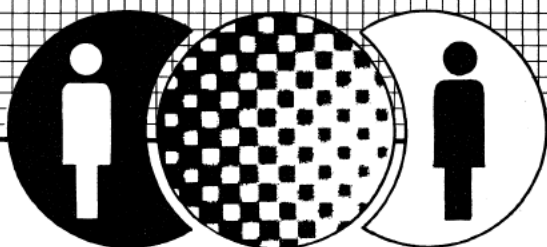


AMERICAN
PSYCHIATRIC
ASSOCIATION



OUR PATIENTS IN A CHANGING WORLD

138 TH ANNUAL MEETING
DALLAS • TEXAS
MAY 18-24, 1985

NEW RESEARCH PROGRAM & ABSTRACTS

**PROGRAM
AND
PAPERS ON NEW RESEARCH**

IN SUMMARY FORM

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

**DALLAS, TEXAS
MAY 18-24, 1985**

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.

**ADVISORY COMMITTEE FOR THE
NEW RESEARCH PROGRAM:**

Robert E. Hales, M.D.
Washington, DC

John Morihisa, M.D.
Washington, DC

Susan Fiester, M.D.
Bethesda, MD

Allen J. Frances, M.D.
New York, NY

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Fort Gordon, GA

Robert Freedman, M.D.
Denver, CO

M. Katherine Shear, M.D.
New Rochelle, NY

Charles A. Kaufmann, M.D.
Washington, DC

Tuesday, May 21, 1985, 12 Noon-2:00 p.m.

New Research 2—Poster Session—Room E-301, Level III, Convention Center

Evaluator: Peter S. Jensen, M.D.

- NR13 CHARACTERISTICS OF VERY POOR OUTCOME SCHIZOPHRENIA
Kenneth L. Davis, M.D., Richard S.E. Keefe, Michael Davidson, M.D., Miklos F. Losonczy, M.D., Thomas B. Horvath, M.D., Richard C. Mohs, Ph.D.
- NR14 EARLY NEUROLEPTIC RESPONSE: CLINICAL PROFILES
Malcolm Bowers, Jr., M.D., Mary E. Sungar, M.D., Peter I. Jatlow, M.D., Frederick Hoffman, B.A., Nora Goicoechea, M.S.N.
- NR15 SYMPTOMS AND PROGNOSTIC FACTORS IN SCHIZOPHRENIA
Sam Castellani, M.D., J. Alexander Boeringa, Ph.D., Beryl Silkey, A. James Giannini, M.D., Jean Endicott, Ph.D.
- NR16 FAMILIAL SCHIZOPHRENIA AND TREATMENT RESPONSE
Jeremy A. Silverman, Richard Mohs, Ph.D., John C.S. Breitner, M.D., Kenneth L. Davis, M.D.
- NR17 NEGATIVE SYMPTOMS IN THE GENERAL POPULATION
Gerald A. Nestadt, M.D., Alan J. Romanoski, M.D., Paul McHugh, M.D., William Eaton, Ph.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D.
- NR18 DISTRACTIBILITY IN SCHIZOPHRENICS AND RELATIVES
Bonnie Spring, Ph.D.
- NR19 CLINICAL SIGNIFICANCE OF COMMAND HALLUCINATIONS
David J. Hellerstein, M.D., William Frosch, M.D., Harold Koenigsberg, M.D.
- NR20 AUDITORY HALLUCINATIONS ARE SUBVOCALIZED SPEECH
Peter A. Bick, M.D., Marcel Kinsbourne, M.D.
- NR21 SENSORY GATING IN RATS: PARALLELS WITH PSYCHOSIS
Lawrence E. Adler, M.D., Gregory M. Rose, Ph.D., Robert Freedman, M.D.
- NR22 CEREBRAL GLUCOGRAPHY OF ACUTE SCHIZOPHRENICS
John M. Cleghorn, M.D.
- NR23 MAGNETIC RESONANCE IMAGING INTENSITY VALUES IN SCHIZOPHRENIC BRAINS
Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Stephen C. Olson, M.D., Val Dunn, Ph.D., James C. Ehrhardt, M.D.
- NR24 DYNAMIC CT SCANS IN SCHIZOPHRENIA: BLOOD-BRAIN BARRIER EVALUATION
Elizabeth M. Burns, Ph.D., Henry A. Nasrallah, M.D., Mary H. Kathol, M.D., Thomas W. Kruckeberg, M.S., Suzanne Chapman, B.S.N.
- NR25 BRAIN OT₁ IN SCHIZOPHRENIC AND NORMAL CONTROLS
Marian K. DeMyer, M.D., Richard L. Gilmor, M.D., Hugh C. Hendrie, M.B., Ch.B., Forrest T. Meiere, Ph.D., William E. DeMyer, M.D.
- NR26 OLFACTORY RECALL DEFICITS AND VBR IN SCHIZOPHRENIA
Paul J. Moberg, M.A., Godfrey D. Pearlson, M.D., Won S. Kim, M.D., Larry E. Tune, M.D.
- NR27 CT DENSITY AND VENTRICLES OF SCHIZOPHRENIA IN JAPAN
Shigenobu Kanba, M.D., Satoru Shima, M.D., Yutaka Masuda, M.D., Daizo Tsukumo, M.D., Toshinori Kitamura, M.D., Masahiro Asai, M.D.
- NR28 BRAIN CT SCANS IN PSYCHIATRIC INPATIENTS
Thomas P. Beresford, M.D., Richard C.W. Hall, M.D., Frederic C. Blow, Ph.D., Linda Nichols, Ph.D., James Langston, M.D.
- NR29 COMPUTERIZED EEG SYNCHRONY AND MENTAL DISORDERS
Martin R. Ford, Ph.D., John W. Goethe, M.D., Debra Dekker, M.A.
- NR30 ERRORS IN MAPPING OF BRAIN ELECTRICAL ACTIVITY
E. Michael Kahn, M.D., Richard D. Weiner, M.D., Richard D. Coppola, Sc.D.
- NR31 CALCIUM BLOCKERS PREVENT DOPAMINE HYPERSENSITIVITY
Jack A. Grebb, M.D., Richard C. Shelton, M.D., William J. Freed, Ph.D.
- NR32 MESOLIMBIC DOPAMINE ACTIVITY AND SCHIZOPHRENIA
Neal Swerdlow, David L. Braff, M.D., Mark A. Geyer, Ph.D., George F. Koob, Ph.D.

- NR33 NEW METHOD TO ASSESS CENTRAL DOPAMINERGIC FUNCTION
Mark A. Riddle, M.D., James F. Leckman, M.D., Donald J. Cohen, M.D., George M. Anderson, Ph.D., Sharon Ort, R.N., Bennett A. Shaywitz, M.D.
- NR34 LOWER ALPHA 2 AGONIST BINDING IN SCHIZOPHRENIC BRAINS
Grant N. Ko, M.D., James R. Unnerstall, Michael J. Kuhar, Ph.D., Richard Jed Wyatt, M.D., Henry H. Holcomb, M.D., Joel E. Kleinman, M.D.
- NR35 LYMPHOCYTE 3H-SPIROPERIDOL BINDING IN SCHIZOPHRENIA
Ed Rotstein, M.D., Ram K. Mishra, Ph.D., Dharam P. Singal, Ph.D., Dory Barone, R.T.
- NR36 TRIHEXYPHENIDYL INCREASES PLASMA CHLORPROMAZINE
Lawrence H. Rockland, M.D., Thomas Cooper, David Weber, M.D., Timothy Sullivan, M.D., Barbara Murray, M.D., Matthew Keats, M.D.
- NR37 NEUROLEPTIC DYSPHORIA AS AN OUTCOME PREDICTOR
Peter J. Weiden, M.D.
- NR38 HISTORY OF EPS PREDICTS FUTURE EPISODES
George A. Keepers, M.D., Daniel E. Casey, M.D.
- NR39 SELF-LIMITED NEUROLEPTIC MALIGNANT SYNDROME WITH CONTINUED USE OF NEUROLEPTIC
Gerard Addonizio, M.D., Virginia Susman, M.D., Steven D. Roth, M.D.
- NR40 TARDIVE DYSKINESIA: A FIVE-YEAR FOLLOW-UP
H.A. Grossman, M.D., X. Fornazzari, M.D., J. Thornton, M.D., M. Seeman, M.D.
- NR41 ACUTE TREATMENT OF SCHIZOPHRENIA WITH CLOZAPINE
Jeffrey A. Lieberman, M.D., Thomas B. Cooper, M.A., John M. Kane, M.D., William Florio, M.D., Ronald Brenner, M.D., Jacque Vital-Herne, M.D., Celeste Johns, M.D.
- NR42 TREATMENT OF TARDIVE DYSKINESIA WITH BROMOCRIPTINE
Jeffrey Lieberman, M.D., John Kane, M.D., William Florio, M.D., Sukdeb Mukherjee, M.D.
- NR43 DRUG HOLIDAYS AND TARDIVE DYSKINESIA
Bruce I. Diamond, Ph.D., Chandresh Shah, M.D., Ana Hitri, Ph.D., Richard L. Borison, M.D.
- NR44 TARGET WEIGHT PROGRAM PREVENTS WATER INTOXICATION
Morris B. Goldman, M.D., Daniel J. Luchins, M.D.
- NR45 BODY WEIGHT REGULATION IN SCHIZOPHRENIA
William B. Lawson, M.D., Charles A. Kaufmann, M.D., Craig Karson, M.D., Daniel R. Weinberger, M.D., Markku Linnoila, M.D.
- NR46 MALIGNANT HYPERTHERMIA SUSCEPTIBILITY IN NEUROLEPTIC MALIGNANT SYNDROME
Stanley N. Caroff, M.D., Henry Rosenberg, M.D., Jeffrey Fletcher, Ph.D., Merrill Hilf, B.A., Terry D. Heiman-Patterson, M.D.
- NR47 METHADONE IN TREATMENT RESISTANT SCHIZOPHRENIA
David A. Brizer, M.D., Neil Hartman, M.D., John Sweeney, Ph.D., Robert B. Millman, M.D.
- NR48 CARBAMAZEPINE LOWERS PLASMA HALOPERIDOL LEVELS
George W. Arana, M.D., Donald Goff, M.D., Hylar Friedman, M.D., Marjorie Ornstein, B.A., Bruce Black, M.D., Leslie Hocking, M.D., David J. Greenblatt, M.D., Richard I. Shader, M.D.
- NR49 CHRONOPHARMACOLOGY OF HALOPERIDOL TREATMENT
R. Swami Nathan, M.D., James M. Perel, Ph.D., Richard Stiller, Ph.D., Jeffrey L. Peters, M.D., Theresa McCarthy, R.N., Suzanne Currah, M.S.
- NR50 THIOTHIXENE DOSE STUDY: TX-RESISTANT SCHIZOPHRENIA
Chuong C. Huang, M.D., Richard P. Gerhardtstein, M.D., David Y. Kim, M.D., Leo Hollister, M.D.
- NR51 POSITIVE/NEGATIVE SYMPTOMS IN INTERICTAL PSYCHOSIS
C. Edward Coffey, M.D., James J. McGough, B.A., Elizabeth Sumner, B.A., Susan Pelton
- NR52 A DOMINANT GENE FOR ALZHEIMER'S DISEASE
Richard C. Mohs, Ph.D., Jeremy A. Silverman, M.A., John C.S. Breitner, M.D., Kenneth L. Davis, M.D.
- NR53 SUBTYPES OF ALZHEIMER'S DISEASE
William Bondareff, M.D., Christopher Q. Mountjoy, M.B.
- NR54 CARBOHYDRATE METABOLISM IN ALZHEIMER'S DISEASE
M. Fisman, M.D., Bruce Gordon, M.D., Thomas MacDonald, M.D., John Dupre, M.D., Edward Helmes, Ph.D.

- NR55 HEPATIC POLYPLOIDY IN ALZHEIMER'S DISEASE
M. Fisman, M.D., Hildegard Enesco, Ph.D., Marie Laskey, M.Sc.
- NR56 CORTICAL ATROPHY AND PLATELET MAO IN DEMENTIA
Robert C. Young, M.D., George S. Alexopoulos, M.D., Kenneth W. Lieberman, Ph.D., Charles A. Shamoian, M.D., Robert Roe, M.D., Michael Deck, M.D.
- NR57 VBR COGNITIVE AND NEUROLOGICAL DEFICITS IN MULTIPLE SCLEROSIS
Godfrey D. Pearlson, M.D., Won S. Kim, M.D., Peter V. Rabins, M.D., John R. Lipsey, M.D., Paul J. Moberg, M.A., Benjamin Brooks, M.D.
- NR58 CEREBRAL VBR'S AND ACETYLCHOLINESTERASE ACTIVITY IN SENILE DEMENTIA
Larry E. Tune, M.D., G. Pearlson, M.D.
- NR59 PSYCHIATRIC SYMPTOMS IN DEMENTIA SYNDROMES
Larry E. Tune, M.D., C. Steele, R.N., M.J. Lucas, R.N.
- NR60 CAN ECT CURE PARKINSON'S DISEASE?
David E. Raskin, M.D.
- NR61 REM SLEEP IN ALZHEIMER'S-TYPE DEMENTIA
Michael Serby, M.D., John Adler, Ph.D.
- NR62 ANTICHOLINERGIC DRUG EFFECTS ON MEMORY IN ELDERLY
Bharat R.S. Nakra, M.D., Ron Margolis, Ph.D., George T. Grossberg, Lindbergh S. Sata, M.D.
- NR63 TRH TEST IN DEMENTIA: ELDERLY DEPRESSED AND CONTROLS
Trey Sunderland, M.D., Pierre N. Tariot, M.D., Edward A. Mueller, M.D., Dennis L. Murphy, M.D., Paul Newhouse, M.D., Robert M. Cohen, M.D.
- NR64 HYDERGINE IN HIGH DOSES IN MILD DEMENTIA
Ole J. Thienhaus, M.D., Beverly Wheeler, M.D., Sandra Simon, O.T., Frank Zemlan, Ph.D., James T. Hartford, M.D.
- NR65 DEPRESSION WITH REVERSIBLE DEMENTIA: PHENOMENOLOGY
George S. Alexopoulos, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.
- NR66 DEXAMETHASONE SUPPRESSION IN DEMENTIA
Gerard A. Charles, M.D., A. John Rush, M.D.
- NR67 TRH TEST, DST, AND RESPONSE TO DESIPRAMINE IN DEMENTIA
T.W. McAllister, M.D., Lon Hays, M.D.
- NR68 SPECIFICITY OF BENZODIAZEPINE DISRUPTION OF MEMORY
Owen M. Wolkowitz, M.D., Herbert Weingartner, Ph.D., Daniel W. Hommer, M.D.
- NR69 ANTEROGRADE AMNESIA WITH ORAL LORAZEPAM
Daljit S. Mac, M.D., Rajiv Kumar, M.D., Donald W. Goodwin, M.D.
- NR70 PARENTS OF A DOWN'S SYNDROME CHILD
S. Brandon, M.D., Mary Newell
- NR71 CLINICAL EFFICACY OF ALPRAZOLAM IN PTSD PATIENTS
Frederick J. Dunner, M.D., Warren P. Edwards, Ph.D., Paul C. Copeland, D.O.

Tuesday, May 21, 1985, 2:00 p.m.-5:00 p.m.

New Research 3—Oral/Slide Session, Room E-301, Level III, Convention Center

Chp.: M. Katherine Shear, M.D.

Co-Chp.: Nina R. Schooler, M.D.

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| NR72 | PANIC: PREVALENCE RISK FACTORS AND TREATMENT RATES Jeffrey H. Boyd, M.D. | 2:00 p.m. |
| NR73 | THE NATURAL COURSE OF AGORAPHOBIA-PANIC DISORDERS Alan Breier, M.D., Dennis S. Charney, M.D. | 2:15 p.m. |
| NR74 | BUSPIRONE, CLORAZEPATE AND WITHDRAWAL Karl Rickels, M.D., Irma Csanalosi, M.D., Hack Chung, M.D., Warren G. Case, M.D., Edward Schweizer, M.D. | 2:30 p.m. |
| NR75 | EEG OF PANIC DISORDER AND NARCOLEPSY John R. Adams, M.D., Victor S. Wahby, M.D., Earl L. Giller, M.D. | 2:45 p.m. |
| NR76 | EXCESS MORTALITY IN PANIC DISORDER William Coryell, M.D., Russell Noyes, Jr., M.D., Daniel House, Ph.D. | 3:00 p.m. |
| NR77 | CO-2 CHEMOCEPTOR SENSITIVITY IN PANIC PATIENTS Scott W. Woods, M.D., Dennis S. Charney, M.D., Jacob Loke, M.D., Wayne K. Goodman, M.D., D. Eugene Redmond, M.D., George R. Heninger, M.D. | 3:15 p.m. |
| NR78 | SUMMARY OF MULTICENTER STUDY OF ALPRAZOLAM Malcolm Lader, M.D. | 3:30 p.m. |
| NR79 | NEW RESEARCH STRATEGIES IN ANXIETY DISORDERS Gerald L. Klerman, M.D. | 3:45 p.m. |
| NR80 | ALPRAZOLAM LEVELS: OUTCOME IN PANIC David J. Greenblatt, M.D., Randall B. Smith, Ph.D., Richard I. Shader, M.D. | 4:00 p.m. |
| NR81 | ALPRAZOLAM WITHDRAWAL IN PANIC DISORDER PATIENTS Robert L. DuPont, Jr., M.D., John C. Pecknold, M.D. | 4:15 p.m. |
| NR82 | ADVERSE EFFECTS AND PATIENT ACCEPTANCE Graham D. Burrows, M.D., Arthur Rifkin, M.D., Russell Noyes, Jr., M.D. | 4:30 p.m. |
| NR83 | CLINICAL EFFICACY AND OUTCOME James C. Ballenger, M.D., Robert T. Rubin, M.D., Richard P. Swinson, M.D. | 4:45 p.m. |

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

New Research 4—Poster Session—Room E-301, Level III, Convention Center

Evaluator: John M. Morihisa, M.D.

- NR84 ARGININE VASOPRESSIN CHALLENGE IN DEPRESSION
William H. Meller, M.D., Roger G. Kathol, M.D., Richard S. Jaeckle, M.D., Juan F. Lopez, M.D.
- NR85 CORTISOL RESPONSE TO YOHIMBINE IN DEPRESSION
Lawrence Price, M.D., George R. Heninger, M.D.
- NR86 TSH IS LOWER AT NIGHT IN DEPRESSION
David A. Sack, M.D., Steven P. James, M.D., Norman E. Rosenthal, M.D., Thomas A. Wehr, M.D.
- NR87 CSF SOMATOSTATIN AND ABNORMAL RESPONSE TO DST
Allen R. Doran, M.D., David R. Rubinow, M.D., Alec Roy, M.B., David Pickar, M.D.
- NR88 INTRAVENOUS PROCAINE AS A PROBE OF LIMBIC ACTIVITY
Charles H. Kellner, M.D., Mitchel Kling, M.D., Robert M. Post, M.D., Rex Cowdry, M.D., David Gardner, M.D., Frank Putnam, M.D., Richard Coppola, Ph.D.
- NR89 MELATONIN AND AGING
G.F. Oxenkrug, M.D., I.M. McIntyre, A.K. Jain, M.D., R. Balon, M.D., L.P. Taylor, Ph.D., S. Gershon, M.D.
- NR90 PROLACTIN RESPONSE DURING DST
Peter E. Stokes, M.D., Betty Lasley, Ph.D., Peter M. Stoll
- NR91 AGE, DST AND DIAGNOSTIC HETEROGENEITY
Gabor I. Keitner, M.D., Ivan W. Miller, Ph.D., Walter A. Brown, M.D., William H. Norman, Ph.D., Alan E. Fruzzetti, B.A.
- NR92 DEPRESSION IN UNTREATED AND TREATED ALCOHOLICS
Alan J. Romanoski, M.D., Barry Rovner, M.D., Gerald A. Nestadt, M.D., Marshal Folstein, M.D.
- NR93 DEPRESSIVE SUBTYPES AND RANGES OF DST RESPONSE
Thomas C. Bond, M.D., Anthony J. Rothchild, M.D., Jan Lerbinger, B.S., Alan F. Schatzberg, M.D.
- NR94 DST PREDICTS POOR PLACEBO RESPONSE IN DEPRESSION
Ram K. Shrivastava, M.D., Rita Schwimmer, M.S., Walter Armin Brown, M.D., Mihaly Arato, M.D.
- NR95 DST AND INTOLERANCE TO SEROTONIN UPTAKE INHIBITION
Walter Armin Brown, M.D., Ram K. Shrivastava, M.D., Mihaly Arato, M.D.
- NR96 IS DST OUTCOME AFFECTED BY SEVERITY OF SYMPTOMS?
George W. Arana, M.D., Paul J. Barrerira, M.D., Joseph Lipinski, M.D., Hyme Schachter, B.S., Bruce M. Cohen, M.D.
- NR97 SEVERITY OF DEPRESSION AND THE DST
Kevin Kerber, M.D., Pam Flegel, B.S., Leon Grunhaus, M.D., John F. Greden, M.D.
- NR98 EEG SLEEP IN RECURRENT DEPRESSION
James E. Shipley, M.D., David J. Kupfer, M.D., Ellen Frank, Ph.D., David B. Jarrett, M.D., James M. Perel, Ph.D., Victoria J. Grochocinski, Ph.D.
- NR99 SLEEP AND DEPRESSION DURING TREATMENT WITH TCA'S
J. Catesby Ware, Ph.D., Frederick W. Brown, M.D., Philip J. Moorad, M.D., Joe Tom Pittard, M.D., B. Cobert, M.D.
- NR100 CLINICAL CORRELATES OF ONE-CARBON METABOLISM
William G. Walter-Ryan, M.D., Donna A. Morere, M.S., Renato D. Alarcon, M.D., Marva Steele, R.N., John A. Monti, Ph.D., Leland C. Tolbert, Ph.D.
- NR101 DESIPRAMINE ALTERS PLASMA NOREPINEPHRINE KINETICS
Richard C. Veith, M.D., Jeffrey B. Halter, M.D., Michele Murburg, M.D., Robert F. Barnes, M.D., Enrique Villacres, M.D., Frank Backus, M.D.
- NR102 3H-IMIPRAMINE BINDING IN DEPRESSED ELDERLY
L. S. Schneider, M.D., James A. Severson, Ph.D., Fred Staples, Ph.D., Eric Fredrickson, B.S., R. Bruce Sloane, M.D.

- NR103 LEARNED HELPLESSNESS AND HIGH MHPG DEPRESSIONS
Jacqueline Samson, Ph.D., Steven Mirin, M.D., Stuart Hauser, M.D., Brenda Fenton, Benjamin Gerson, M.D., Joseph J. Schildkraut, M.D.
- NR104 NEUROENDOCRINE RESPONSE TO MAXIMAL EXERCISE STRESS
Marvin A. Oleshansky, M.D., James L. Meyerhoff, M.D., Edward H. Mougey, M.S., Robert L. Herman, M.D., Jerel L. Zoltick, M.D.
- NR105 MHPG EXCRETION IN LATE LIFE DEPRESSION
Robert C. Young, M.D., George S. Alexopoulos, M.D., Charles A. Shamoian, M.D., J. John Mann, M.D.
- NR106 PLASMA MELATONIN AND CORTISOL RHYTHMS IN AGING
N.P.V. Nair, M.D., N. Hariharasubramanian, M.D., Carmencita Pilapil, M.Sc., Ramsey Yassa, M.D.
- NR107 BUPROPION METABOLITES, HVA AND CLINICAL RESPONSE
Robert N. Golden, M.D., C. Lindsay DeVane, Pharm.D., Matthew V. Rudorfer, M.D., Michael A. Sherer, M.D., S. Casey Laizure, Pharm.D., Markku Linnoila, M.D., William Z. Potter, M.D.
- NR108 BUPROPION IN PATIENTS WITH HEART FAILURE
Steven P. Roose, M.D., Alexander H. Glassman, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N.
- NR109 BUPROPION: CONCENTRATION-RESPONSE RELATIONSHIP
R. Kumar, M.D., Sheldon H. Preskorn, M.D., Carroll W. Hughes, Ph.D., Sieglinde C. Othmer, Ph.D., Ekkehard Othmer, M.D.
- NR110 COHERENCE (1 TO 8Hz) AS QUANTITATIVE ELECTROENCEPHALOGRAPHY MARKER OF MAJOR DEPRESSION
Arnold L. Lieber, M.D., Leslie S. Prichep, Ph.D., Kenneth Alper, M.D.
- NR111 BRAIN SPECT AND MAGNETIC RESONANCE IMAGING IN DEPRESSION
C. Edward Coffey, M.D., Burton P. Drayer, M.D., Daniel Gianturco, M.D., Daniel Sullivan, M.D.
- NR112 CLINICAL AND DST CORRELATES OF ECT RESPONSE
Leon Grunhaus, M.D., Kirsten Alcsér, Ph.D., Roger F. Haskett, M.D., John F. Greden, M.D., Thomas Zelnik, M.D.
- NR113 LEICESTER (UK) CLINICAL TRIAL OF ECT VERSUS DUMMY ECT
S. Brandon, M.D., R.L. Palmer, M.D., P. Crowley, M.B., S. Eason, M.B.
- NR114 CT CHANGES IN LATE LIFE DEPRESSION
Peter V. Rabins, M.D., Godfrey Pearlson, M.D., Paul Moberg, M.A., Won Kim, M.D.
- NR115 SEIZURE DURATION AND THE CLINICAL EFFECTS OF ECT
Alexander L. Miller, M.D., Raymond Faber, M.D., John Hatch, Ph.D., Harold Alexander, M.D.
- NR116 TRANLYCYPROMINE: KINETICS AND HYPOTENSIVE ACTIONS
Alan G. Mallinger, M.D., David J. Edwards, Ph.D., Jonathan M. Himmelhoch, M.D., Steven Knopf, B.S., Joan Ehler, M.D.
- NR117 TARGETING IMIPRAMINE DOSE IN DEPRESSED CHILDREN
Floyd R. Sallee, M.D., Michael D. Rancurello, M.D., Richard L. Stiller, Ph.D., James M. Perel, Ph.D.
- NR118 RAPID DOSING TRICYCLIC ANTIDEPRESSANT LEADS TO EARLY RESPONSE
Jack Hirschowitz, M.D., Jerry A. Bennett, Pharm.D., Frank Zemlan, Ph.D., David L. Garver, M.D.
- NR119 CLOMIPRAMINE: AN INTRAVENOUS PULSE LOADING REGIMEN
Bruce G. Pollock, M.D., James M. Perel, Ph.D., Michael Shostak, M.D., David J. Kupfer, M.D., Duane Spiker, M.D., Seymour Antelman, Ph.D.
- NR120 RESPONSE TO T₃ IN IMIPRAMINE RESISTANT DEPRESSION
Michael E. Thase, M.D., David J. Kupfer, M.D., David B. Jarrett, M.D., Ellen Frank, Ph.D.
- NR121 DOSE EFFECT OF AMOXAPINE ON DOPAMINE BLOCKADE
Raymond F. Anton, M.D., Bruce I. Diamond, Ph.D., Ana Hitri, Ph.D., Mark Shelhorse, M.D.
- NR122 SEASONAL AFFECTIVE DISORDER AND LIGHT TREATMENT IN CHILDREN
N.E. Rosenthal, M.D., Constance J. Carpenter, B.S., Steven P. James, M.D., Barbara L. Parry, M.D., Susan Rogers, R.N., Thomas A. Wehr, M.D.
- NR123 BIOLOGICAL EFFECTS OF BRIGHT LIGHTS
William F. Byerley, M.D., Daniel F. Kripke, M.D., Craig S. Risch, M.D., J. Christian Gillin, M.D., David S. Janowsky, M.D., Donal Parker, M.D., Lawrence G. Rossman, M.S.
- NR124 CORNELL SCALE OF DEPRESSION IN DEMENTIA (CSDD)
George S. Alexopoulos, M.D., Robert C. Abrams, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.

- NR125 PREVALENCE OF PREMENSTRUAL SYNDROMES
Cheryl M. McChesney, M.D., Susan R. Johnson, M.D., Raymond R. Crowe, M.D.
- NR126 CHARACTERISTICS OF PROBABLE ENDOGENOUS DEPRESSION
Donna E. Giles, Ph.D., A. John Rush, M.D., Michael A. Schlessler, M.D., Paul J. Orsulak, Ph.D., Howard P. Roffwarg, M.D.
- NR127 CHRONIC STRESS DOES NOT CAUSE MAJOR DEPRESSION
Naomi Breslau, Ph.D., Glenn Davis, M.D.
- NR128 PERSONALITY TRAITS AND ANTIDEPRESSANT RESPONSE
Eric D. Peselow, M.D., Faouzia Barouche, M.D., Jill Munroe, Ronald R. Fieve, M.D.
- NR129 DOPAMINE D2 RECEPTOR PET SCANS IN BIPOLARS
Godfrey D. Pearlson, M.D., Dean F. Wong, M.D., Robert F. Dannals, Ph.D., Larry E. Tune, M.D., Frederick Schaefer, M.D., Henry N. Wagner, Jr., M.D.
- NR130 NEUROPSYCHOLOGICAL EFFECTS OF LITHIUM
Eric D. Shaw, Ph.D., J. John Mann, M.D., Peter E. Stokes, M.D., Alan Z.A. Manevitz, M.D.
- NR131 LITHIUM IN PSYCHOTIC REFRACTORY DEPRESSION
Carolyn Mazure, Ph.D., J. Craig Nelson, M.D.
- NR132 NEW TREATMENT FOR LITHIUM PROBLEM BIPOLAR PATIENTS
Ekkehard Othmer, M.D., Sieglinde C. Othmer, Ph.D., Cherilyn DeSonna, M.D.
- NR133 BIPOLAR DISORDER FOLLOWING HEAD TRAUMA
Sashi Shukla, M.D., Sukdib Mukherjee, M.D., Charles Godwin, M.D., Morton Miller, M.D.
- NR134 SALIVA LITHIUM MONITORING IN PREPUBERTAL CHILDREN
Elizabeth B. Weller, M.D., Ronald A. Weller, M.D., Mary A. Fristad, M.A., Michael Cantwell, M.D., Sheridan Tucker, M.D.
- NR135 EXACERBATION OF EXTRAPYRAMIDAL SYMPTOMS WITH ADDITION OF LITHIUM
Gerard Addonizio, M.D., Steven D. Roth, M.D., Peter E. Stokes, M.D., Peter M. Stoll
- NR136 PREMENSTRUAL SYMPTOMS AND MENTAL DISORDERS
Thomas B. Mackenzie, M.D., Kimerly Wilcox, Ph.D., Howard Baron, B.S.
- NR137 PREVALENCE OF ANOREXIA NERVOSA: A NATIONAL SURVEY
Laurie Humphries, M.D., Scott N. Mohler, Ph.D., Carol L. Elam, M.A.
- NR138 PLASMA BETA-ENDORPHIN IN BULIMIA
David A. Waller, M.D., R. Sanford Kiser, M.D., Bettie W. Hardy, Ph.D., Ingbert Fuchs, M.D., Linda Parkin Feigenbaum, R.N.
- NR139 THE DEXAMETHASONE SUPPRESSION TEST IN BULIMIA
C. David Lindy, M.D., Alexander H. Glassman, M.D., B. Timothy Walsh, M.D., Steven P. Roose, M.D., Madeline Gladis, M.A.
- NR140 NEUROENDOCRINE RESPONSES IN BULIMIA
Allan S. Kaplan, M.D., Paul E. Garfinkel, M.D., Jerry Warsh, M.D., Gregory M. Brown, M.D.
- NR141 SLEEP EEG IN BULIMIA
James I. Hudson, M.D., Jeffrey M. Jonas, M.D., Harrison G. Pope, Jr., M.D., Victoria Grochochinski, Ph.D.
- NR142 TASTE DIFFERENCES IN ANOREXIA AND BULIMIA NERVOSA
Katherine A. Halmi, M.D., Adam Drewnowski, Ph.D., Beverly Pierce, M.A., James Gibbs, M.D., Gerard Smith, M.D.
- NR143 TREATMENT OF BULIMIA WITH NOMIFENSINE
Harrison G. Pope, Jr., M.D., Peter L. Herridge, M.D., James I. Hudson, M.D., Regene Fontaine, M.D., Deborah Yurgelun-Todd, M.A.
- NR144 HUNGER AND SATIETY IN ANOREXIA AND BULIMIA NERVOSA
William Owen, M.D., Katherine A. Halmi, M.D., James Gibbs, M.D., Gerard Smith, M.D.
- NR145 SEXUAL MOLESTATION OF BOYS BY FEMALES
Diane Shrier, M.D., Robert L. Johnson, M.D.
- NR146 EVALUATION OF BENEFIT FROM A JCAH REGULATION
George Wilson, M.D.

Wednesday, May 22, 2:00 p.m.-5:00 p.m.

New Research 5—Oral/ Slide Session—Room E-301, Level III, Convention Center

Chp.: Robert Freedman, M.D.

Co-Chp.: Lewellyn B. Bigelow, M.D.

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| NR147 | A STUDY OF DISTINCT QUALITY OF MOOD IN MELANCHOLIA Robert L. Spitzer, M.D., Miriam Gibbon, M.S.W., Janet B.W. Williams, D.S.W. | 2:00 p.m. |
| NR148 | PSYCHOSIS AND SUICIDE Eli Robins, M.D. | 2:15 p.m. |
| NR149 | BRIGHT LIGHT THERAPY OF CHRONOBIOLOGIC DISORDERS Alfred J. Lewy, M.D., Robert L. Sack, M.D., Clifford Singer, M.D. | 2:30 p.m. |
| NR150 | SITE OF ACTION OF ANTIDEPRESSANT DRUGS IN ANIMALS Fritz A. Henn, M.D., Emmeline Edwards, Ph.D., Joel Johnson, Eliot Siegel | 2:45 p.m. |
| NR151 | PLATELET SEROTONIN UPTAKE AND IMPRAMINE BINDING Herbert Y. Meltzer, M.D., R.C. Arora, Ph.D., Alan G. Robertson, M.D. | 3:00 p.m. |
| NR152 | DST, TRH-ST AND REM LATENCY IN DEPRESSION A. John Rush, M.D., Michael A. Schlessner, M.D., Donna E. Giles, Ph.D., Paul J. Orsulak, Ph.D., Carol J. Fairchild, M.S.N., Howard P. Roffwarg, M.D. | 3:15 p.m. |
| NR153 | TCA DOSE ADJUSTMENT USING 24 HOUR DRUG LEVELS J. Craig Nelson, M.D., Peter Jatlow, M.D., Carolyn Mazure, Ph.D. | 3:30 P.M. |
| NR154 | DESIMPRAMINE PLASMA LEVELS AND CLINICAL RESPONSE William Coryell, M.D., Rick D. Turner, M.D., Arnold Sherman, Ph.D. | 3:45 P.M. |
| NR155 | LIFE EVENTS: CSF METABOLITES AND DST IN DEPRESSION Alec Roy, M.B., David Pickar, M.D., Markku Linnoila, M.D., Allen Doran, M.D., Steven M. Paul, M.D. | 4:00 p.m. |
| NR156 | AGE, ALCOHOL, CATECHOLS, MEMORY, AND NEUROANATOMIC CHANGE T. Peter Bridge, M.D., Elizabeth S. Parker, Ph.D., Beth J. Soldo, Ph.D., Loring Ingraham, M.A., Charles E. Bickham, M.D. | 4:15 p.m. |
| NR157 | HOW RESPONSES TO STIMULANTS CHANGE WITH AGE Enoch Callaway, M.D., Roy Halliday, Ph.D., Hilary Naylor, Ph.D. | 4:30 p.m. |
| NR158 | DECREASE IN SELECTIVE ATTENTION PRODUCES ANALGESIA Lewis L. Judd, M.D., David S. Segal, Ph.D., Byron Budnick, LouAnn McAdams, Ph.D., S. Craig Risch, M.D., David S. Janowsky, M.D., Steven Hillyard, Ph.D. | 4:45 p.m. |

Thursday, May 23, 1985, 12 Noon-2:00 p.m.

New Research 6—Poster Session—Room E-301, Level III, Convention Center

Evaluator: Rege S. Stewart, M.D.

- NR159 VALIDITY OF AFFECTIVE BORDERLINE SUBTYPES
Paul Skevington Links, M.D., Meir Steiner, M.D., David R. Offord, M.D., Alan B. Eppel, M.B., Jan Mitton, R.N., Audrey Hendershot, R.N., Marilyn Korzekwa, M.D.
- NR160 SLEEP EEG VERSUS DST IN BORDERLINES WITH MELANCHOLIA
Kenneth R. Silk, M.D., Michael Feinberg, M.D., Naomi E. Lohr, Ph.D., Margaret C. Buitenheim, Ph.D., Karen Saakvitne
- NR161 STABILITY OF DSM-III ON BORDERLINE PERSONALITY DISORDER
Alan Barasch, M.D., Allen J. Frances, M.D., John Clarkin, Ph.D., Stephen W. Hurt, Ph.D., Sandra Cohen, M.D.
- NR162 SYMPTOMS OF SCHIZOTYPAL PERSONALITY DISORDER
L.B. Jacobsberg, M.D., Paul Hymowitz, Ph.D., Allen J. Frances, M.D., Mary Sickles, M.D., Alan Barasch, M.D.
- NR163 CAN AMPHETAMINE SOLVE BORDERLINE HETEROGENEITY?
S. Charles Schulz, M.D., Jack Cornelius, M.D., Richard Brenner, M.D., Paul Soloff, M.D.
- NR164 BORDERLINE TRAITS IN RELATIVES OF BORDERLINES
Patricia M. Schulz, M.S.W., S. Charles Schulz, M.D., Richard F. Ulrich, M.S., Robert O. Friedel, M.D., Robert Resnick, Ph.D., Solomon Goldberg, Ph.D.
- NR165 HETEROGENEITY OF BORDERLINE PERSONALITY DISORDER
Minna R. Fyer, M.D., Allen J. Frances, M.D., Timothy Sullivan, M.D., Steven W. Hurt, Ph.D., John Clarkin, Ph.D.
- NR166 CRITERIA FOR DIAGNOSING PERSONALITY DISORDERS
W. John Livesley, M.B., Ch.B.
- NR167 CORE CRITERIA FOR DIAGNOSING BORDERLINE PATIENTS
H. George Nurnberg, M.D., Aileen Feldman, M.D., Stephen W. Hurt, Ph.D., Ryang Suh, M.D.
- NR168 A STUDY CHARACTERIZING DSM-III-R CRITERIA FOR PANIC DISORDER PATIENTS
Mary E. Hanrahan, A.C.S.W., M. Katherine Shear, M.D.
- NR169 DIURNAL VARIATION OF ABNORMAL ANXIETY
Oliver G. Cameron, M.D., Joan Kotun, M.D., Myung A. Lee, M.D., Shelia Murphy, B.S.
- NR170 PSYCHOBIOLOGIC CHANGES DURING SPONTANEOUS PANIC
Oliver G. Cameron, M.D., Myung A. Lee, M.D., George C. Curtis, M.D., Daisy S. McCann, Ph.D.
- NR171 PHYSIOLOGICAL CONCOMITANTS OF ANXIETY
Donna L. Moreau, M.D.
- NR172 ELEVATED NOREPINEPHRINE/CORTISOL RATIO IN PTSD
John Mason, M.D., Earl L. Giller, M.D., Thomas R. Kosten, M.D., Robert B. Ostroff, M.D., Laurie Harness, M.S.W.
- NR173 GENETIC AND FAMILIAL RISK FOR ANXIETY DISORDERS
Jeffrey Boyd, M.D.
- NR174 PANIC DISORDER AND MITRAL VALVE PROLAPSE
William Matuzas, M.D., Jafar Al-Sadir, M.D., E.H. Uhlenhuth, M.D., Richard M. Glass, M.D., Ronald J. Ganellen, Ph.D.
- NR175 ANXIETY IN CHILDREN AND ADOLESCENTS
Evanne Hoehn-Saric, M.D., Mohammad Maisami, M.D., Diane Wiegand, B.S.
- NR176 PLASMA GABA ABNORMALITIES IN PSYCHIATRIC ILLNESS
Frederick Petty, M.D.
- NR177 CO₂ AS A TRIGGER FOR PANIC IN PANIC PATIENTS
Anke Ehlers, M.D., Jurgen Margraf, M.D., Walton T. Roth, M.D., C. Barr Taylor, M.D., Richard J. Maddock, M.D., Bert S. Kopell, M.D.

- NR178 TREATED HEROIN ADDICTS FOLLOWED FOR 15 YEARS
Charles Rohrs, M.D.
- NR179 PROBATIONERS AND DRUGS IN A MAJOR URBAN COUNTY
Kenneth R. Kaufman, M.D., Phyllis Sherman Raschke, M.P.A.
- NR180 NEUROCHEMICAL CHANGES IN COCAINE AND OPIATE ABUSE
Todd Wilk Estroff, M.D., Charles A. Dackis, M.D., Donald R. Sweeney, M.D., A.L.C. Pottash, M.D.
- NR181 HYPERPROLACTINEMIA IN COCAINE ABUSE
Charles A. Dackis, M.D., Todd W. Estroff, M.D., Mark S. Gold, M.D.
- NR182 EXCRETION OF PTERINS DURING METHADONE MAINTENANCE
Kenneth J. Krajewski, M.D., Robert W. Guynn, M.D.
- NR183 COCAINE ABUSE TREATMENT OUTCOME
Arnold M. Washton, Ph.D., A.L.C. Pottash, M.D.
- NR184 PSYCHIATRIC PATIENTS AND NICOTINE: USE AND EFFECTS
Susanna Goldstein, M.D., Stephen H. Geisler, M.D., Simcha Pollack, Ph.D.
- NR185 PROSTAGLANDINS AND RECOVERY FROM ALCOHOLISM
James P. MacMurray, Ph.D., John E. Crowder, M.D., Michael D. Schultz, M.D., Jonathan D. Berman, M.D., Roland C. Aloia, Ph.D., Louis P. Bozzetti, M.D.
- NR186 PREDICTORS OF DRIVING ACCIDENTS IN ALCOHOLICS
William R. Yates, M.D., Russell Noyes, Jr., M.D., Fred Petty, M.D., Keith Brown
- NR187 PROSTAGLANDIN CHANGES IN RECOVERING ALCOHOLICS
Jonathan D. Berman, M.D., James P. MacMurray, Ph.D., Roland C. Aloia, Ph.D., Paul A. Stein, Ph.D., John E. Crowder, M.D., Louis P. Bozzetti, M.D.
- NR188 AMINO ACIDS AND HALLUCINATIONS IN ALCOHOLICS
L. Branchey, M.D., M. Branchey, M.D., D. Zucker, M.D., S. Shaw, M.D., C.S. Lieber, M.D.
- NR189 PRIMARY AND SECONDARY DEPRESSION IN ALCOHOLICS
Marsha R. Read, Ph.D., Barbara J. Powell, Ph.D., Elizabeth C. Penick, Ph.D., Barry I. Liskow, M.D., Stephen F. Bingham, Ph.D., Audrey S. Rice, M.A.
- NR190 SEPARATION AND ALCOHOL CONSUMPTION IN MONKEYS
William T. McKinney, M.D., Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., C. Raymond Lake, M.D.
- NR191 MENTAL DISORDERS IN RIVER VICTIMS
Ellen Frank, Ph.D., Barbara Anderson, M.S., Patricia Cluss, Ph.D., Jane Ergood, M.A., Ana Rivera-Tovar, M.S., Barbara Duffy Stewart, M.P.H.
- NR192 SEASONAL CHANGES IN VIOLENCE AGAINST FEMALE FOSTER WIVES
Richard P. Michael, M.D., Doris Zumpe, Ph.D.
- NR193 PELVIC PHYSIOLOGICAL CHANGES DURING FEMALE AROUSAL
Ismet Karacan, M.D., Constance Moore, M.D., Sezai Sahmay, M.D.
- NR194 ASSAULT HISTORIES OF INPATIENTS: INTERVIEW DATA
Andrea Jacobson, M.D., Jill Koehler, B.S., Curt Pinchuck, B.A.
- NR195 ISOLATION, AGGRESSION AND ANTIBODY RESPONSE IN MICE
Michael A. Fauman, M.D.
- NR196 IRRITABLE BABY AND ADULT PSYCHOPATHOLOGY
George U. Balis, M.D., Spyros J. Monopolis, M.D.
- NR197 COMMUNITY DEMORALIZATION AND DSM-III DIAGNOSIS
Andrew E. Skodol, M.D., Patrick E. Shrout, Ph.D., Bruce P. Dohrenwend, Ph.D., Janet B.W. Williams, D.S.W., Miriam Gibbon, M.S.W., Frederick Kass, M.D.
- NR198 NATURAL DISASTERS: EMOTIONAL IMPACT ON CHILDREN
Sudhakar Madakasira, M.D., Lesly T. Mega, M.D., Kevin O'Brien, Ph.D.
- NR199 LITIGATION AS A STRESS IN MEDICAL PRACTICE
Sara C. Charles, M.D., Richard B. Warnecke, Ph.D., Jeffrey Wilbert, M.A., Carlos DeJesus, M.A.
- NR200 MEDICAL STUDENT PERCEPTIONS OF PSYCHIATRIST'S ROLE
Linda F. Pessar, M.D., Seymour Axelrod, Ph.D., Marvin I. Herz, M.D.

- NR201 DEPRESSION IN MEDICAL STUDENTS
Mark Zoccolillo, M.D., George Murphy, M.D., Richard Wetzel, Ph.D.
- NR202 THE LIFETIME CREATIVITY SCALES: NEW RESEARCH TOOLS
Ruth L. Richards, M.D., Dennis K. Kinney, Ph.D., Inge Lunde, M.D., Maria E. Benet, A.B., Ann P.C. Merzel, A.B.
- NR203 THE SADS-L AND THE DIS: HOW DO THEY COMPARE?
Deborah S. Hasin, M.S., Bridget F. Grant, Ph.D., Gary Harsey, M.D., Jerry Warsh, M.D., Harvey Stancer, M.D., Robert Cook, E. Persad, M.D., Theola Jorna
- NR204 CAN CHRONIC INPATIENTS LEARN WHAT THEY TAKE?
James C. Beck, M.D., Robert Staffin, A.B.
- NR205 FAMILY DIAGNOSES MISSED BY PSYCHIATRIC RESIDENTS
Neil J. Baker, M.D., Sandra L. Berry, M.S.W., Lawrence E. Adler, M.D., Ronald Franks, M.D., Merilyne C. Waldo, M.A., Robert Freedman, M.D.
- NR206 MICRO-BASED DATA SYSTEM FOR A PSYCHIATRIC CLINIC
E. Michael Kahn, M.D., Jacqueline Holland, R.N., Thomas L. Droege, Edward Goldenberg, M.D.
- NR207 SHORT-TERM PSYCHOTHERAPY: PROCESS AND OUTCOME
Manuel Trujillo, M.D., Arnold Winston, M.D., Leigh McCullough, Ph.D., Harold Been, M.D., Jerome Pollack, M.D., Richard Kestenbaum, Ph.D.
- NR208 SOCIAL SKILLS TRAINING FOR SCHIZOPHRENICS
Robert P. Liberman, M.D., Charles J. Wallace, Ph.D.
- NR209 PSYCHOTHERAPY FOR DEPRESSED INPATIENTS
Ivan W. Miller, Ph.D., William H. Norman, Ph.D., Gabor Keitner, M.D.
- NR210 FOCAL FAMILY THERAPY IN FAMILIES OF SCHIZOPHRENICS
Judith E. Levene, M.S.W., Frances Newman, M.A., Joel J. Jeffries, M.B.
- NR211 CONSOLIDATED HEALTH CARE FOR ADOLESCENTS
Felton Earls, M.D., Arlene R. Stiffman, Ph.D.
- NR212 PSYCHIATRIC ILLNESS IN SEVERELY ASTHMATIC CHILDREN
David A. Mrazek, M.D.
- NR213 UNDIAGNOSED MEDICAL ILLNESS ON A CHRONIC CARE WARD
Richard L. Borison, M.D., Mark E. Shelhorse, M.D., Chandresh Shah, M.D., Ana Hitri, Ph.D., Bruce I. Diamond, Ph.D.
- NR214 SOMATIC TREATMENT NEEDS OF A COMMUNITY SAMPLE
Alan J. Romanoski, M.D., Gerald A. Nestadt, M.D., Marshal F. Folstein, M.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D.
- NR215 CLOSING THE MENTAL HOSPITAL
S. Brandon, M.D., Liam Donaldson, M.D.
- NR216 SCHIZOPHRENIA: P300 TEMPORAL LOBE DEFICIT CONFIRMED
Michael W. Torello, Ph.D., Martha E. Shenton, Ph.D., Geraldine P. Cassens, Ph.D., Frank H. Duffy, M.D., Robert W. McCarley, M.D.

Thursday, May 23, 1985, 2:00 p.m.-5:00 p.m.

New Research 7—Oral/Slide Session—Room E-301, Level III, Convention Center

Chp.: Susan Fiester, M.D.

Co-Chp.: Donald Sweeney, M.D.

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| NR217 | EXPLOSIVE VIOLENCE IN PRIMATES William T. McKinney, M.D., Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., C. Raymond Lake, M.D. | 2:00 p.m. |
| NR218 | BEHAVIORAL FAMILY THERAPY FOR SCHIZOPHRENICS Ian R.H. Falloon, M.D., Christine McGill, Ph.D., Jeffrey Boyd, Ph.D., Robert P. Liberman, M.D. | 2:15 p.m. |
| NR219 | CHILD ABUSE EPIDEMIOLOGY: SOME NEW PERSPECTIVES Nicholas A. Green, M.D., L. Ralph Jones, M.D., Lee W. Badger, M.S.W. | 2:30 p.m. |
| NR220 | PARASUICIDE CHANGES DURING A TEEN SUICIDE CLUSTER Lucy Davidson, M.D. | 2:45 p.m. |
| NR221 | PSYCHIATRISTS FIND 27% OF COMMUNITY NEED TREATMENT Alan J. Romanoski, M.D., Gerald A. Nestadt, M.D., Marshal F. Folstein, M.D., Michael Von Korff, Sc.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D. | 3:00 p.m. |
| NR222 | THE ECOLOGY OF SUICIDE IN CANADA Isaac Sakinofsky, M.D., Robin Roberts | 3:15 p.m. |
| NR223 | CONSENT RATES IN SCHIZOPHRENIC AND CONTROL GROUPS Llewellyn B. Bigelow, M.D., Tammy L. Braun, B.A. | 3:30 p.m. |
| NR224 | HYPNOTIC HALLUCINATION ALTERS EVOKED POTENTIALS David Spiegel, M.D., Steven Cutcomb, Ph.D., Chuan Ren, M.D., Karl Pribram, M.D. | 3:45 p.m. |
| NR225 | FAMILIES OF THE CHRONICALLY HOMELESS Howard Dichter, M.D., A. Anthony Arce, M.D. | 4:00 p.m. |
| NR226 | WOODSHEDDING: A PHASE IN RECOVERY FROM PSYCHOSIS John S. Strauss, M.D., Joshua Sparrow, Courtenay M. Harding, Ph.D., Hisham Hafez, M.D., Paul Lieberman, M.D. | 4:15 p.m. |
| NR227 | TESTING SYMPTOM CRITERIA FOR DSM-III SCHIZOTYPAL AND BORDERLINE PERSONALITY DISORDERS Thomas H. McGlashan, M.D. | 4:30 p.m. |
| NR228 | NEW SUPPORT FOR A SCHIZOTYPAL/BORDERLINE DICHOTOMY David L. Braff, M.D. | 4:45 p.m. |

NEW RESEARCH PAPERS

in Summary Form

**NR1
FRONTAL LOBE STRUCTURE AND FUNCTION IN SCHIZOPHRENIA**

Monday, May 20, 2:00 p.m.

Karen Faith Berman, M.D., Neuropsychiatry Branch, NIMH, St. Elizabeths Hospital, WAW Bldg., Room 536, Washington, D.C. 20032, Richard C. Shelton, M.D., Ronald F. Zec, Ph.D., Daniel R. Weinberger, M.D.

Summary:

Recent research in schizophrenia has identified two relatively consistent brain abnormalities: 1) structural abnormalities such as enlarged ventricles (VBRs) and cortical atrophy, especially of frontal lobes, on CT scan; and 2) functional abnormality of frontal cortex in studies employing techniques such as regional cerebral blood flow (rCBF) that investigate cortical physiology of the living human brain. These findings of structural and functional abnormalities are potentially important to the understanding of schizophrenia, but it has not been clear whether they are related.

The present study combined determinations of cortical metabolism via Xenon 133 inhalation rCBF with investigation of structure by CT scan. Eighteen medication-free and 22 neuroleptic treated chronic schizophrenic patients underwent rCBF procedures during a variety of cognitive tasks and conditions. CT scans were measured by an investigator who was unaware of the rCBF results.

In the medication-free patients blood flow to all cortical areas was found to vary inversely with the degree of frontal atrophy on CT. This was true for all cognitive activation conditions, but the relationship was most robust ($r < -.55$, $p < .02$) during a task specifically linked to dorsolateral prefrontal cortical function, the Wisconsin Card Sort (WCS). A relationship between rCBF and frontal atrophy was not found in patients on neuroleptics. However, in this group rCBF to prefrontal cortex varied with VBR, particularly during the WCS ($r = -.55$, $p < .008$).

These results indicate that physiological observations of reduced prefrontal blood flow are related to structural pathology. These data also strongly suggest that dorsolateral prefrontal cortex is abnormal both structurally and functionally in schizophrenia, that these abnormalities are linked, and that they are important biological underpinnings of this illness.

**NR2
INTERREGIONAL BRAIN METABOLISM IN SCHIZOPHRENIA**

Monday, May 20, 2:15 p.m.

Henry H. Holcomb, M.D., Room 4N-317, Building 10, NIMH, Bethesda, Maryland 20205, W.E. Semple, M.A., M.S. Buchsbaum, M.D., R.M. Cohen, M.D., C.M. Clark, Ph.D., L.E. DeLisi, M.D.

Summary:

Because patients with schizophrenia differ from normals in their appreciation of pain we have used positron emission tomography of fluorine-18 2-deoxyglucose utilization in conjunction with a prolonged, repetitive, noxious, cutaneous, electrical stimulation design (Buchsbaum, et al., Arch. Gen. Psych. 1984, 41:1159-1166) to assess functional interregional coupling between various brain regions. Analysis of 14 drug free, severely ill schizophrenics and 15 age/sex matched normal volunteers, using a $p < 0.05$, revealed a systematic, significant difference in interregional correlation patterns between the two groups. These correlation matrices revealed a marked divergence between the two groups in their coupling between the right parietal, and left or right frontal cortex. Normals receiving right forearm stimulation exhibit negative or zero correlations between the left and right frontal cortical regions and the right parietal cortex. Schizophrenics, however, exhibit highly coupled correlations between those regions. Aberrant correlational patterns may reflect abnormal sensory processing in this syndrome.

NR3**Monday, May 20, 2:30 p.m.****MAGNETIC RESONANCE IMAGING IN SCHIZOPHRENIA: SMALLER CEREBRAL SIZE IN MALES**

Stephen C. Olson, M.D., Univ. of Iowa College of Medicine, Dept. of Psychiatry, 500 Newton Road, Iowa City, IA 52242, Nancy C. Andreasen, M.D., Henry A. Nasrallah, M.D., Jeffrey A. Coffman, M.D., William M. Grove, Ph.D., Val Dunn, M.D., James C. Ehrhardt, Ph.D.

Summary:

Magnetic resonance imaging (MRI) as compared to CT imaging offers enhanced tissue contrast, visualization of the brain in all planes, and absence of bone artifact, allowing measurement of brain structures previously limited to post-mortem examination. We report here the comparison of brain area measurements in 28 males and 10 females (age 19-52) with DSM-III schizophrenia (SCZ) and 25 male and 24 female control subjects (age 19-40) scanned using a Picker 0.5 tesla MRI system. The midsagittal inversion recovery image was used to measure the area of the mesial surface of the cerebral hemisphere subdivided into occipital, parietal and frontal cortex, as well as midsagittal areas of the corpus callosum, cerebellum, ventricle, thalamus, and cranium.

We found mean cerebral area to be smaller in SCZ males than control males ($\bar{x} \pm S.D = 86.5 \pm 11.4 \text{ cm}^2$ vs. $96.3 \pm 9.4 \text{ cm}^2$; $T = 3.410$, $p = .001$), while SCZ and control females did not differ ($85.8 \pm 8.8 \text{ cm}^2$ vs. $85.8 \pm 9.3 \text{ cm}^2$, respectively). A size difference of equivalent magnitude was observed in cranial area (SCZ males: $159.2 \pm 11.2 \text{ cm}^2$ vs. control males: $171.6 \pm 13.0 \text{ cm}^2$; $T = 3.717$, $p = .0005$), suggesting that smaller brain size in SCZ males may be due to developmental hypoplasia rather than brain atrophy. The MRI findings will be compared to previously reported VBR measures by axial CT of this SCZ sample. Absolute area and ratio and ratio measurements of other CNS structures (e.g. VBR) will be presented and compared by diagnosis, sex, height, and clinical variables, and implications of these findings will be discussed.

NR4**Monday, May 20, 2:45 p.m.****THE DOPAMINE INFLUENCE ON CNS METABOLISM IN SCHIZOPHRENIA**

Adam Wolkin, M.D., New York VAMC, Psychiatry Service (116A), 24th St. & 1st Ave., New York, NY 10010, Burton Angrist, M.D., Barbara Jordan, R.N., John Rotrosen, M.D., Judith Jaeger, Ph.D., Jonathan Brodie, M.D., Alfred Wolf, Ph.D.

Summary:

The dopamine (DA) hypothesis of schizophrenia is largely based upon the clinical and pharmacological effects of DA agonists and antagonists. We have used positron emission tomography (PET) in conjunction with DA agonists and antagonists in order to evaluate the metabolic correlates of DA system activity and its relevance to schizophrenia.

Medication-free chronic schizophrenics have decreased cerebral metabolism, with the most significant deficits in the left frontal and temporal areas. After several months of neuroleptic treatment, metabolic rates increased to levels seen in normals except in the frontal region.

Effects of a DA agonist, d-amphetamine, were assessed in a separate group of chronic schizophrenics. Using a same day test-retest paradigm, medication-free subjects underwent two PET scans with C11-deoxyglucose. Prior to the second scan, patients received either placebo or d-amphetamine .5mg/kg (double blind). Abrams and Taylor negative symptoms, BPRS, and AIMS scores were obtained in conjunction with each scan.

Following amphetamine, both positive symptoms and involuntary movements increased, whereas negative symptoms decreased. Metabolic activity decreased in all regions of interest. As compared to placebo, this decrease was significant for the right frontal, temporal, and striatal regions.

The metabolic changes induced by amphetamine were in the direction of the abnormalities observed in chronic schizophrenics and opposite to the metabolic changes associated with neuroleptic treatment. The relationship of these changes to psychopathology, and the metabolic effects of DA agonists in normals will also be presented.

NR5
PEPTIDES IN SUBSTANTIA NIGRA FROM SCHIZOPHRENICS

Monday, May 20, 3:00 p.m.

Michael J. Iadarola, Ph.D., Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, WAW Bldg., Washington, D.C. 20032, Joel E. Kleinman, M.D., Hsiu-Ying T. Yang, Ph.D.

Summary:

Substance P and dynorphin are particularly enriched in pars reticulata of rat substantia nigra (SN); these peptides are located in afferent terminals arising from striatal perikarya (J.S. Hong *et al.*, 1977; M. Palkovits *et al.*, 1984). The source of nigral enkephalin peptides, which are derived from pre-proenkephalin A has not been clearly defined. However, in rat they do not appear to come from striatal efferents. Preclinical studies have shown that chronic neuroleptic treatment decreases substance P content in the SN (J.S. Hong *et al.*, 1978). Such an observation suggests that nigro-striatal dopaminergic innervation regulates striatal peptidergic efferents and that this may be altered in schizophrenia. We have examined this possibility by a post-mortem analysis of substance P, dynorphin A 1-8 and met⁵-enkephalin-arg⁶-gly⁷-leu⁸ (MERGL) in human SN in 14 normals (mean age 40 yrs; post-mortem interval 18 hrs) and 14 schizophrenics (mean age 33 yrs; post-mortem interval 16 hrs). Three small pieces (15 mg) were removed from each SN while frozen; where possible the pieces were dissected from the pigmented portion of the SN. Samples were assayed by RIAs specific for each peptide. The mean (\pm SEM) picomoles/mg protein for nigral substance P was 11.8 ± 3.1 in controls and 11.6 ± 1.8 in schizophrenics; for dynorphin A 1-8 mean content was 4.3 ± 1.3 in controls and 3.6 ± 0.7 in schizophrenics. Although there were no significant differences in the above two peptides, a significant increase (120% over control) in nigral MERGL content was observed in the schizophrenics ($0.294 \pm .05$) compared to controls ($0.134 \pm .03$). Not all schizophrenic SNs showed the increase, but five patients were more than two standard deviations away from the control mean. Our data indicate that nigral dynorphin and substance P are not altered in schizophrenics, while nigral met⁵-enkephalin-arg⁶-gly⁷-leu⁸ is increased. The relationship of this peptide to dopaminergic regulation appears to be distinct from that of dynorphin or substance P. It is possible that the increase in nigral MERGL and by inference other pre-proenkephalin-derived peptides is related to some portion of the schizophrenic process.

NR6
PLASMA ANTIPSYCHOTIC-SIGMOIDAL RESPONSE CURVES

Monday, May 20, 3:15 p.m.

David L. Garver, M.D., Dept. Psychiatry, ML #559, 231 Bethesda Ave., University of Cincinnati College of Med., Cincinnati, OH 45267, Robert M. Hitzemann, Ph.D., Michael V. Mavroidis, M.D., Jack Hirschowitz, M.D.

Summary:

Sigmoidal dose-response curves for antipsychotic drugs have been consistently reported. In contrast, all studies of antipsychotic drug *plasma level*-response relationships utilizing studies with predetermined fixed X2 daily "average" doses and chemical assays have found non-sigmoidal, inverted "U" shaped curves for haloperidol, fluphenazine and thiothixene; diminished response at higher plasma antipsychotic levels.

The radioreceptor assay (RA) utilized in the present study measures the quantity of D₂ blocking potency (bound and free) in plasma. It monitors both parent compound (as does chemical assays) and active metabolites, functionally summing relative affinities for D₂ concentration of each active/inhibiting component. With rat (rather than calf) caudate as source of D₂ receptors and H-spiroperidol as the ligand, assay sensitivity was 1 ng haloperidol eq (Heq)/ml plasma.

Forty-four DSM-III schizophrenics newly admitted received predetermined fixed doses of haloperidol, fluphenazine and thiothixene ranging from 1/2 to X2 "average" doses of drug. Psychotic symptom change was monitored by serial NHSI. RA results are mean of days 7 & 14 in ng Heq/ml.

Thirty-two of 44 schizophrenic subjects fell on a clear sigmoidal drug level-response curve: linear portion, 3-10 ng Heq/ml (n = 18); plateau, 10-43 ng Heq/ml (n = 10). Two subjects at high blood levels had <25% improvement. Ten subjects with plasma levels <1-4.2 ng Heq/ml were on an independent curve whose linear portion was both steeped, and shifted to the left (0.5-2 ng Heq/ml).

In addition to verifying a sigmoidal antipsychotic drug plasma level-response relationship in the majority of schizophrenics, the data suggests such drug level-response relationships may aid in discriminating among types of psychotic illnesses whose curves are at variance with those of the majority of schizophrenics: drug non-responders (at any level) and a group of "dopamine psychotics" with curves shifted left.

NR7

Monday, May 20, 3:30 p.m.

HALOPERIDOL: PLASMA LEVELS AND CLINICAL RESPONSE

Michael Shostak, M.D., Assistant Professor of Psychiatry, Medical Director, OERP, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15213, James M. Perel, Ph.D., Richard L. Stiller, Ph.D., Wendy Wyman, R.N., Suzanne Curran, M.S.

Summary:

The response of 17 acutely psychotic inpatients to a fixed oral dose of haloperidol (HA), 5 mg BID, was studied over four weeks. Eleven males and six females, mean age 37.4 ± 12.1 , gave informed consent. The DSM III diagnoses were 1 paranoid psychosis, 1 chronic undifferentiated and 15 paranoid schizophrenics. Psychopathology ratings and plasma samples were obtained twice weekly. From day 17 on, all patients received benztropine 3 mg BID. Plasma was assayed by solvent extraction radioimmunoassay (RIA) specifically for (HA) and by a direct RIA which yields total = (HA) plus the reduced metabolite. The latter is the only known metabolite which has (partial) activity. Baseline BPRS was 54 ± 9.7 , final BPRS 40 ± 12.6 . Mean steady-state plasma levels at 2½ weeks (just before starting benztropine) were: HA 5.6 ± 3.0 ; reduced metabolite 10.5 ± 3.7 ; total 16.0 ± 6.1 (all in ng/ml). The corresponding levels at 4 weeks were HA 6.87 ± 2.7 ; metabolite 13.0 ± 4.8 ; total 19.8 ± 6.1 (all in ng/ml). None of these changes were statistically significant (paired t-test, $p > .2$). Nine patients were judged to be clinically recovered (56%) using global impression/discharge readiness/no medication change as criteria. Their BPRS was 29 ± 5.9 at four weeks; for those not recovered it was 50 ± 8.3 . At 4 weeks the linear correlation coefficient between % improvement relative to baseline and log plasma levels was: HA 0.35 (ns); metabolite .43 (ns); total .55 ($p = .05$). There was no suggestion of a curvilinear response over the range studied, nor did benztropine have any effect on clinical state or any of the plasma levels. These results also indicate that reduced HA is usually present in much greater amounts than the parent drug and contributes significantly to the overall clinical effect/plasma level response relationship.

NRS

Monday, May 20, 3:45 p.m.

CLINICAL APPLICATIONS OF I-125 FLUPHENAZINE RIA

William Glazer, M.D., Yale University, 34 Park Street, New Haven, Connecticut 06519, John Brennan, Ph.D., Jan-I Tu, Ph.D., Marc Aronson, M.D., Kenneth Duchin, Ph.D., Judith Steinbach, M.T., Rita Jewart, M.A., Sydney Gilman, Ph.D., Eileen L. Nickoloff, Ph.D.

Summary:

A rapid, very sensitive and direct radioimmunoassay (RIA) for fluphenazine in human serum has been developed for clinical studies. The RIA requires no sample pretreatment and utilizes an ^{125}I fluphenazine derivative as the radiolabel. Standard curve, controls and patient samples are processed quickly using a computerized multiwell gamma counter. The direct ^{125}I results from patients given fluphenazine decanoate are highly correlated with the results on a ^3H -fluphenazine reference immunoassay.

The direct ^{125}I RIA was used to obtain pharmacokinetic profiles of 8 chronic schizophrenic patients (age range 26 to 45 years, 7 males/1 female, 2 white/6 black) who are receiving 25 mg biweekly injections of fluphenazine decanoate. For these patients, trough concentrations of fluphenazine (C_{\min}) equal 0.93 ± 0.50 ng/ml (mean \pm 0.94 hours) after drug administration. In another study, fluphenazine serum levels at steady state were compared in a group of 17 patients with tardive dyskinesia (TD) and 22 patients without this condition (NTD).

No significant difference in mean drug levels was observed between the groups (2.9 ng/ml vs. 2.5 ng/ml, respectively). Additional demographic (age, race, sex) and clinical variables (drug dosage and timing) that could influence the relationship between serum fluphenazine and TD were also investigated. None was found to be statistically significant. Future clinical studies of fluphenazine decanoate could be aided by this sensitive ^{125}I RIA.

NR9

Monday, May 20, 4:00 p.m.

EMOTIONAL BLUNTING: NEUROLEPTICS AND SCHIZOPHRENIA

Alan Breier, M.D., National Institute of Mental Health, NIH Bldg. 10, 4N-214, 9000 Rockville Pike, Bethesda, MD 20205-1000, David Pickar, M.D., John Boronow, M.D., Daniel W. Hommer, M.D., Allen Doran, M.D., Owen Wolkowitz, M.D., Alec Roy, M.B., Steven M. Paul, M.D.

Summary:

Emotional blunting, a common clinical feature of schizophrenia, has in recent years been viewed as unresponsive to neuroleptic treatment and thus hypothesized to be unrelated to the dopamine system. We have examined the effects of double-blind, placebo controlled fluphenazine administration ($n = 18$) and withdrawal ($n = 12$) on ratings of emotional blunting in patients with DSM-III diagnosed schizophrenia and attempted to link these changes to biological variables.

Emotional blunting, as determined by blind physician ratings using the Abrams Taylor Rating Scale (ATRS) and the withdrawal-retardation subscale of the BPRS (W-R), were each significantly increased 4 weeks following fluphenazine withdrawal ($p < 0.01$ and $p < 0.05$, respectively). Similarly, doctor's psychosis ratings were also significantly increased ($p < 0.01$). Four weeks of fluphenazine treatment was associated with significant improvement in measures of emotional blunting (ATRS $p < 0.02$, W-R $p < 0.01$), doctor's psychosis ($p < 0.001$) and BPRS thought disorder (TD) ($p < 0.001$). Improvement in the ATRS and W-R did not significantly correlate with the improvement in doctor's psychosis or TD, suggesting the possibility that change in emotional blunting was not simply a factor of change in positive psychotic symptoms. Neither lateral ventricular brain ratio nor third ventricular size was related to neuroleptic response or the effect of neuroleptic withdrawal as reflected by ATRS, W-R, doctor's psychosis, or TD ratings. We have recently reported neuroleptic-induced time-dependent decreases in levels of plasma homovanillic acid (HVA). In this study we have observed high correlations between changes in plasma HVA and changes in the ATRS: med-free to 5th week of fluphenazine treatment ($r = 0.68$, $p < 0.01$); and from neuroleptic treatment to 5th week med-free ($r = 0.84$, $p < 0.001$). These data suggest dopaminergic involvement not only in more positive psychotic symptoms but also in negative symptoms such as emotional blunting.

NR10

Monday, May 20, 4:15 p.m.

VASOPRESSIN TREATMENT OF SCHIZOPHRENIA

Andrei-C. Iager, M.D., Neuropsychiatry Branch, NIMH, St. Eliz. Hospital, Washington, D.C. 20032, Darrell G. Kirch, M.D., Neil Pliskin, Llewellyn B. Bigelow, M.D., Richard Jed Wyatt, M.D., Craig N. Karson, M.D.

Summary:

Introduction: Although neuroleptics are effective antipsychotics, many treated chronic schizophrenic patients will continue to exhibit a variety of negative symptoms. Vasopressin alone was used with some success by Forizs as early as 1937 in the treatment of such symptoms in a group of patients with "schizophrenia with deterioration." A more recent study by Vranka *et al.* (1979) confirmed these results. The spectrum of efficacy of vasopressin may not overlap with that of the neuroleptics. To test this hypothesis we administered a vasopressin analogue to chronic schizophrenic patients.

Methods: Ten chronic schizophrenic patients diagnosed according to DSM III and Research Diagnostic Criteria gave written informed consent for this study. The patients were recruited from the NIMH research wards, Saint Elizabeths Hospital. They were physically healthy and stable on a fixed dose of antipsychotic which was maintained throughout this study. The patient's behavior and performance was scored on The Negative Symptom Rating Scale and on the Brief Psychiatric Rating Scale (BPRS). I-Desamine D8 Arginine Vasopressin and placebo prepared by Ferring and furnished by Armour Pharmaceuticals was administered for three months to the patients in a double-blind ABA design.

Results: Preliminary data from this study indicate that negative symptoms decrease significantly ($p < 0.05$) during active vasopressin treatment. The BPRS Mean Item Scores also decreased significantly ($p < 0.05$) suggesting that vasopressin may have a broader psychotropic effect in patients with schizophrenia. Additionally, some individual patients showed marked improvement in the positive symptoms. Preliminary data from the neuropsychological tests will be presented.

NR11**Monday, May 20, 4:30 p.m.****PHASE II: CLINICAL TRIAL OF REMOXIPRIDE IN SCHIZOPHRENIA**

G. Chouinard, M.D., Allan Memorial Institute, 1025 Pine Ave., W. Montreal, Quebec, Canada, L. Turnier, M.D.

Summary:

Twenty hospitalized schizophrenic patients, satisfying DSM-III criteria, underwent a 4-day placebo washout before being treated for six weeks with remoxipride, a new benzamide derivative. All patients completed the clinical trial. Ten patients showed marked improvement in schizophrenic symptoms, and there was a significant ($p < .05$) reduction in the mean score for CGI and BPRS total score suggesting that remoxipride has an antipsychotic effect. Results also showed a decline in parkinsonism consistent with the hypothesis that remoxipride has little effect on the nigrostriatal system. Dyskinetic movements increased slightly during treatment and this can be explained by the uncovering effect of neuroleptic withdrawal. Absence of steady state plasma prolactin elevations indicates that remoxipride differs from classical neuroleptics and sulpiride. The lack of serum neuroleptic activity using [^3H]spiperone binding suggests that the agonist [^3H]n-propylnorapomorphine should be used as a ligand for D_2 receptors in human studies of remoxipride.

NR12**Monday, May 20, 4:45 p.m.****OBSESSIVE/COMPULSIVE SYMPTOMS IN SCHIZOPHRENIA**

Wayne S. Fenton, M.D., Chestnut Lodge & Chestnut Lodge Research Institute, 500 W. Montgomery Ave., Rockville, MD 20850, Thomas H. McGlashan, M.D.

Summary:

Although the occurrence of obsessive/compulsive (OC) symptomatology in schizophrenia has been described for over 60 years, the clinical significance of these phenomena has yet to be explored systematically. This report details clinical characteristics and long term course of a group of 21 DSM-III schizophrenic patients with prominent OC symptoms from the Chestnut Lodge Follow-Up Study. Their condition at admission was assessed and rated in relation to a variety of demographic/predictor variables, and outcome was blindly evaluated from multiple perspectives an average of 15 years later. While schizophrenic patients with OC symptomatology differed only minimally from schizophrenic patients without OC symptoms at admission, their long term outcome in the areas of social relations, employment, psychopathology, and global functioning was significantly and almost uniformly poorer. Persistent OC symptoms thus appear to be a powerful predictor of poor prognosis in schizophrenia. The authors provide a descriptive typology of obsessive phenomena observed and discuss possible explanations of this somewhat unexpected finding.

NR13
CHARACTERISTICS OF VERY POOR OUTCOME SCHIZOPHRENIA

Tuesday, May 21, 12 Noon-2:00 p.m.

Kenneth L. Davis, M.D., Psychiatry Service (116A), VA Medical Center, Bronx, New York 10468, Richard S.E. Keefe, Michael Davidson, M.D., Miklos F. Losonczy, M.D., Thomas B. Horvath, M.D., Richard C. Mohs, Ph.D.

Summary:

Biologic, diagnostic and psychosocial variables were assessed in 65 drug free patients meeting RDC and/or Feighner criteria for schizophrenia. Thirteen were identified prior to assessment as very poor outcome "Kraepelinian" patients because for the past 5 years they: (1) showed no evidence of a remission, (2) did no useful work, and (3) were either (a) continuously hospitalized or (b) dependent on others for food, shelter and clothing. All patients were given diagnoses by RDC, DSM-III, Feighner, IPSS, Langfeldt, and Schneiderian criteria. In most cases Kraepelinian patients were positive and negative symptoms. Nine RDC schizoaffectives were found among the acutely exacerbated patients but none were found among Kraepelinians ($p < .10$). A six week treatment study with standardized doses of Haldol demonstrated that Kraepelinian patients were less responsive to this dopamine blocker than were other exacerbated schizophrenics ($p < .05$). Two thirds of the Kraepelinians but only 30% of the other schizophrenic had a positive family history for schizophrenia. Ventricular assymetry on CT scan was more common in Kraepelinians than other patients ($p < .01$). These findings indicate that very poor outcome schizophrenics have a genetic abnormality resulting in symptoms of all types which are not dopamine mediated.

NR14
EARLY NEUROLEPTIC RESPONSE: CLINICAL PROFILES

Tuesday, May 21, 12 Noon-2:00 p.m.

Malcolm Bowers, Jr., M.D., 620 Grace Bldg., Yale-New Haven Hosp., 25 Park St., New Haven, CT 06519, Mary E. Sungar, M.D., Peter I. Jatlow, M.D., Frederick Hoffman, B.A., Nora Goicoechea, M.S.N.

Summary:

We have studied 47 inpatients who required neuroleptic treatment for acute psychotic disorders. Twenty were categorized as good early responders. Eighteen had significant residual symptoms at ten days and were called poor early responders. Mean neuroleptic dose for the two groups was not significantly different. Twenty clinical items were compared in the two groups. In contrast to good early responders, poor responders were significantly younger at illness onset and index admission, more schizoid during development, less often married, and less frequently diagnosed psychosis with affective features or atypical psychosis. Diagnosis may have been influenced by early drug response, however. By contrast there were *no significant differences* between the groups with regard to symptom profiles rated on admission, family history of major psychiatric disorder in first degree relatives, hallucinogen use, or I.Q. Plasma free HVA on admission was significantly higher in the good early responders and free plasma MHPG showed a similar trend. To our knowledge, this is the first demonstration that a laboratory test may be more effective than symptom profiles in predicting early neuroleptic response in psychotic patients.

NR15
SYMPTOMS AND PROGNOSTIC FACTORS IN SCHIZOPHRENIA

Tuesday, May 21, 12 Noon-2:00 p.m.

Sam Castellani, M.D., Associate Professor, Department of Psychiatry, UKSM-W, 1010 North Kansas, Wichita, Kansas 67214, J. Alexander Boeringa, Ph.D., Beryl Silkey, A. James Giannini, M.D., Jean Endicott, Ph.D.

Summary:

Schneiderian first rank symptoms (FRS), formal thought disorder (FTD) and emotional blunting (EB) were examined in relation to epidemiological and prognostic factors in 63 patients diagnosed as schizophrenic by the Research Diagnostic Criteria (RDC). Data were obtained using the Schedule for Affective Disorders and Schizophrenia and emotional blunting scale of Abrams and Taylor.

FRS were associated with lower age, greater depression and lower severity on prognostic factors (length of illness, length of past hospitalization, work function, social relations), while FTD and EB were associated with greater age, less depression and higher severity on prognostic factors. Negative correlations were found between FRS and both FTD and EB. These results suggest that FRS and FTD/EB tend to fall into separate clusters in RDC-diagnosed schizophrenic patients, and may represent different phenotypic manifestations and/or temporal stages of the schizophrenic process.

NR16
FAMILIAL SCHIZOPHRENIA AND TREATMENT RESPONSE

Tuesday, May 21, 12 Noon-2:00 p.m.

Jeremy A. Silverman, Psychiatry Service - 116A, VA Medical Center, 130 W. Kingsbridge Road, Bronx, New York 10468, Richard Mohs, Ph.D., John C.S. Breitner, M.D., Kenneth L. Davis, M.D.

Summary:

Despite the large body of evidence for a genetic etiology, there are still no known biological correlates of familial schizophrenia. To investigate one possible link, 35 hospitalized RDC or Feighner-positive schizophrenics were assessed for family history of schizophrenia spectrum disorder (SSD) and response to a 6-week standardized dose schedule of haloperidol (10 mg bid week 1-4, 15 mg bid week 5, 20 mg bid week 6). Subjects showing a 12 point for 20% decrease from baseline scores of the BPRS at any time were considered Responders (R), and other Non-Responders (NR). Family history of SSD - comprising schizophrenia, schizoaffective disorder, unspecified functional psychosis, and schizophrenia-related personality - was assessed by blind, semi-structured interview with multiple informants. Fifteen (15) of 35 (43%) cases had one or more Family History RDC positive 1° or 2° relatives with SSD. Thirteen (13) of these 15 were NR's ($p < .005$). Because FH-subjects might have failed to show familial predisposition, owing to small family size, incomplete family history or other causes, aggregate familial morbid risk of SSD was examined among NR and R proband families. The risk was 16.3% among NR 1° relatives but only 3.5% in R families ($p < .01$). These results suggest that familial schizophrenia may be less responsive to neuroleptic treatment than sporadic disease.

NR17
NEGATIVE SYMPTOMS IN THE GENERAL POPULATION

Tuesday, May 21, 12 Noon-2:00 p.m.

Gerald A. Nestadt, M.D., Department of Psychiatry & Behavioral Sciences, The Johns Hopkins Hospitals, Baltimore, Maryland 21205, Alan J. Romanoski, M.D., Paul McHugh, M.D., William Eaton, Ph.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D.

Summary:

A complete psychiatric examination was performed on 810 subjects by one of four specially trained research psychiatrists in a two-stage morbidity survey conducted in 1981 as a component of the Eastern Baltimore Mental Health Survey of the ECA program.

DSM-III diagnoses were made on each of the subjects using the Standardized Psychiatric Examination (SPE) which included the entire Present State Examination (PSE-9). All subjects were examined for 14 different negative symptoms derived from PSE-9.

At least one negative symptom so defined was found in every schizophrenic subject; however, at least one negative symptom was found in 60% of the dementia/delirium subjects, 78% of the affective disorder subjects, 10% of the personality disorder subjects and in 7% of the 380 subjects with no DSM-III Axis I or Axis II diagnosis. The schizophrenic subjects were found to have three negative symptoms on average. The particular negative symptoms often found in schizophrenic subjects were different from those in the other diagnostic groups.

This study indicates that these symptoms are not individually characteristic of any psychiatric disorder although schizophrenic patients have more of these symptoms and may be more severely afflicted by certain of them. It is not clear that any of these symptoms can be employed for the diagnosis of or considered essential to schizophrenia.

**NR18
DISTRACTIBILITY IN SCHIZOPHRENICS AND RELATIVES**

Tuesday, May 21, 12 Noon-2:00 p.m.

Bonnie Spring, Ph.D., Texas Tech University, Department of Psychology, Lubbock, Texas 79409-4100

Summary:

Two studies are presented on distractibility as a marker of vulnerability to schizophrenia. In Study I, 12 schizophrenics, 15 schizo-affectives, 10 depressives, 15 normal controls, and 14 siblings of schizophrenics performed a dichotic listening task. When asked to immediately repeat words heard in one ear and to ignore distractor words presented to the other ear, both schizophrenics and their siblings interjected more phonemes from the distractor message (intrusions) than did normals. Study II involved 19 schizophrenics, 21 manic-depressives, 20 unipolar depressives, 20 matched normals, as well as parents and siblings of patients (33 relatives of schizophrenics, 26 relatives of manic-depressives, 19 relatives of unipolar depressives) and 19 matched normals. Even without distraction, schizophrenics repeated the main message less accurately than any other group when no distractor and distractor tasks were matched on discriminating power. Paranoid and undifferentiated schizophrenics manifested distractibility differently. Only paranoids exceeded normals in intrusions of distractor phonemes, but only undifferentiated schizophrenics showed decrements in repeating the main message when distraction was introduced. Relatives of schizophrenics repeated the main message as accurately as normals but were the only group to exceed normals in intrusions of distractor phonemes. Relatives of highly delusional schizophrenics interjected the most distractors. Intrusions were correlated between schizophrenics and relatives at $r = .58$ in Study I ($r = .84$ excluding three depressed siblings) and at $r = .69$ in Study II. We conclude that distractibility shows promise as a familiarly transmitted marker of schizophrenia. Since relatives of schizophrenics occasionally interject distractors without showing marked impairments at repeating the main message, we suggest that their distractibility may reflect a style of allocating greater than normal attentional capacity to distractors.

**NR19
CLINICAL SIGNIFICANCE OF COMMAND HALLUCINATIONS**

Tuesday, May 21, 12 Noon-2:00 p.m.

David J. Hellerstein, M.D., Fellow in Public Psychiatry, NY State Psychiatric Institute, 722 West 168th St., New York, N.Y. 10032, William Frosch, M.D., Harold Koenigsberg, M.D.

Summary:

Command hallucinations (CH) are auditory hallucinations in which a voice instructs a patient to act in a particular manner, often violently or self-destructively. It is commonly assumed in clinical practice that such patients are at increased risk for acting on the basis of CH, and thus require hospitalization and close observation. No research, however, documents this clinical impression. Our study retrospectively reviewed 789 consecutive inpatient admissions over a 1 year period; of 150 patients with auditory hallucinations, 58 heard commands. Demographic variables, diagnoses, symptoms and pre and in-hospital behavior were analyzed for CH and non-CH patients. CH patients were not significantly different from non-CH patients on these variables. There was no evidence for increased violent or self-destructive behavior in CH patients. In contrast, the presence or absence of auditory hallucinations correlated strongly with many demographic, diagnostic and behavioral variables. The clinical and research implications of these findings are discussed.

NR20**Tuesday, May 21, 12 Noon-2:00 p.m.****AUDITORY HALLUCINATIONS ARE SUBVOCALIZED SPEECH**

Peter A. Bick, M.D., Research Fellow, Harvard Medical School, MMHC, 74 Fenwood Road, Boston, MA 02115, Marcel Kinsbourne, M.D.

Summary:

In many schizophrenic patients, auditory hallucinations can be a disabling and treatment refractory phenomenon. It has been claimed that these hallucinations can be extinguished by stereo headphones or distracting sounds but no theoretical rationale has been offered for this. Evidence that covert subvocal speech occurs in hallucinating schizophrenics is reviewed and a theory is presented, suggesting that when schizophrenics hallucinate, they are in fact listening to their own subvocalisations. 18 hallucinating schizophrenics were asked to report if the intensity of their 'voices' was affected by holding their mouth wide open, a maneuver that has been shown to abolish subvocalisations. 2 control maneuvers not predicted to effect auditory hallucinations were also given. Mouth opening abolished the voices in 14 patients ($p < 0.05$, sign test). In another study, 21 college students were hypnotized and told that they could hear voices. Mouth opening abolished the voices in 18 subjects, ($p < 0.01$). Conceptualizing auditory hallucinations as subvocalisations may help in deriving coping strategies for this symptom.

NR21**Tuesday, May 21, 12 Noon-2:00 p.m.****SENSORY GATING IN RATS: PARALLELS WITH PSYCHOSIS**

Lawrence E. Adler, M.D., Instructor/Research Assoc., Dept. of Psychiatry C268, Univ. Colo. Health Sci. Ctr., 4200 E. Ninth Ave., Denver, CO 80262, Gregory M. Rose, Ph.D., Robert Freedman, M.D.

Summary:

Central inhibitory mechanisms were assessed in Sprague-Dawley rats by an evoked potential technique which we have previously used to show diminished inhibitory sensory gating in psychotic patients. Middle latency (P35-N50) auditory evoked potential responses were recorded at the vertex in unanesthetized freely-moving animals. Inhibitory mechanisms were assessed in a conditioning-testing paradigm by measuring the change in response to a 70 dB click test stimulus following an earlier conditioning stimulus at 0.5 sec intervals. The rats demonstrated significant suppression of the P35-N50 response to the second auditory stimulus (mean decrement ratio 68.2%). Amphetamine significantly interfered with the suppression of the response to the second stimulus; haloperidol, injected after the amphetamine returned the conditioning-testing ratio toward more normal values. Phencyclidine caused a similar decrease in suppression and was similarly antagonized by haloperidol. These results with psychotomimetic drugs in an animal model parallel abnormalities in sensory gating previously observed in schizophrenics and acutely psychotic manics.

NR22**Tuesday, May 21, 12 Noon-2:00 p.m.****CEREBRAL GLUCOGRAPHY OF ACUTE SCHIZOPHRENICS**

John M. Cleghorn, M.D., McMaster University, 1200 Main Street, West, Hamilton, Ontario, Canada L8N 3Z5

Summary:

This study employs positron emission tomography with fluorine labelled 2-deoxy-glucose (FDG) to describe uptake of glucose in brains of drug-free, acute, first admission schizophrenics (SCZ) who have never received neuroleptic medication. We examined the effect on glucose uptake of a single-dose of a dopamine agonist, apomorphine hydrochloride (APO) and placebo saline in balanced order on 2 successive days. Six right-handed, male SCZ meeting RDC were examined within days of first admission for acute, positive psychotic symptoms. Controls were 10 age-matched, right-handed men who demonstrated no psychiatric disorder on examination and no family history of same. No effect of APO on regional brain glucose consumption could be detected. However regional brain glucose uptake changed from day 1 to day 2 in 5 of 6 SCZ. On day 1 they showed high levels of activity in either left or right frontal cortex. On day 2, 5 of 6 subjects demonstrated high levels in both frontal cortices symmetrically. Controls showed more right or left frontal activity on both days. There was no evidence of frontal hypometabolism which has been reported in several studies of chronic SCZ and no consistent lateralization which has been reported in single scans of acute patients. Anxiety levels were not different in patients and controls and cortisol was not elevated on either day. Increased and symmetrical frontal glucose uptake characterized acute SCZ patients the second time they encountered the scan situation.

NR23 **Tuesday, May 21, 12 Noon-2:00 p.m.**
MAGNETIC RESONANCE IMAGING INTENSITY VALUES IN SCHIZOPHRENIC BRAINS

Jeffrey A. Coffman, M.D., 500 Newton Road, Room 1-290, Univ. of Iowa College of Medicine, Iowa City, IA 52242, Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Stephen C. Olson, M.D., Val Dunn, Ph.D., James C. Ehrhardt, M.D.

Summary:

A number of recent CT studies have suggested subtle differences in brain structure when schizophrenics and normal controls are compared (Coffman, et al, 1984). Magnetic resonance imaging, in addition to offering excellent in vivo anatomical data regarding gross brain structure, provides opportunity for assessment of several signal characteristics which reflect local physiochemical environments. We report here a study of tissue biochemical structural parameters in schizophrenic and control subjects utilizing magnetic resonance imaging techniques.

Twenty four schizophrenic and 21 healthy males (age 20-45) were scanned using a Picker 0.5 tesla MR system using an inversion-recovery (T_1 weighted) pulse sequence. Mid-sagittal, coronal and transverse images were obtained. Mean intensity values were obtained for gray and white matter tissue regions of interest (0.3 cm^2) in the frontal, temporal and parietal lobes as well as the cerebellum. Due to wide day to day and patient to patient variability, image intensity ratios were calculated for each patient using values for the splenium of the corpus callosum as the denominator. Interlabar, interhemispheric and intergroup comparisons have been made. Preliminary analysis of the data for the schizophrenic group reveals few interhemispheric or interlobar differences. Intergroup comparisons are currently being analyzed. In addition to presentation of measurements, methodological issues relating to regional tissue assessments by MR will be discussed and an attempt will be made to integrate the results with our previous CT findings.

NR24 **Tuesday, May 21, 12 Noon-2:00 p.m.**
DYNAMIC CT SCANS IN SCHIZOPHRENIA: BLOOD-BRAIN BARRIER EVALUATION

Elizabeth M. Burns, Ph.D., The University of Iowa, College of Nursing, Rm. 494, Iowa City, IA 52242, Henry A. Nasrallah, M.D., Mary H. Kathol, M.D., Thomas W. Kruckeberg, M.S., Suzanne Chapman, B.S.N.

Summary:

Rapid rotational computed tomography (CT) was used to perform dynamic brain scans in ten consenting right-handed males (mean age 36 years) fulfilling DSM III criteria for chronic schizophrenia. Subjects had a drug wash-out for 10-14 days prior to scanning.

Hypaque, 32 ml, was given via a mechanical injector over 4 seconds. Using a Picker 1200SX scanner, a series of 30 rapid-sequence scans of a pre-selected transverse brain section (15° from the canthomeatal line) was obtained. Graphs of changes in brain density over time in ten bilateral brain regions were generated by computer.

Significantly higher perfusion was observed in the right compared with the left temporal lobe in the patient sample. A similar asymmetry was also detected in the right versus left cerebellum and cerebellar vermis. Evaluation of these findings relative to the integrity of the blood-brain barrier will be discussed.

NR25 **Tuesday, May 21, 12 Noon-2:00 p.m.**
BRAIN OT_1 IN SCHIZOPHRENIC AND NORMAL CONTROLS

Marian K. DeMyer, M.D., 791 Union Drive, Institute of Psychiatric Research, Indianapolis, IN 46223, Richard L. Gilmor, M.D., Hugh C. Hendrie, M.B., Ch.B., Forrest T. Meiere, Ph.D., William E. DeMyer, M.D.

Summary:

Brains of 11 young adult schizophrenics and their normal controls were imaged with Technicare's .15 Tesla Nuclear Magnetic Resonance imager using a combination of spin echo and inversion recovery sequences. OT_1 values from 23 brain areas, each 107 pixels, were computer-averaged from the caudate nucleus, thalamus and gray and white matter from the temporal, frontal, posterior-frontal/anterior-parietal and occipital areas bilaterally.

Results: Sch had higher combined white matter OT_1 than Nr ($368.0 \pm 14 \text{ msec}$ vs. $355.9 \pm 10 \text{ msec}$; $p = .027$ two-tailed). Four brain areas contributed most to this difference. Possible meanings of this result, major sources of measurement error, contributions of neuroleptic treatment to the result and attempts at validation will be discussed. Replication trials, additional reliability studies and other areas measurements, including spin density modality, are in process and additional findings will be reported.

NR26**Tuesday, May 21, 12 Noon-2:00 p.m.****OLFACTORY RECALL DEFICITS AND VBR IN SCHIZOPHRENIA**

Paul J. Moberg, M.A., Research Associate, The Johns Hopkins Hospital Meyer 279, Baltimore, Maryland 21205, Godfrey D. Pearlson, M.D., Won S. Kim, M.D., Larry E. Tune, M.D.

Summary:

Nineteen schizophrenics, and 19 age and sex matched normal controls, received CT scans and were concurrently administered three similarly structured recognition memory tasks. Visual and verbal recognition were measured implementing abbreviated forms of the Rey Auditory Verbal Task (1964) and Kimura's Figures (1963). The third recognition task was an olfactory paradigm of the authors' design. All subjects were screened, and performed normally on an odor discrimination task. Recognition accuracy for all recognition tasks was represented using d'scores.

Schizophrenics performed significantly worse than controls on all recognition memory tasks, but were most impaired on olfactory recognition. Only olfactory recognition was significantly correlated with cerebral atrophy assessed by VBR on CT ($r = -.69, p < .001$). These data may support evidence for limbic/subcortical involvement in schizophrenia.

NR27**Tuesday, May 21, 12 Noon-2:00 p.m.****CT DENSITY AND VENTRICLES OF SCHIZOPHRENIA IN JAPAN**

Shigenobu Kanba, M.D., Depts. of Psychiatry and Psychology, Mayo Clinic, Rochester, MN 55905, Satoru Shima, M.D., Yutaka Masuda, M.D., Diazo Tsukumo, M.D., Toshinori Kitamura, M.D., Masahiro Asai, M.D.

Summary:

Brain CT density, ventricular size and asymmetry of cerebral hemispheres were measured by CT scans in 46 chronic schizophrenic inpatients (DSM III Criteria) and age and sex matched controls. We found significantly lower CT density in the bilateral frontal and occipital regions in the schizophrenic patients ($P < 0.01$); however, no significant difference was observed in the CT density laterality. There was no correlation between CT density and age, drug dosage, duration of illness, age of onset or ECT. There was no significant difference in VBR, Ewans' index, CMI or asymmetry. The finding that schizophrenic patients with lower brain CT density had normal ventricles and asymmetry is of great interest and awaits explanation. Meanwhile, we may postulate that the lower CT density occurs as a primary structural deficit before the measurable secondary gross structural changes occur; i.e. enlarged brain ventricles, cerebral atrophy.

NR28**Tuesday, May 21, 12 Noon-2:00 p.m.****BRAIN CT SCANS IN PSYCHIATRIC INPATIENTS**

Thomas P. Beresford, M.D., Chief, Psychiatry Service, VA Medical Center, 1030 Jefferson Ave., Memphis, TN 38104, Richard C.W. Hall, M.D., Frederic C. Blow, Ph.D., Linda Nichols, Ph.D., James Langston, M.D.

Summary:

The authors reviewed brain CT studies from 156 patients admitted to psychiatric inpatient wards. This comprised 3.5% of 4,600 total admissions during a 2½ year period. Forty-nine scans were abnormal (31.4%). Twenty-seven scans (17.3%) showed a lateralizing abnormality, and 22 scans (14.1%) a bilateral abnormality. Scan results changed diagnosis in 28 cases (17.9%), confirmed a suspected diagnosis in 17 cases (10.9%) and ruled out a specific clinical diagnosis in 69 cases (44.2%).

Contrary to current belief, lateralizing neurologic signs on physical examination, were not associated with CT lesion laterality. Clinical symptoms associated with positive CT result were cognitive impairment (34 of 49, 69.4%), visual or other non-auditory hallucinations (17 of 49, 34.7%), and recent behavioral change (16 of 49, 32.7%). Taken together, mental status findings correlated with positive scan readings ($p < 0.05$).

The authors conclude that (1) the study psychiatrists used CT scanning conservatively, (2) the absence of lateralizing findings should not obviate CT scanning and (3) mental status exam, especially with respect to cognitive impairment, offers the best guide for CT scan use.

**NR29
COMPUTERIZED EEG SYNCHRONY AND MENTAL DISORDERS**

Tuesday, May 21, 12 Noon-2:00 p.m.

Martin R. Ford, Ph.D., The Institute of Living, 400 Washington Street, Hartford, CT 06106, John W. Goethe, M.D., Debra Dekker, M.A.

Summary:

Recent evidence indicates that computer-assisted analysis of EEG activity in psychiatric patients can greatly augment our understanding of neurophysiological processes in relation to behavioral symptomatology. This report focuses on a computer-derived measure of EEG synchrony (SYN, a phase-dependent measure of the degree of coupling between two EEG signals). Eight-channel, eyes-closed, resting EEG recordings were obtained from patients within two weeks of admission. Dependent measures of percent SYN, number and pattern of inter-lead SYN correlations, and region of relative SYN abundance significantly discriminated paranoid schizophrenic, major depressive, dysthymic, and geriatric groups (n = 56). Other significant differences were: schizophrenics vs. depressives (all on neuroleptics; n = 34), and depressives on neuroleptics vs. those on tricyclics vs. those on medications (n = 35). EEG SYN is a unique measure of regional cortical communication which may enhance our understanding of the electro-physiological concomitants of mental disorders.

**NR30
ERRORS IN MAPPING OF BRAIN ELECTRICAL ACTIVITY**

Tuesday, May 21, 12 Noon-2:00 p.m.

E. Michael Kahn, M.D., Box 3173, Duke Univ. Med. Ctr., Durham, NC 27710, Richard D. Weiner, M.D., Richard D. Coppola, Sc.D.

Summary:

Topographic display of brain electrical activity (EEG and event-related potentials) is an intuitively powerful mode of data presentation. Simultaneously, these techniques are quite sensitive to distortion and error. Data from ongoing studies of depressed and schizophrenic subjects, and patients with neurologic diseases, will be used to demonstrate the impact of artifact, map construction strategy, and choice of reference on topograms. Recognition of the limitations of these techniques facilitates accurate clinical appraisal of the findings.

Artifact: Sources include blinking, eye movement, and muscle activity. Observation of raw EEG facilitates rejection of artifact-contaminated epochs; however, apparently minor interference may be highlighted by topographic technique.

Map construction: The many pixels displayed in a single map may represent data from as few as 11 electrodes. Map appearance is quite sensitive to the computational strategies used to interpolate values for the pixels. Electrophysiologic features may be exaggerated by scaling of values for plotting, with incumbent truncation and roundings errors. Finally, the scheme by which lead locations are mapped from the three dimensions of the head onto the video screen affects resolution of brain areas and accuracy of anatomic localization.

Reference: Electrodes near the reference site will have low amplitude activity relative to more distant sites. A change in reference schemes may result in an apparent shift of localization of activity. Source derivation has been suggested as a "reference free" technique. In practice, results appear similar to average reference constructions. Non-cephalic (sternovertebral) reference may be unsatisfactory because of EKG artifact.

Knowledge of these factors allow choice of recording and data presentation schemes which augment clarity of the maps produced.

NR31**Tuesday, May 21, 12 Noon-2:00 p.m.****CALCIUM BLOCKERS PREVENT DOPAMINE HYPERSENSITIVITY**

Jack A. Grebb, M.D., Neuropsychiatry Branch, NIMH, WAW Bldg., St. Eliz. Hospital, Washington, D.C. 20032, Richard C. Shelton, M.D., William J. Freed, Ph.D.

Summary:

Chronic Thioridazine (TDZ) treatment in animals produces much less dopaminergic supersensitivity than other neuroleptics. We hypothesized that this difference is due to the potent calcium channel inhibitory effect of TDZ. If this hypothesis were correct, the effects of TDZ would be mimicked by co-administration of calcium channel blocker (CCB) drugs (e.g., diltiazem, nifedipine, verapamil) with haloperidol (HAL), a neuroleptic without CCB activity.

Methods: Swiss-Webster mice (n = 163) were treated chronically (28d) with CCB's and/or HAL. Following three days of drug withdrawal, mice were tested for amphetamine-induced locomotion and apomorphine-induced cage climbing.

Results: Co-administration of diltiazem or verapamil (but not nifedipine) prevented the development of HAL-induced apomorphine supersensitivity ($p < 0.05$), but not the development of HAL-induced amphetamine supersensitivity.

Discussion: The results suggest a complex interaction between CCB's and dopaminergic systems. Insofar as neuroleptic-induced apomorphine supersensitivity is an animal model of tardive dyskinesia, these data suggest a potential role for CCB's in the prophylaxis and treatment of this movement disorder.

NR32**Tuesday, May 21, 12 Noon-2:00 p.m.****MESOLIMBIC DOPAMINE ACTIVITY AND SCHIZOPHRENIA**

Neal Swerdlow, Medical Scientist Training Prog., University of California, San Diego, La Jolla, CA 92093, David L. Braff, M.D., Mark A. Geyer, Ph.D., George F. Koob, Ph.D.

Summary:

While overactivity within central dopamine-containing neural systems and, specifically, within the mesolimbic dopamine system has been repeatedly implicated in the pathophysiology of schizophrenia, direct evidence for such an involvement has been scarce.

Our studies of the acoustic startle response (ASR) in humans have revealed that schizophrenic patients do not exhibit the inhibition of the ASR that normally occurs when the startle stimulus is preceded by a weak pre-pulse. In the present study, we show an elimination of this "pre-pulse inhibition" of the ASR in rats during stimulation of supersensitive dopamine terminal regions. Dopamine receptor stimulation in forebrain regions was achieved with the direct agonist apomorphine after producing a state of denervation supersensitivity using intracerebral injections of the catecholamine neurotoxin, 6-hydroxydopamine. Our results suggest that the ASR may be a useful animal model of schizophrenia based on the parallels between schizophrenic patients and dopaminergically stimulated rats.

NR33**Tuesday, May 21, 12 Noon-2:00 p.m.****NEW METHOD TO ASSESS CENTRAL DOPAMINERGIC FUNCTION**

Mark A. Riddle, M.D., Assistant Prof. of Psychiatry & Pediatrics, Yale Child Study Center, P.O.B. 3333, New Haven, CT 06510, James F. Leckman, M.D., Donald J. Cohen, M.D., George M. Anderson, Ph.D., Sharon Ort, R.N., Bennett A. Shaywitz, M.D.

Summary:

This report describes a novel strategy for assessing central dopaminergic (DA) function in 12 patients (ages 7-45) with Tourette Syndrome (TS) using debrisoquin (DBQ) loading and plasma-free homovanillic acid (PF-HVA) levels. DBQ is a peripherally active antihypertensive agent. Plasma-free 3-methoxy-4-hydroxyphenethyleneglycol (PF-M-PG), urinary catecholamines, monoamine metabolites (4 patients), and cardiovascular status were also measured. DBQ loading resulted in significant decreases in PF-HVA (56%) and PF-M-PG (68%) from the initial baseline to the 4-hour post-loading value. Cerebrospinal fluid monoamine metabolites data suggest that DBQ does not cross the blood-brain barrier in man. The potential usefulness of this strategy is illustrated by its use in combination with centrally active DA agents. After treatment with haloperidol, pre-DBQ PF-HVA decreased by 28%, while post-DBQ PF-HVA increased by 23%. The results of the urinary measures are compatible with DBQ's mechanism of action involving postganglionic blockade, but not MAO inhibition. The DBQ loading method appears to be a safe and potentially effective technique for evaluating central DA function.

NR34

Tuesday, May 21, 12 Noon-2:00 p.m.

LOWER ALPHA 2 AGONIST BINDING IN SCHIZOPHRENIC BRAINS

Grant N. Ko, M.D., Neuropsychiatry Branch, NIMH, St. Eliz. Hosp., WAW Bldg., Room 536, Washington, D.C. 20032, James R. Unnerstall, Michael J. Kuhar, Ph.D., Richard Jed Wyatt, M.D., Henry H. Holcomb, M.D., Joel E. Kleinman, M.D.

Summary:

Introduction: One neurochemical hypotheses of the schizophrenic syndrome suggests that increased norepinephrine (NE) may account for some of the psychopathology. One possible mechanism for increased NE is decreased inhibitory receptors on cell bodies in the locus coeruleus (LC). In order to test this hypothesis, inhibitory receptors (alpha-2 adrenergic) were measured in postmortem schizophrenic brains.

Methods: Unfixed pontine material was obtained from the D.C. Medical Examiner's Office. The pons was cut and mounted on brass microtome chucks with brain paste, and using a cryostat, coronal sections of 16 micro thickness were thaw mounted on subbed microscope slides and allowed to air dry at room temperature before they were stored. [³H] para-aminoclonidine (PAC, 40 Ci/mmol) was used to label alpha-2 adrenergic binding sites in the mounted tissue sections. The mean age at the time of death and post mortem delay was 43 years and 19 hours, respectively for the schizophrenic patients, 52 years and 20 hours for the suicide victims, and 45 years and 21 hours for normal controls.

Results: The mean and standard error for PAC binding to LC, expressed as femtomoles/mg protein, in normal controls was 887 ± 315 (n=6), in suicide victims was 647 ± 270 (n=7), and in schizophrenic patients was 190 ± 19 (n=5).

Conclusion: The preliminary data from this pilot study suggest fewer alpha-2 binding sites at the LC of schizophrenic patients than controls. Additional samples are currently being analyzed. The implications of this finding will be discussed.

NR35

Tuesday, May 21, 12 Noon-2:00 p.m.

LYMPHOCYTE 3H-SPIROPERIDOL BINDING IN SCHIZOPHRENIA

Ed Rotstein, M.D., Department of Psychiatry, McMaster University, Hamilton, Ontario, Canada, Ram K. Mishra, Ph.D., Dharam P. Singal, Ph.D., Dory Barone, R.T.

Summary:

When ³H-spiroperidol binding sites were found on human lymphocytes that appeared to meet the criteria for a dopamine receptor, it became possible to test the hypothesis in living patients that an increased number of dopamine receptors was involved in the pathogenesis of the acute schizophrenic syndrome.

Specific binding was found to be significantly increased (p<.01) in 20 unmedicated schizophrenic patients meeting Research Diagnostic Criteria compared to 24 healthy controls particularly in the paranoid subtype (p<.001). No significant difference in binding was found between patients who had never previously taken neuroleptics from those who had. Neither was any significant correlation found between binding and age, chronicity of illness, blink rate or severity of negative or positive symptoms.

Displacement studies, the lack of stereospecificity and the need for an intact lymphocyte indicated that this binding site was different from the dopamine receptor characterized in the brain, and that results from assays done on intact cells were prone to misinterpretation due to uptake phenomena. Nevertheless increased lymphocyte ³H-spiroperidol binding in schizophrenic patients compared to controls has now been reported by three separate investigators indicating a biological abnormality.

NR36

Tuesday, May 21, 12 Noon-2:00 p.m.

TRIHEXYPHENIDYL INCREASES PLASMA CHLORPROMAZINE

Lawrence H. Rockland, M.D., The New York Hospital-Cornell Medical Center, 21 Bloomingdale Road, White Plains, NY 10605, Thomas Cooper, David Weber, M.D., Timothy Sullivan, M.D., Barbara Murray, M.D., Matthew Keats, M.D.

Summary:

Anti-parkinsonian agents inhibit (Singh), or don't affect (Simpson), neuroleptic efficacy. APs decrease (Rivera-Calimlim), increase (Kolakowaka) or don't affect (Simpson) neuroleptic levels. CPZ levels drop 50% over first month (Sakalis).

Methods: 20 acute or subchronic DSM III schizophrenic or schizophreniform Ss, 19-30 y.o. Constant CPZ dosage. Double-blind, placebo-controlled, cross-over design. CPZ (300-1500 mgm) and trihexyphenidyl (9mgm/day)/placebo liquid, 1,5,9 p.m.

| Washout | CPZ Buildup | X ₁ | X ₂ | Placebo |
|---------|-------------|--------------------------------------|----------------|------------|
| I | II | III | IV | V |
| Day 0 | 7 | CPZ CONSTANT DOSE 21 trihex/Pl 31 | tri/Pl 42 | Placebo 52 |

Bloods for CPZ level, clinical interviews BIW before 1st daily doses. Ratings BPRS (r = .92), GAS (r = .90), EPS Scale (r = .90). CPZ level by gas chromatography, nitrogen detector, 2,4, dichlorpromazine standard.

Results: (1st 12 subjects—20 just completed). Trihexyphenidyl increased CPZ plasma levels; \bar{x} (Pl) = 83.75, \bar{x} (trihexyphenidyl) = 115.42 p < .05. Nine S's higher trihexyphenidyl, 2 lower, 1 tie; Sign Test = .033. No clinical change on trihexyphenidyl; BPRS: \bar{x} (Pl) = 18.25, \bar{x} (trihexyphenidyl) = 29.92, NS; GAS: \bar{x} (Pl) = 35.17, \bar{x} (trihexyphenidyl) = 33.75, NS; EPS: \bar{x} (Pl) = 1.71, \bar{x} (trihexyphenidyl) = 1.67, NS. No fall off of CPZ levels; \bar{x} CPZ levels: Stage III = 106.58, Stage IV 92.58, Stage V = 103.17; Last Level Stage II, \bar{x} = 107.17; last level State V, \bar{x} = 104.58, NS.

Comment: Only Simpson had adequate design. Discrepant results probably due to chronicity of their S's, our younger acutes and subchronics. Unable to replicate Sakalis' results; not due to neuroleptics before study. 4 of 5 S's, no drug >3 weeks before study, had rising levels.

NR37

Tuesday, May 21, 12 Noon-2:00 p.m.

NEUROLEPTIC DYSPHORIA AS AN OUTCOME PREDICTOR

Peter J. Weiden, M.D., Payne Whitney Clinic, 525 East 68th St., New York, NY 10021

Summary:

A prospective study evaluated subjective dysphoria, objective neuroleptic-induced motoric effects, and clinical outcome in acute psychotic inpatients.

Methods: 58 consecutive admissions with an initial diagnosis including schizophrenia were assessed weekly with standard Parkinsons, akinesia, akathisia, and subjective dysphoria scales.

Results: Of 54 patients rated, 13 (24%) experienced severe dysphoria. 4 out of 6 patients discharged AMA were dysphoric responders (p < .02). However, the remaining 9 dysphoric patients remained and received significantly lower maintenance neuroleptic doses than the non-dysphoric group (878 vs. 1455 mg. CPZ equivalents p < .05). Mean objective side effect scores were significantly lower in this group as well (1.1 vs. 1.85, p < .05) yet overall improvement rates were identical (66% vs. 70%). Objective rating data revealed that severe Parkinsonian and/or akinetic patients complained less of their specific side effects or general drug-induced dysphoria than patients with moderate or lower objective scores.

Significance: This study replicates previous findings demonstrating neuroleptic dysphoria as a predictor of future noncompliance. However, there appears to be another subgroup of dysphoric patients who comply, receive lower doses, and do as well clinically as non-dysphorics. Conversely, severely akinetic patients are relatively unable to complain about disabling side effects. These data suggest that a subgroup of dysphoric patients clinically benefit from such a response.

**NR38
HISTORY OF EPS PREDICTS FUTURE EPISODES**

Tuesday, May 21, 12 Noon-2:00 p.m.

George A. Keepers, M.D., Psychiatry Service, VA Medical Center, Portland, OR 97207, Daniel E. Casey, M.D.

Summary:

Controversy surrounds prophylactic anti-EPS drug prescription for neuroleptic-induced EPS, in part because EPS occurrence in individual patients seems unpredictable. Various factors (age, sex, neuroleptic dose, and potency) affect the likelihood of EPS but do not reliably predict those patients who will have EPS and who should receive prophylaxis. Individual vulnerability to EPS has been assumed to explain this variation but the utility of past history for predicting future occurrence of EPS has not previously been studied.

We reviewed charts of all patients diagnosed with schizophrenia and medicated with neuroleptics at our hospital in 1979, finding 63 patients for whom records of multiple treatments were available. EPS, neuroleptic and anticholinergic drug doses were recorded for the first 21 days in each treatment episode. The average age of the sample was 29 years and 51% were female.

Neuroleptic treatment resulted in EPS in 55% of the cases. Occurrence or absence of EPS in earlier hospitalizations correctly predicted EPS in subsequent treatments in 84% of the cases. Variation in neuroleptic potency, neuroleptic dose, and anticholinergic dose between hospitalizations partially explained incorrect predictions. Additional analyses have shown the relative importance of prior history as a predictive factor in comparison to age, sex, neuroleptic potency, neuroleptic dose, and prophylaxis with anticholinergic drugs.

These results strongly support the concept of individual susceptibility as a major predictor of EPS and indicate who should receive anti-EPS prophylaxis: patients with a history of EPS.

**NR39
SELF-LIMITED NEUROLEPTIC MALIGNANT SYNDROME WITH CONTINUED USE OF NEUROLEPTIC**

Tuesday, May 21, 12 Noon-2:00 p.m.

Gerard Addonizio, M.D., The New York Hospital-Cornell Medical Center, 21 Bloomingdale Road, White Plains, NY 10605, Virginia Susman, M.D., Steven D. Roth, M.D.

Summary:

Increasing recognition of Neuroleptic Malignant Syndrome (NMS) suggests it may be much more common than previously realized. Our experience indicates that a milder, self-limited form of NMS exists. This study, a retrospective chart review of 82 consecutive patients, assesses the spectrum and incidence of NMS. Inclusion criteria were: males on neuroleptics, age 16-35, DSM-III diagnoses of schizophrenia, bipolar disorder, schizoaffective disorder, brief reactive psychosis and atypical psychosis. Patients were evaluated for episodes of elevated temperature, extrapyramidal symptoms, tachycardia, elevated blood pressure, disphoresis, incontinence, leukocytosis, confusion, and elevated CPK. To diagnose NMS, five of these items, including EPS and elevated temperature, must have occurred within a 48 hour period with no other medical illness accounting for symptoms. Two patients (2.4%), the only two with a previous history of NMS, had NMS diagnosed this admission and neuroleptic stopped. One immediately improved and one continued to have symptoms. In addition, eight patients (9.8%) fulfilled our criteria but had cessation of symptoms without stopping neuroleptic. Temperatures in these patients ranged from 99° to 101.8°F with three patients $\geq 100.0^\circ$. Of 82 patients, 30% had affective diagnoses and 20% were treated with lithium. By contrast, of these eight patients 63% had affective diagnoses and 50% were treated with lithium. This data describes a milder, self-limited form of NMS, sometimes without marked temperature elevation, which terminates without cessation of neuroleptic. Also, affective diagnoses and lithium may be risk factors. In addition, this data supports the suspicion that the incidence of NMS is greater than the frequently reported 0.5%-1.0%. We are conducting a prospective study which should help clarify whether this self-limited form of NMS is itself a risk factor for development of the full blown syndrome.

**NR40
TARDIVE DYSKINESIA: A FIVE-YEAR FOLLOW-UP**

Tuesday, May 21, 12 Noon-2:00 p.m.

H.A. Grossman, M.D., St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, Canada, M5B 1W8, X. Fornazzari, M.D., J. Thornton, M.D., M. Seeman, M.D.

Summary:

This is a five year follow-up study of twenty-two out patients with Tardive Dyskinesia all of whom were on continuing long term neuroleptic treatment. We employed a standardized videotaped examination and used the Smith Scale for T.D. as well as the Abnormal Involuntary Movement Scale. Our data tended to demonstrate three main results. First, using the Smith Scale, a majority (68%) improved. Secondly, our male patients tended to show the most deterioration while the females young and old all improved. Lastly, there was no apparent correlation between score changes and the average dose over five years through the current dose tended to be less than the average dose in those that improved in T.D. ratings.

**NR41
ACUTE TREATMENT OF SCHIZOPHRENIA WITH CLOZAPINE**

Tuesday, May 21, 12 Noon-2:00 p.m.

Jeffrey A. Lieberman, M.D., Long Island Jewish-Hillside Medical Center, Hillside Division, P.O. Box 38, Glen Oaks, NY 11004, Thomas B. Cooper, M.A., John M. Kane, M.D., William Florio, M.D., Ronald Brenner, M.D., Jacque Vital-Herne, M.D., Celeste Johns, M.D.

Summary:

Though neuroleptic drugs have proven antipsychotic efficacy there are many patients who are unresponsive to treatment or suffer debilitating side effects from their use.

Preclinical and clinical studies have shown clozapine to be a novel neuroleptic compound. Its putative clinical atypicality stems from reports that it has antipsychotic efficacy in patients who are treatment resistant to adequate conventional neuroleptic treatment; that it has therapeutic efficacy and is tolerated by patients who are intolerant—due to acute side effects—to therapeutic doses of conventional neuroleptics; and that it may not have the side effect liability of tardive dyskinesia as do conventional neuroleptics.

We have studied 21 patients with chronic schizophrenia (ages 19-39, mean 28.4 16 male 5 female) who have met criteria for being neuroleptic refractory or intolerant in an open 6 week treatment trial of clozapine at controlled doses (500-900 mg/d). Eighteen patients also had clinically significant definite persistent TD. Clinical status (behavioral and neurologic) and blood levels of homovanillic acid (HVA) prolactin, growth hormone and neuroleptic levels were evaluated following a drug free interval at baseline prior to and weekly after initiation of clozapine treatment. The results of this trial will be presented and discussed.

**NR42
TREATMENT OF TARDIVE DYSKINESIA WITH BROMCRIPTINE**

Tuesday, May 21, 12 Noon-2:00 p.m.

Jeffrey Lieberman, M.D., Long Island Jewish-Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004, John Kane, M.D., William Florio, M.D., Sukdeb Mukherjee, M.D.

Summary:

Tardive dyskinesia (TD) occurs in approximately 20% of patients chronically exposed to neuroleptic drugs. At present there is no treatment with consistently demonstrated efficacy. Dopamine supersensitivity at specific neuroanatomical locations secondary to neuroleptic treatment has been implicated in the pathogenesis of TD. Based on this etiologic hypothesis a receptor modification strategy for treatment has been proposed utilizing dopamine agonist drugs. To test the efficacy of dopamine agonist receptor modification treatment, we studied 11 patients with clinically significant TD. After a 4-12 week drug free interval patients were randomly assigned to 10 weeks of treatment with bromocriptine or placebo and thioridazine 100mg/d under double blind conditions. Dose was titrated for the first 6 weeks to a target dose between 40 and 60mg/d where it was held constant for 4 weeks. After 10 weeks of treatment meds were stopped and patients followed for 8 weeks. At baseline and throughout the 18 week period patients were evaluated clinically (behavioral and neurologic status) and with blood samples for drug level and endocrine hormones. Results of this study will be presented and discussed.

**NR43
DRUG HOLIDAYS AND TARDIVE DYSKINESIA**

Tuesday, May 21, 12 Noon-2:00 p.m.

Bruce I. Diamond, Ph.D., VA Medical Center, Psychiatry Service, 116A-D, Augusta, Georgia 30910, Chandresh Shah, M.D., Ana Hitri, Ph.D., Richard L. Borison, M.D.

Summary:

It is controversial whether drug holidays decrease the risk for tardive dyskinesia. We tested the effect of continuous versus intermittent treatment in male Sprague-Dawley rats with daily haloperidol (1.0 mg/kg). The continuous group received the drug over eight weeks while the intermittent group had two one week holidays over the same period. Dopamine receptor hypersensitivity was tested behaviorally with apomorphine and biochemically by receptor binding studies. The continuous treatment resulted in a 52% increase in dopamine D₂ receptors whereas the intermittent treatment resulted in a 22% increase over controls. The behavioral data paralleled the biochemical findings indicating that drug holidays may lessen the risk of developing tardive dyskinesia.

**NR44
TARGET WEIGHT PROGRAM PREVENTS WATER INTOXICATION**

Tuesday, May 21, 12 Noon-2:00 p.m.

Morris B. Goldman, M.D., Dept. of Psychiatry (Box 411), Univ. of Chicago Medical Center, 5841 S. Maryland, Chicago, IL 60637, Daniel J. Luchins, M.D.

Summary:

The electrolyte imbalance associated with water intoxication (WI) can be life threatening and frequently leads to medical hospitalizations in 3 to 7% of chronically hospitalized psychotics. We've developed a simple and effective program for preventing WI. Baseline body weights and simultaneous serum sodium concentrations are used to predict the weight at which a patient is likely to become dangerously hyponatremic (range 3.5 - 5 Kg above the mean baseline weight). The patient is then weighed three times weekly. If the weight exceeds the predetermined value, a stat sodium is obtained. If this value is below the dangerous level, intake is limited by isolating the patient for 24 hours.

We've instituted the program with 11 male chronic schizophrenics with a history of recent WI. For the five months prior to, and since starting, the program patients were taking stable doses of neuroleptics; and were on no other medications and had no medical conditions known to effect water intake or excretion. The linear relationship between percent change in body weight (%CBW) and the percent change in serum sodium concentration (%CSS) was assessed by obtaining simultaneous weights and sodiums every two weeks. We found the %CSS = (-.82)%CBW (n = 128, r = .71, p < (.001). In the five months prior to the program, there were nine episodes of WI requiring transfer to a medical facility (2 seizures, 2 protracted vomiting, 5 stupor or coma). In the five subsequent months, there have been no episodes of WI. The theoretical basis of the program, as well as its practical implementation will be discussed.

**NR45
BODY WEIGHT REGULATION IN SCHIZOPHRENIA**

Tuesday, May 21, 12 Noon-2:00 p.m.

William B. Lawson, M.D., Metropolitan State Hospital, 11400 S. Norwalk Blvd., Norwalk, CA 90650, Charles A. Kaufmann, M.D., Craig Karson, M.D., Daniel R. Weinberger, M.D., Markku Linnoila, M.D.

Summary:

Schizophrenic patients become anorectic and psychotic when drug free, and gain weight while recovering with neuroleptics. Various biological parameters including drug free cerebral spinal fluid (CSF) metabolites and computer tomography (CT) were determined in 35 chronic schizophrenic patients undergoing a 6-week drug free period followed by a .4mg/kg haloperidol treatment. Weight changes correlated positively with caloric intake, but not measures of fluid shifts. Weight loss consistently occurred in the drug free period and was negatively correlated with subsequent neuroleptic response. Weight gain was positively correlated with neuroleptic response. Drug free patients with normal CT were significantly more likely to be underweight. All weight changes were attenuated in patients with enlarged ventricles on CT. CSF 5HIAA was significantly lower in underweight patients. HVA and DOPAC showed significant negative correlations with neuroleptic related weight gain. Recent attempts to subtype schizophrenia with CT and the role of central dopamine in eating disturbances and psychosis will be discussed.

NR46**Tuesday, May 21, 12 Noon-2:00 p.m.****MALIGNANT HYPERTHERMIA SUSCEPTIBILITY IN NEUROLEPTIC MALIGNANT SYNDROME**

Stanley N. Caroff, M.D., V.A. Medical Center (116A), University of Pennsylvania, University Ave., Phila., PA 19104, Henry Rosenberg, M.D., Jeffrey Fletcher, Ph.D., Merrill Hilf, B.A., Terry D. Heiman-Patterson, M.D.

Summary:

In order to investigate whether similarities exist in the mechanisms underlying the neuroleptic malignant syndrome (NMS) and anesthetic-induced malignant hyperthermia (MH), we compared the in-vitro contracture responses of skeletal muscle obtained from patients with NMS (N = 5) or MH (N = 5) susceptibility and from controls (N = 12). Muscle strips weighing 25-230 mg were dissected free from biopsy specimens of the quadriceps or vastus lateralis, mounted in a tissue bath containing Krebs Ringer's solution at 37°C, and bubbled with 95% O₂-5% CO₂. All strips were electrically stimulated at 0.2 hz. In each subject group, we measured the contracture tension response of separate strips exposed to halothane (1-3%), or incremental doses of caffeine (0.125-16mM) or fluphenazine (0.2-25.6mM). Four of the 5 NMS patients were judged to be MH-susceptible based on a contracture response greater than 0.5 g following halothane administration. There were no significant difference in the responses to caffeine or fluphenazine between NMS, MH and control groups. These findings indicate that the standard halothane-contracture screening test for MH-susceptibility is positive in some NMS patients. This supports an association between MH and the NMS and implies that some NMS patients may be at risk for MH during anesthesia. In addition, the pathophysiology underlying the NMS may involve a peripheral skeletal muscle component. Finally, the halothane-contracture test may prove useful in confirming the diagnosis of the NMS in questionable cases.

NR47**Tuesday, May 21, 12 Noon-2:00 p.m.****METHADONE IN TREATMENT RESISTANT SCHIZOPHRENIA**

David A. Brizer, M.D., 24 West 70th Street, New York, N.Y. 10023, Neil Hartman, M.D., John Sweeney, Ph.D., Robert B. Millman, M.D.

Summary:

Case reports of patients who self-medicate with opiates, observations in methadone programs, and clinical and neuroendocrine studies suggest that methadone may exert an antipsychotic effect. To test this hypothesis, seven inpatients with chronic paranoid schizophrenia (RDC criteria) received either methadone (maximum daily dose, 40 mg) or placebo plus a fixed dose of neuroleptic for up to three weeks in a double-blind single crossover study. Mean baseline BPRS score was 69.3 ± 6.7 despite continuous neuroleptic treatment (mean daily dose, 2600 chlorpromazine equivalents per day) during the previous two months.

Patients were rated weekly on BPRS and CGI scales by two psychiatrists; patients who were 'much improved' or 'very much improved' on CGI and who showed greater than 33% reduction of baseline BPRS score while receiving methadone could remain on methadone as outpatients. Other patients would have their methadone dose tapered over one week.

Percent change in patients' global BPRS score after three weeks (N = 6) or 9 days (N = 1) on methadone plus neuroleptic was significantly greater than that seen after three weeks on placebo plus neuroleptic ($p < .01$). Global BPRS was significantly reduced after 9 days or three weeks on methadone compared to baseline rating ($p < .005$). One patient was discharged to outpatient care on methadone, and six patients were withdrawn from methadone without difficulty. Methadone may be a useful adjunct in some patients with treatment-resistant chronic paranoid schizophrenia.

NR48
CARBAMAZEPINE LOWERS PLASMA HALOPERIDOL LEVELS

Tuesday, May 21, 12 Noon-2:00 p.m.

George W. Arana, M.D., Boston VA Medical Center, Department of Psychiatry (116A), 150 South Huntington Avenue, Boston, MA 02130, Donald Goff, M.D., Hylar Friedman, M.D., Marjorie Ornstein, B.A., Bruce Black, M.D., Leslie Hocking, M.D., David J. Greenblatt, M.D., Richard I. Shader, M.D.

Summary:

Recent findings suggest that carbamazepine (CBZ) may be used in combination with haloperidol (HAL) for the treatment of agitated psychotic disorders. Because CBZ is known to induce hepatic microsomal enzymes affecting the metabolism of certain drugs, we assessed the plasma levels of HAL in seven psychotic patients treated with both HAL and CBZ.

HAL levels were measured using gas liquid chromatography yielding a sensitivity of 1.0 ng/ml. HAL daily doses ranged from 10-40 mg with a mean of 19.2 mg; CBZ daily doses ranged from 400-1000 mg with a mean plasma level of 8.6 ug/ml.

Mean HAL plasma levels was reduced by more than 50% (range: 18% to 100%) compared to the pre-CBZ levels, yielding statistical significance at the $p < .01$ level. Monitoring HAL levels may be necessary among patients who receive concurrent treatment with CBZ.

NR49
CHRONOPHARMACOLOGY OF HALOPERIDOL TREATMENT

Tuesday, May 21, 12 Noon-2:00 p.m.

R. Swami Nathan, M.D., Assistant Professor of Psychiatry, Western Psychiatric Institute, 3811 O'Hara Street, Univ. of Pgh., Pittsburgh, PA 15213, James M. Perel, Ph.D., Richard Stiller, Ph.D., Jeffrey L. Peters, M.D., Theresa McCarthy, R.N., Suzanne Curran, M.S.

Summary:

There is some evidence that the therapeutic effects of haloperidol (HAL) may be related to the plasma HAL levels. One of the factors that would influence the blood drug level is the time of drug administration. As part of a larger ongoing study, we investigated the effect of time of HAL administration in seven medically healthy schizophrenic patients on their plasma HAL levels. Three of them received 10 mg of HAL once a day at 0900 hours for eight days and four patients received the same oral dose, once a day at 1800 hours for eight days. Blood samples were collected on days 4 and 8 prior to giving medication to determine the HAL steady-state levels. After receiving their last dose on day 8, all patients were maintained drug-free for 72 hours during which time seven blood samples were collected. The mean steady-state HAL levels measured on days 4 and 8 were 5.7 ± 1.4 ng/ml for the patients receiving HAL in the morning (morning group) and 10.5 ± 4.5 ng/ml for those receiving it in the evening (evening group). Plasma HAL levels during the 72 hours after the last dose of HAL on day 8 were plotted to determine the area under the HAL curve. The evening group achieved 69% higher plasma HAL levels ($AUC 623 \pm 321$) compared to the morning group ($AUC 369 \pm 77$). Half life ($t_{1/2}$) of HAL was 18.2 ± 1.9 for the morning group and 21.5 ± 5.6 for the evening group. The observed peak HAL plasma levels were also higher for the evening group (21.5) compared to the morning group (19.5). Our preliminary data suggest that evening time of HAL administration may result in higher plasma HAL concentration with longer half-life. If this trend is confirmed in a larger sample, the clinical implications of our findings are that the manipulation of time on HAL administration may be utilized to enhance the therapeutic advantage in some schizophrenic patients by increasing the HAL bioavailability.

NR50**Tuesday, May 21, 12 Noon-2:00 p.m.****THIOTHIXENE DOSE STUDY: TX-RESISTANT SCHIZOPHRENIA**

Chuong C. Huang, M.D., Medical College of Wisconsin, 9191 Watertown Plank Road, Milwaukee, WI 53226, Richard P. Gerhardstein, M.D., David Y. Kim, M.D., Leo Hollister, M.D.

Summary:

This is a double blind study designed to evaluate the differential response of acutely decompensated treatment-resistant hospitalized schizophrenic patients to two regimens of thiothixene (60 mg qd vs >60 mg qd dose). Fifty schizophrenic inpatients by DSM-III criteria from Milwaukee County Mental Health Complex were chosen for the study. They were mentally ill for 2 years or more and were treatment-resistant by drug history and did not have major medical or other psychiatric illness. After one week of washout period all patients entered 2 week single blind phase of study when the thiothixene was increased from 15 mg qd to 60 mg qd. Then they were randomly assigned to two different groups, A & B. The group A patient received 60 mg qd thiothixene up to 11th week. The group B patient received increasing dose of thiothixene up to 400 mg qd. The plasma concentrations of thiothixene were measured weekly. The Roerig Global, Brief Psychiatric Rating Scale and Nurses Observational Scale for Inpatient Evaluation were used to evaluate the patients' symptoms weekly. No severe side effect was found. The common side effects were dystonia, blurred vision, dry mouth and drowsiness which usually occurred in the first 6 weeks of the study. Analysis of efficacy revealed that there is statistically significant difference between the high and low dose antipsychotic effects in resistant patients. The plasma assay data in general correlate with the dosage of thiothixene that were given to the patients. The clinical implications from this study will be discussed.

NR51**Tuesday, May 21, 12 Noon-2:00 p.m.****POSITIVE/NEGATIVE SYMPTOMS IN INTERICTAL PSYCHOSIS**

C. Edward Coffey, M.D., P.O. Box 3920, Duke Medical Center, Durham, NC 27710, James J. McGough, B.A., Elizabeth Sumner, B.A., Susan Pelton

Summary:

Positive and negative symptoms have been useful in differentiating subtypes and schizophrenia, but have not been applied to the study of interictal psychosis in temporal lobe epilepsy (TLE). We reviewed published reports of interictal psychosis in patients with TLE and identified 83 cases with sufficient data for further analysis. Symptoms reported were categorized as positive or negative, and grouped by laterality of epileptogenic focus. Positive symptoms dominated the clinical picture, with delusions and hallucinations occurring in 87% and 67% respectively. Catatonic and bizarre behavior were relatively infrequent. Affective flattening was the only negative symptom reported and occurred in 31% of cases. There was no correlation between type of symptom and laterality of lesion. These data suggest that the "schizophrenic-like" psychosis of interictal TLE is more appropriately termed a "paranoid-hallucinatory syndrome." These findings may have implications for understanding the pathophysiology of interictal psychosis in TLE.

NR52
A DOMINANT GENE FOR ALZHEIMER'S DISEASE

Tuesday, May 21, 12 Noon-2:00 p.m.

Richard C. Mohs, Ph.D., Psychiatry Service - 116A, VA Medical Center, 130 W. Kingsbridge Road, Bronx, NY 10468, Jeremy A. Silverman, M.A., John C.S. Breitner, M.D., Kenneth L. Davis, M.D.

Summary:

The age-specific familial risk of Alzheimer Dementia (AD) was determined among the first degree relatives of 27 clinically diagnosed AD probands and 21 age-matched controls. Occurrence of AD in relatives was assessed by the family history method using multiple informants to improve accuracy in reporting. Inter-informant agreement was high, both on particular AD symptoms in relatives ($Kappa = 0.83, p < .001$) and on age of onset ($r = 0.96, p < .001$). Twelve (9.8%) of 122 AD proband relatives aged 45+ had presumed AD, but only 21 (2.1%) of 95 control relatives were affected ($X^2 - 5.3, p < .03$). The 90 year lifetime incidence of presumed AD in proband relatives was 48%, a figure which deviates only insignificantly from the 50%+ expected in a dominant genetic illness. The age-dependent manifestation of AD among relatives was readily explained by a biomathematical model that assumed: 1) AD is transmitted by a single autosomal dominant gene; and 2) onset in genetically predisposed individuals is determined by the cumulative effect of a number of (environmental?) insults ("hits"), each of which has an exponentially distributed waiting time. The model accounted for over 99% of the variance in age-specific incidence and yielded estimates for the mean age of onset (80.1 yrs) and age of peak incidence (79.7 yrs.) consistent with other reported data on AD. These findings suggest that the available data on familial aggregation of AD are completely consistent with an autosomal dominant mode of genetic transmission.

NR53
SUBTYPES OF ALZHEIMER'S DISEASE

Tuesday, May 21, 12 Noon-2:00 p.m.

William Bondareff, M.D., USC School of Medicine, 2025 Zonal Avenue, Hoffman 101, Los Angeles, CA 90033, Christopher Q. Mountjoy, M.B.

Summary:

DSM-III recognizes two types of *Primary Degenerative Dementia*; early and late onset. They are characterized by identical histopathology and often referred to collectively as Alzheimer's Disease (AD). Although early onset may define a more pernicious type of AD, recent findings suggest that subtypes can be more reliably differentiated by histopathological criteria.

Brains of histologically confirmed cases of AD were examined. Those with less than 5000 locus ceruleus (LC) neurons (AD-2) had less NE and ChAT and more plaques and tangles in cerebral cortex than those with more neurons (AD-1). An apparently severe form of neurofibrillary degeneration was found in AD-2. It was characterized by non-argyrophilic, loose tangles that were weakly metachromatic and indirectly correlated with the number of surviving neurons. A disproportionate reduction in the amount of cortical NE per surviving LC neuron suggested an especially severe degree of functional impairment. As AD-2 appears to occur more frequently, but not exclusively, in younger persons, the identification of AD subtypes by age in DSM-III is of questionable utility.

NR54
CARBOHYDRATE METABOLISM IN ALZHEIMER'S DISEASE

Tuesday, May 21, 12 Noon-2:00 p.m.

M. Fisman, M.D., London Psychiatric Hospital, P.O. Box 2532, Terminal A, London, Ontario, Canada N6A 4H1, Bruce Gordon, M.D., Thomas MacDonald, M.D., John Dupre, M.D., Edward Helmes, Ph.D.

Summary:

Investigators have observed reduced fasting blood sugar values and a reduced area under the glucose tolerance curve in Alzheimer's Disease (AD) patients compared to controls; they have also suggested that the clinical coincidence of AD and diabetes mellitus is unusual. We report the results of a study to further evaluate this "hypoglycemic" phenomenon in AD.

Nine patients meeting inclusion and exclusion criteria for the diagnosis of AD with normal to low normal fasting and postprandial blood sugars and nine age and sex matched controls were involved in this study. Subjects received a 200 g carbohydrate diet for three days preceding a 24 hour fast. Venous blood was taken one hour after supper on day 1 and three hourly intervals on day 2 for measurement of glucose, beta-hydroxybutyrate, acetoacetate, lactate, pyruvate, insulin and glucagon. Multivariate analysis showed patients with AD to have significantly elevated glucose ($p < .05$) and a trend to elevation of acetoacetate ($p < .07$), compared to controls at 21 and 24 hours after starting the fast; serum insulin levels were significantly lower 24 hours after starting the fast in AD and patients compared to controls ($p < .004$). No significant differences between AD and controls were noted for any of the other compounds measured.

The present findings conflict with those reported in the literature and possible causes for these differences will be discussed, as well as possible implications in relation to other metabolic changes found in AD.

NR55
HEPATIC POLYPLOIDY IN ALZHEIMER'S DISEASE

Tuesday, May 21, 12 Noon-2:00 p.m.

M. Fisman, M.D., London Psychiatric Hospital, P.O. Box 2532 Terminal A, London, Ontario, Canada N6A 4H1, Hildegard Enesco, Ph.D., Marie Laskey, M.Sc.

Summary:

Several authors have suggested multiorgan involvement in Alzheimer's Disease (AD), including possible hepatic dysfunction. As an increase in hepatic polyploidy as a function of age has been widely reported in mammals, including man, an investigation of hepatic polyploidy in AD was undertaken.

We compared the liver ploidy in 19 subjects with clinically and neuropathologically identified AD with the findings in 18 age and sex matched autopsy controls without evidence of AD at autopsy.

Ten micron liver sections, stained with haematoxylin and eosin, were number coded. Nuclear diameters of randomly selected parenchymal nuclei were measured by ML, who was blind to the diagnoses. These measurements were then evaluated to determine whether the nuclei formed the regular groupings characterizing a polyploid series. Chi square contingency test showed a significant difference between the two groups ($X^2 = 12.49$, 2 d.f., $p < .005$). The AD group appears to differ from the control group in having a greater than expected 4N class and a smaller than expected 2N class. Since increased polyploidy is age associated, these findings suggest that the AD patients may be biologically older than their nondemented peers.

These findings should be interpreted in terms of possible nutritional and hormonal influences on hepatic polyploidy; and are discussed in the context of the increased lymphocytic aneuploidy reported in AD, the increased polyploidy reported in Werners syndrome and the concept of increased aging associated changes outside the brain in patients with AD.

NR56
CORTICAL ATROPHY AND PLATELET MAO IN DEMENTIA

Tuesday, May 21, 12 Noon-2:00 p.m.

Robert C. Young, M.D., Division of Geriatric Services, The New York Hospital-Cornell Medical Center, Westchester Division, 21 Bloomingdale Rd., White Plains, NY 10605, George S. Alexopoulos, M.D., Kenneth W. Lieberman, Ph.D., Charles A. Shamoian, M.D., Robert Roe, M.D., Michael Deck, M.D.

Summary:

Atrophic changes on computerized tomographic (CT) scan of brain and increased platelet monoamine oxidase (MAO) activity have both been described in patients with primary degenerative dementia compared to same age controls. However, neither of these is found in all cases. Therefore CT scan findings were compared with platelet MAO activity in 35 psychiatric inpatients who met DSM III criteria for primary degenerative dementia. Platelet MAO activity (nmoles/mg protein/hr) was determined using benzylamine as substrate. Platelet MAO activity was higher in patients with at least moderate rated widening of cortical sulci (mean \pm S.D.: 77.3 ± 21.1 ; $n = 18$) than in those with no or minimal abnormality (62.8 ± 20.6 ; $n = 17$; $t = 2.056$, $df = 33$, $p < .05$). It also tended to be higher in those with at least moderate rated increase in size of the lateral ventricles (76.8 ± 20.8 ; $n = 17$) than in those with no or minimal abnormality (64.1 ± 21.5 ; $n = 18$; $t = 1.782$, $df = 33$, $p < .10$). There was no such relationship between platelet MAO activity and size of the third ventricle. These preliminary data suggest an association between cortical atrophy and platelet MAO activity in degenerative dementia.

NR57
VBR COGNITIVE AND NEUROLOGICAL DEFICITS IN MULTIPLE SCLEROSIS

Tuesday, May 21, 12 Noon-2:00 p.m.

Godfrey D. Pearlson, M.D., 600 N. Wolfe Street, Johns Hopkins Hospital, Meyer 279, Baltimore, Maryland 21205, Won S. Kim, M.D., Peter V. Rabins, M.D., John R. Lipsey, M.D., Paul J. Moberg, M.A., Benjamin Brooks, M.D.

Summary:

38 patients from an outpatient Multiple Sclerosis clinic who were subjects in a longitudinal study, were referred for cranial CT scans during a 2 year period. MS patients were compared to 36 age and sex group-matched screened normal volunteer controls. Planimetric VBR was blindly assessed on all CT scans. The mean MS VBR was significantly larger (p 2-tailed $< .001$) than that of controls. 50% of MS patients had VBR values ≥ 2 SC's above the control mean; they were significantly more likely to have the progressive, as opposed to the relapsing/remitting form of MS. In MS patients, VBR correlated significantly with cognitive impairment on the Mini-Mental Status (MMSE), $r = -.45$, and disability (.43), and neurological impairment (.48), on the Kurtzke Scales, all $< .01$. Canonical discriminant function analysis using MMS and neurological dysfunction scores, correctly classified the presence of ventricular enlargement (as defined above) in 77% of cases.

NR58
CEREBRAL VBR'S AND ACETYLCHOLINESTERASE ACTIVITY IN SENILE DEMENTIA

Tuesday, May 21, 12 Noon-2:00 p.m.

Larry E. Tune, M.D., Johns Hopkins University, Sch. of Medicine, 600 N. Wolfe St., Osler 320, Baltimore, MD 21205, G. Pearlson, M.D.

Summary:

In 16 patients with the diagnosis of senile dementia of the Alzheimer's type (SDAT), computerized tomography scans were rated blind to clinical and laboratory data, and lateral ventricular-to-brain ratios (VBR) were calculated. Cerebrospinal fluid (CSF) acetylcholinesterase (AChE) activity was measured by radioenzymatic assays in all patients. The degree of dementia was quantified using the Mini-Mental Status Examination of Folstein, et al. Significant correlations were found between cerebral atrophy as assessed by the VBR's and CSF AChE activity (Pearson's $r = -0.59$, $p < .01$). Cognitive impairment as quantified by the MMSE score also correlated significantly with VBR ($r = -0.46$, $p < .05$). These correlations were not accounted for by the age or duration of illness. This relationship between VBR and AChE activity demonstrates an association between two independently determined clinical measures in senile dementia of the Alzheimer's type.

NR59
PSYCHIATRIC SYMPTOMS IN DEMENTIA SYNDROMES

Tuesday, May 21, 12 Noon-2:00 p.m.

Larry E. Tune, M.D., Johns Hopkins University, Sch. of Medicine, 600 N. Wolfe St., Osler 320, Baltimore, MD 21205, C. Steele, R.N., M.J. Lucas, R.N.

Summary:

Significant differences were found in the prevalence of psychiatric symptoms in systematically diagnosed (DSM-III) patients with primary degenerative dementia (PDD) and multi-infarct dementia (MID). MID patients had more symptoms (95%) than PDD cases (77%). Symptom profiles for males and females with PDD differed markedly with males having more hallucinations and delusions than females. In a pilot study comparing thioridazine and haloperidol in control of target psychiatric symptoms in the above population, both proved effective. However, patients treated with haloperidol exhibited prominent extrapyramidal side effects at low doses: 1, 2 mg prior to control of symptoms. Thus, while roughly equally effective in controlling behavioral symptoms, therapeutic doses of thioridazine resulted in fewer side effects. These unique studies address important management issues and have implications for increased knowledge about sub-types of dementia.

NR60
CAN ECT CURE PARKINSON'S DISEASE?

Tuesday, May 21, 12 Noon-2:00 p.m.

David E. Raskin, M.D., Department of Psychiatry, Wilmington Medical Center, P.O. Box 1668, Wilmington, DE 19899

Summary:

Many studies have indicated that electroconvulsive therapy will successfully ameliorate the symptoms of Parkinson's disease. A patient with idiopathic Parkinsonism was seen because of the presence of a concurrent major depressive episode with melancholia. The patient was successfully treated with electroconvulsive therapy. A relapse of Parkinson's disease and depressive disorder occurred 2½ months later. Another course of ECT was successful in terminating both the Parkinson's disease and the depressive episode. In March, 1984, and June, July, 1984, two courses of ECT were necessary. It was decided that after 4 periods of ECT with an average interval of symptom free behavior of 2 months, the patient would be a candidate for maintenance ECT. One treatment was administered every 2 weeks; the frequency was subsequently shifted to once a month. Although the patient's major depressive episode has resolved on maintenance ECT, he was continuing symptoms of dysthymic disorder. His Parkinsonism, however, has *completely resolved*. Objective ratings of Parkinson's disease are provided which demonstrate both the immediate effects of ECT on his Parkinson's disease, and the sustained 6 month remission in Parkinson's with the use of maintenance ECT. This research, although on an individual patient, nevertheless demonstrates the dramatic effect of ECT in some patients with Parkinson's disease and the capacity for maintenance ECT to prevent recurrences of Parkinson's disease. Research needs to be extended to larger groups of patients in order to identify Parkinson's subgroups who are candidates for this intervention.

NR61
REM SLEEP IN ALZHEIMER'S-TYPE DEMENTIA

Tuesday, May 21, 12 Noon-2:00 p.m.

Michael Serby, M.D. Psychiatry Svce., New York V.A. Medical Center, N.Y., NY 10010, John Adler, Ph.D.

Summary:

Rapid Eye Movement (REM) sleep is of theoretical interest in Alzheimer's type dementia (ATD) because of cholinergic mechanisms involved in the initiation and maintenance of the REM state. REM sleep has been shown to be sensitive to cholinergic manipulation (physostigmine and arecoline shorten and scopolamine prolongs REM latency). ATD is a disorder with a demonstrated central cholinergic deficit.

Significant changes for REM sleep measures have previously been reported in moderately to severely demented ATD patients. Decreased REM time and percents were found to correlate with the degree of cognitive impairment, and REM sleep differences discriminated ATD patients from normal controls and patients with major depressive disorder (MDD). Given the importance of REM sleep measures for MDD, these REM sleep findings in ATD were believed to be potentially meaningful for the differential diagnosis of ATD versus depression in the elderly.

Six moderately to severely demented non-depressed ATD in-patients were polysomnographically studied for nocturnal sleep measures at the New York Veterans Administration Medical Center. Subjects were recorded for 3-5 nights following adaptation using standard recording techniques.

Findings for total REM time, REM percent, and REM latency were markedly variable, both between and within subjects. Mean REM sleep amounts were substantially greater than in previous reports for this population, and for some subjects REM amounts were within the normal range.

Further investigation is required to evaluate the diagnostic utility of REM parameters in the elderly and the general significance of REM sleep in ATD.

NR62
ANTICHOLINERGIC DRUG EFFECTS ON MEMORY IN ELDERLY

Tuesday, May 21, 12 Noon-2:00 p.m.

Bharat R.S. Nakra, M.D., Asst. Professor Psychiatry, St. Louis University Hospital, 1221 S. Grand, St. Louis, MO 63104, Ron Margolis, Ph.D., George T. Grossberg, Lindbergh S. Sata, M.D.

Summary:

Elderly people are more susceptible to such side effects because of lower levels of acetylcholine in the aging brain. We report results of a study in which 20 healthy elderly subjects (age range 61-78) received 2 mg. of trihexyphenidyl or placebo in a double blind trial. Each subject served as his own control. 90 minutes after administration of the drug (or placebo), the Wechsler Memory Scale was administered. The results suggest that Trihexyphenidyl significantly impaired logical memory, visual reproduction and visual reproduction after 30 minute delay. Immediate memory and past memory were not impaired. This study highlights the adverse consequences of using anticholinergic drugs in the elderly. If a single, 2 mg. dose of Trihexyphenidyl can impair recall of new information what happens if and when these drugs are prescribed on a regular basis to the elderly.

NR63**Tuesday, May 21, 12 Noon-2:00 p.m.****TRH TEST IN DEMENTIA: ELDERLY DEPRESSED AND CONTROLS**

Trey Sunderland, M.D., Clin. Neuropharmacology Section, Laboratory of Clinical Sciences, National Inst. of Mental Health, Bethesda, Md. 20205, Pierre N. Tariot, M.D., Edward A. Mueller, M.D., Dennis L. Murphy, M.D., Paul Newhouse, M.D., Robert M. Cohen, M.D.

Summary:

Symptoms of depression have frequently been noted in patients with dementia of the Alzheimer type (DAT). Previous reports have revealed "positive" findings in a percentage of DAT patients with both the DST and REM latency tests. Results of TRH stimulation will be presented in Alzheimer patients, elderly depressed patients and elderly controls. 15 DAT patients (mean age: 63.4 years), 11 depressed patients (mean age: 59.1 years), and 10 elderly normal volunteers (mean age 61.3 years) were administered 500 μ g IV protirelin (TRH) after baseline thyroid and depression measures were obtained. Samples for RIA measurement of TSH were drawn at -15, 0, +15, +20, +30 and +45 minutes.

The DAT patients had peak Δ TSH responses which are significantly lower than normal controls ($9.1 \pm 1.2 \mu$ IU/ml SEM versus 14.7 ± 2.3 , $p < 0.05$) but not significantly different from depressed subjects (8.8 ± 1.3 , $p > 0.1$). The serial TSH levels in the DAT and depressed groups were significantly different from the control group but not from each other at +20, +30 and +45 minutes ($p < 0.05$). No significant differences were found between groups in baseline thyroid measures, and Hamilton depression ratings failed to show a significant correlation with Δ TSH in these subjects.

This study demonstrates new evidence that both DAT and elderly depressed patients have a blunted response to TRH stimulation which approximates that previously found in young depressed patients. This blunting is apparently not caused by aging alone and cannot be explained simply by baseline thyroid abnormalities or measurable levels of observable depression in either group.

NR64**Tuesday, May 21, 12 Noon-2:00 p.m.****HYDERGINE IN HIGH DOSES IN MILD DEMENTIA**

Ole J. Thienhaus, M.D., Dept. of Psychiatry, University of Cincinnati, Cincinnati, Ohio 45267-0559, Beverly Wheeler, M.D., Sandra Simon, O.T., Frank Zemlan, Ph.D., James T. Hartford, M.D.

Summary:

In a double blind study of 41 outpatients aged 55 to 80 with mild memory impairment, the efficacy of dihydroergotoxin mesylate (DEM, Hydergine^R)₂ at 6 mg p.o. per day was tested during a twelve week period. Specific etiologies for the amnesic syndrome were ruled out by history, physical examination and laboratory tests. Subjects with a Hamilton Depression Scale rating above 16, i.e. possible pseudodementia, were excluded. Physician rating of memory, employing the Inventory of Psychic and Somatic Complaints in the Elderly (IPSC-E), indicated marked clinical improvement of memory function in DEM-treated subjects (N=22) versus those on placebo (N=19), (F=3.34; df=1,39; $p < .04$). In contrast, structured testing of recent memory using Digit Symbol Substitution and Zahlenverbindungs Test (ZVT) showed improvement in both groups ($p < .001$) with no significant intergroup differences ($p < .10$). Our results indicate that in cases of mild though subjectively distressing impairment, DEM at higher dosages may help to enhance memory function.

NR65 **Tuesday, May 21, 12 Noon-2:00 p.m.**
DEPRESSION WITH REVERSIBLE DEMENTIA: PHENOMENOLOGY

George S. Alexopoulos, M.D., Cornell University Medical College, 21 Bloomingdale Road, White Plains, NY 10650, Robert C. Young, M.D., Charles A. Shamoian, M.D.

Summary:

A considerable percentage of geriatric depressed patients develop a dementia syndrome which subsides when symptoms of depression improve. While anecdotal reports suggest that depression with reversible dementia (DRD) has a distinct presentation, there have been no systematic studies. We studied 168 geriatric inpatients with unipolar major depression diagnosed by two psychiatrists using Research Diagnostic Criteria (RDC) and DSM III. Subjects who also met criteria for dementia were classified as DRD if their cognitive dysfunction improved (Δ Cognitive Capacity Screening Examination (CCSE) ≥ 3 and final CCSE > 23) after amelioration of depression (Δ Hamilton Depression Rating Scale (HRDS) ≥ 10 or final HDRS < 12). Subjects with depression and dementia who remained cognitively impaired (final CCSE < 24) even after improvement of depression (Δ HDRS ≥ 10 or final HDRS < 12) were considered to have a permanent organic mental syndrome, DRD (N=32) subjects had significantly more retardation, helplessness, hopelessness, depersonalization, and paranoid symptoms, and significantly less insight than cognitively unimpaired depressives (D)(N=77) who responded to antidepressant treatment. With the exception of helplessness, DD subjects (N=18) had similar HDRS item scores with D patients. Psychotic ($\chi^2_p = 9.32$ df=2, $P < 0.01$) and retarded RDC subtypes ($\chi^2_p = 8.71$ df=2, $P < 0.02$) were differently distributed in DRD, DD, and D subjects. DRD patients more frequently had a psychotic ($\chi^2_{dif} = 7.20$ df=2, $p < .05$) or a retarded depression ($\chi^2_{dif} = 8.58$, df=2, $P < 0.02$) than the DD and D group combined. There were no differences in the proportions of psychotic ($\chi^2_{group} = 2.12$) or retarded RDC subtypes ($\chi^2_{group} = 0.11$) among DD and D subjects. The remaining RDC subtypes, duration of current episode, course of illness, and family history were similar in DRD, DD, and D subjects. The data suggest that a certain constellation of depressive symptoms is associated with the development of transient cognitive dysfunction in geriatric patients.

NR66 **Tuesday, May 21, 12 Noon-2:00 p.m.**
DEXAMETHASONE SUPPRESSION IN DEMENTIA

Gerard A. Charles, M.D., Univ. TX Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235, A. John Rush, M.D.

Summary:

Sixty-four nondepressed, carefully selected senile demented inpatients underwent 1.0 mg. overnight dexamethasone suppression tests (DSTs) separated by 7 days. These patients were in a clinically stable and drug-free state for at least six months prior to testing. The Modified Ischemic Scale score and ICD-9 criteria for Alzheimer's disease were used to dichotomize subjects into Alzheimer's and multi-infarct types of dementia. Patients with vascular dementias were significantly more likely to evidence DST nonsuppression. Furthermore, DSTs in this group were less reproducible from week to week than DSTs in Alzheimer's patients.

These data indicate that: 1) the DST may be a useful laboratory adjunct to differentiate vascular and less severe parenchymatous dementias; 2) if pseudodementia is associated with a high frequency of DST nonsuppression, the DST may be of great clinical use in distinguishing early mild dementias from pseudodementias; and 3) diffuse, widespread neuronal degeneration is associated with a high, albeit inconsistent, degree of DST nonsuppression.

NR67**Tuesday, May 21, 12 Noon-2:00 p.m.****TRH TEST, DST, AND RESPONSE TO DESIPRAMINE IN DEMENTIA**

T.W. McAllister, M.D., Lexington VA Medical Center, 116A, Lexington, KY 40511, Lon Hays, M.D.

Summary:

Neuroendocrine testing to differentiate Alzheimer's disease (SDAT) and depressive illness is controversial. Spar (1982) and Raskind (1982) reported abnormal DSTs in patients with SDAT, Carnes (1983) the opposite. The possibility that some of the DST (+) SDAT patients have pseudodementia has not been tested, nor have other neuroendocrine tests been studied.

We report preliminary results from a prospective, blind study of the relationship between TRH Stimulation-Tests (TST), DST, and response to Desipramine (DMI) in patients with SDAT and Major Depressive Disorder (MDD).

Elderly patients, who met DSM-III criteria for SDAT or MDD, and were free of conditions which affect the neuroendocrine tests were included. Clinical status was evaluated before and after a four week trial of DMI using the Mini-Mental Status Exam (MMSE), the Hamilton Rating Scale (HRS), the Ward Function Inventory (WFI), and a modified Global Deterioration Scale (GDS). TSTs and DSTs were performed in standard fashion.

10 patients with SDAT and 8 patients with MDD have been studied. 50% of the SDAT patients, 17% of the MDD patients had blunted TSTs prior to treatment. 78% of the SDAT and 75% of the MDD had (+) DSTs prior to treatment. SDAT patients showed no response to DMI in terms of changes in GDS, WFI, HRS or MMSE scores. MDD patients showed an expected significant drop in HRS (24.7/9.4). These results suggest that the TST and DST are not useful predictors of response to DMI and SDAT, and confirm that these tests are probably not useful diagnostic aids in separating depressed and demented inpatients.

NR68**Tuesday, May 21, 12 Noon-2:00 p.m.****SPECIFICITY OF BENZODIAZEPINE DISRUPTION OF MEMORY**

Owen M. Wolkowitz, M.D., National Institute Mental Health, NIH Bldg 10, 4N214, 9000 Rockville Pike, Bethesda, MD 20205-1000, Herbert Weingartner, Ph.D., Daniel W. Hommer, M.D.

Summary:

Benzodiazepines produce anterograde memory-learning impairments that model "classic" amnesias, such as Korsakoff's disease. For example, diazepam disrupts aspects of attention and episodic memory (memory for recently acquired events) without altering access to previous learning in long-term memory. This model of memory failure is in sharp contrast to the memory disorder seen in patients with dementia of the Alzheimer's type, whose forgetting of recent events is directly linked to loss of previously acquired information in long-term memory. Anticholinergic drugs model this cognitive failure.

The neuropharmacological findings that support this analysis of the psychobiology of cognitive failures are as follows: 10 normal volunteers were administered increasing doses of intravenous diazepam (8.8 μ g/kg, 35 μ g/kg, 140 μ g/kg cumulative doses) and were tested following each dose. The test used had been previously standardized. Reliable decrements were observed in attention and in several measures of episodic memory. However, subjects were totally unimpaired in their effectiveness in remembering previously acquired knowledge. Scopolamine disrupts all of these cognitive functions. Specifically, the deficits in episodic memory are all reliably linked to impairments in accessing knowledge memory.

These findings provide a framework for defining specific psychobiological determinants of types of cognitive failure.

NR69
ANTEROGRADE AMNESIA WITH ORAL LORAZEPAM

Tuesday, May 21, 12 Noon-2:00 p.m.

Daljit S. Mac, M.D., Univ. of Kansas Medical Center, 39th & Rainbow Blvd., Kansas City, KS 66103, Rajiv Kumar, M.D., Donald W. Goodwin, M.D.

Summary:

Some benzodiazepines have been reported to produce anterograde amnesia. Twelve healthy volunteers were enrolled in this double blind, placebo controlled study to evaluate the amnestic effects of orally administered lorazepam. Subjects were randomly assigned to receive either placebo (N=6) or 2 mg of lorazepam (N=6). A standard 16-word list was used to assess immediate and delayed recall. Each list consisted of a particular category, e.g. places, which served as a retrieval cue for delayed recall. At the end of the word list subjects were instructed to recall in any order as many words as they could remember from the list, in a period of 45 seconds. The mean percent of the words recalled at each testing time was compared for both groups. The two groups did not differ when tested for immediate recall at any of the testing times. The groups were also compared for delayed recall. Subjects on lorazepam recalled fewer words when compared to the placebo group, $t(9)=3.36, p<.01$. The results show that lorazepam has a deleterious effect on short term recall of verbal material. This has implications for students and others preparing for tests or doing mental work, while taking therapeutic doses of lorazepam.

NR70
PARENTS OF A DOWN'S SYNDROME CHILD

Tuesday, May 21, 12 Noon-2:00 p.m.

S. Brandon, M.D., Dept. of Psychiatry, Clinical Sciences, Leicester Royal Infirmary, Leicester, England, Mary Newell

Summary:

Of 36 Down's children born in a defined community 4 were rejected by parents and 7 families refused to cooperate. 1 mother was aged over 40 years, seven aged over 35 years. 40% of parents were opposed to prenatal diagnosis or abortion on principle, confirming that amniocentesis does not reach the majority at risk and a substantial minority refuse termination. Most parents wished to be fully informed partners in all matters concerning the management of their child but 56% (cf. 59% Gallup Poll) believe that severely mentally or physically handicapped children should be allowed to die and 26% (cf. 32% Gallup) insisted that all possible measures should be invoked to keep their child alive. Only 44% of parents were unchanged in health. 28% of mothers reported significant psychiatric morbidity, 16% experienced severe somatic symptoms. 12% of fathers reported significant psychiatric morbidity. The attitudes of parents and involved professionals over a 10 year period are reviewed and the needs and wishes of parents are considered in light of this and other data.

**NR71
CLINICAL EFFICACY OF ALPRAZOLAM IN PTSD PATIENTS**

Tuesday, May 21, 1985, 2:00 p.m.

Frederick J. Dunner, M.D., Psychiatry Service 116A, VA Medical Center, Iowa City, IA 52240, Warren P. Edwards, Ph.D., Paul C. Copeland, D.O.

Summary:

This research project is an open label 8 week study to evaluate the clinical efficacy of alprazolam (Xanax) in the treatment of subjects with Post-Traumatic Stress Disorder (PTSD). Consenting outpatient male Vietnam veterans with a DSM-III diagnosis of PTSD were placed on an initial dosage of alprazolam 1.5 mg/day (with a maximum dose of 4.5 mg/day). Evaluations were made at weeks 0, 1, 3, 5 & 8 and these included subject self ratings (SCL-90 & patient CGI) and physician ratings (Hamilton Anxiety and Depression Rating Scales, sleep and side effect questionnaires and physician CGI).

Preliminary findings of 18 subjects (13 completers) will be discussed. Significant improvement in mean rating scale scores was seen comparing week 0 to weeks 1 and 3. This initial improvement was also maintained for the rest of the study period through week 8. Additional findings will be discussed during the presentation.

**NR72
PANIC: PREVALENCE RISK FACTORS AND TREATMENT RATES**

Tuesday, May 21, 1985, 2:00 p.m.

Jeffrey H. Boyd, M.D., Room 18-105, 5600 Fishers Lane, Rockville, MD 20857

Summary:

Four studies of panic disorder were undertaken, as part of the Epidemiologic Catchment Area (ECA) program, with a total sample size of 15,440 community residents. DIS panic disorder has a one month prevalence between 0.4% and 0.7%. There is a unimodal normally distributed age of onset, with a mode of 15 to 19 years, and a mean of 24 years. Prevalence rates are higher among women age less than 65, people who are separated or divorced, and people with low socioeconomic status. More than half of the DIS panic is found in conjunction with another current DIS disorder, most notably, somatization disorder.

Panic disorder leads the list of psychiatric disorders for which people get mental health treatment. Panic disorder is treated at rates comparable to or exceeding treatment rates of somatization, schizophrenia, or major affective disorders. Co-existing panic is why many people with other psychiatric disorders seek treatment.

**NR73
THE NATURAL COURSE OF AGORAPHOBIA-PANIC DISORDERS**

Tuesday, May 21, 1985, 2:15 p.m.

Alan Breier, M.D., Yale University and Connecticut Mental Health Center, Ribicoff Res. Fac., 34 Park Street, New Haven, CT 06510, Dennis S. Charney, M.D.

Summary:

This study examined the development and longitudinal course of agoraphobia-panic disorder (AGR-PD) and the temperal occurrence of other lifetime psychiatric disorders. Sixty patients who met Research Diagnostic Criteria for agoraphobia (AGR), mixed phobia, or panic disorder (PD), were interviewed using a modified version of the SADS-L and a semistructured interview developed by the authors. The occurrence of disorders occurring prior to the onset of AGR-PD were: major depression (MD) 30%, generalized anxiety disorder (GAD) 30%, alcoholism 13%, and obsessive compulsive disorder (OCD) 5%. Patients with episodes occurring after the onset of AGR-PD were: PD 95%, anticipatory anxiety 90%, AGR 90%, GAD 57%, MD 40%, OCD 12%, social phobia 5%, alcoholism 4%. AGR, anticipatory anxiety, and PD were without remission in 88%, 85%, and 70% of patients, respectively. Only 38% and 5% of patients had unremitting courses of GAD and MD, respectively. The first panic attack (PA) occurred spontaneously in 78% of the patients. The number of spontaneous type PAs decreased over the course of AGR-PD. 75% of the sample had predominantly spontaneous type PAs throughout the first year but, of the 28 patients with a duration of AGR-PD of 10 years or longer, only 25% of all PAs were predominantly spontaneous throughout the 10th year. Patients with a history of childhood separation disorder (CSD) had an earlier age of onset of the first PA, AGR, anticipatory anxiety, and GAD. Menstruation was associated with worsening generalized anxiety symptoms (51%) and an increase in PAs (33%). Caffeine worsened generalized anxiety (54%) and was associated with precipitating PAs (17%). It is concluded that a variety of anxiety disorders, MD, and alcoholism commonly occur in patients with AGR-PD and that the syndrome of agoraphobia, PAs, and anticipatory anxiety has a chronic unremitting course that is affected by the type of first PA, childhood separation, the menstrual cycle, and caffeine.

NR74
BUSPIRONE, CLORAZEPATE AND WITHDRAWAL

Tuesday, May 21, 1985, 2:30 p.m.

Karl Rickels, M.D., Univ. of Penna., 203 Piersol, 3400 Spruce Street, Philadelphia, PA 19104, Irma Csanalosi, M.D., Hack Chung, M.D., Warrent G. Case, M.D., Edward Schweizer, M.D.

Summary:

GAD patients treated for 6 months with the BZ clorazepate and the non-BZ buspirone were abruptly switched to 3 weeks of placebo under double-blind conditions. They completed daily checklists and were evaluated weekly. Results obtained support clearly the hypothesis that clorazepate but not buspirone caused significant rebound anxiety and/or withdrawal symptoms when patients are switched from active drugs to placebo. Compared to buspirone (26.3 mg/d) patients, clorazepate (20.5 mg/d) patients had higher HAM-A scores ($p < .03$) and higher daily checklist scores (6 day repeated measures analysis, $p < .001$) after 1 week on placebo. Under double-blind conditions, patients were rated on whether or not they experienced withdrawal. Highly significant differences between clorazepate and buspirone patients were obtained in favor of buspirone ($p < .001$).

NR75
EEG OF PANIC DISORDER AND NARCOLEPSY

Tuesday, May 21, 1985, 2:45 p.m.

John R. Adams, M.D., VA Medical Center, West Haven, CT 06516, Victor S. Wahby, M.D., Earl L. Giller, M.D.

Summary:

Purpose: To compare standard and sleep polygraphic recordings in panic disorder and narcolepsy.

Rationale: Excessive daytime sleepiness, a manifestation of narcolepsy, is a common complaint in panic disorder.

Methods: Two age and sex matched groups of patients were investigated by clinical evaluation, neurological examination and a sleep EEG. Group A ($n = 61$) had panic disorder (DSM-III) and Group B ($n = 28$) had narcolepsy. The Stanford University Sleep Disorder Narcolepsy Protocol was used for standard polygraphic control and included 10 channels EEG, mylohyoid electromyogram (EMG), electrocardiogram (EKG) and electrooculogram (EOG). All patients had normal neurological and medical examinations and were not on any psychoactive medications.

Results: For Group A 18% ($n = 11$) had normal EEG's and 62% ($n = 38$) had REM onset sleep, 11% ($n = 7$) had left temporal spikes and 21% ($n = 13$) had right temporal spikes. For Group B 28% ($n = 8$) had normal EEG, 57% ($n = 16$) had REM onset sleep, 3% ($n = 1$) had left temporal spikes and 17% ($n = 5$) had right temporal spikes. These findings were not significantly different in the 2 groups.

Conclusions: The electroencephalographic findings were similar in both groups. The polygraphic results in the narcolepsy group were compatible with established literature. Similar results in the panic group may suggest a common electrocortical etiology.

NR76
EXCESS MORTALITY IN PANIC DISORDER

Tuesday, May 21, 1985, 3:00 p.m.

William Coryell, M.D., Univ. of Iowa College of Medicine, 500 Newton Road, Iowa City, IA 52242, Russell Noyes, Jr., M.D., Daniel House, Ph.D.

Summary:

We found excess mortality among males with panic disorder followed an average of 35 years after psychiatric hospitalization (Coryell et al, 1982). In contrast to age and sex-matched controls with primary depression, much of this excess mortality was due to cardiovascular disease; the remainder was due to suicide.

We have since confirmed these findings in a separate, outpatient cohort. 155 outpatients with panic disorder were matched by age and sex to surgical controls and over 80% in each group were located an average of 12.5 years later. Four deaths were observed among the males with this disorder though only 1.8 were expected based on Iowa Vital Statistics. Moreover, when compared to controls, death among males with panic disorder were significantly more likely to involve cardiovascular disease (3 observed) or suicide (1 observed) ($p = .014$). As with the first cohort, females with panic disorder did not display excess mortality.

NR77

Tuesday, May 21, 1985, 3:15 p.m.

CO-2 CHEMOCEPTOR SENSITIVITY IN PANIC PATIENTS

Scott W. Woods, M.D., Yale University, 34 Park Street, New Haven, CT 06508, Dennis S. Charney, M.D., Jacob Loke, M.D., Wayne K. Goodman, M.D., D. Eugene Redmond, M.D., George R. Heninger, M.D.

Summary:

CO-2 chemoceptor sensitivity may be related to the pathophysiology of anxiety disorders. In panic anxiety patients, breathing 5% CO-2 has been reported to increase anxiety. CO-2 chemoceptor sensitivity can be compared in panic patients and controls by measuring the ventilatory response to increasing inspired CO-2 concentration (FiCO-2) caused by rebreathing.

Method: Using DSM-III criteria, 14 medication-free agoraphobia with panic attacks (APA) patients and 13 age- and sex-matched controls were selected. After giving informed consent, subjects underwent a rebreathing test modified from Read's (1967) method, raising FiCO-2 to 7-10%. In 10 patients and 12 controls, subjective and objective anxiety ratings were obtained 30 min. before and immediately after rebreathing.

Results: Ventilatory response to Co-2 was 1.58 ± 0.60 l/min/mm Hg (mean \pm S.D.) in APA patients and 1.74 ± 0.68 l/min/mm Hg in controls ($t = -0.630$, n.s.). Patients were able to continue rebreathing 3.90 ± 1.12 min.; controls lasted 4.98 ± 1.28 min. ($t = 2.353$, $p < .05$). In both groups, rebreathing produced significant increase over baseline for anxiety, nervousness, fear, autonomic symptoms, and clinician-rated anxiety. However, in patients compared to controls, the increase was not significantly different on any measure. Nine of 10 patients and 11 of 12 controls met DSM-III criteria for a panic attack during rebreathing.

Conclusions: At the relatively high concentrations achieved here, CO-2 robustly increased anxiety in both healthy controls and APA patients. Patients tolerated rebreathing a shorter time, possibly indicating increased behavioral sensitivity to CO-2 as reported by others. Ventilatory response was similar in patients and controls, suggesting that behavioral sensitivity to CO-2 may occur despite normal CO-2 chemoceptor sensitivity.

NR78

Tuesday, May 21, 1985, 3:30 p.m.

SUMMARY OF MULTICENTER STUDY OF ALPRAZOLAM

Malcolm Lader, M.D., Maudsley Hospital, Department of Pharmacology, London, England

Summary:

A multicenter study comparing alprazolam with placebo in 500 patients studied in eight centers in the U.S., Canada and Australia has established the general efficacy of alprazolam in this relatively newly characterized disorder. Side effects, for the most part typical of the benzodiazepine class, were less troublesome than those expected of the tricyclic antidepressants hitherto standard treatment for panic disorder. Special diagnostic procedures, an elaborate protocol and extensive training of the participating investigators have been developed and carried to a successful conclusion.

The results of the study will be discussed and placed in a broader perspective with a critical analysis drawing on the author's extensive background in clinical research with benzodiazepines.

NR79
NEW RESEARCH STRATEGIES IN ANXIETY DISORDERS

Tuesday, May 21, 1985, 3:45 p.m.

Gerald L. Klerman, M.D., Department of Psychiatry, Massachusetts General Hospital, Fruit Street, Boston, MA 02114

Summary:

The separation of panic and agoraphobia from the large group of generalized anxiety disorders is the basic concept embodied in the design of the multinational, multicenter trial comparing alprazolam to placebo in the treatment of panic disorders. Although this concept deviates from what has been the consensus of the psychiatric field from World War I through the early 1980s, there is increasing evidence supporting this view. Other than alprazolam, anxiolytic benzodiazepines have thus far shown only limited effect on panic attacks, while the monoamine oxidase inhibitors and the tricyclic antidepressants have shown efficacy in panic attacks and agoraphobia. Panic attacks can be induced in the laboratory setting by giving susceptible patients lactate infusion, yohimbine, caffeine, or carbon dioxide; these laboratory-induced attacks can be blocked by giving monoamine oxidase inhibitors, tricyclic antidepressants, or alprazolam. Epidemiological evidence has identified some risk factors associated with panic disorders and has indicated their prevalence in the population. Although no genetic markers have been identified, family studies suggest there may be a genetic vulnerability to panic disorders. Follow-up studies have associated panic disorders with increased morbidity and mortality. The decision to mount the collaborative study of alprazolam vs placebo in the treatment of panic disorders has been supported by evidence that suggests this is a distinct entity with clinical significance.

NR80
ALPRAZOLAM LEVELS: OUTCOME IN PANIC

Tuesday, May 21, 1985, 4:00 p.m.

David J. Greenblatt, M.D., Division of Clinical Psychopharm, Box 1007, Tufts-New England Med. Ctr., 171 Harrison St., Boston, MA 02111, Randall B. Smith, Ph.D., Richard I. Shader, M.D.

Summary:

Alprazolam is a triazolobenzodiazepine currently under evaluation in the treatment of panic disorders. Although alprazolam kinetics within an individual are very predictable and consistent, considerable interindividual variation in the half-life and clearance of alprazolam implies variation between individuals in steady-state plasma concentration at any given daily dosage. Steady-state plasma concentrations of alprazolam and other benzodiazepines were determined coincident with clinical assessment at several points during this multicenter study of alprazolam in the treatment of panic disorders for two reasons: to measure each patient's compliance, and to determine if a relationship exists between plasma concentrations of alprazolam and clinical outcome (measured by number of panic attacks per week). We conclude that compliance to treatment in the panic study was excellent as determined by plasma concentrations of alprazolam and other benzodiazepines; steady-state plasma concentration was highly correlated to the dose administered ($r^2 = 0.81$); sex, age, or race did not contribute to intersubject variability in this study; there was no statistically significant difference between the plasma concentration of alprazolam in responders (zero panic attacks) and the plasma concentration of alprazolam in nonresponders; and there was a significant but not predictive relationship between plasma concentration of a alprazolam and total number of panic attacks per week.

NR81**Tuesday, May 21, 1985, 4:15 p.m.****ALPRAZOLAM WITHDRAWAL IN PANIC DISORDER PATIENTS**

Robert L. DuPont, Jr., M.D., 6191 Executive Blvd., Rockville, MD 20852, John C. Pecknold, M.D

Summary:

Patients with anxiety disorders treated with benzodiazepines may experience an increase in symptoms during drug taper and withdrawal was categorized as uncomplicated, symptomatic taper and withdrawal. Increased symptoms may be due to a transient withdrawal syndrome, to a recurrence of the original disorder or to a combination of both. A multicenter, placebo-controlled clinical trial of alprazolam (1 to 10mg/day) was conducted in 559 patients with panic disorder, many of whom had agoraphobia. As part of this trial, alprazolam taper and withdrawal were studied in 303 patients, 134 of whom were treated acutely for two months and 169 of whom were treated chronically for three to 14 months. The maximum rate of dose reduction was 1mg every three days. In the acute group the final dose averaged 5.8 ± 2.3 mg/day. Symptom intensity in baseline, treatment, taper and post-taper periods will be compared in the acute treatment group. Clinical course during taper and withdrawal was categorized as uncomplicated, symptomatic, taper refused, or unevaluable due to dropout, etc. The distribution of these types of clinical course varied greatly among the eight sites. Generally, patients who received chronic treatment experience more difficulty withdrawing than did patients in the acute group. Management of patients whose symptoms increased during taper and who wished to resume medication, a problem handled differently at the eight trial sites, will be discussed. The possibility that panic disorder requires chronic treatment will be addressed.

NR82**Tuesday, May 21, 1985, 4:30 p.m.****ADVERSE EFFECTS AND PATIENT ACCEPTANCE**

Graham D. Burrows, M.D., Department of Psychiatry, University of Melbourne at Austin, Melbourne, Australia, Arthur Rifkin, M.D., Russell Noyes, Jr., M.D.

Summary:

In the cross-national study of alprazolam vs. placebo in the treatment of panic disorder daily doses were substantially larger than doses used in previous studies (mean, approximately 6 mg); however, relatively few adverse effects were seen. While over 500 patients participated in the study, only six patients reported severe or unexpected adverse reactions; five of the patients were taking alprazolam and one was taking placebo. Excluded from this total are reports of withdrawal reactions, which are not part of this discussion. Four percent of alprazolam-treated patients and 1.5% of placebo-treated patients in the study dropped out because of adverse effects. Sedation was the most common adverse effect reported by patients taking alprazolam. This effect decreased with time throughout the study even though the alprazolam dose was gradually increased. Infrequent adverse effects reported by alprazolam-treated patients included ataxia, increased appetite, and slurred speech. Adverse effects reported by patients in the placebo group were clearly signs of increased anxiety: depression, diarrhea, excitement, faintness, headache, insomnia, menstrual irregularity, nausea, vomiting, sleep disturbance, palpitations, tremor, and weakness. Although other drugs demonstrating efficacy in the treatment of panic disorders (i.e., imipramine and phenelzine) have reportedly produced a 15% to 20% incidence of overstimulatory response in patients, there was only one instance of this adverse reaction reported during our study.

**NR83
CLINICAL EFFICACY AND OUTCOME**

Tuesday, May 21, 1985, 4:45 p.m.

James C. Ballenger, M.D., Department of Psychiatry, Medical University of South Carolina, Charleston, SC 29425, Robert T. Rubin, M.D., Richard P. Swinson, M.D.

Summary:

The efficacy of alprazolam in the treatment of panic disorder and agoraphobia with panic attacks has been clearly demonstrated in a double-blind, placebo-controlled trial involving over 500 patients. Sixty-eight percent of alprazolam-treated patients and 72% of placebo-treated patients were experiencing one or more spontaneous panic attacks per week at the start of the study. After only one week on study medication, 37% of alprazolam-treated patients and 58% of placebo-treated patients were experiencing spontaneous panic attacks. By the end of the eight-week study, only 16% of alprazolam-treated patients and 25% of placebo-treated patients were still experiencing spontaneous attacks. Efficacy of alprazolam was also shown by the elimination of situational panic attacks; while 82% of the alprazolam-treated patients were experiencing situational panic attacks at the start of the study, this portion was reduced to 57% by the end of week one and to 33% by the end of week eight. In the placebo-treated group, 78% of patients were experiencing situational attacks at the start of the study, 65% were experiencing these attacks at the end of week one, and 42% were still experiencing situational panic attacks at the end of week eight. Approximately 50% to 60% of the total improvement seen during the study in the alprazolam-treated group occurred in the first week of treatment. Alprazolam was also superior to placebo in improving ratings of phobic anxiety, general anxiety, and functional, social, and work disabilities.

**NR84
ARGININE-VASOPRESSIN CHALLENGE IN DEPRESSION**

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

William H. Meller, M.D., Psychiatric Hospital, The University of Iowa, Iowa City, IA 52240, Roger G. Kathol, M.D., Richard S. Jaeckle, M.D., Juan F. Lopez, M.D.

Summary:

It has been established that AVP stimulates the pituitary adrenal axis to release ACTH and cortisol. Because major depressive disorder (MDD) is associated with hypersecretion of ACTH and cortisol, we investigated the ACTH and cortisol secretory response to AVP (0.18 u/kg IM at 1600 hours) in 13 patients who met DSM-III criteria for MDD and in 6 controls (C). Six of the MDD patients were DST nonsuppressors (NS) and 7 were DST suppressors (S). The MDD group had a significantly higher mean maximal cortisol increase after AVP than the C group. Furthermore, the distribution of maximal cortisol increments separated the MDD group into two subgroups. One subgroup had hyperresponse (mean Δ max. \pm standard error [SE] 15.2 mcg/dl \pm .9 mcg/dl) and one had normal or low cortisol response (mean Δ max. SE 5.1 mcg/dl \pm .3 mcg/dl). The control Δ max. \pm SE was 5.8 mcg/dl \pm 1.4 mcg/dl. 83% of NS and 43% of S fell into the hyperresponse group.

There was no significant difference in the mean maximal ACTH increase after AVP administration between the MDD and C group; however, 50% of the NS, 57% of the S and 0% of C had mean max. ACTH increases >12.5 pg/ml ($p < .1$ MDD vs. C Fisher's exact). These findings suggest that there is a subgroup of patients with MDD who have hypersecretion of cortisol when challenged with AVP.

NR85

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

CORTISOL RESPONSE TO YOHIMBINE IN DEPRESSION

Lawrence H. Price, M.D., Yale University, Connecticut Mental Health Center, Ribicoff Res. Fac., 34 Park Street, New Haven, CT 06519, George R. Heninger, M.D.

Summary:

Hypothalamic-pituitary-adrenal (HPA) axis abnormalities are associated with depression. These abnormalities may be related to changes in neurotransmitter receptor function in depressed patients. Yohimbine, which increases brain norepinephrine by blocking alpha-2 adrenoceptors, was given to depressed patients and healthy controls to determine whether effects on cortisol secretion differed between groups.

Methods: Using DSM III criteria, 40 patients with major depression (18 melancholic, 22 nonmelancholic) and 19 healthy subjects were selected after giving voluntary informed consent. All subjects were free of psychotropic medications for 3 weeks before testing. On 2 different days, after an overnight fast, each subject received yohimbine 20 mg orally or a matching placebo. Plasma cortisol and free 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) were measured before and for 4 hours after the dose.

Results: Yohimbine caused a greater net peak increase in cortisol in melancholics ($4.5 \pm SD 7.0$ ug/dl, $p < .006$) and nonmelancholics ($2.2 \pm SD 5.0$ ug/dl, $p < .03$) compared with controls (-1.3 ± 4.2 ug/dl). There was no significant difference between depressive subtypes or between dexamethasone suppressors and nonsuppressors. Net peak cortisol response to yohimbine was positively correlated with net peak MHPG response in melancholics ($r = .57$, $p < .02$) but not in nonmelancholics ($r = .25$, n.s.) or normals ($r = .33$, n.s.). Net peak MHPG response did not differ between depressives and healthy controls.

Conclusions: The cortisol response to yohimbine differed significantly between depressed patients and controls, despite similar MHPG responses between groups. Correlations between cortisol and MHPG responses differed substantially between groups. These data suggest that the functional interaction between norepinephrine and the HPA axis is abnormal in depression.

NR86

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

TSH IS LOWER AT NIGHT IN DEPRESSION

David A. Sack, M.D., NIMH, DIRP, Clinical Psychobiology Branch, Bldg. 10/4S239, 9000 Rockville Pike, Bethesda, MD 20205, Steven P. James, M.D., Norman E. Rosenthal, M.D., Thomas A. Wehr, M.D.

Summary:

A blunted TSH response to TRH is found in depressed patients but baseline TSH does not differ from normal controls. TSH has a circadian rhythm with peak secretion occurring at night. Sleep dampens the nocturnal rise of TSH so that TSH is highest when subjects are kept awake at night. We have studied the profiles of TSH in 9 drug free bipolar women and 6 healthy women of similar ages. Daytime secretion of TSH was the same for both groups but normals secreted significantly higher amounts of TSH between midnight and 7:00 a.m. than did the patients. Sleep deprivation increased nocturnal TSH in both groups but more so in the control group. Sleep deprivation, which improves depression, raised TSH in the depressed group to levels seen in the normals at baseline. Thus, the basal and stimulated secretion of TSH at night is reduced in depressives, an abnormality which may result from reduced secretion of TRH, increased secretion of dopamine, or from altered pituitary responsiveness.

NR87
CSF SOMATOSTATIN AND ABNORMAL RESPONSE TO DST

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Allen R. Doran, M.D., National Institute Mental Health, NIH Bldg. 10, 4N214, 9000 Rockville Pike, Bethesda, MD 20205-1000, David R. Rubinow, M.D., Alec Roy, M.B., David Pickar, M.D.

Summary:

Somatostatin is a neuropeptide that exerts numerous effects in brain and has been shown to interact with other neurotransmitters and hormones including ACTH. Somatostatin has been observed to inhibit the activity or secretion of several of these substances through different mechanisms. Decreased levels of CSF somatostatin have recently been reported and replicated in depressed patients and nonsuppression on the dexamethasone suppression test continues to be a commonly reported neuroendocrine alteration in this patient group. *In vitro* studies have shown that somatostatin inhibits ACTH secretion, which prompted us to also administer the DST to a group of neuropsychiatric patients, allowing us to assess whether there was a relationship between CSF somatostatin and hypothalamic-pituitary-adrenal (HPA) axis activity as measured by the DST. Consequently, we measured levels of CSF somatostatin in patients with depression and schizophrenia. In DST nonsuppressors lower levels of CSF somatostatin were found regardless of diagnosis and this was negatively correlated with maximum postdexamethasone cortisol values in the total patient group. These data suggest a functional relationship between HPA hyperactivity and reduced CSF somatostatin.

NR88
INTRAVENOUS-PROCAINE AS A PROBE OF LIMBIC ACTIVITY

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Charles H. Kellner, M.D., Asst. Prof., Chief C/L Psychiatry, Medical University of S.C., Charleston, SC 29425, Mitchel Kling, M.D., Robert M. Post, M.D., Rex Cowdry, M.D., David Gardner, M.D., Frank Putnam, M.D., Richard Coppola, Ph.D.

Summary:

Considerable evidence has been accumulated in both animal and human experiments to show that procaine hydrochloride and other local anesthetics selectively affect limbic system structures. There are now extensive data to suggest the involvement of limbic and temporal lobe mechanisms in the modulation of affect. Moreover, carbamazepine, an effective anticonvulsant for limbic seizures, is effective in treating some patients with affective disorders. We therefore postulated that intravenous procaine might produce symptoms or experiential phenomenon referable to limbic system activation in psychiatric patients and that physiological or behavioral responses might be useful as predictors of clinical response to carbamazepine.

We administered a series of intravenous bolus doses of procaine hydrochloride to 8 patients with affective disorders, 17 patients with borderline personality disorder and 8 healthy normal volunteers. 16-lead EEG recordings were done throughout the procedure, blood samples for neuroendocrine studies were obtained at regular intervals and a rating questionnaire that was designed to evaluate mood, sensory-perceptual, and cognitive changes was administered after each dose.

Emotional responses were mainly dysphoric but included some positive experiences. Unformed auditory hallucinations were common. Olfactory and gustatory hallucinations were also reported. Endocrine responses included consistent increases in ACTH, cortisol and prolactin across all groups but no change in growth hormone. Power spectral analysis of the EEG data showed specific increases in fast activity over the temporal lobes which correlated with the degree of dysphoria experienced ($r = .65$, $p < .001$, $n = 21$). We will discuss these preliminary results and their theoretical and potential clinical implications.

**NR89
MELATONIN AND AGING**

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

G.F. Oxenkrug, M.D., 951 East Lafayette, Detroit, MI 48207, I.M. McIntyre, Ph.D., A.K. Jain, M.D., R. Balon, M.D., L.P. Taylor, Ph.D., S. Gershon, M.D.

Summary:

Melatonin synthesis from serotonin in the pineal gland decreases with aging. Our data suggest that this decline in melatonin production might trigger the age-associated activation of the hypothalamic-pituitary-adrenal (HPA) axis. HPA stimulation might contribute to the development of such age-associated pathology as hyperlipidemia, late onset diabetes, impairment of immunodefense and cognitive function. The mechanisms causing age-associated decrease of melatonin synthesis have not been thoroughly investigated. The effects of serotonin precursors and selective monoamine oxidase inhibitors on pineal melatonin synthesis in young and old rats exposed to constant light, cold and stress was assessed by HPLC-fluorometric determination of the pineal indoles and measurement of NAT and HIOMT activity. The data will be discussed in relation to the mechanisms of normal and precocious aging in senile dementia of Alzheimer's type and Down's syndrome.

**NR90
PROLACTIN RESPONSE DURING DST**

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Peter E. Stokes, M.D., Cornell University Medical Ctr., 525 East 68th Street, New York, NY 10021, Betty Lasley, Ph.D., Peter M. Stoll

Summary:

Prior studies have demonstrated that basal prolactin (PRL) levels and PRL release after insulin or stress can be inhibited by pretreatment with corticosteroids including dexamethasone (DEX). One report noted increased basal PRL levels in bipolar (BP) as compared to unipolar (UP) depressed. Meltzer et al. (Am J Psychiat 139:6, 1982) reported increased basal PRL levels in both UP and BP depressed patients and in non-depressed psychiatric patients as compared to healthy normal controls (HNC). Patients who were cortisol nonsuppressors also showed nonsuppression of PRL in the same plasma sample. In a preliminary study we found a highly significant correlation ($r = .75$, $p = .01$) between post-DEX A.M. plasma cortisol level and absolute plasma PRL in a series of 10 depressed patients undergoing a 1 mg overnight DST. We are now extending these findings in depressed comparison patient groups, and HNC using various doses of DEX. The results of this ongoing study will be presented. Our pilot study findings are compatible with Meltzer's suggestion of a broad but reversible failure of neuroendocrine regulation in major depressive illness. However the possible association of post-DEX PRL nonsuppression with depressive subtype may provide an additional interesting and perhaps useful neuroendocrine marker of depressive illness.

**NR91
AGE, DST AND DIAGNOSTIC HETEROGENEITY**

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906, Ivan W. Miller, Ph.D., Walter A. Brown, M.D., William H. Norman, Ph.D., Alan E. Fruzzetti, B.A.

Summary:

Several studies have indicated a positive correlation between age and cortisol hypersecretion as assessed by the Dexamethasone Suppression Test (DST). There is disagreement, however, concerning the age cutoff at which changes in serum cortisol become significant. Most studies have reported on homogeneous populations in comparison with nonpsychiatric control groups. A 1 or 2 mg DST was administered to a diagnostically heterogeneous sample of 229 psychiatric inpatients. Serum cortisol was measured at 4 and 11:30 pm next day. Older patients with an affective disorder (major unipolar depression, bipolar depression, schizoaffective or dysthymic disorder) showed significantly higher rates of nonsuppression (serum cortisol >5 ug/dl) than younger patients with affective disorders ($p < .001$), but only when using age 65 or higher as a cutoff. Non-affective patients also showed a trend ($p < .10$) toward increased nonsuppression rates with older age, but at a significantly lower rate than the affective patients. The sensitivity of the DST for major depression in those under age 65 was 33% and in those over age 65, 75%. However, the specificity in the over 65 age group was only 46%. These findings suggest that the DST is not a useful tool for the differential diagnosis of major depression in those over 65 years due to an increased rate of nonsuppression in all elderly inpatients.

NR92

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

DEPRESSION IN UNTREATED AND TREATED ALCOHOLICS

Alan J. Romanoski, M.D., Dept. of Psychiatry & Behavioral Sciences, The Johns Hopkins Hospitals, Baltimore, MD 21205, Barry Rovner, M.D., Gerald A. Nestadt, M.D., Marshal Folstein, M.D.

Summary:

Studies demonstrating increased prevalence of depression among alcoholics and their families have generally been based on alcoholic probands drawn from patient samples. Is there also an increased prevalence of depression among *untreated* alcoholics in the general population, or has Berksonian bias been at play? We offer data on this question.

Four specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N = 810) of 175,000 eastern Baltimore residents over 18 years of age. Their mission was to identify each subject's DSM-III-defined disorder after conducting a standardized psychiatric examination which averaged two hours in duration. The Standardized Psychiatric Examination (SPE) format and record was developed as a validation study of the NIMH Diagnostic Interview Schedule in the eastern Baltimore site of the Epidemiologic Catchment Area studies. The subjects were research volunteers for whom the research psychiatrists had no clinical responsibility. A random sample of abstinent alcoholic outpatients in treatment at the Baltimore City Hospitals Alcoholism Treatment Services, who resided in the same catchment area was examined by a research psychiatrist who used the identical (SPE) examination format.

Depressive symptoms in general, and DSM-III major depressive symptoms in particular, were no more prevalent among untreated community alcoholics than among non-alcoholic community residents. Depression was much more prevalent among treated alcoholics from both the community and clinic samples than among untreated community alcoholics. There was no difference in prevalence of depression among treated alcoholic and community residents receiving mental health specialty care for any other reason.

NR93

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

DEPRESSIVE SUBTYPES AND RANGES OF DST RESPONSE

Thomas C. Bond, M.D., McLean Hospital, 115 Mill Street, Belmont, MA. 02178, Anthony J. Rothchild, M.D., Jan Lerbinger, B.S., Alan F. Schatzberg, M.D.

Summary:

There has been considerable debate recently whether dexamethasone suppression test (DST) results, classified by suppression vs. nonsuppression alone, discriminate among depressive subtypes. One issue has been the relationship of DST results to three proposed familial subtypes, which were defined by Schlessler, Winokur et al on the basis of the presence of absence of depression, alcoholism or sociopathy in first-degree relatives. Other investigators have failed to confirm their data. Recently, our group reported that patients with markedly elevated 4 p.m. post-dexamethasone cortisol levels ($\geq 15 \mu\text{g/dL}$) were often psychotic, suggesting that ranges of DST results may provide better discrimination among subtypes than suppression vs. nonsuppression.

65 unipolar depressed patients were studied to determine familial prevalence for depression and alcoholism in psychotic and non-psychotic probands. The results were then correlated with three different ranges of DST response ($\geq 4.9 \mu\text{g/dL}$, 5.0 - 14.9 $\mu\text{g/dL}$, $\geq 15.0 \mu\text{g/dL}$) as well as suppression vs. nonsuppression alone. A subgroup of patients with markedly elevated DST responses ($\geq 15.0 \mu\text{g/dL}$) was identified who had (1) significantly increased familial prevalence for depression; (2) significantly decreased familial prevalence for alcoholism; and (3) increased incidence for psychosis (43.8%). Patients with intermediate DST responses (5.0 - 14.9 $\mu\text{g/dL}$) had: (1) significantly increased familial prevalence for alcoholism; and (2) no increased familial prevalence for depression. DST suppression vs. nonsuppression did not discriminate among familial subtypes. However, depressive spectrum disorder could be separated from familial pure depression disorder and sporadic depressive disorder at the level of $\geq 15.0 \mu\text{g/dL}$. These data lend support to relationships between DST responses and familial subtypes but only using very high cortisol levels.

NR94**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****DST PREDICTS POOR PLACEBO RESPONSE IN DEPRESSION**

Ram K. Shrivastava, M.D., Park Lexington Regional Research Center, 133 East 73 Street, Suite 210, New York, NY 10021, Rita Schwimmer, M.S., Walter Armin Brown, M.D., Mihaly Arato, M.D.

Summary:

Although depressed patients with a positive dexamethasone suppression test (DST) respond better to antidepressants than do suppressors (S) in some studies, it is unknown whether non-suppressors (NS) and S differ in placebo response or spontaneous recovery. As part of a clinical psychopharmacological study 31 outpatients with major depression and scores of 18 on the Hamilton Rating Scale for Depression (HRS) and a minimum score of 4 on the Clinical Global Impressions (CGI) had a DST and were randomly assigned to placebo on a double-blind basis for 6 weeks. NS and S did not differ significantly in initial HRS scores (29.8 + 6.5 vs 25.9 + 3.8). Patients were assessed weekly and were considered placebo responders if they showed a 50% decrease and a final score of 10 on the HRS. Ten patients (32%) were placebo responders. None of the 9 NS, but 10/22 S (45%) were placebo responders ($\chi^2 = 4.14$ p .05). Our findings suggest that DST NS are likely to require antidepressant treatment whereas S show a relatively frequent placebo response and spontaneous recovery from depression.

NR95**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****DST AND INTOLERANCE TO SEROTONIN UPTAKE INHIBITION**

Walter Armin Brown, M.D., VAMC, Davis Park, Providence, RI 02908, Ram K. Shrivastava, M.D., Mihaly Arato, M.D.

Summary:

A few studies have suggested that non-suppressors (NS) respond poorly to relatively "serotonergic" antidepressants, but the response of suppressors (S) and NS to an antidepressant with selective effects on serotonin activity in vivo has not yet been examined. In a double-blind placebo controlled study 81 outpatients with Major Depression had a DST and were randomly placed on imipramine, placebo or fluvoxamine, a selective serotonin uptake inhibitor. Thirteen of the 24 S (54%) but only 3 of the 9 NS (33%) had a good response to fluvoxamine. Most striking, however, was the high proportion of NS (56%) as compared to S (13%) who had to discontinue fluvoxamine due to side effects, primarily nausea, which are considered to be serotonin related ($\chi^2 = 4.47$, $p < .05$). The drop out rate for side effects did not differ significantly between NS and S on imipramine (17% vs 27%) or NS and S on placebo (10% vs 5%). Pituitary-adrenocortical disinhibition may identify a depressive subtype associated with increased serotonergic activity and intolerance to serotonergic drugs.

NR96**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****IS DST OUTCOME AFFECTED BY SEVERITY OF SYMPTOMS?**

George W. Arana, M.D., Boston VA Medical Center, Department of Psychiatry (116A), 150 South Huntington Avenue, Boston, MA 02130, Paul J. Barrerira, M.D., Joseph Lipinski, M.D., Hyme Schachter, B.S., Bruce M. Cohen, M.D.

Summary:

Although it is known that cortisol release is reactive to psychological stress, it is not known to what degree cortisol dysregulation in psychiatric disorders is a consequence of disease-specific abnormalities or is secondary to non-specific effects. To determine whether there was a relationship between the severity or type of psychiatric symptoms and non-suppression of cortisol post-dexamethasone (DST), we studied a total of 31 psychiatric inpatients on an acute inpatient psychiatry service with DSM-III diagnoses of depressive, bipolar, schizophrenic, and atypical psychotic disorders. BPRS and Hamilton Depression Scales (HDS) were used to assess severity of symptoms on the day of DST.

Neither BPRS nor HDS total or subscale scores correlated with the DST. No significant relationships were seen between severity of symptoms and DST status (Fisher's t-test and Spearman coefficients). The authors conclude that severity of symptoms and DST outcome are not correlated.

NR97
SEVERITY OF DEPRESSION AND THE DST

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Kevin Kerber, M.D., Department of Psychiatry, University Hospitals, Box 011, 1405 E. Ann, Ann Arbor, MI 48109, Pam Flegel, B.S., Leon Grunhaus, M.D., John F. Greden, M.D.

Summary:

Early DST articles failed to find significant relationships between absolute post-dexamethasone plasma cortisol levels and clinical severity. Recent pilot reports, however, indicate that DST values might reflect clinical severity, with higher levels associated with more severe depression. These reports are somewhat plagued by small sample sizes, concurrent use of medications, or diagnostic heterogeneity.

To examine this question systematically, we studied 66 drug-free (>10 days) patients with major depressive disorder, endogenous subtype (SADS/RDC). We correlated four rating scales (Hamilton and Carroll Depression scales, 100 mm line scale and Global Assessment scale) with post-dexamethasone cortisol levels prior to treatment and at discharge. We found: (1) moderate ($r = .25$ to $r = .49$) but significant ($p < .05$) correlations between the Hamilton and Carroll scales for depression and pretreatment DST cortisol levels in the total sample; (2) all significant correlations disappeared in the total sample at discharge; (3) those patients who "failed to normalize" despite treatment, however, continued to show significant correlations at discharge; (4) patients' self-ratings supported clinicians' ratings in most cases.

These data confirm the growing consensus that absolute post-dexamethasone cortisol levels do reflect severity to a moderate degree, but only in patients with non-suppressive hypothalamic-pituitary adrenal dysregulation.

NR98
EEG SLEEP IN RECURRENT DEPRESSION

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

James E. Shipley, M.D., Assistant Professor of Psychiatry, Western Psychiatric Institute & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, David J. Kupfer, M.D., Ellen Frank, Ph.D. David B. Jarrett, M.D., James M. Perel, Ph.D., Victoria J. Grochocinski, Ph.D.

Summary:

As part of an ongoing study of maintenance therapy in recurrent unipolar depression, we now report data for 22 patients, each in at least their third episode, who achieved symptomatic remission during treatment with imipramine (IMI) for the index episode. After a two-week drug free washout, EEG sleep was then recorded (Sleep 0) and patients were begun on IMI. Patients were declared in symptomatic remission if their HRS was < 7 for three consecutive weeks ($\bar{X} \pm SD$ dose = 222 ± 43 mg/dl), and EEG sleep was then repeated (Sleep 1). Patients were maintained on IMI and continued in symptomatic remission for an additional four months ($\bar{X} \pm SD$ dose = 226 ± 49 mg/d), whereupon EEG sleep was again recorded (Sleep 2). Daily dosage ($r = .92$) and plasma levels ($r = .81$) were highly correlated between Sleep 1 and Sleep 2. For either Sleep 1 or Sleep 2 compared to Sleep 0, IMI was not sedative but was potent in suppressing REM sleep. There were no mean differences for sleep measures for Sleep 1 and Sleep 2. Sleep continuity and architecture measures for Sleep 1 and Sleep 2 were significantly correlated, while REM measures were not. Higher plasma levels at initial symptomatic remission (Sleep 1) were correlated with lower REM time and increased stage 2 sleep. After continued symptomatic remission (Sleep 2), significant correlations of prolonged REM latency and REM cycle time with plasma levels were noted. These results suggest that (1) IMI has significant effects on EEG sleep of recurrent depressives; (2) the sleep of individual patients is consistent during continued treatment with regard to sleep continuity and architecture measures; (3) despite nearly identical dosing and plasma levels, the pattern of correlations between EEG sleep and plasma levels changed over time, suggesting an alteration in CNS function with continued treatment.

NR99**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****SLEEP AND DEPRESSION DURING TREATMENT WITH TCA's**

J. Catesby Ware, Ph.D., 1303 McCullough, Suite 447, San Antonio, TX 78212, Frederick W. Brown, M.D., Philip J. Moorad, M.D. Joe Tom Pittard, M.D., B. Cobert, M.D.

Summary:

Thirty depressed anxious insomniac patients received in a random double blind manner either trimipramine (TRI) or imipramine (IMI) for 6 weeks following a 12 day placebo period from which responders were dropped. The dose was increased gradually up to 200 mgs., q.h.s. as tolerated; a minimum dose of 100 mgs., q.h.s. was required to stay in the study. Both groups improved similarly in measures of depression and anxiety (Hamilton, Profile of Moods Scale, Covi Anxiety, Global Clinical Assessment). However, polysomnographic evaluations during the study indicated that only the TRI group improved significantly in terms of sleep parameters (e.g. total sleep time, sleep latency, number of awakenings). Also, no REM sleep suppression occurred with TRI as it did with IMI. Both groups had an initial increase in sleep related periodic leg movements (nocturnal myoclonus) that gradually decreased over the course of treatment. The data, therefore, indicate that although TCA's may have similar effects on depression, they can be differentiated in terms of their physiological effects on sleep.

NR100**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****CLINICAL CORRELATES OF ONE-CARBON METABOLISM**

William G. Walter-Ryan, M.D., Department of Psychiatry, Univ. of Alabama School of Medicine, Birmingham, AL, 35294, Donna A. Morere, M.S., Renato D. Alarcon, M.D., Marva Steele, R.N., John A. Monti, Ph.D., Leland C. Tolbert, Ph.D.

Summary:

Work from our group has shown decreased erythrocyte methionine adenosyltransferase (MAT) activity (V_{max}) and phosphatidylcholine (PC) levels in major depression and schizophrenia, and elevated MAT activity and PC in mania. Pre-post-medication comparisons demonstrated that these abnormalities were not simply medication effects: medication usage (tricyclics, neuroleptics, and lithium) was associated with one-carbon metabolism findings closer to those from controls. This study focused on the association between change in clinical status and the above parameters. Inpatients were diagnosed by DSM-III with schizophrenia (N = 14), major depression (N = 7) or mania (N = 6). Paired blood samples were drawn on admission (medication-free), and on discharge. Several reliable instruments, including the BPRS, NOSIE, Ham-D, and Mania Scale, were used at regular intervals as measures of psychopathology. Clinical change was measured by subtracting admission from discharge scores, then comparing this to similar change in V_{max} and PC between admission and discharge. The results indicate that clear-cut clinical improvement, reflected in a negative score, was related to an increase in V_{max} and percent PC in depressed and schizophrenic patients, and in manic patients, to a decrease.

NR101 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
DESIPRAMINE ALTERS PLASMA NOREPINEPHINE KINETICS

Richard C. Veith, M.D., G.R.E.C.C. 182B, VA Medical Ctr., 1660 So. Columbian Way, Seattle, WA 98108, Jeffrey B. Halter, M.D., Michele Murburg, M.D. Robert F. Barnes, M.D., Enrique Villacres, M.D., Frank Backus, M.D.

Summary:

Elevations of plasma norepinephrine (NE) in Major Depression might represent increased sympathetic (SNS) outflow, if elevated NE is due to increased plasma NE appearance rate and not reduced plasma NE clearance. If SNS outflow is increased, acute blockade of CNS neuronal NE re-uptake by desipramine (DMI) might suppress plasma NE by activating α_2 pathways which inhibit SNS outflow. To test these hypotheses, arterialized plasma NE kinetics were measured in 6 male patients with Major Depression (55 ± 7 yr, $\bar{x} \pm$ SEM) and 14 male controls of similar age and weight using a tritium-labelled NE infusion technique. Measurements were repeated in patients after two days of DMI (50 mg/hs). Trends toward higher basal plasma NE (317 ± 60 vs 279 ± 34 pg/ml) and NE appearance rate ($.41 \pm .09$ vs $.35 \pm .05$ $\mu\text{g}/\text{m}^2/\text{min}$) in patients did not reach statistical significance. However, close correlations between basal NE and NE appearance in patients and controls ($r > .93$, $p < .001$) indicated that higher plasma NE levels were associated with increased NE appearance. Plasma NE clearance was similar in patients and controls ($1.24 \pm .09$ vs $1.24 \pm .07$ L/ m^2/min , $p = \text{NS}$). As expected, DMI decreased NE clearance by 18% from $1.24 \pm .09$ to $1.02 \pm .08$ L/ m^2/min ($p < .02$). Plasma NE fell by 12% from 317 ± 60 to 278 ± 65 pg/ml ($p < .05$) because NE appearance rate was suppressed by 27% from $.41 \pm .09$ vs $.29 \pm .08$ $\mu\text{g}/\text{m}^2/\text{min}$ ($p .01$). We conclude that elevated plasma NE in Major Depression is due to increased NE appearance rate. DMI acutely suppresses plasma NE, despite a fall in NE clearance. Increased synaptic NE resulting from re-uptake blockade might stimulate CNS α_2 pathways to inhibit SNS outflow and/or activate pre-synaptic inhibitory feedback mechanisms regulating peripheral SNS neurons.

NR102 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
3H-IMIPRAMINE BINDING IN DEPRESSED ELDERLY

L.S. Schneider, M.D., Assistant Professor of Psychiatry, USC School of Medicine, 1934 Hospital Pl., Los Angeles, CA 90033, James A. Severson, Ph.D. Fred Staples, Ph.D., Eric Fredrickson, B.S., R. Bruce Sloane, M.D.

Summary:

Specific binding sites for 3H-imipramine have been demonstrated in human brain and platelets. These are observed to be significantly decreased in depressed patients and may be a site of tricyclic antidepressant activity. This study is intended to assess a change in platelet 3H-imipramine binding (B_{max}) with age and in depressed elderly. 35 ambulatory, unmedicated subjects at least 60 years of age, who met RDC criteria for major depression of one-month duration, and with Hamilton Depression Rating Scores (HDRS) of > 18 were treated with either nortriptyline (NT) or interpersonal psychotherapy (IPT) for 16 weeks. B_{max} was determined in 17 subjects before treatment, in 18 subjects an average of 22 weeks after beginning treatment, in 10 age-matched controls, and in 11 younger controls (mean age 33).

Results: B_{max} was greater in elderly controls compared with the younger group, and lesser in the depressed than in the elderly controls. No correlation was found between B_{max} and HDRS either before or after treatment. There was no difference in B_{max} between subjects who received NT and those who received IPT; or between those who had an 3H-imipramine binding assay before treatment and those who had it about 22 weeks after treatment began. An unexpected result is that treatment responders as measured by HDRS at 16 weeks had significantly lower B_{max} than those who did not respond, regardless of the treatment received. 14 of 18 depressed subjects with a low B_{max} responded while only 3 of 14 with a higher B_{max} responded. The B_{max} of subjects who failed to respond was not significantly different from elderly controls.

Conclusions: 3H-imipramine binding is greater in the elderly, and among depressed elderly it is significantly lower than in age-matched controls. Within the depressed group, lower B_{max} is associated with significant clinical response. Implications are discussed.

NR103**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****LEARNED HELPLESSNESS AND HIGH MHPG DEPRESSIONS**

Jacqueline Samson, Ph.D., Rsch. Fellow, Harvard Med. School, Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115, Steven Mirin, M.D., Stuart Hauser, M.D., Brenda Fenton, Benjamin Gerson, M.D., Joseph J. Schildkraut, M.D.

Summary:

Studies from our laboratory, using the learned helplessness paradigm in animals, have shown that increases in brain levels of MHPG result from exposure to uncontrollable stressors and that these alterations may be conditioned. This suggests that depressions characterized by high urinary MHPG levels may represent conditioned responses to uncontrollable environmental stressors and may be associated with generalized expectations of powerlessness. In a preliminary study, feelings of powerlessness and locus of control beliefs were assessed prior to treatment in 18 clinically depressed patients using the Kobasa Hardiness Questionnaire and the Rotter Internal-External Control scale. Concurrently, urinary MHPG levels and platelet MAO activity were determined under drug-free conditions. Higher MHPG levels were associated with feeling of powerlessness ($r = .47$, $p = .05$) and with lower social status ($r = .57$, $p < .01$). Although external control scores showed a significant correlation with feelings of powerlessness ($r = .62$, $p < .01$), they did not correlate strongly with MHPG levels ($r = .22$, N.S.). However, high external control scores were significantly associated with low platelet MAO activity ($r = .55$, $p < .05$). These findings will be discussed in terms of a conditioned vulnerability model of depressions.

NR104**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****NEUROENDOCRINE RESPONSE TO MAXIMAL EXERCISE STRESS**

Marvin A. Oleshansky, M.D., Div. NP, WRAIR, WRAMC, Washington, DC 20307-5100, James L. Meyerhoff, M.D., Edward H. Mougey, M.S., Robert L. Herman, M.D., Jerel L. Zoltick, M.D.

Summary:

Plasma β -lipotropin (β -LPH) and β -endorphin (β -END) levels during and after maximal exercise were measured in healthy volunteers to characterize the extent and duration of hypothalamic/pituitary (H/P) responses to stress. Since previous studies have noted an effect of prior physical training on H/P responses, a range of highly fit to non-fit subjects was studied.

A maximal exercise treadmill test (ETT) was performed on ten healthy male subjects, mean age 39.4 ± 3.5 years (range 24-61 years). Maximal ETT time provides an index of fitness. The exercise was performed on a treadmill at a constant rate of 3.3 mile/hr with a 5% increase in grade every three min until exhaustion. Plasma was collected for β -LPH and β -END immediately prior to exercise (baseline), immediately following the completion of exercise (maximal exercise) and fifteen min after exercise (recovery). β -LPH and β -END were assayed individually by RIA after extraction from plasma. Mean maximal ETT time was 15.4 ± 0.9 min (range 11-19 min). Mean increases in plasma β -LPH and β -END levels from baseline to maximal exercise were 190.4 ± 36.9 and 34.2 ± 6.4 pg/ml respectively. These values were poorly correlated with ETT time with R coefficients of 0.37 (n.s.) and 0.16 (n.s.). The mean changes of plasma β -LPH and β -END levels from maximal exercise to recovery were 2.5 ± 41.1 (range -136 to +243) and -2.6 ± 7.8 (range -33 to +37) pg/ml and were correlated with ETT time with R coefficients of -0.79 ($p < 0.01$) and -0.79 ($p < 0.01$) respectively.

Recent work from several laboratories has identified an alteration in the regulation of H/P activity in depression. The current finding that changes in plasma β -LPH and β -END levels during a fifteen minute recovery period after exercise are highly inversely correlated with fitness as expressed by maximal ETT time suggest that future studies on H/P activity need to take into account the fitness of subjects and time of sampling after the termination of stress.

NR105
MHPG EXCRETION IN LATE LIFE DEPRESSION

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Robert C. Young, M.D., Division of Geriatric Services, The New York Hospital-Cornell Medical Center, Westchester Division, 21 Bloomingdale Rd., White Plains, NY 10605, George S. Alexopoulos, M.D., Charles A. Shamoian, M.D., J. John Mann, M.D.

Summary:

Dysfunction of brain monoamine neurotransmitters including noradrenaline (NE) may be part of the pathophysiology of major depression of late life especially. Urinary excretion of the metabolite of NE, 3-methoxy-4-hydroxyphenylethylene glycol (MHPG), has been used as one indirect measure of brain and peripheral NE metabolism. Therefore urinary excretion of MHPG was measured in geriatric depressed patients. The subjects were eleven psychiatric inpatients with major depression by DSM III criteria, whose first episode of illness was at ≥ 60 years of age. Their mean age was 78.1 yrs. \pm 5.8 yrs. (S.D.); ten were female. Serial 24 hour urine collections were obtained on a tyramine-free diet. MHPG was detected by gas chromatography-mass spectrometry. Average individual urinary MHPG excretions ranged tenfold. MHPG excretion was not significantly correlated with age ($r_p = -.28$) or total (21 item) Hamilton Depression Rating Scale score ($r_s = .06$). However it was positively correlated with Minimental State score ($r_s = 0.62$, $p < .05$). Treatment with nortriptyline, which inhibits NE reuptake, was associated with reduction in urinary MHPG excretion after four weeks in four of five patients ($t = 2.361$, $df = 4$, $p < .10$). Reduction of MHPG excretion was inversely correlated with plasma nortriptyline concentration (80-281 ng/ml) in this sample ($r_p = -0.82$). These preliminary data suggest a relationship between urinary MHPG excretion and Minimental State scores in symptomatic late life depressives. They also suggest that treatment with nortriptyline is associated with a concentration-dependent reduction in urinary MHPG excretion.

NR106
PLASMA MELATONIN AND CORTISOL RHYTHMS IN AGING

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

N.P.V. Nair, M.D., Douglas Hospital Research Centre, 6875 LaSalle Blvd., Verdun, Quebec, Canada H4H 1R3, N. Hariharasubramanian, M.D., Carmencita Pilapil, M.Sc., Ramsey Yassa, M.D.

Summary:

The circadian rhythm of plasma melatonin and cortisol were investigated in 7 normal young men (mean age: 21.1 years) and in 4 normal older men (mean age: 64 years). The day length at the time of study was 11 hours and the subjects were indoor with lights of 500 lux. The findings: there was a significant reduction in 24 hour secretion ($p = 0.003$) and peak levels ($p = 0.03$) of melatonin in the elderly compared to the young subjects. Also in the elderly, there was a greater lag in the onset of significant nocturnal elevation, from sunset time (4.4 hours) than in the young (2.5 hours), as well as a delay in the time of nocturnal peak, at 04:00 a.m. in the elderly as compared to 02:00 a.m. in the young men. *The cortisol rhythm did not show any significant age related changes.* These changes in melatonin rhythm may reflect age related alterations in neurochemical events specifically associated with melatonin production. It is proposed that plasma melatonin rhythm may be a useful index of brain aging.

NR107

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

BUPROPION METABOLITES, HVA AND CLINICAL RESPONSE

Robert N. Golden, M.D., LCS/NIMH, Bldg. 10, Rm 4S239, 9000 Rockville Pike, Bethesda, MD 20205-1000, C. Lindsay DeVane, Pharm.D., Matthew V. Rudorfer, M.D., Michael A. Sherer, M.D., S. Casey Laizure, Pharm. D., Markku Linnoila, M.D., William Z. Potter, M.D.

Summary:

Bupropion (BUP) is a new antidepressant characterized preclinically as a weak inhibitor of dopamine (DA) reuptake with appreciable effects on norepinephrine or serotonin reuptake or on monoamine oxidase activity. We have studied the relationships among BUP and its metabolites, hemovanillic acid (HVA), and clinical response in depressed patients.

Changes in plasma levels of the DA metabolite HVA following treatment distinguished non-responders from responders. In 4 non-responders, HVA rose from 52.1 ± 5.6 pmol/ml to 70.9 ± 5.6 following BUP treatment ($p < .02$). In contrast, responders did not show a significant change in plasma HVA (pretreatment HVA = 41.7 ± 4.0 pmol/ml; post-treatment HVA = 42.1 ± 3.3 ; $n=6$).

Following 4 weeks of treatment, metabolites predominated over BUP in the CSF of the 6 subjects in whom samples were obtained: threohydrobupropion (T-B) concentration was 40 times greater than BUP concentration; hydroxybupropion (OH-B) and erythrohydrobupropion (E-B) concentrations were 6 times greater than that of BUP. There was a strong correlation between CSF and plasma metabolite concentrations (T-B plasma vs CSF $r = .94$, $p < .01$; OH-B $r = .83$, $p < .05$; E-B $r = .82$, $p < .05$), indicating that plasma levels of metabolite reflect CSF concentrations.

Plasma levels of BUP itself did not appear to be related to outcome. However, higher plasma levels of OH-B and E-B and of the sum of the metabolites were associated with poor response. Strikingly, OH-B levels were > 1200 ng/ml in all 5 non-responders and < 1200 in all 7 responders ($p < .002$). Further, OH-B plasma levels correlated with post-treatment plasma HVA levels ($r = .71$, $p < .05$). Thus OH-B, perhaps through activation of DA systems, appears to be associated with poor clinical outcome when present in high concentrations in depressed patients receiving bupropion treatment.

NR108

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

BUPROPION IN PATIENTS WITH HEART FAILURE

Steven P. Roose, M.D., 722 W. 168th St., New York, NY 10032, Alexander H. Glassman, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N.

Summary:

The safe and effective pharmacological treatment of the depressed patient with cardiovascular disease remains a significant clinical problem. In patients with pre-existing bundle branch block, standard tricyclic treatment carries a significant risk of serious conduction complications, specifically 2 to 1 heart block. In patients with left ventricular impairment, there have been two studies demonstrating that imipramine does not cause deterioration of left ventricular function as measured by radionuclide ejection fraction. However, in the patient with congestive heart failure, imipramine is far from safe because of a 50% rate of TCA-induced orthostatic hypotension.

Bupropion is a new antidepressant, of the aminoketone class with a chemical structure that is unrelated to the tricyclics, which has been approved by the FDA for release and should soon be available to the clinician. To date, bupropion has not caused adverse cardiac complications in patients free from cardiovascular disease. The question remained, however, would bupropion be safer than a tricyclic in a patient population with severe left ventricular impairment. Therefore, we compared the effect of bupropion and imipramine in a double-blind placebo cross-over study in a group of depressed patient with congestive heart failure. Left ventricular ejection fraction as determined by radionuclide was done at baseline and repeated on each drug. Lying and five minutes standing blood pressures were collected three times a day throughout baseline and drug treatment.

The baseline ejection fraction of the group of 12 patients was 34%, on bupropion 33%, and on imipramine 30%. Thus, neither drug had a significant adverse effect on left ventricular performance. However, 6 of 12 (50%) patients could not tolerate imipramine because of severe orthostatic hypotension whereas none of the 12 patients treated with bupropion had similar problems. Thus, in patients with impaired left ventricular performance, bupropion appears to be an antidepressant that does not cause adverse effect on left ventricular performance and, most significantly, does not induce orthostatic hypotension.

NR109**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****BUPROPION: CONCENTRATION-RESPONSE RELATIONSHIP**

R. Kumar, M.D., Kansas Univ. Med. Center, 39th & Rainbow Blvd., Dept. of Psychiatry, Kansas City, KS 66103, Sheldon H. Preskorn, M.D., Carroll W. Hughes, Ph.D., Sieglinde C. Othmer, Ph.D., Ekkehard Othmer, MD.

Summary:

Antidepressant efficacy of bupropion (Welbutrin) was evaluated in an amitriptyline-controlled, double-blind, random assignment study of hospitalized adult patients meeting DSM-III criteria for major depressive disorder. Steady-state trough plasma levels of bupropion were drawn 11-12 hours after the last dose on days 14, 21, and 28 of treatment and assayed using an antibody specific for the parent compound. Patients were evaluated at baseline and on days 14, 21, and 28 using Hamilton depression and anxiety scales (HAM-D and HAM-A) and Zung self-rating scales for depression and anxiety (Zung-D and Zung-A.) This analysis is based on 15 of the 21 bupropion-treated patients. The percent change in scores from baseline were plotted as a function of plasma levels and regression analyses were performed revealing correlation between antidepressant response and increasing drug concentration. The best fit was achieved on day 21 (Table A.) The data for Day 21 was further divided into three groups based on plasma drug concentration: (a) less than 100 ng/ml, (I), (b) 100-200 ng/ml, (II), and (c) more than 200 ng/ml, (III.) A better antidepressant response was observed in patients with high as compared to low blood levels of bupropion (Table B.) Group III differed from group I on the HAM-D ($p < .01$) and Zung-D ($p < .05$.) Maximum antidepressant response occurred at concentrations above 200 ng/ml of bupropion. Significant linear relationships were observed between antidepressant response and steady-state plasma bupropion levels.

Table A

HAM-D: $y = 33.6 \pm 0.19x$, $r = .58$
 $F(1,13) = 6.8$, $p < .02$

ZUNG-D: $y = 5.9 \pm 0.11x$, $r = .47$
 $F(1,13) = 4.3$, $p < .06$

| | I (n=5) | II (n=5) | III (n=5) |
|--------|---------|----------|------------------|
| HAM-D | 45(10) | 59(14) | 82(5) I vs. III* |
| HAM-A | 40(14) | 61(18) | 68(7) |
| ZUNG-D | 15(5) | 17(10) | 36(7) I vs. III* |
| ZUNG-A | 12(8) | 27(7) | 28(4) |

Table B

$y = \% \text{ change in score.}$
 $x = \text{bupropion plasma conc.}$

Mean \pm (SEM), * = $p < .05$ one tail student t-test

NR110**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****COHERENCE (1 TO 8Hz) AS QUANTITATIVE ELECTROENCEPHALOGRAPHY MARKER OF MAJOR DEPRESSION**

Arnold L. Lieber, M.D., St. Francis Hospital, 250 West 63rd Street, Miami Beach, FL 33141, Leslie S. Prichep, Ph.D., Kenneth Alper, M.D.

Summary:

Seventy-six inpatient RDC major depressives (51 primary and 25 secondary), drug free for at least seven days, were examined by quantitative electroencephalography (QEEG). Multivariate analyses of variance were performed on several QEEG variables identified in an earlier study as discriminators of major depressive subtypes. Inter-hemispheric incoherence (wave shape asymmetry) in the delta and theta frequency bands was present to a statistically significant degree in all of the subjects. Secondary major depressives had significantly less delta incoherence than primary major depressives in both anterior and posterior brain regions. Depression secondary to OBS was distinguished from other secondary depression by the presence of significant slow wave excess in the former only. The ability of beta activity to discriminate unipolar from bipolar major depression was confirmed.

NR111

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

BRAIN SPECT AND MAGNETIC RESONANCE IMAGING IN DEPRESSION

C. Edward Coffey, M.D., P.O. Box 3920, Duke Medical Center, Durham, NC 27710, Burton P. Drayer, M.D., Daniel Gianturco, M.D., Daniel Sullivan, M.D.

Summary:

Patients referred for ECT at our institution undergo thorough neurologic assessment prior to the therapy and, in the presence of focal CNS deficits, are studied further with brain CT scanning. Recently we have extended this work-up to include more detailed anatomic assessment with brain nuclear magnetic resonance imaging (MRI) and determination of cerebral blood flow (CBF) with single photon emission computed tomography (SPECT). We will describe a series of patients with major depression and negative neurologic histories who had focal CNS deficits on examination, but in whom brain CT scans were entirely normal. Further neuroimaging assessment with SPECT revealed evidence of hemispheric asymmetry in CBF which correlated with the side of the focal deficits; in some of these cases MRI revealed lesions that had not been apparent on CT and which correlated with the asymmetric CBF. The significance of these findings for the pathophysiology of depression remains unclear. However, the technologies of SPECT and MRI will be available to most general psychiatric practices in the near future, and it will be important to establish their role in the clinical assessment of patients with major psychiatric disturbances and focal CNS deficits.

NR112

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

CLINICAL AND DST CORRELATES OF ECT RESPONSE

Leon Grunhaus, M.D., Assistant Professor of Psychiatry, Director, Inpatient Service, Clinical Studies Unit, University of Michigan Hospital, 1405 E. Ann St., Ann Arbor, MI 48109, Kirsten Alcser, Ph.D., Roger F. Haskett, M.D., John F. Greden, M.D., Thomas Zelnik, M.D.

Summary:

The prediction of ECT response is an important element of psychiatric practice. Clinical features and neuroendocrine responses have been suggested as predictors of ECT response. Good responders to ECT are usually those with endogenous, retarded and delusional clinical features, while poor responders are those with neurotic, anxious and atypical clinical features. Studies using DST values as predictors of ECT response have produced ambiguous results, both DST suppression and non-suppression have been associated with favorable outcome. To test these response predictors, we studied 26 markedly depressed medication non-responsive patients treated with modified ECT. All patients met RDC/SADS diagnosis of MDD and had an HRSD score of 20 or more. Clinical ratings and 1 mg DST were performed weekly, not on ECT days. Raters were blind to research data.

Results: 58% of patients were good responders (patients categorized as good or partial/poor responders according to changes in the 17-item HRSD); they were more often psychotic and retarded, had distinct quality of mood and lower somatic anxiety ratings. When pre-ECT HRSD psychic and somatic anxiety scores totaled, higher values predicted poorer ECT response. There was no difference in pre-ECT total HRSD scores between good responders and partial/poor responders. All DST suppressors and 50% of the non-suppressors responded well to ECT.

Conclusions: 1) Specific clinical features are suggestive of good and poor response to ECT's and 2) DST suppression seems to predict good response to ECT's while non-suppression associates to poorer response and may be an expression of a more severe form of depressive illness.

NR113 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
LEICESTER (UK) CLINICAL TRIAL OF ECT VERSUS DUMMY ECT

S. Brandon, M.D., Dept. of Psychiatry, Clinical Sciences, Leicester Royal Infirmary, Leicester, England, R.L. Palmer, M.D., P. Crowley, M.B., S. Eason, M.B.

Summary:

In a double blind clinical trial all patients referred for electro-convulsive therapy were randomly allocated to real or dummy E.C.T. Of 186 patients referred 48 did not participate. 95 met the criteria for a depressive episode and 22 for schizophrenia. Treatment was twice weekly to a maximum of eight shocks, no antidepressants were prescribed during the trial. Schizophrenic patients remained on baseline medication. In depressed patients improvement was significantly greater at 2 and 4 weeks in the real treatment group. For the schizophrenic patients those receiving real E.C.T. were substantially better on the Montgomery Asberg Schizophrenia scale, the visual analogue global psychopathology scale and the depression scale. The differences on the MASS and visual analogue global psychopathology scale were not due to improvement in depressive symptoms. The implication of these findings is discussed.

NR114 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
CT CHANGES IN LATE LIFE DEPRESSION

Peter V. Rabins, M.D., Meyer 279, Johns Hopkins Hospital, Baltimore, MD 21205, Godfrey Pearlson, M.D., Paul Moberg, M.A., Won Kim, M.D.

Summary:

We compared head CT scan attenuation numbers of 10 patients with senile dementia of the Alzheimer's type (SDAT), 7 elderly patients with DSM-III major depression and 17 age and sex matched normals. Depressed patients (like those with SDAT) had significantly lower mean CT attenuation numbers (MAN) in each of 7 brain regions studied compared to normal controls ($p < .05$ to $< .001$). MAN of depressed patients were not significantly different from those of patients with SDAT. This confirms Levy's (1982) previous reports of abnormal "brain density" in elderly depressives. Depressed patients also had increased ventricle-to-brain ratios (VBR) compared to normals ($p < .05$), but less than the SDAT dementia group ($p < .05$)

Normals showed no correlation between VBR and mean attenuation numbers ($r = .00$). In demented patients, as predicted, there was a negative correlation between VBR and MAN ($r = -.82$, $p < .005$) suggesting that parenchymal loss accounts for ventricular dilation. This relationship was reversed in the depressives where VBR correlated positively with MAN ($r = .71$, $p < .05$). In late life depression, enlarged ventricles and diminished MAN may result from a different process than in SDAT.

NR115 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
SEIZURE DURATION AND THE CLINICAL EFFECTS OF ECT

Alexander L. Miller, M.D., Associate Professor, Department of Psychiatry, Univ. of TX Health Science Center, San Antonio, TX 78284, Raymond Faber, M.D., John Hatch, Ph.D., Harold Alexander, M.D.

Summary:

It is generally agreed that a brain seizure is essential for ECT efficacy, but it is unclear how the duration of the seizures relates to the clinical effects of ECT. Data from patients receiving multiple monitored ECT have suggested that cumulative seizure duration (SD) must exceed a threshold before improvement occurs and that improvement is a function of SD over a large range above this threshold (Maletsky, *Compr. Psych.* 19, 541).

We studied 29 depressed patients given unilateral ECT. SD was measured by EEG for each patient's first six treatments. Hamilton ratings of depression were done before the first and after the third and sixth treatments. Twenty min prior to each treatment the patients learned new verbal and non-verbal material, and were tested for recall at 20 min and 4 h after each treatment. After the 4 h testing they learned new material, on which they were tested at 24 h (no intervening treatment).

We found that forgetting of non-verbal material correlated significantly with SD. Forgetting of verbal material did not correlate with SD. No relationship between SD and changes in Hamilton ratings was found.

Since the conclusion from these data is that longer SD increases acute amnesic effects of ECT but not efficacy, we looked for treatment variables that affect SD. Both methohexital dose and succinylcholine dose correlated inversely with SD. Methohexital dose, however, correlated positively with forgetting scores when SD was partialled out. Thus, increasing the dose of methohexital would not accomplish the goal of lessening ECT-produced amnesia, whereas increasing the dose of succinylcholine may be helpful.

NR116**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****TRANLYCYPROMINE: KINETICS AND HYPOTENSIVE ACTIONS**

Alan G. Mallinger, M.D., Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, David J. Edwards, Ph.D., Jonathan M. Himmelhoch, M.D., Steven Knopf, B.S., Joan Ehler, M.D.

Summary:

Tranlycypromine (TCP) (Parnate®) produces irreversible inhibition of MAO, yet other clinically important actions of this drug may be concentration-dependent. Therefore, we investigated the pharmacokinetics of TCP (about which little is known at present) in 9 depressed subjects, following oral administration of a 20 mg dose. Blood was collected at 16-17 points over an interval from 0-10 hrs. Plasma TCP was measured in duplicate using gas chromatography/mass spectrometry. We found that TCP was rapidly absorbed; peak levels ranging from 64.5-190 ng/ml (mean \pm SD = 112 ± 41 ng/ml) were attained within 0.67-3.50 hrs (mean \pm SD = 1.55 ± 0.99 hrs). Absorption was biphasic in 7 of the 9 subjects, but the early peak was much larger in all but 2 subjects. Elimination of TCP was also rapid, with a half-life ranging from 1.54-3.16 hrs (mean \pm SD = 2.45 ± 0.57 hrs). Blood pressure (BP) and pulse (P) were measured over the course of each experiment. During the interval from 2-7 hrs post-dose, standing systolic and diastolic BPs were significantly lowered, and standing P was significantly raised, compared to baseline (paired t-tests). For individual subjects, the time of onset for the hypotensive effect on standing systolic BP was correlated with the time of the peak plasma TCP concentration ($n=9$, $r=0.93$, $p<0.001$). Significant postural lowering of systolic BP (sitting vs. standing), compared to baseline, was found at 1, 2, and 3 hrs post-dose, but not at later times (paired t-test). For the overall subject group, mean postural lowering of systolic BP was correlated with mean plasma TCP concentrations measured at the same time points ($n=7$, $r=0.88$, $p<0.01$). Thus, at least some effects of TCP on BP appear to be concentration-dependent (perhaps due to a receptor-mediated action). In practical terms, our findings suggest that patients who experience clinically significant hypotensive reactions to TCP may benefit from changes in their dose regimen aimed at minimizing peak drug levels.

NR117**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****TARGETING IMIPRAMINE DOSE IN DEPRESSED CHILDREN**

Floyd R. Sallee, M.D., Assistant Professor of Child Psychiatry; Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, Michael D. Rancurello, M.D., Richard L. Stiller, Ph.D., James M. Perel, Ph.D.

Summary:

Recent research has shown a minimum therapeutic plasma conc. range for imipramine plus desipramine of 150-250 ng/ml in children. To achieve this level rapidly and safely, pharmacokinetic data from each individual patient is utilized to empirically estimate IMI dose. Pharmacokinetic studies consist of a 25 mg test dose of IMI with multiple time-concentration samples over a 30 hour period. In a pilot sample of 12 children, mean age 11.1 ± 1.5 elimination half-life of IMI + DMI was 13.27 ± 6.26 hr. In a subset in which absorption kinetics was also obtained mean plasma clearance of IMI + DMI was $.0166 \pm .0066$ ml/min/kg ($N=8$). Using elimination half-life and clearance values along with IMI + DMI levels at 24 hours, we have been able to estimate steady-state IMI + DMI levels in children. We have found this method useful in reducing total time needed to achieve targeted IMI + DMI levels in children and for higher potentially therapeutic levels of 350 ng/ml in prepubertal depression with hallucinatory episodes.

NR118**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****RAPID DOSING TRICYCLIC ANTIDEPRESSANT LEADS TO EARLY RESPONSE**

Jack Hirschowitz, M.D., Dept. of Psychiatry, University of Cincinnati Medical Center, Mail Loc. #559, Cinti., OH 45267, Jerry A. Bennett, Pharm. D., Frank Zemlan, Ph.D., David L. Garver, M.D.

Summary:

A rapid onset of antidepressant action is of primary concern in the treatment of depression. Our study compares a rapid dosing of desipramine (DMI) to a more traditional dosing schedule to assess potential earlier onset of action.

In this preliminary report of our ongoing study 17 patients with a DSM III diagnosis of major depressive disorder with melancholia were randomly assigned to either rapid dose DMI (50 mg twice a day and 100 mg at bedtime) or a traditional dosing regimen (50 mg at bedtime for 2 days, then 50 mg twice daily for 2 days, then 50 mg three times daily for 2 days, then 100 mg twice daily). Patients were required to achieve a HAM-D score greater than 17 and undergo 4 days of drug free hospitalization prior to random group assignment.

HAM-D ratings were performed by the same rater on days 7, 14 and 21 of the study.

Analysis of variance of the HAM-D scores of the two groups with repeated measures across all weeks revealed a significant improvement in depression ratings across weeks of drug administration ($F = 22.32$; $df = 2, 6$; $p < 0.0001$) and a significant interaction between drug treatment and time on drug ($F = 4.37$; $df = 2, 6$; $p < 0.04$). Individual comparison of the two drug treatments indicated the rapid dosing group ($N = 11$) improved more significantly than the traditional dosing group ($N = 6$), ($p < 0.02$) at the end of one week.

This higher level of improvement was maintained over the 3 week study with no difference in intergroup side effects.

Our finding does confirm an earlier antidepressant response when higher doses of DMI are administered from day one.

NR119**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****CLOMIPRAMINE: AN INTRAVENOUS PULSE LOADING REGIMEN**

Bruce G. Pollock, M.D., Assistant Professor of Psychiatry, Clinical Pharmacology Program, Western Psychiatric Institute & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, James M. Perel, Ph.D., Michael Shostak, M.D., David J. Kupfer, M.D., Duane Spiker, M.D., Seymour Antelman, Ph.D.

Summary:

The relative contribution of pharmacokinetic vs. pharmacodynamic factors in therapeutic onset to tricyclic antidepressants was examined using a pulse-loading dose strategy with intravenous (IV) clomipramine (CMI). Five depressed inpatients (1 male, 4 female, \bar{x} age 43.4 ± 6.6 yrs) were found by two independent psychiatrists to meet DSM III criteria for Major Depressive Episode (\bar{x} duration of the index episode 6.4 ± 2.7 months). After giving informed consent, all patients were maintained drug free for 2 weeks, receiving only supportive treatment. At the conclusion of this 14 day period, the \bar{x} HRS score was 22.6 ± 2.4 and all patients manifested typical disturbances in their sleep EEGs consistent with moderately severe depression. An evening infusion of 75 mg CMI was then administered, followed by 200 mg IV the next evening. The infusions were well tolerated, transient nausea being the only significant side effect. Half-life of CMI was 28.3 ± 4.6 hr; the desmethyl metabolite was *not* detected after the initial 2 infusions. Sleep was effected immediately with a profound suppression of REM. On the morning after receiving the second infusion, patients reported an improvement in their sleep and \bar{x} HRS scores had dropped to 14.6 ± 5.5 . All five consecutively treated patients continued to improve *without any further medication*; 11 days after receiving the second infusion \bar{x} HRS was 6.8 ± 1.5 . The patients then received 8 days of further IV CMI after which their \bar{x} HRS was 4 ± 1.1 . This data is highly significant when compared to matched, control patients receiving IV saline. The pattern of response to IV pulse-loading with CMI approximates a pharmacodynamic, anticlockwise hysteresis. This suggests that Major Depression may be managed rapidly with small total doses of medication, provided they are strategically administered.

NR120**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****RESPONSE TO T₃ IN IMIPRAMINE RESISTANT DEPRESSION**

Michael E. Thase, M.D., Dept. of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213, David J. Kupfer, M.D., David B. Jarrett, M.D., Ellen Frank, Ph.D.

Summary:

The value of L-triiodothyronine (T₃; 25 mcg/d) as an adjunctive treatment for tricyclic resistant depression was studied in 20 outpatient recurrent major depressives (RDC/DSM-III). Patients had not responded to ≥ 12 weeks imipramine treatment at maximum tolerated dosage (\bar{x} 240 mg/d, plasma levels > 225 ng/ml). Mean pre-T₃ Hamilton (HRS) score was 16.9 (± 5.4). All patients were euthyroid; none had an exaggerated TSH response to TRH. IMI dosage was held constant over 2.4 weeks of adjunctive T₃ treatment. Results were compared to a sample of 12 matched historical controls who received continued IMI but not T₃. Mean HRS scores did not significantly improve on T₃ (Δ HRS = 4.0); only 5 patients remitted. Control rates were virtually identical (Δ HRS = 5.1; 4/12 remitted). Outcome was not associated with TSH response to TRH. Eight T₃ nonresponders subsequently remitted with alternative treatments. Failure of T₃ to enhance response to IMI in this sample may be related to the fact that all patients were euthyroid or the length and intensity of initial IMI treatment.

NR121**Wednesday, May 22, 1985, 12 Noon-2:00 p.m.****DOSE EFFECT OF AMOXAPINE ON DOPAMINE BLOCKADE**

Raymond F. Anton, M.D., Psychiatry Service, VA Medical Center, Charleston, SC 29403, Bruce I. Diamond, Ph.D., Ana Hitri, Ph.D., Mark Shelhorse, M.D.

Summary:

We have shown previously that amoxapine treated patients have elevated prolactin and neuroleptic activity in their serum. The purpose of this study was to examine in a dose dependent manner the dopamine blockade efficiency of amoxapine.

Fourteen inpatients diagnosed by DSM III as major depressives (9 with psychotic features) were given single blind divided daily doses of placebo for 5 days, then sequential amoxapine doses of 300 mg (2 wks), 400 mg (1 wk), and 500 mg (1 wk). Blood was drawn at 8 AM prior to the AM dose twice during the placebo and each dosing period. Split serum was measured for prolactin (PRL) by RIA and serum neuroleptic activity (SNA) utilizing a radio-receptor assay with chlorpromazine (CPZ) standardization. The values of PRL and SNA obtained on each amoxapine dose were averaged and differences between doses were analyzed by repeated measures ANOVA. Mean \pm S.E. for PRL (ng/ml) at baseline, 300, 400, 500 mg amoxapine were, respectively, 4.2 ± 0.8 , 13.2 ± 1.9 , 12.9 ± 2.2 , 14.9 ± 2.0 ($p < 0.01$). There was a significant main effect of treatment with amoxapine causing a mean 3-fold (range 2-10 fold) increase in PRL but with no difference between doses. Mean \pm S.E. for SNA (ng/ml CPZ-EQ) at baseline, 300, 400, 500 mg amoxapine were, respectively, 1.9 ± 1.0 , 10.6 ± 4.6 , 8.1 ± 2.3 , 17.0 ± 6.7 ($p < 0.01$). There was a main effect of treatment with amoxapine showing a significant SNA (range 0-74 ng/ml CPZ-EQ) at every dose but no significant difference between doses was observed. The overall correlation between PRL and SNA across all patients and doses was $R = 0.3$ (N.S.).

The data support other evidence that amoxapine possesses dopamine blocking capability in man. However, there appears to be no relationship between dose (300-500 mg) and efficacy of dopamine blockade. Also, PRL elevation and SNA appear to be independent measurements of amoxapine's neuroleptic potential.

NR122 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
SEASONAL AFFECTIVE DISORDER AND LIGHT TREATMENT IN CHILDREN

N.E. Rosenthal, M.D., 9000 Rockville Pike, Room 4S-239, Building 10, Bethesda, MD 20205-1000, Constance J. Carpenter, B.S., Steven P. James, M.D., Barbara L. Parry, M.D., Susan Rogers, R.N., Thomas A. Wehr, M.D.

Summary:

We have encountered 7 children with seasonal affective disorder (S.A.D.). Five have at least one parent with S.A.D. Age range is 6-14 years and age of onset ranges from 2-10. Four are boys and three girls. Commonly patients present with school difficulties and fatigue in the fall semester. They want to sleep longer and have a hard time getting up in the morning. Parents report decreased activity level, sadness, irritability, anxiety, social withdrawal, crying spells and headaches. Children usually perceive these changes as coming from the external world eg, unfair demands and overwhelming work load. January and February are the worst months. Five out of seven patients have used bright (2500 lux) full-spectrum light in the early morning and evening hours with extremely beneficial effects. All symptoms are reversed and parents, teachers and children have commented on the change. It seems that children require less exposure to light than adults with S.A.D.; one hour a day may be sufficient. It is important for educators, counselors and clinicians to recognize this condition in the differential diagnosis of school difficulties in fall and winter, especially as it appears to be so readily reversible. Case histories will be presented and discussed.

NR123 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
BIOLOGICAL EFFECTS OF BRIGHT LIGHTS

William F. Byerley, M.D., Department of Psychiatry M-003, University of California, San Diego, San Diego, CA 92093, Daniel F. Kripke, M.D., Craig S. Risch, M.D., J. Christian Gillin, M.D., David S. Janowsky, M.D., Donal Parker, M.D., Lawrence G. Rossman, M.S.

Summary:

Bright light decreases plasma melatonin levels in normal subjects (Lewy et al 80) and ameliorates symptoms of depressed patients (Lewy et al 82, Kripke et al 83, Rosenthal et al 84). One minute of light suppresses melatonin production in the rat and hamster; therefore, we decided to test 5 minute light exposures. 8 normal male subjects (mean age 28) were studied on 2 nights. Each night blood samples were collected at 1:30, 1:40, 1:50, 2:20, 2:40 and 3AM. At 2AM subjects were exposed to bright light (2500 - 7500 lux) for 5 minutes; the other night only artificial room light (<500 lux). The sequence was counterbalanced. Plasma melatonin and ACTH levels were determined using RIAs. 5 minutes of bright light compared to room light significantly decreased plasma melatonin concentrations — an analysis of variance for repeated measure revealed a significant ($p < 0.0365$) interaction effect between sequential values and treatment conditions — but levels ACTH were unchanged. Our finding has implication for psychiatric and endocrine therapy.

NR124 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
CORNELL SCALE OF DEPRESSION IN DEMENTIA (CSDD)

George S. Alexopoulos, M.D., New York Hospital-Cornell Med. Ctr., 21 Bloomingdale Road, White Plains, NY 10605, Robert C. Abrams, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.

Summary:

Depression and dementia frequently coexist. Depression is often found in demented patients while a considerable percentage of geriatric depressives develop a transient dementia syndrome. Depression rating scales have limited value for demented patients because they rely on responses from individuals with impaired memory and judgment. To avoid this problem, we have developed the CSDD, a 19-item instrument which can quantify depression using an interview with patients' caretakers. The CSDD was tested on 48 demented subjects (20 psychiatrically hospitalized, and 28 in nursing homes). The correlation (Cohen's Kappa) of total CSDD scores obtained by two independent psychiatrists was 0.64 and ranged from 0.88 to 0.96 in the individual items. The CSDD had high internal consistency (Kuder-Richardson coefficient 0.96). The concurrent validity of CSDD was tested by correlating CSDD scores with an independent global rating ($r_s = 0.83$), and with depression classified in four groups according to Research Diagnostic Criteria (RDC) ($r_s = 0.83$). CSDD scores of each group classified by RDC were significantly different from scores of each adjacent group; while the Hamilton Depression Rating Scale failed to make such differentiations. At total score 8, the sensitivity of CCSE was 84% and the specificity was 96%. We expect that CSDD will be a useful instrument in the investigation of heterogeneous groups of patients with permanent or transient cognitive dysfunction and psychopharmacological studies.

NR125
PREVALENCE OF PREMENSTRUAL SYNDROMES

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Cheryl M. McChesney, M.D., Univ. of Iowa College of Med., Dept. of Psychiatry, 500 Newton Road, Iowa City, IA 52242, Susan R. Johnson, M.D., Raymond R. Crowe, M.D.

Summary:

Halbreich and Endicott propose research criteria for 18 premenstrual syndromes. No population-based prevalence studies of these premenstrual syndromes or subtypes have previously been reported. We studied a stratified-random sample consisting of 996 women, ages 18 to early 50's, to determine the prevalence of these 18 premenstrual syndromes. These women were mailed two questionnaires: one designed by us concerning their menstrual, past medical, and socio-economic histories; and the Premenstrual Assessment Form (PAF), a 95 item questionnaire designed by Halbreich and Endicott. Preliminary analysis indicates close to 75% response rate of the women contacted. Women who were pregnant, postmenopausal, or not menstruating for other reasons were excluded (N=111). The results of the remaining women (N=581) were then classified according to Halbreich and Endicott's research criteria. Only 4% of this remaining sample had no significant change in symptoms from their usual nonpremenstrual state. For 25% of the sample, there was no suitable PMS category. 26% met PAF Major Depressive Syndrome, 2% had PAF Anxiety Syndrome, and 1% had PAF Angry Irritable Syndrome. Prevalence of the remaining PMS categories will be presented. This data suggests that while premenstrual symptoms are quite common, there is differentiation in the prevalence of the various PAF Premenstrual Syndromes.

NR126
CHARACTERISTICS OF PROBABLE ENDOGENOUS DEPRESSION

Wednesday, May 22, 1985, 12 Noon-2:00 p.m.

Donna E. Giles, Ph.D., Univ. TX Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235, A. John Rush, M.D., Michael A. Schlessler, M.D., Paul J. Orsulak, Ph.D., Howard P. Roffwarg, M.D.

Summary:

Discrepancies in findings concerning the RDC endogenous/nonendogenous classification may result from, among other factors, group assignment decisions. Some studies classify patients as Endogenous if they meet criteria for Probable Endogenous while other studies include these same patients in the Nonendogenous group.

We have compared RDC "definite endogenous," "probable endogenous," and "nonendogenous" patients using reduced REM latency (≤ 65.0 minutes) and dexamethasone nonsuppression (> 4.0 ug/dl) findings. Our purpose was to examine the biological validity of the Probable Endogenous category.

| | DEXAMETHASONE NONSUPPRESSION (%) | REDUCED REM LATENCY (%) |
|----------------------------|-------------------------------------|----------------------------|
| DEFINITE ENDOGENOUS (n=63) | 36.5 | 69.8 |
| PROBABLE ENDOGENOUS (n=46) | 23.9 | 37.0 |
| NONENDOGENOUS (n=36) | 11.1 | 36.1 |

These data will be discussed in light of our current understanding of biologic abnormalities in depression.

NR127 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
CHRONIC STRESS DOES NOT CAUSE MAJOR DEPRESSION

Naomi Breslau, Ph.D., Case Western Reserve University, Assoc. Prof., Dept. of Psychiatry, Cleveland, OH 44106, Glenn Davis, M.D.

Summary:

The "reactive-endogenous" dichotomy in depression was not incorporated in DSM III in part because the etiologic distinction was not supported by research. Nevertheless, stress has been proposed 1) as an *etiologic agent* in the genesis of the disorder and 2) as a *precipitant of episodes*. We compared the *rate, age of onset, and # of episodes* of Major Depression (MDD) in mothers of severely disabled children (chronic stress sample) with those in a geographically based probability sample of mothers (controls). DSM III MDD was ascertained by NIMH-DIS. Rates of MDD and age of onset were not significantly different in the 2 groups. # of lifetime episodes was significantly higher in MDD positives in the chronic stress sample, but # symptoms in worst episode was not.

| | n | age | 6 mo rate | Lifetime rate | Onset (yrs) | #episodes* | #Sx |
|----------------|-----|------|-----------|---------------|-------------|------------|---------|
| Chronic stress | 319 | 42±8 | 8.4% | 18.4% | 27±8.6 | 16±28 | 9.1±2.7 |
| Controls | 357 | 43±9 | 6.8% | 16.6% | 29±9.9 | 6.5±13 | 8.4±2.5 |

*p<.03

Rates of 16 MDD symptoms in depressed mothers in the 2 samples were not significantly different (p set at .003, Bonferroni inequality). With the exception of the difference in # of episodes, the findings support neither an etiologic nor a precipitant role for chronic stress in MDD.

NR128 **Wednesday, May 22, 1985, 12 Noon-2:00 p.m.**
PERSONALITY TRAITS AND ANTIDEPRESSANT RESPONSE

Eric D. Peselow, M.D., 1322 East 84th St., Brooklyn, NY 11236, Faouzia Barouche, M.D., Jill Munroe, Ronald R. Fieve, M.D.

Summary:

The purpose of this paper is to evaluate whether certain personality traits have any short-term (4-5 weeks) or long-term (6 month) predictive value in individuals with major depression who are treated with tricyclic antidepressants.

Over the past 2 years, we have examined 85 outpatients with major depression. At their initial visits all patients were rated with a Structured Interview for DSM III Personality Disorders (SIDP), which examined personality traits in all 11 DSM III personality disorder diagnosis.

Following a 7-10 day observation period & following a 7-10 day period on low-dose desipramine (50 mg) all patients still depressed were treated with 150-300 mg of desipramine over 4-5 weeks. Of 60 who remained on this regimen, 35 improved and 25 did not. Of the 35 who improved, 20 were able to sustain that improvement.

Our analysis noted that no personality trait predicted short-term response, but individuals with borderline, histrionic and narcissistic traits relapsed within 6 months following initial apparent clinical recovery.

NR129**Wednesday, May 22, 12 Noon-2:00 p.m.****DOPAMINE D2 RECEPTOR PET SCANS IN BIPOLARS**

Godfrey D. Pearlson, M.D., Assistant Professor of Psy., Meyer 279, The Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21205, Dean F. Wong, M.D., Robert F. Dannals, Ph.D., Larry E. Tune, M.D., Frederick Schaerf, M.D., Henry N. Wagner, Jr., M.D.

Summary:

Sixteen DSM III bipolar patients were studied with C-11 N-Methylspiperone PET imaging. Two had never received neuroleptics; 4 had been completely drug-free for at least 1 month at the time of scanning; of these 3 were acutely manic; the remainder were on stable lithium treatment. The dopamine D2 and serotonin S2 binding was estimated by the 43 min. caudate/cerebellum (Ca/Cb) and frontal/cerebellum (FC/Cb) ratios, respectively. No statistically significant difference was detected when patients were compared to 44 age and sex-matched controls. Ca/Cb ratio was significantly inversely correlated to the inter-episodic SANS (negative symptom score) ($<.01$) Pearson $r = -.8$ ($n = 9$). This correlation remained significant when a partial correlation for ventricular/brain ratio on CT scan was carried out.

NR130**Wednesday, May 22, 12 Noon-2:00 p.m.****NEUROPSYCHOLOGICAL EFFECTS OF LITHIUM**

Eric D. Shaw, Ph.D., Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021, J. John Mann, M.D., Peter E. Stokes, M.D., Alan Z.A. Manevitz, M.D.

Summary:

Bipolar patients in remission were assessed over a five-week period starting at their current lithium dosage, twice during a blind placebo and twice after their lithium was restarted. All patients were blind to their medication status. The test battery included: the Finger Oscillation or Tapping Test (motor speed), the Paced Auditory Serial Addition Task (information processing speed), the Buschke selective reminding protocol (long-term memory), and written associations to two target words within 60 seconds each (associational productivity and idiosyncrinity). Mood was assessed at each session using clinical interview, the Hamilton Depression Scale, the Longitudinal Rating of Manic States Scale and a Subjective State Questionnaire. Lithium level was measured by atomic absorption spectrophotometry. Lithium had a statistically significant detrimental effect on motor speed, memory and associational productivity and idiosyncrinity, and a clinically observable effect on information processing speed, such that these measures improved when lithium was discontinued and declined again when lithium was reintroduced.

NR131**Wednesday, May 22, 12 Noon-2:00 p.m.****LITHIUM IN PSYCHOTIC REFRACTORY DEPRESSION**

Carolyn Mazure, Ph.D., Dept. of Psychiatry, Yale-New Haven Hospital, 20 York Street, New Haven, CT 06504, J. Craig Nelson, M.D.

Summary:

A recent report indicated lithium augmentation was an effective treatment for some delusionally depressed cases refractory to neuroleptic-antidepressant treatment. The current retrospective study determined response rates to lithium augmentation (+Li) in 8 bipolar (BP) and 13 unipolar (UP) DSM III psychotic depressives refractory to 3 weeks of neuroleptic-desipramine treatment. These rates were compared with those for ECT - the usual treatment for nonresponsive delusional depression - in 15 UP psychotic depressives. In the patients receiving +Li, 6 of 8 BP patients responded while 2 of 13 UP patients responded, a significant difference (Fisher Exact Test, $p < .025$). Response in UP patients to ECT (9 of 15) was significantly greater than response to +Li (2 of 13) ($X^2 = 4.09$, $p < .05$). These data provide evidence that +Li is of practical value for BP psychotic depressives who do not respond to antipsychotic-antidepressant treatment, and show that ECT is the superior treatment for refractory UP delusional patients. The data also indicate that in future studies of +Li efficacy, UP and BP patients must be evaluated independently.

NR132 **Wednesday, May 22, 12 Noon-2:00 p.m.**
NEW TREATMENT FOR LITHIUM PROBLEM BIPOLAR PATIENTS

Ekkehard Othmer, M.D., Univ. of Kansas Medical Center, 39th & Rainbow, Kansas City, KS 66103, Sieglinde C. Othmer, Ph.D., Cheryl DeSouza, M.D.

Summary:

Lithium is the treatment of choice for prophylaxis of recurrent bipolar disorder. However, shortcomings of lithium treatment are: 1. Up to 20% of bipolar patients are resistant to lithium. 2. Severe side effects may necessitate drug discontinuation; 3. Recurrent depressive episodes while on lithium may necessitate additional antidepressant treatment.

This study reports preliminary results on the prophylactic properties of the monocyclic antidepressant bupropion in bipolar patients.

Method: For ethical reasons, only bipolar patients (DSM-III criteria, at least once hospitalized for mania) were enrolled who had either severe side effects to lithium or for whom lithium lacked prophylactic efficacy for mania, depression, or both. More than half of these patients showed marked deterioration in social and professional functioning. At this time, 27 of the expected total of 50 adult patients have entered the double-blind, randomly assigned, placebo controlled two-year out-patient study. Baseline assessments included physical examination, vital signs, EEG, EKG, laboratory screen, a 58-item adverse experience scale, the Hamilton Depression Scale, the manic behavior scale, the Global Assessment Scale (GAS), the SCL-90 and a social adjustment scale. All measurements were repeated at regular intervals. Study drug (bupropion or placebo) was started at 300mg/day and then titrated according to response (range 450-700mg/day).

Results: In a preliminary comparison with placebo, bupropion has statistically significant prophylaxis against mania. Patients on placebo experienced a manic breakdown after an average of 8 weeks. A manic relapse occurred in 11 of the 27 patients. 2 of these patients were on BUP, 9 were on placebo. 7 of these patients were crossed-over to open label BUP. Only 1 of these patients had a manic relapse and this patient was non-compliant with bupropion treatment.

Conclusion: Bupropion may be a viable alternative for bipolar out-patients who have severe side effects or fail to respond entirely to chronic lithium treatment.

NR133 **Wednesday, May 22, 12 Noon-2:00 p.m.**
BIPOLAR DISORDER FOLLOWING HEAD TRAUMA

Sashi Shukla, M.D., Dept. of Psychiatry & Beh. Sci., University Hosp., HSC T 10/020, Stony Brook, NY 11794-8101, Sukdib Mukherjee, M.D., Charles Godwin, M.D., Morton Miller, M.D.

Summary:

Although a high incidence of behavioral abnormalities following head trauma is recognized, there is no systematic data on bipolar disorder associated with head trauma. This is the first such report on 20 patients who met RDC diagnoses of Bipolar Disorder following closed head trauma.

Patients were selected from the neuropsychiatric clinics of two hospitals between March 1980 to March 1984. Severity of head trauma was classified on the basis of a review of the neurologic literature as mild, moderate and severe using length of post traumatic amnesia as the measure of severity. Family history of psychiatric illness was determined by interview of 85 first degree relatives.

Mean age at head trauma was 23 years (median 19.5) and 27.5 years (median 24) at onset of psychiatric illness. Onset of affective disorder followed head trauma by a mean duration of 4.4 years (median 2). BP-I illness was associated with a higher incidence of severe head trauma, abnormal EEGs, and post traumatic seizure disorder and a unipolar manic course of illness. The predominant mood during manic episodes was irritable rather than euphoric and less than a third of the patients showed psychosis. BP-I illness was associated with mild trauma and normal EEGs. The sample showed an absence of family history of Bipolar Disorder, Unipolar Depression being present in 22 relatives.

Neurologic findings were consistent with the neurologic literature on closed head trauma. Possible etiologic associations, lateralization findings and medicolegal implications are discussed.

NR134**Wednesday, May 22, 12 Noon-2:00 p.m.****SALIVA LITHIUM MONITORING IN PREPUBERTAL CHILDREN**

Elizabeth B. Weller, M.D., Department of Psychiatry, University of Kansas Medical Center, 39th & Rainbow, Kansas City, KS 66103, Ronald A. Weller, M.D., Mary A. Fristad, M.A., Michael Cantwell, M.D., Sheridan Tucker, M.D.

Summary:

Saliva lithium levels have been studied in adults as an alternative to plasma lithium monitoring. The saliva-serum lithium ratio is approximately 2:1 (range, 1.8-3.35) and is unaffected by lithium dose, saliva flow rate, and psychiatric diagnosis. This study compares saliva to plasma lithium levels in 14 prepubertal children aged 6-12 treated with lithium carbonate. 119 concomitant plasma and saliva lithium determinations were obtained during the study. Correlation coefficients, saliva:serum ratios, and regression equations were calculated with data from all subjects combined, and also for each subject individually. Both of these methods found saliva levels were correlated with serum levels. The relationship was greater when individual regression equations were used ($r = .83$). Saliva levels accurately and significantly predicted serum levels in 80% of individual regression equations. Greater variability was noted in saliva compared to serum lithium levels. Based on this study saliva monitoring may be possible for children treated with lithium.

NR135**Wednesday, May 22, 12 Noon-2:00 p.m.****EXACERBATION OF EXTRAPYRAMIDAL SYMPTOMS WITH ADDITION OF LITHIUM**

Gerard Addonizio, M.D., The New York Hospital-Cornell Medical Center, 21 Bloomingdale Road, White Plains, NY 10605, Steven D. Roth, M.D., Peter E. Stokes, M.D., Peter M. Stoll

Summary:

Although increased extrapyramidal symptoms (EPS) with the lithium-neuroleptic combination have been anecdotally reported, this is the first prospective study examining this interaction. Ten patients on a steady dose of neuroleptics for a mean of 9.8 days (range 5-19) were rated with a modified Simpson-Angus rating scale for extrapyramidal side effects the day before and the day after the addition of lithium, and every three days thereafter, for a total of four post-lithium measurements. Raters were blind and inter-rater reliability was good. Patients remained on steady or decreasing dose of neuroleptic during this period of time. A control group of five patients received neuroleptic alone. Results in lithium-treated patients:

| Day | 1 | 3 | 6 | 9 | 12 |
|------------------------------|----------|-----------|-----------|-----------|-----------|
| m EPS score | 0.8±0.36 | 0.97±0.44 | 1.05±0.49 | 1.17±0.48 | 1.27±0.51 |
| n | 10 | 10 | 10 | 10 | 9 |
| p value (paired t) vs. day 1 | | .03 | .03 | .02 | .003 |
| m Li level | 0 | 0.65 | 0.80 | 0.89 | 0.92 |

Mean EPS ratings increased steadily after the initiation of lithium and were significantly elevated compared to baseline. Controls showed no significant change. Rating scale items showing most frequent change with lithium treatment were elbow rigidity, shoulder shaking, tremor and gait. In conclusion, these findings demonstrate that, in some patients, lithium significantly worsens neuroleptic-induced extrapyramidal symptoms.

**NR136
PREMENSTRUAL SYMPTOMS AND MENTAL DISORDERS**

Wednesday, May 22, 12 Noon-2:00 p.m.

Thomas B. Mackenzie, M.D., Associate Professor of Psychiatry, University of Minnesota Medical School, Box 393 Mayo, 420 Delaware St., S.E., Minneapolis, MN 55455, Kimerly Wilcox, Ph.D., Howard Baron, B.S.

Summary:

To date studies of women with premenstrual symptoms show an increased prevalence of affective disorders. These studies, however, were undisguised and involved college-age women. Our study examined the lifetime prevalence of psychopathology in women blind to its purpose at peak risk for premenstrual syndromes (30-40 yr). Fifty-eight women recruited by advertisement for a "daily changes study" were covertly selected based on their report of "premenstrual or menstrual difficulties." The latter inquiry was buried in a medical screening interview. Women reporting non-mild difficulties (n=29) were compared to those reporting moderate-severe difficulties (n=29). Diagnoses were made using the Diagnostic Interview Schedule. Women rated moderate-severe not only had a greater lifetime prevalence of affective disorders (45% v 21%; p=.05) but also showed an increase in drug abuse (21% v 0%; p=.01). The former association has not been reported in 30-40 yr persons blind to the study design. An association with substance abuse appears to be a new finding.

**NR137
PREVALENCE OF ANOREXIA NERVOSA: A NATIONAL SURVEY**

Wednesday, May 22, 12 Noon-2:00 p.m.

Laurie Humphries, M.D., Department of Psychiatry, University of Ky. Medical Center, MN 365, 800 Rose St., Lexington, KY 40536, Scott N. Mohler, Ph.D., Carol L. Elam, M.A.

Summary:

A total of 5,377 female volunteers from 120 colleges and universities across the continental U.S. completed questionnaires, including the Eating Disorder Inventory (EDI), the Zung Self-Rating Depression Scale (SDS), and the Zung Self-Rating Anxiety Scale (SAS). Findings from the EDI suggest that there exists an extensive preoccupation with weight in college-age women accompanied by a substantial amount of weight restriction. The prevalence of anorexia nervosa was estimated to be 2.1% for this sample, with nonpsychopathological restrictive dieting occurring in another 5.1% of these individuals. A regional difference was also found, suggesting that weight-preoccupation may be more prevalent among females in the southern U.S. Analysis of the SDS and SAS data suggests a moderate linear relationship between weight and these measures of depression and anxiety. However, depression and anxiety were found to be strongly associated with respondents classified as having anorexia nervosa compared to those categorized as normal dieters.

**NR138
PLASMA BETA-ENDORPHIN IN BULIMIA**

Wednesday, May 22, 12 Noon-2:00 p.m.

David A. Waller, M.D., Dept. of Psychiatry, U. Texas, Southwestern Medical School, 5323 Harry Hines Blvd., Dallas, TX 75235, R. Sanford Kiser, M.D., Bettie W. Hardy, Ph.D., Ingbert Fuchs, M.D., Linda Parkin Feigenbaum, R.N.

Summary:

Endogenous opioid peptides such as beta-endorphin (BE) have been linked in animal studies to feeding behavior, and in human studies to glucoregulation. To investigate the hypothesis that abnormalities in BE regulation of eating might underlie the "addictive" behavior of bulimia, we measured plasma BE immunoreactivity by radioimmunoassay in 34 female normal-weight bulimics (DSM-III-R) and in an age- and weight-matched control group of 34 normal females. Blood was drawn at 10 AM to control for diurnal variation. The mean plasma BE immunoreactivity for bulimics (59.6 pg/ml, S.E.M. 5.6) was significantly lower than for controls (79.5 pg/ml, S.E.M. 8.5, p<.05). Within the bulimic group, a significant inverse relationship was found between severity of bulimic symptomatology as measured by the Bulimia Subscale (Factor II) of the Eating Attitudes Test, and plasma BE immunoreactivity (R= -.34, p<.05). This study suggests that uncontrolled binge-eating and vomiting is associated with low levels of plasma beta-endorphin immunoreactivity.

NR139
THE DEXAMETHASONE SUPPRESSION TEST IN BULIMIA

Wednesday, May 22, 12 Noon-2:00 p.m.

C. David Lindy, M.D., 722 W. 168th St., New York, NY 10032, Alexander H. Glassman, M.D., B. Timothy Walsh, M.D., Steven P. Roose, M.D., Madeline Gladis, M.A.

Summary:

Several recent studies examining the dexamethasone suppression test (DST) in normal weight bulimic patients have reported DST non-suppression rates of 44-67% vs. less than 10% in normal controls. Two possible explanations for this finding in bulimics are: 1) the concurrent presence of depressive illness and/or 2) significant weight fluctuations, both of which are known to be associated with bulimia and with DST non-suppression. Therefore, we performed the DST in bulimic patients while simultaneously measuring serial weights and determining presence or absence of major depression using the SADS and RDC criteria.

We determined the rate of DST non-suppression after a dose of 1 mg dexamethasone in 55 normal weight bulimic women. Nineteen (35%) demonstrated DST non-suppression. The weight change over the week prior to the DST averaged -0.3 lbs with no significant difference between suppressors and non-suppressors. There was a higher frequency of RDC major depression among non-suppressors than suppressors (36% vs. 9%, respectively) but this difference did not quite reach statistical significance (chi-square with Yates = 3.0, $p < 0.08$). No significant differences were found between the DST suppression and non-suppression groups with respect to age, duration of illness, eating scale scores, weight, percent of ideal body weight, or history of anorexia nervosa. These data suggest that no single clinical factor has been identified which explains the abnormally high rate of DST non-suppression in bulimia. Thus, our findings imply that bulimia can be added to the growing list of psychiatric syndromes associated with cortisol non-suppression.

NR140
NEUROENDOCRINE RESPONSES IN BULIMIA

Wednesday, May 22, 12 Noon-2:00 p.m.

Allan S. Kaplan, M.D., Toronto General Hospital, 200 Elizabeth Street, Toronto, Ontario, Canada, M5G 2C4, Paul E. Garfinkel, M.D., Jerry Warsh, M.D., Gregory M. Brown, M.D.

Summary:

Bulimia is linked to affective illness by its clinical presentation, family history profile and response to anti-depressant pharmacotherapy. As well, neuroendocrine responses to pharmacologic challenges have been found to be abnormal in a subgroup of depressed patients. It is of theoretical and possibly therapeutic value to assess these responses in patients with normal weight bulimia.

We conducted the TSH response to IV TRH, the growth hormone and plasma MHPG response to IV clonidine and the dexamethasone suppression test (DST) in a group of patients with normal weight bulimia and a group of controls matched on demographic and weight-related variables. The bulimic group (N = 13) demonstrated significantly blunted mean peak TSH responses to TRH compared to controls (N = 8) (ANOVA, $p < .05$). The bulimics (N = 11) showed a trend towards blunted GH response and evidence of prolonged suppression in MHPG following clonidine administration compared to controls (N = 6). The bulimics (N = 20) also had significantly more non-suppression in the DST than the controls (N = 20) (Fishers Exact Probability, $p < .05$). To our knowledge, this is the first report of blunted TSH response to TRH in a group of normal weight bulimics compared to a matched control group. It is also the first report of GH and MHPG responses in a bulimic population.

This data supports the hypotheses that there may be noradrenergic dysfunction in a subgroup of patients with normal weight bulimia, and provides further evidence for a biological link with depression. Further studies in a larger patient sample are indicated to elucidate these findings.

NR141
SLEEP EEG IN BULIMIA

Wednesday, May 22, 12 Noon-2:00 p.m.

James I. Hudson, M.D., Mailman Research Center, McLean Hospital, Belmont, MA 02178, Jeffrey M. Jonas, M.D., Harrison G. Pope, Jr., M.D., Victoria Grochochinski, Ph.D.

Summary:

To investigate sleep architecture in bulimia, all-night sleep EEG's were obtained on 8 women (mean age 26.3 yrs) meeting DSM-III criteria for bulimia, and on 26 normal women (mean age 30.8 yrs) on 2 consecutive nights. Concurrent major depression was present in 4 bulimic subjects. Analysis of data from the second night of sleep revealed a mean REM latency of 59.8 min (SE 4.2) among bulimics, which was significantly less than the 73.2 min (SE 3.7) found among controls ($p < .05$, Student's t-test, one-tailed). There was no significant difference in REM latency between bulimics with and without concurrent major depression (57.9 min vs. 61.7 min).

Decreased REM latency has been consistently reported in major depression. Thus, bulimia may share sleep architecture abnormalities in common with major affective disorder.

NR142
TASTE DIFFERENCES IN ANOREXIA AND BULIMIA NERVOSA

Wednesday, May 22, 12 Noon-2:00 p.m.

Katherine A. Halmi, M.D., Associate Professor Psychiatry, Cornell University Medical Center - Westchester, 21 Bloomingdale Road, White Plains, NY 10605, Adam Drewnowski, Ph.D., Beverly Pierce, M.A., James Gibbs, M.D., Gerard Smith, M.D.

Summary:

Taste responses of young women with anorexia and bulimia nervosa were examined using a range of sucrose and lipid-containing stimuli before and after weight gain. No differences in perception of increasing sweetness or fatness intensity were present among the eating disorder groups pre- and post-treatment and normal female controls. In contrast, *taste preference* varied across subject groups. Bulimic patients gave the highest pleasantness scores and showed an enhanced liking for intensely sweet stimuli (20% sucrose w/w). Exclusive dieting anorectics consistently rated all sucrose and fat stimuli more unpleasant than controls or bulimics. These differences were not altered by body weight gain during treatment. Taste preferences to sugar and fat appear linked to eating patterns which define the Eating Disorder Groups and thus may provide psychobiological marker of these diagnostic groups. In addition, the recognition of differences in taste preferences may lead to the development of more effective treatment strategies for these patients.

NR143
TREATMENT OF BULIMIA WITH NOMIFENSINE

Wednesday, May 22, 12 Noon-2:00 p.m.

Harrison G. Pope, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178, Peter L. Herridge, M.D., James I. Hudson, M.D., Regene Fontaine, M.D., Deborah Yurgelun-Todd, M.A.

Summary:

Several double-blind studies have found tricyclic antidepressants and monoamine oxidase inhibitors effective for bulimia—but often at the cost of annoying side effects. Recently, nomifensine, an antidepressant with few side effects, has been approved for American use.

We treated 12 consecutive bulimic outpatients, who had been symptomatic for 2-18 years, with nomifensine 150-300mg per day. Two patients developed high fevers (40°C) on the 14th day of treatment (a reaction previously described with nomifensine) and were promptly withdrawn from the drug. Of the remaining 10 patients, 6 experienced a remission of their bulimia, 2 a marked improvement (75% decrease in binge-eating), and 2 a moderate improvement (50% decrease). On follow-up of 1-3 months, 8 patients maintained their response, but 2 of the initially remitted patients relapsed—one partially and one completely. Aside from headaches in one woman, side effects were minimal in the 10 patients. These observations suggest that nomifensine deserves further study as a possible new treatment for bulimia.

NR144

Wednesday, May 22, 12 Noon-2:00 p.m.

HUNGER AND SATIETY IN ANOREXIA AND BULIMIA NERVOSA

William Owen, M.D., Research Fellow in Psychiatry, New York Hospital - Westchester Div., Cornell University Medical Ctr., 21 Bloomingdale Road, White Plains, NY 10605, Katherine A. Halmi, M.D., James Gibbs, M.D., Gerard Smith, M.D.

Summary:

Anorectic patients that were restrictors (R) or bulimics (B) ingested a liquid test meal and reported their sensations of hunger and fullness before, during and at the end of the meal using visual analog scales. Prior to treatment, R tended to eat larger meals than B ($\bar{x}R = 730\text{ml}$, $n = 5$; $\bar{x}B = 406\text{ml}$, $n = 6$). After reaching normal weight, R tended to eat smaller meals than B ($\bar{x}R = 156\text{ml}$, $n = 4$; $\bar{x}B = 380\text{ml}$, $n = 5$). Thus treatment resulted in a large change in meal size in R but not in B. Prior to treatment, R showed a greater change than B in both hunger and fullness ratings during the meal. After reaching normal weight R showed much less change than B in these ratings. Treatment resulted in larger changes in hunger and fullness ratings in R than in B. The results suggest the change in hunger and fullness perception in R is related to weight gain and/or ingestion of smaller meals. Why R, but not B, eat extremely small test meals and report only slight changes in hunger and fullness ratings when *both* groups have returned to a normal weight is puzzling and requires further study.

NR145

Thursday, May 23, 12 Noon-2:00 p.m.

SEXUAL MOLESTATION OF BOYS BY FEMALES

Diane Shrier, M.D., 543 Park Street, Upper Montclair, NJ 07043, Robert L. Johnson, M.D.

Summary:

All adolescent males (12-20 years) attending an adolescent medicine clinic in a large inner city facility were routinely questioned as to whether they had ever been raped, sexually abused or forced to have sex. A group of adolescent males who had been sexually molested by females, either during latency or adolescence, was identified. The characteristics of the assault and its perceived impact on the boys are described and contrasted with a group drawn from the same adolescent medicine clinic population who reported having been molested by males.

In both the male and female molested groups the assailant was usually a familiar person and force was rarely used. Few of the boys had informed anyone of the molestation and none had been reported to professionals or community agencies. The boys in both groups appeared to currently function satisfactorily in most areas of their lives but there was an increased rate of sexual dysfunction and sexually related psychosocial problems compared to a non-molested control group. Both groups felt the molestation experience had a significant and sustained impact on their lives, especially in the areas of trusting interpersonal relationships and their capacity to function sexually.

Differences between the male and female molested groups included the fact that the male molestations were more likely to be single episodes, while the female molestations were often repeated. Also, an increased rate of homosexuality or bisexuality was found only in the male molested group.

This preliminary data is presented because to date little information is available on sexual molestation of boys outside of a psychiatric, prison, or sexual offender population.

NR146

Thursday, May 23, 12 Noon-2:00 p.m.

EVALUATION OF BENEFIT FROM A JCAH REGULATION

George Wilson, M.D., Carrier Foundation, Belle Mead, NJ 08502

Summary:

Medical services are under increasing cost/benefit scrutiny. At the same time, regulatory agencies are increasingly involved in requiring specific formats for treatment. For example, the 1982 Carrier Foundation JCAH report required a change in the multidisciplinary Treatment Planning Conferences (TPC's), requiring more structure and a more detailed report. In a prospective study, the benefits of the "old" ($N = 92$) vs. the "new" ($N = 91$) TPC's were compared, obtaining ratings from patients, psychiatrists, and other staff. Ratings were of improvement from different modalities of treatment (e.g., medication, psychotherapy), helpfulness of the TPC, and the extent to which treatment was well coordinated. Results did not indicate any benefit from the new TPC's. Given the need for increased staff time, the cost/benefit ratio for the new TPC's was poor. While not definitive, this study suggests that regulatory agency requirements, when feasible, should be subjected to study, and cost/benefit analysis, prior to widespread implementation.

NR147
A STUDY OF DISTINCT QUALITY OF MOOD IN MELANCHOLIA

Wednesday, May 22, 2:00 p.m.

Robert L. Spitzer, M.D., NYS Psychiatric Institute, 722 West 168th Street, New York, NY 10032, Miriam Gibbon, M.S.W., Janet B.W. Williams, D.S.W.

Summary:

For several decades the clinical concept of distinct quality of mood has been considered to be one of the defining features of "endogenous" depression. It is included in the Newcastle Diagnostic Scale, the Feinberg and Carroll criteria, and the Research Diagnostic Criteria for endogenous depression, as well as the DSM-III criteria for melancholia. The lack of a consensus as to how the concept should be operationalized in a clinical interview and uncertainty about the value of the concept for making a diagnosis of melancholia led to this study. An interview that included 11 items, each corresponding to a different way of operationalizing the concept, was administered to 100 depressed patients—50 with DSM-III melancholia and 50 without. The low intercorrelation among the 11 items and the low predictive value of each item for the diagnosis of melancholia casts doubt on the diagnostic usefulness of the concept of distinct quality.

NR148
PSYCHOSIS AND SUICIDE

Wednesday, May 22, 2:15 p.m.

Eli Robins, M.D., Washington Univ. School of Medicine, Department of Psychiatry, 4940 Audubon Avenue, St. Louis, MO 63110

Summary:

The prevalence and characteristics of psychosis were observed in a population of 134 subjects who committed suicide in St. Louis in a one-year period.

Psychosis was diagnosed if a subject had, in the period just prior to his suicide, experienced any of the following: delusions; hallucinations; bizarre behavior; disorientation, confusion, or memory loss; or formal thought disorder. Using these criteria, the investigator found that 25 (19%) of the 134 subjects were psychotic at the time of suicide.

Although only three of the 134 suicide subjects had been diagnosed as having had schizophrenia and only five organic brain syndrome, all eight of these subjects were found to have been psychotic at the time of their suicides. In the two largest diagnostic groups the prevalence of psychosis was less: of the 63 subjects with affective disorder, depressed phase, ten (16%) were psychotic; of the 33 with alcoholism, five (15%) were psychotic. Of the 20 psychiatrically undiagnosed subjects, two (10%) were found to be psychotic. None of the five terminally medically ill or the three apparently well subjects were found to have been psychotic.

NR149
BRIGHT LIGHT THERAPY OF CHRONOBIOLOGIC DISORDERS

Wednesday, May 22, 2:30 p.m.

Alfred J. Lewy, M.D., Department of Psychiatry, Oregon Health Sciences University, Portland, OR 97201, Robert L. Sack, M.D., Clifford Singer, M.D.

Summary:

Whereas psychiatrists have long thought that chronobiology was relevant in the understanding of bipolar depression, until recently its practical applications have not been encouraging. Using melatonin production as a marker for circadian phase position, the baseline circadian phase position of 10 subjects was determined and the shift in phase position in response to bright light exposure was measured. Other circadian phase markers, such as REM latency and the core body temperature rhythm also shifted in the same direction. In both normal volunteers and in patients with melancholia and winter depression, bright light exposure in the morning advanced their circadian rhythms (shifted them to an earlier time) and bright light exposure in the evening delayed their rhythms (shifted them to a later time). Patients with winter depression have morning hypersomnia and tend to be phase delayed. Bright light exposure in the morning causes a robust antidepressant effect in such patients.

NR150

Wednesday, May 22, 2:45 p.m.

SITE OF ACTION OF ANTIDEPRESSANT DRUGS IN ANIMALS

Fritz A. Henn, M.D., Professor and Chairman, Dept. of Psychiatry, HSC, School of Medicine, SUNY at Stony Brook, Stony Brook, NY 11794-8101, Emmeline Edwards, Ph.D., Joel Johnson, Eliot Siegel

Summary:

The development of an animal model of depression with phenomenological accuracy and pharmacological specificity allowed an investigation of the neurobiological effects seen in the CNS of affected animals. These studies have demonstrated that in a model having both genetic and environmental factors, the environmental stressors can cause long-term changes in CNS structure whose time course parallels that of the altered animal behavior. These changes are specific and localized, the most pronounced being an upregulation of beta receptors in the hippocampus. The model is responsive to a range of antidepressants. It was found that both imipramine and mianserin are effective and down regulate the beta receptor. In the case of mianserin, a compound which does not normally down regulate receptors, this effect occurs and appears to operate through the 5-HT system. The effect of a cognitive form of psychotherapy was also examined behaviorally and neurochemically. These results suggest beta receptor regulation in the hippocampus may be an important location for the control of mood and suggest new approaches to antidepressant pharmacology which will be presented.

NR151

Wednesday, May 22, 3:00 p.m.

PLATELET SEROTONIN UPTAKE AND IMIPRAMINE BINDING

Herbert Y. Meltzer, M.D., Dept. of Psychiatry, University of Chicago, School of Medicine, 5841 S. Maryland, Chicago, IL 60637, R.C. Arora, Ph.D., Alan G. Robertson, M.D.

Summary:

Platelet serotonin (5-HT) uptake and H-imipramine binding (IB) have been proposed to be biological markers for major depression. They may be described by their kinetic constants: V_{max} and B_{max} (measures of number of 5-HT and IB uptake sites, respectively) and K_M and K_D (inversely correlated with affinity for 5-HT and imipramine, respectively).

V_{max} was significantly decreased in bipolar (8.5 ± 2.8 pmoles/10 platelets/min, $N=37$) and unipolar (10.4 ± 2.8 , $N=63$) depressed and manic (9.8 ± 2.4 , $N=38$) patients, compared to normal controls (12.5 ± 2.8 , $N=140$). Psychotic and nonpsychotic depressives did not differ significantly in V_{max} . B_{max} was significantly negatively correlated with age for all depressions ($r = -0.29$, $N=62$, $p=0.02$) and for manics ($r = -0.44$, $N=22$, $p=0.04$) but not in normals ($r=0.003$, $N=56$, $p=NS$). B_{max} was not significantly different in manics, depressed and normal controls after the effect of age was covaried out, although there was a trend for low B_{max} in unipolar psychotic depressives.

V_{max} was correlated with the Paranoia rating of the Hamilton Scale (HDRS) in major depression ($\rho = -0.42$, $N=91$, $p=0.0001$). K_D was correlated with HDRS Suicide ratings in major depression ($\rho = 0.36$, $N=51$, $p=0.01$). Both correlations were significant for unipolar, bipolar and psychotic depressives as well.

These results suggest V_{max} is a more likely candidate as a biological marker for affective disorder than B_{max} .

NR152
DST, TRH-ST AND REM LATENCY IN DEPRESSION

Wednesday, May 22, 3:15 p.m.

A. John Rush, M.D., Univ. TX Health Science Center, 5323 Harry Hines Blvd., Dallas, TX 75235, Michael A. Schlessler, M.D., Donna E. Giles, Ph.D., Paul J. Orsulak, Ph.D., Carol J. Fairchild, M.S.N., Howard P. Roffwarg, M.D.

Summary:

203 in- and outpatients received both the 1 mg. DST and the 500 mcg. TRH-ST. DST-nonsuppression rates were 46% - UP-Endog.; 13% - UP-Nonendog.; 56% - BP-Depressed; 17% - BP-Manic; 100% - BP-Mixed; and 0% - Other. TRH-ST blunting ($\Delta \text{max} < 5.0 \text{ luU/ml}$) occurred in 25% (UP-E); 9% (UP-NE); 44% (BP-D); 44% (BP-M); 67% (BP-MX); and 33% (0). Within the combined UP-E and BP-D group, 30 of 144 patients (26%) evidenced DST nonsuppression (DST-NS) without TRH-ST blunting. Nine (8%) revealed TRH-ST blunting without DST nonsuppression.

REM latency, DST and TRH-ST were measured in 67 endogenous patients (BP-D or UP-E). 21 (31%) had no abnormalities. 3 (4%) had all 3 abnormalities. RL or DST-NS detected 66%, RL or TRH-ST detected 58%, and TRH-ST or DST detected 49%. TRH-ST detected only 2 patients not detected by DST or RL.

This study suggests: (a) RL and DST are each more sensitive than TRH-ST; (b) DST followed by sleep EEG is the most cost-effective "laboratory battery;" (c) blunted TRH-ST is not simply a consequence of DST-NS; and (d) the endogenous/nonendogenous dichotomy is validated by all 3 tests.

NR153
TCA DOSE ADJUSTMENT USING 24 HOUR DRUG LEVELS

Wednesday, May 22, 3:30 p.m.

J. Craig Nelson, M.D., Dept. of Psychiatry, Yale-New Haven Hospital, 20 York Street, New Haven, CT 06504, Peter Jatlow, M.D., Carolyn Mazure, Ph.D.

Summary:

Prior studies indicate antidepressant response to desipramine (DMI) occurs above a plasma level threshold. Rapid dose adjustment to reach that threshold quickly might reduce time spent at subtherapeutic levels and increase the likelihood of response to the initial dose. Other studies indicate plasma drug levels 24 hours after a single dose may be predictive of steady state levels and thus useful for dose adjustment, but this strategy has not been tested.

We confirmed the correlation of plasma DMI levels 24 hours after a single dose with steady state DMI levels in 16 inpatients ($r = .88$). The derived regression equation was applied to 24 hour levels in a second series of inpatients to calculate the dose needed to reach a target level of 140 ng/ml. That dosage (100 to 500 mg/day) was then administered. The pharmacokinetic limitations of this approach were mitigated because we were aiming for a broad therapeutic range of about 115-250. 15 patients completed the study. All 15 reached the threshold level of 115 ng/ml; 13 of the 15 patients achieved a level between 115 and 233 ng/ml. Remarkable side effects appeared to be associated with rapid dose adjustment in only one patient. Use of 24 hour plasma levels to rapidly adjust dosage was clinically feasible, safe, and resulted in plasma levels in the therapeutic range.

NR154
DESIMPAMINE PLASMA LEVELS AND CLINICAL RESPONSE

Wednesday, May 22, 3:45 p.m.

William Coryell, M.D., Univ. of Iowa College of Med., 500 Newton Road, Iowa City, IA 52242, Rick D. Turner, M.D., Arnold Sherman, Ph.D.

Summary:

Thirty outpatients with major depression completed a six week, fixed dose trial of desimpramine. Recovery after six weeks, defined in either of two ways, corresponded to lower desimpramine levels while clinical status at four weeks bore no apparent relationship to plasma levels. A plasma level of 140 ng/ml at either four or six weeks best discriminated patients who recovered at six weeks from those who did not according to a global assessment while 155 ng/ml provided the best discrimination when recovery was defined using an alternative threshold. Since the therapeutic range for desimpramine plasma levels have a lower limit, these findings support a curvilinear relationship. Differences across studies in the distribution of desimpramine levels may have produced many of the differences in conclusions. These conclusions may, in fact, be reconcilable and consistent with an upper therapeutic limit between 140 and 160 ng/ml.

NR155**Wednesday, May 22, 4:00 p.m.****LIFE EVENTS: CSF METABOLITES AND DST IN DEPRESSION**

Alec Roy, M.B., National Institute of Mental Health, Bldg. 10, 4N-214, 9000 Rockville Pike, Bethesda, MD 20205-1000, David Pickar, M.D., Markku Linnoila, M.D., Allen Doran, M.D., Steven M. Paul, M.D.

Summary:

The cerebrospinal fluid levels of norepinephrine and six monoamine metabolites were measured in 23 patients meeting DSM-III criteria for major depressive episode, 15 of whom also met criteria for melancholia. Life events during the six-month period prior to the onset of depression were recorded using Paykel's method. However, depressed patients who did not have a life event in the six months prior to the onset of their depression had significantly lower levels of the dopamine metabolite, homovanillic acid and the serotonin metabolite, 5-hydroxyindoleacetic acid, than those patients with life events. The incidence of nonsuppression on the dexamethasone suppression test was also significantly greater in those patients with a major depressive episode who did not have an undesirable life event (83.3%) than in those who did (16.6%). Thus, within an apparently homogenous group of depressed patients the presence or absence of life events led to a separation into biologically distinct groups.

NR156**Wednesday, May 22, 4:15 p.m.****AGE, ALCOHOL, CATECHOLS, MEMORY, AND NEUROANATOMIC CHANGE**

T. Peter Bridge, M.D., ADAMHA, Rm. 13C-23, 5600 Fishers Lane, Rockville, MD 20857, Elizabeth S. Parker, Ph.D., Beth J. Soldo, Ph.D., Loring Ingraham, M.A., Charles E. Bickham, M.D.

Summary:

Reported here are data from 43 white male and female subjects aged 45-79 who are free from psychiatric illness, substance abuse, space occupying/tissue destructive CNS disease. They were evaluated for brain CT scan, cognitive performance, alcohol use, and plasma DBH activity. Data from these subjects indicate that increased cerebral ventricular volume (VBR) was associated with frequent alcohol use and reduced levels of DBH activity. Predicted VBR scores are more than three times as large for those who drink 4 or more times/week and have low DBH activity compared to other older subjects. Frequent drinkers also showed decreased density of both grey and white matter in frontal lobe measurements ($r = -0.365, p = .005$), which, in turn, were associated with reduced abstraction performance ($r = .249, r = .042$) and reduced memory performance ($r = .420, p = .002$). These data indicate that frequent alcohol use and reduced DBH activity are associated with increased VBR, reduced frontal lobe tissue density, and impaired cognitive performance in the elderly.

NR157**Wednesday, May 22, 4:30 p.m.****HOW RESPONSES TO STIMULANTS CHANGE WITH AGE**

Enoch Callaway, M.D., Langley Porter Psychiatric Inst., 401 Parnassus Avenue, San Francisco, CA 94143, Roy Halliday, Ph.D., Hilary Naylor, Ph.D.

Summary:

We report 3 studies of stimulants based on a serial information processing model. All drugs were given orally, double-blind and with placebo (PL) controls. All tests were done before and then repeated starting 45 min after drug. The 1st study used women; 8 aged 30 to 40 and 8 aged 60 to 70. They were tested with PL, 5, 10 and 20 mgm methylphenidate (MP). On a choice reaction time task that combined 2 levels of stimulus complexity and 2 levels of response complexity to provide 4 subtasks, young women had reaction times (RT) speeded by 10 and 20 mgm MP. MP did not speed RT for old subjects, nor did it change P3 latency for either group. The 2nd study used men; 12 aged 20 to 30 and 12 aged 60 to 70. They were tested with PL, 10 mgm MP and 10 mgm d-amphetamine (dAMP). Again, stimulants speeded choice RT for young men but not for old. In both studies, age interacted with stimulus complexity, and stimulant effect interacted with response complexity. The 2nd study included a continuous performance task (CPT) and a simple motor task designed to maximize response preparation before stimulus delivery. On the CPT, stimulants reduced false positives in young and increased them in the old. MP speeded RT of both the old and young men on the motor task. In Study 3, six of the same old men were tested in the afternoon with PL and 10 mgm dAMP. Again choice RT was, if anything, slowed by dAMP, but CPT performance was improved. Thus, in age, responses to stimulants seem qualitatively different from those of young subjects.

NR158

Wednesday, May 22, 4:45 p.m.

DECREASE IN SELECTIVE ATTENTION PRODUCES ANALGESIA

Lewis L. Judd, M.D., Dept. of Psychiatry (M-003), University of CA, San Diego, La Jolla, CA 92093, David S. Segal, Ph.D., Byron Budnick, LouAnn McAdams, Ph.D., S. Craig Risch, M.D., David S. Janowsky, M.D., Steven Hillyard, Ph.D.

Summary:

There is evidence that the endogenous opioid peptide neurotransmitter systems are involved in the regulation of attention in both animals and man. Recently we reported that Naloxone, an opiate antagonist, improved selective attention in normal subjects. Here we report the effect of Methadone, an opiate agonist, on the same selective attention variables.

Method: 10 normal subjects were administered 2.5 mg of Methadone-HCl or an inert placebo IM in two experimental sessions under double blind. In a sound-attenuated chamber auditory event related potentials (AERPs) were recorded while the subjects were attending to specific auditory stimuli while ignoring others. The change in the N-100 wave of the AERP under these conditions is the "attention effect."

Results: A strong attention effect on the N-100 amplitude and area was present during the placebo session. Methadone significantly attenuated this attention effect on N-100 amplitude ($F(1,9) = 32.63; p < .0003$) and peak area ($F(1,9) = 13.33; p < .0053$).

Discussion: Methadone impaired the capacity of these subjects to selectively attend to auditory stimuli in the presence of competing stimuli. This effect is consistent with reports in the literature that opiates produce difficulty in mental concentration. Further, patients administered narcotic analgesics often report that their pain is still present, but they are less able to focus upon it. Naloxone and methadone had opposite effects on selective attention which suggest a discrete and specific role of the μ -opioid peptide neurotransmitters systems in the regulation of attentional behaviors. We hypothesize that the effect of opiate agonists on selective attention may be one of the central mechanisms by which these compounds promote analgesia.

NR159

Thursday, May 23, 12 Noon-2:00 p.m.

VALIDITY OF AFFECTIVE BORDERLINE SUBTYPE

Paul Skevington Links, M.D., 3rd Fl., Fontbonne Building, St. Joseph's Hospital, 50 Charlton Ave. East, Hamilton, Ontario, Canada L8N 4A6, Meir Steiner, M.D., David R. Offord, M.D., Alan B. Eppel, M.B., Jan Mitton, R.N., Audrey Hendershot, R.N., Marilyn Korzekwa, M.D.

Summary:

Controversy about the validity of subtypes within the Borderline Personality Disorder (BPD) still exists. The present study reports on the initial findings on the following hypotheses: the subgroup of BPD with concomitant Major Depressive Disorder (MDD) will be differentiated from pure BPD (without concomitant MDD) on the basis of clinical characteristics, childhood antecedents, response to Dexamethasone Suppression Test (DST), and prevalence of psychiatric illness in first degree relatives.

A large representative sample of psychiatric inpatients was examined using the Diagnostic Interview for Borderlines (DIB), Research Diagnostic Criteria, and direct interviews with relatives. Initial results indicated that of the 54 patients positive for DIB diagnosis, 82% (44 patients) showed concomitant MDD. Although the patients with MDD had significantly more dysphoric affect, both the affective and pure subtypes exhibited high levels of social withdrawal, anhedonia, and anger. For the 54 borderline subjects, 45% came from non-intact homes, 34% reported being physically abused by primary caretakers during childhood, and 21% reported being sexually abused by their caretakers. There was a trend for sexual abuse to be more frequently reported by the pure subgroup. The results of the DST indicated that of 42 borderline patients tested, 24% (10) had positive DST's, with 23% (8/35) and 29% (2/7) positive results in the affective and pure subtypes, respectively.

No clear affective subtype was differentiated based on clinical characteristics, childhood antecedents, and response to DST. The frequent occurrence of concomitant MDD in our inpatient sample challenges the credibility of this definition of the affective subtype. Other clinical characteristics which may define a more valid affective subtype will be discussed.

NR160

Thursday, May 23, 12 Noon-2:00 p.m.

SLEEP EEG VERSUS DST IN BORDERLINES WITH MELANCHOLIA

Kenneth R. Silk, M.D., Univ. of Mich./Ann Arbor VAMC, 2215 Fuller Road (116A), Ann Arbor, MI 48105, Michael Feinberg, M.D., Naomi E. Lohr, Ph.D., Margaret C. Buitenheim, Ph.D., Karen Saakvitne

Summary:

While there is growing evidence that a large group of borderline patients also meet Axis I criteria for an affective diagnosis, there are indications that many non-melancholic borderlines have false positive results on the DST. We questioned whether other physiologic tests, particularly the sleep EEG, might be more accurate than DST in discriminating endogenous depression among borderlines.

This report is from an ongoing study that compares affective and non-affective borderlines with each other and with non-borderline affective (NBA) controls on a series of biological, phenomenological and psychological parameters. Among 25 borderlines prospectively identified with the DIB, we found that only 2 of the 12 DST+ patients had an RDC diagnosis of Major Depressive Disorder with endogenous features (MDD/E), while 8 of the 12 were non-endogenous MDD (MDD/NE). By contrast, among 17 simultaneously tested NBA controls, 7 of the 8 DST+ patients were MDD/E.

We compared the relationship of RDC diagnoses to both the DST and sleep EEG results in 20 borderlines. 3 were prospectively diagnosed using the DIB; 17 were retrospectively identified by Gunderson and Singer criteria. Sleep EEG findings indicative of endogenous depression were determined by a discriminant function which includes REM latency and REM density (Feinberg et al, 1982). Results of the sleep EEG were consistent with results generally found in purely affective patients. Nine borderlines had positive sleep ($DF < 1$) of whom 6 were MDD/E. Two were MDD/NE; one was MDD. Three other MDD/E patients had negative sleep. Only one MDD/E patient was DST+, though the DST was positive in four others.

Though the sample is small, our preliminary evidence suggests that the sleep EEG may be a more accurate indicator of melancholia than the DST in borderline patients.

NR161

Thursday, May 23, 12 Noon-2:00 p.m.

STABILITY OF DSM-III ON BORDERLINE PERSONALITY DISORDER

Alan Barasch, M.D., 449 East 68th Street, New York, NY 10021, Allen J. Frances, M.D., John Clarkin, Ph.D., Stephen Hurt, Ph.D., Sandra Cohen, M.D.

Summary:

This three year follow-up study presents data on three measures of the diagnostic validity of Borderline Personality Disorder (BPD)—diagnostic stability over time, distinctness from affective disorder, and level of functional impairment—for a group of BPD patients in comparison to a challenging reference group limited to patients with other personality disorders (OPDs).

Methods: Thirty patients with personality disorders and without Axis I disorders were assessed at index and at three year follow-up for DSM-III diagnosis, GAS, and affective data.

Results: Of 10 patients with BPD, 6 still met full DSM-III criteria (5 of 8 items) and three others had 4 items positive. Of 20 patients with OPDs, 16 were still diagnosed as an OPD, and three newly met criteria for BPD. Forty percent of the BPDs and also 40% of the OPDs reported episodes of MAD during follow-up. There was no difference in level of function by GAS.

Significance: BPD is relatively stable over three year follow-up and does not predispose to MAD any more than do OPDs. BPD is relatively distinct from OPDs by pattern and not severity of psychopathology. These data lend support to the usefulness of the DSM-III BPD construct.

NR162
SYMPTOMS OF SCHIZOTYPAL PERSONALITY DISORDER

Thursday, May 23, 12 Noon-2:00 p.m.

L.B. Jacobsberg, M.D., Payne Whitney Psychiatric Clinic, 525 E. 68th Street, New York, NY 10021, Paul Hymowitz, Ph.D., Allen J. Frances, M.D., Mary Sickles, M.D., Alan Barasch, M.D.

Summary:

Goal: This study examines the discriminatory descriptive characteristics of patients with schizotypal (SPD) and borderline (BPD) personality disorder.

Method: 64 personality disordered patients were evaluated with clinical interview, family history assessment, and the SIB, a semi-structured interview operationalizing the DSM-III criteria for schizotypal and borderline personality disorder.

Results: All schizotypal scales, except social anxiety, discriminated SPD from the control group of other Axis II disorders. In addition, SPD was discriminated by the borderline items 1) compulsive sociability, 2) boredom, 3) mood elevation when praised, and 4) identity disturbance. None of the schizotypal items discriminated the borderline patients from the controls, whereas the borderline symptoms of 1) self-damage, 2) affective instability, 3) hostility, and 4) rejection sensitivity did. These results support the validity of the schizotypal diagnosis. The findings contrast with recent observations based on non-clinical, familial samples that schizotypals are best characterized by negative symptoms (e.g. social isolation and impaired functioning). In this clinical patient sample positive symptoms (e.g. illusions, ideas of reference, magical thinking, and odd communication) are found to be equally valid discriminators. When a pure SPD subgroup was compared with the mixed SPD/borderline group, there was no difference on any of the schizotypal items, with only self-damaging behavior discriminating between the two groups. Thus the symptoms reported by the SPD's were not contaminated by the overlap with the borderline group.

There was no additional incidence of schizophrenia in the parents or grandparents of the schizotypal patients compared with the controls, whereas the borderline patients reported twice as many instances of affective illness among their families in relation to all other patients.

Significance: The findings contradict recent suggestions that SPD be redefined in DSM-III-R to increase emphasis on negative symptoms and also suggest that clinical SPD samples differ from familial ones.

NR163
CAN AMPHETAMINE SOLVE BORDERLINE HETEROGENEITY?

Thursday, May 23, 12 Noon-2:00 p.m.

S. Charles Schulz, M.D., Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213, Jack Cornelius, M.D., Richard Brenner, M.D., Paul Soloff, M.D.

Summary:

Introduction: The "amphetamine test" research strategy has been useful to advance understanding of depression and schizophrenia. To investigate the characteristics of borderline personality disorder we compared the response to amphetamine of DIB identified borderline patients (N = 8) compared to normals (N = 10). We found the borderline patients were significantly more sensitive to the effects of amphetamine and that 4 of the 8 patients experienced psychotic symptoms. We now report on an extension of this study which shows a heterogeneous response to amphetamine in borderline patients.

Methods: Seven borderline personality disorder patients (DIB \geq 7) participated in a double-blind placebo-controlled experiment in which they received either amphetamine 30 mg or placebo. Behavior was rated using the BPRS and patients completed the HSCL.

Results: 1) The borderline patients had a significant increase in BPRS of 12.6 ± 3.14 SEM ($p < 0.01$). 2) Three of the seven patients became frankly psychotic during the testing, a finding similar to our original investigation. 3) Upon examination of all 15 patients studied to date we noted a bi-modal pattern of response to amphetamine. Six patients noticed a dramatic increase in well being, while 5 reported dysphoria.

Discussion: Neuroendocrine and pharmacotherapy studies suggest that borderline personality disorder is a heterogeneous disorder. The results of this study demonstrate that the pharmacodynamic probe of the amphetamine test can objectively subdivide this complicated group.

NR164

Thursday, May 23, 12 Noon-2:00 p.m.

BORDERLINE TRAITS IN RELATIVES OF BORDERLINES

Patricia M. Schulz, M.S.W., Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, S. Charles Schulz, M.D., Richard F. Ulrich, M.S., Robert Hamer, Ph.D., Robert O. Friedel, M.D., Solomon Goldberg, Ph.D.

Summary:

The purpose of this study is the evaluation of relatives of mixed borderline and schizotypal (BPD/STPD) patients for the presence of borderline traits. The 21 BPD/STPD patients and 44 of their relatives with and without major affective disorder (MAD) were compared to 22 patients with MAD and 15 of their relatives on the Schedule for Interviewing Borderlines (SIB).

Results: Patients: Using the cut-off of 5 or more DSM-III traits for BPD and 4 or more traits for STPD, the BPD/STPD group had more borderline traits ($X^2=22.5$, $p<.001$) than the depressed patients. The BPD/STPD group also had more schizotypal traits ($X^2=22.8$, $p<.001$) than the depressed patients.

Results: Relatives: 16% of the BPD patients' relatives had >5 STPD traits, 54% had 1-4 traits, 30% had none. Of these same relatives 11% had >5 BPD traits, 48% had 1-4, 41% had none. There was no difference between the relative groups (BPD vs MAD) for the presence of BPD traits ($X^2 = .6854$, $p = .40$) or STPD traits ($X^2 = .9$, $p = .13$). Twenty one percent (21%) of depressed patients' relatives had MAD compared to 51% of BPD relatives. When controlling for the presence of affective disorder in the relatives of both groups interviewed, the STPD traits were found in the relatives who had DSM-III MAD ($X^2 = 7.5$, $p < .01$). The BPD traits were not associated with MAD in either relative group ($N = 59$) ($X^2 = .2$, $p = .6$). Schizotypal traits in the relatives of BPD/STPD patients ($N = 44$) were associated with MAD ($X^2 = 3.86$, $p = .05$). Borderline traits, however, were not associated with the MAD in the relatives of BPD/STPD patients ($X^2 = .9$, $p = .34$). The depressed patients' relative group was not too small to test independently on these measures.

NR165

Thursday, May 23, 12 Noon-2:00 p.m.

HETEROGENEITY OF BORDERLINE PERSONALITY DISORDER

Minna R. Fyer, M.D., N.Y. State Psychiatric Institute, 722 W. 168th Street, New York, NY 10032, Allen J. Frances, M.D., Timothy Sullivan, M.D., Steven Hurt, Ph.D., John Clarkin, Ph.D.

Summary:

Goals: To determine whether borderline personality disorder (BPD) is a homogeneous diagnostic entity with clear boundaries and to address some of the methodologic limitations of previous studies which assume that BPD is homogeneous.

Method: Diagnostic, demographic, course and treatment data were gathered by chart review on 200 BPD inpatients. Diagnoses were compared to a control group of 550 inpatients in the same hospital during the same time period.

Results: 94% of BPDs had at least one, and 40% had two or more additional diagnoses. In BPDs the incidence of other diagnoses was: 68% affective, 40% substance abuse, 29% substance dependence, 18% organic, 17% other personality disorders and 12% non-affective psychotic disorders. As has also been found by other investigators, the rate of affective disorder in BPDs was high. However, there was no significant difference between BPDs and controls or between BPDs and other personality disorder patients in the rate of affective disorder.

Significance: BPD appears to be a heterogeneous category with unclear boundaries, overlapping with many disorders but without a specific association with any Axis I disorder proposed by other investigators. This evidence casts doubt on the construct validity of the BPD diagnosis and inspires caution in interpretation of results from studies of BPD that do not systematically report base rates and coexisting diagnoses.

NR166
CRITERIA FOR DIAGNOSING PERSONALITY DISORDERS

Thursday, May 23, 12 Noon-2:00 p.m.

W. John Livesley, M.B., Ch.B., 841 Centre Ave. East, Calgary, Alberta, Canada T2E 0A1

Summary:

This paper reports a survey of the features used to diagnose personality disorders. Two research questions were addressed: i) do psychiatrists agree on the prototypical features of the different personality disorders? and ii) do psychiatrists agree on the behavioral features of each disorder? Trait and behavioral descriptions of each DSM-III category were developed through content analysis of the clinical literature and nominating techniques. These were mailed to a random sample of 2960 psychiatrists who were asked to rate each item for prototypicality of the disorder in question. 936 psychiatrists responded. The reliability coefficients for trait and behavioral ratings were comparable, demonstrating the feasibility of developing behavioral criteria. The highly prototypical behaviors were then used to construct a self-report inventory. The data from 150 subjects were analyzed to provide information on the internal consistency of each scale. The results provide only partial support for DSM-III categories.

NR167
CORE CRITERIA FOR DIAGNOSING BORDERLINE PATIENTS

Thursday, May 23, 12 Noon-2:00 p.m.

H. George Nurnberg, M.D., Associate Professor of Clinical Psychiatry, 241 Central Park West, New York, NY 10024, Aileen Feldman, M.D., Stephen W. Hurt, Ph.D., Ryang Suh, M.D.

Summary:

This study compares 17 hospitalized borderline personality disorder (BPD) patients with 20 normal controls. Four criteria sets of DSM III, Grinker, Gunderson and Kernberg were combined and used with the DIB Scale. The following features were most prominent among the BPD patients: 1) impulsive episodes, 2) unstable relationships, 3) chronic feelings of depressive emptiness/loneliness, 4) acting out behavior and less prevalent 5) identity disturbance.

BPD patients can be discriminated by different patterns of disturbance while sharing features with controls. While DSM III requires 5 of 8 items for BPD diagnosis from the above features significantly less made a positive diagnosis. Optimal balance between sensitivity and specificity, for these data, was any combination of 3 criteria or the combination of criteria 1 and 2. They give approximately equal and high values for positive and negative predictive power (.94 and .95, respectively).

The results and techniques illustrate that while there may be many features associated with the syndrome, some characteristics, and particularly some combinations of characteristics may be more prototypical of the syndrome's expression than others. These combinations have a high probability of leading to accurate diagnosis to the degree that they are distinctive and regularly occur in combination in individuals with the disorder and not among those without the disorder. BPD seems to identify a heterogeneous patient group with behavioral disturbances without particular personality specificity having in common certain core characteristics among which additional features may further subtype component members.

NR168

Thursday, May 23, 12 Noon-2:00 p.m.

A STUDY CHARACTERIZING DSM-III R CRITERIA FOR PANIC DISORDER PATIENTS

Mary E. Hanrahan, A.C.S.W., Payne Whitney Clinic NYH, 525 East 68th Street, New York, NY 10021, M. Katherine Shear, M.D.

Summary:

There is a clear relationship between patients who meet DSM-III criteria for panic disorder and patients who meet criteria for Agoraphobia, i.e. most panic patients develop phobic avoidance and most agoraphobics experience panic symptoms. Current plans for revision of DSM-III will highlight this connection. Specifically, the diagnosis of panic disorder will be subdivided into patients with 1) no phobic avoidance, 2) limited phobic avoidance and 3) extensive phobic avoidance. The latter category will encompass agoraphobics who have had panic attacks. This classification views panic disorder as continuing a spectrum of panic-phobic symptomatology and raises the interesting question of what determines which symptoms a given patient will experience. The purpose of this study is to begin to address this question by further characterizing patients in the panic disorder spectrum.

Methods: *Subjects:* 85 patients evaluated in the Payne Whitney Clinic Anxiety Disorder Clinic from 1982 - 1984.

Procedures: Charts were reviewed to establish 1) DSM-III R diagnosis, 2) age and sex distribution of each group, 3) presence or absence of non-panic somatic symptoms in each group, 4) Axis II and Axis III diagnoses.

Results: 1) patients (4 men, mean age 28; 14 women, mean age 36) had panic disorder with no phobic avoidance, 2) patients (15 men, mean age 30; 21 women, mean age 33) had panic disorder with limited avoidance and 3) patients (14 men, mean age 36 and 18 women, mean age 33) had panic disorder with extensive avoidance. 4) 40% of patients in all three groups had prominent non-panic somatic sx. 5) Significantly more patients with limited phobic avoidance had Axis II and Axis III diagnoses than patients in other 2 groups.

Findings: These findings support the homogeneity of the reviewed panic disorder grouping and suggest further study of patients with limited phobic avoidance.

NR169

Thursday, May 23, 12 Noon-2:00 p.m.

DIURNAL VARIATION OF ABNORMAL ANXIETY

Oliver G. Cameron, M.D., Dept. of Psychiatry, U. of Michigan Hospitals, 1405 E. Ann St., Ann Arbor, MI 48109-0010, Joan Kotun, M.D., Myung A. Lee, M.D., Sheila Murphy, B.S.

Summary:

Diurnal variation is present in many patients with melancholic depression, involving a worsening of symptoms in the morning. Three studies with DSM-III defined anxiety disorder patients without major depression were conducted to determine if anxiety also fluctuated during the day. In the first study, 34 patients were studied retrospectively (27 women, 7 men; mean age = 36.5 years; mean duration = 10.2 years; 24 had panic attacks with or without agoraphobia). There was a significant fluctuation ($p < .02$) with the highest rating in the later afternoon to early evening. In a prospective study a second group of panic disorder patients (9 women, 2 men; mean age = 34.9 years; mean duration = approximately 15 years) and 6 controls (4 women, 2 men; mean age = 31.8) were studied. Anxiety, temperature and pulse were measured at 5 points during the day. The 3 P.M. rating for anxiety was significantly ($p < .02$) greater than the 7 A.M. rating in the panic disorder group, but not different in the control group. Temperature and pulse did not differ between the two groups. In a third group of 12 prospectively studied patients only 7% of 88 panic attacks occurred prior to 10 A.M. and the mean time of occurrence was mid-afternoon. These results indicate a midafternoon peak in anxiety patients' symptom level. This diurnal variation in a psychiatric patient population other than depressives may warrant further investigation into circadian rhythms of biologic parameters in anxiety as well as other psychiatric disorders.

NR170
PSYCHOBIOLOGIC CHANGES DURING SPONTANEOUS PANIC

Thursday, May 23, 12 Noon-2:00 p.m.

Oliver G. Cameron, M.D., Asst. Prof. Dept of Psychiatry, U. of Michigan Medical Center, 1405 E. Ann St., Ann Arbor, MI 48109, Myung A. Lee, M.D., George C. Curtis, M.D., Daisy S. McCann, Ph.D.

Summary:

Physiological and endocrine changes are associated with "stress" or "anxiety" in normal humans. Recent advances in diagnosis and treatment have generated interest in the pathophysiology of disorders of anxiety, especially panic attacks. Although a few studies of basal hormonal and cardiovascular function in people with panic disorder and changes produced by pharmacologically-induced panic attacks have appeared, no studies of hormone changes during "spontaneous" panic have been reported. We, therefore, measured pulse (P), blood pressure (BP), oral temperature (T), and plasma epinephrine (E), norepinephrine (NE), MHPG, cortisol (cort), growth hormone (GH), and somatostatin (ST), during nine panic attacks (average severity = 6.2, maximum = 10) in four patients with DSM-III defined panic and daily attack frequency. Interpolation of values obtained at 4-hour intervals throughout the experimental period were used as baseline. All patients were otherwise healthy, drug-free, at bedrest with indwelling venous catheters, and on low catecholamine diets in a clinical research center during the study.

No measure showed uniform increases or decreases across all patients. The most consistent changes across patients were small *increases* in BP, cort, NE, and MHPG, and *decreases* in T. Individual differences were prominent; for example, one patient showed distinct GH as well as cort, NE, and T changes, but no P, BP, or MHPG changes in several variables but not GH, and the fourth only minimal changes on any variable except T. Surprisingly, no E (or ST) changes were observed in any patient. Further study with more patients is needed, paying particular attention to patterns of response between and within patients and individual differences between patients. Study of pattern changes during "spontaneous" panic may permit inferences concerning pathophysiological CNS mechanisms of anxiety.

NR171
PHYSIOLOGICAL CONCOMITANTS OF ANXIETY

Thursday, May 23, 12 Noon-2:00 p.m.

Donna L. Moreau, M.D., Dept. Child Psychiatry, New York Hospital/Payne, Whitney Clinic, 525 East 68th Street, New York, NY 10021

Summary:

Goals: This study measures whether anxiety disorder patients: 1. are differentially responsive to physiological, cognitive, psychological challenges 2. have subjective states consonant with physiological state 3. differ in baseline physiological values and physiological reactivity from normal controls.

Methods: 14 panic disorder patients were compared to 10 normal controls. Physiological and mood measures were taken while subjects were exposed to: 1. physiologic stimulus (auditory tone, light touch, startle) 2. cognitive stimulus (mental arithmetic) 3. psychological stimulus.

Results: 1. Anxiety patients showed significant physiological responsiveness to cognitive and psychological but not to physiological challenges. 2. Patients were discordant for physiologic reactivity and subjective state with mood being more sensitive. 3. There were no significant differences between patients and controls at baseline or during the challenges. Both subjectively experienced significantly more tension during the physiologic stimulus.

Significance: Findings provide further evidence for central rather than peripheral dysfunction in anxiety disorders.

NR172
ELEVATED NOREPINEPHRINE/CORTISOL RATIO IN PTSD

Thursday, May 23, 12 Noon-2:00 p.m.

John Mason, M.D., West Haven V.A. Hospital, Psychiatry - 116A, West Haven, CT 06516, Earl L. Giller, M.D., Thomas R. Kosten, M.D., Robert B. Ostroff, M.D., Laurie Harness, M.S.W.

Summary:

Accompanying the sympathetic NS arousal (high norepinephrine) (N) that has been reported in post traumatic stress disorder (PTSD), we expected high urinary free cortisol (C) levels, but found low levels ($\bar{X} = 34.9$, s.d. = $4.9 \mu\text{g/day}$). High N with low C was unusual compared to four other diagnoses. Using the 24 hr urinary N to C ratio (NCR) during hospitalization (avg = 8 weeks), biweekly urines in PTSD patients ($n = 9$) showed higher NCR (2.54 ± 0.42) than in mania (1.18 , $n = 8$), depression (0.89 , $n = 8$), or schizophrenia - paranoid (1.06 , $n = 12$) and undifferentiated (0.81 , $n = 7$) ($F(4,43) = 6.9$, $p < 0.0003$). The NCR from the first urine during hospitalization, when no patients were on antidepressants or lithium, was also highest for PTSD ($\bar{X} = 2.3$) ($F = 3.3$, $p < 0.02$). The NCR for the 30 patients receiving antipsychotics ($\bar{X} = 1.27$) was similar to the 14 not receiving them ($\bar{X} = 1.14$) ($t = 0.4$, ns). Physical activity measured by BPRS item was not associated with NCR ($r = -0.13$, ns). We conclude that the NCR may be a useful biological index in PTSD.

NR173
GENETIC AND FAMILIAL RISK FOR ANXIETY DISORDERS

Thursday, May 23, 12 Noon-2:00 p.m.

Jeffrey Boyd, M.D., Room 18-105, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20817

Summary:

This is a review of the state of the art of genetic and familial research in anxiety disorders. There is evidence from four twin studies and 10 family studies that panic disorder tends to run in families, and that genetic transmission may be involved. Six family studies indicate that obsessive compulsive disorder is familial and seven out of nine twin studies indicate genetic involvement. The evidence for a genetic factor in the phobias is controversial: 3 twin studies suggest no inheritance, whereas 4 twin studies do suggest inheritance; 2 family studies find an increase of phobias among first degree relatives, a third study does not. The one twin study of generalized anxiety disorder does not suggest a strong genetic component. Several animal models (Maudsley reactive rats, C57 Black mice from Jackson Labs, and NIH-Swiss-Webster mice from the NIH stock) are available for study of the molecular genetics of anxiety disorders.

NR174
PANIC DISORDER AND MITRAL VALVE PROLAPSE

Thursday, May 23, 12 Noon-2:00 p.m.

William Matuzas, M.D., Dept. of Psychiatry, Univ. of Chicago, 5841 S. Maryland, Chicago, IL 60637, Jafar Al-Sadir, M.D., E. H. Uhlenhuth, M.D., Richard M. Glass, M.D., Ronald J. Ganellen, Ph.D.

Summary:

Recent observations have suggested an association between panic disorder and both mitral valve prolapse (MVP) and thyroid dysfunction. These observations have been limited by small patient groups and/or variable criteria for cardiac or thyroid diagnoses. Furthermore, cardiac and thyroid status have not been assessed simultaneously in spite of evidence that MVP and thyroiditis are associated. We examined a consecutive series of 65 self-referred patients with panic attacks and various DSM III diagnoses. Thirty-seven of 65 had MVP by echocardiography (M-mode and 2-D); 30 of 48 by auscultation (systolic click with or without murmur); and 24 of 48 by both. Seven of 55 had an abnormal thyroid status with elevated thyroid hormones ($n = 2$), history of thyroid illness ($n = 3$), or high titers of thyroid antibodies ($n = 7$). These results do not suggest etiologic associations, but do suggest these syndromes may be associated because of a common etiology with broad systemic manifestations.

NR175
ANXIETY IN CHILDREN AND ADOLESCENTS

Thursday, May 23, 12 Noon-2:00 p.m.

Evanne Hoehn-Saric, M.D., The Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21205, Mohammad Maisami, M.D., Diane Wiegand, B.S.

Summary:

The contribution of anxiety to psychopathology in children and adolescents is less well understood than in adults. The Children's Anxiety Evaluation Form (CAEF), based on history, signs and symptoms obtained through semi-structured interviews, was developed to measure anxiety levels in nonpsychotic children of normal intelligence. Sixty-three inpatients, average age 11.6, were assessed using the CAEF, and the self-rated State-Trait Inventory for Children (STAIC) and Reynolds and Richmonds Revised Measure of Children's Manifest Anxiety (RMCMA). CAEF scores differentiated patients independently diagnosed on discharge as anxiety disorders from the total population (p .0005), oppositional disorder (p .0005), nonaggressive conduct disorders (NCD)(p .0005) and aggressive conduct disorders (ACD)(p .01). NCD scored lower on the CAEF than did ACD(p .05). Despite a positive correlation between CAEF and STAIC Trait scores($r = .38, p .001$) and with RMCMA($r = .25, p .05$), the STAIC and RMCMA failed to differentiate diagnostic groups. The data support the importance of interviewing in assessment of anxiety levels. The different anxiety levels in two groups of conduct disorders may have important therapeutic implications.

NR176
PLASMA GABA ABNORMALITIES IN PSYCHIATRIC ILLNESS

Thursday, May 23, 12 Noon-2:00 p.m.

Frederick Petty, M.D., V.A. Medical Center, 4500 S. Lancaster, Dallas, TX 75216

Summary:

A role for gamma-aminobutyric acid or GABA, the major inhibitory neurotransmitter in mammalian brain, has been postulated in affective disorders. We here report a summary of studies during the last three years on plasma GABA in patients with several psychiatric illnesses. Patients with alcoholism have levels even lower than those of patients with depression. Patients with secondary depression or bipolar depression, on the other hand, have values in the control range. Bipolar patients had levels significantly above control both while manic and while in clinical remission on lithium. Patients with anorexia nervosa had levels similar to control.

These findings are discussed in the context of a biochemical relationship between alcoholism and depression, and the possibility that elevated GABA levels may be developed into a useful trait marker for bipolar affective disorder. Additionally, relative advantages of various assay procedures will be discussed.

NR177
CO2 AS A TRIGGER FOR PANIC IN PANIC PATIENTS

Thursday, May 23, 12 Noon-2:00 p.m.

Anke Ehlers, M.D., Research Scholar in Psychiatry & Behavioral Sciences, Stanford Univ. School of Medicine, Stanford, CA 94305, Jurgen Margraf, M.D., Walton T. Roth, M.D., C. Barr Taylor, M.D., Richard J. Maddock, M.D., Bert S. Kopell, M.D.

Summary:

A focus of recent research on Panic Disorder has been the experimental provocation of panic attacks. Our study examines CO2 inhalation as a panic induction technique and compares its effects to standard stress tests. We record physiological, behavioral, and subjective responses of patients with Panic Disorder or Agoraphobia with Panic Attacks and matched control subjects. Our preliminary results confirm earlier findings that CO2 raises anxiety levels and physiological arousal in these patients. However, responses were moderate and few patients asked to stop because of panic. Cold Pressor and Mental Arithmetic tests also produced considerable increases in anxiety and physiological arousal. These results and our recent findings with lactate infusions lead us to conclude that CO2 and lactate effectively increase anxiety in both panic patients and controls but that they are not specific triggers for panic attacks. Thus, response to these provocations does not appear to be a biological marker for Panic Disorder.

**NR178
TREATED HEROIN ADDICTS FOLLOWED FOR 15 YEARS**

Thursday, May 23, 12 Noon-2:00 p.m.

Charles Rohrs, M.D., Department of Psychiatry, NYU Medical Center, 550 1st Avenue, New York, NY 10016

Summary:

28 adult male heroin addicts were followed regularly as a group for 15 years between 1969 and 1983. All had a history of at least 2 years of intravenous heroin addiction (range 2 to 17 yrs) and all entered drug free therapeutic community involuntarily (court ordered) where they remained totally abstinent during inpatient treatment (range 13 to 32 mos, mean 22 mos). Subsequently patients were seen weekly for 5 years, then monthly until 1983. By the 5th post-residential treatment year 3 distinct outcome groups emerged. 40% were designated true responders; they maintained total abstinence throughout the follow-up period and were judged to have made successful adaptations to drug-free life. 20% were designated recidivists; they were unable to remain off heroin after supports of residential treatment were relaxed, even with intense group support. 40% were designated relapsing responder patients who relapsed to heroin re-addiction or alcoholism but responded then to either methadone maintenance, AA, or lithium. Treatment and follow-up were identical for all. No differences were noted among groups at the time of admission by demographics, history, psychological testing, or clinical rating scales. However, after 18 mos of residential abstinence a significant difference appeared in depression scale scores between recidivists and the responder groups. Data from this study suggest 1) addiction does not predict recidivism, 2) evaluation during prolonged abstinence has predictive outcome potential, 3) efficacy of involuntary treatment, 4) significant psychological differences among heroin addicts.

**NR179
PROBATIONERS AND DRUGS IN A MAJOR URBAN COUNTY**

Thursday, May 23, 12 Noon-2:00 p.m.

Kenneth R. Kaufman, M.D., 8635 West Third St., #985, Los Angeles, CA 90048, Phyllis Sherman Raschke, M.P.A.

Summary:

The authors reviewed a twenty-two month period during which time urine drug tests were administered to probationers convicted of a criminal offense in Los Angeles County with the nature of the offense or investigation indicating drug abuse. These individuals had been granted probation with the condition that they "submit to periodic anti-narcotic tests as directed by the probation officer." Of 114,433 samples, there were 22,967 positives (20%) representing 26,961 identified drugs. The monthly percentage of positive samples ranged between 17 and 22 without significant increase over the study period. The most prevalent drug was phencyclidine (PCP) which represented 37.4% of all identified drugs. Cocaine represented only 7% during the first half of the study; however, during the second eleven months cocaine represented 22% of all identified drugs. Further, an inverse relationship between PCP and cocaine frequency was noted. Geographic migration of positive samples was also found. The authors present preliminary analysis of this data with implications for general drug abuse in a major urban county.

**NR180
NEUROCHEMICAL CHANGES IN COCAINE AND OPIATE ABUSE**

Thursday, May 23, 12 Noon-2:00 p.m.

Todd Wilk Estroff, M.D., Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901, Charles A. Dackis, M.D., Donald R. Sweeney, M.D., A. L. C. Pottash, M.D.

Summary:

In order to determine if neurochemical differences exist in drug abuse disorders 23 severe cocaine abusers (A) (greater than 1 gm/day) were compared to 16 high dose methadone maintenance (greater than 80 mg/d) patients (B) and 20 normal controls (C) with regard to 4 measures. The cocaine abusers had confirmatory blood levels, were not dependent on other substances and had no other psychiatric diagnosis. The cocaine group had significantly elevated prolactin levels compared to the other two groups (A: 19.76 ± 10.14 ; B: 13.11 ± 9.02 ; C: 7.05 ± 5.03 ; $p = .001$). Methadone patients demonstrated significantly low MAO levels compared to both other groups (A: 28.83 ± 10.61 ; B: 20.56 ± 9.06 ; C: 33.00 ± 19.04 ; $p = .034$), and significantly decreased Platelet Serotonin Transporter compared to the cocaine group (A: 23.91 ± 9.37 ; B: 14.36 ± 9.27 ; C: 18.97 ± 5.99 $p = .007$) as well as prolactin levels which were significantly above the control group and significantly below the cocaine group. There were no differences in tyrosine levels (A: 1.73 ± 0.53 ; B: 1.61 ± 0.41 ; C: 1.62 ± 0.37 $p = 0.671$). Repeat measurements after two weeks of cocaine abstinence revealed no significant difference on any parameter. These data are consistent with significant neurochemical disruption occurring among cocaine and opiate abusers and that each substance may have its own individual pattern of abnormality. The cocaine addicts' elevated prolactin levels may be due to chronic cocaine induced dopamine depletion. Low MAO levels may account for the reported antidepressant effects of methadone.

**NR181
HYPERPROLACTINEMIA IN COCAINE ABUSE**

Thursday, May 23, 12 Noon-2:00 p.m.

Charles A. Dackis, M.D., Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901, Todd W. Estroff, M.D., Mark S. Gold, M.D.

Summary:

The secretion of prolactin is tonically inhibited by dopamine (DA) and cocaine acts upon DA neurons. We studied 8 a.m. prolactin levels in 18 male cocaine abusers without other substance abuse, and 20 normal male controls. Prolactin levels were drawn within 72 hours of admission and determined by radioimmunoassay.

Prolactin levels in the cocaine patients (mean \pm SD; 35.4 ± 26.9 ng/ml) were significantly greater ($t = 4.62$, $df = 36$, $p < 0.001$) than those of the controls (mean \pm SD; 7.0 ± 5.0). Using a cut-off of 20 mg/ml, 12 of 18 patients (67%) had elevated prolactin levels.

Chronic cocaine exposure has been shown to reduce DA levels and increase postsynaptic DA receptor density. These findings are consistent with DA inhibition. Elevated prolactin levels reported here are also consistent with DA inhibition by cocaine.

Given the dramatic elevation of prolactin in chronic cocaine abuse, this measure may prove useful in understanding the nature of cocaine-induced neuroendocrine and neurotransmitter disruptions. The duration of hyperprolactinemia after the cessation of cocaine abuse may correspond with "psychological" withdrawal states associated with the abrupt discontinuation of cocaine.

NR182

Thursday, May 23, 12 Noon-2:00 p.m.

EXCRETION OF PTERINS DURING METHADONE MAINTENANCE

Kenneth J. Krajewski, M.D., Dept. of Psychiatry, Univ. of Texas Medical School at Houston, P.O. Box 20708, Houston, TX 77225, Robert W. Guynn, M.D.

Summary:

The current work explores the hypothesis that methadone maintenance is mediated via or, at least affects the immune system and evidence for this relationship can be found through measurement of urinary excretion of neopterin. Though not widely investigated, there has been a growing body of evidence suggesting that pterin metabolism may be involved in some psychiatric disturbances. Neopterin and biopterin are naturally occurring pterins which have been associated with immune functioning and biogenic amine synthesis, respectively. Urinary neopterin or the neopterin/biopterin ratio appears to be commonly elevated in malignant disorders, especially of the hematologic system, and in conditions in which the immune system is taxed (e.g. AIDS). Urinary excretion in normal subjects appears to be under strict metabolic controls and confined within a relatively small range. There has been increasing evidence that methadone dependence involves and possibly is mediated by the immune system. Morning urinary biopterin and neopterin were measured in 12 subjects on methadone maintenance and 16 controls matched for age, race and sex. Employing high pressure liquid chromatography, results of urinary neopterin revealed a two-fold increase in methadone subjects (633 nmole/mole creatine) when compared to control (271 nmole/mole creatine) $F = 18.85$ (1,23 DF) $P < .001$. There was 1.3 fold increase in urinary biopterin in methadone subjects (650 nmole/mole creatine) compared to control (491 nmole/mole creatine) $F = 6.45$ (1,23 DF) $P < .02$. These results suggest: 1) patients on the methadone maintenance may have a significant alteration in immune functioning as measured by urinary neopterin, 2) the high rate of Acquired Immune Deficiency (AIDS) in I.V. drug abusers may be in part related to immunoreactive activity of opiates, and 3) further study of immune functioning may be important in the study of the pathogenesis of opiate dependence.

NR183

Thursday, May 23, 12 Noon-2:00 p.m.

COCAINE ABUSE TREATMENT OUTCOME

Arnold M. Washton, Ph. D., The Regent Hospital, 425 E. 61st St., New York, NY 10021, A.L.C. Pottash, M.D.

Summary:

Although cocaine abuse has become a major public health problem in recent years, almost no studies of cocaine abuse treatment outcome have appeared in the literature. This paper describes a treatment outcome study of 63 employed middle and upper class cocaine abusers who entered a specialized outpatient treatment program. The treatment program focused on immediate and complete abstinence from all mood-altering chemicals and employed a variety of interventions including urine monitoring, drug education, supportive therapy, cocaine recovery groups, and specific relapse prevention strategies. Data are presented on treatment retention and drug-free success rates at 7-13 months after program entry. Results are discussed in terms of factors contributing to successful outcomes and the effectiveness of outpatient treatment as either an alternative or sequel to hospitalization in selected cocaine abusers.

NR184 **Thursday, May 23, 12 Noon-2:00 p.m.**
PSYCHIATRIC PATIENTS AND NICOTINE: USE AND EFFECTS

Susanna Goldstein, M.D., Long Island Jewish-Hillside Medical Center, 263rd Street & 76th Avenue, Glen Oaks, NY 11004, Stephen H. Geisler, M.D., Simcha Pollack, Ph.D.

Summary:

Nicotine intake (smoking) has a variety of effects on CNS functions: *Neurochem.*-stimulates release of NE and DA and depending on dose, may increase or inhibit the release of Ach. *Neurophysiol.*-causes an alerting pattern in the EEG and a decrease in skeletal muscle tone and deep tendon reflexes. *Neuroendocr.*-increases plasma of GH, ADH, ACTH cortisol, NE, E. Although there is an adaptation of the glucocorticoid response to chronic nicotine intake as little as 12 hours of abstinence results in increased level of plasma glucocorticoid when nicotine is reintroduced. *Neuropharm.*-smokers metabolize some psychotropic drugs faster than non smokers, they are less sedated by CPZ and benzodiazepines and they are less sensitive to the hypotensive effects of CPZ. *Behavioral*-facilitates memory and reduces hostility and aggression. Cessation of smoking may be followed by a withdrawal syndrome which includes insomnia, increased hostility and inability to concentrate.

Smoking is an addictive behavior with negative health consequences. On the other hand, nicotine may have some function in the behavioral regulation of physiological homeostasis and habitual smoking may be symptomatic of a physiologic need. The present study shows, in agreement with clinical observation that the prevalence of smoking in psychiatric inpatients is significantly higher ($p < 0.01$) than in the general population and they are heavier smokers ($p < 0.05$). The smokers required significantly higher ($p < 0.01$) doses of neuroleptics and yet fewer required antiparkinsonian medication. In presenting this data we attempt to highlight the need for further research of this interesting drug that our patient population is using so prevalently and to draw attention to the necessity to take smoking into consideration in drug treatment studies and in neuroendocrine studies.

NR185 **Thursday, May 23, 12 Noon-2:00 p.m.**
PROSTAGLANDINS AND RECOVERY FROM ALCOHOLISM

James P. MacMurray, Ph.D., Psychiatry Service (116A1), Jerry L. Pettis Mem. Veterans Hospital, 11201 Benton Street, Loma Linda, CA 92357, John E. Crowder, M.D., Michael D. Schultz, M.D., Jonathan D. Berman, M.D., Roland C. Aloia, Ph.D., Louis P. Bozzetti, M.D.

Summary:

Prostaglandins (PG) for the E series have previously been implicated in the etiology of alcoholism and in the mediation of mood states in bi-polar affective disorder. Lithium has been shown to be a potent anti-prostaglandin agent, and other studies have found that alcoholics on lithium report less intoxication following an alcohol challenge. Those study findings suggest that depressed PG titers may be associated with increased ethanol tolerance. Increased tolerance, in turn, is considered a major component of the alcoholic's compulsion to drink. The authors studied $\text{PGF}_2\alpha$ titers in 27 inpatient alcoholics in an effort to explore aspects of the relationship between PG synthesis and abstinence behavior. Blood samples were obtained, spun down and frozen at -70° until assayed by radioimmunoassay method. The PG titers were then correlated with a variety of drinking history and treatment outcome variables. The most salient finding was a significant relationship between $\text{PGF}_2\alpha$ titers and treatment outcome. Those patients with elevated titers during the first month of abstinence had a successful treatment outcome significantly more often than those with depressed titers ($P < .005$). Also, the PG titers were negatively related to history of depression ($P < .05$). On the basis of these findings we hypothesize that the positive relationship between $\text{PGF}_2\alpha$ titers and treatment outcome reflects an increased ethanol tolerance and heightened need to drink in abstinent alcoholics with depressed $\text{PGF}_2\alpha$ titers.

NR186
PREDICTORS OF DRIVING ACCIDENTS IN ALCOHOLICS

Thursday, May 23, 12 Noon-2:00 p.m.

William R. Yates, M.D., Resident in Psychiatry, Department of Psychiatry, University of Iowa Hospitals and Clinics, Iowa City, IA 52240, Russell Noyes, Jr., M.D., Fred Petty, M.D., Keith Brown

Summary:

Public pressure to address the problem of drunk drivers is increasing. The purpose of this study was to evaluate a group of alcoholics to determine if there was a group of high risk drivers who could be distinguished by historical or behavioral factors. Alcoholics admitted to a Veterans Administration alcohol treatment facility in Knoxville, Iowa, were given detailed drug, medical, and psychiatric interview. Of 262 consecutively admitted alcoholics, 57 reported a history of personal injury motor vehicle accidents while intoxicated. Their histories were compared with the remaining 205 patients with no history of personal injury accidents.

Results of the study revealed that drivers with a history of accidents were significantly more likely to begin drinking early in life, have histories of suicide attempts, antisocial behavior, and a history of aggressive behavior in adolescence and while intoxicated. Multiple regression analysis demonstrated that early onset of heavy drinking, frequent job loss because of drinking, and childhood fighting best predicted report of previous accidents while intoxicated. A prospective study to confirm these findings may allow identification of a high risk group of drivers who deserve special attention in attacking the national drunk driving problem.

NR187
PROSTAGLANDIN CHANGES IN RECOVERING ALCOHOLICS

Thursday, May 23, 12 Noon-2:00 p.m.

Jonathan D. Berman, M.D., Substance Abuse Fellow, Psychiatry Service 116A, V.A. Med. Center, West Haven, CT 06516, James P. MacMurray, Ph.D., Roland C. Aloia, Ph.D., Paul A. Stein, Ph.D., John E. Crowder, M.D., Louis P. Bozzetti, M.D.

Summary:

In vitro studies have shown that repeated ethanol exposure decreases prostaglandin (PG) synthesis through precursor depletion despite an initial PG-stimulating action. Since PG levels have been reported decreased in depressed bipolar patients, several authors have proposed that chronic alcohol intake creates a PG-deficiency dysphoria, relieved by further drinking, which is central to the development of dependence. To examine the clinical relationship between alcoholism and PG, the authors measured serum PGE and PGF₂ levels in three groups of male alcoholics, sober for less than one, one to four, and more than four weeks respectively, plus 18 age-matched male controls. A highly significant elevation in PGF₂, but not PGE, was seen in the 1-4 week group, compared with both controls and other patient groups, which did not differ significantly among themselves. These findings suggest that abstinence results in release from PG "down-regulation" and are consistent with *in vitro* data. A link between PG and alcohol-related mood states appears plausible but has yet to be definitely established.

NR188
AMINO ACIDS AND HALLUCINATIONS IN ALCOHOLICS

Thursday, May 23, 12 Noon-2:00 p.m.

L. Branchey, M.D., Alcohol Research Center, VA Med. Center, 130 West Kingsbridge Rd., Bronx, NY 10468, M. Branchey, M.D., D. Zucker, M.D., S. Shaw, M.D., C. S. Lieber, M.D.

Summary:

Hallucinations have been attributed to an increased serotonergic tone as well as to a decreased dopaminergic tone in patients undergoing dopaminergic therapy for Parkinson's disease and in subjects ingesting hallucinogenic substances. For this reason, we decided to investigate whether serotonin and dopamine pathways are modified in alcoholics with a history of hallucinations. Brain serotonin has been shown to depend on the availability from the circulation of its precursor tryptophan and on the plasma concentration of other amino acids (AA) competing with it for brain entry: tyrosine, phenylalanine, valine, leucine and isoleucine. The ratio of tryptophan over these AA (tryptophan ratio) correlates with brain serotonin. Similarly, brain dopamine depends on the availability of its precursors tyrosine and phenylalanine. We assessed whether alcoholics who had experienced hallucinations have a lower tryptophan ratio and a higher tyrosine + phenylalanine ratio than patients without such a history. All amino acids were determined after an overnight fast. Data analyzed by an analysis of covariance (with the amount of alcohol consumed as covariate) showed that patients with a history of hallucinations have a tryptophan ratio significantly lower than patients without such a history ($x \pm SD = .102 \pm .029$ vs $.121 \pm .029$, $p < .001$) and a tyrosine + phenylalanine ratio significantly higher. Changes in the ratios were due primarily to increases in tyrosine and phenylalanine in patients with hallucinations (tyrosine $x \pm SD = 107.7 \pm 55.1$ nmoles/ml vs 84.3 ± 25.1 , $p < .001$; phenylalanine $x \pm SD = 98.6 \pm 77.6$ vs 70.6 ± 41.5 , $p < .025$). Age, number of years of excessive drinking and liver biopsies did not differentiate among the 2 patient groups. Thus, our data suggest that amino acid abnormalities believed to result in a decreased brain serotonin and in an increased brain dopamine render certain individuals more vulnerable to hallucinatory experiences.

NR189
PRIMARY AND SECONDARY DEPRESSION IN ALCOHOLICS

Thursday, May 23, 12 Noon-2:00 p.m.

Marsha R. Read, Ph.D., Department of Psychiatry, Kansas University Medical Center, 39th and Rainbow Boulevard, Kansas City, KS 66103, Barbara J. Powell, Ph.D., Elizabeth C. Penick, Ph.D., Barry I. Liskow, M.D., Stephen F. Bingham, Ph.D., Audrey S. Rice, M.A

Summary:

Five-hundred-sixty-five hospitalized, male VA alcoholics were administered: (1) A criterion-based structured, psychiatric diagnostic interview (2) An interview including information about social-demographic characteristics, history of drinking and family history. Forty-two percent ($N = 238$) met inclusive criteria for major depression. One-hundred-sixty of these were eliminated (67%) because they met criteria for other syndromes *in addition* to alcoholism and depression. This left a sample of 78 men positive only for alcoholism and depression who were then divided into three independent groups according to the reported onset of the two disorders: PRIMARY depression = onset of depression two or more years *before* the onset of alcoholism ($N = 24$). CONCURRENT depression = onset of depression within plus or minus two years of alcoholism ($N = 23$). SECONDARY depression = onset of depression two or more years *after* the onset of alcoholism ($N = 31$). Few differences were found between the three groups with respect to socio-demographic features, number and type of symptoms reported, or family history. Slightly more of the primary group received psychiatric treatment for non alcohol-related problems. Our findings suggest that the primary/secondary distinction among alcoholics with depression may have little clinical significance.

**NR190
SEPARATION AND ALCOHOL CONSUMPTION IN MONKEYS**

Thursday, May 23, 12 Noon-2:00 p.m.

William T. McKinney, M.D., Department of Psychiatry, Clinical Sciences Center, University of Wisconsin Medical School, 600 Highland Avenue, Madison, WI 53792, Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., C. Raymond Lake, M.D.

Summary:

Alcohol alters the response of rhesus monkeys to social separation. Low dose alcohol has antidepressant effects similar to those of imipramine, whereas high dose alcohol is a depressant similar to alpha-methylparatyrosine. In this study, social separation was found to increase the voluntary consumption of alcohol by rhesus monkeys.

Sixteen monkeys were studied. They were mother reared for the first six months of life and then housed in peer groups. Twelve were intermittently separated from their social groups while four were individually housed throughout the study. Refrigerated water or aspartame sweetened water (vehicle) containing 6% alcohol (w/v) were presented after 4.5 hours of fluid deprivation.

Over six separations, three with alcohol and three with water available, the intermittently separated monkeys progressively drank more alcohol when they were separated than when they were together. Initial consumption rates did not predict which subjects would develop high or low consumption rates over repeated separations. That is, the monkeys that drank the most water or vehicle were not the subjects that drank the most alcohol/vehicle.

Previous work has established that vulnerability to increased alcohol consumption in rhesus monkeys is related to some underlying neurobiological characteristics, namely lower CSF norepinephrine levels. This study provides data to support the role of a specific social stressor, namely, social separation as an additional risk factor. The combination of neurobiological vulnerability and exposure to this type of social stressor is suggested as particularly hazardous in terms of the potential for significantly increased alcohol consumption.

**NR191
MENTAL DISORDERS IN RAPE VICTIMS**

Thursday, May 23, 12 Noon-2:00 p.m.

Ellen Frank, Ph.D., Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, Barbara Anderson, M.S., Patricia Cluss, Ph.D., Jane Ergood, M.A., Ana Rivera-Tovar, M.S., Barbara Duffy Stewart, M.P.H.

Summary:

While it has frequently been noted that the incidence of rape in the histories of psychiatrically ill women is high, no one has studied the converse: is the incidence of past psychiatric illness high in women who are raped? To answer this question we assessed 60 recent rape victims and 31 matched controls using the Diagnostic Interview Schedule (DIS). A test of proportions revealed no significant differences between the groups with respect to *prior* diagnoses of generalized anxiety disorder, major depression, phobia, alcohol abuse/dependence or drug abuse/dependence. However, when the period of the *past month only* was explored, rape victims differed from controls in the prevalence of several diagnoses: major depressive episode ($z = 2.20, p \leq .05$), generalized anxiety disorder ($z = 4.76, p \leq .05$), (DSM-III duration and age criteria removed), drug abuse/dependence and agoraphobia ($z = 4.63, p \leq .05$). The two groups did not differ on generalized anxiety disorder (all DSM-III criteria applied), alcohol abuse/dependence, social phobia or simple phobia.

W I T H D R A W N

NR192
SEASONAL CHANGES IN VIOLENCE BY MEN TOWARD WIVES

Thursday, May 23, 12 Noon-2:00 p.m.

Richard P. Michael, M.D., Dept. of Psychiatry, Emory University Medical School, Atlanta, GA 30322, Doris Zumpfe, Ph.D.

Summary:

We reported (*Am. J. Psychiat.*, 140,883, 1983) that rapes and assaults showed annual rhythms with maxima in the summer. These rhythms were statistically related to annual temperature changes. We suggested a neuroendocrine basis for the behavioral rhythms, but this view was criticized because people interact more in summer, spend more time outdoors and wear scantier clothing: an obvious explanation but one not supported by the fact that rapes and assaults, corrected for population, do not increase in hotter climates as one proceeds south. If the opportunity for interactions were the major factor, violence *within* the family should remain rather constant throughout the year. To study this, we obtained monthly totals of crisis calls from 19 shelters for abused women in three states in the USA. In Georgia and Texas, crisis calls from abused women showed significant annual rhythms (cosinor analysis: $F(2,9) = 14.2$ and 22.0 , $P < 0.005$ and < 0.0001 respectively) with 14% increases above the annual means in mid-July. The dates of the maxima were within a few days of the annual temperature maxima and within 3 weeks of the previously reported rape and assault maxima. Control measures showed no annual rhythmicity. In California, requests for shelter also showed an annual rhythm ($F(2,9) = 7.1$, $P < 0.025$). These results from an ongoing study suggest that summer increases in male violence towards live-in female partners may not depend primarily on an increased opportunity for social interactions.

W I T H D R A W N

NR193
PELVIC PHYSIOLOGICAL CHANGES DURING FEMALE AROUSAL

Thursday, May 23, 12 Noon-2:00 p.m.

Ismet Karacan, M.D., Director, Sleep Disorders & Research Center, Baylor College of Medicine, Texas Medical Center, One Baylor Plaza, Houston, TX 77030, Constance Moore, M.D., Sezai Sahmay, M.D.

Summary:

We have recently developed electronic technology to monitor the physiological activity of the female pelvis. This formed the basis of a recent examination of healthy orgasmic women. We measured vaginal muscle activity, clitoral activity, uterine tonus, vaginal blood flow and clitoral blood flow, during (1) sleep and (2) sexual excitement and subsequent orgasm. To our knowledge, this was the first attempt to monitor such variables.

We found that muscle tonus had three basic and concurrent cycles of change: one occurring every 1-2 minutes, one occurring every 5-10 minutes, and one every 3-4 hours. Other patterns were as follows: (1) when blood flow activity increased because of sexual arousal, muscle tonus increased and clitoral activity decreased, but occasional brief bursts of clitoral activity still occurred; (2) when uterine muscle activity increased, vaginal and clitoral blood flow decreased; (3) at the height of vaginal blood flow, clitoral activity decreased.

These complex but predictable interrelationships appear to be the normal pattern for orgasmic women. Such findings are the first data regarding female pelvic activity during arousal and orgasm.

NR194
ASSAULT HISTORIES OF INPATIENTS: INTERVIEW DATA

Thursday, May 23, 12 Noon-2:00 p.m.

Andrea Jacobson, M.D., Department of Psychiatry, SUNY/Buffalo School of Medicine, 462 Grider Street, Buffalo, NY 14215, Jill Koehler, B.S., Curt Pinchuck, B.A.

Summary:

100 male and female psychiatric in-patients were interviewed to determine the frequency, severity, interpersonal circumstances and perceived current effects of four kinds of assault experiences: physical-child, physical-adult, sexual-child, sexual-adult. The extent and severity of assault experiences substantially exceeded previously published data on the psychiatric population (often based on retrospective record review); the data obtained also exceeded baseline assault rates for the general, non-psychiatric population. The majority of the patients reported severe physical assault, either as a child or as an adult. Rates for severe sexual assault of women patients were also high, with 34% of the women reporting such assault as children, and 52% as adults. The inclusion in the data analysis of non-severe, but still significant, assault results in even higher rates. Assault history was perceived by patients as highly relevant to their current functioning; 40% of the patients reported at least one assault experience that they believed continued to have major effects on their current life. And 20% of the patients described permanent physical damage secondary to assault experiences. There were significant gender differences in many areas of the data, including differences in prevalence of assault experiences, site of assault (home vs. out-of-home), current feelings of guilt or shame. A detailed breakdown of data by assault type and gender is presented. The implications of the data for *routine* inquiry regarding physical and sexual assault history are discussed.

NR195
ISOLATION, AGGRESSION AND ANTIBODY RESPONSE IN MICE

Thursday, May 23, 12 Noon-2:00 p.m.

Michael A. Fauman, M.D., 25824 Dundee Road, Huntington Woods, MI 48070

Summary:

Male Balb/c mice (n = 24) were isolated on day 0. On day 20, 16 mice were grouped 4 to a cage and the dominant mouse, if any, in each cage identified. On day 22, a 5th group (n = 4) received 2 hours of intermittent shock (0.5 ma, 1 sec./min.). A 6th control group (n = 4) remained isolated. Following the shock all 24 mice were given 10.0 ug IV of Keyhole Limpet Haemocyanin (KLH). On day 29 anti-KLH IgG (aK-IgG) levels were determined by ELISA. The aK-IgG levels of the shocked mice and one cage of grouped mice which had no fighting nor dominance were significantly lower (t = 3.02, p < 0.05; t = 4.71, p < 0.01 respectively) than the controls. The aK-IgG levels of the 3 dominant males in the 3 other grouped cages were significantly lower than the non-dominant males (p < 0.02 Mann-Whitney U test). The most frequently attacked mouse had an aK-IgG level 100X > the dominant male in the same cage and 4X > the control. Further studies confirmed that dominant and submissive behaviors are correlated with opposite effects on antibody response in mice.

NR196
IRRITABLE BABY AND ADULT PSYCHOPATHOLOGY

Thursday, May 23, 12 Noon-2:00 p.m.

George U. Balis, M.D., University of Maryland, Dept. of Psychiatry, 645 W. Redwood Street, Baltimore, MD 21201,
Spyros J. Monopolis, M.D.

Summary:

Recent reports on the "irritable baby" (IB) as a predictor of childhood disorders, stimulated interest in its relationship to adult psychopathology. As part of a larger study involving 500 patients evaluated for episodic disturbances, we compared in this study 70 patients with a history of IB with 378 patients without such a history (NIB) through self-reported questionnaires and physician-reported data.

Results: *Physician data:* The following diagnoses occurred with higher statistical significance among IB versus NIB subjects: borderline personality disorder ($p < .000$), schizotypal personality ($p < .005$), schizoid disorder of adolescence ($p < .005$), phobic disorder ($p < .02$), avoidant personality ($p < .02$), schizoaffective disorder ($p < .002$), substance dependence ($p < .008$), affective disorder ($p < .07$), organic hallucinosis ($p < .045$). Also IB patients showed higher scores of $p < .001$ in: explosivity/impulsivity, generalized aggressiveness, violent dyscontrol, suicidal attempts, self-inflicted injuries, and episodic mood swings. *Self-reported data:* IB subjects showed higher scores in all scales of psychopathology, most of which at $p < .001$ level or greater. Symptom scales included paranoid, schizophreniform, compulsive, phobic, anxiety, depressive, and dissociative symptoms. Trait scales included paranoid, schizoid, passivity, egocentricity, sociopathy, cathectic lability, emotional lability, impulsivity, and emotional excitability traits. Affect/impulse dyscontrol scales included paroxysmal affective episodes, violent dyscontrol (self-directed and other-directed), and generalized aggression. Differences were more representative of males.

Discussion: A history of IB appears to be a major precursor of serious psychopathology not only in childhood but also in adolescence and adulthood, and is characterized by polysymptomatic presentation with prominent impulsivity and generalized aggressive dyscontrol.

NR197
COMMUNITY DEMORALIZATION AND DSM-III DIAGNOSIS

Thursday, May 23, 12 Noon-2:00 p.m.

Andrew E. Skodol, M.D., NYS Psychiatric Institute, 722 W. 168th Street, New York, NY 10032, Patrick E. Shrout, Ph.D., Bruce P. Dohrenwend, Ph.D., Janet B. W. Williams, D.S.W., Miriam Gibbon, M.S.W., Frederick Kass, M.D.

Summary:

This study investigates the relationship of demoralization, as measured by a scale of the Psychiatric Epidemiology Research Interview (PERI), and DSM-III diagnosis in a group of community subjects. 96 of 429 subjects who scored above an empirically-derived cut-score on the 27-item PERI demoralization scale and 55 randomly-selected subjects with scores below the cut were blindly re-interviewed using the DIS, supplemented with questions designed to make additional DSM-III diagnoses in the depressive spectrum. Current and lifetime diagnoses were made on the basis of the DIS data by two experts in DSM-III diagnosis, also blind to the demoralization status of the subjects. 17 of 96 demoralized subjects had a current major depressive episode, compared to only 1 of 55 not demoralized. This corresponds to a sensitivity of PERI demoralization for current MD of .78, a specificity of .76, an overall diagnostic power of .76 and a prevalence of current major depression of 6.3%. Other disorders from the DSM-III classes of affective, anxiety, and personality disorders also occurred significantly more frequently in the demoralized than in the not-demoralized group. In addition, of 40 highly demoralized community subjects without a current diagnosis, nearly half had past diagnoses of DSM-III major depression. This study adds to our understanding of what screening scales in the community measure in terms of standard psychiatric nosological categories. Demoralization continues to represent a measure of non-specific psychological distress, sometimes indicating current mental disorder, but also possibly representing the residual of prior illness, especially major depression.

NR198

Thursday, May 23, 12 Noon-2:00 p.m.

NATURAL DISASTERS: EMOTIONAL IMPACT ON CHILDREN

Sudhakar Madakasira, M.D., ECU School of Medicine, Department Psychiatric Med., Greenville, NC 27834, Lesly T. Mega, M.D., Kevin O'Brien, Ph.D.

Summary:

The eastern part of North Carolina was devastated on March 28, 1984 by a series of tornadoes that left a few people dead and hundreds injured or homeless. The emotional reactions in school children of kindergarten through 9th grade were assessed two-six weeks later in the tornado affected and closeby nonaffected areas. Of the 4085 children enrolled, 3752 (92%) filed out, with the help of their teachers, a self-report survey which included DSM-III symptoms for posttraumatic stress disorder (PTSD). Children of the tornado affected areas (n = 1833) reported a significantly higher frequency of irritability, intrusive thoughts and depressed feeling when compared to those (n = 1919) in nonaffected areas ($X^2 = 8.9, 6.6$ and 7.6 respectively, $p < 0.05$). The converse was seen with withdrawal and decreased appetite ($X^2 = 23.6$ and 20.4 respectively, $p < 0.001$). A total of 862 children (23%) met the criteria for PTSD but did not differ with regard to area ($X^2 = 0.3$, NS). Children, whose households were directly hit by the tornado (n = 377), were then compared to those not hit (n = 3367). The former reported a significantly higher frequency of several symptoms (intrusive thoughts, recurrent dreams, trouble concentrating, startle response, depression, separation anxiety, and sleep disturbance, all $p < 0.001$). More children from the former group also met the criteria for PTSD ($X^2 = 34.2$, $p < 0.001$). Prepubertal age (<12 years) and female gender were also significantly associated with PTSD ($X^2 = 43.1$ and 26.8 respectively, $p < 0.001$). These findings confirm that children directly involved in a natural disaster show a greater incidence of emotional reactions and suggest that younger children and girls may be also at a higher risk.

NR199

Thursday, May 23, 12 Noon-2:00 p.m.

LITIGATION AS A STRESS IN MEDICAL PRACTICE

Sara C. Charles, M.D., University of Illinois, Department of Psychiatry, 912 South Wood Street, Chicago, IL 60612, Richard B. Warnecke, Ph.D., Jeffrey Wilbert, M.A., Carlos DeJesus, M.A.

Summary:

Eighty physicians, all members of an original survey sample (in press), drawn randomly from the membership of the Chicago Medical Society, were interviewed to assess stresses - especially malpractice litigation - in their medical practices. Stresses in practice were divided into two main areas: 1) those which they anticipated and for which they feel relatively well prepared such as working with dying patients, interacting with patients' families, poor surgical outcome, and the pressure of time limitations; and 2) those which were unanticipated and for which they feel inadequately prepared such as the economic aspects of medical practice, interaction with office personnel and administrators, demands of academic life and the threat and actual involvement with the legal process. 52 of the 80 physicians had already been sued. Statistical analysis of data obtained comparing sued and non-sued doctors on a number of variables is in process. In addition, interview data that assesses common coping mechanisms and defensive styles as well as the doctor's own evaluation of his capacity to deal with stress is being analyzed. It is anticipated that the findings may provide a data base for stress reduction education in undergraduate and residency training programs as well as for programs for physicians already in practice.

NR200 **Thursday, May 23, 12 Noon-2:00 p.m.**
MEDICAL STUDENT PERCEPTIONS OF PSYCHIATRIST'S ROLE

Linda F. Pessar, M.D., Assistant Professor, Dept. of Psychiatry, SUNY, Erie County Medical Center, 462 Grider St., Buffalo, NY 14215, Seymour Axelrod, Ph.D., Marvin I. Herz, M.D.

Summary:

Does the psychiatric clerkship cause medical students to devalue the psychiatrist's role because of role confusion engendered by the team approach? For each of 33 clinical situations requiring intervention by mental health professionals, 76 psychiatry clerks rated the likelihood that it would be performed by (a) psychiatrist, (b) psychologist/social worker, (c) nurse/paraprofessional. Ratings were made before and after rotations on in-patient settings which use a non-egalitarian team approach.

Results showed that for interventions traditionally performed by only one of the three groups, significant pre-post changes indicated *increased* professional role differentiation. *Both* pre- and post-clerkship, functions often shared by psychiatrists and psychologists/social workers (e.g., psychotherapy) were judged more likely to be performed by psychiatrists. Post-clerkship attitudes toward psychiatry were significantly more positive than those reported in the literature.

Conclusion: A clerkship on hospital units using a modified team approach may *enhance* students' perceptions of role differentiation, and need not denigrate psychiatry as a medical specialty because of role confusion.

NR201 **Thursday, May 23, 12 Noon-2:00 p.m.**
DEPRESSION IN MEDICAL STUDENTS

Mark Zoccolillo, M.D., Dept. of Psychiatry, 4940 Audubon Avenue, St. Louis, MO 63110, George Murphy, M.D., Richard Wetzel, Ph.D.

Summary:

We prospectively assessed first and second year medical students for depression with a monthly Beck Depression Inventory. Students scoring above nine and a control group were interviewed using the NIMH Diagnostic Interview Schedule. 79% (389) of the students participated. Three cohorts were assessed during two years; one first year class, one second year class, and one cohort for both years. The incidence of major depression or probable major depression (3/4 symptoms) by DSM-III criteria during the first two years of medical school was 11%. The lifetime prevalence was 16%. A family history of treated depression was common among the depressed students (48% vs 17%, $P < .01$). 87% of the depressed students had a family history of treated depression or an episode of depression prior to their first or second year of medical school (70%). The mean age of onset of the first episode of depression was 19.4 years. Depression in medical students is more common than in the general population. A selection bias as seen by a family history of depression or a previous history of depression is an important factor in this increased prevalence. Many of the depressed students delayed or did not seek treatment; two depressed students ultimately left medical school.

NR202

Thursday, May 23, 12 Noon-2:00 p.m.

THE LIFETIME CREATIVITY SCALES: NEW RESEARCH TOOLS

Ruth L. Richards, M.D., Laboratories for Psychiatric Research, McLean Hospital, Belmont, MA 02178, Dennis K. Kinney, Ph.D., Inge Lunde, M.D., Maria E. Benet, A.B., Ann P. C. Merzel, A.B.

Summary:

A new instrument, The Lifetime Creativity Scales (LCS), is presented. Scales address a broad innovative capability as reflected in real-life accomplishment. The LCS rationale is based on evidence for a "disposition toward originality" found across diverse fields of endeavor. "Creative" activities meet criteria for (a) originality, and (b) meaningfulness to others. Previous measures have focused on specific areas such as the arts, sciences, and leadership, or have required that "creative" activities meet criteria for social recognition. The LCS has a much wider range of applicability. LCS ratings, made on six-point scales, reflect the peak level and the extent of vocational and avocational creativity over the adult lifetime; summary ratings are provided as well. Specific criteria and multiple examples are given for each rating level. Data is presented from an interviewed sample of 175 subjects. There is evidence for high interrater reliability, and for construct validity using several documented predictors of adult creativity, measures of education and intelligence, and Holland's primary interest styles. Factor analytic results upheld an hypothesized distinction between vocational and avocational creativity; quantity and quality of creative activity were associated in each of these areas. Illustrations of the use of primary and summary LCS ratings in psychiatric research are given. Of interest are apparent preferences for vocational or avocational creativity within different psychodiagnostic groups. The LCS will be made available to interested professionals for research purposes.

NR203

Thursday, May 23, 12 Noon-2:00 p.m.

THE SADS-L AND THE DIS: HOW DO THEY COMPARE?

Deborah S. Hasin, M.S., New York State Psychiatric Institute (DRAT), 722 W. 168th St., New York, NY 10032, Bridget F. Grant, Ph.D., Gary Hasey, Jerry Warsh, M.D., Harvey Stancer, M.D., Robert Cook, E. Persad, M.D., Theola Jorna

Summary:

We compared the results of two diagnostic interview procedures, the lifetime version of the Schedule for Affective Disorders and Schizophrenia (SADS-L) and the Diagnostic Interview Schedule (DIS) in a sample of 120 substance abuse inpatients during their third week of hospitalization (about two-thirds had been detoxified immediately prior to this admission). Lay interviewers administered the DIS and the DIS computer programs produced non-hierarchical DSM-III diagnoses. Two raters administered the SADS-L, one with several years of experience in the use of the instrument, the other extensively trained for this study. Inter-rater reliability was virtually perfect; these interviewers assigned RDC diagnoses. Kappa values of agreement between the SADS-L and the DIS varied considerably from diagnosis to diagnosis, reaching a high of .67 for drug abuse and/or dependence, and a low of -.03 for atypical bipolar disorder/bipolar II. In general, agreement for affective disorders, anxiety disorders (with the exception of panic disorder) and anti-social personality disorder was low, while agreement for drug abuse and/or dependence, alcohol abuse and/or dependence, and panic disorder was fairly good. Reasons for the diagnostic discrepancies between the instruments included criterion differences between the RDC and DSM-III, but the manner in which the two instruments operationalized the diagnostic criteria also contributed substantially to disagreement, where it occurred. Some causes of disagreement between the SADS-L and the DIS would pertain to any sample, while others are more specifically related to problems of diagnosis in individuals with substance abuse disorders. These and implications of the findings are discussed.

NR204
CAN CHRONIC INPATIENTS LEARN WHAT THEY TAKE?

Thursday, May 23, 12 Noon-2:00 p.m.

James C. Beck, M.D., Cambridge Hospital, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA 02139, Robert Staffin, A.B.

Summary:

Geller showed that State Hospital Patients do not know what medicine they take or what it does. No one has previously studied whether state hospital patients will learn about their medicine if they are taught.

We interviewed 57 State Hospital Patients about their anti-psychotic medication. 42 patients were given three educational sessions in which the name of the medicine, and risks and benefits were presented. All patients were reinterviewed one week and one month later.

Only 11 of 57 patients could initially identify the name of their antipsychotic medication and one therapeutic and one side effect. After the education sessions, only three additional patients could recall this information correctly.

Most of these patients do not meet Roth's definition of competence to consent to treatment. Our results suggest that, in Massachusetts, under the recent Rogers Decision, a majority of state hospital patients will require a court hearing and a judge's order to continue on medication. We question the utility of this procedure, and suggest an alternative.

NR205
FAMILY DIAGNOSES MISSED BY PSYCHIATRIC RESIDENTS

Thursday, May 23, 12 Noon-2:00 p.m.

Neil J. Baker, M.D., Assistant Professor, Dept. of Psychiatry, C268 Univ. Colo. Health Sci. Ctr., 4200 E. Ninth Avenue, Denver, CO 80262, Sandra L. Berry, M.S.W., Lawrence E. Adler, M.D., Ronald Franks, M.D., Merilyne C. Waldo, M.A., Robert Freedman, M.D.

Summary:

A family psychiatric history is a crucial aid to accurate diagnosis and treatment. Little is known about the utility of a standard clinical interview in detecting psychopathology in patients' relatives. We obtained family histories from 64 consecutively admitted adult psychiatric inpatients treated by PGY-3 residents who independently obtained family data while unaware of the research methods or goals. The residents generally asked the patients or a relative about psychiatric treatment or symptoms in the family, but rarely drew family trees. Using two informants, a family tree for all first- and second-degree relatives, and screening questions based on the Family History-Research Diagnostic Criteria (FH-RDC), our research team made almost four times as many diagnoses as the residents. Of the 23 relatives who had FH-RDC diagnoses of schizophrenia, other major psychotic disorder, bipolar disorder, or recurrent unipolar disorder, 13 were missed by the residents. Similarly, less than 40% of other affective disorders were detected by the residents. The results suggest that residents will miss a significant number of critical diagnoses unless a strategy of constructing a family tree and using a second informant is taught.

**NR206
MICRO-BASED DATA SYSTEM FOR A PSYCHIATRIC CLINIC**

Thursday, May 23, 12 Noon-2:00 p.m.

E. Michael Kahn, M.D., Box 3173, Duke University, Medical Center, Durham, NC 27710, Jacqueline Holland, R.N., Thomas L. Droege, Edward Goldenberg, M.D.

Summary:

Evolution of computer hardware and software, affording improved access to computer services at modest cost, provided impetus for development of a microcomputer-based record system for the Duke Psychiatric Outpatient Clinic. The clinic, a training site with more than 250 active patients, had previously been served by a remote job entry mainframe system. Goals for design were: 1) reduction in cost, 2) improved responsiveness and flexibility, 3) independence from external facilities, and 4) quality assurance. These were met through the development of a data management system using an IBM PC-XT (R) and dBase III (C).

The system: 1) records demographic, diagnostic, treatment plan, and medication information for each patient, 2) performs appointment scheduling, 3) maintains progress notes for each visit, 4) generates billing summaries, 5) facilitates administrative review of caseloads and training experience, and 6) provides printed documentation of the treatment process. It is menu-driven, and data are entered and retrieved by clerical personnel who were trained on site. Medication and diagnostic dictionaries improve accuracy of information entered, and cross-indexing facilitates review for completeness and consistency. Confidentiality is assured by limiting physical access to the computer and password protection of files. The system is unique in its admixture of defined data fields and free text fields. The switch to the new system from manual records took three months. Approximate hardware costs were \$6000 and software development costs were \$5000. Since the system is written in a widely known database management language, it may be modified to meet new needs and settings easily.

The process of design and implementation of the system will be detailed in this presentation. Factors which led to relevance and ease of use, responsible for its success, will be stressed.

**NR207
SHORT-TERM PSYCHOTHERAPY: PROCESS AND OUTCOME**

Thursday, May 23, 12 Noon-2:00 p.m.

Manuel Trujillo, M.D., Beth Israel Medical Center, 10 Nathan D. Perlman Place, New York, NY 10003, Arnold Winston, M.D., Leigh McCullough, Ph.D., Harold Been, M.D., Jerome Pollack, M.D., Richard Kestenbaum, Ph.D.

Summary:

Experimental outcome data of the psychotherapeutic treatment of patients suffering from personality disorders is scarce. This is equally true for long- and short-term forms of psychotherapy. Building on clinical and research insights developed by Sifneos, Malan and Davanloo, we designed a study to test process and outcome of two specific forms of short-term therapy applied to patients suffering from personality disorders (avoidant, dependent, compulsive and passive-aggressive; personality disorders which are characterized by inhibition of emotional expression and interpersonal difficulties). 20 patients were randomly assigned to waiting list control and two experimental groups. Both consisted of two forms of short-term therapy (maximum 40 one/week sessions) based on psychoanalytic psychodynamics. Multiple outcome measures were used at baseline, midphase, termination, and follow-up. We will demonstrate the differences in process and outcome of specific psychotherapeutic techniques. A careful analysis will delineate the impact of those technical ingredients which enhance emotional expression (use of confrontation, focus on affect, focus on patient-therapist relationship) vs. the impact of those technical ingredients enhancing cognitive awareness (use of non-confrontational interpretation: focus on cognition).

NR208
SOCIAL SKILLS TRAINING FOR SCHIZOPHRENICS

Thursday, May 23, 12 Noon-2:00 p.m.

Robert P. Liberman, M.D., Rehabilitation Service (691/B117), Brentwood VA Medical Center, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073, Charles J. Wallace, Ph.D.

Summary:

A controlled clinical trial of intensive social skills training vs. holistic health therapy, both combined with optimal neuroleptic drug therapy, was conducted with 28 schizophrenic patients diagnosed with the Present State Examination. The patients were at high risk for relapse because of histories of multiple hospitalization and their living with relatives who were high on "expressed emotion." Measures were taken before and after the 9 weeks of inpatient treatment and at six month intervals thereafter for a two year follow-up. Ratings were made of social skills, psychopathology, and community adjustment.

Compared to patients who received an equally intensive regimen of jogging, meditation, and other stress reduction modalities, the social skills patients learned the social problem-solving skills and retained these skills over the follow-up period. Improvements also favored the patients who received social skills training on social and community adjustment, relapse and rehospitalization.

NR209
PSYCHOTHERAPY FOR DEPRESSED INPATIENTS

Thursday, May 23, 12 Noon-2:00 p.m.

Ivan W. Miller, Ph.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906, William H. Norman, Ph.D., Gabor Keitner, M.D.

Summary:

No previous study has investigated the efficacy of psychotherapy for a severely depressed *inpatient* sample.

In this study, 47 inpatients who met DSM-III criteria for major depression were randomly assigned to one of three conditions: a) Standard Treatment, consisting of antidepressant medication and brief contacts with a psychiatrist, b) Cognitive Therapy + Standard Treatment, or c) Social Skills Training + Standard Treatment. Patients began these treatment protocols while in the hospital and continued them for 20 weeks after discharge. For comparison purposes, an "Assessment Only" group of 27 inpatients with a diagnosis of major depression received the same assessment battery as the patients in the treatment conditions, but no attempt was made to specify their treatment.

At the end of treatment (20 weeks post discharge from the hospital), the following results were obtained. 1) The Standard Treatment group had a lower rate of noncompliance than the Social Skill Training group. 2) While the means of all groups were in the nondepressed range, there were no significant differences between groups in level of depression. 3) The Standard Treatment and Cognitive Therapy groups had a significantly higher proportion of patients who made a complete recovery than did the Assessment Only group.

NR210**Thursday, May 23, 12 Noon-2:00 p.m.****FOCAL FAMILY THERAPY IN FAMILIES OF SCHIZOPHRENICS**

Judith E. Levene, M.S.W., Clarke Institute of Psychiatry, 250 College St., Toronto, Ontario, M5T 1R8 Canada, Frances Newman, M.A., Joel J. Jeffries, M.B.

Summary:

Recent evidence suggests that in the treatment of schizophrenics, 1) family interactions play an important role in the course of the illness and the outcome of treatment, and 2) schizophrenics in treatment do best when the treatment combines pharmacological and psychosocial components.

Our family therapy outcome study compares the benefits of two forms of family therapy combined with neuroleptic medication for adult schizophrenics. This study has yielded preliminary findings bearing on important aspects of the treatment of schizophrenics: 1) Families are helped to become, and to be experienced by the patients as, important sources of support when family therapy centers on redefining family structure and supporting parental roles as parents temporarily and flexibly "prop up" impaired ego functions of the patients; 2) Family therapy is most effective when the therapy is tailored to the needs of each family based on the stage of the patient's illness, the level of the family's understanding about the illness, and the dynamics of family life.

Family and therapist are aided in their collaboration when a dynamic focus for understanding and intervention is formulated to guide the therapy.

Preliminary data from this study comparing two forms of family therapy—Focal Family Therapy and Supportive Management Counselling—will be presented to 1) demonstrate their efficacy compared to other psychosocial therapies and 2) demonstrate the long-term effects of the therapies as measured by patient and family variables.

NR211**Thursday, May 23, 12 Noon-2:00 p.m.****CONSOLIDATED HEALTH CARE FOR ADOLESCENTS**

Felton Earls, M.D., Washington University School of Medicine, Department of Psychiatry, 4940 Audubon Avenue, St. Louis, MO 63110, Arlene R. Stiffman, Ph.D.

Summary:

The Robert Wood Johnson Foundation, recognizing that the rate of mortality was increasing among adolescents, funded a national project that enabled 20 medical schools to consolidate academic and community services to improve health care for this age group.

This poster session gives results from the first stage of a controlled study to evaluate this project. Over 3000 randomly selected youth using both consolidated and nonconsolidated services are being interviewed at two points in time to determine how successfully their problems are identified and treated. Several illustrative posters will be presented outlining the different patterns of medical and psychiatric staffing between clinics, the distribution of behavioral, social and health problems, and the relationship between staffing patterns and problem identification. Discussion will center on difficulties in mounting such experimental field evaluations, as well as on understanding the behavioral and social dimensions of adolescent health problems.

NR212**Thursday, May 23, 12 Noon-2:00 p.m.****PSYCHIATRIC ILLNESS IN SEVERELY ASTHMATIC CHILDREN**

David A. Mrazek, M.D., National Jewish Hosp. & Res. Center, 3800 East Colfax Ave., Denver, CO 80206

Summary:

A consecutive sample of 35 moderate to severely asthmatic children aged 6 to 17 was assessed using DSM-III diagnostic criteria. Three broad categories based on Axis I diagnoses were compiled: 1) children with no psychiatric diagnosis (22%); children with either a diagnosis of adjustment disorder or psychological factors affecting physical condition (49%); and 3) those with more serious psychiatric illness (29%). The predominant diagnosis in the last group was dysthymic disorder (n = 8).

Each child's level of adaptation was assessed using the Child Global Assessment Scale (CGAS), which identified subgroups with good, intermediate, and maladaptive adjustment. A strong relationship between severity of psychiatric diagnosis and competence in school and interpersonal relationships was demonstrated ($p < .001$). Comparing the CGAS scores of those children with dysthymic disorder to the others yielded a highly significant differentiation ($p < .01$). These findings support the clinical observation that the simultaneous occurrence of both depressive illness and serious physical illness is likely to have a highly disorganizing impact on a child's capacity to function. Consequently, more intensive intervention would seem justified than what would be required to treat either disease in isolation.

NR213 **Thursday, May 23, 12 Noon-2:00 p.m.**
UNDIAGNOSED MEDICAL ILLNESS ON A CHRONIC CARE WARD

Richard L. Borison, M.D., VA Medical Center, Psychiatry Service, 116A-D, Augusta, GA 30910, Mark E. Shelhorse, M.D., Chandresh Shah, M.D., Ana Hitri, Ph.D., Bruce I. Diamond, Ph.D

Summary:

It has been suggested that patients in custodial settings receiving regular medical care are as competently treated as patients in more medically intensive settings. This concept was tested when a 43-bed unit of chronic schizophrenics became a psychopharmacology research unit. Patients previously received annual physical exams and biannual lab exams. For research purposes all patients underwent physical and laboratory examinations. We found that 93% of patients had undiagnosed tardive dyskinesia and that 23% of patients had abnormal indices on CBC consistent with anemia that went undiagnosed. Cardiac exams revealed many difficulties not previously noted, including, bundle block in 7%, myocardial infarctions in 5%, arterial enlargement in 12%, ventricular enlargement in 5%, as well as several cases of undiagnosed premature arterial or ventricular contractions and even heart block. Urinalysis revealed 5% of patients with hematuria and 56% of patients with changes consistent with urinary tract infection. It would appear that more intensive programs lead to superior medical care.

NR214 **Thursday, May 23, 12 Noon-2:00 p.m.**
SOMATIC TREATMENT NEEDS OF A COMMUNITY SAMPLE

Alan J. Romanoski, M.D., Dept. of Psychiatry & Behavioral Sciences, The Johns Hopkins Hospitals, Baltimore, MD 21205, Gerald A. Nestadt, M.D., Marshal F. Folstein, M.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D.

Summary:

A medication's effect on a mental disorder's course is studied in patients. Do these patients differ from cases of the same disorder who are not in treatment? We offer data on this question.

Four specially selected and trained research psychiatrists examined a multistage stratified probability sample (N=810) of 175,000 eastern Baltimore residents over 18 years of age. Their mission was to identify each subject's DSM-III defined disorder after a standardized 2-hour examination. The standard examination format and record was developed as a validation study of the NIMH Diagnostic Interview Schedule in the Eastern Baltimore site of the Epidemiologic Catchment Area Studies. The subjects were research volunteers for whom the research psychiatrists had no clinical responsibility. Their selection (by others) in the prior stage was such that about 1/2 would show mental disorders. The last items on each record form asked the examining psychiatrist for treatment recommendations if he/she were psychiatric consultants. Somatic treatments were recommended for 126 subjects. The examiners felt morally obliged to transmit recommendations in 80 instances despite our "no-clinical-intervention" rule.

By weighted calculations, 8.0% of eastern Baltimore adults need pharmacologic treatment for a mental disorder, only 3/5 of whom were getting the recommended type of treatment.

The paper describes how the frequency of people recommended neuroleptics (1.3%), antidepressants (1.9%), sedatives or hypnotics (4.5%) or other somatic treatments (0.7%) vary by age, sex, race and diagnosis. The characteristics which distinguish people not receiving the recommended treatment from those who do are emphasized.

NR215
CLOSING THE MENTAL HOSPITAL

Thursday, May 23, 12 Noon-2:00 p.m.

S. Brandon, M.D., Dept. of Psychiatry, Clinical Sciences, Leicester Royal Infirmary, Leicester, England LE2 7LX, Liam Donaldson, M.D.

Summary:

With the long threatened hospital closures, services to an English county of 860,000 are reviewed. Two large hospitals provide 1090 beds. 57.5% residents are over 65 years and 2/3 of these are demented. 20% are over 75 years. 30.4% over 65 years have been in hospital for less than 1 year but 72% are severely incapacitated. Only 9% patients over 65 were in hospital for less than 1 year and had low social withdrawal scores. 19% under 65 and hospitalized under 1 year were severely disabled but 54% of those between 1 & 2 years. The lowest disability rate 14% was in those with a hospital stay between 5 and 10 years. 20% of those in hospital less than 1 year or 1 to 2 years were first admitted more than 5 years ago. 26% of beds in the system were designated as acute but 71% of patients suffered from schizophrenia, organic states or dementia. Discharged long stay patients after a rehabilitation programme experienced a quality of life in the community worse than in hospital. This policy attributed to "therapeutic radicals and fiscal conservatives" is likely to please neither.

NR216
SCHIZOPHRENIA: P300 TEMPORAL LOBE DEFICIT CONFIRMED

Thursday, May 23, 12 Noon-2:00 p.m.

Michael W. Torello, Ph.D., Harvard Medical School, Mass. Mental Health Center, 74 Fenwood Rd., Boston, MA 02115, Martha E. Shenton, Ph.D., Geraldine P. Cassens, Ph.D., Frank H. Duffy, M.D., Robert W. McCarley, M.D.

Summary:

Using the new non-invasive technique of brain electrical activity mapping (BEAM) we discovered a deficiency of integrated left temporal amplitude (LTA) of P300 waveform (an index of information processing) in chronic, medicated schizophrenics (SZ). This LTA feature also correctly diagnosed 9/10 individual SZ and 9/10 controls. We are now testing its diagnostic validity on a new sample. To date, we have tested 5 new medicated psychotic subjects: for the 3 subjects diagnosed as SZ on DSM III, RDC, and Feighner criteria these preliminary data show a left temporal deficiency of the P300 wave in *each* subject that, on statistical analysis, corresponds exactly to the left temporal region defined in the first study, thus tentatively confirming it. Furthermore, neuropsychological tests show deficits compatible with temporal lobe dysfunction.

NR217
EXPLOSIVE VIOLENCE IN PRIMATES

Thursday, May 23, 2:00 p.m.

William T. McKinney, M.D., Department of Psychiatry, Clinical Sciences Center, University of Wisconsin Medical School, 600 Highland Avenue, Madison, WI 53792, Gary W. Kraemer, Ph.D., Michael H. Ebert, M.D., C. Raymond Lake, M.D.

Summary:

The effects of early social deprivation are seen across a broad spectrum of clinical diagnostic categories but have rarely been investigated prospectively.

Adolescent male rhesus monkeys with a history of social deprivation for one month in the second six months of life were given two doses of d-amphetamine (1.5 mg/kg six hours apart). There was no reason to expect problems since the monkeys had been living together for years and had stable levels of affiliative behaviors, typical of peer-reared monkeys. After the second dose, unanticipated violence left one monkey dead and two in severe shock. The remaining subject, the dominant monkey, was severely wounded. Acute, lethal violence of this kind is not normal in rhesus monkeys at any age and illustrates the nature of the explosive violence syndrome. These episodes did not occur in monkeys reared socially without a period of social deprivation when they were given comparable doses of d-amphetamine. Even doses as low as 0.5 mg/kg can precipitate these bouts of severe aggression in animals with a history of social deprivation.

Subsequent work has demonstrated that d-amphetamine produces large increases in CSF norepinephrine in socially deprived monkeys but not in socially reared monkeys until they receive doses six times higher.

Alterations in rearing conditions may alter underlying neurobiological systems thus leading to increased vulnerability to later stressors. These alterations are masked but become apparent with challenge. There are major implications for understanding the long-term effects of alteration of early rearing conditions.

NR218
BEHAVIORAL FAMILY THERAPY FOR SCHIZOPHRENICS

Thursday, May 23, 2:15 p.m.

Ian R. H. Falloon, M.D., Buckingham Hospital, High Street, Buckingham, MK18-1NU England, Christine McGill, Ph.D., Jeffrey Boyd, Ph.D., Robert P. Liberman, M.D.

Summary:

A controlled clinical trial of home-based behavioral family therapy—comprising education about schizophrenia, training in communication skills and problem-solving skills—combined with optimal neuroleptic therapy, crisis intervention and case management was conducted with 36 schizophrenic patients. The control therapy was equally frequent sessions of clinic-based supportive individual therapy. Therapy sessions were conducted every week for 3 months, biweekly for 6 months, then monthly for the remainder of the 2-year period of treatment. Measures were taken blindly on psychopathology as well as on a variety of dimensions of community adjustment, social functioning, family interaction and coping, and relapse.

Results indicated that, after two years 11% of the patients receiving behavioral family therapy relapsed vs. 78% of patients receiving individual therapy. Statistically significant advantages in outcome also accrued to the patients and relatives in the family therapy condition on social functioning, coping, family burden, and rehospitalization. Cost effectiveness was significantly better for the behavioral family therapy as well.

NR219
CHILD ABUSE EPIDEMIOLOGY: SOME NEW PERSPECTIVES

Thursday, May 23, 2:30 p.m.

Nicholas A. Green, M.D., The University of Alabama, College of Community Health Sciences, Box 6291, University, AL 35486, L. Ralph Jones, M.D., Lee W. Badger, M.S.W.

Summary:

By factor analysis, a sample of all Alabama reports of child abuse and neglect for 1982 (23,000) was derived, which included 25-67 counties (6,818 records). Of 2,409 reports of physical/sexual abuse, there were 864 confirmed cases. The state-specific rates for a number of epidemiologic variables were considerably higher in Alabama than in the literature. Examination by actual town size instead of by SMSA/non SMSA revealed increased risk for both sexual and physical child abuse, regardless of race, in small towns of 10,000 to 50,000 located outside of metropolitan areas. Most physical injuries in either form of abuse were not severe, as commonly reported, but most abuse was chronic, with implications about the consequences for the child victim. Female-headed families of both races were at high risk, but the majority of physical and sexual abuse involved two-parent white families. The results of this study suggest entirely new perspectives on descriptive variables in child abuse epidemiology.

NR220
PARASUICIDE CHANGES DURING A TEEN SUICIDE CLUSTER

Thursday, May 23, 2:45 p.m.

Lucy Davidson, M.D., Violence Epidemiology Br., Centers for Disease Control, Atlanta, GA 30333

Summary:

Data from non-criminal police reports were used to compare parasuicides in 1982 and 1983 in a suburban community. These reports were generated by calls directly to the police, calls to the community's ambulance service or presentation to the area's general hospital. Thus, the reported parasuicides represent a more broadly based population than previously studied. The 1982 parasuicides preceded a widely-publicized cluster of teen suicides in 1983. Comparison of the two years' data shows an increase in the number and rate of reported parasuicides and a reduction in the mean age at time of attempt. Geographic clustering of parasuicides by neighborhood occurred. Enrollment in the same school as a teen suicide was also positively correlated with parasuicide. Specific social linkages among some of the parasuicides and suicides can be demonstrated.

NR221

Thursday, May 23, 3:00 p.m.

PSYCHIATRISTS FIND 27% OF COMMUNITY NEED TREATMENT

Alan J. Romanoski, M.D., Dept. of Psychiatry & Behavioral Sciences, The Johns Hopkins Hospitals, Baltimore, MD 21205, Gerald A. Nestadt, M.D., Marshal F. Folstein, M.D., Michael Von Korff, Sc.D., Morton Kramer, Sc.D., Ernest M. Gruenberg, M.D.

Summary:

For the first time, estimates of psychiatric treatment needs for a population have been based on direct clinical examinations of community subjects.

Four specially selected and trained research psychiatrists examined a multi-stage stratified probability sample (N-810) of 175,000 Eastern Baltimore residents over 18 years of age. Their mission was to identify each subject's DSM-III-defined disorder after conducting a standardized psychiatric examination which averaged two hours in duration. The Standard Psychiatric Examination (SPE) format and record was developed as a validation study of the NIMH Diagnostic Interview Schedule in the Eastern Baltimore site of the Epidemiologic Catchment Area studies. The subjects were research volunteers for whom the research psychiatrists had no clinical responsibility. At the conclusion of each examination, each psychiatrist wrote a treatment plan for each subject as if he were acting as a consulting psychiatrist making recommendations to the subject's primary care physician. These treatment plans were recorded on pre-coded forms.

Aggregating the 810 treatment plans, weighting each subject according to the strata and response rates, and adjusting to the 1980 census produced an estimate that 27% of the population of eastern Baltimore could be expected to benefit from treatment for their mental disorders: 19.8% from psychological or behavioral treatments, 12.7% from adjunctive medical evaluation or treatment, 8.0% from psychopharmacologic treatments, and 8.2% from social or rehabilitative interventions. Whether the treatment need is met or unmet, the clinical DSM-III diagnoses, and some personal characteristics are presented.

NR222

Thursday, May 23, 3:15 p.m.

THE ECOLOGY OF SUICIDE IN CANADA

Isaac Sakinofsky, M.D., Professor, Psychiatrist-in-Chief, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, Canada M5B 1W8, Robin Roberts

Summary:

The present study follows in the tradition of Emile Durkheim's epoch-making study (1897) of suicide in the "departments" of Western Europe but uses data analysis methods not available to him in an attempt to shed light on the social causation of suicide. Standardized averaged suicide rates for the provinces of Canada for the pre-censal periods 1969-71 and 1979-81 were calculated and these rates related to social, economic, and cultural data collected during the two public census' across the decade. Certain of the provinces have increased their suicide rates and these can be shown to be related to changes in the socio-cultural matrix. The data analysis included principal component analysis of 178 social variables and regression of these principal components on the male and female suicide rates. 88.3% of the variance in male suicide and 88.71% of the variance in female suicide could be explained.

NR223
CONSENT RATES IN SCHIZOPHRENIC AND CONTROL GROUPS

Thursday, May 23, 3:30 p.m.

Llewellyn B. Bigelow, M.D., William A. White Division, St. Elizabeths Hospital, Washington, DC 20032, Tammy L. Braun, B.A.

Summary:

Important and potentially controversial research conducted in mentally disabled persons include studies with no direct benefit to the participants. Studies of hypothetical consent rates indicate no difference between medically and mentally ill groups in a wide range of risk categories. We report a comparison of actual consent rates in schizophrenic patients with hypothetical consent rates in two control groups.

Methods: Inpatients (n=56) at the NIMH Neuropsychiatry Branch were asked to consent to the following procedures: 24-hour urine samples, multiple venipuncture, a head CT scan, electroretinogram, and lumbar puncture. These procedures produce no direct benefit to the subject, but are designed to develop general knowledge about the illness. Two control groups were given questionnaires and sample consent forms for the same procedures. Respondents were asked to indicate their consent under four conditions: 1) a random sampling, 2) paid random sample, 3) having a serious illness of unknown cause, and 4) a relative having a serious illness of unknown cause. One control group consisted of attendees at an Institutional Review Board conference (n=23); the other was a sample of research staff (n=20).

Results: The control groups consent rates varied strongly depending upon the procedure and the condition proposed. Consent rates of the schizophrenic patients were not significantly different from the controls under condition 3: having a serious illness of unknown etiology. Our results support a conclusion that severely ill schizophrenic persons do make choices and that their decisions are similar to those made by persons without mental disability.

NR224
HYPNOTIC HALLUCINATION ALTERS EVOKED POTENTIALS

Thursday, May 23, 3:45 p.m.

David Spiegel, M.D., Psychiatry TD114, Stanford School of Medicine, Stanford, CA 94305, Steven Cutcomb, Ph.D., Chuan Ren, M.D., Karl Pribram, M.D.

Summary:

Brain electrical potentials evoked by visual stimulation were analyzed to study the neurophysiological mechanism associated with hypnotic hallucination. The visual evoked responses of 6 high and 6 low hypnotizable subjects were compared in three hypnotic conditions: stimulus enhancement, stimulus diminution, and stimulus elimination (obstructive hallucination). Highly hypnotizable individuals demonstrated significant suppression of the later components of the evoked response (N_2 and P_3) while experiencing obstructive hallucinations, indicating a change in information processing. This effect was significantly greater in the right, as compared to the left, occipital region.

NR225
FAMILIES OF THE CHRONICALLY HOMELESS

Thursday, May 23, 4:00 p.m.

Howard Dichter, M.D., Hahnemann University, Dept. of Psychiatry, Mail Stop 350, Broad and Vine Sts., Philadelphia, PA 19102, A. Anthony Arce, M.D.

Summary:

There has been increasing public concern over the problem of homelessness. Recent reports have shown that there is a high incidence of psychiatric illness among this population. Little is known about the relationship between disturbed homeless persons (HP's) and their families. We will report findings from a pilot study designed to examine some aspects of this relationship.

Family members of ten hospitalized chronically homeless persons admitted to a psychiatric unit were interviewed. Chronic homelessness was defined as greater than thirty consecutive days of living without shelter. Schizophrenia, substance abuse and severe personality disorder were the most common diagnoses among these HP's.

The change from stable family living to homelessness was explored. Familial problems, psychiatric illness and economic strain were common factors which appeared related to the development of homelessness. Evidence of family problems preceded the beginning of homelessness by years. Psychiatric illness among the parents of the HP's was frequent. Few of the families of HP's were intact. Sometimes homelessness appeared to facilitate stability of the family unit.

Ongoing contact between HP's and their families appeared more frequent than was previously expected. Often the relationship between the HP and their families was angry and hostile. Some families maintained large networks which tracked their HP's. These families were sophisticated in their use of available community resources. Many families persisted in caring about their HP thereby providing an opportunity for family involvement. The role of families in the treatment of homelessness will be explored.

NR226
WOODSHEDDING: A PHASE IN RECOVERY FROM PSYCHOSIS

Thursday, May 23, 4:15 p.m.

John S. Strauss, M.D., Yale University, Dept. of Psychiatry, 25 Park Street, New Haven, CT 06519, Joshua Sparrow, Courtenay M. Harding, Ph.D., Hisham Hafez, M.D., Paul Lieberman, M.D.

Summary:

Until recently amazingly little attention has been paid to the evolution of patients' disorders after a psychotic episode. And yet research with such a focus may provide key information about processes of recovery and recurrence. This report describes findings from a study carried out to chart the evolution of patients' lives and illnesses in the year following hospitalization for severe psychiatric disorder. In this study 28 subjects were assessed with standardized interviews at bimonthly intervals over a one-year period. A final follow-up was carried out two years after hospital discharge.

Findings suggested that specific phases through which patients passed during that period could be identified. One of the most important of these was the "woodshedding" phase. During this phase, the patient appeared to be at a plateau. No measurable improvements in symptomatology or social functioning could be identified. But the assessments also indicated that subtle changes were occurring. These changes led to increasing abilities and pressures in the patient to make major life changes. The identification of the "woodshedding" phase has several major implications for treatment as well as for understanding the process of recovery from psychosis. Expectations of the patient by clinicians and family members can be modified, phase-specific treatment can be considered, and the processes requiring an apparent plateau during recovery can be identified. These and other implications of the woodshedding phase will be discussed.

NR227 **Thursday, May 23, 4:30 p.m.**
TESTING SYMPTOM CRITERIA FOR DSM-III SCHIZOTYPAL AND BORDERLINE PERSONALITY DISORDERS

Thomas H. McGlashan, M.D., Chestnut Lodge Research Institute, 500 West Montgomery Avenue, Rockville, MD 20850

Summary:

Schizotypal and borderline personality disorders (SPD & BPD) appear to be different by follow-up, yet are poorly discriminated from each other by current DSM-III symptom criteria. In the Chestnut Lodge Follow-Up Study, three Axis II study cohorts (pure SPD, n = 10; pure BPD, n = 81; mixed SPD/BPD, n = 18) with distinctive outcomes are defined using current borderline diagnostic systems (DSM-III SPD, DSM-III BPD, Gunderson et al. borderline). This study compares the relative frequency (strengths) with which *individual* symptom criteria from each system discriminate (by χ^2 analysis) across these study cohorts.

Results support the retention of some but the elimination of other symptom diagnostic criteria in DSM-III SPD and BPD (specifics to be detailed). The findings, in conjunction with recent literature (also to be detailed) suggest: (1) the most characteristic (core) symptoms for DSM-III SPD are odd communication, suspicious/paranoid, and social isolation while the least discriminating is illusions/depersonalization/ derealization. (2) The core symptoms for DSM-III BPD are unstable relationships, impulsivity and self-damaging acts while the least discriminating is inappropriate anger. (3) The symptom, depression (Gunderson et al. criterion), does *not* discriminate SPD and BPD and (4) transient psychoses (the Gunderson et al. criteria of brief paranoid experiences and regression in treatment) discriminate for SPD but against BPD and therefore fit better as SPD criteria. Implications for future modifications of DSM-III SPD and BPD criteria are discussed.

NR228 **Thursday, May 23, 4:45 p.m.**
NEW SUPPORT FOR A SCHIZOTYPAL/BORDERLINE DICHOTOMY

David L. Braff, M.D., UCSD Medical Center, 225 Dickinson Street, San Diego, CA 92103

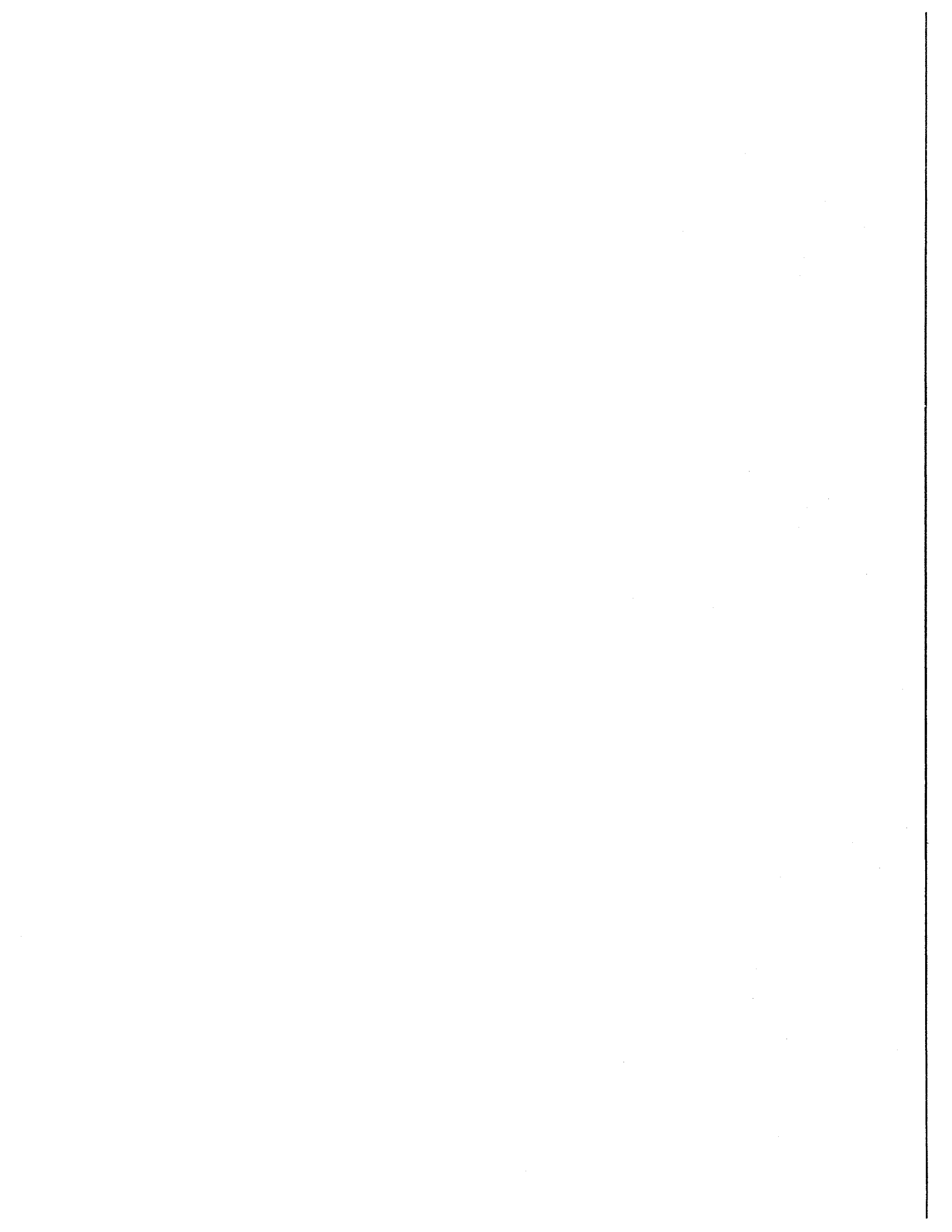
Summary:

One of the most vexing problems in modern biological psychiatry is the attempt to find reliable markers that differentiate schizotypal from borderline disordered patients. In this study, such differentiating data are reported using a visual backward masking technique that reliably measures a subject's attentional/information processing capacity. Sixteen schizotypal and 16 borderline patients were tested and measures of visual thresholds (the critical stimulus duration or CSD) and speed of information processing were obtained. The information processing data were analyzed by ANOVA; 1) The schizotypals scored in the slow (impaired) range, typical of schizophrenic patients. 2) In distinction, the borderlines scored significantly better (p .01) and were in the range of minor depressive patients. Measures of gross psychopathology, medication effect, age, and IQ did not account for the observed differences. These results offer novel, biologically based support for the schizotypal/borderline distinction of Spitzer et al. and the DSM-III.

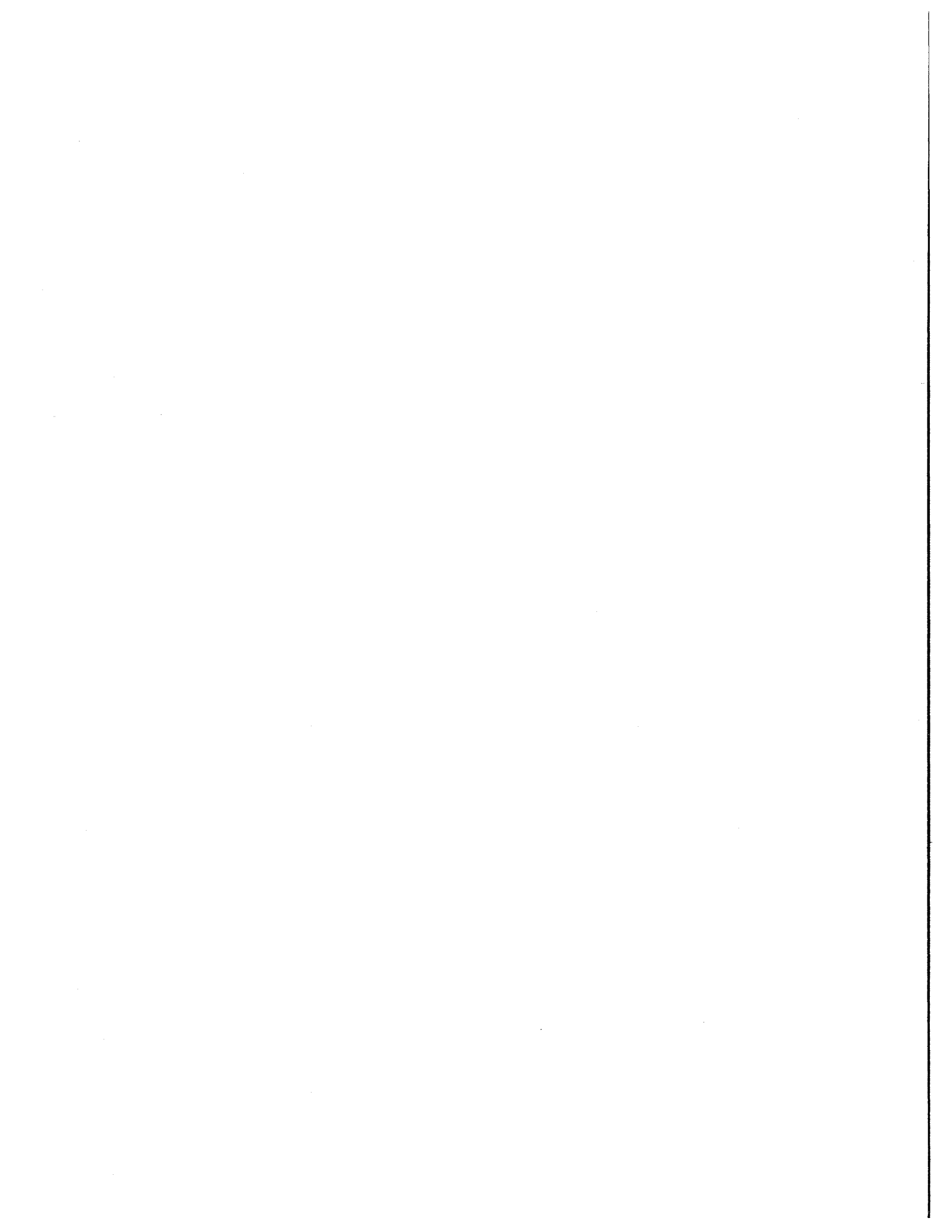
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