March 1, 1975

psycho pharma cology division 28 newsletter

## BY-LAW CHANGES APPROVED

The proposed changes in Division 28 by-laws have been approved by an overwhelming majority. 85% of those voting approved the changes in terms of office, 15% disapproving. 87% of those voting approved the by-laws concerning student member status and a student on the Executive Committee.

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## NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

Albert Pawlowski has indicated in recent informal contacts with the Newsletter staff that some new directions of research in which NIAAA is interested are the following:

1) Alcoholism and alcohol abuse among youth and the aged.

2) Alcoholism and alcohol abuse in connection with the retirement years.

3) Effects of the association of heavy drinking and cancer and heart disease.

4) The role alcohol plays in the family--it may at times be of beneficial use.

5) Fetal alcohol syndrome: Recent evidence indicates that pregnant women who are heavy drinkers may have offspring with alcohol syndrome.

6) The alcoholic woman: How is she different from the alcoholic male? There may be causes of her alcoholism different from those of the male's. If so, could treatments differ?

## NIAAA RESEARCH GRANTS, FY 1974, RELEVANT TO PSYCHOPHARMACOLOGY

Alteration of alcoholic patients' drinking behavior (R01 AA00179)
George E. Bigelow
Baltimore City Hospitals

Brain stimulation and alcohol preference (R01 AA00203)
Roy A. Wise
Sir George William University

Studies of habituation to alcohol (R01 AA00215)
R.J. Senter
University of Cincinnati

Alcohol intoxication and dependence in animals (P01 AA00231)
Fred W. Ellis
University of North Carolina

Ethanol effects on motor control and on polydipsia (R01 AA00253)
John L. Falk
Rutgers - The State University

Alcohol and behavior: A genetic and biochemical study (R01 AA00293)
Gerald E. McClearn
University of Colorado

Variables related to ethanol self-administration (R01 AA00299)
Travis I. Thompson and R.A. Meisch
University of Minnesota

Opiate addiction and alcoholism: Concurrent treatment (P01 AA00379)
Ira A. Liebson
Baltimore City Hospital

Community-reinforcement for treating alcoholic persons (R18 AA00457)
Nathan H. Azrin
Anna State Hospital

Investigations of experimental alcohol dependence (R01 AA01217)
Wilbur M. Davis
University of Mississippi

antagonist blockade and unblocked conditions. Because of the limitation in generalizing about behavior observed in one setting to that in other more complicated settings, patients are followed after discharge in order to determine the relationship (if any) between behavior observed on the research ward and behavior which occurs in the community. The design also permits the correlation of biological factors (drug metabolism, endocrine homeostasis, sleep-wakefulness patterns, catecholamine metabolism and other biochemical and physiological variables) with behavioral observations during a drug-free period and cycles of heroin administration, methadone assisted withdrawal, and narcotic blockade.

The program is currently concerned with: 1. A clarification of conditioning factors and their role in the addiction process; and 2. a better definition of the conditions under which one may define a successful outcome with narcotic antagonist treatment.

Basic Behavioral Studies: Dr. Nancy K. Mello has recently joined the Center research staff and is in the process of setting up a behavioral science laboratory for animal studies of drug abuse. This research program will parallel and complement the clinical research programs. The program will initially focus on the behavioral and biological effects of antagonists in an operant self-administration framework.

BEHAVIORAL PHARMACOLOGY RESEARCH UNIT
UNIVERSITY OF OTTAWA
contributed by Roger Stretch

The Behavioral Pharmacology Research Unit (Director, Dr. Roger Stretch; Senior Research Associate, Dr. Gary J. Gerber) is supported by Grant 1212-5-103 from the Non-Medical Use of Drugs Directorate, Health and Welfare, Canada. The project that we are undertaking is entitled Experimental Investigations of the Behavioral and Pharmacological Determinants of Drug Dependence in Monkeys.

This project includes three basic categories of experiments. The first category concerns experiments dealing primarily with the acquisition and maintenance of drug self-administration behavior in squirrel monkeys, using a chronic i.v. cannulation procedure (Stretch, R. and Gerber, G.J., Canad. J. Physiol. Pharmacol., 1970, 48, 575-581). Current investigations, employing discrete-trial, second-order schedules of drug reinforcement, are being undertaken in an effort to quantify the relative reinforcing effects of several representative drugs with dependence-producing properties (narcotic analgesic drugs; psychomotor stimulant drugs). Experiments are also being done employing schedule-induced polydipsia as a means of engendering oral intake of dependence-producing drugs such as morphine, and the effects of drugs with antagonist properties. The third category of experiments involves comparison of drug-induced changes in operant baselines maintained by schedules of food or electric-shock presentation.

GEORGIA INSTITUTE OF TECHNOLOGY
EMORY UNIVERSITY
DEPARTMENT OF PHARMACOLOGY
YERKES REGIONAL PRIMATE RESEARCH CENTER
contributed by Larry D. Byrd

Behavioral pharmacology in Atlanta is characterized by the work underway at three institutions. Laboratories actively studying the effects of drugs on behavior exist at Georgia Institute of Technology, and the Department of Pharmacology and Yerkes Regional Primate Research Center of Emory University.

Jack Marr, an Associate Professor in the Department of Psychology at Georgia Tech, has an ongoing program

to morphine and related drugs. Jim O'Callaghan, another graduate student, has shown that rats exposed to morphine *in utero* exhibit less analgesia when tested with morphine at 5-6 weeks of age than comparable handled offspring of mothers that were treated with saline. Dose-response curves for morphine have been determined in the offspring, and Jim has been able to demonstrate that the prenatal effects of morphine persist in offspring that have been reared by cross-fostering.

Experiments in behavioral pharmacology at the Yerkes Regional Primate Research Center include a continuation of the work I had been doing at the New England Regional Primate Research Center, and studies by Al Pieper on physical dependence on ethanol in the rhesus monkey. To develop the oral intake of ethanol, monkeys were surgically prepared with chronically indwelling venous catheters. Whenever the subject accepted water from a drinking tube, ethanol was injected via the catheter. Subsequently, the concentration of ethanol in the water was gradually increased as the amount of ethanol was received orally. Preference testing using a three-bottle choice procedure showed in some subjects an enhanced oral intake of ethanol for 4-8 weeks after terminating the injection of ethanol via the catheter.

More recently, the effect of withdrawel from chronic ethanol administration on tremor in skeletal muscle has been studied. Blood ethanol was maintained at elevated levels in the rhesus monkey for several days by continuously infusing ethanol via a venous catheter. Following abrupt termination of the infusion, tremor was measured during hourly periods from a transducer attached to leg muscle. The frequency of tremor tended to be a function of the blood ethanol level maintained prior to withdrawel.

My work comparing the effects of drugs on schedule-controlled behavior in apes and monkeys is continuing here at the Yerkes Center. Studies completed and reported so far have described the effects of d-amphetamine, chlorpromazine and morphine on responding under a multiple fixed-interval, fixed-ratio schedule of food presentation in the chimpanzee. The effects of d-amphetamine on responding in the chimpanzee were similar to the effects typically observed in monkeys; response rates increased as a function of drug dose, and the changes in responding were rate-dependent. The effects of chlorpromazine and morphine in the chimpanzee contrasted with the effects of these drugs in squirrel and rhesus monkeys and baboons. Whereas morphine and chlorpromazine decrease mean rates of responding maintained by food presentation in monkeys, the two drugs markedly increased responding in the chimpanzee. Yet, a direct comparison of the effects of morphine on responding in the chimpanzee and the baboon showed the drug to have rate-dependent effects in both species.

The effects of drugs on schedule-induced drinking have also been studied in these experiments in the chimpanzee, and the results show that drugs can be differentiated in terms of their effects on drinking. d-Amphetamine and chlorpromazine each decreased schedule-induced drinking in the chimpanzee, but the dose-effect curves for the two drugs differed. d-Amphetamine decreased drinking to near zero levels at a dose that had the maximum increasing effect on responding, but chlorpromazine had little effect on drinking until the dose was high enough to disrupt and markedly decrease responding.

The disruption in laboratory activity associated with the move to the Yerkes Center last fall is still being felt. However, experiments are gradually being resumed as animals are released from quarantine and equipment and laboratory space are put in order. The availability of a larger number of apes and of three different species of apes here at the Yerkes Center will contribute to the continuation of these comparative studies.

Leavitt, F. Drugs and Behavior. Philadelphia: W.B. Saunders, 1974.

Drugs and Behavior is an introductory textbook on psychopharmacology written at the level of advanced undergraduate students. It assumes no prior knowledge of pharmacology.

The book begins with four chapters on basic psychopharmacology, which include classification, principles, drug effects, and toxicology. It then addresses the more clinical topics of drug abuse and psychopharmacotherapy. The remaining chapters consider studies of psychoactive drug effects in areas usually studied in physiological psychology, a few of which are learning and memory, aggression, sleep and electrical brain self-stimulation.

There is extensive referencing of material in each individual chapter. Additional material is provided in an appendix on organic chemistry and another on psychoactive drugs. The author has also compiled a manual containing 615 objective questions designed to test mastery of this material.

McMillan, D.E. Central Nervous System Pharmacology: A Self-Instruction Text. Boston: Little, Brown, and Company, 1974.

Central Nervous System Pharmacology is an introduction to principles and applications of CNS pharmacology. Divided into sixteen short chapters, the book begins with some of the unifying principles of behavioral pharmacology, i.e., CNS transmitter theory, dose dependent effects and rate dependency effects. Each subsequent chapter is a conspectus of the current body of knowledge in some area of CNS pharmacology. Topics include stimulants and antidepressants, analgesics, sedatives and hypnotics, antiparkinson agents, anesthesia, and drug abuse.

Within each area explored, mechanisms of drug action are suggested, as well as their proposed involvement in the currently accepted disease etiologies. Generic and trade names of available drug preparations are used and a comparison of advantages and contraindications of the various drugs is provided.

As a self-instruction text, Central Nervous System Pharmacology is a noteworthy achievement. A fundamental working vocabulary will be obtained from its format of introduction, explanation, and review of each topic. The programmed sequence follows a logical order that is interesting while not overly simplified.

This text was prepared for students in medicine, dentistry, and pharmacy, but would be suggested for any person desiring an introduction or review of this interdisciplinary field.

Gibbins, R.J., Israel, Y., Kalant, H., Popham, R.E., Schmidt, W., and Smart, R.G.(Eds.). Research Advances in Alcohol and Drug Problems. Somerset, N.J.: Wiley-Interscience, 1974.

This book, the first volume of a proposed annual series intended to deal with recent advances in alcohol and drug problems, focuses in particular on drug addiction. The series is aimed at a truly interdisciplinary audience, but one which lacks expertise in the particular areas discussed. The level of difficulty appears appropriate to advanced undergraduate and graduate student readers who have some background in the areas drawn upon by psychopharmacology.

Research Advances in Alcohol and Drug Problems deals with selected areas in which recent progress has been made and is not intended to be a comprehensive review. The analyses range from the biochemical level to the psychological and sociological levels.

support for the study of clinical pharmacology and clinical pharmacy, and to provide for review of drug prescribing; and to amend the Federal Food, Drug, and Cosmetic Act to provide for additional regulation of drug promotions, to provide for recordkeeping and reporting for all drugs, to provide for certification of programs respecting manufactures' representatives, to provide for the submission of data relating to therapeutic equivalence of drugs, to provide for the certification of certain drugs, to provide for a national drug compendium, to provide additional drug information to consumers, to establish a code system for the identification of all drugs, to provide for a recall of adulterated or misbranded foods, drugs, and cosmetics (To Interstate and Foreign Commerce).

S 32 Introduced 1/15/75
by Kennedy, Magnuson, Moss (Utah), Tunney, Bentsen, Brooke, Cannon, Case, Cranston, Culver, Hart (Mich.), Hatfield, Humphrey, Inouye, Javits, Johnston, Leahy, Mansfield, McGee, McGovern, Mondale, Montoya, Pell, Randolph, Sparkman, Stafford, Weicker, and Williams
To establish a framework for the formulation of national policy and priorities for science and technology (To Labor and Public Welfare; Aeronautical and Space Sciences; and Commerce).

The information in this column was taken from the Congressional Index and Major Legislation of the 93rd Congress, a Congressional Research Service monthly.

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Travis Thompson, Ph.D., Editor
Mary Rice, Assistant Editor

Box 392 Mayo
University of Minnesota
Minneapolis, Minnesota 55455

DR VICTOR G LATIES
U OF ROCH M
DEPT RADIAT BIOLO
ROCHESTER N Y 14642

CSO 2336

## WANT ADS

### POSITION DESIRED

MA in psychology, 10 years experience in physiological psychology. Including work in CNS and psychopharmacology. Desires position. Contact Viola F. Hayhurst, NICHD, Baltimore, Md. 21224.

Send any Position Available or Position Desired ads to be included in the next Newsletter to:

Ms. Mary Rice
Psychiatry Research Unit
Box 392 Mayo
University of Minnesota
Minneapolis, Minnesota 55455

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## ON THE LEGISLATIVE FRONT

### LAWS PASSED BY THE 93RD CONGRESS RELEVANT TO RESEARCH IN PSYCHOPHARMACOLOGY

PL 93-281 Passed 5/14/74
Amends the Controlled Substances Act to provide for the separate registration of practitioners who use narcotic drugs in the treatment of addicts (designed principally to prevent diversion of methadone).

PL 93-282 Passed 5/14/74
Amends the Comprehensive Alcohol Abuse and Alcoholism Treatment, Prevention, and Rehabilitation Act to extend the authorizations for project grants and contracts and the state formula grants through FY 1976. Authorizes additional grants to those states which adopt the basic provisions of the Uniform Alcoholism and Intoxication Treatment Act (Commission on Uniform State Laws). Transfers the contracts and project grants authorities under Part C of the Community Mental Health Center Act to this Act. Provides that the efforts of the federal government to deal with the problems of alcoholism be coordinated through the National Institute of Alcohol Abuse and Alcoholism. Establishes the Addiction and Mental Health Administration to administer mental health, alcohol, and drug abuse programs. Strengthens the provisions that prohibit the exclusion of alcoholics who need medical attention from hospitals.

PL 93-348 Passed 7/12/74
National Biomedical Research Fellowship, Traineeship and Training Act. Provides for the protection of human subjects in biomedical research and establishes a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Establishes a national program of health research fellowships and traineeships.

### BILLS OF SPECIAL INTEREST INTRODUCED IN THE 94TH CONGRESS AS OF 2/14/75

H 1592 Introduced 1/17/75
by Carney
To amend the Act of August 24, 1966, as amended, to assure humane treatment of certain animals (To Agriculture).

HCR 42 Introduced 1/14/75
by Whitehurst
Pertaining to the methods used on animals in research (To Science and Technology).

H 561 Introduced 1/14/75
by Koch
To amend certain provisions of the Controlled Substances Act relating to Marihuana (To Interstate and Foreign Commerce).

H 865 Introduced 1/14/75
by Peyser and Rangel
To prevent the use of Heroin for any drug maintenance program (To Interstate and Foreign Commerce).

H 556 Introduced 1/14/75
by Koch
To amend the Public Health Service Act to provide for a National Center for Clinical Pharmacology, to provide

## SURVEY OF AVAILABILITY OF TRAINING IN PSYCHOPHARMACOLOGY

Division 28 is compiling a listing of psychology departments that offer formal training in psychopharmacology. The listing will be made available to students desiring to specialize in psychopharmacology. If your department presently offers any courses (graduate or undergraduate) dealing directly with psychopharmacology, we would appreciate receiving this information for inclusion in the listing. Send information to:

Roy Pickens, Secretary
Box 392 Mayo
University of Minnesota
Minneapolis, Minn. 55455

In response to the initial request the following institutions have indicated that formal training is available in psychopharmacology:

- Indiana University (George Heise)
- Lakehead University (Paul Satinder)
- Rutgers University (Bernard Beer)
- Southern Illinois University at Carbondale (Robert Levitt)
- Texas Tech University (Richard Carlson)
- University of Chicago (C.R. Schuster)
- University of Illinois at Chicago Circle (Alexander Rosen)
- University of Maryland (Lewis Gollub and James Barrett)
- University of Minnesota (Travis Thompson)
- University of South Carolina (James Appel)
- University of Waterloo (M. Vogel-Sprott)

Additional institutions will be added to the list as such information becomes available. Keep those cards and letters coming in, folks!

## SUMMARIES OF RECENT PUBLICATIONS OF SPECIAL INTEREST

Abel, E.L. Drugs and Behavior: A Primer in Neuropsychopharmacology. Somerset, N.J.: Wiley-Interscience, 1974.

The stated goal of this text is a description of drug action in terms of the neurochemical changes which occur "between the chemical stimulus and the behavioral response." The author presents a nonselective review of neurophysiology and of the basic principles and mechanisms of drug action and a brief clinical characterization of several classes of centrally active drugs. Little space is devoted to behavioral mechanisms of drug action. The author assumes a prior knowledge of physiology and psychology on the part of the reader. The instructional usefulness of the text is diminished by its erratic placement of emphasis and by errors (e.g., mistatement of the rate dependence hypothesis (p. 141) and the description of the mechanism of action of the tricyclic antidepressants (p. 161)).

Hoffmann, F.G. A Handbook on Drug and Alcohol Abuse: The Biomedical Aspects. London: Oxford University Press, 1975.

As the subtitle indicates, this book focuses on the biological (as opposed to psychological or sociological) aspects of drug dependence. It provides a broad, but not superficial, introduction to drug abuse, including the names and classifications of drugs, basic pharmacology, and the problem of illicit channels of distribution. Extended sections deal with biological aspects of dependence on narcotics, CNS depressants, inhalants, hallucinogens (including marihuana), and CNS stimulants.

This text is suitable for the medical and graduate school levels. It does not deal with behavioral components of drug dependence.

of research focusing on the effects of drugs on operant behavior controlled by simple and complex schedules. In a study recently completed, responding in the pigeon was maintained under a temporal discrimination procedure in which correct responses were reinforced under a fixed-interval schedule. Changes in correct and incorrect responses due to chlorpromazine were a function of the rate at which the responses occurred under control conditions, i.e., the effects were rate dependent. Another experiment, on the effectiveness of chlorpromazine in enhancing the development and maintenance of responding in the pigeon under a large fixed-ratio schedule is underway. In this experiment, chlorpromazine is administered chronically to facilitate the abrupt transition from responding under continuous reinforcement to responding under a large fixed-ratio schedule.

Di Anne Bradford, a graduate student, has recently completed a study of the effects of imipramine on second-order schedule performance in the pigeon. A fixed-ratio schedule comprised individual components of the second-order schedule and food was presented upon completion of the first fixed-ratio component after a fixed time had elapsed. The results of the experiment showed imipramine to have rate-dependent effects on the behavior.

Another graduate student, Bob Witner, has developed a stable and putatively appropriate baseline condition for demonstrating the effects of ethanol. He is comparing the effects of oral doses of ethanol and pentobarbital on multiple schedule performance involving punishment in the rat.

Nearby, in the Department of Pharmacology at Emory University, Steve Holtzman is studying the effects of morphine and morphine antagonists on motor activity and operant behavior in the rat and squirrel monkey. In a series of experiments, the results of which have been reported over the last few years, the effects of morphine and morphine antagonists with mixed agonist properties were examined on locomotor activity and continuous avoidance behavior in the rat, and on the disposition of monoamines in the rat brain. All drugs, including morphine, increased the rate of continuous avoidance responding in a dose-dependent manner. This action could be blocked by the "pure" antagonist naloxone. Observations are now being extended to squirrel monkeys trained under schedules similar to those employed with the rats. Experiments with morphine, nalorphine, cyclazocine and naloxone indicate that the effects of these drugs on avoidance behavior are similar in the two species.

Harlan Shannon, a graduate student, has developed a two-choice discrete-trial avoidance procedure for evaluating the discriminative properties of morphine and related drugs. Rats have been trained to discriminate between saline and 3.0 mg/kg of morphine injected subcutaneously. The stimulus effect produced by morphine has all of the characteristics of a specific narcotic effect: a) rats respond on the drug lever when other narcotics are substituted for morphine; b) morphine discrimination is blocked by naloxone; c) the development of tolerance and cross-tolerance to the discriminative effects of morphine can be demonstrated; d) the rats respond on the saline lever or on both levers at chance levels when tested with non-narcotic isomers and structural analogues of narcotic analgesics, or with non-opioid psychoactive drugs such as amphetamine and phenobarbital. Similar discrimination experiments are now being planned for squirrel monkeys. If the discriminative properties of morphine in the rat are at all analogous to morphine's subjective effects in man, he may have a valuable animal model for studying this important component of drug action.

Another major line of investigation has been the effects of prenatal morphine administration on the subsequent responsiveness of the offspring

Alcohol effects on behavior: Biochemical correlates (R01 AA01245)
Irving Geller
Texas Tech University
School of Medicine

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## WHAT'S HAPPENING AT...

ALCOHOL AND DRUG ABUSE RESEARCH CENTER
HARVARD MEDICAL SCHOOL
THE MCLEAN HOSPITAL
contributed by Isaac Greenberg

For the past year and a half, the Alcohol and Drug Abuse Research Center at Harvard Medical School and the McLean Hospital has been engaged in a multi-faceted, multi-disciplinary research program on the behavioral and biological aspects of drug use and abuse. Under the direction of Dr. Jack H. Mendelson and co-direction of Dr. Roger E. Meyer and Dr. Nancy K. Mello, the Center is presently involved in examining the effects of alcohol, heroin, barbiturates, and marijuana on behavioral, biochemical, and physiological variables. The Center consists of a clinical research program, an animal research program, and biochemistry and electrophysiology laboratories.

Marihuana Research: Volunteer male subjects are admitted in groups of four to a research ward for a 31-day stay. Within the obvious constraints which research paradigms impose, efforts are made to simulate a "normal" environment employing a modified token-economy system. In this system, the subjects, who are either heavy or casual marihuana users, have continuous access to a semi-portable operant manipulandum. The points accumulated through operant responding are exchangeable either for money at the termination of the study or for marihuana cigarettes which are continuously available for 21 of the 31 days. The various possible influences of marihuana are analyzed using a wide spectrum of measures including operant response magnitude and distribution patterns, social and interpersonal interactions among the subjects, subject mood reports, programmed observations throughout the day and night, psychomotor-testing, etc. Biochemical assessments of the androgen levels are being studied as are potential chromosomal and neurological abnormalities.

Alcohol Research: In a design similar to that described for the marihuana studies, either heavy or casual alcohol users are admitted to the research ward for 30 days, and alcohol is for sale during 20 days of their stay. The operant manipulandum is fully portable in this study and is carried about by the subjects virtually everywhere on the ward area. Because alcohol addicts have been shown to spend all their point or token accumulation on sporadic binge drinking intervals, special attention is being paid to drinking patterns of the heavy drinkers when alcohol is priced at 50 cents per drink and during "happy hours" when the price is halved. Preliminary data suggest that the "happy hour" may be important in initiating drinking bouts, but even these rarely approach the "binging" patterns previously described in alcoholics.

Narcotics Research and Treatment Evaluation: Under the direction of Dr. Roger E. Meyer, a program evaluating the value of various narcotic antagonists in the treatment of heroin addicts in now underway.

This project is an attempt to develop a paradigm which might be useful in determining the potential therapeutic benefits of narcotic antagonists in preventing relapse behavior in heroin addicts who had previously failed in other types of rehabilitation. The techniques of operant analysis of behavior have been applied to studies of heroin-seeking under