CONSCIOUSNESS. J. H. Woods. University of Michigan, Ann Arbor, MI.

Phencyclidine and ketamine induce in humans a profound change in central nervous system function that resembles anesthesia, i.e., loss of sensitivity to pain and a total amnesia for events during intoxication. Ketamine continues to be used in medicine as an anesthetic in many places in the world and is used in the U.S. extensively in children when burn wounds are treated. In many different species of animals both phencyclidine and ketamine can be used as anesthetics for many kinds of surgical interventions. The mechanism for this profound change in consciousness for these drugs is unkown. An increasingly impressive body of knowledge is accruing that suggest that some of the behavioral effects of excitatory amino anatagonists (NMDA-type) resemble some actions of phencyclidine and ketamine. The presentation will illustrate that an NMDA antagonist, CGS 19755 (Lehmann *et al.*, J. Pharmacol. Exp. Ther. 245:65–76; 1988), can produce an anesthetic state in rhesus monkeys that resembles that produced by ketamine and phencyclidine. (Research supported by NIDA Grant DA-05325.)

YOUNG PSYCHOPHARMACOLOGIST AWARD AND INVITED ADDRESS

Chair: *Larry Byrd,* Yerkes Regional Primate Research Center, Emory University, Atlanta, GA

BEHAVIORAL MEASURES OF OPIOID DEPENDENCE AND WITHDRAWAL. Charles P. France. University of Michigan, Ann Arbor, MI.

Discriminative stimulus effects of opioid agonists and antagonists were studied in morphine-treated rhesus monkeys discriminating between 0.01 mg/kg of naltrexone and saline while responding under a schedule of stimulus-shock termination. Opioid antagonists substituted completely for the naltrexone discriminative stimulus and the effective discriminative doses were the same as the doses reported to precipitate directly-observable signs of withdrawal in morphine-dependent monkeys. Opioid agonists as well as nonopioids produced responding on the saline lever. Substitution of saline for the daily injection of morphine resulted in a time-dependent switch to the naltrexone lever and this effect was reversed by opioid agonists. Comparison of studies in which antagonists were substituted for naltrexone and studies in which antagonists were used to attenuate the withdrawal-reversing actions of agonists in morphine-abstinent monkeys showed a strong relationship between these methods for estimating antagonist affinities. Moreover, pA_2 values determined under these conditions support the notion that the same receptor subtype mediates a wide variety of behavioral effects of morphine in monkeys. (Supported by USPHS Grant 05018.)

FRIDAY P.M.

NEW FELLOWS ADDRESS

Chair: *James E. Smith,* Wake Forest University, Bowman Gray School of Medicine, Winston-Salem, NC

WHAT OPERANT "MICROSCOPY" REVEALS ABOUT THE BEHAVIORAL EFFECTS OF ANTIPSYCHOTICS. Stephen C. Fowler. University of Mississippi, University, MS.

Behavioral pharmacological studies using an operant microscope (i.e., an operant chamber equipped with a force transducer operandum and serviced by a laboratory computer) are reviewed. This work demonstrates the utility of a dynamic, microanalytic, multimeasurement methodology in behavior analysis. More specifically, experiments aimed at understanding the associative, incentive/motivational, and motor effects of dopamine-receptor blocking neuroleptics suggest that the predominant effect of these drugs in rats, even at low doses, is a motor impairment remarkably similar to Parkinson's disease symptoms in human beings. These findings should facilitate the development of preclinical screens for identifying and eventually eliminating antipsychotics' extrapyramidal side effects.

INVITED ADDRESS

Chair: *Nancy Ator,* The Johns Hopkins University School of Medicine, Baltimore, MD

DIFFERENTIAL EFFECTS OF BENZODIAZEPINES ON LEARNING AND MEMORY. J. M. Moerschbaecher. LSU Medical Center, New Orleans, LA.

The effects of various benzodiazepines, administered orally, were investigated in patas monkeys responding under a multiple schedule of repeated acquisition and performance of conditional discriminations. In both components of the multiple schedule, alprazolam, lorazepam, temazepam and triazolam produced dose-related decreases in overall response rate. At lower doses, alprazolam, triazolam and lorazepam also increased errors in acquisition while having no effect on errors in performance. Temazepam had no effect on errors except at doses which produced substantial decreases in response rate. In contrast, diazepam, flurazepam and oxazepam had little or no effect on responding. In a second series of experiments the effects of alprazolam, temazepam and triazolam on the retention of conditional discriminations were evaluated. Each of these drugs were found to produce both dose- and delay-dependent disruptive effects on retention, as measured by percent savings in errors to criterion. The data suggest that inherent differences exist among the benzodiazepines in terms of their effects on complex behavioral processes. Such differences may constitute a significant health-related consequence of their use in the outpatient or drug abuser.

SYMPOSIUM

The Reinforcing Efficacy of Drugs

Chair: *William Woolverton,* University of Chicago, Chicago, IL

INTRODUCTION.

Drugs of abuse can function as positive reinforcers in humans and other animals. Behavior that is maintained by drugs is comparable to behavior maintained by standard reinforcers. Further, behavioral variables that influence operant responding have similar effects on behavior controlled by drug delivery. However, it has been problematic to assess the strength of this behavior in response to environmental and pharmacological interventions and to compare the ability of different drugs to control responding. This difficulty has arisen in part from using rate of responding as a measure of reinforcing efficacy. Rate of responding maintained by a drug reinforcer is determined not only by its reinforcing effects, but by nonspecific rate-modifying effects as well. Thus, dose-response functions are typically inverse under ratio and

interval schedules with the lowest rates of responding maintained by higher and presumably more reinforcing doses of the drug. As a result, many investigators have attempted to use other measures for assessing the relative strength of different reinforcers to control behavior. The major independent variables in these studies have been magnitude (dose) of reinforcement and relative availability of other reinforcers and the goal has been to determine how changes in these variables affect a presumed measure of response strength. The present symposium is designed to review these studies and evaluate the utility of the concept of reinforcing efficacy. Meisch and Lemaire will present findings from a series of studies altering response cost and concurrent access to other drug doses in order to assess the relative reinforcing strength of different doses of pentobarbital. Johanson and Nader will discuss the results of choice experiments which have evaluated the effectiveness of response cost, punishment, and alternative reinforcers to reduce cocaine choice. Vuchinich and Tucker will discuss the effectiveness of alcohol to maintain behavior as a function of the availability of other reinforcers and their relative constraints. The implications of their findings for the treatment of alcoholism will also be considered. Finally, Katz will discuss the merits of methods that have been used to assess strength, the usefulness of the concept of reinforcing efficacy, and the implication of this analysis for the prediction of abuse potential.

RELATIVE REINFORCING EFFECT OF DIFFERENT AMOUNTS OF PENTOBARBITAL. Richard A. Meisch and Gregory A. Lemaire. University of Texas Health Science Center, Houston, TX.
(Abstract not available)

REDUCING COCAINE CHOICE IN MONKEYS. Chris-Ellyn Johanson and Michael Nader. Uniformed Services University of the Health Sciences, Bethesda, MD.
(Abstract not available)

REINFORCEMENT CONTEXT AND HUMAN ALCOHOL ABUSE. Rudy E. Vuchinich and Jalie A. Tucker. Wayne State University, Detroit, MI.
(Abstract not available)

CAN WE SCALE REINFORCING EFFICACY OF DRUGS AND DOES IT TELL US ANYTHING ABOUT ABUSE LIABILITY? Jonathan Katz. National Institute on Drug Abuse Addiction Research Center, Baltimore, MD.
(Abstract not available)

PRESIDENTIAL ADDRESS
Chair: *George E. Bigelow,* The Johns Hopkins University/Key Medical Center, Baltimore, MD

OPIOID ANALGESICS: INFERRING RECEPTOR-MEDIATED ACTIVITY FROM BEHAVIORAL DATA. Linda A. Dykstra. University of North Carolina at Chapel Hill, Chapel Hill, NC.

Differences between the profiles of activity exhibited by opioids suggest that the effects of these compounds are mediated through one or more opioid receptor systems. For example, research within our laboratory has shown that opioids produce analgesia through at least two different opioid receptor types, in particular the mu and kappa opioid receptors. We have used a number of pharmacological techniques to relate the analgesic effects of opioid compounds to presumed activity at different opioid receptor types. These have included studies in which the dose of antagonist required to reverse the analgesic effects of mu versus kappa opioids has been quantified as well as studies in which animals have been made tolerant to a mu agonist and cross tolerance to kappa agonist has been determined.

INFORMAL PAPER SESSION—HOSPITALITY SUITE

SATURDAY A.M.

INVITED ADDRESS
Chair: *Chris-Ellyn Johanson,* Uniformed Services University of the Health Sciences, Bethesda, MD

DOPAMINE RECEPTORS AND BEHAVIOR. William Woolverton. University of Chicago, Chicago, IL.
(Abstract not available)

SYMPOSIUM
Role of Behavioral Pharmacology in Drug Development
Co-Chair: *Linda A. Dykstra,* University of North Carolina at Chapel Hill, Chapel Hill, NC
Co-Chair: *J. David Leander,* Lilly Research Labs, Eli Lilly and Company, Indianapolis, IN
Discussant: *Dennis Zimmerman,* Lilly Research Labs, Eli Lilly and Company, Indianapolis, IN
Discussant: *Robert L. Balster,* Medical College of Virginia, Richmond, VA

INTRODUCTION. Linda A. Dykstra. University of North Carolina at Chapel Hill, Chapel Hill, NC.

The number and use of behaviorally active drugs has increased tremendously during the past 35–40 years. As a result, interest in the scientific investigation of these drugs has also increased. Presently, the investigation of behaviorally active drugs draws on a number of disciplines, including pharmacology, psychiatry, biochemistry, physiology and, of course, psychology. Information gained from these investigations has had a very important impact on the development of new compounds to be used in the treatment of various behavior disorders. As a result, a number of fruitful collaborations have developed between behavioral scientists and members of the pharmaceutical industry. The proposed symposium will focus on the role of behavioral pharmacology in drug development, with special emphasis on the behavioral technology which has helped to advance this interaction. The symposium will begin with a historical account of this collaboration which will be followed by 3 presentations, each from psychologists now employed in the pharmaceutical industry. Each of these presenters will discuss an individual drug class (antianxiety agents, cognitive enhancers and NMDA antagonists), with emphasis on the models that have been used in the development of new compounds within that class.

IMPACT OF BEHAVIORAL PHARMACOLOGY IN THE PHARMACEUTICAL INDUSTRY. Francis C. Colpaert. Neurobiology Division, FONDAX, Groupe de Recherche Servier, 7, rue Ampère, 92800 Puteaux, France.

Behavioral pharmacology is one of the several approaches and corresponding methodologies that are being used in the pharmaceutical industry to discover new C.N.S. drugs through preclinical research. Most of the important pharmacological principles (e.g.,