

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 unknown. An increasingly impressive body of knowledge is accruing that suggests that some of the behavioral effects of excitatory amino antagonists (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