SYMPOSIUM

Current Research on the Behavioral Pharmacology of Benzodiazepines

Chair: *John D. Roache,* University of Texas Health Science Center, Houston, TX.

Discussant: *Kimberly C. Kirby,* University of Texas Health Science Center, Houston, TX.

DRUG REINFORCEMENT AND DRUG DISCRIMINATION WITH BENZODIAZEPINES IN THE BABOON. Nancy A. Ator. The Johns Hopkins University School of Medicine, Baltimore, MD.

Studies of drug self-administration and drug discrimination with benzodiazepines in the baboon will be reviewed with an eye to pointing out the commonalities and differences among benzodiazepines in relation to other sedative/anxiolytic drugs. The relationship between conclusions drawn under one procedure to those drawn under another procedure also will be explored. Data on the effect of a history of drug discrimination on drug self-administration and vice versa will be presented. Of the 11 benzodiazepines studied in the intravenous self-administration procedure, all maintained at least moderate daily rates of self-injection that were higher than those maintained by the drug vehicle, but the more quickly eliminated benzodiazepines (triazolam and midazolam) maintained the highest daily rates of drug-taking. Under the oral self-administration procedure, all three benzodiazepines studied (alprazolam, triazolam, diazepam) maintained stable daily patterns of drug ingestion that resulted in physiological dependence to the benzodiazepine, but alprazolam seemed to be the most efficacious reinforcer in comparison to the drug vehicle. In drug discrimination procedures, baboons trained to discriminate lorazepam generalized to all other benzodiazepines tested but did not generalize reliably to barbiturates nor to other anxiolytics except for certain benzodiazepine-receptor ligands. These data will be related to data from the drug discrimination literature with sedative/anxiolytic drugs as a whole to emphasize the relative specificity in generalization profiles among benzodiazepines. When drug discrimination and drug self-administration procedures were studied sequentially, sensitivity to discriminative stimulus effects increased after a history of self-administration but probability of self-administration did not increase after drug discrimination training.

REINFORCING AND STIMULUS EFFECTS OF BENZODIAZEPINES IN HUMANS. John D. Roache. University of Texas Health Science Center, Houston, TX.

Previous research in human subjects has shown that benzodiazepines reinforce self-administration behavior in sedative abusers but not in nonabuser populations. Abuse liability studies have employed subject-rated questionnaires to measure subjective experiences presumably related to the reinforcing effects of sedatives. Empirical studies are needed to assess the relationship between the reinforcing and interoceptive stimulus effects of benzodiazepines. Consistent with the lesser abuse potential and reinforcing efficacy of benzodiazepines as compared to barbiturates, both abuser and nonabuser populations, show evidence that benzodiazepines produce a lesser magniude and somewhat different subjective experience. Benzodiazepines were reported to produce differential subjective effects in nonabuser subjects who did versus those who did not self-administer these drugs. In sedative abusers, diazepam and triazolam were similarly self-administered although these drugs produced differential profiles of adverse subjective effects. Also in sedative abusers, the extent of benzodiazepine self-administration has been correlated with subject ratings of drug liking. Together, these results indicate some concordance between subject ratings and reinforcing effects of benzodiazepines. However, the modest strength of the correlations certainly indicate that acute dose-induced subject ratings do not completely covary with self-administration behavior.

BENZODIAZEPINE-INDUCED AMNESIA IN HUMANS: A COMPARISON WITH OTHER AMNESIAS. Richard G. Lister. NIAA, Bethesda, MD.

Psychopharmacological studies in which drugs are administered to normal volunteers can enhance our understanding of the mechanisms of learning and memory. Such studies have an advantage over neuropsychological studies in patients in that drug effects are reversible. Subjects are, therefore, able to serve as their own controls. The presentation will focus on the effects of benzodiazepines on different aspects of cognition. The impairments seen in explicit tests of memory will be compared to observations of intact memory assessed implicity. The effects of the benzodiazepine triazolam on meta cognitive processes will be examined. Finally comparisons will be made between benzodiazepine-induced amnesia, various organic amnesias, and the amnesias caused by scopolamine and alcohol.

ASSESSMENT OF BENZODIAZEPINE PHYSICAL DEPENDENCE IN BABOONS. C. A. Sannerud*† and R. R. Griffiths.* *The Johns Hopkins University Medical School and †NIDA Addiction Research Center, Baltimore, MD.

It has been estimated that over 2% of the U.S. adult population is exposed to benzodiazepine (BZ) drugs chronically, and, therefore, may be at risk for the development of physical dependence. Physical dependence on BZ was assessed in male baboons after continuous drug infusions via IG catheters. Behavior was scored during observational sessions using rating scales. Flumazenil precipitated a withdrawal (WD) syndrome, including retching, vomiting, tremor, and abnormal postures, after only 4–7 days of high dose administration of midazolam, triazolam, and diazepam. The precipitated WD syndrome appeared to be more severe after chronic administration of higher BZ doses than after lower BZ doses. Severity of precipitated WD syndrome was also a function of flumazenil dose. Higher flumazenil doses given after administration of 20 mg/kg/day diazepam produced myoclonic jerks and seizures. Lower flumazenil doses did not precipitate a WD syndrome in diazepam-dependent baboons. Signs of spontaneous WD began to appear within 7 days after termination of 20 mg/kg/day diazepam treatment, and was characterized by increases in abnormal postures and tremor, and substantial decreases in food intake. Spontaneous WD syndrome after high doses of diazepam was less severe, but more protracted than the precipitated WD syndrome. (Supported by NIDA Grant DA 01147 and NIDA NRSA Award DA 05293.)

SYMPOSIUM

The Etiology of Alcoholism: Definition of Risk Factors

Chair: *Steven L. Schandler,* Chapman College, Orange, CA.

Discussant: *Michael J. Cohen,* VA Medical Center, Long Beach, CA.

ALCOHOLISM RISK AND PSYCHOPHYSIOLOGICAL COR-