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DIAZEPAM SELF-ADMINISTRATION IN RHESUS MONKEYS. Jack Bergman, Department of Pharmacological and Physiological Sciences, The University of Chicago, The Pritzker School of Medicine, Chicago, IL 60637; Chris E. Johanson, Department of Psychiatry, The University of Chicago, The Pritzker School of Medicine, Chicago, IL 60637; and Charles R. Schuster, Departments of Psychiatry and Pharmacological and Physiological Sciences, The University of Chicago, The Pritzker School of Medicine, Chicago, IL 60637.

These studies were designed to assess the ability of diazepam to maintain responding in rhesus monkeys. Six monkeys were trained to self-administer cocaine (baseline drug) under a fixed ratio 10 schedule of reinforcement in three-hour daily sessions. When diazepam (6.25–400 μg/kg/inj) was substituted for cocaine for 7–10 sessions, responding was well-maintained at doses between 12.5 and 50 μg/kg in one monkey. In the other five monkeys, however, diazepam across the entire dose range did not maintain consistent responding above vehicle levels. Next several manipulations were performed which have been shown in previous studies to modify the reinforcing properties of drugs. Two monkeys were food-deprived to 80% of their free-feeding body weights. Although cocaine self-administration increased significantly under the deprivation condition, diazepam continued to maintain only vehicle levels of self-administration. Next, responding was maintained by IV pentobarbital (250 μg/kg/inj) as the baseline drug in three monkeys. However, when diazepam was substituted, responding was still not maintained in a consistent manner. Subsequently, the FR requirement for drug delivery was lowered from 10 to 1. Although pentobarbital intake increased, responding was not maintained by diazepam. In summary, diazepam across a wide range of doses did not maintain responding when substituted for either cocaine or pentobarbital in rhesus monkeys. Furthermore, although drug self-administration increased when monkeys were food-deprived (cocaine), or response requirements lowered (pentobarbital), diazepam self-administration did not. This failure to demonstrate that diazepam has positive reinforcing properties is similar to results found in self-administration studies with diazepam using normal humans. The results taken as a whole have implications for the abuse liability of diazepam.

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A SCREENING TEST FOR DRUG REINFORCERS USING RATS. R. J. Collins, J. R. Weeks and R. R. Russell, The Upjohn Company, Kalamazoo, MI 49001.

We described earlier a method for evaluation of the reinforcing properties of drugs in rats (CPDD Meeting, 1978). Naive rats were offered drug by intravenous self-administration for 5 days, the dose reduced 10-fold for 4 days, and finally 2 days each at FR-2 and FR-4. A potent reinforcing agent generates response rates greater than that maintained by saline, the rate increasing with reduction of dose and the FR schedule. A scoring system gave a dose-related expression of reinforcing activity. We report here an improved protocol which decreases the variability of the test. A similar scoring system was used. Naive rats were offered saline injections for 3 days. Rats were accepted if injections taken averaged $\geq$4 and $\leq$50 daily. Of 295 rats, 3% were >50 and 12% <4 injections. Rats were offered drug for 5 days, then the dose reduced 0.5 log (3.2-fold) for an additional 5 days. Under both protocols, saline rate averaged about 10/day. A rate significantly greater ($p<0.1$) than saline was reduced from 73 to 32 injections/day. Other measures of reinforcement were the percentage of rats showing a drug effect and whether the group mean injection rate was significantly greater than saline. The approximate order of reinforcing potency was: narcotic analgesics > partial opiate agonists > CNS stimulants > barbiturates. Benzodiazepines, ethanol, caffeine and haloperidol were marginally effective. As a class, the partial agonist opiate analgesics appear to be more potent reinforcers in the rat than in the monkey. Finally, extinction lever-pressing activity was examined. Rats from the above study were returned to their home cages for 2 weeks, and then again offered the lever for saline for one hour. Rats offered saline during the "drug period" averaged 3 responses and >9 responses were significantly greater ($p<0.1$). Of 113 rats which were reinforced, 76% responded >9 times in contrast to 12% of 157 rats which were not reinforced. This extinction responding was highly correlated with response rate, but poorly correlated with the drug dose.