Behavioral Studies of Cathinone in Monkeys and Rats

Schuster, C. R; Johanson, C. E.

As has been pointed out by previous speakers, it is now apparent that the principal pharmacologically active agent in the Khat plant is l-cathinone.

For the last year our laboratory has been investigating the behavioral actions of dl-and l-cathinone. Because cathinone is structurally and pharmacologically similar to d-amphetamine, these studies have attempted to compare the effects of cathinone to those of d-amphetamine.

To date, three behavioral procedures have been used. These are: 1) food-reinforced responding in rhesus monkeys, 2) drug self-administration in monkeys 3) studies of tolerance and cross-tolerance to the anorexic effects of cathinone and d-amphetamine in rats.

I. FOOD REINFORCED RESPONDING IN RHESUS MONKEYS

Three rhesus monkeys were trained to lever press under a multiple fixed-interval (FI) 5 min. fixed-ratio (FR) 30 schedule of food delivery. Specifically, in the presence of a red light animals were reinforced for the first response occuring after five minutes had elapsed from the preceding food delivery. Following completion of the FI component, the stimulus lights turned green and the animals were reinforced with food after completion of 30 lever presses. The FI and FR components alternated throughout a two hour daily session.

After behavior stabilized under the multiple schedule, dose-response curves were obtained for d-amphetamine and dl-and l-cathinone. Doses of drugs were given-intravenously 5 minutes before selected daily drugs.

All three drugs produced a dose-related decrease in responding under both the FI and FR conditions. dl-and 1-Cathinone appeared to be approximately equal in potency whereas d-amphetamine was twice as potent.

II. DRUG SELF-ADMINISTRATION STUDIES

Three rhesus monkeys surgically prepared with indwelling venous catheters served as subjects. All animals had been previously trained to lever press under an FR 10 schedule of cocaine delivery during a 3-hr daily session. Various doses of d-amphetamine, dl-

and l-cathinone as well as saline were substituted for cocaine for 5 consecutive sessions. All drugs maintained responding at levels significantly above those seen when saline was substituted. Both dl-and l-cathinone maintained rates of responding significantly higher than those generated by cocaine and d-amphetamine. Further, l-cathinone appeared to be more potent than either dl-cathinone or d-amphetamine.

III. TOLERANCE STUDIES

In two separate studies, cross-tolerance between d-amphetamine and dl-cathinone was studied. In these studies, the anorexic effects of the two drugs were studied in rats by determining their efficacy in decreasing the animal's intake of sweetened condensed milk made available for 15 minutes on a daily basis. Both d-amphetamine and dl-cathinone produced a dose-related decrement in milk intake In both studies dose-response curves for both drugs were obtained before, during and after a period of repeated administration of drug. In the first study, d-amphetamine (2.0 mg/kg/) was given daily. In the second study, dl-cathinone was given daily. In both studies, tolerance was demonstrated by a diminution in the effect of the chronically administered drug and as well by a shift in the dose-response curve to the right. In the case of d-amphetamine, this shift was approximately two-fold whereas with dl-cathinone, a much larger shift was obtained (8-12 fold). In both studies cross-tolerance between dl-cathinone and d-amphetamine was observed.

In summary, dl-cathinone shares with d-amphetamine the ability to: 1) disrupt food reinforced lever pressing behavior in monkeys; 2) serve as a positive reinforcer in drug self-administration experiments; 3) produce a decrement in milk intake in rats; and 4) produce tolerance to its anorexic effects. In addition, there is cross-tolerance between cathinone and amphetamine.

AUTHORS

C. R. Schuster, Ph.D.
C. E. Johanson, Ph.D.
Department of Psychiatry
The University of Chicago
950 East 59th Street
Chicago, Illinois 60637