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BRIEF COMMUNICATION

Effects of *d*-Amphetamine on Schedule Induced Polydipsia[1]

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WAYNER, M. J., I. GREENBERG AND J. TROWBRIDGE. *Effects of d-amphetamine on schedule induced polydipsia.* PHARMAC. BIOCHEM. BEHAV. 1(1) 109–111, 1973.–Two female Sprague-Dawley albino rats were selected in terms of the amount of schedule induced polydipsia which developed on an FI-1 min food reinforcement schedule at 80% of their initial body weights. The effects of six different doses of *d*-amphetamine administered intraperitoneally, 0.05, 0.25, 0.50, 1.00, 1.50, and 2.00 mg/kg on bar presses and schedule induced licking and water consumption were determined and compared to results obtained during baseline and following placebo injections. In the animal which displayed less schedule induced polydipsia during preinjection baseline, results indicate that amphetamine in low doses tended to enhance adjunctive licking and water consumption whereas higher doses decreased the same behavior. There was no obvious enhancement in the other animal, which displayed more adjunctive licking during baseline, and drinking as well as licking decreased with increasing dose. Both animals displayed a similar dose related increase in bar presses with a maximum at 1.50 mg/kg.

d-Amphetamine Schedule induced polydipsia Adjunctive drinking Drinking Licking Lateral hypothalamus

WHEN animals are partially deprived of food and thereby reduced in body weight and the daily ration is delivered intermittently on a fixed interval one min schedule, very strong and persistent post pellet drinking develops. The phenomenon has been referred to as schedule induced polydipsia and is one of a general class of adjunctive behaviors [3]. A possible role of lateral hypothalamic motor control functions in the mediation of this behavior has been described [4]. Relatively little, if anything, is known about the effects of centrally active drugs on this type of behavior. Both pentobarbital (2.0 mg) and methamphetamine (0.5 mg) eliminated post pellet drinking when administered 15 min before the session whereas there was no obvious change in the associated variable interval bar pressing performance [2]. Atropine sulfate and atropine methyl nitrate (3, 6, 9 mg/kg) had a similar effect on schedule induced water consumption but the depression of licking was more variable [1]. Ethyl alcohol and Δ^9-tetrahydrocannabinol in relatively small quantities tend to enhance recovered adjunctive drinking [5]. The purpose of the present experiment was to determine the effects of various amounts of *d*-amphetamine on FI-1 min bar pressing and the associated schedule induced drinking. Results indicate a dose related effect on both measures.

METHOD

Animals

Two Sprague-Dawley female albino rats 280 g in weight were employed. Animals were fed a reduced ration of food once per day in order to maintain body weight at 80% of their initial weight. Animals were trained to depress a lever in order to obtain a 45 mg Noyes pellet of food in a standard medium size LVE test chamber equipped with a food cup, three signal lights, an overhead light, background white noise, and a stainless steel ball tipped drinking spout attached to a eudiometer tube and drinkometer. All of the test and programming equipment were the same as that described in previous experiments [5]. Animals were tested once each day until relatively stable bar pressing and schedule induced polydipsia occurred on an FI-1 min schedule. Session length was determined by the time required to obtain 50 pellets but not longer than 60 min. The total number of licks, bar presses, and water consumed during the session were measured. Home cage water intake and daily body weight were also recorded. After the animals had adjusted to the schedule and displayed stable bar pressing and polydipsia for at least 10 days the first injection was administered. The two animals were selected

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for this experiment in terms of their baseline performance. One animal displayed a relatively high level of schedule induced licking whereas the other was considered to be a moderate drinker under these conditions. The following six doses of *d*-amphetamine HCl (K and K Laboratories, Jamaica, N. Y.) dissolved in distilled water were employed: 0.05, 0.25, 0.50, 1.00, 1.50 and 2.00 mg/kg. The doses were injected intraperitoneally 30 min before the test session in a nonsystematic order once per week. Each dose was administered three times. Each animal was also injected with a comparable volume of buffered rat ringers every other week. Therefore each animal was injected 36 times, 18 times with *d*-amphetamine and 18 times with buffered rat ringers over a 36 week period.

RESULTS

The data are summarized for the first animal in Fig. 1 and the second animal in Fig. 2. In each figure the mean of the three values obtained with the three injections at each dose for bar presses (solid points connected by a broken line), licks (solid points connected by a solid line), and the water consumed (HOH in ml, thin solid line) are presented as a function of dose. In addition the mean of the comparable values for the 18 ringers injections (S) and for the 10 baseline days (B) are also included.

For the animal in Fig. 1, 0.05, 0.25 and 1.00 mg/kg of *d*-amphetamine enhanced licking as compared to baseline and following the placebo injections of ringers solution. Adjunctive licking was definitely decreased by the two large doses of 1.50 and 2.00 mg/kg. Water consumption was closely related to licking except for a clear dissociation at the two highest doses. The differences are large and represent a decrease in licking from 5922 to about 3330 licks. The enhancement of licking at smaller doses was not as great but represented an increase of 860 licks at 0.05 mg/kg. The increase in bar presses was also substantial and dose related with an optimum increase at 1.50 mg/kg. The increase was 657 presses, from 660 at 0.05 to 1317 presses at 1.50 mg/kg.

The second animal in Fig. 2 displays an identical effect on bar pressing; however, the drug affects adjunctive licking differently. There is no apparent enhancement of licking at low doses but a continuous and almost linear decrease from 0.05–1.50 mg/kg. The amount of water consumed is closely related to licking over the same range. The results at 2.00 mg/kg are interesting. A clear dissociation occurred between licking and water consumption which in this case can be attributed to stereotypy, a common occurrance with high doses of amphetamine.

DISCUSSION

These results demonstrate that *d*-amphetamine affects schedule dependent and schedule induced behavior differently. In the animal in Fig. 1, low doses enhance drinking more than in the other animal of Fig. 2 and the decrease occurs abruptly at 1.50 and 2.00 mg/kg. There was no obvious stereotyped drinking in this animal at these two doses. The animal in Fig. 2 had a much higher lick rate with a mean of 10,516 for the 18 placebo injections (S) as compared to 5430 for the other animal. Only the smallest dose seemed to increase licking. Larger doses produced a progressive decrease. The increase in licking without an

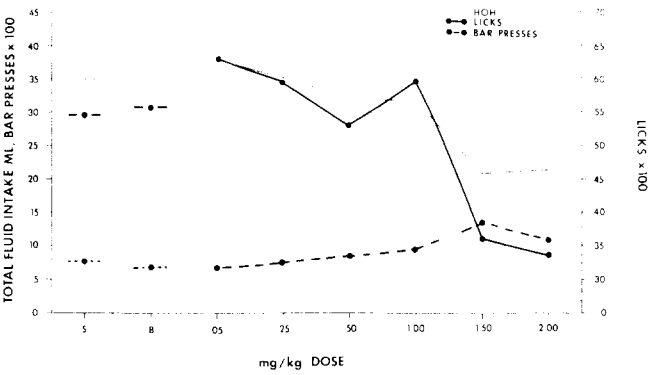

FIG. 1. Mean number of bar presses, licks and water consumed as a function of the amount of *d*-amphetamine injected intraperitoneally. Each point based upon 3 injections. (S) equals the mean of 18 placebo injections. (B) equals the mean of 10 preinjection days or baseline.

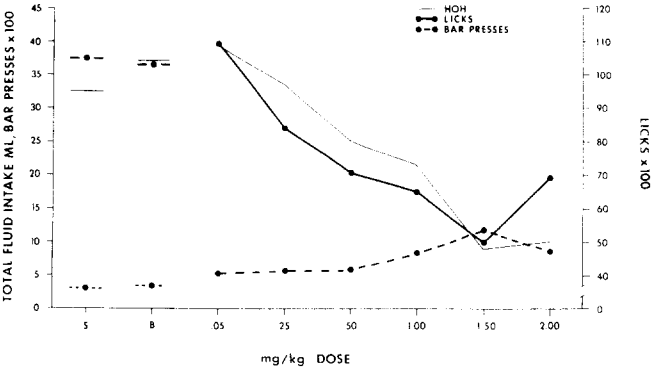

FIG. 2. Same as Fig. 1 except for a different animal.

increase in consumption at 2.00 mg/kg can be attributed to the stereotypy of the behavior. In larger doses, licking under these conditions was observed to become exaggerated to the point where animals licked continuously at the food cup for several hours. Both animals displayed similar increases in bar pressing with increasing dose with a maximum at 1.50 mg/kg. The major difference between the two animals appears to be the higher rate of baseline licking in the animal of Fig. 2 which is also correlated with a smaller amount of bar pressing. Within limits under these conditions bar pressing and schedule induced licking are inversely related.

In the animal which displayed the moderately low level of schedule induced polydipsia, the fact that bar pressing increased with increasing doses up to a maximum at 1.50 mg/kg while adjunctive licking and water consumption appeared to be enhanced at only relatively low doses, is similar in some respects to effects of ethyl alcohol and Δ^9-tetrahydrocannabinol on adjunctive drinking [5]. The possibility that the three drugs are affecting the same mechanism is very appealing and indicates that comparisons should be made under more similar experimental conditions in the future.

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