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Effects of Caffeine on FT-1 Min Schedule Induced Drinking at Different Body Weights[1,2]

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BARONE, F. C., M. J. WAYNER AND S. KLEINROCK. *Effects of caffeine on FT-1 min schedule induced drinking at different body weights.* PHARMAC. BIOCHEM. BEHAV. 11(3) 347–350, 1979.—The effects of caffeine (3.125, 6.25, 12.5, 25.0, 50.0, and 100.0 mg/kg) on lever pressing, schedule induced licking, and water consumption induced by a fixed time 1 min schedule of food reinforcement were studied. Changes in these dependent variables were assessed when animals were reduced to 80% of their initial body weight by partial food deprivation and when body weight recovered after the animals were returned to conditions of ad lib feeding. Results indicate similar decreases in licking and drinking at the highest doses of caffeine under both feeding and body weight conditions. The results were compared to previous research which evaluated the effects of caffeine on adjunctive behavior.

Caffeine Schedule induced polydipsia Adjunctive drinking Licking Drinking Fixed time 1 min schedule

CAFFEINE inhibits the enzyme cyclic nucleotide phosphodiesterase which converts 3', 5' adenosine monophosphate to 5' adenosine monophosphate and consequently accounts for the widespread pharmacological effects of the drug [4,6]. Heart rate, muscle contraction, gastric secretion, and repiration tend to be increased by caffeine and tolerence due to repeated administration develops. Caffeine also has a diuretic action due to an increased rate of sodium and chloride excretion. In the central nervous system, caffeine stimulates the activity of the cortex and medulla and increases reflex excitability. Investigations on the behavioral effects of caffeine have been concentrated primarily on the enhancing effects of the drug on motor activity [1, 2, 3, 8]. A few studies have examined the effects of caffeine on schedule dependent behaviors [5, 7, 13] and feeding [3]. Only one study has evaluated the effects of caffeine on schedule induced behavior [10]. In this study, the effects of caffeine on lever pressing, schedule induced licking and water consumption induced by a fixed interval 1 min food reinforcement generator schedule were determined for animals reduced to 80% of their initial body weight by partial food deprivation and when body weight recovered after animals were returned to conditions of ad lib feeding. The results of the experiment indicated differential effects of the drug between animals at 80% body weight and when they were permitted to recover body weight. Under both conditions the highest dose, 100.00 mg/kg, decreased all dependent variables. Also, the lowest dose, 3.125 mg/kg, increased all dependent variables at recovered body weight and had no effects on the same measures when animals were at 80% body weight.

The purpose of the present study was to investigate the effects of several doses of caffeine administered intraperitoneally on schedule induced licking and drinking. The effects of the drug were assessed in a similar manner to the previous study [10] except that the generator schedule was changed from fixed interval to fixed time. Delivering the food pellets automatically controlled for the number of pellets delivered under the different body weight conditions which made possible direct comparisons between the different body weights for the different doses. In addition, schedule dependent lever pressing was eliminated. Specifically, the effects of caffeine on schedule induced licking and water consumption on lever pressing on a fixed time 1 min generator schedule were determined for rats partially food deprived to 80% body weight and for the same dependent variables in the same test chamber when body weight recovered following a return to ad lib feeding. Results indicate similar effects for animals at 80% body weight and when they are permitted to recover body weight.

EXPERIMENT 1

The purpose of Experiment 1 was to measure the effects of six doses of caffeine—3.125, 6.25, 12.5, 25.0, 50.0 and 100.0 mg/kg—on lever pressing, schedule induced licking, and water consumption in a 1 hr test session when animals were at 80% body weight due to partial food deprivation. Animals were subjected to a fixed time 1 min food reinforcement schedule in a standard test chamber. Doses of caffeine were selected on the basis of previously published data on locomotor activity [8] and schedule induced licking and drinking [10].

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[2]Reprint requests to Dr. M. J. Wayner at the above address.

METHOD

Animals

Six male hooded rats were selected from our colony and placed in individual living cages. Their body weights were 261, 263, 276, 274, 251, and 268 g.

Procedure

The animals were allowed to adapt to the individual living cages and daily handling. Food, water, and body weight were recorded daily for one month. Animals were then reduced to 80% of ad lib feeding body weights by gradually restricting daily rations of food. The ad lib feeding body weights were 350, 392, 346, 350, 348, and 368 g. Water was continously availble. Water consumption and body weight were recorded daily.

On the tenth day of restricted feeding daily 1 hr testing sessions were initiated. A fixed time 1 min generator schedule was used and Noyes food pellets, 45 mg, were delivered every minute during the 1 hr test session for a total of 60 pellets per session. Test sessions were conducted between 0600 and 1000 hr. The test chamber consisted of a standard LVE 1469 medium size test cage and matching sound attenuating cubicle with a lever and pellet dispensing mechanism. A food cup, delivery mechanism, test lights, and lever were mounted in a standard fashion on one wall as provided by the manufacturer. A glass insulated stainless steel ball point drinking spout attached to a graduated eudiometer tube was placed in the center of the adjacent wall of the test cage, 4.0 cm above the grid floor and protruded 1.5 cm into the cage. Total number of licks were recorded and amount of water consumed in ml during the daily 1 hr session was measured. Lever pressing, although not reinforced, does occur under these conditions [11] and was also recorded. In addition, total number of pellets consumed during the testing session and the 23 hr home cage water consumption in ml which occurred on each injection day was also recorded.

After schedule induced licking and drinking and lever pressing stabilized, a series of intraperitoneal injections was initiated. Injections were administered every other day, 40 min prior to test session. First the animals received eight 1 cc/kg of 0.9% saline injections. Results on the last 3 days of saline injection constituted the predrug baseline condition. The following doses of caffeine were then administered as 1 cc/kg; 3.125, 6.25, 12.5, 25.0, 50.0, and 100.0 mg/kg. The drug was dissolved in 0.9% saline. The order of administration of the six doses varied for each animal. Finally, three 1 cc/kg 0.9% saline injections were administered and constituted the postdrug baseline condition.

RESULTS

Data were analyzed by means of single factor ANOVAs having repeated measures. One analysis was carried out for each of the three test session dependent variables; total number of lever presses and licks and water consumed in ml during the 1 hr sessions. Eight levels of the factors were included in the analysis: predrug baseline, each of the six doses of caffeine, and the post drug baseline. The main effects for licks, $F(7,35)=10.32$, and water consumed, $F(7,35)=20.29$, were significant, $p<0.01$. The main effects for lever presses were not significant, $F(7,35)=1.78$, $p>0.10$. Post hoc Dunnett tests were then performed for each dependent variable. In each case the predrug baseline condition

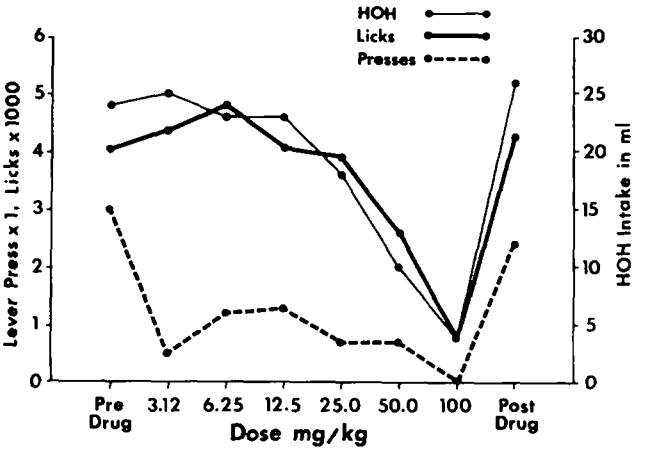

FIG. 1. Mean number of presses, licks, and mean water consumed in ml for the 6 animals in Experiment 1 during the 1 hr test sessions presented as a function of the pre- and postdrug baseline conditions and the 6 doses of caffeine.

TABLE 1

MEAN ± S.D. NUMBER OF PELLETS CONSUMED DURING 1 HR SESSIONS ON INJECTION DAYS OF EXPERIMENTS 1 AND 2

Doses (mg/kg)	Experiment 1 (Reduced Weight)	Experiment 2 (Ad Lib Weight)
Predrug Baseline	60.0 ± 0.0	60.0 ± 0.0
3.125	60.0 ± 0.0	60.0 ± 0.0
6.25	60.0 ± 0.0	60.0 ± 0.0
12.5	60.0 ± 0.0	60.0 ± 0.0
25.0	60.0 ± 0.0	60.0 ± 0.0
50.0	60.0 ± 0.0	59.7 ± 0.8
100.0	60.0 ± 0.0	56.0 ± 8.0
Postdrug Baseline	60.0 ± 0.0	60.0 ± 0.0

was considered as the control treatment for comparisons with all other doses and the postdrug baseline condition. These tests revealed that the 100.0 mg/kg dose of caffeine significantly decreased licking, and that the 50.0 and 100.0 mg/kg dose of caffeine significantly decreased water consumption, $p<0.01$. These effects are illustrated in Fig. 1 where the mean number of lever presses, licks, and water consumed in ml for all animals are presented as a function of the pre- and postdrug baseline and the six doses of caffeine. The mean numbers of pellets consumed during the 1 hr test sessions in Experiment 1 are listed in Table 1. All animals consumed all 60 pellets at each baseline and caffeine dose administered. Therefore, the decreases in drinking and licking at higher doses cannot be attributed to a decrease in the number of pellets consumed under these conditions. The fact that pre-and postdrug data did not differ indicates that there was no overall change in responding during the course of the experiment which could be attributed to drug administrations or other factors.

The mean home cage water consumption in ml for all animals as a function of the pre- and postdrug baseline and the six doses of caffeine is presented in Fig. 2. A one-way

FIG. 2. Mean home cage 23 hr water consumed in ml for the 6 animals in Experiment 1 presented as a function of the pre- and postdrug baseline conditions and the 6 doses of caffeine

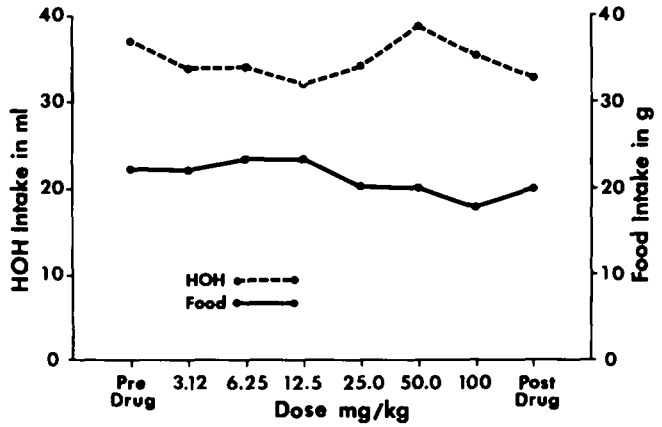

FIG. 4. Same as Fig. 2 including food consumption except for experiment 2.

ANOVA with repeated measures revealed significant differences, $F(7,35)=2.83$, $p<0.05$. A post hoc Dunnett test indicated that only the 25.0 mg/kg dose produced a significant increase in home cage intake as compared to the predrug baseline data, $p<0.01$. Pre- and postdrug intakes did not differ.

EXPERIMENT 2

The purpose of this experiment was to examine the effects of the same six doses of caffeine on the same dependent variables in the same animals utilized in Experiment 1 but after they had recovered body weight following a return to ad lib eating. Schedule induced drinking under these conditions has been described elsewhere [9, 10, 12]. Briefly, when animals recover predeprivation body weights under ad lib eating condition, they are then returned to the identical test chamber for 1 hr test sessions every day. Therefore, the effects of the drug are assessed in relatively normal animals with a built in predisposition to respond in certain ways. Thus, drug effects are not confounded by food deprivation. Results of caffeine injections are similar to those in Experiment 1.

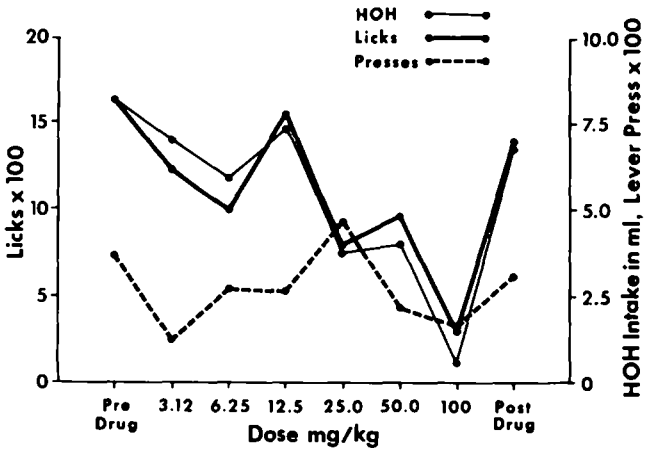

FIG. 3. Same as Fig. 1 except for Experiment 2.

METHOD

Animals

The same 6 animals after completion of Experiment 1 were utilized in this experiment.

Procedure

Following the termination of the first experiment animals were brought back to their ad lib feeding weight over a period of 6 days by gradually increasing their daily ration of food. At the end of this period body weights were 340, 356, 342, 369, 334, and 350 g. Animals were then tested again for 60 min daily test sessions at their free feeding weights. The experimental chamber, pellet delivery mechanism, drinking spout, and FT-1 min generator schedule were identical to that utilized in Experiment 1. When lever presses and schedule induced licking and drinking had stabilized under these conditions over a period of 12 days, a new sequence of injections was initiated. As in Experiment 1, animals received intraperitoneal injections every other day, 40 min before the daily test session. The last three of five 1 cc/kg 0.9% saline injections constituted the precaffeine baseline condition. Following the administration in a non-systematic order of the 6 doses of caffeine—3.125, 6.25, 12.5, 25.0, 50.0, and 100.0 mg/kg administered as 1 cc/kg dissolved in 0.9% saline—animals received three 1 cc/kg 0.9% saline injections which comprised the postdrug baseline condition.

RESULTS

The same statistical procedures as described in Experiment 1 were applied to the data of the present experiment. The main effects for licks, $F(7,35)=7.97$, and water consumed, $F(7,35)=6.74$, were significant, $p<0.01$. The main effects for lever presses were not significant, $F(7,35)=1.19$, $p>0.25$. Post hoc Dunnett tests indicated that the 25.0 and 100.0 mg/kg dose of caffeine significantly decreased licking, and that the 25.0 and 50.0 ($p<0.05$) and the 100.0 mg/kg ($p<0.01$) doses significantly decreased water consumption. These effects are illustrated in Fig. 3 where the mean numbers of lever presses, licks, and water consumed in ml for all animals are presented as a function of the pre- and postdrug baselines and the six doses of caffeine. The mean numbers of pellets consumed during the 1 hr test sessions are listed in Table 1. All animals consumed all 60 pellets except at the

50.0 and 100.0 mg/kg doses. Differences in pellet consumption at the 50.0 mg/kg dose were not significant and differences at the 100.0 mg/kg dose were due to only one animal that consumed only 40 of the 60 pellets during the test session. This particular animal was the one that received the highest 100.0 mg/kg dose first in the series of injections. Therefore, decreases in drinking and licking at the higher doses were not related significantly to the number of pellets consumed under these conditions. The mean home cage food and water consumption for all animals as a function of the pre- and postdrug baseline and the six doses of caffeine is presented in Fig. 4. The main effects for home cage water, $F(7,35)=0.868$, $p>0.25$, and food, $F(7,35)=1.88$, $0.05<p<0.10$, consumption were not significant. Pre- and postdrug measures were not different for any of the dependent variables studied.

DISCUSSION

The data on schedule induced licking and drinking when animals are at 80% body weight indicate that caffeine significantly decreases licking at the highest, 100.0 mg/kg, dose and water consumption at the 50.0 and 100.0 mg/kg doses. Lever pressing which occurred under these conditions was not affected. These differences were not associated with the number of pellets ingested and animals ate all 60 pellets during the test sessions at each caffeine dose. The 25.0 mg/kg dose of caffeine produced increased drinking in the home cage.

The effects of caffeine on lever presses, licks and water intakes when body weight recovers due to ad lib eating are similar. However, it appears that licking and drinking are more sensitive to the drug under these conditions. Significant decreases occurred for licks at the 25.0 and 100.0 mg/kg doses and for water consumption at the 25.0, 50.0 and 100.0 mg/kg doses. The number of pellets consumed during test sessions and home cage water and food consumption were not affected by caffeine injections.

When compared to previous experiments [10], the present study illustrates that the decreases in licking and drinking observed in an FI-1 min schedule of food reinforcement in previous experiments [10] cannot be due to the decreased number of lever presses, pellets received and pellets eaten. All 60 pellets were always delivered and consumed during the 1 hr test session on the FT-1 min schedule at reduced and ad lib eating body weight in the present experiments and decreases in licking and drinking still occurred, although at lower doses than those preiously reported [10]. The fact that increases in licking and drinking did not occur at lower doses [10] is interesting. The different number of pellets received by animals in the two experiments might explain the differential results. In the FI-1 min study [10], the number of pellets received and eaten under baseline conditons were 58 at reduced body weight and 42 at recovered body weight. In the present study utilizing an FT-1 min schedule, 60 pellets were received and eaten during baseline test sessions under both body weight conditions. Apparently, increased lever pressing during the FI-1 min schedule [10] interacts with pellet consumption, licking and drinking, and the effects of caffeine to produce increases at the lowest dose which has no effect on animals during the FT-1 min schedule. The increased home cage water consumption produced at reduced body weight at the 25.0 mg/kg dose of caffeine can probably be attributed to the diuretic effect of caffeine. The increase was not associated with decreased test box water consumption [10].

The results of these experiments indicate that caffeine is a complex stimulus which interacts with body weight and test schedule conditions. Because animals exhibit rapid tolerence to the behavioral effects of caffeine following one injection [10], more work is required on the effects of single caffeine dose injections on independent groups of animals under similar experimental conditions.

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