Pharmacology Biochemistry & Behavior, Vol. 14, pp. 235–240. Printed in the U.S.A.

Effects of Caffeine Administration on Food and Water Consumption Under Various Experimental Conditions[1,2]

A. D. MERKEL,[3] M. J. WAYNER, F. B. JOLICOEUR[3] AND R. MINTZ

Brain Research Laboratory, Syracuse University, 601 University Avenue, Syracuse, NY 13210

Received 1 March 1980

MERKEL, A. D., M. J. WAYNER, F. B. JOLICOEUR AND R. MINTZ. *Effects of caffeine administration on food and water consumption under various experimental conditions.* PHARMAC. BIOCHEM. BEHAV. **14**(2) 235–240, 1981.—The effects of caffeine on food and water intake were assessed in rats maintained under several experimental conditions. In Experiment 1, caffeine, 3.125, 6.25, 12.5, 25.0, 50.0 or 100.0 mg/kg was injected into 23 hr food deprived, 23 hr water deprived or ad lib animals. In Experiment 2, animals were adapted to a 21 hr food deprivation schedule and administered the same doses of caffeine as were used in Experiment 1. Results indicate that caffeine both enhances and decreases food and water intake and that the effects observed depend on the experimental circumstances.

Caffeine Feeding Drinking

CAFFEINE, 1,3,7 trimethylxanthine, is a widely used drug found in coffee, tea, cola nuts, and cocoa. The drug is generally considered to be a central nervous system stimulant [21,27]. Although there is little direct evidence supporting this assumption, it has been shown that the drug can alter cortical EEG recordings [4] and can increase the percentage of spontaneously firing units in the sensorimotor cortex [3]. The fact that caffeine increases locomotor activity in animals in a dose related manner has also been cited as support for a central stimulating action of the drug [7, 13, 14, 19, 22, 24].

In the periphery caffeine has marked pharmacological effects. Among these, caffeine alters both carbohydrate and lipid metabolism. The drug promotes both glycogenolysis [6,15] and lipolysis [5, 10, 12] through activation of phosphorylase and lipase, respectively. Furthermore, under certain circumstances caffeine inhibits the effect of insulin on glucose metabolism, which in certain species induces hyperglycemia [2,25].

Considering caffeine's effects on carbohydrate metabolism, it seems likely that it would affect eating and food intake. However, there have been few studies concerned with the possible influence of the drug on ingestive behavior and the effects which have been observed are contradictory. In one study caffeine's effect on food intake was measured directly in ad lib animals. The results indicated that a toxic sublethal dose of 185 mg/kg produced a transient 3 day decrease in food consumption [20]. More recently, the effects of caffeine on 2 hr food intake were investigated in both ad lib and food deprived mice. Results demonstrated that caffeine, 10, 20 and 40 mg/kg, increased diurnal but not nocturnal food consumption of ad lib mice and had no effect in food deprived animals [11].

Studies on the effects of caffeine on water intake are also sparse. Results of one study indicated that low doses of the drug decrease water consumption in rats [20]. In a more recent study, 3.125 mg/kg of caffeine increased schedule induced drinking in ad lib animals but not in animals reduced to 80% body weight. On the other hand, a high dose of 100 mg/kg reduced schedule induced drinking under both conditions [26].

In view of the known effects of caffeine on metabolic processes and the paucity of other available information, further investigation of the effects of caffeine on ingestive behavior seemed necessary. The purpose of the present study was to examine the effects of several doses of caffeine on food and water consumption under a variety of experimental conditions. Results indicate that caffeine significantly affects ingestive behavior and that these effects are dependent upon the dose administered and the experimental conditions.

EXPERIMENT 1

The purpose of Experiment 1 was to examine the effects of 6 doses of caffeine, 3.125, 6.25, 12.5, 25.0, 50.0 and 100.0 mg/kg on food and water intake in 23 hr food deprived, 23 hr water deprived, and ad lib animals.

[1]This work was supported by NSF Grant No. BNS 76-18520 and NIMH Training Grant No. MH-14258.
[2]Reprint requests to Dr. M. J. Wayner at above address.
[3]Now at Institut de Recherches Cliniques de Montreal, P.Q., Canada.

TABLE 1

MEAN ± SD FOOD INTAKE (g) FOR EXPERIMENT 1

Treatment	Food Deprived 1 Hr	Water Deprived 1 Hr	Water Deprived 23 Hr	Ad Lib 1 Hr	Ad Lib 23 Hr
Predrug Saline	16.04 ± 2.83	7.00 ± 0.75	15.68 ± 1.6	1.78 ± 1.41	25.25 ± 3.01
3.125	14.14 ± 7.21	7.06 ± 1.40	16.71 ± 1.6	3.0 ± 1.66	20.51 ± 7.39
6.25	16.60 ± 3.19	7.05 ± 1.72	16.48 ± 1.5	2.0 ± 1.78	25.11 ± 4.97
12.5	15.38 ± 3.64	6.80 ± 1.69	16.28 ± 2.24	2.83 ± 1.12	24.16 ± 4.3
25.0	15.08 ± 2.24	7.30 ± 2.49	14.92 ± 2.68	2.76 ± 1.18	23.48 ± 2.7
50.0	15.22 ± 1.51	5.70 ± 1.70	13.75 ± 2.35	2.83 ± 1.19	19.1 ± 3.9 *
100.0	5.78 ± 4.08†	1.06 ± 1.43†	9.00 ± 4.3 †	0.26 ± 0.66‡	15.73 ± 7.29†
Post drug	15.32 ± 2.62	6.83 ± 0.51	16.90 ± 1.15	1.83 ± 0.72	24.38 ± 3.48

*$p<0.05$ Post hoc Dunnett's Test.
†$p<0.01$ Post hoc Dunnett's Test.
‡$p<0.01$ Tukey A test indicated that this dose of caffeine decreased food intake compared to the 3.125, 12.5, 25.0 and 50.0 mg/kg doses.

Method

Animals. Eighteen male hooded rats, 300–350 g, were placed in individual cages in a temperature controlled room, 21° ± 1°C, on a 12 hr light/dark cycle. During a 10 day adaptation period food and water was available ad lib.

Procedure. Following the adaptation period, animals were divided into three groups of six animals each: Group 1, 23 hr chronic food deprivation; Group 2, 23 hr chronic water deprivation; Group 3, ad lib food and water. Once food and water intakes stabilized in all groups, a series of IP injections was initiated. First, all animals received 3 injections of 0.9% saline. The data obtained on these days constituted pre-drug baseline measures to which subsequent drug injection data were compared. Then, animals in each group were administered one of six doses of caffeine, 3.125, 6.25, 12.5, 25.0, 50.0 or 100.0 mg/kg in a counterbalanced order. Injections were given every third day, 30 min prior to the test session.

Caffeine was dissolved in 0.9% saline and administered in a volume of 1 ml/kg. Food intake to 0.1 g and water intake to 1 ml were measured immediately following the test session for all groups. All animals were weighed daily prior to the test session. Where appropriate, 23 hr food and water intakes were recorded.

Results

For each group results were analyzed by means of one-way ANOVA's with repeated measures. Data collected under pre-drug saline conditions, with each of the 6 doses of caffeine, and under the post-drug saline condition constituted the 8 levels of the analyses. Post hoc comparisons were made between pre-drug saline and drug injection data using two-tailed Dunnett's test or Tukey A tests where appropriate.

For Group 1, 23 hr food deprived animals, individual analyses were performed on 1 hr food intake, 1 hr water intake, and 23 hr water intake. For 1 hr food intake the main effect was significant: $F(7,35)=4.64$, $p<0.01$. A Dunnett's test indicated that only the 100 mg/kg dose of caffeine decreased food consumption, $p<0.01$. Water intake was also significantly affected during the 1 hr test session, $F(7,35)=35.84$, $p<0.01$. A Dunnett's test revealed that water consumption was significantly reduced by the 100 mg/kg dose of the drug, $p<0.01$. However, 23 hr water intake was not significantly affected.

For Group 2, 23 hr water deprived animals, individual analyses were performed on 1 hr water intake, 1 hr food intake, and 23 hr food intake. For 1 hr water intake, the main effect was significant, $F(7,35)=103.9$, $p<0.01$. A Dunnett's test indicated that the highest dose of caffeine, 100 mg/kg, significantly reduced water intake during this interval, $p<0.01$, and that the lowest dose of the drug, 3.125 mg/kg significantly increased water intake, $p<0.05$. The main effect 1 hr food intake analysis was significant: $F(7,35)=16.7$, $p<0.01$. A Dunnett's test revealed that 100 mg/kg caffeine significantly decreased food intake during the first hour, $p<0.01$. The main effect for 23 hr food intake was also significant, $F(7,35)=14.9$, $p<0.01$. A Dunnett's test indicated that 23 hr food intake was significantly reduced by 100 mg/kg caffeine.

For Group 3, ad lib animals, individual analyses were carried out on both food and water intake data for the 1 hr test session and the remaining 23 hr. All main effects resulting from the food intake analyses were significant: 1 hr, $F(7,35)=4.57$, $p<0.01$; and 23 hr, $F(7,35)=6.45$, $p<0.01$. A Dunnett's test performed on the 1 hr food intake data indicated that there were no significant differences between pre-drug saline values and those obtained following any drug injection. However, a Tukey A test revealed that the highest dose of caffeine, 100 mg/kg, resulted in lower mean food intake when compared to the 3.125, 12.5, 25.0 and 50.0 mg/kg doses, $p<0.01$. A Dunnett's test performed on 23 hr food intake data indicated that both the 50 mg/kg and the 100 mg/kg doses of caffeine significantly decreased food intake, $p<0.05$ and $p<0.01$, respectively. The main effect of caffeine on 1 hr water intake was significant: $F(7,35)=3.84$, $p<0.01$. Dunnett's test revealed that only the 12.5 mg/kg dose of caffeine significantly increased water intake during the 1 hr test session. Water intake was not affected by caffeine during the remaining 23 hr.

The data for each group for both food and water intakes are presented in Tables 1 and 2, respectively.

In summary, these results indicate that 100 mg/kg caffeine significantly reduced food intake during the 1 hr test period in food deprived, water deprived, and ad lib animals. Fur-

TABLE 2

MEAN ± SD WATER INTAKE (ml) FOR EXPERIMENT 1

Treatment	Food Deprived 1 Hr	Food Deprived 23 Hr	Water Deprived 1 Hr	Ad Lib 1 Hr	Ad Lib 23 Hr
Predrug Saline	12.72 ± 1.72	23.6 ± 3.46	22.2 ± 1.75	1.56 ± 1.46	42.5 ± 10.0
3.125	14.00 ± 3.79	21.2 ± 2.78	25.0 ± 1.2 *	2.33 ± 1.21	42.3 ± 10.0
6.25	13.40 ± 2.03	26.6 ± 6.05	24.0 ± 1.69	2.33 ± 1.21	39.5 ± 8.5
12.5	13.80 ± 1.22	22.4 ± 10.17	24.9 ± 2.49	3.83 ± 2.32*	41.2 ± 9.7
25.0	14.40 ± 2.31	28.6 ± 6.00	22.3 ± 3.37	1.83 ± 1.47	45.0 ± 9.6
50.0	12.40 ± 2.57	28.2 ± 10.01	20.5 ± 2.47	1.5 ± 1.76	36.6 ± 12.6
100.0	1.20 ± 0.93†	29.0 ± 11.72	4.2 ± 2.54†	0.66 ± 0.41	35.5 ± 14.4
Post drug	13.02 ± 1.69	24.5 ± 3.46	23.0 ± 2.32	1.96 ± 1.33	44.0 ± 9.9

*$p<0.05$ Post hoc Dunnett's Test.
†$p<0.01$ Post hoc Dunnett's Test.

thermore, 100 and 50 mg/kg of caffeine significantly decreased food intake in ad lib animals 23 hr following the 1 hr test session. Water intakes during the 1 hr test period were decreased by the highest dose of caffeine in both food deprived and water deprived animals. Increased water intakes were seen in water deprived animals with 3.125 mg/kg caffeine and in ad lib animals with 12.5 mg/kg.

EXPERIMENT 2

The previous experiment demonstrated that caffeine in high doses can decrease food and water intake. Although lower doses increased water consumption in ad lib and water deprived animals, no significant effects of caffeine on food consumption were seen with smaller doses of the drug. However, a more detailed examination of the data revealed sporadic but dramatic increases in food intake following administration of small doses of caffeine, 3.125 to 25.0 mg/kg. These increases were seen only in animals receiving the small doses as their first injection in the counterbalanced design. This enhancing effect of small doses was not observed in animals who had previously received the two highest doses of the drug, 50 or 100 mg/kg. The development of tolerance in these animals might explain the ineffectiveness of low doses in augmenting food intake. Indeed, it has been shown that tolerance occurs rapidly to certain pharmacological effects of caffeine including the activity stimulating effect [23] and the diuretic effect [21]. Also, the effect of the drug on schedule dependent and schedule induced behaviors dissipates following repeated administration of caffeine [26]. The purpose of the present experiment was to investigate the effects of acute injections of caffeine on food and water intake in food deprived rats. The same six doses of caffeine utilized in Experiment 1 were administered.

Method

Animals. Thirty-six male hooded rats, 300–350 g, were placed in individual cages in a temperature controlled room, 21° ± 1°C, maintained on a 12 hr light/dark cycle. Purina Rat Chow was presented ad lib for a brief adaptation period and was presented in galvanized hanging feeders attached to the outside front of the cage. Water was available ad lib and presented in 100 ml graduated plastic cylinders. Body weight in g, food intake to 0.1 g, and water intake in ml were recorded daily.

Procedure. Once animals had habituated to the feeders a 21 hr food deprivation schedule was imposed. Each day thereafter, animals were weighed and water tubes removed. One half hour later, premeasured rat chow was placed in the feeding cups for 3 hr and water tubes were returned. Food intake was measured after 30 min, 1 hr, 2 hr, and 3 hr of the 3 hr feeding session. Water intakes were measured after the same intervals and also after 23½ hr.

Once total 3 hr food intake stabilized, animals were divided into six equal groups matched according to 3 hr food intake on the last 3 days of the stabilization period. The data collected on these days represented baseline data and were a control for the effects of injection. On the next three days, animals were injected with 0.9% saline IP, 30 min prior to the test session. The data obtained on these days constituted pre-drug saline measures to which subsequent drug injection data were compared. On the Treatment Day, each group was injected with one of the following doses of caffeine, 3.125, 6.25, 12.5, 25.0, 50.0 or 100.0 mg/kg IP, 30 min prior to food presentation. Caffeine was dissolved in 0.9% saline and injected in a volume of 1 ml/kg. On the following 3 days no injections were administered. The data collected on these days constituted post drug measures of any residual effect of caffeine.

Results

Three hour cumulative food intake data were analyzed by means of a 6×6 ANOVA with repeated measures on the last factor. The factors included in the analysis were Doses and Days. Each of the six doses of caffeine administered on the Treatment Day contributed to one level of the dose factor. Data collected under baseline, pre-drug saline, Treatment, and each of the 3 post drug days constituted the levels of the Day factor. Results indicated a significant main effect for both factors: Dose, $F(5,30)=2.82$, $p<0.05$, and Day, $F(5,150)=10.98$, $p<0.01$. A significant Dose×Day interaction was also obtained, $F(25,150)=2.19$, $p<0.01$, and was further analyzed by means of simple main effects analyses at each level of the Dose factor. Except for the lowest dose, 3.125 mg/kg, significant main effects were found at each level

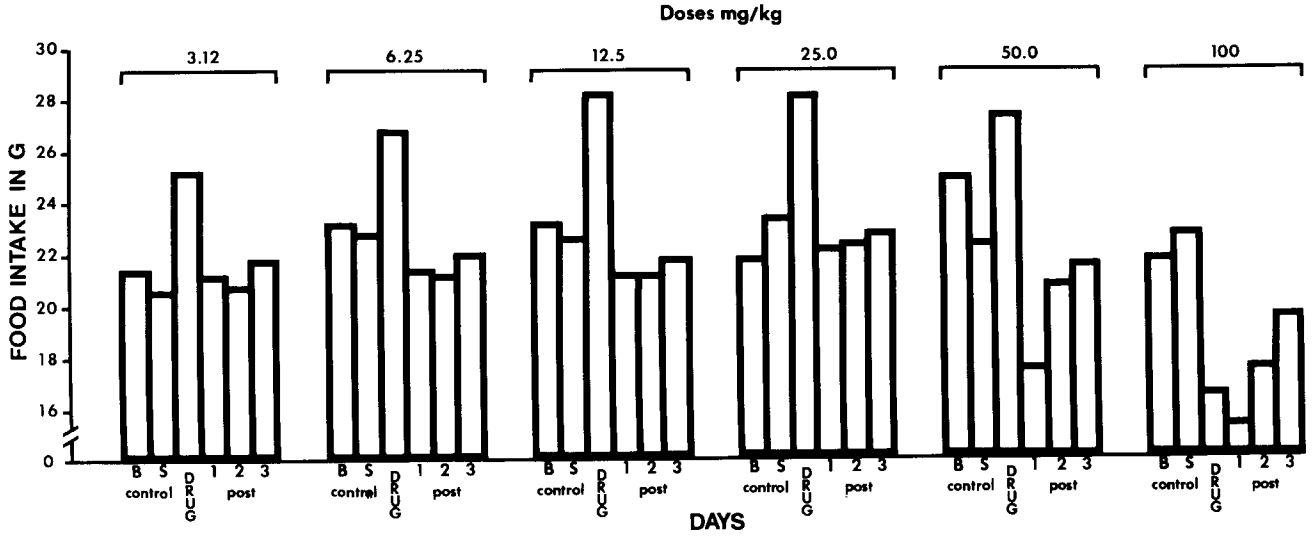

FIG. 1. Mean cumulative 3 hr food intake g presented for each dose as a function of Days: Control, Baseline and Saline; Drug; and Post Treatment Days.

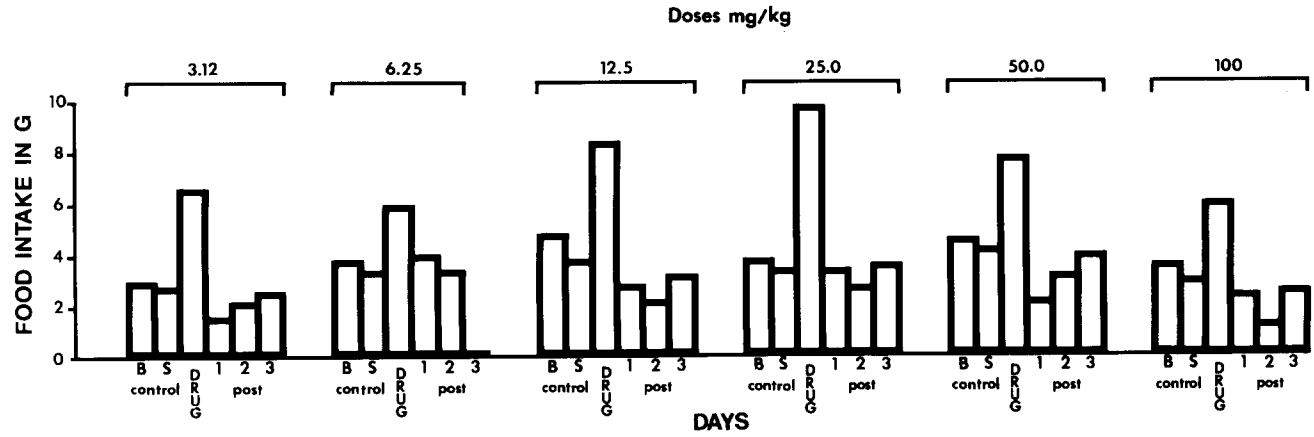

FIG. 2. Mean cumulative 2 hr food intake g presented for each dose as a function of Days: Control, Baseline and Saline; Drug; and Post Treatment Days.

of the factor: 6.25 mg/kg, $F(5,150)=2.27$, $p<0.05$; 12.5 mg/kg, $F(5,150)=4.9$, $p<0.01$; 25.0 mg/kg, $F(5,150)=3.92$, $p<0.01$; 50.0 mg/kg, $F(5,150)=8.4$, $p<0.01$; and 100 mg/kg, $F(5,150)=6.59$, $p<0.01$. Post hoc Dunnett's tests were then performed and revealed that in comparison to pre-drug saline day, the cumulative food consumption of Treatment Day was significantly increased by 6.125 ($p<0.05$), 12.5 ($p<0.05$), 25.0 ($p<0.01$), and 50 mg/kg ($p<0.05$) doses. In addition, the administration of the 50 mg/kg dose resulted in a significant decrease in 3 hr food intake on the first post drug day ($p<0.05$). Finally, the 100 mg/kg dose of caffeine significantly decreased cumulative 3 hr food intake on the Treatment Day ($p<0.01$) and this effect endured for the next two post drug days ($p<0.01$). These results are illustrated in Fig. 1, where mean cumulative 3 hr food intake is presented for each dose as a function of days.

Individual 6×6 ANOVA's with repeated measures were also performed on the food intake data obtained during the 1st hr, 2nd hr, and 3rd hr of the test session. Only the 2nd hr analysis proved significant: Days, $F(5,150)=42.94$, $p<0.01$; Dose×Days, $F(25,150)=1.75$, $p<0.05$. The significant interaction was analyzed by simple main effects analyses carried out at each level of the dose factor. Significant main effects were found at each level of this factor: 3.125 mg/kg, $F(5,150)=4.75$, $p<0.01$; 6.25 mg/kg, $F(5,150)=2.61$, $p<0.05$; 12.5 mg/kg, $F(5,150)=11.21$, $p<0.01$; 25.0 mg/kg, $F(5,150)=22.25$, $p<0.01$; 50 mg/kg, $F(5,150)=7.46$, $p<0.01$; and 100 mg/kg, $F(5,150)=4.12$, $p<0.01$. Post hoc Dunnett's tests indicated that each dose tested, including the 100 mg/kg, increased 2nd hr food intake on the Treatment Day, $p<0.01$. These results are illustrated in Fig. 2 where mean cumulative 2nd hr food intake is presented for each dose as a function of Days.

The effects of caffeine on water intake were also exam-

TABLE 3

MEAN ± SD CUMULATIVE 3 HR WATER INTAKES (ml) IN 21 HR FOOD DEPRIVED RATS

Dose mg/kg	Baseline	Predrug Saline	Treatment Day	Postdrug Day 1	Postdrug Day 2	Postdrug Day 3
3.125	21.3 ± 2.8	20.0 ± 1.7	26.0 ± 3.7*	19.6 ± 10.3	23.6 ± 3.1	20.8 ± 2.9
6.25	23.0 ± 6.1	22.2 ± 5.4	29.3 ± 5.3*	23.6 ± 3.0	24.3 ± 4.3	23.2 ± 2.9
12.5	24.8 ± 2.0	25.0 ± 2.5	30.8 ± 1.9*	22.3 ± 4.2	23.2 ± 3.7	26.5 ± 6.5
25.0	23.3 ± 3.0	23.5 ± 2.7	26.8 ± 2.3	22.0 ± 1.2	23.5 ± 4.3	24.0 ± 3.5
50.0	24.1 ± 2.1	24.1 ± 1.7	21.5 ± 2.8	21.2 ± 2.5	22.2 ± 2.1	24.2 ± 2.3
100.0	23.8 ± 1.5	24.6 ± 2.4	14.0 ± 10.0†	18.8 ± 2.1	22.1 ± 4.6	24.2 ± 1.3

*$p<0.05$ Post hoc Dunnett's Test.
†$p<0.01$ Post hoc Dunnett's Test.

ined. Individual 6×6 ANOVA's with repeated measures on the Day factor were performed on the 1st hr, 2nd hr, 3rd hr cumulative 3 hr and remaining 20½ hr water intake data. Significant results were found only in the cumulative 3 hr water intake data: Day factor, $F(5,25)=4.17$, $p<0.01$; and Dose×Day interaction, $F(25,150)=5.54$, $p<0.01$. Simple main effects analyses at each level of the Dose factor revealed the following significant effects: 3.125 mg/kg, $F(5,150)=4.63$, $p<0.01$; 6.25 mg/kg, $F(5,150)=5.09$, $p<0.01$; 12.5 mg/kg, $F(5,150)=7.06$, $p<0.01$; and 100 mg/kg, $F(5,150)=13.27$, $p<0.01$. Post hoc Dunnett's tests demonstrated that 3.125 mg/kg, 6.25 mg/kg, and 12.5 mg/kg increased cumulative 3 hr water intakes on the Treatment Day ($p<0.01$) and that 100 mg/kg decreased water intake on the Treatment Day ($p<0.01$). No other comparisons were significant. These results are presented in Table 3.

In summary, caffeine administered in doses of 6.25, 12.5, 25.0 and 50.0 mg/kg significantly increases cumulative 3 hr food intake in 21 hr food deprived rats, while 100 mg/kg of the drug significantly decreases 3 hr food intake. The administration of 50 mg/kg of caffeine on the Treatment Day results in a significant reduction in 3 hr food intake on the first post drug day. Injection of 100 mg/kg produced a more prolonged effect, such that 3 hr food intakes were significantly depressed on the 2 subsequent post drug days. The effects of caffeine on 3 hr food intake are most pronounced during the 2nd hr of feeding, where all doses of the drug significantly enhanced food consumption. Water intake was similarly affected by caffeine administration. However only cumulative 3 hr water intakes were altered by the drug and the 3 lowest doses produced a significant increase in water consumption and the highest dose produced a significant decrease.

DISCUSSION

Results demonstrate that caffeine can affect ingestive behavior and the effects depend upon the experimental circumstances. In Experiment 1, several doses of caffeine were injected in a counterbalanced order in 23 hr food deprived, 23 hr water deprived, and ad lib animals. Only the highest dose administered, 100 mg/kg, decreased both food and water intakes during the 1 hr test session. Also, in this experiment, a slight but significant increase in 1 hr water consumption was observed following the injection of 3.125 mg/kg in water deprived animals and 12.5 mg/kg in ad lib animals. Long term effects of caffeine on ingestive behavior were also observed. The decreased effect of 100 mg/kg on food intake persisted in both ad lib and water deprived animals throughout the remaining 23 hr while the effect of the drug on water intake was no longer apparent. Prolonged effects were also obtained following the administration of 50 mg/kg caffeine. While this dose was ineffective in altering either food or water intake in any group during the 1 hr test session, it produced a significant decrease in food consumption during the remaining 23 hr for both ad lib and water deprived animals.

The effects of caffeine on food consumption were more pronounced in Experiment 2 where the same doses were administered acutely to 21 hr food deprived animals. In that experiment, 6.25, 12.5, 25.0 and 50.0 mg/kg caffeine significantly increased cumulative 3 hr food intake on the Treatment Day while 100 mg/kg significantly decreased consumption on this day. On the first post drug day, the results demonstrated that both 50 and 100 mg/kg doses significantly decreased cumulative 3 hr food intake. The diminished food consumption produced by the 100 mg/kg dose persisted throughout the 2nd post drug day. The effects of the drug on water intake were similar but less prominent. The 3 lowest doses tested significantly increased cumulative 3 hr water consumption while the highest dose significantly decreased water intake. No long term effects of the drug on water intake were observed.

The immediate anorexia produced by the 100 mg/kg dose of caffeine in both experiments is consistent with the results of other studies which have demonstrated both decreased activity [13,22] and decreased food intake [20] following high doses of the drug. The prolonged decrease in food intake observed following the administration of both the 50 and 100 mg/kg doses is more difficult to explain. This effect, which was seen up to 2 days following drug injection, cannot be attributed to a direct pharmacological action of the drug since the half-life of the drug is approximately 2 to 2.8 hr. Thus no significant amount of the drug remains 24 hr after administration [9,21]. A residual conditioned taste aversion might account for the post drug day decreased consumption. However, such an explanation is unlikely since it has been shown that aversion to a taste stimulus cannot be produced to a taste stimulus to which animals have been adapted prior to conditioning [1], as was the case in this experiment. Thus, the basis for the observed anorexia induced by high doses of the drug remains obscure.

The results of Experiment 2 are especially interesting be-

cause they demonstrate that low doses of caffeine enhance food intake of 21 hr food deprived animals. This finding is inconsistent with previously reported results which indicated that caffeine administration increased food intake of ad lib but not 21 hr food deprived mice [11]. This discrepancy might be due to procedural differences including species utilized, length of test session, and time of injection.

The increase in activity associated with caffeine administration might have contributed to the augmented feeding response observed following the injection of 6.25, 12.5, 25.0 and 50.0 mg/kg of the drug. However, it has been shown that amphetamine, another central nervous system stimulant, induces marked anorexia at doses which result in hyperactivity. This effect of amphetamine has been reported to occur in both food deprived and satiated animals [8,11]. Therefore, an activity increase does not provide an adequate explanation of the results obtained in Experiment 2.

The increase in food intake might be related indirectly to the less prominent but significant increase in water consumption. Possibly, the relatively weak diuretic effect of caffeine [21] induced animals to drink more which then led to enhanced food consumption. But this hypothesis is tenuous. While the lowest dose tested, 3.125 mg/kg increased drinking, it did not affect food intake. Also, both 25.0 and 50.0 mg/kg caffeine significantly increased 3 hr food consumption without producing a concomitant increase in water intake. Therefore, in this Experiment at least, the effects of the drug on food intake can be readily dissociated from the less obvious effects of the drug on drinking behavior.

The results of Experiment 2 might reflect a direct effect of caffeine on metabolic processes. It has been shown, both in vitro and in vivo, that caffeine can produce a decrease in blood glucose levels. In vitro, caffeine introduced into a medium containing various glucose concentrations induces insulin release from pancreatic beta cells but only when the concentration of glucose approximates or exceeds physiological levels of 100 mg/100 ml [18]. In vivo, administration of caffeine results in a marked hyperglycemic response in genetically bred obese mice but a significant decrease in blood glucose concentrations in their lean littermates [17]. It is possible that the enhanced consumption of food observed in Experiment 2 was in response to a caffeine induced hypoglycemia.

Obviously, further experimentation is required before the relationship between caffeine's pharmacological effects and its effects on ingestive behavior can be firmly established.

REFERENCES

1. Ahlers, R. H. and P. J. Best. Novelty vs. temporal contiguity in learned taste aversion. *Psychon. Sci.* **25:** 34–36, 1971.
2. Anderson, J., G. Hollifield and J. A. Owens. The effects of caffeine, deoxyribose nucleic acid and insulin on the metabolism of glucose by adipose tissue in vitro. *Metabolism* **15:** 30–38, 1968.
3. Arushanyan, E. B., A. Y. Belozertsev and K. G. Arvazov. Comparative effect of amphetamine and caffeine on spontaneous activity of sensorimotor cortical units and their responses to stimulation of the caudate nucleus. *Bull. exp. Biol. Med.* **78:** 776–779, 1974.
4. Ashton, H., J. E. Millman, P. Telford and J. W. Thompson. The effect of caffeine, nitrazepam and cigarette smoking on the contingent negative variation in man. *Electroenceph. clin. Neurophysiol.* **37:** 59–61, 1974.
5. Bellet, S., J. Aspe, A. Kershbaum and D. Zanuttini. Effect of caffeine on free fatty acids. *Circulation* **30:** Suppl. 3, 45–52, 1964.
6. Berthet, J., E. W. Sutherland and T. W. Rall. The assay of glucagon and epinephrine with use of liver homogenates. *J. biol. Chem.* **229:** 351–354, 1957.
7. Boissier, J. R. and P. Simon. Influence de la caffeine sur le comportement en situation libre de la souris. *Archs int. Pharmacodyn.* **166:** 363–369, 1967.
8. Booth, D. A. Amphetamine anorexia by direct action on the adrenergic feeding system of rat hypothalamus. *Nature, Lond.* **217:** 869–870, 1968.
9. Burg, A. W. Physiological disposition of caffeine. *Drug Met. Rev.* **4:** 199–228, 1975.
10. Davies, J. I. In vitro regulation of the lipolysis of adipose tissue. *Nature* **218:** 349–352, 1968.
11. Dobrzanski, S. and N. S. Doggett. The effects of (D)-amphetamine and fenfluramine on feeding in starved and satiated mice. *Psychopharmacology* **48:** 283–286, 1976.
12. Dole, V. P. Effect of nucleic acid metabolites on lipolyses in adipose tissue. *J. biol. Chem.* **236:** 3125–3128, 1961.
13. Eicheler, D. *Kaffee und Koffein.* Berlin: Springer, 1975.
14. Estler, C. J. Effect of α and β-adrenergic blocking agents and parachlorophenylalanine on morphine and caffeine stimulated locomotor activity in mice. *Psychopharmacology* **28:** 261–268, 1973.
15. Gemmill, C. L. The effects of caffeine and theobromine derivatives on glycolysis in muscle. *J. Pharmac. exp. Ther.* **91:** 292, 1947.
16. Gubareff, T. and W. Sleator, Jr. Effects of caffeine on mammalian atrial muscle and its interaction with calcium. *J. Pharmac. exp. Ther.* **148:** 202–214, 1965.
17. Kuftinec, D. M. and J. Mayer. Extreme sensitivity of obese hyperglycemic mice to caffeine and coffee. *Metabolism* **13:** 1369–1371, 1964.
18. Malaisse, W. J., F. Malaisse-Lagae and D. Mayhew. A possible role for the adenylcyclase system in insulin secretion. *J. clin. Invest.* **46:** 1724–1734, 1967.
19. Natsuno, Y. and S. Inada. Influence of caffeine upon spontaneous motor activity of mice. *Jap. J. vet. Sci.* **34:** 234–253, 1972.
20. Peters, J. M. Factors affecting caffeine toxicity: A review of the literature. *J. clin. Pharmac.* **7:** 131–141, 1967.
21. Ritchie, J. M. The xanthines. In: *The Pharmacological Basis of Therapeutics,* edited by L. S. Goodman and A. Gilman. New York: MacMillan, 1975, pp. 367–378.
22. Strom, S. Studies of spontaneous activity with a modified squirrel wheel technique with special regards to screening and follow up studies. *Acta pharmaceut. Suec.* **1:** Suppl. 1, 22–31, 1964.
23. Tainter, M. L. Effects of certain analeptic drugs on spontaneous running activity of the white rat. *J. comp. physiol. Psychol.* **36:** 143–155, 1943.
24. Thethapandha, A., H. M. Maling and J. R. Gilette. Effects of caffeine and theophylline on activity of rats in relation to brain xanthine concentrations. *Proc. exp. biol. Med.* **139:** 582–586, 1972.
25. Vaugn, M. Effects of hormones on glucose metabolism in adipose tissue. *J. biol. Chem.* **236:** 2196, 1961.
26. Wayner, M. J., F. B. Jolicoeur, D. B. Rondeau and F. C. Barone. Effects of acute and chronic administration of caffeine on schedule dependent and schedule induced behavior. *Pharmac. Biochem. Behav.* **5:** 343–348, 1976.
27. Weiss, B. and V. G. Laties. Enhancement of human performance by caffeine and the amphetamines. *Pharmac. Rev.* **14:** 1–36, 1962.