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Effects of Methylphenidate on Food and Water Consumption at Different Body Weights[1,2]

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BARONE, F C , M J WAYNER, H K LEE, W H TSAI, D L DEHAVEN AND W WOODSON *Effects of methylphenidate on food and water consumption at different body weights* PHARMAC BIOCHEM BEHAV 10(4) 591–595, 1979 —The effects of intraperitoneally administered methylphenidate at 0, 1 5, 3 0, 6 0, and 12 0 mg/kg were studied in two experiments Experiment 1 determined the effects of methylphenidate on 0 5, 1 0, 2 0, and 24 hr post injection food and water consumption in rats at ad lib feeding body weights Experiment 2 determined the post injection effects of methylphenidate on 0 5, 1 0 and 2 0 hr food and water and 24 hr water consumption in rats maintained at 80% ad lib feeding body weight due to partial food deprivation The results of Experiment 1 indicate that when animals are feeding ad lib at normal body weight food and water consumption is decreased for 2 hr following the administration of the lowest 1 5 mg/kg dose of methylphenidate Methylphenidate in doses as high as 12 0 mg/kg has no effect on 24 hr food and water consumption under these conditions The results of Experiment 2 indicate that when animals are maintained at reduced body weight due to partial food deprivation, food consumption for 2 hr is significantly decreased by the highest, 12 0 mg/kg, dose of methylphenidate These effects are observed within the first 30 min post injection when methylphenidate decreases food consumption in a dose dependent manner Methylphenidate has no effect on water consumption under these conditions The effects of methylphenidate on ingestive behavior are discussed in terms of previous experiments and the possible differential effects on motor activity at different body weights under different stimulus conditions

Methylphenidate Eating Drinking Body weight Food deprivation

METHYLPHENIDATE, a piperidine derivative, is classified as a mild central nervous system stimulant having pharmacological properties similar to amphetamine [8] The central dopaminergic effects of methylphenidate have been demonstrated. Methylphenidate causes a significant release of dopamine from striatal synaptosomes and might directly stimulate receptor sites [5,6] In addition to preferentially affecting dopaminergic systems, methylphenidate also stimulates the release of growth hormone [2,3]. Several behavioral effects of methylphenidate have been observed It has been shown to increase activity [7, 9, 10, 14] and induce stereotyped behaviors such as grooming, sniffing, and licking in mice and rats [4, 7, 11, 16] Methylphenidate also facilitates active avoidance and water maze performance [13]. Lever pressing for water in fluid deprived animals was increased [1, 15, 17] and discriminative responding for food in weanling rats was decreased [12] by methylphenidate. Recently, it has been demonstrated that methylphenidate affects schedule dependent and schedule induced behaviors differently [18]. Schedule induced licking and drinking are decreased by methylphenidate when animals are tested at 80% body weight and following a return to ad lib feeding. Lever pressing under the same conditions was not affected. The effects of methylphenidate on food and water consumption under these conditions have not been investigated The purpose of this study was to examine the effects of several doses of methylphenidate on the consumption of available food and water. These effects were assessed in rats maintained at ad lib feeding body weight and in animals partially food deprived to 80% body weight. Results indicate that at ad lib feeding body weight the lowest, 1.5 mg/kg, dose of methylphenidate significantly decreases both eating and drinking. At reduced body weight, a dose related decrease in food consumption occurred with the highest, 12 0 mg/kg, dose causing the greatest decrease Water consumption was not affected.

EXPERIMENT 1

The purpose of this experiment was to study the effects of 1 5, 3.0, 6.0, and 12 0 mg/kg of methylphenidate administered intraperitoneally on ad lib food and water consumption

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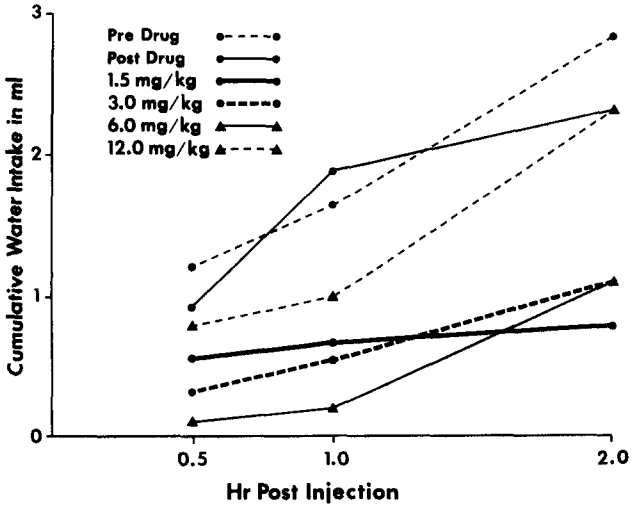

FIG 1 Mean cumulative water consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection in the 9 ad lib animals in Experiment 1

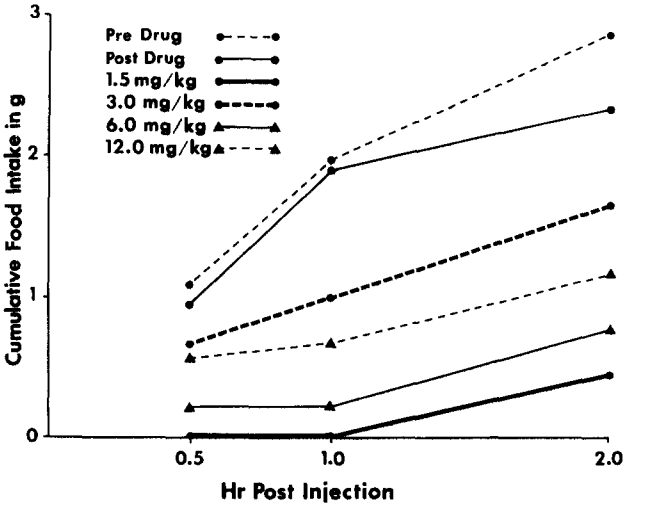

FIG 3 Mean cumulative food consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection period in the 9 ad lib animals in Experiment 1

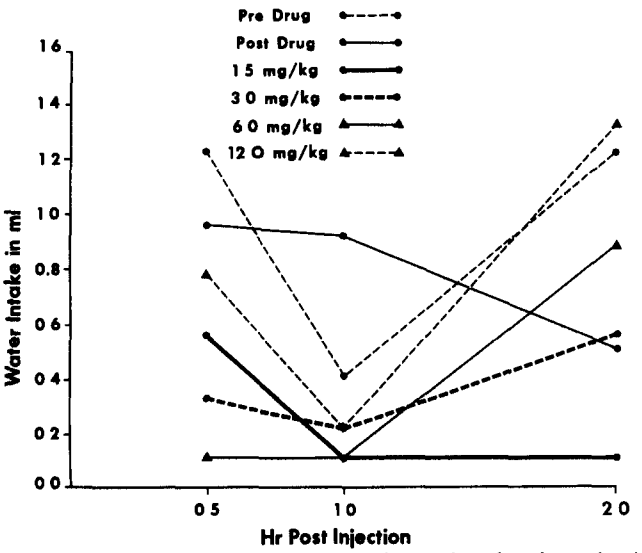

FIG 2 Mean water consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection in the 9 ad lib animals in Experiment 1

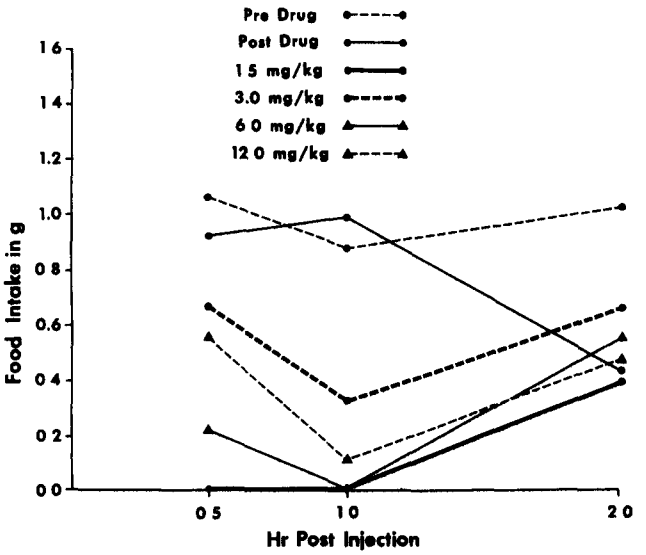

FIG 4 Mean food consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2.0 hr post injection in the 9 ad lib animals in Experiment 1

METHOD

Animals

Nine male hooded rats, approximately 4 months old, were selected from our colony and placed in individual living cages, 25×28×30 cm. A 12 hr light-dark cycle began at 0700 and was followed by a 12 hr dark phase. The room temperature was maintained at 21 ± 1°C

Procedure

Animals were adapted to handling and isolated housing for 5 days. During this period and for the duration of the experiment Purina lab chow consumption in g, tap water consumption in ml, and body weight in g were measured daily between 1200 and 1500 hr Following the adaptation period the animals had a mean body weight of 425 ± 54.3 g (SD). A series of intraperitoneal injections was then initiated. Injections were administered in a volume of 1 ml/kg every other day. First, animals received five 0.9% NaCl injections. Results on the last 3 days of saline injection constituted the predrug baseline condition. The following doses of methylphenidate were then administered: 1.5, 3.0, 6.0, and 12 0 mg/kg. The drug was dissolved in 0 9% NaCl. The order of administration of the four doses of methylphenidate was varied for each rat according to a balanced lattice square incomplete block design. Finally, three 0.9% NaCl injections were administered, and they constituted the post drug baseline condition Food and water consumption were measured 0 5, 1.0, 2.0, and 24 hr following all injections

RESULTS

The data for 2 hr post injection water and food consumption were analyzed by two-way ANOVA's with repeated measures The factors were doses, six levels consisting of predrug baseline, 1 5, 3 0, 6.0, and 12.0 mg/kg methylphenidate, and post drug baseline, and time, three levels consisting of 0 5, 1 0 and 2.0 hr post injection consumption measures The analysis of water consumption indicated that the main effects for doses was significant, $F(5,40)=3.09$, $p<0\ 05$ The main effects for time, $F(2,16)=2\ 07$, $p>0\ 10$, and the dose by time interaction, $F(10,80)=1\ 59$, $p>0.10$, were not significant. The analysis of food consumption indicated that the main effects for doses was significant, $F(5,40)=2.93$, $p<0\ 05$ The main effect for time, $F(2,16)=0\ 77$, $p>0\ 25$, and the dose by time interaction, $F(10,80)=0\ 74$, $p>0\ 25$, were not significant. Separate Dunnett tests were performed to determine dose effects The predrug baseline condition was considered as the control treatment for comparisons with the drug doses and the post drug condition These tests revealed that in comparison to baseline both food and water consumption were significantly decreased by 1 5 mg/kg methylphenidate, $p<0\ 02$ In both cases post drug data did not differ from predrug baseline These results are illustrated in Figs. 1, 2, 3 and 4 In Figs 1 and 2 the cumulative and non-cumulative mean water intakes are presented as a function of time post injection Figures 3 and 4 illustrate the same effects for food intakes

The data for 24 hr post injection food and water consumption were analyzed by one-way ANOVA's with repeated measures Six levels of the dose factor were included in each analysis: predrug baseline, each of the four doses of methylphenidate, and the post drug condition There were no significant dose effects for 24 hr water, $F(5,40)=1\ 355$, $p>0\ 25$, or food, $F(5,40)=1\ 920$, $p>0\ 10$, consumption

To summarize, when animals are feeding ad lib at normal body weight, food and water consumption is decreased for 2 hr following the administration of the lowest 1 5 mg/kg dose of methylphenidate. Methylphenidate in doses as high as 12 0 mg/kg has no effect on 24 hr food and water consumption under these conditions

EXPERIMENT 2

The purpose of this experiment was to investigate the effects of the same 4 doses of methylphenidate on the same dependent variables as in Experiment 1 in animals which were partially food deprived and maintained at a reduced body weight

METHOD

Animals

Ten male hooded rats, approximately 4 months old, were selected from our colony and placed in individual living cages The light-dark cycle and room temperature were the same as in Experiment 1

Procedure

Animals were allowed to adapt for 5 days as described in Experiment 1 Following the adaptation period animals had a mean body weight of 398 ± 12 8 g (SD) Animals were then reduced to 80% of ad lib feeding body weight over an 8 day period by gradually restricting the daily rations of food Water was continuously available The food ration was administered and the daily water consumption in ml and body weight in g was measured daily between 1200 and 1500 hr Following 3 additional days at reduced body weight a series of intraperitoneal injections was initiated Injection procedures were similar to those utilized in the first experiment However, animals received 1 0 ml/kg injections every third day instead of every other day Following the injections food was presented for a 2 hr period and consumption was meas-

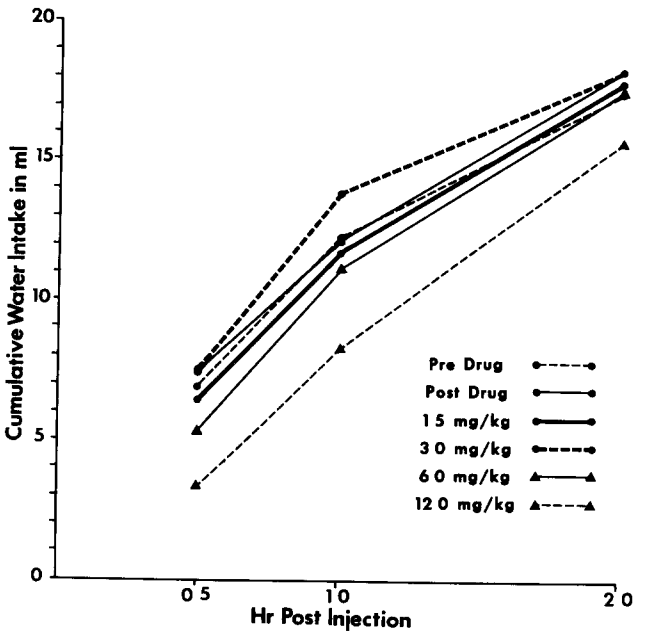

FIG 5 Mean cumulative water consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection period in the 10 reduced body weight animals in Experiment 2

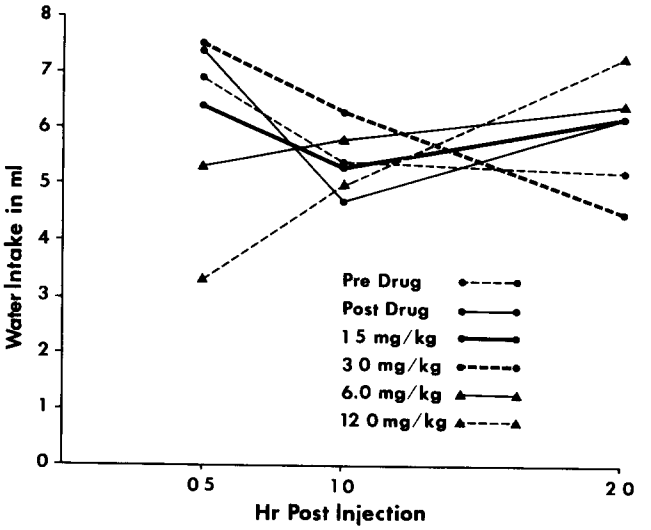

FIG 6 Mean water consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection in the 10 reduced body weight animals in Experiment 2

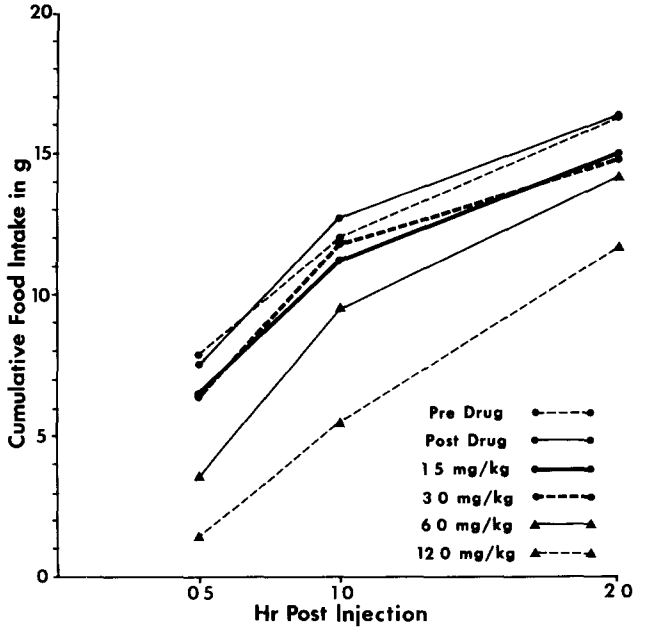

FIG 7 Mean cumulative food consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection period in the 10 reduced body weight animals in Experiment 2

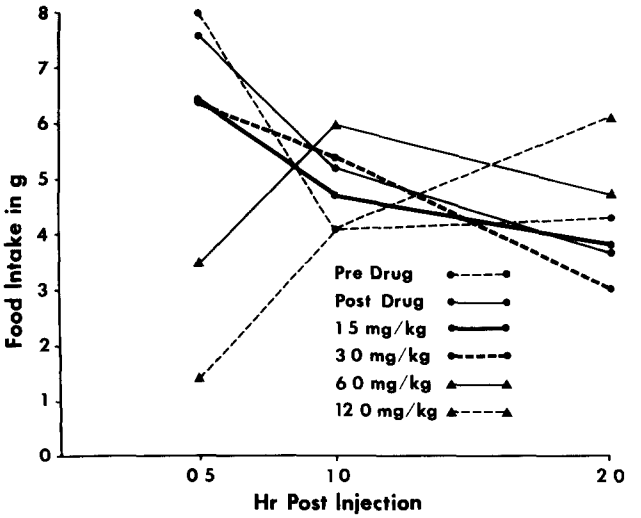

FIG 8 Mean food consumption for the predrug baseline, the 4 doses of methylphenidate, and the post drug baseline which occurred at 0 5, 1 0 and 2 0 hr post injection in the 10 reduced body weight animals in Experiment 2

ured at 0 5, 1 0 and 2 0 hr Water consumption was measured at 0 5, 1 0, 2 0, and 24 hr post injection Again the last 3 of 5 pre-methylphenidate 0 9% NaCl injections constituted the predrug baseline condition Following the administration of methylphenidate in a nonsystematic order as described in the first experiment, three 0 9% NaCl injections were administered which comprised the post drug baseline condition On the two days which occurred between injection days food rations were further adjusted in order to maintain 80% body weight for each injection day These adjustments due to the eating during the tests were relatively small and insignificant

RESULTS

The data for 2 hr post injection water and food consumption were anlayzed as described in Experiment 1. The analysis of water consumption indicated that the main effects for doses, $F(5,45)=0\ 70$, $p>0\ 25$, time, $F(2,18)=0\ 62$, $p>0\ 25$, and the dose by time interaction, $F(10,90)=1\ 94$, $0\ 10>p>0\ 05$, were not significant These results are illustrated in Figs 5 and 6 where the cumulative and noncumulative mean water intakes are presented as a function of time post injection The analysis of food consumption indicated that the main effect for doses was significant, $F(5,45)=3.73$, $p<0\ 01$ Dunnett tests were then performed utilizing the predrug baseline as the control treatment Results indicated that the 12 0 mg/kg dose of methylphenidate significantly decreased food consumption The post drug data did not differ from predrug baseline The main effect for time, $F(2,18)=2\ 44$, $p>0\ 10$, was not significant The dose by time interaction was significant, $F(10,90)=7\ 57$, $p<0\ 01$ Simple main effects analyses of doses at each time period indicated that doses at 0 5 hr were significant, $F(5\ 90)=13\ 60$, $p<0.01$, doses at 1 0 hr were not significant, $F(5,90)=1\ 17$, $p>0\ 25$, and doses at 2 0 hr were significant, $F(5,90)=2\ 48$, $p<0\ 05$ Tukey A tests were then conducted to determine dose effects at 0 5 and 2 0 hr At 0 5 hr the food consumption following 6.0 and 12 0 mg/kg methylphenidate was decreased below both the pre and post drug baselines, $p<0\ 01$ The 12 0 mg/kg dose also decreased consumption when compared to the 1 5 and 3 0 mg/kg doses indicating a dose related effect, $p<0\ 01$ At 2 0 hr no significant differences between doses were observed. These results are illustrated in Figs 7 and 8 where the cumulative and noncumulative mean food intakes are presented as a function of time post injection The data for 24 hr post injection water consumption were also analyzed as described in Experiment 1 There was no significant dose effect for 24 hr water consumption, $F(5,45)=2\ 09$, $0\ 10>p>0\ 05$

To summarize, when animals are maintained at reduced body weight due to partial food deprivation, food consumption over a 2 hr period is significantly decreased by the highest 12 0 mg/kg dose of methylphenidate These effects are observed within the first 30 min following injections when methylphenidate decreases food consumption in a dose dependent manner Methylphenidate in doses as high as 12 0 mg/kg has no effect on water consumption under these conditions

DISCUSSION

Free access food and water consumption when animals are at ad lib feeding body weight is decreased by methylphenidate It is interesting that under these conditions the lowest dose studied was the most effective in decreasing both measures over a 2 hr post injection period The effects of methylphenidate on free access food and water consumption when animals are at 80% body weight due to partial food deprivation are different Food consumption is decreased for 2 hr post injection by the highest dose studied These effects are attributed to a dose related decrease in eating which occurs from 0 to 30 min post injection. It is also interesting that water consumption was not affected by any dose of

methylphenidate when animals are at reduced body weight. The effects of these same doses of methylphenidate on activity must also be determined as a possible explanation for the decrease in eating and drinking Visual inspection of the animals seemed to indicate an increase in activity at only the large dose

These results demonstrate that the effects of methylphenidate on lever pressing, licking and drinking observed in previous experiments [18] cannot be attributed to concurrent changes in food and water consumption For example, animals at reduced body weight trained to press a lever for 45 mg food pellets on an FI 1 min schedule exhibit a significant decrease in schedule induced licking and drinking following the administration of methylphenidate Lever pressing for food was unaffected by methylphenidate under these conditions. In the present study, methylphenidate did not affect water consumption and decreased food consumption in animals maintained under the same reduced body weight conditions Consequently, the decrease in schedule induced licking and drinking appear to be due to some central effect of methylphenidate which is independent of any effects on food and water ingestion Additional studies on other adjunctive behaviors are in progress

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