

Effects of Methylphenidate on Schedule Dependent and Schedule Induced Behavior^{1,2}

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(Received 11 May 1978)

WAYNER, M. J., R. B. MINTZ, F. B. JOLICOEUR AND D. B. RONDEAU. *Effects of methylphenidate on schedule dependent and schedule induced behavior*. PHARMAC. BIOCHEM. BEHAV. 10(2) 299-302, 1979.—The effects of methylphenidate, 1.5, 3.0, 6.0 and 12.0 mg/kg, on lever pressing, schedule induced licking, and drinking were studied. The generator schedule was a fixed interval 1 min food reinforcement schedule. The effects were assessed when animals were reduced to 80% body weight by partial food deprivation and when allowed to recover body weight under conditions of ad lib eating. Results indicate that under both body weight conditions methylphenidate significantly decreases schedule induced licking and drinking but does not affect lever pressing.

Methylphenidate	Schedule induced drinking	Adjunctive drinking	Eating	Drinking
Schedule dependent behavior				

METHYLPHENIDATE is a piperidine derivative traditionally classified as a central nervous system stimulant [5]. Clinically, this drug is widely utilized in the treatment of so-called hyperactive children [3, 14, 20]. Several behavioral effects of methylphenidate in laboratory animals have been documented. Methylphenidate administered in relatively small doses, 2.0 to 16.0 mg/kg, has been shown to increase various components of general activity in rats [4, 6, 7, 11]. When administered in higher doses, 50 to 100 mg/kg, methylphenidate induces stereotype behaviors such as gnawing, sniffing, and licking in mice and rats [2, 4, 8, 13]. Studies on the effects of methylphenidate on behavior maintained by schedules of food or water reinforcement have been relatively sparse. Methylphenidate increases lever pressing for water in fluid deprived animals placed on various schedules of reinforcement [1, 12, 15]. Discriminative responding for food in weanling rats was found to be impaired following the administration of 2.0 and 5.0 mg/kg of methylphenidate [10]. The effects of methylphenidate on schedule induced behavior have not been investigated. The purpose of this study was to examine the effects of several doses of methylphenidate on schedule dependent lever pressing and on schedule induced licking and drinking. These effects were assessed in rats when partially food deprived to 80% body weight and when allowed to recover body weight following a return to ad lib feeding. Results indicate that under both body weight conditions methylphenidate does not affect lever pressing but significantly reduces schedule induced behavior.

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 on lever pressing, schedule induced licking, and water consumption in animals at 80% body weight due to partial food deprivation. Animals were subjected to a fixed interval 1 min food reinforcement schedule during 1 hr test sessions.

METHOD

Animals

Four male hooded rats were selected from our colony and placed in individual living cages in a temperature controlled room, 20 ± 1°C, with a 12 hr light-dark cycle. Body weights were 407, 457, 401 and 423 g.

Procedure

After a 10 day period of adaptation, animals were reduced to 80% of ad lib feeding body weight by gradually restricting the daily rations of food. Water was continuously available. Water intakes and body weights were measured daily. After 3 days of shaping on a continuous food reinforcement schedule, animals were tested daily for 1 hr on a fixed interval 1 min food reinforcement schedule for 45 mg Noyes pellets. The test chamber consisted of a standard LVE 1469 medium size test cage with a lever and pellet dispensing mechanism in a sound attenuating cubicle. Food cup, deliv-

¹Supported in part by NSF Grant No. BNS 76-18520

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ery mechanism, test lights and lever were mounted on one wall. A glass insulated stainless steel ball point drinking spout attached to a graduated cylinder was placed in the center of the adjacent wall of the test cage, 4.0 cm above the grid floor and protruding 1.5 cm into the cage. Licks were measured by a contact lickometer. Total number of licks and presses were recorded and amount of water consumed in ml during the daily 1 hr sessions was measured.

After lever presses and schedule induced behavior stabilized, a series of intraperitoneal injections was initiated. Injections were administered as 1 ml/kg every other day, 20 min prior to the test session. 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 was varied for each rat. Finally, three 0.9% NaCl injections were administered and they constituted the post drug baseline condition.

RESULTS

Data were analyzed by means of one way ANOVA's with repeated measures. One analysis was carried out for each of the four dependent variables, lever presses, licks, and water consumed in ml during the 1 hr sessions, and 24 hr home cage water consumption. Six levels of the dose factor were included in each analysis: predrug, baseline, each of the four doses of methylphenidate, and the postdrug condition. Significant main effects were found for licks, $F(5,15)=5.93$, $p<0.01$; as well as for water consumed during the test session, $F(5,15)=47.02$, $p<0.01$, and in the home cage, $F(5,15)=7.18$, $p<0.01$. The main effect for lever presses was not significant ($p>0.05$). Separate Dunnett tests were performed for licks and water consumed. In each case the predrug baseline condition was considered as the control treatment for comparisons with the drug doses and the postdrug condition. These tests revealed that in comparison to baseline licking was significantly decreased by the 12.0 mg/kg dose ($p<0.01$) and water consumed in the test cage was significantly reduced by 3.0, 6.0 and 12.0 mg/kg methylphenidate ($p<0.01$). Water consumed in the home cage was significantly increased by the 6.0 and 12.0 mg/kg doses ($p<0.01$). The test cage results are illustrated in Fig. 1 where the mean number of presses (thin continuous line), mean number of licks (solid points connected by a solid line) and mean water intakes (solid points connected by a broken line) for all animals are presented as a function of the predrug saline baseline data and the 4 doses of methylphenidate. In summary, these results indicate that, when animals are tested at reduced body weights, methylphenidate significantly decreases schedule induced licking and drinking but does not substantially affect schedule dependent lever pressing. The increased drinking in the home cage which occurred at the higher doses of methylphenidate is related to the decreased water consumption which occurred in the test cage at the same doses.

EXPERIMENT 2

The purpose of this experiment was to investigate the effects of the same 4 doses of methylphenidate on the same dependent variables in the animals utilized in Experiment 1

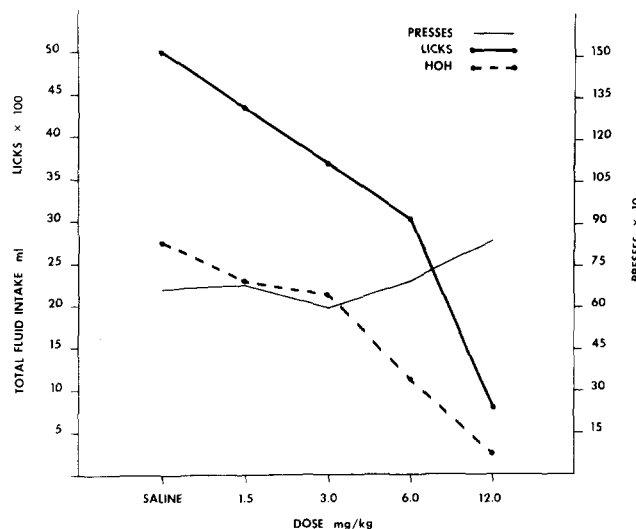


FIG. 1. Mean number of presses and licks and mean water consumed in ml for the 4 animals in Experiment 1 when tested at 80% body weight presented as a function of the predrug saline baseline data and the four doses of methylphenidate administered.

but after they had recovered body weight following a return to ad lib eating. The procedures involved to obtain schedule dependent and schedule induced behavior under these conditions have been described previously [19]. Briefly, when animals recover predeprivation body weights under free feeding conditions, they are then retested in the identical test chamber for 1 hr daily sessions.

METHOD

Animals

The same 4 animals of Experiment 1 were utilized in this experiment.

Procedure

Following the completion of the first experiment, animals were brought back to their ad lib feeding body weight over a period of 6 days by gradually increasing their daily ration of food. Animals were not tested in the experimental chamber on these days. At the end of this period body weights were 405, 451, 413 and 412 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 generator schedule were identical to that utilized in Experiment 1. When lever presses and schedule induced behavior had stabilized under these conditions a new sequence of injections was initiated. Injection procedures were the same as those utilized in the first experiment; that is, animals received 1 ml/kg intraperitoneal injections every other day, 20 min before the daily session. Results on the last three days of the five saline injections constituted the predrug baseline condition. Following the administration of a non-systematic order of the same four doses of methylphenidate, three 0.9% NaCl injections were given which comprised the post drug baseline condition.

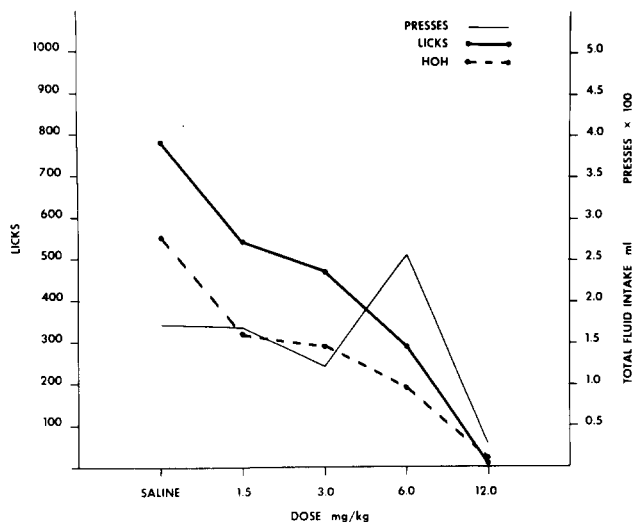


FIG. 2. Same as Fig. 1 except the same 4 animals in Experiment 2 were tested at recovered body weight following a return to ad lib eating.

RESULTS

The same statistical procedures as described in Experiment 1 were applied to the data of the present experiment. In addition, 24 hr home cage food consumption was also analyzed. Significant main effects were found for licks, $F(5,15)=5.24$, $p<0.01$, and for test cage water consumed, $F(5,15)=4.89$, $p<0.01$. The main effect for lever pressing was not significant ($p>0.05$). The main effects for home cage water, $F(5,15)=2.87$, $p>0.05$, and food, $F(5,15)=0.98$, $p>0.25$, were not significant. Post hoc Dunnett tests revealed that in comparison to baseline, licks and water consumed were significantly decreased by 6.0 and 12.0 mg/kg methylphenidate. No significant changes in lever presses were produced by any of the doses tested. In all cases post drug data did not differ significantly from the predrug baseline condition. The test cage results are illustrated in Fig. 2 where mean number of lever presses (thin continuous line), mean number of licks (solid points connected by a solid line), and mean water intakes (solid points connected by a

broken line) for all animals are presented as a function of the predrug saline baseline condition and the four doses of methylphenidate. It can be seen that the effects of methylphenidate in recovered body weight free feeding animals are similar to those observed under conditions of food deprivation. Schedule induced licking and drinking are decreased by relatively high doses of the drug whereas lever pressing is not affected by methylphenidate.

DISCUSSION

These results demonstrate that methylphenidate affects schedule dependent and schedule induced behaviors differently. Schedule induced behaviors were significantly decreased by methylphenidate both when animals were tested at 80% body weight and following a return to ad lib feeding. Although lever pressing under the conditions of both experiments was not affected significantly by methylphenidate, the observed increase in Fig. 2 which occurred at the 6.0 mg/kg dose was due to the excessive stereotyped lever pressing of one animal. If this animal were eliminated at this particular dose, lever pressing under ad lib feeding conditions would also decrease gradually with larger doses of the drug, as does licking and drinking (Fig. 2). Since the animals in Experiment 2 are not at 80% body weight lever pressing, licking, and drinking might all be considered adjunctive [17,19]. Home cage water consumption was not increased at the higher doses of methylphenidate in Experiment 2. An increase might not have occurred, as it did in Experiment 1, because animals on ad lib eating and drinking consume less in the test chamber. Animals at 80% body weight drink much more in the test chamber and consequently drink less in the home cage. The higher doses of methylphenidate apparently enhance home cage drinking to compensate for the decreased drinking in the test cage. The effects of methylphenidate on home cage eating and drinking in normal and reduced body weight rats will be published in a subsequent report.

Similar effects were found with amphetamine on schedule dependent lever pressing and schedule induced licking and drinking [18]. It is interesting that drugs which have been found to be clinically effective in treating hyperactive children systematically decrease adjunctive behaviors in experimental animals [20]. This fact suggests that adjunctive behavior in animals might constitute an experimental model for the study of bizarre behaviors in general [9,16].

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