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BRIEF COMMUNICATION

Prewatering and Haloperidol Have Similar Effects on Rats' Response Rate and Duration

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JACKSON, D. E. AND S. E. BOWEN. *Prewatering and haloperidol have similar effects on rats' response rate and duration.* PHARMACOL BIOCHEM BEHAV 47(3) 761-763, 1994. – Haloperidol (0.1 mg/kg) and 5-min prewatering were given to 12 rats on three occasions each to determine effects on fixed ratio 15 (FR 15) responding for water. Compared to baseline, both treatments significantly reduced rate (prewatering slightly more) and both significantly increased duration. Though similar, drug and prewatering effects showed enough differences to suggest that there are both anhedonic and motoric deficit components to haloperidol's effects on rats' lever-pressing behavior for water.

Neuroleptics Haloperidol Prewatering Response duration Within-session effects Anhedonia Motoric deficit Rats

IT IS well known that rats given haloperidol show operant rate attenuation (2,6), increases in emitted peak force (4), and increases in response duration, the time the lever microswitch is closed (3,5).

Haloperidol is a dopamine D_2 receptor blocker frequently used as an antipsychotic. Explanations for haloperidol's effect on rat operant behavior are generally seen as motivational or motoric. Wise's (6) anhedonia hypothesis suggests that reinforcers' effects are degraded by neuroleptics. By contrast, a motor deficit interpretation is preferred by others [e.g., (1,4)].

A recent study by Liao and Fowler (5) reported that haloperidol produced within-session changes in operant response rate (decreases) and duration (increases) in rats working on a fixed ratio 20 (FR 20) schedule for food, and the authors interpreted these findings as supportive of the motor deficit hypothesis. "Furthermore, the increase in duration that occurred as the responding progresses within a session indicates that the motoric deficit grows as a function of the amount of behavior emitted" [(5), p. 201]. Using these data to support a motor deficit interpretation rests on the assumption that these effects cannot be generated by motivational manipulations. The purpose of the present study was to test this notion by comparing haloperidol's effects on rats' response rate and duration with those produced by a clearly motivational intervention. The motivational intervention selected was the prewatering of the rats prior to their operant session of working for water on a FR schedule. While it is reasonable that overall response rate will be affected by prewatering, the effects prewatering will have on duration are unknown.

METHOD

Subjects

Twelve male albino rats obtained from the Holtzman Co. (Madison, WI) served as subjects. On arrival they were individually housed with constant access to food and water. They were subsequently water-deprived and initially maintained at 85% of free-feeding weights through limited watering following each session. Subsequently, a weight gain of 3 g/week was targeted so that on the first day of haloperidol injection the rats had a mean weight of 405 g (range 359-452 g) and were approximately 194 days old. The rats were run between 0730 and 0900 daily during the light portion (0715-1930) of the vivarium light-dark cycle.

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Apparatus

The four identical operant chambers used measured 28 × 26 × 29 cm (Gerbrands Model G7410). The side walls of each chamber were clear plastic and the front and back panels were aluminum; the floor consisted of steel grids. The recessed water dipper was centered on the front wall of the chamber 2 cm above the floor. The response lever was 9 cm from the floor immediately above the dipper. The dipper operated on the release of the lever (18–22 g was required to close the switch), providing 0.1 ml of water. The dipper remained available for 3 s. A clear 24-V dc lamp (CM 1819) located outside the chamber provided illumination. Each chamber was housed in a blower-ventilated, sound-attenuating enclosure (Gerbrands Model 7210). The chambers were controlled and data were collected by a Model Z-159 Zenith computer. Response duration was measured to the nearest 0.02 s.

Procedure

All rats self-trained (dipper available for 6 s) to a criterion of 60 reinforcers on a continuous reinforcement schedule (CRF). After an additional CRF session of 50 reinforcers (3-s access to the dipper), the rats began daily 15-min sessions on a FR 15 schedule which continued throughout the experiment. Fifteen FR days preceded the first prewatering day. Three prewatering days were followed by three drug days, with two baseline recovery days following each treatment (both prewater and drug).

Prewatering treatment. On prewatering days, rats were given access to water in home cages for 5 min. They were then immediately placed in operant chambers at the usual time.

Haloperidol treatment. All injections were given IP 45 min prior to chamber placement. The dose was 0.1 mg/kg at a concentration of 0.48 mg/ml. Haloperidol (McNeil Laboratory, Inc., Fort Washington, PA) was prepared in a vehicle solution of warm lactic acid (0.002 M).

Parameter justification. Five minutes of prewatering was selected because pilot work indicated that this amount of prewatering would lead to approximately the same degree of response rate attenuation as the haloperidol dose selected. A 0.1-mg/kg dose of haloperidol was selected because it approximated the dosage in the Liao and Fowler (5) study that maximized the within-session effect on duration.

RESULTS

Mean response rate and duration were computed for each subject for each of the three 5-min intervals making up the 15-min session. Figures 1 and 2 show the mean rate and duration collapsed over days for the three time intervals for each treatment (baseline, drug, prewatering).

An attempt was made to make rate comparable for the drug and prewatering treatments. A 2 (Treatments) × 3 (Days) × 3 (Time) within-subjects analysis of variance (ANOVA) revealed nonsignificant treatment and day effects. There was a significant time effect, $F(2, 22) = 17.49$, $p < 0.001$. Since comparability was demonstrated, no further analyses were conducted on rate data.

A Treatment × Days × Time within-subjects analysis of variance was conducted on duration data in order to obtain the error terms preparatory to a series of planned orthogonal comparisons. Three baseline days were randomly selected from the six that immediately preceded each treatment, producing a 3 (Treatments) × 3 (Days) × 3 (Time Periods) × 12 (Subjects) design. Since duration is known to increase within session and across days following haloperidol treatment (2), comparisons involving time were T1 versus T2 + T3 and T2 versus T3. Comparisons involving days were D1 versus D2 + D3 and D2 versus D3. Comparisons involving treatment were baseline versus drug + watering and drug versus watering. Each two-way interaction answers six questions, each with 2 comparisons (12 comparisons). For example, the Treatment × Time interaction specifically answers whether the treatments differed at times 1, 2, and 3 (2 comparisons for each time) and whether a specific treatment differed over time (2 comparisons for each treatment). Thus, there were a total of 36 comparisons in the analysis of duration data. Twelve of the 36 comparisons were significant and are summarized in Table 1.

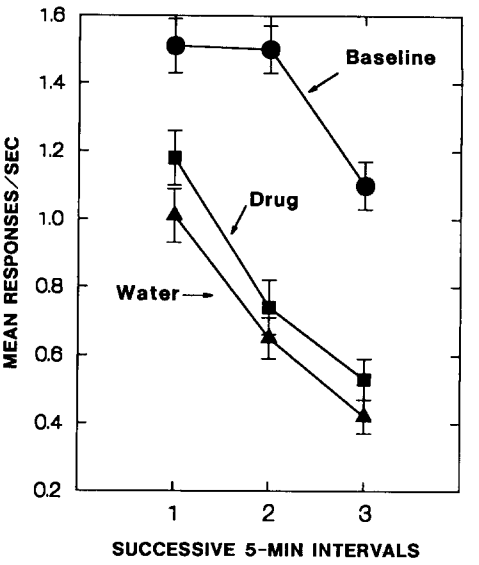

FIG. 1. Mean response rates of 12 rats collapsed over three days showing both treatment (baseline, prewatering, drug) and within-session (first, second, and third 5-min intervals) effects.

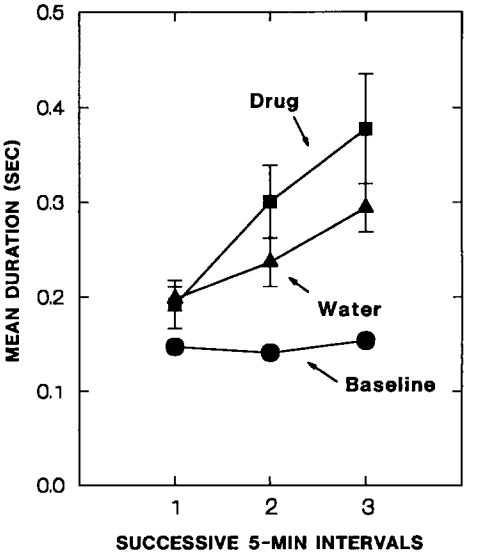

FIG. 2. Mean durations of 12 rats collapsed over three days showing both treatment (baseline, prewatering, drug) and within-session (first, second, and third 5-min intervals) effects.

TABLE 1

SUMMARY OF THE 12 SIGNIFICANT PLANNED COMPARISONS FROM TWO-WAY INTERACTIONS

	F	*p* Value
Treatment × Time		
1. Treatments differed at time 2		
Baseline < Drug + Water	11.96	<0.01
2. Treatments differed at time 3		
Baseline < Drug + Water	24.06	<0.001
3. Drug changed over time		
T1 < T2 + T3	15.76	<0.001
Treatment × Day		
1. Drug changed over days		
D1 < D2 + D3	13.48	<0.01
D2 < D3	5.84	<0.05
2. Water changed over days		
D2 > D3	5.84	<0.05
3. Treatments differed on day 1		
Baseline < Drug + Water	9.36	<0.01
4. Treatments differed on day 2		
Baseline < Drug + Water	28.23	<0.001
5. Treatments differed on day 3		
Baseline < Drug + Water	26.94	<0.001
Water < Drug	25.89	<0.001
Day × Time		
1. Times differed during day 2		
T1 < T2 + T3	9.17	<0.01
2. Times differed during day 3		
T1 < T2 + T3	6.46	<0.05

All *F*s have 1 and 44 degrees of freedom.

DISCUSSION

It is clear from Fig. 1 and the ANOVA on rate that prewatering reduced response rate in a manner very similar to that produced by haloperidol. The decrease in baseline rate during the last 5 min could reflect some combination of satiation and grooming effects. However, since no direct observations were made of the rats, exactly what the rats did is unknown.

For duration data, the planned comparisons provided several significant findings. First, consider the Treatment × Time interaction as shown in Table 1 and illustrated in Fig. 2. The treatments did not differ at T1. However, the drug + water conditions showed higher durations than baseline at both T2 and T3, but did not differ from each other. Further, neither baseline nor watering changed over time, but drug did when T1 was compared to T2 + T3.

The Treatment × Days interaction produced seven significant comparisons. Baseline did not change over days, but drug did, as was expected. That watering showed higher durations on day 2 than on day 3 is inexplicable. The two treatment groups differed from baseline on days 1, 2, and 3, but from each other only on day 3, with drug showing longer durations than watering on that day.

The Day × Time interaction produced only two significant comparisons (out of 12): On both days 2 and 3, T1 had durations significantly lower than T2 + T3.

Figure 2 and the planned comparisons provide a clear picture of the effects both drug and watering have on duration. Although the pattern shown by the drug and watering treatments are similar, only drug produced significant within-session increases. Since watering reduced rate even more than drug, this finding is not based on differences in rate. However, the two treatments did not differ significantly from each other at any of the three time levels. A further difference between drug and watering was found over days. Only drug produced systematic increases in duration over days. Taken together, these findings suggest that haloperidol's effect on duration has both an anhedonic (that part that can be duplicated by watering) and a motoric component (that part that is not duplicated by watering).

Although these results demonstrated within-session increases in duration, as did Liao and Fowler (5), several procedural differences in the two studies should be noted. Perhaps because Liao and Fowler used four different doses on each rat, three of their six rats stopped responding before the 30-min session was over for the 0.08 dose; all six stopped for the 0.16 dose. Therefore, for their analyses they took the total responses emitted and computed means for duration on the first, middle, and final thirds of the responses.

All 12 rats in the present study showed at least some responding during the final 5 min of the three 15-min drug sessions, and thus the analyses were based on the responses which occurred during the three consecutive 5-min periods. This procedural difference produced an accentuation of the within-session effect for duration in the Liao and Fowler study; however, they made no direct comparisons of drug with vehicle during the three separate intervals. Visual inspection suggests that the 0.08 dose produced durations which differed from vehicle only for the final third of the responses.

Further differences between the two studies included the FR requirement (20 vs. 15), session duration (30 vs. 15 min), and reinforcer (food vs. water). Given these differences, that the results of the two studies were so similar is a testimony to the robustness of the effect.

Whether these water versus drug results will generalize to other dosages (and consequently different amounts of prewatering) or other reinforcement schedules remains to be seen. In any event, it seems that increases in duration, even within-session ones, should not be taken as an unambiguous measure of motoric deficit.

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