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Use of Operant Response Duration to Distinguish the Effects of Haloperidol from Nonreward

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FAUSTMAN, W. O. AND S. C. FOWLER. *Use of operant response duration to distinguish the effects of haloperidol from nonreward.* PHARMAC. BIOCHEM. BEHAV. 15(2) 327–329, 1981.—Prior experimentation, making exclusive use of operant response rate, has offered conflicting evidence regarding the role of reinforcement and motor effects in neuroleptic-induced changes in operant responding. In the present work, response rate and response duration were recorded for 12 rats responding under a fixed-ratio 10 schedule of food reinforcement. On six consecutive days separate groups of animals were given haloperidol or saline-with-extinction. Although both drug treatment and extinction produced elevated durations compared to pre-treatment baseline, the haloperidol group exhibited response durations that were significantly higher than those of the no-drug-extinction group. In view of these results, and since prior work has shown that response duration provides information which is nonredundant with response rate, it is suggested that response duration may be a valuable tool in future work attempting to partial out the motivational and motor effects of neuroleptics on operant responding.

Extinction Haloperidol Rats Response duration

SEVERAL investigations have attributed the operant rate-reducing effects of neuroleptics (e.g., pimozide, haloperidol) to a decrement in the rewarding qualities of primary reinforcers [5, 6, 14] or, more recently, to decrements in the efficacy of secondary reinforcers [7]. Though there is increasing evidence for a role for dopamine in brain reward mechanisms (for review see [2]), several experiments point to the importance of motor effects in neuroleptics' reducing operant rates [3, 8, 10, 12]. One difficulty in sorting out the relative contribution of motor vis a vis reinforcement effects of neuroleptics lies in the fact that changes in response rate can be taken as measures of either motor effects or reinforcement effects depending on one's purposes. In order to circumvent this procedural dilemma, what is needed is a measure of operant behavior which provides information about motor or reinforcement effects that is separate from response rate. A candidate dependent variable for this purpose is average response duration (i.e., the amount of time a rat keeps the operant microswitch in the closed position, divided by the number of responses in a session—hereafter referred to simply as response duration; see [9]). Previous work has shown that response duration is influenced by extinction [9] and by various drugs [4] and that it provides behavioral information on drug effects not available from the rate measure alone [13]. Although response duration has not been thoroughly researched, it is presumed to reflect, at least in part, the motor features of individual responses [4]. In view of the foregoing, the purpose of the present methodological work was to examine response duration along with response rate in an experimental paradigm in which the effects of extinction are compared with the effects of a neuroleptic (haloperidol) on reinforced responding. This paradigm has been used frequently to test the hypothesis that neuroleptics have their behavioral effects primarily on reward processes [11].

METHOD

Animals

The animals were 12 male Sprague-Dawley rats (Holtzman Co.) with body weights averaging approximately 300 g. All animals were food deprived and maintained at 80% of their free feeding weight. Water was continuously available in the individual home cages.

Apparatus

The apparatus consisted of four simultaneously operative operant chambers. Each chamber measured 23 cm long, 20 cm wide, and 19 cm high and was fitted with stainless steel rods running parallel to the front of the chamber. The front panels were constructed of aluminum while the remaining sides were clear Plexiglas. The top of the manipulandum (Gerbrands Co., Rat Lever G6312) was 8 cm above the grid

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floor and was positioned in the center of the front panel, extending 1.5 cm beyond the panel wall. The lever was adjusted for a 20 G force requirement. The food hopper was located behind a rectangular opening (4.5×4.5 cm) in the lower left corner of the front panel. Reinforcers (Noyes Co., 45 mg standard rodent formula food pellets) were delivered by Ledex Co. and Gerbrands Co. food dispensers. Each operant chamber and pellet dispenser was enclosed in a ventilated, sound attenuating compartment.

Programming of contingencies and recording of data were accomplished with a laboratory computer (PDP 8/e) and associated peripherals. This system recorded the number of bar press responses and the amount of time the manipulandum microswitch was held in the closed position during each session. The latter was divided by the number of responses in a session to yield an average response duration.

Procedure

The animals were shaped by the method of successive approximations and were subsequently placed on a fixed-ratio 10 schedule of reinforcement with 10 minute sessions. Reinforcers were delivered upon bar release. If the reinforcer had been presented at the instant of lever depression, it seems likely that the solenoid noise would have become an S^D for the rat to terminate the response, thereby possibly relegating response duration to control by solenoid operation and limiting the extent to which this dependent variable would be free to vary. All animals were trained to stability (2–3 weeks), and, during the last 3 days of predrug baseline, all were injected (IP) with saline (0.9%, 1 ml/kg) 4 hours before data collection. Following baseline, the animals were assigned to 2 groups of 6 animals each. For 6 consecutive days one group of animals received saline (0.9%, 1 ml/kg IP) 4 hours before a session in which primary reinforcement was withheld (the magazine was still operative). During these same 6 days, the other group of animals received haloperidol (0.5 mg/kg free base, IP) 4 hours before a session in which FR 10 reinforcement was maintained. Haloperidol (Janssen) was mixed in a solution of methylparaben-propylparaben, lactic acid and sterile water prior to initiation of the experiment. The presently employed haloperidol dosing procedure has been satisfactorily used in a prior investigation [1].

RESULTS AND DISCUSSION

The results for both the rate and duration variable are plotted in Fig. 1. A two-way analysis of variance (drug vs extinction × six sessions) of the rate data generally confirmed the graphic impression in that there was a significant decline in responding over the six sessions, $F(5,50)=5.649$, $p<0.01$, with a significant condition-by-sessions interaction, $F(5,50)=6.222$, $p<0.01$. Even though the main effect of drug vs extinction was not significant, $F(1,10)=2.450$, $p>0.05$, the interaction effect suggests that changes in rate produced by haloperidol clearly differed from rate changes engendered by extinction over the course of six sessions. These data are in agreement with prior work [11] that demonstrated the nonequivalence of pimozide and extinction for fixed ratio trained rats. Thus, it appears that nonreward and neuroleptics show similar response patterns only when a continuous reinforcement schedule is employed (e.g., [14]).

For the duration data the analysis of variance revealed a significant difference between drug and extinction conditions, $F(1,10)=15.503$, $p<0.01$, a significant sessions effect, $F(5,50)=3.116$, $p<0.01$, but no interaction, $F(5,50)=1.683$, $p>0.05$. These data, therefore, show that the dose of haloperidol used here had much larger effects on response duration than did exposure to nonreward. The data in Fig. 1 show that on days 4, 5, and 6 there was an approximately equal degree of response rate suppression as a result of haloperidol and extinction. However, corresponding response duration levels for these response rates show a large difference, suggesting a difference in the characteristics of the lever response. This observation indicates that neuroleptics and extinction may produce operant rate reduction by means of differing mechanisms. The relatively greater durations seen for the reinforced drug group cannot be attributed to cumulative drug effects because response durations for the first day of haloperidol treatment were significantly higher than they were for the first extinction session, $t(10)=2.846$, $p<0.05$. Consistent with previous findings [9], nonreward per se did elevate duration over baseline values; mean durations for the three baseline days and for the six extinction sessions shown were, respectively, 0.466 sec and 0.541 sec, with all rats exhibiting such an increase, $t(5)=5.131$, $p<0.05$.

Insofar as response duration can be viewed as reflective of motor features of operant behavior, the current data suggest that haloperidol can have relatively pronounced motor effects that cannot be observed simply in terms of

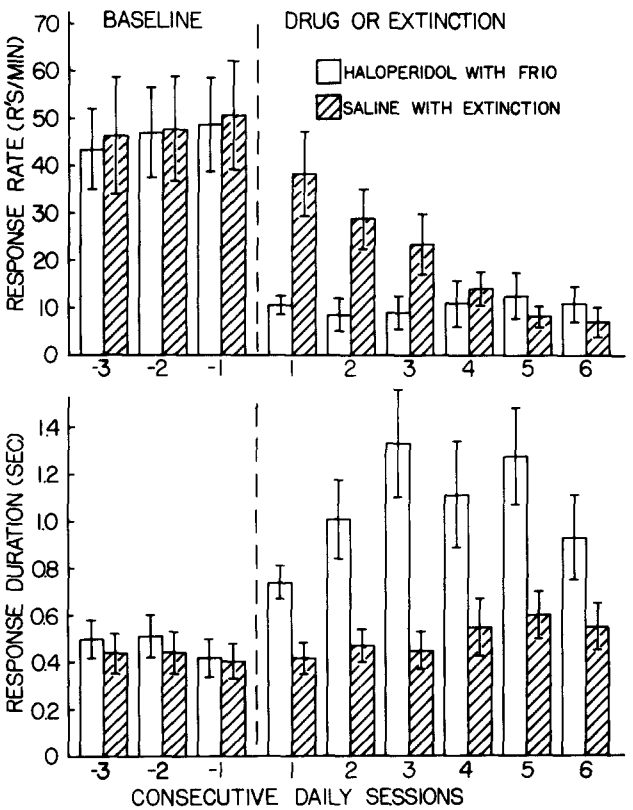

FIG. 1. Mean response rate (top) and mean response duration as a function of daily sessions for two separate groups of six rats each. The vertical bars represent ±1 SEM. During baseline both groups received saline injections and responded on a fixed ratio 10 schedule of food reinforcement. Over the next six consecutive days one group received saline injections and extinction, while the other received haloperidol (0.5 mg/kg, IP) and continuation of fixed ratio 10.

changes in response rate, and these motor effects at the dose used are not equivalent to those seen in extinction. Since rate and duration of response provide non-redundant information about behavior [13], experiments designed to determine the relative motor vis a vis putative anhedonic effects of neuroleptics could benefit from the inclusion of the response duration variable.

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