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Haloperidol and Nonreinforcement Produce Different Patterns of Response Slowing in a Food Reinforced Runway Task[1]

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WIRTSHAFTER, D. AND K. E. ASIN. *Haloperidol and nonreinforcement produce different patterns of response slowing in a food reinforced runway task.* PHARMACOL BIOCHEM BEHAV 22(5)661–663, 1985.—Rats were trained to traverse a runway for food reward and speeds were measured in the start, run and goal segments of the alley. After eight days of acquisition training, subjects were tested for four days under conditions of either extinction or haloperidol pretreatment. Although both haloperidol and extinction produced a suppression of the running response, the pattern of this suppression in the three alley segments was quite different for the two conditions. Haloperidol tended to be more effective than extinction in slowing start speeds but less effective than extinction in reducing run and goal speeds. This differential effect of haloperidol and extinction on speeds in different alley segments provides further evidence that haloperidol-induced impairments in performance cannot result entirely from a blunting of primary reinforcement.

Haloperidol Reinforcement Anhedonia Dopamine Extinction Neuroleptics

CONSIDERABLE recent interest has been focused on the view that dopaminergic mechanisms may be involved in mediating the reinforcing effects of natural rewards such as food and water. The original experimental support for this notion arose from the finding that injections of dopamine antagonists such as haloperidol or pimozide produce effects on positively reinforced responding which are at least superficially similar to those seen during extinction [13]. The earliest theory offered to account for these findings proposed that neuroleptics may block the effects of primary reinforcers, but more recent findings, such as the additive effects of nonreinforcement and neuroleptics in suppressing responding [5,7], have forced several modifications of the original theory [12]. None-the-less, the resemblance of the effects of neuroleptics and nonreward still remains as the most basic evidence supporting the "anhedonia theory" of the action of dopamine antagonists on operant behavior.

In the current study we attempted to compare, in more detail than has been done previously, the effects of haloperidol treatment and reward omission on behavior in a food reinforced straight alley task. The results of this study demonstrate the existence of certain qualitative differences between extinction and neuroleptic treatment, and support other evidence suggesting that the effects of neuroleptic drugs on operant behavior cannot be due soley to an interference with reward mechanisms.

METHOD

Animals

Subjects were 32 adult, male Sprague Dawley derived rats obtained from a colony maintained by the University of Illinois. At the beginning of the experiment rats weighed 330±30 g and were individually housed in wire mesh cages under a 12:12 hour light:dark cycle. Water was available ad lib.

Apparatus

The straight alley was constructed of clear Plexiglas except for the floor which was composed of 2 mm diameter metal rods spaced 10 mm apart. The alley was partitioned by metal guillotine doors to form a start box (16×11.5×10 cm), a runway (110×11.5×10 cm) and a goal box (30.3×15×10 cm). A small glass coaster was located in the rear of the goal box in which a single Froot Loop (Kellogs) was placed on reinforced trials. Photobeams were located 14 and 104 cm beyond the start box door and 20 cm past the goal box door. Opening of the start box door was detected by a microswitch. Digital circuitry allowed for measurements of start, run and goal latencies to the nearest one-hundredth of a second. For purposes of analysis, data were converted to reciprocal latencies (speeds).

Procedure

Rats were allowed access to food (Wayne Lab Blocks) for one hour per day. After eight days on this restricted feeding schedule rats were individually placed in the alley with all doors opened and allowed to explore it for five minutes. On the following two days rats were confined in the goal box until they had consumed a Froot Loop placed in the coaster. Rats were fed for one hour following removal from the alley. Acquisition training was begun on the following day. Each rat was placed in the start box facing away from the lowered guillotine door. Thirty seconds later the door was opened. After the animal left the start box the door was

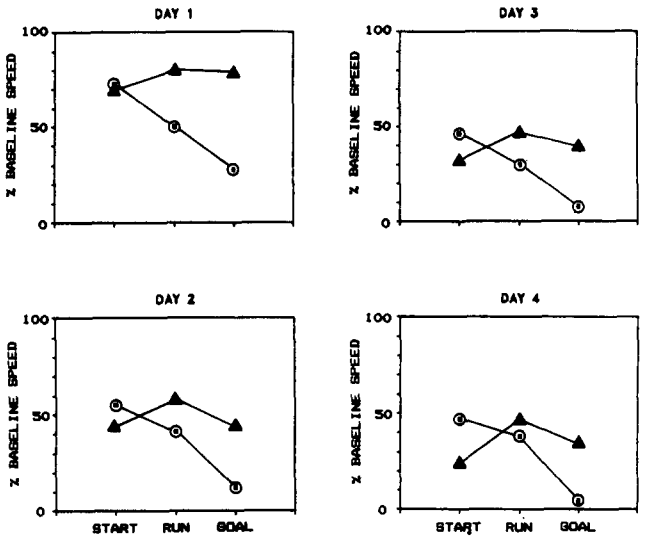

FIG. 1. Mean speeds, expressed as a percent of baseline, in the start, run, and goal segments of the alley across the four days of testing for rats receiving extinction (circles) or haloperidol (triangles) treatments.

lowered to prevent retracing. After the animal entered the goal box, the door to that compartment was lowered and the rat was confined to the goal box until the reward was consumed. The subjects was then replaced into the start box and 30 sec later the door was opened, initiating another trial. On the first two days of acquisition training rats were given three such trials per day, and six trials per day were given for the next 6 days.

Following the 42 trials of acquisition training, by which time stable baselines had been achieved, rats were divided into three groups matched as closely as possible on speeds in each of the three alley segments. Eleven subjects were assigned to the extinction group, ten to the low dose haloperidol group and eleven to the high dose haloperidol group. For the next four days subjects in the extinction group received six extinction trials per day. Extinction trials were identical to those described above except that no food was present and rats were confined to the goal box for 15 sec before replacement into the start box. Subjects in the haloperidol groups were injected IP with haloperidol (Haldol) at a dose of either 0.10 or 0.15 mg/kg. Forty-five minutes following drug treatment these animals were each given six reinforced trials identical to those in the acquisition phase of the experiment. As with the extinction group, animals were tested under haloperidol for four days.

RESULTS

In order to allow comparison of the effects of nonreinforcement and extinction in different segments of the alley, data for the test phase of the experiment were converted into percents of baseline speeds on the last day of acquisition. Preliminary analysis indicated that the effects of treatment with the low or high doses of haloperidol did not differ ($p>0.4$), therefore data for these two groups were combined.

The results of this experiment are shown in Fig. 1 which displays start, run and goal speeds, as percents of baseline, across the four days of extinction or drug testing. The data were analyzed using a 2×4×3 (drug/extinction × days × alley segment) repeated measures analysis of variance using the unweighed means solution for unequal numbers of subjects. The analysis indicated a highly significant effect of days, $F(3,90)=30$, $p<0.001$, and a highly significant drug × position interaction, $F(2,60)=24.64$, $p<0.001$. The drug × days × position interaction failed to approach significance, $F<1$. Examination of Fig. 1 shows that the drug × position interaction resulted from the fact that haloperidol and extinction produced very different patterns of slowing across the three alley segments. These data were analyzed further using a simple main effects analysis. Since the degrees of freedom for the relevant mean squares both exceeded 30, critical values for the resulting t statistic were taken from a table of the normal distribution, as suggested by Winer [11]. This analysis indicated that, for extinction animals, speeds were significantly more suppressed in the run than the start segment ($t=3.04$, $p<0.01$), and significantly more suppressed in the goal than the run segment ($t=5.42$, $p<0.001$). In contrast, haloperidol treated rats were significantly more suppressed in the start than in the run segment ($t=3.16$, $p<0.01$), whereas other comparisons did not reach significance. Examination of Fig. 1 also indicates that while haloperidol tended to be more effective than extinction in suppressing start speeds, it was less effective in reducing goal and run speeds.

DISCUSSION

The results of the current experiment indicate the existence of qualitative differences in the effects of haloperidol and extinction on behavior in a food reinforced straight alley task. Omission of the reinforcer resulted in a slowing of speeds, relative to baseline, which was maximal in the goal segment, less pronounced in the run segment, and still less marked in the start segment. This pattern of results probably reflects the fact that the primary defining event of extinction, i.e., the nonoccurrence of an expected reward, occurs in the goal box itself and affects behavior in earlier segments of the alley only through indirect mechanisms, such as stimulus generalization. In marked contrast, haloperidol tended to exert its greatest effect on start speeds, while suppression of run and goal speeds did not differ significantly from each other. These results are compatable with those of Mogenson [8] who found that injections of low doses of spiroperidol into the nucleus accumbens reduced start but not run speeds. One possible interpretation of these findings is that the suppression of the alley habit by haloperidol does not result from an event occurring in the goal box, such as a blunting of the reinforcing effects of the food. It is also possible that haloperidol exerts effects, in addition to a blockage of primary reinforcement, which might distort the pattern of declines in speed until it no longer resembles that seen in extinction. For example, haloperidol might both attenuate reinforcement, slowing run and goal speeds, and produce an impairment in the ability to initiate movements, accounting for the large effect on start speeds. A number of workers, based on different types of evidence, have indeed suggested that neuroleptic treatment may act both to blunt reinforcement and to alter other behavioral mechanisms such as "motor capacity" [3], "general arousal" [2], or "willingness to exert effort" [9].

Consistant with the current findings, several other studies which have made a detailed comparison of extinction and other neuroleptic treatment have also found that the effects

of these two types of manipulations differ in a number of ways. For example, extinction and neuroleptic treatment result in different patterns of changes in response duration in a food reinforced operant task [4], and lead to very different patterns of responding in a chronic self-stimulation paradigm [6]. Additionally, extinction and neuroleptic-induced "pseudoextinction" are differentially affected by a number of experimental manipulations including partial reinforcement [5,10] and prior response force requirements [1]. These findings, together with others [5,7], suggest that the "simple anhedonia theory," i.e., the notion that at low doses neuroleptics act only to blunt primary reinforcement, cannot be correct. It is possible that, with sufficient ingenuity, the current results could in some way be accounted for by the "extended verison of the anhedonia theory," [12] which suggests that neuroleptics act both to block primary reinforcement and to reduce incentive motivation, but our findings certainly could not be construed as providing direct support for this viewpoint.

The results of the current study indicate that whereas both haloperidol and reinforcer omission lead to decrements in performance which increase over successive trials, the pattern of decrements produced by these two treatments is considerably different. These findings suggest that further examination of the nature of the effects of neuroleptics on speeds in different alley segments may provide a useful tool for studies attempting to clarify the role of dopaminergic mechanisms in operant behavior.

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