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BRIEF COMMUNICATION

Evidence for Dopamine Involvement in Reinforcement Obtained Using a Latent Extinction Paradigm

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ASIN, K. E. AND D. WIRTSHAFTER. *Evidence for dopamine involvement in reinforcement obtained using a latent extinction paradigm.* PHARMACOL BIOCHEM BEHAV **36**(2) 417–420, 1990.—The current experiment utilized a modified latent extinction method to examine the question of whether neuroleptic treatment blunts the reinforcing properties of food. Deprived rats were trained to traverse a runway for food reward and were then injected with haloperidol and given ten reinforced direct placements either into the goal box of the alley or into a novel cage with food present. The animals, while still under the influence of the haloperidol, were then given six standard trials of running down the alley. Animals who received goal box placements showed slower run speeds during the test trials than did the subjects who received placements into a neutral cage. These results suggest that placing the haloperidol treated rats into the baited goalbox resulted in a reduced expectation of reward and are compatible with the "anhedonia" theory of neuroleptic action.

Reinforcement Anhedonia Dopamine Neuroleptics Latent extinction

THE nature of the neurochemical basis of reinforcement is one of the most debated topics in behavioral neuroscience. One major hypothesis regarding reward mechanisms is the "anhedonia" theory proposed by Wise (15–18). The basic tenent of current versions of this theory is that the dopaminergic system is involved in the behavioral effects of both primary and secondary reinforcement. The primary evidence which has been taken to support this claim is the fact that, under a number of experimental conditions, neuroleptic treatment results in a gradual decrement in response output resembling that seen in extinction. Other investigators, however, have cogently argued that the response decline seen after neuroleptic treatment represents an interaction with motoric systems which interferes with ongoing behavior [e.g., (3, 9, 13)]. These two possibilities have proven difficult to untangle experimentally since, in many behavioral paradigms, certain types of drug-induced motor impairments could lead to behavioral effects similar to those which would be expected to occur after interference with reward mechanisms. For example, dopamine receptor blockade might cause motor responses to become aversive or more difficult than normal (9). This aversiveness or difficulty might then become conditioned to responses made under the influence of neuroleptics with the result that the subject might gradually come to withhold such responses. This type of notion, of course, bears a certain similarity to the Hullian concept of reactive inhibition (7).

Thus, whereas the reinforcement theorist would suggest that gradual decrements in response output under neuroleptic treatment reflect an extinction of reward expectation, the motor theorist would propose that they reflect merely the animal's repeated experience with responding under the influence of the drug. In order to distinguish between these possibilities it would be useful to determine whether mere exposure to reinforcement under neuroleptic treatment is sufficient to produce a decrement in later performance, or whether the actual instrumental response must be made under the influence of the drug for the decrement to occur.

In the current studies we attempted to investigate this question using a modification of the latent extinction paradigm. In the classic latent extinction study animals are trained to traverse a runway for food reward. The experimental animals are then given a number of placements directly into the goal box without food present. Rats are then allowed to run down the alley under conditions of conventional extinction. Compared to control animals, who have received placements into an unbaited neutral box, the experimental subjects display a facilitation of extinction. This

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effect is generally believed to represent the extinction of reward anticipation or expectancy as a result of experience with the empty goal box (8, 10, 11). Historically, latent extinction studies played an important role in the demise of Hull's reactive inhibition theory of extinction (4).

In the present study we reasoned that if neuroleptic pretreatment blunts the effect of reward, placing a haloperidol-treated animal in a baited goal box might be analogous to placing an undrugged animal into an unbaited goal box. In both cases the direct goal box placements should lead to a reduced expectancy of reward. Were this the case it should be possible to demonstrate an effect analogous to latent extinction in neuroleptic treated rats. Since no response other than eating would be required of the drugged rats during the goal box placements, it is unlikely that any subsequent effects of these placements would reflect motor difficulties.

In the current experiments, we first demonstrated the phenomenon of conventional latent extinction and then examined the effects of haloperidol using a modification of this paradigm. The results of these studies support dopaminergic involvement in reinforcement. A preliminary version of the present report was presented at the 1986 meeting of the Society for Neuroscience (1).

METHOD

Subjects

Subjects were 27 adult male Sprague-Dawley derived rats weighing about 350 g at the start of the study.

Apparatus

The straight alley was constructed of clear Plexiglas except for the floor which was constructed of metal rods 2 mm in diameter spaced 10 mm apart. The start box ($16 \times 11.5 \times 10$ cm) and the goal box ($30.3 \times 15 \times 10$ cm) could be isolated from the remainder of the alley ($110 \times 15 \times 10$ cm) by metal guillotine doors. The sides and top of the goal box were covered with diagonal strips of black electrical tape 0.75 inches in diameter and separated from each other by the same distance. [Latent extinction can be demonstrated more easily when the goal box is clearly distinct from the remainder of the alley (8).] Latencies were evaluated by means of two photocells situated 15 and 105 cm from the start box. Opening the door of the start box started a timer which ran until the first photobeam had been broken. Interruption of this beam in turn started another timer which ran until the second photobeam had been broken.

Preliminary Training

All subjects were placed on a one hour per day feeding schedule. After eight days of restricted feeding, each rat was individually placed in the alley with all doors open, and allowed to explore it for 5 min. On the following two days, rats were placed in the goal box and confined there until they had consumed a Froot Loop (Kellogg's). Acquisition training began the following day. An animal was placed in the start box facing away from the lowered partition, which was raised when the animal oriented towards it. After entrance into the goal box, the door to it was closed to prevent retracing. Following consumption of the reward, the animal was replaced in the start box and one minute later the door to that compartment was again opened initiating another trial. Rats were given six acquisition trials per day for 10 days, their daily ration of food being given to them at the end of their training sessions.

Latent Extinction

Twelve rats were used to study conventional latent extinction. Following preliminary training, subjects were divided into experimental and control groups matched on start and run speeds on the last day of training. On the following day, experimental subjects received 10, 30-sec placements into the unbaited goal box of the alley. Placements were separated from each other by one minute, during which the rat was placed in its home cage. Control subjects received 10 similar placements into an empty plastic cage. One minute after their last placement, all subjects received 6 extinction trials in the alley. Extinction trials were conducted in the same fashion as acquisition trials except that the goal box was unbaited. Subjects were restrained in the goal box for 30 sec after entry, and any animal failing to enter the goal box within 2 min of the start of a trial was placed there and assigned a run latency of 120 sec.

Modified Latent Extinction

Fifteen animals were used to study the effects of haloperidol. Following preliminary training, they were divided into two groups matched on start and run speeds. The following day subjects received injections of 0.15 mg/kg of haloperidol (SC). This dose was chosen based on previous studies which indicated that it produced a clear suppression of run speeds (14). Thirty min later experimental subjects ($n = 8$) were placed in the baited goal box ten times and restrained there until a single Froot Loop had been eaten. Placements were separated from each other by one min. Control animals were given 10 placements into a novel plastic cage and, in like fashion, were restrained there until a single Froot Loop had been eaten. All subjects then received six trials in the alley with reinforcement present.

RESULTS

Conventional Latent Extinction

Data were analyzed by a $2 \times 2 \times 6$ (group $\times$ alley segment $\times$ trial) multivariate profile analysis of variance, with repeated measures on the trial factor. The MANOVA indicated that for start speeds there were no significant group ($F<1$) or trial, $F(5,5) = 2.123$, $p<0.214$, effects and no significant interaction term ($F<1$). Seward and Levy (11), using a similar paradigm, also failed to obtain differences in start speeds between groups. With regard to run speeds, the MANOVA indicated a significant group effect, $F(1,9) = 7.596$, $p<0.022$, and a significant trials effect, $F(5,5) = 7.095$, $p<0.03$; the group $\times$ trials interaction did not approach significance, $F(5,5) = 1.403$, $p<0.37$. As may be seen in Fig. 1, rats which had been placed in the nonrewarded goal box of the alley showed slower run speeds across the extinction trials then did the animals placed in a nonrewarded neutral box.

Modified Latent Extinction

Start and run speeds across the six "haloperidol latent extinction" trials were analyzed using a $2 \times 2 \times 6$ MANOVA, as described above. With regard to start speeds, neither the group, $F(1,12) = 3.164$, $p<0.101$, nor group $\times$ trial interaction, $F(5,8) = 2.225$, $p<0.150$, term was significant. A significant trial effect was obtained, $F(5,8) = 7.287$, $p<0.008$, indicating that start speeds declined similarly for both groups across trials. Analysis of run speeds indicated significant group, $F(1,12) = 4.848$, $p<0.048$, and trial effects, $F(5,8) = 3.990$, $p<0.041$, but no significant group $\times$ trials interaction ($F<1$). Group mean running speeds are shown in Fig. 2. It can be seen that, following haloperidol treatment, the animals given direct goal box placements showed slower alley running speeds than did animals given placements into a neutral box.

DISCUSSION

The first experiment of the present study demonstrated robust

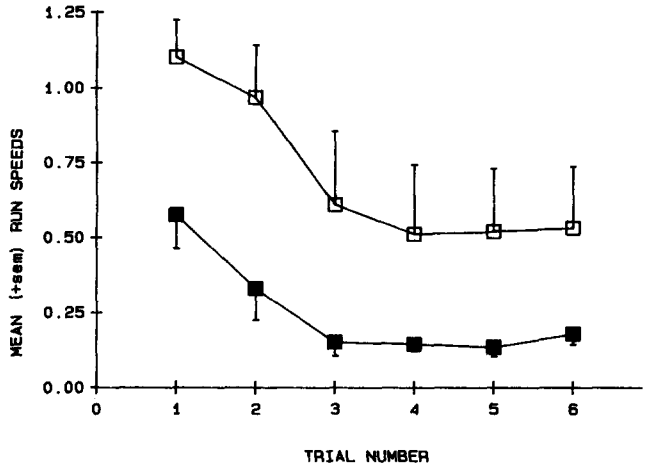

FIG. 1. Run speeds across the six extinction trials for control subjects (open symbols) and animals receiving direct goal box placements. Vertical lines indicate S.E.M.'s.

latent extinction. Animals were first trained to run down an alley for food reward after which they were given 10 placements directly into either the unbaited goal box or a neutral box. On the test day, rats given the goal box placements showed significantly slower run speeds during extinction then did control rats. In the next experiment we examined neuroleptic-induced "pseudoextinction" using a similar paradigm. As in the first experiment, rats were trained to run down a straight alley for food reward. On the test day, all of the animals were treated with haloperidol. Thirty minutes later, half of the animals were given 10 placements in the baited goal box and half were placed in a novel box, also with reinforcement present. Following these placements, rats were allowed to run the alley for food reward. It was reasoned that if dopamine receptor blockade impairs reinforcement mechanisms, then haloperidol-treated animals placed directly into the goal box should subsequently show evidence for "latent pseudoextinction" when allowed to traverse the alley, since the animals would have had an opportunity to learn that the food in the goal box was less reinforcing then it had been previously. On the other hand, if haloperidol's depression of run speeds was entirely due to interference with motor systems, the two drugged groups should show similar run speeds since the previous motor output of the two groups (i.e., eating) was similar. Our results support the hypothesis that haloperidol reduces the rewarding value of the food, as evidenced by the greater reduction in running speeds shown by the injected animals given pretest goal box placements.

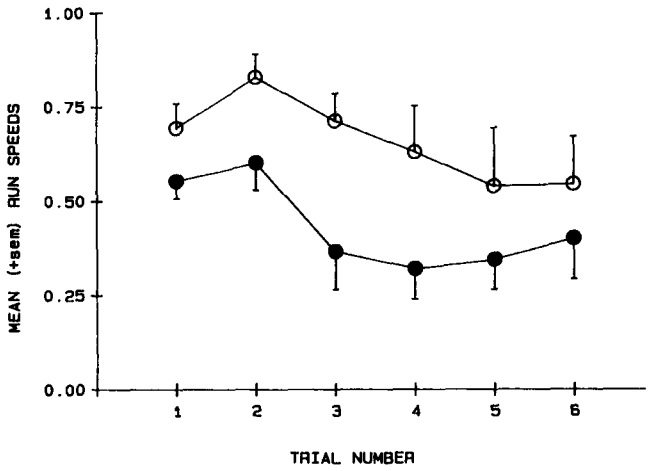

FIG. 2. Run speeds across the six haloperidol trials for control animals (open symbols) and subjects receiving direct goal box placements. Vertical lines indicate S.E.M.'s.

It is unlikely that the reduction in run speeds shown by rats placed directly into the goal box reflects an aversion to a place associated with an unpleasant state produced by haloperidol, since it has been demonstrated that injections of haloperidol fail to produce a conditioned place aversion (12).

Our current findings are in agreement with several other studies which have demonstrated neuroleptic-induced effects which are not easily explained on the basis of motor impairments. For example, it has been reported (12) that haloperidol treatment blocks the formation of a conditioned place preference to an environment paired with food, and other workers have found that neuroleptic treatment attenuates the ability of stimuli paired with food delivery to serve as secondary reinforcers (2,5). Additionally, pimozide has been found to block the response reinstating ("priming") effects produced by a reinforced trial in animals previously subjected to extinction (6). It is important to note that, in contrast to these studies, the current findings cannot be explained by drug-induced impairments in associational mechanisms. All of these results suggest that the effects of neuroleptics on behavior cannot result entirely from motor impairments and are compatible with the notion that blockade of dopamine receptors may blunt the reinforcing capacity of environmental stimuli. This conclusion is supported by the fact that, under certain experimental conditions, neuroleptic-induced reductions in response output do not seem to interact with the motor demands of the task being studied (1). It should be stressed that the present study does not provide evidence that neuroleptics affect only reinforcement mechanisms; indeed, certain evidence suggests that this is not the case [e.g., (14)]. It should also be stressed that acceptance of the view that blockade of dopamine receptors blunts reinforcement by no means entails acceptance of the far stronger position that release of dopamine is involved in the effectiveness of natural reinforcing stimuli. It is possible, for example, that the role of dopamine in reinforcement may be permissive rather that causal. Further studies will be necessary to investigate these questions.

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