Pharmacology Biochemistry & Behavior, Vol. 26, pp. 241–246. Copyright © Pergamon Journals Ltd., 1987. Printed in the U.S.A. 0091-3057/87 $3.00 + .00

Facilitation of the Expression But Not the Acquisition of Latent Inhibition by Haloperidol in Rats

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Received 15 September 1986

WEINER, I., J. FELDON AND Y. KATZ. *Facilitation of the expression but not the acquisition of latent inhibition by haloperidol in rats.* PHARMACOL BIOCHEM BEHAV **26**(2) 241–246, 1987.—In the latent inhibition (LI) paradigm, nonreinforced preexposure to a stimulus retards subsequent conditioning to that stimulus. The administration of haloperidol in both the preexposure and the conditioning stages was found to enhance LI in the conditioned emotional response (CER) procedure (Weiner and Feldon, 1986). The present experiments investigated the effects of 0.1 mg/kg haloperidol administration on LI in a two-way avoidance procedure, consisting of two stages: preexposure, in which the to-be-conditioned stimulus, tone, was repeatedly presented without reinforcement; and conditioning, in which the animals acquired a two-way avoidance response with the tone serving as the warning signal. Experiments 1 and 2 tested whether the administration of haloperidol confined to the preexposure stage, where learning to ignore the nonreinforced stimulus takes place, would suffice to enhance the LI effect. In Experiment 1, preexposure and conditioning were conducted 24 hr apart. LI was obtained in both the placebo and haloperidol conditions, but the effect was not more pronounced under the drug. In addition, haloperidol-treated animals exhibited impaired avoidance performance. In Experiment 2, preexposure and conditioning were given 72 hr apart. With this interval, haloperidol did not affect avoidance performance. However, also under these conditions, the magnitude of the LI effect was not larger in the haloperidol-treated groups, indicating that the administration of the drug in the preexposure stage alone did not suffice to enhance LI. In Experiment 3, haloperidol was administered in both the preexposure and the conditioning stages, given 24 hr apart. In addition, animals were re-tested in avoidance 24 hr later without the drug. Haloperidol-treated animals showed poorer avoidance performance in both the initial conditioning and the re-test. However, in both tests, haloperidol groups showed a significantly larger LI effect than placebo controls. The implications of these findings for the effects of haloperidol on LI and learning are discussed.

Haloperidol Latent inhibition Two-way active avoidance Rat

THE two most emphasized behavioral actions of neuroleptics are motor impairment (blockade of response initiation and/or maintenance) and a reduction of the rewarding value of primary reinforcers. However, in spite of the extensive research directed towards differentiating between these two effects of the neuroleptic drugs, their mechanism of action has remained a matter of debate (e.g., [3, 4, 6–8, 10–14, 27, 33, 35, 38, 43, 44].

In two recent experiments, we tested the effects of haloperidol on the development of latent inhibition (LI) in a conditioned emotional response (CER) procedure [40]. In the LI paradigm, nonreinforced preexposure to a stimulus retards subsequent conditioning to that stimulus when it is paired with a reinforcer [17]. For example, if an animal is preexposed to a series of tones, these tones lose their capability to enter into associations with other stimuli, such as shock, or responses such as shuttle avoidance. The choice of the LI paradigm was prompted by two reasons. First, the LI paradigm is uniquely suited for elucidating drug action unconfounded with motivational effects. Nonreinforced preexposure reduces the attention value, or the associability, of the to-be-conditioned stimulus without altering its associative strength, i.e., without endowing it with either inhibitory or excitatory effects [21, 28, 29, 31, 39]. This decremental process is considered to reflect a process of learning not to attend to, ignore, or tune out irrelevant stimuli [18, 20–23]. Thus, the LI phenomenon provides an instance of learning which is devoid of a motivational component, since it is learning in the absence of any reinforcement. Consequently, the use of LI allows determining the effect of neuroleptics on learning that does not involve reinforcement, and thus is not susceptible to these drugs' action of primary reinforcement blockade. In addition, since the control (nonpreexposed) group in the LI paradigm involves regular conditioning, it is possible, within a single experimental design, to assess the drug effects on learning involving reinforcement. Second, we have shown that LI is disrupted by 1.5 mg/kg dl-amphetamine [41,42]. Since amphetamine in relatively low doses seems to exert behavioral effects opposite to those of neuroleptics, i.e., it increases motor activity [15] and enhances the rewarding properties of reinforcement (e.g., [9,34]), it was of interest to test whether haloperidol would act on LI in an opposite manner to that of amphetamine.

Indeed, our experiments [40] showed that haloperidol facilitated the development of LI. Moreover, this enhancement was obtained both under conditions which gave rise to

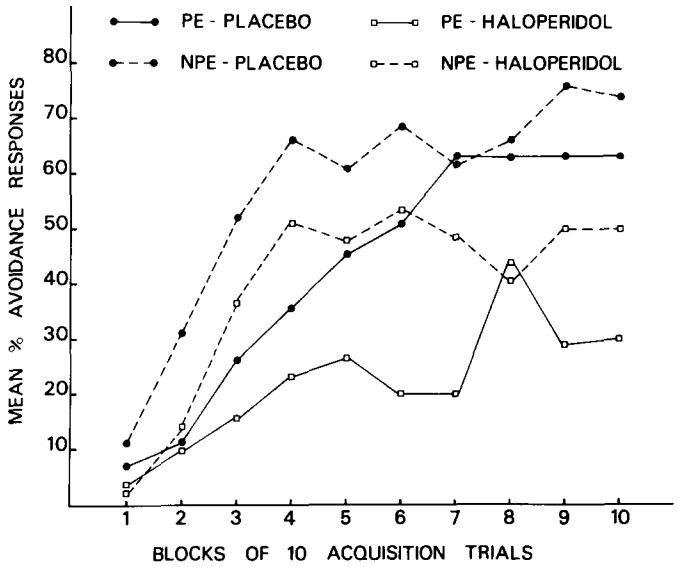

FIG. 1. Mean percent of avoidance responses over 10 blocks of 10 trials of the preexposed and nonpreexposed groups in two drug conditions: Placebo and Haloperidol (0.1 mg/kg). Avoidance conditioning was given 24 hr after preexposure. Drugs were administered in preexposure only.

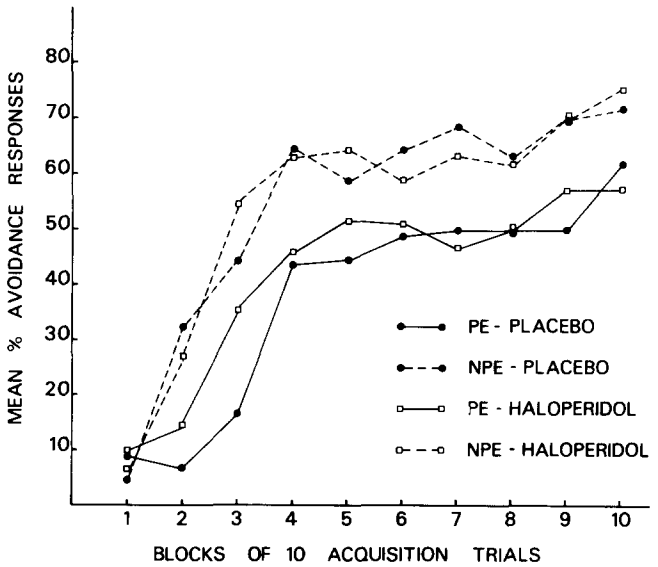

FIG. 2. Mean percent of avoidance responses over 10 blocks of 10 trials of the preexposed and nonpreexposed groups in two drug conditions: Placebo and Haloperidol. Avoidance conditioning was given 72 hr after preexposure. Drugs were administered in preexposure only.

LI in normal animals, i.e, following 40 nonreinforced CS preexposures, and under conditions in which normal animals failed to develop LI, i.e., following 10 CS preexposures. These results suggested that haloperidol enhanced the ability of animals to learn to ignore an irrelevant stimulus. The present experiments were designed to test this suggestion by determining whether the administration of haloperidol confined to the nonreinforced preexposure stage, where learning to ignore the irrelevant stimulus takes place, would suffice to facilitate LI. In addition, we sought to demonstate haloperidol-produced enhancement of LI using a different test, namely, two-way active avoidance. In our previous experiments we used an off-base-line CER procedure in which animals were not required to perform an overt response in either the preexposure or the conditioning stage, in order to minimize any possible motor effects of haloperidol. The use of two-way avoidance was aimed at testing whether the facilitatory effect of haloperidol on LI would also be evident in a procedure that involves motor responding and which is known to be disrupted by neuroleptics [8, 9, 13].

EXPERIMENT 1

METHOD

Subjects

Thirty-six male Long Evans rats (bred in the animal colony of the Psychology department, Tel-Aviv University, Israel), approximately 4 months old, were used. They were housed one to a cage under reversed cycle lighting for the duration of the experiment.

Apparatus

The two-way active avoidance apparatus consisted of three identical Campden Instruments shuttle boxes, measuring 48.5×23×20 cm. The barrier between the two compartments of the box consisted of an aluminum wall, with a central inverted U-shaped gate (10×7 cm). Each box was set in a ventilated, sound-insulated chest. The preexposed to-be-conditioned stimulus was a 5-sec, 2.8 kHz tone produced by a Sonalert module (Model SC 628). Shock was supplied to the grid floor by a Campden Instruments scrambled shock generator (Model 521C) set at 1 mA intensity. A Rockwell AIM 65 microprocessor was used for equipment programming and data recording.

Procedure

The LI procedure consisted of two stages: preexposure and avoidance conditioning test.

Preexposure

Each animal was placed in the shuttle box with the house lights on and received 50, 5-sec tone presentations on a variable interval (VI) 60 sec schedule, ranging from 20 to 100 sec. The nonpreexposed (NPE) animals were confined to the shuttle box for an identical period of time, but did not receive the tones. At the end of the preexposure session, animals were returned to their home cages.

Test

Twenty-four hr after preexposure, each animal was placed in the shuttle box with the house lights on and received 100 avoidance trials, presented on a VI 60-sec schedule ranging from 30 to 90 sec. Each avoidance trial started with a 5-sec tone followed by a 30-sec shock, the tone remaining on with the shock. If the animals crossed the barrier to the opposite compartment during the 5-sec tone, the tone was terminated and no shock was delivered. A crossing

response during shock terminated the tone and the shock. If the animal failed to cross during the entire tone-shock trial, the tone and the shock terminated automatically after 35 sec.

The latencies of the avoidance/escape responses were recorded. The 100 trials were divided into 10 blocks of 10 trials, and all analyses were carried out on the percentage of avoidances in each of the ten 10-trial blocks, with blocks as a repeated measurements factor.

The animals were randomly assigned to 4 experimental groups in a 2×2 design, consisting of preexposure-no preexposure and drug-no drug in preexposure. The appropriate drug treatment, either 0.1 mg/kg haloperidol dissolved in 1 ml of isotonic saline or an equivalent volume of saline, was administered IP 45 min prior to the start of preexposure. Avoidance conditioning was conducted without drugs.

RESULTS

Figure 1 presents the mean percent of avoidance responses over 10 blocks of 10 trials for the preexposed and nonpreexposed animals in the Haloperidol and Placebo conditions. The data were analyzed by a 2×2×10 ANOVA, with main factors of preexposure and drug condition and a repeated measurements factor of blocks. As can be seen in Fig. 1, the administration of haloperidol 24 hr prior to avoidance conditioning, led to poorer avoidance performance in both the preexposed and the nonpreexposed animals. This was supported by a significant main effect of Drug, $F(1,32)=5.10$, $p<0.03$, a significant Drug × Blocks interaction, $F(9,288)=1.99$, $p=0.04$, and the significant linear component of this interaction, $F(1,32)=6.78$, $p<0.02$. In addition, the LI effect, i.e., poorer acquisition of avoidance responding in the preexposed as compared to the nonpreexposed groups, was evident in both the Placebo and Haloperidol conditions. This was supported by a significant main effect of Preexposure, $F(1,32)=4.10$, $p<0.05$, and a significant Preexposure × Blocks interaction, $F(9,288)=2.02$, $p<0.04$. However, there was no indication in the ANOVA, or in the trend analysis, of a Preexposure × Drug interaction. Thus, there was no evidence for a facilitatory effect of haloperidol on LI, when the administration of the drug was confined to the preexposure stage.

EXPERIMENT 2

This experiment tested whether the absence of a facilitatory effect of haloperidol on LI in Experiment 1 could be related to the drug-induced impairment of avoidance conditioning. Consequently, in Experiment 2, avoidance conditioning was conducted 72 hr after preexposure, in which haloperidol was administered.

METHOD

Experiment 2 was identical in all respects to Experiment 1, except that preexposure and conditioning were separated by 72 hr.

RESULTS

Figure 2 presents the mean percent of avoidance responses over 10 blocks of 10 trials for the preexposed and nonpreexposed animals in the Haloperidol and Placebo conditions. The data were analyzed by a 2×2×10 ANOVA, with main factors of preexposure and drug condition and a repeated measurements factor of blocks. As can be seen in Fig. 2, 72 hr following haloperidol administration, there was no trace of haloperidol-produced interference of avoidance. LI was obtained in both the Placebo and Haloperidol conditions, but again, there were no appreciable differences between the magnitude of the effect in the two drug conditions. This was supported by a 2×2×10 ANOVA with main factors of preexposure and drug condition and a repeated measurements factor of blocks, which yielded only a significant main effect of Preexposure, $F(1,32)=4.12$, $p<0.05$.

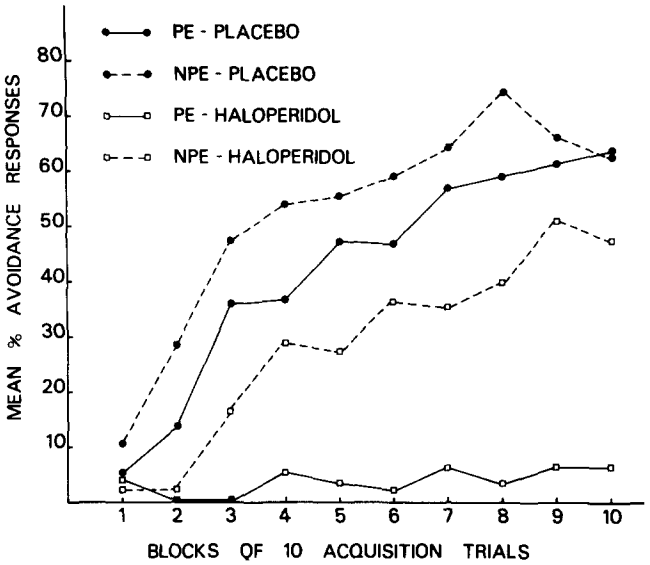

FIG. 3. Mean percent of avoidance responses over 10 blocks of 10 trials of the preexposed and nonpreexposed groups in two drug conditions: Placebo and Haloperidol. Avoidance conditioning was given 24 hr after preexposure. Drugs were administered in both the preexposure and conditioning stages.

EXPERIMENT 3

The results of Experiments 1 and 2 showed conclusively that when haloperidol was administered only in the preexposure stage, the LI effect was not enhanced. This result markedly contrasts with the dramatic facilitation of LI obtained in our CER experiments in which the drug was administered in both the preexposure and conditioning stages [40]. Consequently, such administration was used in Experiment 3 in order to determine whether the facilitatory effect of the drug depends on its presence throughout the LI procedure. In addition, 24 hr after conditioning, animals were re-tested in the absence of the drug.

METHOD

Subjects

Forty-four male Long Evans rats were used.

Apparatus

This was the same as in Experiment 1.

Procedure

The procedure was identical to that of Experiment 1, with two changes: (a) the drugs were administered 45 min prior to preexposure and 45 min prior to avoidance conditioning; (b) 24 hr following conditioning, all animals were re-tested in avoidance, without drugs.

RESULTS

Avoidance Conditioning

Figure 3 presents the mean percent of avoidance responses over 10 blocks for 10 trials of the preexposed and nonpreexposed animals in the Haloperidol and Placebo conditions. The data were analyzed by a 2×2×10 ANOVA, with main factors of preexposure and drug condition and a repeated measurements factor of blocks.

As can be seen in Fig. 3, haloperidol interfered with avoidance. This was supported by a significant main effect of Drug, $F(1,40)=16.97$, $p<0.001$, a significant Drug × Blocks interaction, $F(9,360)=4.60$, $p<0.001$, and a significant linear component of this interaction, $F(1,40)=9.47$, $p<0.005$. In addition, the existence of LI, i.e., poorer avoidance acquisition of the preexposed as compared to the nonpreexposed animals, was supported by the significant main effect of Preexposure, $F(1,40)=5.19$, $p<0.03$, a significant Preexposure × Blocks interaction, $F(9,360)=2.03$, $p<0.04$, and by the significant linear component of this interaction, $F(1,40)=4.83$, $p<0.04$. However, as can be seen in Fig. 3, when haloperidol was administered in both preexposure and conditioning, the difference between the preexposed and nonpreexposed groups, i.e., the magnitude of LI, was much larger in the Haloperidol than in the Placebo condition. This was supported by the significant Drug × Preexposure × Blocks interaction, $F(9,360)=2.83$, $p<0.004$, as well as by a significant linear component of this interaction, $F(1,40)=9.17$, $p<0.005$.

Re-Test

Figure 4 presents the mean percent of avoidance responses over 10 blocks of 10 trials of the preexposed and nonpreexposed animals in the Haloperidol and Placebo conditions. The data were analyzed by a 2×2×10 ANOVA, with main factors of preexposure and drug condition and a repeated measurements factor of blocks. The presence of LI in the re-test was supported by a signficant main effect of Preexposure, $F(1,40)=11.87$, $p<0.002$. Haloperidol-treated groups exhibited poorer avoidance performance in the re-test. This was supported by a significant main effect of Drug, $F(1,40)=8.86$, $p<0.005$, and a significant Drug × Blocks interaction, $F(9,360)=3.63$, $p<0.001$, as well as by the significant linear component of this interaction, $F(1,40)=7.06$, $p<0.02$. However, as can be seen in Fig. 4, the effect of haloperidol was mainly on the PE group, thereby again producing a larger LI effect. This was indicated by the interaction of Drug × PE which approached significance, $F(1,40)=2.99$, $p<0.10$. It should be noted that the mean number of avoidance responses out of 100 acquisition trials in the re-test for the 4 groups were: NPE-Sal—90; PE-Sal—78; Hal-NPE—81; Hal-PE—49.

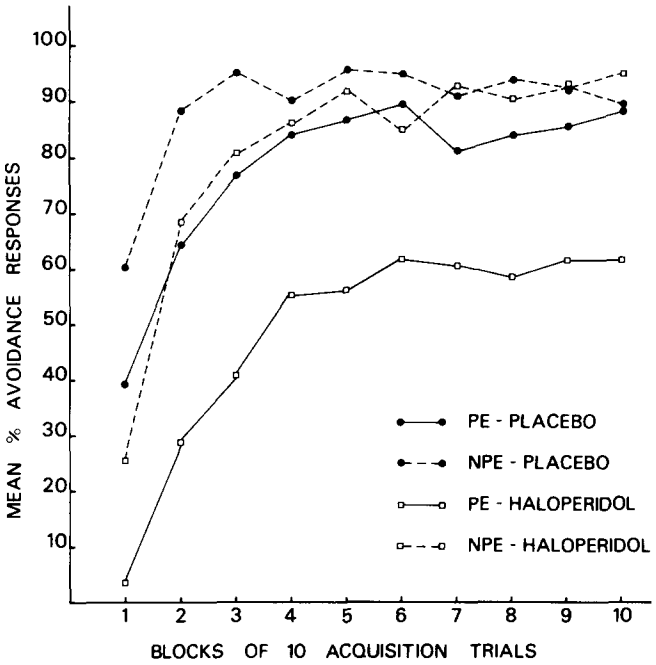

FIG. 4. Mean percent of avoidance responses over 10 blocks of 10 trials of the preexposed and nonpreexposed groups in two drug conditions: Placebo and Haloperidol, in avoidance retest. Re-test was given 24 hr after avoidance conditioning. No drugs were administered in re-test.

DISCUSSION

In line with previous reports on the disruptive effects of neuroleptics on avoidance (e.g. [8, 9, 13, 24]), haloperidol was found to impair two-way active avoidance. The impairment was evident 24 hr after drug administration but disappeared 72 hr later.

Latent inhibition, i.e., poorer avoidance acquisition of the preexposed (PE) as compared to the nonpreexposed (NPE) groups, was obtained in both the placebo- and haloperidol-treated animals. Moreover, the development of LI in haloperidol-treated animals was independent of the drug effects on avoidance performance. Thus, in Experiments 1 and 3, haloperidol impaired avoidance acquisition in *both* the nonpreexposed and the preexposed groups, but the impairment was much greater in the preexposed groups, resulting in the LI effect. Indeed, the present results demonstrate a dissociation between the effects of haloperidol on avoidance and on LI. In Experiment 2, when avoidance conditioning was conducted 72 hr following preexposure, avoidance performance of the NPE-haloperidol group did not differ from that of the NPE-placebo group, yet the PE-haloperidol group continued to exhibit impaired avoidance. Likewise, in Experiment 3, when animals were re-tested in the absence of the drug, avoidance performance of the NPE-haloperidol group was similar to that of the NPE-placebo, whereas the PE-haloperidol group still showed pronounced retardation.

Beninger *et al.* [8,9] showed that neuroleptics do not affect the formation of CS-US (shock) association and suggested that neuroleptic-induced deficits in avoidance are related to impairment of motor responding. The present results demonstrate that also the retardation of CS-US association, normally obtained following nonreinforced CS preexposure, is not affected, or is even enhanced, under haloperidol, and that this retardation persists also when the drug-induced impairment of avoidance is alleviated.

The administration of haloperidol in both the nonreinforced preexposure and conditioning (avoidance) stages enhanced the LI effect, replicating our previous results with the conditioned suppression procedure [40]. However, animals receiving the nonreinforced preexposure under haloperidol but conditioned without the drug, showed a normal, non-facilitated, LI effect. Thus, haloperidol-produced facilitation of LI is not due to enhanced learning to ignore irrelevant stimuli, which takes place in the nonreinforced preexposure stage. We suggested elsewhere [25,42] that the critical feature of LI is that the animal is exposed to two opposite environmental contingencies in the preexposure and the conditioning stages. In the former, the target stimulus is consistently followed by nonreinforcement; and, in the latter, the same stimulus is followed by reinforcement. The central point here is that, while during preexposure, the animal must learn that the stimulus signals no event of consequence and is, therfore, irrelevant, this acquired stimulus irrelevance must control the animal's behavior in conditioning, in spite of the fact that the stimulus comes to signal a significant outcome, reinforcement. The finding that haloperidol does not enhance LI when given only in preexposure, but facilitates the LI effect when administered in both the preexposure and conditioning stages, implies that the drug does not enhance animals' ability to learn that a given stimulus is irrelevant but, instead, facilitates the ability to continue and respond to this stimulus as irrelevant under changed contingencies of reinforcement.

These results fit extremely well with those obtained with amphetamine. Animals preexposed under amphetamine but conditioned without the drug show a normal LI effect. In contrast, the administration of amphetamine in both the preexposure and conditioning stages abolishes LI [42]. Thus, both amphetamine and haloperidol do not affect animals' ability to learn to ignore an irrelevant stimulus, but the two drugs exert opposite effects on subsequent control by such stimuli, haloperidol enhancing and amphetamine disrupting animals' ability to continue to respond to a stimulus as irrelevant when it is followed by reinforcement.

Haloperidol, at the low dose used in the present experiments (0.1 mg/kg), selectively blocks DA receptors [2] whereas low doses of amphetamine enhance neurotransmitter activity at dopaminergic receptors [16]. The finding that the two drugs exert opposite effects on LI, provides additional evidence that LI is mediated by the dopaminergic system [30,32]. Moreover, the fact that both effects are dependent on drug administration in both the nonreinforced preexposure and conditioning stages suggests that the dopaminergic system is involved in the expression (control over behavior by irrelevant stimuli) rather than in the acquisition (learning to ignore) of LI.

Finally, the present results add to the increasing body of evidence that neuroleptics do not affect associative learning [1, 5, 7–9, 36, 37]: Haloperidol does not affect animals' capacity to learn that a stimulus signals nonreinforcement and, moreover, enhances subsequent control of such a stimulus over behavior. The possibility that neuroleptics may, in general, enhance the effects on behavior of nonreinforcement or stimuli associated with nonreinforcement is in line with the findings that the effects of haloperidol, administered in extinction, summate with those of nonreinforcement to produce very rapid extinction [26] and that pimozide reduces resistance to extinction obtained following intermittent reinforcement training [35].

ACKNOWLEDGEMENTS

This study was supported by a grant from the Israel Institute for Psychobiology, Charles E. Smith Family Foundation 6/84 to I. Weiner. Experiment 3 was conducted by B. Froman. We thank Prof. R. E. Lubow for his valuable comments on this manuscript.

REFERENCES

1. Ahlenius, S., J. Engel and M. Zoller. Effects of apomorphine and haloperidol on exploratory behavior and latent learning in mice. *Physiol Psychol* **5**: 290–294, 1977.
2. Anden, N. E., S. G. Butcher, H. Corrodi, K. Fuxe and U. Ungerstedt. Receptor activity and turnover of dopamine and noradrenaline after neuroleptics. *Eur J Pharmacol* **11**: 303–314, 1970.
3. Anisman, H., G. Remington and L. S. Sklar. Effects of inescapable shock on subsequent escape performance: Catecholaminergic and cholinergic mediation of response initiation and maintenance. *Psychopharmacology (Berlin)* **61**: 107–124, 1979.
4. Anisman, H. and R. M. Zacharko. Stimulus change influences escape performance: Deficits induced by uncontrollable stress and by haloperidol. *Pharmacol Biochem Behav* **17**: 263–269, 1982.
5. Beninger, R. J. The role of dopamine in locomotor activity and learning. *Brain Res Rev* **6**: 173–196, 1983.
6. Beninger, R. J. and N. L. Freedman. The use of two operants to examine the nature of pimozide-induced decreases in responding for brain stimulation. *Physiol Psychol* **10**: 409–412, 1982.
7. Beninger, R. J., A. J. MacLennan and J. P. J. Pinnel. The use of conditioned defensive burying to test the effects of pimozide on associative learning. *Pharmacol Biochem Behav* **12**: 445–448, 1980.
8. Beninger, R. J., S. T. Mason, A. G. Phillips and H. C. Fibiger. The use of extinction to investigate the nature of neuroleptic-induced avoidance deficits. *Psychopharmacology (Berlin)* **69**: 11–18, 1980.
9. Beninger, R. J., S. T. Mason, A. G. Phillips and H. C. Fibiger. Use of conditioned suppression to evaluate the nature of neuroleptic-induced avoidance deficits. *J Pharmacol Exp Ther* **213**: 623–627, 1980.
10. Corradini, A., T. N. Tombaugh and H. Anisman. Effects of pimozide on escape and discrimination performance in a water-escape task. *Behav Neurosci* **98**: 96–106, 1984.
11. Ettenberg, A., G. F. Koob and F. E. Bloom. Response artifact in the measurement of neuroleptic-induced anhedonia. *Science* **213**: 357–359, 1981.
12. Fibiger, H. C. Drugs and reinforcement: A critical review of the catecholamine theory. *Annu Rev Pharmacol Toxicol* **18**: 37–56, 1978.
13. Fibiger, H. C., A. P. Zis and A. F. Phillips. Haloperidol induced disruption of conditioned avoidance responding: Attenuation by prior training or by anti-cholinergic drugs. *Eur J Pharmacol* **38**: 309–314, 1975.
14. Franklin, K. B. J. and S. N. McCoy. Pimozide-induced extinction in rats: Stimulus control of responding rules out motor deficit. *Pharmacol Biochem Behav* **11**: 71–75, 1979.
15. Groves, P. M. and G. V. Rebec. Biochemistry and behavior: Some central actions of amphetamines and antipsychotic drugs. *Annu Rev Psychol* **27**: 91–127, 1976.
16. Kuczenski, R. Biochemical actions of amphetamine and other stimulants. In: *Stimulants: Neurochemical, Behavioral and Clinical Perspectives*, edited by I. Creese, New York: Raven Press, 1983, pp. 31–62.

17. Lubow, R. E. Latent inhibition. *Psychol Bull* **79:** 398–407, 1973.
18. Lubow, R. E., I. Weiner and P. Schnur. Conditioned attention theory. In: *The Psychology of Learning and Motivation,* vol 15, edited by G. H. Bower. New York: Academic Press, 1981, pp. 1–49.
19. Mackey, W. B. and D. van der Kooy. Neuroleptics block the positive reinforcing effects of amphetamine but not of morphine as measured by place conditioning. *Pharmacol Biochem Behav* **22:** 101–105, 1985.
20. Mackintosh, N. J. Stimulus selection: learning to ignore stimuli that predict no change in reinforcement. In: *Constraints on Learning: Limitations and Predispositions,* edited by R. A. Hinde and J. S. Hinde. Cambridge: Academic Press, 1973, pp. 79–100.
21. Mackintosh, N. J. A theory of attention: variations in the associability of stimuli with reinforcement. *Psychol Rev* **82:** 276–298, 1975.
22. Mackintosh, N. J. *Conditioning and Associative Learning.* New York: Oxford University Press, 1983.
23. Moore, J. W. Brain processes and conditioning. In: *Mechanisms of Learning and Motivation: A Memorial Volume for Jerzy Konorski,* edited by A. Dickinson and R. A. Boakes. Hillsdale: Earlbaum, 1979, pp. 111–142.
24. Niemegeers, C. J. E., F. J. Verbruggen and P. A. J. Janssen. The influence of various neuroleptic drugs on shock avoidance responding in rats. *Psychopharmacologia* **16:** 161–164, 1969.
25. Ohad, D., I. Weiner, R. E. Lubow and J. Feldon. The effects of amphetamine on blocking. *Physiol Psychol,* in press.
26. Phillips, A. G. and H. C. Fibiger. Decreased resistance to extinction after haloperidol: Implications for the role of dopamine in reinforcement. *Pharmacol Biochem Behav* **10:** 751–760, 1979.
27. Phillips, A. G., A. C. McDonald and D. M. Wilkie. Disruption of autoshaped responding to a signal of brain-stimulation reward by neuroleptic drugs. *Pharmacol Biochem Behav* **14:** 543–548, 1981.
28. Reiss, S. and A. R. Wagner. CS habituation produces a "latent inhibition effect" but no active "conditioned inhibition." *Learn Motiv* **3:** 237–245, 1972.
29. Rescorla, R. A. Summation and retardation tests of latent inhibition. *J Comp Physiol Psychol* **75:** 77–81, 1971.
30. Solomon, P. R., A. Crider, J. W. Winkelman, A. Turi, R. M. Kamer and L. J. Kaplan. Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: relationship to schizophrenic attention disorder. *Biol Psychiatry* **16:** 519–537, 1981.
31. Solomon, P. R., C. A. Lohr and J. W. Moore. Latent inhibition of the rabbit's nictitating response: Summation tests for active inhibition as a function of a number of CS preexposures. *Bull Psychon Soc* **4:** 557–559, 1974.
32. Solomon, P. R. and D. M. Staton. Differential effects of microinjections of d-amphetamine into the nucleus accumbens or the caudate putamen on the rat's ability to ignore an irrelevant stimulus. *Biol Psychiatry* **17:** 743–756, 1982.
33. Spyraki, C., H. C. Fibiger and A. G. Phillips. Attenuation of place preference conditioning using food reinforcement. *Psychopharmacology (Berlin)* **77:** 379–382, 1982.
34. Taylor, J. R. and T. W. Robbins. Enhanced behavioral control by conditioned reinforcers following microinjections of d-amphetamine into the nucleus accumbens. *Psychopharmacology (Berlin)* **84:** 405–412, 1984.
35. Tombaugh, T. N., H. Anisman and J. Tombaugh. Extinction and dopamine receptor blockade after intermittent reinforcement training: Failure to observe functional equivalence. *Psychopharmacology (Berlin)* **70:** 19–28, 1980.
36. Tombaugh, T. N., L. J. Grandmaison and K. A. Zito. The establishment of secondary reinforcement in sign tracking and place preference tests following pimozide treatment. *Pharmacol Biochem Behav* **17:** 665–670, 1982.
37. Tombaugh, T. N., C. Szostak and P. Mills. Failure of pimozide to disrupt the acquisition of light-dark and spatial discrimination problems. *Psychopharmacology (Berlin)* **79:** 161–168, 1983.
38. Tombaugh, T. N., J. Tombaugh and H. Anisman. Effects of dopamine receptor blockade on alimentary behaviors: Home cage food consumption, magazine training, operant acquisition, and performance. *Psychopharmacology (Berlin)* **66:** 219–225, 1979.
39. Wagner, A. R. and R. A. Rescorla. Inhibition in Pavlovian conditioning: Application of a theory. In: *Inhibition and Learning,* edited by R. A. Boakes and M. S. Halliday. London: Academic Press, 1972, pp. 301–336.
40. Weiner, I. and J. Feldon. Facilitation of latent inhibition by haloperidol. *Psychopharmacology,* in press.
41. Weiner, I., R. E. Lubow and J. Feldon. Chronic amphetamine and latent inhibition. *Behav Brain Res* **2:** 285–286, 1981.
42. Weiner, I., R. E. Lubow and J. Feldon. Abolition of the expression but not the acquisition of latent inhibition by chronic amphetamine in rats. *Psychopharmacology (Berlin)* **83:** 194–199, 1984.
43. Wise, R. A. Catecholamine theories of reward: A critical review. *Brain Res* **152:** 215–247, 1978.
44. Wise, R. A. Neuroleptics and operant behavior. *Behav Brain Sci* **5:** 39–87, 1982.