APRIL, 1963

## IMMOBILITY AS AN AVOIDANCE RESPONSE, AND ITS DISRUPTION BY DRUGS<sup>1</sup>

# DALBIR BINDRA<sup>2</sup> AND HARVEY ANCHEL

#### MC GILL UNIVERSITY

Much of the available literature on avoidance behavior is based on responses which require the animal to run, lever-press, or to make some active response to avoid noxious stimulation. The purpose of Experiment I reported in this paper was to determine whether animals can learn to sit or stand motionless in order to escape or avoid electric shock. Five experimental rats were given escape-avoidance training, while five yoked control animals received electric shocks without any response-related contingency. It was shown that an immobility avoidance response, as distinct from the unconditioned "freezing" response to shock, can be trained. The results of Experiment II (30 rats) revealed that this response is more readily acquired at higher shock intensities than at lower ones, provided escape by jumping is prevented at the high shock intensities. The effects of six doses of each of three drugs on the immobility avoidance response were studied in Experiment III (13 rats). Methylphenidate, chlorpromazine, and imipramine all produced a decrement in the immobility response, but the pattern and amount of the effects of the three drugs were quite different, one from the other. The implications of these findings for a general theory of avoidance behavior and for drug screening are discussed.

In a typical avoidance learning experiment, the animal is required to run from one side of a shuttle box to the other, or to press a bar, or to make some active response in order to terminate or avoid noxious stimulation (e.g., electric shock). Much of the available literature on avoidance behavior deals with the characteristics of such active responses. The purpose of the present study was to determine whether animals can also learn to sit or stand motionless to escape or avoid electric shock. Blough (1958) has shown that pigeons can be trained to stand motionless in order to receive a food reinforcement; thus it appears not inconceivable that an immobility avoidance response can also be trained. In the present study, experimental rats were given escapeavoidance training, while control yoked animals received electric shocks without opportunity to escape or avoid them. The effects of shock intensity on the acquisition of the immobility response, as well as the influence of three drugs (chlorpromazine, imipramine, and methylphenidate) on the performance of the response, were studied.

#### EXPERIMENT I

The purpose of the first, preliminary, experiment was to determine whether immobility as an avoidance response to a specific stimulus situation could be learned by the rat.

#### Subjects

Ten naive adult male hooded rats, each weighing about 200 gm, were used. They were housed in small wire mesh cages, two to a cage. An experimental and a control animal comprised a cage pair.

#### **Apparatus**

The training was conducted in a wooden box, 38 in. long, 6 in. wide, and 20 in. deep. It was divided into two equal compartments, each 19 in. long. The box had a grid floor, through which a 0.75 ma (420 VAC) "scrambled" electric shock could be delivered. A single switch was used to turn the shock on or off simultaneously in both compartments.

<sup>&</sup>lt;sup>1</sup>This research was supported by a grant (MH-03238) from the United States Public Health Service. Chlorpromazine (Largactil) was supplied without charge by Poulenc, Ltd., imipramine (Tofranil) by Geigy (Canada), Ltd., and methylphenidate (Ritalin) by Ciba, Ltd.

<sup>&</sup>lt;sup>2</sup>For reprints write Dalbir Bindra, Department of Psychology, McGill University, Montreal 2, P.Q., Canada.

### Procedure and Results

For training, the experimental animal of a pair was placed in one compartment and the control animal in the other. Each animal of the pair was left in its respective compartment for a period of 10 min on each of 14 training sessions, one session per day. During a session, the experimenter observed the experimental animal and occasionally looked at the control animal. Shock was applied whenever the experimental animal walked, reared, sniffed, or was otherwise active in some way. The shock was terminated as soon as the animal stood or sat motionless; rats frequently sit motionless momentarily in the course of frantic jumping and running. Each time the experimental animal was shocked. the control animal also received the shock regardless of what it was doing; thus, the shocks received by the control animal were not consistently contingent on any specific behavior. The duration in seconds for which it was necessary to keep the shock on (i.e., the time the experimental animal spent making any observable movements) was recorded by a running-time-meter connected to the shock switch; the time spent sitting motionless was calculated by subtracting this figure from 600 sec-the total duration of a session.

From the first to the second training session, there was a marked increase in immobility; both the experimental and the control animals remained motionless during more than 50% of the second session. On the third training session, it was noticed that, though the duration of immobility continued to increase in the experimental animals, the control animals began to move around. By the 14th session, all experimental animals had learned the response; each remained motionless for 9.99 min of the 10-min session. Clearly, like running or jumping, immobility can be trained as an avoidance response. In no case did the immobility represent lying flat on the grid, as rats sometimes do while they are being shocked; the observed immobility could more accurately be described as sitting rigidly motionless.

In order to determine how far the observed immobility was a response to the specific training situation, all animals were observed in four test sessions following training. One of the tests was given in the training situation and three in situations that differed from it in their stimulus characteristics. Each test was preceded and followed by a retraining session. using the original training procedure. During the retraining sessions all experimental animals maintained the 9.99/10-min performance level. During a test session, the experimenter recorded subject's action (e.g., walking, rearing, grooming, sitting or standing motionless, etc.) at the end of each successive 6-sec interval; the click of a timer indicated each 6-sec interval. The reliability of this method has been discussed before (Bindra and Blond, 1958). All animals, experimental and control, were observed individually for a 10-min period, and the number of "motionless" entries was counted. No shock was given in any of the test sessions.

The results of the four test sessions are presented in Table 1. The figures describe the

Table	1
-------	---

Means and Ranges of the Frequencies of "Motionless" Entries in Test Sessions 1-4, and the Significance Level of Differences Between Experimental and Control Groups.

Test Session No.	Experimental Condition	Experimental Animals	Control Animals	p-values (t-test; two-tailed)
1	Same as training	96.6 (9 <b>3</b> -100)	11.8 (0- <b>3</b> 2)	<.001
2	Square shallow box	70.2 ( <b>3</b> -100)	21.8 (9- <b>36</b> )	<.05
3	Same as training but with a card- board floor	62.2 (34-84)	12.4 (0-42)	<.01
4	Wire-mesh (living) cage	9.4 (1-15)	9.2 (2-21)	n.s.

mean number of protocol entries (out of a total of 100) in which the animals were observed to be motionless. The results of Test Session 1, conducted in the training situation, clearly show the difference between the experimental and the control animals. Note that most of the experimental animals also displayed the immobility response in a square shallow box (Test Session 2), which had a grid floor similar to the one in the training situation, as well as in a situation in which the grid of the training box had been covered by a cardboard (Test Session 3). However, the response did not occur to any considerable extent in the wire-mesh cage (Test Session 4), which was identical to the ones in which the animals normally lived and was quite different from the training box.

### Conclusion

The difference between control and experimental animals shows that immobility response in the experimental animals was not an unconditioned "freezing" response to electric shock. The differences in the incidence of immobility between Test Session 1 and the other test sessions, especially Sessions 3 and 4, indicate that the response was specifically associated with the situation in which it was trained.

#### **EXPERIMENT II**

This experiment was designed to determine the relation between shock intensity and the acquisition of the immobility response.

### Subjects and Apparatus

Thirty naive male hooded rats, each weighing about 200 gm, served. The apparatus described under Exp. I was used.

#### Procedure

Twenty-four of the 30 rats were divided into four groups, A, B, C, and D. Each of Groups A, B, and D contained four animals; Group C contained 12. The remaining six rats, Group Y, served as yoked-control animals for six of the animals in Group C. Though the voltage of the shock generator was kept constant at 420 VAC, the shock intensity was different for the various groups: Group A, 0.50 ma; Group B, 0.75 ma; Groups C and Y, 2.00 ma, and Group D, 2.65 ma. The training procedure for the six yoked pairs replicated that used in Exp. I. In the case of Groups A, B, D, and the six non-paired animals of Group C, only one compartment of the training box was used, but in every other respect the procedure was the same as in Exp. I. In the course of daily training sessions, when an animal remained motionless for 9.99 min in the 10-min session of a particular day, it was considered to have learned the immobility response.

The day after an animal reached the above learning criterion, it was given a test session. The time-sample method for recording the animal's behavior was the same as that used in Exp. I; the number of "motionless" and "rearing" entries during the test session was determined for each animal. No shock was given during the test session.

### Results

Six of the 16 rats in Groups C and D failed to acquire the immobility response. All these non-learners managed to jump out of the training box when they were shocked during the first training session. Though they were immediately placed back into the box, each continued this jumping behavior and showed no signs of learning the required response even after 30 training sessions. The data from these non-learners are not included in the following analysis.

The general course of learning in the case of all learners, in Group A, B, C and D was the same as that observed in the first experi-



Fig. 1. The cumulative proportion of animals that reached the criterion of learning (remaining motionless for 9.99 min out of 10 min) on each of the successive training sessions. Groups A and B (N = 8) were trained under low shock intensity; Groups C and D (N = 10) under high shock intensity.

ment. The duration of immobility increased rapidly during the first two sessions, and then continued to increase more slowly. There appeared to be no remarkable difference between Groups A and B, or between Groups C and D; therefore, the data for each of these two sets of groups were combined. The cumulative proportion of animals that reached the criterion of learning on each successive training session is shown in Fig. 1. It is clear that Groups A and B, which received a lower intensity of shock, did not learn the immobility response as readily as did the animals that received the two higher intensities of shock (Groups C and D). It also appeared that miscellaneous environmental disturbances were more likely to disrupt immobility in Groups A and B than in C and D; the higher intensities produced more stable responses.

Every animal in Groups A, B, C, and D that had reached the learning criterion remained motionless for at least 95% of the time (95% of the time-sample entries) during the test session. The yoked animals, Group Y, remained motionless significantly less than the paired animals in Group C (p < .01; two-tailed t-test). The yoked animals also reared significantly more than their paired experimental animals (p < .01). These results are shown in Table 2.

#### Table 2

Comparison of the Frequency of "Motionless" and "Rearing" Responses of the Trained and the Yoked-Control Animals at the End of Training.

Responses	Experimental Animals Mean (Range)	Control Animals Mean (Range)	þ
"Motionless"	96.1 (89-100)	5 <b>3</b> .7 (44-65)	<.01
"Rearing"	0.8 (0-4)	22.4 (17-70)	<.01

## Conclusion

Considering only the animals that did not successfully escape the shock by jumping, the higher intensities of shock clearly produced quicker learning of the immobility response. However, shock intensity also seems to determine the probability of occurrence of the jumping response. Further, even at a high intensity of shock, the difference between the yoked-controlled animals and the experimental animals, in the case of which shock termination is contingent on their remaining motionless, is maintained; thus, a genuine learning of the immobility response is again demonstrated.

## **EXPERIMENT III**

Active escape-avoidance responses, such as alley running, have been shown to be enhanced by stimulant drugs (Hamilton, 1960) and impaired by depressant drugs (Ader and Clink, 1957; Cook and Weidley, 1957; Irwin, 1961). The purpose of this experiment was to determine the effects of three commonly used drugs, methylphenidate, an amphetamine-like stimulant, chlorpromazine, a mild depressant or "tranquilizer", and imipramine, an "antidepressant" on the immobility avoidance response. Six dose levels of each of these drugs were used.

## Subjects and Apparatus

Thirteen naive adult male hooded rats, weighing about 200 gm each, served. The apparatus used is described under Exp. 1.

### Procedure

The training procedure was the same as employed in training Groups A, B, C and D of Exp. II, except that only one shock intensity, 0.75 ma, was used—the same intensity as was used in Exp. I. When all animals had learned the immobility avoidance response, they were divided into two groups, Group L, of five rats, and Group H, of eight rats. Group L was tested at the three lower drug doses, and Group H at the three higher drug doses.

All animals were tested in a series of sessions extending over about four/weeks. Each test session was followed (and preceded) by a retraining session; the procedure for the retraining sessions was the same as that used in the original training. The retraining sessions ensured the maintenance of the avoidance response at a high performance level (9.99/10 min). The time-sample method used to record the occurrence of the motionless response in the test sessions has been described in Exp. I. No shocks were administered during the test sessions.

Every animal was given 11 test sessions; the first and the last of these were control tests (*i.e.*, no drug injections were given on these

Group	Chlorpromazine Hydrochloride	Imipramine Hydrochloride	Methylphenidate Hydrochloride	
L	2, 4, or 6 mg/kg	15, 20, or 25 mg/kg	4, 6, or 8 mg/kg	
н	8, 10, or 12 mg/kg	30, 35, or 40 mg/kg	10, 12, or 14 mg/kg	

Table 3Schedule of Drug Injections.

days). On the days of the other nine experimental test sessions, the animals in Group L and H were injected with the three drugs according to the schedule presented in Table 3. All animals in each group were given all the injections for that group in a scrambled order. The interval between the injection and the test was 30 min in the case of chlorpromazine and imipramine, and 15 min in the case of methylphenidate. All drugs were administered intraperitoneally.

### Results

As in Exp. I, in which the same shock intensity was used, all the animals reached the criterion of learning (remaining motionless for 9.99 min in 10 min) by the 17th training session. In the retraining sessions, all the animals maintained this criterion.

Figure 2 shows the mean frequencies of occurrence of the immobility response during the control session and under the influence of the six doses of each of the three drugs. The



Fig. 2. The mean and S.D. (vertical lines) of frequency of occurrence of the immobility response during the control sessions and under the influence of the six doses of each of the three drugs. The doses were as follows:

Chlorpromazine 2, 4, 6, 8, 10, or 12 mg/kg;

Imipramine 15, 20, 25, 30, 35, or 40 mg/kg; and Methylphenidate 4, 6, 8, 10, 12, or 14 mg/kg.

Group L was tested at the three lower doses of each drug, and Group H at the three higher doses of each drug. A control session was given at the beginning, and again at the end, of the test sessions.

points for the three lower doses are based on Group L animals, and those for the three higher doses on Group H animals. It is clear that all three drugs produced a decrement in immobility. Within the limit of drug doses employed, this decrement was, roughly speaking, a direct monotonic function of dose in the case of methylphenidate, and an inverse monotonic function of dose in the case of chlorpromazine. Imipramine affected the response to about the same degree at all dose levels, except the lowest. Correspondingly, the variability of immobility scores decreased markedly at the higher doses of chlorpromazine and methylphenidate, but remained large at the higher doses of imipramine (see Fig. 2). Response decrement was significantly greater under the influence of the most potent dose of methylphenidate than under influence of the most potent dose of imipramine (p < .01) and of chlorpromazine (p < .01); under the influence of imipramine it was significantly greater than under the influence of chlorpromazine (p < .06). Every animal showed a marked decrement (compared to its own control score) in the avoidance response under the influence of chlorpromazine and of methylphenidate; only one animal in Group L failed to show a decrement under the influence of any of the three lower doses of imipramine.

#### Discussion

Methylphenidate is known to increase the level of spontaneous activity (Bindra and Baran, 1959); the decrement in the immobility response in the present experiment is most simply attributed to the hyperactivity induced by this drug.

Chlorpromazine is known to impair active avoidance responses (Ader and Clink, 1957); in general, the higher the dose, the greater the impairment. However, the present experiment shows that chlorpromazine reduces the occurrence of the immobility avoidance response only at extremely low doses. Irwin (1961) has shown that, in the case of an active avoidance response, the degree of impairment produced by phenothiazines is directly proportional to the extent to which they decrease spontaneous activity. Though the decrease in spontaneous activity produced by chlorpromazine is a direct function of the dose (Bindra and Baran, 1959), the impairment of the immobility avoidance response seems to be an inverse function of the dose.

Inasmuch as the effects of methylphenidate, as well as of chlorpromazine at certain doses, on the immobility avoidance response are opposite to the effects of these drugs on other, more active, avoidance responses, these effects must depend upon the exact behavioral components that make up different types of responses and on the effect that the drug has on each of those behavioral components (Bindra, 1961). In the light of this, the theoretical formulations, suggesting that drugs influence avoidance responding by modulating anxiety (Miller, Murphy, and Mirsky, 1957), must be re-examined.

Imipramine, which has been shown to resemble chlorpromazine in many of its behavioral effects (Herr, Stewart, and Charest, 1961), displayed a distinctive effect on the immobility avoidance response used in the present experiment. Though it is likely that at still higher doses imipramine, like chlorpromazine, may act as a sedative and have no decremental effect on the immobility response, the fact that it had this decremental effect over a wider range of doses than did chlorpromazine is notable and may have significance for drug screening (see Herr, Stewart and Charest, 1961). The usefulness of imipramine in the treatment of depressed patients (Kuhn, 1958) and the parallel between clinical depression and immobility as produced in the present experiment is also suggestive.

#### REFERENCES

- Ader, R., and Clink, D. W. Effects of chlorpromazine on the acquisition and extinction of an avoidance response in the rat. J. Pharmacol. exp. Therap., 1957, 121, 144-148.
- Bindra, D. Components of general activity and the analysis of behavior. Psychol. Rev., 1961, 68, 205-215.
- Bindra, D., and Baran, D. Effects of methylphenidylacetate and chlorpromazine on certain components of general activity. J. exp. Anal. Behav., 1959, 2, 343-350.
- Bindra, D., and Blond, Joyce. A time-sample method for measuring general activity and its components. *Canadian J. Psychol.*, 1958, **12**, 74-76.
- Blough, D. S. New test for tranquilizers. *Science*, 1958, 127, 586-587.
- Cook, C., and Weidley, E. Behavioral effects of some psychopharmacological agents. Ann. N.Y. Acad. Sci., 1957, 66, 740-752.
- Herr, F., Stewart, Jane, and Charest, Marie-Paule. Tranquilizers and antidepressants: A pharmacological comparison. Arch. int. Pharmacodyn., 1961, 134, 328-342.
- Hamilton, C. L. Effects of LSD-25 and amphetamine on a running response in the rat. Am. Med. Assn. Archiv., 1960, 2, 104-109.
- Irwin, S. Correlation in rats between the locomotor and avoidance-suppressant potencies of eight phenothiazine tranquilizers. Arch. int. Pharmacodyn., 1961, 132, 279-286.
- Kuhn, R. The treatment of depressive states with G22355 (Imipramine hydrochloride). Am. J. Psychiat., 1958, 115, 459-464.
- Miller, R. E., Murphy, J. V., and Mirsky, I. A. The effects of chlorpromazine on fear-motivated behavior in rats. J. Pharmacol. exp. Therap., 1957, 120, 379-387.

Received May 20, 1962