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Criterion for Learned Helplessness in the Rat: A Redefinition

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MUSTY, R. E., M. P. JORDAN AND R. H. LENOX. *Criterion for learned helplessness in the rat: A redefinition*. PHARMACOL BIOCHEM BEHAV 36(4) 739–744, 1990.—Numerous investigators have reported difficulty obtaining reliable learned helplessness. Various laboratories have used differing test environments and criteria, making comparisons among experiments difficult. Some use an escape deficit criterion, in which escape is slowed down in a shuttle box, while others have used an escape failure criterion, in which rats do not escape at all on most test trials. Little work has been done to test the validity of LH, i.e., the prediction of persistence of escape failure after exposure to uncontrollable shock. The present studies demonstrate that the reliability and validity of learned helplessness can be improved by 1) modifying the shuttle box to increase task difficulty and decrease random escape behavior and 2) adopting a new escape failure criterion for helpless behavior which is based on statistical prediction of the persistence of escape deficits.

Learned helplessness   Depression   Rat model of depression

THE phenomenon known as learned helplessness (LH) has been widely studied, yet several problems have made it a subject of considerable controversy. Katz (11) and Wilner (30,31) both argued that an animal model of depression should be examined according to the ground rules proposed by McKinney and Bunney (15); models should be based on observable behavior, have objective criteria, and be reproducible. Divergent criteria, however, have been used to define LH in rats. Seligman and Beagley (23) reported that rats exhibited slower escape latencies after receiving inescapable shock. In their study, however, some rats did not escape in the 60-second test trial and these were referred to as *escape failures*. The group having received uncontrollable shock exhibited a greater number of escape failures than the control group, which had not been administered uncontrollable shock. They also reported that 63% of the rats showed escape failure on more than 25% of the total number of test trials, i.e., at least 5 failures in 20 trials. Later researchers, who were concerned with using LH as a psychopharmacological model, developed a criterion measure for helplessness (25). An *escape failure* was redefined, by these authors, as a latency of greater than 20 seconds in a 45-second test trial. Their criteria for LH was defined as 6 or more escape failures in 15 trials. Others have continued to use similar approaches (10,29). Some researchers have used escape latencies as a measure of helplessness (31), while others have used a classification variable, i.e., helpless vs. not helpless, based on an arbitrarily defined latency within the test. Consequently, it is difficult to compare studies of learned helplessness using these differing definitions of escape failure. In view of this difference, it is important to determine whether or not the reproducibility of learned helplessness differs as a consequence of the criteria used to define it.

In regard to the question of reproducibility, LH results have been inconsistent. Published reports have observed ranges of LH from 12.5% (23) to as high as 85% (25). Freda and Kline (7) found that LH was difficult to replicate Weiland *et al.* (29) reported that various researchers have had difficulty in finding reproducible performance deficits. Task difficulty is one variable which seems to be involved. Anisman *et al.* (2), for example, found that adding a hurdle to the shuttle box test improved the reproducibility of LH. In pilot studies, we found poor replication to replication stability of LH in a shuttle box without a midpoint hurdle or barrier. In the present experiment, we have compared the outcome using a barrier as compared with no barrier in the shuttle box.

In addition to the question of reproducibility, the LH model has been criticized in the area of validity (30,31). Wilner has pointed out that there is considerable variability in "estimates of how long helplessness effects last." This issue is certainly an important aspect of validity for an animal model of depression. To the best of our knowledge, no one has attempted to examine potential criteria for LH using the persistence of escape deficits as the criterion measure.

The present studies were designed to examine potential criteria for learned helplessness in order to improve the reliability, reproducibility, and validity of the procedure.

METHOD

Subjects

Two hundred and sixty outbred male adult Sprague-Dawley

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rats were purchased from Charles River. They were housed in plastic shoe-box cages 20 × 16 × 8½", 5 animals per cage in a room maintained at constant temperature (75 ± 4°F) and controlled lighting (12-hour light-dark cycle). Food and water were provided ad lib except during training and testing. All animals were treated in accordance with *Ethical Principles for the Care and Use of Animals* of the American Psychological Association, and the procedures were approved by the University of Vermont Animal Care and Use Committee.

Apparatus

A shuttle box was used which had 2 adjacent compartments with inside dimensions of 19.5 × 15.5 × 15.5 cm each. The floor was constructed of brass rods 2 mm in diameter and spaced 1 cm apart. Walls were constructed of clear Plexiglas to permit observation during experiments. The shuttle box was enclosed in a sound-attenuated environmental chamber (71 × 34 × 31 cm) with a window to permit remote observation of subjects. Lighting for each chamber was provided by a 1-W light bulb located directly above the shuttle box. Shock was delivered to the grid floor by a Grason-Stadler shock generator (Model E1064GS). A NEDCO ABLE-40 computer controlled the shuttle boxes and recorded response measures. In a second condition of the experiment, a 15.5 × 15.5 cm copper barrier with a 7.6 × 7.6 cm open doorway centered at the floor level of the shuttle box was inserted.

Procedures

Rats were tested in multiple replications in subgroups ranging from 5–18 rats each over the period of two years. Subgroups were those tested with inescapable preshock without the barrier (PNB, n = 55); no preshock without the barrier (NPNB, n = 56); preshock with the barrier (PB, n = 81); and no preshock with the barrier (NPB, n = 68). In previous studies, investigators have employed a yoked control group, in which a group of rats is given *escapable* shock equal to those given *inescapable* shock. Since rats treated with escapable shock do not show LH (10,25), these were not included in this series of studies. Four replications were run with PNB and NPNB subgroups, 4 replications were run with all four subgroups, and 2 additional replications were run with PB and NPB subgroups.

Pretest day. Animals were randomly assigned to receive either inescapable shock (PNB, PB) or no shock (NPNB, NPB) in a shuttle box with one half closed off with an electrified copper wall. These preshock groups received 80 inescapable shocks (5-sec duration at 2.0 mA) which were delivered on a variable interval 60-sec (VI-60) schedule with a range of 10–110 sec. The no preshock rats were placed in an identical shuttle box for an equivalent amount of time without receiving any shock. All rats were tested 24 hr after the pretest day.

Testing. Twenty-four hours after pretest, all animals were tested individually for acquisition of an escape response. One testing session consisted of 20 trials, in which the rat was required to cross from one side to the other and back (FR2) to escape the shock. Shock was preceded by a 5-sec CS tone (4000 Hz, 70 dB) which remained on until shock was terminated. During testing the shock intensity was 1.3 mA on a VI-60-sec schedule. If the appropriate response was not made within 45 sec, the shock was automatically turned off. The dependent measure was the latency to perform the FR2 response. Procedures for testing subgroups with the barrier in place were identical for those tested in the no-barrier conditions.

Retesting. In order to test the stability of LH, animals were retested for escape behavior 7 and 14 days following the initial test. Subgroups were as follows: PNB, n = 35; NPNB, n = 35; PB, n = 30; and NPB, n = 30. Retests were conducted over four replications of 5–10 animals per subgroup.

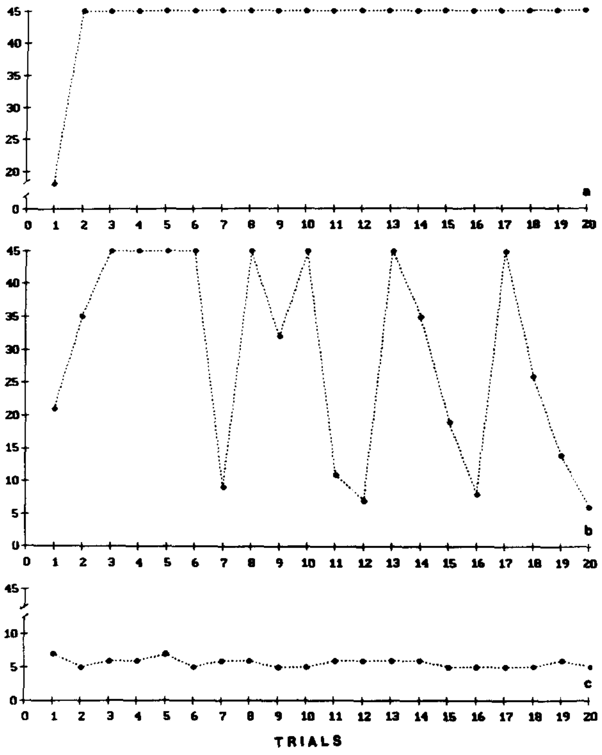

FIG. 1. Individual plots of latency to escape for three representative rats of each type. Plots for 20 trials on the test day. (a) An FP (failure pattern) rat with escape failures on 19/20 trials. (b) A DP (deficit pattern) rat with successful escapes on many trials. (c) An ES (escaper) rat with consistent escape performance. See text for explanation of FP, DP, and ES.

RESULTS

Using analyses of the individual behavior of each rat, three patterns of behavior were observed on the test day. Actual plots from individual rats which are representative of these patterns are shown in Fig. 1. These were: 1) a pattern of failure to escape, i.e., variable early escape followed by "giving up" (making very few to no escapes after trial five) (Fig. 1a); 2) a pattern of intermittent escapes throughout the session in which some animals had decreasing escape latencies and others irregular latencies (Fig. 1b); 3) a pattern of consistent escape (Fig. 1c).

From examination of these patterns, we developed two criteria for helpless behavior. The first criterion is based on a pattern like that shown in Fig. 1a and the second is based on the criterion for LH used by Sherman, Sacquitine and Petty (25) (Fig. 1a, b). In order to clarify the confused definitions of escape behavior on a single trial, we refer to a latency of >20 sec in a 45-sec trial as an *escape deficit.* If the rat has a latency of 45 sec (no escape in the allotted time) we refer to this as an *escape failure* (Table 1). Thus, there can be two criteria for helpless behavior, based on performance on multiple trials (Table 1). We refer to the criterion of Sherman, Sacquitine and Petty (25) as a *deficit pattern* (DP) (Fig. 1b); i.e., latencies of >20 sec on at least 13/20 or more trials. The new criterion is referred to as a *failure pattern* (FP)

TABLE 1

CRITERIA FOR LEARNED HELPLESSNESS

Criterion Type:	Deficit Criterion	Escape Criterion
Behavior on a Single Trial	Escape Deficit (ED) Latency >20 sec. ↓	Escape Failure Latency = 45 sec. ↓
Behavior on Multiple Trials	Deficit Pattern (DP) Escape deficit on at least 13/20 (65%) trials.	Failure Pattern (FP) Escape failure At least one in first 5 trials *and* on at least 12/15 (80%) on trials 6–20.

(Fig. 1a), a latency = 45 sec at least once in the first five trials *and* latencies = 45 sec on at least 12/15 (80%) of the remaining trials.

Rats not meeting the DP criterion were defined as escapers (ES) (Fig. 1c). These rats were those showing relatively consistent escape responses throughout the test session, i.e., those showing latencies of >20 sec on no more than 12/20 trials.

Statistical analysis was subsequently conducted in two steps. First, if the barrier condition has an effect on reproducibility, greater amounts of variance accounted for would be expected in the barrier condition, in comparison with the no barrier condition. Validity of LH would be improved if test day latencies predict performance one and two weeks later. Similarly, if latencies are used as statistical predictors for those animals meeting the DP and FP criteria, greater amounts of variance should be accounted for in animals exhibiting the longest latencies on the initial test day (FP animals) in comparison with the animals showing more variable latencies (DP animals). Second, in order to test the categorization of animals as helpless or not, each was classified as helpless or not, based on DP and FP criteria and outcomes were examined using categorical analysis (chi-square).

Mean latencies over trials 1–20 of the initial test day were used as predictors in a regression analysis, in which the dependent variables were the mean latencies on trials 6–20 on retests, 7 and 14 days after the initial test. Data from trials 6–20 were used to eliminate warm-up effects. The greatest amount of predicted variance (R^2) was found in the barrier condition (Table 2). Note that the amount of variance predicted was 47% and 42%, across the 7-day and 14-day tests, respectively, but the variance predicted in the nonbarrier condition did *not* remain stable and was not statistically significant on the 14-day test.

The optimal criterion for defining learned helplessness would be one which best predicts long escape latencies one and two weeks after the initial test. Thus, regression analyses were run for all animals which were retested at 7 and 14 days. Mean latencies for trials 1–20 were used as predictors of the latencies of trials 6–20, 7 and 14 days after the initial test. As stated above, it was hypothesized that initial test day latencies would be the best predictors of retest latencies in the FP criterion group. The hypothesis was confirmed as shown in Table 3. Note that the R^2 is stable and statistically significant for the latencies at both 7 and 14 days after the initial test, but that R^2 for the DP criterion was not significant at either of these times.

TABLE 2

REGRESSION COEFFICIENTS OBTAINED FROM REGRESSION ANALYSES

	Week 1	Week 2
PB	.47*	.42*
PNB	.49*	.07
NPB	.33**	.15
NPNB	.22	.16

PB = preshock/barrier; PNB = preshock/no barrier; NPB = no preshock/barrier; NPNB = no preshock/no barrier.
*$p<0.0001$.**$p<0.005$.

TABLE 3

REGRESSION COEFFICIENTS OBTAINED AT 7 AND 14 DAYS AFTER THE INITIAL TEST IN FP AND DP GROUPS

	Week 1	Week 2
FP	.20*	.21*
DP	.05	.05

FP = Failure pattern; DP = Deficit pattern.
*$p<0.02$.

The fact that the DP criterion does not predict latencies at retest 7 and 14 days following the initial test, is likely due to the extreme variability of behavior which was observed in the trial by trial plot of these data. To test this possibility, variances were calculated for all 20 trials combined for those animals in each criterion group. In this comparison, the DP group data included *all* animals which are considered helpless using this criterion. The variances were 731.8 for the DP group and 502.0 for the FP group. The variance for the FP group is significantly less than the variance in the DP group where $F(25)=4.82$, $p<0.01$ [F-test for difference among variances (6)].

An analysis of variance of the mean latencies to escape revealed that LH persisted using the FP criterion (Fig. 2). On the other hand, those animals meeting the DP criterion only had latencies which significantly decreased between the initial test day and the two-week test, indicating that these animals were learning to escape shock. Similarly, the mean latencies of ES rats significantly decreased between the initial test and the two-week test. It is clear that these animals were learning as well.

When subjects were categorized using the FP and DP criteria, no statistically significant differences in the frequency of LH was found between criterion type (DP vs. FP) in the nonbarrier subgroups. These data demonstrate that reliable LH is not produced in nonbarrier conditions. Helpless behavior was obtained using the FP criterion in the preshock barrier condition (PB) shown in Fig. 3. LH frequency was significantly greater than the frequency obtained in the no preshock condition (NPB). Using the DP criterion, the frequency of escape deficit response increased in both preshock and no preshock conditions (PB and NPB), but no significant differences were found between these subgroups. These data clearly show that LH is produced only under conditions using the failure pattern (FP) criterion in the barrier condition.

DISCUSSION

These experiments have demonstrated that a barrier in the shuttle box combined with the adoption of the FP criterion for helpless behavior increases the reliability and validity of obtaining LH. As Anisman (1) and Glazer and Weiss (8,9) have previously noted, the use of a hurdle or barrier with a small doorway in the shuttle box test reduces random escape behavior in which a rat

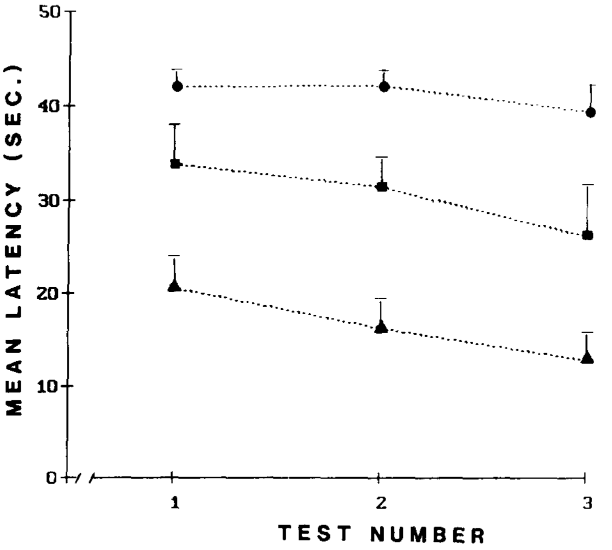

FIG. 2. Mean latency for subgroups classified as LH using the FP (failure pattern) criterion (circles), the DP (deficit pattern) criterion (squares), and ES (escapers) (triangles) on the day of initial test (Week 1) and on the two subsequent weeks (2 and 3). S.E.M. is shown above each mean. Two-way analysis of variance demonstrated a significant subgroup effect, $F(1,11) = 14.84$, $p<0.003$, and a significant effect of week, $F(2,26) = 3.19$, $p<0.03$ (one-tailed). Neuman-Keuls comparisons demonstrated that FP animals had larger mean latencies than DP animals ($p<0.01$) and ES animals ($p<0.01$). Newman-Keuls comparisons within each subgroup FP, DP, and ES over weeks 1–3 demonstrated no significant decrease in latencies for FP; a significant decrease in latencies between week 1 and 3 for DP ($p<0.05$) and a significant decrease in latencies between weeks 1 and 2 and 1 and 3 for ES ($p<0.05$ in both cases).

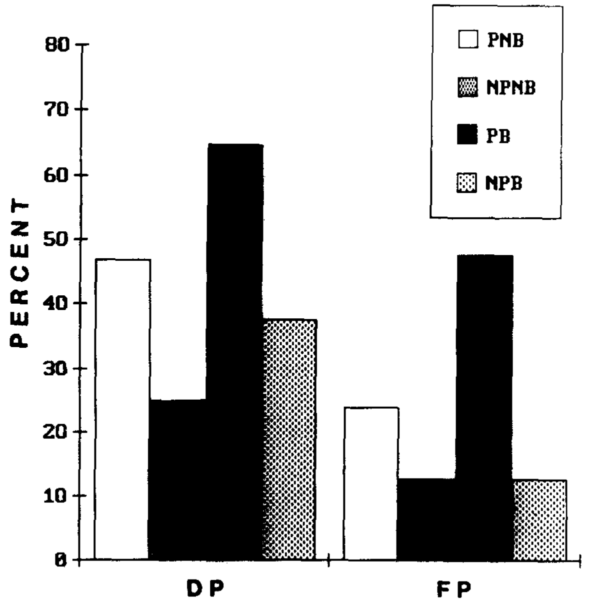

FIG. 3. Overall percent of rats with LH using the DP (deficit pattern) criterion and FP (failure pattern) criterion in the no-barrier condition (preshock, no-barrier; PNB and no preshock, no-barrier; NPNB), and in the barrier condition (preshock-barrier, PB and preshock no-barrier, PNB). A chi-square analysis of the number of rats classified as LH with the FP criterion vs. the DP criterion by barrier condition was significant, $\chi^2(1) = 3.25$, $p<0.03$, indicating that a greater number of rats show LH in the barrier condition only.

jumps around the shuttle box and accidentally makes an FR2 response to terminate shock. The doorway forces the rat to orient toward it, cross to the other side of the shuttle box through it, then turn around and repeat this sequence to reach the other side of the shuttle box. From careful observation of our animals, we concluded that the barrier reduces random behavior which terminates shock and increases the difficulty of the task. This conclusion was supported by the regression analysis which showed that latencies from the initial test were not predictive of latencies at 14 days in the nonbarrier condition. The amount of variance accounted for in the barrier condition, however, was high *and* stable across the two weeks of retesting. It is likely that random responses lead to the termination of shock in lever-press escape paradigms used by other researchers as well (10,25). Thus, under FP criteria in the barrier condition, the present analyses have demonstrated a rate for LH of approximately 50%. This rate of LH is particularly well suited to studies examining interventions meant to increase or decrease the manifestation of helpless behavior.

Next, it was shown that the mean latency for all trials of subjects in the FP criterion group were predictive of behavior one and two weeks after exposure to uncontrollable shock. Optimal predictions were obtained in the preshock-barrier condition. These analyses clearly demonstrate that a criterion which takes into account the temporal pattern of failure to respond early in the test session may be a critical factor in obtaining clear deficits in performance over time. This conclusion was strengthened by the fact that variability in performance using DP criterion was significantly higher than in the FP criterion condition. Finally, when latencies to respond were examined in the FP, DP, and ES criterion groups, a clear separation of the latencies over test sessions were found. Animals in the DP group showed evidence of learning in weeks two and three, suggesting that they should not be included in analyses of LH.

When using the categorical approach, the FP criterion eliminates false positive classification of rats as LH (Fig. 3), since those animals which are falsely classified using the DP criterion are learning, but more slowly than escapers. It is of note that under DP criteria, the percent of helpless behavior increased equally in the preshock and *no* preshock animals upon moving to the barrier condition (Fig. 3). However, under FP criteria there was a significant increase in animals' percentage of showing helpless behavior in the preshock group in the barrier condition; this increase was not observed in the *no* preshock group. Thus, increased task difficulty under DP criteria resulted in an increase in escape deficits randomly distributed between the preshock and no preshock groups, suggesting an erroneous classification of the animals showing LH. Using FP criteria, addition of the barrier served to specifically increase the percentage of animals showing LH (preshock), with the rate of spontaneous helplessness (no preshock) remaining unchanged independent of task difficulty. Several studies currently suggest a genetic predisposition for induction of LH, and it is likely that its true prevalence is characteristic of the animal species and strain (22,29).

Using FP criteria with the animals used in this investigation would suggest that approximately 10% show a baseline of spontaneous helplessness. Therefore, it is important to note that animals classified as LH in the preshock group constitute a baseline of spontaneous helplessness (10%) and another 40% in which the helpless behavior was dependent upon the exposure to the uncontrollable shock experience on the pretest day. Interpretation of pharmacological or behavioral effects on helpless behavior must account for the inclusion of spontaneous helplessness in animals within the LH group.

Several other variables have been examined which appear to play a role in the degree to which LH is observed. Any one of these variables could account for the high variability from one study to another and from one laboratory to another. Seligman and Beagley (23) found that task difficulty was an important variable: the more difficult the response the greater the number of rats showing LH. Seligman, Rosellini and Kozak (24) and Kirk and Blampied (12) have demonstrated that prior experience with escape from shock reduced the degree and rates of LH. There are large variations from laboratory to laboratory in the number, intensity, and temporal intervals between inescapable shocks in the pretest situation. Maier, Albin and Testa (14) reported that these variables contribute little to the outcome of LH, but shock intensity used in the uncontrollable shock condition, relative to test day shock intensities (21), has been shown to play a role in the degree of LH. Finally, there has been little standardization of testing apparatuses for learned helplessness. Seligman, Rosellini and Kozak (24), Sherman, Sacquitine and Petty (25) and Henn *et al.* (10) have used a lever press avoidance response in an operant conditioning chamber; Anisman *et al.* (2), Weiland *et al.* (29) and Martin *et al.* (16) have used a shuttle-box environment.

On the theoretical side, some have argued that LH in animals is used "to describe the interference of adaptive responses produced by inescapable shock and . . . to describe the process that we believe underlies the behavior" (18). In their view, LH is defined by two types of behavior: failure "to initiate responses to escape shock" or slower escape responses *and* more trouble learning that responding is effective. Seligman's view is that LH parallels depression in which the individual feels loss of control of the reinforcers. Alternatively, Weiss and his colleagues have argued that the failure to escape is due to a motor activation deficit (inactivity) due in large part to changes in central norepinephrine system function (26,27). Others have taken a more behavioral view, suggesting that the observed behavior following inescapable shock (or stress) leads to performance deficits, described as escape interference (3) or competing motor responses (19).

The development of a new failure pattern criterion in the present studies raises several interesting questions for further research. Martin, Soubrie and Simon (16,17) use the number of escape failures on an FR1 schedule in the shuttle box. The measure of impairment is the absence of an escape response following a 3-sec light CS and a 3-sec shock. They argue that the "very first seconds following shock onset seem to be critical for detecting interference effects in animals preexposed to inescapable shocks, especially under a simple FR1 schedule." This procedure seems to be a variant of the failure pattern approach used in the present study since the rats fail to initiate an escape response. The difference between this specific procedure and our paradigm is a matter of speculation which should be subjected to a parametric comparison in future studies.

The literature is conflicting in regard to the possibility that activity plays a role in the emergence of these behavior patterns. Weiss, Kriekhaus and Conte (28) have shown that intertrial activity prior to shock is predictive of successful performance in the shuttle box. Kovachich *et al.* (13) and Cierpial *et al.* (5) have demonstrated that animals bred for high activity show deficits in swim test performance after uncontrollable shock, while those bred for low activity do not show a deficit. Rosellini and DeCola (20) reported that there were no differences in activity in the intertrial periods during shuttle box performance among groups that had been administered inescapable shock when compared with controls. Thus, it would seem worthwhile to examine the activity among the animals showing the aforementioned escape patterns by measuring both general and intertrial activity. Phenotypic characteristics other than activity may play a role in the emergence of these patterns of escape. Weiland, Boren, Consroe and Martin (29) reported that the strain of rats contributes considerably to the outcome. Brush *et al.* (4) studied rats selectively bred for high or low performance in shuttle box avoidance. They concluded that the major phenotypic difference was greater emotional reactivity in the low avoidance line. Scott, Cierpial and Weiss (22) have shown that susceptibility to the effects of uncontrollable shock, as measured by the swim test, is heritable. It would seem that future work should focus on inbreeding studies to determine whether or not activity or emotionality are phenotypes which play a role in the emergence of these patterns.

Regardless of which view is adopted, the present study has improved the reliability of measuring escape deficits. It has also improved the validity of learned helplessness by demonstrating that behavior is consistently poor after defining LH using a failure pattern criterion. While the classification of LH using an FP criterion may underestimate actual LH, escape latencies are more stable at both retest times than the DP group and thus the FP criterion is representative of a more consistent population; less vulnerable to the variability associated with previous studies of LH (29) and more appropriate for research using LH as a procedure to examine the neuropharmacological substrates and biobehavioral mechanisms of this phenomenon.

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REFERENCES

1. Anisman, H. Vulnerability to depression: contribution of stress. In: Post, R. M.; Ballenger, J. C., eds. Neurobiology of mood disorders. New York: Williams & Wilkins; 1984:407–431.
2. Anisman, H.; deCatanzaro, D.; Remington, G. Escape performance following inescapable shock: Deficits in motor response maintenance. J. Exp. Psychol. [Anim. Behav. Proc.] 4:197–218; 1978.
3. Anisman, H.; Glazier, S. J.; Sklar, L. S. Cholinergic influences on escape deficits produced by uncontrollable stress. Psychopharmacology (Berlin) 74:81–87; 1981.
4. Brush, F. R.; Baron, S.; Froehlich, J. C.; Ison, J. R.; Pellegrino, L. J.; Phillips, D. S.; Sakellaris, P. C.; Williams, V. N. Genetic differences in avoidance learning by *Rattus norvegicus*: escape/avoidance responding, sensitivity to electric shock, and open field behavior. J. Comp. Psychol. 99:60–73; 1985.
5. Cierpial, M. A.; Simson, P. E.; Rankin, L. A.; Carpenter, M. D.; Scott, P. A.; Weiss, J. M. Selective breeding for high and low motor activity in a swim test: behavioral, electrophysiological and pharmacological effects. Soc. Neurosci. Abstr. 15(Part II):1176; 1989.
6. Ferguson, G. A. Statistical analysis in psychology and education. New York: McGraw-Hill; 1966.
7. Freda, J. S.; Klein, S. B. Generality of the failure to escape (helplessness) phenomena in rats. Anim. Learn. Behav. 4:401–406; 1976.
8. Glazer, H. I.; Weiss, J. M. Long-term and transitory interference effects. J. Exp. Psychol. [Anim. Behav. Proc.] 2:191–201; 1976.
9. Glazer, H. I.; Weiss, J. M. The long-term interference effect: An alternative to "learned helplessness." J. Exp. Psychol. [Anim. Behav. Proc.] 2:202–213; 1976.
10. Henn, F. A.; Johnson, J.; Edwards, E.; Anderson, A. Melancholia in rodents: Neurobiology and pharmacology. Psychopharmacol. Bull. 21:3; 1985.
11. Katz, R. J. Animal models of human depressive disorders. Neurosci.

Biobehav. Rev. 5:231–246; 1981.

12. Kirk, R. C.; Blampied, N. M. Transituational immunization against the interference effect (learned helplessness) by prior passive and active escape. Psychol. Rec. 36:103–214; 1986.
13. Kovachich, G. B.; Cierpial, M. A.; Aronson, C. E.; Frazer, A.; Weiss, J. M. Selective breeding of rats for high and low motor activity in a swim test: quantitative autoradiographic analysis of alpha-2 adrenoreceptors in the locus coeruleus. Soc. Neurosci. Abstr. 15(Part II):1175; 1989.
14. Maier, S. F.; Albin, R. W.; Testa, T. J. Failure to learn to escape in rats previously exposed to inescapable shock depends on nature of escape response. J. Comp. Physiol. Psychol. 85:581–592; 1973.
15. McKinney, W. T., Jr.; Bunney, W. E. Animal model of depression: Review of evidence and implications for research. Arch. Gen. Psychiatry 21:240–248; 1969.
16. Martin, P.; Soubrie, P.; Simon, P. Shuttle-box deficits induced by inescapable shocks in rats: Reversal by the beta-adrenoreceptor stimulants Clenbuteral and Salbutamol. Pharmacol. Biochem. Behav. 24:177–181; 1986.
17. Martin, P.; Soubrie, P.; Simon, P. Noradrenergic and opioid mediation of tricyclic-induced reversal of escape deficits caused by inescapable shock pretreatment in rats. Psychopharmacology (Berlin) 90: 90–94; 1986.
18. Miller, W. R.; Rosellini, A.; Seligman, M. E. P. Learned helplessness and depression. In: Maser, J. D.; Seligman, M. E. P., eds. Psychopathology: Experimental models. San Francisco: W. H. Freeman and Company; 1977:104–130.
19. Miller, N. E.; Weiss, J. M. Effects of somatic or visceral responses to punishment. In: Campbell, B. A.; Church, R. M., eds. Punishment and aversive behavior. New York: Appleton-Century-Crofts; 1969: 343–372.
20. Rosellini, R. A.; DeCola, J. P. Inescapable shock interferes with the acquisition of a low-activity response in an appetitive context. Anim. Learn. Behav. 9:487–490; 1981.
21. Rosellini, R.; Seligman, M. E. P. Frustration and learned helplessness. J. Exp. Psychol. [Anim. Behav. Proc.] 1:149–157; 1975.
22. Scott, P. A.; Cierpial, M. A.; Weiss, J. M. Selective breeding for susceptibility to the effects of uncontrollable shock. Soc. Neurosci. Abstr. 15(Part I):801; 1989.
23. Seligman, M. E. P.; Beagley, G. Learned helplessness in the rat. J. Comp. Physiol. Psychol. 88:534–541; 1975.
24. Seligman, M. E. P.; Rosellini, R. A.; Kozak, M. Learned helplessness in the rat: time course, immunization, and reversibility. J. Comp. Physiol. Psychol. 88:542–547; 1975.
25. Sherman, A. D.; Sacquitine, J. L.; Petty, F. Specificity of the learned helplessness model of depression. Pharmacol. Biochem. Behav. 16:449–454; 1982.
26. Weiss, J. M.; Glaser, L. A.; Pohorecky, L. A.; Brick, J.; Miller, N. E. Effects of chronic exposure to stressors on avoidance-escape behaviors and on brain norepinephrine. Psychosom. Med. 37:522–534; 1975.
27. Weiss, J. M.; Glazer, H. I.; Pohorecky, L. A. Coping behavior and neurochemical changes: An alternative explanation for the original "learned helplessness" experiments. In: Serban, G.; King, A., eds. Animal models in human psychobiology. New York: Plenum Press; 1976:141–173.
28. Weiss, J. M.; Kriekhaus, E. E.; Conte, R. Effects of fear conditioning on subsequent avoidance behavior and movement. J. Comp. Physiol. Psychol. 65:413–421; 1968.
29. Wieland, S.; Boren, J. L.; Consroe, P. F.; Martin, A. A stock differences in the susceptibility of rats to learned helplessness training. Life Sci. 39:937–944; 1987.
30. Willner, P. The validity of animal models of depression. Psychopharmacology (Berlin) 83:1–16; 1984.
31. Willner, P. Depression, a psychobiological synthesis. New York: John Wiley; 1985.