AN EVALUATION OF LEARNED HELPLESSNESS AS A MODEL OF DEPRESSION IN THE RAT

By

H. RYAN WAGNER II

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DISSERTATION

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AN EVALUATION OF LEARNED HELPLESSNESS

Title

AS A MODEL OF DEPRESSION IN THE RAT

H. Ryan Wagner II

Candidate

Psychology

Department

Richard Spolsky

Dean

December 4, 1975

Date

Committee

Chairman

Frank A. Logan

Eugene C. Palmer

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Abstract

H. Ryan Wagner II, Ph.D.
Department of Psychology
The University of New Mexico, 1975

Two experiments were conducted assessing the appropriateness of the learned helplessness paradigm as an animal (rat) analogue to states of clinical depression. Using decreases in appetitive and activity variables to functionally define depression, Experiment 1 assessed food consumption, water intake, weight gain, number of cage crossings, and shuttle avoidance learning in rats over an 18 hr interval immediately following exposure to a session of inescapable shock (IS). Control measures were obtained in nonshocked (NS) animals and in yoked counterparts subjected to equivalent amounts of escapable shock (ES).

Results showed significant decreases in appetitive functions and learning abilities of IS rats when compared against both shocked and nonshocked control groups. Furthermore, postshock treatment of the former group (IS) with electroconvulsive shock (ECS) or the tricyclic antidepressant compound desmethyl imipramine (DMI) effectively eliminated postshock differences on dependent variables between escapably and inescapably shocked rats. However, inspection of the data suggested the latter effect to primarily reflect a selective decremental influence of the antidepressants on appetitive functions in ES animals rather than an increase ("cure") of such deficits in IS rats.

Reasoning that failure to observe amelioration of the effects of IS through antidepressant manipulations in Experiment 1 may have been a function of their acute administration (whereas clinical applications of both ECS and the tricyclics involve repeated administrations), rats in Experiment 2 were subjected to a 12-day schedule of chronic DMI administration prior to shock exposure. In addition to providing a closer approximation to the therapeutic situation, this procedure, by housing rats in the test environment prior to shock, provided opportunity to compare postshock functions with a preshock baseline. Despite pretreatment on the chronic DMI regimen, differential postshock drug effects were not observed between ES and IS rats. More importantly, shock differentials were no longer apparent on appetitive measures in undrugged control animals.

Based on these findings, it is suggested that inescapable shock is inherently more stressful than equivalent amounts of escapable shock. Accordingly, IS rats have less tolerance for coping with subsequent stress situations than do their ES counterparts. Reinterpeting the results of Experiment 1 within this context, it is argued that the novelty of the postshock test was itself a source of stress, which, through interaction with the impaired coping abilities of IS animals, produced decremental effects on appetitive functions in the latter animals. In contrast, rats in Experiment 2, having been previously habituated to the postshock environment, were not stressed by such, and, consequently, failed to demonstrate differential shock effects. These findings argue against the viability of the learned helplessness paradigm as a model of depression in the rat.

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In 1967 Seligman and associates (Overmier & Seligman, 1967; Seligman & Maier, 1967) reported the presence of escape-avoidance deficits in mongrel dogs exposed to an a priori episode of inescapable shock. In this work, dogs, while suspended immobile in a sling, were subjected to a session of multiple shocks through electrodes affixed securely to their foot pads. When subsequently tested on a shuttle-avoidance task, such animals demonstrated impaired acquisition in comparison with both nonshocked control dogs (Overmier & Seligman, 1967; Seligman & Maier, 1967) and with dogs exposed to equivalent amounts of avoidable shock (Seligman & Maier, 1967). Initially, postshock learning impairments appeared to be a transient phenomenon, disappearing somewhere between 24 and 48 hr after exposure to stress (Overmier, 1968; Overmier & Seligman, 1967; Seligman, Maier & Geer, 1968). However, Seligman and Groves (1970) subsequently reported finding deficits in dogs tested as much as one week following exposure to inescapable shock. Moreover, dogs failing to acquire avoidance tasks during the initial poststress session continued to show impairment in such tasks upon retesting for periods of up to 25 days (Seligman et al., 1968). Interestingly, these latter deficits could be ameliorated by forced exposure of the animal to escape contingencies (Seligman et al., 1968).

After the manner of Rescorla (1967), Seligman has proposed that, during sessions of inescapable shock, dogs learn that shock onset and offset are independent of their responding. Formally, the conditional probability of the occurrence of an aversive event, given a response, is equal to the conditional probability of the occurrence of that event,

given no response. In a less rigorous vein, Seligman has suggested that, in fact, what an inescapably shocked animal learns in this situation is that it is helpless.

In addition to the above reports, learning deficits following episodes of uncontrollable aversive stimulation have been claimed across a variety of species including goldfish (Behrend & Bitterman, 1963; Padilla, Padilla, Ketterer, & Giacalone, 1970), cats (Seward & Humphrey, 1967), mice (Braud, Wepman, & Russo, 1969), chickens (Maser & Gallup, 1974), and man (Hiroto, 1974; Miller & Seligman, 1975; Thornton & Jacobs, 1971). Despite the apparent generality of the effect, initial attempts to demonstrate learned helplessness phenomena in the rat met with failure (Anisman, 1973; Weiss, Krieckhaus, & Conte, 1968). Recently, however, Maier's group (Maier, Albin, & Testa, 1973; Testa, Juraska, & Maier, 1974) not only conclusively demonstrated escape-avoidance deficits in rats following episodes of uncontrollable shock but was also able to relate previous failures in finding this effect to species- and task-specific variables.

Specifically, Maier found that rats tested in standard one-way and shuttle-avoidance tasks showed no deficits in acquisition of such tasks following sessions of inescapable preshock. Noting the failure of these animals to demonstrate learning increments over trials on such tasks, Maier proposed that the flight response required in both the one-way and shuttle-avoidance task was almost reflexive in the frightened rat and, consequently, limited learning opportunities. That is, rats respond almost instinctively to grid shock by running. On one-way and shuttle-avoidance tasks this often results in consistently

successful short latency responding from the first trial on. Despite high performance levels, rats in such situations may be slow to recognize contingencies between responding and shock offset. In this sense, simple shuttle tasks may sample performance rather than learning variables. Accordingly, Maier found that when shuttling was made more difficult (by requiring rats to shuttle to one side of the box and back again on a single trial), or when the coping response was of a less reflexive nature (e.g., bar pressing or turning of a wheel manipulandum), inescapable shock in rats did indeed produce learning impairments as compared against both unshocked control animals (Maier et al., 1973; Testa et al., 1974) and yoked control animals subjected to equivalent amounts of avoidable shock (Testa et al., 1974). Seligman's group has subsequently not only replicated helplessness effects in rats using a bar press escape task (Seligman & Beagley, 1975; Seligman, Rossellini, & Kozak, 1975), but also extended the paradigm by demonstrating a number of characteristics previously reported only in dogs including permanency of the effect (up to an interval of at least one week), immunization against preshock effects, and "cure" following a series of forced exposures to response contingencies (Seligman et al., 1975). While providing apparent resolution of previously reported inabilities to find helplessness effects in rats, these studies also caution against across-the-board application of the phenomenon without regard for species and task variables.

In addition to learning deficits, "helpless" animals have been reported to display subjectively different postshock behavior patterns. For example, Seligman (Overmier & Seligman, 1967; Seligman, 1974, pp. 24-25; Seligman et al., 1968) described considerable struggling

and vocalizing in dogs during initial periods of shock. In animals provided with coping contingencies against such shock, struggling and vocalizing gradually ceased as the animal began to master the task at hand, i.e., avoid shock. In contrast, inescapably shocked dogs appeared after the first few trials to give up and were commonly observed to sit and passively endure subsequent shock without further attempts at struggling or escaping. Moreover, such behavior generalized beyond the experimental environment. "Helpless" dogs, when approached prior to testing on the day following preshock, wilted, sunk to the bottom of their cages, assumed submissive postures, and presented little resistance at attempts to handle them. In marked contrast, dogs provided with preshock coping contingencies responded to subsequent handling in their home cages with considerable resistance and aggressive behavior.

From these basic data, Seligman has proposed that learned helplessness provides an animal analogue to states of clinical depression (Seligman, 1972, 1974). According to this formulation, an animal, when initially confronted with an aversive situation, responds with fear. If that animal subsequently learns that it has some control over its situation, fear dissipates. If it instead "realizes" that it has no control over that situation, fear is replaced by "depression" (Seligman, 1974, pp. 53-54). In his initial monograph, Seligman (1972) proposed the paradigm as an animal analogue to clinical states of reactive depression (i.e., depressions characterized by some identifiable precipitating event). However, in the more recent formulation (Seligman, 1974), the model has been broadened by the suggestion that both reactive and endogenous depressions, at least at a psychological level, share common elements. (Indeed, this position

reflects current lack of nosological agreement on depression. For instance, Kendell [1968] has proposed that reactive and endogenous depressions share bipolar positions on a unidimensional continuum running in increasing severity from the reactive to endogenous pole. Kiloh and Garside [1963] have argued in contrast that the two entities are independent and separate disease processes.)

While Seligman has presented a compelling case for the validity of his model, many of his arguments remain limited by a lack of systematic investigations between the behavior of "helpless" animals and observable clinical indices of depression. With that preface, the current work describes an evaluation of the viability of learned helplessness as an animal analogue of depression in the rat.

Prerequisite to this problem is the establishment of a functional definition outlining the overt manifestations of depression. Toward that end, decreases in both psychomotor activity and appetite (with correlated weight loss) not only are common to a variety of depressive disorders (Wittenborn, 1965) but also provide an easily measured set of behavioral correlates in the rat. Accordingly, it is proposed that a functionally depressed rat should demonstrate decreased levels of food consumption, water intake, weight gain, and number of cage crossings in the period following exposure to a session of inescapable shock (i.e., induction of "depression").

Of course, presence of the above syndrome is not by itself sufficient support for the existence of a "depressed" state; indeed, there exist a variety of disorders aside from depression which exhibit similar behavioral manifestations. Recognizing this problem, Seligman (1974 , p. 80) has himself suggested that validation of an animal model of a clinical state requires the demonstration of similarities

between that condition and its animal analogue along four relevant dimensions, i.e., physical manifestations of the disorder, etiology, prevention, and cure.

With specific attention to the fourth of these points, it follows that if inescapable shock does induce an analogous state of depression in the rat, then intervention into that state via standard antidepressant manipulations shown efficacious in the clinic should likewise prove effective in ameliorating behavioral indices of depression in inescapably shocked rats (at least to the extent that those indices reflect the existence of biological substrates analogous with those of the clinical condition). Hence, treatment of "depressed" rats with electroconvulsive shock (ECS) or the antidepressant tricyclic desmethyl imipramine (DMI) should predictably reverse decreases in dependent measures induced following exposure to an episode of inescapable shock. (Regarding the latter manipulations, ECS remains a highly efficacious tool in the treatment of depression [Fink, 1974]. Although its application is primarily indicated in cases of endogenous depression, it nevertheless has been reported to produce significant improvement in populations with diagnosed reactive depressions [Mendels, 1967; Rose, 1963]. Similarly, the tricyclic compounds are highly successful in antidepressant therapy. Like ECS, their use is most often indicated in endogenous/psychotic varieties of depression, although [again like ECS] clinical improvement has also been reported in diagnosed populations of reactive depressions [Klerman & Cole, 1965].)

While the helplessness position is consistent with a large body of data, the paradigm is nevertheless not without its critics. Regarding learning impairments, both Weiss (Weiss et al., 1968) and Anisman (Anisman & Waller, 1973) have demonstrated high correlations between

activity levels of rats during episodes of inescapable shock and subsequent rates of acquisition in avoidance learning. Weiss found this relationship to hold for activity measures obtained only during the presentation of a conditioned stimulus in preshock while Anisman has reported high correlations between activity and learning both during conditioned stimulus presentations and during the interstimulus interval (Anisman & Waller, 1971a, 1971b, 1972). Anisman has also shown similar relationships to hold during sessions of inescapable shock conducted without explicit conditioning stimuli (1971b).

Based on these findings, Weiss has suggested that the learning deficits seen following episodes of inescapable shock reflect a generalization of fear-induced freezing from the preshock session to the test situation (Weiss et al., 1968). In an extension of this position, Anisman (Anisman & Waller, 1973) has argued that inescapable shock increases probabilities of freezing in subsequent aversive situations and that it is this tendency to freeze rather than prior learning about experimental contingencies which provides sources of proactive interference during subsequent escape-avoidance testing. Borrowing from Bolles (1970), Anisman goes on to suggest that both freezing and flight in rats represent species-specific prepotent responses to aversive situations. Within this formulation, preshock affects subsequent performance by altering the probability of the occurrence of one or the other of these prepotent responses. Facilitation of escape-avoidance acquisition results when preshock encourages performance of a prepotent response compatible with the task at hand; conversely, performance decrements when the situation elicits a prepotent response incompatible with the required response (e.g., freezing during a shuttle-avoidance task). Learned helplessness,

if Anisman's position is correct, becomes nothing more than an artifact of the experimental situation. Accordingly, learning impairments should not occur in inescapably shocked animals if subsequent testing requires performance on tasks conducive to neither freezing nor flight. In this vein, it is important to note that recent reports claiming "helplessness" effects in the rat (Maier et al., 1973; Seligman & Beagley, 1970 ; Seligman et al., 197 ; Testa et al., 1974), all involve test procedures which facilitate development of freezing responses.

If, as reasoned by Weiss and Anisman, decrements in acquisition of avoidance tasks reflect differential amounts of fear, then manipulations which reduce fear should similarly improve acquisition. Toward that end, the current work examined avoidance acquisition in preshocked rats following the administration of a benzodiazepine antianxiety agent (Librium).

EXPERIMENT 1

Method

Subjects

Male albino rats (96) obtained from commercial suppliers were used in all conditions. Weights at time of testing were approximately 300 g.

Apparatus

Preshock was administered in galvanized steel boxes 23 cm in length and 8 cm wide fashioned after Weiss, Stone, and Harrell (1970). A turning wheel 14 cm in diameter and 5 cm in width was mounted at the front of each box while a Plexiglas lid provided for continuous observation. Shock was administered through metal plates affixed on each side of the center hole of a 4 cm Plexiglas ring designed to fit over the rat's tail. After applying electrode paste to the inside of each plate, the ring was slipped over the tail and taped in place. When securely affixed, the plate restricted movement of rats such that, when placed in the shock chamber, animals were facing toward the front with forepaws resting on the turning wheel. Sitting and turning in the experimental apparatus, while possible, were severely restricted. Shock intensity was maintained at 2 mA as delivered through a constant current stimulation unit (BRS). Shock onset and offset were automatically programmed to occur on a 1 min fixed interval schedule and to terminate after a wheel turn of the prescribed parameters or, in the event of no response, after 30 sec.

Escape-avoidance testing was conducted in standard shuttle boxes measuring 19 cm X 18 cm X 18 cm. Shock was passed through a floor

grid consisting of 3 mm stainless steel rods spaced at 1.5 cm intervals. Each compartment was separated by a divider with a 5 cm X 7 cm oval door at its center. A 12 V lamp located above each door was programmed to appear 5 sec before shock onset and to terminate with its offset. Scrambled shock was applied through 150 kΩ of fixed resistance (Campbell & Church, 1968) using a Foringer constant voltage source. Current was continually monitored to 1 mA with a step-down resistor connected in parallel to a storage oscilloscope.

Activity measures were obtained in standard holding cages which had been modified by the addition of a movable floor unit centered on a crosswise fulcrum. Movement of a rat to the front or rear of the cage caused a slight (3 mm) depression of the floor which activated a microswitch located just beneath the cage. Each switch was in turn connected to a bank of counters programmed to record the number of cage crossings over an 18 hr test interval. Food (Wayne Lab-Blox) was weighed prior to each session and placed in a feeding tray at the front of the activity cage. At the conclusion of the session, the remaining pellets, spillage, and residue were collected and reweighed to determine the amount of food consumed. Water was similarly available in calibrated drinking tubes located at the front of each cage. At the conclusion of the experiment, the tubes were removed and water intake was measured. Both food and water were available ad lib throughout this phase of the experiment.

Procedure

Upon receipt, rats were weighed and placed in individual housing. Groups of three rats were selected such that animals in a

given group differed by no more than 25 g. One group of three was randomly selected and deprived of food and water for 24 hr prior to experimentation. At the start of the session, rats in that group were affixed with tail electrodes and placed in the preshock device located in a sound-attenuating chamber. At this point each animal was assigned by random procedure to one of three preshock conditions as follows:

1. Group ES rats (escapable shock) were given standard escape training. At shock onset it was possible for rats in this condition to terminate shock by turning the wheel manipulandum. Initially, escape parameters required one-half turn of the wheel. Following a minimum of 30 consecutive escape responses, criterion was raised one-half turn. The session continued until all animals had reached a minimum criterion of 2½ turns. At the start of each shock session and after increases in criterion level, it was often necessary to shape responding. In general, this entailed a brief increase in current intensity. Typically, after a few trials with this procedure escape responding appeared (or resumed) at short latency. All animals reached criterion within approximately 6 hr.

2. Group IS rats (inescapable shock) were connected in series with ES rats insuring that both animals received equivalent amounts of current. However, IS rats, unlike their yoked counterparts, were not able to terminate shock themselves and consequently continued to receive current until their ES partner responded or until 30 sec had elapsed. Thus, shock offset remained controlled by the performance of the ES animal. Some pseudoconditioning was evident in IS rats although this usually dropped out as criterion for the ES animal increased.

3. Group NS rats (nonshock) were weighed, affixed with electrodes, and placed into the preshock device in the same manner as IS and ES animals and remained there for the duration of the preshock session. However, in contrast to the former two groups, NS animals at no time received shock. Responding by NS rats, while possible, was minimal with such animals generally preferring to curl up in the experimental chamber in a resting position.

Following termination of this portion of the experiment, all rats were removed from the shock chamber, reweighed, and placed in holding cages for a period of 30 min. Following this, the entire group was randomly assigned to one of four postshock conditions as follows:

1. Group C rats (control) were removed from holding cages, injected with isotonic saline (2 ml, ip) and placed back in their holding cages for an additional 30 min. Following this, animals were again removed from holding cages and placed directly into activity cages for the next 18 hr. This was done at the beginning of the dark phase of the animals' normal 12 hr diurnal cycles. At the end of 18 hr, all rats in this group were removed from their cages and measures were obtained on food and water intake, weight gain, and number of cage crossings for the 18 hr postshock period. All three animals were then given 40 trials of escape-avoidance training after the method of Maier et al. (1973).

Briefly, each rat received five initial trials of standard shuttle-avoidance training. Movement of the animal to the opposite compartment at any time after the onset of a 5 sec conditioned stimulus (light onset) precluded shock onset. If an avoidance response did not occur during this period, the animal was able to terminate the ensuing shock by performance of the same response. If

an animal failed to respond within 30 sec after shock onset, the trial was automatically terminated and a latency to respond of 35 sec was recorded. After five trials under these conditions, response requirements were increased such that escape or avoidance was now contingent on the performance of a shuttle response to the opposite compartment with subsequent return (fixed ratio-2; Maier et al., 1973). An additional 35 trials were conducted under these contingencies with response latencies recorded for each trial. All other conditions remained the same.

2. Group DMI rats (desmethyl imipramine) were treated identically to C animals with the single exception that all rats in this group, upon removal from their holding cages, received an injection of the tricyclic compound desmethyl imipramine (20 mg/kg, ip). Following this, DMI animals were returned to their holding cages for an additional 30 min whereupon they were transferred to activity cages for postshock analyses and escape-avoidance training as described above.

3. Group ECS rats (electroconvulsive shock) were removed from holding cages after 30 min and given a single treatment of electroconvulsive shock (50 mA dc administered by Grass stimulator and constant current unit through alligator clips affixed across the ears). This procedure consistently produced full-blown tonic-clonic seizures of approximately 30 sec duration. Following this, ECS rats were returned to holding cages for 30 min and thereafter transferred to activity cages as described above.

4. Group LIB rats (Librium) were removed from holding cages, handled, and returned to their cages for an additional 30 min after which they were transferred to activity cages as described above.

Eighteen hr later, LIB animals were removed, injected with the benzodiazepine compound chloradiazepoxide hydrochloride (Librium, 5 mg/kg, ip) and placed in holding cages for an additional 3 hr. Thereafter, escape-avoidance testing was conducted as described above.

Results

Appetitive and Activity Measures

Orthogonal planned comparisons were conducted for simple treatment effects both over levels of therapeutic manipulation (C - DMI; C - ECS; DMI - ECS) and over levels of shock conditions (NS - ES; NS - IS; ES - IS). In the case of group C, no significant differences were found between saline-injected and LIB animals (the latter were injected with a benzodiazepine agent just prior to avoidance testing) on dependent measures (food: $F[1,46] = 1.21$, $p > .50$; water: $F[1,46] < 1$, $p > 75$; weight gain: $F[1,46] > 1$, $p > .50$; cage crossings: $F[1,46] = 1.14$, $p > .50$). Accordingly, data from both groups were combined to form a pooled control group for use in subsequent analyses; all tests on the latter data were conducted using adjusted unweighted means (Winer, 1967, pp. 402-404). Additional planned comparisons were carried out contrasting the effects of shock conditions (NS - ES; NS - IS; ES - IS) within each level of therapeutic treatment condition and on the effects of therapeutic treatments (C - DMI; C - ECS; DMI - ECS) within each shock level. As the latter comparisons generally involved sufficiently large sample sizes, estimates of error variability were taken from the particular level under analysis (Winer, 1967, pp. 387-388).

Experimental shock effects (NS - ES; NS - IS; ES - IS) --simple effects across therapeutic treatment conditions (C + DMI + ECS).

Figure 1a shows the effects of shock on dependent variables irrespective of therapeutic treatment conditions. In general, exposure to experimental shock produced one of two effects, i.e., a general decremental effect uninfluenced by the nature of the shock (whether it was escapable or inescapable) and a more specific decremental effect associated exclusively with inescapable shock. Across all levels of therapeutic treatment conditions, a general shock effect was apparent for both food consumption and level of activity. Specifically, food intake in both shock conditions (ES and IS) was significantly decreased below NS control levels (ES: $F[1,93] = 13.95$, $p < .001$; IS: $F[1,93] = 22.48$, $p < .001$) while differences between the former two groups (ES - IS) remained nonsignificant ($F[1,93] < 1$, $p > .50$). Similarly, number of cage crossings was reliably decreased over control values by both ES ($F[1,93] = 17.13$, $p < .001$) and IS ($F[1,93] = 16.87$, $p < .001$) with differences arising between the latter two groups (ES - IS) again nonsignificant ($F[1,93] < 1$, $p > .50$). Water consumption and weight gain, in contrast, demonstrated significant decreases only in experimental groups exposed to conditions of inescapable shock (water: $F[1,93] = 8.18$, $p < .01$; weight gain: $F[1,93] = 10.02$, $p < .005$). No significant differences on these latter two variables were found between control and ES animals nor between ES animals and their yoked (IS) counterparts.

Weight loss during shock showed a general shock effect with both ES ($F[1,93] = 27.4$, $p < .001$) and IS ($F[1,93] = 11.2$, $p < .005$)

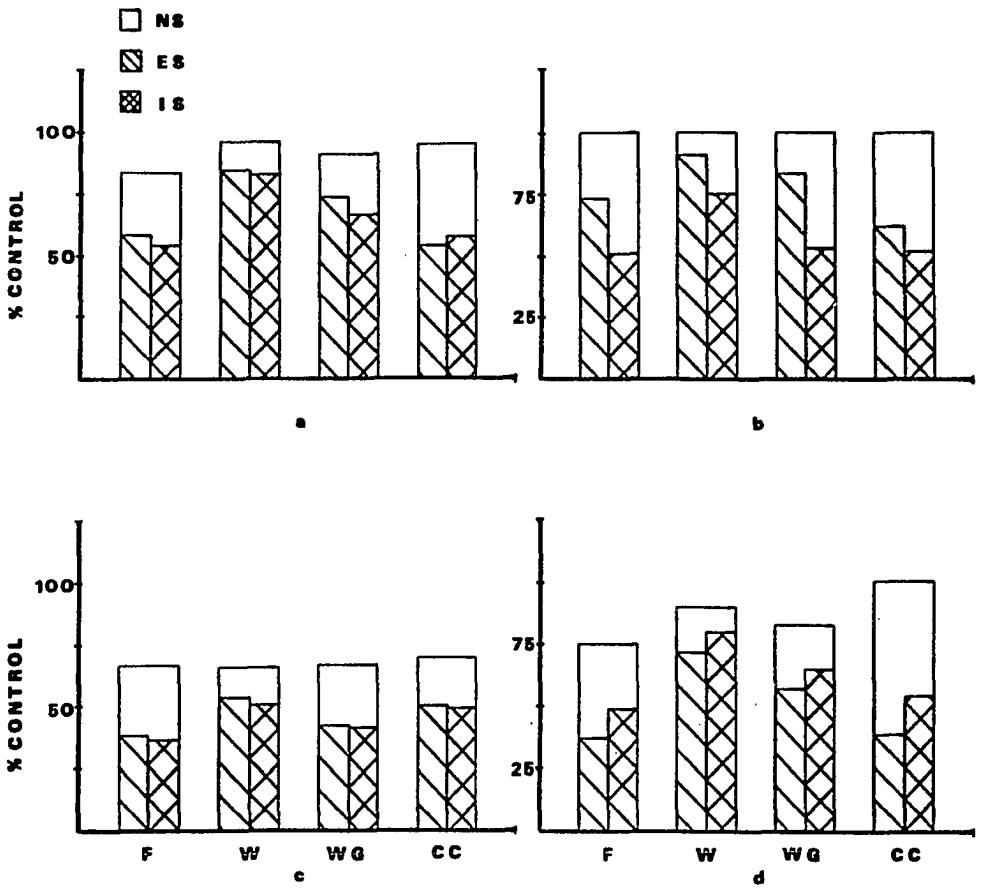

Figure 1. Effects of NS, ES, and IS on appetitive and activity measures (a) across all levels of therapeutic treatments, (b) in control animals, (c) in DMI-injected rats, and (d) in ECS animals. All measures are expressed as percent NS control values.

significantly reduced below NS levels. Differences between the former two groups did not reach significance ($F[1,93] = 3.56$, $p < .10$).

Experimental shock effects within therapeutic treatment conditions (Control). The effects of inescapable shock on dependent measures is clearly seen in Figure 1b. Specifically, appetitive measures in the control (saline + Librium) condition, displayed highly specific effects to inescapable shock. Food consumption, water intake, and correlated weight gain were all significantly reduced by inescapable shock below control values ($F[1,45] = 22.96$, $p < .001$; $F[1,45] = 13.01$, $p < .001$; $F[1.45] = 12.13$, $p < .005$, respectively). More importantly, appetitive measures in IS animals were also significantly reduced ($F[1,45] = 4.68$, $p < .05$; $F[1,45] = 4.37$, $p < .05$; $F[1,45] = 4.89$, $p < .05$, respectively) below levels obtained in animals exposed to similar amounts of escapable shock (ES - IS). On the other hand, only food intake was significantly reduced by exposure to escapable shock in comparison with NS control values ($F[1,45] = 6.91$, $p < .025$).

Activity measures, in contrast to appetitive functions, showed only a general shock effect at the control level with statistically reliable decreases in number of cage crossings below NS values noted for both ES ($F[1,21] = 7.97$, $p < .01$) and IS ($F[1,21] = 11.06$, $p < .005$) groups; differences between the latter two groups (ES - IS) remained nonsignificant ($F[1,21] < 1$, $p > .25$).

Experimental shock effects within therapeutic treatment conditions (DMI). DMI-evoked change on the effects of shock on dependent measures is shown in Figure 1c. Specifically, the pattern of Figure 1b was only partially altered by antidepressant intervention. Both food intake and weight gain continued to show significant reductions below

NS control values in the IS condition despite DMI treatment ($F[1,21] = 4.53$, $p < .05$; $F[1,21] = 8.15$, $p < .01$). However, differences in the latter measures no longer existed between escapably and inescapably (ES - IS) shocked groups ($F[1,21] < 1$, $p > .25$; $F[1,21] = 1.88$, $p > .10$). Moreover, DMI was found to eliminate all differences between treatment levels for both water intake and number of cage crossings.

Experimental shock effects within therapeutic treatment conditions (ECS). ECS-evoked change on the effects of shock on dependent measures is seen in Figure 1d. Effects following administration of a single session of ECS were even more pronounced than above. Specifically, the latter treatment eliminated virtually all differentials in appetitive measures between shock treatment levels (with the single exception of food consumption in the ES group which remained significantly below NS control values ($F[1,21] = 4.92$, $p < .05$). Despite this, a general shock effect remained apparent in activity in the ECS condition with number of cage crossings significantly decreased below NS control values by both ES ($F[1,21] = 8.57$, $p < .01$) and IS ($F[1,21] = 4.58$, $p < .05$).

In summary, inescapable shock was generally found to produce a selective decrease in appetitive functions below both corresponding NS control levels and below levels obtained in animals exposed to equivalent amounts of escapable shock. Activity, on the other hand, while decreased by shock, was not differentially affected by the type of shock (ES vs. IS). Both DMI and ECS were in varying degrees, capable of altering this pattern. Specifically DMI, while not completely eliminating the effects of inescapable shock, nevertheless

eliminated all differentials between escapably and inescapably shocked animals (thus suggesting that only a general shock effect remained). ECS was even more striking in this respect and effectively eliminated virtually all shock differentials in appetitive measures including general shock effects. In both cases, elimination of ES - IS differentials appeared to occur primarily through a selective decremental effect of antidepressant agents on appetitive functions in escapably shocked animals (compare Figures 1c and 1d with Figure 1b).

Therapeutic treatment effects (C - DMI; C - ESC; DMI - ECS)-- simple effects across experimental shock conditions (NS + ES + IS). Figure 2a shows the nonspecific decreases produced by antidepressant manipulations on dependent measures. Of the two manipulations, DMI produced the most pronounced effects on dependent measures. Summing over all levels of shock, DMI generated significant decreases in all appetitive variables in comparison with nondrug control levels (food: $F[1,93] = 10.37$, $p < .005$; water: $F[1,93] = 27.91$, $p < .001$; weight gain: $F[1,93] = 7.00$, $p < .01$). ECS in contrast, while significantly decreasing food consumption ($F[1,93] = 4.54$, $p < .05$), failed to significantly alter either water intake ($F[1,93] = 1.05$, $p > .50$) or weight gain ($F[1,93] < 1$, $p > .50$) over comparable control levels. In comparing between the two treatments (DMI - ECS), only water consumption in the DMI treated animals was reliably reduced below intake levels in ECS rats ($F[1,93] = 18.14$), $p < .001$). Neither experimental treatment was found to produce a significant difference in activity in comparison with control animals (C - DMI: $F[1,93] = 1.24$, $p > .50$; C - ECS: $F[1,93] < 1$, $p > .50$).

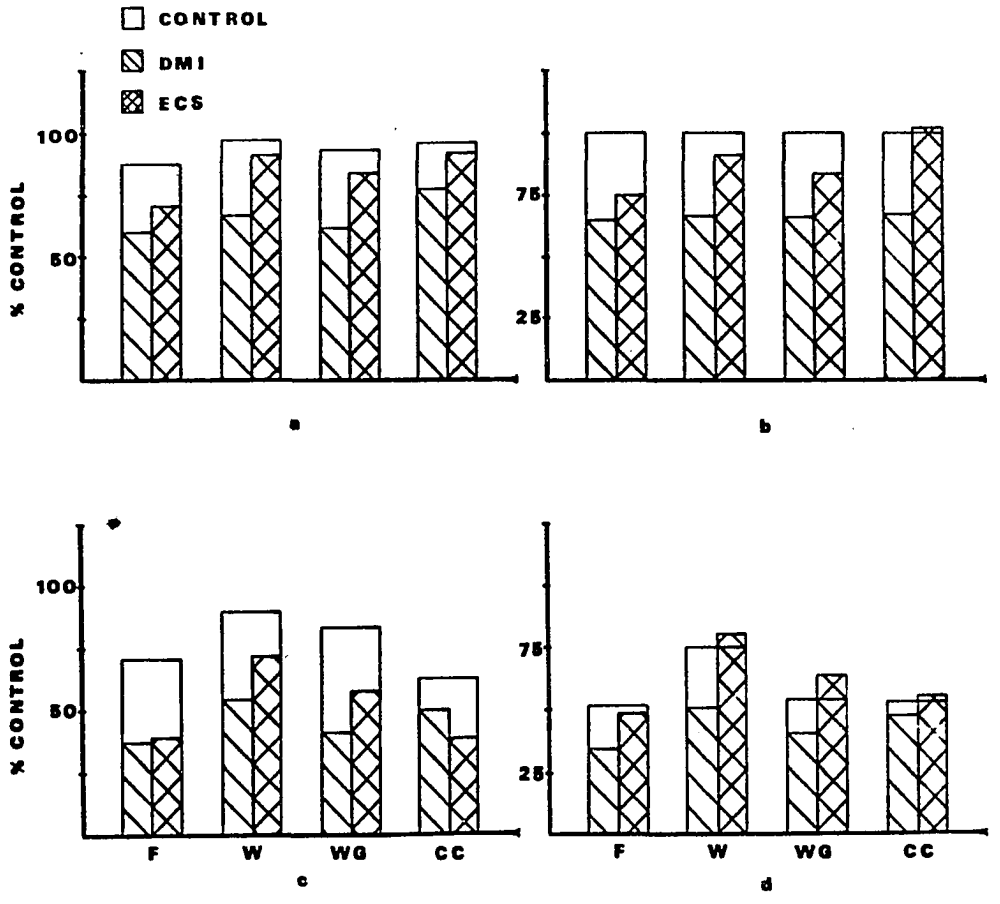

Figure 2. Effects of therapeutic treatments on appetitive and activity measures (a) across all levels of experimental shock, (b) in NS animals, (c) in ES rats, and (d) in animals given IS. All measures are expressed as percent NS control values.

Therapeutic treatment effects within experimental shock conditions (NS). Effects of DMI and ECS on dependent measures can be seen by examining their effects on unshocked animals in Figure 2b. Specifically, DMI produced significant reductions in both food intake and water consumption ($F[1,29] = 5.21$, $p < .05$; $f[1,29] = 10.22$, $p < .005$) as compared with undrugged (C) rats. ECS at the same shock level failed to generate reliable reductions in any appetitive measure. (In fact, water consumption in the DMI group was significantly reduced below levels displayed by ECS animals ($F[1,29] = 6.78$, $p < .025$).)

Therapeutic treatment effects within experimental shock conditions (ES). The selective effects of antidepressant manipulations on escapably shocked animals is apparent in Figure 2c. Specifically, both water intake ($F[1,29] = 18.78$, $p < .001$) and weight gain ($F[1,29 = 6.78$, $p < .025$) were significantly reduced by DMI below nondrug control levels. Water consumption was also significantly reduced by DMI below ECS intake levels in the ES condition ($F[1,29] = 7.94$, $p < .01$). As above, no significant effects on activity were noted for either antidepressant treatment (C - DMI: $F[1,29] = 4.03$, $p > .10$; C - ECS: $F[1,29] = 1.07$, $p > .50$).

Therapeutic treatment effects within experimental shock conditions (IS). Figure 2d shows the inability of antidepressant agents to alleviate ("cure") shock effects in helpless animals. In this regard, water consumption in DMI treated rats was significantly reduced below both nondrug control levels ($F[1,29] = 5.63$, $p < .025$) and levels displayed by ECS animals ($F[1,29] = 7.94$, $p < .01$). No other differences in appetitive or activity measures obtained significance, an outcome which reflects the decremental effects of antidepressant manipulations

(compare Figure 2d with Figures 2b and 2c) on appetitive functions in NS and ES rats.

In summary, DMI effected a selective decrease in food and water intake in NS control conditions. A similar effect was seen for ECS although in most cases reductions generated by the latter manipulation remained nonsignificant in comparison with nondrug control levels. Differences in the level of activity remained nonsignificant regardless of therapeutic manipulation or level of shock applied.

Analyses of Learning Effects

Planned orthogonal comparisons were conducted for simple treatment effects both over shock conditions (NS - ES; NS - IS; ES - IS) and therapeutic conditions (C - DMI; C - ECS; C - LIB). Further analyses were conducted for differential shock effects within each level of therapeutic treatment. As preliminary work had shown differential shock effects only during the latter part of avoidance training, all analyses were conducted over mean scores generated over the final four blocks (trials 21-40) of avoidance training.

Experimental shock effects NS - ES; NS - IS; ES - IS--simple effects across therapeutic treatment conditions (C + DMI + ECS + LIB). As is apparent in Figure 3a, exposure to shock, when considered irrespective of therapeutic manipulation, slowed avoidance learning. Specifically, latency scores were reliably increased by both ES ($F[1,93] = 6.51$, $p < .025$) and IS ($F[1,93] = 18.80$, $p < .001$) over NS levels while differences between the former two groups (ES - IS) remained nonsignificant ($F[1,93] = 3.18$, $p > .10$). This overall pattern was characteristic of a general shock effect.

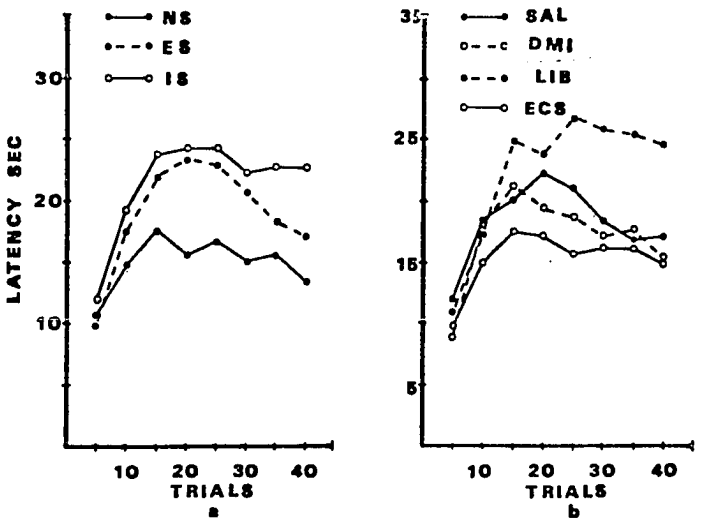

Figure 3. Effects on avoidance learning of (a) experimental shock across all conditions of therapeutic treatments, and (b) therapeutic treatments across all conditions of experimental shock.

Experimental shock effects within therapeutic treatment conditions (C). Figure 4a clearly illustrates the impaired learning of inescapably shocked rats in the control condition. Specifically, IS rats were significantly slower to escape-avoid than NS ($F[1,21] = 14.36$, $p < .005$) and ES ($F[1,21) = 8.31$, $p < .01$) counterparts. Moreover, significant differences were not found between the latter (NS - ES) two groups ($F[1,21] < 1$, $p > .50$) thus pointing up a selective deficit in escape-avoidance acquisition in inescapably shocked rats.

Experimental shock effects within therapeutic treatment conditions (LIB). The inability of the antianxiety agent (Librium) to eliminate the effects of inescapable shock on avoidance learning is seen in Figure 4b. Although generally slowed by drug injection at all shock levels (Figure 3b), IS animals nevertheless remained significantly slower in comparison with NS ($F[1,21] = 8.18$, $p < .01$) and ES ($F[1,21] = 6.41$, $p < .025$) groups; differences between the latter two groups (NS - ES) again remained nonsignificant ($F[1,21] < 1$, $p > .50$).

Experimental shock effects within therapeutic treatment conditions (DMI and ECS). Figures 4c and 4d in contrast show the elimination of avoidance deficits by both ECS and DMI. Specifically, groups treated with either antidepressant agent failed to show selective deficits in the IS condition. In this regard, ECS rats did not differ significantly between any experimental shock condition. Similarly, DMI rats did not differ significantly between NS and IS groups although a specific decremental drug effect was observed for ES rats relative to the other two groups (NS - ES: $F[1,21] = 12.89$, $p < .005$; ES - IS: $F[1,21] = 7.71$, $p < .025$).

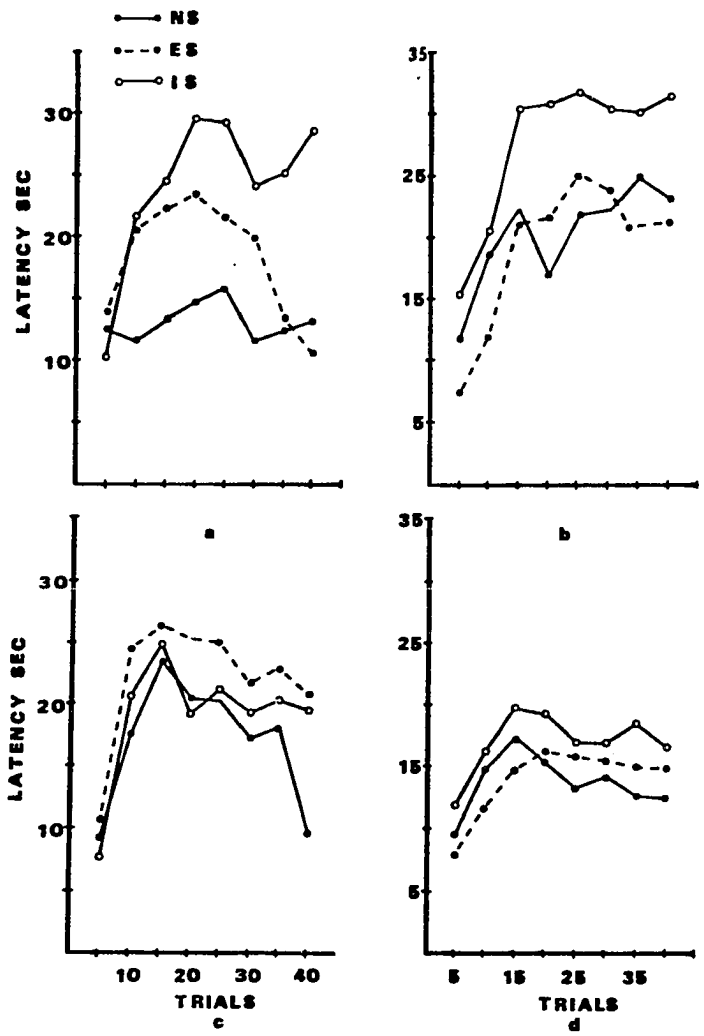

Figure 4. Effects on avoidance learning of (a) SAL, (b) LIB, (c) DMI, and (d) ECS.

Thus, inescapable shock systematically increased shuttle avoidance latency in undrugged control animals relative to both nonshocked and escapably shocked counterparts. Pretreatment with a benzodiazepine antianxiety agent, while increasing latency in all shock treatment groups, nevertheless failed to eliminate the selective effects of IS on avoidance acquisition. In contrast, escape-avoidance latency of inescapably shocked rats in ECS and DMI groups was not significantly different from NS control levels.

Therapeutic treatment effects (C - DMI; C - ECS; C - LIB)--simple effects across experimental shock conditions (NS + ES + IS). Figure 3b clearly illustrates the detrimental effect of Librium on avoidance learning irrespective of the level of shock. Specifically, over all conditions of shock, LIB rats were significantly slower on latency measures ($F[1,92] = 13.66$, $p < .001$) in comparison with nondrugged control animals (Figure 4b). In contrast, animals receiving antidepressant agents were slightly facilitated by such treatments although effects were not significantly different from control levels (C - DMI: $F[1,92] < 1$, $p > .50$; C - ECS: $F[1,92] = 2.96$, $p > .10$). No further comparisons were conducted at this level nor between therapeutic treatment conditions within levels of experimental shock.

Correlational Analyses

As can be seen in Table 1, significant correlations existed between all appetitive measures. Specifically, food consumption correlated highly with both water intake ($r = .53$, $p < .001$) and weight gain ($r = .56$, $p < .001$); relationships between the latter two variables was higher yet ($r = .89$, $p < .001$). Correlations between

appetitive functions and number of cage crossings, while not as pronounced, were, nevertheless, significant (food intake: $r = .37$, $p < .001$; water intake: $r = .44$, $p < .001$; weight gain: $r = .42$, $p < .001$). Significant correlations were also found between weight loss during experimental shock and both appetitive and activity variables (food intake: $r = .28$, $p < .05$; water intake: $r = .33$, $p < .001$; weight gain: $r = .27$, $p < .05$; cage crossings: $r = .36$, $p < .001$). Finally, correlations of the above variables with shuttle latency measures in all cases failed to reach significance at $p < .05$.

Discussion

Differential shock effects on appetitive measures were generally consistent with prior findings in this area. Food consumption, water intake, and correlated weight gain were all significantly decreased by exposure to inescapable shock in comparison with both nonshocked animals and with yoked counterparts exposed to equivalent amounts of escapable shock (the latter rats differed significantly from NS animals only in amount of food consumed). In contrast, motor activity appeared to be a relatively insensitive gage of ES - IS differentials as reflected by significant decreases in the number of cage crossings for both IS and ES groups relative to NS controls (with the difference between the former two groups remaining nonsignificant).

Intervention with antidepressant agents produced only a partial alteration of the above pattern. Specifically, DMI successfully eliminated ES - IS differentials on appetitive measures (although IS animals remained significantly below NS controls on all such measures). ECS was even more effective in this regard and eliminated differentials

between all shock conditions. In almost every case, these effects did not result from increases in consumption levels in IS animals but rather from a decrease in such functions in NS and/or ES control groups (see Figures 1b, 1c, and 1d).

Unfortunately, these findings fail to clarify the etiology of ES - IS differentials. Decreased appetitive functions are equally well accounted for by postulated stress differentials between escapable and inescapable shock or by induction of a condition of depression. Antidepressant manipulations, while removing shock differentials, appeared to do so by preferentially affecting dependent measures in control animals rather than through any selective increase ("curing") of such functions in the IS condition. From the latter data, it can be argued on the one hand that the differential effects of the antidepressants on control (NS and ES) animals reflects interaction of such agents with an analogous state of depression in IS rats. In this regard, different responses obtain between depressed and nondepressed subjects to both ECS and the tricyclics (DiMascio, Heninger, & Klerman, 1964; Fink, 1974; Poldinger, 1963). Alternatively, it may follow that responses to the antidepressants are limited in appetitive functions of inescapably shocked rats through a "basement" effect. In support of this latter possibility, consumption levels of ES rats in most cases were observed to undergo a decrease down to approximately equivalent IS levels. In any event, the inability of Experiment 1 to clarify the above issues suggests the need for further experimentation.

Table 1

Correlation Matrix:

Experiment 1

	Food Intake	Water Intake	Weight Gain	Cage Crossings	Shock Weight Loss	Shuttle Latency
Food Intake	1.0	.53**	.56**	.37**	.28*	.02
Water Intake	.53**	1.0	.89**	.44**	.33**	-.05
Weight Gain	.56**	.89**	1.0	.42**	.27*	-.08
Cage Crossings	.37**	.44**	.42**	1.0	.36**	-.06
Shock Weight Loss	.28*	.33**	.27*	.36**	1.0	.13
Shuttle Latency	.02	-.05	-.08	-.06	.13	1.0

* $p < .05$

** $p < .001$

EXPERIMENT 2

Therapeutic efficacy of both ECS and the tricyclic compounds in clinical settings appears only after several treatments. Similarly, differential effects of the tricyclics obtain in the rat following episodes of acute and chronic administration (Schildkraut, Winokur, Draskoczy, & Hensle, 1971). Accordingly, failure in Experiment 1 of antidepressant manipulations to ameliorate the effects of inescapable shock on rats may have been simply a function of their acute (one-time) application.

Experiment 2 was thusly designed to assess the effects of one of these agents (DMI) on appetitive measures in inescapably shocked rats following a sequence of chronic treatment. In addition to giving a much closer approximation to clinical applications, this design also provided opportunity to examine the extent and magnitude of ES - IS differentials in rats habituated to the experimental environment prior to shock administration. Relevance of the latter point relates to the demonstrated stressor qualities of novelty on rats (Levine, 1965; Moyer, 1965) on appetitive functions. In fact, the latter works suggest that differential effects of IS on appetitive functions reported in Experiment 1 may simply reflect an impairment in the ability of such animals to cope with subsequent stress situations. Accordingly, to the extent that preadaptation eliminates the stress (novelty) characteristics of the test situation, ES - IS differentials should also be eliminated.

Method

Subjects

Male albino rats (28) obtained from commercial suppliers were used in all conditions. Weights at the beginning of testing were approximately 300 g. All rats were maintained in individual housing throughout all phases of the experiment.

Apparatus

Equipment remained as described in Experiment 1.

Procedure

Prior to testing, rats were separated into weight-matched pairs with a maximum difference of 25 mg between rats in any one pair and then separated into two equivalent groups of seven pairs each. Rats in experimental conditions were subjected to daily injections (15 mg/kg, ip) of desmethyl imipramine (DMI) for 12 consecutive days; control animals received equivalent injections of isotonic saline (2 ml). During Day 1 through Day 5 of this sequence, animals remained in colony housing. Subsequently, on Day 6 a pair of weight-matched animals was removed and placed in activity cages where measures were taken for the remainder of the injection sequence on food consumption, water intake, weight gain, and number of cage crossings. To control for handling and deprivation effects, each pair of rats was removed daily from activity cages in the morning and placed in holding cages for a 7 hr period whereafter they were returned to activity cages. On the morning of Day 12, the pair was removed as usual and placed in the shock apparatus. One member of each pair was randomly assigned to the ES condition and the second to the IS group

(as the basic interest in Experiment 2 was between differential effects of escapable and inescapable shock, no nonshock group was run). Following completion of the shock sequence (as described in Experiment 1), animals were removed, injected, and returned to activity cages for assessment of appetitive and activity functions over the next 18 hr. Avoidance learning was not evaluated in Experiment 2.

Results

Difference scores for all dependent measures were obtained by subtracting postshock measures from the mean score of the corresponding preshock measure as computed from levels obtained on the three days immediately prior to shock, i.e., difference score = $\left[\left[(\text{Day } 9 + \text{Day } 10 + \text{Day } 11)/3\right] - \text{Day } 12\right]$. In this regard, preliminary work had indicated that dependent measures were initially depressed upon placement in activity cages (Figure 5) and that such measures increased to stabilized levels within three days of habituation. Consequently, only data from the three days immediately prior to shock exposure were used in computing baseline data. It was hoped that difference scores would provide a more sensitive metric of shock differentials than the between-groups comparisons of postshock scores analyzed in Experiment 1.

Subsequently, orthogonal planned comparisons were conducted for shock effects (ES - IS) within each therapeutic condition and for therapeutic effects (C - DMI) within each shock condition. In no case did any of these sixteen comparisons reach significance at the $p < .05$ level (Figure 6a). More precisely, nonsignificant differences were found for shock effects (ES - IS) in both saline-treated groups and in DMI-injected animals. Similarly, nonsignificant differences obtained for drug effects (C - DMI) irrespective of shock level. These patterns

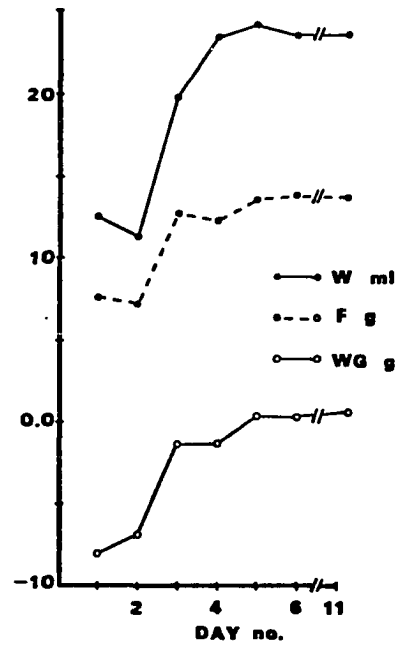

Figure 5. Preliminary data showing the recovery of appetitive functions following initial placement of rats into test cages (n = 6).

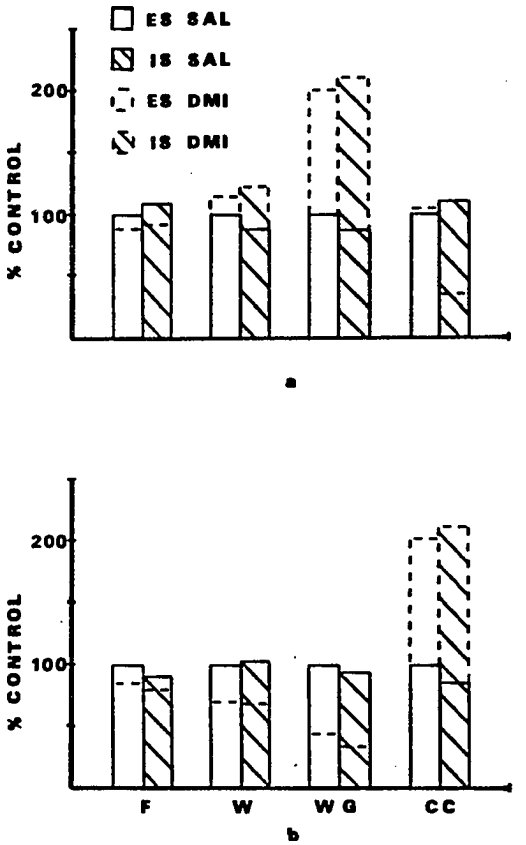

Figure 6. Effects of SAL and DMI on appetitive and activity measures in ES and IS rats of Experiment 2 as reflected in (a) preshock-postshock difference scores, and (b) postshock measures only. All values are expressed as percent ES-SAL values.

held for all dependent measures including food consumption, water intake, weight gain, and number of cage crossings.

Because of the considerable divergence of these findings from the pattern of results displayed in Experiment 1, a post hoc analysis based only on postshock scores (i.e., the dependent measures of Experiment 1) was conducted to determine if findings reflected some manner of measurement artifact. As above (Figure 6b), outcomes on the latter measures failed to indicate the existence of a significant shock effect (ES - IS) within either the control (saline) or drug (DMI) condition. However, treatment effects now appeared for drug condition (C - DMI) with both water intake ($F(1,24) = 8.80$, $p < .01$) and weight gain ($F(1,24) = 5.39$, $p < .05$) significantly decreased by DMI regardless of shock condition. Conversely, number of cage crossings in DMI animals showed a significant increase over saline-treated controls ($F(1,24) = 8.75$, $p < .01$), again irrespective of level of shock. Thus, chronic DMI treatment produced significant decreases in both water intake and weight gain and a significant increase in level of activity. Despite this, no differentials on appetitive measures were observed between ES - IS shock conditions in control animals nor were any differential drug effects evident between escapably and inescapably shocked animals.

Discussion

Failure to obtain a differential shock effect on dependent measures between saline-treated control animals in Experiment 2 contrasts sharply with the outcome of Experiment 1 and suggests habituation to the experimental environment as a critical component of shock-related effects. Precisely, inescapable shock appears to

create stress differentials which lead to impairment in the ability to cope with subsequent stressors. Indeed, Weiss (Weiss, Glazer, & Pohorecky, 1974) has posed a similar suggestion following demonstrations of avoidance deficits only on tasks requiring strenuous motor activity after a period of swim stress (rats performing on avoidance tasks requiring minimal amounts of physical efforts did not show deficits). In the present experiments, stress differentials became manifest in animals confronted with adaptation to a novel situation but not in rats previously adapted to that same environment. The data of Experiment 2 both support the above position and are consistent with prior reports describing increased stress indices in rats during exposure to novelty (indeed, appetitive functions were consistently depressed following initial transfer of animals to activity cages [Figure 5] in Experiment 2).

Experiment 2 also failed to provide evidence of differential drug effects between ES and IS following a two-week schedule of daily injections of DMI. Specifically, DMI-treated rats, after exposure to an episode of inescapable shock, showed no evidence of differential drug responses along measured dimensions from escapably shocked counterparts. To the extent that inescapable shock is able to induce biological substrates analogous with those underlying clinical depression, DMI should have been efficacious in modifying that substrate. Experiment 2 provided no support for such a process and strongly suggests that inescapably shocked rats, although differentially stressed by their experience, are not in an analogous state of depression.

GENERAL DISCUSSION

Taken together, the present findings fail to support suggestions (Seligman, 1972, 1974) proposing the learned helplessness paradigm as an animal model of clinical depression in the rat. Conversely, results are consistent with the development of a differential stress syndrome arising from the inherently more severe characteristics of inescapable shock (Weiss, 1968, 1971a, 1971b, 1971c).

A variety of observations support this conclusion. Inescapable shock was observed to produce a consistent and significant decrease in all appetitive measures in contrast to both unshocked rats and to yoked animals exposed to equivalent amounts of escapable shock. Most importantly, this effect was strikingly eliminated by a simple preadaptation procedure designed to habituate animals to the experimental environment prior to shock exposure. This suggests, as pointed out above (see Discussion--Experiment 2), that the stress of novelty is itself a requisite and necessary factor in the demonstration of ES - IS differentials. In fact, previous reports have described similar relationships between appetitive functions and stress. Both water (Amsel, 1950; Levine, 1957, 1958, 1965; Moyer, 1965; Weiss, 1968, 1970a; Weiss, Stone, & Harrell, 1970) and food consumption (Mowrer & Viek, 1948; Weiss, 1968, 1970a; Weiss et al., 1970) have been decreased following exposure to inescapable shock. In this regard Moyer (1965) and Levine (1965) have related consummatory behavior in novel situations to a complex interaction encompassing both history of prior stress and experimental novelty. Of particular relevance to the present work are their findings describing elimination

of novelty-induced decreases in water consumption following habituation of rats to drinking cages.

The observed effects of habituation on appetitive variables also argue strongly against a role for depression in the etiology of shock differentials. In this respect, clinical depression transcends environment, i.e., depression is not "cured" simply by returning the patient to a familiar environment (although it can be argued that removal of stress [novelty] might alleviate neurotic/reactive depressions).

In addition to habituation findings, neither DMI nor ECS were successful in eliminating shock effects on appetitive measures. Specifically, both treatments, when administered on an acute basis, effectively removed ES - IS differentials. Despite this, IS rats injected with DMI remained significantly decreased on dependent measures relative to NS animals. Moreover, elimination of ES - IS and NS - IS differentials by both agents appeared to occur through a selective decrease of appetitive functions in control (NS and ES) groups down to IS levels rather than through any increase in such functions for the latter animals as would be expected if, in fact, they were "cured" of their depression. As noted above (see Discussion--Experiment 2), the latter observations in part parallel differential effects obtaining between administration of anti-depressant agents in nondepressed and depressed subjects and provided speculative support for the existence of a depressed substrate in IS rats. However, subsequent findings of Experiment 2 failed to substantiate such a position. In fact, failure to obtain a differential drug effect between escapably and inescapably shocked rats following chronic DMI administration (a situation much closer to

clinical applications) provides instead additional evidence against the existence of an analogous state of depression in inescapably shocked rats.

With respect to avoidance acquisition, inescapably shocked rats demonstrated a selective deficit in performance of an FR-2 shuttle avoidance task in comparison with escapably shocked counterparts (although this differential became clearly apparent only over the final few trials; see Figure 4a) of training and clearly indicate that experimental conditions were sufficient to produce typical helplessness effects as described by Seligman (1974). Interestingly, this difference was not altered through benzodiazepine administration but was eliminated by both antidepressant agents, a finding which suggests that "helplessness" effects are not a function of fear-induced alterations in behavior as argued by Weiss et al. (1968) and Anisman (1973). However, it does not necessarily follow that such deficits reflect proactive interference related to previously learned environmental noncontingencies. In fact, both DMI and ECS gave some evidence of facilitating levels of motor activity (see ECS in Figure 2b; also recall the significant increase in activity occurring in chronically treated DMI rats in Experiment 2). In this regard, high correlations have previously been demonstrated between levels of activity and avoidance learning (Miller & Weiss, 1969); additionally, agents which elevate activity levels (e.g., amphetamine) facilitate acquisition of shuttle avoidance tasks (Krieckhaus, Miller, & Zimmerman, 1965; it is interesting to note that DMI, ECS, and amphetamine all appear in some degree to facilitate catecholaminergic systems.) In the present work, animals pretreated with a benzodiazepine compound subjectively appeared to be markedly decreased

in overall activity levels. Concurrently, avoidance acquisition in such animals was impaired at all levels of shock (Figures 3a and 4b).

While the present experiments leave issues unresolved with respect to the nature of learning impairments seen following exposure to inescapable shock, it is nevertheless apparent that performance differentials (and their absence) in the above data can be explained without recourse to "helplessness" explanations. In fact, learning data, when considered in context with the remainder of the present findings, can more reasonably be argued to reflect factors other than learned helplessness (although learning that responding is noncontingent is not necessarily mutually exclusive to other sources of proactive interference nor mutually inclusive of the existence of an analogous state of depression).

In summary, the above data show differential decrements in both appetitive functions and in acquisition of a shuttle avoidance task (but not in activity levels) in inescapably shocked rats relative to both unshocked rats and to rats exposed to equivalent amounts of escapable shock. Despite this, application of two standard somatic antidepressants failed to ameliorate effects of inescapable shock on appetitive functions. In contrast, such effects were eliminated through use of simple preadaptation procedures designed to allow animals to habituate to the experimental environment. These several observations combine to suggest that exposure to inescapable shock does produce stress differentials in rats but that such states bear little resemblance (at least at a biological level) to those forms of depression which are favorably influenced by electroconvulsive shock treatment and tricyclic medication.

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APPENDICES

APPENDIX 1

REVIEW OF LITERATURE

Introduction

In 1967, Seligman and his associates (Overmier & Seligman, 1967; Seligman & Maier, 1967) published a pair of papers describing resultant behavioral manifestations of exposure to an episode of inescapable shock in dogs. Briefly, such shock produced impaired escape-avoidance learning in the 24 hr period immediately following shock experience. After relatively few trials, inescapably shocked dogs ceased struggling and barking, choosing to accept subsequent shocks in a passive fasion characterized by sitting and whining during shock (even following increases in shock intensity). In a cognitive sense, such animals were described as appearing to have "given up." Moreover, this effect was not a function of exposure to shock per se as dogs provided with an escape contingency during the stress session subsequently demonstrated neither learning impairments nor the passive behaviors of inescapably shocked counterparts (Seligman & Maier, 1967).

In explanation of these phenomena, it was proposed that inescapably shocked animals had learned that shock onset and offset were completely independent of responding. That is, the dogs had learned a state of helplessness which, during subsequent escape-avoidance learning, produced a source of proactive interference with that learning (Seligman & Maier, 1967).

More recently, Seligman (1972, 1974) has proposed that this state (learned helplessness) provides an animal analogue of clinical depression. Accordingly, this paradigm, per Seligman, provides a

potentially important tool in studying and understanding the psychopathology of depression. However, despite these suggestions and their numerous extrapolations (see Seligman, 1974), scant work has been done toward relating the behavior of "helpless" animals to any of the overt clinical manifestations of human depression.

With that preface, this paper discusses literature pertinent to the evaluation of the learned helplessness paradigm as a viable animal model of depression in the rat. As a preface, Seligman has suggested that legitimate extrapolation from an animal model of pathology to the clinical state requires the demonstration of parallels along four dimensions, i.e., etiology, physical manifestations of the disorder, cure, and prevention (Seligman, 1974, p. 80). It is to the behavioral manifestations and their subsequent amelioration ("cure") to which the present work is addressed. Toward that end, depression has been functionally defined as a condition of decreased food and water consumption, decreased levels of activity (as measured by number of cage crossings), weight loss, and learning impairment in inescapably shocked animals. Regarding this definition, psychomotor retardation and decreased appetite are common to a number of depressive states (Seligman, 1974, pp. 82-83; Wittenborn, 1965). Weight loss has also been reported (Kiloh & Garside, 1963) although this factor may also be indicative of high levels of stress (Peters & Finch, 1961). Learning deficits, on the other hand, are not commonly associated with depressive syndromes. Although cognitive impairment may occur with psychotic ideation, it is not generally seen as an integral component of depression. However, within Seligman's helplessness context such deficits become central to depressive etiology. For instance, Seligman (1974) has argued that it is precisely the inability

to recognize contingencies between responding and reinforcement which subsequently leads to feelings of hoplessness, helplessness, and despair. Accordingly, it becomes incumbent on an evaluation of this model to include assessment of poststress learning capacities.

This latter point also raises important nosological issues. In its original form, Seligman (1972) proposed learned helplessness as a model of reactive depression (i.e., depression precipitated by some identifiable external event). In subsequent formulations (Seligman, 1974), this position has been modified to preclude strict distinctions between reactive and endogenous types of depression (i.e., depression whose onset cannot be linked to any identifiable event). It is important to note in this regard that nosological systems employing reactive-endogenous dichotomies contain, in part, implicit etiological statements (contrast this for example against phenomenological systems based on neurotic-psychotic distinctions). Learned helplessness, with its specific etiological statement, is in this sense consistent with reactive depressions. Nevertheless, problems of classification in the psychopathologies remain, for the most part, unresolved. Accordingly, it comes as no surprise to find reactive-endogenous distinctions conceptualized on both a unidimensional continuum (Garmany, 1963; Kendell, 1968) and as functionally independent entities (Kiloh & Garside, 1963). Aside from pointing to the existence of these controversies, it is not within the purview of this review to enter its nosological disputes. Decreases in activity and appetite are common to a variety of depressions including both reactive and endogenous types and, consequently, are independent of rigorous diagnostic statements.

Nevertheless, the hallmark of depression remains a subjective phenomenon of affect with determination of this state in infrahuman species, accordingly, restricted to the level of inference. Consequently, no amount of detail in outlining behavioral indices can eliminate the possibility of mislabeling unrelated syndromes synonomous only in external manifestations and, in turn, the problem must be circumvented at a second level. In this regard, Seligman has pointed to cure as one of the requisites for establishing the validity of an animal model with its clinical analogue. Accordingly, if inescapable shock in fact produces an analogous condition of animal depression at biological substrates, then those somatic interventions indicated as efficacious in states of human depression should likewise prove efficacious in alleviating functional depression in the rat. "Treatment" of inescapably shocked animals with electroconvulsive shock (ECS) or antidepressant drugs should predictably reduce shock-induced decreases in dependent measures if, indeed, such decreases do reflect clinical analogues.

With the above as a brief introduction to the problem, this paper will turn to a more detailed survey into the relationship between learned helplessness and depression including a review of the basic data of learned helplessness and alternative explanations of those findings. Regarding dependent measures, changes in weight, appetite, and activity have not been investigated within a helplessness context but have been extensively examined under a variety of related stress situations. Pertinent findings from this literature will accordingly be reviewed. Finally, the effects of both electroconvulsive shock and anti-depressant drug therapy on depression will be discussed. This will include survey of these effects in man and in experimental animals

with specific focus on the interrelationship between the biochemical aspects of these manipulations to both learned helplessness and current biological conceptualizations of depression.

Learned Helplessness: The Basic Findings

Initial discovery of learned helplessness phenomena occurred during the course of a series of studies investigating relationships between Pavlovian fear conditioning and instrumental responding (Seligman, 1974, p. 21). In the earliest studies (Overmier & Seligman, 1967), mongrel dogs were suspended in hammocks and subjected to 1 hr stress sessions comprising a series of unsignalled and inescapable shocks (6.0 mA) applied through electrodes affixed to the animals' feet. Experimental groups received one of three combinations of shock density while a fourth group served as an untreated control. Twenty-four hours following this initial session, all animals were given 10 trials on a shuttle-avoidance task. In all cases, preshocked (PS) groups showed increases in both response latency and number of failures to escape. Dogs receiving lighter shock densities exhibited a slight trend toward less severe impairment although differences between experimental groups on the above measures were not significant. Additionally, increasing the intensity of shock by 2 mA during escape-avoidance testing failed to eliminate PS-related deficits, thus arguing against habituation to shock.

Initially, helplessness effects demonstrated stringent temporal restraints, consistently appearing in animals tested within 24 hrs following the initial session of inescapable shock but not at 48, 72, or 144 hr intervals after such shock. Despite this, performance deficits in escape-avoidance responding, once they had occurred, were

relatively permanent and could be demonstrated up to 7 days after the first poststress test session (Seligman & Maier, 1967). In partial replication, Overmier (1968) using almost identical preshock procedures, also failed to find avoidance deficits in dogs tested at 72 or 144 hr intervals following preshock. However, in contrast to earlier work, Overmier found significant impairment at the 48 hr interval (although the deficit was not as pronounced as that seen after 24 hr). Subsequently, Seligman and Groves (1970) successfully demonstrated a nontransient helplessness effect with initial escape-avoidance deficits apparent 1 week after the last of a multiple session of inescapable shocks. (As an aside, Overmier's avoidance task did not contain an escape provision. This latter variation was incorporated in response to criticism that previous demonstrations of helplessness had tested dogs in escape-avoidance training using the traditional "method of emergence," i.e., avoidance behavior developed from performance of the escape task at increasingly shorter latencies. PS animals had, per this argument, been taught to be unresponsive only during shock. Overmier did not find this to be a factor.)

Anticipating arguments attributing the above effects to shock habituation or the development of unauthorized coping responses during the PS session, Overmier and Seligman (1967) were able to demonstrate escape-avoidance deficits in dogs paralyzed with neuromuscular blocking agents during PS and in animals tested on a shuttle task at shock intensities 2 mA above those applied during PS. In neither of these cases was magnitude of the postshock deficit influenced by the presence or absence of a warning signal during the preshock session.

In a second report, Seligman and Maier (1967) were not only able to replicate initial findings of impaired shuttle-avoidance performance

but, in an important extension, were able to demonstrate that the presence of an escape contingency during PS (in this case allowing dogs to escape shock while suspended in their hammock by pressing a panel with their head), eliminated subsequent performance deficits in shuttle acquisition. In fact, performance of escaping dogs did not differ significantly from levels displayed by nonshocked control animals. Moreover, dogs given shuttle-avoidance training prior to exposure to inescapable shock also failed to show subsequent performance deficits upon retesting. This latter finding has been suggested by Seligman (1972) as being analogous to an immunization technique against adverse PS effects.

In related fashion, Seligman et al. (1968) reported "curing" chronic shuttle avoidance deficits in dogs through forced exposure to escape/avoidance contingencies. Precisely, "helpless" dogs were coaxed, or in more extreme cases, forcibly dragged over a shuttle barrier. Following up to 50 trials of such procedures, previously impaired dogs were able to demonstrate asymptotic avoidance performance indistinguishable from that of nonshocked animals. (However, Testa, Juraska, and Maier [1974] have subsequently reported evidence suggesting that the effects of PS, while reduced by such procedures, cannot be completely eliminated.)

Interestingly, the above reports also note subjectively different behavior between escapably and inescapably shocked animals both during and following the PS session. Specifically, all dogs responded to the first few trials of shock with considerable vocalizing and struggling. However, as inescapable shock continued, dogs began to sit passively and whine during subsequent applications of shock. Dogs provided with a coping contingency during PS, in contrast, continued to bark and

struggle until escape-avoidance learning was considerably progressed; at no time did coping animals give indication of passively acquiescing to their situation. Differential behavior also generalized to conditions outside the stress situation. Coping dogs, when approached after their PS experiences, barked, ran to the rear of their cages, and generally resisted any attempt at handling. In contrast, dogs not provided with escape-avoidance contingencies lay on their cage floor when approached, adopted submissive postures, and did not resist handling (Seligman, 1974, pp. 24-25).

In explanation of these diverse effects, it has been proposed (Seligman & Solomon, 1969; Seligman, 1974; Seligman, Maier, & Solomon, 1971) that learning deficits observed after exposure to episodes of inescapable shock reflect a type of proactive interference based on prior shock experience. Precisely, animals learn during sessions of inescapable shock that responding and shock onset/offset are independent of one another. Formally posed, the conditional probability of reinforcement (escape or avoidance), given a response, is equal to the conditional probability of reinforcement, not given a response. Less rigorously, the probability of receiving or not receiving reinforcement is entirely unrelated to any response that an animal may or may not choose to emit. In this regard, traditional learning theories have viewed learning as occurring only when two events occur in contiguity (S-S) or when a stimulus event is followed by a reinforced response (S-R). Borrowing from Rescorla (1967), Seligman (1974) has suggested learned helplessness as an extension of these positions wherein subjects come to learn the presence of noncontingent response events. At a motivational level, Seligman has furthermore speculated that inescapably shocked animals develop a set

of response-limiting expectancies. That is, when an animal expects that his responding will not alter his environment, he subsequently loses the motivation to initiate voluntary responses. Generalization of this set of expectancies and its accompanying amotivational state to situations outside of the initial stress situation becomes a source of proactive interference in subsequent escape-avoidance situations.

Reinterpreting the above data within this context, it is apparent that exposure to shock per se is not a critical factor as the helplessness effect is seen only in yoked animals deprived of coping contingencies; control groups with available contingencies do not become "helpless" despite exposure to equivalent amounts of shock. Also, the effect has been shown to be relatively permanent (as would be expected if it is, indeed, a learned behavior). Once an inescapably shocked animal has failed to learn in an escape-avoidance task, the impairment continues for as much as 25 days after the initial postshock test session (Seligman et al., 1968; Seligman & Maier, 1967). In related fashion, initial postshock test impairment has been found at intervals of up to 7 days following conclusion of a series of sessions of inescapable shock. (Importantly, dogs limited to only one such session showed transient 24 hr helplessness [Seligman & Groves, 1970].) These latter reports describing nontransient helplessness effects remain consistent with learning formulations and argue, for instance, against mediation of the effect by transient physiological artifact as others (Miller &Weiss, 1969) have suggested.

In addition, forced exposure of "helpless" dogs to previously ignored escape-avoidance contingencies resulted in the elimination of existing performance deficits (Seligman et al., 1968), while dogs given

escape training (immunized) prior to exposure to inescapable shock were not impaired during subsequent testing (Seligman & Maier, 1967). Within a helplessness context, these latter findings suggest, in the first case, that dogs extinguish previously learned sets of expectations and replace them with an appropriate set including now-in-effect contingencies. In a similar vein, animals given preliminary escape training fail, according to Seligman (1974), to establish noncontingent expectations during subsequent episodes of inescapable shock.

Interestingly, approximately one-third of all dogs tested failed to develop learned helplessness (Overmier & Seligman, 1967; Seligman, 1974, p. 24; Seligman & Maier, 1967). In explanation of this, Overmier and Seligman (1967) have argued that this finding reflects differential learning histories of the dogs prior to impoundment. Per this logic, mongrel dogs, having an extensive past history of "coping" would not be as susceptible to the effects of inescapable shock as would dogs not having such a background. Consistent with this, Seligman and Groves (1970) were able to systematically demonstrate that cage-raised beagles, restricted from birth from contact with handlers and peers, incurred significantly more learning impairment following a single session of inescapable shock than did mongrel counterparts with unknown prelaboratory histories.

Learned Helplessness in the Rat

Following initial reports outlining the basic effects and parameters of learned helplessness in the dog, the generality of the phenomenon has been expanded across several species and over a variety of paradigms. Learning impairments following inescapable shock

have been reported in goldfish tested in both a Sidman shuttle-avoidance task (Behrend & Bitterman, 1963) and in a one-way shuttle task (Padilla, Padilla, & Ketterer, 1970), in cats tested on a wheel turning task (Seward & Humphrey, 1967), in mice performing a water escape task (Braud, Wepman, & Russo, 1969), in chickens (Maser & Gallup, 1974), and in humans on a reaction time task following finger shock (Thornton & Jacobs, 1971) and on a finger maze task following exposure to an aversive level of noise (Hiroto, 1974).

In the rat, however, the situation has not been as lucid. Several authors reported finding only marginal deficits (Kurtz & Walters, 1962; Mullin & Mogenson, 1963; Weiss, Krieckhaus & Conte, 1968) following inescapable shock. Indeed, in several instances such procedures produced facilitation (Anderson & Paden, 1966; Blanchard & Blanchard, 1968; Brookshire, Littman, & Stewart, 1961; de Toledo & Black, 1967; Slotnick, 1968). On the other hand, Dinsmoor and Campbell (1956), Looney and Cohen (1972), McCulloch and Bruner, (1939), and Mowrer (1940) have all reported impaired acquisition following sessions of inescapable shock.

It remained for Maier (Maier, Albin, & Testa, 1973) to resolve (at least in part) the issue. Maier pointed out that dogs performing in shuttle-avoidance tasks produced data clearly demonstrating incrementing learning during acquisition. Rats, on the other hand, when tested on similar tasks, did not generate data in the form of a learning curve and instead often performed at short latencies from the very first trial. This suggested, as correctly pointed out by Maier, that crossing a shuttle box is a very different response for a rat than for a dog and that failure to take such species and tasks differences into consideration accounted, at least in part, for

discrepant findings between the two species. In support of this, instances failing to find learning impairments in rats following preshock experience have used test tasks requiring short latency shuttle responding, a response that may be almost reflexive in the frightened rat (Bolles, 1971; Turner & Solomon, 1962). In turn, this suggests that the amount and nature of learning required in some avoidance learning tasks may be minimal.

Specifically, directing themselves to this question, Maier et al. (1973) subjected rats to inescapable shock over a wide variety of parametric intensities and densities, none of which were found to produce subsequent avoidance deficits in comparison with nonshocked control animals tested on a standard shuttle task. As expected, learning curves obtained during avoidance testing were almost completely flat, reflecting the tendency for most animals to perform at short latency from the first test trial. This was not the case, however, when rats were tested on more complex tasks. Precisely, Maier found that increasing response contingencies to require not only a cross into the opposite compartment but subsequent return on a single trial (fixed ratio-2; Maier et al., 1973) produced learning curves in unshocked rats and learning deficits in inescapably shocked rats. A similar outcome obtained when shock offset was linked to manipulation of a turning wheel. In support of his findings, Maier critically noted that reports describing learning impairments following PS in rats have not employed shuttle tasks in subsequent testing (i.e., bar pressing: Dinsmoor & Campbell, 1956; Mowrer, 1940; water maze performance: McCulloch & Bruner, 1939; platform jumping: Looney & Cohen, 1972).

These findings have subsequently been replicated on a variety of escape-avoidance tasks and extended by demonstrating that such deficits

are produced by the inescapable nature of shock (Seligman & Beagley, 1975; Seligman, Rossellini, & Kozak, 1975; Testa et al., 1974), that the effects are relatively permanent (at least up to intervals of 1 week), that rats can be immunized against PS effects, and that rats can be "cured" by forced exposure to escape-avoidance contingencies (Seligman et al., 1975).

In summary, this work adds the rat to the growing list of species for which helplessness effects have been claimed although the controversies leading to this demonstration should provide a caution in across-the-board applications of the paradigm without proper consideration for species and task differences. This concludes discussion of the paradigm itself and sets the stage for exposition and discussion of the several alternative explanations advanced to account for these effects.

Learned Helplessness Phenomena: Alternative Explanations

Adaptation Hypotheses

Adaptation hypotheses suggest that animals may during inescapable shock somehow become adapted or desensitized to further shock (Quinsey, 1970). Accordingly, shock may not produce sufficient motivation to learn during subsequent escape-avoidance training.

Several facts argue against this. Church, LoLordo, Overmier, Solomon, and Turner (1966) failed to find adaptation of cardiac responses in curarized dogs during a sequence of inescapable shocks. Moreover, increasing the intensities of shock during escape-avoidance training over PS levels has not been reported to alleviate learning deficits in inescapably shocked dogs (Overmier & Seligman, 1967) or in rats (Anisman & Waller, 1972). In fact, Anisman and Waller found

decreased performance at higher intensities. If, indeed, animals had become adapted during PS, then increased shock during subsequent testing should lead to opposite effects. Accordingly, these findings are difficult to reconcile with adaptation theories and suggest that the latter provide an inadequate account of the helplessness data.

Exhaustion Hypotheses

Exhaustion hypotheses argue that stresses associated with inescapable shock produce shortlasting emotional and/or physiological exhaustion which in turn reduces the ability of animals to cope with subsequent stress situations. Initial impetus for such explanations arose from initial reports describing a transient (24-48 hr) nature for helplessness effects (Overmier, 1968; Overmier & Seligman, 1967; Padilla et al., 1970). Despite the subsequent demonstration (Seligman & Groves, 1970) of nontransient learned helplessness, two schools of the exhaustion hypothesis remain popular.

The first proposes that learned helplessness deficits reflect stress-induced over-reactions of the parasympathetic nervous system. This explanation is reminiscent of the earlier work of Brush and his associates investigating correlations between corticosteroid levels and the Kamin effect (i.e., deficits in avoidance performance appearing 1-6 hr following completion of an initial avoidance learning session [Kamin, 1957]).

In this regard, increases in levels of circulating corticosteroids following exposure to stress have been widely documented. For instance, Rabinovici (1951) described decreased levels of adrenal ketosteroids in rats following exposure to cold, x-ray irradiation, and intraperitoneal injections of adrenocorticosteroid hormones (ACTH).

In a related vein, Haltmeyer, Denenberg and Zarrow (1967) demonstrated increased levels of circulating corticosteroids in rats following a session of grid shock. Maximum rates of increase occurred in the first 15 min following shock termination with asymptotic levels approached at 45 min. Adrenal release remained constant over several intensities of shock. Similar increases in plasma 17-hydroxycorticosteroids in monkeys have been reported following both Pavlovian fear conditioning and avoidance responding (Mason, Brady, & Sidman, 1957). In agreement with Haltmeyer et al. (1967) steroid release in the latter study approached maximum levels under both conditions (as measured by control injections of ACTH); baseline levels returned approximately 1-2 hr after completion of the test session.

With regard to steroid levels during learning, Brush and Levine (1966) demonstrated a correlation between plasma corticosteroid concentrations and the descending arm of a U-shaped avoidance function for a 1 hr period following a session of Pavlovian fear conditioning. In later work (Levine & Brush, 1967), a similar relationship was found following an initial period of avoidance learning. It was, moreover, possible to alter avoidance learning in similar fashion with ACTH injections.

However, despite these latter findings, several observations argue against the autonomic nervous system playing a significant role in learned helplessness. For instance, Brush, Myer, and Palmer (1963) reported finding no Kamin effect after an episode of escape learning although it was clearly present following a single episode of fear conditioning. Avoidance deficits also occurred immediately following training on an unsignalled escape task in spite of elevations in plasma

corticosteroids (Brush & Levine, 1966). In contrast to the critical role played by fear conditioning in mediating autonomic effects, learning impairments following PS in the learned helplessness paradigm consistently have been shown to be independent of the presence or absence of a conditioned stimulus (Overmier & Seligman, 1967).

Finally, original impetus for exhaustion-type theories arose from initial reports on the transient nature of helplessness phenomena. However, nontransient effects of up to 1 week have subsequently been reported in both the dog (Seligman & Groves, 1970) and rat (Seligman et al., 1975). Both these findings and the demonstration of continued deficits in escape-avoidance responding for periods of up to 30 days following an initial test failure (Seligman et al., 1968; Seligman & Maier, 1967) are difficult to reconcile with the much shorter time courses displayed by autonomic phenomena and strongly suggest that the role of hormonal factors in learned helplessness is minimal.

In a second major variation of the exhaustion hypothesis, Weiss, Stone, and Harrel (1970) have proposed mediation of PS learning deficits through decreased levels of central brain norepinephrine (NE). As a preface to this position, stress-induced decreases in NE have been widely documented (Barchas & Freedman, 1963; Bliss & Zwanziger, 1966; Maynert & Levi, 1964; Ordy, Samorajski & Schroeder, 1966; Stone, 1970) and appear to reflect increased rates of transmitter release. In this regard, rates of NE synthesis are generally adequate to maintain endogenous NE levels during episodes of mild stress. However, during severe stress (or during mild stress with pharmacologically-impaired synthesis; [Gordon, Spector, Sjoerdsma, & Undenfriend, 1966]), rates of NE release and degradation exceed the capacity of the brain to synthesize new transmitter with consequent

depletion of endogenous NE pools (Barchas & Freedman, 1965; Gordon et al., 1966; Maynert & Levi, 1964; Stone, 1970).

In this regard, Weiss (Weiss et al., 1970) reported finding decreased levels of whole brain NE in rats following a 48 hr session of inescapable shock. Surprisingly, yoked rats receiving equivalent avoidable shock showed significant increases in NE over nonshocked control animals. Based on these findings, Weiss has subsequently proposed that learned helplessness in fact reflects nothing more than stress-induced short-term decreases in brain NE (Weiss, Glazer, & Pohorecky, 1974).

While appealing in its simplicity, several related findings argue that such an isomorphism between brain chemistry and behavior is, unfortunately, inadequate. To this point, numerous reports have described relationships between impairments in avoidance learning and decreases in brain catecholamine levels (Cooper, Breese, Grant, & Howard, 1973; Seiden & Peterson, 1968) and between central levels of NE and general activity (Cooper et al., 1973; Krieckhaus, Miller, & Zimmerman, 1965). On the other hand, Cooper et al. (1973) reported significant increases in both the level of general activity and in avoidance performance despite a 50% reduction in brain NE. Increased motor activity has also been reported following a period of chronic reserpine treatment despite continued reductions in monoamine levels (Segal, Sullivan, Kuzenski, & Mandell, 1971).

These findings suggest that Weiss' position is incomplete and that the relationship between NE and behavior cannot be so simple. Several additional factors argue against a mediation of helplessness by hormonal factors. The time course of stress-induced decreases in NE, variously estimated between 1-6 hr (Barchas & Freedman, 1963;

Maynert & Levi, 1964; Ordy et al., 1966) is inconsistent with both reported short-term (24-48 hr) helplessness effects and the more permanent variety (7-25 days) reported by Seligman and his group. Moreover, both forms of the exhaustion hypotheses are difficult to reconcile with improved performance following forced exposure to escape-avoidance contingencies (Seligman et al., 1968).

Competing Motor Response Theories

As with exhaustion theories, there are several variations on the competing motor response hypothesis. Nevertheless, these positions share the basic tenet that animals, during periods of inescapable shock, learn a response which subsequently provides a source of proactive interference with escape-avoidance learning.

For instance, it has been suggested (Dinsmoor & Campbell, 1956; Mullin & Mogenson, 1963) that inescapably shocked animals learn to escape and/or reduce shock via some "unauthorized" response (e.g., rearing, crouching, rolling over on the heavy fur on its back, etc.) and that it is these responses which subsequently interfere with avoidance learning. Less viable versions of this theme have proposed that shock offset leads to the development of superstitious responding or, alternatively, that active responding is sometimes adventiously punished by shock offset and, hence, is decreased in the test situation (see Seligman et al., 1971 for a more detailed discussion of such issues).

Such arguments encounter numerous difficulties. For instance, initial shock application produces considerable running and struggling in rats. This activity, beginning at some point after shock onset and often continuing for the duration of the shock, should be adventiously reinforced by shock offset and, therefore, increase in

frequency. Yet running in inescapably shocked rats, instead of increasing over trials, most commonly decreases and is replaced by immobility and "prancing" (Trabasso & Thompson, 1962). Moreover, paralysis to both dogs (Overmier & Seligman, 1967) and rats (Anisman, 1972) during PS has been shown to produce learning impairments similar in magnitude to those obtained following PS in unparalyzed animals. Although the use of neuromuscular blocking agents has been criticized as a technique for precluding kinesthetic learning (Black, 1967), findings in this regard are not readily accounted for in the above formulations.

Directly addressing himself to these arguments, Maier (1970) noted that if proactive interference from incompatible motor responses was indeed a source of subsequent learning deficits in learned helplessness, then animals systematically taught a skeletal response incompatible with an avoidance task should subsequently demonstrate impaired acquisition of that task. If, on the other hand, recognizing the existence of contingencies between responding and shock offset was the critical variable (as suggested within a helplessness formulation), then avoidance learning should remain unaffected. Accordingly, Maier systematically trained dogs to terminate shock by holding their heads immobile. Subsequent escape-avoidance learning was somewhat impaired in such dogs in comparison to unshocked dogs but this difference disappeared over trials such that later performance of experimental dogs was indistinguishable from unshocked control animals. In striking contrast, over 50% of yoked dogs exposed to inescapable shock were still failing in the escape-avoidance task when the experiment was terminated after 130 trials. However in criticism, it has been pointed out (Anisman &

Waller, 1973) that the inescapably shocked animals in Maier's study may have learned a more pronounced freezing response than their escaping counterparts and that this in turn could have accounted for the differential learning observed between the two groups.

In discussing this issue at a subjective level, Seligman (Seligman et al., 1971), citing the numerous studies of his group, noted that "helpless" dogs did not appear to be performing competing motor responses of any type; instead, more than anything, such animals seemed to have given up. Maier (1970) in this same vein, reported that the only dogs consistently observed to adopt shock-reducing postures were animals given coping contingencies during preshock treatment.

While such rebuttals fail to completely refute competing response hypotheses, they, nevertheless, severely restrict their scope (i.e., the competing response is reduced to some marginal (currently unobservable) adjustment of the skeletal musculature).

Two later versions of this hypothesis, however, fair much better under criticism and, indeed, appear as substantial as the helplessness position itself in accounting for existing data. Quite simply, Weiss et al. (1968) have proposed that the avoidance deficits seen following episodes of inescapable shock in rats result from extensive freezing in the presence of a conditioned stimulus (CS) previously involved in classical fear conditioning. As a test of this, Weiss subjected rats to 2 days of fear conditioning (four trials per day). Control groups received equal presentations of the CS by itself, a session of unsignalled shock, or fear conditioning to a CS different from that to be used in subsequent avoidance training. On the day following completion of these pretest sessions, all animals

were given daily avoidance training for 1 week (150 trials in total). Movement ratings were obtained on general activity for 10 sec epochs prior to, during, and after the CS on each animal throughout both pretest and avoidance sessions.

Weiss found, not surprisingly, that the performance of the group receiving fear conditioning and subsequent avoidance training in the presence of the same CS was markedly below that of the other three groups. More importantly, movement ratings for the prefear group during the CS were depressed both in fear conditioning and later avoidance training. Movement in this latter group correlated highly (r = .83) with total number of avoidance responses and provided a strong predictor of acquisition in the avoidance task. Significant correlations were not found in control groups.

Noting the sometimes transient nature of learned helplessness, Weiss was also able to repeat these findings using a temporally spaced procedure during both pretest sessions and avoidance sessions. As before, movement during the CS in the experimental group remained an excellent predictor of subsequent avoidance performance. Moreover, Weiss reported that it was possible to eliminate avoidance deficits (in fact, avoidance learning was facilitated) by training rats on an avoidance task prior to fear conditioning. In this latter case, activity ratings during the CS were not suppressed in subsequent avoidance training.

This work suggests then that PS effects in learned helplessness may reflect nothing more than proactive interference with shuttle responding arising from fear-induced freezing in the rat. However, Weiss' findings, relying on the presence of a CS, remain limited by the demonstration (Overmier & Seligman, 1967) of equivalent learning

impairment following sessions of both signalled and unsignalled inescapable shock. In this regard, it can be argued that fear during PS is conditioned to static apparatus and environmental cues and that such conditioning subsequently generalizes to test situations (McAllister & McAllister, 1963). However, Weiss' demonstration of avoidance deficits only in rats given fear conditioning to the avoidance CS suggests that this latter explanation is incomplete.

Anisman (Anisman & Waller, 1973), borrowing conceptually from Bolles (1971), has critically expanded this position by suggesting that PS effects are mediated by changes in the probability of occurrence of certain species specific defensive reactions (SSDR). As a preface, Bolles (1971) has pointed out that rats exhibit one of three prepotent species specific defensive reactions when frightened (i.e., flight, freezing, or fighting) and that the particular response forthcoming is contingent on the context of a given situation. Bolles notes, furthermore, that many aversive situations are characterized by a conflict in such SSDRs (for instance, rats shocked in a shuttle box have competing predispositions to both run away and to freeze when subsequently placed in that same situation). To the extent that a given task favors one SSDR over another, the more quickly such conflicts will be resolved. Toward this end, bar pressing is typically compatible with freezing while turning wheels and one-way avoidance tasks encourage fleeing. Shuttle-avoidance, by requiring animals to reenter a compartment where they have previously received shock, provides a clear example of the conflict between flight and freezing.

Bolles' position has received considerable support from a series of studies by Blanchard and Blanchard investigating the behavior of rats under a variety of aversive situations. Using a moving shock prod as a CS, Blanchard and Blanchard (1969a, 1969b) demonstrated enhanced avoidance responding following a session of prior fear conditioning to the prod. Activity levels during avoidance training (as measured by grid crossings in the experimental chamber) were significantly depressed during intertrial intervals but, nevertheless, correlated significantly with the number of avoidance responses made by experimental groups. In contrast, rats subjected to fear conditioning (again, to the prod) outside of the experimental chamber showed significant increases in both activity levels and avoidance responding when tested against rats receiving equivalent fear conditioning within the test chamber. These findings point to the relationship between freezing behavior and the number of situational cues present during prior fear conditioning. In later work, Blanchards suggest, as did Bolles earlier, that freezing and fleeing often conflict and that the presence of one over the other is contingent on both the test situation (Blanchard & Blanchard, 1971) and the discriminability of threat objects (Blanchard & Blanchard, 1970a, 1970b).

Within this conceptual format, Anisman has systematically investigated the role of PS variables in subsequent learning. Resultant findings have strengthened and extended Weiss' initial suggestions and presently provide a compelling indictment of helplessness effects in the rat. As a starting point, Anisman, like Weiss, found PS activity levels highly correlated with subsequent avoidance learning (Anisman & Waller, 1971a, 1971b, 1972). However,

in contrast to Weiss, Anisman also found a high correlation between learning and levels of activity during interstimulus intervals. Indeed, indirect support for this position had already been previously provided by Cicala (Cicala, Masterson, & Kubitsky, 1971; Cicala & Ulm, 1971) with the demonstration of an increase in activity during the CS over levels obtained during the interstimulus interval (although overall activity of shocked animals was depressed relative to nonshock controls.) These findings implied that freezing was not conditioned only to the CS as proposed by Weiss, but also appeared to generalize to the entire PS situation. Importantly, Anisman and Waller (1971b) also found decreased activity levels in the interstimulus interval following exposure to unsignalled PS. As with signalled shock, such activity correlated well with subsequent escape-avoidance learning. In all cases, correlations between learning and activity in unshocked rats remained nonsignificant.

Anisman further extended these findings to a systematic evaluation of PS effects on stimulus and response variables in both one-way and shuttle-avoidance learning. Not surprisingly, PS facilitated avoidance tasks when animals were required to run away from the previously dangerous stimulus (Anisman, 1973; Anisman & Waller, 1972; de Toledo & Black [1967, 1970] have reported similar findings). On the response side, punishment of the to-be-required response enhanced learning impairments while escape training during PS facilitated learning (i.e., training or punishing the to-be-required response amplified PS effects). These findings indicate that the effects of PS are not only species- and task-specific (recall Maier et al., 1973) but are also sensitive to specific stimulus and response characteristics of a given task.

Finally, Anisman (1973) has shown facilitation of shuttle-avoidance is eliminated when PS is administered to restrained rats. In contrast, facilitation of one-way avoidance remained unaffected by restraint. In analysis of both freezing and number of cage crossings (measured during repeated presentations of preshock CS without accompanying US), Anisman found that freezing was significantly elevated in restrained rats. Conversely, number of cage crossings were elevated in unrestrained rats but differed significantly from controls only during the actual presentation of the CS.

Anisman has subsequently integrated these findings into a unified activity hypothesis (Anisman & Waller, 1973) directed toward an explanation of equivocal findings in rat avoidance behavior. As most investigations of learned helplessness in the rat have involved escape-avoidance tasks, the thrust of much of Anisman's theory is thus also applicable to helplessness findings. Specifically, Anisman and Waller suggest, as did Bolles (1971), that learning in an aversive situation is, for the rat, highly correlated with the compatibility between the required avoidance task and prepotent SSDRs. Or to paraphrase, learning and performance in a given paradigm reflects the relative dominance of one SSDR (e.g., flight) over another (e.g., freezing). To the extent that a given situation elicits an incompatible SSDR, that task will be relatively more difficult to learn since animals will not only have to learn to produce the correct response but will also have to learn to suppress the inappropriate SSDR.

In this regard, it is of interest that amphetamine has been reported to facilitate shuttle-avoidance performance (Anisman & Waller, 1971a; Hearst, 1963; Krieckhaus et al., 1965) and that this effect

appears to be mediated by a drug-induced decrease in freezing behavior (Anisman & Waller, 1971a; Krieckhaus et al., 1965). Indeed, the former authors have described a state-dependent effect wherein rats trained to avoid under amphetamine, subsequently demonstrated impaired performance when tested in an undrugged state. The authors described improved avoidance responding only after such rats had activity learned to suppress freezing. Similarly, Anisman & Waller (1972a) reported PS facilitation of both shuttle- and one-way avoidance learning in hood, Wistar, Holtzman, and Sasco strains but not in Sprague-Dawley animals. Importantly, shock-induced freezing was excessive only in the latter strain.

Finally, the widely reported negative correlation between intensity of shock and avoidance acquisition (Anisman & Waller, 1972a; Levine, 1966; Moyer & Korn, 1964; Theios, Lynch, & Lower, 1966) has been attributed to increased freezing at higher shock intensities (Anisman & Waller, 1972a; Theios et al., 1966). In a systematic investigation of this relationship, the latter authors in fact have described activity as a monotonically decreasing function of shock intensity.

In summary, Anisman's activity theory provides a comprehensive alternative explanation of learned helplessness phenomena in the rat. All reported instances of learning impairment following an episode of inescapable PS in the rat have used complex escape-avoidance tasks. One-way avoidance and, in some cases, shuttle-avoidance are more often than not facilitated by PS (see Anisman & Waller, 1973). In this regard, Bolles (1970, 1971) has noted that fear-induced freezing responses can be easily suppressed in one-way avoidance tasks. Accordingly, flight reactions remain relatively unopposed and account

for rapid acquisition. More complex tasks, on the other hand, do not lend themselves as readily to suppression of fear-induced freezing and lead to an antagonism between competing SSDRs. These tasks are, not surprisingly, far more difficult for PS rats to solve.

Addressing himself specifically to these criticisms, Seligman (1974) noted the demonstration of learned helplessness in a variety of nonshock paradigms (i.e., Braud et al., 1969, in mice negotiating a water escape task; Hiroto, 1974, in humans performing on a finger maze; and McCulloch & Bruner, 1939, with rats swimming in a water maze). These instances are not, however, compelling. For instance, Seligman's assertion that deficits in human subjects performing on a finger maze task following a single session of exposure to inescapable tone (Hiroto, 1974) reflects development of a set of expectations that their responding has become noncontingent is not appealing. Indeed, one-third of Seligman's mongrel dogs did not succumb to a state of helplessness during severe shock. Attributing this latter finding to a prelaboratory history of successful coping, Seligman, nevertheless, is willing to submit that 1 hr exposure to an obnoxious tone can, in man, be more disruptive than applications of strong shock to dogs suspended immobile in a hammock. Regarding Braud's swimming task, mice were required to swim across a tub to a lighted platform. Importantly, over five test trials Braud failed to find a difference between inescapably shocked mice and coping controls in the first two test trials; escape latencies for the former group increased significantly only over the final three trials. It is thus impossible to separate learning deficits from fatigue factors. In the most direct challenge to the freezing hypothesis, McCulloch and Bruner (1939) required rats to perform a brightness discrimination in a water maze after several

daily sessions of shock. Results showed impaired acquisition for PS rats but this finding remained compromised as performance of inescapably shocked rats was compared only against an equivalent group of unshocked animals. Hence, it becomes impossible to discriminate effects related to the inescapable nature of shock from effects of shock per se. Moreover, incorrect maze performance in both groups resulted in application of a shock as a rat pulled himself out of the water. Obviously the latter task was not shock free and may have interacted with PS effects to produce unforeseeable sources of confounding.

Also, in contrast to the above work, Anderson and Paden (1966) reported facilitated acquisition of a passive avoidance task in mice previously subjected to extended sessions of inescapable tumbling. In addition, preliminary findings by this author have failed to disclose systematic differences in performance of a water maze brightness discrimination escape task between groups of escapably and inescapably shocked rats providing water temperature was kept elevated and precautions were taken to keep rats warm between trials (see also Stone, 1970). On the other hand, rats subjected to identical PS conditions demonstrated learning deficits when tested on an FR-2 shuttle-escape task.

Thus, freezing theories present a viable alternative to learned helplessness in the rat. Whether this also holds across other species remains to be determined. For instance, preshock effects in the dog have not been as extensively documented as in the rat nor does an extensive literature exist regarding behavior of the dog under shock conditions (for example, correlations have not been established on the activity levels of dogs during preshock and subsequent learning

performance). Such observations, of course, restrict the applicability of the freezing hypothesis to rats but, within that species, it remains at this juncture as an equally tenable explanation of preshock-related learning deficits.

Stress Effects and Dependent Measures

Although appetitive functions, weight change, and level of motor activity have not been specifically investigated within the context of learned helplessness, a considerable body of relevant data nevertheless exists on related effects of general stress and fear on such measures. Discussion of relevant work from this area accordingly follows.

Stress and Coping Behavior

Perhaps the most widely discussed study on the psychological effects of stress concerned the executive monkey phenomenon (Brady, Porter, Conrad, & Mason, 1958). In this work, two monkeys were affixed in series with shock electrodes. One animal in each pair was then given a Sidman avoidance contingency; his yoked partner received equivalent shock but had no means of preventing or terminating such. After several weeks of performance on this task, Brady found that his "executive" (i.e., avoiding monkey) had developed significantly more gastric ulceration than had its yoked nonavoiding counterparts.

This work has subsequently been severely criticized for Brady's unfortunate use of a biasing selection technique (discussed below) which may have systematically assigned ulcer-prone monkeys to the executive chair. Indeed, several subsequent investigators, in contrast to Brady, have shown an alleviation of stress pathology in animals provided with contingencies for coping with aversive stimuli. For instance, Weiss

(1968) reported finding significant decreases in gastric ulceration in rats given an avoidance contingency during a 21 hr stress session. Gastric pathology was uniformly more pronounced in yoked rats. Escape-avoidance rats, in turn, showed more pathology than rats restrained but not shocked during the experimental period although this latter difference was not significant. These findings have subsequently been replicated by Weiss (1971a) over a longer stress period (48 hr) using a different avoidance task (wheel turning versus a nose manipulandum), and with a higher density and intensity of shock. As before, yoked animals demonstrated significantly more gastric pathology than did either escape-avoidance or nonshocked counterparts. However, in contrast with earlier findings, avoiding animals, under these more severe conditions, showed significantly more ulceration than did unshocked rats. Interestingly, application of a single brief shock following performance of each avoidance response in coping rats eliminated stress-reducing characteristics of the avoidance situation and increased ulceration beyond even that observed in inescapably shocked rats (Weiss, 1971b). In explanation of this latter finding, Weiss has suggested that response contingent shock provides a source of negative feedback and that the conflict introduced (i.e., avoiding at a price) produces a marked increase in stress characteristics of the situation.

In discussing the discrepancies in his findings against those of Brady, Weiss noted that Brady systematically selected monkeys with high response rates to serve as the avoidance animal. In this vein, Sines, Cleeland, and Adkins (1963) have reported that rats demonstrating the highest rates of avoidance responding were also the most susceptible to ulceration. In fact, Weiss (1971a) reported finding, post hoc,

higher incidences of ulceration in 9 of 36 avoiding rats over yoked counterparts. This percentage is precisely predicted by assuming that, for each two pairs of animals, one higher responder was selected (as Brady systematically did) as the avoidance animal. Thus, it appears that the availability of a coping contingency in an aversive situation does in fact reduce the stress characteristics of that situation (at least in the rat). Whether this is also the case in primates awaits replication of Brady's experiment under proper experimental controls.

Stress and Warning Signals

Stress differentials arising through the availability or nonavilability of a coping response have parallels with stress differentials occurring between sessions of signalled and unsignalled shock. Precisely, ulceration produced by inescapable shock is reduced in severity when shock is systematically preceded by a warning signal (Gliner, 1972; Mezinskis, Gliner, & Shemburg, 1971; Seligman & Meyer, 1970; Weiss, 1970, 1971b). Moreover, rats in preference situations consistently select signalled over unsignalled shock (Gliner, 1972; Lockard, 1965; Perkins, Levis, & Seymann, 1963), although not if the former is associated with higher shock intensities (Lockard, 1965).

These reports stand in contrast to earlier findings in the rat (Brady, Thornton, & DeFisher, 1962; Pare, 1964, 1965) and mouse (Friedman & Ader, 1965) reporting increased ulceration in the presence of warning signals. In explanation of these inconsistencies, Weiss (1970) has correctly pointed out that those reports describing increases in gastric pathology during signalled shock have failed to exercise stringent yoking procedures. Indeed, applying tail shock to

yoked rats connected in series with experimental counterparts (thus equating current in the two animals), Weiss (1970, 1971a) has consistently found higher levels of ulceration in unsignalled conditions.

In this regard, Weiss (1971a) has proposed that stress is inversely related to relevant information; unsignalled shock, of course, provides rats with less information than signalled shock and, hence, is more stressful. In a related interpretation, Seligman and Meyers (1970) noting reductions in rates of operant bar pressing during unsignalled shock, proposed that rats in the signalled condition were afraid (i.e., stressed) only in the presence of the CS, having quickly learned that non-CS periods are "safe." In contrast, rats receiving unsignalled shock remained in continuous fear. Regardless of interpretations, the weight of current evidence suggests that unsignalled shock produces a higher level of stress than does signalled shock and that this finding may be analogous to differentials in the inherent aversiveness or stress characteristics found between controllable and uncontrollable shock.

Stress and Consummatory Behavior

Inescapable shock also appears to produce decreases in appetitive functions although documentation of these effects remains partially unresolved. For example, increases have been reported in both water consumption (Amsel & Maltzman, 1950; Levine, 1965; Moyer, 1965; Moyer & Baenninger, 1963; Siegel & Siegel, 1949) and food consumption (Siegel & Brantley, 1951; Strongman, Coles, Remington, & Wookey, 1970; Weiss, 1970a) following exposure to inescapable shock. In contrast, other researchers have described decreased water consumption (Amsel,

1950; Levine, 1957, 1958, 1965; Lerman, 1974; Moyer, 1965; Weiss, 1968, 1970; Weiss et al., 1970) and food consumption (Lerman, 1974; Mowrer & Viek, 1948; Weiss, 1968, 1970a; Weiss et al., 1968) following similar experiences.

Several factors contribute to these ambiguities. Both Amsel (1950) and Mowrer and Viek (1948) have presented evidence showing decreased food and water intake in the presence of stimuli previously involved in fear conditioning. In further explication, Moyer (1965) and Levine (1957, 1958, 1965) have related consummatory behavior to a complex interaction including prior stress experience and experimental novelty. Specifically, rats handled in infancy, when subsequently confronted with stress, demonstrated less emotionality and responsiveness than did nonhandled rats. Accordingly, water consumption in handled rats showed less fluctuation in response to stress. Moreover, novelty has also been shown to produce decreased water intake (Levine, 1965; Moyer, 1965). Conversely, habituation to novelty resulted in restoration of baseline rates. In fact, numerous reports have described increased levels of water consumption over nonstress baseline levels during episodes of repeated stress (Amsel & Maltzman, 1950; Levine, 1965; Moyer, 1965; Siegel & Brantley, 1951; Siegel & Siegel, 1949). Interestingly, in all cases, rats in these latter reports received extensive handling prior to testing.

In summary, data suggest that consummatory behavior is reduced by high levels of stress although such effects remain influenced by a complex interaction between prior histories of experimental animals, novelty of the experimental situation, and the presence of fear-inducing cues.

In a different vein, Weiss has systematically investigated changes in appetitive measures as a combined function of informational content of conditioned stimuli and the amount of controllability provided to experimental animals. In this regard, Weiss (1970) reported significant decreases in both food and water intake in consecutive 24 hr periods following shock (although significant decreases in water appeared only during the second 24 hr period). No significant differences were found between rats receiving signalled shock and those exposed to unsignalled shock. In a continuation of this, Weiss then subjected rats to two shorter duration stress sessions separated from each other by 24 hr. Again, both appetitive measures were significantly decreased with respect to nonshocked control animals and yet failed to differ significantly from each other (although food and water intake were lower in animals receiving unsignalled shock). This strongly suggests a shock-related effect irrespective of the presence or absence of a warning signal. (As an aside, Weiss obtained his measures over an extended period of time. This contrasts with most prior work wherein consummatory responding has remained restricted to a prescribed period of the day--and seldom in excess of 1 hr).

Pare (1965), in similar work, reported finding a significant decrease in water consumption of shocked animals over nonshocked rats, again, irrespective of the presence or absence of a warning signal. However, in contrast to Weiss, Pare also reported a significant decrease in food consumption, but only for animals receiving signalled shock. Rats exposed to unsignalled shock in turn ate less that unshocked animals although this latter difference was not significant.

As noted above, comparability between Weiss' findings and those of Pare remain limited by failure of the latter author to use adequate yoking procedures. Despite this, both workers have reported nontransient decreases in food and water consumption following exposure to shock; whether or not such decreases are enhanced or reduced by the presence of a warning signal remains undetermined.

In a similar set of investigations, Weiss has also examined differences in consummatory behavior arising from the availability or nonavailability of coping contingencies during stress. In this regard, Weiss (1968) reported finding significant decreases in 24 hr food intake in rats subjected to a 3 hr session of inescapable shock. Control rats receiving equivalent avoidable shock did not differ from nonshock animals (although these measures were lower for avoiding animals). These results have subsequently been partially replicated (Weiss et al., 1970) over a considerably shorter poststress epoch. Looking at both food and water intake in the 1 hr period immediately following termination of a 3 hr stress period, Weiss again found a significant decrease in food consumption in inescapably shocked rats. However, in contrast to his earlier report (Weiss, 1968), avoiding animals also showed significant decreases in food intake. Water consumption, which had not differed in previous work, was now significantly decreased in inescapably shocked rats. On the other hand, Weiss (1971a) reported significant increases in water consumption in both yoked and avoiding rats during a 48 hr. session of continuous shock. Importantly, rats in the latter study were allowed ad lib access to water for the duration of the experiment but were without food. In this regard Deaux and Kakolewski (1970) have previously shown that water consumption in the absence of food is increased by stress.

Consistent with this, Lerman (1974) has reported decreases in both food and water intake over an eight day period in rats exposed to 24 hr. day shock.

Whether findings in these latter studies are applicable to poststress situations remains an open issue although available evidence does suggest that decreases in food intake following a period of stress are ameliorated by the availability of coping contingencies during stress. This may also be the case for water intake although the evidence is not as compelling.

Stress and Weight Change

In contrast to appetitive functions, stress effects on body weight remain unambiguous. Almost all reports in this area describe decreased body weight following exposure to an episode of stress (Brady et al., 1962; Friedman & Ader, 1965; Gliner, 1970; Pare, 1965; Pare & Temple, 1973; Peters & Finch, 1961; Weiss, 1970). Of these reports, both Pare (1965) and Brady et al. (1962) have described significant and differential decreases in rats exposed to signalled shock (Friedman and Ader [1965] have reported similar findings in mice). Both groups also reported finding significant weight decreases in rats receiving unsignalled shock in comparison with nonshocked controls.

The latter findings have not, however, been substantiated by other workers. For instance, Gliner (1972) was able to find no difference in postshock weight loss between rats in unsignalled and signalled conditions while Weiss (1970) reported significant decreases in weight in unpredictably shocked rats below yoked animals receiving predictable shock. Despite this, both Weiss and Gliner found shock to

significantly decrease weight (irrespective of predictability) in comparison to unshocked animals. Weiss also found significant decreases in weight gain during the stress session. This latter effect was noted only in animals receiving unpredictable shock. Rats in predictable shock conditions did not differ from each other despite 48 hr of continuous shock application (Weiss, 1971a).

With regard to this latter point, all reports describing increased stress effects (as measured by weight loss) to signalled shock (Brady et al., 1962; Friedman & Ader, 1965; Pare, 1965) have neglected to separate postshock weight change from weight losses incurred during the stress session; this, of course, limits the generality of this work.

Lastly, Weiss (1968) has reported significant decreases in weight in inescapably shocked animals in comparison with both avoiding and unshocked control rats; these differences were apparent at both 16 and 24 hr intervals after shock. Avoiding animals showed a consistent but nonsignificant decrease below nonshocked controls. While this suggests that coping contingencies may partially reduce shock-induced weight loss, findings in this regard remain preliminary and ambiguous.

Stress and Activity

Most work examining the relationships between stress and levels of activity has used movement in an open field task as a metric of activity. Commonly, animals are placed on a demarcated area for a period of some minutes and count is taken on the number of grid crossings. This type of task appears particularly sensitive to measurement of exploratory behavior and to suppression of the latter by the introduction of fear conditioned cues. While this may serve as

an adequate index of emotionality, inferences from such tasks to general levels of psychomotor activity appear limited and must be considered in that spirit.

With that preface, Peters and Finch (1961) found significant decreases in grid crossings in rats previously subjected to a single session of inescapable shock in the test chamber. Strikingly, this effect was present for a period of 25 days. A second experimental group, subjected to shock at slightly less than one-half the intensity of the above group, showed depressions in activity in comparison with nonshocked control rats although the effects were not as severe or as long lasting as those seen in rats subjected to higher intensities of shock.

In a similar tact, Blanchard and Blanchard, elaborating on the above work, reported decreases in exploratory activity (again, as reflected in number of grid crossings) when fear eliciting stimuli were of a poorly discriminable nature (e.g., environmental cues in a shock box). On the other hand, when dangerous cues were clearly discriminable and localized, exploratory activity remained unaffected although animals passively avoided the dangerous area (Blanchard & Blanchard, 1969b, 1970a, 1970b). Similarly, Bindra and Palfai (1967) reported increases in preambulatory behavior in rats during presentation of a CS previously paired with an appetitive US. Conversely, presentation of a CS previously associated with shock lead to corresponding decreases in such behavior. Davitz, Mason, Mowrer, and Viek (1957), in like fashion, noted decreased locomotor exploratory behavior during presentation of a light previously associated with shock. While the above findings clearly indicate decreased locomotor activity following stress episodes, they remain

confounded with fear-induced suppression of movement. Accordingly, their comparability to postshock activity levels in "helpless" animals is limited.

Summary

In general summary, findings have consistently shown poststress suppressions of both food consumption and weight gain in rats. Water intake, while subject to variations in environmental contingencies, also appears to be decreased by shock episodes. Activity levels may also be subject to poststress reductions but data here remain highly speculative. Regarding effects of coping provisions on these measures, Weiss has shown alleviation of shock-induced reductions in appetitive functions and weight loss in escape-avoidance rats over yoked counterparts. However, divergent findings persist in the area and issues remain unresolved.

Therapeutic Manipulations and Depression

Tricyclic compounds (e.g., imipramine, desipramine) and electroconvulsive shock therapy (ECS) remain the two most common somatic interventions in the treatment of depression. Each has been demonstrated to produce significant amelioration of depressive symptomology over placebo interventions (Hurwitz, 1974; Klerman & Cole, 1965; Morris & Beck, 1974; Wittenborn, 1965). Nevertheless, efficacy of a given treatment for a given patient appears to reflect a complex and poorly understood relationship between treatment, type of depression, and individual patient differences. For instance, both ECS and tricyclic intervention are predominantly used in endogenous/psychotic varieties of depressions (Fink, 1974; Jarvik, 1970). Despite

this, there are reports of clinical improvement in patients with diagnosed neurotic/reactive depressions following treatment with one of the above somatic interventions (Klerman & Cole, 1965; Mendels, 1967).

Comparative studies between the two approaches suggest ECS as slightly more efficacious than antidepressant drugs as a means of intervention across "equivalent" patient groups (Hurwitz, 1974; Jarvik, 1970). In this regard, clinical improvement following ECS is reported in a range of 70-90% of treated patients (Fink, 1974; Hurwitz, 1974). Similar figures for tricyclic treatments range from 60-70% (Jarvik, 1970; Morris & Beck). Interestingly, patients failing to respond to one type of therapy may improve when switched to the other although pharmacological intervention is almost exclusively the initial therapy of choice due to undesirable side effects associated with ECS (Wittenborn, 1965).

Regarding modes of action, it can summarily be stated that this remains in the realm of speculation for both ECS and tricyclic agents although a large and overlapping literature is beginning to accumulate in this regard.

At a biochemical level, Welch, Hendley, and Turek (1974) reported finding a decreased membrane affinity for NE in the rat brain following a single application of ECS. Schildkraut and Draskoczy (1974), in addition to replicating these findings, also reported decreased levels of endogenous NE with commissurate increases in O-methylated catabolites (i.e., normetanephrine). These data combine to suggest that ECS may produce increased rates of release of NE into synaptic spaces. This, along with a reduced membrane affinity for the NE molecule, account for increased levels of O-methylated NE metabolites.

In addition to alterations in noradrenergic mechanisms, ECS has also been consistently reported to produce elevations in whole brain levels of 5-hydroxytryptamine (Bertaccini, 1959; Valzelli & Garattini, 1974). Such an increase, combined with reported increases in 5-hydroxyindole acetic acid (Valzelli & Garattini, 1974) and free plasma tryptophan (Stelmasiak & Curzon, 1974) presents a picture of an increase in both turnover and endogeous levels of 5-hydroxytryptamine (5-HT).

Interestingly, parallels exist between ECS-induced modifications in brain chemistry and putative mechanisms of the tricyclics. Specifically, the latter have been extensively reported to block neuronal reuptake of brain monoamines (Bopp & Biel, 1974; Lidbrink, Jonsson, & Fuxe, 1971; Longo, 1972). Early reports proposed this effect to be most pronounced in noradrenergic systems. However, this position has been modified by subsequent findings to suggest that imipramine-type drugs with secondary amine characterics (e.g., desipramine; protriptyline) preferentially inhibit the NE membrane pump for central noradrenergic neurons while compounds with tertiary amine characteristics (e.g., imipramine; chlorimipramine) preferentially inhibit membrane pumping of 5-HT (Lidbrink et al., 1971). Importantly, these latter effects are obtained in clinical dose ranges. At higher concentrations, competitive blocking has been observed at the postsynaptic receptor (Longo, 1972), although this mechanism is not thought to be involved in the drug's clinical actions.

It is of particular interest that Schildkraut and his associates (Schildkraut, Winokur, & Applegate, 1970; Schildkraut, Winokur, Draskoczy, & Hensle, 1971) have, in contract to the above findings, reported increases in NE turnover following a course of chronic

tricyclic administration (rats were dosed twice daily for a 3 week period). Critically, the time course of these events paralleled the time course of clinical improvement commonly reported for such agents. The relationship between this latter finding and the therapeutic efficacy of the tricyclics remains to be determined.

As a relevant aside, recent advances in outlining modes of action of clinically effective antidepressant drugs, combined with increasing knowledge into the metabolism of chemical systems of the brain, have lead to recent formulations of several biological theories of depression. These have included suggestions of impaired NE metabolism (Schildkraut & Kety, 1967), impaired serotonin metabolism (Lapin & Oxenkrug, 1969), or a combined imbalance in both systems (Bueno & Himwich, 1967). While such theories are intriguing, they remain incomplete and, consequently, are yet to significantly contribute to improvements in the understanding and clinical treatment of depression.

Summary

In summary, review of relevant findings on learned helplessness remain unresolved with regard to both the validity of the theoretical basis of the phenomenon and to the viability of the paradigm as a model of depression. In this regard, several issues are pertinent.

1. Learned helplessness (i.e., learning that responding is noncontingent) has yet to be convincingly demonstrated in the rat without accompanying shock artifact. In this regard, it has been suggested that learning deficits following inescapable shock reflect prepotent freezing in the presence of fear-inducing stimuli. Such explanations appear to provide a highly viable alternative to the helplessness explanation and suggest the need for further experimentation.

2. Providing animals with some type of coping contingency during PS has been reported to eliminate subsequent learning deficits (an effect described by proponents of the model as "therapeutic"). However, it is possible to argue that rats allowed to escape and/or avoid during PS are not, in fact, learning that their responding in an aversive situation is effective in dealing with that situation (as suggested by a helplessness explanation) but, instead, may simply be learning to suppress prepotent tendencies to freeze while afraid. When subsequently retested, such rats perform at a higher level than inescapably shocked counterparts. This may simply reflect proactive facilitation occurring as a result of having previously learned to suppress freezing tendencies.

3. Shock per se has consistently been demonstrated to suppress appetite (food and water intake), increase weight loss, and suppress activity. However, findings remain equivocal with respect to differential effects of controllable and uncontrollable shock (and stress) on these measures. In this regard, it remains to be clearly demonstrated that the psychological effects of controllable shock differentially effect these variables in contrast to uncontrollable shock.

4. Both tricyclic intervention and ECS have been shown to be efficacious in dealing with a variety of depressive disorders. If, indeed, subjecting animals to inescapable shock does produce an animal analogue of clinical depression, then the above manipulations should likewise produce an amelioration of that state (at least to the extent that the two conditions share common biological substrates).

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APPENDIX 2

CURRICULUM VITA

Personal:

Born: March 5, 1944

Marital Status: Single

Education:

University of California at Los Angeles,
Bachelor of Science, 1967.

American River College (Sacramento, California),
Associates Arts, 1965.

Appointments:

Teaching Associate. Department of Psychology, University of New Mexico. 1975-1976.

Graduate Assistant. Department of Psychology, University of New Mexico. 1972-1975.

Publications:

Feeney, D. M., Wagner, H. R., McNamara, M. C. & Weiss, G. Effects of tetrahyrocannabinol on hippocampal evoked afterdischarges in cats. Experimental Neurology, 1974, 41, 357-365.

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