SOME EFFECTS OF ADRENOCORTICOTROPHIC HORMONE AND DEXAMETHASONE ON BEHAVIOR OF THE RAT IN THE CONDITIONED EMOTIONAL RESPONSE SITUATION

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In an attempt to clarify the relative influences of adrenocorticotrophic hormone (ACTH) and adrenal corticoids on aversively controlled responses, fifty-four experimentally naive male hooded rats were trained in an Estes-Skinner conditioned emotional response (CER) task. The mean suppression ratios and bar-presses were measured daily. Dexamethasone 21-phosphate (200 μg), Zinc Corticotrophin Hydroxide (12 I.U.) and dexamethasone, and saline were injected either in extinction (Experiment I) or in acquisition (Experiment II) in the respective treatment groups. The data were analyzed by analysis of variance. ACTH significantly increased suppression ratios only during acquisition. Dexamethasone had no effect on suppression. Both hormones produced decreases in the number of bar-presses made in extinction, regardless of when given. These results together with previous findings were interpreted as indicating that whereas ACTH has some direct effects on "fear", adrenal corticoids have a general effect on instrumental responding.

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INTRODUCTION

Interest in the influence of pituitary and adrenal hormones on emotional behavior has grown considerably with the introduction of improved biochemical and behavioral investigational techniques within the last ten years. The origins of this interest, however, can be traced to the recognition by James (1890), Watson, (1929) and Cannon (1927) that physiological states play an important role in the determination of emotions. Workers in psychiatry (Rome and Braceland, 1952) general medicine (Selye, 1950), psychosomatic medicine (Goolker and Schein, 1953; Pincus and Hoagland, 1949) and psychology (Levine, 1962: Schacter and Singer, 1962) have since speculated on the possible relations between exaggerated stress responses, especially pituitary-adrenal responses, and the occurrence of intense emotional states or of actual emotional disorders. "The commonness of mental disturbances associated with disorders of the endocrine system as a whole, and the pituitary-adrenocortical axis in particular, gave further support to an attractive thesis which originally centered its focus on these sites." (Rome and Robinson, 1959, p. 1281). Not only was it suggested that pituitary and adrenal hormones figured prominently in the overall stress response (Selye, 1950) and in the onset of psychosis (Rome and Braceland, 1952), but also that these hormones might in general be implicated in the control of behavior governed by aversive stimuli (Mirsky, Miller and Stein, 1953). As knowledge of the physiology of these and related endocrine systems improved, such speculations become more specific.

Adrenocorticotrophic hormone (ACTH) of the anterior pituitary and adrenalin of the adrenal medulla are known to be released rapidly in

response to stress. Some of the processes related to this hormonal response to stress are better understood than others. Adrenalin may be involved in the actual release of ACTH. It is known that ACTH governs the synthesis and provokes the release of gluco-corticoids of the adrenal cortex. In the absence of ACTH, corticoid function is minimal. High levels of ACTH are measured either by high plasma corticoid levels, or by large depletion of a corticoid precursor, adrenal ascorbic acid, upon the application of a standard stress. High ACTH levels are often associated with efficient avoidance performance on both active and passive avoidance tasks (Levine, 1969).

While the release of ACTH occurs within a few minutes of the onset of stress, corticoid levels in plasma do not rise appreciably until at least 15 minutes to an hour later. In their turn, high corticoid concentrations suppress the release of ACTH by the anterior pituitary, forming a negative feedback loop. Both hypothalamic and thalamic centers have been implicated in this feedback suppression (Davidson, Jones and Levine, 1968; Usher, Kasper and Birmingham, 1967; Bohus and de Wied, 1967; Von Wimersma-Greidanus and de Wied, 1969). It may be that corticoids also act at one or several of these loci to inhibit the behavioral effects of already circulating ACTH.

In studies of the effects of pituitary-adrenal hormones on behavior, a main problem, imperfectly recognized, has been to isolate the minimal set of hormone changes responsible for the observed effects. The interrelations of these few hormones with each other and with other endocrine systems are discouragingly complex, calling for the broadest possible perspective of their relative physiology (Mason, 1968, esp. p. 791-808). However, when one is concerned with a specific class

of behavior, it is imperative to seek more precise descriptions of the relations between any specific hormone and a particular behavior, while not ignoring basic confusions. Three kinds of imprecision deserve particular attention in this context.

First, effects of ACTH and of corticoids have not been clearly separated. Elevations in plasma ACTH, as occur during prolonged stress, directly raise plasma corticoid levels. Conversely, continued high plasma corticoid levels are an index of sustained ACTH secretory responses. Hence the behavior said to be associated with large injections of ACTH or with measured high corticoids may in fact be due to either hormone, or to both.

Second, there is the question of the technique by which the effects of ACTH or corticoids may best be examined. Correlational studies have the advantage of leaving the organism relatively undisturbed, but do not necessarily point out causal relationships. Such studies have value largely in displaying the functions which are worth examining by more manipulative methods (Mason, Brady, and Sidman, 1957), or in confirming that findings of the latter kind are consistent with naturally-occurring relationships (Wertheim, Conner and Levine, 1969).

Ablation techniques, although they offer valuable information as to the behavior of the organism in the absence of certain hormones, involve formidable difficulties of interpretation, which do not hinge merely on the problem of the added trauma of surgical intervention. The adrenal cortex, which makes and stores gluco-corticoids, also makes mineralo-corticoids which are necessary for normal plasma sodium balance and, hence, are partly responsible for normal sensory-motor function. Apart from the cortex, the adrenal gland also houses the medulla and its hormones, adrenalin and noradrenalin.

Adrenalin itself has been implicated in the development and maintenance of emotional responses. Hence the results of adrenalectomy, a favorite strategy for removing gluco-corticoids from the system, are confounded by the removal of two other important sets of hormones. They are also confounded by post-surgical rises in ACTH (Gemzell, Van Dyke, Tobias, and Evans, 1951; Barrett, Hodges, and Sayers, 1957; Ulrich and Slusher, 1964). Thus it is not clear whether any difference in behavior observed in adrenalectomized animals is due to the fall in corticoids or to this rise in ACTH. The period of recovery to normal levels of ACTH secretion is some four to five weeks. Analogous difficulties stem from the fact that the anterior pituitary, which stores ACTH, also governs the gonads and the thyroid via trophic hormones. Not only are there other anterior pituitary hormones beside these, but there are two posterior lobe hormones as well, which can both influence (or complement) anterior lobe functions (de Wied, 1965, 1966; de Wied and Bohus, 1966). The results of hypophysectomy (removal of the whole pituitary) or even adenohypophysectomy (removal of the anterior lobe) are thus incredibly complex metabolically, and to cite ACTH absence alone as the cause of the ensuing behavioral changes is perhaps overly optimistic of a simple explanation.

Injection techniques have the advantage of simplicity and directness, but it would be foolish to assume that only one endocrine function is selectively affected. In the typical injection study on the pituitary-adrenal system (in early work, usually combined with ablations, e.g., Miller and Ogawa, 1962), as has been pointed out, the effects of ACTH and of corticoids have not always been clearly separated. It is also the case that, as could be said equally of other techniques, effects on acquisition and on retention of the response in question have

usually been indiscriminately confounded. If the experimenter injects (or ablates) in or prior to the period of acquisition, and observes some effect in extinction (e.g., Miller and Ogawa), at what point has he influenced the response he observes?

Third, and very important, in most discussions of the effects of pituitary-adrenal hormones on behavior under aversive control a number of responses have been lumped together. Levine (1969) in a recent review attempted some separation of the effects of the individual hormones and of the classes of behavior affected; however, many of the confusions just cited remain unresolved.

In spite of all the foregoing difficulties, some trends do appear when one examines the data which have so far been obtained. The majority of the studies reported were carried out on rats.

Active Avoidance

De Wied (1964) attempted to extend previous findings concerning changes in the acquisition of a two-way active avoidance (shuttle) response following removal of ACTH by pituitary ablations. Appelzweig and Baudry (1955) and Appelzweig and Moeller (1959) had observed significant impairment of acquisition of the shuttle response following hypophysectomy. Daily ACTH treatment largely prevented this deficit, but had no significant effect on acquisition in normal animals. However, the number of animals was small and the whole pituitary had been removed. De Wied (1964) was able to demonstrate an impairment of acquisition by removing only the anterior pituitary. The deficit was minimized in animals treated with either ACTH or a "cocktail" of three pituitary-governed hormones. This "cocktail" included a 250 µg dose of cortisone acetate equivalent gluco-corticoid activity to about 500 µg of

corticosterone (Frawley, 1967), the principal gluco-corticoid of the rat adrenal gland. On the basis of this study, de Wied questioned whether ACTH exerts a critical influence on the acquisition of the avoidance response. The effect of anterior pituitary removal could be due either to the lack of ACTH, to the lack of the corticoids which ACTH releases, or to the lack of other hormones in the "cocktail."

In an experiment using injections and no ablations, Murphy and Miller (1955) observed that ACTH given to animals during the acquisition of a shuttle response, or during both the acquisition and extinction periods, produced a significant increase in the number of conditioned avoidance responses (CAR's) made in extinction. Treatment only in extinction had no such effect. In no case did ACTH treatments significantly affect the acquisition of the response. Miller and Ogawa (1962) showed that this effect in extinction and absence of an effect in acquisition could be demonstrated in adrenalectomized animals treated only in acquisition with ACTH. Thus, the ACTH effect in extinction appeared to be independent of corticoid activity. However, the manner in which an acquisition treatment might affect only extinction behavior remains unclear. Additional complications were introduced by the operation, as already discussed.

The effects of ACTH treatments on behavior in extinction, however they may originate, appear to be highly reliable. De Wied (1966) demonstrated that treatment only in extinction with a variety of substances, each containing at least the active amino acid sequence ACTH 4 - 10 (which is the central portion of the natural peptide ACTH 1 - 24), led to a significant increase in the number of CAR's in extinction. Bohus and de Wied (1966) not only repeated this result, but also showed that injection of a stereoisomeric ACTH molecule, with a change in a

single mid-chain amino acid, led to a significant decrease in the number of CAR's exhibited. De Wied (1967) obtained results indicating that in animals in which ACTH was maintained at a high level during extinction, either through injection or as a result of recent adrenalectomy, the shuttle response was strongly resistant to extinction. Furthermore, in a group of animals hypophysectomized (no ACTH) prior to acquisition, extinction was rapid. It would appear, therefore, that ACTH was crucial in the maintenance of the CAR in extinction.

However, the hypophysectomized animals were maintained on the previously mentioned "cocktail" containing cortisone. There is reason to believe from evidence in the same study that the decreased resistance to extinction in hypophysectomized animals could be due to the presence of the corticoid rather than to the absence of ACTH. Treatment of normal animals during extinction with either dexamethasone, a potent synthetic corticoid, or with corticosterone, was associated with a dose-dependent decrease in resistance to extinction of the CAR. It is possible, then, that corticoids have effects on active avoidance independent of ACTH. That these effects are related to gluco-corticoid activity specifically appears to be demonstrated by the fact that large doses of aldosterone (which has only slight gluco-corticoid function) were required to reduce resistance to extinction significantly.

To summarize, it is not clear whether ACTH alone is sufficient to allow normal acquisition of a two-way response, or whether corticoids are also necessary. A very clear and persistent finding is that ACTH maintains the CAR in extinction, regardless of the period in which it is given. High levels of corticoids, on the other hand, have been associated with a decrease in resistance to extinction of the CAR when

injected in that period.

A number of studies employing the one-way active avoidance response lend support to these specific conclusions. Measuring adrenal output of corticosterone, Bohus, Endroczi and Lissak (1964) observed a high positive correlation between the level of this corticoid after extinction and the number of CAR's made during extinction. Bohus and Lissak (1968) obtained results which they interpreted to mean that the absence of corticoids rather than the increases in ACTH following adrenalectomy were the reason for the increased resistance to extinction of the one-way response. They observed a persistence of the CAR in animals adrenalectomized after training, whether saline was given, or deoxycorticosterone acetate (DOCA). The authors stated that DOCA, a sodium-retaining, aldosterone-like mineralo-corticoid, having no gluco-corticoid activity, suppresses ACTH. They argued from this that facilitation of the extinction of the response after adrenalectomy is independent of the increase in ACTH which follows removal of feedback control of corticoids, and that "changes in the rate of avoidance extinction are elicited by the excess or absence of gluco-corticosteroids" (p. 305). However, it should be noted that DOCA, because it lacks gluco-corticoid activity, has no pituitary suppressive effect whatsoever (Frawley, 1967). Thus ACTH increases may complement corticosteroid decreases in the maintenance of the response in extinction in adrenalectomized animals, or ACTH alone may be responsible. The definitive experiment has not been done.

Another type of active avoidance task which has been examined in relation to these hormones is the Sidman (unsignalled) bar-press response. The findings with this response parallel those with other active avoidance tasks but leave as many questions undecided. In a classic experiment

Sidman, Mason, Brady and Thach (1962) showed that plasma corticoid levels (indicating high ACTH levels) covaried with the bar-press rate in the Sidman schedule during both the acquisition and extinction of the response. They found higher corticoids and increased bar-pressing after any sudden change to a shorter response-shock interval, when free shocks were applied, or during spontaneous recovery in extinction. Wertheim, Conner and Levine (1967) found that ACTH treatment led to dose-dependent increases in responding on a Sidman schedule. In the same study they demonstrated a dose-dependent decrease in responding after dexamethasone treatment. In another study (Wertheim, Conner and Levine, 1969) they observed that animals who exhibited significantly greater corticoid responses to ether stress (larger ACTH secretory responses) prior to acquisition training, as well as a higher resting level of corticosterone during acquisition, avoided more shocks than other animals. This effect, of course, might be due to either ACTH or corticoid.

Passive Avoidance and Related Measures

The "passive avoidance response" is studied by making an aversive stimulus contingent on the animal performing some predefined, usually appetitive, response. The degree to which the animal subsequently withholds, or "suppresses" the predefined response is taken as the measure of passive avoidance. In passive avoidance and in the conditioned emotional response (CER) situation (suppression of ongoing appetitively motivated behavior during presentation of a classically conditioned aversive stimulus), the measure of fear is perhaps more direct than in active avoidance, since such withholding of responses would seem to be more primitive.

Endroczi, Telegdy, and Lissak (1957), by pairing shock with a previously positive CS, inhibited an established appetitive response. In animals injected with ACTH throughout the experiment they found a significantly longer inhibition of the appetitive response than in control animals. In agreement with this result, Koranyi, Endroczi, Lissak, and Szepes (1967) observed that treatment with ACTH on either the last trial of acquisition or the first trial of extinction significantly augmented a passive avoidance response in extinction.

However, a more precise study by Levine and Jones (1965), replicated with some variations by Anderson, Winn and Tam (1968), allows a somewhat clearer judgment of the relative contributions of ACTH and of corticoids to passive avoidance responses. Levine and Jones made shock contingent on a bar-press response for water. A group injected with ACTH during the shock session only (ACTH-terminated) was compared during extinction with a control group. A bimodal distribution was observed in both groups; some animals resumed appetitive responding within two or three days, while others remained inhibited for at least six days. Among the animals who resumed appetitive responding earlier, those from the ACTH-terminated group made significantly more bar-presses in extinction than the early-returning control animals. When ACTH treatment was continued until the end of extinction, however, the inhibition of responding was prolonged. To interpret these results Levine (1969) suggested that, with sudden withdrawal of exogenous hormone following long-term treatment, ACTH-terminated animals were deficient in the release of endogenous ACTH, and that this led to lesser response suppression.

To determine whether ACTH sustains the passive avoidance response,

or whether the convarying corticoids are responsible, Anderson, Winn and Tam (1968) repeated the Levine and Jones experiment in animals hypophysectomized prior to training. In such animals, the appetitive response was only minimally suppressed during the extinction period. Continuous hydrocortisone treatment beginning prior to acquisition did not increase this suppression; while ACTH or ACTH and hydrocortisone treatment throughout acquisition and extinction led to prolonged suppression. From the studies just mentioned, it seems that ACTH is to be implicated in the control of passive avoidance, with corticoids playing little part in sustaining the response. Anderson, Winn, and Tam's finding clearly contradicts the implications of those studies on active avoidance which would suggest that corticoids do have an effect on avoidance responding in extinction antagonistic to that of ACTH. It does not stand alone, however. Weiss, McEwen, Silva and Kalkut (1969) observed that by altering situational cues between training and test so as to reduce available "fear" cues, they could better distinguish between animals adrenalectomized, hypophysectomized or untreated prior to the acquisition of a psssive avoidance response. Adrenalectomized animals showed significantly greater response inhibition in the "low fear" situation. Under "high fear" conditions they were equivalent to normal animals. Hypophysectomized animals showed less response inhibition than normal animals under either condition. Weiss et al. briefly reported that with the same treatments and a CER measure, suppression of operant responding for food and water to a tone presented several seconds before a "strong shock" was intense and did not differentiate the three hormone conditions. However, suppression to the box alone where the tone-shock pairings were given did differentiate adrenalectomized, hypophysectomized and normal

animals. The details of the latter experiment have not yet been published. Since corticoid levels are minimal in both adrenalectomized and hypophysectomized animals, Weiss et al.'s findings relate apparent differences in fear arousal to differences in the level of ACTH only. Weiss et al.'s study and the one by Anderson, Winn and Tam (1968) imply a minimal role for corticoids in the control of passive avoidance responses. In both cases, the results may be confounded by the fact that ablations were made before training. It may be that when only injections are employed the effects will be analogous to those found in active avoidance studies.

Aims of the Present Study

In the light of the previously mentioned findings, the present study was aimed at answering three main questions: (1) To what extent does the alteration of hormone states during the acquisition of an aversive response account for observed changes in extinction performance? This question relates to confusions arising from such treatments as preacquisition adrenalectomy or hypophysectomy, as well as to studies in which hormone treatments are given during both the acquisition and extinction periods. Could comparable effects be observed when hormones were manipulated in only one of these periods?

(2) When the experimenter resorts to gland removal, to what extent does the loss of other major hormones contribute to performance changes which have been attributed uniquely to changes in ACTH or corticoids? Could comparable effects be demonstrated when only specific hormones were manipulated without surgical intervention?

(3) How is it possible to determine the prepotency of either ACTH or the corticoids when, as usually occurs in stress, the levels of

both are high? This is an important question, to which only one imperfect answer has been given. Anderson, Winn and Tam (1968) found ACTH prepotent over corticoid, inasmuch as increased resistance to extinction of a passive avoidance response was observed in the group given both corticoid and ACTH, while no effect was observed in the group given only corticoid. In the Anderson, Winn and Tam study, however, the animals were hypophysectomized prior to the experiment and were injected during both the acquisition and extinction of the response.

Rationale for the Method

The Estes-Skinner (1941) CER technique was chosen as a relatively sensitive measure of acquired "fear" of a CS (Annau and Kamin, 1961; Kamin and Schaub, 1963). It is assumed that suppression of ongoing appetitively motivated behavior during presentation of a classically-conditioned aversive CS reflects acquired "fear", in that the respondents associated with the aversive CS interfere with the ongoing appetitive respondents. For example, intense orienting responses to the CS may interfere with an ongoing bar-press response for food. As one investigator has succinctly described it, "the CER pits 'hunger' against 'fear'" (Kamin, 1965). In accordance with the unpublished finding cited in Weiss et al. (1969) that changes in pituitary-adrenal hormones could be more clearly seen to influence a CER under "low fear" than under "high fear" conditions, two levels of shock were chosen which are different in terms of the expected suppression with a 70 db white noise CS (Annau and Kamin, 1961).

Animals were treated with dexamethasone, with dexamethasone plus ACTH, and with only saline, since then a comparison could be made

between the degree of suppression observed in a high corticoid-low ACTH group (the dexamethasone-injected), a high corticoid-high ACTH group (the animals given both hormones) and a normal group. Since injected ACTH would itself release endogenous corticoid, ACTH "override" of any observed corticoid effect would be a severe test of its prepotency.

In addition to the suppression data, additional observations on the daily number of bar-presses and of reinforcements were considered of interest. These observations were suggested by the results of experiments by Wertheim, Conner and Levine (1967, 1969) relating injected corticoid, or high levels of endogenous corticoids, to superior timing behavior on a Sidman bar-press shock avoidance schedule. As well, there is a suggestion in data briefly cited by Levine (1969) that pituitary-adrenal hormones may have effects on non-emotional behavior, in that they influence the timing of bar-press responses on certain appetitive schedules. More information on these effects might prove valuable.

To separate the effects of the drugs on acquisition and extinction of the response, the hormone treatments were given in only one of these periods rather than in both. Since so many previous results had indicated the effects of these hormones on extinction to be the most reliable, extinction treatments were chosen for study in the first experiment, with acquisition treatments reserved for a second.

THE EXPERIMENTS

Method

Subjects

The subjects used in these experiments were experimentally naive male hooded rats from the Quebec breeding farms (St. Eustache, P.Q.) weighing from 275-375 grams. Thirty animals were used to make up matched groups in Experiment I; 26 in Experiment II. They were housed in individual cages and maintained on a diet of Purina Lab Chow (#5001 pellets) and water supplemented with liquid vitamins (Ostoco Vitamin Drops: C. E. Frosst, Montreal) and an antibiotic (Terramycin: Pfizer, Montreal). The colony room was darkened from 12:30 a.m. to 8:30 a.m. daily. All testing was conducted between 11:30 a.m. and approximately 11:30 p.m. each day.

All animals were maintained on 24-hour food deprivation at 75 per cent of their ad libitum weight and were taught to bar-press on a 2.0-minute VI schedule. A stable rate of bar-pressing was achieved with five to seven daily 2-hour sessions of VI training, after which CER training was begun.

Apparatus

Standard Grason-Stadler relay equipment was used to control the eight rat stations that were housed in individual sound-attenuating chambers in an adjoining closed room. A Grason-Stadler constant-current shock generator and scrambler (model E1064GS) was used for each box. The CS was provided by a single Grason-Stadler (model 901B) noise generator with output separately adjusted for each box via a multiple "audio splitter." The CS intensity was measured in each box (with all box

ventilation fans off) with a General Radio sound-level meter (G.R. Co., Concord, Mass., model 1551-C).

CER Procedures

The CS was a 3-minute 70 db white noise first presented on the Pretest Day (without US). The length of the CS and the schedule of presentation were the same for the Pretest Day and each day thereafter: a CS was presented four times in the usual two-hour bar-press session, at 17, 41, 67, and 97 minutes from the start of the session. It was preceded by an unsignalled 3-minute "pre-CS" period during which baseline bar-press rates were counted. The suppression ratios comparing "CS" (B) and "pre-CS" (A) bar-press rates were calculated as $\frac{B}{A + B}$ for each of the four daily CS presentations, and then averaged to obtain a "daily ratio" for each animal. A ratio of 0.50 indicates no suppression; a ratio of 0.00 indicates total suppression during the CS. Ratios between 0.50 and 0.00 indicate intermediate degrees of suppression. It is theoretically possible to have a ratio of 1.00, indicating that the animal pressed during the "CS" but <u>not</u> in the "pre-CS" period.

<u>Pretest</u>: This day's session included four CS presentations without us. The ratios from this Pretest Day are considered to reflect the "innate suppressiveness" of the CS employed, before any pairing of the CS with shock. Kamin (1965) has observed that, when backward conditioning is attempted with these white noise stimuli (presentation of the CS alone following training sessions in which <u>unsignalled</u> shock has been given), CS presentations lead to a relative <u>increase</u>, not a decrease, in the bar-press rate.

Conditioning: For three days, Ss were given four CS-US pairings per day. The offset of the CS initiated a 0.5 second, 0.5 or 1.0 ma scrambled shock delivered through the grid floor of the box.

Extinction: There were six extinction sessions. Each day, the CS was presented four times on the usual schedule, but without US.

Total bar-presses and total reinforcements were recorded throughout the experiment. Mean suppression ratios were calculated daily for each animal from the Pretest Day until the end of extinction.

EXPERIMENT I

Treatments and Design

Six groups of five animals each were matched on the basis of the number of bar-presses made on the last day of VI training. Both the group mean and the range were taken into account in the selection of groups. An analysis of variance performed on the bar-press data for this day confirmed that there were no significant differences between these six groups ($F = 0.22$; $df = 5/24$; $p > .05$; $F = 2.62$ required). All hormone injections were given in the extinction period; physiological saline was given during the acquisition period of the CER. Table 1 outlines the groups and their treatments. For three of the groups, 0.5 ma shock was the US used during acquisition. For the three other groups, 1.0 ma shock was used. At each shock level, animals in two of the three groups were first given a 0.2 ml subcutaneous injection containing 200 µg of dexamethasone 21-phosphate (Hexadrol: Organon, Montreal) 75-90 minutes prior to the first CS presentation on each day of extinction. For one of these groups at each shock level, this injection was followed by a second subcutaneous

TABLE 1

DESIGN OF EXPERIMENT I
(HORMONE TREATMENTS IN EXTINCTION)

	Shock level in ma	
	0.5	1.0
Injection	Saline	Acetate Buffer
	Dexamethasone	Dexamethasone
	Dexamethasone & ACTH	Dexamethasone & ACTH

injection of 0.3 ml containing 12 I.U. of Zn-ACTH (Corticotrophin Zinc Hydroxide Suspension: Organon, Montreal) 20-30 minutes prior to the first CS ("Dex-ACTH 0.5", and "Dex-ACTH 1.0" Extinction Groups); for the other, by a subcutaneous injection of 0.3 ml of saline ("Dex 0.5" and "Dex 1.0" Extinction Groups). For the third group of animals at the 0.5 ma shock level ("Control 0.5" Group) the two injections were saline in the appropriate volumes. The animals in the third group at the 1.0 ma shock level ("Control 1.0" Group) were derived originally from a concurrent experiment employing the same training parameters. They were injected with a 0.2 M, pH 4 sodium acetate buffer in the appropriate volumes rather than with saline, as they were originally to have been compared with a group given the drug Elipten (aminoglutethimide) suspended in this buffer. To induce adaptation to the injections themselves, all animals were injected with saline, from at least the present day, on the same schedule as that arranged for the hormone injections in extinction.

The dose levels and the schedule of injections were arranged to produce a maximal or near-maximal effect of the hormones during at least the central 80-minute period of the daily session which bounded the four CS presentations (Wertheim, Conner and Levine, 1967).

Results

The daily mean suppression ratios for each of the six extinction-injected groups are shown in Figure 1. Figure 2 shows the daily mean number of bar-presses made by these same six groups. As is evident from the mean suppression ratios for the Pretest Day, there was no appreciable tendency for these animals to suppress to the CS until the application of shock in acquisition.

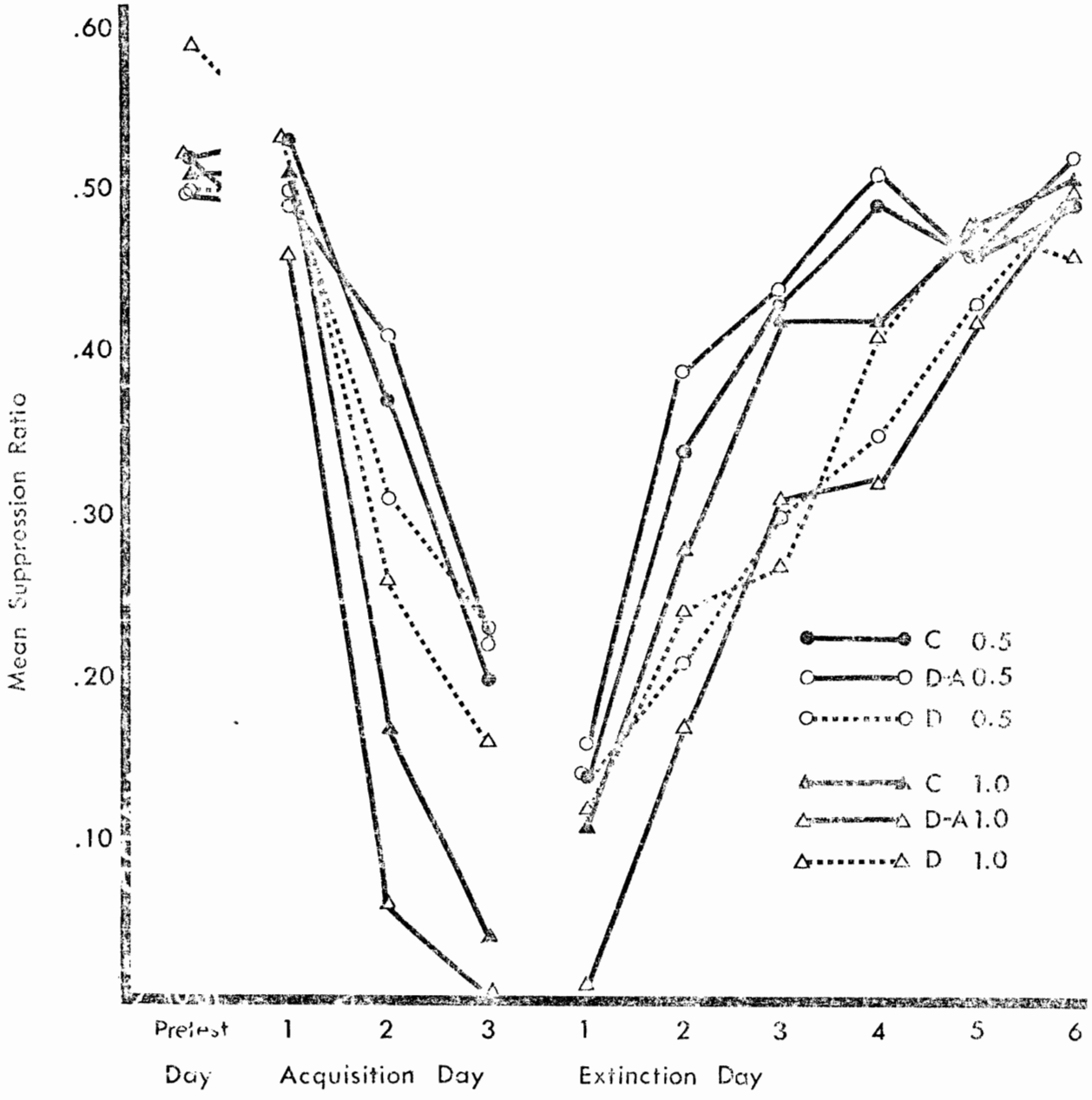

Figure 1. Mean suppression ratios in each of the six extinction-injected groups. C, Control Group; D-A, Dex-ACTH Group; D, Dex Group.

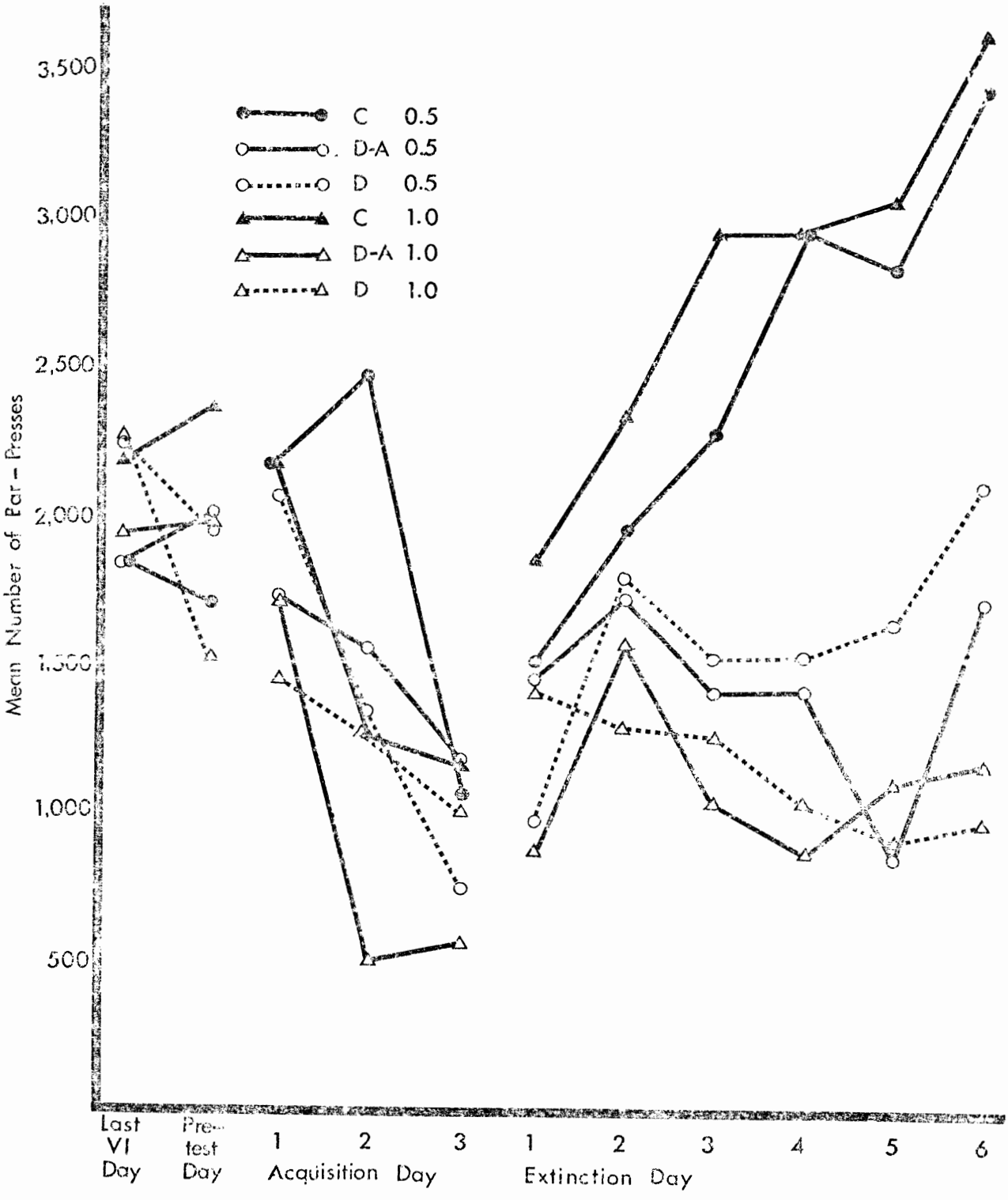

Figure 2. Mean number of bar-presses made by each of the extinction-injected groups. C, Control Group; D-A, Dex-ACTH Group; D, Dex Group.

Separate 3-way analyses of variance (shock x treatment x days) were carried out on the daily mean suppression ratios and on the daily total number of bar-presses for these six groups for the acquisition period of the CER, and then for the period of extinction. For acquisition Days 2 and 3, prior to any hormone treatment, the analysis of variance of the suppression data (Table 2) revealed that 1.0 ma shock led to significantly greater suppression ($F = 14.92$; $df = 1/24$; $p < .001$) and that suppression was greater in all groups across the three days of training ($F = 37.16$; $df = 1/24$; $p < .001$). The treatment groups did not differ; and all interactions were nonsignificant. For the six days of extinction, the analysis of the suppression ratios of these same groups (Table 3) revealed only a significant deepening of suppression across days ($F = 98.29$; $df = 5/120$; $p < .001$).

The analysis of the bar-press data on Days 2 and 3 of acquisition of the CER (Table 4) indicated that 1.0 ma shock produced a relative increase in suppression which fell just short of significance ($F = 4.22$; $df = 1/24$; $p > .05$; $F = 4.26$ required). Again, suppression increased across days ($F = 10.49$; $df = 1/24$; $p < .005$), and there was a significant shock x days interaction ($F = 6.38$; $df = 1/24$; $p < .05$). An examination of this interaction (see Figure 3) indicates that whereas the mean number of bar-presses was reduced on Day 2 for the 1.0 ma shock groups, the mean for the 0.5 ma shock groups did not reach a comparable low level until Day 3 of acquisition.

The analysis of the bar-press data on the six extinction days (Table 5) showed that the following effects were significant: a treatment effect ($F = 8.91$; $df = 2/24$; $p < .005$), a days effect ($F = 11.49$; $df = 5/120$; $p < .001$), a treatment x days interaction ($F = 8.47$; $df = 10/120$; $p < .001$), and a shock x treatment x days

TABLE 2

MEAN SUPPRESSION RATIOS ON ACQUISITION DAYS 2 AND 3 IN EXTINCTION-INJECTED GROUPS
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		29		
Shock	4558.81	1	4,558.81	14.92##
Treatment	494.43	2	247.22	0.81
Shock x Treatment	1266.64	2	633.32	2.07
Subjects within groups (error between)	7334.20	24	305.59	
Within Subjects		30		
Days	2220.41	1	2220.41	37.16##
Shock x Days	43.76	1	43.76	0.73
Treatment x Days	98.24	2	49.12	0.82
Shock x Treatment x Days	201.89	2	100.95	1.69
Days x Subjects within groups (error within)	1434.20	24	59.76	

##p < .001

TABLE 3

MEAN SUPPRESSION RATIOS ON EXTINCTION DAYS 1 TO 6 IN EXTINCTION-INJECTED GROUPS
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		29		
Shock	897.80	1	897.80	2.12
Treatment	1,041.81	2	520.91	1.23
Shock x Treatment	1,513.04	2	756.52	1.78
Subjects within groups (error between)	10,182.66	24	424.28	
Within Subjects		150		
Days	27,736.91	5	5,547.38	98.29##
Shock x Days	424.07	5	84.81	1.50
Treatment x Days	838.66	10	83.87	1.49
Shock x Treatment x Days	572.49	10	57.25	1.01
Days x Subjects within groups (error within)	6,772.54	120	56.44	

##$p < .001$

TABLE 4

TOTAL BAR-PRESSES ON ACQUISITION DAYS 2 AND 3 IN EXTINCTION-INJECTED GROUPS
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		29		
Shock	2,826,642	1	2,826,642	4.22
Treatment	3,115,249	2	1,557,625	2.32
Shock x Treatment	2,288,786	2	1,114,393	1.66
Subjects within groups (error between)	16,083,555	24	670,148	
Within Subjects		30		
Days	2,966,371	1	2,966,371	10.49#
Shock x Days	1,803,707	1	1,803,707	6.38*
Treatment x Days	892,314	2	446,157	1.58
Shock x Treatment x Days	721,367	2	360,684	1.27
Days x Subjects within groups (error within)	6,789,758	24	282,907	

#p < .005
*p < .05

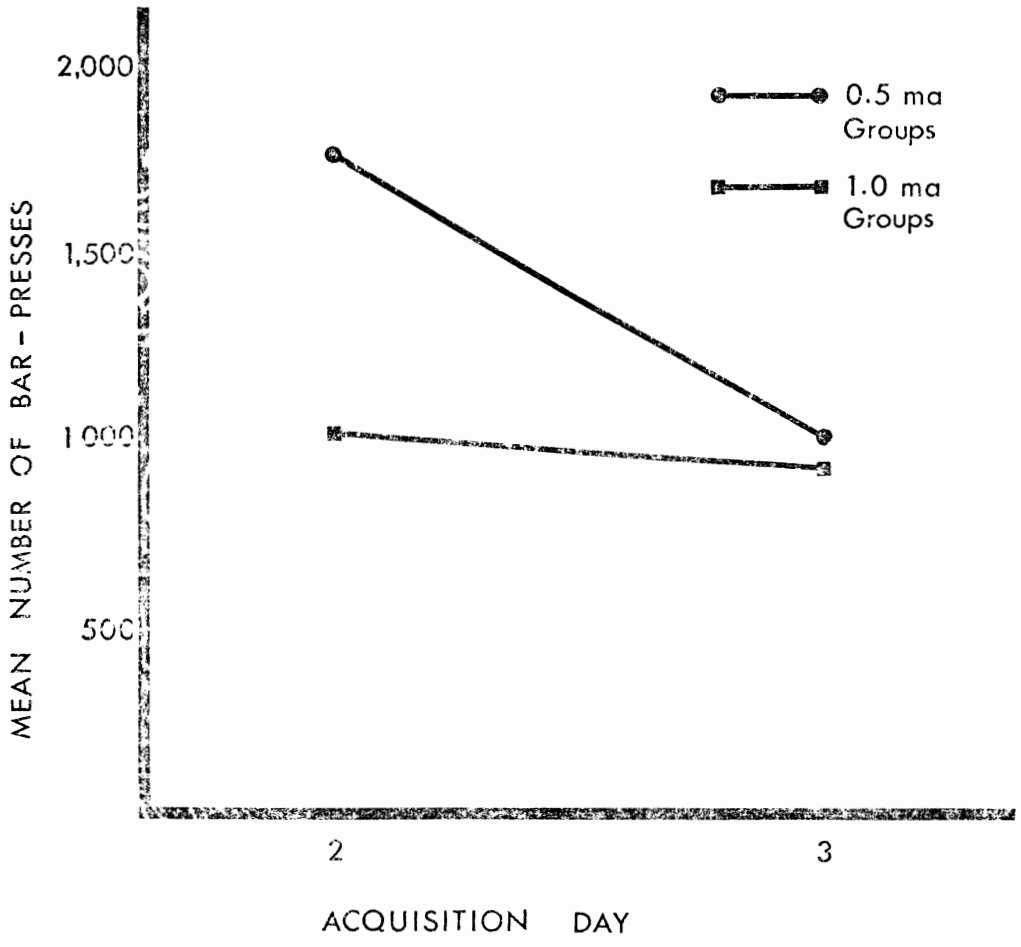

Figure 3. Shock x days interaction in the bar-presses made on Days 2 and 3 of acquisition by the extinction-injected groups.

TABLE 5

TOTAL BAR-PRESSES ON EXTINCTION DAYS 1 TO 6 IN EXTINCTION-INJECTED GROUPS
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		29		
Shock	1,103,090	1	1,103,090	0.28
Treatment	70,055,189	2	35,027,595	8.91#
Shock x Treatment	4,751,311	2	2,375,656	0.60
Subjects within groups (error between)	94,299,949	24	3,929,165	
Within Subjects		150		
Days	10,296,432	5	2,059,286	11.49##
Shock x Days	1,731,108	5	346,222	1.93
Treatment x Days	15,188,989	10	1,518,899	8.47##
Shock x Treatment x Days	3,491,959	10	349,196	1.95*
Days x Subjects within groups (error within)	21,515,964	120	179,300	

#p < .005
##p < .001
*p < .05

interaction ($F = 1.95$; $df = 10/120$; $p < .05$). The source of the treatment effect can be seen from inspection of Figure 2. The curves for the Control Groups in extinction are clearly higher than those of the hormone-treated groups indicating more overall bar-pressing. Within the four hormone-treated groups, the "Dex-ACTH" curve at each shock level is beneath the "Dex" curve. The teatment x days effect (see Figure 4) arises from the fact that there is a steady daily increase in the number of bar-presses made by the Control Groups, while the number of bar-presses made by the hormone-injected groups remains stable, or declines. The three-way interaction (shock x treatment x days) may be due to the tendency in the hormone-treated groups for the 1.0 ma shock animals to bar-press less than the 0.5 ma shock animals (see Figure 2). Paradoxically, this tendency is reversed in the Control Groups: the 1.0 ma Control Group exhibits the higher daily means.

Discussion

That stronger shock should lead to significantly lower mean suppression ratios in acquisition, and to a lower baseline rate of bar-pressing, was expected (Annau and Kamin, 1961). The finding that the shock effect was no longer significant in extinction might be explained by the short period of acquisition training used in the present study (three days) in contrast with that of Annau and Kamin (ten days).

The significant days effects in the suppression data merely reflect acquisition of the CER and recovery from it in extinction. The same can be said of the bar-press data in acquisition, which appear to reflect the conditioning of fear to situational cues other than the CS.

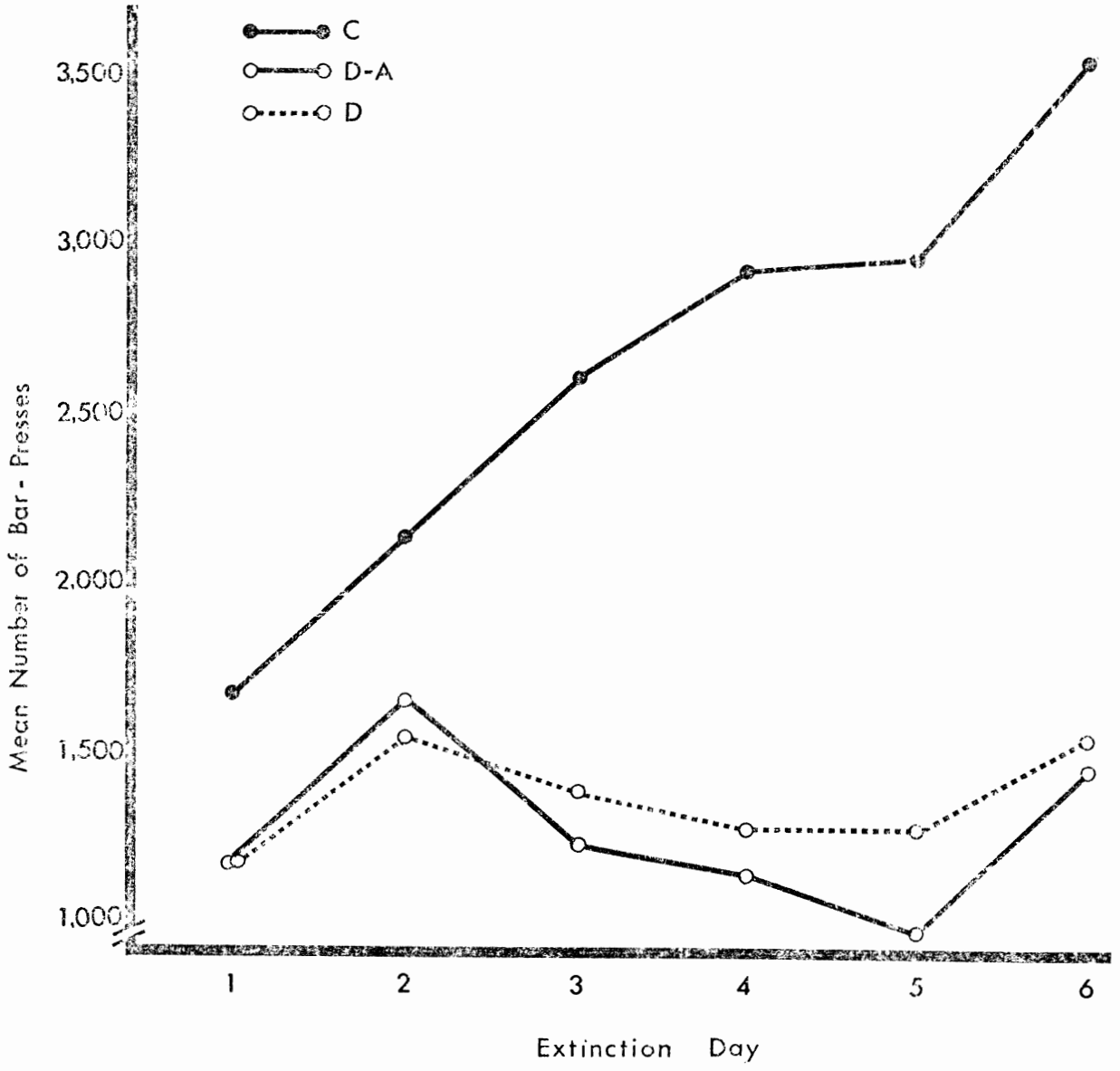

Figure 4. Treatment x days interaction in the bar-presses made on Days 1 to 6 of extinction by the extinction-injected groups. C, Control Groups; D-A, Dex-ACTH Groups; D, Dex Groups.

However, in the bar-press data of the extinction period, the days effects indicate some persistent change in the behavior of the hormone-treated groups unrelated to the measure of "fear" obtained in the suppression ratios.

This becomes apparent when one considers, in the extinction bar-press data, the two interactions involving the days effect—both of which, for these extinction-injected groups, also involve the effect of treatments. It is principally because treatments are having an effect in extinction that four of the bar-press curves in Figure 2 do not reflect the anticipated recovery from the low levels reached in acquisition. That recovery is observed only in the Control Groups.

The findings of Experiment I which are of greatest interest relate to the effect of the hormone treatments on the two response measures. When suppression ratios are considered, there is an absence of any significant effect in extinction of either dexamethasone or dexamethasone and ACTH given during this period. At first sight, this is surprising. Studies by de Wied (1966, 1967), Koranyi, Endroczi, Lissak and Svepes (1967), and Bohus, Nyakas and Endroczi (1968) have demonstrated that both corticoid treatments and ACTH treatments given during the extinction of other responses based on aversive stimuli did alter the resistance to extinction of these responses.

If this lack of an affect on suppression is considered together with the marked effect of hormone treatments on the bar-press measure, one is led to question previous interpretations of the effects of these hormones on responses under aversive control. In the present experiment dexamethasone did not facilitate extinction of a CER; nor did ACTH in combination with dexamethasone increase the resistance to extinction. Both hormone treatments, however reduced overall bar-press responding.

The possible implications of these findings will be discussed following the report of Experiment II.

EXPERIMENT II

One aim of Experiment II was to study the effects on the acquisition and extinction of a CER of hormone treatment in acquisition only. The selection of groups for this experiment was based on the following rationale. If corticoids act to attenuate responses to aversive stimuli, animals treated with dexamethasone might be expected to show less response suppression than control animals when trained under high shock conditions. Furthermore, if ACTH acts to augment responses to aversive stimuli, animals treated with ACTH might be expected to show more suppression than control animals when trained under low shock conditions. As explained in the Introduction, ACTH-treated animals were also injected with dexamethasone in order to reaffirm the prepotency of ACTH over any corticoid effect (Anderson, Winn and Tam, 1968).

A second aim of Experiment II was to follow up the observation in Experiment I that the hormone treatments had a profound effect on the recovery of bar-pressing in extinction. It was considered worthwhile to determine whether this effect in extinction was a direct result of the presence of the hormones.

Treatments and Design

As in Experiment I, the groups were matched as well as possible on the basis of the number of bar-presses made on the last day of VI training. An analysis of variance performed on the bar-press data for this day confirmed that there were no significant differences between the groups ($F = 0.15$; $df = 3/20$; $p > .05$; $F = 3.10$ required). In this

experiment, animals were treated with the same hormones as in the first experiment. However, all hormone injections were given during the acquisition of the CER; physiological saline injections were given on the same schedule during the extinction period. Table 6 outlines the groups and their treatment. For two of the groups, 0.5 ma shock was the US used during acquisition; for the other two, 1.0 ma shock was used. At the 0.5 ma shock level, one group was given a 0.2 ml injection containing 200 µg of dexamethasone 21-phosphate 75-90 minutes prior to the first CS presentation on each day of acquisition. This was followed by a 0.3 ml subcutaneous injection containing 12 I.U. of Zn-ACTH 20-30 minutes prior to the first CS ("Dex-ACTH 0.5" Acquisition Group). The other 0.5 ma shock group received physiological saline at the same times and in the appropriate volumes ("Control 0.5" Group). One group at the 1.0 ma shock level received the dexamethasone injection as described above, followed by physiological saline 20-30 minutes prior to the first CS ("Dex 1.0" Acquisition Group); the other received physiological saline at the same times and in the appropriate volumes ("Control 1.0" group). As in Experiment 1, to induce adaptation to the injections themselves, all animals were injected with saline from the last day of VI training on the same schedule as that arranged for the acquisition and extinction injections.

Results

The daily mean suppression ratios for each of the four acquisition-injected groups are shown in Figure 5. Figure 6 shows the daily mean number of bar-presses for these same groups. As is evident from the mean ratios for the Pretest Day, there was no appreciable tendency in any of the acquisition-injected groups for animals to suppress to the CS

TABLE 6

DESIGN OF EXPERIMENT I
(HORMONE TREATMENTS IN ACQUISITION)

	Shock level in ma	
	0.5	1.0
Injection		
	Saline (n = 6)	Saline (n = 4)
	Dexamethasone & ACTH (n = 7)	Dexamethasone (n = 7)

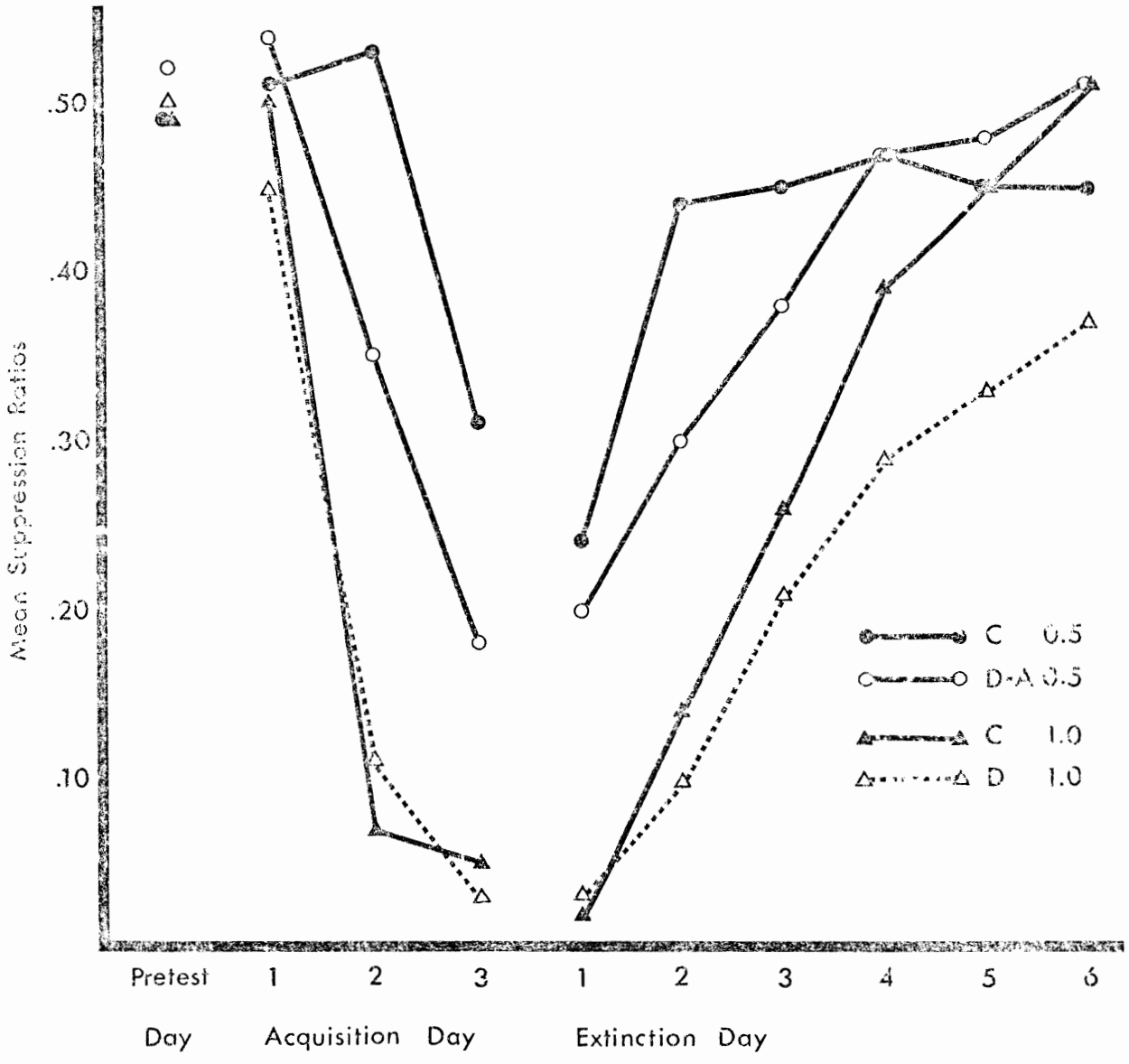

Figure 5. Mean suppression ratios in each of the four acquisition-injected groups. C, Control Group; D-A, Dex-ACTH Group; D, Dex Group.

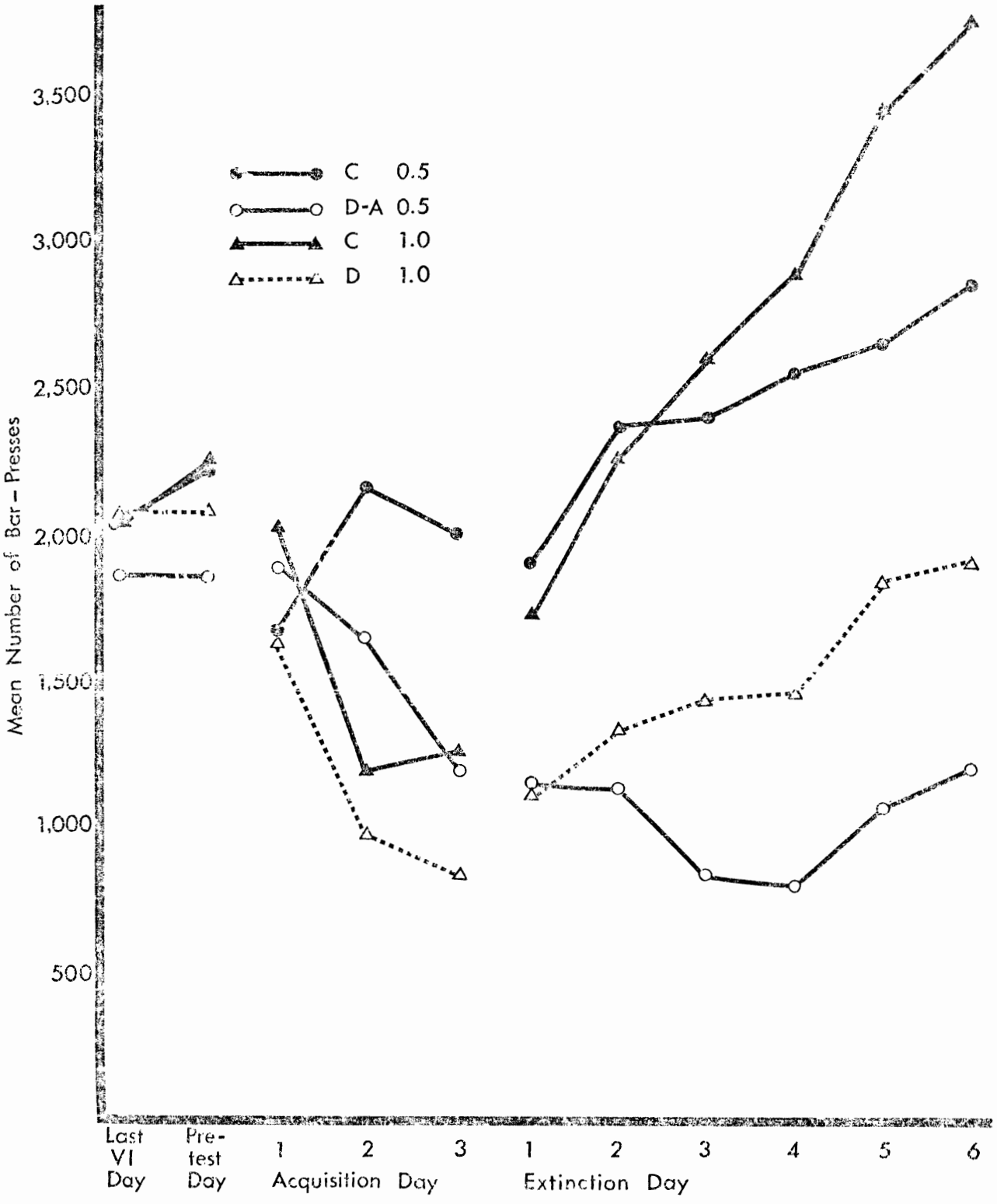

Figure 6. Mean number of bar-presses made by each of the acquisition-injected groups. C, Control Group; D-A, Dex-ACTH Group; D, Dex Group.

prior to the application of shock in acquisition.

Separate analyses of variance were performed on the suppression data and the bar-press data at each shock level. On Days 2 and 3 of acquisition, the analysis of the suppression data from the 0.5 ma groups (Table 7) revealed a significantly greater suppression in the Dex-ACTH 0.5 Group ($F = 4.92$; $df = 1/11$; $p < .05$) than in the Control Group. Suppression increased significantly across days ($F = 18.22$; $df = 1/11$; $p < .005$). This days effect was the only significant effect observed in any subsequent analysis of variance of the suppression data. In acquisition, there were no significant effects on suppression ratios in the 1.0 ma shock groups (Table 8). Despite the significantly greater suppression observed in the Dex-ACTH 0.5 Group in acquisition, and the apparent trend in early extinction (Figure 5), only the days effect could be shown to be significant in the suppression data of the 0.5 ma groups on extinction Days 1 to 6 (Table 9a: $F = 11.88$; $df = 5/55$; $p < .001$), on Days 1 to 3 (Table 9b: $F = 18.89$; $df = 2/22$; $p < .001$), or even on Days 1 and 2 (Table 9c: $F = 23.20$; $df = 1/11$; $p < .001$). For extinction Days 1 to 6, the analysis of the suppression data for the 1.0 ma groups (Table 10) revealed only a large days effect ($F = 44.73$; $df = 5/45$; $p < .001$).

As in the first experiment, the days effects in the suppression data reflect the acquisition and extinction of the CER. The absence of the effect in the 1.0 ma groups during acquisition is explained by the fact that the suppression in these two groups was almost complete by Day 2.

When the bar-press data from Days 2 and 3 of acquisition were analyzed, no significant effect of treatment (or of days) was found in either the 0.5 ma groups (Table 11) or the 1.0 ma groups (Table 12).

TABLE 7

MEAN SUPPRESSION RATIOS ON ACQUISITION DAYS 2 AND 3 IN ACQUISITION-INJECTED GROUPS GIVEN 0.5 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	1,486	1	1,486	4.92*
Subjects within groups (error between)	3,324	11	302	
Within Subjects		13		
Days	2,430	1	2,430	18.22#
Treatment x Days	45	1	45	0.34
Days x Subjects within groups (error within)	1,467	11	133	

*$p < .05$
#$p < .005$

TABLE 8

MEAN SUPPRESSION RATIOS ON ACQUISITION DAYS 2 AND 3 IN ACQUISITION-INJECTED GROUPS GIVEN 1.0 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		10		
Treatment	8.96	1	8.96	0.08
Subjects within groups (error between)	964.93	9	107.21	
Within Subjects		11		
Days	138.48	1	138.48	1.94
Treatment x Days	52.54	1	52.54	0.74
Days x Subjects within groups (error within)	640.86	9	71.21	

TABLE 9a

MEAN SUPPRESSION RATIOS ON EXTINCTION DAYS 1 TO 6 IN ACQUISITION-INJECTED GROUPS GIVEN 0.5 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	116	1	116	0.15
Subjects within groups (error between)	8,446	11	768	
Within Subjects		65		
Days	6,275	5	1,255	11.88##
Treatment x Days	821	5	164	1.55
Days x Subjects within groups (error within)	5,811	55	106	

##p < .001

TABLE 9b

MEAN SUPPRESSION RATIOS ON EXTINCTION DAYS 1 TO 3 IN ACQUISITION-INJECTED GROUPS GIVEN 0.5 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	628.11	1	628.11	0.83
Subjects within groups (error between)	8,329.61	11	757.24	
Within Subjects		26		
Days	2,652.78	2	1,326.39	18.89##
Treatment x Days	156.38	2	78.19	1.11
Days x Subjects within groups (error within)	1,545.13	22	70.23	

##p < .001

TABLE 9c

MEAN SUPPRESSION RATIOS ON EXTINCTION DAYS 1 AND 2 IN ACQUISITION-INJECTED GROUPS GIVEN 0.5 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	499.32	1	499.32	0.85
Subjects within groups (error between)	6,452.28	11	586.57	
Within Subjects		13		
Days	1,405.87	1	1,405.87	23.20##
Treatment x Days	145.72	1	145.72	2.40
Days x Subjects within groups (error within)	666.75	11	60.61	

##$p < .001$

TABLE 10

MEAN SUPPRESSION RATIOS ON EXTINCTION DAYS 1 TO 6 IN ACQUISITION-INJECTED GROUPS GIVEN 1.0 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		10		
Treatment	723	1	723	0.98
Subjects within groups (error between)	6,625	9	736	
Within Subjects		55		
Days	13,313	5	2,663	44.73##
Treatment x Days	448	5	90	1.51
Days x Subjects within groups (error within)	2,679	45	60	

##p $<$.001

TABLE 11

TOTAL BAR-PRESSES ON ACQUISITION DAYS 2 AND 3 IN ACQUISITION-INJECTED GROUPS GIVEN 1.0 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	2,806,324	1	2,806,324	2.25
Subjects within groups (error between)	13,714,763	11	1,246,797	
Within Subjects		13		
Days	593,270	1	593,270	2.19
Treatment x Days	143,462	1	143,462	0.53
Days x Subjects within groups (error within)	2,980,086	11	270,917	

TABLE 12

TOTAL BAR-PRESSES ON ACQUISITION DAYS 2 AND 3 IN ACQUISITION-INJECTED GROUPS GIVEN 1.0 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		10		
Treatment	508,358	1	508,358	1.00
Subjects within groups (error Between)	4,555,656	9	506,184	
Within Subjects		11		
Days	14,845	1	14,845	0.06
Treatment x Days	56,127	1	56,127	0.22
Days x Subjects within groups (error within)	2,275,920	9	252,880	

In extinction (Days 1 to 6), animals in the Dex-ACTH 0.5 Group pressed significantly less than those in the Control Group ($F = 5.92$; $df = 1/11$; $p < .05$); no other significant effects appeared in this analysis (Table 13). Animals in the Dex 1.0 Group pressed significantly less in extinction than control animals at that shock level (Table 14: $F = 7.02$; $df = 1/9$; $p < .05$). This dexamethasone effect was augmented by the days effect, as seen in Figure 6 in the (significant) divergence of the bar-press curves across days in the 1.0 ma groups (Table 14: $F = 9.20$; $df = 5/45$; $p < .001$).

Discussion

An important result of Experiment II was the finding that animals treated during acquisition with ACTH (and dexamethasone) showed reliable greater suppression in acquisition than did their control animals. However, in spite of the trend apparent in Figure 5, this effect did not approach significance in extinction, when hormone treatments were discontinued. The fact that ACTH augmented suppression in these animals had been expected on the basis of observations which suggested that ACTH increases fear. However, to find this effect in acquisition alone was unexpected. The finding of an effect on acquisition performance and no effect on extinction performance when hormone treatments were given only in acquisition does not agree with the observations of Murphy and Miller (1955), who studied a two-way active avoidance response. They found that ACTH given only in acquisition had no significant effect on trials to criterion in acquisition, but did significantly increase the resistance to extinction. With acquisition treatments alone, Koranyi et al. (1967) observed that ACTH interfered significantly with the acquisition of this active response, but

TABLE 13

TOTAL BAR-PRESSES ON EXTINCTION DAYS 1 TO 6 IN ACQUISITION-INJECTED GROUPS GIVEN 0.5 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		12		
Treatment	39,467,053	1	39,467,053	5.92*
Subjects within groups (error between)	73,368,556	11	6,669,869	
Within Subjects		65		
Days	2,083,110	5	416,622	2.20
Treatment x Days	2,231,845	5	446,369	2.36
Days x Subjects within groups (error within)	10,412,599	55	189,320	

*$p < .05$

TABLE 14

TOTAL BAR-PRESSES ON EXTINCTION DAYS 1 TO 6 IN ACQUISITION-INJECTED GROUPS GIVEN 1.0 ma SHOCK
ANALYSIS OF VARIANCE

Source	SS	df	MS	F
Between Subjects		10		
Treatment	24,138,065	1	24,138,065	7.02*
Subjects within groups (error between)	30,939,289	9	3,437,699	
Within Subjects		55		
Days	14,870,510	5	2,974,102	9.20##
Treatment x Days	2,312,246	5	462,449	1.43
Days x Subjects within groups (error within)	14,551,930	45	323,376	

* $p < .05$
$p < .001$

paradoxically (and in agreement with our own finding) augmented the acquisition of a passive avoidance response, as measured in extinction. There is, therefore, meagre support for the present finding in previous work.

Dexamethasone treatment given in acquisition in our study did not attenuate CER suppression during either training or extinction. As mentioned in the introduction to this experiment, previous work had suggested that corticoids in some way attenuate fear. However, a close analysis of the actual studies in which dexamethasone or other corticoids were given reveals that this apparent effect on fear can be observed only in active avoidance extinction (de Wied, 1967). A study by Wertheim, Conner and Levine (1967) demonstrated that in a Sidman (unsignalled) bar-press avoidance task, dexamethasone treatment indeed led to fewer overall responses with an increase in the proportion of long inter-response times, but also led to fewer shocks. This would not appear to be an attenuation of fear. Compare the typical effects of the tranquilizer chlorpromazine on Sidman bar-press avoidance: The animal exhibits decreased responding and a correlated increase in shock, both dose-dependent (Hanson, 1961). Furthermore, Bohus and Lissak (1968) report that corticosterone had no effect on the number of CAR's observed in the acquisition of a one-way active avoidance response, although it did cause a large and significant reduction in inter-trial responding. Kasper-Pandi, Hansing, and Usher (1970) found that a large dose of dexamethasone did not affect the acquisition of a two-way active avoidance response. Conner and Levine (1969), also studying this active (shuttle) response, observed that their data "failed to provide any evidence that dexamethasone injections reliably influenced conditioned

avoidance behavior" in acquisition.

Keeping these findings in mind, consider now the bar-press data from animals treated in acquisition. The effects of treatments on bar-pressing were not significant during the period of the injections, although at both levels of shock there was a tendency for the hormone-treated animals to have lower bar-press scores in acquisition than their respective control animals. The lack of significance of this tendency could be due to the overall decrease in bar-pressing which occurs in all animals shocked in CER acquisition (Annau and Kamin, 1961). Most startling was the failure of the animals treated in acquisition to recover normal bar-pressing in extinction. Despite this, they continued to receive the same number of reinforcements as the control animals. This finding is reminiscent of that of Wertheim et al. (1967), who observed a decrease in response rate but efficient avoidance performance (Sidman schedule) in animals treated with dexamethasone. It would appear that the CER technique may help unravel existing confusions at least about the effects of dexamethasone. The two measures made available by this technique allow a separation of the "fear" component and the active response component which are necessarily confounded by an active avoidance technique. The significance of these effects and the ACTH effects on bar-pressing during extinction in acquisition-treated animals will be discussed in the context of the reinterpretation of our own and other observations which will follow.

GENERAL DISCUSSION

To review briefly: the CER task provides a measure of the suppression of an appetitive bar-press response to a classically conditioned aversive stimulus (the "fear" measure), and a measure of overall bar-press responding (an "active response" unrelated to fear except that fear periodically interrupts it). When the suppression measure was considered, it was found that ACTH and dexamethasone given together during acquisition augmented "fear." Since dexamethasone alone did not have any significant effect on the suppression measure, ACTH would appear to be responsible, and the effect of ACTH prepotent over any corticoid effect. This effect of ACTH on "fear" was not maintained in extinction in acquisition-treated animals; nor could it be demonstrated in animals treated only in extinction. Dexamethasone did not attenuate "fear" during the acquisition of the CER, or during extinction, regardless of the period of treatment. These results indicate that only ACTH had an affect on the fear measure (short-term), and confirm that corticoids do not affect fear directly (Wertheim et al., 1967, 1969; Weiss et al., 1969).

The bar-press data demonstrate that dexamethasone decreases overall bar-press responding in extinction. Thus it is plausible to suggest that corticoids exert their apparent effects on "fear" in the active avoidance response by decreasing instrumental response output. This effect of corticoids is not limited to behaviour under aversive control. Levine (1968) briefly cites an unpublished finding that animals treated with dexamethasone exhibited improved performance on a differential reinforcement of low rate (DRL) schedule, so that they were able to obtain more reinforcements under these conditions.

The decrease in bar-pressing produced by the combined injections of ACTH and dexamethasone was the same as that produced by dexamethasone alone. Thus, from these results, it cannot be determined whether ACTH itself had an independent effect on instrumental response output in extinction, perhaps by increasing mild generalized fear (Weiss et al., 1969), or whether, in the absence of the US, the effects of dexamethasone on active responding were predominant.

Most of the apparent contradictions between these results and previous findings were seen to disappear when the foregoing distinction was made between effects on fear and effects on active responding. The fact that an apparent effect of dexamethasone on fear could only be demonstrated elsewhere in active avoidance extinction, especially considered together with the present findings, indicated that diminished active responding might have been confused with attenuated fear in previous interpretations. It was noticed that in nearly every case in which previous work disagreed with the suppression data (the "fear" measure), it agreed well with the bar-press data (the "active response" measure). Furthermore, it was observed that where previous findings agreed with the present ones, the task was usually a passive response in the case of the suppression data, and an active response in the case of the bar-press data.

This distinction between effects of ACTH and corticoids on fear and on active responding certainly merits further investigation. Of special interest, also, is the possible independence of mild generalized fear and intense specific fear, suggested elsewhere (Weiss et al., 1969) as well as in these results. Finally, the observation that the effect of these drugs on fear is in acquisition and appears to be a short-term effect gives great weight to objections raised in the Introduction concerning

the use of treatments affecting the pituitary-adrenal state of the animal in the acquisition period when extinction data are to be examined. The present results have shown that acquisition treatments may affect measures taken during the extinction of a CER without affecting measures taken during the acquisition of the CER. Thus it is not enough to show that there was no significant effect of prior treatments on acquisition, or to assume that other treatments, given only in extinction, are responsible. Many previously observed effects, which were assumed to be direct effects on extinction, may now need to be carefully reconsidered.

SUMMARY

In an attempt to clarify the relative influences of adrenocorticotrophic hormone (ACTH) and adrenal corticoids on aversively controlled respones, fifty-four experimentally naive male hooded rats were trained in an Estes-Skinner conditioned emotional response (CER) task. The mean suppression ratios and bar-presses were measured daily. Dexamethasone 21-phosphate (200 μg), Zinc Corticotrophin Hydroxide (12 I.U.) and dexamethasone, and saline were injected either in extinction (Experiment I) or in acquisition (Experiment II) in the respective treatment groups. The data were analyzed by analysis of variance. ACTH significantly increased suppression ratios only during acquisition. Dexamethasone had no effect on suppression. Both hormones produced decreases in the number of bar-presses made in extinction, regardless of when given. These results together with previous findings were interpreted as indicating that whereas ACTH has some direct effects on "fear", adrenal corticoids have a general effect on instrumental responding.

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APPENDIX A

RAW DATA: EXPERIMENT I

(In all cases, the decimal point, which comes before the two digits has been omitted in the suppression ratios. These were dealt with in the form of percentages.

SUPPRESSION RATIO DATA

"DEX-ACTH 0.5" EXTINCTION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	52	45	49	32	13	44	46	58	45	55
2	46	47	49	17	15	44	45	59	47	49
3	50	52	33	25	24	38	35	41	41	*
4	50	50	30	13	15	38	45	53	57	49
5	53	53	46	23	13	32	47	44	38	55

*This animal died on Day 6 of Extinction

"DEX 0.5" EXTINCTION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	50	54	38	17	03	16	06	27	30	36
2	54	43	04	01	09	29	45	37	50	53
3	46	46	31	47	32	16	36	35	49	51
4	47	46	52	32	16	16	27	*	*	*
5	51	51	31	20	10	30	35	41	44	49

*This animal died on Day 4 of Extinction

"CONTROL 0.5" GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	51	55	14	00	03	25	45	52	52	53
2	51	47	49	22	16	43	31	44	47	50
3	56	50	28	08	11	32	45	50	46	45
4	49	54	44	32	30	45	51	55	45	49
5	53	57	49	38	11	26	41	46	41	50

"DEX-ACTH 1.0" EXTINCTION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	49	53	00	00	01	23	43	48	49	52
2	57	48	00	00	02	02	25	31	39	43
3	47	42	10	00	16	30	42	10	24	33
4	50	45	20	01	07	25	23	32	48	52
5	55	40	01	00	01	04	24	37	40	58

"DEX 1.0" EXTINCTION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	54	42	09	20	00	03	02	07	17	29
2	50	69	47	29	31	37	44	48	52	51
3	60	53	20	00	00	13	00	25	42	41
4	66	50	04	00	15	34	49	71	64	58
5	63	50	51	33	15	34	41	52	63	51

"CONTROL 1.0" GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	52	52	14	10	10	22	48	42	49	56
2	52	51	25	00	00	22	43	38	49	52
3	46	52	31	10	13	14	23	32	44	46
4	53	54	16	00	09	44	46	49	48	51
5	50	46	00	00	22	40	49	51	52	51

BAR-PRESS DATA

"DEX-ACTH 0.5" EXTINCTION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1322	1840	1155	1159	799	1434	1628	754	710	259	1178
2	1960	1226	1505	1577	1225	1620	1036	#	1447	1230	2249
3	2740	2884	1968	1021	997	1021	1387	875	678	290	*
4	2079	2682	2760	2695	1604	1697	2659	2576	2634	1833	2730
5	954	1386	1197	1326	1296	1505	1860	1216	1558	657	663

*This animal died on Day 6 of Extinction
These data were lost because of equipment failure

"DEX 0.5" EXTINCTION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1603	1748	1071	1384	723	1079	1218	897	1215	1264	1027
2	2750	2403	2449	1337	1205	1097	2097	1943	1032	972	1830
3	3653	3378	2127	658	490	1076	2727	2091	2747	3226	4271
4	1985	1014	3707	2471	549	927	1911	1783	*	*	*
5	1142	1187	1036	831	738	704	1022	891	1080	1135	1297

*This animal died on Day 4 of Extinction

"CONTROL 0.5" GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1870	1132	1845	1676	1076	1384	1430	1735	2237	1464	1908
2	1709	1526	1629	4601	946	1520	1115	#	#	3599	3634
3	1999	2101	3245	2870	1227	2063	2171	2663	3819	4158	5251
4	2771	2743	2770	1725	1134	1659	3364	3101	3641	2880	4215
5	820	969	1417	1471	921	940	1638	1622	2046	2018	2189

#These data were lost because of equipment failure.

"DEX-ACTH 1.0" EXTINCTION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1257	1304	1294	253	154	1216	1773	978	1114	1321	1085
2	1626	1025	1048	330	399	589	520	522	429	501	553
3	3409	4185	3189	442	417	670	2422	1701	1136	1687	2415
4	1462	1514	1195	276	593	665	1350	1010	645	1072	982
5	2485	1766	1769	1199	1239	1248	1892	969	1023	893	810

"DEX 1.0" EXTINCTION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day			Extinction Day					
			1	2	3	1	2	3	4	5	6
1	888	1026	1094	674	991	593	719	727	390	561	489
2	2052	1662	1973	1459	1432	1771	2847	2728	2468	1993	2162
3	3337	1232	1042	1091	566	610	994	345	775	491	594
4	773	528	669	323	339	810	409	483	256	358	421
5	4153	3114	2486	2758	1688	3195	1480	2001	1302	1122	1271

"CONTROL 1.0" GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1338	1253	1172	1127	802	528	899	1166	1246	1384	1875
2	2160	2255	999	159	69	592	1258	1513	1929	2331	3049
3	2942	3484	3432	2238	1191	2212	2999	3821	3647	3140	4014
4	2150	2151	2363	1189	1281	2291	2674	3160	3352	3752	3994
5	2352	2624	2928	1571	2459	3611	3776	5039	4484	4706	5134

APPENDIX B

RAW DATA: EXPERIMENT II

(In all cases, the decimal point, which comes before the two digits has been omitted in the suppression ratios. These were dealt with in the form of percentages).

SUPPRESSION RATIO DATA

"DEX-ACTH 0.5" ACQUISITION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	55	48	33	18	37	51	54	51	48	47
2	50	51	44	23	34	28	51	50	47	49
3	48	53	14	23	25	31	46	55	53	44
4	55	58	52	19	02	22	33	60	53	48
5	42	61	55	29	37	46	55	48	52	58
6	57	54	27	06	07	34	24	42	46	49
7	56	56	18	09	00	00	06	23	40	64

"CONTROL 0.5" GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	45	66	68	56	39	59	40	52	46	51
2	54	55	43	42	45	50	56	55	54	58
3	51	48	54	48	45	58	56	52	47	52
4	52	53	52	27	16	51	50	50	49	53
5	45	44	46	00	00	27	24	26	29	03
6	48	37	53	10	01	18	44	46	47	54

"DEX 1.0" ACQUISITION GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	56	20	43	08	08	20	34	42	49	54
2	49	47	11	03	02	03	11	21	26	33
3	48	47	03	01	05	04	14	18	28	31
4	47	51	15	00	00	15	21	46	51	48
5	49	51	00	00	00	00	00	06	00	03
6	49	46	04	08	00	10	25	24	29	38
7	52	50	03	00	09	22	40	48	51	50

"CONTROL 1.0" GROUP

MEAN SUPPRESSION RATIOS

Subject	Pretest Day	Acquisition Day			Extinction Day					
		1	2	3	1	2	3	4	5	6
1	45	48	08	01	01	22	40	49	52	50
2	45	51	01	02	01	23	29	36	39	47
3	50	56	14	03	01	10	33	52	51	56
4	54	45	04	13	03	00	01	17	39	50

BAR-PRESS DATA

"DEX-ACTH 0.5" ACQUISITION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1799	2032	2593	1639	1246	1708	859	962	765	1104	771
2	2584	1962	1680	807	664	420	306	263	446	658	343
3	2186	2162	2545	2553	1982	2320	1902	1590	1652	1788	1969
4	1067	1863	1508	2296	991	712	642	1157	724	736	1311
5	1521	1669	1760	1691	1314	929	1438	399	304	798	713
6	2048	2414	2487	1369	1551	1748	2415	1212	1483	2173	3036
7	1792	852	679	1173	614	184	296	313	237	312	271

"CONTROL 0.5" GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1389	1950	1697	1404	2014	2168	2164	2147	2239	2650	2595
2	1577	1684	1563	1475	1591	1589	1578	1479	1420	1635	1427
3	2362	3221	3326	3202	3434	3410	3968	3914	4558	4675	4877
4	2662	2852	1938	1873	2217	2682	2706	2033	1799	2294	2121
5	848	885	742	815	401	216	501	877	916	734	513
6	3275	2693	754	4171	2360	1923	3364	3974	4511	3932	5557

"DEX 1.0" ACQUISITION GROUP

NUMBER OF BAR PRESSES

Subject	Last Day of VI	Pretest Day	Acquisition Day 1	Acquisition Day 2	Acquisition Day 3	Extinction Day 1	Extinction Day 2	Extinction Day 3	Extinction Day 4	Extinction Day 5	Extinction Day 6
1	1527	1433	417	1765	1097	1796	1607	1722	1193	1897	1830
2	2014	2209	2175	1148	1239	1294	1204	1289	1460	1723	1379
3	2524	2439	1027	175	444	1088	1668	2194	1975	2400	2542
4	1387	1822	1066	678	405	792	1157	912	1262	1412	1555
5	1704	1864	1332	127	17	9	103	174	273	444	661
6	2627	2430	2798	1695	793	835	1264	1547	1586	2501	3186
7	2750	2394	2643	1299	1778	1987	2248	2144	2506	2530	2911

"CONTROL 1.0" GROUP

NUMBER OF BAR PRESSES

Subject	*Last Day* of VI	*Pretest* Day	Acquisition Day			Extinction Day					
			1	2	3	1	2	3	4	5	6
1	1479	1791	1834	1159	1391	1626	1861	2689	3455	3660	2862
2	1898	2210	1927	763	1517	1893	2441	2716	2776	3266	2954
3	2663	2777	2585	585	1232	1345	2071	1902	1738	1804	1962
4	2085	2143	1752	2273	844	2047	2736	3119	3601	5146	7216