Ph. D. PSYCHOLOGY

Joel Kaplan

APPROACH AND INHIBITORY REACTIONS AFTER HIPPOCAMPAL DAMAGE

APPROACH AND INHIBITORY REACTIONS IN RATS AFTER BILATERAL HIPPOCAMPAL DAMAGE

by

Joel Kaplan

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Department of Psychology
McGill University
Montreal

November, 1966

Acknowledgements

The assistance of the following people in the preparation of this paper is gratefully acknowledged: Dr. J. Corson and Mr. H. Buchtel for their critical readings of the manuscript; Mr. W. Mundl for his design and construction of much of the equipment; and Mrs. A. Szikita for her typing of the manuscript.

I am especially indebted to my wife Dorothy for her endless encouragement throughout the course of this research.

TABLE OF CONTENTS

INTRODUCTION..... 1

The Present Investigation.....13

GENERAL SURGICAL AND HISTOLOGICAL PROCEDURES.....15

EXPERIMENT I.

The Effects of Hippocampal Damage on Activity in Two Situations.....18

EXPERIMENT II.

The Effect of Introducing a Novel Visual Stimulus During Directed and Undirected Activity.....25

EXPERIMENT III.

Reaction to an Air-blast, and the Acquisition and Extinction of a Conditioned "Freezing" Response.....32

EXPERIMENT IV.

Avoidance Conditioning.....37

DISCUSSION.....40

SUMMARY.....52

REFERENCES.....54

FIGURES AND TABLES.....61

Various behavioral changes have been observed in mammals after damage to the hippocampus. The most striking change has been found with human patients who, after undergoing surgical removal of the hippocampus and related structures, have shown extreme difficulty in retaining new information (Milner, 1962; in press). However, experiments with hippocampectomized infrahuman mammals have been relatively unsuccessful in reproducing the severe "memory" disturbance found with human patients. From the literature on infrahuman subjects, Isaacson (1966) concludes that "hippocampal destruction does not interfere with any mechanism of learning or memory, but rather influences the animals in ways such that they will be more or less influenced by certain environmental changes. Thus, the lesions affect performance." One of the most noticeable changes in performance found with hippocampectomized animals, particularly with rats, has been their enhanced and persistent tendency to respond to conditions which normally produce "response-suppression."

Some measures which have demonstrated enhanced and persistent response tendencies have included intermittent reinforcement schedules and tests of "passive avoidance," extinction, reversal, and alternation behavior. However,

there has even been a lack of consistency and agreement with results obtained with these behavioral measures. Some of the conflicting reports might be attributed to slight variations in behavioral techniques (Isaacson, Schmaltz, & Douglas, in press; Snyder & Isaacson, 1965; Kimble, Kirkby, & Stein, 1966), differences in extent (Snyder & Isaacson, 1965) and location (Kimura, 1958) of hippocampal damage, or differences in the methods used for destroying hippocampal tissue (Douglas & Isaacson, 1964).

The earliest report of a passive avoidance impairment by rats with hippocampal lesions, came from Kimura (1958), who found that posterior dorsal, but not anterior dorsal, hippocampal lesions significantly interfered with the subject's (S's) ability to inhibit a previously learned approach response. Similar deficits have since been reported by others (Isaacson & Wickelgren, 1962; Kimble, 1963; Kimble et al., 1966; Snyder & Isaacson, 1965) who have tested rats with extensive bilateral hippocampal ablations. Lack of an apparent deficit with small anterior dorsal lesions has also been reported (Kaada, Rasmussen, & Kveim, 1962; Kveim, Setekliev, & Kaada, 1964). In contrast, Teitelbaum & Milner (1963) have found that rats with rather small

anterior dorsal hippocampal lesions were impaired in inhibiting a response which led to foot-shock, but the authors did suggest that the larger lesions produced greater deficits.

Along with the important variables of lesion size and lesion locus within the hippocampus, it has also been found that (a) the kind of passive avoidance task used (Snyder & Isaacson, 1965) and, (b) the amount of pretraining before the onset of aversive stimulation (Isaacson, Olton, Bauer, & Swart, 1966; Kimble et al., 1966) contribute to the degree of impairment. Kimble et al. (1966) found that hippocampectomized rats were able to inhibit a response that required no previous training, but were impaired when required to inhibit a previously trained approach response. The untrained response in their study consisted of Ss stepping off of a perch and through a hole onto an electrified floor. No appetitive reward was associated with the response, and all Ss "spontaneously" stepped through the hole after being placed on the perch. The latency of movement through the hole on the day following shock was used as a measure of passive avoidance. The trained task, which revealed a deficit, consisted of shocking Ss at a water spout at the end of a runway, after they had previously been trained to run down the runway for water reinforcement. Although by using these

different tasks the authors were able to dissociate the effects of hippocampal damage, interpretation might have been more straightforward had they simply varied the amount of pretraining experience in the runway. This would have eliminated the possibility that the deficit they found with the hippocampectomized rats was a result of the Ss' increased motivation for water. With respect to this question, Isaacson et al. (1966) have varied the amount of pretraining in a passive avoidance situation, and measured its effect on the ability of hippocampectomized rats to withhold a response. In their experiment a "quivering" runway was used to motivate the Ss to jump into a stable compartment. On either the first, twenty-first, or forty-first jump, foot-shock was delivered in the compartment. Using this procedure it was found that the hippocampectomized Ss returned more rapidly than controls to the compartment, on the trial following shock, regardless of whether 0, 20, or 40 training trials were previously given. It was noted however, that the hippocampectomized Ss returned relatively sooner if they had received some pretraining experience. Teitelbaum & Milner (1963) have also found that rats with hippocampal lesions require no prior training in order to show a deficit in passive avoidance. They found that rats with lesions in the

dorsal hippocampus descended from a "safe" platform onto an electrified grid floor more often than control Ss. The point to be made here is that the lack of suppression on the part of the Ss with hippocampal damage was not dependent on the prior establishment of responses associated with the platform.

Further evidence which suggests that specific prior training is not essential for hippocampectomized rats to show a lack of "suppressive" behavior, comes from experiments in which these Ss have been found to persist in activity for longer periods of time than control Ss (Douglas & Isaacson, 1964; Roberts, Dember, & Brodwick, 1962; Teitelbaum & Milner, 1963). Although it has not been clear why hippocampectomized rats display this behavior, it is interesting to note that situations which have revealed prolonged activity have measured activity in fairly large chambers (Douglas & Isaacson, 1964; Teitelbaum & Milner, 1963) or in mazes (Roberts et al., 1962). On the other hand, measures which have demonstrated no differences in activity between hippocampectomized rats and control Ss have been based on data taken with either very small chambers (Kim, 1960) or with running wheels (Kaada, Rasmussen, & Kveim, 1961; Leaton, 1963). It is possible that the situations which have shown this behavior have been relatively more

"attractive" to the Ss, suggesting that conditions which enhance "approach" behavior would be more likely to reveal prolonged activity in hippocampectomized rats.

Although prior training of a specific response does not appear to be essential for hippocampectomized Ss to show impaired response-suppression, it does seem to contribute to this form of maladaptive behavior. In addition to the relatively greater impairment produced in passive avoidance situations, pretraining experience has also been shown to interfere with other forms of behavior that require some degree of response-suppression. For example, Ellen & Wilson (1963) found that rats with hippocampal lesions were unable to learn an "active avoidance" response because these Ss continued to respond in a previously trained manner, which interfered with the new response to be learned. Furthermore, reversal problems which have required S to shift his spatial orientation away from previously rewarded responses have revealed deficits with rats (Kimble & Kimble, 1965; Thompson & Langer, 1963), cats (Teitelbaum, 1964; Webster & Voneida, 1964), and monkeys (Mahut & Cordeau, 1963) with hippocampal lesions; and in rats during electrical stimulation of the hippocampus (Rabe, 1963).

Other evidence that pretraining influences the later behavior of hippocampectomized Ss, comes from experiments which have shown that rats with extensive bilateral hippo-

campal ablations respond at much higher rates than control Ss after being switched from a continuous to an intermittent reinforcement schedule (Clark & Isaacson, 1965; Jarrard, 1965; Schmaltz & Isaacson, 1966). For example, Clark & Isaacson (1965) have reported that hippocampectomized rats were unable to learn to delay their responses on a "differential reinforcement of low rates" (DRL) operant schedule after being switched from continuous reinforcement. In this task S receives a reward only if he has refrained from responding for a predetermined delay period. Responses during the delay interval go unrewarded and each response during this interval resets the timers back to the beginning of the delay. Although the results found by Clark & Isaacson could be interpreted in terms of retarded learning per se or impaired temporal discrimination, Schmaltz & Isaacson (1966) have recently demonstrated that the deficit on this task is directly related to Ss' pretraining experience. These latter authors found that hippocampectomized rats that were allowed 20 consecutive continuous reinforcement sessions before switching to DRL training were impaired in learning the new task. However, rats with identical lesions that were trained on DRL immediately after learning to bar-press for food were no different from control Ss either in (a) number of reinforce-

ments obtained or, (b) percentage of reinforced responses. These Ss did, however, bar-press significantly more than control Ss during DRL performance, as did the hippocampectomized Ss that were switched to DRL after extensive bar-pressing experience with continuous reinforcement. These results are in accord with those reported by Jarrard (1965) who found that hippocampectomized rats, after being switched from continuous reinforcement, demonstrated significantly higher food-reinforced bar-pressing rates on a variable interval schedule, when compared with control Ss.

Based on much of the evidence cited above, Kimble (1966) has characterized the animal with hippocampal damage as one who perseverates in performing previously learned responses. However, it is clear that in switching from a continuous to an intermittent reinforcement schedule, rats with hippocampal damage show a high increase in response rates, and do not just "perseverate" at the previous rate associated with continuous reinforcement. Furthermore, Kimble's formulation would not appear to account for the lack of "spontaneous" alternation found with hippocampectomized rats (Douglas & Isaacson, 1964; Roberts et al., 1962), since this behavior, although possibly related to an increased tendency to perseverate, does not involve the establishment

of a previously learned response. As mentioned earlier, impaired passive avoidance without prior training of an approach response, and prolonged activity in certain situations, similarly cannot be described as perseveration of a previously trained response.

Slower extinction of instrumental acts found with hippocampectomized rats (Jarrard, Isaacson, & Wickelgren, 1964; Jarrard & Isaacson, 1965; Niki, 1965; Teitelbaum, 1961) and cats (Peretz, 1965) has also been interpreted as evidence of perseveration of previously trained responses (Kimble, 1966). For example, Jarrard et al. (1964) found that hippocampectomized rats persisted in showing short running latencies in a runway when food was no longer presented in the goal-box. Similarly, Teitelbaum (1961) found that rats with dorsal hippocampal lesions continued to bar-press at high rates when food was no longer contingent upon the bar-pressing response. In another study, Isaacson, Douglas, & Moore (1961) found that hippocampectomized rats displayed shorter latencies than control Ss on extinction trials of a previously trained shuttle avoidance response. These results raise a question which concerns the nature of the response that is perseverated. The common feature with all of these experiments has been

that the response which is perseverated by hippocampectomized Ss during extinction, is one that has undergone formal training and which consists of a directed act. Would hippocampectomized Ss also show slower extinction (i.e. greater perseveration) of nondirected conditioned behavior which has not been formally trained? For example, a rat will generally "freeze" if he is returned to a place that was previously associated with a noxious stimulus. Would such a conditioned "freezing" response (which requires no formal training and which is not directed at a "goal") be perseverated by Ss with hippocampal damage after the noxious stimulus had been permanently removed from the situation? According to a "perseveration" hypothesis, it might be expected that "freezing" would take longer to extinguish in hippocampectomized Ss. The lack of "inhibition" found with hippocampectomized Ss under various conditions suggests that hippocampal damage interferes in some way with a "braking" mechanism; and interference with such a mechanism might therefore be expected to produce faster, rather than slower, extinction of conditioned "freezing."

It is possible that the extent to which "response" tendencies are modified in rats after hippocampal damage, depends on conditions which modify S's level of "arousal."

It has been shown that the hippocampus acts to inhibit ascending activity from the brainstem reticular formation (Adey, Segundo, & Livingston, 1957; Redding, 1964), as well as afferent conduction into the hypothalamus (Feldman, 1962). Interference with such an inhibitory mechanism might make Ss more responsive to conditions which tend to increase arousal. In this respect, Teitelbaum & Milner (1963) have reported that sudden noises, such as hand clapping, greatly increased the frequency with which rats with hippocampal lesions jumped off a platform onto an electrified grid. Similarly, Raphelson, Isaacson, & Douglas (1965) have reported that the introduction of a new visual stimulus into a runway increased the running speed of rats with extensive hippocampal damage. On the other hand, they found that operated and unoperated control Ss typically reduced their speeds when the novel stimulus was first introduced. However, the suggestion that the behavior of hippocampectomized Ss is related to a reduction in the inhibitory regulation of "arousal systems" has only indirect support: from electrophysiological experiments. To the best of my knowledge, there have been no experiments in which physiological changes have been monitored concomitantly with the behavioral changes observed in hippocampectomized animals. Such experiments should provide valuable

information regarding the relationship between changes in arousal and the behavior of these brain-damaged Ss.

The overall picture from the behavioral evidence cited above, is that infrahuman animals with bilateral hippocampal damage show an increased and persistent tendency to continue making some responses that "normal" animals stop making fairly rapidly. This behavior is very similar to that found after brain damage to other structures which are intimately related to the hippocampus. For example, changes found after septal damage are so similar that McCleary (in press) has stated that "perseverative characteristics of the animal with bilateral hippocampal lesions cannot as yet be differentiated convincingly from those of the subject with septal damage."

Again, it should be mentioned that the striking "memory" disturbance found in human patients with hippocampal damage has received little confirmation from experiments with infrahuman subjects. However, both acquisition deficits (Kaada et al., 1961; Kimble, 1963; Kveim et al., 1964; Stein & Kimble, 1966; Spiegel, Hostetter, & Thomas, 1966) and retention deficits (Isaacson, Schmaltz, & Douglas, in press; Kaada et al., 1961) have been found with hippocampectomized rats in various maze problems, which suggests that in order to get a "memory"

deficit in infrahuman subjects, the problem must contain some level of complexity.

The Present Investigation

Aspects of "perseveration" found after hippocampal damage would appear to need clarification in order to reach a better understanding of hippocampal "function." For instance, it would be useful to know more precisely the conditions that are responsible for producing more persistent activity in animals following damage to the hippocampus. Roberts et al. (1962) have suggested that rats with hippocampal lesions are "hyperexploratory," but the effects of varying exploratory incentive have not been examined. The persistent activity of hippocampectomized rats has also been interpreted as a failure to habituate to novelty (Leaton, 1965), suggesting that hippocampectomized Ss would be more reactive to the introduction of a novel stimulus. However, Wickelgren & Isaacson (1963) and Raphelson et al. (1965) have found that under certain conditions hippocampectomized rats react less to the introduction of a novel stimulus. It would therefore be valuable to determine more precisely the circumstances in which rats with hippocampal damage do or do not react to novel stimulation. Furthermore, as was mentioned

earlier, experiments which have shown that hippocampectomized Ss perseverate during extinction conditions have always measured trained goal-directed responses; and it would therefore be informative to know whether untrained nondirected behavior, such as conditioned "freezing" would also persist during extinction procedures.

It was with the purpose of seeking answers to some of these questions that experiments in the present investigation were designed. In the first experiment, activity was measured in two situations: one which facilitated exploration and one which limited exploration. In the second experiment reactions to a novel visual stimulus were measured during goal-directed and undirected activity. In the third experiment acquisition and extinction of a conditioned "freezing" response and reactions to the noxious stimulus, itself, were measured. Finally, in the fourth experiment, active avoidance conditioning was studied.

General Surgical and Histological Procedures

Subjects in all experiments were male hooded rats obtained from either the Quebec Breeding Farm or from the McIntyre Medical Center, McGill University. At the time of surgery, weights ranged from 275-310 grams. Subjects were anesthetized with nembutal (60 mg/ml) given IP, and placed in a Kopf stereotaxic instrument. The skull was exposed after a scalp incision and trephine holes were drilled at desired locations. One group of Ss received bilateral electrolytic lesions in the dorsal hippocampus (Hp Les. group). Another group had the electrode lowered into the hippocampus without the current being turned on (Sham group). A third group of Ss had the dorsal hippocampus and overlying neocortex removed bilaterally by means of aspiration (Hp + Cort. group), while a fourth group had only the cortex above the hippocampus aspirated (Cort. group). Electrolytic lesions were produced by passing a two milliampere anodal current for 20 sec. through a stainless-steel formvar-insulated electrode, which was exposed only at the tip. The electrode was lowered perpendicular to the incisor bar, once on either side of the sagittal suture, 2 mm. posterior to bregma, 2 mm. lateral from the midline, and 3 mm. below the dura. Cortical ablations and combined cortical and hippocampal ablations

were produced by sucking out the tissue with a glass pipette which was attached to a vacuum source. No attempt was made to remove the same amount of tissue in the cortical ablations as was removed in the cortical-hippocampal ablations. Following surgery, the holes in the skull were covered with either gelfoam or gelfilm, the skin sutured together, and penicillin administered IM.

Upon completion of testing, Ss with brain damage were sacrificed with ether and perfused with saline followed by 10% formol-saline. Brains were removed and placed in 10% formalin for a day, after which they were frozen and sectioned at 40 micra in the De Groot plane (De Groot, 1959). Every fifth section through a lesion was saved and stained with either luxol fast blue and 1% neutral red, or with thionin. Each S's lesion was then reconstructed on representative sections, obtained from De Groot's atlas of the rat brain. Graph paper, arranged in .5 cm. squares, was placed over each of the De Groot diagrams for each S, and the number of squares contained within the area of the lesion was counted and used as an index of brain damage. Table 1 presents the averaged amount of hippocampal and cortical damage, as determined by the number of squares, for each operated group. The rostro-caudal extent of hippocampal damage produced by aspiration

was generally greater than that produced electrolytically, although both types of damage were similar with respect to width and depth of the lesion. Furthermore, the greatest amount of total brain damage was produced in the group with combined hippocampal and cortical destruction. A few of the Ss in each of the groups with hippocampal damage were also found to have minor thalamic damage. These Ss were not discarded since thalamic damage was always relatively small and never consistent between Ss. Thalamic nuclei sometimes damaged included posterior, lateral, and pretectal areas. Figures 1-3 show coronal sections of brain damage in the various groups. The sections which present hippocampal damage were chosen to show those lesions which contained the greatest amount of thalamic damage. Figure 4 presents a dorsal view of a brain with combined hippocampal and cortical damage, and one with only cortical damage.

Experiment I. The Effects of Hippocampal Damage on Activity in Two Situations

Under certain conditions, but not under others, rats with bilateral hippocampal damage have been found to persist in activity for longer periods of time than control subjects. Positive results have been obtained from measurement of activity in relatively large areas, while negative results have been obtained from measurement of activity in very small chambers or running wheels. One possible explanation for this divergence of findings is that hippocampectomized rats are "hyperexploratory" and not merely hyperactive. However, to the best of my knowledge, situations which provide different degrees of opportunity to "explore," have not been compared systematically. Therefore, the first experiment was designed to compare the activity of rats with and without hippocampal damage in: (a) a situation which facilitated exploration and, (b) one which limited this type of behavior.

Subjects

Subjects were 60 male hooded rats caged separately and having constant access to food and water. The number of Ss in each group were as follows: Unoperated group, 11; Sham

group, 13; Cort. group, 10; Hp + Cort. group, 10; Hp Les. group, 16. Testing began approximately three weeks after surgery.

Procedure

Movement recorder

The apparatus consisted of a metal cylinder 12 in. high and 11 in. in diameter with a plywood cover. A window cut into the cylinder permitted observation of the Ss. Any movement by S caused displacement of a spring-suspended floor, and an acceleration transducer attached to the bottom of the wire mesh floor measured activity in terms of dynamic energy output (Mundl, 1966). A Dymec voltage-to-frequency converter, model 2210, connected to a Dynac variable time base counter, model dy-2500, provided activity scores in numerical form which were printed out every minute from a Hewlett Packard model 560A digital recorder. This apparatus was designed to limit exploratory activity, by restricting area, and amount of varied sensory stimulation.

To further reduce varied sensory stimulation, Ss were tested in a fairly dark room and extraneous sounds were masked by steady noise provided by a Grason Stadler model 901B white noise generator. Movement was measured at the same time each day on five consecutive days in 15 min. sessions. Groups

were compared by means of analyses of variance on measures of inter- and intrasession habituation.

Exploration apparatus

In contrast to the previous apparatus which was designed to restrict exploration, this apparatus was designed to facilitate it. Four identical chambers were used to measure "exploratory" activity. Each chamber was constructed of ¼ in. plywood painted flat black, and measured 16 in. x 11 in. x 24 in. high. A hole 1½ in. in diameter was cut into each of the four walls. On the long sides the hole was located midway, 5 in. above the floor, and on the short sides it was located midway, 3½ in. above the floor. An "exploratory" response consisted of S inserting his head through a hole and breaking a light beam. A 4 sec. delay followed each response, before the next response could be counted. This delay was incorporated into the circuitry of the system to reduce movement artifact once S's head was through a hole.

The testing room was well illuminated and masking noise was provided in the manner previously described. Responses were counted and printed out every 5 min. from a three channel Grason Stadler print-out counter, model E12505A, and from a single channel Pressin print-out counter, both located in an adjacent room. The number of head insertions was recorded in

1 hr. sessions on five consecutive days, and as with the other apparatus, each S was tested in the same chamber at the same time each day. Again, groups were compared by means of analyses of variance on measures of inter- and intrasession habituation.

Testing procedure

Subjects were first tested in one activity situation for five consecutive sessions, then after one week of not being tested at all, were tested in the other activity situation for five sessions. Half of the Ss in each group was first tested in the "exploration chamber," while the other half was first tested in the movement recorder. Subjects with cortical ablations were tested only in the movement recorder, while two unoperated Ss and two Ss with combined hippocampal and cortical lesions were tested only in the head insertion apparatus. One S from the sham operated group died after first being tested in the movement recorder.

Results

Subjects with combined hippocampal and cortical ablations and Ss with electrolytic lesions in the hippocampus habituated significantly more slowly than either operated or unoperated control Ss in the "exploration chamber" but not in the movement recorder. This deficit (i.e. perseveration of explora-

tion) was most striking during the first session for both groups with hippocampal damage. In contrast to the Ss with hippocampal electrolytic lesions, however, the Ss with combined hippocampal and cortical ablations continued to show a deficit in habituation through the second and third sessions.

Figure 5 presents "exploratory" activity for five sessions for each of the four groups. An analysis of variance on the activity over five sessions showed that the groups were significantly different ($p < .01$, $F = 5.55$, $df = 3/45$). Scheffé's test of multiple comparisons, with $p < .10$ used as the level for rejecting the null hypothesis (Scheffé, 1959), further revealed no difference between the two groups with different types of hippocampal damage, as well as no difference between the operated and unoperated control groups. Similarly, no difference was found between the hippocampal electrolytic lesioned group and either one of the control groups when activity was compared over the five sessions. Subjects with combined hippocampal and cortical damage however, were significantly different from either the operated ($p < .05$, Scheffé) or unoperated ($p < .01$, Scheffé) control subjects. A day-by-day comparison between the groups revealed that they differed significantly on day

1 ($p < .01$, $F = 16.23$, $df = 3/45$), day 2 ($p < .01$, $F = 7.26$, $df = 3/45$), and day 3 ($p < .05$, $F = 3.30$, $df = 3/45$), but not on days four or five. The overall trend showing decreased activity for five sessions was significant ($p < .01$).

Figures 6, 7, and 8, show intrasession scores for sessions 1, 2, and 3, respectively. As mentioned above, differences in habituation between the groups was significant during sessions 1, 2, and 3, but not during sessions four or five. Scheffé's test of multiple comparisons for session one revealed no difference between the two groups differing with respect to hippocampal damage, as well as no difference between the two control groups. However, either group with hippocampal damage differed significantly from either one of the control groups ($p < .01$, Scheffé). Intrasession scores for session two revealed that the group with combined hippocampal and cortical damage differed significantly from the operated ($p < .05$, Scheffé) and unoperated ($p < .01$, Scheffé) groups, as well as from the group with hippocampal electrolytic lesions ($p < .10$ Scheffé). On the other hand, the group with hippocampal electrolytic lesions did not differ from either of the control groups, when habituation over the second 1 hr. session was recorded. It should be noted however, that the Hp Les. group was more active than either one of the

control groups during the first 15 min. of this session. Intrasession scores for the third session showed no difference between the two groups with hippocampal damage, and no difference between the Hp Les. group with either one of the control groups. The Hp + Cort. group however, continued to differ from either of the control groups ($p < .05$, Scheffé).

Figure 9 presents activity in the movement recorder for five sessions for each of the five groups, and Fig. 10 shows changes in activity during the first session in this apparatus. Neither the overall nor the day-by-day analysis revealed any differences between any of the groups on either intersession or intrasession activity scores.

Experiment II. The Effect of Introducing a Novel Visual Stimulus During Directed and Undirected Activity

Results from the previous experiment suggest that the lack of habituation found with rats suffering hippocampal damage is related to the amount of exploration permitted by the activity chamber. It is possible that the holes in the "exploration" chamber acted as "exciting" stimuli that maintained a high level of arousal in the hippocampectomized Ss. However, the design of the first experiment did not provide definitive analysis of the stimulus effect, per se.

The following experiment, therefore, was designed to compare the reactions of hippocampal Ss with control Ss, to the presentation of a novel irrelevant visual stimulus. In the "undirected" condition the initial reaction and habituation to the visual stimulus was measured in terms of a change in activity, after Ss had become relatively inactive. In the "directed" condition, reaction to the stimulus was measured with respect to suppression of bar-presses for food.

Subjects

Subjects in both parts of this experiment consisted

mainly of those Ss that had been tested in the previous experiment. In all cases, novelty reactions were first measured in the "undirected" condition. Subjects tested in the "undirected" condition consisted of 13 operated control Ss, 10 Ss with posterior cortical ablations, 8 Ss with combined hippocampal and cortical ablations, and 16 Ss with bilateral hippocampal lesions produced electrolytically. One S from the group with cortical ablations died before being tested in the "directed" condition. Furthermore, 9 additional experimentally naive Ss with combined hippocampal and cortical damage were tested in the "directed" condition, along with 15 experimentally naive unoperated Ss. Four operated control Ss were not used in the "directed" condition because of illness which appeared subsequent to their being tested in the "undirected" condition.

Procedure

Undirected activity

The apparatus consisted of the movement recorder described in the previous experiment, with one minor change. Three amber lights, each containing a 6 v., .15 amp. lamp, were inserted at equal distances around the inside perimeter, 4 in. above the floor of the chamber. Novel visual stimula-

tion was presented by these lights and consisted of ½ sec. on - ½ sec. off flashes.

Approximately two weeks after being tested in Experiment I, Ss were tested in this situation. Specifically, after S had been in the movement recorder for 10 min., the lights came on and flashed for the remainder of a 15 min. session. Subjects were tested in this manner on three consecutive days. Movement, before and during visual stimulation, was measured and recorded as in Experiment I.

Directed activity

The apparatus consisted of an operant conditioning chamber constructed of wood, 10 in. long x 8½ in. deep x 18 in. high, with a clear plexiglass front. A lever was mounted on the left wall 2 in. from the grid floor, and a food cup was located 1¼ in. to the side of the lever. A Gerbrands model D food dispenser was located at the side of the box and both the conditioning chamber and food dispenser were housed inside a sound-proof chamber, which also accommodated a house light, a blower for circulating air, and a masking noise source. Novel visual stimulation was presented by a ½ sec. on - ½ sec. off flashing amber light, 28 v., .07 amp., located 4 in. above the lever in the conditioning chamber.

Two weeks before they were trained to bar-press for food, Ss were put on a food deprivation schedule. They were given enough food in the form of dry lab blocks once per day for their weights to stabilize to about 85% of their normal weights. After testing began, each S received two blocks of lab chow following each experimental session. Water was present in the individual home cages at all times.

Subjects "trained" themselves to bar-press in order to obtain a 45 mg. pellet of food. After S had learned to bar-press for food on a continuous reinforcement schedule, three more days of training, 10 min. per day, were allowed before records were taken. On the fourth day, presses for 10 min. were recorded and used as an index of food motivation. On days 5, 6, and 7, visual stimulation was turned on after the third minute of bar-pressing, and remained on for three minutes. Suppression ratios, measuring bar-presses before and during visual stimulation, were used as an index of the amount of distraction produced by the visual stimulus. Since it was observed that even normal Ss would usually not remain distracted for more than one minute after onset of the visual stimulus, suppression ratios only included a comparison of bar-presses one minute after stimulus onset with bar-presses one minute prior to stimulus onset.

Results

While bar-pressing for food, both the Hp + Cort. group and the Hp Les. group were less distracted by the onset of the novel visual stimulus than any of the other groups. However, the Ss with hippocampal damage were not different from the other Ss in reacting to the visual stimulus while in the movement recorder.

Directed activity

The lack of distraction found in the two groups of Ss with hippocampal damage cannot be attributed to increased food motivation in these Ss, since no difference was found between any of the groups in the number of food-reinforced bar-presses during the 10 min. session on day four. The mean number of bar-presses for this session were 96.9, 96.5, 98.7, 97.7, and 96.0 for Ss with combined hippocampal and cortical damage, Ss with hippocampal electrolytic lesions, Ss with posterior cortical ablations, Ss that received sham operations, and unoperated Ss respectively.

Suppression of bar-presses was calculated by using the ratio $\frac{A}{A + B}$, where "A" represents responses emitted during the minute prior to the onset of the visual stimulus, and "B" represents the number of presses during the first minute after the onset of the stimulus. With this ratio, complete suppress-

ion of bar-pressing during "B", yields an index of 1.00. When the number of presses during "B" is the same as the number during "A", an index of .50 is obtained.

Figure 11 presents suppression ratios for one session prior to the first test session, and for the three test sessions. Although the groups did not differ with respect to the control session (P), an analysis of variance showed a significant Group effect ($F = 9.93$, $df = 4/61$, $p < .01$), and a significant Interaction effect ($F = 8.78$, $df = 8/122$, $p < .01$), when the groups were compared over the three sessions. All three groups without hippocampal damage showed almost complete suppression of bar-presses when first presented with the flashing light, but were less affected by the visual stimulus with each succeeding session. These Ss typically "froze" when the flashing light was initially introduced, then explored the area surrounding the light before starting to bar-press again. In contrast, the introduction of the flashing light caused little change in the bar-pressing behavior of either group with hippocampal damage, even upon initial exposure. There was a slight decrease in bar-presses with both hippocampal groups when the light was first introduced, which typically represented a brief startle reaction followed by orientation towards the light. However, from general observa-

tion of the hippocampectomized Ss, it appeared that they did not remain "frozen" for as long as the control Ss after the stimulus came on.

Undirected activity

Figure 12 presents changes in activity after the onset of the visual stimulus along with subsequent habituation as the stimulus remained on, for each of the three test sessions. It is clear that all groups reacted similarly to the introduction of the flashing lights. Activity first increased with the onset of visual stimulation and then decreased as the lights continued to flash. Analyses of variance revealed that the groups did not differ with respect to either the change in activity which accompanied stimulus onset or with respect to the decrement in activity as the stimulus remained on, for any of the three sessions.

Experiment III. Reaction to an Air-blast, and the Acquisition and Extinction of a Conditioned "Freezing" Response

Results from the previous experiment suggest that under certain conditions rats with hippocampal damage are less affected by changes in environmental stimulation when compared with control Ss. The preceding experiment was concerned with behavioral changes associated with the introduction of an irrelevant nonaversive stimulus. The present experiment deals with unconditioned reactions to an aversive stimulus, and to the development and extinction of a conditioned "freezing" response (CFR).

Unconditioned reactions to stress, such as "freezing" observed in Ss after the presentation of an aversive stimulus, have not, as far as I know, been carefully compared in hippocampectomized and control Ss. One purpose of the present experiment therefore, was to compare the activity of rats with and without hippocampal damage, after the presentation of an air-blast. When a noxious stimulus, such as an air-blast, is repeated in a particular location, a CFR to that location is likely to develop. As mentioned earlier, it would be of interest to know whether this type of a condi-

tioned response would persist in Ss with hippocampal lesions during extinction procedures, as has been found with other responses.

Subjects

Subjects were 44 experimentally naive male hooded rats. One group consisted of 21 Ss with bilateral electrolytic lesions in the dorsal hippocampus. Another group consisted of 13 Ss with sham operations. A third group made up of 10 unoperated Ss was also used, but these Ss were tested at an earlier date and were not subjected to the extinction phase of the experiment.

Procedure

The apparatus used was the cylindrical movement recorder used in both previous experiments, with a slight addition. Two pieces of ¼ in. copper tubing, fitted with brass nozzles, were draped over the chamber pointing downward. The tubing was connected to a solenoid actuated valve which was, in turn, connected to a tank of compressed air.

Subjects were first habituated to the activity chamber for 10 min. a day on eight consecutive days. On days 9-13, a one sec. air-blast at 60 lbs. of pressure was delivered through the nozzles after the seventh minute. On days 14-18

no air-blast was delivered.

Air-blasts were automatically controlled by a series of timers, and activity was printed out every minute as described previously. Analyses of variance were performed on the activity data of minutes 8-10 on; (a) three days prior to air-blasts (sessions 1-3), (b) the five days that air-blasts occurred (sessions 4-8), and (c) the final five days when air-blasts no longer occurred (sessions 9-13).

Since a CFR to the situation occurred following days that an air-blast was delivered, the CFR was measured in terms of the activity during the first three minutes of those sessions that followed air-blast sessions. Analyses of variance were then carried out to compare the first three minutes of each group's mean activity on the days before air-blasts were delivered (sessions 1-4), on the days which followed an air-blast (sessions 5-9), and on the days when air-blasts no longer occurred (sessions 10-13).

Results

Subjects with hippocampal damage lost their CFR faster than Ss with sham operations as measured by the first three minutes of activity in sessions 10-13. However, no difference was found between hippocampal, sham, and unoperated groups in

either their initial reaction to the air-blast, or in their developing a CFR after repeated presentations of the air-blast.

Results for each group's activity during minutes 8-10, and during minutes 1-3, are presented in Figs. 13 and 14 respectively. Analyses of variance revealed no differences between the groups for minutes 8-10 on sessions prior to the air-blast, on sessions that contained an air-blast, or on sessions in which the air-blast was omitted. All Ss typically "froze" after an air-blast, but increased their activity steadily, during minutes 8-10, over the five extinction sessions. Analyses of variance also revealed no differences between the groups in either the development of the CFR, or for the first three minutes during sessions before CFR development. All Ss typically became very inactive as soon as they were placed into the activity chamber if the session had followed one in which they were blasted with air. An analysis of variance on the first three minutes of the extinction sessions however, revealed a significant Interaction effect ($F = 7.08$, $df = 3/78$, $p < .01$) between the hippocampal and sham groups, but not a significant Group effect. As can be seen from Fig. 14, the group with hippocampal lesions became increasingly more active during the first three minutes with each additional extinction session. In contrast, the activity of the sham operated group remained low throughout the four extinction sessions. This inactivity

found with the sham group cannot be explained in terms of their merely habituating to the situation as a whole, since these same Ss increased their activity during minutes 8-10 on the same extinction days (Fig. 13).

It should again be stressed that the difference found between the two groups during extinction sessions depended critically on the minutes during which behavior was sampled. If it was sampled during the first three minutes of the extinction sessions, the groups were found to differ. However, if behavior was sampled during minutes 8-10, no difference was found.

Experiment IV. Avoidance Conditioning

The previous experiment showed that rats with hippocampal damage reduced their "freezing" more rapidly than sham operated Ss during extinction of a CFR. This result, coupled with some pilot work which will be described below, suggested that the Ss with hippocampal lesions might be impaired in acquiring an active avoidance response.

Subjects

Subjects were the same 21 Ss with hippocampal lesions and 13 Ss with sham operations that were used in the previous experiment.

Procedure

The apparatus consisted of a 28 in. x 5½ in. x 12 in. high alley, divided in the middle by an opaque sliding door. At one end of the alley three pieces of ¼ in. copper tubing with brass nozzles protruded ¼ in. into the chamber and were located 1¼ in. above the wire mesh floor. The copper tubing was connected to a tank of compressed air, and a hand actuated valve permitted the presentation of air-blasts to be controlled by the experimenter.

Subjects began training in this apparatus approximately

three weeks after the conclusion of the last experiment. Each S was first allowed to explore the entire alley for three minutes. The partition was then lowered and S was placed, with his back towards the partition, into the compartment that contained the air nozzles. After 5 sec. the partition was raised, and if S did not turn around and move into the other compartment within another 5 sec., a short air-blast of approximately 2 sec., at 60 lbs. of pressure, was delivered. If S failed to escape after the first air-blast, which happened only rarely, additional blasts were presented until he did escape. After the S moved into the safe compartment, he remained there for 30 sec. before the next trial began. Thirty trials were given for the first session, and if a criterion of five out of six avoidance responses was not reached within this session, an additional 20 trials were given the next day. Testing was concluded after 50 trials whether or not the criterion was attained.

It was observed from a pilot study that unoperated Ss that learned to avoid under these conditions fastest, were Ss that tended to "freeze" in the safe compartment after making either escape or avoidance responses. Although the Ss with hippocampal lesions were not different from control Ss in

"freezing" after the air-blast in Experiment III, it is still possible that this response was weaker in the lesioned Ss since they lost it faster during extinction sessions. This, in turn, might be revealed as impaired avoidance behavior under the conditions of the present experiment. Therefore, the amount of time spent immobile in the safe compartment on the first two escape trials was recorded, and correlations were obtained for each group comparing the number of trials to criterion with the total amount of time spent "frozen." The two groups were also compared with regard to the number of trials required to reach criterion.

Results

No difference was found between the two groups in the number of trials required to reach criterion (Table 2). Four of the operated control Ss and four Ss with hippocampal lesions failed to reach criterion within the 50 trials. Correlation coefficients of the amount of time spent "frozen" after the first two escape responses and the rate of avoidance learning, were .67 and .55 (Spearman's rho) for the group with sham operations and for the group with hippocampal lesions respectively. Both correlation coefficients deviated significantly from chance, indicating that the Ss that "froze" more after making a response, irrespective of surgical treatments, learned the avoidance response fastest.

Discussion

The present results have helped clarify to some degree the conditions in which "perseverative" behavior is found in rats after hippocampal damage. In Experiment I the Ss with hippocampal damage habituated more slowly than control Ss in the "exploration" apparatus, but not in the movement recorder. The behavior generated by cues in each of these environments was markedly different, as were the cues themselves. Holes in the walls of the "exploration" apparatus provided a means for visual exploration. No such specific cues were provided by the movement recorder. In addition, the movement recorder measured every movement made by the S, whereas the "exploration" apparatus measured only a discrete "goal directed" response. Since the movement recorder measured every response, it is possible that while in this apparatus, the Ss with hippocampal damage were actually engaged in exploratory activities while the other Ss were engaged in some other forms of activity. Therefore, a difference in patterns of behavior might exist despite the finding that the groups did not differ in their rates of habituation. However, from observation of the Ss through the window in the apparatus, it did not appear that the Ss with hippocampal damage differed from the controls in their patterns

of activity.

Although both the Hp Les. group and the Hp + Cort. group were slower than control Ss in reducing their activity in the "exploration" apparatus, the Hp + Cort. group was more impaired. Since a control group with only cortical damage was not tested in this apparatus, the possibility that Ss with damage restricted to the cortex might also have exhibited poor habituation must be considered. Fortunately, there are some data from our laboratory that bear on this point. Musty (personal communication) found no difference between unoperated Ss and Ss with brain damage restricted to the cortex above the hippocampus, when habituation was measured under the same conditions and in the same "exploration" chambers as those used in the present investigation. There are a number of possibilities to account for the difference found between the Hp + Cort. and the Hp Les. groups, but it seems reasonable that the most likely cause for this difference was the greater amount of hippocampal tissue removed in the Hp + Cort. group. This possibility is supported by other experiments (Roberts et al., 1962; Teitelbaum & Milner, 1963) which have also suggested that larger hippocampal lesions in rats produced greater persistence in "exploratory" activity than smaller lesions. It is also true that, in the present experiment, Ss in the Hp + Cort. group had more

total brain tissue removed than Ss in the Hp Les. group. The possibility that a "mass action" effect caused a greater impairment in habituation cannot be eliminated. However, this possibility seems unlikely since Douglas & Isaacson (1964) controlled for total amount of tissue removed and still found slower habituation in rats with cortical-hippocampal ablations, compared with rats with only neocortical damage. That the greater impairment found with the Hp + Cort. group in the present experiment was related to some interaction between the hippocampus and its overlying cortex remains a possibility, of course.

Regardless of the difference found between the Hp + Cort. and the Hp Les. groups in the "exploration" apparatus, it is clear that both groups habituated more slowly in this apparatus than either the operated or unoperated control groups. The slower habituation could be related to the nature of the cues in the chamber, to the nature of the response permitted by the chamber, or to an interaction between these factors. It seems plausible that the holes in the "exploration" chambers served as "rewarding" stimuli which facilitated approach tendencies to a greater extent than cues provided in the movement recorder. If hippocampal damage strengthens response tendencies associated with approach

behavior, it is not surprising that the "exploration" apparatus, which provided cues to facilitate this behavior, would be more likely to differentiate between Ss with and without hippocampal lesions. Since the Ss with hippocampal damage did not show persistent activity in the movement recorder, their behavior cannot be explained in terms of a general increase in activity, as suggested by Teitelbaum & Milner (1963) and by Niki (1962).

Interpretation of the slower habituation found with hippocampectomized Ss in the "exploration" apparatus is somewhat confounded by the result that these same Ss habituated like controls to flashing lights which were presented in the movement recorder (Experiment II). It might have been expected that exploratory responses directed towards the lights when they first came on would persist in the Ss with hippocampal damage. However, all groups rapidly habituated to the lights as indicated by the reduction in movement scores. A possible explanation for this discrepancy might be that the flashing lights did not provide as much stimulus variety or permit as much directed motor activity as the "exploration" chambers. In this respect, the relatively homogeneous nature of the flashing lights might be more analagous to the conditions which originally showed no differences in habituation in the movement

recorder (Experiment I).

Leaton (1965) has suggested that hippocampectomized rats habituate more slowly than control Ss to novel stimuli. In his experiment Leaton measured forced-trial choice-point speed in a T-maze and found that Ss with hippocampal damage, unlike controls, did not decrease their speeds from one trial to the next. However, the results from Experiment II suggest that, under certain conditions, rats with hippocampal damage can habituate as well as controls to the introduction of a novel stimulus. In Leaton's experiment the Ss were engaged in directed motor activity, and it was this activity which persisted in the rats with hippocampal damage. This result is similar to the impaired habituation found with hippocampectomized Ss in Experiment I, in that both the "exploration" apparatus and Leaton's T-maze facilitated directed motor behavior.

Recently, Isaacson (1966) has offered an explanation to account for the variety of deficits found after hippocampal damage. He suggests that abnormal behavior is exhibited by hippocampectomized Ss when environmental conditions become incongruent with an animal's expectancies. Under such conditions, according to Isaacson, the hippocampus normally acts "as a specific effector mechanism" which helps the animal to

modify his behavior appropriately. This explanation accounts very satisfactorily for much of the behavior found after hippocampal damage, particularly in experiments which have shown maladaptive behavior to sudden changes in environmental contingencies. However, it seems difficult to account in this way for (a) the lack of habituation found in Experiment I, and (b) the faster reduction of "freezing" found in Experiment III. Firstly, the slower habituation exhibited by the Ss with hippocampal damage would not seem to entail the disruption of previous expectancies directly. Isaacson does mention however, that "expectancies" can be determined by "genetic endowment" and "early life experiences" as well as by formal laboratory training. Secondly, the increased activity found in the Ss with hippocampal lesions during extinction sessions (Experiment III, Fig. 14) might be interpreted as better adaptation to an environmental change (cessation of air-blast) rather than as maladaptive behavior.

Kimble (1966) has suggested that Ss with hippocampal damage perseverate learned responses and are therefore less flexible in modifying their behavior with changes in the environment. This interpretation is quite similar to that proposed by Isaacson, and again, does explain many of the deficits found after hippocampal lesions. However, the

development of previous response patterns was not necessary for the hippocampectomized rats of the present investigation to show persistent responses in the "exploration" apparatus. Furthermore, their "freezing" behavior did not persist, even as long as controls, when the air-blast was removed (Experiment III, Fig. 14). According to a "perseverative" hypothesis it might have been expected that "freezing" would be prolonged rather than diminished.

The results of Experiment I and Experiment III suggest therefore, that the failure of hippocampectomized rats to suppress responses does not necessarily require the "build-up" of a particular response pattern. In Experiment I, the poor habituation of Ss with hippocampal damage appeared to be related to environmental conditions which facilitated approach tendencies, and, as mentioned earlier, it is possible that the tendency to make responses which are directed at a "rewarding" goal (i.e. holes for exploring) is relatively strengthened after hippocampal damage. Along with an increase in "response strength" it would also appear that hippocampal damage weakens inhibitory or "braking" reactions which might normally be associated with "alarming" or noxious stimuli. For example, under the conditions of Experiment III, the Ss with hippocampal lesions failed to show the persistence of "freezing" that the

control Ss showed. Other explanations in terms of a disruption in "memory," or a reduction in "emotionality," should be considered; but the Ss with hippocampal lesions in Experiment III did "freeze" to the same extent as controls immediately after the air-blast and at the beginning of sessions which followed air-blast sessions, which suggests that (a) they were not less "emotional," and (b) they were able to remember the consequences of the previous day. A memory deficit cannot be totally ruled out, however, since it is possible that the Ss with hippocampal lesions might require day-to-day exposure to the unconditioned stimulus (air-blast) for them to demonstrate good retention. Continued exposure to the air-blast, of course, did not occur during extinction sessions. In order to test more specifically for a memory deficit it would be of interest to measure S's retention at various intervals after the last air-blast session. Again, however, it is clear that the Ss with hippocampal lesions were able to retain information concerning the air-blast for at least 24 hours.

Another possible indication that "braking" reactions to "alarming" stimuli are weakened after hippocampal destruction, comes from the result which showed that the Ss with hippocampal damage did not react very strongly to the flashing light when it was presented during bar-pressing performance.

These Ss typically startled and oriented towards the flashing light when it was first introduced, but did not appear to remain "frozen" for as long as the control Ss. Although latencies were not taken between the time bar-pressing stopped and then started again, this impression is supported by the fact that the hippocampectomized Ss pressed more than controls in the minute following stimulus onset. Similar results have recently been reported by Raphelson et al. (1965). These authors found that rats with extensive hippocampal damage did not react to the introduction of a novel visual stimulus while they were running down an alley for food. Subjects with dorsal hippocampal damage, like the Ss with similar brain damage in the present experiments, initially reacted to the new stimulus, but recovered significantly faster than the control Ss. A general decrease in reactivity to novel stimulation cannot explain the results obtained by Raphelson et al., or the fact that in the present experiment the Ss with hippocampal damage did not differ from any of the control Ss in reacting to the flashing lights when they were presented in the movement recorder. In this latter situation "freezing" was not observed in any of the Ss when the lights were initially introduced. Instead, all Ss typically explored the area surrounding the lights when they came on;

which accounts for the initial increase in movement scores. It must be remembered that the lights were introduced into this situation when the Ss were relatively inactive and not engaged in directed activities. It is possible that under such conditions the sudden introduction of a novel stimulus would cause less of an "alarm" or "startle" reaction than if presented when the S was "attending" to some other stimulus in his environment.

It seems highly probable that the nature of the stimulus as well as the response is important in determining the extent to which rats with hippocampal damage will react to a new stimulus; and factors related to the intensity, complexity, and relevance of the stimulus should be investigated. For instance, the novel stimulus in the second experiment consisted simply of a flashing light to which Ss had not attached any particular significance, and it would be of considerable interest to determine whether Ss with hippocampal damage would have been more distracted from bar-pressing had the light been previously paired with "reinforcement" in another situation.

As mentioned previously, the result that the Ss with hippocampal lesions reduced their "freezing" during extinction sessions more rapidly than the sham operated Ss (Experiment III), suggested that these same Ss might also be retarded in acquiring

an active avoidance response. However, this was not the case, as shown by the results of Experiment IV. In contrast to the present results, McNew & Thompson (1966) have recently reported that rats with hippocampal lesions were inferior to unoperated control Ss in learning an active avoidance response which was similar to the one used in the present investigation. One difficulty in reconciling these results involves the fact that McNew & Thompson did not present any histological data for the hippocampal lesions of their Ss. Furthermore, air-blasts were used in the present experiment to motivate the Ss whereas McNew & Thompson used foot-shock. In comparing the two experiments, it would appear that "normal" rats learn to avoid a foot-shock much more rapidly than an air-blast, which suggests that hippocampectomized rats would be more likely to show an impairment in avoidance tasks which "normal" Ss learn rapidly. However, this would not explain the result that hippocampectomized rats acquire a shuttle avoidance response faster than control Ss (Isaacson, Douglas, & Moore, 1961).

In general, the present results suggest that "approach" tendencies are relatively strengthened after hippocampal damage in rats, and that "braking" reactions are relatively weakened. There are obvious similarities between this and

other explanations which have attributed the behavior of hippocampectomized Ss to a lack of "response inhibition" or to an enhancement of "response perseveration." It is clear, however, that a general "disinhibition" of behavior does not follow hippocampal damage. If this were the case, the Ss with hippocampal damage in Experiment I would have shown persistent activity in the movement recorder as well as in the "exploration" apparatus. Furthermore, as was mentioned earlier, the Ss with hippocampal lesions in Experiment III did not "perseverate" the conditioned "freezing" response but, instead, lost it during extinction sessions faster than control Ss. In contrast to this latter result, hippocampectomized Ss extinguish other kinds of previously learned responses slower than control Ss (Jarrard et al., 1964; Jarrard & Isaacson, 1965; Niki, 1965; Peretz, 1965; Teitelbaum, 1961). These conflicting data, as well as the results of Experiments I and II, suggest that the nature of the "response" should be investigated more closely in order to reach a better understanding of hippocampal "function."

Summary

Rats with bilateral dorsal hippocampal damage habituated more slowly than control subjects in a situation which provided opportunities for visual exploration, but were indistinguishable from controls when habituation was measured in a small enclosed platform activity recorder. The hippocampectomized subjects were also less distracted by the introduction of a flashing light, while they were bar-pressing for food. However, no difference was found between the hippocampectomized and control groups in either their initial reaction or subsequent habituation to flashing lights that were presented after all subjects had become relatively inactive in a movement recorder. The subjects with hippocampal lesions also lost a conditioned "freezing" response faster than control subjects, although no differences were found in either their initial freezing to the aversive stimulus (air-blast) or in their acquiring the conditioned "freezing" reaction. Furthermore, no differences were found between hippocampectomized and control subjects in acquiring an active avoidance response motivated by air-blast. The composite results of these experiments suggest that "approach" tendencies are relatively strengthened after hippocampal damage, and that "braking" reactions, which may possibly be associated with

aversive or "alarming" stimuli, are relatively weakened.

References

Adey, W. R., Segundo, J. P., & Livingston, R. B. Corticifugal influences on intrinsic brainstem conduction in cat and monkey. J. Neurophysiol., 1957, 20, 1-16.

Clark, C. V. H., & Isaacson, R. L. Effect of bilateral hippocampal ablation on DRL performance. J. comp. physiol. Psychol., 1965, 59, 137-140.

De Groot, J. The rat forebrain in stereotaxic coordinates. Koninkluke Nederlandse Akademie van Wetenschapped, Afd. Neturrkunds. Tweede Reeds, 1959, LII (4), 1-40.

Douglas, R. J., & Isaacson, R. L. Hippocampal lesions and activity. Psychon. Sci., 1964, 1, 187-188.

Ellen, P., & Wilson, A. S. Perseveration in the rat following hippocampal lesions. Exp. Neurol., 1963, 8, 310-317.

Feldman, S. Neurophysiological mechanisms modifying afferent hypothalamo-hippocampal conduction. Exp. Neurol., 1962, 5, 269-291.

Isaacson, R. L. Hippocampal contributions to the mechanisms of behavior. Paper read at Amer. Psychol. Ass., New York, Sept., 1966.

Isaacson, R. L., & Wickelgren, W.O. Hippocampal ablation and passive avoidance. Science, 1962, 138, 1104-1106.

Isaacson, R. L., Douglas, R. J., & Moore, R. Y. The effect of radical hippocampal ablation on acquisition of avoidance responses. J. comp. physiol. Psychol., 1961, 54, 625-628.

Isaacson, R. L., Olton, D. S., Bauer, B., & Swart, P. The effect of training trials on passive avoidance deficits in the hippocampectomized rat. Psychon. Sci., 1966, 5, 419-420.

Isaacson, R. L., Schmaltz, L. W., & Douglas, R. J. The retention of a successive discrimination problem in two maze situations by hippocampectomized and neodecorticate rats. Psychol. Rep., in press.

Jarrard, L. E. Hippocampal ablation and operant behavior in the rat. Psychon. Sci., 1965, 2, 115-116.

Jarrard, L. E., & Isaacson, R. L. Hippocampal ablation in rats: effects of intertrial interval. Nature, 1965, 207, 109-110.

Jarrard, L. E., Isaacson, R. L., & Wickelgren, W. O. Effects of hippocampal ablation and intertrial interval on runway acquisition and extinction. J. comp. physiol. Psychol., 1964, 57, 442-444.

Kaada, B. R., Rasmussen, E. W., & Kveim, O. Effects of hippocampal lesions on maze learning and retention in rats. Exp. Neurol., 1961, 3, 333-355.

Kaada, B. R., Rasmussen, E. W., & Kveim, O. Impaired acquisition of passive avoidance behavior by subcallosal, septal, hypothalamic and insular lesions in rats. J. comp. physiol. Psychol., 1962, 55, 661-670.

Kim, D. Nest building, general activity, and salt preference of rats following hippocampal ablation. J. comp. physiol. Psychol., 1960, 53, 11-16.

Kimble, D. P. The effects of bilateral hippocampal lesions in rats. J. comp. physiol. Psychol., 1963, 56, 273-283.

Kimble, D. P. The effects of bilateral hippocampal lesions in rats. Paper presented at the General Biology Seminar, California Institute of Technology, Jan. 1966.

Kimble, D. P., & Kimble, R. J. Hippocampectomy and response perseveration in the rat. J. comp. physiol. Psychol., 1965, 60, 474-476.

Kimble, D. P., Kirkby, R. J., & Stein, D. G. Response perseveration interpretation of passive avoidance deficits in hippocampectomized rats. J. comp. physiol. Psychol., 1966, 61, 141-143.

Kimura, D. Effects of selective hippocampal damage on avoidance behavior in the rat. Canad. J. Psychol., 1958, 12, 213-217.

Kveim, O., Setekliev, J., & Kaada, B. R. Differential effects of hippocampal lesions on maze and passive avoidance learning in rats. Exp. Neurol., 1964, 9, 59-72.

Leaton, R. N. Exploratory behavior in rats with hippocampal lesions. J. comp. physiol. Psychol., 1965, 59, 325-330.

Leaton, R. N. The effects of hippocampal lesions on reactions to novelty in the rat. Unpublished doctoral dissertation, Yale University, 1963.

McCleary, R. A. Response-modulating functions of the limbic-system: initiation and suppression. In E. Stellar and J. M. Sprague (Eds.) Progress in Physiological Psychology, in press.

McNew, J. J., & Thompson, R. Role of the limbic system in active and passive avoidance conditioning in the rat. J. comp. physiol. Psychol., 1966, 61, 173-180.

Mahut, H., & Cordeau, J. P. Spatial reversal deficits in monkeys with amygdalo-hippocampal ablations. Exp. Neurol., 1963, 7, 426-434.

Milner, B. Amnesia following operation on the temporal lobes. In O. L. Zangwill and C. W. M. Whitty (Eds.), Amnesia. London: Butterworths, in press.

Milner, B. Les troubles de la memoire accompagnant des lesions hippocampiques bilaterales. In P. Passouant (Ed.),

Physiologie de l'hippocampe. Paris: Du centre national de la recherche scientifique, 1962, pp. 257-272.

Mundl, W. J. Technical note: activity of small animals measured with accelerometer. Med. Electron. & Biol. Engin., 1966, 4, 209-212.

Niki, H. The effects of hippocampal ablation on the behavior of the rat. Japan. Psychol. Res., 1962, 4, 139-153.

Niki, H. The effects of hippocampal ablation on the inhibitory control of operant behavior in the rat. Japan. Psychol. Res., 1965, 7, 126-137.

Peretz, E. Extinction of food-reinforced responses in hippocampectomized cats. J. comp. physiol. Psychol., 1965, 60, 182-185.

Rabe, A. Effects of bilateral hippocampal stimulation on discrimination reversal learning in the rat. Paper read at Eastern Psychological Association, 1963.

Raphelson, A. C., Isaacson, R. L., & Douglas, R. G. The effect of distracting stimuli on the runway performance of limbic damaged rats. Psychon. Sci., 1965, 3, 483-484.

Redding, F. K. Neurophysiological studies on the role of the hippocampus in sensory perception in the cat. Unpublished doctoral dissertation, McGill University, 1964.

Roberts, W. W., Dember, W. N., & Brodwick, M. Alternation and exploration in rats with hippocampal lesions. J. comp. physiol. Psychol., 1962, 55, 695-700.

Scheffé, H. The analysis of variance. New York: John Wiley & Sons, 1959.

Schmaltz, L. W., & Isaacson, R.L. The effects of preliminary training conditions upon DRL-20 performance in the hippocampectomized rat. Physiol. Behav., 1966, 1, 175-182.

Snyder, D. R., & Isaacson, R. L. The effects of large and small bilateral hippocampal lesions on two types of passive avoidance responses. Psychol. Rep., 1965, 16, 1277-1290.

Spiegel, T. A., Hostetter, G., & Thomas, G. J. Effects of bilateral lesions in the hippocampus on acquisition of two maze problems. Psychon. Sci., 1966, 6, 205-206.

Stein, D. G., & Kimble, D. P. Effects of hippocampal lesions and posttrial strychnine administration on maze behavior in the rat. J. comp. physiol. Psychol., 1966, 62, 243-249.

Teitelbaum, H. A comparison of the effects of orbitofrontal and hippocampal lesions upon discrimination learning and reversal in the cat. Exp. Neurol., 1964, 9, 452-462.

Teitelbaum, H. A study of hippocampal function in the rat. Unpublished doctoral dissertation, McGill University, 1961.

Teitelbaum, H., & Milner, P. Activity changes following partial hippocampal lesions in rats. J. comp. physiol. Psychol., 1963, 56, 284-289.

Thompson, R., & Langer, S. K. Deficits in position reversal learning following lesions of the limbic system. J. comp. physiol. Psychol., 1963, 56, 987-995.

Webster, D. B., & Voneida, T. J. Learning deficits following hippocampal lesions in split-brain cats. Exp. Neurol., 1964, 10, 170-182.

Wickelgren, W. O., & Isaacson, R. L. Effect of the introduction of an irrelevant stimulus upon runway performance of the hippocampectomized rat. Nature, 1963, 200, 48-50.

Figures and Tables

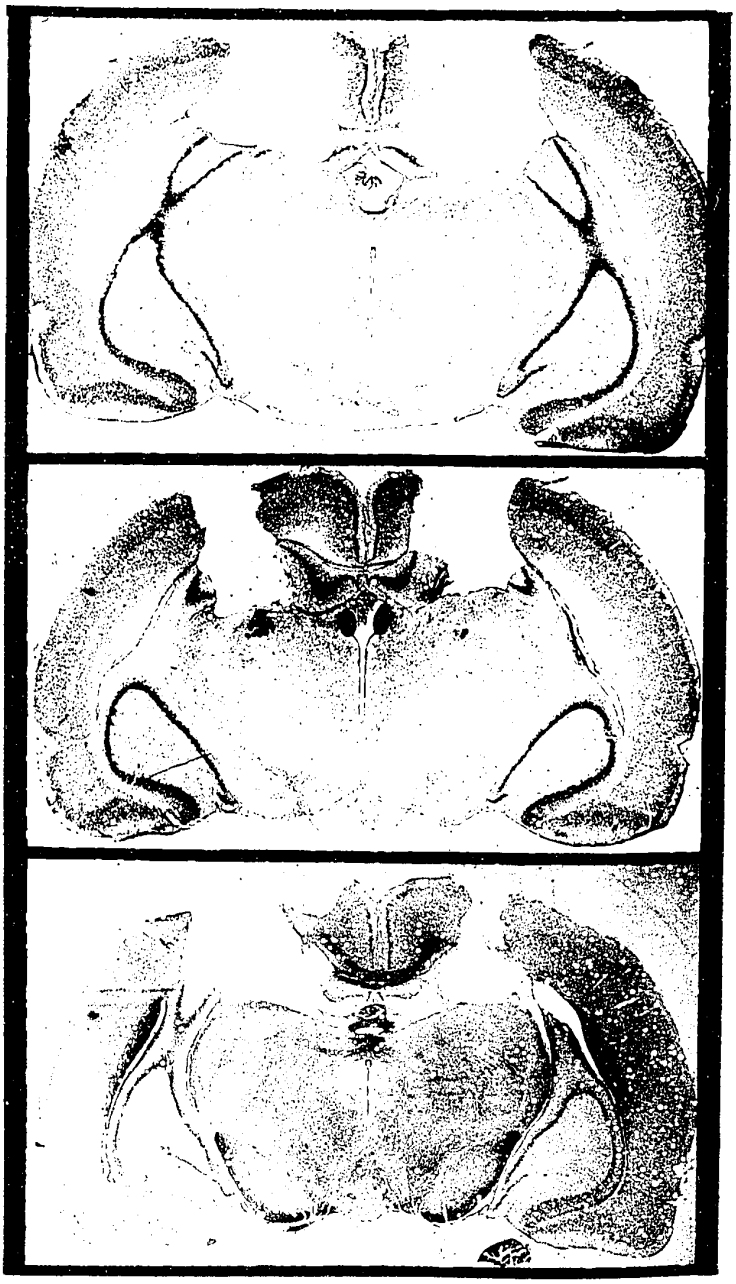

Fig. 1. Coronal sections sliced at 40 μ showing cortical and hippocampal damage in three different Ss.

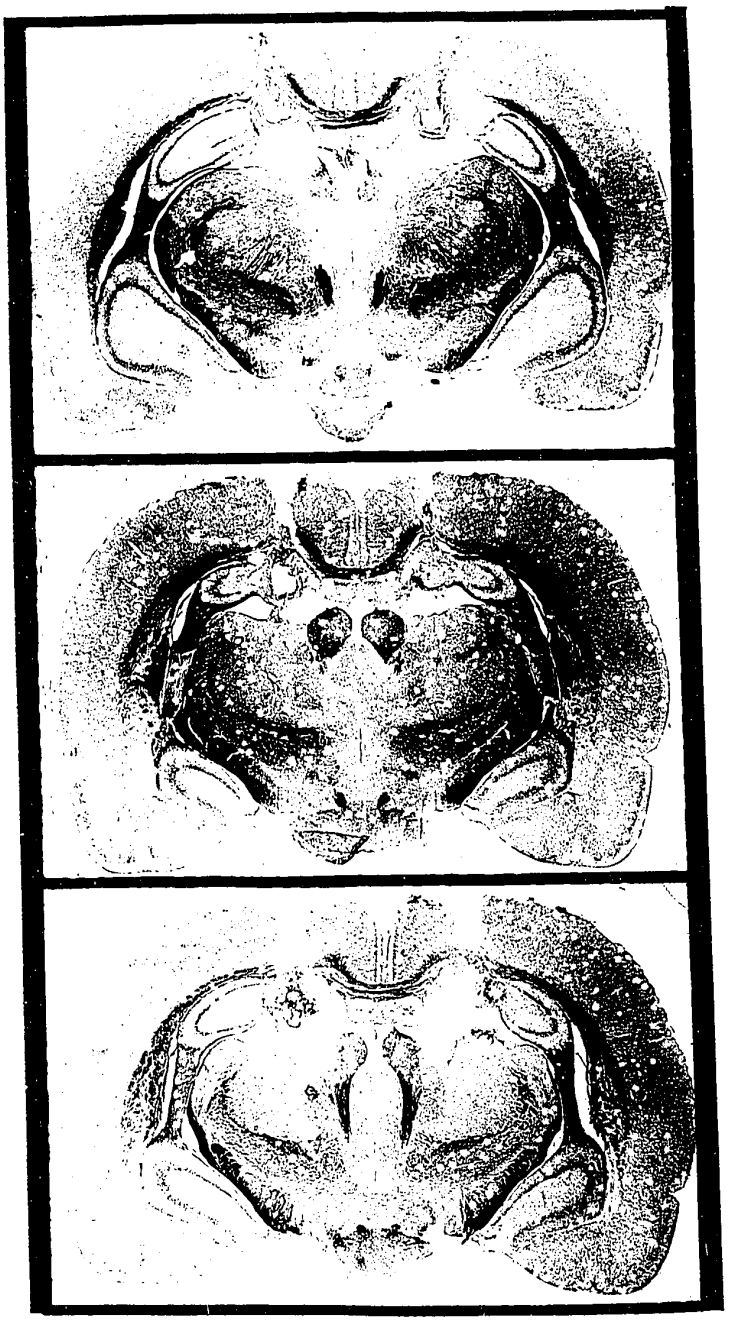

Fig. 2. Coronal sections sliced at 40 μ showing damage produced by electrolytic lesions aimed at the dorsal hippocampus, in three different Ss.

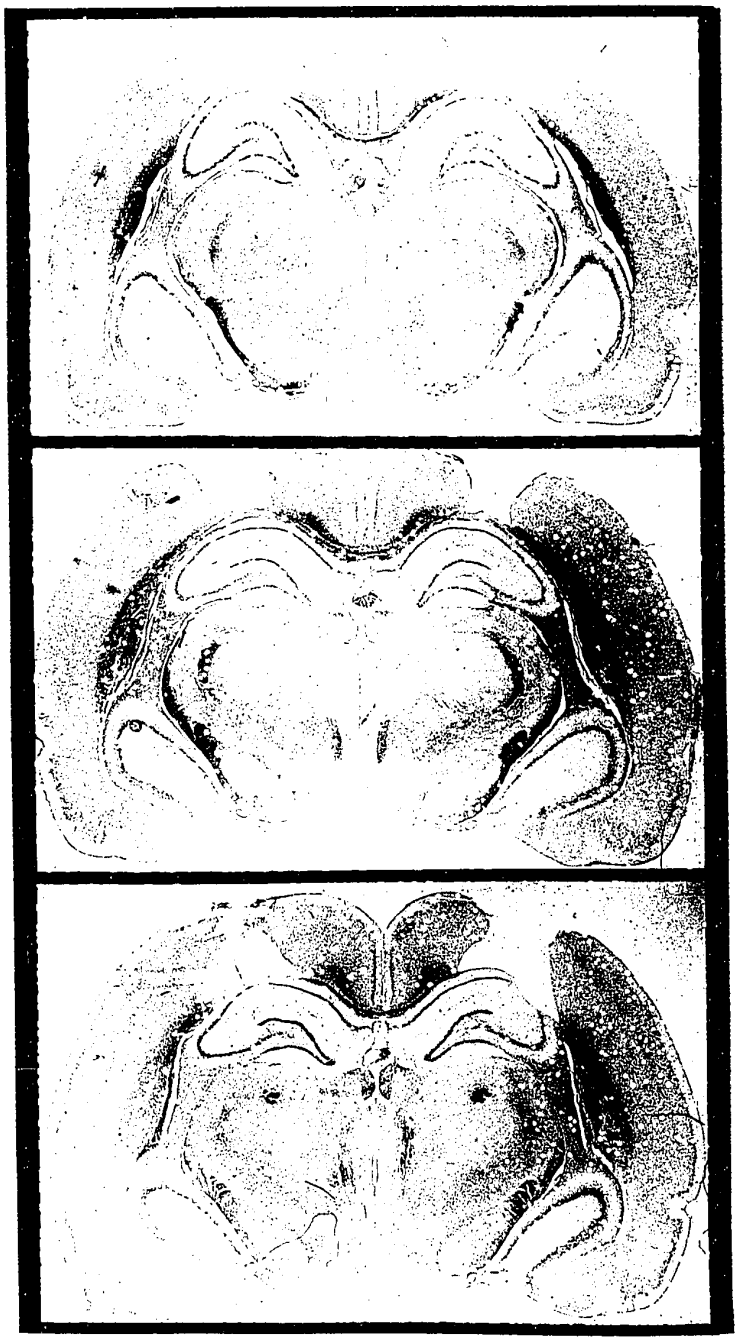

Fig. 3. Coronal sections sliced at 40 μ showing cortical damage in three different Ss.

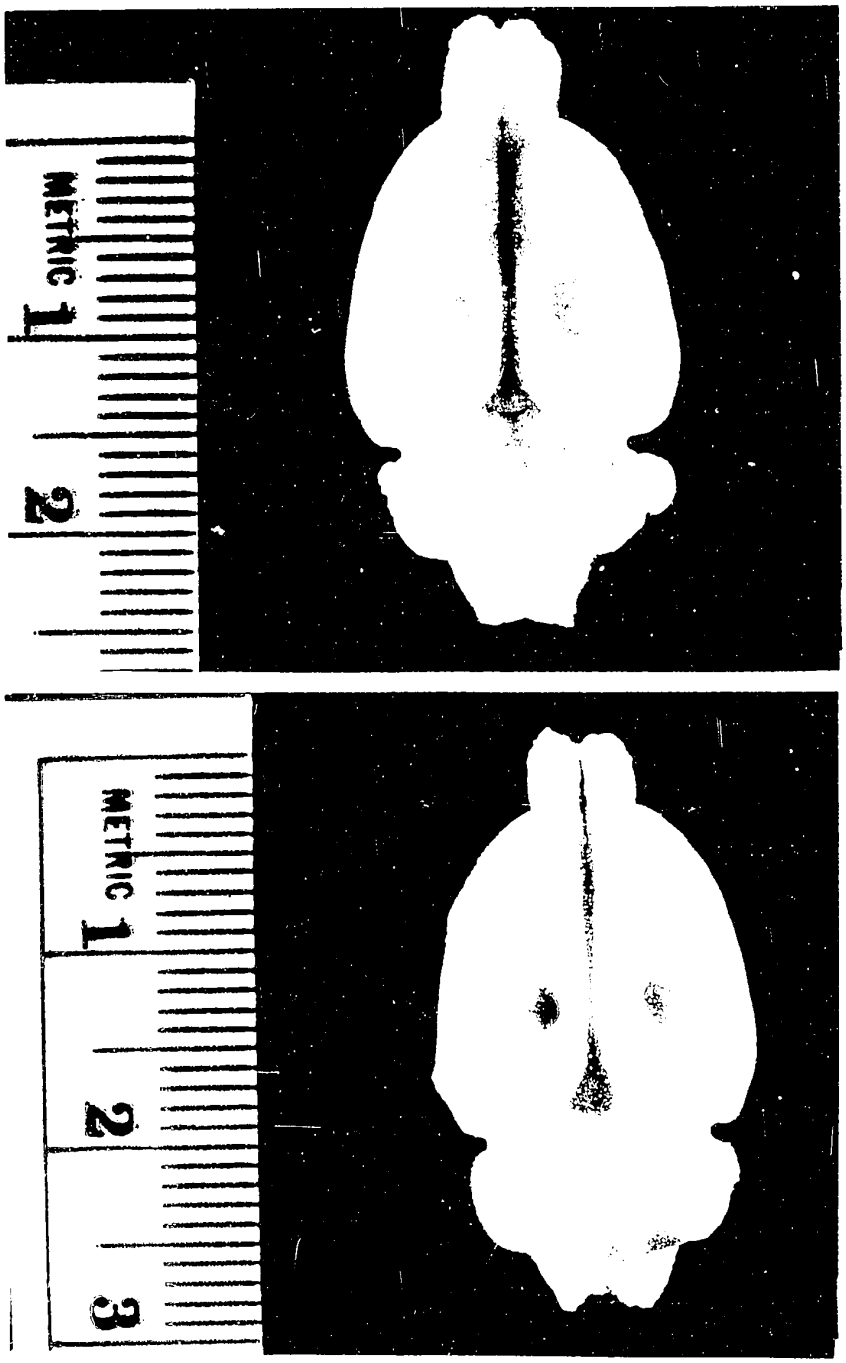

Fig. 4. Dorsal view of a rat brain with a bilateral cortical ablation (above), and one with a combined cortical and hippocampal ablation (below).

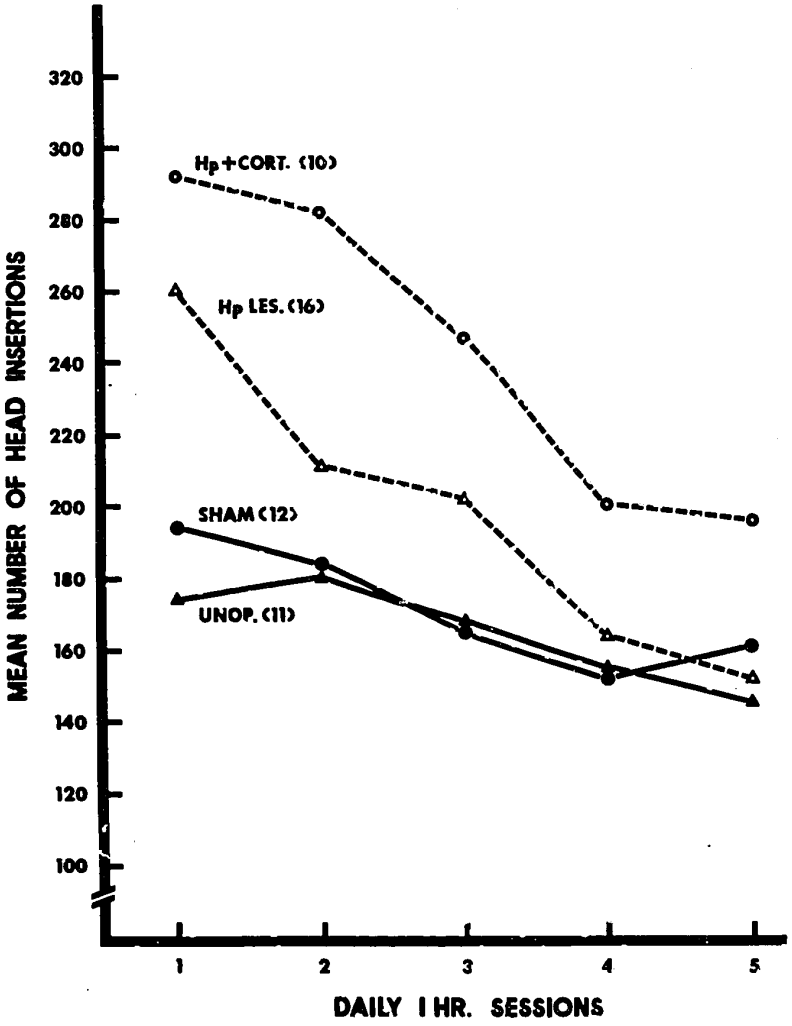

Fig. 5. Activity in exploration apparatus (Hp + Cort.= Ss with combined bilateral hippocampal and cortical ablations; Hp Les.= Ss with bilateral electrolytic lesions in the dorsal hippocampus; Unop.= unoperated Ss; Sham = Ss with electrodes inserted into the hippocampus and then removed).

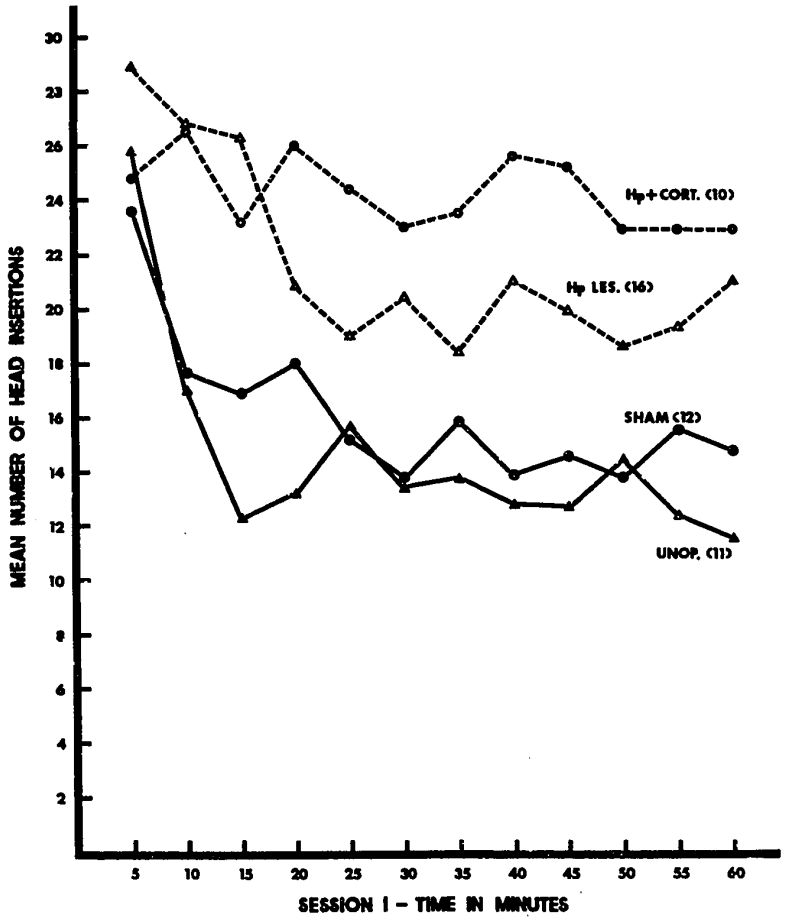

Fig. 6. Activity in exploration apparatus. Number of head insertions were printed out at 5 min. intervals. (Hp + Cort.= Ss with combined bilateral hippocampal and cortical ablations; Hp Les.= Ss with bilateral electrolytic lesions in the dorsal hippocampus; Unop.= unoperated Ss; Sham = Ss with electrodes inserted into the hippocampus and then removed).

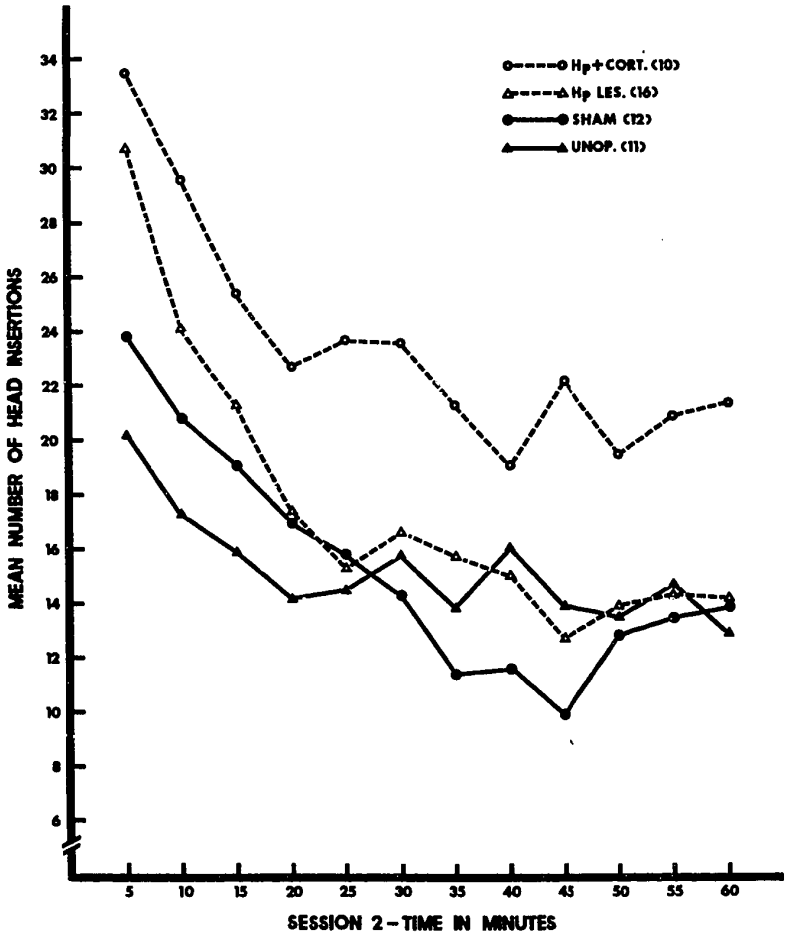

Fig. 7. Activity in exploration apparatus. Number of head insertions were printed out at 5 min. intervals. (Hp + Cort.= Ss with combined bilateral hippocampal and cortical ablations; Hp Les.= Ss with bilateral electrolytic lesions in the dorsal hippocampus; Unop.= unoperated Ss; Sham = Ss with electrodes inserted into the hippocampus and then removed).

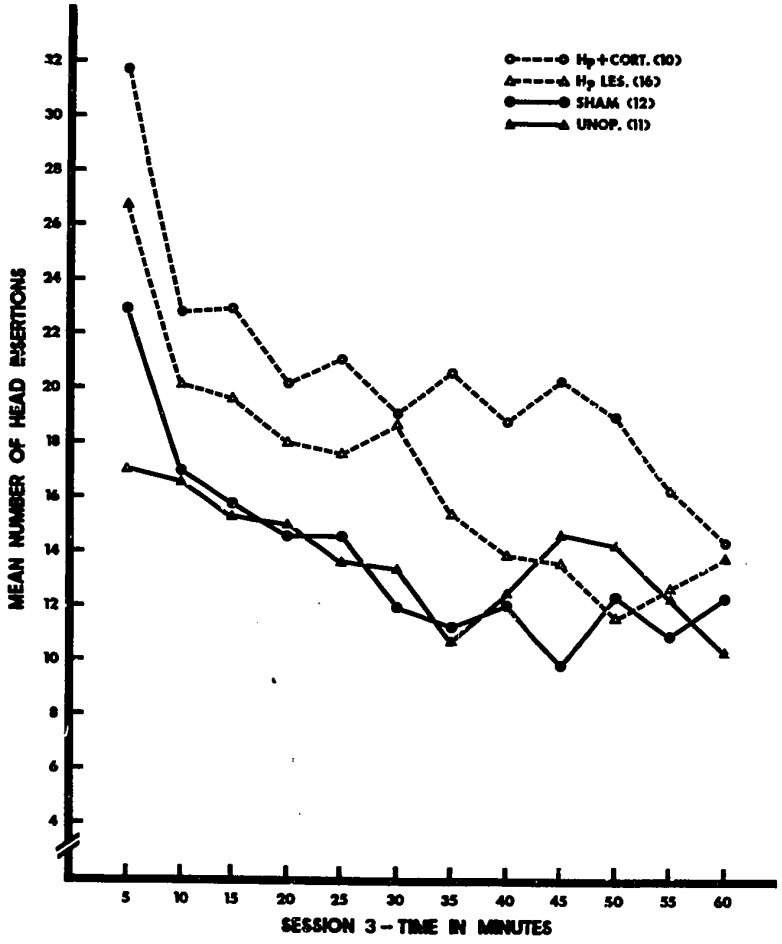

Fig. 8. Activity in exploration apparatus. Number of head insertions were printed out at 5 min. intervals. (Hp + Cort.= Ss with combined bilateral hippocampal and cortical ablations; Hp Les.= Ss with bilateral electrolytic lesions in the dorsal hippocampus; Unop.= unoperated Ss; Sham = Ss with electrodes inserted into the hippocampus and then removed).

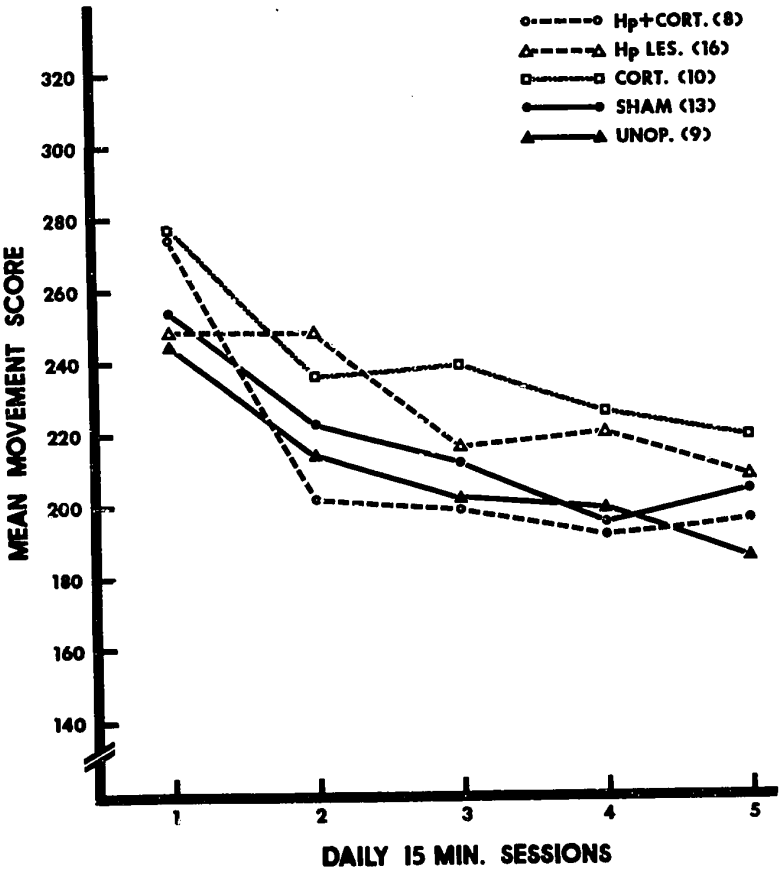

Fig. 9. Activity in movement recorder. (Hp + Cort.= Ss with combined bilateral hippocampal and cortical ablations; Hp Les.= Ss with bilateral electrolytic lesions in the dorsal hippocampus; Cort.= Ss with bilateral cortical ablations; Unop.= unoperated Ss; Sham = Ss with electrodes inserted into the hippocampus and then removed).

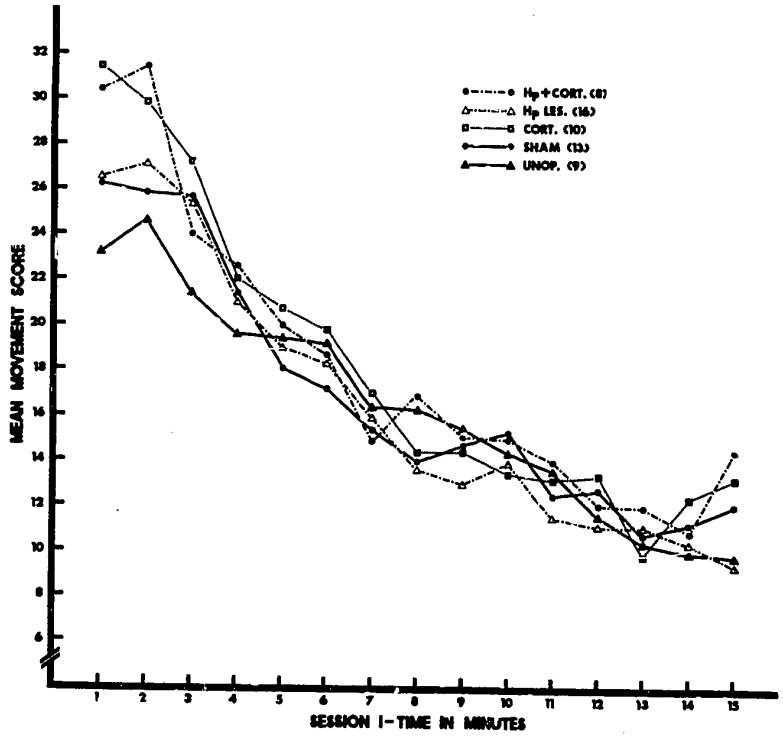

Fig. 10. Activity in movement recorder. Scores printed out at one minute intervals.

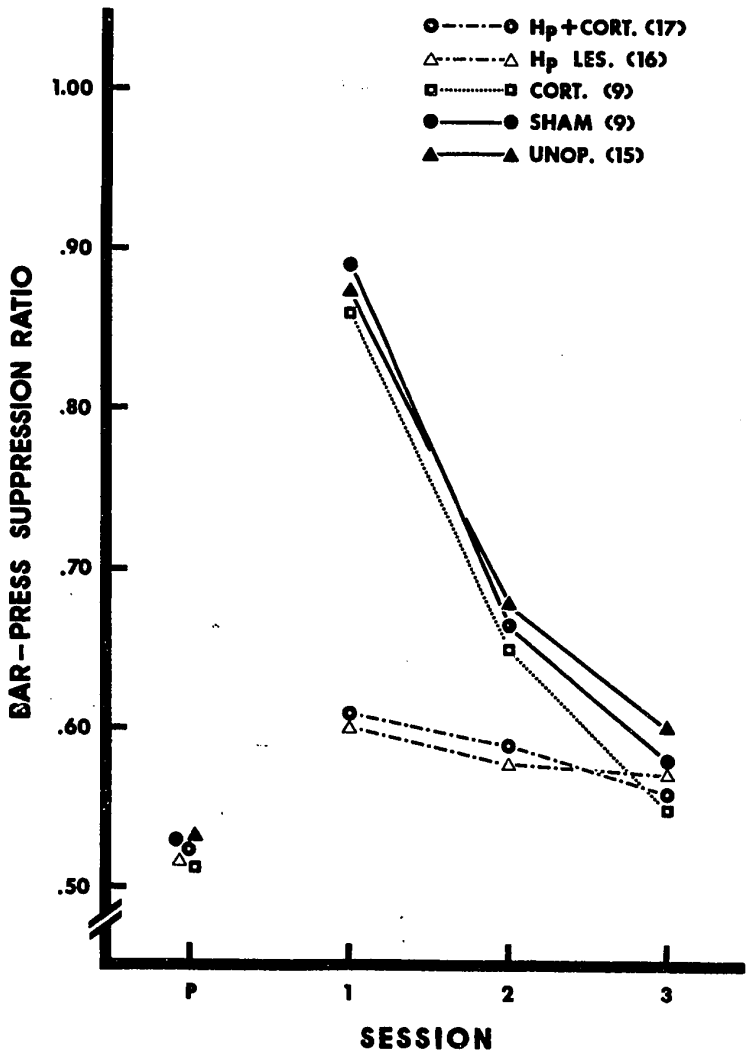

Fig. 11. Reaction to flashing light during food-reinforced bar-press performance. Bar-press suppression ratio = $\frac{A}{A + B}$ where A = number of presses in the minute prior to light onset, and B = number of presses during the first minute of light onset. P = control session.

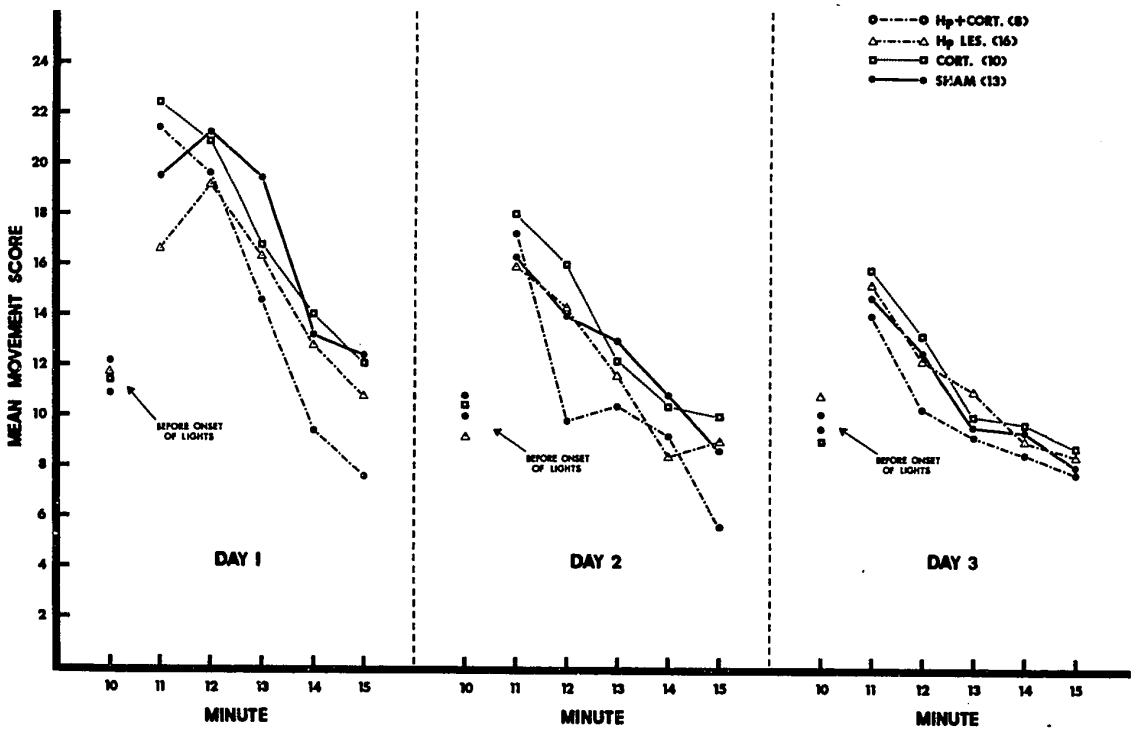

Fig. 12. Reactions to flashing lights in movement recorder. Lights began to flash after Ss were in recorder for 10 minutes.

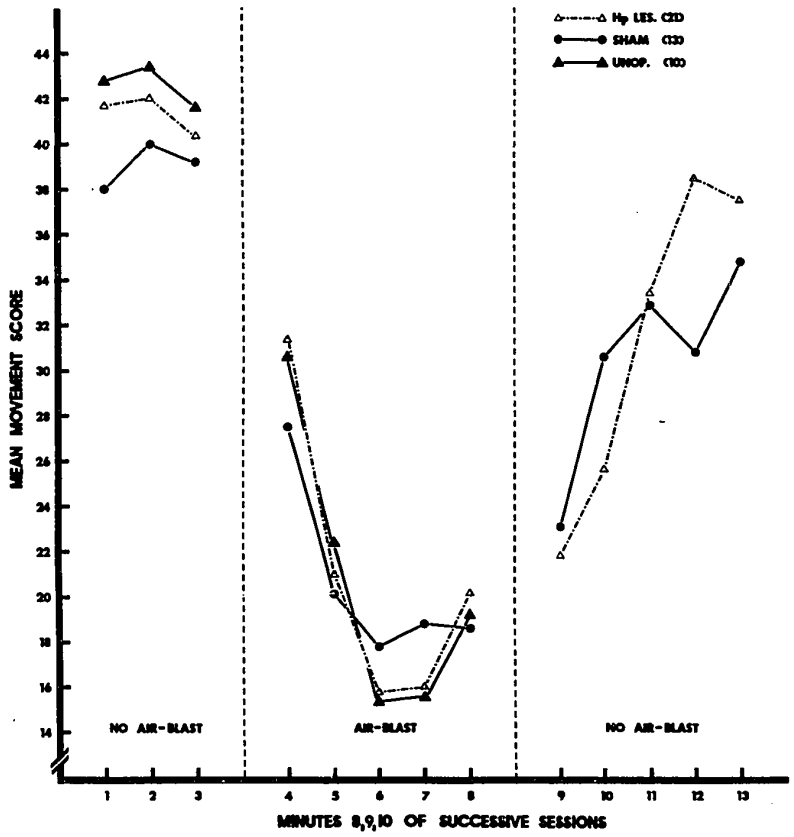

Fig. 13. Development and extinction of reactions to an air-blast. Air-blast was presented on sessions 4-8 after the seventh minute of each session, and the total activity for minutes 8-10 was used as a measure of S's immediate reaction.

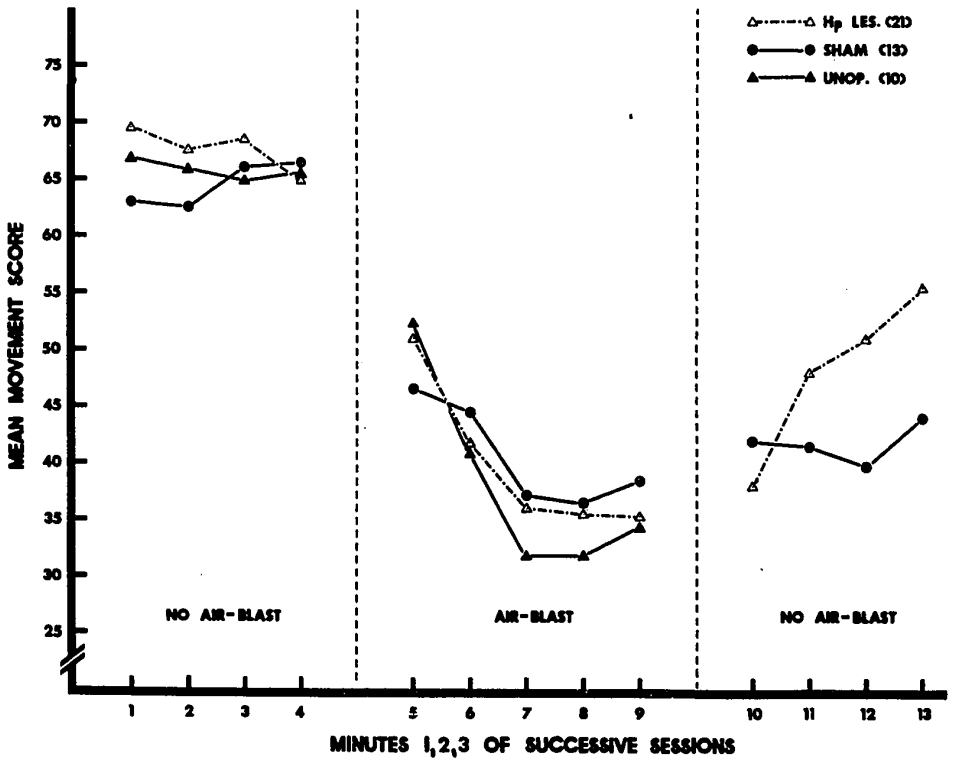

Fig. 14. Development and extinction of a conditioned "freezing" reaction. Air-blast was presented in sessions 4-8 after the seventh minute of each session, and the total activity for minutes 1-3 in sessions that followed an air-blast session was used as a measure of conditioned "freezing."

Table 1

Mean Brain Damage Determined by Number of .5 cm. Squares

Experiment I and II

Group	Hippocampal damage	Cortical damage	Thalamic damage
Hp + Cort.	548.6	284.8	4.6
Hp Les.	311.0	12.6	8.4
Cort.	2.2	327.4	-

Experiment III and IV

Hp Les.	329.3	9.5	12.3

Table 2

Trials to Criterion in Active

Avoidance Conditioning

Group	N	Mean	Range
Hp Les.	21	28.6	4-50
Sham	13	27.2	5-50