FORNIX LESIONS AND RESPONSE TO ENVIRONMENTAL CHANGE

BEHAVIORAL AND ADRENOCORTICAL RESPONSES OF RATS WITH FORNIX LESIONS TO CHANGES IN ENVIRONMENTAL STIMULATION

by

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Abstract

The behavior of animals with hippocampal damage differs from that of normal animals across a variety of behavioral tasks. However, the indices of learning and performance used to assess the effects of hippocampal damage are limited in information content, and are easily subsumed by several current theories of hippocampal function. The approach taken in the present series of experiments was to utilize tasks that consistently result in behavioral deficits in animals with hippocampal damage, but to increase the amount of information. The experiments analyzed the response of rats with total fornix lesions to the transition from acquisition to extinction of a response. Detailed observations of the behavior and measurement of corticosterone levels allowed a more complete picture of the hippocampal deficit to emerge.

Experiment 1 examined acquisition and extinction of an operant lever press response in a standard operant chamber. Fornix lesioned rats made fewer responses during acquisition and had increased resistance to extinction. Detailed analysis revealed many other differences in the behavior of control and lesioned rats. Control rats reacted to the transition to extinction with decreased frequency of bouts of food related behaviors, increased bout durations of all behaviors, changed topography of lever presses from acquisition type presses to biting responses, changed sequential organization of behaviors, and behaviors labelled as emotional. Control rats also responded to the transition with increased plasma corticosterone levels, an increase that was negatively correlated with response burst duration and amount of biting, and positively related to the

maintenance of acquisition responses. Fornix lesioned rats exhibited more random behavioral organization in both acquisition and extinction. Following the transition to extinction, lesioned rats did not exhibit the behavioral flexibility, corticosterone increases, or behavior-corticosterone relationships exhibited by control rats.

Experiment 2 maintained the same task requirements but in a large, enriched environment. Less efficient behavioral organization resulted in lesioned rats again receiving fewer reinforcements during acquisition. Both groups extinguished faster in the large enriched environment than in Experiment 1, but lesioned rats maintained food related behaviors longer than controls. Lesioned rats exhibited only acquisition type responses interspersed with short trips away from the lever and food cup. Controls exhibted two modes of response interspersed with long duration trips away. During trips away, the groups differed in their interactions with objects in the environment in terms of frequency, duration, intensity and temporal and sequential organizations.

Experiment 3 examined exploratory behavior patterns during initial exposure to the experimental environment of Experiment 2. The groups again differed in frequency, quality and organization of their interactions with objects in the environment. Control rat exploratory patterns were similar to those during extinction, but lesioned rat patterns differed.

Experiment 4 examined the response of lesioned and control rats to environmental change in a simple appetitive consummatory task. After being allowed to eat, the rat's consummatory response was blocked

while the cues controlling behavior were maintained. The groups differed in the frequency, duration and organization of their behavior. Controls responded to the change with increased corticosterone and altered behavioral strategies while lesioned rats showed neither.

Experiments 4, 5 and 6 examined alternative explanations of the differences in corticosterone response profiles of control and lesioned rats during acquisition and extinction. These differences appear not to have resulted from 1) differences in conditioning to the sampling procedure, 2) a general attenuation of responsiveness in lesioned rats, or 3) differences in response to the novel aspects of the testing environment.

The detailed analysis of behavior suggests that fornix lesioned rats differ from controls in the organization of behavior and in response to changes in environmental demands. The results are used to address contradictory issues in current theories of hippocampal function.

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Chapter 1

Introduction

During the 1950's, Scoville and coworkers (Scoville, 1954; Scoville and Milner, 1957; Penfield and Milner, 1958) reported profound memory losses in patients who had undergone bilateral medial temporal lobe resections for the relief of psychotic or epileptic disorders. This memory loss was striking not only in degree but in specificity, involving complete and permanent anterograde amnesia, with some retrograde amnesia. Immediate and long term memory, as well as general perceptual and intellectual functioning, were left intact. Although these resections involved varying degrees of damage (i.e. unilateral or bilateral removal of all or portions of the uncus, amygdala, hippocampus and parahippocampal gyrus), the pattern of results indicated that the memory loss was proportional to the degree of bilateral damage to the hippocampal formation.

These findings appeared to be a step toward solving the problem of the physiology of memory. Penfield and Milner (1958) stated that they had "thrown welcome light on the location of some portion at least of the ganglionic record of current experience (p. 496)". Since both immediate and long term memory were intact, the retrieval process still seemed to be functioning after temporal lobe resection. This reasoning led Milner (1970) to conclude that the hippocampal damage interfered with the consolidation of recent or immediate experience into memory.

As Douglas (1967) points out, this conceptualization of recent memory was indistinguishable from the ability to learn. "Each implies an ability to store new material more or less permanently and to recall correctly upon demand. No permanent learning is possible unless there is a capacity for permanent storage (p. 423)". Consequently, many experimenters attempted to study the effects of hippocampal ablation in animals on a variety of learning tasks. Before reviewing the results of these attempts, a brief description of the hippocampal formation, its connections and the possible differences in types of hippocampal damage will be provided.

The hippocampal formation is allocortical tissue located within and axially following, bilaterally around the thalamus, the curvature of the lateral ventricles. It is contiguous with the septum rostrally via the fimbria fornix and terminates in the temporal horn of the lateral ventricles. The actual location varies with species. In primates, neocortical development has forced the hippocampal formation ventrally and laterally such that the entire formation is located in the medial temporal lobes. In lower mammals the dorsal hippocampus, that part located dorsal to the thalamus, is the more prominent. In cross-section perpendicular to this curved longitudinal axis, the hippocampal formation resembles two interlocking U's, one composed of the hippocampal gyrus and subiculum, the other the fascia dentata or dentata gyrus. The subiculum merges with cortical tissue through the presubiculum, parasubiculum and entorhinal area. As you move from the subiculum to the hippocampal gyrus you encounter a characteristic pyramidal cell layer that has been further differentiated into

subfields CA1, CA2,. CA3, and CA4, by Lorente de No (See Blackstad, 1956) on the basis of structure and connections. CA4 is then capped by the dentate gyrus with its equally conspicuous densely packed granule cell layer.

Since the early work of Ramon y Cajal (See Andersen, 1975) the flow of information through the hippocampal formation was considered to be rostral. Perforant path fibers from the entorhinal cortex carry information from all sensory modalities (See MacLean, 1975) and project to the dentate gyrus. The dentate sends axons to regio inferior of the hippocampus proper, regio inferior sends axons rostrally through the fimbria-fornix and collaterals to CA1; and CA1 then sends axons via the alveus to join the regio inferior rostral projections. These rostral projections terminate in the medial and lateral septum or continue via the pre- and post- commisural fornix to lower hypothalamic and midbrain structures (Raisman et al, 1966). Hippocampal afferents also arrive from these structures rostrally and distribute to all portions of the hippocampus (Raisman, 1966). More recent additions to this description include the lamellar organization of the hippocampus along its axial extent (Lomo, 1971), differential distribution of fibers from dorsal and ventral hippocampus (Siegal and Tassoni, 1971; Deadwyler et al, 1975), a change in emphasis on distribution of subfield CA1 output from rostral to subicular targets (Hjorth-Simonsen, 1973; Andersen et al, 1973), and a change in hypothalamic and mammillary afferents from origins in the hippocampus proper to origins in the subiculum (Swanson and Cowan, 1975).

This is only a brief description of the hippocampus and its connections (for more detail see Raisman, 1966; Raisman et al, 1966; Siegal and Tassoni, 1971; Hjorth-Simonsen, 1973; or current reviews by Chronister and White, 1975; Powell and Hines, 1975; Andersen, 1975), but it provides a basis for distinguishing different lesions. Electrolytic or aspiration lesions of the hippocampal formation should disrupt hippocampal function in proportion to the extent of damage (keeping in mind possibly differing functions for different regions). With dorsal lesions, the extent of fimbria fornix damage may be critical. Total fornicotomy not only deafferents and deefferents rostrally, but also partially deafferents the intact subicular projections from CA1 and transects subicular projections to the hypothalamus. Similarly, entorhinal lesions deefferent entorhinally as well as partially deafferent intact rostral projections. The majority of hippocampal lesions (see Douglas, 1967) damage the hippocampal gyrus, the dentate gyrus and to some extent the subiculum. As pointed out by Altman et al, (1973), the actual extent of damage for hippocampal lesions reported in the literature varies from small lesions that leave most of the hippocampus intact to large lesions that destroy not only all the hippocampal formation but result in extensive damage to surrounding structures.

The early studies of animals with hippocampal lesions revealed that the behavior of these animals differed from that of controls both in a wide variety of learning tasks, as well as in a number of situations that did not involve traditional learning paradigms. In appetitive learning tasks animals with hippocampal damage appeared to

have little difficulty learning to traverse a simple runway (Niki, 1962; Jarrard et al, 1964), to press a lever (Schmaltz and Isaacson, 1966) or to learn some forms of simple simultaneous discrimination (Kimble, 1963; Teitelbaum, 1964). On many other aspects of appetitive tasks, hippocampally damaged animals were reported to differ from normal animals. The lesioned animals were slower at extinguishing learned responses when the response was no longer reinforced (Niki, 1962; Jarrard et al, 1964; Raphaelson et al, 1966), they were less efficient at spacing responses on fixed interval and differential reinforcement of low rate operant schedules that call for withholding responses (Jarrard, 1965; Clark and Isaacson, 1965; Haddad and Rabe, 1969) but were superior on fixed ratio operant schedules that call for rapid responding (Rabe and Haddad, 1968). Hippocampally damaged animals were also reported to be slower to learn to navigate complex mazes (Niki, 1962; Kimble, 1963; Jarrard and Lewis 1967), to learn discriminations if the stimuli are presented successively as in go/no go tasks (Niki, 1965; Swanson and Isaacson, 1967) or if the response was conditional (e.g. go right when black, left when white) (Kimble, 1963), and to learn to reverse a discrimination (Teitelbaum, 1964; Kimble and Kimble, 1965; Douglas and Pribram, 1966).

Hippocampal lesions also lead to varied results on aversively motivated learning tasks. These tasks can be loosely classified as active or passive avoidance. In active avoidance the animal actively avoids punishment by making a response (e.g. runs from a dangerous place). Animals with hippocampal lesions were found to be superior at two-way avoidance where the animal must shuttle back and forth between

two compartments that are alternately safe and dangerous (Isaacson et al., 1961; Green et al., 1967) but were found to exhibit either normal performance (Niki, 1962) or deficits (McNew and Thompson, 1966) in one-way avoidance where the safe and dangerous aspects of the compartments remain constant. In passive avoidance a response is punished and learning is evidenced by the animal refraining from engaging in the punished behavior. Hippocampally damaged animals were generally found to exhibit deficits in passive avoidance (Kimura, 1958; Isaacson and Wickelgren, 1962; Kimble, 1963).

In these early studies there were also reports of differences between normal and hippocampally damaged animals in a number of environmental contexts not directly related to learning paradigms. For example, animals with hippocampal damage were reported to be more active in the home cage (Kim, 1960; Jarrard, 1968) and in open fields (Kimble, 1963; Teitelbaum and Milner, 1963; Jarrard, 1968), not to exhibit spontaneous alternations of responses in a T-maze (Roberts et al, 1962) and not to be distracted by novel stimuli when engaged in appetitive tasks (Wickelgren and Isaacson, 1963; Raphaelson et al, 1965).

The studies reported above concerning the behavioral effects of hippocampal damage in appetitive and aversively motivated learning tasks and in response to environmental stimulation are not intended to be exhaustive but representative. They illustrate the type of problems facing early hippocampal theorists, and the set of lesion effects that form the core of what may be characterized as the "hippocampal syndrome". More recently, Black, et al, (1977) in their review of the

literature on avoidance learning and punishment list thirty studies that have examined the response of hippocampally damaged animals in two-way avoidance. These studies are almost without exception, in agreement with the early Isaacson et al (1961) results. Other results are not so consistent with earlier findings. The early studies do not, for example, make distinctions that have since been realized as important, such as, differences in types of passive avoidance (e.g. withholding punished responses that have been preceded by no training or by appetitive or escape training).

Many aspects of this hippocampal syndrome were consistent with a failure of memory consolidation hypothesis. Among these were failure to exhibit spontaneous alternations,difference in open field behavior and deficits in passive avoidance. For example, if an animal is punished for stepping down from a platform or for a consummatory behavior like drinking from a water spout, then a failure of memory consolidation could lead to a "passive avoidance" deficit. A large number of passive avoidance experiments employing intact animals with various experimental treatments to the hippocampus (e.g. stimulation, injections of protein synthesis inhibitors) have successfully disrupted passive avoidance behavior and have been interpreted as having disrupted memory consolidation (see Nakajima, 1975 for a review). However, animals with hippocampal lesions do not exhibit deficits on many of these types of passive avoidance tasks (Nadel et al, 1975; Black, et al, 1977).

More damaging to memory consolidation interpretations were the many reported instances of normal learning in hippocampally damaged

animals. These tasks included intertrial intervals of sufficient duration that the task could not be solved in the time frame of immediate memory and, more importantly, many of the experiments specifically tested for and found long term retention (e.g. Kimble, 1963; Niki, 1962). In addition, a memory consolidation interpretation would appear to have a great deal of difficulty accounting for those instances where animals with hippocampal lesions were superior to normals as in two-way avoidance.

More successful and certainly more enduring accounts of the many deficits following hippocampal damage utilized the concept of inhibition (Douglas and Pribram, 1966; Douglas, 1967; 1972; Kimble, 1968; Isaacson and Kimble, 1972; Altman et al, 1973; Solomon, 1977). The early inhibition theories (Douglas and Pribram, 1966; Douglas, 1967 and Kimble, 1968) postulated that animals with hippocampal damage were unable to inhibit responding to stimuli that signalled non-reinforcement. This process was considered to be synonymous with internal inhibition (Pavlov, 1927) and, though less formally stated with Hull's (1943) concept of reactive inhibition (see Kimble, 1968). These theories as least at a descriptive level appeared to provide a reasonably good acount of the data, predicting as stated by Douglas (1967) "hippocampectomized animals to excell over normals on tasks in which a disruptive inhibitory tendency is present, normal on tasks in which no inhibition is involved, and inferior to normals on tasks demanding an inhibitory tendency (p. 428)". Normal acquisition of simple responses (e.g. running in a runway for food) or of simultaneous discriminations reflect the animals normal response to stimuli

associated with reinforcement. Non-reinforcement in extinction and in tasks with extinction components (reversals, certain schedules, go/no-go discrimination) was assumed to result in a build-up of inhibition which subsequently leads to a cessation of responding. A lack of inhibition in animals with hippocampal damage was seen to account for the over-responding of hippocampals on those tasks. Similarly, exploration in an open field, spontaneous alternation in a T-maze and maze learning, all involve exposure to stimuli without reinforcement and consequently a build-up of inhibition in normal animals. Inhibitory theories would then predict the deficits exhibited by animals with hippocampal lesions on these tasks. To account for the indistractability of hippocampals in ongoing appetitive tasks, inhibitory theories postulated that the distracting stimuli were external inhibitors and further assumed that external inhibitors were mediated through internal inhibition (See Douglas, 1972). In the two-way avoidance task the hippocampal animals were considerd superior in that they did not have the disruptive inhibitory tendency of normals (freezing). The passive avoidance deficit would appear to present a problem for a theory based on lack of responsiveness to non-reinforcement in that delivering an aversive reinforcer for an appetitively motivated response would not constitute non-reinforcement. Recognizing this, Douglas (1972) simply changed the theory from an inability of hippocampals to respond appropriately to stimuli signalling non-reinforcement to include an inability to respond to any alteration in the significance of the stimulus controlling behavior.

Other current inhibitory theories are those of Altman et al (1973) and Solomon (1977). Altman et al (1973), in contrast to earlier theories discussed above, postulated that in animals with hippocampal damage the primary inhibitory deficit was motor not sensory. They suggested that when hippocampal animals are aroused they tend to "act out" or emit learned or unlearned responses that are prepotent in the situation. Sensory problems, such as reduced attentiveness or indistractability, are secondary deficits resulting from this inability to "brake" ongoing behavior. Solomon (1977) postulated just the reverse, the primary deficit was in sensory processing. Specifically, the hippocampal animal is able to respond appropriately to many stimulus situations but is unable to tune out stimuli that are no longer of significance.

In addition to the inhibitory theories listed above, there are a number of theories that attempt to explain the hippocampal syndrome in terms of underlying motivational deficits (Jarrard, 1973; Isaacson and Kimble, 1972; Gray, 1970, in press) or in terms of more cognitive differences in information processing strategies between lesioned and normal animals (Hirsh, 1974; O'Keefe and Nadel, 1974, in press). Isaacson and Kimble (1972) suggest, as do other inhibitory theorists, that hippocampal animals cannot inhibit ongoing activity, but the activity is not limited to specific responses but to higher level hypotheses or response strategies. Runaway activity in this framework reflects an ergotropic (excitatory center) bias that results from lack of hippocampal inhibition. It is suggested that the animals are superfrustrated or aroused by non-reward and this accentuation of

frustration leads to an increase in stereotyped or fixated behavior patterns of the type described by Maier (1964). In contrast, Gray (1970, in press) suggests that animals with hippocampal damage do not exhibit a frustrative response to stimuli that signal non-reward. According to Gray, information about non-reward or punishment is transmitted to the hippocampus from the septum, the hippocampus is then responsible for response decrement in a manner similar to that proposed by Amsel (1962).

In contrast to the theories mentioned above, the information processing theories (Hirsh, 1974 and O'Keefe and Nadel, 1974, in press) suggest that the deficits following hippocampal damage do not result from a failure of inhibitory mechanisms but instead result from differences in properties of the learning systems employed by normal animals and the residual systems relied on by animals with hippocampal damage. The residual systems of hippocampals are able to utilize only S-R strategies which are less flexible than those employed by normal animals. Normal strategies are postulated by O'Keefe and Nadel to involve spatial mapping and by Hirsh to involve contextual memory storage and retrieval.

The data base from which all of these theories were formulated has not been given in detail; to do so would be unduly lengthy. The point is that utilizing basically the same data base an enormous variety of theoretical treatments have emerged, from motor inhibitions on one extreme to complex cognitive theories on the other. As Elmes et al (1975) point out, the number of behavioral deficits following hippocampal damage only slightly exceed the number of theories

attempting to account for them. Elmes et al (1975) suggest that there are two reasons for this "theoretical imbroglio". The first concerns the insensitivity or inappropriateness of many of the behavior measures and the second the widely differing amount and localization of damage to the hippocampus.

With respect to the first of these points, the data obtained with traditional measures have been somewhat less than successful in determining or limiting theory. Kimble (1975) states that "in reviewing the results across a wide vareity of situations it appears that the situations in which hippocampally damaged rats are most markedly different from their controls are those in which environmental contingencies require the cessation of one behavior and/or the initiation of a different behavior (p. 312)". Perhaps the clearest example of the situations to which Kimble is referring, is the environmental shift from continuous reinforcement to non-reinforcement of a response. The behavioral requirements in response to this change appear to be easily specified, the animal simply has to refrain from making the response that is no longer reinforced.

Easily specified task requirements and stress on objective measurements has led researchers to measure resistance to extinction in terms of the number of responses and/or the latency of response until some arbitrary criterion has been reached. Studies that have examined the response of animals with hippocampal damage to extinction following continuous reinforcement are summarized in Table 1. Studies that have involved tasks with extinction components (e.g. reversals or schedules) and extinction following more complex tasks, although both usually

Table 1

CRI -- Extinction Studies Involving Hippocampal and Fornix Lesions

Study	Subject	Lesion	Task	Result	Comment
Brown, Hautmann & Marco, 1969	cats	total hippo.	discrete trial operant	deficit	
Brunner, Hughlock & Gazzara, 1974	rats	dentate granule cells	runway	deficit	
Cohen, 1970	rats	total hippo	runs	deficit	
Coover, Goldman & Levine, 1971	rats	total hippo	free operant	deficit	
Fried, 1972	rats	dorsal, ventral, total, hippo	runway	mixed	dorsals show deficit, total or ventrals showed deficit or facilitation, depending on whether acquisition occurred before or after surgery respectively.
Gaffan, 1972	rats	fornix	runway, operant	mixed	deficit on extinction in runway, but not on nose poke operant
Henke & Bunnell, 1971	rats	total hippo	free operant	deficit	
Isaacson, Nonneman & Schmaltz, 1968	cats	total hippo	runway	mixed	deficit in adults, not in neonates
Jarrard & Isaacson, 1965	rats	total hippo.	runway	deficit	
Jarrard, Isaacson & Wickelgren, 196-	rats	total hippo.	runway	mixed	no deficit with 10 sec ITI, but extinction deficit with 10 min. delay between trials
Jarrard & Lewis, 1967	rats	total hippo.	maze	deficit	
Niki, 1962	rats	mostly dorsal hippo.	runway	deficit	
Niki, 1965	rats	total hippo.	free operant	deficit	
Peretz, 1965	cats	total hippo.	operant	deficit	
Raphelson, Isaacson & Douglas, 1966	rats	total, dorsal	lever, runway	mild deficit	dorsals look like normals, combined data gives deficit
Ross, Grossman & Grossman, 1975	rats	fornix	see for cats	no deficit	Response was conservation level press-shuttle behavior. Fornicals had less acquisition and showed ~50 more responses in extinction but not significant
Schmaltz & Isaacson 1967	rats	total hippo.	free operant	mild def., deficit	Repeated CRI → extinction showing increasing deficit with repeated change
Warburton, 1972	rats	rostral ventral hippo	discrete trial operant	deficit	
Winocur & Mills, 1969	rats	total hippo	runway	deficit	

result in deficits in animals with hippocampal lesions (see Altman et al. 1973 or Hirsh, 1974 for reviews), are not included. Examination of Table 1 reveals that in both rats and cats and for both operant and instrumental responses, there is general agreement that damage to the hippocampal formation results in extinction deficits--the hippocampally damaged animals perseverate or continue to make the no longer reinforced response longer than do controls. Consequently, the extinction deficit must be taken into account in any attempt at theorizing about the function of the hippocampal formation.

Current theories of hippocampal function, however, account for this deficit with surprising ease, partially of course, because the extinction deficit is part of the data base from which the theories were formed , but also as a result of the less informative measures employed. These traditional measures (e.g. number of responses or response latencies until criterion) are, without doubt, useful as a scaling technique or metric for assessing variables that affect associability or performance; they seem less appropriate if one is interested in brain function. The processes that underlie this performance deficit as assessed by traditional measures could, for example, involve sensory, motivational or motor systems, either exclusively or in combination. In fact, as reviewed above, current theories that attempt to account for the deficits following hippocampal damage differentially appeal to deficiencies in each of these. The response perseveration in extinction has been postulated to result from inability to inhibit ongoing behavior at the motor level (Altman et al., 1973), a failure of internal inhibition (Douglas, 1967, 1972;

Kimble, 1968), superfrustration (Isaacson and Kimble, 1972), lack of frustration (Gray, 1970) and reliance on non-spatial or S-R strategies (O'Keefe and Nadel, 1974, in press; Hirsh, 1974). The traditional measures convey little information useful for addressing underlying processes and consequently, the extinction deficit can be easily subsumed by theory, by resorting to speculation (often contradictory) about unmeasured but measurable aspects of the animals behavior.

The Elmes et al (1975) solution to the problem of lack of useful information was to utilize what they considered to be a more sensitive task. An alternative approach was taken in the present series of experiments. This approach was to remain with tasks such as extinction that are central to the "hippocampal syndrome" and consistently result in behavioral deficits in animals with hippocampal damage, but to increase the amount of useful information. Two techniques that increase information (Jensen, 1970) are the addition of physiological dependent variables and the approach taken by ethologists of simultaneous observation and recording of many behavioral variables.

The observational approach has been used successfully by experimenters interested in the behavioral correlates of hippocampal electrical activity (See Vanderwolf et al., 1975, Black, 1975 and Ranck, 1975 for reviews). In rats, hippocampal theta (6-12 HZ rhythmic slow activity) accompanies what Vanderwolf (1971) called voluntary behavior but later classified descriptively as Type 1 which includes head movement, walking, manipulative behaviors and changes in posture. Hippocampal theta does not accompany more automatic behaviors like licking, scratching, face-washing or shivering. These Type 1 behaviors

occur in animals with hippocampal lesions; consequently the motor patterns must originate elsewhere. But, the hippocampus may be involved in the sequencing or organization of these behaviors (See Vanderwolf et al, 1978). Grooming in rats, for example, involves an orderly sequence of behaviors whose units are not accompanied by hippocampal theta and these units are present in animals with hippocampal lesions. The transitions between units (such as postural shifts) are, however, accompanied by theta, and the grooming sequence in animals with hippocampal damage is disorganized (Vanderwolf, et al., 1978). Organizational deficits in animals with hippocampal lesions have also been reported for sexual behavior (Michal, 1973) and hoarding and nest building (Shipley and Kolb, 1977). Shipley and Kolb report that "although these animals have no difficulty performing the discrete motor acts of walking to the objects, picking them up and so on, they do have difficulty in chaining these acts together to perform a unified behavioral sequence (p. 1071)".

Similar relationships between behavior and hippocampal single cell activity have been observed (Ranck, 1973, Feder and Ranck, 1973; Ranck, 1975). Firing patterns were recorded from both theta cells and complex spike cells (these being differentiated on the basis of firing patterns and relationships to hippocampal theta) during general activity and during acquisition and extinction of responses. The theta cells fired in conjunction with the theta related behaviors described previously. Different complex spike cells were found to fire during four different categories of behavior 1) during consummatory behavior or successful behavior associated with consummatory behavior, 2) during

these same behaviors but also during unsuccessful behavior associated with these, 3) during approach and orienting but not during consummatory behavior, and 4) at the end of orienting behaviors or when behaviors changed direction. These specific relationships between behavior and single cell activity led Ranck (1975) to suggest that the hippocampus is involved in sequencing of automatic and nonautomatic behaviors and in altering these patterns in a flexible way.

These behavioral observations show that the hippocampus is active during many components of general activity and suggest that the hippocampus may be involved in the organization of these components both in species typical behavioral sequences as well as in learned tasks. As Bindra (1961) has pointed out, learning and extinction of even simple tasks involves refinement in organization of preexisting behaviors from the general activity matrix of the animal. Bindra suggests that the "change in the performance of any given response brought about by an experimental manipulation can be fully understood only if the effects of that manipulation on the occurrence of the components of general activity are known. A more "molecular" analysis of the response and general activity is indicated (p. 214)".

Examination of the hippocampal extinction literature reveals that this approach has not been employed. For example, in not a single experiment listed in Table 1 was any behavior of the animals recorded other than the specific task requirements. The absence of such data in the hippocampal literature probably reflects the absence of emphasis on such data in the learning literature. In general, although theoretical accounts of acquisition and extinction stress the importance of

competing, (collateral) and emotional behavior (See Amsel, 1962), the occurrence of such behavior is often not observed directly and must be inferred. Wong has recently demonstrated that these behaviors are systematically involved in the acquisition and extinction strategies of normal animals (Wong, 1977; 1978). Since differences in both emotional behavior and in strategies between normal and hippocampally damaged animals are postulated in theories of hippocampal function (for example - Isaacson and Kimble, 1972; Isaacson, 1974; O'Keefe and Nadel, in press, Hirsh, 1974), observational data during learning tasks would appear to be especially useful not only in potentially providing a more accurate characterization of the deficit following hippocampal damage but also in addressing specific issues in theories of hippocampal function.

Similarly, although several theories of hippocampal function postulate increased or decreased arousal in hippocampal animals in comparison to controls (Isaacson, 1974; Gray, 1970; Jarrard, 1973), few experimenters have attempted to examine whether or not the changes in environmental demands result in differences in arousal. One reliable, non-specific index of arousal is an increase in plasma corticosterone levels (Levine et al, 1972; Houser and Pare, 1974; Hennessy et al, 1977a; Hennessy et al, 1977b). Recently it has been demonstrated by Levine and coworkers (Coover et al, 1971a; Levine et al, 1972; Goldman et al, 1973; Davis et al, 1976) that in normal animals, the corticosterone response occurs rapidly when reinforcement contingencies for well established behaviors are changed, and that the response can be bidirectional. Serum corticosterone decreased when rats were

switched to a higher rate of reinforcement and increased when they were switched to a lower rate of reinforcement. These changes were shown to reflect a violation of the rats expectation rather than a change in density of reinforcement. The corticosterone response of hippocampal animals to environmental change could then directly address the issue of whether hippocampal animals show increased arousal (Isaacson, 1974), decreased arousal (Gray, 1970), or normal arousal (Altman et al. 1973' O'Keefe and Nadel, in press) as well as whether or not hippocampal animals fail to develop expectations as stated by Hirsh (1974).

The second reason suggested by Elmes et al (1975) to account for the current "theoretical imbroglio" was comparison of results from studies employing hippocampal damage of widely differing amounts and localization. Recent anatomical and electrophysiological studies suggest differential distribution of output along the axial extent of the hippocampus (Siegal and Tassoni, 1971; Siegal and Flynn, 1968), differential distribution of output from the major hippocampal subfields (Anderson et al, 1973; Hjorth-Simonsen, 1973) and possible differential field distribution depending on dorsal-ventral location (Deadwyler et al, 1975). As Jarrard (1976) points out, the assumption that the hippocampal complex functions as a unit has led to a general disregard for such factors. For, example, hippocampal lesions and fornix transections are often used interchangeably (See O'Keefe and Nadel, in press or Gaffen, 1973). Behavioral studies that have examined the effects of selective disruption of hippocampal fields or projections (Van Hoesen et al, 1972, Myhrer, 1975; Jarrard, 1976; Ross and Grossman, 1975; Ross et al 1975) have reported disassociation on

many of the behavioral tasks that constitute the total hippocampal syndrome. On tasks referred to by Kimble (1975) as resulting in the most marked difference in the behavior between hippocampals and normals, and specifically the transition from acquisition to extinction the results are unclear. For example, both deficits and no deficits in extinction have been reported in animals with total fornix transection (Gaffan, 1972, Ross et al, 1975). Normal extinction behavior following fornicotomy occurred in tasks that differed considerably from those usually employed by other researchers. In the present studies total fornix transections are used, both to address this disparity in the literature and to provide baseline data for further, more discrete lesions.

Chapter 2

Effects of total fornix lesions on the acquisition and extinction of a lever press response in a standard operant chamber

Experiment I

Introduction

While there are numerous reports in the literature showing that hippocampal lesions result in increased resistance to extinction following continuous reinforcement of an operant or instrumental response, only two experiments on fornical lesions have been reported and no differences (Ross, Grossman, Grossman, 1975) between control and lesioned animals or mixed results (Gaffan, 1972) were reported (see Table 1). One explanation for these differences might be in terms of type of lesion. Before one can conclude, however, that these differences are related to the type of lesion, one must rule out the possibility that they are related to other factors. For example, in the tasks where no deficits were found Gaffan and Ross _et al_. employed somewhat atypical operant responses - poking the nose into a hole in the former case and shuttling back and forth between two locations and pressing a lever in the latter case. Hippocampal lesion experiments typically employed running in a straight alley or a manipulative operant response such as lever pressing. The present experiment examined the effects of fornix lesions on the performance and extinction of an operantly conditioned lever press response as a first step in determining whether there is a difference in extinction between

the effects of fornical and hippocampal lesions. A deficit on lever press extinction for fornix lesioned rats would suggest that differences in the literature reflect procedural differences and not differences in the effects of different types of hippocampal damage.

In the present experiment direct, detailed and systematic observations of the actual behavior patterns displayed by the animals were made in addition to recording automatically the frequency of operant responses. As pointed out in the introduction, a detailed behavioral analysis could provide a more accurate characterization of the behavioral deficit following hippocampal damage and such observations of behavior would be especially useful in evaluating theories of hippocampal function. For example, frustration during extinction is considered to be the unconditioned response to the nonoccurrence of anticipated reinforcement and, in normal animals, is considered to be aversive (Adelman and Maatsch, 1956) and to be accompanied by increased corticosterone levels (Coover et al., 1971a) and increased displacement and emotional responses (Falk, 1972; McFarland, 1966). Gray (1970) has proposed that hippocampal damage results in deficits in the development of conditioned frustration responses. In contrast, Isaacson (1974) has proposed that hippocampal damage increases an animal's susceptibility to frustration and that such increased frustration leads to the development of stereotyped perseverative responding as described by Maier (1964). Data on frustration related behaviours (e.g. corticosterone response, displacement and agressive behavior) and on the stereotypy of sequential behavior patterns should, then, help decide which of these

views, if either, is correct. Similarly, a detailed behavioral analysis might provide insight into theories of hippocampal function that involve inhibition of responding (Douglas, 1972; Altman, Brunner and Bayer, 1973) or information processing (O'Keefe and Nadel, 1974; in press; Hirsh, 1974).

Experiment 1, therefore, examined the effects of lesions of the fornix on the performance and extinction of an operantly conditioned lever-press response. The traditional measure of number of lever presses was supplemented by concomitant measurement of corticosterone levels and by a detailed analysis of the animals behavior.

Method

Subjects:

The subjects were twenty-six naive, male hooded rats of the Long-Evans strain obtained from the McMaster colony. At the time of surgery the rats weighed 200-250 g. Thirteen rats received complete transection of the fornix[1] and thirteen rats served as operated controls. Data for two lesioned rats were discarded because fornical damage was unilateral, and for two control rats because fornical damage occurred. As a result, there were eleven rats in each group. The experiment was carried out in two replications. There were five experimental and three control rats in the first instance; there were six experimental and eight control rats in the second. There was one

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[1]The fornical lesions involve damage to the dorsal and medial fornix, anterior extensions of the fimbria, and to the ventral hippocampal commissure. There is not complete agreement as to the terminology that should be employed to label this region. I shall refer to it as the fornix.

difference between the two experimental series. In the first, the rats were housed in individual cages in a free access colony room with a 14-10 hour light-dark cycle following surgery. In the second, the rats were housed in individual cages in a restricted access colony room with a 12-12 hour light-dark cycle following surgery. This change in housing conditions was made in order to reduce the effects of uncontrolled environmental changes on corticosterone levels (Seggie, Shaw, Uhlir and Brown, 1974). All rats were handled and weighed daily.

Surgery

Surgery was performed using sodium pentobarbital anesthesia (60 mg/kg.). Lesions were made using a specially designed knife which allowed a lateral approach to the fornix. The knife, which was permanently mounted on a sterotaxic tower, consisted of two juxtaposed stainless steel L-shaped blades. The blades were triangular in cross-section, the base of the upper blade was .6 mm across and its height was .5 mm; the base of the lower blade was .6 mm and and its height .8 mm. Each blade was 20 mm long, but when the knife was in a closed position only the distal 8 mm of each blade made contact. This procedure minimized the amount of cortical damage. A small hole was made in the side of the skull at the following coordinates: 1.5 mm posterior to bregma and 3.9 mm ventral to the surface of the skull. The open knife was then inserted into the brain laterally for a distance of 11 mm from the point at which the knife touched the dura. For the fornix lesioned rats the knife was closed for 30 seconds, opened and removed; for the operated controls the procedure was identical except that the knife remained open in position for the 30

second period. Prior to surgery .05 cc of atropine sulfate (concentration .6 mg/ml) was given to minimize respiratory complications, and following surgery .2 cc Strepenalean (MTC Pharmaceuticals, Hamilton, Canada) suspension was given to prevent infection. All animals were given a two week recovery period during which time food and water were available ad libitum.

Histology

At the conclusion of the experiment, the rats were sacrificed, the brains perfused, embedded in gelatin, frozen and were cut in 40 micron coronal sections. Every second slice throughout the damaged area was saved and fiber stained with hematoxylin using a modified Weil procedure (Wolf, 1971).

Apparatus

Training was carried out in a standard operant chamber measuring 21 x 28 x 40 cm with a grid floor. The walls of the chamber were made of transparent plastic. The chamber was equipped with a food cup centered on one wall 9 cm above the grid and a bar press lever located at the same level and 9 cm to the left of the food cup. 45 mg Noyes food pellets served as the reinforcement.

The chamber was located in a sound attenuated room under constant lighting and 70 db white noise. A Sony Viewfinder video camera provided constant monitoring of subject behaviour. Selected sessions were recorded using a Sony AV-3600 Videorecorder. BRS-Foringer logic circuitry located in an adjacent room was used to record data and deliver reinforcements.

Procedure

Post-operative recovery: During the third postoperative week all rats were reduced to 75% of their projected ad lib weight and maintained at this level throughout the experiment. In order to determine projected ad lib weights, additional groups of rats with fornical lesions and operated controls were maintained on ad lib feeding and their weights recorded daily. Curves based on these weights were employed to estimate the projected weights of deprived rats.

Conditioning: Before each session the rat was removed from the home cage, placed in a transport box, weighed and then carried to the experimental apparatus. The rats were first shaped to bar press by reinforcing successive approximations of the desired response. They were allowed to make 50 reinforced bar press responses on a continuous reinforcement schedule (CRF). For the following ten days the rats were given daily 20 minutes sessions of acquisition training on a CRF schedule. On day 11, after 5 reinforced responses the rats were switched to extinction; the feeder mechanism continued to operate but did not deliver food. The rats remained on extinction for 5 daily 20 minute sessions. All training was carried out between the hours of 1500 and 2100 hours. Times of each daily session remained constant for each animal; equal numbers of fornicals and controls were run at a given time.

Recording: Videotape recordings were made of behaviour on day 9 of acquisition and day 1 of extinction. The behaviour of the rats was classified in terms of the animal's movements and the outcomes of these movements. The following responses were considered:

1. pressing the lever - activation of the lever by any means
2. biting the lever - lever activation while biting
3. food cup check - approaching the food-cup and moving the head over it or into it
4. grooming
5. rearing
6. nose poke - placing the nose in a hole in the wall of the apparatus
7. trips away from and to the food cup and bar press area
8. jumping

Certain behaviours which one might have expected to appear on this list were omitted for the following reasons. Eating was not analyzed since it occurred only in acquisition and the primary interest was in the comparison between acquisition and extinction. Immobility was omitted because it occurred very rarely. Walking and running were omitted because they usually occurred in conjunction with other behaviours.

In addition to dealing with individual responses, bouts of responding were treated as a unit. A bout of responding was defined as a series of uninterrupted responses of a given type. Each bout began when the animal switched from another response to the response of concern and terminated when the animal switched responses again. The number of bouts of a given response (which is equivalent to the number of transitions from that response to or from others) was recorded. In addition, the length of each bout was recorded. For some responses bout length was measured by the number of responses in the bout and in

others by temporal duration. The measure employed in each case depended on the ease with which discrete responses could be isolated.

Stereotypy of the behaviour was analyzed using information analyses (Attneave, 1959). The information analyses allow one to estimate mathematically the amount of information in a sequence of events. To describe behaviour in a situation as stereotyped implies that if one were to categorize all the behaviours in that situation and record their sequence of occurrence, then particular behaviours or particular sequences would be highly probable or predictable. To the extent that events are predictable they convey little information in the sense of reducing uncertainty. In the present experiment the behavioural sequence was recorded with bouts of particular behaviours as the events, and first and second order estimates of information content of the sequence were calculated. First order analyses give an estimate of the predictability of the behaviour based on the relative probabilities of the behaviours themselves. Second order analyses give an estimate of the predictability of a response given that another response has occurred. Stereotypy or predictability of behaviour is reflected in low values of information content.

Videotape data for one lesioned rat was incomplete and was not obtained for another, due to technical difficulties.

Blood sampling and corticosterone assays

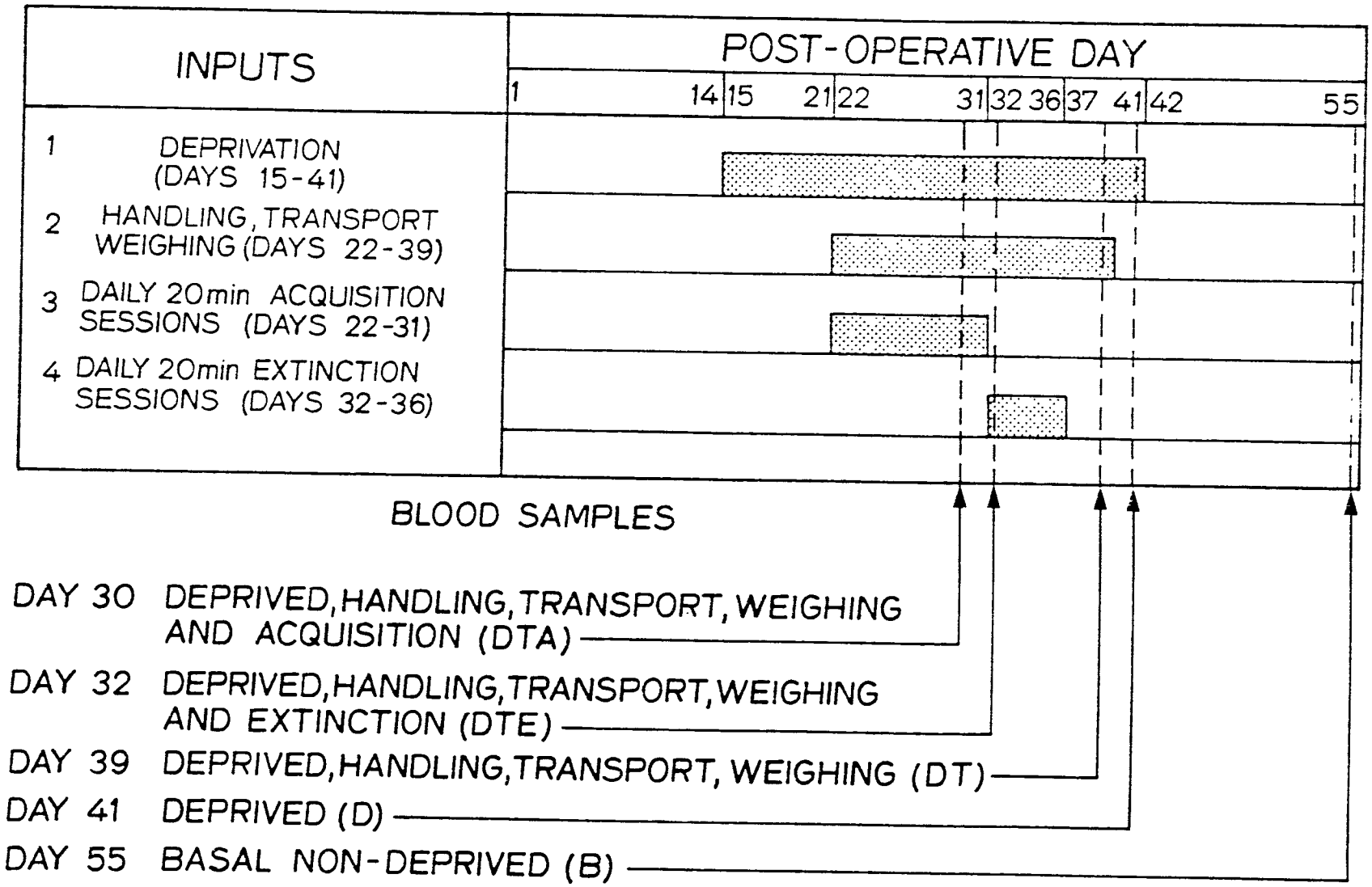
To obtain blood samples, rats were placed in a restraint box, the tail nicked, and approximately 100 microliters of blood collected in heparinized capillary tubes. The sampling procedure took less than two minutes which was brief enough to prevent a rise in corticosterone

from the sampling procedure to affect the assay (Davidson, Jones & Levine, 1968). The blood was centrifuged immediately and the extracted plasma frozen until assayed. Corticosterone levels were measured by a competitive protein binding method using a modified version of the procedure described by Murphy (1967). The serum was treated with ethanol and the precipitated protein removed by centrifuging. The supernatant was transferred to a clean tube, evaporated to dryness and the assay performed on the residue. The corticosterone was made to compete with radioactive cortisol for the transcortin binding sites. The transcortin bound protein was separated from the free fraction using dextran treated charcoal. The radioactivity of the bound fraction was measured and the amount of corticosterone obtained from a standard curve. Each assay required 20 microliters of serum and was performed in duplicate by Dr. T. Sivakumaran at Henderson General Hospital, Hamilton, Ontario, who had no knowledge of experimental status of individual rats from which the samples were obtained.

Five blood samples from each rat were taken as illustrated in Figure 1. As the figure indicates all samples were taken at least three weeks post-operatively. This delay allows full recovery from the temporary disruptive effects in diurnal rhythms attributed to the fornical lesion (Lengvari & Halasz, 1973). In order to assess the effect of the transition from continuous reinforcement to extinction, blood samples were taken immediately following the ninth acquisition session (sample 1: DTA) and immediately following the first extinction session (sample 2: DTE).

Figure 1

Time course for stimulus inputs and blood samples. Shaded bars indicate days that stimulus inputs were present; vertical lines indicate inputs that were present for each blood sample. Rats in the first replication did not receive the last two samples.


INPUTS
POST-OPERATIVE DAY
1
14
15
21
22
31
32
36
37
41
42
55
1 DEPRIVATION (DAYS 15-41)
2 HANDLING, TRANSPORT WEIGHING (DAYS 22-39)
3 DAILY 20min ACQUISITION SESSIONS (DAYS 22-31)
4 DAILY 20min EXTINCTION SESSIONS (DAYS 32-36)
BLOOD SAMPLES
DAY 30 DEPRIVED, HANDLING, TRANSPORT, WEIGHING AND ACQUISITION (DTA)
DAY 32 DEPRIVED, HANDLING, TRANSPORT, WEIGHING AND EXTINCTION (DTE)
DAY 39 DEPRIVED, HANDLING, TRANSPORT, WEIGHING (DT)
DAY 41 DEPRIVED (D)
DAY 55 BASAL NON-DEPRIVED (B)

Experimental sessions occurred between 1500 and 2100 hours. Since diurnal levels vary during this time (Wilson & Critchlow, 1973/74) all experimental session and blood sampling times remained constant for individual animals for the five samples taken; also, these times were counterbalanced across lesioned and control groups.

In addition to diurnal fluctuations, other potential influences on corticosterone levels were present during the experiment. The rats were maintained on a chronic food deprivation schedule and prior to each experimental session the rats were removed by hand from the home cage, weighed and transported to the experimental situation. Three additional blood samples on each rat were obtained to assess the contribution of these variables. The first sample was collected three days after the last extinction session. The deprived rats were handled, transported, weighed, returned to the home cage and the samples taken 20 min later (sample 3: DT)[2]. The second sample was taken five days after the last extinction session in order to assess the effects of deprivation. The deprived rats were removed from the home cage and a sample was obtained immediately (sample 4: D). The

[2]The corticosterone responses to the experimental manipulations not only are diverging from the elevated baseline resulting from chronic deprivation (Sakellaris & Vernikos-Danellis, 1974) but also coincide with the rise in corticosterone resulting from handling and transport to a new experimental environment. The time course for the corticosterone response may vary with intensity and type of stressor (Ader & Friedman, 1968). The blood samples were taken 20 minutes after initiation of stimulation (at the end of the 20 minute experimental sessions or 20 minutes after handling and transport). This time should be appropriate to register both the effects of the initial handling and transport and the cumulative effects of the 20 minute sessions. It is, of course, possible that the fornix lesions may change the time course of the corticosterone response.

rats were returned to ad lib feeding and two weeks later a non-deprived baseline sample was taken; the rats were removed from the home cage and the blood sampled immediately (sample 5: B).

Results

Histology:

Figure 2a presents an example of a fornical lesion, and Figure 2b an example of an operated control. All eleven of the lesioned rats received

total transections of the fornix. None of the eleven operated controls had any fornical damage. Extra-fornical damage for the eleven animals with fornix lesions included partial damage to stria medullaris in four, complete damage to stria medullaris in two, partial damage to stria terminalis in six, complete damage to stria terminalis in three, partial damage to the cingulum in six and slight septal damage in one rat. Extra fornical damage to operated controls consisted of partial damage to stria medullaris in two animals. Because of the design of the knife, cortical damage in all animals was slight and unilateral. There were no obvious correlations between behavioural effects and extra-fornical damage. (See Appendix 1 for detailed evaluation).

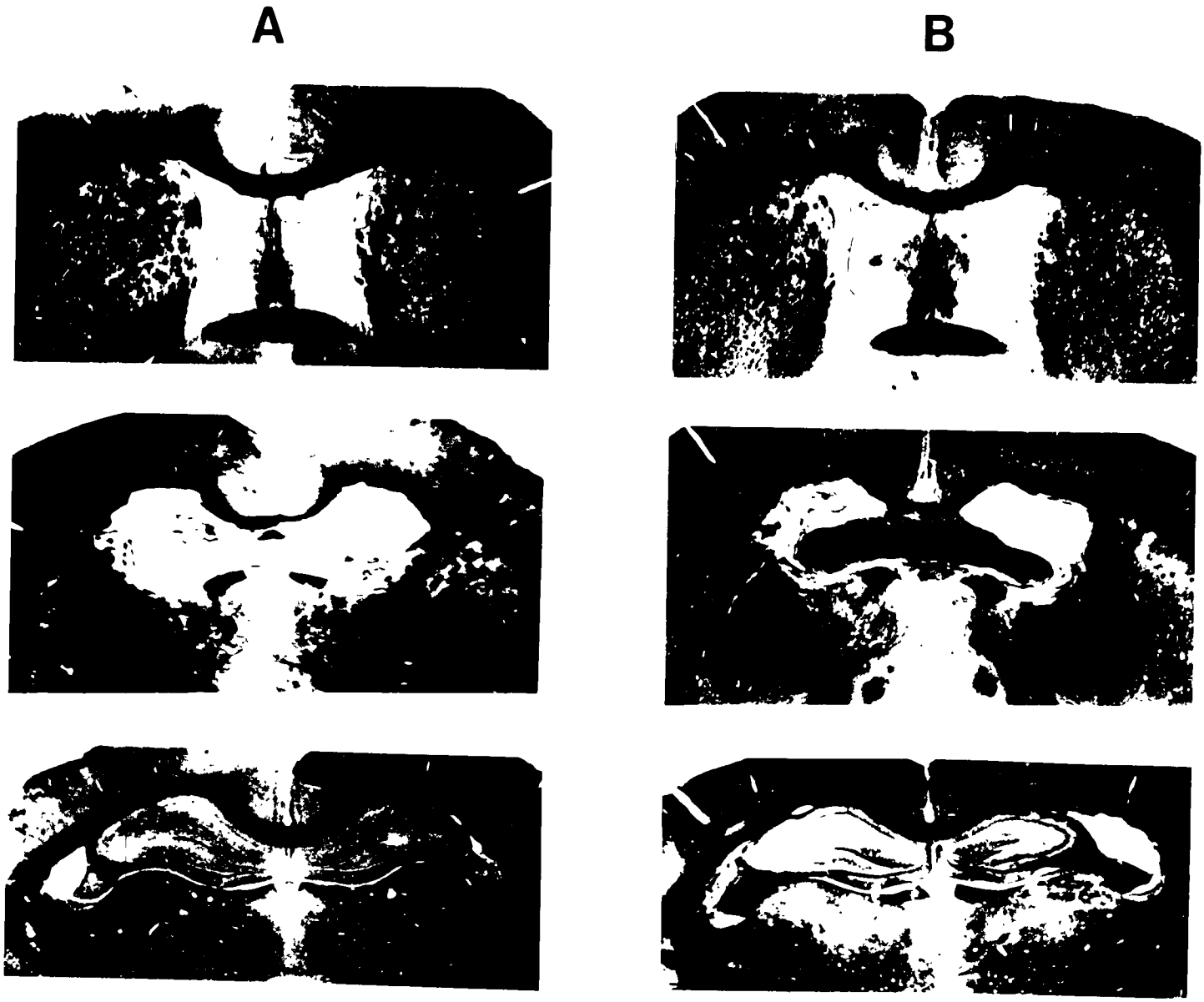
Behavioural Data:

Rate of lever pressing, the traditional measure of learning and extinction, will be discussed first. Then, more detailed data will be presented on what are considered to be the three major response categories - lever pressing, food cup checks and trips away. The relative frquency and duration of each response category as well as

Figure 2

A. Frontal sections (modified Weil stain for myelinated fibers) from brain of a fornix lesioned rat showing the septal area anterior to the lesion (top); the area of maximal lesion size (middle); the hippocampal area posterior to the lesion (bottom). Notice the lightly stained fimbria fibers in bottom section indicating extensive demyelination.

B. Frontal sections from the brain of an operated control rat showing the septal area (top); the fornix area (middle); the hippocampal area (bottom). Note dark stained fibers.


A
B

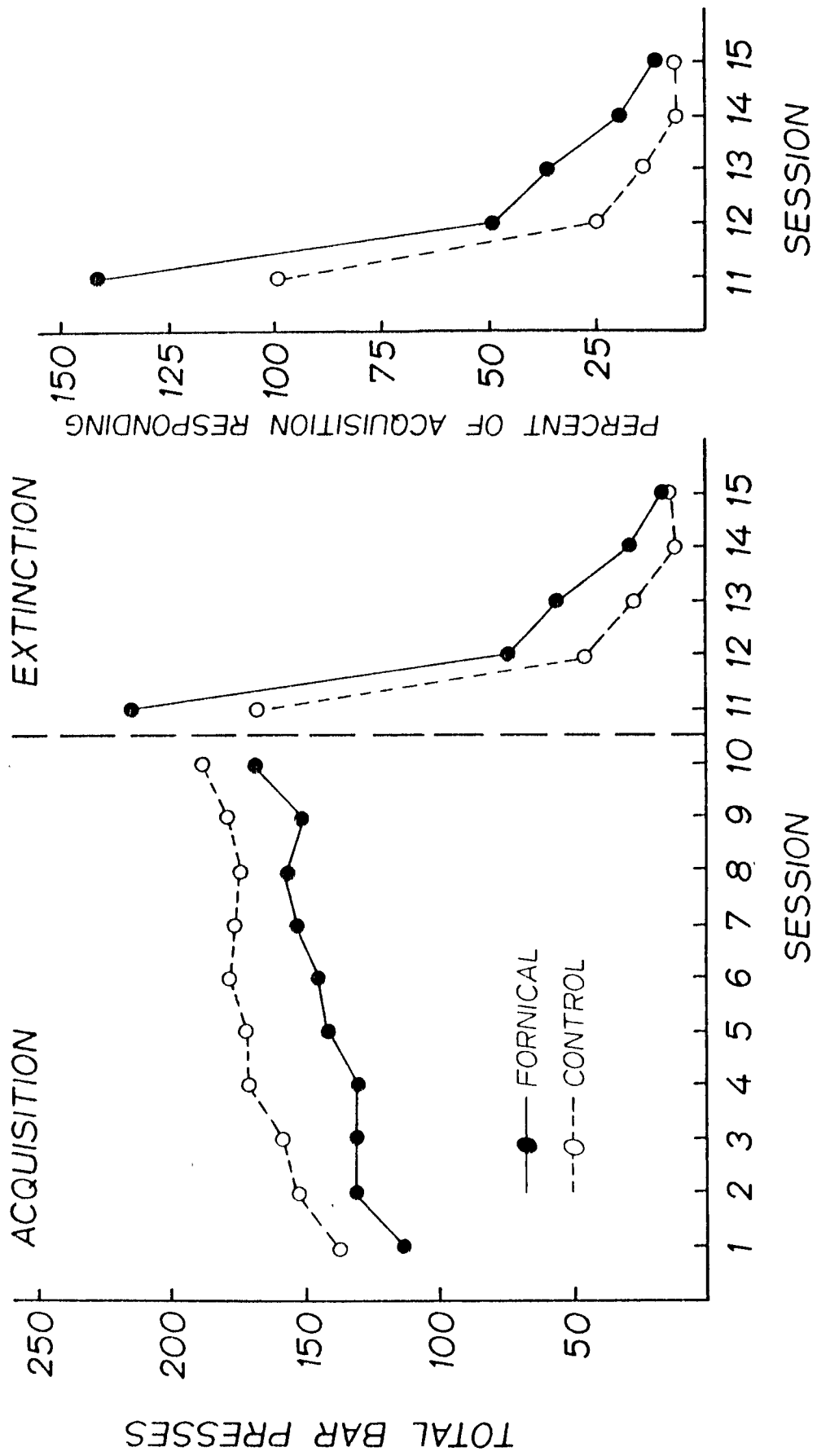
their sequential relationships will be described. In addition, data will be presented for other responses which occurred during trips away.

Lever-pressing: The absolute number of lever presses during each 20 minute session of acquisition and extinction are shown in the left hand panel of Figure 3. The number of responses during extinction expressed as a percentage of the terminal acquisition performance on day 9 are shown in the right hand panel. A two by ten analysis of variance was carried out on the acquisition data with lesion and days of training being the main factors. There was a significant effect for days of training ($F = 14.0$, $p < .001$). In addition, there was a significant lesion effect; controls responded at a higher rate than fornicals ($F = 4.51$, $p < .05$).

Because of the significant difference between control and lesioned rats in rate of lever-pressing during acquisition, analysis of variance for extinction data was carried out on lever-pressing expressed as a percentage of terminal acquisition performance as well as on absolute levels of lever-pressing. A two by five analysis of variance was carried out in each case with lesion and days of extinction as the main factors. For absolute levels, there was a significant days of extinction effect ($F = 83.7$, $P < .001$) but no significant lesion effect ($F = 3.60$, $p < .10$). For extinction, lever pressing expressed as a percentage of terminal acquisition performance, there was a significanat days of extinction effect ($F = 83.4$, $p < .001$) and a significant lesion effect ($F = 8.19$, $p < .01$). Therefore, if one takes terminal acquisition performance into account, one can conclude that operated controls extinguished more rapidly than rats with fornical lesions.

Figure 3

Mean lever presses during acquisition and extinction in a standard operant chamber for fornix lesioned and control rats. Left panel shows total lever presses during acquisition and extinction; right panel shows extinction responding expressed as a percentage of asymptotic acquisition rate.


ACQUISITION
EXTINCTION
TOTAL BAR PRESSES
PERCENT OF ACQUISITION RESPONDING
SESSION
SESSION
FORNICAL
CONTROL
250
200
150
100
50
150
125
100
75
50
25
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
11 12 13 14 15

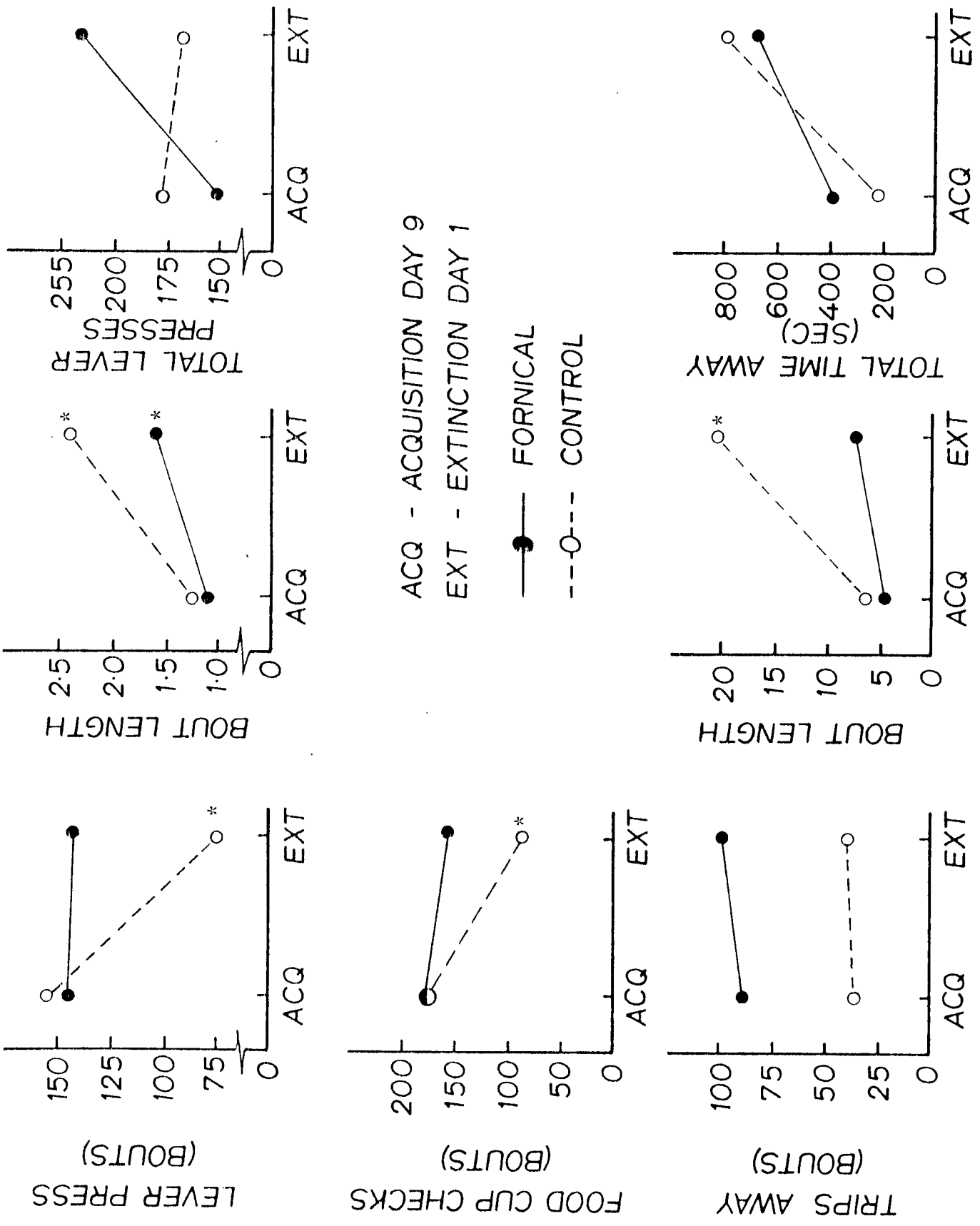
Analysis of major response categories: The three major response categories as defined by the task requirements are lever pressing, food cup checks and trips away from the bar and food cup area. Data on the mean number of bouts of each response, the mean bout length and the total number of lever presses and total time away during the ninth 20 minute acquisition session and first 20 minute extinction session are presented in Figure 4. Because total duration is determined jointly by number of bouts and bout lengths, I shall not discuss it further.

In general, the transition from acquisition to extinction resulted in more changes in behaviour for control rats than for rats with fornical lesions. The operated controls showed a decrease in number of bouts of lever pressing and food cup checks but no change in number of trips away; the lesioned rats showed no change in number of bouts of any of the three responses. In addition, the operated controls showed an increase in bout length of lever pressing and trips away; the lesioned rats showing a smaller increase in the lever press bout length and no change in trips away bout length.

Analysis of variance carried out on each measure confirmed the above description of the data. The interactions between training conditions (acquisition vs. extinction) and lesion (operated controls vs. fornicals) were significant for number of bouts of lever pressing ($F = 14.0$, $p < .005$), number of food cup checks ($F = 12.7$, $p < .005$), bout duration of lever pressing ($F = 12.36$, $p < .005$) and bout duration of trips away ($F = 31.22$, $p < .001$). Examination of Figure 4 suggests that the significant interactions in each case reflect greater changes

Figure 4

Changes in number of bouts, bout length and total number of major responses as a result of the transition from acquisition to extinction. Major responses are defined with respect to task requirements (see text for explanation). An asterisk indicates a significant change from acquisition to extinction.


ACQ - ACQUISITION DAY 9
EXT - EXTINCTION DAY 1
FORNICAL
CONTROL
TOTAL LEVER PRESSES
BOUT LENGTH
TOTAL TIME AWAY (SEC)
BOUT LENGTH
LEVER PRESS (BOUTS)
FOOD CUP CHECKS (BOUTS)
TRIPS AWAY (BOUTS)
ACQ
EXT

in the behaviour of controls following the transition to extinction. The only measure for which the interaction was not significant was number of trips away. In this case the main effect of lesions was significant ($F = 51.01$, $p < .001$). Tests of simple main effects (Winer, 1962) also supported the above conclusions. In each case, within group comparisons of acquisition vs. extinction performance were made. Those which were significant ($p < .05$) are marked with an asterisk in Figure 4. (The five percent significance level was employed in this and subsequent tests of simple effects.)

Further analyses of lever pressing and trips away: The transition from acquisition to extinction resulted in a change in the topography of lever-pressing. Whereas during acquisition the typical lever press involved the use of one or both paws, many of the lever presses that occurred during extinction involved biting the bar which never occurred during acquisition. Table 2 shows the percentage of two types of lever-presses (regular pressing with the paws and pressing as a result of biting the lever) for control and lesioned groups in both acquisition and extinction. A two by two analysis of variance of the data on percent biting showed a significant interaction ($F = 5.61$, $p < .05$). An analysis of simple main effects suggests that this interaction occurred because controls displayed significantly more biting in extinction than in acquisition while rats with fornical lesions did not.

Frequency of bouts and bout length for behaviours emitted during trips away are presented in Figure 5. Data are shown only for activities that had relatively high frequencies - nose poking, rearing

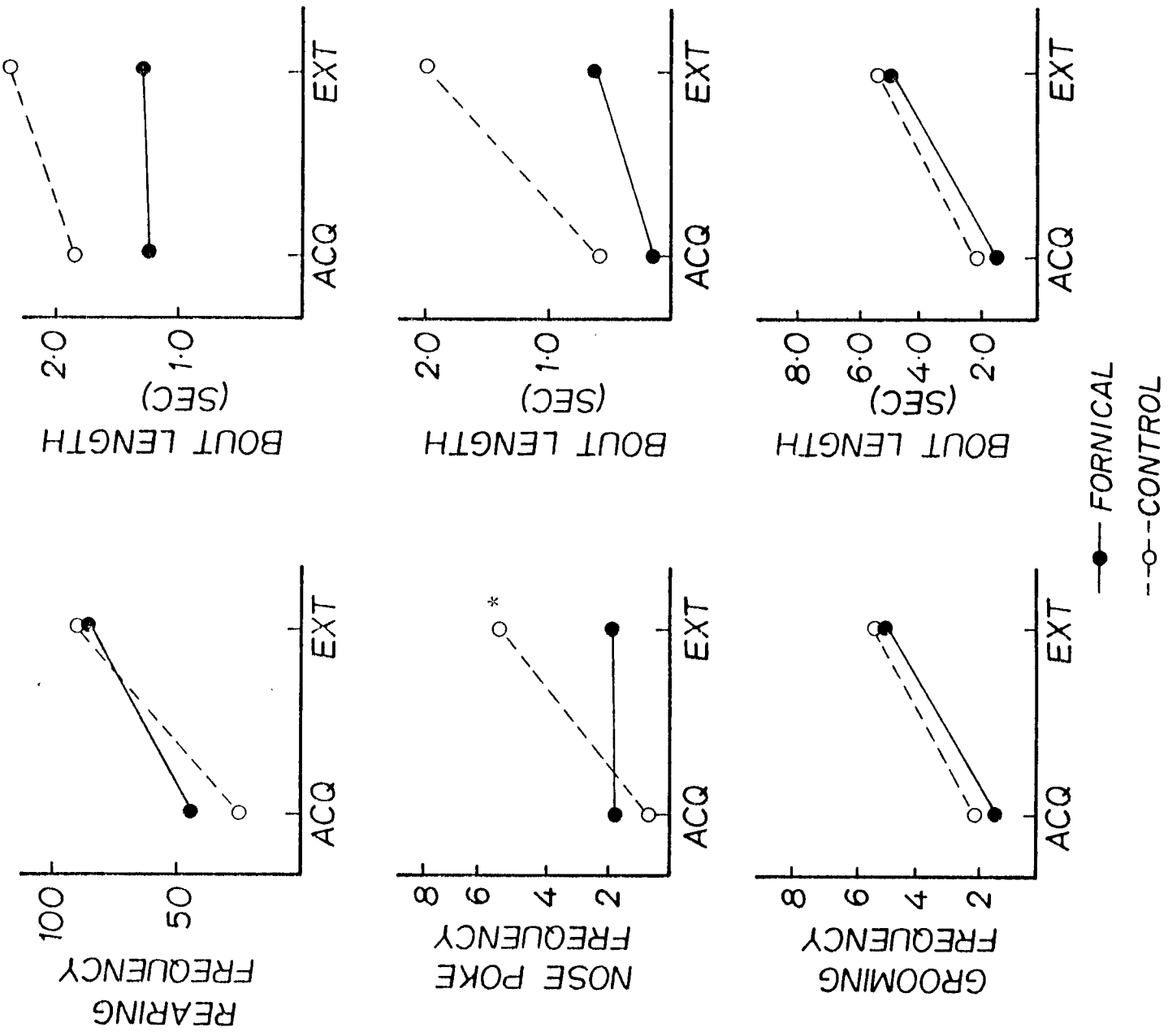
TABLE 2

Percentage of the two types of lever press mode during acquisition and extinction

GROUP	RESPONSE	ACQUSITION	EXTINCTION
FORNICAL	Regular bar press	100	91.7
	Biting bar press	0	8.3
CONTROL	Regular bar press	100	75.2
	Biting bar press	0	24.8

Figure 5

Frequency and bout length of response made during trips away from the bar and food cup area. An asterisk indicates a significant change from acquisition to extinction.


BOUT LENGTH (SEC)
8·0
6·0
4·0
2·0
ACQ
EXT
GROOMING FREQUENCY
8
6
4
2
BOUT LENGTH (SEC)
2·0
1·0
NOSE POKE FREQUENCY
8
6
4
2
*
REARING FREQUENCY
100
50
FORNICAL
CONTROL

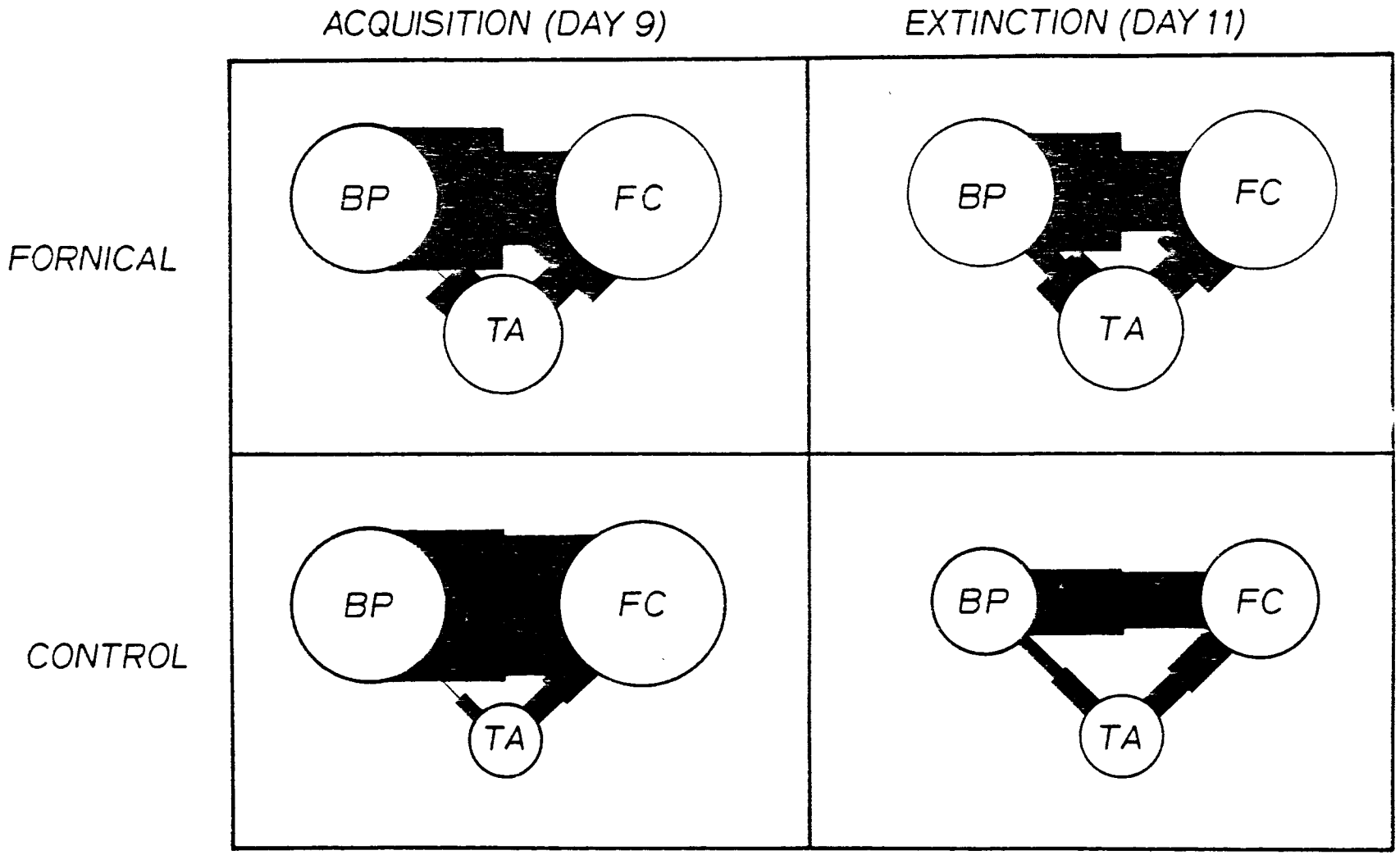
and grooming. Since controls spent more time away in extinction, the increase in number of bouts could simply reflect the increase in total time away rather than an actual increase in the density of bouts. In order to control for this possibility, analyses were carried out on the number of bouts normalized with respect to total time away. The only response for which there was a significant change as a consequence of the transition to extinction was nose poking. There was a significant interaction between lesion and condition ($F = 5.32$, $p < .05$). An analyses of simple main effects suggests that this interaction occurred because controls displayed a significant increase in nose poking as a consequence of the switch from acquisition to extinction while rats with fornical lesions displayed a slight but not significant decrease.

For bout length, the lesion vs. control main effect was significant for rearing ($F = 20.1$, $p < .001$) and nose poking ($F = 8.01$, $p < .025$). In addition, the acquisition vs extinction main effect was significant for bout length of all three responses (rearing: $F = 6.7$, $p < .025$); nose poke: $F = 4.42$, $p < .05$; grooming: $F = 29.8$, $p < .001$). The latter results suggest that rats with lesions of the fornix and control rats showed increased bout durations during extinction. However, individual comparisons of acquisition and extinction for each group indicated no significant difference for rats with fornical lesions on bout lengths of rearing and nose-poking.

Certain responses occurred with a frequency that was too low to permit them to be included in the formal analysis. One such response was attempting to escape from the apparatus. Four of the eleven control rats attempted to do this on 15 occasions after the beginning

Figure 6

Sequential patterns of major responses for fornix lesioned and control rats during acquisition and extinction. The area of the circle is proportional to the frequency of bout initiation. The band widths are proportional to the frequency of transitions (See text).



BP-BAR PRESS BOUTS FC-FOOD CUP CHECKS TA-TRIPS AWAY

of extinction. Two fornical rats did this on one occasion each.

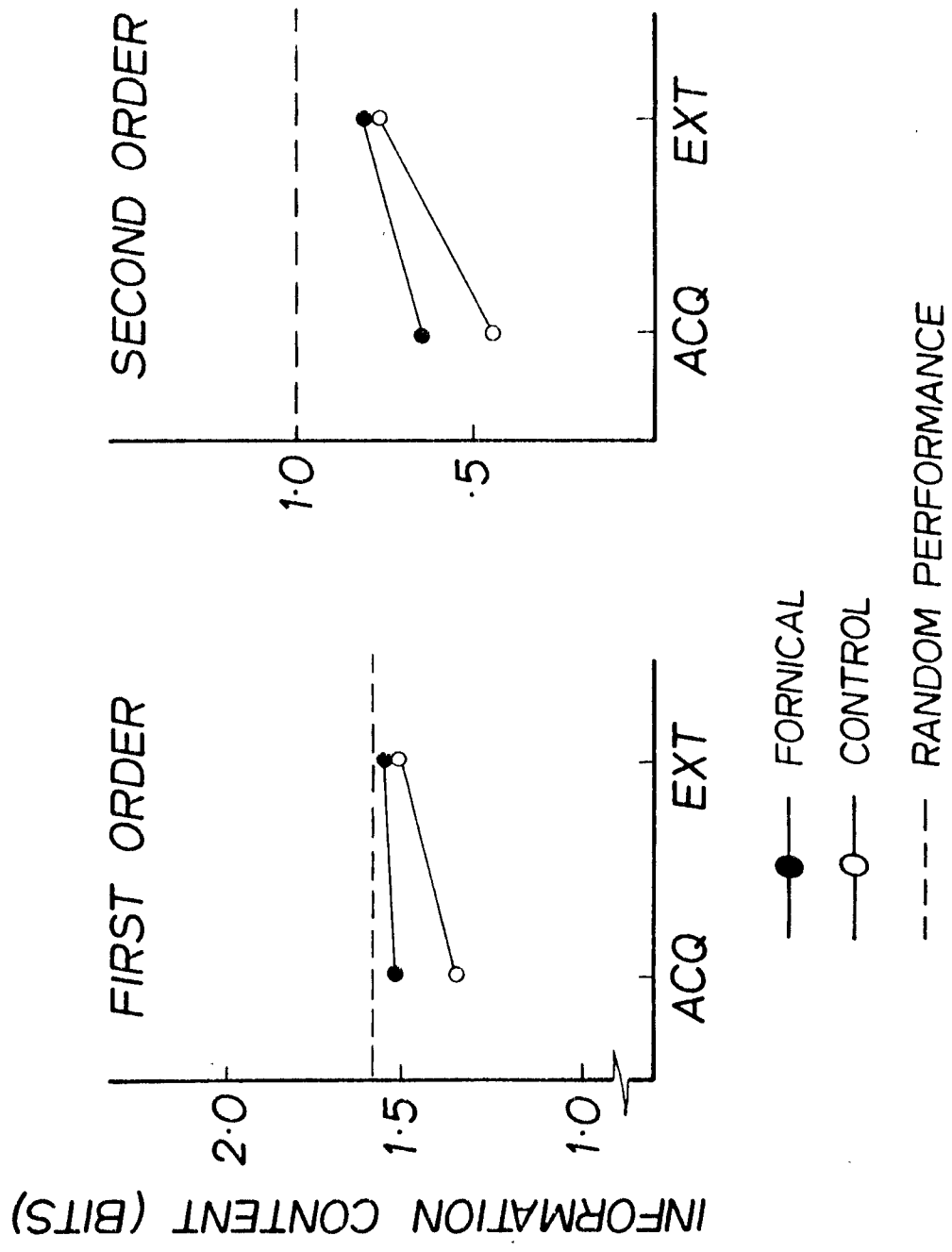
Sequential patterns: The transitions from a bout of one of the major responses to another are shown in Figure 6. The area of each circle is proportional to the frequency of bouts of a particular response. The number of times that an animal switched from a given act to one of the other two acts is indicated by the width of the dark band joining two circles. Each of these bands is divided into two sections; the width of the half nearest a given circle indicates the frequency of transition from the activity represented by that circle to the activity represented by the other circle. For example, the number of times that an animal switched from lever pressing to food cup checking is given by the width of the band adjacent to the lever press circle; the number of times that an animal switched from food cup checking to lever pressing is given by the width of the band adjacent to the food cup check circle.

In acquisition, control animals tended to go to the food cup when they left the lever; they tended to go to the lever when they left the food cup. Finally, after a trip away they tended to go to the food cup. During acquisition, animals with lesions of the fornix were similar to controls in that they tended to move from the lever to the food cup and from the food cup to the lever. They differed from controls after a trip away in that they tended to return to the lever rather than to the food cup. In extinction, these patterns of responding were maintained by the animals, but the dominance of one choice over another was greatly reduced, especially for animals in the control group.

This description is supported by information analyses of the first and second order predictability of the responses. First order analyses give an estimate of the predictability of the animal's behaviour based on the relative probabilities of the behaviours themselves; second order analyses give estimates based on the predictability of a response given that another response has occurred. Separate informational analyses were performed on each animal in both acquisition and extinction. These data were then averaged and are presented in Figure 7 which compares the patterns of both lesioned and control rats with random performance. Two by two analyses of variance were then carried out on the obtained information content with lesion (presence vs. absence) and condition (acqusition vs. extinction) as the main variables. Significant main effects of lesion ($F = 14.3$, $p < .005$; $F = 7.0$, $p < .025$), condition ($F = 50.5$, $p < .001$; $F = 60.2$, $p < .001$) and lesion x condition interaction ($F = 18.4$, $p < .001$; $F = 5.5$, $p < .05$) were obtained for both first and second order measures, respectively. An analysis of simple main effects indicates that both groups displayed a significant decrease in second order predictability but only controls displayed a significant decrease in first order predictability. These results suggest that the interaction for the measure of first order predictability occurred because the transition to extinction resulted in a decrease in predictability among controls but not lesioned rats; the interaction for the second order measure occurred because extinction resulted in a significant decrease in second order predictability for both control rats and rats with lesions of the fornix, but the decrease was much greater in magnitude for the control rats.

Figure 7

Information analyses of acquisition and extinction performance for fornix lesioned and control rats. First and second order analyses were performed on the behavioural sequences of each rat; group means are presented and compared to random performance.


INFORMATION CONTENT (BITS)
2·0
1·5
1·0
FIRST ORDER
ACQ
EXT
SECOND ORDER
1·0
·5
ACQ
EXT
FORNICAL
CONTROL
RANDOM PERFORMANCE

Corticosterone

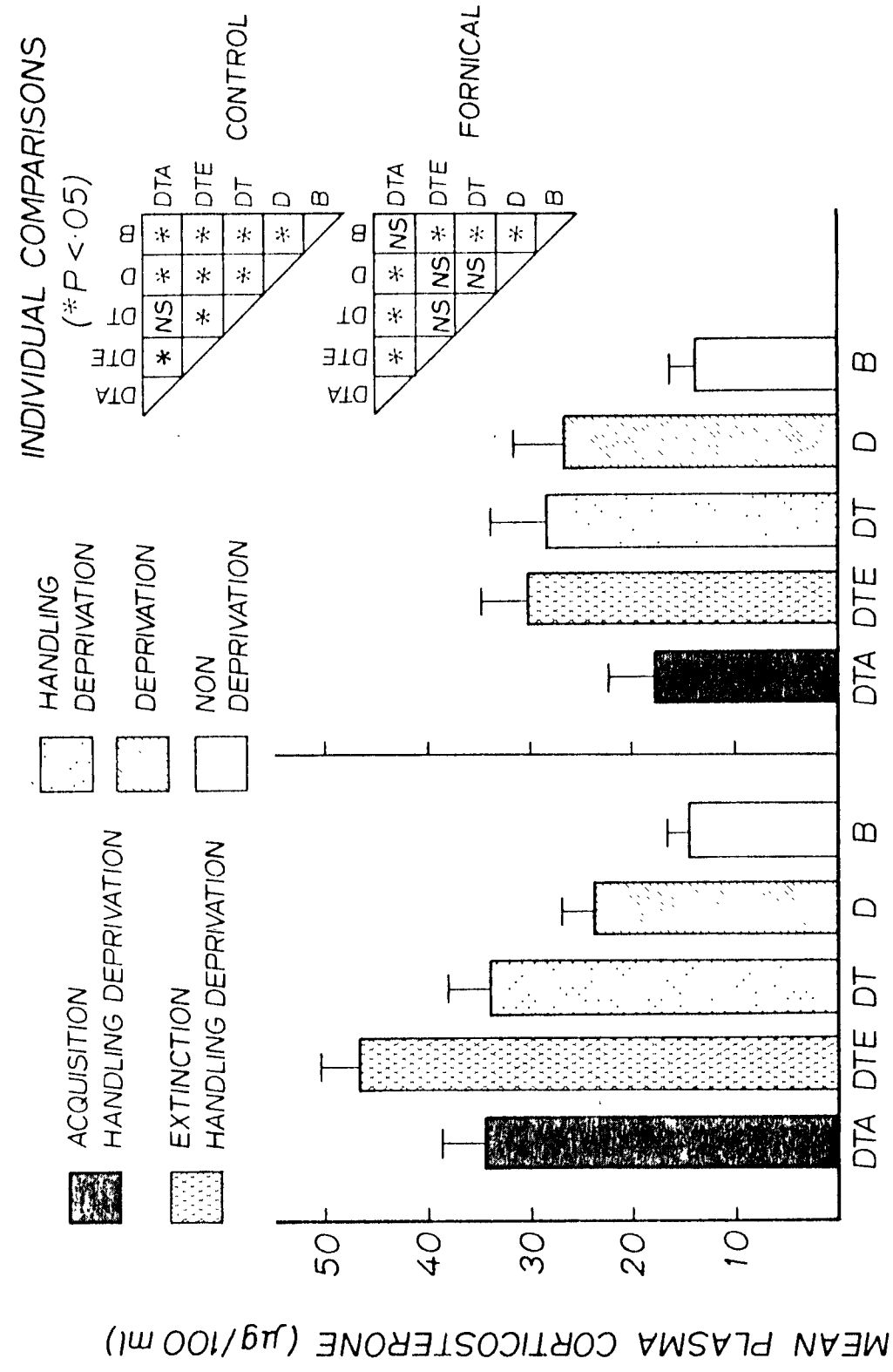
Mean plasma corticosterone levels for all samples from operated controls and rats with fornical lesions are presented in Figure 8. A two by five analysis of variance was carried out on this data with lesion and condition as the main factors. The analysis yielded a significant effect of treatment ($F = 20.7$, $p < .001$) and a significant treatment by lesion interaction ($F = 4.95$, $p < .005$). Both groups were responsive to the experimental manipulations, but the response profiles of control and lesioned animals differed.

In order to specify more precisely the nature of the differences in profile, within group comparisons for individual treatments were made using Neuman-Keuls comparisons ($p < .05$); these are summarized at the top of the figure. Starting from the non-deprived condition (B) which represents the non-stressed diurnal baseline level, control rats responded to each additional stimulus with a significant increase in corticosterone. This pattern held for the addition of deprivation (D), handling and transport (DT), and extinction (DTE). In acquisition (DTA), the corticosterone levels of controls were significantly lower than in extinction but not different from the deprived handling basal level (DT).

Lesioned rats, like controls, showed a significant corticosterone elevation to deprivation. Unlike controls, the manipulations of handling and transport and extinction did not result in additional corticosterone elevations. The effect of acquisition for lesioned rats was to reduce corticosterone levels significantly below the deprived-handled basal level to a level not significantly different from the non-deprived baseline level.

Figure 8

Mean plasma corticosterone as a function of condition for control and fornix lesioned rats. Significance levels for individual comparisons are shown at the right. Bars indicate standard error of the mean. B-basal non-deprived; D-deprived; DT - deprived, handling, transport, weighing; DTE - deprived, handling, transport, weighing and extinction; DTA - deprived, handling, transport, weighing and acquisition. Data are reported only for rats who received all five samples; data from rats in the first replication are not included.

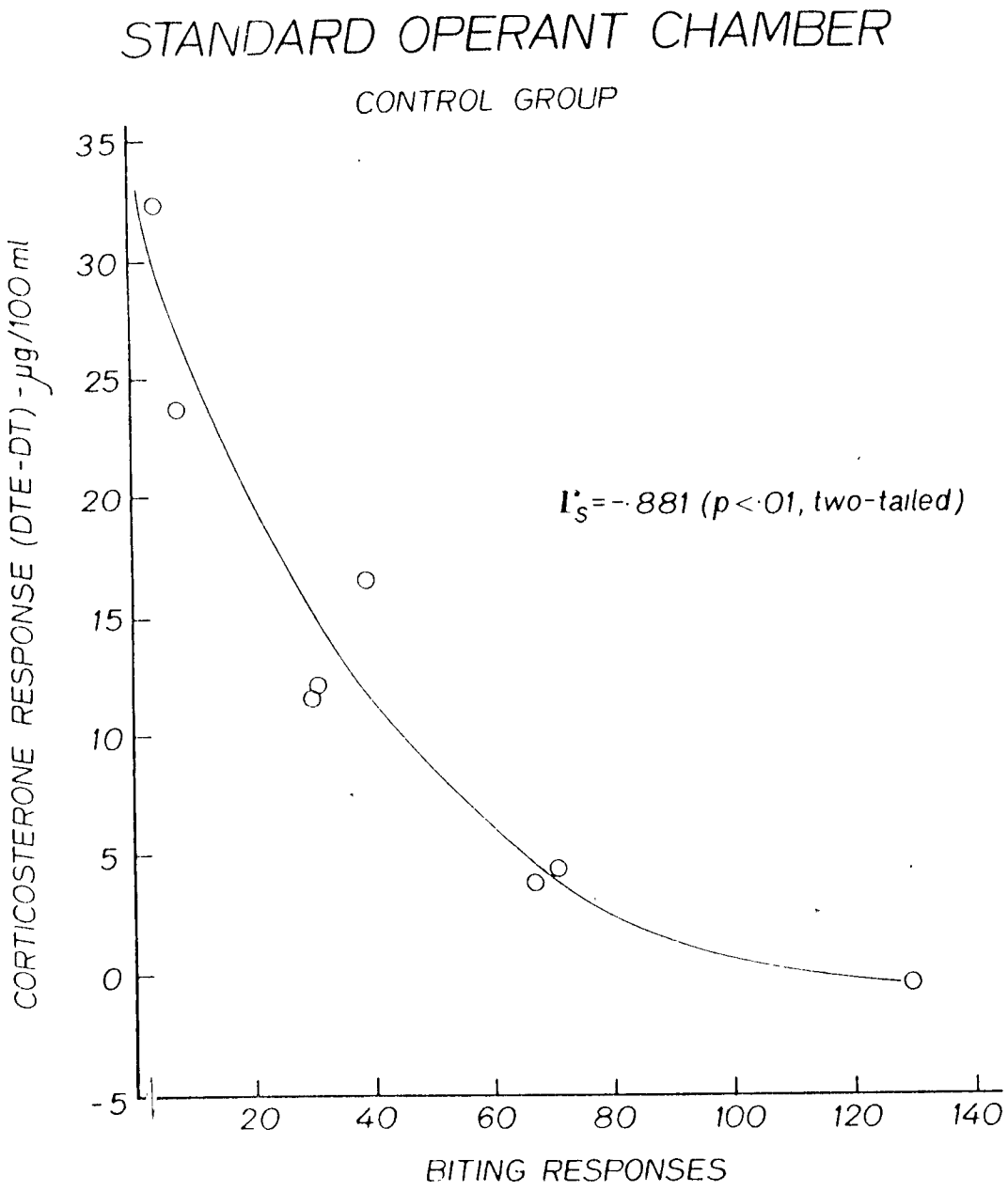

MEAN PLASMA CORTICOSTERONE (µg/100 ml)
50
40
30
20
10
DTA DTE DT D B
CONTROL
DTA DTE DT D B
FORNICAL
ACQUISITION
HANDLING DEPRIVATION
EXTINCTION
HANDLING DEPRIVATION
HANDLING DEPRIVATION
DEPRIVATION
NON DEPRIVATION
INDIVIDUAL COMPARISONS
(*P < .05)
CONTROL
FORNICAL
DTA
DTE
DT
D
B
*
NS

Since both corticosterone and emotional behavior have been used as indicators of a frustrative response to extinction, correlations between the corticosterone responses in extinction and these measures of behaviour in extinction (biting the lever, nose poking and bouts of lever pressing) were calculated. For the control group, significant negative correlations were found for the three behaviour indices (biting of the lever, $r_s = -.881$, $p < .01$; nose poking, $r^S = -.74$, $p < .05$; lever press bout length, $r_s = -.81$, $p < .05$). An example of this relationship is presented in Figure 9 which shows the corticosterone response as a function of amount of biting.

The high negative correlations between the corticosterone response and the measures of altered response topography (i.e. biting and response bout length) prompted further examinations for relationships between corticosterone response and original response topography and for relationships between response topographies. For control rats, both the number of regular lever presses and the number of food cup checks, the behaviours most likely to result in primary frustration, were positively correlated with the corticosterone response but these failed to reach significance ($r_s = .47$ and $r_s = .52$, respectively). The number of responses in each of the response modes (regular lever pressing and biting lever pressing) were negatively correlated for controls ($r_s = -.40$) but were positively correlated for lesioned rats ($r_s = .85$, $p < .01$). There were no significant correlations between the corticosterone response and any measures of behaviour for lesioned rats.

Figure 9

The relationship between the corticosterone response to extinction and the amount of lever biting during extinction for control rats. The corticosterone response to extinction is the difference between extinction levels and handled baseline (DTE-DT).


STANDARD OPERANT CHAMBER
CONTROL GROUP
CORTICOSTERONE RESPONSE (DTE-DT) - µg/100 ml
35
30
25
20
15
10
5
0
-5
20
40
60
80
100
120
140
BITING RESPONSES
$r'_s = -.881$ ($p < .01$, two-tailed)

Discussion

In the discussion of the present experiment, as well as the discussions of individual experiments to follow, I shall limit myself to a consideration of the possible interpretations of the data. A discussion of the implications of the data for general theories of hippocampal function will be deferred to the general discussion in Chapter 6.

As pointed out in the introduction, Gaffan (1972) and Ross et al (1975) found no effect of fornix lesions on resistance to extinction following continuous reinforcement; in contrast, the present results did find an effect of fornix lesions on resistance to extinction when terminal acquisition response rates were considered. The present results suggest, therefore, that the difference between experiments involving fornical lesions (Gaffan, 1972; Ross et al, 1975) and those involving hippocampal lesions (Table 1) may have arisen from differences in type of response or procedure rather than type of lesion. In the Ross et al study, in addition to the unusual task requirements, the lesioned rats received significantly less training during acquisition than did controls. Even with this difference in response strength, lesioned rats made approximately 50% more responses in extinction but this large difference did not reach significance. In the Gaffan study, the fornix lesioned rats exhibited an extinction deficit when the response was running in a straight alley but not when the response was nose poking in an operant chamber. The present data suggest that nose poking was increased by the transition to extinction of lever pressing in control but not in lesioned animals. Perhaps some

nose pokes may have been elicited in Gaffan's controls rats by the transition to extinction, and increased the response total to a level equivalent to that of the lesioned rats. In this sense, the elicited nose poke in Gaffan's study may have played the same function role as biting the lever in the present study.

The present experiment reports a number of behavioural differences between control rats and rats with lesions of the fornix in addition to the traditional measure of resistance to extinction that is discussed above. These results can be summarized by answering two questions. First, what differential effects did the transition to extinction have on control rats and rats with lesions of the fornix? Second, what differences were seen between control rats and rats with lesions of the fornix that were maintained across both acquisition and extinction.

One can note in response to the first of these questions that the changes in behaviour that were produced by extinction in control rats were absent or smaller in magnitude in rats with lesions of the fornix. This conclusion also holds true for corticosterone measures.

The transition to extinction resulted in three types of behavioural differences between lesioned and control rats. First, the frequency of bouts of a given behavior changed markedly. Control rats showed a decrease in the number of bouts of previously reinforced responses - lever presses and food cup checks. On the other hand, these rats showed an increase in the number of bouts of what might be called "emotional" responses such as biting the lever and nose poking. Rats with lesions of the fornix, however, failed to show a change in the

frequency of bouts of these responses following the transition to extinction. The second type of measure, duration of bouts or responding, increased for all responses measured in control rats. For lesioned rats, bout lengths of all behaviours that were measured failed to increase, or increased less than those of control rats (with the exception of grooming bout length). The third type of measure is the predictability of response sequences, and both control rats and rats with lesions of the fornix showed decreases in sequential predictability of behaviour during extinction. However, the decreases were greater in magnitude for the control rats, primarily because the control rats were more predictable in acquisition.

The transition to extinction also resulted in differences in the corticosterone responses of lesioned and control rats. Control rats displayed increases in corticosterone levels to the D condition (deprivation) and to the DT condition (deprivation plus weighing, handling and transport to a new environment). Since exposure to the combined condition (DT) produced a greater effect than exposure to the D condition, the DT condition provides the appropriate baseline for assessing the corticosterone response to acquisition and extinction. When baseline levels from the DT condition were compared to those during the learning situations, there was a clear-cut effect of extinction on corticosterone levels in control rats but no effect of acquisition. For rats with lesions of the fornix, there was no increase during extinction in corticosterone levels over the DT condition. Corticosterone levels were elevated for all conditions in which the lesioned rats were deprived and not permitted to eat (D),

(DT) and (DTE). A lower corticosterone level occurred when the lesioned rats were not deprived (B) and when they were deprived and permitted to eat during acquisition (DTA). One may conclude from these results that extinction did not affect the corticosterone levels of rats with lesions of the fornix. However, other interpretations of these data are possible. The higher corticosterone levels for control rats during both acquisition and extinction could simply reflect either response attenuation or a ceiling effect in lesioned rats. This pattern would also be obtained if controls exhibited higher baselines in both conditioning situations coupled with a normal response to extinction for both groups. Lastly, the increased corticosterone levels in extinction could reflect a conditioned response to the aversive blood sampling procedure independent of the changed environmental demands. These alternatives will be examined in later experiments (Chapters 4 and 5).

Increases in emotional behaviour and in corticosterone levels seen in controls following the transition to exxtinction were absent in lesioned rats. However, the behavioural and corticosterone measures cannot both passively reflect an emotional response in control rats to the withdrawal of expected reinforcement since they were negatively correlated. A number of experiments have previously reported negative relationships between corticosterone and certain types of behaviour (Coover et al, 1973; Ursin et al, 1975; Davis et al, 1977). For example, Davis et al (1977) reported decreased corticosterone levels in rats with extended training sessions on a shock escape task in comparison to initial training session levels. The decreased

corticosterone levels were not found in yoked control rats with identical shock histories. Such results are often interpreted as evidence for the view that "coping behaviour" results in lower corticosterone levels. One could apply the same interpretation to the present results by arguing that lever biting, nose poking and long bursts of lever pressing are examples of "coping behaviour". But these behaviours were not successful in altering reinforcement delivery and thus seem to alter the definition of what is meant by coping considerably. The interpretation of this correlation will be discussed later.

The second question posed above concerned differences between control rats and rats with lesions of the fornix that were maintained during acquisition and extinction. Such differences were surprisingly few in number; in most cases interactions occurred with the two groups being very similar under one of the conditions and different under the other. There were, however, some behavioural differences between groups that were common to both acquisition and extinction. In general, rats with lesions to the fornix initiated shorter bouts of activity than controls; they switched from one activity to another more quickly. Also, they tended to be less predictable than controls in moving among the three major task defined behaviours; that is, a given act was less accurately predicted from a knowledge of the previous act for the fornix lesioned rat.

The detailed behavioural analysis provides information relevant to the question of what are the basic characteristics attributed to the hippocampal syndrome. Among the most frequently suggested attributes

are frustration, stereotypy and a lack of response inhibition. Frustration is considered to be the unconditioned response to the nonoccurrence of anticipated reinforcement. It is also considered to be an aversive state (Mackintosh, 1974) and to be accompanied by emotional and displacement responses (Falk, 1972; McFarland, 1966). Rats with lesions of the fornix showed fewer emotional and displacement activities as evidenced by less biting, less nose poking and fewer attempts to escape from the apparatus. The failure to show the normal corticosterone rise in response to extinction also suggests that the fornix lesioned rats were less emotional. One can conclude from these data, in direct opposition to certain theories of hippocampal function (Isaacson, 1974; Isaacson & Kimble, 1972), that fornix lesioned rats, unlike controls, were not frustrated during extinction. The important question then concerns whether this lack of response in lesioned rats can be attributed to some disruption of motivational systems per se, or to an interference with the detection of the changed environmental demands. If motivational systems are disrupted by damage to the hippocampal formation, the disruption must be selective because motivational and emotional responding in hippocampal lesioned animals is normal under some conditions. For example, emotional responses to electric shock are unaffected by hippocampal lesions (Blanchard, Blanchard & Fial, 1970). In addition, rats with fornical lesions showed a normal corticosterone increase in response to deprivation in the present experiment even though they did not show one to extinction. Furthermore, Ely et al. (1977) recently reported that mice with hippocampal lesions have a greater corticosterone response to crowding

than do controls. Such a selective deficit, on the other hand, could be accounted for if the motivational systems were intact and if lesioned animals could detect or interpret some of the inputs that result in the activation of motivation systems but not other inputs. This possibility will be examined further in chapter 4.

The present data are also relevant to the concepts of behavioural inhibition and response stereotypy. Hippocampally damaged rats are often characterized as persistent, inflexible, predictable, locked into particular patterns of behaviours or particular strategies, or unable to inhibit particular responses (See Kimble, 1975 or Isaacson and Kimble, 1972). Certain aspects of the data of the present experiment are consistent with this characterization. The behavior of fornix lesioned rats changed less than that of controls after extinction began. Not only did the lesioned rats continue the acquisition mode of responding, but the total number of responses in this mode far exceeded that of controls. At the same time, other aspects of the data were inconsistent with this characterization. If rats with lesions of the fornix are inflexible and unable to inhibit or switch responses, should they not have performed longer bouts of responding rather than shorter bouts of responding than controls? Of course long bouts would not be expected if sequences of short bouts of responses formed units which persisted in extinction. But if response sequences form units for animals with lesions of the fornix, the sequential pattern of responding should have been predictable and remained so throughout the experiment. However, the data on sequential predictability indicate that it did not; lesioned rats were less

predictable than controls throughout the experiment. A more general question with respect to response inhibition concerns the many qualitative differences between lesioned and control rats in the present experiment. Response inhibition interpretations assume, at least where the response requirements are well defined, that the differences between normal and lesioned rats are quantitative; the lesioned rats simply exhibit more of the task defined behaviour than do controls. This misconception follows directly from the use of less informative measures like total number of lever presses. The extent to which the qualitative differences in behaviour between groups contribute to the extinction deficit will be examined in Chapter 3.

To summarize, the present experiment showed that rats with fornix lesions exhibit a deficit in the extinction of a lever press response even when traditional measures are employed. The additional measures support this conclusion and provide information on which to evaluate some theories of hippocampal function. A number of questions arise from this experiment. First, to what extent do the many behavioural differences in the lesioned and control rats' response to the changed environmental demands contribute to the traditionally defined "extinction deficit". This question will be explored in Chapter 3. Second, it was suggested that there were several alternative interpretations of the corticosterone results. Due to the importance of these data to the evaluation of motivational theories of hippocampal function, these alternatives are explored in Chapters 4 and 5. Finally, the nature of the behavioural and hormonal response of fornix lesioned rats to frustrating environmental changes is explored in Chapter 4.

Chapter 3

Effects of total fornix lesions on exploration and lever press extinction in an enriched experimental environment

Experiment 2

The results of the previous experiment indicated that rats with fornix lesions exhibited greater resistance to extinction when either traditional or detailed measures of behaviour were employed. The detailed behavioural analyses performed in the previous experiment also revealed a number of additional differences between lesioned and control rats in this situation. The groups differed in the organization of their behaviour in terms of frequencies, durations and sequential dependencies, in the use of the experimental environment away from the lever and food cup, in topography shifts in existing behaviour, and in the emergence of emotional and displacement responses. The extent to which these additional behavioural differences contributed to the traditionally defined extinction deficit (i.e. animals with hippocampal damage exhibiting a greater number of lever presses during extinction) is not clear. Current learning theories of extinction would appear to be of limited utility in answering this question. Of the three most dominant theories, the reactive inhibition theory (Hull, 1943), the generalization decrement theory (Capaldi, 1967) and frustration theory (Amsel, 1967), only the latter addresses the issue of behaviours outside the specific task requirements. Within the framework of frustration theory, many of these behaviours would be relegated to the role of competing responses.

As Mackintosh (1974) points out, it is difficult to account for suppression of the reinforced response solely on the basis of competing response tendencies, and in addition, it is also difficult to class many of the behavioural differences observed in Experiment 1 as competing responses (i.e., biting falls within the operant response class). Recent work by Wong (1977, 1978) suggests that many of the behaviours that differed between lesioned and control rats in Experiment 1 are systematically involved in the acquisition and extinction strategies of normal rats.

One way to evaluate the contribution of these behavioural differences to the extinction deficit, would be to determine the effects on extinction responding when the opportunity to engage in these alternative responses is altered experimentally. In Experiment 1 these behavioural differences were observed even though the apparatus used tended to minimize their involvement. The present experiment maintains the same task requirements but in an enlarged, enriched experimental environment designed, on the basis of previous exploratory and adjunctive research (see Walsh and Cummins, 1976 and Falk, 1977 for reviews), to enhance the additional behavioural differences observed in Experiment 1. If these additional behaviours are involved in the acquisition and extinction strategies of normal rats as suggested by Wong (1978), then altering the opportunity and consequently the occurrence of these behaviours, should elucidate their role and, provide information on which, in any, of these differences contribute to the extinction deficit.

Methods

Subjects:

Twenty-five experimentally naive, male hooded rats of the Long-Evans strain obtained from Canadian Breeding Farms, St. Constant, Quebec were used. At the time of surgery, the rats weighed 200-250 g. As in Experiment 1, this experiment was carried out in two replications; there were no procedural differences between these.

Procedure:

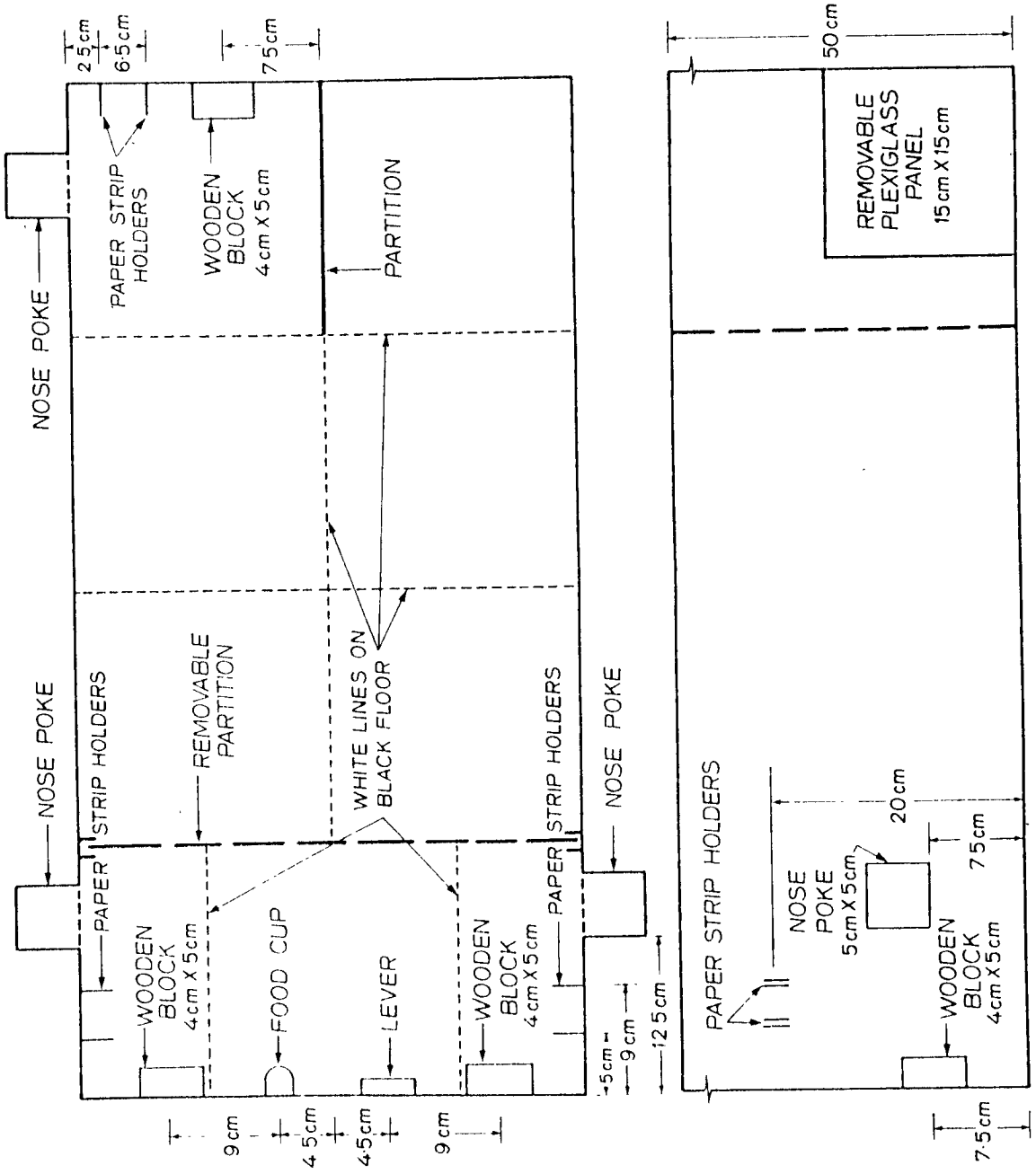
The experimental procedure was similar to that used in Experiment 1 except that slight changes in pretraining and data collection were dictated by the change in experimental environment. Housing conditions and surgical, deprivation, conditioning, histological, blood sampling and assay procedures were identical to those described in Experiment 1.

Apparatus:

Training was carried out in a large chamber measuring 40 x 80 x 50 cm with a wood floor. The walls of the chamber were transparent plastic and the floor painted black to aid video analyses of behaviour. The chamber was equipped with the standard lever and food cup and, in addition, a number of environmental supports for species typical behaviours were provided. The environmental supports are identified together with their spatial arrangement in Figure 10. The wood blocks were soft pine; the paper strips were 3 x 20 cm pieces of corregated cardboard. The effectiveness of all three objects (wood blocks, paper and darkened box) as adequate environmental supports for collateral behaviour has previously been demonstrated (Falk, 1972; Wong, 1977).

Figure 10

Diagram of enriched experimental environment. Environment consisted of 40 x 80 x 50 cm transparent plastic chamber equipped with standard lever and food cup and three sets of environmental supports for species typical behaviours. The environmental supports were soft pine blocks, 3 x 20 cm pieces of cardboard, and 5 x 5 x 5 cm dark interior boxes.


NOSE POKE
PAPER STRIP HOLDERS
WOODEN BLOCK 4cm X 5cm
PARTITION
2.5cm
6.5cm
7.5cm
NOSE POKE
STRIP HOLDERS
REMOVABLE PARTITION
WHITE LINES ON BLACK FLOOR
PAPER
WOODEN BLOCK 4cm X 5cm
FOOD CUP
LEVER
WOODEN BLOCK 4cm X 5cm
PAPER
STRIP HOLDERS
NOSE POKE
9 cm
4.5cm
4.5cm
9 cm
5cm
9 cm
12.5 cm
50 cm
REMOVABLE PLEXIGLASS PANEL 15cm X 15cm
PAPER STRIP HOLDERS
NOSE POKE 5cm X 5cm
20 cm
7.5cm
WOODEN BLOCK 4cm X 5cm
7.5cm

Pretraining:

Two days before acquisition training the rats were adapted to the experimental apparatus for ten minutes. On the next day, the rats were shaped to lever press and allowed to make 50 reinforced lever press responses on a continuous reinforcement schedule. During the shaping session, the removable plastic partition was inserted; during the previous adaptation and subsequent conditioning sessions the partition was removed. These changes from the preconditioning procedure reported in Experiment 1 were made to facilitate shaping of the lever press response as well as to facilitate the transition to the acquisition phase in the enriched experimental environment.

Video-tape analyses:

As in Experiment 1, the behaviour of the rats was classified in terms of the animals' movements and the outcome of these movements. Behaviours directed toward the additional environmental supports in this more enriched environment were added to the behavioural list of Experiment 1. Grooming and rearing were deleted; grooming because it occurred infrequently with respect to other behaviours and rearing because it occurred as an integral part of many separate behaviours. The frequency, duration, quality, and sequential order of the behavioural interactions were recorded. The rating for quality of interaction with objects was the following:

1. orient and approach object
2. nose sniff but no contact
3. brief contact (<1 sec)
4. long contact (> 1 sec)
5. biting or pawing object

Jumping and climbing, although they often involved object contact, were treated as a separate category.

Results

Histology

Of the sixteen lesioned rats, ten received complete transection of the fornix; damage to the remaining six was unilateral and their data were not included in the analysis. The extra-fornical damage to the ten rats with complete fornix lesions included partial damage to stria medullaris in two, complete damage to stria medularis in five, partial damage to stria terminalis in seven, complete damage to stria terminalis in two animals. There was no damage to the septum or cingulum in the lesioned rats and only slight unilateral cortical damage. The nine operated controls received no damage to the fornix or to extra-fornical structures with the exception of slight unilateral cortical damage.

Lever-pressing

The number of lever presses during the acquisition and extinction sessions are presented in the left panel of Figure 11. The right panel of Figure 11 shows extinction lever pressing expressed as a percentage of terminal acquisition performance.

A two by ten analysis of variance of acquisition data was carried out with lesion and days of training as the main factors. Controls responded at a higher rate during acquisition than did the lesioned rats ($F = 19.8$, $p < .001$). While both groups increased responding as a function of days ($F = 69.2$, $p < .001$), the change across days of training was greater for controls than for lesioned

Figure 11

Mean lever presses during acquisition and extinction in enriched experimental environment for fornix lesioned and control rats. Left panel shows total lever presses during acquisition and extinction; right panel shows extinction responding expressed as a percentage of asymptotic acquisition rate.

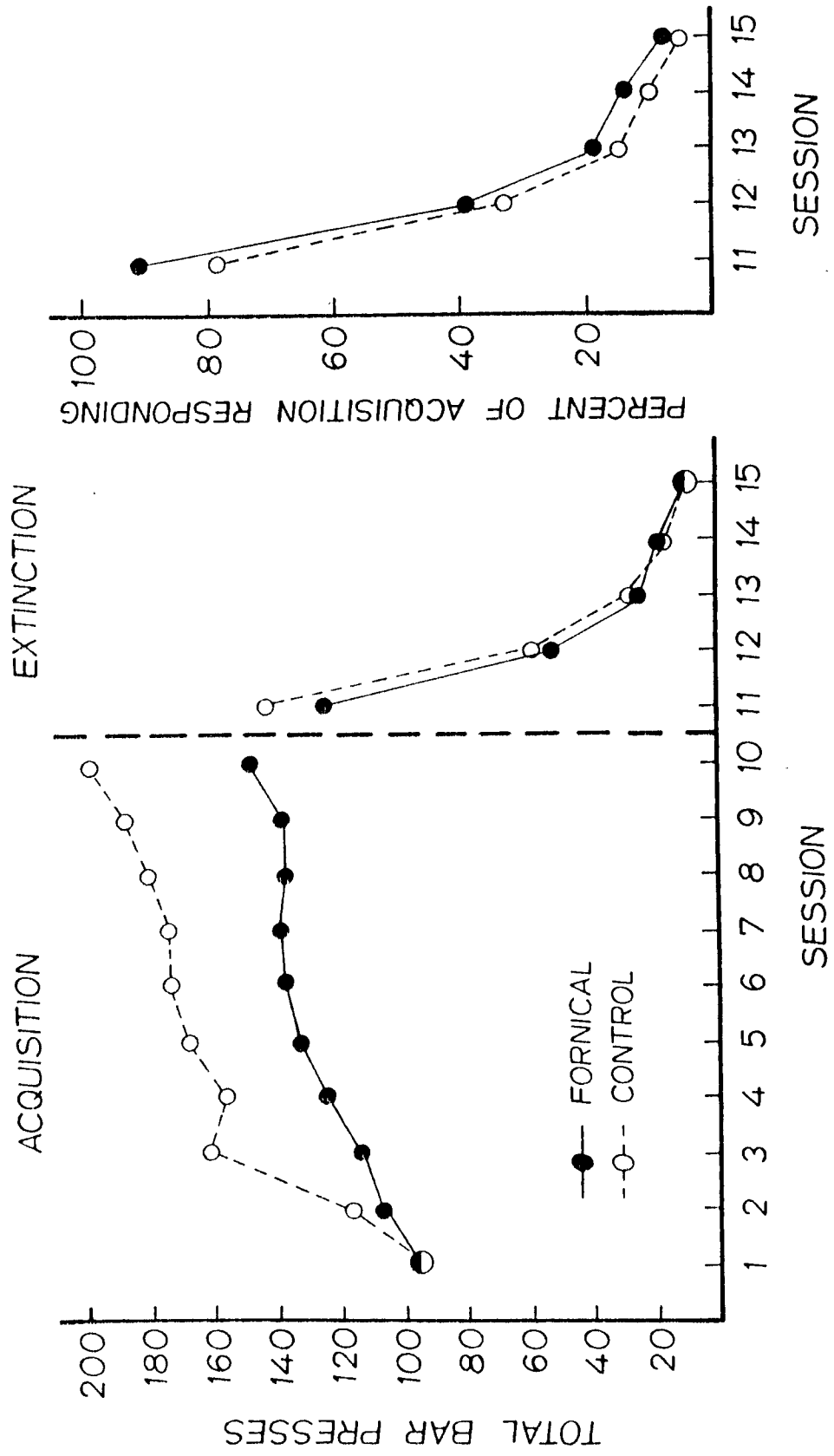
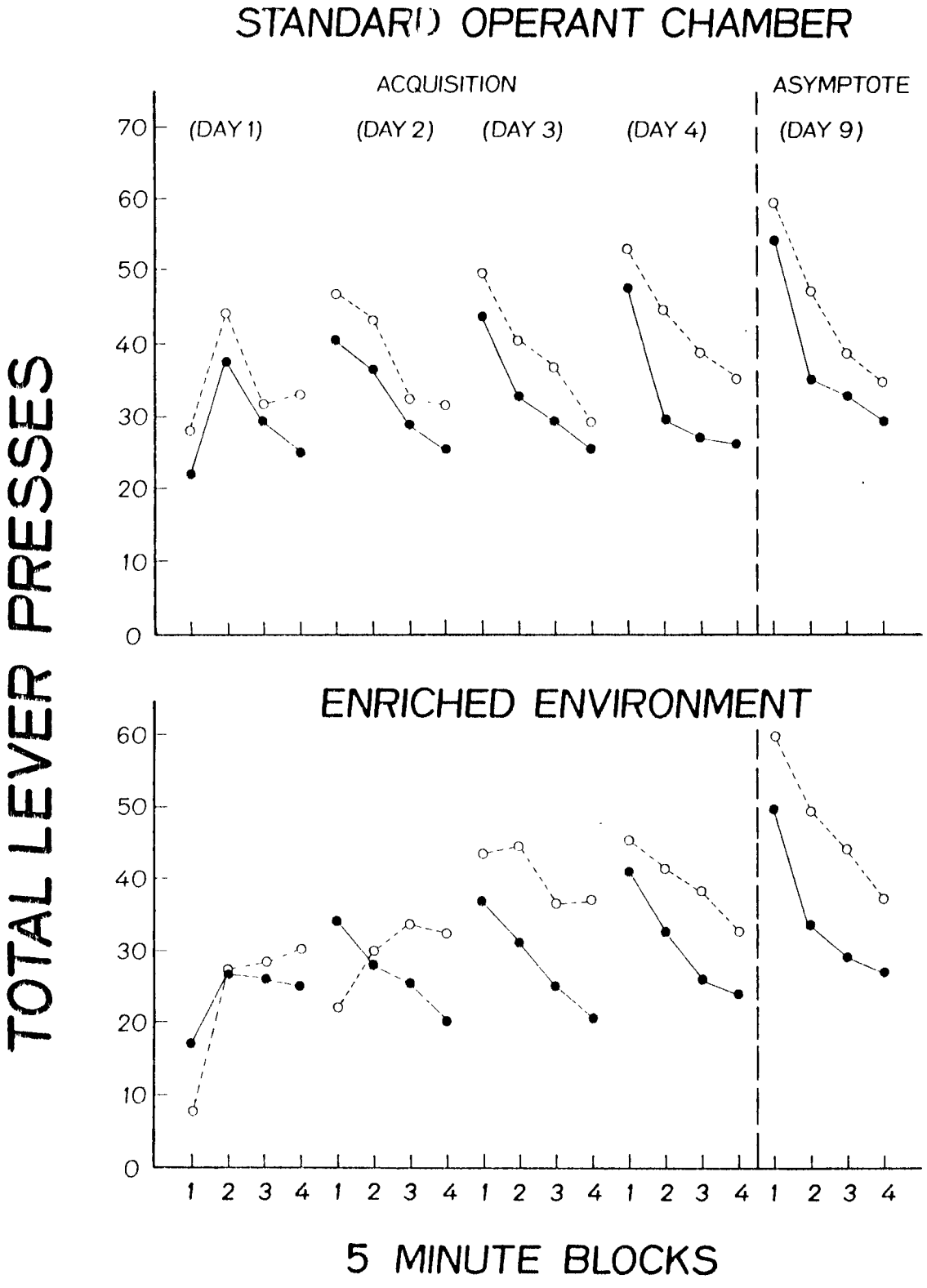

ACQUISITION
EXTINCTION
TOTAL BAR PRESSES
PERCENT OF ACQUISITION RESPONDING
SESSION
SESSION
FORNICAL
CONTROL
200
180
160
140
120
100
80
60
40
20
100
80
60
40
20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
11 12 13 14 15

Figure 12

Comparison between the within session acquisition lever press response patterns exhibited by rats in the standard operant chamber of Experiment 1 and those exhibited by rats in the enriched environment of Experiment 2. Fornix lesioned rats - dark circles, solid lines; Control rats - open circle, dotted line.


STANDARD OPERANT CHAMBER
ACQUISITION
ASYMPTOTE
(DAY 1)
(DAY 2)
(DAY 3)
(DAY 4)
(DAY 9)
70
60
50
40
30
20
10
0
ENRICHED ENVIRONMENT
60
50
40
30
20
10
0
1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4
TOTAL LEVER PRESSES
5 MINUTE BLOCKS

rats, as is evident in Figure 11 and supported by a significant day X group interaction ($F = 8.9$, $p < .001$). This difference in acquisition responding across days is more clearly seen in Figure 12 which presents daily response rates broken down into five minute intervals. Within session response patterns for early acquisition sessions are compared to asymptotic patterns for both the present experiment and previous groups from Experiment 1 trained in a small standard operant chamber. Asymptotic within session patterns are similar in both the standard and enriched experimental environments, but with controls responding at a higher rate than rats with fornix lesions. With the exception of the first five minutes on Day 1, lesioned rats in both environments and control rats in the standard environment adopt this monotonically descending pattern even in the early sessions. Control rats in the enriched environment, however, do not develop this pattern until the fourth experimental session. The difference is most obvious on Day 2 where the patterns of lesioned and control rats were reversed. Analyses of variance for individual days reveal a significant five-minute-block X group interaction on Day 2 ($F = 6.8$, $p < .001$) and interactions that approach significance on Days 1 and 3.

As is evident from Figure 11, lesioned and control rats did not differ in total number of lever press responses emitted during the five days of extinction. Analyses of variance for absolute levels or for extinction lever pressing expressed as a percentage of terminal acquisition levels yielded significant effects only for days of extinction ($F = 122.0$, $p < .001$; $F = 121.1$, $p < .001$, respectively).

In contrast to the failure to find a difference in responding using total lever presses, further analyses of the lever press data revealed clear differences between lesioned and control rats both during extinction and in response to the transition from acquisition to extinction. First, the groups differed in the distribution of responses within the extinction sessions. Total responses broken into five minute blocks for the first extinction session are presented in Figure 13. Lesioned rats responded at higher rates during the early part of the session but controls responded at higher rates later in the session. Analyses of variance yielded significant five minute block X group interaction ($F = 3.0$, $p < .05$). This within session difference in pattern of response was paralleled by changes in the response topography. Lever pressing was categorized into regular lever pressing (made with the paw) and biting lever pressing (activation of the feeder mechanism as a result of biting the lever). These data for both acquisition and extinction are presented in Table 3. The transition from acquisition to extinction resulted in operated controls exhibiting a greater decrease in regular lever pressing and a greater increase in biting presses. These differences are supported by two by two analyses of variance with condition and lesion as the main factors which showed significant condition (acquisition vs extinction) X lesion interactions for regular presses ($F = 14.7$, $p < .005$) and biting presses ($F = 24.7$, $p < .001$). Within the extinction session the proportion of responses that resulted from lever biting showed significant increases ($F = 3.2$, $p < .05$) for controls but not for lesioned rats.

Figure 13

Mean lever press responses of fornix lesioned and control rats during the first day of extinction in the enriched environment broken down into five minute blocks.

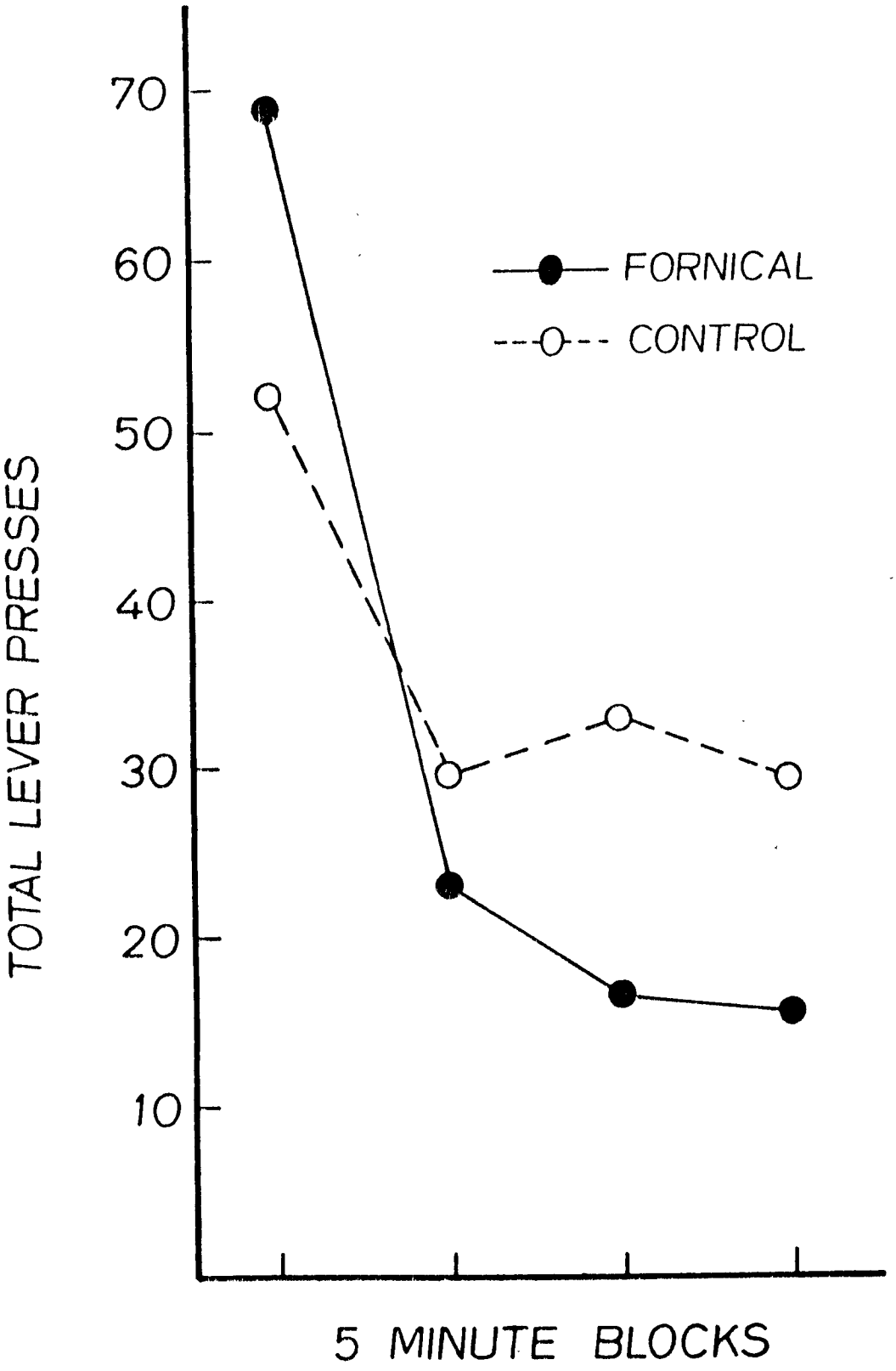

70
60
50
40
30
20
10
TOTAL LEVER PRESSES
FORNICAL
CONTROL
5 MINUTE BLOCKS

Table 3

Percentage of the two types of lever press mode during acquisition and extinction in the enriched experimental environment

GROUP	RESPONSE	ACQUISITION					EXTINCTION				
		5 MIN BLOCK				TOTAL	5 MIN BLOCK				TOTAL
		1	2	3	4		1	2	3	4	
FORNICAL	Regular Bar Press	44.3	33.3	28.7	27.0	138.3	68.8	23.2	16.4	15.8	124.2
	Biting Bar Press	0	0	0	0	~0	~0	~0	~0	~0	0.6
	Percent Biting	0	0	0	0	~0	~0	~0	~0	~0	0.5
CONTROL	Regular Bar Press	59.4	49.0	43.9	36.9	189.2	46.3	19.4	22.6	15.7	104.0
	Biting Bar Press	0	0	0	0	0	6.0	10.-	10.6	13.4	40.4
	Percent Biting	0	0	0	0	0	9.2	20.8	34.0	34.7	29.0

A comparison of the within session acquisition (Day 9) and extinction (Day 1) patterns under standard and enriched environmental conditions for both control and lesioned rats is presented in Figure 14. As is evident from the figure the asymptotic acquisition patterns within groups did not differ between environmental conditions. They did, however, differ in extinction as a result of the changed environment. For lesioned rats, enrichment of the experimental environment did not change the shape of the extinction curve but only lowered the number of responses emitted. For controls the opposite results were obtained; the total responses did not differ but the shape of the extinction curve changed. These differences are supported by analyses of variance with experimental environment and within session block as the main factors. Lesioned rat data yielded a significant effect of environment ($F = 7.9$, $p < .01$) and block ($F = 35.3$, $p < .001$) but no significant interaction ($F = 0.7$, $p > .05$,). Control data yielded a significant effect of block ($F = 13.0$, $p < .001$) and block X environment interaction ($F = 2.9$, $p < .05$) but no effect of environment ($F = 1.4$, $p > .05$).

Detailed behaviour analyses

Major responses: The major responses as defined by the schedule requirements are lever pressing, food cup checks and trips away from the lever and food cup area. The mean number of bouts, mean bout duration and mean total responses for each major response are presented in Figure 15.

For both lesioned and control groups, the transition from acquisition to extinction resulted in changes in the number of bouts of

Figure 14

Comparison between the within session response patterns exhibited by rats in the standard operant chamber of Experiment 1 and those exhibited by rats in the enriched environment of Experiment 2.

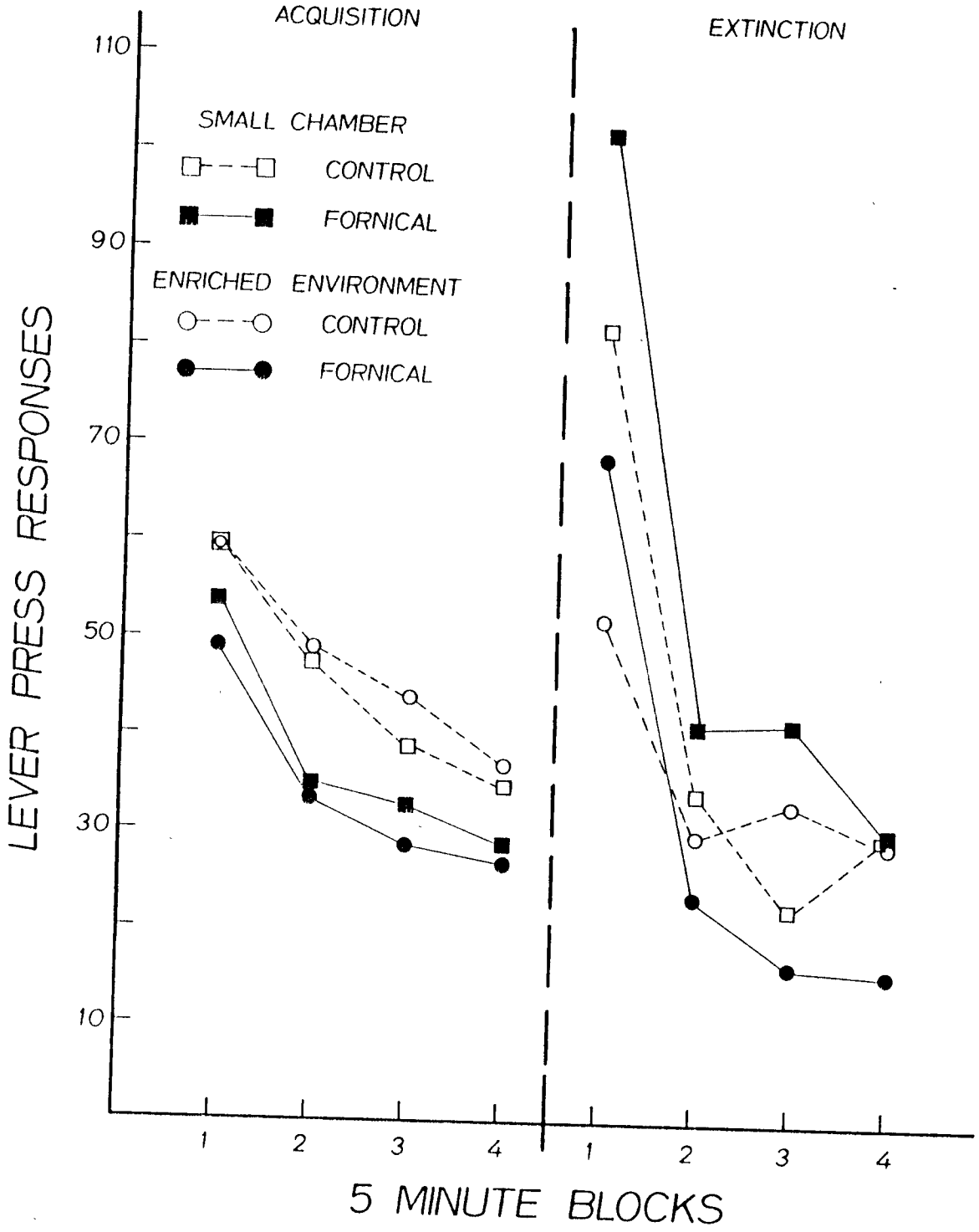
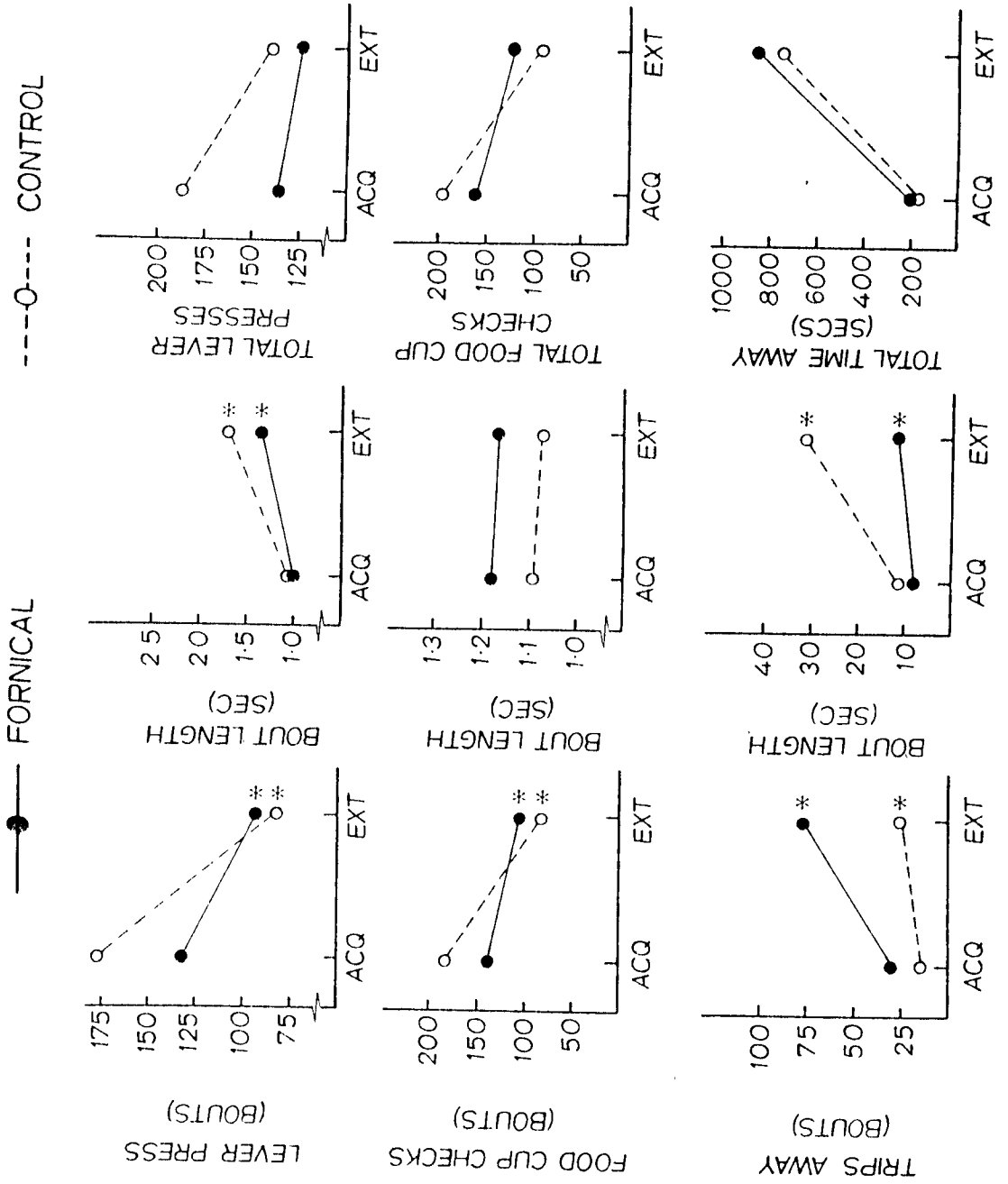

ACQUISITION
EXTINCTION
110
90
70
50
30
10
SMALL CHAMBER
CONTROL
FORNICAL
ENRICHED ENVIRONMENT
CONTROL
FORNICAL
LEVER PRESS RESPONSES
1
2
3
4
1
2
3
4
5 MINUTE BLOCKS

Figure 15

Changes in number of bouts, bout length and total number of major responses as a result of the transition from acquisition to extinction in an enriched environment. An asterisk indicates a significant change from acquisition to extinction.


FORNICAL
CONTROL
LEVER PRESS (BOUTS)
BOUT LENGTH (SEC)
TOTAL LEVER PRESSES
FOOD CUP CHECKS (BOUTS)
BOUT LENGTH (SEC)
TOTAL FOOD CUP CHECKS
TRIPS AWAY (BOUTS)
BOUT LENGTH (SEC)
TOTAL TIME AWAY (SECS)
ACQ
EXT

both food related behaviours (lever pressing and food cup checks) and in trips away from the lever and food cup area. Lesioned rats showed less of a reduction in food related behaviours but a larger increase in number of trips away. These differences were supported by two by two analyses of variance with lesion and condition as the main factors which yielded significant groups X condition interactions for lever press bouts ($F = 16.1$, $p < .001$), food cup bouts ($F = 17.8$, $p < .001$) and trips away ($F = 31.2$, $p < .001$). Tests of simple main effects ($p < .05$) indicate that the response to the transition is significant for both groups on all three measures. The significant interactions result from differences in magnitude of change.

The mean duration of lever press bouts and trips away also changes as a result of the transition from acquisition to extinction. Bout lengths increase as a result of the transition to extinction for both groups but the increase was much larger for operated controls than for lesioned rats. This description is supported by two by two analysis of variance with lesion and condition as the main factors which yielded significant interactions for lever press bout length ($F = 5.06$, $p < .05$) and trip duration ($F = 38.0$, $p < .001$) and tests for simple main effects which yielded significant ($p < .05$) increases during extinction for both groups on both measures. Again the significant interactions reflect differences in magnitude of the change. Food cup behaviour involved eating during acquisition but not during extinction. Consequently, two measures of duration of food cup checks were calculated. When the duration is defined as the number of food cup checks emitted before switching to another response (this is

the measure presented in Figure 15), the transition to extinction did not result in a change in bout duration, but lesioned rats were more likely to repeat a check of the food cup during both acquisition and extinction. Analysis of variance of this measure of food cup bout length yielded a significant effect only for lesion ($F = 8.2$, $p < .05$). When bout duration is defined as the time elapsed (seconds) during each bout, lesion rats show significantly longer bouts during acquisition (means: fornical 6.54, control 4.73, Mann-Whitney $U = 13$, $p < .02$) but shorter bouts during extinction (means: fornical 1.65, control 2.55, Mann-Whitney $U = 12$, $p < .02$).

Total number of responses in each category are also presented in Figure 15. Total time away increases dramatically following the transition to extinction ($F = 503.3$, $p < .001$) but not differentially with respect to lesioned and control groups (group X condition interaction not significant, $F = 1.8$, $p > .05$). The lesioned rats do show a tendency to spend more time away during both acquisition and extinction but this difference did not reach significance ($F = 3.6$, $.05 < p < .1$). Further tests indicate that lesioned rats spent more time away during extinction ($F = 8.1$, $p < .05$) but not during acquisition. This difference is opposite to that seen in the small operant chamber in Experiment 1, where control rats spent more time away during extinction than did lesioned rats. A comparison of time away during extintion between Experiments 1 and 2 indicates that control rats do not differ in amount of time spent away from the lever and food cup ($F < 1$) but lesioned rats spent more time away in the large enriched environment than in the small operant chamber ($F = 14.3$, $p < .005$).

Sequential patterns for major responses:

The major responses with respect to the imposed schedule requirements are lever press, food cup check and trip away from lever and food cup area. The frequency of bouts of major responses and the frequency of transitions between these responses are presented in Figure 16.

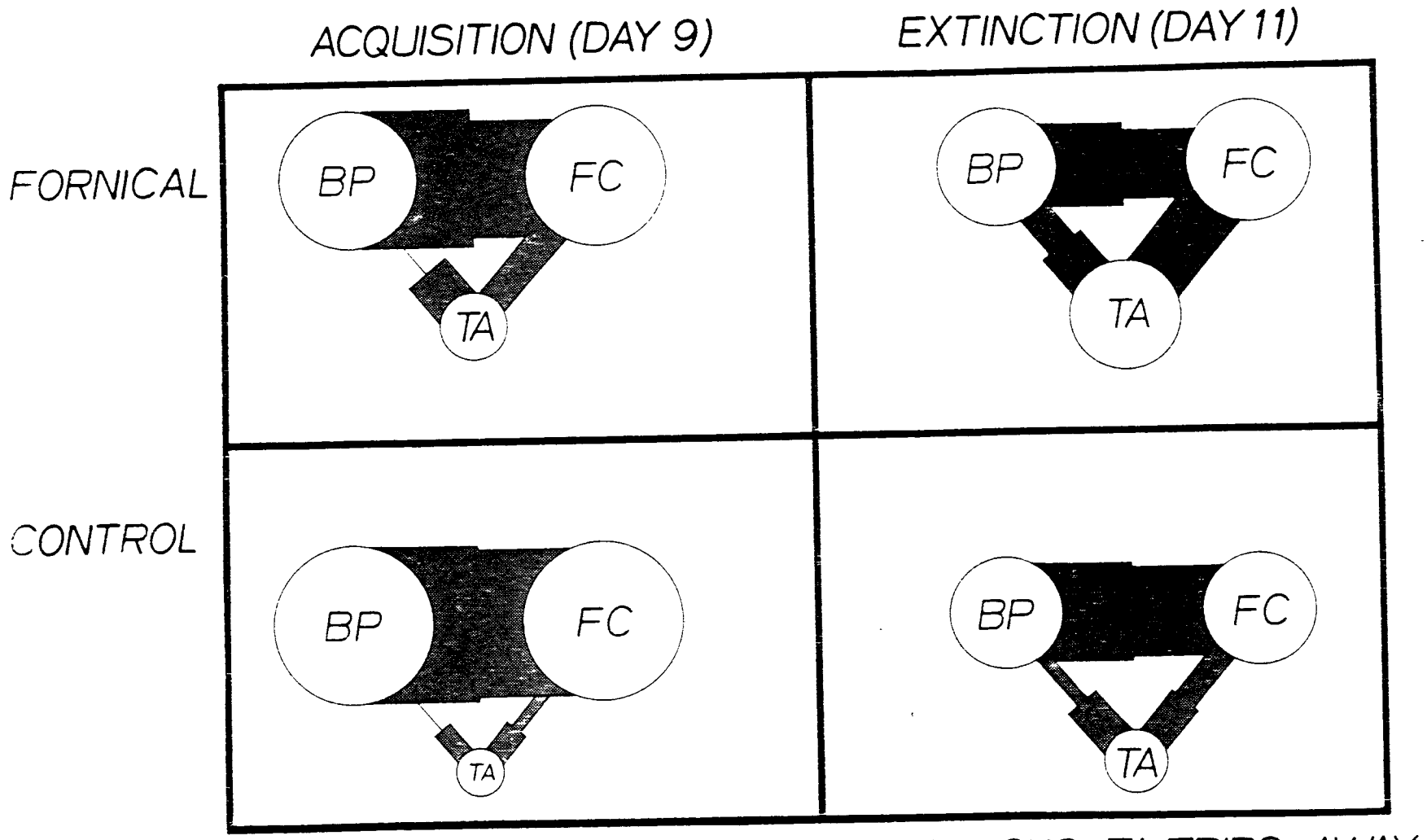
The behaviour of control rats during acquisition was "efficient" with respect to the schedule requirements. Lever presses are followed by movement to the food cup, food cup checks by movement back to the lever, and trips away are small in proportion to food related behaviours. In extinction, the control rats decrease the frequency of food related behaviours, increase the frequency of trips away and transitions between behaviours tend to be more random.

The behaviour of the lesioned rats was less structured than that of controls in both acquisition and extinction (the frequency of bouts and of transitions are more equally represented), but particularly in extinction.

This description is supported by information analyses of the first and second order predictability of responses. Separate information analyses were performed for each rat in both acquisition and extinction. These data are presented in Figure 17. As is evident from Figure 17, the behaviour of the fornix lesioned and control rats became more random in extinction, but lesioned rats were more random in both first and second order predictability measures during acquisition and extinction. Analyses of variance with lesion (lesioned vs. control) and condition (acquisition vs extinction) as the main factors

Figure 16

Sequential patterns of major responses for fornix lesioned and control rats during acquisition and extinction in the enriched experimental environment. The area of the circle is proportional to the frequency of bout initiation. The band widths are proportional to the frequency of transitions (see text for details).



BP-BAR PRESS BOUTS FC-FOOD CUP CHECKS TA-TRIPS AWAY

Figure 17

Information analyses of major response sequences during acquisition and extinction in the enriched experimental environment for fornix lesioned and control rats. First and second order analyses were performed on the behavioural sequences of each rat; group means are presented and compared to random performance.

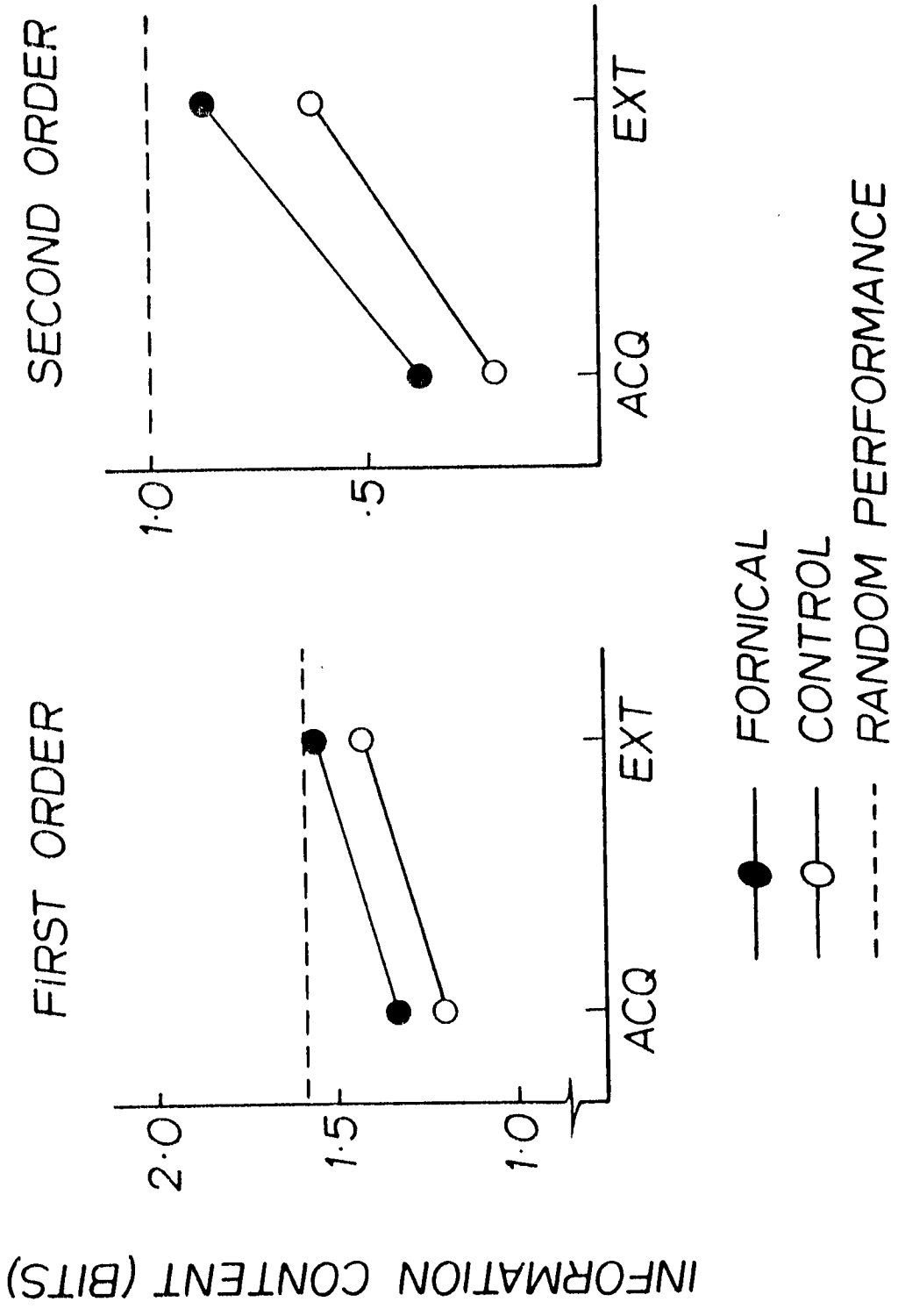
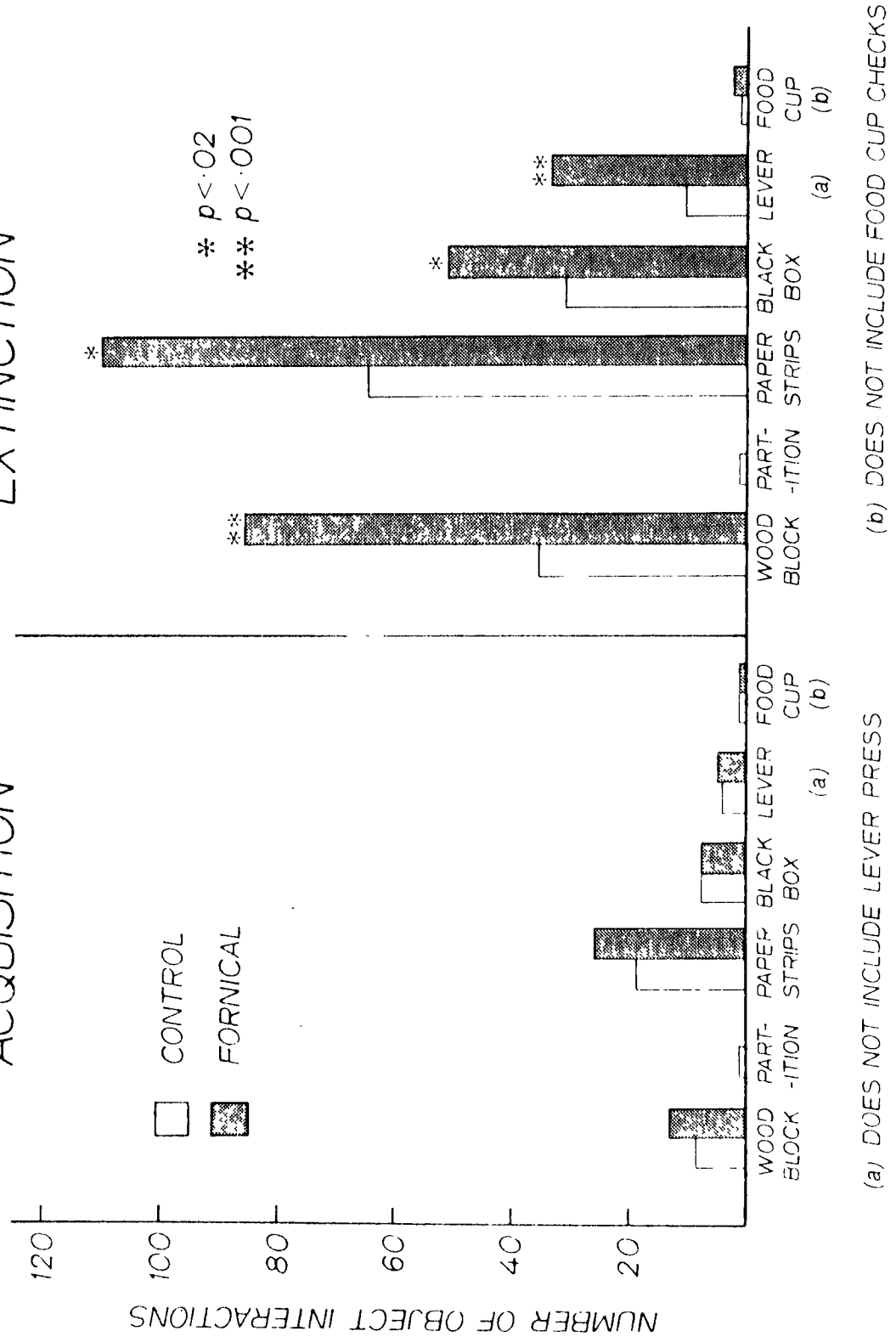

SECOND ORDER
FIRST ORDER
1·0
·5
ACQ
EXT
2·0
1·5
1·0
ACQ
EXT
FORNICAL
CONTROL
RANDOM PERFORMANCE
INFORMATION CONTENT (BITS)

Figure 18

Mean frequencies of interactions with objects in the experimental environment during trips away. These data are collapsed across identical objects in different locations and across different intensities of interactions. Lever presses and food cup checks are not included since they by definition end a trip away; however, food cup or lever interactions that do not fit the definition of lever press or food cup check are included.



(a) DOES NOT INCLUDE LEVER PRESS

(b) DOES NOT INCLUDE FOOD CUP CHECKS

yielded significant effects of lesion ($F = 46.6$, $p < .001$; $F = 79.5$, $p < .001$) and condition ($F = 118.2$, $p < .001$; $F = 195.0$, $p < .001$) for both first and second order measures, respectively.

Behaviours emitted during trips away:

Behavioural interactions with objects in the experimental environment were analyzed with respect to frequency of occurrence, quality, and temporal and sequential order. The Mann-Whitney U statistic ($\alpha = .05$) was employed in these analyses.

Rats with fornix lesions did not differ from control rats on any measure of object interaction during acquisition. The transition to extinction, however, resulted in differences between lesioned and control rats on the four measures of object interactions listed above.

The mean frequencies of object interaction, collapsed across identical objects in different locations, are presented in Figure 18. Lesioned rats showed significantly more object interactions than controls for four of the six object categories. Lesioned rats had more total time away during extinction than did controls, but accumulated this time away by making significantly more trips of significantly shorter duration. This pattern resulted in lesioned rats interacting with more objects per minute (fornical 19.6, control 11.3, $U = 2$, $p < .002$) but fewer objects per trip (fornical 3.5, control 5.5, $U = 20$, $p < .05$).

The increase in rate of emission of object interaction can be accounted for in terms of the quality and duration of these behaviours.

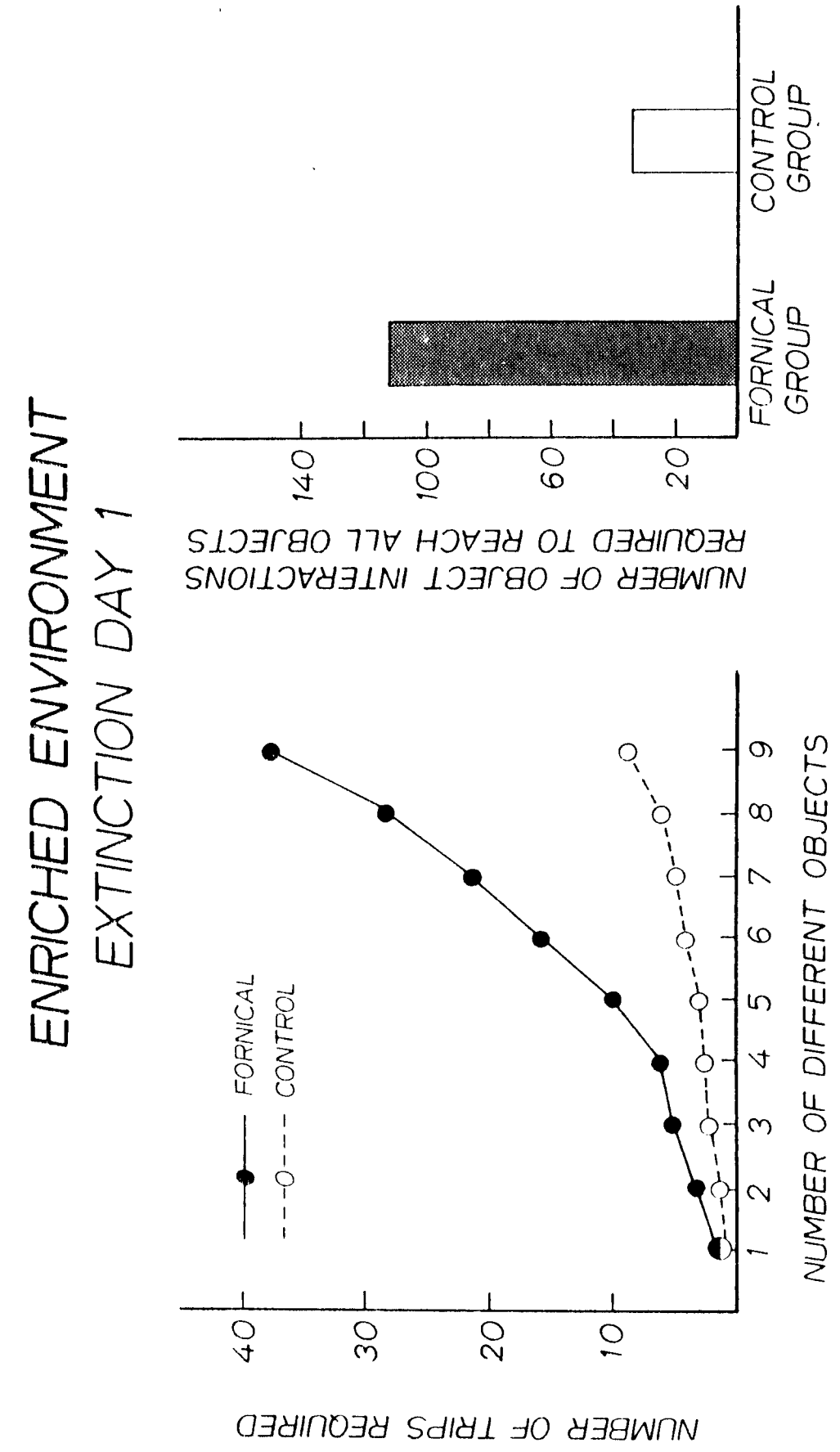
The frequency of lower quality interactions (those involving approach, approach and nose, or brief contact) were significantly greater for lesioned rats. There were no differences between lesioned and control rats in the frequencies of higher quality categories (involving long contact and/or manipulation) but the duration of those behaviours were greater for control rats (for example contact with the paper strips averaged 3.6 seconds for controls and 1.9 seconds for lesioned rats, $U = 9$, $p < .01$).

Jumping and climbing behaviour during extinction often involved interactions with objects but were analyzed separately as they appeared to be attempts to escape the experimental environment. These behaviours were made almost exclusively by controls (controls $\bar{X} = 3.8$, fornical $\bar{X} = 0.5$, $U = 14$, $p < .05$).

Interactions with objects in the experimental environment during extinction also differed with respect to temporal and sequential order. Temporal order data for both groups are presented on the left panel of Figure 19. These data represent cumulatively the number of trips required to interact with N different objects (N = 1-9). As is evident from this figure, lesioned rats required many more trips away from the bar and food cup area before interactions with all objects had occurred. Analysis of variance with number of objects explored and lesion as the main factors revealed significant effects of lesion ($F = 11.5$, $p < .005$), of object number ($F = 21.2$, $p < .001$) and a significant lesion X object interaction ($F = 9.4$, $p < .001$). The total number of objects interacted with during this time is presented in the right panel of Figure 19. Lesioned rats required significantly more

Figure 19

Cumulative number of trips required to interact with the different objects in the experimental environment during extinction day 1 (left panel) and total number of objects interacted with before all objects were reached (right panel).


ENRICHED ENVIRONMENT
EXTINCTION DAY 1
FORNICAL
CONTROL
NUMBER OF TRIPS REQUIRED
40
30
20
10
1 2 3 4 5 6 7 8 9
NUMBER OF DIFFERENT OBJECTS
NUMBER OF OBJECT INTERACTIONS
REQUIRED TO REACH ALL OBJECTS
140
100
60
20
FORNICAL GROUP
CONTROL GROUP

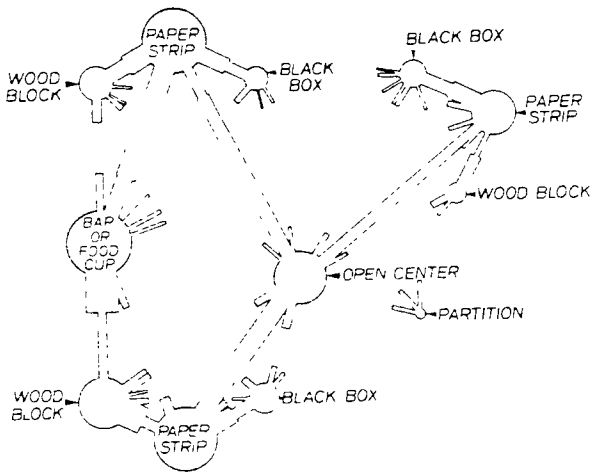
object interactions than did controls ($U = 9$, $p < .005$) to reach all objects. Since the lesioned rats made significantly more object interactions during this time, the temporal order differences do not simply reflect the short trip duration of the lesioned rats.

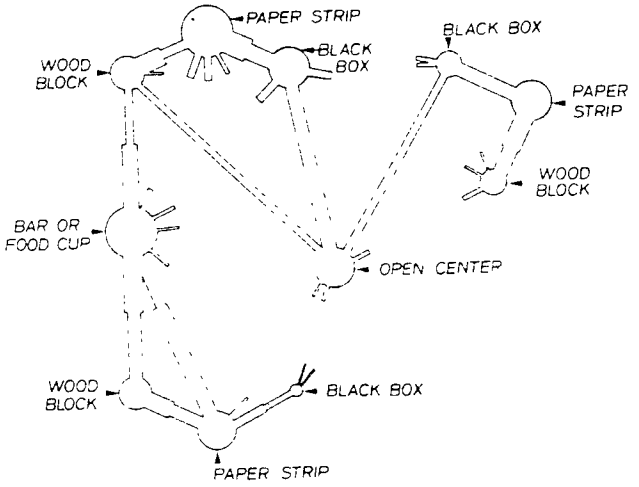
The differences in temporal order during the extinction session can be understood by considering the differences in the sequential behavioural patterns between the groups. The sequential patterns were analyzed using information analyses. Frequency of interactions with all objects and frequency of transitions between objects were obtained for each rat. Representative data for two lesioned and two control rats are presented in Figure 20. Frequency of interactions is represented by the size of the circles; frequency of transitions by the width of the adjoining bands. The circles are arranged to approximate the actual spatial arrangement of the objects in the experimental environment. Control rats tended to interact with all objects equally but exhibited predictable sequential patterns. The transition data show spatial clustering with transitions primarily directed toward adjacent objects. The lesioned rats, unlike the controls, exhibited a large number of interactions with certain objects and neglected others. The patterns differed for different lesioned rats but in all rats the bar and food cup was the dominant choice. In fact, the behaviour of the lesioned rats tended to be structured around the bar and food cup. The lesioned rats, like controls, showed predictable transitions but the predictability was derived from the tendency of lesioned rats to return to the bar and food cup regardless of the previous behaviour or location of the rats.

Figure 20

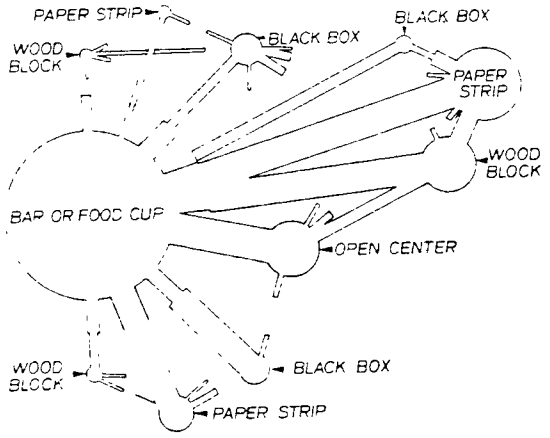
Sequential patterns of behaviours emitted during extinction in the enriched environment for two lesioned and two control rats. Only major transition paths are connected, less frequent transitions are represented by broken bands. Note the structuring of the behaviour of the lesioned rats about the bar and food cup and the relative neglect of these by controls.

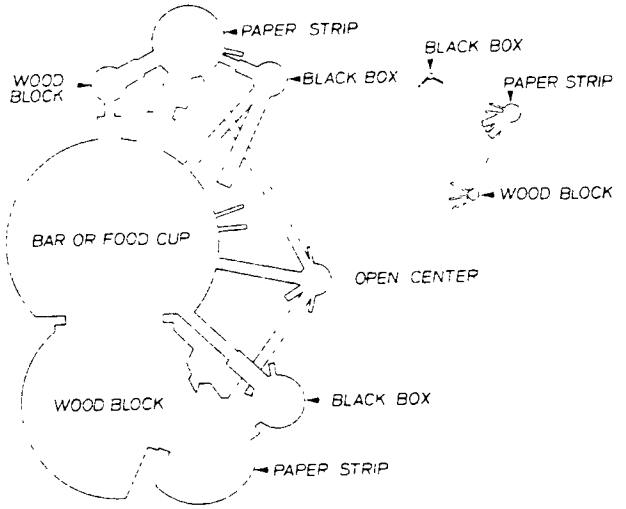
CONTROL





FORNICAL





These descriptions were supported by information analyses of first and second order predictability. Information content was calculated for each rat for first and second order sequences and between group comparisons made with the Mann-Whitney U statistic. Lesioned rats were more predictable on first order measures ($U = 16$, $p < .02$) but did not differ from controls on second order measures ($U = 38$, $p > .1$).

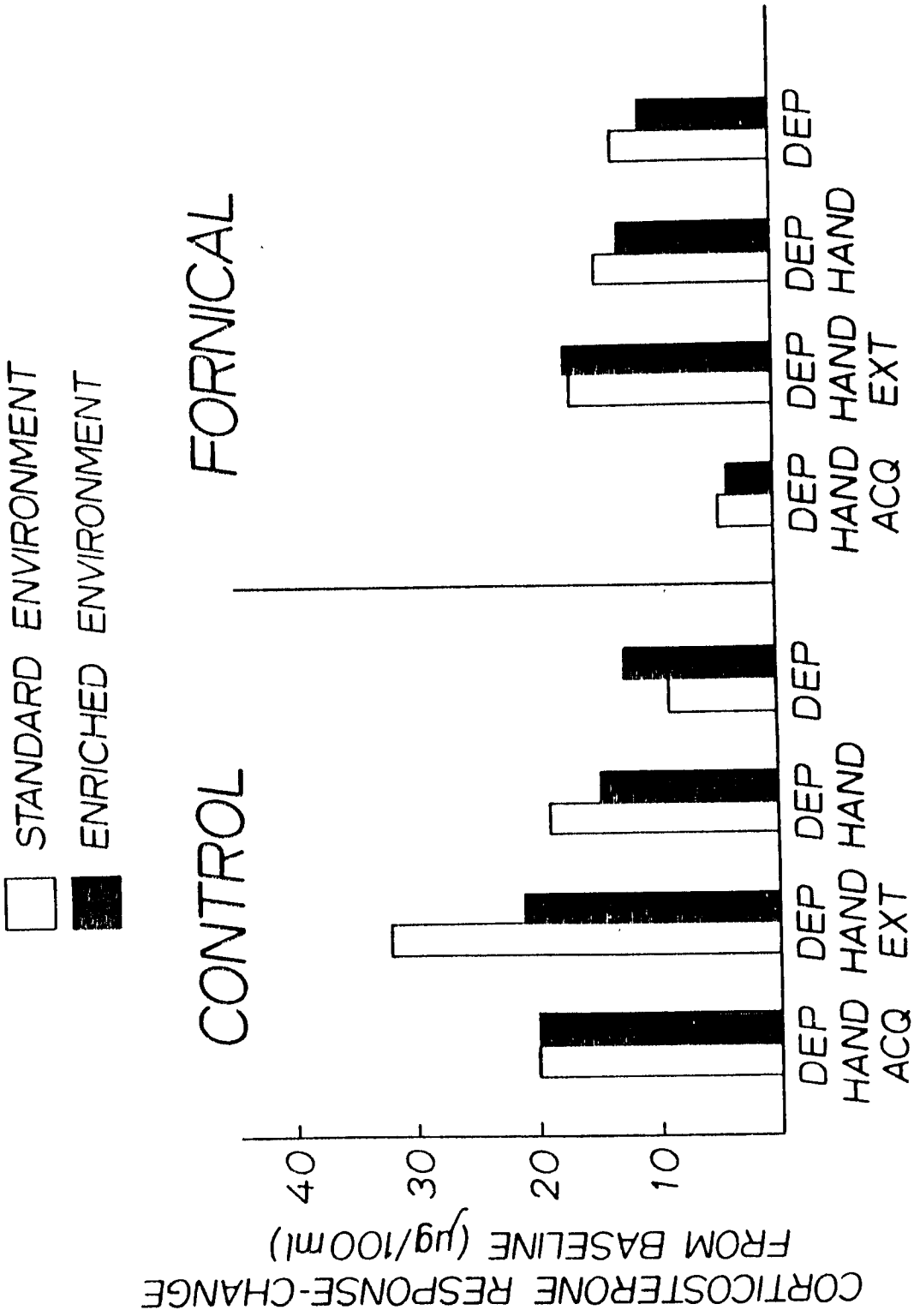
Corticosterone

The mean corticosterone responses of lesioned and control rats are presented in Figure 21. Although analyses were performed on the raw data, the figure presents the increase in corticosterone in response to the experimental treatments (i.e., the difference between the treatment level and non-stimulated basal level). The corticosterone levels from the different phases of Experiment 1 are also presented for comparison.

The response profile of the lesioned rats was similar to that exhibited in Experiment 1. Deprivation, deprivation plus handling and/or extinction increased corticosterone levels and acquisition decreased corticosterone toward basal values. For the control rats, the response profile differed from that of Experiment 1 most notably in the absence of the large corticosterone increase during extinction. The control responses with the exception of the high corticosterone levels during acquisition were similar to those of the lesioned rats. Analysis of variance with lesion and treatment condition as the main factors yielded a significant effect only for treatment conditions($F = 8.14$, $p < .001$); there was no effect of lesion ($F < 1$) nor was there a lesion X treatment interaction ($F = 1.9$, $.05 < p < .1$). Subsequent

Figure 21

Mean plasma corticosterone responses of lesioned and control rats to the experimental treatments and control conditions. Experiment 1 data are also presented for comparison. These data represent the response over the non-deprived basal levels (for example, DEP is the response to deprivation, deprived levels - non-deprived basal levels).


STANDARD ENVIRONMENT
ENRICHED ENVIRONMENT
CONTROL
FORNICAL
CORTICOSTERONE RESPONSE-CHANGE FROM BASELINE (μg/100ml)
40
30
20
10
DEP HAND ACQ
DEP HAND EXT
DEP HAND
DEP
DEP HAND ACQ
DEP HAND EXT
DEP HAND
DEP

individual Neuman-Keuls comparisons ($p < .05$) confirmed the above description. There were increased corticosterone levels over the non-deprived basal levels for all treatments. The only significant difference between treatments was a decrease in corticosterone levels during acquisition in the lesioned rats.

Correlations between the corticosterone response to the extinction procedure and measures of behavior during extinction were calculated. For the control group, as in Experiment 1, significant negative correlations were found for biting the lever ($r_s = -.74$, $p < .025$) and lever press bout length ($r_s = -.83$, $p < .01$) but a positive correlation was found for object interactions ($r_s = .6$, $p < .05$). There were no significant correlations between the corticosterone response and behaviour for the lesioned rats.

Discussion

Bindra (1961) suggested that an exact and meaningful analysis of a learning task is likely to occur only if the components of general activity in the specific task context are taken into consideration. The results of the present experiment emphasize the importance of the specific environmental context in which the learning task is performed. Even though the task requirements remained constant between Experiment 1 and the present experiment, the independent manipulation of experimental environment resulted in dramatic shifts in some components of the behaviour of both lesioned and control rats, while other components remained relatively unchanged. More importantly, the specific components that changed and those that remained constant

differed between lesioned and control rats[3].

During acquisition, the behaviour of both lesioned and control rats in the present experiment was very similar to that seen in Experiment 1. Lesioned rats again received fewer reinforcements during acquisition than did controls. This difference may be accounted for by the more "efficient" behaviour of control rats both with respect to the sequential organization of major responses and the amount of time required to consume each reinforcement. The only observed difference in acquisition between experiments was that control rats in the enriched environment were slower to adopt the typical asymptotic acquisition response patterns during the early acquisition sessions. Wong (1977) reported that during appetitive acquisition in an enriched environment, normal rats engage in collateral behaviour and that this collateral behaviour diminishes with continued training. It seems likely that the response pattern of the control rats during early acquisition represents competition between exploration and task behaviour in the early sessions. This tendency for controls to engage in collateral behaviour together with the indistractability of rats with hippocampal damage (Raphelson et al., 1965; Cohen, 1970) would account for the differences described above.

During extinction there were instructive differences and

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[3]It is recognized that ideally the experimental environment manipulation should be a within rather than between experiment variable. Although it seems unlikely, some additional uncontrolled variable may have contributed to the observed differences. Consequently, conclusions based on these comparisons should be considered tentative rather than conclusive.

similarities between the present results and those of Experiment 1. From the detailed analysis, one could conclude that lesioned rats again exhibited an extinction deficit. Relative to control rats, the lesioned rats maintained food related behaviours (lever press and food cup checks) and, in general, showed smaller changes in behaviour. When the traditional measure of total lever presses is considered, however, lesioned rats did not show an extinction deficit.

These different measures lead to apparent contradictory conclusions only if one considers extinction to involve a single process. The detailed measures suggest that this is not the case. Control rats exhibited two distinctly different types of responding during extinction both in the present experiment and in Experiment 1. Initially, control rats maintained the mode of responding present during acquisition. Following continued nonreinforcement of the acquisition operant, control rats then switched into altered response topographies interspersed with exploratory bouts of the experimental environment. Lesioned rats did not exhibit the flexibility of controls, but, in general, continued to respond in the acquisition mode. This difference is most clearly seen in the distinction between regular and biting responding. Control rats initially exhibited regular presses (the topography of acquisition), but as the extinction session continued, there was a progressive increase in biting responses (a response topography never seen during acquisition). Fornix lesioned rats, in contrast, showed greater maintenance of regular pressing and did not exhibit biting responses. Support for this distinction in modes is also seen in the greater tendency of control rats to exhibit

bursts of responding as evidenced by the greater decrease in frequency of lever press bouts and increase in bout durations for controls during extinction. Evidence for exploratory bouts for control but not lesioned rats comes from the longer trip durations for controls and the many quantitative and qualitative differences between groups in the patterns of object interactions during extinction.

When extinction responding in the standard operant chamber and in the enriched environment are compared, one can conclude that the extinction environmental manipulation only affected the first type of responding. Extinction in the enriched environment simply lowered the number of responses for lesioned rats. Extinction in the enriched environment also lowered the number of responses of this first type for controls as it did for lesioned rats, but did not affect the amount of responding of the second type. Consequently the traditional measure of total lever presses shows an extinction deficit in Experiment 1, but not in the present experiment.

The behaviour of control rats in the present experiment was consistent, at least descriptively, with a recent model of extinction proposed by Wong (1978). Wong's model differs from current S-R theories (Capaldi, 1967; Amsel, 1972) in that it was based on detailed behavioural analyses and emphasizes disconfirmation of expectancies and concomitant new learning (factors which Mackintosh (1974) points out as the failure of current S-R theory). Wong's model depicts three qualitatively different stages during extinction. The first stage (habit) involves invigorated repetition of the previously reinforced response and is considered to be automatic. The habit phase is then

followed by a trial and error strategy characterized by response topography changes (initially within the operant class and later outside) and the initiation of exploration and aggression. These behavioural changes then tend to diminish in the later resolution phase, the characteristics of which are less clear, but involve increased avoidance and an increase in other consummatory behaviours or inactivity.

Not only is the behaviour of control rats in agreement with the conceptualization, but within this framework, the correlations between behavioural and corticosterone responses to extinction in the present series of experiments no longer seem anomalous. For controls in the small operant chamber of Experiment 1, the acquisition mode of responding was positively related to the corticosterone response, the altered mode was negatively related to the corticosterone response, and the corticosterone levels were significantly elevated. In the enriched environment of the present experiment, the controls decreased first mode responding, maintained the altered mode, the corticosterone levels were no longer significantly elevated but the residual corticosterone levels were again negatively related to the amount of responding in the altered mode. These data suggest that corticosterone increases result from the violation of the expectation of reinforcement; and the magnitude of the response is related to both the degree to which the rat maintains the habitual response mode (i.e. receives negative feedback) and the degree to which he engages in altered "coping" behavioural strategies..

The behaviour of fornix lesioned rats was not consistent with Wong's model. The lesioned rats did not appear to exhibit exploratory bouts during extinction, nor did they show the behavioral flexibility of altered mode responding, the corticosterone response or the behavior-corticosterone relationships. In contrast, the lesioned rats, in Wong's terminology, appeared to exhibit only the habitual automatic first stage behavior. In this respect, the extinction behavior of lesioned rats in the present experiment was very similar to that exhibited by lesioned rats in the standard operant chamber of Experiment 1.

Extinction in the large, enriched experimental environment did, however, result in the lesioned rats making fewer lever press responses in comparison to lesioned rats of Experiment 1. This difference can best be understood by examining the organization of the behavior of lesioned rats. In both experiments, the extinction behavior of lesioned rats was essentially random with respect to task defined behaviors; food related behaviors are interrupted by a high frequency of trips away from the lever and food cup (see Figures 6 and 16). Although the frequency and sequential nature of the trips away are comparable between experiments, this pattern resulted in the lesioned rats in the large experimental environment spending significantly more time away then lesioned rats in the small operant chamber (i.e. each trip takes up more time in the large environment of Experiment 2). Consequently, lesioned rats in the large environment have approximately 40% less time at the bar and food cup. It is suggested that this difference alone may account for the difference between experiments in

number of lever presses exhibited by lesioned rats during extinction.

Experiment 3

During extinction, in the previous experiment, lesioned and control rats differed in the organization of their behavioural interactions with objects in the enriched experimental environment. Control rats made fewer but longer duration trips from the bar and food cup. During these trips, control rats initiated more object interactions per trip, and their object interactions were of higher quality. The patterns of these interactions also differed; they were structured with respect to the spatial arrangement of objects for controls, but with respect to the lever and food cup for lesioned rats. It was concluded from these data that the novelty of the transition to extinction resulted in controls but not lesioned rats initiating bouts of exploration.

Alternative explanations of these results are possible. For example, the novelty of the transition to extinction could have resulted in exploratory bouts for both groups, but with lesioned and control rats exhibiting qualitatively different exploratory patterns. Hippocampally damaged rats have previously been reported to differ from normal rats during exploration (for examaple, Kimble, 1963; Teitelbaum and Milner, 1963; Strong and Jackson, 1970). However, these experiments employed the number of grid crossings or photocell interruptions as behavioral measures. On the basis of these indirect activity measures and anecdotal reports (Kimble, 1963; O'Keefe and Nadel, in press), hippocampally damaged rats are considered to be

hyperactive but hypoexploratory, exhibiting more but less directed activity. Comparable data to those of Experiment 2 are not available.

The present experiment was designed to examine the above alternatives by providing data on the exploratory behavior patterns for both fornix lesioned and control rats during initial exposure to the experimental environment of Experiment 2. If the transition to extinction elicits exploration in controls but not in lesioned rats, as suggested in Experiment 2, then the exploration patterns in the present experiment should be similar to those during extinction for control rats but dissimilar for lesioned rats. Any other pattern of results for the present experiment would not support the interpretation offered in Experiment 2. In addition, the recording of the actual behavior patterns during exploration in the present experiment should more directly address the issue of whether hippocampally damaged rats are hypoexploratory in addition to hyperactive. Evidence for hypoexploratory behavior in lesioned rats would be decreased frequency and quality of interactions with objects in the experimental environment, as well as, alterations in temporal and sequential behavior patterns.

Methods

Subjects:

Thirteen experimentally naive, male hooded rats of the Long-Evans strain obtained from Canadian Breeding Farms, St. Constant, Quebec, were used. At the time of surgery the rats weighed 200-250 g. Nine of the rats received total fornix transection, four were operated controls.

Apparatus:

Testing was carried out in the large chamber used in Experiment 2 and described previously. The chamber was located in a sound attentuated room under constant lighting and 70 db white noise.

Procedure:

Housing conditions, surgical, deprivation and histological procedures were the same as Experiment 1 and 2.

The testing procedure consisted of placing the rats in the large chamber for a ten minute period. Ten minutes approximates the amount of time spent away from the lever and food cup in Experiment 2. All rats were placed in the center of the chamber facing the rear. As in previous experiments the chamber was cleaned and the floor washed between animals.

Video-analysis:

The ten minute exploration period was videotaped using a Sony Viewfinder camera and Sony AV-3600 recorder.

Behaviours directed toward the experimental environment were used as an index of exploratory behaviour. As in Experiment 2 these behaviours were analyzed in terms of frequency of occurrence, quality, temporal and sequential order. The rating for quality of interactions was the following:

1. orient and approach
2. nose, sniff but no contact
3. brief contact (< 1 sec)
4. long contact (> 1 sec)
5. manipulatory (biting or pawing object).

Results

Histology:

All nine lesioned rats received complete fornix transections; none of

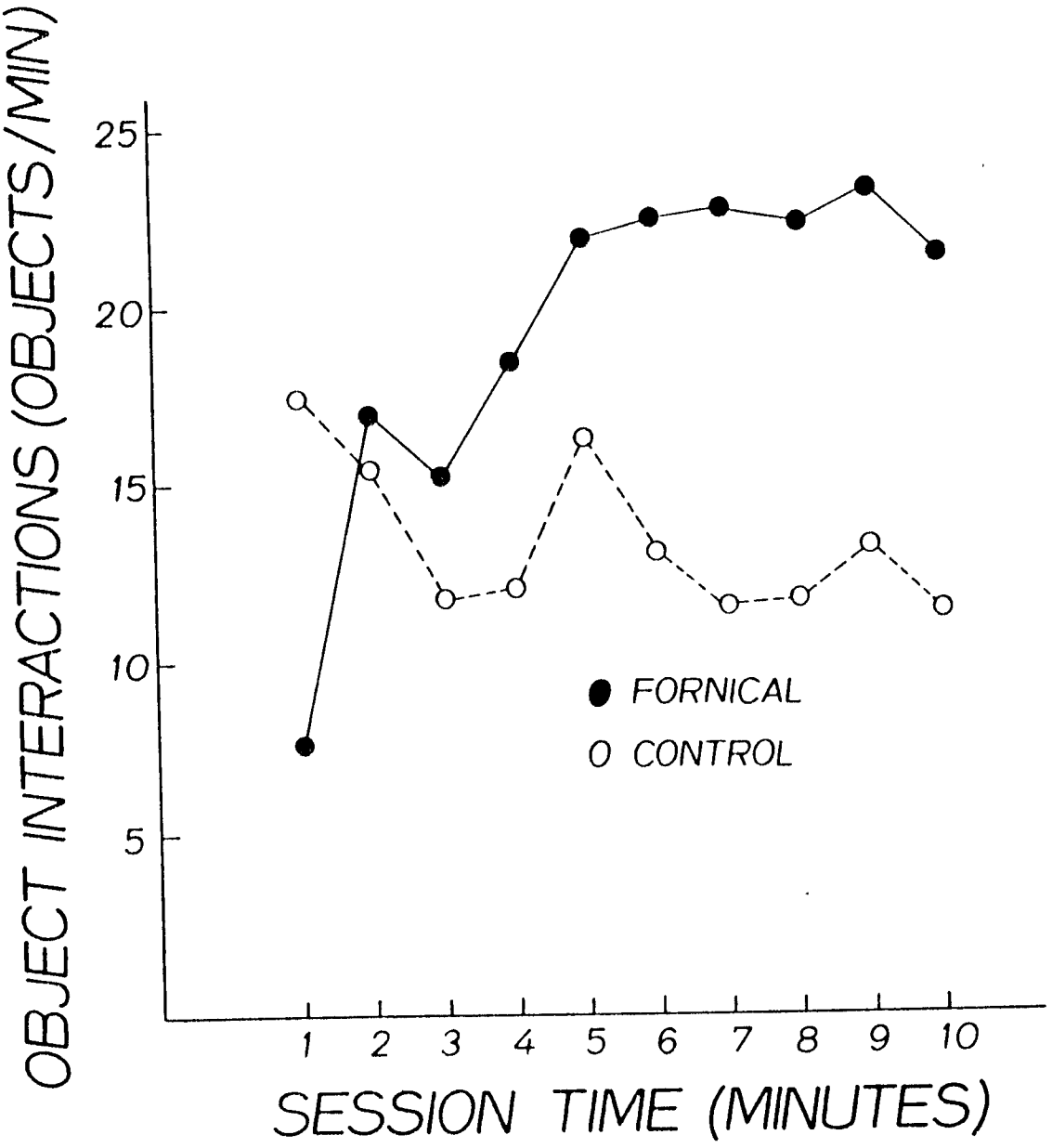
the operated controls received fornix damage. Extra-fornical damage to the lesioned rats included partial damage to stria medullaris in two, complete damage to stria medullaris in four, partial damage to stria terminalis in six, complete stria terminalis damage in two and slight unilateral cortical damage in all rats. The operated controls received no extra-fornical damage with the exception of slight unilateral cortical damage.

Behaviour:

Exploratory behaviour of the rats was quantified by measuring the number of interactions the rats made with objects in the experimental environment. The number of object interactions collapsed across all objects and all quality categories as a function of time in the novel environment are presented in Figure 22 for both lesioned and control rats. As is evident from the figure, both lesioned and control rats interacted with objects in the experimental environment, but the frequency of interactions was greater for lesioned rats. Control rats showed a slight tendency to decrease the frequency of interactions with time in the environment, while lesioned rats increased their frequency of interactions. Analysis of variance of the interaction data with lesion and time in the environment as the main factors yielded a significant effect of lesion ($F = 5.4$, $p < .05$) and a significant lesion X time interaction ($F = 3.5$, $p < .005$). The lower frequency of interactions of the lesioned rats in comparison to controls in the first minute may have resulted from the tendency of lesioned rats to freeze on being placed in the novel environment. Lesioned rats had a mean of 14 seconds that they were freezing and controls only 4 seconds, but these differences did not reach significance (Mann-Whitney-Wilcoxon $T_X = 17.5$, $.1 < p < .15$, two tailed).

Figure 22

Mean frequency of interactions with objects during initial exposure to the enriched environment as a function of time.


OBJECT INTERACTIONS (OBJECTS/MIN)
25
20
15
10
5
FORNICAL
CONTROL
1
2
3
4
5
6
7
8
9
10
SESSION TIME (MINUTES)

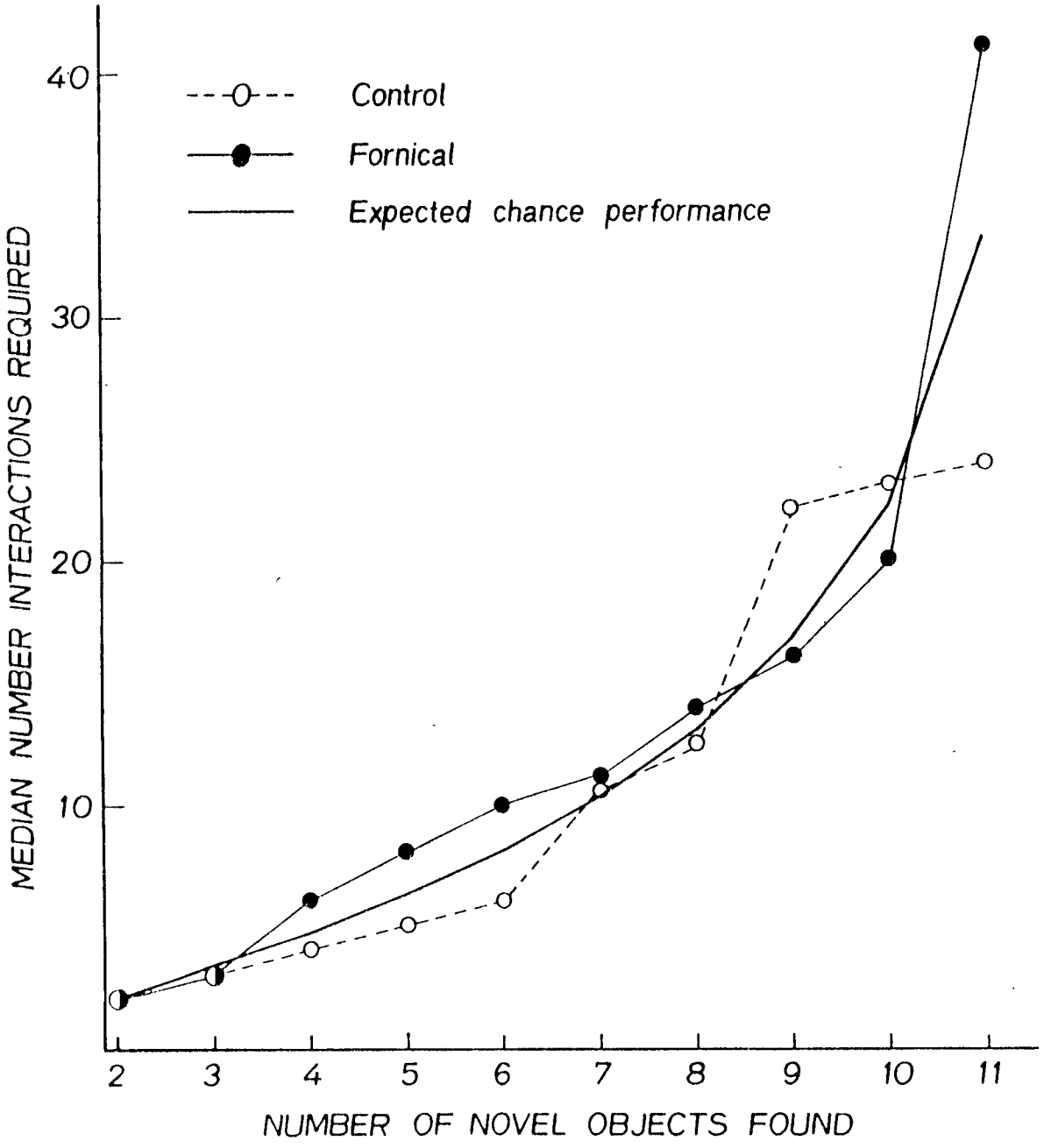
Since the above data represent pooled interactions of all qualities across all objects, these results could have been obtained by different types of interactions between the groups. Therefore, different object categories and different qualities of interactions were examined separately. Lesioned rats were found to interact with all objects more frequently than controls. The increased frequency of interactions was significant only for the food cup (Mann-Whitney-Wilcoxon, T_X = 13.5, $p < .04$, two tailed) but approached significance for both wood blocks and paper strips.

The object interactions were rated into separate quality categories (see Methods for categories) but for analysis these categories were combined into those of short duration (approach and/or nose and/or brief contact) and those of longer duration (long contact and/or manipulations). Lesioned rats were found to exhibit more interactions of short duration (T_X = 15, p = .05, two-tailed) but no differences between groups were found for frequency of longer durations interactions. While the frequency of these longer duration initiations did not differ, their durations were shorter for lesioned rats. For example, paper strip interactions were the most frequent for both lesioned and control rats, but lesioned rats spent significantly less time in actual contact with the paper (Mann-Whitney-Wilcoxon, T_X = 40, p = .038).

The temporal and sequential order of the rats' behaviour were also examined. Temporal order data for both groups are presented in Figure 23. These data represent cumulatively the median number of interactions required to locate each of the novel objects in the experimental environment. An object was considered novel only if it had not been interacted

Figure 23

Cumulatively, the median number of interactions required by lesioned and control rats to interact with objects on first exposure to the enriched environment. Theoretical values for chance interactions (based on geometric distribution) with objects are presented for comparison purposes.

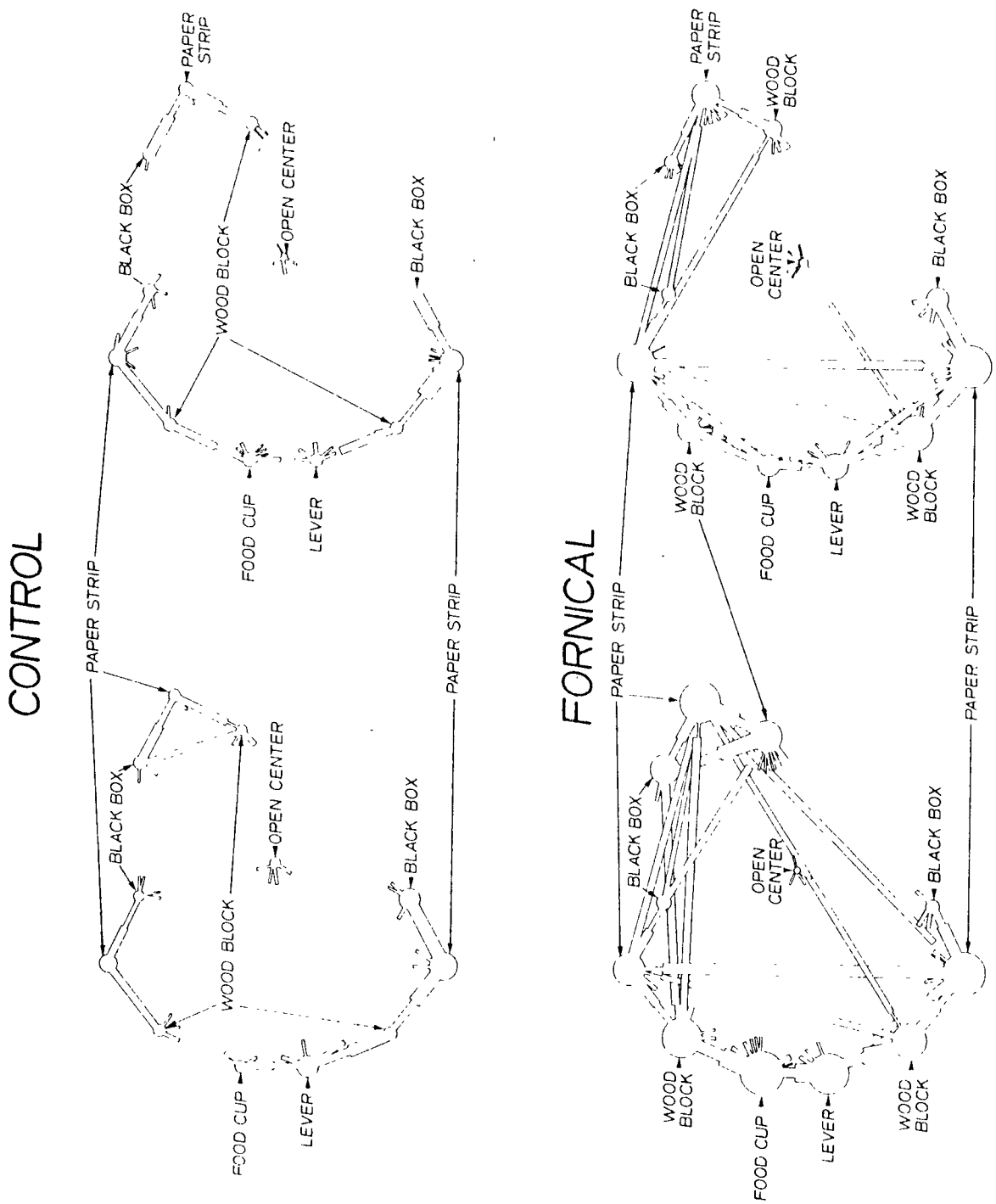

Control
Fornical
Expected chance performance
MEDIAN NUMBER INTERACTIONS REQUIRED
40
30
20
10
2
3
4
5
6
7
8
9
10
11
NUMBER OF NOVEL OBJECTS FOUND

with previously. Using this definition, the rat could exhibit a tendency to seek novel objects, to repeat interactions with familiar objects, or encounter objects on a more or less random basis. Examination of Figure 23 indicates that both lesioned and control rats tend to do the latter; their cumulative data tend to oscillate about the theoretically expected values for chance interactions with novel objects. The reasons for using medians in the present case is because one lesioned rat met the criteria for a statistical outlier on six of the ten points plotted, and, thus, medians were considered to be more representative of group performance than were means. The groups were compared at each point (including the aberrant lesioned rats data) using the Mann-Whitney-Wilcoxon statistic ($p = .05$, two-tailed). The groups were significantly different at only two of the ten points, both indicating a slight tendency for lesioned rats to repeat interactions with familiar objects. The total number of interactions required by control and lesioned rats to interact with all objects were compared to the data for extinction (the data of Experiment 2). The present data of control rats did not differ from extinction data of controls ($t = 1.16$, $p < .05$) but lesioned rats required more interactions during extinction than did lesioned rats during exploration ($t = 4.4$, $p < .01$).

Sequential order or patterning in the exploration data was analyzed using information analyses. Frequency of interactions with all objects and frequency of transitions were obtained for each rat; representative data for two lesioned and two control rats are presented in Figure 24. Frequency of interactions is proportional to the size of the circle and frequency of transition between objects is proportional to the width of the adjoining bands.

Figure 24

Sequential patterns of behaviours emitted during first exposure to the enriched environment for two lesioned and two control rats. Frequency of interactions are proportional to circle size, frequency of transitions to band widths. Only major transition paths are connected, less frequent transitions are represented by broken bands.


CONTROL
PAPER STRIP
BLACK BOX
WOOD BLOCK
OPEN CENTER
FOOD CUP
LEVER
FORNICAL
PAPER STRIP
BLACK BOX
WOOD BLOCK
OPEN CENTER
FOOD CUP
LEVER

As the figure indicates, control rats tended to interact with all objects more or less equally but exhibited predictable sequential patterns. The transition data show spatial clustering with transitions primarily directed toward adjacent objects. Lesioned rats, in contrast, tend to exhibit slight preferences for some objects and the transitions between objects are more random. This description was supported by information analyses on first and second order predictability. First order analyses give an estimate of the predictability of the rat's behaviour based on the relative probabilities of the behaviours themselves; second order analyses give estimates based on the predictability of a response given that another response has occurred. Separate information analyses were performed on each rat. Control rats were more predictable than lesioned rats on second order measures (Mann-Whitney-Wilcoxon, $T_X = 16$, $p = .04$) and tended to be more random on first order measures but this difference only approached significance (Mann-Whitney-Wilcoxon, $T_X = 38$, $p = .07$).

The behaviour of the rats during ten minutes exposure to the novel environment may be summarized as follows. Control rats approach, nose, contact and manipulate all objects in the environment. Their interactions appeared to be random with respect to the objects (first order information analyses) and to whether or not the objects had been subject to previous interactions (temporal analyses), but were structured with respect to sequential choice (second order information analyses) and tended to decline across the session. Lesioned rats exhibited similar behaviours as controls. Lesioned rats differed from controls, however, in that 1) the frequency of interactions was higher and did not decline during the session 2) there was a tendency for preference both for certain objects and for

objects interacted with previously and 3) there was less predictability in their behaviour sequences.

Discussion

In order to compare the behavioural organization in the present experiment with that in extinction, it is useful to distinguish two separate types of differences. The first type concerns differences between lesioned and control rats that were present during both exploration and extinction. The second, and more important type, concerns differences between the organization of behaviour in exploration and in extinction.

Among the differences between lesioned and control rats that were observed in both situations are the following. In both exploration and extinction lesioned rats, unlike controls, did not interact with all objects equally (some objects were preferred, others neglected). Lesioned rats, however, initiated more object interactions, but these interactions in exploration, as in extinction, were of lower quality and shorter duration.

Differences in the behavioral organization between situations occurred almost exclusively in lesioned rats. Control rats, in addition to the behaviours listed above, did not differ between exploration and extinction in either their temporal patterning of object interactions or in their sequential organization. The only observed difference in environment interaction in controls between situations was the absence of "emotional" behaviours (jumping, climbing, etc.) during exploration. Lesioned rats, in contrast, differed in both temporal and sequential organization of behaviour between exploration and extinction. Both of these differences appear to reflect experience-related structuring of the lesioned rat's

behavior during extinction. The temporal and sequential patterns of lesioned rats during extinction are both organized with respect to the lever and food cup area. In the absence of special significance for the food cup and lever, lesioned rats during exploration are similar to controls in their temporal order of object interactions but more random than controls in their sequential organization. These data are consistent with the interpretation presented in Experiment 2 that non-reinforcement in extinction elicits bouts of exploration in controls but not in lesioned rats.

The present between group differences in behavior patterns during exploration are instructive when compared to other experiments that show deficits in hippocampally damaged rats in open field situations. Since in the present experiment the objects in the environment were spatially separated and lesioned rats were more random in their object to object sequencing, the higher frequency of object interactions in lesioned rats also reflects higher activity. These data, then, are in agreement with the general consensus in the literature that hippocampally damaged rats are hyperactive in open fields (Kimble, 1963; Teitelbaum and Milner, 1963; Jarrard, 1968; Strong and Jackson, 1970).

As pointed out earlier, a number of experimenters have postulated that hippocampally lesioned rats are also hypoexploratory (Kimble, 1963; Cohen, 1970; O'Keefe & Nadel, in press). The less informative activity measures (grid crossings or photocell interruptions) of most experiments cannot easily address the issue of exploration. When studies employing these measures are eliminated, one is left with only anecdotal reports of open field exploration differences between control and hippocampally lesioned

rats.[4] Kimble (1963, 1975) for example, states that lesioned rats exhibited only stereotyped repetitive running, while controls explored one area, moved to another randomly with many bursts and stops. This description of controls is close to the quantified behavioural results for controls in the present experiment. The detailed measures for lesioned rats in the present experiment do not, however, agree with subjective reports, even though the behavioural measures of the present experiment are designed especially to quantify these types of behavioural differences. In fact, lesioned rats interact with more objects in the experimental environment than do controls. The primary difference between groups was more subtle; the behaviour differed in terms of quality, duration and sequencing. These differences have been observed by the present experimenter to occur in many contexts and subjectively often give the impression that lesioned rats are 'doing nothing but repetitive running'. The data stress the importance of measuring quantifiable aspects of the rats behaviour rather than relying on subjective impressions.

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[4] Hippocampally damaged gerbils have been shown to exhibit a decrement in reactivity to novel objects placed in the home cage (Glickman et al., 1970). Glickman et al. also examined open field behaviour in this study, but unfortunately they too used grid crossings as the dependent measure.

Chapter 4

Effects of fornix lesions on the violation of an expectancy in a simple appetitive consummatory task

Experiment 4

According to Mackintosh (1974), the most important effect of appetitive reinforcers is to act as goals for instrumental responses. This goal-directing function of appetitive reinforcement was evident in the behaviour of control rats in the previous experiments. When reinforcement was withheld the control rats exhibited increased levels of corticosterone, a response demonstrated to be sensitive to violations of expectations (Levine et al., 1972). In addition, the control rats appeared to exhibit what Wong (1978) characterized as a transition from response persistence to goal-persistence. Evidence for this goal-persistence comes from the alterations in the responses exhibited by controls both within and outside the operant class and the negative relationship between these response changes and the corticosterone response. In contrast, the goal-directing function of reinforcement was not evident in the behaviour of fornix lesioned rats. During extinction, lesioned rats did not show the corticosterone elevations, the behavioural alterations or the behavioural-corticosterone relationships exhibited by controls. These data lead one to conclude that lesioned rats either do not develop expectations that their responses will result in reinforcement, or they do not exhibit the normal response to violations of these expectations once developed.

This interpretation is central to the information processing theories of hippocampal function of both O'Keefe and Nadel (in press) and Hirsh (1974), but stands in marked opposition to some of the inhibitory notions of hippocampal function based on traditional S-R learning theory (for example, Douglas, 1972). Hirsh (1974) takes the strong position that animals with hippocampal damage do not develop expectations. O'Keefe and Nadel (in press), in contrast, imply that animals with hippocampal damage can exhibit increased, decreased or normal frustrative responses (i.e., the response to the violation of an expectation) presumably dependent upon the type of task and the strategies employed by normal and lesioned animals. Hippocampally damaged animals are suggested to be able to alter their behavior appropriately when they see the reward objects or when consummatory behavior alone is considered, but should differ in tasks that have spatial components and/or involve the cognitive mapping system. It would then be useful to obtain data on the response of lesioned and control rats to the violation of an expectation in a situation not involving spatial components or prior instrumental or operant response requirements. Of course, this situation cannot be achieved but it can be approximated by moving closer to a pure consummatory behaviour. The expectation of food as a goal object for a deprived rat, for example, can be evoked by the immediately present stimuli (i.e., the sight and smell of the food) without recourse to previous experience (Tolman, 1932). The primary purpose of the present experiment was to examine the response of fornix lesioned and control rats to the violation of an expectation in this simple situation. The rats were first allowed to

eat from a food container. The consumatory response was then blocked while retaining the sight and smell of the food by placing a transparent, perforated cover on the food cup. If hippocampally damaged animals do not form expectations then the lesioned rats, unlike controls, should not respond to the blocked eating session. On the other hand, this situation would appear to meet the requirements for one in which lesioned rats, according to o'Keefe and Nadel (in press), should show normal frustrative responses. Of course, if neither lesioned or control rats respond to the blocked eating session, then this situation apparently does not involve expectations and is not an appropriate test.

A second and unrelated purpose of the present experiment was to carry out an additional control for the interpretation of the corticosterone response to extinction. The sampling procedure, itself, has been shown to be a highly potent activator of the pituitary-adrenal system (for example, Kearley et al., 1974; Lanier et al., 1975), and the extinction blood sample was by necessity taken after the rats had been previously exposed to the sampling procedure during acquisition. Although it seems unlikely, it is possible that the elevated levels of corticosterone during extinction in control rats could have been a conditioned response to the sampling procedure rather than a response to the environmental change. This possibility can be investigated by taking identically spaced samples on changed or constant environmental baselines.

Methods

Subjects:

Eighteen naive, male hooded rats, obtained from Canadian

Breeding Farms, St. Constant, Quebec were used. At the time of surgery, the rats weighed 200-250 g. Ten rats received total fornix transection; eight served as operated controls.

Procedure:

Housing conditions, surgical, deprivation, histological, blood sampling and assay procedures were identical to those of Experiments 1-3.

Training was carried out in the large chamber of Experiment 2 but with the shaping partition blocking off the lever-food cup area of the chamber. A 10 x 10 x 4 cm perforated plastic food cup containing ten Purina lab blocks (approximately 50 g) was placed in the center of the chamber at the beginning of each session.

The rats were given 18 daily 20 min sessions. For sessions 1-10 and 14-18 the rats were allowed to eat from the container. For sessions 11-13 the food was present but a perforated plastic cover prevented access.

Recording:

Videotape recordings were made on day 9 and day 11. The behaviour of the rats was classified in terms of the animal's movements and the outcomes of these movements. The following responses were considered:

1. eating
2. interaction with the blocked food cup
3. trips away from the food cup
4. moving the food cup with paws or mouth
5. interactions with other objects in the environment.

Food consumption and latency to start eating were recorded daily.

Blood Samples

Blood samples for corticosterone assay were taken immediately following eating session 9 and blocked eating session 11. To control for possible contaminating effects of experience with day 9 sampling on day 11 corticosterone levels, two additional eating samples were taken two days apart on eating days 16 and 18. Deprived and non-deprived basal samples were taken 3 and 17 days, respectively, after the last experimental session. For these samples the rat was removed from the home cage at the session time and sampled immediately. Session times were between 1100 and 1900 hrs. These times remained constant for individual rats throughout the experiment and were counterbalanced across groups.

Results

Histology

Seven of the ten lesioned rats received total fornix transections; three received only partial lesions and their data were not included in the analyses. None of the eight control rats received fornix damage. Extra fornical damage to lesioned rats included partial damage to stria medullaris in one, complete damage to stria medullaris in six, partial damage to stria terminals in four, complete damage to stria terminalis in three rats. There was no septal or cingulum damage in the lesioned rats. All rats received slight unilateral cortical damage. No further extra-fornical damage was observed in control rats.

Behaviour:

During eating sessions there were no differences between control and lesioned rats in amount consumed, but there were

differences between groups in their eating behaviour. Control rats typically removed a pellet from the food dish, carried the pellet to a particular location, alternated between eating and exploratory behaviour, then returned to the food dish to remove another pellet. Food pellets were not completely eaten before additional pellets were taken. This hoarding behaviour typically resulted in several partially eaten pellets being left in the eating location at the end of the session. Lesioned rats also alternated between eating bouts and trips around the experimental chamber but food was typically eaten from the food container without pellet removal. Control rats were also slightly more hesitant to initiate eating in the early sessions.

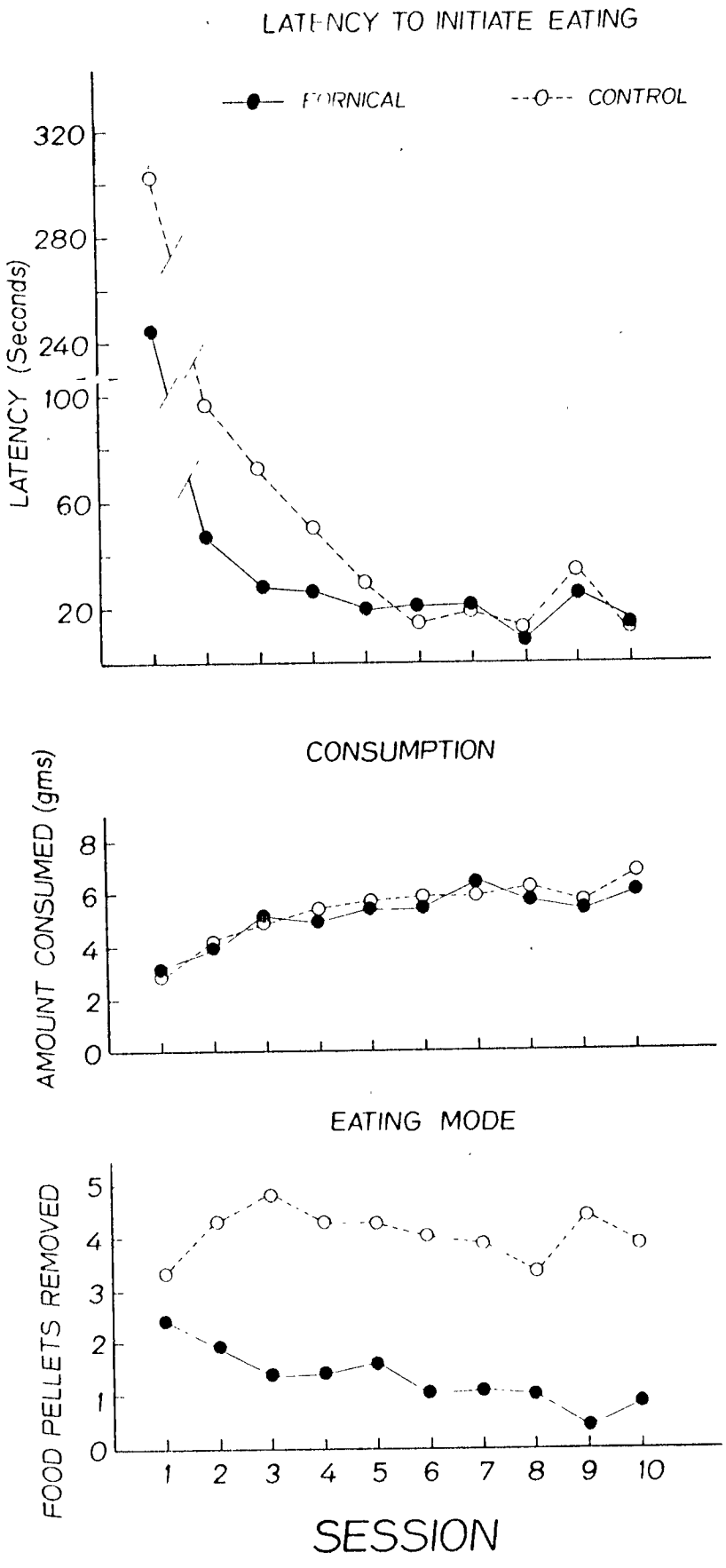
Data on food consumption, latency to eat and eating mode, as measured by number of pellets removed, during eating sessions 1-10 are presented in Figure 25 for both lesioned and control rats. Analyses of variance of these data with lesion and session as the main factors support the above description. For amount consumed there was a significant effect only for session ($F = 6.3$, $p < .001$) but no effect of lesion or lesion by session interaction (F's < 1). Analysis of latency to eat data yielded a significant effect of session ($F = 58.9$, $p < .001$) but the larger latencies for control rats did not reach significance ($F = 2.64$, $p > .05$). Analysis of number of pellets removed, the measure of hoarding behaviour, yielded a significant effect of lesion ($F = 26.6$, $p < .001$) but no effect of session or lesion X session interaction (F's < 1).

Detailed behavioural analyses:

Data from detailed behavioural analyses of lesioned and control rats during both asymptotic eating (session 9) and blocked eating

Figure 25

Behaviours of lesioned and control rats during the ten eating sessions. TOP - latency to initiate eating at start of session; MIDDLE - amount of food consumed; BOTTOM - difference in eating modes as measured by number of food pellets removed from the food cup.


LATENCY TO INITIATE EATING
FORNICAL
CONTROL
LATENCY (Seconds)
320
280
240
100
60
20
CONSUMPTION
AMOUNT CONSUMED (gms)
8
6
4
2
0
EATING MODE
FOOD PELLETS REMOVED
5
4
3
2
1
0
1 2 3 4 5 6 7 8 9 10
SESSION

(session 11) are presented in Table 4. During the eating session and particularly during the blocked eating session, lesioned rats initiated more bouts of behaviours, but these bouts were of shorter duration. This generalization holds for all behaviours recorded.

In addition to these quantitative changes, qualitative differences between groups were observed for food cup interactions during the blocked eating sessions. Controls rats sniffed, pawed and bit the closed food container with an intensity sufficient to move the 300 g food container around the experimental chamber. Lesioned rats also sniffed the container, but the typical interaction involved walking over the food cup. The qualitative differences were quantified by measuring the actual movement of the food cup. As shown in table 4, control rats moved the food cup significantly more than the rats with fornix lesions (Mann-Whitney $U = 3$, $p < .001$, two tailed).

Sequential patterns of behaviour during the blocked eating sesion were analyzed using information analyses. Frequency of behavioural bouts and frequency of transitions were obtained for each rat; representative data are presented in Figure 26. As the figure indicates the most obvious difference between the lesioned and control rats was in absolute frequency of emitted behaviours. First and second order information content of the behavioural patterns were calculated for each rat. The lesioned rats tended to be more random than controls in their transitions but these differences did not reach significance ($U = 18$, $p > .05$). There was no difference in first order predictability between groups.

Table 4

Mean frequency and durations of behaviours during eating and blocked eating sessions

	Control	Fornical	Significance Level
Eating (session 9)			
frequency of trips away from food cup	30.4	51.1	*
trip duration (seconds)	11.5	6.0	*
frequency of eating bouts (preferred mode)	19.5	39.3	***
eating bout length (preferred mode - seconds)	54.7	22.7	**
Blocked eating (session 11)			
frequency of trips away from food cup	58.3	110.7	***
trip duration	14.5	6.5	***
frequency of food cup interactions	57.9	109.1	***
duration of food cup interactions (seconds)	7.5	4.9	**
frequency of object interactions (total)	51.8	129.4	***
a) short duration (< 1 sec)	29.9	105.1	***
b) long duration (> 1 sec)	22.9	24.3	NS
movement of food cup (inches)	14.7	2.6	***

* approached significance .05 $p < .1$

** $p < .05$

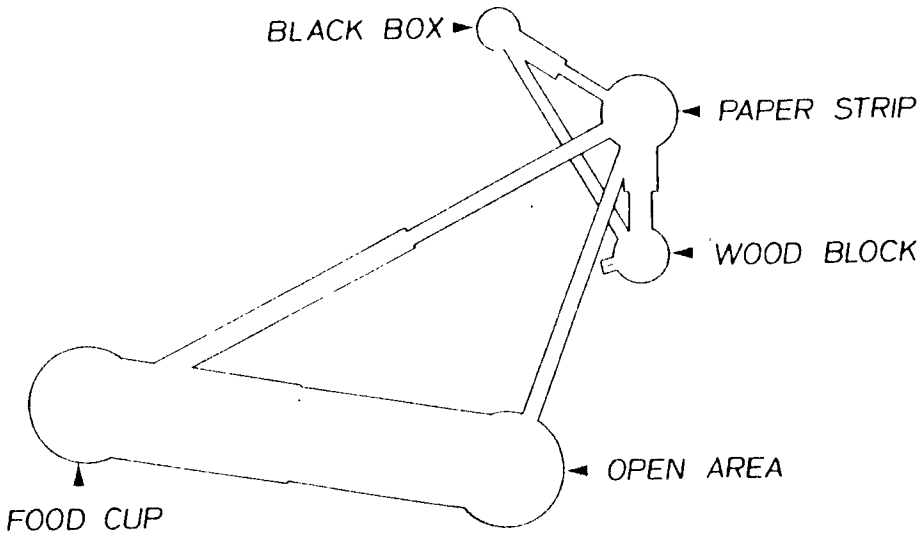
*** $p < .005$

All comparisons are made using the Mann-Whitney U statistic

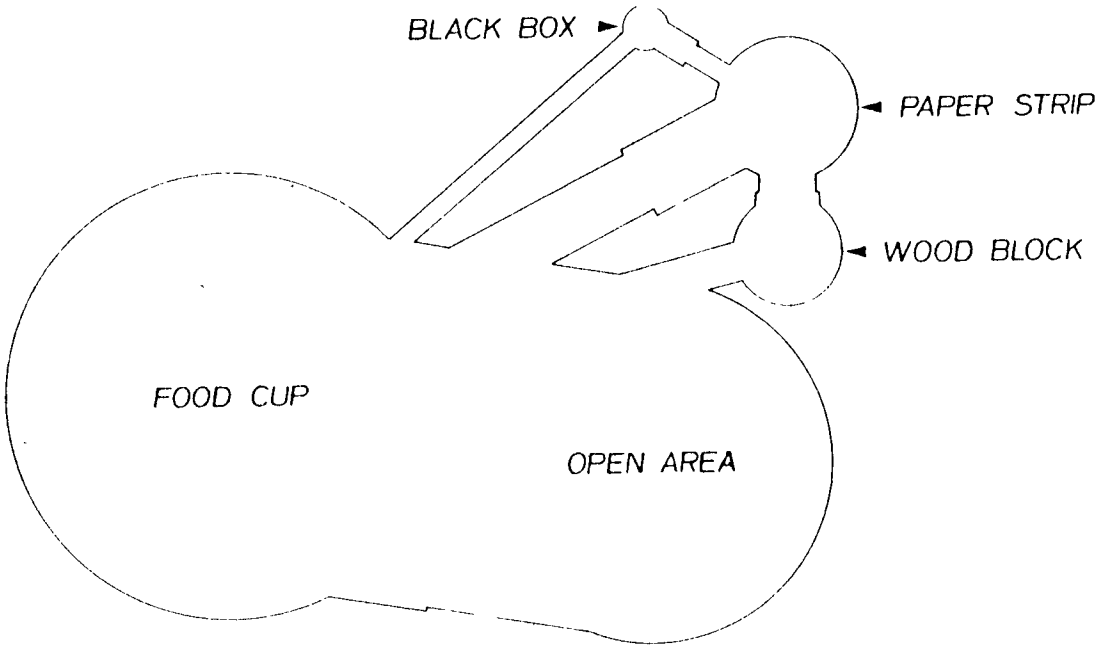
Figure 26

Sequential patterns of behaviours emitted during the first blocked eating session for a representative rat from the lesioned and control groups. Note the large difference in frequency of initiation of behaviours.

CONTROL



FORNICAL



Corticosterone

Mean plasma corticosterone levels of lesioned and control rats for the three eating session (sessions 9, 16 and 18) are presented in Figure 27. As is evident from the figure, repeated corticosterone sampling had no effect on subsequent corticosterone levels; comparable conditions led to comparable corticosterone levels for both control and lesioned rats. Analysis of variance of these data support this description yielding no effect of condition on corticosterone levels ($F = 2.0$, $p > .1$).

Mean plasma corticosterone levels of lesioned and control rats for all conditions are presented in Figure 28. Analysis of variance of these data with lesioned and treatment as the main factors yielded a significant effect of condition ($F = 36.3$, $p < .001$) and a lesion X condition interaction ($F = 3.9$, $p < .05$). Both lesioned and control rats respond to the experimental treatments with changes in corticosterone but the response profiles differed.

Further analyses of profile differences were made using within group Neuman-Keuls comparisons ($p < .05$); these are summarized at the top of the figure. These data indicate that both groups responded to deprivation with increased corticosterone. The control rats also exhibited higher corticosterone levels during eating and even higher levels during blocked eating. These responses were not seen in the lesioned rats. The lesioned rats tended to exhibit lower corticosterone levels during eating than either the blocked eating or deprivation conditions but these differences failed to reach significance.

Figure 27

Mean plasma corticosterone levels for lesioned and control rats during three eating sessions. E 1 - sample taken immediately following eating session 9; E 2 - sample taken immediately following eating session 16; E 3 - sample taken immediately following eating session 18.

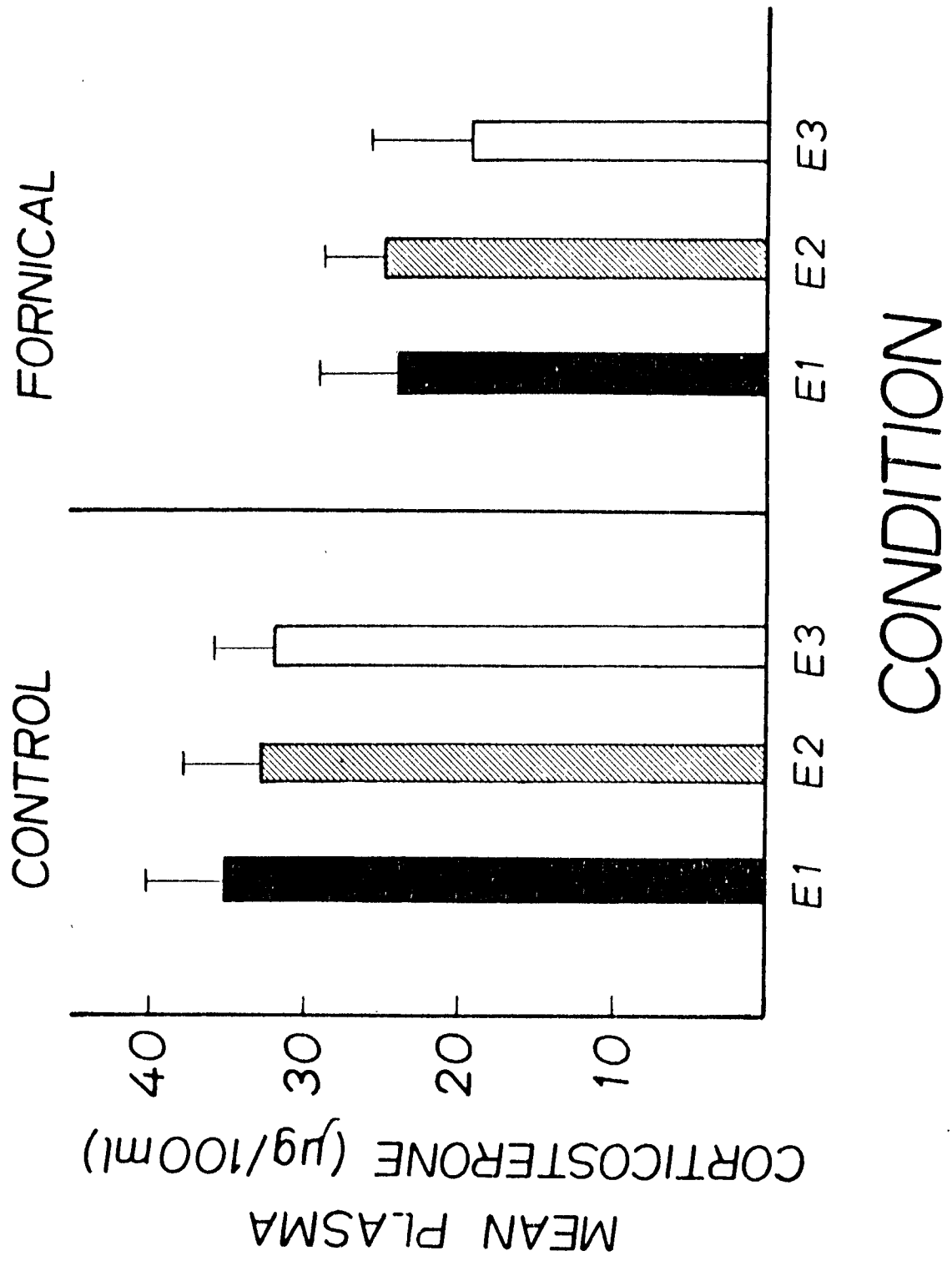
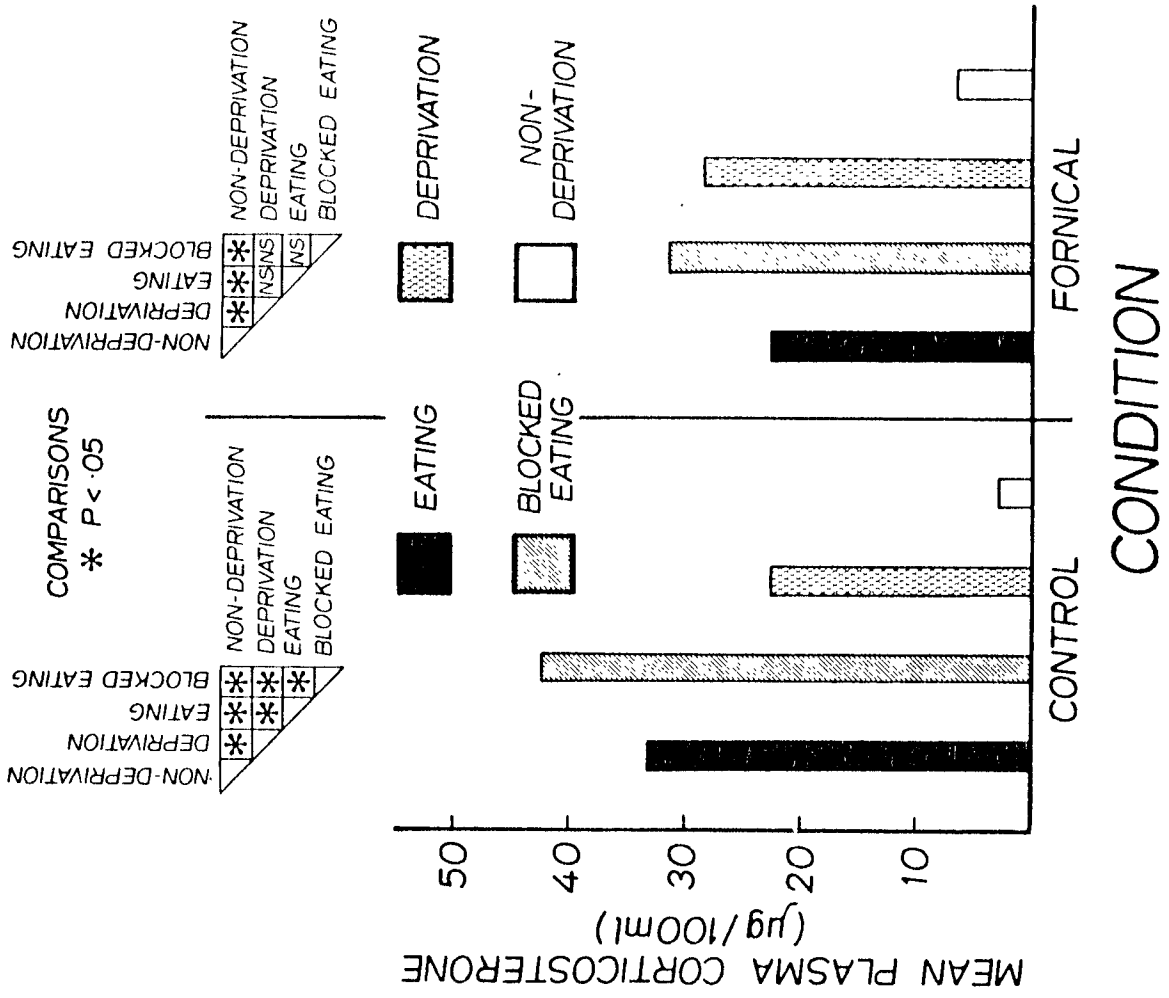

MEAN PLASMA
CORTICOSTERONE (µg/100ml)
40
30
20
10
CONTROL
FORNICAL
E1
E2
E3
E1
E2
E3
CONDITION

Figure 28

Mean plasma corticosterone levels for lesioned and control rats as a function of treatment condition. Individual comparisons between treatment levels are presented at the top of the figure.


MEAN PLASMA CORTICOSTERONE (µg/100ml)
50
40
30
20
10
CONTROL
FORNICAL
CONDITION
EATING
BLOCKED EATING
DEPRIVATION
NON-DEPRIVATION
COMPARISONS
* P < ·05
NON-DEPRIVATION
DEPRIVATION
EATING
BLOCKED EATING
NS
NSNS
*

Correlations between the corticosterone response and the behavioural responses to the food cup (food cup movement) during the blocked eating session were calculated for both lesioned and control rats. No signficant correlations were observed for either group.

Discussion

As stated earlier, the purpose of the present experiment was twofold. The data on both aspects of the experiment (corticosterone control and expectancy violations) tend to support the interpretations of previous experiments.

The present results offer no support for a conditioning interpretation of the corticosterone results obtained in the previous experiments. Support for such an interpretation would be of the form of increased corticosterone levels as a function of number of previous samplings. Yet, in the present experiment, the three asymptotic eating corticosterone measurements did not differ for either control or fornix lesioned rats regardless of the number of prior samples (1,2, or 3). These data demonstrate the reproducibility of the corticosterone response under constant environmental conditions and suggest that changes in corticosterone levels must then reflect changes in environmental stimulation. The possibility of a conditioned corticosterone response to the sampling procedure is, of course, not negated, only the likelihood of its occurrence under the sampling regime of the present series of experiments.

Second, the present results are consistent with the interpretation that the blocked eating session violated an expectation for control rats. The control rats responded to this session with

increases in corticosterone and altered goal-directed behavior. However, the behavior of rats with fornix lesions does not fit this interpretation. The lesioned rats did not show either the corticosterone response or the altered goal-directed behavior as a result of the blocked eating session.

In addition to these differences in the behaviour of lesioned and control rats in response to the change from eating to blocked eating, a number of other differences between groups occurred during both the eating and the blocked eating sessions. These differences were characteristic of the differences in the organization of behaviour between groups observed in previous experiments. Lesioned rats again exhibited more total behavioural initiations (of all behaviours) but of short durations and rapid transitions. The only new behavioural difference between lesioned and control rats was the difference in hoarding behaviour during the eating sessions. Similar deficits in hoarding in rats with hippocampal damage was reported by Vanderwolf et al (1978). Rats tend to take food under cover or to safe locations before eating and the presence of the hoarded food seems to act as a goal for this behaviour (Barnett, 1975). One could speculate on the significance of this loss in hippocampally damaged rats but it seems more appropriate to group this disruption with other, as yet unexplained, disruptions in the organization of species' typical behaviours (grooming, Vanderwolf, et al., 1978; sexual behaviour, Michal, 1973) that result from hippocampal damage.

Chapter 5

Examination of alternative explanations for the differences in acquisition-extinction corticosterone response profiles of lesioned and control rats

In Experiment 1, the corticosterone levels of lesioned rats were lower than those of control rats during both acquisition and extinction (See Figure 8). This pattern of results is open to a number of interpretations. Perhaps the simplest interpretation of these data would be that the corticosterone responses of lesioned rats are either attenuated or subject to a ceiling effect. Both possibilities seem unlikely. In the previous experiments, lesioned rats responded normally to deprivation and in a number of experiments in the literature rats with damage to the hippocampal formation have been shown to exhibit normal corticosterone responses to a variety of stressors and some of these responses have been of greater magnitude than those of the present study (Endroczi, 1972; Lanier et al, 1975; Coover et al, 1971b; Kearley et al., 1974).

Other interpretations must postulate the operation of more than one factor to account for the observed outcome. The interpretation offered in Experiment 1 was that the lesioned rats, unlike controls, did not respond to extinction but exhibited a greater than normal decrease in corticosterone levels during acquisition. This interpretation was based on the observed basal corticosterone levels but was consistent with the observed behavioural differences between lesioned and control rats during extinction. It does, however, leave

unexplained the greater than normal decrease in corticosterone levels of lesioned rats during acquisition. Greater than normal decreases in corticosterone levels during acquisition have been reported previously for rats with hippocampal damage (Coover et al, 1971b). Coover et al attributed this difference to the greater number of reinforcements received by lesioned rats, but the lesioned rats of Experiment 1 received less not more reinforcement in comparison to controls. Lesioned and controls could, however, differ in either their conditioned or unconditioned response to food presentation, both of which have been reported for normal rats (Levine & Coover, 1976; Coover et al., 1977).

Another possibility is that there was a factor present during both acquisition and extinction to which controls but not lesioned rats were responding with increased corticosterone. This difference in acquisition and extinction baseline could then be coupled with a normal response to the transition to extinction in both groups to give the observed pattern of results.

Since the presence or absence of an extinction response in lesioned rats is crucial to the interpretation of previous results, two additional experiments were carried out to examine these alternative explanations of the data.

Experiment 5

It is well established that the corticosterone levels of normal animals increase following exposure to a novel environment (Mason, 1968). The data on the corticosterone response to novelty in animals with damage to the hippocampal formation, however, show little

agreement; normal (Coover et al., 1971b); greater than normal (Bohus et al., 1968), and lower than normal (Iuvone & Van Hartesveldt, 1976) corticosterone levels have been reported. These studies, however, differ in the amount of exposure to the novel environment the animals had experienced at the time of testing. The greater than normal corticosterone levels reported by Bohus et al. (1968) occurred following first exposure to the novel environment and the lower levels reported by Iuvone and Van Hartesveldt (1976) occurred following the twelfth exposure to an open field.

In Experiment 1 the acquisition and extinction sessions were carried out in a novel environment to which the rats had been habituated. Therefore, the lower corticosterone levels during acquisition and extinction seen in fornix lesioned rats could have resulted from lowered responsiveness to the novel aspects of the testing situation coupled with a normal response to the transition from acquisition to extinction.

The present experiment examined the corticosterone levels of fornix lesioned and control rats following habituated exposure to a novel environment where both exposure time and experimental environment were comparable to those of Experiment 1. If the corticosterone levels of lesioned rats are lower than those of normal rats following habituation to novelty, then the above alternative explanation of the results of Experiment 1 would be supported. If, on the other hand, the corticosterone levels of lesioned and control rats did not differ following habituation to novelty, then the alternative explanation of the Experiment 1 results would seem unlikely.

Method

Subjects

Eighteen naive, male hooded rats of the Long-Evans strain obtained from Canadian Breeding Farms, St. Constant, Quebec were used. At the time of surgery the rats weighed 200-250 g. The rats had free access to food and water in their home cages at all times. Ten of the rats received total fornix transection, the remaining eight served as operated controls.

Procedure

Housing conditions, surgical, recovery, histological, blood sampling and assay procedures were previously described.

The rats were given eight daily exposures to a novel environment. Each day the rat was removed from the home cage, placed in a transport box, weighed, and carried to the experimental environment where it was placed for 20 minutes in the operant chamber used in Experiment 1.

Blood samples for corticosterone assay were taken immediately following the first (HTN) and the last experimental session ($\overline{HTN}$). Two additional basal samples were taken. The first was a basal non-stimulated sample (B), and was taken two weeks prior to the first experimental session - the rat being sampled immediately after removal from the home cage. The second was a handle-transport control sample (HT) and was taken one week prior to the first experimental session - the rat being weighed and transported and returned to the home cage and the sample taken 20 minutes later.

The experimental sessions occurred between 1200 and 1800 hours. The sample times remained constant for each rat across all samples and these times were counterbalanced across groups.

Results

Histology:

The histological results are similar to those of the first experiment as illustrated in Figure 2. The ten rats of the lesioned group received total transection of the fornix, none of the operated controls received fornix damage. Extra-fornical damage for the ten rats with fornix lesions included partial damage to stria medullaris in four, complete damage to stria medullaris in five, partial damage to stria terminalis in six, complete damage to stria terminalis in three, slight posterior septal damage in three, and partial cingulum damage in one. Both control and fornix lesioned rats received slight unilateral cortical damage from the knife insertion. There was no additional extra-fornical damage to the operated controls.

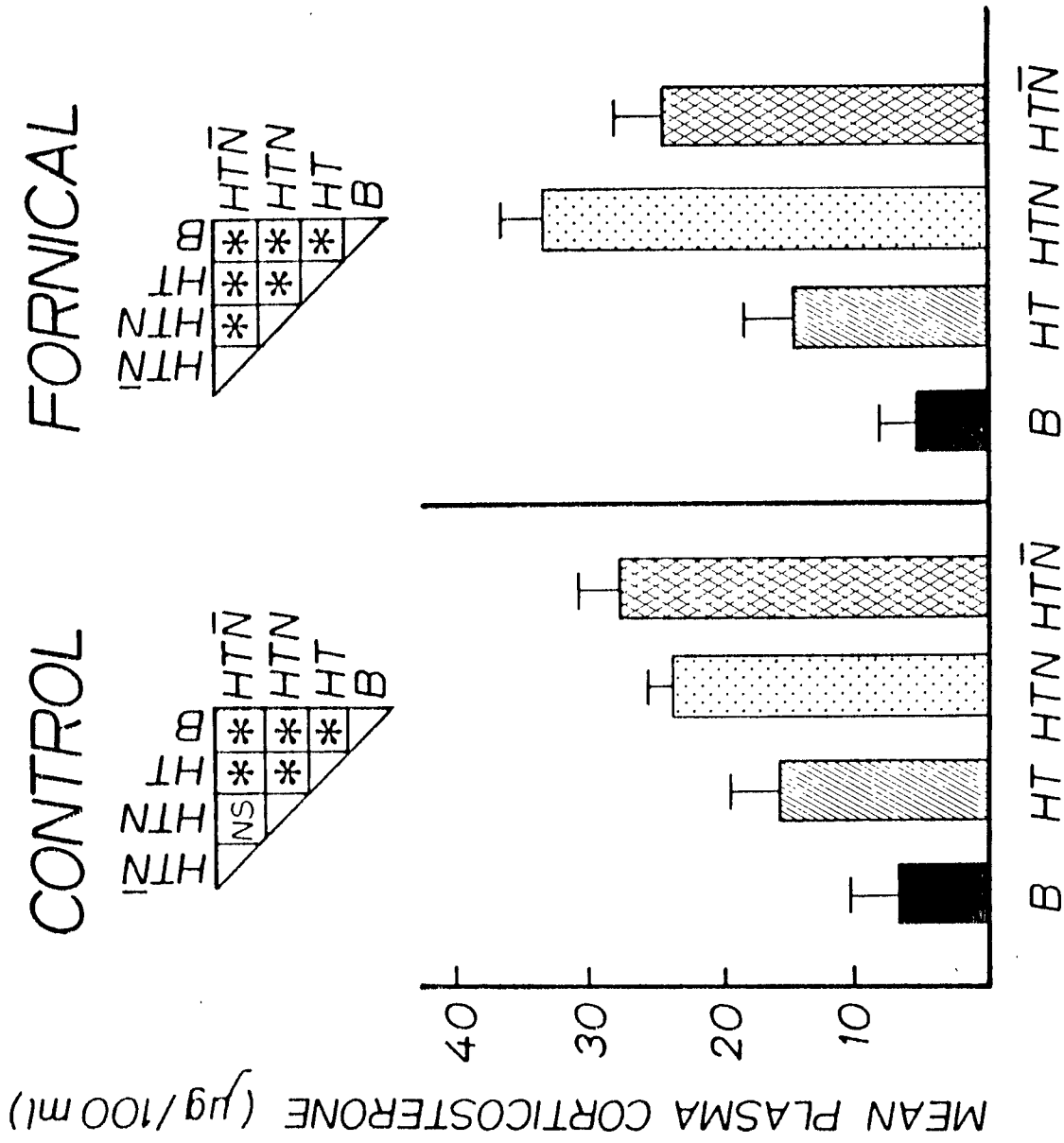
Corticosterone:

Mean plasma corticosterone for operated controls and animals with lesions of the fornix for all four treatment conditions are presented in Figure 29.

As can be seen from the figure, both lesioned and control rats responded to the treatments but the response profiles of lesioned and control rats differed. Analysis of variance of this data with lesion and treatment as the main factors yielded a significant effect of treatment ($F = 36.8$, $p < .001$) and a significant treatment X lesion interaction ($F = 3.07$, $p < .05$). Within group comparisons for the

Figure 29

Mean plasma corticosterone for lesioned and control rats for all treatment conditions. Individual comparisons between treatments are presented at top of figure B - non-stimulated basal level; HT - handled, transport and weighing; HTN - handled, transport, weighing and first exposure to novel environment. $\overline{\text{HTN}}$ - handled, transport weighing and eighth exposure to "novel" environment.


FORNICAL
CONTROL
B
HT
HTN
HTN̄
B
HT
HTN
HTN̄
*
NS
MEAN PLASMA CORTICOSTERONE (μg/100 ml)
40
30
20
10
B
HT
HTN
HTN̄

individual treatments were made using Newman-Keuls tests (α = .05) and are summarized at the top of the figure. Both groups showed significant corticosterone elevations over baseline (B) for the handling-transport (HT) condition. For both groups, both the first (HTN) and eighth ($\overline{\text{HTN}}$) exposures to the novel environment resulted in additional corticosterone elevations over the HT baseline. The corticosterone levels of lesioned rats to the first exposure were significantly higher than to the eighth exposures, but corticosterone levels of controls did not differ for the two exposures. Between group comparisons indicate that the corticosterone levels of lesioned rats to the first exposure were significantly higher than those of control rats. There were no differences between groups for the other conditions.

Discussion

The results of this experiment show that rats with lesions of fornix and control rats respond to a novel environment with corticosterone elevations, that these responses are still present after eight days habituation, and that at this time the magnitude of the response did not differ between lesioned and control rats. Since the amount of habituation to the novel environment experienced by rats in the present experiment was comparable to that in Experiment 1, it seems unlikely that a differential response to a habituated novel environment could account for the large difference in corticosterone levels seen between groups in Experiment 1.

The greater than normal corticosterone levels seen in lesioned rats after first exposure to novelty was consistent with the greater

than normal response of hippocampal rats under this condition reported by Bohus et al, (1968). This supernormal response adds further support to the selective nature of the corticosterone response of rats with damage to the hippocampal formation and argues strongly against any simple attentuation or ceiling effect on corticosterone responsivity in hippocampally damaged rats.

Habituation to the experimental environment did have a differential effect on lesioned and control rats. The corticosterone response of lesioned rats was lower after habituation than on first exposure. Unlike the Iuvone and Van Hartesveldt (1979) results, the corticosterone levels of lesioned rats following habituated exposure were not below the levels of controls. Since the present study was intended to examine the effect of habituation experience comparable to that of Experiment 1, and not designed to replicate Iuvone and Van Hartesveldt, the studies differ in the number of habituation sessions. The difference in corticosterone levels in the two experiments may be due to this procedural difference.

The corticosterone response of control rats, unlike that of lesioned rats, did not decrease as a result of habituation. This lack of change was been reported previously but no satisfactory explanation has been offered. The initial exposure has been considered to elicit a fear response in the rat and this response, as evidenced by defecation scores, declines over exposures (see Roseerans, 1970, or, for a review, Walsh & Cummins, 1976). It seems unlikely then that the high corticosterone levels after habituated exposure reflect fear in normal rats. Strong and Jackson (1970) reported behavioural data that tend to

parallel these corticosterone results. Control rats in their experiment exhibited qualitative shifts in behaviour with repeated exposure to a novel environment. By the sixth exposure the control rats averaged 24 attempts to jump out of the apparatus. These attempts were not present initially, nor were they present in rats with hippocampal lesions. The decline in defecation, the maintenance of high corticosterone, the behavioural shifts and recent evidence that corticosterone measures reflect non-specific arousal rather than a particular emotional state (Levine, et al., 1972; Hennessy et al., 1977a; Hennessy et al., 1977b) all suggest that the initial and final high levels of corticosterone may reflect qualitatively different arousal states in normal rats.

Experiment 6

The purpose of this experiment was to examine the possibility that the lower corticosterone levels of lesioned rats during acquisition resulted from differential responsiveness to food consumption. If this were true, one would predict that lesioned rats would exhibit greater than normal corticosterone decreases in response to food presentation even in the absence of the operant training procedures. In the present experiment, this prediction was tested by examining the corticosterone responses of control and fornix lesioned rats following home cage feeding sessions.

Method

Subjects:

Sixteen naive, male hooded rats obtained from the McMaster colony were used. The rats weighed 200-250 g at the time of surgery.

Eight rats received total lesion of the fornix and eight served as operated controls.

Procedure:

The housing conditions and surgical, histological and assay procedures have been reported preveiously. As in previous experiments, a repeated measures design was employed. During the third post-operative week the rats were reduced to 75% of their ad lib weight corrected for growth. After adapting to the deprivation schedule twenty daily 20 min eating sessions in the home cage were given. Supplementary nightly feeding (at 2200 hrs) was given during this time to maintain 75% projected weights. The rats were then returned to ad lib feeding. Water was available in the home cage at all times.

Three blood samples were taken from each rat. The experimental eating session and blood sample times occurred between 1700 and 2100 hrs. These remained constant for individual animals and were counterbalanced across groups. Corticosterone levels were measured: 1) when the rats were not deprived (B), 2) when they were deprived (D), 3) when they were deprived but permitted to eat; immediately following the nineteenth 20minute eating session (DC).

Results

Histology:

The histological results are similar to those of the first experiment as illustrated in Figure 2. Seven of the eight lesioned rats received total fornix transections; one received unilateral damage and the data from this rat were not included in the analysis. None of the eight operated control rats received fornix damage. Extra-fornical

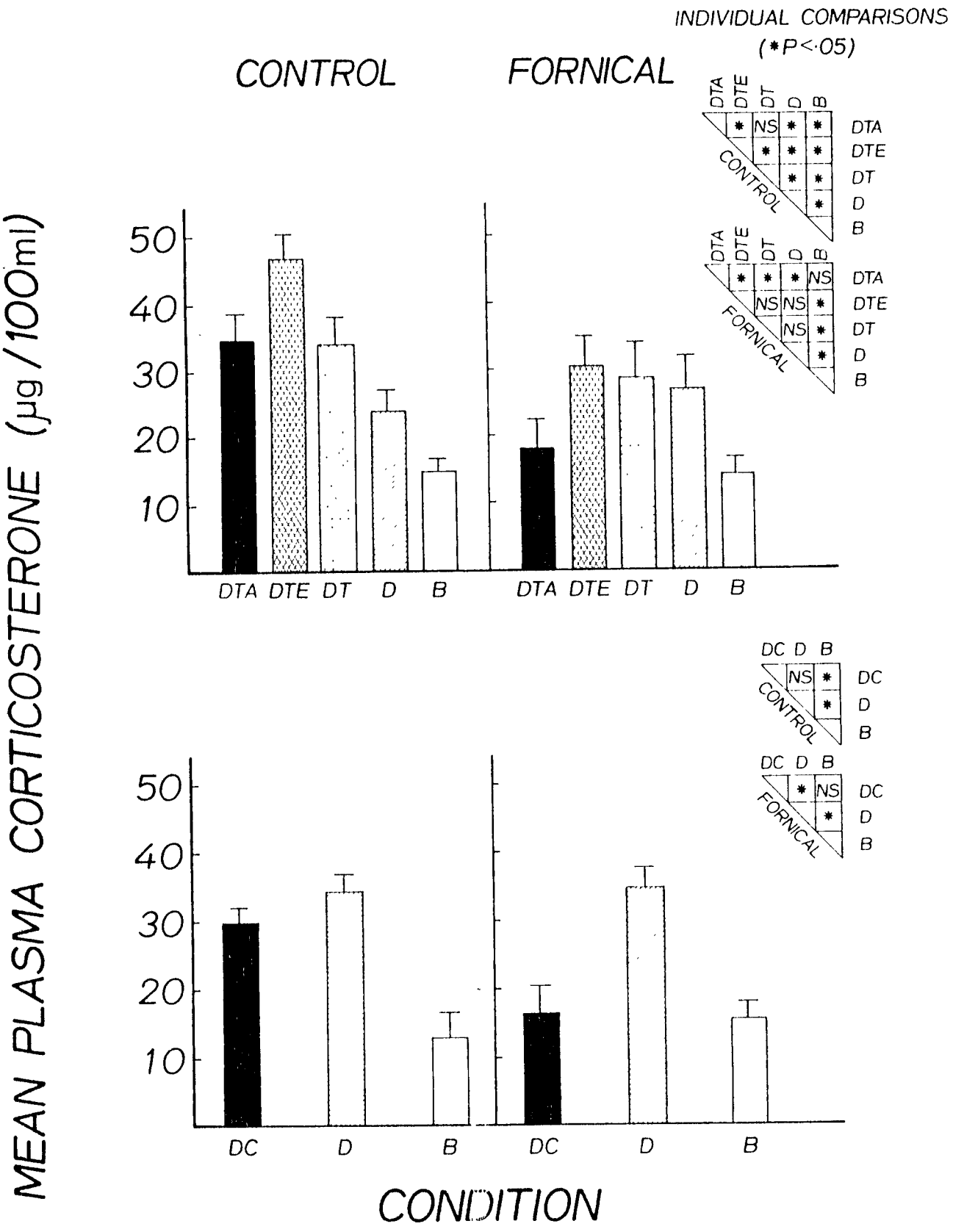
damage to lesioned rats included partial damage to stria medullaris in one, complete damage to stria medullaris in five, partial damage to stria terminalis in four, complete damage to stria terminalis in two, and slight septal damage in one rat. There was no cingulum damage in the lesioned rats. All rats received slight unilateral cortical damage. No further extra-fornical was observed in control rats.

Corticosterone:

Mean plasma corticosterone levels for operated controls and rats with fornix lesions for the three treatment conditions are present in the bottom panel of Figure 30. The corticosterone results from Experiment 1 are also presented in Figure 30 for comparison purposes. Lesioned and control rats did not differ in their response to deprivation. They did, however, differ in their response to the 20 minute eating session. An analysis of variance of these data yielded a significant effect of treatment ($F = 35.3$, $p < .001$) and a significant treatment X lesion interaction ($F = 6.2$, $p < .02$). Within group comparisons for individual treatments were made using Newman-Keuls tests with a significance level equal to .05. These comparisons showed significant differences in deprived (D) and nondeprived (B) corticosterone levels for both lesioned and control rats. For controls, eating while deprived (DC) corticosterone levels were significantly higher than nondeprived levels, but did not differ from deprived levels. The reverse was true for lesioned animals; eating while deprived (DC) corticosterone levels did not differ from nondeprived levels (B), but were significantly lower than deprived levels (D).

Figure 30

Mean plasma corticosterone levels as a function of experimental conditions. (BOTTOM). Results of Experiment 6; B - non-deprived basal; D - deprived basal level; DC - deprived but following 20 min home cage eating session. (TOP). Results of Experiment 1 for comparison purposes (see Figure 8)


INDIVIDUAL COMPARISONS
(*P<.05)
CONTROL
FORNICAL
DTA DTE DT D B
DTA
DTE
DT
D
B
CONTROL
FORNICAL
DC D B
DC
D
B
MEAN PLASMA CORTICOSTERONE (µg/100ml)
50
40
30
20
10
DTA DTE DT D B
DC D B
CONDITION

Discussion

The prediction that lesioned and control rats respond differentially to eating alone was supported. Both the amount of food consumed and the pattern of corticosterone response in the present experiment were comparable to those of Experiment 1. It therefore seems reasonable to conclude that eating during aquisition was responsible for the lower than baseline acquisition corticosterone levels of lesioned rats.

The data on the effect of eating in control rats was somewhat ambiguous. The Neuman-Keuls test showed no significant effect of eating; on the other hand, all of the control rats showed lower corticosterone levels during eating than during the baseline deprivation condition. One might conclude from these results, tentatively, that eating produced a slight decrease in corticosterone levels in control rats. If this conclusion is accepted, one could then argue that a marginal change in eating in Experiment 1 was cancelled by an increase during acquisition, possibly a residual effect of novelty as seen in Experiment 5.

This small effect of eating in control rats raises further questions. Why were corticosterone responses small in controls as compared to rats with lesions of the fornix? And why were corticosterone responses small in the present experiment as compared to others in which eating resulted in large decreases (Levine & Coover, 1976)? The following hypothesis, if it is correct, would answer both of these questions. Eating in control rats results in a decrease in corticosterone levels that is a function of the expected decrease in

deprivation level. If eating results in satiation, as is normally the case, a marked reduction on corticosterone levels will be seen in control animals that have had experience on such a schedule. But, if satiation is not permitted, as in the present experiment, the rat should not expect to be satiated and the corticosterone drop should be small. The data are consistent with this proposal. Levine and Coover (1976), for example, provided animals with 28 g of wet mash for a one hour period on each of 25 daily test sessions, and a marked drop in corticosterone levels was found on the 25th session. In the present study, 5 g of dry food was provided over 20 minutes on each daily test session, and a much smaller drop resulted on the 19th session. Control rats do show drops in corticosterone to the first few exposures to the 5 g schedule (unpublished data). I suggest further that rats with lesions of the fornix may not develop such differential expectations or may develop them very slowly; their corticosterone levels will respond, therefore, as though eating will result in satiation.

Discussion

The data presented in this experiment counter alternative explanations of the corticosterone results of Experiment 1. The corticosterone response profile of the fornix lesioned rats in Experiment 1 does not appear to have resulted either from a general attenuation of corticosterone responsivity or to a failure of lesioned rats to respond to some factor common to acquisition and extinction coupled with a normal corticosterone response to extinction. Rather, it appears that lesioned rats do not respond to extinction but respond to eating during acquisition with greater than normal decreases in corticosterone.

In general, the present series of experiments suggest that the corticosterone responsivity of rats with lesions of the fornix differs from that of control rats in terms of the influence of behaviourally significant situations. It can be suggested that after fornix damage certain stimuli no longer affect the pituitary-adrenal system, while other stimuli do. Another possibility is that there are multiple parallel pituitary-adrenal regulatory systems only one of which involves the fornix. Stimuli may or may not be channeled into the regulatory system involving the hippocampus. No matter which of these hypotheses is correct, behaviourally significant stimuli can be divided into at least two categories on the basis of the role of the fornix in mediating their effects. The first category does not involve the fornix and seems to concern direct inputs concerned with primary motivation - ether stress, for example, which seems to be mediated by the hypothalamus (Halasz, 1969), as well as electric shock (Nakadata & De Groot, 1973) and deprivation (Coover et al., 1971b). It is premature to identify stimuli which involve the hippocampus. The category may be characterized as more complex and having indirect modes of action. For example, it may involve stimuli which elicit expectancies about motivationally significant events and the violation of such expectancies (Levine et al., 1972), or mismatches between what is expected and what occurs in a given situation (O'Keefe & Nadel, in press).

Chapter 6

General Discussion

The present series of experiments analyzed behavioral and physiological differences between rats with total fornix lesions and control rats in their response to the transition from acquisition to extinction of an operant response. As Kimble (1975) has pointed out, this specific change in environmental demands is characteristic of those tasks where animals with hippocampal damage exhibit the most striking behavioral deficits. The approach taken in the present series of experiments was to increase the amount of information about the behavior of the rats in order to provide a more accurate characterization of the behavioral deficit following fornix transection, and to provide information that would be useful in addressing contradictory issues in current theories of hippocampal function. These aspects of the work presented here will be discussed separately; the relevance of individual experiments to the literature was included in the discussion of the individual experiments and will not be repeated.

The detailed analysis of behavior employed in the experiments indicated that rats with total fornix lesions differed from control rats on a large number of behavioral measures across a variety of situations including acquisition of an operant response, extinction of an operant response, exploration, home cage and open field eating and blocked eating. These behavioral differences can be grouped into two

categories, although these categories are not mutually exclusive.

The first category of differences that distinguishes lesioned and control rat are those differences that were present under essentially all environmental conditions. These differences may tentatively be characterized as differences in the organization of behavior. Recent behavioral organization models, admittedly in their infancy (see de Ruiter et al, 1974), utilize as units of analysis the frequency of initiation of different bouts of behavior, the durations of these bouts and their sequencing. The actual observed behavior is the single channel product of an active integrative decision making process and is affected by the current internal and external stimulus complex. Disturbances in the organization of behavior would then not necessarily remain constant across situations but instead could be reflected in differences in absolute or relative frequencies of different behaviors, in their absolute or relative durations and in their sequencing. In the present series of experiments the lesioned rats differed from controls on all of these measures. These differences were apparent whether one considered more general task defined behaviors (e.g. lever bouts or trips away) or more specific individual behavioral units (e.g. interactions with objects in the experimental environment). During acquisition the lesioned rats in comparison to controls exhibited increased frequency of irrelevant behaviors (trips away from bar and food cup) but decreased frequency of relevant behaviors (lever press and food cup checks), and the durations of eating bouts were longer than for controls. During extinction for all behaviors measured, the lesioned rats exhibited increased

frequencies, decreased durations and differences in sequential patterning with respect to controls. Similar differences were seen during exploration and during the eating or blocked eating sessions in the open field. These differences in organization of behavior are consistent with the reports in the literature that show hippocampal damage to result in deficits in the organization of species typical behaviors such as sexual behavior (Michal, 1973), food hoarding (Vanderwolf et al, 1978, Shipley and Kolb, 1977), grooming (Vanderwolf et al., 1978) and nest building (Shipley and Kolb, 1977). That the organizational differences between lesioned and control rats in the present series of experiments interact with task defined behavior is obvious during some situations (like eating in the open field in Experiment 4) but is also evident in the other situations. For example, during lever press acquisition in Experiments 1 and 2 the lesioned rats received significantly fewer reinforcements than did controls. This difference can be accounted for by the more efficient performance patterns of controls (i.e. the shorter duration eating behavior, the decreased frequency of irrelevant behaviors and the more predictable sequencing).

These behavioral organization problems do not, however, seem to be specific to damage to the hippocampal formation. Increased frequency of behavioral initiations, decreased durations, and increased or decreased randomness of behavioral sequencing have also been reported following amphetamine injections (Norton, 1973), catecholamine manipulation (Antelman and Caggiula, 1977), cortical lesions (Vanderwolf et al, 1978), lateral hypothalamic lesions (Rowland, 1977)

or x-irradiation, carbon monoxide or pallidal lesions (Norton et al, 1976). Regardless of the lack of specificity of these behavioral organization deficits, they must be taken into account in attempts to explain deficits following hippocampal damage, since the present experiments indicate that they interact with specific task requirements across a variety of tasks.

The second category of behavioral differences between lesioned and control rats evident in the present series of experiments was the difference in behavioral response to changes in environmental demands. In general, when the environmental demands changed, the behavior of control rats changed more than did the behavior of lesioned rats. First, the transition from acquistion to extinction resulted in an extinction deficit in fornix lesioned rats. In the standard operant chamber of Experiment 1, this was reflected in both the traditional measure of resistance to extinction (total number of lever presses) and in the detailed measures (number of lever bouts and number of food cup checks). The transition from acquisition to extinction in the enriched environment of Experiment 2 also resulted in an extinction deficit when the detailed measures (lever bouts and food cup checks) are considered that was not evident from traditional measures. More importantly, the detailed analysis revealed more about the nature of the extinction deficit. The lesioned rats, unlike controls, did not exhibit increased arousal as measured by the corticosterone response, nor did they exhibit the behavioral flexibility of control rats. These differences were present not only following the transition from acquisition to extinction of the lever press response but also in the simpler eating-blocked eating transition in Experiment 4.

As pointed out in Chapter 3, the behavior of the control rats was descriptively at least consistent with the recent extinction model of Wong (1978). Using Wong's terminology, the control rats exhibited both response persistence and goal persistence. The response persistence, as defined by Wong, consists of continuation of the response in the acquisition topography; goal persistence consists of the pursuit of the initial goal but with altered response topographies and interspersed exploratory bouts. For control rats in the present experiments, response persistence in extinction was positively related to the corticosterone response to extinction, but goal persistence was negatively related to the corticosterone response. Lesioned rats appeared to exhibit only response persistence in extinction. They showed neither the behavioral flexibility, the corticosterone response, nor the behavior-corticosterone relationships but, instead, continued to respond in the acquisition mode during extinction.

These data would suggest that extinction, at least in control rats, does not reflect a passive decline in control over responding by the environmental stimuli as a result of non-reinforcement. Rather, for controls, the data suggest that the changed environmental demands result in the violation of the rats expectation that responses will result in reinforcement, that this violation is reflected by increased corticosterone and altered behavioral strategies. The magnitude of the corticosterone response is positively related to the degree that the rat maintains the habitual response mode (receives negative feedback) and negatively related to the degree to which he engages in altered "coping" behavioral strategies. The behavior of lesioned rats in

extinction, in contrast, would appear to be consistent with a passive S-R account of extinction.

Since the present results suggest that the effects of fornical lesions are similar to those of hippocampal lesions in extinction, it seems reasonable to attempt to explain these data in terms of general hypotheses about the functions of the hippocampal formation. Although these theories will be discussed separately, this is not to imply that they are mutually exclusive nor that the hipocampal formation is concerned with a single function.

The present results are relevant to certain theories that relate hippocampal function to motivational and emotional processes (Gray, 1970; Jarrard, 1973; Isaacson & Kimble, 1972; Isaacson, 1974) Isaacson and Kimble (1972) and Isaacson (1974), for example, have suggested that damage to the hippocampal formation leads to an accentuation of the frustration response and that this, in turn, leads to increased stereotopy or fixated behavior patterns of the type described by Maier (1964). In extinction, the result of this response is the increased levels of lever pressing in hippocampally damaged animals. The detailed observations of behavior provided by the present series of experiments certainly cast doubt on this interpretation. Three of the experiments specifically involved violations of expectations, the conditions presumed necessary to evoke a frustration response and in neither experiment was there evidence in the behaviour of lesioned rats of increased frustration as described above. First, one would expect frustration to be accompanied by heightened emotional and displacement responses (Falk, 1972; McFarland, 1966). As has been

pointed out previously, the lesioned rats exhibited less, not more, of these behaviors (for example, less biting, fewer attempts to escape the apparatus, less movement of the food cup, etc). Second, since frustration has been demonstrated to be aversive (Adelman & Maatsch, 1956), and corticosterone levels are assumed to increase in aversive situations, one would expect supernormal frustration to be accompanied by supernormal corticosterone responses. Unlike controls, the lesioned rats in the present series of experiments did not exhibit corticosterone elevations to the changed environmental demands but were demonstrated to exhibit normal corticosterone responses in other situations. Finally, the lesioned rats did not exhibit fixated behaviour patterns of greater than normal stereotypy. In fact, the lesioned rats were less stereotyped, as measured by the information analyses, in both acquisition and extinction and the transition to extinction resulted in decreased rather than increased stereotypy. Not only do the present results not support a supernormal frustrative response, they are in direct opposition. Both the behavioural and hormonal data are more consistent with the view suggested by Gray (1970) that lesions of the fornix lead to a reduced frustration response.

It is interesting in view of these diametrically opposed accounts that other experimenters have asserted that hippocampally damaged rats exhibit normal frustration (for example, Gaffan, 1973; O'Keefe & Nadel, in press). At this point, one could make a strong argument for ignoring the construct of frustration, if evidence for increased, decreased and normal responses following hippocampal damage

can be gleaned from the same literature. In view of the consistency and replicability of the behavioural and hormonal data in the present series of experiments, it seems more appropriate to re-examine the data from which the above discrepant conclusions were drawn.

First, Swanson and Isaacson (1967) reported that rats with hippocampal lesions responded during S^{Δ} periods with bar press rates that were 15% higher than their response rate during reinforcement periods, while controls during S^{Δ} decreased their response rates by 15%. These data, were interpreted as evidence for increased frustration. Lesioned rats in Experiment 1 showed no evidence of frustration yet responded at higher rates during extinction than during acquisition, controls showed the opposite. An obvious alternative explanation for the results of both experiments is that eating during reinforced periods takes more time than checking the food cup during non-reinforcement periods. In Experiment 2, it was found that either individual food cup bouts or total time at the food cup was approximately three times longer during acquisition than during extinction. A 15% increase in response rate does not represent increased frustration but simply reflects the large increase in time available for lever pressing during non-reinforcement. The remaining evidence for increased frustration in hippocampal rats appears to be based on the lack of behaviour flexibility in lesioned rats that could reflect fixated behaviour of the type described by Maier (1964). This has already been discussed, and the lack of behavioural flexibility will be returned to later in the discussion of information processing theories of hippocampal function.

In contrast to the paucity of data to support heightened frustrative responses there are a large number of experiments to suggest normal frustration in hippocampally damaged rats. Evidence for a normal frustrative response comes from positive results in the "frustration effect" (i.e. faster run times in the second alley of a double runway when food is omitted in the first goal box than when food is present, Amsel & Roussel, 1952) or in positive behavioural contrast (i.e. responding more vigorously than would be expected when reinforcement has been either deleted or reduced).

A "frustration effect" in rats with hippocampal lesions was reported by Swanson and Isaacson (1969). These results can be questioned on a number of grounds. First, as the authors themselves point out, the lesions are considerably smaller than those that result in extinction deficits, averaging 10-65% damage. Second, it was not shown statistically that any individual group exhibited a frustration effect. Lastly, the observed trend did not emerge in hippocampal rats until the fifth and sixth day of testing. This trend seems opposite to what would be expected for a frustration effect.

Positive behavioural contrast following either the initiation of go-no-go discrimination training or following a reduction in reward magnitude can also be taken as evidence for frustration if proper control procedures are employed (see Mackintosh, 1974). Gaffan (1973) reported normal contrast in rats with fornix lesions following the initiation of go-no go discrimination training. Unfortunately Gaffan employed an alternating VI-ext schedule which has been argued (Mackintosh, 1974; Staddon, 1970) and demonstrated (Kello, 1972) not to

reflect behavioural contrast but to simply reflect the characteristic control over responding exhibited by this schedule. Similar problems of interpretation are evident in a recent study by Van Hartesveldt (1973), who reported that hippocampal rats were able to respond appropriately to changes in magnitude of reinforcement. This study does not have the appropriate control for contrast (ie. a group that was maintained at the lower reinforcement level throughout) nor does Van Hartesveldt note that the relative change in behavior was much greater for controls. When controls for these criticisms are instituted, hippocampally damaged rats do not show behavioural contrast (Murphy & Brown, 1970; Franchina & Brown, 1971; Henke & Bunnell, 1971). One can see that the literature does not support an interpretation of heightened or even normal frustrative responses in hippocampally damaged rats. The results in the literature, instead, agree with the detailed observations of the present series of experiments that show the absence of a frustrative response in lesioned rats.

The present data are also relevant to the hypothesis that the hippocampus is involved in the inhibition of behavior (McCleary, 1966; Douglas, 1967, 1972; Kimble, 1968, 1975; Isaacson and Kimble, 1972; Altman, Brunner and Bayer, 1973; Solomon, 1977). Although these theories are grouped together in that they make somewhat similar predictions concerning the results of the present series of experiments, they do differ with respect to underlying processes (e.g. Pavlovian internal inhibition, tuning out of stimuli, response braking), to what is being inhibited and to the extent to which they are testable. Douglas (1967, 1972), for example, suggests that animals

with hippocampal damage lack Pavlovian internal inhibition. Internal inhibition is considered to be an activity generated process to counteract excitation and functions to reduce the control over behavior by stimuli that no longer signal reinforcement. Procedures are available (See Rescorla, 1969) for distinguishing between different forms of internal inhibition and these have been used to demonstrate that not all forms are absent in hippocampally damaged animals (Solomon, 1977). Solomon's demonstration that hippocampal rats show normal conditioned inhibition makes it unlikely that the general hippocampal syndrome results simply from lack of responsivity to stimuli signalling non-reinforcement. Similarly, the response braking theory of Altman et al (1973) makes rather precise predictions concerning if not underlying mechanisms at least the behavior of hippocampally damaged animals. Hippocampal animals will exhibit a greater than normal tendency to "act out", or emit overt responses when aroused. It is apparently this type of inhibition model that Elmes et al (1975) were addressing when they argued that inhibition models could not account for increased susceptibility to learned helplessness in hippocampally damaged rats. In this task, exaggerated helplessness in the contingent phase following non-contingent training is, of course, opposite what one would expect for animals who have a greater than normal tendency to emit overt responses when aroused. Other inhibition theories, like Isaacson and Kimble (1972), are much more flexible in their predictions of behavior following hippocampal damage. Isaacson and Kimble also suggest that hippocampal animals cannot inhibit activity, but the activity is not limited to specific responses but to

higher level hypothesis or response strategies. To postulate a behavioral sequence or behavioral strategy activator allows considerable flexibility in accounting for behavioral deficits following hippocampal damage, but at the same time the physiological basis for such a postulate may be questioned.

Regardless of these differences among inhibition theories, disruption of underlying processes is thought to manifest itself primarily in two behavioral syndromes. The first is a tendency for the animal to continue to do what it has been doing in the past even when conditions change, and to be inflexible, predictable, and locked into particular patterns of behavior or into particular strategies. The second is a tendency for the animal to be hyperactive - to make a large number of active skeletal responses and to not remain immobile for any period of time. The data of the present series of experiments are, to a certain extent, consistent with both descriptions. For example, when the environmental demands changed on the transition to extinction, the fornix lesioned rats were more active than controls and their behavior changed less than the behavior of controls. In this sense the present results are consistant with inhibition theories. As pointed out in Chapter 2, other aspects of the data raise questions for inhibition theories. The detailed analyses revealed that lesioned rats exhibited shorter not longer bouts of responding in comparison to controls, their sequential patterns of responding were less not more predictable than controls and the transition to extinction resulted in less not more predictability in patterning. These results seem in direct contradiction to inhibitory theory characterizations of hippocampally

damaged rats. Other aspects of the present series of experiments do not seem to be directly addressed by inhibition theories. These theories, for example, would not predict the absence of a corticosterone response to extinction in lesioned rats nor would they predict the differing results brought about by the change in experimental environments between Experiments 1 and 2. Part of the problem for response inhibition interpretations of the present results would appear to stem from the assumption, at least in simple situations, that the lesioned rats simply exhibit more of the task defined behavior than do controls. The detailed analyses presented in Experiments 1-4 demonstrated that this was not the case.

Another account of the persistence of the fornix lesioned rats is provided by the hypothesis that animals with hippocampal damage cannot employ the information processing systems that are used by normal animals (Hirsh, 1974; O'Keefe and Nadel, in press). According to this view, the lesioned animals must employ residual systems in learning tasks, systems that have properties that differ from the properties of the more versatile information processing systems of normal animals. Both Hirsh and O'Keefe and Nadel have proposed that the residual systems involve S-R learning and extinction. However, while these theorists agree on some of the characteristics of the residual S-R systems, they disagree on others. Unlike contemporary formulations of S-R theory, Hirsh takes the strong position that the residual mechanisms of hippocampally damaged animals do not involve expectations. Reinforcement does not function as a goal for responses, but simply strengthens associations between stimuli and responses.

O'Keefe and Nadel are less clear in their formulation but would not appear to exclude any contemporary S-R mechanisms. Both O'Keefe and Nadel and Hirsh agree, however, that non-reinforcement during extinction results in weakening the ability of stimuli to evoke the response, presumably, through a build-up of inhibition similar to Hullian "reactive inhibition". In this sense, both theories are consistent with current S-R theory, in that, extinction is seen to be a passive process; learned responses are inhibited without the occurrence of concomitant new learning. Both theories also postulate active new learning to be involved in the more flexible extinction strategies of normal animals.

According to O'Keefe and Nadel, normal animals may use spatial strategies to solve tasks, in addition to the residual S-R strategies. The animals form a representation of the spatial layout of the environment, or cognitive map, and use this representation to guide their behavior. Reinforcement in this system appears to serve only as information. In the event of environmental change, the spatial system registers the change and exploration is triggered to update the cognitive map and incorporate the changes. Therefore, the spatial theory must not only specify the distinguishing features of the two strategies but must also specify a priori the conditions under which the different strategies will be employed by normal animals. The data of the present series of experiments appear to be relevant to both issues. The behavior of lesioned rats appears to be consistant with an S-R characterization, and the behavior of controls with an interplay between S-R and spatial strategies. This is evident from the

continuation of the acquisition mode of responding for lesioned rats and two different modes with interspersed exploration for controls. Other aspects of the data are inconsistant with the O'Keefe and Nadel hypothesis. They imply that lesioned rats exhibit normal frustration when there is no spatial separation between signal and goal. The evidence against this assumption has already been discussed. They also suggest that lesioned rats show either no deficit or at best a slight deficit in operant tasks whereas large deficits appear in runways. The difference between tasks is seen by O'Keefe and Nadel to involve difference in the domination of spatial hypotheses in runways and S-R type hypotheses in operant tasks. I disagree with this interpretation on two accounts. First, the literature review (see Table 1) suggests that lesioned rats are no more likely to show deficits in the runway than in the operant chamber. Second, the large difference in magnitude of the lesioned rat deficit between operant and runway tasks could result from a difference in the sensitivity of the measures employed. In the runway, latency measures are used while in the operant chamber total number of lever presses. The present results suggest that response variation in controls, in the form of lever biting will detract from the difference between lesioned and control rats in this task. In the runway, in contrast, response variation (Wong, 1977, 1978) takes the form of alternate routes and responses incompatible with running, thus enhancing latency differences between lesioned and control rats. In addition, O'Keefe and Nadel would predict that the enlarged enriched environment of Experiment 2 should enhance the deficit in lesioned rats. Controls should benefit from this

environmental change as a result of the use of the cognitive mapping system, lesioned rat should not. The results were inconsistent with this prediction.

The present data are also relevant to the contextual memory theory of Hirsh (1974). According to Hirsh, normal animals operate with two distinct but interactive information processing modes. The "on line performance" mode uses only information currently available in the sensorium. This mode can form associations but only of an S-R type. The "contextual mode" transfers information to and from the "on line" mode. This second system thus allows the animal use of information not directly present in the sensorium; the animal forms expectations which perscribe current strategies to the on line system. In the event of changed environmental demands, the interactive system registers the changes and rapidly alters the prescribed performance line behavior based on observed changes, past experience, motivational context and such subtle variables as the nature of the problem. Animals with hippocampal damage have access only to the on line system and as such their behavior, in the event of an environmental change, must passively decrease in a traditional S-R fashion before new behavior occurs.

As Hirsh points out, experimental evidence that bears directly on these basic assumptions is sketchy. However, some of the data of the present series of experiments are consistant with specific predictions that could be derived from Hirsh's formulation. For example, the behavior of controls should reflect the violation of an expectancy and rapid change in behavior in the face of this violation. The rapid decline in acquistion mode responding, the emergent emotional

and displacement activities, the increased corticosterone levels, the altered modes of responding and the behavioral-hormonal correlates of control rats in the present experiments are consistent with this prediction. In contrast, the behavior of lesioned rats should reflect the absence of expectations and support of simple S-R type behavioral strategies. As discussed previously, there is no evidence in the literature for expectations in lesioned rats (i.e. absence of frustration, behavioral contrasts, etc.), nor was there supportive evidence in the present experiments. With environmental change, lesioned rats maintained previous modes of responding, did not show emotional behavior or corticosterone responses, displayed response persistance but not goal persistance. This pattern in the behavior of lesioned rats is consistent with what would be expected if lesioned rats did not form expectations but operated instead on simple S-R strategies. Other aspects of the behavioral differences between fornix lesioned and control rats in the present series of experiments are either contradictory or are not addressed by the contextual retrieval theory. As pointed out earlier, one of the more consistent differences between lesioned and control rats were differences in the organization of their behavior. It is difficult to see why relying on a performance line strategy should result in such differences, especially under constant environmental demands.

One is left with the conclusion that no current theory of hippocampal function can account for the many behavioral differences between control and lesioned rats that were observed in the present series of experiments. This inability of current theory to account for

the present data stems, in part, from the different methodological approach employed in the present experiments. Typically, crucial experiments are designed to test specific hypotheses. The data derived from these experiments allow inference about the validity of the hypotheses being tested, but are limited in information content and are useful only to the extent that the conceptualization guiding the design of the experiment is correct. Observational data, on the other hand, convey a large amount of information and are less restricted by prior conceptualization. For example, Ranck employing the observational approach concluded that "hippocampal transformations would seem to be involved in solving such problems as how to sequence these various automatic behaviors appropriately, how to sequence automatic and nonautomatic behaviors appropriately, how to test the appropriateness of an automatic behavior or sequence and stop or change it if need be, how to shift from one behavior to another, how to combine automatic and nonautomatic behaviors into new patterns, how to use behaviors which are being learned along with older behaviors, or in general how to use automatic and nonautomatic behaviors in a flexible way and to avoid being too rigid (Ranck, 1975, p. 240)". Ranck's statement lacks the precision of some current theories of hippocampal function, but in the sense that it reflects a broader data base, may more accurately characterize the deficit following hippocampal damage. In the present series of experiments, experimentation was supplemented by observation. As the previous discussion indicates, this approach can provide a less restricted characterization of the behavioral deficit and, in addition, can address current theory, if not by disproof, by making particular theories less tenable or less attractive.

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Appendix I

The surgical procedure for fornix lesioned and operated control rats was identical with the exception of knife closure. This procedure controlled for surgical insult and cortical damage and was intended to control for extra-fornical damage as well. However, lesioned rats, as a group, experienced greater extra-fornical damage (i.e. damage to stria medullaris, stria terminalis and cingulum) than did the operated controls. As a result, it was deemed necessary to examine the possible extent to which this extra-fornical damage might have contributed to the observed behavioural differences between groups.

The extent of the extra-fornical damage to fornix lesioned rats varied from no damage to total bilateral damage for both stria medullaris and stria terminalis and from no damage to partial bilateral cingulum damage. While there were no obvious correlations between behaviour and extra-fornical damage, the difficulty in rating extent of damage (i.e. would bilateral partial damage be more or less severe than total unilateral damage) prevented formal correlations.

Instead, the behaviour of fornical rats with no damage to stria medullaris, no damage to stria terminalis or no cingulum damage was compared to the means for the lesioned and control groups. Table A.1. presents these comparisons for some of the behavioural measures that most readily distinguish lesioned and control group differences. One would expect that if damage to these pathways rather than fornix damage was important for the behavioural results, then fornix lesioned rats with no damge should resemble controls on these measures. Inspection of Table A.1. clearly reveals that this was not the case. One can

conclude from these comparisons that the behavioural differences between lesioned and control rats must, in fact, result from fornix damage and not from damage to extra-fornical structures.

Table A.1. Comparison of lesioned rats with intact stria medullaris, intact stria terminalis or intact cingulum with lesioned and control groups on measures that reflect group differences.

Behavioural measure*	Fornix lesioned group	Operated control group	Fornix lesioned rats with intact		
			stria medullaris	stria terminalis	cingulum
Number of trips away during acquisition	86.7	36.1	76	102	98
Number of trips away during extinction	98.3	40.3	103	87	106
Extinction trip duration	7.2	20.4	7.0	7.1	7.6
Percent biting during extinction	7.6	26.4	9.8	7.0	5.0
Lever press bout length during extinction	1.57	2.51	1.70	1.44	1.57
Corticosterone response to extinction (over baseline)	2.0	12.9	2.8	2.0	2.4

* All values presented are means for the appropriate groups.