THE ROLE OF THE HIPPOCAMPUS AND SEPTUM IN RESPONSE INHIBITION

by

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INTRODUCTION

Experimental psychologists have long concerned themselves with the initiation of behavior. There is another aspect of behavior, however, that merits equal attention and has only recently gained recognition as a major problem in psychology. This is the phenomenon of response inhibition. How is a response pattern eliminated when it is no longer appropriate? For example, a rat is taught to go through a white door and avoid a black one. If the reinforcement conditions are then reversed, the rat must inhibit his tendency to go through the previously correct white door in order to receive a reward or avoid punishment. How does he do it?

The general problem of response inhibition has been approached from a variety of directions, but one of the main lines of inquiry has been neuropsychological: what brain structures are involved in response inhibition and what is the nature of the deficit in behavior produced by damage of these structures? Three regions have received most attention: the hippocampus, the septum, and the frontal lobes. There is still considerable controversy, however, about the exact nature of the deficit in response inhibition produced by lesions of these structures.

The purpose of the present thesis is to describe the effects of lesions of hippocampal and septal structures on the ability of rats to reverse a number of different habits. In each case the rat must learn that the response that was previously right is now wrong, and inhibit it, while the response that was previously wrong is now right. A comparison of the effects of hippocampal and septal lesions on the

ability of rats to inhibit different kinds of responses should provide important information about the functions of these structures.

Before proceeding with an analysis of the notion of response inhibition, it should be noted that the hippocampal and septal regions have been ascribed roles in a wide variety of functions. Because of their close anatomical relation with the olfactory system, both structures were once classified as important parts of the rhinencephalon and were thus implicated as higher organs of smell. However, rats with septal or hippocampal lesions (Swann, 1934) and dogs with large hippocampal lesions (Allen, 1941) were found to be able to make olfactory discriminations as well as normal animals. Thereafter, a number of different functions have been attributed to these structures.

The hippocampus has been thought to be important in the elaboration and expression of emotion (Papez, 1937; Gol, Kellaway, Shapiro & Hurst, 1963), the control of instinctive behavior (Kim, 1960), and the consolidation of learning (Milner & Penfield, 1955). It is also believed to have some special role in the early stages of learning (Hunt, Diamond, Moore & Harvey, 1957; John & Killam, 1959). The septum has been thought to be important in preventing hyper-emotionality (Brady & Nauta, 1953) and as a "pleasure center" (Olds & Milner, 1954). These conceptions may all have some validity. However, recent experiments have provided considerable evidence that an important function of both the hippocampus and the septum of infra-human animals is also to enable them to inhibit response (Teitelbaum, 1961, 1964; Kaada, Rasmussen, & Kveim, 1962; Kasper, 1963; Kimble, 1963; Douglas & Isaacson, 1964).

Theories of the effects of brain lesions on response inhibition

There are at least four different views of the nature of the deficit that underlies the inability of an animal to inhibit his responses after a lesion of the brain: 1) that the lesion produces a deficit in the ability of an animal to inhibit any kind of response or "central set" that is temporarily dominant; 2) that it produces an inability to inhibit responses or to switch sets quickly; 3) that the animal is especially unable to habituate to novel stimuli; and 4) that the deficit is in the ability to inhibit movements, so that the animal is good in active responses but poor in situations requiring passivity.

Theory of perseveration of central sets

Mishkin (1964) reviewed his and his colleagues' studies of the effects of frontal-lobe lesions on the ability of monkeys to learn a variety of tasks, and concluded that the frontal lobes are important in the ability of an animal to give up any response tendency or central set that is temporarily dominant. If the normal animal has a strong tendency to choose the same stimulus continually in a test situation, so does the monkey with a frontal lesion, except that extinction of the tendency is more difficult. If the normal animal's dominant tendency is to choose the novel stimulus in a test situation, the same is again true for the monkey with a frontal lesion and now this tendency is more difficult to extinguish. According to this view, the frontal lobes are unimportant in determining the nature of the dominant response tendency; they are important only in extinguishing it.

Such a theory is inadequate as a complete explanation of the

effects of frontal lesions. For example, such lesions do not always produce a deficit in the ability to reverse a habit (Gross, 1963b) or to extinguish a bar-pressing response (Butler, Mishkin & Rosvold, 1963). Furthermore, monkeys with frontal damage may perform poorly on a delayed alternation task without perseverating excessively on either the left or right side (Gross & Weiskrantz, 1964).

When we turn to the hippocampus and the septum, the theory of perseveration of central sets becomes even less plausible. For example, thirsty rats with septal lesions may show poor response inhibition by taking many more shocks at an electrified water spout than normal animals (Kaada et al., 1962), which is consistent with the perseveration idea. However, the same rats may learn a complicated maze as well as normal animals, showing no tendency to perseverate on any originally preferred but incorrect response (Kaada, Rasmussen, & Kveim, 1961; see also Thomas, Moore, Harvey & Hunt, 1959). On the other hand, rats with hippocampal lesions may show a strong tendency to perseverate on an incorrect response in a maze (Kaada et al., 1961; Kimble, 1963; Kveim, Setekleiv & Kaada, 1964), yet are able to inhibit their responses about as well as normal animals when the water spout is electrified (Kaada et al., 1962; Kveim et al., 1964).

A general perseveration theory predicts that lesions will impair response inhibition in all tasks that require it. Kaada's studies indicate that the hippocampus and septum may not be identical in function, but rather may make possible the inhibition of different kinds of responses. Clearly, any explanation in terms of a general perseveration of central sets is inadequate to explain the observed dissociation.

Theory of a defect of quick inhibition

The second view of the way a brain lesion may impair response inhibition is that it decreases an animal's ability to learn to inhibit a response quickly, or in few trials. It is not too unreasonable to assume that the ability to switch rapidly from one response (or central set) to another involves a more sophisticated and complex mechanism than the ability to learn gradually, in a more rote fashion, that the dominant response is incorrect and must be replaced by a different one. The second hypothesis, then, is that the lesion, contrary to the usual effect of brain damage, produces a greater deficit in tasks in which normal animals perform well, such as quick reversal learning, than in tasks in which normal animals perform poorly, such as reversal learning which takes many trials.

Most of the experiments which support the theory are studies of the effects of frontal-lobe lesions in monkeys. For example, it has been found that monkeys with frontal lesions are impaired when required to reverse simple discriminations (Harlow & Dagnon, 1943; Settlage, Zable & Harlow, 1948) which normal monkeys learn in just a few trials, but are not impaired in the reversal of more difficult discriminations (Gross, 1963a, b). Similarly, Gross (1963b) found that during repeated reversals of an object-discrimination, monkeys with frontal damage were at first able to reverse as well as the control animals. Only after many reversals, when the control animals were performing exceedingly well, did the frontal animals show a significant deficit. Also, repeated reversals of an object discrimination were tested in

which the speed of reversal learning for all animals was increased by giving them fewer and fewer criterion trials before each reversal (Pribram, 1961). Again, there were no differences between the monkeys with frontal and control lesions except when the control animals reversed within only a few trials. Much of the evidence thus seems to support the notion that the monkey's frontal cortex is especially important in the ability of an animal to reverse a habit quickly.

There have been just a few studies of reversal learning following hippocampal or septal lesions. Teitelbaum (1964) found that cats with large hippocampal lesions were poor in reversing a number of tactual discriminations, as were cats with orbital frontal damage. Similar results were reported by Webster and Voneida (1964), even for an animal with just slight hippocampal damage. There were no significant differences in task difficulty between the different tests, however, so the importance of speed of reversal could not be analyzed.

Thompson and Langer (1963) found that rats with either hippocampal or septal lesions were considerably impaired in the successive reversal of a simple position habit. The normal and cortical control animals averaged only about 0.20 shocks per reversal in addition to the necessary "informing" shock, while the rats with hippocampal or septal damage averaged about 1.20 extra shocks per reversal. There was no overlap between the scores of the experimental and control animals. Again, it is not clear how the rats would have done on the reversal of more difficult tasks.

Extinction and passive avoidance tasks are also relevant to the problem of the importance of speed of switching responses. Butler et al. (1963) found that monkeys with orbital frontal damage extinguished a bar-pressing response as well as control animals when first tested. However, after repeated conditioning and extinction, the control animals extinguished more and more quickly, while the monkeys with orbital frontal lesions actually got worse in their ability to extinguish. Curiously, monkeys with lateral frontal lesions (Butler et al., 1963) and cats with septal lesions (Zucker, 1964) were found to be normal on both the first slow and succeeding quicker extinctions of a food-reinforced response. Rats with anterior hippocampal lesions, though, show a deficit analogous to that of the monkeys with orbital frontal lesions. Teitelbaum (1962) found that these rats were normal in the first extinction of a bar-pressing response, but were relatively slow to extinguish in later tests when the normal animals were extinguishing more quickly.

A study by Jarrard, Isaacson, and Wickelgren (1964) demonstrates that a quick inhibition theory is probably inadequate to explain the effects of hippocampal lesions on extinction. Studying the acquisition and extinction of a runway response for food, they found that varying the inter-trial interval had no effect on the extinction responses of cortical control animals. However, with response latency as the measure, rats with cortical-hippocampal lesions extinguished very poorly when the trials were separated by 10 minutes, while they extinguished as well as the control animals when the trials were separated by only 10 seconds. Thus the speed of extinction of the control animals

was not important, but the intertrial interval did play a role in determining the effects of hippocampal lesions on response inhibition. Another experiment which proves the same point was reported by Thompson, Langer, and Rich (1964). They found that the deficit in the reversal learning of a simple position habit produced by hippocampal lesions was more pronounced when the intertrial interval was 30 minutes than when it was 30 seconds. The control animals again performed just as well under the spaced as under the massed conditions.

The possibility that the rat's septum is important for the quick inhibition of responses appears to be supported by one experiment. Schwartzbaum and Spieth (1964) studied the effects of septal lesions in the rat on the animal's ability to inhibit a bar-pressing response when the response was followed by shock. The rats with lesions showed significant impairment only in the conditions or sessions in which the normal animals performed extraordinarily well.

In general, then, the notion that a brain lesion may impair the rapid learning of a task which requires response inhibition or a switch of set seems to describe the effects of frontal-lobe lesions in the monkey fairly well. The evidence concerning the hippocampus and septum is much more scanty. It appears that, for the rat, the theory may possibly apply to the septum but probably not to the hippocampus.

Theory of poor habituation to novelty

The third theory of the role of the hippocampus and septum in response inhibition may be considered a special case of the fourth hypothesis discussed below, that they are important in inhibiting active responses and supporting passive behavior. However, it seems to warrant

special consideration. This is the theory that both structures help the animal to habituate to novel stimuli. There is strong evidence that lends support to this view. However, there is evidence that these structures also help the animal to initiate activity in familiar environments.

First, experiments suggest that the hippocampal theta waves, of four to seven cycles per second, and recorded primarily in the dorsal hippocampus, are highly correlated with exploratory, orienting, or "searching" activity (Grastyan, 1959; Grastyan, Lissak, Madarasz, & Donhoffer, 1959). Theta waves are driven by large cells in the medial septum (Petsche, Stumpf & Gogolak, 1962) and are also often (Green & Arduini, 1954) but not always (Redding, 1964) elicited by stimulation of the reticular system. Theta waves sometimes disappear when searching movements no longer occur (Grastyan, 1959), and at other times continue before or during more goal-directed behavior (Adey, 1961). Whether these waves represent an "activated" or "de-activated" state of the hippocampus is controversial. In either case, the high correlation of their occurrence with searching movements would indicate that the septum and hippocampus may be especially important in the initiation or extinction of exploratory behavior.

The effects of lesions of these structures generally support the view that they are important in the extinction of exploratory behavior, or habituation. Septal lesions in the rat (Thomas et al., 1959), though not in the cat (Zucker, 1964), seem to produce hyperactivity in a novel environment (however, see Kenyon, 1962). Similarly,

hippocampal lesions in the rat may increase general activity in a novel environment (Teitelbaum, 1961; Kimble, 1963; Douglas & Isaacson, 1964) and may also slow down the rate of habituation (Roberts, Dember, & Brodwick, 1962; Douglas & Isaacson, 1964; however, see Wickelgren & Isaacson, 1963). Hyperactivity is found even if the lesion is limited to the anterior part of the hippocampus (Teitelbaum, 1961; Douglas & Isaacson, 1964). This is an area in which lesions have no noticeable effect on such common tests of response inhibition as passive avoidance (Kimura, 1958; Kaada et al., 1962) and bar-pressing under a reinforcement schedule which requires a low rate of responding (Ellen, Wilson & Powell, 1964). Moreover, hippocampal lesions in the cat may slow down or prevent habituation of the orienting response to the CS in either approach or avoidance learning tests (Grastyan, 1959; Grastyan & Karmos, 1962). These data indicate that removal of the hippocampus or septum may result in increased exploratory behavior and a decreased rate of habituation to novel stimuli.

On the other hand, septal and hippocampal lesions are often found to produce hypo-active animals. Septal damage in the rat decreases general activity in the dark (Kenyon, 1962) and in the home cage (Thomas et al., 1959). Hippocampal lesions in the cat, baboon, and monkey also result in generally apathetic animals (Votaw, 1959; Gols et al., 1963). It seems that, although there are many exceptions, perhaps the most consistent general description of animals with septal or hippocampal lesions is that they are slow to habituate and may be hyper-responsive to novel stimuli, but when the environment is familiar or does not contain much novelty, they show little exploration and are generally apathetic.

In this respect, the effects of hippocampal ablation in man and animal may not be very different. Patients with bilateral hippocampal ablation appear to have great difficulty in consolidating their experiences into permanent memories (Milner & Penfield, 1955; Scoville & Milner, 1957; Penfield & Milner, 1958). Their learning deficit, however, is not quite complete. One such patient was found to improve normally in a mirror-drawing task, and this improvement was retained and continued over days, despite the subject's claim of complete unfamiliarity with the situation whenever it was presented (Milner, 1962). Perhaps the failure to consolidate memory traces may be interpreted partly as an indication of poor ability to habituate--the unfamiliar never becomes familiar. However, these patients also are apathetic and lack normal curiosity (Milner, 1962). Thus, the apparently great differences in the effects of hippocampal ablation in man and animal may, at least in some respects, be differences in degree only.

In general, then, the evidence seems to indicate that the hippocampus and septum may be important in the ability of an animal both to habituate to novel stimuli and to maintain activity in a familiar environment. However, the relation between these functions of the hippocampus and septum and the importance of these structures in the inhibition or activation of more goal-directed responses has yet to be determined.

Theory of poor inhibition of movement

Perhaps the most common view of the role that the hippocampus and septum play in response inhibition is that they aid the animal in its ability to remain motionless; that is, they inhibit active responses and help produce immobile or withholding behavior. There is considerable evidence both for and against this theory.

Evidence for the theory. First, strong stimulation of the septum (Austin & Jasper, 1950) and sometimes of the hippocampus (Grastyan, 1959) results in an "arrest reaction" in which the animal is immobile. He is then unreactive to external stimuli and the effects of stimulation of the motor cortex may be considerably reduced. Furthermore, stimulation of either the hippocampus (MacLean, Flanigan, Flynn, Kim, & Stevens, 1955-56; Grastyan, 1959; Andy & Mitchell, 1960; Flynn, MacLean, & Kim, 1961) or septum (Andy & Mitchell, 1960) often prevents an animal from performing a well-learned avoidance reaction. Even the autonomic component of the response may be inhibited (MacLean et al., 1955-56).

The generalized response inhibition produced by stimulation is thought to be mediated by inhibition of the reticular system (Grastyan, 1959). Some physiological support of this idea is available, at least for the hippocampus. Adey, Segundo, & Livingston (1957) found that stimulation of the hippocampal gyrus of cats and monkeys decreased the effect of later reticular stimulation on activity in the centrum medianum. Similarly, Redding (1964), using the encéphale isolé preparation, found that in the cat brain hippocampal stimulation decreases subsequent evoked potentials in the visual cortex. On the other hand, the evoked potential produced by optic tract stimulation is enhanced by preceding reticular stimulation. The suppressing effect produced by hippocampal stimulation disappears and is even replaced by facilitation if the cerveau isolé preparation is used; that is, one in which the reticular system is cut off from the hippocampus and visual system. Redding concludes that stimulation of the hippocampus has a strong inhibitory effect on the reticular system.

One experiment seems to indicate that hippocampal stimulation does not affect the learning process itself, but only inhibits the response. Flynn and Wasman (1960) tried to train cats by presenting a combination of buzzer and shock to the paw after strong stimulation of the hippocampus. Paw withdrawals rarely or never occurred during the CS after even hundreds of trials. However, if the CS was then presented without preceding hippocampal stimulation, though still followed by the shock, avoidance paw withdrawals occurred on about 50 per cent of the first 20 trials. Since normal naive cats without hippocampal stimulation usually failed to show avoidance responses during the first 20 trials of CS-US presentation, Flynn and Wasman concluded that some learning must have occurred during the initial trials with hippocampal stimulation. However, the possibility of sensitization was not eliminated since cats that are given forepaw shock alone after hippocampal stimulation for hundreds of trials might also show 50 per cent avoidance reactions if then presented with the buzzer-shock combination. Thus the experiment did not conclusively demonstrate that some learning of the CS-US association occurred after the hippocampal stimulation.

Further behavioral evidence that the hippocampus and septum are normally involved in the inhibition of active responses and support of passive behavior is the finding that lesions of these areas sometimes impair passive-avoidance learning and facilitate the learning of an active avoidance. First, passive avoidance: here the question is whether a punishing shock or two is sufficient to make an animal give up a dominant approach response; if not, what number of shocks is needed

before such a response is given up? McCleary (1961) found that one or two shocks would make normal cats stop running down a runway for food. Cats with lesions in the septum (Zucker, 1964) or septal-callosal region (McCleary, 1961) usually continue to run for food after two shocks and thus demonstrate poor passive avoidance. Kimura (1958) and Isaacson and Wickelgren (1962) reported similar findings with rats who had either posterior hippocampal or large hippocampal damage. Kaada et al. (1962) observed the number of shocks a thirsty rat would take at a charged water spout, and found that normal subjects took from 1 to 4 shocks while those with septal damage took from 8 to more than 100 shocks at the water spout. Kasper (1963) found that continuous low-voltage septal stimulation also makes ~~thirsty~~ rats take more shocks than normal animals at a charged water spout. Thus, both septal and hippocampal disturbances have been found to impair passive avoidance learning.

Other studies have demonstrated that rats with septal lesions learn a shuttle-box active avoidance response considerably faster than normal animals (King, 1958; Kenyon, 1962; Krieckhaus, Simmons, Thomas, & Kenyon, 1964). Isaacson, Douglas, and Moore (1961) got similar results using rats with large cortical-hippocampal lesions.

In general, the observations that stimulation of the hippocampus or septum may result in the reduction of spontaneous, cortically-induced, or learned motor responses, that it may inhibit the activity of the reticular system, and that lesions of these structures may depress passive-avoidance behavior and facilitate active--avoidance, all lead to the conclusion that these structures are important in the

inhibition of active responses and the production of immobile or withholding behavior.

Evidence against the theory. Despite the strong evidence that active behavior is inhibited and passive behavior supported by the hippocampus and septum, there is also opposing evidence. First, radical disruption of the normal activity of the rat's hippocampus, produced by bilateral hippocampal spreading depression, has been found to result in an animal that is extraordinarily unresponsive (Bures, 1959). Not only are avoidance reactions eliminated but even escape reactions take about a half minute to perform. In addition, hippocampal spreading depression has little effect on the rate of firing of reticular cells (Bures, Buresova, & Fifkova, 1961). These results may be contrasted with the effects of bilateral cortical spreading depression. With the cortical depression, escape reactions are performed with relative ease and the majority of reticular cells show a considerable increase in their average rate of firing (Bures, 1959; Bures et al., 1961). Cortical spreading depression thus produces an increase in reticular arousal, and although the animal is then somewhat unresponsive, the increased midbrain activity maintains its responsiveness to shock and permits good escape behavior. Hippocampal spreading depression, on the other hand, does not produce an increase of reticular activity; the animal is barely responsive to shock. Disruption of the normal functions of the hippocampus by spreading depression may thus produce a very unresponsive animal.

Ablation studies provide further evidence opposed to the conclusion that the hippocampus and septum inhibit active responses and support

passive behavior. For example, simple active avoidance-learning in the rat may be impaired by either unilateral hippocampal lesions (Buresova, Bures, Vinogradova, & Weiss, 1962) or by septal lesions (Kenyon, 1962; Vanderwolf, 1964). These tasks are different from the shuttle-box test in two ways: first, the same region of the apparatus is always the one to be avoided, while in the shuttle-box the region that gives shock on one trial is the safe region on the next; and secondly, there are no special CSs which precede and signal the onset of shock and thus elicit the final avoidance behavior. The rats are simply placed in one area and must move to another area within 5 or 10 seconds in order to avoid shock. These studies make it clear that hippocampal and septal lesions may disrupt the learning of active avoidance tasks, and may thus be important in initiating behavior.

The evidence that ablation of the hippocampus and septum impair the ability of an animal to withhold its responses is also equivocal. Hippocampal lesions do not always result in poor passive avoidance learning (Kimura, 1958; Kaada et al., 1962; Kveim et al., 1964). Zucker (1964) has shown that cats with septal lesions extinguish an active—avoidance response as well as normal animals, while Moore (1964) found that cats with septal lesions will sometimes freeze rather than escape shock in an active avoidance test. Finally, rats with septal lesions sometimes, though not always, suppress their bar-pressing behavior as well as normal animals in tests of a conditioned emotional response, or CER (Brady & Nauta, 1955; Harvey, Jacobson, & Hunt, 1961). In fact, under certain weak shock conditions, rats with

septal lesions show a stronger CER than normal rats, presumably due to a lower pain threshold (Harvey, 1964).

These results make it necessary to reexamine the fact that hippocampal or septal stimulation sometimes results in strong motor inhibition. Such an inhibiting effect is maximally produced by intense stimulation which almost always results in large bilateral seizures in these structures (Flynn & Wasman, 1960; Flynn et al., 1961). Motor inhibition following stimulation thus may be just a mild version of the motor deficits produced by spreading depression. It appears unlikely that such response-inhibiting effects of stimulation are similar to any which may be produced naturally by the activity of these structures. This view is supported by the fact that rats with either septal or hippocampal lesions have sometimes been found to be poor in initiating active avoidance responses and at other times they have been observed to inhibit their activity as well as normal animals.

In summary, then, though there is considerable evidence in support of it, the theory that the major role of the hippocampus and septum is to inhibit active responses and maintain withholding behavior is subject to some doubt. The experimental results reported in this thesis will give further evidence that the theory is inadequate.

THE PRESENT INVESTIGATION

Four theories of the effects of brain lesions on response inhibition have been examined in detail. The following conclusions have been reached: 1) the theory of "perseveration of central sets" is probably inadequate to explain the effects of frontal, hippocampal, or septal lesions; 2) the theory that frontal lesions may produce a deficit in the ability of monkeys to inhibit a response or switch sets quickly or after only a few negative trials appears well-substantiated, while the evidence concerning the effects of hippocampal and septal lesions is much more scanty; 3) the theory that lesions of the hippocampus and septum produce hyper-responsiveness and slow habituation to novel stimuli has considerable support; however, such animals are also often hypo-responsive in an environment that does not contain much novelty; and 4) though there is much evidence that supports the theory that the hippocampus and septum act to inhibit responses and support passive behavior, the hypothesis is still subject to doubt.

As we see, the exact nature of the role of the hippocampus and septum in the ability of an animal to inhibit its responses is not yet clear. Two reasons for the present state of uncertainty are: first, the general confusion concerning the importance of these structures in active vs. passive avoidance; second, the paucity of evidence concerning the effects of such lesions on the ability of animals to reverse habits of various levels of difficulty.

The present experiments were designed to test the ability of rats with hippocampal or septal lesions to reverse a variety of habits. One

group of animals was tested for their ability to learn a simple active avoidance response. The task was then reversed and became a test of simple passive avoidance. This was in turn reversed and the active avoidance had to be relearned. Altogether, each animal was tested on six reversals from active to passive and six reversals from passive to active avoidance. Animals of another group were tested for their ability to learn and reverse a simple position habit, a black-white simultaneous discrimination, and a black-white successive discrimination. The simultaneous black—white and position reversals were then repeated to test improvement in the speed of reversal learning with added training. These experiments should help clarify the role of the hippocampus and septum in response inhibition.

METHOD

The subjects were 82 naive male hooded rats, obtained from the Quebec Breeding Farm. They were housed four or five to a cage, with food and water ad libitum. The number of animals in each group is given in Tables I and II.

Surgical and histological procedures and results

The animals weighed between 210 and 260 grams at the time of operation. The rat was anesthetized with nembutal and placed in the Johnson-Krieg stereotaxic instrument. A scalp incision was made and holes of appropriate size were drilled at the desired location in the skull. The septal, anterior hippocampal, and posterior hippocampal lesions were made electrolytically by a stainless-steel wire insulated except at the tip. The cortical and cortical-hippocampal lesions were made by suction. The electrolytic lesions were made with 2 to 2.4 milliamperes of direct current for 20 seconds. The septal and the anterior hippocampal lesions were essentially the same in both studies. The co-ordinates of the septal lesions in relation to bregma were: A1.8, L.0.7, and H5.2 mm. from the surface of the skull. The anterior hippocampal lesions were P1.5, L1.5, and H3.8. In the active-passive avoidance study, the posterior hippocampal lesions were P4.5, L4.6, and H4.1. The posterior hippocampal lesions were slightly more posterior, lateral, and deeper in the discrimination reversal study.

Suction lesions were made by drilling a large hole over the posterior cortex, cutting the dura with a scalpel, and then aspirating the exposed cortex. In the cortical-hippocampal group the underlying hippocampus was similarly aspirated. In the active-passive study, which was done last, more care was taken to avoid the midline cortex in both suction groups, and in the cortical-hippocampal group less of the cortex and more of the posterior hippocampus was removed than in the discrimination-reversal study. After bleeding subsided, gelfoam was packed into the skull holes. The sham operated control animals had holes drilled in their skulls but their brains were not damaged. At the end of each operation, the scalp was closed with wound clips and antibiotics were administered intramuscularly.

On completion of the testing schedule, each experimental animal was perfused first with normal saline and then with formal-saline and the brain was removed. After fixing for several days, coronal sections of about 1 to 2 mm. thick were cut by a razor blade. Photographs were taken of the dorsal view of the suction lesions and of the anterior and posterior views of the relevant sections, and estimates were made of the size of the lesion. Photographs of representative lesions from the two studies are presented in Figs. 1 and 2.

The septal lesions were consistently large, with the lateral and medial septal areas being almost completely removed. In most animals, the fornix was also interrupted, though those with no damage to the fornix showed at least as great a deficit as the other animals

with septal lesions. The corpus callosum, the anterior commissure, and the caudate nucleus were rarely damaged.

The anterior hippocampal lesions were usually small, ranging from 1 to 2 mm. in diameter. The posterior hippocampal lesions in the active-passive avoidance study were also from 1 to 2 mm. in diameter, while those in the discrimination-reversal study were usually 2 to 3 mm. in diameter.

In the discrimination--reversal study, both the cortical and the cortical-hippocampal lesions usually included the retrosplenial and some posterior cingulate cortex. Furthermore, though the hippocampal damage was fairly extensive, almost all the animals in the cortical-hippocampal group had much of the posterior hippocampus spared. In the active-passive avoidance study, the medial cortex was almost always spared in the suction groups. Also, there was usually less cortical and more posterior hippocampal damage in this cortical-hippocampal group than in the previous one.

The data obtained from all animals with hippocampal lesions in which the lesions did not penetrate to the thalamus were discarded. Also, the results of all animals with cortical control lesions in which there was bilateral damage to the hippocampus were discarded.

Training procedures

Apparatus

An avoidance box, similar to the one used by Vanderwolf (1962), was employed for the active-passive avoidance study. It was 38" long, 12" wide, and 20" high, and had a grid floor through which a 0.33 ma

shock could be administered to the paws of the animal. A removable partition in the middle of the box divided it into a black and a white side. It was wired so that the black or white side could be electrified separately.

For the discrimination—reversal study, a modified version of the discrimination apparatus first described by Thompson and Bryant (1955) was used. It consists of a V-shaped choice chamber with a grid floor, and a goal chamber with a wooden floor. The grid in the choice chamber delivered a 0.8 ma shock, while separately wired grids under the left and right windows through which the animal entered the goal chamber delivered a 0.4 ma shock. The windows, which measured 4" x 5", were separated by a partition which protuded 4" out into the choice chamber. Black, white, or horizontally-striated cards were placed behind the windows, with the incorrect card locked in place. The background surrounding the cards was light grey.

General procedure

In the active-passive avoidance study, the animal was always placed in the white side with his back towards the black side. In the active avoidance tests, if the rat had not moved to the black side after five seconds, intermittent shock was given. After avoidance or escape, the partition was put in place to prevent back-tracking. Twenty—five seconds later, the rat was placed on the feeding stand for five seconds and then a new trial was started.

In the passive avoidance tests, in order to avoid shock the animal had to stay on the white side and avoid going into the black for 25 seconds. If he succeeded, the partition was put in place and

the rat was placed on the feeding stand for five seconds before a new trial began. If the animal made an error by going from the white to the black side, it was shocked intermittently until it re-entered the white side, or for a 30-second period, after which it was gently pushed into the white side. Then the partition was immediately put in place and the animal stayed in the correct compartment for 25 seconds, after which it was placed on the feeding stand for five seconds before the next trial began. The total inter-trial interval thus varied from about 30 to 60 seconds.

The criterion for active or passive avoidance was always five out of six correct consecutive trials. Within each day the active and passive avoidance tests succeeded each other without intermission. In both the active and passive tests, if 30 errors were made before criterion was reached, training was stopped and continued the next day. If 60 errors were made in the original active avoidance learning, training was simply stopped and that animal was not given the complete series of passive and active reversal tests.

In the discrimination--reversal study, the animal was placed in the choice chamber with his back to the cards and goal-chamber. E tapped on the box if S made no choice after about five seconds, and then gave intermittent shocks if no choice was made after 10 to 15 seconds . The animal was shocked automatically by a constantly charged grid if he approached the wrong door, which was counted as an error. As in the active-passive avoidance study, no more than one error was counted per trial. The correction method was used so that the trial was terminated after the animal pushed over the correct card and

entered the goal chamber. After about five seconds the animal was taken out of the goal chamber and placed on the feeding stand while another animal was tested. Four or five rats were run one after the other for each trial, so the inter—trial interval varied from one to three minutes.

Specific training

In the active-passive avoidance study, training began from 10 days to four months (for some of the septal rats) after the operation. On the first day, active avoidance was taught until criterion was reached. The animal was then trained on passive avoidance, which was followed by another active avoidance test. On the second day, each animal was retrained on active avoidance and was then given passive, active, passive, active, and passive avoidance tests. On the third day, the passive avoidance response was re—established and the rats were given a sequence of active, passive, active,passive, and active avoidance tests. Altogether there were six reversals from active to passive avoidance and six reversals from passive to active avoidance.

In the discrimination—reversal study, training began 14 to 20 days after the operation. On the first day all animals were taught to enter the goal chamber through open windows until three successive avoidance responses were achieved. The next day, each animal was trained to knock down horizontally-striated cards until he made three successive avoidances without shock. Except during the position-reversal tests, all animals were then given 30 trials a day. On all the visual discrimination tests, the sequence of correct responses was: 5L, 5R, 5L, 5R, then 10 "random" trials (LRLRRLRRLL); on

alternate days, the right side was correct on the first five trials. The learning criterion was either 25 correct responses out of 30 or 9 correct out of the last 10 trials. The day after criterion was achieved on one task, the next task began. Each animal was usually tested five or six days per week. The order of the tasks was as follows:

1) Position reversals. On the day after pre-training, all animals were trained to go to the left until they achieved a criterion of 5 out of 6 correct; then, using the same criterion, the animals were trained to go to the right, to the left, and to the right again. Horizontally-striated cards were behind both windows. Training was stopped if 30 errors were made on any reversal. Thus each animal's score was simply the greatest number of errors made on any of the reversals.

2) Black-white simultaneous discrimination. Some rats in each group had black correct, others had white.

3) Reversal of B-W simultaneous discrimination.

4) Successive discrimination: when both sides were black, the left side was correct; both white, the right was correct.

5) Successive discrimination: reversal of preceding (4). Training on this task stopped if 150 or more errors were made.

6) Black-white simultaneous discrimination (same as 3).

7) Reversal of B-W simultaneous descrimination (same as 2).

8) Position reversals (same as 1).

RESULTS

Active avoidance learning

Table I shows that, in the active-passive avoidance study, almost all rats with septal lesions and some of the rats with hippocampal lesions performed very poorly in the original learning of the active avoidance response (see Vanderwolf, 1964). In fact, one rat with a septal lesion, one with a posterior hippocampal lesion, and two with cortical-hippocampal lesions, never did reach criterion on the first active avoidance test. A simple active avoidance response was also taught to all groups at the beginning of the discrimination-reversal study. In that condition, E always tapped on the box for at least five seconds before applying shock. No deficit was then observed in the learning of active avoidance by any animal, and the rats with septal lesions even appeared to learn faster than the others.

These contrary results made it probable that the rats in the active-passive study who did not learn the active--avoidance response would have made avoidance responses if the box had been tapped. These animals were then trained on passive avoidance by tapping on the box throughout the trial and shocking any resulting active-avoidance response. The rat with the septal lesion which previously never made any active avoidance responses required 33 shocked trials before learning to inhibit its response under these conditions, while the three rats with hippocampal lesions took two, six and seven shocks. Two normal animals which were tested under similar conditions took

two and three shocks. Therefore, at least for the septal rat, the excessive freezing behavior indicated by poor active avoidance was very difficult to maintain in the presence of a disinhibiting stimulus. These results indicate that septal lesions and sometimes hippocampal lesions produce a deficit in the acquisition of an active avoidance response as long as no arousing or disinhibiting stimulus precedes the application of the shock.

Active and passive reversals

In general, the animals which performed poorly on the reversals from the active to the passive avoidance also did poorly on the reversals from the passive to the active avoidance. Thus, as Table I shows, both the septal group and the cortical-hippocampal group performed considerably worse than their control groups on both sets of reversals. Unfortunately, the effects of the cortical-hippocampal lesions cannot be unambiguously attributed to the hippocampal damage since two of the nine animals with only cortical lesions also performed very poorly on reversals of both the active and the passive avoidance.

The group with posterior hippocampal lesions performed significantly worse than the control or anterior hippocampal groups on the passive tasks, though it was still significantly superior to the septal or cortical-hippocampal groups on those reversals (see Kimura, 1958). Their performance on the reversals to the active avoidance was highly variable. In general, the group data clearly show that poor performance on one set of reversals was usually associated with poor performance on the other set.

There were some striking individual exceptions to this general

result. One rat with a septal lesion and one with a cortical-hippocampal lesion performed very poorly on the passive tests, yet relatively well on the active avoidance tests. On the other hand, one rat with a posterior hippocampal lesion performed comparatively well on the passive tests but was extremely poor on the active tests. These glaring exceptions, combined with some preliminary results on the effects of lesions of other parts of the brain using these tasks, make it difficult to conclude that a single mechanism controls the ability of an animal to switch both from active to passive and from passive to active avoidance. However, the results described here clearly disprove the contention that a deficit in passive avoidance leads to a facilitation of active avoidance behavior.

Discrimination reversals

Table II summarizes the performances of all groups on the various discrimination tests. The performance of the rats with septal lesions on the reversals of the various discriminations makes it clear that a lesion which produces a large deficit in passive avoidance behavior does not necessarily produce a deficit in all reversal tasks. In fact, rats with septal lesions performed quite poorly in the reversal tests which normal rats found very easy (active and passive avoidance and the position reversals) while they performed quite well in the reversal tests which normal rats found comparatively difficult (the visual-discrimination reversals). This result appears analogous to the effect of frontal lobe lesions in the monkey, and leads one to the conclusion that the rat's septum may be especially important in the ability of the

animal to quickly inhibit or switch sets.

In contrast to the group with septal lesions, the cortical-hippocampal animals were significantly worse than their control group on almost all of the reversal tests. They performed extremely poorly on both the simplest (position reversal) and most difficult (reversal of the successive discrimination) tests, so their deficit appears more general than that of the septal group.

Though almost all animals with either anterior or posterior hippocampal lesions performed outside of the normal range on at least one reversal task, these groups were rarely significantly worse than the control animals. Both electrolytic hippocampal groups, however, did tend to perform poorly on the reversal of the successive discrimination, though this was not statistically significant ($P < .10$).

In general, then, septal lesions produced striking deficits only in the simpler reversal tasks, while hippocampal lesions resulted in a more general impairment of reversal learning.

The "non-reversal" discrimination tasks

All groups performed quite alike on the original learning of the black-white simultaneous discrimination. This result indicates that, at least in this situation, none of the lesions had any significant effect on the ability of rats to learn to avoid the incorrect stimulus.

The behavior of the experimental groups on the later learning of the successive discrimination (task 4) and relearning of the simultaneous discrimination (task 6) deserves special comment. First, it should be noted that the control animals generally performed extremely well on both tasks, indicating considerable positive transfer from the

previously-learned tasks. Except for the poor successive-discrimination learning of the cortical-hippocampal group, none of the experimental groups were significantly worse than the control animals on either task 4 or 6. All animals with limbic lesions, though, except for one with posterior hippocampal damage, scored outside of the normal range on at least one of these two tasks. Yet only one septal animal and two with cortical-hippocampal lesions were outside of the control range on both tasks. As Table III indicates, the almost universal pattern was to perform very well on one of these tests and yet quite poorly on the other.

This result can best be explained by the apparently very strong tendency of animals with limbic lesions to base their choice on either the left or the right--side cues and virtually to ignore other stimuli. Thus, when an animal was taught to go to the white card and avoid the black one, and its choices were based primarily on the stimuli shown on the right side, then it found the following successive discrimination (both sides black, go to left, both sides white, go to right) exceptionally easy since it already had a strong tendency to go through the right side if it was white and to avoid it if it was black. However, if the rat learned the previous discrimination on the basis of the cues shown at the left side, the successive discrimination was then very difficult to learn. The same description applies when an animal was taught the simultaneous discrimination after learning a successive one.

The order of tasks was arranged so that as long as an animal continued to base his choices on the cues shown on the same side, he would perform well (strong positive transfer) one one task but poorly

(strong negative transfer) on the other. As we see, this is what almost all of the animals with limbic lesions did. Furthermore, at least one of the few exceptions was clearly due to a switch of the preferred side during the learning of the reversal of the successive discrimination. It appears, then, that: a) rats with limbic lesions apparently attend only to the cues on one or the other side when solving a two-choice discrimination problem; and b) these animals learn to approach one cue and avoid the other, indicating that probably both positive and negative emotions control their behavior in such a situation.

Summary of results

1. Septal lesions and sometimes hippocampal lesions produce a deficit in the acquisition of a simple active avoidance response as long as there is no disinhibiting CS to "trigger" the response.

2. Rats with septal or hippocampal lesions that are very poor in reversing from active to passive avoidance are usually also poor in reversing from passive to active avoidance.

3. Septal lesions produce a large deficit in reversal tasks which normal rats find simple, but produce little or no deficit in more difficult reversal tasks.

4. Hippocampal lesions may produce a deficit in both the simple and more difficult reversal tests.

5. Both septal and hippocampal lesions seem to reduce the range of cues used in the solution of a two—choice discrimination problem to those appearing on either the left or the right side, but not on both sides.

DISCUSSION

The results of these experiments have implications for a number of issues. First is the relation between passive and active avoidance behavior. The commonly held opinion is that animals that perform poorly in passive avoidance tasks, and are thus poor at inhibiting their responses, perform as well or better than normal animals in tests of active avoidance. The present experiments demonstrate, however, that this is not necessarily so. The same septal or hippocampal lesion that impairs passive avoidance may also impair active avoidance behavior.

It seems probable that the apparent facilitation of active avoidance by such lesions is due to an increase in the arousing effects of a CS: in the present experiments, the auditory stimulation of tapping on the box before presenting shock. Krieckhaus et al.(1964) have presented two arguments against this possibility: first, that after septal lesions the hyper-reactive rat (with a "septal syndrome") does not perform much better in the shuttle-box than the less reactive animal (lacking the syndrome). It seems however that there is no necessary relation between the hyper-reactivity and the effect of stimulation in disinhibiting a freezing response. Krieckhaus's second argument is that a visual stimulus can be used as a CS, rather than the more arousing auditory stimulus; but this also seems not to be decisive, since the visual stimulation appears to be less effective —— has a smaller facilitating effect on avoidance learning -- than the auditory stimulation (Kenyon, 1962; Krieckhaus et al., 1964). Thus, these objections do not necessarily invalidate an "excessive disinhibition"

explanation of how brain lesions may sometimes facilitate active avoidance learning.

The finding that septal lesions in the rat had little or no effect on the ability of animals to reverse the relatively difficult visual discriminations is surprising, especially when one considers how poorly these animals inhibit their response in the passive avoidance test. This pattern of the effects of septal lesions on different tests of perseveration may not apply to other species. For example, Zucker (1964) found that septal lesions in the cat may produce a deficit in the learning and reversal of a difficult discrimination though not of a simple one. Furthermore, Zucker found that his cats with septal lesions could learn to inhibit a well-trained active avoidance response as well as normal cats. In Zucker's study, a buzzer was always presented as a CS. Under such conditions, rats with septal lesions would undoubtedly perform even worse on passive avoidance than they did in the present active-passive tests in which there was no such disinhibiting CS. We find, then, that rats and cats do not show the same effects of septal lesions on response inhibition.

The performance of the rats with septal damage in these experiments generally support the odd view derived from studies of frontal lesions in monkeys that a brain lesion may impair the learning of simple reversals but not difficult ones. The interpretation given here of this fact, however, is different from the one proposed by Gross and Weiskrantz (1964). They regard such results as indicating that the lesion produces a deficit in the ability of an animal to profit from his short--term memory store. The view presented here is that the ability

to switch sets quickly requires a more sophisticated and thus more disruptable mechanism than does the ability of an animal to inhibit his dominant tendency more gradually.

Gross points out, though, that the monkeys with frontal lesions are not only poor in reversing, but they are also poor in learning discrimination problems that normal animals solve after only a few trials. Similarly, rats with septal lesions are also poor in learning a simple active avoidance response. How can these results be reconciled with the "quick-switching" theory? In the avoidance situation, it seems as if normal rats develop, but very quickly inhibit, a freezing or withholding tendency after the first couple of shocks. As long as there is no disinhibiting stimulus, rats with septal lesions also develop a freezing tendency but are slower to give it up. Perhaps in the discrimination tests, the monkeys with frontal damage are slower to give up their incorrect response tendencies in the condition in which normal monkeys give theirs up very quickly. Thus the finding of poor learning does not disprove the quick-inhibition interpretation. Although it is unlikely that all, or perhaps even most, of the effects of septal lesions in the rat or frontal lesions in the monkey are explicable by such a theory, it is clearly a viewpoint that deserves serious consideration.

The role of the hippocampus in response inhibition appears to be even more difficult to understand than that of the septum. The rats in the present experiments with large cortical-hippocampal lesions clearly found reversal learning of all sorts considerably more difficult than did those with lesions confined to the cortex, while the effects of the smaller anterior and posterior hippocampal lesions were usually much

slighter or even negligible. However, one cannot conclude from these results that an ablation of the hippocampus, as long as it is large enough, will invariably result in poor response inhibition. The reasons are: (1) in the present experiments almost all of the rats with large cortical-hippocampal lesions would sometimes perform surprisingly well on a reversal-learning task; (2) Jarrard et al. (1964) found that rats with similar lesions will under some conditions extinguish an operant response as well as cortical control rats; (3) Lash (1964) found that under some conditions rats with cortical-hippocampal lesions would show more spontaneous alternation and perform better on a successive brightness discrimination than rats with cortical lesions alone; and (4) Webster and Voneida (1964) found that, in the cat, an extremely small lesion of the hippocampus, one that does not even penetrate to the thalamus, may cause a grave deficit in tests of reversal learning.

Further difficulty emerges if one concentrates one's attention on the anterior hippocampus. Lesions restricted to this area of the rat's brain have been found to produce poor rapid extinction of a bar-pressing response (Teitelbaum, 1961), hyper-activity (Teitelbaum & Milner, 1963; Douglas & Isaacson, 1964); poor maze learning (Kaada et al., 1961; Kveim et al., 1964), and poor spontaneous alternation (Gold, 1961; Douglas & Isaacson, 1964). Together, these results seem to indicate that this area is important in response inhibition. However, such lesions do not produce a deficit in passive avoidance learning (Kimura, 1958; Kaada et al., 1962; Kveim et al., 1964; and the present experiment). On the different reversal tests of this experiment, the group as a whole was never significantly worse than the control group, though some of the

animals did sometimes perform very poorly. In general, then, it seems that the exact role of the hippocampus, or of different parts of the hippocampus, in response inhibition is a problem that only future research can clarify.

SUMMARY

Rats with septal, anterior hippocampal, posterior hippocampal, cortical, and cortical-hippocampal lesions were trained on a number of different reversal tests. In one study the rats were taught to alternate active and passive avoidance responses. In another study the rats were trained on a position reversal and various visual-discrimination reversal tests. The major results and conclusions are as follows:

1. As long as there is no disinhibiting CS to "trigger" the response, septal lesions and sometimes hippocampal lesions produce a deficit in the acquisition of a simple active avoidance response. The tendency of rats with septal lesions to be excessively disinhibited by arousing stimuli probably explains their excellent performance in the shuttle-box avoidance situation.

2. Rats with septal and hippocampal lesions that are very poor in reversing from active to passive avoidance are usually also poor in reversing from passive to active avoidance. Thus the theory that animals that are poor in inhibiting their responses are better than normal in initiating responses is not supported.

3. Septal lesions produce a large deficit in reversal tasks which normal rats find simple, but produce little or no deficit in more difficult reversal tasks. Therefore septal lesions in the rat, like frontal lesions in the monkey, appear to produce a deficit in the ability of animals to switch sets quickly.

4. Hippocampal lesions may produce a deficit in both the simpler

and the more difficult reversal tests. However, the role of the hippocampus in response inhibition is still very unclear.

5. Both septal and hippocampal lesions seem to reduce the range of cues used in the solution of a two-choice discrimination problem to those appearing on either the left or the right side, but not on both sides.

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Table I. Median and range (in brackets) of errors to criterion for active and passive avoidance.

	Original active avoidance	Mean of six reversals from active to passive	Mean of six reversals from passive to active
Sham-Op (N-10)	4.5 (3-8)	1.5 (1.2-2.0)	1.8 (1.3-5.0)
Septum (N-7)[1]	20[b] (5-60)	10.0[b] (5.2-21.5)	7.5[b] (4.8-16.0)
Ant Hipp (N-5)	8 (4-11)	1.5 (1.0-2.0)	2.7 (1.8-4.5)
Post Hipp (N-8)[1]	7.5[a] (4-60)	2.5[b] (2.2-3.0)	3.6 (1.3-16.7)
Post Cort (N-9)	7 (3-13)	2.3 (1.7-12.0)	2.8 (1.7-6.5)
Cort Hipp (N-11)[2]	11 (4-60)	8.3[d] (3.0-24.8)	5.5[c] (3.5-9.8)

[a] Different from sham-op at .05 level (Mann-Whitney U, 2-tailed).

[b] Ditto at .002 level.

[c] Different from post cort at .05 level (Mann-Whitney U, 2-tailed).

[d] Ditto at .02 level.

[1] One subject not trained on reversal tasks.

[2] Two subjects not trained on reversal tasks.

Table II. Median and range (in brackets) of errors to criterion for each of the discriminations and reversals.

	Sham-Op (N-5)	Septum (N-7)	AntHipp (N-5)	PostHipp (N-5)	PostCort (N-5)	CortHipp (N-5)
1) Position reversal	9 (6-22)	27[a] (15-30)	19 (12-30)	10 (9-30)	11 (8-18)	25[b] (15-30)
2) Simult. B-W	15 (9-20)	17 (8-24)	10 (7-19)	10 (7-35)	11 (7-29)	14 (6-31)
3) Reversal of (2)	44 (26-56)	37 (28-59)	35 (21-49)	64 (28-98)	28 (20-48)	63 (27-94)
4) Success. B-W	10 (3-24)	28 (5--67)	36 (8-76)	14 (7-95)	18 (5-38)	59[b] (16-107)
5) Reversal of (4)	43 (19-63)	61 (51-82)	70 (44-95)	67 (49-133)	45 (31-69)	136[b] (67-150)
6) Simult. B-W	7 (3-15)	34 (0-62)	4 (1-28)	6 (4-35)	4 (1-11)	22 (0-59)
7) Reversal of (6)	24 (7-44)	42 (28-54)	29 (25-58)	45 (33-82)	13 (6-24)	60[b] (26-101)
8) Position reversal	5 (4--7)	9[a] (5-14)	7 (6-13)	9[a] (6-11)	6 (2-8)	21[b] (7-30)

[a] Different from sham-op at .05 level (Mann-Whitney U, 2--tailed)

[b] Different from post cort at .05 level (Mann-Whitney U, 2-tailed)

Table III. Number of animals with limbic lesions that performed either well (within control range) or poorly (outside of control range) on both Tasks 4 and 6, vs. number that performed well on one task but poorly on the other.

Well on both	Poorly on both	Well on 4, Poorly on 6	Poorly on 4, Well on 6
1	3	8	10
Total	4	18	

Chi-square - 8.9, df - 1, $P < .01$.

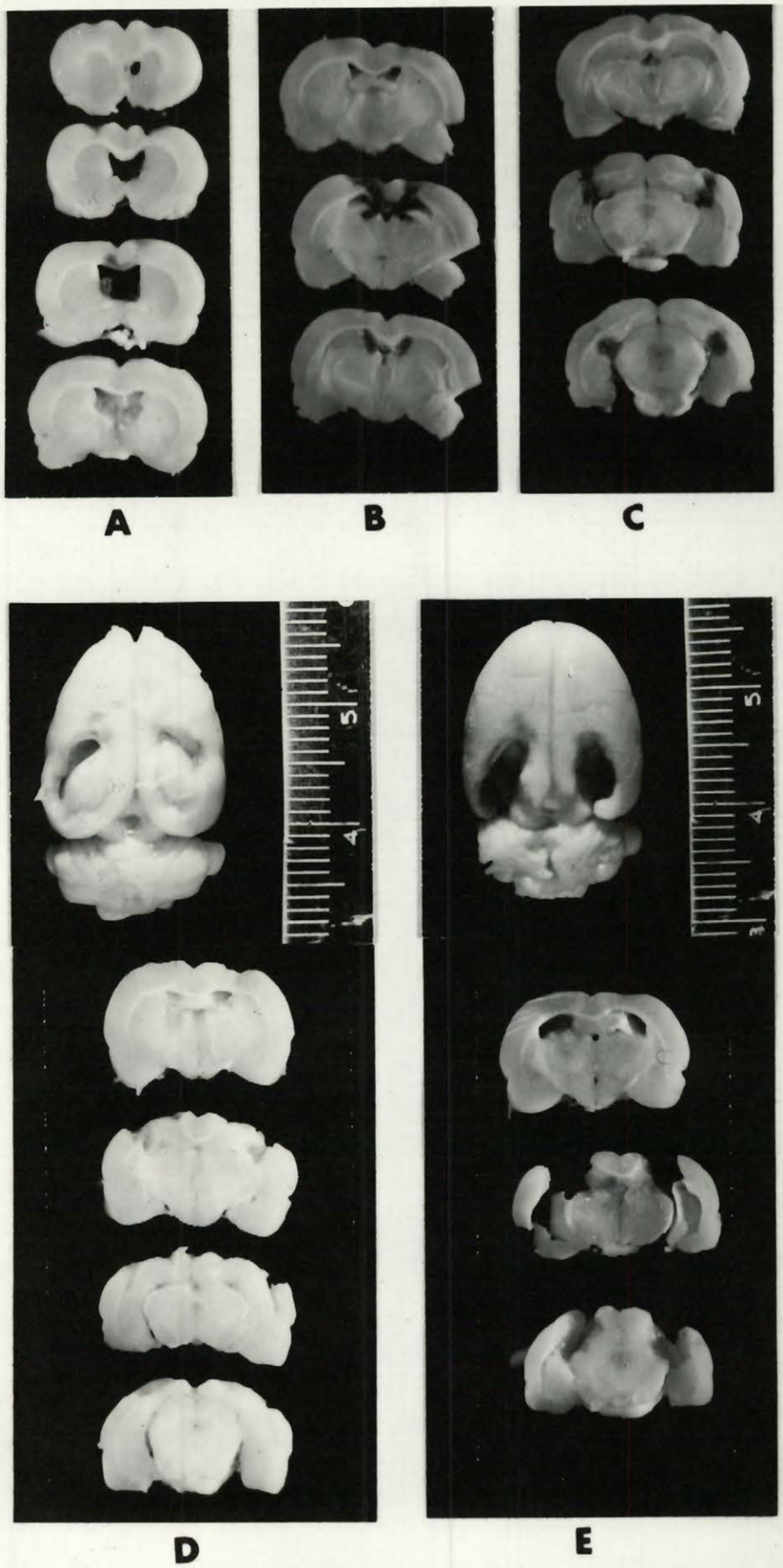

Fig. 1. Representative lesions from the active-passive avoidance study: A. Septum; B. Anterior Hippocampus; C. Posterior Hippocampus; D. Posterior Cortex; E. Cortical-Hippocampal.

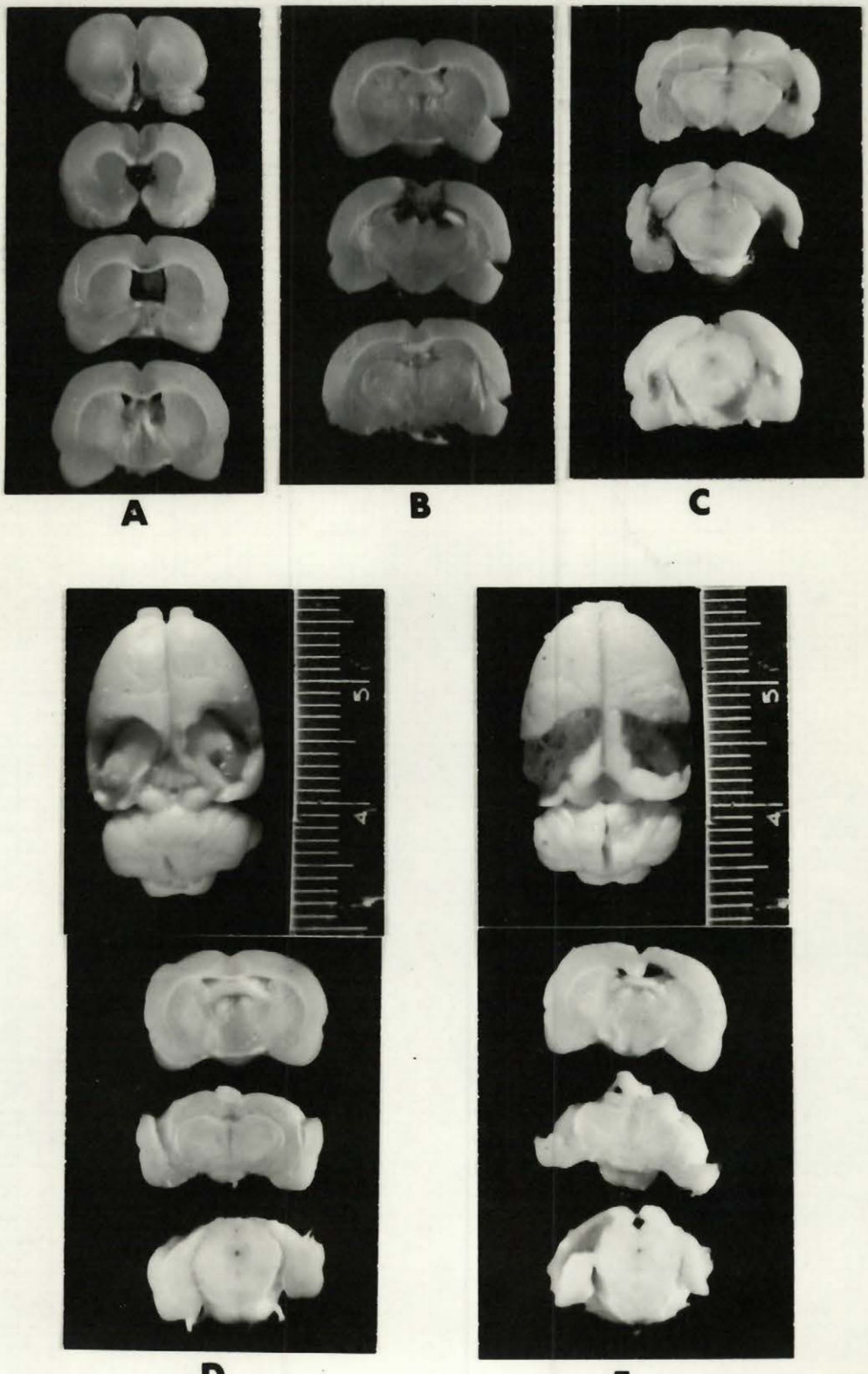

Fig. 2. Representative lesions from the discrimination-reversal study: A. Septum; B. Anterior Hippocampus; C. Posterior Hippocampus; D. Posterior Cortex; E. Cortical-Hippocampal.

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Feindel,

Visual Function of the Forebrain Commissures in the Chimpanzee

Abstract. *Interocular transfer of learned pattern discrimination tasks in chimpanzees with sectioned optic chiasma is dependent on the forebrain commissures. This function is sustained by the splenium and the anterior commissure, the former pathway being the more capable.*

That the commissures of the forebrain play a vital role in the transmission of patterns of visual experience between the cerebral hemispheres has been established in the cat and in the monkey (*1*). In a study of the localization of this visual function in the commissure of the cat, the posterior half of the corpus callosum was found to participate (*2*). This distribution probably relates to the disposition of visually related cortex on gyrus lateralis of the cat. Work with the monkey suggested that the anterior commissure, as well as corpus callosum, may transmit visual information (*3*). Apart from the suggestion that the anterior commissure may participate in visual transmissions, the contribution of the various segments of corpus callosum to transfer of visual information in the primate has not been analyzed previously. The present study was therefore undertaken to determine the pattern of localization of visual transfer functions in the forebrain commissures of a higher primate.

Eight young adult chimpanzees were subjected to midsagittal section of the optic chiasma, whereby the visual sensory input from the two eyes was restricted to the separate hemispheres over the remaining uncrossed pathways. To assess the role of particular parts of the forebrain commissures, seven of the animals underwent surgical section of varying portions of the corpus callosum. In four of the seven, the anterior commissure was also sectioned. One animal served as a control, with only the optic chiasma sectioned.

Training on visual discrimination problems began 2 weeks after surgery. The training apparatus was designed to limit the subject's viewing of the discriminanda to one eye. The visual stimulus-objects consisted of pairs of patterns mounted on two separate lids covering adjacent metal cups. The cup covered by the "correct" lid was baited with food. An opaque sliding door between the animal and the stimulus objects was raised to permit response. The animals were allowed to use the hand contralateral to the viewing eye, both the visual afferent and motor efferent projections thereby being related to the same hemisphere. The location of the lids containing the two stimulus choices was shifted from right to left positions according to a chance sequence. Each animal was given 100 trials daily. When an animal achieved 17 or more correct trials in 20 (criterion of learned performance), it received four additional days of "overtraining" to stabilize performance through the eye and hand receiving the training.

Transfer-of-training tests were then carried out through the, heretofore, untrained opposite eye and hand. High-level transfer-of-training occurred when there was immediate recognition of the discrimination task through the second eye and hand. Interocular transfer was impaired or absent when additional trials were required for learning.

For the discrimination training, a series of two pairs of black and white, flat patterns were employed: problem A, two rectangles versus a single rectangle; and problem B, a triangle versus a square. The first-mentioned member of each pair was arbitrarily selected as "correct"—that is, it would yield a reward. The patterns of each pair were equated as to the total areas of black and white surfaces, so that luminous reflectance was balanced. The animals were trained and tested on problem A before going on to problem B. After achieving criterion performance on transfer-testing for the first problem, the animals were given additional trials in order to expose each cerebral hemisphere to equal amounts of direct experience with the problem. By thus assuring equivalent training for the two hemispheres, generalization effects from one problem to the next were thereby balanced for the two brain halves.

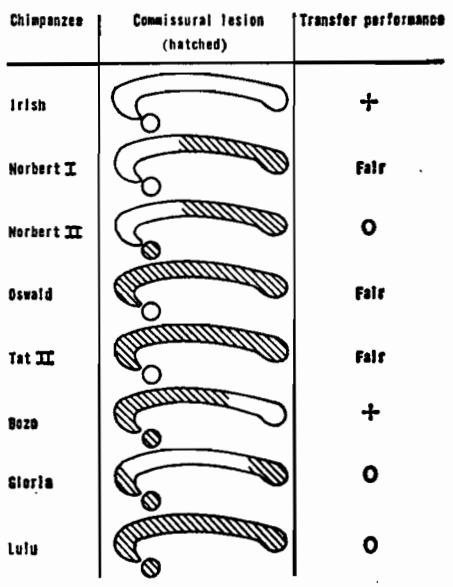

Fig. 1. Correlation of extent of transection of corpus callosum and anterior commissure with the degree of transfer of pattern discrimination training between the two eyes in chiasma-sectioned chimpanzees. Symbols: +, 90 to 100 percent saving of learning on transfer-testing; fair, 60 to 85 percent saving; 0, virtual failure—that is, minus 7 percent to plus 15 percent saving of learning.

Table 1. Scores for learning and transfer-of-learning on each of two visual pattern discrimination problems, A and B.

Problem	Trials for: Primary learning	Trials for: Transfer	Percentage of saving in relearning
	Irish		
A	880	20	98
B	80	0	100
	Norbert I		
A	380	120	68
B	260	40	85
	Norbert II		
A	40	40	0
B	300	320	−7
	Oswald		
A	1500	600	60
B	1700	280	84
	Tat II		
A	340	120	65
B	60	20	67
	Bozo		
A	520	0	100
B	200	20	90
	Gloria		
A	400	340	15
B	360	340	6
	Lulu		
A	1200	1060	12
B	400	420	−5

The scores of training and transfer-testing for each animal are presented in Table 1. The set of 20 trials in which criterion performance was achieved is excluded: thus, a score of "0" indicates that performance at criterion level or better was attained during the very first set of 20 trials. The percentage saving of learning is derived by dividing the difference between the scores for primary learning and learning on transfer-testing by the score for primary learning, and multiplying by 100. A minus value indicates that a greater number of trials was required for relearning than for pri-

mary acquisition. The degree of transfer-of-training is schematically correlated with the type of commissural lesion in Fig. 1.

Complete transection of the forebrain commissures virtually abolished interocular transfer of the pattern discrimination tasks, as seen in animal Lulu. Division of a 1-cm segment of splenium (24 percent of corpus callosum) combined with division of the anterior commissure likewise eliminated interocular transfer in Gloria. On the other hand, the intact splenium alone (Bozo) sustained pattern transfer-of-training at a high level. The anterior commissure, by itself, also supported visual transfer, though at a reduced level (Oswald and Tat II). Other than the splenium and anterior commissure, the remaining sectors of the interhemispheric pathways did not contribute to transfer of pattern discrimination learning (see particularly Gloria). It seems clear, then, that of the fiber bundles of the forebrain commissures, it is splenium and anterior commissure that participate in visual transfer. Of the two, the splenium appears the more potent in information transmission, since in isolation it supported a higher level of transfer of pattern discrimination learning than did the anterior commissure alone.

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References and Notes

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