

**LEARNING DEFICITS IN CATS WITH
BILATERAL ASSOCIATION AREA LESIONS**

by

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A THESIS

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INTRODUCTION

The purpose of this thesis is to study the effects of bilateral association response area lesions in cats on three learning tasks. The past ten years have witnessed the careful description of four electrophysiologically well-differentiated cortical association response areas. Termed "association areas," two of them are found on the middle suprasylvian gyrus, one on the anterior lateral gyrus, and one around the pericruciate sulcus. They are, of course, found on each cerebral hemisphere, although the exact location may vary from species to species.

Speaking in electrophysiological terms, their uniqueness lies partly in the fact that under chloralose, curare, or the normal waking state, peripheral stimuli from auditory, visual, and tactile modalities all yield equivalent and undifferentiated responses in these four areas. Moreover, it would appear that while the gross electrophysiology of the sensory association system is rather well delineated, the evidence relating these areas to behavior is much less clear.

This is true for the following reasons. For example, there is an interspecies-comparison difficulty that is inherent in all comparative work. More precisely, it is difficult to compare lesions made in the association areas (electrically defined) of cats to those made in the association areas of monkeys, because the cortical homologies between cats and primates have not been adequately established (Akert, 1964). This is unfortunate because the majority of lesion studies have involved primates, although most of the electrophysiological data on association areas has been derived from studies on the cat. Even here, on the basic

electrophysiological level, Thompson¹ has found a discrepancy between cat and monkey association responses. It seems that the foci of long latency association evoked potentials in the squirrel monkey (Saimiri sciureus) do not include the homologue of the suprasylvian association area in the cat. The role of the association cortex in behavior could vary widely among species, and the chance that lesions in structural homologous association areas have different effects in various species cannot be excluded a priori. To avoid possible misinterpretation and confusion, this review will be limited to behavioral studies pertaining to the cat, except where it is expected that the addition of other studies will contribute unquestionably to a clearer understanding of the thesis problem.

Three separate measures of learning were designed to present a wide range of tasks in order to pinpoint more exactly the type of deficit resulting from bilateral extirpation of the association areas: visual discrimination learning set, delayed response, and auditory discrimination "go - no go."

Learning set. The learning set problem was comprehensively described in a primate study by Harlow (1949) and has since become a common learning task in studies utilizing the Wisconsin General Testing Apparatus (WGTA). It emphasizes the ability to transfer information from problem to problem. Using naive monkeys with temporal neocortical lesions, Meyer (1958) found a marked initial impairment in learning set performance. However, as time progressed, there was a good deal of recovery. Harlow (1959) found neither a gain nor a loss in learning set performance following bilateral prefrontal lobectomy in rhesus monkeys.

¹ K. F. Thompson. Personal Communication. 1967

Cats acquiring the learning set discriminations make great use of visual cues. According to Hara and Warren (1961), cats with bilateral lesions in the suprasylvian gyrus showed significantly greater median savings scores (in trials to relearn) than did the normal controls on a WGTA task involving visual figure discrimination. In another paper, the same investigators (1961 a) trained cats in discriminations involving form, size and brightness before subjecting them to suprasylvian lesions. They were not significantly inferior to unoperated controls upon retesting. Preoperatively, brightness was dominant over form and size, but operated animals no longer showed such a preference.

The discrimination reversal task is closely related to the learning set problem. The correct object must be discriminated from a dissimilar pair in both tests, but in the reversal task, the non-rewarded object becomes the rewarded object when the same pair of objects is presented later. Warren (1960) trained cats on a series of discrimination reversal problems with 80 pairs of dissimilar objects. After frontal lesions, there was no suggestion of a decrease in performance when compared with normal cats. The frontal preparations were significantly inferior to controls only when tested with the same familiar objects for several days. Whether this deficit is in part related to the association response area most proximal to the frontal areas remains to be demonstrated.

From these studies emerges the possibility that individual association area ablations may have little effect on postoperative visual discriminations, although Warren and Sinha (1957) found that lesions in the suprasylvian gyrus increased the threshold in visual size discriminations. However, Hara (1962) reported that cats which were preoperatively trained and postoperatively tested with pre-striate (middle suprasylvian) areas ablated showed a transient change in size discrimination. There was no

difference in brightness thresholds, but the animals did display a marked loss of form discrimination. Nevertheless, it is important to stress the point that these studies have dealt only with partial removal of the association system. With the current supposition of extreme cortical lability, it is not difficult to imagine the functions of an ablated cortical area being transferred to another. This is especially true when one considers that characteristics of the association response (e.g., waveform, amplitude variability, areal distribution) are the same in all cortical association fields to all modalities of stimulation (Thompson et al., 1963).

Results of total vs. partial association area ablations are described by Johnson (1962) in which rats were presented a conditional learning problem which involved an escape response to a simultaneous presentation of light and tone but not to either alone. Although it took partially ablated animals longer than normals to learn the task, the totally ablated animals were unable to learn. One valid conclusion that might be drawn is the necessity for total ablation of these areas for the demonstration of striking behavioral differences.

Delayed response. If one is forced to state the most dominant, non-variant fact that has resulted from over twenty years of lesion studies, it is this: frontal lesions disrupt delayed-response performance. This point has resulted from a vast number of delayed-response primate studies, although, even here, it has been argued that the impairment of delayed responses is due not to the lack of "immediate memory" but to the enhanced distractibility of frontal animals (Malmo, 1942; Wade, 1947; Harlow et al., 1952) to their hypermotility (Wade, 1947) or to the impairment of associative functions (Hissen et al., 1938; Finnan, 1942). The

delayed response deficit following lesions in primates is unique to the frontal cortex - it does not occur if lesions are made in other regions of the cortex (Pribram et al., 1955). Pribram (1964) hypothesized that the frontal areas contain a mechanism that "allows stimuli to be temporarily compounded." This is an "association" view. The compounding process involves the method by which stimuli are associated and is not to be confused with a more permanent storage mechanism.

Feline studies involving frontal and prefrontal lesions are somewhat fewer than primate studies. Although the following feline studies make use of tasks other than the delayed response, it is interesting to note the other effects of frontal lesions. Cats with frontal lesions seem incapable of retaining an avoidance response learned preoperatively and are unable to relearn such a task (Brady et al., 1954). Billet and Warren (1956) compared cats with prefrontal lesions and cats with prestriate lesions to normal cats with regard to performance on an Umweg problem in a Hebb-Williams maze. The cats with prefrontal lesions were inferior to the normal control group both in original learning and retention, and the cats with suprasylvian lesions were inferior to both of the other groups. Finally, Warren and Warren (1966) have reported that normal cats and cats with lesions in the frontal association cortex do not differ in the efficiency of their searching behavior as measured by performance on the Hamilton search test.

Thompson and Kramer (1965) found that total ablation of association areas abolished the subsequent ability of cats to exhibit sensory preconditioning and suggested that association areas appear to play a role in "attentional" aspects of behavior. Therefore, these areas may be postulated to be involved in the delayed-response test. However, Warren et al.

(1962) reported that cats show no significant difference between normal, frontal, and pretriate lesion groups in the postoperative learning of a delayed-response task. In summary, although in the monkey frontal cortical lesions specifically and quite regularly result in severe impairment of the delayed response task, no such deficit has been demonstrated in the cat.

Auditory discrimination. The third problem was an auditory discrimination task. The "go - no go" testing paradigm was chosen to make the resultant data at least partially comparable to previous cat data obtained in a Brogden-Culler rotating cage using shock avoidance training. The auditory "go - no go" procedure is a difficult task. For example, Battig *et al.* (1962) found that frontal monkeys in such a situation did very poorly. Using diffuse visual cues, however, frontal and control animals performed the task equally well. Chorazyna and Stepien (as reported by Konorski, 1964) found that bilateral ablation of anterior and posterior sylvian gyri in dogs abolished their ability to differentiate between pairs of identical tones and different tones in a "go - no go" procedure. However, ablation of the prefrontal areas did not seem to impair performance on this test. In cats, Goldberg *et al.* (1957) removed bilaterally the ventral portions of the temporal region and found that the ability to discriminate between groups of tones, which differed only in temporal patterning, was lost. Simple tonal discriminations were preserved.

Thompson (1959) compared three methods of presenting a frequency discrimination problem and found that the discrimination between 1,000 cps and 1,500 cps tones was more easily learned with a repetitive procedure than with an alternation procedure. In the repetitive procedure, the 1,000 cps tone was on for 1 sec. and then off for 1 sec. throughout all training. The 1,500 cps tones, when given, were presented alternatively

with the 1,000 cps tone. In the alternation procedure, the cat was given eight presentations of a tone. The presentation was either eight tones of 1,000 cps or an alternation of 1,000 cps and 1,500 cps with four presentations of each frequency. There was 370 msec. of silence between two consecutive tones in the eight tone series.

These results suggested the use of the repetition procedure which will be more completely described in the next chapter. Thompson and Smith (1967) found that cats with lesions similar to those described in this study could discriminate between a 250 cps tone requiring a shock avoidance response, and a 2,000 cps tone requiring no response. They were, however, unable to discriminate the 250 cps tone when it was presented as an alternation with a continuously repeated 2,000 cps tone.

Although the following studies are not specifically related to the three aforementioned tasks, they seem at least partially relevant in that the major lesioned area included the suprasylvian gyrus. In the previously described Billet and Warren paper (1956), cats with suprasylvian lesions were found to be inferior to prefrontal, prestriate and normals in a Hebb-Williams maze. Warren, Warren and Akert (1961) found that cats with bilateral suprasylvian lesions were inferior to both normal cats and cats with orbitofrontal lesions. These cats were also trained in a Hebb-Williams maze, and the inferiority of the suprasylvian animals represents difficulty on the original learning task. Upon retesting about seven months later, the cats with suprasylvian lesions were still found to be inferior to both groups.

Interestingly enough, two cats which were subjected to suprasylvian lesions after training showed no loss in retention at postoperative testing. Thus, lesions in the suprasylvian gyrus interfered more with initial

learning than with retention. This is an attribute very similar to that proposed by Pribram for the frontal cortex.

MATERIALS AND METHODS

Subjects

The subjects were 6 pure-bred Burmese cats (2 male and 4 female)¹. They were the products of two separate litters and were obtained in Eugene, Oregon. The fact that all six cats were pure-bred implies a good degree of inter-subject genetic control. All cats were adults (weight over 2 kg.) and with the exception of the immediate post-operative period, the animals received routine care provided by the animal quarters, i.e. all animals were maintained ad libitum on standard laboratory chow.

The cats came to this lab with considerable experience in the WETA apparatus. Their previous experience included a variety of object discrimination and learning set trials over a period of three years (Stevens, 1965) but to this E's knowledge, the cats had never experienced an auditory discrimination or "go - no go" type of task. In the WETA, all cats, except one (IV), worked for small chunks of raw, fresh beef liver. The lone exception found liver distasteful and was partial to a commercially prepared canned cat food.

Apparatus

The testing apparatus was a Wisconsin General Testing Apparatus (WETA) with an 8" Wharfedale speaker mounted on the ceiling of the stimulus compartment. The auditory stimuli were generated by a Hewlett Packard wide range oscillator and filtered high and low by a Spencer-Kennedy variable electronic filter. A Grasson Stadler electronic switch provided a rise-fall time of 60 msec. The two frequencies (1,000 and 1,800 cps) were alternated

¹ One of the females (III) died in surgery. Cats I and VI were male; cats II, IV and V were female.

manually while a continuous background of white noise was provided throughout the experiment.

Stimulus objects for both the delayed response and visual discrimination portions of the testing procedure were randomly drawn from a collection of objects used in previous discrimination tasks at the University of Oregon in Eugene. The objects varied with regard to size, shape, color, and texture. No object was ever used for more than one learning set problem in the entire pre- and postoperative series. Finally, the 2 sec. and 10 sec. delayed response presentations were made with the aid of a Universal "Gra - Lab" laboratory timer mounted on top of the WCTA in full view of the E.

Testing Procedure

The daily testing procedure for all cats was divided into three sections (learning set, delayed response, auditory "go - no go") that were presented in random order on successive days. The testing procedures were given for 12 days preoperatively and 12 days following a 15 day postoperative recovery period. A second testing period was begun 5 months postoperatively. It also consisted of 12 testing days.

The delayed response section consisted of 16 trials/day. The reward was displayed to the cat, placed in a foodwell, and both foodwells were then covered by an identical stimulus object. The opaque screen was never closed. For 8 of the 16 trials, the total elapsed time between the covering of the reward and the placement of the tray within the cat's reach was 2 sec. For the other 8 trials, this interval was 10 sec. The 2 intervals and the position of the baited foodwell were varied according to a modified balanced Gellerman series. Twelve days each of pre- and postoperative testing yielded a total of 192 pre- and 192

postoperative trials for each of the two testing sessions.

The daily learning set section consisted of 6 trials each of 6 separate problems for a total of 36 daily trials. On the first trial of each problem a single stimulus object covering either a baited or non-baited foodwell was presented. The next 5 trials for each problem included both the object presented in the first trial and a second object. If the object in the first trial was baited, it became the correct object on the following five trials. If the object on the first trial was not baited, the second object became the correct object on the following five trials. A new pair of stimulus objects was used for each trial over a 12 day period (i.e. 72 pairs). Three trial - 1 problems were "baited" and three were "non-baited." All stimulus object positions were randomly varied. Twelve days each of pre- and postoperative testing yielded performance data on a total of 72 pre- and 72 postoperative problems which each included 432 trials/cat.

The auditory discrimination portion of the testing procedure used two different auditory stimuli to signal a "go - no go" discrimination in which the reinforcement depended on the cat's displacing an object over a single food well during the "go" portion of the trial. During the "no go" portion of the trial, the object covering the single food well was fastened with a draw-string that was invisible to the cat. The animal was therefore incapable of moving the object. Each trial lasted a total of 60 sec. It included the "no - go" stimulus which consisted of a 1,000 cps tone that was on for 1.25 sec. and off for 1.25 sec. This sequence was repeated. The onset of the "go" period was varied randomly during the "no go" period. The "go" period

consisted of the following sequence: 1.25 sec. 1,800 cps tone, 1.25 sec. of silence, 1.25 sec. of 1,000 cps tone, 1.25 sec. silence (presented for three cycles, i.e. 15 sec.). If the animal did not retrieve the food during the "go" period, the response was scored as incorrect. On such trials, the "no-go" signal recurred and the 60-sec. cycle went to completion. If the animal made a response during the recurrence of the "no-go" signal, the screen was lowered and the trial terminated.

"No-go" trials were exactly the same as "go" trials except for the absence of the 15-sec. "go" signal. The criterion for a response on a "no-go" trial was contact between a paw and the foodwell cover. Whenever this response occurred during a "no-go" signal, the screen was lowered, the trial was ended, and an error was scored. Of the 40 trials given each cat on each day only 10 contained a "go" stimulus. This somewhat unorthodox testing procedure was necessary to compensate for the "go" tendency of the cats who had always previously been given training to make the "go" response in the WGTA. At one point, when this response tendency seemed to have been overcome, the eighth and ninth days of preoperative testing included 20 rather than 10 "go" trials. However, it was difficult to maintain this schedule, and the last three days included only 10 "go" trials out of the total 40 trials. In order to assure a comparable evaluation of post- and preoperative data, the 3-week and 5-month postoperative testing was made to conform to the preoperative schedule, i.e. 20 rather than 10 "go" trials were presented on days eight and nine. Forty trials/day for 12 days yielded a total of 480 pre- and 480 postoperative trials. Each 480 trials included 140 trials on which reward was available.

Operation

The cats were anesthetized with pentobarbital sodium (40 mg./kg.)

injected intraperitoneally. After anaesthesia was obtained, atropine (.04 mg./kg.) was injected intra-muscularly, and the head was shaved to remove all scalp hair. The animal was placed in a head holder, which did not traumatize the tympanic membrane or infra-orbital nerves. The scalp was then prepared for surgery.

Surgery took place under sterile conditions in the operating room in the University of Oregon Medical School animal quarters. The cat was first draped, and the midline scalp was incised from the nasion to the occipital ridge. The scalp was retracted laterally and the temporalis muscle freed from its anterior and midline facial attachments. The muscle was then retracted and the bone scraped free of periosteum. Bilateral trephine holes were placed over the frontal sinuses and the bone removed with rongeurs to the frontal sinus wall. The sinus membrane was freed and removed, and the sinus was dried. All necessary hemostasis was obtained with bone wax. Each nasal sinus foramen was covered with acrylic resin cement which was allowed to harden. The instruments were then re-sterilized.

For the ablations, bilateral trephine holes were placed in the temporo-parietal areas and the bone removed with rongeurs, exposing dura posteriorly to the occipital area, anteriorly to include the posterior wall of the frontal sinus, medially to within 2 mm. of the midline and laterally to the ectosylvian gyrus.

The dura was incised and retracted, and the pia opened. Number 18 and 19 needles with blunted tips were used to gently aspirate the cortex. Suction was provided by a Sklar compression unit. Brain hemostasis was obtained with the aid of oxidized cellulose (Oxyeel) and Gelfoam. After aspiration, the dura was reapproximated and sutured with 6-0 silk

and an atraumatic curved needle. The wound was then closed in anatomical layers and sprayed with a plastic bandage.

Following operation 300,000 units of bicillin were administered intramuscularly and the animal was allowed to regain consciousness, a period varying from 12 to 36 hours, under an infra-red heat lamp. The animals were then fed milk and somagen by hand using a rubber syringe, until they could eat without aid. In all three operated cats, motor control seemed impaired and none of them regained ambulatory facility until 5 days postoperatively, at which time they were returned to their individual home cages in the animal quarters. All three cats begin the postoperative testing session 15 days after the operation.

Lesions

Anatomically, the lesioned areas were designed to include the following: middle suprasylvian gyrus, the anterior third of the lateral gyrus, and both banks of the cruciate sulcus. On the medial wall of the hemisphere the lesioned areas included tissue slightly dorsal to the cruciate sulcus and slightly ventral to it on the anterior cingulate gyrus. After completion of testing, the animals were given a brief neurological examination, the brains were perfused, and were examined grossly. The brains were then imbedded in celloidin, sectioned at 30 μ , and stained by the Nissl method for study of the lesions and retrograde thalamic degeneration.

RESULTS

Behavioral

The responses of the individual cats to each of the three learning problems are presented in Tables I, II, and III of the Appendix. Table I contains the preoperative data, Table II the postoperative (3 week) data, and Table III the 5-month postoperative data. The entries in these tables are mean percent correct scores taken over three consecutive four-day intervals.

The comparison of the mean percent correct scores for each task over the twelve preoperative days is as follows:

	Learning Set	Delayed Response	Auditory Discrimination
Unoperates	74.8%	77.4%	70.9%
Operates	73.3%	76.4%	69.8%

The mean percent scores over the twelve days of the 3-week postoperative period are:

Unoperates	76.4%	78.4%	68.0%
Operates	57.7%	55.6%	52.0%

Finally, the mean percent scores over the twelve days of the 5-month postoperative period:

Unoperates	72.2%	73.5%	70.8%
Operates	62.5%	61.0%	57.6%

A summary of the above data is presented graphically in Figures I, II, and III.

Figure I is designed to display the differences between the operates and unoperates on the learning set problem. An analysis of

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variance was applied that took into account the fact that the data contained unequal group sizes. The analysis chosen was that of an unweighted means solution (Table I). The between subjects' F score for the learning task was clearly significant at greater than the .05 level. In fact, it approached the .01 level. This analysis shows the difference between lesioned and non-lesioned animals on this task. No other interaction was found to be significant in this variance analysis. This would include any variance possibly attributed to uncontrolled variables in the testing procedure.

TABLE I

	Source of Variation	M. S.	F
<u>ANALYSIS</u>	Between Ss		
	A	405.5	25.18*
	Subjects w. groups	16.1	
	Within Ss		
	B	23.5	
	AB	5.8	
	B x Subjects w. groups	209.7	
	C	289.0	
	AC	130.1	
	C x Subjects w. groups	2,741.0	
<u>DISCRIMINATION</u>	BC	12.7	
	ABC	11.2	
	BC x Subjects w. groups	11.9	
	Between Ss		
	A	364.9	31.45*
	Subjects w. groups	11.6	
	Within Ss		
	B	29.1	
	AB	2.6	
	B x Subjects w. groups	54.6	
<u>SET</u>	C	65.1	
	AC	107.7	
	C x Subjects w. groups	1,151.0	
	BC	8.0	
	ABC	4.15	
	BC x subjects w. groups	12.3	
	Between Ss		
	A	166.1	8.34
	Subjects w. groups	19.9	
	Within Ss		
B	11.2		
AB	.33		
B x subjects w. groups	16.8		
<u>DELAYED RESPONSE</u>	C	43.3	
	AC	44.8	
	C x subjects w. groups	163.5	
	BC	.22	
	ABC	5.15	
	BC x subjects w. groups	7.2	

A = Subjects df = 1

B = Testing Days 1-12 df = 11

C = Preoperative and Postoperative
Testing Sessions df = 2

* p = .05

FIGURE I
COMPARISON BETWEEN LESIONED AND NON-LESIONED
CATS ON LEARNING SET PROBLEM

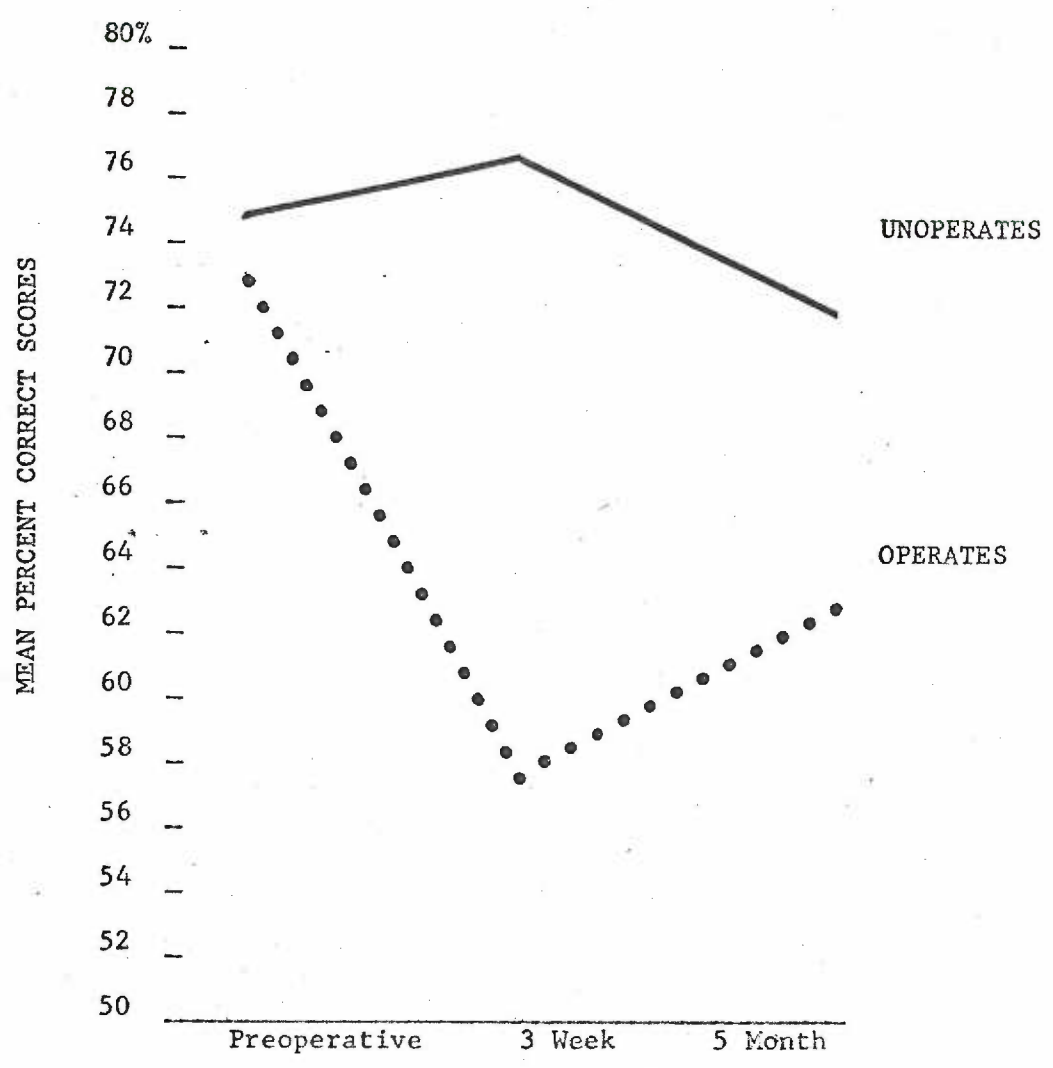


Figure II is designed to display the differences between the operates and unoperates on the delayed response problem. An analysis of variance procedure for data containing unequal group sizes (i.e., unweighted means solution) revealed a between subjects *F* score that came very close to the .05 level (Table I). No other interactions, including those possibly related to uncontrolled variables, were found to be significant.

Figure III is designed to display the differences between the operates and unoperates on the auditory discrimination problem. An analysis of variance of the same type as described above was used to analyze the data (Table I). The between subjects *F* score for this task was clearly significant at the .05 level. Once again, no other interactions were found to be significant in this variance analysis. The use of one-tailed tests in the analyses described in this thesis was deemed permissible because of the prior assumption that the lesioned animals would perform at lower level than the unoperated animals.¹

Figures I - V in the Appendix are graphic presentations of the mean correct percent scores taken over three consecutive four-day intervals for individual animals. Figures I and II display data from the two unoperated animals. Figures III, IV, and V display data from the three operated animals. Note the very definite separation between the pre- and postoperative curves on Figures III, IV, and V (operates) and the lack of separation in curves on Figures I and II (nonoperates).

Because of the small number of subjects and a hesitancy to assume normal distribution of the scores, a nonparametric test (the Mann-

¹The use of a one-tailed test applies only to the Mann-Whitney test. All analyses of variance were derived from a two-tailed table.

Whitney U test) was chosen to analyze a portion of the data. P-scores were calculated for the following group comparisons:

1. Experimental (preoperative) vs. Experimental (3 weeks postoperative)
2. Experimental (preoperative) vs. Experimental (5 months postoperative)
3. Experimental (3 weeks post-operative) vs. Experimental (5 months postoperative)
4. Control vs. Experimental (Preoperative)
5. Control vs. Experimental (3 weeks postoperative)
6. Control vs. Experimental (5 months postoperative)

In each of the six cases a p-score was calculated for each four-day group of scores for each of the three tasks. Tables II and IV each present the entire 36 p-scores. Table II displays comparisons listed above as 1 - 3, and Table III displays comparisons 4 - 6. Because of the very small sample, a special table was used to calculate these p-scores (Table J, Appendix, Siegel, 1956).

Unfortunately, with such a small N, many of the p-scores, although being as significant as possible under these conditions, fail to reach a p of .05 or better. Therefore, the discussion will first be limited to those situations in which a p-score of .05 was possible (i.e. Table II).

In the comparison of the experimental preoperative scores with the 3-week post-lesion scores of the same animals, Table II shows a difference at the .05 level for all three tasks indicating a significant lesion effect over this period. In the comparison of the experimental preoperative scores with the 5-month post-lesion scores of the same animals, Table II shows a difference at the .05 level for all three tasks. This result again indicates a significant deficit in performance after the lesions. In the comparison of the scores determined in the 3-week post-operative testing period with those determined in the 5-month post-lesion period, no significant difference was found, although Figures, I,

FIGURE II

COMPARISON BETWEEN LESIONED AND NON-LESIONED
CATS ON DELAYED RESPONSE PROBLEM

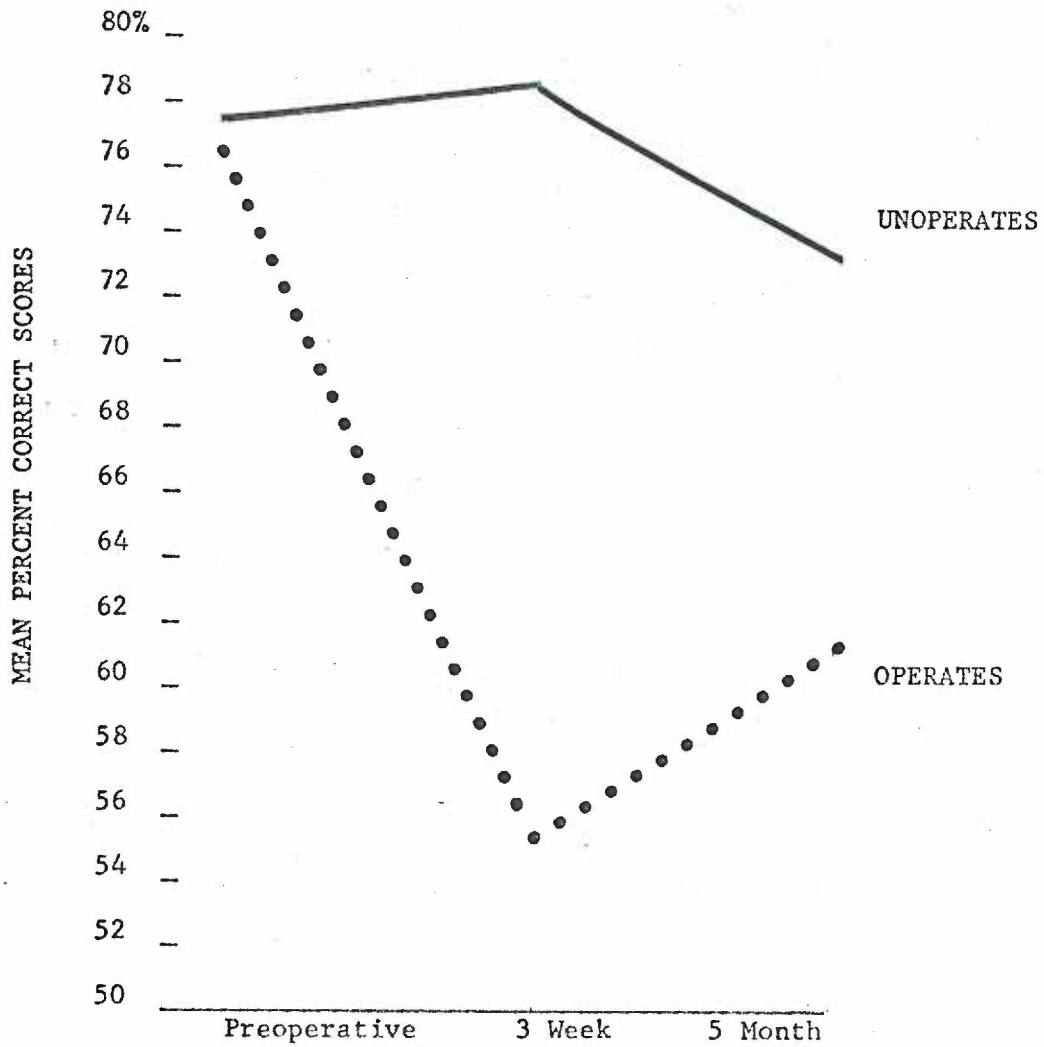
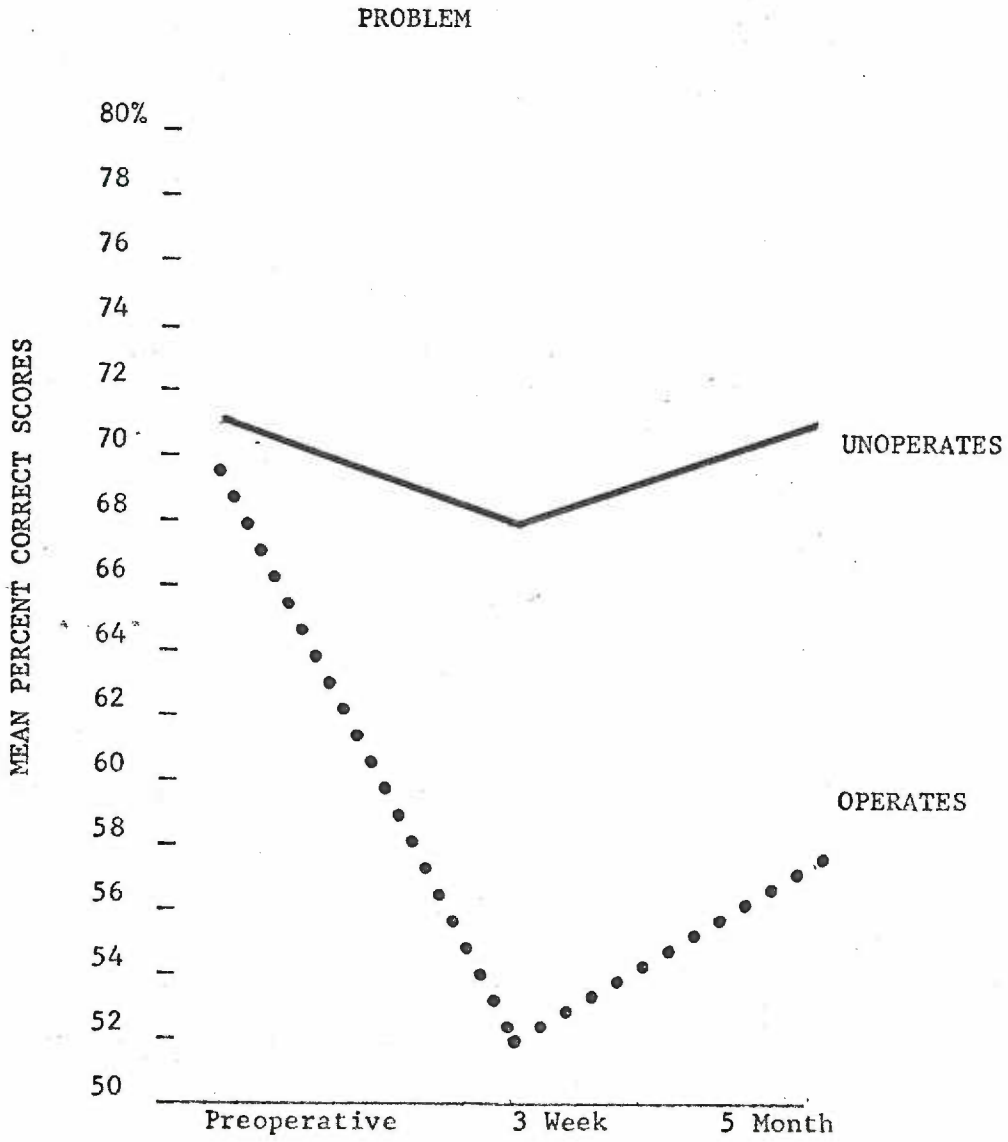


FIGURE III

COMPARISON BETWEEN LESIONED AND NON-LESIONED
CATS ON AUDITORY DISCRIMINATION



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II and III seem to indicate at least a slight improvement in performance between these groups.

As reported before, the lack of an adequate N in the non-operated control group prohibited the possibility of a significant comparison in certain cases, however, certain trends seem to be suggested. During the first twelve days of testing, there are no significant differences between the controls and the non-operated experimentals. This is true for all three tasks ($p = .35, .35, .5$ Table III). It indicates that the animals for the two groups were drawn in a random fashion. In the comparisons of the 3-week controls with the 3-week experimentals, all tasks showed a $p = .1$ (Table III). This p-score is as significant as the number of subjects will allow. This is also the case in the comparison of 5-month controls with 5-month experimentals (Table III), where p again is equal to .1 for all three tasks. These last two p scores indicate that the deficit displayed by the operates was a direct result of the lesions and not some other variable operating during the postoperative period.

Anatomical.

Photographs of the gross brains of the three lesioned animals are presented in the Appendix. For each of these cats, photographs were taken of three views of the gross brain, viz. superior, left lateral, and right lateral. These brains are being processed for cortical reconstruction and subcortical degeneration studies. Although all lesions were deemed complete at surgery, distortion due to healing helps render gross examination an inadequate means of checking lesion limits.

TABLE XI

COMPARISONS OF PERFORMANCE OF LESIONED CATS
BETWEEN PRE- AND POSTOPERATIVE TEST-
ING SESSIONS USING THE MANN-WHITNEY
U TEST

1. Experimental (preoperative) vs. Experimental (3 week postoperative)

	Days 1-4		Days 5-8		Days 9-12		Days 1-12	
	U	P	U	P	U	P	U	P
Learning Set	0	.05	0	.05	0	.05	0	.05
Delayed Resp.	0	.05	0	.05	0	.05	0	.05
Aud. Disc.	0	.05	0	.05	0	.05	0	.05

2. Experimental (preoperative) vs. Experimental (5 months postoperative)

Learning Set	0	.05	3	.35	0	.05	0	.05
Delayed Resp.	0	.05	0	.05	0	.05	0	.05
Aud. Disc.	0	.05	1	.10	0	.05	0	.05

3. Experimental (3 weeks postoperative) vs. Experimental (5 month postop.)

Learning Set	0	.50	1	.10	0	.05	0	.35
Delayed Resp.	0	.20	1	.10	1	.10	1	.10
Aud. Disc.	0	.10	1	.10	3	.35	1	.10

TABLE III

COMPARISONS OF PERFORMANCE BETWEEN LESIONED AND NON-LESIONED CATS AT PRE- AND POSTOPERATIVE TESTING SESSIONS USING MANN-WHITNEY U TEST

1. Control (preoperative) vs. Experimental (preoperative)

	Days 1-4		Days 5-8		Days 9-12		Days 1-12	
	U	p	U	p	U	p	U	p
Learning Set	4	.50	3	.35	2	.20	3	.35
Delayed Resp.	2	.20	3	.35	0	.05	3	.35
Aud. Disc.	1	.10	3	.35	3	.35	3	.35

2. Control (3 week postoperative) vs. Experimental (3 week postoperative)

Learning Set	0	.10	0	.10	0	.10	0	.10
Delayed Resp.	0	.10	0	.10	0	.10	0	.10
Aud. Disc.	0	.10	0	.10	1	.20	0	.10

3. Control (5 months postoperative) vs. Experimental (5 month postoperative)

Learning Set	0	.10	1	.20	0	.10	0	.10
Delayed Resp.	0	.10	0	.10	0	.10	0	.10
Aud. Disc.	0	.10	0	.10	0	.10	0	.10

CONCLUSION

Given the statistical handicaps inherent in any study which attempts to use a small number of animals, certain conclusions may still be tentatively drawn here. Bilateral association area lesions do disrupt the behavior measured by learning tasks.

The auditory discrimination "go - no go" task is interesting because it combines two learning processes. The first is the auditory discrimination itself, and the second is a temporal distinction between "go" and "no go" periods. In this sense, perhaps this problem is the most difficult of the three. If we assume that more complex learning processes are most affected by association area lesions we should expect this task to be most seriously affected by the lesions.

In a partially analogous study by Johnson (1962), cats with bilateral association area lesions learned to respond in a Brogden-Culler wheel in the presence of auditory stimuli similar to those used in this study. After extensive training, most of his unoperated animals reached a 75% criterion level. This is very close to the correct-response level of the cats in this study. Furthermore, Johnson's lesioned animals also showed a distinct deficit in the post-lesion auditory discrimination task, but his data in this situation are confounded by the addition of a light stimulus.

It is interesting to compare the Brogden-Culler wheel vs. the WETA "go-no go" paradigms. Thompson (1964) points out that in studies testing frequency discrimination after complete auditory cortex lesions, the conditions of training seem to have a crucial effect. Studies which demonstrate

a loss of frequency discrimination require a response to the positive stimulus and response inhibition to the negative stimulus. Studies demonstrating postoperative relearning of the auditory discrimination used methods involving a change from a background negative stimulus. In one sense, the paradigm described in this study is a combination of both procedures. Whereas the task used here required the animal to inhibit a negative response, it also involved learning to respond only to a change in an ongoing background negative stimulus. Thompson's prediction (1964) that

"Ablation of the association areas alone will impair frequency discrimination learning by repetitive training procedures, even if the primary auditory cortex is intact."

seems to be borne out by this study. One question that has relevance for understanding the nature of the deficit is whether the association area lesions affect the "go - no go" portion of the test rather than the auditory discrimination per se. That is to say, animals without these areas are incapable of inhibiting a response during the "no go" portion of the trial. It might be possible to tease out this type of information from the raw data if records were kept regarding the type and time of errors made during the testing procedure. Unfortunately, this was not done.

The learning set task was also significantly affected by the lesions. It is not difficult to explain why, especially if one considers "learning to learn" as a more complex learning process. It is interesting to note that the operates showed a good deal of recovery in the four months between postoperative testing periods (Figure VI). This result is similar to that found by Meyer (1958) on learning set performance

by monkeys having temporal neocortical lesions. Perhaps these results are partially due to the fact that the cats had extensive experience on a learning set task (over 1,000 problems) before they came to this lab.

The delayed response problem demonstrated the smallest post-lesion deficit according to the analysis of variance. Warren et al. (1962) have shown that cats with frontal lesions display no deficit in this type of task. It is difficult to make an exact comparison, but there is little doubt that Warren's frontal lesions and the lesions in this study are at least partially overlapping, especially in the pericruciate area (PCA).

Johnson found that his partially ablated animals were able to learn, but it took them significantly longer than normal or somatic cortex ablated controls. The totally ablated animals were unable to learn to his (Johnson's) established criteria. The cats did show responses to simultaneous stimuli from two modalities but did not inhibit responses to an independent presentation. However, they showed a statistically significant tendency toward differential responses in the direction of learning. Johnson mentioned that perhaps the totally ablated group had some difficulty in connecting the conditioning stimuli with the shock, but that the only valid conclusion that might be drawn was the necessity for total ablation in the demonstration of behavioral differences.

Perhaps the reason for the failure of Warren et al. to find a delayed response deficit was that they had made an incomplete association response area lesion. Of course, in contrast, many primate studies have shown delayed response deficits with frontal lesions (i.e. a partial association response area lesion). However, this may represent nothing more than a phylogenetic lability that decreases as one goes

up the evolutionary scale. This decreasing lability does seem to be a fairly reliable generality - as far as the cortex is concerned anyway.

The lesions, although somewhat varied in extent, appear to have fulfilled their purpose. It must be emphasized that the correlations of individual animal behavior with lesion size cannot be attempted without adequate histological examination, and then only if the vast amount of intra-animal variability is kept closely in mind.

BIBLIOGRAPHY

1. Akert, K. Comparative anatomy of the frontal cortex and thalamo-cortical connections. In F. M. Warren and K. Akert (eds) *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964. pp. 372-396.
2. Battig, K., Rosvold, H. E. and Mishkin, M. Comparison of the effects of frontal and caudate lesions on discrimination learning in monkeys. *J. comp. physiol. Psych.*, 1962. 55, 458-463.
3. Billett, H. and Warren, F. M. Usage behavior in normal and brain operated cats after prolonged postoperative recovery. *Am. Psychologist*, 1956, 11, 440. (Abstract)
4. Brady, F. V., Schreiner, L., Geller, I. and Kling, A. Subcortical mechanisms in emotional behavior: The effect of rhinencephalic injury upon the acquisition and retention of a conditioned avoidance response in cats. *J. comp. physiol. Psych.*, 1954. 47, 179-186.
5. Finnan, F. L. Delayed response of pre-delay reinforcement in monkeys after the removal of the frontal lobes. *Amer. J. Psychol.*, 1942. 55, 202-214.
6. Goldberg, J. M., Diamond, I. T. and Hoff, W. D. Auditory discrimination after ablation of temporal and insular cortex in cat. *Fed. Proc.*, 1954. 16, 47.
7. Harva, K. Visual defects resulting from prestriate cortical lesions in cats. *J. comp. physiol. Psych.*, 1962. 55, 293-298.
8. Harva, K. and Warren, J. M. Equivalence reactions by normal and brain-injured cats. *J. comp. physiol. Psych.*, 1961. 54, 86-90.
9. Harva, K. and Warren, J. M. Stimulus additivity and dominance in discrimination performance by cats. *J. comp. physiol. Psych.*, 1961. 54, 86-90.
10. Harlow, H. F. The development of learning in the rhesus monkey. *Amer. Scientist*, 1959. 47, 459-479.
11. Harlow, H. F. The formation of learning sets. *Psychol. Rev.*, 1949. 56, 51-65.
12. Harlow, H. F., Davis, R. T., Settlage, P. H. and Meyer, D. R. Analysis of frontal and posterior association syndromes in brain-damaged monkeys. *J. comp. physiol. Psych.*, 1952. 45, 419-429.
13. Johnson, R. H. Role of association cortex in conditional discriminations in the cat. Unpublished Master's thesis, Univ. Oregon Medical School, 1962.

14. Konorski, J. Analysis of errors by refrontal animals on the delayed-response test. In P. M. Warren and K. Akert (eds.) *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964. pp. 271-294.
15. Malmo, R. B. Interference factors in delayed response in monkeys after removal of frontal lobes. *J. Neurophysiol.*, 1942. 5, 295-308.
16. Meyer, D. R. Some psychological determinants of sparing and loss following damage to the brain. In H. F. Harlow and C. N. Woolsey (eds.) *Biological and biochemical bases of behavior*. Madison: University of Wisconsin Press, 1958. pp. 173-192.
17. Nicson, H. W., Riesen, A. H. and Nowlis, V. Delayed response and discrimination learning by chimpanzees. *J. comp. physiol. Psych.*, 1938. 26, 361-386.
18. Pribram, K. H. A progress report on the neurological processes disturbed by frontal lesions in primates. In J. M. Warren and K. Akert (eds.) *The frontal granular cortex and behavior*. New York: McGraw-Hill Book Co., 1964. pp. 26-55.
19. Pribram, K. H., Kruger, L., Robinson, F. and Berman, A. J. The effects of precentral lesions on the behavior of monkeys. *Yale J. Biol. Med.*, 1955. 28, 428-443.
20. Siegel, S. *Nonparametric statistics for the behavioral sciences*. New York: McGraw-Hill Book Co., 1956.
21. Stevens, D. A. A comparison of learning in rhesus monkeys, *Cebus* monkeys, lemurs, and Burmese cats. Unpublished Doctoral thesis, Univ. Oregon, Eugene, 1965.
22. Thompson, R. F. The effect of training procedure upon auditory frequency discrimination in the cat. *J. comp. physiol. Psych.*, 1959. 52, 186-190.
23. Thompson, R. F. Role of cortical association fields in auditory frequency discrimination. *J. comp. physiol. Psych.*, 1964. 57, 335-339.
24. Thompson, R. F. and Kramer, R. Role of association cortex in sensory preconditioning. *J. comp. physiol. Psych.*, 1965. 60, 186-191.
25. Thompson, R. F. and Smith, H. E. Effects of association area lesions on auditory frequency discrimination in the cat. *Psychon. Sci.*, 1967, in press.
26. Thompson, R. F., Smith, H. E. and Bliss, D. Auditory, somatic sensory, and visual response interactions and interrelations in association and primary cortical fields of the cat. *J. Neurophysiol.*, 1963. 26, 365-378.

27. Wade, M. The effect of sedatives upon delayed response in monkeys following removal of the prefrontal lobes. *J. Neurophysiol.*, 1947. 10, 57-61.
28. Warren, J. M. Oddity learning set in a cat. *J. comp. physiol. Psych.*, 1960. 53, 433-434.
29. Warren, J. M. and Sinha, M. M. Effect of differential reinforcement on size preferences in cats. *Percept. Mot. Skills*, 1957. 7, 17-22.
30. Warren, J. M. and Warren, H. B. Performance of immature and adult cats on the Hamilton search test. *Psychon. Sci.*, 1966. 6, 5-6.
31. Warren, J. M., Warren, H. and Akert, K. Orbitofrontal cortical lesions and learning in cats. *J. comp. Neurol.*, 1962. 118, 17.
32. Warren, J. M., Warren, H. B. and Akert, K. Umweg learning by cats with lesions in the prestriate cortex. *J. comp. physiol. Psych.*, 1961. 54, 629, 632.

APPENDIX

1. The first part of the appendix
describes the general principles of the
method used in the study.

2. The second part of the appendix
describes the specific procedures used
in the study.

3. The third part of the appendix
describes the results of the study.

TABLE I
Preoperative
Percent Correct Responses

<u>LEARNING SET</u>				
Cat	Days 1-4	Days 5-8	Days 9-12	Days 1-12
I	75.8%	70.8%	81.6%	76.1%
VI	65.1	65.1	82.5	<u>70.9</u>
II	70.8	74.2	75.0	$\bar{X}=74.8\%$ 73.3
IV	70.0	72.5	81.6	74.7
V	65.1	70.8	76.5	<u>70.8</u> $\bar{X}=73.3\%$
<u>DELAYED RESPONSE</u>				
I	76.6%	70.3%	76.6%	74.5%
VI	76.6	82.8	81.2	<u>80.2</u>
II	68.8	78.1	87.5	$\bar{X}=77.4\%$ 78.1
IV	64.1	78.1	84.4	75.5
V	67.2	76.6	82.8	<u>75.5</u> $\bar{X}=76.4$
<u>AUDITORY DISCRIMINATION</u>				
I	71.9%	63.1%	75.0%	70.0%
VI	66.9	75.6	72.5	<u>71.7</u>
II	70.0	65.0	75.0	$\bar{X}=70.9\%$ 70.0
IV	73.1	64.4	53.1	63.5
V	73.1	71.2	77.5	<u>73.9</u> $\bar{X}=69.8\%$

N.B. Animals II, IV, and V were chosen for lesions. Animals I and VI were chosen as unoperated controls.

TABLE II
Postoperative - 3 weeks
Percent Correct Responses

<u>LEARNING SET</u>				
Cat	Days 1-4	Days 5-8	Days 9-12	Days 1-12
I	76.7%	71.0%	81.7%	76.5%
VI	68.3	76.7	84.2	<u>76.4</u>
II	57.5	55.8	61.7	$\bar{X}=57.7$ 58.3
IV	53.5	54.2	61.7	56.5
V	53.5	60.8	60.9	<u>58.4</u> $\bar{X}=76.4$
<u>DELAYED RESPONSE</u>				
I	68.8%	73.4%	81.3%	74.5%
VI	81.3	81.3	84.4	<u>82.3</u>
II	51.6	53.1	59.4	$\bar{X}=78.4$ 54.7
IV	53.1	53.1	57.8	54.7
V	53.1	62.5	56.2	<u>57.3</u> $\bar{X}=55.6$
<u>AUDITORY DISCRIMINATION</u>				
I	73.1%	61.2%	73.8%	69.4%
VI	63.1	75.0	61.9	<u>66.7</u>
II	45.6	53.1	53.1	$\bar{X}=68.0$ 50.6
IV	43.8	46.2	53.8	47.9
V	51.9	58.8	61.9	<u>57.5</u> $\bar{X}=52.0$

N. B. Animals II, IV, and V were lesioned. Animals I and VI were the unoperated controls.

TABLE III
Postoperative - 5 months
Percent Correct Responses

LEARNING SET

Cat	Days 1-4	Days 5-8	Days 9-12	Days 1-12
I	69.0%	80.0%	76.8%	73.9%
VI	65.8	70.0	75.8	$\frac{70.5}{\bar{X}=72.2}$
II	54.2	73.3	67.7	65.1
IV	50.0	65.0	70.0	61.7
V	56.7	60.9	65.0	$\frac{60.5}{\bar{X}=62.5}$

DELAYED RESPONSE

I	64.1%	73.4%	78.1%	71.9%
VI	71.9	75.0	78.1	$\frac{75.0}{\bar{X}=73.5}$
II	54.7	67.2	64.1	62.0
IV	59.5	68.8	67.2	65.2
V	51.6	56.2	59.4	$\frac{55.7}{\bar{X}=61.0}$

AUDITORY DISCRIMINATION

I	65.6%	68.8%	70.0%	68.1%
VI	98.1	69.1	63.8	$\frac{73.3}{\bar{X}=70.8}$
II	53.8	63.8	57.5	58.4
IV	55.6	62.5	61.3	59.8
V	50.6	56.3	57.5	$\frac{54.8}{\bar{X}=57.6}$

N. B. Animals II, IV, and V were lesioned. Animals I and VI were the unoperated controls.

FIGURE I

Cat I - Unoperated Control

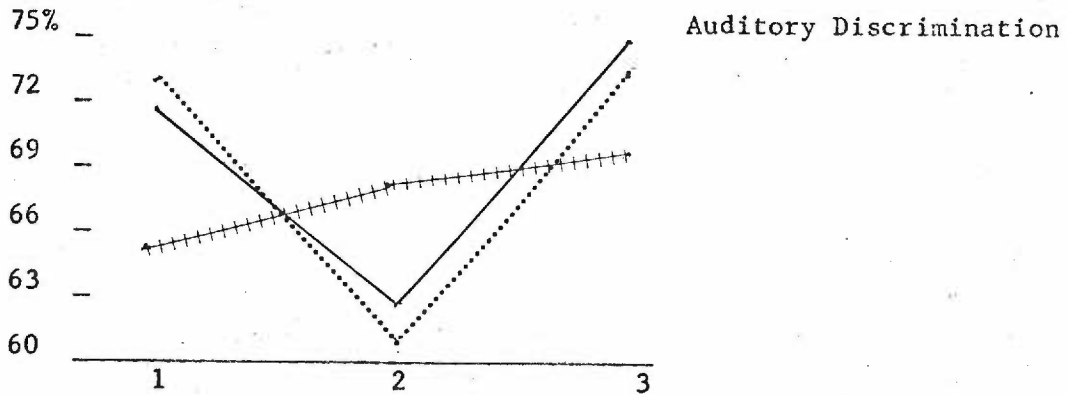
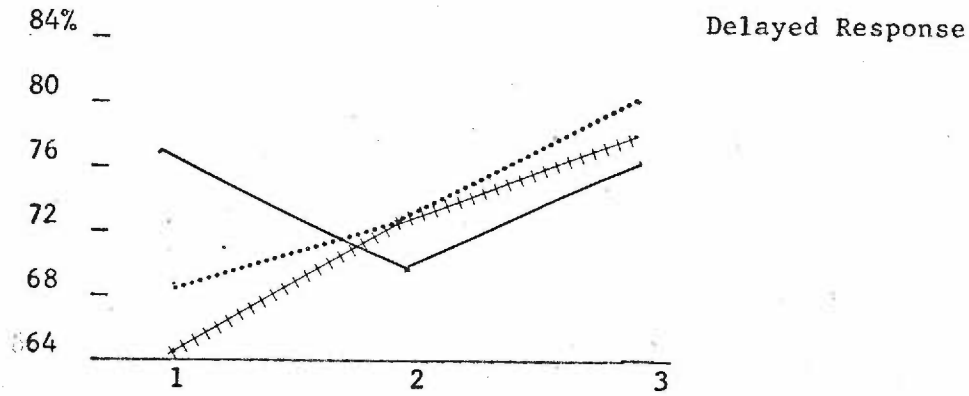
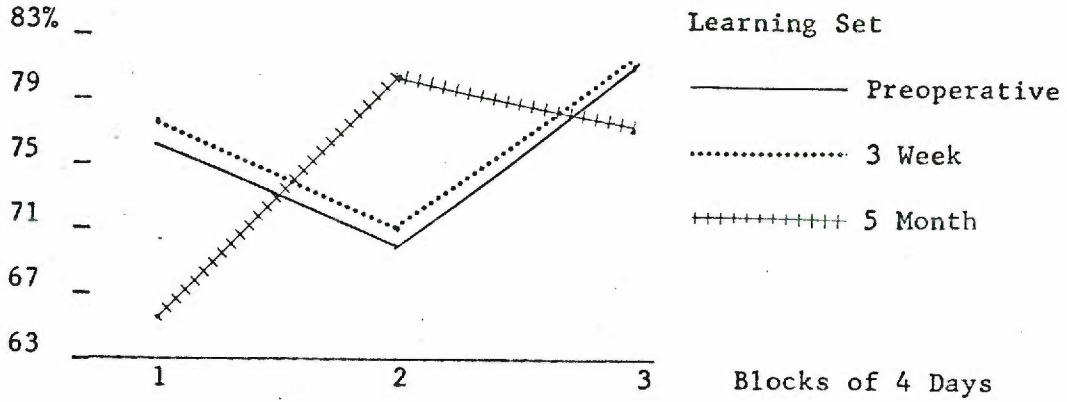


FIGURE II

Cat II - Operate

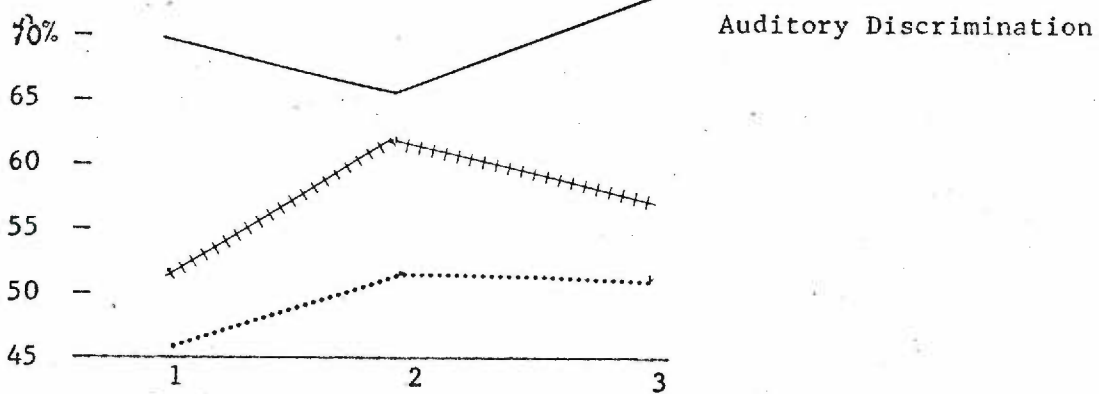
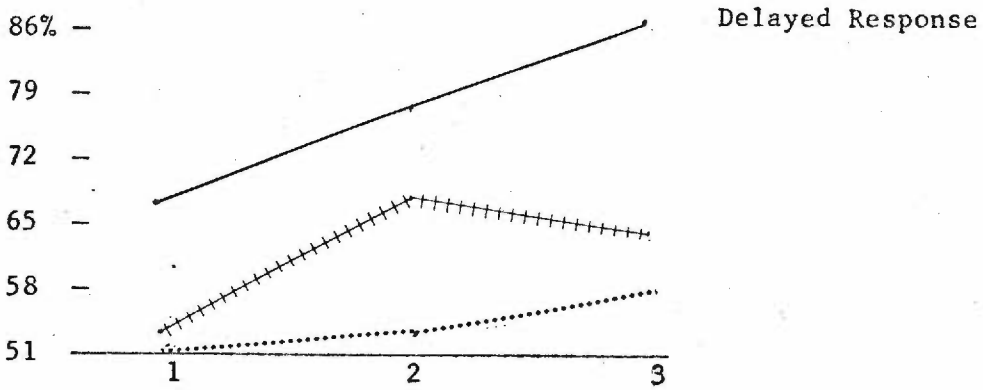
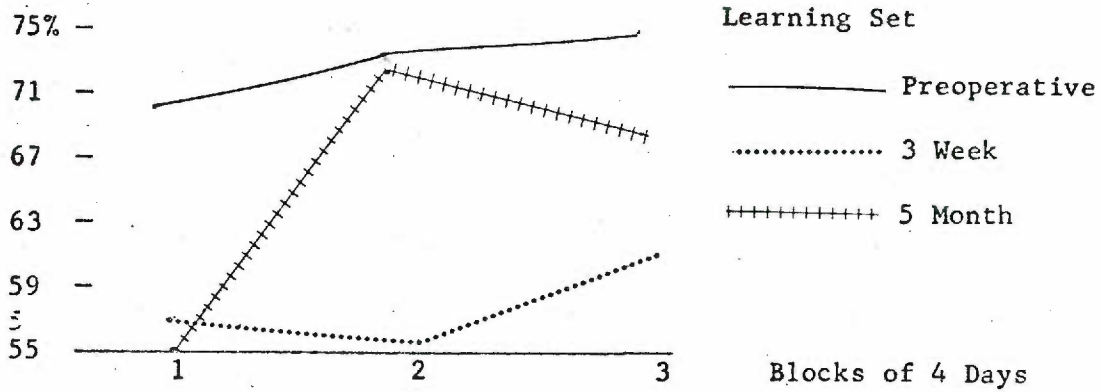


FIGURE III

Cat IV - Operate

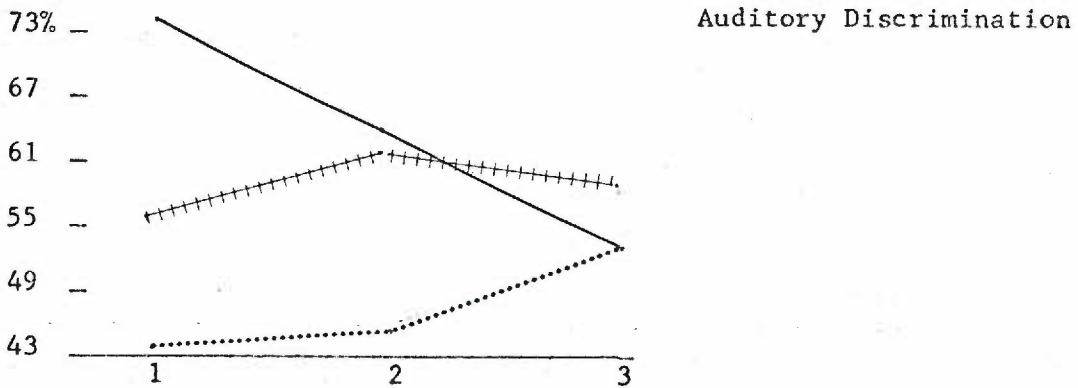
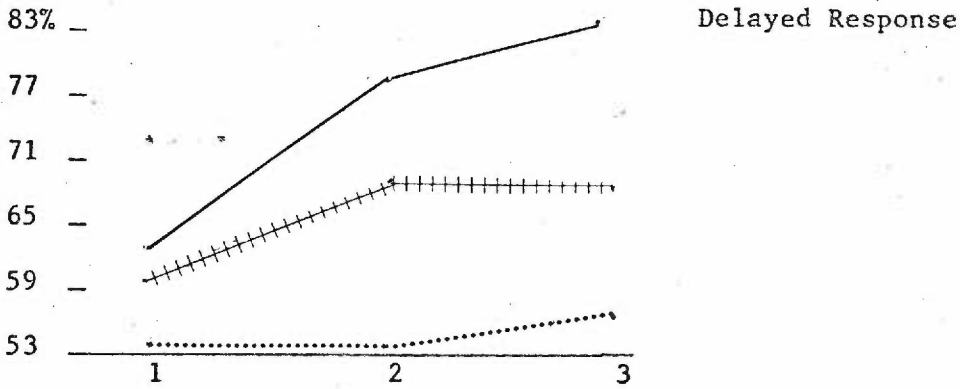
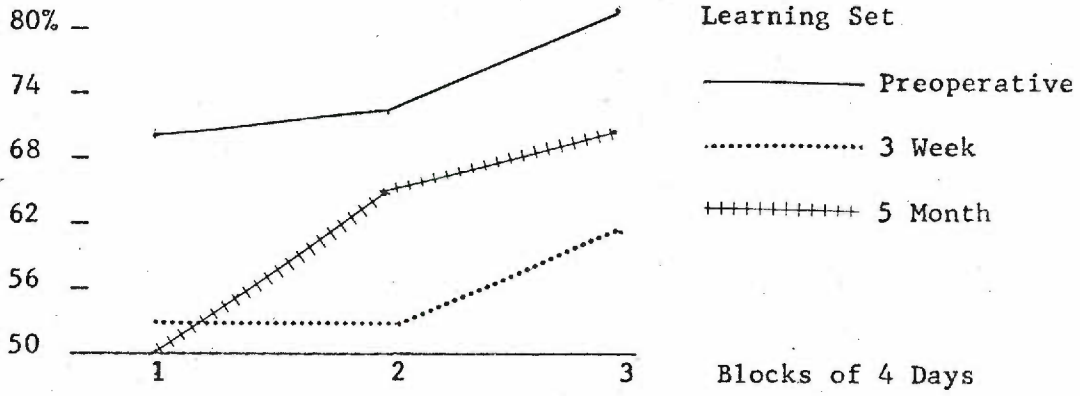


FIGURE IV

Cat V - Operate

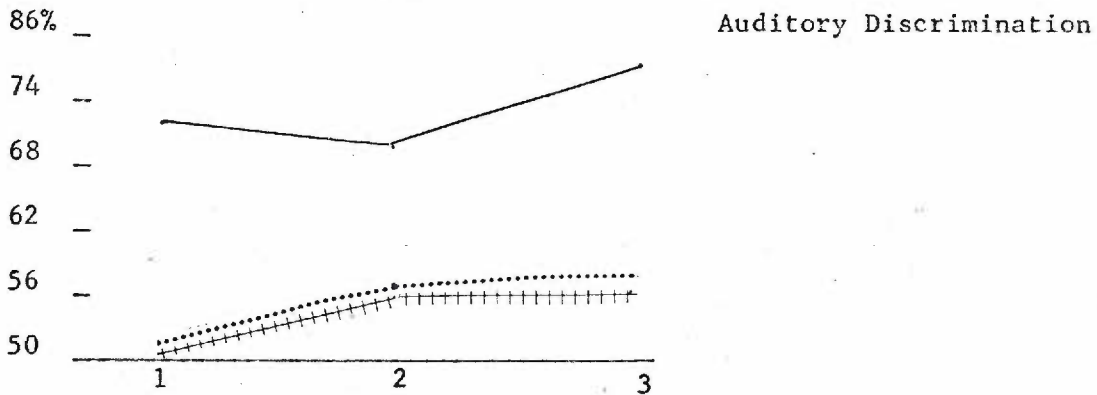
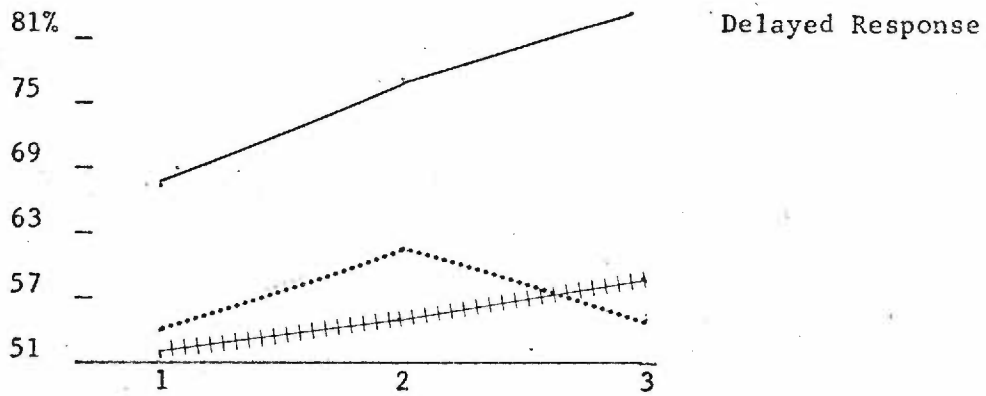
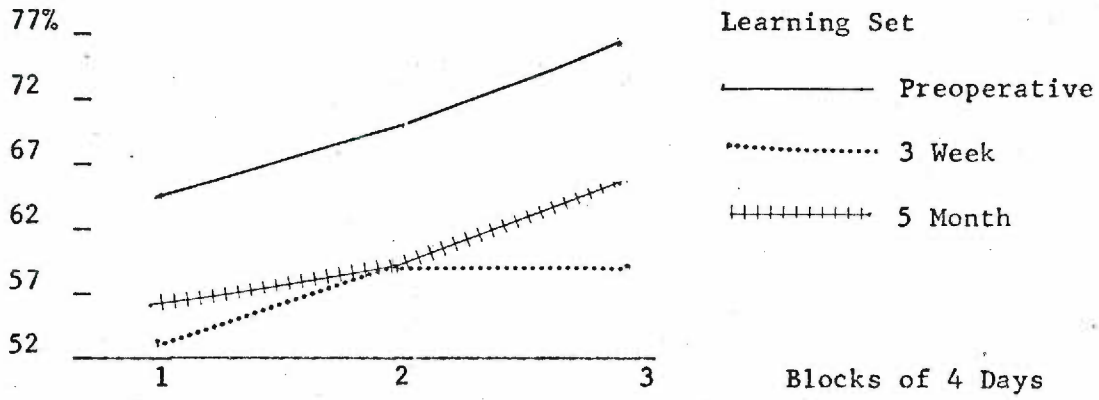
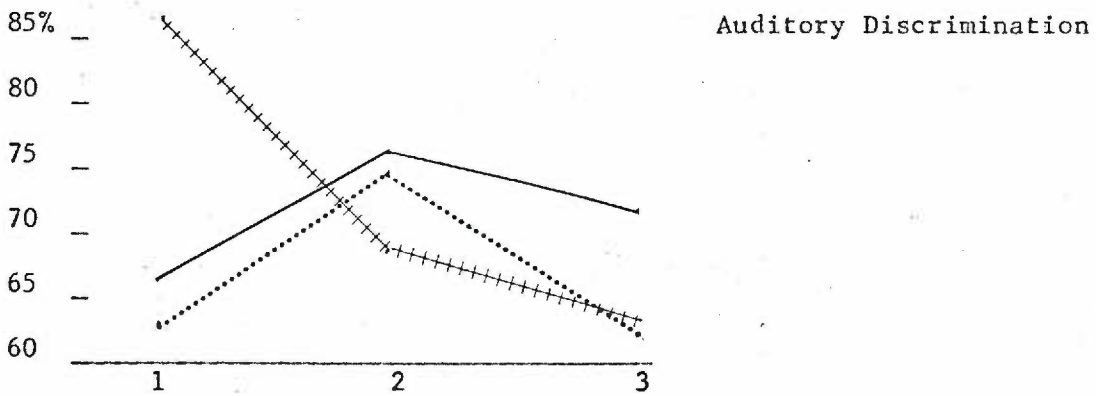
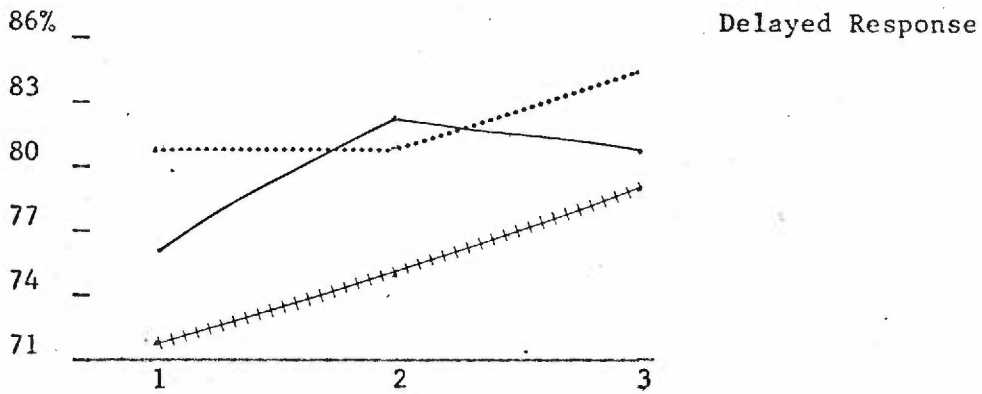
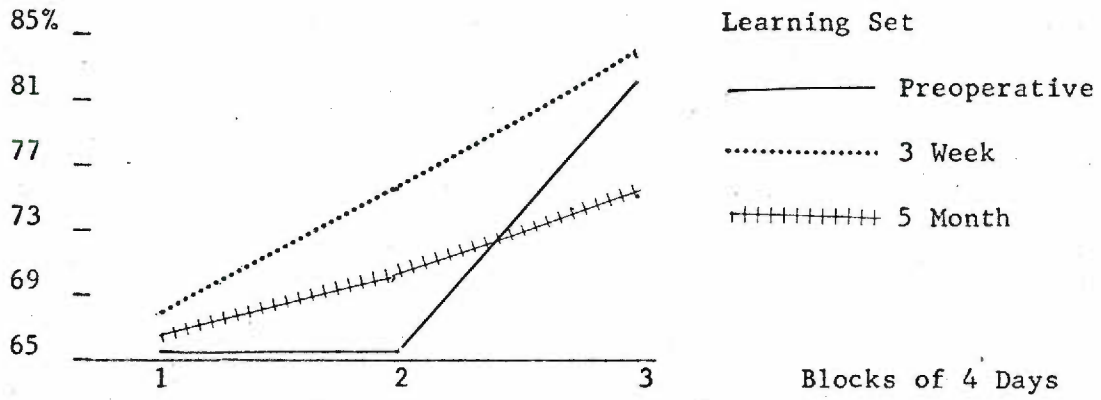


FIGURE V

Cat VI - Unoperated Control



"Go - No Go" Training Procedure

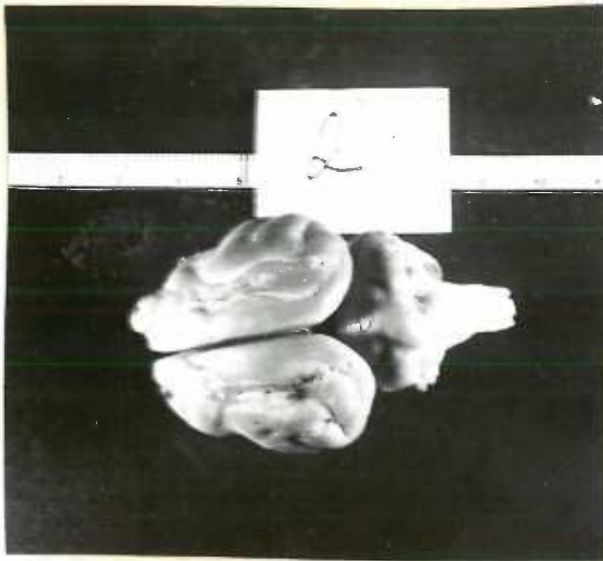
Although the cats came to this lab with a great deal of WETA experience, they had never performed in a "go - no go" situation. They had been required on previous tasks to "go" to the correct object whenever the tray was presented. One major problem in getting the animals to perform well in the "go - no go" setting was the extinguishing of that predisposition for making an immediate "go" response.

A variety of procedures were tried to shape the "no - go" behavior when the difficulty first became evident. At first, the single object was presented many times in the hope that the response would extinguish when no food reward was found. However, one reinforcement would always begin a series of many responses to the unbaited object.

Secondly, the object was hinged at the back to the board so that it could only move in a pivot around the hinge, thereby uncovering the food well. More importantly, a piece of string was fastened to the front of the stimulus object, run through a hole in the tray beneath the object and back to the observer. In this manner the observer was able to lock the object by placing tension on the string, but the cat was unable to discern whether the object was locked or not.

The cats were then subjected to "go" extinction trials with the locked object. After several hundred trials, approximately 90% of which consisted of the presentation of the object in the locked position, the dominant "go" response to this situation was extinguished.

PLATE I



Both Hemispheres



Left Hemisphere



Right Hemisphere

PLATE III



Both Hemispheres



Left Hemisphere



Right Hemisphere

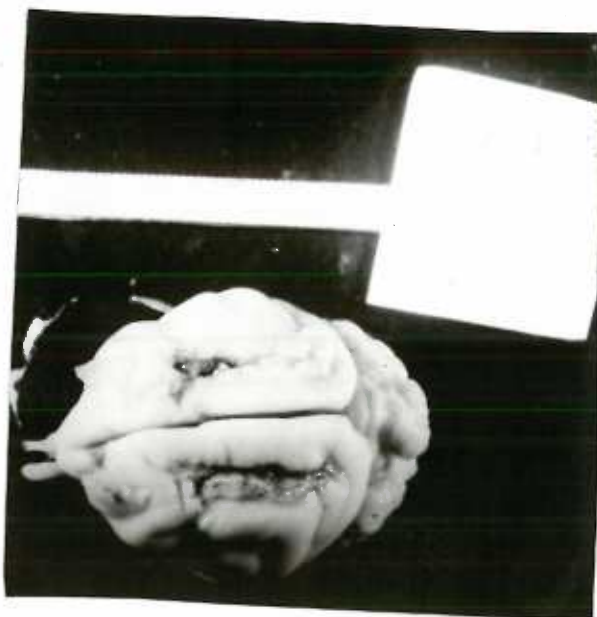
Cat IV

Left Hemisphere. The middle suprasylvian gyrus shows loss of contour and substance. The lateral gyrus appears almost totally intact with the exception of the anterior 1/5th of its more lateral extent. The pericruciate areas seem totally ablated extending to and including the anterior cingulate gyrus.

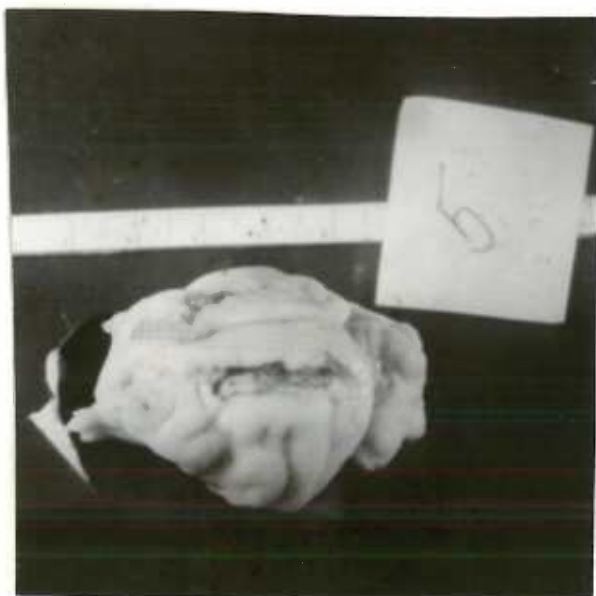
Right Hemisphere. The middle suprasylvian gyrus shows loss of contour and substance. The lateral gyrus seems almost totally intact, again with the exception of its more medial extent. The pericruciate areas seem totally ablated down to and including the superior lip of the anterior cingulate gyrus.

Comment. The lesion seems adequate with the exception of its lack of destruction of the anterior lateral sensory association areas.

PLATE II



Both Hemispheres



Left Hemisphere



Right Hemisphere

Cat V

Left Hemisphere. There appears to be total loss of substance in the middle suprasylvian gyrus. The lateral gyrus shows loss of structure and content in its anterior 1/5th extending medially to include part of the cingulate gyrus. There is total loss of substance surrounding the perieruciate areas.

Right Hemisphere. There is total loss of substance of the middle suprasylvian gyrus. The lateral gyrus shows loss of substance in its anterior 1/5th which extends medially to include the cingulate gyrus. There is total loss of substance about the perieruciate areas matching that of its contralateral hemisphere.

Comment. The lesions seem to cover the intended areas.

APPENDIX II*

*Analyses done subsequent to the completion of the thesis.

TABLE I

SUMMARY OF 2 SEC. AND 10 SEC. DELAYED RESPONSE DATA

Correct Responses				
Normals	Postoperative 3 week			\bar{X}
	Days 1-4	Days 5-8	Days 9-12	
Cat I 2 sec.	23	24	30	77
	21	23	22	66
Cat VI	29	28	28	85
	17	20	22	59
<u>Lesioned</u>				
Cat II	14	19	23	56
	19	15	14	48
Cat IV	17	22	23	62
	17	12	14	43
Cat V	19	26	22	67
	15	14	14	43
Postoperative 5 Month				
<u>Normals</u>				
Cat I	24	24	27	75
	17	21	23	61
Cat VI	26	29	33	88
	26	23	24	73
<u>Lesioned</u>				
Cat II	21	26	20	67
	22	15	15	52
Cat IV	22	23	23	68
	16	21	20	57
Cat V	21	24	25	70
	12	12	13	37

TABLE II

SUMMARY OF RESPONSES ON TRIALS 2 AND 2-6 INCLUSIVE
DEPENDENT ON WHETHER INITIAL OBJECT IS REWARDED (+) OR NOT (-)

Correct Responses

Cat #	3 Week				5 Month			
	Trial 2		Trials 2-6		Trial 2		Trials 2-6	
	+	-	+	-	+	-	+	-
I	25	28	136	128	29	31	135	131
VI	<u>31</u>	<u>29</u>	<u>141</u>	<u>131</u>	<u>29</u>	<u>28</u>	<u>127</u>	<u>127</u>
	56	57	277	259	58	59	263	258
II	18	22	95	105	21	22	115	114
IV	19	25	104	101	22	22	115	107
V	<u>22</u>	<u>20</u>	<u>111</u>	<u>99</u>	<u>24</u>	<u>22</u>	<u>103</u>	<u>115</u>
	59	67	310	305	67	66	333	336

TABLE III

Comparison Between 3-Week and 5-Month Operates and Unoperates

Auditory Discrimination

<u>Source of Variation</u>	<u>SS</u>	<u>df</u>	<u>Mean Sq.</u>	<u>F</u>
Between operates and unoperates	2,900.0	1	2,900.0	67.6**
Between Ss in same group	<u>132.3</u>	3	44.1	
Total between Ss	3,112.3	4		
Between 3-week and 5-month	176.2	1	176.2	
Interaction (operates and unoperates)				
X (3-week + 5-month)	577.3	1	577.3	
Interaction: pooled Ss X trials	<u>2,691.0</u>	3	897.0	
Total within Ss	3,444.5	5		

Learning Set

Between operates and unoperates	2,652.0	1	2,652.0	63.6**
Between Ss in same group	<u>125.0</u>	3	41.7	
Total between Ss	2,777.0	4		
Between 3-week and 5-month	1.3	1	1.3	
Interaction (operates and unoperates)				
X (3-week + 5-month)	525.0	1	525.0	
Interaction: pooled Ss X trials	<u>2,389.5</u>	3	796.5	
Total within Ss	2,915.8	5		

Delayed Response

Between operates and unoperates	1,040.0	1	1,040.0	20.5*
Between Ss in same group	<u>152.0</u>	3	50.7	
Total between Ss	1,192.0	4		
Between 3-week and 5-month	1.6	1	1.6	
Interaction: (operates and unoperates)				
X (3-week + 5-month)	125.2	1	125.2	
Interaction: pooled Ss X trials	<u>972.0</u>	3	324.0	
Total within Ss	1,098.6	5		

* Significant at .95

** Significant at .99