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Effect of Frontal Lesions on Performance of Sequential Tasks by Monkeys

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Sequential behavior was studied in monkeys with frontal and inferotemporal lesions. An automated discrimination apparatus was used for training. Postoperative retention was assessed in two types of test; one, which required the subject to so order his response that without repetitions he had to push all of several cued panels (internally ordered sequence test) and another, in which the exact order of pushing a series of panels was determined by cues displayed on the panels (externally ordered sequence test). In some animals original learning of this last test was studied postoperatively. The prediction was that the monkeys with frontal lesions would fail internally ordered sequence task but would be able to follow a sequence where external cues can guide the behavior sequence. Those with inferotemporal lesions would show a deficit in the latter test due to their known handicap in visual discrimination problems. The results obtained on those with frontal lesions on the *non-cued* task confirmed our hypothesis. The subjects with inferotemporal lesions showed no deficit on this task. On the cued task, monkeys with frontal lesions had good postoperative retention; the other group varied a great deal on their performance. The pattern of errors of subjects with frontal lesions on the internally ordered sequence revealed a failure in the completion of a task rather than a tendency towards perseveration. Interpretation of the results in those with frontal lesions, suggests a lack of internal representation in order to anticipate the next step of a sequence; this is not compatible with a simple explanation in terms of a defective recent memory.

Introduction

Jacobsen, Wolfe and Jackson (2) studied behavior sequences in two well-known chimpanzees ("Becky" and "Lucy") which had been given

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frontal lobectomies. The tests employed were the two-platform, single-stick problem, and the opening of a problem box requiring a sequence of actions performed in a precise order. They concluded that removal of the "frontal areas seriously impaired adjustment to situations involving temporal organizations of behavior."

It appeared worth while to explore further the experimental conditions under which behavior sequences are disturbed by frontal lesions. To this end, monkeys with a dorsolateral granular frontal ablation were trained in two variations of a sequential task. As controls, four with inferotemporal lesions were also trained on these problems. Some of these tasks required the animals to so order their responses that without repetitions during any trial, they should push *all* of several cued panels to obtain reward; we refer to this as the "internally" ordered sequence test. In the other type of sequential task the exact order of pushing a series of panels was prescribed by cues displayed on the panels; we called this the "externally" ordered sequence task. The prediction was made that monkeys with frontal lesions would more easily learn and retain a task where distinctive external cues prescribe the sequence; that those with inferotemporal lesions, on the other hand, should show no difficulty in performing the internally ordered sequence test but might have a deficit in the extrenally ordered task due to their known deficits on visual discrimination problems.

Material and Methods

Ten immature monkeys (*Macaca mulatta*) were used.

The apparatus was an automated discrimination apparatus (DADTA), (11). On this machine, one to twelve stimuli (displayed on 1.5 × 2.5 inch lucite panels) can be presented in scrambled order over sixteen positions. The pattern of stimuli and reinforcement presentation can be preprogrammed. The subject responds by pressing a panel; the stimuli display and the correct and erroneous responses are recorded on punched paper tape for ready processing by a general purpose computer. Peanuts are used as reinforcement.

Because of the complexity of the test, the monkeys had to be progressively "shaped" to perform the various tasks; they were trained preoperatively on the following series of tasks: (a) press one red panel for a reinforcement; (b) discriminate between the numerals "7" and "8"; (c) press an "O" and a green circle, without repetition in either order (simple internally ordered sequence O–G); (d) press "O", green circle, and the numeral "4" without repetition in any order (internally ordered sequence

O–G–4); (e) press, without repetition, three red circles (internally ordered R–R–R). Finally, three monkeys were trained to press first a green circle then a red circle (the externally ordered task) and seven others (three with frontal and four with posterior lesions) were given this task only postoperatively.

The criterion for adequate discrimination learning was forty-five correct responses in one fifty-trial session; the criterion for adequate performance of the sequence tests was ten consecutive correct trials in a session for the "two cues" sequence and nine consecutive trials for the "three." All were given preoperative retention tests, in the same order as in the original learning part of the experiment.

Six of the ten animals were given ablations of the dorsolateral frontal cortex, and four, ablations of the inferotemporal cortex. Approximately 10 days after surgery, postoperative retention tests were begun. The subjects which did not reach criterion in the postoperative retention tests were retrained; two orders of retraining were used to evaluate transfer effects.

The tasks were given in the following order. Group I, three monkeys with frontal and two with inferotemporal lesions: discrimination ("7" positive); internally ordered sequences: R–R–R, G–O, G–O–4; externally ordered sequences, G–R. Group II, three monkeys with frontal and two with inferotemporal lesions: discrimination ("8" positive); ordered sequence: G–R; nonordered sequences: G–O, G–O–4, R–R–R.

The frontal lesions were symmetrical and quite similar in extent from one animal to another; only monkey No. 113 had slight subcortical damage (Fig. 1). Thalamic degeneration of the nucleus medialis dorsalis was studied. Cells of the middle and lateral portion of the nuclei were absent; the most medial magnocellular portion had a normal aspect (Fig. 1).

Inferotemporal preparations were made somewhat variable intentionally. The lesions were kept small so as not to interfere completely with discrimination, yet hopefully large enough to produce some effect. Thus, monkey No. 110 had the smallest lesion, while the other three had received ablations roughly comparable in extent (Fig. 1).

Results

Discrimination Task. All monkeys with frontal lesions showed complete retention or relearned with considerable saving (Table 1). The temporal-lesion subjects were not so uniform. Monkey No. 110 showed only mode-

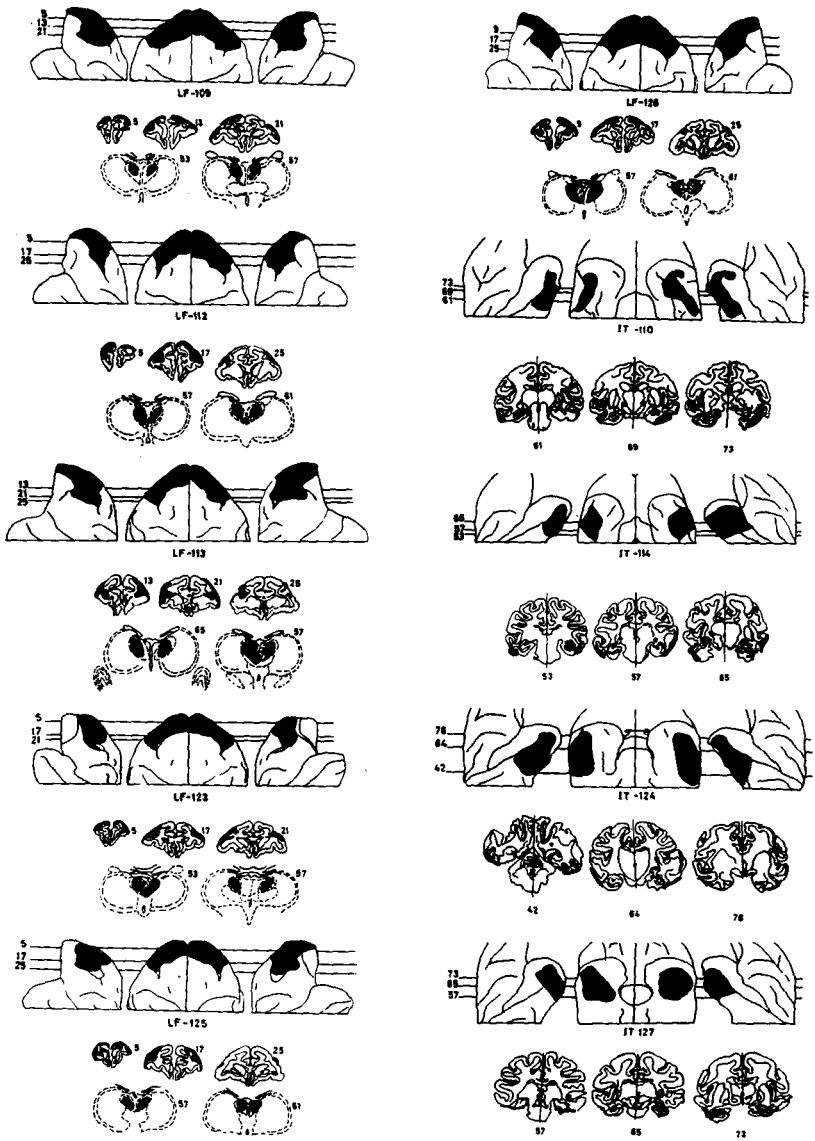

FIG. 1. Reconstruction of lesions for six monkeys with lateral frontal (LF) and four with inferotemporal (IT) lesions. Representative cross sections for each animal and medio dorsal nuclei degeneration for the frontal group are shown.

rate impairment on this task; No. 124 completely retained the discrimination; and No. 114 and No. 127 had clear deficits.

TABLE 1

TOTAL NUMBER OF TRIALS TO REACH CRITERION IN THE DISCRIMINATION TEST FOR NORMALS (WHICH WERE SUBSEQUENTLY OPERATED), FRONTALS, AND INFEROTEMPORALS

Monkeys	113	112	109	123	125	126	114	110	124	127	Avg.	SD
Normals	400	250	250	250	200	100	500	230	200	200	260	106
Frontals	150	200	100	0	50	0					83	74
Temporals							850	150	0	200	300	325

Original Learning of an Externally Ordered Sequence. Both the subjects with frontal and temporal lesions were slightly inferior to the unoperated controls (Table 2). The controls averaged 571 trials, while the frontal group averaged 730 trials and the temporal group, 888 trials. However, none of these differences reached statistical significance at the 0.1 level.

Error Analysis. The types of errors possible on the externally ordered sequence test are selection of red first and repetition of green. An analysis of the errors showed that the distribution of responses varied radically from the hypothetical probability of one-half red failure (X^2 goodness of fit, 2 *df*, $p < 0.001$).

Retention and Relearning of an Externally Ordered Sequence. No significant deficit was found between pre- and postoperative scores (Fig. 2). Monkeys with frontal lesions relearned this task with considerable saving (average 240 trials), (Table 2).

The Retention and Relearning of an Internally Ordered Sequence. Retention tests for the frontally and inferotemporally damage subjects in the internally ordered sequence tests are depicted in Fig. 3. There is a significant difference both between pre- and postoperative scores for the frontal group ($t = 13{,}34$, 5 *df*, $p < 0.001$), and between the two operated groups ($t = 6{,}46$, 7 *df*, $p < 0.001$).

On the "two unlike cues" task, the frontal group took ninety-eight trials to rereach criterion; the temporal group showed immediate and complete retention (Table 3).

On the "three unlike cues" (G–"0"–"4"), the frontal group averaged 749 trials to reach criterion, while their temporal lobe controls took an average of only 130 trials (Table 3). On the "three like cues" (R–R–R) task, monkeys with frontal lesions averaged 667 trials to rereach criterion,

TABLE 2

LEARNING OF AN EXTERNALLY ORDERED SEQUENCE TASK

A. Total Number of Trials to Reach Criterion for Normals, Frontals, and Temporals

	Normals			Avg.	SD	Frontals			Avg.	SD	Temporals				Avg.	SD
Monkey	123	125	126			113	112	109			114	110	124	127		
Trials	892	220	600	571	275	650	643	897	730	118	1350	486	679	1039	888	332

B. Total Number of Trials for the Frontal Group on Postoperative Relearning

	Frontals			Avg.	SD
	123	125	126		
	70	582	68	240	242

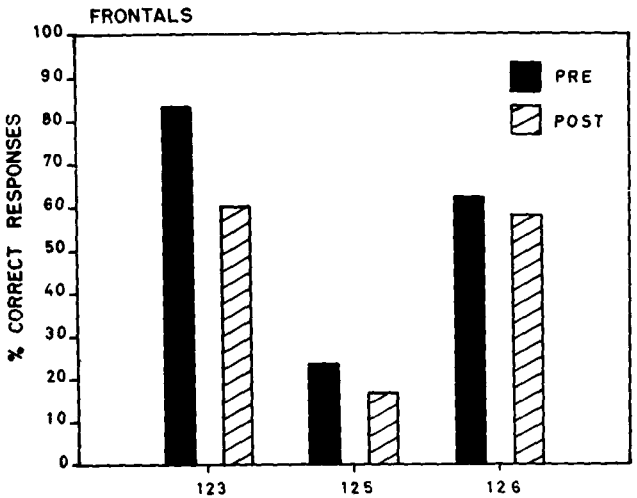

FIG. 2. Percentage of correct responses in the pre- and postoperative retention test for three monkeys with frontal lesions on the externally ordered sequence: G–R.

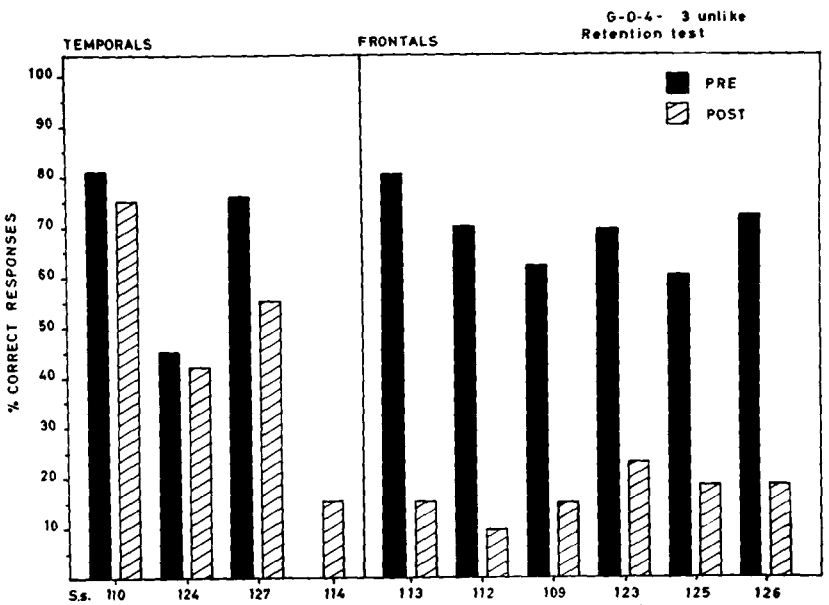

FIG. 3. Percentage of correct responses in the pre- and postoperative retention test for the frontal and temporal groups on the internally ordered sequence: G–O–"4".

and their inferotemporal controls only needed an average of 77 trials (Table 3).

TABLE 3

TOTAL NUMBER OF TRIALS TO REACH CRITERION PRE- AND POSTOPERATIVELY IN THE FRONTAL AND TEMPORAL GROUPS ON THE INTERNALLY ORDERED SEQUENCE TASKS

	2 Unlike		*3 Unlike*		*3 Like*	
	Preop.	Postop.[a]	Preop.	Postop.	Preop.	Postop.
Frontals						
113	317	—	200	1500[b]	33	1500[b]
112	280	170	1732	924	61	1250
109	122	120	1698	263	749	829
123	376	96	800	375	32	130
125	190	47	1068	693	35	75
126	162	57	159	735	59	220
Average	241	98	943	749	162	667
	SD 98	SD 49	SD 692	SD 441	SD 287	SD 616
Temporals						
114	126	—	794	65	65	9
110	314	10	1281	50	29	135
124	341	10	419	189	28	114
127	391	10	926	214	156	50
Average	293	10	855	130	70	77
	SD 115	SD 0	SD 356	SD 83	SD 62	SD 58

[a] —, Not tested.

[b] Subject did not meet criterion.

Order of presentation of tasks (Groups I and II) is indicated in Table 4. A clear transfer effect was found between the first and second test run (internally ordered); this effect was clearer for Group II. This result made it possible to compare the total number of relearning trials for the frontal group with those of the temporal group on the *first* internally ordered sequence task irrespective of whether it was a G–O–4 or R–R–R problem. This difference between the two operated groups is significant (*Fisher sign test*, $p < 0.004$, one-tailed test).

Error Analysis for the "Three Unlike" Task. The type of error that subjects can commit in this test can be of three kinds: to hit twice the first panel selected (1–1 type error, normal $p = \frac{1}{8}$); to repeat the second (1–2–2, normal $p = \frac{2}{9}$); and to return to the first after the second was pushed (1–2–1, normal $p = \frac{2}{9}$).

An analysis of the distribution of errors over the last 25 per cent of

the trials indicated that normal subjects made more 1–2–1 errors than 1–2–2 or 1–1 errors. Seven subjects were studied. Using a two-tailed binomial distribution, there was a significantly higher number of 1–2–1 errors over 1–1 errors ($p < 0.001$). The occurrence of 1–2–1 over 1–2–2 type errors was also significantly higher ($p < 0.02$) (normal $p = \frac{1}{2}$).

TABLE 4

EFFECT OF ORDER OF TASKS ON AVERAGE TOTAL NUMBER OF TRIALS ON THE INTERNALLY ORDERED SEQUENCE TASK TO REACH CRITERION IN THE TWO GROUPS OF OPERATED ANIMALS

Group I				
	Frontals		Temporals	
	Like	Unlike	Like	Unlike
Avg.	1193	896	72	58
SD	277	505	63	8
Group II				
	Frontals		Temporals	
	Unlike	Like	Unlike	Like
Avg.	601	142	202	82
SD	161	60	13	32

The distribution of errors in the two operated groups is different. Three monkeys of the temporal group had 1–2–1 errors more frequently than 1–1 errors; this difference though, is not significant at the 0.1 level (one-tail binomial, $p = 125$). Two out of these three animals showed 1–2–1 errors more often than 1–2–2 errors, but again the differences are not significant (one-tail binomial, $p = 50$).

On the other hand, all monkeys with frontal lesions during the last 25 per cent of the trials made more 1–2–1 type errors than the *sum* of 1–2–2 plus 1–1 errors. The difference is highly significant ($p < 0.001$, two-tail binomial).

Thus, monkeys with frontal lesions tend to reproduce the pattern of error performed in original learning, though the proportion of 1–2–1 error is different after the operation. A comparison can be made of the proportion of 1–2–1 against repetitive errors (1–1 and 1–2–2) over the first quartile: Unoperated normal subjects give a 1:1 relation; inferotemporally operated subjects show a 2:1 ratio; and those with frontal lesions mount to 3:1. The same analysis made over the last quartile gave a

proportion of 2:1 for the normal group, 2:1 for the temporal group and 4:1 for the frontal group.

The error analysis for the three like cued task was not done in this detailed a fashion but also indicates a larger proportion of 1–2–1 errors, both for the normal and frontal groups, with that of the frontal group markedly greater.

Discussion

Good postoperative retention was found on subjects with frontal lesions on the externally ordered sequence task. On original learning of this task, the results are not conclusive since the scores obtained differed only slightly and the number of animals in each group was small. Two of the inferotemporally operated monkeys showed a clear handicap on visual discrimination, and these also were deficient in this externally ordered sequence task. Error analysis on the original learning of the task yielded no difference between subjects with frontal lesions and those with inferotemporal lesions; both operated groups selected the red cue significantly more frequently, which eliminates a simple color discrimination deficit as a possible cause of the failure for the animals with temporal lesions. Results on the internally ordered sequence task indicate that inferotemporal operates have no deficit on performing motor sequences, but they might well have difficulty on problems involving *sensory* sequences.

The internally ordered sequence task clearly separated the groups with anterior and posterior lesions from one another. These two operated groups differed significantly in their postoperative scores and in their error patterns. As training progressed, the frontal group increased its proportion of 1–2–1 errors and decreased its proportion of the repetitive (1–2–2 and 1–1) errors. These results exclude perseveration as a possible explanation for the frontal group's difficulty.

A pertinent question to ask is: what are the relevant factors that may account for the different retention scores obtained by monkeys with frontal lesions on these two types of sequences? On the externally ordered sequence task, the order is prescribed distinctively by the cues displayed; the "instructions" are stored, at least in part. The animal can learn the sensory sequence and use it as a guide for his motor sequence.

On the internally ordered sequence task, on the other hand, there are no such external guides to behavior. Here the animal may choose any cue panel for his first response, but whether the following responses are correct or wrong is contingent only on his previous action. Any fixed spatial

strategy is precluded on this task due to the scrambled order in which cues are displayed. Delayed alternation shares some of the characteristics of this task: there is a recurrent sequence, no particular cue is constantly related to reward and the correct response is contingent only on the previous action. Konorski (4) claimed recent-memory deficit for directional cues as a typical frontal deficit; the significantly larger number of 1–2–1 errors of the subjects with frontal lesions makes this unlikely. Rather, the deficit appears in completing a task. Any serial activity requires as much to remember what has already been done as to know what remains to be done. Representative functions are essential in order to anticipate next action. Denny Brown (1) describes the frontal deficit in human patients as the inability to visualize the consequences of his actions. Pribram (7) found that monkeys with frontal lesions keep on pressing a lever after the apparatus has run out of peanuts; the author interpreted this as a failure to be guided by the outcome of his actions. Our results emphasize another aspect, which is the need of some adequate internal representation (i.e., plan) in order to carry out, step by step, the whole of a behavioral sequence. Human beings performing some serial activity (e.g., when reciting poetry) start all over again whenever they are unable to proceed. And on tasks similar to those tested here, lobotomized patients show marked deficits in performance (5, 6, 10).

Is the frontal cortex the only neural structure involved in the guiding of behavior sequences? Pribram (8, 9) has suggested that the frontal cortex is the "association area" for the limbic formations of the forebrain. Recent experimental results have supported this suggestion. Alternation behavior is disturbed not only by frontal but by a variety of limbic system lesions (12) and in fact, hippocampal ablations interfere with the performance of the tasks used in the current study (3). The similarities and differences between these effects and those obtained from subjects with frontal lesions should help clarify the mechanism by which sequential behavior is organized.

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