Reprinted from EXPERIMENTAL NEUROLOGY Volume 11, Number 2, February 1965

EXPERIMENTAL NEUROLOGY 11, 217 229 (1965)

Effects of Frontal Lobotomy in Man on the Performance of a Multiple Choice Task

R. L. POPPEN, K. H. PRIBRAM, AND R. S. ROBINSON

Stanford University, Palo Alto, California

Received August 17, 1964

Using a small special purpose computer (DADTA) a series of multiple choice problems was presented to a group of twenty lobotomized subjects and their matched controls. The problems were similar to those given in a previous experiment to monkeys with frontal lesions. Human problem solving just as monkeys' was found markedly impaired by the frontal surgery, although some differences between its effects on man and beast were also noted.

Introduction

In a recent review of the effects of psychosurgery on behavior, Willet (4) points out that relatively few studies with human subjects have been concerned with identifying the functions of the frontal lobes, and then only incidentally to the principle aim of assessing the therapeutic effect of the surgery. It is no surprise that such is the case because of the inherent disadvantages in a human study: No preoperative behavioral measures are available; operations are carried out on subjects with existing cerebral or behavioral pathology or both; little control can be exerted over the preoperative and postoperative environment and experience of the subjects; and comparability between experimental and control subjects is impossible to guarantee. These difficulties are easily circumvented by the use of infrahuman subjects (8) and therefore much of our knowledge and theory of brain function is based on nonhuman primates. The present experiment is an attempt to replicate some findings from well-controlled animal studies with less reliable human subjects; the hypothesis is that similarity of results will increase the generalizability of our knowledge across phylogenetic levels.

This experiment is based on a multiple-choice study with monkeys that has been described elsewhere (5) but a brief review is necessary here. Using a modified Wisconsin general test apparatus (1) Pribram trained four rhesus monkeys with anterofrontal lesions and four controls to

select the one of two objects that concealed a peanut. These objects were randomly placed over twelve possible positions. The peanut remained under a particular object until criterion performance of five correct consecutive responses was reached, after which the reward was switched to the other object. When criterion was reached on that cue, a third object was added and rewarded. Each of the objects in turn became the positive cue and, after criterion performance on each, another object was added. This procedure was continued until twelve objects were present. The problem was conceived as requiring an alternation of two strategies: searching through the displayed objects until the rewarded one is found; and persisting on the rewarded cue until it is no longer correct. The results showed that the monkeys with frontal lesions tended to persist briefly in their previous strategy after it was no longer appropriate; i.e., they were less likely to return to the positive cue after receiving a reward, and when they finally did select the correct cue five times in succession, they were less likely to leave that cue when it was no longer rewarded. However, an exception to the second finding occurred whenever a new object was introduced into the situation. The subjects with frontal lesions then chose that cue just as rapidly as did the controls (6).

Method

Subjects. Forty chronic schizophrenic male patients of the Menlo Park Veterans Administration Hospital, Menlo Park, California, were used in this experiment. Twenty-two of them had undergone bilateral frontal lobotomy 9–14 years (10.87 = mean) before the study. These subjects

TABLE 1
DESCRIPTIVE DATA ON SUBJECTS OF EXPERIMENT

		Lobot.	Control
Age in years:	Mean	41.17	41.54
	Range	34.50–45.44	36.00–46.25
Length of hospitalization in years (from date of first VA admission):	Mean	16.07	16.48
	Range	10.75–23.33	10.83–19.58
Education in years:	Mean	10.71	10.17
	Range	6–14	4–13
Nurses' ratings on "degree of pathology" (from 1—less severe, to 5—greatly impaired):	Mean	3.3	2.6
	Range	1–5	1–5

were matched as closely as possible with respect to age, diagnosis, length of hospitalization, education, medication, and ward head nurses' ratings of "degree of pathology," by an equal number (except in four cases) of nonoperated ward-mate controls. The control group thus consisted of eighteen patients. Table 1 summarizes the descriptive data.

Apparatus. The equipment used was an automated discrimination apparatus for discrete trial analysis (DADTA), (7). DADTA is a switch-programmed, special purpose relay computer which automatically controls stimulus presentation, determines reinforcement as a function of response, and records stimuli, response, and reinforcement on punched paper tape. Data on paper tape are then transferred to punched cards using an IBM 046 tape-to-card converter. Once on cards, the data may be verified immediately using standard punched card equipment and tabulation and statistical analyses can be done conveniently using BALGOL and Stanford's Burroughs 220 and IBM 7090 computers.

DADTA consists of two sections, a display unit and a control console. The display unit consists of sixteen clear plastic windows, 1¾ × 2½ in., in a four by four arrangement. Each window is hinged and activates a microswitch when slight pressure is applied to it. Behind each window is an Industrial Electronic Engineers, in-line readout projection unit which can display any of twelve different figures, depending on the setting of the control console. A Foringer feeder mechanism was concealed in the top of a wood box 25 in. tall, 21 in. wide and 17 in. long, painted black, which covered the display unit except for the face, in order to protect it. Candies ("M & M") were delivered by the feeder to a metal tray located in the center of the display panel. The display unit was placed on a table in the experimental room and connected by cables to the control console approximately 40 feet away in an adjoining room. The control console recorded on punched tape which window was pressed, the figure projected on that window, and whether or not that response was rewarded. Changes in "program" were automatically controlled and recorded by the console (see Procedure).

A computer program was written in the Burroughs ALGOL-58 (BALGOL) compiler language and run on a Burroughs 220 digital computer to aid in analysis of the experimental data. The data from each trial were read from punched cards, and by task (program), each response was tallied according to symbol chosen until the first reward had been achieved (search) and until criterion had been met (post-search). Simultaneously with the response tallying, cue and position perseveration detection tests

were applied. At the conclusion of each task (program) the response summaries were tabulated and per cent response to cues within search, post-search, and total program calculated. The results of each program were then listed on an on-line IBM 047 accounting machine (Table 2).

Procedure. Each subject was met on his ward by the experimenter who asked him if he would like to participate in a game in which he could win free candy. If the patient agreed, the two walked to the building in which the experimental rooms were set up. The subject was seated in an upholstered easy chair facing the display unit. Six differently colored geometric figures were displayed and he was asked to name the colors as the experimenter pointed to them in order to determine if the subject was color blind. The experimenter then explained the "rules" as follows:

> "This is a game in which you can win free candy. All you have to do is hit the right design, like this. (The experimenter demonstrated by pressing one of the lighted windows and received an "M&M".) Now you try it. (The subject then

TABLE 2

EXAMPLE OF COMPUTER PRINTOUT

	Cue								
	1	3	4	5	8	12	9	2	Total
Search	0	0	0	1	0	0	0	0	1
Postsearch	7	2	2	4	3	3	0	0	21
Program	7	2	2	5	3	3	0	0	22
Per cent S	0.0	0.0	0.0	100.0	0.0	0.0	0.0	0.0	
Per cent PS	33.3	9.5	9.5	19.0	14.2	14.2	0.0	0.0	
Per cent PG	31.8	9.0	9.0	22.7	13.6	13.6	0.0	0.0	
Symbol perseveration									
Position perseveration									
Number of re-entries		0		Rewarded cue 1					
Run number 2906	Type C +			Problem number 1			Program number 2		

	Cue								
	1	3	4	5	8	12	9	2	Total
Search	0	0	2	1	1	1	0	0	5
Postsearch	6	0	2	0	0	0	0		8
Program	6	0	4	1	1	1	0	0	13
Per cent S	0.0	0.0	40.0	20.0	20.0	20.0	0.0	0.0	
Per cent PS	75.0	0.0	25.0	0.0	0.0	0.0	0.0	0.0	
Per cent PG	46.1	0.0	30.7	7.6	7.6	7.6	0.0	0.0	
Symbol perseveration		1							
Position perseveration									
Number of re-entries		0		Rewarded cue 1					
Run number 2897	Type L +			Problem number 2			Program number 10		

pushed one of the figures and was rewarded.) When you press the right design the machine pays off with candy. Try to win as much candy as you can. You may eat it here or put it in this bag. (A waxed sandwich bag lay in front of the unit.) OK, see how much you can win."

The experimenter took a chair about 5 feet to the left rear of the subject where he could see and record the subject's responses; the latter could see the experimenter without difficulty if he wished. If the subject tried to hit more than one window at a time he was told, "Only one counts." If he pressed blank windows he was told, "Only the designs count." If he complained that he could not win any more, or that the machine was broken, he was encouraged to continue by saying he was doing fine, or that he had to find the right one, or, if such were the case, that he was almost finished. Breaks were permitted for a trip to the toilet, a drink of water, or a cup of coffee. The subjects were permitted to smoke.

The task confronting the subject was a sequence of twenty "programs." In each program one of the cues that was displayed was rewarded whenever the window on which it was projected was pressed, regardless of the position of the window. Every response resulted in the display panel becoming blank for a 5-sec intertrial interval, after which the figures reappeared in a different, randomized, position. When the positive cue was selected to a criterion of five times in succession the program changed so that another of the cues was now positive. When five of the six initial cues had been rewarded, i.e., on the sixth program, a seventh figure was added as the positive cue. After criterion on this program the cycle started over again: The figure that was positive in program one became positive in program seven, the positive cue in program eight had also been correct in program two, etc., up to program thirteen when an eighth cue was introduced as correct. The sequence was again repeated in the same order as before, for a total of twenty programs.

The experimental session was terminated after a maximum of 2 hours, whether or not the subject had completed all twenty programs. Also, if less than six programs had been completed in 90 min., a seventh figure was added as the positive cue to determine the response to novelty of those who did not complete the task.

Results

The first and most apparent result is that only half of the lobotomized patients completed all twenty programs whereas fourteen of the eighteen

controls finished the task. This yields an $X^2 = 3.27$ which for $df = 1$ is significant at the 0.07 level. For ease of exposition, lobotomized subjects who completed the task will be referred to as L+ and those who failed to complete it will be designated as L—. Similarly, control subjects will be designated as C+ and C—.

Table 1 shows that control subjects have a mean nurses' rating of 2.6 whereas the average rating for the lobotomized group is 3.3. The t for this difference is 1.70 which for $df = 38$ yields a $p < 0.10$. Further, in comparing the average rating of the four subgroups (L+, L—, C+, C—) the largest difference occurs between C+ (mean = 2.3) and L— (mean = 3.6). A t-test for this difference (a questionable procedure, *cf.* Reference 3) yields a $p < 0.05$. It thus could be argued that completion of the task is a function of "degree of pathology" and that the lobotomized group was simply more impaired than were the controls. However, when the pass–fail criterion is applied to the ratings (Table 3) an X^2 of 2.56 is obtained which for $df = 4$ yields a $p < 0.80$. This is taken to mean that nurses' ratings do not predict completion of task.

TABLE 3

NURSES' RATINGS FOR "DEGREE OF PATHOLOGY" COMPARED TO COMPLETION OR NONCOMPLETION OF THE TWENTY PROGRAMS

	Rating					
	1	2	3	4	5	
No. subjects completing task	6	7	4	4	4	25
No. subjects failing task	2	2	4	3	4	15
	8	9	8	7	8	

Nor does an analysis of the medication given to the subjects account in any simple fashion for the differences between those who completed and those who failed to complete the task. Table 4 is a drug and dosage record of the patients studied.

Table 5 summarizes the results for those subjects who completed the task, the L+ and C+ groups. First, it is seen that lobotomized patients took many more trials to complete the twenty programs than did controls. The L+ subjects made significantly more responses searching for the correct cue, and significantly more responses after they found it, than did C+ subjects, on programs in which no new cue was introduced. On new-cue programs, the number of search and post-search responses dropped significantly for both groups, with L+ subjects doing just as well as the controls.

The types of errors leading to these differences were then analyzed. A "search error" is defined as any repetition of a response to the same unrewarded cue before the first response to the positive cue of that program. In other words, the subject had to search through the available cues until he found the correct one; more than one response to any unrewarded cue is counted as a search error. A "post-search error" occurred whenever he responded to a cue other than the positive one after he had once hit the correct cue for that program. Table 6 shows that L+ subjects made more search errors and post-search errors than did C+ subjects on the eighteen programs in which no new cues were added. But considering the two programs in which a new cue was introduced, it is seen that L+ subjects made significantly fewer search errors and post-search errors than on non-new-cue programs, and did not differ from controls. The C+ group made fewer post-search errors on new-cue programs, but their number of search errors did not drop significantly.

A "perseverative error" is a form of search error in which the subject persists in responding to the previously positive cue after the program has changed and that cue is no longer rewarded. One would expect him to make one perserverative response on each program which would tell him that the program had changed; more than one response would be an error. *Immediate* perseverative errors are those which occur in succession immediately after program change. Table 7 shows that L+ subjects did not significantly differ in the number of immediate perseverative errors on new-cue as opposed to non-new-cue programs, nor did they differ from C+ subjects in this respect. But when the number of responses during search to the previously rewarded cue, aside from those occurring immediately after program change, i.e., the number of *returns* to the previously rewarded cue, are counted, a pattern similar to that found for over-all search errors emerges. The L+ subjects make significantly more such returns than do C+ subjects on both new-cue and non-new-cue programs. And both groups make significantly fewer return errors on programs in which a new cue is introduced. These results are summarized in the second part of Table 7.

A possible source of the increased totals of the L+ group, aside from errors, is the number of different cues sampled by the subject in his search for the correct one. When the average number of cues sampled per program is considered (Table 8), L+ subjects do not differ from the C+ group on non-new-cue programs nor do they search through a smaller variety of cues on new-cue programs as one might expect. The C+

TABLE 4

DRUGS AND DOSES V.A. HUMAN LOBOTOMY STUDY

L +	Thorazine	Stelazine	Mellaril	Thioridazine	Akineton	Chlorpromazine
2888	200 mg TID	10 mg TID	200 mg TID	—	—	—
2892	200 mg TID	10 mg QD	100 mg TID	—	2 mg QD	—
2897	200 mg BID	—	300 mg BID	—	—	—
2903	—	—	—	—	—	200 mg QD
2904	—	—	—	400 mg BID	—	—
2907	400 mg TID	—	—	—	—	—
2910	—	—	—	—	2 mg TID	300 mg QD
2911	—	—	—	200 mg TID	—	—
2912	100 mg BID	—	—	—	—	200 mg BID
2916	—	—	—	—	—	200 mg BID
2926	—	—	—	—	—	—
L —						
2887	—	—	—	—	—	—
2891	300 mg TID	—	200 mg TID	—	—	—
2895	500 mg TID	—	200 mg TID	—	2 mg TID	—
2898	300 mg TID	10 mg QD	—	—	2 mg BID	—
2902	—	—	—	—	2 mg BID	400 mg BID
2908	—	20 mg QD	—	—	—	—
2909	400 mg TID	10 mg QD	—	—	—	—
2913	200 mg TID	—	—	—	—	—
2914	—	—	—	200 mg TID	—	—
2915	—	—	—	—	—	—
2927	300 mg TID	—	—	—	—	—
C +						
2889	200 mg TID	—	200 mg TID	—	—	—
2893	200 mg QD	—	200 mg BID	—	—	—
2894	300 mg TID	—	—	—	2 mg TID	—
2896	400 mg TID	5 mg QD	—	—	—	—
2899	300 mg TID	—	—	—	—	—
2900	200 mg TID	—	—	—	—	—
2901	400 mg TID	—	100 mg TID	—	—	—
2905	—	—	—	400 mg QD	—	300 mg HS
2906	—	—	—	300 mg BID	—	—
2921	—	—	—	100 mg TID	—	100 mg TID
2923	—	—	—	—	—	—
2924	—	5 mg BID	—	—	—	200 mg BID
2928	—	10 mg QD	200 mg TID	—	2 mg BID	—
2930	—	—	—	—	—	300 mg BID
C —						
2920	—	—	—	—	—	250 mg TID
2922	—	—	—	—	—	—
2929	300 mg TID	—	—	—	2 mg QD	—
2933	400 mg TID	1	100 mg BID	—	2 mg TID	—

TABLE 4 (*continued*)

Phenobarbital	Dilantin	Other	Other
—	—	—	—
—	—	—	—
—	—	—	—
—	—	—	—
1 g BID	3 caps. BID	—	—
3.2 g HS	100 mg TID	Cogentin 2mg OD	—
—	100 mg TID	Surfak 240mg BID	—
1.5 g HS	—	INH-379 300mg TID	Mesatoin 200mg BID
—	—	—	—
—	—	Cogentin 1mg BID	Trifluoperazine 0.5g BID
100 mg TID	100 mg QD	Mysoline 250mg TID	Prolixin 2.5mg BID
—	—	Cogentin 2mg QD	Proketazine 50mg BID
—	—	Cogentin 2mg QD	Prolixin 2.5mg TID
—	100 mg BID	Doxinate 240mg QD	—
—	—	—	Prolixin 2.5mg TID
—	—	—	—
60 mg TID	100 mg TID	Mysoline 250mg QD	
—	—	Cogentin 12mg QD	—
1.5 g BID	100 mg TID	Reserpine 2mg BID	—
0.5 g BID	1.5 g BID	Cogentin 2mg QD	Probencid 0.5g BID
1.5 g BID	—	Doxinate 240mg QD	Mesantoin 300mg QD
—	—	Secanol 1.5g	—
30 mg BID	100 mg TID	Mysoline 250mg BID	—
—	—	—	—
—	—	Benedryl 100mg HS	Metrazol 100mg TID
—	—	Cogentin 2mg QD	Niamide 100mg QD
—	—	—	—
—	—	(Ritalin 20mg QD, Dexadrine 10mg, QD, Trilafon 4mg TID)	Prolixin 2.5mg BID
—	—	—	—
—	—	Surfak 240mg QD	
—	—	Surfak 240mg QD	—
—	—	—	—
—	—	Librium 125mg BID	Meprobamate 400mg TID
—	—	Surfak 1 cap. QD	—
—	—	Tofranil 50mg HS	—
—	—	Trifluoperazne 10mg BID	—
—	—	Cogentin 1mg QD	—
—	—	(Ritalin 20mg QD, Cogentin Trilafon 32mg TID 20mg QD)	
—	—	—	—
—	—	Doxinate 240mg QD	—

subjects, however, do significantly decrease in the number of different cues through which they search when a new cue is introduced. The variety of cues searched on new-cue programs is significantly less than on non-new-cue programs, and is significantly less than the variety of cues searched on new-cue programs by the L+ group.

It is difficult to analyze the results of those subjects who did not complete the task to the same extent as the above analyses of the L+ and C+

TABLE 5

PERFORMANCE OF LOBOTOMIZED AND CONTROL SUBJECTS WHO COMPLETED THE TASK

	L+	C+
Mean total responses	625.9	359.2
Mean average search responses per program on non-new-cue programs	8.8	5.9
Mean average search responses per program on new-cue programs	6.1	4.2
Mean average post-search responses per program on non-new-cue programs	24.7	12.9
Mean average post-search responses per program on new-cue programs	3.7	5.9

TABLE 6

MEAN NUMBER OF SEARCH AND POST SEARCH ERRORS PER PROGRAM

	L+	C+
Average search errors for non-new-cue programs	5.4	2.7
Average search errors for new-cue programs	3.0	2.1
Average post-search errors for non-new-cue programs	16.2	6.9
Average post-search errors for new-cue programs	0.8	1.3

TABLE 7

PERSEVERATIVE TYPES OF SEARCH ERRORS; MEAN AVERAGE PER PROGRAM

		L+	C+
Immediate perseverative errors	Non-new-cue programs	0.79	0.65
	New-cue programs	0.41	0.68
Return perseverative errors	Non-new-cue programs	1.66	0.79
	New-cue programs	0.95	0.29

TABLE 8
AVERAGE NUMBER OF DIFFERENT CUES SEARCHED PER PROGRAM

Non-new-cue programs	3.4	3.2
New-cue programs	3.0	2.0

groups because of the highly variable number of programs completed in the 2-hour testing session. Most subjects in the L— and C— groups failed to reach criterion on one or more programs. Four L— subjects failed to reach criterion on the first program presented; all C— subjects got at least that far. As mentioned previously, if a subject had not progressed through the first five programs in 1.5 hours, a new-cue program was introduced anyway. Four L— subjects and one C— subject failed to reach criterion on the new-cue program that was introduced 30 min before the end of the session. Four L— subjects progressed satisfactorily past six programs or more and then became "hung up" and were unable to reach criterion on a particular program; in such cases a second new-cue program was introduced and completed before the session was concluded. Two (an L— and a C—) had response rates so low that although they made criterion on every program that occurred, the 2-hour session terminated before they could complete the entire task. Table 9 presents some of the data for the "failure" groups.

TABLE 9
DESCRIPTIVE DATA ON THOSE SUBJECTS THAT FAILED TO COMPLETE THE TWENTY PROGRAMS IN 2 HOURS

	L—	C—
Mean non-new-cue programs completed	3.54	2.75
Range	0–11	1–6
Mean new-cue programs completed	1.0	0.75
Range	0–2	0–1
Mean total responses	539.0	459.5
N	11	4

Discussion

The aim of this experiment was to ascertain whether a frontal lesion in man produces the same sort of behavioral deficit that such procedures induce in nonhuman primates. The results in this group of patients, on this particular procedure, were for the most part affirmative. However, differences were also obtained.

Lobotomized patients, just as monkeys with frontal lesions, have greater difficulty in performing a multiple choice task than their matched controls. In this study, fewer lobotomized human subjects finished the task and those that did finish made more repetitive errors of all kinds except when novel cues were introduced.

Monkeys in this situation also show an especial difficulty in maintaining the strategy required to complete the task to criterion; they also show the exception to this effect when novel cues are introduced (5). However, in contrast to human beings, sampling and search strategies are only minimally affected (6). We cannot at this time account reasonably for this difference in the effects of frontal lesions on sampling and search in man and beast. Despite this difference, or perhaps even reassured by it, we feel encouraged. The statement has appeared so often in the literature that frontal lobotomy (or leukotomy) produces effects only on the psychiatric illness of the patient—that "intellectual" processes such as those involved in problem solving remain intact (2, 4). This statement is at such variance with the mass of data obtained on nonhuman primates that the suspicion has grown that either the animal studies are irrelevant to the human, or that the latter have been woefully inadequate due to the paucity of appropriate techniques. Already one study (6) has suggested that the existing data obtained in man are lacking; the results of this experiment support this view.

References

1. HARLOW, H. F., and P. H. SETTLAGE. 1948. Effect of extirpation of frontal areas upon learning performance of monkeys. *Res. Publ. Assoc. Res. Nervous Mental Disease* **27**: 446-459.
2. HEBB, D. O., and W. PENFIELD. 1940. Human behavior after extensive bilateral removal from the frontal lobes. *A.M.A. Arch. Neurol. Psychiat.* **44**: 421-438.
3. MC NEMAR, Q. 1962. "Psychological Statistics." Wiley, New York.
4. METTLER, F. A. [ed.]. 1949. "Selective Partial Ablation of the Frontal Cortex." Harper (Hoeber), New York.
5. PRIBRAM, K. H. 1960. The intrinsic systems of the forebrain: an alternative to the concept of cortical association areas, pp. 1323-1344. *In "Handbook of Physiology Sect. 1, Neuropsychology."* Vol. 2 J. Field, H. W. Magoun, and V. E. Hall, [eds.]. Am. Physiol. Soc. Washington, D.C.
6. PRIBRAM, K. H., A. AHUMADA, J. HARTOG, and L. ROOS. 1964. A progress report on the neurological processes disturbed by frontal lesions in primates, pp. 28-55. *In "The Frontal Granular Cortex and Behavior."* J. M. Warren, and K. Akert, [eds.]. McGraw Hill, New York.

7. PRIBRAM, K. H., K. W. GARDNER, G. L. PRESSMAN, and M. BAGSHAW. 1962. An automated discrimination apparatus for discrete trial analysis (DADTA). *Psychol. Rept.* **11**: 247-250.
8. WARREN, J. M., and K. AKERT [eds.]. 1964. "*The Frontal Granular Cortex and Behavior*." McGraw Hill, New York.
9. WILLET, R. 1961. Psychosurgical procedures, pp. —. *In* "*Handbook of Abnormal Psychology: An Experimental Approach*," H. J. Eysenck [ed.]. Basic Books, New York.