

VISUALLY-GUIDED MAZE LEARNING IN MAN: EFFECTS OF BILATERAL HIPPOCAMPAL, BILATERAL FRONTAL, AND UNILATERAL CEREBRAL LESIONS

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Abstract—Seventy-nine patients with different cerebral lesions were trained on a visually-guided stylus maze. The main findings were: (1) bilateral hippocampal lesions produced the most severe impairment, with one patient showing no progress in 215 trials; (2) right temporal lobectomy produced a significant deficit, particularly when the underlying hippocampus was radically excised, whereas patients with left temporal-lobe lesions of equal extent, or with small parietal-lobe lesions of either hemisphere, obtained normal scores; (3) larger lesions of frontal or right posterior cortex severely impaired maze learning, suggesting that size as well as locus of cortical lesion may be a factor in maze-performance; (4) only frontal-lobe lesions affected the ability to follow test instructions.

1. INTRODUCTION

THIS study arose from the need to investigate more systematically the learning ability of patients with bilateral hippocampal lesions, preferably on a task which was not primarily verbal and which permitted the use of massed trials. On clinical examination, patients with these lesions show a severe and generalized memory disorder, those with the most extensive lesions being unable to recall or recognise test material after a lapse of five minutes or less, if their attention has been diverted elsewhere in the meantime, and showing a continuous anterograde amnesia for the events of daily life (SCOVILLE and MILNER [1]; PENFIELD and MILNER [2]; MILNER [3]). On formal testing with verbal material, they fail to progress over many trials. Maze-learning seemed a convenient and objective method of study, the results of which would complement our other findings.

The maze-learning performance of the patients with hippocampal lesions was compared, not only with that of normal subjects, but also with that of a long series of patients who had undergone cortical excisions of varying locus and extent, for the relief of focal seizures. The excisions sampled all parts of the right cerebral cortex and the left frontal and anterior temporal and parietal regions of the dominant hemisphere, but spared Broca's area and the posterior temporal and parietal speech zones. This restriction on elective surgery means that we do not have, and cannot expect to have, any lesions comparable to those of the left posterior-parietal and parieto-temporal gunshot-wound cases in Prof. Teuber's population. This study does, however, include extensive parietal-lobe lesions in the left hemisphere, when that hemisphere is not dominant for speech.

The task chosen was a stylus-maze problem of the stepping-stone kind (BARKER, [4]), the subjects being trained over many trials until they could traverse the maze without error. The resulting data confirmed the profound learning deficit of the hippocampal patients but

also brought to light important differences in maze-learning proficiency among the different cortical-lesion groups, depending upon the locus, laterality and possibly the size of the lesion. These findings form the substance of the present paper.

Route-finding difficulties have traditionally been associated with parietal-lobe lesions and SEMMES, WEINSTEIN, GHENT and TEUBER [5] have demonstrated residual impairment on spatial orientation tasks in men who had sustained penetrating missile wounds of the parietal lobes many years before, men with wounds sparing this region being unimpaired. The tasks required the subject to walk along specific routes on the basis of a series of maps, which could be either visually or tactually presented. Left and right parietal-lobe wounds were equally damaging to performance on these locomotor tasks. However, on a pencil-and-paper lattice-maze task, ELITHORN [6, 7] and BENTON, ELITHORN, FOGEL and KERR [8] found that patients with right-hemisphere lesions were more impaired than patients with left, a finding which is consistent with many clinical observations concerning topographical orientation in acute cerebral disease (e.g. PATERSON and ZANGWILL [9]; MCFIE, PIERCY and ZANGWILL [10]; HÉCAEN, PENFIELD, BERTRAND and MALMO [11]; ETTLINGER, WARRINGTON and ZANGWILL [12]; HÉCAEN [13]; WHITTY and NEWCOMBE [14]).

HÉCAEN [13] discusses post-Rolandic lesions only, and SEMMES *et al.* [5] find no evidence of anterior brain wounds impairing orientation in extrapersonal space, although orientation with respect to the subject's own body may be disturbed (SEMMES, WEINSTEIN, GHENT and TEUBER [15]). ELITHORN [7], however, reports equal impairment with frontal and posterior cerebral lesions, but finds some maze items differentially sensitive to frontal, others to posterior lesions, suggesting a different source of difficulty for the two groups. The Porteus mazes resemble ELITHORN's [7] perceptual mazes in requiring implicit trial-and-error for their solution; it is therefore of interest that a transient defect in Porteus-maze performance follows frontal lobotomy (LANDIS and ERLICK [16]; PORTEUS [17] pp. 52-82). There may, however, be many factors other than spatial ones which could account for this deficit.

The maze task in the present study poses a learning problem primarily, since it requires the repeated tracing of a constant path until the most direct route from starting-point to goal has been mastered. In this it resembles the maze-learning problems used in animal work rather than the more perceptual tasks devised for the study of human patients with cerebral lesions. For this reason, performance may be less affected by minor deficits of spatial orientation than by difficulty in remembering the correct sequence of turns from one trial to the next, although these two facets of maze performance cannot be isolated too strictly from one another, and patients with marked spatial disorientation would be expected to find any spatial maze difficult to learn. These issues will be further discussed in the context of the data to be presented here.

2. SUBJECTS

The main group consisted of 74 patients with unilateral cortical excisions carried out for the relief of focal epilepsy due to static, atrophic lesions. Cases of brain tumour were excluded. A further five patients, two with bilateral frontal and three with bilateral hippocampal lesions, complete the patient population. Table 1 gives the sex, age and Wechsler intelligence ratings for the 79 patients, subdivided according to locus of lesion.

The 11 normal control subjects (3 male, 8 female) had had a high school education and were probably a little above average in intelligence; they ranged in age from 18 to 45 years, with a mean of 22.2 years.

Table 1. Sex, age, and intelligence data for patients grouped according to locus of cerebral lesion

Group	No. of cases	Sex		Age		Wechsler I.Q.	
		M	F	Mean	Range	Mean	Range
<i>Unilateral</i>							
Left temporal	26	20	6	26.2	13-54	102.2	79-128
Right temporal	15	8	7	25.0	13-51	107.9	94-124
Parietal	12	9	3	22.2	16-31	98.4	71-114
Right parieto-temporo-occipital	6	4	2	27.2	19-38	102.8	96-118
Frontal	15	11	4	22.3	13-33	94.3	74-124
<i>Bilateral</i>							
Frontal	2	2	0	47.0	42, 50	111.2	126, 97
Hippocampal	3	3	0	43.0	34-55	117.7	109-123

2.1 Cases of Unilateral Lesion

Table 2 indicates the probable etiology of the original lesions in patients classified on the basis of subsequent cerebral excision as right temporal, left temporal, parietal, right parieto-temporo-occipital, or frontal-lobe cases. These epileptogenic lesions typically date from early life, with onset of habitual seizures in late childhood or early adolescence, and

Table 2. Probable etiology of epileptogenic lesions in unilateral groups

Group	Brain injury				Febrile illness	Brain abscess	A-V malfn	Pial angiomatosis
	Birth or 1st yr	1-7 yr	8-15 yr	21 yr				
					0-9 yr			
Right temporal	11	1	-	-	2	-	1	-
Left temporal	14	3	1	-	4	-	1	3
Parietal	8	-	1	-	2	-	1	-
Right parieto-temporo-occipital	2	1	-	1	-	1	-	1
Frontal	8	1	4	-	-	1	1	-
Total	43	6	6	1	8	2	4	4

the distribution of lesions is similar in the various lesion groups, except for a rather high incidence of late-childhood trauma in the frontal-lobe group. Table 3 shows the mean number of years of habitual preoperative seizures for patients classified in the same way. There are no salient group differences, the left and right temporal-lobe groups being particularly well-matched.

2.1.1. Cortical excisions

2.1.1.1. *Temporal-lobe groups.* The 41 temporal lobectomies were relatively uniform, usually involving the anterior 5 to 6 cm of the temporal lobe and including at least the uncus and amygdala on the mesial surface. In 10 left- and 7 right-sided cases, a radical excision of the hippocampus was carried out. In the left temporal group, all 26 removals were in the dominant hemisphere for speech and all 15 right temporal lobectomies were in the minor hemisphere, five additional temporal-lobe patients having been omitted because they were found to have bilateral speech representation. Only patients with well-lateralized epileptogenic foci were included.

Table 3. Mean duration of preoperative seizures (yr) for different unilateral lesion groups

Group	No. of cases	Preoperative seizures (yr)	
		Mean	S.D.
Right temporal	15	11.5	8.68
Left temporal	26	11.2	8.61
Parietal	12	9.4	6.73
Right parieto-temporo-occipital	6	11.3	4.54
Frontal	15	9.5	6.76

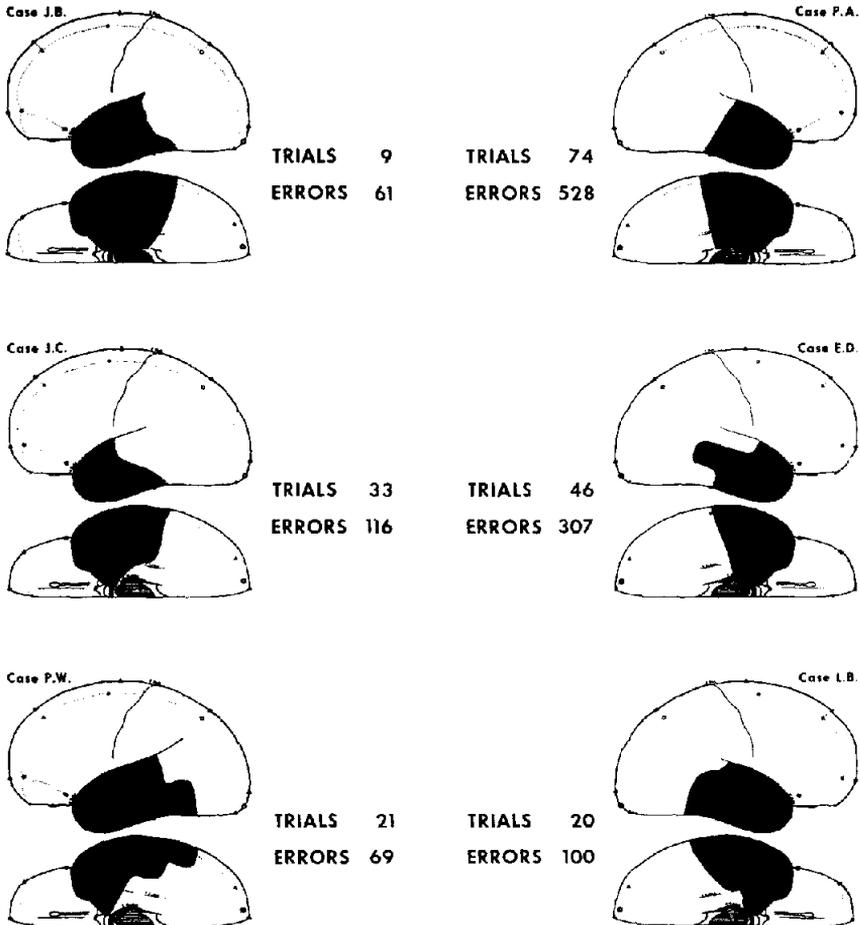


FIG. 1. Diagrams based on the surgeon's drawings at the time of operation, showing the estimated extent of temporal-lobe ablation (lateral and inferior views) in 6 representative cases. Case J. B., left temporal lobectomy, hippocampus excised; Case J. C., small left temporal lobectomy, sparing hippocampus; Case P. W., large left temporal lobectomy, sparing hippocampus; Case P. A., right temporal lobectomy, hippocampus excised; Case E. D., right temporal lobectomy, invading anterior hippocampus only; Case L. B., large right temporal lobectomy, sparing hippocampus. In this figure (and in Figs. 2-4), the maze scores for each patient are indicated beside the appropriate brain map.

Figure 1 shows some representative temporal lobectomies. The removals on the left ranged from 4 to 9 cm along the Sylvian fissure, with a mean of 5.2 cm, and from 4–10.5 cm along the base of the brain, with a mean of 6.1 cm. The corresponding figures for the right temporal lobe are 4–7 cm along the Sylvian fissure, with a mean of 5.7 cm, and 5–7.5 cm along the base, with a mean of 6.2 cm. Thus, some lesions on the left were actually larger than any lesion on the right and there are no significant differences between the two temporal-lobe groups with respect to lesion size.

Seven left temporal-lobe patients were tested in follow-up study, from one to five years postoperatively, at which time only one was still having seizures; the other 34 patients were tested from two to three weeks after operation.

2.1.1.2. *Parietal-lobe group.* The parietal-lobe removals were quite variable in locus and extent. The group comprised 12 patients, 9 with left-sided lesions and 3 with right, 3 of the left parietal excisions being in the non-dominant hemisphere for speech.

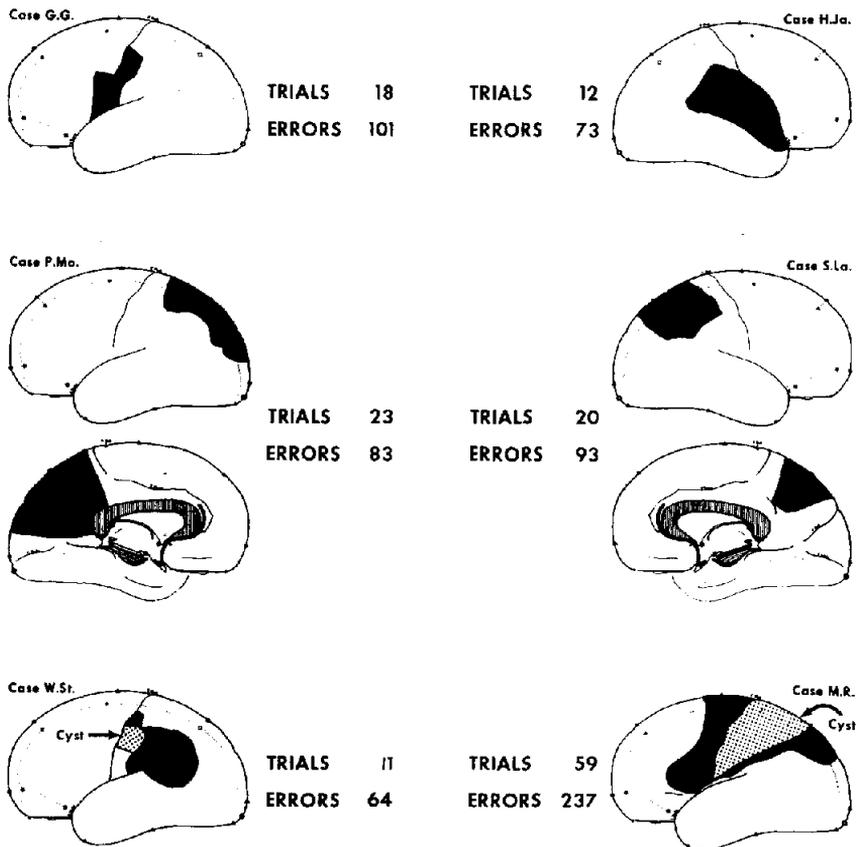


FIG. 2. Diagrams showing estimated extent of cortical excision in 6 of the 12 parietal-lobe cases. Case G. G., left central; Case H. Ja., right Sylvian; Cases P. Mo., S. La., left and right parasagittal, respectively (lateral and mesial views); Cases W. St., M. R., left, non-dominant, parietal lobectomies.

Figure 2 illustrates the range of lesions sampled. In all instances the parietal lobe was primarily involved, although occasionally, as in Cases H. Ja. and M. R., the lesion encroached upon the neighbouring superior temporal or inferior frontal cortex. In the dominant left parietal lobe there were three lower central excisions (cf. Case G. G.) and three parasagittal ones (cf. Case P. Mo.). In the right parietal lobe there were two parasagittal excisions (cf. Case S. La.) and one, Case H. Ja., in the posterior Sylvian region. The three non-dominant left parietal lesions were more extensive (cf. Cases W. St. and M. R.).

Nine patients (including the six whose removals are shown in Fig. 2) were tested from one to seven years after operation, at which time they were seizure-free; the other three patients were tested from two to three weeks post-operatively.

2.1.1.3. *Right parieto-temporo-occipital group.* The removals in these six patients are shown in Fig. 3. All were large lesions, involving parts of the parietal, temporal and occipital cortex and, in Case D. L., invading also the orbito-frontal region. Case J. St. M. is the one instance of adult brain injury in the unilateral lesion groups. This 38-year old man had developed seizures as a sequel to a penetrating missile wound sustained in World War II, at the age of 21.

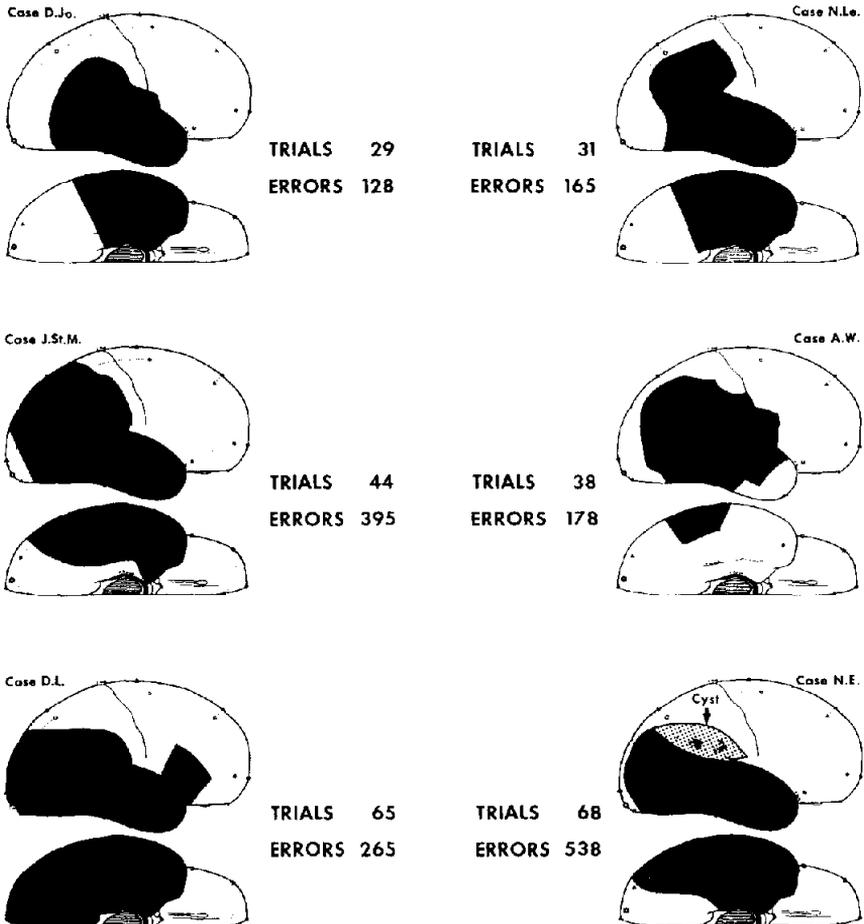


FIG. 3. Diagrams showing estimated extent of ablation (lateral and inferior) in the 6 cases of right parieto-temporo-occipital excision.

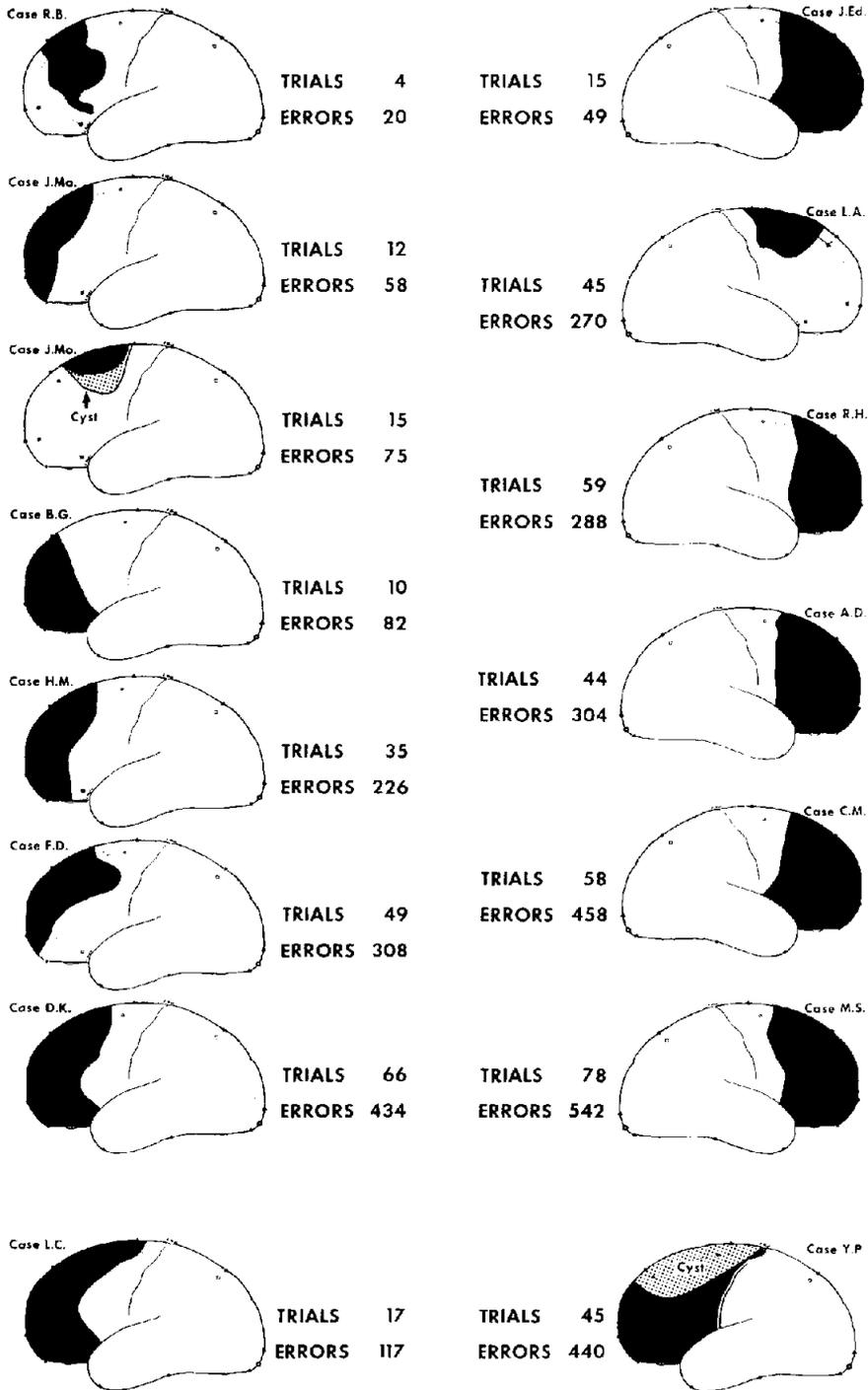


FIG. 4. Diagrams showing lateral extent of excision in the 15 cases of unilateral frontal lobectomy. Cases R. B. to D. K., dominant left frontal; Cases J. Ed. to M. S., right frontal; Case L. C., left frontal, possibly non-dominant; Case Y. P., left frontal, non-dominant.

Cases N. Lc., J. St. M. and N. E. were tested in the early post-operative period, the other three patients in follow-up study from 4 to 13 years later, at which time Cases D. L. and D. Jo. were seizure-free and Case A. W. was having only occasional minor attacks.

2.1.1.4. *Frontal-lobe group.* The lateral extent of removal in each of the 15 cases is shown in Fig. 4. Seven left frontal lobectomies were in the dominant hemisphere for speech, two in the non-dominant; all six right frontal lobectomies were in the minor hemisphere.

Except for Case L. A., the right frontal removals were large, typically extending back to within 1 cm of the precentral gyrus on the lateral surface and including parts of the anterior cingulate and subcallosal gyri on the mesial aspect of the hemisphere. The dominant left frontal lobectomies spared Broca's area (as mapped out by speech testing at operation), but, except for Cases R. B. and J. Mo. with small lesions, the mesial extent of removal was the same as in the right frontal group. All lesions involved at least the dorsolateral aspect of the frontal lobe.

Seven patients (Cases R. B., D. K., J. Mo., M. S., L. C. and Y. P.) were tested from 1 to 14 years after operation, the remaining 8 patients in the early postoperative period. Case D. K. was still having some seizures, but the other follow-up patients were essentially seizure-free.

2.2. *Cases of Bilateral Lesion*

2.2.1. *Bilateral frontal-lobe lesions.* Two patients were tested. The first, Case K. M., had developed seizures after a severe brain injury at the age of 16. Ten years later, in 1938, a bilateral excision of the anterior one-third of both frontal lobes was carried out (HEBB and PENFIELD [18]). Since then he has been seizure-free, except for one attack when he was in the Canadian army and all anti-convulsant medication had been withdrawn. The second patient, Case A. N., sustained a penetrating shell wound of both frontal lobes in 1945, at the age of 22, and necrotic tissue amounting to roughly one-third of the right and one-fifth of the left frontal lobe was excised. This patient belongs to the brain-injured group studied so extensively by Prof. Teuber and his associates. He now has occasional seizures.

2.2.2. *Bilateral hippocampal lesions.* The three patients in this group all had generalized postoperative memory impairment, which was most marked in Case H. M., who in 1955, at the age of 27, had undergone a bilateral medial temporal-lobe resection (SCOVILLE and MILNER [1]). The removal was said to extend back 8 cm along the mesial surface of both temporal lobes, destroying the uncus, amygdala and anterior two-thirds of the hippocampus and hippocampal gyrus bilaterally, but sparing the temporal neocortex. This radical operation was carried out by Dr. William Scoville in an attempt to relieve intractable seizures, and these have in fact been considerably reduced.

Cases F. C. and P. B. (PENFIELD and MILNER [2]) had undergone unilateral (left) temporal lobectomy for the relief of long-standing seizures, but they differed from our regular series of temporal-lobe cases in having active epileptogenic foci in the opposite, unoperated temporal lobe. PENFIELD and MILNER [2] attributed the postoperative memory disorder to a pre-existing lesion in the right hippocampal region, so that the left hippocampal excision effectively produced a bilateral lesion. Support for this view comes from the preliminary pathological findings on Case P. B. who died on April 24, 1965, of a massive pulmonary

4. RESULTS

4.1. *Trials to criterion and error-scores: unilateral lesion groups*

No relationship was found between maze performance and either etiology of lesion, duration of habitual seizures, or time since operation. For 49 patients and 11 normal control subjects who were tested both on this visual maze and, later, on a tactual maze (CORKIN [19]), the Pearson product-moment correlation between age and trials to criterion on the visual maze was -0.07 and between age and errors it was $+0.02$. For the same 49 patients, the correlation between both trials and errors on the visual maze and I.Q. was -0.20 .

In contrast to these negative findings, locus of lesion proved to be a highly significant factor in maze performance. Table 4 shows the mean trials and errors to criterion for the various unilateral lesion groups. The scores for the parietal and left temporal-lobe groups approximate those of the normal control group, whereas the performance of the right temporal, right parieto-temporo-occipital, and frontal-lobe groups appears to be markedly impaired.

Table 4. Maze learning after different unilateral cortical excisions

Group	No. of cases	Trials		Errors	
		Mean	Range	Mean	Range
Left temporal	26	22.4	7-57	103.0	48-248
Right temporal	15	33.8	5-89	224.7	23-605
Parietal (6L, 3R, 3LND)	12	22.0	11-59	97.3	64-237
Right parieto-temporo-occipital	6	45.8	29-68	278.2	128-538
Frontal (7L, 6R, 2LND)	15	36.8	4-78	244.7	20-542
Normal control	11	17.0	6-27	91.8	21-175

Simple analysis of variance confirmed that there were significant group differences in trials to criterion ($F=4.46$, $P<0.01$). Analysis of variance was also carried out on the error scores after these had been subjected to the square-root transformation, $y=\sqrt{x}$, where x is the original score and y the score analysed, thus reducing the skewness of the distributions (BARTLETT [20]). The resulting F-score of 6.43 is significant beyond the 0.001 level. Subsequent t -tests showed that the parietal and left temporal-lobe groups did not differ from the normal control group with respect to either trials or errors. The other three lesion groups were however significantly impaired relative to the normal subjects on both these measures (Right temporal group: Trials, $t=2.55$, $P<0.02$; errors, $t=2.71$, $P<0.02$. Right parieto-temporo-occipital group: Trials, $t=3.42$, $P<0.01$; errors, $t=3.39$, $P<0.01$. Frontal group; Trials, $t=3.02$, $P<0.01$; errors, $t=2.95$, $P<0.01$). Although from inspection of the mean scores in Table 4 the right parieto-temporo-occipital group appears to be more impaired than either the right temporal or frontal-lobe groups, there are in fact no significant differences in score between these three groups, presumably because of the small number of subjects with right parieto-temporo-occipital lesions.

4.1.1. *Comparison of left and right temporal-lobe groups.* Since the right and left temporal lobe groups were so well-matched with respect to lesion size and clinical history, any consistent differences in task performance between these groups are of particular interest. On this maze-learning test, the right temporal group required significantly more trials ($t=2.09$, $P<0.05$) and made significantly more errors ($t=3.19$, $P<0.01$) than the left temporal-lobe group; nevertheless, there was considerable overlap in the distribution of scores for the two groups, with five right temporal-lobe patients obtaining scores near to the mean of the normal control group. The individual differences in maze performance in the right temporal group were unrelated to extent of removal of lateral temporal cortex but were related to how much of the underlying hippocampus had been excised. When the right temporal group was subdivided into those patients with radical excision of the hippocampus and those in whom the hippocampus had been spared or minimally destroyed, the patients with radical excision were found to take significantly more trials to learn the maze (Mann-Whitney $U=13$, $P<0.05$ for a two-tailed test) than did those with the hippocampus essentially spared. For the error scores, the difference between the right hippocampus-spared and right hippocampus-removed groups just failed to reach significance ($U=14$, $P=0.064$, for a two-tailed test). There was no significant difference in score between the left temporal-lobe patients with the hippocampus spared and those with hippocampus radically excised. For example, in Fig. 1, both Case J. B. with radical excision of the left hippocampus and Case P. W. with hippocampus spared but with an extensive removal of the left temporal neocortex had scores better than the average of the normal control subjects. Case P. A., on the other hand, with a radical excision of the right hippocampus, made 528 errors and required 78 trials to learn the maze, whereas Case L. B., with a slightly larger removal on the lateral surface but with the right hippocampus spared, obtained a normal score.

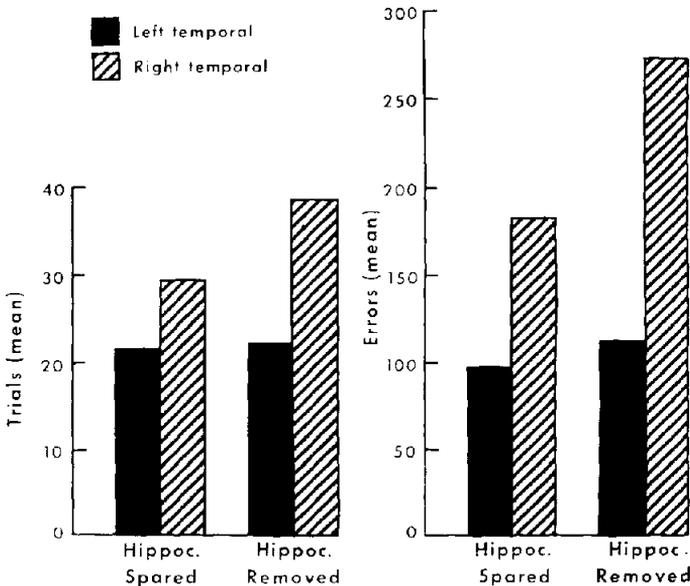


FIG. 6. Maze learning after temporal lobectomy: detrimental effects of hippocampal excision in the right temporal group. Left temporal: hippocampus spared, $N=16$; removed, $N=10$. Right temporal: hippocampus spared, $N=8$, removed, $N=7$.

These findings are summarized in Fig. 6, which shows the detrimental effect of right hippocampectomy on maze performance. The scores for the right temporal group with hippocampus excised are significantly worse than those of the corresponding left temporal group (trials: $U=5$, $P<0.002$; errors: $U=8$, $P<0.02$, for two-tailed tests), whereas there is no significant difference between the right and left temporal groups with hippocampus essentially spared. Thus, whether or not a major portion of the underlying hippocampus is included in the removal is a critical factor in maze learning after right temporal lobectomy.

4.2. *Trials to criterion and error scores: bilateral lesion groups*

Table 5 lists the individual learning scores of the five patients with bilateral lesions. Of the two frontal-lobe patients, Case K. M. is clearly impaired, with scores outside the normal range; his performance is, however, well within the range of the patients with radical unilateral frontal lobectomies. Case A. N. has normal scores, although, as will be seen below, other aspects of his maze performance were impaired. The three patients with bilateral hippocampal lesions show a profound learning disability, which correlates with the relative severity of their memory disorder to clinical examination. Case H. M. failed to learn the correct path through the maze within the limits of testing; Cases F. C. and P. B. did eventually reach criterion, but the number of trials required falls outside the range for the other subjects tested.

Table 5. Maze-learning scores for 5 subjects with bilateral lesions

Group	No. of cases	Trials	Errors
Bilateral frontal	2		
Case K. M.		73	381
Case A. N.		18	91
Bilateral hippocampal	3		
Case H. M.		215+	2,877+
Case F. C.		183	828
Case P. B.		102	377

Case H. M. not only failed to learn the maze; he failed to show any improvement within each testing session of 25 massed trials, so that he was making as many errors per trial at the end of three days of testing as he had done at the outset.

These findings are illustrated in Fig. 7 which shows the error curve for Case H. M. plotted over 215 trials.

4.2.1. *Time scores: unilateral lesion groups.* For most patients, the time scores added little new information and they were therefore not subjected to any detailed statistical treatment. All subjects reduced their time per trial considerably with repeated practice on the maze, but there was a high correlation between initial and final scores, with some subjects consistently preferring to work slowly and others to work fast. Table 6 shows the mean time scores for the first and last five trials for the different unilateral lesion groups.

It should be pointed out that the high initial time-scores of the frontal-lobe reflects the inability of these patients to obey the rules in the early stages of training, a point which will be discussed more fully below.

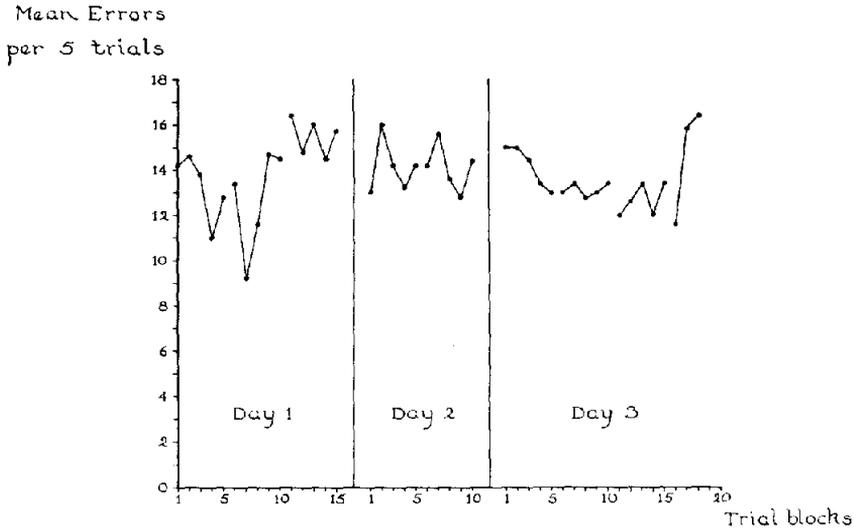


FIG. 7. Learning curve for Case H. M. (bilateral hippocampal excision), showing no decrease in errors over a 3-day period. Each point on the curve represents 5 successive trials.

Table 6. Mean time scores (sec) for different unilateral lesion groups

Group	First 5 trials		Last 5 trials	
	Mean	Range	Mean	Range
Left temporal	70	36-154	25	13-70
Right temporal	88	52-148	31	14-70
Parietal	74	42-131	27	15-56
Right parieto-temporo-occipital	88	51-138	25	17-31
Frontal	108	54-187	25	15-72
Normal control	66	35-170	20	15-56

4.3. Time scores: bilateral lesion group

The time scores at the beginning and end of training for the five patients with bilateral lesions are shown individually in Table 7. The scores for Case K. M., with a bilateral-frontal-lobe lesion, are unremarkable, comparing favourably with the average performance

Table 7. Mean time scores (sec) for first 5 and last 5 trials, for patients with bilateral lesions

Group	First 5 trials	Last 5 trials
Bilateral frontal		
Case K. M.	87	13
Case A. N.	226	67
Bilateral hippocampal		
Case H. M.	70	58
Case F. C.	88	19
Case P. B.	144	46

of the unilateral frontal-lobe group. Case A. N., however, has a higher initial time-score than any other subject tested. This patient had a strong tendency to back-track all the way to the starting-point during the first few trials, in order, as he explained, to rehearse the correct moves before proceeding further. When he was prevented from doing this, he remained "frozen" in the middle of the maze, reluctant to move farther away from the starting-point. This is a striking instance of the difficulty in adapting themselves to test instructions shown by many patients with frontal-lobe lesions.

In the bilateral hippocampal group, Cases F. C. and P. B. showed an appreciable reduction in time score by the time they had completed their lengthy training, although P. B. characteristically worked slowly on this as on many other tasks. Case H. M., on the other hand, showed almost as little progress with respect to time as he did with respect to errors, as can be seen from Fig. 8, in which the mean time for successive blocks of five trials is plotted for the 3-day period.

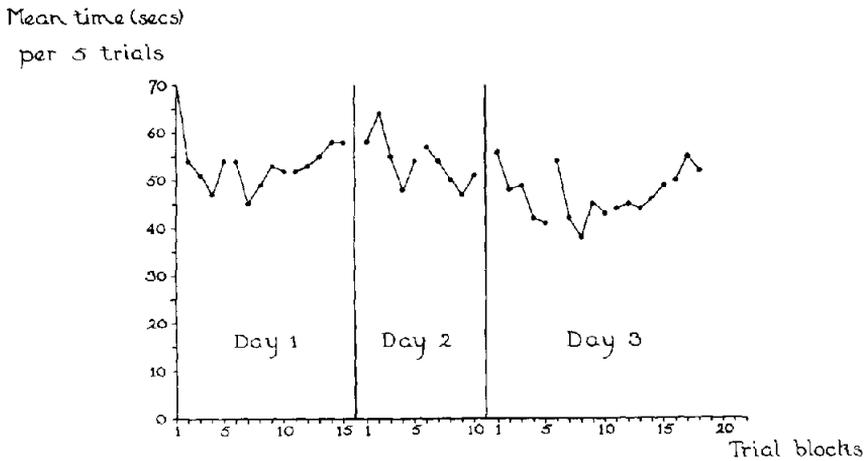


FIG. 8. Learning curve for Case H. M., showing no reduction in time score after the first block of trials, for a 3-day period.

There was some reduction in time from the first trial to the third, which reflected increasing dexterity in the use of the stylus, but from then on there was no consistent change.

4.4. Broken rules and repetitive errors

We turn now to a consideration of certain aspects of test behaviour which were specific to the frontal-lobe group. These concern compliance with test instructions. The instructions for the maze task seemed simple enough and, until the first patient with a frontal lobectomy was tested, there was no reason to believe that they might prove a stumbling-block. This patient, however, repeatedly failed to go back to the preceding bolthead when the error counter clicked, although he knew that he was supposed to do so. Thenceforth all such instances of "rule-breaking" were systematically recorded. Some patients with frontal-lobe lesions persisted in back-tracking towards the starting-point (cf. Case A. N.); others omitted some of the steps on the route, or made diagonal moves in an attempt to approach the

goal more directly. Many disregarded the clicking of the counter and the subsequent warning cries of the experimenter. These findings are illustrated in Fig. 9, which depicts the mean number of broken rules for the different lesion groups. It can be seen that subjects with intact frontal lobes rarely, if ever, failed to carry out the test instructions, and the ability of the patients with bilateral hippocampal lesions to follow instruction is particularly noteworthy, in view of their difficulty in learning the correct path. Simple analysis of variance on these scores yielded an F -ratio of 17.6 ($P < 0.001$) and subsequent t -tests showed the frontal-lobe group's mean score to be significantly higher than that of the other subjects tested. (Frontal group vs Normal control group: $t = 5.39$, $P < 0.001$).

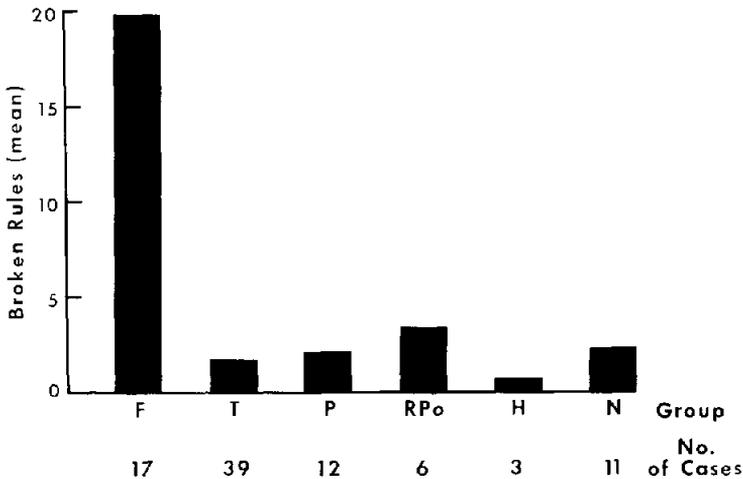


FIG. 9. Incidence of "broken rules", as related to locus of lesion. F, frontal; T, temporal; P, parietal; RPo, right parieto-temporo-occipital; H, bilateral hippocampal; N, normal control.

One of the consequences of the rule-breaking was an increase in repetitive errors within a single trial. Thus, if a patient retraced a portion of the correct path and then approached the same choice-point for the second time, he was liable to repeat his previous error. Not all instances of intratrial repetitive errors were of this type, however. Some frontal-lobe patients would go back only one step after making an error (thus complying with the rules), but then, after a brief pause, would repeat their previous incorrect response. This kind of behaviour was rarely exhibited by the other subjects, although occasionally a patient with a large right-posterior lesion might appear to lose his bearings in the maze and either back-track or make the same error twice, after trying another incorrect bolthead first, and being seemingly quite unaware that he was repeating a response that had already proved unsuccessful.

Figure 10 shows the mean number of intratrial repetitive errors for the various groups of subjects. Apart from the right posterior group, only the frontal-lobe patients show any tendency to make repetitive responses and, as described above, the behaviour appears to have a different basis in the two groups. Analysis of variance showed the group differences to be significant beyond the 0.001 level ($F = 16.2$). The right posterior group's mean score was not significantly higher than that of the temporal, parietal, or normal control groups and was significantly lower than that of the frontal group ($t = 2.81$, $P < 0.02$). The frontal-lobe mean differed from that of the temporal, parietal and normal groups at well beyond the 0.001 level of probability.

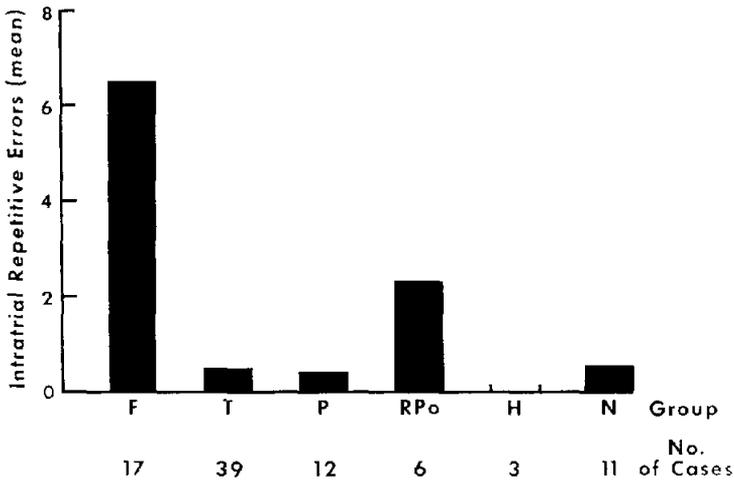


FIG. 10. Incidence of intratrial repetitive errors, as related to locus of lesion. F, frontal; T, temporal; P, parietal; RPo, right parieto-temporo-occipital; H, bilateral hippocampal; N, normal control.

5. DISCUSSION

The findings reported here attest to the severity of the learning defect in patients with bilateral hippocampal lesions. Case H. M., with a bilateral medial temporal lobectomy, not only failed to progress from one training session to another, but also showed no improvement within each set of 25 massed trials, although each trial lasted only about 60 sec. At the end of eight training sessions, he was still "having a little argument with himself" about which direction to take at the first choice-point. This lack of progress is presumably related to the complexity of the maze, in which there are 28 choice-points. Although it is possible by various mnemonics to reduce considerably the number of turns which have to be remembered, the whole route can still not readily be brought within the normal attention span. This means that experience in the latter part of the maze interferes with the effective rehearsal of the first part of the path, so that a patient such as H. M., who seems to rely entirely upon verbal rehearsal to bridge a temporal gap, must start each new trial as if it were a fresh problem.

All subjects but H. M. reduced their time scores in the course of training, but the reduction was due essentially to a decrease in decision time rather than to a gain in motor skill. It is therefore understandable that, in the case of H. M., not only the error scores, but also the time scores failed to improve after the slight degree of additional dexterity needed to manipulate the stylus accurately has been acquired. In contrast to these maze-learning data, the results for the same patient on a mirror-drawing task showed a normal reduction in time and errors with repeated practice, and this reduction carried over from one day to the next, although the patient himself did not remember ever having done the task before (MILNER [21]).

There have been numerous attempts to replicate the human memory loss in experimental animals with hippocampal lesions, the results of which have been largely negative. It is therefore of interest that KAADA, RASMUSSEN and KVEIM [22] have demonstrated a marked impairment of multiple-choice maze-learning in rats with hippocampal lesions, a defect

which seems not to be accountable for in terms of emotional or motivational change (KVEIM, SETEKLEIV and KAADA [23]). These maze-learning tests are of course all sequential tasks, and KIMBLE and PRIBRAM [24] have data consistent with the notion that, in the monkey hippocampal lesions interfere with the acquisition of behaviour sequences, whether internally or externally regulated, whereas on a non-sequential task, discrimination learning, animals with these lesions are unimpaired. However, although the maze-learning difficulty of patients with bilateral hippocampal lesions, considered in isolation, could be described as a disturbance of sequential behaviour, so restrictive a concept can hardly do justice to the wide diversity of situations in which these patients are abnormally forgetful.

The severe impairment of learning exhibited by the bilateral hippocampal patients answered the question which initially motivated this study, but some equally interesting findings emerged from consideration of the scores of the different cortical-lesion groups which had been intended as patient controls.

The impairment seen on this spatial learning task after right-temporal lobectomy, but not after left, is consistent with earlier findings of visual, nonverbal learning deficits in patients with right temporal-lobe lesions (KIMURA [25]) and it contrasts with the verbal learning deficits seen after left temporal lobectomy, but not after right (MEYER and YATES [26]; MILNER [27]; MILNER and KIMURA [28]). In the context it should be noted that many of the patients in the left temporal-lobe group (and two in the left parietal group) were still markedly dysphasic at the time they were learning the maze, and even those who were not dysphasic had sufficient verbal memory impairment to prevent them from learning the maze by the use of verbal mediating cues. Despite these verbal limitations, the maze learning scores of the left-temporal group did not differ from those of normal control subjects. The right temporal patients, on the other hand, repeatedly resorted to overt counting and other verbal devices to learn the correct path, and yet proved to be inefficient learners.

The further discovery in the present study, that the occurrence of an appreciable maze-learning impairment after right temporal lobectomy is contingent upon the inclusion of a large part of the underlying hippocampus in the removal, emphasizes afresh the importance of this structure for human learning processes. With unilateral excisions, however, the learning deficit is specific rather than general, suggesting that each hippocampus is concerned in the major functions of its own hemisphere.

The frontal-lobe group, which was not originally subdivided into left- and right-sided cases, was also found to be significantly impaired. There were, however, marked individual differences in maze-learning scores within the group, which may be related to side of lesion, size of lesion, or both. Figure 4 shows the extent of removal for each patient, together with the corresponding maze scores, the drawings being arranged in order of decreasing proficiency of maze performance within the left and right groups, respectively. The right frontal-lobe group tends to be the more impaired, with all scores but one outside the normal range, but there is much overlap in the scores of the two groups, and no significant difference in mean score was found. It is interesting, however, that the right-left difference was more clear-cut in the same patients on a tactual maze learning task (CORKIN [19]).*

* There were two additional cases, each representing a combination of lesions in frontal and temporal areas, one on the left, Case J. Eu., and the other on the right, Case L. P. Their scores were not included in the statistical analyses, since the lesions were unique. However, their scores on the visual maze were instructive: for the left fronto-temporal case, J. Eu., there were 11 trials and 61 errors; for the right fronto-temporal case, L. P., 29 trials, 202 errors. The brain diagrams for these cases can be found in the paper by CORKIN [19], Fig. 1, this issue, p. 341.

The interpretation of any differences between the right and left frontal groups is rendered more difficult by the fact that, with the exception of Case L. A., all the removals on the right are large, whereas some of those on the left (and notably those in patients with normal maze-learning scores) are small. Thus, it could be argued that lesion size, rather than laterality, is the important factor in lowering maze performance after frontal lobectomy. The fact that the two patients with bilateral injury to the frontal lobes, Cases K. M. and A. N., were less impaired than some cases of right frontal lobectomy, might suggest that side and not size is the important variable; however, this argument is not conclusive, since it is not certain that more tissue was destroyed in these bilateral lesions than in a radical unilateral lobectomy.

What relationship the high error scores of the frontal-lobe patients bear to their inability to follow rules is unclear. Breaking rules does not directly increase the error score to any appreciable extent. However, this tendency may reflect an underlying dysfunction which is responsible also for the slow learning, but which is different in kind from that produced by other lesions. It may be, for example, that the frontal-lobe patients are initially less interested than others in avoiding errors (MILNER [29]).

It should be noted that this behaviour on the maze task is dissociable, in individual cases, from the perseverative behaviour shown by frontal-lobe patients on the Wisconsin Card Sorting Test (MILNER [30]). Thus, Case M. S., with a radical right frontal lobectomy obtained a combined score of 70 broken rules and intratrial repetitive errors on the maze, but showed normal flexibility of response on the sorting test, whereas Cases R. B. and J. Mo., with small left superior-frontal lesions, performed normally on the maze, but made an exceedingly high number of perseverative errors on the sorting test.

The good performance of the group of patients with parietal-lobe lesions was unexpected, in view of the clinical literature. It is true that 9 of the 12 parietal patients were tested several years after operation, when they had been seizure-free for some time; however, the three parietal patients who were tested only 18 days after operation also obtained normal scores, even though one of them was severely aphasic at the time. Inspection of the individual scores suggests, rather, that the small size of the lesions may be the main reason why the parietal-lobe patients performed so well; the only patient with scores outside the normal range is Case M. R., who had what was certainly the largest lesion. This patient, moreover, was tested four years after operation and was no longer having seizures, but his scores indicate a marked impairment of maze learning.

The possibility the lesion size in the posterior cortex is a relevant factor in maze learning derives further support from the very poor performance of the small group of patients with large right posterior lesions involving the parietal, temporal and occipital lobes. It is true that four of the six patients in this group had also had the hippocampus radically excised, but the tendency of some patients to lose their bearings in the maze suggested more than a learning deficit.

The defective maze performance of the right posterior group also raises the question of the possible interfering role of visual field defects in maze performance. Partial homonymous upper quadrant defects on the side contralateral to the lesion were demonstrated in about half the cases of unilateral temporal lobectomy. These defects occurred no more often with right-sided lesions than with left and bore no relation to maze performance. There were fewer patients with lower quadrant or hemianopic defects, but these of course are the defects which might be expected to produce most disturbance on visual route-following tasks. Two left parietal patients had right lower-quadrant defects: one, Case P. Mo., performed

normally; the other, Case M. R., (with a larger lesion) was impaired. Amongst the right-hemisphere cases, only the six patients in the right posterior cortical group had lower quadrant or hemianopic defects, and, although their error scores on the maze were high, the mean was a little smaller than that of the right frontal-lobe group. Moreover, these patients did not show any neglect of the left half of visual space. These data suggest that the field defects of the right posterior group, though coincidental with maze defects, were not influential in producing them.

Since WEINSTEIN, SEMMES, GHENT and TEUBER [31] had found impairment on their tactual and visual route-finding tasks to be positively correlated with deficits in two-point discrimination on the hand, it was decided to investigate the relationship between maze-learning scores and two-point discrimination thresholds for the 62 patients for whom such data were available. It can be seen from Table 8 that the mean number of trials to criterion and the mean number of errors for patients with significant discrimination defects

Table 8. Comparison of maze-learning scores for unilateral groups with and without defects in 2-point discrimination.

Group	No. of cases	Mean scores	
		Trials	Errors
With defect	18	24.2	156
Without defect	44	30.9	179

are slightly lower than those for the group without such defects. Since sensory defects, in this patient population, occurred most frequently with lesions invading the Rolandic cortex, and since most of the small parietal-lobe lesions were of this kind, it is not surprising that two-point discrimination defects did not correlate positively with impaired maze performance. It seems likely, then, that the positive relationship between route-finding difficulty and two-point loss, found by WEINSTEIN *et al.*, merely reflects a partial coincidence of the loci of lesion responsible for the two defects, as the authors themselves suggest (SEMMES *et al.* [15]).

The maze used here differs from the route-finding tasks used by SEMMES *et al.* [5] not only in being a learning task (as has already been pointed out), but also in being a stylus and not a locomotor task. It is known from the work of ORBACH [33] that locomotor-maze performance of peripherally blinded monkeys is more vulnerable than stylus-maze performance to occipital lesions. Moreover, in the stylus-maze there was no need for the subject to be constantly shifting from one set of coordinates to another. At all times the entire maze was visible and its position relative to the subject's own body remained fixed. It seems reasonable, therefore, that this stepping-stone stylus maze would be less likely to uncover mild disorders of spatial orientation than would the map-reading tasks used by SEMMES and her co-workers [5]. This difference in task could perhaps account for the apparent contradiction between the finding of SEMMES *et al.* [5] that patients with parietal-lobe lesions (and only these patients) showed a residual impairment on the map-reading tasks years after penetrating brain wounds and the present finding of normal performance on the stylus maze in the parietal-lobe group. Nevertheless the possible importance of size of parietal-lobe lesion in producing this difference cannot lightly be dismissed. We have seen that some of the patients with large right-posterior cortical excisions did in fact lose their bearings in the stylus maze during the early stages of training, and, more

recently, we have had a striking example of this behaviour from a patient with a large cortical excision limited to the parietal lobe.

The data for this 16-year-old-girl, Case J. Du., were not included in the present analyses because she is one of a new series of patients who are learning the visual maze only after having first been trained on Dr. Suzanne Corkin's tactual maze. However, her test behaviour is so pertinent to the present discussion that it will be described here.

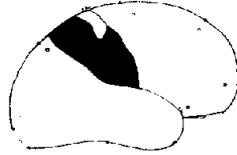


FIG. 11. Case J. Du., right parietal lobectomy. Not included in this study because tested after previous training on tactual maze. Visual maze scores: 52 trials, 400 errors.

Figure 11 shows the lateral extent of the parietal cortical excision, in this case, the removal on the mesial surface being small. It can be seen that the area excised is roughly the sum of the two small right parietal-lobe excisions of Cases S. La. and H. Ja. shown in Fig. 2, though sparing the temporal lobe completely.

It should be pointed out that this patient did not lose her way in the hospital; her visual fields showed only very slight peripheral constriction, in the left lower quadrant, and she had no tendency to neglect the left half of extrapersonal space. Her performance on a number of visual learning tasks and on the Wisconsin Card Sorting Tests was entirely normal. Yet both maze tasks proved extremely difficult and stressful for her.

Three weeks after operation, after prior training on the tactual maze, she learned the visual maze in 52 trials with 400 errors. During the course of this slow acquisition, she lost her way many times and became very discouraged, the testing being interrupted by frequent bouts of weeping. She referred to the maze as a "jungle" and doubted that she would ever learn it. In the early trials she built up a total of 20 broken rules and 4 intratrial repetitive errors, mainly at the most difficult choice points, in the middle of the maze, where she clearly did not know which way she had come nor which way to turn next. This behaviour shows that the stylus-maze task is sensitive to relatively mild forms of spatial disorientation, even if less so than a locomotor maze.

The findings in Case J. Du., whose parietal-lobe lesion was large, suggest that lesion size may indeed be a critical factor in determining the degree of spatial disorientation after a parietal-lobe lesion. This fact, together with the differing spatial demands of the two tasks may reconcile the present findings with those of SEMMES *et al.* [5].

The finding of an impairment in maze learning after large lesions of the right posterior cortex is consistent with earlier work on topographical orientation in cases of cerebral disease (PATERSON and ZANGWILL [9]; MCFIE *et al.* [10]; HÉCAEN *et al.* [11]; ETLINGER *et al.* [12]; HÉCAEN [13]; WHITTY and NEWCOMBE [14]). The fact that the present study does not include comparable lesions in the left posterior cortex prevents an assessment of the relative contribution of the two hemispheres to maze learning. For the temporal lobe, however, a greater effect from right-sided lesions is clearly shown and there is a suggestion that this holds true for the frontal lobe also. Although large removals anywhere in the right hemisphere impair maze performance, it does not follow that they do so for the same reasons; instead, it seems likely that the anterior and posterior regions contribute in qualitatively different ways to performance on this spatial learning task.

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Résumé—L'apprentissage d'un labyrinthe sous contrôle visuel a été étudié chez 79 malades avec différentes lésions cérébrales. Résultats: (1) les lésions bilatérales de l'hippocampe produisent le déficit le plus important, un malade ne manifestant aucun apprentissage au cours de 215 essais; (2) les lobectomies temporales droites produisent un déficit significatif, plus particulièrement lorsqu'elles sont accompagnées de l'ablation radicale de l'hippocampe sous-jacent. Par contre, les malades ayant une lésion temporale gauche de même étendue, ou une lésion pariétale (droite ou gauche) de faibles dimensions, donnent des résultats normaux; (3) des lésions plus grandes d'un lobe frontal ou du cortex postérieur droit ralentissent fortement l'apprentissage—ces données suggèrent que non seulement la localisation mais également l'étendue d'une lésion corticale influencent l'apprentissage du labyrinthe; (4) seules les lésions frontales affectent la capacité à suivre les consignes reçues.

Zusammenfassung—Das Erlernen eines Labyrinthes mit visueller Darbietung wurde bei 79 Patienten mit verschiedenen Hirnläsionen untersucht. Die wichtigsten Befunde sind: (1) beidseitige Läsionen des Hippocampus führen zur grössten Lernschwierigkeit; im Verlauf von 215 Einzelversuchen war bei einem Patienten überhaupt kein Lerneffekt sichtbar; (2) Abtragungen des rechten Temporallappens führen zu einer signifikanten Verlangsamung des Lernens, ganz besonders wenn sie von einer radikalen Abtragung des daruntergelegenen Hippocampus begleitet sind. Hingegen weisen Patienten mit gleich grossen Läsionen des linken Temporallappens oder mit geringen Läsionen des linken oder rechten Parietallappens normale Resultate auf; (3) grössere Läsionen eines Frontallappens oder der rechten hinteren Hirnrinde verlangsamen das Lernen stark—dies führt zum Schluss, dass nicht nur die Lokalisation, sondern auch die Ausdehnung einer Hirnrindenläsion das Erlernen des Labyrinthes beeinflussen; (4) nur Frontallappenläsionen erschweren das korrekte Ausführen der erhaltenen Instruktionen.