FURTHER ANALYSIS OF THE HIPPOCAMPAL AMNESIC SYNDROME: 14-YEAR FOLLOW-UP STUDY OF H.M.*

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Abstract—The report attempts to delineate certain residual learning capacities of H.M., a young man who became amnesic in 1953 following a bilateral removal in the hippocampal zone. In addition to being able to acquire new motor skills (CORKIN [2]), this patient shows some evidence of perceptual learning. He also achieves some retention of very simple visual and tactual mazes in which the sequence of required turns is short enough to fit into his immediate memory span; even then, the rate of acquisition is extremely slow. These vestigial abilities, which have their occasional parallels in the patient's everyday life, are assessed against the background of his continuing profound amnesia for most on-going events, an amnesia that persists in spite of above-average intelligence and superior performance on many perceptual tasks.

THE PRESENT report has three aims. In the first place, it describes the persistent features of a severe amnesic syndrome acquired 14 years ago, following bilateral mesial temporal lobectomy (SCOVILLE [28]). Secondly, the report attempts to give further substance to our previously held belief that the patient's perceptual and intellectual capacities remain intact, as manifested by normal or superior performance on a fairly wide range of experimental tasks. Thirdly, we are exploring the nature of the memory defect in some detail by trying to discover which learning tasks the patient can master, as compared with those on which he always fails.

INTERVAL HISTORY

Since the onset of his amnesia in 1953, we have twice had the opportunity of bringing this patient under intensive observation. In 1962, he spent one week at the Montreal Neurological Institute, and most results of these and earlier examinations have already been reported (CORKIN [1]; MILNER [16, 18, 19]). Extensive testing was again carried out in 1966, during a two-week admission to the Clinical Research Center at M.I.T. Findings obtained during that period, supplemented later by visits to the patient's home, form the basis of the present report.

H.M.'s severe anterograde amnesia persists, although his mother has noted (and we can confirm) a slight but distinct improvement during the past two or three years. He still fails to recognize people who are close neighbours or family friends but who got to know him only after the operation. When questioned, he tries to use accent as a clue to a person's place of origin and weather as a clue to the time of year. Although he gives his date of birth unhesitatingly and accurately, he always underestimates his own age and can only make wild guesses as to the date.

There does not appear to have been any change in H.M.'s capacity to recall remote events antedating his operation, such as incidents from his early school years, a high-school attachment, or jobs he held in his late teens and early twenties. His memory seems vague for the two years immediately preceding the operation (performed when he was 27 years old), but this apparent retrograde loss is becoming increasingly difficult to delineate.

In social settings, H.M. is quiet, and appears at ease, except for his frequent apologies for what he fears may be considered lapses from good manners, such as forgetting the names of persons to whom he has just been introduced. It is clear that he has not lost any of the social graces he acquired in his youth. He keeps himself neat, although he has to be reminded when to shave. He speaks in a monotone, but with good articulation and a vocabulary that is in keeping with his above-average intelligence. His comprehension of language is undisturbed: he can repeat and transform sentences with complex syntax, and he gets the point of jokes, including those turning on semantic ambiguity.

H.M. rarely mentions being hungry, even when his meals have been somewhat delayed; however, when food is put before him he eats in a normal manner. He does not report physical pain, such as headache or stomach-ache, but at times describes feelings of apprehension to which it is difficult for others to assign a cause. His apparent lack of sexual interest and activity has been commented upon by SCOVILLE [29].

Recall of salient personal events

H.M. has been cared for all this time by his mother, who usually accompanies him wherever he goes. It so happened, however, that in 1966 the mother was in Hartford Hospital, recovering from a minor operation, just when H.M. was about to leave for Boston. It was his father, therefore, who packed H.M.'s clothes for him and brought him to meet us at Dr. Scoville's office prior to the journey. The father had also taken the patient to visit his mother in hospital that very morning, the third such visit within a week. Yet when we questioned H.M., he seemed not to remember any of these visits, although he expressed a vague idea that something might have happened to his mother. On the journey to Boston, he kept saying that he felt a little uneasy and wondered if something might be wrong with one of his parents, though he could not be sure which one. On being asked who had packed his bag for the trip he said "Seems like it was my mother. But then that's what I'm not sure about. If there is something wrong with my mother, then it could have been my father." Despite our explaining the situation to him repeatedly during the journey, H.M. was never able to give a clear account of what had happened, and was still feeling "uneasy" when he reached Boston, wondering if something was "wrong" with one of his parents. Gradually, this uneasiness wore off, and although he was told repeatedly that he could telephone home any time he wished, he no longer seemed to know why he should do so. Next day he appeared completely unaware that there had been any question of illness in his family. When asked again who had packed his suitcase, he said "It must have been my mother. She always does these things." It seemed to us instructive how the emotional tone (one

of concern and uneasiness), which was associated with the vague knowledge of his mother's illness, appeared to fade away nearly as rapidly as his knowledge of the events provoking it.

During three of the nights at the Clinical Research Center, the patient rang for the night nurse, asking her, with many apologies, if she would tell him where he was and how he came to be there. He clearly realized that he was in a hospital but seemed unable to reconstruct any of the events of the previous day. On another occasion he remarked "Every day is alone in itself, whatever enjoyment I've had, and whatever sorrow I've had." Our own impression is that many events fade for him long before the day is over. He often volunteers stereotyped descriptions of his own state, by saying that it is "like waking from a dream." His experience seems to be that of a person who is just becoming aware of his surroundings without fully comprehending the situation, because he does not remember what went before.

In December, 1967 (eighteen months after the visit to Boston), H.M.'s father died suddenly, and H.M. is said to have become temporarily quite irritable and intractable, rushing out of the house in anger one evening. The cause of the anger was finding that some of his guns were missing. These had been prize possessions of which he often spoke and which he had kept in his room for many years, but an uncle had claimed them as his legacy after the father's death. The patient was upset by what to him was an inexplicable loss, but became calm when they were replaced in his room. Since then, he has been his usual even-tempered self. When questioned about his parents two months later, he seemed to be dimly aware of his father's death. In these and similar respects, he demonstrates some capacity to set up traces of constant features of his immediate environment. In this instance, the continued absence of one of his parents may have served as an unusually effective clue. Until then, H.M.'s entire life had been spent at home with his father and mother.

After his father's death, H.M. was given protected employment in a state rehabilitation centre, where he spends week-days participating in rather monotonous work, programmed for severely retarded patients. A typical task is the mounting of cigarette-lighters on card-board frames for display. It is characteristic that he cannot give us any description of his place of work, the nature of his job, or the route along which he is driven each day, to and from the centre.

In contrast to the inability to describe a job after six months of daily exposure (except for week-ends), H.M. is able to draw an accurate floor plan of the bungalow in which he has lived for the past eight years. He also seems to be familiar with the topography of the immediate neighbourhood, at least within two or three blocks of his home, but is lost beyond that. His limitations in this respect are illustrated by the manner in which he attempted to guide us to his house, in June, 1966, when we were driving him back from Boston. After leaving the main highway, we asked him for help in locating his house. He promptly and courteously indicated to us several turns, until we arrived at a street which he said was quite familiar to him. At the same time, he admitted that we were not at the right address. A phone call to his mother revealed that we were on the street where he used to live before his operation. With her directions, we made our way to the residential area where H.M. now lives. He did not get his bearings until we were within two short blocks of the house, which he could just glimpse through the trees.

Recall of public events

As one might expect, the patient shows little awareness of even major national or international events. Nevertheless, his mother tells us that he occasionally surprises her by knowing of some occurrence that she did not think he would remember. In February,

1968, when shown the head on a Kennedy half-dollar, he said, correctly, that the person portrayed on the coin was President Kennedy. We asked him whether President Kennedy was dead or alive, and he answered, without hesitation, that Kennedy had been assassinated, but he was unable to tell us anything about the event, including the supposed killer, or about Kennedy's successor. He merely said "It must have been the vice-president, because that's the law." In a similar way, he recalled various other public events, such as the death of Pope John (soon after the event), and recognized the name of one of the astronauts, but his performance in these respects was quite variable.

Neurological examinations

Between 1953 and 1968, H.M.'s neurologic status has been repeatedly assessed, without revealing any significant changes from one examination to another. All functions subserved by the cranial nerves are intact, with two possible exceptions. (1) Although he seemed able to detect smells, two different examiners noted independently that he could not identify the odoriferous substances by name. In the absence of norms, this apparent failure is difficult to evaluate. (2) One examiner noted some mild difficulty with the patient's vertical upward gaze, but this observation was not reported by other examiners who saw the patient at other times.

The patient's coordination and motor power show mild impairment in the upper, and somewhat more marked impairment in the lower extremities; he walks cautiously, with broad-based gait. His sensory status appears normal on cursory examination, except for loss of position sense and vibratory sensitivity in the hallux of both feet. More systematic quantitative assessment of thresholds for light touch and two-point discrimination revealed some elevation of thresholds on the patient's hands for these two aspects of somatic sensation, and more conspicuous losses of sensitivity in his feet (where two-point thresholds were unobtainable). On double simultaneous stimulation with supraliminal tactile stimuli (applied either to homologous or heterologous body parts), the patient shows frequent extinction, more often on the left than on the right, especially on simultaneous stimulation of both feet, but also on stimulation of the hands.

Nearly all examiners ventured the opinion that the sensory and motor symptoms may have antedated this patient's mesial temporal-lobe resection; in fact, the total pattern of symptoms is not incompatible with some damage to the cord. A myelogram was suggested (in 1966) but not carried out because of the non-progressive nature of the symptoms.

The most obvious effect of the operation performed in 1953 is the reduction in the frequency and severity of H.M.'s seizures. During the 11 years preceding the surgery, the patient had more than 50 generalized convulsions each year and numerous minor attacks during each day, in spite of massive anticonvulsive medication at near-toxic levels. Over the 14 years since the bilateral mesial temporal lobectomy, he has been kept on more moderate doses of dilantin; generalized convulsions have occurred about once every two or three years, and the minor attacks are seen perhaps once or twice a day. Electroencephalography continues to disclose diffuse bilateral abnormalities, rather than indicating a focal epileptogenic area.

FORMAL TESTS AND EXPERIMENTAL PROCEDURES

As has been pointed out already, H.M.'s memory defect is not accompanied by any general intellectual loss. In 1953, shortly before his operation, he obtained an intelligence quotient of 104 on Form I of the Wechsler-Bellevue Intelligence Scale; the verbal quotient

was 101 and the performance quotient 106. When tested again in 1955, two years after the operation, he achieved a full-scale quotient of 112, with a verbal quotient of 107 and a performance quotient of 114. This postoperative improvement may well have been due to a reduction in the frequency of his minor attacks, which preoperatively had been observed to occur as often as 12 times during a single two-hour testing session. Seven years later, in 1962, he showed further improvement; when tested with Form II of the Wechsler Intelligence Scale, his full-scale I.Q. was 118, the verbal and performance quotients being 109 and 125, respectively. On the corresponding form of the Memory Scale (STONE et al. [31]), given at the same time, he achieved a memory quotient of 64, which is a grossly abnormal rating standing in marked contrast to his above-average intelligence.

We should note that H.M. did particularly well on such timed tasks as the Block-Design subtest of the Wechsler Scale, or Milner's version of Hebb's triangular-blocks task (HEBB [8], p. 278; MILNER [14]). His success on these tests clearly indicates that spatial relationships as such cause him little trouble.

Sorting Tasks

H.M. does not appear to have any difficulty with sorting tasks that require frequent changes of method for their solution. He has twice taken the Wisconsin Card Sorting Test (GRANT and BERG [7]), which is a quantitative and more difficult version of WEIGL's [37] well-known procedure. The first time, in 1955, he was having numerous small seizures that manifested themselves as momentary lapses of attention; yet he was able to shift appropriately from one category to another, completing four of the six stages of the test, and obtaining a normal error score (MILNER [17]). When retested seven years later, in 1962, he did not of course remember having done the test before. On that occasion he was not handicapped by seizures and completed the six stages of the task without difficulty, achieving the criterion of 10 consecutive correct responses to each of the three categories of colour, form, and number, twice in 84 cards. In spite of this superior performance, he did not realize at the end of the test that he had been constantly changing his method of solution in response to cues from the examiner, but assumed that he had been using the same principle of classification throughout.

A notable feature of H.M.'s sorting behaviour was the unusually small number of perseverative errors; that is to say, of errors made through continuing to sort to the previously correct category. From this standpoint, H.M.'s profound anterograde amnesia was probably an advantage to him, because it meant that he rapidly forgot a method of solution once it had ceased to work. Low perseverative error scores were also obtained on this test by P.B. and F.C., the two patients of Dr. Wilder Penfield who developed amnesic syndromes after unilateral temporal lobectomy, in the presence of a lesion in the temporal lobe of the opposite hemisphere (PENFIELD and MILNER [26]).

The flexible approach to the Card Sorting task exhibited by the patients with bilateral hippocampal lesions stands in sharp contrast to the test behaviour of K.M., a patient in whom Dr. Penfield had removed the anterior portion of both frontal lobes 23 years earlier, as a treatment for post-traumatic epilepsy (HEBB and PENFIELD [9]). K.M. showed to an unusual degree the perseverative tendencies so frequently observed after lesions of the dorsolateral frontal cortex (MILNER [17]; but see TEUBER et al. [32] for a different view).

Figure 1 shows, on the left, the contrasting performance of K.M. and of the three hippocampal patients, with respect to the incidence of perseverative errors on the Wisconsin Card Sorting Test. On the right is shown the converse effect for a memory task: the delayed

matching of photographed faces of college students (MILNER [20]; MUNN [23], pp. 212 and and 608). On the face-recognition task, K.M. made only one mistake in selecting, from an array of 25 faces, the 12 faces that he had been shown 90 sec before. H.M., like P.B. and F.C., has a marked impairment on this visual memory task, and his performance fell to a chance level when the test was repeated a few days later with a distracting task inter-polated between the presentation of the two sets of photographs. It is evident, then, that the performance of the patients on the two tests yields a double dissociation between the effects of bilateral frontal and bilateral hippocampal ablations.
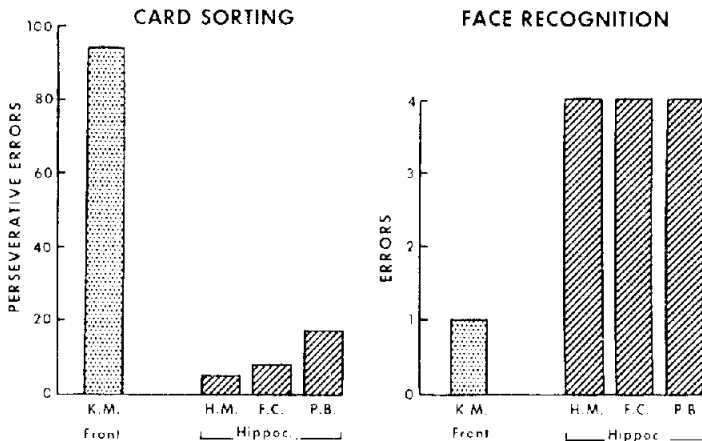

FIG. 1. Contrasting effects of bilateral hippocampal and bilateral frontal-lobe lesions on the performance of two tasks: the Wisconsin Card Sorting Test (GRANT and BERG [7]), and a delayed face recognition task (MILNER [20]). K.M. had sustained bilateral removal of the anterior portion of both frontal lobes, for post-traumatic epilepsy (HEBB and PENFIELD [9]); P.B. and F.C. each had left temporal lobectomies, with persisting electrographic abnormalities in the right temporal lobe (PENFIELD and MILNER [26]); H.M. is the case of bilateral mesial temporal-lobe excision. K.M.'s lesion impairs sorting behaviour but not memory for faces; the bilateral mesial temporal-lobe lesions have the converse effects.

Perceptual Tasks

Because a mesial temporal-lobe excision could easily damage neighbouring neocortical tissue on the inferior aspect of the temporal lobes, it is especially important to point out that H.M. achieved normal, or above normal, scores on perceptual tasks believed to be sensitive to lesions of the right temporal neocortex. Unlike patients with right-temporal-lobe epilepsy (MILNER [15]), H.M. was quick to detect the anomalous features of cartoon drawings, and on tests of tachistoscopic letter recognition (cf. DORFF *et al.* [3]), and letter masking, his performance was considered by Dr. Peter Schiller to be equivalent to that of normal control subjects with the same visual acuity.

Mooney face-perception task

More clearcut evidence of visual efficiency on a perceptual task comes from the MOONEY "Closure" task [22], in which the subject has to organize a face out of a chaotic black and white pattern with incomplete contour. Figure 2 shows a typical item from the series of 44 faces; the subject is required to give the sex and approximate age of the person whose face he sees. On this task there is evidence of some lasting impairment after right temporal

lobectomy (LANSDELL [12]); similarly, NEWCOMBE [24] finds residual deficits in men with penetrating missile wounds of the right temporo-occipital region, but not after corresponding wounds of the left hemisphere.

FIG. 2. Sample of an easy item from the face-perception test (MOONEY [22]).

H.M. responded quickly and accurately to this rather difficult perceptual task, making only four errors and completing the series in less than seven minutes. Because performance on the task may well be age-sensitive, we have compared H.M.'s scores with those of eight normal control subjects of his own age. As can be seen from Table 1, H.M.'s performance is superior to that of every one of these control subjects, both in number of correct responses and in time taken to complete the test.

Table 1. Performance of H.M. on Mooney's face-perception test, as compared with that of 8 normal control subjects matched for age and sex (Maximum score: 44)

Subjects	Age (yr)		No. correct responses		Total time	
H.M.	40		40		6′40″	
	Mean	Range	Mean	Range	Mean	Range
Normal control	41.4	39–45	36.2	33–39	9′53″	8′10″–12′40″

Metacontrast

These additional visual studies were carried out at M.I.T. by Dr. Peter Schiller and his associates, who reported that H.M. showed normal interaction between two stimuli (a disk and a ring) when they were briefly exposed, one after the other, with the interval between stimuli varying from 30 to 200 msec. Each stimulus was exposed for 10 msec, the disk always preceding the ring. H.M. was able to see the disk at all inter-stimulus intervals except 60 msec, a finding which is in accord with data for normal subjects.

Hidden-figures test

In contrast to his efficient performance on so many other visual tasks, H.M. showed marked impairment on a modified form of Gottschaldt's hidden-figures task (GOTTSCHALDT [6]; TEUBER and WEINSTEIN [34]), in which particular geometric patterns have to be discovered and traced out within a network of embedding and overlapping lines. H.M.'s poor performance on this task is discussed elsewhere in this issue (TEUBER *et al.* [33]). His score of 23 compares unfavourably with that of N.A., the patient with a much milder amnesic syndrome caused by a stabwound in the base of the brain. It should be pointed out that N.A. took the test when he was 24 years old, H.M. when he was 39.

H.M.'s difficulty with the hidden-figures test could not have been predicted on the basis of his performance on other visual tasks, but it can be argued that this particular task is not merely testing perception. Indeed, its sensitivity to lesions in any part of either cerebral hemisphere (TEUBER and WEINSTEIN [34]; VIGNOLO [35]) suggests that performance may be impaired for a variety of reasons. In the case of H.M., one wonders whether the need to keep one particular geometric figure in mind whilst analysing another more complex figure might not overtax his short-term memory system, with consequent slowing and errors. In addition, the small number of items that H.M. completed within the time limits reflects his general slowness on paper-and-pencil tasks (CORKIN [2]). It is, however, quite possible that the deficits responsible for H.M.'s poor performance on the hidden-figures task antedate his brain operation and are unrelated to the amnesic syndrome, which followed it.

Learning and memory

The essential integrity of H.M.'s performance on most of the perceptual tasks under-scores our previous impression that this patient's defect is selective to the sphere of memory. At the same time, it seemed to us important to determine on which tasks and under what conditions some residual learning capacity might be demonstrable. His success on a mirror-drawing task seven years after the operation demonstrated that the acquisition of a motor skill was possible in the presence of severe anterograde amnesia for ongoing events. This observation has since been confirmed and extended by CORKIN [2] and will not be pursued further here. Likewise, we cannot discuss at this stage the question of whether H.M. would show normal conditioning with appropriate experimental techniques. An abortive attempt to answer this question was made in 1962. At that time. Dr. Doreen Kimura tried using electric shock to elicit galvanic skin responses in H.M., as a prelude to conditioning this response to previously indifferent stimuli. These experiments were performed in Dr. R. B. Malmo's laboratory at the Allan Memorial Institute, with the assistance of Dr. J. M. Weiffenbach. The experiments were initiated in that setting because the apparatus and procedures needed for conditioning studies of this kind were then in routine use at that institute. Nevertheless the experiments had to be abandoned after it turned out that H.M.

showed no galvanic skin responses to electric shock, even at intensity-levels that normal control subjects found disagreeably painful. H.M. appeared to notice the shocks but did not complain at all of being subjected to this procedure. More information will be needed to determine whether these findings reflect a more general lack of responsiveness to pain, or whether we are dealing with a specific alteration of autonomic reactivity. In any event, this abnormality may be attributable to the removal of the amygdaloid complex, rather than to the removal of the hippocampus itself, both of these structures having been involved in the bilateral mesial temporal-lobe resection. It should also be noted in this connection that bilateral removals limited to the amygdala do not produce amnesia (SCOVILLE and MILNER [30]), so that the observed changes in autonomic responsiveness and the amnesia may well be dissociable.

As to the amnesia itself, it has always been clear that this patient's forgetfulness encompasses verbal as well as nonverbal material. Previous studies have shown that he is severely deficient on tests of verbal learning and recall (SCOVILLE and MILNER [30]), and that he cannot master digit-sequences beyond his immediate span (DRACHMAN and ARBIT [4]). Similarly, he failed completely on such essentially nonverbal tasks as the delayed recall of a complex geometric design (REY [27]; OSTERRIETH [25]) and the recognition of recurrent nonsense patterns (KIMURA [11]; TEUBER et al. [33]).

The gravity of the learning defect has been more systematically explored by means of two maze-learning problems, one permitting the use of vision, the other not. In 1960, H.M. was trained on the visual stepping-stone maze shown in Fig. 3, which is mastered by control subjects of comparable age and intelligence in less than 25 trials. We have argued elsewhere (MILNER and TEUBER [21]) that this task can be a sensitive indicator of memory disorders in patients whose spatial orientation is intact and who can follow the rather simple test instructions. H.M. failed to show any improvement in 215 trials spread over 3 days of training (MILNER [16, 18]). Similarly, he failed to reduce his errors in 80 trials (spread equally over eight consecutive days) on a tactual stylus-maze (CORKIN [1]). These maze tasks, the tactual as well as the visual, require the memorization of a sequence of turns that clearly exceeds the immediate memory span. It was therefore decided, in 1966, to retest this patient with shortened versions of these mazes, in which the total number of turns to be memorized would fall within his immediate memory span; we could then ask whether with intensive training some cumulative learning might be possible.

Shortened visual mazes

The visual maze in its original form, with its 28 choice-points, was reduced to a path containing only 8 choice-points; this aim was achieved by covering the major portion of the maze with a board, in which an aperture exposed the section (Short Maze A) shown in Fig. 4. The sequence of turns could be reduced further if the subject resorted to verbal coding (as, for example, by saying "2 down, 3 across, 2 up, 2 across").

As can be seen from Fig. 5, H.M. showed little evidence of learning this shortened maze over 125 trials; we therefore reduced the path still further by exposing only the area shown in Fig. 6 (Short Maze B). The starting-point was unchanged, so that H.M. did not have to unlearn any response-tendencies he might have acquired during his previous training on Short Maze A. Training was carried out in blocks of 25 trials, given 4 times daily; after 155 trials, H.M. reached the required criterion of 3 successive errorless runs.
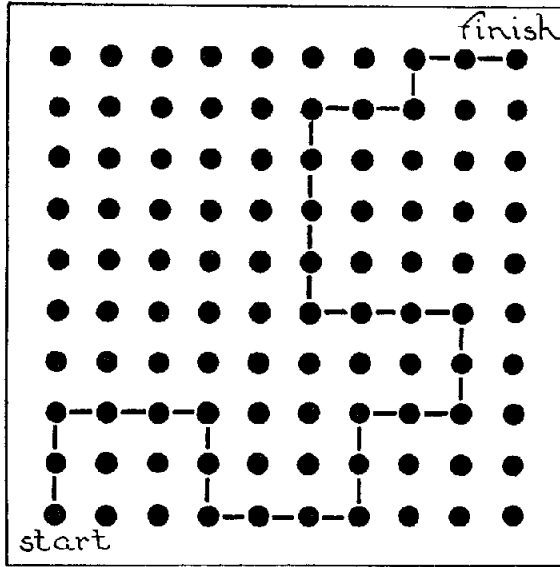
FIG. 3. Plan of visual stepping-stone stylus maze. The black spots are metal bolt-heads on a wooden base. The subject must discover and remember the correct route (indicated here by the black line). He proceeds from bolt-head to bolt-head, with the click of an error-counter to signal whenever he makes a mistake. H.M. failed to reduce his error score in 215 trials (MILNER [18]).
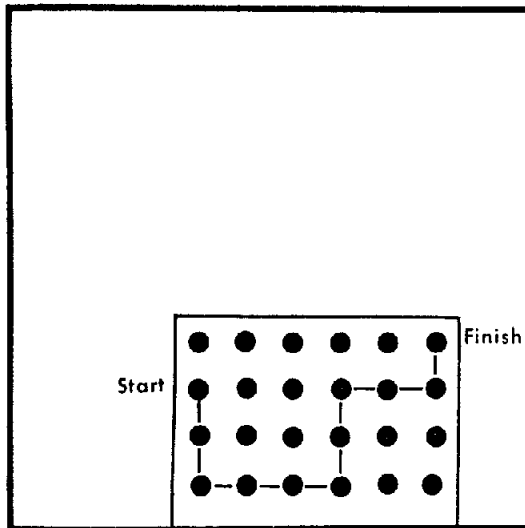

FIG. 4. Short Maze A. The rest of the visual maze (Fig. 3) has now been covered with a board. The light black line indicates the route to be learned, and the heavy black line the outline of the whole board.
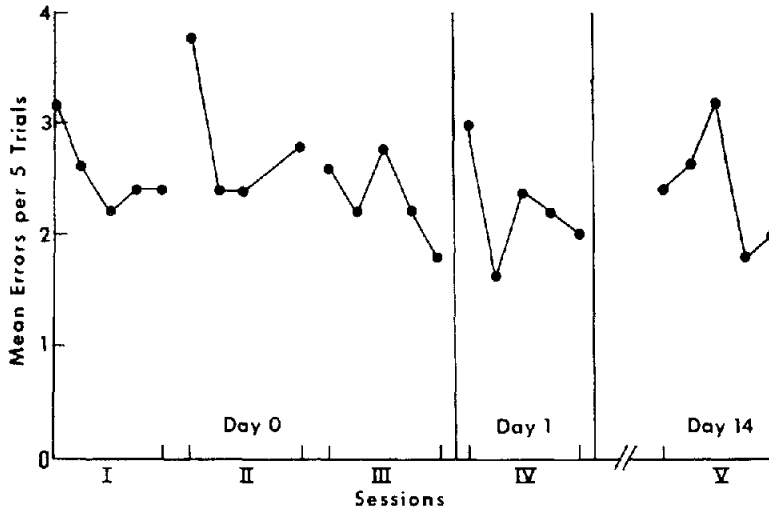
FIG. 5. Short Maze A. Graph showing error scores for H.M., plotted over successive blocks of five trials. There is little evidence of learning after 125 trials. The last 25 trials, performed after training on Short Maze B, also show no progress.
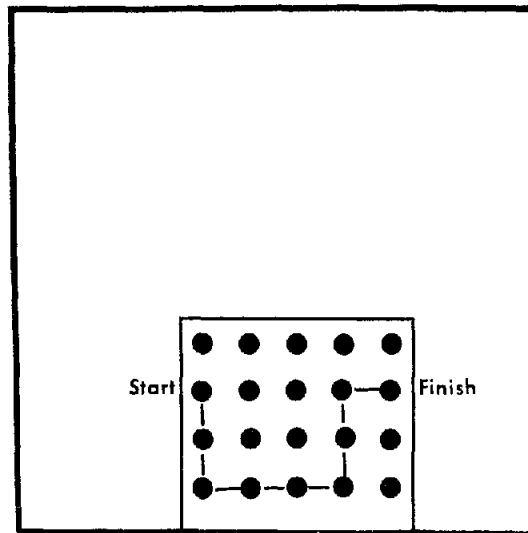

FIG. 6. Short Maze B. Still more of the maze has been shielded from view. The subject must now learn the very simple route indicated by the black line.

Short Maze B clearly comes within the span of immediate memory, even without verbal recoding. Although the slow acquisition is further proof of the severity of the patient's learning defect, the fact that he did eventually learn the maze allowed us to test his retention. He was therefore brought to criterion again on the following day (Day 3, Fig. 7) and again on Days 5, 8 and 14. It is quite evident (from Fig. 7) that he showed retention in the form of marked savings, even after the inter-test interval had been lengthened to six days. On the other hand he did not show a completely errorless performance on any of the days

on which retention was tested. Control subjects, including normal adults and those with various unilateral cortical excisions, show perfect or near-perfect retention of the 28-choice-point maze after 24 hours.
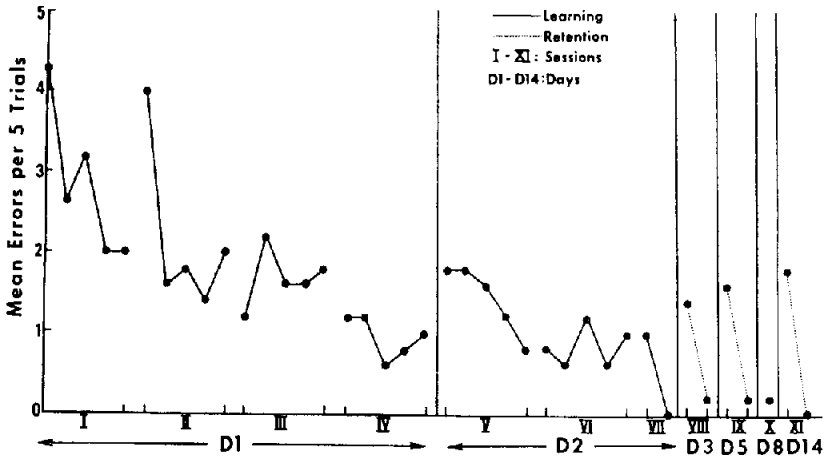

FIG. 7. Short Maze B. Learning and retention curves for H.M. The patient reached criterion in 155 trials, and showed considerable retention on retesting at 1, 2, 3 and 6-day intervals.

On Day 14, immediately after the last retention test on Short Maze B, the patient was given another 25 trials on the slightly longer maze (Short Maze A), in the expectation that some transfer of training would be demonstrable. As Fig. 5 indicates (in the last portion of the graph), the patient showed no evidence of such transfer.

Distribution of errors on Short Maze B. Figure 8 shows the number of times H.M. made mistakes at the various choice-points of Short Maze B before he eventually learned the path. There is a high build-up of anticipatory errors at the end, rather than a random distribution of wrong choices. This pattern of results could be described as showing
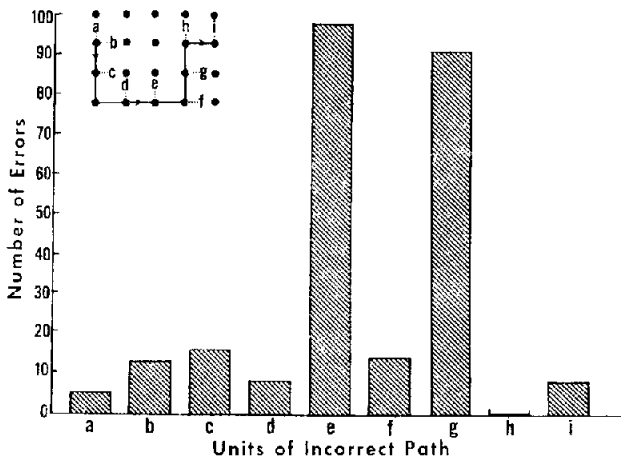

FIG. 8. Short Maze B. Distribution of errors made by H.M. during the 155 training trials needed for him to learn the correct path.

response perseveration (KIMBLE [10]; MAHUT and CORDEAU [13]), but it must be remembered that H.M. was abnormally nonperseverative on the Card Sorting Task (Fig. 1). It seems more likely that the persistence of these particular errors on the maze merely reflects H.M.'s great difficulty in remembering the correct sequence of turns, combined with his visual impression (from surveying the entire small maze) that turns in the direction of the point marked "Finish" would have to be made. The fact that H.M., unlike patients with frontal-lobe lesions, made no repetitive errors within a single trial, argues against attributing his impairment in maze learning to response perseveration (MILNER [18]).

Shortened tactual maze

The same reasoning that led us to predict H.M.'s relative success in learning a shortened version of the visual maze prompted us to test him also with a shortened version of the original tactual maze. As indicated in Fig. 9, this shortening was accomplished by the simple device of blocking the path through the maze half way between the starting-point and the finish, thus providing a new end-point, which differed from the end of a blind alley by being made of rubber. The patient's hand, with the stylus in it, was initially guided
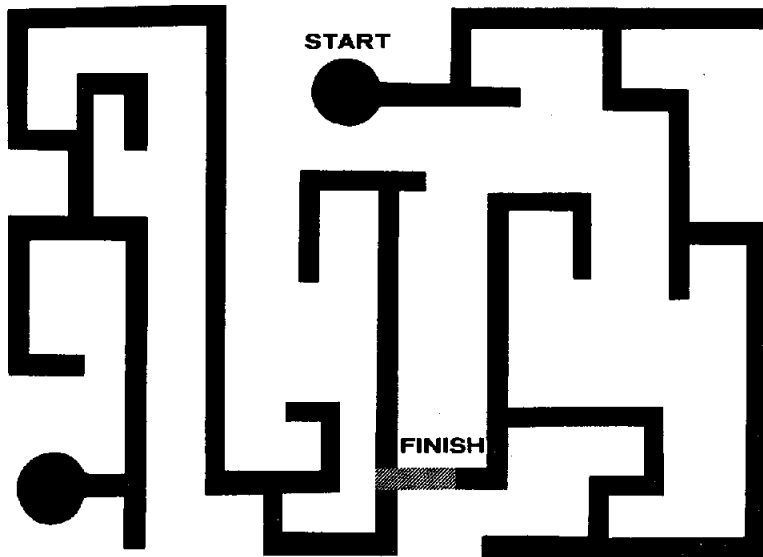

FIG. 9. Tactual Maze (shortened form). An eraser (lightly shaded) blocks the route after the fifth choice point, to indicate the finish. On the complete maze, which has 10 choice points, H.M. failed to reduce his error-scores in 80 trials (CORKIN [1]).

to the starting-area and then lifted off and placed in the finishing area. His hand was then lifted back to the starting-point and he was told to trace the path from start to finish. He was warned that every time he made an incorrect turn, a bell would ring. Vision of the apparatus was excluded at all times by concealing the maze behind a black curtain, under which the patient had to reach with his hand.

Figure 10 shows that H.M. failed to reach the criterion of 3 consecutive errorless runs in 30 training sessions (each consisting of 10 trials) spread over 10 days. Yet he did become increasingly efficient in tracing the shortened path: On all days but Day 7 his total error score for 30 trials is lower than that for the preceding day.

In spite of his difficulty in memorizing the path, H.M. seemed to have little trouble in remembering instructions within a session, and his recognition of the maze task from one session to another improved during training. At the beginning of each session, he was asked by the examiner what purpose the stylus served (the stylus being a ball-point pen). Before
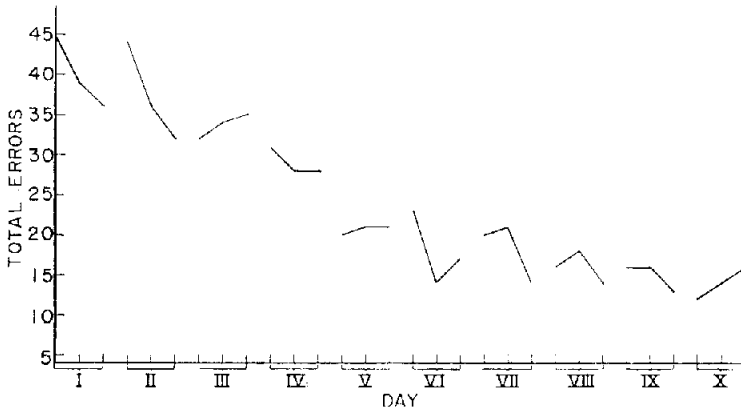

FIG. 10. Shortened Tactual Maze. Learning curve for H.M., plotted as total error scores for successive blocks of 10 trials. Testing was carried out in three sessions per day, for 10 consecutive days. H.M. showed significant progress over the 10 days, but failed to reach the criterion of 3 successive errorless runs in 300 trials.

Trial 81, his reply was "to write it down." Before Trial 91, he said "to trace the right route, making the fewest mistakes."

A similar instance of remembering instructions occurred in the course of tests for tactual sensitivity. When the examiner asked H.M. to hold out his hands (so that they could be touched with Von Frey hairs), the patient promptly closed his eyes as well, just as he had been told to do on other occasions earlier in the day for other sensory tests.

At no time during the 300 trials was H.M. aware of the large number of trials he had completed. From Day 1 onwards he remembered that he had done the test before, but his estimate of the number of completed trials was usually "a few." On the other hand, he greatly overestimated the number of turns between the start and finish, his guess being 23 turns on one occasion and 36 turns on two other occasions.

We must conclude from the tactual maze data as from the visual that even when the number of choice-points falls within the span of immediate memory, H.M. can still only learn very slowly. In the first 50 trials of the shortened tactual maze, he made 200 errors, whereas CORKIN's [1] normal control subjects averaged 90 errors for the full-length maze, which they mastered in about 30 trials.

Gollin incomplete-pictures task

WARRINGTON and WEISKRANTZ [36] have recently found that amnesic patients with Korsakoff's psychosis can learn to recognize fragmented drawings of common objects, despite not remembering doing the task before. It therefore seemed worthwhile to explore H.M.'s capacities with a similar task, to ascertain how far such perceptual learning might be preserved in the presence of a severe anterograde amnesia. H.M. was just 42 years old when he was tested, in February 1968; his performance will be compared with that of 10 normal male subjects, ranging in age from 39 to 46 years, with a mean age of 42.5 years.

Material and procedure. The material was derived from the series of incomplete drawings of objects and animals first devised by GOLLIN [5] for use with children, and later taken over by WARRINGTON and WEISKRANTZ [36] to assess perceptual learning in amnesic patients. The complete test series consists of 20 realistic line drawings, each of which can be presented in a series graded in difficulty from 1 (the most sketchy outline) to 5 (the complete, easily recognisable picture). There are also 3 practice items (a cow, a chair, and a hen), graded in the same way.

Each drawing occupies approximately the same area of an 8 in. × 10 in. card. The total series thus comprises 5 sets of 20 drawings, Set 1 containing the most fragmented versions and Set 5 the complete figures. Figure 11 shows a typical item from the test series: a sketchy representation of an aeroplane, which becomes progressively more clearly defined, from its first presentation in Set 1 to its final presentation in Set 5.

Set 1   Set 2

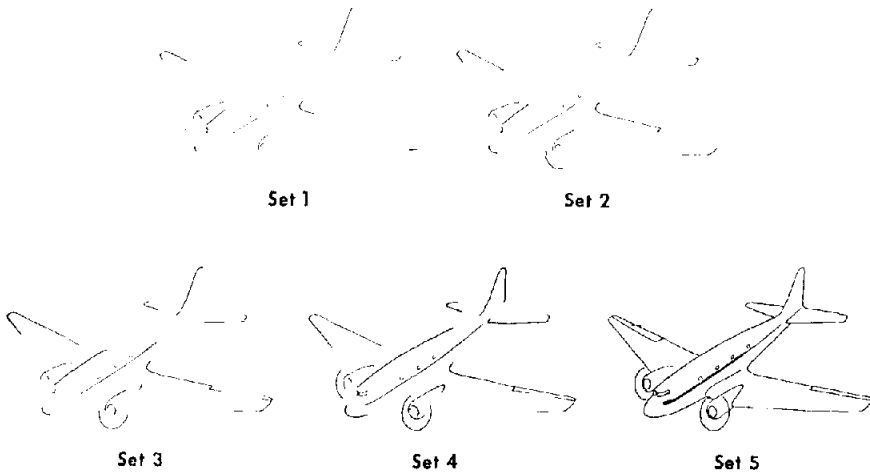Set 3   Set 4   Set 5

FIG. 11. Sample item from the incomplete-pictures task (GOLLIN [5]).

The subject is shown all the most difficult cards first (Set 1), one at a time. He is allowed to look at each card for approximately 1 sec and encouraged to say immediately what he thinks the sketchy drawing might represent. After all 20 cards of Set 1 have been shown, the subject is told that the pictures will now become a little easier to identify. Set 2 is then presented in the same way as Set 1, but the order of cards changes from set to set, so that it is impossible for the subject to anticipate which drawing will be coming next. This procedure is continued through successively easier sets of cards, until all 20 drawings of a given series have been correctly identified.

One hour later and without forewarning, the entire test is repeated, using exactly the same procedure as before. In the present study, the control subjects occupied themselves with various other activities in the interval, but did not do any other visual task. H.M. had a short neurological examination and also tried to answer some questions about recent events.

Results. Table 2 shows that H.M.'s performance on the initial test was slightly above the average of normal control subjects of the same age: H.M. made 21 errors; the control group averaged 25.5 errors, with a range from 15 to 37. This finding constitutes further proof that H.M.'s perceptual abilities are largely intact.

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Table 2. Test-retest error scores on Gollin incomplete-pictures task: data for H.M. and for 10 normal control subjects matched for age and sex (Intertest interval: 1 hour)

| Subjects | Errors | | | | Reduction in errors on retest (%) | |
	Initial test		Retest			
H.M.	21		11		48	
	Mean	Range	Mean	Range	Mean	Range
Normal control	25.5	15–37	3.6	1–15	77.6	52–93

When shown the pictures again, one hour later, H.M.'s performance improved by 48 per cent (Table 2), although he did not remember having taken the test before. Every normal subject showed a greater practice effect than H.M., but a scrutiny of the individual scores revealed that subjects who were poor at identifying the pictures in the first place also profited less from their experience than did those whose initial competence was greater. Hence it seemed desirable to compare H.M.'s performance, on retesting, only with that of normal subjects whose initial scores were close to his own. Four of the control subjects obtained error-scores between 18 and 23 on the initial test; they were therefore selected to be a more appropriately matched control group for H.M.

Figure 12 shows how errors are related to increasing clarity of the pictures, on initial testing and on retest, for H.M. and the matched control subjects (whose scores are averaged). On the first exposure to the task, H.M.'s performance is almost indistinguishable from that of the control subjects, but on retest he shows considerably less improvement than they do.
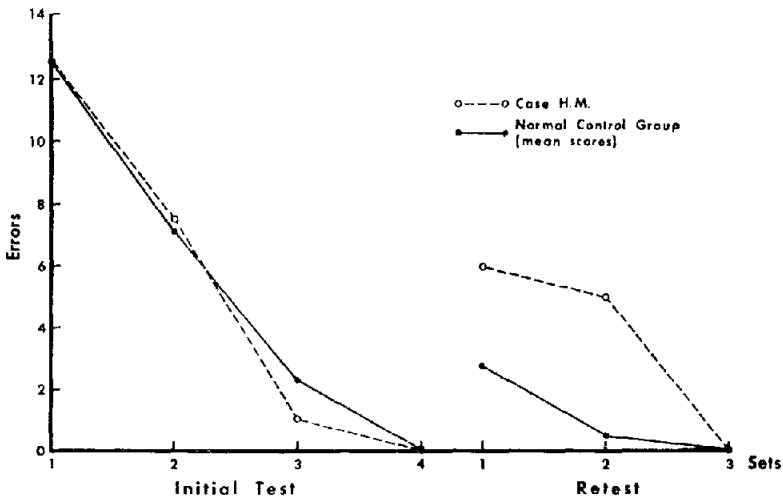

FIG. 12. Graph showing H.M.'s performance on the incomplete-pictures task, as compared with that of a group of four normal control subjects matched for age, sex, and initial error score on this test. Both H.M. and the control subjects made fewer errors on re-testing, one hour after the initial test, but H.M.'s performance did not improve as much as that of the control subjects.

One can, however, argue that this is a very different learning task for normal subjects, who can rely on verbal memory as a guide, than it is for an amnesic patient. Once the normal subject has identified a picture, the name of the object is facilitated, so that when the most sketchy versions are presented a second time, he has many of the correct names ready to try out. Since the items of Set 1 are not similar to each other, normal subjects will be aided in their guessing by the limited choice of verbal labels. We do not know if they would fare any better than H.M. without this added prop.

DISCUSSION

This patient with bilateral mesial temporal-lobe resection and severe anterograde amnesia has now been followed for 14 years. His condition has remained essentially the same, although our interval history (based on home visits and a two-week hospitalization for more intensive study) reveals some very slight improvement, remarkable perhaps only because it seemed to occur at such late date. The central feature of the amnesia continues to be a failure in long-term retention for most ongoing events, in the absence of any general intellectual loss or perceptual disorder. The lack of intellectual deterioration is underscored by the fact that on standard tests of intelligence H.M. does better now than before the operation, and that his performance on such tests, as also on special tests of sorting and categorizing, is above average. The integrity of his perceptual capacities has been established on a wide range of visual and auditory tasks. A particularly instructive instance, encountered in the course of the present studies, is his ability to perceive poorly-defined silhouettes of faces. In sharp contrast to such an achievement, we noted his complete inability to remember photographs of new faces after a delay as short as two minutes, if some distracting task was introduced during the interval. It is equally characteristic of this patient that memories from his early life before the operation appear to be intact, and can be retrieved at will, except for an ill-defined period of retrograde amnesia covering the one or two years just before the operation.

In this and similar cases, in spite of a severe anterograde amnesia, short-term memory (as measured by digit span and related tasks) is essentially unimpaired (DRACHMAN and ARBIT [4]; MILNER [19]; TEUBER et al. [33]; WICKELGREN [38]). It is true that H.M.'s span of six digits forward and five back is rather low for his intelligence level, but it is actually higher now than before the operation, when he was having many more small attacks. Moreover, superior performance on span tests has been observed in other cases of anterograde amnesia produced by bilateral damage to the hippocampal zone (PENFIELD and MILNER [26]). In the case of P.B., a civil engineer, the amnesia developed after left mesial temporal-lobe resection, involving the uncus, amygdala, hippocampus and hippocampal gyrus, and it persisted until his death, from unrelated causes, some fifteen years later. At autopsy, Dr. Gordon Mathieson found that the right hippocampus was atrophic, the extent of the destruction actually exceeding that on the left caused by the surgical removal. This patient, whose amnesia resembled that of H.M., was able, nevertheless, to repeat 9 digits forward and 7 back, and to perform complicated mental arithmetic quickly and accurately.

The intact capacity for immediate registration can also be demonstrated on the Seashore Tonal Memory test, in which a short melody of three to five notes is played twice in rapid succession and the subject's task is to say which note changed at the second playing. As was noted in an earlier report (MILNER [19]), H.M.'s performance on this task was

normal, and so was that of the amnesic patients, P.B. and F.C., described by PENFIELD and MILNER [26].

All of these observations support the view that the essential difficulty of these patients is not in primary registration, or short-term memory as such, but in some secondary process by which the normal subject achieves the transition to long-term storage of information. On the other hand, some of the new observations on H.M. that are reported here suggest that his failure to establish long-term traces is not absolute. The relative sparing of motor learning is now clearly established (CORKIN [2]). In addition, H.M.'s performance on the Gollin incomplete-pictures test shows that he is capable of some perceptual learning. Lastly, even for material that he ordinarily does not retain, some vestiges of learning can be demonstrated with intensive practice. By radically shortening a visual and a tactual maze, so as to bring the sequence of required turns within his immediate memory span, we have demonstrated some learning, with partial retention over one or several days; but acquisition of these short sequences was extremely slow, and it is not known how far his capacity for partial recall would have extended beyond the intervals employed in these experiments.

The patient's behaviour in test situations was in many respects parallel to his performance in everyday life. He seems to have learned something about the constant features of his environment, such as the general arrangement of rooms and furniture in his home. He also occasionally appears to remember some outstanding personal or public event, though with little consistency from day to day. When at home he realizes that his father is dead; he once recognized President Kennedy's profile on a coin and seemed to be familiar with the name of one of the most prominent astronauts. Just as in test situations, these achievements appear to depend on frequent repetition of the items and their embedding in a constant framework. His retention of test instructions seemed to be of this sort, as when he closed his eyes unasked during the later stages of sensory examinations, or when he correctly described the use of a stylus and a bell after prolonged training on one of the mazes.

Another parallel between test situation and real life was evident in the pattern of H.M.'s wrong turns on the tactual maze. This maze, unlike the visual one used in this study, does not afford an overall appreciation of the array of choice-points and possible routes, and in this respect it resembles more closely the actual situation of finding one's way in a city. H.M. had abnormal difficulty at the initial choice-points on the tactual maze but made relatively few mistakes at the choice-points near the finish of the path. Similarly he lost his way when trying to guide us to his home; he could not find the way at first, but got his bearings in the immediate vicinity of his house.

Our emphasis upon some residual learning capacities, shown in the laboratory and in real life, should not detract from the continuing gravity of H.M.'s amnesic state. Despite the fact that even this radical bilateral removal from the hippocampal zone was incomplete, and that 14 years have elapsed since the operation, the patient still lives from moment to moment and remains totally incapable of looking after himself. Among the residual capacities tested, those involving the learning of motor skill were probably the least affected and it is questionable whether an even more drastic removal in the same region would have disturbed them seriously. In contrast, the very slight learning on other tasks, only demonstrable with intensive training, may well reflect the incompleteness of the lesion, which permits some recovery of function with time. In comparing H.M. with other patients whose amnesia also resulted from bilateral involvement of the hippocampal region, it

becomes evident that some of the associated symptoms in H.M.'s case are not a necessary part of the memory disorder. His sensory defects may have antedated the operation and corresponding sensory changes were absent in other cases (PENFIELD and MILNER [26]). The significance of what appear to be a diminished responsiveness to pain and a lack of sexual interest is more difficult to assess, although other patients, such as P.B., have shown a combination of postoperative amnesia with reduction in sexual drive.

All in all, we remain impressed with the central role of the learning impairment in these patients; we believe that any associated changes in drive or initiative, or the relative evenness of their temperaments, cannot account for the profound forgetfulness that envelops most aspects of their lives.

REFERENCES

1. CORKIN, SUZANNE. Tactually-guided maze-learning in man: Effects of unilateral cortical excisions and bilateral hippocampal lesions. *Neuropsychologia* 3, 339–351, 1965.
2. CORKIN, SUZANNE. Acquisition of motor skill after bilateral medial temporal-lobe excision. *Neuropsychologia* 6, 255–265, 1968.
3. DORFF, J. E., MIRSKY, A. F. and MISHKIN, M. Effects of unilateral temporal lobe lesions. *Neuropsychologia* 3, 39–52, 1965.
4. DRACHMAN, D. A. and ARBIT, J. Memory and the hippocampal complex. *Arch. Neurol.* 15, 52–61, 1966.
5. GOLLIN, E. S. Developmental studies of visual recognition of incomplete objects. *Percept. Mot. Skills* 11, 289–298, 1960.
6. GOTTSCHALDT, K. Über den Einfluss der Erfahrung auf die Wahrnehmung von Figuren. *Psychol. Forsch.* 8, 261–317, 1926; 12, 1–87, 1929.
7. GRANT, D. A. and BERG, ESTA. A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. *J. exp. Psychol.* 38, 404–411, 1948.
8. HEBB, D. O. *The Organization of Behavior*. John Wiley, New York, 1949.
9. HEBB, D. O. and PENFIELD, W. Human behavior after extensive bilateral removals from the frontal lobes. *Arch. Neurol. Psychiat.* 44, 421–438, 1940.
10. KIMBLE, D. P. The effects of bilateral hippocampal lesions in rats. *J. comp. physiol. Psychol.* 56, 273–283, 1963.
11. KIMURA, DOREEN. Right temporal-lobe damage. *Arch. Neurol.* 8, 264–271, 1963.
12. LANSDELL, H. C. Effect of extent of temporal lobe ablations on two lateralized deficits. *Physiol. Behav.* 3, 271–273, 1968.
13. MAHUT, HELEN and CORDEAU, J. P. Spatial reversal deficit in monkeys with amygdalo-hippocampal ablations. *Exp. Neurol.* 7, 426–434, 1963.
14. MILNER, BRENDA. Intellectual function of the temporal lobes. *Psychol. Bull.* 51, 42–62, 1954.
15. MILNER, BRENDA. Psychological defects produced by temporal lobe excision. *Res. Publ. Ass. Res. nerv. ment. Dis.* 36, 244–257, 1958.
16. MILNER, BRENDA. Les troubles de la mémoire accompagnant des lésions hippocampiques bilatérales. In *Physiologie de l'Hippocampe*, pp. 257–272. Centre National de la Recherche Scientifique, Paris, 1962.
17. MILNER, BRENDA. Effects of different brain lesions on card sorting. *Arch. Neurol.* 9, 90–100, 1963.
18. MILNER, BRENDA. Visually-guided maze learning in man: effects of bilateral hippocampal, bilateral frontal, and unilateral cerebral lesions. *Neuropsychologia* 3, 317–338, 1965.
19. MILNER, BRENDA. Amnesia following operation on the temporal lobes. In *Amnesia*, C. W. M. WHITTY and O. L. ZANGWILL (Editors), pp. 109–133. Butterworths, London, 1966.
20. MILNER, BRENDA. Visual recognition and recall after right temporal-lobe excision in man. *Neuropsychologia* 6, 191–209, 1968.
21. MILNER, BRENDA and TEUBER, H.-L. Alteration of perception and memory in man: reflections on methods. In *Analysis of Behavioral Change*, L. WEISKRANTZ (Editor), pp. 268–375. Harper and Rowe, New York, 1968.
22. MOONEY, C. M. Closure with negative after-images under flickering light. *Canad. J. Psychol.* 10, 191–199, 1956.
23. MUNN, N. L. *Psychology*, (2nd Ed.). Houghton-Mifflin, Boston, 1951.
24. NEWCOMBE, FREDA. Double dissociation after focal cerebral injury. In *Hemispheric Asymmetry of Function*, M. KINSBOURNE (Editor). Tavistock, London (in press).

25. OSTERRIETH, P. Le test de copie d'une figure complexe. *Arch. Psychol.* **30**, 206–356, 1944.
26. PENFIELD, W. and MILNER, BRENDA. Memory deficit produced by bilateral lesions in the hippocampal zone. *A.M.A. Arch. Neurol. Psychiat.* **79**, 475–497, 1958.
27. REY, A. L'examen psychologique dans les cas d'encéphalopathie traumatique. *Arch. Psychol.* **28**, No. 112, 1942.
28. SCOVILLE, W. B. The limbic lobe in man. *J. Neurosurg.* **11**, 64–66, 1954.
29. SCOVILLE, W. B. Amnesia after bilateral mesial temporal-lobe excision: Introduction to Case H.M. *Neuropsychologia* **6**, 211–213, 1968.
30. SCOVILLE, W. B. and MILNER, BRENDA. Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiat.* **20**, 11–21, 1957.
31. STONE, C. P., GIRDNER, J. and ALBRECHT, RUTH. An alternate form of the Wechsler Memory Scale. *J. Psychol.* **22**, 199–206, 1946.
32. TEUBER, H.-L., BATTERSBY, W. S. and BENDER, M. B. Performance of complex visual tasks after cerebral lesions. *J. nerv. ment. Dis.* **114**, 413–429, 1951.
33. TEUBER, H.-L., MILNER, BRENDA and VAUGHAN, H. G., JR. Persistent anterograde amnesia after stabwound of the basal brain. *Neuropsychologia* **6**, 267–282, 1968.
34. TEUBER, H.-L. and WEINSTEIN, S. Ability to discover hidden figures after cerebral lesions. *A.M.A. Arch. Neurol. Psychiat.* **76**, 369–379, 1956.
35. VIGNOLO, L. A. Factors underlying impairment of visual figure-ground discrimination and sorting tasks in hemisphere-damaged patients. In *Hemispheric Asymmetry of Function*, M. KINSBOURNE (Editor). Tavistock, London, (in press).
36. WARRINGTON, ELIZABETH K. and WEISKRANTZ, L. New method of testing long-term retention with special reference to amnesic patients. *Nature* **217**, 972–974, 1968.
37. WEIGL, E. On the psychology of so-called processes of abstraction. *J. abn. soc. Psychol.* **36**, 3–33, 1941, translated by Margaret J. Rioch from Zur Psychologie sogenannter Abstraktionsprozesse. *Z. Psychol.* **103**, 2–45, 1927.
38. WICKELGREN, W. A. Sparing of short-term memory in an amnesic patient: implications for strength theory of memory. *Neuropsychologia* **6**, 235–244, 1968.

Résumé—Cet article a pour but de délimiter certaines possibilités résiduelles d'apprentissage chez H.M., jeune homme devenu amnésique en 1953, à la suite d'une ablation bilatérale de la région de l'hippocampe. En plus d'être capable d'acquérir de nouvelles habiletés motrices (CORKIN [2]), ce malade manifeste un certain degré d'apprentissage perceptif. Il manifeste aussi un progrès réel dans la maîtrise de labyrinthes visuel et tactile très simples, où la série des tournants obligatoires est suffisamment courte pour s'inscrire dans le champ d'appréhension de la mémoire immédiate. Même dans ce cas, l'acquisition est extrêmement lente. Ces vestiges d'aptitudes, qui réapparaissent à l'occasion dans la vie quotidienne du malade, sont évalués sur un fond d'amnésie profonde atteignant la plupart des évènements courants, amnésie qui persiste en dépit d'une intelligence au-dessus de la moyenne et d'un rendement supérieur dans l'exécution de plusieurs tâches perceptives.

Zusammenfassung—Dieser Bericht versucht die übrig gebliebenen Lernfähigkeiten im Fall H.M. zu kennzeichnen, bei dem ein amnestisches Syndrom im Jahr 1953 nach beidseitiger Abtragung der Ammonshornrinde auftrat. Ausser der fortdauernden Fähigkeit, neue motorische Geschicklichkeiten zu erwerben (CORKIN [2], war es dem Patienten möglich, gewisse Lernfähigkeiten an Wahrnehmungsprüfungen aufzuweisen. Er brachte es auch zustande (obwohl ausserordentlich langsam) einige sehr einfache visuell und taktil dargebotene Labyrinthe zu behalten, bei denen die Zahl der sukzessiven Wendepunkte so verringert wurde, dass sie in das kurzfristige Gedächtnis des Patienten passte. Diese Spuren von langfristigen Gedächtnisleistungen, die ihre gelegentlichen Parallelen im gewöhnlichen Tageslauf des Patienten fanden, werden der weitgehenden Amnesie gegenübergestellt, die trotz überdurchschnittlicher Intelligenz und hervorragender Wahrnehmungsleistungen weiter andauert.