Clinical Cases That Reveal the Anatomical Substrate for Declarative Memories

The Case of H.M.

At the age of 27, H.M., who had suffered minor seizures since age 10 and major seizures since age 16, underwent surgery to correct his increasingly debilitating epilepsy. A high school graduate, H.M. had been working as a technician in a small electrical business until shortly before the time of his operation. His attacks involved generalized convulsions with tongue biting, incontinence, and loss of consciousness (all typical of grand mal seizures). Despite a variety of medications, the seizures remained uncontrolled and increased in severity. A few weeks before his surgery, H.M. became unable to work and had to quit his job.

On September 1, 1953, a bilateral medial temporal lobe resection was carried out in which the amygdala, uncus, hippocampal gyrus, and anterior two-thirds of the hippocampus were removed. At the time, it was unclear that bilateral surgery of this kind would cause a profound memory defect. Severe amnesia was evident, however, upon H.M.'s recovery from the operation, and his life was changed radically.

The first formal psychological exam of H.M. was conducted nearly 2 years after the operation, at which time a profound memory defect was still obvious. Just before the examination, for instance, H.M. had been talking to the psychologist; yet he had no recollection of this experience a few minutes later, denying that anyone had spoken to him. He gave the date as March 1953 and seemed oblivious to the fact that he had undergone an operation, or that he had become incapacitated as a result. Nonetheless, his score on the Wechsler-Bellevue Intelligence Scale was 112, a value not significantly different from his preoperative IQ. Various psychological tests failed to reveal any deficiencies in perception, abstract thinking, or reasoning; he seemed highly motivated and, in the context of casual conversation, normal. Importantly, he also performed well on tests of the ability to learn new skills, such as mirror writing or puzzle solving (that is, his ability to form procedural memories was intact). Moreover, his early memories were easily recalled, showing that the structures removed during H.M.'s operation are not a permanent repository for such information. On the Wechsler Memory Scale (a specific test of declarative memory), however, he performed very poorly, and he could not recall a preceding test-set once he had turned his attention to another part of the exam. These deficits, along with his obvious inability to recall events in his daily life, all indicate a profound loss of short-term declarative memory function.

During the subsequent decades, H.M. has been studied extensively, primarily by Brenda Milner and her colleagues at the Montreal Neurological Institute. His memory deficiency has continued unabated, and, according to Milner, he has little idea who she is in spite of their acquaintance for nearly 50 years. Sadly, he has gradually come to appreciate his predicament. “Every day is alone,” H.M. reports, “whatever enjoyment I've had and whatever sorrow I've had.” TOP

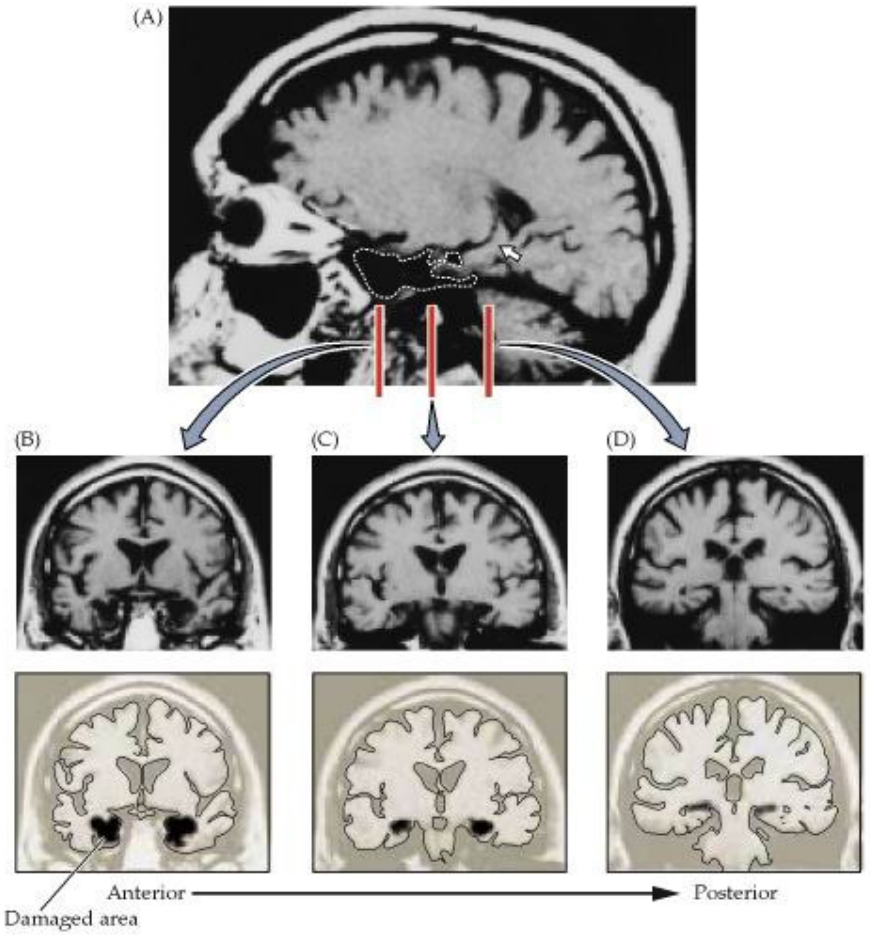
The Case of N.A.

N.A. was born in 1938 and grew up with his mother and stepfather, attending public schools in California. After a year of junior college, he joined the Air Force. In October of 1959 he was assigned to the Azores as a radar technician and remained there until December 1960, when a bizarre accident made him a celebrated neurological case. N.A. was assembling a model airplane in his barracks room while his roommate, unbeknownst to him, was making thrusts and parries with a miniature fencing foil behind N.A.'s chair. N.A. turned suddenly and was stabbed through the right nostril. The foil penetrated the cribriform plate (the structure through which the olfactory nerve enters the brain) and took an upward course into the left forebrain. N.A. lost consciousness within a few minutes (presumably because of bleeding in the region of brain injury) and was taken to a hospital. There he exhibited a right-sided weakness and paralysis of the right eye muscles innervated by the third cranial nerve. Exploratory surgery was undertaken and the dural tear repaired. Gradually he recovered and was sent home to California. After some months, his only general neurological deficits were some weakness of upward gaze and mild double vision. He retained, however, a severe anterograde amnesia for declarative memories. MRI studies first carried out in 1986 showed extensive damage to the thalamus and the medial temporal lobe, mostly on the right side; the mammillary bodies also appeared to be missing bilaterally. The exact extent of his lesion, however, is not known, as N.A. remains alive and well.

N.A.'s memory from the time of his injury over 40 years ago to the present has remained impaired, and like H.M. he fails badly on formal tests of new learning ability. His IQ is 124, and he shows no defects in language skills, perception, or other measures of intelligence. He can also learn new procedural skills quite normally. His amnesia is not as dense as that of H.M. and is more verbal than spatial. He can, for example, draw accurate diagrams of material presented to him earlier. Nonetheless, he loses track of his possessions, forgets what he has done, and tends to forget who has come to visit him. He has only vague impressions of political, social, and sporting events that have occurred since his injury. Watching television is difficult because he tends to forget the storyline during commercials. On the other hand, his memory for events prior to 1960 is extremely good; indeed, his lifestyle tends to reflect the 1950s. TOP

The Case of R.B.

At the age of 52, R.B. suffered an ischemic episode during cardiac bypass surgery. Following recovery from anesthesia, a profound amnesic disorder was apparent. As in the cases of H.M. and N.A., his IQ was normal (111), and he showed no evidence of cognitive defects other than memory impairment. R.B. was tested extensively for the next five years, and, while his amnesia was not as severe as that of H.M. or N.A., he consistently failed the standard tests of the ability to establish new declarative memories. When R.B. died in 1983 of congestive heart failure, a detailed examination of his brain was carried out. The only significant finding was bilateral lesions of the hippocampus—specifically, cell loss in the CA1 region that extended the full rostral-caudal length of the hippocampus on both sides. The amygdala, thalamus, and mammillary bodies, as well as the structures of the basal forebrain, were normal. R.B.'s case is particularly important because it suggests that hippocampal lesions alone can result in profound anterograde amnesia for declarative memory.



MRI images of the brain of patient H.M. (A) Sagittal view of the right hemisphere; the area of the anterior temporal lobectomy is indicated by the white dotted line. The intact posterior hippocampus is the banana-shaped object indicated by the white arrow. (B-D) Coronal sections at approximately the levels indicated by the red lines in (A). Image (B) is the most rostral and is at the level of the amygdala. The amygdala and the associated cortex are entirely missing. Image (C) is at the level of the rostral hippocampus; again, this structure and the associated cortex have been removed. Image (D) is at the caudal level of the hippocampus; the posterior hippocampus appears intact, although somewhat shrunken. Outlines below give a clearer indication of the parts of H.M.'s brain that have been ablated (black shading). (From Corkin et al., 1997.) TOP

References

S. Corkin. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H.M *Semin. Neurol.* 4: 249-259.

S. Corkin, D. G. Amaral, R. G. González, K. A. Johnson, and B. T. Hyman. (1997). H. M's medial temporal lobe lesion: Findings from MRI. J *Neurosci.* 17: 3964-3979.

Hilts, P. J. (1995) *Memory's Ghost: The Strange Tale of Mr. M. and the Nature of Memory* . New York: Simon and Schuster.

B. Milner, S. Corkin, and H.-L. Teuber. (1968). Further analysis of the hippocampal amnesic syndrome: A 14-year follow-up study of H.M *Neuropsychologia* 6: 215-234.

W. B. Scoville and B. Milner. (1957). Loss of recent memory after bilateral hippocampal lesions *J. Neurol. Neurosurg. Psychiat.* 20: 11-21.

L. R. Squire, D. G. Amaral, S. M. ZolaMorgan, M. Kritchevsky, and G. Press. (1989). Description of brain injury in the amnesic patient N.A based on magnetic resonance imaging *Exp. Neurol.* 105: 23-35. (PubMed)

H. L. Teuber, B. Milner, and H. G. Vaughn. (1968). Persistent anterograde amnesia after stab wound of the basal brain *Neuropsychologia* 6: 267-282.

S. Zola-Morgan, L. R. Squire, and D. Amaral. (1986). Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to the CA1 field of the hippocampus *J. Neurosci.* 6: 2950-2967. (PubMed)