COMMENTARY


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Since publication of the landmark article describing his severe memory impairment (Scoville and Milner, 1957), patient H.M. has been a touchstone for research on amnesia and memory systems (Corkin, 2002). After surgical resection of a majority of his medial temporal lobes, H.M. experienced profound forgetfulness. Yet it was the observation of spared cognitive abilities such as attention and language combined with the subsequent demonstration of intact skill learning (e.g., Milner, 1962) that made his case surprising and truly fascinating. The dramatic combination of severity and purity in his memory impairment spurred decades of research in humans and animals that has lead to our current understanding of memory systems. The medial temporal lobe structures that were damaged in patient H.M. support what one typically thinks of as memory, a capacity termed declarative memory, but are not critically involved in examples of nondeclarative memory such as priming or habit learning or in other nonmemory cognitive abilities (Squire, 1992; Gabrieli, 1998; Eichenbaum and Cohen, 2001).

Almost as impressive as the initial breakthrough is the fact that H.M. continues to contribute to the study of memory. In this issue of Hippocampus, O’Kane, Kinsinger, and Corkin present new findings showing that H.M. has learned knowledge about the world that could have been acquired only after his surgery. The authors asked H.M. to recall last names of famous individuals when cued either by the individual’s first name or by first name plus a brief description. H.M. recalled 12 of 35 names (e.g., Johnson) when cued by first name (e.g., Lyndon) and 11 of the remaining 23 (23 of 35 total) when additionally cued with a brief description of the individual. In a second experiment, H.M. recalled extra factual information for a number of famous names that he correctly recognized. For example, he described John F. Kennedy (J.F.K.) as a Catholic president who was assassinated. That his learning is below normal is not surprising. What is surprising is that he learned at all.

Why are the findings surprising? First, previous accounts of H.M.’s impairment reported almost no learning of factual information (e.g., Gabrieli et al., 1988). The current findings are the first in five decades of study to report substantive and unmistakable postmorbid declarative learning in patient H.M. Second, H.M.’s medial temporal lobe damage is extensive and includes partial damage to the perihinal cortex, complete destruction of the entorhinal cortex, and a combination of damage and disconnection that has left the hippocampus nonfunctional. Thus, the learning was supported either by the parahippocampal cortex and damaged perihinal cortex or by structures outside the medial temporal lobe. Third, his ability to retrieve day-to-day memory is reportedly nonexistent.

The latter two findings are consistent with the view that the hippocampus contributes crucially to episodic memory, but not to semantic memory (Vargha-Khadem et al., 1997; Tulving and Markowitsch, 1998), an interpretation considered by O’Kane et al. (this issue). Episodic memory refers to the ability to reexperience the first-hand specifics of an event. Semantic memory refers to knowledge about the world that is not necessarily tied to a particular incident. H.M. acquired knowledge about the world despite an inability to recollect details of specific instances. Thus, it is possible that damage to the hippocampus and other medial temporal lobe structures eliminated his capacity for episodic remembering but left partially intact his ability to acquire new semantic memory. If so, the results of the study support the connection that has been argued to exist between the specialized anatomy and plasticity of the hippocampus and the uniqueness of episodic memory (Mishkin et al., 1998; Nadel et al., 2000).

The authors also consider the possibility that the difference between the knowledge that H.M. was able to acquire and the episodic details that invariably escape him might have more to do with the opportunities for learning rather than the category of retrieval (Alvarez and Squire, 1994; McClelland et al., 1995; Holdstock et al., 2002). The information that H.M. has learned since his surgery could have been encountered numerous times over the decades. In contrast, episodic memory by definition can draw on only a single incident. Thus, it is possible that H.M.’s damage did not impair episodic memory per se but rather severely disrupted declarative memory in such a way that one-trial learning was abolished, allowing learning only through extended repetition.

The results of the article by O’Kane et al. cannot distinguish between the two possibilities, and the authors do not consider the alternatives to be incompatible. Indeed, the similarity between the concepts of episodic memory and single-trial declarative memory would make resolving the alternatives challenging. Nevertheless, it is useful to consider whether episodic memory captures the entirety of the contribution made by the hippocampus to declarative memory or whether a more general, mechanistic description of its function is warranted. Several points are worth discussing.

First, H.M. shows the opposite pattern of performance as compared to his controls. H.M.’s best performance comes from the decades immediately following his surgery whereas
controls performed best on names from the most recent decades. H.M. would have been exposed to news of these famous individuals on numerous occasions, and his learning may have been possible only through repeated exposure over several decades. Indeed, the authors suggest that the repeated availability of the famous names may have allowed H.M. to perform better than he has in previous experiments in which he had less opportunities to encode the test material.

Second, although it may not be ultimately necessary, it seems that the hippocampus ordinarily contributes to the acquisition of semantic memory in healthy individuals. H.M.’s knowledge of individuals who became famous after his surgery is surprising in light of the extreme severity of his amnesia, yet it is nevertheless well below normal. Indeed, the typical finding with other memory-impaired patients is that, although they are able to acquire some factual information, they do so at a slower pace than healthy individuals (Manns and Squire, 2002; see Baddeley et al., 2001, for an example of moderately slowed but otherwise good semantic learning in a case of developmental amnesia). Of course, it is possible that H.M. and other patients performed worse than their controls because of damage to structures other than the hippocampus. However, in a recent study patients with damage thought to be relatively restricted to the hippocampal region (CA fields, dentate gyrus, subicular complex) showed reduced acquisition of factual information after they became amnesic, even when their performance was compared to the subset of control responses that could not have been aided by episodic detail (Manns et al., 2003). Thus, although it may yet make some unique contribution to episodic memory, the hippocampus appears also to be involved in semantic memory.

Third, structures other than the hippocampus appear to make important contributions to episodic memory. Patients with damage to the hippocampal region, including patients for whom neurohistological analysis revealed neuronal loss in all cell fields of the hippocampus (Baddeley et al., 2001), often display residual episodic memory (e.g., Shimamura and Squire, 1991). Thus, the structures in the medial temporal lobe other than the hippocampus appear to be able to support some degree of episodic memory when the extrahippocampal damage is less severe than that of patient H.M. Further, patients with frontal lobe damage are impaired at retrieving the source of information that they have learned (e.g., Janowsky et al., 1989), a capacity that is a crucial component of episodic remembering.

The hippocampus enjoys a position of anatomical privilege and undoubtedly offers a contribution to declarative memory that is unavailable to the other structures within the medial temporal lobe. The surprising findings with patient H.M. suggest that this contribution is important for day-to-day memory but is not ultimately necessary for slow acquisition of factual knowledge. However, the distinction between episodic memory and semantic memory does not provide a clear dissociation between the contributions to declarative memory of the hippocampus and other structures important for memory. Indeed, the hierarchical arrangement and thick interconnectivity of the medial temporal lobe (Lavenex and Amaral, 2000) would make any clean dissociation unlikely. It remains possible that the contribution of the hippocampus is simultaneously unique in its mechanistic detail and pervasive with respect to the examples of declarative memory in which it participates. If so, the capabilities of the hippocampus may be understood in part by defining the limitations of the other structures within the medial temporal lobe. Although the results of the study by O’Kane et al. do not provide clear evidence for a distinction between episodic and semantic memory, H.M.’s apparent inability to learn factual information from a single exposure suggests an intriguing limitation for his intact parahippocampal cortex.

REFERENCES


