



## In Praise of the Amnesia Case Study

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*As clinicians, we can daily apply knowledge learned from a few patients with pure amnesia to patients we see often—those who have memory deficits, such as so-called Mild Cognitive Impairment and neurodegenerative diseases, such as Alzheimer's.*

We know them by their initials. Hardly ever will we know their names during their lives. But our knowledge about memory functioning owes them a significant debt.

There are few instances in clinical neurology and neuropsychology where so much was learned from so few than in the essential individual case studies about amnesia. Most of us will never see a person with "pure" amnesia in our practices. Their rarity belies the impact they have had on our current understanding of what memory is in its normal functioning and in its pathological states.

Of course, it all starts with Henry.



Henry Molaison – patient H.M. -- in 1953 before surgery. (Wikipedia)

Henry. Patient H.M. as he was known from the mid-1950s until his death in 2008; Henry Molaison thereafter. A smattering of case studies can be found in the memory literature as it stood before him, but Henry was our pivot point. An inquisitive neurosurgeon not satisfied with accepting the status quo and a young, energetic neuropsychologist (who is still performing research today, now in her mid-90s) together presented the case of H.M. to the neurological community; we still reap the benefits of what they began. William Scoville, a New England neurosurgeon, was engaged in determining the impact of temporal lobe resections in the early 1950s for patients with epilepsy intractable to the limited medications of the day. A mid-twenties man, H.M., was one such individual. Dr. Scoville removed H.M.'s bilateral medial temporal lobe tissue, including significant amounts of his left and right hippocampus. Reduction in seizure activity was significant. However, Scoville noted a serious behavioral change in H.M. after the surgery—he was unable to retain new information and this did not resolve over time.

The neuropsychologist, Brenda Milner, performed cognitive assessments of H.M. Drs. Scoville and Milner reported their results in one of most frequently cited papers in the neurosciences, Scoville & Milner (1957),<sup>1</sup> wherein both H.M.'s operation and subsequent total anterograde amnesia was detailed. Thus, being unable to form new memories (anterograde amnesia) was on its way to becoming the hallmark feature of what was to become known as hippocampal amnesia, the prototype of a permanent amnesia due to brain damage.

Over the decades, studying Henry offered novel findings that led to our current knowledge of amnesia and memory. His retrograde amnesia (ie, loss of access to what had been previously learned and remembered) turned out to be far more substantial than initially thought. In addition, Milner's creativity in using tests elicited entire domains in what we now call "motor" or "non-declarative" learning wherein H.M. showed evidence of learning via improved performance (rather than recollection) as well as did neurologically intact persons.<sup>2</sup> (Corkin, 2013). Henry's brain was preserved in whole at death, sectioned into 2401 slices a year later, and in early 2014 presented as an online 3-D digital archive accessible by

But Henry is not alone in his contribution to contemporary behavioral neurology.

There was Patient R.B. studied by Drs Stuart Zola-Morgan and Larry Squire of San Diego, Clive Wearing studied by Cambridge's Dr Barbara Wilson, Patient K.C. studied by Dr Endel Tulving of Toronto, and a small community of other patients who continue to instruct us with the collected knowledge accumulated by their detailed individual study.

While Henry was key to opening the story relating amnesia to the hippocampus and surrounding medial temporal lobe, R.B. demonstrated the specificity of the key role of the CA1 field within the hippocampus.<sup>3</sup> (Zola-Morgan and colleagues, 1986).

Clive Wearing, unlike Henry and R.B., had nothing really to hold on to but the present moment. Wearing—a public figure in the UK prior to the herpes simplex encephalopathy, which resulted in full anterograde and retrograde amnesia—was the public face of amnesia for many years. He appeared in various British science documentaries and on American *60 Minutes*. He would constantly, moment by moment, experience the sense of becoming awake, as he noted in his diary, "for the first time ever!"<sup>4</sup> (Sacks, 2007).

Patient K.C., who died earlier this year and who was identified posthumously as Kent Cochrane, became central to our understanding of episodic memory. He was studied for many years by Endel Tulving and his colleagues<sup>5</sup> (1988), who developed the concept and operationalization of episodic memory. K.C., who sustained an amnesia syndrome following severe traumatic brain injury, showed the curious existence of someone who retained semantic knowledge about events and episodes in his life prior to the injury, but without any personal autobiographical sense of having lived them. Like watching old videos of someone else going through their daily life, K.C. lost the ability to retrieve the subjective, personally valuable sense of these episodes of his life prior to the injury.

These rare individuals are instructive not only for the science of behavioral neurology, but for reminding us of the value of knowing our patients. Contemporary practice rarely allows us time to replace our medical history with biographical narrative, but these cases point to the richness of lives that are impacted by neurological disease in and of itself. They show how this richness has created the fuller sense of memory function as being multifaceted both in health and in damage or disease. As clinicians, we can daily apply this knowledge with those patients far, far more commonly seen in practice for whom memory weaknesses and deficits are present, such as so-called Mild Cognitive Impairment and neurodegenerative diseases such as Alzheimer's.

## References:

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5. Tulving E, et al. Priming of semantic autobiographical knowledge: a case study of retrograde amnesia. *Brain Cognition.* 1988;8:3-20.

# A Systematic Review of the Prediction of Brain Amyloid Status: Michael Weiner, MD

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