The Anatomy of Amnesia

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The Anatomy of AMNESIA

New findings on people with a damaged hippocampus suggest a bold rethinking of the way we map the brain By Felipe De Brigard

ILLUSTRATION BY EIKO OJALA

An attractive way to think of the brain is as an atlas of the mind.

In 19th-century views of neuroanatomy, mental faculties were housed in specific regions of the brain. Though roundly debunked, recent thinking in neuroscience has similarly tended to identify brain areas with psychological concepts, such as memory and emotion.

Continents of brain cells are given monikers such as "emotion" and "perception." Within them, independent countries go by names such as "vision" and "audition."

The labels are not without reason. Landmark cases of people with unique forms of brain damage have allowed neuroscientists to isolate specific regions that appear vital to a particular skill or psychological process. And no case is more famous in neuroscience than that of Henry Molaison, better known as H.M.

H.M. suffered from severe epilepsy. In 1953 neurosurgeons tried out a new technique to ease his seizures, which involved surgically removing his hippocampus, a small, C-shaped structure in the middle of the brain, and some adjacent areas. Little did they know that the procedure would knock out H.M.'s ability to form new memories.

He could still remember experiences of his childhood, though. In numerous tests, he demonstrated that other cognitive functions, such as working memory, language, perception and reasoning, remained intact as well. With great practice, he could acquire new skills, although he never became aware of his own learning. As a result, psychologists and neuroscientists concluded that the hippocampus is dedicated to acquiring long-term conscious memories but is unnecessary for pretty much anything else.

This claim became part of the core doctrine of neuroscience. It has featured, unquestioned, in almost every brain science textbook of the past 50 years. A growing body of evidence, however, is challenging the idea that the hip-

FAST FACTS
THE SEAT OF MEMORY?

1. A brain region called the hippocampus has primarily been viewed as a mechanism for acquiring long-term conscious memories.
2. Recent findings, however, suggest that the hippocampus also plays a role in imagination, language, vision and numerous other mental functions.
3. These results indicate that areas in the brain most likely do not map neatly to psychological terms such as memory and perception.

JONATHAN KITCHEN *Getty Images*

pocampus is the seat of memory. It now seems that this brain area is key to a dazzling array of skills tied to basic human experience. Which brings us to an inevitable question: What does the hippocampus do?

The Brain's Sea Horse

When Venetian neuroanatomist Julius Caesar Aranzi first described these seven centimeters of brain tissue in 1587, he likened the structure to a sea horse (or *hippo,* "horse," and *kampus,* "sea monster"). It is nestled in the middle of the brain within the limbic system, a set of areas that serve to regulate emotions, among other basic processes. Before H.M.'s surgery, the function of the human hippocampus was largely unknown. Indeed, until the 1930s the prevailing belief was that the hippocampal region supported our sense of smell or, perhaps, our capacity to navigate.

Observations of H.M.'s amnesia gave rise to the idea that the hippocampus and its neighboring areas—termed the hippocampal complex—were necessary for encoding new memories of a certain type, those that require conscious and voluntary processing. These recollections, such as thinking back on one's first day in school or knowing that the capital of France is Paris, are called declarative memories. Nondeclarative (or implicit) memory was spared for H.M.: in one test, he demonstrated that with sufficient practice he could learn to draw a complicated and unfamiliar star-shaped pattern. He even managed to retain this proficiency for up to a year, despite the fact that he never remembered—declaratively, that is—having performed the task before.

H.M. also scored on par with healthy control subjects on a wide number of visual and linguistic tasks. In a comprehensive report published 14 years after his surgery, H.M's neuropsychologist, Brenda Milner, and her colleagues wrote that his linguistic comprehension remained "undisturbed: he can repeat and transform sentences with complex syntax, and he gets the point of jokes, including those turning on semantic ambiguity." We were also told that his capacity to retain information for a short time—his working memory—was preserved, as was his intellectual capacity. It seemed quite clear that the hippocampus's job was to encode declarative information.

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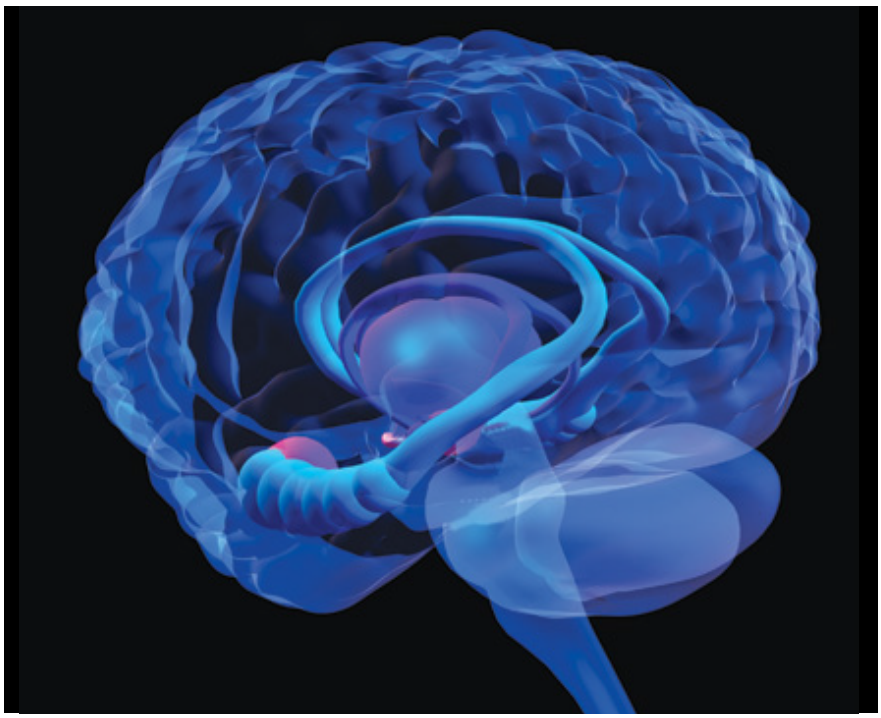
If only it were so simple. As H.M. aged (he lived until he was 82), his language faculties decayed more rapidly than did those of other people his age, revealing that the hippocampus helps us communicate. [For more on H.M.'s language abilities, see "The Engine of Memory," by Donald G. MacKay, on page 30.] Or consider the claim that the hippocampus is not involved in learning a new skill through repetition. Although he could technically pick up new skills, it took H.M. three or four times as long to reach the same level of mastery as healthy people.

Moreover, H.M. might have been less flexible than people normally are in their skill learning. In a 2010 study neuropsychologists Shumita Roy and Norman Park of York University in Toronto introduced seven people to several unfamiliar tools. One participant had a damaged hippocampus, and the other six served as controls. As expected, with practice all



AP PHOTO

The hippocampus, highlighted here with a rattlelike section toward the front of the brain, is a key structure in the formation of memories. Yet it also does much more.

THE AUTHOR

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People with damage to their hippocampus often have trouble identifying odd features in scenes. And when they are asked to imagine themselves in a certain scenario, such as relaxing on a sunny beach, their descriptions are far less vivid than those of healthy people.

"As for seeing, I can't really, apart from the sky. I can hear the sound of seagulls and of the sea … um … I can feel the grains of sand between my fingers …"

seven people got better at using these novel tools. Yet when tested a few days later, only the healthy subjects could still operate the tools. The affected patient could not even recall how to grasp them, let alone how to handle them. In short, adopting a new skill is not simply rehearsing something until it becomes automatic. We need to be able to bring other information back to mind as well.

The timing of a task can also wreak havoc on learning if a hippocampus is not around to help. A 2013 study by psychologist Karin Foerde of Columbia University and her colleagues revealed that individuals with hippocampal damage are unable to learn from feedback if it is delayed by even six seconds, as opposed to provided immediately. This was yet another ability that H.M. was believed to have retained, perhaps erroneously.

A Jack of All Trades?

The hippocampus even appears to help us see. Cognitive neuroscientist Morgan Barense of the University of Toronto, for example, compared the visual acuity of people with and without damage to the hippocampus. She observed that when a visual scene is complex, with objects overlapping and occluding one another, the patients' performance fell well below that of healthy subjects. A study from 2009 also supports the notion of a perceptual role for the hippocampus. Psychologists Donald G. MacKay of the University of California, Los Angeles, and Lori E. James of the University of Colorado Colorado Springs showed H.M. and several control subjects pictures of odd scenes, such as a bird flying inside a fishbowl or a door with its hinges on the same side as its knob. The task was to identify all the elements of the image that were wrong.

JOHN WILHELM *Getty Images (top)*; ALFONSE PAGANO *Getty Images (bottom)*

H.M. fared significantly worse than his healthy counterparts in two ways. He identified fewer wrong elements and misidentified as wrong more correct elements. In both studies, he seemed to struggle when trying to make sense of familiar pieces of information assembled in a manner or context that was novel.

What about reasoning and higher-order cognition, which appeared to be preserved in H.M.? One exception is imagination. In a striking demonstration published in 2007, Demis Hassabis, then at University College London, and his colleagues asked five individuals with hippocampal damage and 10 control participants to picture themselves in a certain place. In a representative response to the cue, "Imagine you are lying on a white sandy beach in a beautiful tropical bay," one patient replied:

"As for seeing, I can't really, apart from the sky. I can hear the sound of seagulls and of the sea … um … I can feel the grains of sand between my fingers … um … I can hear one of the ship's hooters [laughter] … um … that's about it."

When a researcher asked the patient, "Are you seeing this in your mind's eye?" the person said, "No, the only thing I see is blue."

In stark contrast, a healthy subject began a lengthy response in this way:

"It's very hot, and the sun is beating down on me. The sand underneath me is almost unbearably hot. I can hear the sounds of small wavelets lapping on the beach. The sea is a gorgeous aquamarine color. Behind me is a row of palm trees, and I can hear rustling every so often in the slight breeze."

Yet not all aspects of imagination are equally affected, as researcher Elizabeth Race of Boston University and her collaborators found in 2011. They compared how individuals with hippocampal damage and healthy participants fared when thinking about hypothetical events in their own life versus imagining a story based on a picture of others, such as a family at a picnic. Those who had damage struggled to imagine events in which they themselves might have participated, but they had no trouble weaving a narrative around the picnicking strangers.

Perhaps most surprising is the considerable body of research that now suggests that even working memory involves the hippocampus. Multiple neuropsychological tests had suggested that H.M.'s working memory was intact because he was able to follow simple sequential instructions and perform basic mental arithmetic without trouble. But keeping in mind unfamiliar objects for a few seconds or briefly retaining a complex scene seems to pose a challenge to people with hippocampal damage. Perhaps because the initial studies on H.M. used well-known items and familiar information, his probable deficits in these areas never surfaced.

A New Way of Thinking

So the lesson we thought we had learned from H.M., namely that the hippocampus's role is to encode declarative information into long-term memory, has been muddled by recent evidence. So what does the hippocampus in fact do?

One hypothesis is that it helps us bind together new information and integrate it with that which we have already learned. It might also allow us to connect information about individual items recorded in memory with new contexts. There may be others. Given the variety of cognitive activities for which the hippocampus appears to be essential, discovering the right conceptual framework remains a fascinating question—one that H.M. helped to formulate.

Perhaps, then, the real lesson of H.M. is the opposite of what was long taught: that we should be very careful when identifying mental terms—such as memory—with specific neural structures, such as the hippocampus. Neuroscientists widely accept that virtually every mental process invokes multiple brain regions. Yet we all, scientists and laypeople alike, rely on familiar notions such as memory and perception to frame our investigations of the mind and brain.

At a time in which so many scientific projects—the BRAIN Initiative in the U.S. and the Human Brain Project in Europe, among others—aim to produce "maps of the brain," we best not forget this lesson from H.M. The organizational principles of the brain might not mirror the categories we use to describe the mind's many functions. The brain is not an atlas of the mind. M

Perhaps the real lesson of H.M. is the opposite of what was long taught: that we should be careful when identifying mental terms—such as memory—with neural structures, such as the hippocampus.

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