

Studies say old memory can be lost

By Carey Goldberg,
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That schoolyard fight. That first date. That wild night in Vegas. Such memories seem immutable, like videotapes that can be taken down from a shelf in the mind and played over and over, always the same, until death or dementia erases them.

But one of the hottest topics in brain science is a spate of experiments in animals that seem to suggest that a seemingly permanent memory is not only vulnerable to change, but becomes vulnerable every time it is called to mind.

In essence, "your memory is only as good as your last memory, rather than based on your initial memory," said Joseph LeDoux, a prominent New York University neuroscientist at the forefront of the recent research.

It has long been known that memory can deceive. But the new research uses modern techniques of brain experimentation to show how a memory can be put at risk when it is recalled and then placed back into storage, or reconsolidated. Researchers have found that in rats, crabs, and chicks, long-term memories can be erased if they are recalled and then the brain is blocked from making the proteins apparently needed to lay down a memory.

"Psychologists have known for a long time about the changeability and malleability of memory, but we haven't had as striking a way of linking it to the brain mechanisms as this provides," said Daniel L. Schacter, chairman of Harvard's psychology department and author of "The Seven Sins of Memory."

Though the phenomenon has not yet been demonstrated in humans, LeDoux and others propose that a new understanding of memory's physical vulnerability could translate into clinical help. For example, he said, someone traumatized by a terrible memory might be able to call it up and then, while it was still in a vulnerable or labile state, erase the memory using drugs that kept it from being reconsolidated.

The work on reconsolidation is also likely to contribute to a broad sea change in how people think about memory, much as experiments demonstrating the formation of false memories in humans did, said Robert Stickgold, an assistant professor of psychiatry at Harvard Medical School .

The current research challenges a century-old notion that memory begins in an early, shaky, fragile stage and then may be consolidated, a one-time event, into a more stable, permanent memory.

Researchers first showed in animal experiments a generation ago that when long-term memories were called up they could be erased. But the research, which used electric shocks, fizzled.

Then, three years ago, the notion of reconsolidation came back.

In Ledoux's lab, Karim Nader and Glenn Shafe trained rats to expect that when they

heard a tone they would receive an electric shock to their feet. On hearing the tone, the rats would freeze in fear. Days later, when that fear memory was already consolidated, the researchers played the tone again to reactivate the memory. Soon after, they gave the rats a drug to prevent the amygdala, the part of the brain that stores fear memories, from making the proteins apparently needed for storage.

The results: The old, supposedly well-established fear memories disappeared, and the tone lost all terror for the rats.

"Our findings show that consolidated fear memories, when reactivated, return to a labile state" that needs new proteins to be stored all over again, the authors wrote in the journal *Nature* in 2000.

Since then, similar results have been found in crabs and chicks, as well as in rats, when the new proteins are blocked in a different part of the brain crucial for memory, the hippocampus.

That is enough replication to convince many that the phenomenon is real. But now "people are arguing about what reconsolidation actually is," said Vadim Bolshakov, director of the Cellular Neurobiology Laboratory at McLean Hospital, who researches the mechanisms of memory.

"Some people argue that every time we recall a memory, the old memory is erased and a new memory is created," he said. Others argue that the same old memory is being stored again. Some even hypothesize that the old memory is not destroyed, but that many copies of the same memory could exist in parallel.

In recent years, scientists have made progress toward understanding how memory works at the level of neurons and their connections. But too much remains unclear, Bolshakov said, even the identity of the proteins needed to lay down memories.

It is also open to argument, he said, whether the elaborate process of reconsolidation ultimately makes for better memories, because they have been reinforced by the new proteins, or worse memories, because they have been subject to distortion or erasure.

Stickgold said the reconsolidation research may cast light on the formation of false memories.

"Maybe false memories start as true memories, and because they're being reactivated and reactivated and having the chance to be erased, maybe this is a mechanism that explains how all these little changes over time take place," he speculated.

It will be a challenge to replicate the rat and crab results in humans, researchers noted.

For now, it remains "an open question: Does this extend to humans? What is the range of situations or tasks over which the phenomenon occurs?" Schacter said. "We just don't know that."

But even with those questions unanswered, the recent work "does highlight the view that many of us take, that we should not think of memory as something you pull up

and put back in the same way you would a computer file," he said. "It's much more dynamic."