Researchers identify method of creating long-lasting memories

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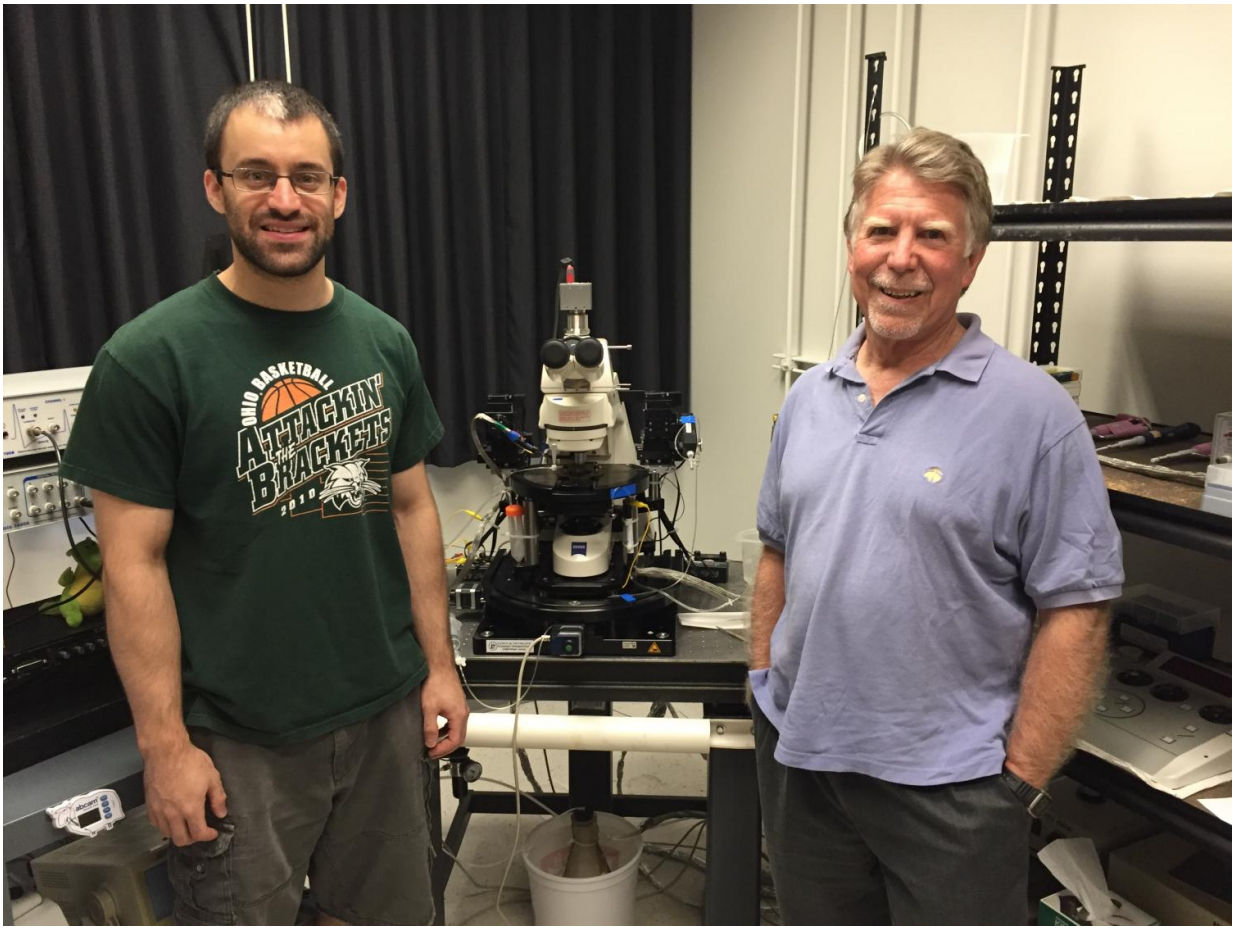

Dr. Robert Greene (right), Professor of Psychiatry and Neurosciences at UT Southwestern Medical Center, and Alex Sonneborn, in the UTSW neuroscience graduate program, stand next to a Zeiss Axoskop2, optogenetic stimulating and electrophysiology recording equipment that allows them to monitor and manipulate live neurons. Greene and Sonneborn are senior and lead authors, respectively, in a study that found attention-grabbing experiences trigger the

release of memory-enhancing chemicals to help etch memories into the brain. Credit: UT Southwestern Medical Center

Imagine if playing a new video game or riding a rollercoaster could help you prepare for an exam or remember other critical information.

A new study in mice shows this link may be possible.

Attention-grabbing experiences trigger the release of memory-enhancing chemicals. Those chemicals can etch memories into the brain that occur just before or soon after the experience, regardless of whether they were related to the event, according to researchers at UT Southwestern Medical Center's Peter O'Donnell Jr. Brain Institute.

The findings, published in *Nature*, hold intriguing implications for methods of learning in classrooms as well as an array of potential uses in the workplace and personal life, researchers said.

The trick to creating long-lasting memories is to find something interesting enough to activate the release of dopamine from the brain's locus coeruleus (LC) region.

"Activation of the locus coeruleus increases our memory of events that happen at the time of activation and may also increase the recall of those memories at a later time," said Dr. Robert Greene, the study's co-senior author and a Professor of Psychiatry and Neurosciences with the O'Donnell Brain Institute.

The study explains at the molecular level why people tend to remember certain events in their lives with particular clarity as well as unrelated details surrounding those events: for instance, what they were doing in

the hours before the Sept. 11, 2001, terrorist attacks; or where they were when John F. Kennedy was assassinated.

"The degree to which these memories are enhanced probably has to do with the degree of activation of the LC," said Dr. Greene, holder of the Sherry Gold Knopf Crasilneck Distinguished Chair in Psychiatry, in Honor of Mollie and Murray Gold, and the Sherry Knopf Crasilneck Distinguished Chair in Psychiatry, in Honor of Albert Knopf. "When the New York World Trade Center came down on 9/11, that was high activation."

But life-changing events aren't the only way to trigger the release of dopamine in this part of the brain. It could be as simple as a student playing a new video game during a quick break while studying for a crucial exam, or a company executive playing tennis right after trying to memorize a big speech.

"In general, anything that will grab your attention in a persistent kind of way can lead to activation," Dr. Greene said.

Scientists have known dopamine plays a large role in memory enhancement, though where the chemical originates and how it's triggered have been points of study over the years.

Dr. Greene led a study published in 2012 that identified the locus coeruleus as a third key source for dopamine in the brain, besides the ventral tegmental area and the substantia nigra. That research demonstrated the drug amphetamine could pharmacologically trigger the brain's release of dopamine from the LC.

The latest study builds upon those findings, establishing that dopamine in this area of the brain can be naturally activated through behavioral actions and that these actions enhance memory retention.

The new study suggests that drugs targeting neurons in the locus coeruleus may affect learning and memory as well. The LC is located in the brain stem and has a range of functions that affect a person's emotions, anxiety levels, sleep patterns, memory and other aspects of behavior.

The study tested 120 mice to establish a link between locus coeruleus neurons and neuronal circuits of the hippocampus - the region of the brain responsible for recording memories—that receive dopamine from the LC.

One part of the research involved putting the mice in an arena to search for food hidden in sand that changed location each day. The study found that mice that were given a "novel experience"—exploring an unfamiliar floor surface 30 minutes after being trained to remember the food location—did better in remembering where to find the food the next day.

Researchers correlated this memory enhancement to a molecular process in the brain by injecting the mice with a genetically encoded light-sensitive activator called channelrhodopsin. This sensor allowed them to selectively activate dopamine-carrying neurons of the locus coeruleus that go to the hippocampus and to see first-hand which neurons were responsible for the memory enhancement.

They found that selectively activating the channelrhodopsin-labeled neurons with blue light (a technique called optogenetics) could substitute for the novelty experience as a memory enhancer in mice. They also found that this activation could cause a direct, long-lasting synaptic strengthening—an enhancement of memory-relevant communication occurring at the junctions between neurons in the hippocampus. This process can mediate improvement of learning and memory.

Some next steps include investigating how big an impact this finding can have on human learning, whether it can eventually lead to an understanding of how patients can develop failing memories, and how to better target effective therapies for these patients, said Dr. Greene.

More information: Tomonori Takeuchi et al. Locus coeruleus and dopaminergic consolidation of everyday memory, *Nature* (2016). DOI: 10.1038/nature19325

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