Optogenetics Provides Evidence of the Biology Behind Making and Losing Memories

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A team at the University of California, San Diego, that included 2013 NARSAD Young Investigator Grantee Christophe D. Proulx, Ph.D., has applied the breakthrough new technology optogenetics to confirm a long-held but previously unproven theory that memories are made—and lost—based on the strength of connections between neurons. The research was published online on June 1st in the journal Nature.

Nerve cells, or neurons, communicate with neighboring neurons across a slender gap called the synapse. It has been proposed since the 1960s that memories are encoded or erased by changes in cellular mechanisms such as long-term potentiation (LTP), which strengthens the neuronal message, and long-term depression (LTD), which weakens it. However, the causal link between these synaptic processes and memory has been difficult to demonstrate until now. With this new study, the San Diego team, led by Roberto Malinow, M.D., Ph.D., was able to demonstrate the link.

“This is the best evidence so far available, period,” says Eric Kandel, M.D., Brain & Behavior Research Foundation Scientific Council member and Nobel Laureate for pioneering memory research. He was not involved in the current study but calls it “a major advance.”
Optogenetics (research-update/karl-deisseroth-using-optogenetics-to-reveal-the-circuitry-of-depression-in-the), developed by Karl Deisseroth, M.D., Ph.D. (http://www.stanford.edu/group/dlab/about_pi.html), with the early support of a NARSAD Grant, is a process in which laboratory animals are genetically engineered to react to light signals. A gene that produces a light-sensitive protein, derived from a fluorescent organism, is inserted into the animal’s brain; researchers are then able to use light to rapidly open and close the membrane channels that make neurons fire and cease firing. This offers precise control over brain circuitry and allows for observation of the effects on behavior in awake, behaving animals.

In this research, rats were conditioned to associate a foot shock with optogenetic stimulation of sound cues targeted to the amygdala, the brain’s fear center, to arouse a fear memory. Subsequent optogenetic delivery of LTD conditioning inactivated the memory of the shock. Then, with optogenetic delivery of LTP conditioning the researchers were able to reactivate the memory. Says Dr. Malinow: “We were playing with memory like a yo-yo.”

The study has been receiving widespread attention. National Institute of Mental Health Director Thomas R. Insel, M.D. (http://www.nimh.nih.gov/about/director/bio/index.shtml), stated: “Beyond potential applications in disorders of memory deficiency, such as dementia, this improved understanding of how memory works may hold clues to taking control of runaway emotional memories in mental illnesses, such as post-traumatic stress disorder (ptsd).”

Read the paper abstract. (http://www.nature.com/nature/journal/vaop/ncurrent/full/nature13294.html)

Read press releases about this research from the University of California (http://ucsdnews.ucsd.edu/pressrelease/how_to_erase_a_memory_and_restore_it), San Diego and from the National Institute of Mental Health (http://www.nimh.nih.gov/news/science-news/2014/shining-a-light-on-memory.shtml).

Read articles on this research from The Huffington Post (http://www.huffingtonpost.com/2014/06/02/erase-restore-memories_n_5432430.html) and from Nature (http://www.nature.com/news/flashes-of-light-show-how-memories-are-made-1.15330).

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