Scientists decode memory-forming brain cell conversations

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Modern human brain. Credit: Univ. of Wisconsin-Madison Brain Collection.

The conversations neurons have as they form and recall memories have been decoded by Medical College of Georgia scientists.

The breakthrough in recognizing in real time the formation and recollection of a memory opens the door to objective, thorough memory studies and eventually better therapies, said Dr. Joe Tsien, neuroscientist and co-director of MCG's Brain & Behavior Discovery Institute. He is corresponding author on the study published Dec. 16 in PLoS ONE.

"It's a beginning, a first glimpse of a memory," Dr. Tsien said. "For the first time it gives us the ability to look at the brain dynamic and tell what kind of memory is formed, what are the components of the memory and how the memory is retrieved at the network level." The finding could help pinpoint at what stage memory formation is flawed and whether drugs are improving it.

For their studies, MCG scientists combined new technology and computational methods with century-old Pavlovian conditioning.

In the memory center of the brain, they used 128 electrodes capable of monitoring a handful of neurons each to simultaneously record the conversations of 200 to 300 neurons as mice learned to associate a certain tone with a mild foot shock 20 seconds later.

A computational algorithm translated the neuronal chatter into a discernable and dynamic activity pattern that provided scientists a trace or picture of what the memory looked like as it was formed and recalled.

"By listening to the neuronal activity we were able to decipher the real-time dynamic pattern and the meaning of those conversations so this is really satisfying," said Dr. Tsien, the Georgia Research Alliance Eminent Scholar in Cognitive and Systems Neurobiology.

The trace changed slightly each time it was recalled - likely as the mood or situation of the rodent changed - but still remained recognizable as a specific memory.

The scientists later correlated retrieval of the memory with the mice's actions, such as freezing upon hearing the tone or returning to the chamber where the foot shock occurred. They found the traces tightly correlated with memory scores: the mice that had lower scores predictably had a fainter trace and those with stronger traces had better behavioral performance, such as freezing in anticipation of a shock. "At the behavioral level he is just frozen, but with this technique of decoding the real-time memory, it will tell you exactly what he is thinking," Dr.

Tsien said.

As expected, when mice were returned one hour later to the chamber where conditioning took place, they repeatedly froze, on average, 1.4 seconds after the recall pattern emerged in the brain. When placed in a setting with no history of the foot shock, the mice would freeze after they heard the tone.

One of the most surprising findings was that the memory trace of the foot shock was the sole memory that emerged in their brains 20 seconds after hearing the tone: just when the mild shock would have followed. "You think we are the only ones that can tell time?" Dr. Tsien said of this unexpected evidence of memory of time.

Problems with memory, the most fundamental cognitive function, can occur at any level - learning, consolidating, storing or retrieving. The ability to watch memories being made in real time should help pinpoint where problems lie, enabling more targeted research and eventual treatment, Dr. Tsien said.

"If you don't know the basic biomarkers such as blood glucose or insulin level, it's hard to assess and study diabetes. Without knowing what memory traces are, you really don't have the precise physiological biomarkers to study memory and to reliably evaluate the effectiveness of treatment of memory disorders. We all know that behavior can be quite misleading sometime." The ability to tell what memory is produced and how good that memory is could also dramatically shape development of machines that are controlled directly by the mind, rather than those using hands as an intermediary, he noted.

Studies were done in the CA1 region of the hippocampus, a well-documented center for forming associative memories. Similar tests are needed in other memory regions, Dr. Tsien said.

Related technology is already advancing patient care. For instance, primate studies of essential motor neuron connections are advancing the development of mind-controlled prosthetic limbs and electrodes can help identify where seizures originate. But it will take time and improved non-invasive recording technology before Dr. Tsien's memory tests can be done on humans.

More information: http://dx.plos.org/10.1371/journal.pone.0008256

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