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How our brains store recent memories, cell by single cell

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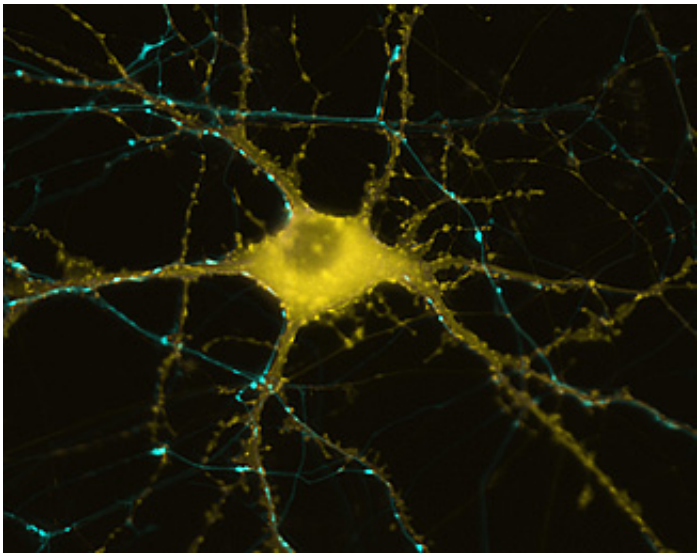

This is a human neuron showing actin formation in response to stimulation. Credit: Michael A. Colicos, UC San Diego

Confirming what neurocomputational theorists have long suspected, researchers at the Dignity Health Barrow Neurological Institute in Phoenix, Ariz. and University of California, San Diego School of Medicine report that the human brain locks down episodic memories in the hippocampus, committing each recollection to a distinct, distributed fraction of individual cells.

The findings, published in the June 16 Early Edition of *PNAS*, further

illuminate the neural basis of human memory and may, ultimately, shed light on new treatments for diseases and conditions that adversely affect it, such as Alzheimer's disease and epilepsy.

"To really understand how the brain represents memory, we must understand how memory is represented by the fundamental computational units of the brain – single neurons – and their networks," said Peter N. Steinmetz, MD, PhD, program director of neuroengineering at Barrow and senior author of the study. "Knowing the mechanism of memory storage and retrieval is a critical step in understanding how to better treat the dementing illnesses affecting our growing elderly population."

Steinmetz, with first author John T. Wixted, PhD, Distinguished Professor of Psychology, Larry R. Squire, PhD, professor in the departments of neurosciences, psychiatry and psychology, both at UC San Diego, and colleagues, assessed nine patients with epilepsy whose brains had been implanted with electrodes to monitor seizures. The monitoring recorded activity at the level of single neurons.

The patients memorized a list of words on a computer screen, then viewed a second, longer list that contained those words and others. They were asked to identify words they had seen earlier, and to indicate how well they remembered them. The observed difference in the cell-firing activity between words seen on the first list and those not on the list clearly indicated that cells in the hippocampus were representing the patients' memories of the words.

The researchers found that recently viewed words were stored in a distributed fashion throughout the hippocampus, with a small fraction of cells, about 2 percent, responding to any one word and a small fraction of words, about 3 percent, producing a strong change in firing in these cells.

"Intuitively, one might expect to find that any neuron that responds to one item from the list would also respond to the other items from the list, but our results did not look anything like that. The amazing thing about these counterintuitive findings is that they could not be more in line with what influential neurocomputational theorists long ago predicted must be true," said Wixted.

Although only a small fraction of cells coded recent memory for any one word, the scientists said the absolute number of cells coding memory for each word was large nonetheless – on the order of hundreds of thousands at least. Thus, the loss of any one cell, they noted, would have a negligible impact on a person's ability to remember specific words recently seen.

Ultimately, the scientists said their goal is to fully understand how the human brain forms and represents memories of places and things in everyday life, which cells are involved and how those cells are affected by illness and disease. The researchers will next attempt to determine whether similar coding is involved in memories of pictures of people and landmarks and how hippocampal cells representing memory are impacted in patients with more severe forms of epilepsy.

More information: Sparse and distributed coding of episodic memory in neurons of the human hippocampus, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1408365111

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