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Neuroscientists uncover possible basis of short-term memory

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Ben W. Strowbridge, PhD, associate professor of neuroscience and physiology/biophysics, and Phillip Larimer, PhD, a MD/PhD student in the neurosciences graduate program at Case Western Reserve University School of Medicine, are the first to create stimulus-specific sustained activity patterns in brain circuits maintained in vitro.

Neuroscientists often classify human memory into three types: declarative memory, such as storing facts or remembering specific events; procedural memory, such as learning how to play the piano or shoot basketballs; and working memory, a type of short-term storage like remembering a phone number. With this particular study, Strowbridge and Larimer, were interested in identifying the specific circuits that could be responsible for working memory.

Using isolated pieces of rodent brain tissue, Larimer discovered a way to recreate a type of working memory in vitro. He was studying a particular type of brain neuron, called mossy cells, which are often damaged in people with epilepsy and are part of the hippocampus.

"Seeing the memory deficits that so many people with epilepsy suffer from led me to wonder if there might be a fundamental connection between hippocampal mossy cells and memory circuits", said Larimer.

Mossy cells are unusual because they maintain much of their normal activity even when kept alive in thin brain slices. The spontaneous electrical activity Larimer and Strowbridge found in mossy cells was

critical to their discovery of memory traces in this brain region.

When stimulating electrodes were inserted in the hippocampal brain slice the spontaneous activity in the mossy cells remembered which electrode had been activated. The memory in vitro lasted about 10 seconds, about as long as many types of working memories studied in people.

"This is the first time anyone has stored information in spontaneously active pieces of mammalian brain tissue. It is probably not a coincidence that we were able to show this memory effect in the hippocampus, the brain region most associated with human memory," said Strowbridge.

The scientists measured the frequency of synaptic inputs onto the mossy cells to determine whether or not the hippocampus had retained memory.

"Memory was not evident in one cell but it was evident in a population of cells," said Strowbridge.

Larimer, who had just published another paper with Strowbridge on experiments recording electrical signals simultaneously inside four brain cells (Journal of Neuroscience, November 2008, "Nonrandom local circuits in the dentate gyrus"), was already familiar with recording from multiple cells/neurons.

"Like our own memories, the memories we created in isolated brain slices were stored in many different neurons or cells, that's why we had to watch several different cells to see the stored information," said Strowbridge.

Larimer and Strowbridge also found the brain circuit that enabled the hippocampus to remember which input pathway had been activated. The

memory effect occurred because of a rare type of brain cell called semilunar granule cells, described in 1893 by the father of neuroscience, Ramón y Cajal. The semilunar granule cells have an unusual form of persistent activity, allowing them to maintain memory and connect to the mossy cells. That was the foundation for this paper. The semilunar granule cells remained an obscurity for more than a century until Strowbridge's group rediscovered them in a paper they published in 2007.

Semilunar granule cells are the third type of brain cell that Strowbridge's group has uncovered. In 2006, Strowbridge's group published a report in the journal Neuron about Blanes cells, which Cajal named for one of his medical students that are involved in the sense of smell. That study opened a new approach to understanding the memory impairment in Alzheimer's disease, a disease that often involves changes in the perception of smells.

Strowbridge's group is now looking into how much information they can store in the hippocampus.

"It took us four years to be able to reproducibly store two bits of information for 10 seconds" says Larimer. "Our findings should progress faster now that we know what to look for and have found the brain circuit that actually holds the memory."

More information: The study, entitled, "Representing information in cell assemblies: Persistent activity mediated by semilunar granule cells" will be published in the February 2010 issue of *Nature Neuroscience*.

Source: Case Western Reserve University