Electrical oscillations critical for storing spatial memories in brain: study

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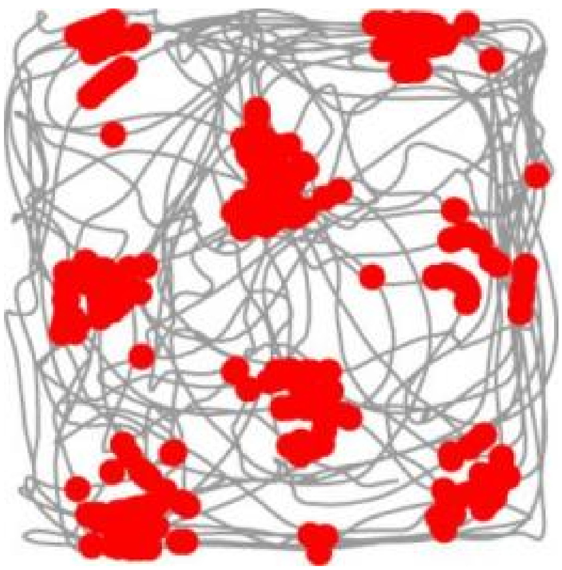

Red dots signal the location of electrical impulses generated within this grid cell, which are needed for the brain to store information about the rat's physical environment. Credit: UC San Diego

Biologists at UC San Diego have discovered that electrical oscillations in the brain, long thought to play a role in organizing cognitive functions such as memory, are critically important for the brain to store the information that allows us to navigate through our physical environment.

The scientists report in the April 29 issue of the journal *Science* that neurons called "grid cells" that create maps of the external environment in one portion of our brain require precisely timed electrical oscillations in order to function properly from another part of the brain that serves as a kind of neural pacemaker.

Their discovery has important implications for understanding the underlying causes of neurological diseases such as Alzheimer's disease and for restoring memory in areas of the brain that are necessary for orientation.

"This work is the first to demonstrate that oscillatory activity has a well-defined function in brain areas that store memories," says Stefan Leutgeb, an assistant professor of biology at UCSD who headed the team of researchers.

Scientists have long known that among the first brain areas to degenerate in Alzheimer's disease, leading to symptoms such as memory loss and disorientation, are the hippocampus and the nearby entorhinal cortex, important structures for the formation of memory. Those two regions of the brain contain three types of neurons that contribute to the formation of spatial memories and the spatial information in episodic memories from our life experiences.

These three types of neurons provide an internal GPS system to the brain. For example, one type of neuron, called "place cells," generates electrical activity only when an animal is at a certain position, while another type, called "head direction cells," acts like a compass. A third class of neurons, called "grid cells," provides grid-like patterns for the brain to store memories of physical dimensions of the external environment. The most striking feature about these cells is that their electrical activity is distributed at equidistant, periodic locations within each cell (shown in the figure). Grid cells were discovered by Norwegian scientists in rats in 2005, but in 2010 researchers in London detected groups of cells in human entorhinal cortex that share the same characteristics.

Leutgeb and his team of UCSD biologists—postdoctoral researcher Julie Koenig, undergraduate student Ashley Linder and Jill Leutgeb, an assistant professor of biology—were motivated to understand the function of electrical oscillations in the brain, which are routinely measured in clinical settings to diagnose neurological disorders.

Leutgeb's group demonstrated that neurons called grid cells in the entorhinal cortex that create maps of the external environment require precisely timed electrical oscillatory input signals from a neural pacemaker in the subcortex of the brain to function properly.

"Our findings represent a major milestone in understanding memory processing, and they will guide efforts to restore memory function when cells in the entorhinal cortex are damaged," says Stefan Leutgeb.

A group of scientists from Boston University reports related findings in a companion paper in the same April 29th issue of *Science*.

The UCSD researchers monitored the electrical activity of grid cells in rats that explored a small four-foot by four-foot enclosure. Grid cells, located in the entorhinal cortex just adjacent to the hippocampus, maintain an internal representation of the external environment. This representation is a grid-like map made of repeating equilateral triangles that tile the space in a hexagonal pattern. As an animal navigates through its environment, a given grid cell becomes active when the animal's position coincides with any of the vertices within the grid.

The scientists silenced the oscillatory input by manipulating a small group of pacemaker cells in the brain and observed a significant deterioration of the grid cells' maps of the environment.

Surprisingly, silencing the oscillatory input did not disrupt brain signals that indicate precise location (provided by place cells) and the compass signal (provided by head direction cells).

"It has been thought that the hippocampus is under control of the entorhinal cortex, so there was the assumption that grid cells would have a very large impact on place cells. We are surprised at how the function of place cells is maintained in the face of significant disruption in grid cell function," says Leutgeb.

"This important result shows that, in general, you can eliminate a substantial amount of incoming information to a brain circuit without that brain circuit losing a majority of its functionality," he adds. "The implication of this finding is that restoring memory function does not require that we exactly reassemble damaged neural circuitry, rather we can regain function by preserving or restoring key components."

"Our findings are a major step towards identifying these key components in an effort to preserve memory function in aging individuals and in patients with neurodegenerative diseases," he says.

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