NEWS

Wireless Miniscope ties seizures to spatial memory problems

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A wireless miniature microscope lets researchers peer into the brains of mice as they run along a 25-foot track.

Researchers used the device, called a **Miniscope**, to spy on neurons that fire when a mouse is in a specific location. They found that these neurons, called place cells, are disrupted in a mouse model of **epilepsy**.

“We know that epileptic patients have seizures, but they also have cognitive deficits,” says **Tristan Shuman**, assistant professor of neuroscience at the Icahn School of Medicine at Mount Sinai in

New York City. “We’re interested in how the brain is altered to cause these cognitive deficits.”

Shuman performed the work in **Peyman Golshani**’s lab at the University of California, Los Angeles. He presented the unpublished findings today at the **2017 Society for Neuroscience annual meeting** in Washington, D.C.

The work represents one of the first applications of the **Miniscope** to study brain circuits involved in a specific behavior. The device snaps onto a mouse’s head and records neural activity in its brain. Other labs are using the device to study social interactions in mice.

About a third of people with autism have **seizures**. There is evidence that repeated seizures can lead to problems with **learning and memory and social deficits**, but the mechanism is unclear.

Shuman and his colleagues used a wireless Miniscope to track the activity of place cells, which reside in the brain’s memory hub, called the **hippocampus**. They recorded place-cell firing in control mice and in mice treated with the drug pilocarpine, which makes them prone to seizures. The mice with seizures perform poorly on memory tests, including the Morris water maze, in which they must learn the location of a hidden platform in a water tank.

Place holders:

The lens of the Miniscope is surgically implanted into the animal’s brain just above the neurons of interest. The rest of the device snaps onto a baseplate in the animal’s skull. It contains a minicomputer, a battery and a micro SD card that can store up to 20 minutes of imaging data.

The researchers injected a virus into the neurons of interest so the cells glow green when they fire. In control mice, particular place cells light up when the mouse reaches specific points along the track. The same place cell lights up every time the mouse reaches the location that cell monitors, even if a week has passed since the animal last ran the course.

In mice with seizures, place-cell firing is more random. Some cells fire whenever the mouse is at any of various locations. The researchers saw this more random pattern 30 minutes after the animal last ran the course, indicating that the animal never formed a map of the track.

“We think this is driving some of the cognitive deficits [in the mice],” Shuman says. “The cells essentially don’t contain the information of where they are, so the animals don’t know where they are in space.”

Place cells reside in the upper layer of the hippocampus. The place cells receive signals that originate in neurons in a deep layer of the hippocampus called the dentate gyrus.

Restoring synchrony:

Shuman and his colleagues investigated whether neurons in the dentate gyrus are also altered in mice with seizures. They implanted an array of 256 electrodes to measure neurons firing in sync. Studies show that synchronized firing in the dentate gyrus is important for memory and cognition.

To make their recordings, they had to fix the animals' heads in place. So they used virtual reality to recreate the track experiment as the mice ran in place atop a spinning Styrofoam ball. Then they recorded from inhibitory neurons, which dampen brain activity, in each mouse's brain. The recordings revealed that inhibitory neurons in the dentate gyrus fire out of sync in mice with seizures.

"These cells are not firing at the same time, and that doesn't allow the information to flow through the circuit," Shuman says. "And that's probably what's leading to some of the place-cell deficits we see."

The researchers then injected neurons from a brain region in fetal mice that gives rise to inhibitory neurons. This restored some synchronous firing in mice with seizures. The neurons "go in and form functional connections, and basically provide new inhibition to the circuit," Shuman says. Other researchers have shown that this cellular therapy **eases seizures and cognitive deficits** in the mice.

Autism is thought to arise from a **lack of inhibitory brain signaling**. So transplanting inhibitory neurons into certain brain regions also could, in theory, improve features of autism, Shuman says.

*For more reports from the 2017 Society for Neuroscience annual meeting, please **click here**.*