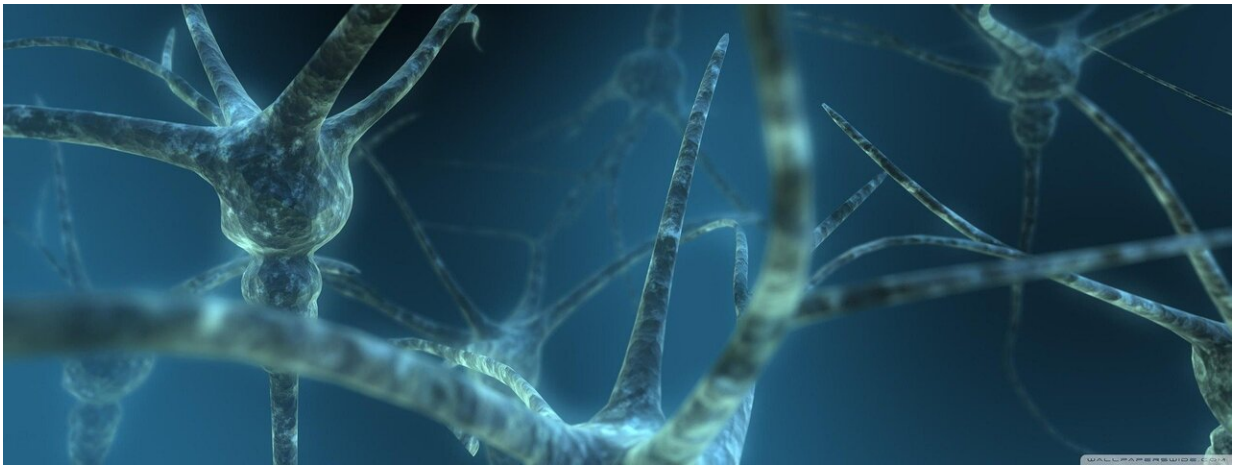


Study yields tiny targets for healing human memory

August 3 2021



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The discovery could offer a way to measure the effectiveness of memory-restoring therapies including medications and deep-brain stimulation. It also could be a step toward recovering lost memory among patients with a variety of brain conditions. The study was published online July 21 by the journal *Epilepsia*.

More than 3 million people in the U.S. have epilepsy, a [seizure disorder](#) in which the brain experiences abnormal bursts of electrical signals. In patients with [temporal lobe epilepsy](#), those bursts are focused in one of the two lobes of the brain that sit close to ear level within the skull.

Because the temporal lobes preserve [long-term memory](#), and patients' [memory](#) problems usually persist even after their seizures have been successfully treated, experts suspect the seizures damage brain circuits. To learn whether this is the case, researchers recorded the activity of individual neurons in the temporal lobes of 62 patients with epilepsy, 37 of whom have TLE.

The patients had electrodes surgically inserted into their brains to determine the focal point of their seizures, and researchers added additional smaller electrodes to monitor the electrical activity of individual neurons, which are smaller than the width of a human hair, while the patients took visual memory tests.

"This is a very rare and special opportunity to study and understand the human brain at the single-cell level," said Ueli Rutishauser, Ph.D., professor of Neurosurgery, Neurology and Biomedical Sciences at Cedars-Sinai. "Single-neuron recordings is a technique that we are uniquely positioned to use at Cedars-Sinai and this was a rare opportunity for us to work with patients and watch their neurons at work."

To gather enough data for the study, Rutishauser and colleagues collaborated with Neurosurgeon Taufik A. Valiante, MD, Ph.D., at the University of Toronto to include additional patients as part of a multi-institutional BRAIN Initiative consortium to study memory in humans at the single-cell level, funded by the National Institutes of Health and led by Cedars-Sinai.

Patients viewed 100 images they had not seen before and then, after a break, were shown 50 of those images again, plus 50 new images. During the viewing, researchers recorded the activity of two types of neurons responsible for two different aspects of memory.

Visually selective neurons put images into categories. "They say it's an animal, a tree or a face, and those are the features out of which memories are built," said Rutishauser, also the Board of Governors Chair in Neurosciences and interim director of the Center for Neural Science and Medicine at Cedars-Sinai.

Memory-selective neurons, meanwhile, signal whether a person has previously seen a landscape, object or person. "A good illustration of this effect is when you feel like you know a person, but you don't know why and cannot recall their name," Rutishauser said.

Patients whose seizures began in the right hemisphere of the brain, which is important for visual memories, showed normal activity in their visually selective neurons and could categorize the images they saw as animals, vehicles, food, people or buildings. However, the activity of their memory-selective neurons was impaired, and they had trouble remembering which images they had seen before with high confidence.

In the brains of patients whose seizures began in the left hemisphere, which is important for verbal memories and language skills, both types of neurons behaved normally, and patients performed well on both portions of the visual test.

"One question that remains to be answered is whether, if you used a verbal memory test, you would find memory deficits and different behavior in memory-selective cells in patients whose seizures began on the left," said Adam Mamelak, MD, professor of Neurosurgery at Cedars-Sinai and co-author of the study. "If so, that would be very important."

Another open question is whether these differences are related to brain dominance. Rutishauser said that 80% of people have left-side dominance, and that this study didn't include enough patients to

determine whether, in the small percentage of people with right-side dominance, the memory deficit was more likely to appear in the left hemisphere.

As a next step, Rutishauser and colleagues are attempting to rescue memory in patients with epilepsy through electrical stimulation that preferentially affects memory-selective neurons.

"Now we have a target," he said. "We have reason to believe it is possible to align the activity of these [neurons](#) to a [brain](#) oscillation called their 'Theta rhythm.' This is a rhythm seen in connection with memory, and it could be a way to rescue their function and help patients retrieve memories that they previously couldn't."

If this works, the same technique could be studied in [patients](#) with other conditions, including Alzheimer's disease, Rutishauser said.

The co-first authors of the study are Seung J. Lee, MD and Danielle E. Beam of Cedars-Sinai.

More information: Seung J. Lee et al, Single-neuron correlate of epilepsy-related cognitive deficits in visual recognition memory in right mesial temporal lobe, *Epilepsia* (2021). [DOI: 10.1111/epi.17010](https://doi.org/10.1111/epi.17010)

Provided by Cedars-Sinai Medical Center

Citation: Study yields tiny targets for healing human memory (2021, August 3) retrieved 26 June 2024 from <https://medicalxpress.com/news/2021-08-yields-tiny-human-memory.html>

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