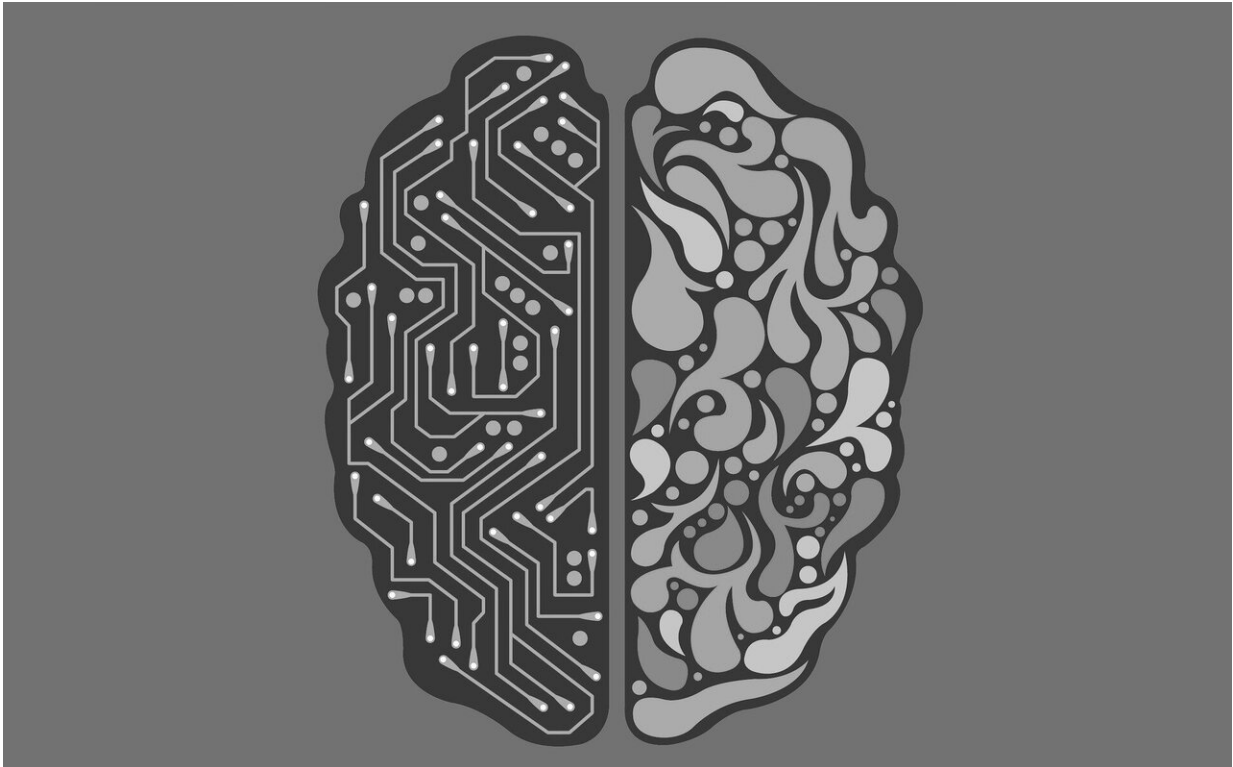


# How does the brain make memories?

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In a study led by Cedars-Sinai, researchers have discovered two types of brain cells that play a key role in dividing continuous human experience into distinct segments that can be recalled later. The discovery provides new promise as a path toward development of novel treatments for memory disorders such as dementia and Alzheimer's disease.

The study, part of a multi-institutional BRAIN Initiative consortium funded by the National Institutes of Health and led by Cedars-Sinai, was published in the peer-reviewed journal *Nature Neuroscience*. As part of ongoing research into how [memory](#) works, Ueli Rutishauser, Ph.D., professor of Neurosurgery, Neurology, and Biomedical Sciences at Cedars-Sinai, and co-investigators looked at how [brain cells](#) react as memories are formed.

"One of the reasons we can't offer significant help for somebody who suffers from a memory disorder is that we don't know enough about how the memory system works," said Rutishauser, senior author of the study, adding that memory is foundational to us as human beings.

Human experience is continuous, but psychologists believe, based on observations of people's behavior, that memories are divided by the brain into distinct events, a concept known as event segmentation. Working with 19 patients with drug-resistant epilepsy, Rutishauser and his team were able to study how neurons perform during this process.

Patients participating in the study had electrodes surgically inserted into their brains to help locate the focus of their epileptic seizures, allowing investigators to record the activity of individual neurons while the patients viewed film clips that included cognitive boundaries.

While these boundaries in daily life are nuanced, for research purposes, the investigators focused on "hard" and "soft" boundaries.

"An example of a soft boundary would be a scene with two people walking down a hallway and talking, and in the next scene, a third person joins them, but it is still part of the same overall narrative," said Rutishauser, interim director of the Center for Neural Science and Medicine and the Board of Governors Chair in Neurosciences at Cedars-Sinai.

In the case of a hard boundary, the second scene might involve a completely different set of people riding in a car. "The difference between hard and soft boundaries is in the size of the deviation from the ongoing narrative," Rutishauser said. "Is it a totally different story, or like a new scene from the same story?"

When study participants watched film clips, investigators noted that certain neurons in the brain, which they labeled "boundary cells," increased their activity after both hard and soft boundaries. Another group of neurons, labeled "event cells," increased their activity only in response to hard boundaries, but not soft boundaries.

Rutishauser and his co-investigators theorize that peaks in the activity of boundary and event cells—which are highest after hard boundaries, when both types of cells fire—send the brain into the proper state for initiating a new memory.

"A boundary response is kind of like creating a new folder on your computer," said Rutishauser. "You can then deposit files in there. And when another boundary comes around, you close the first folder and create another one."

To retrieve memories, the brain uses boundary peaks as what Rutishauser calls "anchors for [mental time travel](#)."

"When you try to remember something, it causes [brain cells](#) to fire," Rutishauser said. "The memory system then compares this pattern of activity to all the previous firing peaks that happened shortly after boundaries. If it finds one that is similar, it opens that folder. You go back for a few seconds to that point in time, and things that happened then come into focus."

To test their theory, investigators gave study participants two memory

tests.

They first showed participants a series of still images and asked them whether or not they had seen them in the film clips they had viewed. Study participants were more likely to remember images that closely followed a hard or soft boundary, when a new "memory folder" would have been created.

Investigators also showed participants pairs of images from film clips they had viewed and asked which of the images appeared first. Participants had difficulty remembering the correct order of images that appeared on opposite sides of a hard boundary, possibly because the brain had segmented those images into separate memory folders.

Rutishauser said that therapies that improve event segmentation could help patients with memory disorders. Even something as simple as a change in atmosphere can amplify event boundaries, he explained.

"The effect of context is actually quite strong," Rutishauser said. "If you study in a new place, where you have never been before, instead of on your couch where everything is familiar, you will create a much stronger memory of the material."

The research team included postdoctoral fellow Jie Zheng, Ph.D., and neuroscientist Gabriel Kreiman, Ph.D., from Boston Children's Hospital; neurosurgeon Taufik A. Valiante, MD, Ph.D., of the University of Toronto; and Adam Mamelak, MD, professor of Neurosurgery and director of the Functional Neurosurgery Program at Cedars-Sinai.

In follow-up studies, the team plans to test the theory that boundary and event cells activate dopamine neurons when they fire, and that dopamine, a chemical that sends messages between cells, might be used as a therapy to strengthen memory formation.

Rutishauser and his team also noted during this study that when event cells fired in time with one of the brain's internal rhythms, the theta rhythm—a repetitive pattern of activity linked to learning, memory and navigation—subjects were better able to remember the order of images they had seen. This is an important new insight because it shows that deep brain stimulation that adjusts theta rhythms could prove therapeutic for [memory disorders](#).

"Theta rhythms are thought to be the 'temporal glue' for episodic memory," said Zheng, first author of the study. "We think that firing of event cells in synchrony with the theta rhythm builds time-based links across different memory folders."

**More information:** Gabriel Kreiman, Neurons detect cognitive boundaries to structure episodic memories in humans, *Nature Neuroscience* (2022). [DOI: 10.1038/s41593-022-01020-w](https://doi.org/10.1038/s41593-022-01020-w).  
[www.nature.com/articles/s41593-022-01020-w](https://www.nature.com/articles/s41593-022-01020-w)

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