Research reveals how the brain remembers fearful experiences

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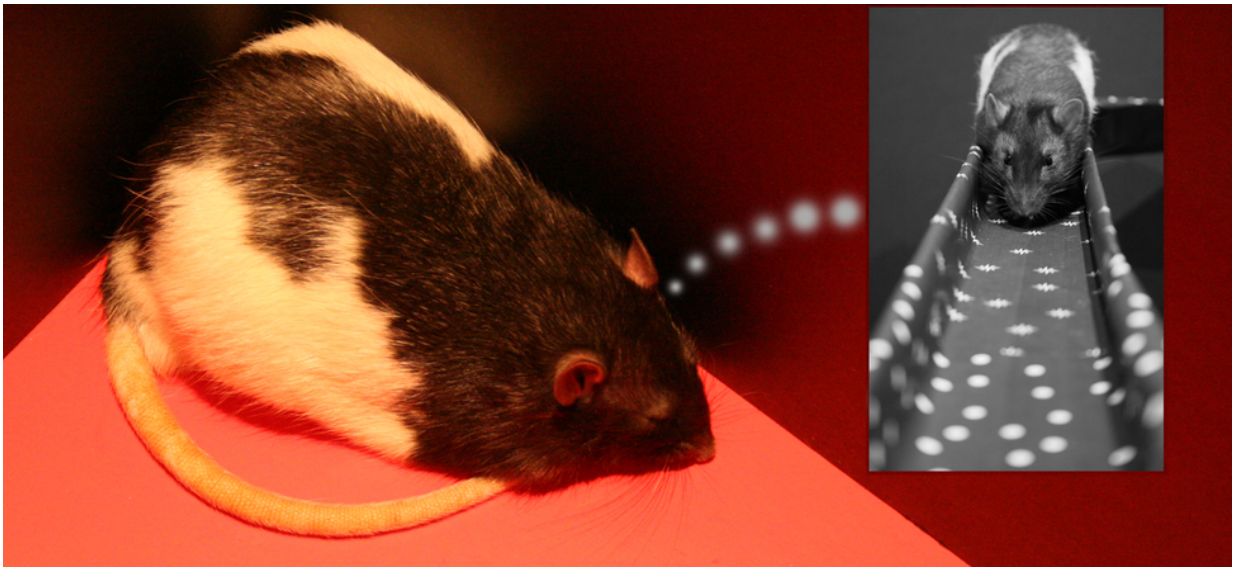

The Ji Lab investigates how the neural circuits in the brain encode, consolidate, and retrieve memories. Credit: The Ji Lab/Baylor College of Medicine

Understanding how the brain remembers can one day shed light on what went wrong when memory fails, such as it occurs in Alzheimer's disease. Researchers at Baylor College of Medicine and Rice University reveal for the first time the specific patterns of electrical activity in rat brains that are associated with specific memories, in this case a fearful experience. They discovered that before rats avoid a place in which they had a fearful experience, the brain recalled memories of the physical

location where the experience occurred. The results appear in *Nature Neuroscience*.

"We recall memories all the time," said senior author Dr. Daoyun Ji, associate professor of molecular and cellular biology at Baylor. "For example, I can recall the route I take from home to work every morning, but what are the brain signals at this moment when I hold this memory in my mind?"

Studying the workings of the brain in people is difficult, so scientists have turned to the laboratory rat. They have learned that when the animal is in a particular place, neurons in the hippocampus, appropriately called place cells, generate pulses of activity.

"A number of place cells generates electrical activity called a 'spiking pattern,'" Ji said. "When the rat is in a certain place, a group of neurons generates a specific pattern of spikes and when it moves to a different place, a different group of neurons generates another pattern of spikes. The patterns are very distinct. We can predict where the animal is by looking at its pattern of brain activity."

But, are these spiking patterns involved in memory?

How to know what a rat is thinking

"Our laboratory rats cannot tell us what memory they are recalling at any particular time," Ji said. "To overcome that, we designed an experiment that would allow us to know what was going on in the animal's brain right before a certain event."

In the experiment, conducted by first author Chun-Ting Wu, graduate researcher at the Ji lab, a rat walked along a track, back and forth. After a period of rest, the rat walked the same track again, but when the

animal approached the end of the track, it received a mild shock. After it rested again, the rat was placed back on the track. This time, however, when it approached the end of the track where it had received the mild shock before, the rat stopped and turned around, avoiding crossing the fearful path.

"Before a rat walked the tracks the first time, we inserted tiny probes into its hippocampus to record the electrical signals generated by groups of active neurons," Ji said. "By recording these brain signals while the animal walked the track for the first time we could examine the patterns that emerged in its brain - we could see what patterns were associated with each location on the track, including the location where the animal later got shocked."

"Because the rat turns around and avoids stepping on the end of the track after the shocks, we can reasonably assume that the animal is thinking about the place where it got shocked at the precise moment that it stops walking and turns away," Ji said. "Our observations confirmed this idea."

When the researchers, in collaboration with co-author Dr. Caleb Kemere at Rice University, looked at the brain activity in place neurons at this moment, they found that the spiking patterns corresponding to the location in which the rat had received the shock re-emerged, even though this time the animal was only stopping and thinking about the location.

"Interestingly, from the brain activity we can tell that the animal was 'mentally traveling' from its current location to the shock place. These patterns corresponding to the shock place re-emerged right at the moment when a specific memory is remembered," Ji said.

Future directions

The next goal of the researchers is to investigate whether the spiking pattern they identified is absolutely required for the animals to behave the way they did.

"If we disrupt the pattern, will the animal still avoid stepping into the zone it had learned to avoid?" Ji said. "We are also interested in determining how the spiking patterns of place neurons in the hippocampus can be used by other parts of the brain, such as those involved in making decisions."

Ji and his colleagues are also planning on exploring what role spiking patterns in the hippocampus might play in diseases that involve memory loss, such as Alzheimer's disease.

"We want to determine whether this kind of mechanism is altered in animal models of Alzheimer's disease. Some evidence shows that it is not that the animals don't have a memory, but that somehow they cannot recall it. Using our system to read spiking patterns in the brains of animal models of the disease, we hope to determine whether a specific spiking pattern exists during memory recall. If not, we will explore the possibility that damaged brain circuits are preventing the animal from recalling the memory and look at ways to allow the animal to recall the specific activity patterns, the memory, again."

More information: Hippocampal awake replay in fear memory retrieval, *Nature Neuroscience*, nature.com/articles/doi:10.1038/nn.4507

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