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New Findings Reveal How The Brain's Memory Center Filters Out Unimportant Details

A study in mice that sheds light on how the brain remembers key details could one day help treat disorders impacting memory

NEW YORK, December 8, 2021

Imagine trying to find a restaurant without a map or GPS. You've been there before, a few times. So you might conjure up some dependable landmarks connected with that spot: the park you always pass, the gas station down the road, maybe even the ice cream truck that's usually stationed nearby. You would likely not use (or even remember) random details, such as what the clouds looked like overhead or who happened to be on the street the last time you were there.

Now, scientists at Columbia's Zuckerman Institute studying mice have discovered new secrets about how the brain remembers useful details and discards insignificant ones. Researchers who study this tend to focus on how we filter what sensory details we collect from the world. But the new work, which appeared Dec. 8 in *Nature*, reveals a selection process that kicks in later, as our memories consolidate, thanks to cells in the brain's memory center.

"Our research suggests that these cells are key to the brain's ability to be flexible and learn what matters — and what doesn't — in a new situation," said postdoctoral researcher Satoshi Terada, PhD, who led the work in the Losonczy lab.

A better fundamental understanding of how the brain records these memories could help shed light on disorders relating to or impacting memory, such as post-traumatic stress disorder, epilepsy, schizophrenia and Alzheimer's.

Making Associations

The scent of freshly baked brownies may remind you of grandma's house. This reflects how the brain forms associative memories, which link sets of details together. Associative memory is vital in guiding us toward rewards or away from dangers.

"Associative memory is fundamental to our everyday lives," said Attila Losonczy, MD, PhD, a principal investigator at Columbia's Zuckerman Institute. "We remember events such as eating at a restaurant by associating places with items, people and other details."

Disorders such as epilepsy, schizophrenia and Alzheimer's can disrupt associative memory. It can also go awry in post-traumatic stress disorder, when people associate harmless situations such as fireworks displays with fearful memories such as those of battlefields.

Much remains unknown about how associative learning discerns which connections are useful enough to be remembered and which are not.

"If I wanted to remember the location of a restaurant, I should not look for, say, a yellow cab I previously saw on the way there because it may not be there the next time,," said Dr. Losonczy, who is also a professor of neuroscience at Columbia's Vagelos College of Physicians and Surgeons. “My brain must select and remember reliable details.”

Reliable or Not?

In the new study, the scientists investigated mice, focusing on the hippocampus, a seahorse-shaped region of the brain central to memory.

"Specifically, we analyzed the hippocampal region CA3, which plays a key role in encoding associative memories," Dr. Terada said.

In experiments, the mice walked on treadmills where the researchers could deliver flashes of blue light and puffs of citrus, banana or mint scents. The treadmill belts were either featureless bands of fabric or burlap strips decorated with patches of felt or velvet that could provide tactile sensory cues to the mice.

In some experiments, the mice repeatedly received a reward in the form of a sip of water at a predictable amount of time after a light, smell or tactile cue was given on specific positions on the treadmills. The cues thus served as trustworthy information signaling that water was coming. In other experiments, the reward was given a random amount of time after these sensory cues, making the cues unreliable.

One challenge with imaging activity in CA3 is that it's buried deep in the brain and quite difficult to examine with conventional methods. Dr. Terada developed a technique to analyze CA3 brain cell activity in mice by focusing on long threadlike parts of these cells known as axons that extend into and convey information to CA1, the part of the hippocampus closest to the brain's surface.

CA3 Cells

The researchers found that CA3 axons were active during both experiments, responding to both reliable and unreliable sensory cues.

However, the cells behaved differently as the mice rested after the experiments, when CA3 replayed the memories to figure out which ones should be stored in long-term memory. The

CA3 axons remained active in mice that had seen reliable cues. In contrast, CA3 axons linked with the unreliable random cues were suppressed during this process of memory replay.

"The current model of how the brain selects useful information for remembering is focused on what we selectively pay attention to in the moment as we experience the world," Dr. Losonczy said. "Our findings also show that the hippocampus has a filtering mechanism that excludes insignificant details as our experiences are later transferred to long-term storage."

Why does the brain's memory center react to these sensory cues even if they appear irrelevant? Although such details might not appear immediately useful, they may have utility later on.

"The hippocampus does not just adapt to and tune out apparently irrelevant stimuli," Dr. Losonczy said. "Something that appears unimportant now can gain relevance later. So the hippocampus has the ability to rapidly associate apparently useless sensory stimuli with utility. The hippocampus is an adaptive, fast-learning machine."

In the future, the scientists aim to map out which specific groups of cells the brains of mice use to filter apparently useful and useless information for long-term memory. Such research could eventually help uncover the ways in which human disorders affect memory.

"Down the road, we could identify the brain circuits and molecular mechanisms underlying associative memory, which could prove targets for therapies," Dr. Losonczy said.

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This paper, "Adaptive stimulus selection for consolidation in the hippocampus," appeared on Dec. 8 in *Nature*. The work was supported by National Institutes of Health grants T32GM007367, National Institute of Mental Health grants 1R01MH124047, 1R01MH124867, F30MH125628 and F32MH118716, National Institute of Neurological Disorders and Stroke grants 1U19NS104590, 1U01NS115530 and F31NS120783-01, a JSPS Overseas Fellowship and the Kavli Foundation. The authors declare no competing interests.