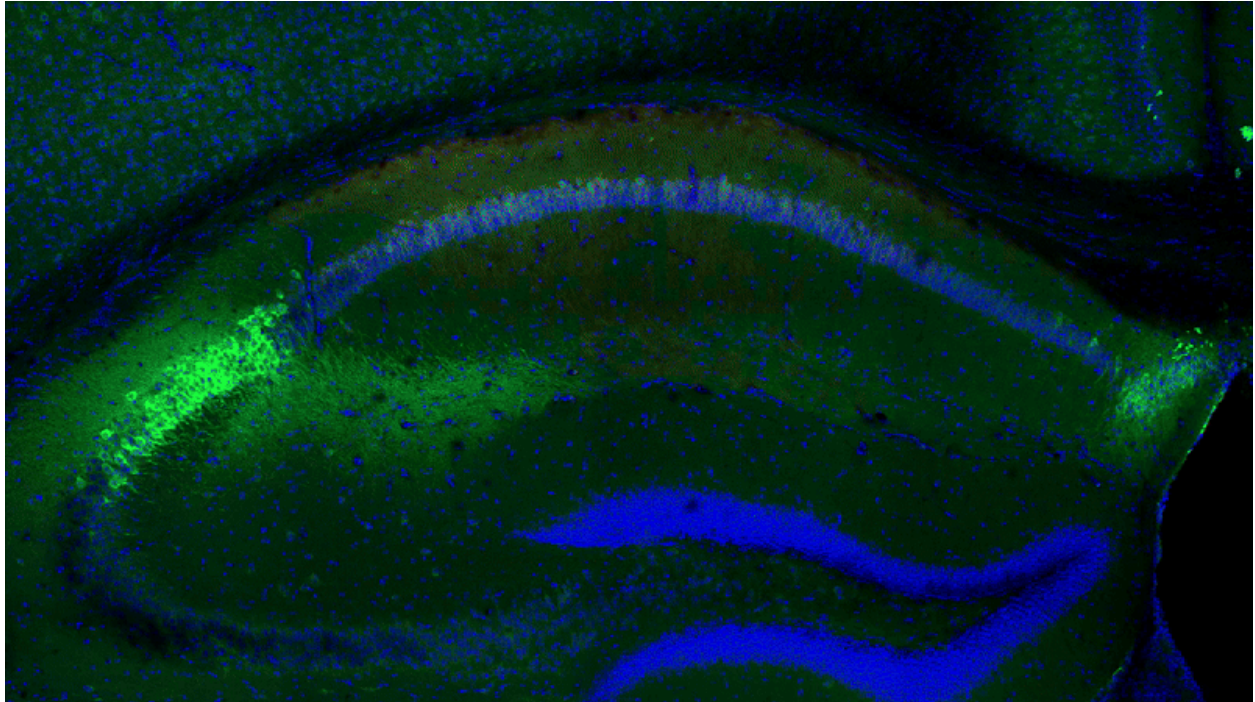


## Fearful Memories of Others Seen in Mouse Brain

*Temporarily silencing brain regions helped scientists pinpoint where different types of memories originate*



*The memory center of a mouse brain. A region that helps remember social interactions is in green. An area important for remembering locations is in red. (Credit: P. Kassraian et al., Columbia's Zuckerman Institute.)*

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NEW YORK, NY — How do we distinguish threat from safety? It's a question important not just in our daily lives, but for human disorders linked with fear of others, such as social anxiety or post-traumatic stress disorder (PTSD). The microscope image above, from the laboratory of [Steven A. Siegelbaum](#), PhD, at Columbia's Zuckerman Institute, displays a powerful technique scientists used to help us find an answer.

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The scientists were investigating the hippocampus, a brain area that plays a key role in memory in humans and mice. Specifically, they focused on the CA2 region, which is significant for [social memory](#), the ability to remember other individuals, and the CA1 region, which is important for remembering places.

In this new study, the researchers for the first time reveal that CA1 and CA2 respectively encode the locations and individuals linked with a threatening experience. The results show that, beyond simply recognizing individuals, CA2 helps record more complex aspects of social memory: in this case, whether another individual is safe or risky. The scientists published [their findings](#) October 15 in the journal *Nature Neuroscience*.

"It's vital to all species that live in social communities, including mice and humans, to have social memories that can help one avoid future experiences with others that might prove harmful while keeping ourselves open to individuals who may be beneficial," said [Pegah Kassraian](#), PhD, a postdoctoral research fellow in the Siegelbaum lab and lead author of the new study. "Fearful memories are important for survival and help to keep us safe."

To investigate where fearful social memories originate in the brain, Dr. Kassraian and her colleagues gave individual mice a choice. They could scamper to one place, meet another mouse that was unknown to them, and receive a mild foot shock (much like a static electricity zap people might get after walking on a carpet and touching a doorknob). Scurrying in the opposite direction to meet a different stranger was safe. Normally, the mice quickly learned to avoid the strangers and locations that were associated with the shocks, and these memories lasted for at least 24 hours.

To determine where in the hippocampus these memories were stored, the researchers genetically altered the mice to enable them to selectively suppress the CA1 or CA2 regions. Surprisingly, turning off each region had very different effects. When the scientists silenced CA1, the mice could no longer remember where they were zapped, but they could still remember which stranger was associated with the threat. When they silenced CA2, the mice remembered where they were shocked, but became indiscriminately afraid of both strangers they met.

These new findings reveal that CA2 helps mice remember whether past encounters with others were threatening or safe. The results also are consistent with prior research detailing how CA1 is home to place cells, which encode locations.

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Previous research has implicated CA2 in various neuropsychiatric conditions such as [schizophrenia](#) and [autism](#). The new study suggests that further investigating CA2 might help scientists better understand social anxiety, post-traumatic stress disorder and other conditions that can lead to social withdrawal.

"It's possible that social withdrawal symptoms are related to an inability to discriminate between who is a threat and who is not," said Dr. Siegelbaum, who is also a professor and chair of the department of neuroscience at Columbia's Vagelos College of Physicians and Surgeons. "Targeting CA2 could be a useful way of diagnosing or treating disorders linked with a fear of others."

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The [paper](#), "The hippocampal CA2 region discriminates social threat from social safety," was published online in *Nature Neuroscience* on October 15, 2024.

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The authors report no conflicts of interest.