Turning off major memory switch dulls memories

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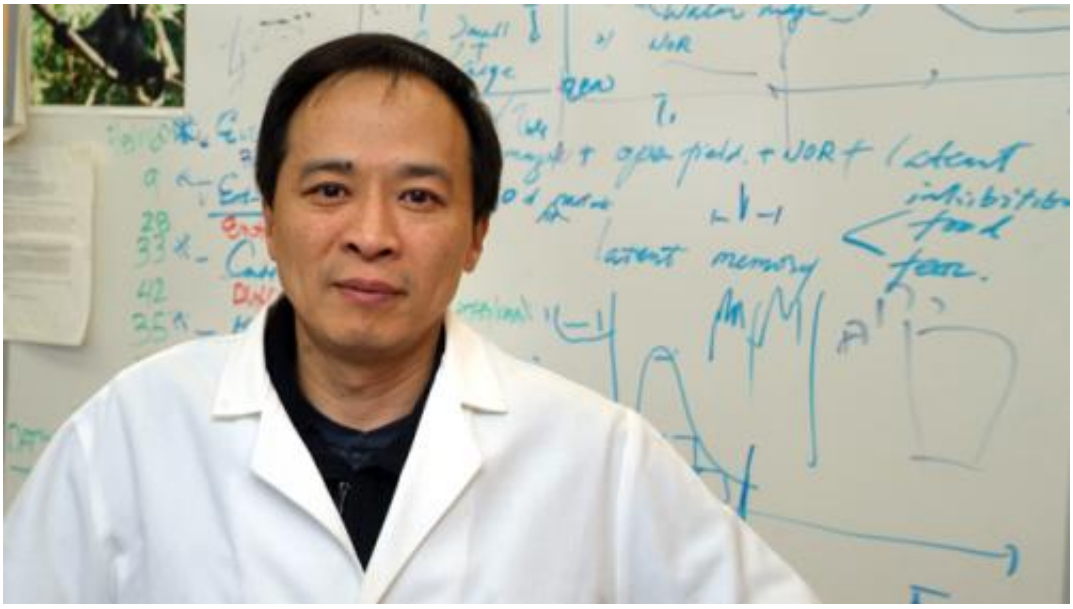

Dr. Joe Tsien is a neuroscientist at the Medical College of Georgia at Georgia Regents University and Co-Director of the GRU Brain & Behavior Discovery Institute. Credit: Phil Jones

A faultily formed memory sounds like hitting random notes on a keyboard while a proper one sounds more like a song, scientists say.

When they turned off a major switch for learning and memory, brain cells communicated, but the relationship was superficial, said Dr. Joe Tsien, neuroscientist at the Medical College of Georgia at Georgia Regents University and Co-Director of the GRU Brain & Behavior

Discovery Institute.

"We have begun to crack the neural code, which allows us to look in real time at how thoughts happen and how memories are made," Tsien said. "That has enabled us to understand for the first time how and whether the right keys are struck at the right time and in the right place and manner to make the beautiful sound of coherent memories and to compare what happens when a key element is missing."

With the NMDA receptor intact, chatter reverberates, associations are made and helpful memories – like how touching a hot stove results in a burn – are easily retrieved.

"You see a face and think of a name, you see your office, and you think you need to work; everything is associative," said Tsien, corresponding author of the study in the journal *PLOS ONE*. "But in mice lacking an NMDA receptor, you can tell the memory patterns are dull and dissociated."

Using the century-old Pavlovian conditioning model that first showed how repetition creates association, they found that mice lacking a functioning NMDA receptor in the hippocampus, the brain's center of learning and memory, could not recollect even something fearful.

When they played a tone, followed 20 seconds later by a mild foot shock, normal mice quickly made the association, down to the timing. The connection essentially never registered with mice lacking the NMDA receptor.

"They form the initial patterns, but don't rehearse them," said Tsien. "Their tones are flat, the association is poor, while everything we register in the healthy brain is associative." To illustrate just how flat, Postdoctoral Fellow Hui Kuang assigned musical notes to the memory

activity of each, which resulted in random noise by the NMDA knockout mice compared to a dynamic rhythm from normal mice. Hear the recordings below:

"By knowing what these patterns look like and what they mean, you can use this signature to measure, for example, during aging, why we begin to lose memory and to identify and test drugs that are truly effective at aiding memory," Tsien said.

"You can tell whether there is an issue with reverberation, whether your brain is repeating what you need to remember, or repeats it but somehow stores it badly, so it's not associated with the right things. This study has revealed a lot of fascinating details about what neuroscientists call the brain's neural code" Tsien said."

He wants to look at how aging affects these processes as a next step. The research team also is looking at Doogie, a mouse genetically bred by Tsien and his team in 1999 to be exceptionally smart, to see if they can also learn more about how super memories are made and what they look like.

This ability to decode how and what the brain is remembering, should one day help physicians better assess and treat conditions such as Alzheimer's and schizophrenia, Tsien said. They may find that some answers are already out there, such as drugs that boost reverberation, or a stimulant like caffeine to help retrieve a memory, Tsien said.

His team first reported decoding brain cell conversations as memories were formed and recalled in *PLOS ONE* in 2009. As with the new study, they used a computational algorithm to translate the neuronal conversations into some of the first pictures of what memories look like.

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