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Lasers reactivate 'lost' memories in mice with Alzheimer's

It was thought that Alzheimer's completely erases memories, but a mouse experiment suggests the condition messes with our ability to recall them instead

Helpful, but lasers might be better
Dana Hanna/Getty

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FORGOTTEN memories have been reawakened in mice with symptoms resembling Alzheimer's disease. The feat suggests the condition may not destroy memories, but instead impair our ability to recall them.

It has long been assumed that Alzheimer's completely erases memories. The disease involves clumps of proteins accumulating in the brain, where they are thought to destroy the neurons that store our memories.

But work by Christine Denny at Columbia University and her team suggests memories may not be wiped by Alzheimer's disease, but instead become harder to access. What's more, they can be artificially reawakened.

The finding could be revolutionary, says Ralph Martins at Edith Cowan University in Australia. "It has the potential to lead to drug development to help regain memories," he says.

To examine how memory is affected by Alzheimer's disease, the researchers developed a way of visualising individual memories in mouse brains. They genetically engineered mice so that neurons glowed yellow when storing a memory, and red when recalling one. Two sets of these mice were created – one that was healthy, and one with a condition resembling Alzheimer's disease.

> **"This technique could be revolutionary. It may lead to drugs that help us regain memories"**

Both sets of mice took a memory test. First, they were exposed to a lemon scent and given electric shocks. Then, a week later, they were exposed to the same lemon scent. Most of the healthy mice immediately froze in anticipation of being shocked. But almost half as many of the Alzheimer's-like mice froze,

suggesting they did not remember the link between the smell and shock so strongly.

This behaviour matched what the team saw in the hippocampi of the mice – the brain regions that record memories. In healthy animals, the red and yellow neurons overlapped, showing that the mice were retrieving the lemon-shock memory from the same place it had been stored. But in the Alzheimer's mice, different cells glowed red during recall, suggesting that they were calling up the wrong memories.

This might explain why people with Alzheimer's often experience false memories, says Denny. For example, many people with the condition incorrectly remember where they were during the 9/11 attacks. These new findings suggest this may be because they are retrieving information from the wrong brain cells.

Memory reboot

Using a genetic engineering technique called optogenetics, Denny's team went on to reactivate the lemon-shock memory in the Alzheimer's mice. By shining a blue laser down a fibre-optic cable into the brain, they were able to stimulate the yellow memory-storing neurons, prompting the mice to freeze when they smelled lemon (*Hippocampus*, doi.org/b9w8).

This shows that "lost" memories may still exist in the brain, and can be recovered. For now, optogenetics cannot be used in people because it isn't yet safe or practical to tinker with our neurons or stick lasers in our brains. But in future, targeted drugs or techniques like deep-brain stimulation may help people with Alzheimer's access forgotten memories, says Denny.

However, mouse Alzheimer's models do not perfectly reflect the condition in humans, warns Martins. The number of neurons that die in Alzheimer's mice is far lower than in people, he says.

But there are already clues that lost memories can be reawakened in people with Alzheimer's, Martins says. "Music is the best example, which has attracted a lot of attention as a way for retrieving memories of the past in these

patients – so it makes sense."

If something like Denny's technique can be made to work in humans, it could have other uses, such as helping witnesses remember crime scenes. We may even be able to tap into memories from early childhood.

However, it's unlikely we could selectively reactivate memories, because we wouldn't know which neurons they were stored in, and some neurons may hold multiple memories, says Denny. "You would not want to bring back bad memories too."

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