Amnesia caused by head injury reversed in early mouse study

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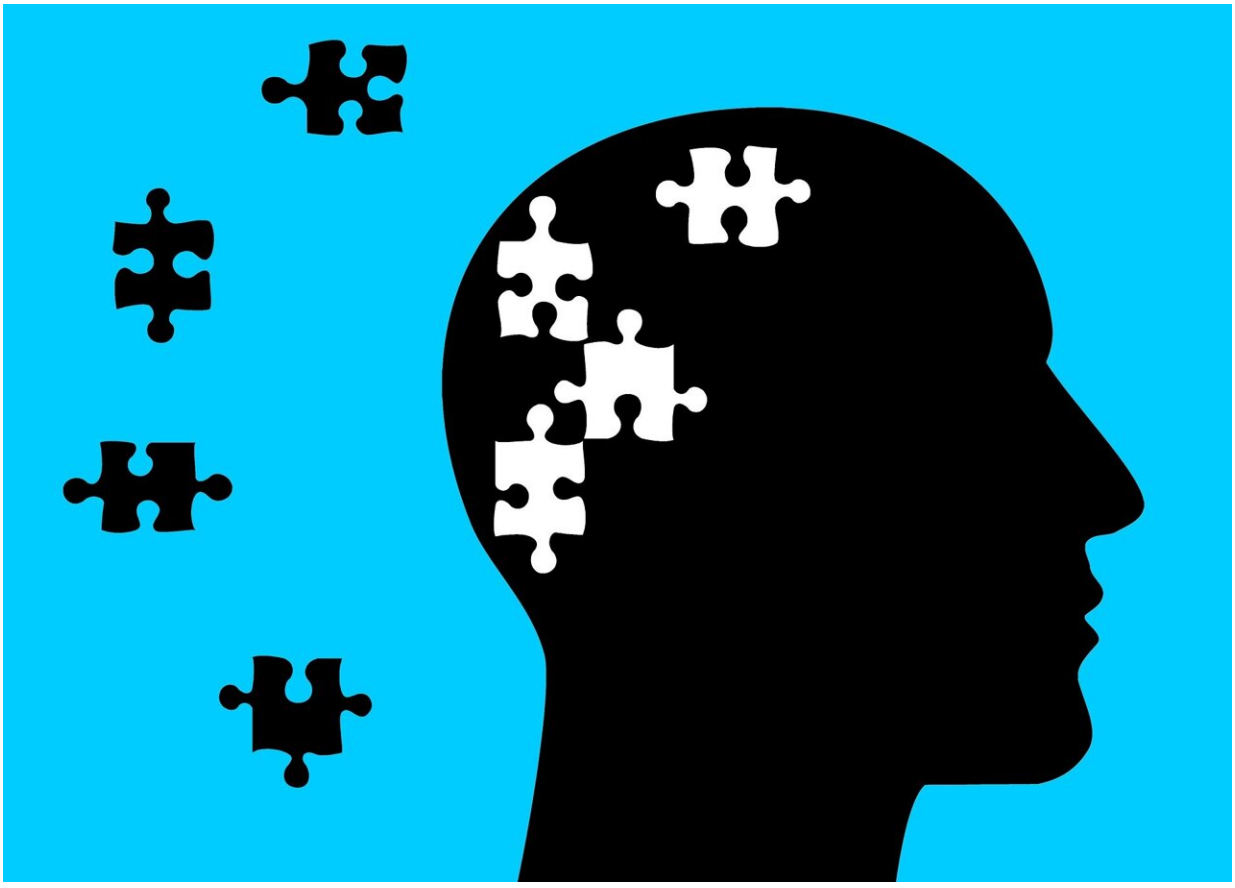

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A mouse study designed to shed light on memory loss in people who experience repeated head impacts, such as athletes, suggests the

condition could potentially be reversed. The research in mice finds that amnesia and poor memory following head injury are due to inadequate reactivation of neurons involved in forming memories.

The study, conducted by researchers at Georgetown University Medical Center in collaboration with Trinity College Dublin, Ireland, is reported January 16, 2024, in *The Journal of Neuroscience*.

Importantly for diagnostic and treatment purposes, the researchers found that the memory loss attributed to head injury was not a permanent pathological event driven by a neurodegenerative disease. Indeed, the researchers could reverse the amnesia to allow the mice to recall the lost memory, potentially allowing cognitive impairment caused by head impact to be clinically reversed.

The Georgetown investigators had previously found that the brain adapts to repeated head impacts by changing the way the synapses in the brain operate. This can cause trouble in forming new memories and remembering existing memories. In their new study, investigators were able to trigger mice to remember memories that had been forgotten due to head impacts.

"Our research gives us hope that we can design treatments to return the head-impact brain to its normal condition and recover cognitive function in humans that have poor memory caused by repeated head impacts," says the study's senior investigator, Mark Burns, Ph.D., a professor and Vice-Chair in Georgetown's Department of Neuroscience and director of the Laboratory for Brain Injury and Dementia.

In the new study, the scientists gave two groups of mice a new memory by training them in a test they had never seen before. One group was exposed to a high frequency of mild head impacts for one week (similar to contact sport exposure in people) and one group were controls that

didn't receive the impacts. The impacted mice were unable to recall the new memory a week later.

"Most research in this area has been in human brains with chronic traumatic encephalopathy (CTE), which is a degenerative brain disease found in people with a history of repetitive head impact," said Burns. "By contrast, our goal was to understand how the brain changes in response to the low-level head impacts that many young football players regularly experience."

Researchers have found that, on average, college football players receive 21 head impacts per week with defensive ends receiving 41 head impacts per week. The number of head impacts to mice in this study was designed to mimic a week of exposure for a college football player, and each single head impact by itself was extraordinarily mild.

Using genetically modified mice allowed the researchers to see the neurons involved in learning new memories, and they found that these memory neurons (the "memory engram") were equally present in both the control mice and the experimental mice.

To understand the physiology underlying these memory changes, the study's first author, Daniel P. Chapman, Ph.D., said, "We are good at associating memories with places, and that's because being in a place, or seeing a photo of a place, causes a reactivation of our memory engrams."

"This is why we examined the engram neurons to look for the specific signature of an activated neuron. When the mice see the room where they first learned the memory, the control mice are able to activate their memory engram, but the head impact mice were not. This is what was causing the amnesia."

The researchers were able to reverse the amnesia to allow the mice to

remember the lost memory using lasers to activate the engram cells. "We used an invasive technique to reverse memory loss in our mice, and unfortunately this is not translatable to humans," Burns adds.

"We are currently studying a number of non-invasive techniques to try to communicate to the brain that it is no longer in danger, and to open a window of plasticity that can reset the brain to its former state."

More information: Amnesia after repeated head impact is caused by impaired synaptic plasticity in the memory engram, *The Journal of Neuroscience* (2024). doi.org/10.1523/JNEUROSCI.1560-23.2024

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