

Structured Unlearning: Marijuana May Impair Memory via the Brain's Non-Firing Cells

A new study suggests that pot makes users forgetful by binding not to neurons but to the brain's supporting glial cells called astrocytes

By [Ferris Jabr](#) | March 1, 2012 | [15](#)



BLUNTED MEMORY: Few studies have investigated exactly how marijuana impairs working memory. Now it seems the answer **might involve non-neuronal brain cells called astrocytes**. Image: Khalid Mahmood, Wikimedia Commons

In a 2006, season 2 episode of *The Office* entitled "Drug Testing," Dwight Schrute interrogates his fellow employees about the partially smoked joint he found in the parking lot. Dwight is determined to identify the culprit, but Jim Halpert turns the tables:

Jim: I'm just saying that you can't be sure that it wasn't you.

Dwight: That's ridiculous. Of course it wasn't me.

Jim: Marijuana is a memory-loss drug, so maybe you just don't remember.

Dwight: I would remember.

Jim: Well how could you if it just erased your memory?

Dwight: That's not how it works!

Half a joint is unlikely to obliterate entire memories, but studies have shown that **regularly smoking marijuana for many years does impair working memory** the ability to temporarily hold information in your head, such as a telephone number or the name of someone you just met. Exactly **what marijuana does to the brain to muddle up memory formation has remained unclear**. Now, a team of researchers has **proposed** that marijuana hinders the process **not by acting on neurons, but rather by acting on non-neuronal brain cells called astrocytes**. The finding adds to a **growing heap of evidence that such non-electrical structural cells, collectively known as glia, play a far more active role in neural activity than researchers once realized**.

Memory depends on a balance of two opposing cellular processes: long-term potentiation, in which connected neurons learn to fire in sync, and long-term depression, the weakening of unnecessary connections among neurons. Xia Zhang of the University of Ottawa Institute of Mental Health Research and his colleagues think that marijuana impairs working memory by throwing off this balance, bolstering **long-term depression (LTD)** at the expense of **long-term potentiation (LTP)**. Their **new study suggests that marijuana increases LTD by triggering a chemical cascade that starts in astrocytes.**

"It's probably the first time it's been shown that astrocytes are involved in the primary event [that regulates] memory," says Giovanni Marsicano of INSERM (The French National Institute for Health and Medical Research), one of Zhang's co-authors. Their study appears in the March 2 issue of *Cell*.

Zhang and his colleagues reached this conclusion after **injecting mice with tetrahydrocannabinol (THC)**, the active component of marijuana, and giving them a series of memory tests, such as forcing the mice to remember the location of an underwater platform in order to emerge from a miniature swimming pool. THC fits like a puzzle piece into tiny cellular structures called **cannabinoid type 1 receptors (CB1)**, which are **found on both neurons and astrocytes in the hippocampus** a part of the brain crucial for memory. Marsicano genetically modified one group of mice to lack CB1 receptors on astrocytes and altered another group of mice to lack these receptors on neurons. To the researchers' surprise, **mice lacking CB1s on astrocytes did much better on the memory tests than mice lacking the receptors on their neurons. In other words, marijuana impaired working memory only when it was able to bind to astrocytes.**

Zhang and his colleagues describe a cascade of chemical changes in the brain that might explain how THC binding to astrocytes results in memory deficits. **When THC binds to an astrocyte, the researchers propose, the astrocyte begins spewing a neurotransmitter called glutamate**, which in turn binds to a glutamate receptor called NMDA on nearby neurons. As a consequence, the neurons begin absorbing another kind of glutamate receptor, called AMPA, which is a key process in the kind of long-term depression that eventually leads to impaired working memory.

Some earlier research suggests that this chain of events is plausible, but Zhang and his colleagues have not yet worked out all the details; **it remains unclear why THC invokes this cascade when it binds to CB1 receptors on astrocytes but not CB1 receptors on neurons.** *Another unresolved issue is that some previous research contradicts the new findings.* Studies by Alfonso Araque of the Cajal Institute in Spain suggest that *stimulating the natural production of endocannabinoids the brain molecules that the marijuana plant imitates induces long-term potentiation, not long-term depression.* Zhang and his colleagues speculate that the discrepancy could be due to the fact that Araque studied slices of brain tissue, rather than studying living animals with intact brains. Slicing up brains might have damaged the connections between astrocytes and neurons, Zhang and his colleagues argue, but they don't have good evidence that this is true. Regardless, **future studies must address** the new evidence that marijuana only impairs memory if it has access to CB1 receptors on astrocytes.

R. Douglas Fields, an internationally recognized authority on neural glial interactions at the National Institutes of Health, found the new study very interesting. "This fits it in with what we have been learning about astrocytes regulating synaptic function," he says.