

How marijuana impairs memory

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A major downside of the medical use of marijuana is the drug's ill effects on working memory, the ability to transiently hold and process information for reasoning, comprehension and learning. Researchers reporting in the March 2 print issue of the Cell Press journal *Cell* provide new insight into the source of those memory lapses. The answer comes as quite a surprise: Marijuana's major psychoactive ingredient (THC) impairs memory independently of its direct effects on neurons. The side effects stem instead from the drug's action on astroglia, passive support cells long believed to play second fiddle to active neurons.

The findings offer important new insight into the [brain](#) and raise the possibility that marijuana's benefits for the treatment of pain, [seizures](#) and other [ailments](#) might some day be attained without hurting memory, the researchers say.

With these experiments in mice, "we have found that the starting point for this phenomenon – the effect of marijuana on working memory – is the astroglial [cells](#)," said Giovanni Marsicano of INSERM in France.

"This is the first direct evidence that astrocytes modulate working memory," added Xia Zhang of the University of Ottawa in Canada.

The new findings aren't the first to suggest astroglia had been given short shrift. Astroglial cells (also known as astrocytes) have been viewed as cells that support, protect and feed neurons for the last 100 to 150 years, Marsicano explained. Over the last decade, evidence has accumulated that these cells play a more active role in forging the connections from

one neuron to another.

The researchers didn't set out to discover how marijuana causes its cognitive side effects. Rather, they wanted to learn why receptors that respond to both THC and signals naturally produced in the brain are found on astroglial cells. These cannabinoid type-1 (CB1R) receptors are very abundant in the brain, primarily on neurons of various types.

Zhang and Marsicano now show that [mice](#) lacking CB1Rs only on astroglial cells of the brain are protected from the impairments to spatial working memory that usually follow a dose of [THC](#). In contrast, animals lacking CB1Rs in neurons still suffer the usual lapses. Given that different cell types express different variants of CB1Rs, there might be a way to therapeutically activate the receptors on neurons while leaving the astroglial cells out, Marsicano said.

"The study shows that one of the most common effects of cannabinoid intoxication is due to activation of astroglial CB1Rs," the researchers wrote.

The findings further suggest that astrocytes might be playing unexpected roles in other forms of memory in addition to spatial working memory, Zhang said.

The researchers hope to explore the activities of endogenous endocannabinoids, which naturally trigger CB1Rs, on astroglial and other cells. The endocannabinoid system is involved in appetite, pain, mood, memory and many other functions. "Just about any physiological function you can think of in the body, it's likely at some point endocannabinoids are involved," Marsicano said.

And that means an understanding of how those natural signaling molecules act on astroglial and other cells could have a real impact. For

instance, Zhang said, "we may find a way to deal with [working memory](#) problems in Alzheimer's."

More information: Han et al.: "Acute Cannabinoids Impair Working Memory through Astroglial CB1 Receptor Modulation of Hippocampal LTD."

Provided by Cell Press

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