

How do cannabinoids make us feel that way?

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Marijuana and its main psychoactive component, THC, exert a plethora of behavioral and autonomic effects on humans and animals. Some of these effects are the cause of the widespread illicit use of marijuana, while others might be involved in the potential therapeutic use of this drug for the treatment of several neuronal disorders.

The great majority of these effects of THC are mediated by cannabinoid receptor type 1 (CB1), which is abundantly expressed in the central nervous system. The exact anatomical and neuronal substrates of each action, however, were previously unknown.

Using an advanced genetic approach, Krisztina Monory and colleagues at the Johannes Gutenberg University Mainz discovered that specific neuronal subpopulations mediate the distinct effects of THC. Their work is published online this week in the open-access journal *PLoS Biology*.

In their study, the researchers generated mutant mice lacking CB1 expression in defined neuronal subpopulations but not in others. These mice were treated with THC, and typical effects of the drug on motor behavior, pain, and thermal sensation were scored. Their discovery of the neural substrates underlying specific effects of THC could lead to a refined interpretation of the pharmacological actions of cannabinoids. Moreover, these data might provide the rationale for the development of drugs capable of selectively activating CB1 in specific neuronal subpopulations, thereby better exploiting cannabinoids' potential therapeutic properties.

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