

Study finds link between marijuana abuse and blunted dopamine response

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Credit: Rice University

(Medical Xpress)—People who use marijuana heavily experience a blunted response to dopamine, according to researchers at Brookhaven National Laboratory, New York University Langone Medical Center and the National Institute on Alcohol Abuse and Alcoholism. When marijuana abusers took methylphenidate, a drug that stimulates dopamine production, they did not experience the cardiovascular, behavioral and brain changes usually associated with an increase in dopamine levels. The research appears in the *Proceedings of the National Academy of Sciences*.

Scientists don't know much about how excessive use of marijuana affects the brain. Marijuana doesn't seem to affect the brain in the same way that other drugs of abuse do. Other drugs stimulate the release of [dopamine](#), a neurotransmitter associated with feelings of pleasure, in a region of the forebrain known as the striatum. While some earlier studies have shown that marijuana does this as well, other studies have shown that marijuana does not have this effect. People who abuse alcohol, nicotine, cocaine, methamphetamine and heroin experience a decreased ability to produce dopamine. However, scientists have never found a link between marijuana use and reduced dopamine production.

Joanne Fowler of Brookhaven National Laboratory and her colleagues wanted to see if marijuana abusers have a different response to dopamine than other people do. To do this, they gave 24 marijuana abusers, who had been smoking a median of about five joints a day, five days a week for 10 years, the drug methylphenidate. This drug, also known as Ritalin, stimulates the production of dopamine. Fowler's team gave 24 control subjects methylphenidate as well.

When the researchers compared the two groups' reactions to methylphenidate, they found that members of the control group experienced greater increases in heart rate and [diastolic blood pressure](#) than the marijuana abusers did. Members of the control group reported

feeling more high, restless, anxious and affected by the drug than the marijuana abusers did.

PET scans showed that [methylphenidate](#) caused changes in the striatum and the cerebellum of the controls. These changes were significantly smaller in the marijuana abusers.

The research suggests that people who use marijuana excessively have problems with the reward circuitry in their brains. Even when their brains produce large amounts of dopamine, marijuana abusers don't respond to it normally. Personality tests showed that the marijuana abusers in the study were more likely to experience negative emotions, including depression, anxiety and irritability, than the controls were. This is a sign that marijuana abusers find it harder to experience pleasure than most people do.

It's not clear whether excessive marijuana use damages the brain's reward circuitry, or whether people who already have damaged reward circuitry use [marijuana](#) to make themselves feel better.

More information: Decreased dopamine brain reactivity in marijuana abusers is associated with negative emotionality and addiction severity, *PNAS*, www.pnas.org/content/early/2014/07/10/1411228111

Abstract

Moves to legalize marijuana highlight the urgency to investigate effects of chronic marijuana in the human brain. Here, we challenged 48 participants (24 controls and 24 marijuana abusers) with methylphenidate (MP), a drug that elevates extracellular dopamine (DA) as a surrogate for probing the reactivity of the brain to DA stimulation. We compared the subjective, cardiovascular, and brain DA responses (measured with PET and [¹¹C]raclopride) to MP between controls and marijuana abusers. Although baseline (placebo) measures of striatal DA

D2 receptor availability did not differ between groups, the marijuana abusers showed markedly blunted responses when challenged with MP. Specifically, compared with controls, marijuana abusers had significantly attenuated behavioral ("self-reports" for high, drug effects, anxiety, and restlessness), cardiovascular (pulse rate and diastolic blood pressure), and brain DA [reduced decreases in distribution volumes (DVs) of [¹¹C]raclopride, although normal reductions in striatal nondisplaceable binding potential (BPND)] responses to MP. In ventral striatum (key brain reward region), MP-induced reductions in DVs and BPND (reflecting DA increases) were inversely correlated with scores of negative emotionality, which were significantly higher for marijuana abusers than controls. In marijuana abusers, DA responses in ventral striatum were also inversely correlated with addiction severity and craving. The attenuated responses to MP, including reduced decreases in striatal DVs, are consistent with decreased brain reactivity to the DA stimulation in marijuana abusers that might contribute to their negative emotionality (increased stress reactivity and irritability) and addictive behaviors.

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