

## The challenges of studying marijuana's effects on the heart and brain

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Over the past decade, marijuana use, both recreational and medicinal, has grown as state governments across the U.S. have legalized its use. But while it might be legal for adults to light up, the question of whether



it is harmful or helpful in many cases remains unanswered.

Researchers say the truth is complicated.

Though it has been studied for decades, much remains unknown about how marijuana, or cannabis, affects heart and brain health. And there are significant challenges to finding clear answers.

"The evidence that has been emerging from animal models show ramifications in the brain and in the heart, but the data for humans is more murky," said Dr. Fernando Daniel Testai, a neurologist at the University of Chicago Department of Neurology and Rehabilitation. Testai was lead author on an American Heart Association scientific statement last year that detailed what's known, and not known, about marijuana's effects on brain health.

"So many things factor into the equation," said Staci Gruber, an associate professor of psychiatry at Harvard Medical School in Boston. She oversees the Marijuana Investigations for Neuroscientific Discovery (MIND) program at McLean Hospital in Belmont, Massachusetts, which studies the effects of medical marijuana on clinical and cognitive measures, as well as brain structure and function and quality of life.

Differences in how people use marijuana, concentrations of the products they use, the active ingredients they contain, how often they use them and for how long, as well as age all may play a role in determining how health is affected, Gruber said. It's up to researchers to drill down in each of these areas, but legal, ethical and other hurdles make it difficult to do so.

More than 48 million people in the U.S. over the age of 12 reported using marijuana in 2019, according to the <u>Substance Abuse and Mental Health Administration</u>. That's roughly 18% of the population, which is



up from 11% two decades ago.

Also known as pot or weed, marijuana can be used recreationally or for medicinal purposes, such as to reduce nausea or ease chronic pain in people with cancer. It can be smoked in cigarette form or through pipes or water pipes, vaped, or infused into baked goods, gummy candies or drinks. Its compounds can be extracted to make oils and concentrates, which can also be vaped or smoked. Little is known about the safety of one method compared to another, though there is evidence the combustion from smoking marijuana can be harmful.

Gruber said some of the confusion stems from what people mean when they use the word "marijuana." Marijuana refers to the dried flowers, leaves, stems and seeds of the cannabis plant, which contains more than 100 chemical compounds. The two most recognized are tetrahydrocannabinol—THC—responsible for the plant's mind-altering effects, and cannabidiol—CBD—which does not produce a "high" but has been used to treat pediatric seizure disorders, anxiety, pain and inflammation.

"We often use the terms 'marijuana' or 'cannabis' to describe anything that comes from the plant, but different compounds from the plant have different effects," Gruber said.

When discussing health impacts, it's also important to distinguish between recreational and medicinal use, she said. "Recreational users tend to look for high THC content in the products they use. Medical users may or may not. They don't typically want to get high, but want to alleviate symptoms so they can do everyday things like go to the store and remember why they are there."

<u>Some studies suggest</u> chronic, heavy recreational use can harm cognitive function—especially if that use begins during adolescence. But research



shows adult medical cannabis patients may experience some cognitive benefits. Gruber was the senior author of a <u>study published 2018 in the Frontiers of Pharmacology journal</u> that showed people who used medical cannabis experienced improvements in executive function over time, with no deficits in verbal learning or memory.

There also are differences in how different types of use affect heart health.

Though the high levels of THC exposure from recreational use may cause a rise in blood pressure, said Gruber, a study last year in Israel found people age 60 and older who used medical marijuana for three months had a reduction in blood pressure. A 2020 scientific statement from the AHA said observational studies have linked marijuana use to an increased risk of heart attacks, atrial fibrillation and heart failure, but acknowledged its impact on the heart and blood vessels was not well understood due to a lack of adequate research.

A study that directly compares the effects of medical marijuana use to recreational use would help, Testai said. As would a clearer definition of what chronic, heavy recreational use really means.

"Most studies measure exposure to marijuana based on self-reported use," he said. "There's no objective data for how much people are consuming."

Another challenge is people who use it recreationally may use other drugs or substances, such as cigarettes or other mind-altering drugs. That makes it difficult to tease out which impacts come from which substances, Testai said.

How often a person uses marijuana, how much they use and for how long matters, Gruber said. For example, people may initially experience



a rapid heart rate, called tachycardia, from products containing THC. But consistent use may result in tolerance to that effect, often after a few days or weeks.

In clinical studies, researchers measure and control what people are consuming. But because the federal government still classifies marijuana as a schedule 1 substance, meaning it is considered to have a high potential for abuse, researchers face tough restrictions on the products they can give study participants.

The National Institute on Drug Abuse Drug Supply Program provides marijuana for research purposes, Gruber said. But research-grade marijuana isn't what people are consuming in their homes.

"Unlike alcohol, which is pretty straightforward, cannabis is many different things," she said. She asks people who use recreational marijuana in her observational studies to submit samples of the products they use most often so they can be analyzed to better measure what's going into their bodies.

Age also plays an important role, Gruber said. Evidence suggests using marijuana during key periods of brain development may harm cognition more than it would if use began in adulthood.

Testai said researchers face another obstacle: the inability to assign a control group to placebo.

"The most fundamental or clear way to practice research is a randomized study with placebo," he said. But with marijuana, "there is no way you can actually mask its effect. Doing high-quality research in this field is confounded by the way <u>marijuana</u> works, not to mention the ethics."

Until there's a better solution, said Gruber, researchers "have to be



creative thinkers. We have to try to capture observational data as closely and rigorously as we can as well as conduct empirically sound clinical trials."

## Provided by American Heart Association

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