

Scientists find anticonvulsant drug helps marijuana smokers kick the habit

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Scientists at The Scripps Research Institute have found clinical evidence that the drug gabapentin, currently on the market to treat neuropathic pain and epilepsy, helps people to quit smoking marijuana (cannabis). Unlike traditional addiction treatments, gabapentin targets stress systems in the brain that are activated by drug withdrawal.

In a 12-week trial of 50 treatment-seeking cannabis users, those who took [gabapentin](#) used less cannabis, experienced fewer withdrawal symptoms such as sleeplessness, and scored higher on tests of attention, [impulse-control](#), and other [cognitive skills](#), compared to patients who received a placebo. If these results are confirmed by ongoing larger trials, gabapentin could become the first FDA-approved [pharmaceutical treatment](#) for cannabis dependence.

"A lot of other drugs have been tested for their ability to decrease cannabis use and withdrawal, but this is the first to show these key effects in a controlled treatment study," said Barbara J. Mason, the Pearson Family Chair and Co-Director of the Pearson Center for Alcoholism and [Addiction Research](#) at Scripps Research. "The other nice thing about gabapentin is that it is already widely prescribed, so its safety is less likely to be an issue."

Mason led the new gabapentin study, recently published online ahead of print by the journal [Neuropsychopharmacology](#).

Stress Circuits

Addiction researchers have long known that [recreational drugs](#) hook users by disrupting the normal tuning of their brains' reward and motivation circuitry. But as scientists at Scripps Research and other institutions have shown in animal studies, cannabis withdrawal after prolonged heavy use also leads to the long-term activation of basic stress circuits. "In human cannabis users who try to quit, this [stress response](#) is reflected in reports of [drug craving](#), [sleep disturbances](#), anxiety, irritability, and dysphoria, any one of which can motivate a person to return to using, because cannabis will quiet these symptoms," said Mason.

A 2008 study by Pearson Center Co-Director George Koob and his colleagues found that gabapentin, an FDA-approved anticonvulsant [drug](#) that resembles the neurotransmitter GABA, can quiet this withdrawal-related activation in stress circuitry in alcohol-dependent rats. That finding motivated Mason to set up a pilot trial of gabapentin in cannabis-dependent individuals, whose withdrawal syndrome features a similar over-activation of stress circuits.

She and her colleagues recruited cannabis users with local newspaper and web ads headlined: "Smoking too much pot? We want to help you stop." "We needed only 50 subjects, but we quickly got more than 700 queries from cannabis users who were eager to quit," Mason said. "Some people deny that cannabis can be addictive, but surveys show that between 16 and 25 percent of substance use treatment admissions around the world every year involve people with primary cannabis dependence."

Twice as Many Abstinent from Cannabis Use

The trial was based at Mason's laboratory at The Scripps Research Institute. Half of the 50 recruits were randomly assigned to take 1,200 mg/day of gabapentin; the rest were given identical-looking placebo

capsules. Over 12 weeks, Mason and her colleagues, including a medical team from the nearby Scripps Clinic, monitored the subjects with tests. Using standard behavioral therapy techniques, they also counseled the patients to stay off cannabis.

The subjects' self-reports and more objective urine tests revealed that gabapentin, compared to placebo, significantly reduced their continuing cannabis use. "Urine metabolite readings indicate about twice as many of the gabapentin subjects had no new cannabis use during the entire study, and, in the last four weeks of the study, all of the gabapentin subjects who completed the study stayed abstinent," Mason said.

Gabapentin also clearly reduced the reported symptoms of withdrawal such as sleep disturbances, drug cravings, and dysphoria. And even though gabapentin normally is thought of as a brain-quieting drug that can cause sleepiness as a side effect, there was some evidence that it sharpened cognition among the cannabis users. Seven gabapentin and ten placebo patients sat for tests of attention, impulse-control, and other executive functions just before the start of the trial and at week four. While the placebo patients tended to score lower after four weeks of attempted abstinence, the gabapentin patients generally scored higher.

Help Resisting Cravings

Addiction researchers now recognize that one of the effects of repeated drug use is the weakening of executive functions-which can happen through the over-activation of reward circuitry as well as by withdrawal-related stress. "That weakening of self-control-related circuits makes it even harder for people to resist drug cravings when they're trying to quit, but gabapentin may help restore those circuits, by reducing stress and enabling patients to sleep better, so that they function better while awake," Mason said.

She is now conducting a larger, confirmatory study of gabapentin in [cannabis users](#), as well as a new study of a novel drug that targets the same stress circuitry.

"People in the treatment community have told me that they're eager for these trial results to come out, because until now nothing has been shown to work against both relapse and withdrawal symptoms," Mason said.

More information: "A Proof-of-Concept Randomized Controlled Study of Gabapentin: Effects on Cannabis Use, Withdrawal and Executive Function Deficits in Cannabis-Dependent Adults", *Neuropsychopharmacology*.

Provided by The Scripps Research Institute

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