

*Possible help for Parkinson's, but a hard regulatory road*

# Neurology Researcher Works to Cut through the Cannabis Research Maze

*By Tyler Smith*

The legalization of marijuana in Colorado has opened the door for researchers to investigate the potential medical benefits – and risks – of the drug and its derivatives. But a study developed by a neurologist at the University of Colorado School of Medicine shows that launching a cannabis-based study requires persistence and a willingness to blaze new trails.



*UCH neurologist Maureen Leehey, MD, is working to clear a number of hurdles for a study of cannabidiol, a non-psychoactive compound of marijuana that could decrease tremors in patients with Parkinson's disease.*

And the study doesn't involve marijuana, at least in the form that most people know it. [Maureen Leehey](#), MD, a neurologist at University of Colorado Hospital and professor of neurology with the CU School of Medicine, has approval for a study involving cannabidiol (CBD), one of the dozens of compounds found in the cannabis plant. She wants to see if anecdotal evidence suggesting that CBD decreases tremor in patients with Parkinson's disease proves out.

Some animal studies point to a variety of [therapeutic benefits](#) that CBD might offer, including protection against neurodegenerative disorders. In addition, CBD acts on different areas of the brain than its better-known cousin THC, the psychoactive compound in marijuana. That makes CBD a potential alternative for patients who want relief from their symptoms without being saddled with an unwanted high from smoking or eating marijuana.

"Pre-clinical trials of CBD in animals have been promising," said Leehey's neurology colleague [Benzi Kluger](#), MD, MS. He noted CBD could also be an alternative to approved neurologic medications that produce other unwanted side effects. "For some people, CBD may be a better option than standard pharmaceuticals," Kluger said.

**Patients lead the way.** Those factors made CBD a natural source of interest for Leehey, who said many of her patients with Parkinson's have told her they take "different marijuana substances" to manage their symptoms.

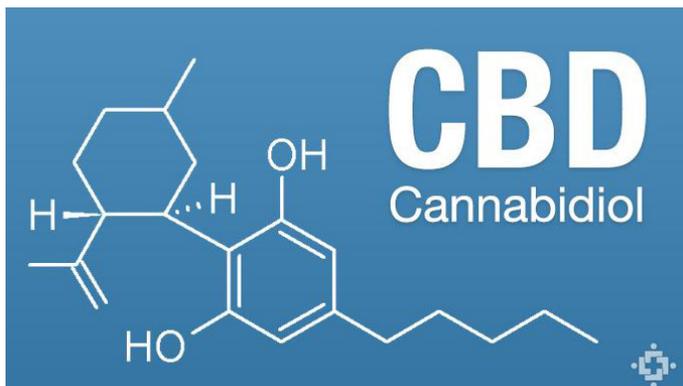
A broad survey Kluger conducted of neurology patients showed that 5 percent of Parkinson's patients – Leehey suspects the percentage is higher – take marijuana to relieve their disease symptoms. Many told Leehey, however, that they don't like to get high because of the side effects, such as dizziness and loss of balance. That was particularly true among Parkinson's patients, which are the largest group treated at the hospital's [Movement Disorders Center](#). However, some patients said they like a CBD formulation that helps them sleep and relieves symptoms such as tremor and anxiety without getting them stoned.

A fruitful research path opened for Leehey, marked first by a paucity of medical literature about the effects of CBD and THC in mitigating symptoms of Parkinson's disease, and second by

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the availability of grant dollars from the Colorado Department of Public Health and Environment (CDPHE) to study the [medical effects of marijuana](#).

The CDPHE approved Leehey's proposal for a randomized trial of CBD's effectiveness in controlling tremor in patients with Parkinson's disease. She plans to conduct a randomized, double-blind, placebo controlled study of 50 patients to measure what effect, if any, CBD has in decreasing tremor, as measured by specific tremor items in the [Unified Parkinsons Disease Rating Scale](#). It's a crossover study, meaning that it will be conducted in two phases, with each patient being part of both the placebo group and the group that receives CBD.



*Cannabidiol is one of dozens of compounds found in cannabis.*

**Marijuana maze.** But the three-year grant, worth a little more than \$1 million, has not yet gotten off the ground as Leehey proceeds through regulatory thickets made even denser by society's ambivalence toward marijuana.

She first discovered that the official government marijuana source for researchers is a [National Institute for Drug Abuse](#) (NIDA) farm operated under a contract with the University of Mississippi. To purchase the product from NIDA, Leehey would have to complete an approval process, but that point became moot when she found that NIDA produces CBD that contains too much THC for the patients she wants to study.

That turned her attention to two commercial drug companies, [INSYS Therapeutics, Inc.](#), which produces pure synthetic CBD; and [GW Pharmaceuticals](#), which manufactures a natural, high-CBD liquid. Leehey said she's working with the two companies to see if it is possible to use one of their products, which patients take orally, for the study.

She also needs Institutional Review Board approval to begin the trial, but she can't move forward with that process until she knows the products that will be used and can document how they will be stored and distributed and how patients will take them. In addition, Leehey will also need Investigational New Drug (IND) approval from the Food and Drug Administration to use CBD for the purpose of her trial.

Perhaps the strangest challenges trace to the fact that under federal law, Leehey must treat CBD as she would marijuana, despite its lack of standing as a party drug. She will need to get special approval from the Drug Enforcement Agency (DEA), which considers CBD a Schedule 1 drug under the Controlled Substances Act, just as it does marijuana.

When the trial begins – Leehey hopes by this fall – the CBD supplier will ship the product directly to Leehey's office, where she will lock it up and store it. Pharmacists will divide the CBD into doses as needed, and the medications will have to be specially transported to the clinic to dispense to patients. Any leftover drugs will be picked up and destroyed by companies approved by the DEA.

As a safety measure, Leehey will conduct an initial 10-patient study that will include driving tests. That might sound a little like testing the effect of non-alcoholic beer on driving, but Leehey said the problem is the lack of clinical understanding of the effects of CBD. If it turns out CBD does affect driving ability, it's better to know that in advance, she added, as the study would have to recommend that patients who enroll stay out of their cars after taking their medications.

**Search for a standard.** Leehey said the stringent study preparations are part of the price to pay for gaining a greater understanding of the therapeutic benefits, if any, of CBD and other cannabis products for her patients. Today, they are nearly impossible to assess because patients use them to self-medicate with products that are not rigorously tested, as other commercially available pharmaceuticals are. And there is no such thing as an established therapeutic dose of CBD to treat any condition.

The situation is complicated by the market in Colorado for marijuana products. Patients can obtain CBD from medical marijuana dispensaries, but products in the dose range that Leehey plans to study would be prohibitively expensive for most, she said. In addition, dispensaries' CBD products are not pure CBD, but

instead have varying concentrations of the compound and other marijuana components, she added.

Patients visiting a dispensary can get advice on products that treat particular symptoms, such as pain, fatigue, sleeplessness – not from physicians, but from dispensary staff who rely on experience and anecdotal evidence, due to a lack of informative studies.

“I have concerns about the self-medicating,” Leehey said. “Some patients tell me the products are helping them, and in that case I don’t want to tell them not to take them, but CBD is like all the other herbal products sold over the counter – it is a medication.”



She added she’s concerned not only by inconsistent doses and hit-or-miss therapeutic choices, but also by the potential interactions with other drugs and potential side effects. CBD, for example, has been linked to effects on the liver.

“It’s important for physicians to understand what their patients are taking,” Leehey said. “I ask the patients in the clinic, ‘What exactly are you taking?’ and they usually don’t know.”

Kluger believes Leehey’s study offers a rare opportunity to fill the mostly black box that is CBD with a better understanding of what the drug does and how clinicians might administer it safely to patients with Parkinson’s. He plans to work with Leehey on studying the effects of CBD on memory, motor speed, attention, and ability to multitask.

“Hopefully, Maureen will pave new ground for people to do other studies,” Kluger said. “This is a unique opportunity for CU researchers to get a leg up in an area where little is known across the board. There are many regulatory hurdles, but the boundaries are worth pushing through.”