



Q&A: Yasmin Hurd

A better treatment for opioid addiction

Yasmin Hurd, a neuropsychopharmacologist and director of the Addiction Institute of Mount Sinai in New York City, is exploring the cannabis-derived chemical cannabidiol as a treatment for opioid addiction.

How did you come to study cannabidiol?

Friends tease me because I've never smoked marijuana, yet study it. I started out looking at the impact of tetrahydrocannabinol (THC) — the cannabinoid present at the highest concentrations in the cannabis plant — on the developing brain. My question was: is there something going on such that your brain encountering THC before ever seeing an opioid changes your sensitivity to that opioid? I wanted to compare THC with another cannabinoid, so we looked at the second most prevalent cannabinoid in cannabis — cannabidiol (CBD). When we gave rats CBD, their heroin-seeking behaviour declined, opposite to THC.

What have your studies in people found?

We showed that CBD could decrease cravings prompted in heroin users when showing them videos of drug paraphernalia (Y. L. Hurd *et al. Neurotherapeutics* 12, 807–815; 2015). One week after their last dose of CBD, their cravings were still reduced, as was any prompt-induced anxiety. CBD has a protracted effect.

What does CBD do in the brain?

Many labs worldwide are racing to work out

CBD's full mechanism of action. It affects multiple systems: the CB₁, CB₂, and GPR55 cannabinoid receptors, vanilloid receptor 1 and the 5-HT_{1A} receptor. It also enhances adenosine levels through the adenosine A₁ receptor. But it's not really potent at any one of these, and that's something that I find fascinating. Neuropsychopharmacologists are trained that when something is high, they should get a hammer and knock it down. And when something is low, they need to get something big to drive it up. CBD operates in a milder way. Perhaps the reason that it doesn't have considerable side effects is that it's not dramatically knocking something down or pushing something up. It's just fine-tuning different systems.

What are the challenges in CBD research?

The stigma and government regulations are big obstacles. In the United States, researchers had to get a licence for CBD: because it comes from the cannabis plant, it is classified as a schedule 1 controlled substance — even though, unlike THC, it doesn't produce intoxication and isn't addictive. Bureaucracy added at least six months to our studies. We had to get a specific type of safe for storing the CBD. A guard

had to follow my clinical coordinator. I had to get an import licence, and an export licence.

What has changed in the past year?

The US Agriculture Improvement Act of 2018 means that hemp (cannabis containing a low level of THC) is no longer classified, so if you're studying hemp-derived CBD, you no longer need a licence. That has made a huge difference. The US National Institutes of Health has put out a request for grant applications on cannabinoid-related science. Now everybody is writing a CBD paper! But there's a considerable shortage of medicinal-quality hemp-derived CBD. And CBD derived from cannabis is still a schedule 1 drug.

Does hemp-derived CBD differ from CBD derived from cannabis?

No, and this is the thing: chemistry is chemistry. If you're only extracting and using CBD, and you can prove that you don't have any THC in there, or less than 0.3%, it shouldn't matter. Federally, CBD should not be classified at all. I think that its complete declassification would have a huge impact on being able to conduct the research that's needed.

What are you working at the moment?

In our rat model, we observed that CBD reverses some of the glutamate-related changes that heroin induces in the brain (J. Ren *et al. J. Neurosci.* 29, 14764–14769; 2009). So, we will study the neurotransmitter glutamate directly in the brain using neuroimaging in people with opioid-use disorder. We'll complement that with studies in animals to get a handle on how CBD is working. Now that we have replicated the effects of CBD on drug craving and anxiety in pilot human studies, I want to see whether it works in the real world. We are seeking funding for a large study of CBD treatment in hundreds of people with heroin-use disorder, including those being treated with the heroin substitute methadone. Methadone doesn't completely block cravings — it's about harm reduction. Although methadone is an opioid, it is more manageable than heroin. We will be able to see, in a large population of people who are also on methadone, whether CBD can help to reduce the amount of opioids that they consume.

What drives your work on CBD?

Addiction is such a tough disorder. It's not about morals. I don't understand why we're so nonchalant about the fact that in the past decade, almost half a million people in the United States have died from opioid drug overdoses. I think that if we can better understand addiction, we will be able to develop non-addictive treatments. When we have those medications, the stigma will be decreased. People will realize that someone can function normally. You won't even know that they had a substance-use disorder.

INTERVIEW BY ANNA NOWOGRODZKI

This interview has been edited for length and clarity.