The Science of Cannabis, Pain, and the Endocannabinoid System Transcript

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Introduction and guest background

CBD has been highly exploited without a lot of good scientific backing for the things that it's being exploited for. For instance, pain. So it has really never been shown to be a good analgesic.

One study out of Sydney, Australia in an emergency room department administered I think 400 milligrams of CBD to people who came in with low back pain Hi there, it's Dr.

Jenn. Welcome back to the Healthy by Dr Jenn podcast. Today, if you are curious about cannabis and how it can be used medically, please stay tuned. Today we have Michelle Sexton, Dr.

Michelle, she is a medical staff professional at the Center for Integrative Medicine at The University of California San Diego. And she's the first naturopathic doctor hired at UCSD, formerly an ADCIS adjunct professor at Department of Anesthesiology.

After she got her naturopathic medicine degree at Baster University in Seattle, she completed a postdoctoral fellowship at the University of Washington in the departments of pharmacology, psychiatry, and behavioral services.

There she studied the endocannabinoid system and its roles in neuroinflammation and neurodegeneration. Her NIH-funded predoctoral and post-doctoral research investigated cannabis effects on immune parameters in patients with multiple sclerosis.

Welcome, Dr. Sexton, so excited to have you here. That's amazing. So you are kind of a trailblazer going in there at the University of San Diego, right?

Or were you all accepted? Was that easy?

Cannabis medicine and the endocannabinoid system

Yeah, and it was really the The research in cannabis that I had done that You know opened that door for me during the opioid epidemic back about 2015 and 16 and the pain division at UCSD Looking, you know for ways to help people exit opioids and they needed somebody to give patients expert guidance rather than just telling them to use cannabis with no information about how to do it.

Right, just go get it off the street, which no, that would not be good. So when you went in there for teaching, you're teaching the doctors that there are alternatives to opiates, and then teaching them why scientifically it helps.

Yeah, I mean, we've done a lot of that research at UCSD as well, but I do like we have a pain fellowship. And so every year I, do a grand rounds to the fellows so that they understand, you know, that this is a medicine to be used in pain medicine and how to do it.

Then they have to go back to, or they leave their fellowship to wherever they're going. the cannabis legality, you know, wherever they are. Yeah. Has it been well received by the fellows and the management?

Oh, yeah. That's great. Because I think when the medical school is, providing it as education, then it gives us some validity. And so I teach about five or six different groups of fellows, including geriatrics, geriatric, palliative care, you know, it's an area for a lot of different reasons cannabis can be helpful there, oncology and addiction medicine.

That's great. So what exactly is the endocannabinoid system? Because some people think it's just to get high or something, but it is actually a system in our body that is connecting with this plant.

Absolutely, yeah. So it kind of followed the history of how morphine was isolated, which happened in the early 1800s. And then it wasn't until, I believe, the 1970s, where a female scientist, Candace Pert, first identified that we had an opioid receptor.

And so that's where this concept of plant compounds and the biologic interaction is because we have protein receptors that are interacting with these botanical compounds.

So that's how the endocannabinoid system first got described was finding a protein receptor and then over time learning that this is a survival based system to provide that we eat, sleep, relax, protect and forget.

and it's in every tissue in our body, and its providing a homeostatic relay or feedback for all kinds of chemical signaling across the body. So for not utilizing that system, you think it is hurting the patient in a way?

What do you mean by not utilizing it? If we're not exploring this avenue because it is there and using instead stronger medications, is that doing a disservice?

Because it's a homeostatic system, it can be modulated. But in most instances, its pretty hard to turn it off. So, we are modulating it all the time. It has been shown to be modulated by acupuncture, by osteopathic manipulation, and by exercise, things that we eat, our social interactions.

So it's being modulate all of the times, but it is hard to permanently down-regulate it because of its homeostatic roles. That's one reason it makes it a little more attractive.

some other drugs because the withdrawal nowhere compares to the type of withdrawal that occurs like benzodiazepines and opioids. So people can use it and then stop using it without a lot of worry that there's going to be very negative impacts on their physiology and functioning.

So in that case, like opiates, you develop kind of a resistance in a way to it, or you need stronger and stronger doses.

THC dosing, tolerance, and product potency

Is cannabis like that? I think it depends, you know, on what people are using, because in my talk, I talked a lot about dose, so you can have absolutely opposite effects of, for instance, THC, the main psychoactive component, at a low dose versus a high dose.

Way to you know illustrate that is anxiety that at low doses it tends to really calm anxiety But as you go up in the dose you can you? Know it can be angiogenic and then beyond that people can become paranoid and at the furthest extreme psychotic So dose really matters because you don't want to like suppress the system.

We really just want it to be toning it and occasionally hacking it. Got it, so tonning it is not just cannabis for this system, it's like you said interactions and Yeah, everything that we're doing can tone it, you know, just like physical touch and massage releases, they're like endorphins, the opioid compounds that make us feel good.

They are part of the runner's high. You know they go up when you do moderate exercise, so it's part our feel-good system in our body. So we want to make sure that it is functioning and that were promoting its function, but we don't want suppress the function.

And then when people are in pain and we've done everything from a root cause state that we can, I guess, when do you recommend cannabis so it can improve this endo-nanoboids system more?

So that's a matter of debate. Some people think people should have to fail opioids before they're given the opportunity to try cannabis. But really the paradigm where I work is why ever start the opioids?

Because you do develop that tolerance and the dose has to keep going up. And then over the long term, opioids

have negative effects on our physical function.

The best data that we have on this is from a drug called Sativex, which is an oral mucosal spray that's made from the cannabis plant, and it was designed for people with multiple sclerosis.

It was produced in Great Britain. And that was your studies that that wasn't your study. We were not studying Satevex in my study, we were just studying people using cannabis.

So There is some like longitudinal data of use of Sativex. And so what that data has found is that once people find that dose that really works for them, that after six months, they were not having to keep increasing that dos.

So it doesn't seem like the same type of tolerance is occurring as with some other drugs. They're staying on that does and it's helped helping them modulate their chronic pain.

Yeah, for multiple sclerosis, spasticity, pain, sleep would probably be the top three. But we also know that it's modulating immune function. So, you know, we know in a neuroinflammatory disease like multiple-scleriosis, to be able to turn down the volume on pro-inflammatories molecules is probably also a piece of what the Sativex or other cannabis extracts may be doing.

And overall inflammation because pain is usually from inflammation. I tell people that using cannabis to think of it kind of like a combination ibuprofen Tylenol, which apparently they have in Australia and we don't have it in the United States.

But you do get that anti-inflammatory benefit plus the analgesic benefit. Now, cannabis affects the brain. What are some negative concerns with it? Because, you know, we do read about, kids smoking hot and affecting their dopamine and effecting their brains.

So, I mean, but that's recreational use. I guess, how do we decide? And what are the side effects that we should be concerned about? Because it's out there.

You can get it anywhere. One thing about decision is age. So I think cannabis is a drug best used after brain development is done. And, what age is that?

28 to 30, potentially. But yeah, the younger the brain, probably the more detrimental the impacts. And so there are cases where there children with intractable pain.

And there occasions where we do employ it for children, but always under adult supervision. But teenagers out there using it are most often accessing You know illegal sources black market sources and there's a lot of problems with that.

CBD evidence and limitations

There's contaminant problems There is the potency issue and so because we know how involved the endocannabinoid system is in developing Networks in the brain and brain pathways that any exposure starting in The womb is probably we're gonna learn over time detrimental Okay, so what I heard you saying is basically wait until the brain has developed 30. So, I mean, we shouldn't have college students using this for sleep.

They should be looking for other things to wait. I think again thinking about dose is really key. Okay. You know, because a lot of times we think about cannabis in the existing literature and a of it was just, these are just cannabis smokers.

And, you know, we have a lot of other options now in terms of what people are using, like very low potency stuff and frequency. Like if they're just using it once a night for sleep, that's going to be very different from somebody who is hitting a vape pen all day long, for instance.

So dose matters, I think, is the takeaway. What do you think about just now that it's more widely available, you probably think well that's good, but then it is kind of crazy, right?

There's like, like you said, it in vapes and it like on every corner all these stores are popping up and people aren't working with a doctor to use it correctly.

So what are your thoughts on that and what's the solution? Well, I think on the one hand, you can think of it as harm reduction sometimes, because actually it's a less detrimental substance to our human body than alcohol.

Fair point. Or some other recreational substances people may be using. But the easiest way are these vape pens. And so this is now a botanical extract that may or may not be purified, especially if people are just buying it in a smoke shop and not a licensed dispensary.

So sometimes they're using solvents, other chemical processes, even to convert CBD to THC, but not measuring what are all of the byproducts of these chemical conversions.

And so people who are ingesting things, we have no idea what they are. Right. If you try to like say, well, this is cannabis. And you go back to the historical context of what cannabis was.

We're not even talking about the same thing anymore. When the University of Mississippi first started testing cannabis, this was after THC was isolated in 1964, The highest potency of a plant they tested in this one paper was 11% THC.

You will barely ever find that in a store. Most of the cannabis now, the flower itself will be 20% and above. So it's really, it has now been bred for this high potence, and in breeding it for high-potency THCs, you're down-regulating all the other minor cannabinoids that were there in a complex mixture.

So I argue that should we even be calling this cannabis anymore? Yeah, that's true. Can you explain, just so we have clarity for the listeners, what does it mean THC and the different percentages and why that is a concern or something to look at?

So THC, or tetrahydrocannabinol, was identified as the active ingredient. So for a long time, just like finding morphine in opium poppy, we knew what the act of ingredient was, but with cannabis we didn't.

There were a ton of pharmaceutical preparations on the market in the United States in early 1900s. But because nobody could control the potency, of the THC molecule because we couldn't measure it, they really fell out of favor.

So, you know, it was hard to have a standardized dosing when you don't have the standardized component you're looking for. That compound is considered an agonist at our cannabinoid receptors.

There's two main receptors, the cannibinoids one receptor is the most highly expressed receptor type G protein couple receptors in the brain. It's all across the Brain because it's homeostatic for neurotransmission.

You know, you think, okay, serotonin is flooding the synapse. How does how do you get the message back to say, okay, you can turn off the serotonin now or the dopamine or glutamate.

Driving, reproduction, and developmental concerns

It's that endocannabinoid system on demand, traveling retrograde and closing calcium channels. So it's just this simple negative feedback loop. So our endogenous compounds do that, but THC is much more highly potent than our indigenous compounds.

And this is why you don't need a lot of it to get the same effect that our body would naturally have. Okay, so Would the side effects come from higher THC now?

Yeah, yeah. So as it was demonstrated with the drug Sativex, if you start people at a low dose, so one spray of Satevex is 2.5 milligrams or 2 point, I think it's 2.5 mg of TH C along with 2 0.7 milligrams of CBD.

It's kind of a one-to-one mixture. 2.5 can be too much for some people, especially I found in cancer patients, their tolerance really comes down. As we get older and our endocannabinoid function starts to wane like everything else, we can more susceptible.

So people who were users in the 60s and 70s with lower potency cannabis and they come back now and try it and there just hit too hard. Yeah. This is what people need to understand.

But starting with a really low dose, and hold that dose for a few days, your body gets tolerant to the side effects. And then if you're not getting pain benefit at that low dose, you just bump it up a little bit and you do this consistently over a period of a couple of weeks.

What often happens is that people develop tolerance to side-effects and at the same time they're getting the therapeutic benefit. Now, what about CBD just with no THC, like cannabis that, because that is a lot of what's out in the market right now or over the counter.

What are your thoughts on, as that positive? Well, CBD has been highly exploited without a a good scientific backing for the things that it's being exploited for.

For instance, pain. So it has really never been shown to be a One study out of Sydney, Australia in an emergency room department administered, I think, 400 milligrams of CBD to people who came in with low back pain.

Every single one had to have rescue medication because it did not do anything for their lower back. That's pretty bad then, yeah. I think placebo would work better.

Might have. Okay. So I there's a misconception about what CBD does and what it's good for. And honestly, from a research perspective and human data, we still really don't know a lot.

It is approved as a drug, Epidiolex, for the treatment of treatment-resistant epilepsies in children to two different epilepsy types. And other than that, it hasn't been approved by the FDA for anything else.

Interesting. So if someone's like, oh, yeah, I tried cannabis. I'm on CBD, like no THC. You think that that is, it's just kind of unfounded, right? Is that what you're saying?

I think there's a big placebo effect. There's so much hype around it that I'd think people have such an expectation. Yes. Oh, placebo is strong. All right, interesting.

And then, so side effects, if you are on an actual cannabis with THC, you should not be operating heavy machinery, driving, right? I mean… So there's a lot of conflict in the research about that.

There are only a couple of per se driving laws, I think, in United States where if there is any THCs, it's the DUI. Because the researchers hasn't really been able to parse out a good test, right?

Like, you could get pulled over, for erratic driving, and then you'll get a drug screen. And if there's any amount of THC, may have contributed to impairment I think is in question.

So we've done those studies at UCSD, the Center for Medical Cannabis Research, driving simulator, people were told just to smoke a joint as they usually would.

As they would, sorry. Yeah, so these are all cannabis users. Well, no, they're not usually. They're used to driving. You worried me, I was like, like you always do, just smoking that.

They may be doing that, but no, in the research setting, they were in another room, and they smoked the cannabis.

The caveat being that the cannibis that we can use for research has come from our federal government.

Oh, cool. And the potency of that has been usually, no. No, not good. 10% THC or less. Oh, interesting. And what people are buying in the marketplace is often 20% or more.

Right. Wow. So anyway, they still smugged this joint of, you know, research-grade cannabis. Yeah. And what they found in the driving simulator was often that people drove slower and maybe were more cautious.

Oh, okay. And definitely less, you know, side-to-side weaving than occurs with alcohol. Maybe a little bit slowed reaction times, but it's not a strong central nervous system depressant.

Wow. So, nothing like with the alcohol and benzodiazepine or an opioid. So yeah, do people get driving instructions when they're given a prescription for opioids?

No. But we do tell people, you should probably wait about four hours after ingesting it, because that's the longest time until the peak concentration in the blood.

Inhaling, probably two hours afterward to drive, just to make sure. people are out there driving on cannabis all the time. I know. It's crazy. Wow. As with alcohol.

Yeah. So what about cannabis and reproduction? Does it affect reproduction at all? Absolutely. Absolutely in a negative way? So one thing we know that it affects in men is Cannabinoid receptors are probably involved in sperm swim, reduce sperm count.

In women undergoing in vitro fertilization, those with higher levels of endocannabinodes were less likely to conceive than those lower levels. So there's something immune-related going on in implantation with the endocannabinoid system.

So then, you know, my thought is always, as with a developing brain, we've got these normal endo-cannibinoids that have a lower potency at the receptor, but then if you're hitting it hard with THC and high doses, you can impact fertility.

Would this be the same as CBD or we don't know the studies on that? I don' think we know as much. But I would say just stay away. Well, CBD is not directly interacting with the cannabinoid receptors.

Like cannabis and THC. Yeah. And that's your thing. Is it even doing anything at all if you're just taking… Okay, okay. It's what we call a promiscuous molecule.

Okay. I mean, you could look it up and find it binds to 20 different receptors, Oh, okay. Yeah, we don't even know what it's doing in there. So cannabis, which we're talking about, is just what's found in the plant.

Cannabis for menopause, sleep, and tapering

You're not extracting anything out. It's just a different… Yeah. That is going to affect fertility. People rolling up joints in high school, that's affecting their fertility, Is that permanent or is it…

No, probably because this system can recover pretty quickly, because remember, it's a homeostatic system. We need it to function to survive. But the system could bounce back pretty quick.

So the other thing involved in reproduction is the developing brain. And again, when these neurons are just starting to be formed and the Every organism with a notochord has an endocannabinoid system.

So as soon as that notchord is developing by week eight of the embryo, you know, cannabis use is going to have an impact. On the leading edge of neurons is the CB1 receptor, and it is guiding neurons out to make their connections.

Again, my question is you've got anandamide or 2AG calling the neurons, but now you throw THC into the mix. And we're learning through, you know, preclinical animal research, the effects specifically on dopaminergic functioning in the developing brain.

But also think about… And developing, I mean, teenagers even, too. Even teenagers, absolutely. Or even 20-year-olds. Yeah. That's so interesting. Because we think, for some reason, it's usually boys, men, young men that that go to this marijuana.

No, but women are, you know, have really grown as users and pregnant women. It is really because they think it's safe because there is a perception that because cannabis is that natural plant that is totally safe.

That's crazy. Well, let's wrap up and talk a little bit about women and the menopause transition. Perfect time of life. Yes. You have found that this is helping women.

Absolutely. One of the first thing that happens in the perimenopaus before menstrual cycles have changed at all, the brain already starts changing. So one of our earliest things that happened with women is insomnia.

And so this is where cannabis can, you know, really be helpful. Also we know from animal data that binding the CB1 receptor with THC kind of lowers body temperature.

So potential impact for helping with night sweats. mood, low dose again, because I think the impact on the adrenal glands of elevating FSH levels can cause a lot of anxiety for women.

So just going back to toning that hypothalamic-pituitary-adrenal axis, so helping with mood anxiety, sleep, And, you know, actually as a substitute for alcohol because we know how negatively alcohol can impact sleep.

And women may start really turning to that in the perimenopause because it's calming them down and they may think that it is really helping their sleep, but those aldehydes are just so bad for our brain.

Yeah. So if you're taking it for sleep I think is helpful because it's sleep, you're going to wake up and not have the THC is going be done out of your system.

How would they know what dose to start at? So for sleep, I'm usually using ingestion because when you ingest it, there's a significant first pass effect and there is an active metabolite of THC that hangs around in the bloodstream a lot longer.

And so when your inhale, the duration of effects can be limited to three or four hours. But with ingession, it can more like six to eight. So I am usually telling people, you know, do you want to just ingested the last thing before you brush your teeth?

So that you get to sleep. The effects come on after you're sleeping and it helps you sustain your sleep or get back into sleep more quickly. And I think a good starting dose is about two and a half milligrams of THC.

I usually have people hold that dose for a few nights. If they're not sleeping better, then they could go up to five. Most of the states have adopted a standard 10-milligram unit for a single dose, but 10 is way too much to start with.

Now, is cannabis something that someone can just stop cold turkey? Should they take breaks from it, or can they just take it forever? Yeah, that's a great question.

I have a 94-year-old patient. He was a cardiovascular surgeon. Having significant back pain, degeneration, he still runs five miles a day. Oh, wow. And the thing that helped him was naproxen, but he didn't want to have to be taking that all the time.

So he started the cannabis, got significant relief. Well, he comes back to me after a period of time and he's now up to taking 33 milligrams twice a day.

He did develop significant tolerance. You can have people taper off, take a break so that endocannabinoid system can reset. and then maybe introduce again back at a low dose.

So he's back, at low-dose again. He was able to totally discontinue his naproxen. Withdrawal, like people using it for pain, often at the doses we're using medically, there's not a strong withdrawal syndrome.

It's usually people that are heavy users, you know, hitting those vape pens or smoking all day long. And the biggest impact is on sleep. There is a significant rebound REM effect, so people may have very vivid dreaming for a period of time, from days to weeks.

It's going to be good or bad depending on the dreams you have, right? just entertaining or interesting. But we know that that REM sleep is important. At high doses, THC may inhibit REMs sleep, but at lower doses that doesn't appear to be happening.

Other things that could happen, like if it was treating symptoms of something, those symptoms are likely to return.

Rapid-fire wrap-up and resources

Like if they're treating nausea, for instance. And agitation is also a part. It's in the DSM-5 as a withdrawal syndrome. That's interesting. Well, Dr.

Sexton, this has been awesome. So cool. I would love to have a few rapid fire questions with you. Okay, whatever that means. What is your favorite biohack?

that actually works? Swimming. Okay. Yes. Well, you're in San Diego, so you can swim all year round. That's right. If you could eliminate one toxin in the world, what would it be?

Plastics. I know, it's everywhere, plastics everywhere. And then what is one word you would like to leave our listeners with? I think I'll go with the Sanskrit meaning of anandamide, one of our primary endocannabinoids, which is bliss.

Oh, I love that. Yeah. Well, thank you so much. I learned a lot, and I loved having an expert to talk to about this because there's so many conflicting information out there.

Absolutely. And you are research heavy. Where could people find some of this research you were talking about? How could they find you? Can they work with you I primarily now only see patients at UCSD, I just closed my private practice recently.

Congrats. I still have a website, msextonnd.com, and so I have published a book. It's called Eat, Sleep, Relax, Protect, Forget, A System's Guide to Wholeness for Women.

Love it. Well, thank you so much. We appreciate it so. Absolutely. Much. it was so great. Thanks for having me.