

The Effects of Cannabis (Marijuana) on the Brain & Body | Huberman Lab Podcast #92

In this episode, I discuss cannabis (aka marijuana), including the biological mechanisms underlying its effects on the mind and body, its known medical applications, its impact on libido, creativity, hunger, hormones and more. I also cover the known adverse health consequences of chronic and even acute (one-time) use and the factors that determine if cannabis is helpful or harmful. Additionally, I detail how the various strains of cannabis: sativa, indica and hybrid strains, can produce such divergent effects depending on the strain type, THC-to-CBD ratio, total dosage, and frequency of use. I review why cannabis can impact speech patterns and one's propensity to develop anxiety/depression during and after use and, in some individuals, paranoia. As the legal landscape for cannabis is rapidly evolving, this episode should interest a wide audience, including former/current cannabis users, those in the medical, sports, law enforcement, and educational communities and, of course, children, teenagers, and parents.

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Other Links and Resources

NSDR Protocol with Dr. Huberman on YouTube: <https://youtu.be/AKGmY8OSHM>

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- Welcome to the Huberman Lab Podcast. where we discuss science and science-based tools for everyday life. [bright music] I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today, we are discussing cannabis, also referred to as marijuana. Cannabis includes many different compounds that have profound impact on the brain and body, so while many of you have probably heard of THC, there are also compounds in cannabis such as CBD, and of course there are different types or strains of cannabis, including sativa strains and indica strains and hybrid strains, and believe it or not, nowadays, there is also an entire literature, meaning a scientific and medicinal literature about type one, type two and type three strains. I'll explain what all of that is and how they work. I'll talk about some of the medicinal applications of different strains of cannabis and combinations of cannabis

strains, as well as some of the potential health hazards of cannabis use. I want to emphasize that any discussion about cannabis has to be framed within the context that the legality of cannabis varies tremendously depending on where you are in the world, so depending on which country you're in and even which state you're in or which area within a country, possessing and using and certainly selling cannabis can be either highly illegal or entirely legal or decriminalized or largely overlooked. You, of course, are obligated to know what those local laws are for you, where you live and where you travel. With that said, today's discussion really will include a full picture as to where cannabis and the various and even very specific compounds within cannabis can be extremely useful in the treatment of some ailments and where certain compounds in cannabis can be extremely dangerous for certain individuals to use, in particular, individuals that have preexisting, genetic propensity for psychosis. That theme is going to come up again and again, but we are also going to talk about the role of cannabis in anxiety and depression, both positive and negative effects. We'll talk about sex differences in terms of women versus men and how they react differently to cannabis, and I would be entirely remiss if I didn't include a conversation about cannabis, meaning THC, CBD, hybrid strains, et cetera in creativity and different modes of thinking, because as many of you probably know or at least have heard about, cannabis can impact the way that we think, the types of memory systems we can access and what's called convergent and divergent thinking, which is one way of conceptualizing what is commonly referred to as creativity. So today's discussion is going to include a lot of information, but I promise to make it clear and accessible to all of you, regardless of whether or not you have a background in biology or not, and today's discussion will also be quite nuanced. You'll find me routinely reading directly from specific research papers, something that of course we always do on this podcast, but today I'm really going to dig into some of the finer points of the methodology in papers and some of the statistics that were used and the specific populations of people that were studied, because as it turns out, there are instances that we will discuss in which the use of cannabis can be immensely beneficial to one group and yet can be entirely detrimental to another group, even at equivalent dosages and depending on a number of different factors, so we will discuss what those factors are. Just to give you a brief overview of the kind of structure I'm going to put on today's episode, we will review of course, cannabis and its various forms. I'll talk about some of the biology, but we are going to really drill into how dosage, that is the concentration of THC relative to CBD, impacts whether or not cannabis is

going to have one effect or another. We will also talk about the frequency of use, daily use, multiple times per day use, weekly use or monthly or occasional use. We will also talk about different professions and how some people may have a little bit more leeway in terms of whether or not they decide to use cannabis or any of its various component chemical constituents, that is CBD or THC, et cetera. And for other professions, it might be entirely inappropriate because of the particular kinds of cognitive tasks those professions demand. We will also talk about genetic predisposition, again, sex differences, hormone effects, and I will also touch on what I think is the most important variable in determining whether or not cannabis is right or wrong for you, and that is your age at which you are considering starting or continuing use or ceasing use. What I can assure you is that by the end of today's podcast, you will have a quite thorough understanding of cannabis, how it works, what it does, what its potential benefits can be, what its potential hazards are,

00:04:46 New Huberman Lab Premium Membership

and whether or not it's right for you and the people that you know. I'm excited to announce that the Huberman Lab Podcast has now launched a premium channel. The purpose of the premium channel is severalfold. First of all, I will be hosting regular AMAs, Ask Me Anythings, where you can ask me anything, and I will provide answers in depth to your specific questions about science and science related tools for mental health, physical health and performance. Now, there is a nominal cost to the premium channel. It's \$10 per month, or you can pay \$100 for the entire year. I should mention, however, that a significant portion of the funds raised through the premium channel are going to support not just the "Huberman Lab Podcast," which we will continue to release every Monday on schedule of zero cost to all consumers' content on mental health, physical health and performance, but proceeds from the premium channel will also be used to fund research, in particular research done on human beings, so not animal models, but on human beings, which I think we all agree is a species that we are most interested in. And, we are going to specifically fund research that is aimed toward developing further protocols for mental health, physical health and performance, and those protocols will be distributed through all channels, not just the premium channel, but through all channels, Huberman Lab Podcast and other media channels. So the idea here is to give you information to your burning questions in depth and allow you the

opportunity to support the kind of research that provides those kinds of answers in the first place. Now, an especially exciting feature of the premium channel is that the Tiny Foundation has generously offered to do a dollar-for-dollar match on all funds raised for research through the premium channel. So this is a terrific way that they're going to amplify whatever funds come in through the premium channel to further support research for science and science-related tools for mental health, physical health and performance. If you'd like to sign up for the Huberman Lab premium channel, again, there's a cost of \$10 per month or you can pay \$100 upfront for the entire year. That will give you access to all the AMAs. You can ask questions and get answers to your questions, and you'll of course get answers to all the questions that other people ask as well. There will also be some premium content, such as transcripts of the AMAs and various transcripts and protocols of Huberman Lab Podcast episodes and not found elsewhere. And again, you'll be supporting research for mental health, physical health and performance. You can sign up for the premium channel

00:07:03 Tool: Non-Sleep Deep Rest (NSDR), Sleep & Anxiety

by going to hubermanlab.com/premium, again, that's hubermanlab.com/premium. Before diving into all of that, I'd like to highlight a new, what I think is a very useful and zero cost resource. This resource is what's called Non-Sleep Deep Rest or NSDR protocol. I've talked many times before on the Huberman Lab Podcast about Non-Sleep Deep Rest, AKA, NSDR. NSDR is sort of an umbrella term for a variety of different practices, so these are behavioral practices that allow you to direct your brain and body into a particular state, and most typically, that state is one of deep relaxation, but also one in which you can access your bodily and brain systems for teaching yourself how to relax in real time and how to recover some of the sleep that you may not be getting at night, and to restore levels of dopamine in particular areas of the brain that are involved in motivation and cognitive and motor control. Basically, NSDR is a wonderfully restorative tool. This has been demonstrated many times over now through quality peer-reviewed science, and there are neurochemical benefits, and there are physical benefits, and there are certainly psychological benefits. I highly recommend NSDR to anybody that has trouble falling asleep or that wakes up in the middle of the night and needs to get better at falling back asleep, as well as to anyone out there that has issues with anxiety or self-regulation of any kind. And if you don't have any of those issues, it's also

immensely beneficial just as a restorative for leaning back into focused work of any kind. Now, a number of people have reached out about finding NSDR protocols, and there are a number of different good ones out there floating around. I've decided to put a zero-cost NSDR script out there on the internet for people to access, so you can find it by going to YouTube and simply put my last name, 'Huberman' and 'NSDR' into the search function. This is a YouTube channel that's hosted by Virtusan, which has a terrific app that includes NSDR and a number of other health and wellness protocols, but they've been quite generous in hosting a 10 minute NSDR, read by me. This NSDR is distinct from, although I should say, similar to yoga nidra, which some of you are familiar with. This NSDR is different than yoga nidra in the sense that it doesn't have intentions. There's no mystical component, and I describe a little bit of the science and why specific components of the NSDR are included, things like long exhale breathing, I talk about perceptual shifts and how to move from thinking and planning to pure sensation. If none of that makes sense right now, it'll make total sense after listening to the NSDR script. Again, it's a 10 minute NSDR script, read by me. You can do this first thing in the morning when you wake up, especially if you didn't get enough sleep that night, and you're feeling a little bit fatigued, and you need to lean into the day with full vigor. You could do it at any point during the day or if you wake up in the middle of the night. Again, this is a zero-cost resource for you. You can find it by going to YouTube, put my last name in and NSDR. I encourage you to try it, and if you like it or frankly, if you don't, you can just put that in the comment section there on YouTube, and I've put it there as a free resource to you, so that you can benefit from the research-backed,

00:10:08 Levels, Thesis, InsideTracker

peer-reviewed studies that point to NSDR as a very useful practice. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero-cost to consumer information about science and science-related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is Levels. Levels is a program that lets you see how different foods affect your health by giving you real-time feedback on your diet using a continuous glucose monitor. One of the most important factors in your immediate and long-term health is how well you're managing your blood glucose or blood sugar. I started using Levels about a year ago as

a way to see how different foods and different lifestyle factors were impacting my blood glucose levels. So for instance, it allowed me to see how different foods and particular macronutrients and combinations of macronutrients would either peak or trough my blood sugar or keep my blood sugar steady. It also allowed me to see how working out with weights or running, how that impacted my blood glucose. So for me, it was a fascinating experiment unto myself as to how my meal schedule, the specific foods I was eating, different combinations of food, as I mentioned before, and exercise were combining to regulate this thing that we call blood sugar and that's so vital to our health. I think anyone that tries Levels will find that you learn an immense amount about what you're doing and what you ought to be doing differently in order to optimize your immediate feelings of wellbeing and your health trajectory. If you're interested in learning more about Levels and trying a CGM yourself, go to levels.link/huberman, that's levels.link, L-I-N-K, /huberman. Today's episode is also brought to us by Thesis. Thesis makes custom nootropics that are designed for your particular needs. I am not a fan of the word nootropics, because nootropics literally means smart drugs or smart drug, and frankly, as a neuroscientist, I know and every other neuroscientist knows that there is no neural circuit or chemical in the brain for being smart. There are, for instance, neural circuits and chemicals that increase your ability to focus or your ability to task switch. Thesis understands this and therefore, has designed custom nootropics that vary and are tailored to you so that, for instance, if you want to achieve focus and clarity for one particular type of work, there is a Nootropic for that. Or if you'd like to have more energy and have more focus, there's a different Nootropic for that. If you'd like to get your own personalized nootropics starter kit, you can go online to takethesis.com/huberman, take that three minute quiz, and Thesis will send you four different formulas to try in your first month, and then they'll work with you and iterate to find the best formulas for you to take ongoing. Again, that's takethesis.com/huberman and use the code 'huberman' at checkout to get 10% off your first box. Today's episode is also brought to us by InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals. I've long been a believer in getting regular blood work done for the simple reason that many of the factors that impact your immediate and long-term health can only be analyzed with a quality blood test. With a lot of blood tests and DNA tests out there, however, an issue is you get information back about lipids and hormones, et cetera, but you don't know what to do with that information. With InsideTracker, they

have a personalized platform that makes interpreting your data and then acting on that data very straightforward and very directed toward specific protocols. What I mean by that is you'll get information back about hormone levels and metabolic factors, lipids, et cetera, and then you can look to nutritional changes, supplementation changes, exercise protocol changes and other lifestyle features that combine or work on their own to start to try and shift those numbers into the range that's appropriate for you. If you'd like to try InsideTracker, you can visit insidetracker.com/huberman to get 20% off any of InsideTracker plans. Just use the code 'huberman' at checkout.

00:14:01 Momentous Supplements

Again, that's insidetracker.com/huberman to get 20% off and use the code 'huberman' at checkout. On many episodes of the Huberman Lab Podcast, we talk about supplements. While supplements aren't necessary for everybody, many people derive tremendous benefit from them, things like enhancing sleep and the depth of sleep, or for enhancing focus and cognitive ability, or for enhancing energy or adjusting hormone levels to optimal range for you. The Huberman Lab Podcast is now partnered with Momentous Supplements. We partnered with Momentous for a number of important reasons. First of all, the quality of their ingredients is exceptional, it's really second to none. Second of all, they ship internationally, and that was important to us, because a number of you reside outside of the United States. Third, we've worked with Momentous very closely to develop single-ingredient formulations. Now, this turns out to be very important, because if you're going to take supplements, you want to know what's working for you and what isn't. And of course, you want to optimize the cost efficiency and the biological efficiency of those supplements. To find the supplements we discuss on the Huberman Lab Podcast, you can go to [livemomentous](https://livemomentous.com/huberman) spelled O-U-S, livemomentous.com/huberman, and I should just mention that the library

00:15:08 Cannabis Strains, Psychoactive Compounds: THC & CBD

of those supplements is constantly expanding. Again, that's livemomentous.com/huberman. Let's talk about cannabis, and when we refer to cannabis, we are indeed referring to marijuana or the marijuana plant. Now, cannabis plants come in different strains or different varieties, and those different strains are

indeed different genetic strains. So just as animals and humans have different genetic backgrounds, and they can be crossed to one another to yield further genetic variation in the offspring, plants can be hybridized to one another in various ways through grafting or through the use of different types of seed combinations, et cetera, in order to generate different strains. There are also naturally occurring differences in the strains of plants, and the cannabis plant is no exception. So for instance, in the context of the discussion about cannabis and its medicinal uses and recreational uses, we need to distinguish between the sativa variety, the indica variety, a variety called ruderalis that's not often discussed, and hybrids of sativa, indica and ruderalis. Before diving into the different strains of cannabis and how they impact the brain embody, both similarly and differently, I want to emphasize that the cannabis plant contains a number of different psychoactive compounds. Now, the most powerful of those compounds is THC. The technical name for it is delta-9-tetrahydrocannabinol. But THC, as I'll refer to it, is just one of the psychoactive and biologically active compounds within cannabis plants. There's also CBD, which is technically referred to as cannabidiol, and cannabidiol, CBD, is known to be used for things like pain management, anxiety management and other medicinal purposes. We will talk about the efficacy of CBD for those purposes, as well as some of, believe it or not, some of the dangers of CBD, depending on where it's sourced and the dosage, et cetera. So we've got THC, CBD and also CBN or cannabinol. CBN is less often discussed. You're going to hear a lot less about CBN containing products out there, CBN containing medicines, but it is relevant to today's discussion, so it will come up a bit. Now, I will be sure to provide more specificity to what I'm about to say, but very broadly speaking, THC is largely responsible for the psychoactive effects of cannabis, that is the changes in mood, the changes in bodily state and sensation, et cetera. Whereas CBD and to some extent, CBN, have profound effects on the brain and body, but they don't tend to give people the sensation of altered perception, altered mood, et cetera. Some people might say they are not the component of cannabis that, quote unquote, gets you high, although today, we will really drill into what the high itself represents in terms of chemical systems in the brain body. And what we will soon learn is that what we think of as being high actually includes a number of different changes in the brain and body, some of which can be best explained by CBD, not by THC, which runs counter to what most people out there know and believe. So broadly speaking, we have THC, CBD and CBN. But I want to point out that the cannabis plant has over 70, seven-zero, 70 different psychoactive compounds, many of which still have not been

studied in isolation and in detail. So there's a big future of research for cannabis and for THC and THC-related psychoactive compounds, as well as for CBD and CBN. Today we're mainly going to focus on THC and CBD, as I mentioned before. I should also point out that the cannabis plant has over 400 biologically active compounds. So these are biologically active compounds that may or may not have psychoactive properties, that may or may not be useful for pain relief, et cetera. Again, there is a vast landscape for exploration of the cannabis plant and of hemp for what they include that could be beneficial to us or detrimental to us, so again, a lot more work to do. Today, we're going to really try and stay on target with what we already know and where there are certain exciting mysteries or intriguing mysteries

00:19:34 Sativa vs. Indica, Stimulant vs. Relaxation Effects

about what we ought to explore more. I will certainly highlight those. Let's go back to the different strains of the cannabis plant, sativa, indica and ruderalis and explore how each of those differentially impacts the brain and body, because therein I think we can start to learn a lot about this incredible plant that is the cannabis plant. And whether or not you are a user of cannabis or whether or not you are entirely opposed to cannabis use, understanding how cannabis works in the brain and body, itself, is absolutely fascinating and can teach you a lot about how your brain and body work at a basic level and can tell you a lot about how your brain and body will react to different life events and how your mood is established and stabilized, and how your appetite is established and stabilized and so on. So we have the three major strains of cannabis, sativa, indica and ruderalis. And for sake of today's conversation, we can pretty much cross off ruderalis. It's not often consumed, and components of ruderalis are not often consumed for medicinal or recreational purposes. Let's focus on sativa and indica. People will consume the sativa variety of cannabis either by edible or by smoking cannabis, or they will consume the indica variety of cannabis, again by edible or by smoking cannabis, or sometimes they will take it in a transdermal form or a sublingual form. There are a bunch of different ways to get the cannabis into the body, but there's a clear distinction between sativa and indica that actually shows up first in the structure of the plant. At their extremes, meaning in a pure strain of sativa, it tends to be a taller plant, a longer stock, believe it or not, and actually the length of the leaves is quite a bit longer, whereas the indica plant tends to be more short and stout. And, for those aficionados out there, I'm sure you know a lot of the

other specific features of sativa versus indica, but already what we're talking about is the same plant, cannabis, with two very different morphologies or shapes. You might say, "Well, why is this interesting or important "to how it affects me or affects other people "for medicinal or recreational purposes?" Well, it turns out that even though they are the same plant, these two different genetic varieties, because of the way that they grow and the way they capture sunlight and the way, believe it or not, that the different plants within that strain interact with one another, 'cause believe it or not, plants are interacting with one another, they actually bring different elements of the psychoactive compounds to different components within the leaves and the so-called buds. The takeaway is that when consumed, and when I say consumed, I want to be very clear, I don't necessarily just mean oral consumption or eating cannabis sativa by edible, I also mean smoking it, and that could be... people will, just like with tobacco, the way that they bring the psychoactive components into their bloodstream and into their brain and body is to essentially heat the dried leaves of the cannabis plant. Then the heat liberates some of the psychoactive components that when inhaled into the lungs, because the lungs include a lot of vasculature, a lot of basically blood vessels and capillaries, that the psychoactive components are actually directly absorbed from the lungs into the bloodstream, and they can cross into the bloodstream and permeate throughout the body and cross the so-called blood brain barrier. So in other words, burning the plant liberates the smoke that contains the psychoactive compounds, and those are inhaled into the lungs and then get into the brain and body and act on the brain and body. And the major effect of sativa varieties are to create a high, if you will, and I'm putting this in air quotes for those of you that are listening, but to also act as a stimulant. The sativa varieties tend to make people feel invigorated, somewhat alert. It doesn't tend to be as much of a sedative as some of the other varieties. Some people report heightened sense of focus or heightened sense of creativity. We'll talk a little bit later on as to whether or not they actually are achieving heightened levels of focus and creativity, or whether or not they just perceive themselves to have heightened levels of focus and creativity. The sativa varieties tend to make people feel a little bit less susceptible to pain and noxious stimuli, which are basically stimuli that you don't like. So the sativa varieties are often prescribed or are used in the recreational context for pain management and relief. Basically, the sativa variety is known to include a head biased effect. So here, we're talking about subjective effects, and of course these will vary from one individual to the next. Some people will smoke cannabis sativa or ingest cannabis sativa orally and

will feel an entirely different array of effects, but most people, the majority of people experience a head-centered high, alertness, focus and a sense that they're more creative. Contrast that with the indica varieties of cannabis, and when people smoke or eat or ingest indica varieties, the psychoactive components of indica, and again, this is pure indica, so not hybridized with sativa at all, but just pure indica, tend to lead to more full-bodied effects. People report feeling more complete, full-body relaxation, more of a sedative effect. Indica cannabis is often prescribed and/or used recreationally in order to achieve a state of sleep or to help relieve anxiety, so less of a stimulant effect. And we will talk about why, literally, the underlying neural circuits that lead to the sativa variety causing more of a elevated mood and a head high, if you will, and the indica variety as being more full body relaxation. One of the ways to remember the distinction between the effects of cannabis sativa and cannabis indica was relayed to me by a friend who actually was a chronic, meaning every day, all day, consumer of marijuana. He basically smoked marijuana for 20 years before quitting about four or five years ago, and he said that indica is often referred to as 'in-da-couch,' meaning laid back in the couch. And that can help you remember that the indica varieties of cannabis

00:25:55 Hybrid Cannabis Strains, Type 1, 2 & 3 Strains

do tend to be more sedative in their effects. Okay, so there's sativa and there's indica, and then now there are hybrid strains. So marijuana growers and people who specialize in creating novel varieties of the cannabis plant, again, I'm using the words cannabis and marijuana more or less interchangeably here, they are very good at creating new strains of plant that might be 25% sativa and 75% indica or vice versa, or 50/50 or 90/10. Essentially, what's happening nowadays is that through plant biology, plant genetics, I should say, growers are getting quite efficient at creating a variety of different strains of the marijuana plant that give rise to very nuanced and distinct effects on brain and body. In fact, so much so, that there's now a new nomenclature, a new language emerging around cannabis and the development of novel strains of cannabis for medicinal and/or recreational purposes. And while this might sound a little bit medical or a little bit clinical to some people, believe it or not, this is the nomenclature that is now typically used. People still refer to the sativa, indica and hybrid strains, but there's now also a description of so-called type one, type two and type three strains for any given sativa, indica or hybrid strain. Okay, so just to put this clearly in your mind, you've got sativa

varieties, that is pure sativa varieties. You have indica varieties, again, pure indica, and then you have hybrid varieties, and beneath each of those, you have type one, type two and type three strains of indica, sativa or hybrid varieties. What are type one, type two and type three? Well, type one, type two and type three strains are strains that have varying amounts or ratios of THC to CBD. So for instance, type one strain, so for instance, you could have a pure sativa, type one, or a type one pure sativa or a type one indica. Those are going to have the greatest amount of THC relative to CBD. And I really want to emphasize this, understanding the ratio of THC to CBD can help explain a lot or even predict a lot about how a given strain of cannabis will impact somebody. For instance, because THC is largely responsible for the typical psychoactive components of cannabis, so what I mean here is, if somebody's ingesting sativa, and it routinely makes them feel more energized, elevates their mood, it gives them a heightened sense of creativity, if that's what they experience, and they're taking a type one version of that, that means that it's quite rich in THC and very little CBD. However, if they were to take a type one version of sativa, and it feels far too strong, like too much energy, or they felt like they were too much in their head, nowadays, there are strains of sativa that have been genetically engineered, and I don't mean by an engineer tinkering away with gene engineering in a CRISPR creating mutants, but literally by hybridizing, crossing different plants to one another, creating in a natural context, the same way plants in the outside world would sometimes hybridize to one another, creating a variety that's perhaps type two, which is going to have less THC and more CBD, or a type three, which is going to be very high CBD and very little THC, and the same is also true for the indica varieties. So I want to make sure that everyone understands this, because it becomes very important for understanding the biology of cannabis and predicting positive versus negative effects of cannabis. Sativa has this stimulant-like effect and tends to be more of a head high, if you will. Indica tends to be more full-body, then lead to more in-da-couch, as I refer to it before, pun intended, deep relaxation, reduce insomnia, et cetera. Now, within each of those sativa and indica, you have type one, type two and type three, and that has everything to do with how much THC, which is the dominant psychoactive compound, versus CBD, which has other effects, mainly on the body, but not so much on the brain and modes of thinking and mood, et cetera, how much THC versus CBD is present. And again, type one is THC dominant, type two, equal ratios, if you will, of THC and CBD, and type three tend to be high CBD. Okay, so already we've got some categorization here that hopefully isn't overwhelming to you, but this turns out to be

extremely important

00:30:41 AG1 (Athletic Greens)

if you want to understand how cannabis works and predict the effects of cannabis. I'd like to take a quick break and acknowledge one of our sponsors, Athletic Greens. Athletic Greens, now called AG1, is a vitamin mineral probiotic drink that covers all of your foundational nutritional needs. I've been taking Athletic Greens since 2012, so I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens, and the reason I still take Athletic Greens, once are usually twice a day, is that it gets to me the probiotics that I need for gut health. Our gut is very important. It's populated by gut microbiota that communicate with the brain, the immune system, and basically all the biological systems of our body to strongly impact our immediate and long-term health, and those probiotics in Athletic Greens are optimal and vital for microbiotic health. In addition, Athletic Greens contains a number of adaptogens, vitamins and minerals that make sure that all of my foundational and nutritional needs are met, and it tastes great. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman, and they'll give you five free travel packs that make it really easy to mix up Athletic Greens while you're on the road, in the car, on the plane, et cetera, and they'll give you a year's supply of vitamin D3 K2. Again, that's athleticgreens.com/huberman

00:31:56 Naturally Occurring Receptors: Nicotinic & Cannabinoid Receptors (CB1)

to get the five free travel packs and the year's supply of vitamin D3 K2. Okay, so somewhat surprisingly, we're going to set aside cannabis. We're going to take what we know about sativa, indica, type one, type two, type three, CBD, et cetera, and we're just going to set that aside for a moment. Why would we do that? Well, we have to ask ourselves, why would any of these plants, why would any of these compounds, THC, CBD, sativa, indica, et cetera, why would any of that have any effect on us at all? And this discussion that we're about to have very much resembles the discussion that we had on a previous episode about nicotine, because as many of you know, nicotine is a commonly used substance. In fact, if we were to look at the three most commonly used drugs, alcohol will be at the top of the list. Many billions of people regularly use alcohol

or occasionally use alcohol. Many billions of people also use nicotine. It's the second most consumed drug, so more than 1 billion and probably closer to 2 billion people consume nicotine, and then the third most consumed drug is cannabis in one form or another. And many of you are probably shouting, "What about caffeine? What about caffeine?" Well, in the context of drugs, and in particular, addictive drugs, caffeine doesn't quite rise to the list, but if we were to look at caffeine and include it in that list, caffeine would be above all of those. But the most commonly used drugs are alcohol, second after that is nicotine and then cannabis. Nicotine, as some of you may know, if you listen to the episode on nicotine, but even if you didn't, nicotine comes from the tobacco plant, and there are a few other plants that include nicotine, and typically it's brought into the brain and body by smoking tobacco, dipping tobacco, snuffing tobacco or vaping nicotine. Nicotine exists in the outside world in these plants, the tobacco plants, but the reason it has an effect on the body is that there are so-called nicotinic receptors in the body. Now, those nicotinic receptors were named after nicotine, the compound, but they existed in the brain and body, not because of the existence of a tobacco plant, but because there are other chemicals in the body that naturally occur, namely acetylcholine that bind the nicotine receptor. Those chemicals, such as acetylcholine, that bind the nicotinic receptor in your brain and body create an enhanced sense of focus, et cetera, et cetera. But, nicotine from tobacco binds that same receptor, but with much greater affinity, and therefore also creates a state of focus, but a much greater one than we can achieve without nicotine. So you can see the nicotine episode if you want to learn more about that. In a very similar way, all of our brains and bodies, from the time that we are conceived, believe it or not, very shortly after conception, if we want to be accurate, very early conception, when you were in the womb, and still now, if you're listening to this, you have what are called cannabinoid receptors, because you also have endogenous cannabinoids. What do we mean by that? You have receptors, which are like little parking spots that are present on cells in your brain and body, and what we call a ligand, which is basically just a chemical that's released, parks in that receptor and causes a number of different biological effects. Cannabis contains compounds that also bind to those receptors, but here I want to make a really clear distinction. We have what are called endogenous ligands, those just mean chemicals from within us that we make naturally, even if we never go near the cannabis plant or any other source of cannabis, we have chemicals that are created in us that park in those receptors and cause biological effects on mood, on perception, on the immune

system, on hunger, et cetera, again, without ever going anywhere near cannabis, we have these endogenous cannabinoids. So endogenous cannabinoids are floating around in us, or I should say, they are released in us in particular ways, bind to these receptors and cause changes in mood, appetite, et cetera. They have many different effects on the brain and body, and we'll talk about those. But just like with nicotine, there are substances in the outside world, in this case, cannabis contains these substances, so things like THC and like CBD, that when ingested by smoking or vaping or by ingesting edibles also will park in those same receptors, the cannabinoid receptors and lead to biological effects. Now, it's a little bit misleading, because we call them cannabinoid receptors as if they were there to bind cannabis, or just like we call the nicotine receptors, nicotinic receptors, it makes it seem as if they were there in order to bind nicotine from tobacco, but that's not the way our brains and bodies evolved. Our brains and bodies evolved for these receptors to make use of chemicals that exist within us, called again, endogenous chemicals, and those endogenous chemicals lead to certain effects, as I mentioned before. The key thing here, if you haven't understood anything I've set up until now, please understand this, the key thing is that THC and CBD and the other components of cannabis bind to those receptors, those endogenous cannabinoid receptors, the ones that we naturally make, with much greater affinity and exert a vastly greater potency and effect on mood and perception, et cetera, than do our endogenous cannabinoids. Another analogy that one could take in order to understand this would be hormones, like testosterone and estrogen. Many people, I would say all people, make testosterone and estrogen to varying degrees. It's going to depend on whether or not you're male, female, your age, whether or not you've gone through puberty, et cetera, et cetera, but let's just take testosterone for example. There's testosterone circulating in your body. That's true if you're male or female, and there are receptors called androgen receptors, we could even call them testosterone receptors. And the testosterone binds to those receptors and has effects on cells. It causes hair growth, changes the voice. It can affect libido. It affects all sorts of things in the brain and body, depending on which organ and tissue you're talking about. But of course, there are people that take synthetic testosterone or derivatives of testosterone, and some of those derivatives, for instance, in the body building community and the sports community, they will take things like Dianabol. These are modified versions of testosterone that can bind to the testosterone receptor with much greater affinity, or I should say the androgen receptor with much greater affinity, and have supra physiological effects, effects that would essentially never

be seen from testosterone that was endogenously, excuse me, endogenously released within the body. We could say the same thing for estrogen. There are estrogen receptors, they bind estrogen, but if someone were to take synthetic estrogen or to ingest a plant compound that contains various estrogenic compounds, and those plants certainly exist out there, they can have supra physiological effects on those receptors. Why am I telling you this? Well, many people believe that because cannabis, marijuana is a plant, and plants grow out of the ground, and they're naturally occurring, and because we have receptors in our body that are there without the need to engineer them from some external source, they're in our genome. They're program for it, and we're born with these things, and we keep these our entire life. Many people mistakenly think, ah, these plant compounds are safer for us or better for us, or are somehow appropriate for us to ingest, but that's simply not true, and here, I'm not saying that cannabis is always a bad idea for people. There are certain populations and certain people for which it can be relatively safe recreationally, that's the truth, and there are other populations for which it can be downright dangerous, recreationally or medicinally. And of course, there are medicinal purposes that are being explored, and we'll talk more about that. But this is vital to understand, because I think that when we hear, "Oh, it's from a plant, it's natural," and then you also have a receptor for these, endogenous cannabinoid receptors, and therefore, the marriage of those two, the coming together of the chemical THC or CBD or both with these receptors is somehow supposed to happen as if this was a purpose of having these receptors, but it's simply not the case. In the same way that the nicotinic receptors are not there because nicotine is good for us, they're there because there are compounds

00:40:35 THC, CBD vs. Endogenous Cannabinoids, Dependence

that exist within us that are good to bind to those receptors from time to time. Now, here's the key thing about, I guess today, I'm saying there are a lot of key things, but here's another key thing about understanding cannabis and the way that it works, which is that THC and CBD, when they're brought into the brain and body by smoking or edible, et cetera, they bind to those receptors, those endogenous cannabinoid receptors, and they tap into the same systems that your endogenous cannabinoids would tap into, the ones that affect mood and energy and creativity and relaxation, et cetera, but they do so with thousand fold greater potency. And as a consequence of that, your endogenous

cannabinoids are outcompeted. They really get no opportunity to interact with those receptors. And understanding that, can lead to a very clear understanding of why, for instance, when people use cannabis to relieve anxiety, or they use cannabis to enter a certain brain state for creativity or to enter sleep, why a dependence on cannabis starts to emerge. Because if they don't ingest cannabis, and again, ingest could mean smoke to bring THC in, or CBD in, or ingest orally or even transdermal or tincture or one of the other varieties, if they don't do that, then what happens is not only are the receptors not stimulated to the same degree or with the same potency that they normally are, but the endogenous cannabinoids can no longer have their effect, so people experience heightened levels of anxiety, disrupted mood, disrupted brain state, and so on. Now, again, I want to be very clear that I'm not trying to paint a picture of cannabis as all bad or even partially bad. What I want to do today is give you as much information I can as to how cannabis works, how its different component parts work, how the different types of cannabis work, and point to some of the valid medicinal uses and some of the recreational uses, and then lay out the landscape for you as to who is really most at risk in terms of psychoactive components, immune components and so on and so forth, so that you can make the most informed choice for you. I am not here to tell you what to do or what not to do. As I like to say, do as you wish, I mean, don't do as you wish if it harms other people or yourself, but do as you wish, but know what you're doing, so that's really my goal here. So as we begin to dive further into the biology, I think you'll start to get a clearer picture of why cannabis is so effective in some context, but also why it can create such massive suffering in other contexts because of the way

00:43:14 Endogenous Cannabinoids, Cannabinoid Receptors & Nervous System Function

that it out-competes your own natural endogenous cannabinoid systems. So let's talk about those endogenous cannabinoid systems, what they are and how they work, because that will give us a lens into what the higher potency or maximum impact of the various cannabis plant varieties and strains in THC and CBD and so forth, how and why those work. So what are the endogenous cannabinoids, these chemical substances that everybody makes? You make them, I make them. You've been making them basically from the time that you were conceived, and you are going to make them until the time that you die. Whether or not they have the impact and the biological functions that I'm

about to describe will depend a lot on whether or not you are using your own endogenous cannabinoids to park in those receptors that you also have from birth until death, or whether or not you are tickling those receptors or strongly activating those receptors using some external source like cannabis and THC, et cetera. The two main endogenous cannabinoids that we want to consider are anandamide, which we will refer to as EAE, so anandamide, and another one, which is arachidonoyl-glycerol, arachidonoyl-glycerol, which we will abbreviate 2-AG. So let's just take EAE and 2-AG, lump them together and talk about the endogenous cannabinoids, just to make it simple. But if you want to do the deep dive on anadamide versus 2-AG, please be my guest.

The endogenous cannabinoids are released from neurons. What are neurons? Neurons are nerve cells. And nerve cells should be conceptualized like this. You have presynaptic neurons and postsynaptic neurons. Presynaptic neurons basically contain little vesicles, little bubbles full of neurotransmitter, which are chemicals, and when neurons are stimulated electrically, and that could be from a thought, it could be from the desire to move, it could be because of a drug, it could be because you're hungry, the relevant neurons will vomit out or will fuse, as we say, those little packets, those little bubbles of neurotransmitter into the gap between the pre and postsynaptic neuron, and we call that a synaptic cleft or the synapse. It's a little gap, a little space, and the neurotransmitter flows across that synapse, and some of it will park in the little parking spots that we call receptors on the postsynaptic neuron side. Depending on which neurotransmitter it is, and a bunch of other things not worth going into right now, the parking of that chemical and those neurotransmitter receptors will either cause that neuron on the postsynaptic side to itself, release neurotransmitter elsewhere, or it will quiet it down, so-called excitation and inhibition. That's kind of neuro transmission in a nutshell. If you don't understand it, no big deal. It's not going to prevent you from understanding today's discussion. If you understand even a small fraction of what I've just said, then it's going to allow you to understand not just today's discussion, but a lot of neuroscience with a lot more nuance and depth of understanding. The key thing to know about the endogenous cannabinoids is that unlike most neurotransmitters, they are released from the postsynaptic side. So what happens is neurotransmitter goes from presynaptic neuron to postsynaptic neuron, but under certain conditions, the postsynaptic neuron, itself, releases a chemical, and that chemical goes backward, what we call retrogradely, to the presynaptic neuron, binds to receptors there and changes the probability that the presynaptic neuron will release neurotransmitter. Put simply, endogenous cannabinoids

tend to decrease the probability that a neuron will release neurotransmitter. They're a break on the system. They're a way of shutting down the communication between neurons, regulating it, not to make it completely quiet, but to adjust the levels with a lot of nuance. Now, the other thing that the endogenous cannabinoids do is a mind bender, because we're talking about cannabis, and a commonly known feature of cannabis and marijuana consumption is disruptions in short-term memory, and there is essentially zero debate as to whether or not that occurs, and we'll talk about the mechanisms a little bit later. And yet, endogenous cannabinoids, the chemicals that you naturally release from these postsynaptic neurons that travel retrogradely back to the presynaptic neuron, actually can lead to strengthening of connections between the presynaptic neuron and the postsynaptic neuron through a process called long-term potentiation, or LTP. They can also cause what's called depression of communication between a presynaptic neuron and a postsynaptic neuron. Long-term depression has nothing to do with depression as a psychological state or as a illness. Long-term potentiation and long-term depression simply refer to the probability that one neuron will be able to stimulate and activate another neuron. And, as I just told you, the endogenous cannabinoids can either turn up the dial or turn down the dial. They can either increase the probability or decrease the probability that a given connection between neurons will function more or will function less. So if you think about the communication between neurons as crosstalk, as a conversation, well, the endogenous cannabinoids can dictate whether or not that conversation is likely to occur or not to occur. Think of them as either putting someone at the top of your text chain in your phone, which would be long-term potentiation, or essentially blocking their number, which would essentially be long-term depression. So, if you're getting the impression that the endogenous cannabinoids are working in a number of different ways, and it's not very straightforward, you're right. In fact, that's the message that I'd like you to take away. The endogenous cannabinoids are sometimes increasing neuronal communication. This can lead to increases in mood or increases in the likelihood that someone will talk a certain way or behave a certain way or feel a certain way. That can also lead to decreases in synaptic transmission, that is communication between neurons, in ways that will make somebody's mood lower, or will make them less hungry or more hungry. And, here's the really key thing, there are two kinds of endogenous cannabinoid receptors, referred to as CB1 and CB2, and we can say with confidence that CB1 is highly enriched in the nervous system, and especially within the brain. It's found not everywhere, but almost everywhere in the brain

and elsewhere in the nervous system, so spinal cord and other aspects of the nervous system. CB2, the cannabinoid receptor, CB2 is largely located in the tissues of the body, including the immune system, the liver, even the genitals, et cetera. So what this means is that the endogenous cannabinoids are having these sorts of effects on neurons that I talked about, but they are also having effects on immune cells, on reproductive organs, on liver, on digestion, on hunger, et cetera, through mechanisms that are divorced from the function of the nervous system of neurons. Now, in reality, no system of the brain and body is divorced from the nervous system, because the nervous system is controlling everything. It is really the master controller, and everything's feeding back to the nervous system, so it's a two way street. But the simple way to think about it is CB1 receptors are mainly in the nervous system, and CB2 receptors are mainly in the body and endogenous cannabinoids, again, EAE, anandamide, and 2-AG, arachidonoyl-glycerol, are impacting CB1 and CB2 receptors. Today we're mainly going to talk about CB1 receptors, 'cause they are the ones that are responsible for most of the familiar effects of cannabis, but the key takeaway at this point is to really understand that the major effects of your endogenous cannabinoids on these receptors in this particular CB1 are very nuanced. It depends on context, depends on which neurons. It's sometimes increasing communication between neurons, sometimes decreasing it, and then along comes cannabis, and that cannabis, again, can arrive by smoking, by vaping, by edible. And cannabis contains THC and CBD that potently bind the CB1 receptor, and now the effects of the CB1 receptor being occupied by THC or being occupied by CBD, are not very nuanced. In fact, they are very predictable and especially important is to understand that they are so strong, and they park in that receptor with such affinity, with such force and precision and stubbornness and refusal to leave that receptor that they completely outcompete the endogenous cannabinoid system. In fact, they leave the endogenous cannabinoid system essentially dysfunctional, which, in some cases, may be a good thing, but in most cases, is going to lead to problems of various kinds, and we'll talk about what sorts of problems. And again, I feel obligated to say, this is not me saying don't ingest cannabis or THC or CBD. That's not what I'm saying. What I'm saying is if you evaluate the potency that is in technical terms, it would be the affinity with which these compounds, THC and CBD and CBN, bind to these endogenous receptors, that would be like a howitzer gun, like a cannon going off, as compared to endogenous cannabinoid, whether or not it's EAE or 2-AG, which is more like a cap gun level of activation, at least in this analogy. So now you have what at least I would like to think is

a fairly complete understanding of the different varieties of cannabis, at least at a broad sweep, and the different biological effects that they can have,

00:53:07 Biological Effects of Cannabis

at least in terms of the major receptors and in retrograde signaling, et cetera, et cetera. Now, let's take a step back into the real world and evaluate or think about what happens when somebody smokes cannabis or ingests cannabis by way of edible or tincture or something of that sort. Cannabis is very fast to enter the bloodstream. In fact, within 30 seconds, it's going to enter the brain and permeate throughout the brain and body. That's very, very fast. I mean, when you contrast that with something like alcohol or even nicotine, depending on how the nicotine is delivered, that is a very fast delivery of the psychoactive and biologically active compound, which in this case is THC and CBD and probably some other things as well. So within 30 seconds, it reaches the brain and bodily tissues, and within 30 to 60 minutes, it's going to reach its peak concentrations and have its peak biological effects. Those aren't always the same thing, but in the case of cannabis, again here I'm using cannabis as an umbrella term for THC and CBD, the effects are going to peak at about 30 to 60 minutes after bringing those compounds into the body in some way or another. And the effects tend to last anywhere from three to four hours, although there's some variation on that, depending on individual metabolism, whether or not somebody is familiar with the compound, believe it or not, psychologically familiar, but also biologically familiar, or whether or not it's a first time use or occasional use and so on. THC and CBD and other components of cannabis are highly what we call lipophilic. That is, they have an affinity toward, and they can actually pass through fatty tissues. Now, every cell in your body, but especially neurons, have a double layer of fat on their outside. And of course, when people hear "fat," they always think, ooh, fat's bad. Most of the world seems to want to lose fat or bodily fat. Here we're talking about the fatty membrane, the barrier around each tissue, in this case we're talking particularly about neurons. And THC and CBD and the other components of cannabis are highly lipophilic, so they can get into essentially all cells just simply by flowing into them. They will also remain in those cells for a long time. So, I know that a number of people, depending on whether or not they get tested for work or for sport or otherwise for cannabis or CBD and THC, don't take this as a strict number, but typically, if one ingests CBD or THC, smokes cannabis, ingests by orally, et cetera, doesn't matter, it's going to

stay in that fatty tissue and can be detected for at least as long as 80 days after ingestion, and there's a whole industry as to how to accelerate the clearance, and I should just tell you that just losing bodily fat isn't going to eliminate it from your system, maybe partially in those fat cells, but certainly intravisceral fat and other fatty tissue that's in around the brain and body is going to harbor that THC molecule and the CBD molecule for quite a long while, at least 80 days. So, if someone smokes cannabis or they ingest cannabis, it very rapidly gets into the bloodstream, and the components that are psychoactive get into the bloodstream and are immediately able to access neurons and other cells and start having these effects

00:56:29 Cannabis Sativa & Subjective Effects: Mood, Stress, Alertness, Paranoia

of parking at those endogenous cannabinoid receptors and impacting the signaling between neurons, which leads to the subjective effects of cannabis, including THC and CBDs, so let's talk about what those different subjective effects are. Again, this is going to vary depending on whether or not people are ingesting sativa varieties of cannabis, just to remind you, those tend to be elevated mood, alertness, talkativeness. People who take sativa varieties tend to talk a lot more than they would otherwise. Again, there are exceptions to this, of course there are exceptions. I'm sure there are people out there shouting, although I guess if you're the quiet people who don't talk too much, you're probably not shouting, or if you're not, you're not doing on sativa, Joe contended, but in any event, there are exceptions, but there are also general rules. And the sativas tend to make people's mood elevated, energetic, again, this sort of head high, and indica varieties tend to do the opposite. more of a sedative, relaxant, et cetera. Why and how would they do that? Well, without going into an extensive deep dive into the different neurotransmitter systems of the brain and body, what we know for sure is that CB1 receptors are present on an enormous number of different neurons in brain structures in neural circuits, so that the sativa varieties that act as a stimulant, making people feel happy, 'cause in general, they do tend to elevate mood, at least at certain dosages, talkative, tend to make people feel like they have ideas that are interesting, that they might want to share, tend to narrow their context, so we tend to increase focus. This is something that's not often discussed about cannabis, but especially the sativa varieties can increase people's level of focus to particular things, something they're watching or something they're doing or music, it allows them to narrow their sense of focus. That's

going to occur by activation of CB1 receptors in the so-called prefrontal cortex, which is just behind the forehead, and the prefrontal cortex acts as a strong modulator of so-called limbic circuitry and other circuitry that is more stress oriented. The way to think about the stress and limbic circuitry, such as the amygdala, which many people have heard about, is that they aren't really circuits for fear and stress. They are circuits that are constantly evaluating one's own internal state, heart rate, et cetera, and what's happening externally, and, sorry to say, but the default of those systems is to detect danger, so threat detection systems. And then the prefrontal cortex largely acts as a brake on those systems, so like the reins pulling back on a steed of horses that would otherwise just take off. And so, the sativa varieties tend to increase CB1 activation in the prefrontal cortex and in other circuitry that then leads to an overall reduction in stress, because of the way that prefrontal circuitry can reduce activation of the amygdala. Now that, of course, does not explain why some people become very stressed and very paranoid when they smoke sativa varieties or other varieties of cannabis or ingest other varieties of cannabis. We'll talk about the paranoid effect and why that occurs and who might predict that would occur to them in a little bit. But I just want to give you a sense of how this is working, because as I mentioned before, THC and/or CBD are going to bind that CB1 receptor, let's say in prefrontal cortex, the neurons of the prefrontal cortex, it's going to bind there, and then they'll be a retrograde signaling back to the presynaptic neuron, and in the case of prefrontal cortex, what's happening is it's increasing transmission, increasing the release of neurotransmitter in the prefrontal cortex. However, at the same time, the very same THC and CBD that was brought into the system is binding the very same type of receptors, CB1 receptors, in other brain structures, such as the amygdala and causing retrograde signaling back to the presynaptic neurons in the amygdala, but it's quieting the activation of those neurons, so this is interesting. We have the same compounds, THC and/or CBD, brought into the body and brain, binding the same receptors, in this case the CB1 receptors, but depending on where those receptors are located and which brain areas we're referring to, they are either causing heightened levels of alertness and activation of systems that are designed to make you talkative and alertness and mood, et cetera, focus, or they're causing suppression of those circuitries. So we have kind of a seesaw effect here where the same compound is increasing mood and alertness and focus in the prefrontal cortex and is decreasing stress and threat detection in the amygdala, and that's one of the reasons why, especially the sativa varieties of cannabis, allow people to enter these

states of focus, some might even say flow, although I don't want to go into what flow states really are. That's for a different discussion, and it's very poorly defined as it is. And I certainly don't want to give people the impression that cannabis increases flow states, because that's not always the case, and certainly most often is not going to be the case. But the idea here is that this molecule comes into our brain and is shifting everything towards a state of focus, elevated mood of heightened sense of importance about whatever it is that we happen to be doing. And now of course, whatever we could happen to be doing could be writing a song, writing poetry, communicating with somebody, but it could also be something as trivial as watching cartoons or watching a movie, which is not trivial in its own right, but in terms of thinking about the creative aspects or the creativity stimulating aspects of cannabis, not productivity oriented. So narrowed focus, elevated mood, more relaxed and yet energetic, that's the major effects of the sativa varieties, except, and this is a really big boldface, triple underlined 'except,' except in some individuals, depending on dosage, but also depending on preexisting neural circuitry and propensity for anxiety, some people ingest or smoke sativa varieties, and regardless of whether or not it's a type one, type two or type three variety, regardless of the ratio between THC and CBD, people will experience intense anxiety and paranoia. Now, how do you predict who will experience intense anxiety and paranoia and who will experience intense relaxation, focus and sense of creativity from ingesting or smoking a type one, type two or type three sativa? Well, there is no way to predict that, and there's a lot of what I would call street lore or dorm room lore or not peer reviewed, but peer discussed among friends and people and acquaintances lore out there that what one needs to do is simply smoke more, or just ingest more. You hear that, "Oh, well listen, if it makes you paranoid, "you simply need to use more," that is absolutely categorically false. Everything we know about the way that THC and CBD work is that they tend to potentiate, that is increase the effects of these different systems at given synapses and in different areas of the brain and body. That is, if someone experiences paranoia or anxiety from a given strain of the marijuana plant or from ingesting an edible in a particular way or a particular kind of edible, that person is very likely to experience the same effect every time they ingest that strain or variety. This is part of what's led to this enormous industry. I mean, there are a number of different reasons, but this is part of what's led to this enormous industry of highly customized cannabis where people will spend some time really seeking out the different strains of cannabis and hybrids of cannabis that work best for them and work best for them in

particular context. I wish I could tell you that if you are a person who is between 5' 7" and 6' tall, and you have blue eyes or brown eyes, that the sativa varieties are going to be right for you, or that sativa varieties are going to give you panic attacks, I can't do that. The only way to determine it would be to actually experience ingesting those or smoking those, which is certainly also not what I'm suggesting. That's up to you. I'm not telling you what to do or what not to do, but there are no good predictors. In fact, if you look in the literature, it is not at all clear that people who have a heightened level of anxiety when they do not smoke cannabis will experience cannabis as less paranoia inducing or more relaxing.

01:04:58 Cannabis Indica & Subjective Effects, Memory, Dosage

That's simply not the case. Now, what we can say for sure is that general categories of effects, such as increased focus and reduced anxiety are largely due to activation of areas like the prefrontal cortex. Now, unlike other compounds like nicotine or alcohol or neurotransmitter systems like dopamine, when we talk about the cannabinoid system, and I say effects, biological effects, psychoactive effects, I want you to keep in mind always, please, please, please keep in mind that those effects can be varied and often opposite in direction, so let's just give an example of that. I just mentioned that when people smoke or eat sativa, that it tends to lead to one specific set, or generally leads to one specific set of effects, heightened focus, mood, et cetera. Whereas when they ingest or smoke indica and its components, again, we're still talking about THC and CBD in varying ratios, but now indica cannabis, and you say, "Well, why would it improve the transition time to sleep?" Or at least give people the impression that it improves the transition time to sleep. We'll talk about what indica actually does for sleep in a little bit, but indica also tends to suppress activation of the amygdala and threat detection centers in the brain, again, binding the same CB1 receptors in those retrograde signaling mechanisms that I talked about before, but it also tends to shut down the hippocampus, an area of the brain associated with memory, which is why indica varieties lead to pronounced, or I should say profound defects in short-term memory and sometimes in long-term memory as well, if it's consumed over long periods of time. We'll talk about short, medium and long-term consumption, occasional consumption going forward. So what I'd like you to take away from this component of the discussion is first of all, the mechanism of action by which cannabis impacts the brain and body, but in particular the

brain, is going to be through CB1 receptors, and those CB1 receptors can lead to either an acceleration or a brake on particular biological mechanisms. And there are going to be a constellation of different accelerations and braking of different neural systems in the brain and body, depending on whether or not people ingest sativa or indica or some hybrid strain. And perhaps most importantly, even if you didn't understand anything that I've said about the biology of these different strains in the receptors, please do understand that there is no way to predict what the effect of a given strain will be on an individual. There has been extensive exploration as to whether or not people who are so called mellow or more anxious or any number of different personality dimensions will respond in one way or the other, but, in fact, there is no way to tell. Layer on top of that the fact that dosing THC and CBD can be fairly straightforward in the form of edibles, because there can be, at least if it's a controlled source, a defined number of milligrams of THC, a defined number of milligrams of CBD. That's true for ingestibles. It's much harder to gauge that from the smokeable forms of cannabis, especially if those smokeable forms of cannabis are obtained through sources where there isn't a lot of clear information about the total amount of THC in that product. Now, this is all changing quite a lot nowadays because of the commercialization of of THC and CBD products and cannabis in a number of different areas, including in the United States. But still, many people are ingesting cannabis, THC, CBD through sources where they don't really know how much they're bringing into their system. And so, whether or not someone gets incredible anxiety relief, enhanced sense of mood and focus and wellbeing, pain relief, et cetera, or whether or not they have full blown panic attacks, et cetera, is very hard to predict based on dosage information alone. Now, of course, we can create broad categories, and we are going to talk about studies that create broad categories of low dose, moderate dose, and high dose. frequent use and infrequent use, but unlike alcohol, unlike nicotine, we can't really point to specificity of X amount of alcohol, grams of alcohol per week, which is safe, or X amount of alcohol, which is not safe. And so I know a lot of people out there are wondering, how often can they smoke cannabis, or how often can they eat cannabis or THC or CBD in any number of its different forms and products, safely? Well, we have to really define what 'safely' means, and we have to really acknowledge that there's a pretty loose set of controls over what one is bringing into their brain and body as they ingest THC and CBD,

01:09:41 Brain Areas Affected by THC & CBD, Side Effects

but even under conditions in which it's very controlled, it's very hard to predict what those effects will be. So before moving into specifics of taking cannabis or not taking cannabis, who should, who shouldn't, what the medicinal purposes are and what some of the newer, exciting data point to, I just briefly want to make a list, and I promise very briefly, I know I'm not often concise, but I do try to be thorough for your sake. I want to make a very brief list of the different brain areas that are impacted by THC and CBD and why THC and CBD have the various effects they do. When somebody smokes or ingests cannabis, doesn't matter what the THC or CBD ratio is, if they experience deficits in memory, and that's almost always present, that's going to be because of reductions in electrical activity within this brain region we call the hippocampus. Hippocampus means seahorse. It's shaped like a seahorse. Anatomists like to name things after what things look like, but hippocampus memory, memory is reduced, in particular short-term memory. That's true regardless of whether or not one is using sativa indica or some hybrid. In general, the prefrontal cortex is going to be activated by the sativa varieties, which is going to increase thinking and narrowly constrain focus to some activity, and that's more commonly associated with the sativa varieties. The indica varieties, as I mentioned before, tend to lead to a suppression of activity in prefrontal cortex, believe it or not, and turn off thinking and planning. This is why indica varieties are often used for relaxation and for promoting sleep. Regardless of whether or not sativa or indica variety, and again, regardless of the ratio of THC to CBD, there is a general suppression of neural circuits within the so-called basal ganglia and cerebellum. Basal ganglia and cerebellum are areas of the brain that are involved in action planning and withholding action, so that would be the basal ganglia, so-called go, no go circuitry, and the cerebellum, which is involved in balance, but also motor planning and motor sequencing. This is why people who smoke marijuana, regardless of the strain, will tend to be less physically mobile. Other common effects are reddening of the eyes, dryness of the mouth, that's actually caused by the same general mechanism, which is a reduction in the secretion of saliva and of tears and lubrication of the eyes from the lacrimal glands of the eyes because of the presence of largely CB2, but also CB1 receptors in the mouth and on the eyes. And there tends to be, especially with certain strains of cannabis, increase in appetite, so-called munchies, and that has everything to do with very, very high density of CB1 receptors in the hypothalamus, and in particular areas of the hypothalamus, like the arcuate nucleus of the hypothalamus, other areas as well, of

course, that have tons of CB1 receptors, bind THC and CBD and activate the neurons that strongly stimulate appetite through two mechanisms, one is a cognitive mechanism of creating a preoccupation with food in anticipation of taste, as well as the experience of taste. So the narrowing of focus to what you want to go eat. You really crave, I dunno, pizza. It seems to be high fat, high carbohydrate foods, but really crave pizza and narrowing of focus, so that you're not thinking about anything else, but also signaling from the hypothalamus to the gut to neurons within the stomach, itself, that regulate blood sugar, so there are strong effects on blood sugar of THC and CBD that generally lead to increases in appetite, so two parallel mechanisms, one within the brain, one within the body, increasing appetite, so there's an array of different effects. And as I mentioned before, CB1 receptors are present all over the nervous system in the brain, the spinal cord. In fact, the presence of CB1 receptors in the spinal cord largely explains the fact that THC and CBD, to some extent, although it's not very well studied, can provide some pain relief. I say some, because a lot of people perceive or believe that they experience more pain relief from cannabis than they actually do. It actually has a lot to do with a perceptual shift to basically focusing on other things, but there does seem to be some antinociceptive, meaning anti pain effects of cannabis, THC in particular, and that is exerted largely through effects on CB1 receptors in neurons of the spinal cord. So a broad array of effects are taking place, regardless of what strain you take and whether or not you eat the cannabis or you smoke the cannabis. And the broad array of effects can be explained by the fact that that retrograde signaling can lead to activation or suppression of activity in various neurons. So now I'd like to take a step back from the biology of cannabis and THC and CBD and all the signaling and receptors, et cetera, and really just focus on cannabis use, and wherever possible, I will point to the specific strains that have been studied and the ratios of THC to CBD, but I have to say that unfortunately, most studies of marijuana, of cannabis, while they have been very careful to detail the amount of THC, low dose, medium dose, or high dose, and actually getting very specific, right down to the number of milligrams or even how much circulating THC is present after somebody smokes a joint or ingests cannabis, most studies have not distinguished between sativa and indica strains. And that's unfortunate, because in the real world, people are distinguishing between sativa and indica strains in their patterns of use and what they prefer and what they don't prefer, or even what they prefer to smoke during the day or ingest during the day versus night. Believe it or not, there are people who are using certain strains during the day and other strains at night, but the science is

yet to catch up to that, or I should say, more accurately, the general public and the themes that are emerging and the practices that are emerging around cannabis, especially in states where it's decriminalized or legalized, are occurring at such a rapid rate that there's absolutely no way that the science could keep up. This is a naturally occurring experiment, not to say that it's natural, like people should do it, but it's an experiment that's happening in real time in the real world, much faster than controlled studies

01:16:08 Creativity: Convergent vs. Divergent Thinking & Dopamine

within university laboratories and other laboratories can keep up. So at this point, I think it's appropriate to ask ourselves, why do people even use cannabis? What are they trying to achieve? Is it always about not feeling pain? Is it always about reducing anxiety? Well, sometimes it is, but oftentimes people are using cannabis in order to achieve a particular state. And we could use a broad brush and say, "Well, they just like being high," but while that may be true in a lot of circumstances, and I have to believe it actually is true in a lot of circumstances, there are a lot of people who use cannabis in a very directed way, or they get, quote unquote, high, in order to achieve states that to them are particularly attractive, and one such state is a state of creativity. And this brings us to a broader theme, which is, does cannabis increase creativity? And if so, is it the THC, the CBD, what's the appropriate ratio or the best ratio for accessing creativity? This is an interesting and important discussion, I believe, because creativity is one of the more sought after and more elusive states that humans can experience. And yet, if you look at human evolution, you look at our progression in terms of technology development and culture and music and poetry, et cetera, we really can look to creativity as the state that fostered so much of that evolution. So whether or not you're into technology, or you're into art or music, whether or not you're just somebody who wants to expand their understanding or their experience of life in some way, creativity is a fundamentally important state to try and access and to try and access regularly and to try and tap into, in order to eventually produce something, in order to create something of meaning that exists not just in that creative state, but to yourself after that creative state has gone away, so the painting that you paint in the creative state hopefully is a painting that still inspires and has impact after you exit that creative state and that will inspire others, and this could be true for any number of different things, not just painting. So does cannabis

increase creativity? The short answer is, it depends. First of all, we need to define creativity. Here we are, thinking as scientists, if not already scientists, and there are basically two modes of thinking that are associated with creativity, and they don't completely explain creativity. But if you look in the research, the psychology research and the neuroscience research, you'll hear about convergent thinking and divergent thinking. Convergent thinking is taking loose ideas and kind of braiding them together, finding a common thread, synthesizing, and organizing those different ideas into some common or specific framework in order to get or create some specific outcome. So convergent thinking is basically the person in the room who's listening to all the ideas and taking them all in. Maybe it's a panel of, how should we get a certain product out to market? Or what are the different motifs that we should include in a piece of music? Or what should we do in terms of rearchitecting a given physical space? Taking in those different opinions, those different ideas from different people, and then synthesizing them and coming up with one or a small subset of coherent ideas that incorporate some or all of the ones that they heard, so that's convergent thinking. It doesn't have to involve a panel of people talking to you. I use that as an example of what goes on inside your own head when you are engaging in convergent thinking. You're thinking, well, so and so said this, and I think that, and you're braiding them through and trying to get some common themes, some common vector to emerge from that. Divergent thinking, on the other hand, is best described as brainstorming. It's exploring ideas and continuing to move into the variation and the vastness of ideas in hopes of eventually being able to converge on some novel idea or framework. So these are similar and related, but typically the creativity process involves first brainstorming and divergent thinking, and then in order to arrive at something, to actually create something, the verb 'create,' not just thinking about what you might create, which occurs during divergent thinking, but actually creating something, a specific painting, a specific song, a specific body of literature, a specific scientific project or experiment and so on, that usually involves convergent thinking. Now these can be explored in the laboratory, and they can be explored in the laboratories through sets of different types of questionnaires or even tasks that you can give human subjects, and this has been done extensively and across the entire body of data, and by that I mean, literally hundreds of studies that have explored the relationship between particular neuro circuits and neurochemicals, convergent and divergent thinking. We can arrive at a principle, and the principle involves a molecule that many of you have heard about before, which is dopamine.

Dopamine is a neuromodulator. It's involved in motivation, and it tends to direct our attention to things outside of us, but it's also closely related to convergent thinking and divergent thinking and to the creative process. And therefore, it should come as no surprise that diseases of the nervous system, excuse me, such as bipolar disorder, which we've done in episode all about bipolar disorder or schizophrenia or mood disorders that impact the levels of dopamine, either make it way, way too high or way, way too low, strongly impact whether or not people will be creative. And I think the short takeaway that makes the most sense in terms of framing this, and we covered this on the episode on bipolar disorder, sometimes called bipolar depression, is that in professions where there's a lot of creativity required in order to succeed, so again, musicians, composers, artists, et cetera, you tend to find more manic depression, and manic depression, at least in the manic states, the hyperactive states, are correlated with elevated levels of dopamine. Likewise, it has been seen over and over throughout history that individuals that have mild forms of schizophrenia, or even full-blown schizophrenia, many famous painters for instance, or musicians, they are known to have elevated levels of dopamine, and they are quite creative. Now, that doesn't mean everybody who's creative has elevated levels of dopamine, although it's likely that their levels of dopamine are at least not diminished, and it doesn't mean that non-creative people have low levels of dopamine, so don't get carried away with the interpretation here. But the point is this, dopamine levels strongly relate to the probability that you can engage in convergent and divergent thinking, and they do so in the following way. When dopamine levels are high, divergent thinking is more likely. That is, when people have a lot of dopamine circulating in their system, they tend to be very expansive with their ideas, they tend to brainstorm a lot, they tend to be comfortable and even want to, or reflexively throw out a lot of ideas so that sometimes even seem a little disconnected. Some people might think of this as attention deficit, but it's not. It's really the idea of throwing out disparate ideas. You hear sometimes, you throw things against the wall and see what sticks, that's a obviously an analogy, but people are throwing lots of things against the wall and seeing what stick, and then seeing how the things that stick fit together, that's divergent thinking, and elevations in dopamine tend to increase divergent thinking. However, they tend to do this in an inverted U-shape way. For those of you either watching on YouTube, I'm just drawing a hump, obviously, and for those of you listening, just imagine a U, the shape of a letter U, and then just flip it upside down, so it looks like a bump. Turns out that when dopamine levels are very low, there's a low

probability of divergent thinking. When dopamine levels are high, as I mentioned before, there's a high level or probability of divergent thinking. But when dopamine levels go very, very high, then there's again, a reduction in divergent thinking. In other words, there's a sweet spot of elevated dopamine for divergent thinking. And again, divergent thinking is critical for the creativity process, because creativity by definition is taking a novel set of ideas and arranging them in a particular way, or taking existing ideas and arranging them in a novel way that then you eventually converge on some new product, new idea, new song, et cetera. Now, convergent thinking follows a very different pattern. When dopamine levels are high, convergent thinking is not very likely. And when dopamine levels are low, convergent thinking is very likely. So here, using arguably a very reductionist view, we're looking at all of this thing we're calling creativity through a very neuroscience reductionist lens, we can say this. The creative process involves going into a state where you're willing to consider a lot of options, many of which seem distantly or not even connected to one another, and dopamine facilitates that divergent thinking state in which you are perfectly happy and in fact, experience a joy, or elation, a comfort and a pleasure in organizing all these different ideas that to anyone else might seem not that related. But when your dopamine levels are elevated, these all seem like great ideas and that maybe there are connections there. You're not accepting all of them as true and valid and interesting in combining them, but there's this idea that it's worth entertaining the possibility, at least for moments. And then, as dopamine levels drop, there is the process of convergent thinking, which is taking options down off the wall saying, "No, no, that doesn't fit with that, "that doesn't fit with that, "but ah, that fits with that, and that can work. "That feels right or sounds right or looks right." That's the creativity process. And so, I think this is not just important for understanding cannabis, which we'll get back to in a moment, but it's important for understanding creativity and brain states in general. Brain states are not, as we would say, a square wave function. You don't just drop into a trench of creativity. Creativity is not an event, it's a process. And what I'm telling you is that it's a process that involves divergent thinking and consideration of a lot of different ideas. That's correlated with high but not too high dopamine. And then, one has to transition into a state of convergent thinking, which is really honing in on the ideas that seem to have validity or that could have validity and getting rid of everything else, and that's associated with low dopamine.

01:26:41 Does Cannabis Increase Creativity?

It's more about logical implementation and consideration as opposed to thinking about and considering everything. So let's now return to the question of whether or not cannabis and its different components increase creativity. And when you look at the literature on this, you find studies that very clearly point to a yes, it increases creativity, and it's not surprising, therefore, that cannabis can increase dopamine transmission, that is dopamine levels, in certain brain areas, in particular brain areas involved in thinking and planning. So cannabis increases dopamine in these areas. Elevated dopamine increases divergent thinking, and divergent thinking is associated with creativity, and there are studies that support the idea that cannabis can increase creativity. However, there are at least as many studies that say that cannabis does not increase creativity, that cannabis increases consideration of multiple ideas, perhaps through elevation of dopamine and related systems, but that ultimately the ideas that converge from that are not truly creative ideas, at least they don't meet the criteria for creative brainstorming and extraction of ideas that are truly novel, so it doesn't increase creativity, so which one is it? Well, fortunately, there's an entirely distinct set of literature that has taken all the other literature into consideration, and here's where we arrive. So there's a really nice study that explored creativity in cannabis users, and we will provide a link to this study. First author is Emily LaFrance, and the title of the paper, somewhat amusing in its own right, which is, it starts with a question, inspired by Mary Jane, of course, Mary Jane being one of the old school versions or ways of talking about cannabis or marijuana. Nowadays, people refer to it mainly as pot, as other names too, of course, and the title of the paper is, "Inspired by Mary Jane Mechanisms Underlying Enhanced Creativity in Cannabis Users." And I really like this study for a couple of reasons. First of all, they looked at people who did not use cannabis as well as people who used cannabis, so they had two different groups, but they did not evaluate creativity of the cannabis users while they were under the influence of cannabis. They looked at the level of creativity in these cannabis users when they were not under the influence of cannabis and asked whether or not their ability to be creative was enhanced by cannabis. Now we're going to compare this to studies in which people come into the laboratory and actually use cannabis, and then they evaluate creativity under that context. But this study has some unique takeaways that I think are really interesting. First of all, they did, yes, see evidence for enhanced creativity, and when I say enhanced creativity, I mean within the context of this divergent thinking thing that I talked about a moment ago. And when I say

enhanced, I mean significantly greater than in non-users, so people that don't use cannabis. So right now I can imagine that all the cannabis users are cheering, "Yes, cannabis increases creativity, "makes people more creative than they would be otherwise." Well, this is interesting. We have to ask ourselves how that was accomplished. And it turns out that one of the major ways in which it was accomplished is that cannabis users, even if they're not under the influence of cannabis, are far more open to novel ideas, and they have a more explorative and reduced anxiety, or I should say lower anxiety mode of thinking when they explore novel ideas, which is essential for divergent thinking. So they observed both enhanced divergent and convergent creative type thinking in cannabis users. And the source of that, they conclude is, and here, I'll just quote, "Cannabis users' higher levels "of openness to experience are responsible "for their enhanced self-reported creativity "and convergent thinking test performance." So it's not necessarily that cannabis is increasing the capacity of the brain areas that are associated with creativity, but rather, cannabis appears to be increasing an openness and probably doing that in part through lowering anxiety in particular people, and that openness is leading to inclusion of more ideas during the divergent thinking process. They're willing to consider throwing up more things on the wall to see if they stick, so to speak. So in their conclusions, they have a really nice statement. Again, I'll just read from the paper, because they said it better than I ever could, quote, "While mainstream media has propagated the idea "that cannabis expands the mind and enhances creativity, "our results show the link between cannabis and creativity "is largely a spurious correlation," meaning that it's not the case that cannabis increases creativity, but, and I inserted the 'but' in this quote, but "driven by differences in personality "that are related to cannabis use. "For example, openness to experience that are related "to both cannabis use and augmented creativity." This is a real chicken/egg argument. What do I mean by that? What I mean is, this paper finds that people who are more open to experience are more likely to use cannabis, and people who use cannabis are going to be more open to new experiences, and that combination of features, openness to experience, and what that openness to new experiences brings, enhances the convergent and divergent thinking that is characteristic of the creative process. So in short, cannabis increases creativity, but through changes in personality that tap into the creative process, rather than directly impacting the neural circuits that, for instance, turn on creativity. And I have to say, this study is really important, because by exploring cannabis users, not while under the influence of cannabis, they were able to tap into this

very important, what I believe to be fact. Because if you think about a study in which you would have one group using cannabis and another group not using cannabis, and then you give them some task that taps into creativity, you will see effects and very likely, you'll see effects where cannabis might even increase divergent and convergent thinking and creativity. Those results have actually been published many times before. But given the varied effects of cannabis and THC that we talked about earlier, through all of that complex signaling stuff, you can imagine that there will also be other studies, and in fact, there are, where divergent and convergent thinking and creativity is not assisted by cannabis and might even be reduced by ingesting cannabis. However, if one considers that divergent thinking is absolutely crucial to the creativity process and the range of things that one will explore will be enhanced by openness and by reduced levels of anxiety, so a willingness to explore different options, some of which might seem completely crazy, and cannabis increases the personality types and reduces the anxiety that create that sense of openness, well then it makes perfect sense why cannabis would increase creativity in certain individuals, but not directly. And this study, the one I just referred to, which I should say was published in the journal, "Consciousness and Cognition," and again, we'll provide a link to it, did a wonderful job of teasing out this impact of cannabis on personality, which then impacts creativity. So if somebody asks you, or if you're wondering, or if you feel like cannabis increases creativity, in some sense the answer is 'yes,' but the answer is 'yes' because of the ways that it shapes openness to new ideas and can, I should say 'can,' because not in everybody, but can, in some individuals, reduce anxiety. What this means is that if you are somebody who experiences anxiety or increased levels of focus from cannabis, regardless of the strain, and here I have to imagine people are exploring different strains, if they're exploring them at all, exploring different modes of delivery, smoking or ingestible, et cetera. If you're somebody who experiences anxiety, it's very likely that you won't have the increased openness to experience and divergent ideas that will facilitate creativity. However, if you are somebody who achieves heightened levels of relaxation and reduced levels of anxiety from cannabis, regardless of which strain we happen to be talking about, well then, yes, it will position you

01:35:08 Chronic Cannabis Use & Changes in Speech Patterns

to be in a heightened state of creativity, at least as defined by convergent and divergent

thinking. One of the more characteristic, or I should say stereotype qualities of people that smoke a lot of marijuana or ingest cannabis through other means is there changed patterns of speech. In fact, there's a lore in the clinical realm that you can predict or get some strong indication as to whether or not somebody is a cannabis user or pot smoker based on their voice and their particular tone of voice and their lack of inflection. There's a lot of speculation here, but fortunately, it's been studied. So I'd like to discuss now whether or not cannabis can impact patterns of speech, both acutely, meaning while under the influence of cannabis, and over time, in chronic cannabis users. And when I say 'chronic cannabis use,' I want to be very specific what I mean. Chronic cannabis use does not necessarily mean that people are smoking cannabis or ingesting cannabis every day, although certainly if they are, that qualifies as chronic use. Chronic use is regular use over time of anywhere from twice a week or more. So using cannabis once a month would not be considered chronic use, even if it's for many, many years. Using cannabis or ingesting cannabis in some way or form twice a week would be considered chronic use. Then of course, some of you out there are going to ask me to split hairs and say, "Well, what if somebody uses it twice a month?" Well, listen, the clinical literature, and the scientific literature don't get that specific. And of course, they're an infinite number of ways to arrange one's cannabis use, everything from zero, none at all, to constantly, every day, all day and everywhere in between. But think of chronic use as twice a week or more. Think of occasional use as less than that and realize that within the realm of chronic use, excuse me, that 'or more' can be anywhere from twice a week, to every day, to just in the evenings, et cetera. The effects of chronic use of cannabis, as I just defined it, on speech have been studied. Because of this characteristic, drawing out of certain syllables, a slowing of speech, and in many cases a total change or alteration in the way that people speak and use language, both when under the influence of cannabis and when not under the influence of cannabis if they're chronic users. And here we really want to distinguish between THC and CBD and just make it really simple and say that CBD is not responsible for most of the psychoactive effects of cannabis, whereas THC is, and again, the ratio of CBD to THC is going to be relevant there, but let's just think about cannabis and THC as one in the same for this portion of the discussion, realizing that, of course, they are not exactly the same thing. There's an excellent study entitled, "Adults with History of Recreational Cannabis Use "Have Altered Speech Production," and we will provide a link to that, first author, Adam Vogel, really like this paper. It was published in the journal, "Drug and Alcohol Dependence." We will

provide a link to it for you if you'd like to peruse it in more detail. The title itself, "Adults with a History of Recreational "Cannabis Use Have Altered Speech Production," tells you pretty much everything you need to know, except there's some important nuance in here, because, as I mentioned earlier, people who smoke sativa varieties of cannabis oftentimes will become more talkative, much more talkative. However, whether or not people tend to rely on sativa cannabis use or indica cannabis use, there is a very consistent finding that people who are chronic users, again twice a week or more, recreational use or medicinal use, undergo pretty profound changes in the way that they speak, but in a very specific set of ways. Now, first of all, the changes in speech shouldn't surprise us at all, because both sativa varieties of cannabis and indica varieties of cannabis impact those brain centers involved in movement, the basal ganglia, remember the go, no-go circuitry, the circuitry that makes you want to do things, and the circuitry that makes you want to withhold action? And it tends to shift the body and brain toward more inaction. And cannabis impacts CB1 receptors in the cerebellum, which is involved in motor planning, execution and balance. So, regardless of whether or not people are using cannabis of the sativa or the indica variety, there are disruptions in motor circuitry. And, as you may have heard, if you listened to our episode with Rockefeller professor, Dr. Erich Jarvis, who works on speech and movement, speech is movement. The movements of the mouth, the movements of the hands, those are intimately related in terms of our speech. In fact, the centers of the brain involved in hand movements are part of the speech areas and vice versa. Erich actually pointed out that if you put your hands behind your back, provided you normally do have use of your hands, it actually will reduce your fluidity of speech, and so I'm going to put them back in front of me now. The point is, smoking marijuana or consuming marijuana by edible changes one's speech and does it in a very specific way. And in this study by Adam Vogel and colleagues, they explored a huge different variety of aspects of speech. And this can be done using spectral processing, which is fancy nerd speak for looking at how much inflection there is or looking at how long people hold vowels or consonants, et cetera, and again, these are people not under the influence of cannabis, but rather people who tend to be under the influence of cannabis when not participating in the study, in other words, chronic recreational cannabis users. So what are the two major shifts that cannabis causes on our patterns of speech? Well, the first one is a change in what's called spectral tilt. Again, that's fancy nerd speak for vocal effort and intensity. So, I'm not a pot smoker, I confess, but if I were to say the sentence, "Vocal effort and

intensity "are important components of speech," that's the way I would say that sentence if I was striving to enunciate very carefully and to accent certain words and syllables. A pot smoker or somebody who uses recreational cannabis fairly often would have reduced spectral tilt, AKA, vocal effort intensity, and might say, [mumbling] "Spectral tilt is vocal effort in intensity, "and it differed between groups and appeared to change "in line with the duration of abstinence from cannabis use." That I think is not a far cry from the change in spectral tilt that they observed here. In addition, there are changes in verbal timing, that is pronunciation of words and accenting particular syllables of words in people that consume cannabis or smoke cannabis. So rather than emphasize particular words within a sentence, so again, I'll just use a sentence from the paper so that you can gain more knowledge from the paper, "Cannabis," and I'll say it the way that I would say it, since I'm not a cannabis user. "Cannabis, marijuana, is the most commonly used, "illicit drug in the world with approximately 4% of adults, "aged 15 to 64 years reporting recent use, "and the citation is from the United Nations Office "on Drugs and Crime, 2019." So that would be the way that I would typically read that sentence. And having gone into the data on this paper, and of course evaluated references therein and listened to some of the spectral analysis that they include as data, you can literally go into these papers online and hear recordings of people who are cannabis users or non-cannabis users, and I'll try and give you a a clear sense without picking an extreme example of how somebody who's a fairly consistent or even occasional cannabis user might read that very same sentence. "Cannabis, marijuana, is the most commonly used "illicit drug in the world with approximately 4% of adults "age 15 to 64 years reporting recent use, "and the citation comes from the United Nation Office "on Drugs and Crime in 2019." Now you'll notice that wasn't a dramatic difference. And, of course I could have taken the liberty to pick an extreme example of the sort that they did occasionally observe in evaluating subjects for this paper. I could have said something like, [mumbling in low tone] "Cannabis, marijuana, "is the most commonly used illicit drug," but frankly that would've been selecting an outlier example, and I don't want to do that. I don't want to skew the data as they say. Rather, if you heard the first time I read the sentence and the second time I read the sentence, what's mainly different is the difference in the amount of enunciation and accenting of particular words and symbols within a sentence. So the total content that's delivered is exactly the same, and while I wasn't measuring my pace, the overall rate of communication is essentially the same, but there's less lilt and falling of the voice and less accenting. That's the major

consistent effect of cannabis use. Now of course, there are examples of people who are using a lot of cannabis, and it impacts brain centers involved in movement and speech, so much so that they really do have the really drawn out kind of, nah, and oftentimes this will be detected in the laugh. There's this stereotypical stoner laugh, as it's sometimes called. Rather than say "Ha, ha, ha" or that's a fake laugh, obviously. It's hard to make myself laugh if something's not actually funny. I'll have to think of something funny. When people say like, "Ha!" That's a bit more of the way I might laugh, like, "Ha," sort of the inspiratory laugh or the, "Ha," which is expiratory laugh. People who use cannabis chronically will often do that, "Haa," which is the back of the throat, [laughs raspily] it's neither inspiratory nor expiratory laugh, and believe it or not, there's an entire literature on inspiratory, inhaling, versus expiratory laughs, and there's also a literature on cannabis altering the pattern of inspiratory and expiratory laughs. It almost sounds like a sarcastic laugh when, in fact, they may not be feeling sarcastic at all. And I have a very close friend and colleague who's a phenomenal neurosurgeon and neuroscientist by the name of Dr. Eddie Chang. He's the chair of neurosurgery at UCSF, and his lab and him are expert in the study of neuroscience controlling language and speech. And he often tells me that he can predict, with almost certainty, whether or not somebody is a regular cannabis user based, not just on the patterns of speech that they use, but even just by recording specific neurons in their brain that underlie the laugh reflex and certain patterns of speech. So this idea that cannabis use changes your ability to speak and enunciate clearly does appear to be true. And the stereotype that cannabis use tends to create more of a drawl or, if you will, a laziness in the laugh, and some of the reflexive enunciations that people use, does also appear to be true. And I say all that, of course, with the caveat that many people out there will know individuals or perhaps you, yourselves, are individuals that may use cannabis but that have incredible articulation, probably better than mine and better than other people out there who speak for a living, so I'm not saying that 100% of people that use cannabis regularly can't speak well or clearly. That's simply not what I'm saying, and I don't want to communicate that idea at all, but it is the case that people who are regular cannabis users are impacting the neural circuits involved in movement.

01:46:46 Cannabis & Libido, Dopamine & Prolactin

Movement also controls speech, and therefore, cannabis is impacting speech. Now I'd

like to turn our attention to whether or not cannabis can increase sexual activity, sexual desire, and/or sexual function, so we're going to be talking about libido, about sexual desire and about effects of cannabis on hormones. And while this might sound like a discussion that's purely oriented towards recreational use of cannabis, that is people using cannabis to heighten or increase their sense of arousal for sexual activity, it actually ventures into the clinical realm too, meaning there have been excellent peer-reviewed studies that I'll describe to you in a moment exploring the use of cannabis or THC, more specifically, for something called hypoactive sexual desire disorder, which refers to a persistent or recurrent deficiency or absence of sexual fantasies and thoughts and/or desire for, or receptivity to, sexual activity. This is a disorder that is fairly common, anywhere from 6% to 9% of people, both males and females. It used to be considered higher prevalence in females than in males, but now those numbers seem to be evening out. So basically, there are anywhere from 6% to 9% of people out there who have very diminished sexual desire. And so, a number of those people are interested in figuring out ways to increase their amount of sexual desire, and of course, there are people in the general population who may not have hyperactive sexual desire disorder who are interested in using cannabis recreationally in order to increase their desire for, or their experience of, sexual activity. Now first we have to acknowledge that sexual desire and activity is a complex set of processes, meaning it's not just one event, sex, the verb. It involves arousal, it involves sex, the verb, and it involves a whole set of mindsets and emotional states that vary tremendously between individuals. But once again, we can distill out a few basic principles, and I should emphasize, these are by no means the only chemicals and neuro circuits involved in the sexual arc, as we'll call it, desire, the act of sex, et cetera, but they are central to it, they are vital to it. They would be considered what I would call necessary but not sufficient, so there'll be other chemicals involved too, but the main chemicals in neuro circuits are those involved in dopamine, so the so-called mesolimbic reward pathway, in particular, a brain structure called nucleus accumbens, which we'll talk about more in a moment, is vital to all motivated behaviors and to the seeking out of all particular types of pleasurable experiences, and sex is no exception. So when we hear that the nucleus accumbens is activated, that almost always means that dopamine has been released in that area and other areas of the brain body, and we can consider dopamine central to the desire for, pursuit of, an act of sex. In addition to that, there are molecules like oxytocin, which are involved in pair bonding, and they're going to be neural circuit specific to the oxytocin

circuitry, but in terms of sexual arousal and sexual behavior, it's really the dopamine pathway in this nucleus accumbens, which are especially vital. That allows us to address the question, does cannabis increase, decrease, or have no effect on sexual desire and/or the ability to have sex? And therein, we will find some very interesting answers, and because, once again, it will point to the fact that the effects of cannabis on different individuals can be highly divergent, meaning in one set of individuals, cannabis will make them far less anxious. And in another set of individuals, the same strain of cannabis, at the same dosage, will make them extremely anxious. The same can be said also of sexual activity. And this was beautifully illustrated in the context of sexual desire in the journal, "Psycho-pharmacology," in a paper published in 2017. The title of this paper is, "Individual Prolactin Reactivity "Modulates Response of Nucleus Accumbens to Erotic Stimuli "During Acute Cannabis Intoxication, an fMRI Pilot Study." So I'll give a little bit of definition to some of the terms in the title that will make it easier for you to understand the paper, but then I'll just march through the results, because they're very straightforward and easy to understand and very interesting. fMRI is just functional magnetic resonance imaging, so basically subjects in this experiment came into the laboratory. They were either people who had not used cannabis before or who had used cannabis before. They were placed into a brain scanner, one of these fMRI devices. It looks like a tube that people are backed up into and then they can view images in there, and their brain can be imaged without having to remove any skull or drill into the skull, no neurosurgery. The participants in this study were grouped according to whether or not they had experienced any aphrodisiac effects during the intoxication with cannabis, so that would be the first group, Group A, they literally called it group A for aphrodisiac. And then the second group, and this is the only thing I don't like about this study, is rather than call it group B, they called them 'group non A,' which just gets a little confusing. So I'll try and simplify all this. There are two groups, and one group experiences sexual arousal when under the influence of cannabis, THC specifically. The other group does not. And it turns out this is a very commonly observed divergence of effects of cannabis. Some people experience a lot of sexual arousal from cannabis and THC in particular, and some people do not, in fact, they experience suppression of sexual desire, and it's always been a little bit mysterious as to why that is. Well, in this study, they showed people in both groups erotic images, and they measured sexual arousal through a number of different measures. We won't go into all that. It was largely subjective. There have been other studies where they've actually measured things like

erections in males and vaginal lubrication in females, so-called autonomic responses that people can't lie about, so to speak, and that tap into other aspects of the so-called sexual arousal process. In this study, they also took blood samples to look at the concentration of things like cannabinoids, so this is a really nice study in that they actually measured how much THC was in the bloodstream in different individuals who reacted to these erotic stimuli in different ways. And they measured hormones, namely cortisol, which is a stress hormone, which tends to negatively correlate with sexual arousal and prolactin. And the interesting takeaway from the study was that for people, and it didn't matter if it was males or females, 'cause they looked at both, for people that experienced elevated prolactin levels under cannabis intoxication, that's how they refer to it. People take cannabis, they measured prolactin. Some people had elevated prolactin and some people did not. For the people that had elevated levels of prolactin, they did not observe activation of brain areas associated with sexual arousal, in this case, the right nucleus accumbens, so you have two nucleus accumbi, I guess they would be called, one on each side of the brain, and the activation of that brain area is strongly associated with dopamine and with arousal and sexual arousal in particular in this study, and if people had elevated prolactin, they did not experience activation of nucleus accumbens, and they did not report feeling sexually aroused to those pictures, at least not to the same degree as the other group. So some people's prolactin levels go up when they ingest cannabis, and those people do not achieve elevated levels of sexual arousal when under the influence of cannabis, even if they're looking at erotic stimuli. That makes sense, because prolactin is mutually inhibitory, as we would say. It's kind of in a push-pull with dopamine. When dopamine levels are high, prolactin levels tend to be low, and when prolactin levels are high, dopamine levels tend to be low. The other group, so-called Group A, that experienced elevated levels of sexual arousal when under the influence of cannabis and viewing erotic stimuli, that group did not show elevated levels of prolactin in response to cannabis. So this, I believe, resolves a longstanding controversy in the field, which is, does cannabis increase sexual arousal? Well, it depends. If you fall into the category of person who has elevated levels of prolactin in response to cannabis, then no, actually cannabis will suppress your sexual response and desire. If, however, you are in the category of person that does not have elevated levels of prolactin in response to cannabis, well then, erotic stimuli can potentially and in fact, do increase sexual arousal in the majority of individuals. Now, many of you are probably hearing this and wondering whether or not you fall into one

category of individual or another. And the key thing here to understand is that levels of prolactin heading into the study did not predict whether or not people would respond to cannabis with elevated or non elevated or even reduced levels of sexual arousal. It was whether or not people's prolactin levels went up or did not go up, that predicted whether or not their levels of arousal would go up or not. So if you are somebody who, yes, does experience elevated levels of sexual arousal and function went under the influence of cannabis, well that's very likely that cannabis does not increase your prolactin levels, at least not to a significant degree while you're taking it. And if you're somebody who does not experience increases in sexual arousal or function or even diminished sexual arousal and function when under the influence of cannabis, it's very likely that cannabis is increasing your levels of prolactin. Unfortunately, there's no way to know or predict based on some other measure. I think the outcome measure, that is increased or not increased

01:56:55 Cannabis & Hormones: Prolactin, Testosterone, Estrogen & Fertility

or even reduced sexual arousal is really the litmus test by which one can figure that out. While we are on the topic of the effects of cannabis on sexual function and hormones like prolactin, it's probably worth mentioning that cannabis has been studied extensively for its impact on other hormones, and we can summarize those literature in the following way. And here I'm referring to studies only on adults. We'll talk about the developing brain and body in a little bit, but it is very clear that smoking cannabis increases prolactin levels. Very, very clear. Now, you might say, "Didn't, you just describe a study "about a set of individuals whose prolactin didn't increase "and as a consequence, "their level of sexual desire went up?" Yes, there are a subset of individuals for which that's true, but people who smoke cannabis do experience increases in prolactin, and that's especially pronounced in people that smoke cannabis more than twice a week. So this is important, prolactin, as I referred to earlier, is reciprocal or mutually inhibitory with dopamine. One way to think about this is in the context of the normal sexual arousal arc whereby dopamine is increased when people are sexually aroused, but then after orgasm, both in males and females, prolactin levels skyrocket. This is actually what creates the so-called refractory period for males during which they cannot achieve erection again for some period of time. That relates directly to how long the prolactin increase lasts. Prolactin is also increased in new parents of all species, including humans, which at least partially,

explains some of the reported or typical reductions in sexual desire and activity in new parents. Now, there are other reasons for that too, sleep deprivation, but nature is smart and has arranged a set of hormones and circuits in the brain and body, such that when tending to a newborn is the most important thing, it relegates, it reduces the importance of producing more children and sexual activity in those moments and days and weeks, sometimes longer. So when prolactin levels are up, dopamine levels are down. Smoking marijuana more than twice a week significantly increases prolactin. There are fewer studies exploring whether or not edible marijuana has the same effect, although the preliminary evidence suggests that it does not. I get into this in a lot more detail in a future episode, all about hormones with Dr. Kyle Gillett, who's been on this podcast before. But he verified that, and my read of the literature is that the edible forms of marijuana, cannabis, probably again, let's put an asterisks next to this, but it appears do not have as much of a prolactin elevating effect and therefore, not as much of a dopamine suppressive effect and therefore, not as much of a testosterone suppressing effect, and that gets to the issue of testosterone. Does cannabis, marijuana suppress testosterone? And this is a very controversial literature and here's why. Some studies say, "Yes, it suppresses testosterone "in males and females," and keep in mind that testosterone in females is vital for libido and cognitive function, cellular repair, et cetera, so it's not just important in males, of course. However, other studies say that cannabis does not decrease testosterone, and it seems to depend on whether or not the cannabis is brought into the system by way of smoking or edible. And it seems to depend on whether or not the cannabis is used chronically by an individual or acutely. And here I just want to zoom out and say that studies on cannabis or drugs of any kind in humans are really complicated. If you think about it, someone has to come into the laboratory, and let's say you want to study chronic cannabis use. Well, you can't keep them in the laboratory all the time, so you have to rely on their self-report of how often they use cannabis and in what form, and you can't really control from one individual to the next of how much cannabis and THC they're bringing into their system. One person might smoke cannabis out of a bong and take big, deep, lungs-full bong inhalations or such. Other people might smoke joints. Other people might use edibles. It becomes very complicated to know what people have done and that they're reporting it accurately, and no joke here, especially if marijuana is impacting the short-term memory systems. They might not actually remember. They might not be tracking it that well. Contrast that with studies of the acute use of cannabis and THC, where people who are not regular users

come into the laboratory and now suddenly, with institutional guidelines and safety protocols, are under the influence of THC and cannabis. Well, now you're dealing with a person who may not have experience with the elevated heart rate and blood pressure that's characteristic of cannabis, 'cause it is a stimulant, at least when initially brought into the system, even if it might eventually lead to relaxation. So now you've got someone who's anxious or somebody who's not anxious, who's deeply relaxed, and you're trying to study these effects, so it's a moving target of sorts, and it's very complicated to study marijuana and cannabis in its various derivatives in this way. Now you can probably appreciate better as to why there's so little nuanced data about sativa versus indica, versus different ratios of CBD and THC. It's really difficult to do these studies in the first place. That said, the general rules are smoking marijuana increases prolactin in men and women, which will reduce dopamine and testosterone. Smoking marijuana chronically, meaning more than twice a week, does appear to reduce testosterone significantly and elevate so-called aromatase enzymes, which are the enzymes that convert testosterone into estrogen. This might partially explain the effect that occurs in about 35% of males, which is gynecomastia, which is a development of breast tissue in males, in particular young males, who have elevated levels of testosterone or who are taking exogenous testosterone for testosterone replacement therapy or if they're taking high doses, anabolic steroids, or in females, the increase in breast size, which is due to additional estrogen from testosterone converted to estrogen. So it does appear that marijuana and cannabis increase estrogen, reduce testosterone, increase prolactin, especially in chronic users. Now, I'm sure that some people out there will say, well, their testosterone levels are exceedingly high or they are fine, meaning the constellation of symptoms associated with low testosterone and elevated estrogen are not present in them. That probably means one of two things, or both. They either had elevated levels of testosterone to begin with, so their ceiling was higher, so bringing it down didn't have that much of effect, or that they have very low levels of aromatase in their system. There are some anecdotal evidence that smoking particular parts of the marijuana plant, in particular, the seeds, can increase aromatase in the conversion of testosterone to estrogen. I think in the old days, the lore was the seeds make you sterile, and I think that was related to what I just told you, this increase in conversion of testosterone to estrogen. There's a vast literature on the effects of cannabis on fertility. Yes, it does seem to alter sperm motility and sperm health and function when taken chronically, more than twice per week, in particular high doses of high potency THC.

This is something we will cover in far more detail on a future episode all about fertility. And in females, there's an increase in estrogen as a consequence of smoking marijuana and increasing prolactin and estrogen in parallel. Whether or not that's detrimental isn't clear, although I point out that elevated estrogen and prolactin can be associated, again, can be associated, not necessarily, and certainly, not causative, but can be associated with elevated levels or frequency of breast cancer detection. So cannabis and its effects on hormones are not without consequence. There are effects of cannabis on cortisol in some individuals. It greatly increases cortisol due the anxiety and paranoia it can create, and in other individuals it reduces cortisol. Again, we have these divergent effects. But I want to be very clear, the effects on prolactin, meaning elevated prolactin, the effects on testosterone, meaning, at least most studies point to, reduced levels of testosterone and increased estrogen. That seems to be true for most all individuals that chronically use cannabis, whereas the effects on cortisol tend to be divergent. Cannabis increases cortisol in some individuals and decreases cortisol in others. In general, increases in cortisol that are ongoing are not healthy for us and so on. And then of course, there are other effects on hormones, and I'll just briefly summarize those, that THC in particular, not CBD, but THC in particular, is known to be strongly inhibitory for something called gonadotropin-releasing hormone. This is a hormone that's released from the brain, from the hypothalamus that then feeds onto, or I should say signals to the pituitary gland, which is also near the roof of your mouth, a lot of stuff happening near the roof of your mouth it turns out, biologically, and reduced levels of gonadotropin-releasing hormone caused by cannabis use, reduced levels of LH luteinizing hormone and FSH, which reduce levels of testosterone and sperm production in males and egg health and ovulation and menstrual function in females. Now, I'm sure there are a number of women out there who will say they have perfectly normal menstrual cycles despite using cannabis. I'm certainly not going to dispute that, but if you are somebody who's trying to maximize fertility or regulate or balance hormones, marijuana and cannabis reduces GnRH. That is the gonadotropin-release from the hypothalamus and thereby reduces luteinizing hormone and follicle stimulating hormone, which are released from the pituitary and travel in the bloodstream to support normal ovarian function and health

02:06:53 Smoking/Vaping Tobacco or Cannabis & Negative Health Consequences

and normal testicular function and health in females and males, respectively. Up until

now I've been discussing the biological and psychological effects of cannabis. Now I'd like to shift our attention to some of the negative health effects of cannabis and shine light on some of the individuals or groups out there that need to be especially wary of and probably avoid cannabis use entirely, including ingestion of cannabis by way of edible. And I frame things that way, because I think there is an increasingly large number of people out there that appreciate that smoking tobacco or smoking cannabis, vaping tobacco, yes, vaping tobacco, or vaping cannabis, each and all have negative health consequences on the lungs and on the so-called endothelial cells of the body, the cells that make up the vasculature, the capillaries and blood vessels. If you don't already know this, I'll make it very clear, and I'll make it very brief. Whether or not you smoke or vape tobacco or cannabis, you are severely impairing the function of endothelial cells that make up the capillaries and blood vessels of your brain and body, and that is known to decrease cognitive capacity over time, increase probability of strokes, severely impact lung function, and also lead to things like peripheral neuropathies. It leads to sexual dysfunction, because of lack of blood flow to the genitals, can lead to other aspects of reproductive damage, including to the ovaries and testes. Essentially, there is no other way to state it, except that smoking and vaping have negative health consequences that are independent of the substances that people are trying to get into their bloodstream by smoking or vaping. So people smoke and vape tobacco, and people smoke and vape cannabis, and in both cases, if we just set aside the direct effects of tobacco and the direct effects of cannabis, we can confidently say that the process of smoking, of inhaling smoke into the lungs, and yes, also vaping, bringing the chemicals that transport nicotine, or in this case, cannabis, into the lungs by way of vaping are both severely detrimental to endothelial cells. I think a few years ago, when vaping wasn't as prominent, there was this question and this idea that maybe vaping was going to be far healthier or at least not as bad as smoking, but now we can see a huge number of negative health effects of vaping, some of which are distinct from the effects of smoking. So if you'd like more information on smoking versus vaping, please see the episode that I did on nicotine. We will also do an entire episode all about vaping in the future, but there's really no way to slice it and dice it or candy coat it. The fact of the matter is that smoking has clear and severe negative health consequences, regardless of whether or not you're smoking tobacco or cannabis, THC, and vaping has negative health consequences, whether or not you're using the vape to bring in nicotine

02:10:06 Avoiding Cannabis During Pregnancy/Breastfeeding, Fetal Neural Development

or THC or some combination of THC and CBD. That's simply the way it is. With that said, now I'd like to focus our attention on the direct effects that cannabis has, either by way of THC action or by way of CBD action in terms of positive or negative health effects on the brain and body, and we're going to explore that first as a function of age. And the reason we're going to do that is related to a fact that I mentioned at the beginning of the episode, which is that the CB1 and the CB2 receptors, the two receptors for cannabis to which THC and CBD and CBN and all other psychoactive compounds of cannabis bind to to have their actions are present throughout development. Believe it or not, they are present very soon after conception, and the CB1 and CB2 receptors actually play a critical role in the development of the fetus. Now, you might wonder why that is, because of course, the developing fetus doesn't necessarily expect to see cannabis or to be exposed to cannabis and THC and CBD. But, as you recall, endogenous cannabinoids are present in the adult brain and body and endogenous cannabinoids, it turns out, are also present in the developing fetus. In fact, endogenous cannabinoids are present at much greater levels in the developing fetus than they are after a child is born, and levels of endogenous cannabinoids actually go down across development. I find this really interesting. What this means is that endogenous cannabinoids and activation of the CB1 and CB2 receptors are an integral part of neural development, and this is going to become especially relevant in considering whether or not pregnant mothers should or should not use cannabis or CBD, and it also points to some very interesting biology in terms of how the brain develops and how the body develops. Now the development of the brain and nervous system and body is a fascinating and vast literature, certainly far too vast to cover in today's episode, especially at this late hour as it were, but we will have a future episode all about brain development. In terms of the effects of cannabis, it's sufficient to say that cannabinoid receptors are present and active in the developing fetus. They're present and active in the newborn. They're present and active in adolescence. And across that time, from conception until adolescence, endogenous cannabinoids are mainly responsible for the actions of those cannabinoid receptors. During that time, the cannabinoid receptors are having very specific effects that are distinct from their effects later in life, and those effects can largely be explained in terms of neural development. Again, we don't have time for an entire lecture on this now, but

during development, your body was a collection of a bunch of cells. It's actually called a blastula, which means a ball of cells, and then those cells actually have to grow out connections and duplicate themselves, and this is a very interesting process by which neurons initially are situated far apart, and then they grow out connections and make contacts with one another. They remove certain connections, depending on what kind of life events you're exposed to. If you have a wonderful event early in life or a traumatic early life, those connections change, et cetera. The important point for today's discussion is that the CB1 receptor, in particular, is expressed on every neuron in the developing brain and has been shown to be important for every aspect of neural development, from the proliferation of cells, meaning getting enough cells to create a brain, to the outgrowth of the so-called axons, the little wires that connect up neurons with one another, to the steering, the direction which those axons go in development, which is essential, and even so far as to explain the connections that form between neurons, the so-called synapses, and then how those synapses work. So the basic statement here is that endogenous cannabinoids and CB1 receptor activation are critical for every aspect of brain wiring and development. With that in mind, the statement I'm about to make is absolutely terrifying, at least to me, and frankly, it should be terrifying to you as well. And the statement is, the current statistics on cannabis use in pregnant mothers is absolutely shocking. The most recent survey of pregnant mothers in the United States show that 15%, one-five, 15% of pregnant mothers report using cannabis in some form or another, either smoking it or more likely ingestion of in edible, because they are aware of the negative effects of smoking on the developing fetus, ingestion of an edible to increase THC and/or CBD during pregnancy, which to me, I have to say, as a developmental neurobiologist is, frankly, it's scary. It's absolutely scary, because that CB1 receptor is not just a minor player in neural development. It is absolutely central to every critical aspect of brain wiring and development. Now, the long-term implications or even the short-term implications of this, 15% of mothers self-reporting the use of cannabis at some point during pregnancy are not yet known. This is, as we would say, an experiment that's ongoing. But I'd be remiss if I didn't point out these data and just implore you, please, please, please, if you are pregnant or considering getting pregnant, you're a cannabis user, whether or not you're using edibles, if you're a CBD user, please do whatever is necessary to not ingest cannabis or smoke cannabis or ingest CBD during pregnancy. Now, there may be certain clinical indications by which your physician and your OB/GYN, and the pediatrician that will eventually be the pediatrician for your

child will prescribe CBD, although it's hard to imagine what those are. I contacted a number of different pediatricians and OB/GYNs and not a single one said they would ever suggest, and in fact would strongly discourage their patients from using cannabis during pregnancy. But I think that the advent of edible forms of cannabis, and the combination of THC and CBD in certain products, and the fact that most people view CBD as safer, because it does not include, or does not have, I should say, the psychoactive effects that THC does, has led to a situation where you have 15% of pregnant mothers using cannabis at some point during pregnancy and maybe even frequently throughout pregnancy, and the effects on the developing fetus are completely unknown. But recall that cannabis and THC and CBD outcompete, meaning they park in the receptor for endogenous cannabinoids and prevent endogenous cannabinoids from having their normal level and pattern of action, so this is absolutely critical. I cannot encourage you enough, or rather, I should say, I cannot discourage enough the use of cannabis and any related compounds in cannabis, edible or smoked, certainly not smoked, but even edible during pregnancy, and certainly in breastfeeding, lactating mothers, the same is also true. Recall that cannabis and THC and CBD are incredibly lipophilic. They're fat soluble, and they get into cells very readily, and they cross the blood brain barrier. They cross the blood placental barrier. So when I encountered this statistic, I had to kind of wipe my eyes a few times. I could not believe it, and yet I crosschecked that number with a few other studies. A few others have come in a little bit lower at somewhere like 13% to 14%, and a few have come in a little bit higher, but the average of 15% is both striking and shocking, so I don't know how to make the message more clear. I hope that is clear. Please do not use any cannabis, THC

02:18:13 Negative Health Consequences of Cannabis, Anxiety & Depression, Tolerance

or related things including CBD, smoked or edible if you're pregnant, lactating, et cetera. Now we are at the point where we need to consider some of the negative health effects of cannabis that have been well documented in peer-reviewed studies. And before I do this, I want to return to a point that I made earlier, which is that nothing I am about to say relates directly to issues of legality. If we consider alcohol, for instance, alcohol is legal in most areas of the world. It's certainly legal in the US, and yet there's an age limit for its use. Typically, it's not available to people until they're 21 or older. It's not to say that certain people don't use it before age 21, but it's not legal. It is illegal to buy or possess

alcohol, consume alcohol before age 21, and I think with good reason, because the brain is still developing. Likewise, we can have an informed discussion about cannabis and its various components that can fully acknowledge the reality, which is that one of the major harms of cannabis in the past has been the legal ramifications of cannabis being illegal. That's a statement that is no longer controversial, and this is not a discussion about legalization or non-legalization. If you look to the scientific literature, the epidemiological literature, there are wonderful data out of Carleton University and elsewhere in Canada showing that many of the negative effects of marijuana and THC are due to the criminal justice system, itself, that is the creation of illicit drug businesses, the creation of organized crime, the creation of a number of different features related to the illegality of cannabis. And again, this isn't the topic of today's episode, but that should be acknowledged. And at the same time, we need to acknowledge that when a compound, a drug or whatever you want to call it becomes legal, there's a tendency to assume that it's safe and safe for everybody. And with respect to cannabis and THC and perhaps even CBD, but certainly for THC and cannabis that's smoked or vaped or consumed in edible form, that is simply not the case. There are clear data pointing to negative health effects of cannabis use and THC use, which again, is not to say that there are not positive effects on mood, anxiety, pain relief, et cetera. Those are out there and they exist, and we will mention some of those of course, and we've talked about some of those, creativity for instance, et cetera. But if we do not acknowledge the negative health effects that are documented in the literature, then we are overlooking some very important data, especially as it relates to the development of psychosis in certain individuals. So, with that said, there are very strong data, and I will provide links to these resources, pointing to the fact that for people who are chronic users of cannabis, that is using it twice a week or more, that over time, their levels of anxiety actually increase, and this is true even for individuals that are using strains of cannabis, that while under the influence of cannabis, reduce anxiety. Over time, meaning over the course of 12 or more months, there is a well-documented effect of the anxiety relief that cannabis and THC initially brought, being less and less potent. That is people need to smoke more of it or ingest more THC in order to achieve the same level of anxiety relief, and in some cases, a switch from anxiety relief to increase in anxiety, and again, that's increase in anxiety, not just when the drug is not being consumed, but also while under the influence of the drug. Why would that be? We have to go back to our understanding of the CB1 receptor and the potency with which THC binds to that CB1 receptor. When THC is

brought into the system over and over again, meaning twice a week or more, the binding of THC, that CB1 receptor, eventually causes a habituation or attenuation of the entire process of binding the receptor and creating the psychoactive effects. So initially it creates anxiety relief, but over time, the affinity for the receptor doesn't change, meaning it can still park in that slot with a lot of affinity, a lot of strength, but there are fewer receptors available, and then the signaling that's downstream of those receptors becomes less and less robust. Now this is a topic we didn't get into in too much detail today, because I didn't want to include even more biological detail, but the CB1 receptor is a so-called G protein-coupled receptor. That's a mouthful, but a G protein-coupled receptor basically is like a bucket brigade. So while some receptors in the brain and body are such that when something, a chemical binds to them, that receptor has a direct action, like it opens and allows stuff to rush into the cell, increases the excitability of the cell, so called fast effects, these G protein-coupled receptors, and CB1 is a G protein-coupled receptor, they are more like a bucket brigade where they kick off a process through one molecule that then is handed off to another molecule that then is handed off to another molecule. It's a long chain or cascade of events. Those long chains or cascades of events have a lot of opportunity for regulation, for adjustment. Receptor systems in the brain and body, especially receptor systems like the cannabinoid system that are used to being tickled, not punched, tickled by endogenous cannabinoids, every once in a while some binds, has an effect, but certainly not bound with incredible potency and over and over again as they are when THC is coming into the system. Well those systems eventually, over time, they adjust themselves so that the body and those cells can achieve so-called homeostasis. So when people are using THC more than twice a week, what ends up happening is those G protein-coupled receptors in the downstream signaling mechanisms start to adjust themselves, and it requires more and more drug, so either higher dosages or more frequent use, and a lot of the positive effects, the so-called decrease in anxiety, increased focus, increased creativity, some of that starts to wane, it starts to dissipate, and people wonder why they have to use so much cannabis just to achieve a fraction of the effect that they used to be able to achieve with even a lower dose. So anxiety is getting worse over time, and that's anxiety during the drug use and outside of the drug use. Some people work around that or try to work around that by using varying strains of cannabis or changing the pattern of delivery from smoking to vaping or from vaping to edible and from edible to transdermal. Anyway, they go through a lot of gymnastics and writhing and seeking, but nonetheless, anxiety

increases over time. Also, it's very clear that depression increases over time and especially, this is surprising to me, but especially for individuals that were not depressed at the the outset of their use. In other words, they didn't start using cannabis because they were depressed, but rather the depression starts to emerge as a consequence of the cannabis and THC use. So that's serious, in fact, we now know, based on really solid epidemiological evidence, that depression is not a strong predictor of seeking out cannabis. It doesn't drive terribly many people to seek out cannabis use,

02:25:57 Cannabis Use & Adolescence/Young Adulthood, Predisposition to Psychosis

but cannabis use, itself, makes people four times likelier to develop a chronic major depression. So anxiety is increasing, depression is increasing, and this turns out to be especially relevant and important to young people. Why do I say that? Well, if you look at the data, and again, I think some of the strongest data are data to come out of the Canadian system. They've done some really beautiful controlled studies. I really hope to invite some of the people who arranged and ran those studies as guests onto the Huberman Lab Podcast. But if you look at the data out of Canada, or you look at some of the data out of Northern Europe and the US, what you find is that the probability that somebody will use cannabis and then go on to use it chronically, correlates very strongly with age. So for instance, some of the highest degree of cannabis use is among individuals 16 to 24 years old. In fact, in individuals who are 16 to 24 years old, and in particular, in students and people who are working, surprising, more than in unemployed populations, being young, 16 to 24, at least to me that's young, and being a student or working doubles the likelihood that somebody is going to use cannabis on a regular basis, twice or more per week. The typical age of initiating cannabis use nowadays is about 19 years old, so 18.7, and about 20% of people in that age bracket, of 16 to 24 years old, are using cannabis daily, either by vaping, by smoking or by edible. That's an enormous number, at least by my read. It's an enormous number, and here's why it's of really serious concern. During the ages of 16 to 24, the cannabinoid receptors are still available. They are not being as strongly driven by endogenous cannabinoids, but by ingestion of THC and/or CBD, there are downstream effects on the signaling within those cells that all the data point to creating a much, much higher likelihood of developing major depression, severe anxiety or psychosis at later ages. So to be very clear, cannabis use, between the ages of 16 to 24, in both males and females is

increasing anxiety, increasing depression in the immediate years and within the one year's time or so, so much so that people are using the cannabis ongoing in an attempt to reduce that anxiety and reduce that depression, but in addition to that, the cannabis use, and because of the signaling mechanisms involved are predisposing those individuals to psychosis later in life. If you look at individuals who start using cannabis, even younger, age 14, or even as young as 12, the probability of psychosis later in life, in particular schizophrenic or schizophrenic-like episodes more than doubles, so this is of really serious concern, and this is completely aside from any so-called positive effects or beneficial effects of cannabis that people might derive from occasional use as adults, meaning people older than 25. So for the person who's older than 25, who eats an edible every once in a while, or who smokes cannabis every once in a while, and people love to make the argument, it's not as bad as alcohol, which frankly, is a terrible argument, because if you saw our episode on alcohol, [laughs] alcohol is pretty bad, but even so, it's just not a good argument. It's saying that something is good, because it's not as bad as something else is simply just not a good or valid argument, at least not biologically speaking. The use of cannabis in young populations is very strongly predisposing people to psychotic episodes, and we know the mechanism by which this occurs. This occurs by a thinning of the so-called gray matter, and it's called gray matter because with neurons, nerve cells, they have a so-called cell body, that's the part that contains the DNA and manufactures all the neurotransmitters, et cetera. And those are shipped out to the other parts of the neuron that include the axon, the wires between axons, and those axons under the microscope, because they have a lot of fatty tissue around them, and this is healthy fatty tissue that allows electrical transmission to be fast, that fatty tissue, those portions of the cells, are called white matter, so you have gray matter and white matter. Gray matter are the so-called cell bodies where the DNA and all the stuff is manufactured. White matter or the axons or the wires through which all the key components are shipped out to the synapse, et cetera. Wonderful data and I do say wonderful, because it is part of a large scale consortium, and we will provide a link to the paper. This was published in "Translational Psychiatry" just this year, point to the fact that adolescent cannabis use accelerates the thinning of the prefrontal cortex and the gray matter in particular. So what this means is, while during normal development, the gray matter, the prefrontal cortex and all the cells there are indeed intended, it's a normal process for it to thicken and then thin a little bit as connections are adjusted and people learn and mature and grow up, this is part of the normal healthy maturation process,

independent of cannabis use. When kids, 'cause these really are kids, use cannabis, and it doesn't matter the mode of cannabis delivery, whether or not it's vaping or smoking or edible, that gray matter thins at a much, much greater rate. And the reason I like this paper published in "Translational Psychiatry" this year so much is that they link the amount of cannabis use, heavy, moderate, light or no cannabis use, to the rate of prefrontal cortical thinning, and it's absolutely clear from these data that the more often young people, meaning individuals between the age of 14 and 25, the more often they consume or smoke or vape cannabis, the faster and the more extreme that cortical thinning is. And the cortical thinning is occurring in exactly the area of the brain that's involved in planning, in control over one's emotions, in reflexes, in organizing one's life in a number of different ways, anywhere from cleaning one's room, literally, knowing what goes where, to making plans that extend out through the day, through the week, through a year, essentially becoming a functional human being involves using your prefrontal cortex in a variety of different contexts and different time domains, the time domain of an hour, the time domain of a day. Making plans and being able to execute plans is fundamental to being a healthy human being, and it's absolutely clear from these data that the more cannabis one uses, the more impaired those neural circuits are. There's simply no other way to view these data. In fact, so much so, that even small amounts of cannabis use are associated with rates of cortical thinning and degrees of cortical thinning that are really detrimental and concerning for normal cognitive processes. If you were somebody who smoked marijuana or consumed cannabis in any form or another during adolescence, does that mean that your prefrontal cortex can never be rescued, that it can't come back? Well, the short answer is, it probably can be rescued to some degree. It will depend on how much cannabis you were using and how often and what strains of cannabis, et cetera. There's really no traveling back in time, as my graduate advisor used to say. Time machines are broken. At least for now, we don't have time machines. So all you can really do is try and emphasize, first of all, quitting cannabis in any form and focusing on behaviors that emphasize endothelial cell blood flow health to the brain, so that would be cardiovascular exercise, adequate nutrition, not smoking nicotine, and there are a number of other things that one can do. We will do an entire episode all about trying to reverse the effects of cannabis and other drug use during adolescence. We don't have time to do a deep dive on that right now, but all the things that standardize and promote health, adequate sleep, good social connection, regular cardiovascular and weight training exercise, healthy nutrition, and what that represents

to you, healthy metabolic function and weight, et cetera, those are all going to facilitate some recovery of brain function, in particular, prefrontal cortical function, by way of all the positive effects that those behaviors and choices have. But with that said, if you are in the age bracket that I've been referring to, this 14 to 25 year old age bracket, and you are an occasional even or chronic cannabis user,

02:34:36 Adolescent Cannabis Use: Brain Development & Mental Health Disorders

you should be very, very careful and concerned about the long-term effects that that could potentially have. That statement is bolstered by another statistic, which is that unlike a lot of other drugs, the rate of cannabis use is strongly related to how dangerous people perceive cannabis to be. Now, that might seem obvious, on the one hand, if you think something is very, very dangerous, you would expect that the probability that somebody would use it would be very, very low, and if they think something is safe, the probability would be high. But that isn't necessarily the case. If you think about it, cannabis is a unique instance in which nowadays we are hearing, yes, it's becoming legal in a number of areas, and we talked earlier about why that's probably a good thing in most circumstances, but that we aren't just hearing that cannabis is safe, or it's not just being implied that cannabis is safer, but many more people are talking about the positive effects of cannabis without a lot of discussion about the negative effects of cannabis. And I realize that saying this is going to upset some people out there, because I know that there are a number of people who fought very hard for the legalization process, and I want to acknowledge that. I also want to acknowledge the many known positive effects of cannabis in adults with very occasional use, provided it is delivered safely and in the safe context and setting and with legality. That is entirely distinct from the issue of whether or not cannabis is safe for the developing brain and body. Again, I'm not demonizing anybody for using cannabis, but I want to make the point very simply and very directly. It is far and away a different circumstance for the brain for an individual to be 25 years or older and using cannabis in whatever form, occasionally or maybe even frequently, than it is for a young person, aged 14 to 25, to be using cannabis, either by smoking or vaping or by edible or any other form, on the brain and body. It's absolutely clear that the brain continues to develop at least until age 25, and that a huge number of systems related to mood regulation, so-called executive function, the ability to organize one's thoughts, plan and execute plans, essentially to become a functional

human being, that's one portion of becoming a functional human being, but certainly an essential one. All of that relies on the fine tuning of this neural circuitry that we've been talking about up until now, and it's abundantly clear that cannabis and THC in particular, dramatically disrupt those processes. So if this isn't clear enough, just from my statements, I'd like to point to a particular paper. This is one of the more impactful papers in this area in recent years. This is a paper published in "Lancet Psychiatry" in 2022. Title is "Association of Cannabis Potency with Mental Ill Health and Addiction, A Systematic Review." There are a number of very important points in this very fine paper. "Lancet Psychiatry" is one of the premier medical journals out there, and they evaluated a huge number of studies. They actually looked at more than 4,000 studies. They selected the ones that were only the most rigorous in terms of study design and analysis and rigor of conclusions, and they looked at how early use of cannabis impacted later probability of development of psychosis and other psychiatric conditions, and the takeaways from this study are very clear. First of all, chronic cannabis use, so more than twice per week, has consistently been associated with mental health disorders. I'm pulling some phrases directly from the paper. Heavy cannabis use, meaning cannabis use more frequent than twice per week, has been associated with four times the risk of psychosis later in life, in particular, schizophrenia and bipolar-like episodes. Now, we've done an episode on bipolar disorder. It's also called bipolar depression. We have not yet done one on schizophrenia, but both bipolar disorder and schizophrenia have a very, very strong genetic component. There's a 30, three-zero, 30 times greater likelihood that you'll have bipolar disorder if you have a first relative who has bipolar disorder. And then, it's also the case that using cannabis, especially during adolescents and the teen years, and up until age 25, create a four times greater risk of psychosis for those that have a predisposition to bipolar disorder and/or schizophrenia. Now, I don't hear very much about this in the media. This paper got some attention and then it got swept away. I don't think that was an intentional sweeping way. There's just a lot of events in the world as you well know. But I think it's a particularly important set of findings, because obviously, in looking at so many studies, it distills out the strongest findings that are out there and really pulls the consistent messages that are arriving from all these different studies. And as they point out, and again, I'm paraphrasing here, this is the first systematic review of the association of cannabis potency, and all of the data point to a very clear conclusion, which is the more potent the THC concentration, the higher probability of developing psychosis or a major depressive episode or a major anxiety disorder later in life. That

should be of particular concern, because we know, we are absolutely clear about the fact that with the advent of all these new strains of cannabis, and with the engineering and availability of cannabis at much higher potency, meaning THC potency, the risk of psychosis is going up and up and is likely to continue going up unless something is done to reduce the frequency of cannabis use to zero, ideally, or to very low frequency, very low potency in adolescence and teens and people age 25 or younger. I know a lot of people don't want to hear this message, because first of all, it's alarming, and second of all, as I mentioned earlier, the statistics tell us that the greatest number of people that are starting to use cannabis are in the age bracket of 16 to 24. Many of them are functional in other areas of life. They're students, they are employed, et cetera. But when you couple that with the fact that the most frequent adopters of cannabis use are in this age bracket of 16 to 24, they're twice as likely to use as other individuals or to start using cannabis as are other individuals. Plus, the general perception out there, because of the way that cannabis is discussed in the media and by sports figures and by celebrities and by politicians, et cetera, that it's not as bad as alcohol and maybe not that bad and maybe even has health benefits, then you're essentially setting up a system where young people are far more likely to adopt and continue cannabis use

02:41:44 Cannabis & Pain Management, Divergent Effects of Cannabis

without realizing these serious health consequences that await them later. With all of that said, I, of course, again want to acknowledge that there have been well-demonstrated effects of cannabis for reducing pain, in particular in chemotherapy and in the context of reducing nausea in people suffering from cancer or chemotherapy. There is a well-known effect that one can generally point to as positive, using cannabis for things like glaucoma, for lowering intraocular pressure and offsetting the loss of neurons that would lead to blindness, although there are other tools, of course, that don't involve cannabis use that can accomplish that as well, so called intraocular pressure lowering drugs or drops. There is a list of probably a dozen or more psychological and bodily ailments that can be aided by cannabis use, in particular edible cannabis use of particular strains. I, of course, am going to address each and every one of those in episodes where I'm talking, for instance, about eye disease or about chronic pain. I am in no way, shape or form trying to rob the incredible efforts of the laboratories and people that have worked very hard to study and establish the valid uses of cannabis for

treating various ailments and that continue to study cannabis in order to try and ameliorate the symptoms of different ailments. But today, I really wanted to emphasize the biology of cannabis, some of the often discussed effects, I guess one could call them positive effects, things like enhanced creativity and really point to the nuance and actually the divergence of people who take cannabis and some experience heightened levels of creativity and some do not. Some people experience heightened levels of sexual arousal and some people experience the exact opposite, and so on and so forth, rather than focus on all the potential positive and emerging positive data about cannabis in different medical contexts. And at the same time, I strongly feel that it's important to acknowledge the shocking, because there's really no other way to describe it, the shocking effects of cannabis use on the developing fetus and the fact that so many pregnant and lactating mothers are using cannabis. I mean, that number 15% still has me dizzy with disbelief, and yet we need to acknowledge this and address this immediately. And I think it's vital to understand that cannabis use through any delivery mechanism, smoking or vaping or edible or otherwise, is very, very concerning, in fact, dangerous to the developing brain, certainly for the fetal brain and for the baby brain, but also for the adolescent brain and for the teen and young adult brain, not just because of the effects that it can have in the immediate term, those slow creeping increases in anxiety and depression, brought on by cannabis use, but also the time release, if you will,

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on the development of psychosis and other types of major psychiatric disorders later in life. I acknowledge we've covered a lot of ground today, and yet there's still far more ground that we could have covered and that we will indeed cover in future episodes. Nevertheless, if you are learning from and are enjoying this podcast, please subscribe to our YouTube channel. That's a terrific zero-cost way to support us. In addition, please subscribe to the podcast on both Spotify and Apple, and on both Spotify and Apple, you can leave us up to a five-star review. If you have questions for us or comments or feedback of any kind, please put that in the comment section on YouTube. We do read all the comments. Please also check out the sponsors mentioned at the beginning of

today's episode. That's the best way to support this podcast. As mentioned earlier, the Huberman Lab Podcast now has a premium channel. You can subscribe to that by going to hubermanlab.com/premium. There, for \$10 a month or \$100 for the entire year, you can get access to all of the monthly AMAs, and you'll be supporting peer-reviewed research to develop further protocols for mental, physical health and performance. Again, that's hubermanlab.com/premium. Not so much today, but in many previous episodes of the Huberman Lab Podcast, we talk about supplements. While supplements aren't necessary for everybody, many people derive tremendous benefit from them for things like enhancing sleep and focus and hormone optimization. The Huberman Lab Podcast has partnered with Momentous supplements. If you'd like to see the supplements that the Huberman Lab Podcast has partnered with Momentous on, you can go to [livemomentous](https://livemomentous.com/huberman), spelled O-U-S, so livemomentous.com/huberman, and there you'll see a number of the supplements that we talk about regularly on the podcast. I should just mention that that catalog of supplements is constantly being updated. If you haven't already signed up for the Neural Network Newsletter, this is a monthly Huberman Lab Podcast newsletter in which you get some brief show note summaries as well as a lot of actionable tools in summary form. Many people find these very useful for distilling out the vast amount of information that we cover on the podcast. So for instance, if you go to hubermanlab.com, you can click on the menu, click to Neural Network Newsletter or simply newsletter, and you can sign up, just give us your email. We do not share your email with anybody. And again, it's completely zero-cost. We also have examples of previous newsletters that you can download immediately without having to sign up for anything and decide whether or not you want to sign up. Again, that's the Neural Network Newsletter at hubermanlab.com. If you're not already following us on social media, we are @hubermanlab on Instagram, on Twitter, on Facebook and on LinkedIn. And especially on Instagram and on Twitter, I cover many of the tools that are discussed on the Huberman Lab Podcast, but also a lot of science and science-based tools not covered on the Huberman Lab Podcast. Again, it's @hubermanlab on all platforms. So once again, thank you for joining me for today's discussion all about cannabis. And as always, thank you for your interest in science. [bright music]