

How Marijuana Affects the Brain & Body | Dr. Andrew Huberman

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 if 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 in 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 a kind of 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 3 to 4 hours Although there's some variation on that depending on individual metabolism whether or not somebody is uh 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 then of course when people say here fat they always think oh fat's bad fats you know 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 also remain in those cells for a long time So I know that a number of people depend 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 it doesn't matter it's gonna 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 you

know how to accelerate the clearance And um uh I should just tell you that just losing bodily fat isn't going to um eliminate it from your system uh maybe partially in those fat cells But uh certainly in uh intravital fat and other fatty tissue that's uh in and around the brain and body is going to harbor that uh THC molecule and the CBD molecule for quite a long while at least 80 days Ok So if someone smokes cannabis or they ingest cannabis 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 of parking at those endogenous cannabinoid receptors and impacting the signaling between neurons which leads to the subjective effects of cannabis including THC and CBD So let's talk about what those different subjective effects are Again this is going to vary depending on whether or not people are adjusting 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 meet people sort of mood elevated energetic Again the 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 Ok 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 CB one receptors are present on an enormous number of different neurons and brain structures and neural circuits So that the sativa varieties that act as sort of a stimulant making people feel happy because in general they do tend to elevate mood at least at certain dosages talkative uh tend to make people feel um like they have ideas that are interesting that they might wanna share um tend to narrow their context So we tend to increase focus This is something that's not often discussed about cannabis but it can especially the sativa varieties can increase people's level of focus to particular things that something they're watching or something they're doing or music allows them to narrow their sense of focus that's going to occur by activation of CB one 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 Uh the way to think about the

stress in 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 the sort of threat detection systems and then the prefrontal cortex largely acts as a break on those systems sort of like the reins pulling back on a steed of horses that would otherwise just kind of take off And so the sativa varieties tend to increase CB one activation in the prefrontal cortex and in other circuitry that then leads to a kind of 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 in a little bit But I just wanna give you a sense of how this is working because as I mentioned before THC and or CBD are gonna bind that CB one receptor let's say in prefrontal cortex and neurons of prefrontal cortex is gonna bind there and then there will 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 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 CB one 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 right We have the same compounds THC and or CBD brought into the body and brain binding the same receptors In this case the CB one 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 are 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 gonna 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 you know not trivial in its own right But in terms of thinking about the creative aspects or the creativity stimulating aspects of cannabis not um sort of 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 bold faced triple underline except except in some individuals depending on dosage but also depending on pre existing 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 OK 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 in type one type two or type three sativa Well there is no way to predict that and there's a lot of kind of what I would call street lore or dorm room lore or kind of um pure not peer reviewed uh but uh sort of pure disgust I mean among friends and people and acquaintances lore out there that what one needs to do is simply smoke more right 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 strainer 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 hy 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 you know between 5 ft

seven and 6 ft tall and uh you have blue eyes or brown eyes that the sativa varieties are gonna be right for you or that the sativa varieties are gonna 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 right 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 That's simply not the case Now what we can say for sure is that uh 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 or eat sativa that it tends to lead to one specific set of or generally leads to one specific set of effects heightened focus mood et cetera Whereas when they ingest or smoke indica and its components right Again we're still talking about THC and CBD and varying ratios But now Indica cannabis and say well why would it improve the transition time to sleep or at least give people the impression that it improved 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 CB one receptors and those retrograde signaling mechanisms that 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 CB one receptors and those CB one receptors can lead to either an acceleration or a break on particular biological mechanisms And there are going to be a constellation of different accelerations and breaking 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 and 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 mellower 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 right Because there can 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 ingestible It's much harder to gauge that from the smokable forms of cannabis especially if those smokable 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 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 well being 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're gonna 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 you know 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 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 wanna 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 anatomist 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 you 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 sort of tears and lubrication of the eyes from the lacrimal glands of the eyes because of the presence of largely CB two but also CB one 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 CB one 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 CB one 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 and anticipation of taste as well as the experience of taste So the narrowing of focus to what you want to go eat right You really crave I don't know pizza it seems to be high fat high carbohydrate foods but really crave

pizza and narrowing the 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 And so there's an array of different effects And as I mentioned before CB one receptors are present all over the nervous system in the brain the spinal cord in fact the presence of CB one 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 should 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 CB one receptors in neurons of the spinal cord So a broad array of effects are taking place regardless of what strain you take and what 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