Guest: Yasmin Hurd, Ph.D., is a professor of psychiatry, neuroscience, and pharmacological sciences at the Icahn School of Medicine at Mount Sinai in New York City; director of the Addiction Institute at the Mount Sinai Behavioral Health System; Ward-Coleman Chair of Translational Neuroscience at Mount Sinai; and a member of the Dana Alliance for Brain Initiatives. She has conducted pioneering research on the neurobiology of opioid abuse, the neurodevelopmental (and cross-generational) effects of cannabis, and potential treatments for opioid addiction. A member of the National Academy of Medicine, Hurd and her research have been featured on NPR, ABC, and CNN, and in the *New York Times, Time,* and *Discover.*

Host: Bill Glovin serves as editor of *Cerebrum* magazine and as executive editor of the Dana Foundation. He was formerly senior editor of *Rutgers Magazine,* managing editor of *New Jersey Success,* editor of *New Jersey Business* magazine, and a staff writer at *The Record* newspaper in Hackensack, NJ. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

[Intro] Bill Glovin: What is addiction and how does it affect and even change the brain? Why are some brains more vulnerable to substance abuse and addiction? What is the role of stress in addiction? Welcome to the Cerebrum Podcast where we explore matters of brain science with leaders in the field. I'm Cerebrum editor-in-chief, Bill Glovin, and today's big topic is obviously addiction. But more specifically, addiction as it relates to substance abuse in this seemingly never-ending pandemic. And to address this most important issue is our guest, Yasmin Hurd, who has conducted pioneering research on the neurobiology of opioid abuse.

[Clip] Yasmin Hurd: We know that it's THC that is leading to the increased risk for opioid use. Unfortunately, the cannabis on the streets today, the THC potency in them is incredible. So before, in the '60s, '70s, even up to the '90s, THC concentration was about 4%. Now it's like 24% and there are products in dispensaries and the way in which some kids even use cannabis in terms of dabbing. You can get nearly 70 to 80% THC. So that's a completely different drug.

Bill Glovin: Yasmin is a professor of psychiatry, neuroscience, and pharmacological sciences at the Icahn School of Medicine at Mount Sinai, as well as director of the
Addiction Institute at the Mount Sinai Behavioral Health System, which is four locations—count them four—in New York City. She is also Ward-Coleman Chair of Translational Neuroscience at Mount Sinai. And, last but not least, she's co-author along with her colleague at the Addiction Institute, Timothy Brennan, of our *Cerebrum* magazine cover story in our winter issue, which recently posted on Dana.org. It's called, “Covid and Addiction: The Perfect Storm.”

Welcome to the podcast, Yasmin. First, let me just say what a great job you did on the story and on your Secret Science Club appearance.

Yasmin Hurd: Thank you so much, I really appreciate it. Thanks for the invitation.

Bill Glovin: There's just so much to address on this topic. I guess the most pressing issue is tied to what you refer to in your article as “the perfect storm.” More than 100,000 Americans died of drug overdoses in a 12-month period that ended in April, up almost 30% from the 78,000 deaths from the year before. Why are things getting worse year after year? And what can we do about it? I know that's a big question.

Yasmin Hurd: Yeah, that's a huge question. And for me, it comes back to, in the aspects of a perfect storm. I think in our society today, we have increased stress. The stress levels that the average person faces are just enormous. And even before Covid; but Covid brought in a new era of this fear, of this very contagious and deadly virus. The isolation that so many people went through and still go through. Also, the economic downturn, kids not being able to see their friends and all these aspects of social connectivity that were lost. All of those increases stress, and stress increases the risk for substance use; isolation increases the risk for substance use, even for those who didn't have a substance use disorder before all of these lockdowns. So, it's a big, big question of how we're going to deal with it. It will take us another hour to discuss.

Bill Glovin: We all have chemicals in our brain. One that flows through brain tissue is called dopamine. It's weird that a chemical is called a reward pathway. Do some of us have more of it than others? And how does it relate to addiction?

Yasmin Hurd: Yeah, so dopamine is that neurotransmitter that even the regular person in the street might even know, it is associated with reward. When you feel good, dopamine levels are elevated. At least the prediction of even getting something positive, your dopamine levels go up. And what drugs of abuse do is that they artificially elevate dopamine, and they elevate it to a much greater level than our normal happy place would bring us. And so, the brain thinks, oh my gosh,
I’ve gotten something incredible. And then it’s that search for that dopamine again, that initial dopamine high, that many people then get trapped in addiction. We all have differences in our genetic makeup that can lead to increases or decreases in our baseline dopamine levels. And the receptors that pass along, that those dopamine signals differ in all of us.

And for example, we know that people who have a substance use disorder, characteristically, there’s a dopamine receptor that’s reduced in their brains. And everybody thinks that—You know, there’s this fight, the chicken or the egg, what came first? Is it that these people are born with this reduced dopamine receptors that make them vulnerable? Or is it the drug that induces that? And it’s a combination of both.

Bill Glovin: You’re saying that there is a genetic predisposition possibly to addiction. Is there also a cultural tie?

Yasmin Hurd: There’s not a cultural vulnerability to substance use disorder, but there is an environmental. So, for example, that same dopamine receptor that is associated with substance use vulnerability, we also see that that changes depending on whether or not you are in a socially very oppressive environment versus if you’re in the same environment and you’re dominant. So just that aspect of the environment can change how your genes, whether or not they’re turned on and off—and we call that mechanism epigenetics—as compared to your genetic inheritance from your parents, where your DNA sequence, you inherit from them. But the environment can actually put tags on your DNA and change how those genes are indeed turned on and off. So, you can now increase your risk for addiction because your environment is so oppressive that it changes some of the DNA, the genes turn on and off, and make you more vulnerable to addiction.

Bill Glovin: What are some of the situations where someone is in an environment that is conducive to addiction, and how can they maybe change that environment?

Yasmin Hurd: This is one of the things I think that it’s not about just that person trying to change that environment, it’s about our society making sure that we have environments that’s enriching for all. And it starts off even with children because the greatest vulnerability for most psychiatric disorders that people don’t realize actually occurs during development. We may diagnose these disorders, and they may exacerbate like addiction when they become adults, but they start early. So even having better enriched environments at schools, the school system has become very pathological for most children, especially in certain communities where parents don’t have the money to send their kids to
private school, where they're stimulated in ways that increases their cognitive creativity, that they feel protected, where kids go to school and they're stressed that they're going to get shot...Those are not the environments that would be nurturing for the developing brain.

So, it's not just what the person can do to change their environment. It's how we, as a society needs to change these environments, especially for children and young adults.

Bill Glovin: Do you see the publicity that has come along with what happened with the Sacklers, for example, and the book *Dopesick*, and then the Hulu series, and those kinds of law enforcement efforts... Do you see a decrease in prescriptions for opioids?

Yasmin Hurd: So, the Sackler and Purdue Pharma that contributed that to the opioid epidemic that we still have definitely that has led to changes in the law. So, for example, now clinicians are educated more because of this opioid epidemic that really started with physicians over-prescribing opioids. So, the education for clinicians has helped to decrease their prescription rates and so on of opioids are monitored very strongly. So, all of those things have contributed to reducing the number of opioid prescriptions written every year. There’s still more than the population of adults in the country so we still have some work to do. But I think that now people realize that while opioids are an essential valuable tool clinically for acute pain, they're really not meant for chronic management of chronic pain because they do then increase the risk of addiction. So just educating clinicians, educating patients and politicians, they have definitely decreased the number of opioid prescriptions.

Bill Glovin: So, there's less prescriptions, but it seems like the problem continues if not getting worse. So why is that happening?

Yasmin Hurd: I mean, two parts. One, there are definitely unscrupulous people out there that still provide opioids in ways that can get around certain laws. Two, you have an illegal market that has indeed blossomed because people did become addicted, for lack of another word, in terms of the people who then needed these opioids and so they started going to the illegal market. And we now have an increase of fentanyl that is placed in these illicit opioids, even the pain medications actually as well so it's not just “heroin.” And fentanyl is 100 times more potent than morphine and so that also keeps people addicted more. The stronger the potency of these opioids, the greater the vulnerability to develop a substance use disorder.
Bill Glovin: You've done a lot of research into cannabinoids and marijuana. Is marijuana, in your mind, connected to opioid addiction in any way?

Yasmin Hurd: So, when you look on a statistical epidemiological level, of course you can see that a number of adults that have an opioid use disorder, they started off with cannabis use earlier in life. But those individuals also experimented a little bit more with alcohol or even cigarettes. From our animal models, we do know that THC, the main cycle active cannabinoid in the cannabis plant, does increase the risk of sensitivity to opioids, meaning that even animals that had adolescent exposure to THC in the majority would then self-administer more heroin. So, we know neurobiologically that there is a link between the cannabinoid system and opioid sensitivity. But it's not a done-deal that just because you had used cannabis, you're going to develop an opioid use disorder.

And also, we know that it's THC that is leading to the increased risk for opioid use. Unfortunately, the cannabis on the streets today, the THC potency in them is incredible. So before, in the '60s, '70s, even up to the '90s, THC concentration was about 4%. Now it's like 24% and there are products and dispensaries and the way in which some kids even use cannabis in terms of dabbing. You can get nearly 70-80% THC, so that's a completely different drug. And that's probably, what's also contributing to the greater risk for developing an opioid use disorder.

And it's a long answer, but cannabis is a complex plant. And we've seen that another cannabinoid in the cannabis plant, CBD, cannabidiol, actually reduced craving in animal models. Also, not just in our human studies, but we saw it in animal models. It reduced drug-seeking behavior. So, cannabis can definitely increase opioid risk, but there's a cannabinoid in the cannabis plant that is being investigated as a potential treatment for opioid addiction.

Bill Glovin: So that would be CBD oil? The use of it is so widespread now in products, food products, pills, edibles, all kinds of forms—

Yasmin Hurd: Yeah, unfortunately.

Bill Glovin: And that is not addictive?

Yasmin Hurd: No. So, CBD is not addictive. We and others, many people now have studied CBD in many different ways in animals and human subjects. And we've not seen that even at very high doses that it has an addictive potential. But like you just
said, CBD now is everywhere, in your water, in your coffee. And that also becomes a problem because people take it as if it is completely benign. And in developing it as a potential medication for opioid craving and anxiety, it's a different dose range than what you can buy in your CBD coffee or so on. It's a completely different dose range. So, we need to make sure we understand medicine and the medicinal characteristics that's needed for CBD or any other drug that's going to be considered medicine, that we need to go through all these clinical trials. But it's going to be at a very different dose range than what people are selling. So many people think you can just go buy this gummy bear, and it's going to treat your anxiety. It's not in the same way.

Bill Glovin: So, what does it do? I mean, a lot of people use it for sleep, for example, but do they use it for decreasing stress?

Yasmin Hurd: People use CBD for decreasing their stress, definitely for increasing sleep. There are other cannabinoids that are also being tested, but yeah, I think for the most part, people are using CBD for this relief of stress and for promoting sleep.

Bill Glovin: We know that marijuana impacts the developing brain in a percentage of young people. Since I don't believe there's really a realistic way of keeping it out of the hands of young people, now that it's mostly legal, what do you suggest is a realistic approach? Or maybe, even better, what would you tell your own 14-year-old about the use of marijuana?

Yasmin Hurd: I would say, wait until you're a little older, because marijuana or cannabis has a very different effect on your adolescent brain than it does on the adult brain. And we don't know why, but that is true.

And so, give yourself a little time, because I know when you tell kids don't do something or tell anybody don't do something they're going to be even more drawn to doing it. So, my thing is showing a little biology to say, this is what your... not, “This is what your brain looks like on drugs,” as the egg and the frying pan, but that, “Wait. Give your brain a little more time to mature,” because we know that cannabis and other drugs and stress has a very different effect on the brain of a teenager than in an adult. And so, when you pass by that sensitive window, you're hopefully then less of a risk for developing an addiction and other psychiatric disorders that we see linked with early cannabis use.

So, I would tell them, just wait, but know that this is a time and period for you and your brain to get to its full mature potential. I think this is the thing in our
society today, I think we take away people's potential by not really giving the support that's needed to succeed during their teenage lives or childhood, not really giving them safe places. This is the time period when they should be protected the most. And we're throwing things at kids as if they're adults, and they're not. Their brains are not developed in the way that the adult brain is in order to address all of the challenges and the toxins that are being thrown at them, both in a drug manner and just in their daily environment with negative aspects of social media and so on.

Bill Glovin: What are your thoughts about legalization in terms of—I mean, really it is impossible to keep it out of the hands of young people.

Yasmin Hurd: For me, I was against legalization of cannabis because obviously I come from it from the part where we're looking at people in the hospital who have a cannabis use disorder, or comorbid psychiatric disorder that cannabis contributes a lot to. So, we come from it from a pathological point of view and yes, not everybody who uses cannabis develops a psychiatric issue. But for me, it's about safety, and we are taught that we're here to try to help people. But one of the things that legalization aspect has done is to stop the imprisonment and arrests of especially young, Black and Brown young men for possession when every race used cannabis in the same manner. So, this bias that then itself leads to brain issues and health issues by arrests and imprisonment, I think it's horrible.

Yasmin Hurd: And also, the fact that as a researcher, ironically, we couldn't get cannabis to work on as easily as someone could just go buy it on the street or just buy it anywhere. So, the legalization has definitely changed the access for research. And since it's already out there, like you said, it's tough to put that genie back into the bottle. So, for me, the legalization has to have certain parameters and boundaries. It has to clearly come with information about what the impact of that drug is on the brain, especially on the developing brain.

I think they need to have restrictions on the potency of the THC. There's no limit to what THC, and now, like I said, with plants that are no longer cannabis. People keep calling it cannabis, it's really not. It's a completely different drug.

And so, we are fooling ourselves when we... Is cannabis clinical safer than opioids? You're not going to die normally from a cannabis overdose as you can for the opioid overdose. But we just need children to understand that it's still a drug. It still can impact their brain. It can still impact the development, the full
maturity, their full potential in their lives. And that's one of the things I think that we need to do a better job of educating.

Bill Glovin: Let's switch hats for a second and talk about alcohol. Years ago when I was an editor at Rutgers Magazine, I did a feature story on the Center for Alcohol Abuse that Rutgers has, and it was very prominent. And the story was about a movement called Moderation Management, which was the idea that people did not have to stop drinking cold turkey, go to AA meetings to quit drinking. And I have to say that that was maybe one of the most controversial articles I had ever done in my career because it spurred all kinds of passionate responses about it. Many of them negative from alcoholics. And in fact, somebody who was a prominent donor threatened to pull her money out of the center that we were talking about because they were sort of open to this idea that it was possible. So, I'm wondering from where you sit, is that something you believe is possible or no?

Yasmin Hurd: I mean, is moderation possible for someone that has a substance use disorder? Yes, but it's challenging, it's challenging. And it comes back to the individual. It comes back also to the drug, to which that they have a problem with. So many people, a horrible phrase as I said, once you have this problem you have this problem for life. And so that helps a lot of people stay sober as much as possible. But I think that we have to be flexible in treatment and recognize that everyone is different. And so there are different subcategories of patients who actually can have a moderation type of approach to their "sobriety".

So, I don't think that we should just be so penalized in that one lapse and that's it, you're out of a program. That to me is the worst thing. You want to make everything inclusive and help people work towards full sobriety, but understand that depending on the person, depending on the drug that they're using, depending on where they are in their phase of their substance use disorder, that moderation may indeed be a better strategy for that time period for that person.

Bill Glovin: So, you're not closing the door on the idea that it can't work.

Yasmin Hurd: Yeah, I'm not closing the door. I think that I always say, and it's the bad answer that I say, we need research on this. And just like I said, it's going to be subgroups of people who can benefit. And so it's to identify those individuals, whether there are aspects of genetics and how the monitoring goes for such individuals. I am not closing the door because we need to have multiple alternatives to realize in substance use treatment often it's the same pathway.
for what someone... they overdose, they detox, rehab and the cycle continues. And at one point we have to start stepping back and going that there must be different roads for different individuals in that circle. And so for this particular group, this strategy might be more effective versus another strategy for another group.

So, I really think that just like in the treatment of cancers, there are many different alternatives and we need to have more alternatives to give clinicians and their patients more tools to address really very challenging disorders.

Bill Glovin: With the pandemic it's such a seesaw. It seems now the momentum is shifting again to no restrictions, but for a while, things seem to be opening up much more, you point out in the article that the lifestyle change of people being home much more. And you could have a glass of wine at 3:00 o'clock instead of waiting until 7:00 o'clock or 8:00 o'clock and that didn't help things. Do you see that maybe with the pandemic lessening, the problem of substance abuse lessens?

Yasmin Hurd: I hope so. The problem that we know is that last year we did see more people developing a problem with the substance use than we did before Covid. And so the question is, are these people since many of the people were probably in the early phase of developing this disorder, that as Covid the clutches have gone down in part, they may be going back up with Omicron, hopefully it means that they're getting early help. They're talking to their clinicians to try to start reducing their substance use, their alcohol use, their drug use and that might help. For the people who relapsed during Covid, there have been a number of programs developed for telemedicine and so on to try to decrease that isolation, group meetings now are... there a number of online group meetings that people can attend no matter where they are in the country. So as these programs expand, hopefully individuals will get... they won't be alone anymore in trying to deal with their substance use problem.

Bill Glovin: Interestingly, we have another feature in this issue of Cerebrum about telemedicine and Covid and how that's changed things. And you've addressed that also in your article in terms of it offers access to a lot more people, but then there's other people say it's not quite as effective as live and in person kind of therapies.

Yasmin Hurd: Without a doubt, you need both. So, if someone is locked up with Covid is better something than nothing.
Bill Glovin: Right. Did you have anything to do with the opening of the nation’s first two supervised treatment centers for substance abuse in New York city? And this seems similar to marijuana in the way that it sort of goes against the federal laws against drugs, but here is government trying to take action because the problem is so widespread.

Yasmin Hurd: Yeah. I didn’t have anything to do with the opening up of those centers in New York. And basically, it’s providing people with an opioid use disorder a safe haven to use their drug and to make sure their drug is safe before they use it. As I mentioned before, there’s a terrible toxin that’s put into a lot of drugs these days, fentanyl, that’s very addictive and very deadly. So, this is a safe haven. And I think that governments understand it. At the end of the day, we’re all after the same thing, the safety of the public, the safety of our citizens.

So, if you think that people dying in such large numbers is a problem, then you have to think of ways to address it. That may not have been something you would’ve done a year ago, 10 years ago, but today you’re saying, okay, we want to prevent overdoses. It also gives access to people to get treatment. So, when they’ll come in, it’s in a non-stigmatizing environment and then they can get information about what treatment might also be available. So, it’s that access as well that I think is important. So, it’s meeting the people where they are in order to then help them get to the next step to getting treatment, and hopefully not needing the drug anymore.

Bill Glovin: So, this is kind of a pilot when they’re talking about opening these kinds of centers in other cities across the country. And you would say that’s a good idea.

Yasmin Hurd: I think that any place that has this issue of all these overdose deaths and all... it’s horrible in our community. A number of places and I’m banking on the percent in Vancouver, they’ve done a really great job in protecting their citizens with a very similar program that’s been running for years. So I think that there is a foundation that’s already there, but this yes, is a pilot project in the US. And so we’ll see how it works. But I do think that it is the role of the government to try to provide safe haven for their citizens. It doesn’t matter what persona they have.

And when people come in then they can get access to treatment for people who may never have gone in. So now that’s again, meeting the people where they’re needed and providing care. Is it ideal? No, but we’re not dealing in an ideal world right now. We have to deal with practicalities, and we have to deal with how do we save people’s lives? And it comes back to sometimes just thinking
outside of the box, but it's the more you can get people to access, to come in, to access some aspect of care. It goes a long way for getting them into full treatment programs and therefore getting them to be drug-free.

Bill Glovin: In terms of your own work, what you do at the Addiction Institute in terms of research, day to day, tell us what you're working on and what is most out there in terms of what we need to still learn?

Yasmin Hurd: Oh boy, there's so much that we still need to learn. And that's why I love being a scientist in one way, even though it becomes frustrated in another because you wish that you had certain tools. In the future they'll look at us like why do we use this tool to understand more about the brain? So, there are two things I think, the research that we do that's critical for me. One, it comes back to the developing brain and it's very challenging. And as I said earlier, we now know that the Genesis of most psychiatric disorders begins during early development. Yes, though we didn't really understand the human, the neuro developing brain, a big part of our program is looking at the neurobiology, looking at what happens to the children of women who are exposed to substances in utero, for example, looking at adolescent brain development.

And I think that that's really important because the more that we can understand these neurobiological changes, the earlier we can go in for treatment intervention. Intervention is critical, but so is treatments. So the other arm of our research program comes into looking at novel strategies for treatment mentioned like CBD. We're doing clinical trials in the large populations to see who CBD might be benefiting in terms of those who have opioid use disorders and who not and trying to find the dose range and the treatment protocol. And this would be great because you're having a non-opioid treatment that can help the masses. Because since it's non-addictive, we can then have programs that are not as restrictive as we have now for programs with methadone, for example.

And also, we are looking at the human brain and how CBD may be working using neuro imaging in people who have a hair and use disorder. So I think that developing new treatments that are non-addictive, that deals with aspects of even the craving and the anxiety that leads to a long relapse. That's one of the things that our program at Sinai that we're working very hard on and it's really about translating a lot of the amount of amazing sites that we have identified into practicalities for clinicians on a day to day. And that hopefully can go across to the community. And we have programs now run by, [unintelligible 00:30:47], who's working with the school system close to Sinai. And those things are really
critical in terms of what we've learned in the clinic. How can we implement that in real life, in helping kids? So those are some of the research programs to we are running.

Bill Glovin: So that's a lot of hats you wear, for sure.

Yasmin Hurd: Yes. So, I should need a lot of CBD for sleep. I definitely need more sleep, but this is the problem. I need to start trying it on myself.

Bill Glovin: I think our listeners also would be interested in hearing your path to neuroscience and a little bit about your background, where you grew up and how you ended up in Sinai.

Yasmin Hurd: I mean, it's a long story. I was a weird kid, I always say that. I was always interested in the brain for whatever reason. I don't come from a family of physicians or scientists. I was born in Jamaica and, as I said, even there, I was just interested in why people were... why they acted in the way they did, because I wanted to know what was happening in their brain. And then I came to the US, we moved to New York, and I love New York. And I think for me--

Bill Glovin: How old were you when you made that move?

Yasmin Hurd: About 12.

Bill Glovin: Oh, wow. Okay.

Yasmin Hurd: Yeah. About 12, 11. And the thing that New York gives you possibilities, and I didn't fit into the normal box of what a science geeky kid should look like, but that's one thing. The US, it gives you opportunities that hard work, fight against the stigmas, you can actually follow your dream and you don't even realize it. So I actually went to upstate soon being to, and a professor there was really so supportive of me because I was working to make money and taking care of the animals that were being used for research. And I kept on asking all these questions and he's like, "Oh, you're asking better questions than my postdocs. Do you want to come and work in the lab?" And I couldn't, I said, I need to make money.

He organized for me to have a work study, so to work and do research and get paid for it. And that's how it got started and it's just changed my life. I would read about science, but now here I was actually doing it. I also finished my doctorate at the Karolinska Institute in Sweden, long story. And I worked at NIH
in my post-op time period. And then I went back to Sweden, was professor there and Sinai recruited me. I remember being called one evening and asked, would I be willing to move back across the pole? And because they were starting to develop a substance use research program and they wanted me to head that. So you never know life. It takes you in many different places, but I just kept on pursuing the research questions that intrigued me and just followed that path.

Bill Glovin: And that's our Cerebrum podcast. I can't thank Yasmin Hurd enough. She is just a wonderful advocate and researcher for this issue. We're very lucky to have her. Remember to check out our winter issue of Cerebrum at Dana.org. And once again, thank you very much for listening. Have a great new year and so long for now.