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STIMULANTS: FROM CAFFEINE TO COCAINE AND ECSTASY

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[video transcript]

00:08

And now I will introduce our speaker for today. So welcome again for 'Stimulants from Caffeine to Cocaine and Ecstasy.' I'm going to be introducing our speaker, Dr. Petros Levounis. So Dr. Levounis serves as Professor and Chair of the Department of Psychiatry at Rutgers New Jersey Medical School. A Phi Beta Kappa graduate of Stanford University, he studied chemistry and biophysics before receiving his medical education at Stanford, and the Medical College of Pennsylvania. He trained in Psychiatry at Columbia University, and further specialized in Addiction Psychiatry at NYU. Dr. Levounis served as Director of the Addiction Institute of New York from 2002 to 2013. And in 2017, was elected as an honorary member of the World Psychiatric Association. Dr. Levounis has published 13 books, including the textbook of Substance Dependence and Co-occurring Psychiatric Disorders, and the Pocket Guide to LGBTQ Mental Health: Understanding the Spectrum of Gender and Sexuality. His books have been translated into French, German, Hungarian, Japanese, Portuguese, and Spanish. So thank you very much Dr. Levounis for being here and taking the time today, I will turn it over to you.

01:31

Thank you so much, Emily, it's a privilege to come back to this program. And thank you very much for for inviting me. So no disclosures, and some learning objectives about intoxication withdrawal and neurobiological mechanisms, as well as treatments. Alright, the way that this, we have a three part sequence, which is fantastic. Very rarely we're given this kind of luxury to go into these drugs of abuse in some detail. So today, we're going to be covering caffeine, cocaine, and ecstasy. And then in next week, next Thursday, we're going to be delving into crystal methamphetamine and bath salts. The last session is going to be two weeks from today, it's going to be more of a clinical practicum, we're going to be talking about clinical cases. I'm going to bring up some cases myself, but I very much would like to invite the audience, for you, to bring up complex problems that you may see in your clinical practice, issues of dual diagnosis, the intersection of different drugs of abuse. And maybe I'll have some ideas that could be of help. Okay, so that's the plan. And for each particular drug, or class of drugs, we will have a general roadmap. We always start with the desirable effects. What is this drug good for? If there weren't anything good about the drug, people were not going to be using, they wouldn't go into the legal trouble and the expense and non medical consequences unless there was something good for them. And we rarely have an opportunity to understand our patient unless we start with why they're using the drug, what is the benefit to them. Then a few words about neurobiology, and I have to apologize to people who really are allergic to chemical structures and get the PTSD from organic chemistry in college classes. But I am going to be using some chemical structures, primarily because the nerd in me cannot do otherwise. But also there is some structure function correlations I would like to make. And then we're going to intoxication. What intoxication looks like, what can be done about it, if anything. Withdrawal, what it looks like, and what can be done about it, if anything. And then long term effects and treatments, what they look like, what can be done about. The major major blocks of Addiction Medicine for each class of drugs. And then we're going to close with some special topics that are unique to the particular class of drugs that we're going to be discussing.

04:43

So this general roadmap can be applied not only to stimulants, can be applied to alcohol, benzodiazepines, Cannabis, the opioids, pretty much any class of drug abuse. Okay, and maybe even to some of the behavioral addictions like gambling, sex and the internet. So let's start with the oldest stimulant in the world, as far as we know, caffeine. It got officially recognized as such in the 1400s, and not all caffeine is created equal. Here's the differential concentration of caffeine in different preparations. And you see that Starbucks is half as strong as Deathwish coffee, which is probably the the strongest one we have identified in 2021. Here it is, I have tasted, I have some at home, it is very tasteful. And I couldn't really tell the fact that it is the strongest coffee that they will have available.

06:00

All right, what are the desirable effects? Mental alertness, wakefulness. And of course, the idea that caffeine belongs into one of those psychoactive drugs that characterized as GRAS, generally considered as safe. It gives you pep, it gives you energy. You know, I drink my tea right now, which is about a third of caffeine than than coffee. And I can convince myself that it helps me give a better lecture. Who knows?

06:38

All right, in terms of neurobiology, caffeine is an adenosine antagonist. And why is that so important here? This is our first structure function correlation, this is caffeine. This is the molecular structure of caffeine, a complicated molecule. But when you compare it with adenosine, you see this is adenosine, which is a drowsiness master of the brain. This is what makes us sleepy. It's a natural, of course, nucleoside in our brains. And if you see here, this is something that looks very, very, very much like caffeine. So what happens is caffeine comes in, substitutes these moiety right here, and therefore kills the drowsiness master in the brain. It's a drowsiness master antagonist. So that is mechanism of action.

07:40

Alright, what do we have a terms of intoxication? DSM five characterized as well in excess of 250 milligrams of caffeine. If you remember, a Starbucks cup of coffee has about 20 milligrams per ounce. So it's about 20 times as much for that. It's a pretty low number, actually. And most of us would think that the well in excess of 250 probably means well in excess of 500 milligrams of caffeine, although some smaller people, some people who are more sensitive to it may get quite intoxicated at 250. What do we get? The classic things that all of us know from insomnia, diuresis, tachycardia. I love the symptom of periods of inexhaustibility. Periods of inexhaustibility, of course followed by the crash. No indication for treatment. We just ride it out.

08:45

Alright. What do we get from withdraw? The most classic one, everybody who has tried to stop drinking coffee or cutting down, knows that headaches are the sinequanone of caffeine withdrawal. But also we get the opposite of the intoxication like you would expect, fatigue, dysphoria, some kind of flu like symptoms. Very self limited, nothing to write home about, and we get over it. Okay. Again, of course, no indication for treatment.

09:25

Now, here comes some interesting things about caffeine in the long term chapter of the roadmap. As of 2021, there is no official caffeine addiction, there is no such thing as caffeine use disorder, although it does live in section three of the DSM five, which is a section for disorders that need more research before they can be elevated to a true disorder in the DSM. For people who are into nosology, remember that binge eating was one of those disorders that needed further study in the DSM four, and then the DSM five it became a full blown kind of legal diagnosis and main part of the DSM five. So stay tuned, some people feel that there is such thing as caffeine addiction, and people who have significant negative consequences from their caffeine use in terms of tachycardia. Let me have my tea help me here. In terms of arrhythmias that they may have, they need no caffeine and they still cannot stop using.

10:48

Now, I would like to introduce the idea of the differential tolerance. Most of you know about the differential tolerance in opioids. For example, people who use a lot of opioids, they get used to the analgesic properties of opioids, they get used to the euphoria of opioids much faster than they get used to the respiratory depression effect of opioids. So what very often happens is somebody keeps on popping the opioids or keeps on injecting, they don't feel particularly euphoric anymore. They don't particularly feel the analgesic effects of opioids. So they say, let me take a couple of more pills so to help my lower back pain. Meanwhile, the respiratory depression has not been subjected to a equivalent level of tolerance, they overdose, coma, and sometimes death. Very often, overdose in opioids happens because of this differential tolerance. How does this work in caffeine? Best way to think about it is the good things about caffeine and the bad things about caffeine. So unfortunately, we develop greater tolerance, faster tolerance to the good things about caffeine, the pep, the energy, the concentration, than the bad things of caffeine, which is the anxiety, the irritability, the edginess, this kind of thing, the insomnia, of course, that comes with caffeine. So if you're drinking just two cups of coffee a day, you get two cups worth of good stuff, two cups worth of bad stuff. But if you elevate and you, let's say, drink 10 cups of coffee a day, you're only going to be getting two or three cups worth of good stuff, while you're going to be getting seven or eight cups worth of the bad stuff. So the more coffee you drink, the worse the cost benefit analysis becomes for you. So people who drink a lot of coffee, if they can bring down their level of caffeine, they are very pleasantly surprised that they haven't dropped that much the energy, and the pep, and the concentration and the excitement of coffee, while at the same time they have reduced significantly the irritability, and anxiety, and insomnia due to caffeine. So that is the concept of differential tolerance. I should say here, no treatment, of course, for any kind of disorder. It's not even a disorder at this point.

14:06

Okay, let's move on to stronger stuff. 1980s we saw the emergence of cocaine. Here it is, these are packets that come from the Andean region of South America. Courtney Love once said 'cocaine is like really evil coffee.' So you can take whatever we said about coffee and amplify it, and that will probably give you cocaine. So what you get? You get the euphoria, you get the idea that you know about things, sense of mastery, something that we see of course with mania

as well, and that's why being intoxicated with cocaine is quite similar to a manic episode. You get, of course, the sexual arousal that comes with cocaine and the appetite suppression, all things that people are find very pleasurable.

15:14

In terms of the neurobiology of cocaine, this is a complicated slide here, but it really does show what's going on with cocaine. Here we have a classic neurotransmission, dopaminergic neurotransmission, this is the presynaptic neuron, there is a message coming down, there is an excitement that comes down and when it comes down, it releases dopamine, depicted here with the orange little balls into the synaptic cleft. The orange balls, the dopamine molecules, find receptors in the postsynaptic cell, they activate these receptors, and boom, they propagate the message. This is normal neurotransmission. Some of this dopamine gets recycled, right here in a reuptake system, in a transporter system. So the dopamine comes back and gets stored in these vesicles, ready to be released again. What cocaine does, depicted here in the white circles with a spike on them, the cocaine blocks the reuptake of dopamine, forcing the dopamine that exists in the synaptic cleft to stay there much longer. Thus, potentiating the downstream effect, potentiating the postsynaptic neurotransmission and therefore getting a much much more vigorous effect than the original signal intended. Of course, something that we see therapeutically with SSRIs, when we think about depression, where instead of dopamine we have serotonin molecules, and the SSRIs block the reuptake of serotonin, forcing certain stay in the synaptic cleft longer and therefore potentiating whatever message comes down the pike for the patient.

17:20

All right. Routes of administration, we all know about the the nasal insufflation. The snorting of cocaine, but that's not the only way that it gets used. We, of course, have the free base, the crack cocaine, which gets through inhalation, essentially smoked cocaine, which is very, very powerful. You can inject cocaine, although it does have vasoconstrictive effects. And very often people have little trouble with just shooting up cocaine, but it's very often showed up with heroin, and that's of course called speedballs. Oral cocaine is not quite as effective, it doesn't have as much bioavailability, but it does have some, and people use Coca Tea. Something that's quite popular again, in South America, and people chew leaves, coca leaves, as well. And they do get some high from them. Suppository use of cocaine, not quite as common outside some subpopulations who seem to be particularly prone to it, of course, you get the high right away, it's a very effective way of delivering cocaine to your system, especially the anal suppository pathway more than the vaginal one.

18:53

Okay, what do we get in intoxication? Why do we get in withdrawal? The way to remember that is that you get psychosis and seizures when you're up with the uppers. When you're intoxicated with the stimulants, you get seizures and psychosis. And you get seizures and psychosis when you're down with the downers, when you're withdrawing from sedatives, alcohol, benzodiazepines and the like. So with cocaine, of course, you get the euphoria we talked about before, but we also get a sense of hyper vigilance and suspicion and that can progress to full blown frank paranoia, at times indistinguishable from a schizophrenic exacerbation or a manic

episode with psychotic features. The decreased appetite and seizures. Cocaine lowers the seizure threshold and people become more prone to have a really significant medical condition due to seizures.

20:02

The withdrawal from cocaine is a psychological withdrawal. That's why, believe it or not, DSM one and DSM two felt that there was no such thing as addiction to cocaine, because at that time, people thought that you have to have physical manifestations of withdrawal like of course you have alcohol, the BDs, or you have with opioids with a horrible physical withdrawal syndrome. With cocaine, their withdrawal syndrome is very well described, very characteristic, but it's a psychological one, not a physiological one. The late Herb Cleaver was the first one that described the withdrawal from cocaine as a full syndrome, and then cocaine did become an addictive substance. That is, of course, very well recognized today. What do you get? The opposite of euphoria, you get dysphoria and depressed mood, the psychomotor retardation, you get increased appetite. Intoxication gave you the decreased appetite. Withdrawal will give you an increased appetite after a cocaine binge.

21:16

Now, in the long term, cocaine is a little special. Most drugs of abuse are subject to tolerance, meaning the more alcohol you use, the less the effect, or you need more alcohol in order to achieve the same level of effect. Same with opioids. Same with a lot of drugs abuse. However, cocaine is special in that people who use cocaine develop tolerance to some effects of cocaine, and they develop sensitization to other effects of cocaine. Sensitization is the opposite of tolerance. The more you use a drug, the easier it is to get an effect. So the more you use cocaine, the lower the seizure threshold, the easier it is to get a seizure episode. The more you use cocaine, the easier it is to get psychotic with tactile, auditory, visual hallucinations, and a situation indistinguishable from schizophrenia. And the stereotypical behaviors, the twitching of the eyes, the bruxism, the grinding of the teeth, these stereotypical behaviors also become subject to sensitization in people who use cocaine long term. Contrast that with tolerance, where people develop micro tolerance to cocaine, the first dose effect meaning that within the same evening, you snort a line of cocaine and you feel the cardiovascular effects, that euphoria, and so on, and then maybe half an hour later, you have another line, you feel less of cardiovascular effect, less of sense of mastery, less euphoria. And unfortunately, people think, 'oh, my God, I didn't get enough.' And they have more and more and more, and they may get actually to serious trouble with overdose from cocaine. But we do not think that you develop long term tolerance, the way that you develop long term tolerances to barbiturates, and benzodiazepines, and alcohol, and opioids, and all these drugs. Unfortunately, you also develop tolerance to the anorectic effects of cocaine. So the more you use cocaine, the less the weight loss that a lot of people desire when they use cocaine.

23:52

All right. Treatments. Treatments for cocaine, the primary treatment of cocaine is cognitive behavioral therapy. And I'm not going to teach you about cognitive behavioral therapy here, I'm sure you have, at some point, been taught about CBT. Trying to connect thoughts, behaviors, and feelings. Analyze the automaticity of thoughts, behaviors, and feelings, trying to give people

alternatives or help the patient come up with alternatives to automatic thoughts, behaviors, and feelings. What are we talking about here? It's four o'clock in the afternoon on Friday, and the cravings come in and all I can think of is using cocaine, and I go on autopilot. And I go straight to my dealers home, and I buy cocaine, and then I go home, and I use it so that the wife doesn't notice, but of course she does. Blah, blah, blah, all this automatic thing that happens from 4pm on Friday, all the way to Saturday morning when you crash after the cocaine binge of Friday night. And there's an automaticity of thoughts, behaviors, and feelings, that needs to be explicated and need to be slowed down, we call that a functional analysis. And then we help the patient create alternatives to this automaticity. The major blocks of CBT, the two parts of functional analysis that I just described, and of course, the skills building, how to distract yourself, how to cope with difficult situations, do some role playing on how to deal with your dealers and not necessarily have to say yes to everything they suggest, relaxation techniques and the like. Functional analysis, skills building, the major blocks of CBT, very, very helpful in cocaine treatment.

26:03

All this is nice and good, with the exception, that in order to enter a successful CBT treatment, the patient does need to have some significant motivation to change. CBT requires structure, requires homework, it requires commitment. And so it works well for people who are in the preparation stage of change or beyond. Action maintenance. People who live in the pre contemplation or contemplation stage of change, do not really respond to CBT quite as well. I don't know if you remember the horrible thing that we used to tell patients, 'come see me when you're ready. I've got nothing to offer to you, unless you are ready to change.' It wasn't because we're mean people. It was because we did not have the technology to actually help people who were in the pre contemplation or contemplation stage of change. If all we knew was CBT, we require the patient to have some commitment to change before we can work with them. Enter motivational interviewing. Motivational interviewing, has been a technology that really addresses this major gap in the work of CBT. It addresses people in pre contemplation, contemplation stage of change, and then it morphs more into classic CBT as you go to preparation, action, and maintenance. And all of you have been trained in motivational interviewing, I just have in front of me here one of my favorite techniques of motivational interviewing. You ask the patient on a scale from one to 10, how ready are you to change? And the patient may say something like a two or three out of 10. Classic CBT would say, okay, you are at two or three out of 10, what can I do to make you a four or a five or a six? What kind of obstacles can I remove from in front of you so that you can advance in your commitment to change? Motivational interviewing turns the whole thing to its head and says huh, you are a two to three out of 10, how come you're a 2 and not 1? Forcing the person to put the little crumbs of motivation that they have in their own words, and then capitalizing on those little discrepancies that you find in motivational interviewing between where the patient is at and where the patient would like to be, a wonderful intervention. Very helpful in stimulant use disorder, including of course, cocaine.

29:04

MAT, motivational assisted treatment, not helpful for cocaine use disorder. We keep on trying and trying and trying and we keep on finding possible subpopulations of people for whom you know, this particular medication may have some effect. And if you stand on one leg and you

squint your eyes and you look at the data again and again, you may find some pockets of promise. Very often, things fizzle out after a few months and the whole thing is put aside. I'm bringing this study for all of you, not because it was a successful study actually was an unsuccessful study, but what's fascinating to me about it is that it was a 24 week study. But if it were to stop at 12 weeks and a lot of pharmacological studies are only going on for three months, then you could convince yourself that the placebo arm, which here in the black line, was considerably worse than the medication, which in this case is the blue and the orange line. Just imagine the experiment having stopped right here, you would reasonably say 'huh, kind of promising, I can see the black line going down while I can see the blue and the orange line pretty much staying the same.' You play the tape out to 24 weeks, and you see pretty much that everything converges, and there's not really very much of a difference between placebo and medication. So be leery of studies that are short lived. Demand, expect, kind of trust studies that go for at least six months if not longer.

30:54

Alright, a word about depression and anxiety. Very often, cocaine use disorder does come with co-occurring depression and anxiety, about a third to two thirds of patients with cocaine use disorder will also suffer from depression and/or anxiety. And of course, we do use medications to treat those disorders. This is not called MAT, if you're hearing about MAT that means meditation specifically addressing the addiction, which we do not have any for cocaine use disorder. But we do use medications to treat co occurring other psychiatric disorders. Now, when I was a first year medical student out in California in 1986, we were taught that for depression we'll give antidepressants and for anxiety we will give anxiolytics like benzodiazepines. This has been completely thrown out the window. And today, for depression we give antidepressants, for anxiety we give antidepressants. If you conceptualize depression is being preoccupation about the past, and anxiety as being preoccupation about the future, both of them seem to share a common underlying mechanism. They both include and involve the serotonin system. And they both seem to be responding to similar medications, namely the antidepressants, SSRIs, SNRIs, bupropion, mirtazapine, our main fare of medications in 2021.

32:40

Alright, a couple of special topics about cocaine, this trafficking route that hasn't changed very much in the past 10 years. As I mentioned before, primarily coming out of the Andean region of South America. This is one way of bringing cocaine into the country. If you see here, people have swallowed these condoms, this condom packets filled with cocaine, they ingest them on the flight into the other country, and then they pass them and transport the cocaine. These are called mules. And there is a wonderful, wonderful movie called Maria Full of Grace. Grace is also a nickname for cocaine and heroin at times. So the greatest part is kind of a little leaf in that part, but it's a wonderful, wonderful movie about this practice. Interestingly, when these packets burst, on occasion of course, they burst and you would expect that the person would die on the spot because of the huge amount of cocaine released in the GI tract. Interestingly, surprisingly, some of them die, but the majority of them live. And the reason is that as we mentioned before, cocaine does not have such good oral and GI bioavailability, you do need to snort it, or you need to use the suppository, or you need to inject it, you will not get as much by eating it.

34:23

And fast forward to today's day. The major issue that we see with cocaine has been the introduction of fentanyl. Fentanyl is found itself in a lot of cocaine preparations, as well as crystal methamphetamine as we're gonna see next week. So when you see somebody with an overdose from cocaine, not a bad idea to give them some Naloxone for the potential that this cocaine was mixed with fentanyl and there's not much you can do about the cocaine, you can just offer supportive treatment to the patient. But there's a lot that we can do about the fentanyl, we can certainly reverse it with doubling the dose of Naloxone that we're used to.

35:18

Alright. And finally, a few words about ecstasy. Methylenedioxy-methamphetamine. Here are the pills, they very often have funny kind of inscriptions on them to make them particularly attractive to the younger generation, up close and personal. There's another saying about methylenedioxy-methamphetamine, 'freshmen love it, sophomores like it, juniors are ambivalent, and seniors are afraid.' This reflects the neurobiology of ecstasy, in that ecstasy floods the brain with serotonin. And at earliest stages, a person gets a lot of serotonin and they get all the nice effects of ecstasy. But as you progress in your ecstasy use disorder, then you deplete your serotonin stores in your brain. And then you end up with a deficiency in serotonin, which is a pretty horrific state to be, very much akin to depression and panic disorder, and you end up with seniors being afraid.

36:32

So how to think about ecstasy, you think about it as half an attenuated form of cocaine, and half an attenuated form of LSD. Yes, you get high with ecstasy, but not nearly as high as you would with a cocaine. And you do get some perceptual disturbances with ecstasy, akin to LSD, but you don't really see things on the wall or hear music and sound. It's just that the whole world is a notch up, everything looks more beautiful, the sounds are more interesting, the smells are more pungent, the colors are more colorful, that kind of life. The main effect of ecstasy is not really an ecstatic one it's more of an empathic one. People who are high on ecstasy report feelings of love and affection. I love you, you love me, we're all in it together. This is a wonderful world, we're all family, this kind of sweetness. And it was used in the past in psychotherapy, the idea there being that highly, highly obsessive people are just so wound up that they cannot really do the transference neurosis and the work of psychotherapy, and you know, love their therapist, and use that kind of love to help them love other people outside, that kind of idea. You would give them a little bit of ecstasy before the session, they would loosen up their obsessiveness, they would come to a session and be able to relate much more closely with a therapist, and therefore do the work of psychotherapy and use that to improve their lives on the outside. Not a bad idea in terms of efficacy. And a lot of studies, as you probably know, are using now ecstasy for the treatment of PTSD, especially the VA system. And we're not there yet, but there's some really, really promising results in this in these studies. The main problem is the issue of toxicity, at what level is ecstasy non toxic, so that we can actually use the beneficial effects and not suffer the neurotoxic effects of ecstasy.

39:00

Alright, here's the molecule. Sorry for that for people who get PTSD from chemical structures. It's a methylene, this methylene moiety right here. Methylene dioxy, the two oxygens, methamphetamine. This part here is methamphetamine. And as we're going to see next week, when we talk about crystal methamphetamine, this is a structure of crystal methamphetamine, an aromatic ring, a phenyl ring, separated from a nitrogen by two carbons. Every time you see an aromatic ring separated from an amino group by two carbons, this may very, very well have psychotropic properties. So here it is methylenedioxy-methamphetamine, the official name of ecstasy, and I just want you to compare it with methamphetamine, which is the prototype as I mentioned before, just this molecule without the methylene dioxy part on the left.

40:03

Alright, something we've talked already beforehand that it increases serotonin at earlier stages, blocking the reuptake, releasing neurotransmitter in the synaptic cleft. But then it chronically decreases serotonin levels, by depleting the serotonin stores, inhibiting the senses of new serotonin, and people end up with a depression of the serotonin system. But the most interesting part here is the neurotoxicity due to ecstasy. Look what happens here. On the left, we have neurons that are normal. And they're beautifully arranged in the cortex in a columnar fashion, one next to the other, one next to the other, one next to the other. People use ecstasy, and they kill those axon terminals, the obliterate axon terminals. And then in the long run, some of these axon terminals regenerate, but they regenerate in a dendritic fashion, like trees, that they are not quite as effective as the original, very columnar, tall and slim and skinny axons that we have in the normal brain. And that's the problem with ecstasy. I showed that to a patient of mine we used a lot of ecstasy, happened to be a gay man, a young gay man, who told me the following, he said, 'Doug, I grew up in a highly homophobic environment. And actually, I welcome the ability to rearrange some of my neurons in a more creative, more imaginative way than what I was brought that was very, very strict.' I appreciate the analogy, I appreciate the imagery. But let me tell you, rearranging your neurons in the way that it's shown here on the third panel is nothing good for our brains. And that's exactly the focus of the research on ecstasy in 2021, how are we going to find a dosing schedule that is not going to subject people to this kind of neurotoxicity?

42:21

Alright, just to be faithful to our own roadmap, what do we get with intoxication. We do get diarrhea, sometimes called disco dump, because we use of course a lot as a party drug, as a club drug. Bruxism, I mentioned before the grinding of the teeth, of course, the stimulant effect of the wakefulness, the endurance, the energy, the good stuff about cocaine, but we see some of those in ecstasy as well. But you do get the serotonin syndrome, and that can be lethal. Serotonin syndrome very often happens for people who combine ecstasy with cocaine, and they get too much serotonin in their brain, or they use ecstasy in the context of dehydration. They don't have enough to drink, they bump their serotonin level way up, and they end up having a serotonin syndrome, which can be a medical emergency. Essentially, you go into hyperthermia, your fever goes way, way up, and you need to cool the patient down. You hydrate them, you cool them with cooling blankets, you drug sedate them so that you don't have any kind of movement. And we do not use beta blockers like we used to do in the past. That's for people who may be doing emergency medicine. Just remember that part.

43:53

In terms of withdrawal, very much what we expected. We expected to have anything like we expect to have the reverse of the excitement and the mood and the love and affection, you have a depressed mood, anhedonia, you feel miserable, you feel fatigued. Rarely would see frank suicidality with ecstasy withdrawal, what we mostly see is a co occurring major depressive disorder with an excess use disorder and that can very well lead in to suicidality. But ecstasy alone very rarely would give you suicidality. No invitation for treatment, we observe the patient, make sure that they are safe, and then we discharge them from the hospital.

44:41

And finally, the long term effects of ecstasy not very well described for many reasons. Number one, the majority of people who use ecstasy also use a bunch of other drugs of abuse. Very rarely you will have somebody who just uses ecstasy. They may use ketamine, GhB, cocaine, alcohol. So you never know what's up, what's down. But the second reason is that you would have to wait a long time to see these long term effects. Very few studies would ever wait that long to see what happens 20 years down the line. All this being said, panic disorder seems to be the one that's mostly associated as a long term effect of ecstasy use, you get all these other things that you see in front of you, but panic disorder would be the one to remember, if you remember one long term effect of ecstasy. No medications, we use our good all of the psychotherapeutic modalities as I described for cocaine, and they have been very successful in ecstasy use disorder as well. Alright, and with that, I think we still have 10 minutes for q&a. But I think Emily has a few things to say before we close. So go ahead, Emily, should I go the next slide?

46:02

Yeah, perfect. Thank you very much, Dr. Levounis, that was a great presentation. So these are just a few points that I wanted to make for everyone that joined today, we have a new Drug User Health podcast called Any Positive Change that our Medical Director Linda Wong is host for. So I will send out information about that in the follow up email, you can go to the next slide. The picture didn't come up, but we have a new Buprenorphine Clinical Card that just got approved. And I'll send all this information in the follow up email as well, because I definitely want to make sure there's time for questions, because we've got quite a bit of questions. I'm not sure if we'll be able to get to them all. And then you could go on. That's okay. And this is just the CEI line. I'm sure everyone already has seen this flyer multiple times before, it's on about every one of our webinar ending slides. So if you ever have a question about HIV, PEP, PrEP, sexual health, HCV, or Drug User Health, feel free to call that line and we can answer any clinical questions you might have. And now we will get to all of the questions. Great. So the first one was, is there any treatment for cocaine use?

47:24

Yes, yes, yes, I'm sure if I didn't be more specific about that. We're talking about whenever we think about treatment of addiction, we think in three major buckets, medications, psychotherapy and counseling, and 12 step programs. So treatments for cocaine, nothing of the medication side, we do not have any medications for cocaine, but we have very successful psychotherapy

and counseling, primarily CBT, cognitive behavioral therapy and motivational interviewing. The major blocks of treatment for cocaine use disorder. The 12 step programs for cocaine have been quite successful as well, not as much evidence based as alcohol. Alcoholics Anonymous have been very, very well studied, and we certainly recommend that as a robust intervention for the treatment of alcohol use disorder. And I personally feel that Cocaine Anonymous is a very good way to go, but the evidence is not quite as high as it is with Alcoholics Anonymous. Major treatment for cocaine use disorder, CBT and motivational interviewing, and contingency management. But I'm going to spend more time on contingency management next week, when talk about crystal methamphetamine, but also contingency management.

48:39

Thank you. All right. The next question was 'hello, I was wondering if you could explain how stimulants work to treat disorders like ADHD?'

48:51

Different situations. I mean, the amphetamines and methylphenidate, the other amphetamines that we have for the treatment of ADHD. But the dosing is very different than the crystal methamphetamine that we're gonna be talking about next week. The route of administration is quite different when you just have an oral pill, instead of shooting it up or smoking it. And the context is different between let's say crystal methamphetamine and when we use ADHD for the treatment of a medical disorder. So there are significant differences between how people take the medication as prescribed for the treatment of medical disorder and recreational use. This being said, you can very, very well get addicted to medications for ADHD as well. They have clinical indication in the same way that opioids have clinical indications and benzodiazapines have clinical indication, but people can very well get addicted to them.

49:50

Thank you. Alright, another question. And for the people, there's a lot of questions. So I don't think we're going to be able to get to all of them within this next 10 minutes. So if there's any questions afterwards, I can always connect with email after, if that's alright with you, I'll email you the questions and then you could connect and answer the questions afterwards. Alright, so the next question is 'in the rehab setting a common complaint is insomnia. Do you think it is important to eliminate caffeine as an available substance within the rehabilitation setting? Otherwise, we are in the position of dealing with sedating medications which are not evidence based being given to patients simply to sedate them? Quetiapine being the prime offender.

50:39

I couldn't agree more with you that quetiapine is the major offender, it's an anti psychotic medication, does not have the indication for insomnia, should not be used in insomnia. I know a lot of patients love it. Even at lower doses of just 50 milligrams of quetiapine, not a very good idea. So what do we do for insomnia in rehabilitation centers. Obviously, sleep hygiene, we teach our patients sleep hygiene. We use CBT for insomnia, which also helps. And if we're forced to use a medication, what we do is we first of all, if a patient's already on an antidepressant, instead of using an activating antidepressants, like for example, sertraline, we're going to use a sedating antidepressant, for example, paroxetine. So we change the

psychopharmacology if the patient has a co occurring psychiatric disorder to be able to help them with their sleep. The other thing that some people believe in, I am almost there myself is the Z drugs. The Z drugs, I'm talking about zolpidem, zaleplon, and zopiclone with the commercial names of Ambien, Sonata, Lunesta, and things of that sort, they may have a lower addictive potential than benzodiazepines at lower doses. So what I'm talking about is zolpidem, Ambien, at five milligrams, maybe 10 milligrams a day, because they seem like they have a receptor specificity that just helps with insomnia without necessarily having that much of an addictive potential. This has been studied in animals, we're not so sure if it's the same thing for humans, but what seems to be the case that if you elevate the dose, if you go to 15 milligrams of zolpidem, or 20 milligrams a day, then most likely they flood all kinds of different receptors and they end up behaving very much like benzodiazepines. Not 100% sure about what all this is all about. But if you have to use a benzodiazepine, or if you have to use a sleeping agent, perhaps the Z drugs are a better choice. Caffeine, go with a decaf. A lot of decaf has placebo properties to it. The patients will know it's decaf, but their tolerance after a while, we're talking about an inpatient rehabilitation is going to go so low that even the minuet amount of caffeine in the decaf coffee will probably do the trick.

53:08

Thank you alright, this one's a long one. The first step to drug use relapse is the relapse of irrational thought patterns and addictive thinking, b&w thinking, all or nothing, rationalization, etc. Because this happens before the addict begins using drugs again, in this case, specifically cocaine, the addict frequently doesn't recognize the slide back into addictive thought patterns and behavior. How do we prepare people in recovery to expect and recognize the mental shift and recognize it as the first step to relapse? The inability to recognize the same old thoughts and rationalizations, behaviors returned before the user actually uses the drug is a major barrier to catching flood before use resumes. The thought pattern and behaviors are as harmful as the actual drug use to their recovery.

54:08

Very, very good points there. Good counseling, good psychotherapy of the CBT kind does address all these behaviors before the patient relapses. The seemingly irrelevant decisions that we're very often talking about in cognitive behavioral therapy are so helpful in unpacking these behaviors, thoughts, and feelings before the person relapses. Two things that are particularly helpful here. One is group psychotherapy. The smartest psychiatrist, the smartest counselor can be duped by a patient. A group of peers has a little bit more resistance to this kind of duping, so group psychotherapy is particularly helpful for what you're talking about. And of course 12 step program. 12 step programs have great tradition and expertise and technology in addressing these pre use changes. I mean, basically, you know, you show up in a 12 step program meeting and a mutual help program, really, and the people go like, 'Whoa, I can see the nails started looking like the nails that you had when you were thinking and drugging, and the hair, and the attitude and the behaviors,' and they can really call you on these things and help you go back to your sobriety. Absolutely.

55:28

I think there was a follow up question to the previous question about stopping caffeine use completely in rehab. They said they're still wondering if you recommend to stop caffeine completely in rehab. I know you spoke about decaf.

55:40

I worked in rehab for 10 years, when I was at the Addiction Institute of New York. There are just so many things that you can end up spending tremendous amounts of energy, fighting with a patient's about minutiae of this and this and that and giving people the option of caf versus decaf. And then having a stratification of status of 'I am a patient who has the badge that I can actually drink real coffee, and you are one of those people who cannot drink coffee,' simplify the whole thing and just use decaf. That was my solution back then, when I was the Director of the Addiction Institute in New York. I don't there are any double blind, placebo controlled trials that can guide us as to what to do exactly with coffee in inpatient settings, but I would go with a decaf option. It does have some caffeine in it decaf, it's not completely decaf. Let's remember that. Mark Gold from Florida started this in great detail.

56:43

Here to close us out, and I just want to thank you, Dr. Levounis for a great presentation.

[End]