

Neurobiology - Levounis (With CME)

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SUMMARY KEYWORDS

addiction, part, insula, people, brain, patients, frontal lobes, pathways, neurotransmitters, cravings, person, cognitive behavioral therapy, dopaminergic, cortex, limbic system, give, somatic, forces, nucleus accumbens, opioid

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This presentation is entitled neurobiology of addiction, key concepts and models. I will now turn it over to Dr. Petros Levounis to begin our presentation.

 00:10

Hello, everyone. First of all, thank you for having me here and giving this talk on the neurobiology of addiction, key concepts and models. I have no financial disclosures. And the key objective is to identify the major neurotransmitters and brain pathways that are involved in the addictive process as we understand them, in 2023. The way we're gonna go about that is first talk about neurotransmitters, then the fundamental model of how we understand addiction, then add to it three novel concepts, before we conclude with some ideas about treatments and how they relate to the neurobiology of addiction.

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So, let's start with neurotransmitters. Neurotransmitters, a favorite topic for people who write exam questions. And here it is, you need to memorize this table. And there's no way to really explain much of it. It is just an association between substances that people use and have significant addictive potential, and their counterpart in the endogenous system, endogenous neurotransmitters and how the substances mimic the work of the endogenous neurotransmitters. This is it. Only one slide for this section, I have no other words of wisdom, other than to say that you just need to memorize this table. Okay. And also have to say that, as you go through the course, and different presenters talk about opioids or talk about alcohol, they will be making more of this association with the endogenous neurotransmitters. The other thing I forgot to say is that if you have any comments, or any thoughts, or any questions, please type them in the chat function of this course. And we'll we'll go through them.

 02:20

Well, let's start with the fundamental model. Up until 1980 or so people thought that addiction was a boring failure. The weaklings of the world that people could not resist the temptations of drugs and

alcohol would be the ones who would succumb to addiction. And somewhere around 1980 science came around, medicine came around said no, no, no, no. Addiction is a chronic relapsing illness, very much like diabetes and hypertension and depression. And the true causes of addiction are these biopsychosocial forces. It's a prototypical biopsychosocial illness, biological forces, primarily genetics. If both your parents had alcohol use disorder, you have a much, much higher chance of the general public to have an alcohol use disorder yourself. Psychological forces, people don't do drugs just to get high people also do drugs, in order to self medicate. The self medication hypothesis of addiction that says, people don't do drugs in order to escape, people do drugs in order to arrive. It's not that people feel normal, and they want to jump to an outside world. People feel alienated, people feel depressed, anxious, and they use the drugs in order to normalize the classic premise of the self medication hypothesis at the core of our psychological understanding of addiction.

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These being said, there are also situations where people do drugs in order to get high. So appreciate both sides of this psychological side of addiction. And finally, social forces, the micro environments, the subcultures, the neighborhoods, within which we all live and love and play and work that contribute to the addiction. So when these three forces, the biopsychosocial forces come together in a particularly complex and nightmarish fashion, they change something in the brain. They flip the brain switch on. And from that point, the addiction tends to have a life of its own, to a very large extent, independent of the forces that set it in motion to begin with. And you say that again. We have this biopsychosocial forces, vulnerabilities, risk factors. And when they come together, and they flip the brain switch on, the addiction tends to stay on for a long, long time, if not, for the rest of the person's life.

 05:05

Don't take me wrong here. I'm not saying that people with addiction do not recover. In fact, the majority of people who at some point in their lives met criteria for a substance use disorder or a behavioral addiction will end up beating the disorder. But the vulnerability to go back to using stays with you for a long, long time, if not for the rest of your life. Model for model- that's what we use. That's how we see addiction. Very helpful in clinical practice.

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But taken to the extreme, it has a major flaw. It suggests that in the absence of significant biopsychosocial factors, the risk of addiction is negligible. What I'm saying here is not just theoretical, it's exactly what we find at the core, or the root cause of the opioid disaster. What you have in front of you is one of the most frequently cited pieces of medical literature. It's not an article, it's a letter to the editor, 10 and a half lines, 10 and a half of the most damaging lines in all of medicine. Why? Because it gave us a ratio. And it said that if you don't have a particularly strong vulnerability due to genetics, psychological factors or social factors, your risk of addiction to opioids is 12,000 to four, now infamous Porter and Jick ratio of 12,000 to four. Of course, this has been discredited, has been put aside, but the damage has been done. Generations of physicians have grown up believing that if you don't have significant biological, psychological, or social vulnerabilities, then there's nothing to fear, you can prescribe, prescribe, prescribe, opioids and the ratio of addiction will be 12,000 to four. And

that's why we have added use of the drug itself, the very molecules entering your body as an additional independent force, that along with biopsychosocial vulnerabilities can very well trigger and flip the brain switch on. And that's a more complete model of addiction as we see today, today.

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Alright, let's try to unpack the brain switch- what's going on in there. All of us have these wonderful pleasure-reward pathways in our brains.

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They live at the basal ganglia, they hover around the nucleus accumbens.

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They are dopaminergic systems, and they essentially scan the world at all times for things that are pleasurable, rewarding and salient- important to us. Imagine your very own dopamine level at the nucleus accumbens this very moment, Nothing too good is happening, nothing too bad is happening is around 100%. If you had an amazing meal right now, chances are that your dopamine level of a nucleus accumbens would jump to about 150% of its baseline. Sex does twice the job of food and jumps the dopamine level of the nucleus accumbens to about 200% of its baseline. Now, out of 30 million chemicals that we have identified in all of the universe, there are only about 250 or so that have this particular ability to go exactly at the very same centers in the brain and activate them as a limbic system, the pleasure-reward pathways of the brain in a way very, very similar to food and sex. They go above that- usual jumped the dopamine levels to 250. In the case of cocaine, 300% of its baseline. And essentially, from a neurobiological perspective, addiction is the hijacking of the pleasure-reward pathways of the brain. These days, we feel that the behavioral addictions things like gambling, and sex and the Internet, most likely run through very, very similar pathways in the brain.

 09:31

Alright, right. Far, far away from this whole kind of situation that happens in the more primitive part of the brain are the frontal lobes. And the frontal lobes are responsible for obstruction, executive function, planning, rational thinking. They're the most civilized part of our existence. Fortunately, or unfortunately, the frontal lobes are not very well-connected to the more primitive parts of the brain.

 10:05

The basal ganglia, very closely related to the hippocampus, the memory center of the brain, and the limbic system, the emotional center of the brain, are the ones that they're particularly responsible for the permanence of the hijacked pleasure reward pathways of the brain. So, as I was saying before, the frontal lobes are not very well connected to this more primitive apparatus, this more limbic system-driven apparatus. And before, before the age of 22, we feel that not even the hardware is fully developed between the frontal lobes and the limbic system. The cables, the neurons may not be fully developed between the frontal lobes and the limbic system. That's how we start to understand

the adolescent, the adolescent who falls in love, and fails to see the light at the end of the tunnel is not so much, because they don't have fully developed frontal lobes. This is part of it. But most importantly, they lack the connection between the frontal lobes and the limbic system, and the ability to modulate an explosive limbic function.

 11:17

Now, this is something that persists in adulthood in one way or another. And in some ways, it's not all bad news. How do we start to understand the appreciation of the arts or sporting events or music, unless you have the ability to- or even having sex, unless we can isolate the effects of the frontal lobes from the more primitive activity of the brain. It's so nice and good, until somebody gets addicted to either a substance or behavior, at which point the one agency that will have that it can keep the brakes on the more primitive part of the brain is not all that available to us because of this disconnect that I just described.

 12:05

Ultimately, the war on drugs from a neurobiological perspective is a war between the hijacked pleasure reward pathways of the brain that scream "I want, I want, I want; I need, I need, I need" and the frontal lobes that try to keep the person safe. When the hijacked pleasure reward pathways win, the person relapses; when the frontal lobes win, the person is in recovery. This is the fundamental two-part equation of addiction. And when you have a person who lives with an addiction in front of you, you may want to visualize in your hand, in your head, how strong are their hijacked pleasure reward pathways of their brains? Versus how strong are the frontal lobes that try to keep them safe. Once again, when the hijacked pleasure reward pathways win, the person relapses; when the frontal lobes win, the person is in recovery.

 13:06

Alright, this is pretty much how we understand addiction in 2023. But we have also included three novel concepts to the fundamental idea of the neurobiology of addiction. It has to do with motivation, the circuitry, and the reward pathways, and the concept of interoception. And I'm going to spend a few minutes in each one of them and try to make sense of them. All right. The way that I presented the the model up until now is if the substances or the behaviors come in, hijack the pleasure reward pathways of the brain, and they leave the frontal lobes to fend for themselves. As it turns out, we rather recently have identified motivational circuitry, especially on the medial orbitofrontal cortex, that is, in fact, affected by substances and behaviors. And they give you a false sense of rational thinking. Narcotics Anonymous have talked about the stinking thinking of addiction many, many years before neurobiology caught up with things. And this is part of the medial orbitofrontal cortex function that gives you this false sense of rational thinking. A lot of the work that we do in addiction treatment with seemingly irrelevant decisions have to do, has to do with this faulty, rational thinking of part of the frontal lobes, especially in the medial orbitofrontal cortex. Of course, as you can anticipate, motivational interviewing, can very well do a great work with this kind of faulty motivations.

 15:01

All right, the second part has to do with the anti-reward pathways and the extended amygdala. This is a complicated slide here. And perhaps the most difficult one to explain. But this is a very, very active area of research in the 2020s. In blue, you have the classic hijacked pleasure reward pathways of the brain, the dopaminergic system and the basal ganglia. In green, you have the prefrontal cortex and this visually represents the two parts of the, of the war, the neurobiological war that I described before. There's a third part and that has to do with the extended amygdala that involves the hippocampus with the memories, the limbic system, with emotions, and a number of other things that are becoming more and more evident to us.

 15:53

In this particular work by George Koob genetics, epigenetics, childhood trauma, psychiatric comorbidities, that give the person this ongoing hyperkatifeia as he calls this ongoing sense of discomfort, which is the work of the anti reward pathways of the brain. Not very well understood, still a work in progress, but let me try to demonstrate it if I can, with a little game that we're gonna play. Let's play the games. And we'll put them together in a second. Okay, so just trust me here. We'll play the games, and then we will, we'll see how they have to do with what they have to do with addiction.

 16:39

Alright. Game number- there are two games- Game Number one, I give you a choice. Either a sure gain of 250 bucks for you to keep no questions asked. Or you have to gamble, option B, you have to gamble. And if you decide to gamble, you have 25% chance of gaining \$1,000, 75% chance of gaining nothing.

 17:07

Let it sit for a second. All right. And if you are like most people, you probably went for the sure gain of 250. About 84% of the people went for the sure thing; 16% went for the gambling. Tversky and Kahneman, both, both psychologists ended up getting the Nobel Prize in Economics, because they showed with this kind of brain distortions, if you can use them in a particular economic fashion, you can end up you know, making millions.

 17:42

Alright, let's erase this game from our heads like it didn't happen. And let's play a completely completely different game. Alright, Game Two, I give you two options. Option A, you give me 750 bucks, write a little check for me to cash. Option B, you have to gamble. And if you decide to gamble, you have 25% chance of losing nothing and 75% chance of losing \$1,000 Let it sit for a second. All right. If you're like most people, you will probably go for the gambling part and not for the sure loss.

 18:24

All right, what happened here? When it came to the game one you and most people are very risk averse. And they want to make sure that they're going to actually keep this little pellet of fun. When

you visualized, or when you thought of having this 250 bucks, for sure, there was a little bit of a dopaminergic uptick at your nucleus accumbens, and you will do everything you can to safeguard that little uptick of pleasure of the 250 bucks.

 19:03

Game two played with a very, very different part of your brain, the anti reward pathways of the brain. And it seems like when it went to that, that kind of giving me 750 bucks, I hope that you felt the discomfort and the annoyance and the irritability, and the anxiety and the the hyperkatifeia that George Koob describes are having to give me 750 bucks. And when it comes to this activation of the anti reward pathways, then you will do anything under the sun to avoid that definite pain, including of course gambling. Now, there's a psychology, psychology trumps probability. Because if you were to play these games over and over and over again, you wouldn't make or lose any money. They're completely money neutral.

 20:01

All right. Well, actually, let me just say how, how directly that that applies to addiction. As it turns out, what seems to happen is that in the earlier parts of a person's trajectory into addiction, the dopaminergic upticks of the reward system, mask, whatever downticks you may have, depicting the activation of the anti reward pathways of the brain. But as the addiction progresses and consolidates at the nucleus accumbens, the dopaminergic upticks of the reward systems become less and less and less prominent. And the downticks of the anti reward pathways keep on becoming more and more and more prominent. As it turns out, addiction morphs from a pursuit of excitation, pleasure and reward, to essentially a desperate attempt to avoid definite pain.

 21:11

The patient who comes to my office and says, Doc, I save, save save all week. So I can go out on Friday night and buy as much cocaine as I can. So I can feel at home... has very little to do with any kind of dopaminergic optics and everything to do with the activation of the anti reward pathways of the brain that are have given the person this chronic sense of discomfort, and dysphoria and irritability, and annoyance and hyperkatifeia, and then that person will really take great risks in order to avoid that definite pain.

 21:50

As I mentioned before this is work in progress. But perhaps one of the most fruitful parts of the neurobiology of addiction, because of course, it ties very well to lots of other areas of great interest having to do with trauma, adverse childhood experiences, epigenetics, and so on.

 22:13

Alright, finally, the third part, the ultimate gatekeeper of the insula. The insula that sits in between the inner and outer parts of our brains, is responsible for interoception. Interoception is a sense very much like taste and touch and smell and vision. It's an integrative sense that takes all kinds of

much like taste and touch, and, and smell, and vision. It's an integrative sense, that takes all kinds of somatic signals, and decides which ones have meaning and which ones do not have meaning. What am I talking about? Yeah, the room is too hot, the room is too cold, I have a little pain on my leg, I have a fleeting sexual thought, I have a craving for cigarettes, if you're a cigarette smoker, all these things are somatic signals. Now they are sent, they come to the insula, through the concept of interception, through the sense of interception, the insula decides which ones have meaning and which ones do not.

 23:16

I would like to demonstrate that concept of interception with a little exercise, the last exercise, trust me, so you know, we have the games and this the exercise, when I say so you're gonna get up from wherever you are, probably you're sitting down somewhere. And for 10 seconds, I would like you to survey your body from the very, very top of your head all the way down to your feet. For somatic signals. The idea there is that, hopefully, for the past, I don't know, 25 minutes or so, your insula had been ignoring all kinds of other somatic signals in favor of the neurobiology of addiction in favor of the lecture you're just being presented with. But when you have this 10 seconds, when you're not going to be hearing me talk or you're going to not going to think about anything else, just saving your body for somatic signals, then these somatic signals will come alive. All right. Let's try to close your eyes as well, just so that it's just simply somatic sensations that you're going to be saving. So I'll get up as well. All right. So get up and close your eyes.

 24:41

Alright, you can open your eyes and you can sit down. Alright. So I hope that some of you at least appreciated some somatic signals that were new. Actually they were not new. They have been there for... it's highly unlikely that all of the sudden you realize that you have to go to the bathroom. We just saw- that that has been building up. But when you had no other- nothing else, to compete with that kind of somatic sensation, then boom, it was given meaning and was given experience. That is the work of interoception. And that happens at the level of the insula.

 25:19

A way to think about addiction is that you have the persons the person who is afflicted by a substance use disorder or behavioral addiction. And you have all these forces battling it out in their brains, you have the hijacked pleasure reward pathways of the brain, you have the hippocampus with the memories, you have the limbic system with the emotions, you have the the medial orbitofrontal cortex with a faulty sense of rationality, you have a lateral part, which is actually the one that is your friend, the one that really is trying to keep you safe. You have the anti reward pathways of the brain with a with a concept of hyperkatifeia all these things battling it out to see whether the person is going to use or not use a particular substance. But at the very end, all these forces, they have to ascend at the insula. It's the insula's responsibility to say these have meaning versus those that do not have meaning.

 26:17

One of the most powerful studies in all of Addiction Medicine, was the work of Nasir Naqvi, that

showed that heavy heavy heavy smokers who have a stroke at the insula and survive the stroke, emerge on the other side, and a lot of them do not have any cravings for cigarettes. What an amazing finding. I mean, a lot of people quit smoking after catastrophic events like heart attacks and strokes, but not even having cravings for cigarettes. The way we understand that is that if you have a stroke at the insula, all these cravings that you have for cigarettes, they're there. The pleasure reward pathways have been hijacked, and the whole machinery of addiction is in place. But at the very, very last minute, when that kind of craving has to go through the insula through the concept of interoception. The insula is not available to give it meaning. And that's why the person does not experience a particular craving for cigarettes.

 27:19

You can start imagining how this will have therapeutic implications. And I'll get that in a moment. We're not suggesting psychosurgery. Nobody's suggesting going in there and obliterating anybody's insula. But we may have ways of tricking the insula into ignoring cravings. We do that through mindfulness. It's kind of a preview of what's coming.

 27:45

All right. Let's go into treatments. First Wave psychoanalysis, all the way back in the 1950s, 1960s... All we could offer was analysis- put the person on the couch and hope for the best. Absolute disaster. It did not work. It actually made people more anxious- made people worse. Why did psychoanalysis not work for addiction? Well, think about it. Psychoanalysis does its best job by shrinking the frontal lobes. That's why we're called shrinks. We're shrinking the frontal lobes, and we allow the more primitive parts of the brain to take over. We'll give people permission to break some rules. Go out there, have some fun and be happier. For particularly obsessive people, that is pretty straightforward. We kind of shrink all the do's and don'ts of life. And we allow the more visceral part of our humanity to see the light of the day.

 28:51

If you tell an addicted person, that's what I want to do with you. I want to shrink your frontal lobe so it can allow the more primitive part to take over they're going to look at you as if you have three heads. I mean, if anything, the task is exactly the opposite- is to beef those frontal lobes especially the lateral part of the orbitofrontal cortex, so that you can keep the beast at bay. This failure of psychoanalysis to treat addiction actually had pretty sinister results in that gave people the false idea that addiction has no treatment. If you have one and only one treatment, and that treatment does not work, then you make the conclusion that your illness is untreatable. Of course in 2023, nothing would be further from- the farther from the from the truth. But the failure of psychoanalysis to treat addiction still has stayed with parts of the population that believe that addiction is not treatable.

 29:53

All right. Second wave- the bootcamps- started in California with a synanon model: let's lock them up, break down those defenses, confront the denial, slap them around, sometimes physically, in order to rebuild the person from scratch. Terrible idea. It was put aside, it was a failure through and through.

Very few people survived the whole treatment. And even for among those who survived the treatment, we're not quite sure, that they were in better shape after the the synanon experience than before.

 30:39

And that brings us to today's treatment where we have safe and effective interventions for addiction. And they can be conceptualized in three major parts: medications, psychotherapy and counseling, and mutual help- the three parts of safe and effective interventions for addiction in 2023.

 31:04

I want to spend a little time on each one of those before we conclude. First of all: medications. The classic two strategies of medications psychopharmacotherapy of addiction is the following. On one hand, there is an agonist strategy. Let me give you a molecule that's going to mimic the substance of use and activate the receptor in a way very, very, very similar to that substance so that your cravings come down. The nicotine patch, the gum for tobacco use disorder, methadone for opioid use disorder, classic examples of an agonist strategy in the pharmacotherapy of addiction.

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The other end of the spectrum, you have an antagonist strategy- let me give you a molecule that's going to block the receptors. So you're going to try to shoot up while you're on, let's say naltrexone, for opioid use disorder, a classic antagonist of the mu opioid receptor, you try to shut up, nothing happens. You say this, too much money, too much trouble, too much legal exposure, and you stop using.

 32:17

And then rather recently, you have the introduction of a third strategy. Something that's a little bit of both- are actually a lot of both: partial agonists varenicline, for tobacco use disorder, buprenorphine, for opioid use disorder, that actually gives you somewhat of a shield that blocks the receptors. But at the same time, they activate the receptor at the 40% level, and therefore cuts down the cravings. A wonderful intervention for primarily tobacco use disorder and opioid use disorder that has really revolutionized the pharmacotherapy of addiction.

 33:08

All right, finally, mutual help, naturally will have the psychotherapy and counseling still developed. In terms of mutual help,

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this is an older study from Bellevue Hospital, where I trained in my talentos group, and in that

particular study, we asked medical staff to rank 11 things that are most important in people's recovery. And as you see here on the left hand side: housing, government, medical services on top of the list. Inner peace, God, spirituality and AAA at the bottom of the list. And then we ask patients to rank those 11 things that are most important for the recovery. And a very, very different picture emerged, where inner peace and God and AA were very high up on the list, and then job and government and housing people at the bottom of the list. So very different value systems, between what the medical staff believe and what patients believe is most important for recovery.

 34:16

And then

 34:16

Lisa Goldfarb had the amazing idea of going back and asking the medical staff the following question: what do you think patients think is most important for the recovery? And if you see on the right hand side here, once again, housing and outpatient services on the top of the list, God, spirituality, at the bottom of the list. So not only we live on a very different page than our patients, who don't even have a clue what that page is, that our patients live in. A huge disconnect between the medical staff and our patients. Bottom line here, our patients respect AA much more than medical staff in general and we owe it to our patients to recommend and support 12 Step mutual help engagement of our patients, which of course, as you know, has helped millions of people across the globe.

 35:15

All right. And finally, in terms of psychotherapy and counseling, the cornerstone of psychotherapy and counseling is cognitive behavioral therapy. You're gonna hear much more about cognitive behavioral therapy, we connect thoughts, behaviors and feelings. We identify automatic thoughts, behaviors and feelings. And we try to find alternatives to that to that automaticity that our patients experience. Of course, we have added motivational interviewing as a powerful way of augmenting cognitive behavioral therapy, especially for patients who live in the pre contemplation or contemplation stage of change.

 36:01

You may remember, way back, or you may not remember, but we used to say or medicine used to say to patients, come see me when you're ready, I've got nothing to offer to you unless you are ready to change. And that's not because doctors were mean people. It's just because we did not have the technology to really address patients who had very little motivation to change. Cognitive behavioral therapy, as wonderful as it is, it does require some motivation. It's a lot of homework, a lot of structure, a lot of tables to fill. And so you need to have some motivation to meaningfully engage in, in cognitive behavioral therapy. Enter motivational interviewing, and motivational interviewing really can work with people with very little interest in changing anything in their lives. And once again, you're going to hear much more about motivational interviewing. Later on.

36:59

These days, we'll have taken this a step further. And we now can work with even with patients who do not come to see us at all. We work with families, and loved ones, in order to get the particular identified patient to eventually get motivated enough to come to see us. We have added to this model here, mindfulness and mindfulness exercises. As promised before, these are ways of tricking the insula into giving us a little time, so that the person can ride the wave of the craving. What I'm saying here is through mindfulness exercises, we can actually get the person to sharpen their observing ego, tricking the insula, allowing for the cravings to have a beginning and a middle and an end. So that the person does not use. We haven't crossed all our T's and dotted all our I's yet, in terms of mindfulness, but it seems like a very promising area for the treatment of addiction. Here it is, in some ways you can think about mindfulness as working at that very, very small interface right before the hijacked pleasure reward pathways of the brain are about to overwhelm the frontal lobes, and in that very, very, very small space there, if we buy some time with mindfulness exercises, who can keep the person safe.

38:30

All right. Another direction we're going in these days is the digital therapeutics and CBT apps, again, we haven't crossed all our T's and dotted all our I's yet, so we cannot fully recommend them. But they seem to have a lot of promise, they can very much help with the structure that I mentioned, that CBT requires. And a lot of research is directed into this digital therapeutics, I'm talking about the CBT apps, primarily. We don't feel that that advertisement that you do your CBT app, and you won't need a clinician whatsoever, are very solid or sound, but there may be certainly a place for them in the treatment of addiction.

39:24

And this is my last slide here. That perhaps we'll have a renewed appreciation for psychodynamic psychotherapy- good old Freudian style psychotherapy- for some of our patients, at least. So here is a complicated slide. But it shows on the left is for women, on the right is for men, and it shows substance use disorders as a function of sexual attraction, not so much sexual identity or sexual behavior but sexual attraction- more of a, an inner way of feeling along a Kinsey scale, whether you're entirely attracted to people of the opposite sex, or of the same sex or somewhere in between. And again, let's- let's focus on the left side of this diagram, the shape of the curve is very similar to the one on the right. So what we have on the left is in light blue, we have fully gay. In orange, we have fully straight. In dark blue, we have bisexual. And here we'll have this very interesting areas of people who are almost gay, but not entirely. And right here, people who are almost straight, but not entirely. And it seems like for people who live in those areas, they may be at the highest risk of substance use disorders and perhaps psychodynamically-oriented psychotherapy does a great job in working with people's inner motives may actually work to reduce the stress in their lives. And, by extension, help them with substance use disorders. Again, it's not something that we are fully confident to support at this point. But this is something that we're working on.

41:21

And with that, I want to thank you very, very much. But before doing that before, thank you very much, once again, a plug for neurotransmitters, this identical slide to what you saw in the beginning, just make sure that you recognize this table before you take the course. And now with that, I just want

just make sure that you memorize this table before you take the exam. And now with that, I just want to summarize what we've talked about in this five areas of Addiction Medicine, of the neurobiology of addiction medicine.

 41:51

In the most basic fashion. In the most basic fashion, we can think about the neurobiology of addiction as having two major parts, the hijacking of the pleasure reward pathways of the brain at the basal ganglia, as contrasted to the frontal lobes and the attempt of the frontal lobes to keep the person safe.

 42:18

We've added three novel concepts to the fundamental neurobiological understanding of addiction motivational circuitry, the anti reward pathways of the brain, and the concept of interoception. In terms of treatments, on the pharmacology- on the pharmacotherapy of addiction will have agonist antagonist and partial agonists and in terms of the psychosocial treatments of addiction we have mutual help, going to behavioral therapy, motivational interviewing, and the emerging area of mindfulness. And once again, I know you're, you've heard me say it enough times now. Know your neurotransmitters.

 43:00

Alright. Alright, so let's check the knowledge now that you have acquired from this lecture. Three questions. First one, at her tenth college reunion, Anna bumps into Marie, her old roommate from her junior year abroad. "Anna," Marie exclaims, "Do you remember sipping wine and snacking on brie and crackers at the cafe by the Seine? That waiter, Jack, mon dieu."

 43:25

Anna has been sober for several years, but suddenly feels an intense craving for alcohol. What part of Anna's brain was most likely activated by Jack, the hot waiter, just now? A- the medial orbitofrontal cortex. B- the lateral orbitofrontal cortex. C- the hippocampus and extended amygdala? Or D- the insula?

 43:46

Have you read it once again. On her tenth college reunion, Anna bumps into Marie, her old roommate from their junior year abroad. "Anna," Marie exclaims, "Do you remember sipping wine and snacking on bread and crackers at the cafe by the Seine, and that waiter, Jack, mon dieu?" Anna has been sober for several years but suddenly feels an intense craving for alcohol. What part of Anna's brain was most likely get activated by Jack, the hot waiter just now. The medial orbitofrontal cortex, the lateral orbitofrontal cortex, the hippocampus and extended amygdala or the insula.

 44:17

And the answer here is the hippocampus and extended amygdala. Clearly this was a memory so that is part of the hippocampus. But also more than a memory, it's more of a visceral limbic system excitement with Jack. This whole apparatus of the more primitive part of the brain that surrounds the nucleus accumbens gets activated and brought Anna all the way back to where she was when she was actually drinking alcohol. And that may very well be responsible for the intense craving that she just experienced.

 44:54

Alright, second question. Robert has been addicted to Candy Crush Saga since high school. He must also study for the ABPM boards on Friday. It's now 10pm on Thursday evening, and hasn't started looking at the lectures. Hmm, he thinks to himself. If I get some Swedish fish to grab some candies, I can reach Lollipop Meadow by midnight, which will give me such a sense of accomplishment that I will have a clear head tomorrow to tackle any question. Perfect plan- to Lollipop Meadow it is. What part of Roberts brain was activated by Lollipop Meadow? Was it the medial orbitofrontal cortex, the lateral prefrontal cortex, the hippocampus and extended amygdala, or the insula.

 45:33

Let me read once again. Robert has been addicted to Candy Crush Saga since high school. He must also study for the ABPM boards of Friday. It's now 10pm on Thursday evening, and he hasn't started looking at the lectures. He thinks for himself, if I get some Swedish fish to grab some candies, I can reach Lollipop Meadow by midnight, which will give me such a sense of accomplishment, I will have the clear head tomorrow to tackle any question. Perfect plan- to Lolipop Meadow it is. What part of Roberts brain was activated by Lollipop Meadow: the medial orbitofrontal cortex, the lateral orbitofrontal cortex, the hippocampus and extended amygdala, or the insula?

 46:10


Well, what I tried to portray here

 46:12

is the stinking thinking of addiction. That part of the medial orbitofrontal cortex. The correct answer is A. It's that faulty motivation that actually can get people in trouble.

 46:27

Alright, and final question, which part of the brain is responsible for integrating, giving meaning and helping people understand sensations such as hot, cold, hungry, full and thirsty, along with cravings for a drug such as tobacco? The medial orbitofrontal cortex, the lateral orbitofrontal cortex, the hippocampus and extended amygdala or the insula?

 46:48

Let me read it again. Which part of the brain is responsible for integrating, giving meaning and helping people understand sensations such as hot, cold, hungry, full and thirsty, along with cravings for a drug such as tobacco? It's the medial orbitofrontal cortex, the lateral orbitofrontal cortex, the hippocampus and extended amygdala or the insula?

 47:09

And the answer here is D, the insula, this is pretty much the definition of interoception. That special sense that integrates somatic sensations. And with that, wanted to thank you very, very, very much. Thank you for spending the last 45 minutes with me here, and all the best. Good luck with the exam if you're taking the exam. All right. Bye bye now.