# Other Classes of Drugs - Levesque

Fri, Jul 21, 2023 10:34AM 30:45

**SUMMARY KEYWORDS**

hallucinogens, people, substance, drugs, experience, pcp, steroid, symptoms, effect, patients, lsd, nmda receptor, treatment, mdma, delirium, sedatives, receptor, significant, sensory, group

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00:00

This presentation is entitled Other Classes of Drugs: Pharmacology and Epidemiology. I will now turn it over to Dr. Annie Levesque to begin our presentation

00:10

Hi, everyone. My name is Angela Annie Levesque, I work at Mount Sinai West Hospital in New York City.

00:16

I have no financial disclosure. This is the learning objective for today. And today I will be talking about other classes of drugs. Before we begin the presentation, I just want to remind everyone to feel free to ask any questions during the presentation. Just write them into the chat and I will get to them as soon as I can.

00:43

So as I mentioned, I will be talking about other classes of drugs. So it's a group of substances that is very diverse. It includes substances that don't really fit into bigger categories. So they are substances that we don't see as frequently in our clinical practice. So I think it's really important that we talk about it today. It's a lot easier to recognize, recognize the common drugs that we hear about frequently that we see in clinic regularly, but substances in this group still can have a significant impact on our patients. But they may be much more difficult to recognize, especially if we don't know what we're looking for.

01:23

So there are four classes of drugs that we will talk about today: hallucinogens, dissociatives, inhalants, and anabolic-androgenic steroids.

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This gives us a sense of the prevalence of some some of the substances that we will talk about today. Surprisingly past year use of hallucinogens is much more common than than drugs that we hear more about, like cocaine or sedative hypnotics. On the other hand, if you look at the bottom of this list, inhalants are less commonly used.

02:02

This is something to keep in mind to know the neurotransmitters that are implicated and the different classes of drugs. There is some overlap but for the most part, when we talk about stimulants, the main neurotransmitters that are involved are dopamine and norepinephrine. For sedatives, it is GABA, which is the brake of the nervous system. The main neurotransmitter involved in hallucinogens is serotonin, which as we know also plays a major role in the world of depression and anxiety treatment. And when it comes to dissociatives, and inhalants, the main neurotransmitters are glutamate and NMDA.

02:42

We will be starting with hallucinogens and we will begin with a question. So I will read the question and then you will have some time to vote on your computer. LSD and psilocybin are: A- serotonin 5HT-2A receptor agonists, B- dopamine transporter reuptake inhibitors, C- NMDA receptor antagonists, or D- opioid mu-receptor agonists? So again, serotonin 5HT-2A receptor agonists, dopamine transporter reuptake inhibitors, NMDA receptor antagonists, or opioid mu-receptor agonists?

03:30

So if you picked A, you're correct, serotonin is the main neurotransmitter involved in hallucinogenic effects. It's a class of drugs that produce alterations in thought mood and perception. They also produce minimal autonomic side effects and very little craving. So it's much more of a sensory experience than it is a physical one. The drugs in this class don't cause much sedation or central stimulation. So you're not going to see significant changes in blood pressure, heart rate, and people are not going to seem as impaired as they would with drugs like sedatives or alcohol.

04:14

Some people suggested that a better term for hallucinogens would be illusionogen. Because when we think about the definition of the words, hallucination describes a perception in the absence of a stimuli, whereas illusions is a- an alteration or an enhancement of an existing sensory perception. So hallucinogen is seeing something that's not there. And illusion is more like misinterpreting a cue. So for example, there is a shadow there, but I think it's a person. So hallucinogens are much more likely to produce illusions, which is possibly a more accurate term.

04:58

04:58

Interestingly, with hallucinogens, reality testing is usually intact. So that means that individuals are able to realize that the experience they're having is a result of a substance use rather than believing that it's a real perception. Another interesting element is that the quality of the experience changes a lot depending on the context in which people use. So a low simulation environment or environment that feel safe and protected helps people to have a more positive experience rather than something more frightening or a stressful experience.

05:34

As we talked about earlier, hallucinogens work in activation of the 5HT-2A serotonin receptors. Classical hallucinogens fall within the group of chemical compounds that is called arylalkylamines, which also includes other substances that bind the same receptors but are not all hallucinogens. So there are members of this class that will act more like stimulants or and pathogens like ecstasy or MDMA. So those are not hallucinogens, but they still go in the same receptor and share the same same or similar chemical properties.

06:12

When using hallucinogens, people can have different experiences. They can see altered shapes and colors, they can experience synesthesia, which is like a crossing of sensory stream. So people will say things like they can see music or they can taste colors. People can also have some positive or negative mood alterations, as we saw earlier, depending a lot on the- on the context in which they use. There can be an alteration in the sense of time, where, for example, people will feel like no time at all, has past when it's actually been many hours.

06:49

I'm mentioned that somatic effects are not predominant, but there still can be some, and one of the most significant would be nausea and vomiting. And that is particularly common with hallucinogens like ayahuasca.

07:04

So now we're going to talk about some of the different types of hallucinogens in more details starting with DMT, which is often used in research on hallucinogens. This is a naturally occurring substance. It's found in some plants, and it's even found in the secretions of certain kinds of toads. So some people actually lick toads to feel intoxicated. It has a very rapid onset in less than five minutes and a short duration of action. It's most commonly used by inhalation, but it can also be injected. It can be taken orally, but in order to be processed and to be active, it needs to be taken in combination with an MAO inhibitor.

07:49

Now ayahuasca is a combination drug. It's consumed as a tea that contains different types of hallucinogens with DMT, and a MAO inhibitor, because as we saw in the last slide, DMT is not active o-

hallucinogens with DMT, and a MAO inhibitor, because as we saw in the last slide, DMT is not active o- orally unless it's taken with MAO inhibitor. It's used in certain religions, and it's also used by people we're seeking a spiritual journey. So you often hear about patients who want to do an ayahuasca retreat, traveled to South America in the pursuit of that sort of spiritual journey. There can be significant vomiting with ayahuasca.

08:29

Psilocybin is a naturally occurring substance that is found in a certain type of mushrooms. It can cause a detachment from reality that can sometimes leads to panic attack or psychosis. So the reality testing is not as intact with psilocybin as it is with other hallucinogens. There is a rapid tolerance to the effect of psilocybin and interestingly, there was a cross tolerance with LSD. So if people use this drug with regularity, they may be able to tolerate tolerate the effect a little better over time and they also tolerate the effects of LSD a little better. The effect lasts a lot longer than with the hallucinogens that we talked about earlier, so up to four to six hours.

09:17

LSD is probably the most known hallucinogen. It is water soluble, clear white, odorless crystal. It can come in different forms. It can come as a thin blotter paper where solution of LSD is dropped onto it and dried. It can come in the form of mints, sugar cubes. It can be pressed into pills or come as gelatin squares. As the image shows, different makers of LSD will put different figures of- or colors to identify their batch of drugs. It has a onset of action of about 30 to 60 minutes and then it peaks at two to four hours, and the effect is very long it can last eight to 12 hours. So, if people have in a negative experience they need to sit with it much longer.

10:12

Mescaline or peyote comes from a cactus. The buttons or the top of the plants are removed from the cactus and dried, and then people chew it or they can also be soaked in water and people can drink the water. So the term peyote refers to the cactus, and the term mescaline is the drug. But the terms are often used interchangeably to talk about the drug. It takes about six to 10 buttons for intoxication. There is a slow onset of action of about 30 to 60 minutes and then during the first hour, people will feel some minor perceptual changes. We'll see increase in respiratory rate, some nausea, and then over the next five to 10 hours there is an onset of visual illusions, hallucinations, synesthesia and others- other symptoms.

11:05

DOM is a chemical modification to mescaline-like substances. It's extremely potent. It is often used as a model of hallucinogens in drug discrimination studies, but it is not widely used recreationally, so we don't see it very commonly in clinical practice.

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MDA is the parent drug that can be modified into MDMA. So MDMA, which is also known as ecstasy.

This is a substance that has both stimulant and hallucinogenic effects. It can produce an effect that can be somewhat similar to combining cocaine and LSD. And like MDMA, it also has some empathogenic effects, which- which is like the sense of feeling connected to others or understanding others. It's sometimes sold as MDMA, but it has more of an hallucinogenic effect than MDMA does.

12:04

Salvia is a beautiful plant that grows naturally in the US. It is legal, some of you may have it in your garden. It can be ingested by chewing, or drinking a juice made of it. It can also be smoked. The main active ingredient is salvinorin, which is a kappa opioid agonist. The effect of salvia is very intense and short lived. So it comes up very quickly, under a minute, and then it lasts for about 30 minutes.

12:36

Okay, so just to summarize, as we talked about, hallucinogens, we see a clear sensorium, intact memory. People are hyperalert so very different from sedated. We see intact reality testing. For the most part, people can be reasoned with or calmed by talking with them. Visual hallucinations are much more common compared with auditory hallucinations.

13:05

People sometimes talk about flashbacks from the experience. So the real name for that is "hallucinogen persisting perception disorder", so HPPD. This is when someone re-experiences perceptual symptoms that were experienced while intoxicated after the user stopped.

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It is not related to the dose or the number of exposures, and it's usually resolved within one to two years after the last use- which is actually pretty long and can be quite scary for some people. It can be triggered by other substance use. So a patient with past hallucinogen use now uses marijuana, and it feels as though they are using hallucinogens again.

13:49

Moving on to the next class of drugs, which is dissociatives. And again, we will begin with a question. So again, I will read the question and you can vote on your computer: PCP and ketamine are: serotonin 5HT-2A receptor agonists, dopamine transporter reuptake inhibitors, NMDA receptor antagonists or opioid mu-receptor agonists?

14:19

So, again, A- serotonin 5HT-2A receptor agonists, B- dopamine transporter reuptake inhibitors, C- NMDA receptor antagonists, or D- opioid mu-receptor agonists?

14:33

The answer is C. So PCP and ketamine are NMDA receptor antagonists. And by definition, the dissociatives are all NMDA receptor antagonists. So these are the most complicated of all the substances we'll talk about today in terms of mechanism of action and neurotransmitters. Glutamate activates NMDA receptors, and it helps filter sensory stimuli, and when you take a dissociative, there is a noncompetitive block of the NMDA receptors. So you basically shut off the ability to filter sensory stimuli. So the outcome is a sensory overflow, and the body responds by dissociating. So rather than stopping the sensory input like one may think it does, it actually floods the sensory system. And the response is shutting down and dissociating from being able to process all that sensory input.

15:30

Members of this class include PCP, ketamine, also dextromethorphan, which is a widely available and over the counter cough suppressant, and also nitrous oxide, which we'll talk about more in the inhaling group.

15:47

The- the effect of this class of drugs are a dissociation: so, sensory isolation, mental distortion... Again, just like for hallucinogens, most of the effects is usually sensory, but you can also see some somatic effects like increase of heart rate, blood pressure and temperature.

16:09

So let's start start with PCP, which was developed as an IV anesthetic. It is no longer FDA approved. It is now a schedule one substance, and the reason for that is that there was an association with a prolonged delirium after it was used as an anaesthetic. And there is also a risk of seizure and and even that's from PCP use. So now it is not used medically anymore.

16:36

The effect of this- of PCP varies depending on the dose. So you can go from confusion, delirium, or psychosis all the way up to coma or even seizure, which is more rare but can happen at a higher dose. PCP intoxication mimics the symptom of psychosis. So it can cause the positive symptoms of psychosis like delusion or hallucination, and it can also cause negative symptoms like a blunted effect and being asocial.

17:06

We can see different kinds of nystagmus on physical exam, so horizontal, vertical, and even rotary, which is more rare. We can also see hyperreflexia, high blood pressure... People often present with a feeling of invulnerability. And when it comes to treatment, we really talk about keeping people in a

low-stimulus environment, maybe administer sedatives as needed and really wait for the effect of PCP to wear off.

17:39

Now ketamine. It's a substance that has an indication for anesthesia in humans. It's a schedule three medication. And when we use it in a medical setting, we usually use it either IV, IM, or as a topical agent. When it is used as a substance of abuse, we- people usually use it by inhalation smoking, or they administer it orally. It's less potent and shorter acting than PCP.

18:08

So it can cause a spacey feeling that people call K-hole. And then it can also cause amnesia, and even delirium at higher doses. On physical examination, we can also see a nystagmus just like we could see with PCP, but only the vertical and horizontal kind. It can also be associated with some pretty significant kidney complications. And I believe it will be discussed in some other sessions a little more in depth.

18:41

Now dextromethorphan is what I really want to talk about today, because many of us may have it in our pharmacy cabinet. It's the DM and Robitussin DM, it's also in NyQuil, and it can be bought as a single product for cough suppression. The recommended dose is 10 to 20 milligrams every four hours for a maximum dose of 120 milligrams a day. And there is quite a low toxicity.

19:08

And so we'll start seeing symptoms of dissociation or PCP-like symptoms with a dose of 300 milligram or more. So basically, people can start feeling intoxicated with the equivalent of about a single bottle of pills. So it makes it a particularly high risk substance for kids because it's available over the counter.

19:33

Another thing to keep in mind is that dextromethorphan has significant serotoninergic properties. So it increases serotonin synthesis and release and it also decreases its reuptake. So something to keep in mind with our patients who're on SSRIs treatment. There has been cases of deaths that were reported too with larger doses like more than 200 times the recommended dose.

20:02

Now we are going to talk about inhalants. And once again, we will start with a question. So, many abused inhalants produce an intoxication that closely resembles which of the following: alcohol, cocaine, cannabis or LSD- so you can vote. Again, the answers are: alcohol, cocaine, cannabis or LSD?

20:31

So the answer is A- most inhalants produce a rapid high that resembles alcohol intoxication. So the initial symptoms will be excitation and then people will experience drowsiness, disinhibition, lightheadedness, and even agitation. They are breathable chemicals. So this picture shows many articles that you may even have at home. So they don't- all those articles could be used as inhalants. They're everywhere. So there were household products, cooking supplies, office supplies, styling products. They- they have different names: Whippets, poppers, and many other names. So this is just a partial list of sorts of inhalants and what chemicals they contain.

21:19

So as I said, Why are they available. So this is some terminology you should know about when it comes to inhalants. So first, "sniffing" is just taking a container and smelling it. "Huffing" is taking a fabric that is soaked with a substance and then, or that was sprayed with a substance, and using it to inhale the substance. And then "bagging" is spraying into a bag to concentrate the vapors and then inhaling into the bag. So the person on the picture is bagging.

21:54

When you look at the age distribution, it is much more of an adolescent syndrome. So the most common age group is the 12 to 17 age group. And then we see, we really see, a decrease as people get older. So most people seem to have an experience when they will try it as adolescence and eventually let it go. But for those who continue using, chronic use really has a neg- some negative long term consequences.

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Inhalants have a high abuse potential, especially for adolescents because they're cheap, they're available. And it's also very difficult to test for it. You have to do some specialized testing. They don't come up on our regular panels. They don't come up with a regular immunoassay.

22:43

They're also perceived as low risk. So adolescents often don't think of it as using drugs the same way they would about... like smoking a joint or using stimulants or things like that. So if you do adolescent medicine, inquire about inhalant use, specifically. They may not think that they're doing anything problematic. So you can really provide the kids and the parents with education about the consequences of use.

23:11

They are highly lipophilic. So they're rapidly absorbed through the lungs and then quickly cross the blood brain barrier. And because they're lipophilic, they can accumulate in the brain and the liver and

blood brain barrier. And because they're lipophilic, they can accumulate in the brain and the liver and the fatty tissue, and then they continue to be released for some time after the person stopped using. There is a rapid onset, a short duration, so that leads to many, many episodes of use throughout the day. And there can be a synergic effect with alcohol or benzos.

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Acutely, the effects are euphoria, disinhibition, dizziness, slurred speech, ataxia... So as I mentioned earlier, very similar to alcohol intoxication. Use can also lead to toxic effects and even overdose in some cases, so respiratory depression, arrhythmia, asphyxia, and even cardiac arrest and that's... so certainly not as benign as as some people may think.

24:13

They are very damageable for different systems of the body when they are used repeatedly so they can cause arrhythmia, cardiomyopathy, skin problems, hepatorenal syndrome, rhabdomyolysis.

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Pulmonary, GU, hematologic consequences can happen. We can see neuro problems like peripheral neuropathy, delirium, dementia, cerebellar atrophy and even some irreversible whi- white matter changes. So you can actually see dementia and white matter atrophy at ages like 30s or 40s for people who use when they were young and used repeatedly.

24:53

And because as I mentioned, there is an accumulation in the fatty tissues, patients can experience a prolonged withdrawal effects. Many of us who do full time addiction medicine, we don't have a lot of experience treating inhalants, because it's relatively rare and patients also don't- are less likely to seek treatment for it. Also, treatment is very difficult in this group. So there can be some profound neurological impairments, and they may be irreversible. So it's an indicator to assess for the cognition at baseline and reassess cognition throughout the course of treatment. And patients may not do well in group therapy or individual therapy, because they may have shorter attention span or poor impulse cont- impulse control, sometimes poor social skills as a result of their use of inhalants. And unfortunately, there's also no medication that's approved for the treatment of this condition.

25:54

Now, the final group that we will talk about today is androgenic-anabolic steroids. So let's- let's break down those two words. So anabolic refers to skeletal muscle building and androgenic means masculinizing. They include testosterone and more than 100 related compounds. They are a schedule three medication so they can be prescribed legally for hypogonadism.

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When they're misused, people often take them for an enhancement of their physical appearance or for to improve their performance. They are often taken 10 to 100 times the intended dose.

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So there are three main groups of users. First, there are people who want to improve their performance in a sport. There are those who want to improve their physical appearance, so we are talking often about adolescents in that case. And then finally, those who want to increase their aggression or their job performance. So we're talking about law enforcement or security officers.

27:03

There's a lot of side effects from steroid use. So acne, liver damage, some significant hypercholesterolemia. There can be complications at the site of injection. Some people will develop aggressive or violent behaviors. And you can see some significant psychiatric symptoms like hypomania, mania, paranoia, or extreme irritability that can develop from repeated steroid use. When people develop that kind of psychiatric symptoms, we can use mood stabilisers or anti-psychotic to treat some of those symptoms. But really the main treatment is to stop using steroids and wait for it to wear off. And usually for someone who's psychiatrically healthy, the symptoms will go away within one or two weeks.

27:53

The side effects are different between genders. So in women, we'll see masculinizing features, deepening of the voice, facial hair, menstrual changes, male-pattern baldness and genital hypertrophy. And then for men, you can see testicular atrophy, prostatic hypertrophy, gynecomastia, baldness, and even infertility.

28:20

Steroid withdrawal-associated depression can occur when people stop using steroids. It's a relatively new, newly discovered phenomenon. There have been some cases of people having pretty severe clinical depression and even suicide in that period of steroid withdrawal. The patients can be responsive to SSRIs. So that could be a treatment option if there is enough symptoms. There was also a high rate of comorbid substance use disorder in this group, especially opioids. And that's because of people in this group may tend to work out a lot or have very physical jobs. And there's a lot of physical injuries. So people are more likely to use opioids for that- for that reason.

29:07

You can also see a body dysmorphic disorder, especially in men who may have the feeling of being too small or not musc- muscular enough. Again, more common in adolescent populations in that case.

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One thing that is quite unique is in this group when you compare to other substances is that there's no immediate euphoric effect to the substance, so people don't feel high from it. They don't use it for a direct rewarding effect. It's rather used for long-term reward that is associated with the long-term physical changes. So so people using steroids are rarely involved in treatment.

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And it's also often socially acceptable or seen as positive. People will get positive feedback. They'll be like, people will say, "Oh, it's great. You're working out. You're, you're taking care of your body." So they are not likely to see it as a negative thing. We often find out about steroid use because of medical complications. So things like high cholesterol or liver problems will come up and then we'll realize that it comes from steroid use, so they are much less likely to seek direct addiction treatment.

30:20

So, in summary, these four classes of drugs that we've seen, they're a very diverse group of substances that we don't see very frequently in clinical practice, but very important to familiarize yourself with them because we need to be able to recognize them. They can have a big impact on our patients. This concludes my talk for today. Thank you all for listening.