

TITLE: Opioid Addiction as an Attachment Disorder: Part II

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Interviewer: Hello and welcome to today's webinar, Opioid Addiction as an Attachment Disorder: Part II. This webinar is paid for by Newport Healthcare. Newport Healthcare is the national leader in teen and young adult behavioral health treatment, providing sustainable healing for mental health and co-occurring disorders. Some important points before we get started, APA does not endorse any products or services. The content was created by Newport Healthcare and does not reflect the views of APA or its editorial staff. Email advertising@apa.org, if you would like to learn more.

Next, this program does not offer CE, however, we will email everyone watching live today a certificate of attendance. Certificates will only be issued to those who watch for a minimum of 45 minutes. A recording of this presentation will be emailed to everyone in about two weeks' time. That email will also include a copy of the presentation slides. During our time together, you will be on mute. You can communicate with us using the Q&A box located on your webinar screen. If you have a question for our presenters, we ask that you type them in using that same Q&A box on your webinar screen.

We will also provide a link to the presentation slides in the chat box. If you miss them, don't worry, we will email them to you along with the recording. With that, I would like to introduce today's presenter, Dr. Michael Roeske. He is a senior director at Newport Healthcare Center for Research and Innovation. Since 2003, he has worked and studied in a variety of treatment settings, including adult substance use disorder and adolescent mental health programs, community-based psychological services, and inpatient psychiatric hospitals. He is trained as a full battery assessor of children to older adults and has functioned as a supervisor, clinical director, educator, presenter, and operator. Welcome, Dr. Roeske.

Dr. Michael Roeske: Thank you. I appreciate the time with everybody today. This is part II, so everybody take out your notes from part I. Just kidding, of course, this is a standalone. We'll cover the basic parts of the first presentation and then we'll get into some additional parts. The first part really talked about explanation for the origin of the opioid epidemic and really using two discrete, but in my view, interrelated lenses of, with respect to socio and circular changes in United States that have left us maybe more disconnected.

Then attachment theory, and particularly I think called the brain opioid theory of social attachment, which says that when we're socially isolated, our base of opioid levels go down. Then when we get social stimulation, it goes up. Then we'll cover into some additional topics such as the role of medications in treatment of opioid use disorders, the ideas around trauma, early stress, genetics, and epigenetics in the origins of opioid disorders, how we think about things like chronic pain, and then the role of social factors, and particularly the absence of social factors in research around this topic.

In the last, in part I, I offered implications for treatment as well. To give an example of that, you'll hear people, especially in early recovery, talk about their relationship to

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opioids as if it's an actual person, as a relationship that has been lost. I found it often quite useful to use basic principles of grief counseling. For example, one of them might be honoring the positives so if you've ever been in a bad relationship yourself and got out of it, and then had friends come up to you and say, "Well, hey, I'm really glad that you're no longer in that relationship. That person was never good for you. They had all these particular faults." You'll notice that your mind automatically went to the opposite.

Well, you immediately either say this out loud or to yourself, well they really weren't that bad. You didn't get to know them. It's an important thing to do when you're working with somebody with opioid use disorder, that special general recovery. I'll do that as we go through the different segments here, offer similar implications for treatment. Let's start at the beginning. Back in 1978, there was a group of researchers who had a theory about their relationship between social aspect in the brain opioid system based upon the strong resemblance between people with close social relationships and narcotic addicts.

What they did was they gave rat pups, small doses of an opioid and removed them from their mother, and measured what's called distress vocalizations. The idea was that these distress vocalizations were essentially an attachment alarm because of vulnerability when they're so young that they need to stay connected. That this crying out was a way to stay in proximity to the person elected the person know. They found that increased and in fact went down and they came to the conclusion that functionally administration of morphine to young puppies simulates the presence of the mother.

In 2004 in a similar but a different line of research, there was two neuroscientists who noticed that languages seemed to share an overlap between social and physical pain. Things like, you hurt my feelings, you broke my heart. There also is a, or certainly back then as well, a mounting evidence of human neuroimaging and animal lesion studies to suggest that social and physical pain shared some similar underlying neural pathways and essentially borrowed potentially from the opioid system to create this sort of attachment system.

They concluded that basically a lot of these things are the same and it really isn't even social isolation that really even produces that. It can be exclusion, it can be rejection, both of those things so it can produce pain in an individual. Then probably the best review of BOTSA was written in 2011. The authors of this recognize that it still relies upon rodent studies and obviously rodents are different in terms of pair-bonding than humans. They're more sensory stimuli and environmentally controlled with the things around them versus the higher taxa of mammal like primates we're much more cognitive and metacognitive.

That person said this particular thing to me. Should I set that back? Are they interested in me? That type of thing. They ultimately concluded that not only did BOTSA was supported by the research, it actually seemed more central to the higher taxa of mammal-like primates than it did in the lower ones. Even beyond that, it was interesting. They also concluded that oxytocin was very important for onset of relationships but they felt that the brain opioid system actually was more important

when you think about pair-bonding over the lifetime which, of course, mammals was more likely to do.

Also because we're dependent upon caretakers or parents for a much longer period of time let's say a rat. I have a eight-year-old son and if a large house cat could take him out, he's not going to be able to take care of himself for a long period of time. Mammals are particularly susceptible for long periods of time. Then more recent research suggests that it's not necessarily even just social stimuli that does this but really has to do with the salience of the social target and around the proximity the closeness so that it's close others if it's a romantic partner, if it's a parent, a child, a close friend, close coworker, those are the people that really are impacted or impact us in terms of our basal opioid levels.

Now, we'll get into a group of questions or assumptions that I've gotten over the years either from patients or students or supervisees, or maybe these are questions that I've asked colleagues or colleagues have asked me. The first one is an assumption that genetics offers an explanation as to why some and not others end up with a compulsion to use substances. Even beyond that why a smaller subset within that particular group ends up with a chronic relapsing condition that we typically know as addiction?

Basically what we tend to think is that yes, that's generally the case. I do want to provide a little caveat here that even within it is really only a small percentage of recreational opioid users that end up with a compulsion to use or addiction. I think there's like a 2016 Volkow and McLellan article that go again a little further, suggesting that it's not only a small percentage but even people with preexisting vulnerabilities. It's relatively infrequent that people end up with addiction. The reason I bring that up is I do think that we've probably over-corrected a bit in our view of the dangerousness of opioids.

Certainly, we can point through something like Purdue Pharma and say, "Look, they had reprehensible marketing and business strategy. They weren't honest in terms of the safety profile," but the fact is that they're actually probably a lot more safe than many people view today. When it comes to genetic studies, a lot of them rely upon family or adoption or twin studies, which obvious they have limitations. The most obvious of which is that they don't actually rely upon genes. They take a look at the relationships. Obviously, if there's adoption, it provides really good data for us.

What those authors typically conclude is that addictions have a moderate to high heritability and it really has to do with the genetic closeness you are to the person so if you're a parent or if you're a parent has a severe substance use disorder, you're much more likely to end up with a substance use disorder than let's say if it's a cousin or a grandparent. Then we can take a look at this other piece, which is epigenetics, and really this is a evolutionarily valuable thing that happens with our genes so that over the course of the lifetime of somebody, the body is able to be adaptive to environmental experiences so that it turns on some genes, it turns off others.

What we typically believe at this point is that it does look like there are early experiences or environmental experiences or random developmental events that do

produce permanent changes in brain function that confer vulnerability to compulsive use. When we actually try to consider what it means from a genetic perspective, it likely resides at hundreds of genetic loci and each one only contributing a minute fraction in terms of the overall vulnerability of the organism. To date, we've only mapped a small percentage of them. We do know at this point generally what those environmental vulnerabilities are and we'll get into that next.

We do know that beginning even 1940s and on, there is a growing body of literature both from animal and human studies to suggest that when there is caretaker deprivation or abuse or neglect long-term chronic stress, it really has a deleterious effect on the adult organism. Probably one of the most impactful for me whenever I read it, was René Spitz's study on what he called *Hospitalism*. Spitz was very influential to Harlow and Bowlby and what he did was he looked at four different populations, two in the general population and two from institutions.

When he held from the institutions' things like housing, clothing, and food, and actually the one institution had better staffing. The children actually came from better backgrounds. They saw spectacular deterioration of these kids and the other institution actually was in a prison where those kids ended up being fairly developmentally normal. The only real difference that René Spitz could attribute these really graphic horrific responses to the environment was that the children in what they called the founding home lied flat in a crib all day.

There was a lot of death because of disease and infection and so they felt like if they kept them separated from each other and didn't have a lot of human interaction or adult interaction, it would get an infection as much and so they basically said in their cribs all day, didn't have a lot of contact with others, a lot of eye contact and playing and all those things.

At that point, René Spitz said, "Boy, it's not so much that we're pleasure-seeking or trying to avoid pain, but we're really people-seeking." Then, of course, we know the, I guess now the seminal and famous story of Felitti, who was the head of preventative medicine at Kaiser in San Diego, where he had the most successful weight loss people leaving the program. He didn't quite understand why, so they were interviewed and showed really high rates of sexual abuse histories, and of course, created the 10-question ACEs, which is a characterized around three subscales or so abuse, neglect, and household dysfunction.

When we think about it in those senses, really we're talking about attachment ruptures, and the results were staggering and still are, so that there's 10 questions of the 10 points, if you have a 6 on the ACE versus a 0, you are 4600% more likely to stick a needle on your arm and do inject drugs. Now, there are other notable self-report measures that show similar type of results, but really none are as productive, particularly with the dose-response converging toward the impact on the adult phenotype.

There are key limitations to ACEs. I know that some of them, it doesn't do a very good job of teasing out the differences between really what is the impact of the genetics versus the environment. It doesn't take into consideration the developmental timing of when the particular event occurred or the duration of the

particular incident, but still, it provides at least a gross understanding of that relationship, particularly early on to stress and trauma, and the impact on it and the vulnerability that it confers to people particularly around, we could certainly say opioid use disorders.

What are the implications for all this? Well, the first one is that it's very clear that early experiences in genetics are important in terms of who ends up why some and not others who recreationally use opioids or maybe use it as a consequence of an injury that maybe takes a long time to heal or really, really any particular time, and so it's really incumbent upon the clinician to take a thorough family history. You're going to obviously find family histories of substance use disorders, but you're going to see similar things. Sometimes I often find a similarity with eating disorder vulnerabilities in there.

The other piece in there is obviously trauma histories and there's different measures you can do around that, but people with trauma histories and genetic vulnerabilities are important to monitor, you understand in terms of what diagnosis and prognosis. Is this a mild opioid use disorder that will maybe potentially resolve itself? The person had just developed physical dependence, or is this something that's going to cascade and become recurring and problematic?

The other piece I typically had done over the years is asked about the subjective experience of the patient, so I ask around those particular things around exclusion or the subjective feeling of exclusion, rejection, or isolation as a child, and then I ask them also now as an adult, if particularly in the experience if they are off of all opioids, if you know what that experience is. As we know, a lot of times if people have those particular vulnerabilities and they're pervasive and they go across different relationship groupings, and they still have it, it's likely going to continue in recovery. Meaning they're going to be experiencing vulnerabilities too, exclusion and isolation, and it really is never going to go away.

Now, when I switch to medication-assisted treatments, this is somewhat of a divisive topic. Some people call it a third rail. I don't know how many people know that metaphor, I've used it sometimes. Sometimes people don't really haven't heard it before. Essentially, all it means is in some subway systems, they run through electricity and it's basically through a rail, so you have the two rails and the wheels sit and there's a third rail that pushes the train along. Obviously, there's enough electricity to move that thing, so if you touch it, it's very dangerous, and so the idea, this is something maybe you shouldn't even touch, touch this particular topic.

To give you an example, I know there might be people on this chat right now. There are even the word assisted is problematic for some, they feel as though it should be just called medications or if they're using an agonist, an agonist treatment, things like that. My hope is to be able to talk about these things in a balanced dispassionate way. That's helpful because it's really difficult to talk about opioid use disorders and is difficult to talk about the brain opioid theory of social attachment without covering this particular topic.

Let's get right into why there's strong advocacy. This study from 2000 took a look at substances of choice or drugs of choice, and it's the correlate to treatment, retention,

and outcomes. They found very clearly that there were some substances that tended to do really poorly when it came to how long you stayed in treatment or how well you did in the outcome. As you might have suspected, opioids was what they identified, the people with opioid use disorders, that was the biggest predictor in terms of treatment outcomes.

Clinically in my experience, I've also found that with methamphetamine users, a lot of times at day five, we would prepare for what we call a rabbit, that we get rabbit and then meaning that they would suddenly just, "I'm going to go." The reason that these are cold, and I touched it on it with referring to that study, but the reason that medication-assisted treatments are called the gold standard. This is against other types of treatment or no treatment, and this is against any of the four types of treatment, it's antagonist, partial agonist, combination of the two, full agonist, is because they do better, they reduced mortality and keep people in treatment.

It's really hard to argue that position that people stay alive and they stay in treatment. You can see why there's a real desire to communicate or advocate for these medications in the course of treatment. There are four types. You have an agonist, antagonist here, and what that essentially is, it's a substance that attaches to the opioid receptor and blocks an opioid from coming in. They take naltrexone and then they shoot some heroin. The heroin does not attach to it just washes out. The person is fine.

Just real quickly, there are three types of opioid receptors, the mu, delta, and kappa, the primary analgesic effect takes place when opioids are attached to the mu-opioid receptor or MOR as is commonly called. Then you have a partial agonist like buprenorphine. What that means is it has a ceiling effect. We'll talk a little bit more about that. Then a combination of the two. The United States was the first country to use a widespread distribution of the combination of the two, like buprenorphine and naloxone. Naloxone being another antagonist.

The reason it might seem it might seem to be confusing to you as to why you could use a partial agonist, an antagonist at the same time, the medication like Suboxone, there's a Zubsolv and Bunavail. There's generic versions is done through a sublingual film. You put it underneath the tongue and it dissolves the bioavailability. In other words, the ability of the body to make use of the medication for the antagonist is very low sublingually, but if you were to inject it, then it would have a much greater effect and you would throw so into withdrawal.

The primary benefit of adding the antagonist to something like Suboxone is that it cuts down on IV use. People can get really sick if they do it which obviously is an important intervention. Then you have things like full agonists, like methadone. We'll primarily cover or talk in a little more detail about the first three. When we are talking about medication-assisted treatments, and when I speak about the divisiveness that is sometimes in the field, what we're really talking about is buprenorphine. It has some additional advantages, it has a high affinity, partial agonist with a long half-life.

What do those three things mean? A high affinity means that it's very, very sticky. That if you take buprenorphine and it attaches the receptors and then you take something, I've seen some studies that show even fentanyl obviously depends on

the amount. It won't dislocate the buprenorphine, it stays in there. The partial agonist means that it's safe at high doses. I've seen some studies where they've given 70 times the recommended amount with no adverse effects. Again, you don't have a risk of overdose with it, and it has a long half-life, which means you only have to do daily dosing, which obviously something with a shorter half like heroin where people have to every 48 hours depending.

It is common for diversion and misuse. Diversion essentially means that it's not used for its intended purpose, so somebody gets a prescription for something like buprenorphine or more commonly like Suboxone, and they give it out to somebody else or they sell it or misuse. This is illicit use, so same thing. Somebody is purchasing Suboxone on the street. Now, a lot of researchers suggest that the reason this is done is to prevent withdrawal, that it's not an effort to get high. It's somewhat misleading to point to the research around how common it is to divert and misuse.

In my experience, that's a partial explanation. People do actually use it and for the effect that it produces. If it is just a bridge to getting to other opioids when it's out on the street, and I use that to talk about any illicit use. It really is not different than any other opioid at that point. In the recovery community, we talk about a thing called gift of desperation. In other words, a lot of times when a really bad thing happens, people are more willing to maybe get into treatment, or try something different. A lot of times the precipitating events that come with opioid use disorders is the fear of withdrawal.

If you're able to get the buprenorphine or Suboxone as the bridged over, my experience is that will maybe prevent someone and that would've maybe sought treatment earlier. Then there are just some general dilemmas. In Europe, they've used buprenorphine much longer than United States. In Finland, it became an epidemic in its own rate. Now, there's mixed data in terms of whether or not people use other substances like alcohol. I've read a good very large methodologically sound longitudinal study, 17 years and so increasing alcohol use over time. That is my clinical experience, and then you just have some other thing.

One, it's very difficult to get off of so that if you do want to have an exit plan with it, it's much harder to get off of than heroin. Most people do relapse upon discontinuation. If people are in recovery in the 12-step community, there's mixed acceptances. Right or wrong sometimes there's judgment by members in the 12-step community about people that are on those. It can make people feel rejected and excluded. It only requires an eight-hour online course from the prescriber. I know some people have argued that that has prevented more widespread distribution of the medication, which they feel is very helpful.

To put it in context, I've worked directly or indirectly with hundreds of people with opioid disorders for almost 20 years now, off and on. I'm still learning every day. An eight-hour course is not a tremendous amount of time, especially if you don't have a lot of experience with opioid use disorders or substance use disorders. After a period of time, prescribers can be eligible to treat as many as 275, which I'm trying to think about how I would keep track of that many patients in my mind and the individual

needs that they may have. Then finally, not always, but I found at times that there's a lack of informed consent.

I remember I interviewed a woman, she was 23 years old. She had gone to her father when she was 18 and said, "Hey, I got myself into a big mess here, I'm addicted to heroin. What do we do?" The father called up a local psychiatrist, a good reputation. Now this is her report, I wasn't there, obviously. She said she went there with her father. He took a 15-minute history and pronounced to her that she needed to be on Suboxone for the remainder of her life, and didn't tell her about some of the risks associated with the challenges of getting off or other treatment options.

By the time I had interviewed her, she was frustrated, after a year she wanted to get off, it took her a year to get off of it, but again, it's really hard to argue that people stay alive and stay in treatment, so I certainly understand the advocacy. Then you have things like naltrexone and Vivitrol. Naltrexone is an antagonist, Vivitrol, long-acting naltrexone. Naltrexone and Vivitrol are a little interesting, you have to detox fully off of it if you were to start that too soon, I've seen it happen, you get thrown into a pretty bad withdrawal, you feel terrible, and you have to be pretty motivated to do it.

Now, Vivitrol, because it is a monthly injection, one of the good things is that it does have good blood levels throughout the course of the 30 days, so that, let's say at day 29, a person suddenly had a real strong desire to use heroin and goes and shoots the heroin, the Vivitrol would be sufficiently in the system still. When we take a look at some of the research around it, with things like Naltrexone that's similar to initial and sustained abstinence to something like buprenorphine and with Vivitrol, this is effective for relapse prevention.

Vivitrol can be a little-- It's not always covered by insurances, when I was last at a place that was a big user of Vivitrol, it wasn't always the easiest process to get authorization or get in place. Implications for treatment. When we go back to 1978 with Panksepp, he felt like the theory could be strengthened if they gave naloxone to the animals and they saw an increase in distress vocalization. In other words, they would interpret that as feeling more disconnected, the attachment alarm is going louder and that's essentially what they found.

There is research to researchers who argue that people that are on the antagonist feel more disconnected and I've talked to colleagues who report similar anecdotal things from their patients. Then if you think about just the vulnerability to again, rejection and exclusion and isolation, and if something like buprenorphine makes people feel connected, it makes people-- That might be a very important piece, particularly when they're vulnerable early in recovery, they're going into, let's say, treatment environments where they don't know people, they're having to be vulnerable. That might be an explanation as to why they stay in treatment longer and try it because it might be the difference between relapse and not.

Moving to chronic pain. The Institute of Medicine, which is the health arm of the National Academy of Scientists, says, this is the most common reason people seek care. The CDC posts this 2018 study with a little more moderate around there, but they still say it's one of the most common reasons that people do so. Even at 20.4%,

that's pretty striking, one out of five Americans reports having chronic pain. Pain itself is a response to tissue damage or an inflammatory process, and it helps with healing, therefore, it has evolutionary value.

It is not agreed upon when acute pain transitions into chronic pain, but typically there's a time period between when you expect acute injury or tissue damage to heal and pain is still persisting. Most people look to the ICD-11, which gives a three-month marker so that if you had a particular injury and it's physically healed in three months have gone by, three and half months, now we've gone into a disease process and evolutionarily chronic pain is no value. Most of us operate from a biopsychosocial model of the human organism, that they're all interpenetrating, this is a biopsychosocial model of chronic pain and a lot of people certainly know that chronic pain can lead to anxiety and depression in people.

What is less commonly known is that trauma, people with histories of trauma, that trauma can lead to chronic pain and that chronic pain is very much associated with poor social supports. These things, if we go back again to this model about what makes people vulnerable to opioid use disorders, both those things, lack of social support and trauma, we can begin to see the relevance see here with something like BOTSA. There are four categories of pain, there's nociceptive. Nociceptive is the most common type of chronic pain. It's usually from activity and then neural pathways, arthritis, most types of spinal pain are nociceptive.

Then you have neuropathic and this is a disease process of any of the somatosensory systems and you hear terms like lancinating or shooting, the most what we probably all recognize or have heard before like diabetic neuropathy. Then you have nociplastic, nociplastic is essentially, in the absence of identifiable tissue damage or disease, it's abnormal processing of pain signals and maybe the two most common diagnoses that are associated with nociplastic or things like fibromyalgia, and irritable bowel syndrome.

Nociplastic tends to come with the poor outcomes and then really, the more that pain is studied, the view is that a lot of pain conditions typically have mixed of these three, so you get the fourth pain category. Now, I want to make a caveat to cancer versus non-cancer pain. The CDC does make a distinction in terms of guidelines or recommendations for use of opioids, between cancer and noncancer types, but physiologically, and the FDA, even kind of comments on this, there really is no difference between the two different types.

The explanation largely has to do with the existential nature of cancers. Cancer, you're talking about with the prognosis, and a lot of times the concerns are on treatment outcomes and so a lot of times it really is just that and not necessarily based on medicine, we're particularly researchers, it's really just how do we want to think about this for the person going through there.

When it comes to pain management, a lot of these recommendations are going to be self-directed. When it comes to self-correcting pieces, your exercise is the most common, or one of the most common, or most likely the most common, it doesn't really matter what kind of exercise you do. I say this for all of us because the tendency is when you get pain is to be self-protective, so you actually want to move

less, and the opposite of what really needs to happen. It doesn't really matter what kind of exercise you do, if there's chronic pain, you want to keep people moving, and then psychotherapy CBT like in other domains, much more commonly studied and tends to show some efficacy to help with it.

When it comes to medications, the first line of medications or antidepressants and anti-epileptic drugs. Gabapentin or Neurontin is the anti-epileptic drug, the antidepressants tend to have more flexibility, particularly with like neuropathic and nociceptive effectiveness. Opioids are not considered a first-line medication through any chronic pain condition but obviously, they're still important for acute pain conditions.

One reason I want to emphasize that if you go back to the risk profile, I know what happens is a lot of people, and even for physician, to now get letters from medical boards if somebody overdoses from an opioid and so there's a lot of fear and concern about whether or not, so much it takes them but really it is important to know that they are typically very safe and for acute pain conditions are still the drug of choice. They have non-surgical and surgical epidural-like bone fusion processes and different things like that.

Implications for treatment. Well, this seems pretty clear to me when you think about the fact that exclusion and rejection and isolation make people feel pain or are painful or increase pain for people and then you add in that trauma and lack of social supports, can be the origin of pain conditions is important to look at it from a treatment perspective. I'm going back to that salient of the social target. It's not just anybody but it's close others. Understanding who those people are in their lives, making sure that they have people in their lives that are helpful which obviously can be difficult depending on the family environment or how isolated they are.

There should be an important part of the treatment approach. I think about that too when I interviewed kids, I just want to hear one safe adult in their life whether it was an uncle, a teacher, a grandparent, a coach. I just need to know that there was at least one person that was in there to help me have a more positive view of prognosis. Now we're going to switch gears a little bit. I know I'm going to talk next about trends in research and I'm going to be referencing the 1993 article something almost 30 years old but I still find it really interesting and useful and I don't necessarily think a lot has changed based on what they said.

In the 1960s, there was a thing called the Community Mental Health Movement which largely looked at social factors in mental health. Now they might think about maybe social justice perspective, lacked opportunities, the stress of maybe an urban environment. In the 1980s, a lot of that funding was cut and NIH followed suit by saying essentially that proposals that had social factors in their research design were not a high priority.

Essentially, what they said as well is that our view, our focus going forward is a biomedical perspective of mental health and substance use disorders. Which I argue has not changed really since and it takes us to what we might call an internal defect model. Now a lot of us might repudiate being associated with an internal defect model something like the Temperance Movement where people were viewed as

having being morally weak or not spiritually strong enough or and that's the reason for the substance use disorder. Let's look at it maybe differently.

In 1997, Leshner, the former head of NIDA, said addiction is a brain disease. Now a lot of us think that was good. It had a lot of moral financial legislative value for the field. He told a family member, "Hey, look, your husband didn't choose opioids over your children. Your husband has a disease." "Okay. That makes me feel better. It's not a personal thing." The challenges though and this is what I argue is that once you do that though, your interventions are intraindividuals. You're talking therapy and medications and you extract out social factors and takes us to the other piece where the public eye goes, the money and publications flow.

I am not trying to suggest in the fairest relationship between researchers and the government but it's clear that most neuroscientists would agree that social factors play a role in substance use disorders and clinicians as well. The fact is that there's not a lot of research that takes a look at social factors as neurobiological intervention or clinicians that understand that maybe the value of a 12-step community or not the value but a part of the value of 12 **[unintelligible 00:44:38]** community is that the person gets to develop these post relationships which actually raises both based on opioid levels and that it is a neurobiological intervention.

When we look at things like social epidemiology, the literature is very clear that there is a very strong link between substance misuse and the amount of social integration a person has. Again, going back to this community mental health movement and not just fully extract out the social justice component because that this doesn't feel, I don't want to, because that's certainly a very important and relevant piece. Just sticking to the idea at a very basic level that people that have these close others are less likely to misuse opioids. I ended part I with this same 2016 article and I just appreciate it so much. I wanted to do it again.

This is an opinion piece, but I want to stop and read through it real quick, "If an aversive experience of social rejection and exclusion can be buffered by MOR activation, mu-opioid receptor, then people with impaired endogenous opioid function, exposure to social stress or both will experience relief or distress when taking drugs that directly or indirectly activate MOR. When you talk to people that are what we call white-knuckling it or don't have these connections in recovery and then they use opioids, they say, "I got relief," because again, their base opioids levels were down.

If we activate and keep those higher when they use, they won't get that same sense of relief and they'd be much more likely to get back into treatment sooner or from this other perspective here. Thus, social integration by restoring normal function of endogenous opioid systems can decrease the need to activate these systems through alcohol or opioid use, and subsequently, it can decrease drug use and relapse."

If we get them up there much less likely, there's a same I remember this, I've heard this before, if you're in Baltimore or I'm outside of Philadelphia. If you're in Philadelphia and someone hands you a plane ticket to Philadelphia and they say, "Do you want this?" You're going to not take it because you're going to say, "I'm

already in Philadelphia. What am I want this ticket for?" That's the same idea here. If your opioid levels are already here, you're not seeking or craving that particular experience. You're not going to take that ticket. You're already in Philadelphia. Implications here are again, very straightforward.

I think both clinicians and social researchers and ultimately NIH or NIMH need to reprioritize social factors in the origination, continuation, and treatment of opioid use disorders. How do we think about all these things? I think it's very clear that the environment now, I argue that over the last, 60, 70 years, we've become increasingly disconnected from each other. When we think about BOTSA, where that creates lower basal opioid levels, and then we have this opportunity to when we add in three different events that led to an increase in access to opioids.

The first one, Purdue Pharma with OxyContin, which everybody knows that story, but the same time, James Campbell gave his presidential address to the influential American Pain Society where he advocated to have pain be the fifth vital sign. By the mid-2000s, chronic pain was an industry, and at the same time and let's talk about drug gangs at the same time, change their marketing approach or a different strategy where they realized a big reason people didn't use heroin was because you had to use it intravenously. They realized if they upped the purity enough, you could use it intranasally. That's what they did.

In a place like Philadelphia, in 1985, the average purity was about 7%. By 1995, it was 70%. The consequence was that of that was that people who were afraid of needles started to experiment with heroin, you had a shift in demographic from inner city minority to Caucasian, urban and suburban. We talked about different questions then. How do we make sense of this particular model of opioid use disorders when it comes to things like genetics and epigenetics and trauma and early-life stress? Well, it's very clear that these things are important in terms of vulnerability to opioid use disorders.

It's important from a societal perspective in terms of how we protect children and adolescents. It's important from a clinician's perspective in terms of taking good histories and understanding the subjective experience of our clients. We talked about medications and the pros and cons that they have. Most strikingly they help people stay alive and stay in treatment, but they come with some risks. One, it's very difficult to get off of and then we looked at chronic pain which very clearly is impacted by the theory of BOTSA which posits that exclusion and separation and disconnection are going to create painful experiences in people.

Then you add in, people have trauma histories and it changes their genetics, their epigenetic responses that confer vulnerability permanent brain function changes that lead to compulsive use. We need to take good histories in terms of these core people in people's lives, try to help people reconnect to these things or understand as protective factors that people that have these close people or others are less likely to use because you think about two people in recovery, they have to get surgery, or they get into a car accident and need to use opioids.

If people have these things in place, they're much less likely to relapse. Social epidemiology and social factors and relapse research, it's very clear that these things

are linked together. The question is, how do we use that as clinicians, or how do we use that as researchers to impress upon the resources available to us? Do we look at things like sober living environments, which are largely unregulated, unstudied environments, but that can be really helpful but also problematic in these things? We conclude with, okay, where do we go from here? What do we--

I've spent two hours talking about this and I probably have three or four other topics that we weren't able to get to. I don't necessarily have an answer to it. What I can say is that for me, the opportunity to present some of the ideas in terms of what works and when I work with others or have the opportunity to treat. These are important considerations that I have, that I found work clinically. Hopefully, together as a community, we begin to think about these things or have conversations and can be collegial even when we don't agree upon everyone's opinion about it.

For that, I wanted to say thank you for your time. Again, know it's valuable. It's a Friday afternoon and here in the Northeast, it's a beautiful, sunny, 70-degree day. I'm sure a lot of people are looking forward to the weekend. Thank you.

Interviewer: Thank you so much Dr. Roeske. we do have time for a couple of questions. I will read the first one. If the addiction to substances subsides, how do we prevent people from becoming addicted to something else?

Dr. Roeske: That's a great question. One that's plagued clinicians and physicians for a long period of time. My general experience is meaning and connection so that if people are engaged in meaningful activities and going back this idea, if they're connected to a stable group of others that they can not actually, egalitarian in nature where they feel like they can have reciprocal honest communication. You're going to be less likely to have the need to go to another substance or behavioral whether it's exercise or overworking, gambling, sexual compulsive behaviors.

Again, if these things have been with you since childhood, we also know there's no cure, per se, for life these things, and people will typically be vulnerable to them.

Interviewer: Great. Thank you. Are there any early signs for those who have this vulnerability?

Dr. Roeske: Yes. I do think that there are. Certainly, there's no research to take a look at attachment styles. Obviously secure is typically not one we would look to. Is it more likely to be disorganized or anxious? Obviously, you have the RAD diagnosis. I don't necessarily know that. What I can say is that certainly the kids with trauma histories who end up with the feeling of disconnection or vulnerability or exclusion, that's subjective experience that typically translates well. Obviously, if there's family members that are also identifiable, those things make me very concerned when they come into me for assessment. as to what really the prognosis of this is?

Interviewer: Great, thank you. Could you also take some time to explain if this same thought process applies to alcohol overuse?

Dr. Roeske: It's a good question and it actually does. One of the explanations in the study the [inaudible 00:55:21] I referenced around increasing opioid use, copious

amounts of alcohol actually activate the more system. You'll see that with people who try to use alcohol to come off of opioids which is not an uncommon effort They'll drink just really large amounts of alcohol. Again some of you in the audience maybe at times maybe have gotten really, really, really intoxicated. At that point, you have activated the MOR system, so that just whoa type of experience actually replicates the experience of opioid use.

Interviewer: I think we have time for maybe one or two more. Someone asked about your thinking on methadone in attachment research.

Dr. Roeske: I haven't seen a lot specific to methadone. A lot of the research that I've read is around those three the partial agonists in the antagonist or the combination of those two. My suspicion, it's the same, I think it's less valued because it typically they're in more impoverished locations just cause of cost and they're associated with more criminal element at times. I think it's the same value. I think the studies that I do see so that it is actually more effective than buprenorphine for both of those things if I recall correctly for treatment retention and lower mortality for what it's worth.

Interviewer: I think we've done for one more, so we'll end on everyone's favorite topic. How do you think that the COVID pandemic plays into this?

Dr. Roeske: It's a great one. I've read some good research. There's a great Cigna study, very large I think 20,000 and 10,000 subsequent years that just show just massive amounts of people feeling disconnected and isolated and largely do lack of meaningful engagement with others and lack of social supports or those are very big ones. I definitely think that's contributed. I know for me when I worked on-site, I'm remote now, like I don't even interact with people always.

When I was in site we used to have these long tables where everyone would come together for lunch and there'd be laughter, that never recovered, that never reemerged. Such a loss of community around these things here that are really, really important not just for people with opioid disorders but we know that these things are salubrious for all of us and particularly around just general pain, the emotional pain of feeling just buffeted and comforted. I think we're still feeling echoes of that.

Interviewer: Thank you so much, Dr. Roeske, for your wonderful presentation and for answering those questions. Thank you to everyone on the line for your participation and for asking those great questions and thank you to Newport Healthcare for making today's webinar possible. Recording of the presentation will be emailed to everyone in about two weeks and that email will also include a copy of the presentation slides.

As soon as the webinar is ended a short survey will appear on your screen, we ask that you take that survey and give us your feedback. Thank you again so much for your attention and to Dr. Roeske for joining us today and we hope you all have a wonderful rest of your day and weekend.

[00:59:23] [END OF AUDIO]