

# NEUROLOGICAL CONSEQUENCES OF REPETITIVE OPIOID USE

## Understanding the Challenges are the Keys to Treatment

BY MISTI STORIE, MS, NCC, NAADAC DIRECTOR OF TRAINING AND PROFESSIONAL DEVELOPMENT



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I was asked by a friend the other day what I like most about working at NAADAC. After a few minutes of thought, the answer put a grin on my face. I responded, “I most love training addiction professionals about medication-assisted treatment and recovery. Picture a day where I am presenting an all-day training in Anytown, USA that required planes, trains and cabs to reach. At the beginning of every training, it seems like there is always at least one counselor who feels compelled to inform me that medications are not appropriate for addiction treatment, despite his attendance at my training. I most love watching the transition this counselor experiences over the next eight hours together. I can physically see his mind shift from closed...to cracked...to open. And better yet, I can pinpoint the precise moment that light shines through. Like clockwork, when the training reaches the climax of explaining how opioid dependence develops in the brain and the FDA-approved medications are designed to work in tandem with these changes, it is impossible for him not to envision one client in his case-

load who could benefit from this technological advancement. The rest of our time together in the training is just helping him figure out which clients are the best fit. It doesn't get any more gratifying than that for me.”

Currently, the Food and Drug Administration (FDA) has approved medications to help treat dependence on alcohol, opioids and tobacco. As more medications are being developed and tested for substance use disorders, the need for addiction professionals to understand the science behind them becomes more paramount. As such, NAADAC places medication-assisted treatment and recovery at the top of our educational priority list. Over the past seven years, NAADAC has developed several face-to-face trainings, online courses, webinars and independent study courses about medication-assisted treatment and recovery to keep pace with the ever-evolving arena of addiction medicine. Our philosophy is *“the more you know, the better you can help your clients.”*

In this spirit, below is an excerpt from NAADAC's *New Innovations In Opioid Treatment: Buprenorphine* that outlines how opioid dependence develops in the brain. With this understanding, it is hard to deny the biological components of addiction and therefore, the necessary treatments designed to assist the brain in reversing the patterns established by excessive use.

### Starting at the Beginning

To understand how opioids affect the brain, one needs to review basic brain functioning. Psychoactive chemicals mostly affect the central nervous system, which consists of the brain and spinal cord. As you probably know, the central nervous system is primarily responsible for:

- thinking, learning and judgment
- emotions (happiness, paranoia, anger, anxiety, fear, love)
- voluntary movements (walking, running, reaching, sitting)
- sensory inputs (smelling, tasting, hearing, feeling)

To ensure the human body responds appropriately to the outside world, the brain manages itself by rapidly sending chemical signals or messages to billions of neurons that are located throughout the human body. These messages are relayed via neurotransmitters and instruct the neuron to take action. Neurons can either be activated or suppressed naturally by neurotransmitters or artificially through the introduction of drugs or medications.

Neurons are commonly referred to as the building blocks of the entire nervous system, and each has its own shape, size and function specific to the type of chemical signals (neurotransmitters) it can receive.

There are three main neurotransmitters relevant to this discussion of opioid consumption and dependence:

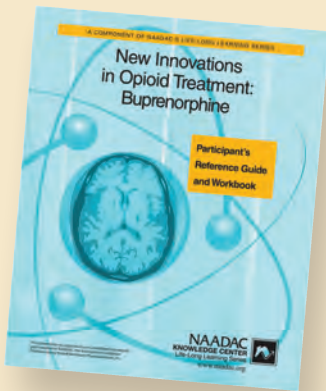
- **dopamine** – regulates motivation and pleasure; most addictive psychoactive chemicals increase dopamine, as do eating, gambling and sex
- **endogenous opioids** – produces euphoria and is a naturally occurring pain reducer that are naturally increased when one feels pain or experiences pleasure
- **noradrenaline** – also known as norepinephrine, contributes to the “fight or flight response,” stimulates wakefulness, breathing, blood pressure and alertness

### Effects of Opioid Consumption in the Brain During Use

When opioids are consumed, there are two main neuronal activities that take place in the brain simultaneously — there are others, but I will only discuss these two for the purpose of this article.

#### The first main neuronal activity is as follows:

1. Opioids are ingested.
2. Opioids bind to opioid receptors.
3. Neurons located in the area of the brain called the locus ceruleus (LC) are suppressed and unable to release noradrenaline to various parts of the brain.



*When opioids are repeatedly consumed, the regulation of dopamine and noradrenaline is altered in the brain and result in opioid dependence and subsequent withdrawal.*

4. The individual experiences drowsiness/nodding, slowed breathing and drop in blood pressure.

#### The second main neuronal activity is as follows:

1. Opioids are ingested.
2. Opioids bind to the opioid receptors.
3. The increase in opioid stimulation activates two areas of the brain called the ventral tegmental area (VTA) and the nucleus accumbens, resulting in the release of dopamine.
4. Since dopamine is a main reward neurotransmitter, increases in the nucleus accumbens makes the opioid user feel happier.
5. The brain remembers those good feelings caused by increased dopamine and opioid activity.
6. The brain of the opioid user desires to repeat the behavior again to get the same good feelings.
7. The cycle of opioid dependence begins or ends, depending upon the frequency of consumption.

#### Onset of Opioid Dependence

In the absence of drugs, the human brain carefully coordinates the activity of the billions of neurons throughout the body. When the brain is exposed to external substances, such as opioids, the brain is overridden and functioning is altered. Typically, when a person does not chronically abuse opioids, the brain is able to return to normal levels of functioning after the opioids have been detoxified from the body.

When a person repeatedly consumes opioids, the brain is in a constant state of imbalance. The brain naturally seeks to always function in a state of equilibrium, called homeostasis, and it will work to restore the balance in spite of the presence of opioids. ***Opioid dependence is established when the brain adapts to the constant presence of opioids.***

1. Since the neurons located in the locus ceruleus (LC) are constantly being suppressed and unable to distribute noradrenaline, they adjust by increasing their level of activity in an effort to regain homeostasis.
2. Roughly normal amounts of noradrenaline can now be distributed throughout the body, and the opioid dependent feels more or less like normal.
3. Also, the opioid receptors gradually become less responsive to opioids because of the constant over-activity. This means that the same amount of opioids no longer produces the same level of stimulation. This adaptation is called tolerance.
4. Since the opioid receptors are not as responsive to opioids as they used to be, the VTA and nucleus accumbens are not being activated with the same intensity.
5. As a result, not as much dopamine is released.
6. The opioid dependent person does not feel the same level of pleasure as previously experienced.
7. Often, the dependent will consume a greater amount of opioids in an effort to achieve the same level of “high” as previously experienced before the onset of tolerance. This phenomenon is commonly referred to by opioid dependents as “chasing the high.”

*Note:* Opioids produce cross-tolerance, meaning that once tolerance develops for one opioid, the opioid dependent will experience tolerance to all opioids. This occurrence is important to remember given that legitimately prescribed pain medications, as well as medication-assisted treatments for opioid dependence, will need to be adjusted appropriately to compensate for the dependent’s level of tolerance.

#### Manifestations of Opioid Withdrawal

When opioid dependent clients stop consuming opioids, the brain is once again forced to experience an imbalance.

1. When opioids are not present, neurons located in the locus ceruleus (LC) are free to behave normally.
2. This causes the amount of noradrenaline released and distributed throughout the body to increase dramatically.
3. The opioid dependent experiences withdrawal symptoms, such as jitters, anxiety, muscle cramps and diarrhea.

The intensity of opioid withdrawal symptoms will depend on the type, amount and frequency of opioid consumed, as well as the duration of abuse. Withdrawal symptoms are basi-

#### Questions to consider while reading this article

1. Which neurotransmitter produces euphoria and is a naturally occurring pain reducer that is naturally increased when one feels pain or experiences pleasure?
2. What is the state of equilibrium the brain naturally seeks called?
3. Rapid heart rate, increased blood pressure and fever are symptoms of what?
4. What do the abbreviations VTA and LC stand for in the article?
5. What are the main neurotransmitters discussed in the article that are relevant to opioid consumption and dependence?
6. What is the main “reward” neurotransmitter?
7. True or false: Opioids with short half-lives have acute withdrawal symptoms for longer periods of time; whereas, opioids with long half-lives have acute withdrawal symptoms for shorter periods of time?
8. What is the half-life of heroin?
9. Which FDA-approved medications for opioid dependence are currently used in the United States?
10. True or false: the FDA-approved medications buprenorphine, naltrexone and methadone work by reducing or eliminating the euphoric effects from illicit use or eliminate withdrawal symptoms that often lead to relapse?

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cally a resurfacing of functions that have been suppressed or altered by opioid consumption. Even though opioid withdrawal symptoms are incredibly uncomfortable, they are not life threatening for individuals who are otherwise generally healthy.

Opioid withdrawal symptoms are experienced in two phases: acute opioid withdrawal and protracted opioid withdrawal. Acute opi-



oid withdrawal symptoms are the opposite of acute intoxication symptoms, including:

- anxiety
- fever
- muscular spasms
- chills
- gooseflesh
- rapid heart rate
- craving
- headache
- runny nose
- diarrhea
- increased blood pressure
- stomach cramps
- dilated pupils
- insomnia
- sweating
- dizziness
- irritability
- vomiting
- exaggerated pain response
- loss of appetite
- watery eyes
- extreme fatigue
- yawning

Most opioid dependents consume their next dose of an opioid when half of the last dose has been removed from the body, known as half-life. The length of time an opioid dependent client experiences acute withdrawal symptoms depends on the half-life of the opioid last consumed. If the brain is accustomed to the constant presence of opioids, more opioids must be consumed at this time to avoid withdrawal symptoms. Opioids with short half-lives have acute withdrawal symptoms for shorter periods of time; whereas, opioids with long half-lives have acute withdrawal symptoms for longer periods of time. Below are the half-lives of some commonly used opioids:

- heroin – three to four hours
- codeine – 2.5 to three hours
- morphine – two hours
- hydromorphone – 2.6 hours
- oxycodone – 3.51 hours
- hydrocodone – 3.8 hours

Protracted opioid withdrawal symptoms are generally less severe than acute withdrawal symptoms, but they can still be very uncomfortable. Symptoms can include:

- craving
- decreased blood pressure
- decreased body temperature
- decreased heart rate
- deep muscle aches
- depressed mood
- impotence
- inability to have an orgasm
- insomnia
- overall lack of pleasure
- poor appetite
- reduced libido

Regardless of the length of the time acute withdrawal symptoms persist, protracted withdrawal symptoms occur for weeks or months after the last opioid is consumed.

### Scientifically Developed Pharmacotherapies

The three FDA-approved medications for opioid dependence that are currently used in the United States are naltrexone, methadone and buprenorphine. These medications work in the brain through the same neuronal pathways as described above, but instead reduce or eliminate the euphoric effects from illicit use or eliminate withdrawal symptoms that often lead to relapse. Granted, these medications are not appropriate for everyone. However, by understanding the biological changes that occur in the brain after repeated use of opioids, the discussion about medication-assisted treatments with your clients becomes more relevant and useful.

To learn more about these pharmacotherapies and medication-assisted treatment and recovery for opioid dependence, watch the free webinar on this topic (free CE credit for NAADAC members), complete the online course (free to NAADAC members) or order the *New Innovations In Opioid Treatment: Buprenorphine Independent Study Course*.



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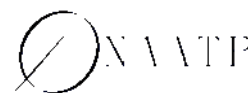
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