

# OPEN

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## GUIDE

# NEUROBIOLOGY OF ADDICTION



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Overdose Prevention Engagement Network

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# KEY TAKEAWAYS

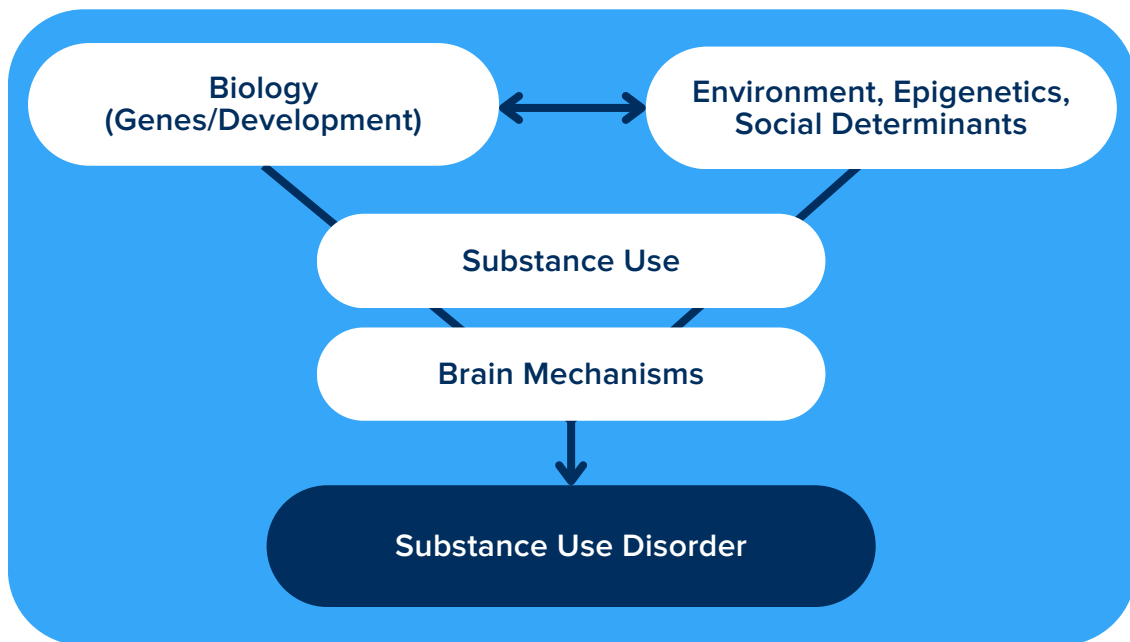


- Addiction and substance use disorders are characterized by intense cravings and compulsion to use despite negative consequences.
  - Each person who uses substances does not develop addiction.
  - People can experience a tolerance to substances and withdrawal without addiction.
- Structures and reward pathways in the brain are negatively affected by substances that are beyond a person’s conscious control.
- Addiction can be treated using a multidisciplinary approach including
  - Treatment medications.
  - Therapy to rebuild and strengthen areas of the brain damaged by addictive substances.
  - Taking part in meaningful, fulfilling activities that can weaken the strong reward pathways focused on addiction.

# NEUROBIOLOGY OF ADDICTION

According to ASAM, “Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual’s life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.” A key piece to understanding and treating addiction is learning how the subconscious processes in the brain drives a person to continue to use regardless of consequence. (1)

Central to addiction is the brain's reward system, primarily the mesolimbic dopamine pathway. Each time a person uses an addictive substance, it causes a release of [dopamine](#), which is a neurotransmitter made in the brain. Dopamine causes a desire to use again regardless of the consequences.

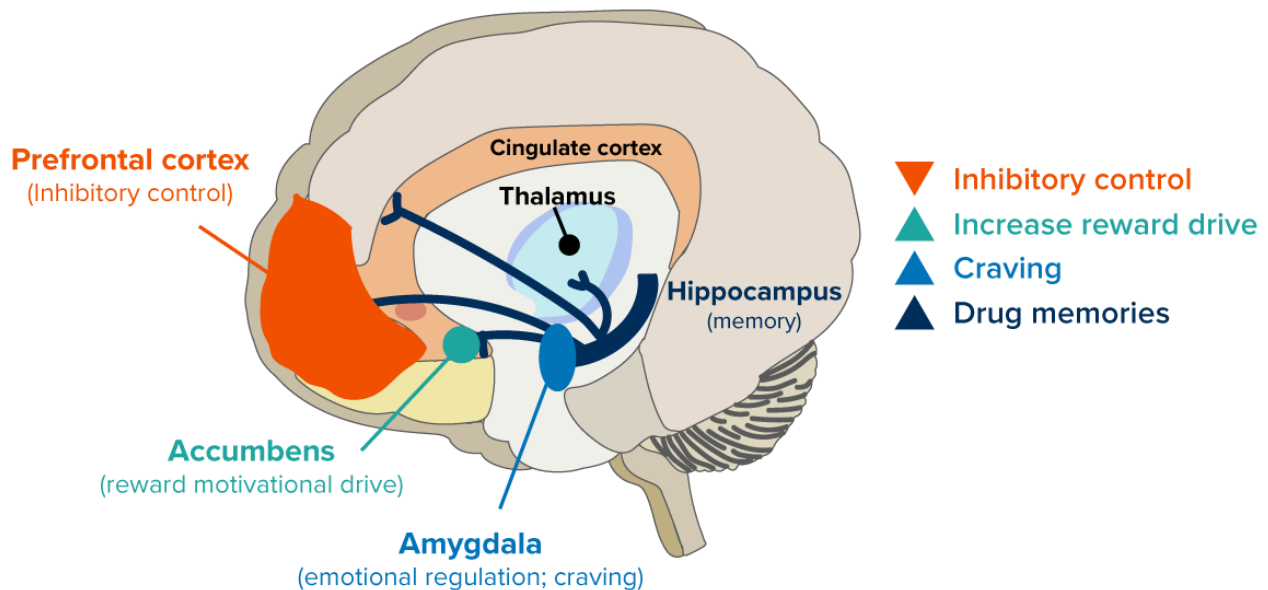


Additionally, addiction involves changes in the [frontal cortex](#), impairing decision-making and impulse control. The [amygdala](#) and [hippocampus](#) are also affected, contributing to the emotional and memory-related aspects of addiction. These neurobiological changes create a cycle of craving, withdrawal, and relapse, making addiction a persistent and challenging condition to treat.

# BASIC UNDERSTANDING OF BRAIN FUNCTIONS CONTRIBUTING TO ADDICTION

## Nucleus Accumbens

The nucleus accumbens is part of the mesolimbic system and receives dopamine from the ventral tegmental area (VTA) in the brainstem. Release of dopamine in the nucleus accumbens is critical in mediating positive reinforcement or desire for both natural rewards such as food or sex and substances of abuse such as alcohol and cocaine.



## Dopamine

The sensation of pleasure typically accompanies advantageous behaviors, such as eating, socializing, and engaging in sexual activity. Our brains are designed to increase the likelihood that we will repeat enjoyable activities. The neurotransmitter, dopamine, plays a crucial role in this process. When the reward circuit is stimulated by a positive or pleasurable experience, a surge of dopamine signals that something significant is occurring that should be remembered. This dopamine signal brings about changes in neural connections, facilitating the repetition of the behavior unconsciously, thereby forming habits.

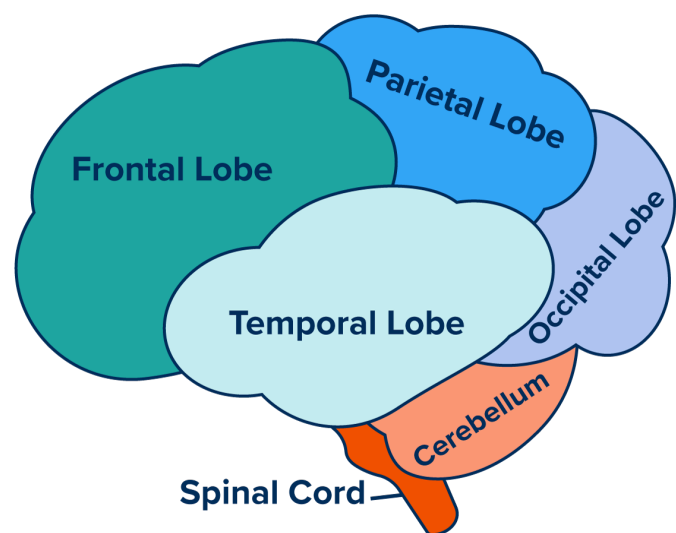
While some drugs induce intense euphoria, they also trigger large surges of dopamine in the nucleus accumbens, strongly reinforcing the link between drug consumption, the resulting pleasure, and all associated external cues. These substantial dopamine surges motivate the brain to prioritize substance use over other, more beneficial goals and activities. Critically, addictive drugs release dopamine regardless of whether the experience was pleasurable. Even after tolerance develops and the drug is no longer enjoyable, drug use continues to increase dopamine release and fuel an ever-intensifying desire to use again.

### Hippocampus and Amygdala

These areas of the brain are responsible for attaching emotions, memories, and previous experiences to stimuli received in the brain. Such contexts can evoke intense desires to use substances, thus acting as a powerful driving force for continued use and return to use.

### Prefrontal Cortex

The prefrontal cortex is responsible for complex cognitive processes described as “executive control” or “conscious self”. Executive function is the ability to organize thoughts and activities, prioritize tasks, manage time, make decisions, and regulate one's actions, emotions, and impulses.

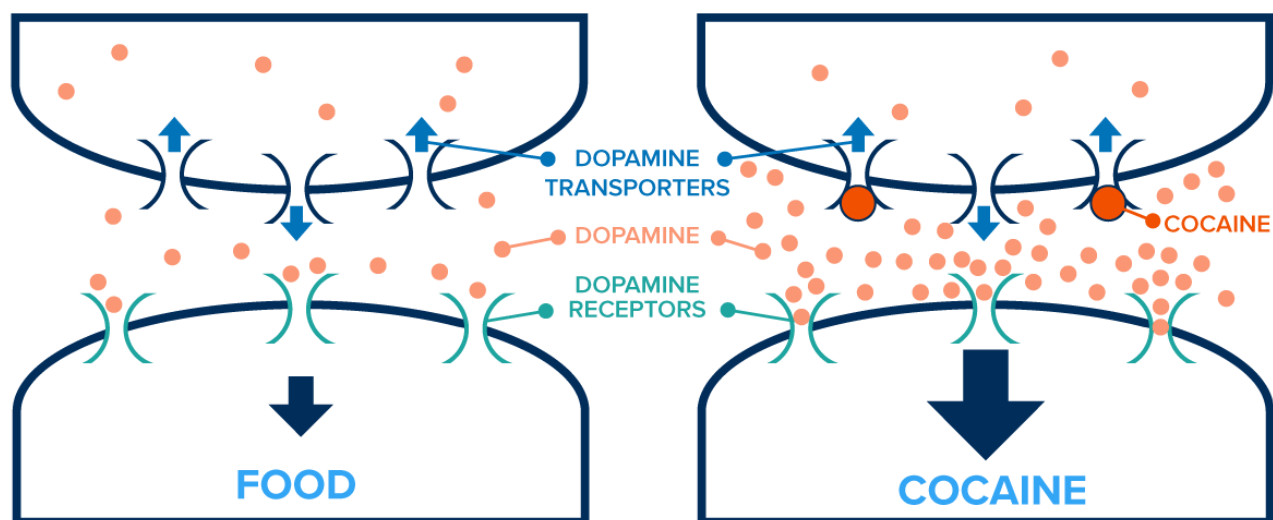


This is also the last part of the brain to mature, making teens most vulnerable to substance use. [This area of the brain becomes damaged by substances and causes a decrease in function and ability to communicate with the accumbens and stop potentially detrimental behaviors.](#) Therapy, that is often part of SUD treatment, focuses on strengthening this area of the brain to control urges to use. Talking about urges and envisioning future consequences engages the cortex and can help to counteract other brain signals related to the urge to use substances.

# PUTTING THE PIECES TOGETHER

Normally, dopamine release is triggered psychologically by some feeling of pleasure or satisfaction and released in the accumbens. Consider natural rewards, such as food, socializing, and sex - these things increase dopamine levels in the accumbens. [Dopamine in the accumbens motivates an individual to want to repeat the experience they just had.](#) For example, when we eat foods, this is satisfying which releases dopamine. This dopamine release encourages you to eat again in the future.

In the case of using addictive substances, these substances cause a direct release of dopamine. Not only does this cause a desire to use again, regardless of the consequences, these substances cause dopamine to flood the reward circuit up to [10 times](#) more than a natural reward. As a person continues to use substances, there is an even stronger release of dopamine which is called “dopamine sensitization”. This equates to an even stronger craving or motivation to continue using substances due to the amount of dopamine release.



### DOPAMINE RELEASE EXPLAINED (3)

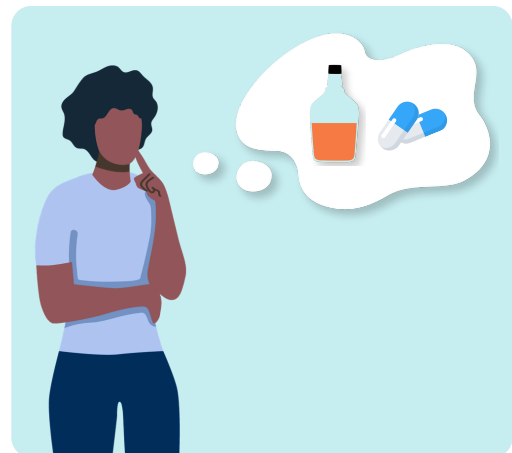
All drugs of abuse increase dopamine release in the nucleus accumbens (NAcc), which normally mediates responses to natural reinforcers like food and sex.

<p><b>Normal</b></p>	<p>Some activities cause pleasure → Pleasure causes dopamine release → Dopamine causes a desire to repeat the activity</p>
<p><b>Addiction</b></p>	<p>Drugs directly release dopamine → Dopamine causes a desire to use drugs again regardless of the consequences</p>

A person's ability to experience pleasure from naturally rewarding (i.e., reinforcing) healthy activities is also reduced due to the brain's reward circuit being hijacked by addictive substances. This is why a person who misuses substances may describe feeling flat, having a lack of motivation, and/or unable to enjoy things that were previously pleasurable. Now, the person needs to keep using substances to experience even a normal level of reward, and this process only worsens over time due to the hijacked reward circuit. In addition, the person will often need to take larger amounts of the substance to produce the familiar high. This resistance to the pleasurable aspects of drug use is known as tolerance.

In cases of addiction, everyday environmental or situational cues that have been associated with drug use due to alterations in the reward circuitry can spark intense cravings whenever an individual encounters these stimuli, even when the drug is not present.

This conditioned response can persist for extended periods, affecting individuals who have been abstinent for several years. For instance, a person who has abstained from drug use for ten years might still experience cravings when revisiting a former neighborhood or residence where they previously used drugs. Often, individuals may not consciously recognize the connection between these cues and their past drug use. The brain retains these associations, much like it remembers how to ride a bicycle.(2)



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3. Nestler, E. J., Hyman, S. E., & Malenka, R. C. (2009). Molecular Neuropharmacology: A Foundation for Clinical Neuroscience. New York: McGraw-Hill Medical.

## WEBINAR

### A MODERN UNDERSTANDING OF THE ADDICTED BRAIN

This free, 1-hour CME course outlines the basics the human brain works and how substance use alters normal brain function.

- Discuss the basic, motivational neurocircuitry activated by substance use.
- Describe how common triggers interact with motivational circuits to produce drug-seeking behavior.
- Outline how chronic drug use alters motivational neurocircuitry to perpetuate drug-seeking behavior.



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