UNDER THE HOOD:
A Look Inside the Brain of Your Patient Suffering from Substance Use Disorder

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NORTH DAKOTA ACADEMY OF FAMILY PHYSICIANS
STRONG MEDICINE FOR NORTH DAKOTA

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My name is John Hagan. I am an internal medicine physician. I have worked in corrections since 2003. I work in an environment where 85 percent of my patients suffer from substance use disorder.

As a primary care provider, you are on the front lines of health care delivery.

There is no question that this remark is true. **Question:** With the show of hands, how many of you work in emergency departments? **Question:** How many work in same day or walk-in clinics? **Question:** How many work in primary care clinics? **Question:** How many work for hospitalist services? **Question:** Now, how many of the rest of you provide the ongoing and chronic care for patients who are seeing a specialist? The truth is, we all talk about managing health care. You don't just manage it, you deliver it.

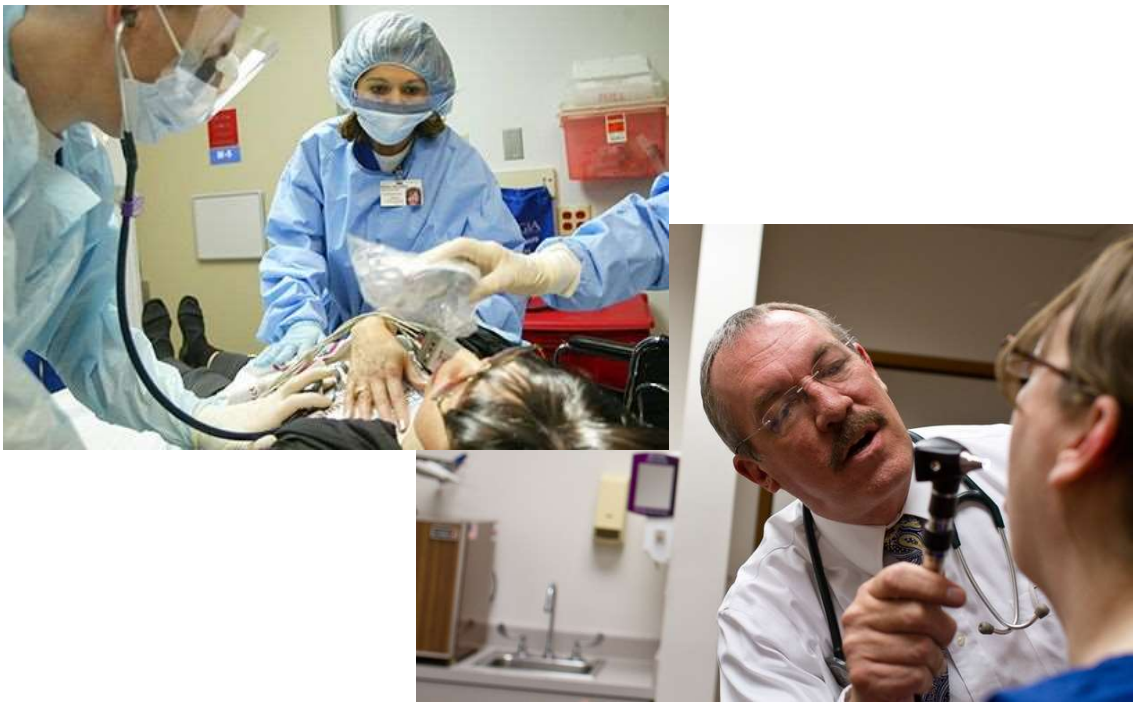
You treat many patients who suffer from obvious or hidden addictions.

Addicted patients come in all shapes, ages and sizes. Drug and alcohol experimentation that leads to addiction often begins in the teenage years. Some patients develop an addiction to opiates after exposure to these products. They may have been given a prescription for pain following injury or surgery. Many of our patients have been introduced to the world of addiction by a significant other in a new relationship.

Patients that you see in your daily practice may be suffering from addiction.

Addicts come from all walks of life. Drugs know no gender preference and have no geographic bias. Education offers no protection. I have cared for inmates who are addicts from all walks of life, including business owners, teachers, tradesmen, ranchers, physicians, nurses, lawyers, law officers and judges.

You want to deliver effective emergent and routine care to these patients.



In healthcare delivery, we see people as they are. We treat them when they are at their best; we often stand beside them on their darkest days. I have come to believe that addiction is part of the human condition, every bit as much as is heart disease, diabetes and obesity. No child in grade school ever said, “I want to be a socially dysfunctional addict when I grow up!“ The Question is, “How can I deliver effective care to my addicted patients?”

Expand your knowledge about

how substance use affects the health and behavior of your patients.

You have already enrolled in the refresher course. I guarantee success in 3 easy lessons or your money back.

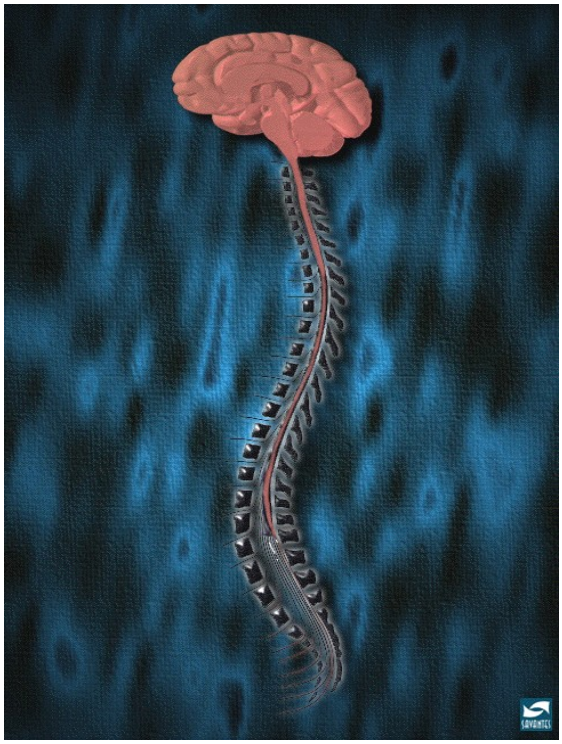
Recall that all substances of abuse act on the nervous system.

Lesson 1: Willy Sutton, a famous bank robber was once asked, “Why do you rob banks?” He responded, “That’s where the money is.” If a substance doesn’t interact with your brain, it is unlikely to be abused. Let’s review some relevant anatomy.

We need a brief review of neuroanatomy.

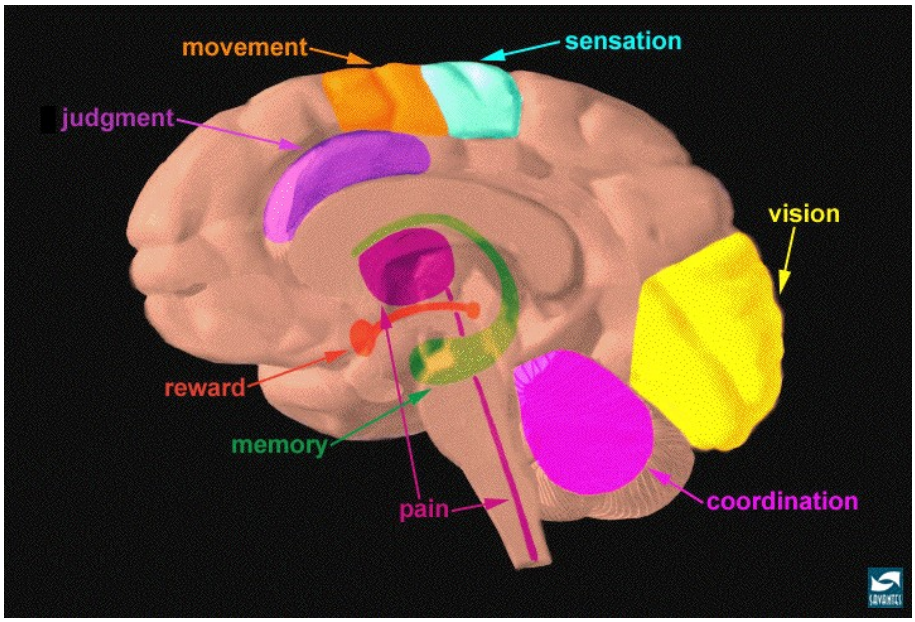
A is for anatomy.

Our central nervous system acts and reacts to our environment.



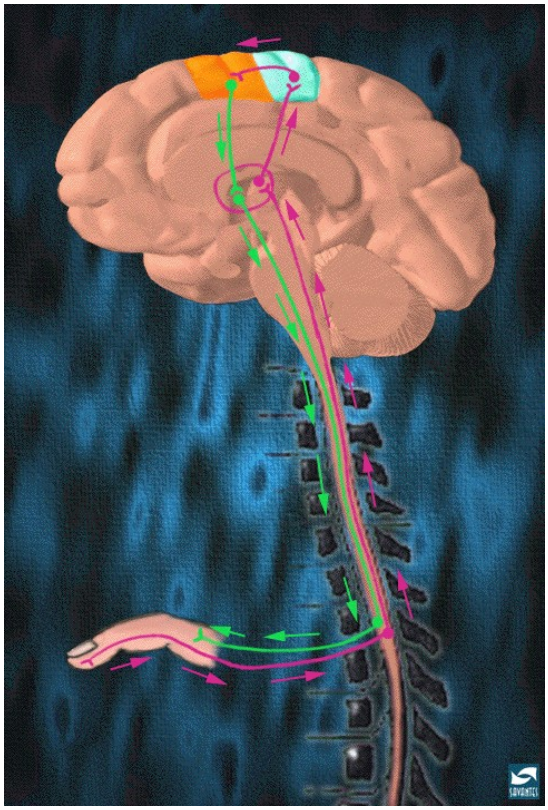
The central nervous system includes both the brain and the spinal cord. Billions of nerve cells communicate with each other using electrical and chemical signals. Everything we sense, feel, and do we do with this organ. It is how we communicate with our body and our world.

The brain is divided into functional areas.



Distinct parts of the brain govern specific functions. Note sensory, motor, and visual cortex. Separate centers exist for coordination, pain and memory. One important pathway is the reward pathway. Another is the thalamus. Let's take a closer look.

Different areas communicate to get the job done.

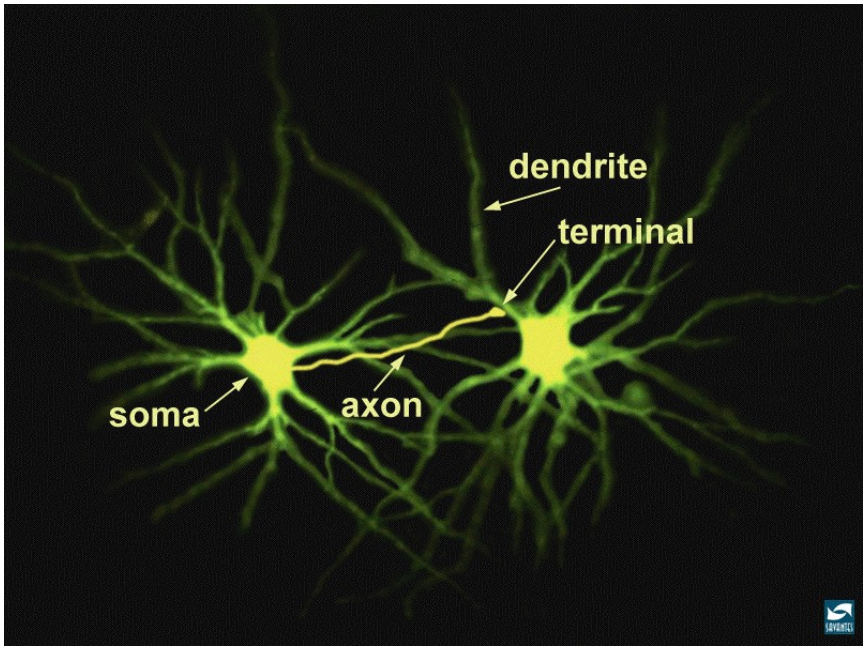


This is a long pathway. I want you to bite your finger. C'mon, do it! Ow! Nerve endings in the finger sense the injury and connect to other neurons heading up into the brain. These end in the thalamus, forming a synapse with other neurons. The thalamus organizes this information and sends it to the sensory cortex (in blue), which interprets this as pain. It sends that information to the nearby motor cortex directing it to send motor information back to the thalamus. Again, the thalamus recognizes the incoming information and sends it back down the spinal cord by a different route, directing neurons in the finger, hand and arm to react to the pain.

Nerves communicate with each other by releasing chemicals as a signal.

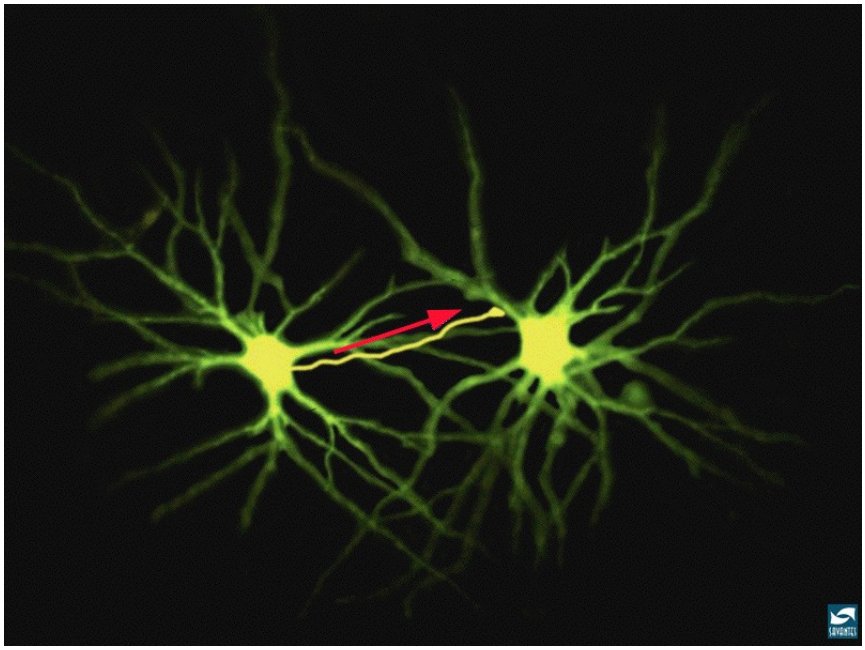
Let us review briefly the anatomy of neurons and, specifically, the end plates at the synapse. It is here that the critical steps leading to addiction occur.

Neurons are living cells that conduct signals.



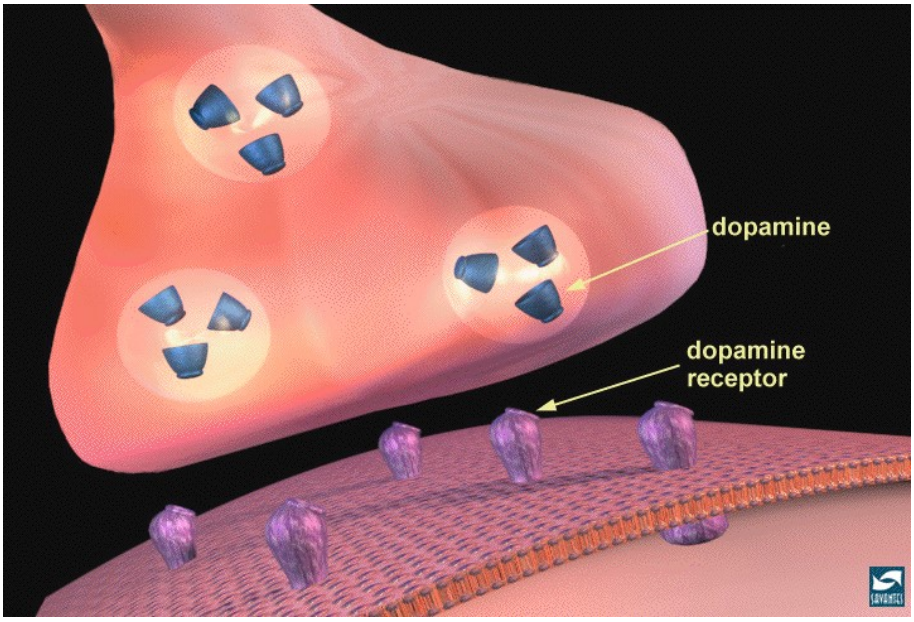
All hig speed signaling pathways use neurons. Neurons have dendrites, to receive information, cell bodies to power the cell, and axons, which are the live wires that reach to the next neuron. This is a picture of real neurons in the thalamus.

Signals flow from one neuron to the next.



The axon is the key path for information transit. It may land on another cell's dendrite, soma or axon. Most go to dendrites. A wave of electrical energy travels down the axon to the terminal, called the synapse.

The synapse, where one nerve connects to the next is the key.

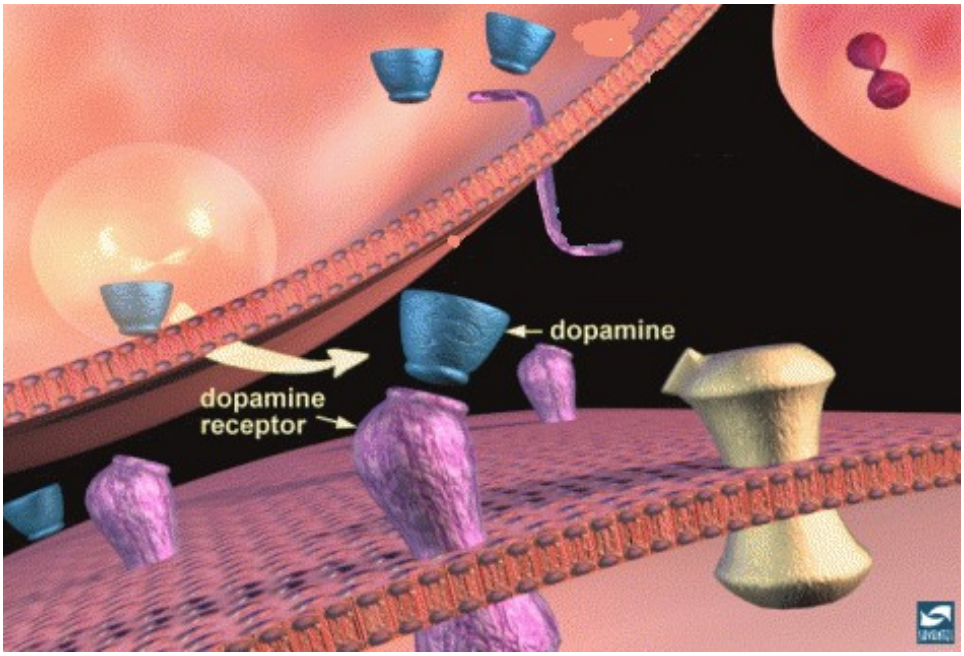


This is a close up of the terminal, or synapse. In the terminal, the wave of incoming electrical energy triggers the vesicles filled with the neurotransmitter to fuse with the cell membrane and dump the dopamine (in this case) into the very small space between the neurons. The neurotransmitter molecules bind to the receptors and the receptors initiate the electrical impulse down the line.

Dopamine transmission is a central issue.

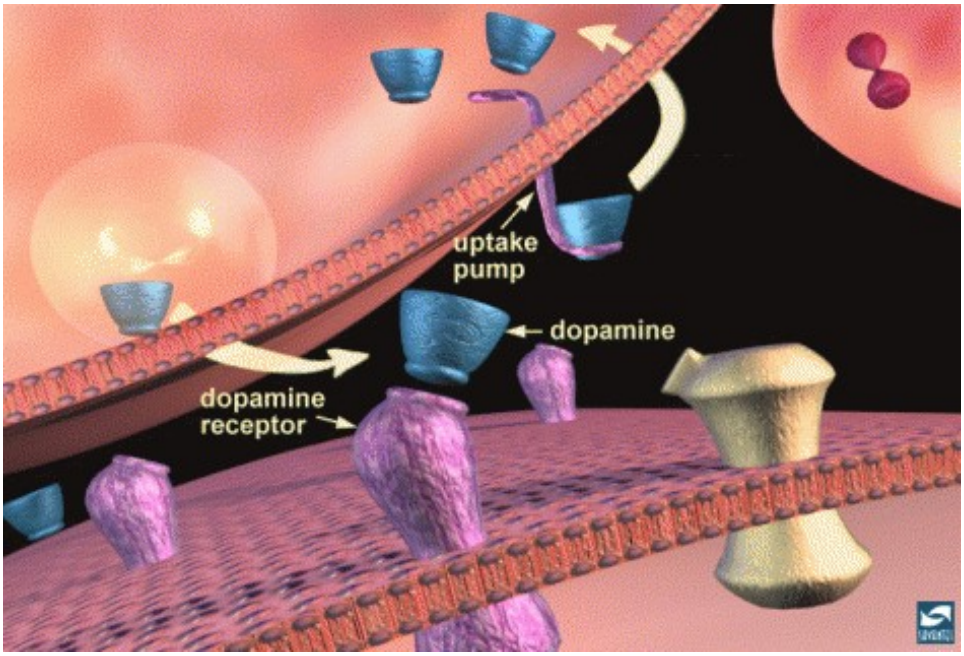
There are many different chemicals in the body that are used as neurotransmitters. We are going to zero in on one that plays a major part in addiction medicine.

Dopamine is the chemical that is released to send the signal.



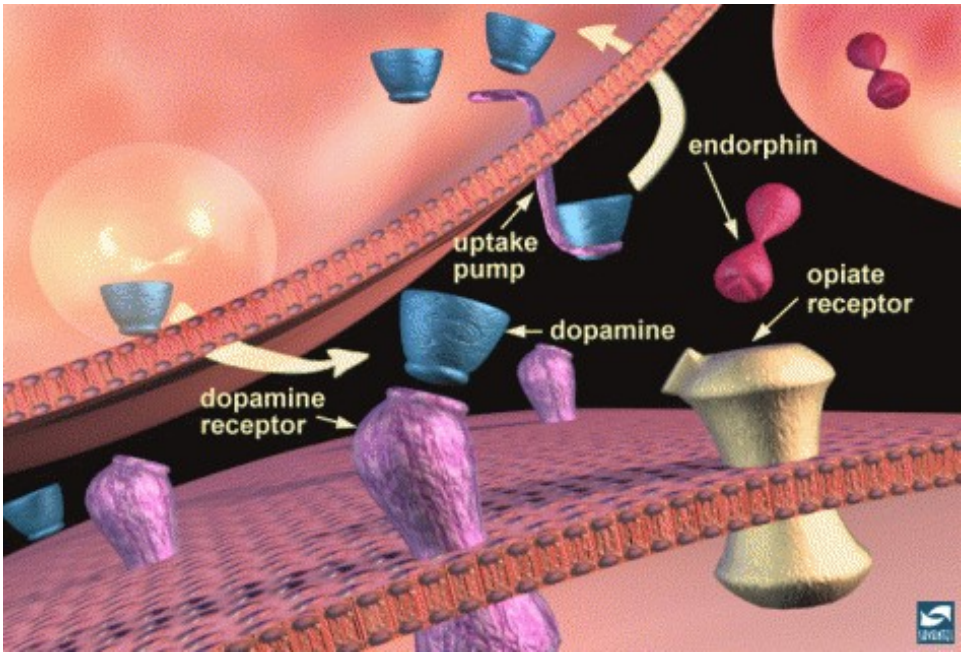
Here we see dopamine, a neurotransmitter, being released into the cleft, the space between the neurons. It is a microscopic space, and only takes moments for the dopamine to be released and travel across the space.

Dopamine receptors receive the signal.



The dopamine receptors bind the dopamine, and the message is passed. The dopamine doesn't stick permanently, but releases back into the cleft. Here it is taken up back into the presynaptic cell by means of a re-entry pump.

Endorphins and other transmitters can effect the signal.



The cleft is a complex area. More than one neuron may end at the same place, releasing their own neurotransmitters that may magnify or lessen the effect of the main signal.

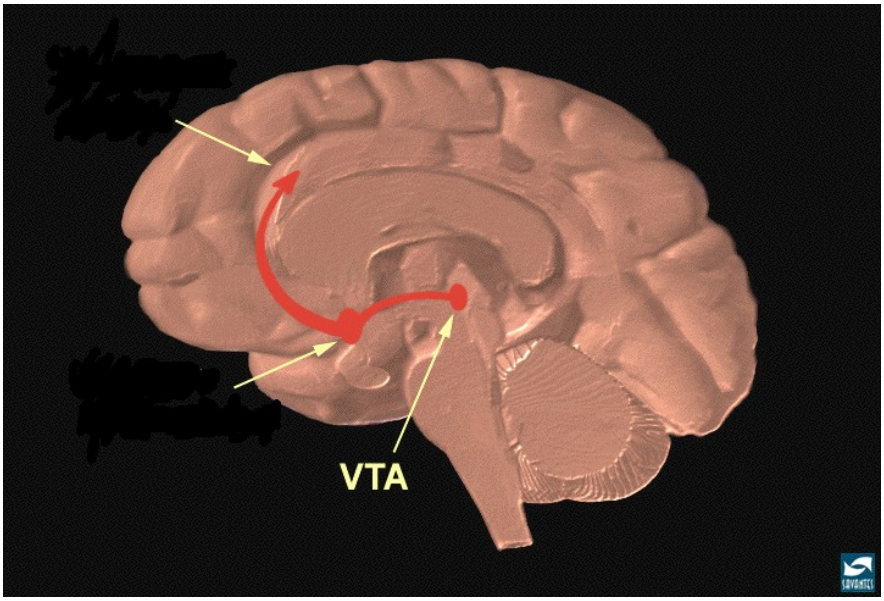
The reward pathway is the critical brain pathway involved in substance abuse.

Our area of interest in regard to drug abuse involves the reward pathway. It is a naturally occurring structure in all animals above amphibians in the evolutionary ladder. This includes dogs, cats, birds, and people.

The reward pathway has three essential structures.

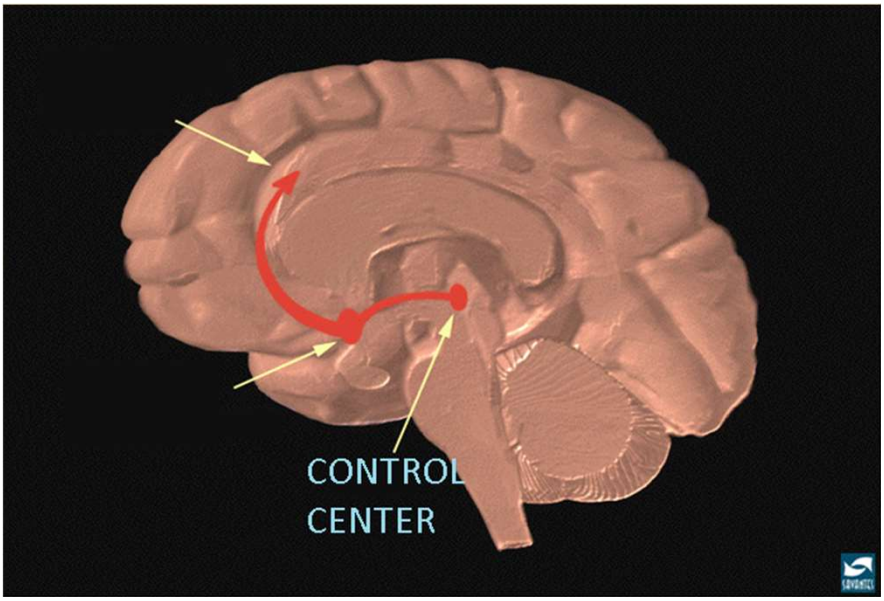
The reward pathway is what makes positive reinforcement possible.

The VTA receives information about sensations from the spinal cord via the thalamus.



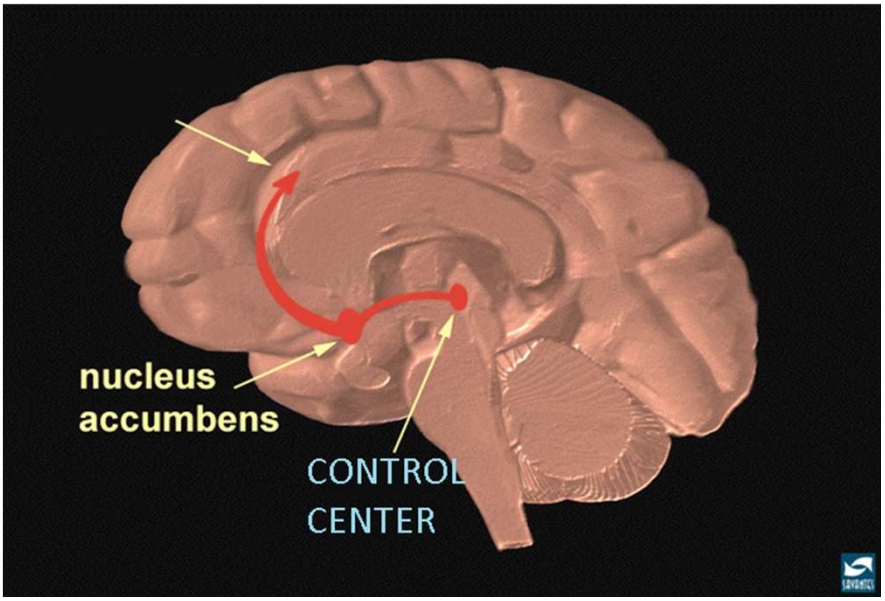
The VTA is hard wired to the thalamus, which you will remember was just activated when we bit our fingers. The VTA receives a signal from other parts of the thalamus when a sensation is determined to be pleasurable. The VTA uses dopamine as its major neurotransmitter.

The VTA receives information about sensations from the spinal cord via the thalamus.



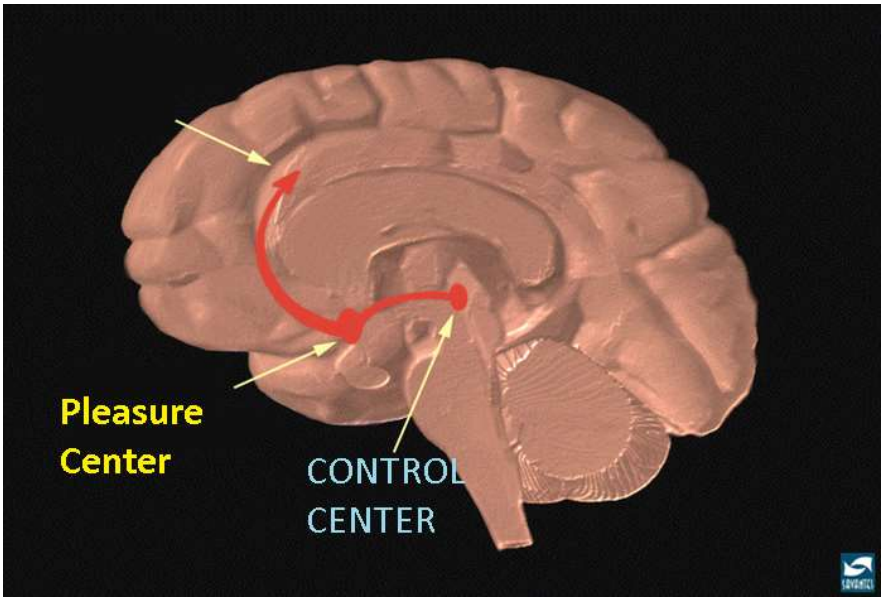
It is the control center; it looks at the information coming in, considers the situation, and initiates the response.

The nucleus accumbens is the pleasure center that is stimulated in reward.



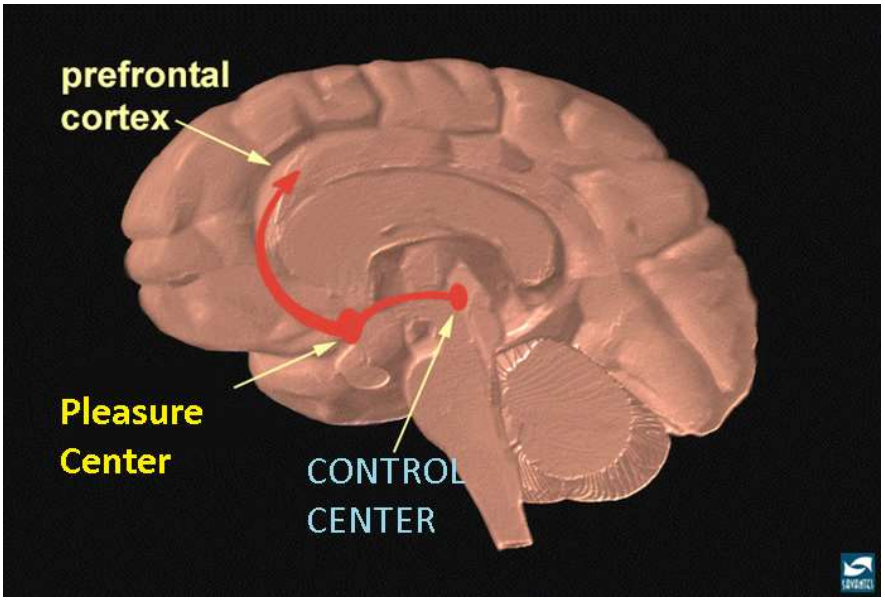
This area, called the nucleus accumbens, is where the VTA axons send their signal. When the VTA neurons release their signal, the nucleus accumbens is activated. The stronger the signal, the stronger the activation and response.

The nucleus accumbens is the pleasure center that is stimulated in reward.



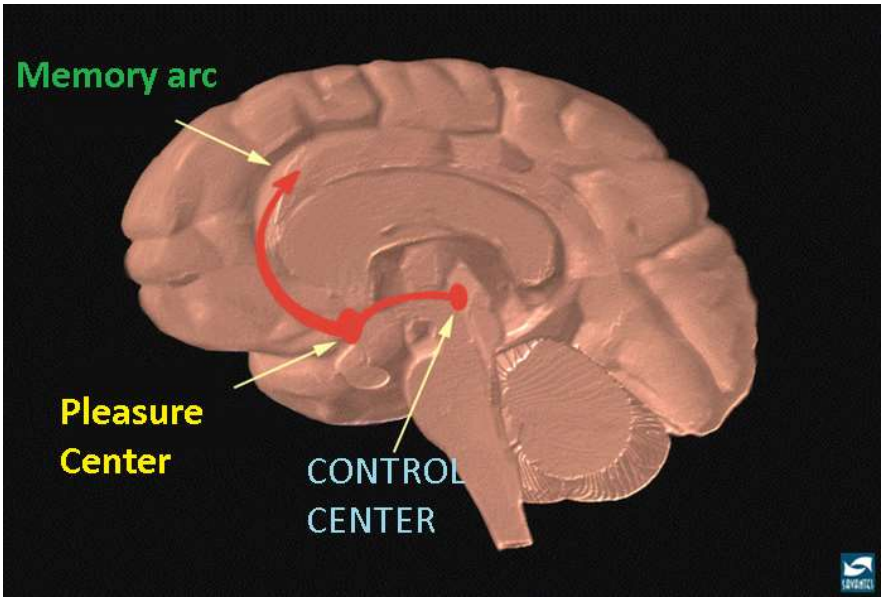
The nucleus accumbens is our brain's pleasure center. Stimulating this area informs us that the sensations we are experiencing are pleasurable.

The prefrontal cortex controls attention, recognition, and triggers remembering.



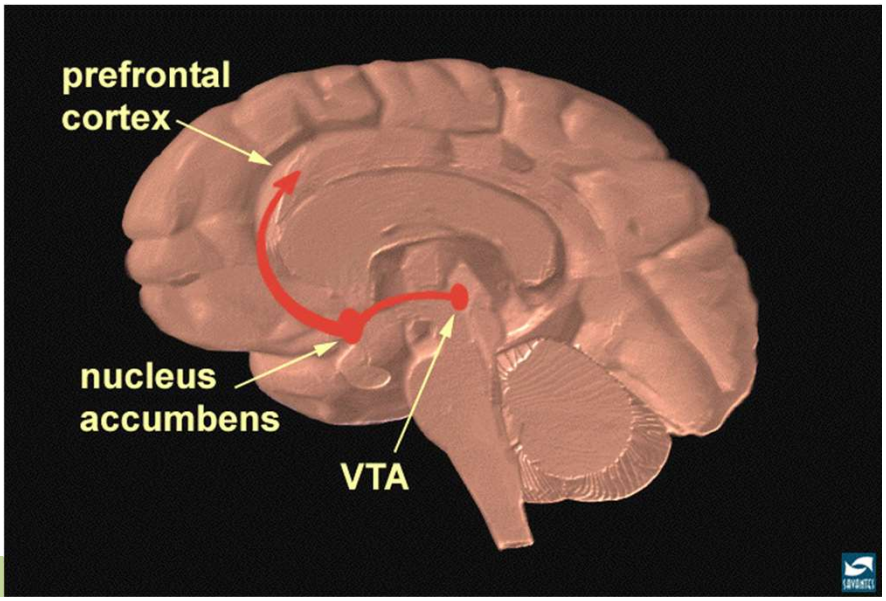
The nucleus accumbens, or pleasure and reward center, sends its axons to the prefrontal cortex. This is the area that directs our conscious thought. It triggers us to pay attention, then to recognize both the pleasure signal and the circumstance that created it.

The prefrontal cortex controls attention, recognition, and triggers remembering.



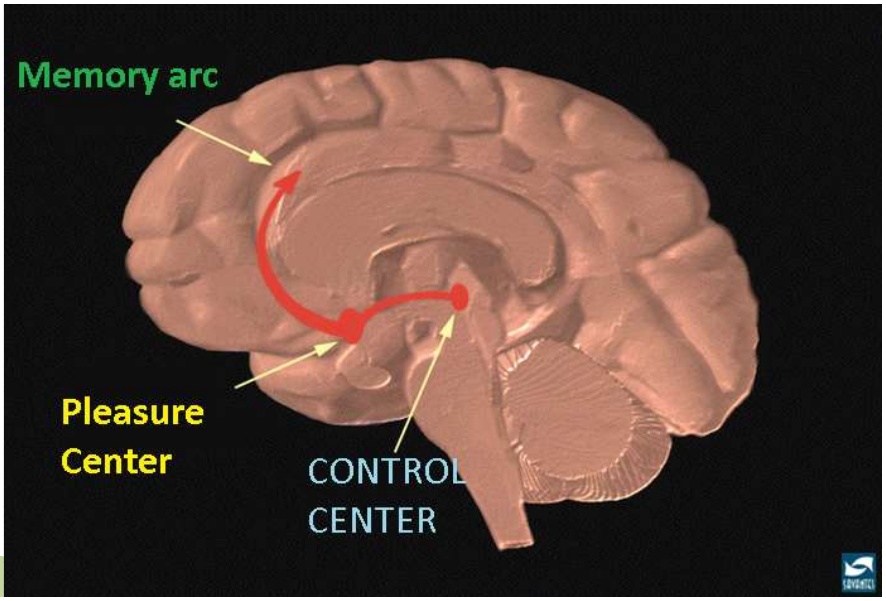
This arcs onward to create and store a pleasurable memory of what occurred. So, the prefrontal cortex is where we debrief and figure out just what occurred, and what the circumstances were that brought this about. Then we store the memory for future use.

Dopamine is the key player in the brain's reflex arc to reinforce pleasurable activities.



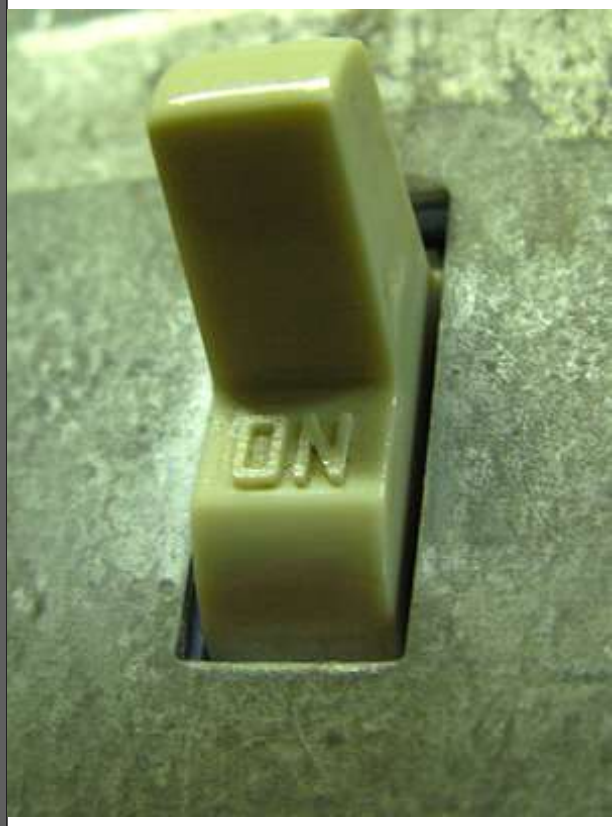
FOLKS, THIS IS THE MONEY SLIDE. The cingulate gyrus and the limbic system are the key players in the human reward pathway.

Dopamine is the key player in the brain's reflex arc to reinforce pleasurable activities.



All pleasurable sensations enter the brain through the spinal cord to the **hypothalamus**. Pleasurable sensations are forwarded to the **nucleus accumbens**. **THIS IS THE PLEASURE CENTER**. Good food, good sex, good music, good sensations of any kind will result in the release of dopamine into the synaptic clefts of the nucleus accumbens. The reflex arc leads to areas of attention, registration and finally long term memory storage. This is how we train animals. This is also how we train people. **QUESTION:** Who has watched people playing slot machines at the casino? Note, humans have the capacity to remember pleasant experiences, and the ability to imagine them in the future. **EVERY DRUG OF ABUSE IN HUMANS HIJACKS THIS PATHWAY**.

The reward pathway can be activated in a number of ways.

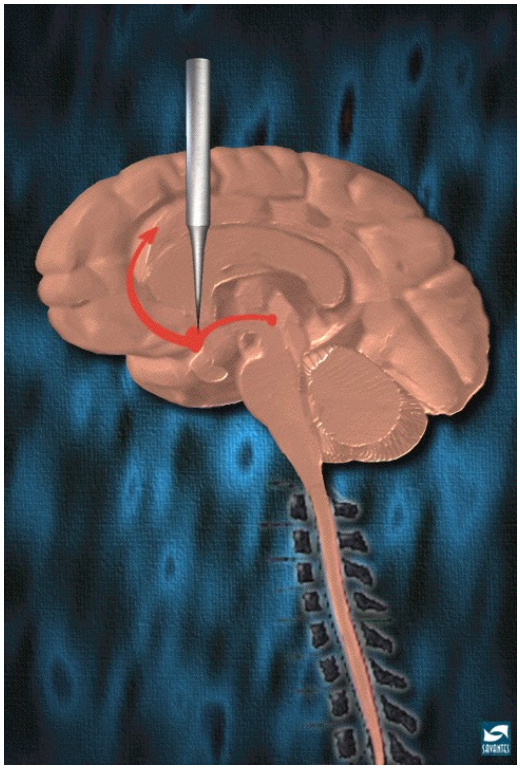


It is safe to say that there are many ways to find pleasure in this world. Humans and other organisms engage in behaviors that are rewarding. These pleasurable feelings are remembered to provide positive reinforcement so that the behavior is repeated.

Natural rewards occur when pleasant sensations cause the VTA to signal the nucleus accumbens.

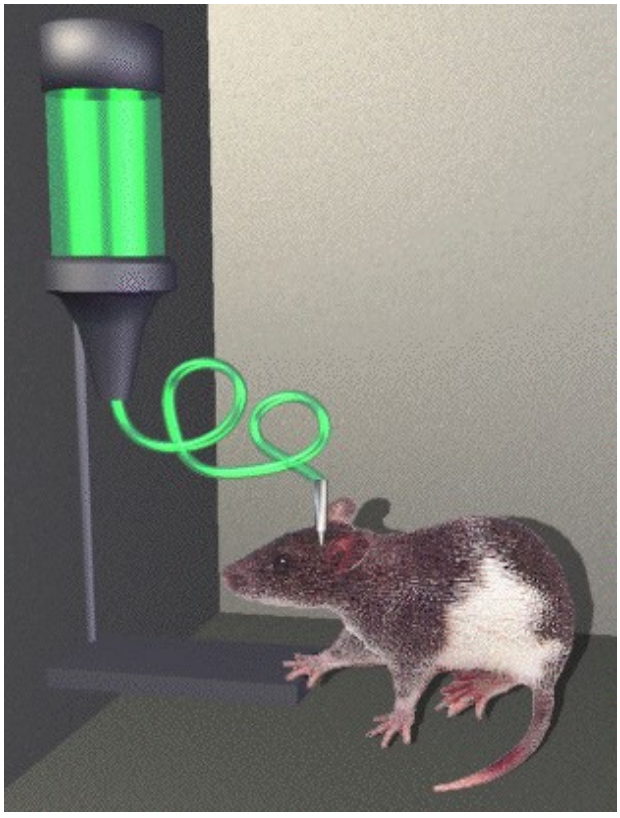
Natural rewards such as food, water, sex and nurturing allow the organism to feel pleasure when eating, drinking, procreating and being nurtured. These are essential behaviors for species survival.

Electrical stimulation of the nucleus accumbens by an electrode can also release dopamine.



Remember, the nucleus accumbens is the pleasure center. No matter how it is stimulated, pleasurable memories result. So, if I train a rat to press a lever and get food, it will press the lever often. If an electrode is placed in the rat's brain and it learns that by pressing a lever, it can get a small electrical jolt to activate the nucleus accumbens, it will press the lever in the same way. If we move the electrode 2 mm away from the nucleus accumbens, the rat will stop pressing.

Stimulation by any chemical that triggers the VTA or nucleus accumbens triggers a reward.



Any chemical introduced into the synapses of the nucleus accumbens that either triggers the dopamine receptors or prevents the reuptake of dopamine that is already there will activate the pleasure center. Cocaine is one such drug; others, like meth, imitate dopamine at the receptors and prevents its reuptake at the pumps.

Addiction occurs when drugs of abuse hijack the reward pathway.

Drug abuse truly means using chemicals to abuse our brain’s reward pathway.

Addiction is a state in which an individual engages in a compulsive behavior.

This can be repetitive drinking, drug use, or behaviors such as gambling.

In the addictive state, the behavior is reinforcing (rewarding or pleasurable).

For a behavior to become addictive, it MUST activate the nucleus accumbens, leading to the attention, recognition and creation of pleasurable memories.

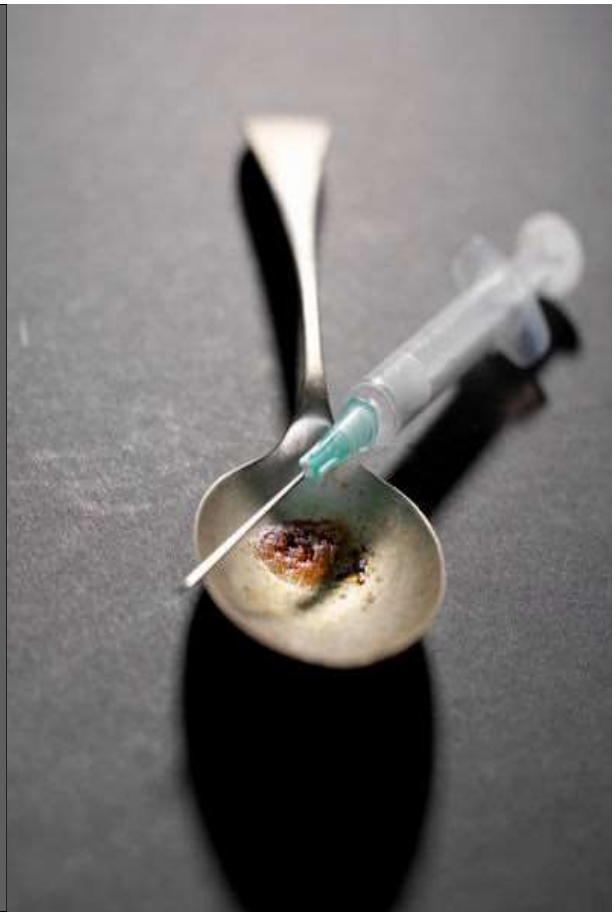
The individual loses control over limiting intake.

It is the loss of control that is the key. Addicted individuals continue this behavior in spite of the fact that they recognize the negative outcomes.

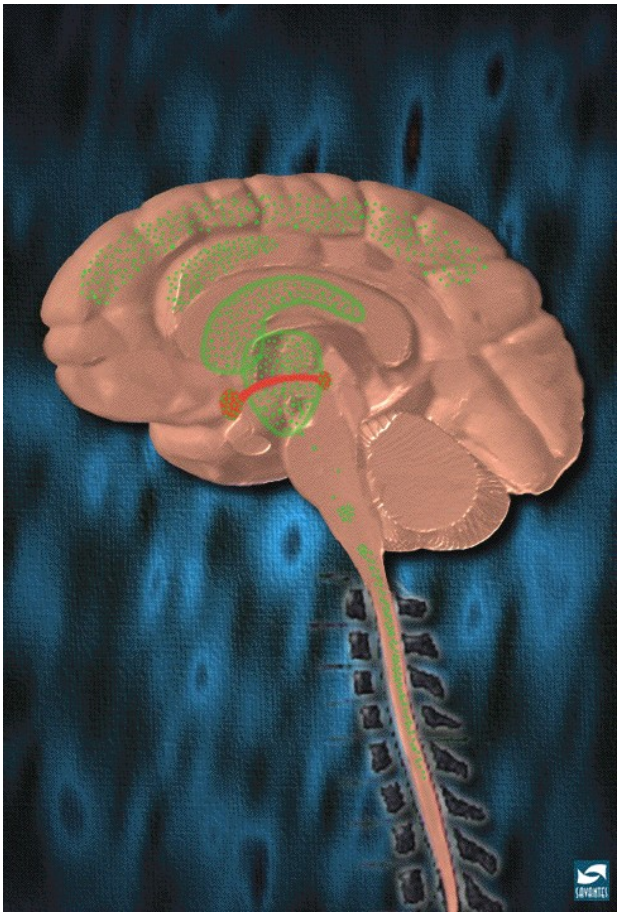
Understand how drugs of abuse act on the brain to cause addiction, tolerance and dependence.

Let us explore the actions of some drugs common to our patients.

heroin is a highly addictive drug that produces euphoria, blocks pain and interacts with the reward pathways.



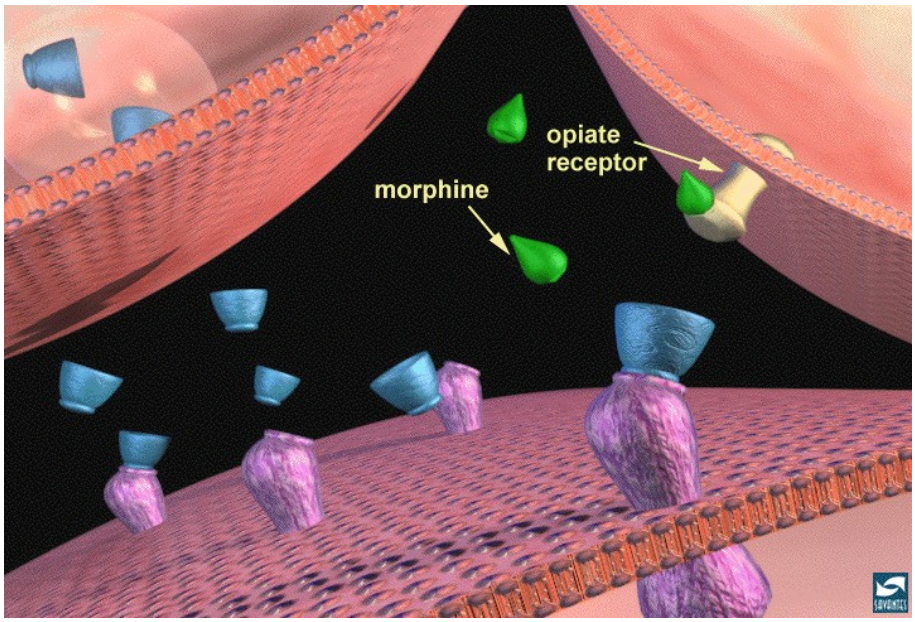
heroin is the prototype drug for all opiates. It becomes morphine in the bloodstream. Oxycodone, oxycontin, dilaudid, opana and other narcotic pain medications are all in the same class.



Heroin localizes its effect in the brain.

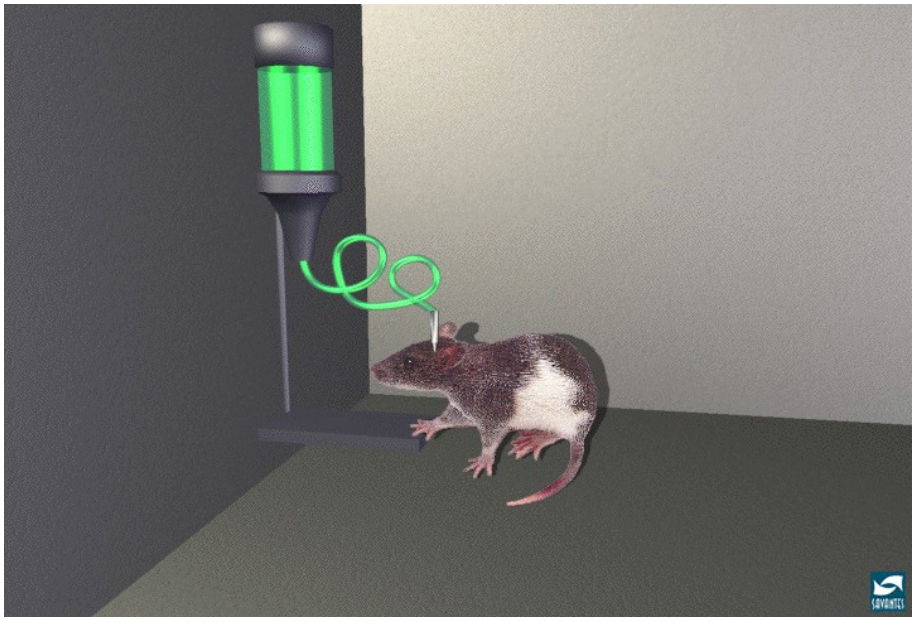
heroin and other drugs like it become morphine in the brain. Morphine binds to opiate receptors in the thalamus, brainstem and spinal cord to block pain signals. It also binds to areas of the cerebral cortex, VTA, nucleus accumbens where is has predictable effects.

Opiates bind to receptors in the nucleus accumbens.



In the nucleus accumbens, opiate receptors exist on neurons neighboring the dopamine neurons coming from the VTA. These neurons usually have an inhibiting effect on the dopamine neuron from the VTA. When opiate receptors are triggered, this neighboring cell sends a signal to the presynaptic dopamine neuron to increase its release of dopamine. This activates the pleasure center directly. This initiates the reflex arc of attention, recognition and memory, creating a powerful positive reinforcement pattern.

Tolerance and dependence occur.

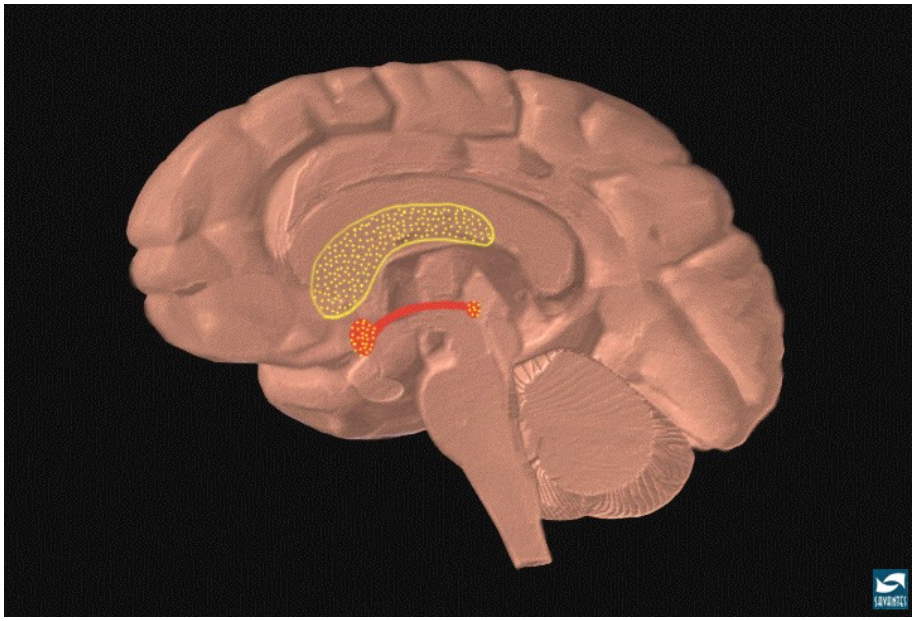


Here, a rat is receiving morphine directly into his nucleus accumbens, or pleasure center. He will learn that pressing the lever is pleasurable. He will then show addictive behavior, pressing it as often as he can. He will ignore food levers, as they are not as pleasurable. He craves the morphine. This is addiction. Over time, he will need larger and larger doses to get the same result. This is due to changes in the receptor sites, and dwindling supplies of dopamine. This is known as tolerance. Finally, he will reach a point where his body and mind cannot function in the absence of this drug. This is known as dependence. We will discuss this further in the next section.

Meth and cocaine produce euphoria and interact with the reward pathways.

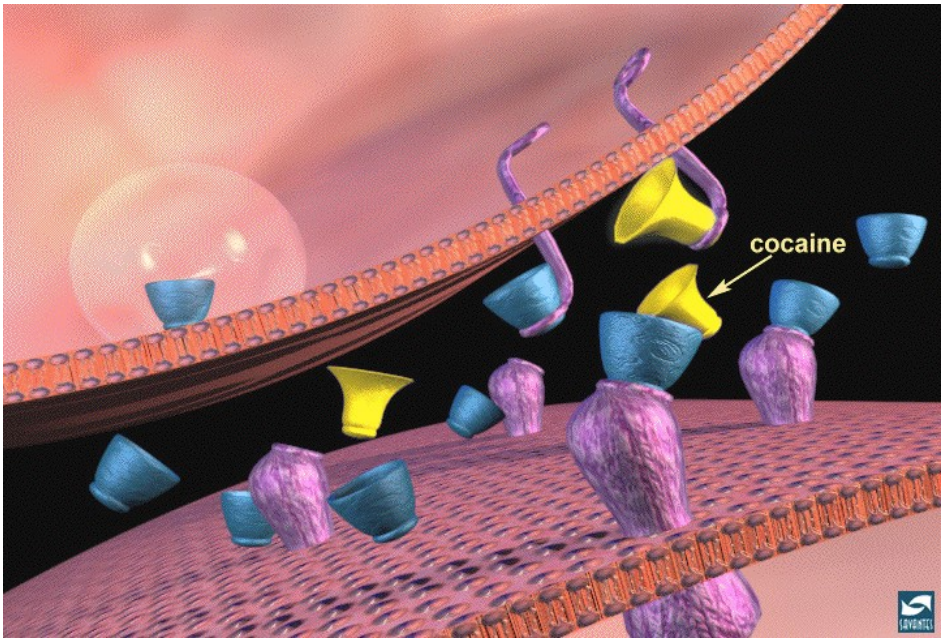
Methamphetamines (meth or crank, ecstacy and similar drugs) are all called sympathemimetics. This is because they trigger the body's sympathetic nervous system, which is responsible for fight or flight. In the body it imitates adrenaline. In the brain, it imitates dopamine.

Meth and cocaine reach the brain quickly when smoked or injected.



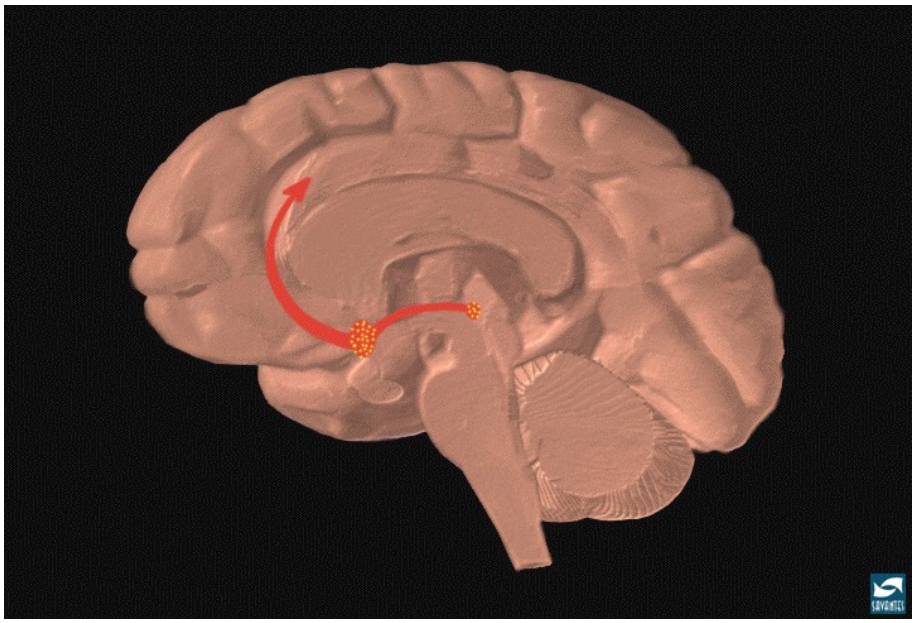
When smoked or injected, meth reaches the brain quickly. Its main binding sites are in the reward pathway. It also binds in the caudate nucleus. This area tends to trigger repetitive behaviors such as pacing, nail biting, scratching and picking.

Meth and cocaine act directly on the nucleus accumbens.



IN the case of cocaine, the molecule enters the cleft and blocks the pumps from removing the dopamine that has already been released and recycling it. As a result, more dopamine stays in the cleft, repeatedly binding to the receptors and activating the pleasure center. Meth molecules are even more potent – They imitate dopamine and both bind to the receptors and prevent reuptake.

Repeated use leads to addiction and dependence.



Just as in the opiate example above, repeated cycles of use lead to addiction, tolerance and dependence. Although the two drugs act in different ways, the final common pathway is the same. With repeated use, the body comes to rely on the drug to maintain reward feelings. The person no longer gets pleasure from natural sources. He has anhedonia. This is the state of dependence. To avoid this, the user goes back to using.

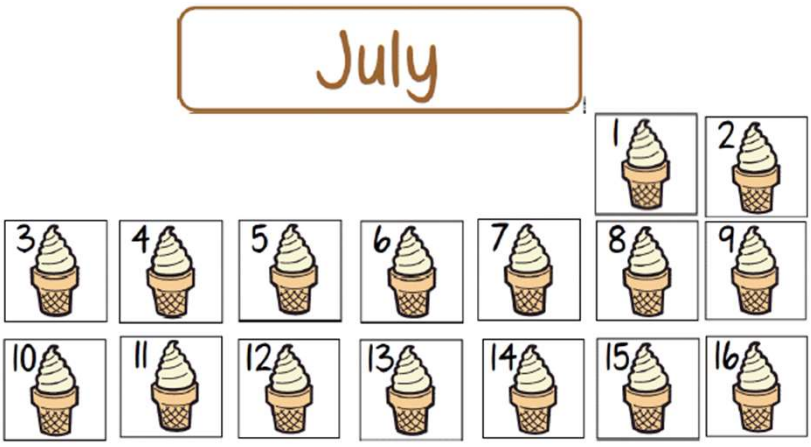
Addiction, tolerance and dependence are separate but related features of drug use.

For instance, oncology patients with chronic pain will develop tolerance and dependence, but not necessarily addiction.

Tolerance occurs when larger doses of medication are required to achieve the effect.

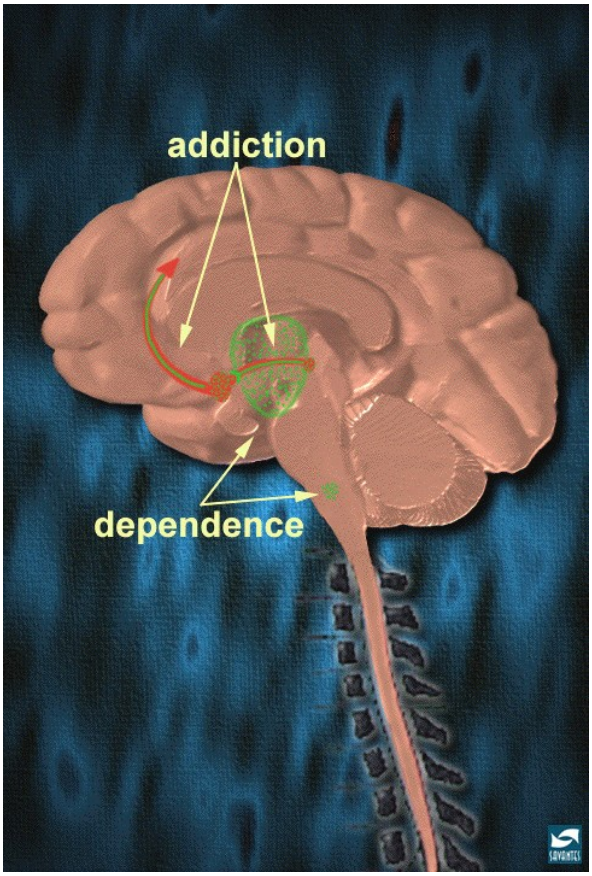
If addiction is the craving, then tolerance leads to the need for increased amounts to satisfy the craving.

Dependence is not the same as tolerance or addiction.



In dependence, the organism cannot function normally without the substance. Chronic daily alcohol use is a good example.

Drug dependence and addiction occur in different areas.



Here we see that the sites for addiction and dependence for our two example drug classes.

So, when you new client presents like this …

And your history and interactions suggest this …

Use the knowledge you have gained here to recognize addiction driven behaviors and to intervene!

Your actions can help to prevent this!

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