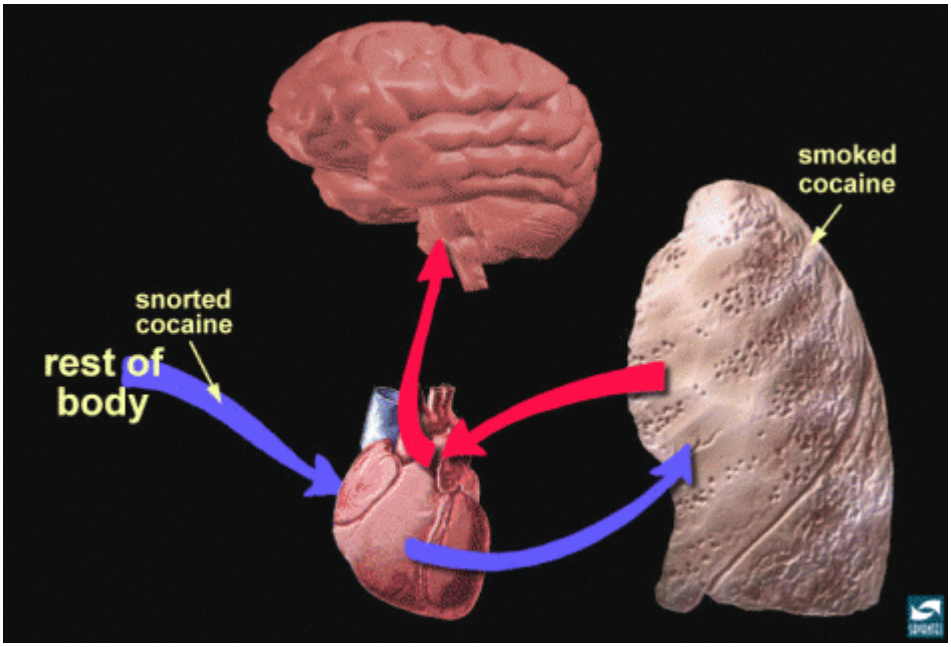
NIDA NATIONAL INSTITUTE ON DRUG ABUSE
The Science of Drug Abuse & Addiction

The Neurobiology of Drug Addiction

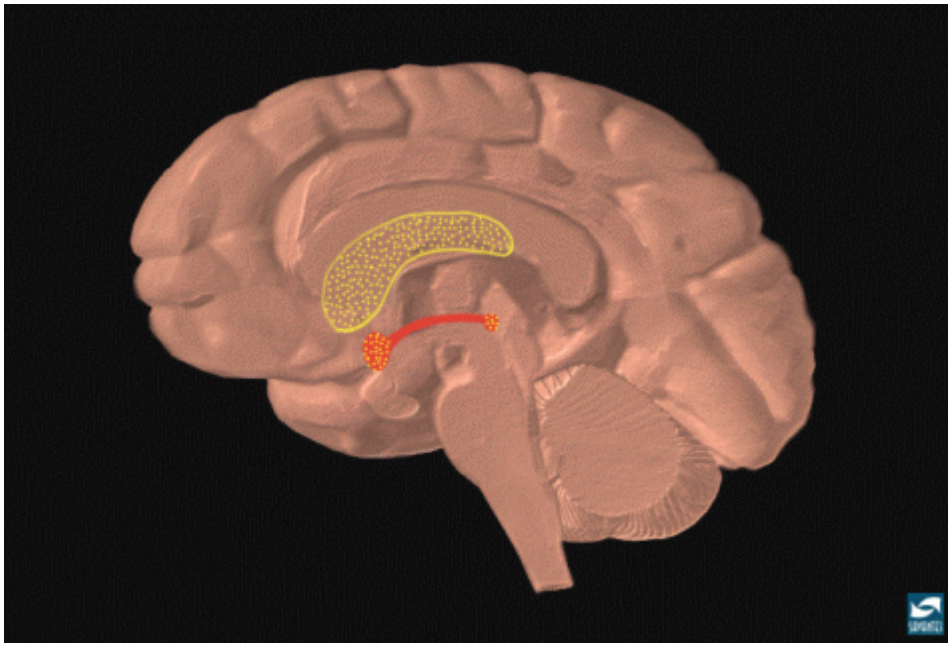
Cocaine is also an addictive drug, and like heroin, not all users become addicted. However, with the advent of crack cocaine (the freebase), the rate of addiction to cocaine has increased considerably.

2: Snorting vs smoking cocaine: different addictive liabilities



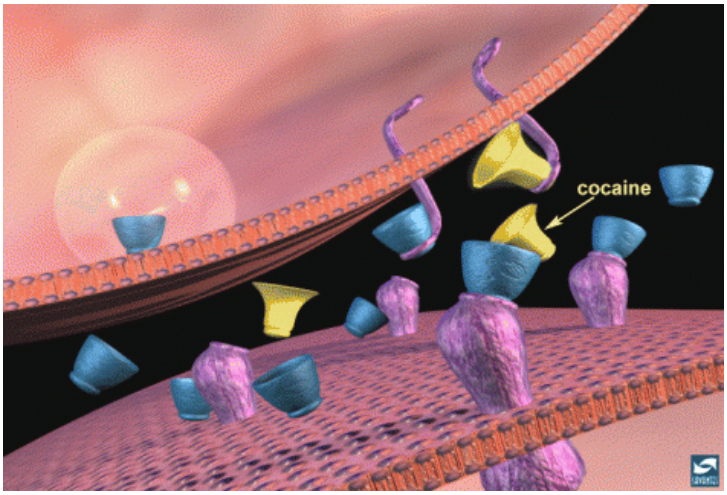
Historically cocaine abuse involved snorting the powdered form (the hydrochloride salt). When cocaine is processed to form the freebase, it can be smoked. Heating the hydrochloride salt form of cocaine will destroy it; the freebase can be volatilized at high temperature without any destruction of the compound. Smoking gets the drug to the brain more quickly than does snorting. Show the audience why this happens. Snorting requires that the cocaine travels from the blood vessels in the nose to the heart (purple arrow), where it gets pumped to the lungs (purple arrow) to be oxygenated. The oxygenated blood (red arrows) carrying the cocaine then travels back to the heart where it is pumped out to the organs of the body, including the brain. However, smoking bypasses much of this, the cocaine goes from the lungs directly to the heart and up to the brain. The faster a drug with addictive liability reaches the brain, the more likely it will be abused. Thus, the time between taking the drug and the positive reinforcing or rewarding effects that are produced can determine the likelihood of abuse.

3: Localization of cocaine "binding sites"



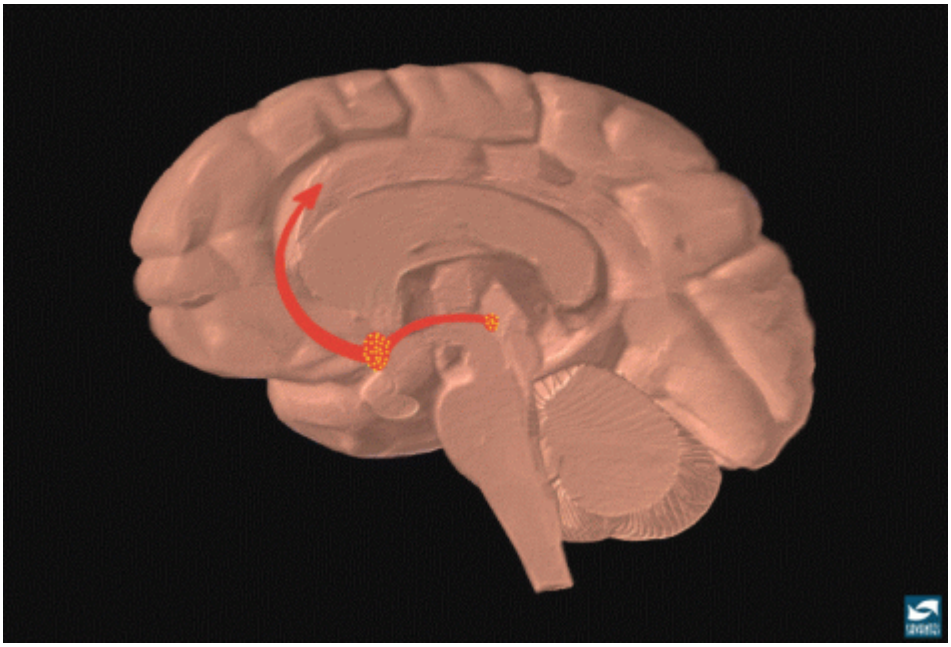
When a person smokes or snorts cocaine, it reaches all areas of the brain, but it binds to sites in some very specific areas. These are highlighted with the yellow dots: the VTA, the nucleus accumbens, and the caudate nucleus (the largest structure). Point out that cocaine binds especially in the reward areas that you have just discussed. The binding of cocaine in other areas such as the caudate nucleus can explain other effects such as increased stereotypic (or repetitive) behaviors (pacing, nail-biting, scratching, etc..)

4: Dopamine binding to receptors and uptake pumps in the nucleus accumbens: the action of cocaine



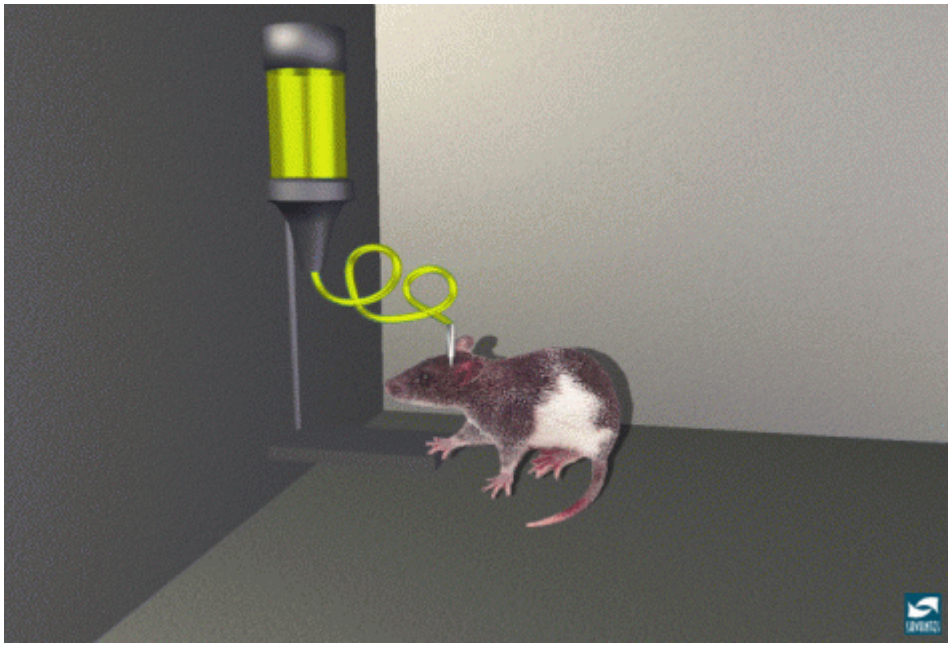
Explain that cocaine binds to sites in areas of the brain that are rich in dopamine synapses such as the VTA and the nucleus accumbens. Review dopamine transmission in the close-up of a synapse in the nucleus accumbens. Point to dopamine (inside the terminal) that is released into the synaptic space. The dopamine binds to dopamine receptors and then is taken up by uptake pumps back into the terminal. Now show what happens when cocaine is present (yellow). Cocaine binds to the uptake pumps and prevents them from transporting dopamine back into the neuron terminal. So more dopamine builds up in the synaptic space and it is free to activate more dopamine receptors. This is the same effect that you showed in an earlier image with morphine, where morphine increased dopamine release from the terminal to produce more dopamine in the synaptic space.

5: Cocaine dependence and activation of the reward pathway



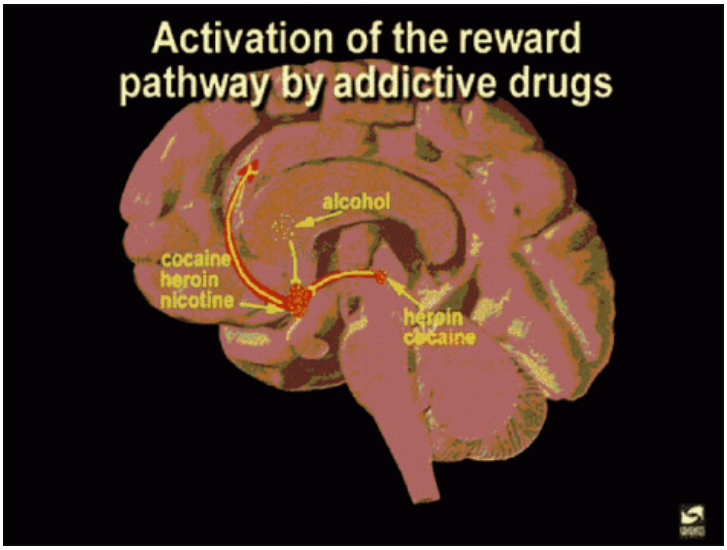
Review where cocaine binds within the reward pathway (the VTA and the nucleus accumbens). As a result of cocaine's actions in the nucleus accumbens (point to the dots of cocaine in the VTA and nucleus accumbens), there are increased impulses leaving the nucleus accumbens to activate the reward system. This pathway can be activated even in the absence of cocaine (i.e., during craving). Indicate that with repeated use of cocaine, the body relies on this drug to maintain rewarding feelings. The person is no longer able to feel the positive reinforcement or pleasurable feelings of natural rewards (i.e. food, water, sex)--the person is only able to feel pleasure from the cocaine. Thus the user becomes dependent and when the cocaine is no longer present, anhedonia (inability to feel pleasure) and depression emerge as part of a withdrawal syndrome. To avoid this, the user goes back to the cocaine. Unlike the example for morphine, cocaine addiction (i.e., craving) and dependence (i.e., anhedonia) both involve structures in the reward pathway.

6: Rats self-administer cocaine



Scientists have measured increased dopamine levels in the synapses of the reward pathway in rats self-administering cocaine. Just as they did for heroin, rats will press a bar to receive injections of cocaine directly into areas of the reward pathway such as the nucleus accumbens and the VTA. Again, if the injection needle is placed near these regions (but not in them), the rat will not press the bar to receive the cocaine. The ability of rats to self-administer cocaine is an excellent predictor of the addictive potential of this drug.

7: Summary: addictive drugs activate the reward system via increasing dopamine neurotransmission



In this last image, the reward pathway is shown along with several drugs that have addictive potential. Just as heroin or morphine and cocaine activate the reward pathway in the VTA and nucleus accumbens, other drugs such as nicotine and alcohol activate this pathway as well, although sometimes indirectly (point to the globus pallidus, an area activated by alcohol that connects to the reward pathway). Although each drug has a different mechanism of action, each drug increases the activity of the reward pathway by increasing dopamine transmission. Because of the way our brains are designed, and because these drugs activate this particular brain pathway for reward, they have the ability to be abused. Thus, addiction is truly a disease of the brain. As scientists learn more about this disease, they may help to find an effective treatment strategy for the recovering addict.

Background Information for the Presenter

Objectives

The objective of the teaching packet is to illustrate to the audience the basic function of the brain, the neurobiological basis for addiction and the actions of heroin and cocaine. The packet is arranged in 4 sections. The first section introduces the brain and presents some basic neurobiology, the second introduces the reward pathway and the third and fourth present the mechanism of action of heroin and cocaine and how each affects the reward system.

Before Using the Teaching Packet

- Know your target audience. Be prepared to adjust your presentation depending on the degree of education and training of your audience.
- Read the narrative script and practice the presentation. Be prepared to define any word used in the presentation. If you need additional information, several reference materials are also included at the end.

General Instructions

- The presentation should take approximately 30-40 minutes (without questions).
- Use the narrative text as a guide, it need not be repeated word-for-word.

Additional Reference Material

1. G. Hanson and P.J. Venturelli. Drugs and Society, Jones and Barlett Publishers, Boston, 1995.
2. O. Ray and C. Ksir. Drugs, Society, and Human Behavior, Mosby, St. Louis, 1996.
3. R.R. Levine, C.A. Walsh and R.D. Schwartz. Pharmacology: Drug Actions and Reactions, Parthenon Publishing Group, New York, 1996.