



STIMULANTS

The Brain's Response to Drugs

BACKGROUND

Stimulant drugs such as cocaine, "crack," amphetamines, and caffeine are substances that speed up activity in the brain and spinal cord. This, in turn, can cause the heart to beat faster and blood pressure and metabolism to increase. Stimulants often influence a person to be more talkative and anxious and to experience feelings of exhilaration.

Use of cocaine and other stimulants can cause the heart to beat abnormally fast and at an unsteady rate. Use of these drugs also narrows blood vessels, reducing the flow of blood and oxygen to the heart, which results in "starving" the heart muscle. Even professional athletes whose bodies are well-conditioned have succumbed to cocaine's ability to cause heart failure. Researchers currently have no way to detect who may be more susceptible to these effects.

MECHANISM OF ACTION

Cocaine acts on the pleasure circuit to prevent reabsorption of the neurotransmitter dopamine after its release from nerve cells. Normally, neurons that are part of the pleasure circuit release dopamine, which then crosses the synapse to stimulate another neuron in the pleasure circuit. Once this has been accomplished, the dopamine is picked up by a transporter molecule and carried back into the original neuron. However, because cocaine binds to the dopamine transporter molecule, it prevents the reabsorption of dopamine. This causes a build up of dopamine in the synapse, which results in strong feelings of pleasure and even euphoria. The excess dopamine that accumulates in the synapse causes the neurons that have dopamine receptors to decrease the number of receptors they make. This is called

down regulation. When cocaine is no longer taken and dopamine levels return to their normal (i.e., lower) concentration, the smaller number of dopamine receptors that are available for the neurotransmitter to bind to is insufficient to fully activate nerve cells. This results in a drug "craving," which is a way of telling the addict to get the level of dopamine back up by taking cocaine. Cocaine also binds to the transporters for other neurotransmitters, including serotonin and norepinephrine, and blocks their re-uptake. Scientists are still unsure about the effects of cocaine's inter-action with these other neurotransmitters.

Cocaine has also been found to specifically affect the prefrontal cortex and amygdala, which are involved in aspects of memory and learning. The amygdala has been linked to emotional aspects of memory. Researchers believe that a neural network involving these brain regions reacts to environmental cues and activates memories, and this triggers biochemical changes that result in cocaine craving.



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Amphetamines, such as methamphetamine, also act on the pleasure circuit by altering the levels of certain neurotransmitters present in the synapse, but the mechanism is different from that of cocaine. Chemically, methamphetamine is closely related to amphetamine, but it has greater effects on the brain. Methamphetamine is also chemically similar to dopamine and another neurotransmitter, norepinephrine. It produces its effects by causing dopamine and norepinephrine to be released into the synapse in several areas of the brain, including the nucleus accumbens, prefrontal cortex, and the striatum, a brain area involved in movement. Specifically, methamphetamine enters nerve terminals by passing directly through nerve cell membranes. It is also carried into the nerve terminals by transporter molecules that normally carry dopamine or norepinephrine from the synapse back into the nerve terminal. Once in the nerve terminal, methamphetamine enters dopamine and norepinephrine containing vesicles and causes the release of these neurotransmitters. Excess dopamine and norepinephrine would normally be destroyed by enzymes in the cell, however, methamphetamine blocks this breakdown. The excess neurotransmitters are then carried by transporter molecules out of the neuron and into the synapse. Once in the synapse, the high concentration of dopamine causes feelings of pleasure and euphoria. The excess norepinephrine may be responsible for the alertness and anti-fatigue effects of methamphetamine.

Methamphetamine can also affect the brain in other ways. It can cause:

- cerebral edema
- brain hemorrhage
- paranoia
- hallucinations

Some of methamphetamine's effects on the brain may be long-lasting and even permanent. Research with laboratory animals has demonstrated that exposure to a single, high-dose of methamphetamine or prolonged exposure at low doses destroys up to fifty percent of the dopamine-producing neurons in certain parts of the brain. Studies are currently underway to study the long-term effects of chronic methamphetamine abuse in humans. Although the damage of chronic methamphetamine abuse may not be immediately apparent in humans,

scientists believe that the progressive decrease in numbers of dopamine-producing neurons may lead to Parkinson's disease.

Methamphetamine also has widespread effects on other parts of the body. It can cause:

- high blood pressure
- arrhythmias
- chest pain
- shortness of breath
- nausea, vomiting, and diarrhea
- increased body temperature which can be lethal in overdose situations



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