

Scientists seek to manage dopamine's good and bad sides

October 7 2009, By Robert S. Boyd

The good, the bad and the ugly: That's a quick summary of the effects of dopamine, a natural brain chemical that's linked to pleasure, addiction and disease.

This little molecule -- it consists of only 22 atoms -- is essential to life but can be a curse sometimes. Too much or too little of it can lead to [drug abuse](#), reckless thrill-seeking, obesity, the tremors of Parkinson's disease, even restless leg syndrome, an irresistible urge to move your legs.

Although [dopamine](#) was identified almost a century ago, brain scientists are still trying to figure out how to manage its undesirable effects, such as cocaine or [nicotine addiction](#).

"There is no currently approved medication for treating cocaine addiction," Nora Volkow, the director of the National Institute on Drug Abuse, said Monday as she announced the successful preliminary test of a possible future vaccine for the dangerous drug.

"We are looking at the potential for new medications that reduce the brain's sensitivity to these conditioned drug cues and would give patients a fighting chance to manage their urges," Anna Childress, a psychiatrist at the University of Pennsylvania School of Medicine in Philadelphia, told a conference of [neuroscientists](#) in Washington. "We have a brain hard-wired to appreciate rewards, and cocaine and other drugs of abuse latch onto this system."

Dopamine is the key to that system. A "neurotransmitter" that helps brain cells, or neurons, communicate with one another, dopamine is released into the brain by pleasurable experiences such as eating, having sex or indulging in drugs.

Its presence creates feelings of satisfaction, enjoyment or excitement, and so motivates people to repeat behavior, good or bad.

Dr. Jay Giedd, a psychiatrist at the National Institute of Mental Health in Rockville, Md., explained dopamine's effects in a radio interview earlier this year:

"If we make good decisions, our dopamine goes up. It tells our brain, you know, 'good call, that was the right move, you know, do that again next time,' and it literally changes the anatomy of the brain. It strengthens certain connections. It decreases others."

The problem is that behavior that shouldn't be repeated also releases dopamine.

Researchers are studying dopamine's role in conditions such as the following:

ADDICTION

Drugs such as cocaine, amphetamines and nicotine flood nerve circuits in the brain with dopamine. This produces the euphoric effects that smokers and drug users crave and motivates them to repeat the behavior.

"Repeated exposures to cocaine result in excessive dopamine levels at nerve terminals," said Deirdre McCarthy, a neuroscientist at Massachusetts General Hospital in Charlestown.

Here's how excess dopamine leads to addiction:

A brain cell sends dopamine molecules across a narrow gap to places called "receptors" on the surface of another cell, generating an electric signal. Usually, "transporters" then collect unused dopamine and ship it back to the sending cell. Cocaine blocks the transporters, however, leaving more of the drug in the spaces between cells. This dopamine overload gives users their cocaine "high."

The potential vaccine for cocaine abusers that Volkow announced Monday blocks cocaine that's injected or inhaled into the bloodstream from crossing the "blood-brain barrier," which protects the brain from contamination by undesirable substances.

In a related move, the National Institute on Drug Abuse granted \$10 million last week to a small pharmaceutical firm in Rockville, Md., for an advanced trial of a vaccine for nicotine addiction.

OBESITY

Recent studies show a connection between obesity and low dopamine levels in the brain.

Experiments with rats show that a weakened dopamine system reduced the pleasurable feeling associated with eating. The rats compensated by overeating and soon became obese, according to Emmanuel Pothos, a neuroscientist at Tufts University School of Medicine in Boston.

Pothos said there was evidence that obese humans also had a shortage of dopamine. "These findings have important implications in our understanding of the obesity epidemic," he said.

"We eat not only for nourishment but also for pleasure," wrote Gerald

Weissmann, the editor in chief of The FASEB Journal, an experimental biology publication. "Now we know why so many people stay addicted to food: it fuels the midbrain pleasure machinery."

GAMBLING

Prescription medications that stimulate dopamine production can have a strange side effect, occasionally turning people into reckless gamblers.

"Some ordinary people with regular lives taking this medication all at once started to gamble and engage in hazardous games of luck, a behavior that stopped after discontinuing the drug," Birgit Abler, a researcher at the University of Ulm, Germany, told the neuroscientists' conference.

Dopamine also plays a role in other serious ailments. Scientists hope to discover ways to ease their effects.

PARKINSON'S DISEASE

Parkinson's disease is a slow-developing movement disorder caused by the gradual deaths of neurons that supply dopamine, according to James Surmeier, a Parkinson's expert at Northwestern University in Evanston, Ill. Patients suffer uncontrollable trembling and stiffness of the limbs.

Researchers are seeking drugs that slow down the loss of dopamine neurons, said Marina Picciotto, a neuroscientist at Yale University in New Haven, Conn.

The herbal supplement L-Dopa, also known as Levodopa, may be taken to create more dopamine, thereby relieving the shortage that leads to Parkinson's.

ADHD

A brain imaging study at Brookhaven National Laboratory in Upton, N.Y., found low levels of dopamine in people with attention deficit hyperactivity disorder.

"These deficits in the brain's reward system may help explain the clinical symptoms of ADHD, including inattention and reduced motivation, as well as the propensity for complications such as drug abuse and obesity among ADHD patients," Volkow reported in the Sept. 9 issue of the *Journal of the American Medical Association*.

ON THE WEB

University of Texas dopamine research:

www.utexas.edu/research/asrec/dopamine.html

Dopamine and addiction: www.drugabuse.gov/scienceofaddiction/

National Institute on Drug Abuse:

www.nida.nih.gov/Infofacts/understand.html

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