MedicalXpress

Meth addiction mechanism discovered

April 9 2008

Researchers have identified, for the first time, long-term changes in the brain circuitry of methamphetamine-addicted mice that can explain why the craving of addiction is so stubborn and long-lived. The research could lead to more effective treatments for addiction to methamphetamine and related drugs.

Nigel Bamford and colleagues published their findings in the April 10, 2008, issue of the journal *Neuron*, published by Cell Press.

In their experiments, the researchers treated mice with methamphetamine and studied how long exposure to the drug affected levels of the brain chemical dopamine. Researchers have long known that methamphetamine and amphetamine enhance release of dopamine at the connections between neurons, called synapses. Dopamine is one of the brain's major neurotransmitters, the chemical messengers by which one neuron triggers its neighbor to fire a nerve impulse.

The researchers concentrated on the dopamine machinery in the brain's corticostriatal region, believed to harbor the "habit" circuitry central to the compulsive drug-seeking of addiction to methamphetamine and amphetamine.

To reveal the flow of dopamine, they used a fluorescent tracer dye that is taken up by the same microscopic sacs, called vesicles, that store and release dopamine in the process of signaling between neurons. Using microscopy to follow the movement of the dye, they could study how methamphetamine affected the dopamine transport machinery in the

brain.

Their studies revealed that giving the animals the drug long enough to cause chronic effects caused a depression of the synaptic dopamine machinery in the corticostriatal region that lasted for months after the drug was withdrawn. However, giving the animals a dose of methamphetamine reversed the depressive effects on the synaptic machinery.

The researchers' experiments also revealed details of how the drug produced its long-term effect—by altering specific types of receptors for dopamine and another neurotransmitter, acetylcholine.

They concluded that the mechanism they discovered "might provide a synaptic basis that underlies addiction and habit learning and their long-term maintenance."

In a preview of the article in the same issue of *Neuron*, Jeremy Day and Regina Carelli speculated that the drug effects that the researchers discovered might disrupt the normal machinery for learning in the brain, "leading to aberrant reward processing and action selection. If so, the discovery of methods to reverse this plasticity may be a promising avenue for addiction treatment," they wrote.

Source: Cell Press