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Like Methamphetamine, "Ecstasy" May Cause Long-Term Brain Damage

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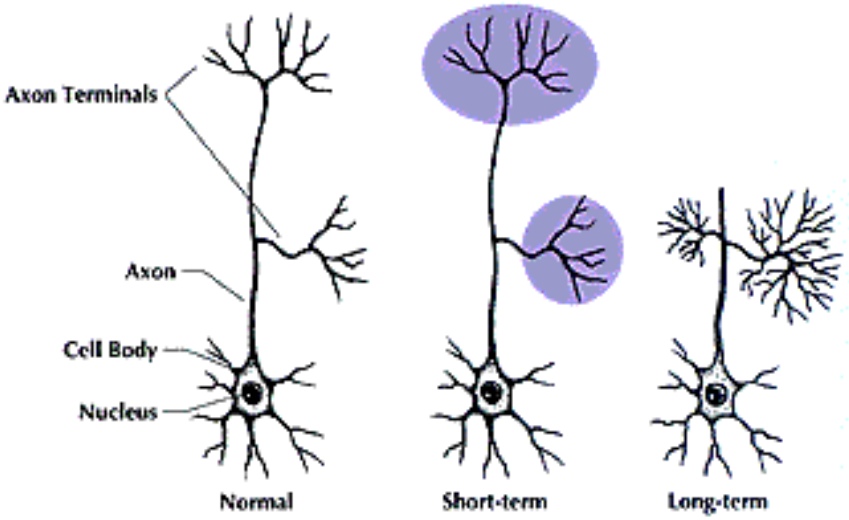
Heavy users of ecstasy, a synthetic drug that is structurally similar to methamphetamine and the hallucinogen mescaline, may be risking brain damage that remains long after the high has worn off, according to NIDA-supported research.

In a series of studies conducted with rats and nonhuman primates, Dr. George Ricaurte and his colleagues at Johns Hopkins Medical Institutions first determined that a single dose of MDMA (3,4-methylenedioxymethamphetamine), only slightly higher than the size of doses taken by humans, significantly damaged brain cells called neurons that produce serotonin. Serotonin is a major neurotransmitter, or chemical messenger, in the brain that is thought to influence mood, appetite, sleep, and other important functions. Then Dr. Ricaurte reported that 12 to 18 months after the brains of squirrel monkeys had been damaged by MDMA, serotonin-producing nerve fibers had regrown abnormally in some brain regions and failed to regrow at all in others.

Unlike methamphetamine, which damages brain neurons that produce both serotonin and another important chemical messenger called dopamine, "MDMA selectively damages serotonin neurons in virtually all species examined to date," Dr. Ricaurte says.



Dr. Ricaurte's studies have found that MDMA damages serotonin-producing neurons in the brains of nonhuman primates. The illustration on the left shows a normal neuron. The shaded area in the middle illustration shows the axon terminals of the neuron that are damaged by MDMA. The illustration on the right shows how, 12 to 18 months after being damaged by MDMA, serotonin-producing nerve fibers have regrown excessively in some areas and not at all in others.

"With MDMA, the doses that people take very closely approach the doses known to produce neurotoxic effects in animals," Dr. Ricaurte says.

"At this point, the major question is whether the neuronal changes we see in animals from methamphetamine and MDMA exposure occur in human beings who use these drugs," he says.

To help answer that question, he is conducting separate clinical studies using brain imaging techniques to evaluate the possibility of long-term brain damage in humans who have previously used either methamphetamine or MDMA. These studies also are assessing the potential functional consequences of such neuronal damage on aspects of mood, movement, memory, impulse control, aggression, and sleep cycles.

Determining the functional consequences of MDMA exposure may be more complex than previously thought, Dr. Ricaurte says. The long-term study with squirrel monkeys indicated that in some brain areas, such as those containing structures involved in memory and learning, damaged neurons failed to recover. However, in other brain areas, specifically those involved in regulating such functions as sleep and appetite, damaged neurons regrew nerve fiber excessively, resulting in an overabundance of serotonin being released. "This means that when we evaluate humans previously exposed to high doses of MDMA, we should be looking for loss of serotonin function in some brain regions, but perhaps normal or increased serotonin function in other regions," Dr. Ricaurte says.

Determining the possible damaging effects of ecstasy has become more important in recent years because the pattern of MDMA use has changed, points out Dr. Ricaurte. Although ecstasy has been available as a street drug

since the 1980s, its use escalated in the 1990s among college students and young adults, particularly those who participate in all-night dance parties called "raves." In 1995, 2.3 percent of college students said they had used ecstasy at some time during the year, more than quadruple the 0.5 percent of students who reported using the drug in 1994, according to NIDA's latest Monitoring the Future study. The percentage of young adults, ages 19 to 28, who used ecstasy in the past year also jumped significantly to 1.6 percent in 1995 from 0.7 percent in 1994, according to the survey.

Source:

Fischer, C.; Hatzidimitriou, G.; Wlos, J.; Katz, J.; and Ricaurte, G. Reorganization of ascending 5-HT axon projections in animals previously exposed to recreational drug 3,4-methelenedioxymetham-phetamine (MDMA, "Ecstasy"). *Journal of Neuroscience* 15:5476-5485, 1995.

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