

Ecstasy drug produces lasting toxicity in the brain

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Recreational use of Ecstasy - the illegal "rave" drug that produces feelings of euphoria and emotional warmth - is associated with chronic changes in the human brain, Vanderbilt University investigators have discovered.

The findings, reported online Dec. 5 in the *Archives of General Psychiatry*, add to the growing evidence that Ecstasy produces long-lasting serotonin neurotoxicity in humans, said Ronald Cowan, M.D., Ph.D., associate professor of Psychiatry.

"Our study provides some of the strongest evidence to date that the drug causes chronic loss of serotonin in humans."

The neurotransmitter serotonin, a critical signaling molecule, has roles in regulating mood, appetite, sleep, learning and memory.

The current study is important, Cowan said, because MDMA (Ecstasy's chemical name) may have therapeutic benefits and is now being tested as a treatment for post-traumatic stress disorder and anxiety associated with cancer.

"It's essential that we understand the risk associated with using Ecstasy," Cowan said. "If news keeps coming out that MDMA is being tested therapeutically and is safe, more people will tend to self-administer the drug. We need to know the dose at which this drug becomes toxic."

"Our studies suggest that if you use Ecstasy recreationally, the more you use, the more brain changes you get."

In the current study, Cowan and colleagues used positron emission tomography (PET) imaging to examine the levels of serotonin-2A receptors in various brain regions, in females who had used Ecstasy (but not in the 90 days prior to imaging) and in females who had never used the drug. They limited their studies to females because previous

work has shown gender-specific differences in serotonin receptor levels.

They found that Ecstasy users had increased levels of serotonin-2A receptors and that higher lifetime use of the drug (higher doses) correlated with higher serotonin receptor levels. The findings are consistent with some studies in animal models, with receptor levels increasing to compensate for the loss of serotonin, Cowan said.

Cowan and colleagues reported earlier this year that Ecstasy increased brain activation in three brain areas associated with visual processing, which suggested a loss in brain efficiency. Together, the two studies provide compelling evidence that Ecstasy causes lasting changes in brain serotonin function, Cowan said.

"It's really critical to know whether or not this drug is causing long-term [brain](#) damage because millions of people are using it," he said.

The 2010 National Survey on Drug Use and Health estimated that 15.9 million individuals 12 years or older in the United States had used Ecstasy in their lifetime; 695,000 people had used Ecstasy in the month prior to being surveyed.

Cowan is interested in determining the doses of [Ecstasy](#) that are toxic, and whether there are genetic vulnerabilities to [toxicity](#). If clinical trials show that the drug has therapeutic benefits, it's critical to know the risks, he said.

Provided by Vanderbilt University Medical Center

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