Ecstasy associated with chronic change in brain function

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Ronald Cowan, M.D., Ph.D., and colleagues report in the May issue of *Neuropsychopharmacology* that recreational Ecstasy use is associated with a chronic change in brain function. Credit: Vanderbilt University

the illegal "rave" drug that produces feelings of euphoria and emotional warmth - has been in the news recently as a potential therapeutic. Clinical trials are testing Ecstasy in the treatment of post-traumatic stress disorder.

But headlines like one in Time magazine's health section in February - "Ecstasy as therapy: have some of its negative effects been overblown?" - concern Ronald Cowan, M.D., Ph.D., associate professor of Psychiatry.

His team reports in the May issue of *Neuropsychopharmacology* that recreational Ecstasy use is associated with a chronic change in brain function.

"There's tension in the fields of psychiatry and psychotherapy between those who think Ecstasy could be a valuable therapeutic that's not being tested because of overblown fears, and those who are concerned about the drug's potentially harmful effects," Cowan said.

"We're not on one side or the other; we're just trying to find out what's going on in the brain - is there any evidence for long-lasting changes in the brain?"

The message in news reports needs to be accurate, Cowan said. His team's studies suggest that the current message should be: "If you use Ecstasy recreationally, the more you use, the more brain changes you get."

Cowan and his colleagues examined brain activation during visual stimulation, using functional magnetic resonance imaging (fMRI), in subjects who had previously used Ecstasy (but not in the two weeks prior to imaging) and in subjects who had not previously used Ecstasy.

They found increased brain activation in three brain areas associated with visual processing in Ecstasy users with the highest lifetime exposure to the drug. The findings were consistent with the investigators' predictions based on results from animal models: that Ecstasy use is associated with a loss of serotonin signaling, which leads to hyper-excitability (increased activation) in the brain.

The hyper-excitability suggests a loss in brain efficiency, Cowan said, "meaning that it takes more brain area to process information or perform a task."

The investigators found that this shift in brain excitability did not return to normal in subjects who had not used Ecstasy in more than a year.

"We think this shift in cortical excitability may be chronic, long-lasting, and even permanent, which is a real worry," Cowan said, noting that the Ecstasy users in the study are young (18 to 35 years old). "The question is what will happen to their brains as they age over the next 60 years."

Cowan said that the pattern of hyper-excitability is similar to that observed in fMRI studies of

individuals at risk for, or with early, Alzheimer's disease.

"I'm not saying that these people are at increased risk for dementia, but that there's a loss of brain efficiency in both recreational Ecstasy use and early Alzheimer's."

The findings suggest that brain hyper-excitability (increased activation in fMRI scans) may be a useful biomarker for Ecstasy-induced neurotoxicity, which the investigators will continue to study.

"Our goal is to be able to let people know whether or not the drug is causing long-term brain damage," Cowan said. "That's really critical because millions of people are using it."

The 2009 National Survey on Drug Use and Health estimated that 14.2 million individuals 12 years or older in the United States had used Ecstasy in their lifetime; 760,000 people had used Ecstasy in the month prior to being surveyed.

Cowan is also 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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