Minimal Ecstasy Use Linked to Cognitive Deficits

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VIENNA — Even a few low doses of the drug ecstasy were associated with a decline in verbal memory function in a unique prospective study of first-time users, Thelma Schilt said at the annual congress of the European College of Neuropsychopharmacology.

Carriers of the methionine allele of the catechol-O-methyltransferase (COMT) gene polymorphism proved far more sensitive to this adverse drug effect than were people who possessed the valine allele, added Ms. Schilt of the Amsterdam Institute for Addiction Research and the University of Amsterdam.

Ecstasy (3,4-methylenedioxymethamphetamine), also known as MDMA, is an inexpensive illicit recreational drug that's popular in the dance club/rave scene. Users report feelings of happiness and connection to others. Animal studies suggest that ecstasy is neurotoxic, producing long-term damage to the distal axons of serotonergic neurons.

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MS. SCHILT

Cognitive deficits have been documented in recreational users. However, such studies have either been cross-sectional or retrospective, and have mostly involved heavy users of ecstasy and multiple other potentially confounding drugs, including cocaine, alcohol, cannabis, and amphetamines.

For this reason, Ms. Schilt and her coinvestigators performed a prospective observational cohort study in 188 ecstasy-naive subjects as part of the larger Netherlands XTC Toxicity Study. Participants, whose mean age was 22 years, were recruited at places such as dance clubs and university campuses. Participants had to indicate an interest in trying ecstasy in the future, have a history of only minimal exposure to other recreational drugs, and undergo baseline neuropsychologic testing and brain-imaging studies.

During 11 months of follow-up, 58 subjects took ecstasy. Their usage was modest: a mean cumulative dose of 3.2 tablets and a median of 1.5. They underwent neuropsychologic testing roughly 12 weeks after their most recent use of the drug, as did a matched group of 60 subjects who remained persistently ecstasy naive. The participants were queried about drug use during follow-up, and underwent drug screening to validate their self-reported minimal use of other drugs.

At baseline, the two groups had similar neuropsychologic test scores. However, at follow-up the ecstasy users had significantly lower scores on immediate and delayed verbal recall and verbal recognition. Other cognitive domains were unaffected.

"The changes are small. You would not notice in everyday life that their memory had declined," Ms. Schilt stressed.

Nonetheless, the test results suggest even a low cumulative dose of ecstasy could be neurotoxic. Further follow-up will show whether the deficits remain after longer periods of abstinence. Also worthy of further study is the possibility that ecstasy accelerates the decline in verbal memory that's part of the normal aging process. Answers to these questions will have a bearing on ongoing clinical studies exploring the use of MDMA to facilitate psychotherapy, she continued.

Because ecstasy's pleasurable effects are attributable to a boost of serotonin in the brain, it was initially hypothesized that the serotonin transport promoter gene was involved in the drug's adverse effects upon memory. When other investigators demonstrated that that was not the case, Ms. Schilt and coinvestigators decided to study the effects of COMT gene polymorphisms in their subjects. They found the neuropsychologic test abnormalities associated with ecstasy use were most pronounced in people homozygous for the methionine or met allele.

This finding makes sense, Ms. Schilt explained, because the met allele is associated with low COMT activity and thus relatively high synaptic dopamine levels.

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