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Letters to the Editors

Ecstasy Use–Parkinson's Disease Link Tenuous

Recently, *Movement* Disorders published the third case report of Parkinson's symptoms in an individual who reported prior (+/−) 3,4-methylenedioxymethamphetamine (MDMA or "Ecstasy") use,[1] and an excellent accompanying editorial that critically examined claims of causality made in case reports.[2]

We have contacted the authors of both previous case reports and learned that the amount of Ecstasy consumed by both cases was below that required for enrollment in studies that were designed to look for but failed to find dopamine toxicity in Ecstasy users. Amounts consumed were also below doses (3 doses in 3-hour intervals of up to 8.6 mg/kg p.o., 25.8 mg/kg in total; 4.0 mg/kg s.c. injections, 12 mg/kg in total) that failed to produce dopamine toxicity in nonhuman primates.[3,4] One case report was of an individual who took Ecstasy on 10 occasions over a year.[5] Although precise data on the amount consumed each time are not available,[6] based on data collected in Ecstasy users around this period (see for example Gerra et al.[7] and Wareing et al.[8]), estimated consumption probably ranged from 1 to 3.5 tablets per use. Another case report[9,10] was of an individual who took just 1 to 2 tablets twice monthly for approximately 6 months. Assuming a 75-kg body weight and 80 mg tablets, a dose at or above typical Ecstasy pills of the times,[11,12] neither case is likely to have consumed more than 3.7 mg/kg per occasion.

Based on the available evidence, the link between Ecstasy use and Parkinson's disease seems especially tenuous.

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References

1. O'Suilleabhain P, Giller C. Rapidly progressive parkinsonism in a self-reported user of ecstasy and other drugs. Mov Disord 2003; 18:1378–1403.
2. Kish SJ. What is the evidence that Ecstasy (MDMA) can cause Parkinson's disease? Mov Disord 2003;18:1217–1223.
3. Ricaurte GA, Yuan J, Hatzidimitriou G, Cord BJ, McCann UD. Retraction. Science 2003;301:1429.
4. Ricaurte GA. Grant progress report submitted to NIDA for Grant DA0507-12, 15 July 2003. p 1–12 [obtained via Freedom of Information Act Request; response received 21 January 2004].
5. Mintzer S, Hickenbottom S, Gilman S. Parkinsonism after taking ecstasy. N Engl J Med 1999;340:1443.
6. Mintzer S. Personal communication via e-mail to L. Jerome, December 23, 2003.
7. Gerra G, Zaimovic A, Giucastro G, et al. Serotonin function after (+/−) 3,4-methylenedioxymethamphetamine ("Ecstasy") in humans. Int Clin Psychopharmacol 1998;13:1–9.
8. Wareing M, Fisk J, Murphy PN. Working memory deficits in current and previous users of MDMA ("Ecstasy"). Br J Psychol 2000;91:181–188.
9. Kuniyoshi SM, Jankovic J. MDMA and parkinsonism. N Engl J Med 2003;349:96–97.
10. Kuniyoshi SM. Personal communication to L. Jerome, July 14, 2003.
11. Baggott M, Heifets B, Jones RT, Mendelson J, Sferios E, Zehnder J. Chemical analysis of ecstasy pills. JAMA 2000;284:2190.
12. Cole JC, Bailey M, Sumnall HR, Wagstaff GF, King LA. The content of ecstasy tablets: implications for the study of their long-term effects. Addiction 2002;97:1531 1536.

Ecstasy and Acute Dystonia

I read with interest the article by O'Suilleabhain and Giller[1] regarding the possibility that Ecstasy can cause parkinsonism. Because the use of this illicit recreational substance with known action in some neurotransmitters[2] is increasing worldwide, it is noteworthy that there are only few reports of Ecstasy-induced movement disorders. In a recent editorial, Kish has reviewed and discussed the few cases of possible Ecstasy-induced parkinsonism.[3] Priori and colleagues reported some years ago a man with an acute dystonic reaction to Ecstasy.[4] Demirkiran and colleagues described a case with overlapping symptoms of neuroleptic malignant syndrome and serotonin syndrome after a single exposure.[5] One case of leg myoclonus after an acute high-dose exposure was also reported.[6] Since then, there is no other report, at least through the Medline database.

I would like to report on an 18-year-old woman who had no personal or family history of neurological disease. She accepted occasional consumption of Ecstasy starting a year ago. Approximately 24 hours after ingesting three tablets of Ecstasy in a period of approximately 8 hours, she developed painless spasmodic torticollis to the left and brief episodes of oculogyric crisis. There was no tremor of the head or upper limbs. The rest of the neurological examination was

normal. Torticollis improved markedly after a single intravenous dose of biperiden.

The present case and others[4,5] suggest an acute dystonic reaction to an antidopaminergic-like drug. Emergency physicians see more frequently acute side effects of Ecstasy, which are basically a sympathomimetic reaction with tachycardia, high blood pressure, and cardiac arrhythmia as well as fever, respiratory and renal insufficiency, cerebral edema, and seizures, but movement disorders are very rarely reported, so it seems that they remain unreported or underdiagnosed. Movement disorder specialists must try to establish the real frequency of acute and long-term movement disorders induced by Ecstasy.

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References

1. O'Suilleabhain P, Giller C. Rapidly progressive parkinsonism in a self-reported user of ecstasy and other drugs. Mov Disord 2003;18: 1378–1381.
2. White SR, Obradovic T, Imel KM, Whetaon MJ. The effects of methylenedioxymethamphetamine (MDMA, "Ecstasy") on monoaminergic neurotransmission in the central nervous system. Prog Neuorobiol 1996;49:455–479.
3. Kish S. What is the evidence that ecstasy (MDMA) can cause Parkinson's disease. Mov Disord 2003;18:1219–1223.
4. Priori A, Bertolasi L, Berardelli A, Manfredi M. Acute dystonic reaction to ecstasy. Mov Disord 1995;10:353.
5. Demirkiran M, Jankovic J, Dean JM. Ecstasy intoxication: an overlap between serotonin syndrome and neuroleptic malignant syndrome. Clin Neuropharmacol 1996;19:157–164.
6. Hinkelbein J, Gabel A, Volz M, Ellinger K. Suicide attempt with high-dose ecstasy. Anaesthesist 2003;52:51–54.

Reply: Ecstasy and Acute Dystonia

Dr. Cosentino describes a young woman with an acute dystonic syndrome which, assuming it is organic, could plausibly be attributed to the drugs ingested shortly beforehand. However, before citing a specific toxin one should note that the Ecstasy tablets this woman (and our patient) took might have contained MDMA or other neuroactive drugs, as is commonly the case. Dr. Cosentino suggests that the handful of case reports of extrapyramidal complications after Ecstasy ingestion may under-represent their true prevalence. We are biased to believe that striking syndromes such as the ones he and we describe must affect only a tiny minority of the approximately 10% of teenagers who have used Ecstasy. As long as the plausibility of extrapyramidal toxicity is being debated, it is reasonable that neurologists raise their antennae for such an association: teenagers and young adults with unexplained parkinsonism or dystonia syndromes should be asked about prior use of Ecstasy. If suspicion regarding a link intensifies, more rigorous systematic epidemiologic studies will be easily justified.

Dr. Jerome and colleagues question the plausibility of a causal link based on the argument that most people who take Ecstasy do not develop complications. Cohorts of a few dozen users of ecstasy found only equivocal and transient motor complications in a minority of the cases, and the modest numbers of primates experimentally exposed to MDMA did not develop parkinsonism or dystonia. Extrapyramidal side-effects of Ecstasy, if they occur, appear to be rare and perhaps idiosyncratic and based on individual susceptibilities.

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