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Parkinsonism after Taking Ecstasy

To the Editor: Recreational use of 3,4-methylenedioxymethamphetamine (MDMA, or "ecstasy"), a hallucinogen, has increased both in Europe and the United States.[1] This substance is manufactured in illicit laboratories from a variety of organic ketone precursors. MDMA, which is structurally related both to the stimulant amphetamine and to the hallucinogen mescaline, promotes the release of both serotonin and dopamine from synaptic terminals.[2] We report a case of parkinsonism after repeated use of this drug.

A 29-year-old man had slight clumsiness of his upper and lower extremities in August 1998. During the following four weeks he began to have difficulty walking and lost the ability to write and to drive. He was unable to continue his work in retail merchandising and then could not live independently. The results of magnetic resonance imaging, electroencephalography, lumbar puncture, and positron-emission tomography with [^{18}F]fluorodeoxyglucose were normal. Tests for antibodies to the human immunodeficiency virus were negative on two occasions. Eleven weeks after the onset of symptoms, examination revealed a disturbance in gait and impairment of fine coordination. The patient's condition continued to worsen, and eight weeks later examination revealed bradykinesia of the face and limbs, absence of blinking, hypokinesia in relation to speech, postural instability, and a markedly parkinsonian gait. Cognitive function was normal, and there was no tremor.

The patient had ingested MDMA nine times in 1997 and once more in May 1998. He denied having used any other illicit substances except cannabis. Treatment with the maximal tolerated doses of levodopa and pramipexole did not improve his symptoms.

Parkinsonism has not previously been associated with the use of MDMA. Although we have no firm evidence of a causal relation between this patient's drug use and his parkinsonism, there are no other tenable explanations. Idiopathic Parkinson's disease rarely develops in this age group and is responsive to medication, and neither it nor parkinsonism of any other neurodegenerative cause progresses this rapidly. Our patient's condition most closely resembled the parkinsonism produced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, a byproduct of the illicit manufacture of meperidine, which is highly toxic to neurons of the substantia nigra. Positron-emission tomographic studies have shown that even subclinical exposure to this substance produces progressive nigrostriatal damage, making the subject vulnerable to subsequent parkinsonism.[3]

We hypothesize that our patient may have had parkinsonism as a result of a delayed neurotoxic effect of MDMA on the substantia nigra and striatum. There is evidence for such dopaminergic neurotoxicity in animals,[4,5] and delayed neurotoxicity in humans could occur as a result of neuronal damage induced by free radicals.[5] Recent research regarding the neurotoxic effects of this substance has focused on serotonergic neurotoxicity and impairment of memory.[6] This patient's case suggests that the effects of MDMA on dopaminergic systems should be studied further to characterize more fully the dangers of its use.

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Carvedilol

To the Editor: In his review of carvedilol, Frishman (Dec. 10 issue)[1] did not adequately distinguish the effects of the drug in patients with dilated cardiomyopathy from those in patients with ischemic cardiomyopathy. Bristow et al.[2] have shown that there are differences between these two disorders in β-adrenergic activation. The Australia–New Zealand Heart Failure Research Collaborative Group[3,4] has assessed the efficacy of carvedilol in patients with ischemic cardiomyopathy. The investigators reported an increase in symptoms of congestive heart failure with carvedilol as compared with placebo. Carvedilol did result in an increase in left ventricular ejection fraction and a decrease in ventricular size, but both of these effects may have been due to the lower heart rate and lower blood pressure in these relatively healthy patients. In addition, neither maximal nor submaximal exercise performance changed with use of the drug. These results argue against the efficacy of carvedilol for relieving symptoms of congestive heart failure in patients with ischemic cardiomyopathy.

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Dr. Frishman replies:

To the Editor: Dr. Cohn suggests that the benefit of carvedilol may vary according to the cause of heart failure. In particular, he suggests that patients with ischemic cardiomyopathy may respond less well than others, citing the Australia–New Zealand study to support that position.[1,2] In the Australia–New Zealand study, symptoms of heart failure did increase in slightly more patients in the carvedilol group at 6 months, though not at 12 months.