later (five months after the diagnosis of spinal epidural lipomatosis), the patient was asymptomatic, the findings on the neurologic examination were normal, and MRI studies of the thoracic and lumbar spine (Fig. 1B) showed that the thickness of the epidural fat was normal (3 mm).

Cushing's syndrome typically causes an accumulation of fat that involves the face, neck, and trunk, and it also causes hypertrophy of adipose tissue normally present in the spinal canal. In one study, MRI evaluation of the thoracolumbar spine showed that the mean thickness of the epidural fat in the sagittal plane was 4.6 mm (range, 3 to 6) in normal subjects, whereas the thickness was more than 6 mm (range, 7 to 15) in patients with spinal epidural lipomatosis.[5] The mechanism by which hypercortisolism induces epidural lipomatosis is unclear. We recommend careful neurologic examination of patients with Cushing's syndrome and the performance of spinal MRI studies for the detection of spinal epidural lipomatosis, if there is a neurologic deficit.

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1. Hierholzer J, Benndorf G, Lehmann T, et al. Epidural lipomatosis: case report and literature review. Neuroradiology 1996;38:343-8.
2. Doppman JL. Epidural lipomatosis. Radiology 1989;171:581-2.
3. Noel P, Pepersack T, Vanbinst A, Alle JL. Spinal epidural lipomatosis in Cushing's syndrome secondary to an adrenal tumor. Neurology 1992;42:1250-1.
4. Sivakumar K, Sheinart K, Lidov M, Cohen B. Symptomatic spinal epidural lipomatosis in a patient with Cushing's disease. Neurology 1995;45:2281-3.
5. Robertson SC, Traynelis VC, Follett KA, Menezes AH. Idiopathic spinal epidural lipomatosis. Neurosurgery 1997;41:68-75.

More about Parkinsonism after Taking Ecstasy

To the Editor: I am the 29-year-old patient who was discussed in the letter "Parkinsonism after Taking Ecstasy" (May 6 issue).[1] I believe it is important to clear up some incorrect statements made by the doctors who wrote the letter.

In their letter, the doctors claim, "He denied having used any other illicit substances except cannabis." This is untrue, because I have never used cannabis. And if they believed that I had used cannabis, why wasn't it looked into as a possible cause of my illness? Another question is, if I never responded to levodopa and pramipexole, and all the brain scans were negative, why wasn't another possibility of illness considered?

At the time I became ill, I was a very healthy 29-year-old man who had been lifting weights since the age of 16. I was using creatine and Thermadrine (which contains ephedrine, caffeine, and aspirin) and had tried dehydroepiandrosterone for a week (it made me lightheaded). At the University of Michigan they neglected to test these substances (now being tested at another medical center), even though there is no national standard for testing their purity.

I find it hard to believe that physicians at an institution like the University of Michigan would submit such a letter about me without telling me beforehand and then use incorrect information to make their claim.

In no way do I advocate drug abuse, but if someone is going to make such a claim, then I feel they should be more accurate and have more solid evidence.

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1. Mintzer S, Hickenbottom S, Gilman S. Parkinsonism after taking ecstasy. N Engl J Med 1999;340:1443.

To the Editor: Mintzer et al. hypothesized that their patient had parkinsonism as a result of a delayed neurotoxic effect of 3,4-methylenedioxymethamphetamine (MDMA) on his basal ganglia and noted that his condition most closely resembled nigrostriatal damage induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). We question this conclusion. The patient's positron-emission tomographic scan was normal, and his condition did not respond to antiparkinsonian agents, unlike MPTP-induced parkinsonism. There is currently no evidence to suggest that MDMA damages dopaminergic neurons, and none of the thousands of animals or humans exposed to MDMA have shown evidence of parkinsonism.

MDMA is a phenethylamine, MPTP a phenylpiperidine. Aside from a coincidental similarity in their acronyms, they are chemically unrelated and have in common neither precursors nor intermediates. The purity of street drugs is far from perfect, and since no chemical analysis was performed, we have no evidence that this patient ingested either MDMA or MPTP. Samples of putative MDMA obtained and analyzed in January 1998 found that 29 of 35 pills (83 percent) contained no MDMA whatsoever,[1] and more detailed analyses of street MDMA by high-performance liquid chromatography show a wide variety of non-MDMA contaminants.[2] The patient probably ingested a wide variety of chemicals, any one of which might have been responsible for his parkinsonian symptoms. Whether MPTP is the culprit is doubtful, because the metabolite MPP^+ (1-methyl-4-phenylpyridinium), thought to be responsible for the parkinsonism induced by MPTP, does not appear to be present in the brain after oral administration.[3]

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1. Saunders N. Trends in quality in January 1998. (See: http://www.ecstasy.org/testing/analysis.html.)
2. Rothe M, Pragst F, Spiegel K, Harrach T, Fischer K, Kunkel J. Hair concentrations and self-reported abuse history of 20 amphetamine and ecstasy users. Forensic Sci Int 1997;89(1-2):111-28.
3. Fuller RW, Hemrick-Luecke SK, Perry KW. Tissue concentrations of MPTP and MPP+ in relation to catecholamine depletion after the oral or subcutaneous administration of MPTP to mice. Life Sci 1989;45:2077-83.

To the Editor: It is important to note that use of MDMA was not confirmed in this case, as might have been done by hair analysis. Amphetamines are well known to cause

dopaminergic neurotoxicity in animals and are sometimes sold as MDMA. However, amphetamines have not previously been associated with parkinsonism, despite more than 60 years of therapeutic and illicit use worldwide.

One isolated case, with symptoms beginning eight weeks after drug exposure, does not fit the expected pattern of drug toxicity. Despite the widespread use of MDMA, parkinsonism induced by this drug has not been previously reported. Therefore, any toxicity would probably have been caused by a contaminant or a highly idiosyncratic reaction. If the toxicity were due to a contaminant, a cluster of cases would have been expected, as with MPTP. If this were an idiosyncratic case of MDMA toxicity, symptoms would probably have appeared soon after use of the drug. Parkinsonism after use of MPTP had an onset time of several days, probably because the toxic metabolite accumulated in the substantia nigra over this period. Any toxic effects of MDMA, which in animals produces free radicals within hours,[1] would likewise be expected to occur soon after drug exposure.

Although it is tempting to ascribe adverse health consequences to socially disapproved behaviors, such as illicit drug use, the best interests of science are poorly served when this is done with no evidence other than a very loose, unconfirmed temporal association.

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1. Colado MI, O'Shea E, Granados R, Murray TK, Green AR. In vivo evidence for free radical involvement in the degeneration of rat brain 5-HT following administration of MDMA ('ecstasy') and p-chloroamphetamine but not the degeneration following fenfluramine. Br J Pharmacol 1997; 121:889-900.

The authors reply:

To the Editor: Sewell and Cozzi state that no link exists between MDMA and dopaminergic neuronal damage, but studies in laboratory animals suggest that MDMA may be toxic to dopaminergic neurons[1] and may cause enduring changes in neuronal responses to dopamine.[2] The fact that parkinsonism after use of MDMA has not been reported previously does not exclude the possibility that such an association exists. Clinical evidence of parkinsonism can be missed, particularly when the disorder is mild and, as in our patient, when tremor is absent. The first full report of parkinsonism in persons with long-term use of valproate did not appear until 18 years after its introduction in this country,[3] even though it had been prescribed for many patients by neurologists and psychiatrists, the very specialists who should be most adept at identifying signs of parkinsonism.

We mentioned MPTP as an example of a substance that may have delayed neurotoxic effects on monoaminergic neurons, without intending to suggest that MDMA acts chemically in the same manner as MPTP. We agree with Sewell and Cozzi that MPTP was not the culprit in this case, since our patient denied any intravenous drug use and MPTP is not orally active. We also agree that an MDMA contaminant may have been the agent truly responsible, but this possibility also merits attention, since it has not been reported previously. Moreover, if symptoms can be produced by an MDMA contaminant that is sometimes present in ecstasy, users are at risk. There is no reason to believe, as Baggott et al. state, that an idiosyncratic reaction would produce symptoms rapidly; the time course depends on the mechanism.

Our patient denied having used cannabis. During a clinic visit with two of us, however, his companion described the patient's past cannabis use in his presence, and the patient made no objection. The reasons for the misunderstanding are not clear. There is no evidence in the literature to suggest that any of the other substances mentioned by our patient would have any effect on the nigrostriatal dopamine system. Our patient believes that he should have been informed about our letter before we sent it to the *Journal.* We followed the current practice for publishing clinical observations, which does not include a requirement to inform the patient about the submission. Moreover, we assiduously protected the patient's confidentiality. We did not identify him by name, we published no photographs of him, and we provided no information that would enable any reader to determine his identity.

The hypothesis that MDMA caused this patient's illness requires confirmation by additional reports. For now, it remains only a single observation. We reported the finding to alert other physicians to the possibility of MDMA-induced parkinsonism and to prompt further investigation into the dopaminergic effects of this substance.

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1. Commins DL, Vosmer G, Virus RM, Woolverton WL, Schuster CR, Seiden LS. Biochemical and histological evidence that methylenedioxymethylamphetamine (MDMA) is toxic to neurons in the rat brain. J Pharmacol Exp Ther 1987;241:338-45.
2. Obradovic T, Imel KM, White SR. Repeated exposure to methylenedioxymethamphetamine (MDMA) alters nucleus accumbens neuronal responses to dopamine and serotonin. Brain Res 1998;785:1-9.
3. Armon C, Shin C, Miller P, et al. Reversible parkinsonism and cognitive impairment with chronic valproate use. Neurology 1996;47:626-35.