

Acute Dystonic Reaction to Ecstasy

To the Editor:

Ecstasy (3,4-methylenedioxymethamphetamine) is a recreational drug widely used in Europe and the United States. Intake of ecstasy frequently causes trismus or bruxism, muscle stiffness, and ataxia, and may also cause psychiatric side effects such as paranoia, depression, or psychosis (1). Occasional reports describe more severe ecstasy-related adverse effects, including convulsions, collapse, hyperthermia, disseminated intravascular coagulation, hypotension, and hepatotoxicity (1). In the patient, described here consumption of ecstasy led to an unusual neurological complication.

A 22-year-old man, who had no personal or family history of neurological or systemic disease, but who admitted being an occasional cocaine user, took two tablets of ecstasy. Several months had elapsed since his last intake of cocaine, and he had never taken ecstasy before. Approximately 11 h after ingesting ecstasy, he awoke from a normal night's sleep with a feeling of restlessness, accompanied by difficulty in turning his head and mild dysphagia. Neurological examination on the same day showed spasmodic torticollis to the right with laterocollis and a coarse action tremor of the right upper limb. These manifestations responded promptly to intramuscular anticholinergic treatment (biperidene lactate, 10 mg). The tremor and dysphagia disappeared gradually within 4 days, the torticollis within 11 days. When treatment was interrupted 19 days after the onset of symptoms, the patient complained only of discomfort on turning his head to the left, a symptom that disappeared completely within 2 weeks. Eight months after taking ecstasy, he remained symptom-free.

Our patient's clinical picture resembles an acute dystonic reaction to antidopaminergic neuroleptic drugs. The effectiveness of the symptomatic anticholinergic treatment also suggests a basal ganglia dysfunction. Interestingly, his disorder had a longer recovery course than that usually seen in patients with neuroleptic-induced dystonic reactions. The long time course might depend not upon pharmacokinetic mechanisms but on underlying changes in receptor sensitivity. Ecstasy stimulates serotonin release (2), and serotonergic pathways innervate the substantia nigra and globus pallidus (3), the two major output structures of the basal ganglia. Although ecstasy, like other amphetamine derivatives, exerts major effects on serotonin release, it also influences dopaminergic systems. In the case reported here, the fact that the patient had consumed cocaine—a well-known dopamine stimulant (4)—without complaining of adverse effects makes it unlikely that stimulation of the dopaminergic system precipitated his acute ecstasy-related dystonic reaction. Unusual dystonic reactions of this kind, presumably occur, as do neuroleptic-induced reactions, only in predisposed individuals (5). Alternatively, ecstasy-related acute dystonia might go unreported because drug users tend to underestimate self-limiting complications. Whatever the explanation, acute dystonia induced by ecstasy hardly surprises, considering that another psychostimulant, co-

caine, can precipitate or even induce hyperkinetic movement disorders (6). This case report suggests that young adults with acute-onset dystonia should be questioned about possible ecstasy intake.

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Diabetes Mellitus Presenting as Paroxysmal Kinesigenic Dystonic Choreoathetosis

Paroxysmal kinesigenic dystonic choreoathetosis (PKC) is a disorder that is characterized by attacks of chorea, dystonia, or tonic posturing lasting <5 min and triggered by sudden movements or startle (1). These episodes can occur up to 100 times a day and can be preceded by paresthesias or vague sensory phenomenon. Some patients have pain associated with the dystonia. Both familial and sporadic cases can occur. Sensorium is not altered during the episodes. Patients are asymptomatic between attacks (2). PKC has been reported in patients with thalamic infarcts (3), multiple sclerosis (4), progressive supranuclear palsy (5), basal ganglia calcifications (6), thyrotoxicosis (7), and hypoglycemia (8). Nonketotic hyperglycemia can cause seizures, visual hallucinations, focal neurologic signs, disturbance of con-

sciousness, choreoathetosis, and myoclonic twitches (9,10). We describe a patient with PKC affecting the right arm secondary to new onset diabetes mellitus.

A 68-year-old right-handed man presented with right arm intermittent paresthesias that started in the fingers and moved up to involve the entire arm. Several hours later, numbness was followed by severe pain and then involuntary right arm movements. The episodes of involuntary movements occurred eight to 10 times a day and lasted 3–5 min. They were precipitated by movement of that arm as when grasping for a glass of water and when stressed or excited. There was a history of essential hypertension for which he was taking nifedipine extended release tablet 120 mg/day. He had polyuria and polydipsia for 2–3 weeks. He had no history of seizures or myocardial infarction. He denied fever, chills, sweats, cold intolerance, muscle cramps, or extremity weakness. He quit smoking 30 years ago. On examination, blood pressure was 132/86 mm/Hg, pulse 82 beats/min and regular, and respirations were 18/min. He was afebrile. On neurological examination, he was alert and oriented without cognitive deficits. Muscle strength was normal, except in the right hand, where it was 4/5. Abnormal movements were characterized by internal rotation of the right arm, extension at the elbow, and pronation of the hand 360° so that the ventral aspect of the hand faced upward. The dystonic posture of the right arm persisted throughout the 3–5-min period. The patient reported no paresthesias or dysesthesias between attacks, and his neurologic exam was normal, except for mild right hand weakness, which had been present for many years. There was no rigidity, bradykinesia, or tremor. Deep tendon reflexes were symmetric and decreased. Plantar reflexes were flexor. Laboratory was significant for a serum glucose = 688 mg/dl, BUN = 30 mg/dl, and creatine = 1.6. Serum osmolality was calculated to be 310 mOsm/kg H₂O. Serum acetone was negative. MRI of the head revealed a circular lesion in the left posterior parietal white matter and prominence of the left Sylvian fissure consistent with left hemispheric atrophy (Fig. 1). Note was made of small lesions in the basal ganglia thought to be consistent with Virchow-Robin spaces. Electroencephalogram, recorded during an episode of dystonia, was normal. The patient was hydrated and treated with insulin. His abnormal movements decreased in frequency and severity over the next 7 days.

At the time of discharge, his serum glucose was 198 mg/dl and his PKC had resolved. His diabetes was managed with glipizide 10 mg bid and diet. There was no recurrence on follow-up at 6 months.

Discussion

Nonketotic hyperglycemia can cause diffuse alterations in many parts of the central nervous system. Coma and seizures can be associated with nonketotic hyperglycemia and occurs more commonly than in ketotic hyperglycemia. Aphasia, hemiparesis, hemisensory loss, hemianopsia, nystagmus, and tonic eye deviation have also been reported (9). Focal neurologic changes in the absence of seizure activity can often be seen as a presenting symptom of nonketotic coma (11). The mean age of patients with nonketotic coma is 62 years (12). Most of these patients have old infarcts, cerebral arteriosclerosis, or lacunar states. These lesions expose certain neuronal groups to the adverse biochemical conditions of nonketotic hyperglycemia. Our patient had left cortical atrophy secondary to a previous infarct. Thus, the left hemisphere most likely was more susceptible to metabolic changes.

PKC has been described in patients with multiple sclerosis (4), head trauma (13), thyrotoxicosis (7), hypoparathyroidism (14), hypoglycemia (8), and basal ganglia calcifications (6). In addition, specific ischemic lesions have been associated with PKC and include lesions of the putamen, right frontoparietal region, thalamus, and brainstem (3). Morres et al. (15) described what they thought was PKC as a manifestation of nonketotic hyperglycemia but their patient experienced shaking and jerking of the right arm and leg. Their patient had no dystonic posturing. They later mention that the patient probably had "movement induced myoclonic jerking" (15). Rector et al. (10) described three patients with choreoathetosis or ballism secondary to nonketotic hyperglycemia. Their patients symptoms were not paroxysmal and not precipitated by movement (10). To our knowledge, this is the first report of PKC as the presenting symptom of diabetes mellitus.

Two changes are proposed, one metabolic and the other circulatory, that attempt to explain the focal right arm dystonic choreoathetosis that occurred during nonketotic hyperglycemia. The biochemical alterations vary depending on whether the hyperglycemia is associated

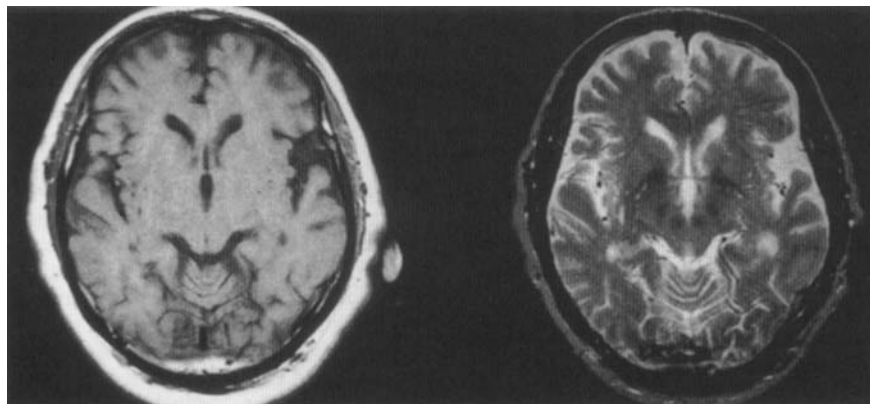


FIG. 1. Cranial MRI showing a subcortical infarct in the left posterior parietal lobe. T1-weighted image on the left (TR = 683, TE = 16) with decreased intensity and T2-weighted image on the right (TR = 2500, TE = 90) demonstrate high-intensity characteristics of the lesion. There is prominence of the left Sylvian fissure consistent with left cortical atrophy. The small rounded lesions in the basal ganglia are most likely Virchow-Robin spaces.

with ketosis or nonketosis. In nonketotic states gamma amino n-butyric acid (GABA) becomes depleted. GABA and L-glutamic acid are both amino acids and are present in high concentrations in nervous tissue. During the stress of nonketotic hyperglycemia the energy requirements change due to inhibition of the Krebs cycle thought to be the result of a direct influence from a hyperosmolar environment. Brain tissue then resorts to using ketone bodies and amino acids for metabolism. GABA is metabolized to succinic acid via the succinic semialdehyde pathway (GABA shunt) (12). This shunt can be used as an alternative pathway to the Krebs cycle and can generate as much as 40% of the total energy requirements in brain tissue. As a consequence to the greater utilization of the GABA shunt, GABA is depleted.

In patients with Huntington's disease with chorea type, neuronal subpopulations that utilize GABA as a neurotransmitter are preferentially lost in striatal neurons projecting to the globus pallidus externa (GPe) via the indirect pathway of the motor circuit of the basal ganglia-thalamocortical circuit (16,17). In primates, forty-seven percent of the GPe neurons are allocated to the active movement of the arm. In comparison, ten per cent are involved with active leg movements (18). Because of the relatively large number of GPe neurons functionally arranged in parallel circuits for both the execution and preparation of limb movement, these neurons are most susceptible to GABA depletion. As to why the dystonia involved the right arm, the patient could have either had lesions in the left basal ganglia not seen on MRI or the infarct in the left subcortical white matter could have interfered with the circuitry of the basal ganglia-thalamocortical pathway.

Hyperglycemia has been shown to decrease cerebral regional blood flow independent of changes in serum osmolality. Statistically significant ($p < 0.01$) blood flow decreases occurred in the globus pallidus and thalamus (19). Therefore, hyperglycemia induced regional blood flow pallidal and thalamic decreases could also contribute to the dysfunction of susceptible neurons. Again, due to the relatively high number of GPe neurons controlling active arm movements, these neurons would be rendered most susceptible to diminished regional blood flow.

We describe a unique case of paroxysmal kinesigenic dystonic choreoathetosis as the presenting symptom of diabetes mellitus first appearing as non-ketotic hyperglycemia.

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Does Fluoxetine Aggravate Parkinson's Disease? A Pilot Prospective Study

To the Editor:

The number of drugs able to induce parkinsonism or aggravate Parkinson's disease is now rapidly growing. Besides reserpine, tetrabenazine, and classical neurolept-