CASE REPORT

MDMA ("Ecstasy") and Panic Disorder: Induction by a Single Dose

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Introduction

(±)3,4-Methylenedioxymethamphetamine (MDMA) is a synthetic amphetamine analogue used recreationally by humans in the United States (Peroutka 1987) and Western Europe (Anon 1992), and is thought by some to have potential utility as a psychotherapeutic adjunct (Grinspoon and Bakalar 1986). It is generally believed that MDMA acts via central monoamines, primarily by inducing transmitter release and interfering with monoamine reuptake inactivation (Johnson et al 1991; McKenna and Peroutka 1990). In animals, MDMA has been shown to damage brain serotonin neurons, and in the monkey the neurotoxic dose closely approximates the dose typically ingested by humans (Ricaurte et al 1988). Concern that MDMA may damage serotonin neurons in the human brain is largely responsible for MDMA's Schedule I status in the United States, and consequently, the dearth of controlled studies comparing the risks of MDMA to its possible benefit as a therapeutic adjunct.

There have been several recent reports of lasting adverse neuropsychiatric sequelae in humans who have taken repeated (usually high) doses of MDMA (Creighton et al 1991; Benazzi and Mazzoli 1991; McGuire and Fahy 1991; Schifano 1991; McCann and Ricaurte 1991). These reports suggest that individuals with prior psychiatric histories may have an increased susceptibility to MDMA's adverse effects. Lingering psychiatric syndromes associated with MDMA ingestion have included chronic paranoid psychosis (Schifano 1991; McGuire and Fahy 1991), recurrent acute paranoid psychosis (Creighton et al 1991), depression with suicidality (Benazzi and Mazzoli 1991), and panic disorder with secondary depression (McCann and Ricaurte 1991).

Although untoward effects of high neurotoxic doses of MDMA might be anticipated, particularly in vulnerable individuals, enduring psychiatric illness following a single moderate dose of MDMA in a healthy individual has not been reported. We describe an individual with no prior psychiatric history who developed panic disorder after ingesting a single typical dose of MDMA.

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Case Report

The patient is a 23-year-old college student with no personal or family history of psychiatric illness, and no history of illicit drug use except for sporadic marijuana use before age 21. The patient's symptoms started shortly after ingesting MDMA with 2 friends in a local drinking establishment. Acutely (within 45 min), he experienced jaw clenching and excitement, euphoria, a sense of "closeness to everyone," distortion of his visual fields, and hot and cold flashes. The following day, he felt fatigued and had trouble concentrating. These symptoms persisted for 4 days, when he felt a sudden sense of extreme anxiety, with palpitations, tremulousness and nausea, leading him to believe that MDMA had damaged his heart. Continued symptoms prompted him to visit an emergency room, where a thorough medical evaluation (including a physical examination, an electrocardiogram, and routine urine and blood tests), was unrevealing. He was discharged with the diagnosis of anxiety. Further evaluation by his general practitioner, including magnetic resonance imaging of the head and thyroid function tests revealed no organic pathology.

Symptoms persisted for several weeks and were particularly severe in the morning. Periods of anxiety lasted from 1–3 hr, and were punctuated by several discrete episodes of panic, occurring on a daily basis. Panic attacks were characterized by sudden waves of nausea, "emotional intensity," palpitations, tremors, anxiety, and a desire to be alone. Panic attacks were followed by intense feelings of depression lasting for up to an hour.

Psychiatric treatment was sought, and several combinations of lorazepam and haloperidol were tried over a 4-week period, and were unsuccessful in abating symptoms of anxiety and panic. Ultimately, alprazolam, at a dose of 0.25 mg–0.5 mg four times daily provided relief to the point that the patient discontinued medications abruptly, hoping that treatment was no longer necessary. Clinical improvement continued until he ingested two over-the-counter cold remedies (to treat an upper respiratory tract infection) containing pseudoephedrine and phenylpropanolamine. Within 1 hr after taking medication he became anxious, and within 2 hrs, he experienced his first of a second series of panic attacks.

Since the reemergence of his symptoms, the patient has been treated with alprazolam 0.25 mg TID with imipramine 25 mg TID. Over 3 months after taking MDMA, he now describes feeling "pretty close to normal" while on medication. He has had no "full blown panic attacks" for over 1 month. Several attempts to wean himself from medications have failed, secondary to the reappearance of persistent anxiety.

Discussion

There have been two previous reports of panic attacks associated with MDMA. The first report, by Whitaker-Azmitia and Aronson (1989), described three individuals who experienced panic while under the acute influence of MDMA. Unlike the current case, panic in these individuals occurred while under the influence of the drug, and did not evolve into a chronic case of panic disorder. The second report (McCann and Ricaurte 1991) described an individual with prior psychiatric disturbance following ingestion of high dose (600–850 mg) MDMA. Given the high dose used and the history of previous psychiatric problems, this case may represent toxic effects of MDMA in a predisposed individual. The present case differs from previous reports in that it suggests that in certain

individuals without prior psychiatric history, a single pharmacologic dose of MDMA may be sufficient to produce an enduring psychiatric illness (which meets DSM-III-R criteria for panic disorder).

Although it is possible that serotonergic neurotoxicity underlies the development of panic disorder in this patient, the single low dose taken makes this unlikely. The lowest dose of MDMA reported to damage serotonin neurons in nonhuman primates is 5 mg/kg (Ricaurte et al 1988), more than two times the dose typically taken by humans. Instead it is more likely that MDMA's pharmacological properties played a role in the development of panic disorder. More specifically, the observation that two over-the-counter cold medications containing sympathomimetics exacerbated the patient's symptoms suggests that altered catecholamine function was involved. This hypothesis is appealing, as dysfunctional central noradrenergic function has been implicated in patients with spontaneously occurring panic disorder (Charney and Heninger 1986), and panic disorder has recently been reported following a recreational dose of cocaine, another drug that enhances catecholaminergic neurotransmission (Geracioti and Post 1991).

Several aspects of this case should be addressed. First, the possibility that the present case in fact represents spontaneous panic disorder which might have occurred without MDMA cannot be excluded. However, the temporal association between MDMA and first panic attack, and the absence of a family history mitigate against this possibility. Second, because no formal psychiatric assessment was performed prior to the onset of panic disorder, the possibility that a subtle psychiatric disturbance had gone undetected should be considered. However, the patient's high level of functioning prior to the onset of illness argue against this possibility. Finally, the differential diagnosis for panic disorder is lengthy, and includes organic illnesses such as hypoglycemia, cardiac disease, hyperthyroidism, pheochromocytoma, epilepsy, and drug intoxication, as well as psychiatric illnesses such as schizophrenia and avoidant or paranoid personality disorder. Given the extensive medical evaluation performed in the emergency room and by his internist, an organic etiology for this patient's anxiety and panic is less likely. Although schizophrenia or personality disorder should not be ruled out as forming the basis of this patient's symptoms, the history of high premorbid functioning, the lack of response to antipsychotic therapy, and the beneficial response to a combination of benzodiazepines and antidepressants make panic disorder the more likely diagnosis.

In summary, the present case suggests that a single pharmacologic dose of MDMA is sufficient to cause panic disorder in a previously healthy individual. Given the increasing popularity of MDMA in the United States and abroad, the case herein described suggests that MDMA use should be considered in the differential diagnosis of new onset drug-induced panic disorder.

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