Persistent Psychosis and Medical Complications After a Single Ingestion of MDMA "Ecstasy"—A Case Report and Review of the Literature

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ABSTRACT

We describe a case report of persistent psychosis and severe medical complications in a previously healthy, 19-year-old African-American man after a single ingestion of what was purported to be "Ecstasy." We detail the psychiatric symptoms and medical complications that resulted in several weeks of hospitalization in both medical intensive care and psychiatric units. Furthermore, we describe changes in the demographics of the use of Ecstasy and present the current understanding of the cause of neurotoxicity after Ecstasy use when it occurs. We conclude by suggesting actions clinicians can take to ameliorate the negative consequences of Ecstasy use.

INTRODUCTION

This case report describes both persistent psychosis and severe medical complications in a previously healthy, 19-year-old, African-American man after a single ingestion of the street drug "Ecstasy" (3,4-methylenedioxymethamphetamine, MDMA).

Although Ecstasy is often regarded as a "safe" drug within youth culture,

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persistent psychosis after even a single use has been increasingly documented in medicine.[1,2] In addition to the case presentation, this report also details important epidemiological trends regarding the shift of Ecstasy use in minority groups as well as a hypothesis of how Ecstasy causes psychiatric and medical insults to vulnerable users.

CASE PRESENTATION

In July 2008, a 19-year-old African-American man without remarkable psychiatric or medical history obtained Ecstasy from his girlfriend and ingested the tablet. Shortly thereafter, he began hearing voices and behaving bizarrely, leading to his incarceration for trespassing and resisting arrest.

In October 2008, all charges were dropped and the patient was taken directly from a corrections center to a local emergency department (ED) for evaluation of his behavior. The ED physician found that the patient was awake and alert, but could not meaningfully communicate. Lab testing showed no alcohol or drugs present. Liver enzymes were elevated, and electrocardiogram (EKG) showed sinus bradycardia and a right bundle branch block. The patient also had marked bilateral ankle edema. Overnight, the patient was then transferred to an acute-care inpatient psychiatric unit, apparently before receiving medical clearance. On the psychiatric unit the next morning, the patient had a seizure and was urgently transferred to an intensive care unit (ICU).

At the ICU, the patient was found to have metabolic alkalosis, significantly elevated creatinine kinase (>2000 units/liter [UL]), and elevated liver function. Cardiac abnormalities and bilateral lower extremity swelling were still present with sinus bradycardia alternating with tachycardia, right bundle branch block, and dilated cardiomyopathy with reduced ejection fraction of 30 to 35 percent.

In the ICU, the patient continued to display bizarre behavior. He frequently assumed unusual postures by putting his hands and feet beneath his buttocks while pushing his pelvis upwards. He also attempted to eat EKG leads, catheters, ink pens, and other inedible objects. The patient would also chew on his buccal mucosa and pick at his nostrils producing blood, as well as handling and smearing his feces. Whatever speech he had was nonsensical, and the patient appeared to be responding strongly to internal stimuli.

After psychiatric consultation, an aggressive psychotropic medication regime was instituted with olanzapine 20mg orally (PO) every 12 hours and haloperidol 10mg intramuscular twice a day. Lorazapem 2mg was also employed on an as needed basis (PRN) administered frequently over a several day period. Our medication choices were informed by published reports of successful treatments [see Discussion section]. After several days of this medication regimen, more normal behavior and even responsive conversation was observed but was still interspersed with agitation and confusion.

Given the seizure, neurological work up was pursued. Electroencephalogram was without epileptiform discharges. Imaging of the brain and lumbar puncture were normal. Other laboratory indicators of central nervous system (CNS) vasculitis were also normal. Neurology service felt the patient did not have any obvious neurological basis for the seizure or infection of the CNS.

The patient remained in the ICU for two weeks. His medical conditions stabilized and his mental state improved modestly, but he still frequently needed restraints and close staff supervision. In November 2008, the patient was transferred back to the acute-care inpatient psychiatric unit. Fortunately, the unit's psychiatric team was the same team that had been consulted by the ICU. After his transfer back to the psychiatric unit, the patient continued to require restraints on several occasions due to agitation and nonresponsiveness to verbal redirection. The patient was also observed to be staring off blankly into space or making stereotypic movements while screaming. Because of this continued unpredictable behavior, valproate syrup 500mg PO three times daily (TID) was added for the treatment of this agitation.

Slowly, the patient made improvements, such as no longer assuming odd positions or displaying stereotypic behaviors. Episodes of agitation were less frequent as he became more cooperative. The patient was also able to describe recent hallucinatory experiences, including auditory hallucinations telling him to "Get out of the restraints" and "Eat, eat, eat," visual hallucinations of "ghosts and shadows," and tactile hallucinations of bugs crawling on his skin. The patient also said that he had used "Wiggle," another street name for Ecstasy. He stated that he had used the drug just once back in July and he began having behavior problems shortly thereafter. He was unclear as to what happened during his incarceration but remembers "not being with it" most of the time. Because of this persistent psychosis after one Ecstasy use, hallucinogen-induced persistent perceptual disorder was diagnosed. The patient's multiaxial assessment is presented in Table 1.

In the days before discharge, the patient again showed improvement of symptoms and increased insight. The patient was well groomed with good hygiene and communicated his thoughts more accurately. Since the patient's symptoms were resolving, the haloperidol was discontinued and olanzapine was reduced to 10mg twice daily (BID) and valproate syrup continued at 500mg BID.

The family arranged to have an attendant be with the patient daily for months after discharge. As of the time of the writing of this article, the patient no longer required an attendant and was continuing to make slow improvements in cognition and functioning but had sustained episodes of dysphoria and depressed mood. His medical conditions improved, but he also continued to have marked cardiac abnormalities that required regular medical follow up and monitoring.

DISCUSSION

Ecstasy was discovered in 1912 and was originally intended for use in

TABLE 1. Patient multiaxial assessment

AXIS I	Substance-induced delirium due to Ecstasy ingestion
	Hallucinogen-induced persistent perceptual disorder
AXIS II	No mental retardation or personality disorder identified
AXIS III	Dilated cardiomyopathy with right bundle-branch block
	Metabolic alkalosis
	Elevated liver function tests and creatinine kinase
	Single tonic-clonic seizure witnessed by staff with micturation
AXIS IV	Involved in casual drug use prior to MDMA exposure
	Requires supervision of activities of daily life due to sequellae from Ecstasy Ingestion
AXIS V	Global assessment of functioning at presentation to hospital was 30 due to profound psychosis and severe impairments in functioning, including inability to bathe, clothe, or feed himself
	Global assessment of functioning at discharge was 50 with resolution of psychosis but with ongoing major impairments in day-to-day functioning, requiring close supervision of activities

clotting treatments or to modify smooth muscle contraction.[3] Beginning in 1976, famed biochemist and psychopharmacologist Alexander Shulgin resynthesized it as MDMA and, along with deceased psychotherapist Leo Zeff, popularized its usage in psychotherapy.[4] Once it was discovered that Ecstasy has possibilities for serious brain damage, the Drug Enforcement Administration banned this drug for all but research purposes in 1985.[4,5]

Active research in MDMA has continued, both in the US and worldwide. Some of this research challenges whether the absolute ban on MDMA should continue or whether there could be narrowly defined, appropriate clinical uses for MDMA in light of its unique profile of benefits versus possible risks.[4] Reflecting this strong and ongoing disagreement among scientists, law enforcement officials, and health policy makers, there are ongoing trials exploring the therapeutic use of MDMA in targeted clinical populations, including patients with posttraumatic stress disorder[6] and anxiety related to advanced stage cancer.[7] It should be noted that the drug being given in these trials is MDMA synthesized in a controlled setting and given in prespecified dosages.

Street names for Ecstasy are numerous, and include Wiggle (used by our patient and his peers), X, E, Beans, Adam, Hug Drug, Disco Biscuit, and Love Drug.[8] Ecstasy use is most common in the 18- to 25-year-old age group, with 3.7 percent of 18 to 25 year olds admitting to use in 2007.[9] Although rates of use are unacceptably high, they are lower than peak use, which occurred in 2001.[9,10] In recent years, Ecstasy's use has spread from white youths to various ethnic groups, with the sharpest increase in use by African American adults ages 20 to 30.[10]

An alarming fact of Ecstasy use is that what is consumed is often not MDMA, but a mixture of MDMA and similar compounds, or other adulterants, that can cause medical and psychiatric complications far greater than MDMA itself. This occurs as a result of the illicit manufacturing process where other substances are used to amplify or prolong the "high." One study found MDMA and at least two additional compounds, 3,4-methylenedioxyamphetamine (MDA), and 1-(3,4-methylenedioxyphyl)-2-propanalol, in an Ecstasy tablet.[11] Other substances that have been found in ecstasy include methamphetamine, caffeine, dextromethorphan, ephedrine, cocaine, aspirin, pseudoephedrine, ketamine, lysergic acid diethylamide (LSD), and paramethoxyamphetamine.[12,13]

MDMA is thought to cause persistent damage to serotonergic neurons in the human brain, as it has been shown to cause this damage in laboratory animals.[13–15] MDMA acts by binding to presynaptic monoamine transporters—most strongly to serotonin receptor transporter (SERT)—inducing rapid release and subsequent depletion of serotonin and dopamine from presynaptic terminals.[14–17] Further damage is caused by a peripheral metabolite that is taken up by CNS serotonin nerve terminals and generates free radicals, thus exhausting the antioxidant capacity of brain tissues.[14.] Serious psychiatric illness implicated with Ecstasy use includes paranoid psychosis, delirium, panic attacks, perceptual disturbances, and depression with suicidal ideations. Medical complications reported with Ecstasy use include fulminant hyperthermia, convulsions, disseminated intravascular coagulation, rhabdomyolysis, renal and liver failure, intracranial hemorrhage, fatal arrhythmias, myocardial infarctions, and cerebral edema.[2,15,18]

The presented case demonstrates several important aspects of present-day Ecstasy use. The patient is a member of a minority group that is the fastest growing segment of Ecstasy use nationally.[12] As is often the case, the patient's age in this case pointed toward different possible etiologies. The patient's age is consistent with first-break schizophrenia. However, the complete lack of prodrome, the medical complications, and good premorbid functioning demanded an investigation into causes other than schizophrenia. The patient's age was also consistent with CNS infection or encephalitis, but he had no laboratory indicators of this diagnosis.

The patient's age, his good premorbid functioning, and his pattern of medical complications supported exposure to Ecstasy as a cause of his symptoms. There was no laboratory toxicology evidence of MDMA exposure, but the patient was incarcerated during the period that MDMA could have been detected by toxicology. Furthermore, presumptive diagnoses of Ecstasy ingestion/intoxication are often made without toxicological evidence. Unlike other illicit substances, such as cocaine and phencyclidine, most routine toxicology screens do not screen for Ecstasy. Instead, clinicians rely on careful interviewing of patients, their families, and their peer groups as well as working with public health and law enforcement officials in following trends of illicit drug use within different geographic and demographic communities.[9,10]

In our patient, we were able to support Ecstasy exposure through repeated and detailed discussions with the patient, his friends, and his parents. We also contacted local law enforcement who confirmed a growing trend of Ecstasy use in the patient's age group within the Greater New Orleans area, mirroring a growing trend of drug abuse in post-Katrina New Orleans.[19, 20] Furthermore, the patient's complete resolution of psychosis but continued dysphoria is also consistent with Ecstasy complications. However, we acknowledge that the patient's imprisonment for several months complicates the establishment of the diagnosis, and diagnostic certainty would be greater if the patient had been continually in a healthcare setting instead of imprisoned on minor charges for several months. This situation is not surprising, as described in an article by Potash[21] of the shunting of mental health and substance abuse issues in New Orleans from healthcare settings to prisons and jails, and in a recent issue of *Psychiatric Services* is dedicated to examining the high prevalence of mental illness in criminal justice settings nationwide.[22]

Establishing a diagnosis that accounted for the patient's persistent psychotic symptoms and medical complications was obviously challenging. We consulted the text of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (*DSM-IV-TR*) to diagnose hallucinogen-induced persistent perceptual disorder.[23] In particular, we noted that the patient's continued auditory, visual, and tactile hallucinations satisfied Criterion A. There is additional discussion in the Associated Features and Disorders section that this diagnosis often presents with severe medical/physiological complications, such as those found in our patient, and that MDMA is a commonly used hallucinogen in this class.

Once we concluded that the patient's symptoms were due to Ecstasy use, we reviewed published research—mostly case reports—to determine which treatment leads to the fastest and most complete amelioration of symptoms. We found several case reports that documented the use of high-dose, antipsychotic medication (haloperidol and olanzapine, specifically) and anticonvulsants in the treatment of psychiatric symptoms after Ecstasy use.[1,15,18]

CONCLUSION

This paper describes persistent psychosis and serious medical complications after a presumptive single ingestion of Ecstasy in a previously healthy 19-year-old man. Despite decades of literature demonstrating possible complications of Ecstasy, its illicit use remains high. Furthermore, the demographics of Ecstasy use have drifted from white, middle-class youth to minority groups within various socioeconomic backgrounds. What has not changed is that the possible consequences of Ecstasy use are poorly appreciated by the drug's users. Whether these complications are due to MDMA directly, caused by chemically related compounds, or caused by unrelated adulterants added in an illicit manufacturing process is an area of ongoing debate and research. Furthermore, part of that ongoing research is focused on whether there is a therapeutic use for MDMA in specially selected situations.

When illicit use of Ecstasy is suspected because of lab testing, psychiatric presentation, medical complications, or verbal reports, it demands close collaboration between psychiatrists and medical specialists. When this type of collaboration is obtained, it can prevent further disintegration of mental functioning, worsening of medical complications, or death. What remains to be seen is how we can best promote full recovery in individuals exposed to Ecstasy who have these complications, and this offers opportunities for future research.

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