

IMPLICATIONS OF RESEARCH FOR TREATMENT: *ECSTASY*

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Ecstasy (3, 4-methylenedioxy-methamphetamine) (MDMA) (also called Adam, E, X, eccie) is a synthetic, psychoactive drug with both stimulant and hallucinogenic properties similar to methamphetamine and mescaline. Similar compounds include MDA and MDEA (Eve). Most tablets containing MDMA are produced in clandestine laboratories in Belgium, Luxemburg, or in Asia and the tablets may contain only MDMA or MDA or they may contain either of those drugs and acetaminophen, caffeine, codeine, ketamine, methamphetamine, MDE, pseudoephedrine, or nothing.

LATEST RESEARCH FINDINGS

Adverse Effects

Common adverse physical effects of MDMA include agitation, anxiety, tachycardia and hypertension; more serious adverse reactions include hyperthermia, rhabdomyolysis, disseminated intravascular coagulation, renal failure, cardiac complications, intracranial hemorrhage, and hepatotoxicity [1, 2, 3]. Another term used to describe these adverse effects is “serotonin syndrome,” which is characterized by enhanced physical activity, sweating, lack of coordination, mental confusion, trismus, jaw clenching, agitation, hyperreflexia, hyperthermia, shivering, rhabdomyolysis, metabolic acidosis, myoclonus, tremor, and nystagmus [4].

Cognitive/Psychiatric Associations

Long-term neurotoxic effects of MDMA, particularly in the serotonergic system, are not fully known. One study found ecstasy polydrug users were significantly more impaired on a recognition task for complex visual patterns and spatial working memory as a function of task difficulty. They also showed a trend towards impairment on several learning paradigms. They remained relatively unimpaired on most measures associated with prefrontal functioning, with the exception of verbal fluency “letter” generation [5]. The

observed impairment may be attributable to a combination of reversible acute effects of MDMA resolving over a period of 2-3 weeks and more long-term changes associated with extent of lifetime consumption [6]. Evidence has also been found that MDMA use may be associated with deficits in executive functioning (planning, initiation, and self-regulation of goal-directed behavior) [7].

Studies have suggested use of MDMA affects depression, other mood disorders, impulsiveness or hostility, psychotic symptoms, anxiety and panic disorders, and other psychopathologic disturbances. The selective impairments of neuropsychological performance associated with regular ecstasy use have been found not to be reversed by prolonged abstinence, which is consistent with evidence that ecstasy has potent and selective neurotoxic effects on brain serotonergic systems in humans [8]. A prospective-longitudinal study of mental disorders in ecstasy users found users were at significantly increased risk of DSM-IV substance-related disorders and at higher risk of alcohol use disorders than users of other illicit substances. They also had significantly higher rates for almost all DSM-IV mental disorders than did non-users or users of other illicit drugs. However, the ecstasy use might be associated with use of multiple substances and onset of mental disorder is more likely to precede rather than follow use of ecstasy and related substances [9]. Individuals who have taken a larger number of MDMA

tablets have a higher risk of developing psychiatric disorders, and polydrug use itself may lead to different problems. It may be beneficial to assess the consequences of ecstasy use within the wider context of recreational drug use as a whole [10].

A review of studies of chronic recreational use of MDMA showed repeated use of ecstasy to be associated with sleep, mood, and anxiety disturbances, elevated impulsiveness, memory deficits, and attention problems which may persist for up to two years after cessation. In a subset of humans, particularly adolescents, depletion of serotonin by MDMA use may hasten or enhance vulnerability to a wide array of neuropsychiatric problems such as persistent depression of mood, manifestations of anxiety, psychosis, increases in impulsiveness, hostility, aggression, and sleep disturbances [11].

The levels of past use of ecstasy affect psychological problems. In a web-based survey of 282 ecstasy users, depression, memory problems, anxiety, mood fluctuation, poor concentration, infections, tremors/twitches, and weight loss were all significantly associated with the extent of ecstasy use [12]. Former chronic ecstasy users who had not consumed ecstasy in the last 14 days had higher levels of depression than their matched controls and might be at risk with regard to the development of a more severe depressive syndrome [13]. Another study found that ex-users of ecstasy could be divided into two groups: those who had quit for mental health reasons and those who had quit for circumstantial reasons. Half of those who quit for mental health reasons scored in the range for clinical depression and current levels of depression and anxiety correlated significantly with the cumulative amount of MDMA they had taken several years previously. This study suggests that some users may either be more vulnerable to the adverse effects of MDMA or have pre-existing mental health problems for which they self-medicate by using ecstasy. Some of these users experienced mental health impairment that persisted for years after they stopped using the drug [14].

The long-term effects most frequently reported included the development of tolerance to MDMA (59%), impaired ability to concentrate (38%), depression (37%), and “feeling more open towards

people” (31%). The most prominent concern of the users was the drug’s long-term effects on mental health [15]. Heavy ecstasy polydrug users reported significantly higher scores than non-drug users on several Symptom Checklist-90 (SCL-90) factors, including phobic anxiety, obsessive-compulsive behavior, anxiety, psychosis, somatisation, and significantly higher rates of “loss of sex or pleasure” [16].

MDMA users are reported to be taking selective serotonin reuptake inhibitors (SSRI) such as fluoxetine or sertraline or antioxidants such as vitamin C or vitamin E to minimize their risks. Animal experiments suggest these substances may reduce serotonin depletion by MDMA but they have not shown they protect against brain damage and SSRIs may block the metabolism of MDMA by the liver [17] as well as facilitate the occurrence of serotonin syndrome [18]. Underground websites give specific information as to “preloading” and “postloading” and the use of over-the-counter supplements such as 5-hydroxytryptophan (5-HTP), although this information does not appear to have been medically evaluated.

TREATMENT IMPLICATIONS

There is no antidote for MDMA, only supportive care similar to treatment of amphetamine or methamphetamine overdose [2]. No withdrawal syndrome from MDMA has been reported [19], although a study of 173 adolescents and young adults interviewed with the Composite International Diagnostic Interview, Substance Module, found that 43% met the DSM-IV criteria for dependence on ecstasy and 34% met the criteria for abuse of ecstasy [20]. While studies have suggested recreational ecstasy use is related to depression and poorer memory as well as learning and attention abilities (one study found feelings of depression approached clinical levels of depression [21]), articles on evidence-based treatment for persons seeking help for ecstasy dependence do not appear to exist [22].

An analysis of characteristics of clients entering TCADA programs with a primary, secondary, or tertiary problem with ecstasy between 1988 and 2003 found that these clients reported using the drug on eight

days in the past month, which equals weekend use [23]. However, 80% reported that marijuana, alcohol, powder cocaine, or methamphetamine was their primary problem drug, a relationship which would affect their treatment prognosis. Clinicians should be prepared to provide treatment for these combinations. In addition, ecstasy use has spread beyond the club culture into the community, as shown by the increasing proportions of persons of color. In 1990, 88% of clients with any problem with ecstasy were White, 8% were Hispanic, and 4% were Black; in 2003, 63% were White, 19% were Hispanic, and 16% were Black. Clinicians should be prepared to provide services which are culturally relevant to these users.

Clients who used ecstasy were more likely at admission to enter residential programs, but only 39% completed treatment even though they had a longer length of stay. Six percent had received a DSM diagnosis of depression, and 5% received anti-depressants. Given the correlation of use of ecstasy and depression and other psychological problems as cited in the literature, it would seem that more clients should be assessed for depression and wider use of anti-depressant medications should be evaluated. In addition, the research findings about impaired concentration indicate that treatment techniques used for individuals with cognitive disabilities would be appropriate in some cases [24].

GLOSSARY

dependence—a pattern of substance misuse characterized by a combination of factors, such as withdrawal, tolerance, cravings, out-control use, and use despite negative effects.

depression—a mood disorder characterized by poor appetite or overeating, sleeplessness or hypersomnia, low energy or fatigue, low self-esteem, feelings of hopelessness, and difficulty concentrating or making decisions.

disseminated intravascular coagulation—a complex and controversial systemic thrombohemorrhagic disorder involving the generation of intravascular fibrin and the consumption of procoagulants and platelets. It is seen with a number of well-defined clinical situations, including sepsis and major trauma.

DSM-IV—Diagnostic and Statistical Manual, 4th edition, which is the diagnostic criteria of psychiatric disorders published by the American Psychiatric Association.

executive functioning—associated with mental operations such as planning, working memory, and initiation and self-regulation of goal-directed behavior.

5-HT—serotonin.

hepatotoxicity—a state of toxic damage to the liver, a common cause of acute liver disease, morbidity and mortality.

hypertension—high blood pressure.

hyperthermia—exceptionally high fever.

metabolic acidosis—a disturbance of the body acid-base balance in which there is excessive acidity of the blood. Metabolic acidosis can occur as a result of many different diseases, such as kidney failure, poisoning, diabetic ketoacidosis, and shock.

myoclonus—irregular involuntary contraction of a muscle usually resulting from functional disorder of controlling motoneurons.

nystagmus—a rapid involuntary oscillation of the eyeballs.

neurotransmission—the transmission of nerve impulses across a synapse.

psychosis—a thought disorder in which reality is grossly distorted. Symptoms can include seeing, hearing, smelling, or tasting things that are not there; paranoia; delusions. Psychosis can occur as a result of brain injury or disease, and is seen particularly in [schizophrenia](#) and bipolar disorders.

rhabdomyolysis—the breakdown of muscle fibers with leakage of potentially toxic cellular contents into the systemic circulation.

serotonin—a phenolic amine neurotransmitter $C_{10}H_{12}N_2O$ that is a powerful vasoconstrictor and is found especially in the brain, blood serum, and gastric mucous membrane of mammals; called also 5-HT 5-hydroxytryptamine.

serotonin syndrome—characterized by enhanced physical activity, sweating, lack of coordination, mental confusion, trismus, jaw clenching, agitation, hyperreflexia, hyperthermia, shivering, rhabdomyolysis, metabolic acidosis, myoclonus, tremor and nystagmus.

SERT—serotonin transporter.

somatization—The unconscious process by which psychologic distress is manifested as physical symptoms.

somnolence—drowsiness.

SSRI—selective serotonin reuptake inhibitors.

tachycardia—relatively rapid heart action whether physiological (as after exercise) or pathological.

verbal fluency letter generation—a classic neuropsychological test of language production which involves subjects generating and articulating a word in response to a cue the Verbal Fluency Task. As an example, in the letter category, participants are asked to produce as many words as possible beginning with a specified letter in one minute.

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