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## Research Report Series: MDMA (Ecstasy) Abuse

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The so-called "club drug" MDMA continues to be used by millions of Americans across the country despite growing evidence of its potential harmful effects. 3,4-Methylenedioxymethamphetamine (MDMA, or "Ecstasy") has gained a deceptive reputation as a "safe" drug among its users. This illegal drug, which has both stimulant and psychedelic properties, is often taken for the feelings of well-being, stimulation, as well as the distortions in time and sensory perceptions that it produces. MDMA first became popular in the "rave" and all-night party scene, but its use has now spread to a wide range of settings and demographic subgroups. According to the 2002 National Survey on Drug Use and Health, more than 10 million people have tried MDMA at least once.

Myths abound about both the acute effects and long-term consequences of this drug, often called "Ecstasy" or "X". Indeed, one reason for the rapid rise in the drug's popularity is that many young people believe that MDMA is a new safe drug. But MDMA is not new to the scientific community, with many laboratories beginning their investigations of this drug in the

1980s, and the picture emerging from their efforts is of a drug that is far from benign. For example, MDMA can cause a dangerous increase in body temperature that can lead to cardiovascular failure. MDMA can also increase heart rate, blood pressure, and heart wall stress. Animal studies show that MDMA can damage specific neurons in the brain. In humans, the research is not conclusive at this time; however, a number of studies show that long-term heavy MDMA users suffer cognitive deficits, including problems with memory.

NIDA-supported research is developing a clearer picture of the potential dangers of MDMA, and this Research Report summarizes the latest findings. We hope that this compilation of scientific information will inform readers and help the public recognize the risks of MDMA use.

**Nora D. Volkow, M.D.**

Director

National Institute on Drug Abuse

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Chapter 1: What is MDMA?

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MDMA is an illegal drug that acts as both a stimulant and hallucinogen, producing an energizing effect, as well as distortions in time and perception and enhanced enjoyment from tactile experiences. Typically, MDMA (an acronym for its chemical name 3,4-methylenedioxymethamphetamine) is taken orally, usually in a tablet or capsule, and its effects last approximately 3 to 6 hours. The average reported dose is one to two tablets, with each tablet typically containing between 60 and 120 milligrams of MDMA. It is not uncommon for users to take a second dose of the drug as the effects of the first dose begin to fade.

MDMA can affect the brain by altering the activity of chemical messengers, or neurotransmitters, which enable nerve cells in many regions of the brain to communicate with one another. Research in animals has shown that MDMA in moderate to high doses can be toxic to nerve cells that contain serotonin and can cause long-lasting damage to them. Further, MDMA can interfere with the body's ability to control its temperature, which has on rare occasions led to severe medical consequences, including death. Also, MDMA causes the release of another neurotransmitter, norepinephrine, which is likely what causes the increase in heart rate and blood pressure that often accompanies MDMA use.

Although MDMA is known universally among users as Ecstasy, researchers have determined that many Ecstasy tablets contain not only MDMA but a number of other drugs or drug combinations that can be harmful as well. Adulterants found in MDMA tablets purchased on the street include methamphetamine, caffeine, the over the counter cough suppressant dextromethorphan, the diet drug ephedrine, and cocaine. Also, as with many other drugs of abuse, MDMA is rarely used alone. It is not uncommon for users to mix MDMA with other substances, such as alcohol and marijuana.

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MDMA was developed in Germany in the early 1900s as a parent compound to be used to synthesize other

pharmaceuticals. During the 1970s in the United States some psychiatrists began using MDMA as a psychotherapeutic tool despite the fact that the drug had never undergone formal clinical trials nor received approval from the U.S. Food and Drug Administration (FDA) for use in people. In fact, it was only in late 2000 that the FDA approved the first small clinical trial for MDMA that will determine if the drug can be used safely under carefully monitored conditions to treat post-traumatic stress disorder. Nevertheless, the drug gained a small following among psychiatrists in the late 1970s and early 1980s, with some even calling it "penicillin for the soul" because it was perceived to enhance communication in patient sessions and reportedly allowed users to achieve insights about their problems. It was also during this time that MDMA first started becoming available on the street. In 1985, the U.S. Drug Enforcement Agency banned the drug, placing it on the list of Schedule I drugs with no proven therapeutic value.

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It is difficult to determine the exact scope of this problem because MDMA is often used in combination with other substances, and does not appear in some traditional data sources, such as treatment admission rates. MDMA does, however, appear to be a drug that has increased in popularity and become more widespread, particularly among people under the age of 25.

In 2002, over 10 million persons aged 12 or older reported using Ecstasy at least once in their lifetime according to the 2002 National Survey on Drug Use and Health, up from 6.4 million in 2000. The number of current users in 2002 was estimated to be 676,000. The initiation of Ecstasy use in the U.S. has been rising steadily since 1992, with 1.8 million new users in 2001.

The Drug Abuse Warning Network, maintained by the Substance Abuse and Mental Health Services Administration, reported that mentions of MDMA in drug abuse related cases in hospital emergency departments increased 94% from 1999 to 2001 (from 2,850 to 5,542); 86% of these cases also involved other substances, such as alcohol, marijuana, cocaine and heroin. More than three-quarters (77%) of the patients who came to emergency departments mentioning MDMA as a factor in their admission in 2001 were age 25 and under, suggesting that MDMA is used predominantly by adolescents and young adults.

There is, however, some encouraging news from NIDA's Monitoring the Future Study (MTF), an annual survey used to track drug abuse trends among adolescents in middle and high schools across the country. Over the last 2 years Ecstasy use decreased by almost 50% in 8th, 10th, and 12th graders combined. In fact, rates of MDMA use decreased significantly from 2002 to 2003 in all three grades surveyed. For 12th graders past year use declined from 7.4 percent to 4.5 percent. These decreases may be due in part to negative attitudes about MDMA use and increased awareness about the harmful consequences associated with this drug. Disapproval of MDMA use increased significantly from 2002 to 2003 for 8th and 10th graders but remained stable for 12th graders, and perceived risk associated with use increased in selected categories in each grade. For example, 56 percent of 12th graders said they were aware of the harm associated with the drug, an increase of 18 percentage points over three years ago. The percent of 12th graders who felt they could easily obtain the drug remained stable at 59% and 58% in 2002 and 2003, respectively, whereas the perceived availability among 10th

graders decreased from 41% in 2002 to 36.3% in 2003. While the rates of MDMA use may be declining in high school students, the drug is still easy to get, and its use remains prevalent. The MTF data also show that MDMA use extends across many demographic subgroups. Among 12th graders, for example, 6.4 percent of Whites, 5.3 percent of Hispanic students, and 1.4 percent of African Americans reported using MDMA in the year prior to the survey.

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MDMA first gained popularity among adolescents and young adults in the nightclub scene or weekend-long dance parties known as raves. However, recently the profile of the typical MDMA user has been changing. Community-level data from NIDA's Community Epidemiology Workgroup (CEWG), reported in June 2003, indicate that use of MDMA has spread beyond the rave and nightclub scene to a variety of urban, suburban and rural areas throughout the country, including greater use on college campuses. For example, reports from Chicago suggest that Ecstasy, or drugs sold as Ecstasy, are widely available among high school and college students.

Use of this drug has also increased among different ethnic groups. For example, reports from Texas indicate use spreading beyond predominantly White youth to a broader range of ethnic groups. In Chicago, where a single MDMA pill can be purchased for about \$12 to \$15, the drug continues to be predominantly used by White youth, but there are increasing reports of its use by African American adults in their twenties and thirties. Also indicators in New York suggest that both the distribution and use of club drugs are becoming more common in non-White communities.

MDMA has also become a more popular drug among urban gay males. Reports have shown that some gay and bisexual men take MDMA and other club-drugs in myriad venues. This is concerning given that the use of club drugs has been linked to high-risk sexual behaviors that may lead to HIV or other sexually transmitted diseases. Many gay males in big cities report using MDMA as part of a multiple-drug experience that includes marijuana, cocaine, methamphetamine, ketamine, and other legal and illegal substances.

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MDMA has become a popular drug, in part because of the positive effects that a person experiences within an hour or so after taking a single dose. Those effects include feelings of mental stimulation, emotional warmth, empathy toward others, a general sense of well being, and decreased anxiety. In addition, users report enhanced sensory perception as a hallmark of the MDMA experience. Because of the drug's stimulant properties, when used in club or dance settings MDMA can also enable users to dance for extended periods. However, there are some users who report undesirable effects immediately, including anxiety, agitation, and recklessness.

As noted, MDMA is not a benign drug. MDMA can produce a variety of adverse health effects, including nausea, chills, sweating, involuntary teeth clenching, muscle cramping, and blurred vision. MDMA overdose can also occur - the symptoms can include high blood pressure, faintness, panic attacks, and in severe cases, a loss of consciousness, and seizures.

Because of its stimulant properties and the environment in which it is often taken, MDMA is associated with vigorous physical activity for extended periods. This can lead to one of the most significant, although rare, acute adverse effects -- a marked rise in body temperature (hyperthermia). Treatment of hyperthermia requires prompt medical attention, as it can rapidly lead to muscle breakdown, which can in turn result in kidney failure. In addition, dehydration, hypertension, and heart failure may occur in susceptible individuals. MDMA can also reduce the pumping efficiency of the heart, of particular concern during periods of increased physical activity, thereby further complicating these problems.

MDMA is rapidly absorbed into the human blood stream, but once in the body MDMA interferes with the body's ability to metabolize, or break down, the drug. As a result, additional doses of MDMA can produce unexpectedly high blood levels, which could worsen the cardiovascular and other toxic effects of this drug. MDMA also interferes with the metabolism of other drugs, including some of the adulterants that may be found in MDMA tablets.

In the hours after taking the drug, MDMA produces significant reductions in mental abilities. These changes, particularly those affecting memory, can last for up to a week, and possibly longer in regular users. The fact that MDMA markedly impairs information processing emphasizes the potential dangers of performing complex or even skilled activities, such as driving a car, while under the influence of this drug.

Over the course of the week following moderate use of the drug, many MDMA users report feeling a range of emotions, including anxiety, restlessness, irritability, and sadness that in some individuals can be as severe as true clinical depression. Similarly, elevated anxiety, impulsiveness, and aggression, as well as sleep disturbances, lack of appetite and reduced interest in and pleasure from sex have been observed in regular MDMA users. Some of these disturbances may not be directly attributable to MDMA, but may be related to some of the other drugs often used in combination with MDMA, such as cocaine or marijuana, or to potential adulterants found in MDMA tablets.

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MDMA affects the brain by increasing the activity of at least three neurotransmitters (the chemical messengers of brain cells): serotonin, dopamine, and norepinephrine. Like amphetamines, MDMA causes these neurotransmitters to be released from their storage sites in neurons resulting in increased neurotransmitter activity. Compared to the very potent stimulant, methamphetamine, MDMA causes greater serotonin release and somewhat lesser dopamine release. Serotonin is a neurotransmitter that plays an important role in the regulation of mood, sleep, pain, emotion, appetite, and other behaviors. The excess release of serotonin by MDMA likely causes the mood elevating effects experienced by MDMA users. However, by releasing large amounts of serotonin, MDMA causes the brain to become significantly depleted of this important neurotransmitter, contributing to the negative behavioral aftereffects that users often experience for several days after taking MDMA.

Numerous studies in animals have demonstrated that MDMA can damage serotonin-containing neurons; some of these studies have shown these effects to be long-lasting. This suggests that such damage may occur in humans as well -- however, with the technologies currently available, measuring serotonin damage in humans is more difficult. Studies have

shown that some heavy MDMA users experience long lasting confusion, depression, and selective impairment of working memory and attention processes. Such memory impairments have been associated with a decrease in serotonin metabolites or other markers of serotonin function. Imaging studies in MDMA users have shown changes in brain activity in regions involved in cognition, emotion, and motor function. However, improved imaging technologies and more research is needed to confirm these findings and to elucidate the exact nature of the effects of MDMA on the human brain. It is also important to keep in mind that many users of Ecstasy may unknowingly be taking other drugs that are sold as Ecstasy, and/or they may intentionally use other drugs, such as marijuana, which could contribute to these behavioral effects. Additionally, most studies in people do not have behavioral measures from before the users began taking drugs, making it difficult to rule out pre-existing conditions.

Factors such as gender, dosage, frequency and intensity of use, age at which use began, the use of other drugs, as well as genetic and environmental factors all may play a role in some of the cognitive deficits that result from MDMA use and should be taken into consideration when studying the effects of MDMA in humans.

Given that most MDMA users are young and in their reproductive years, it is possible that some female users may be pregnant when they take MDMA, either inadvertently or intentionally because of the misperception that it is a safe drug. The potential adverse effects of MDMA on the developing fetus are of great concern. Behavioral studies in animals have found significant adverse effects on tests of learning and memory from exposure to MDMA during a developmental period equivalent to the third trimester in humans. However, the effects of MDMA on animals earlier in development are unclear, therefore, more research is needed to determine what the effects of MDMA are on the developing human nervous system.

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For some people, MDMA can be addictive. A survey of young adult and adolescent MDMA users found that 43 percent of those who reported ecstasy use met the accepted diagnostic criteria for dependence, as evidenced by continued use despite knowledge of physical or psychological harm, withdrawal effects, and tolerance (or diminished response), and 34 percent met the criteria for drug abuse. Almost 60 percent of people who use MDMA report withdrawal symptoms, including fatigue, loss of appetite, depressed feelings, and trouble concentrating.

MDMA affects many of the same neurotransmitters systems in the brain that are targeted by other addictive drugs. Experiments have shown that animals prefer MDMA, much like they do cocaine, over other pleasurable stimuli, another hallmark of most addictive drugs.

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Because social context and networks seem to be an important component of MDMA use, the use of peer led advocacy and drug prevention programs may be a promising approach to reduce MDMA use among adolescents and young adults. High schools and colleges can serve as important venues for delivering messages about the effects of MDMA use. Providing accurate scientific information regarding the effects of MDMA is important if we hope to reduce the damaging effects of this

drug. Education is one of the most important tools for use in preventing MDMA

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There are no specific treatments for MDMA abuse. The most effective treatments for drug abuse and addiction are cognitive behavioral interventions that are designed to help modify the patient's thinking, expectancies, and behaviors, and to increase skills in coping with life's stressors. Drug abuse recovery support groups may be effective in combination with behavioral interventions to support long-term, drug-free recovery. There are currently no pharmacological treatments for dependence on MDMA. Antidepressant medications might be helpful in combating the depressive symptoms frequently seen in MDMA users who have recently become abstinent.

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