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RESEARCH FILE

Ecstasy: What We Know and Don't Know About MDMA - A Scientific Review

A number of our Nation's best monitoring mechanisms have detected an alarming increase in the popularity of MDMA (3,4-methylenedioxymethamphetamine), particularly among young Americans. Unfortunately, myths abound about both the acute effects and long-term consequences of this drug, also known as "Ecstasy," with many young people believing that MDMA is safe, offering nothing but a pleasant high for the $25 cost of a single tablet. But MDMA is not new to the scientific community, with many laboratories beginning their investigations of this drug in the mid 1980s, and the picture emerging from their efforts paints a much different image of this drug, one that is far from benign.

This report, *Ecstasy: What We Know and Don't Know About MDMA*, represents a scientific review of what research has discovered about how this drug works in the brain and what requires further study to fully understand the consequences of using this illicit substance. This report discusses what scientists know and don't know about MDMA's acute effects on the brain and behavior from laboratory studies in both animals and humans. The report also reviews the long-term effects on the brain, again in both laboratory animals and humans, as well as long-term behavioral consequences detected in chronic MDMA users.

MDMA, a relatively simple chemical belonging to the amphetamine family of compounds, has properties of both stimulants and hallucinogens. While MDMA does not cause true hallucinations, many people have reported distorted time and perception while under the influence of this drug. The vast majority of people take MDMA orally, and its effects last approximately four to six hours. Many users will "bump" the drug, taking a second dose when the effects of the initial dose begin to fade. The typical dose is between one and two tablets, with each containing approximately 60-120 milligrams of MDMA. However, tablets of what users call Ecstasy often contain not only MDMA but a number of other drugs, including methamphetamine, caffeine, dextromethorphan, ephedrine, and cocaine.

One of the more alarming facts about MDMA is that despite its known detrimental effects, there are increasing numbers of students and young adults who continue to use the drug. Results from the 2000 Monitoring the Future survey indicate that MDMA use increased among students in the 12th, 10th, and 8th grades. African Americans show considerably lower rates of MDMA use than do either whites or Hispanics. The recent CEWG data showed a large increase in use among Hispanics that may represent an important change.

Effects of Acute Doses of MDMA

MDMA works in the brain by increasing the activity levels of at least three neurotransmitters: serotonin, dopamine, and norepinepherine. Much like other amphetamines, MDMA causes these neurotransmitters to be released from their storage sites in neurons, increasing brain activity. Compared to the potent stimulant methamphetamine, MDMA triggers a larger increase in serotonin and a smaller increase in dopamine. Serotonin is a major neurotransmitter involved in regulating mood, sleep, pain, emotion, and appetite, as well as other behaviors. By releasing large amounts of serotonin, and also interfering with its synthesis, MDMA leads to a significant depletion of this important neurotransmitter. As a result, it takes the human brain a significant amount of time to rebuild the store of serotonin needed to perform important physiological and psychological functions.

One hypothesis to explain the long-lasting neurotoxicity of MDMA on serotonergic systems is that MDMA induces both oxidative and metabolic stress in serotonin neurons that, in turn, adversely affect the ability of these neurons to produce serotonin. Support for this hypothesis comes from a variety of studies, including those showing that MDMA perturbs the activity of various antioxidant enzymes; artificially boosting the levels of these enzymes reduces MDMA's effects on serotonin and dopamine neurons. Also, stress appears to increase the oxidative damage caused by MDMA.

It has been difficult to study the effects of MDMA in humans under controlled conditions, and virtually impossible until recently to conduct simultaneous neurochemical studies. However, several groups of researchers have chosen to study the behavioral pharmacology of MDMA in various animal species, showing that MDMA and related compounds produce a unique behavioral profile in rodents. Studies in non-human primates suggests that acute doses of MDMA may have subtle effects on higher cognitive functions, including memory and learning. Other experiments in laboratory animals suggest that MDMA is a drug that humans are likely to abuse, and that humans may develop tolerance to MDMA's reinforcing effects. Limited studies in humans have shown that MDMA negatively impacts short-term performance on a variety of measures of cognitive ability.

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