Ecstasy damages the brain and impares memory in humans.

By Robert Mathias

NIDA NOTES Staff Writer

A NIDA-supported study has provided the first direct evidence that chronic use of MDMA, popularly known as "ecstasy," causes brain damage in people. Using advanced brain imaging techniques, the study found that MDMA harms neurons that release serotonin, a brain chemical thought to play an important role in regulating memory and other functions. In a related study, researchers found that heavy MDMA users have memory problems that persist for at least two weeks after they have stopped using the drug. Both studies suggest that the extent of damage is directly correlated with the amount of MDMA use.

"The message from these studies is that MDMA does change the brain and it looks like there are functional consequences to these changes," says Dr. Joseph Frascella of NIDA's Division of Treatment Research and Development. That message is particularly significant for young people who participate in large, all-night dance parties known as "raves," which are popular in many cities around the Nation. NIDA's epidemiologic studies indicate that MDMA (3,4-methylenedioxymethamphetamine) use

has escalated in recent years among college students and young adults who attend these social gatherings.

In the brain imaging study, researchers used positron emission tomography (PET) to take brain scans of 14 MDMA users who had not used any psychoactive drug, including MDMA, for at least three weeks. Brain images also were taken of 15 people who had never used MDMA. Both groups were similar in age and level of education and had comparable numbers of men and women.

In people who had used MDMA, the PET images showed significant reductions in the number of serotonin transporters, the sites on neuron surfaces that reabsorb serotonin from the space between cells after it has completed its work. The lasting reduction of serotonin transporters occurred throughout the brain, and people who had used MDMA more often lost more serotonin transporters than those who had used the drug less.

Previous PET studies with baboons also produced images indicating MDMA had induced long-term reductions in the number of serotonin transporters. Examinations of brain tissue from the animals provided further confirmation that the decrease in serotonin transporters seen in the PET images corresponded to actual loss of serotonin nerve endings containing transporters in the baboons' brains. "Based on what we found with our animal studies, we maintain that the changes revealed by PET imaging are probably related to damage of serotonin nerve endings in humans who had used MDMA," says Dr. George Ricaurte of The Johns Hopkins Medical Institutions in Baltimore. Dr. Ricaurte is the principal investigator for both studies, which are part of a clinical research project that is assessing the long-term effects of MDMA.

"The real question in all imaging studies is what these changes mean when it comes to functional consequences," says NIDA's Dr. Frascella. To help answer that question, a team of researchers, which included scientists from Johns Hopkins and the National Institute of Mental Health who had worked on the imaging study, attempted to assess the effects of chronic MDMA use on memory. In this study, researchers administered several standardized memory tests to 24 MDMA users who had not used the drug for at least two weeks and 24 people who had never used the drug. Both groups were matched for age, gender, education, and vocabulary scores.

The study found that, compared to the nonusers, heavy MDMA users had significant impairments in visual and verbal memory. As had been found in the brain imaging study, MDMA's harmful effects were dose related, the more MDMA people used, the greater difficulty they had in recalling what they had seen and heard during testing.

The memory impairments found in MDMA users are among the first functional consequences of MDMA-induced damage of serotonin neurons to emerge. Recent studies conducted in the United Kingdom also have reported memory problems in MDMA users assessed within a few days of their last drug use. "Our study extends the MDMA-induced memory impairment to at least two weeks since last drug use and thus shows that MDMA's effects on memory cannot be attributed to withdrawal or residual drug effects," says Dr. Karen Bolla of Johns Hopkins, who helped conduct the study.

The Johns Hopkins/NIMH researchers also were able to link poorer memory performance by MDMA users to loss of brain serotonin function by measuring the levels of a serotonin metabolite in study participants' spinal fluid. These measurements showed that MDMA users had lower levels of the metabolite than people who had not used the drug; that the more MDMA they reported using, the lower the level of the metabolite; and, that the people with the lowest levels of the metabolite had the poorest memory performance. Taken together, these findings support the conclusion that MDMA induced brain serotonin neurotoxicity may account for the persistent memory impairment found in MDMA users, according to Dr Bolla.

Research on the functional consequences of MDMA-induced damage of serotonin-producing neurons in humans is at an early stage, and the scientists who conducted the studies cannot say definitively that the harm to brain serotonin neurons shown in theimaging study accounts for the memory impairments found among chronic users of the drug. However, "that's the concern, and it's certainly the most obvious basis for the memory problems that some MDMA users have developed," Dr. Ricaurte says.

Findings from another Johns Hopkins/NIMH study now suggest that MDMA use may lead to impairments in other cognitive functions besides memory, such as the ability to reason verbally or sustain attention. Researchers are continuing to examine the effects of chronic MDMA use on memory and other functions in which serotonin has been implicated, such as mood, impulse control, and sleep cycles.

How long MDMA-induced brain damage persists and the long-term consequences of that damage are other questions researchers are trying to answer. Animal studies, which first documented the neurotoxic effects of the drug, suggest that the loss of serotonin neurons in humans may last for many years and possibly be permanent. "We now know that brain damage is still present in monkeys seven years after discontinuing the drug," Dr. Ricaurte says. "We don't know just yet if we're dealing with such a long-lasting effect in people."

Sources

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