# The Chicago connectio

**Research**

# U. of C. studies led to ban on designer dru

By Jon Van
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"Ecstasy," a street drug touted for enhancing empathy and self-understanding, found its most influential critics among people who have little interest in or knowledge of so-called "street drugs."

But their basic studies into the nature of how the brain works led them to information that Ecstasy, no matter how good it may make a person feel, likely is producing long-term brain deterioration.

Ten years of study of the aging and death of brain cells led Chicago scientists to make conclusions about Ecstasy that influenced the recent federal action to make sales of the drug illegal.

Ecstasy is known chemically as 3,4-methylenedioxymethamphetamine, or MDMA. It was given an emergency one-year Schedule 1 controlled substance listing by the federal Drug Enforcement Administration after the agency received research information from Charles Schuster and Lewis Seiden, two pharmacological researchers at the University of Chicago.

Schedule 1 is the most restrictive category and is used for drugs with high abuse potential and no therapeutic value. Such drugs as heroin, LSD and MDA, a close chemical cousin of MDMA, are in the Schedule 1 category. Hearings are scheduled for later in the summer to determine what permanent category the DEA will assign MDMA.

Backers of Ecstasy, including some psychiatrists, have hired a lawyer to fight restrictive classification of the substance that would preclude its experimental use in humans.

The drug, a derivative of oil of sassafras or oil of nutmeg, is related chemically to both amphetamines and mescaline. It is produced in the private chemical laboratories of people who specialize in making so-called "designer drugs" and is said to be especially popular in California.

The substance had no standing as a regulated drug and was legal to produce and sell until the drug agency action, which takes effect July 1. Seiden said he doubts the government action will stop street sales and use of the substance. However, it may stop licensed therapists such as psychiatrists from giving it to patients, Seiden said, "and that is a good thing."

It will be easy for chemists to add another molecule to the drug's basic make-up, producing an analog that will again be legal to make and sell, Seiden said.

This represents a dark side of what drug researchers do regularly in their labs. Legitimate researchers produce chemical cousins or analogs of a substance to enhance therapeutic value while eliminating side effects. Designer-drug chemists do the same, but to evade legal constraints rather than to make their products safer or more therapeutic.

The Chicago research, sponsored by the National Institute of Drug Abuse, has examined effects of various drugs in the amphetamine family on the brains of rats and other animals.

It was work with MDA that caused Seiden, Schuster and their colleagues to warn federal authorities of the probable dangers of MDMA. Rats given regular doses of MDA exhibit a 50 percent reduction in their production of serotonin, a brain chemical that plays a role in regulating sleep, aggression, sexual arousal and other vital functions.

Most startling was the finding that the reduced serotonin production persisted six months after the rats had their last dose of MDA. The likelihood is that brain cells manufacturing serotonin are killed when the MDA is administered, Seiden said, and pictures of brain tissue from dead rats support that conclusion.

Methylamphetamine, or MA, another chemical cousin of MDMA, has been shown by Seiden and Georgetta Vosmer to kill brain cells producing dopamine, a brain chemical that helps regulate body movement. Loss of dopamine production can result in symptoms found in patients with Parkinson's disease.

It is natural for some brain cells to die as a person ages, and Seiden is concerned that even though taking Ecstasy might have no immediate effect on someone's neurologic health, it could be devastating in the future when normal aging further depletes the user's brain cells.

Ten years of research into brain function and reaction to several drugs have given Seiden and his colleagues insights into how aging and cell death may occur and what strategies might work to prevent it. They originally began their experiments to determine how the brain [illegible] become tolerant of certain [illegible] over time.

They found that use of drugs like MDA, MDMA and their cousins may speed up the normal aging process in the brain, providing scientists a clearer picture of how brain cells die naturally.

When a person takes MDA, it causes cells to produce brain chemicals called neurotransmitters at an accelerated pace. This overproduction of neurotransmitters produces the pharmacologic effect that some describe as euphoric, Seiden said.

In this flood of brain chemicals, Chicago researchers have proven that some of them combine with oxygen and hydrogen to form new and toxic substances that return to the cells of their origin and kill them.

This occurs at an accelerated pace when chemical stimulants like MDA and MA are administered, but Seiden said it may also occur during normal brain functions, providing a cause for cell death with aging.

"We are trying to pin this down and to find ways to block it or reverse it," said Seiden. "This is nitty-gritty cellular chemistry."

If the researchers can prove their theories and learn just how brain chemicals turned toxic manage to kill their parent cells, it should be possible to produce other chemicals that can come to the assistance of the brain cells, stopping the toxins before they do any damage.

Studies by the Chicago researchers and other groups have used a variety of chemicals closely related to MDMA in five animal species, and all have demonstrated an ability to kill the cells that produce vital brain chemicals.

Although MDMA's ability to kill human brain cells has not been shown with direct evidence, the work on animals is highly suggestive that MDMA would have that effect on humans, Seiden and his colleagues advised the drug agency.

"Use of any drug is a matter of risks and benefits," Seiden said. "If you had a drug with the probable risks of MDMA, you might justify using it if a person could expect a large benefit, such as if you thought it might cure cancer and the patient had no alternative therapy available.

"But what are the benefits of MDMA? Personal insights? Feeling better? These are vague and certainly not worth the high risks of this drug. It reminds me very much of the claims made for LSD when it was first used."