MDMA: Compound raises medical, legal issues

BRAIN MIND bulletin
FRONTIERS OF RESEARCH, THEORY AND PRACTICE
April 15, 1985 Volume 10, Number 8

MDMA, a compound sometimes known as Adam or XTC, is in the eye of a paradoxical hurricane. It appears likely to become tightly restricted just as it is gaining attention as a possible pharmacological breakthrough.

The drug—technically 3,4-methylenedioxy-methamphetamine—is derived from oil of sassafras or oil of nutmeg. Increasingly, psychiatrists and counselors are praising its therapeutic efficacy. Clinical use is being investigated independently by therapists in the U.S., England, Chile, Germany, France and Australia.

Meanwhile the U.S. Drug Enforcement Administration has begun hearings on its possible scheduling as a controlled substance. It also is under international regulatory consideration by the World Health Organization.

DEA officials expressed astonishment at the number of protests from mental-health professionals when the proposed scheduling was announced. Research proponents of the drug requested a hearing through Dewey, Ballantine, Bushby, Palmer & Wood, a prestigious Washington, D.C., law firm.

"We were not aware of the quasi-therapeutic use of the drug until after we proposed scheduling last July," DEA spokesman Frank Sapienza told *B/MB*.

Sapienza said the agency had known of the drug since the 1970's but had not seen reports of its experimental use until recently.

MDMA was one of eight compounds investigated in Michigan animal studies in 1953-54, funded by the Army Chemical Center. The studies were declassified in 1969 and reported in a technical journal in 1973.

The spread of MDMA use and its possible outlawing have provoked a journalistic flurry. *Newsweek, Psychology Today, People, Rolling Stone, California Magazine, L.A. Weekly* and *Omni* are among the publications that have scheduled articles on MDMA.

Separate stories in this issue deal with MDMA's unique characteristics, its purported therapeutic potential and the issues surrounding its current legal status.

Because MDMA's 1914 patent by Merck & Co. has long since lapsed and the compound is now in the public domain, pharmaceutical manufacturers are not motivated to spend the millions of dollars necessary to demonstrate efficacy or safety. In that sense it is what has been called an "orphan drug."

Used legally by psychiatrists in some states and unofficially by non-MD therapists, MDMA has been described by some researchers as an aid to communication and clarity.

Reported therapeutic benefits include insight into problems, pain reduction, motivation, improved couple and family relationships, enhanced body awareness, diminution of fear and treatment of addiction.

The effects of a 100-mg. dose of MDMA last for about four hours. Therapeutically the drug is not taken regularly like a tranquilizer but is used episodically in two or three sessions. The drug does not lend itself to abuse because the brain

Continued on Page 2

Psychiatrists report on drug's clinical outcome

Four psychiatrists who use MDMA in clinical practice reported on the findings of more than 1,000 sessions at a recent California conference sponsored by the Earth Metabolic Design Laboratory.

Their overall conclusions, as phrased in an article in press: "The reports of MDMA's facilitation of psychotherapy were impressive. Many subjects experienced classic retrieval of lost traumatic memories, followed by relief of emotional symptoms."

Psychotherapist Alise Agar will coordinate a follow-up meeting of psychiatrists, psychologists, chemists and others in June to synthesize the findings to date.

MDMA currently is used for cancer patients as an adjunct to conventional therapy. Patients say the experience alters their sense of hopelessness. Some have significantly outlived their prognoses. One reported becoming pain-free during the session after a year of intense pain. With the help of self-hypnosis and two more MDMA sessions, he has been able to maintain the pain at a low level for six months.

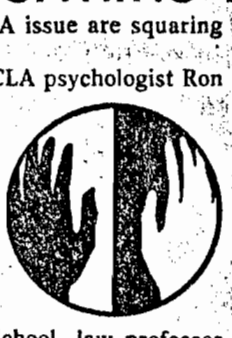
Psychiatrist George Greer concluded that his study of 29 patients demonstrated "a potential use for MDMA as a safe and effective adjunct to therapy, especially for the prevention and treatment of interpersonal problems and substance-use

Continued on Page 3

Hearing to determine MDMA research status

Witnesses on both sides of the MDMA issue are squaring off.

In the upcoming MDMA hearings, UCLA psychologist Ron Siegel will testify on abuse by recreational users he has interviewed. Government witnesses will testify that its use as a treatment adjunct has not been established. They also will cite animal tests showing "similar qualitative effects" between MDMA and MDA.



MDMA researchers — psychiatrists George Greer of Santa Fe, N.M., and Lester Grinspoon of Harvard Medical School, law professor James Bakalar of Harvard, educational psychologist Thomas Roberts of Northern Illinois University—maintain that MDMA does not have a high potential for abuse. "At most it has a low or moderate potential." That position also will be taken by psychiatrist Lance Wright of the drug and alcohol treatment unit of the Philadelphia VA Medical Center and physician Richard Seymour of the Haight-Ashbury Free Medical Clinic.

The investigators also will argue that, judging by current use of MDMA by practicing psychiatrists, the compound is safe under medical supervision and has shown significant therapeutic value.

According to Grinspoon, the government has performed no controlled studies on the substance. In late March the National Institute on Drug Abuse allocated $25,000 to determine dependency potential in rats and monkeys.

The research proponents will cite a new study on rats that appears to contradict the earlier finding of similarity to MDA. First, scientists trained the animals to differentiate between LSD and a saline solution. When the animals were then given MDA, they behaved as if they had been given LSD. MDMA produced a different effect.

MDMA issue. . .

Continued from Page 1

develops a rapid tolerance with frequent use. Positive effects diminish, and side effects become more uncomfortable.

Preliminary medical studies indicate that the substance has relatively mild side effects. (See box, this page.)

Clinical investigators estimate that the substance has been used more than one million times since it became available in the 1970's.

According to the Drug Abuse Warning Network, a federal agency that tracks emergency-room admissions, no reports have been filed on MDMA since 1981. One overdose death with complications has been attributed to the sole use of MDMA; in four post-mortems MDMA was one of a combination of drugs found.

MDMA is being used primarily by four groups, with some overlap:

- Therapists, as an adjunct to treatment.
- Transpersonally oriented individuals and groups, as a tool for spiritual insight.
- Working teams, for creativity and bonding.
- Social users, for mood elevation and purported enhancement of interpersonal warmth and confidence.

* * *

Psychiatrists and others interested in the therapeutic effects have raised medicolegal questions about the regulatory procedure and the constraints on research. They maintain that the drug itself is not the therapeutic focus but rather a catalyst—an adjunct that increases the patient's ability to articulate and integrate insight.

"These drugs are a milieu, not a treatment," said psychiatrist George Greer of Santa Fe, N.M. "It's part of a procedure. This is comparable to the use of certain drugs as part of a surgical procedure."

Mental health professionals complain of a Catch-22 in the law: They say that the DEA cannot determine medical efficacy because the agency has no review committee versed in the medical use of psycho-chemicals. The research proponents suggest setting up a review committee of research psychiatrists for future DEA inquiries into little-known substances.

Because of the required hearing, the substance is not likely to be scheduled before early 1986.

Resources

A collection of pertinent papers on MDMA is available for $15 from Earth Metabolic Design Foundation. EDML also offers a computerized survey to clinicians using MDMA and is helping coordinate the testimony at the DEA hearings to be held in three U.S. cities. Licensed psychotherapists or psychiatrists can write to EDML: 3484 Monroe Ave., Lafayette, Calif. 94549, (415) 420-9739.

For information on the government's position: Frank Sapienza, Drug Enforcement Administration, Dept. of Justice, 1405 I St. NW, Washington, D.C. 20537. The proposed scheduling is 49 Fed. Reg. 30210.

MDMA study shows low toxicity

Preliminary physiological tests of MDMA show low toxicity. Long-term toxicity studies remain to be done, however, and relatively little is known of its effectiveness in the severely disturbed.

A medical study of 21 people showed a moderate rise in pulse and blood pressure. Eighty per cent reported transient jaw tension, periodic uncontrollable eye movements and headache. None had visual illusions with their eyes open, but all reported a strong sensual or kinesthetic awareness. Reflexes were fast and motor strength normal. Most had a loss of appetite, and one reported nausea and vomiting. A three-month follow-up study showed no lasting physical effects.

Six subjects reported major personal changes in the months after the sessions, especially better communication with people close to them. Ninety per cent said their relationships had improved, especially in terms of more generous feelings.

"Our findings support the impression that this is a safe agent for positive mood changes when used sparingly and episodically," said physicians Jack Downing and Phil Wolfson and psychotherapist Alise Agar, who conducted the study.

Production process eliminates MDMA's psychedelic properties, biochemist says

In the next month or two, MDMA will be variously described in national magazines from hundreds of points of view: those of therapists, drug enforcement officials, researchers and recreational users.

What is it? Is it a substance of abuse, a therapeutic aid, an aphrodisiac, a psychedelic, an antidepressant?

MDMA is a member of the phenethylamine family. Most manufacturers use a pharmaceutical product refined several steps beyond the oil of sassafras and oil of nutmeg from which the drug is derived.

MDMA is not a psychedelic. It is sometimes confused with MDA, a mildly psychedelic substance first used in the 1960's. (MDMA rarely triggers visual or auditory distortions.) According to David Nichols, a Purdue University pharmaceutical chemist, MDMA goes through an additional chemical transformation not used in the manufacture of MDA.

"The psychedelic properties are removed from the active isomer by adding a methyl group to the nitrogen," he said. "There are subjective similarities to MDA, but the two substances are pharmacologically distinct."

Alexander Shulgin, a psychopharmacologist, pointed out that MDMA, MDA and pseudoephedrine (Sudafed, an antihistamine) share certain chemical features, but each has distinct properties.

MDMA is not a true amphetamine. DEA officials maintain that it produces behavioral changes in animals similar to amphetamines. Biochemists, however, say that it only shares a similar carbon skeletal structure. Chemically, it is an amphetamine. Pharmacologically—that is, in terms of its action in a biological system—it is not.

MDMA may represent a new class of substances. According to Nichols, researchers are looking for a name for a class of compounds that clarify emotions. "Recently we coined the term entactogen—from the Greek for 'touch within.'"

Nichols reported in a 1983 anthology, *Medicinal Chemistry and Structure-Activity Relationships of Hallucinogens*, that MDMA and its close analogs produce "only minor disruptions of normal sensory processing. They apparently amplify empathy and would seem ideal candidates as an adjunct to psychotherapy."

MDMA may work by altering timing mechanisms in the brain. Structurally it resembles the neurotransmitters dopamine and norepinephrine, researchers say, and seems to trigger the release of serotonin.

Frank Barr, physician and author of the melanin hypothesis of brain function (see *B/MB*, July 11-Aug. 1, 1983), speculated that MDMA, because of its chemical structure, binds to melanin.

Melanin, which Barr has postulated as a major organizing factor in biological systems, is known to regulate the timing of the neurotransmitters. They in turn control the neuroendocrine system (the endorphins and other peptides). Therefore, MDMA would indirectly affect the normal phased release of peptides reaching the brain's hippocampus and frontal cortex regions.

In the April 1 *Leading Edge*: Special Issue: 'Cake-sharing' disarmament plan by inventor Stephen Salter of the University of Edinburgh includes obstacles to arms cuts, verification and military rivalry. Single copies $1.50; send stamped, self-addressed envelope to Box 42211, Los Angeles 90042.

DEA, clinicians disagree on MDMA schedulin

The legal controversy surrounding MDMA raises provocative questions: Who should control the use of new therapeutic agents? Who should define "potential for abuse" or "accepted medical use"?

According to U.S. law, foods and drugs are regulated for safety by the Food and Drug Administration. The Drug Enforcement Administration, as part of the Justice Department, is responsible for enforcing laws.

A qualified researcher or pharmaceutical company files a request to investigate a new drug. Animal studies explore chronic toxicity, determining which organs are damaged after prolonged use. After animal toxicity levels are established, researchers can investigate safety and efficacy in human subjects.

The typical procedure to get a new drug approved costs the pharmaceutical manufacturer some $12 million. Because MDMA was first patented in 1914 and is now in the public domain, there is little incentive for a manufacturer to seek its approval.

(When lithium, a natural element, was found to be effective in the treatment of manic-depressive illness, psychiatrists were frustrated because manufacturers had no financial motivation to process it and verify its purity. As a known compound, it could not be patented. However, a special spansule form was finally patented to get around the problem.)

Canada is the only country in which MDMA is illegal. The substance was scheduled there in 1979 after unofficial manufacture came to light.

Since it is not yet scheduled in the U.S., MDMA is in a legal twilight zone. It can be used on human subjects in states where physicians are allowed to administer drugs they have manufactured to consenting patients. State laws require them, however, to gain informed consent and peer review of their work.

All other investigations are necessarily off the record and cannot be officially considered by the DEA. Therefore there is no body of data on safety and medical efficacy for most new substances.

Drugs with no official standing are subject to being "scheduled"—that is, made illegal except for use by registered researchers—if a potential for abuse is uncovered. A drug is proposed for Schedule 1 if it is considered to have high abuse potential and no medical efficacy, Sched 2 if it has high abuse potential and knowledged medical utility. LSD is Sch ule 1; morphine, cocaine and amphetam are Schedule 2.

Schedules 3, 4 and 5 cover drugs o decreasing abuse potential and broad er—almost lay—medical use. The do not even require triplicate prescrip tions.

The DEA points out that qualified searchers technically can study Schedul drugs. However, research proponents that the stringent Schedule 1 proto discourage study. They point out that drug has ever been removed from Sched 1.

Only one researcher in the U.S., Fra DiLeo of the University of Maryland M cal School, has obtained permissior investigate LSD. DiLeo is studying its in the terminally ill.

BRAIN MIND bulletin

Brain/Mind Bulletin (USPS 124-350) is published every three weeks except the second week in November, with the third week in January and first week in February combined, by Interface Press, Box 42211, 4717 N. Figueroa St., Los Angeles, Calif. 90042. Telephone (213) 223-2500. Subscriptions: $25 per year ($30 first-class mail) in North America, $35 all other (airmail). Back issues $1.50 each with self-addressed envelope.

Editorial: Marilyn Ferguson, Publisher
Connie Zweig, Executive Editor
Chris Berka, Contributing Editor
Administration: Anita V. Storey
Staff: Glenn Bassett, Larry Crane, Marine Derrick, June DeWitt, Lynn Ferguson, Ed Fowler, Denise Purdy.

Therapists see MDMA as useful. . .

Continued from Page 1

disorders."

The most common benefits: improved communication and intimacy between family members and couples. Aftereffects included higher self-esteem, positive mood and a decreased use of addictive substances.

Most subjects reported an expanded mental perspective or insight. Several said they felt undesirable emotional symptoms, such as anxiety during the sessions and sadness or fatigue afterward. Five described transcendent experiences.

All nine with specific psychiatric disorders reported significant relief from their problems. Two said they had full and lasting remissions.

"When we are in altered states, our habits don't work the same," Greer said. "It's like putting a program into a computer that has been rewired or is operating at a different frequency.

"The usual pattern of flow keeps running into dead ends. The computer keeps asking the operator what to do, so the operator has to make a choice

purpose is, the experience can be diffic The difficulty pushes us either to cha our purpose or to change ourselves in or to move nearer our chosen goal.

"Through this experience, one can cide to learn simpler, more efficient w of being able to recognize and m choices—without having to spend a lo time in a drug-induced state."

David Katzin, a Los Angeles physic who directs a drug detoxification cli suggested that MDMA may prove us for substance abuse. Another physic has already used it successfully to as cocaine withdrawal.

A Benedictine monk working in a st prison has suggested using MDMA in rehabilitation of prisoners. An un study of psychiatric residents at Har University will examine the usefulness the compound as a training tool for cli cians, and a West Coast psychiatrist cently proposed a study of MDMA as motivational tool for vocational rehab tation.

In Brief

Psycho-Intuitive Training May 4-5; advanced ver May 6-8, "demystification of the psychic proces with Anne and Jim Armstrong, **Paradise Valley, A**

BOOKS

Psychology moves from upset mind to broken brain

THE BROKEN BRAIN by Nancy Andreasen ($16.95 from Harper & Row, 10 East 53rd St., NYC 10022).

Drugs are reshaping the direction of psychiatry. "Designer drugs," made precisely to fit the brain's receptors, can alter moods in exact ways, providing relief from alarming disorders. They may one day be used to heighten specific kinds of awareness or enhance specific skills.

This highly accessible book on the biological revolution in psychiatry is a good introduction. But it is clearly biased: Andreasen, a psychiatry professor, believes that most mental illness is *caused* by abnormalities in brain structure or chemistry. As psychiatry moves from a psychological to a neuroscience explanation, she says, it is moving from the "troubled mind" to the "broken brain."

Andreasen aims to remove the stigma from mental illness—and to remove the stigma from using drugs to treat it.

After reviewing the two other schools of thought on mental disorders—psychoanalysis and behaviorism—she introduces the biological model: Psychiatric illnesses are medical diseases just like diabetes, heart disease and cancer. They are not due to "bad habits," bad parenting or weakness of will, she asserts. Therefore, they should be treated by "somatic therapies."

Andreasen contrasts these three approaches, introducing beginners to the brain and its array of neurotransmitters, and reviewing the history of new pharmacological treatments.

In her enthusiasm for these breakthroughs, however, she may be oversimplifying this issue. Depression, schizophrenia and anxiety cannot be explained away on purely materialistic bases. Given the great body of evidence for the role of stress and attitude in physical illnesses, it is unreasonable to seek a single biological cause for mental illness.

Andreasen does not differentiate between *cause* and *symptom*. She assumes, rather, that the cause is always in the physical brain.

Revolutionary new drugs may alter brain function in a way that enables people to work, focus and generally feel better. But do they "cure" people? What is the therapeutic competence in the world of mental disease? And do biological psychiatrists continue to seek answers to these questions while easing life for their patients? —C.Z.

Tomatoes, tradition and curiosity

The reason tomatoes were not accepted until relatively recently in North America is simple: They were poisonous. Everyone knew they were poisonous, at least everyone in North America. It was obvious.

Tomatoes belong to the nightshade family. . . . The fact that the French and Italians were eating them in increasing quantities without seeming harm did not encourage colonial Americans to try them. It simply did not make sense to eat poisonous food.

Not until 1820, when Robert Gibbon Johnson ate a tomato on the steps of the courthouse in Salem, N.J., and survived, did the people of America begin, grudgingly, we suspect, to consume tomatoes.

The tomato effect in medicine occurs when an efficacious treatment for a certain disease is ignored or rejected because it does not 'make sense' in light of accepted theories of disease mechanism and drug action. The tomato was ignored because it was clearly poisonous; it would have been foolish to eat one. In analogous fashion, there have been many therapies in the history of medicine that, while later proved efficacious, were at one time rejected because they did not make sense.

We cannot progress in medicine without a theoretical structure. Structure by necessity limits our peripheral vision while allowing us to focus on a particular path. The benefit of such a structure far outweighs the detriment. However, we can reduce the detriment by asking, almost in ritual fashion, certain questions. Before we accept a treatment, we should ask, "Is this a placebo?"; before we reject a treatment we should ask, "Is this a tomato?"

—*Journal of the American Medical Assn.*, May 11; reprinted in *Advances* 2:1

WHO to rule on 28 phenethylamines

International attempts to regulate MDMA and a family of related compounds are under way.

In the late 60's and early 70's, 40 nations signed treaties to coordinate drug controls worldwide. With the International Convention of Psychotropic Substances, scheduling procedures became uniform.

Rulings by the World Health Organization take precedence over national ones. A country can favor higher national recommendations but not lower ones.

Late this month in Geneva the Expert Committee on Drug Dependence will convene to recommend various levels of control over MDMA and 27 other phenethylamines. Next February member nations will meet for official voting.

In 1958 a WHO technical report on psychoactive drugs in psychiatry explored the relationship between altered states and religious experiences and noted the reluctance of scientists to enter into full-scale investigation of these areas.

Last May WHO passed a resolution urging the recognition of "the spiritual dimension of health." Richard Doblin, a spokesman for the Earth Metabolic Design foundation, suggests that the resolution is a context in which WHO could update the 1958 report by reviewing the medical aspects of the new compounds.

BRAIN MIND bulletin
P. O. Box 42211
Los Angeles, Calif. 90042

Our 10th Year

ATTENTION MAIL ROOM:
This is a paid subscription—please expedite.