LSD and Ecstasy: Pharmacology, Phenomenology, and Treatment

A hallucination is a false perception, and these drugs induce exaggerated and "unreal" sensory phenomena including visual, auditory, and tactile hallucinations.

by NORMAN S. MILLER, MD, and MARK S. GOLD, MD

LSD and Ecstasy (MDMA) are hallucinogens and stimulants, according to pharmacological classification. The hallucinogens comprise a broadly defined class of drugs that cross pharmacological boundaries. These drugs are grouped together as much for historical reasons as for their psychological effects. By strict definition, the hallucinogens alter and distort perceptions in space and time. A hallucination is a false perception, and these drugs induce exaggerated and "unreal" sensory phenomena including visual, auditory, and tactile hallucinations. These perceptions originate internally from drug-induced neurochemical changes in the brain and, as in hallucinations, project onto an external reality.[1]

Dr. Miller is an Associate Professor in the Departments of Psychiatry and Neurology, University of Illinois at Chicago. Dr. Gold is a Professor at the Brain Institute, Departments of Neuroscience and Psychiatry, University of Florida, College of Medicine, Gainesville, Florida.

Address reprint requests to Norman S. Miller, MD, Department of Psychiatry (M/C 913), University of Illinois at Chicago, 912 S. Wood St., Chicago, IL 60612-7327.

MDMA, LSD, AND CANDY FLIPPING

In the late 1980s, psychedelic dances called "raves" were being held at so-called "acid houses" in England, spreading quickly to Germany. The drug used at acid houses was Ecstasy or MDMA, not LSD. Unlike the acid tests of the 1960s where LSD was provided to all, Ecstasy and LSD are sold alongside a variety of bottled water, smart drinks, fruit juices, vitamins, and amino acids. The "street" reasoning is that drinks should contain amino acid building blocks depleted by MDMA and that continual hydration is an important preventative measure.

While acid tests of the '60s were predominantly psychedelic experiences, raves are cybernetic. The music is electronic and rhythmic without an obvious ethnic or cultural origin. Raves can last for three or four days, but 12 or 24 hours of continuous dancing and switching between MDMA and LSD—candy flipping or trolling (tripping and rolling)—is common. The idea is to keep going. The energy to dance nonstop and to continue to move while hot, tired, and hallucinating is provided by MDMA and/or methamphetamine packaged as MDMA.

This practice of concurrent drug use is very common but is not limited to LSD and Ecstasy. Alcohol, marijuana, cocaine, seda-

LSD is one of the most potent psychoactive drugs known in pharmacology.

tives/hypnotics (benzodiazepines), barbiturates, quaaludes, and antidepressants are drugs frequently taken by the hallucinogen users. The occurrence of multiple drug use and addiction is much more likely to be the rule than the exception by the contemporary alcoholic and drug addict, including the hallucinogen user.[2]

LSD: INTOXICATION AND TOXICITY

The fact that LSD use is increasing is of particular interest since it is one of the most potent psychoactive drugs known in pharmacology.[3] A 10-mg dose produces euphoria and decreased inhibition; 50 to 100 mg is the minimal hallucinogenic dose, whereas 400 to 500 mg produces the full hallucinogenic effect. LSD is well absorbed orally.

Like MDMA, LSD primarily alters the serotonin system. LSD has a high affinity for both serotonin receptors (5-HT_{2A} and 5-HT_{2C}). In this volume, the neuropharmacology of LSD is reviewed by Aghajanian[4] and psychopharmacology, by Gold.[5] The most constant psychological effect of LSD is the perceptual distortions and visual hallucinations. Objects undulate, their boundaries are lost and merge; people's faces and body parts appear distorted.[6,7] The sensory acuity is heightened for all modalities. Perceptions are more vivid. There is an acute attentiveness to details with overvalued attribution of meaning to ordinary objects and events; usual thoughts become novel and profound.[8]

Disrupted concentration, decreased recent memory, impaired insight and judgment, depersonalization, and derealization are common occurrences. At times, a fragmentation or loss of self-identity may promote mystical experiences. Suspiciousness and frank paranoid delusions may occur, particularly with chronic and repetitive use.[9] The effects on mood are unpredictable, including euphoria, anxiety, panic, and depression alternating in an intense mood lability with irritability and sometimes suicidal ideation and actions.[7]

ECSTASY: INTOXICATION AND TOXICITY

MDMA(3,4-methylenedioxymethamphetamine) (also known as Ecstasy, X, Adam) use appears confined to suburban youth (well educated at present) and gay youth on both coasts. In the US, accurate estimates of usage are difficult to determine; however, some estimate that 100,000 doses a month are sold.

Mechanism of action is very much like amphetamine, although the compound is more of a hybrid mescaline plus amphetamine. MDMA causes the release of serotonin and also blocks reuptake—like a more specific amphetamine targeted to the 5-HT system.

One problem in MDMA research is that the neurochemical effects are greater for monkeys than for rodents; in fact, many of the neurochemical findings only became clear in monkeys and man.[1,10] At the highest doses studied MDMA can reduce brain 5-HT by 90% with long-lasting decreases for 12 to 18 months in hippocampus and cortex—time needed to regrow axons.[11] MDMA toxicity in humans is predicted by studies in animals. Studies using doses in monkeys similar to doses taken by humans show clear neurotoxic effects. Clear deficits and major neurotoxicity appear related to total exposure or dose and are cumulative.

Consistent with this is Una McCann's recent report[12] at the Society for Neuroscience: MDMA produces a 30% to 35% drop in 5-HT metabolism in humans (decreased 5-HIAA). MDMA effects in women are much greater than those observed for men, with a 50% decrease in 5-HT in women users, although less body weight and more frequent use may be the explanation for these remarkable sex differences. MDMA produces marked sleep stage changes and changes in sleep—total sleep and Stage 2 sleep decrease although users are unaware of these changes and say that they are sleeping well. Personality changes were also clear and remarkable—increased conformity and decreased impulsivity, more sense of belonging to a group or cult.

MDMA is associated with 5-HT long-lasting neurotoxicity.[11] Silver stains in animals and scans in humans show loss of 5-HT organization and cortical 5-HT.

The methamphetamine derivatives are frequently sold as MDMA since they all produce an intense euphoria. Ecstasy replaced MDA in the 1970s and 1980s, but MDA use still persists.[10] Acute MDMA problems include jitteriness, anxiety, jaw clenching, and fear, and may occur at any dose. At high doses visual distortions may occur; objects may appear to be shimmering, shiny, or moving and shaking. Suspicion and even frank paranoid reactions can occur. Some people report that they at first desire to be alone and then are concerned that people are noticing their odd behavior. At higher doses they may experience panic with tachycardia, psychosis, paranoia, and violence. While these effects are not commonly reported now, it is likely that this will be seen more in the future. Treatment is symptomatic; panic and/or anxiety are treated

with reassurance and/or minor tranquilizers, and psychosis or psychotic symptoms are treated with haloperidol.

Effects of prolonged use of Ecstasy and/or LSD are now coming to attention. Use for a week or two can lead to confusion, loss of interest in hygiene, fatigue, memory impairment, and sleep dysfunction. Other psychological symptoms include bizarre and poorly formed geometric patterns and complex visual images, especially with closed eyes, similar to other hallucinogens. Physical symptoms are common and include jaw-clenching, bruxism, sweating, ataxia, nausea, and dizziness in addition to the sympathomimetic effects of tachycardia, hypertension, hyperflexia, and tremor.[1,10] Other adverse effects include residual withdrawal effects that can last for weeks, including exhaustion, depression, fatigue, nausea, and numbness.

Because of the sympathomimetic effects, certain medical conditions may be aggravated by MDMA, MDA, and other hallucinogens. These include diabetes mellitus, liver disease, seizure disorders, glaucoma, cardiovascular disease, hypertension, hypoglycemia, hyperthyroidism, and pregnancy.[1,10] Other toxic manifestations include ataxia, nystagmus, emotional lability, vomiting, and paresthesias. Overdose reactions include tachycardia, palpitations, hypertension, hypotension, hyperthermia, renal failure, disseminated intravascular coagulation, and rhabdomyolyses.[1,10]

The adverse psychological reactions are similar to those of classic hallucinogens, and include panic dissociative and psychotic reactions, insomnia, rage reactions, and delusions.[2,9] Suicidal actions are prominent, particularly with methamphetamine. The expression "speed kills" is an outgrowth of the intense feelings of depression with despair, hopelessness, helplessness, and paranoid delusions that may accompany chronic use of these drugs.[9,12]

DIAGNOSIS

The diagnosis is made by applying the same criteria for addiction, tolerance, and dependence that are used for all drugs as in DSM-III-R. Urine confirmation is ideal. Hallucinogens are rarely the first drugs used by the patient and usually there is a progression of use from other drugs such as alcohol and marijuana. Alcohol is often the first drug used and frequently in combination with the hallucinogens.

INTERVENTION AND TREATMENT

Patients with LSD or MDMA "bad trips" based on loss of control and anxiety are treated with reassurance and a comforting environment. Those who have marked changes in cognition and aberrant judgment can also be treated by placing the user in a safe environment without impeding freedom of movement. Getting up, sitting, walking, rocking may actually be helpful for the MDMA or LSD-toxic patient as you try to deflect concern and attention from the frightening elements or "visual nightmare." Ice baths and rehydration are often necessary after the use of Ecstasy at all-night raves. However, benzodiazepines such as lorazepam or diazepam may be employed for agitation, panic, and other symptoms of anxiety accompanying the use of these drugs.[2]

Long-term consequences of LSD have also been described and include prolonged psychosis, severe depression, flashbacks ("free trips"), exacerbation of preexisting psychiatric illness, and the posthallucinogen perceptual disorder (PHPD), which has been described as living in a "purple haze." Chronic and severe episodes of panic, phobias, and depression have been described for LSD and Ecstasy.

The treatment of withdrawal is supportive and usually does not require pharmacological therapy. It is important to recognize that most hallucinogen users are multiple-drug addicts/alcoholics who must be assessed for their other addictions and their medical complications. These patients may be referred for traditional inpatient and outpatient treatment for drug and alcohol addiction as well as long-term participation in Alcoholics Anonymous and Narcotics Anonymous.[2]

REFERENCES

1. Hollister L. Effects of hallucinogens in humans. In: Jacobs B, ed. *Hallucinogens: Neurochemical, Behavioral and Clinical Perspectives*. New York, NY: Raven Press; 1984.
2. Miller NS, Gold MS. *Drugs of Abuse: A Comprehensive Series for Clinicians*. Vol II. New York, NY: Plenum Medical Book Company; 1991.
3. Gold MS, Schuchard K, Gleaton T. LSD in the USA: Déjà vu again? *Biol Psychiatry*. 1993; 33:6-15.
4. Aghajanian GK. Serotonin and the action of LSD in the brain. *Psychiatric Annals*. 1994; 24:137-141.
5. Gold MS. The epidemiology, attitudes, and pharmacology of LSD use in the 1990s. *Psychiatric Annals*. 1994; 24:124-126.
6. Bowers MD Jr, Freedman DX. "Psychedelic" experiences in acute psychoses. *Arch Gen Psychiatry*. 1966; 15:240-248.
7. Bowers MG Jr. Acute psychosis induced by psychotomimetic drug abuse. *Arch Gen Psychiatry*. 1972; 27:437-442.
8. Smith DE, Seymour RD. Dream becomes nightmare: adverse reactions of LSD. *Psychoactive Drugs*. 1985; 17:297-303.
9. Hayner GN, McKinney H. MDMA: the dark side of ecstasy. *Psychoactive Drugs*. 1986; 18:341-347.
10. Redda KK, Walker CA, Barnet G. *Cocaine, Marijuana, Designer Drugs: Chemistry, Pharmacology and Behavior*. Boca Raton, Fla: CRC Press; 1989.
11. Ricaurate GA, Fischer CA, Hadzidimitrio G, Katz JL. Reorganization of ascending 5-HT projections after MDMA injury. *Society for Neuroscience Abstracts*. 1993; 19(482.2):1169.
12. McCann UD, Ridenour A, Shaham Y, et al. Evidence for serotonin neurotoxicity in recreational MDMA ("Ecstasy") users: a controlled study. *Society for Neuroscience Abstracts*. 1993; 19(482.1):1169.