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Hallucinogens

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In Brief

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The hallucinogens comprise a group of drugs that alters perception, cognition, and mood. Despite their name, hallucinogens only sometimes cause true hallucinations, defined as perceiving experiences that do not occur. These substances exert their mind-altering effects primarily through agonism at serotonin receptors (specifically 5-HT_{2a}) in the central nervous system. There is some controversy over which drugs of abuse fit neatly into the category of hallucinogens. Although phencyclidine (PCP) may cause hallucinations, it is classified as a dissociative drug. Other drugs of abuse such as cocaine, anticholinergics, marijuana, and methylenedioxymethamphetamine (MDMA or "ecstasy") can alter perception or produce hallucinations, but these drugs are not classified as hallucinogens because of different mechanisms of action and numerous other important physiologic and toxicologic effects.

The best-known hallucinogen is the semisynthetic compound lysergic acid diethylamide (LSD). Naturally occurring hallucinogens include psilocybin, obtained from *Psilocybe cubensis* or "magic mushrooms," and mescaline, derived from the peyote cactus. Lesser known but similar compounds include N,N-dimethyltryptamine (DMT), derived from many botanical sources, and lysergic acid amide (LSA), derived from morning glory seeds. Although most of these compounds are ingested, DMT is smoked or inhaled nasally.

Historically, hallucinogens have been used for religious ceremonies, recreational abuse, and even research purposes to induce alterations of perception. The Monitoring the Future Survey of the National Institute on Drug Abuse provides an annual assessment of the extent of drug use among 8th-, 10th-, and 12th-grade students nationwide. The use by adolescents of hallucinogens as a class, and specifically of LSD, began to decline in the 1990s. Use of these drugs has remained stable at historically low levels of lifetime use: 3.5% of 8th graders and 9.7% of 12th graders stated use on data collected from 2002 through 2004.

Physiologic effects of hallucinogen use include paresthesias, dizziness, weakness, drowsiness, nausea, and blurred vision. The desired effect is altered perception by the user. Typical perceptual symptoms include distortion of shapes and colors and hallucinations that usually are visual. A classic, although uncommon, hallucinogen-induced perceptual change is synesthesia, in which one sense is perceived as another. For example, a user who has synesthesia may feel that he or she is "hearing" colors or "seeing" smells. Hallucinogen users may experience distorted cognition and have difficulty expressing thoughts or an imprecise sense of time. Users may describe a transcendent or dreamlike state. Mood often is affected greatly and varies from euphoria to a "bad trip," in which the user experiences profound anxiety or fear.

Unlike many other drugs of abuse, no current evidence suggests direct end-organ toxicity or overdose fatalities from hallucinogens. The acute danger of hallucinogens, instead, comes from their effect on judgment while the individual is in an altered state. Although reports are relatively rare, the unsupervised, altered patient may have a deadly accident, as in an attempt to fly. Irreversible ocular damage has been reported from staring at the sun. There is no evidence that these substances are physiologically addictive or produce a withdrawal syndrome.

A long-term adverse outcome of hallucinogen use is the occurrence of "flashbacks," now more appropriately referred to as hallucinogen persisting perception disorder. This condition consists of episodes of re-experiencing one or more of the perceptual symptoms previously induced by hallucinogen use after the drug has worn off and in the absence of another disorder, such as psychiatric illness. Although case reports of this phenomenon exist, it is believed to be rare.

Symptoms of hallucinogen intoxication may be difficult to distinguish from those of psychiatric illness, particularly schizophrenia. Lack of a family history of psychiatric disorders, absence of

symptoms when the drug has cleared, and variable severity of symptoms that can be related to an ingestion suggest hallucinogen toxicity. Although hallucinogens may cause visual perceptual disturbances and visual hallucinations, they do not cause the disorganized thinking, true delusions, and auditory hallucinations that are typical of schizophrenia.

The treatment of a patient who is suspected of being under the influence of a hallucinogen is primarily supportive. Acutely intoxicated patients should be placed in a calm, quiet, protected environment and provided contact with familiar people and objects. Those experiencing a "bad trip" may benefit from benzodiazepines.

Comment: The word hallucinogen, derived from Latin, means to wander in mind or talk idly. Research on hallucinogens has been challenging because these preparations exert varying effects, depending on the perception of the user and the setting where the use has taken place. The therapeutic benefits of these drugs have been debated. Additional research is needed to explore the neurocognitive effects of hallucinogens in an attempt to understand consciousness better, reduce anxiety in terminally ill patients facing death, and perhaps understand the mechanisms of certain mental illnesses, such as psychoses and schizophrenia.

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In Brief

Drug Interactions

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A drug interaction occurs when one drug alters the effectiveness or toxicity of another. Clinically significant drug interactions, which pose potential harm to the patient, may result from changes in pharmaceutical, pharmacokinetic, or pharmacodynamic properties. Required in vitro studies conducted by drug manufacturers help predict the potential occurrence of a drug interaction, but they do not confirm the clinical relevance for patients, and they are not sufficiently sensitive to identify all potentially serious interactions, especially in the pediatric population.

Patient factors that increase the risk for drug interactions include being critically ill; receiving polypharmacy; having impaired hepatic or renal function, hypoxemia, or metabolic disturbances; and being elderly. Given the paucity of data on drug interactions in pediatric patients, children also should be considered at special risk. Drug characteristics that contribute to interactions include high potency, wide usage, action on vital organ functions, narrow therapeutic index, saturable hepatic metabolism, and extensive protein binding (>90%).

Drug interactions can be used strategically to benefit patients. For example, a lower dosage of a primary drug (saquinavir) can be used to avoid adverse effects when a second drug (cimetidine) inhibits the clearance of the more toxic agent. Therapeutic effects also can be enhanced with desirable drug interactions, such as vitamin C increasing iron absorption.

More commonly, drug interactions may lead to adverse events. Many unacceptable drug interactions can be avoided simply by spacing the administration times of medications; other interactions are inevitable and require dosage adjustments or even discontinuation of one or more agents. Prescription drugs usually are implicated

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