HALLUCINOGEN-RELATED DISORDERS

Psychosis is a disturbance in the perception of reality, evidenced by hallucinations (false sensory perceptions), delusions (false beliefs that are not shared with any other people), or disorganized thoughts. Psychotic states brought on by hallucinogen use are often referred to as "trips" by recreational users, and they may be accompanied by agitation, aggression, and other forms of behavioral impairment. Trips generally involve existential experiences, distortions in perception, and synesthesias (blending of the senses).

Hallucinogens alter perceptions without causing any major metabolic changes (Abraham, Aldridge, & Gogia, 1996). They come in many different shapes and forms, ranging from common household items to plant and animal extracts to synthetic derivatives of natural products. The classic hallucinogens include lysergic acid diethylamide, or LSD ("acid"), which is the prototypical hallucinogen, as well as psilocybin ("magic mushrooms") and mescaline ("peyote"). There are three different classes of "designer" drugs (recreational drugs that are derivatives of legal compounds): molecules containing phenylethyl amine scaffolds, synthetic derivatives of opiates, and arylhexylamines such as phencyclidine (PCP). In addition, volatile substances or those that emit vapors (e.g., paint thinners, diethyl ether, gasoline, certain glues, felt tip pens, nitrous oxide, and aerosol containers) can be sniffed, bagged, huffed, or sprayed to induce a hallucinogenic experience (Anderson & Loomis, 2003).

A number of hallucinogens were discovered during the course of routine pharmaceutical research. For example, Albert Hofman first synthesized LSD while investigating the pharmaceutical properties of lysergic acid derivatives, and he subsequently used LSD-induced hallucinations as a model to gain insight into the pathophysiology of schizophrenia. However, the discovery of LSD paved the way for easy synthesis and distribution of hallucinogens to the general public, allowing hallucinogen use to transcend its previous geographical or spiritual boundaries (Abraham, Aldridge, & Gogia, 1996). The affinity of LSD for serotonin receptors, especially the 5-HT_2 family of G-protein-coupled receptors, has been well-documented; however, it is still unclear how LSD exerts its effects on perception, mood, and thought processes (Backstrom, Chu, Niswender, & Sanders-Bush, 1999).

Similarly, amphetamine derivatives have their origins in pharmacological research, where it was found that subtle variations of phenylethylamine could produce molecules with properties that ranged from stimulation of the sympathetic nervous system to changes in cognition. Amphetamine, methamphetamine, 3,4-methylenedioxyamphetamine, or MDA, and 3,4-methylenedioxymethamphetamine, or MDMA ("X," "E," "Ecstasy"), have since found their way into recreational use. These drugs can quickly deplete the brain's stores of serotonin through a combination of increased release of serotonin into the synapse with decreased serotonin production and recycling (Britt, 2005).

Another class of designer drugs is the arylhexylamines, which include phencyclidine, or PCP ("angel dust," "peace pill," "whack"), and ketamine ("Special K," "cat valium"). These compounds noncompetitively inhibit the N-methyl-D-aspartate (NMDA) receptor complexes of the central nervous system, leading to increased release of neurotransmitters such as dopamine, serotonin, and norepinephrine in the prefrontal cortex and midbrain. Like the lysergic acid and amphetamine derivatives, arylhexylamines are metabolized in the liver cytochrome P450 system and excreted by the kidneys (Britt & McCance-Katz, 2005).

Inhalants are readily absorbed through the lungs and rapidly metabolized in the liver cytochrome P450 system. With the exception of nitrates, inhalants are depressants that act directly on the central nervous system, with hypothesized effects on opiate, GABA, and NMDA receptors. Nitrates work to produce sensations of floating by dilating blood vessels and relaxing smooth muscles. Adverse and lethal events related to inhalant abuse are related to their anesthetic and gaseous properties; these include sudden sniffing death syndrome, arrhythmias, asphyxia, and serious accidental injuries. Chronic inhalant abuse can damage the heart, kidneys, liver, bone marrow, and nervous system (Williams & Storck, 2007).

The main purpose of hallucinogen use, regardless of whether it is for recreational purposes or in religion, is to induce the hallucinogenic experience. Religious use by shamans of hallucinogens such as ayahuasca, psilocybin, lysergic acid amide, and peyote has been well documented. Sacramental use of psilocybin can be traced back to the Aztecs, and the use of these mushrooms continues to this day among some indigenous tribes of the Oaxaca region of Mexico. Ayahuasca use has traditionally been located along the Amazon and in Latin America, and its use is in religious ceremonies to help with spiritual cleansing and physical detoxification, such as recovery from alcoholism. Peyote is consumed chiefly in the context of Native American religious ceremonies that either celebrate special occasions such as birthdays or serve a particular purpose such as promoting the health of a loved one or ensuring the safety of church members serving in the military. For those who do not ingest peyote, a few drops of the tea may be placed on the lips as a blessing. Religious use of both ayahuasca and peyote is exempted from prosecution by federal law, which has excited controversy through the intersection of the United States's war on drugs with freedom of religion (Halpern & Sewell, 2005).

Recreationally, hallucinogen use is popular among adolescents and young adults because hallucinogens can produce feelings of euphoria and energy, as well as a desire to socialize, without any withdrawal symptoms or memory

The Corsini Encyclopedia of Psychology, edited by Irving B. Weiner and W. Edward Craighead.

impairment. Although hallucinogen abuse dropped off in the 1970s and remained at low levels during the 1980s, there has since been a reemergence in hallucinogen use. This increase is hypothesized to be due to generational forgetting, whereby the current generation of youths has not had opportunities to learn from older peers about bad trips and other adverse consequences of hallucinogen use (Rickert, Siqueira, Dale, & Wiemann, 2003).

Volatile hallucinogen abuse is prevalent among teenagers; almost 20% of teenagers have experimented with inhaled substances. Inhalant abuse can also be found in industrial factory workers who bring home solvents for recreational use. The use of inhalants is equally common among members of both sexes. Non-Hispanic Caucasians are more likely to report inhalant use than are members of other race or ethnic groups (Neumark, Delva, & Anthony, 1998). Inhalant abuse typically causes a euphoric feeling and can become habit-forming (Anderson & Loomis, 2003).

Hallucinogen-induced psychosis is often accompanied by abuse of other drugs, risky or impaired behavior, and physical symptoms such as increased blood pressure, seizures, and balance problems. Flashbacks, a sudden unexpected re-experience of a previous hallucinogen experience, can be common, but they tend to fade over time as long as no additional hallucinogen is taken (Britt & McCance-Katz, 2005). The National Institute on Drug Abuse does not consider classical hallucinogens to be drugs of addiction, because they do not produce compulsive drug-seeking behavior. Over time, most recreational users decrease or completely stop taking hallucinogens (Griffiths, Richards, McCann, & Jesse, 2006).

The acute treatment for hallucinogen and inhalant intoxication revolves around clearing the body of the drugs and their metabolites combined with psychosocial support. Clearance methods depend on the drug abused. For example, inhalant abusers should be placed on supplemental oxygen (Anderson & Loomis, 2003), whereas patients who are intoxicated with PCP should have their urine acidified. Acutely intoxicated patients are in a state of sensory hyperstimulation and are thus easily agitated; treatment should take place in a minimally stimulating environment, such as a quiet, dimly lighted room.

Long-term treatment of hallucinogen abuse and dependence is similar to the treatment of alcohol abuse and includes individual counseling, support groups, and referral to Narcotics Anonymous. The treatment of a prolonged hallucinogen-induced psychotic episode is based around the use of antipsychotic medications for symptom and behavioral management and the promotion of clearance of the hallucinogen from the body of the patient. Treatment of chronic inhalant abuse also relies on support and counseling. Education can help decrease adolescent experimentation with inhalants (Anderson & Loomis, 2003); however, many substance-abuse treatment programs feel that they do not have the resources to address the issues of inhalant abuse or dependence (Beauvais, Jumper-Thurman, Plested, & Helm, 2002).

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See also: **Drug Addiction; Psychotic Disorders**