Club Drugs, Ecstasy, and Hallucinogens

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Hallucinogens - LSD, Peyote, Psilocybin, and PCP

Hallucinogenic compounds found in some plants and mushrooms (or their extracts) have been used—mostly during religious rituals-for centuries. Almost all hallucinogens contain nitrogen and are classified as alkaloids. Many hallucinogens have chemical structures similar to those of natural neurotransmitters (e.g., acetylcholine-, serotonin-, or catecholaminelike). While the exact mechanisms by which hallucinogens exert their effects remain unclear, research suggests that these drugs work, at least partially, by temporarily interfering with neurotransmitter action or by binding to their receptor sites. This DrugFacts will discuss four common types of hallucinogens:

- LSD (d-lysergic acid diethylamide) is one of the most potent mood-changing chemicals. It was discovered in 1938 and is manufactured from lysergic acid, which is found in ergot, a fungus that grows on rye and other grains.
- Peyote is a small, spineless cactus in which the principal active ingredient is mescaline. This plant has been used by natives in northern Mexico and the southwestern United States as a part of religious ceremonies. Mescaline can also be produced through chemical synthesis.

- Psilocybin (4-phosphoryloxy-N,Ndimethyltryptamine) is obtained from certain types of mushrooms that are indigenous to tropical and subtropical regions of South America, Mexico, and the United States. These mushrooms typically contain less than 0.5 percent psilocybin plus trace amounts of psilocin, another hallucinogenic substance.
- PCP (phencyclidine) was developed in the 1950s as an intravenous anesthetic. Its use has since been discontinued due to serious adverse effects.

How Are Hallucinogens Abused?

The very same characteristics that led to the incorporation of hallucinogens into ritualistic or spiritual traditions have also led to their propagation as drugs of abuse. Importantly, and unlike most other drugs, the effects of hallucinogens are highly variable and unreliable, producing different effects in different people at different times. This is mainly due to the significant variations in amount and composition of active compounds, particularly in the hallucinogens derived from plants and mushrooms. Because of their unpredictable nature, the use of hallucinogens can be particularly dangerous.

- LSD is sold in tablets, capsules, and, occasionally, liquid form; thus, it is usually taken orally. LSD is often added to absorbent paper, which is then divided into decorated pieces, each equivalent to one dose. The experiences, often referred to as "trips," are long; typically, they end after about 12 hours.
- **Peyote:** The top of the peyote cactus, also referred to as the crown, consists of disc-shaped buttons that are cut from the roots and dried. These buttons are generally chewed or soaked in water to produce an intoxicating liquid. The hallucinogenic dose of mescaline is about 0.3 to 0.5 grams, and its effects last about 12 hours. Because the extract is so bitter, some individuals prefer to prepare a tea by boiling the cacti for several hours.
- Psilocybin: Mushrooms containing psilocybin are available fresh or dried and are typically taken orally. Psilocybin (4-phosphoryloxy-N,Ndimethyltryptamine) and its biologically active form, psilocin (4hydroxy-N,N-dimethyltryptamine), cannot be inactivated by cooking or freezing preparations. Thus, they may also be brewed as a tea or added to other foods to mask their bitter flavor. The effects of psilocybin, which appear within 20 minutes of ingestion, last approximately 6 hours.
- PCP is a white crystalline powder that is readily soluble in water or alcohol. It has a distinctive bitter chemical taste. PCP can be mixed easily with dyes and is often sold on the illicit drug market in a variety of tablet, capsule, and colored powder forms that are normally snorted, smoked, or orally ingested. For smoking, PCP is often applied to a leafy material such as mint, parsley, oregano, or marijuana. Depending upon how much

and by what route PCP is taken, its effects can last approximately 4–6 hours.

How Do Hallucinogens Affect the Brain?

LSD, peyote, psilocybin, and PCP are drugs that cause hallucinations, which are profound distortions in a person's perception of reality. Under the influence of hallucinogens, people see images, hear sounds, and feel sensations that seem real but are not. Some hallucinogens also produce rapid, intense emotional swings. LSD, peyote, and psilocybin cause their effects by initially disrupting the interaction of nerve cells and the neurotransmitter serotonin.¹ Distributed throughout the brain and spinal cord, the serotonin system is involved in the control of behavioral, perceptual, and regulatory systems, including mood, hunger, body temperature, sexual behavior. muscle control. and sensory perception. On the other hand, PCP acts mainly through a type of glutamate receptor in the brain that is important for the perception of pain, responses to the environment, and learning and memory.

There have been no properly controlled research studies on the specific effects of these drugs on the human brain, but smaller studies and several case reports have been published documenting some of the effects associated with the use of hallucinogens.

LSD: Sensations and feelings change much more dramatically than the physical signs in people under the influence of LSD. The user may feel several different emotions at once or swing rapidly from one emotion to another. If taken in large enough doses, the drug produces delusions and visual hallucinations. The user's sense of time and self is altered. Experiences may seem to "cross over" different senses, giving the user the feeling of hearing colors and seeing sounds. These changes can be frightening and can cause panic. Some LSD users experience severe, terrifying thoughts and feelings of despair, fear of losing control, or fear of insanity and death while using LSD.

LSD users can also experience flashbacks, or recurrences of certain aspects of the drug experience. Flashbacks occur suddenly, often without warning, and may do so within a few days or more than a year after LSD use. In some individuals, the flashbacks can persist and cause significant distress or impairment in social or occupational functioning, a condition known as hallucinogen-induced persisting perceptual disorder (HPPD).

Most users of LSD voluntarily decrease or stop its use over time. LSD is not considered an addictive drug since it does not produce compulsive drug-seeking behavior. However, LSD does produce tolerance, so some users who take the drug repeatedly must take progressively higher doses to achieve the state of intoxication that they had previously achieved. This is an extremely dangerous practice, given the unpredictability of the drug. In addition, cross-tolerance between LSD and other hallucinogens has been reported.

Peyote: The long-term residual psychological and cognitive effects of mescaline, peyote's principal active ingredient, remain poorly understood. A recent study found no evidence of psychological or cognitive deficits among Native Americans that use peyote regularly in a religious setting.² It should be mentioned, however, that these findings may not generalize to those who repeatedly abuse the drug for recreational purposes. Peyote abusers may also experience flashbacks.

Psilocybin: The active compounds in psilocybin-containing "magic" mushrooms have LSD-like properties and produce alterations of autonomic function, motor

reflexes, behavior, and perception.³ The psychological consequences of psilocybin use include hallucinations, an altered perception of time, and an inability to discern fantasy from reality. Panic reactions and psychosis also may occur, particularly if a user ingests a large dose. Long-term effects such as flashbacks, risk of psychiatric illness, impaired memory, and tolerance have been described in case reports.

PCP: The use of PCP as an approved anesthetic in humans was discontinued in 1965 because patients often became agitated, delusional, and irrational while recovering from its anesthetic effects. PCP is a "dissociative drug," meaning that it distorts perceptions of sight and sound and produces feelings of detachment (dissociation) from the environment and self. First introduced as a street drug in the 1960s. PCP quickly gained a reputation as a drug that could cause bad reactions and was not worth the risk. However, some abusers continue to use PCP due to the feelings of strength, power, and invulnerability as well as a numbing effect on the mind that PCP can induce. Among the adverse psychological effects reported are—

- Symptoms that mimic schizophrenia, such as delusions, hallucinations, paranoia, disordered thinking, and a sensation of distance from one's environment.
- Mood disturbances: Approximately 50 percent of individuals brought to emergency rooms because of PCPinduced problems—related to use within the past 48 hours—report significant elevations in anxiety symptoms.⁴
- People who have abused PCP for long periods of time have reported memory loss, difficulties with speech and thinking, depression, and weight loss. These symptoms can persist up to one year after stopping PCP abuse.

• Addiction: PCP is addictive—its repeated abuse can lead to craving and compulsive PCP-seeking behavior, despite severe adverse consequences.

What Other Adverse Effects Do Hallucinogens Have on Health?

Unpleasant adverse effects as a result of the use of hallucinogens are not uncommon. These may be due to the large number of psychoactive ingredients in any single source of hallucinogen.³

- LSD: The effects of LSD depend largely on the amount taken. LSD causes dilated pupils; can raise body temperature and increase heart rate and blood pressure; and can cause profuse sweating, loss of appetite, sleeplessness, dry mouth, and tremors.
- **Peyote:** Its effects can be similar to those of LSD, including increased body temperature and heart rate, uncoordinated movements (ataxia), profound sweating, and flushing. The active ingredient mescaline has also been associated, in at least one report, to fetal abnormalities.⁵
- **Psilocybin:** It can produce muscle relaxation or weakness, ataxia, excessive pupil dilation, nausea, vomiting, and drowsiness. Individuals who abuse psilocybin mushrooms also risk poisoning if one of many existing varieties of poisonous mushrooms is incorrectly identified as a psilocybin mushroom.
- **PCP:** At low-to-moderate doses, physiological effects of PCP include a slight increase in breathing rate and a pronounced rise in blood pressure and pulse rate. Breathing becomes shallow; flushing and profuse sweating, generalized numbness of the extremities, and loss of muscular coordination may occur.

At high doses, blood pressure, pulse rate, and respiration drop. This may be accompanied by nausea, vomiting, blurred vision, flicking up and down of the eyes, drooling, loss of balance, and dizziness. PCP abusers are often brought to emergency rooms because of overdose or because of the drug's severe untoward psychological effects. While intoxicated, PCP abusers may become violent or suicidal and are therefore dangerous to themselves and others. High doses of PCP can also cause seizures, coma, and death (though death more often results from accidental injury or suicide during PCP intoxication). Because PCP can also have sedative effects. interactions with other central nervous system depressants, such as alcohol and benzodiazepines. can also lead to coma.

What Treatment Options Exist?

Treatment for alkaloid hallucinogen (such as psilocybin) intoxication—which is mostly symptomatic—is often sought as a result of bad "trips," during which a patient may, for example, hurt him- or herself.⁶ Treatment is usually supportive: provision of a quiet room with little sensory stimulation. Occasionally, benzodiazepines are used to control extreme agitation or seizures.

There is very little published data on treatment outcomes for PCP intoxication. Doctors should consider that acute adverse reactions may be the result of drug synergy with alcohol.⁷ Current research efforts to manage a life-threatening PCP overdose are focused on a passive immunization approach through the development of anti-PCP antibodies.⁸ There are no specific treatments for PCP abuse and addiction, but inpatient and/or behavioral treatments can be helpful for patients with a variety of addictions, including that to PCP.

How Widespread Is the Abuse of Hallucinogens?

According to the 2013 National Survey on Drug Use and Health (NSDUH)*, more than 1.1 million people aged 12 or older reported using hallucinogens within the past 12 months.

LSD

In 2013, more than 24.8 million people aged 12 or older reported they had used LSD in their lifetime (9.4 percent) according to NSDUH. More than 1.1 million people had used the drug in the past year. Between 2012 and 2013, the number of past-year initiates of LSD increased only slightly.

Peyote and Psilocybin

It is difficult to gauge the extent of use of these hallucinogens because most data sources that quantify drug use exclude these drugs.

PCP

In 2013, 6.5 million people aged 12 or older reported that they had used PCP in their lifetime (2.5 percent) according to NSDUH. However, only 90,000 people reported use in the past year—a decrease from 172,000 in 2012.

Learn More

For more information on hallucinogens, please visit <u>http://www.drugabuse.gov/drugs-abuse/hallucinogens</u>.

Other Data Sources

* NSDUH (formerly known as the National Household Survey on Drug Abuse) is an annual survey of Americans age 12 and older conducted by the Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services. This survey is available on line at <u>www.samhsa.gov</u>.

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Club Drugs (GHB, Ketamine, and Rohypnol)

Club drugs are a pharmacologically heterogeneous group of psychoactive drugs that tend to be abused by teens and young adults at bars, nightclubs, concerts, and parties. Gamma hydroxybutyrate (GHB), Rohypnol, ketamine, as well as MDMA (ecstasy) and methamphetamine (which are featured in separate DrugFacts) are some of the drugs included in this group.

- GHB (Xyrem) is a central nervous • system (CNS) depressant that was approved by the Food and Drug Administration (FDA) in 2002 for use in the treatment of narcolepsy (a sleep disorder). This approval came with severe restrictions, including its use only for the treatment of narcolepsy, and the requirement for a patient registry monitored by the FDA. GHB is also a metabolite of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). It exists naturally in the brain. but at much lower concentrations than those found when GHB is abused.
- Rohypnol (flunitrazepam) use began gaining popularity in the United States in the early 1990s. It is a benzodiazepine (chemically similar to sedative-hypnotic drugs such as Valium or Xanax), but it is not approved for

medical use in this country, and its importation is banned.

• Ketamine is a dissociative anesthetic, mostly used in veterinary practice.

How Are Club Drugs Abused?

- GHB and Rohypnol are available in odorless, colorless, and tasteless forms that are frequently combined with alcohol and other beverages. Both drugs have been used to commit sexual assaults (also known as "date rape," "drug rape," "acquaintance rape," or "drug-assisted" assault) due to their ability to sedate and incapacitate unsuspecting victims, preventing them from resisting sexual assault.
- GHB is usually ingested orally, either in liquid or powder form, while Rohypnol is typically taken orally in pill form. Recent reports, however, have shown that Rohypnol is being ground up and snorted.
- Both GHB and Rohypnol are also abused for their intoxicating effects, similar to other CNS depressants.
- GHB also has anabolic effects (it stimulates protein synthesis) and has been used by bodybuilders to aid in fat reduction and muscle building.

• Ketamine is usually snorted or injected intramuscularly.

How Do Club Drugs Affect the Brain?

- GHB acts on at least two sites in the brain: the GABA_B receptor and a specific GHB binding site. At high doses, GHB's sedative effects may result in sleep, coma, or death.
- Rohypnol, like other benzodiazepines, acts at the GABA_A receptor. It can produce anterograde amnesia, in which individuals may not remember events they experienced while under the influence of the drug.
- Ketamine is a dissociative anesthetic, so called because it distorts perceptions of sight and sound and produces feelings of detachment from the environment and self. Ketamine acts on a type of glutamate receptor (NMDA receptor) to produce its effects, which are similar to those of the drug PCP.^{1,2} Low-dose intoxication results in impaired attention, learning ability, and memory. At higher doses, ketamine can cause dreamlike states and hallucinations; and at higher doses still, ketamine can cause delirium and amnesia.

Addictive Potential

- Repeated use of GHB may lead to withdrawal effects, including insomnia, anxiety, tremors, and sweating. Severe withdrawal reactions have been reported among patients presenting from an overdose of GHB or related compounds, especially if other drugs or alcohol are involved.³
- Like other benzodiazepines, chronic use of Rohypnol can produce tolerance, physical dependence, and addiction.
- There have been reports of people binging on ketamine, a behavior that is similar to that seen in some cocaine- or amphetamine-dependent individuals.

Ketamine users can develop signs of tolerance and cravings for the drug.⁴

What Other Adverse Effects Do Club Drugs Have on Health?

Uncertainties about the sources, chemicals, and possible contaminants used to manufacture many club drugs make it extremely difficult to determine toxicity and associated medical consequences. Nonetheless, we do know that:

- Coma and seizures can occur following use of GHB. Combined use with other drugs such as alcohol can result in nausea and breathing difficulties. GHB and two of its precursors, gamma butyrolactone (GBL) and 1,4 butanediol (BD), have been involved in poisonings, overdoses, date rapes, and deaths.
- Rohypnol may be lethal when mixed with alcohol and/or other CNS depressants.
- Ketamine, in high doses, can cause impaired motor function, high blood pressure, and potentially fatal respiratory problems.

What Treatment Options Exist?

There is very little information available in the scientific literature about treatment for persons who abuse or are dependent upon club drugs.

- There are no GHB detection tests for use in emergency rooms, and as many clinicians are unfamiliar with the drug, many GHB incidents likely go undetected. According to case reports, however, patients who abuse GHB appear to present both a mixed picture of severe problems upon admission and a good response to treatment, which often involves residential services.³
- Treatment for Rohypnol follows accepted protocols for any benzodiazepine, which may consist of a 3- to 5-day inpatient detoxification

program with 24-hour intensive medical monitoring and management of withdrawal symptoms, since withdrawal from benzodiazepines can be life-threatening.³

 Patients with a ketamine overdose are managed through supportive care for acute symptoms, with special attention to cardiac and respiratory functions.⁵

How Widespread Is Club Drug Abuse?

Monitoring the Future (MTF) Survey*

MTF has reported consistently low levels of abuse of these club drugs since they were added to the survey. For GHB and ketamine, this occurred in 2000; for Rohypnol, 1996. According to results of the 2014 MTF survey, 1.0 percent of 12th-grade students reported past-year use of GHB, a statistically significant decrease from peakyear use of 2.0 percent in 2004. GHB use among 8th- and 10th-grade students was not reported.

Past-year use of ketamine was reported by 1.4 percent of 12th-graders in 2014. This also represents a significant decrease from

the peak year of 2002, in which 2.6 percent reported past-year use.

For Rohypnol, 0.3 percent of 8th-graders, 0.5 percent of 10th-graders, and 0.7 percent of 12th-graders reported past-year use, also down from peak use in 1996 for 8thgraders (1.0 percent), 1997 for 10thgraders (1.3 percent), and 2002 and 2004 for 12th-graders (1.6 percent).

Learn More

For additional information about club drugs, visit <u>www.drugabuse.gov/drugs-abuse/club-drugs</u>.

Data Sources

* These data are from the 2014 Monitoring the Future survey, funded by the National Institute on Drug Abuse, National Institutes of Health, U.S. Department of Health and Human Services, and conducted annually by the University of Michigan's Institute for Social Research. The survey has tracked 12th-graders' illicit drug use and related attitudes since 1975; in 1991, 8th- and 10th-graders were added to the study.

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MDMA ("Ecstasy" or "Molly")

MDMA (3,4-methylenedioxymethamphetamine), popularly known as ecstasy or, more recently, as Molly, is a synthetic, psychoactive drug that has similarities to both the stimulant amphetamine and the hallucinogen mescaline. It produces feelings of increased energy, euphoria, emotional warmth and empathy toward others, and distortions in sensory and time perception.

MDMA was initially popular among White adolescents and young adults in the nightclub scene or at "raves" (long dance parties), but the drug now affects a broader range of users and ethnicities.

How Is MDMA Abused?

MDMA is taken orally, usually as a capsule or tablet. The popular term Molly (slang for "molecular") refers to the pure crystalline powder form of MDMA, usually sold in capsules. The drug's effects last approximately 3 to 6 hours, although it is not uncommon for users to take a second dose of the drug as the effects of the first dose begin to fade. It is commonly taken in combination with other drugs. For example some urban gay and bisexual men report using MDMA as part of a multiple-drug experience that includes cocaine, GHB, methamphetamine, ketamine, and the erectile-dysfunction drug sildenafil (Viagra).

How Does MDMA Affect the Brain?

MDMA acts by increasing the activity of three neurotransmitters, serotonin, dopamine, and norepinephrine. The emotional and pro-social effects of MDMA are likely caused directly or indirectly by the release of large amounts of serotonin, which influences mood (as well as other functions such as appetite and sleep). Serotonin also triggers the release of the hormones oxytocin and vasopressin, which play important roles in love, trust, sexual arousal, and other social experiences. This may account for the characteristic feelings of emotional

Is MDMA Addictive?

Research thus far on MDMA's addictive properties has shown varying results, but we do know that some users report symptoms of dependence, including continued use despite knowledge of physical or psychological harm, tolerance (or diminished response), and withdrawal effects.

The neurotransmitter systems targeted by MDMA are the same as those targeted by other addictive drugs. Experiments have shown that animals will selfadminister MDMA—an important indicator of a drug's abuse potential—although the degree of self-administration is less than some other drugs of abuse such as cocaine. closeness and empathy produced by the drug; studies in both rats and humans have shown that MDMA raises the levels of these hormones.

The surge of serotonin caused by taking MDMA depletes the brain of this important chemical, however, causing negative aftereffects—including confusion, depression, sleep problems, drug craving, and anxiety—that may occur soon after taking the drug or during the days or even weeks thereafter.

Some heavy MDMA users experience long-lasting confusion, depression, sleep abnormalities, and problems with attention and memory, although it is possible that some of these effects may be due to the use of other drugs in combination with MDMA (especially marijuana).

What Are the Other Health Effects of MDMA?

MDMA can have many of the same physical effects as other stimulants like cocaine and amphetamines. These include increases in heart rate and blood pressure, which are particularly risky for people with circulatory problems or heart disease. MDMA users may experience other symptoms such as muscle tension, involuntary teeth clenching, nausea, blurred vision, faintness, and chills or sweating.

In high doses, MDMA can interfere with the body's ability to regulate temperature. On rare but unpredictable occasions, this can lead to a sharp increase in body temperature (hyperthermia), which can result in liver, kidney, or cardiovascular system failure or even death. MDMA can interfere with its own metabolism (breakdown within the body), causing potentially harmful levels to build up in the body if it is taken repeatedly within short periods of time.

Compounding the risks is the fact that ecstasy tablets and even capsules of supposedly pure "Molly" sometimes actually contain other drugs instead or in addition. Those may include ephedrine (a stimulant), dextromethorphan (a cough suppressant), ketamine, caffeine, cocaine, methamphetamine, or even, most recently, synthetic cathinones (the psychoactive ingredients in "bath salts"). These substances are harmful alone and may be particularly dangerous mixed with MDMA. Users who intentionally or unknowingly combine such a mixture with additional substances such as marijuana and alcohol may be putting themselves at even higher risk for adverse health effects.

Does MDMA Have Therapeutic Value?

MDMA was first used in the 1970s. not as a recreational drug but as an aid in psychotherapy—although without the support of clinical trial research or FDA approval. In 1985, the Drug Enforcement Administration labeled MDMA a Schedule I substance, or a drug with high abuse potential and no recognized medicinal use. Some researchers remain interested in its potential therapeutic value when administered under carefully monitored conditions. It is currently in clinical trials as a possible pharmacotherapy aid to treat posttraumatic stress disorder (PTSD) and anxiety in terminal cancer patients.

Additionally, the closeness-promoting effects of MDMA and its use in sexually charged contexts (and especially in combination with sildenafil) may encourage unsafe sex, which is a risk factor for contracting or spreading HIV and hepatitis.

Learn More

For additional information on MDMA, please see drugabuse.gov/publications /research-reports/mdma-ecstasy-abuse