Long-Term Effects of Hallucinogens
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National Institute on Drug Abuse

Research Report Series

from the director:

Hallucinogens and dissociative drugs—which have street names like acid, angel dust, and vitamin K—distort the way a user perceives time, motion, colors, sounds, and self. These drugs can disrupt a person's ability to think and communicate rationally, or even to recognize reality, sometimes resulting in bizarre or dangerous behavior. Hallucinogens such as LSD, psilocybin, peyote, DMT, and ayahuasca cause emotions to swing wildly and real-world sensations to appear unreal, sometimes frightening. Dissociative drugs like PCP, ketamine, dextromethorphan, and *Salvia divinorum* may make a user feel out of control and disconnected from their body and environment.

In addition to their short-term effects on perception and mood, hallucinogenic drugs are associated with psychotic-like episodes that can occur long after a person has taken the drug, and dissociative drugs can cause respiratory depression, heart rate abnormalities, and a withdrawal syndrome. The good news is that use of hallucinogenic and dissociative drugs among U.S. high school students, in general, has remained relatively low in recent years. However, the introduction of new hallucinogenic and dissociative drugs is of particular concern.

NIDA research is developing a clearer picture of the dangers of hallucinogenic and dissociative drugs. We have compiled the scientific information in this report to inform readers and hopefully prevent the use of these drugs.

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Director
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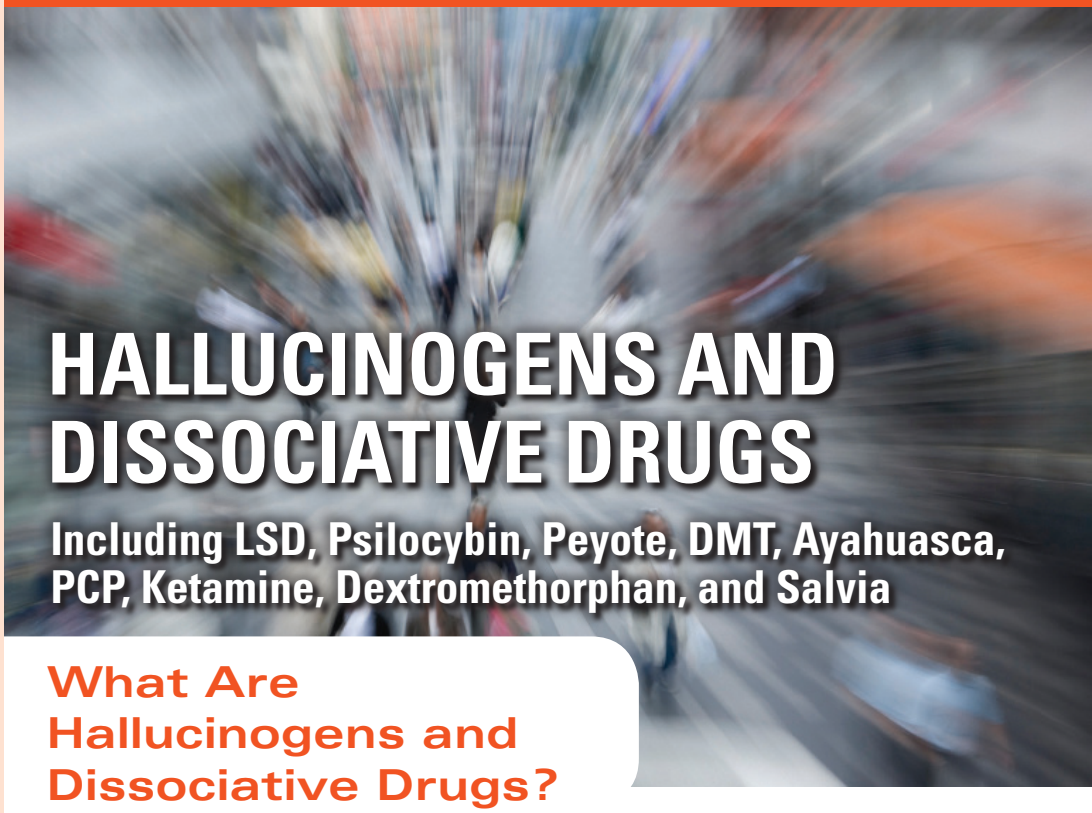


HALLUCINOGENS AND DISSOCIATIVE DRUGS

Including LSD, Psilocybin, Peyote, DMT, Ayahuasca, PCP, Ketamine, Dextromethorphan, and Salvia

What Are Hallucinogens and Dissociative Drugs?

Hallucinogens are a class of drugs that cause hallucinations—profound distortions in a person's perceptions of reality. Hallucinogens can be found in some plants and mushrooms (or their extracts) or can be man-made, and they are commonly divided into two broad categories: classic hallucinogens (such as LSD) and dissociative drugs (such as PCP). When under the influence of either type of drug, people often report rapid, intense emotional swings and seeing images, hearing sounds, and feeling sensations that seem real but are not.

While the exact mechanisms by which hallucinogens and dissociative drugs cause their effects are not yet clearly understood, research suggests that they work at least partially by temporarily disrupting communication between neurotransmitter systems throughout the brain and spinal cord that regulate mood, sensory perception, sleep, hunger, body temperature, sexual behavior, and muscle control.

Psilocybin mushrooms, LSD, and Salvia divinorum *are commonly used hallucinogenic and dissociative compounds.*

Common Hallucinogens and Dissociative Drugs

Classic Hallucinogens*

LSD (d-lysergic acid diethylamide)—also known as acid, blotter, doses, hits, microdots, sugar cubes, trips, tabs, or window panes—is one of the most potent mood- and perception-altering hallucinogenic drugs. It is a clear or white, odorless, water-soluble material synthesized from lysergic acid, a compound derived from a rye fungus. LSD is initially produced in crystalline form, which can then be used to produce tablets known as "microdots" or thin squares of gelatin called "window panes." It can also be diluted with water or alcohol and sold in liquid form. The most common form, however, is LSD-soaked paper punched into small individual squares, known as "blotters."

Psilocybin (4-phosphoryloxy-N, N-dimethyltryptamine)—also known as magic mushrooms, shrooms, boomers, or little smoke—is extracted from certain types of mushrooms found in tropical and subtropical regions of South America, Mexico, and the United States. In the past, psilocybin was ingested during religious ceremonies by indigenous cultures from Mexico and Central America. Psilocybin can either be dried or fresh and eaten raw, mixed with food, or brewed into a tea, and produces similar effects to LSD.

Peyote (Mescaline)—also known as buttons, cactus, and mesc—is a small, spineless cactus with mescaline as its main ingredient. It has been used by natives in northern Mexico and the southwestern United States as a part of religious ceremonies. The top, or "crown," of the peyote cactus has disc-shaped buttons that are cut out, dried, and usually chewed or soaked in water to produce an intoxicating liquid. Because the extract is so bitter, some users prepare a tea by boiling the plant for several hours. Mescaline can also be produced through chemical synthesis.

DMT (Dimethyltryptamine)—also known as Dimitri—is a powerful hallucinogenic chemical found naturally occurring in some Amazonian plant species (see "Ayahuasca") and also synthesized in the laboratory. Synthetic DMT usually takes the form of a white crystalline powder and is typically vaporized or smoked in a pipe.

Ayahuasca—also known as hoasca, aya, and yagé—is a hallucinogenic brew made from one of several Amazonian plants containing DMT (the primary psychoactive ingredient) along with a vine containing a natural alkaloid that prevents the normal breakdown of DMT in the digestive tract. Ayahuasca tea has traditionally been used for healing and religious purposes in indigenous South American cultures, mainly in the Amazon region.

Dissociative Drugs

PCP (Phencyclidine)—also known as ozone, rocket fuel, love boat, hog, embalming fluid, or superweed—was originally developed in the 1950s as a general anesthetic for surgery. While it can be found in a variety of forms, including tablets or capsules, it is usually sold as a liquid or powder. PCP can be snorted, smoked, injected, or swallowed. It is sometimes smoked after being sprinkled on marijuana, tobacco, or parsley.

Ketamine—also known as K, Special K, or cat Valium—is a dissociative currently used as an anesthetic for humans as well as animals. Much of the ketamine sold on the street has been diverted from veterinary offices. Although it is manufactured as an injectable liquid, ketamine is generally evaporated to form a powder that is snorted or compressed into pills for illicit use. Because ketamine is odorless and tasteless and has amnesia-inducing properties, it is sometimes added to drinks to facilitate sexual assault.

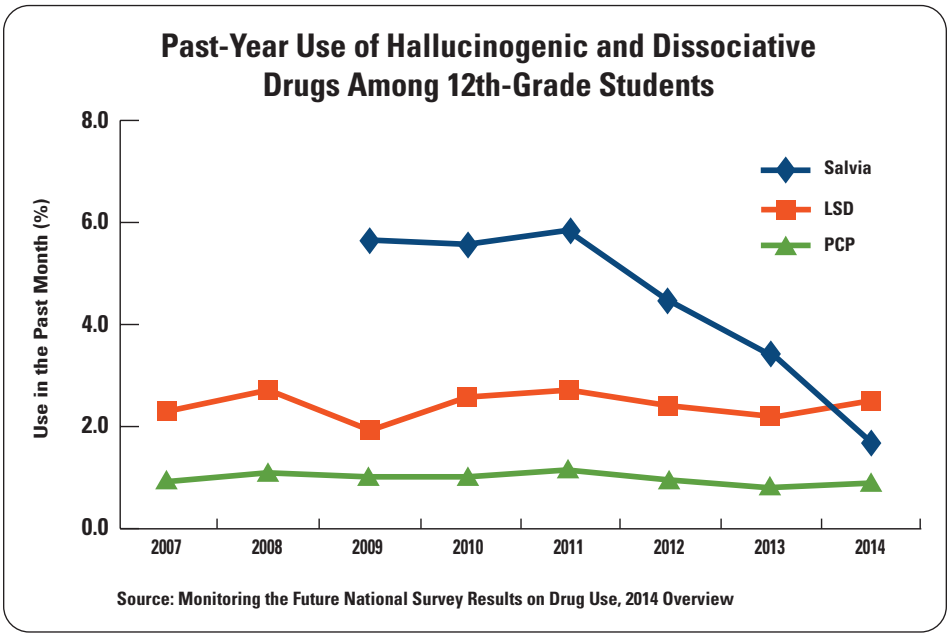
*In this report, the term "hallucinogen" will refer to the classic hallucinogenic drugs LSD and Psilocybin.

DXM (Dextromethorphan)—also known as robo—is a cough suppressant and expectorant ingredient in some over-the-counter (OTC) cold and cough medications that are often abused by adolescents and young adults. The most common sources of abused DXM are "extra-strength" cough syrup, which typically contains around 15 milligrams of DXM per teaspoon, and pills and gel capsules, which typically contain 15 milligrams of DXM per pill. OTC medications that contain DXM often also contain antihistamines and decongestants.

Salvia divinorum—also known as diviner's sage, Maria Pastora, Sally-D, or magic mint—is a psychoactive plant common to southern Mexico and Central and South America. Salvia is typically ingested by chewing fresh leaves or by drinking their extracted juices. The dried leaves of salvia can also be smoked or vaporized and inhaled.

How Widespread Is the Abuse of Hallucinogens and Dissociative Drugs?

According to the 2013 National Survey on Drug Use and Health, 229,000 Americans ages 12 and older reported current (past-month) use of LSD and 33,000 reported current use of PCP (Substance Abuse and Mental Health Services Administration, 2013). Among high school seniors, salvia was significantly more popular than LSD or PCP when it was added to the Monitoring the Future survey in 2009. Past-year use was reported to be 5.9 percent for salvia, 2.7 percent for LSD, and 1.3 percent for PCP. Fortunately, rates have dropped significantly for saliva—to 1.8 percent in 2014—with LSD and PCP use dropping slightly (Johnston, 2014).



While regular use of hallucinogenic and dissociative drugs in general has remained relatively low in recent years, one study reported that the United States ranks first among 36 nations in the proportion of high school students ever using LSD or other hallucinogens in their lifetime (6 percent versus 2 percent in Europe) (Hibell, 2012).

Additionally, tourism to the Amazon for the purpose of using ayahuasca has become increasingly popular among Americans and Europeans in recent years, and ayahuasca use has also been reported in major cities in Brazil and abroad (Barbosa, 2012; McKenna, 2004). Although DMT is a schedule I drug, plants containing DMT are not scheduled, and there is ambiguity over ayahuasca's legal status in the United States (McKenna, 2004). Two U.S. Brazilian churches have obtained permission to import and use these plants in their ceremonies.

Why Do People Take Hallucinogenic or Dissociative Drugs?

Hallucinogenic and dissociative drugs have been used for a variety of reasons (Bogenschutz, 2012; Bonson, 2001). Historically, hallucinogenic plants have been used for religious rituals to induce states of detachment from reality and precipitate "visions" thought to provide mystical insight or enable contact with a spirit world or "higher power." More recently, people report using hallucinogenic drugs for more social or recreational purposes, including to have fun, help them deal with stress, or enable them to enter into what they perceive as a more enlightened sense of thinking or being. Hallucinogens have also been investigated as therapeutic agents to treat diseases associated with perceptual distortions, such as schizophrenia, obsessive-compulsive disorder, bipolar disorder, and dementia. Anecdotal reports and small studies have suggested that ayahuasca may be a potential treatment for substance use disorders and other mental health issues, but no large-scale research has verified its efficacy (Barbosa, 2012).

How Do Hallucinogens (LSD, Psilocybin, Peyote, DMT, and Ayahuasca) Affect the Brain and Body?

How Do Hallucinogens Work?

Classic hallucinogens are thought to produce their perception-altering effects by acting on neural circuits in the brain that use the neurotransmitter serotonin (Passie, 2008; Nichols, 2004; Schindler, 2012; Lee, 2012). Specifically, some of their most prominent effects occur in the prefrontal cortex—an area involved in mood, cognition, and perception—as well as other regions important in regulating arousal and physiological responses to stress and panic.

What are the Short-Term Effects of Hallucinogens?

Ingesting hallucinogenic drugs can cause users to see images, hear sounds, and feel sensations that seem real but do not exist. Their effects typically begin within 20 to 90 minutes of ingestion and can last as long as 12 hours. Experiences are often unpredictable and may vary with the amount ingested and the user's personality, mood, expectations, and surroundings. The effects of hallucinogens like LSD can be described as drug-induced psychosis—distortion or disorganization of a person's capacity to recognize reality, think rationally, or communicate with others. Users refer to LSD and other hallucinogenic experiences as "trips" and to acute adverse or unpleasant experiences as "bad trips." On some trips, users experience sensations that are enjoyable and mentally stimulating and that produce a sense of heightened understanding. Bad trips, however, include terrifying thoughts and nightmarish feelings of anxiety and despair that include fears of losing control, insanity, or death.

Like LSD and psilocybin, DMT produces its effects through action at serotonin (5-HT) receptors in the brain (Strassman, 1996). Some research has suggested that DMT occurs naturally in the human brain in small quantities, leading to the hypothesis that release of endogenous DMT may be involved in reports of alien abductions, spontaneous mystical experiences, and near-death experiences, but this remains controversial (Barker, 2012).

Short-Term General Effects of Hallucinogens

Sensory Effects

- Hallucinations, including seeing, hearing, touching, or smelling things in a distorted way or perceiving things that do not exist
- Intensified feelings and sensory experiences (brighter colors, sharper sounds)
- Mixed senses ("seeing" sounds or "hearing" colors)
- Changes in sense or perception of time (time goes by slowly)

Physical Effects

- Increased energy and heart rate
- Nausea

Specific short-term effects of LSD, psilocybin, peyote, DMT, and ayahuasca include:

LSD

- Increased blood pressure, heart rate, and body temperature
- Dizziness and sleeplessness
- Loss of appetite, dry mouth, and sweating
- Numbness, weakness, and tremors
- Impulsiveness and rapid emotional shifts that can range from fear to euphoria, with transitions so rapid that the user may seem to experience several emotions simultaneously

Psilocybin†

- Feelings of relaxation (similar to effects of low doses of marijuana)
- Nervousness, paranoia, and panic reactions
- Introspective/spiritual experiences
- Misidentification of poisonous mushrooms resembling psilocybin could lead to unintentional, potentially fatal poisoning

Peyote

- Increased body temperature and heart rate
- Uncoordinated movements (ataxia)
- Profound sweating
- Flushing

DMT

- Increased heart rate
- Agitation
- Hallucinations frequently involving radically altered environments as well as body and spatial distortions

Ayahuasca

- Increased blood pressure
- Severe vomiting (induced by the tea)
- Profoundly altered state of awareness and perceptions of otherworldly imagery

†Misidentification of poisonous mushrooms resembling psilocybin could lead to unintentional, potentially fatal poisoning.

What Are the Long-Term Effects of Hallucinogens?

LSD users quickly develop a high degree of tolerance to the drug's effects, such that repeated use requires increasingly larger doses to produce similar effects. Use of hallucinogenic drugs also produces tolerance to other drugs in this class, including psilocybin and peyote. Use of classic hallucinogens does not, however, produce tolerance to drugs that do not act directly on the same brain cell receptors. In other words, there is no cross-tolerance to drugs that act on other neurotransmitter systems, such as marijuana, amphetamines, or PCP, among others. Furthermore, tolerance for hallucinogenic drugs is short-lived—it is lost if the user stops taking the drugs for several days—and physical withdrawal symptoms are not typically experienced when chronic use is stopped.

The long-term residual psychological and cognitive effects of peyote remain poorly understood. Although one study found no evidence of psychological or cognitive deficits among Native Americans who use peyote regularly in a religious setting, those findings may not generalize to those who repeatedly abuse the drug for recreational purposes (Halpern, 2005). Peyote users may also experience hallucinogen persisting perception disorder (HPPD)—also often referred to as *flashbacks*. The active ingredient mescaline has also been associated, in at least one report, to fetal abnormalities (Gilmore, 2001).

Long-term effects of DMT use and abuse and addiction liability are currently unknown. Unlike most other hallucinogens, DMT does not appear to induce tolerance (Winstock, 2013).

As with some other hallucinogens, there is little information to suggest that ayahuasca use creates lasting physiological or neurological deficits, especially among those using the brew for religious activities.

Overall, two long-term effects—persistent psychosis and HPPD—have been associated with use of classic hallucinogens (see sidebar). Although occurrence of either is rare, it is also unpredictable and may happen more often than previously thought, and sometimes both conditions occur together. While the exact causes are not known, both conditions are more often seen in individuals with a history of psychological problems but can happen to anyone, even after a single exposure. There is no established treatment for HPPD, in which flashbacks may occur spontaneously and repeatedly although less intensely than their initial occurrence. Some antidepressant and antipsychotic drugs can be prescribed to help improve mood and treat psychoses, however. Psychotherapy may also help patients cope with fear or confusion associated with visual disturbances or other consequences of long-term LSD use. More research on the causes, incidence, and long-term effects of both disorders is being conducted.

Long-Term Effects of Hallucinogens

Persistent psychosis

- Visual disturbances
- Disorganized thinking
- Paranoia
- Mood disturbances

Hallucinogen Persisting Perception Disorder (HPPD)

- Hallucinations
- Other visual disturbances (such as seeing halos or trails attached to moving objects)
- Symptoms sometimes mistaken for neurological disorders (such as stroke or brain tumor)

What Are the Effects of Common Dissociative Drugs on the Brain and Body?

How Do Dissociative Drugs Work?

Laboratory studies suggest that dissociative drugs, including PCP, ketamine, and DXM, cause their effects by disrupting the actions of the brain chemical glutamate at certain types of receptors—called N-methyl-D-aspartate (NMDA) receptors—on nerve cells throughout the brain (Morgan, 2012; Morris, 2005). Glutamate plays a major role in cognition (including learning and memory), emotion, and the perception of pain (the latter via activation of pain-regulating cells outside of the brain). PCP also alters the actions of dopamine, a neurotransmitter responsible for the euphoria and "rush" associated with many abused drugs.

Salvia divinorum works differently. While classified as a dissociative drug, salvia causes its effects by activating the kappa opioid receptor on nerve cells (Cunningham, 2011; MacLean, 2013). These receptors differ from those activated by the more commonly known opioids such as heroin and morphine.

What Are the Short-Term Effects of Dissociative Drugs?

Dissociative drugs can produce visual and auditory distortions and a sense of floating and dissociation (feeling detached from reality) in users. Use of dissociative drugs can also cause anxiety, memory loss, and impaired motor function, including body tremors and numbness. These effects, which depend on the amount of the drug taken, are also unpredictable—typically beginning within minutes of ingestion and lasting for several hours, although some users report feeling the drug's effects for days. See text box for general effects of dissociative drugs.

General Common Effects of Dissociative Drugs

Low to Moderate Doses	High Doses
Numbness	Hallucinations
Disorientation, confusion, and loss of coordination	Memory loss
Dizziness, nausea, vomiting	Physical distress, including dangerous changes in blood pressure, heart rate, respiration, and body temperature
Changes in sensory perceptions (such as sight, sound, shapes, time, and body image)	Marked psychological distress, including feelings of extreme panic, fear, anxiety, paranoia, invulnerability, exaggerated strength, and aggression
Hallucinations	Use with high doses of alcohol or other central nervous system depressants can lead to respiratory distress or arrest, resulting in death
Feelings of detachment from self and environment	
Increase in blood pressure, heart rate, respiration, and body temperature	

In addition to these general effects, different dissociative drugs can produce a variety of distinct and dangerous effects. For example, at moderate to high doses, PCP can cause a user to have seizures or severe muscle contractions, become aggressive or violent, or even experience psychotic symptoms similar to schizophrenia. At moderate to high doses, ketamine can cause sedation, immobility, and amnesia. At high doses, ketamine users also report experiencing terrifying feelings of almost complete sensory detachment likened to a near-death experience (called a "K-hole," similar to a bad LSD trip). Salvia users report intense but short-lived effects—up to 30 minutes—including emotional mood swings ranging from sadness to uncontrolled laughter.

DXM, which is safe and effective as a cough suppressant and expectorant when used at recommended doses (typically 15 to 30 milligrams), can lead to serious side effects when abused. For example, use of DXM at doses from 200 to 1,500 milligrams can produce dissociative effects similar to PCP and ketamine and increase the risk of serious central nervous system and cardiovascular effects such as respiratory distress, seizures, and increased heart rate from the antihistamines found in cough medicines.

What Are the Long-Term Effects of Dissociative Drugs?

While the long-term use of most dissociative drugs has not been investigated systematically, research shows that repeated use of PCP can lead to tolerance and the development of a substance use disorder that includes a withdrawal syndrome (including craving for the drug, headaches, and sweating) when drug use is stopped. Other effects of long-term PCP use include persistent speech difficulties, memory loss, depression, suicidal thoughts, anxiety, and social withdrawal that may persist for a year or more after chronic use stops.

Glossary

Central Nervous System: The brain and spinal cord.

Cerebral cortex: The region of the brain responsible for cognitive functions including reasoning, mood, and perception of stimuli.

Dissociative: a type of compound, such as phencyclidine or ketamine, that produces an anesthetic effect characterized by a feeling of being detached from the physical self.

DXM: A common street name for dextromethorphan.

Flashback: A sudden but temporary recurrence of aspects of a drug experience (including sights, sounds, and feelings) that may occur days, weeks, or even more than a year after hallucinogenic drug use.

Glutamate: An excitatory neurotransmitter found throughout the brain that influences the reward system and is involved in learning and memory, among other functions.

Hallucinogen: A drug that produces hallucinations—distortions in perception of sights and sounds—and disturbances in emotion, judgment, and memory.

HPPD: Hallucinogen persisting perception disorder; the spontaneous and sometimes continuous recurrence of perceptual effects of LSD long after an individual has ingested the drug.

Kappa opioid receptor: A receptor on nerve cells that is activated by certain opioid-like compounds produced in the body. These receptors differ from those activated by the more commonly known opioids, such as heroin and morphine.

Neurotransmitter: A chemical compound that acts as a messenger to carry signals from one nerve cell to another.

NMDA receptors: N-methyl-D-aspartate receptors, a type of glutamate receptor that is important for learning and memory; it is the target of drugs such as PCP and ketamine.

Persistent psychosis: Unpredictable and long-lasting visual disturbances, dramatic mood swings, and hallucinations experienced by some LSD users after they have discontinued use of the drug.

Serotonin: A neurotransmitter involved in a broad range of effects on perception, movement, and emotions. Serotonin and its receptors are the targets of most hallucinogens.

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Where can I get further information about hallucinogens?

To learn more about hallucinogens and other drugs of abuse, visit the NIDA website at **www.drugabuse.gov** or contact the *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).

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NIDA's website includes:

- Information on drugs of abuse and related health consequences
- NIDA publications, news, and events
- Resources for health care professionals, educators, and patients and families
- Funding information (including program announcements and deadlines)
- International activities
- Links to related websites (access to websites of many other organizations in the field)
- Information in Spanish (en español)

NIDA Websites and Webpages

www.drugabuse.gov
www.teens.drugabuse.gov
www.easyread.drugabuse.gov
www.drugabuse.gov/drugs-abuse/hallucinogens
www.drugabuse.gov/publications/term/160/DrugFacts
www.hiv.drugabuse.gov/
www.researchstudies.drugabuse.gov/
www.irp.drugabuse.gov/

For Physician Information
NIDAMED
www.drugabuse.gov/nidamed

Other Websites

Information on hallucingens and dissociative drugs is also available through:

- Substance Abuse and Mental Health Services Administration: *www.samhsa.gov*
- Drug Enforcement Administration: *www.deadiversion.usdoj.gov*
- Monitoring the Future: *www.monitoringthefuture.org/*
- The Partnership at Drug Free.org: *www.drugfree.org/drug-guide*

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