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HALLUCINOGENS AND DISSOCIATIVE DRUGS*

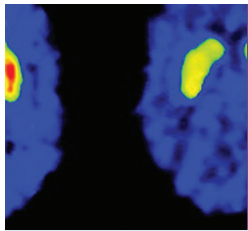
THE NATIONAL INSTITUTE ON DRUG
ABUSE RESEARCH REPORT SERIES:
COCAINE

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ABUSE RESEARCH REPORT SERIES:
INHALANTS

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HALLUCINOGENS AND DISSOCIATIVE
DRUGS

ABOUT THIS READING MATERIAL:

These three research reports were produced by the National Institute on Drug Abuse. You can access this material directly on the NIDA website. We combined these three readings into a single PDF in December of 2015



Cocaine's stimulant and addictive effects explained.
See page 2.

Research Report Series

from the director:

Cocaine abuse and addiction continue to plague our Nation. In 2008, almost 15 percent of Americans had tried cocaine, with 6 percent having tried it by their senior year of high school. Recent discoveries about the inner workings of the brain and the harmful effects of cocaine offer us unprecedented opportunities for addressing this persistent public health problem.

Genetic studies continue to provide critical information about hereditary influences on the risk of addiction to psychoactive substances, including cocaine. But genetic risk is far less rigid than previously thought. More recent epigenetic research has begun to shed light on the power of environmental factors (e.g., nutrition, chronic stress, parenting style) to influence gene expression and thus, genetic risk. Furthermore, sophisticated imaging technologies have allowed scientists to visualize the brain changes that result from chronic drug exposure or that occur when an addicted person is exposed to drug-associated "cues" that can trigger craving and lead to relapse. By mapping genetic factors, epigenetic mechanisms, and brain regions responsible for the multiple effects of cocaine, we are gaining fundamental insights that can help us identify new targets for treating cocaine addiction.

NIDA remains vigilant in its quest for more effective strategies to address the serious public health issues linked to cocaine abuse. We not only support a wide range of basic and clinical research, but also facilitate the translation of these research findings into real-world settings. To this end, we strive to keep the public informed of the latest scientific advances in the field of addiction. We hope that this compilation of scientific information on cocaine abuse will inform readers and bolster our efforts to tackle the personal and social devastation caused by drug abuse and addiction.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse



Cocaine

What Is Cocaine?

Cocaine is a powerfully addictive stimulant that directly affects the brain. Cocaine was labeled the drug of the 1980s and 1990s because of its extensive popularity and use during that period. However, cocaine is not a new drug. In fact, it is one of the oldest known psychoactive substances. Coca leaves, the source of cocaine, have been chewed and ingested for thousands of years, and the purified chemical, cocaine hydrochloride, has been an abused substance for more than 100 years. In the early 1900s, for example, purified cocaine was the main active ingredient in most of the tonics and elixirs

continued inside

that were developed to treat a wide variety of illnesses.

Pure cocaine was originally extracted from the leaf of the *Erythroxylon* coca bush, which grew primarily in Peru and Bolivia. After the 1990s, and following crop reduction efforts in those countries, Colombia became the nation with the largest cultivated coca crop. Today, cocaine is a Schedule II drug, which means that it has high potential for abuse but can be administered by a doctor for legitimate medical uses, such as local anesthesia for some eye, ear, and throat surgeries.

Cocaine is generally sold on the street as a fine, white, crystalline powder and is also known as “coke,” “C,” “snow,” “flake,” or “blow.” Street dealers generally dilute it with inert substances such as cornstarch, talcum powder, or sugar, or with active drugs such as procaine (a

chemically related local anesthetic) or amphetamine (another stimulant). Some users combine cocaine with heroin—in what is termed a “speedball.”

There are two chemical forms of cocaine that are abused: the water-soluble hydrochloride salt and the water-insoluble cocaine base (or freebase). When abused, the hydrochloride salt, or powdered form of cocaine, can be injected or snorted. The base form of cocaine has been processed with ammonia or sodium bicarbonate (baking soda) and water, and then heated to remove the hydrochloride to produce a smokable substance. The term “crack,” which is the street name given to freebase cocaine, refers to the crackling sound heard when the mixture is smoked.

Cocaine use ranges from occasional to repeated or compulsive use, with a variety of patterns between these extremes. Other than medical uses, there is no safe way to use cocaine. Any route of administration can lead to absorption of toxic amounts of cocaine, possible acute cardiovascular or cerebrovascular emergencies, and seizures—all of which can result in sudden death.

How Does Cocaine Produce Its Effects?

Research has led to a clear understanding of how cocaine produces its pleasurable effects and why it is so addictive. Scientists have discovered regions within the brain that are stimulated by all types of reinforcing stimuli such as food, sex, and many drugs of abuse. One neural system that appears to be most affected by cocaine originates in a region of the midbrain called the ventral tegmental area (VTA). Nerve fibers originating in the VTA extend to a region known as the nucleus accumbens, one of the brain’s key areas involved in reward. Animal studies show that rewards increase levels of the brain chemical (or neurotransmitter) dopamine, thereby increasing neural activity in the nucleus accumbens. In the normal communication process, dopamine is released by a neuron into the synapse (the small gap between two neurons), where it binds to specialized proteins (called dopamine receptors) on the neighboring neuron and sends a signal to that neuron. Dopamine is then

How Is Cocaine Abused?

The principal routes of cocaine administration are oral, intranasal, intravenous, and inhalation. Snorting, or intranasal administration, is the process of inhaling cocaine powder through the nostrils, where it is absorbed into the bloodstream through the nasal tissues. The drug also can be rubbed onto mucous tissues. Injecting, or intravenous use, releases the drug directly into the bloodstream and heightens the intensity of its effects. Smoking involves inhaling cocaine vapor or smoke into the lungs, where absorption into the bloodstream is as rapid as by injection. This rather immediate and euphoric effect is one of the reasons that crack became enormously popular in the mid-1980s.



Coca bush



removed from the synapse to be recycled for further use. Drugs of abuse can interfere with this normal communication process. For example, scientists have discovered that cocaine acts by blocking the removal of dopamine from the synapse, which results in an accumulation of dopamine and an amplified signal

to the receiving neurons (see image on page 4, “Cocaine in the brain”). This is what causes the initial euphoria commonly reported by cocaine abusers.

small amounts, cocaine usually makes the user feel euphoric, energetic, talkative, and mentally alert, especially to the sensations of sight, sound, and touch. It can also temporarily decrease the need for food and sleep. Some users find that the drug helps them perform simple physical and intellectual tasks more quickly, although others experience the opposite effect.

What Are the Short-Term Effects of Cocaine Use?

Cocaine’s effects appear almost immediately after a single dose and disappear within a few minutes to an hour. Taken in

The duration of cocaine’s euphoric effects depend upon the route of administration. The faster the drug is absorbed, the more intense the resulting high, but also

What Is the Scope of Cocaine Use in the United States?

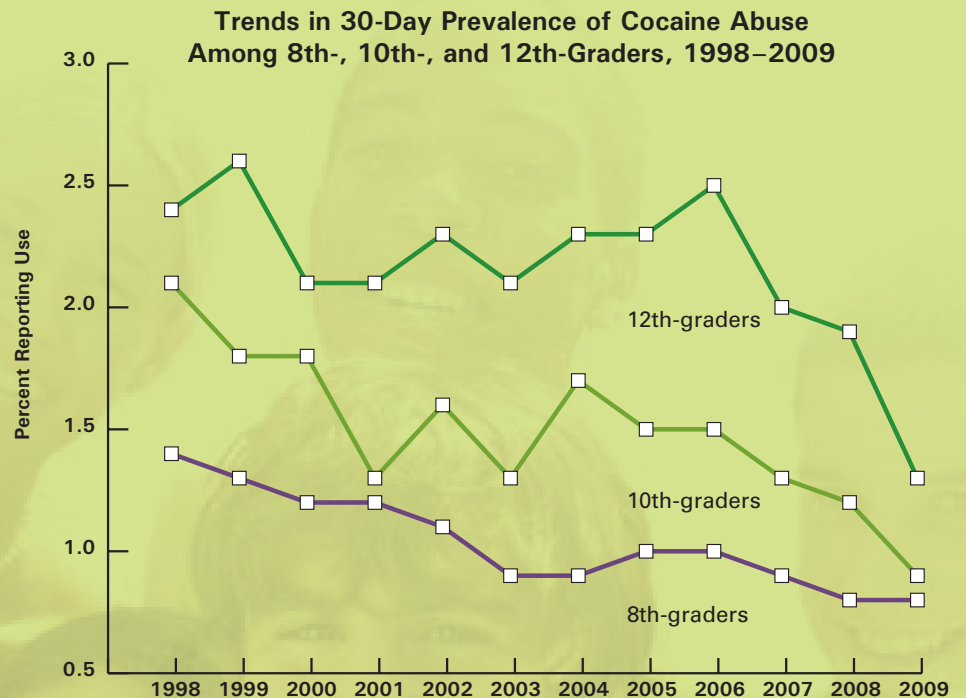
The National Survey on Drug Use and Health (NSDUH) estimates that in 2008 there were 1.9 million current (past month) cocaine users, of which approximately 359,000 were current crack users. Adults aged 18 to 25 years have a higher rate of current cocaine use than any other age group, with 1.5 percent of young adults reporting past-month cocaine use. Overall, men report higher rates of current cocaine use than women.

The 2009 Monitoring the Future survey, which annually surveys teen attitudes and drug use, reports a significant decline in 30-day prevalence of powder cocaine use among 8th-, 10th-, and 12th-graders from peak use in the late 1990s, as well as significant declines in past-month use among 10th- and 12th-graders from 2008 to 2009.

Repeated cocaine use can produce addiction and other adverse health consequences. In 2008, according

to the NSDUH, about 1.4 million Americans met the *Diagnostic and Statistical Manual of Mental Disorders* criteria for dependence or abuse of cocaine (in any form) in the past 12 months. Further, data from the 2008 Drug Abuse Warning Network (DAWN) report showed that cocaine was involved

in 482,188 of the nearly 2 million visits to emergency departments for drug misuse or abuse. This translates to almost one in four drug misuse or abuse emergency department visits (24 percent) that involved cocaine.



Source: University of Michigan, 2009 Monitoring the Future Survey.

the shorter the duration. The high from snorting is relatively slow to arrive, but it may last from 15 to 30 minutes; in contrast, the effects from smoking are more immediate but may last only 5 to 10 minutes.

The short-term physiological effects of cocaine use include constricted blood vessels; dilated pupils; and increased body temperature, heart rate, and blood pressure. Large amounts of cocaine may intensify the user's high but can also lead to bizarre, erratic, and violent behavior. Some cocaine users report feelings of restlessness, irritability, anxiety, panic, and paranoia. Users may also experience tremors, vertigo, and muscle twitches.

There also can be severe medical complications associated with cocaine abuse. Some of the most frequent are cardiovascular effects, including disturbances in heart rhythm and heart attacks; neurological effects, including strokes, seizures, headaches, and coma; and gastrointestinal complications, including abdominal pain and nausea. In rare instances, sudden death can occur on the first use of cocaine or unexpectedly thereafter. Cocaine-related deaths are often a result of cardiac arrest or seizures followed by respiratory arrest.

In addition, research has also revealed a potentially dangerous interaction between cocaine and alcohol. This mixture is the most common two-drug combination that results in drug-related death.

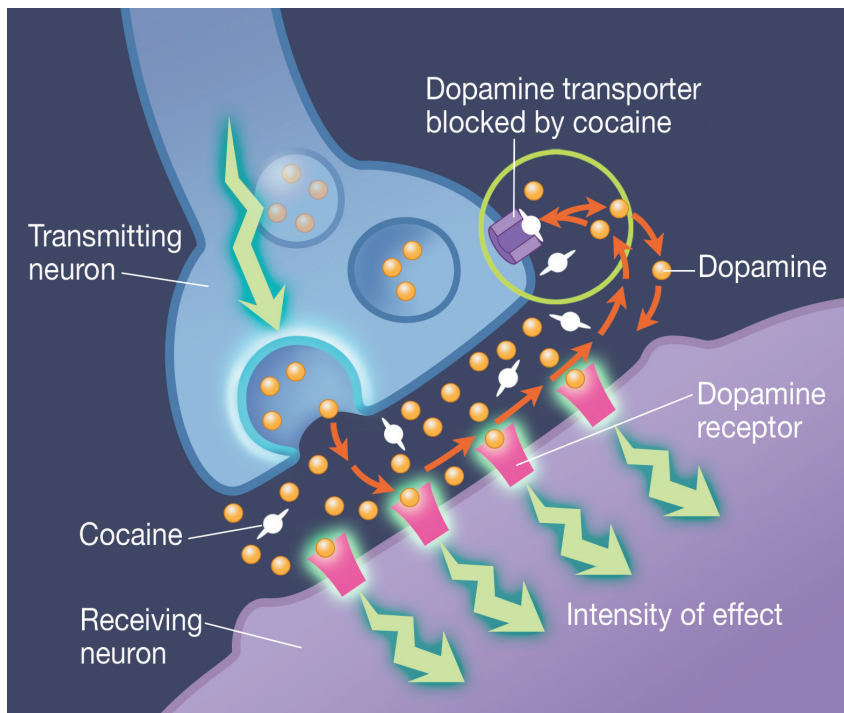
What Are the Long-Term Effects of Cocaine Use?

Cocaine is a powerfully addictive drug. Thus, it is unlikely that an individual will be able to reliably predict or control the extent to which he or she will continue to want or use the drug. And, if addiction takes hold, the risk for relapse is high even following long periods of abstinence. Recent studies have shown that during periods of abstinence, the memory of the cocaine experience or exposure to cues associated with drug use can trigger tremendous craving and relapse to drug use.

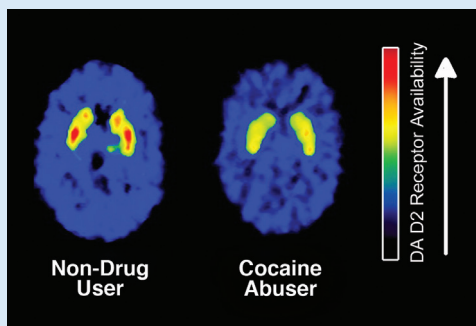
With repeated exposure to cocaine, the brain starts to adapt, and the reward pathway becomes less sensitive to natural reinforcers and to the drug itself. Tolerance may develop—this means that higher doses and/or more frequent use of cocaine is needed to register the same level of pleasure experienced during initial use. At the same time, users can also become more sensitive (sensitization) to cocaine's anxiety-producing, convulsant, and other toxic effects.

Users take cocaine in “binges,” during which the cocaine is used repeatedly and at increasingly higher doses. This can lead to increased irritability, restlessness, panic attacks, and paranoia—even a full-blown psychosis, in which the individual loses touch with reality and experiences auditory hallucinations. With increasing dosages or frequency of use, the risk of adverse psychological or physiological effects increases.

Different routes of cocaine administration can produce different adverse effects. Regularly snorting cocaine, for example, can lead to loss of sense of smell; nosebleeds; problems with swallowing;



Cocaine in the brain—In the normal communication process, dopamine is released by a neuron into the synapse, where it can bind to dopamine receptors on neighboring neurons. Normally, dopamine is then recycled back into the transmitting neuron by a specialized protein called the dopamine transporter. If cocaine is present, it attaches to the dopamine transporter and blocks the normal recycling process, resulting in a buildup of dopamine in the synapse, which contributes to the pleasurable effects of cocaine.



Brain images showing decreased dopamine (D₂) receptors in the brain of a person addicted to cocaine versus a nondrug user. The dopamine system is important for conditioning and motivation, and alterations such as this are likely responsible, in part, for the diminished sensitivity to natural rewards that develops with addiction.

hoarseness; and an overall irritation of the nasal septum, which could result in a chronically inflamed, runny nose. Ingested cocaine can cause severe bowel gangrene due to reduced blood flow. Persons who inject cocaine have puncture marks called “tracks,” most commonly in their forearms, and may experience allergic reactions, either to the drug or to some additive in street cocaine, which in severe cases can result in death. Many chronic cocaine users lose their appetite and experience significant weight loss and malnourishment.

Are Cocaine Abusers at Risk for Contracting HIV/AIDS and Hepatitis?

Yes, cocaine abusers are at increased risk for contracting such infectious diseases as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and viral hepatitis. This risk stems not only from sharing contaminated needles and drug paraphernalia but also from engaging in risky behaviors as a result of intoxication. Research has shown that drug intoxication and addiction can compromise judgment and decisionmaking,

and potentially lead to risky sexual encounters, needle sharing, and trading sex for drugs—by both men and women. In fact, some studies are showing that among drug abusers, those who do not inject drugs are contracting HIV at rates equal to those who do inject drugs, further highlighting the role of sexual transmission of HIV in this population.

Additionally, hepatitis C (HCV) has spread rapidly among injecting drug users. Risk begins with the first injection, and within 2 years, nearly 40 percent of injection drug users (IDUs) are exposed to HCV. By the time IDUs have been injecting for 5 years, their chances of being infected with HCV are between 50 and 80 percent. Although treatment for HCV is not effective for everyone and can have significant side effects, medical followup is essential for all those who are infected. There is no vaccine for the hepatitis C virus, and it is highly transmissible via injection; thus, HCV testing is recommended for any individual who has ever injected drugs.

What Treatments Are Effective for Cocaine Abusers?

In 2007, cocaine accounted for about 13 percent of all admissions to drug abuse treatment programs.

The majority of individuals (72 percent in 2007) who seek treatment for cocaine abuse smoke crack and are likely to be polydrug abusers, or users of more than one substance. The widespread abuse of cocaine has stimulated extensive efforts to develop treatment programs for cocaine. As with any drug addiction, this is a complex disease that involves biological changes in the brain as well as myriad social, familial, and other environmental problems. Therefore, treatment of cocaine addiction must be comprehensive, and strategies need to assess the neurobiological, social, and medical aspects of the patient’s drug abuse. Moreover, patients who have a variety of addictions often have other co-occurring mental disorders that require additional behavioral or pharmacological interventions.

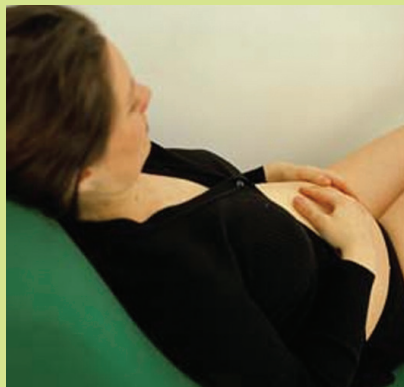
Pharmacological Approaches

Presently, there are no FDA-approved medications to treat cocaine addiction. Consequently, NIDA is working aggressively to identify and test new medications to treat cocaine addiction safely and effectively. Several medications marketed for other diseases (e.g., vigabatrin, modafinil, tiagabine, disulfiram, and topiramate) show promise and have been reported to reduce cocaine use in controlled clinical trials. Among these, disulfiram (used to treat alcoholism) has produced the most consistent reductions in cocaine abuse. On the other hand, new knowledge of how the brain is changed by cocaine is directing attention to novel targets for medications development. Compounds that are currently being tested for addiction treatment take advantage of underlying cocaine-induced adaptations in the brain that disturb the balance between excitatory (glutamate) and inhibitory (gamma-aminobutyric acid) neurotransmission. Also,

What Are the Effects of Maternal Cocaine Use?

The full extent of the effects of prenatal cocaine exposure on a child is not completely known, but many scientific studies have documented that babies born to mothers who abuse cocaine during pregnancy are often prematurely delivered, have low birth weights and smaller head circumferences, and are shorter in length than babies born to mothers who do not abuse cocaine.

Nevertheless, it is difficult to estimate the full extent of the consequences of maternal drug abuse and to determine the specific hazard of a particular drug to the unborn child. This is because multiple factors—



such as the amount and number of *all* drugs abused, including nicotine; extent of prenatal care; possible neglect or abuse of the child; exposure to violence in the environment; socioeconomic conditions; maternal nutrition; other health conditions; and exposure to sexually transmitted diseases—can all interact to impact maternal, fetal, and child outcomes.

Some may recall that “crack babies,” or babies born to mothers who abused crack cocaine while pregnant, were at one time written off as a lost generation. They were predicted to suffer from severe, irreversible damage, including reduced intelligence and social skills. It was later found that this was a gross exaggeration. However, the fact that most of these children appear normal should not be overinterpreted to indicate that there is no cause for concern. Using sophisticated technologies, scientists are now finding that exposure to cocaine during fetal development may lead to subtle, yet significant, later deficits in some children, including deficits in some aspects of cognitive performance, information processing, and attention to tasks—abilities that are important for the realization of a child’s full potential.

dopamine D₃ receptors (a subtype of dopamine receptor) constitute a novel molecular target of high interest. Medications that act at these receptors are now being tested for safety in humans. Finally, a cocaine vaccine that prevents entry of cocaine into the brain holds great promise for reducing the risk of relapse. In addition to treatments for addiction, medical treatments are being developed to address the acute emergencies that result from cocaine overdose each year.

Behavioral Interventions

Many behavioral treatments for cocaine addiction have proven to be effective in both residential and outpatient settings. Indeed, behavioral therapies are often the only available and effective treatments for many drug problems, including stimulant addictions. However, the integration of behavioral and pharmacological treatments may ultimately prove to be the most effective approach.

Presently, there are no proven medications to treat cocaine addiction. Consequently, NIDA is working aggressively to identify and test new medications.

One form of behavioral therapy that is showing positive results in cocaine-addicted populations is contingency management, or motivational incentives (MI). MI may be particularly useful for helping patients achieve initial abstinence from cocaine and for helping patients stay in treatment. Programs use a voucher or prize-based system that rewards patients who abstain from cocaine and other drug use. On the basis of drug-free urine tests, the patients earn points, or chips, which can be exchanged for items that encourage healthy living, such as a gym membership,

movie tickets, or dinner at a local restaurant. This approach has recently been shown to be practical and effective in community treatment programs.

Cognitive-behavioral therapy (CBT) is an effective approach for preventing relapse. CBT is focused on helping cocaine-addicted individuals abstain—and remain abstinent—from cocaine and other substances. The underlying assumption is that learning processes play an important role in the development and continuation of cocaine abuse and addiction. These same learning processes can be harnessed to help individuals reduce drug use and successfully prevent relapse. This approach attempts to help patients recognize, avoid, and cope; that is, they recognize the situations in which they are most likely to use cocaine, avoid these situations when appropriate, and cope more effectively with a range of problems and problematic behaviors associated with drug abuse. This

therapy is also noteworthy because of its compatibility with a range of other treatments patients may receive.

Therapeutic communities (TCs), or residential programs, offer another alternative to persons in need of treatment for cocaine addiction. TCs usually require a 6- or 12-month stay and use the program's entire "community" as active components of treatment.

They can include onsite vocational rehabilitation and other supportive services and focus on successful re-integration of the individual into society.

Community-based recovery groups—such as Cocaine Anonymous—that use a 12-step program can also be helpful to people trying to sustain abstinence. Participants may benefit from the supportive fellowship and from

sharing with those experiencing common problems and issues.

It is important that patients receive services that match all of their treatment needs. For example, if a patient is unemployed, it may be helpful to provide vocational rehabilitation or career counseling along with addiction treatment. If a patient has marital problems, it may be important to offer couples counseling.

Glossary

Addiction: A chronic, relapsing disease characterized by compulsive drug seeking and use and by long-lasting changes in the brain.

Anesthetic: An agent that causes insensitivity to pain and is used for surgeries and other medical procedures.

Coca: The plant, *Erythroxylon*, from which cocaine is derived. Also refers to the leaves of this plant.

Crack: The slang term for a smokable form of cocaine.

Craving: A powerful, often uncontrollable, desire for drugs.

Dopamine: A brain chemical, classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

Freebase: A solid, water-insoluble, and smokable form of cocaine that is produced when its hydrochloride salt form is processed with ammonia or sodium bicarbonate and water, then heated to remove the hydrochloride. (Also, see "crack.")

Frontal cortex: The front part of the brain involved with reasoning, planning, problemsolving, and other higher cognitive functions.

Gamma-aminobutyric acid (GABA): The main inhibitory neurotransmitter in the central nervous system. GABA provides the needed counterbalance to the actions of other systems, particularly the excitatory neurotransmitter glutamate.

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

Hydrochloride salt: A powdered, water-soluble form of cocaine that can be injected or snorted.

Neuron: A nerve cell.

Nucleus accumbens: A brain region involved in motivation and reward. Nearly all drugs of abuse directly or indirectly increase dopamine in the nucleus accumbens, contributing to their addictive properties.

Polydrug user: An individual who uses more than one drug.

Rush: A surge of pleasure (euphoria) that rapidly follows the administration of some drugs.

Stimulant: A class of drugs that enhances the activity of monoamines (such as dopamine) in the brain, increasing arousal, heart rate, blood pressure, and respiration, and decreasing appetite; includes some medications used to treat attention-deficit hyperactivity disorder (e.g., methylphenidate and amphetamines), as well as cocaine and methamphetamine.

Tolerance: A condition in which higher doses of a drug are required to produce the same effect achieved during initial use.

Vertigo: The sensation of dizziness.

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Where can I get further information about cocaine?

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

NATIONAL INSTITUTE ON DRUG ABUSE



RESEARCH DISSEMINATION CENTER

What's New on the NIDA Web Site

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

NIDA Web Sites

www.drugabuse.gov

www.backtoschool.drugabuse.gov

www.teens.drugabuse.gov

For Physician Information

NIDAMED 

www.drugabuse.gov/nidamed

Other Web Sites

Information on cocaine abuse and addiction is also available through the following Web site:

- Substance Abuse and Mental Health Services Administration Health Information Network: www.samhsa.gov/shin



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How can
inhalant abuse
be recognized?
See page 4.

Research Report Series

from the director:

Although many parents are appropriately concerned about illicit drugs such as marijuana, cocaine, and LSD, they often ignore the dangers posed to their children from common household products that contain volatile solvents or aerosols. Products such as glues, nail polish remover, lighter fluid, spray paints, deodorant and hair sprays, whipped cream canisters, and cleaning fluids are widely available yet far from innocuous. Many young people inhale the vapors from these sources in search of quick intoxication without being aware that using inhalants, even once, can have serious health consequences.

National surveys indicate that nearly 21.7 million Americans aged 12 and older have used inhalants at least once in their lives. NIDA's 2011 Monitoring the Future (MTF) survey reveals that 13.1 percent of 8th-graders have used inhalants. Parents and children need to know that even sporadic or single episodes of inhalant abuse can be extremely dangerous. Inhalants can disrupt heart rhythms and cause death from cardiac arrest, or lower oxygen levels enough to cause suffocation. Regular abuse of these substances can result in serious harm to vital organs, including the brain, heart, kidneys, and liver.

Through scientific research, we have learned much about the nature and extent of inhalant abuse, its pharmacology, and its consequences. This research has brought the picture of inhalant abuse in the Nation into focus and pointed to the dangers and the warning signs for parents, educators, and clinicians. We hope this compilation of the latest scientific information will help alert readers to inhalant abuse and its harmful effects and aid efforts to deal with this problem effectively.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

Inhalants

What Are Inhalants?

Inhalants are volatile substances that produce chemical vapors that can be inhaled to induce a psychoactive, or mind-altering, effect. Although other abused substances can be inhaled, the term “inhalants” is used to describe a variety of substances whose main common characteristic is that they are rarely, if ever, taken by any route other than inhalation. This definition encompasses a broad range of chemicals that may have different pharmacological effects and are found in hundreds of different products. As a result, precise categorization of inhalants is difficult. One classification system lists four general categories of inhalants—volatile solvents, aerosols, gases, and nitrites—based on the forms in which they are often found in household, industrial, and medical products.

continued inside

Volatile solvents are liquids that vaporize at room temperature. They are found in a multitude of inexpensive, easily available products used for common household and industrial purposes. These include paint thinners and removers, dry-cleaning fluids, degreasers, gasoline, glues, correction fluids, and felt-tip markers.

Aerosols are sprays that contain propellants and solvents. They include spray paints, deodorant and hair sprays, vegetable oil sprays for cooking, and fabric protector sprays.

Gases include medical anesthetics as well as gases used in household or commercial products. Medical anesthetics include ether, chloroform, halothane, and nitrous oxide (commonly called “laughing gas”). Nitrous oxide is the most abused of these gases and can be found in whipped cream dispensers and products that boost octane levels in racing cars. Other household or commercial products containing gases include butane lighters, propane tanks, and refrigerants.

Nitrites often are considered a special class of inhalants. Unlike most other inhalants, which act directly on the central nervous system (CNS), nitrites act primarily to dilate blood vessels and relax the muscles. While other inhalants are used to alter mood, nitrites are used primarily as sexual enhancers. Nitrites include cyclohexyl nitrite, isoamyl (amyl) nitrite, and isobutyl (butyl) nitrite and are commonly known as “poppers” or “snappers.” Amyl nitrite is used in certain diagnostic procedures and was prescribed in the past to treat some patients for heart pain. Nitrites now are prohibited by the Consumer Product Safety Commission but can still be found, sold in small bottles labeled as “video head cleaner,” “room odorizer,” “leather cleaner,” or “liquid aroma.”

Generally, inhalant abusers will abuse any available substance. However, effects produced by individual inhalants vary, and some users will go out of their way to obtain their favorite inhalant. For example, in certain parts of the country, “Texas shoeshine,” a shoe-shining spray containing the chemical toluene, is a local favorite.

What Is the Scope of Inhalant Abuse?

According to the 2010 National Survey on Drug Use and Health (NSDUH), there were 793,000 persons aged 12 or older who had used inhalants for the first time within the past 12 months; 68.4 percent were under the age of 18.

In fact, inhalants—particularly volatile solvents, gases, and aerosols—are often the easiest and first options for abuse among young children who use drugs. NIDA’s annual MTF survey of 8th-, 10th-, and 12th-graders consistently reports the highest rates of current, past-year, and lifetime inhalant use among 8th-graders.

Inhalant use has decreased significantly among 8th-, 10th-, and 12th-graders compared to its peak years in the mid-1990s (see figure, page 3). According to the 2011 MTF survey, past-year use was reported as 7.0, 4.5, and 3.2 percent, for 8th-, 10th-, and 12th-graders, respectively. Data compiled by the National Capital Poison Center also show a decrease in the prevalence of inhalant cases reported to U.S. poison control centers—down 33 percent from 1993 to 2008. The prevalence was highest among children aged 12 to 17, peaking among 14-year-olds.

Demographic differences in inhalant use have been identified at different ages. The MTF survey indicates that in 2011, 8.6 percent of 8th-grade females reported using inhalants in the past year, compared with 5.5 percent of 8th-grade males.

In terms of ethnicity, Hispanics have the highest rates of past-year use among 8th- and 10th-graders, compared to both Blacks and Whites.

People from both urban and rural settings abuse inhalants. Further, research on factors contributing to inhalant abuse suggests that adverse socioeconomic conditions, a history of childhood abuse, poor grades, and school dropout are associated with inhalant abuse.



How Are Inhalants Used?

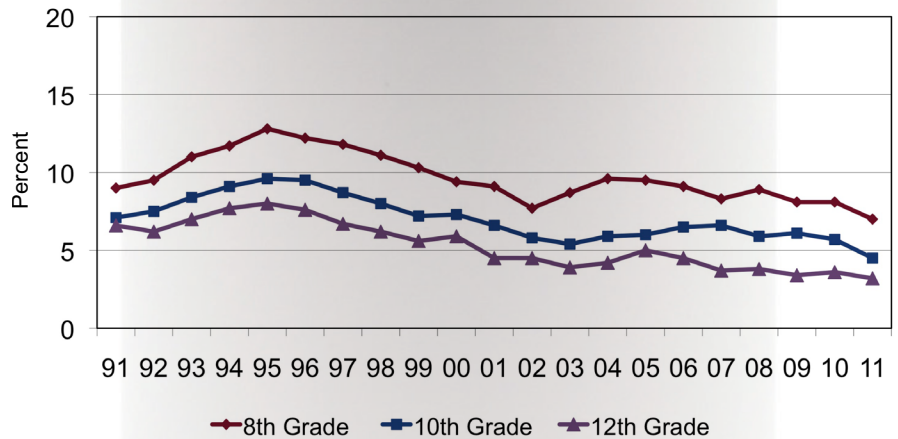
Inhalants can be breathed in through the nose or the mouth in a variety of ways, such as—

- “sniffing” or “snorting” fumes from containers;
- spraying aerosols directly into the nose or mouth;
- “bagging”—sniffing or inhaling fumes from substances sprayed or deposited inside a plastic or paper bag;
- “huffing” from an inhalant-soaked rag stuffed in the mouth; and
- inhaling from balloons filled with nitrous oxide.

Inhaled chemicals are absorbed rapidly into the bloodstream through the lungs and are quickly distributed to the brain and other organs. Within seconds of inhalation, the user experiences intoxication along with other effects similar to those produced by alcohol. Alcohol-like effects may include slurred speech; the inability to coordinate movements; euphoria; and dizziness. In addition, users may experience lightheadedness, hallucinations, and delusions.

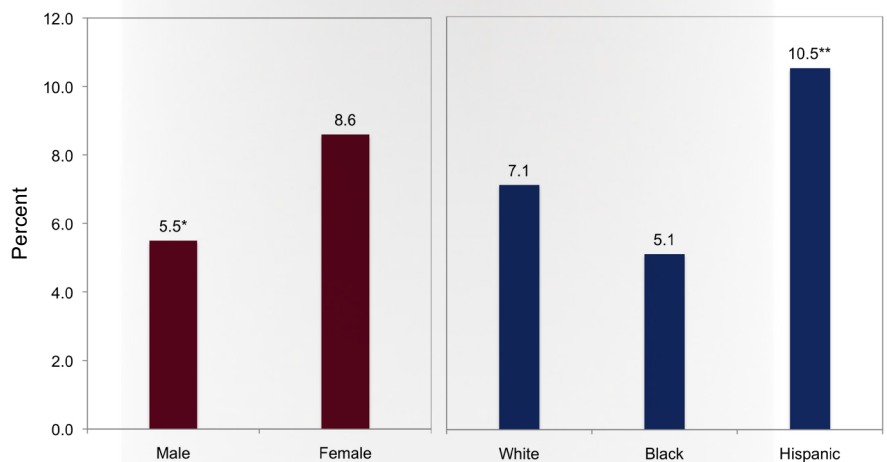
Because intoxication lasts only a few minutes, abusers frequently seek to prolong the high by inhaling repeatedly over the course of several hours, which is a very dangerous practice. With successive inhalations, abusers can suffer loss of consciousness and possibly even death. At the least, they will feel less inhibited and

Past-Year Inhalant Use Among 8th-, 10th-, and 12th-Graders, 1991–2011



Source: University of Michigan, 2011 Monitoring the Future Survey.

Gender and Race/Ethnicity Differences in Past-Year Inhalant Use Among 8th-Graders, 2011



*Level of significance of difference between Male and Female = .05

** Level of significance of difference between Whites and Hispanics and Blacks and Hispanics = .001

Source: University of Michigan, 2011 Monitoring the Future Survey.



Most inhalants produce a rapid high that resembles alcohol intoxication, with initial excitation then drowsiness, disinhibition, lightheadedness, and agitation.

less in control. After heavy use of inhalants, abusers may feel drowsy for several hours and experience a lingering headache.

How Do Inhalants Produce Their Effects?

Many brain systems may be involved in the anesthetic, intoxicating, and reinforcing effects of different inhalants. Nearly all abused inhalants (other than nitrites) produce a pleasurable effect by depressing the CNS. Nitrites, in contrast, dilate and relax blood vessels rather than act as anesthetic agents.

Evidence from animal studies suggests that a number of commonly abused volatile solvents and anesthetic gases have neurobehavioral effects and mechanisms of action similar to those produced by CNS depressants, which include alcohol and medications such as sedatives and anesthetics.

A 2007 animal study indicates that toluene, a solvent found in many commonly abused inhalants—including model airplane glue, paint sprays, and paint and nail polish removers—activates the brain's dopamine system. The dopamine system has been shown to play a role in the rewarding effects of nearly all drugs of abuse.

What Are the Short- and Long-Term Effects of Inhalant Use?

Although the chemical substances found in inhalants may produce various pharmacological effects, most inhalants produce a rapid high that resembles alcohol intoxication, with initial excitation followed by drowsiness, disinhibition, lightheadedness, and agitation. If sufficient amounts are inhaled, nearly all solvents and gases produce anesthesia—a loss of sensation—and can lead to unconsciousness.



How Can Inhalant Abuse Be Recognized?

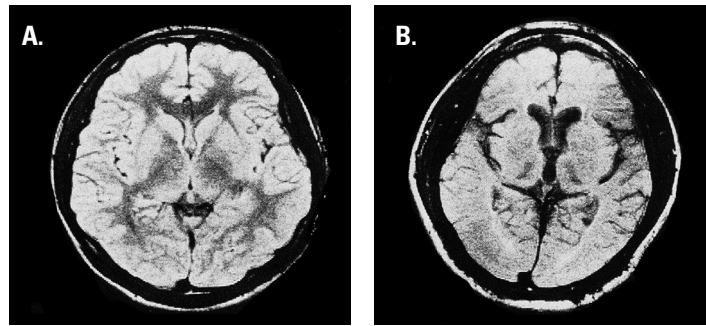
Early identification and intervention are the best ways to stop inhalant abuse before it causes serious health consequences. Parents, educators, family physicians, and other health care practitioners should be alert to the following signs:

- Chemical odors on breath or clothing
- Paint or other stains on face, hands, or clothes
- Hidden empty spray paint or solvent containers, and chemical-soaked rags or clothing
- Drunk or disoriented appearance
- Slurred speech
- Nausea or loss of appetite
- Inattentiveness, lack of coordination, irritability, and depression

The chemicals found in solvents, aerosol sprays, and gases can produce a variety of additional effects during or shortly after use. These effects are related to inhalant intoxication and may include belligerence, apathy, impaired judgment, and impaired functioning in work or social situations; nausea and vomiting are other common side effects. Exposure to high doses can cause confusion and delirium. In addition, inhalant abusers may experience dizziness, drowsiness, slurred speech, lethargy, depressed reflexes, general muscle weakness, and stupor. For example, research shows that toluene can produce headache, euphoria, giddy feelings, and the inability to coordinate movements.

Inhaled nitrites dilate blood vessels, increase heart rate, and produce a sensation of heat and excitement that can last for several minutes. Other effects can include flush, dizziness, and headache.

A strong need to continue using inhalants has been reported by many individuals, particularly those who have abused inhalants for prolonged periods over many days. Compulsive use and a mild withdrawal syndrome can occur with long-term inhalant abuse. A recent survey of 43,000 American adults suggests that inhalant users, on average, initiate use of cigarettes, alcohol, and almost all other drugs at younger ages and display a higher lifetime prevalence of substance use disorders, including abuse of prescription drugs, when compared with substance abusers without a history of inhalant use.



Compared with the brain of an individual with no history of inhalant abuse (A), that of a chronic toluene abuser (B) is smaller and fills less of the space inside the skull (the white outer circle in each image). Courtesy of Neil Rosenberg, M.D., NIDA Research Report (NIH 05-3818).

What Are the Other Medical Consequences of Inhalant Abuse?

Inhalant abusers risk an array of other devastating medical consequences. The highly concentrated chemicals in solvents or aerosol sprays can induce irregular and rapid heart rhythms and lead to fatal heart failure within minutes of a session of prolonged sniffing. This syndrome, known as “sudden sniffing death,” can result from a single session of inhalant use by an otherwise healthy young person. Sudden sniffing death is associated particularly with the abuse of butane, propane, and chemicals in aerosols. Inhalant abuse also can cause death by—

- **asphyxiation**—from repeated inhalations that lead to high concentrations of inhaled fumes, which displace available oxygen in the lungs;
- **suffocation**—from blocking air from entering the lungs when inhaling fumes from a plastic bag placed over the head;

- **convulsions or seizures**—from abnormal electrical discharges in the brain;
- **coma**—from the brain shutting down all but the most vital functions;
- **choking**—from inhalation of vomit after inhalant use; or
- **fatal injury**—from accidents, including motor vehicle fatalities, suffered while intoxicated.

Based on independent studies performed over a 10-year period in three different states, the number of inhalant-related fatalities in the United States is approximately 100–200 per year.

Animal and human research shows that most inhalants are extremely toxic. Perhaps the most significant toxic effect of chronic exposure to inhalants is widespread and long-lasting damage to the brain and other parts of the nervous system (see figure). For example, chronic abuse of volatile solvents, such as toluene or naphthalene (the volatile ingredient in mothballs), damages the protective sheath

Hazards of Chemicals Found in Commonly Abused Inhalants

amyl nitrite, butyl nitrite

(*"poppers," "video head cleaner"*)

sudden sniffing death syndrome, suppressed immunologic function, injury to red blood cells (interfering with oxygen supply to vital tissues)

benzene

(*found in gasoline*)

bone marrow injury, impaired immunologic function, increased risk of leukemia, reproductive system toxicity

butane, propane

(*found in lighter fluid, hair and paint sprays*)

sudden sniffing death syndrome via cardiac effects, serious burn injuries (because of flammability)

freon

(*used as a refrigerant and aerosol propellant*)

sudden sniffing death syndrome, respiratory obstruction and death (from sudden cooling/cold injury to airways), liver damage

methylene chloride

(*found in paint thinners and removers, degreasers*)

reduction of oxygen-carrying capacity of blood, changes to the heart muscle and heartbeat

nitrous oxide ("laughing gas"), hexane

death from lack of oxygen to the brain, altered perception and motor coordination, loss of sensation, limb spasms, blackouts caused by blood pressure changes, depression of heart muscle functioning

toluene

(*found in gasoline, paint thinners and removers, correction fluid*)

brain damage (loss of brain tissue mass, impaired cognition, gait disturbance, loss of coordination, loss of equilibrium, limb spasms, hearing and vision loss), liver and kidney damage

trichloroethylene

(*found in spot removers, degreasers*)

sudden sniffing death syndrome, cirrhosis of the liver, reproductive complications, hearing and vision damage

around certain nerve fibers in the brain and peripheral nervous system. This extensive destruction of nerve fibers is clinically similar to that seen with neurological diseases such as multiple sclerosis.

The neurotoxic effects of prolonged inhalant abuse include neurological syndromes that reflect damage to parts of the brain involved in controlling cognition, movement, vision, and hearing. Cognitive abnormalities can range from mild impairment to severe dementia.

Inhalants also are highly toxic to other organs. Chronic exposure can produce significant damage to the heart, lungs, liver, and kidneys. Although some inhalant-induced damage to the nervous and other organ systems may be at least partially

reversible when inhalant abuse is stopped, many syndromes caused by repeated or prolonged abuse are irreversible.

Abuse of inhalants during pregnancy also may place infants and children at increased risk of developmental harm. Animal studies designed to simulate human patterns of inhalant abuse suggest that prenatal exposure to toluene can result in reduced birth weights, occasional skeletal abnormalities, delayed neurobehavioral development, and altered regulation of metabolism and body composition in males, as well as food intake and weight gain in both sexes. A number of case reports note abnormalities in newborns of mothers who

chronically abuse solvents, and there is evidence of subsequent developmental impairment in some of these children. However, no well-controlled prospective study of the effects of prenatal exposure to inhalants in humans has been conducted, and it is not possible to link prenatal exposure to a particular chemical to a specific birth defect or developmental problem.

Finally, a 2008 survey of over 13,000 high school students has identified an association between disordered eating (defined as a positive response to one or more of three questions about engaging in inappropriate behaviors for weight control during the past 30 days) and inhalant use among both male and female students.

What Are the Unique Risks Associated With Nitrite Abuse?

Nitrites are abused mainly by older adolescents and adults. Typically, individuals who abuse nitrites are seeking to enhance sexual function

and pleasure. Research shows that abuse of these drugs in this context is associated with unsafe sexual practices that greatly increase the risk of contracting and spreading infectious diseases such as HIV/AIDS and hepatitis.

Animal research raises the possibility that there may also be a link between abuse of nitrites and the development and progression

of infectious diseases and tumors. The research indicates that inhaling nitrites depletes many cells in the immune system and impairs mechanisms that fight infectious diseases. A study found that even a relatively small number of exposures to butyl nitrite can produce dramatic increases in tumor incidence and growth rate in animals.

Glossary

Anesthetic: An agent that causes insensitivity to pain and is used for surgeries and other medical procedures.

Central nervous system: The brain and spinal cord.

Dementia: A condition of deteriorated mental function.

Dopamine: A brain chemical, classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

Naphthalene: Volatile, active ingredient in mothballs.

Toxic: Causing temporary or permanent effects detrimental to the functioning of a body organ or group of organs.

Withdrawal: Symptoms that occur after chronic use of a drug is reduced abruptly or stopped.

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Where can I get further information about inhalants?

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

NATIONAL INSTITUTE ON DRUG ABUSE



RESEARCH DISSEMINATION CENTER

What's New on the NIDA Web Site

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

NIDA Web Sites

www.drugabuse.gov
www.inhalants.drugabuse.gov
www.steroidabuse.gov
www.clubdrugs.gov
www.backtoschool.drugabuse.gov
www.teens.drugabuse.gov

Other Web Sites

Information on inhalant abuse is also available through these other Web sites:

- Centers for Disease Control and Prevention: www.cdc.gov
- National Inhalant Prevention Coalition: www.inhalants.org
- Substance Abuse and Mental Health Services Administration Health Information Network: www.samhsa.gov/shin



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Revised July 2010, Revised July 2012.

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.

Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

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.

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.



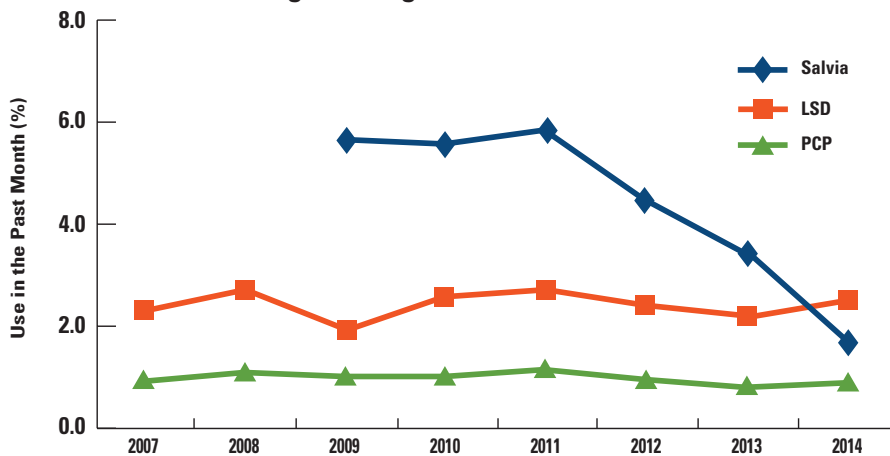
Salvia divinorum—also known as divinor’s sage, Maria Pastora, Sally-D, or magic mint—is a

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 salvia—to 1.8 percent in 2014—with LSD and PCP use dropping slightly (Johnston, 2014).

Past-Year Use of Hallucinogenic and Dissociative Drugs Among 12th-Grade Students



Source: Monitoring the Future National Survey Results on Drug Use, 2014 Overview

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

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.

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



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)

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).

NATIONAL INSTITUTE ON DRUG ABUSE



RESEARCH DISSEMINATION CENTER

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 hallucinogens 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



National Institute
on Drug Abuse

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