

Research Report

SERIES

In the 1970s, the baby boom generation was coming of age, and its drug of choice was marijuana. By 1979, more than 60 percent of 12th-graders had tried marijuana at least once in their lives. From this peak, the percentage of 12th-graders who had ever used marijuana decreased for more than a decade, dropping to a low of 33 percent in 1992. However, in 1993, first-time marijuana use by 12th-graders was on the upswing, reaching 50 percent by 1997. Although the percentage of 12th-graders who have experience with marijuana has remained roughly level since then, there is still reason to be concerned. In 1999, more than 2 million Americans used marijuana for the first time. Two-thirds of them were between the ages of 12 and 17. Furthermore, the marijuana that is available today can be 5 times more potent than the marijuana of the 1970s.

The use of marijuana can produce adverse physical, mental, emotional, and behavioral changes, and—contrary to popular belief—it can be addictive. Marijuana smoke, like cigarette smoke, can harm the lungs. The use of marijuana can impair short-term memory, verbal skills, and judgment and distort perception. It also may weaken the immune system and possibly increase a user's likelihood of developing cancer. Finally, the increasing use of marijuana by very young teens may have a profoundly negative effect upon their development.

We hope that this research report will help make readers aware of our current knowledge of marijuana abuse and its harmful effects.

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MARIJUANA

Abuse

What is marijuana?

Marijuana—often called *pot, grass, reefer, weed, herb, mary jane, or mj*—is a greenish-gray mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis sativa*, the hemp plant. Most users smoke marijuana in hand-rolled cigarettes called *joints*, among other names; some use pipes or water pipes called *bongs*. Marijuana cigars called *blunts* have also become popular. To make blunts, users slice open cigars and replace the tobacco with marijuana, often combined with another drug, such as crack cocaine. Marijuana also is used

to brew tea and is sometimes mixed into foods.

The major active chemical in marijuana is delta-9-tetrahydrocannabinol (THC), which causes the mind-altering effects of marijuana intoxication. The amount of THC (which is also the psychoactive ingredient in hashish) determines the potency and, therefore, the effects of marijuana. Between 1980 and 1997, the amount of THC in marijuana available in the United States rose dramatically.

What is the scope of marijuana use in the United States?

Marijuana is the Nation's most commonly used illicit drug. More than 83 million Americans (37 percent) age 12 and older have tried marijuana at least once, according to the 2001 National Household Survey on Drug Abuse (NHSDA).



Marijuana use is widespread among adolescents and young adults. The percentage of middle-school students who reported using marijuana increased throughout the early 1990s. In the past few years, according to the 2001 Monitoring the Future Study, an annual survey of drug use among the Nation's middle- and high-school students, illicit drug use by 8th-, 10th-, and 12th-graders has leveled off. Still, in 2001, 20 percent of 8th-graders reported that they had tried marijuana, and 9 percent were current users (defined as having used the drug in the 30 days preceding the survey). Among 10th-graders, 40 percent had tried marijuana sometime in their lives, and almost 20 percent were current users. As would be expected, rates of use among 12th-graders were higher still: Nearly half had

tried marijuana at some time, and 22 percent were current users.

The Drug Abuse Warning Network (DAWN), a system for monitoring the health impact of drugs, estimated that, in 2001, marijuana was a contributing factor in more than 110,000 emergency department (ED) visits in the United States, with about 15 percent of the patients between the ages of 12 and 17, and almost two-thirds male.

In 1999, the National Institute of Justice's Arrestee Drug Abuse Monitoring Program (ADAM), which collects data from 34 sites on the number of adult arrestees testing positive for various drugs, found that, on average, 39 percent of adult male arrestees and 26 percent of adult female arrestees tested positive for marijuana. ADAM collected data on juvenile arrestees in nine sites and found that marijuana was the most com-

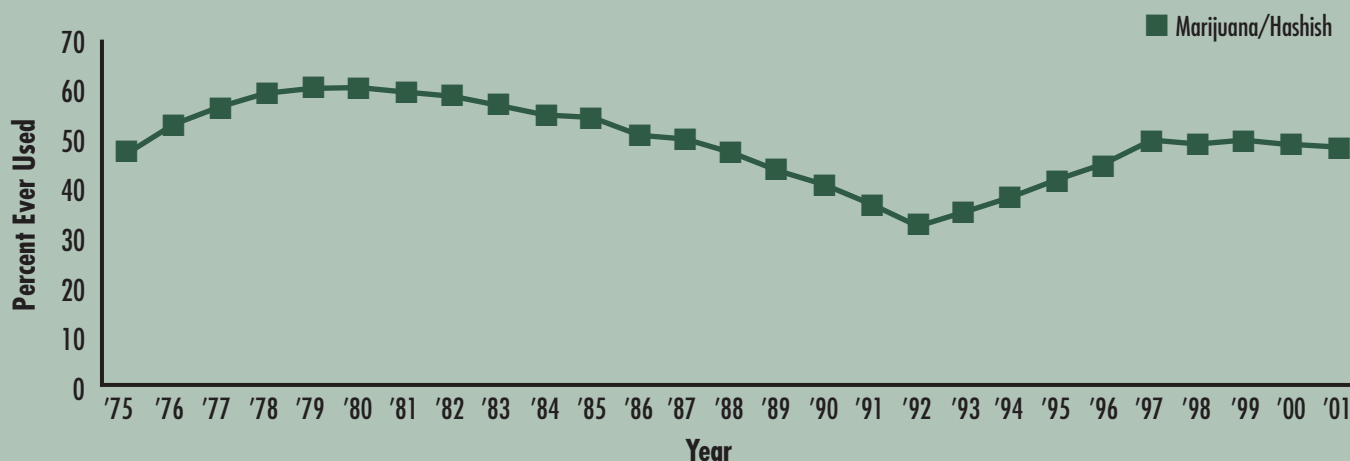
monly used drug among these youths. On average, 53 percent of juvenile male and 38 percent of juvenile female arrestees tested positive for marijuana.

NIDA's Community Epidemiology Work Group (CEWG), a network of researchers that tracks trends in the nature and patterns of drug use in major U.S. cities, consistently reports that marijuana frequently is combined with other drugs, such as crack cocaine, PCP, formaldehyde, and codeine cough syrup, sometimes without the user being aware of it. Thus, the risks associated with marijuana use may be compounded by the risks of added drugs, as well.

How does marijuana affect the brain?

Scientists have learned a great deal about how THC acts in the brain to produce its

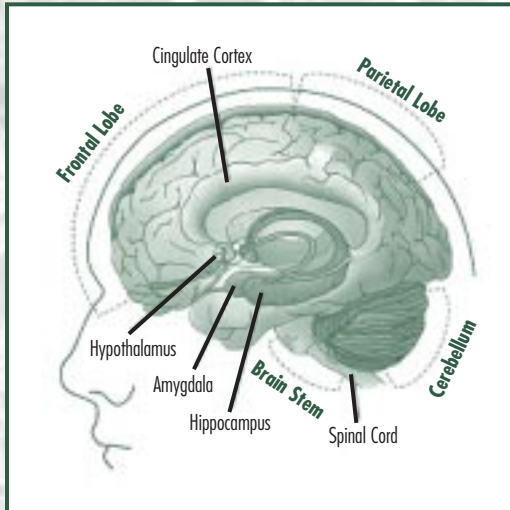
Long-Term Trends in Lifetime* Marijuana Use by 12th-Graders



* at least once in a lifetime

Source: The Monitoring the Future Study, the University of Michigan

Marijuana's Effects on the Brain



When marijuana is smoked, its active ingredient THC travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.

Brain Region	Functions Associated With Region
Brain regions in which cannabinoid receptors are abundant	
Cerebellum	Body movement coordination
Hippocampus	Learning and memory
Cerebral cortex, especially cingulate, frontal, and parietal regions	Higher cognitive functions
Nucleus accumbens	Reward
Basal ganglia Substantia nigra pars reticulata Entopeduncular nucleus Globus pallidus Putamen	Movement control
Brain regions in which cannabinoid receptors are moderately concentrated	
Hypothalamus	Body housekeeping functions (body temperature regulation, salt and water balance, reproductive function)
Amygdala	Emotional response, fear
Spinal cord	Peripheral sensation, including pain
Brain stem	Sleep and arousal, temperature regulation, motor control
Central gray	Analgesia
Nucleus of the solitary tract	Visceral sensation, nausea and vomiting

many effects. When someone smokes marijuana, THC rapidly passes from the lungs into the bloodstream, which carries the chemical to organs throughout the body, including the brain. In the brain, THC connects to specific sites called *cannabinoid receptors* on nerve cells and thereby influences the activity of those cells. Some brain areas have many cannabinoid receptors; others have few or none. Many cannabinoid receptors are found in the parts of the brain that influence pleasure, memory, thought, concentration, sensory and time perception, and coordinated movement.

What are the acute effects of marijuana use?

Marijuana's effects begin immediately after the drug enters the brain and last from 1 to 3 hours. If marijuana is consumed in food or drink, the short-term effects begin more slowly, usually in ½ to 1 hour, and last longer, for as long as 4 hours. Smoking marijuana deposits several times more THC into the blood than does eating or drinking the drug.

Within a few minutes after inhaling marijuana smoke, an

individual's heart begins beating more rapidly, the bronchial passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look red. The heart rate, normally 70 to 80 beats per minute, may increase by 20 to 50 beats per minute or, in some cases, even double. This effect can be greater if other drugs are taken with marijuana.

As THC enters the brain, it causes a user to feel euphoric—or "high"—by acting in the brain's reward system, areas of the brain that respond to stimuli such as food and drink as well as most drugs of abuse. THC activates the reward system in

the same way that nearly all drugs of abuse do, by stimulating brain cells to release the chemical dopamine.

A marijuana user may experience pleasant sensations, colors and sounds may seem more intense, and time appears to pass very slowly. The user's mouth feels dry, and he or she may suddenly become very hungry and thirsty. His or her hands may tremble and grow cold. The euphoria passes after awhile, and then the user may feel sleepy or depressed. Occasionally, marijuana use produces anxiety, fear, distrust, or panic.

Marijuana use impairs a person's ability to form memories, recall events (see Marijuana, Memory, and the Hippocampus), and shift attention from one thing to another. THC also disrupts coordination and balance by binding to receptors in the cerebellum and basal ganglia, parts of the brain that regulate balance, posture, coordination of movement, and reaction time. Through its effects on the brain and body, marijuana intoxication can cause accidents. Studies show that approximately 6 to 11 percent of fatal accident victims test positive for THC. In many of these cases, alcohol is detected as well.

In a study conducted by the National Highway Traffic Safety Administration, a moderate dose of marijuana alone was shown to impair driving performance; however, the effects of even a low dose of marijuana combined with alcohol were markedly greater than for either drug alone. Driving indices measured included reaction time, visual search frequency (driver checking side streets), and the ability

Marijuana, Memory, and the Hippocampus

Marijuana's damage to short-term memory seems to occur because THC alters the way in which information is processed by the hippocampus, a brain area responsible for memory formation. Laboratory rats treated with THC displayed the same reduced ability to perform tasks requiring short-term memory as other rats showed after nerve cells in their hippocampus were destroyed. In addition, the THC-treated rats had the greatest difficulty with the tasks precisely during the time when the drug was interfering most with the normal functioning of cells in the hippocampus.

As people age, they normally lose neurons in the hippocampus, which decreases their ability to remember events. Chronic THC exposure may hasten the age-related loss of hippocampal neurons. In one series of studies, rats exposed to THC every day for 8 months (approximately 30 percent of their lifespan), when examined at 11 to 12 months of age, showed nerve cell loss equivalent to that of unexposed animals twice their age.

to perceive and/or respond to changes in the relative velocity of other vehicles.

Marijuana users who have taken high doses of the drug may experience acute toxic psychosis, which includes hallucinations, delusions, and depersonalization—a loss of the sense of personal identity, or self-recognition. Although the specific causes of these symptoms remain unknown, they appear to occur more frequently when a high dose of cannabis is consumed in food or drink rather than smoked.

How does marijuana use affect physical health?

Marijuana use has been shown to increase users' difficulty in trying to quit smoking tobacco. This was recently reported in a study com-

paring smoking cessation in adults who smoked both marijuana and tobacco with those who smoked only tobacco. The relationship between marijuana use and continued smoking was particularly strong in those who smoked marijuana daily at the time of the initial interview, 13 years prior to the followup interview.

A study of 450 individuals found that people who smoke marijuana frequently but do not smoke tobacco have more health problems and miss more days of work than nonsmokers do. Many of the extra sick days used by the marijuana smokers in the study were for respiratory illnesses.

Even infrequent marijuana use can cause burning and stinging of the mouth and throat, often accompanied by a heavy cough. Someone who smokes marijuana regularly may have many of the same respiratory problems that tobacco smokers do, such as

daily cough and phlegm production, more frequent acute chest illnesses, a heightened risk of lung infections, and a greater tendency toward obstructed airways.

Cancer of the respiratory tract and lungs may also be promoted by marijuana smoke. A study comparing 173 cancer patients and 176 healthy individuals produced strong evidence that smoking marijuana increases the likelihood of developing cancer of the head or neck, and that the more marijuana smoked, the greater the increase. A statistical analysis of the data suggested that marijuana smoking doubled or tripled the risk of these cancers.

Marijuana has the potential to promote cancer of the lungs and other parts of the respiratory tract because it contains irritants and carcinogens. In fact, marijuana smoke contains 50 percent to 70 percent more carcinogenic hydrocarbons than does tobacco smoke. It also produces high levels of an enzyme that converts certain hydrocarbons into their carcinogenic form, levels that may accelerate the changes that

ultimately produce malignant cells. Marijuana users usually inhale more deeply and hold their breath longer than tobacco smokers do, which increases the lungs' exposure to carcinogenic smoke. These facts suggest that, puff for puff, smoking marijuana may increase the risk of cancer more than smoking tobacco does.

Some adverse health effects caused by marijuana may occur because THC impairs the immune system's ability to fight off infectious diseases and cancer. In laboratory experiments that exposed animal and human cells to THC or other marijuana ingredients, the normal disease-preventing reactions of many of the key types of immune cells were inhibited. In other studies, mice exposed to THC or related substances were more likely than unexposed mice to develop bacterial infections and tumors.

One study has indicated that a person's risk of heart attack during the first hour after smoking marijuana is four times his or her usual risk. The researchers suggest that a heart attack might occur,

in part, because marijuana raises blood pressure and heart rate and reduces the oxygen-carrying capacity of blood.

The Science of Medical Marijuana

THC, the main active ingredient in marijuana, produces effects that potentially can be useful for treating a variety of medical conditions. It is the main ingredient in a medication that is currently used to treat nausea and increase appetite in patients with wasting due to cancer chemotherapy or AIDS, to relieve pain, and to treat glaucoma. Scientists are investigating other potential medical uses for cannabinoids, including treating brain damage due to stroke and neurological disorders such as Parkinson's disease and Tourette's syndrome.

Some clinical trials of smoked marijuana for therapy are underway, but the inconsistency of THC dosage in different marijuana samples poses a major hindrance to valid trials and to the safe and effective use of the drug. Moreover, the adverse effects of marijuana smoke on the respiratory system will offset the helpfulness of smoked marijuana for some patients. Finally, little is known about the many chemicals besides THC that are in marijuana, or their possible deleterious impact on patients with medical conditions.

Health Consequences of Marijuana Abuse

Acute (present during intoxication)

- Impairs short-term memory
- Impairs attention, judgment, and other cognitive functions
- Impairs coordination and balance
- Increases heart rate

Persistent (lasting longer than intoxication, but may not be permanent)

- Impairs memory and learning skills

Long-term (cumulative, potentially permanent effects of chronic abuse)

- Can lead to addiction
- Increases risk of chronic cough, bronchitis, and emphysema
- Increases risk of cancer of the head, neck, and lungs

How does marijuana use affect school, work, and social life?

Students who smoke marijuana get lower grades and are less likely to graduate from high school, compared with their nonsmoking peers. In one study, researchers compared marijuana smoking and nonsmoking 12th-graders' scores on standardized tests of verbal and mathematical skills. Although all of the students had scored equally well in 4th grade, the smokers' scores were significantly lower in 12th grade than the nonsmokers' scores were.

Workers who smoke marijuana are more likely than their co-workers to have problems on the job. Several studies have associated workers' marijuana smoking with increased absences, tardiness, accidents, workers' compensation claims, and job turnover. A study among municipal workers found that employees who smoked marijuana on or off the job reported more "withdrawal behaviors"—such as leaving work without permission, daydreaming, spending work time on personal matters, and shirking tasks—that adversely affect productivity and morale.

Depression, anxiety, and personality disturbances are all associated with marijuana use. Research clearly demonstrates that marijuana use has the potential to cause problems in daily life or make a person's existing problems worse. Because marijuana compromises the ability to learn and remember information, the more a person uses marijuana the more he or she is likely to

fall behind in accumulating intellectual, job, or social skills. Moreover, research has shown that marijuana's adverse impact on memory and learning can last for days or weeks after the acute effects of the drug wear off.

For example, a study of 129 college students found that among heavy users of marijuana, those who smoked the drug at least 27 of the preceding 30 days, critical skills related to attention, memory, and learning were significantly impaired, even after they had not used the drug for at least 24 hours. The heavy marijuana users in the study had more trouble sustaining and shifting their attention and in registering, organizing, and using information than did the study participants who had used marijuana no more than 3 of the previous 30 days. As a result, someone who smokes marijuana once daily may be functioning at a reduced intellectual level all of the time. More recently, the same researchers showed that a group of long-term heavy marijuana users' ability to recall words from a list was impaired 1 week following cessation of marijuana use, but returned to normal by 4 weeks. An implication of this finding is that even after long-term heavy marijuana use, if an individual quits marijuana use, some cognitive abilities may be recovered.

Another study produced additional evidence that marijuana's effects on the brain can cause cumulative deterioration of critical life skills in the long run. Researchers gave students a battery of tests measuring problem-solving and emotional skills in 8th grade and again in 12th grade. The results showed that the students who were already drinking alcohol plus smoking marijuana in

8th grade started off slightly behind their peers but that the distance separating these two groups grew significantly by their senior year in high school. The analysis

The Body's Natural THC-Like Chemicals

THC owes many of its effects to its similarity to a family of chemicals called the *endogenous cannabinoids*, which are natural *Cannabis*-like chemicals. Because a THC molecule is shaped like these endogenous cannabinoids, it interacts with the same receptors on nerve cells, the cannabinoid receptors, that endogenous cannabinoids do, and it influences many of the same processes. Research has shown that the endogenous cannabinoids help control a wide array of mental and physical processes in the brain and throughout the body, including memory and perception, fine motor coordination, pain sensations, immunity to disease, and reproduction.

When someone smokes marijuana, THC overstimulates the cannabinoid receptors, leading to a disruption of the endogenous cannabinoids' normal control. This overstimulation produces the intoxication experienced by marijuana smokers. Over time, it may degrade some cannabinoid receptors, possibly producing permanent adverse effects and contributing to addiction and risk for a withdrawal syndrome.

linked marijuana use, independently of alcohol use, to reduced capacity for self-reinforcement, a group of psychological skills that enable individuals to maintain confidence and persevere in the pursuit of goals.

Can marijuana use during pregnancy harm the baby?

Research has shown that babies born to women who used marijuana during their pregnancies display altered responses to visual stimuli, increased tremulousness, and a high-pitched cry, which may indicate problems with neurological development. During infancy and preschool years, marijuana-exposed children have been observed to have more behavioral problems and to perform tasks of visual perception, language comprehension, sustained attention, and memory more poorly than nonexposed children do. In school, these children are more likely to exhibit deficits in decision-making skills, memory, and the ability to remain attentive.

Is marijuana use addictive?

Long-term marijuana use can lead to addiction for some people; that is, they use the drug compulsively even though it often interferes with family, school, work, and recreational activities. According to the 2001 National Household Survey on Drug Abuse, an estimated 5.6 million Americans age 12 or older reported problems with illicit drug use in the past year. Of these,

3.6 million met diagnostic criteria for dependence on an illicit drug. More than 2 million met diagnostic criteria for dependence on marijuana/hashish. In 1999, more than 220,000 people entering drug abuse treatment programs reported that marijuana was their primary drug of abuse.

Along with craving, withdrawal symptoms can make it hard for long-term marijuana smokers to stop using the drug. People trying to quit report irritability, difficulty sleeping, and anxiety. They also display increased aggression on psychological tests, peaking approximately 1 week after they last used the drug.

What treatments are available for marijuana abusers?

Treatment programs directed at marijuana abuse are rare, partly because many who use marijuana do so in combination with other drugs, such as cocaine and alcohol. However, with more people seeking help to control marijuana abuse, research has focused on ways to overcome problems with abuse of this drug.

One study of adult marijuana users found comparable benefits from a 14-session cognitive-behavioral group treatment and a 2-session individual treatment that included motivational interviewing and advice on ways to reduce marijuana use. Participants were mostly men in their early thirties who had smoked marijuana daily for over 10 years. By increasing patients' awareness of what triggers their marijuana use, both treatments

sought to help them devise avoidance strategies. Use, dependence symptoms, and psychosocial problems decreased for at least 1 year after both treatments. About 30 percent of users were abstinent during the last 3-month followup period. Another study suggests that giving patients vouchers for abstaining from marijuana can improve outcomes. Vouchers can be redeemed for such goods as movie passes, sports equipment, or vocational training.

No medications are now available to treat marijuana abuse. However, recent discoveries about the workings of THC receptors have raised the possibility that scientists may eventually develop a medication that will block THC's intoxicating effects. Such a medication might be used to prevent relapse to marijuana abuse by reducing or eliminating its appeal.

Where can I get further scientific information about marijuana?

Fact sheets on marijuana, other illicit drugs, and related topics are available free, in English and Spanish, by calling NIDA Infofax at 1-888-NIH-NIDA (1-888-644-6432) or, for those with hearing impairment, 1-888-TTY-NIDA (1-888-889-6432).

Information on marijuana and related topics also can be obtained through NIDA's home page, www.drugabuse.gov, and from the National Clearinghouse for Alcohol and Drug Information (NCADI) at 1-800-729-6686. NCADI's Web site is www.health.org.

Glossary

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

Cannabinoids: Chemicals that help control mental and physical processes when produced naturally by the body and that produce intoxication and other effects when absorbed from marijuana.

Carcinogen: Any substance that causes cancer.

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

Hippocampus: An area of the brain crucial for learning and memory.

Hydrocarbon: Any chemical compound containing only hydrogen and carbon.

Psychoactive: Having a specific effect on the mind.

THC: Delta-9-tetrahydrocannabinol; the main active ingredient in marijuana, which acts on the brain to produce its effects.

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

Access information on the Internet

- What's new on the NIDA Web site
- Information on drugs of abuse
- Publications and communications (including NIDA NOTES)
- Calendar of events
- Links to NIDA organizational units
- 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.marijuana-info.org
www.steroidabuse.org
www.clubdrugs.org

NCADI
Web Site: www.health.org
Phone No.: 1-800-729-6686

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