Marijuana Update

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How does marijuana use affect school, work, and social life?
See page 7.

National Institute on Drug Abuse

Research Report Series

Marijuana

from the director:

Changes in marijuana policies across states legalizing marijuana for medical and/or recreational use suggest that marijuana is gaining greater acceptance in our society. Thus, it is particularly important for people to understand what is known about both the adverse health effects and the potential therapeutic benefits linked to marijuana.

Because marijuana impairs short-term memory and judgment and distorts perception, it can impair performance in school or at work and make it dangerous to drive an automobile. It also affects brain systems that are still maturing through young adulthood, so regular use by teens may have a negative and long-lasting effect on their cognitive development, putting them at a competitive disadvantage and possibly interfering with their well-being in other ways. Also, contrary to popular belief, marijuana can be addictive, and its use during adolescence may make other forms of drug abuse or addiction more likely.

Whether smoking or otherwise consuming marijuana has therapeutic benefits that outweigh its health risks is still an open question that science has not resolved. Although many states now permit dispensing marijuana for medicinal purposes and there is mounting anecdotal evidence for the efficacy of marijuana-derived compounds, there are currently no FDA-approved indications for "medical marijuana." However, safe medicines based on cannabinoid chemicals derived from the marijuana plant have been available for decades and more are being developed.

This Research Report is intended as a useful summary of what the most up-to-date science has to say about marijuana and its effects on those who use it—both young and old.

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What is marijuana?

Marijuana—also called *weed, herb, pot, grass, bud, ganja, Mary Jane,* and a vast number of other slang terms—is a greenish-gray mixture of the dried, shredded leaves and flowers of *Cannabis sativa*—the hemp plant. Some users smoke marijuana in hand-rolled cigarettes called *joints*; many use pipes, water pipes (sometimes called *bongs*), or marijuana cigars called *blunts* (often made by slicing open cigars and replacing some or all of the tobacco with marijuana).[1] Marijuana can also be used to brew tea and, particularly when it is sold or consumed for medicinal purposes, is frequently mixed into foods ("edibles") such as brownies, cookies, or candies. In addition, concentrated resins containing high doses of marijuana's active ingredients, including honey-like "hash oil," waxy "budder," and hard amber-like "shatter," are increasingly popular among both recreational and medical users.

The main *psychoactive* (mind-altering) chemical in marijuana, responsible for most of the intoxicating effects sought by recreational users, is delta-9-tetrahydro-cannabinol (THC). The chemical is found in resin produced by the leaves and buds primarily of the female cannabis plant. The plant also contains more than 500 other chemicals, including over 100 compounds that are chemically related to THC, called *cannabinoids*.[2]

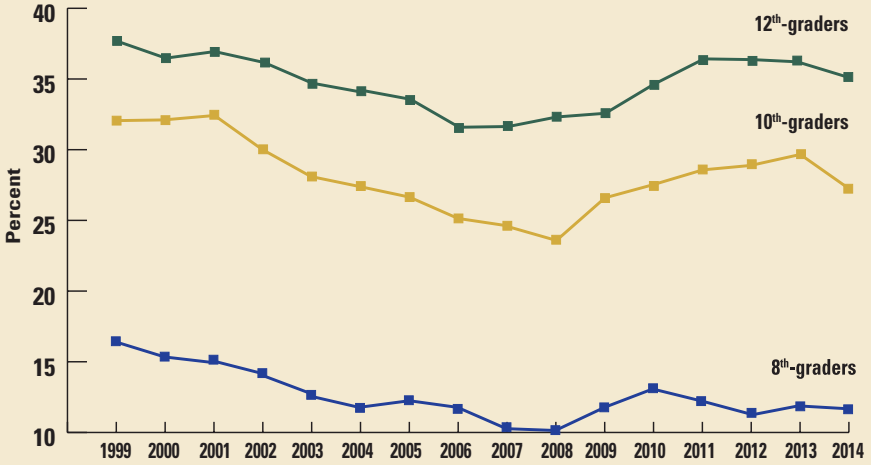
continued inside

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

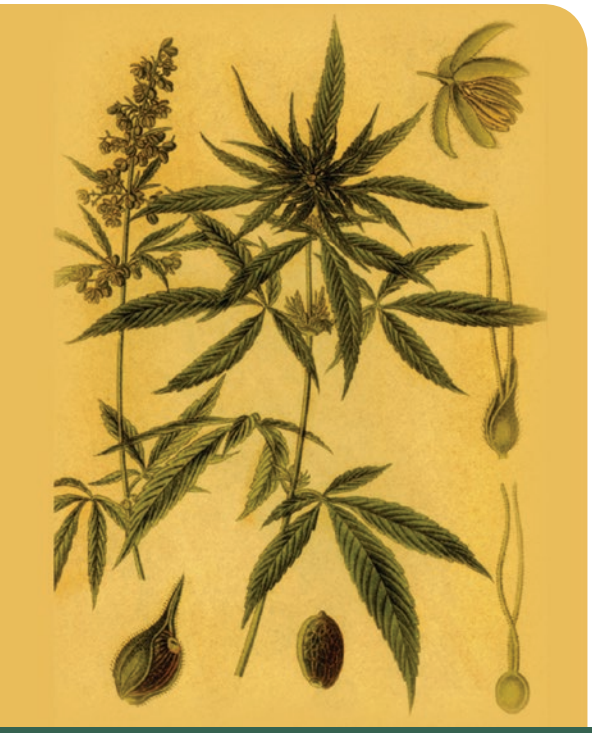
Marijuana is the most commonly used illicit drug (19.8 million past-month users) according to the 2013 National Survey on Drug Use and Health (NSDUH).[3] That year, marijuana was used by 81.0 percent of current illicit drug users (defined as having used a drug at some time in the 30 days before the survey) and was the only drug used by 64.7 percent of them.

Marijuana use is widespread among adolescents and young adults. According to the Monitoring the Future survey—an annual survey of drug use and attitudes among the Nation's middle and high school students—most measures of marijuana use by 8th-, 10th-, and 12th-graders have held steady in the past few years following several years of increase in the previous decade. Teens' perceptions of the risks of marijuana use have steadily declined over the past decade, possibly related to increasing public debate about legalizing or loosening restrictions on marijuana for medicinal and recreational use. In 2014, 11.7 percent of 8th-graders reported marijuana use in the past year and 6.5 percent were current users. Among 10th-graders, 27.3 percent had used marijuana in the past year and 16.6 percent were current users. Rates of use among 12th-graders were higher still: 35.1 percent had used marijuana during the year prior to the survey and 21.2 percent were current users; 5.8 percent said they used marijuana daily or near-daily.[4]

Long-Term Trends in Annual* Marijuana Use Among 8th-, 10th-, and 12th-Graders



*use in the past 12 months
Source: University of Michigan, 2014 Monitoring the Future Survey.



Medical emergencies possibly related to marijuana use have also increased. The Drug Abuse Warning Network (DAWN), a system for monitoring the health impact of drugs, estimated that in 2011, there were nearly 456,000 drug-related emergency department visits in the United States in which marijuana use was mentioned in the medical record (a 21 percent increase over 2009). About two-thirds of patients were male and 13 percent were between the ages of 12 and 17.[5] It is unknown whether this increase is due to increased use, increased *potency* of marijuana (amount of THC it contains), or other factors. It should be noted, however, that mentions of marijuana in medical records do not necessarily indicate that these emergencies were directly related to marijuana intoxication.

What are marijuana effects?

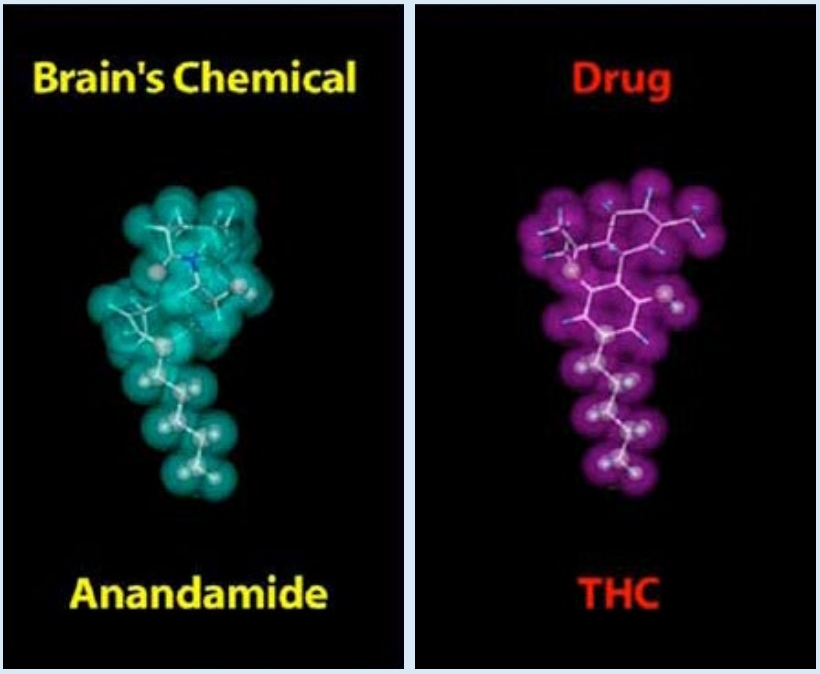
- When marijuana is smoked, THC and other chemicals in the plant pass from the lungs into the bloodstream, which rapidly carries them throughout the body and to the brain. The user begins to experience their effects almost immediately **(see "How does marijuana produce its effects?")**. Many users experience a pleasant euphoria and sense of relaxation. Other common effects, which may vary dramatically among different users, include heightened sensory perception (e.g., brighter colors), laughter, altered perception of time, and increased appetite.
- If marijuana is consumed in foods or beverages, these effects are somewhat delayed—usually appearing after 30 minutes to 1 hour—because the drug must first pass through the digestive system. Eating or drinking marijuana delivers significantly less THC into the bloodstream than smoking an equivalent amount of the plant. Because of the delayed effects, users may inadvertently consume more THC than they intend to.
- Pleasant experiences with marijuana are by no means universal. Instead of relaxation and euphoria, some users experience anxiety, fear, distrust, or panic. These effects are more common when too much is taken, the marijuana has an unexpectedly high potency, or a user is inexperienced. People who have taken large doses of marijuana may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity. These unpleasant but temporary reactions are distinct from longer-lasting psychotic disorders, such as schizophrenia, that may be associated with the use of marijuana in vulnerable individuals. **(See "Is there a link between marijuana use and mental illness?")**

Although detectable amounts of THC may remain in the body for days or even weeks after use, the noticeable effects of smoked marijuana generally last from 1 to 3 hours and those of marijuana consumed in food or drink may last for many hours.

How does marijuana produce its effects?

THC and other cannabinoid chemicals in marijuana are similar to cannabinoid chemicals that naturally occur in the body. These *endogenous cannabinoids* (such as anandamide; **see figure below**) function as *neurotransmitters* because they send chemical messages between nerve cells (*neurons*) throughout the nervous system. They affect brain areas that influence pleasure, memory, thinking, concentration, movement, coordination, and sensory and time perception. Because of this similarity, THC is able to attach to molecules called *cannabinoid receptors* on neurons in these brain areas and activate them, disrupting various mental and physical functions and causing the effects described earlier. The neural communication network that uses these cannabinoid neurotransmitters, known as the *endocannabinoid system*, plays a critical role in the nervous system's normal functioning, so interfering with it can have profound effects.

For example, THC is able to alter the functioning of the hippocampus **(see "Marijuana, Memory, and the Hippocampus")** and orbitofrontal cortex, brain areas that enable a person to form new memories and shift their attentional focus. As a result,



THC's chemical structure is similar to the brain chemical anandamide. Similarity in structure allows drugs to be recognized by the body and to alter normal brain communication

Marijuana users who have taken large doses of the drug may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity.

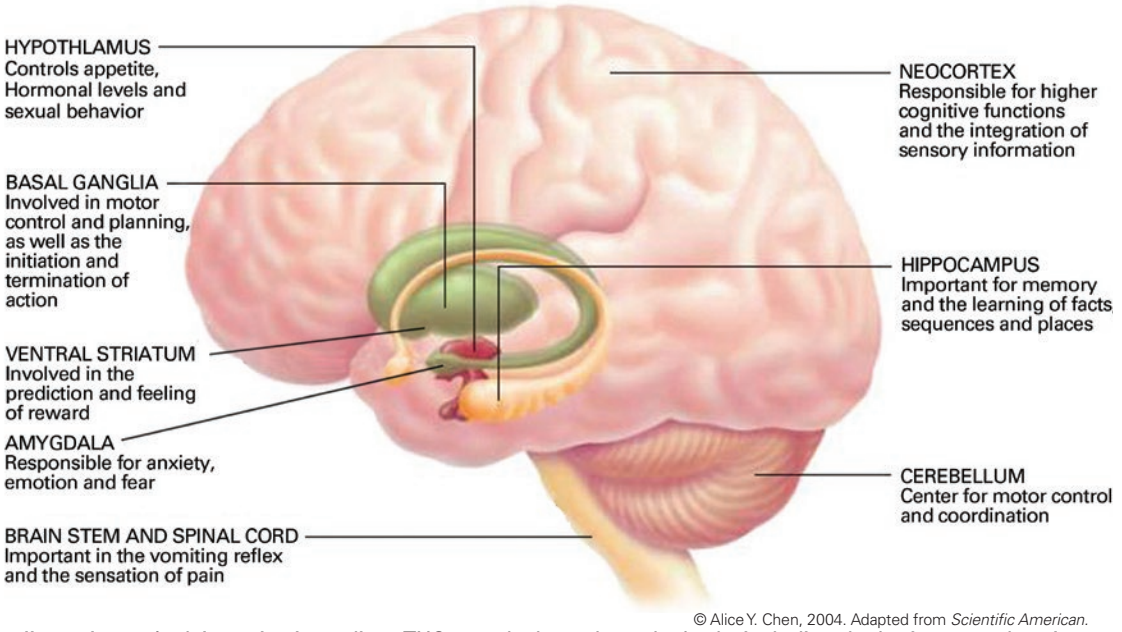
using marijuana causes impaired thinking and interferes with a user's ability to learn and to perform complicated tasks. THC also disrupts functioning of the cerebellum and basal ganglia, brain areas that regulate balance, posture, coordination, and reaction time. This is the reason people who have used marijuana may not be able to drive a car safely **(see "Does marijuana use affect driving?")** and may be impaired at playing sports or other physical activities.

THC, acting through cannabinoid receptors, also activates the brain's reward system, which includes regions that govern the response to healthy pleasurable behaviors like sex and eating. Like most other drugs of abuse, THC stimulates neurons in the reward system to release the signaling chemical *dopamine* at levels higher than typically observed in response to natural stimuli. This flood of dopamine contributes to the pleasurable "high" that recreational marijuana users seek.

Does marijuana use affect driving?

Marijuana significantly impairs judgment, motor coordination, and reaction time, and studies have found a direct relationship between blood THC concentration and impaired driving ability.[6,7] Marijuana is the illicit drug most frequently found in the blood of drivers who have been involved in accidents, including fatal ones[8] (although it is important to note that marijuana can remain detectable in body fluids for days or even weeks after acute intoxication). A meta-analysis of multiple studies found that the risk of being involved in an accident roughly doubles after marijuana use.[9]

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.

Accident-involved drivers with THC in their blood, particularly higher levels, are three to seven times more likely to be responsible for the accident than drivers who had not used drugs or alcohol. The risk associated with marijuana in combination with alcohol appears to be greater than that for either drug by itself.[7]

Is marijuana addictive?

Yes. Over time, overstimulation of the endocannabinoid system by marijuana use can cause changes in the brain that lead to *addiction*, a condition in which a person cannot stop using a drug even though it interferes with many aspects of his or her life. It is estimated that 9 percent of people who use marijuana will become dependent on it.[10,11] The number goes up to about 17 percent in those who start using young (in their teens) and to 25 to 50 percent among daily users.[12,13] According to the 2013 NSDUH, marijuana accounted for 4.2 million of the estimated 6.9 million Americans dependent on or abusing illicit drugs.[3]

Marijuana addiction is linked to a mild withdrawal syndrome. Frequent marijuana users often report irritability, mood and sleep difficulties, decreased appetite, cravings, restlessness, and/or various forms of physical discomfort that peak within the first week after quitting and last up to 2 weeks.[14,15]

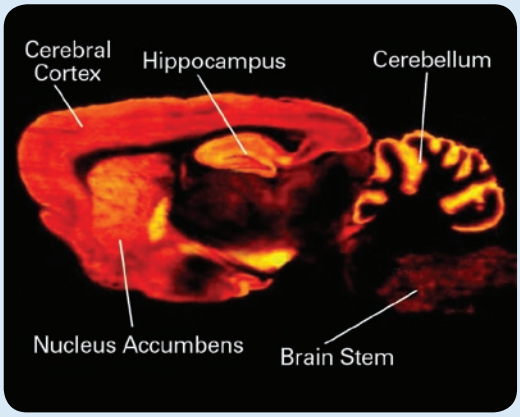
Rising Potency

Marijuana potency, as detected in confiscated samples, has steadily increased over the past few decades.[2] In the early 1990s, the average THC content in confiscated cannabis samples was roughly 3.7 percent for marijuana and 7.5 percent for sinsemilla (a higher potency marijuana from specially tended female plants). In 2013, it was 9.6 percent for marijuana and 16 percent for sinsemilla.[16] Also, newly popular methods of smoking or eating THC-rich hash oil extracted from the marijuana plant (a practice called "dabbing") may deliver very high levels of THC to the user. The average marijuana extract contains over 50 percent THC, with some samples exceeding 80 percent. These trends raise concerns that the consequences of marijuana use could be worse than in the past, particularly among new users or in young people, whose brains are still developing (see "What are marijuana's long-term effects on the brain?").

Researchers do not yet know the full extent of the consequences when the body and brain (especially the developing brain) are exposed to high concentrations of THC or whether the recent increases in emergency department visits by people testing positive for marijuana are related to rising potency. The extent to which marijuana users adjust for increased potency by using less or by smoking it differently is also unknown. Recent studies suggest that experienced users may adjust the amount they smoke and how much they inhale based on the believed strength of the marijuana they are using, but are not able to fully compensate for variations in potency.[17,18]

What are marijuana's long-term effects on the brain?

Substantial evidence from animal research and a growing number of studies in humans indicate that marijuana exposure during development can cause long-term or possibly permanent adverse changes in the brain. Rats exposed to THC before birth, soon after birth, or during adolescence show notable problems with specific learning and memory tasks later in life.[19–21] Cognitive impairments in adult rats exposed to THC during adolescence are associated with structural and functional changes in the hippocampus.[22–24] Studies in rats also show that adolescent exposure to THC is associated with an altered reward system, increasing the likelihood that an animal will self-administer other drugs (e.g., heroin) when given an opportunity **(see "Is marijuana a gateway drug?")**. Imaging studies in human adolescents show that regular marijuana users display impaired neural connectivity in specific brain regions involved in a broad range



Distribution of cannabinoid receptors in the rat brain. Brain image reveals high levels (shown in orange and yellow) of cannabinoid receptors in many areas, including the cortex, hippocampus, cerebellum, and nucleus accumbens (ventral striatum).

Marijuana, Memory, and the Hippocampus

Memory impairment from marijuana use occurs because THC alters how information is processed in the hippocampus, a brain area responsible for memory formation.

Most of the evidence supporting this assertion comes from animal studies. For example, rats exposed to THC in utero, soon after birth, or during adolescence, show notable problems with specific learning/memory tasks later in life. Moreover, cognitive impairment in adult rats is associated with structural and functional changes in the hippocampus from THC exposure during adolescence.

As people age, they lose neurons in the hippocampus, which decreases their ability to learn new information. Chronic THC exposure may hasten age-related loss of hippocampal neurons. In one study, rats exposed to THC every day for 8 months (approximately 30 percent of their life-span) showed a level of nerve cell loss (at 11 to 12 months of age) that equaled that of unexposed animals twice their age.

of executive functions like memory, learning, and impulse control compared to non-users.[25]

The latter findings may help explain the results of a large longitudinal study conducted in New Zealand, which found that frequent and persistent marijuana use starting in adolescence was associated with a loss of an average of 8 IQ points measured in mid-adulthood.[26] Significantly, in that study, those who used marijuana heavily as teenagers and quit using as adults did not recover the lost IQ points. Users who only began using marijuana heavily in adulthood did not lose IQ points. These results suggest that marijuana has its strongest long-term impact on young users whose brains are still busy building new connections and maturing in other ways. The endocannabinoid system is known to play an important role in the proper formation of synapses (the connections between neurons) during early brain development, and a similar role has been proposed for the refinement of neural connections during adolescence. If confirmed by future research, this may be one avenue by which marijuana use during adolescence produces its long-term effects.[27]

The ability to draw definitive conclusions about marijuana's long-term impact on the human brain from past studies is often limited by the fact that study participants use multiple substances, and there is often limited data about the participants' health or mental functioning prior to the study. Over the next decade, the National Institutes of Health is planning to fund a major longitudinal study that will track a large sample of young Americans from late childhood (before first use of drugs) to early adulthood. The study will use neuroimaging and other advanced tools to clarify precisely how and to what extent marijuana and other substances, alone and in combination, affect adolescent brain development.

Is marijuana a gateway drug?

Early exposure to cannabinoids in adolescent rodents decreases the reactivity of brain dopamine reward centers later in adulthood.[28] To the extent that these findings generalize to humans, this could help explain early marijuana initiates' increased vulnerability for drug abuse and addiction to other substances of abuse later in life that has been reported by most epidemiological studies.[29] It is also consistent with animal experiments showing THC's ability to "prime" the brain for enhanced responses to other drugs.[30] For example, rats previously administered THC show heightened behavioral response not only when further exposed to THC but also when exposed to other drugs such as morphine—a phenomenon called *cross-sensitization*.[31]

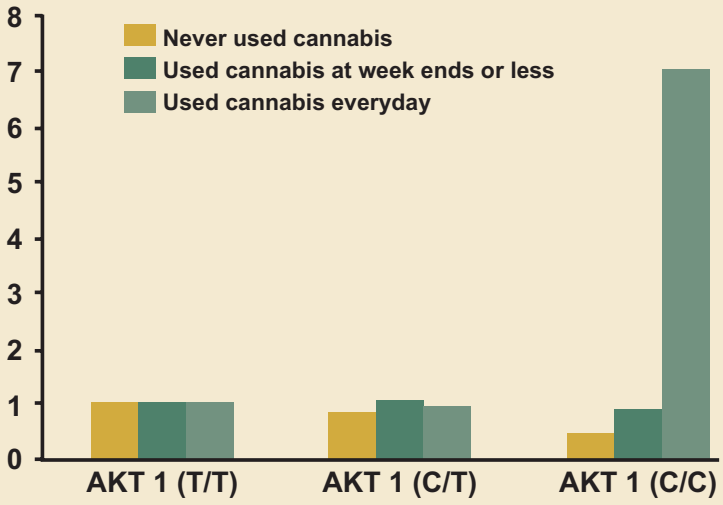
These findings are consistent with the idea of marijuana as a "gateway drug." However, most people who use marijuana do not go on to use other, "harder" substances. Also, cross-sensitization is not unique to marijuana. Alcohol and nicotine also prime the brain for a heightened response to other drugs[32] and are, like marijuana, also typically used before a person progresses to other, more harmful substances.

It is important to note that other factors besides biological mechanisms, such as a person's social environment, are also critical in a person's risk for drug use. An alternative to the gateway-drug hypothesis is that people who are more vulnerable to drug-taking are simply more likely to start with readily available substances like marijuana, tobacco, or alcohol, and their subsequent social interactions with other drug users increases their chances of trying other drugs. Further research is needed to explore this question.

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

Research has shown that marijuana's negative effects on attention, memory, and learning can last for days or weeks after the acute effects of the drug wear off, depending on the user's history with the drug.[33] Consequently, someone who smokes marijuana daily may be functioning at a reduced intellectual level most or all of the time. Considerable evidence suggests that students who smoke marijuana have poorer educational outcomes than their nonsmoking peers. For example, a review of 48 relevant studies found marijuana use to be associated with reduced educational attainment (i.e. reduced chances of graduating).[34] A recent analysis using data from three large studies in Australia and New Zealand found that adolescents who used marijuana regularly were significantly less likely than their non-using peers to finish high school or obtain a degree. They also had a much higher chance of later developing dependence, using other drugs, and attempting suicide.[35] Several studies have also linked heavy marijuana use to lower income, greater welfare dependence, unemployment, criminal behavior, and lower life satisfaction.[36,37]

To what degree marijuana use is directly causal in these associations remains an open question requiring further research. It is possible that other factors independently predispose people to both marijuana use and various negative life outcomes such as school dropout.[38] That said, marijuana users themselves report a perceived influence of their marijuana use on poor outcomes on a variety of life satisfaction and achievement measures. One study, for example, compared current and former long-term, heavy users of marijuana with a control group who reported smoking marijuana at least once in their lives but not more than 50 times.[39] All participants had similar



Whether adolescent marijuana use can contribute to developing psychosis later in adulthood appears to depend on whether a person already has a genetically based vulnerability to the disorder. The AKT1 gene governs an enzyme that affects brain signaling involving the neurotransmitter dopamine. Altered dopamine signaling is known to be involved in schizophrenia. AKT1 can take one of three forms in a specific region of the gene implicated in susceptibility to schizophrenia: T/T, C/T, and C/C. Daily users of marijuana (green bars) with the C/C variant have a seven times higher risk of developing psychosis than infrequent marijuana users or nonusers. The risk for psychosis among those with the T/T variant was unaffected by whether they used marijuana.

Source: Di Forti et al. Biol Psychiatry. 2012.

education and income backgrounds, but significant differences were found in their educational attainment: Fewer of the heavy cannabis users completed college and more had yearly household incomes less than $30,000. When asked how marijuana affected their cognitive abilities, career achievements, social lives, and physical and mental health, the majority of heavy users reported that marijuana had negative effects in all these areas of their lives.

Studies have also suggested specific links between marijuana use and adverse consequences in the workplace, such as increased risk for injury or accidents.[40] One study among postal workers found that employees who tested positive for marijuana on a pre-employment urine drug test had 55 percent more industrial accidents, 85 percent more injuries, and 75 percent greater absenteeism compared with those who tested negative for marijuana use.[41]

Is there a link between marijuana use and mental illness?

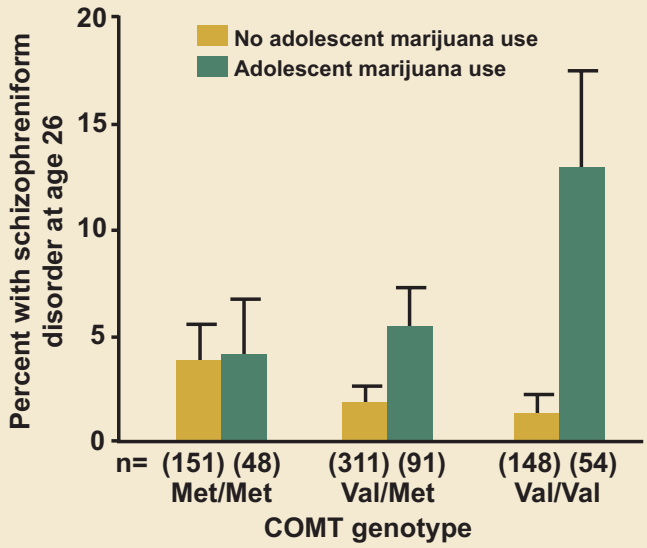
Several studies have linked marijuana use to increased risk for mental illnesses, including psychosis (schizophrenia), depression, and anxiety, but whether and to what extent it actually causes these conditions is not always easy to determine.[19] The amount of drug used, the age at first use, and genetic vulnerability have all been shown to influence this relationship. The strongest evidence to date concerns the link between marijuana use and psychotic disorders in those with a preexisting genetic or other vulnerability.[42] Recent research **(see AKT1 Gene Variations and Psychosis)** has found that marijuana users who carry a specific variant of the *AKT1* gene, which codes for an enzyme that affects dopamine signaling in the *striatum*, are at increased risk of developing psychosis. The striatum is an area of the brain that becomes activated and flooded with dopamine when certain stimuli are present. One study found that the risk for those with this variant was seven times higher for daily marijuana users compared with infrequent- or non-users.[43]

Another study found an increased risk of psychosis among adults who had used marijuana in adolescence and also carried a specific variant of the gene for catechol-O-methyltransferase (COMT), an enzyme that degrades neurotransmitters such as dopamine

and norepinephrine.[44] **(see Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs).** Marijuana use has also been shown to worsen the course of illness in patients who already have schizophrenia. As mentioned previously, marijuana can also produce a brief psychotic reaction in non-schizophrenic users, especially at high doses, although this fades as the drug wears off.

Other, less consistent associations have been reported between marijuana use and depression, anxiety, suicidal thoughts among teens, and personality disorders. Marijuana has also been associated with an *amotivational syndrome*, defined as a diminished or absent drive to engage in typically rewarding activities. Because of the role of the endocannabinoid system in regulating mood and reward, it is logical to hypothesize the existence of such a link underpinned by brain changes, but more research is needed to confirm and better understand it.

Genetic Variation in COMT Influences the Harmful Effects of Abused Drugs



The influence of adolescent marijuana use on adult psychosis is affected by genetic variables. This figure shows that variations in a gene can affect the likelihood of developing psychosis in adulthood, following exposure to cannabis in adolescence. The COMT gene governs an enzyme that breaks down dopamine, a brain chemical involved in schizophrenia. It comes in two forms: "Met" and "Val." Individuals with one or two copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence (dark bars). Those with only the Met variant were unaffected by cannabis use.[7]

Source: Caspi et al. Biol Psychiatry. 2005.

Adverse Consequences of Marijuana Use

Acute (present during intoxication)

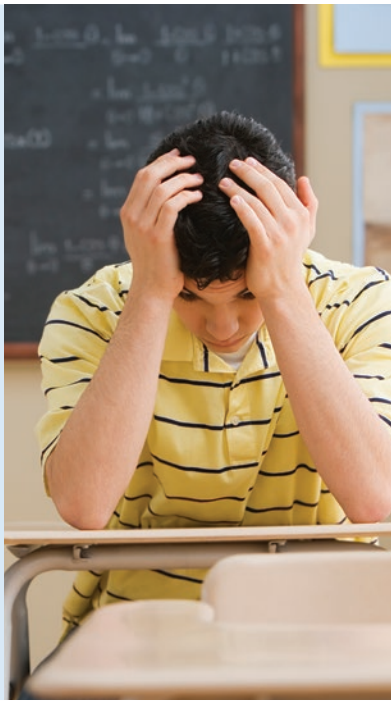
- Impaired short-term memory
- Impaired attention, judgment, and other cognitive functions
- Impaired coordination and balance
- Increased heart rate
- Anxiety, paranoia
- Psychosis (uncommon)

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

- Impaired learning and coordination
- Sleep problems

Long-term (cumulative effects of repeated use)

- Potential for addiction
- Potential loss of IQ
- Increased risk of chronic cough, bronchitis
- Increased risk of schizophrenia in vulnerable people*
- Potentially increased risk of anxiety, depression, and amotivational syndrome*



**These are often reported co-occurring symptoms/disorders with chronic marijuana use. However, research has not yet determined whether marijuana is causal or just associated with these mental problems.*

What are marijuana's effects on general physical health?

Within a few minutes after inhaling marijuana smoke, a person's heart rate speeds up, the breathing passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look bloodshot (red). The heart rate—normally 70 to 80 beats per minute—may increase by 20 to 50 beats per minute or may even double in some cases. Taking other drugs with marijuana can amplify this effect.

Limited evidence suggests that a person's risk of heart attack during the first hour after smoking marijuana is nearly five times his or her usual risk.[45] This observation could be partly explained by marijuana raising blood pressure (in some cases) and heart rate and reducing the blood's capacity to carry oxygen.[46] Marijuana may also cause *orthostatic hypotension* (head rush or dizziness on standing up), possibly raising danger from fainting and falls. Tolerance to some cardiovascular effects often develops with repeated exposure.[47] These health effects need to be examined more closely, particularly given the increasing use of "medical marijuana" by people with health issues and older adults who may have increased baseline vulnerability due to age-related cardiovascular risk factors **(see "Marijuana as Medicine")**.

Marijuana smoke, like tobacco smoke, is an irritant to the throat and lungs and can cause a heavy cough during use. It also contains toxic gases and particles that can damage the lungs. Marijuana smoking is associated with large airway inflammation, increased airway resistance, and lung hyperinflation, and regular marijuana smokers report more symptoms of chronic bronchitis than non-smokers.[48] Smoking marijuana may also reduce the respiratory system's immune response, increasing the likelihood of the user acquiring respiratory infections, including pneumonia.[49] One study found that frequent marijuana smokers used more sick days than other people, often because of respiratory illnesses.[50]

Whether smoking marijuana causes lung cancer, as cigarette smoking does, is less certain. Although marijuana smoke contains *carcinogenic* (cancer-causing) combustion products, evidence for a link between marijuana use and lung cancer has thus far been inconclusive.[51] The very different ways marijuana and tobacco are used, including factors like how frequently they are smoked during the day and how long the smoke is

held in the lungs, as well as the fact that many people use both substances make determining marijuana's precise contribution to lung cancer risk, if any, difficult to establish. This is an area that will require more research.

However, a few studies have shown a clear link between marijuana use in adolescence and increased risk for an aggressive form of testicular cancer (non-seminomatous testicular germ cell tumor) that predominantly strikes young adult males.[52,53] The early onset of testicular cancers compared to lung and most other cancers indicates that, whatever the nature of marijuana's contribution, it may accumulate over just a few years of use.

Can marijuana use during pregnancy harm the baby?

Animal research suggests that the body's endocannabinoid system plays a role in the control of brain maturation, particularly in the development of emotional responses. Thus THC exposure very early in life may negatively affect brain development. Research in rats suggests that exposure to even low concentrations of THC late in pregnancy could have profound and long-lasting consequences for both

Marijuana as Medicine

The potential medicinal properties of marijuana and its components have been the subject of research and heated debate for decades. THC itself has proven medical benefits in particular formulations. There are two FDA-approved, THC-based medications, dronabinol (Marinol®) and nabilone (Cesamet®), prescribed for the treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS.

In addition, several other marijuana-based medications have been approved or are undergoing clinical trials. Nabiximols (Sativex®), which is currently available in the United Kingdom, Canada, and several European countries for treating the spasticity and neuropathic pain that may accompany multiple sclerosis, combines THC with another chemical found in marijuana called cannabidiol (CBD). CBD does not have the rewarding properties of THC, and anecdotal reports indicate it may have promise for the treatment of seizure disorders, among other conditions. A CBD-based medication called Epidiolex is currently being tested in the United States for the treatment of two forms of severe childhood epilepsy, Dravet syndrome and Lennox-Gastaut syndrome.

Medications like these, which use purified chemicals derived from or based on those in the marijuana plant, are generally considered by researchers to be more promising therapeutically than use of the whole marijuana plant or its crude extracts. Development of drugs from botanicals such as the marijuana plant poses numerous challenges. Botanicals may contain hundreds of unknown, active chemicals, and it can be difficult to develop a product with accurate and consistent doses of these chemicals. Use of marijuana as medicine also poses other problems such as the adverse health effects of smoking and THC-induced cognitive impairment. Nevertheless, a growing number of states have legalized dispensing of marijuana or its extracts to people with a range of medical conditions.

An additional concern with "medical marijuana" is that little is known about the long-term impact of marijuana use by people with health- and/or age-related vulnerabilities to whom it is dispensed—such as older adults or people with cancer, AIDS, cardiovascular disease, multiple sclerosis, or other neurodegenerative diseases. Further research will be needed to determine whether people whose health has been compromised by disease or its treatment (e.g., chemotherapy) are at greater risk for adverse health outcomes from marijuana use.

brain and behavior of offspring.[54] Human studies have shown that some babies born to women who used marijuana during their pregnancies respond differently to visual stimuli, tremble more, and have a high-pitched cry, which could indicate problems with neurological development.[55,56] In school, children prenatally exposed to marijuana are more likely to show gaps in problem-solving skills, memory, and the ability to remain attentive.[57,58] More research is needed, however, to disentangle marijuana's specific effects from other environmental factors, including maternal nutrition, exposure to nurturing/neglect, and use of other substances by mothers.[59] Establishing marijuana's effects on prenatal development is important, because roughly half of U.S. pregnancies are unplanned, with the rate considerably higher for teens and young adults,[60] so many women may use marijuana without knowing they are pregnant.

Available Treatments for Marijuana Use Disorders

Marijuana addiction appears to be very similar to other substance use disorders, although the long-term clinical outcomes may be less severe. On average, adults seeking treatment for marijuana use disorders have used marijuana nearly every day for more than 10 years and have attempted to quit more than six times.[61] People with marijuana use disorders, especially adolescents, often also suffer from other psychiatric disorders (comorbidity).[62] They may also abuse or be addicted to other substances, such as cocaine or alcohol. Available studies indicate that effectively treating the mental health disorder with standard treatments involving medications and behavioral therapies may help reduce marijuana use, particularly among heavy users and those with more chronic mental disorders. The following behavioral treatments have shown promise:

- **Cognitive-behavioral therapy:** A form of psychotherapy that teaches people strategies to identify and correct problematic behaviors in order to enhance self-control, stop drug use, and address a range of other problems that often co-occur with them.
- **Contingency management:** A therapeutic management approach based on frequent monitoring of the target behavior and the provision (or removal) of tangible, positive rewards when the target behavior occurs (or does not).
- **Motivational enhancement therapy:** A systematic form of intervention designed to produce rapid, internally motivated change; the therapy does not attempt to treat the person, but rather mobilize their own internal resources for change and engagement in treatment.

Currently, no medications are indicated for the treatment of marijuana use disorder, but research is active in this area. Because sleep problems feature prominently in marijuana withdrawal, some studies are examining the effectiveness of medications that aid in sleep. Medications that have shown promise in early studies or small clinical trials include the sleep aid zolpidem (Ambien®), an anti-anxiety/anti-stress medication called buspirone (BuSpar®), and an anti-epileptic drug called gabapentin (Horizant®, Neurotin®) that may improve sleep and, possibly, executive function. Other agents being studied include the nutritional supplement N-acetyl-cysteine and chemicals called FAAH inhibitors, which may reduce withdrawal by inhibiting the breakdown of the body's own cannabinoids. Future directions include the study of substances called *allosteric modulators* that interact with cannabinoid receptors to inhibit THC's rewarding effects.

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Where can I get further information about marijuana?

To learn more about marijuana 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
NIDA DRUGPUBS
RESEARCH DISSEMINATION CENTER

NIDA'S website includes:

- Information on drugs of abuse and related health consequences
- NIDA publications, news, and events
- Resources for researchers, health care professionals, educators, and patients and families.
- Information on NIDA research studies and clinical trials.
- 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/marijuana
www.hiv.drugabuse.gov
www.researchstudies.drugabuse.gov
www.irp.drugabuse.gov

For Physician Information

NIDAMED
www.drugabuse.gov/nidamed

Other websites

Information on marijuana is also available through the

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

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