Marijuana and Cannabinoids

- The main psychoactive chemical in marijuana that produces the intoxicating effects desired by recreational users is delta-9-tetrahydro-cannabinol (THC).¹
- Marijuana contains more than 500 other chemicals, including more than 100 compounds chemically related to THC, called cannabinoids.¹
- The human body produces cannabinoids that are similar to those found in the marijuana plant. The areas of the brain that influence pleasure, memory, thinking, concentration, movement, coordination and sensory and time perception are affected by these endogenous cannabinoids. THC is able to take advantage of this similarity and attach to cannabinoid receptors on neurons in these brain areas, activating them and thus disrupting various mental and physical functions.¹
- Acting through the cannabinoid receptors, THC also activates the brain’s reward system, which includes parts of the brain that respond to healthy pleasurable behaviors like sex and eating. THC is similar to other drugs of abuse in that it 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 effects that recreational marijuana users seek.¹

Patterns of Use

- Marijuana is the most commonly used illicit drug in the country. In 2014, 22.2 million Americans aged 12 or older were current marijuana users.²
- Marijuana use is widespread among adolescents and young adults. While the previous decade had several years of increased marijuana use, most measures of marijuana use have held steady in the past few years. However, as there has been an increase in public debate about legalizing or loosening restrictions on medical and recreational marijuana use, teens' perceptions of the risks associated with such use have steadily declined over the past decade.³

Medical emergencies possibly related to marijuana use have also increased. There were nearly 456,000 drug-related emergency department visits in 2011 in the US in which marijuana use was mentioned in the medical record, a 21% increase over 2009. It is unknown if this increase is a result of increased use, increased THC content or other factors. It must also be noted that mentions of marijuana in medical records do not necessarily indicate that these emergencies were directly related to marijuana use.

Acute Effects

- When smoked, THC and other chemicals in marijuana pass from the lungs into the bloodstream, and are then quickly carried throughout the body and to the brain. The effects are felt almost immediately. Many users experience a pleasant euphoria and sense of relaxation. Other common effects that vary among users are heightened sensory perception, laughter, altered perception of time and increased appetite.

• Consuming marijuana in foods or beverages delays these effects for 30 minutes to 1 hour, as 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 drug. Users may inadvertently consume more THC than they intend to as a result of the unknown delay in effects.

• While THC may remain in the body for days or weeks after use, the noticeable effects of smoked marijuana generally last from 1 to 3 hours and those of consumed marijuana last for several hours.

• Not all users experience pleasant effects. Instead of relaxation and euphoria, some users experience anxiety, fear, distrust and panic. These effects can happen 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 can include 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 (continued in “Neurological Effects”).

Long-Term Effects

• Developmental Effects
  o Marijuana use during adolescence can cause long-term or possibly permanent adverse changes in brain development.
  o THC alters how information is processed in the hippocampus, a brain area responsible for memory formation, thus causing memory impairment. Evidence from animal studies demonstrates that rats exposed to THC in utero, soon after birth or during adolescence, show notable problems with specific learning and memory tasks later in life. Additionally, cognitive impairment in adult rats is associated with structural and functional changes in the hippocampus from exposure to THC during adolescence.
  o Imaging studies of human adolescents reveal that regular marijuana use results in impaired neural connectivity in specific brain regions that govern executive functions like memory, learning and impulse control compared to non-users.
  o Brain development may be negatively affected by THC exposure very early in life. Research in rats suggests that exposure to even low concentrations of THC late in pregnancy could have profound and long-term consequences for both brain development and behavior of offspring.
  o Evidence from human studies shows that pregnant women who use marijuana have babies that respond differently to visual stimuli, tremble more and have a high-pitched cry, suggesting problems with neurological development.

---

Children who were prenatally exposed to marijuana are more likely to show gaps in problem-solving skills, memory and the ability to remain attentive in school.\(^8\)

- **Neurological Effects**
  - It is estimated that 9% of people who use marijuana will become dependent on it.\(^9\) The number goes up to about 17% in those who start using in their youth and to 25%-50% among daily users.\(^10\) Of the 7.1 million Americans with an illicit drug use disorder in 2014, 4.2 million had disorders related to their marijuana use.\(^2\)
  - Addiction involving marijuana is linked to a mild withdrawal syndrome. Frequent marijuana users can experience 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.\(^11\)
  - Marijuana use has been linked to increased risk for mental illnesses, including psychosis/schizophrenia, depression and anxiety. Yet it is unknown whether and to what extent it actually causes these conditions.\(^12\) The amount of marijuana used, the age at first use and genetic vulnerability have all been shown to influence this relationship.
  - A person who already has a genetically-based vulnerability to a mental disorder can determine whether adolescent marijuana use contributes to developing a 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 the susceptibility to schizophrenia: T/T, C/T and C/C. Daily marijuana users 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 marijuana use.\(^13\) Marijuana use has also been shown to worsen the course of illness in patients who already have schizophrenia.
  - Adults who carried a specific variant of the gene catechol-O-methyltransferase, an enzyme that degrades neurotransmitters such as dopamine and norepinephrine, had an increased risk of psychosis if they used marijuana in adolescence. The gene 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 marijuana.

---


during adolescence. Those with only the Met variant were unaffected by marijuana use.14

○ Marijuana has also been associated with amotivational syndrome, defined as a diminished or absent drive to engage in typically rewarding activities. However, more research is needed to confirm this correlation in order to understand it.1

- Physical Effects
  ○ Like tobacco smoke, marijuana smoke is an irritant to the throat and lungs, causing a heavy cough during use and containing toxic gases and particles that can damage the lungs. Smoking marijuana is associated with large airway inflammation, increased airway resistance and lung hyperinflation, in addition to symptoms of chronic bronchitis for regular marijuana smokers.15 Smoking marijuana can increase the chance of the user acquiring respiratory infections, including pneumonia, due to a reduced immune response from the respiratory system.16
  ○ Although marijuana smoke contains carcinogenic combustion products, there is no current evidence of a link between marijuana use and lung cancer. So, whether smoking marijuana causes lung cancer, as cigarette smoking does, is unknown.17