

Medicinal and Recreational Marijuana: What are the Risks?

By Shawn Van Gerpen, MD, Tamara Vik, MD;
and Timothy J. Soundy, MD

Abstract

With the recent legalization of recreational marijuana in Colorado, Washington, Alaska, the District of Columbia and legislation pending for both medical and recreational marijuana in several other states, it is important for the facts regarding its potential for serious mental health consequences to be known. Little has been said about the psychiatric risks of this substance, particularly in youth. Several studies have shown increased rates of depression, anxiety and schizophrenia among those who use marijuana on a regular basis. In addition, permanent loss of IQ and structural changes in the brain have been demonstrated with habitual use. Legalization of marijuana for recreational use can influence an adolescent's perception of this substance as "safe." In states that have legalized marijuana for medical purposes, there is the very real problem of "diversion." As many as 34 percent of 12th-graders who use marijuana in states with legalized marijuana had obtained it from a person who had received it through a prescription.

Introduction

With the recent legalization of recreational marijuana in Colorado and Washington and the legal use of medical marijuana in 23 states, South Dakota will likely face another concerted effort to legalize marijuana for both medical and recreational purposes. Proponents of marijuana legalization state that marijuana is no different than alcohol and would increase tax revenues and lower the expense of prosecuting users. However, there are significant deleterious effects to the use of this substance that weigh heavily in favor of keeping the laws in South Dakota as they are.

Background

While known by a variety of different names (cannabis, pot, Mary Jane, weed, etc.) marijuana is a drug that is familiar to most people. Research into the use of this drug is bringing to light a number of very serious concerns, especially within the adolescent population, that many familiar with the drug have failed to recognize in the past. The legalization of marijuana, compounded with the continued illegal use of cannabis, continues to have a major impact on the lives of the youth that we treat in our

medical practices and interact with in our communities. Many users of the drug consider it to be a "safe" alternative to "hard core" drugs or alcohol; however, this belief is in stark contrast to the reputable research findings being published on this topic.

Review

According to data published by the Centers for Disease Control and Prevention's (CDC) Youth Risk Behavior Surveillance (YRBS) survey in 2013 which surveyed ninth through 12th grade students in public and private schools throughout the U.S., 40.7 percent of ninth through 12th grade students reported that they had used marijuana one or more times during their lifetime – 8.6 percent of which indicated that they had tried marijuana for the first time prior to age 13. These percentages were noted to be slightly lower in South Dakota's adolescent population with 29.6 percent of ninth through 12th grade students reporting having used cannabis one or more times in their life, and 7.2 percent of those indicating that they had first used marijuana prior to age 13.¹

One of the leading arguments of proponents for legalized marijuana is that the regulated, legal use of cannabis

obtained through legal channels will result in a decrease in the overall amount of marijuana being used due to the disruption of the underground market by which people currently obtain the drug. One study, published between 2002 and 2008, which looked at adolescent marijuana use, showed that the use was lower and the perception of its riskiness was higher in states where medical marijuana was not legal. On the other hand, adolescent marijuana use was noted to be “higher and perception of its riskiness lower” in states where medical marijuana was legal.² Gil Kerlikowske, director of the White House Office of National Drug Control Policy stated, “Today...there is evidence suggesting that regulation schemes that have been promoted by the marijuana legalization lobby are not succeeding in preventing the diversion of marijuana into the hands of young people, as was promised to the voters.” Of interest, it should be noted that “34 percent of the 12th-graders who used marijuana and lived in states with medical marijuana laws reported that they obtained the drug through someone else’s prescription – and 6 percent said they had their own prescription”.³

Not only are there a growing number of adolescents reporting cannabis use, but the perceived dangers of this drug are shifting as well. According to a Feb. 6, 2013 article in *JAMA*, adolescent attitudes toward marijuana use seem to be changing. When looking at adolescent attitudes towards marijuana use, this article indicated that only 41.7 percent of eighth-graders felt that occasional marijuana use was dangerous.⁴ One of the greatest misconceptions surrounding marijuana safety is a false belief that the marijuana of the boomer generation is the same marijuana that is being used by our youth today. According to a report by the National Institute on Drug Abuse, “The amount of tetrahydrocannabinol (THC) in marijuana samples confiscated by police has been increasing steadily over the past few decades. In 2012, THC concentrations in marijuana averaged close to 15 percent, compared to around 4 percent in the 1980s.”⁵

Marijuana, or cannabis, is a derivative of the plant *cannabis sativa*.⁶ Cannabis exists in many forms and levels of potency with herbal cannabis being the most commonly used form.⁷ The active ingredient in cannabis is Δ^9 -tetrahydrocannabinol.⁷ Research has demonstrated that the effects of cannabis on the human body are related to the agonistic effects at the cannabinoid receptors (CB1 and CB2).⁸ The CB1 receptor is a pre-synaptic receptor that is found in large quantities in the striatum, hippocampus and cerebellum and also in lesser amounts in peripheral tissues, liver adipocytes, the pancreas, the gastrointestinal

tract, skeletal muscle and in immune cells.⁸ In contrast, CB2 receptors are located mainly in the immune cells in tissues such as the spleen and liver.⁸

Cannabinoid receptors found in neurons are activated by the neurotransmitter anandamide.⁷ It is the endocannabinoid system that has been identified as one of the key components “for cortical development, neuronal migration, connectivity and synaptogenesis. During adolescence, many brain regions undergo dramatic levels of growth and synaptic remodeling,” particularly in the prefrontal cortex.⁹ THC, the active ingredient in cannabis, acts like anandamide and leads to activation of the neuron. It is activation of the CB1 receptor that leads to the psychoactive effects of cannabis.⁷ One theory that explains how this occurs is that by stimulating the cannabinoid receptors, the glutamate and gamma-aminobutyric acid functioning is altered. This in turn leads to structural changes within the brain of adolescent patients using marijuana.¹⁰ It is these changes in neuronal structure that may account for many of the very serious neurological effects that can accompany adolescent marijuana use. It is also the large number of CB receptors in the striatum, amygdale, hippocampus, cerebellum, and prefrontal cortex that give rise to the brain’s pleasure and reward centers, contributing to the addictive potential of the drug.⁷ It is worth noting that there exists an abundance of cannabinoid receptors in the prefrontal cortex, a region of the brain that has been identified in the development of schizophrenia.⁹

Research looking at the effects of marijuana use on the developing brain support the theory noted above. In a recent study at Northwestern University, it was reported that teens who smoked marijuana daily for a three year period had abnormal changes in the structure of their brain compared to teens in the control group. Brain abnormalities and memory problems were observed in these individuals in their early twenties, two years after they had stopped using marijuana. The cannabis users were noted to have striatal, globus pallidus, and thalamus changes showing these brain regions appearing to shrink and collapse inward. These individuals also had poorer working memory. The earlier the age of cannabis use, the more dramatic the brain changes and memory deficits were noted to be.¹¹

Although many proponents of cannabis legalization have refuted the claim that cannabis is a “gateway drug” to using even more dangerous and addictive substances of abuse, studies that have looked at substance use trends

among cannabis users seem to support the “gateway drug” theory. Not only does it appear that cannabis use itself is a potential precursor to future drug use, but the age of first use of cannabis and the frequency of cannabis use seem to also be predictors of future substance abuse issues. Studies have shown that over two-thirds of those under the age of 18 who have been admitted to a drug treatment program identify cannabis as their substance of choice. It is estimated that the “risk for illicit drug initiation appeared 21 times higher among cannabis experimenters and 124 times higher among daily cannabis users than among nonusers.”⁷

Data from the Treatment Episode Data Set (TEDS), which is a national data base of annual admissions to substance abuse treatment facilities in the U.S., shows that among adults who first used marijuana at the age of 14 or younger, 13.2 percent went on to develop drug dependence or abuse. This rate was noted to be six times higher than that of adults who first used marijuana starting after the age of 18. A 2011 review of demographic data looking at age showed that 74 percent of those surveyed in drug treatment facilities across the U.S. reported that they had first started to use substances of abuse at the age of 17 or younger, with 34.1 percent reporting they had first used substances of abuse between that ages of 15-17 and 29.7 percent reporting their first use between the ages of 12-14. Another 10.2 percent reported that they had first begun using substances of abuse before they were 11 years of age. Of those surveyed, only 26 percent reported that they began using substances of abuse at the age of 18 or older.¹²

Another claim that is often made by those in favor of marijuana legalization is that cannabis is not an addictive drug. Popular belief is that cannabis use is safe and does not carry any long term addictive potential. Credible research contradicts this belief. According to *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*, the current criteria for a substance use disorder is a “cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance related problems.” One important characteristic that defines a substance use disorder is “an underlying change in brain circuits that may persist beyond detoxification, particularly in individuals with severe disorder.” These brain changes may be demonstrated by “the repeated relapses and intense drug craving when the individuals are exposed to drug-related stimuli.” As indicated earlier in this article, the activation by THC of

the CB receptors in the striatum, amygdale, hippocampus, cerebellum and prefrontal cortex areas, which are known to give rise to the brain’s pleasure and reward center, contribute to the addictive potential of the drug.¹³

DSM-5 has defined cannabis-related disorders by the following diagnostic criteria:

A. A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
4. Craving, or a strong desire or urge to use cannabis.
5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school or home.
6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
8. Recurrent cannabis use in situations in which it is physically hazardous.
9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
 - b. Markedly diminished effect with continued use of the same amount of cannabis.
11. Withdrawal, as manifested by either of the following:
 - a. The characteristic withdrawal syndrome from cannabis.

- b. Cannabis is taken to relieve or avoid withdrawal.¹³

While many of the acute effects of cannabis tend to be reversible (increased heart rate, blood shot eyes, euphoria and relaxation) proponents and opponents of marijuana legalization tend to disagree on cannabis's ability to cause withdrawal symptoms once the drug has been discontinued. Research has identified a number of symptoms related to cannabis withdrawal such as irritability, anger, aggression, anxiety, depressed mood, restlessness, sleep difficulty and decreased appetite or weight loss. These withdrawal symptoms typically begin within 24-48 hours after discontinuation of the drug and typically last between one and three weeks. These symptoms may cause the user of the drug significant distress and contribute to relapse among those trying to abstain.⁷

For those who do choose to use cannabis, the use of this drug does not come without the potential for serious health risks. Research has shown that there is nearly a five time increased risk of myocardial infarction in the hour after one uses marijuana. Cannabis smokers are also exposed to many of the same harmful chemicals that cigarette smokers are exposed to. This exposure to chemicals puts one at a greater risk for developing cancer, bronchitis and recurrent lung infections.⁷

Marijuana has also been shown to affect one's level of cognition and motivation. Consider for a moment the image that comes to mind when you think of the term "pot head," a slang term often used to describe someone that frequently smokes marijuana. This phrase, often used as a comedic portrayal of a marijuana user, depicts these frequent users of the drug as being extremely laid back, unmotivated, lazy, excessively hungry and as having poor memory.¹⁴ Research shows that there is a connection between marijuana use and one's motivation. Many experts agree that excessive use of marijuana, as well as a number of other "psychoactive" drugs, can lead to amotivational syndrome, a term used to describe the "variety of changes in personality, emotions and cognitive functions such as lack of activity, inward-turning, avolition, apathy, incoherence, blunted affect, inability to concentrate and memory disturbance" that is noted in chronic users of these drugs.¹⁵

Not only does marijuana affect one's motivation, but also one's cognitive ability. Marijuana use has been shown to affect adolescent academic performance. Results from the U.S. National Survey on Drug Use and Health showed

that "youth with poor academic results were more than four times likely to have used cannabis in the past year than youth with average or higher grades." Cannabis use has also been shown to lead to decreased attention span, slower reaction times and motor/coordination deficits. Studies have also demonstrated that the use of cannabis may result in a decrease in adolescent IQ. It has also been shown that adolescents who are heavy users of marijuana have "poorer complex attention functioning, as well as poor sequencing ability, slower psychomotor speed, and difficulties in verbal story memory."⁷

The motivation and cognitive affects of cannabis are also seen in adults who use marijuana. Studies indicate that a strong correlation exists between chronic cannabis use and unemployment, increased dependency on social welfare programs, and a decrease in life satisfaction rates.⁷ The National Institute on Drug Abuse has also released studies showing that employees who used cannabis were more likely to have increased absences, accidents, worker's compensation claims and job turnover when compared to non-cannabis users.⁷

In recent years there has been more research into the role that marijuana plays in the development of mood disorders, anxiety disorders and psychosis. In one study of over 50,000 Swedish patients published by Zammit et al., a link was identified between marijuana use and the development of schizophrenia, a risk that was notably greater with increased marijuana use.¹⁶ In fact, in one published article, it was noted that of the research subjects who used cannabis over 50 times, there was a sevenfold increase in the risk for developing schizophrenia.¹⁶ In another study, performed by Arseneault et al., it was demonstrated that in those subjects who used marijuana prior to the age of 15, there was a four times increased risk of developing schizophrenia by age 26.¹⁶

Not only has marijuana been linked to increased rates of psychosis and schizophrenia, but more evidence is being reported on the link between cannabis and other mental health conditions. A study in Australia demonstrated that there was a relationship that existed in adolescent males and females with regard to the daily use of marijuana and the development of depression.⁸ This relationship was found to be the most profound in adolescent girls. In fact, in girls under the age of 15, it was found that there was a significant increase in suicidal ideation or attempts over the course of the next 15 years of their life.⁸ Another research study performed in Australia found that in teens ages 13-17 who had used marijuana, there was a three

times increased risk of developing depression when compared to those teenagers who had never used the drug.⁸ Increased levels of anxiety have also been linked to marijuana use. For those adolescents who used cannabis on a weekly basis and who continued to use until the age of 29, there was a significantly increased likelihood of developing an anxiety disorder.⁷

From a cognition standpoint, cannabis is known to slow a person's ability to react, decrease their motor coordination, and decrease one's ability to concentrate and focus. This increased level of distractibility, along with slower reaction times, has been shown to be a contributing factor in motor vehicle accidents when users of the drug attempted to drive while under the influence of cannabis. In a laboratory setting, cannabis and THC were noted to "produce dose-related deficits in reaction time, attention, motor performance and coordination, and information processing that can last up to 28 days after abstinence from the drugs."⁷

There are over 60 pharmacologically active cannabinoids in marijuana. One such chemical, cannabidiol (CBD), is a compound that may have anti-anxiety, anti-inflammatory and antispasmodic actions. It has been reported that CBD does not cause cognitive deficits or the perception of feeling "stoned." The level of THC in medically dispensed marijuana is extremely high while CBD is low. THC is the

chemical responsible for euphoria, or the "high" in marijuana. Indications for legally available marijuana for medicinal use vary from state to state and include cancer, glaucoma, AIDS, hepatitis, ALS, seizure disorders, Crohn's disease, Parkinson's disease and multiple sclerosis. Data collected in states where marijuana is legal for medicinal purposes suggests that the majority of those who possess medical marijuana user cards do not have one of these conditions.

Conclusion

There is a significant amount of evidence to support that the long-term use of marijuana is harmful to individuals and society, especially to adolescents. Research has shown that marijuana use can lead to an increased risk of chronic mental illnesses such as schizophrenia, depression, and anxiety by causing structural changes in a young, maturing brain. Adolescent use of marijuana can also lead to decreased intelligence levels and poor working memory which can interfere with educational attainment and create psychosocial and financial problems that no amount of increased tax revenue can offset. Although there are many in society who will lobby for legalization of this drug due to its "safety" profile, the evidence on this topic refutes this claim and we in South Dakota would be wise to continue to defeat any attempt at legalization of this harmful substance.

REFERENCES

- Centers for Disease Control and Prevention. Youth risk behavior surveillance – United States, 2013. Morbidity and Mortality Weekly Report. 2014;63(4): 1-170.
- Wall MM, Poh E, Cerda A, Keyes KM, Galea S, Hasin DS. Adolescent Marijuana Use from 2002 to 2008: Higher in States with Medical Marijuana Laws, Cause Still Unclear. *AEP*. 2011; 21(9): 714-716.
- Brauser D. Regular marijuana use in teens on the rise. *Medscape*. December 18, 2013; 1-3.
- Kuehn B M. Teen perceptions of marijuana risks shift: Use of alcohol, illicit drugs, and tobacco declines. *JAMA*. 2013;309(5): 429-430.
- National Institute on Drug Abuse. Drug facts: Marijuana. January 2014;1-6.
- Cohen M, Rasser PE, Peck G, Carr VJ, Ward PB, Thomson PM, Johnston P, Baker A, Schall U. Cerebellar grey-matter deficits, cannabis use and first-episode schizophrenia in adolescents and young adults. *International Journal of Neuropsychopharmacology*. 2012;15: 297-307.
- Douaihy A. Cannabis revisited. *UPMC Synergies*. 2013;1-11.
- Rubino T, Zamberletti E, Parolaro D. Adolescent exposure to cannabis as a risk factor for psychiatric disorders. *Journal of Psychopharmacology*. 2012;26(1): 177-188.
- Hill MN. Clearing the smoke: What do we know about adolescent cannabis use and schizophrenia? *Journal of Psychiatry Neuroscience*. 2014;133: 75-76.
- Hilt RJ. Cannabis and the adolescent brain. *Pediatric Annals*. 2014;43(3): 89-90.
- Smith MJ, Cobia DJ, Wang L, et al. Cannabis-related working memory deficits and associated subcortical morphological differences in healthy individuals and schizophrenia subjects. *Schizophrenia Bulletin*. 2013;40(2): 287-299.
- SAMHSA. The TEDS report: Age of substance use initiation among treatment admissions aged 18 to 30. 2014;1-8.
- Diagnostic and statistical manual of mental disorders. American Psychiatric Publishing; 5th edition. 2013.
- Merriam-Webster online dictionary. <http://www.merriam-webster.com>. 2014.
- Ozaki S, Wada K. Amotivational syndrome in organic solvent abusers. *Nihon Yakurigaku Zasshi*. 2001;117 (1): 42-48.
- Shapiro GK, Buckley-Hunter L. What every adolescent needs to know: Cannabis can cause psychosis. *Journal of Psychosomatic Research*. 2010;69: 533-539.

About the Authors:

Shawn Van Gerpen, MD, Assistant Professor and Residency Director, Department of Psychiatry, University of South Dakota Sanford School of Medicine.

Tamara Vik, MD, Assistant Professor and Child and Adolescent Residency Director, Department of Psychiatry, University of South Dakota Sanford School of Medicine.

Timothy Soundy, MD, Professor and Chair, Department of Psychiatry, University of South Dakota Sanford School of Medicine.