Effects of Marijuana on Mental Health:
Attention Deficit-Hyperactivity Disorder (ADHD)

ADAI | ALCOHOL & DRUG ABUSE INSTITUTE

Susan A. Stoner, PhD, Research Consultant

Highlights

- Both ADHD and marijuana use are associated with impaired attention, inhibition, and executive function.
- Expectations that marijuana would make symptoms of ADHD worse are not borne out by the scant research available on this topic.
- Evidence suggests that those with ADHD are at increased risk for developing cannabis use disorders.
- Despite widespread belief that marijuana has medicinal benefits for ADHD, there is virtually no research evidence to support this belief.
- Marijuana cannot be safely recommended for the treatment of ADHD at this time; at best, it might be considered as a last-line therapy when all other conventional therapies have failed.[26]

Introduction

Marijuana is the most commonly used drug of abuse in the United States.[1] As found in the 2015 National Survey on Drug Use and Health, 22.2 million people aged 12 and older had used marijuana in the past month.[1] Research suggests that marijuana use has increased over the past decade[2-4] as perceptions of risk of harm from using marijuana among adults in the general population have steadily declined.[4] As of June 2017, 26 states and the District of Columbia have enacted laws that have legalized marijuana use in some form, and 3 additional states have recently passed measures permitting use of medical marijuana.[5] Mental health conditions figure prominently among the reasons given for medical marijuana use[6], yet there is a dearth of rigorous, experimentally controlled studies examining the effects of marijuana on mental health conditions.[7] This research brief will summarize what is known about the effects of marijuana on attention deficit-hyperactivity disorder (ADHD).

Overview of Complexities in Specifying Marijuana Effects

Any summarization of the effects of marijuana on mental health would be lacking without a brief overview of complexities in specifying marijuana effects. Unlike, say, methamphetamine, marijuana is not a single chemical compound. As a plant, marijuana is composed of more than 500 chemical substances.[8] Only a fraction of these have been studied. It is generally understood that the psychotropic substance in marijuana that is primarily responsible for its intoxicating effects is delta-9-tetrahydrocannabinol (THC).[9] More than 100 other compounds have been identified in marijuana that are chemically related to THC, called cannabinoids.[8] Cannabinoids exert their effects through the relatively recently discovered endocannabinoid system; only since the late 1980s has it been recognized that humans and other mammals have cannabinoid receptors throughout the body and endogenous cannabinoids that modulate the effects of neurotransmitters and other cellular mechanisms in ways that are not yet fully understood but that have generated intense interest as potential targets for therapeutic drug development, including drugs for mental health.[9] Of the two known cannabinoid receptors, CB1 and CB2, CB1 is expressed

Table 1. CNS and cardiovascular effects of THC and CBD.

	THC	CBD
Anticonvulsant	+	++
Muscle relaxant	++	+
Analgesic	++	+
Anxiolytic	±	++
Antipsychotic	–	++
Neuroprotective	+	++
Antiemetic	++	+
Sedation	+	–
Bradycardia	–	+
Tachycardia	+	–
Hypertension	+	–
Hypotension	–	+

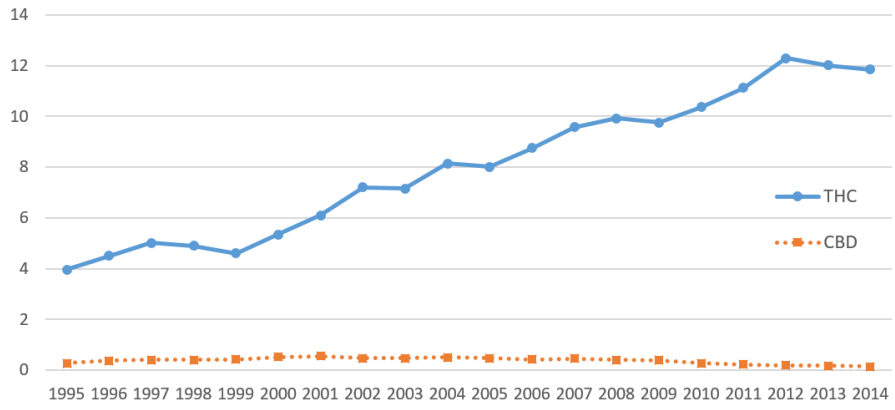
Adapted from Russo E, Guy GW. A tale of two cannabinoids: the therapeutic rationale for combining tetrahydrocannabinol and cannabidiol. Medical Hypotheses. 2006 Dec 31;66(2):234-46.

abundantly in the brain and central nervous system (CNS) while CB2 expression is low in the CNS but high in peripheral immune cells and tissues.[10] Psychoactive effects of marijuana are attributed to CB1 receptors whereas CB2 receptors are non-psychoactive.[9, 10]

Aside from THC, the most studied phytocannabinoid is cannabidiol (CBD).[11] CBD has been described as nonpsychotropic due to the fact that it appears to be non-intoxicating and non-reinforcing, but it does appear to be psychotropic insofar as it appears to have pharmacological benefits with regard to anxiety, schizophrenia, addiction, and depression.[12] Table 1 summarizes the major CNS and cardiovascular effects of THC and CBD.[11] CBD has been demonstrated to attenuate certain effects of THC, including intoxication, sedation, and tachycardia.[11] In modern clinical trials, this has permitted the administration of higher doses of THC in an effort maximize therapeutic effects while minimizing side effects.[11] It is largely unknown how the interaction of THC and CBD plays out in practical use of marijuana by medicinal and recreational marijuana users.

Research on cannabis products seized by the US Drug Enforcement Agency (DEA) shows that the potency of marijuana in common use has increased dramatically in the last 2 decades, at least in terms of THC content.[8] As shown in Figure 1, from 1995 to 2014, the average THC content of seized cannabis products virtually tripled from approximately 4% to approximately 12%.[8] On the other hand, average CBD content fell from approximately 0.28% in 2001 to < 0.15% in 2014, resulting in a change in the THC:CBD ratio of 14:1 in 1995 to approximately 80:1 in 2014.[8] This means that, on average, the cannabis products seized in 2014 were presumably far more intoxicating and than those seized in 1995 – and marijuana and cannabis products that are in common use may bear little resemblance to marijuana supplied by the federal government for marijuana research.[13] In terms of strength, the National Institute on Drug Abuse considers less than 1% to be low, 1-5% to be medium, 5-10% to be high, and over 10% to be very high.[14] An examination of the online menu of one of Seattle's most popular recreational marijuana stores in June 2017 listed over 100 varieties of marijuana "flowers" that were labeled as 20% THC or higher, with THC content going as high as 30%. For many of these, CBD content was not listed. By comparison, there were only 20 varieties with listed THC content under 10%. Marijuana concentrates were labeled as having THC content as high as 97%. From a scientific standpoint, the effects of cannabis products with such levels of THC on mental health have largely not been studied.

Figure 1. Average Concentration (%) of THC and CBD in Cannabis Samples Seized by DEA 1995-2014



Source: ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC. Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the United States. Biological Psychiatry. 2016 Apr 1;79(7):613-9.

Individual differences in objective and subjective effects of marijuana vary by individual, variety/strain, dosage, route of administration, personality, degree of tolerance, and other factors.[9] Many of the psychological effects of cannabis and THC are biphasic and bidirectional.[9] Acute marijuana intoxication is generally associated with euphoria, subjective quickening of associations, relaxation, decreased motor activity, a sense of calm, increased awareness of sensory experience and internal sensations of the body, transient sensory experiences, synesthesia, craving sweet and salty foods, enhanced perception of current activities, increased salience of stimuli, simultaneous focus on multiple things, impaired shifting of focus, fantasies of power, and belief of having arrived at a transcendent insight.[15] With regard to neurocognition, marijuana intoxication is associated with deficits in processing speed, attention, working memory, decision-making, motivation, time-perception, and reality testing.[15] Considering the broad range of effects, one can begin to imagine how marijuana could have beneficial or harmful effects with regard to mental health.

Tolerance to certain effects of marijuana develops with regular use, within several days in some cases,[9] as a function of CB1 receptor expression downregulation.[10] Research suggests that after tolerance develops it can take several

weeks of THC-free recovery for CB1 receptor expression to return to baseline levels.[10] Because of tolerance, the eventual downregulation of CB1 receptors with chronic use means that any benefit derived from THC with regard to mental health could result in symptom exacerbation when users are not under the influence of THC.[10]

The Role of the Endocannabinoid System in ADHD

It is unknown precisely how the endocannabinoid system (ECS) may be involved in ADHD. A small preliminary study found that degradation of the endocannabinoid anandamide (AEA) was impaired in a small sample of drug-free boys with ADHD.[16] AEA impairs memory and attention by reducing the activity of the dopamine transporter system. The ECS may also be involved in ADHD through its involvement in reward circuits in the brain.[10]

Effects of Marijuana on Cognition

Marijuana intoxication has well-documented deleterious effects on cognition, including impairments in attention and inhibition, verbal learning and memory, working memory, executive function, and psychomotor function.[17] Adults who use marijuana chronically have demonstrated poorer performance on tests of attention, executive functions, learning and memory, visuospatial skills, and processing speed. Adolescent marijuana users show attention, working memory, and learning abnormalities that persist at least 6 weeks following cessation of use, but that these deficits may resolve with longer term abstinence.[18]

Most relevant to ADHD, impaired attention is generally considered a hallmark of being under the influence of marijuana. Numerous studies have demonstrated dose-dependent impairments in focused, divided, and sustained attention tasks that may be attenuated with tolerance among daily users. Active adolescent and adult marijuana users as well as those abstinent for several weeks show impairments on measures of sustained and divided attention, processing speed, rapid visual information processing, visual search, tracking, trail making, and paced serial addition. Increasing abstinence is generally associated with improvements in performance.[17]

Executive functions are differentially affected by acute and chronic exposure to marijuana. Several studies have demonstrated impairments in planning, reasoning, interference control, and problem solving tasks with administration of THC. With regard to the chronic effects of marijuana, findings on executive function are less consistent. Studies in which executive dysfunction was detected tended to have older samples than the studies in which no impairments were observed, which included predominantly adolescent and young adult users.[17]

Effects of Marijuana on Cognition in ADHD

Few studies have investigated the neurocognitive performance of individuals with both a history of ADHD and regular marijuana use. Tamm et al.[19] compared young adults with a childhood ADHD diagnosis who did (n=42) and did not (n=45) report marijuana use at least monthly in the past year to a normative comparison group (controls) who did (n=20) and did not (n=21) report past year regular marijuana use on neuropsychological measures. Findings indicated that ADHD group performed worse than controls on measures of verbal memory, processing speed, cognitive interference, decision-making, working memory, and response inhibition. There were no significant effects for marijuana use in either group, and no interactions between ADHD and marijuana use were found. A small study of the effects of ADHD and marijuana use on brain functional architecture in young adults with a similar experimental design produced similar findings that marijuana use does not exacerbate ADHD-related functional alterations in brain architecture.[20]

Opinions on Therapeutic Use of Marijuana by those with ADHD

Clinical and anecdotal evidence suggest an increasingly popular perception that marijuana use is therapeutic for ADHD. A qualitative study of online forum threads regarding ADHD and marijuana found a disproportionate number of comments favoring the therapeutic over harmful effects of marijuana for ADHD that was specific to ADHD and not observed when mood, non-ADHD psychiatric conditions, or general quality of life were considered.[21] Comments extolling the therapeutic effects of marijuana for ADHD predominantly pointed to improvement in inattentive symptoms rather than symptoms of hyperactivity or impulsivity. A number of comments indicated that marijuana was

perceived as being "medicinal" or sanctioned by healthcare providers. Findings suggest that patients seeking information regarding effects of marijuana on ADHD will find information on Internet forums biased toward marijuana improving ADHD that is not reflective of what is found in the medical and research literature.

Interestingly, a qualitative study of marijuana users in Norway (where marijuana use is illegal) found that a considerable proportion of participants reported that they used marijuana for what they perceived as medical reasons, and self-diagnosed ADHD was most prevalent. Traditional ADHD medication was described as having many more negative effects than marijuana. Marijuana use was perceived as reducing symptoms associated with self-diagnosed ADHD, and these effects were taken as evidence for the validity of the self-diagnosis. Using marijuana medicinally for self-diagnosed ADHD was considered less stigmatizing than using it for intoxication and recreation.[22]

As of June 2017, ADHD is not specifically listed as a qualifying condition for a medical marijuana card in any of the states that allow for medicinal use of marijuana.[23] Physicians point out that marijuana can have neurocognitive effects that are, in many cases, the opposite of what patients and parents and trying to achieve, e.g., decreased concentration, irritability, and anxiety. It has been noted that even where there is some good quality evidence beneficial effects of medical marijuana or cannabinoids for certain conditions in adult patients, caution should be used in generalizing the evidence to children and adolescents due to the vulnerability of the developing brain to environmental toxins and substances, wide variation in forms of medical marijuana, and evidence of an association between adolescent marijuana use and later adverse psychosocial outcomes.[24]

Evidence on Therapeutic Use of Marijuana in ADHD

A case report of a 28 year old man with ADHD purported to show improvements in behavior, motor function, mood, and driving skills while under the influence of dronabinol, a synthetic THC analog, compared to when he had abstained from the drug.[25] However, his poorer performance while abstinent may have been reflective of combined ADHD and cannabinoid withdrawal rather than ADHD alone.[26]

A survey of 76 adults (56 men, 20 women) with ADHD examined the relationship between marijuana use and ADHD symptoms and sleep quality. Frequency of marijuana use was positively associated with number of inattentive symptoms among men but women and negatively associated with sleep quality among women but not men. Although intent was not assessed, findings suggest men and women with ADHD may be using marijuana for different reasons, which include an attempt to self-medicate ADHD symptoms.[27]

A large national survey of 2811 marijuana users examined the relationship between subtypes of ADHD and marijuana use.[28] The researchers examined how proportions of daily and nondaily users differ in terms of meeting symptom criteria for specific subtypes of ADHD when not using marijuana. Findings revealed that, overall, daily users met more symptom criteria than non-daily users. A higher proportion of daily users met criteria for the hyperactive-impulsive or combined subtypes than the inattentive subtype. Non-daily users did not show a difference in proportions between subtypes. Casual and moderate users showed no significant difference in the likelihood of meeting symptom criteria for an ADHD diagnosis, which the researchers interpreted as lending further support to the self-medication hypothesis of cannabis use for those affected by the hyperactive-impulsive or combined subtypes of ADHD.

Cooper et al.[29] conducted a recently published pilot randomized double-blind, placebo-controlled trial of Sativex, an oromucosal spray consisting of THC and CBD in a 1:1 ratio, in 30 adults with ADHD in the United Kingdom, investigating effects on cognitive performance, activity level, and behavioral symptoms of ADHD and emotional lability. For ADHD symptoms, in the active group, marginally significant improvements were found for hyperactivity/impulsivity and trends towards improvements were found for inattention and emotional lability. Effect sizes were comparable to those previously reported for treatment of ADHD with stimulant medications. While there was no change in functional impairment, the study period may have been too short to assess functional outcomes. Although participants were intended to be blind to the medication that they received, the investigators noted that the correct guess rate was high, indicating that participants noticed the presence or absence of expected effects, which may have affected their self-reported outcomes. The investigators concluded that the findings provide preliminary support for further investigations of Sativex and other compounds targeting the endocannabinoid system in ADHD.

ADHD and Marijuana Use and Use Disorders

One of the most common problems associated with ADHD is co-occurring substance abuse. In a meta-analytic study childhood ADHD was found predict later development of use disorders for nicotine, alcohol, marijuana, cocaine, and other substances.[30] Conversely, a 25-year prospective longitudinal study found that the extent of marijuana use by age 25 positively predicted the extent of adult ADHD symptoms at age 25, and this association was not explained by social, family, cognitive, or behavioral factors.[31] Current and childhood ADHD symptoms predicted cannabis-related outcomes in a non-clinical sample of young adults.[32] Specifically, current and childhood inattention predicted more severe cannabis outcomes in young adulthood, including higher levels of current use and/or dependence, craving, and use-related problems. Childhood hyperactivity-impulsivity predicted earlier initiation of marijuana use. Individuals with childhood ADHD that persisted into early young adulthood had a greater likelihood of marijuana dependence throughout the young adulthood years (18-22 years old) compared to those without ADHD and those with childhood-limited ADHD.[33]

A representative, population survey of adults in Ontario, Canada, found that hyperactive and impulsive symptoms were associated with problematic cannabis use in men but not women. By contrast, inattentive symptoms predicted problems with cannabis in women but not men.[34] Notzon et al.[35] estimated the prevalence of ADHD in a population of 99 adults seeking treatment for marijuana use disorders using a combination of well-validated questionnaires. Findings yielded an estimated prevalence of adult ADHD in this population of between 34% and 46%, which the authors noted is consistent with estimates of prevalence in two prior studies of marijuana use disorders but higher than those from most studies of substance use disorders as a whole. Similarly, a review of electronic health records of 483 adolescents presenting for treatment for substance use disorders found that 33%, 35%, and 38% of adolescents with marijuana dependence, abuse, and problem use, respectively, were diagnosed with ADHD.[36] It was noted that, because regular use of marijuana produces neurocognitive changes in executive functioning similar to ADHD, making a diagnosis of ADHD in a person actively using or recently abstinent from marijuana is fraught with difficulty. Thus, high apparent comorbidity between marijuana use disorder and ADHD may reflect marijuana-induced neurocognitive disorder rather than true ADHD, or a combination of both.[37]

Conclusions

In summary, both marijuana and ADHD are associated with deficits in cognition. ADHD is associated with impaired attention, inhibition, and executive function. Marijuana use is also known to cause impairments in attention and inhibition, and executive function among other cognitive impairments. Thus, one would expect the effects of marijuana to exacerbate symptoms of ADHD rather than improve them. Surprisingly, the research thus far has not demonstrated this although only a few small studies have been conducted. On the other hand, despite widespread belief that marijuana has medicinal benefits for ADHD, there exists virtually no research evidence to support this belief. Evidence does suggest that those with ADHD are at increased risk for developing cannabis use disorders. Given the current scarcity of data, marijuana cannot be safely recommended for the treatment of ADHD at this time. At best, it might be considered as a last-line therapy when all other conventional therapies have failed.[26]

References

1. Center for Behavioral Health Statistics and Quality. Results from the 2015 National Survey on Drug Use and Health: Detailed Tables. Rockville (MD): SAMHSA; 2016. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf
2. Hasin DS, Saha TD, Kerridge BT et al. Prevalence of marijuana use disorders in the United States between 2001-2002 and 2012-2013. JAMA Psychiatry 2015;72(12):1235-42.
3. Grucza RA, Agrawal A, Bierut LJ. NESARC Findings on Increased Prevalence of Marijuana Use Disorders—Reply: Consistent With Other Sources of Information. JAMA Psychiatry 2016;73(5):532-3.
4. Compton WM, Han B, Jones CM et al. Marijuana use and use disorders in adults in the USA, 2002–14: analysis of annual cross-sectional surveys. The Lancet Psychiatry 2016;3(10):954-64.
5. State Marijuana Laws in 2017 Map. Governing [online magazine] http://www.governing.com/gov-data/state-marijuana-laws-map-medical-recreational.html
6. Reinarman C, Nunberg H, Lanthier F. Heddleston T. Who are medical marijuana patients? Population characteristics from nine California assessment clinics. Journal of Psychoactive Drugs 2011;43(2):128-35.
7. Walsh Z, Gonzalez R, Crosby K et al. Medical cannabis and mental health: A guided systematic review. Clinical Psychology Review 2017;51:15-29.

8. ElSohly MA, Mehmedic Z, Foster S et al. Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the United States. Biological Psychiatry 2016;79(7):613-9.
9. Pacher P, Bátkai S, Kunos G. The endocannabinoid system as an emerging target of pharmacotherapy. Pharmacological Reviews 2006;58(3):389-462.
10. Volkow ND, Hampson AJ, Baler RD. Don't Worry, Be Happy: Endocannabinoids and Cannabis at the Intersection of Stress and Reward. Annual Review of Pharmacology and Toxicology 2017;57:285-308.
11. Russo E, Guy GW. A tale of two cannabinoids: the therapeutic rationale for combining tetrahydrocannabinol and cannabidiol. Medical Hypotheses 2006;66(2):234-46.
12. Russo EB. Cannabidiol Claims and Misconceptions. Trends in Pharmacological Sciences. 2017;38(3):198-201.
13. NIDA's Role in Providing Marijuana for Research. https://www.drugabuse.gov/drugs-abuse/marijuana/nidas-role-in-providing-marijuana-research.
14. Marijuana Plant Material Available from the NIDA Drug Supply Program https://www.drugabuse.gov/researchers/research-resources/nida-drug-supply-program-dsp/marijuana-plant-material-available-nida-drug-supply-program
15. Atkinson DL. Marijuana's effects on the mind. In: Compton M, editor. Marijuana and mental health. Arlington (VA): American Psychiatric Association Publishing, 2016. p. 11-37.
16. Centonze D, Bari M, Di Michele B et al. Altered anandamide degradation in attention-deficit/hyperactivity disorder. Neurology. 2009 Apr 28;72(17):1526-7.
17. Broyd SJ, van Hell HH, Beale C et al. Acute and chronic effects of cannabinoids on human cognition—a systematic review. Biological Psychiatry 2016;79(7):557-67.
18. Schweinsburg AD, Brown SA, Tapert SD. The influence of marijuana on neurocognitive functioning in adolescents. Current Drug Abuse Reviews 2008;1(1):99 – 111.
19. Tamm L, Epstein JN, Lisdahl KM et al. Impact of ADHD and cannabis use on executive functioning in young adults. Drug and Alcohol Dependence 2013;133(2):607-14.
20. Kelly C, Castellanos FX, Tomaselli O et al. Distinct effects of childhood ADHD and cannabis use on brain functional architecture in young adults. NeuroImage: Clinical 2017;13:188-200.
21. Mitchell JT, Sweitzer MM, Tunno AM et al. "I use weed for my ADHD": a qualitative analysis of online forum discussions on cannabis use and ADHD. PLoS ONE 2016;11(5):e0156614.
22. Pedersen W. From badness to illness: Medical cannabis and self-diagnosed attention deficit hyperactivity disorder. Addiction Research & Theory 2015;23(3):177-86.
23. State-by State MMJ Qualifying Conditions (Leafly.com) https://www.leafly.com/news/health/qualifying-conditions-for-medical-marijuana-by-state
24. Nelson T, Liu YH, Bagot KS, Stein MT. Weeding Out the Justification for Marijuana Treatment in Patients with Developmental and Behavioral Conditions. Journal of Developmental & Behavioral Pediatrics 2017;38(6):446-448.
25. Strohbeck-Kuehner P, Skopp G, Mattern R. Cannabis improves symptoms of ADHD. Cannabinoids 2008;3(1):1-3.
26. Hadland SE, Knight JR, Harris SK. Medical marijuana: review of the science and implications for developmental behavioral pediatric practice. Journal of Developmental and Behavioral Pediatrics 2015;36(2):115.
27. Ly C, Gehricke JG. Marijuana use is associated with inattention in men and sleep quality in women with Attention-Deficit/Hyperactivity Disorder: A preliminary study. Psychiatry Research 2013;210(3):1310-2.
28. Loflin M, Earleywine M, De Leo J, Hobkirk A. Subtypes of attention deficit-hyperactivity disorder (ADHD) and cannabis use. Substance Use & Misuse 2014;49(4):427-34.
29. Cooper RE, Williams E, Seegobin S et al. Cannabinoids in attention-deficit/hyperactivity disorder: A randomised-controlled trial. European Neuropsychopharmacology 2017; (8):795-808.
30. Lee SS, Humphreys KL, Flory K et al. Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: a meta-analytic review. Clinical Psychology Review 2011;31(3):328-41.
31. Fergusson DM, Boden JM. Cannabis use and adult ADHD symptoms. Drug and Alcohol Dependence 2008;95(1):90-6.
32. Bidwell LC, Henry EA, Willcutt EG et al. Childhood and current ADHD symptom dimensions are associated with more severe cannabis outcomes in college students. Drug and Alcohol Dependence 2014;135:88-94.
33. Breyer JL, Lee S, Winters KC et al. A longitudinal study of childhood ADHD and substance dependence disorders in early adulthood. Psychology of Addictive Behaviors 2014;28(1):238.
34. Kolla NJ, van der Maas M, Toplak ME et al. Adult attention deficit hyperactivity disorder symptom profiles and concurrent problems with alcohol and cannabis: sex differences in a representative, population survey. BMC Psychiatry 2016;16(1):50.
35. Notzon DP, Pavlicova M, Glass A et al. ADHD is highly prevalent in patients seeking treatment for cannabis use disorders. Journal of Attention Disorders 2016 (in press).
36. Zaman T, Malowney M, Knight J, Boyd JW. Co-occurrence of substance-related and other mental health disorders among adolescent cannabis users. Journal of Addiction Medicine 2015;9(4):317-21.

Citation: Stoner SA. Effects of Marijuana on Mental Health: Attention Deficit-Hyperactivity Disorder (ADHD). Alcohol & Drug Abuse Institute, University of Washington, June 2017. URL: http://adai.uw.edu/pubs/pdf/2017mjadhd.pdf.

This report was produced with support from the Washington State DSHS Division of Behavioral Health and Recovery (DBHR)