

Sorting Through the Science on Marijuana: Facts, Fallacies, and Implications for Legalization

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I. INTRODUCTION

The “War on Drugs” has many critics, but nowhere is there greater consensus about its limitations than with marijuana. Marijuana is the most commonly used illicit drug. In the United States, nearly one-third of the population has used marijuana at least once, and among users of illicit substances, seventy-four percent report using marijuana.¹ Data on marijuana related arrests and incarceration is inconsistent, but many experts suggest that the adverse consequences of criminal sanctions are greater than the adverse consequences of marijuana.² The wide-spread perception that marijuana punishments exceed marijuana’s harms has fuelled popular advocacy for liberalization of marijuana policy.

Amidst all the discussion of marijuana, a series of myths is often perpetuated. Marijuana is sometimes characterized as being harmless and other times characterized as being very harmful. Some express concern that increasing marijuana availability will increase its use, while others suggest that marijuana is already so widely available that increasing its availability will undercut the black market without increasing use. Marijuana is touted as having widespread medicinal benefits by some, while others point to the notion that the evidence for marijuana’s role as a medicinal agent is very limited. Some point to the notion that marijuana causes addiction, while others state that addiction to marijuana does not exist.

Ultimately, policy determinations on marijuana should rest on some objective valuation of its impact on individuals, as well as the public health. The

1. SUBSTANCE ABUSE AND MENTAL HEALTH SERVS. ADMIN., RESULTS FROM THE 2005 NATIONAL SURVEY ON DRUG USE AND HEALTH: NATIONAL FINDINGS 13 (2006), available at <http://oas.samhsa.gov/nsduh/2k5nsduh/2k5results.htm> (on file with the *McGeorge Law Review*).

2. Philippe Bourgois, *The Mystery of Marijuana: Science and the U.S. War on Drugs*, 43 SUBSTANCE USE & MISUSE 581, 582 (2008); Ryan S King, *The War on Marijuana: The Transformation of the War on Drugs in the 1990s*, 3 HARM REDUCTION J. (2006), available at <http://www.harmreductionjournal.com/content/3/1/6> (on file with the *McGeorge Law Review*).

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purpose of this paper is to review the scientific literature on marijuana, focusing on what marijuana is, what it does, its putative benefits, and its potential harms.

II. BIOLOGY OF MARIJUANA

A. *What Is Marijuana?*

Marijuana is produced from cultivation of the *Cannabis sativa* plant. The wide-ranging preparations of marijuana vary in their chemical composition, their agricultural utility and their capacity to cause intoxication. The most common preparation of consumed marijuana is dried leaves, or buds, which can be smoked.

The primary psychoactive component of marijuana, a chemical called tetrahydrocannabinol (THC), was first identified in 1965.³ THC is concentrated in the flowering head of female *Cannabis sativa* plants, and selective cultivation techniques can augment its concentration. It is notable that, while THC is believed to be the primary psychoactive component of marijuana, in fact, marijuana smoke contains many other chemicals and at least sixty other cannabinoids (chemicals that are structurally related to THC).⁴ The role of these chemicals is not well understood, but it is possible that they also contribute to marijuana's effects. One indication of this is the fact that synthetic production of pure THC produces effects that are similar but not exactly the same as marijuana, highlighting the potential role of the other cannabinoids in contributing to the effects of marijuana.⁵

B. *How Does Marijuana Cause a "High"?*

In 1990, researchers identified two distinct brain receptors that are stimulated by THC.⁶ Because the receptors were discovered during investigations of cannabis, they were called cannabinoid receptors. One type of cannabinoid receptor (CB1) was found mostly within the brain, and the other cannabinoid receptor (CB2) was found mostly throughout the body. The role of cannabinoid receptors is not well understood, but it is known that they are stimulated by a hormone called anandamide. Ordinarily, anandamide and cannabinoid receptors regulate many functions of the mind and body, including learning, remembering,

3. Raphael Mechoulam et al., *Chemical Basis of Hashish Activity*, 169 SCI. 611, 611–12 (1970).

4. Mohamed Ben Amar, *Cannabinoids in Medicine: A Review of Their Therapeutic Potential*, 105 J. ETHNOPHARMACOLOGY 1, 2 (2006).

5. Ziva D. Cooper & Margaret Haney, *Cannabis Reinforcement and Dependence: Role of the Cannabinoid CBI Receptor*, 13 ADDICTION BIOLOGY 188, 189–90 (2008).

6. William A. Devane et al., *Isolation and Structure of a Brain Constituent that Binds to the Cannabinoid Receptor*, 258 SCI. 1946, 1946–49 (1992).

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forgetting, pain perception, motor coordination, immune functioning, and reproduction.⁷ Because anandamide and cannabinoid receptors are naturally occurring (endogenous), the network they compose is called the endocannabinoid system.

How does the endocannabinoid system relate to the “high” caused by marijuana? When marijuana is consumed, the THC that is absorbed causes the syndrome of intoxication by stimulating cannabinoid receptors in place of anandamide. The consequence of this receptor stimulation is the experience of mild euphoria, altered perception of time, relaxation, difficulty with memory and concentration, and intensification of sensory experiences. Regular users of marijuana typically find these effects pleasurable or reinforcing. Marijuana intoxication also causes dose-dependant impairments in short-term memory, attention, reaction time, and motor coordination. Additionally, some users experience anxiety, panic, and mild paranoia, and high levels of marijuana intoxication can cause psychosis.

III. MARIJUANA BENEFITS

A. *Is There Any Evidence to Support Medicinal Benefits of Marijuana?*

Given the physiological prevalence of the endocannabinoid system, as well as extensive subjective reports from individuals stating that marijuana alleviates symptoms of diseases, it is hardly surprising that marijuana has been conjectured to have therapeutic utility. The gold standard for establishing the efficacy of medical interventions is controlled and randomized clinical trials. While strict regulation of marijuana has limited the capacity of researchers to investigate it as widely as would otherwise be possible, a growing number of studies in the United States as well as in Europe have demonstrated that marijuana alleviates symptoms of some conditions.⁸ The symptoms for which there is the most substantial evidence include nausea and vomiting, anorexia and wasting, neuropathic pain and muscle spasticity.

Reviewing existing claims and evidence for marijuana’s therapeutic benefits, a number of the leading medical consensus bodies and professional organizations have taken positions supporting additional research and consideration of

7. See Michelle Glass et al., *Cannabinoid Receptors in the Human Brain: a Detailed Anatomical and Quantitative Autoradiographic Study in the Fetal, Neonatal and Adult Human Brain*, 77 *NEUROSCIENCE* 299, 299–300 (1997) (describing the behavioral effects of cannabinoids, such as “enhancement of the senses, errors in judgment of time and space, emotional changes, irresistible impulses, illusions and hallucinations . . . decreased psychomotor performance, an interference in attention space, and a loss of efficient in memory”).

8. See, e.g., Ben Amar, *supra* note 4 (analyzing the therapeutic potential of cannabinoids); Stanley J. Watson et al., *Marijuana and Medicine: Assessing the Science Base: a Summary of the 1999 Institute of Medicine Report*, 57 *ARCH GEN PSYCHIATRY* 547 (2000) (analyzing the benefits and risks of marijuana as a medicine).

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lowering the scheduling status of marijuana. In 2007, following a series of reports published by the Institute of Medicine⁹ and National Institute of Health advocating for more research on marijuana, the American College of Physicians (ACP) published the following position statement:

Position 1: ACP supports programs and funding for rigorous scientific evaluation of the potential therapeutic benefits of medical marijuana and the publication of such findings.

Position 1a: ACP supports increased research for conditions where the efficacy of marijuana has been established to determine optimal dosage and route of delivery.

Position 1b: Medical marijuana research should not only focus on determining drug efficacy and safety but also on determining efficacy in comparison with other available treatments.

Position 2: ACP encourages the use of nonsmoked forms of THC that have proven therapeutic value.

Position 3: ACP supports the current process for obtaining federal research-grade cannabis.

Position 4: ACP urges an evidence-based review of marijuana's status as a Schedule I controlled substance to determine whether it should be reclassified to a different schedule. This review should consider the scientific findings regarding marijuana's safety and efficacy in some clinical conditions as well as evidence on the health risks associated with marijuana consumption, particularly in its smoked form.

Position 5: ACP strongly supports exemption from federal criminal prosecution; civil liability; or professional sanctioning, such as loss of licensure or credentialing, for physicians who prescribe or dispense medical marijuana in accordance with state law. Similarly, ACP strongly urges protection from criminal or civil penalties for patients who use medical marijuana as permitted under state laws.¹⁰

9. DIV. OF NEUROSCIENCE AND BEHAVIORAL HEALTH, INST. OF MED., MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE (Janet E. Joy et al. eds., 1999).

10. TIA TAYLOR, AM. COLL. OF PHYSICIANS, SUPPORTING RESEARCH INTO THE THERAPEUTIC ROLE OF MARIJUANA: A POSITION PAPER OF THE AMERICAN COLLEGE OF PHYSICIANS 1 (2008).

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B. *Are Marijuana's Medical Benefits an Indication for Legalization?*

Since the establishment of the Food, Drug, and Cosmetic Act of 1938,¹¹ the safety and efficacy of medications is assessed by the Food and Drug Administration (FDA) prior to approval for medical applications. This determination is independent of the process for determining whether a substance should be legal for non-medicinal consumption. If the FDA finds that a drug has risk of abuse, it petitions the Drug Enforcement Agency (DEA) to place the drug on the list of controlled substances, where a scheduling system designates the risk associated with the drug. Drugs that are deemed to have abuse potential without medical benefit are placed in Schedule I.

The regulatory function described above is designed to protect the public from medications whose risks are not justified by therapeutic benefit. With respect to marijuana, which resides in Schedule I, the FDA has been criticized for espousing an ideological position in place of rigorous, objective, scientific inquiry.¹² While many would agree that there is now sufficient evidence to justify a re-evaluation of marijuana's scheduling, the regulatory role of the FDA remains of paramount importance to the public health and the precedent of legislating medical interventions is concerning because voters and legislators do not typically have the expertise to determine the safety and efficacy of medical interventions. Ultimately, it is the opinion of this author that those who find the current processes for drug approval in the United States unsatisfactory should work toward reforming, as opposed to circumventing, those processes.

IV. MARIJUANA RISKS

A. *Is It Possible to Be "Addicted" to Marijuana?*

In common language, the term "addiction" is used quite broadly to define any number of compulsive behaviors. In the practice of medicine however, there are generally four lines of evidence that are drawn upon to demonstrate that a particular substance has "addictive" properties. First and foremost, human users demonstrate the clinical features characteristic of addiction. Second, animal studies demonstrate that animals self-administer the substance. Third, the

11. Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (codified in 21 U.S.C. §§ 301–399D).

12. See, e.g., Gregory T. Carter & Bruce Mirken, *Medical Marijuana: Politics Trumps Science at the FDA*, 8 MEDSCAPE GEN. MED. 46 (2006) (arguing that "politics . . . has now completely trumped science" at the FDA); Peter J. Cohen, *Medical Marijuana: The Conflict Between Scientific Evidence and Political Ideology: Part One of Two*, 23 J. PAIN & PALLIATIVE CARE PHARMACOTHERAPY 4 (2009) (discussing the "conflict between the development of policies based on evidence obtained through the use of scientific methods and those grounded on ideological and political considerations that have repeatedly entered the longstanding debate reading the legal status of medical marijuana").

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substance has the capacity to stimulate the biological reward circuitry of the brain. Fourth, epidemiological studies show that the phenomenon is not some local, cultural outlier, but rather a persistent and pervasive syndrome that manifests across the population among people who are exposed to the substance.

*B. Four Lines of Evidence Support the Validity of Marijuana Addiction**1. Clinical Features*

The medical syndrome of addiction is defined in the *Diagnostic Statistical Manual IV-TR (DSM IV)*.¹³ Marijuana addicts manifest the hallmark features of addiction: They complain that they are unable to stop using despite desiring to stop; they report that their marijuana use causes adverse consequences in their lives, and they frequently seek medical help with discontinuation. Consistent, heavy marijuana use generates tolerance, and a withdrawal syndrome follows abrupt cessation.¹⁴ The severity of marijuana withdrawal has been compared to nicotine withdrawal. Like nicotine withdrawal, marijuana withdrawal is not life-threatening, but it is sufficiently uncomfortable to compel a return to use after discontinuation, thus helping to sustain the cycle of addiction.¹⁵ *DSM IV* defines substance dependence (also known as addiction) as follows:

[A] maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same twelve-month period:

1. Tolerance, as defined by either of the following:
 - a. a need for markedly increased amounts of the substance to achieve intoxication or desired effect
 - b. markedly diminished effect with continued use of the same amount of the substance
2. Withdrawal, as manifested by either of the following:
 - a. the characteristic withdrawal syndrome for the substance (this has been defined for marijuana)
 - b. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

13. Deborah Hasin et al., *Substance Use Disorders: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and International Classification of Diseases, Tenth Edition (ICD-10)*, 101 *ADDICTION* 59, 61 (2006).

14. See Alan J. Budney et al., *Review of the Validity and Significance of Cannabis Withdrawal Syndrome*, 161 *AM. J. PSYCHIATRY* 1967 (2004) (analyzing a study illustrating the cannabis withdrawal syndrome).

15. See Alan J. Budney et al., *Comparison of Cannabis and Tobacco Withdrawal: Severity and Contribution to Relapse*, 35 *J. SUBSTANCE ABUSE TREATMENT* 362 (2008) (analyzing study comparing perceptions of withdrawal in cannabis user and tobacco cigarette smokers). *Id.* at 368.

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3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use
5. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. The substance 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 the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

Specify if:

With Physiological Dependence: evidence of tolerance or withdrawal (i.e., either Item 1 or 2 is present)

Without Physiological Dependence: no evidence of tolerance or withdrawal (i.e., neither Item 1 nor 2 is present)[.]¹⁶

2. *Animal Studies*

Animal studies of addiction ascertain the addictive properties of a substance by offering it to animals under controlled circumstances and observing how reinforcing that substance is. For instance, do laboratory animals gravitate towards areas where they received the substance? How hard will they work to receive the substance? Will they use the substance in place of other pleasurable activities, such as eating or drinking? Substances of abuse vary in how strongly reinforcing they are. For instance, studies of cocaine show that addiction develops rapidly and that rodents will work to self-administer cocaine until they reach a state of complete exhaustion or overdose.¹⁷ Marijuana is not as reinforcing as cocaine, but animal models show that it is in fact reinforcing, and they will independently self-administer it.¹⁸

16. AM. PSYCHIATRIC ASS'N, DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS (4th ed., rev. vol. 2000).

17. Hugh O. Petti & Joseph B. Justice, Jr., *Effect of Dose on Cocaine Self-Administration Behavior and Dopamine Levels in the Nucleus Accumbens*, 539 BRAIN RES. 94, 100 (1991).

18. Cooper & Haney, *supra* note 5, at 190.

3. *Neurobiology*

Virtually all drugs associated with addiction share the ability to stimulate the reward center of the brain. Cannabinoid receptors have been found directly within the reward center of the brain.¹⁹ Stimulation of these receptors is associated with dopamine release in the nucleus accumbens (the part of the reward center that assigns value to incoming stimuli), the neurobiological keystone that triggers the addictive machinery of the brain.²⁰ Researchers have ascertained additional validation for this action of marijuana: if cannabinoid receptors in the brain are experimentally blocked, marijuana loses its ability to cause the above described dopamine release, thus proving that THC primarily mediates marijuana's actions on the brain.²¹

4. *Epidemiology*

Population studies have revealed that one out of eleven people (nine percent) who have ever smoked marijuana go on to develop the syndrome of addiction.²² Among people who first start smoking marijuana before the age of eighteen, the incidence of addiction is substantially higher. Marijuana addiction is pervasive and can cause distress. In 2009, marijuana was associated with 122 out of every 100,000 visits to emergency departments.²³

C. What Are the Short-Term Effects of Marijuana Intoxication on the Brain?

Marijuana intoxication is the result of a number of brain changes that occur when marijuana is used. These include alterations in short-term memory, sense of time, sensory perception, attention span, problem solving, verbal fluency, reaction time, and psychomotor control.²⁴ Some users report positive feelings such as mild euphoria and relaxation, while others, particularly naive users, report anxiety, paranoia, and panic reactions.²⁵ The short-term effects of

19. *Id.* at 189.

20. William A. Carlezon, Jr. & Mark J. Thomas, *Biological Substrates of Reward and Aversion: A Nucleus Accumbens Activity Hypothesis*, 56 *NEUROPHARMACOLOGY* 122, 122–23 (2009).

21. Marilyn A. Huestis et al., *Blockade of Effects of Smoked Marijuana by the CBI-Selective Cannabinoid Receptor Antagonist SR141716*, 58 *ARCHIVES GEN. PSYCHIATRY* 322, 322–25 (2001).

22. Ahmed Elkashef et al., *Marijuana Neurobiology and Treatment*, *SUBSTANCE ABUSE*, Dec. 8, 2008, at 17–29 (2008).

23. *SUBSTANCE ABUSE AND MENTAL HEALTH SERVS. ADMIN., DRUG ABUSE AND WARNING NETWORK NATIONAL ESTIMATES OF DRUG-RELATED EMERGENCY DEPARTMENT VISITS, 2004–2009* (Sep. 23, 2010), https://dawninfo.samhsa.gov/data/report.asp?f=Nation/All/Nation_2009_All_ED_Visits_by_Drug (on file with the *McGeorge Law Review*).

24. Leslie Iversen, *Cannabis and the Brain*, 126 *BRAIN* 1252, 1256–59 (2003).

25. Wayne Hall & Louisa Degenhardt, *Adverse Health Effects of Non-Medical Cannabis Use*, 374 *LANCET* 1383, 1383–84 (2009).

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marijuana last approximately one to four hours, depending on potency of the marijuana, the route of administration, and the tolerance of the user. While frequent users develop tolerance to many of marijuana's effects, tolerance is never complete; even users who do not appear or feel intoxicated continue to manifest impairments under testing.²⁶

While marijuana does have a number of physical effects (to be described below), the relative paucity of cannabinoid receptors in the areas of the brain that control vital functions such as breathing²⁷ probably accounts for the fact that there are no reported cases of human deaths attributed to marijuana toxicity.

D. Does Marijuana Intoxication Impact Driving?

A special note of caution is warranted with regards to marijuana and driving. In one recent study, ninety-seven percent of heavy users of marijuana reported driving a car while intoxicated.²⁸ Many users justified their ability to drive by comparing the effects of marijuana to the effects of alcohol. Marijuana does cause less dramatic impairment than alcohol intoxication, but it has nonetheless been associated with a two- to three-fold increase in accidents on the road.²⁹ An association has been found between blood THC levels and likelihood of culpability in fatal traffic accidents involving marijuana users.³⁰ The increase in accidents is likely related to the effects of marijuana on attention, hand-eye coordination, tracking behavior, and reaction time.³¹ Even individuals with tolerance who may not show obvious deficits in these areas, manifest impairment when there is a need to adaptively respond to sudden unexpected emergencies.³² The combination of alcohol and marijuana produces levels of impairment greater

26. Karen I. Bolla et al., *Dose-related Neurocognitive Effects of Marijuana Use*, 59 *NEUROLOGY* 1337, 1340 (2002); Emma J.K. Wadsworth et al., *Cannabis Use, Cognitive Performance, and Mood in a Sample of Workers*, 20 *J. PSYCHOPHARMACOLOGY* 14, 20–21 (2006).

27. Michelle Glass et al., *Cannabinoid Receptors in the Human Brain: A Detailed Anatomical and Quantitative Autoradiographic Study in Fetal, Neonatal, and Adult Human Brains*, 77 *NEUROSCIENCE* 299, 307–310 (1997).

28. Philip Terry & Kay A. Wright, *Self-Reported Driving Behavior and Attitudes Towards Driving Under the Influence of Cannabis Among Three Different User Groups in England*, 30 *ADDICTIVE BEHAVIORS* 619, 619–26 (2005).

29. Olaf H. Drummer et al., *The Involvement of Drugs in Drivers of Motor Vehicles Killed in Australian Road Traffic Crashes*, 36 *ACCIDENT ANALYSIS & PREVENTION* 239, 246 (2004); Jan G. Ramaekers et al., *Dose Related Risk of Motor Vehicle Crashes After Cannabis Use*, 73 *DRUG & ALCOHOL DEPENDENCE* 109, 111–12 (2004).

30. Franjo Grothenhermen et al., *Developing Limits for Driving under Cannabis*, 102 *ADDICTION* 1910, 1912–13 (2007).

31. Ramaekers, *supra* note 29, at 113.

32. Anthony Liguori et al., *Effects of Marijuana on Equilibrium, Psychomotor Performance, and Simulated Driving*, 9 *BEHAV. PHARMACOLOGY* 599, 606–07 (1998).

than their independent sum, and this too has been demonstrated among experienced users with high levels of tolerance.³³

E. Does Repeated Marijuana Use Have Long Term Effects on the Brain?

While there is no question that marijuana causes short-term impairments in brain function, the degree to which these impairments are reversible with chronic use is less clear. Some studies have shown that brain function recovers over time, while others demonstrate persistence of subtle, but important, impairments.³⁴ How is it possible to reconcile the different findings from different studies? These inconsistencies often appear to reflect differences in the sensitivity with which “impairment” is measured. By and large, most of the prominent brain effects of marijuana are short term and do in fact reverse when marijuana is discontinued.³⁵ However, there is increasing evidence that subtle effects, such as slowed information processing, may actually persist long after discontinuation. These effects are difficult to detect because they may only become apparent in the setting of highly complex and demanding brain functions.³⁶

Cannabinoid receptors are most prevalent in the prefrontal cortex, hippocampus, amygdala, basal ganglia, and cerebellum. These brain regions undergo prominent developmental changes throughout childhood and adolescence and thus may be particularly susceptible to the adverse cognitive effects of marijuana. Adolescent humans using marijuana have been found to have increased volumes in the cerebellum, possibly from failure to prune synapses effectively.³⁷ These adolescent marijuana users also show increased brain processing effort on functional magnetic resonance imaging (fMRI) during an inhibition task in the presence of similar task performance, even after twenty-eight days of abstinence.³⁸ Taken together, there is compelling evidence that

33. Anthony Liguori et al., *Separate and Combined Effects of Marijuana and Alcohol on Mood, Equilibrium, and Simulated Driving*, 163 *BEHAV. PSYCHOPHARMACOLOGY* 399, 399, 404 (2002); Jorgen G. Bramness et al., *Impairment Due to Cannabis and Ethanol*, 105 *ADDICTION* 1080, 1080–87 (2009).

34. Robert I. Block et al., *Effects of Frequent Marijuana Use on Memory-Related Regional Cerebral Blood Flow*, 72 *PHARMACOLOGY, BIOCHEMISTRY, & BEHAVIOR* 237, 237–50 (2002); Jeremy Quickfall & Daniel Crockford, *Brain Neuroimaging in Cannabis Use: A Review*, 18 *J. NEUROPSYCHIATRY* 318, 318–32 (2006).

35. Alecia D. Schweinsburg et al., *The Influence of Marijuana Use on Neurocognitive Functioning in Adolescents*, 1 *CURRENT DRUG ABUSE REVS.* 99, 100 (2008).

36. Nadia Solowij et al., *Cognitive Functioning of Long-Term Heavy Cannabis Users Seeking Treatment*, 287 *J. AMER. MED. ASS'N* 1123, 1127 (2002).

37. Krista L. Medina et al., *Abnormal Cerebellar Morphometry in Abstinent Adolescent Marijuana Users*, 182 *PSYCHIATRY RES.: NEUROIMAGING* 152, 152–59 (2010).

38. Susan F. Tapert et al., *Functional MRI of Inhibitory Processing in Abstinent Adolescent Marijuana Users*, 194 *PSYCHOPHARMACOLOGY* 173, 178–79 (2007).

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chronic increases in stimulation of the brain's cannabinoid system can lead to morphologic and physiologic changes especially during adolescence.³⁹

F. *Does Smoking Marijuana Cause Cancer?*

Smoked marijuana irritates the delicate lining of the respiratory tract and causes damage to the cells lining the bronchial passages. This damage impairs the respiratory system's ability to clear toxins and fight off microorganisms. It also leads to inflammatory changes, which are experienced by users as increased phlegm, cough, wheezing, and shortness of breath.⁴⁰ Users of marijuana are at increased risk of both acute and chronic bronchitis.⁴¹

Smoked marijuana is also thought to carry a risk of cancer, particularly lung cancer and cancer of the head and neck.⁴² This concern emerges from the observation that heavy marijuana use causes biochemical and gene alterations in the respiratory tract that are known to be markers of precancerous change.⁴³ Further, marijuana smoke has many of the same carcinogenic hydrocarbons that have been shown to cause lung cancer from tobacco.⁴⁴ However, despite the theoretical cancer risk associated with marijuana, to date there are no high quality studies demonstrating a convincing relationship between marijuana use and cancer.

G. *Does Marijuana Use Pose Any Risks to Pregnant or Breast-Feeding Women?*

Many of the compounds in smoked marijuana readily cross the placenta, where the growing fetus absorbs them and pass into breast milk, where nursing infants ingest them.⁴⁵ Because it is not ethical to give pregnant or nursing women marijuana, most of the studies in this area have followed groups of women who

39. Schweinsburg, *supra* note 35, at 108–09.

40. Harold Kalant, *Adverse Effects of Cannabis on Health: An Update of the Literature Since 1996*, 28 *PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY* 849, 853–53 (2004).

41. D. Robin Taylor et al., *A Longitudinal Study of the Effects of Tobacco and Cannabis Exposure on Lung Function in Young Adults*, 97 *ADDICTION* 1055, 1056, 1059 (2002).

42. Donald P. Tashkin et al., *Respiratory and Immunological Consequences of Marijuana Smoking*, 42 *J. CLINICAL PHARMACOLOGY (SUPPLEMENT)* 71S, 76S–78S (2002); Zuo-Feng Zhang et al., *Marijuana Use and Increased Risk of Squamous Cell Carcinoma of the Head and Neck*, 8 *CANCER EPIDEMIOLOGY, BIOMARKERS, & PREVENTION* 1071, 1076 (1999).

43. Kalant, *supra* note 40, at 853.

44. Mikhail F. Denissenko et al., *Preferential Formation of Benzo[a]pyrene Adducts at Lung Cancer Mutational Hotspots in P53*, 274 *SCI.* 430, 430–32 (1996).

45. Susan J. Astley & Ruth E. Little, *Maternal Marijuana Use During Lactation and Infant Development at Year One*, 12 *NEUROTOXICOLOGY & TERATOLOGY* 161, 161 (1989); Miriam Schneider, *Cannabis Use in Pregnancy and Early Life and Its Consequences: Animal Models*, 259 *EUR. ARCHIVES OF PSYCHIATRY & CLINICAL NEUROSCIENCE* 383 (2009).

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have been identified as smoking marijuana during those risk periods. Pregnant marijuana users are also more likely to use other illicit drugs, tobacco, and alcohol. They are also less likely to receive antenatal care. Such confounding variables limit interpretation of these studies. Nonetheless, studies link marijuana use during pregnancy or breast-feeding with low birth weight, developmental delay, and behavioral problems.⁴⁶ Are these short-term or long-term effects? Monitoring these effects over time suggests that some of these effects may persist throughout a child's development, and that early exposure to marijuana is associated with behavioral problems at age ten,⁴⁷ and an increased risk of marijuana use at age fourteen.⁴⁸ Altogether, the effects of marijuana on child development appear to be subtle but significant, particularly given what is known about the importance of the early years as a critical period for establishing a foundation for growth and function throughout the rest of life.

H. Does Marijuana Use Have Any Impact on Mental Health?

Marijuana is well known to cause fluctuations in mood and anxiety, but the extent to which these fluctuations persist beyond the period of marijuana use is unclear.⁴⁹ Studies show an increase in anxiety and depressive disorders among frequent marijuana users, but there is not sufficient information to determine the direction of causality.⁵⁰ In other words, we cannot yet determine whether marijuana causes an increase in depression and anxiety, or whether individuals who suffer from depression and anxiety tend to use more marijuana.⁵¹ However, heavier marijuana use has been shown to increase the association with anxiety and depression. Weekly or more frequent cannabis use in teenagers predicts an approximately two-fold increase in risk for later depression and anxiety.⁵²

46. David M. Fergusson et al., *Maternal Use of Cannabis and Pregnancy Outcome*, 109 BRIT. J. OBSTETRICS & GYNECOLOGY 21 (2002).

47. Lidush Goldschmidt et al., *Prenatal Marijuana and Alcohol Exposure and Academic Achievement at Age 10*, 101 ADDICTION 521, 528 (2004).

48. Nancy Day et al., *Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14*, 101 ADDICTION 1313, 1320 (2006).

49. Ron De Graaf et al., *Early Cannabis Use and Estimate Risk of Later Onset of Depression Spells: Epidemiological Evidence from the Population-Based World Health Organization World Mental Health Survey Initiative*, 172 AM. J. EPIDEMIOLOGY 149, 155 (2010).

50. Gregory B. Bovasso, *Cannabis Abuse As a Risk Factor for Depressive Symptoms*, 98 AM. J. PSYCHIATRY 2033, 2033–37 (2001).

51. Louisa Degenhardt et al., *Exploring the Association Between Cannabis Use and Depression*, 98 ADDICTION 1493, 1500 (2003).

52. Louisa Degenhardt et al., *The Relationship Between Cannabis Use, Depression, and Anxiety Among Australian Adults: Findings from the National Survey of Mental Health and Well-Being*, 36 SOC. PSYCHIATRY & PSYCHIATRIC EPIDEMIOLOGY 219, 220–26 (2001); George C. Patton et al., *Cannabis and Mental Health in Young People: Cohort Study*, 325 BRIT. MED. J. 1195, 1196–97 (2002).

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In sufficient doses, marijuana can cause psychosis,⁵³ a state of mind characterized by the inability to distinguish between what is real and what is not. Psychosis is concerning for three reasons. First, the loss of connection to reality can be an emotionally terrifying experience. Second, psychosis can stimulate unsafe behavior when the lack of connection to reality inhibits the ability to determine what is safe and what is not. Third, there is mounting evidence that psychosis itself is harmful to the brain and may actually predispose the brain to psychotic disorders.⁵⁴

In addition to causing psychosis, marijuana may also contribute to the development of lifelong psychotic disorders such as schizophrenia.⁵⁵ Schizophrenia is a disorder characterized by deterioration in thinking, disturbances in perception, and impairments in social function. Marijuana can unmask symptoms among individuals who have pre-existing vulnerability (such as a family history) to schizophrenia.⁵⁶ Additionally, marijuana may be an independent risk factor for the development of psychotic disorders such as schizophrenia. Schizophrenia affects approximately one percent of the population across the world, and marijuana has been found to increase the risk of manifesting the illness by 1.4 to 2 fold.⁵⁷ Marijuana use by schizophrenics has been associated with brain volume loss significantly greater than seen in schizophrenics who abstain from marijuana.⁵⁸

I. Are the Effects of Marijuana on Young People Any Different than Its Effects on Adults?

Because adolescent brains are still developing, marijuana use before age eighteen results in higher rates of addiction—up to seventeen percent within two years—and disruption to an individual’s life.⁵⁹ The earlier the use, the greater the risk.

53. Theresa H.M. Moore et al., *Cannabis Use and Risk of Psychotic or Affective Mental Health Outcomes: A Systematic Review*, 370 LANCET 319, 321–25 (2007).

54. Diana O. Perkins et al., *Relationship Between Duration of Untreated Psychosis and Outcome in First-Episode Schizophrenia: A Critical Review and Meta-Analysis*, 162 AM. J. PSYCHIATRY 1785, 1785–1804 (2005).

55. Louisa Degenhard et al., *Testing Hypotheses About the Relationship Between Cannabis Use and Psychosis*, 71 DRUG & ALCOHOL DEPENDENCE 37, 44–45 (2003).

56. Louise Arseneault et al., *Casual Association Between Cannabis and Psychosis: Examination of the Evidence*, 184 BRIT. J. PSYCHIATRY 110, 115 (2004).

57. Moore, *supra* note 53, at 320–21.

58. Monica Rais et al., *Excessive Brain Volume Loss Over Time in Cannabis-Using First Episode Schizophrenia Patients*, 165 AM. J. PSYCHIATRY 490, 494–96 (2008).

59. U.S. DEPT. OF HEALTH & HUM. SERVICES, NAT’L INST. OF DRUG ABUSE, PUB. NO. 06-5882, *MONITORING THE FUTURE: NATIONAL RESULTS ON ADOLESCENT DRUG USE: OVERVIEW OF KEY FINDINGS 2005* (2006).

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A relationship between marijuana and poor educational attainment has been repeatedly demonstrated across many studies.⁶⁰ The relationship appears to hold even when confounding variables are statistically controlled.⁶¹ School performance is a function of many factors, but it is likely that the short-term effects of marijuana intoxication exacerbate existing school difficulties and push poor performance into school failure. On the other hand, analysis of behavioral, socioeconomic, and health outcomes at age twenty-nine all reveal that abstainers consistently have the most favorable outcomes, whereas early high users consistently have the least favorable outcomes.⁶² A twenty-one-year longitudinal study of 1265 New Zealand adolescents found that regular or heavy use, was associated with increased rates of a range of adjustment problems, including other illicit drug use, crime, depression and suicidal behaviors.⁶³

The association between marijuana and other adverse social outcomes (such as unemployment, status of occupation, income, unplanned pregnancy, alcohol and illicit substance use, crime, and incarceration) may, however, be mediated by the downstream impact of school failure and low educational attainment.⁶⁴ Criminalization of marijuana may also contribute to these adverse outcomes via the adverse lifelong consequences of a criminal record or incarceration.⁶⁵

V. IMPLICATIONS FOR LEGALIZATION

A. *What Impact Would Legalization of Marijuana Have on Marijuana Use?*

No industrialized country has legalized marijuana, such that projections on the impact of marijuana legalization are merely speculative. Analysis of regulatory changes and decriminalization in other countries has produced mixed findings, with some suggestions of increased use and others of decreased use.⁶⁶

In 2010, the RAND Corporation, a non-profit institution investigating policy and health services, published a report entitled, *Altered State? Assessing How Marijuana Legalization in California Could Influence Marijuana Consumption*

60. WAYNE HALL ET AL., NAT'L DRUG & ALCOHOL RES. CENTER, THE HEALTH AND PSYCHOLOGICAL EFFECTS OF CANNABIS USE 125 (2nd ed. 2001).

61. David M. Fergusson et al., *Cannabis and Educational Achievement*, 98 ADDICTION 1681, 1690 (2003).

62. Phyllis Erickson et al., *Marijuana Use from Adolescence to Young Adulthood: Multiple Developmental Trajectories and Their Associate Outcomes*, 23 HEALTH PSYCHOL. 299 (2004).

63. David M. Fergusson et al., *Cannabis Use and Psychosocial Adjustment in Adolescence and Young Adulthood*, 97 ADDICTION 1123, 1133 (2002).

64. HALL, *supra* note 60.

65. Robert J. MacCoun, *Drugs and the Law: A Psychological Analysis of Drug Prohibition*, 113 PSYCHOL. BULL. 497, 498–505 (1993).

66. Robert J. MacCoun, *What Can We Learn from the Dutch Cannabis Coffeeshop Experience?* (RAND Drug Policy Research Center, Working Paper July 10, 2010), available at http://www.rand.org/pubs/working_papers/WR768 (on file with *McGeorge Law Review*).

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*and Public Budgets.*⁶⁷ The report acknowledged that its projections were based on estimations of multiple variables, subject to substantial uncertainty. Altogether, the report projected that legalization would likely be followed by a substantial price decline in marijuana, and a concomitant increase in use. Given the fact that approximately nine percent of marijuana users go on to develop addiction, the absolute numbers of people with marijuana dependence would grow.

Marijuana legalization would likely increase the availability of marijuana, and decrease the perception of harm associated with it. This would result in increased use. Thus, the number of people impacted by adverse effects, even if only a small percentage, would likely grow.

B. In the Advent of Legalization, What Measures Might Safeguard the Public's Health?

The adverse effects of marijuana impact a minority of marijuana users. However, any increase in marijuana use is likely to be accompanied by an increase in the absolute number of individuals with marijuana-related problems. Enlightened regulation should seek to attenuate the unintended consequences of increased marijuana use, and should take extra measures to protect at-risk populations. The populations at highest risk of marijuana related consequences are (1) youth, (2) pregnant or breastfeeding women, and (3) individuals at high risk for mental illness.

In 2010, the California Society of Addiction Medicine wrote a statement in response to Proposition 19, the California ballot initiative that, if passed, would have legalized marijuana.⁶⁸ That statement summarized seven core regulatory measures that might help defray the adverse impact of legalization:

(1) *Restriction:* Marijuana use and possession among individuals under the age of twenty-one should be prohibited. Intoxication with marijuana should be prohibited while operating heavy machinery, or working in sensitive occupations.

(2) *Treatment:* Currently only a small percentage of people who need treatment for marijuana addiction actually receive it. Yet treatment works. Any policy change that increases the absolute number of people with addiction should also set forth the mechanism to offer treatment to those who need it.

(3) *Labelling:* Given concerns about adding a new “smokeable” product, and the importance of instilling public awareness of long term risk from the outset. Appropriate labelling should characterize the known quantity, strength, and

67. Beau Kilmer et al., *Altered State? Assessing How Marijuana Legalization in California Could Influence Marijuana Consumption and Public Budgets* (RAND Drug Policy Research Center, Occasional Paper 2010), available at http://www.rand.org/pubs/occasional_papers/OP315 (on file with *McGeorge Law Review*).

68. CAL. SOC'Y OF ADDICTION MED., STATEMENT ON THE MEDICAL ASPECTS OF MARIJUANA LEGALIZATION (Apr. 2010), <http://www.csam-asam.org/pdf/misc/Legalization.pdf> (on file with the *McGeorge Law Review*).

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constituents, and such labelling should be standardized and monitored for accuracy.

(4) *Commerce*: Manufacture, marketing, distribution, and sales of marijuana should be closely regulated to ensure appropriate controls, ranging from safety, to zoning.

(5) *Education*: Widespread educational efforts should be developed to educate the population about marijuana and ensure the public health.

(6) *Research*: Assumptions about the impact of legalization, and the potential effectiveness of the measures described here, are speculative. No major industrialized country has legalized marijuana. In the event of legalization, it would be vital to objectively study the impact of such policy change and the effectiveness of provisions taken to minimize harms. Additionally, a mechanism needs to be established for monitoring and documenting intoxication, for the purpose of ascertaining DUI, or intoxication while involved in other sensitive activities.

(7) *Revenue*: Taxes should be commensurate to the social costs of the drug, and should be applied towards those ends. Given the complexity of regulating and overseeing the principals described above, it would be prudent to establish an appropriations committee to oversee the appropriate allocation of funds.⁶⁹

VI. CONCLUSION

Marijuana is the most widely used illicit substance. In many regions, the widespread perception that criminal sanctions against marijuana users are ineffective and unjustified has generated a re-evaluation of public policy on marijuana. Marijuana has already been decriminalized in some states, and further legalization initiatives are forthcoming.

This article has sought to objectively review the biological and medical characteristics of marijuana. Like most drugs, marijuana has some potential benefits and some potential risks. Marijuana's potential medical benefits merit a re-assessment of its scheduling status by the FDA, but the public health is not well served if the FDA's responsibility to scientifically ascertain safety and efficacy is altogether circumvented. While most of the risks associated with marijuana are moderate in severity,⁷⁰ the prevalence of marijuana use means that a sizeable minority of the population is likely to experience some adverse effects. Furthermore, three populations are particularly at risk for the adverse effects of marijuana: youth, individuals with mental illness, and pregnant or breastfeeding women.

69. *Id.*

70. David Nutt et al., *Development of a Rational Scale to Assess the Harm of Drugs of Potential Misuse*, 369 LANCET 1047 (2007). David Nutt et al., *Drug Harms in the UK: a Multicriteria Decision Analysis*, 376 LANCET 1558 (2010).

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Accurately appraising marijuana's characteristics is vital for ensuring that determinations on marijuana policy are informed by fact rather than ideology. Overall, an enlightened regulatory approach towards marijuana would eliminate the harmful impact of ineffective criminal policy, while protecting the health of at-risk populations, and taking measures to provide resources to those who suffer adverse consequences.