CALIFORNIA ACADEMY of CHILD & ADOLESCENT PSYCHIATRY

The Impact of Cannabis Use During Adolescence:

A Report to the California Academy of Child & Adolescent Psychiatry

From the Cannabis White Paper Task Force

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EXECUTIVE SUMMARY

Introduction

- There are validated psychological and physiological effects of cannabis which lead to altered cognitive states.
- Although research is ongoing to determine the efficacy of cannabis for various medical conditions in adults, no research is ongoing to determine the efficacy of cannabis for medical conditions in children and adolescents.
- At the present time, there is little to no credible, legitimate data to support the use of cannabis for the treatment of any psychiatric condition, especially for children and adolescents.
- There is little to no regulation of dispensaries that sell cannabis in California, and there is little to no regulation of the content, potency, and purity of marketed cannabis.

Epidemiology and Trends of Use

- Cannabis is the most widely used illicit drug in the United States.
- There recently have been slight increases in national prevalence rates of adolescent cannabis use, and patterns of use in California follow national trends.
- Surveys which measure social norms in high school students demonstrate decreased perceptions of cannabis' harm, increased social approval of cannabis use, and increased perceptions of cannabis' availability.
- Frequency of adolescent cannabis use varies from abstinence to regular/heavy use. Earlier age of onset of use and more frequent use lead to higher rates of cannabis abuse, dependence, and psychiatric comorbidities.

Mechanisms of Action

- Δ-9-THC is the main psychoactive compound found in cannabis. This compound is lipophilic and crosses the blood-brain-barrier easily.
- Primary effects are mediated through CB1 and CB2 receptors that mediate endocannabinoids.

The Effects of Cannabis on Brain Development

- Structural brain development continues during the critical period of adolescence.
- Cannabis use during this time disrupts and changes brain structure and physiology.

Effects of Cannabis on Cognition

- There are short term and longer term negative effects on cognitive performance with cannabis use.

- Heavy use (defined as $\geqslant$ 4x/week, or $\geqslant$ 5 joints/week) was associated with lower IQ and worse attention, working memory, verbal memory, and learning. Children and adolescents who began using cannabis daily before age 15 years performed worse than those who started daily use at 15 years or older.
- Some cognitive deficits improved when abstinence from cannabis occurred but some cognitive deficits endured.

Adolescent Cannabis Use and the Development of Mental Illness

- Cannabis use appears correlated with the development of psychotic disorders and may hasten the onset of these disorders.
- The evidence is equivocal as to whether cannabis is correlated with the development of mood and anxiety disorders.
- Other substance use disorders coexist with cannabis use disorders, particularly alcohol and tobacco abuse or dependence.

The Potential for Abuse of Cannabis in Children and Adolescents

- Childhood and adolescence are developmental periods during which children are more vulnerable to developing substance abuse and dependence than adulthood.
- The progression from cannabis use to abuse/dependence can occur more rapidly in adolescents than in adults.
- Effective treatments exist for cannabis abuse and dependence.

The Effects of Adolescent Cannabis Use on Functional Outcomes

- There can be negative later life outcomes associated with adolescent cannabis use.

Conclusions Based on the Existing Literature

- Based on the evidence of physiological, cognitive, and psychological vulnerabilities of children and adolescents, we recommend that cannabis use be minimized or completely avoided in this population. In fact, we recommend that cannabis use be prohibited in those younger than 21 years, similar to alcohol.
- For those physicians who insist on recommending cannabis use in this vulnerable population, we recommend that they:
    - Conform to standards of practice as described in the California Society of Addiction Medicine's "Youth First" paper.
    - Attempt numerous trials of well-accepted, evidence-based treatments for the symptoms or diagnosis they are treating prior to initiating "treatment" with cannabis.
- With regard to the role of physicians (or lack thereof) in the "medical marijuana" process in general (i.e., in adults), we support the recommendations found in the commentary by

Drs. Kleber and DuPont, published in the June 2012 edition of *The American Journal of Psychiatry*.

- We recommend that the United States Drug Enforcement Agency (DEA) consider reclassification of THC so that valid research can proceed.

MISSION STATEMENT

Cal- ACAP's purpose and mission is to represent the interests of the four regional organizations in California's legislation, public policy, advocacy, scientific knowledge and clinical services as they relate to the mental health of California's children, adolescents, and families. State referenda such as Proposition 215 (which passed in 1996) and Senate Bill 420 (which passed in 2003) have permitted "medical" use of cannabis by physician recommendation. Additionally, SB 1449 (which became effective in January 2011) revised and reduced penalties for the possession of cannabis.

This task force was convened to review current scientific knowledge about the impact of cannabis use on children and adolescents, particularly with respect to brain development, cognition, the development of mental illness, and comorbidities with mental illness. A review of relevant literature, consisting of over two hundred eighty research reports and policy papers, was undertaken.

NOTES

Note 1: "Marijuana" is a slang term for the dried leaves and flowers of the cannabis plant. These leaves and flowers have significant quantities of delta-9-tetrahydrocannabinol (a.k.a., Δ-9-THC, or THC). Throughout this position paper, the term "cannabis" will be used, except where use of the term "marijuana" is indicated (e.g., official title of an Act).

Note 2: The brain of a child or adolescent is fundamentally a "work-in-progress." It evolves as ongoing developmental processes help determine its transient and ultimate anatomy and function. Because of this continuing refinement, studies on the effects and safety of drugs in adults cannot be applied directly to children and adolescents. Exposure to drugs that affect the adolescent's brain during this unique developmental period may alter the course of brain development and produce effects that persist into adulthood. Therefore, to assess fully the impact of a drug requires studies of immediate and long-term effects specifically conducted in this population. Unfortunately, as discussed more fully in the body of this paper, such studies currently are limited.

Note 3: For the purposes of this paper "child and adolescent" will be defined as individuals under age 21 years. Although admittedly a somewhat arbitrary definition and not entirely consistent with the definition employed in some of the studies cited in this paper (which define adolescents

as individuals under age 18 years), we utilize it to be consistent with other organizational position papers as well as existing state and national alcohol-use policies.

INTRODUCTION

Tetrahydrocannabinol (THC), the primary active agent found in cannabis, is classified as a "Schedule I Controlled Substance" by the United States Drug Enforcement Agency (DEA). This designation means that, according to the DEA, cannabis does not have an accepted medical use, nor has it been found/declared safe for medical use. Similarly, the Food and Drug Administration (FDA) issued a statement that it has "not approved smoked marijuana for any condition or disease indication" and that "[t]here are alternative FDA-approved medications in existence for treatment of many of the proposed uses of smoked marijuana."

In 1996, California voters passed proposition 215, also known as the Compassionate Use Act, which permits patients with a doctor's recommendation to possess and grow cannabis for personal use. This proposition, along with subsequent bills passed by the California State Legislature and signed into law by sitting governors (e.g., California Senate Bills 420 and 1449), has raised numerous complex legal, regulatory, political, and public health issues. For example, cannabis remains illegal under federal law, which places California state law in direct opposition with federal law and raises the question of whether (and if so, how) the United States Department of Justice will enforce federal regulations within California regarding the cultivation and possession of cannabis.

Proposition 215 also has led to still unresolved issues of how to regulate properly the production and distribution of cannabis. For example, should medical cannabis be taxed and if so, to where (e.g., which state funds or programs) should the revenue be directed? If used, what dose is effective? What safeguards are in place to ensure purity and monitor potency? A recent commentary by Kleber and DuPont articulates these challenges (Kleber and DuPont 2012).

In addition, Proposition 215 appears to assume that there is a medical benefit to using cannabis in patients, hence the popular term "medical marijuana." While there is some evidence for the efficacy of cannabis in particular medical conditions in adults (such as chemotherapy-induced nausea) and research is ongoing (Leung 2011), in children, reports of its therapeutic potential remain anecdotal and largely based on extrapolation from studies in adults. For example, a report from the American Academy of Pediatrics states "[m]arijuana has been touted as ameliorating chemotherapy-induced nausea, wasting and anorexia associated with AIDS, intraocular pressure in glaucoma, and muscle spasticity arising from such conditions as multiple sclerosis" (Joffe and Yancy 2004). To date, there is little to no evidence to support the use of cannabis for the treatment of psychiatric disorders in any population, let alone children and adolescents. It is well-known and empirically validated, however, that "cannabis intoxication can cause distorted perceptions, impaired coordination, difficulty with thinking and problem solving, and problems with learning and memory" (NIDA Info Facts 2010).

Because cannabis can impact negatively the physical and mental health of users and because there are few well-accepted medical indications for cannabis, California physicians are placed in the problematic situation of recommending a substance that has risks and benefits that are not understood fully.

Potential policy solutions to this quandary are discussed elsewhere (e.g., California Society of Addiction Medicine Youth First position paper 2011, California Medical Association position paper 2011) and are beyond the scope of this manuscript. The goal of this paper is to review the current scientific knowledge of the impact of cannabis use on children and adolescents. Emphasis is placed particularly on those with an underlying predisposition to develop psychiatric disorders (and who therefore may be more susceptible to the potential short and long-term negative effects of cannabis use). We will focus on the sequelae of cannabis use on child and adolescent brain development, cognition, the development of substance use disorders, comorbidities and mental illness, and functional outcomes. Information on the treatment of cannabis use disorders during adolescence is beyond the scope of this paper and can be found elsewhere (e.g., Cannabis Youth Treatment Series).

EPIDEMIOLOGY AND TRENDS OF USE

Cannabis is the most widely used illicit drug in the United States. According to the 2010 National Survey on Drug Use and Health (NSDUH), 17.4 million Americans used cannabis in the past month, and the prevalence of use is increasing. Between 2007 and 2010, the prevalence of "past-month use" increased from 5.8% to 6.9% (Administration 2011). Among youth age 12-17 years, the NSDUH revealed that the rate of current cannabis use (defined as past-month use) increased from 6.7 to 7.4% in the same time period (though this rate is down from an 8.2% high in 2002). At the same time, the percentage of people age 12-17 years who perceive great risk in regularly smoking cannabis decreased from 54.7% to 47.5% and almost one-half of these young people report "fairly easy" or "very easy" access to cannabis. In California, the most recently published California Schools Survey estimates the use for year 2009-10 to be 6% in 7th graders, 14% in 9th graders, and 24% in 11th graders. There were small increases in the percentage of individuals in each grade level who reported lifetime use of "seven or more times" and "overall and weekly use in the past 6 months." Among high school juniors, there were increases in reports of "peer use, perceived availability, and lack of harm" (Austin and Skager 2011). A worldwide study describes that "occasional cannabis use has become normative among a substantial minority of adolescents." The article further states that peer acceptance of drug culture "is an important facilitator of cannabis use" and that within a country, "perceived availability [of drug] stands out as the single most important predictor for use" (ter Bogt et al. 2006).

Different typologies of adolescent users have been described (Wittchen et al. 2009; Perkonigg et al. 2007; Kokkevi et al. 2006; Perkonigg et al. 1999). Users are generally grouped along a continuum of frequency of use into either "abstinent/nonusers," "occasional users," or "regular users" (which progressed to "heavy and continued users"). It is interesting to note that there was a wide range in the definitions of "regular" and "heavy use" in the studies reviewed. Some studies divided frequency of cannabis use into "greater than five (5) times in a lifetime" or "less than or equal to five (5) times in a lifetime." Other studies divided frequency of use into "more

than ten (10) times in a lifetime" or "less than or equal to ten (10) times in a lifetime." Still others quantified cannabis use by weekly frequency, such as three (3) times use per week up to five (5) times use per week. One study attempted to divide users into three categories based on lifetime use ("greater than ten (10) but less than 100 times," "between 100 and 200 times," and "greater than 200 times").

Another critical factor found in trends of cannabis use is age of onset of use (e.g., <13 years, 13-15 years; 16-19 years). Tucker et al. identified two periods of particular vulnerability: early adolescence and the transition to adulthood (Tucker et al. 2005). These data suggest that there are different "stages" of use, and effective education, prevention and treatment should be customized accordingly. Self-report data of use frequency should be interpreted with caution, because studies have shown that multiple sources of information are more helpful to validate use amounts that may be both over- and under-reported (Buchan et al, 2002).

Amid these trends in adolescent cannabis use, there appears to be a national trend toward decriminalization of cannabis use for adults. It remains unclear how changes in the legal status of cannabis for adults will affect the prevalence of its use in those under 18 (or 21) years of age. Given this widespread and increasing use, it is important to review the current state of knowledge regarding the impact of cannabis use on child and adolescent brain development, mental health, and social and educational functioning.

MECHANISMS OF ACTION

Although cannabis contains numerous compounds, many of which are likely to be psychoactive, as mentioned previously, the main compound mediating its effects on the brain is delta-9-tetrahydrocannabinol (THC). This lipophilic molecule is rapidly absorbed when cannabis is smoked and more slowly absorbed when eaten (Elkashef et al. 2008). It becomes widely distributed throughout the body, easily crossing the blood-brain barrier and accumulating in fat.

THC and the other cannabinoids in marijuana activate the two known endogenous cannabinoid receptors, CB1 and CB2 (Matsuda et al. 1990). CB2 receptors are found mainly in immune cells (Galiegue et al. 1995; Munro et al. 1993). The CB1 receptor is the primary endocannabinoid receptor in the brain, and CB1 antagonists block the psychoactive effects of cannabis (Huestis et al. 2001). This G-protein coupled receptor is one of the most abundant neuromodulatory receptors in the brain and is found in high concentrations in the hippocampus, amygdaloid complex, frontal cortex, sensory cortex, basal ganglia, and limbic areas (Glass et al. 1997). CB1 receptors are located on the axon terminals of pre-synaptic neurons (Wilson and Nicoll 2002). There, they are activated by the retrograde release of endocannabinoids (such as anandamide and 2-arachidonylglycerol). Activation of CB1 receptors decreases calcium-mediated synaptic vesicle release, thereby modulating pre-synaptic neural activity.

In the neocortex and hippocampus, CB1 receptors are located exclusively on a subpopulation of GABAergic interneurons, the activity of which is believed to have important consequences for perception, cognition, and plasticity (Wilson and Nicoll 2002). These GABAergic neurons are

critical for the synchronization of large neural networks that underlie rapid oscillations in the gamma range, which, in turn, are thought to be important in perception and cognition (Banks et al. 2000; Buzsaki and Chrobak 1995). The CB1 receptor is thought to modulate these oscillations via suppression of inhibitory neurons. Additionally, GABAergic interneurons modulate long-term potentiation, which is thought to be critical for the neural plasticity underlying learning and memory formation. By activating the CB1 receptor, THC exerts its effects on these processes.

THE EFFECTS OF CANNABIS ON BRAIN DEVELOPMENT

Adolescence is a critical period of structural brain development. Environmental exposures, such as cannabis use, may alter the course of this process. A number of research studies have examined the impact of cannabis use on the structure and physiology of the adolescent brain by using neuroimaging techniques. Adolescent and early-adulthood cannabis use is associated with altered cortical gyrification, decreased whole-brain gray matter percentage, and increased whole-brain white matter percentage (Mata et al. 2010; Wilson et al. 2000). Cannabis use during adolescence has been associated with gender-specific effects on pre-frontal cortex volume and alterations in cerebellar size; these effects were correlated with poorer performance on tests of executive functioning and learning (Ashtari et al. 2011; Medina et al. 2009; Medina et al. 2010). Heavy cannabis use during adolescence also appears to disrupt white matter integrity in the arcuate fasciculus (a structure that connects the frontal and temporal lobes) and to lead to decreased hippocampal volumes (Ashtari et al. 2011; Ashtari et al. 2009). Several functional MRI (fMRI) studies have demonstrated altered patterns of cortical activation during cognitive tasks in cannabis-using adolescents; interestingly, the cannabis users' performance matched that of non-users (Jager et al. 2010; Schweinsburg et al. 2010; Tapert et al. 2007). These studies suggest that cannabis use during adolescence may alter the functional circuitry utilized during cognition.

EFFECTS OF CANNABIS ON COGNITION

Because of the diffuse location of cannabinoid receptors in the human brain, cannabis has a wide range of both acute and chronic effects on cognitive processes. Acutely, in adults, THC administration leads to deficits in attention, working memory, and all other stages of memory consolidation/formation (Morrison et al. 2009; Ranganathan and D'Souza 2006), slower processing speed and longer planning times, and increased impulsivity (Crean et al. 2011; McDonald et al. 2003; Ramaekers et al. 2006).

Studies in adolescents also have demonstrated significant effects of cannabis use on cognition. In a longitudinal study, the IQ of young people prior to initiation of cannabis use was compared to their IQ years later (Fried et al. 2002). In this study, current heavy cannabis use was associated with a 4-point decline in IQ compared to gains in IQ in light users, non-users, and former heavy users. Harvey et al. examined the performance of adolescent regular cannabis

users (>1 use/week) on a battery of cognitive tests after 12 hours of abstinence and found that they performed significantly worse on tasks of attention, spatial working memory, and learning than controls (Harvey et al. 2007). In other studies, neuropsychological tests after longer periods of abstinence (up to 3-6 weeks) in adolescents who regularly use cannabis have demonstrated slower processing speed, decreased attention, poorer verbal memory (both working memory and learning), lower verbal IQ, and impaired planning and sequencing (Hanson et al. 2010; Medina et al. 2007; Schwartz et al. 1989). Heavy cannabis smokers had more executive functioning errors and less adaptive responses (Lane et al. 2007). Many of these decrements in performance were correlated positively with the lifetime amount of cannabis use. Some of the deficits normalized after three weeks of abstinence (Hanson et al. 2010).

The effects of cannabis use on cognition may depend upon when during development use begins. Pope et al. found that the verbal IQ of early-onset, long-term adult cannabis users was lower than that of late-onset users and non-users (Pope et al. 2003). Similarly, Fontes et al. compared executive functioning in daily cannabis users who began use before age 15 and those who began at age 15 or older (Fontes et al. 2011). Those individuals who began using prior to age 15 performed significantly worse on tests of attention, impulsivity, and other executive functions. It is not clear whether this worse performance after early-onset use was related to cannabis exposure during a vulnerable developmental period, longer duration of use (i.e., a cumulative effect), or both.

When neuropsychological performance is measured for adolescents who use alcohol and cannabis concurrently, the results are less clear, possibly related to the addition of a confounding variable (i.e., alcohol use). In two studies, marijuana had an independent negative effect on memory different from the poorer attention and executive functioning effects found with alcohol use alone. (Thoma et al. 2011, Schwenisberg et al. 2005). Interestingly, another study suggested that reduced verbal learning and decreased memory performance found in adolescent heavy alcohol use was ameliorated in youth who also had heavy marijuana use (i.e., in addition to heavy alcohol use) (Mahmood et al. 2010).

Many of the aforementioned studies on the effects of cannabis use on cognition are limited by small sample sizes and relatively brief follow-up periods. Therefore, the long-term effects of regular cannabis use on adolescent (and ultimately adult) cognition remain unclear. Additionally, many of these studies are cross-sectional and cannot rule out the possibility that pre-existing differences in cognition pre-disposed certain individuals to use cannabis more frequently (i.e., reverse causation). More longitudinal studies of longer duration are needed to clarify this issue. In spite of these limitations, current evidence suggests that regular cannabis use is detrimental to adolescent cognition and that its effects last well beyond the period of intoxication.

ADOLESCENT CANNABIS USE AND THE DEVELOPMENT OF MENTAL ILLNESS

There is mounting evidence that cannabis use is associated with the development of psychotic illnesses, including schizophrenia. Meta-analyses of longitudinal studies have confirmed that

there is an increased risk of psychosis in people who have used cannabis, with a "dose-response" effect apparent (i.e., the magnitude of the negative effects increases with greater cumulative cannabis use) (Moore et al. 2007). The age of onset of psychosis is 2.7 years younger in cannabis users than in non-users, and the progression to daily cannabis use is associated with the development of prodromal and frank psychotic symptoms (Compton et al. 2009; Large et al. 2011). The aforementioned alterations in brain anatomy and cognitive processing caused by long-term cannabis use appear to be related to the development of psychotic illness.

Anecdotally, cannabis is often thought to alleviate anxiety and depression and these reported effects are often cited as reasons for use. With regard to mood, in adult patients with chronic pain associated with fibromyalgia, THC has been shown to improve mood as well as provide modest pain relief (Kraft 2012). However, in adults, high doses of THC can induce intense anxiety and fear as well as panic attacks. In fact, a significant proportion of individuals experience episodes of anxiety after smoking cannabis (reviewed in Crippa et al. 2009). These symptoms limit its therapeutic use. In adolescents, those with higher levels of "trait anxiety" are more likely to abuse cannabis (Dorad et al. 2008), which suggests that they may be using cannabis to "self-medicate." However, a number of longitudinal studies examining the relationship between cannabis use during adolescence and the later development of depression and anxiety disorders have suggested that adolescents who use or have used cannabis are more prone to develop these disorders than adolescents who do/have not (Fergusson et al. 2002; Hayatbakhsh et al. 2007; Lee et al. 2008; Moore et al. 2007; Patton et al. 2002; Rubino et al. 2012). Although these studies indicate that cannabis use during adolescence is associated with an increased likelihood of mood and anxiety disorders both during adolescence and later in life, it is not currently known whether cannabis use causes the disorders or whether the disorders (or early manifestations thereof) predispose children to use cannabis.

THE POTENTIAL FOR ABUSE OF CANNABIS IN CHILDREN AND ADOLESCENTS

During adolescence, different areas of the brain develop at different rates, with the "reward-hedonic" networks (e.g., nucleus accumbens, striatum) maturing prior to the pre-frontal "control system" (Casey and Jones 2010). The early maturation of the reward system makes adolescents more sensitive to the rewarding experiences of illicit drugs and alcohol at a particularly vulnerable time, when executive control systems required for impulse control and judgment are less well-developed than in adults. This confluence of factors may, in turn, predispose adolescents to develop alcohol or drug abuse/dependence more readily and more frequently than adults.

As with early nicotine and early alcohol use, early cannabis use is associated with an increased risk of developing a cannabis use disorder (Chen et al. 2005). Several studies suggest that use in early adolescence leads to a higher risk of steady, increasing use over time and a higher vulnerability to the development of substance abuse or dependence (i.e., "gateway hypothesis" (Perkonigg et al. 2008, Tucker et al. 2005, Kokkevi et al. 2006, Fergusson et al. 2006, Wittchen et al. 2008; Suris et al. 2007)). Bassiony found that the progression from cannabis use to

cannabis use disorder occurs more quickly in adolescents than in adults, and a study by Behrendt et al. 2009 showed that youth who used cannabis early in adolescence developed cannabis dependence one year faster than those who used tobacco early in adolescence developed nicotine dependence. Data from a recent study suggest that individuals who begin using cannabis between the ages of 12-18 years have at least three times the risk of developing a cannabis use disorder compared with individuals who begin using between ages the ages of 22-26 years.

Cannabis withdrawal symptoms also have been documented in adolescence. Over a four-week period, symptoms such as sleep difficulties, nervousness, excessive perspiring, restlessness (twitches and shakes), anxiety, tension, body aches, nausea, thoughts of cannabis, cravings for cannabis, and malaise declined (Milin et al. 2008). This study seems to suggest that adolescents are more likely than adults to develop withdrawal symptoms. To the extent that the presence of a withdrawal syndrome increases the risk for continued or recurrent use, adolescence appears to be a particularly vulnerable time for the development of substance use disorders (Winters and Lee 2008).

THE EFFECTS OF ADOLESCENT CANNABIS USE ON FUNCTIONAL OUTCOMES

Cannabis' impact on adolescent brain development and cognition, coupled with adolescents' generally heightened vulnerability to develop substance abuse and dependence, can lead to worse functional outcomes later in life. These functional outcomes may have significant ramifications on the socio-economic development of individuals who begin using cannabis during adolescence. The results of a number of longitudinal studies seem to indicate that more frequent use of cannabis is correlated with an increased likelihood of leaving school without a degree, a lower income, greater dependence on welfare and unemployment, and lower life satisfaction as an adult (Brook et al. 2008; Fergusson and Boden 2008; Fergusson et al. 2003). Although these studies attempted to control for co-morbidities and predispositions correlated with cannabis use, the data must be interpreted with caution because of the possibility of unaccounted for correlations.

CONCLUSIONS BASED ON THE EXISTING LITERATURE

Chronic cannabis use during adolescence produces alterations in brain anatomy and functioning that, in turn, impair cognition and that may contribute to the development of mental illness (particularly psychosis). Because children and adolescents have brains that are still developing, they are more sensitive to reinforcement from alcohol or drug use and have a greater propensity to develop substance abuse or dependence than adults. Finally, cannabis use early during adolescence is associated with lower social and occupational functioning in adulthood. Many of these phenomena exhibit dose-response relationships (i.e., the magnitude of the negative effects increases with greater cumulative cannabis use).

Although there is still much to learn about the impact of adolescent cannabis use on brain function, mental health, and functional outcomes, the great majority of evidence from scientific studies indicates that cannabis use should be minimized or completely avoided during this critical period of human development. In fact, we recommend that cannabis use be prohibited in those younger than 21 years, similar to alcohol.

For those physicians who insist on recommending cannabis use in this vulnerable population, we recommend that they conform to standards of practice as described in the California Society of Addiction Medicine's "Youth First" paper. We also advise that these physicians attempt numerous trials of accepted, evidence-based treatments for the diagnosis or symptoms they are treating prior to initiating "treatment" with cannabis. With regard to the role of physicians (or lack thereof) in the "medical marijuana" process in general (i.e., in adults), we support the recommendations found in the commentary by Drs. Kleber and DuPont, published in the June 2012 edition of *The American Journal of Psychiatry*.

Despite the potential risks of cannabis use in childhood and adolescence, the data on cannabis' impact on youths' cognition, development of mental illness and substance use disorders, and overall level of functioning is far from definitive. Therefore, we would recommend reclassifying THC as a Schedule II Controlled Substance so that it can be studied further in the adult population (i.e., those age 21 years and older). Hopefully, some of these future studies can yield useful results which can be extrapolated (to some extent) to the adolescent population in order to guide and refine future local, state, and national policies regarding adolescent cannabis use.

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