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Review of Marijuana Use in the Adolescent Population and Implications of its Legalization in the United States

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Abstract

With the changing attitudes towards the legality of marijuana in the United States (US), there has been an abundance of rhetoric surrounding the potential societal effects of decriminalized cannabis use. These statements vary in degree from visions of the downfall of our moral and productive civilization, to the elimination of drug crime and a windfall of economic growth. From either side of this divisive issue, there has been a strongly expressed concern of the unknown consequences of a more readily available cannabis supply to the adolescent population, followed by what measures should be taken to curtail this risk. Given this country's unique relationship with mind-altering substances, a great deal of comparisons have been made with alcohol, as it is also a substance of recreation as well as abuse that is currently legal but has also gone through a period of prohibition. This paper looks to examine the validity of this comparison, as well as reviews the current research on the effects of early cannabis use on the adolescent brain.

Keywords Marijuana; Teenagers; Legalization; THC

Introduction

As the United States attitude towards marijuana's legality is changing, there has been no scarcity of rhetoric surrounding the potential societal effects of decriminalized cannabis use. These statements vary in degree from visions of the downfall of our moral and productive civilization, to the elimination of drug crime and a windfall of economic growth. From either side of this divisive issue, there has been a strongly expressed concern of the unknown consequences of a more readily available cannabis supply to the adolescent population, followed by what measures should be taken to curtail this risk. Given this country's unique relationship with mind-altering substances, a great deal of comparisons have been made with alcohol, as it is also a substance of recreation as well as abuse that is currently legal but has also gone through a period of prohibition. This paper looks to examine the validity of this comparison, as well as reviews the current research on the effects of early cannabis use on the adolescent brain.

Marijuana is still the highest used illicit substance among adolescents, despite the plethora of data citing its potential risks. Following a decline in usage from the 1990s to the mid-2000s, marijuana use among adolescents is again on the rise as of 2013, with 7.0% of 8th graders, 18.0% of 10th graders, and 22.7% of 12th graders self-reporting marijuana use in the past month. The results in 2008 were 5.8%, 13.8%, and 19.4%, respectively. A more concerning trend are those reporting daily use, 6.5% in 2013, up from 5.0% [1]. In comparison, alcohol use in the past month in 2013 among 8th graders was 10.2%, 10th graders 25.%, and 12th graders 39.2%, with 2.2% of 12th graders reporting daily use [1]. A reasonable hypothesis for the increase in this trend is a reduction in the perceived risk of the drug. The increasing legality of the substance could potentially give adolescents the perception of minimalized risk during a time period when the developing brain is more prone to risk taking in general [2].

We still know relatively little about marijuana's effects on the brain, despite the pervasive nature of cannabis use across our population. It has long been known that some of the direct side effects of marijuana use are impairments of memory, executive functioning, psychomotor speed and dexterity [3]. Where researchers have been able to discern some long-term effects, such as deficits to working memory [4] and overall intelligence quotient [5], it has been difficult to determine what this translates into as far as alterations in structural and neuroendocrine chemistry. With increasing access to imaging techniques, researchers are looking to determine whether there is a definite structural complex that correlates with cannabis's interruption of the maturation of neural tissue, or if the brain is more resilient to the neurotoxic effects of marijuana.

The Adolescent Brain

Adolescence is a time of massive physiologic, neurologic, social, and educational growth whose importance is becoming increasingly illuminated. The advances in brain-imaging technology have further helped to explain how the adolescent differs from the adult. There has been an increased focus in recent years on the continuing development of the brain long after the body reaches physiologic maturity. Whereas skeletal growth of the body generally stops around the average age of 18, the brain continues to develop throughout the mid-twenties [6]. With the increasing availability and improvements in MRI technology, researchers have been able to pinpoint changes in the adolescent/young adult brain that continue long after the body has finished maturing. For example, different parts of the cortex seem to mature at different times, with more rudimentary regions maturing first, such as areas responsible for movement, somatosensory, and information processing [7]. Later progress occurs in regions associated with the

"fine tuning" of behavior, such as impulse control and planning ahead with the maturation of the prefrontal cortex [8].

One of the best substantiated structural changes in this age group is an increase in neuronal white matter, due to increased myelination and axonal organization, which is most pronounced in the prefrontal cortex, internal capsule, basal ganglia, thalamic pathways, ventral visual pathways, and the corpus collosum. These are the areas most associated with attention, motor skills, cognitive ability, and memory [9]. The development of grey matter follows the opposite trajectory of white matter during this time period, as grey matter hits it peak volume and then declines in early adolescence in a process known as "pruning" [7,10]. Where the purpose of this decrease in grey matter is not entirely clear, the hypothesis is that the process is thought to eliminate repetitive connections, and results in a decrease in cortical volume and thickness. The combination of increased white matter connections and reduction of redundant grey matter orchestrates a more efficient adolescent brain, now capable of increased cognitive functioning [7,9,10].

In this light, it stands to be a logical assumption that psychotherapeutic techniques designed for adults to affect neural circuitry, may affect adolescents differently. For example, cognitive behavioral therapy (CBT) is a technique that is commonly used to treat substance use disorders and aims to increase inhibitory control and mediate automatic emotional responses by effectively exercising the prefrontal cortex. In adolescents, the prefrontal cortex is still developing and CBT may help to strengthen these areas that are both developing and may have potentially been damaged by substance abuse [11]. Likewise, mindfulness therapy, which focuses on acknowledging all incoming emotions and accepting them, but avoiding reacting to them, has been shown to disconnect the emotional control of the limbic system from the dopamine-reward circuitry, potentially benefiting the emotionally reactive adolescent [11].

The primary psychoactive compound in cannabis is delta-9-tetrahydrocannabinol (THC), which is an exogenous activator of the cannabinoid system in the brain, whose receptors are found pervasively throughout the brain, most prominently in the hippocampus, amygdala, cortex, basal ganglia and cerebellum [12]. Cannabis use has been found to affect motor coordination and create sensory perception and integration difficulties, features long associated with the cerebellum [13]. Exposure to THC, either smoked or infused, increases cerebellar blood flow and activity [14]. More recently, chronic marijuana exposure during adolescence has been shown to result in abnormal brain structure development. Adolescents with chronic marijuana exposure (>60 lifetime uses) were found to have significantly larger inferior posterior vermis volume than controls after a one-month abstinence [15]. These morphologic changes are particularly concerning based on the idea that they are occurring during a period of neurological development and were obtained after the majority of the lipophilic THC would have passed through the body.

Several studies have found additional evidence of a disruption in these processes in cannabis users. Cousijn et al., 2012 [16] found that grey matter volume in the anterior cerebellum was larger in heavy (10+ days per month) young adult cannabis users in the Netherlands who had not been through a period of abstinence, which is in support of Medina's 2010 study. This study also found differences in the hippocampus (involved in memory) and the amygdala (involved in craving) compared with controls.

White matter changes in adolescent cannabis users have been more difficult to elucidate. MRI studies have shown increases in axonal diameter, myelin sheathe thickness, and improved tract organization producing enhanced signal transduction, and is thought to participate in the intellectual, social, and emotional changes that take place during the adolescent growth period [9,10,17]. Wilson et al. [18] using MRI/PET found that adolescents that began using marijuana before the age of 17 had smaller whole brain and cortical grey matter volumes as well as larger white matter volumes than those who started after the age of 17. Matochik et al. [19] using Voxel-based morphometry analyzed brain tissue in heavy marijuana users and specifically found lower white matter density in the parietal lobe, yet higher density around the parahippocampal and fusiform gyri on the left side. Longer duration was associated with higher white matter tissue density on the left precentral gyrus. However, other studies found no changes in white matter composition [20]. Alcohol's known effects on myelination may further blur the effects of marijuana given the frequent concurrent use in both the adolescent and adult population. This array of findings makes it clear that the topic of THC's effects on CNS maturation needs to be explored further.

Cannabis and Psychosis

A connection between schizophrenia and cannabis use has been known for decades, with articles connecting the two showing up before 1970. Studies have repeatedly shown that those who use cannabis are more likely to become psychotic in their lifetime (OR 2.59) compared to alcohol use (OR 1.93) [21]; as well as those individuals with more severe symptoms of schizotypy are more likely to have used cannabis [22,23]. But a causal relation for this effect has been difficult to elucidate despite years of study.

A longitudinal study of first episode psychosis patients in Italy found that individuals who used cannabis were significantly younger at the time of their first psychotic episode (26.57 years) as opposed to individuals who did not use cannabis (34.13) [24] even after adjusting for age and diagnosis. Similarly, a study from the UK found that a history of cannabis use (with a third of the cannabis-using patients using daily or almost daily) predicted an earlier onset of both the prodromal period as well as the first psychotic episode of 21.22 and 21.97 years, respectively, versus those with no history of cannabis use showing onsets at 26.35 and 27.12 years, respectively [25].

Δ-9-THC has long been recorded to cause symptoms such as perceptual alterations, fragmented thinking, paranoia, and altered perception of time [26] that are remarkably similar to many of the positive symptoms individuals with schizophrenia experience. In addition, the popular cultural stereotype of the chronic cannabis user as apathetic, languid, and amotivational could potentially also be used to describe many of the negative symptoms of schizophrenia [27]. Despite the idea that marijuana causes the positive symptoms usually associated with psychosis, the research has not supported this hypothesis. A history of cannabis abuse in psychotic patients tends to correlate with less severe negative symptoms, but not with more positive symptoms [23,24].

The dopamine system, which is involved in the primary reward complex, has been postulated to be essential in understanding the physiologic causes of psychosis as well as drug addictions. The dopamine hypothesis as an explanation of psychosis, though the details of which are often debated, states that disruption of dopamine and dopaminergic structures are a critical component of the symptoms

of schizophrenia, and more generally, psychosis [28]. These disruptions appear to be significant in the prefrontal cortex [28]. This area appears to undergo a significant amount of maturation during that adolescent period, with dopaminergic connections increasing in the prefrontal cortex throughout maturity [6]. In addition, activity of catechol-O-methyltransferase (COMT), a dopamine degrading enzyme appears to increase after approximately age 30 [29], suggesting a potential decrease in the dopamine/reward inputs as we age. It would be a logical step to postulate that substance use that targets this region of the brain at a time when that region is undergoing significant plasticity and maturing could potentially lead to long term changes that would not be corrected by simple cessation of the drug.

From a treatment perspective, these trends in cannabis use can be difficult to grasp. Traditionally, patients with their first psychotic breaks occurring early in age generally have poorer outcomes, making the correlation between cannabis and age of psychosis rather significant from a treatment perspective [30]. Conversely, the negative symptoms of psychosis are conventionally the most difficult to treat, and those psychotic patients with cannabis histories tend to have less severe negative symptoms [25]. The popular theory at present tends to be that cannabis-use may preemptively induce psychosis in genetically susceptible individuals, and it is at present unlikely and incorrect to make a blanket statement that cannabis causes psychosis [31]. However, more research needs to be done to elucidate these connections.

Conclusion

With the presently changing landscape of marijuana dispensation in the United States, it is prudent to maintain a circumspect approach to the variety of claims surrounding marijuana, or any other substance. Similar to alcohol, marijuana must be looked at pragmatically, considering its pervasive use as well as its complex neurophysiological effects. A 2013 Gallup poll found that 38% of Americans admit to having tried marijuana at some point in their lives, a percentage that remained relatively equal across gender, age groups, education, income, and political viewpoints. The addiction rate of marijuana is 9.1%, compared with nicotine at 31.9%, alcohol at 15.4%, cocaine at 16.7%, and heroin at 23.1% [32]. Although it has the lowest rate of addiction, 9.1% of the 38% of Americans who have admittedly tried it at some point, is not an insignificant number (approximately 119 million). Unlike other substances of potential addiction, cannabis appears to lose its addictive potential as the individual ages, decreasing almost to zero by the age of 25. In contrast, alcohol maintains its addictive potential for decades after young adulthood [27].

There are a myriad of challenges to researching a substance such as cannabis, especially in a highly vulnerable subject group such as adolescents. In the past, adolescents have often been looked at as "small adults", but with the increasing discoveries of the ever-evolving adolescent brain, this misconception has slowly been laid to rest. Studying 'illegal' drug use in particular brings its own challenges.

Seeking causation for any emerging psychopathology is notoriously difficult in this population, as in many cases drug-users tend to "self-select" their drug of choice, making it difficult to prove one is in fact causing the other [33]. In addition, it is often difficult to weed out comorbid substance use and abuse of other drugs from the specific drug being studied. An example used earlier in this paper includes alcohol's long-known effect on myelination, effectively excluding any alcohol use from a study of the effects of cannabis on white matter.

Irrespective of an individual's stance on cannabis decriminalization, efforts need to be made to dismiss the idea of marijuana as a "harmless" substance. However, the current federal illegality of cannabis makes researching it often difficult. Marijuana proponents will describe numerous medicinal uses, yet surprisingly few have even been well researched. The current schedule I classification places marijuana on the same grounds as heroin, LSD, and ecstasy; and defines it with no accepted medical use with a high potential for abuse, despite scientific research that states otherwise. In this context, it is difficult to understand that opiates, amphetamines, and cocaine are considered to have more medical uses and are less dangerous. Despite its scheduled restrictions, the popularity of the substance has allowed for a great deal of 'naturalistic' studies of the endocannabinoid system, as well as its implications on brain development [34,35]. The recent trend of legalization may potentially at least mitigate this current barrier of our understanding of neuroscience. With a growing body of research into the long-term consequences of marijuana use in the adolescent brain, our policy makers can impose age limitations for the legalization of marijuana that are tied to scientifically valid reasoning. By tying policy to reason, age limits can lessen the potential impact of marijuana use in developing people. The current age limitation for alcohol use at 21 years is still several years prior to the termination of neurodevelopment, but the cultural acceptance of this threshold allows for several protective years of neurological maturation. Much like alcohol, marijuana is a substance that is prevalent among the adolescent population [1], with decreasing criminalization, care must be taken to better understand and prevent long-term sequelae of its use in the developing brain.

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