Adolescent Marijuana Use and Vulnerability for Neuropsychiatric Disorders

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An overview of some of the recent scientific data examining the relationship between adolescent marijuana use and later onset of neuropsychiatric disorders.

**CONFERENCE COVERAGE**

In context of the evolving legal regulations on the medical and recreational use of marijuana, there has been an increase in marijuana use and marijuana-related disorders in the US, especially among adolescents, where daily use is at a 30-year high among US high school seniors. Because adolescence represents a period of significant neurodevelopment, the effects of marijuana use during adolescence and possible short- and long-term consequences are a growing concern. Here we discuss some of the recent scientific data examining the relationship between adolescent marijuana use and later onset of neuropsychiatric disorders.

Converging scientific evidence from preclinical studies, human neuroimaging, and large longitudinal studies suggests that adolescent-onset marijuana use, particularly heavy marijuana use, is associated with a number of neuropsychiatric sequelae including neurocognitive deficits and reductions in IQ, increased risk for psychosis, affective disorders, marijuana and non-marijuana drug addiction, and lower academic attainment. Is a relationship between adolescent marijuana use and neuropsychiatric disorders biologically plausible?

In the human brain, cannabinoid 1 receptors, the receptors which marijuana’s biochemical components act on to cause its psychoactive effect, are expressed widely with the highest density of receptors found in the striatum, amygdala, hippocampus, hypothalamus, and cerebellum—all brain regions that are implicated in marijuana addiction and other neuropsychiatric disorders. Neuroimaging studies of adolescent marijuana users have found structural and functional differences in some of these brain regions when compared to matched controls. Preclinical studies have shown that when rodents are exposed to cannabinoid compounds during adolescence, brain and behavioral changes are observed. The animals show signs of being more anxious and depressed in animal behavioral stress tests compared to non-exposed rodents, and their brains show altered maturation of the prefrontal cortex and subcortical structures, as well as altered connections between those structures. The brains of adolescent cannabis-exposed rodents also show changes in a number of different neurotransmitters (eg, dopamine, glutamate, GABA) and the
stress-response system (ie, hypothalamic-pituitary-adrenal gland [HPA] axis). Interestingly, many of these brain and behavior changes do not develop when chronic cannabinoids are administered to older (adult) animals, suggesting an age-dependent vulnerability to adverse effects of marijuana which may be specific to childhood and adolescence.

Perhaps the strongest evidence that links adolescent marijuana use to neuropsychiatric disorders comes from a series of large longitudinal studies, many of which were done in Australia and New Zealand.5,6 These studies have followed children from birth through young adulthood (some for up to 30 years) and many have attempted to control for a number of cofounding variables, allowing for the isolation of the effects of marijuana on specific neuropsychiatric outcomes.

While these studies have consistently shown a dose-response relationship between adolescent marijuana use and increased vulnerability to developing neuropsychiatric disorders, the results are less consistent after controlling for confounding variables, such as childhood adversity and shared risk genes, suggesting that at least some of the risk may be related to common factors.

To better answer questions about the impact of marijuana on neurodevelopment, data from these large cohort studies have recently been pooled for systematic reviews and integrative analyses.5,6 Moore and colleagues5 completed a systematic review that includes 35 studies to examine if marijuana use was associated with psychotic or affective outcomes (both symptoms and disorders), beyond transient intoxication.6

The researchers found that there was an increased risk for psychotic outcomes in individuals who had ever smoked marijuana (1.5 times more likely to develop psychosis) (adjusted odds ratio [OR] = 1.41, 95%CI = 1.54-2.84) with a dose-response such that heavy marijuana use and earlier age of onset were associated with increased risk. While the data was less consistent for affective disorders, there was also association between heavy marijuana use and an increased risk for depression (adjusted OR = 1.49, 95%CI = 1.15-1.94).

An integrative participant-level analysis was recently completed using pooled data from three large longitudinal studies which included 3765 subjects.6 Silins and colleagues6 looked at the maximum frequency of teenage marijuana use (age < 17) and a number of developmental outcomes in young adulthood. They found a dose-response relationship between adolescent marijuana use and a number of adverse outcomes in young adulthood with the heaviest marijuana users (daily use) experiencing the most neuropsychiatric sequelae as young adults.

After controlling for covariates, adolescent daily marijuana users were 18 times more likely to develop a marijuana use disorder (adjusted OR = 17.95, 95%CI = 9.44-34.12); 8 times more likely to use other illicit drugs (adjusted OR = 7.80, 95%CI = 4.46-14.63); and 7 times more likely to attempt suicide (adjusted OR = 6.83, 95%CI = 2.04-22.90) in young adulthood. They were also significantly less likely to graduate high school and achieved lower academic attainment.

These findings linking adolescent-onset marijuana use to neuropsychiatric outcomes in young adulthood, and bridging preclinical, clinical translational, and prospective longitudinal methodologies, underscore the need for increased research in this area and the importance of psychiatrists to help patients with the following:

1. educate youths and their parents about the harms of marijuana
2. screen and provide early treatment to high-risk adolescents
3. increase advocacy
4. involve the scientific community in marijuana-related policy decisions

Dr Hammond will present evidence examining links between cannabis use and mood disorders and anxiety disorders at the 25th Annual Meeting and Symposium of the American Academy of Addiction Psychiatry, in a symposium titled "What is the Evidence of Harm to Adolescents Using Cannabis?"

Disclosures:
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