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Research report

Cannabis and alcohol use, and the developing brain

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ABSTRACT

Sex hormones and white (and grey) matter in the limbic system, cortex and other brain regions undergo changes during adolescence. Some of these changes include ongoing white matter myelination and sexually dimorphic features in grey and white matter. Adolescence is also a period of vulnerability when many are first exposed to alcohol and cannabis, which appear to influence the developing brain. Neuropsychological studies have provided considerable understanding of the effects of alcohol and cannabis on the brain. Advances in neuroimaging have allowed examination of neuroanatomic changes, metabolic and neurotransmitter activity, and neuronal activation during adolescent brain development and substance use. In this review, we examine major differences in brain development between users and non-users, and recent findings on the influence of cannabis and alcohol on the adolescent brain. We also discuss associations that appear to resolve following short-term abstinence, and attentional deficits that appear to persist. These findings can be useful in guiding earlier educational interventions for adolescents, and clarifying the neural sequelae of early alcohol and cannabis use to the general public.

Contents

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1. Introduction

Sex hormones and white (and grey) matter in the limbic system, cortex and other brain regions undergo changes during adolescence [1]. Increasingly high resolution and rapid acquisition neuroimaging techniques have allowed us to examine neuromaturation more carefully than in the past, permitting the identification of sex similarities and differences in brain development.

2. White matter development in adolescence

White matter development and pubertal staging are highly correlated [2]. White matter, consisting of myelin-coated axons, is primarily concentrated in the inner brain and facilitates communication between regions to create neural networks such as the cortico-cortical and cortico-subcortical connections [2]. These cortico-cortical and cortico-subcortical connections are critical in serving cognitive and mood functions [2].

Whole brain analyses have demonstrated age-related increases in white matter volume and fractional anisotropy (FA) bilaterally in a number of fiber tracts including the arcuate fasciculus and corticospinal tract [3]. FA changes are thought to be a consequence of increases in the diameter of axons forming fiber tracts resulting in increases in parallel diffusivity [3]. These observations have occurred in areas supporting speech and motor function (i.e., arcuate fasciculus and corticospinal tract) and are thought to enhance long distance connectivities in white matter tracts [3].

3. Grey matter development in adolescence

Grey matter, consisting predominantly of neuronal cell bodies, dendrites, synapses, and unmyelinated axons, serves to process information by means of directing sensory stimuli to nerve cells [4]. Grey matter also contains glial cells that function to transport nutrients and energy to neurons [4].

Grey matter and intelligence have demonstrated some very interesting correlations. Intelligence quotient (IQ) is positively correlated with grey matter cortical volume in the prefrontal cortex in adolescents [5–7]. Remodeling and ongoing maturation of the central nervous system in adolescence are thought to be mediated in part by age-related grey matter volume changes [3,8]. Overall reductions in cortical grey matter volume have been observed during adolescence [3]. This process has been described as grey matter undergoing synaptic pruning [3]. Synaptic pruning may result in more specialized functional networks and more efficient processing of information as some have suggested [9]. However, others have suggested that cortical volume changes of the scale detected by magnetic resonance imaging (MRI) are unlikely due primarily to synaptic pruning and instead may be the result of increased myelination of intra-cortical axons [10]. For girls, subcortical grey matter forebrain structures have been found to be at adult volumes. For boys, volumes of the same subcortical gray matter structures have been found to be larger than for adult males and are thought to undergo regression into adulthood [11,12]. Girls have significantly smaller volumes of cortical grey matter, but greater extraventricular cerebrospinal fluid (CSF) than boys [8].

Refined analytic approaches show that most brain regions, including mean cortical thickness, appear to demonstrate a linear, monotonic decrease in cortical thickness after 5 years of age and through adolescence [13]. A minority of areas, the bilateral temporo-parietal regions and the right prefrontal cortex, demonstrated cubic trajectories with peaks in cortical thickness at or before age 8 [13]. Males demonstrated faster occipital thinning than females [13].

The limbic system is well known to play an important role in emotion, behavior, motivation, long-term memory, and olfaction [14]. During adolescence, amygdala and hippocampal volume increase for both males and females [15]. However, amygdala volume increases significantly more in males than females while hippocampal volume increases more in females than males [15].

4. Sex differences in adolescent brain development

A number of sex differences in the developing brain have been found. Males have demonstrated volumetric increases in white matter compared to females [8]. However, males have shown faster occipital thinning than females. Differences in total cerebral volume between boys and girls have been noted with 10% larger volume in boys and primarily in the form of increased cortical gray matter [8]. However, after 5 years of age, neither boys nor girls show any major change in total cerebral volume [8]. These findings support the hypothesis that sex differences in brain size are related to cortical neuronal differences. Subcortical nuclei size was found to be the same between boys and girls. However, girls have proportionally greater extraventricular CSF but not ventricular CSF [8,15] compared to boys. Cerebral volumes adjusted for intracranial vault size have been found to differ in the mean volume of the caudate and globus pallidus between males and females; the volume of the caudate has been found to be larger in females whereas the volume of the globus pallidus has been found to be larger in males [15]. Lateral ventricles demonstrated increases in size in males but not in females during development after age 11 [15]. Boys have demonstrated faster increases in white matter volume than girls during adolescence [16]. Using diffusion tensor imaging, greater FA has been noted in white matter regions (including frontal lobe) in boys whereas greater FA has been noted in the splenium of the corpus callosum for girls [17].

In addition, greater mean diffusivity (MD) in boys has been seen in the corticospinal tract and frontal white matter in the right hemisphere [17]. In contrast, girls have shown greater MD in the occipito-parietal lobes and superior aspect of the corticospinal tract of the right hemisphere [17]. Mean diffusivity reflects the rate of water diffusion, independent of directionality and is an inverse measure of membrane density. Mean diffusivity of white matter has been found to correlate with cognitive performance (IQ, executive function) [17]. Mean diffusivity of the corticospinal tract was found to correlate with clinical scores related to motor function [17]. Finally, girls demonstrated greater fiber density increases with age than boys in associative regions based on MD values [11,12,16]. These sex differences may be responsible in part for many of the differences observed in prevalence, onset, and symptoms of psychiatric disorders of adolescence.

5. Effects of cannabis on adolescent brain development

Cannabis has been most well studied in heavy users rather than those who use sporadically where the effect of use is unclear. The most common form of cannabis, smoked, has seen an evolution in its composition over the past few decades. There has been an increase in the psychoactive component (delta-9-tetrahydrocannabinol or THC) and a decrease in the therapeutic component (cannabidiol). Some experts have suggested this has led to an increase in the persistence of neuroanatomic changes in the brain during adolescence [18,19]. We discuss some of these changes here, in addition to alterations in volumetric, grey matter density, and positron emission tomography activity recently observed in the literature.