Impact of substances on the adolescent brain

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Abstract

Adolescence is a critical period of brain development, wherein the prefrontal cortex and hippocampus undergo significant maturation. Exposure to substances, such as alcohol, marijuana, and nicotine during this time can disrupt these maturation processes. This literature review examines the impact of substance use on functions such as memory and decision making as well as brain structure. These findings emphasize the necessity for early intervention and prevention of substance use in adolescents in order to mitigate any long term consequences.

Keywords

Adolescent substance use, alcohol, marijuana, nicotine, brain structure, brain function.

Introduction

Adolescence is a critical time period of brain development, as the brain undergoes significant changes in cognitive functions and neural structure. During this developmental stage, the brain undertakes maturation, particularly in the prefrontal cortex and hippocampus, which are regions of the brain essential for attention, memory, and decision making. The adolescent period is characterized by rapid synaptic pruning, increased myelination and growth in neural networks (Blakemore, 2018). There is a heightened vulnerability to external influences during the adolescent developmental window, contributing to higher risk of substance use. Increased neuroplasticity of the adolescent brain is associated with this vulnerability to peer influence, social pressure, and risk taking behaviors (Casey et al., 2019). As alcohol, marijuana, and nicotine are some of the most commonly used substances during adolescence, the use of these not only disrupts brain development, but also has the potential to lead to long term cognitive and structural changes (Spear, 2018).

Previous research has shown that alcohol, marijuana, and nicotine all contribute to deficits in cognitive performance through different mechanisms. Along with these functional impairments, substance use is linked to structural changes in critical brain regions such as the prefrontal cortex and hippocampus. Comparing adolescents who do and do not use substances can offer valuable insight on the long term consequences substance use can have on the adolescent brain.

Neuroimaging techniques such as magnetic resonance imaging (MRI) and specifically functional MRI (fMRI) reveal differences between adolescents who do and do not use substances. MRI allows for the assessment of physical changes in the brain and fMRI provides insight into differences in brain activation patterns when engaged in cognitive tasks testing memory, attention, and decision making. Understanding these abnormalities is essential to recognizing the implications of adolescent substance use on long term mental health, behavior, and increased risk of substance abuse disorder in the future.

The aim of this review is to evaluate how different substances, including alcohol, marijuana, and nicotine, affect cognitive functions including attention, memory, and decision-making, and brain structure. By analyzing the impact substance abuse has on the adolescent brain function and structure, the broader implications of adolescent drug use will be revealed, which emphasizes how early substance exposure can result in academic challenges, problems with mental health, and increased likelihood of substance use disorder in the future. Early intervention and prevention of substance abuse is essential to protect adolescents during this critical developmental stage.

Methods

Here we conducted a literature review search on the effects of substance use on the adolescent brain. Articles were identified from Google Scholar and PubMed using search terms such as, "substance use impact on adolescent brain", "cognitive function", and "brain structure". Peer reviewed published research papers were selected based upon relevancy of the titles to the impacts of substance use on the adolescent brain and only papers published within the past 20 years were included to ensure inclusion of only current research.

Results

A total of 20 articles were identified and examined for this literature review. Of the 20 papers, 12 met inclusion criteria by examining the effects of substance use on the adolescent brain. Upon review, several themes emerged, including significant negative effects of alcohol, marijuana, and nicotine on cognitive functions like attention, memory, and decision making, as well as on brain structure.

Alcohol's effect on brain structure and function

Adolescence is a critical period of development and maturation in the brain, specifically in the prefrontal cortex and hippocampus, two regions of the brain that are strongly interconnected through neural pathways. The prefrontal cortex is the region of the brain responsible mainly for decision-making and attention, and is especially vulnerable during this time of growth due to the active development taking place. Throughout adolescence, the brain undergoes synaptic pruning, or the elimination of inefficient neural connections, and myelination, which is a process that increases the speed of neural signaling, in order to improve neural networks for efficient cognitive processing. Alcohol use disrupts these developmental processes in the prefrontal cortex and can lead to inefficient pruning and slower myelination. Alcohol use in adolescence has also been found to lead to the retention of extra synapses in the prefrontal cortex (Spear, 2018). These extra synapses can create structural inefficiencies that may negatively impact the development of cognitive control. Slowed myelination has also been found to negatively impact executive functions (Spear, 2018). Extra synapses and slowed myelination have been linked to functional impairments, such as deficits in impulse control and decision making, which may make adolescents more prone to risk-taking behaviors. Moreover, neuroimaging studies have shown decreased activation in the prefrontal cortex during tasks that require cognitive control. Reduced activity may indicate that the prefrontal cortex's ability to allocate neural resources has been compromised as a result of alcohol use.

The hippocampus is a region of the brain essential for memory and learning and has also been found to have structural damage from alcohol use. Alcohol use in adolescence has been found to result in neuroinflammation and oxidative stress in the hippocampus which can contribute to neuronal loss (cell death) and reduced volume of the hippocampus (Guerri et al., 2011). Extensive structural damage to the hippocampus may weaken the region's ability to encode and consolidate memories. Memory encoding is the first critical stage of memory formation and is a process by which information is made into a format that can be stored in the brain for later retrieval. Memory encoding involves several brain regions but particularly the prefrontal cortex and hippocampus. Encoding relies on neural processes that are especially vulnerable to the impacts of substances such as alcohol.

Previous work has suggested that adolescents who engage in heavy drinking (3-4 drinks per occasion) have decreased volume of the hippocampus in comparison to adolescents who do not drink (Hamidullah et al., 2022). The Hamidullah study followed 24 adolescents who reported to have engaged in binge or heavy drinking at least twice in the last month and a control group of 24 adolescents who have no history of alcohol use. Structural MRI was utilized to measure hippocampal volume. The difference in volume was found to be associated with worse performance on memory and learning tasks (Hamidullah et al., 2022). Therefore, adolescents exposed to alcohol's neurotoxic impacts may impair long term potentiation, which is a cellular mechanism important for memory (Guerri et al., 2011). Evidence has shown that there is also reduced activation in the hippocampus during memory encoding tasks, in adolescents exposed to alcohol (Hamidullah et al., 2022). Structural impairments in both the prefrontal cortex and the hippocampus can both result in negative impacts on functional capabilities in these regions. There is an interdependence between structural and functional changes caused by alcohol use in the adolescent brain. Alcohol use may also weaken the neural connectivity between the hippocampus and prefrontal cortex, impacting the ability to integrate memory into decision making. Reduced volume in the hippocampus and reduced white matter weakens the functional connectivity that is required for memory encoding. In the same way, inefficient synaptic pruning and slower myelination in the prefrontal cortex negatively impacts the brain's ability to sustain attention and effectively regulate decision making. Almost as a feedback loop, the structural changes result in functional impairments, such as inability to regulate behavior and impulsivity, which can increase the likelihood of problematic alcohol use later in life resulting in possible further structural damage.

In sum, alcohol's impact on the adolescent brain is complex and multi-faceted. Alcohol use does not simply impact the prefrontal cortex and hippocampus regions, but it also impacts dynamic networks in the brain. Weakened communication between the prefrontal cortex and hippocampus is especially harmful, as it can impact the brain's ability to apply past experiences into future decisions. The changes that have been found to occur due to alcohol use in adolescence may be irreversible, even after stopping use (Guerri et al., 2011).

Marijuana function and structure

Introduction of marijuana during the vulnerable period of adolescence may disrupt neurodevelopment, leading to structural and functional changes that can affect cognitive functions and behavior. The main psychoactive compound in marijuana is Tetrahydrocannabinol (THC) which interacts with Cannabinoid Receptor 1 (CB1) in the hippocampus. As mentioned previously, the hippocampus is a region of the brain critical for learning and memory. Prior studies sought to understand the neural changes to the adolescent brain when using marijuana. To examine this, researchers recruited 63 adolescents, aged 15-18 years, 26 of which were using alcohol and marijuana. The participants were subject to neuroimaging such as MRI to measure hippocampal volume, and cognitive testing such as verbal learning assessments . Adolescents who use marijuana regularly were found to have reduced volume in the hippocampus compared to adolescents who do not use marijuana. Asymmetry in the hippocampus was also found such that marijuana use was associated with a larger left hippocampal volumes (Lisdahl et al., 2013). There is also evidence to show that the age marijuana is first used plays a role in the potential for negative structural changes in the hippocampus as well as the prefrontal cortex (Gruber et al., 2014).

The THC CB1 interaction can impact neurotransmission, which can lead to reduced hippocampal plasticity. The reduction in the plasticity, or the brain's ability to adapt and form new neural connections, can negatively impact processes like memory formation and learning (Meier et al., 2012). Since the brain is still maturing and developing, specifically in the hippocampus, during adolescence, this may be why teens who begin use of marijuana at an earlier age experience more profound and lasting impacts. Additionally, there is evidence that the altered hippocampal structure, due to the use of marijuana, results in short and long term memory deficits. Memory problems are mainly due to the hippocampus' inability to process and store new information as it should. Therefore, the memory deficits are not simply a consequence of intoxication but enforce the permanent changes that are related to the use of marijuana in adolescence (Lisdahl et al., 2013).

Marijuana has also been found to affect the structure of the prefrontal cortex. Evidence shows that marijuana use in adolescence may reduce cortical thickness in the prefrontal cortex, potentially delaying maturation of this important region. The use of marijuana may negatively impact this pruning, hindering the prefrontal cortex's ability to strengthen the necessary neural pathways for developmental progression. Albaugh and colleagues analyzed data from 799 adolescents, aged 14-19 years, to examine changes in cortical thickness. The participants underwent MRI scans at a baseline age of 14, and a follow up scan at age 19. The adolescents who use cannabis were found to have abnormal accelerated cortical thinning in the prefrontal region compared to the adolescents who do not use. The degree to which the thinning occurred was directly associated with the amount of cannabis use present. Furthermore, the study revealed this cortical thinning in the prefrontal cortex was associated with higher levels of attentional impulsiveness 5 years following the initiation of the study (Albaugh et al., 2022). Along with the structural changes, evidence has shown a decreased activation in the prefrontal cortex during tasks that require cognitive control in adolescents who use marijuana compared to those who do not (Lisdahl et al., 2013). Together, these impacts may hinder the development of self-regulation skills, which may result in adolescents becoming more prone to poor decision making and impulsivity.

Nicotine function and structure

Nicotine exposure during the adolescent stage has also been shown to disrupt the vital developmental process taking place in the brain, leading to structural and functional impairments specifically in the prefrontal cortex and hippocampus, like those seen in alcohol and marijuana use. Nicotine activates acetylcholine receptors (nAChRs), which are abundant in the prefrontal cortex and critical for brain development. Overactivation of the nAChRs during adolescence inhibits normal synaptic pruning processes, resulting in a dysregulated neural network (Dwyer et al., 2009). The changes have been found to negatively impact the prefrontal cortex's abilities to mediate cognitive control and regulate impulsivity. Nicotine use may also result in oxidative stress, which is too many free radicals and not enough antioxidants to neutralize them.

Previous research has sought to understand the impacts of nicotine on the adolescent brain. A recent study involving 92 adolescent participants from ages 12-17, revealed through neuroimaging techniques, such as functional and structural MRI scans, a significant difference in brain structure and function between the adolescents who do and do not consume nicotine. The study utilized cognitive tests such as the stroop test (testing selective attention and cognitive flexibility), Go/No-Go task (testing response inhibition and impulse control) and the spatial span test (testing working memory and spatial memory). Neuroimaging scans were collected in a resting state and as well as during the cognitive tasks. The adolescents who smoked regularly showed reduced gray matter volume in the prefrontal cortex and hippocampus compared to the adolescents who do not smoke. Gray matter in the prefrontal cortex was reduced by up to 20% and the hippocampal volume was similarly reduced. These structural changes translated into poorer performance during cognitive tasks involving memory and inhibitory control. The adolescents who use nicotine were found to perform worse than the control on tasks especially related to memory and attention (McGill et al., 2014)

Behavioral studies have also consistently demonstrated that cognitive disruptions common among adolescents smoking nicotine may lead to behaviors, such as increased impulsivity, risk-taking behaviors, and difficulties with attention, that could result in heightened likelihood of continued substance use in the future. Adolescence is also a time period where the hippocampus is experiencing robust neurogenesis, the growth and development of nervous tissue. The use of nicotine may disrupt this process potentially leading to long term impairments in memory and learning. The disruption of this process is due to the exposure of nicotine reducing the proliferation of neural progenitor cells (McGill et al., 2014). Neural progenitor cells are a part of the nervous system that can differentiate into different types of neurons and glial cells, they are key to brain development and maintenance of the nervous system. A reduction in the proliferation of neural progenitor cells can lead to impaired neurogenesis, the formation of new neurons, which can potentially impact brain function. Nicotine has also been shown to lead to reductions in hippocampal cell density and dendritic complexity in the brain of adolescents exposed to nicotine. These structural changes have been found to manifest in negative impacts on memory. Adolescents who smoke have been found to perform worse on verbal and spatial memory tasks compared to their non-smoking peers. There is also evidence that these deficits persist years after cessation, potentially meaning permanent alterations in hippocampal function (McGill et al., 2014).

Limitations

There are limitations to this research paper. The literature review was not fully systematic, as not every available title was analyzed, which could have led to the exclusion of additional relevant studies. Additionally, self reported substance use in adolescents research participants may be unreliable due to fear of legal or parental consequences, affecting the accuracy of numerical data presented. This could potentially understate the true impact substance use has on adolescent brain development.

Prevention and intervention strategies

Preventing adolescent substance use is essential in order to avoid future substance use disorder development. Things like school based education programs can raise awareness of the long term effects of the most commonly used or exposed to substances among adolescents like alcohol, marijuana, and nicotine. Education on the importance of physical exercise may also reduce substance use, as staying active is a way to avoid situations exposed to substances.

Conclusion

In conclusion, adolescent substance use, particularly alcohol, marijuana, and nicotine consumption, can have substantial and lasting impacts on brain structure and function. The substances specifically interfere with critical brain regions including the prefrontal cortex and hippocampus. This interference has been found to result in deficits in memory, attention, decision making, and impulse control. Neuroimaging highlights these structural and functional impacts. Adolescence being a vulnerable period of brain development, early prevention and intervention is necessary. With nearly 60% of adolescents reportedly using alcohol, marijuana, or nicotine before graduating high school, prevention and education is essential. By addressing these issues early on, potential to reduce long term consequences is possible.

Future research is needed to better understand how substance use affects different stages of adolescent brain development, respectively. Tracking adolescents over time could provide deeper insights into the structural and functional brain changes associated with alcohol, marijuana and nicotine use. Additional studies could also further explore the effectiveness of prevention and intervention programs to determine what is most effective.

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