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Cover Page Footnote

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FIU Undergraduate Research Journal

Brain and Behavior: Cognitive Failures are Associated with Sensation Seeking via Adolescent Marijuana Use

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A main concern regarding adolescent marijuana use is its long-term negative health effects, such as alterations to brain structure and function, which can lead to deficits in working memory (e.g., cognitive failures). This raises concerns for the development of proper executive functioning in marijuana-using adolescents. As such, understanding factors leading to adolescent marijuana use, such as personality, can allow for an assessment of predispositions that could pose a threat to their cognitive health. This study examined whether adolescent marijuana use mediates the effect of sensation-seeking on cognitive failures. An adolescent sample (*N*=165; 48.8% Female, 88.6% White, 84.9% Hispanic/Latinx, M_{age}=14.9) from a larger multi-wave study was assessed. Results show that high sensation-seeking tendencies predicted greater marijuana use (effect=0.08, p=0.02), and that marijuana use predicted greater false triggering (effect=0.96, p=0.01). Furthermore, a significant indirect effect between sensation-seeking and false triggering through days of marijuana use (effect=0.08, CI [0.01, 0.20]) was found. Findings suggest that marijuana use can impact executive functioning within the prefrontal cortex via alterations to myelination due to false signaling on oligodendrocytes. Additionally, a mature striatum coupled with an underdeveloped prefrontal cortex during adolescence may predispose sensation-seeking adolescents to try marijuana without considering the risk of memory impairments.

Keywords: *working memory*, *endocannabinoid system*, *prefrontal cortex*, *oligodendroglia*, *marijuana*, *cannabis*, *adolescents*, *sensation-seeking*, *neurobiology*

Cannabis is one of the most popular drugs amongst adolescents, with 16.4% of adolescents aged 12-17 years and 51.9% of individuals aged 18-25 years having used cannabis in their lifetime in the United States (Camchong et al., 2016). Moreover, cannabis has been found to alter the development of the prefrontal cortex (PFC) which can affect the development of proper executive functioning tasks, such as working memory (Bloomfield et al., 2019; Funahashi, 2006). It is important to note that the PFC develops during adolescence, therefore sensitizing this region to molecular-level alterations in the endocannabinoid system due to underdeveloped neural pathways (Duperouzzel et al., 2019).

The endocannabinoid system is responsible for the development of executive functioning in the PFC and is sensitive to any exogenous cannabinoids (exocannabinoids), such as Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD), that may be introduced through cannabis use (Dougherty et al., 2012). Additionally, endogenous cannabinoids (endocannabinoids) – natural cannabinoids that the body produces – attach to cannabinoid receptors in the endocannabinoid system, many of which are found in the PFC (Dougherty et al., 2012). Since cannabis contains exocannabinoids that also attach to the receptors in the endocannabinoid system, the differences in the chemical structure of these compounds can alter working memory after prolonged use. This is especially true if cannabis is consumed earlier in life, as in the case of early-onset cannabis use– use of cannabis prior to age 16 – which may raise the risk of cognitive failures through working memory impairments (Stringfield & Torregrossa, 2021).

Increased concerns exist for the development and health of myelination in adolescent marijuana users due to the presence of cannabinoid receptors on oligodendrocytes (Lubman et al., 2015). That is, impaired working memory may result from false signaling of G-proteins within oligodendrocytes via marijuana use in adolescence, thus affecting the myelination of nearby neurons (Ford, 2021; Lubman et al., 2015). Since the effects of exocannabinoids on the developing brain indicate a probability of memory impairments, concerns are raised for youth with high sensation-seeking tendencies because their internal desire to seek out new and thrilling experiences may predispose them to marijuana use (Curry et al., 2018; Duperrouzel et al., 2019; Zuckerman, 2015). This internal desire can be attributed to the maturation of the striatum – the brain's reward system – before the PFC has finished developing, influencing young adolescents to seek out novel experiences without considering the negative consequences (Galvan, 2010). Additionally, studies find that young adolescents require more stimulation from a reward to receive the same amount of satisfaction if the stimulus were presented to an adult, putting marijuana use at an even greater threat to youth due to hyposensitization (Galvan, 2010).

It is significant to note that much of prior literature focuses on the adverse effects of adolescent marijuana use. However, a neurobiological basis is not always mentioned to explain why these negative effects occur. This article investigates the often-omitted neurobiological basis of sensation-seeking tendencies and how this behavior may lead to adolescent marijuana use and, consequently, cognitive failures from the changes in brain structure and function.

Literature Review

As one of the highest consumed substances amongst adolescents, 10.2% of 8th graders, 18.7% of 10th graders, and 30.5% of 12th graders reported using a cannabis product in 2022 (Johnston et al., 2022). The main concern regarding adolescent cannabis use is the long-term negative health effects on brain structure and function, particularly in cases of younger adolescents (Bloomfield et al., 2019; Camchong et al., 2016; Duperrouzel et al., 2019).

These negative effects include improper functioning of working memory and other higher cortical functions required for healthy mental maturation (Duperrouzel et al., 2019; Zehra et al., 2018). Since much of the PFC develops during adolescence, this region is sensitized to internal and external stimuli. These stimuli include changes in hormone levels, peer influences, external rewards, social contact, and substance use (e.g., marijuana; Widjojo, 2018).

The Endocannabinoid System

The endocannabinoid system produces endogenous cannabinoids to help develop executive functioning in the PFC (Dougherty et al., 2012). Cannabinoid receptors, such as cannabinoid type 1 (CB1) receptors, are found throughout glial cells and neurons in the PFC (Dougherty et al., 2012; Kruk-Slomka et al., 2016; Lubman et al., 2015). Cannabis contains exocannabinoids, such as Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD), that can alter glial cell functionality after prolonged use.

Specifically, oligodendrocytes – the neuroglial cells that make myelin sheaths and attach to axons on neurons to provide synaptic support – contain CB1 receptors within their structure (Ford, 2021; Lubman et al., 2015). As Duperrouzel and colleagues (2019) found, exocannabinoids introduced to the developing adolescent brain disrupt functional connectivity and change brain structure in the PFC. Since CB1 receptors exist on oligodendroglia, cannabis use can potentially lead to alterations in myelination through CB1 receptor activation on oligodendrocytes (Lubman et al., 2015).

The Prefrontal Cortex and Working Memory

The PFC develops throughout most of one's life, from the prenatal period to one's mid-forties when myelination completes; however, most of its development occurs during adolescence (Gibb & Kolb, 2015). Because the PFC is in development during adolescence, higher cortical functions associated with this region, such as working memory, are also in development (Lopez- Larson et al., 2011). Alterations in PFC structure and functionality during adolescence raise concerns for the individual because these alterations affect the development of working memory (Funahashi, 2006). Additionally, working memory is linked to the functioning of related higher cortical tasks including thinking, decision-making, and planning (Funahashi, 2006).

Learning Memory

Prior studies find that marijuana has specific ties to memory alterations through use (Schweinsburg et al., 2008). A study by Schweinsburg and colleagues (2008) finds that heavy marijuana-using adolescents do not improve on short-term memory tasks after six weeks of abstinence. In contrast, other polysubstanceusing adolescents (e.g., alcohol, nicotine, opioids) did not demonstrate as severe deficits as the marijuana-using sample. This finding suggests that cannabis has a direct and unique effect on learning and memory that most other substances do not (Schweinsburg et al., 2008).

Early-Onset Heavy Marijuana Use and Cognitive Failures

Current knowledge about long-term cognitive failures in heavy adolescent marijuana users show that increased dose at an earlier age increases the risk of attentional dysfunction, decreased abilities in sequencing, and impaired verbal story memory into adulthood (Jackson et al., 2016; Schweinsburg et al., 2008). Namely, frequent and heavy use of marijuana during the early stages of adolescence continuing through young adulthood can provoke cognitive failures, even with cessation of use. However, these cognitive declines are not as profound if cessation takes place at an earlier age while the PFC is in development (Jackson et al., 2016; Schweinsburg et al., 2008). Increasing evidence supports the claim that proper development of the PFC is necessary for the maturation of working memory and other higher cognitive processes, and that heavy marijuana use can disturb such maturation when used during adolescence (Schweinsburg et al., 2008; Stringfield & Torregrossa, 2021).

Notably, many studies find that heavy marijuana users have impaired cognition; this is seen primarily in early-onset users– use before the age of 16 years old (Jackson et al., 2016; Schweinsburg et al., 2008; Shrivastava et al., 2011). Cognitive failures such as deficits in IQ, attention, memory, and verbal abilities have been found in such samples (Jackson et al., 2016; Schweinsburg et al., 2008), and may indicate an early development of dependence among young cannabis that most likely continues into adulthood (Shrivastava et al., 2011).

Sensation-Seeking

Prior work has shown that sensation-seeking is a risk factor for adolescent marijuana use (Hampson et al., 2008). Adolescents high in sensation-seeking – defined as the desire to seek stimulation from novel experiences and sensations (Zuckerman, 2015) – possess increased risk of experimenting with marijuana due to its popularity and perception of being a low-risk sensation experience (Hampson et al., 2008; Zuckerman, 2015). Barnum and Armstrong (2019) state that risk appraisal – the consideration of the risks and rewards associated with the behavior – mediates risk taking behavior and sensation-seeking. For a risky behavior to occur, decision-making must take place to determine whether the potential rewards of such behavior will outweigh the potential risks. In this, many adolescents can think about whether the behavior is worth the potential risks of marijuana use (Hampson et al., 2008; Zuckerman, 2015).

Neurobiology of Sensation-Seeking

Sensation-seeking tendencies have a neuronal basis within the PFC and striatum (Coffman et al., 2021; Galvan, 2010). Studies find that the striatum finishes maturation before the PFC, which can explain why young adolescents may participate in risky activities, such as marijuana use, without considering the consequences (Galvan, 2010; Shad et al., 2011). Namely, an underdeveloped PFC does not yet have the maturity to make decisions by itself and depends on the striatum's reward circuitry to help guide the decision- making process

(Galvan, 2010; Shad et al., 2011). Led by internal feelings and desires, young adolescents may engage in marijuana use without considering the potential risks as an effect of underdeveloped neural pathways in the PFC (Galvan, 2010; Shad et al., 2011).

Moreover, the striatum is hyposensitized during early adolescence, meaning rewards must be heightened for adolescents to receive the amount of stimulation that an adult would receive from the same reward (Galvan, 2010). Prior studies have found increased activity of the ventral striatum in adolescents as compared to adults when anticipating a reward (Bjork, 2004). This can explain an adolescent's impulsiveness and reactivity in the presence of a highly stimulating experience, therefore increasing reward-seeking behavior (Galvan, 2010; Shad et al., 2011).

Current Study

The high rate of cannabis use among adolescents is concerning since prior studies show that cannabis disrupts the maturation of the PFC during its developmental period in adolescence (Lopez-Larson et al., 2011). As such, adequate development of working memory in adolescence is critical because proper working memory reduces the risk of improper decision-making and thinking capabilities, allowing for the proper maturation of planning and judgment (Funahashi, 2006; National Research Council (US) and Institute of Medicine (US) Board on Children, Youth, and Families, 1999). This study examined whether adolescent marijuana use mediates the effect of sensation-seeking on cognitive failures, and the neurobiological basis behind these behaviors.

Methods

Participants

The studied sample consisted of a sub-study of 165 adolescents (48.8% female, 88.6% White, 84.9% Hispanic/Latinx, M_{age}=14.9) who completed the first wave (W1) of a larger ongoing multi-wave longitudinal study examining risk and protective factors impacting e-cigarette use. 9th and 10th-grade students (14-16 years old) enrolled in South Florida high schools and their caregivers completed W1 of the larger study. Exclusion criteria for adolescents included: intellectual or physical disabilities, neurological diseases, a learning disorder, severe mental illness, and a lack of English fluency. Moreover, adolescents needed to meet at least one criterion for either having a sibling or friend with prior substance experimentation, personal high levels of impulsivity or personally showing sensation-seeking tendencies. Each of these characteristics has been linked with substance use (Curry et al., 2018). It is worth noting that only 2.6% of adolescents that were screened did not meet a high-risk criterion. Thus, the study sample is likely representative of typical high school students in the region.

Procedures

Recruitment events for the larger multi-wave longitudinal study were performed at public high schools in South Florida. Interested adolescents and their caregivers completed an eligibility screen (where sensation-seeking was assessed) over a brief phone call made a few days after collecting their phone numbers. For those meeting criteria, a first in-person appointment was scheduled for W1-visit 1(W1-V1) data collection;

this subsample of participants visited the facility in-person for two visits during W1. In the first visit (W1-V1), adolescents and caregivers signed an informed consent and assent document before being placed into separate rooms to establish confidentiality of personal answers while completing questionnaires. The adolescent subsample completed their questionnaires within 1.5 hours, and their caregivers within 45 minutes; all participants were allowed to take breaks at any point during the questionnaire and to resume after their break. Participants were scheduled to return within a month of the first visit for W1-visit 2 (W1-V2), in which adolescents completed another set of questionnaires within 15 minutes. iPads were used to conduct questionnaires via REDCap (Research Electronic Data Capture; Harris et al., 2009; Harris et al., 2019). Participants were then compensated monetarily for their participation in the study. The Institutional Review Board approved study procedures at the university (Florida International University).

Measures

Substance Use Risk Profile Scale (SURPS): Raw scores from the SURPS (Woicik et al., 2009) were used to assess adolescents' sensation-seeking at W1 during the eligibility screening (e.g., "*I enjoy new and exciting experiences even if they are unconventional*"). Six (6) items were rated on a 4-point Likert scale (1 = strongly disagree, 4 = strongly agree; Cronbach's $\alpha = 0.54$). Raw scores were determined by finding the sum of the six (6) individual scores for each participant.

Adolescent Marijuana Use: Marijuana use was assessed at W1-V1 using one item adapted from the Population Assessment of Tobacco and Health Survey (PATH; Hyland et al., 2016). Participants were asked, "*In the past year, on how many days did you use marijuana?*" The number of days was entered into a textbox.

Cognitive Failures Questionnaire (CFQ): During the second visit of W1, participants completed the CFQ (Broadbent et al., 1982) to assess levels of cognitive failures. More specifically, the False Triggering subscale was used (e.g., "*Do you bump into people?*"; Cronbach's $\alpha = 0.78$). Eight (8) items were rated on a 5-point Likert scale (4 = very often, 0 = never), and responses were summed to produce a subscale score, with higher scores reflecting greater cognitive failures.

Data Analytic Plan

Mediation analysis was conducted using the PROCESS macro version 3.3 (Hayes, 2019) for SASv9.4 (SASInstitute, 2002-2012). Particularly, we examined whether a participant's self-reported days of marijuana use at W1-V1 (M) mediated the relationship between sensation-seeking assessed during eligibility screening (X) and cognitive failure use at W1-V2 (Y). Study variables were normally distributed (skewness range = -0.34-0.58, kurtosis range = -0.44-0.05) apart from days of marijuana use (skewness = 5.94, kurtosis = 36.41). Given the non-normality of this use variable, a logarithm transformation was applied (Kline, 2016). Adolescents' biological sexes, ages, and ethnicities were included as covariates.

Results

The table presents means, standard deviations, and correlations for study variables. Sensation-seeking was significantly positively correlated with days of marijuana use, and days of marijuana use were significantly positively correlated with cognitive failures. Furthermore, a non-significant positive correlation was found between sensation-seeking and cognitive failures.

Table 1

Means, Standard Deviations, and Correlations for Study Variables

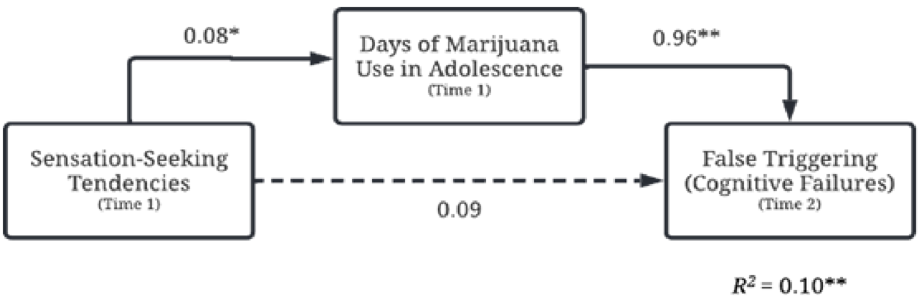
Study Variables	*M*	*SD*	Correlations					
				2	3	4	5	6
I. Sex'(WI)	0.51	0.50						
2. Ethnicityb(WI)	0.85	0.36	-0.11					
3. Age(WI)	14.90	0.68	0.Q2	0.11				
4. Sensation seeking (Screener)	16.23	2.80	0.21••	0.03	0.03			
5. Past year marijuana use (Wl-V!}g	9.95	48.64	*0.15f*	0.06	*0.14f*	0.22••		
6. False triggering (WI-V2)	9.144	5.42	-0.21•••	-0.05	-0.00	0.03	*0.14f*	

Note: t marginal p = 0.06; "*p* < 0.0l; '" *p* < 0.001; WI-VI= Wave I-Visit I, Wl-V2 = Wave I-Visit 2; Female= 0, Male= I; b Hispanic No= 0, Yes= I; Variable represents untransformed value.

The figure further illustrates the mediation of sensation-seeking tendencies and false triggering by days of marijuana use. A significant relationship exists for sensation-seeking adolescents to engage in marijuana use, which then significantly increases the chances of acquiring cognitive failures with a higher frequency of days of marijuana use.

Figure 1

Mediation Model for Sensation-Seeking Impact on Marijuana Use



Youth's self-report of sensation-seeking on false triggering as mediated by days of marijuana use; *p<0.05, **p<0.01.

Discussion

The growing popularity of marijuana raises concerns about the long-term neurobiological effects of marijuana exposure, especially for adolescents who begin to experiment with this substance while their PFCs are in development. As prior studies find, marijuana use is related to false signaling of CB1 receptors on oligodendrocytes, which in turn can cause alterations to the functioning of these cells and affect myelination (Lubman et al., 2015). These morphological changes may impair working memory by changing the functionality of oligodendrocytes in the PFC (Ford, 2021; Lubman et al., 2015). Although brain imaging techniques were not used in this study, it can be presumed that increased cognitive failures in adolescent marijuana users could be linked to alterations in myelination.

Since brain imaging was not used to analyze data for this study, it may discredit some of the proposed alterations to the PFC and myelination as described. Although it is known that alterations to the structure of the PFC can affect its functionality (Camchong et al., 2016; Duperrouzel et al., 2019), it is not yet known whether myelination is majorly influenced by marijuana use, or whether the alterations show an increase or decrease in myelination. Such brain analyses may require invasive procedures and threaten participant well-being after study completion, therefore violating ethical rights. Factors other than alterations to myelination could be involved in the significance of cognitive failures with increased marijuana use. However, only thorough white matter analysis and brain imaging would confirm any changes in myelination or brain structure as a result of marijuana use.

As results show, increased days of marijuana use were associated with increased cognitive failures – or decreased cognitive capabilities –, and that sensation–seeking tendencies were associated with marijuana use. Young sensation-seeking participants may have been influenced by their brain's reward system when deciding to use marijuana (Galvan, 2010). Given that the striatum matures before the PFC, the young sensation-seeking adolescent sample may have been more inclined to experiment with marijuana (Galvan, 2010). An underdeveloped PFC coupled with a mature striatum may have influenced marijuana use in that consideration of its negative consequences would not have taken place. Thus, positive experiences would be highlighted by the brain's reward system which, seeking to provide its host with positive feelings, guides the decision-making process (Galvan, 2010; Shad et al., 2011).

One factor to consider in the analysis is the amount of marijuana used by adolescents in the past year. As studies show, increased marijuana use consistently shows lower scores on learning and memory tests (Schweinsberg et al., 2008). In relation to the Cognitive Failures Questionnaire used in this study, the total amount of days in the past year in which the adolescent used marijuana would account for their false triggering results in total, rather than the duration between their last day of use and the day that the adolescent filled out the questionnaire. However, if a memory test were applied for the adolescents in this sample, results could have been skewed based on the adolescents' last day of marijuana use (e.g., one week ago, one month ago).

Moreover, chemical imbalances in the adolescent's endocannabinoid system through more recent use of marijuana could play a role in lower memory scores. Since a large amount of CB1 receptors are present within the PFC and hippocampus, false signaling of these receptors can lead to altered functionality of these brain regions, which includes proper functionality of memory and learning (Lubman et al. 2015; Prenderville et al., 2015; Widjojo, 2018).

Results also showed that sensation-seeking and cognitive failures are mediated by days of marijuana use, but no significant association between sensation-seeking and cognitive failures was found. The significance of these results demonstrates how individuals high in sensation-seeking are not predisposed to cognitive failures, but rather their decision to use marijuana may predispose them to cognitive failures in the future. This finding is consistent with the findings of Romer (2010), in which sensation-seeking did not directly predict deficits in executive functioning; rather, sensation-seeking predicted substance use, leading to cognitive declines through increased use. These findings, coupled with the results of this study, do not demonstrate impairments in PFC functionality through sensation- seeking alone (Romer, 2010).

Conclusion

Further testing needs to be done to confirm alterations in myelination caused by cannabis use and determine the detrimental extent to the adolescent's future. Even still, youth substance use prevention programs are encouraged to target youth high in sensation-seeking to offset marijuana use. A major limitation of this study is the lack of variability between tested adolescents, in that all the participants were recruited from schools in Miami-Dade County. As such, these results cannot be generalized to the entire population of adolescents who have sensation-seeking tendencies. Furthermore, neurological imaging was not used in this study to determine the severity of cognitive failures within the PFC. In essence, subjective self-reports may not truly display the extent of cognitive failures as an effect of increased days of marijuana use during adolescence. Despite these limitations, the results from this study can be used to further understand motives for and consequences of marijuana use during the PFC's developmental stage. Future studies are encouraged to use neurological imaging techniques to confirm the regions in which cognitive failures arise, as well as measuring blood THC levels to find a relationship between current cognitive deficits and current marijuana use. In this way, a relationship between current marijuana use and cognitive failures can be made, rather than using subjective reports to determine the severity of such.

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