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Research Article

Frequent Marijuana Use and Cognitive Flexibility in Young Adult College Students

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Abstract

Background: Frequent marijuana (MJ) use has been associated with deficits in executive functioning (EF), but few studies have examined the contribution of recent and lifetime MJ use to the magnitude of EF impairment in young adults.

Purpose of current study: We examined cognitive flexibility in 18-22 year old college students, who were heavy marijuana users (MJ+) or healthy controls (HC). We hypothesized MJ+ would have poorer cognitive flexibility compared to HC, which would be related to earlier age at first MJ use, and greater past 30-day and lifetime MJ use.

Methods: 28 MJ+ (68% male) using MJ ≥ 5 times/week and 33 HC (55% male) using MJ ≤ once/month in the past year completed the Modified-Wisconsin Card Sorting Test, and an EF-composite score was calculated based on categories correct and perseverative errors t-scores.

Results: MJ+ had a significantly lower EF-composite score compared to HC ($t(59)=2.50$, $p=0.02$), and this was related to greater past 30-day MJ use (r (26)=-0.38, $p=0.049$).

Conclusion: Impaired cognitive flexibility in MJ+ and greater recent MJ use may contribute to the maintenance of MJ use, making it difficult to choose alternatives to reduce MJ use.

Keywords: marijuana, cognitive flexibility, executive functioning, young adults, WCST

1. Introduction

Marijuana (MJ) use is prevalent in the United States and use rates are on the rise, particularly among young adults. Roughly 6% of individuals 18 years of age and 9% of individuals 21-24 years of age reported daily MJ use in 2017, the highest rates recorded in the past three decades. Among college students, daily MJ use rose from 3.5% in 2007 to 4.4% in 2017 [1]. Despite low perceived risk and a nationwide trend toward legalization, frequent MJ use has been associated with deficits in cognitive functioning (e.g. impaired short term memory, attention, and executive functioning) [2-4], poorer academic outcomes for college students (e.g. higher rates of skipping classes, lower grades, higher drop-out rates) [5, 6], and adverse outcomes for adults (e.g. lower income, higher rate of unemployment, increased welfare dependence) [7, 8]. Frequent MJ use during young adulthood, a critical period for maturation of the prefrontal cortex (PFC) and honing of executive functions (EFs) [9], may interfere with development of cognitive abilities needed for success in college and beyond. Due to the high prevalence of frequent MJ use during this age range and previous research suggesting MJ's deleterious effects on cognitive functioning and academic performance, further research into the effects of chronic MJ use on cognitive functioning in young adult college students is warranted.

Delta-9-tetrahydrocannabinol (THC), the primary psychoactive component of MJ, binds to endocannabinoid type 1 receptors (CB1R) [10] which are widely distributed in the PFC [11]. The endocannabinoid system is thought to play a role in neurodevelopment, suggesting typical brain maturation may be affected by introduction of exogenous cannabinoids such as THC, making young adulthood a particularly vulnerable time to use MJ frequently [4, 12]. Acutely, THC alters dopaminergic activity promoting the release of dopamine, while chronic exposure to THC causes desensitization of CB1R and blunting of the dopamine system. These short- and long-term alterations of the dopaminergic system are thought to be related to cognitive impairment in frequent MJ users [10].

The PFC is critical to functioning of EFs including inhibitory control, working memory, and cognitive flexibility, cognitive domains vital for problem-solving, reasoning, and learning [13]. Cognitive flexibility, one of the core EF domains, involves altering behavior in

response to changing environmental demands and is critical for considering alternatives, avoiding habitual responses, and making adaptive decisions [14]. Several studies have suggested frequent MJ users have impaired cognitive flexibility compared to non-users [15, 16], although questions still remain regarding the contribution of recency and cumulative MJ use to magnitude of impairment. Surprisingly, few studies have examined these associations in young adults [17, 18], despite emerging adulthood being a critical time in protracted maturation of the PFC. Due to the high prevalence of MJ use among college and university students [1] and the importance of EFs for success in college, additional research examining this population is justified.

Previous studies have suggested frequent MJ use in adults is related to poorer cognitive flexibility, with degree of impairment relating to age of onset [15, 16, 19], frequency of MJ use [15, 16, 20], magnitude of MJ use [15, 16], but not duration [20, 21], or cumulative lifetime MJ use [22]. Still, other studies have found no significant difference in performance on tasks assessing cognitive flexibility when comparing frequent MJ users to non-users [21, 23, 24]. Discrepancies among previous findings may be due to differences in participant characteristics across studies, such as age of the participant sample, and age of onset as well as duration of heavy MJ use among participants. While previous findings suggest frequent MJ use may impair cognitive flexibility in adults, the relationship between MJ use characteristics and degree of impairment has yet to be fully understood. Thus, the current study sought to determine whether MJ use characteristics are related to cognitive flexibility in order to better identify future targets for prevention and intervention efforts aimed at reducing the incidence of MJ use among young adults.

Although young adults have the highest prevalence of frequent MJ use [1], few studies have examined cognitive flexibility in this population [17, 18, 25]. Lane (2007) compared adolescent frequent MJ users ages 14-18 with non-using peers and found that users had poorer cognitive flexibility on the WCST relative to controls, although frequency of MJ use and cumulative lifetime MJ exposure were not examined for potential associations with cognitive flexibility [25]. The relationship between frequency of MJ use and cognitive flexibility was assessed in a sample of college students ages 18-28 in a study conducted by Pope [17]. Heavy users of MJ performed worse on the WCST relative to light MJ users, although no control group was included in the study [17]. These findings support a relationship between frequent MJ use and impaired cognitive flexibility in individuals still undergoing PFC development and further illustrate the importance of examining MJ use characteristics for associations with cognitive flexibility.

With the high rates of frequent MJ use among young adults attending college, and associations between frequent MJ use and adverse academic outcomes, further research examining cognitive flexibility in college students who do and do not use MJ frequently is necessary. Furthermore, the associations between MJ use variables and cognitive flexibility have yet to be elucidated. The current study examined cognitive flexibility in young adult college students who do and do not use MJ frequently, and investigated potential associations between age at first MJ use, cumulative lifetime MJ use days, recent MJ use, and cognitive flexibility. We hypothesized MJ users would have poorer cognitive flexibility on the Modified Wisconsin Card Sorting Test (M-WCST) relative to healthy controls, and that earlier age of MJ use onset, greater lifetime MJ use, and greater recent MJ use would be related to poorer cognitive flexibility on the M-WCST.

2. Methods

2.1 Participants

Male and female participants were recruited using flyers, social media, word of mouth, and snowball sampling for a laboratory-based quasi-experimental study examining cognitive flexibility in heavy MJ users and controls. The final sample included 28 frequent MJ users (MJ+) and 33 healthy controls (HC). Inclusionary criteria included age between 18-22 years, fluency in English, and current enrollment in college or university. Exclusionary criteria included self-reported pregnancy, uncorrected visual impairment, neurological condition, serious head injury, learning disability, serious medical conditions, current use of psychotropic medication, lifetime history of a mental health diagnosis, premature birth (<35 weeks gestation), prenatal exposure to drugs or alcohol, and history of bipolar I or schizophrenia in immediate family of biological relatives. MJ+ used MJ ≥ 5 times/week for the past year and reported ≤ 15 lifetime uses combined across any illicit substance other than MJ. In the MJ+ group, 19 participants reported using an illicit substance other than MJ in their lifetime with some participants reporting multiple substances. Lifetime illicit substance use in the MJ+ group included hallucinogens (N=15), cocaine (N=5), methylenedioxymethamphetamine (MDMA) (N=3), amphetamines (N=1), opioids (N=1), and benzodiazepines (N=1). HCs reported using MJ ≤ once/month over the past year, no lifetime occasions of binge drinking (consuming >5 drinks for males and >4 drinks for females during a 2-hour period), lifetime alcohol consumption of ≤ 51 drinks, lifetime cigarette consumption of ≤ 90 cigarettes, and no lifetime use of any illicit substance other than MJ. All MJ+ tested positive for THC and two tested positive for opioids on a 12-panel urine test. One HC who tested positive for THC reported one occasion of MJ use in the past month.

2.2 Measures

Lifetime MJ Use: Participants self-reported total lifetime MJ use days as a measure of cumulative lifetime MJ exposure.

Adult Self-Report (ASR): The ASR [26] assesses adaptive functioning and problems in adults. Three items on the ASR directly assess substance use in the past 6 months (e.g. "How many days in the past 6 months did you use tobacco? Alcohol? Illicit substances?"). Participant responses for past 6-month illicit substance use was used as a measure of past 6-month MJ use. As participants reported 15 or fewer lifetime uses of illicit substances other than MJ, illicit substance use days in the past 6 months closely represent participants' past 6-months MJ use.

Timeline Followback (TLFB): The 30-day TLFB [27, 28], was used to quantify recent MJ and other substance use. Participants reported type and frequency of substance(s) used for each day in the 30 days prior to assessment, including the day of the study visit. Total number of MJ, alcohol, and cigarette use episodes reported on the TLFB was used as measures of recent use for each substance category.

Modified Wisconsin Card Sorting Test (M-WCST): The M-WCST [29] contains 48 of the 128 response cards used in the original WCST, removing the 80 cards that share more than one attribute with a key card, allowing the M-WCST to be quickly administered and scored while retaining equal sensitivity to executive dysfunction [29]. The M-WCST assesses cognitive flexibility by requiring participants to alter problem-solving strategies in response to examiner feedback. The participant sorts response cards by color (C), form (F), or number (N) using four key cards and correct sorting order is determined by the participant's choices, such that the sorting rule chosen first becomes the first rule. Following six consecutive correct responses, the examiner tells the participant to find another rule to sort by. The second rule chosen by the participant, if different than the first, becomes the second correct sorting rule, leaving the remaining sorting rule as the third correct category. Following completion of the third category, participants must sort cards in the same order as chosen previously to complete the task (e.g. C, N, F, C, N, F). The task is completed when a participant competes all six sorting categories or when no more response cards remain. Dependent variables include categories correct (CC), perseverative errors (PE), total errors (TE), percent PE, and an EF-composite score. CC is the number of times the participant completed a sorting category (i.e. six consecutive correct responses). PE occur when a participant is instructed to find a new rule but continues sorting by the current rule or when two errors based on the same sorting rule are made consecutively, indicating impairments in set-shifting. TE includes all errors made during the task, and percent PE measures the percent of total errors that were perseverative. The EF-composite score is a measurement of overall EF adjusted for the participant's sex, age, and level of education.

Wechsler Abbreviated Scale of Intelligence (WASI-II): Participants also completed the 2-subtest version (vocabulary and matrix reasoning) of the WASI-II [30] as a measure of general intelligence.

2.3 Procedure

Participants who met criteria for the MJ+ or HC groups were instructed to remain abstinent from MJ and other substances for 12 hours prior to their study visit, which included questionnaires and neurocognitive tasks of executive functioning. The 12-hour abstinence period was chosen to avoid acute effects of MJ intoxication as well as possible effects of acute MJ withdrawal [15]. All participants provided informed written consent prior to completion of study measures. Following informed consent, a breathalyzer (BACtrack Breathalyzer) was administered to exclude participants acutely intoxicated by alcohol (all participants had breath alcohol concentration of 0.00) and a 12-panel urine screen (CLIA Waived Inc. Rapid Drug Test Cup) was used to assess recent substance use. Participants completed

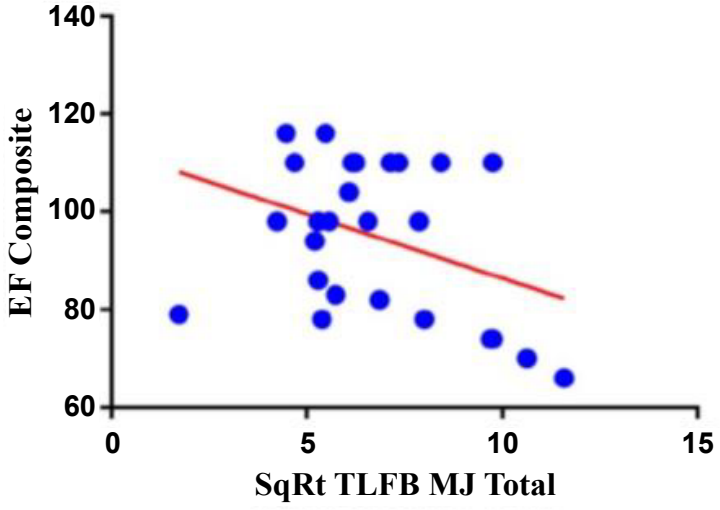

Figure 1: Past 30-day MJ use episodes and EF composite. Greater number of past 30-day MJ use occasions was associated with lower EF-composite scores in MJ+ ($r(26)$=-0.38, p=0.049).

measures assessing demographics, substance use, and neurocognitive functioning. All participants were compensated with an Amazon e-gift card. This study was approved by the Oregon State University Institutional Review Board (IRB) and followed all ethical guidelines of the IRB.

2.4 Statistical analysis

All independent and dependent variables were examined for normal distribution. When skew or kurtosis was ≥ 2 or ≤ -2, Mann-Whitney *U* tests were used to examine group differences in demographics, substance use history, and cognitive functioning. Chi-Square tests were used to examine group differences for categorical variables. For normally distributed continuous variables, independent samples *t*-tests were used to examine group differences. Substance use and neurocognitive variables not meeting normality requirements were log or square root transformed to achieve normal distribution for correlations examining relationships between substance use and cognitive flexibility.

The EF-composite score from the M-WCST, a standardized measure of global cognitive flexibility, was chosen for between and within-group analyses. MJ use variables included recent (past 30-day) MJ use episodes, past 6-month illicit substance use days, and lifetime MJ use days. Between-group differences in the EF-composite score were examined using an independent samples *t*-test. Within MJ+, associations between EF-composite, age of MJ use onset, past 30-day, past 6-month, and lifetime MJ use, as well as other substance (alcohol and cigarette) use variables, were investigated using Pearson's or Spearman's correlations, as appropriate. All analyses were performed using SPSS Statistical Software (Version 24, Armonk, NY: IBM Corp).

3. Results

Demographic characteristics of the MJ+ and HC are presented in Table 1. MJ+ and HC were well matched on sex (X^2 (1, N=61)=1.13, p=0.29), race (X^2 (3, N=61)=1.80, p=0.61), and socioeconomic status (X^2 (4, N=61)=1.66, p=0.80). MJ+ were significantly older than HC (U=231.50, p=0.001). Groups also differed on IQ (t(59)=3.31, p=0.002), such that MJ+ had significantly lower IQ scores relative to HC (Tables 2 and 3). However, neither age (r(26)=-0.12, p=0.55) nor IQ (r(26)=0.10, p=0.62) were significantly correlated with the EF-composite score within the MJ+. Groups also differed in substance use other than MJ with MJ+ reporting greater lifetime and past 30-day alcohol and cigarette use (Table 2).

To examine the influence of frequent MJ use on cognitive flexibility, MJ+ and HC were compared on M-WCST performance using the EF-composite score. Participants

Table 1: Participant demographics.

Variables	MJ+ (N=28)	HC (N=33)	*U* or X^2	*p*
Sex (M/F)	19/9	18/15	1.13	0.29
Age	20.25 (0.22)	19.18 (0.20)	231.50	0.001
Race (N)				
White	22	22		
Asian	1	4	1.80	0.61
More than one race	4	6		
Unknown	1	1		
Socioeconomic Status (N)				
Poor	1	1		
Lower middle class	1	1		
Middle class	14	20	1.66	0.80
Upper middle class	11	11		
Wealthy	1	0		

Mean (SE)

Table 2: Substance use characteristics in MJ+ and HC.

Variables	MJ+ (N=28)	HC (N=33)	*t, U* or X^2	*p*
Ever used MJ (N)	28	6	41.10	<0.001
Lifetime MJ use days	1041.89 (115.19)	23.06 (22.10)	9.50	<0.001
Past 30-day MJ use occasions	48.54 (6.01)	0.06 (0.04)	0.00	<0.001
Age at first MJ use	16.39 (.29)	17.67 (0.61)	1.84	0.08
Ever drank alcohol (N)	28	26	6.71	0.01
Lifetime drinks[1]	409.14 (118.92)	15.67 (3.02)	67.5	<0.001
Past 30-day drinks	19.00 (3.39)	1.98 (0.64)	119.00	<0.001
Ever smoked cigarettes (N)	18	1	26.50	<0.001
Lifetime cigarettes	41.75 (25.55)	0.03 (0.03)	170.00	<0.001
Past 30-day cigarettes	4.61 (3.34)	0.03 (0.03)	391.1	0.05

Mean (SE), MJ=marijuana

[1]Lifetime drinks N=32 for HC, as one participant declined to answer.

in the MJ+ group had a significantly lower EF-composite score compared to HC ($t(59)=2.50$, $p=0.02$, Cohen's $d=0.64$), an effect mainly driven by a lower CC t-score in MJ+ relative to HC (Table 3).

In order to determine whether past 30-day, 6-month, and lifetime MJ use were related to cognitive flexibility, within-group correlations of substance use and the EF-composite score in MJ+ were performed. The EF-composite score was significantly correlated with square root transformed past 30-day MJ use episodes ($r(26)=0.38$, $p=0.049$, Figure 1). Past 6-month illicit substance use days ($r_s(26)=-0.28$, $p=0.14$), log transformed lifetime MJ use days ($r(26)=-0.32$, $p=0.10$), and age at first MJ use ($r(26)=0.10$, $p=0.63$) were not related to the EF-composite score. Together, these finding suggest poorer cognitive flexibility in frequent MJ users may relate to recent (past 30-day) MJ use and not cumulative lifetime MJ use days or age at first MJ use. Correlations assessing a possible association between log transformed lifetime alcohol use ($r(26)=0.16$, $p=0.43$), log transformed past 30-day alcohol use ($r(26)=0.10$, $p=0.70$), lifetime cigarette use ($r_s(26)=-0.10$, $p=0.60$), and past 30-day cigarette use ($r_s(26)=0.10$, $p=0.64$) determined these substance use variables were unrelated to EF-composite scores in MJ+, suggesting no significant influence of substance use other than MJ use on cognitive flexibility.

4. Discussion

The current study examined the effects of frequent MJ use on EF in young adult college students. Young adults using MJ ≥ 5 times/week were compared to peers using MJ ≤ once/month on the M-WCST, a neurocognitive task assessing cognitive flexibility. MJ+ performed more poorly on the M-WCST compared to HC, suggesting the habitual use of MJ may be related to deficits in cognitive flexibility, replicating previous findings in adults [15, 16, 19]. Within MJ+, increased past 30-day MJ use occasions was associated with poorer cognitive flexibility. Age at first MJ use, past 6-month illicit substance use days, and lifetime MJ use days were not related to cognitive flexibility on the M-WCST. Together, these findings suggest frequent MJ users have impaired EF related to recent MJ use. Presence of these impairments in young adults indicate the potential hazards of frequent MJ use during protracted maturation of the PFC and underline the importance of examining the effects of heavy MJ use on EF during young adulthood.

Similar to previous findings in adult populations [15, 16], frequent MJ use was associated with impairments in cognitive flexibility in young adult college students, with greater recent MJ use correlated with poorer EF-composite scores. These deficits may be related to the residual effects of recent cannabinoid use on PFC functioning. Our results support findings of a recent meta-analysis examining cognitive functioning in adolescent and young adult MJ users and the effects of abstinence on these deficits [4]. Results of the meta-analysis suggested a small mean effect size for studies that found impaired cognitive functioning in adolescent and young adult frequent MJ users (Cohen's $d=-0.25$), with deficits in EF-abstract reasoning/shifting having the second largest effect size among previous studies. However, when studies with abstinence periods of greater than 72 hours prior to assessment were examined, effect sizes for cognitive impairment were not significantly different from zero (Cohen's $d=-0.08$). The current results suggest cognitive deficits in frequent MJ users could be related to recent (past month) use of MJ, and future studies will be needed to determine whether these impairments may be reversible with abstinence. The specific effects of abstinence have been previously examined in adult frequent MJ users using a battery of 10 neuropsychological tests, including the WCST [22]. Following 28-days of monitored abstinence, no significant difference in cognitive functioning was observed between abstinent heavy MJ users and controls. Additionally, the absence of a significant relationship between cumulative lifetime MJ use and cognitive flexibility in the current study further supports the hypothesis that observed cognitive deficits in frequent MJ users may be more related to recent heavy MJ use occasions rather than the cumulative effects of lifetime days of MJ use. Contrary to previous studies [15, 16, 19], age at first MJ use was not related to cognitive flexibility. With only 10 MJ+ reporting first use

Table 3: Cognitive functioning scores in MJ+ and HC.

Variables	MJ+ (N=28)	HC (N=33)	*t* or *U*	*p*
WASI-II Full-Scale IQ	106.11 (2.08)	115.91 (2.08)	3.31	0.002
Range	84-135	94-148		
EF composite	95.29 (2.91)	103.97 (2.00)	2.46	0.02
Range	66-116	77-130		
CC T-score	48.43 (1.48)	53.55 (.95)	232.5	0.001
Range	33-56	33-67		
PE T-score	46.86 (1.75)	50.42 (1.51)	0.15	0.88
Range	28-60	31-63		
TE T-score	46.36 (2.37)	50.91 (1.85)	1.54	0.13
Range	30-72	26-74		
%PE T-Score	48.82 (1.44)	49.15 (1.55)	0.154	0.88
Range	33-59	28-59		

Mean (SE), EF=executive functioning, CC=categories correct, PE=perseverative errors, TE=total errors

of MJ before age 16, it is possible that we did not have a sufficient number of MJ users initiating use at an early age to observe deficits in cognitive flexibility related to age at first use. The lack of findings related to age of onset may also be due to measuring MJ onset by age at first use rather than age when regular or frequent use was initiated. A previous study that found a relationship between age of MJ use onset and EF examined age at which regular or frequent MJ use commenced, which may be a more sensitive measure for examining how early exposure to neurotoxic effects of MJ may impair EF [15].

The current findings must be interpreted with regards to some limitations. Firstly, due to the study's cross-sectional design, we are unable to speculate whether deficits in cognitive flexibility in this sample were a result of frequent MJ use or if pre-existing differences in cognitive functioning were present before initiation of MJ use. Second, participants were instructed to remain abstinent from all substance use for 12 hours prior to their study visit. While it is possible participants did not follow these instructions, no participants reported MJ or any other substance use on the TLFB for the day of their study visit nor did anyone appear intoxicated during assessment. Third, while we asked participants to report the number of times they used MJ per week in the past year to determine eligibility for the MJ+, future studies will be needed to better quantify amount of MJ use across different cannabis products and different methods of use (smoking vs. edibles vs. concentrates). This is important as using MJ with higher THC content for shorter periods of time may have different effects on neurocognitive functioning than using MJ with lower THC content for longer periods of time. Lastly, lifetime and past 30-day use of alcohol and cigarettes were significantly higher in MJ+, although these variables were not related to cognitive flexibility in the current study.

The current findings suggest that frequent MJ use among young adult college students is associated with deficits in cognitive flexibility. Impairment in cognitive flexibility in frequent MJ users may contribute to habitual use by making it difficult to consider alternatives to and consequences of MJ use. Elucidating a relationship between frequent MJ use and EF provides a foundation for future longitudinal research examining whether deficits in cognitive flexibility predispose individuals to use substances or if these deficits are consequences of an individual's substance use. A greater understanding of the directionality of these findings may inform clinical research investigating intervention techniques designed to improve cognitive deficits that may be related to the maintenance of MJ use. This is especially critical for informing research within young adult MJ users as MJ use has increased in this age range in recent years [1].

5. Conclusion

In summary, our findings suggest frequent MJ use in young adult college students is related to impaired cognitive flexibility with greater recent MJ use related to greater deficits, but unrelated to the age at which MJ is first used. These results support the hypothesis that deficits in cognitive flexibility in frequent MJ users may be related to the effect of residual cannabinoids on EF, although future research is needed to examine the effects of abstinence on these deficits in young adults. These findings suggest that heavy MJ use among young adults may lead to difficulties in making adaptive decisions when faced with changing environmental demands, thus perpetuating habitual responses that could contribute to the maintenance of MJ use in this population.

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7. Conflicts of Interest

The authors declare that there are no conflicts of interest.

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