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BRIEF COMMUNICATION

Preliminary Evidence for a Sex-Specific Relationship between Amount of Cannabis Use and Neurocognitive Performance in Young Adult Cannabis Users

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Abstract

Accumulating evidence suggests neuropsychological deficits from cannabis use, with a burgeoning area of preclinical research indicating possible sex-differences. However, few studies have examined how cannabis use may differentially impact neurocognition in male and female cannabis users. As such, we examined potential sex-differences in associations between amount of cannabis use (across several time frames) and neurocognitive performance among young adult regular cannabis users. Consistent with previous studies, more cannabis use was generally associated with poorer episodic memory and decision-making, but not other measures of inhibitory control. However, patterns of results suggested sex-specific dissociations. In particular, more cannabis use was more consistently associated with poorer episodic memory performance in females than males. Conversely, more cannabis use was associated with poorer decision-making performance for males, but not females. These results provide further evidence for residual cannabis-associated neurocognitive deficits and suggest the importance of examining the impact of cannabis on neurocognition separately for males and females. (*JINS*, 2013, *19*, 1009–1015)

Keywords: Cannabis, Cognition, Marijuana, Neuropsychology, Sex differences, THC

INTRODUCTION

Cannabis use is prevalent among young adults, with rates of use rising in recent years (Johnston, O'Malley, Bachman, & Schulenberg, 2012). Accumulating evidence suggests neuropsychological deficits from cannabis use (Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd, 2001; Solowij et al., 2002), and a burgeoning area of research points to possible sex-differences. Neurodevelopmental, pharmacological, metabolic, behavioral, and hormonal differences may all be contributing factors (Crane, Schuster, Fusar-Poli, & Gonzalez, 2013). As more states decriminalize use, it is critical that we develop a thorough understanding of the neurocognitive effects of cannabis use. In this study, we examined sex-differences in the impact of cannabis use on episodic memory and inhibitory control: neurocognitive domains thought to be affected by cannabis use and on which healthy males and females often show differences in performance.

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Adverse effects of cannabis on neurocognitive functioning are well documented, but the magnitude, duration, and the specific conditions under which impairment manifests remain unclear. Deficits in episodic memory are some of the most commonly reported, especially with recent use (Crane et al., 2013; Pope et al., 2001). Studies also find problems in inhibitory control among cannabis users (Grant, Chamberlain, Schreiber, & Odlaug, 2012; Verdejo-Garcia et al., 2007; Wesley, Hanlon, & Porrino, 2011; Whitlow et al., 2004) (a predisposition toward unplanned, rapid reactions without regard to negative consequences; Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001), a domain including impulsivity, decision-making, risk-taking, delay-discounting, and motor inhibition. Further evidence of cannabis-associated deficits come from studies reporting relationships between amount of self-reported cannabis use and episodic memory (Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Cunha, Nicastri, de Andrade, & Bolla, 2010; Pope & Yurgelun-Todd, 1996; Solowij et al., 2002; Wagner, Becker, Gouzoulis-Mayfrank, & Daumann, 2010), decision-making (even after 25-days abstinence) (Bolla, Eldreth, Matochik, & Cadet, 2005; Verdejo-Garcia et al., 2007), and motor inhibition (Cunha et al., 2010).

Several lines of evidence suggest females may be more vulnerable than males to cannabis associated neurocognitive deficits. For example, females show greater cannabinoid receptor-1 (CB1) desensitization in several brain regions, including the prefrontal cortex and hippocampus (Burston, Wiley, Craig, Selley, & Sim-Selley, 2010)—regions especially involved in inhibitory control and episodic memory—suggesting they may be more sensitive than males to neural changes from consumption of cannabis. In addition, preclinical evidence indicates that females preferentially metabolize cannabis only to its most highly active metabolite, while males metabolize cannabis to multiple compounds, which may make females more vulnerable to the negative neural effects of cannabis than males (Narimatsu, Watanabe, Yamamoto, & Yoshimura, 1991). However, evidence of pharmacokinetic sex-differences in human studies is not currently well understood (Pigott, Walker, Teitelbaum, & Lu, 2009).

Despite some neuroimaging data suggesting cannabis-related sex-differences, with some evidence that female cannabis users may have larger right amygdala volumes (McQueeny et al., 2011) and prefrontal cortex volumes (Medina et al., 2009) compared to female controls, while male cannabis users had similar amygdalar volumes (McQueeny et al., 2011) and smaller prefrontal cortex volumes (Medina et al., 2009) compared to male controls; many studies to date report no interactions between cannabis using and non-using group status and sex (Pope, Jacobs, Mialet, Yurgelun-Todd, & Gruber, 1997; Solowij et al., 2011; Tait, Mackinnon, & Christensen, 2011). Recently, Lisdahl and Price (2012) examined how amount of cannabis use may differentially affect neurocognition in male and female cannabis users. Although they found cannabis users had poorer immediate recall and interference inhibition than controls, sex did not moderate these relationships. However, they used only one temporal parameter of cannabis use (past year), one measure of inhibitory control, and had a fairly small sample size ($n = 10$ males, 13 females) that may have made it challenging to detect more subtle effects.

In this study, we examined how amount of cannabis use during different periods of time (i.e., lifetime, past year, and past month) may be differentially associated with measures of episodic memory and several aspects of inhibitory control in young adult cannabis users. We hypothesized that recent cannabis use (i.e., past month) will be associated with poorer immediate and delayed recall (but not recognition), while lifetime cannabis use will be associated with poorer decision-making and motor inhibition, and these relationships will be stronger in females. Given the multi-dimensional nature of inhibitory control, we also examined other measures including risk-taking and delay-discounting.

METHODS

Participants

Participants were cannabis users from the Chicago-metropolitan area recruited through word-of-mouth and informational fliers. All participants: (1) were 18–24 years old; (2) had education >8 years; (3) had estimated full-scale IQ >75; (4) had no diagnosis of a learning disability, developmental delay, mental illness (including Attention Deficit Hyperactivity Disorder; ADHD), or neurological condition; (5) had no significant birth complications; (6) had no loss of consciousness >10 min; (7) had no current use of psychotropic medication; (8) demonstrated English fluency; (9) had no significant recent alcohol use (AlcoMate Prestige Model AL6000; Palisades Park, NJ); (10) had no illicit drug use other than cannabis in the past 30 days or >10× in life for each drug class; (11) had no recent illicit drug use other than cannabis (10-panel Drug Check Cup; Express Diagnostics, Blue Earth, Minnesota); (12) used cannabis: >200 in life, >4× per week during peak use, and in the last 45 days; (13) had no cannabis use on testing day; and (14) identified cannabis as their drug of choice. The Institutional Review Board at the University of Illinois at Chicago approved the study and written informed consent was obtained. Additional details regarding the larger study, methods, and participants have been previously reported (Gonzalez et al., 2012).

Demographics, Potential Confounds, and Substance Use

Demographic information, including race/ethnicity, and family of origin information was obtained through an examiner-led questionnaire. The Wechsler Test of Adult Reading assessed premorbid full-scale IQ, current and lifetime substance use were diagnosed with the Structured Clinical Interview for DSM-IV, the Beck Depression Inventory-II and Beck Anxiety Inventory assessed depression and anxiety symptoms, the Barratt Impulsiveness Scale-11 evaluated trait impulsivity, and the Wender-Utah Rating Scale assessed ADHD (scores >46 indicates possible ADHD diagnosis). An examiner-led semi-structured interview collected participants' amount and frequency of alcohol, nicotine, and illicit substance use during their lifetime, the past year, and the past month (Gonzalez et al., 2012).

Laboratory Measures of Neurocognitive Functioning

Verbal episodic memory

The Hopkins Verbal Learning Test-Revised (HVLT-R; Benedict, Schretlen, Groninger, & Brandt, 1998) norm-based, age corrected *Z*-scores for immediate recall (cumulative words recalled over three learning trials), delayed recall (total words recalled after a 20− to 25-min delay), and recognition discrimination (hits minus false positives) indexed verbal episodic memory.

Inhibitory Control

The Iowa Gambling Task (IGT) total net norm-based T-score (choices from advantageous decks minus disadvantageous

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decks) assessed decision-making (Bechara, Damasio, Damasio, & Anderson, 1994). We used the demographically corrected norms that control for age and education. Lower values indicate poorer decision-making or a bias toward immediate versus long-term rewards.

Mean number of pumps, excluding the number of pumps when the balloon "pops" on the Balloon Analogue Risk Task (BART; Lejuez et al., 2002) assessed risk-taking. Higher scores indicate greater risk-taking.

The Monetary Choice Questionnaire (MCQ; Kirby, Petry, & Bickel, 1999) examined participants' delay-discounting. Log-transformed parameter *k* values (representing individual differences in delay-discounting) were used, with higher values suggesting steeper discounting.

Total number of correct inhibitions minus number of "misses" on the "go" trials on the GoStop Task assessed motor inhibition. Higher scores indicate better motor inhibition (Dougherty, Mathias, Marsh, & Jagar, 2005).

General Statistical Procedures

All analyses were carried out using SPSS 20.0 (IBM). Data were inspected for non-normal distribution and outliers. Square-root transformations were used for amount of cannabis, alcohol, and nicotine use and nonparametric procedures were used for analyses of participant characteristics with data that violated assumptions of parametric procedures. Males and females were compared on demographic, substance use, and mental health variables using *t* tests or χ^2 tests as appropriate. In addition, males and females were compared on general neurocognitive performance using separate analysis of variance. We conducted moderated hierarchical multiple regression analyses with centered (a statistical approach of subtracting the mean from continuous predictor variables to help reduce multicollinearity) lifetime, past year, and past month cannabis use entered as separate independent variables in the first block, vectors for sex (i.e., male, female) in the second block, and their interaction in the third block as predictors, and performance on neuropsychological measures as separate dependent variables. In addition, we controlled for alcohol and nicotine use within the same period as the period of cannabis use (i.e., lifetime, past year, past month). To preserve power, non-significant covariates were removed from final models and only reduced models are reported. Results were deemed statistically significant when *p*-values $<.05$.

RESULTS

Demographics, Mental Health, Substance Use and Other Potential Confounds

As evident in Table 1, males and females reported minimal mental health complaints and did not differ on any potential confounds, with the exception that males drank more alcohol in the past 30 days than females.

Relationships between Amount of Cannabis Use, Sex, and Neurocognitive Performance

Neurocognitive performance did not statistically differ by gender, with the exception that females showed better motor inhibition than males (Table 1). It is important to note that in general, males and females demonstrated poorer performance on immediate and delayed recall compared to the normative sample (Table 1) and compared to a non-using control group in a prior analyses from the same parent study (Gonzalez et al., 2012), suggesting mild memory impairments in both groups. On the other hand, mean decision-making performance was not significantly poorer than the normative sample for male or female cannabis users. Measures for risk-taking, delayed discounting, and motor inhibition do not have published normative samples. Of note, cannabis users in this study did not significantly differ from non-using controls on their performance on any of the aforementioned inhibitory control tasks in our parent study (Gonzalez et al., 2012).

We found a significant negative relationship between amount of lifetime, past year, and past month cannabis use and immediate and delayed recall (but not recognition) on the HVLT-R, and decision-making performance on the IGT (Table 2). Cannabis use was not significantly associated with any other neurocognitive measure regardless of time frame (Table 2).

The interaction between lifetime cannabis use and sex trended toward significance on delayed recall and also on decision-making (Table 2). In addition, the interaction between past month cannabis use and sex trended toward significance on decision-making (Table 2).

Given our *a priori* hypotheses of potential sex-differences and multiple trends suggesting such, we performed follow-up exploratory analyses of the simple slopes for interaction terms that trended significance and for interactions where there was a main effect of amount of cannabis use in the model to better understand if neurocognitive measures related to cannabis use may have sex-specific patterns. All analyses used the same covariates as the reduced omnibus models (Table 2).

Immediate recall of both males or females was not associated with cannabis use in the past year ($\beta = -.19$, $t(65) = -1.58$, $p = .12$ and $\beta = -.18$, $t(65) = -1.54$, $p = .13$, respectively) or past month ($\beta = -.21$, $t(65) = -1.76$, $p = .08$ and $\beta = -.15$, $t(65) = -1.22$, $p = .23$, respectively). However, more lifetime cannabis use was associated with poorer immediate and delayed recall for both females (immediate: $\beta = -.30$, $t(65) = -2.59$, $p = .01$; delayed: $\beta = -.41$, $t(65) = -3.81$, $p < .001$) and males (immediate: $\beta = -.23$, $t(65) = -2.01$, $p = .049$; delayed: $\beta = -.28$, $t(65) = -2.59$, $p = .01$). On the other hand, more past year and past month cannabis use was associated with worse delayed recall for females ($\beta = -.32$, $t(65) = -2.72$, $p = .008$ and $\beta = -.30$, $t(65) = -2.56$, $p = .01$, respectively), but not for males ($\beta = -.17$, $t(65)\beta = -1.50$, $p = .15$ and $\beta = -.20$, $t(65) = -1.73$, $p = .09$, respectively). In contrast, poorer decision-making was associated with more lifetime ($\beta = -.38$, $t(65) = -3.32$, $p = .001$), past year ($\beta = -.37$, $t(64) = -3.36$, $p = .001$), and

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Table 1. Participant characteristics

	Male CU ($n = 44$) % or $M \pm SD$ (range)	Female CU ($n = 25$) % or $M \pm SD$ (range)	p-value
Demographics			
Age	20.75 ± 1.89 (18–24)	20.72 ± 1.62 (18–24)	.95
Estimated FSIQ	102.11 ± 10.24 (76–118)	102.80 ± 10.02 (82–120)	.79
Years of education	13.34 ± 1.67 (10–16)	13.64 ± 1.68 (11–18)	.48
Ethnicity/race			.70
Caucasian	43%	36%	
Black	34%	40%	
Hispanic	7%	16%	
Asian	7%	4%	
Other	9%	4%	
Annual household income in thousands of dollars [Md, IQR]	26 [9, 61]	33 [7, 94]	.84
Mother's education	14.23 ± 2.68 (7–18)	14.13 ± 3.00 (5–20)	.89
Mental health			
BDI-II Total Score [Md, IQR]	5 [2.25, 7.75]	5 [1.50, 10]	.81
BAI Total Score [Md, IQR]	4 [2, 9]	5 [3, 8]	.21
WURS, % of scores >46 [IQR]	2% [15.25, 30]	8% [9.50, 18.50]	.27
BIS-11 Total Score	59.48 ± 9.16 (41–82)	59.04 ± 10.58 (37–79)	.86
Substance Use			
Current (30 day) DSM-IV SUD			
Alcohol abuse	11%	0%	.08
Alcohol dependence	0%	0%	1.00
Cannabis abuse	34%	28%	.60
Cannabis dependence	27%	28%	.95
Lifetime DSM-IV SUD			
Alcohol abuse	25%	16%	.38
Alcohol dependence	2%	4%	.68
Cannabis abuse	41%	44%	.80
Cannabis dependence	34%	28%	.60
Years of cannabis use	5.18 ± 2.44 (1–12)	4.68 ± 2.14 (1–9)	.39
Age of 1st cannabis use	15.80 ± 2.12 (11–21)	16.29 ± 2.35 (11–20)	.38
Age of regular cannabis use	17.36 ± 1.98 (13–22)	17.96 ± 2.32 (13–23)	.26
Days since last cannabis use	4.18 ± 4.05 (1–26)	5.52 ± 8.45 (1–45)	.38
% THC+	77%	76%	.90
Lifetime [Md, IQR]			
Alcoholic drinks	569.50 [189.75, 1215]	288 [104.50, 1527.50]	.40
Cigarettes	1512.50 [19.50, 7515]	574 [0, 3186]	.37
Cannabis (grams)	625.15 [198.50, 2219.41]	482.40 [124.63, 1328.70]	.47
Past Year [Md, IQR]			
Alcoholic drinks	132 [33, 291]	80 [24, 210]	.33
Cigarettes	72 [0.50, 1417.50]	48 [0, 540]	.35
Cannabis (grams)	114 [55.65, 440.63]	90 [24, 383.40]	.42
Past 30 days [Md, IQR]			
Alcoholic drinks	11.50 [2.25, 20.75]	3 [0.50, 15]	.04*
Cigarettes	6 [0, 90]	7 [0, 50]	.52
Cannabis (grams)	10.75 [5.15, 36.68]	12 [2.38, 33.55]	.81
Neuropsychological performance			
Verbal Episodic Memory			
HVLT Immediate Recall (z score)	−0.81 ± 1.23 (−3.62–1.51)	−0.77 ± 1.45 (−3.89–1.24)	.90
HVLT Delayed Recall (z score)	−0.83 ± 1.32 (−4.13–0.88)	−0.90 ± 1.26 (−2.88–0.88)	.83
HVLT Recognition Discrimination (z score)	0.01 ± 0.82 (-2.83–0.5)	0.03 ± 0.95 (−2.86–0.5)	.95
Inhibitory Control			
IGT Net Total (T score)	45.59 ± 9.50 (26–63)	45.60 ± 10.26 (22–65)	1.00
BART (Mean Adjusted Pumps)	30.51 ± 12.28 (2.86–58.19)	31.16 ± 13.61 (6.54–56.17)	.84
MCQ (log-transformed k)	−1.50 ± 0.47 (−2.64–-0.67)	−1.41 ± 0.53 (−2.87–−0.80)	.49
Go/Stop (Inhibitions-Misses)	−37.39 ± 21.34 (−78–31)	−26.52 ± 15.08 (−61–5)	.03*

Note: All values are means, standard deviations, or ranges, unless otherwise noted.
CU = cannabis users; Md = Median; IQR = interquartile range; FSIQ = Full Scale IQ; BDI-2 = Beck Depression Inventory-2nd Edition; BAI = Beck Anxiety Inventory; WURS = Wender-Utah Rating Scale; BIS = Barratt Impulsiveness Scale-11th version; DSM-IV SUD = Diagnostic and Statistical Manual IV substance use disorders; THC+ = positive rapid urine toxicology testing. *$p < .05$.

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Table 2. Hierarchical moderated regression models for predicting how amount of cannabis use and sex affect neurocognition

	Lifetime			Past Year			Past Month		
Variable	R^2	β	*p*	R^2	β	*p*	R^2	β	*p*
HVLT (Immediate Recall)									
Block 1- Amount of Cannabis Use	0.13	−0.36	***.002***	0.07	−0.26	***.03***	0.07	−0.25	***.04***
Block 2- Sex/Gender	0.13	−0.02	.88	0.07	0.00	.99	0.07	0.02	.88
Block 3- Cannabis Use x Sex/Gender	0.14	−0.14	.33	0.07	−0.03	.85	0.07	0.05	.78
HVLT (Delayed Recall)									
Block 1- Amount of Cannabis Use	0.21	−0.46	***.001***	0.11	−0.33	***.006***	0.12	−0.35	***.003***
Block 2- Sex/Gender	0.22	−0.07	.54	0.11	−0.04	.71	0.12	−0.02	.84
Block 3- Cannabis Use x Sex/Gender	0.25	−0.22	***.10***	0.13	−0.18	.24	0.13	−0.11	.47
HVLT (Recognition Discrimination)									
Block 1- Amount of Cannabis Use	0.03	−0.16	.19	0.02	−0.14	.25	0.02	−0.13	.30
Block 2- Sex/Gender	0.03	−0.01	.96	0.02	0.00	.99	0.02	0.01	.95
Block 3- Cannabis Use x Sex/Gender	0.03	−0.08	.58	0.03	−0.09	.56	0.02	0.00	.99
IGT (Net Total)									
Block 1- Amount of Cannabis Use	0.09	−0.30	***.01***	0.18	−0.34	***.003***	0.12	−0.35	***.003***
Amount of Alcohol Use	–	–	n/a		0.24	***.04***	–	–	n/a
Block 2- Sex/Gender	0.09	−0.03	.82	0.18	0.01	.95	0.12	0.00	.97
Block 3- Cannabis Use x Sex/Gender	0.15	0.28	***.05***	0.21	0.23	.12	0.16	0.26	***.10***
BART (Mean Adjusted Pumps)									
Block 1- Amount of Cannabis Use	0.01	−0.11	.39	0.00	−0.04	.74	0.01	−0.11	.39
Block 2- Sex/Gender	0.01	0.02	.90	0.00	0.02	.85	0.01	0.03	.83
Block 3- Cannabis Use x Sex/Gender	0.04	−0.19	.20	0.00	0.06	.71	0.04	0.21	.22
MCQ (log-transformed k)									
Block 1- Amount of Cannabis Use	0.00	0.02	.88	0.00	−0.01	.92	0.00	0.05	.69
Block 2- Sex/Gender	0.01	0.87	.48	0.01	0.09	.49	0.01	0.09	.49
Block 3- Cannabis Use x Sex/Gender	0.01	−0.05	.72	0.01	0.01	.95	0.01	0.01	.95
Go/Stop (Inhibitions-Misses)									
Block 1- Amount of Cannabis Use	0.01	0.08	.50	0.01	0.08	.50	0.10	0.01	.92
Amount of Alcohol Use	–	–	n/a	–	–	n/a		−0.32	***.009***
Block 2- Sex/Gender	0.08	0.27	***.02***	0.08	0.27	***.03***	0.14	0.19	.11
Block 3- Cannabis Use x Sex/Gender	0.08	−0.03	.82	0.08	0.01	.94	0.14	0.03	.86

Note: The sex/gender variable was dummy coded, with males serving as the referent group; covariates were only included in models in which they were significant. HVLT = Hopkins Verbal Learning Task; IGT = Iowa Gambling Task; BART = Balloon Analogue Task; MCQ = Monetary Choice Questionnaire; n/a = non-applicable.
Italicized and bold *p*-values are significant or trending significant.

past month (β = −.39, $t(65) = -3.42$, $p = .001$) cannabis use in males, but not females (lifetime: β = .01, $t(65) = 0.11$, $p = .91$; past year: (β = −.08, $t(64) = -0.70$, $p = .48$), past month: β = −.10, $t(65) = -0.85$, $p = .40$).

DISCUSSION

In this study, we examined relationships between amount of cannabis use and neurocognitive functioning on indices of episodic memory and inhibitory control among a non–treatment-seeking, community-dwelling sample of young adult regular cannabis users who had minimal mental health problems or other drug use. We replicated prior findings of poorer episodic memory and decision-making with more cannabis use (Bolla et al., 2002; Cunha et al., 2010; Pope & Yurgelun-Todd, 1996; Solowij et al., 2002; Wagner et al., 2010), indicating decision-making is more strongly associated with cannabis use than other inhibitory control measures. Indeed, we previously found decision-making performance, but not performance on other inhibitory control measures, was associated with more symptoms of cannabis addiction (Gonzalez et al., 2012). Although significant sex by cannabis use interactions were not observed, several trends toward significant interactions point to potential sex-differences in relationships between cannabis use and neurocognitive functioning. Indeed, a more complex pattern of results emerged when examining exploratory relationships among cannabis use parameters and neurocognition for males and females.

When taken together, follow-up exploratory analyses found amount of cannabis use was more consistently associated with poorer episodic memory performance in females than males. Conversely, more cannabis use was associated with poorer decision-making performance for males, but not females. Cannabis use may disrupt estrogen-related dendritic spine maturation in the hippocampus, especially in females (Gillies & McArthur, 2010), while males' protracted neurodevelopment and earlier initiation of use compared to females

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may make them more vulnerable to cannabis-related disruptions in neuromaturation in the orbitofrontal cortex (Crane et al., 2013).

The time frame of cannabis use also had some bearing on the pattern of findings. Immediate recall was only associated with cumulative lifetime use, suggesting it is more influenced by cumulative burden than recent use. On the other hand, poorer delayed recall of females and decision-making performance for males were associated with more cannabis use across all time frames, indicating that more recent use, in addition to cumulative lifetime burden, is relevant to performance.

It is important to keep in mind that, in general, male and female cannabis users in this study demonstrated deficits in episodic memory, especially immediate and delayed recall, but not in decision-making, compared to their non-using counterparts recruited for the parent project (Gonzalez et al., 2012). Of note, there were no group differences, sex-differences, or interaction effects of group and sex between cannabis users in this sample and their non-using counterparts on decision-making, risk-taking, and delayed discounting in the parent project (Gonzalez et al., 2012). When compared to normative data, male and female cannabis users in this study scored in the low average range of abilities, yet a sizable proportion evidenced at least mild impairments in episodic memory (Table 1; *Z*-scores $\leqslant -1.0$ were observed on immediate recall for 45% of male cannabis users and 32% of female cannabis users and on delayed recall for 45% of males and 56% of females). Overall, participants' decision-making was not impaired when compared to the normative sample (Table 1; but 30% of males and 20% of females scored in the mildly impaired range or worse (T-score $\leqslant$40)). This is important because, despite mild overall episodic memory impairment and no overall decision-making impairment in our sample, we still found evidence for important relationships in how cannabis use may differentially impact these domains in a sex-specific manner. It is possible that our findings of poorer episodic memory among cannabis users is due in part to the residual (or semi-acute) effects of cannabis, as many of the participants in this study still tested positive for THC (Table 1), and similar to what other studies have found, participants performance may improve over time with abstinence (Hanson et al., 2010). Due to the fact that these young cannabis users are in their early stages of cannabis use, it is also possible that continued cannabis use may result in the emergence of clinically significant impairments in these domains.

In summary, our study expands on previously reported associations between more cannabis use and poorer episodic memory and decision-making, using a non–treatment-seeking community sample of young adult current cannabis users with minimal mental health problems and use of other substances. Patterns of results across various time frames suggested dissociations between males and females. Although we speculate on potential mechanisms for the observed relationships, our study is limited by its cross-sectional design and requires replication in a larger sample. A limitation of the study is that our sample consists only of young adult cannabis users who began their cannabis use between the ages of 11 and 21, with a mean age of 16. Given evidence of more negative neurocognitive consequences with an earlier onset of use (see Crane et al., 2013), our findings may not be generalizable to individuals who begin cannabis use at a later age or to older cannabis users. In addition, participants earned hypothetical rewards and losses, as opposed to real rewards and losses, on measures of decision-making, risk-taking, and delayed discounting, which may have influenced participant motivation; however, this remains a controversial issue (e.g., Bornovalova et al., 2009; Johnson & Bickel, 2002). Furthermore, family history of substance use was not measured, a factor that may have influenced the results. Ongoing and future studies will use longitudinal designs to better explore mechanisms for the observed patterns of results, including the possible role of sex hormones. The current study provides further evidence for residual cannabis-associated neurocognitive deficits and underscores the importance of examining the impact of cannabis on neurocognition separately for males and females. Sex-differences in the neurocognitive effects of cannabis may mean different functional consequences from use and have implications for intervention efforts.

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