

# Impact of 2 Weeks of Monitored Abstinence on Cognition in Adolescent and Young Adult Cannabis Users

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## Abstract

**Objectives:** Previous research suggests recovery from cannabis-related deficits in verbal learning and memory functioning after periods of cannabis abstinence in adolescents. Here, we examine how cannabis cessation affects cognitive performance over 2 weeks of monitored abstinence compared to controls in adolescents and young adults.

**Methods:** Seventy-four participants (35 cannabis users) aged 16–26 ceased all cannabis, alcohol, and other illicit substance consumption for a 2-week period; abstinence was monitored *via* weekly urinalysis, breath, and sweat patch testing. Starting at baseline, participants completed weekly abbreviated neuropsychological batteries. Measures included tests of attention, inhibition, verbal working memory, and learning. Repeated measures assessed within and between subject effects for time and group status, while controlling for past year alcohol and nicotine use. **Results:** Cannabis users showed increased performance compared to controls on sustained attention tasks after 2 weeks of cannabis use.

**Conclusions:** Deficits in attention, but not verbal learning and memory, recovered after 2 weeks of monitored abstinence. This differs from previous literature, suggesting that other cognitive domains may show signs of recovery after periods of cannabis cessation in adolescents and young adults.

**Keywords:** Cannabis cessation, Marijuana, Neurocognition, Adolescents, Emerging adulthood, Abstinence

Adolescent cannabis use has remained relatively stable at high levels over the past several years, as 36% of high school seniors reported using within the past year (Johnston et al., 2019). The relative popularity of cannabis within adolescents and young adults makes it of interest to parse out the long-term effects of cannabis use, specifically in neurocognition. Adolescence and emerging adulthood is a time of great neurodevelopmental growth, including in the endocannabinoid system (Giedd et al., 1999; Jernigan, Trauner, Hesselink, & Tallal, 1991). Therefore, adolescents may be more susceptible to the effects of repeated and early cannabis use (Ehrenreich et al., 1999; Lisdahl, Wright, Medina-Kirchner, Maple, & Shollenbarger, 2014).

Regular cannabis use during adolescence and early adulthood has been previously associated with neurocognitive deficits (Lisdahl, Gilbert, Wright, & Shollenbarger, 2013; Lisdahl et al., 2014). Specifically, cannabis use during this period has been associated with deficits in processing speed (Gruber, Dahlgren, Sagar, Gönenc, & Killgore, 2012; Lisdahl & Price, 2012; Medina, Hanson et al., 2007), verbal working

memory (Medina, Hanson et al., 2007; Solowij et al., 2011; Tait, Mackinnon, & Christensen, 2011; Thoma et al., 2011), and executive functioning (Gonzalez et al., 2012; Gruber, Dahlgren et al., 2012; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012; Lisdahl & Price, 2012; Mathias et al., 2011; Medina, Hanson et al., 2007; Wade, Wallace, Swartz, & Lisdahl, 2019). Animal models have revealed that chronic cannabis use leads to downregulation of endocannabinoid receptors located within the central nervous system (De Fonseca, Gorriti, Fernandez-Ruiz, Palomo, & Ramos, 1994). This downregulation of receptors may play a role in the observable neurocognitive deficits highlighted above. As adolescence marks a time of great neurodevelopmental growth, teens may be more vulnerable to the effects of cannabis in these receptors as the brain is still undergoing maturation (Casey, Getz, & Galvan, 2008). This point has been emphasized by work investigating early age of onset of cannabis use, which suggests that earlier use is associated with neurocognitive deficits (Fontes et al., 2011; Gruber, Dahlgren et al., 2012).

While differences in neurocognition have been reported across cannabis using samples, the persistence of these deficits following cessation of use has been questioned.

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Some research suggests that cognitive deficits found in cannabis users may no longer be observed following even short periods of abstinence (e.g., 72 hr), suggesting that some effects may be due to residual intoxication (Schreiner & Dunn, 2012; Scott et al., 2018). This residual intoxication is attributed to the fat-soluble properties of delta-9-tetrahydrocannabinol (THC), allowing for it to stay within the human body and slowly release over a period of months (Grotenhermen, 2003). Furthermore, there is some evidence that the downregulation of endocannabinoid receptors may be reversible after monitored abstinence (Hirvonen et al., 2012). However, it is notable that meta-analyses examining the impact of length of abstinence on neurocognitive outcomes include almost exclusively cross-sectional studies that also mix a wide variety of traditional cognitive and magnetic resonance imaging (MRI)-based tasks; thus, the heterogeneity of methodologies may obscure real differences. Furthermore, longitudinal functional studies provide evidence showing differences in cerebral blood flow after cannabis use that persists up to 7 days post-cannabis use compared to controls, suggesting residual effects from cannabis use may be more long-lasting (Sneider et al., 2008). Cross-sectional neuroimaging studies examining cannabis users after a month of abstinence have shown structural (Jacobus, Squeglia, Sorg, Nguyen-Louie, & Tapert, 2014; McQueeney et al., 2011; Medina et al., 2009; Medina, Nagel, & Tapert, 2010) and functional differences (Padula, Schweinsburg, & Tapert, 2007; Tapert et al., 2007), suggesting neural changes remain even after cannabis cessation. This conflicting literature points to a need for more longitudinal studies examining the effects of cannabis use following periods of abstinence.

In an attempt to address these concerns, studies examining how the length of abstinence impacts cognitive performance have gained attention (Ganzer, Bröning, Kraft, Sack, & Thomasius, 2016). Only three known longitudinal studies have examined the impact of monitored sustained abstinence from cannabis use in adolescents and young adults. Hanson et al. (2010) examined neuropsychological function between users and nonusers over 3 weeks of abstinence, assessing verbal learning, verbal working memory, and attention on a weekly basis. Schuster et al. (2018) randomized cannabis users into an abstinence or continuous-using group and examined the impact of sustained abstinence over a 4-week period on memory and attention outcomes measured weekly. Roten, Baker, and Gray (2015) examined cannabis cessation in treatment-seeking adolescents in a placebo-controlled trial comparing cognitive performance of abstinent and nonabstinent adolescents at 4 and 8 weeks. Findings across these three studies suggest that abstinence from cannabis results in verbal learning and memory recovery after 1–2 weeks of abstinence and psychomotor speed after a month of abstinence, while deficits in sustained and selective attention and inhibition endured for at least 3–4 weeks (Hanson et al., 2010; Roten et al., 2015; Schuster et al., 2018). It is worth noting that the effects of continuously monitored cannabis cessation within young adult cannabis users compared to controls have not yet been investigated, as the only study that included

young adults (Schuster et al., 2018) compared abstinent users to still using cannabis users without a healthy control group. Taken together, findings suggest that some cognitive deficits from cannabis use may be from acute intoxication or resolve with abstinence. However, deficits in attention may represent a long-term chronic effect of cannabis use (Hanson et al., 2010; Pope & Yurgelun-Todd, 1996; Schuster et al., 2018). Notably, these studies often neglect to account for length of abstinence leading up to their enrollment in the study, despite the fact that this initial abstinence period may play an important role in the return of cognitive functioning (Ganzer et al., 2016). In order to better address how monitored sustained cannabis abstinence impacts neurocognition in both adolescents and young adults while also taking into considerations for pre-enrollment cannabis abstinence, we have proposed the following study.

The current longitudinal study aimed to investigate how continuous abstinence from cannabis use affects cognitive performance, including measures of attention, inhibition, verbal working memory, and learning in adolescents and young adults. Participants were monitored over a period of 2 weeks, with toxicology-confirmed abstinence. We hypothesized that adolescent and young adult cannabis users would experience improved performance on cognitive tests measuring verbal working memory and learning after 1 week of monitored sustained abstinence but would continue to exhibit deficits in sustained attention compared to controls across the entire 2-week period of monitored abstinence.

## METHOD

### Participants

Participants included seventy-four 16- to 26-year olds (35 cannabis users and 39 controls) balanced for gender (53% male) and predominantly Caucasian (66%). Cannabis users were current users [nearly weekly; (Lisdahl & Price, 2012; Medina, Hanson et al., 2007; Medina, Schweinsburg, Cohen-Zion, Nagel, & Tapert, 2007)] who smoked over 44 times in the last year, over 100 times in their lifetime, and demonstrated negative results or downward trends in THC levels in sweat patch analyses for the period of monitored abstinence. Controls smoked no more than 5 times in the past year and no more than 20 times in their lifetime (Wade, Wallace et al., 2019; Wallace, Wade, Hatcher, & Lisdahl, 2019). Controls who had used cannabis in the past 30 days on the Timeline Followback (TLFB) or had positive toxicology screens at session one (baseline) were excluded from the study. Participants were excluded from the study if they were left-handed, possessed MRI contraindications (claustrophobia, pregnancy, or metal in body), had major medical or neurological conditions (such as seizures, migraines, tumor, chemotherapy exposure, multiple sclerosis, and movement disorders), past head trauma where they experienced unconsciousness for longer than 2 min, independent Axis I mood, anxiety, and attention disorders, prenatal substance use exposure or complications (gestations <35 weeks), or excessive illicit substance

use (>20 lifetime uses across all major drug categories). Inclusion and exclusion criteria were selected based off previous neurocognitive and neuroimaging studies done with cannabis using adolescents and young adults (Lisdahl & Price, 2012). Four participants (three cannabis users and one control) dropped out during the first 3 weeks of the study. Rationale for why participants dropped out was not obtained.

## Procedures

### Screening

Participants were recruited through the local community and university and were required to call in if interested in the study. Interested participants completed initial phone screening wherein they were asked basic questions to verify eligibility for the study. Participants who met initial eligibility requirements were invited to complete written consent (assent for participants under the age of 18) *via* mail and then underwent a more detailed screening. During detailed screening, participants were given the Mini International Neuropsychiatric Interview [MINI (Sheehan et al., 1998)], and adolescents under 18 and their parents were separately given the MINI-Kid (Sheehan et al., 2010). Furthermore, participants were given the Customary Drinking and Drug Use Record (CDDR) to assess for current and lifetime substance use history. All participants were compensated for completing the detailed screening, and participants who met full study inclusion criteria were invited to complete the remainder of the study. Ineligible participants were not informed of study eligibility criteria.

### Study sessions

Participants enrolled into the larger study were required to come in weekly for a brief battery of neuropsychological testing and questionnaires, once a week for 3 weeks (creating a 2-week monitored abstinence period for the current study). During the last visit of the brief neuropsychological battery, participants were given the TLFB to assess for substance use over the past year. Participants were asked to remain abstinent over the course of the study from all substances for the entire study duration, except for nicotine use. Participants were asked to abstain from nicotine use 1 hr prior to testing, so as not to confound results with effects from nicotine withdrawal (Ashare, Falcone, & Lerman, 2014). Abstinence was monitored *via* weekly urinalysis (sessions one, two, and three) drug testing as well as continuous drug sweat patch testing (administered at study sessions one, two, and three); thus, abstinence was confirmed for a minimum of 2 weeks between study sessions one and three. One week after the last brief neuropsychological testing visit, participants went on to complete an expanded neuropsychological battery as well as volume oxygen maximum (VO<sub>2</sub> max) testing (aerobic fitness) and MRI scan [data described in more detail in Wade, Wallace et al. (2019)]. Visits were scheduled approximately 7 days from their previous visit in order to attain at

least 14 days of abstinence between study sessions one and three. Examiners were not blinded to the status of participant's drug use status, in part due to the fact that participants had to report on the date of their last substance use episodes. All data were collected in accordance and with oversight of the local Institutional Review Board.

## Materials

### MINI psychiatric interview

The MINI is a semistructured clinical interview and was utilized during the detailed screener to identify comorbid Axis-I diagnoses (Sheehan et al., 1998). Participants under the age of 18 completed the MINI-Kid separately from their parents, who also completed the MINI-Kid (Sheehan et al., 2010).

### Substance use

- (1) *Customary Drinking and Drug Use Record*. During the detailed screen, participants completed the CDDR, a valid self-report measure for assessing adolescent substance use, to collect age of first use and regular use (defined as using cannabis once a week) as well as the frequency and quantity of the participant's lifetime usage (Brown et al., 1998).
- (2) *Timeline Followback*. The TLFB (Sobell & Sobell, 1992) was used to measure past year use (including the period of monitored abstinence). Trained research assistants utilized holidays and memorable events to the participants (e.g., birthdays, family gatherings, and parties) as anchor points to help the participant remember exact substance use over the past year. Substances were measured by standard units and included alcohol (in number of standard drinks), nicotine (in number of cigarettes and hits of chew/snuff/pipe/cigar/hookah), cannabis {in number of joints [number of cannabis concentrates converted to joints (based on estimated 0.5 gram = 1 joint)]}, and other illicit substances including stimulants, sedatives, gamma-hydroxybutyric acid, ketamine, hallucinogens, ecstasy, methylenedioxy-methamphetamine, opioids, prescription opiates, and inhalants. Last date of use was also collected for each substance.
- (3) *Substance use toxicology measurement*.
  - (1) *Continuous Sweat Patch*. All participants (cannabis users and controls) wore a PharmChek drug patch throughout the course of the study. PharmChek drug patches capture sweat excreted across multiple days, which allows detection of substances that may not be found in weekly urinalysis tests. This form of testing has proven to be a valid and accurate way of detecting substances within users across various substances including THC (Gentili, Mortali, Mastrobattista, Berretta, & Zaami, 2016; Saito et al., 2004). PharmChek drug patches allowed for the quantitative detection of cocaine, benzoyllecgonine, heroin, 6-monoacetylmorphine, morphine, codeine, amphetamines, methamphetamine, THC, and phencyclidine (PCP) at a minimum cutoff of 0.5 ng/ml for THC, 7.5 ng/ml for PCP, and 10 ng/ml for all other drugs tested.

- (2) *Alcohol Breathalyzer*. Participants were required to undergo breathalyzer testing for detection of recent alcohol use before every study session.
- (3) *Urine Toxicology*. Weekly urine samples were collected, and drug toxicology was tested via ACCUTEST SplitCup 10 panel drug tests. Substances that were screened included (minimum cutoffs included) amphetamines (1000 ng/ml), barbiturates (300 ng/ml), benzodiazepines (300 ng/ml), cocaine (300 ng/ml), ecstasy (500 ng/ml), methadone (300 ng/ml), methamphetamines (500 ng/ml), opiates (300 ng/ml), PCP (25 ng/ml), THC (15,000 ng/ml), and 11-Nor-9-carboxy-THC (THC-COOH) (50 ng/ml) as well as nicotine usage through additional testing via Nicalert cotinine urinalysis test strips.
- (3) The Hopkins Verbal Learning Task (HVLT) measures verbal learning and verbal working memory (Brandt & Benedict, 1991). Participants were read a list of 12 words and required to freely recall as many of the words as they can remember. After three trials of being read and asked to recall said list, participants were given a 20- to 25-min delay before being asked to recall the list again. Alternative forms were used every week of testing.
- (4) The Ruff 2&7 measures selective and sustained attention (Ruff & Allen, 1996). Participants were asked to scan across a series of lines containing target and distractor stimuli. Participants were asked to mark the target stimuli (2 and 7) as quickly and accurately as possible while ignoring distractor stimuli (other numbers or letters). Participants were timed on how long it takes to complete each of the 20 given trials. Scores reported are summed *T*-values.

### Abstinence decision-making

Since THC can be detected in the body for several weeks after cessation of cannabis use, participants were allowed to test positive for THC in their system via PharmChek as long as THC levels continued to drop between each study session (session one to two and two to three). If participants tested positive for any other substances, had a breath alcohol concentration higher than 0.000, had an increase in their THC levels during study participation, or self-reported the use of cannabis throughout the 2-week abstinence period, participants were excluded from the present analyses.

### Neuropsychological testing

The neuropsychological tests were selected based off previous research indicating they are sensitive to the effects of cannabis use, are associated with aberrant brain structure results related to cannabis use, and have been used in prior investigations of the role of sustained cannabis abstinence in adolescent users (Hanson et al., 2010; Lisdahl et al., 2013, 2014; Medina, Hanson et al., 2007). The CVLT-II Forced Choice trial was used as an embedded validity measure during the fourth testing session (Wade, Wallace et al., 2019). As no participants were below cutoff scores, participants are believed to have given appropriate effort on testing measures. Examiners were not blinded to whether participants were within the control or cannabis use group.

- (1) The Stroop task was used to measure inhibition and cognitive control (Golden & Freshwater, 2002). Participants were required to correctly identify the ink color of words while suppressing the response to read the word, which was written as an opposing word color. The number of correct responses and incorrect responses within a 60-s time period was recorded.
- (2) Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) Letter-Number Sequencing (LNS) was used to measure verbal working memory (Wechsler, Coalson, & Raiford III, 1997). Participants were asked to remember a series of letters and numbers and repeat them back in alphabetical and serial order. The length of letters and numbers participants were required to remember slowly grew with subsequent trials. Total raw correct responses were measured.

### Statistical analyses

A series of repeated measures analyses of covariance (ANCOVA) were run to examine the interaction between time (three study sessions) and group (cannabis users and controls). The number of past year alcohol and nicotine uses (as measured by the TLFB) was used as separate covariates within the repeated measures model to control for impact of comorbid substance use on recovery rates. Cognitive measures that were used for outcomes included the number of correct responses made during the Stroop task, total score from LNS, total score from immediate free recall and delayed free recall from the HVLT, and total accuracy and total response time from the Ruff 2&7. All statistical differences were made at a *p*-value less than .05.

## RESULTS

### Demographics

Cannabis users and controls did not significantly differ by age, race, gender, or years of education. See Table 1 for more demographic information.

### Substance use

As expected, cannabis users had significantly more cannabis use in the past year [ $t(34) = -7.1, p < .001$ ] as well as lifetime uses [ $t(34) = -5.2, p < .001$ ]. On average, cannabis users had been abstinent from cannabis for 20.7 days by the third session. In the control group, four participants had used cannabis within the past year, and their length of abstinence on average was 153.5 days; there was no reported use during the period of the study. Cannabis users had significantly more past year alcohol ( $t(53) = -4.3, p < .001$ ), nicotine use [ $t(34) = -2.7, p = .01$ ], and session three cotinine levels [ $t(41) = -2.7, p = .01$ ] compared to controls. Due to these differences, past year alcohol and nicotine use was included in the model to account for their potential influence in outcomes. See Table 1 for full substance use information by group.



**Table 1.** Demographics and group descriptors

|                          | Cannabis users<br><i>M (SD) [range]</i> | Controls<br><i>M (SD) [range]</i> |
|--------------------------|---|-----------------------------------|
| Age                      | 21.5 (2.2) [17.0–26.0]                  | 20.8 (2.8) [16.0–25.0]            |
| Gender (male)            | 62.8%                                   | 43.6%                             |
| Race (Caucasian)         | 62.8%                                   | 69.2%                             |
| Years of education       | 14.0 (1.6) [11.0–18.0]                  | 14.2 (2.3) [9.0–19.0]             |
| Past year alcohol use    | 347.4 (298.0) [0.0–1120.5]              | 100.9 (171.2) [0.0–698.5]         |
| Past year nicotine use   | 220.5 (489.5) [0.0–1867.0]              | 0.5 (2.0) [0.0–12.0]              |
| Past year cannabis use   | 353.2 (292.9) [44.7–1394.0]             | 0.2 (0.8) [0.0–4.8]               |
| Lifetime cannabis use    | 1210.4 (1380.7) [101.0–6000.0]          | 1.3 (2.8) [0.0–12.5]              |
| Length of abstinence     | 20.7 (10.1) [12.0–48.0]                 | 153.5 (118.9) [39.0–262.0]        |
| Age of first regular use | 17.4 (1.5) [15.0–21.0]                  | N/A                               |

*Note.* *M* = mean, *SD* = standard deviation. Past year and lifetime substance uses reflect total standard substance uses in the past year (e.g., alcohol in number of standard drinks; nicotine in number of cigarettes and hits of chew/snuff/pipe/cigar/hookah; and cannabis in number of joints). More detail of how this information was collected is reflected in the Method section under TLFB.

**Table 2.** Mean neuropsychological scores across sessions

|                         | Cannabis users |              |              | Controls     |              |              |
|-------------------------|----------------|--------------|--------------|--------------|--------------|--------------|
|                         | Session 1      | Session 2    | Session 3    | Session 1    | Session 2    | Session 3    |
| Letter–number span      | 11.5 (3.1)     | 12.3 (2.9)   | 13.1 (3.1)   | 11.4 (2.4)   | 12.3 (2.4)   | 12.8 (2.4)   |
| Ruff 2&7 total speed    | 94.6 (19.3)    | 104.7 (17.4) | 112.1 (20.4) | 101.0 (19.9) | 110.5 (22.3) | 116.8 (23.7) |
| Ruff 2&7 total accuracy | 80.6 (18.7)    | 90.4 (18.2)  | 98.7 (12.3)  | 82.7 (22.6)  | 88.7 (18.1)  | 94.6 (13.7)  |
| Stroop                  | 51.6 (7.7)     | 55.6 (7.2)   | 58.6 (10.3)  | 52.7 (10.2)  | 55.9 (13.3)  | 60.2 (11.4)  |
| HVLT–total recall       | 28.4 (3.7)     | 28.1 (3.1)   | 27.9 (3.9)   | 28.8 (3.9)   | 28.7 (4.2)   | 28.8 (4.1)   |
| HVLT–delayed recall     | 9.8 (1.7)      | 9.8 (1.8)    | 10.1 (2.2)   | 10.1 (1.8)   | 10.2 (2.1)   | 10.2 (2.0)   |

*Note.* Values include means and standard deviation in the format of mean (standard deviation).

## Repeated measures

### Time

Repeated measures ANCOVAs revealed a significant main effect by time with improved performance over time for LNS performance [ $F(1,69) = 11.73$ ,  $p < .001$ ,  $\eta_p^2 = 0.15$ ], Ruff 2&7 Total Time [ $F(1,69) = 74.03$ ,  $p < .001$ ,  $\eta_p^2 = 0.52$ ], Ruff 2&7 Total Accuracy [ $F(1,69) = 37.41$ ,  $p < .001$ ,  $\eta_p^2 = 0.35$ ], and total Stroop performance [ $F(1,69) = 16.24$ ,  $p < .001$ ,  $\eta_p^2 = 0.19$ ].

### Group effects

There were no significant effects between cannabis group, past year alcohol use, and past year nicotine use on neuropsychological performance (see Table 2).

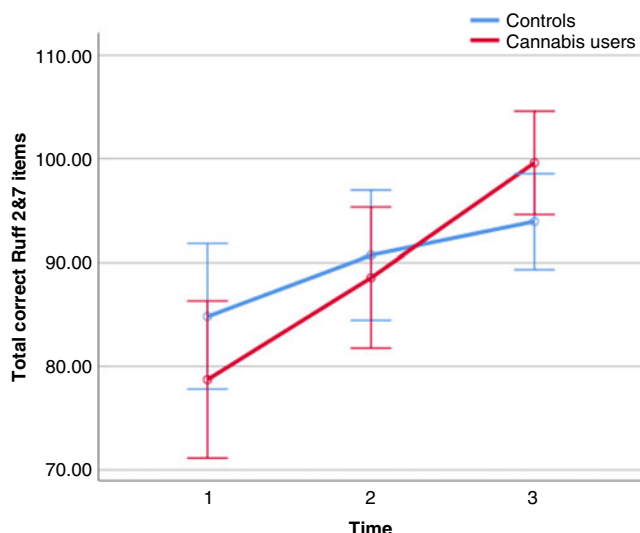
### Interaction effects

There was a significant interaction between time and cannabis group on Ruff 2&7 Total Accuracy [ $F(1,69) = 6.47$ ,  $p = .01$ ,  $\eta_p^2 = 0.09$ ], with cannabis users demonstrating significant improvements in accuracy compared to controls (see Figure 1). There was a significant interaction between

time and past year alcohol use on Ruff 2&7 Total Accuracy [ $F(1,69) = 12.22$ ,  $p = .001$ ,  $\eta_p^2 = 0.15$ ] and HVLT Immediate Free Recall [ $F(1,69) = 4.31$ ,  $p = .04$ ,  $\eta_p^2 = 0.06$ ] with heavier alcohol users showing increased performance with more time. There were no significant interactions with past year nicotine use.

## DISCUSSION

We predicted that cannabis users would have significant deficits in cognitive performance compared to controls at baseline, but that domains of verbal working memory and verbal learning would recover with 1 week of monitored sustained abstinence, but would continue to exhibit deficits in sustained attention compared to controls. However, our findings suggested that cannabis users were not significantly different from controls at baseline on these brief measures [although this same sample did demonstrate some deficits on a more expansive battery at a later time point (Wade, Wallace et al., 2019)], nor did they demonstrate improved performance in verbal working memory and learning tests compared to controls. However, the adolescent and young adult cannabis users in this study did show significant



**Fig. 1.** Ruff 2&7 total accuracy across sessions between cannabis users and controls.

*Note.* Figure highlights the interaction between cannabis use group and time on improved Ruff 2&7 accuracy across all three sessions. Covariates appearing in the model are evaluated at the following values: past year alcohol use = 212.80 and past year nicotine use = 105.95. Error bars: 95% confidence interval. Past year alcohol use and past year nicotine use were measured from the TLFB. More information about how these measures were collected can be found in the Method section.

improvement in their sustained attention performance following the 2-week period of monitored abstinence.

While previous research has suggested sustained deficits in attention following 3 weeks and 1 month of monitored abstinence in a sample of adolescents (Hanson et al., 2010) and a sample of adolescents and young adults (Schuster et al., 2018), respectively, our findings indicate that attentional deficits may continue to recover with continued abstinence in adolescents and young adults. It is also important to note that although our period of *monitored* abstinence was a minimum of 2 weeks, our cannabis users reported that they had on average an additional six and a half days of abstinence prior to enrolling the study, suggesting a total of at least 3 weeks of abstinence prior to the final date of testing. Thus, it is possible that subtle deficits in verbal learning and working memory had already recovered by the first day of testing and could explain the lack of significant neurocognitive differences between cannabis users and controls at any time point. This is consistent with Schuster et al. (2018) who found that these cognitive domains recovered within the first week. However, Hanson et al. (2010) demonstrated at least 2 weeks of sustained abstinence for cognitive recovery in these areas in a younger sample of adolescents. The age difference in the included cannabis user samples (Hanson et al., 2010; mean age = 18.1; present study's mean age = 21.5) may indicate that adolescents may require more time to experience cognitive recovery than their young adult counterparts. Furthermore, the cannabis users within our sample had relatively late onset of regular cannabis use

( $M = 17.4$  years old), which may explain a lack of significant differences in cognitive functioning at baseline due to both later onset of cannabis use and potentially fewer years of cannabis exposure [mean age of regular use was 15.6 for Hanson et al. (2010)]. Consistent with this, age of regular cannabis use and duration of use have been implicated as important factors in attention deficits (Ehrenreich et al., 1999; Solowij, Michie, & Fox, 1995). Taken together, these studies highlight the importance of measuring date of last cannabis use as the length of sustained abstinence depending on age may determine rates and domains of neurocognitive recovery from chronic cannabis use. Furthermore, years of chronic cannabis use may also moderate the above effects. Accordingly, future studies should examine these factors more closely. Finally, it is notable that we did observe cognitive deficits in primarily the same sample following 3 weeks of monitored abstinence on other neuropsychological tasks measuring psychomotor processing speed and sustained attention, including the CPT-2 and D-KEFS Trail Making Test (Wade, Wallace et al., 2019; Wallace et al., 2019). In addition, cannabis users demonstrated impaired working memory on the letter–number sequencing task after controlling for aerobic fitness level, and low-fit cannabis users had impaired verbal memory performance on the CVLT-II (Wade, Wallace et al., 2019). Thus, it is also possible that the tests utilized in the mini-NP battery were not sufficiently sensitive to detect cognitive deficits.

The underlying mechanism explaining recovery of cognitive functioning with continued abstinence from cannabis is most likely due to recovery within the endogenous endocannabinoid system (Hirvonen et al., 2012). Continued cannabis exposure has been shown to downregulate CB1 receptors, which are found largely within frontal and limbic regions of the brain (Howlett et al., 2004). Animal models have shown that this CB1 receptor downregulation may exhibit recovery comparable to controls after 7 days within the striatum and 14 days within the hippocampus after cannabis cessation (Sim-Selley et al., 2006). Due to the timeline and areas of CB1 recovery, this mechanism provides a potential explanation for the relatively rapid recovery of certain domains of cognitive functioning. Still, these findings must first be replicated within human populations. Additional research examining the direct relationship between these mechanism and cognition needs to be done.

Overall, these findings provide a message of hope that cannabis cessation could lead to the recovery of attentional deficits in adolescents and young adults. As research has shown that youth are at particular risk for harm from cannabis use (Turner, Spithoff, & Kahan, 2014), treatment models for adolescents engaging in cannabis use have been established (Diamond et al., 2002). While these programs seem promising, continuous abstinence rates within youth remain low (Budney, Roffman, Stephens, & Walker, 2007). Thus, additional research is needed to encourage continuous abstinence in adolescents and young adults, which may help to attenuate more long-term cognitive deficits that may occur with continued use and as the brain continues to mature.

Interestingly, past year alcohol also significantly predicted improved performance on attention and verbal working memory tasks over the period of abstinence. Recent studies have suggested that co-use of alcohol and cannabis can be an important consideration when disentangling the effects of substance use on cognition (Jacobus et al., 2014; Ramaekers et al., 2011; Wade, Thomas et al., 2020). Our findings highlight that abstinence from concurrent cannabis and alcohol use in co-users may play a role in the recovery of neuropsychological functioning. Patterns of substance use and co-use should be more closely investigated within future studies examining the impact of cannabis on cognition. Though these two issues are entangled in the present design, future studies may want to consider different groups abstaining from alcohol and cannabis separately.

There are limitations to consider within the context of our study. Cannabis users reported at least a week of abstinence from cannabis prior to entering the study; this may have resulted in some recovery of function prior to the monitored abstinence period. Furthermore, we were unable to disentangle the effects of abstaining from alcohol or cannabis use in the current design. Of other note, one study reported that toxicology testing with the sweat patch may miss small doses of edible cannabis (Huestis et al., 2008); however, none of our participants reported recent edible use in the past month, edible use during the past year was very low, and we also conducted urine toxicology analyses weekly. Examiners were not blind to participant drug status, which may have impacted results as recent research has emphasized that neuropsychologists have intrinsic biases on the cognitive effects of chronic cannabis users (Hirst, Watson, Rosen, & Quittner, 2019). Furthermore, no specific validity testing was done until session four. So while appropriate effort was given at session four, we can only infer valid effort during previous neuropsychological testing sessions leading up to session four. Our brief neuropsychological battery did not include measures of psychomotor speed or visual learning and memory, which have also been shown to be impaired in cannabis users (Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Lisdahl & Price, 2012; Wade, Wallace et al., 2019; Winward, Hanson, Tapert, & Brown, 2014). Furthermore, we did not conduct repeated neuroimaging and it is notable that previous studies have reported subtle deficits in brain function, connectivity, and structure following 2–4 weeks of monitored abstinence (Jacobus et al., 2012, 2014; Maple, Thomas, Kangiser, & Lisdahl, 2019; Price et al., 2015; Schweinsburg et al., 2010; Shollenbarger, Price, Wieser, & Lisdahl, 2015; Tapert et al., 2007); thus, additional longitudinal studies utilizing more sensitive measures of neuroimaging are needed before it can be concluded that full recovery is obtained following abstinence.

Research on the impact of sustained abstinence from cannabis on neuropsychological outcomes is understudied. Our findings add to this literature by demonstrating significant recovery in sustained attention deficits in regular adolescent and young adult cannabis users following 2 weeks of monitored abstinence. Further investigations into confirming

the impact of sustained abstinence in samples with an earlier age of cannabis use onset and examining other outcomes, especially neuroimaging, are needed. The implications of these findings are hopeful and suggest that sustained abstinence in late adolescent and young adult regular users can improve cognition in the domain of sustained attention. Thus, programs that promote abstinence in young users should remain a high public health priority.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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