Neurocognition in College-Aged Daily Marijuana Users

A THESIS
SUBMITTED TO THE FACULTY OF THE GRADUATE SCHOOL
UNIVERSITY OF MINNESOTA
BY

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IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER OF ARTS

Advisor: Monica Luciana, Ph.D.

December, 2013

Acknowledgements

My sincere thanks to my advisor, Monica Luciana, PhD, for her patient support and guidance throughout the research and writing process. Thanks also to the members of the Luciana lab for their contribution to data collection and management.

This study was supported by grant R01DA017843 awarded to Monica Luciana by the National Institute on Drug Abuse, by grant R01AA020033 awarded to Monica Luciana by the National Institute on Alcohol Abuse and Alcoholism, and by the University of Minnesota's Center for Neurobehavioral Development.

Abstract

Marijuana is the most commonly used illicit substance in the United States. Use, particularly when it occurs early, has been associated with cognitive impairments in executive functioning, learning, and memory. This study comprehensively measured cognitive ability as well as comorbid psychopathology and substance use history to determine the neurocognitive profile associated with young adult marijuana use. College-aged marijuana users who initiated use prior to age 17 (*n*=35) were compared to demographically-matched controls (*n*=35). Marijuana users were high functioning, demonstrating comparable IQs relative to controls and relatively better processing speed. Marijuana users demonstrated relative cognitive impairments in verbal memory, spatial working memory, spatial planning, and motivated decision-making. Comorbid use of alcohol, which was heavier in marijuana users, was unexpectedly found to be associated with better performance in many of these areas. This study provides additional evidence of neurocognitive impairment in the context of early onset marijuana use. Complications in determining cause-effect associations are discussed.

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Introduction

Marijuana is the most commonly used illicit drug in the United States among adolescents and young adults, with 51.9% of 18-25 year olds reporting use during their lifetimes (Substance Abuse and Mental Health Services Administration, 2012). Currently, adolescents and young adults perceive the risks of marijuana use to be lower, and profess less disapproval of peer marijuana use, than in past years (Johnston, Bachman, & Schulenberg, 2012; Johnston, O'Malley, Bachman, & Schulenberg, 2013). Despite these popular perceptions that marijuana use is not a high-risk activity, a growing body of research indicates that use is associated with cognitive impairments. Given growing advocacy for marijuana's legalization and its prevalence of use, it is crucial to better understand the nature of these impairments.

The primary psychoactive compound in marijuana, delta-9-tetrahydrocannabinol, acts directly on the central and peripheral nervous systems, binding to receptors for endogenous cannabinoids. Dense populations of endocannabinoid system (ECS) receptors are located in the prefrontal cortex, hippocampus, basal ganglia, thalamus, hypothalamus, and cerebellum. Within these regions, the ECS broadly modulates synaptic signaling (Freund, Katona, & Piomelli, 2003; Viveros, Llorente, Moreno, & Marco, 2005). Animal models indicate that the endocannabinoid system undergoes dramatic change during adolescence (Ellgren et al., 2008; Rodriguez de Fonseca, Ramos, Bonnin, & Fernandez-Ruiz, 1993). ECS receptor expression and binding capacity in the striatum, limbic forebrain, and ventral midbrain reach their peaks during adolescence, decreasing afterward to adult levels (Rodriguez de Fonseca et al., 1993). Similarly,

endocannabinoid receptor expression in cortical sensorimotor areas decreases only after the onset of adolescence (Heng, Beverley, Steiner, & Tseng, 2011). In the prefrontal cortex, ECS receptor expression and ECS-mediated synaptic inhibition is reduced in adolescence compared to earlier stages of development (Ellgren et al., 2008; Heng et al., 2011). Together, *in vitro* rat research indicates that ECS receptor expression in adulthood is lower than during earlier stages of development.

ECS receptors in the dorsolateral prefrontal cortex (DLPFC) are located in the presynaptic terminals of inhibitory GABAergic interneurons (Long, Lind, Webster, & Weickert, 2012). When ECS receptors are activated, they produce inhibition of the inhibitory GABAergic interneurons, ultimately leading to excitation. Normative patterns of modulation of the ECS through adolescence may be a mechanism through which greater degrees of cognitive control are achieved. That is, as ECS receptors are pruned as part of the normative changes in brain structure that occur during adolescence (Gogtay & Thompson, 2010), greater neuronal inhibition develops in the DLPFC, increasing capacities for cognitive control and other regulatory functions (Long et al., 2012).

Disruption of the ECS during adolescence through the introduction of outside cannabinoids can have long-term effects on these aspects of synaptic transmission and associated behaviors, leading to persistent alterations in adulthood. In rodents, chronic cannabinoid administration during adolescence is linked to decreased adult serotonergic activity in the brain stem (Bambico, Nguyen, Katz, & Gobbi, 2010) and blunted dopamine activity in the midbrain (Pistis et al., 2004). Rodents exposed to exogenous cannabinoids during adolescence demonstrate decreased memory and learning ability

(Jager & Ramsey, 2008; Rubino et al., 2009; Schneider & Koch, 2003, 2007) as well as decreased inhibitory control (Realini, Rubino, & Parolaro, 2009; Schneider & Koch, 2003) in adulthood.

Similarly, cognitive impairments are noted in human adolescents and young adults in the context of active marijuana use. As might be expected, impairments are evident during acute intoxication, including impaired attention, executive function, decision-making skills, and memory function (Crean, Crane, & Mason, 2011; Morrison et al., 2009; Ramaekers et al., 2006). Beyond acute intoxication, adolescent and young adult marijuana use is associated with numerous impairments, particularly in verbal memory and executive functioning. Marijuana users demonstrate poorer retrospective recall on list-learning tasks (Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Gonzalez et al., 2012; Hanson et al., 2010; Harvey, Sellman, Porter, & Frampton, 2007; Solowij et al., 2011; Takagi et al., 2011) as well as poorer memory for stories (Fried, Watkinson, & Gray, 2005; Medina et al., 2007; Schwartz, Gruenewald, Klitzner, & Fedio, 1989). Similarly, marijuana users display diminished memory for future actions assessed through prospective memory tasks (Bartholomew, Holroyd, & Heffernan, 2010; McHale & Hunt, 2008; Montgomery, Seddon, Fisk, Murphy, & Jansari, 2012).

Executive functioning skills appear to be diminished in marijuana users as well. Users show decreased planning ability on a Tower of London task (Grant, Chamberlain, Schreiber, & Odlaug, 2012) and a task of logical organization (Montgomery et al., 2012). Marijuana users demonstrate less flexibility and abstract reasoning ability than non-users

(Bolla et al., 2002; Pope & Yurgelun-Todd, 1996), and decision-making tends to be more risky (Clark, Roiser, Robbins, & Sahakian, 2009; Grant et al., 2012; Solowij et al., 2012).

Marijuana users demonstrate impairments inconsistently in other cognitive domains, including attention (Bolla et al., 2002; Dougherty et al., 2013; Lisdahl & Price, 2012), processing speed (Fried et al., 2005; Lisdahl & Price, 2012; Medina et al., 2007), and spatial reasoning (Harvey et al., 2007; Pope & Yurgelun-Todd, 1996). It is unclear if performance in these domains is directly related to marijuana use, or if other behaviors associated with marijuana use contribute to these findings.

Deficits remain during early (Cuttler, McLaughlin, & Graf, 2012; Dougherty et al., 2013; Fried et al., 2005; McHale & Hunt, 2008), as well as sustained (Bolla et al., 2002; Hanson et al., 2010; Lisdahl & Price, 2012; Medina et al., 2007) abstinence.

As law-makers grapple with questions about the legalization of marijuana, studies of non-acutely intoxicated users allow us to understand how cognitive functioning may be affected in the context of regular marijuana use. In addressing that question, it is important to consider when individuals began to use the drug. Marijuana users who begin use early in life often demonstrate greater cognitive impairment than marijuana users who begin use later on measures of memory and executive functioning (Ehrenreich et al., 1999; Fontes et al., 2011; Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012; Lisdahl, Gilbart, Wright, & Shollenbarger, 2013; Pope et al., 2003). Given the important role of the ECS during development, it is likely that disruption of the system at a younger age impacts later cognitive performance, particularly executive functions that emerge as frontostriatal brain networks reach their full maturational potential.

Two important difficulties emerge when trying to compare between studies of young adult marijuana users. First, age range tends to vary widely between studies. Studies exploring samples of college-aged subjects commonly use a broad age and developmental range, including people in their late twenties or thirties (Battisti et al., 2010; Bolla et al., 2002; Ehrenreich et al., 1999; Wagner, Becker, Gouzoulis-Mayfrank, & Daumann, 2010; Whitlow et al., 2004). While several studies have focused on adolescent users (Hanson et al., 2010; Harvey et al., 2007; Medina et al., 2007), it is not common to narrowly define age groups in young adult samples. Second, the majority of studies exploring neurocognitive profiles of adolescent marijuana users focus on a limited range of cognitive skills. This approach fails to provide a comprehensive cognitive profile, likely resulting in a limited understanding of any observed cognitive deficits. A broad assessment of cognitive ability can better reveal patterns of weaknesses but also potential strengths.

The current study provides a comprehensive cognitive profile of non-treatment seeking college student marijuana users in a narrow age-range (18-20). Participants were heavy users but had histories of typical development and were low-risk in relation to socioeconomic vulnerabilities, comorbid psychopathology, as well as general cognitive ability. Marijuana use in 18-20 year olds is common, and the assessment of cognition within this selective age band has the benefit of providing information regarding the functional skills and abilities of actively- and heavy-using individuals who are otherwise at low risk for impairment. This information is important to ascertain given the increasing

prevalence of marijuana use on college campuses and the possible further increase in use that could result from legalization.

Users were compared to non-using controls in the context of an assessment battery that included measures of clinical symptoms, other externalizing behaviors, and neurocognition across multiple domains of function.

It was predicted that users would exhibit relative impairments in learning and memory, particularly when such skills recruit executive functions, as well as decision-making, working memory, and planning.

Methods

Participants

Seventy-three individuals, ages 18–20, were studied: healthy non-using controls (n = 37) and heavy marijuana users who began use before age 17 (n = 36). The average age of use onset was 15.2 (Table 1). Participants were recruited through university advertisements, and all were monetarily compensated.

Inclusion criteria included being a native English speaker, right-handed, with normal/corrected-to-normal vision and hearing, and no reported history of neurological problems, mental retardation or current pregnancy. Controls were excluded if they met current or past Axis I DSM-IV-TR (American Psychiatric Association, 2000) criteria for any psychiatric disorder and/or if they reported marijuana use more than once monthly.

Inclusion criteria for marijuana users consisted of self-reported marijuana use of at least 5 times per week for at least 1 year. Use onset was required to be before age 17 so that length of use across study participants would be relatively uniform. Marijuana use

during this age span has been most strongly associated with cognitive impairment (Lisdahl et al., 2013), and use initiation is most common between the ages of 16 and 18 in the United States (Substance Abuse and Mental Health Services Administration, 2012). Marijuana users were excluded if they were daily cigarette smokers, if alcohol use exceeded 4 drinks for females and 5 drinks for males on more than 2 occasions per week, or if they met criteria for current or past substance dependence other than marijuana. One marijuana user met criteria for current and past alcohol dependence, despite meeting the project's use frequency criteria, and was excluded from analyses. Marijuana users were asked to refrain from drug use for at least 12 hours before testing so as not to be acutely high during the assessment. Longer periods of abstinence were not required, because we did not wish to study individuals in the midst of drug withdrawal and because a goal of the study was to capture functional capacities in the context of active use. Formal drug testing was not implemented due to budgetary limitations. This study was approved by the University of Minnesota's Institutional Review Board. Participants provided informed consent prior to participation.

Procedure

Interested participants (those who responded to posted advertisements) completed a phone screening followed by an in-person structured interview, the Kiddie-Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version (K-SADS-PL: Kaufman et al., 1997) to assess for recent and past histories of psychological problems. Current (recent) ratings were based on the previous 2 months for non-substance use related disorders and the previous 6 months for SUDs. In addition, information was

obtained about quantity and frequency of drug use across the past 30 days and past year. Intelligence was estimated by the Vocabulary and Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (WASI: Wechsler, 1999). Participants completed detailed health and demographic questionnaires. Participants who met inclusion criteria returned for a second assessment, including a comprehensive neurocognitive battery. The battery was designed to capture a broad array of functions in the domains of motor behavior, processing speed, attention, spatial and verbal memory, and executive skills.

Neurocognitive Battery

Motor function. *Finger Tapping Test* (Lezak, Howieson, & Loring, 2004). This test measures motor speed. Participants tapped a key as many times as possible within a 10-second period. Three trials were administered for each hand, and the number of taps per trial was recorded. The average of all three trials per hand is reported.

Grooved Pegboard (Lafayette Instrument, 1989). This test measures psychomotor dexterity and speed. Participants were presented with a flat board containing rows of holes and small metal 'pegs' that fit into the holes on the board. The pegs were shaped so that one side is square. Each peg had to be correctly manipulated in order to fit the holes. Under timed conditions, participants used the pegs to fill the holes on the board using first the right hand, then the left hand. Accuracy and response time were recorded.

Processing speed. *Digit Symbol* (WAIS-III Digit Symbol: Lezak et al., 2004; Wechsler, 1997). This test measures psychomotor performance, sustained attention, response speed, and visuomotor coordination. This test was administered according to

WAIS-III standardized procedures. The score recorded is the number of squares filled in correctly out of a total possible 133 squares.

Letter cancellation task (Lezak et al., 2004). This task measures immediate attention and vigilance but is also a speeded test. Participants viewed a piece of paper on which were printed rows of capitalized letters. They were instructed to work as quickly but as accurately as possible and to cross out all occurrences of the letters 'E' and 'C'. Time-to-completion and numbers of errors were recorded.

Verbal fluency. *Controlled oral word association test* (COWAT; Delis, Kramer, Kaplan, & Ober, 2000; Lezak et al., 2004). The COWAT assesses verbal production as well as rule maintenance and response monitoring. It was administered according to standardized procedures using the target letters F, A, and S. A total score for each participant was calculated, representing the total number of words generated across all three trials after deductions for rule violations, set- loss errors (i.e., words not beginning with target letters), and perseverations (i.e., saying the same word more than once).

Verbal attention and working memory. *Digit Span* (WAIS–III Digit Span; Wechsler, 1997). This test measures immediate recall of auditory verbal information. Digit span forward and digit span backward conditions were administered according to WAIS-III standardized procedures.

Verbal learning and memory. *Rey Auditory Verbal Learning Test* (RAVLT; Lezak et al., 2004; Rey, 1993). This test measures acquisition, storage, and retrieval of verbal information. During the learning stage, participants were read a list of 15 words 5 separate times and were asked to recall as many words as they were able after each

presentation. Then, they were read a new (interference trial) list of 15 words once and asked to recall those words. Participants then were asked to freely recall as many words as they could from the first list (immediate recall). Following a 30-minute delay, participants were again asked to recall as many words as they could from the first list. The number of words recalled and errors during the learning trials, interference trial, immediate recall, and delayed recall trials were recorded. The learning trials assessed the participant's immediate learning and temporary storage of verbal information. The interference trial assessed immediate learning of new information, presented only once. The immediate recall trial assessed learning recall when the items not actively rehearsed in working memory. The delayed recall trial performance represented learning that has been consolidated into memory. Intrusion and perseverative errors were also tabulated. Intrusion errors occurred when participants responded with non-list words. Perseverative errors occurred when participants repeated responses during a given trial.

Additional learning and memory variables were calculated to best characterize performance. Loss after consolidation was calculated as the percentage of words recalled during delay relative to words recalled during the final learning trial (Takagi et al., 2011). Retroactive interference (trial 5 vs. immediate recall) and proactive interference (trial 1 vs. interference) were examined. To explore learning efficiency and strategy, bidirectional serial ordering and response consistency were calculated (Delis, Kramer, Kaplan, & Ober, 2000). Bidirectional serial ordering refers to recall of stimulus words in the same order as they are presented, forward or backward. Response consistency measures how often the same words are recalled from trial to trial during free recall as a

percentage of total words recalled during free recall trials:

$$\left(\frac{\text{Conjoint recall of words between trial 6,7}}{\frac{\Sigma T6,T7}{2}} \times 100\right).$$

Spatial memory. *Spatial span*. This test measures immediate recall of visually presented nonverbal information, and is a nonverbal analogue of the digit span test. The version used here was computerized using Eprime version 1.1 (Psychology Software Tools; www.psnet.com). Participants, seated at a computer terminal, viewed arrays of squares on the screen. One by one, some of the squares 'lit up' in a sequence. In the forward condition, participants repeated the sequence by touching the squares in the remembered sequence using a touch-pen device (FastPoint Technologies, Inc.). In the backward condition, participants repeated the sequence in reverse order. The forward and backward memory spans were recorded as the number of items recalled in correct sequence across trials in each condition.

Spatial Recognition (Cambridge Neuropsychological Test Automated Battery, CANTAB; Fray, Robbins, & Sahakian, 1996). This test measures recognition memory for spatial locations. The participant viewed empty boxes at different locations on the screen. Five stimuli were presented in succession at different locations on the screen for 3 seconds each. After a five-second delay, the participant was shown two boxes, one of which was in a location previously displayed in the earlier sequence. The participant indicated which box position was shown previously. Accuracy and response time were recorded. The percentage of correct trials across all four blocks was used as the variable of interest.

Self-Ordered Search (CANTAB; Owen, Downes, Sahakian, Polkey, & Robbins, 1990). This test measures spatial working memory, self-monitoring, and behavioral self-organization. Using a computerized touch-screen, participants searched for blue tokens hidden inside an array of boxes. The task was organized into 4, 6 and 8 box problems, with increased box number corresponding to increased task difficulty. Participants were instructed that at any one time there would be a single token hidden inside one of the boxes. Their task was to search until they found it, at which point the next token would be hidden. Once a given box yielded a token, that box would not be used to hide the token again during the trial. Every box was used once on every trial; thus, the total number of tokens to be found during each trial corresponded to the number of boxes on the screen. A "between-search" error was recorded when participants returned to open a box in which a token had already been found. Additionally, a strategy score was tabulated. The strategy score, which was based on responses to 6 and 8-item searches, reflects the participant's tendency to search through available locations in an organized fashion. Between-search error scores for each level of search complexity, as well as strategy scores, were the variables of interest.

Spatial Delayed Response Task (DRT; Luciana & Collins, 1997; Luciana, Collins, & Depue, 1998). This task measures working memory for the locations of spatial targets. During each of 48 trials, the participant first observed a central fixation point on a computer monitor. Next, a visual cue appeared in their peripheral vision for 200 ms. After the peripheral visual cue, the cue and fixation point disappeared, and the screen blackened for randomly interspersed delay intervals of 500 or 8,000 ms. After the delay

interval, the participant indicated the remembered location of the cue with a touch-pen device (FastPoint Technologies, Inc.). A block of 16 "no delay" trials were also administered prior to the delay trials to measure basic perceptual and visuomotor abilities independent of memory. Average accuracy (in millimeters) and response times (in milliseconds) were recorded for each condition.

Planning. *Tower of London* (CANTAB; Owen et al., 1990). This test measures future planning ability. A full task description can be found in Luciana et al. (2009). Using a computerized touch-screen, participants moved colored balls to match a target display (problem-solving block). Participants were told at the start of each problem-solving trial that the trial should be completed in *X* number of moves, where *X* was the minimum number of moves required to achieve a perfect solution. The total number of problems in which participants responded with the minimum number of moves was recorded and expressed as a proportion of total possible perfect solutions. Participants were instructed not to make the first move until they knew which balls to move and were encouraged to solve the problem correctly on the first try. Time from presentation of the problem to starting to solve the problem (planning time) was recorded. Planning time and percent of perfect solutions were examined.

Motivated decision-making. *Iowa Gambling Task* (IGT: Bechara, Damasio, Damasio, & Anderson, 1994). This task measures motivated decision-making ability. Participants completed a computerized version of the IGT (Hooper et al., 2004) during which they selected from among four decks of cards varying in their amounts of monetary reward and punishment (Bechara et al., 1994). Participants worked to earn real

money (maximum of $5). For each selection from Decks 1 or 2 (the "disadvantageous decks"), participants would win $0.25 but the losses were organized so that over 20 selections from these decks, participants would incur a net loss of $1.25. The difference between Decks 1 and 2 was in the frequency and magnitude of punishment: Deck 1 contained frequent (50% of cards) punishments, whereas Deck 2 contained less frequent (10% of cards) but much larger punishments. For each selection from Decks 3 or 4 (the "advantageous decks"), participants would win either $0.10 or $0.15 and the losses were organized so that over 20 selections from these decks, participants would accrue a net gain of $1.25. Similar to the disadvantageous decks, the two advantageous decks differed from each other in the frequency of punishment, such that small punishments occurred on 50% of the cards in Deck 3 and larger punishments occurred on 10% of the cards in Deck 4. Trials (n= 100) were split into 5 blocks with 20 trials per block. For each block, the number of choices from disadvantageous decks was subtracted from number of choices from advantageous decks. Thus, values above "0" correspond to relatively advantageous choices. In addition, the actual numbers of selections made from each deck were tabulated across the full task to analyze choice preferences.

Together, these measures took several hours to complete.

Self-Report Questionnaire

Participants completed Achenbach's Adult Self-Report (ASR; Achenbach & Rescorla, 2003) questionnaire, which yields answers to substance use questions. Substance use scales consist of self-reported daily tobacco use, number of days drunk, and days using drugs (other than alcohol or tobacco) for the previous 6 months.

Statistical Approach

Data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA), Windows version 19. Distributions of all variables were examined. Error variables for the Letter Cancellation, RAVLT, and COWAT tasks were square root transformed to meet assumptions for parametric analysis. Chi-square tests were used to compare nominal variables (i.e., sex) between users and controls. Mann-Whitney U analyses assessed for group differences in substance use characteristics, in which variances were unequal between groups. Univariate and repeated measures analyses of variance (ANOVA) assessed for group differences in other characteristics. Sex, IQ, and alcohol use were covaried in all group comparisons. To best characterize a wide variety of alcohol use patterns, alcohol use was quantified as an average of two alcohol use variables that were standardized across the whole sample (controls and marijuana users). The first alcohol use variable was calculated by multiplying the participants' self-reported average drinking occasions per week and the average number of alcoholic drinks per occasion for the previous 6 months, as assessed by direct interview. The second alcohol use variable was the number of days that the participant reported being drunk in the last 6 months, as assessed by the ASR questionnaire. Missing data from 2 controls and 1 marijuana user on an alcohol use variable reduced the sample size to 35 participants per group.

To provide a conservative control for the number of statistical comparisons, alpha levels equal to or below 0.01 were considered significant, and alpha levels at or below 0.05 were considered trend effects.

As will be described, levels of alcohol use also differed between groups. Significant group differences were further examined using partial correlations to explore the extent to which alcohol use contributed to those effects. Alcohol use was correlated with task performance in marijuana users, controlling for IQ, sex, and days using drugs in the past 6 months. Scatterplots of residuals were examined to assess for normal distributions, and data were screened for outliers and influential data points.

Results

Demographics (Table 1)

Groups were comparable in age, years of education, race/ethnic distribution, and IQ. Consistent with similar studies of drug users with demographically matched college student controls (Croft, Mackay, Mills, & Gruzelier, 2001), IQs were generally above average, indicating that participants were generally high functioning from a cognitive standpoint. There were significantly more males among marijuana users, consistent with the gender distribution of marijuana users in this age range (Substance Abuse and Mental Health Services Administration, 2011).

Substance Use Characteristics

Alcohol and marijuana use. Marijuana users had significantly higher alcohol use as assessed by averaging the standardized scores of typical alcohol use patterns and days drunk in the past 6 months ($p < 0.001$; Table 1). Additionally, marijuana users had greater tobacco use, days drunk, and days using drugs in the last 6 months compared to controls. As a result of exclusion criteria, controls reported no marijuana use. Marijuana users reported a mean age of initiation of use during mid-adolescence ($M = 15.24$, $SD =$

1.24). Marijuana users reported nearly daily marijuana use during the past 30 days with a mean of 10.20 hits per day; however there was considerable variability in the number of reported hits per day, with a standard deviation of 9.12.

DSM-IV-TR diagnostic characteristics. Marijuana users reported little substance use outside of marijuana and alcohol. The majority of marijuana users had tried other drugs less than 5 times, and no participant had used any other drug more than 15 times (Table 2). Almost all marijuana users met criteria for current and/or past marijuana substance use disorder (SUD) (Table 3) and many met criteria for current and past alcohol abuse. There was high concordance between current and past diagnosis of an SUD within subjects (Table 3). SUD symptom patterns were examined in detail to clarify symptom expression related to both alcohol and marijuana use. Marijuana users exhibited fewer symptoms related to current alcohol use (M = 0.89 symptoms per person, SD = 1.05) than related to marijuana use (M = 4.03 symptoms per person, SD = 1.90; U = 100.5, $p < 0.001$). Similarly, marijuana users reported fewer symptoms related to past alcohol use (M = 1.20 symptoms per person, SD = 1.32) than past marijuana use (M = 4.23 symptoms per person, SD = 1.77; U = 114.0, $p < 0.001$). As a result of exclusion criteria, controls exhibited very few symptoms related to current alcohol use (M = 0.11 symptoms per person, SD = 0.32) or past alcohol use (M = 0.03 symptoms per person, SD = 0.17), and no symptoms related to other drug use.

Comorbid Psychopathology

Given selection procedures, controls were free of psychopathology. Outside of SUDs, marijuana users reported little psychopathology (Table 3). One participant met

criteria for current Bipolar NOS; another met criteria for past Bipolar NOS. Both were due to episodic hypomania, consistent with the reported comorbidity between SUDs and bipolar disorder (Perlis et al., 2004; Wilens et al., 2008). Other psychological disorders included past Oppositional Defiant Disorder (n = 2) and past Specific Phobia (n = 1).

Overall, the sample of marijuana users is notable for its good overall psychological health independent of marijuana use, and for high levels of premorbid functioning (as indicated through estimated verbal IQ scores).

Neurocognitive Performance (Table 4)

Motor Function

Groups were equivalent in Finger Tapping and Grooved Pegboard performance with no evidence of laterality differences.

Processing Speed

Marijuana users demonstrated faster Letter Cancellation completion times. Omission and commission errors were equivalent between groups. Completion times were uncorrelated with overall errors in both groups. Groups were equivalent in Digit Symbol performance.

Verbal Fluency (COWAT)

Marijuana users displayed greater verbal fluency, producing more correct responses. Set-loss errors were only marginally greater among users. Perseverative errors were equivalent between groups.

Verbal Learning and Memory

The groups were equivalent on Digit Span forward and backward.

A repeated measures ANCOVA across RAVLT trials (T1-T5, interference trial, immediate recall, and delayed recall) revealed a group effect, F (1, 65) = 7.31, p = 0.009, η_p^2 = 0.10, and a group by trial interaction, F (1, 65) = 8.74, p = 0.004, η_p^2 = 0.12 (Figure 1). Follow-up analyses revealed that marijuana users had a trend toward poorer performance during list learning trial 5, F (1, 65) = 3.90, p = 0.05, η_p^2 = 0.06. Marijuana users performed worse than controls on the interference trial list. Following interference, marijuana users demonstrated poorer immediate recall and poorer 30-minute delayed recall. Furthermore, there was a trend for marijuana users have greater loss after consolidation, F (1, 65) = 6.30, p = 0.02 , η_p^2 = 0.09 (Marijuana user M = 78.04%, SD = 17.16, Control M = 90.90%, SD = 16.76)

Examining retroactive interference (trial 5 vs. immediate recall) and proactive interference (trial 1 vs. interference) revealed no significant trial by group interaction. No significant group differences were noted during learning or delayed recall for bidirectional serial ordering or response consistency during learning. Marijuana users demonstrated less response consistency between short- and long-term recall, F (1, 65) = 15.78, $p < 0.001$, η_p^2 = 0.20 (Marijuana user M = 80.64%, SD = 14.55, Controls M = 93.73%, SD = 6.58).

Errors during list learning and recall were equivalent between groups.

Spatial Working Memory

No significant group differences were evident on forward or backward Spatial Span, Spatial Recognition, or Spatial Self-Ordered Search. On the DRT, groups were equivalent in their accuracy and response latency for the no delay condition, indicating

that basic sensorimotor functions recruited by the task were similar between groups. Additionally groups displayed equivalent accuracy during the 500 ms delay condition. Marijuana users demonstrated a trend of decreased accuracy on the 8,000 ms delay condition. Marijuana users had significantly longer response latencies after both 500 ms and 8,000 ms delays. Accuracy and response latencies were uncorrelated in marijuana users and controls for the 500 ms and 8,000 ms delay conditions.

Planning

There was a trend for marijuana users to produce fewer perfect solutions on the Tower of London task. Marijuana users made more moves to complete 3-move problems. Additionally, marijuana users had marginally faster initiation times during 5-move problems.

Motivated Decision-Making

On the Iowa Gambling Task, total good minus bad choices over five blocks of the task were examined with block as the within subjects factor and group as the between subjects factor (Figure 2). A significant main effect of group, F (1,64) = 10.97, p = 0.002, η_p^2 = 0.15, was observed with marijuana users displaying poorer performance.

There was a significant group difference in choice of deck 1, F (1,64) = 7.63, p = 0.007, η_p^2 = 0.11, deck 2, F (1,64) = 7.77, p = 0.007, η_p^2 = 0.11, and a marginal group difference in choice of deck 4, F (1,64) = 5.26, p = 0.025, η_p^2 = 0.08. Marijuana users made more choices from disadvantageous decks, decks 1 and 2, and fewer choices from advantageous deck 4 (Figure 3).

Deck choices were compared to choices expected by chance. Both groups showed aversion to frequent punishment decks (1 and 3), choosing from these less often than expected at a significant or trend level (Deck 1: Marijuana user t (34) = -2.12, p = 0.041, Control t (33) = -7.43, $p < 0.001$; Deck 3: Marijuana user t (34) = -3.70, p = 0.001, Control t (33) = -2.26, p = 0.031). Within infrequent punishment decks, controls demonstrated a preference for smaller wins with infrequent smaller punishment (Deck 4: t (33) = 4.24, $p < 0.001$), with choices from deck 4 correlating with overall good choices throughout the task ($r_{\text{sex, alcohol use, IQ}} = 0.80$, $p < 0.001$). Conversely, marijuana users showed a preference for greater wins with infrequent but greater punishment (Deck 2: t (34) = 2.68, p = 0.011).

Associations with Alcohol Use

For all significant group effects described above, alcohol use was examined for associations with task performance within marijuana users (Table 5). For learning and recall measures of the RAVLT and average moves on 3-move problems of the TOL, greater alcohol use was unexpectedly associated with better task performance. Alcohol use was uncorrelated with other task performance variables.

Furthermore, within marijuana users, no group differences in cognitive function were noted between subjects with current alcohol abuse (n = 11) and subjects without current alcohol abuse (n = 24). Similarly, the sum of all SUD symptoms within marijuana users (alcohol and marijuana SUD symptoms) was not a significant predictor of cognitive performance when modeling marijuana users task performance with IQ and sex included as predictors.

Impact of Comorbid Psychopathology

Significant group differences remained essentially unchanged when marijuana users with psychopathology outside of SUDs (n = 5) were excluded.

Discussion

This study employed a comprehensive neurocognitive battery to assess a range of cognitive abilities in a low-risk sample of college-aged daily marijuana users who were studied in the context of active use. The user sample was notable in terms of its relative psychological health, absence of externalizing psychopathology, and above-average levels of general intellect. Several important patterns are evident from the findings. First, despite several cognitive strengths, users demonstrated a number of cognitive deficits relative to demographically-matched controls. In addition, while marijuana users exhibited greater alcohol use than controls, the concomitant use of alcohol had differential effects on specific domains of cognitive performance. Overall, it does not appear that most observed cognitive deficits between marijuana users and controls were due to alcohol-related deficits since for the majority of tasks, alcohol use was unrelated to task performance. However, within the domain of verbal learning, relatively higher levels of self-reported alcohol use in marijuana users were associated with better cognitive functioning on the RAVLT. This pattern is consistent with recent reports of more normative patterns of structural brain integrity in marijuana users who use alcohol versus those who do not (Jacobus et al., 2009; Medina, Schweinsburg, Cohen-Zion, Nagel, & Tapert, 2007). While counterintuitive, this finding may point to specific neural interactions, perhaps involving frontal and temporal lobe circuitry involved in memory

consolidation, between alcohol and marijuana such that alcohol use benefits some areas of function in the context of heavy marijuana use. Importantly, however, the interaction between alcohol and marijuana, if present, does not protect against diminished cognitive performance in other areas of function when users are compared to controls.

Moreover, the cognitive performance in marijuana users was not related to general substance use disorder impairments. A count of SUD symptoms across alcohol and marijuana did not significantly predict marijuana user's cognitive performance, and users with and without current alcohol abuse did not differ in cognitive performance. This indicates that the current findings are not due to general cognitive liability as a result of substance use exposure.

This study's sample was comprised of high functioning marijuana users with above average IQs and minimal non-substance-related psychopathology. Outside of their marijuana-related substance use diagnoses, users were representative of typical university students in the United States. Indeed, marijuana users were comparable to controls in psychomotor function, short-term verbal working memory, as measured with digit span, and several measures of spatial memory and reasoning. They also showed a number of relative cognitive strengths.

Marijuana users performed particularly well on speeded measures, such as letter cancellation and verbal fluency. Both measures are short tasks (< 2 minutes), requiring short-term sustained attention. It is important to note that these tasks are externally motivated, with instructions to work quickly.

On the other hand, users demonstrated many relative deficits: impaired and inconsistent patterns of verbal recall, slower reaction times and increased errors on delayed spatial working memory, difficulty with relatively easy planning problems on the Tower of London task, and strikingly poor Iowa Gambling Task performance. In addition to having memory difficulties, it appears users were generally less motivated and, as a consequence, less persistent in the absence of motivation-enhancing instruction, when tasks required sustained and internally-motivated effort.

For instance, the 3-move Tower of London trials are relatively easy and can be completed using perceptual cues. The observed pattern of better performance in users on more difficult relative to easy trials is reminiscent of motivational problems that can characterize neuropsychological performance (Lezak et al., 2004), where effort-based resources are more strongly allocated to more challenging relative to less challenging problems.

On the other hand, verbal learning performance was characterized by a pattern of sustained performance during early learning trials and a slow but subtle divergence from controls' performance as the task progressed (see Figure 1). Marijuana users and controls acquired verbal learning of the target list at an equivalent rate, difficulty level, and with equivalent consistency on the first 4 trials. However, users had a decreased ability to retain and restate previously learned verbal information. The re-statement of the learned material must be made on the basis of representational knowledge without the use of external cues. Moreover, marijuana users demonstrated greater loss after consolidation, when required to produce learned information after a time delay. Marijuana users'

relatively decreased response consistency between delayed recall trials indicates use of a less efficient recall strategy. While the loss of information may appear to be relatively low in absolute magnitude (1 in 15 presented words), this same degree of information loss in the context of ongoing academic, occupational, and social interactions could have obvious impacts on social function and other areas of achievement. The observation of relatively poor retention of learned material over time is consistent with other reports (Block et al., 2002; Fried et al., 2005; Medina et al., 2007; Pope & Yurgelun-Todd, 1996; Tait et al., 2011; Takagi et al., 2011; Wagner et. al., 2010) and could be explained by a combination of deficits in executive control as well as motivation.

When these findings are considered in relation to the areas where marijuana users demonstrated relative strengths (short-term externally-motivated tasks that required quick performance), it could be that marijuana users are most impaired when tasks require intrinsic motivation for completion and most successful when tasks are enhanced by the provision of motivation-enhancing instructions, such as the instruction to work quickly. Although this suggestion is speculative given that motivation was not directly measured in this study, motivation-enhancing instruction has been found to improve marijuana users' performance, but not that of controls, on a verbal learning and memory task (Macher & Earleywine, 2012).

In addition, the finding of slower response times on the delayed response task, in the context of reduced performance accuracy, supports the conclusion that executive control processes are impaired in users. The reaction time findings indicate that efficiency as well as accuracy of spatial working memory is compromised in marijuana

users. Notably, marijuana users' performance was intact on no-delay trials, ruling out the possibility that basic sensorimotor differences account for this patterning. The spatial delayed response task is heavily influenced by dopamine neurotransmission in frontostriatal circuits, with increased dopamine activity facilitating better performance (Luciana et al., 1998). The observed performance deficits may indicate blunted striatal or frontal dopamine activity in the marijuana users, a finding previously reported in adult marijuana users (Kowal, Colzato, & Hommel, 2011) and consistent with the animal literature (Pistis et al., 2004; Schneider & Koch, 2003).

This conclusion is further supported by the marijuana users' significantly impaired decision-making on the Iowa Gambling Task following reward and punishment feedback. Acute reduction of dopaminergic activity has been found to produce impaired decision-making performance on the Iowa Gambling Task (Sevy et al., 2006), mirroring the disruptions noted in the current study. Throughout the Iowa Gambling task, marijuana users failed to acquire an effective strategy. Marijuana users made more choices from decks providing frequent and/or larger punishments, resulting in poorer choices overall. These decks have the potential to yield high rewards, suggesting that reward feedback was more compelling to marijuana users than was punishment feedback.

The performance deficits observed in the current study cohere with findings from the brain imaging literature indicating less efficient brain activation patterns in marijuana users. Users demonstrate increased activation across a wide range of brain regions and recruit alternative brain networks during task performance (Block et al., 2002; Chang et al., 2006; Harding et al., 2012; Jacobsen et al., 2004; Kanayama et al., 2004; Padula et al.,

2007; Schweinsburg et al., 2010; Tapert et al., 2007). Increased activation and recruitment of alternative pathways may be compensatory and less efficient.

In summary, marijuana users demonstrated an inconsistent pattern in terms of leveraging appropriate strategies to facilitate performance on complex memory, planning, and decision-making tasks. These tasks generally required high levels of self-organization as well as intrinsic motivation as opposed to areas where the users excelled (fast, short-term processing tasks), which were more externally-motivated. These findings suggest that if individuals engage in marijuana use on a daily basis, they may become increasingly dependent upon external sources of reinforcement and motivation to structure their behavior as opposed to intrinsically-driven self-reliance and self-organization. On the other hand, they may excel in settings where external sources of motivation, in the attainment of short-term goals, are high. Users' performance across domains of function suggests the possibility of diminished frontostriatal dopaminergic activity, affecting both decision-making and spatial working memory performance. This may be the mechanism driving the performance deficits noted and may be one avenue through which chronic marijuana use impacts longer-term function.

Limitations

One limitation of the current study is the overrepresentation of males in the user sample. However, this gender distribution is consistent with the gender distribution of marijuana users in the United States (Substance Abuse and Mental Health Services Administration, 2012). Sex was controlled in all statistical analyses; however, findings cannot be readily generalized to female users. A further limitation is that our design does

not permit dose-response associations to be measured in users who tended to be relatively homogeneous in their use patterns. A related issue is that it is difficult to quantify the precise amount of drug ingested by users given that the potency of marijuana is not standard. While many studies have quantified dose by calculating hits per day (which we assessed), this measure does not address potency or the amount of drug ingested during a hit. Marijuana users were required to use marijuana at least 5 days per week, yielding a relatively homogeneous sample of users. There were no requirements for amount of hits during each episode of use.

Additionally, while marijuana users were not acutely high during testing, we cannot rule out the possibility that the cognitive differences observed in our sample are due to residual effects of marijuana use. However, the current assessment provides a comprehensive cognitive profile of otherwise high functioning individuals in the context of frequent current marijuana use. This profile allows us to make real-world inferences about how daily marijuana use might impact cognition. As questions of marijuana legalization are at the forefront of societal debates, understanding how daily marijuana use can impact skills that are important for social, educational, and occupational achievement is important.

Another possible concern is that marijuana users were in active states of withdrawal during testing, affecting the results. Users were asked to abstain for at least a twelve-hour period prior to the study. This possibility appears unlikely given the psychomotor performance exhibited by marijuana users, which is inconsistent with behaviors that individuals in the midst of marijuana withdrawal demonstrate. They tend

to show slowed psychomotor task performance and poor immediate attention (Haney et al., 2001). Finally, we did not employ marijuana drug testing, since the active compound in marijuana remains detectible long after prior use. The level of detail that participants conveyed regarding their use patterns was convincing in terms of the likelihood that they were, indeed, heavy users, an assumption validated by their reports of symptoms of marijuana dependence. However, because we did not employ drug testing, we cannot completely rule out the possibility that actual use in these participants is lower than what they self-reported. Finally, although our findings are suggestive of patterns of impairment that emerge as a consequence of use and replicate findings reported in the literature, cause-effect associations cannot be determined. It could be that premorbid levels of function were impaired in users prior to use onset.

Conclusions

The current study provides a comprehensive cognitive profile of college-aged daily marijuana users. Marijuana users demonstrated strengths relative to controls in processing speed and verbal fluency. Marijuana users also demonstrated numerous cognitive deficits, most notably in verbal memory, engagement and use of efficient strategies with complex tasks, and motivated decision-making. Counterintuitively, alcohol use in the context of heavy marijuana use seemed to protect against some, but not all, of these difficulties. Future dose-response studies in samples that are similarly free of comorbid pathology and in this well-defined age-range would be helpful in clarifying whether a single underlying deficit leads to these distinct behavioral patterns. Pharmacological challenge studies in users versus controls can clarify the role dopamine

activity plays in the observed behavioral patterns; users would be predicted to show blunted responses to dopamine stimulation. Additionally, the relationship between concurrent marijuana and alcohol use and cognitive performance should continue to be explored in early-onset marijuana users to determine the unique and combined effects of the substances on performance and on neural dynamics.

Table 1

Demographic and substance use characteristics of marijuana users and controls

	Control (n = 35)	Marijuana user (n = 35)		
	M (SD) or %	*M (SD)* or %	*F* or χ^2	*U*
Age	19.40 (0.93)	19.52 (0.62)	0.39	
Sex Ratio (male:female)	13:22	22:13	4.63*	
Race (% Caucasian)	77.14%	88.57%	1.61	
Years of education	13.26 (1.24)[a]	13.29 (0.94)[a]	0.01	
Estimated Full Scale IQ[a]	114.73 (9.40)	115.27 (9.56)	0.05	
Vocabulary T-Score[a]	62.10 (6.85)	61.27 (7.88)	0.21	
Matrix reasoning T-Score[a]	54.49 (5.98)	56.09 (5.21)	1.35	
Alcohol Use Average	-0.59 (0.69)	0.59 (0.76)	46.54**	
ASR Substance Use				
Past 6 months: Tobacco use per day	0.00 (0.00)	0.91 (1.55)		385.00**
Past 6 months: Days drunk	5.37 (9.24)	25.07 (18.38)		142.00**
Past 6 months: Days using drugs	0.14 (0.49)	145.94 (40.58)[a]		636.00**
Marijuana Use[b]				
Age First Used		15.24 (1.24)		
Past year: Days MJ used		333.43 (43.61) (range: 208-365)		
Past 30 days: Days MJ used		25.86 (3.24) (range: 20-28)		
Past year: Avg. hits per day		10.09 (8.82) (range: 2-50)		
Past 30 days: Avg. hits per day		10.20 (9.12) (range: 1.5-50)		
Lifetime: Max hits in 24 hours		38.72 (27.52) (range: 6-120)[a]		

Mann–Whitney *Us* were computed when appropriate.
[a]Marginal means presented, controlling for sex. [b]Variables only included for marijuana users.
*$p \leq .05$. **$p \leq .01$.

Table 2

Lifetime other drug usage in marijuana users. Number of participants who used each drug at different usage levels.

Substance	1-5 times	6-10 times	11-15 times	Mean Usage
Cannabis				
Hash	1			0.14 (0.85)
Stimulants				
Adderall	4	1		0.70 (2.06)
Cocaine	2	1		0.33 (1.34)
Opioids				
Vicoden	5			0.39 (1.35)
Codeine	1			0.06 (0.34)
Opium	4			0.26 (0.79)
Oxycodone	2			0.05 (0.24)
Psychedelics				
Mushrooms/LSD	16	3	2	1.24 (2.39)
Salvia	4			0.31 (1.08)
Mescaline	1			0.03 (0.17)
Benzodiazepines				
Xanex	3	1		0.09 (0.28)
Valium	1			0.11 (0.69)
Sedative/Hypnotics				
Ambien	1			0.29 (1.69)
Other				
Ecstasy	12			0.81 (1.48)
Nitrous Oxide	2			0.17 (0.86)

Table 3

DSM-IV-TR Diagnostic characteristics of marijuana users (n = 35)

	Current Diagnosis	Past Diagnosis	Current and Past
Marijuana Dependence	18	18	17
Marijuana Abuse	12	14	12
Alcohol Dependence	0	0	0
Alcohol Abuse	11	16	10
Bipolar NOS	1	1	0
Oppositional Defiant Disorder	0	2	0
Specific Phobia	0	1	0
Comorbidity			
Only Marijuana Dependence	14	9	
Only Marijuana Abuse	6	6	
Only Alcohol Abuse	2	0	
Marijuana Dependence, Alcohol Abuse	3	9	
Marijuana Abuse, Alcohol Abuse	6	7	

Table 4

Neuropsychological battery scores. Means reported are marginal means, controlling for sex, IQ, and alcohol use.

Cognitive Measure	Control *M (SD)*	Marijuana user *M (SD)*	*F*	*p*	η_p^2
Finger Tapping Test					
Dominant hand (# taps)	42.16 (10.19)	46.93 (7.19)	3.01	0.087	0.04
Non-dominant hand (# taps)	42.02 (8.49)	44.76 (7.65)	1.29	0.261	0.02
Grooved Pegboard					
Dominant hand time (seconds)	65.41 (8.14)	64.12 (8.31)	0.32	0.575	0.01
Non-dominant hand time (seconds)[a]	72.97 (9.98)	71.13 (11.55)	0.32	0.572	0.01
Letter Cancellation					
Time (seconds)	111.95 (16.60)	96.79 (18.08)	7.50*	0.008	0.10
Total omissions[c]	1.51 (0.71)	1.49 (0.76)	0.01	0.927	0.00
Total commissions[c]	0.81 (0.27)	0.72 (0.12)	1.42	0.237	0.02
Digit Symbol					
Total correct	87.59 (15.12)	89.35 (13.21)	0.17	0.680	0.00
COWAT – Verbal Fluency					
Total correct words generated	43.24 (8.50)	50.79 (10.98)	6.78*	0.011	0.09
Total set-loss errors[c]	0.82 (0.29)	1.11 (0.52)	4.67^	0.034	0.07
Total perseverative errors[c]	1.03 (0.39)	0.95 (0.41)	0.35	0.557	0.01
Digit Span					
Digits forward (# recalled)	7.52 (0.86)	6.99 (1.03)	3.28	0.075	0.05
Digits backward (# recalled)	5.76 (1.19)	5.24 (1.17)	1.95	0.167	0.03
RAVLT – Verbal Learning and Memory					
Total words: Trial 1-5	55.05 (7.00)	51.29 (8.34)	2.70	0.105	0.04
Total intrusions: Trial 1-5[c]	1.02 (0.58)	1.30 (0.63)	2.26	0.121	0.04
Total perseverative errors: Trial 1-5[c]	1.96 (0.78)	1.81 (1.01)	0.26	0.609	0.00
Total words: Interference trial list	7.40 (1.95)	5.83 (1.86)	9.08*	0.004	0.12

Total words: Immediate recall	12.24 (2.08)	10.56 (2.44)	6.65*	0.012	0.09
Total words: Delayed recall	12.03 (2.13)	9.68 (2.91)	10.47*	0.002	0.14
Spatial Span					
Forward (# recalled)	6.55 (0.98)	6.99 (0.89)	2.17	0.145	0.03
Backward (# recalled)	6.78 (1.22)	6.50 (1.01)	0.66	0.421	0.01
Spatial Recognition[a]					
% Correct recall	86.50 (8.14)	85.66 (7.20)	0.12	0.731	0.00
Self-Ordered Search[a]					
Between search errors 4	0.12 (0.49)	0.18 (0.44)	0.15	0.700	0.00
Between search errors 6	2.79 (3.25)	2.60 (2.67)	0.04	0.835	0.00
Between search errors 8	10.65 (9.02)	9.66 (8.32)	0.13	0.716	0.00
Total between search errors	13.56 (10.21)	12.43 (9.70)	0.13	0.720	0.00
Strategy Score: 6-8	30.28 (5.36)	28.80 (5.52)	0.76	0.386	0.01
Spatial Delayed Response Task					
Error: No delay (millimeters)	2.44 (0.76)	2.55 (0.88)	0.17	0.682	0.00
Error: 500 ms delay (millimeters)	6.44 (2.18)	7.70 (2.23)	3.15	0.080	0.05
Error: 8,000 ms delay (millimeters)	9.87 (3.36)	11.98 (2.55)	4.81^	0.032	0.07
Mean reaction time: No delay	1823.33 (575.62)	1962.42 (419.96)	0.75	0.390	0.01
Mean reaction time: 500 ms delay	1663.24 (352.62)	2034.85 (374.35)	10.93*	0.002	0.14
Mean reaction time: 8,000 ms delay	1733.73 (345.42)	2234.00 (475.77)	15.60*	< 0.000	0.19
Tower of London[a]					
% Perfect Solutions	83.71 (13.33)	74.12 (14.47)	5.24^	0.025	0.08
Average moves 2	2.00 (0.00)	2.00 (0.00)			
Average moves 3	3.00 (0.16)	3.28 (0.39)	8.63*	0.005	0.12
Average moves 4	4.92 (0.89)	5.16 (0.97)	0.72	0.398	0.01
Average moves 5	5.65 (1.00)	6.24 (1.13)	3.11	0.083	0.05
First move initiation time 2	3190.52 (1161.58)	3662.26 (735.35)	2.27	0.137	0.05
First move initiation time 3	5510.37 (2510.15)	5442.88 (1485.40)	0.01	0.920	0.00
First move initiation time 4	8308.17 (5079.47)	8420.53 (3091.36)	0.01	0.935	0.00
First move initiation time 5	12987.90 (6940.13)	8805.07 (5108.86)	4.75^	0.033	0.07

Average first move initiation time	7499.24 (3547.50)	6582.68 (2138.04)	0.94	0.337	0.01
Iowa Gambling Task[b]					
Good Choices-Bad Choices: Block 1	-1.12 (9.58)	-3.56 (7.18)	0.82	0.368	0.01
Good Choices-Bad Choices: Block 2	3.25 (10.36)	-2.13 (7.54)	3.85^	0.054	0.06
Good Choices-Bad Choices: Block 3	3.73 (9.48)	-1.68 (8.67)	3.47	0.067	0.05
Good Choices-Bad Choices: Block 4	9.56 (9.32)	-1.29 (10.09)	12.73*	0.001	0.17
Good Choices-Bad Choices: Block 5	9.80 (10.42)	-0.15 (10.66)	9.89*	0.003	0.13
Good Choices: Total	60.45 (18.17)	49.77 (16.10)	4.01^	0.049	0.06

[a]Data unavailable for 1 marijuana user ($n = 34$). [b]Data unavailable for 1 control ($n = 34$). [c]Square root transformed.
^$p \leq .05$. *$p \leq .01$.

Table 5

Follow-up partial correlations between alcohol use variable and cognitive measure in marijuana users controlling for sex, IQ, and days using drugs in past 6 months.

	Alcohol Use
Letter Cancellation	
Time	0.19
COWAT – Verbal Fluency	
Total words	-0.10
Total set-loss errors[a]	-0.28
RAVLT – Verbal Learning & Memory	
Total Words: Trial 5	0.46*
Total Words: Interference Trial List	0.53*
Total Words: Immediate Recall	0.56*
Total Words: Delayed Recall	0.52*
% of Learning Recalled During Delay	0.35
Delayed Consistency	0.50*
Spatial Delayed Response Task	
Error: 8,000 ms delay	-0.34
Reaction Time: 500 ms delay	-0.25
Reaction Time: 8,000 ms delay	-0.28
Tower of London[b]	
% Perfect Solutions	0.26
Average Moves 3	-0.46^
First move initiation time 5	-0.13
Iowa Gambling Task	
Good Choices-Bad Choices: Block 2	-0.12
Good Choices-Bad Choices: Block 4	0.13
Good Choices-Bad Choices: Block 5	-0.20
Good Choices: Total	-0.24
Deck1 Choices	0.18
Deck 2 Choices	-0.11
Deck 4 Choices	-0.06

[a]Square root transformed. [b]Data unavailable for 1 participant (n = 34).
^$p \leq .05$. *$p \leq .01$.

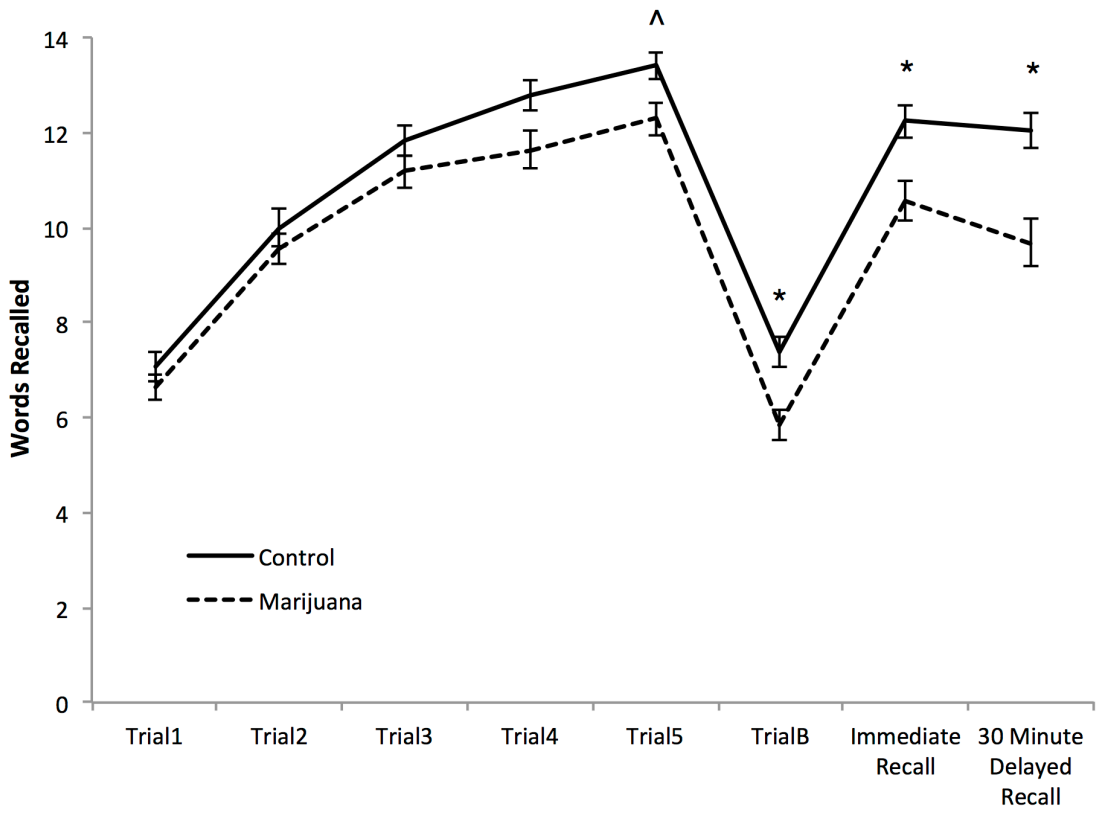

Figure 1. RAVLT Learning Curve. Average words recalled during learning trails 1-5, immediate recall, and 30 minute delayed recall.

^ $p \leq .05$ * $p \leq .01$

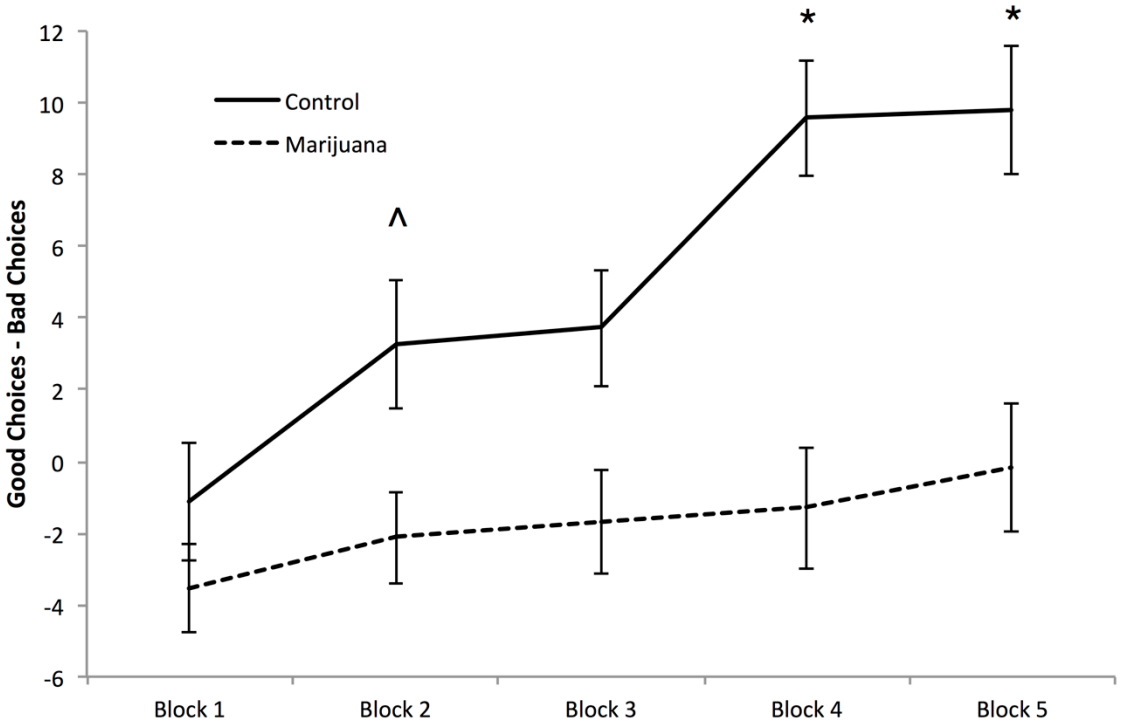

Figure 2. Iowa Gambling Task. Total good choices minus total bad choices over 5 blocks.

^ $p \leq .05$. * $p \leq .01$.

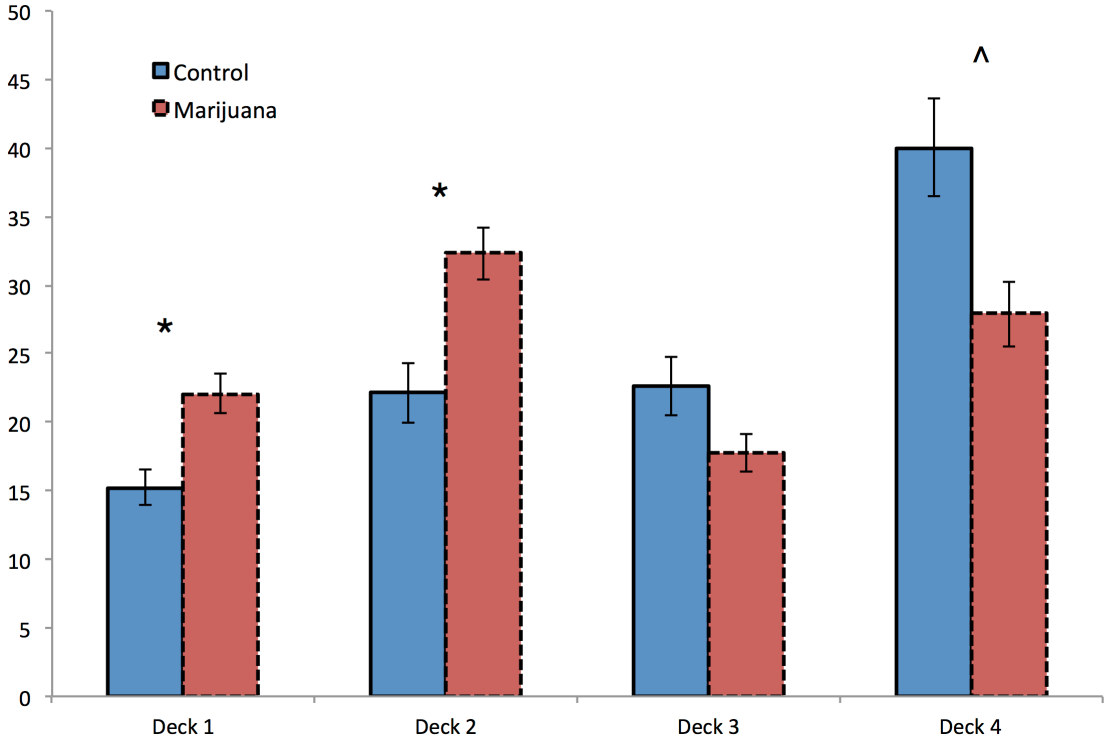

Figure 3. Iowa Gambling Task. Number of choices from each deck across 5 blocks between groups.

^$p \leq .05$. * $p \leq .01$.

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