One Month of Cannabis Abstinence in Adolescents and Young Adults Is Associated With Improved Memory

Randi Melissa Schuster, PhD[a,*]; Jodi Gilman, PhD[a]; David Schoenfeld, PhD[b]; John Evenden, PhD[c]; Maya Hareli, BA[a]; Christine Ulysse, MS[b]; Emily Nip, BA[a]; Ailish Hanly, BA[a,d]; Haiyue Zhang, MS[b]; and A. Eden Evins, MD, MPH[a]

ABSTRACT

Objective: Associations between adolescent cannabis use and poor neurocognitive functioning have been reported from cross-sectional studies that cannot determine causality. Prospective designs can assess whether extended cannabis abstinence has a beneficial effect on cognition.

Methods: Eighty-eight adolescents and young adults (aged 16–25 years) who used cannabis regularly were recruited from the community and a local high school between July 2015 and December 2016. Participants were randomly assigned to 4 weeks of cannabis abstinence, verified by decreasing 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol urine concentration (MJ-Abst; n = 62), or a monitoring control condition with no abstinence requirement (MJ-Mon; n = 26). Attention and memory were assessed at baseline and weekly for 4 weeks with the Cambridge Neuropsychological Test Automated Battery.

Results: Among MJ-Abst participants, 55 (88.7%) met a priori criteria for biochemically confirmed 30-day continuous abstinence. There was an effect of abstinence on verbal memory ($P = .002$) that was consistent across 4 weeks of abstinence, with no time-by-abstinence interaction, and was driven by improved verbal learning in the first week of abstinence. MJ-Abst participants had better memory overall and at weeks 1, 2, 3 than MJ-Mon participants, and only MJ-Abst participants improved in memory from baseline to week 1. There was no effect of abstinence on attention: both groups improved similarly, consistent with a practice effect.

Conclusions: This study suggests that cannabis abstinence is associated with improvements in verbal learning that appear to occur largely in the first week following last use. Future studies are needed to determine whether the improvement in cognition with abstinence is associated with improvement in academic and other functional outcomes.

Trial Registration: ClinicalTrials.gov identifier: NCT03276221

J Clin Psychiatry 2018;79(6):17m11977

To cite: Schuster RM, Gilman J, Schoenfeld D, et al. One month of cannabis abstinence in adolescents and young adults is associated with improved memory. *J Clin Psychiatry*. 2018;79(6):17m11977.

To share: https://doi.org/10.4088/JCP.17m11977

[a]Center for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

[b]Department of Biostatistics, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

[c]Cambridge Cognition, Park City, Utah

[d]University of Massachusetts Medical School, Worcester, Massachusetts

**Corresponding author:* Randi Melissa Schuster, PhD, Center for Addiction Medicine, Massachusetts General Hospital, 101 Merrimac St, Ste 320, Boston, MA 02114 (Rschuster@mgh.harvard.edu).

Cannabis use in adolescence is widespread, and rates of use are likely to increase further as more states move toward legalization. Lifetime, annual, past-month, and daily cannabis use among middle school– and high school–aged students was, respectively, 28.6%, 22.6%, 13.7%, and 3.0% in 2016, with rates of daily use doubling between 8th and 12th grade.[1] Students report very easy accessibility to cannabis, and attitudes of harm perception in 2016 were at or near historic lows, with only 1 in 3 12th-grade students perceiving great risk in regular cannabis use.[1]

Regular cannabis exposure during adolescence may cause greater adverse effects than later exposure due to ongoing neuromaturation occurring well into the third decade of life.[2,3] Gray matter in areas underlying higher-order cognition is last to mature,[4] and increased myelination contributing to white matter development continues through at least the late 20s.[5–9] Cannabis use is thought to affect normal neuromaturation[10] via effects of tetrahydrocannabinol (THC) on endocannabinoid-guided neuromaturation and selective synaptic pruning during adolescence.[11] Exposure to synthetic cannabinoids or THC during adolescence but not later in life is associated with cognitive impairments[12–15] that are linked with biomarkers of aberrant neurodevelopment, including shorter dendrites and reduced spine densities in the hippocampus.[15] Epidemiologic studies have also reported associations between earlier cannabis onset and poor neurocognition[16,17] as well as abnormalities in brain activation patterns[18] (for a review, see Crane et al[19]).

We sought to determine whether neurocognition improves with extended cannabis abstinence. To our knowledge, only 2 studies have prospectively examined patterns of adolescent neurocognitive recovery with cannabis abstinence, 1 in comparison to nonusing controls[20] and 1 in comparison to cannabis users who continue to smoke.[21] In a nonrandomized trial, Hanson and colleagues[20] found remittance of memory deficits after 3 weeks of abstinence among adolescent cannabis users compared to nonusers. The second study,[21] which was designed to evaluate changes in cognitive performance among adolescents enrolled in a randomized, placebo-controlled trial of *N*-acetylcysteine for cannabis cessation, showed improvement in verbal memory and psychomotor speed in those who were abstinent for 4 or 8 weeks compared to those who continued to smoke. These studies provide preliminary evidence that abstinence is associated with improved neurocognitive function. However, no study to date has employed an experimental design in which adolescent participants are randomized to stop using cannabis to control for group differences that might influence performance (eg, learning, baseline neurocognition,

Clinical Points

- It is not known whether adolescents continue to experience cognitive deficits even after they stop using cannabis.
- Patients will very likely experience improvement in thinking abilities, particularly memory for new information, when they stop using cannabis.

amotivation) and assessed neurocognition regularly during abstinence to determine the course of neurocognitive recovery.

We aimed to determine whether cognition improved to a greater degree in adolescent and young adult regular cannabis users randomized to an abstinence condition than in those randomized to a monitoring control condition, and the timing of any improvement. We focused our cognitive assessment on attention and memory, processes critical to academic performance and implicated in early cannabis exposure.

METHODS

Participants

Participants (N = 88) were adolescents and young adults, aged 16 to 25 years, recruited via peer referral and community advertisements and in a public high school in a northwest Boston suburb. Inclusion criteria were assessed via telephone screen and included cannabis use at least weekly, use in the week prior to screening, English fluency, and willingness to be randomized to 30 days of abstinence. Participants were randomized 2:1 to 4 weeks of cannabis abstinence achieved with a contingency management (CM) intervention (MJ-Abst; n = 62) or non-contingent monitoring, matched for contact time, with no abstinence requirement (MJ-Mon; n = 26).

Procedures

Enrollment occurred between July 2015 and December 2016 (ClinicalTrials.gov identifier: NCT03276221). A detailed description of procedures has been described previously.[22] Procedures were approved by the Partners Healthcare Human Subjects Committee. Written informed consent was obtained for participants over the age of 18 years, and written parental consent and participant assent were obtained for individuals under the age of 18 years.

Participants completed 7 visits over approximately 1 month in a private office in the hospital laboratory or on the high school campus. Cognitive testing occurred at baseline (prior to any change in cannabis use), and weekly for 4 consecutive weeks. Participants also met with study staff twice between baseline and the week 1 visit to provide urine samples.

Randomization occurred at the end of the baseline visit. After baseline, those assigned to MJ-Abst were asked to stop using cannabis for 1 month and completed a behavioral contract[23] that listed behaviors to be monitored, a schedule of monitoring, and contingencies to be imposed. MJ-Mon participants were not asked to abstain from cannabis and provided urine samples for toxicology on the same schedule as those assigned to MJ-Abst.

MJ-Abst participants earned incentives on a 2-track system for attendance and abstinence, with static denominations for attendance and escalating denominations for abstinence. The first 35 participants earned $585 for 30 days of abstinence with full attendance ($405 for abstinence and $180 for full attendance). Due to the success of the CM paradigm at eliciting 30 days of cannabis abstinence,[22] the payment schedule was reduced by approximately 30% for the final 27 participants ($315 for 30 days of abstinence and $105 for full attendance). MJ-Mon participants received escalating payments for attendance, totaling $220 for full attendance. Incentives were distributed via reloadable credit cards through Clinical Trials Payer (CT Payer) on the day of the visit for attendance and on receipt of the quantitative urinalysis results confirming abstinence (for MJ-Abst participants; described in the next paragraph).

For MJ-Abst participants, abstinence was indexed by self-reported nonuse and progressively decreasing urine concentrations of 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH), the main secondary THC metabolite and a widely accepted cannabis biomarker. Samples were shipped overnight to Dominion Diagnostics (Kingstown, Rhode Island), where THCCOOH levels were assayed using liquid chromatography/tandem mass spectrometry, normalized to creatinine (CN-THCCOOH).[24] New use was established using a statistical model developed by Schwilke and colleagues.[25]

Assessments

Demographic and background information was assessed at baseline. Full-scale IQ was estimated at baseline using the 2-subtest Wechsler Abbreviated Scale of Intelligence[26] for those recruited through the school and Wechsler Test of Adult Reading[27] for participants recruited from the community. Cannabis and alcohol dependence were assessed at baseline with the Cannabis Use Disorders Identification Test–Revised (CUDIT-R[28]) and Alcohol Use Disorders Identification Test (AUDIT[29]), respectively. A modified Timeline Followback interview[30] was conducted at baseline to approximate quantity and frequency of past-90-day cannabis and alcohol use. Current and lifetime Axis I diagnoses were assessed with the Structured Clinical Interview for *DSM-IV* (SCID-IV)[31] for participants recruited at the hospital.

Cognition was assessed at baseline and weekly for 4 consecutive weeks with the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition [http://www.cambridgecognition.com/cantab/]. Attention was indexed with the Attention Switching Task (AST), a measure of cued attentional set-shifting, and the Rapid Visual Information Processing task (RVP), a measure of visual sustained attention. For the AST, an arrow appeared

Table 1. Participant Descriptives at Baseline[a]

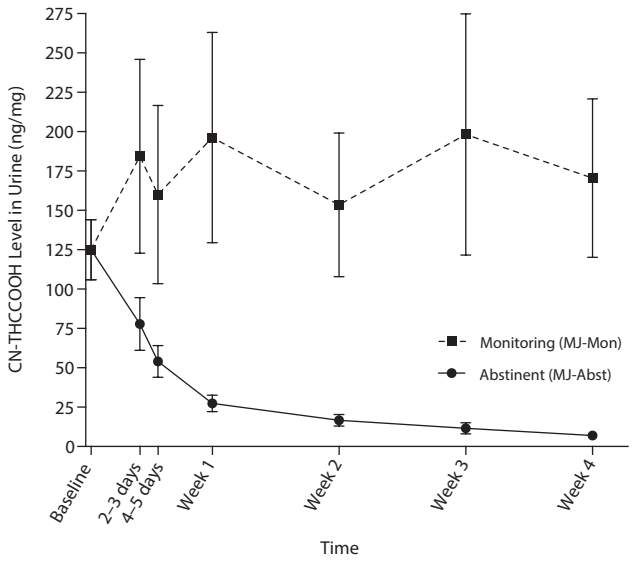
Variable	MJ-Mon (n = 26)	MJ-Abst (n = 62)	*P* Value
Demographic			
Sex, male, n (%)	14 (53.8)	36 (58.1)	.72
Age, y	21.2 (2.3)	20.5 (2)	.20
Education, y	13.9 (2)	14.0 (1.8)	.95
Race, n (%)			.29
White	15 (57.7)	44 (71.0)	
Black	5 (19.2)	7 (11.3)	
Asian	1 (3.9)	2 (3.2)	
More than 1 race	2 (7.7)	8 (12.9)	
Other	3 (11.5)	1 (1.6)	
Ethnicity, Hispanic, n (%)	2 (7.7)	6 (9.7)	.77
Cognition and achievement			
IQ	106.0 (10.7)	107.9 (8.6)	.36
GPA	3.1 (0.6)	3.1 (0.5)	.91
Baseline alcohol use			
Past-90-day alcohol use			
No. of days alcohol consumed	25.3 (20.2)	22.1 (13.8)	.39
No. of drinks consumed, median (IQR)	63 (31–152)	81.8 (48–147)	.48
No. of days since last alcohol use, median (IQR)	3 (2–6)	2 (2–5)	.50
Dependence symptoms, AUDIT score	7.1 (5.4)	8.6 (5.9)	.27
Baseline cannabis use			
Past-90-day cannabis use			
No. of days cannabis consumed	57.5 (27.3)	54.4 (25.1)	.61
No. of times cannabis consumed, median (IQR)	107.5 (46–157)	103 (50–172)	.94
Grams of cannabis consumed, median (IQR)	23.8 (10.9–57.6)	29.6 (10.1–77.5)	.96
Initiated cannabis use at < 16 years, n (%)	7 (26.9)	28 (45.2)	.11
No. of days since last cannabis use, median (IQR)	1 (1–3)	1 (1–2)	.33
Dependence symptoms, CUDIT-R score	13.1 (4.8)	14.4 (5.8)	.32
CN-THCCOOH concentration, median (IQR), ng/mg	104.1 (77.6–274.5)	88.8 (29–212.8)	.12
Current SCID-IV diagnoses, n (%)[b]			
Major depression	1 (4.5)	2 (3.7)	.88
Bipolar disorder	0 (0)	2 (3.7)	.36
Panic disorder	0 (0)	2 (3.7)	.36
Agoraphobia	0 (0)	1 (1.9)	.52
Social phobia	0 (0)	0 (0)	–
Specific phobia	0 (0)	0 (0)	–
OCD	0 (0)	0 (0)	–
PTSD	1 (4.5)	2 (3.7)	.88
Generalized anxiety disorder	1 (4.5)	4 (7.4)	.64
Anorexia	0 (0)	0 (0)	–
Bulimia	0 (0)	1 (1.9)	.52
Psychosis	0 (0)	1 (1.9)	.52

[a]All values shown as mean (SD) unless otherwise noted.
[b]SCID-IV not administered to participants recruited in high schools (Monitoring n = 22, Contingency Management n = 53).
Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, CN-THCCOOH = creatinine-adjusted 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol, CUDIT-R = Cannabis Use Disorders Identification Test-Revised, GPA = grade point average, IQ = intelligence quotient, IQR = interquartile range, MJ-Abst = abstinent from cannabis, MJ-Mon = monitoring, OCD = obsessive-compulsive disorder, PTSD = posttraumatic stress disorder, SCID-IV = Structured Clinical Interview for *DSM-IV*, TLFB = 90-day Timeline Followback.

on one side of the screen, and a cue was presented indicating whether the participant should respond according to the direction of the arrow, or the side of the screen on which the arrow appeared. AST outcome variables included total errors, response latency (in milliseconds), switching cost (difference between response latencies when the rule was switching versus when the rule remained constant; milliseconds), and congruency cost (difference between response latency of congruent versus incongruent trials; milliseconds). For the RVP, digits from 2 to 9 randomly appeared at the rate of 100 digits per minute in the center of the screen for 6 minutes and 30 seconds. Participants registered responses using the press pad every time the last digit in 1 of 3 target sequences (2-4-6, 3-5-7, and 4-6-8) was observed. Sixteen target sequences occurred every 2 minutes, with a total of 27 targets presented. RVP outcome measures included total hits, total false alarms, A′ (ie, signal detection measure of sensitivity to the target), mean response latency (milliseconds), and mean response speed variability (milliseconds).

Memory was measured with the Delayed Matching to Sample task (DMS), Spatial Span task (SSP), and Verbal Recognition Memory task (VRM). The DMS is a test of simultaneous and delayed matching to sample. Participants were shown a complex pattern (the sample) followed by 4 choice patterns. Participants selected the choice pattern identical to the sample as quickly as possible. Latency between presentation of the choice stimuli varied between 0-, 4-, or 12-second delays. Participants were administered

Figure 1. Urine Creatinine-Adjusted THCCOOH Concentrations Among Abstinent and Non-Abstinent Cannabis Users[a]



[a]All values represent means and standard errors. A total of 592 valid urine specimens were collected during the study period, and 552 (93.2%) of the specimens had 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) levels that were quantifiable based on available laboratory methods (range of creatinine-unadjusted THCCOOH levels in quantifiable samples: 0–3,920 ng/mL; range of creatinine-adjusted THCCOOH levels in quantifiable samples: 0–1,765.8 ng/mg). Urine creatinine-adjusted THCCOOH (CN-THCCOOH) concentrations declined during 4 weeks of monitored cannabis abstinence only among those randomized to 4 weeks of cannabis abstinence (MJ-Abst). Values are presented for specimens for which quantifiable THCCOOH and creatinine were available.

24 counterbalanced trials including 8 trials at each delay. DMS outcome variables included number of correct responses and latency to correct response, each at all 3 delay intervals. SSP measures visual span capacity. A pattern of white boxes was shown, and the boxes changed color one at a time in variable sequence. Once the sequence presentation was complete, participants touched the boxes in the order as was originally presented. Each task level comprised 3 possible sequences, and the sequence length at each level increased from 2 to 9 boxes. The task terminated when all 3 sequences at a given level were completed unsuccessfully. Outcome variables included the longest sequence successfully recalled and mean time to last response (in milliseconds). VRM is a measure of immediate and delayed verbal memory. Participants were shown a list of 18 words twice. After each presentation and a 20- to 30-minute delay, participants were asked to recall as many of the words as possible. Outcome variables included initial encoding (number of words recalled after trial 1), total encoding (sum of words recalled in trial 1 and trial 2), and delayed recall.

Alternate forms of CANTAB tasks were administered when available to minimize practice effects. Outcome variables were converted to *z*-scores based on the overall group means and standard deviations at baseline when all participants were non-abstinent. *z*-Scores within each test were averaged at each time point separately by abstinence group to create test score composites and averaged within domain at each time point separately by abstinence group to create attention and memory composites. Primary outcomes were the attention and memory domain composite scores, and secondary analyses focused on test score composites.

Analytic Approach

Data were analyzed using Stata 13.1 (StataCorp, College Station, Texas) and SAS 9.4 (SAS Institute, Cary, North Carolina). At baseline, participants were all considered non-abstinent. At subsequent time points, participants were analyzed per randomized group. Cognitive data from MJ-Abst participants who did not attain 4 weeks of abstinence were included only in analyses from visits with biochemically confirmed abstinence. MJ-Abst participants who dropped out of the study were considered non-abstinent at all visits with missing data. Repeated-measures analyses of variance were conducted to study longitudinal change in cognition from baseline through week 4. Separate models were conducted for attention and memory domain composite scores and, when appropriate, test composite scores. Significant group effects were followed up with pairwise group comparisons at each time point. Significant time effects were followed up by comparing differences in slopes between consecutive time points, separately by group. The α level was set at .05 for all statistical tests.

RESULTS

Participant Characteristics

MJ-Mon and MJ-Abst groups were comparable across demographic, mood, alcohol, and cannabis use indices, including frequency and amount of cannabis consumed in the 90 days prior to the intervention (Table 1), and across measures of cognition at baseline (Supplementary Table 1).

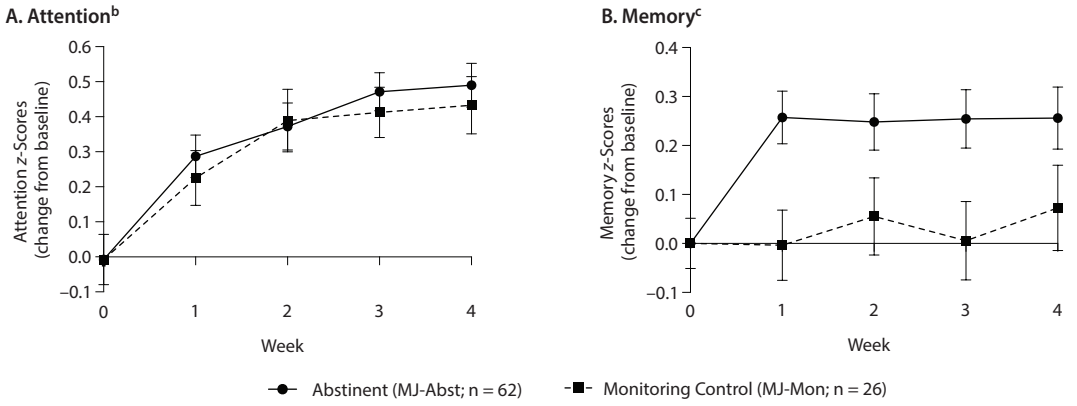
Verification of Cannabis Abstinence

Creatinine-adjusted THCCOOH levels declined across the 4 weeks for MJ-Abst but not MJ-Mon participants (Figure 1). Fifty-five (88.7%) of the 62 participants assigned to MJ-Abst met prespecified criteria for 30-day biochemically confirmed continuous abstinence. Comparison of baseline characteristics of MJ-Abst participants, divided by 30-day continuous abstinence status, is provided in Supplementary Table 2. All participants in the MJ-Mon group used cannabis during the study period, with a mean (SD) of 4.87 (3.15) days of use between visits.

Attention

There was a main effect of time (study week) ($F_{4,88} = 13.80$, $P < .0001$) on attention, but no main effect of abstinence status ($F_{1,88} = 0.37$, $P = .55$) or abstinence status × time interaction ($F_{3,88} = 0.34$, $P = .79$). This finding indicates that attention improved similarly in MJ-Abst and MJ-Mon participants during the 4-week assessment period (Figure 2A).

Figure 2. Change From Baseline in Cognitive Scores During 1 Month of Cannabis Abstinence or Continued Use[a]



Omnibus Model Effects
- **Time (study week):** $F_{4,88} = 13.80$, $P < .0001$
- **Abstinence status:** $F_{1,88} = 0.37$, $P = .55$
- **Abstinence status × time (study week):** $F_{3,88} = 0.34$, $P = .79$

Comparison of Slopes Between Weeks by Group
- **Baseline to week 1:**
  - **MJ-Abst:** $\beta = 0.29$, $t_{88} = 5.42$, $P < .0001$
  - **MJ-Mon:** $\beta = 0.23$, $t_{88} = 3.16$, $P = .002$
- **Week 1 to week 2:**
  - **MJ-Abst:** $\beta = 0.09$, $t_{88} = 1.75$, $P = .08$
  - **MJ-Mon:** $\beta = 0.16$, $t_{88} = 2.20$, $P = .03$
- **Week 2 to week 3:**
  - **MJ-Abst:** $\beta = 0.10$, $t_{88} = 2.07$, $P = .04$
  - **MJ-Mon:** $\beta = 0.02$, $t_{88} = 0.33$, $P = .74$
- **Week 3 to week 4:**
  - **MJ-Abst:** $\beta = 0.02$, $t_{88} = 0.43$, $P = .67$
  - **MJ-Mon:** $\beta = 0.02$, $t_{88} = 0.33$, $P = .74$

Pairwise Group Comparisons at Each Time Point
- **Week 1 (MJ-Abst vs MJ-Mon):** $\beta = 0.06$, $t_{88} = 0.77$, $P = .45$
- **Week 2 (MJ-Abst vs MJ-Mon):** $\beta = -0.02$, $t_{88} = -0.18$, $P = .86$
- **Week 3 (MJ-Abst vs MJ-Mon):** $\beta = 0.06$, $t_{88} = 0.77$, $P = .44$
- **Week 4 (MJ-Abst vs MJ-Mon):** $\beta = 0.06$, $t_{88} = 0.67$, $P = .51$

Omnibus Model Effects
- **Time (study week):** $F_{4,88} = 0.27$, $P = .89$
- **Abstinence status:** $F_{1,88} = 10.75$, $P = .002$
- **Abstinence Status × time (study week):** $F_{3,88} = 0.38$, $P = .77$

Comparison of Slopes Between Weeks by Group
- **Baseline to week 1:**
  - **MJ-Abst:** $\beta = 0.26$, $t_{88} = 5.60$, $P < .0001$
  - **MJ-Mon:** $\beta = -0.004$, $t_{88} = -0.05$, $P = .96$
- **Week 1 to week 2:**
  - **MJ-Abst:** $\beta = -0.01$, $t_{88} = -0.20$, $P = .85$
  - **MJ-Mon:** $\beta = 0.06$, $t_{88} = 0.81$, $P = .42$
- **Week 2 to week 3:**
  - **MJ-Abst:** $\beta = 0.01$, $t_{88} = 0.13$, $P = .90$
  - **MJ-Mon:** $\beta = -0.05$, $t_{88} = -0.68$, $P = .50$
- **Week 3 to week 4:**
  - **MJ-Abst:** $\beta = 0.002$, $t_{88} = 0.03$, $P = .97$
  - **MJ-Mon:** $\beta = 0.07$, $t_{88} = 0.92$, $P = .36$

Pairwise Group Comparisons at Each Time Point
- **Week 1 (MJ-Abst vs MJ-Mon):** $\beta = 0.26$, $t_{88} = 3.43$, $P = .0009$
- **Week 2 (MJ-Abst vs MJ-Mon):** $\beta = 0.19$, $t_{88} = 2.25$, $P = .03$
- **Week 3 (MJ-Abst vs MJ-Mon):** $\beta = 0.25$, $t_{88} = 2.83$, $P = .006$
- **Week 4 (MJ-Abst vs MJ-Mon):** $\beta = 0.18$, $t_{88} = 1.86$, $P = .07$

[a]All values represent means and standard errors.
[b]Attention improved similarly in MJ-Abst and MJ-Mon groups across the 4-week assessment period.
[c]Memory improved only in MJ-Abst participants, and this improvement occurred in the first week of cannabis abstinence.

Memory

There was a main effect of abstinence status on memory ($F_{1,88} = 10.75$, $P = .002$), such that MJ-Abst participants had better memory than MJ-Mon participants overall and at weeks 1, 2, 3, and 4 (trend). There was no main effect of time ($F_{4,88} = 0.27$, $P = .89$) or group × time interaction ($F_{3,88} = 0.38$, $P = .77$). Memory improved in MJ-Abst participants from baseline to week 1 (Figure 2B).

Change in Components of Memory With Abstinence: Exploratory Analysis

To examine the components of memory most impacted by cannabis abstinence, each test that constituted the memory composite was evaluated separately (Table 2). Main effects of abstinence and time on VRM appeared to drive the overall effect of abstinence on memory. The main effect of time on VRM was driven by improvement from baseline to week 1 in MJ-Abst participants only. The main effect of abstinence was such that the MJ-Abst participants performed better than MJ-Mon participants overall and at weeks 1, 2 (trend), 3 (trend), and 4 (trend). For SSP and DMS, there were main effects for time, but the effect of abstinence status and the abstinence status × time interactions were not significant.

To better understand the aspect(s) of declarative memory most impacted by cannabis abstinence, analyses were repeated considering each of the 3 constituting VRM variables separately (Table 3). There was a main effect of abstinence status for initial and total encoding. MJ-Abst participants learned more words after trial 1 and altogether, and this effect was significant overall and at weeks 1, 2 (trend for initial encoding only), 3 (initial encoding only), and 4 (trend for initial and total encoding). The main effect of time and the abstinence status × time interactions were not significant for either initial or total encoding. For delayed recall, there was a main effect of time. Abstinence status and the group × time interaction were not significant, indicating

Table 2. Change in Scores on Tests of Memory by Abstinence Status Across 4-Week Study Period

Variable	Spatial Span	Delayed Matching to Sample	Verbal Recognition Memory
Omnibus model effects			
Time (study week)	$F_{4,88}=5.01$, $P=.001$	$F_{4,88}=4.54$, $P=.002$	$F_{4,88}=2.52$, $P=.047$
Abstinence status	$F_{1,88}=2.95$, $P=.09$	$F_{1,88}=2.84$, $P=.10$	$F_{1,88}=8.65$, $P=.004$
Abstinence status × time	$F_{3,88}=1.74$, $P=.16$	$F_{3,88}=0.26$, $P=.85$	$F_{3,88}=0.58$, $P=.63$
Comparison of slopes between weeks by group			
Baseline to week 1			
MJ-Abst	$\beta=0.28$, $t_{88}=4.58$, $P<.0001$	$\beta=0.31$, $t_{88}=4.81$, $P<.0001$	$\beta=0.24$, $t_{88}=2.36$, $P=.02$
MJ-Mon	$\beta=0.13$, $t_{88}=1.46$, $P=.15$	$\beta=0.21$, $t_{88}=2.49$, $P=.01$	$\beta=-0.36$, $t_{88}=-2.44$, $P=.02$
Week 1 to week 2			
MJ-Abst	$\beta=0.05$, $t_{88}=0.88$, $P=.38$	$\beta=0.13$, $t_{88}=2.17$, $P=.03$	$\beta=-0.24$, $t_{88}=-2.37$, $P=.02$
MJ-Mon	$\beta=0.15$, $t_{88}=1.59$, $P=.12$	$\beta=0.05$, $t_{88}=0.61$, $P=.55$	$\beta=-0.03$, $t_{88}=-0.17$, $P=.87$
Week 2 to week 3			
MJ-Abst	$\beta=0.02$, $t_{88}=0.37$, $P=.71$	$\beta=-0.20$, $t_{88}=-3.77$, $P=.0003$	$\beta=0.19$, $t_{88}=1.53$, $P=.13$
MJ-Mon	$\beta=-0.17$, $t_{88}=-2.07$, $P=.04$	$\beta=-0.13$, $t_{88}=-1.67$, $P=.10$	$\beta=0.16$, $t_{88}=0.82$, $P=.41$
Week 3 to week 4			
MJ-Abst	$\beta=0.08$, $t_{88}=1.32$, $P=.19$	$\beta=0.10$, $t_{88}=1.91$, $P=.06$	$\beta=-0.16$, $t_{88}=-1.15$, $P=.25$
MJ-Mon	$\beta=0.25$, $t_{88}=3.02$, $P=.003$	$\beta=0.11$, $t_{88}=1.39$, $P=.17$	$\beta=-0.16$, $t_{88}=-0.80$, $P=.43$
Pairwise group comparisons at each time point			
Week 1 (MJ-Abst vs MJ-Mon)	$\beta=0.15$, $t_{88}=1.48$, $P=.14$	$\beta=0.10$, $t_{88}=1.06$, $P=.29$	$\beta=0.60$, $t_{88}=3.45$, $P=.0009$
Week 2 (MJ-Abst vs MJ-Mon)	$\beta=0.05$, $t_{88}=0.57$, $P=.57$	$\beta=0.17$, $t_{88}=1.70$, $P=.09$	$\beta=0.38$, $t_{88}=1.93$, $P=.056$
Week 3 (MJ-Abst vs MJ-Mon)	$\beta=0.25$, $t_{88}=2.69$, $P=.009$	$\beta=0.11$, $t_{88}=1.26$, $P=.21$	$\beta=0.42$, $t_{88}=1.95$, $P=.05$
Week 4 (MJ-Abst vs MJ-Mon)	$\beta=0.07$, $t_{88}=0.62$, $P=.54$	$\beta=0.10$, $t_{88}=1.05$, $P=.30$	$\beta=0.42$, $t_{88}=1.83$, $P=.07$

Abbreviations: MJ-Abst = abstinent from cannabis, MJ-Mon = monitoring.

Table 3. Change in Measures of Verbal Declarative Memory by Abstinence Status Across 4-Week Study Period

Variable	Initial Encoding	Total Encoding	Delayed Recall
Omnibus model effects			
Time (study week)	$F_{4,88}=1.13$, $P=.35$	$F_{1,88}=0.82$, $P=.51$	$F_{4,88}=5.56$, $P=.0005$
Abstinence status	$F_{1,88}=10.00$, $P=.002$	$F_{1,88}=5.67$, $P=.02$	$F_{1,88}=2.91$, $P=.09$
Abstinence status × time	$F_{3,88}=0.21$, $P=.89$	$F_{3,88}=1.32$, $P=.27$	$F_{3,88}=1.49$, $P=.22$
Comparison of slopes between weeks by group			
Baseline to week 1			
MJ-Abst	$\beta=0.27$, $t_{88}=2.12$, $P=.04$	$\beta=0.30$, $t_{88}=2.93$, $P=.004$	$\beta=0.08$, $t_{88}=0.68$, $P=.50$
MJ-Mon	$\beta=-0.32$, $t_{88}=1.81$, $P=.07$	$\beta=-0.22$, $t_{88}=-1.46$, $P=.15$	$\beta=-0.47$, $t_{88}=-2.58$, $P=.01$
Week 1 to week 2			
MJ-Abst	$\beta=-0.14$, $t_{88}=-1.09$, $P=.28$	$\beta=-0.26$, $t_{88}=-2.51$, $P=.01$	$\beta=-0.35$, $t_{88}=-2.94$, $P=.004$
MJ-Mon	$\beta=0.03$, $t_{88}=0.14$, $P=.89$	$\beta=0.11$, $t_{88}=0.70$, $P=.49$	$\beta=-0.19$, $t_{88}=-1.08$, $P=.28$
Week 2 to week 3			
MJ-Abst	$\beta=0.23$, $t_{88}=1.31$, $P=.19$	$\beta=0.23$, $t_{88}=1.77$, $P=.08$	$\beta=0.15$, $t_{88}=1.24$, $P=.22$
MJ-Mon	$\beta=0.01$, $t_{88}=0.02$, $P=.98$	$\beta=0.03$, $t_{88}=0.16$, $P=.87$	$\beta=0.39$, $t_{88}=2.17$, $P=.03$
Week 3 to week 4			
MJ-Abst	$\beta=-0.13$, $t_{88}=-0.69$, $P=.49$	$\beta=-0.08$, $t_{88}=-0.58$, $P=.57$	$\beta=-0.30$, $t_{88}=-2.22$, $P=.03$
MJ-Mon	$\beta=-0.02$, $t_{88}=-0.06$, $P=.96$	$\beta=-0.18$, $t_{88}=-0.90$, $P=.37$	$\beta=-0.25$, $t_{88}=-1.28$, $P=.20$
Pairwise group comparisons at each time point			
Week 1 (MJ-Abst vs MJ-Mon)	$\beta=0.59$, $t_{88}=2.95$, $P=.004$	$\beta=0.52$, $t_{88}=3.06$, $P=.003$	$\beta=0.60$, $t_{88}=3.45$, $P=.0009$
Week 2 (MJ-Abst vs MJ-Mon)	$\beta=0.43$, $t_{88}=1.89$, $P=.06$	$\beta=0.15$, $t_{88}=0.73$, $P=.47$	$\beta=0.38$, $t_{88}=1.93$, $P=.056$
Week 3 (MJ-Abst vs MJ-Mon)	$\beta=0.65$, $t_{88}=2.45$, $P=.02$	$\beta=0.34$, $t_{88}=1.59$, $P=.12$	$\beta=0.42$, $t_{88}=1.95$, $P=.05$
Week 4 (MJ-Abst vs MJ-Mon)	$\beta=0.54$, $t_{88}=0.62$, $P=.06$	$\beta=0.45$, $t_{88}=1.95$, $P=.05$	$\beta=0.42$, $t_{88}=1.83$, $P=.07$

Abbreviations: MJ-Abst = abstinent from cannabis, MJ-Mon = monitoring.

that MJ-Abst and MJ-Mon participants' overall abilities to recall words after a delay were comparable and that they changed in their ability to perform this task similarly over time.

DISCUSSION

Memory, but not attention, improved more among adolescents and young adults who abstained from cannabis compared to those who continued to use. This finding is consistent with that of prior studies that indicated neurocognitive dysfunction persists after several days of abstinence,[32–35] particularly in the domain of memory (for reviews, see references 36–38), and with findings that verbal memory improved after 4 or 8 weeks of abstinence.[21] The current study extends this finding by demonstrating that improvement in memory appears to occur with 1 week of continuous cannabis abstinence.

Declarative memory, particularly encoding of novel information, was the aspect of memory most impacted by cannabis abstinence. Those who maintained abstinence learned more words than those who continued to use cannabis. This finding is consistent with those of other studies that suggest a specific effect of cannabis on learning, including recent findings that THC acutely interferes with encoding of verbal memory without interfering with retrieval[39] and that an effect of cannabis on learning accounts for effects on delayed recall.[17] Cannabis use may

impede learning via disruption in the prefrontal, parietal, and temporal cortices, which are implicated in the memory learning network.[40,41] This notion is supported by findings of dense localization of cannabinoid type 1 receptors in the prefrontal cortex as well as frontal gray[42,43] and white matter disruptions in cannabis-using adolescents.[44–47] In contrast, this study found abstinent and non-abstinent individuals to have comparable visual span capacity, short-term visual recognition memory, and verbal recall of information after a delay, and these abilities improved comparably across groups over the 4-week assessment period.

Attention improved over time in both abstinent and non-abstinent groups, a finding that could be consistent with a pilot report that while attention-processing speed was similar between abstinent cannabis users and nonusers, attention accuracy remained lower among users throughout 3 weeks of abstinence.[20] A non–cannabis exposed control group is needed to understand whether young cannabis users experience subcortically mediated attention dysfunction that persists even after 30 days of abstinence.

The primary limitation of this study was the absence of a control group of nonusers. Without comparison to a nonusing sample or knowledge of performance prior to the initiation of cannabis use, it is difficult to interpret the role of cannabis in affecting domains that did not improve more among abstainers compared to non-abstainers, such as tasks of attention, visual span capacity, short-term visual recognition memory, and verbal delayed recall. There are several possible explanations: (1) deficits predate cannabis use, (2) deficits from cannabis exposure are permanent or long-lasting, (3) substantial practice effects in the control group wash out the ability to detect subtle between-group differences, or (4) cannabis does not adversely impact attention or these other domains, thus no improvement over practice effects would be evident with abstinence. Without nonusers, normative score comparisons, and/or knowledge of preuse cognitive functioning, it is difficult to determine whether the extent of improvement in the abstinent group represents a return to baseline. A larger trial currently underway (1K23DA042946, PI: R.M.S.) includes a nonuser comparator group, which will be essential in determining whether the extent of memory change in the first week of abstinence represents a full return to baseline.

An additional limitation of the study is the inability to determine a more precise time point when memory improvement occurred during the first week of abstinence. The current study cannot determine whether improvement represented a reversal of the acute effects of THC or resolution of more persistent cognitive effects. Future studies are warranted that examine cognitive change at more frequent intervals within the first week of abstinence. However, regardless of whether the change observed is a reversal of the early residual effects or recovery from cannabis' persistent effects, findings are still of high clinical significance, as the difference in performance between groups persisted across the entire 1-month assessment period. A final limitation is the possibility that a ceiling effect may have impeded our ability to detect further improvement in memory after the first week of abstinence. The non-abstinent group evidenced no improvement from baseline to week 1, suggesting that they did not benefit at all from practice. Practice effects across the 1-month testing period were more detectable in the attention domain and therefore less prone to a ceiling effect.

The functional significance of the observed memory improvement in abstinent cannabis users is also not known. The larger follow-up trial will determine whether cognitive improvement with cannabis abstinence translates to self-perceived cognitive enhancements, collateral-reported cognitive enhancements, and objective markers of improved academic performance. By design, this study also recruited a more heterogeneous group of cannabis users (in terms of cannabis use severity and comorbidities), enhancing generalizability to the more typical adolescent user. However, this design may have resulted in greater within-group cognitive variability, particularly in the MJ-Mon group, which had fewer participants. The study also was not powered to examine risk factors for poor neurocognitive recovery with abstinence (eg, baseline cognitive reserve, psychiatric comorbidity). Finally, this study focused on changes in memory and attention, as they were hypothesized to be most impacted by cannabis abstinence. Future studies will employ a more comprehensive cognitive battery to determine the specificity of the abstinence impact on memory.

This study provides convincing evidence that adolescents and young adults may experience improvements in their ability to learn new information when they stop using cannabis. Attention does not appear to be impacted by 1 month of cannabis abstinence. It is essential that we develop a better understanding of whether cannabis exposure in adolescence is associated with cognitive deficits and, if so, whether and over what period such deficits improve with abstinence. This knowledge has a potential for high public health impact, including physician advice to adolescents and their parents and local, statewide, and national policymaking.

Submitted: October 19, 2017; accepted May 1, 2018.

Published online: October 30, 2018.

Potential conflicts of interest: At the time the manuscript was written, **Dr Evenden** was an employee of Cambridge Cognition, who supplied the cognitive assessment software for this study. Dr Evenden is the owner of WiltonLogic LLC, has received advisory panel payments from H. Lundbeck A/S, and is a former employee of AstraZeneca. **Dr Evins** has received research grant support to her institution from Pfizer Inc, Forum, and GlaxoSmithKline and honoraria for advisory board work from Pfizer and Reckitt Benckiser for work unrelated to this project. **Drs Schuster**, **Gilman**, and **Schoenfeld** and **Mss Hareli**, **Ulysse**, **Nip**, **Hanly**, and **Zhang** report no competing interests.

Funding/support: This publication was made possible by support from the National Institutes of Health, National Institute on Drug Abuse (1K23DA042946, Dr Schuster; 1K01DA034093 and 1R01DA042043-01A1, Dr Gilman; K24 DA030443, Dr Evins); by the Norman E. Zinberg Fellowship in Addiction Psychiatry and Livingston Fellowship from Harvard Medical School (Dr Schuster); and by the Louis V. Gerstner III Research Scholar Award (Dr Schuster).

Role of the sponsor: The supporters had no role in the design, analysis, interpretation, or publication of this study.

Additional information: Location of work: Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

Supplementary material: Available at PSYCHIATRIST.COM.

REFERENCES

1. Johnston LD, O'Malley PM, Miech RA, et al. *Monitoring the Future National Survey Results on Drug Use, 1975–2016: Overview, Key Findings on Adolescent Drug Use*. Ann Arbor, MI: Institute for Social Research; 2017.
2. Giedd JN, Blumenthal J, Jeffries NO, et al. Brain development during childhood and adolescence: a longitudinal MRI study. *Nat Neurosci*. 1999;2(10):861–863.
3. Sowell ER, Thompson PM, Holmes CJ, et al. Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping. *Neuroimage*. 1999;9(6 pt 1):587–597.
4. Gogtay N, Giedd JN, Lusk L, et al. Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A*. 2004;101(21):8174–8179.
5. Benes FM, Turtle M, Khan Y, et al. Myelination of a key relay zone in the hippocampal formation occurs in the human brain during childhood, adolescence, and adulthood. *Arch Gen Psychiatry*. 1994;51(6):477–484.
6. Durston S, Hulshoff Pol HE, Casey BJ, et al. Anatomical MRI of the developing human brain: what have we learned? *J Am Acad Child Adolesc Psychiatry*. 2001;40(9):1012–1020.
7. Giedd JN. Structural magnetic resonance imaging of the adolescent brain. *Ann N Y Acad Sci*. 2004;1021(1):77–85.
8. Jernigan TL, Gamst AC. Changes in volume with age—consistency and interpretation of observed effects. *Neurobiol Aging*. 2005;26(9):1271–1274, discussion 1275–1278.
9. Pfefferbaum A, Mathalon DH, Sullivan EV, et al. A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. *Arch Neurol*. 1994;51(9):874–887.
10. Bava S, Tapert SF. Adolescent brain development and the risk for alcohol and other drug problems. *Neuropsychol Rev*. 2010;20(4):398–413.
11. Viveros MP, Llorente R, Suarez J, et al. The endocannabinoid system in critical neurodevelopmental periods: sex differences and neuropsychiatric implications. *J Psychopharmacol*. 2012;26(1):164–176.
12. Harte LC, Dow-Edwards D. Sexually dimorphic alterations in locomotion and reversal learning after adolescent tetrahydrocannabinol exposure in the rat. *Neurotoxicol Teratol*. 2010;32(5):515–524.
13. O'Shea M, Singh ME, McGregor IS, et al. Chronic cannabinoid exposure produces lasting memory impairment and increased anxiety in adolescent but not adult rats. *J Psychopharmacol*. 2004;18(4):502–508.
14. Quinn HR, Matsumoto I, Callaghan PD, et al. Adolescent rats find repeated Delta(9)-THC less aversive than adult rats but display greater residual cognitive deficits and changes in hippocampal protein expression following exposure. *Neuropsychopharmacology*. 2008;33(5):1113–1126.
15. Rubino T, Realini N, Braida D, et al. Changes in hippocampal morphology and neuroplasticity induced by adolescent THC treatment are associated with cognitive impairment in adulthood. *Hippocampus*. 2009;19(8):763–772.
16. Gruber SA, Silveri MM, Dahlgren MK, et al. Why so impulsive? white matter alterations are associated with impulsivity in chronic marijuana smokers. *Exp Clin Psychopharmacol*. 2011;19(3):231–242.
17. Schuster RM, Hoeppner SS, Evins AE, et al. Early onset marijuana use is associated with learning inefficiencies. *Neuropsychology*. 2016;30(4):405–415.
18. Gruber SA, Sagar KA, Dahlgren MK, et al. Age of onset of marijuana use and executive function. *Psychol Addict Behav*. 2012;26(3):496–506.
19. Crane NA, Schuster RM, Mermelstein RJ, et al. Neuropsychological sex differences associated with age of initiated use among young adult cannabis users. *J Clin Exp Neuropsychol*. 2015;37(4):389–401.
20. Hanson KL, Winward JL, Schweinsburg AD, et al. Longitudinal study of cognition among adolescent marijuana users over three weeks of abstinence. *Addict Behav*. 2010;35(11):970–976.
21. Roten A, Baker NL, Gray KM. Cognitive performance in a placebo-controlled pharmacotherapy trial for youth with marijuana dependence. *Addict Behav*. 2015;45:119–123.
22. Schuster RM, Hanly A, Gilman J, et al. A contingency management method for 30-days abstinence in non-treatment seeking young adult cannabis users. *Drug Alcohol Depend*. 2016;167:199–206.
23. Petry NM. A comprehensive guide to the application of contingency management procedures in clinical settings. *Drug Alcohol Depend*. 2000;58(1-2):9–25.
24. Huestis MA, Cone EJ. Differentiating new marijuana use from residual drug excretion in occasional marijuana users. *J Anal Toxicol*. 1998;22(6):445–454.
25. Schwilke EW, Gullberg RG, Darwin WD, et al. Differentiating new cannabis use from residual urinary cannabinoid excretion in chronic, daily cannabis users. *Addiction*. 2011;106(3):499–506.
26. Wechsler D. *Wechsler Abbreviated Scale of Intelligence*. New York, NY: The Psychological Corporation: Harcourt Brace & Company; 1999.
27. Wechsler D. *Wechsler Test of Adult Reading*. San Antonio, TX: Pearson; 2001.
28. Adamson SJ, Sellman JD. A prototype screening instrument for cannabis use disorder: the Cannabis Use Disorders Identification Test (CUDIT) in an alcohol-dependent clinical sample. *Drug Alcohol Rev*. 2003;22(3):309–315.
29. Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption—II. *Addiction*. 1993;88(6):791–804.
30. Robinson SM, Sobell LC, Sobell MB, et al. Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychol Addict Behav*. 2014;28(1):154–162.
31. First MB, Spitzer RL, Gibbon M, et al. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Non-Patient Edition (SCID-I/NP)*. New York, NY: Biometrics Research, New York State Psychiatric Institute; 2002.
32. Medina KL, Hanson KL, Schweinsburg AD, et al. Neuropsychological functioning in adolescent marijuana users: subtle deficits detectable after a month of abstinence. *J Int Neuropsychol Soc*. 2007;13(5):807–820.
33. Schwartz RH, Gruenewald PJ, Klitzner M, et al. Short-term memory impairment in cannabis-dependent adolescents. *Am J Dis Child*. 1989;143(10):1214–1219.
34. Solowij N, Jones KA, Rozman ME, et al. Verbal learning and memory in adolescent cannabis users, alcohol users and non-users. *Psychopharmacology (Berl)*. 2011;216(1):131–144.
35. Thoma RJ, Monnig MA, Lysne PA, et al. Adolescent substance abuse: the effects of alcohol and marijuana on neuropsychological performance. *Alcohol Clin Exp Res*. 2011;35(1):39–46.
36. Crane NA, Schuster RM, Fusar-Poli P, et al. Effects of cannabis on neurocognitive functioning: recent advances, neurodevelopmental influences, and sex differences. *Neuropsychol Rev*. 2013;23(2):117–137.
37. Grant I, Gonzalez R, Carey CL, et al. Non-acute (residual) neurocognitive effects of cannabis use: a meta-analytic study. *J Int Neuropsychol Soc*. 2003;9(5):679–689.
38. Schweinsburg AD, Brown SA, Tapert SF. The influence of marijuana use on neurocognitive functioning in adolescents. *Curr Drug Abuse Rev*. 2008;1(1):99–111.
39. Ranganathan M, Radhakrishnan R, Addy PH, et al. Tetrahydrocannabinol (THC) impairs encoding but not retrieval of verbal information. *Prog Neuropsychopharmacol Biol Psychiatry*. 2017;79(pt B):176–183.
40. Dickerson BC, Eichenbaum H. The episodic memory system: neurocircuitry and disorders. *Neuropsychopharmacology*. 2010;35(1):86–104.
41. Uncapher MR, Wagner AD. Posterior parietal cortex and episodic encoding: insights from fMRI subsequent memory effects and dual-attention theory. *Neurobiol Learn Mem*. 2009;91(2):139–154.
42. Bhattacharyya S, Fusar-Poli P, Borgwardt S, et al. Modulation of mediotemporal and ventrostriatal function in humans by Delta9-tetrahydrocannabinol: a neural basis for the effects of Cannabis sativa on learning and psychosis. *Arch Gen Psychiatry*. 2009;66(4):442–451.
43. Bossong MG, Jager G, van Hell HH, et al. Effects of Δ9-tetrahydrocannabinol administration on human encoding and recall memory function: a pharmacological FMRI study. *J Cogn Neurosci*. 2012;24(3):588–599.
44. Ashtari M, Avants B, Cyckowski L, et al. Medial temporal structures and memory functions in adolescents with heavy cannabis use. *J Psychiatr Res*. 2011;45(8):1055–1066.
45. Churchwell JC, Lopez-Larson M, Yurgelun-Todd DA. Altered frontal cortical volume and decision making in adolescent cannabis users. *Front Psychol*. 2010;1:225.
46. Medina KL, Nagel BJ, Tapert SF. Abnormal cerebellar morphometry in abstinent adolescent marijuana users. *Psychiatry Res*. 2010;182(2):152–159.
47. Yücel M, Zalesky A, Takagi MJ, et al. White-matter abnormalities in adolescents with long-term inhalant and cannabis use: a diffusion magnetic resonance imaging study. *J Psychiatry Neurosci*. 2010;35(6):409–412.

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Karen D. Wagner, MD, PhD, at kwagner@psychiatrist.com.

See supplementary material for this article at PSYCHIATRIST.COM.

THE JOURNAL OF
CLINICAL PSYCHIATRY
THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL PSYCHOPHARMACOLOGY

Supplementary Material

Article Title: One Month of Cannabis Abstinence in Adolescents and Young Adults Is Associated With Improved Memory

Author(s): Randi Melissa Schuster, PhD; Jodi Gilman, PhD; David Schoenfeld, PhD; John Evenden, PhD; Maya Hareli, BA; Christine Ulysse, MS; Emily Nip, BA; Ailish Hanly, BA; Haiyue Zhang, MS; and A. Eden Evins MD MPH

DOI Number: https://doi.org/10.4088/JCP.17m11977

List of Supplementary Material for the article

1. Table 1 — Comparison of Baseline Cognitive Functioning Among Participants Randomized to Cannabis Abstinence or Monitoring

2. Table 2 — Baseline Comparison Between MJ-Abst Participants Who Were and Were Not Able to Maintain 30 Days of Cannabis Abstinence

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Table 1. Comparison of Baseline Cognitive Functioning Among Participants Randomized to Cannabis Abstinence or Monitoring

	Monitoring (MJ-Mon; n=26)	Abstinent (MJ-Abst; n=62)	p-values
Memory (z)	-0.01 (0.4)	0.004 (0.5)	0.91
Verbal Recognition Memory (z)	0.03 (0.8)	-0.01 (0.9)	0.85
Trial 1 (raw/z)	9.1 (2.0)/0.2 (0.9)	8.3 (2.2)/-0.1 (1.0)	0.16
Total Encoded (raw/z)	20.6 (4)/0.002 (0.9)	20.6 (4.9)/-0.001 (1.1)	0.99
Delayed Recall (raw/z)	9.9 (2.8)/-0.2 (1.0)	10.5 (3.0)/0.1 (1.0)	0.36
Spatial Span (z)	-0.03 (.4)	0.01 (0.5)	0.71
Span Length(raw/z)	6.9 (1.5)/-0.2 (1.1)	7.2 (1.2)/0.1 (0.9)	0.36
Time to Last Response (raw/z)	7758.5 (1931.1)/0.1 (1.1)	7978.2 (1642.3)/-0.04 (1.0)	0.59
Delayed Matching to Sample (z)	-0.03 (0.5)	0.01 (0.6)	0.80
Total Correct at 0ms Delay (raw Mdn, IQR/ z Mdn, IQR)	7[7, 8]/-0.03[-0.03,0.9]	7[6, 8]]/-0.9[-0.03,0.9]	0.89
Total Correct at 4000ms Delay (raw Mdn, IQR/ z Mdn, IQR)	7[7, 8]]/0.2[0.2,0.9]	7[5, 8]]/-1. 3[0.2,0.9]	0.19
Total Correct at 12000ms Delay (raw Mdn, IQR/ z Mdn, IQR)	7[6, 8]]/-0.02[-0.8,0.8]	8[6, 8]]/0.8[-0.8,0.8]	0.49
Response Latency at 0ms Delay (raw/z)	2701.0 (607.1)/-0.1 (0.9)	2606.0 (743.7)/0.04 (1.1)	0.57
Response Latency at 4000ms Delay (raw/z)	3529.8 (1181.7)/-0.2 (1.2)	3243.9 (886.4)/0.09 (0.9)	0.22
Response Latency at 12000ms Delay (raw/z)	3933.6 (1467.7)/-0.2 (1.2)	3606.9 (1043.6)/0.1 (0.9)	0.24
Attention (z)	-0.08 (0.7)	0.02 (0.7)	0.54
Rapid Visual Processing (z)	-0.10 (1.0)	0.04 (0.7)	0.46
A Prime (raw/z)	0.9 (0.1)/0.02 (1.0)	0.9 (0.1)/-0.01 (1.0)	0.91
Total False Alarms (raw Mdn, IQR/ z Mdn, IQR)	1[0,2]]/0.2[-0.2,0.6]	1[0,2]]/0.2[-0.2,0.6]	0.59
Hits (raw/z)	19.7 (4.5)/0.05 (0.9)	19.4 (5.1)/-0.02 (1.0)	0.75
Response Latency (raw/z)	420.7 (120.4)/-0.2 (1.3)	396.3 (78.7)/0.1 (0.8)	0.27
Response Latency Variability (raw/z)	175.2 (129.6)/-0.1 (1.3)	160.5 (84.8)/0.04 (0.9)	0.53
Attention Switching Task (z)	-0.06 (0.6)	0.02 (0.8)	0.65
Total Errors (raw Mdn, IQR/ z Mdn, IQR)	0[0, 0]]/0.4[0.4,0.4]	0[0, 0]/0.4[0.4,0.4]	0.56
Response Latency (raw/z)	516.3 (80.3)/-0.1 (0.7)	502.2 (121.2)/0.04 (1.1)	0.59
Congruency Cost (raw/z)	50.7 (45.6)/-0.01 (1.1)	50.1 (39.5)/0.004 (1.0)	0.96
Switching Cost (raw/z)	230.4 (124.0)/-0.2 (0.9)	188.5 (140.2)/0.1 (1.0)	0.19

Note. All values represent mean and standard deviations unless otherwise noted.

Supplementary Table 2. Baseline Comparison Between MJ-Abst Participants Who Were and Were Not Able to Maintain 30 Days of Cannabis Abstinence

	Abstinent Participants in MJ-Abst (n = 55)	Non-Abstinent Participants in MJ-Abst (n = 7)	p-values
Demographics			
Sex, male, n (%)	31 (56.4)	5 (71.4)	0.45
Age	20.6 (2.1)	19.9 (1.2)	0.36
Education (in years)	13.9 (1.9)	14.0 (1.0)	0.94
Race, n (%)			
White	42 (76.4)	2 (28.5)	0.002
Black	4 (7.3)	3 (42.9)	
Asian	2 (3.6)	0 (0)	
More than One Race	7 (12.7)	1 (14.3)	
Other	0 (0)	1 (14.3)	
Ethnicity, Hispanic, n (%)	4 (7.3)	2 (28.6)	0.07
Cognition and Achievement			
IQ	109.1 (7.6)	98.9 (10.8)	0.002
GPA	3.2 (0.4)	2.6 (0.5)	0.002
Baseline Alcohol Use			
Past 90 Day Alcohol Use			
Days Alcohol Consumed	22.3 (12.9)	17.1 (18.4)	0.35
Drinks Consumed (Mdn [IQR])	86 [51, 139]	44 [8, 224]	0.27
Days Since Last Alcohol Use (Mdn [IQR])	2 [1, 5]	2 [2, 10]	0.69
Dependence Symptoms (AUDIT)	8.5 (5.6)	9.4 (8.7)	0.71
Baseline Cannabis Use			
Past 90 Day Cannabis Use			
Days Cannabis Consumed	52.7 (24.3)	58.0 (27.4)	0.59
Times Cannabis Consumed (Mdn [IQR])	94 [43, 165]	200 [55, 264]	0.12
Grams of Cannabis Consumed (Mdn [IQR])	24.8 [8.8, 66]	115.7 [51, 160]	0.003
Initiated cannabis use at <16 years, n (%)	25 (45.5)	3 (42.9)	0.90
Days Since Last Cannabis Use (Mdn [IQR])	1 [1, 2]	1 [0, 1]	0.08
Dependence Symptoms (CUDIT-R)	14.3 (5.7)	15.4 (6.5)	0.62
CN-THCCOOH (Mdn [IQR])	45.6 [17.6, 138.4]	257.4 [41.1, 417.6]	0.09
Current SCID-IV Diagnoses, n (%)*			
Major depression	1 (2.1)	1 (16.7)	0.08
Bipolar disorder	2 (4.3)	0 (0)	0.61
Panic disorder	2 (4.3)	0 (0)	0.61
Agoraphobia	1 (2.1)	0 (0)	0.61
Social phobia	0 (0)	0 (0)	--
Specific phobia	0 (0)	0 (0)	--
OCD	0 (0)	0 (0)	--
PTSD	2 (4.3)	0 (0)	0.61
Generalized anxiety disorder	3 (6.4)	1 (16.7)	0.37
Anorexia	0 (0)	0 (0)	--
Bulimia	1 (2.1)	0 (0)	0.72
Psychosis	0 (0)	0 (0)	--

Note: all values are means, standard deviations, unless otherwise noted; AUDIT, Alcohol Use Disorders Identification Test; CN-THCCOOH, Creatinine-adjusted 11-nor-9-carboxy-tetrahydrocannabinol in ng/mg; CUDIT-R, Cannabis Use Disorder Identification Test-Revised; GPA, Grade point average; IQ, Intelligence quotient; IQR, Interquartile range; Mdn, Median; SCID-IV, Structured Clinical Interview for DSM-IV (*SCID-IV not administered to

participants recruited in high schools; Abstinent participants in MJ-Abst n = 47 and non-abstinent participants in MJ-Abst n = 6); TLFB, 90-day Timeline Followback.