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Objective and subjective memory ratings in cannabis-dependent adolescents

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Abstract

Background and Objectives—Cannabis is the most widely used illicit substance worldwide, with an estimated 160 million users. Among adolescents, rates of cannabis use are increasing, while the perception of detrimental effects of cannabis use is declining. Difficulty with memory is one of the most frequently noted cognitive deficits associated with cannabis use, but little data exists exploring how well users can identify their own memory deficits, if present.

Methods—The current secondary analysis sought to characterize objective verbal and visual memory performance via a neurocognitive battery in cannabis-dependent adolescents enrolled in a pharmacotherapeutic cannabis cessation clinical trial (N=112) and compare this to a single self-reported item assessing difficulties with memory loss. Exploratory analyses also assessed dose-dependent effects of cannabis on memory performance.

Results—A small portion of the study sample (10%) endorsed a “serious problem” with memory loss. Those participants reporting “no problem” or “serious problem” scored similarly on visual and verbal memory tasks on the neurocognitive battery. Exploratory analyses suggested a potential relationship between days of cannabis use, amount of cannabis used, and gender with memory performance.

Conclusions and Scientific Significance—This preliminary and exploratory analysis suggests that a sub-set of cannabis users may not accurately perceive difficulties with memory. Further work should test this hypothesis with the use of a control group, comprehensive self-reports of memory problems, and adult populations that may have more years of cannabis use and more severe cognitive deficits.

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Keywords

adolescents; cannabis; memory; cognition; neurocognitive testing

Introduction

Cannabis is the most widely used illicit substance worldwide, with an estimated 160 million users.[1] Within the United States (US), cannabis use among adolescents is increasing, while the perception of the harmful effects of cannabis is declining.[2] Cannabis use is typically initiated during adolescence or young adulthood (18.4 years old)[3], and often persists into adulthood. Despite public perception of general safety, myriad problems are associated with early initiation of regular cannabis use, including higher incidence of cannabis dependence;[4] neurocognitive deficits;[5–7] adverse influence on relationships, employment, and mental health;[8,9] and progression to the use of tobacco.[10] It has been suggested that adolescents may be more vulnerable to neurocognitive deficits and alterations in brain structure and function associated with cannabis use compared to adults, due to their ongoing neurodevelopment. [7,11] Further, recent work is investigating the potential link between cannabis-related brain structure abnormalities and cognitive decrements.[12]

Memory impairment is potentially the most frequently noted cognitive deficit associated with cannabis use. A number of studies assessing memory function in cannabis users have shown deficits associated with chronic use.[13–20] Two of those studies reported on verbal learning and memory among adolescent cannabis users and found impaired memory performance among cannabis users and dose-dependent effects of cannabis on performance.[18,20] While adolescent and adult data strongly suggest memory impairment in cannabis users, the perception of that impairment by the user is not well understood. Agreement between self-reported memory difficulties and objective, neurocognitive assessments has not been extensively explored in the literature. One study with aircraft pilots in a flight simulator showed that cognitive impairment was accurately perceived during acute cannabis intoxication, but impairment was not perceived 24 hours later, even in the presence of continued performance deficits.[21] It may be that cannabis users are not accurately identifying cognitive difficulties, thus biasing their own self-reports. The ability to accurately perceive cognitive difficulties is an important issue that warrants study, especially in adolescents, who are at a critical juncture in their educational and vocational training and advancement.

The current study is an exploratory secondary analysis that assessed memory in cannabis-dependent adolescents enrolled in cannabis cessation clinical trial. Memory performance was characterized using objective and subjective measures. Visual and verbal memory was assessed through a computerized neurocognitive battery (CNS Vital Signs).[22] Visual and verbal memory tasks are recognition-based, rather than recall-based, and are meant to more closely mimic memory impairments experienced during daily activities. Self-reported memory difficulties were rated via one item on The Marijuana Problem Scale (MPS).[23–25] Self-reported ratings of memory loss were compared to objective performance on visual and verbal memory tasks to determine if participants could accurately recognize and report any

memory difficulties. Also, dose-dependent relationships between cannabis use characteristics and memory performance were explored. Based on previous research, it was expected that participants would show deficits in memory compared to previously determined age-matched control values[22], and that there would be a dose-dependent influence of cannabis use on memory performance. It was also predicted that participants would not accurately self-report their own memory difficulties. The current study did not include a control group and was not powered to test memory impairments specifically, so all analyses were exploratory in nature.

Methods

Participants and Procedures

Data for this secondary analysis came from a double-blind, placebo-controlled trial of *N*-acetylcysteine (NAC) for cannabis cessation in treatment-seeking adolescents.[26] Study participants, aged 15–21, who met criteria for cannabis dependence and had no other current clinically significant psychiatric or co-occurring substance use disorder (excluding tobacco) were enrolled (N=116 in the parent trial). Participants were excluded from the study if they were taking medications that may interfere with study medication, currently enrolled in treatment for cannabis dependence, or if they were pregnant or breastfeeding. Participants were randomized to receive active medication (NAC, 1200 mg twice daily) or matched placebo for 8 weeks. Abstinence from cannabis was the primary outcome measure in the parent trial. All memory assessments reported in this analysis were completed prior to randomization. Further details of the study can be found elsewhere.[26]

Measures

Participants completed the self-reported MPS scale[23–25] during the screening visit (prior to cannabis cessation), which assesses difficulties associated with cannabis use. Specifically, the questionnaire asks participants to indicate how much of a problem a particular item has been over the past 30 days. Participants rated 19 items on an ordinal scale (0=no problem, 1=minor problem, 2=serious problem), which results in a total summed score (0–19). This questionnaire has shown excellent internal consistency (α=0.86).[27] Out of 19 items, one item assesses problems with memory (i.e., “memory loss”). While it is not standard practice to assess individual items from the MPS, we were specifically interested in the perception of memory difficulties, though we recognize this as a study limitation.

At screening, participants also completed the CNS Vital Signs, which is a computerized neurocognitive battery of performance tests that assesses subtle changes in mental acuity, learning and memory, psychomotor speed, complex attention, impulsivity, planning and sequencing.[22] Verbal and visual memory tests from this battery are adaptations of the Rey Auditory Verbal Learning Test and the Rey Visual Design Learning Test[28], which is presented with standardized instructions[29] and was adapted for computer delivery.[22] In the verbal task, 15 words are presented, and participants are asked to remember those words (separated by 2 seconds). Then, 30 words are presented with the original 15 words randomly interspersed. The participant pushes the space bar when they see a word they recognize from the previous list (immediate condition). After 20 minutes, the participant is asked again to

respond when they see one of the original 15 words (delay condition). In the visual task, participants are asked to remember 15 geometric shapes and the procedures are similar to those described for the verbal task. Scoring includes correct “hits” and “passes” for the immediate and delayed condition. Verbal and visual memory tasks yield scores that are summed to generate a composite memory score that captures recognition, not recall, through immediate and delayed conditions. This score can range from 60 to 120, with 100 (SD=15) being average for adolescents and young adults.[22]

Recency of cannabis use prior to the screening visit was captured via the Timeline Follow-Back[30] adapted for cannabis use. Approximately 64% of the sample endorsed using cannabis the day prior to the screening assessment. If participants had appeared impaired at screening or reported using cannabis earlier that day, they would not have been consented at that time. Therefore, all memory measurements completed at screening were taken approximately 12–24+ hours since their last cannabis use episode (as determined by self-report).

Additional questions were asked at the screening visit to assess cannabis use history (i.e., years of cannabis use and number of prior quit attempts) and current use patterns (days of use in the past 30 and grams used per day). Days of use (out of the last 30) was determined via responses on the Timeline Follow-Back instrument[30]. Participants were also asked to estimate the quantity of cannabis they purchase at a time and how many days that typically lasts (over the past 30 days). This provided an estimate of grams used per day.

Statistical Analyses

For the current analysis, there was insufficient data for four participants, resulting in a sample of N= 112. Standard descriptive statistics were used to summarize demographic, clinical, and cannabis use characteristics for those enrolled in the parent trial, both in the aggregate and categorized by responses on the memory loss item of the MPS (0, 1, or 2). To screen for potentially confounding factors between self-reported and objective memory difficulties, Pearson chi-squared tests (or Fisher’s exact tests, in cases where expected cell counts were too small) were used to compare MPS memory loss groups on categorical and grouped-continuous demographic and lifetime cannabis use measures. Similarly, a one-way ANOVA test was used to compare mean number of days of cannabis use (out of 30) and Marijuana Craving Questionnaire total score (MCQ)[31] across self-reported memory loss groups.

Verbal and visual memory scores from the neurocognitive battery were compared across MPS memory loss groups with the use of Kruskal-Wallis tests, owing to the non-normal residuals when performing parametric one-way ANOVA tests. Further between-group analyses were conducted with Steel-Dwass tests[32], which is the nonparametric version of Tukey’s HSD post-hoc test.

In order to build a model for predicting verbal and visual memory scores, a linear model was assumed using the memory loss score from the MPS as the response variable and the full set of candidate predictors as explanatory variables, consisting of: age, gender, cigarette smoker, days of cannabis use (out of the past 30), urinary cannabinoid level, grams of

cannabis used per day (past 30 days), MCQ score, modified Fagerström Tolerance Questionnaire total score (FTND)[33], race (grouped: Caucasian vs. non-Caucasian), education (grouped: some college vs. no college), years of cigarette use, and years of cannabis use. A minimum Bayesian Information Criterion (BIC) stopping rule was used with a backward direction stepwise routine. Thus, the algorithm successively removed variables from the full model and updated the model's BIC value until no further removals could decrease the BIC any further. The remaining variables then comprised the selected model.

Results

Sample Characteristics

Demographic and cannabis use characteristics are shown in Table 1 for all participants included in the current analysis, and separated by responses on the memory loss item of the MPS. Out of the 112 participants, 11 (10%) reported experiencing "serious" memory loss problems, while 54 (48%) reported a "minor problem" and 47 (42%) reported having "no problem" with memory loss. Generally, participants had an average (SD) age of 18.9 (1.5) years, 73% were male, and 74% were currently enrolled in school.

Tests of association between the demographic and cannabis use characteristics in Table 1 and self-reported memory loss produced statistically insignificant results. The chi-squared tests found no significant association between self-reported memory loss and gender $\chi^2(2, N = 112) = 5.75$, $p = .0565$; enrollment in school $\chi^2(2, N = 112) = 2.65$, $p = .266$; and grams/day of cannabis (grouped) $\chi^2(2, N = 112) = 2.28$, $p = .320$. Likewise, there was no significant association in the Fisher exact tests between self-reported memory loss and age ($p = .957$); years smoking cannabis ($p = .868$); and number of quit attempts ($p = .145$). The means of days of cannabis use (out of 30) and MCQ total were not significantly different between the memory-loss groups, with test results of $F(2, 107) = 0.26$, $p = 0.772$ and $F(2, 107) = 1.95$, $p = 0.147$, respectively.

Memory Comparisons

Mean verbal and visual memory standardized scores and 95% confidence intervals (CI) derived via the CNS Vital Signs neurocognitive battery for all participants across memory impairment categories are listed in Table 2. Comparisons between groups revealed significant differences between the verbal and visual memory scores among the MPS groups ($p = <0.0081$ and $p = <0.0041$, respectively). Participants reporting minor problems with memory performed better on average on both verbal and visual memory compared to those reporting no problem. Those participants reporting serious memory issues performed worse on average than the other groups.

Post-hoc comparisons between memory difficulty groups showed a significant difference between those reporting "minor problem" and "serious problem" ($Z = -2.69$, $p = .020$) in verbal memory scores, but no differences between those reporting "no problem" and "minor problem" ($Z = 2.16$, $p = .079$) or between those reporting "no problem" and "serious problem" ($Z = -1.46$, $p = .308$). Likewise, there was a significant difference in visual

memory scores between those reporting “minor problem” and “serious problem” ($Z = -2.51$, $p = .032$), but there was also a significant difference between those reporting “no problem” and “minor problem” ($Z = 2.78$, $p = <.015$). Similar to the verbal memory scores, there was no significant difference between those reporting “no problem” and “serious problem” ($Z = -0.38$, $p = .922$).

Predictors of Visual and Verbal Performance

The relevant values for the selected regression models for verbal and visual memory are summarized in Table 3. The stepwise variable selection routine produced a model with gender and days of cannabis use in the past 30 days (and an intercept) predicting verbal memory. The BIC value for this model was 418.249. For visual memory, the best model included gender, days of cannabis used, grams of cannabis used per day, education, and years of cigarette use. The final BIC value was 367.35. It should be emphasized that these results are exploratory in nature and should be interpreted with caution.

Discussion

Cannabis-dependent adolescents enrolled in a cannabis cessation trial generally self-reported mild or no memory impairment (48% and 42%, respectively). Participants who reported “minor” problems with memory loss performed better on average on objective tasks than all other participants, and slightly above the normative values found for healthy individuals in this age group (mean=100, SD=15).[22] Those participants reporting “no problem” with memory loss scored lower on average compared to those reporting a “minor problem”, and their scores were not significantly different from those reporting a “serious problem” with memory loss. Those reporting a “serious problem” also scored the lowest on average on the neurocognitive battery for memory, and compared to normative values[22] were more than one standard deviation from the mean for verbal memory. These results suggest that the majority of participants categorized themselves somewhat inconsistently on the MPS when compared to objective, neurocognitive tasks. Participants reporting “minor” problems demonstrated the strongest performance on the memory tasks. This finding may suggest that these participants may be more likely to recognize or remember difficulties, leading to some endorsement of problems with cannabis, but objectively are not experiencing cognitive deficits. Most notably and of greater concern is that participants reporting “no problem” were not classifying themselves correctly and appeared to have memory deficits when compared to other participants in this trial and normative scores for their age group.

Predictive variables of memory performance were examined using a stepwise variable selection routine, and found that gender and days of cannabis use in the past 30 days were significant predictors of both verbal and visual memory deficits. Frequency of use seems relevant for the prediction of cognitive deficits, which is consistent with some previous literature.[13,34,35] For visual memory deficits, several additional variables emerged, such as grams of cannabis used, education, and years of cigarette use. Gender also emerged as a predictor for memory score in the current study. This result should be interpreted cautiously as the majority of study participants were male (73%), but it does represent and interesting and noteworthy finding. There is some evidence to suggest gender differences in cannabis-

related cognitive effects,[13,36] and a recent study found a relationship between more cannabis use and poorer episodic memory in females compared to males.[37] It may be that frequency of cannabis use and gender should be considered and explored in future research on neurocognitive deficits related to cannabis use.

Some participants in this study appear to recognize their memory difficulties, which may have therapeutic significance. Those individuals who recognize difficulties in cognitive performance related to cannabis use may be more motivated to decrease their use or quit. Of more concern are those individuals who reported “no problem” with memory, while objective tests revealed that they did exhibit slight memory deficits. A substantial portion of the study sample (42%) was not accurately recognizing these deficits. For these individuals, discussion of their objective measures of memory impairment compared to normative controls might be used to enhance motivation to decrease cannabis use. This suggests that the MPS may be useful in categorizing memory difficulties for some individuals, and a comprehensive treatment should include memory improvement strategies or cognitive training.

There are several limitations to the current analysis that should be noted. First, the MPS only contained one item that assessed memory loss issues. Analysis of a single item is not standard practice in the literature, but the current analysis was meant to be exploratory in the assessment of objective and subjective memory comparisons. A more thorough assessment of self-reported memory and associated difficulties will be necessary for adequate comparisons with neurocognitive batteries. Second, this study did not assess other cognitive domains, which are also likely to be affected by cannabis use and should be explored in future studies along with corresponding self-reports of cognitive performance. Third, this study did not include a control group of non-cannabis matched adolescents. Therefore, memory performance among the current study sample can only be compared to age-matched non-cannabis using controls from previous studies.[22] Fourth, the MPS relies on the accurate reporting and perception of memory issues in the patient, and does not differentiate between retrospective, prospective, short- or long-term memory difficulties. Only 11 participants in the current study reported a “serious problem” with memory, which may have biased the neurocognitive results for that group, and may not accurately capture performance among this group. Fifth, the collected neurocognitive data does not account for baseline levels of performance prior to the initiation of cannabis use. However, these data can be compared to normative data for healthy controls for the same test batter in similar age groups[22], which aids in assessing deficits. Finally, estimates of cannabis use were not all obtained through validated methods (i.e., grams used per day). Future studies assessing estimates of cannabis use as predictors should include detailed and validated measures of self-report to account for quantity, potency, and sharing of cannabis among users. It may be wise for future studies to assess several domains of cognitive functioning, as well comprehensive assessments of memory, including both recognition and recall (immediate and delayed conditions).

This preliminary and exploratory post-hoc analysis seems to suggest discrepancies between subjective and objective assessments of memory performance in a sub-set of cannabis-dependent adolescents. While deficits may be subtle among adolescents and young adults, these deficits may worsen with continued cannabis use. Those participants who do not

endorse any deficits may require additional assessment and intervention. Future studies should compare both comprehensive self-report and objective batteries of memory performance to assess accurate perception of deficits, if present, and should pay special attention to potential gender differences in cannabis use and performance. These assessments could then be utilized as diagnostic tools to identify areas for improvement, gauge progress throughout a treatment episode, educate participants regarding their neurocognitive performance, and motivate a cessation attempt. Furthermore, specific attention must be paid to cannabis-dependent adolescents with compromised memory function who do not recognize this impairment. These individuals may need to be specifically targeted for cessation in addition to cognitive training to maximize their likelihood of long-term abstinence from cannabis.

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Table 1

Demographic and cannabis use characteristics as a function of self-reported memory impairments.

		Marijuana Problem Scale – Memory Loss		
	Overall (N=112)	**No problem (N=47)**	**Minor problem (N=54)**	**Serious problem (N=11)**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Age	18.9 ± 1.5	18.8 ± 1.6	19.0 ± 1.5	18.7 ± 1.7
Male %	73.2	80.9	72.2	45.5
Enrolled in School %	74.1	76.6	68.5	90.9
Years Smoking Cannabis	4.2 ± 1.8	3.9 ± 1.7	4.3 ± 1.8	4.6 ± 2.7
# of Quit Attempts	2.4 ± 3.4	1.8 ± 3.4	3.1 ± 3.7	2.0 ± 2.5
Days of Cannabis Use (out of 30)	22.7 ± 7.3	23.2 ± 6.8	22.2 ± 7.8	23.5 ± 6.6
Grams/day of Cannabis	1.9 ± 3.3	1.8 ± 4.1	1.9 ± 2.9	2.0 ± 1.7
Marijuana Craving Questionnaire Total (out of 84)	47.5 ± 14.6	45.9 ± 13.5	47.1 ± 14.9	55.5 ± 16.4

Table 2

Verbal and visual memory standardized scores derived via the CNS Vital Signs neurocognitive battery for all participants across memory impairment categories.

MPS memory group	Verbal Memory Mean (SD)	Verbal Memory 95% CI	Visual Memory Mean (SD)	Visual Memory 95% CI
No problem	92.7 (25.7)	84.7 – 100.7	93.1 (15.7)	88.2 – 98.0
Minor problem	103.7 (17.09)	99.02 – 108.5	102.2 (12.8)	98.6 – 105.9
Serious problem	80.2 (25.4)	62.0 – 98.4	91.3 (10.6)	83.2 – 99.4

Table 3

Regression model summary for verbal and visual memory using only predictors selected by a backwards variable selection.

Verbal Memory						
Source	**df**	**Sum of Squares**	**Mean Squares**	**F Ratio**	***p*-value**	**R^2**
Model	2	909.21	454.61	0.86	0.4260	0.0171
Error	99	52,282.27	528.10			
Total	101	53,191.48				
Visual Memory						
Source	**df**	**Sum of Squares**	**Mean Squares**	**F Ratio**	***p*-value**	**R^2**
Model	5	2,507.04	501.41	2.54	0.0337	0.1237
Error	90	17,758.53	197.32			
Total	95	20,265.58				

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