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Marijuana use associated with worse verbal learning and delayed recall in a sample of young adults

NATALIA LASPADA[1,a], ERIN DELKER[1,b,e], ESTELA BLANCO[1,c,e,f], PAMELA ENCINA[2,b,g], GABRIELA CABALLERO[2,b,g], JORGE DELVA[3,d,h], RAQUEL BURROWS[2,j], BETSY LOZOFF[4,i,j], SHEILA GAHAGAN[1,e,j]

[1]Department of Pediatrics, Division of Child Development and Community Health, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA, USA.
[2]Institute of Nutrition and Food Technology, Unversidad de Chile, Av. El Líbano 5524, Santiago, Chile.
[3]Dean School of Social Work, Director and Paul Farmer Professor for Innovation in Social Work and Health, Boston University, Boston, MA, 02215, USA.
[4]Center for Human Growth and Development, University of Michigan, 300 N. Ingalls Bldg. 1063NE, Ann Arbor, MI, USA.
[a]Psychology and Public Health pre-graduate student
[b]Psychologist.
[c]Epidemiologist.
[d]Social worker.
[e]MPH.
[f]MA.
[g]BS.
[h]PhD.
[i]MS.
[j]MD.

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Correspondence to:
Sheila Gahagan, MD, MPH
Department of Pediatrics, Division of Child Development and Community Health, University of California, San Diego.
4305 University Avenue, Suite 590.
San Diego, CA, USA 92105.
Fax: 619-681-0666
sgahagan@ucsd.edu

ABSTRACT

***Background**: There is concern about the cognitive consequences of marijuana consumption. **Aim:** To assess the influence of current and past marijuana use and frequency on verbal learning and memory in a sample of adults aged 21 years old. **Material and Methods**: Marijuana use was assessed using a clinician administered interview in 654 participants (56% females), who reported frequency of use, age of first use and whether its use led to problems in their lives. The CogState International Shopping List was administered to assess learning and memory. **Results**: Seventy percent reported ever using marijuana, 46% consuming during the past year and 27% during the past 30 days. The latter scored significantly lower on delayed recall. Current and frequent use were significantly associated with lower accuracy in verbal learning and memory. **Conclusions:** In this cohort of adults aged 21 years old, marijuana use was prevalent and related to worse verbal memory.*

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***Key words:** Cannabis; Memory; Verbal Learning; Young Adult; Marijuana Use.*

El consumo de marihuana se asocia a una menor capacidad de aprendizaje verbal y memoria tardía en adultos jóvenes

***Antecedentes:** Existe preocupación acerca de los efectos cognitivos del consumo de marihuana. **Objetivo**: Estudiar el efecto de consumo de marihuana presente o pasado en la capacidad de aprendizaje verbal y memoria en una muestra de adultos de 21 años. **Material y Métodos**: El consumo de marihuana fue evaluado mediante una entrevista médica en 654 adultos de 21 años (56% mujeres), quienes informaron acerca de la frecuencia de consumo, edad de comienzo y si el consumo les ha causado problemas en sus vidas. Se les administró el Cogstate International Shopping List para evaluar aprendizaje y memoria. **Resultados**: El 70% informó haber consumido marihuana alguna vez, 46% la usó durante el último año y el 27% en los últimos 30 días. Estos últimos tuvieron un menor puntaje en memoria tardía. El consumo actual y frecuente se asoció a una menor precisión en la capacidad de aprendizaje verbal y memoria. **Conclusiones**: En esta cohorte de adultos de 21 años, el consumo de marihuana fue prevalente y relacionado a una menor memoria verbal.*

***Palabras clave:** Cannabis; Memoria; Aprendizaje Verbal; Adulto Joven; Uso de la marihuana.*

Marijuana use is increasing in Chile and worldwide, and several countries support decriminalization of the substance. In 2015, Chilean Law 20,000 allowed, for the first time, a small amount of marijuana cultivation, provided proper authorization, for personal use[1]. Among South American countries, Chile reported the highest lifetime marijuana use (28%), with adolescent use doubling in the last decade from 14.8% (2001) to 30.6% (2013)[2]. Furthermore, comprehensive national surveys conducted by SENDA (Servicio Nacional para la Prevención y Rehabilitación del consumo de Dorogas y Alcohol) (2016) reflect systematic increase in the prevalence of marijuana use from 2010 to 2016. In particular, young adults aged 19-25 experienced a statistically significant increase in reported lifetime marijuana use, rising from 24.0% in 2014 to 33.8% in 2016[3]. Given the relative commonality of marijuana use among the young adult population, it is important to understand possible consequences and associations of marijuana use. In particular, our intention was to test for neurocognitive associations of marijuana use within a Chilean young adult sample.

Prior studies have demonstrated negative cognitive outcomes for marijuana users[4-10], including early onset users[9], with effects persisting even after periods of forced abstinence[6]. In a Chilean sample, marijuana use has been related to deficits in fluid intelligence[10]. Cognitive functions affected include task accuracy, psychomotor speed, sequencing ability, sustained attention, and verbal memory[4-7]. In contrast, a recent meta-analysis found that the supposed negative cognitive outcomes of marijuana use may be overstated or due to acute exposure[11]. We assessed cognitive outcomes related to any, frequent, early onset, and problematic marijuana use in a sample of Chilean young adults.

Materials and Methods

Participants were part of a Chilean cohort studied since infancy in either a preventative trial of iron-deficiency anemia or a neuromaturation study[12]. Data were collected from healthy 21-year-olds originally recruited in infancy from four low- to middle-income communities in Santiago, Chile[12,13]. Of 1,790 infants from the original studies, 654 participated in an evaluation of substance use and neurocognitive testing at 21 years. The study was approved by Institutional Review Boards at the Institute for Nutrition and Food Technology, University of Chile, University of Michigan, and University of California San Diego. All participants gave informed consent.

Study variables

Marijuana use was assessed via clinician-administered survey. Participants indicating any marijuana use received questions regarding frequency in the past 30 days and past year. Three or more marijuana uses in the past 30 days was considered frequent use. Problematic marijuana use was ≥1 problems reported in relationships, school, or health measured on a 14-item questionnaire(14; see appendix A).

Verbal learning (International Shopping List [ISL]) and memory (ISL+ Recall [ISLR]) were assessed with the CogState-International Shopping List, which has reliability across translations, as suggested by Lim et al.[15]. The CogState neurocognitive battery has determined validity for measuring cognitive functioning[16]. The ISL assesses immediate and delayed recall of a 12-item list. Immediate recall is measured as the sum of 3 trials. Delayed recall is measured in one trial. Higher scores indicate better verbal learning and memory.

Covariates from infancy (socioeconomic status [SES], Mother's IQ, sex, randomization group) and young adulthood (age, education [high school graduation yes/no], "binge" drinking, lifetime cigarette use) were considered as potential confounding variables. SES was assessed using the Graffar index[17]; higher scores indicate lower SES. Binge drinking was defined as consuming ≥ 4 or 5 drinks on one occasion for females and males, respectively.

Statistical analyses

Univariate and bivariate analyses were used for descriptive statistics. Multivariable generalized linear models tested group differences in learning/memory scores. We compared mean cognitive scores of (1) participants reporting marijuana use over the past year or 30 days to never users; (2) frequent marijuana users to non-frequent or never-users; and (3) problem marijuana users to non-problem or never-users. Analyses adjusted for sex, age at substance use assessment, education, binge drinking, and cigarette use[18]. We utilized SAS version 9.4 and SPSS version 23 software.

Results

Participants, as described in Table 1, were 21 (SD = 0.2) years old on average, 85.5% high school graduates, and 55.6% female. Marijuana use was endorsed by 69.5% (lifetime), 45.8% (past year), and 27.0% (past 30 days).

In adjusted multivariable analyses, we found lower mean memory scores for both past 30-days (p = 0.001) and past-year (p = 0.015) marijuana users, compared to non-users (Table 2). Problematic users had worse scores than non-problematic users on the memory test (p = 0.048) but not on the learning test. Furthermore, there was some indication that early onset users –defined as participants who reported using marijuana for the first time at or prior to age 16[9]– scored worse on the learning (p = 0.135) and memory (p = 0.068) tests when compared with late onset users and never users, but these findings did not achieve statistical significance. Past 30-day frequent users had significantly lower mean learning (p = 0.049) and memory (p = 0.001) scores compared to non-frequent or non-users. We also tested higher levels of use (≥ 6 uses in past 30 days; ≥ 40 uses in past year). More frequent use was consistently associated with lower scores on both tests.

Table 1. Participant characteristics according to lifetime marijuana use

	Yes (n, %) or Mean (SD)	No (n, %) or Mean (SD)	p-value
Infancy			
Socioeconomic status, (range 9-43)[b] (10)	27.3 (SD = 6.5)	27.8 (SD = 6.0)	0.404
Mother's IQ, (range 51-110)	83.9 (SD = 9.7)	84.5 (SD = 9.2)	0.487
Sex			
Male	(222, 76.3)	(69, 23.7)	0.001
Female	(232, 63.9)	(131, 36.1)	
Iron supplementation			
Yes	(138, 30.0)	(322, 70.0)	0.927
No	(51, 30.9)	(114, 69.1)	
Iron deficiency anemia			
Yes	(19, 23.5)	(62, 76.5)	0.154
No	(170, 31.3)	(374, 68.8)	
Young Adult			
Age of cognitive assessment, yr	21.0 (SD = 0.3)	21.0 (SD = 0.3)	0.830
Age of drug assessment, yr	20.9 (SD = 0.2)	21.0 (SD = 0.2)	0.076
Graduate secondary school			
Yes	(379, 67.8)	(180, 32.2)	0.029
No	(75, 79.0)	(20, 21.1)	
Lifetime binge drinking			
Yes	(138, 95.8)	(6, 4.2)	0.000
No	(316, 62.0)	(194, 38.0)	
Lifetime cigarette use			
Yes	(390, 85.0)	(69, 15.0)	0.000
No	(64, 32.8)	(131, 67.2)	

[a]Group differences tested with chi-square (categorical variables) and independent samples t-test (continuous variables). Mean (SD) presented for continuous variables, (n, %) presented for categorical variables. [b]Higher scores indicate more socioeconomic disadvantage.

Table 2. Marijuana use and verbal learning and memory scores in young adulthood*

	Verbal learning	p value	Memory	p value
12-Month marijuana use				
Yes	26.2 (0.2)	0.735	9.4 (0.1)	0.015
No	26.3 (0.2)	--	9.8 (0.1)	--
30-Day marijuana use				
Yes	25.9 (0.3)	0.130	9.2 (0.1)	0.001
No	26.4 (0.2)	--	9.7 (0.1)	--
12-Month frequent use (≥40 uses)				
Yes	24.9 (0.4)	0.000	8.8 (0.2)	<0.001
No	26.5 (0.2)	--	9.7 (0.1)	--
30-Day frequent use (≥ 3 uses)				
Yes	25.6 (0.4)	0.049	9.1 (0.2)	0.001
No	26.4 (0.2)	--	9.7 (0.1)	--
Problematic Use (≥1 problem)				
Yes	26.1 (0.3)	0.471	9.4 (0.1)	0.048
No	26.4 (0.2)	--	9.7 (0.1)	--
Age of onset of marijuana use				
Early (≤16 yr)	25.9 (0.3)	0.135	9.3 (0.1)	0.068
Late (>16 yr)	26.3 (0.2)	--	9.6 (0.1)	--
Never Use	26.7 (0.3)	--	9.8 (0.1)	--

*All models are adjusted for sex, age at substance use assessment, education, binge drinking, and cigarette use.

Discussion

We assessed the association between marijuana use and cognition in this sample of Chilean young adults. Participants who reported marijuana use over the last year or past 30 days performed worse than never-users on a delayed recall task measuring verbal memory. Frequent marijuana use was also associated with worse performance for verbal learning and memory. Assessing varying levels of exposure, we found significant negative effects of marijuana use even for individuals who reported using "at least once" in the past year –relatively lenient criteria compared to other studies. As we altered the cut-off points to focus on more intense marijuana use in the exposed group, the magnitude of the effect increased.

Previous studies found marijuana use to be associated with poorer cognition, yet a large meta-analysis suggests these conclusions may have been overstated. Limitations of previous studies included small sample size (4-6, 8) and varying definitions of marijuana use. Some studies had stringent criteria (4-6 uses/week), while others assessed infrequent users (e.g. 10 joints in past year). Furthermore, there has been an overreliance on defining problematic marijuana use only by frequency of use, rather than by marijuana use causing problems in daily life[19]. Given recent changes in Chilean marijuana legislation, shifting attitudes towards marijuana use, and increasingly prevalent use among Chileans, this study provides important information on the potential adverse effects of such use.

This study has several limitations. Participants cannot be considered representative of the Santiago population. Results should be replicated in other settings to determine generalizability. Furthermore, attrition was a limitation, as this study included only 654 of the original 1,790 infancy cohort participants. However, current study participants did not differ significantly from the original cohort regarding most baseline characteristics, with the exception of supplementation group. Participants that were randomized to high and low iron supplementation in infancy were more likely to be included in this analysis compared to infants randomized to no iron supplementation. Another limitation is that the measures used to quantify exposure (marijuana use)

and outcome (verbal memory performance) were not specifically validated for a Chilean population. However, there is likely cross-cultural validity[15] of verbal memory tasks, such as the CogState ISL. Participants retrospectively reported timing and frequency of marijuana use, thus risking recall bias. Furthermore, some participants may have been experiencing acute effects of marijuana at the time of evaluation, as no abstinence period was enforced[20]. In addition, we analyzed the effect of marijuana use on only one cognitive measure, verbal recall ability, and we were unable to adjust for the level of effort during the evaluation. Observed associations may vary across cognitive domains. Further understanding of these nuances will help elucidate plausible mechanisms. Another limitation is the cross-sectional nature of the analysis. These analyses will be strengthened by further follow-up of participants to test persistence of observed associations. Additionally, the field could benefit from understanding the predictors of marijuana use as well as the effect of marijuana use on later cognitive and functional outcomes[21,22].

Strengths of this study include the relatively large sample size and use of a valid and reliable assessment of verbal learning and memory (CogState-ISL). Marijuana use was defined consistently, and problematic use was based on a validated 14-item questionnaire (see Appendix A). Although participants were not assessed for clinical psychopathology diagnosis or Substance Use Disorder, our study in a non-clinical, non-U.S. sample is relevant to more typical substance use. Considering the continued uncertainty surrounding the short-term and long-term cognitive harms of marijuana, more research is warranted, and this study adds to this research.

In this study of 21-year-olds from Santiago, Chile, marijuana use correlated with poorer cognitive outcomes. A cross-sectional association between increased marijuana use and worse cognitive outcomes implies a need to investigate the relationship between marijuana use and cognitive changes over time. In this era of liberalization of marijuana, scientific research on the effects of marijuana on cognitive, behavioral, psychological, and functional outcomes in adolescence and young adulthood is particularly timely. Such research should expand beyond clinical samples to increase the likelihood of external validity.

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Appendix A. Problematic marijuana use items

The following questions ask the participant (marijuana user) if consuming marijuana has caused any of the following problems during his/her life:

1. You have behaved in some way that you later regretted. (1 = No, 2 = Yes)
2. Has caused problems with your parents. (1 = No, 2 = Yes)
3. Has caused problems with your husband/wife or girlfriend/boyfriend. (1 = No, 2 = Yes)
4. Has caused problems with your friends. (1 = No, 2 = Yes)
5. Has caused problems with your teachers or bosses. (1 = No, 2 = Yes)
6. Has caused you to get together with people who have a bad influence. (1 = No, 2 = Yes)
7. Has caused problems in school or work. (1 = No, 2 = Yes)
8. Has caused you to have less interest in activities where you used to have more interest. (1 = No, 2 = Yes)
9. Has caused emotional instability. (1 = No, 2 = Yes)
10. Has caused you to have less energy. (1 = No, 2 = Yes)
11. Has interfered with your ability to think well. (1 = No, 2 = Yes)
12. Has caused other psychological problems. (1 = No, 2 = Yes)
13. Has caused problems for your health. (1 = No, 2 = Yes)
14. Has caused problems with the police. (1 = No, 2 = Yes)

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