JOURNAL OF PSYCHOACTIVE DRUGS
https://doi.org/10.1080/02791072.2021.1936700

Taylor & Francis
Taylor & Francis Group

Cannabis Consumption Onset and Addiction: Data from the Second Brazilian Drugs and Alcohol Survey (BNADS)

MadrugaClarice Sandi , MiguelAndré de Queiroz Constantino , MassaroLuciana Teixeira Santos , CaetanoRaul , and LaranjeiraRonaldo

ABSTRACT

The objective of this study was to provide rates of cannabis use and dependence and risk factors, proposing a conditional path model for cannabis addiction. A subsample of adult participants from a Brazilian household survey was analyzed to estimate cannabis dependence. Estimation of prevalence rates and association between dependence and age of cannabis use initiation were performed. The conditional model was applied to investigate the mediation of depressive symptoms and alcohol consumption in the association of early cannabis use and dependence. Lifetime and last year cannabis use were 6.47% and 2.81%, respectively. Moderate and severe cannabis dependence were 0.74% and 0.18% in the population, and 26.47% and 6.38% among last year's cannabis users. A Parallel Multiple Mediator Model revealed strong association between cannabis use initiation age and dependence, when depressive symptoms or alcohol consumption mediate this association. The proportion of cannabis users displaying dependence symptoms is elevated and it is associated with the age of cannabis use initiation. The results show the importance of primary prevention interventions, prioritizing the delay of cannabis and alcohol experimentation. Our findings can enrich the debate on drugs policies and legislation, reinforcing the need for stronger restrictions of adolescent drug access and ensuring its enforcement.

ARTICLE HISTORY
Received 6 September 2020
Revised Vxx xxxx xxxx
Accepted 15 March 2021

KEYWORDS
Brazil; household survey; cannabis; substance use disorder; addiction

Introduction

We are currently living a pivotal moment in cannabis history, with drug policies under review in many countries, bringing in with it the relaxation of cannabis legal status. Significant changes have already taken place in several States within the US and at a national level in a few countries such as Uruguay, Netherlands, Portugal, Canada and Chile. Its new legal status worldwide has led to a surge in cannabis-based products, making it one of the fastest growing markets in the world (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2019; Castillo-Carniglia et al. 2020). Within this scenario it is important to highlight how much this drug has changed over time from its natural herbal form with low Tetrahydrocannabinol (THC) concentrations (between 2% and 5%), to a range of new products, ranging from cannabis hybrid strains, cannabis resin developed from new methods of extraction, all considered highly potent, boasting THC concentrations never seen before, and finally to its synthetic analogues. Such drastic change in THC concentrations have had an impact on addiction development (Freeman and Winstock 2015). Evidence also shows that cannabidiol (CBD) concentrations are insignificant in most of the drug sold on the streets as this market demands an ever-increasing psychotropic effect, occurring mainly by higher THC levels as opposed to its medicinal qualities, related to higher levels of CBD (Vindenes et al. 2013).

This new market has influenced the media, affecting the public opinion regarding this drug. Biased information orchestrated by the cannabis industry has become a trending topic, with the diffusion of a one-sided understanding of its effects and underestimating its related health risks. Inadequate perception of risks can impact drug's consumption rates in certain spheres of the population, especially, among adolescents. The combination of lessened risk perception, misleading information, and increased availability may lower the age of experimentation by anticipating it (Castillo-Carniglia 2015).

The consequences of early initiation of cannabis use have been well documented, with findings from long-term cohorts suggesting severe and permanent negative impact on memory and cognition (Lubman, Cheetham, and Yucel 2015; Meier et al. 2012), on life achievements (Fergusson and Boden 2008), and increased chances of developing mental disorders such as psychosis, anxiety, and especially depression (Large et al. 2011; Lev-Ran et al. 2014; Rasic et al. 2013). Early exposure to cannabis is also related to increased chances of developing

CONTACT Clarice Sandi Madruga claricesandi@gmail.com Psychiatry, Universidade Federal de São Paulo Ringgold Standard Institution, 865 Rua Napoleão de Barros, São Paulo 04021-001, Brazil

Table 1. Lifetime and last year cannabis prevalence rates according to socioeconomic and demographic characteristics (2012). Estimates for population aged 15– 64 years.

	Lifetime Use	Last Year Use
	Total % [95% CI]	Total % [95% CI]
Total (3828)	6.47[5.13–8.12]	2.81[2.07–3.79]
Sex		
Men	10.05[7.75–12.93]	5.09[3.66–7.05]
Women	3.12[2.25–4.27]	0.66[0.37–1.18]
Age		
15–24	8.40[6.27–11.16]	5.42[3.69–7.88]
25–34	9.37[6.69–12.99]	3.46[2.22–5.37]
35–44	4.82[3.10–7.42]	1.61[0.74–3.44]
45–64	3.54[2.12–5.87]	0.85[0.34–2.07]
Years of study		
1 to 8 years	4.03[3.02–5.36]	2.65[1.76–3.97]
9 to 12	6.41[4.37–9.31]	3.12[2.02–4.78]
13 or more	7.80[5.69–10.61]	2.68[1.48–4.78]
Marital status		
Single	8.12[5.78–11.31]	4.40[2.95–6.51]
Married/Cohabiting	5.60[4.36–7.16]	1.91[1.35–2.68]
Widowed/Divorced	6.09[3.52–10.36]	2.94[1.19–7.08]
Income		
Up to 3 MW*	6.09[4.63–7.98]	3.33[2.32–4.76]
3 to 4 MW	11.99[6.11–22.17]	2.89[0.76–10.35]
5 or more MW	13.98[4.23–37.43]	2.61[0.35–16.87]
Employed		
Yes	7.73[5.91–10.04]	3.32[2.36–4.67]
No	3.69[2.65–5.10]	1.67[1.01–2.72]
Area		
Urban	6.76[5.22–8.70]	2.98[2.10–4.21]
Rural	2.85[1.47–5.46]	1.20[0.41–3.44]
Age of onset (mean)	17.7 (SD ± 3.7)	16.5 (SD ± 3.3)

*MW – Minimum Wage 2012 (R$622,00 or U$ 304,90).

cannabis dependence (Degenhardt, Ferrari, and Hall 2017). The literature also highlights an association between cannabis consumption and alcohol use disorders, and how this combination can amplify negative effects mentioned above (United Nations Office on Drugs and Crime (UNODC) 2015).

Approximately 9% of those who experiment cannabis will become addicted to it (according to the criteria for dependence in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition) rising to about 17% in those who start using in their teens (National Institute on Drug Abuse (NIDA) and National Institute of Health 2020). Findings from the Monitoring the Future survey found significant increase in cannabis use among adolescents in the US between 2017 and 2019, especially among 10th graders (National Institute on Drug Abuse (NIDA) and National Institute of Health 2019).

There is a scarcity of population-based and in-depth studies regarding cannabis consumption in Latin America (Castillo-Carniglia 2015). A student survey performed in 2010 in all state capitals in Brazil have shown that cannabis use in the country is relatively low compared to most Latin American countries, and most high-income countries, with estimated rates of 5.7% of lifetime use and 3.7% in the last year (Centro Brasileiro de Informações sobre Drogas Psicotrópicas (CEBRID) 2010). The first edition of the Brazilian National and Alcohol Survey (BNADS) performed in 2006 in a nationally representative sample aged 14 years and older found that 2.1% of Brazilians had used cannabis in the previous year (Jungerman and Laranjeira 2008). However, the information regarding cannabis age of initiation and addiction at a national level is still not available for the country.

The debate raised by recent cannabis decriminalization has brought the subject to the spotlight in Brazil, and policies are due to be implemented in a climate of little country-specific scientific evidence. It is, therefore, crucial to enrich the discourse regarding cannabis by ensuring it is backed by concrete and wide-reaching evidence. The aim of this study is to estimate prevalence rates of cannabis use and dependence in a nationally representative sample of the Brazilian population. In addition, the association between age of cannabis use and dependence indicators are investigated. The authors

Table 2. Prevalence rates of other substance use and depression among cannabis users and associations with cannabis use.

	Whole Sample (N = 3828)			Cannabis Users (used in the last year)				
	Men % [95% CI]	Women % [95% CI]	Total % [95% CI]	Men % [95% CI]	Women % [95% CI]	Total % [95% CI]	IRR*** (95%CI)	
Cannabis Dependence (SDS)								
Moderate	1.37[0.8–2.3]	0.15[0.03–0.80]	0.74[0.4–1.2]	26.92 [12.7–38.5]	23.26[11.5–32.20]	26.47[18.5–33.5]	n/a	
Severe	0.25[0.1–1.0]	0.11[0.02–0.50]	0.18[0.1–0.5]	4.92[CI: n/a][1]	16.83[CI: n/a][1]	6.38 [4.4–7.2]		
Depressive Disorder (CES-D)								
	17.0[14.0–20.4]	31.1[28.3–34.0]	24.29[21.8–26.9]	24.75[15.8–36.6]	70.09[41.0–88.7]	30.35[21.0–41.6]	3.1	(1.7–5.6)
Other Substance Use								
Binge Drinking*	65.70[61.2–69.9]	48.56[42.7–54.4]	58.61[54.6–62.5]	83.09[70.6–90.9]	65.21[31.2–88.5]	80.57[68.9–88.6]	5.7	(3.1–10.6)
AUD**	15.50[12.7–18.7]	6.96[5.5–8.7]	11.10[9.6–12.7]	39.15[27.0–52.8]	33.59[11.5–66.2]	38.47[27.5–50.8]	7.6	(4.1–14.3)
Tobacco Use	20.62[18.0–23.5]	12.39[10.7–14.3]	16.37[14.7–18.2]	58.26[44.4–70.9]	64.31[35.8–85.3]	59.0[46.7–70.3]	11.8	(6.2–22.2)
Cocaine Use	3.24[2.2–4.6]	0.65[0.3–1.2]	1.90[1.4–2.6]	45.32[34.3–56.8]	42.07[13.3–77.4]	44.93[34.6–55.7]	2.6	(1.9–3.6)

*Ingestion of 4/5 (women/men) units within 2 hours – among alcohol users.
**Alcohol Use Disorder (DSM-V).
***Multivariate analysis (Poisson regression) was adjusted by sociodemographic characteristics.
Bold = $p < .001$.
[1]Confidence intervals not estimated due to conflict between weighting sample strata.

propose and test a path model to explain the relationship between cannabis age of initiation and dependence, identifying the role of depression and alcohol consumption as possible mediators of this association.

Methods

The second Brazilian National Alcohol and Drugs Survey (II BNADS) was conducted in 2012. A multistage cluster sampling procedure was used to select a representative sample of the Brazilian population aged 14 years and older. The global response rate was 77%. To allow comparisons with main international surveys, the analysis was based on a sub-sample of 3,828 individuals aged 15 to 64 years. Face-to-face interviews of approximately one hour were conducted in the respondent's home by trained interviewers, using a standardized questionnaire. The drug assessment was completed by the participant himself in a separate room, and then returned to the interviewer in a sealed envelope (Abdalla et al. 2014; Madruga et al. 2012).

Measures

Cannabis use was investigated with questions covering the following areas: lifetime and last year use (parameter chosen to indicate current use), and age of consumption onset (age when first tried cannabis). Questions regarding access to cannabis were also included, such as the location where it was last obtained and a likert scale on how easy it was to find it. A question regarding how cannabis was acquired (bought, given or traded) in the last occasion it was consumed was also included in the questionnaire.

Cannabis dependence – Identified by the Brazilian validated version of the Severity of Dependence Scale (SDS) (Ferri et al. 2000), through five questions: 1) "Have you ever though your use of cannabis was out of control?" 2) "Does the prospect of missing a smoke make you very anxious or worried?" 3) "Do you worry about your use of cannabis?" 4) "Do you wish you could stop?" 5) "How difficult would you find it to stop or go without cannabis?" Responses were scored on a four-point likert scale with the following scores for the first four questions: 0 = never or almost never; 1 = sometimes; 2 = often; 3 = always or nearly always. The fifth question had answers ranging as follows: 0 = not difficult; 1 = quite difficult; 2 = very difficult; 3 = impossible.

The two official recommended cutoff scores published for this tool are the score of 3 for adults (17 to 57 years old) proposed by Swift et al. (Swift, Copeland, and Hall 1998) and the score of 4 for adolescents (14 to 18 years old), proposed by Martin et al. (2006). Further, Cuenca-Royo et al. (2012) performed a more sophisticated validation by taking into account the Psychiatric Interview for Mental Disorders (PRISM) as the gold standard for cannabis disorders according to DSM-IV and DSM-V criteria. Taking the paradigm that cannabis dependence varies across a continuum from relatively mild to severe, the dependence index was created using a continuous variable with the sum of all five items, ranging from 0 to 15, with 15 representing the highest level of dependence. This variable is used for all the multivariate and conditional models.

The age of initiation of alcoholic beverages consumption was assessed using the question "At what age did you start drinking alcohol (do not consider when you only tried one or two sips)". The number of drinks consumed in a typical day (alcohol intake) was also measured with the assistance of a unit/drink demonstration chart.

Binge Drinking was defined as the consumption of four alcohol units (drinks) for females and five alcohol units for males within a two-hour period. A drink was defined as a 5-ounce glass of wine, a 12-ounce can of beer, or a 1.5-ounce shot of liquor (National Institute on Alcohol Abuse and Alcoholism (NIAAA) 2005).

Alcohol Use Disorder (AUD) was assessed with the Brazilian version of the Composite International Diagnostic Interview (CIDI 2.1) (Quintana et al. 2004). Although this survey pre-dates DSM-5, the assessment can determine alcohol use disorder according to DSM-5, covering the eleven criteria it demands. In the analysis herein, the presence of 2 or more criteria in the past 12 months was considered a positive diagnosis of AUD.

Being a smoker was defined as an affirmative answer for smoking equal to or more than once a month. Age of onset for smoking and smoking patterns were also included in this session.

Lifetime and past 12 months self-reported use of the following substances was also assessed: Amphetamine Type Stimulants (ATS, defined by the use of amphetamines such as speed, crystal meth, ecstasy and other MDMA alternatives); Crack/cocaine; Cocaine; Solvents (glue and ether-chloride spray), Opioids (heroin and morphine) and Hallucinogens (LSD, magic mushrooms).

Depressive symptoms were assessed using the Brazilian validated version of the 20-item Center for Epidemiological Studies Depression Scale (CES-D) which asks about the frequency of depressive symptoms experienced in the week prior to the interview, ranging from 0 (never) to 4 (most of the time). The score 16 was used as the cutoff point (Batistoni, Neri, and Cupertino 2007; Bradley, Bagnell, and Brannen 2010) for the preliminary analysis as a case indication of depressive

disorder. To obtain the mediating effect in the conditional model the total score (sum of all items) was considered, creating an index accounting for the presence and intensity of depressive symptoms (ranging from 0 to 80).

Statistical analysis

The analysis was performed using the Stata® software, version 13.0, for the weighted prevalence rates estimations and individual associations. The Conditional Process Analysis was performed using Process ("processmacro.org" macro v2.14.) installed in SPSS21. PROCESS is a computational procedure that implements moderation or mediation analysis, as well as their combination in an integrated conditional process model. It uses a path analysis framework similar to the approach described by Hayes and Preacher, which estimates the interference of direct, indirect, and total effects in an independent variable (Hayes and Preacher 2014).

All the analysis accounted for the complex sampling characteristics of the data. Analyses were conducted on data weighted to correct for unequal probabilities of selection into the sample, and a post-stratification weight was applied to correct for non-response and to adjust both samples to known population distributions on demographic variables (education, age, gender and region of the country) according to the Brazilian Censuses of 2010. Cross-tabulations were used to examine lifetime and last year cannabis consumption rates by socioeconomic and demographic characteristics by sex, age, years of study, marital status, income, professional status and living area.

Prevalence rates of depressive disorder, binge drinking, Alcohol Use Disorder (AUD), tobacco and cocaine use were also estimated in the whole sample and among past year cannabis users.

Poisson regression models were used to assess the incidence ratio (IRR), indicating how much belonging to the Cannabis Users category affects the probability of the incidence of other outcomes (depressive disorders, binge drinking, AUD, tobacco and cocaine use), while controlling for sex, age and educational.

The hypothesis was to determine whether the direct association between cannabis consumption age of onset (CAO) and cannabis dependence (CD) could be mediated by depression indication and/or alcohol consumption. To test this hypothesis, we adopted the Parallel Multiple Mediator (PMM) Model from the Conditional Process Analysis algorithms. CAO was considered the predictor (X), CD the outcome (Y), depression indication was considered the mediator (M1) and alcohol consumption the second mediator (M2). All models were calculated as weighted linear composites of scale items. The mediations were conducted to estimate the effect of depression indication and alcohol consumption in the relation between CAO and CD, using the product of coefficients method (Mackinnon and Fairchild 2009). This method involves the multiplication of regression coefficients for the regression of the mediator on the independent variable (a-path) and for the regression of the outcome on the mediator (b-path) with the independent variable included in the model (c-path), and with a*b considered the mediated effect. An effect size, representing proportion of variance explained by the mediated effect, can be calculated by dividing the amount of variance in the outcome explained by the mediated effect by the total amount of variance in the outcome explained by both the mediator and the independent variable. For the serial mediation analysis, the total effect of X on Y is equal to the direct effect of X plus the sum of the two specific indirect effects of the two mediators. All mediation effects were estimated in Process using a maximum likelihood estimator and 10,000 bootstrap draws to obtain confidence intervals for the indirect effect. All models were evaluated using multiple indices of model fit: a non-significant chi-square statistic, comparative fit index (CFI) values greater than 0.95, and standardized root mean square residual (SRMR) values less than 0.08 (Hu and Bentler 1999).

This research protocol was submitted and approved by the Ethics Committee of the Federal University of Sao Paulo and by National Commission of Ethics in Research. The interviews complied with all statements required by the Brazilian Ministry of Health Ethical Committee Office (CAAE: 61909615.0.000.5505).

Results

Cannabis use prevalence rates and user's profile

Lifetime cannabis use was reported by 6.47% [5.13–8.12] of the sample, being 10.05% [7.75–12.93] among men and 3.12% [2.25–4.27] among women. The mean age for cannabis use onset among the lifetime users sample was 17.7 years old (SD ± 3.7). Adult (aged 25 to 34), educated (13 or more years of study), employed, and earning salaries over 5 times the minimum wage males presented the highest rates for lifetime use, reaching nearly 14%.

The last year use was reported by 2.81% [2.07–3.79] of the general population and, again, the consumption rate was higher among men 5.09% [3.66–7.05] as compared to women, of 0.66% [0.37–1.18]. The mean age of onset for cannabis use among recent users was 16.5 years

old (SD ±3.3), with more than half of the sample (59.8%) reported having experimented cannabis for the first time before completing 18 years old.

The adjusted multivariate model identified that age and sex were the only sociodemographic characteristics associated with current cannabis use, as users were more likely to be male (OR: 3.14 [1.60–6.17]), and younger, with chances of consumption decreasing by 0.95 times each successive year of age (OR: 0.95 [0.92–0.98]).

TABLE 1 HERE

Cannabis dependence

Poisson regression models were used to assess the associations between cannabis use, depressive disorder, binge drinking, alcohol use disorder, tobacco and cocaine use while controlling by gender, age, education. The rate of cannabis moderated dependence in the general population was 0.74% [0.4–1.2] with higher rates among men 1.37% [0.8–2.3] as compared to women, 0.15% [0.03–1.8]. Cannabis moderate dependence was identified in 26.47% [18.5–33.5] of current users. We found that 32.6% of the current users have tried to quit without success, whereas over two every ten users (24%) referred history of withdrawal symptoms, such as insomnia, sweating, shivering, anxiety, irritability, palpitation, and tachycardia. Women tended to refer those symptoms more often than men, with 23.9% among men as compared to 29.7% among women (data not shown in the tables). Severe cannabis dependence was identified in more than 6.38% [4.4–7.2] of cannabis users; this rate was over three times higher amongst women when compared to men (16.83% vs 4.92%).

Cannabis and depressive disorder

Depressive Disorder indication was identified in over 30.35% [21.-41.6] of cannabis users, as compared to 24.29% [21.8–26.9] in the whole population. Depressive symptoms were very prevalent among female cannabis users, reaching 70.09% [41.0–88.7]. The multivariate analysis showed that cannabis use and dependence were highly associated with depression IRR:3.1 [1.7–5.6], with users having over three times more chances to present depressive disorder.

Cannabis and use of other drugs

Most cannabis users (85.4%) drank alcohol in the last year, and the majority of them, 80.57% [68.9–88.6], reported binge drinking in the last year. Alcohol Use Disorder (AUD) was identified in over one third of cannabis users (38.47% [27.5–50.8]). The multivariate analysis showed a robust association between cannabis use and binge drinking (IRR: 5.7 [3.1–10.6]), and AUD (IRR:7.6 [4.1–14.3]). Cannabis use had a high and significant association with tobacco smoking (IRR: 11.8 [6.2–22.2]). In the multivariate analysis, we found that there is also a significant association between cannabis cocaine use (IRR: 2.6 [1.9–3.6]).

TABLE 2 HERE

The conditional model

The Parallel Multiple Mediator (PMM) Model allows many effects operating through multiple mechanisms simultaneously (Hayes and Preacher 2014), presenting coefficients for all direct and indirect paths tested with significant *p*-values, even though the R square value was considered low (5%). The PMM Model proposed considered the continuous variables depressive symptoms (index with the CES-D items) and alcohol consumption (AC, doses/units of alcohol ingested in a typical day) as mediators in the association between the predictor X, cannabis use age of onset (CAO), and the outcome Y, Cannabis dependence (CD) (Direct effect:0.0615; SE: 0.0018;t:34.346;p = .0000; LLCI: 0.0580 ULCI 0.0650). Data is consistent with the claim that cannabis age of onset affected the development of cannabis dependence through depressive symptoms independent of alcohol consumption (Indirect effect 1: 0.0002; BootSE: 0.0001; BootLLCI: 0.0001 – BootULCI: 0.0006); and through alcohol consumption independent of depressive symptoms (Indirect effect 3: Effect: 0.0005; BootSE: 0.0003; BootLLCI: 0.0000 – BootULCI: 0.0014). However, no indirect effect was estimated when considering both mediators in series (Indirect effect 2) as seen in Figure 1.

Discussion

This is the first-time cannabis dependence was assessed in a nationally representative sample in Brazil. Further, the risk factors for consumption and dependence were investigated to build an explanatory conditional model demonstrating the relationship between age of cannabis initiation and dependence, revealing the mediating effects of alcohol consumption and depressive symptoms in this association.

Lifetime cannabis use rate was 6.47%, lower than European estimates (27,4%) (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2019), with one in every ten males aged 15 to 64 years old having tried cannabis at least once in their life (10.05%). Consumption of cannabis in the previous year (2011) was 2.81% in the whole sample (5.09% among men as compared to 0.66% among

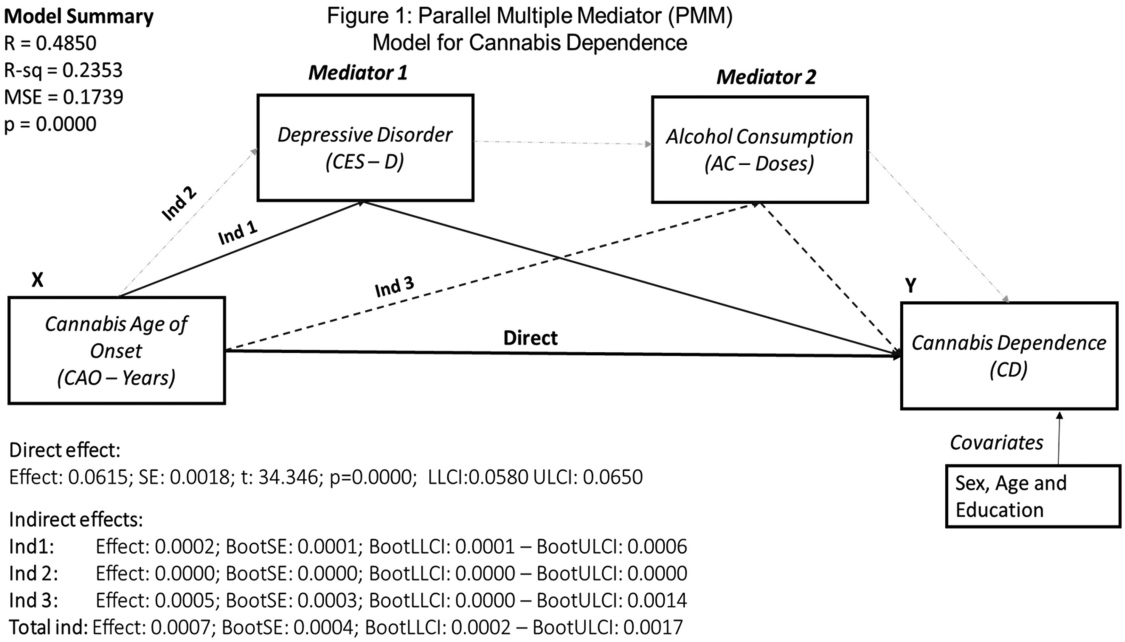

Figure 1. Parallel Multiple Mediator (PMM) Model for cannabis dependance.

women). This prevalence reached 9.18% among young men (15 to 24 years old). Even though higher than previous national estimates (Jungerman and Laranjeira 2008), Brazilian rates were lower than in most South American countries, such as Argentina (6.9%), Uruguay (5.2%) Chile (30.6%) (Castillo-Carniglia 2015; Degenhardt et al. 2011) and Europe (7.4%) at the time of this survey (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2019). Following cannabis, cocaine is the most consumed illegal drug in Brazil, its price making it highly available for adolescents (Abdalla et al. 2014). Current marijuana users were more than twice more likely to use cocaine in the previous year. However, assumptions related to the gateway theory should be avoided, not only due to the fact that causality assertions are not valid in a cross-sectional framework, but also due to the lack of previous evidence of such relationship.

Our findings also showed that cannabis users had nearly twelve times more chances of smoking tobacco cigarettes. This large association was not as expected as it would be in countries where both drugs are typically combined in the same cigarette, such as the United States, England, and most European countries. However, this is not the case in Brazil, where cannabis is usually cheaper, and joints are typically made of the cannabis compound alone, without mixing with tobacco products. In fact, our study showed that at the time the survey was performed, nearly half of cannabis users are not tobacco smokers at all, and actually one in ten have never smoked tobacco in their lives. Looking from the perspective that the use of these drugs is unrelated in Brazil, it becomes relevant to identify cannabis use as a risk factor for tobacco smoking (and vice-versa). Regarding alcohol use, most cannabis users (over 80%) reported binge drinking, and were nearly six times more likely to drink in a harmful pattern than the general population. Furthermore, over one third of cannabis users were identified with alcohol use disorder (AUD). Cannabis dependence was significantly associated with alcohol use disorder, even when adjusting by socioeconomic and demographic characteristics or depressive symptoms.

The mean age of consumption onset of cannabis lifetime users was 17.7 years old, and 16.5 to last year users. Use at an early age is the main concern when analyzing the long-term effects of cannabis use. Young people are more vulnerable to developing adverse effects associated with the use of psychotropic substances, especially from exogenous cannabinoids. The adolescent's developing brain is more vulnerable to the chemical changes that psychotropic substances cause, leading to profound and, sometimes, permanent alterations, which can be associated not only with lower cognitive performance, but also psychiatric disorders and increased risk of developing cannabis dependence (Bossong and Niesink 2010; Lubman, Cheetham, and Yucel 2015; Meier et al. 2012).

Cannabis dependence syndrome has been extensively reported in the literature (Freeman and Winstock 2015; United Nations Office on Drugs and Crime (UNODC) 2015; Volkow et al. 2014). The European Monitoring Center for Drugs and Drug Addiction (EMCDDA) has

promoted the use of scales to measure problematic cannabis use in population surveys. The Severity of Dependence Scale assesses the psychological aspects of substance dependence related to feelings of control, worry and anxiety about consumption, and has been used extensively (Cuenca-Royo et al. 2012; Ferri et al. 2000). In this study we found that 0.74% of the population aged 15 to 65 years old were screened with moderate cannabis dependence, with higher rates among men (1.37%). Dependence was identified in nearly one third of current cannabis users, again with higher rates among men (26.92%) as compared to women (23.26%). The high proportion of users displaying symptoms of dependence can also be explained by the increasingly high concentrations of THC found in the cannabis sold on the streets (Freeman and Winstock 2015; Taschwer and Schmid 2015), in line with recent surveys performed in Chile (Castillo-Carniglia 2015) and in the USA (Hasin et al. 2015). Even though men are more prompt to consume cannabis and to present moderate dependence, severe cannabis dependence was more prevalent among women, affecting nearly two in every 10 female users (16.83%), as compared to just under 5% among men. This finding is in agreement with prior research (Fergusson and Boden 2008; Green et al. 2015; Harder, Stuart, and Anthony 2008) showing that the escalation of addiction is faster in women, even though they present lower rates of experimentation and consumption. Our results also showed that consumption rates are up to five times higher among men compared to women. However, current gender differences may reflect differences in the amount of exposure, rather than vulnerability to addiction. On the other hand, gender was not a risk factor for any of the two levels of dependence assessed, moderate, and severe. In fact, none of the sociodemographic characteristics predicted cannabis dependence. The exploratory association analysis demonstrated that the only predictors for cannabis dependence were age of cannabis use initiation, depressive disorder/symptoms, alcohol use, and AUD, grounding the conditional model proposed.

The proposed conditional model of cannabis addiction has confirmed that the development of cannabis dependence is affected by the age of cannabis use initiation when this relationship is mediated by either depressive symptoms or alcohol consumption, i.e., happening alone, but not concomitantly.

Based on the risk factors identified by the preliminary association analysis, the Parallel Multiple Mediator (PMM) Model proposed considered the age of cannabis initiation (Cannabis age of onset – CAO) as a predictor of dependence (CD). It demonstrated that CD occurrence is predicted by the age of initiation as a direct predictor with an inverse effect: the sooner the initiation of use the higher the chances of developing dependence, with a significant direct effect of 0.06 ($p < .0001$). The hypothesis that this association was mediated by depressive symptoms and alcohol consumption was also confirmed. The indirect effects considering depressive disorder and cannabis dependence and alcohol consumption had a mediation role significantly affecting the outcome CD. Individuals who had an early onset of cannabis use have increased chances to present depressive symptoms and both events predicted cannabis dependence. The parallel multiple mediator model also demonstrated that early onset of cannabis uses increased chances of alcohol consumption and both were associated with cannabis dependence. These results are supported by literature showing that early consumption, mood disorders and the misuse of alcohol can intermediate and trigger addiction (Salom et al. 2015; Zaman et al. 2015). The results reinforce the need for primary drug use prevention strategies in order to inhibit or postpone cannabis (and alcohol) experimentation. Further, it emphasizes the importance of also targeting alcohol consumption and mood disorders to build more effective secondary prevention and treatment approaches for cannabis dependence.

Our findings should be interpreted in the light of study limitations. First, the cross-sectional design of the BNADS rules out the establishment of causality. Therefore, the assumptions brought forward by the conditional model proposed should be interpreted with caution, even though our independent variable comes from a retrospective assessment, considering an event that necessarily happened before our outcome (age of experimentation and addiction). Assessment of illegal drug use by self-report can lead to an underestimation of substance use. However, the strategy of using a separate self-filled response sheet, returned in a sealed envelope in order to guarantee the participant's confidentiality, is likely to mitigate this limitation. Finally, the associations estimated for this manuscript were calculated using different models of adjustment, considering first the sociodemographic characteristics and then the depression symptoms score and alcohol consumption. The sociodemographic variables used were sex, age and education. Other sample characteristics that are potential confounders were not included in the analysis either due low response rate (income) or were not significantly associated with the outcome in the exploratory analysis (marital status and living area). Ethnicity and race could also affect the analysis as confounders, however, the assessment of this characteristics in such an ethnically diverse country such as Brazil leads

to an even worse bias related to self-reporting (Travassos and Williams 2004).

The authors believe that a good approach to minimize the negative, individual and social impacts related to the use of psychoactive substances, should be through education and prevention. We must bring to focus that initiatives prioritizing the delay of the age of drug use onset were in fact, never implemented in the country. Finally, we hope our findings will pave the way for evidence-based drug policies in Brazil and abroad.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the CAPES; CNPq.

ORCID

http://orcid.org/0000-0003-3203-3889
http://orcid.org/0000-0003-2877-2195

References

Abdalla, R., C. Madruga, M. Ribeiro, I. Pinsky, R. Caetano, and R. Laranjeira. 2014. Prevalence of cocaine use in Brazil: Data from the II Brazilian National Alcohol and Drugs Survey (BNADS). *Addictive Behaviors* 39 (1):297–301. doi:10.1016/j.addbeh.2013.10.019.

Batistoni, S. S. T., A. L. Neri, and A. P. F. B. Cupertino. 2007. Validity of the center for epidemiological studies depression scale among Brazilian elderly. *Revista de Saude Publica* 41 (4):598–605. doi:10.1590/S0034-89102007000400014.

Bossong, M. G., and R. J. Niesink. 2010. Adolescent brain maturation, the endogenous cannabinoid system and the neurobiology of cannabis-induced schizophrenia. *Progress in Neurobiology* 92 (3):370–85. doi:10.1016/j.pneurobio.2010.06.010.

Bradley, K. L., A. L. Bagnell, and C. L. Brannen. 2010. Factorial validity of the center for epidemiological studies depression 10 in adolescents. *Issues in Mental Health Nursing* 31 (6):408–12. doi:10.3109/01612840903484105.

Castillo-Carniglia, A. 2015. Large increase in adolescent marijuana use in Chile. *Addiction* 110 (1):185–86. doi:10.1111/add.12765.

Castillo-Carniglia, A., A. Rivera-Aguirre, E. Calvo, R. Queirolo, K. M. Keyes, and M. Cerdá. 2020. Trends in marijuana use in two Latin American countries: An age, period and cohort study. *Addiction* 115 (11):2089–97. doi:10.1111/add.15058.

Centro Brasileiro de Informações sobre Drogas Psicotrópicas (CEBRID). 2010. *VI Levantamento Nacional sobre o Consumo de Drogas Psicotrópicas entre Estudantes do Ensino Fundamental e Médio das Redes Pública e Privada de Ensino nas 27 Capitais Brasileiras*. Sao Paulo: Universidade Federal de São Paulo.

Cuenca-Royo, A. M., A. Sanchez-Niubo, C. G. Forero, M. Torrens, J. M. Suelves, and A. Domingo-Salvany. 2012. Psychometric properties of the CAST and SDS scales in young adult cannabis users. *Addictive Behaviors* 37 (6):709–15. doi:10.1016/j.addbeh.2012.02.012.

Degenhardt, L., A. Ferrari, and W. Hall. 2017. The global epidemiology and disease burden of cannabis use and dependence. In *Handbook of cannabis and related pathologies biology, pharmacology, diagnosis and treatment*, ed. Faculty of Life Sciences and Medicine KsCL, London, United Kingdom, 89–100. London, UK: Faculty of Life Sciences and Medicine, King's College London.

Degenhardt, L., C. Bucello, B. Calabria, P. Nelson, A. Roberts, W. Hall, M. Lynskey, L. Wiessing. 2011. What data are available on the extent of illicit drug use and dependence globally? Results of four systematic reviews. *Drug and Alcohol Dependence*. 117(2–3):85–101. doi:10.1016/j.drugalcdep.2010.11.032.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). 2019. *Developments in the European cannabis market*. Lisbon.

Fergusson, D. M., and J. M. Boden. 2008. Cannabis use and later life outcomes. *Addiction* 103 (6):969–76; discussion 977–8. doi:10.1111/j.1360-0443.2008.02221.x.

Ferri, C. P., J. Marsden, M. de Araujo, R. R. Laranjeira, and M. Gossop. 2000. Validity and reliability of the Severity of Dependence Scale (SDS) in a Brazilian sample of drug users. *Drug and Alcohol Review* 19 (4):451–55. doi:10.1080/713659418.

Freeman, T. P., and A. R. Winstock. 2015. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychological Medicine* 45 (15):3181–89. doi:10.1017/S0033291715001178.

Green, K. M., R. J. Musci, R. M. Johnson, P. A. Matson, B. A. Reboussin, and N. S. Ialongo. 2015. Outcomes associated with adolescent marijuana and alcohol use among urban young adults: A prospective study. *Addictive Behaviors* 53:155–60. doi:10.1016/j.addbeh.2015.10.014.

Harder, V. S., E. A. Stuart, and J. C. Anthony. 2008. Adolescent cannabis problems and young adult depression: Male-female stratified propensity score analyses. *American Journal of Epidemiology* 168 (6):592–601. doi:10.1093/aje/kwn184.

Hasin, D. S., T. D. Saha, B. T. Kerridge, R. B. Goldstein, S. P. Chou, H. Zhang, J. Jung, R. P. Pickering, W. J. Ruan, S. M. Smith, et al.. 2015. Prevalence of marijuana use disorders in the united states between 2001–2002 and 2012–2013. *JAMA Psychiatry*:1–9.

Hayes, A., and K. J. Preacher. 2014. Statistical mediation analysis with a multicategorical independent variable. *British Journal of Mathematical and Statistical Psychology* 67 (3):451–70. doi:10.1111/bmsp.12028.

Hu, L.-T., and P. M. Bentler. 1999. Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal* 6 (1):1–55. doi:10.1080/10705519909540118.

Jungerman, F. S., and R. Laranjeira. 2008. Characteristics of cannabis users seeking treatment in Sao Paulo, Brazil. *Revista Panamericana de Salud Pública* 23 (6):384–93.

Large, M., S. Sharma, M. T. Compton, T. Slade, and O. Nielssen. 2011. Cannabis use and earlier onset of psychosis: A systematic meta-analysis. *Archives of General Psychiatry* 68 (6):555–61. doi:10.1001/archgenpsychiatry.2011.5.

Lev-Ran, S., M. Roerecke, B. Le Foll, T. P. George, K. McKenzie, and J. Rehm. 2014. The association between cannabis use and depression: A systematic review and meta-analysis of longitudinal studies. *Psychological Medicine* 44 (4):797–810. doi:10.1017/S0033291713001438.

Lubman, D. I., A. Cheetham, and M. Yucel. 2015. Cannabis and adolescent brain development. *Pharmacology & Therapeutics* 148:1–16.

Mackinnon, D. P., and A. J. Fairchild. 2009. Current directions in mediation analysis. *Current Directions in Psychological Science* 18 (1):16. doi:10.1111/j.1467-8721.2009.01598.x.

Madruga, C., R. Laranjeira, R. Caetano, I. Pinsky, M. Zaleski, and C. P. Ferri. 2012. Use of licit and illicit substances among adolescents in Brazil — A national survey. *Addictive Behaviors* 37 (10):1171–75. doi:10.1016/j.addbeh.2012.05.008.

Martin, G., J. Copeland, P. Gates, and S. Gilmour. 2006. The Severity of Dependence Scale (SDS) in an adolescent population of cannabis users: Reliability, validity and diagnostic cut-off. *Drug and Alcohol Dependence* 83 (1):90–93. doi:10.1016/j.drugalcdep.2005.10.014.

Meier, M. H., A. Caspi, A. Ambler, H. Harrington, R. Houts, R. S. Keefe, K. McDonald, A. Ward, R. Poulton, T. E. Moffitt. 2012. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proceedings of the National Academy of Sciences of the USA*. 109(40): E2657–2664. doi:10.1073/pnas.1206820109.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). 2005. *Helping patients who drink too much: A clinician's guide*.

National Institute on Drug Abuse (NIDA) and National Institute of Health. 2019. *Monitoring the future 2019*.

National Institute on Drug Abuse (NIDA) and National Institute of Health. 2020. *Marijuana research report*.

Quintana, M. I. A. S., M. R. Jorge, F. L. Gasta, and C. T. Miranda. 2004. The reliability of the Brazilian version of the Composite International Diagnostic Interview (CIDI 2.1). *Brazilian Journal of Medical and Biological Research* 37 (11):1739–45. doi:10.1590/S0100-879X2004001100020.

Rasic, D., S. Weerasinghe, M. Asbridge, and D. B. Langille. 2013. Longitudinal associations of cannabis and illicit drug use with depression, suicidal ideation and suicidal attempts among Nova Scotia high school students. *Drug and Alcohol Dependence* 129 (1–2):49–53. doi:10.1016/j.drugalcdep.2012.09.009.

Salom, C. L., K. S. Betts, G. M. Williams, J. M. Najman, and R. Alati. 2015. Predictors of comorbid polysubstance use and mental health disorders in young adults-a latent class analysis. *Addiction* 111 (1):156–64. doi:10.1111/add.13058.

Swift, W., J. Copeland, and W. Hall. 1998. Choosing a diagnostic cut-off for cannabis dependence. *Addiction* 93 (11):1681–92. doi:10.1046/j.1360-0443.1998.931116816.x.

Taschwer, M., and M. G. Schmid. 2015. Determination of the relative percentage distribution of THCA and Δ9-THC in herbal cannabis seized in Austria – Impact of different storage temperatures on stability. *Forensic Science International* 254:167–71. doi:10.1016/j.forsciint.2015.07.019.

Travassos, C., and D. R. Williams. 2004. The concept and measurement of race and their relationship to public health: A review focused on Brazil and the United States. *Cadernos De Saúde Pública* 20 (3):660–78. doi:10.1590/S0102-311X2004000300003.

United Nations Office on Drugs and Crime (UNODC). 2015. *World drug report 2015*. Vienna.

Vindenes, V., D. H. Strand, L. Kristoffersen, F. Boix, and J. Mørland. 2013. Has the intake of THC by cannabis users changed over the last decade? Evidence of increased exposure by analysis of blood THC concentrations in impaired drivers. *Forensic Science International* 226 (1–3):197–201. doi:10.1016/j.forsciint.2013.01.017.

Volkow, N. D., R. D. Baler, W. M. Compton, and S. R. Weiss. 2014. Adverse health effects of marijuana use. *The New England Journal of Medicine* 370 (23):2219–27. doi:10.1056/NEJMra1402309.

Zaman, T., M. Malowney, J. Knight, and J. W. Boyd. 2015. Co-occurrence of substance-related and other mental health disorders among adolescent cannabis users. *Journal of Addiction Medicine* 9 (4):317–21. doi:10.1097/ADM.0000000000000138.