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Why should we ask binge drinkers if they smoke cannabis? Additive effect of alcohol and cannabis use on college students' neuropsychological performance

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ABSTRACT

Introduction: Binge drinking (BD) and cannabis use are prevalent in European adolescents and students. BD has been shown to have a negative impact on neuropsychological functioning, but little is known about the additive effect when it is combined with cannabis consumption. We therefore investigated the neuropsychological profiles of students who engage in combined BD and cannabis use, in order to explore the potentially harmful additive effects of cannabis use and BD on cognition.

Material and methods: A sample of college students ($N = 298$) completed questionnaires on alcohol and cannabis use, and were screened for neuropsychological impairments using the Brief Evaluation of Alcohol-Related Neuropsychological Impairments (BEARNI). First, after dividing students into three groups according to their alcohol and cannabis use (i.e., light drinkers, binge drinkers, and binge drinkers consuming cannabis), we ran a linear mixed model based on the BEARNI z scores to test the performances of the three groups. Information yielded by the mixed model was supplemented by individual analyses. Second, to explore the heterogeneity of binge drinkers' profiles, we ran a cluster analysis to characterize the alcohol users at higher risk of more severe neuropsychological impairment.

Results: Overall, poorer neuropsychological performances were observed among binge drinkers compared with light drinkers, whether they used cannabis or not. However, flexibility, episodic memory and working memory were particularly affected among binge drinkers who used cannabis.

Conclusions: Results emphasize the importance of asking binge drinkers if they smoke cannabis, in order to adapt care and prevention strategies to their consumption and neuropsychological profile.

1. Introduction

Binge drinking (BD) is mainly observed in adolescents and young adults, and concerns two thirds of college students in France (Tavolacci et al., 2016). BD is usually defined as a pattern of alcohol consumption characterized by intermittent periods of heavy drinking over a short period of time and periods of abstinence (Crego et al., 2009).[1] This specific pattern of consumption is frequently associated with the use of cannabis (Tavolacci et al., 2016), which is the most consumed illicit substance in Europe, with 31% of French students reportedly having smoked it at least once in their lives (EMCDDA, 2019). Both BD and cannabis use have harmful consequences (e.g., academic, social, cognitive, neuropsychological and daily life disturbances; Buckner et al., 2010; Carbia et al., 2018; Stevens et al., 2021), making them a major

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[1] In the United States, BD corresponds to four drinks for women and five drinks for men consumed within a 2-hour interval, according to the National Institute on Alcohol Abuse and Alcoholism (2004). The thresholds in France are six drinks for women and seven drinks for men within a 2-hour interval.

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public health issue. The focus must therefore be on BD and its association with cannabis use.

The neuropsychological impairments induced by BD have been extensively documented in the scientific literature (Amrani et al., 2013; Lees et al., 2019; Salas-Gomez et al., 2016). This problematic drinking pattern can lead to brain atrophy in the prefrontal, temporal and parietal cortices, as well as in the hippocampus, inducing executive and memory disorders (see Carbia et al., 2018, for a review). BD mainly impairs executive functions, with increased impulsivity and a lack of cognitive control related to frontal dysfunction (Gil-Hernandez & Garcia-Moreno, 2016; Parada et al., 2012). Memory impairments have also been reported (Vinader-Caerols et al., 2017), but less consistently than executive disorders. Memory deficits affect the visual and verbal dimensions of both episodic (Mota et al., 2013) and working memory (Carbia et al., 2017; Scaife & Duka, 2009). Chronic cannabis consumption can also lead to brain damage, especially in hippocampal (Yücel et al., 2016) and prefrontal regions (Shollenbarger et al., 2015), resulting in episodic memory impairment (Broyd et al., 2016; Petker et al., 2019; Wade et al., 2020) and executive deficits (Churchwell et al., 2010). According to these studies, using cannabis in addition to BD leads to potentially more severe cognitive consequences.

To sum up, the aforementioned studies describe common memory and executive impairments among BD and cannabis consumers. Although the cognitive deficits seem to be similar in nature, they appear to differ in severity, depending on which substance is used. Memory impairments are reported more than executive deficits in chronic cannabis users (Solowij et al., 2011), with the opposite pattern for BD (Carbia et al., 2018). Their combined use could therefore lead to memory and executive dysfunctions of the same severity, owing to an additive effect. Despite the frequency of alcohol and cannabis use among students, few studies have explored the additive effect of BD and cannabis use on neuropsychological deficits. To our knowledge, only two studies have so far been conducted among adolescents and young adults (Jacobus et al., 2015; Winward et al., 2014), and none with a sample made up solely of college students. Compared with young adults with a history of light and controlled substance use, poorer executive functioning and verbal episodic memory abilities have been observed in young BD and cannabis co-users. In Winward et al. (2014)'s study, BD and cannabis co-use was associated with the executive and episodic memory impairments found in single-substance users (BD or cannabis), but co-users also had specific working memory impairments that are not observed in single users. Overall, these two studies suggest that the consumption of both substances has an additive effect on neuropsychological deficits, and encourage further research to examine co-use in college students and identify the characteristics of those who exhibit the poorest neuropsychological performances. This knowledge is essential for designing appropriate prevention measures.

Thus, for the first time in college students, the present study aimed to (1) improve understanding of the additive effect of BD and cannabis use on neuropsychological functioning, and (2) describe the profiles of student users who are at the greatest risk of neuropsychological deficits. Based on the literature, we first expected to observe executive and episodic memory deficits in college students who engage in BD, whether they smoked cannabis or not. Second, we expected to observe an additive effect of BD and cannabis use in students, resulting in more severe memory and executive function impairments than in BD students who did not consume cannabis. Finally, we expected to find a gradient of severity of neuropsychological impairments among BD students, with those who consumed cannabis performing more poorly.

2. Material and methods

2.1. Procedure and participants

The present study was part of a larger research program exploring substance use among young adults which is still in progress (Alcohol and Drugs at Caen University, ADUC). Participants were 298 volunteer students in their first to fifth year of study at the University of Caen Normandy (see Fig. 1 for inclusion process). They were recruited up to the end of 2020 through an e-mail invitation, and came to the laboratory to fill in the questionnaires and undergo individual neuropsychological testing. All participants were aged 18–36 years, were native French speakers and did not have any medical history (i.e., no neurological, psychiatric, endocrine or infectious disease) that might have an impact on their cognitive functioning. Current anxiety and depression were assessed with the State-Trait Anxiety Inventory (STAI; Bergeron et al., 1976) and the Beck Depression Inventory (BDI; Beck et al., 1961). Tobacco dependence was assessed with the Fagerström Test for Nicotine Dependence (Svicher et al., 2018), and participants were asked to abstain for at least 12 h before undergoing the cognitive tests. They were split into three groups based on their consumption profiles: light drinkers (LD), binge drinkers (BD), and binge drinkers consuming cannabis (BDC; see Measures section for the procedure and a description of these groups).

2.2. Ethics

The data were gathered between 2017 and 2020. All participants were informed about the study, which was approved by the French Data Protection Authority (CNIL; no. u24-20171109-01R1), prior to their inclusion in the study and then provided their written informed consent.[2]

2.3. Measures

2.3.1. Sociodemographic variables

Age, sex, and native language were recorded. Participants differed on sex: there were more men in the BDC group than in either the LD or BD group (see Table 1).

2.3.2. Alcohol- and cannabis-related variables

Alcohol use was assessed with the French version of the *Alcohol Use Disorders Identification Test* (AUDIT; Gache et al., 2005). The AUDIT is a 10-item measure designed to screen for excessive alcohol use. A BD score was also calculated, according to Townshend and Duka's method (2002), by considering the speed at which alcohol units were consumed, the number of times the respondent had become drunk over the previous 6 months, and the percentage of times the respondent had become drunk when consuming alcohol. This score therefore considers consumption quantity and frequency. Repeated withdrawal from alcohol, an aspect that is missing from classic BD measures (see Maurage et al., 2020, for a review of different possible measures of BD), was also considered. Cannabis use was assessed using the *Cannabis Abuse Screening Test* (CAST; Legleye et al., 2011). Three groups of students were formed on the basis of these three measures. Students with an AUDIT score above 19 were excluded from the statistical analysis, to avoid a confounding effect of alcohol use disorder. The LD group contained students who had light and controlled alcohol use (i.e., AUDIT score below 6; Gache et al., 2005) and neither cannabis use nor BD (BD score below 16, and CAST score below 1; Legleye et al., 2011). The BD group engaged in BD (BD score above 24), but without consuming cannabis (CAST score below 1). The BDC group included BD students (BD score above 24) who also consumed cannabis (CAST score equal to or above 5).

[2] Despite there being no legal requirement to seek ethics committee approval for noninterventional research outside of biological and medical development in France, we followed the ethical standards set by the American Psychological Association Ethical Principles of Psychologists and Code of Conduct (APA, 2016) for the ethical treatment of human participants.

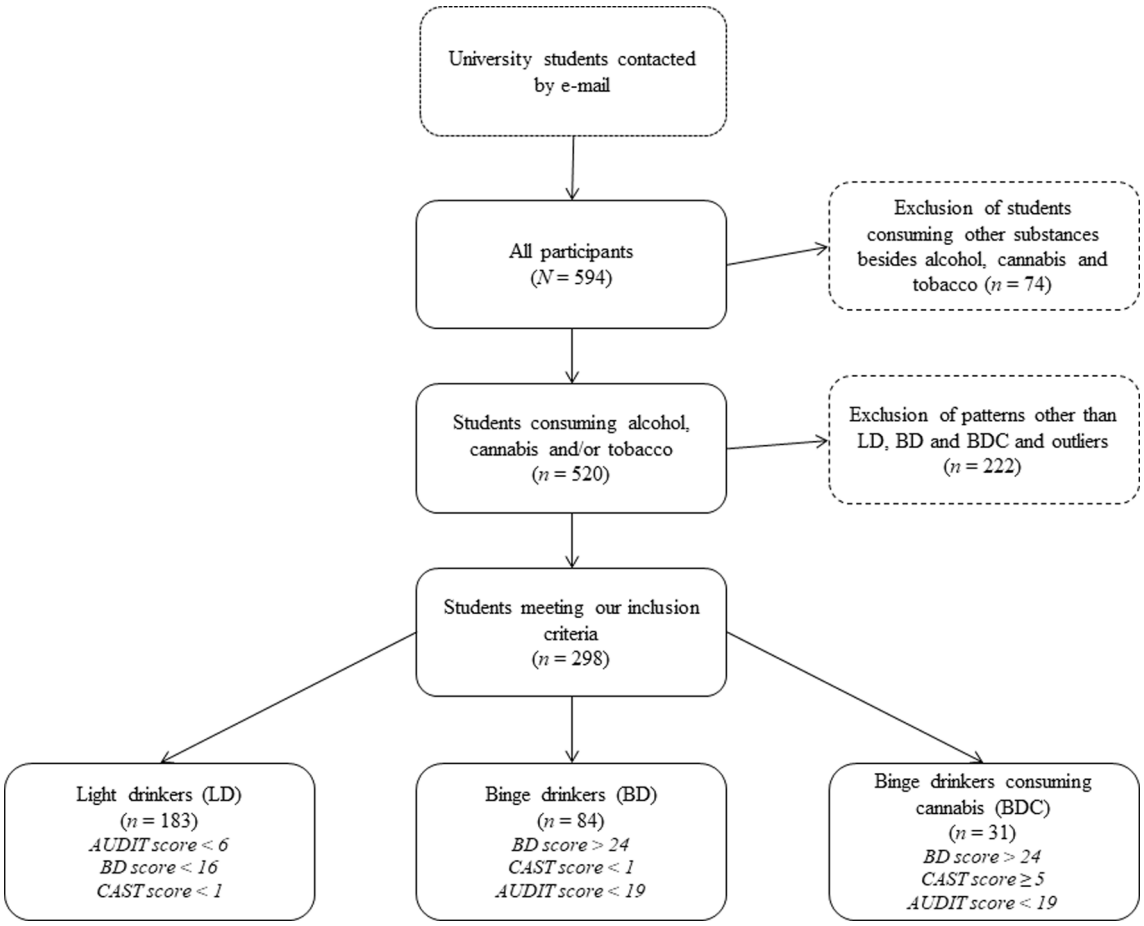

Fig. 1. Flowchart of recruitment process. *Note.* AUDIT: Alcohol Use Disorders Identification Test; BD: binge drinking; CAST: Cannabis Abuse Screening Test.

2.3.3. *Neuropsychological screening – BEARNI*

Neuropsychological impairments were assessed with the Brief Evaluation of Alcohol-Related Neuropsychological Impairments (BEARNI; Ritz et al., 2015). This test was specifically designed to screen for cognitive and motor deficits in patients with alcohol use disorders (i.e., deficits in episodic memory, working memory, executive functions, visuospatial abilities and ataxia). It contains five subtests: verbal episodic memory (maximum score: 6 points), alphabetical span, assessing verbal working memory (maximum score: 5 points), alternating verbal fluency, assessing flexibility abilities (maximum score: 6 points), five complex figures, assessing visuospatial abilities (maximum score: 5 points), and ataxia, assessing balance (maximum score: 8 points). The BEARNI yields six scores: five subscores and a total score (maximum score: 30 points). The BEARNI is a screening tool that facilitates referral for a more detailed neuropsychological assessment. As low drinking does not lead to neuropsychological deficits, participants in the LD group with moderate impairments (cut-off score $\leq$ 17; Ritz et al., 2015) were excluded from the statistical analysis.

2.4. *Data analysis*

First, participants' raw BEARNI scores were transformed into *z* scores. A *z* score was computed for each BEARNI subtest, based on the mean and standard deviation of the LD group (i.e., mean scale scores of zero and standard deviations of one).

Second, we calculated a linear mixed model, with BEARNI subtest *z* score as a within-participants variable, group as between-participants variable, and participant as a random component. Sex (coded female = -0.5, male = 0.5), age, Fagerström score, and BD score were included as covariates, to control for their effects. Including these covariates allowed for a more precise assessment of the effects of our variable of interest on the BEARNI test, by providing estimated means of BEARNI subtests across the three groups, with the covariate effects in the model kept constant. To compare neuropsychological profiles between groups, we used the contrast method recommended by Cohen et al. (2013). More specifically, we use two Helmert contrasts to test our hypotheses. The first contrast (C1) compared the LD group with the set of binge drinkers (i.e., BD and BDC groups), thereby allowing us to test the overall effect of substance use on neuropsychological impairments (LD > BD and BDC). The second contrast (C2) compared the BD group with the BDC group, allowing us to assess the additive effect of BD and cannabis use on neuropsychological impairments (BD > BDC). Regarding the hypotheses set out in the Introduction, we expected the LD group to perform better than both BD and BDC, with no difference between BD and BDC on executive functioning (i.e., statistical significance for C1, but not for C2). As for memory, we expected LD to perform better than both BD and BDC, and BD to perform better than BDC (i.e., statistical significance for both C1 and C2).

Finally, we further explored the heterogeneity of the users' profiles by carrying out two analyses on the BD set (BD and BDC). First, to examine the hypothesis of the additive effect in greater depth, we explored the distribution of the two groups' executive and memory scores. Second, we performed a k-means clustering analysis including the BEARNI subscores. This revealed greater impairment in BDC than in BD. The algorithm was constrained to separate the users into two groups, and we assumed that one contained the less impaired profiles, and the other contained the more impaired profiles. This analysis allowed us to identify BD and BDC participants who were more or less cognitively impacted (chi2 analysis), and to pinpoint their specific characteristics (Student *t* tests) regarding alcohol (i.e., alcohol onset,

Table 1
Demographic, consumption, and psychological variables of the three groups of participants.

Group	LD ($n = 183$)	BD ($n = 84$)	BDC ($n = 31$)	p value	Comparisons (post hoc tests)
Variables					
Sex ratio (men/women)	45/138	22/62	20/11	< 0.001[1]	
Age (in years)	21.57 ± 3.39	20.51 ± 1.93	21.19 ± 2.21	0.180	
Range	18–36	18–26	18–27		
Alcohol onset (age)	15.98 ± 1.91	15.29 ± 1.55	14.61 ± 1.36	< 0.001[2]	LD = BD; LD > BDC; BD = BDC
Range	5–22	11–19	12–18		
Cannabis onset (age)	18.40 ± 2.27	16.25 ± 1.58	15.74 ± 1.29	< 0.001[2]	LD = BD; LD > BDC; BD = BDC
Range	15–22	14–18	14–19		
AUDIT score	3.06 ± 1.20	10.33 ± 4.26	11.58 ± 3.37	< 0.001[2]	LD < BD; LD < BDC; BD = BDC
Range	0–5	2–19	4–18		
Binge drinking score	7.34 ± 3.83	36.16 ± 12.89	48.70 ± 23.44	< 0.001[2]	LD < BD < BDC
Range	1.33–15.50	24.50–107.33	24.50–118		
CAST score	0 ± 0	0 ± 0	11.93 ± 5.19	< 0.001[2]	
Range			5–20		
Fagerström score	0.73 ± 1.48	0.57 ± 1.14	11.93 ± 5.19	< 0.001[2]	LD = BD; LD < BDC; BD < BDC
Range	0–8	0–5	5–20		
BDI score	4.46 ± 4.10	4.68 ± 4.65	6.19 ± 5.70	0.009[2]	LD = BD; LD < BDC; BD < BDC
Range	0–28	0–23	0–18		
STAI-A score	33.72 ± 11.05	32.47 ± 11.85	34.35 ± 14.71	> 0.05[2]	
Range	20–75	20–73	20–77		
STAI-B score	42.32 ± 10.53	44.09 ± 10.27	44.71 ± 13.17	0.015[2]	LD = BD; LD < BDC; BD = BDC
Range	20–67	24–75	23–79		

Note. Data are shown as mean ± standard deviation.
LD: light drinkers; BD: binge drinkers; BDC: binge drinkers using cannabis; BEARNI: Brief Evaluation of Alcohol-Related Neuropsychological Impairments; AUDIT: Alcohol Use Disorders Identification Test; CAST: Cannabis Abuse Screening Test; BDI: Beck Depression Inventory; STAI-A: State–Trait Anxiety Inventory, state score; STAI-B: State–Trait Anxiety Inventory, trait score.
[1] chi[2]; proportion of men was higher in BDC group than in LD and BD groups

[2] ANCOVA with sex and age as covariates. Holm test was used as post hoc.

frequency of consumption per week, and drinks consumed per week), tobacco (i.e., tobacco onset, duration of dependence, and Fagerström score), and cannabis (i.e., cannabis onset, frequency of consumption per week, grams of cannabis consumed, and money spent per week) consumption patterns, as well as anxiety (i.e., STAI A and B scores) and depression (i.e., BDI score). The purpose of these analyses was thus to identify at-risk consumer profiles.

3. Results

3.1. Linear mixed model analysis of BEARNI z scores in the three groups of students

The results of the linear mixed model on adjusted BEARNI *z* scores (with sex, age, and BD and Fagerström scores as covariates) are set out in Table 2.

The linear mixed model revealed significant main effects of the first and second contrasts ($p < .001$). Results indicated that the BD set (BD and BDC) had poorer overall neuropsychological performances on the BEARNI test than the LD group, with poorer overall performances for the BDC group than for the BD group. Regarding the covariates, there were no significant effects of sex ($p = .48$), age ($p = .91$), or Fagerström score ($p = .66$), but a significant effect of the BD score ($B = 0.007$, 95% CI [0.002, 0.013], $p = .012$). We analyzed the effects of the two contrasts on each of the five BEARNI subscores. The first contrast was significant for all five subscores, indicating that the BD set (BD and BDC) had poorer neuropsychological performances than the LD group. The second contrast was significant for the episodic memory subscore ($p < .001$), as well as for the working memory ($p = .041$) and flexibility ($p < .001$) subscores, indicating that the BDC group performed more poorly than the BD group. No significant differences were found between the BD and BDC groups on the visuospatial ($p = .18$) and ataxia ($p = .13$) subscores. These results are reported in Fig. 2.

Table 2
Adjusted *z* scores of BEARNI subtest performances across the three groups.

BEARNI scores	LD group ($n = 183$)	BD group ($n = 84$)	BDC group ($n = 31$)	Contrast 1 (LD > BD, BDC) statistics	Contrast 2 (BD > BDC) statistics
Total score	0.08 ± 0.05	−0.19 ± 0.08	−0.75 ± 0.14	$B = 0.56$, $p < .001$*	$B = 0.55$, $p < .001$*
Confidence interval	[-0.03, 0.19]	[-0.35, −0.04)]	[-1.02, −0.48)]	[0.30, 0.81]	[0.32, 0.83]
Episodic memory	0.07 ± 0.08	−0.11 ± 0.12	−0.93 ± 0.21	$B = 0.59$, $p < .001$*	$B = 0.82$, $p < .001$*
Confidence interval	[-0.10, 0.24]	[-0.36, 0.13]	[-1.35, −0.51]	[0.25, 0.93]	[0.37, 1.27]
Working memory	0.08 ± 0.08	−0.15 ± 0.12	−0.62 ± 0.21	$B = 0.47$, $p = .006$*	$B = 0.47$, $p = .041$*
Confidence interval	[-0.08, 0.25]	[-0.40, 0.10]	[-1.04, −0.21]	[0.13, 0.81]	[0.02, 0.92]
Flexibility	0.09 ± 0.09	−0.33 ± 0.12	−0.85 ± 0.21	$B = 0.53$, $p = .002$*	$B = 0.82$, $p < .001$*
Confidence interval	[-0.08, 0.26]	[-0.28, 0.21]	[-1.27, −0.44]	[0.19, 0.87]	[0.37, 1.27]
Visuospatial abilities	0.09 ± 0.08	−0.19 ± 0.12	−0.50 ± 0.21	$B = 0.44$, $p = .012$*	$B = 0.31$, $p = .18$
Confidence interval	[-0.08, 0.26]	[-0.44, 0.05]	[-0.92, −0.08]	[0.09, 0.78]	[-0.14, 0.76]
Ataxia	0.09 ± 0.08	−0.49 ± 0.12	−0.84 ± 0.21	$B = 0.76$, $p < .001$*	$B = 0.35$, $p = .126$
Confidence interval	[-0.08, 0.26]	[-0.74, −0.24)]	[-1.26, −0.43)]	[0.42, 1.10]	[-0.10, 0.80]

Note. Data are shown as mean ± standard deviation.
The confidence interval was set at 95%.
* indicates statistical significance.
LD: light drinkers; BD: binge drinkers; BDC: binge drinkers using cannabis; BEARNI: Brief Evaluation of Alcohol-Related Neuropsychological Impairments.

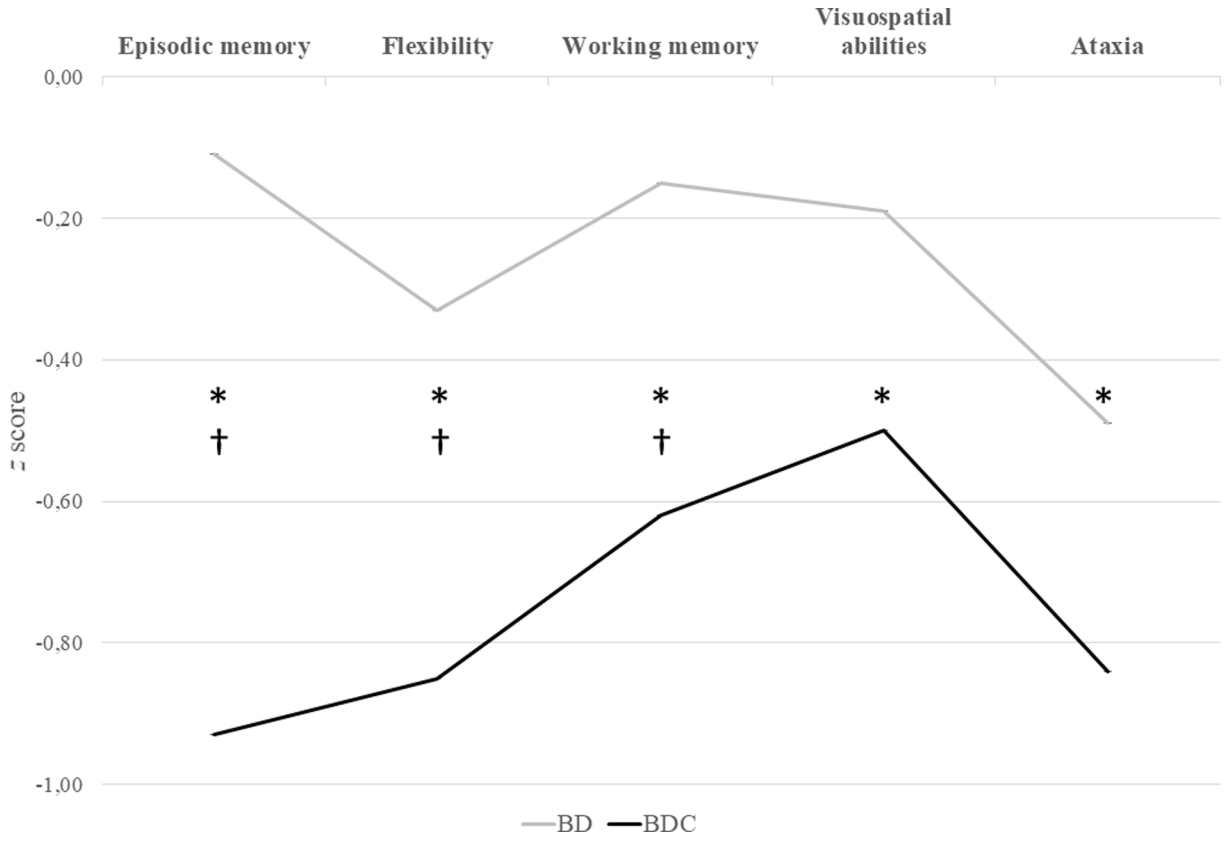

Fig. 2. BEARNI subscores of BD and BDC groups. *Note.* Results of significant Group × Subtest interaction in linear mixed model. Data are shown as mean *z* scores. *Significant Contrast 1 (difference between LD group and BD and BDC groups; $p_s < 0.012$). † Significant Contrast 2 (difference between BD and BDC; $p_s < 0.041$). BEARNI: Brief Evaluation of Alcohol-Related Neuropsychological Impairments; LD: light drinkers; BD: binge drinkers; BDC: binge drinkers consuming cannabis.

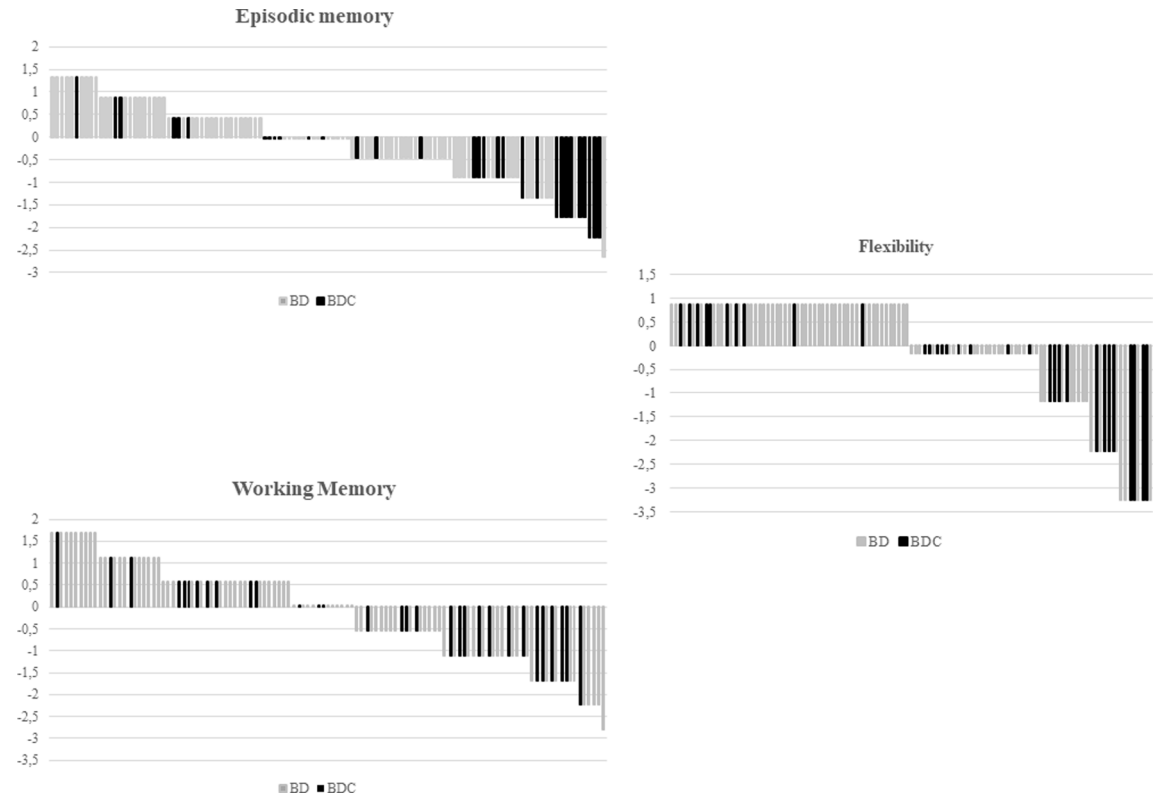

Fig. 3. Distribution of individual performances on BEARNI flexibility, working memory and episodic memory subtests of binge drinkers (BD) and binge drinkers consuming cannabis (BDC). *Note.* BD performances are shown in light gray and BDC performances in black.

3.2. Analyses of individual BD and BC students' episodic and working memory and flexibility scores

We ran individual analyses to examine whether scores indicated a gradient of severity. We predicted that the BDC group would have more severe cognitive impairments than the BD group. Performances of BD and BDC participants on the BEARNI flexibility and episodic and working memory subtests were heterogeneous (see Fig. 3). Results showed a gradient of severity, specifically for the episodic memory subtest. Most BD participants had better scores than BDC, who performed more poorly, but the expected gradient was not found for working memory and flexibility subtests. The separation was not linear: BD and BDC overlapped on both the lowest and highest scores. A few BD participants performed more poorly than other BD, and some of the BDC had preserved performances when others had more severe impairments. This outcome encouraged us to go further to understand the factors that could explain the heterogeneity of cognitive performances found here.

3.3. Cluster analysis on the neuropsychological deficits screened with the BEARNI test among BD and BDC students

We performed a k-means clustering analysis on the BEARNI flexibility, episodic memory and working memory subscores, as these were lower in BDC than in BD (Table 3). Cluster 1 encompassed 23.48% of the sample, while Cluster 2 represented 76.52%, with a larger proportion of BD students in Cluster 2 ($n_{BD} = 72$; $n_{BDC} = 16$) than in Cluster 1 ($n_{BD} = 12$; $n_{BDC} = 15$). Cluster 2 contained participants with the highest BEARNI subscores, whereas Cluster 1 contained those with the lowest subscores (see Table 3). Moreover, Cluster 1 was characterized by higher Fagerström and STAI-B scores than Cluster 2 was. Regarding cannabis use, the analysis was only conducted in the BDC group, and results showed a trend toward significance, with participants in Cluster 1 ($M = 5.93$, $SD = 1.79$) consuming more cannabis per week than those in Cluster 2 ($M = 4.37$, $SD = 2.44$), $t_{(29)} = 2.01$, $p = .054$, $d = 0.72$. A supplementary table describing the BD and BDC subgroups in each cluster is available.

Table 3
K-means clustering analysis of BEARNI flexibility, episodic memory, and working memory subscores in BD set (BD and BDC).

Variables	Cluster 1 ($n = 27$)	Cluster 2 ($n = 88$)	Statistics
BEARNI episodic memory score Range	−1 ± 0.95 −2.66–1.32	0.09 ± 0.77 −1.78–1.32	$t_{(113)} = -6.11$ $p < .001$*, $d = -1.34$
BEARNI working memory score Range	−0.86 ± 0.75 −2.23–0.57	0.11 ± 1.11 −2.79–1.70	$t_{(113)} = -4.27$ $p < .001$*, $d = -0.94$
BEARNI flexibility score Range	−1.79 ± 1.19 −3.25 to −0.15	0.43 ± 0.68 −2.22–0.88	$t_{(113)} = -12.29$ $p < .001$*, $d = -2.70$
Duration of tobacco use (in years) Range	6.07 ± 2.80 0–11	5.25 ± 2.07 1–9	$t_{(70)} = 1.36$ $p = .17$, $d = 0.36$
Fagerström score Range	2.32 ± 2.19 0–6	1 ± 1.66 0–7	$t_{(88)} = 2.99$ $p = .004$*, $d = 0.73$
Alcohol onset Range	15.22 ± 1.55 12–18	15.08 ± 1.53 11–19	$t_{(113)} = 0.42$ $p = .67$, $d = 0.09$
Number of alcoholic drinks per week Range	7.04 ± 8.68 0–30	7.26 ± 7.04 0–40	$t_{(113)} = -0.14$ $p = .89$, $d = -0.03$
Number of days of alcohol use per week Range	2.38 ± 1.79 0–7	2.14 ± 1.16 0–7	$t_{(110)} = 0.80$ $p = .42$, $d = 0.18$
STAI-A score Range	36.29 ± 14.17 21–70	31.95 ± 12.05 20–77	$t_{(112)} = 1.57$ $p = .12$, $d = 0.34$
STAI-B score Range	48.33 ± 9.96 27–70	43.01 ± 11.14 23–79	$t_{(113)} = 2.22$ $p = .028$*, $d = 0.49$
BDI score Range	5.81 ± 5.54 0–23	4.86 ± 4.80 0–22	$t_{(113)} = 0.87$ $p = .39$, $d = 0.19$

Note. Data are shown as mean ± standard deviation.
Cluster 1 contained the poorest BEARNI performances and Cluster 2 the best.
The confidence interval was set at 95%.
* indicates statistical significance
BD: binge drinkers; BDC: binge drinkers using cannabis; BEARNI: Brief Evaluation of Alcohol-Related Neuropsychological Impairments; BDI: Beck Depression Inventory; STAI-A: State–Trait Anxiety Inventory, state score; STAI-B: State–Trait Anxiety Inventory, trait score.

4. Discussion

This was the first study to seek to (1) improve understanding of the additive effect of college students' BD and cannabis use on their neuropsychological functioning, and (2) describe the profiles of student users who are most at risk of neuropsychological deficits. Results showed that college students who engaged in binge drinking behavior with (BDC) or without (BD) cannabis use performed consistently more poorly than LD on all the cognitive domains we assessed (episodic memory, working memory, flexibility, visuospatial abilities, and ataxia). An additive effect of BD and cannabis use was specifically observed on flexibility, episodic memory and working memory, when BD and BDC groups were contrasted. Individual analyses revealed heterogeneous gradients of cognitive impairment severity between BD and BDC. Finally, cluster analyses highlighted more severe neuropsychological deficits in users who frequently consumed tobacco and who had a high level of anxiety.

The present study revealed negative effects of combined alcohol and cannabis use on episodic memory, executive functions, visuospatial skills, ataxia, and working memory in college students. With the exception of ataxia, this observation was in accordance with previous studies conducted among adolescents and young adults identified as BD (Mota et al., 2013; Sneider et al., 2013) or cannabis users (Fried et al., 2005). Ataxia is not usually described in BD, but is regularly reported in alcohol use disorder (Fitzpatrick et al., 2012) and cannabis use (Moreno-Rius, 2019). We hypothesized that BD combined with cannabis use results in more severe memory and flexibility impairments, and results confirmed that BDC students did indeed have greater episodic memory, flexibility and working memory deficits than BD students. As shown in Winward et al. (2014)'s study, combine use seemed to have a negative effect on working memory. However, contrary to their observations, we also found impaired working memory in BD without cannabis use. Flexibility and working memory abilities rely on the prefrontal cortex and cerebellum, which are rich in cannabinoid receptors, thus making them very sensitive to the neurotoxic effects of cannabis (Quickfall & Crockford, 2006). Although other studies conducted in BD have not always clearly reported executive impairments encompassing flexibility and working memory abilities (Gil-Hernandez & Garcia-Moreno, 2016; Vinader-Caerols et al., 2017), cannabis use seems to heighten the negative effect of BD on executive functions. Moreover, the deleterious additive effect on episodic memory in the BDC group is consistent with the literature on chronic cannabis users (Solowij et al., 2011), as well as with our hypothesis. This specific additive effect could be due to the peculiar neurotoxic effects of cannabis on the hippocampus (Lorenzetti et al., 2016; Yücel et al., 2016). The hippocampus is a node of the brain network responsible for episodic memory abilities (Papez circuit; Markowitsch, 1997), and is rich in cannabinoid receptors (Lorenzetti et al., 2016). An additive effect on episodic memory could interfere with scores on flexibility and working memory subtests, as these are not purely executive tasks, but also rely on memory abilities. Further examination is needed, using executive tasks that do not involve memory, in order to disentangle the impact of these results.

This study also deepened our understanding of the specific BDC neuropsychological profile in college students. Individual score analyses showed a gradient of severity, with a larger proportion of BDC students

having poorer episodic memory performances than BD, despite greater heterogeneity than expected. Even among young students, this pattern indicates that adding cannabis consumption to BD mostly affects memory abilities. Together, these two products have an even more harmful effect on the developing brain than BD without cannabis (Terry-McElrath & Patrick, 2018). We expected this gradient of severity to be particularly marked for the working memory subtest, on which BDC performed more poorly overall than single-substance users, as reported by Winward et al. (2014). Surprisingly, the gradient was more mixed and nonlinear for working memory and flexibility, but these subscores still indicated an additive effect of BD and cannabis use. These results point to a significant additive effect of cannabis when consumed with BD, although this does not necessarily lead to new additional impairments. Nevertheless, the present study highlighted heterogeneity, with some BD students having unexpectedly poor performances, and some BDC students having preserved performances. This prompted us to focus on variables that might help us identify the clinical profile of BD college students who are most at risk of developing neuropsychological impairment. Whether they used cannabis or not, results showed that students who had the lowest executive and memory scores were more addicted to tobacco and had higher trait anxiety. An association with tobacco use has been shown to be prevalent in both BD and cannabis users (Goodwin et al., 2018; Gubner et al., 2016). In another context, chronic tobacco smoking was found to be related to neuropsychological impairment, notably for memory and flexibility (Conti et al., 2019). Like tobacco, anxiety can represent a risk factor for neuropsychological impairments, above all by affecting executive functioning (Shields et al., 2016). In the present study, college students who exhibited cognitive impairments tended to be more anxious. Students used alcohol to cope, especially those with higher levels of anxiety (Lechner et al., 2020). The relationship between BD, cannabis use, and anxiety remains unclear, especially in college students (Nourse et al., 2017; Shalit & Lev-Ran, 2020). Tobacco and a high anxiety level, added to BD and/or cannabis use, may worsen the cognitive impairments highlighted in our study, as they seem to impair the same cognitive areas. Although the nature of our study did not allow us to establish any causal relationship between these variables, our results do suggest that they should be taken into account in prevention. The circularity of the possible risk factors for developing cognitive impairments between substance use, anxiety, and substance use to cope with anxiety is alarming, especially so regarding the current health context. With the SARS-CoV-2 pandemic, students have had to contend with high levels of anxiety (Essadek & Rabeyron, 2020). Regardless of context, these findings highlight the importance of prevention, so that students can be identified and psychologically supported at an early stage-even before they indulge in BD or substance use, or develop anxiety. Complementary analyses suggested that students with neuropsychological impairments spent more money on cannabis than those with preserved performance (data not shown). Even if this result has yet to be properly analyzed, it highlights the problem of how to measure cannabis intake. Unlike alcohol, with its standard drink units, cannabis lacks a precise measure that would reflect the actual amount consumed, and this issue needs to be further explored.

One limitation of this study is that some patterns of students' consumption were not represented in our sample, and consumption was self-reported. We chose to divide participants into three groups, based on available data, in order to examine the impact of co-occurring BD and cannabis use on neuropsychological profiles. However, the study sample did not encompass students who consumed cannabis without BD, as this profile is scarce in college students, and was particularly lacking in our sample. Future studies will therefore have to be conducted among cannabis users without BD to further focus on the aggravating effects of combined BD and cannabis use. Moreover, the three groups in our sample differed in size, which may have influenced statistical power and Type I errors. Furthermore, the neuropsychological assessment we used in this study was a screening test (BEARNI; Ritz et al., 2015) with multicomponent tasks that rely on executive and memory abilities. This tool was designed to screen alcohol-related neuropsychological impairments and was not initially intended to assess cannabis consumption. However, the fact that alcohol and cannabis share the same cognitive impairment spectrum encouraged researchers to extend its use. The present study nonetheless represents a first step in understanding the neuropsychological consequences of BD and cannabis co-use. Further research is required to perform more detailed and extended neuropsychological assessments to overcome the above-mentioned limitations. This could be the opportunity to adapt the BEARNI's cut-offs and psychometrics to educated young people.

5. Conclusions

The assessment of neuropsychological impairment among college students engaging in BD associated with cannabis use demonstrated that these two practices have an additive effect, especially for memory and executive impairments. They seem to have specific harmful effects on students' cognition and consumption patterns. As BD and cannabis co-use can lead to cognitive impairments, it may partly explain the reduced academic success reported in the literature (Páramo et al., 2020). Clinical practice could greatly benefit from this information, as it emphasizes the need to better characterize the different consumption and psychological profiles, especially in young students. As we know that neuropsychological impairments can hinder the motivation to quit or reduce consumption (Le Berre et al., 2012) and may also diminish the efficiency of prevention protocols, asking BD if they also use cannabis could be highly beneficial in clinical practice, for both prevention and research. Furthermore, it could allow prevention and care strategies to be adapted to each person's neuropsychological profile. This study suggests that future prevention programs should take memory and executive impairments into account, as well as consumption profiles and anxiety levels, in order to improve the impact and efficiency of these programs in college students.

CRediT authorship contribution statement

Simon Deniel: Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Maxime Mauduy:** Formal analysis, Data curation, Writing - review & editing, Visualization. **Caroline Cheam-Bernière:** Investigation, Resources, Data curation, Writing - review & editing, Visualization. **Nicolas Mauny:** Investigation, Resources, Data curation, Writing - review & editing, Visualization. **Charlotte Montcharmont:** Investigation, Resources, Data curation, Visualization. **Nicolas Cabé:** Conceptualization, Methodology, Resources, Writing - review & editing. **Anaëlle Bazire:** Methodology, Investigation, Resources. **Jessica Mange:** Conceptualization, Methodology, Formal analysis, Resources, Writing - review & editing, Visualization, Supervision. **Anne-Pascale Le Berre:** Methodology, Writing - review & editing. **Denis Jacquet:** Resources, Writing - review & editing. **Virginie Bagneux:** Conceptualization, Methodology, Writing - review & editing. **Pascale Leconte:** Investigation, Writing - review & editing. **Ludivine Ritz:** Conceptualization, Methodology, Formal analysis, Resources, Data curation, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition. **Hélène Beaunieux:** Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

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Declaration of interest

The authors declare no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.abrep.2021.100362.

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