



Binge drinking trajectory and neuropsychological functioning among university students: A longitudinal study



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ABSTRACT

Background: Adolescence is a time of considerable neurodevelopment. Binge drinking (BD) during this period increases the vulnerability to its neurotoxic effects. This longitudinal study aimed to investigate the relationship between BD trajectory over university years and neuropsychological functioning.

Methods: Cohort-study. Two-year follow-up. A total of 89 university students were assessed: 40 Non-BD (at Initial and Follow-up), 16 Ex-BD (BD at Initial but not at Follow-up) and 33 BD (at both times). Neuropsychological assessment of working memory, episodic memory and executive abilities was carried out during their first (Initial) and third (Follow-up) academic year at the University of Santiago de Compostela.

Results: BD subjects performed less well on the Wechsler Memory Scale-III (WMS-III) Logical Memory Subtest (immediate theme recall, $P = .034$; delayed theme recall, $P = .037$; and percent retention, $P = .035$) and committed more perseverative errors on the Self-Ordered Pointing Task (SOPT) ($P = .021$) than Non-BD. There were no differences between Ex-BD and Non-BD.

Conclusions: Binge drinking trajectory during adolescence is associated with neuropsychological performance. Persistent BD, but not Ex-BD, is associated with verbal memory and monitoring difficulties. This is compatible with the hypothesis that heavy alcohol use during adolescence may affect cognitive functions that rely on the temporomesial and dorsolateral prefrontal cortex.

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1. Introduction

Alcohol is the main risk factor for incident disability-adjusted life years (i.e., lost years of healthy life) in young people aged 10–24 years worldwide (Gore et al., 2011). Special attention has been given to binge drinking (BD), which is a prevalent pattern of alcohol consumption in many European countries (Hibell et al., 2009). BD is characterized by the intake of large amounts of alcohol in a short and irregular period of time (e.g., only on some days of the week).

The socio-sanitary relevance of the adverse consequences of BD (Mota et al., 2010; Okoro et al., 2004; World Health Organization, 2000) is highlighted by the evidence of an important degree of neural development during adolescence. Animal and human studies

indicate non-linear decreases in grey matter, which are more marked in frontal regions (Giedd et al., 2009; Sowell et al., 1999; Whitford et al., 2007). Besides, synaptic and cellular changes take place in the hippocampus and prefrontal cortex during late adolescence and continue until adulthood (Kornack and Rakic, 1999; Petanjek et al., 2011). These transformations involve development and strengthening of neural circuits, which are accompanied by improvements in neurocognitive functions related to these areas, such as episodic declarative memory (Anderson and Lajoie, 1996; Sowell et al., 2001), working memory (Conklin et al., 2007; Luciana et al., 2005; Silveri et al., 2004) and executive abilities (Luciana and Nelson, 2002; Welsh et al., 1991).

Binge drinking during adolescence appears to interact with neural development in a way that increases the vulnerability to its neurotoxic effects. Structural abnormalities in prefrontal and mesolimbic areas have been observed in binge drinking animal models (Crews et al., 2000; Taffe et al., 2010). Also, human clinical studies have reported hippocampal and prefrontal abnormalities in

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adolescents with alcohol use disorder (AUD; De Bellis et al., 2000, 2005; Medina et al., 2007, 2008).

Binge drinking is prevalent among students (Wicki et al., 2010) and structural and functional differences (in cerebral activation patterns and in psychophysiological responses to cognitive tasks) between binge drinkers and abstainers or light drinkers have been reported (Ehlers et al., 2007; Crego et al., 2009, 2010; Courtney and Polich, 2010; Maurage et al., 2009; Schweinsburg et al., 2010; Squeglia et al., 2012). These differences are in line with those reported on neuropsychological functioning. Several studies have showed poorer performance among BD students on neuropsychological tasks assessing inhibitory control, cognitive interference, sustained attention, verbal working memory and episodic declarative memory (García-Moreno et al., 2008; Goudriaan et al., 2007; Hartley et al., 2004; Heffernan et al., 2010; Johnson et al., 2008), functions known to be supported by prefrontal and/or hippocampal regions. Consistently, we have recently reported that BD results in poorer performance in neuropsychological tests assessing both verbal declarative memory (i.e., immediate and delayed recall) (Parada et al., 2011) and executive aspects of working memory (Parada et al., 2012), processes known to depend on the integrity of the hippocampus and dorsolateral prefrontal cortex, respectively.

However, despite the fact that adolescent binge drinkers show neurocognitive difficulties in population-based cross-sectional studies, little is known about the evolution of these difficulties in relation to their binge drinking trajectories. A ten-year follow-up study with AUD adolescents has shown that persistent heavy use of alcohol from adolescence to young adulthood is associated with poorer verbal memory over time (Hanson et al., 2011). These authors also suggest that, whereas early abstinence improves the performance at similar levels as healthy youths, heavy alcohol use during certain neurodevelopmental stages may lead to persistent difficulties. Similarly, recovery of neuropsychological functioning in chronic alcoholics seems related to both age and length of abstinence (Rourke and Grant, 2009). Unlike data from clinical studies, so far there is no evidence, to the best of our knowledge, on the effects of the binge drinking trajectory on neuropsychological functioning in general adolescent population. Longitudinal studies providing repeated observations at individual level of both alcohol consumption and neuropsychological performance are more suitable to elucidate causal-relationships, that is, whether neuropsychological deficits represent a consequence of heavy episodic drinking during adolescence.

Considering that prefrontal and hippocampal brain regions continue to develop until adulthood, and both are especially vulnerable to alcohol effects, as shown in clinical and animal studies, we carried out a longitudinal study to investigate the relationship between BD trajectory over a 2-year time period and neuropsychological performance in tests sensitive to temporomesial and prefrontal functioning among university students who began their alcohol consumption pattern during adolescence. This study extends on previous work and allows us to test the following hypotheses: (i) participants with a persistent binge drinking trajectory would show poorer performance in neuropsychological tests related to prefrontal and temporomesial functioning, such as working memory and declarative memory tasks, than participants who left their pattern of consumption and than non-binge drinkers; and (ii) participants who left the binge drinking pattern would improve their performance on these tasks from the initial to the follow-up assessment, to the level of the non-binge drinkers.

2. Methods

2.1. Participants

Participants were part of a longitudinal research project about the epidemiology and neurocognitive effects of binge drinking among university students conducted

at the University of Santiago de Compostela (Caamaño-Isoña et al., 2008). The neuropsychological assessment of students was performed during their first (Initial) and third (Follow-up) academic year of attendance at the University of Santiago de Compostela. At the Initial assessment time, first-year university students were screened by means of an anonymous and confidential questionnaire that they completed in class (see Section 2.2 for details). The classification criteria were based on their responses to the third question of the Alcohol Use Disorders Identification Test (AUDIT) (How often do you have six or more drinks on a single occasion? Never/Less than monthly/Monthly/Weekly/Daily or almost daily) and to one question related to the speed of consumption (drinks per hour). Subjects were classified as binge drinkers if they reported drinking six or more alcoholic drinks on the same occasion weekly, or monthly and during these episodes drank at least three drinks per hour. They were classified as controls (Non-BD) if they reported drinking six alcoholic drinks on the same occasion never, or less than monthly and at a maximum speed of consumption of two drinks per hour. Taking into account that, in Spain, a standard alcoholic drink is equivalent to 10 g of alcohol, six drinks consumed at a speed of more than two drinks per hour brings blood alcohol concentration (BAC) to 0.08 g percent or above. Once classified as a function of BD, participants were interviewed to obtain information about their clinical and sociodemographic status. To reduce the potential confusion of other factors, the following exclusion criteria were considered: personal history of neurological disorders (including loss of consciousness for at least 20 min); history of diagnosis or current psychopathological diseases (DSM-IV-TR Axis I and II; American Psychiatric Association, 2000); current psychopathological symptoms as assessed by the Symptom Checklist-90-R (SCL-90-R; Degoratis, 1983); regular consumption of other drugs (opiates, hallucinogens, cocaine, amphetamine compounds or medically prescribed psychoactive substances), except nicotine and cannabis; alcohol use disorders; severe non-corrected motor or sensory deficits; family history of major mental disorder and history of alcoholism in first- and second-degree relatives. Moreover, an AUDIT score of 20 or over was adopted as a cut-off for identifying possible alcohol abuse or dependence (Babor et al., 2001).

Participants who did not fulfil exclusion criteria were invited to undertake a neurocognitive assessment. Participants were required to not take alcohol or any other drug the day of the assessment, and to attend rested and on good health condition. Two years later, participants were contacted again for a follow-up interview and neuropsychological assessment. The same exclusion criteria were considered. The average time elapsed was 22.01 ± 2.1 months. Ninety-four subjects of the one hundred forty-three assessed in the initial phase (66%) agreed to carry out the follow-up interview. Experimental mortality did not alter the sample representation. According to ANOVAs and chi-square tests, the characteristics of the total sample and follow-up sample at Initial assessment are not significantly different on sex, age, SCL-90-R scores and aspects related to alcohol consumption pattern (AUDIT total score, frequency of six drinks/occasion, drinks per hour, percentage of drunkenness, age of onset of alcohol consumption and cannabis occasional use).

At Follow-up, subjects were reclassified according to their trajectory of alcohol use. Those who reported a binge drinking pattern of consumption at both times (Initial and Follow-up) were considered BD. Those who were classified as binge drinkers at the Initial assessment but not at Follow-up were characterized as Ex-BD. Those who did not report a binge drinking pattern of alcohol consumption were classified as Non-BD. Two subjects were excluded at Follow-up interview because they met exclusion criteria and one subject did not complete the assessment. Besides, for sample consistency, three Non-BD participants at the Initial assessment who reported a binge drinking pattern at Follow-up were excluded from the analysis. Finally, 89 participants were included in the analysis: 40 Non-BD, 16 Ex-BD and 33 BD.

Neuropsychological assessments were performed by psychologists specialized in neuropsychology. All participants gave written informed consent and received monetary compensation for their participation (15€ at the Initial assessment and 30€ at Follow-up). The research was performed in accordance with the ethical principles for research involving human subjects outlined in the Helsinki Declaration, European Council Agreements and Spanish Bioethics Legislation.

2.2. Measures

2.2.1. Sociodemographic and clinical data. Sociodemographic, academic and substance use data were collected through a questionnaire and the Alcohol Use Disorders Identification Test (Babor et al., 2001). The AUDIT is a brief written screening method developed by the World Health Organization (WHO) to identify current harmful and hazardous drinking that has demonstrated reasonable psychometric properties in college students (Kokotailo et al., 2004). The Galician version of the AUDIT (Varela et al., 2005) was used to assess the frequency of binge drinking.

Personal and family history of alcohol use disorder and psychopathological or medical diseases information was collected through a semi-structured interview that included a translated and adapted version of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), Individual Assessment Module (IAM) and Family History Assessment Module (FHAM), designed by the Collaborative Study on the Genetics of Alcoholism (COGA; Bucholz et al., 1994), and the Symptom Checklist-90-R (Degoratis, 1983). The SCL-90-R evaluates a broad range of symptoms of psychopathology and provides a global index of psychological distress.

2.2.2. Neuropsychological battery. Neuropsychological assessment of episodic memory and executive functions included the following tests:

- (a) Verbal and visual episodic memory were assessed by measuring: trials I–V total, immediate recall (trial VI), and delayed recall (trial VII) of Rey Auditory Verbal Learning Task (RAVLT; Rey, 1964); immediate recall, delayed recall and retention of units and themes of Logical Memory Subtests I and II of Wechsler Memory Scales-III (WMS-III; Wechsler, 2004); and immediate recall, delayed recall and retention score of Family Pictures I and II (WMS-III). The RAVLT consists of a five-trial presentation of a 15-word list (List A; trials I–V), each followed by immediate free recall, and a single presentation of an interference list (List B) followed by immediate recall (trial VI) and delayed free recall of list A (trial VII). At Follow-up, List A was replaced by an alternate list (List C). This task assesses immediate and delayed free recall, besides of measuring proactive and retroactive interference effects. Whereas recall has been associated with left hippocampus functioning (Babiloni et al., 2010; Kilpatrick et al., 1997), interference susceptibility has been related to prefrontal functioning (Badre and Wagner, 2005). Logic Memory is a task in which two short stories are presented orally (A and B), with story B presented twice. Subjects are asked to freely recall, as exactly as possible, each story immediately after presentation (Logical Memory I). After 25–35 min, they are asked to repeat what they could remember of both stories (Logical Memory II). This test assesses immediate and delayed verbal episodic declarative memory of contextualized semantic units. Significant correlations between WMS-III Logical Memory and hippocampal volumes have been demonstrated (Griffith et al., 2004). In the Family Pictures subtest, four visual scenes are shown to the subjects for 10 s each. After each scene presentation, subjects are asked to recall which family members were present, what they were doing and their location in a 2×2 grid (Family Pictures I). A 30-min delayed recall is also obtained (Family Pictures II). This task assesses immediate and delayed visuospatial memory and is associated to temporomesial functioning. Recent studies indicate that it also implies verbal components (Chapin et al., 2009; Dulay et al., 2002). In all cases raw scores were analyzed.
- (b) Executive functions: Working memory was assessed by the Digit span backward subtest and the Spatial Location backward subtest of WAIS-III (Wechsler, 1999); monitoring was assessed by total errors and perseverations of the Self-Ordered Pointing Test (SOPT; Petrides and Milner, 1982); and planning was assessed with the raw total score on Zoo Map and Key Search subtests of the Behavioural Assessment of Dysexecutive Syndrome (BADS; Wilson et al., 1996). In Digit span backward, the examiner reads aloud a number sequence that increases in length by one digit from trial to trial. Subjects are asked to repeat each sequence in reverse order. This test provides a verbal working memory index. Spatial Location backward is similar to the Digit span, in which subjects are required to repeat in the reverse order a given sequence of tapings on cubes mounted on a board. This test assesses visuospatial working memory. The index of performance was the number of digits/blocks contained in the longest sequence repeated correctly. Both tasks provide information about parietal cortex and bilateral prefrontal cortex functioning (Cabeza and Nyberg, 2000). In the Self-Ordered Pointing Test – abstract design version, 108 sheets are shown to the subject, each of which shows a series of abstract designs. This task is composed of 4 blocks with 3 trials each, in which the number of stimuli per sheet increases block by block (6, 8, 10 and 12). Stimuli are repeated on every sheet of each trial, but their position changes from sheet to sheet. Participants are required to point to a design on each sheet, without repeating a previous choice. Perseverative errors were defined as the number of errors that occurred as a result of pointing to the same item that was chosen on the immediately preceding page. Total errors score was the sum of perseverative and non-perseverative errors. This task provides information about the ability to regulate behaviour based on plans and strategies. It is related to processing speed and working memory and performance is associated with daily life activities (Strauss et al., 2006). This test is sensitive to dorsolateral prefrontal damage. The Zoo Map test presents two trials on which subjects are shown a map of a zoo and asked to trace the route they would take to visit six out of twelve places following certain written and orally presented rules. The first trial consists of a high-demand version of the task in which subjects have to plan the route. The second one is a low-demand trial in which the route may be completed following the written instructions. This task assesses planning ability. In the Key Search test, subjects are told to imagine that a square drawn on a paper is a big field in which they have lost their keys. They are asked to draw a line, starting from a predetermined position, to show the route they would take to find the keys. This task assesses the ability to plan a course of action in an everyday-like situation, and provides information about the efficiency of searching strategy. For the purpose of the analysis, raw scores were considered.
- (c) Finally, the Vocabulary subtest (WAIS-III; Wechsler, 1999) was administered to estimate premorbid intellectual level. This task assesses accuracy on defining different words and its total scaled score was analyzed.

2.3. Data analysis

Demographic and clinical data were analyzed by a series of one-way analyses of variance (ANOVAs) or χ^2 tests (for categorical data). Neuropsychological data were

analyzed by a series of repeated-measures ANOVAs, with assessment time (Initial and Follow-up) as the within-subjects factor and BD trajectory as the between-subjects factor (Non-BD, Ex-BD and BD).

Whenever appropriate, degrees of freedom were corrected by the conservative Greenhouse–Geisser estimate. All post hoc pair comparisons were performed with the Bonferroni adjustment for multiple comparisons, with an alpha level of 0.05. Pearson's product–moment correlation coefficient was employed to investigate correlations between neuropsychological performance and cannabis use. Statistical analyses were executed with statistical software SPSS 17.0 for Windows (SPSS Inc., 2008).

3. Results

3.1. Demographic and substance use variables

The demographic and substance use variables for subjects from all study groups at the Initial and Follow-up assessments are presented in Table 1. At the Initial assessment, groups differed in age ($F_{(2,86)} = 3.799, p = .026$), AUDIT scores ($F_{(2,86)} = 86.406, p = .0001$), age of onset of alcohol use ($F_{(2,86)} = 8.580, p = .0001$), and cannabis use ($\chi^2_{(2)} = 22.609, p = .0001$). Non-BD subjects scored lower in AUDIT than BD ($p = .0001$) and Ex-BD ($p = .0001$), and reported older age of onset of alcohol use than BD ($p = .0001$) and Ex-BD ($p = .032$). The age-related differences were not confirmed in post hoc comparisons. Groups did not differ in psychopathological symptoms ($F_{(2,86)} = .704, p = .497$) or in estimated intellectual level assessed by the Vocabulary subtest (WAIS-III) ($F_{(2,86)} = .444, p = .643$). At Follow-up, there were group differences on AUDIT scores ($F_{(2,86)} = 68.007, p = .0001$) and cannabis use ($\chi^2_{(2)} = 26.804, p = .0001$). Non-BD ($p = .0001$) and Ex-BD ($p = .0001$) scored lower in AUDIT than BD. Table 2 shows descriptive data for all dependent variables.

Pearson's product–moment correlations were conducted to explore possible relationships between neuropsychological performance and cannabis use at Initial and Follow-up. There were not significant correlations (Pearson's r values ranged from $-.197$ to $.04, p > .05$), so this variable was not considered in the posterior analyses.

3.2. Episodic memory and binge drinking trajectory

3.2.1. Rey-Auditory Verbal Learning Test. Participants scored lower at Follow-up than at the Initial assessment on trials I–V total ($F_{(1,83)} = 5.93, p = .017, \eta^2 = .067$); trial VI ($F_{(1,82)} = 10.57, p = .002, \eta^2 = .114$); and trial VII ($F_{(1,82)} = 10.64, p = .002, \eta^2 = .115$). The results revealed no significant main effect or interaction involving BD trajectory.

3.2.2. Logical Memory I and II. The BD trajectory significantly affected immediate recall of themes ($F_{(2,84)} = 3.80, p = .026, \eta^2 = .083$); delayed recall of themes ($F_{(2,84)} = 3.31, p = .041, \eta^2 = .073$); and retention ($F_{(2,84)} = 3.80, p = .026, \eta^2 = .083$). Post hoc comparisons revealed that BD scored poorer than Non-BD on immediate recall of themes ($p = .034, CI\ 95\% .06, 2.08$), delayed recall of themes ($p = .037, CI\ 95\% .03, 1.55$), and retention ($p = .035, CI\ 95\% .02, 7.28$). A significant effect of assessment time was found on immediate recall of units ($F_{(1,84)} = 4.18, p = .044, \eta^2 = .047$), showing that participants recalled more units at Follow-up than at the Initial assessment. No interaction effects between assessment time and BD trajectory reached significance.

3.2.3. Family Pictures I and II. A significant interaction between assessment time and BD trajectory was observed for the retention score ($F_{(2,84)} = 4.97, p = .009, \eta^2 = .106$). Post hoc analysis indicated that Ex-BD showed a clear improvement in their retention score between the Initial and Follow-up assessment ($p = .010, 95\% CI\ -.842, 5.958$). Participants, regardless of group, also showed

Table 1

Group means (standard deviation) for demographic and clinical data.

	Non-BD n = 40	Ex-BD n = 16	BD n = 33
Gender (m/f)	19/21	4/12	18/15
<i>Initial</i>			
Age*	18.50 (0.56)	18.88 (0.62)	18.82 (0.58)
AUDIT total** ^a	2.75 (2.45)	10.63 (3.63)	11.91 (3.60)
Age at onset of alcohol use** ^b	15.76 (0.94)	14.88 (1.03)	14.67 (1.29)
Occasional cannabis users**	3	8	19
SCL-90-R, Pc	42.85 (29.71)	48.44 (29.42)	51.12 (31.06)
WAIS-III Vocabulary	12.30 (2.39)	12.00 (1.97)	11.85 (1.66)
<i>Follow-up</i>			
Age	20.43 (0.55)	20.63 (0.50)	20.64 (0.78)
AUDIT total** ^c	2.98 (2.83)	6.19 (3.62)	11.39 (3.08)
Occasional cannabis users**	2	9	19
SCL-90-R, Pc	35.13 (29.14)	37.19 (27.32)	40.78 (31.42)

^a Non-BD < Ex-BD ($p = .0001$); Non-BD < BD ($p = .0001$).^b Non-BD > Ex-BD ($p = .032$); Non-BD > BD ($p = .0001$).^c Non-BD < BD ($p = .0001$); Ex-BD < BD ($p = .0001$).* $p = .05$.** $p = .001$.

significantly higher scores in delayed recall at Follow-up than at the Initial assessment ($F_{(1,85)} = 5.60$, $p = .020$, $\eta^2 = .062$).

3.3. Executive functions and binge drinking trajectory

Self-Ordered Pointing Test (SOPT). The BD trajectory had a significant effect on SOPT perseverative errors ($F_{(1,85)} = 3.88$, $p = .024$, $\eta^2 = .084$). Post hoc analysis revealed that BD committed significantly more perseverative errors than Non-BD ($p = .021$, IC 95% –1.30, –.08).

Participants also made less total errors at Follow-up than at the Initial assessment ($F_{(1,85)} = 29.36$, $p < .001$, $\eta^2 = .257$). There were no significant interactions between assessment time and BD trajectory for any of the SOPT variables measured.

With respect to the tests assessing working memory (Digits backward/Spatial location backward) and planning (Zoo Map/Key

Search), neither the main effects of assessment time or BD trajectory nor their interaction were significant.

4. Discussion

The aim of this study was to analyze the relationship between BD trajectory and neuropsychological performance in tests sensitive to temporomesial and prefrontal functioning among university students. Binge drinking adolescents without alcohol use disorders were compared to light/non-drinking controls with no current or lifetime comorbid psychopathology and no family history of alcoholism at first and third year of university (i.e., from late adolescence to young adulthood).

We hypothesized, first, that participants with a persistent binge drinking trajectory over a 2-years time period would perform poorer in memory and executive tasks than participants who gave

Table 2

Descriptive neuropsychological data for BD trajectory at initial and follow-up.

	Non-binge drinking		Ex-binge drinking		Binge drinking	
	Initial	Follow-up	Initial	Follow-up	Initial	Follow-up
<i>Memory</i>						
RAVLT, trial I–V total ^b	59.51 (5.34)	56.25 (7.47)	58.94 (6.92)	59.00 (7.40)	58.41 (6.49)	55.82 (8.40)
RAVLT, VI ^b	13.23 (1.55)	12.33 (1.96)	12.67 (2.06)	11.93 (2.52)	12.47 (2.21)	12.03 (2.54)
RAVLT, VII ^b	13.26 (1.68)	11.83 (2.44)	12.53 (2.23)	12.13 (2.85)	12.78 (1.96)	12.09 (2.47)
RAVLT, B	7.05 (2.15)	7.08 (2.2)	7.57 (2.14)	7.64 (1.55)	6.50 (1.55)	6.94 (2.29)
Logical Memory I, units ^b	53.73 (6.72)	54.79 (8.17)	50.50 (6.53)	54.06 (5.30)	50.78 (6.77)	51.33 (7.49)
Logical Memory I, themes ^{a,*}	16.58 (1.93)	16.87 (2.40)	16.69 (1.78)	16.75 (1.88)	15.47 (1.88)	16.00 (2.56)
Logical Memory II, units	34.95 (4.70)	36.03 (5.87)	32.69 (5.49)	34.63 (4.35)	32.28 (5.77)	33.15 (7.33)
Logical Memory II, themes ^{a,*}	10.70 (1.29)	10.97 (1.90)	10.31 (1.30)	10.94 (1.57)	10.09 (1.49)	10.12 (1.93)
Logical Memory, retention ^{a,*}	93.88 (5.86)	93.95 (6.12)	89.88 (8.27)	91.19 (7.59)	90.66 (8.18)	89.55 (10.48)
Family Pictures I	47.53 (8.81)	51.00 (8.58)	47.27 (8.76)	47.81 (8.77)	46.34 (9.54)	49.06 (8.61)
Family Pictures II ^b	47.40 (9.34)	50.40 (8.64)	47.00 (7.61)	48.38 (9.00)	46.31 (8.92)	49.24 (8.78)
Family Pictures retention ^{c,**}	98.45 (3.46)	97.13 (4.46)	96.13 (5.19)	99.56 (.96)	98.72 (2.67)	98.33 (3.29)
<i>Executive functions</i>						
Digits backward	5.56 (1.27)	5.50 (1.45)	5.44 (1.31)	5.81 (1.56)	5.16 (1.27)	5.55 (1.18)
Spatial location backward	6.03 (1.01)	5.67 (1.33)	6.25 (1.39)	6.13 (.96)	6.06 (1.05)	6.06 (1.03)
SOPT, total errors ^b	9.45 (4.99)	7.23 (4.66)	11.69 (5.60)	7.00 (5.47)	12.97 (7.73)	8.82 (4.95)
SOPT, perseverations ^{a,*}	1.10 (1.24)	1.18 (1.08)	1.88 (1.31)	1.19 (2.43)	2.09 (1.65)	1.55 (1.44)
Zoo Map, raw score	13.35 (3.32)	11.95 (3.80)	12.06 (4.46)	13.31 (3.70)	11.91 (3.86)	12.27 (4.36)
Key Search, raw score	11.48 (2.74)	11.78 (3.49)	13.25 (3.00)	12.94 (1.84)	11.72 (3.26)	11.76 (2.71)

^a BD trajectory main effect, $p < .05$.^b Assessment time main effect, $p < .05$.^c Assessment time $\times$ BD trajectory interaction effect, $p < .05$.* Significant post hoc comparisons ($p < .05$): binge drinking vs. non-binge drinking groups.** Significant post hoc comparisons ($p < .05$): ex-binge drinking group (Initial vs. Follow-up).

up the pattern and than non-binge drinkers. Secondly, we hypothesized that participants who gave up the binge drinking pattern would improve their performance from the initial to the follow-up assessment, to the level of the non-binge drinkers. The results partially confirm our hypotheses. Maintenance of BD was associated with lower verbal episodic memory and response monitoring than Non-BD, although no significant differences were found between BD and Ex-BD. As predicted, Non-BD and Ex-BD groups did not differ significantly in performance.

Regarding episodic memory, persistent binge drinkers recalled less information at immediate and delayed trials of the Logical Memory subtest and showed a lower retention rate than non-binge drinkers. However, no effects of the BD trajectory were found when unstructured, non-contextualized verbal material had to be learned (i.e., recall of a list of unrelated words in the Rey-Auditory Verbal Learning Task). Most of the previous work on this topic has been focused on clinical populations. The association between persistent binge drinking and lower episodic memory performance is consistent with the results of a 10-year follow-up study of adolescents with alcohol and other substance abuse disorders (Hanson et al., 2011). This study found that persistent heavy use of alcohol over time, with little or no other substance use, was associated with poorer immediate recall on the California Verbal Learning Test, a list-learning test that contained semantically related words. Besides, those individuals that, after treatment for alcohol and other substance use disorder, remained abstinent or consumed alcohol and other substances infrequently over the follow-up period performed at similar cognitive levels as youths without any alcohol problem. This pattern resembles that seen in long-term abstinence alcoholics (Rourke and Grant, 2009). The absence of performance differences on the RAVLT in our study may be interpreted in terms of previous proposals that difficulties in learning tasks involving non-contextualized information may be overcome by recruiting alternative neural networks, such as prefrontal regions, that could implement active encoding and retrieval strategies (Schweinsburg et al., 2010). In our previous work reporting the cross-sectional analysis of the Initial assessment on this sample (Parada et al., 2011), binge drinking students showed poorer performance than non-binge drinkers on RAVLT, although differences were restricted to greater interference. The current results may respond to cognitive development that resulted in improved control of interference. Another possibility is that reduced sample size might have limited the power to detect differences across groups. Finally, the finding of difficulties in delayed story recall associated with binge drinking may respond to differences in memory consolidation, a process that has been linked to hippocampal functioning (Alvarez and Squire, 1994; Squire and Zola, 1997; Tulving and Markowitsch, 1998), especially in story recall tasks (Frisk and Milner, 1990; Vannest et al., 2008). The vulnerability of the hippocampus to alcohol binge drinking has been consistently supported by studies in rodents and primates (Chin et al., 2010; Taffe et al., 2010).

Taking all the data together, it is plausible to propose that declarative episodic memory difficulties are subsequent to the establishment of BD and may reflect hippocampal dysfunction. Further support for a causal relationship between binge drinking and memory dysfunction comes from structural neuroimaging data showing a reduced hippocampal volume in young people with alcohol use disorders (De Bellis et al., 2000; Nagel et al., 2005). In line with this proposal, it has been reported that youths with a family history of alcoholism and with minimum consumption of alcohol do not display structural differences in the hippocampus (Hill, 2004). Also, the similarity of the groups as regards psychopathological and demographic aspects that could otherwise influence the results (such as age, gender, educational and intellectual level and socioeconomic status), as well as the absence of family history

of alcoholism in our sample of participants, contributes to this hypothesis.

Regarding prefrontal functions, difficulties in monitoring, as measured by the perseverative errors on the SOPT, were associated with maintenance of BD. Students who gave up the binge drinking pattern performed at similar levels to non-binge drinkers. At our knowledge, only a longitudinal study (Goudriaan et al., 2007) examined the relationship between binge drinking trajectory and prefrontal functions among adolescent students, although it was limited to decision making, a function known to be subserved by ventromedial prefrontal cortices (Bechara and Damasio, 2005). Goudriaan et al. (2007) investigated whether binge drinking was related to disadvantageous decision making, as measured by the Iowa Gambling Task (IGT), and found that stable (over a 2-year time period) high binge-drinkers made less advantageous choices on the IGT than persistent low-binge drinkers. However, as the IGT was only administered once in the referred study, it is not possible to know if performance changes were associated with the trajectory of the binge drinking pattern. As regards longitudinal studies with clinical population, the above-described study by Hanson et al. (2011) on subjects with alcohol and other substance use disorders, found no association between distinct patterns of alcohol and other drugs abuse over 10 years period and executive functions (as measured by Digit Span and Trails B time-to-completion). The few cross-sectional studies using SOPT have not found performance differences as a function of alcohol drinking patterns (Hartley et al., 2004; Johnson et al., 2008). Nonetheless, it is important to note that these studies did not analyze perseverative errors.

Functional activation studies with healthy human subjects and lesion studies with animals have consistently demonstrated specific activity within the mid-dorsolateral region of the frontal cortex (areas 46 and 9) during the performance of tasks requiring monitoring of information within working memory, such as self-ordered tasks (Petrides, 2000). The present results are thus consistent with those of structural and functional neuroimaging studies on binge drinking showing differences in prefrontal volume and fractional anisotropy in frontal white matter among binge drinkers (McQueeney et al., 2009; Squeglia et al., 2012) and AUD adolescents (Medina et al., 2008; De Bellis et al., 2005, 2008) in comparison with control subjects. Interestingly, these differences are associated with variables that characterize the BD pattern, such as higher estimated peak blood alcohol concentration (McQueeney et al., 2009).

Unlike the results reported in a previous work on this sample (Parada et al., 2012), we did not observe differences on verbal span. This could be explained by the development of working memory as a result of brain maturation. Improved performance in working memory tasks during adolescence has been associated with late cortical maturation of the frontal lobes, and with the development of their connecting pathways (Østby et al., 2011). Performance on tasks largely mediated by the dorsolateral prefrontal cortex reaches adult levels later than performance on those tasks mediated by more ventral frontal regions and, among them, tasks that demand high levels of executive control mature later than those that require working memory but decreased control (e.g., backward versus forward digit span and SOPT versus backward span tasks; Conklin et al., 2007). Nonetheless, we cannot discard that this pattern of findings could stem from the lack of sufficient power to detect differences between groups.

One potential limitation of our study is the high prevalence of occasional cannabis use among binge drinkers. Long-term effects of heavy or chronic cannabis use on neuropsychological functioning are well known. Nevertheless, it is important to take into account that the light pattern of cannabis consumption in our sample, characterized by occasional use and short history of use, did not statistically correlate with differences on neuropsychological

scores, as was indicated previously. On other hand, approximately one-third of Spanish adolescents who drink alcohol also consume cannabis (Ministerio de Sanidad, Política Social e Igualdad, 2010), so their exclusion would have made difficult the selection of the BD group, possibly making it less representative.

Binge drinking is an important public health problem. Nevertheless, neuropsychological studies on the consequences of this pattern of alcohol consumption among adolescents from general population are scarce. By controlling confounding factors such as psychopathological symptoms and family history of alcoholism and other psychiatric disorders, the present longitudinal study indicates that maintenance of binge drinking during late adolescence and early adulthood is associated with difficulties in learning/memory and monitoring.

The present results illustrate the negative consequences of binge drinking during adolescence on neurocognitive functioning, and they may be useful for strengthening public prevention programmes and policies on binge drinking, which should focus on delaying age of onset of alcohol use, as well as on reducing the incidence and prevalence of binge drinking in the youth population.

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Contributors

Authors F. Cadaveira, M. Corral and S. Rodríguez-Holguín designed the study and wrote the protocol. Authors N. Mota, M. Parada and A. Crego managed the literature searches and summaries of previous related work. Authors F. Caamaño and S. Doallo undertook the statistical analysis, and author N. Mota wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

No conflict declared.

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