Increased amplitude of P3 event-related potential in young binge drinkers

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A B S T R A C T

The aim of the present study was to determine how binge drinking (BD) affects brain functioning in male and female university students during the performance of a visual discrimination task. Thirty two binge drinkers and 53 controls (non binge drinkers), with no history of other drug use, personal or family history of alcoholism or psychopathological disorders, were selected. Event-related potentials (ERPs) were recorded during the performance of a visual oddball task. The latency and amplitude of the N2 and P3b components of the ERPs were analyzed. There were no differences between the groups in behavioral measures, but P3b amplitudes were significantly larger in binge drinkers than controls. This may suggest the presence of anomalies in neural processes mediating attention processing, or an imbalance (increased) of neuronal activity in P3b generators caused by the presence of BD pattern for a long time.

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Introduction

In recent decades, there has been increasing concern regarding the neurocognitive effects of alcohol intake in adolescents and young people (for a review see Monti et al., 2005) because of the high prevalence of alcohol abuse among this population (Serdula, Brewer, Gillespie, Denny, & Mokdad, 2004). Binge drinking (BD) has become increasingly common among adolescents and college students and refers to the consumption of large amounts of alcohol in a short time, often on Thursdays and at the weekend (Beets et al., 2009), followed by a period of abstinence (Lange et al., 2002; Wechsler, Davenport, Dowdall, Moeykens, & Castillo, 1994; Wechsler et al., 2002).

The most widely accepted operating definition of BD is the consumption of five or more alcoholic drinks (four or more in the case of women) on a single occasion (in the time span of two hours, according to the National Institute on Alcohol Abuse and Alcoholism) at least once in the previous two weeks or month (for a review see Courtney & Polich, 2009; Parada et al., 2011a). Additionally, considering the differences of pure ethanol that one Standard Alcoholic Drink contains in each country (International Center for Alcohol Policies, 2003), it is necessary to adjust the criteria to the location of the investigation.

Although 6–10% of adolescents fulfill diagnostic criteria for alcohol use disorders (Clark, Bukstein, & Cornelius, 2002), BD is much more prevalent in adolescents and young people and often viewed by them as innocuous (Johnston, O'Malley, Bachman, & Schulenberg, 2009). Epidemiological studies across the USA and UK indicate that around 40% of university students are binge drinkers (Gill, 2002; Wechsler et al., 2002). In an epidemiological previous study by our research group in Spain (Caamaño-Isorna, Corral, Parada, & Cadaveira, 2008), 37% of first-year university students (N = 2700) were found to consume large amounts of alcohol ("risky consumption") and 12.2% showed a BD pattern of alcohol consumption, with higher prevalence in males than females (29.9% vs. 8.2% females).

Adolescence is a time of dynamic brain changes that occur in the context of major physiological, psychological, and social transitions. Maturing neural circuitry during this life stage, particularly in the prefrontal cortex, limbic system, and white matter association and projection fibers, is linked with advancements in cognition and behavior (Bava et al., 2010). So, higher-order cognitive functions such as attention, working memory, planning, problem solving, and inhibitory control are developing during adolescence and historically linked to maturation of the frontal lobes (for a review see De Luca & Leventer, 2008). Given the extent of brain maturation occurring during this phase in life, adolescents who use substances

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appear to be vulnerable to alterations in brain functioning, cognition and behavior, and alcohol use may detrimentally influence the developing brain (for a review see Guerri & Pascual, 2010).

Animal studies have demonstrated that the intermittent consumption of high doses of alcohol causes major alterations in the central nervous system (CNS) (Jaatinen, Riikonen, Riihioja, Kajander, & Hervonen, 2003; Roberto, Nelson, Ur, & Gruol, 2002; Tokunaga, Silvers, & Matthews, 2006) and that the adolescent brain is more sensitive to the neurotoxic effects of alcohol and BD than the adult brain (Crews, Braun, Hoplight, Switzer, & Knapp, 2000; White, Ghia, Levin, & Swartzwelder, 2000). Alcohol particularly affects those structures of the brain that mature late on in development, such as the hippocampus and the prefrontal cortex (PFC) (for a review see Monti et al., 2005).

Human studies have revealed the presence of neurostructural and neurocognitive anomalies in adolescents with alcohol use disorders (AUDs). These studies have reported significant reductions in the volume of hippocampus and PFC (De Bellis et al., 2005; Medina et al., 2008; Nagel, Schweinsburg, Phan, & Tapert, 2005), and the presence of neurocognitive deficits in functions related to these brain areas, such as visuospatial attention, and particularly working memory (for a review see Brown & Tapert, 2004), in adolescents with AUD in comparison with paired controls. As regards BD, although few studies have investigated the neurobiological and neurocognitive effects of this pattern of alcohol consumption in non-clinical samples of adolescents and young people, it has been shown that young people who indulge in BD experience difficulty in carrying out tasks involving PFC functions, such as working memory, planning, attention and decision making (Crego et al., 2009, 2010; García-Moreno, Exposito, Sanhueza, & Angulo, 2008; Goudriaan, Grekin, & Sher, 2007; Johnson et al., 2008), or hippocampus function as verbal memory (Parada et al., 2011b).

The event-related potentials (ERP) have been widely used to assess the neurocognitive effects of alcohol in different populations such as alcoholics, abstinent chronic alcoholics and children of alcoholics (for a review see Porjesz et al., 2005). Most studies have focused on the P3b component, a positive wave peaking between 300 and 600 ms after the stimulus onset, with maximum amplitude values at centroparietal sites, and functionally associated with processes of attention and memory access evoked by the evaluation of stimuli in tasks that require some form of action like a covert or overt response (for a review see Polich, 2007). These studies have shown that alcoholism is associated with reduced amplitude and a delayed latency of P3b to task-relevant target stimuli, impairments considered as electrophysiological markers of earlier behavioral results showing that alcoholism is linked to a deficit in higher cognitive (attention and memory) processing (for a review see Campanella et al., 2009; Porjesz et al., 2005). Moreover, reduced P3b amplitude is considered a genetically transmitted marker for the risk of alcoholism (for a review see Polich, Pollock, & Bloom, 1994; Porjesz et al., 2005). Other studies (Cadaveira, Grau, Roso, & Sanchez-Turet, 1991; Cadaveira, Roso, Grau, & Sanchez-Turet, 1992; Cristini, Fournier, Timsit-Berthier, Bailly, & Tujus, 2003; Maurage et al., 2008; Olbrich, Maes, Gann, Hagenbuch, & Feige, 2000), although fewer in number and with more controversial results, have also focused on the N2 component, a negative waveform with a peak latency around 200 to 300 ms related to attentional processes.

With regard to BD, few studies have used ERPs to explore BD in young people. Ehlers et al. (2007) used a facial emotional expression recognition task and evaluated ERPs in young adults with a history of BD during adolescence. They reported that the amplitude of the late P3 component (P3b) was lower in young adults participating in BD during adolescence than in subjects who did not partake in BD during adolescence. The authors suggested that these anomalies may be associated with a loss or delay in the development of inhibitory brain systems in binge drinkers. Recently, Maurage, Pesenti, Philippot, Joassin, & Campanella (2009) used a test–retest paradigm and reported that short-term BD can produce marked cerebral dysfunction that is undetectable by behavioral measures alone. The results of their study revealed that, after 9 months of BD, subjects presented significantly delayed latencies in the P1, N2 and P3 components elicited by emotional auditory stimuli, with respect to controls, with no behavioral differences. These studies have revealed that young binge drinkers show electrophysiological anomalies in the processing of emotional stimuli. Moreover, two previous reports by our research group have revealed that young binge drinkers show anomalous electrophysiological patterns and hypoactivation of the anterior prefrontal cortex during a working memory task (Crego et al., 2009, 2010).

In the present study, the N2 and P3b components of the ERPs elicited in response to a visual oddball task were analyzed in a sample of young people (first-year university students) with and without a BD pattern of alcohol consumption, in order (i) to establish whether ERPs differ between the young binge drinkers and corresponding control subjects, which may reveal any impairment in the process of attention and information processing, and (ii) to determine if the electrophysiological measurements are affected differently by BD in male and female subjects.

Materials and methods

Participants

Eighty-five first-year university students (age range 18–20 years) participated in the study. Thirty-two of the participants (15 females) were classified as binge drinkers and 53 (25 females) as controls.

For sample selection, first-year students at the University of Santiago de Compostela (Galicia, Spain) ($N = 2700$) were asked to complete a questionnaire during class. The initial sample used in the present study is the same as that used in an epidemiological study carried out by our research group (Caamaño-Isorna et al., 2008). The questionnaire included the Galician validated version of the Alcohol Use Disorder Identification Test (AUDIT) (Varela, Braña, Real, & Rial, 2005); items 10, 11 and 12 of the Alcohol Use Questionnaire (AUQ) (Townshend & Duka, 2002), i.e. speed of drinking (average number of drinks consumed per hour), number of times the subject became drunk in the previous 6 months, and percentage (average) number of times the subject became drunk when drinking, as well as other items regarding use of alcohol (frequency of BD episodes in the previous 2 weeks and the previous month, number of drinks per occasion, number of drinks consumed on each day of the last week, age of onset of use, etc.) and other drugs (type of drug use, frequency of consumption, etc.).

According to the quantitative definition of BD used in European countries such as Spain, where a standard alcoholic drink equals about 10 g of alcohol, this study established the criterion of consumption of six or more standard alcoholic drinks on the same occasion (rather than five or more, as in the USA, where one standard alcoholic drink equals about 14 g of alcohol), one or more times per month. This information was obtained from the subject's response to question 3 of the AUDIT ("How often do you have six or more drinks on one occasion? Never/Less than monthly/Monthly/Weekly/Daily or almost daily"). In addition to this quantity/frequency criterion, speed of alcohol consumption was also considered. To be classified as binge drinkers, subjects had to drink at least three drinks per hour during BD episodes. This information was obtained from the subject's response to question 11 of the AUQ,
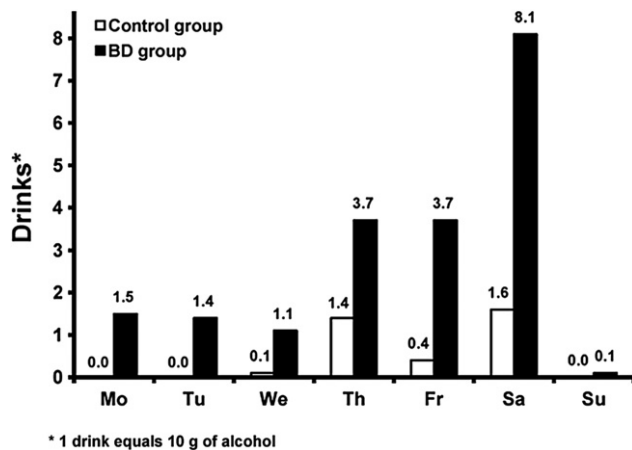
Fig. 1. Mean number of drinks consumed on each day of the last week by the BD and control subjects.

which refers to the speed of drinking (average number of drinks consumed per hour).

Therefore, (1) subjects who drank six or more standard alcoholic drinks on the same occasion one or more times per week, and (2) those who drank six or more standard alcoholic drinks on the same occasion at least once a month and, during these episodes drank at a speed of consumption of at least three drinks per hour, were classified as binge drinkers. Those who drank six standard alcoholic drinks on the same occasion less than once per month and at a maximum speed of consumption of two drinks per hour, were classified as controls (non-BD). The control group was composed of university students who did not meet criteria for BD but not necessarily had to be abstinent, because the latter are scarce amongst young university students (at least in the study population). Thus, the low level of alcohol consumption of most subjects in the control group was representative of most of the students surveyed, and the amounts, frequency and speed at which they drank guaranteed the absence of a BD pattern or any other type of alcohol-related problems. Anyway, an analysis comparing abstainers (13) and light drinkers (40) of the control group was performed, and the results showed no significant differences between them in any parameter (latency or amplitude) of ERPs components analyzed (N2 and P3b).The mean number of drinks that the BD and control subjects consumed on each day of the last week is shown in Fig. 1.

The Symptom Checklist-90-Revised questionnaire (SCL-90-R) (Derogatis, 1994) was applied to the initially selected subjects in order to detect any psychopathological symptoms and compare the different scales in the two groups. Subsequently, the subjects were interviewed about their personal and family history of alcoholism and medical or psychopathological disorders. The interview comprised 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). Questions about individual and familiar psychopathological problems were based on DSM-IV criteria and at least one other diagnostic classification system. Alcohol abuse/dependence was assessed in all subjects, both controls and binge drinkers, by use of the AUDIT. This test has been validated to assess alcohol-related problems or disorders (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001), and specifically in university students (for a review see Reinet & Allen, 2007). AUDIT scores in the range of 8–19 reveal "risky" consumption, while scores of 20 or above warrant further diagnostic evaluation for alcohol dependence. Information on tobacco, cannabis and other drugs use was obtained from the subjects' responses to items about drugs use included in the questionnaire.

The exclusionary criteria were left-handedness, non-corrected sensory deficits, any episode of loss of consciousness for more than 20 min, history of traumatic brain injury or neurological disorder, personal history of psychopathological disorders (DSM-IV Axis I and Axis II disorders), family history of major psychopathological disorders (major depressive disorder, schizophrenia or anxiety disorders according to DSM-IV criteria) in first-degree relatives, family history of first-degree alcoholism or substance abuse, and history of regular or occasional use of drugs (cannabis, opiates, hallucinogens, ecstasy, cocaine, amphetamine compounds or medically prescribed psychoactive substances). With regard to tobacco consumption, subjects with a regular tobacco consumption were excluded, while occasional smokers (who smoke during BD episodes but no in others situations) were controlled but not excluded. As regards alcohol consumption, subjects with AUDs (AUDIT scores $\geq$ 20) were excluded from the study.

The demographic and drinking characteristics of the subjects finally selected to form the BD and control groups are presented in Table 1. With respect to psychological variables, the two groups did not differ either in global severity index (GSI) or any scale of SCL-90-R.

The experiment was undertaken in compliance with Spanish legislation and the code of ethical principles for medical research

Table 1
Demographic and drinking characteristics of the Control and BD groups (mean $\pm$ SD).

	Control	BD
N (females)	53 (25)	32 (15)
Age: years (range)	18.5 $\pm$ 0.5 (18–20)	18.8 $\pm$ 0.6 (18–20)
Handedness (rigth/left)	53/0	32/0
Caucasian ethnicity (%)	100	100
Age of onset on alcohol consumption: years[*]	16 $\pm$ 1	15 $\pm$ 1.3
Quantity of consumption: drinks per occasion[a][**]	1 $\pm$ 1.5	5.1 $\pm$ 2
Drinks in the last week (self-reported)[a][**]	3.5 $\pm$ 1.4	19.7 $\pm$ 4.9
Speed of consumption: drinks per hour[a][**]	0.6 $\pm$ 0.9	3.3 $\pm$ 1.1
BD episodes in the last two weeks[**]	0.02 $\pm$ 0.1	1.4 $\pm$ 1.4
Times drunk in the last 6 months[**]	1.2 $\pm$ 2.7	6.8 $\pm$ 7
Percentage of times became drunk when drinking[**]	5.9 $\pm$ 10.1	42.7 $\pm$ 31.6
Total AUDIT score (range)[**]	2.4 $\pm$ 2.1 (0–9)	11.3 $\pm$ 3.4 (6–18)
Global Score Index (GSI) percentil of SCL-90-R	43.3 $\pm$ 29.7	52.2 $\pm$ 33.9

[*]t < 0.05 significant group differences (Control vs. BD).
[**]t < 0.001 significant group differences (Control vs. BD).
 [a] 1 drink equals 10 g of alcohol.

involving human subjects outlined by the World Medical Association (Declaration of Helsinki: see Williams, 2008). Participants signed an informed consent form and were paid for participating in the experiment.

Tasks and procedure

Participants were asked to abstain from consuming alcohol for 12 h before the experiment and not to have binge drinking episodes in the past 24 hours to prevent acute alcohol intake effects and to rule out withdrawal effects. In addition, they were instructed not to smoke or drink tea or coffee for at least 3 h prior to the experiment. Compliance with these restrictions was self-reported by the subjects. Each subject was seated in a comfortable armchair located in a light- and sound-attenuated electrically shielded room, and a brain cap and electrodes (see below) were fitted to the subject's head. General instructions were given to avoid movements during the test and the task was explained.

A visual oddball task was used. The oddball paradigm is a classical discrimination task, in which two stimuli are presented in a random series such that one of them occurs relatively infrequently and subjects must detect this occasional rare ("target") stimuli occurring against a background of more frequent non-target ("standard") stimuli.

In the oddball task employed, 150 stimuli, size $2.5° \times 2.5°$ visual angle, were presented at random on a black background in the center of a CRT monitor placed 100 cm in front of the subject's eyes. The stimulus duration was 45 ms and the interstimulus interval (ISI) varied between 1000 and 1400 ms. The stimuli consisted of two different figures, a white circle designated as the standard stimulus (probability = 0.8) and a white star designated as the target stimulus (probability = 0.2). Participants were instructed to press a button with the preferred hand when the target stimulus appeared and not to respond when the standard stimulus appeared.

EEG recording

The electroencephalogram (EEG) was recorded with Brain Vision Recorder system using a Braincap with 32 synterized Ag–AgCl electrodes placed at AF3, AFz, AF4, F7, F3, Fz, F4, F8, FC3, FCz, FC4, C3, Cz, C4, CP3, CPz, CP4, T7, T8, P7, P3, Pz, P4, P8, PO7, PO3, POz, PO4, PO8, O1, Oz and O2 (according to the extended 10–20 International System). All active electrodes were referred to the nose tip and grounded with an electrode placed at Fpz. Vertical electrooculographic activity (VEOG) was recorded bipolarly from above and below the left eye to control eye movements and blinks. Electrode impedances were kept below 10 kΩ. EEG signals were continuously amplified and digitized at a rate of 500 Hz, and filtered on-line with a 0.01–100 Hz band pass filter.

Data analysis

Behavioral analysis

Only responses with reaction times (RTs) between 100 and 1000 ms after the onset of a target stimulus were considered as correct. Responses to the standard stimuli were scored as false alarms, and failures to respond to target stimuli were defined as omissions. The RTs, the percentage of correct responses and the percentage of false alarms from the two groups (BD and control) were compared using a Student's t-test for independent samples.

ERP analysis

All EEG data were analyzed with Brain Vision Analyzer software (Version 2.0.1). The EEG was corrected for ocular artefacts by the semiautomatic procedure in Independent Component Analysis

(ICA) (Jung et al., 2000). It was then digitally filtered off-line with a 0.1–30 Hz bandpass filter and segmented into epochs of 1000 ms from 100 ms pre-stimulus to 900 ms post-stimulus. Baseline correction was applied, epochs exceeding ±80 μV at any scalp electrode were rejected (lower than 5% in each task) and EEG epochs corresponding to incorrect responses (omissions or false alarms) were excluded. Average ERPs time-locked to the standard and the target stimuli were computed separately.

The averaged ERPs were analyzed with a semiautomatic peak detection procedure and, subsequently reviewed and manually corrected at each of the 32 electrodes for each participant. The N2 and P3b components were identified and marked in the averaged waveform elicited by the standard and target stimuli as the largest negative peak between 200 and 300 ms after the stimuli onset, and the largest positive peak within a time window of 300-600 ms, respectively. Both amplitudes (μV) and latency (ms) values of these ERP components were organized into three regions, each including six electrode positions: frontal (F3, Fz, F4, FC3, FCz, FC4), central (C3, Cz, C4, CP3, CPz, CP4) and parietal (P3, Pz, P4, PO3, POz, PO4). A mixed model ANOVA with two between-subjects factors and three within-subject factors was used for the statistical analysis of each component. The between-subjects factors were Group (BD and control) and Gender (male and female), and the within-subject factors were Condition (standard and target stimuli), Region (frontal, central and parietal) and Electrode location (six channels). In addition, an independent analysis was performed for each gender.

An alpha level of 0.05 was used and, whenever appropriate, degrees of freedom were corrected by the conservative Greenhouse–Geisser estimate. All post hoc paired comparisons were performed with the Bonferroni adjustment for multiple comparisons, also with an alpha level of 0.05.

Results

Behavioral results

The behavioral data for each group are summarized in Table 2. No significant differences between the control and BD groups were observed for RTs, percentage of correct responses or false alarms.

Electrophysiological results

The grand averages of the ERPs for the standard and target stimuli in the control and BD groups are shown in Figs. 2 and 3, respectively. The grand averages of the ERPs in the two groups for the target stimuli in males and females are compared in Figs. 4 and 5, respectively. The mean and standard derivation (SD) values of amplitude and latency of P3b and N2 components for the two groups are shown in Table 3, and the mean and SD values of P3b amplitude for each gender in each group are shown in Table 4.

The analysis of the N2 amplitude revealed that the factor Condition had a significant effect [$F(1,81) = 20.32$, $p < .001$]. The N2 amplitude was significantly larger in the target than in the standard condition. The analysis also revealed that the factor Region had a significant effect [$F(2,162) = 25.34$, $p < .001$], with higher amplitude

Table 2
Behavioral data from the control and BD groups (mean ± SD).

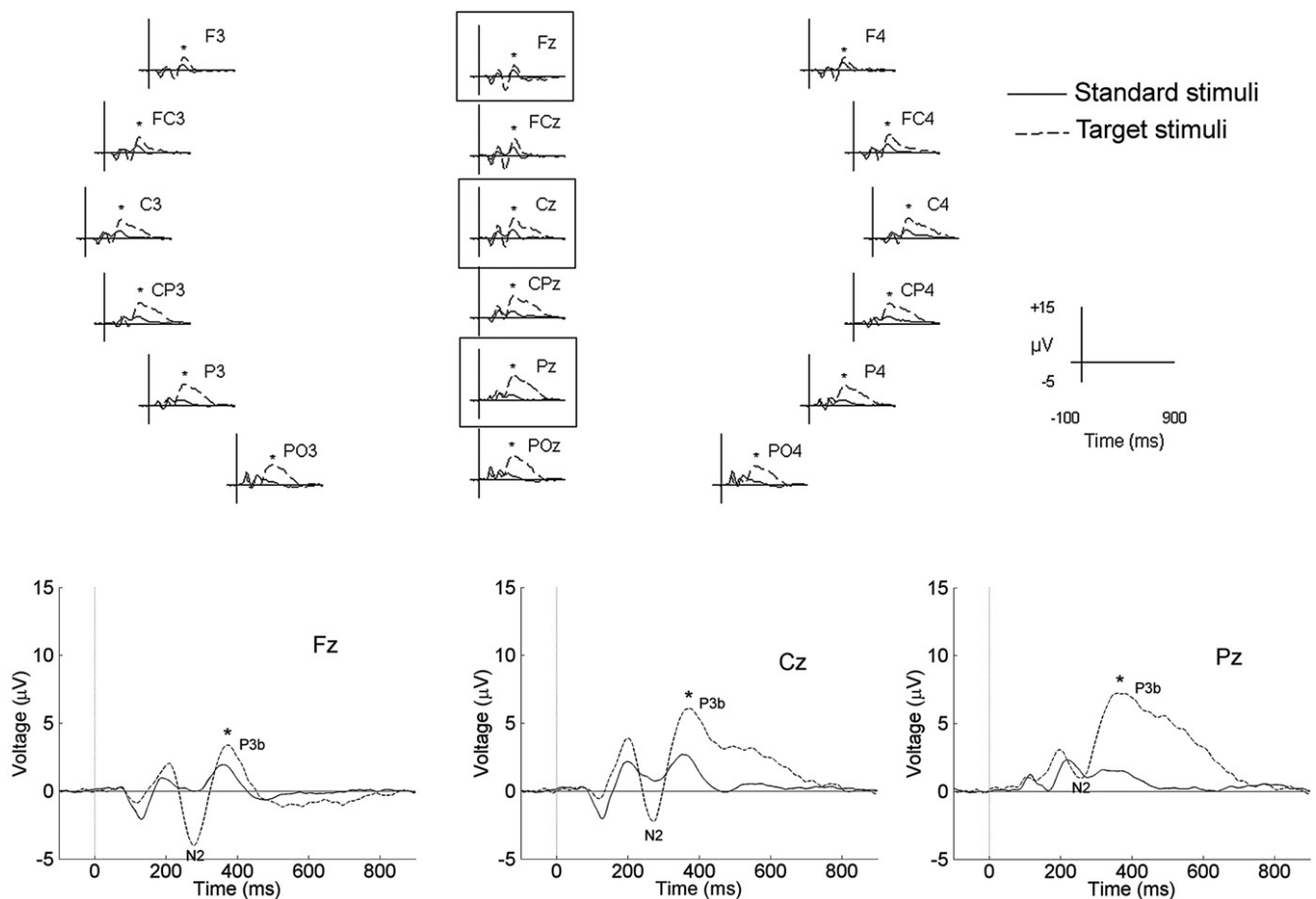| Behavioral performance	Control	BD
Reaction time (ms)	392.6 ± 49.9	392 ± 46.8
% Correct responses	99.2 ± 1.8	99.3 ± 1.6
% False alarms	0.1 ± 0.4	0.2 ± 0.7

Fig. 2. Grand averages of ERPs from the Control group in response to the standard (solid lines) and target stimuli (dashed lines) at the 18 electrodes analyzed. P3b amplitude was larger for the target than the standard stimuli in all the electrodes and regions analyzed.

in anterior than posterior regions (frontal > central > parietal) ($p < .001$ for all pair comparisons).

The N2 latency or amplitude did not differ significantly between groups for any region or condition.

Likewise N2, the P3b latency did not differ significantly between groups at any region or condition.

As regards P3b amplitude, the analysis revealed that the factor Condition had a significant effect [$F(1,81) = 166.06, p < .001$]. The P3b amplitude was significantly larger in the target than in the standard condition. The analysis also revealed that the factor Region had a significant effect [$F(2,162) = 26.48, p < .001$], with larger amplitude in posterior than anterior regions (parietal and central > frontal) ($p < .001$ for all pair comparisons). As regards the factor Group, it had a significant effect [$F(1,81) = 8.04, p < .01$]. The P3b amplitude was significantly larger in the BD than control group. The interaction between Group and Condition also had a significant effect [$F(1,81) = 12.31, p < .001$]. The post hoc multiple comparisons revealed that P3b amplitude was larger in the target than in the standard condition in both groups as was expected ($p < .001$) (see Figs. 2 and 3), and that for the target condition was significantly larger in the BD than in the control group ($p < .001$). There was no significant Group × Condition × Region interaction, and an independent analysis for each region in the target condition confirmed a larger P3b amplitude in the BD group than the control group in the frontal [$F(1,81) = 12.89, p = .001$], central [$F(1,81) = 10.85, p = .001$] and parietal [$F(1,81) = 7.28, p = .008$] regions.

Bearing in mind that previous studies have reported that oddball P3 is reduced among smokers (Anokhin et al. 2000; Polich & Ochoa, 2004), it is increased by acute smoking (Polich & Criado 2006) and

decreased by smoking abstinence (Daurignac, Le Houezec, Perez-Diaz, Lagrue, & Jouvent, 1998), the data were analyzed excluding the occasional smokers (three subjects in the control group and seven subjects in the BD group). The results did not show differences with those including the whole sample. Moreover, the occasional smokers were compared with the no-smokers into each group, and there were not differences in P3b amplitude between the subgroups. Therefore, the occasional smokers were not excluded from the sample.

Finally, with regard to the factor Gender, no significant interactions between Group and Gender were observed on the latency or amplitude of both N2 and P3b components. However, as regards P3b amplitude, the analysis revealed that the interaction between Gender and Condition had a significant effect [$F(1,81) = 4.62, p < .05$], and the post hoc multiple comparisons confirmed, as was expected, that P3b amplitude for the target condition was significantly larger in females than males ($p < .05$). Moreover, independent analyses for each gender showed that the interaction between Group and Condition had a significant effect both in males [$F(1,43) = 4.44, p < .008$] and females [$F(1,38) = 7.48, p = .038$], and the post hoc multiple comparisons confirmed that P3b amplitude for the target condition was significantly larger in the BD than in the control group for both males ($p < .01$) and females ($p < .05$) (see Figs. 4 and 5).

Discussion

Although some neuropsychological studies have revealed that young people with a BD pattern of alcohol consumption show
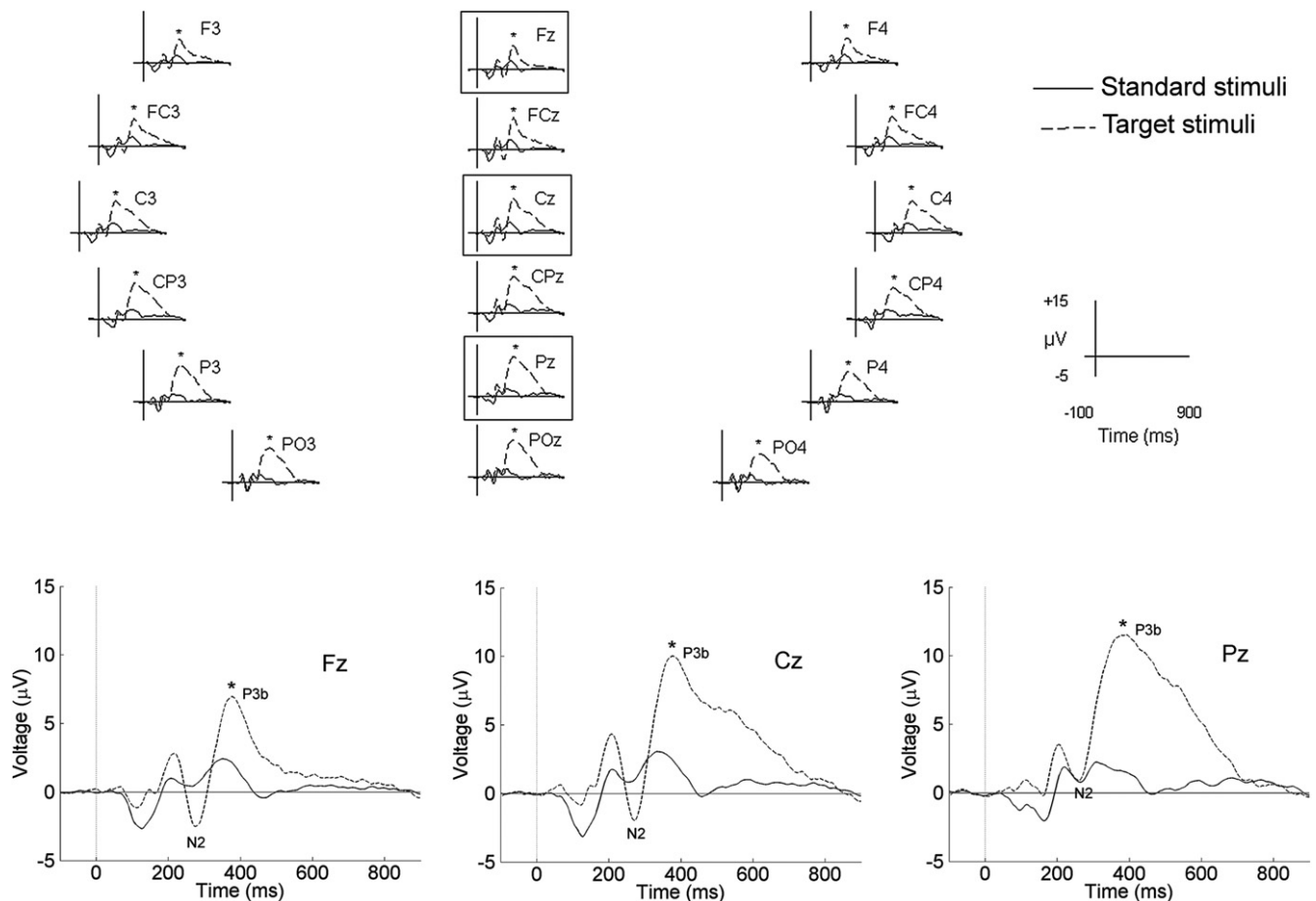
Fig. 3. Grand averages of ERPs from the BD group in response to the standard (solid lines) and target stimuli (dashed lines) at the 18 electrodes analyzed. P3b amplitude was larger for the target than the standard stimuli in all the electrodes and regions analyzed.

behavioral deficits in relation to cognitive functions such as working memory, attention, planning, decision making and verbal memory (García-Moreno et al., 2008; Goudriaan et al., 2007; Johnson et al., 2008; Parada et al., 2011b), in the present study no behavioral differences between BD and control groups were observed. This was not unexpected, since ERPs can reveal neuro-cognitive restrictions undetectable at the behavioral level, and perhaps the tasks employed, although useful for obtaining ERPs related to attentional processes, were not sensitive enough to detect differences in behavioral performance or any possible behavioral impairment.

With regard to ERPs, the results revealed a larger P3b amplitude in the BD group than in the control group in frontal, central and parietal regions during the execution of the visual oddball task. This is surprising because a reduction in the P3b amplitude has long been associated with alcoholism and the risk of alcoholism (for review, see Polich et al., 1994; Porjesz et al., 2005). The P3b amplitude has been considered as an indicator of the allocation of attentional resources to the voluntary selection of relevant stimuli and context updating processes of working memory (for a review see Polich, 2007), and many studies have revealed that abstinent chronic alcoholics, who have significant attentional and memory deficits, show a reduction in the P3b amplitude (for a review see Campanella et al., 2009; Porjesz et al., 2005). However, the relation between alcohol consumption and anomalies in P3b is complex. It has been proposed that, rather than a consequence of alcohol consumption, the reduction in P3b amplitude is an

endophenotype, or a genetically transmitted risk marker for alcoholism (Hesselbrock, Begleiter, Porjesz, O′ Connor, & Bauer, 2001), independent of lifetime alcohol consumption (Perlman, Johnson, & Iacono, 2009; Pfefferbaum, Ford, White, & Mathalon, 1991), and it has been linked to risk for alcoholism across a variety of experimental tasks and in a variety of clinical and epidemiological populations, including adolescents at high familial risk for alcoholism prior to alcohol exposure (Porjesz et al., 1998; Rodríguez Holguín, Corral, & Cadaveira, 1999)

Regarding BD, Ehlers et al. (2007) found that adults with a history of BD during adolescence, with no diagnosed lifetime of drug dependence showed a lower P3b amplitude than adults with no regular BD during adolescence and no drug dependence, in response to an emotional facial expression task. However, the decrease in the amplitude cannot be attributed exclusively to BD during adolescence, because family history of alcohol and conduct disorder or antisocial personality disorder were not excluded and were significant covariates in the analysis. In the present study, in which subjects with AUD or personal history of psychopathological disorders (DSM-IV Axis I and Axis II disorders) and a family history of alcoholism (factors involving the effect of reducing the amplitude of P3b) were excluded, no reduction in P3b amplitude was observed in the BD group. Conversely, the results of this study have revealed that P3b amplitude is larger in young university BD students than in matched paired controls, an anomaly that could be a specific electrophysiological marker of the BD pattern in young people. In this sense, two recent studies of Bartholow and cols., using a visual
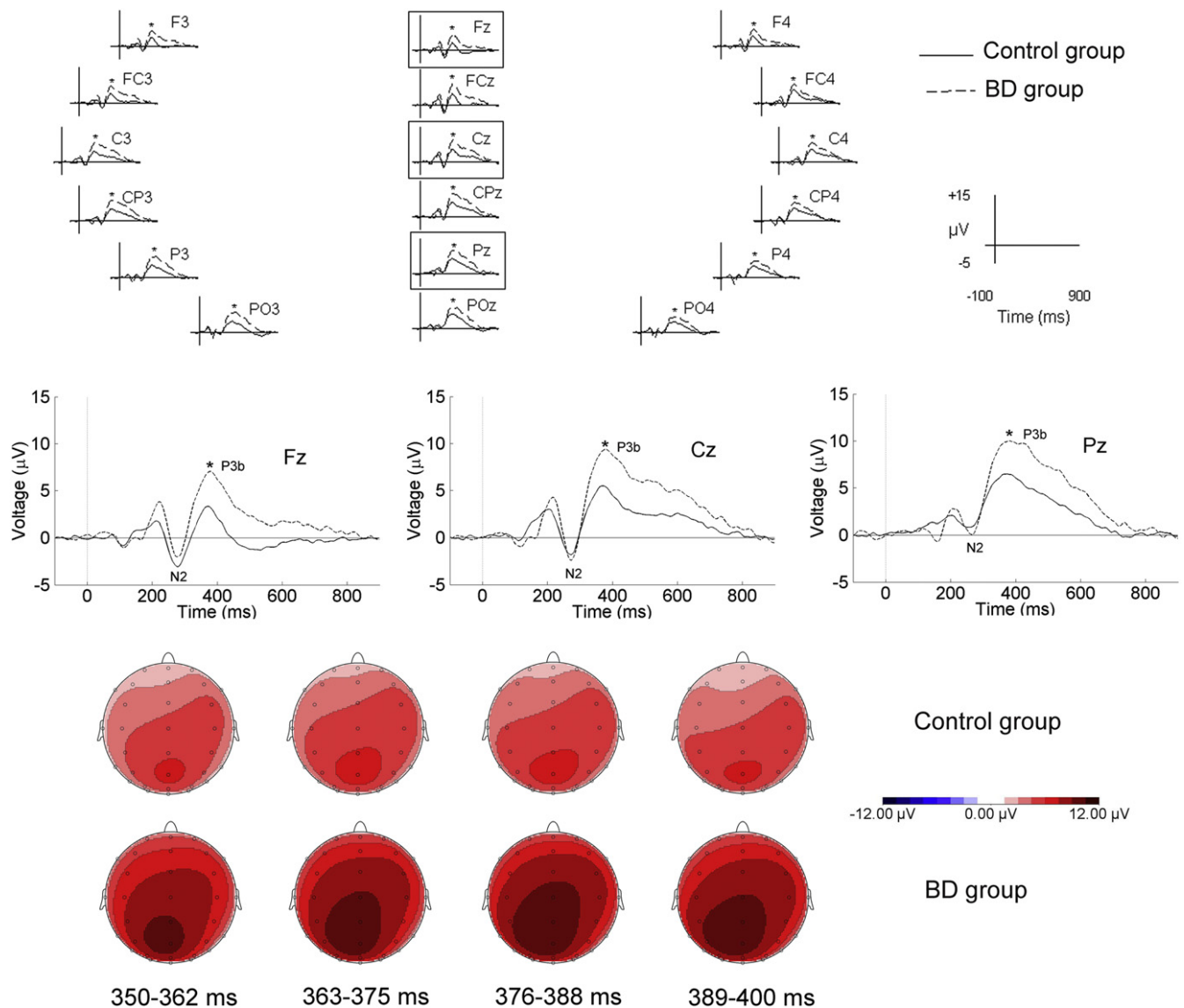
Fig. 4. Grand averages of ERPs and voltage maps corresponding to the peak of P3b component in the males of the control (solid lines) and BD groups (dashed lines) in response to the target stimuli at the 18 electrodes analyzed. Males of the BD group showed larger P3b amplitude in all electrodes and regions analyzed than males of the control group.

oddball task, have found that young university students with low alcohol sensitivity (with an alcohol consumption similar to the BD group in the present study) also showed increased P3b amplitude, but only to alcohol cues (Bartholow, Henry, & Lust, 2007; Bartholow, Lust, & Tragesser, 2010). P3b amplitude elicited by neutral, arousing or non-alcoholic beverage-related images targets did not differ to their high-sensitivity peers (Bartholow et al., 2010). The authors suggested that P3 reactivity to alcohol cues could be a new endophenotype for alcohol use disorder risk. Likewise, increased of P3b amplitude to neutral target stimuli in pure cognitive task also could be a specific electrophysiological marker of the BD pattern in young people and of the alcohol use disorder risk. However, more studies are needed to confirm this result.

A functional explanation of these results would be linked to the results of different fMRI studies by Tapert and cols. (Schweinsburg, Mcqueeny, Nagel, Eyler, & Tapert, 2010; Tapert et al., 2004). These authors reported that adolescents with AUD showed abnormalities in brain response (enhanced BOLD) to a spatial working memory task, despite adequate performance. The authors suggested the involvement of compensatory mechanisms and that binge drinkers

exhibit a greater reliance on alternate memory systems during verbal learning. According to this compensation hypothesis, the larger P3b amplitude observed in the BD group in the present study might suggest that binge drinkers recruit different or wider brain areas associated with attentional processing to compensate the BD-related neurocognitive decline and to successfully complete the specific task. This hypothesis must be further explored with other tasks, perhaps more sensitive to possible behavioral deficits, and complemented with neuroimaging studies before it can be confirmed.

It is also possible that the effects found in the present study were related to an imbalance of neuronal activity in P3b generators. Alcohol generally has a suppressive effect on the CNS: It reduces the activity of excitatory neurotransmitters and their receptors and enhances the activity of inhibitory neurotransmitters and their receptors. After long-term alcohol exposure, a complex set of mechanisms are activated to counteract the effects of the persistent presence of alcohol in the brain. These mechanisms promote the activity of excitatory neurotransmitter systems and suppress the activity of inhibitory neurotransmitter systems, attempting to
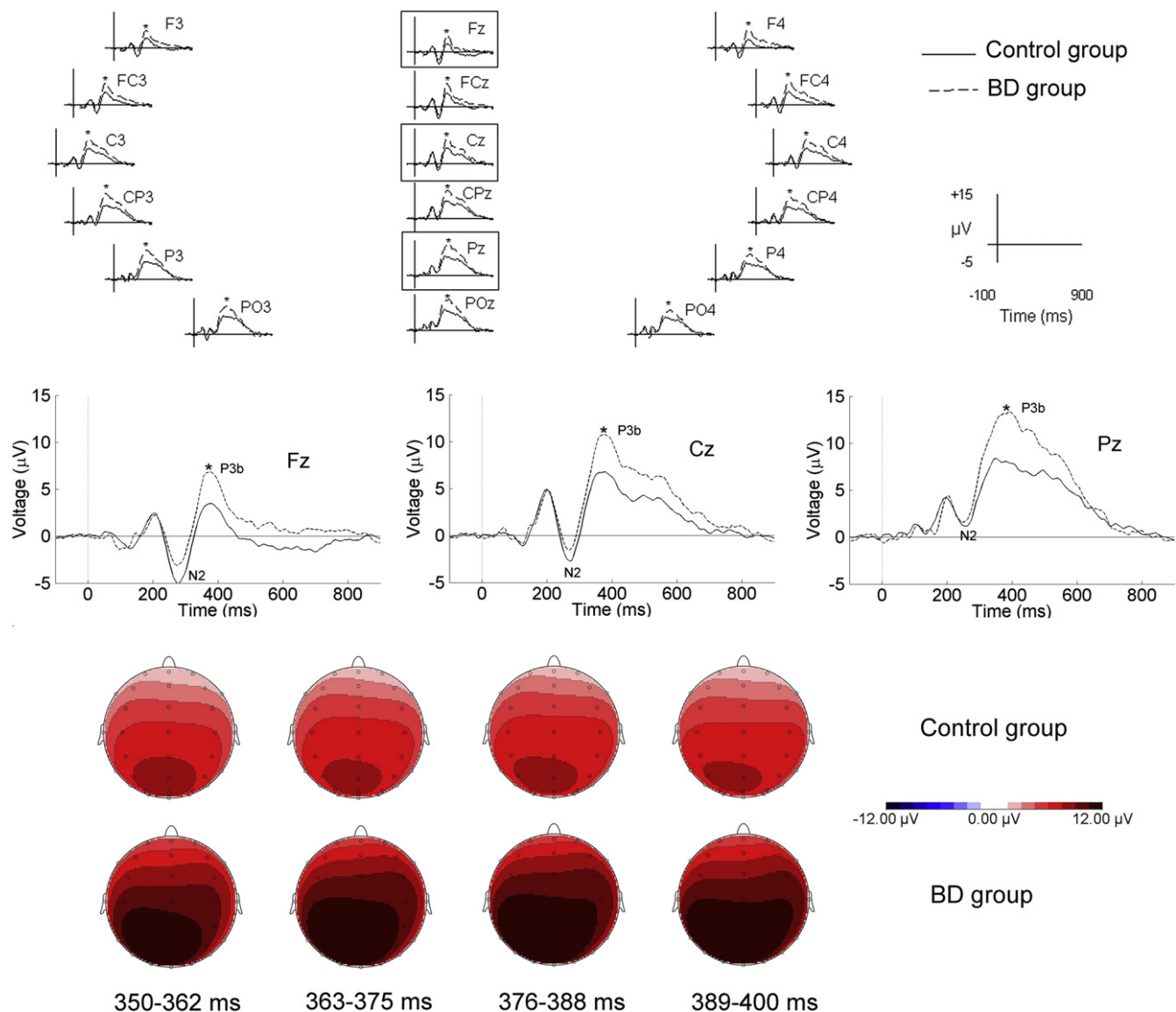
Fig. 5. Grand averages of ERPs and voltage maps corresponding to the peak of P3b component in the females of the control (solid lines) and BD groups (dashed lines) in response to the target stimuli at the 18 electrodes analyzed. Females of the BD group showed larger P3b amplitude in all electrodes and regions analyzed than females of the control group.

return brain function to a "normal" state in the presence of alcohol. When the individual stops drinking, however, these adaptive changes result in an imbalance in inhibitory and excitatory neurotransmission, resulting in CNS hyperexcitability ("kindling effect") that manifests itself as withdrawal symptoms (for a review see Becker, 1998). Binge drinking is characterized by the consumption of large amounts of alcohol within a limited time period followed by a period of abstinence, as opposed to regular drinking, in which a person might consume similar weekly amounts of alcohol but without the extremes of alcohol intoxications and continuous withdrawals. Repeated periods of alcohol binging and withdrawal increase the degree of withdrawal-induced neuronal excitability in several brain areas including amygdala, hippocampus, ventral striatum, periaqueductal gray and frontal cortical areas (for a review see Stephens & Duka, 2008), and the imbalance occurring during withdrawal may accrue with each successive episode and may culminate in a state of persistent increased of neural activity of P3b generators. In this sense, several animal studies have demonstrated increased neural hyperexcitability, alterations in

spontaneous EEG and exacerbation of withdrawal symptoms following repeated withdrawal experiences (Becker & Hale, 1993; Becker & Littleton 1996; Duka et al., 2004). Therefore, taking into account that the total amount of P3b activity represents the summation of the outputs derived from different sources or generators (Johnson, 1993), the larger P3b amplitude observed in the BD group in the present study may be a reflection of an imbalance (increased) of neuronal activity in P3b generators caused by the presence of BD pattern for a long time.

As regards N2, BD did not have any effects on the amplitude of the N2 elicited by standard or targets stimuli. In a previous study by our research group (Crego et al., 2009), the amplitude of N2 was larger in binge drinkers in response to the matching stimuli of a visual pairs-matching continuous task, suggesting higher levels of attentional effort required by these subjects. However, the pairs-matching continuous tasks and the oddball tasks are different in both the level of difficulty and in the nature of the cognitive processes involved, and this might account for the different influence of BD on the N2 amplitude in both experiments.

Table 3
Values of the latency (ms) and amplitude (μV) of the N2 and P3b components (mean ± SD) at the 18 electrodes analyzed in control and BD groups.

| | N2 values for target stimuli | | | | P3b values for target stimuli | | | |
| | Control | | BD | | Control | | BD | |
	Latency	Amplitude	Latency	Amplitude	Latency	Amplitude	Latency	Amplitude
F3	274 ± 27.19	−3.81 ± 3.4	269.69 ± 21.96	−2.64 ± 4.16	379.96 ± 32.6	5.1 ± 4.47	385.31 ± 35.16	8.4 ± 4.42
Fz	277.7 ± 22.62	−4.94 ± 4.06	276.25 ± 17.01	−3.59 ± 4.77	377.81 ± 31.81	4.56 ± 3.99	382.94 ± 32.5	8.28 ± 5.3
F4	271.58 ± 28.22	−4.15 ± 3.7	265.06 ± 26.2	−2.59 ± 4.38	380.23 ± 36.39	5.05 ± 3.66	382 ± 28.42	8.52 ± 4.65
FC3	271.02 ± 27.12	−3.87 ± 3.5	266.75 ± 21.82	−2.75 ± 4.53	377.66 ± 34.09	5.9 ± 5.03	387.5 ± 37.04	9.45 ± 4.82
FCz	272.3 ± 24.66	−5.15 ± 4.25	274.75 ± 17.07	−4.14 ± 5.69	374.04 ± 29.70	6.51 ± 5.04	384 ± 30.14	10.63 ± 6.24
FC4	267.96 ± 24.92	−3.61 ± 3.96	264.56 ± 24.84	−2.55 ± 4.64	379.32 ± 33.16	6.87 ± 4.14	385.37 ± 32.8	9.97 ± 4.9
C3	267.58 ± 27.33	−3.15 ± 3.81	263.87 ± 21.02	−2.57 ± 4.79	379.62 ± 40.72	6.99 ± 5.24	386.75 ± 38.73	10.99 ± 5.06
Cz	269.17 ± 22.15	−3.46 ± 4.6	267 ± 23.15	−3.5 ± 6.32	371.55 ± 35.94	7.71 ± 5.66	386.87 ± 37.54	11.81 ± 6.23
C4	266.75 ± 25.36	−2.72 ± 4.09	264.06 ± 24.91	−2.29 ± 4.94	384.04 ± 39.8	7.53 ± 4.96	388.69 ± 37.58	10.77 ± 5.26
CP3	262.94 ± 26.35	−2.57 ± 3.89	257.75 ± 22.05	−2.36 ± 5.19	375.13 ± 46.89	7.91 ± 5.86	386.75 ± 42.71	12.33 ± 5.09
CPz	263.92 ± 26.27	−1.94 ± 4.54	263.06 ± 21.26	−2.12 ± 6.05	372.87 ± 47.26	8.57 ± 6	385.81 ± 44.72	12.79 ± 6.27
CP4	259.74 ± 26.26	−2.19 ± 4.4	259.81 ± 23.06	−2.03 ± 5.4	375.47 ± 48.74	7.79 ± 5.2	387 ± 40.84	10.91 ± 5.83
P3	254.94 ± 27.9	−2.17 ± 4.02	254.56 ± 22.94	−1.91 ± 5.5	370.34 ± 48.14	8.39 ± 5.94	398.06 ± 45.19	12.68 ± 5.19
Pz	255.58 ± 28.65	−0.81 ± 4.62	259.62 ± 22.43	−0.93 ± 5.85	365.92 ± 50.3	9.57 ± 5.97	387.81 ± 44.14	13.69 ± 6.33
P4	255.85 ± 27.92	−1.58 ± 4.6	256.06 ± 23.09	−1.7 ± 5.77	369.28 ± 53.47	8.11 ± 5.52	395.94 ± 43.77	10.72 ± 5.69
PO3	247.13 ± 27.24	−2.01 ± 4.46	250.31 ± 21.19	−1.69 ± 5.87	368.11 ± 53.61	8.54 ± 5.92	390.44 ± 45.64	12.06 ± 5.57
POz	246.98 ± 26.23	−0.9 ± 4.87	251.87 ± 22.35	−0.64 ± 6.05	364.91 ± 50.79	9.82 ± 6.02	391.81 ± 45.68	12.79 ± 6.29
PO4	248.24 ± 24.89	−1.43 ± 4.86	248.25 ± 22.12	−1.35 ± 6.23	369.55 ± 56.14	8.29 ± 5.77	384. 81 ± 49.69	10.4 ± 5.79

It is well-known that several components contribute to the N2 wave, depending on the type of cognitive processes required by the task. A simple oddball task, such as the one of this study, only requires the categorization of two easily discriminable stimuli, so it is not likely that N2 components associated with processes required in the pairs-matching continuous task, such as maintenance in working memory or conflict monitoring were present in this study (for a review, see Folstein & Van Petten, 2008).

Regarding latency values, which are usually considered an index of the speed of cognitive processing, Maurage et al. (2009) found delayed latencies in the P1, N2 and P3b. The authors compared young adult binge drinkers (more than 10 drinks of 10 g of alcohol at least two times a week) with matched paired controls (both were first-year university students), in a test–retest paradigm over a nine-month period. The potentially biasing variables were controlled and the subjects included met strict selection criteria: no personal or family history of alcoholism, total absence of past or current drug consumption (including tobacco and medication), no

Table 4
Values of P3b amplitude (μV) (mean ± SD) at the 18 electrodes analyzed in males and females of the control and BD groups.

| | P3b values for target stimuli | | | |
| | Control | | BD | |
	Males	Females	Males	Females
F3	4.69 ± 4.1	5.55 ± 4.89	8.24 ± 4.66	8.59 ± 4.29
Fz	4.26 ± 4.19	4.88 ± 3.81	8.48 ± 5.26	8.07 ± 5.52
F4	5.13 ± 3.68	4.96 ± 3.72	8.4 ± 5.18	8.66 ± 4.15
FC3	5.16 ± 4.61	6.73 ± 5.43	8.8 ± 4.58	10.19 ± 5.13
FCz	5.81 ± 5.06	7.29 ± 4.99	10.43 ± 6.01	10.86 ± 6.69
FC4	6.68 ± 4.07	7.08 ± 4.29	9.32 ± 4.93	10.7 ± 4.93
C3	5.94 ± 4.55	8.18 ± 5.78	10.05 ± 4.73	12.05 ± 5.37
Cz	6.87 ± 5.66	8.65 ± 5.62	11.08 ± 5.84	12.65 ± 6.74
C4	6.65 ± 4.16	8.52 ± 5.65	9.79 ± 4.92	11.88 ± 5.58
CP3	6.64 ± 4.88	9.35 ± 6.59	10.78 ± 3.77	14.08 ± 5.91
CPz	7.65 ± 5.63	9.59 ± 6.32	11.56 ± 5.08	14.18 ± 7.32
CP4	6.77 ± 4.32	8.93 ± 5.91	9.45 ± 4.06	12.56 ± 6.31
P3	7.1 ± 4.84	9.84 ± 6.78	10.98 ± 2.92	14.61 ± 6.51
Pz	8.5 ± 5.09	10.77 ± 6.73	11.88 ± 4.23	15.74 ± 7.74
P4	6.82 ± 4.3	9.57 ± 6.42	8.8 ± 3.5	12.89 ± 6.93
PO3	6.92 ± 4.57	10.35 ± 6.79	10.1 ± 2.84	14.28 ± 7.04
POz	8.57 ± 4.69	11.21 ± 7.07	10.68 ± 3.64	15.16 ± 7.8
PO4	6.9 ± 4.56	9.84 ± 6.63	8.51 ± 3.6	12.49 ± 7.1

history of psychiatric disorder and no moderate or high depression-anxiety scores. The results revealed that, although the two groups did not differ in any psychological, behavioral or electrophysiological measures in the first session (before the subjects started binge drinking habits), nine months later, the binge drinkers displayed significantly delayed latency in the P1, N2 and P3 components elicited by emotional auditory stimuli in a discrimination task, although they did not show any differences in amplitude. However, in the present study there were no significant differences in the latency of any component. Perhaps the differences in the specific tasks used by Maurage and cols. (emotional tasks) and in this study (pure cognitive tasks), and even the differences in the sensory modality, would account for the differences in the results relating BD and ERP latencies. In this sense, it must be noted that most of the studies reporting anomalies in ERP latencies in alcoholic populations used auditory stimuli (Cadaveira et al., 1991) or emotional tasks (Maurage et al., 2008).

The assessment of possible gender differences was also of interest in the present study. In the last decade, the prevalence of BD has tended to rank equally among men and women (Wechsler et al., 2002; Young, Morales, McCabe, Boyd, & Darcy, 2005). Several neuropsychological and neuroimaging studies on alcohol consumption have reported that women are more sensitive to the neurotoxic effects of alcohol (Hommer, Momenan, Kaiser, & Rawlings, 2001; Mann et al., 2005; Medina et al., 2008), perform worse in spatial working memory tasks (Townshend & Duka, 2005), and display more anomalous patterns of brain activity than men (Caldwell et al., 2005). However, like in the two previous studies by our research group (Crego et al., 2009, 2010), no significant gender-related differences in the groups were observed in the present study.

Finally, it is important note that the results of this study should be interpreted with caution. Our results need to be generalized and extended and care must be taken in extrapolating the results of this study to other sensory modalities and even to visual stimuli using tasks different from the oddball paradigm.

Conclusions

The results of the present study revealed that young university-student binge drinkers (without AUD, psychopathological comorbilities or family history of alcoholism) show anomalies in ERPs in

comparison with non binge drinking controls. These anomalies are characterized by a larger amplitude of the P3b component, which may suggest that young people with a BD pattern of alcohol consumption during adolescence and early adulthood may experience anomalies in neural processes that mediate attention processing or an imbalance of neuronal activity caused by the presence of BD pattern for a long time. Moreover, taking into account the sensitivity of the ERP technique and the specificity of the effect found, further research is required to confirm these results and to explore the (pre)clinical potential of this electrophysiological marker.

Acknowledgments

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