Addiction

RESEARCH REPORT

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Hyperactivation of right inferior frontal cortex in young binge drinkers during response inhibition: a follow-up study

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ABSTRACT

Aims The objective of this study was to examine brain activity, with particular attention to prefrontal function, during response execution and inhibition in youths who have engaged in binge drinking (BD) for at least 2 years. **Design** Event-related potentials (ERPs) were recorded twice within 3 years, during performance of a Go/NoGo task. **Setting** The study was part of a longitudinal study of the neurocognitive effects of BD. **Participants** A total of 48 undergraduate students, 25 controls (14 females) and 23 binge drinkers (10 females), with no personal or family history of alcoholism or psychopathological disorders. **Measurements** The Go-P3 and NoGo-P3 components of the ERPs were examined by principal component analysis and exact low-resolution tomography analysis (eLORETA). **Findings** Binge drinkers showed larger Go-P3 amplitudes than controls in the first and second evaluations ($P = 0.019$). They also showed larger NoGo-P3 amplitude in the second evaluation ($P = 0.002$). eLORETA analyses in the second evaluation revealed significantly greater activation of the right inferior frontal cortex (rIFC) in binge drinkers than in controls during successful inhibition ($P < 0.05$). **Conclusions** Young binge drinkers appear to show abnormal brain activity as measured by event-related potentials during response execution and inhibition which may represent a neural antecedent of difficulties in impulse control.

Keywords Binge drinking, eLORETA, event-related potentials, inhibitory control, NoGo-P3, prefrontal cortex.

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INTRODUCTION

Alcohol use is common among adolescents and young students. At an age as young as 15–16 years, more than 90% of European students have reportedly drunk alcohol at some point in their lives, on average having their first drink at the age of 12 years, and getting drunk for the first time at 14 years [1]. In a situation similar to that reported in the United States [2] almost half of adolescents in Europe are current drinkers, and approximately 60% of these drinkers follow a pattern of consumption known as binge drinking (BD) [3]. This type of drinking, characterized by the consumption of large amounts of alcohol in a short time followed by a period of abstinence, is generally defined as the consumption of five or more drinks (four or more for females) on one occasion within a 2-hour interval at least once in the last 2 weeks [4].

While neurotoxicity induced by chronic alcoholism has long been known [5], the extent to which BD causes damage is not well known. The main contributions are from animal studies, which have shown that several BD episodes may cause more damage than an equivalent amount of alcohol without withdrawal episodes or consumed on only one occasion [6]. Some studies have also shown that adolescent rats exhibit substantially more alcohol-induced damage than adult rats in brain regions such as the frontal cortex and the limbic system [7–10]. Similarly, young rats are more likely to exhibit cognitive impairment in learning and memory as result of excessive alcohol consumption [11,12].

Recent studies have shown the harmful consequences of alcohol use disorders (AUD) in human adolescents. Such studies reveal that AUD in adolescents can induce brain structure abnormalities and, as in animals, these abnormalities affect mainly the prefrontal cortex (PFC) and the hippocampus [13–16]. Cognitive deficits compatible with damage in these areas have also been revealed consistently in adolescents and youths with AUD [17,18].

Although scarce, studies examining neurocognition in adolescents with a BD pattern emphasize that binge drinkers (BDs) show greater difficulties in neuropsychological tests involving PFC activity, such as working memory, inhibitory control and decision-making [19–25], and in learning and memory tasks associated typically with the hippocampus and the medial temporal lobe [26].

The sensitivity of the adolescent brain to the harmful effects of alcohol appears to be related to the fact that adolescence is a critical period of neuromaturation, during which important changes in structure and function take place [27]. The region experiencing the most noticeable changes is the PFC, which does not reach maturity until early adulthood [28]. Partly as a result of these maturational events in the PFC, executive control processes undergo profound development throughout adolescence [29].

In the present study, event-related potentials (ERPs) were recorded during a Go/NoGo task, in order to identify any possible neurofunctional anomalies in young BDs. This paradigm requires that subjects respond to some trials (Go stimuli) and refrain from responding to others (NoGo stimuli). We chose this task because: (i) to date, no neurofunctional study has evaluated the relationship between inhibitory control and BD; (ii) in addition to the stop-signal task, this is the most suitable task for measuring suppression of a pre-potent response [30]; and (iii) engaging PFC to perform this task has been demonstrated repeatedly [31].

During the task, NoGo stimuli elicit ERPs consisting of a negative deflection (NoGo-N2) at approximately 200–300 ms post-stimulus, with the maximum at fronto-central electrodes, followed by a positive wave (NoGo-P3) between 300–500 ms post-stimulus, with a more fronto-central distribution than the Go-P3 [32]. Although NoGo-N2 has been linked traditionally to response inhibition [33,34], recent evidence relates it to conflict-monitoring processes [35–37]. With regard to NoGo-P3, it has been stated repeatedly to reflect inhibition-related activity [38–40].

Studies using ERPs, transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) have provided evidence that the neural circuits engaged in inhibitory control are included in several PFC areas, especially the right inferior frontal cortex (rIFC) [31,41,42], as well as other regions [43–45].

Neurophysiological dysfunctions have been well established in chronic alcoholics during tasks involving inhibitory control [46,47]. Nevertheless, to our knowledge, response inhibition has not been evaluated from a neurophysiological view in young BDs.

In the present study, the P3 component elicited by ERPs during the performance of a Go/NoGo task and its neural sources, estimated by exact low-resolution electromagnetic tomography analysis (eLORETA), were used to examine the effects of the BD pattern on inhibitory control in young university students. On the basis of the above remarks (disruptive effects of BD on neurocognitive functioning, sensitivity of PFC and vulnerability of immature brain), we predicted that young BDs would exhibit an anomalous prefrontal response during performance of a Go/NoGo task. Similarly, we were interested in assessing whether the possible anomalies related to this consumption pattern were maintained, attenuated or increased over a 2-year follow-up period.

METHODS AND MATERIALS

Participants

Forty-eight undergraduate students participated in the study. Twenty-five were classified as controls (14 females) and 23 as BDs (10 females). The students were evaluated at two different times, when they were aged 18–19 and 20–21 years.

The participants, all students at the University of Santiago de Compostela (Galicia, Spain), were selected on the basis of their responses to a questionnaire that included the Galician validated version of the Alcohol Use Disorder Identification Test (AUDIT) [48], as well as other items regarding use of alcohol and other drugs.

According to the quantitative definition of BD used in European countries such as Spain, where a standard alcoholic drink (SAD) equals about 10 g of alcohol, in the BD group this study included participants who: (i) drank six or more SADs on the same occasion one or more times per week or (ii) drank six or more SADs on the same occasion at least once a month and during these episodes drank at least three drinks per hour. The same criteria were used in both evaluations, so that BDs had to have maintained this drinking pattern for at least 2 years. Participants who drank less than this amount at the time of both assessments were included in the control group.

The participants were also questioned about their personal and family history of alcoholism (FHA) and medical or psychopathological disorders, using the Symptom Checklist-90 revised questionnaire (SCL-90-R) [49] and an adapted version of the Semi-Structured

Assessment for the Genetics of Alcoholism by the Collaborative Study on the Genetics of Alcoholism (COGA) project [50]. The exclusionary criteria are shown in Table 1, and the demographic and drinking characteristics of the selected participants are shown in Table 2 and Fig. 1.

Procedure

Each participant was assessed at two different times within a 2-year interval. They were asked to abstain from consuming drugs and alcohol for 12 hours before the experiment and none of them reported any BD episodes in the 2 days prior to the trial. The participants were also instructed not to smoke or drink tea/coffee for at least 3 hours before the assessments.

A Go/NoGo task was used to evaluate response execution and response inhibition. The participants were instructed to fixate on a small cross located centrally on a CRT monitor. Squares or circles were presented at a visual angle of $3 \times 3°$ for 50 ms over the cross, with a 1000–1400 ms inter-stimulus interval (onset–onset). The number of stimuli ranged between 140 and 160. The participants had to press a button with their preferred hand in response to the Go trials (green circle and blue square) and not to respond to the NoGo trials (blue circle and green square). Stimuli were presented equiprobably in a randomized order.

ERP recording

The electroencephalogram (EEG) was recorded using a Braincap with 32 active electrodes (extended 10–20 International System) referred to the nose tip and grounded with an electrode at Fpz. Vertical and horizontal electro-oculogram readings were also recorded. Electrode impedances were maintained below 10 kΩ. EEG signals were amplified and digitized continuously at a rate of 500 Hz, and filtered with a 0.01–100 Hz band-pass filter.

Table 1 Exclusionary criteria established in the study.

Exclusionary criteria
Family history of first-degree alcoholism or substance abuse
Personal history of psychopathological disorders (according to DSM-IV criteria)
Family history of major psychopathological disorders in first degree relatives
Use of illegal drugs (except cannabis)
Episode of loss of consciousness for more than 20 minutes
History of traumatic brain injury or neurological disorder
Non-corrected sensory deficits
AUDIT scores ≥ 20

AUDIT: Alcohol Use Disorders Identification Test.

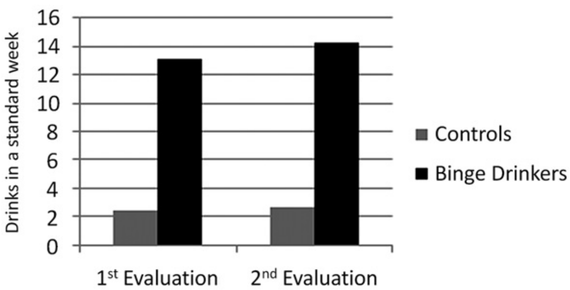

Figure 1 Mean number of drinks consumed by the control and binge drinking subjects during a standard week for the first and second evaluations

Table 2 Demographic and drinking characteristics of the control and binge drinking (BD) groups (mean ± standard deviation).

	First evaluation		*Second evaluation*	
	Controls	*Binge drinkers*	*Controls*	*Binge drinkers*
n (females)	25 (14)	23 (10)	25 (14)	23 (10)
Age	18.6 ± 0.5	18.8 ± 0.5	20.3 ± 0.5	20.7 ± 0.6
Handedness (right/left)	23/2	22/1	23/2	22/1
Caucasian ethnicity (%)	100	100	100	100
Regular tobacco smokers	0	2	1	4
Occasional tobacco smokers	2	5[a]	1	8[a]
Regular use of cannabis	0	4[a]	0	0
Occasional use of cannabis	2	11[a]	1	13[b]
Age of onset on drinking	15.7 ± 0.9	14.6 ± 1.4[a]	15.7 ± 0.9	14.6 ± 1.4[a]
Drinks in a standard week	2.4 ± 3.4	13.2 ± 11.3[b]	2.7 ± 2.2	14.3 ± 5.9[b]
Times consuming six or more drinks per month	0 ± 0.1	2.8 ± 1.5[b]	0.1 ± 0.3	2.9 ± 1.9[b]
Percentage drunkenness	11.5 ± 19.5	55.4 ± 39.5[b]	16.8 ± 26.3	52.5 ± 26.2[b]
Total AUDIT score	2.6 ± 2.3	12.1 ± 3.9[b]	2.6 ± 2.4	10.7 ± 2.7[b]

[a]$t < 0.05$ significant group differences; [b]$t < 0.001$ significant group differences. AUDIT: Alcohol Use Disorders Identification Test.

Data analysis

Behavioural analysis

Only responses occurring between 100 and 1000 ms after the onset of a Go stimulus were considered to be correct responses. The no-responses to NoGo stimuli were rated as correct inhibitions. Reaction times (RT) and percentage of correct responses and inhibitions were analysed by analysis of variance (ANOVA).

ERP analysis

The EEG data were analysed with BrainVision Analyzer software (version 2.0.1). The EEG was corrected for ocular artefacts [51], filtered digitally with a 0.1–30 Hz bandpass filter, segmented into epochs of 1000 ms (100 ms pre-stimulus to 900 ms post-stimulus) and baseline-corrected. Epochs exceeding $\pm 80\ \mu V$ at any scalp electrode were rejected and those corresponding to incorrect responses (omissions or false alarms) were excluded.

The ERPs were examined by temporal principal components analysis (tPCA) to ensure correct identification of the P3 component [52,53]. A covariance matrix-based tPCA was applied separately for both conditions (Go and NoGo). Ten factors, which accounted for 94.2 and 90.9% of the variance of the Go and NoGo conditions, respectively, were selected. Extracted factors were then submitted to Promax rotation. The temporal and spatial characteristics of the components indicated that, for the Go condition, factor 1 corresponded to the Go-P3 component, and for the NoGo condition factor 2 corresponded to the NoGo-P3 component (Fig. 2).

The factor scores corresponding to Go-P3 and NoGo-P3 components were categorized 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 repeated-measures ANOVA with two between-subject factors (group: BD and control; gender: male and female) and two within-subject factors (region: frontal, central and parietal; electrode: six channels) was used to analyse each component (alpha level ≤ 0.05). All *post-hoc* paired comparisons were performed with the Bonferroni adjustment for multiple comparisons, also with an alpha level of 0.05.

eLORETA analysis

eLORETA was used to estimate the cerebral origin of scalp-recorded electrical activity related to the P3 component derived from tPCA for Go and NoGo trials. eLORETA images represent the electric activity at each voxel in the neuroanatomic Montreal Neurological Institute (MNI) space as the exact magnitude of the estimated current density [54].

Voxel × voxel between-group comparisons of the Go-P3 and NoGo-P3 current density distribution were performed. To identify possible between-group differences in the brain electrical activity in Go or NoGo trials, non-parametric statistical analyses of functional eLORETA images (statistical non-parametric mapping; SnPM) were performed, with a *t*-test for independent groups. The results correspond to maps of *t*-scores for each voxel for corrected $P < 0.05$.

RESULTS

Behavioural performance

Behavioural results are summarized in Table 3. There were no significant differences between the control and the BD group, or between genders, for any of the variables

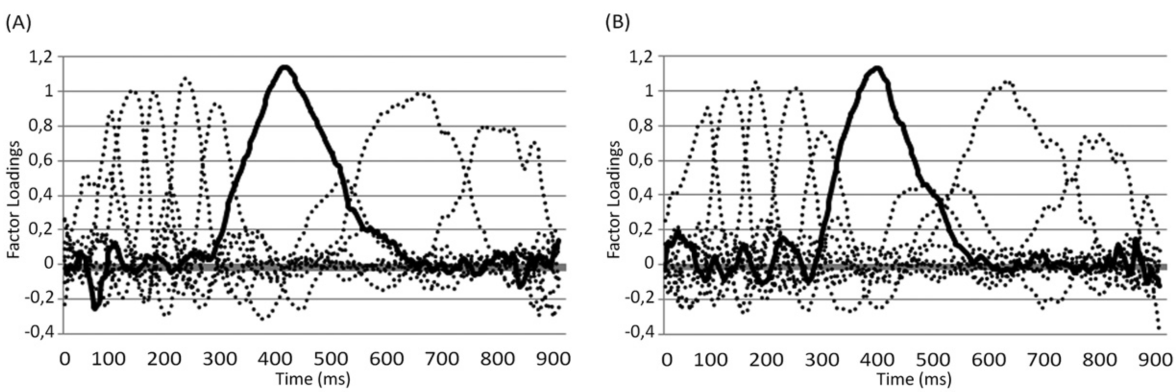

Figure 2 (a) Factor loadings of the ten temporal factors extracted during the Go condition for both the first and second evaluations. Factor 1, associated with the Go-P3 component, is shown as a solid line. (b) Factor loadings of the 10 temporal factors extracted during the NoGo condition for both first and second evaluation. Factor 2, associated with NoGo-P3 component, is shown as a solid line

Table 3 Behavioural data concerning the control and binge drinking (BD) groups in the two evaluations (mean ± standard deviation).

Behavioural performance	*Controls*	*Binge drinkers*
First evaluation		
Response time (ms)	524.22 ± 142.83	528.68 ± 138.61
% Correct responses	94.03 ± 4.85	94.60 ± 4.44
% Correct inhibitions	95.77 ± 5.05	96.81 ± 3.11
Second evaluation		
Response time (ms)	518.96 ± 132.01	519.29 ± 131.14
% Correct responses	95.68 ± 4.87	96.85 ± 3.01
% Correct inhibitions	96.55 ± 4.28	97.42 ± 2.60

analysed (RT and percentage of correct responses and inhibitions) in either of the evaluations.

Electrophysiological results

The grand averages of the ERPs for each group are shown in Figs 3 (first evaluation) and 4 (second evaluation). The components derived from tPCA are shown in Fig. 2.

Analysis of the Go-P3 component in the first and second evaluations revealed significant differences between the groups ($F_{(1,44)} = 5.91$; $P = 0.019$), with higher factor scores in the BD group but no differences between genders. Independent analysis for each evaluation moment confirmed that these differences were significant in both the first and the second assessments. The analysis also revealed significant differences between regions ($F_{(2,88)} = 44.41$; $P < 0.001$), with higher factor scores in the parietal and central regions ($P < 0.001$). Although there were no significant interactions involving region, separate analyses were performed for each, revealing that the differences between the two groups were significant in the central ($F_{(1,44)} = 6.33$, $P = 0.016$) and the parietal ($F_{(1,44)} = 5.69$; $P = 0.021$) regions.

Analysis of the NoGo-P3 component in the first and second evaluations also revealed significant differences between groups ($F_{(1,44)} = 9.33$; $P = 0.004$), but not between genders. However, after independent analysis for each evaluation moment, the differences were significant in the second ($F_{(1,44)} = 11.12$; $P = 0.002$) but not in the first assessments. No differences regarding the region factor were found in this component. Separate analyses for each region in the second evaluation showed significant differences between groups at the three regions: frontal ($F_{(1,44)} = 12.02$; $P = 0.001$), central ($F_{(1,44)} = 11.69$; $P = 0.001$) and parietal ($F_{(1,44)} = 7.47$; $P = 0.009$).

Identical analyses were applied to the N2 component, and there were no significant effects or interactions involving the group factor in either of the two conditions.

eLORETA results

Analysis of the current density distribution revealed significant differences between groups only in the second evaluation, and only for the NoGo trials. Significantly greater activation was observed in the BD than in the control group for the NoGo stimuli, essentially in the right inferior prefrontal gyrus and the insula. The eLORETA maps (SnPM) comparing the neuroelectrical activity of the BD and control groups for NoGo-P3 are shown in Fig. 5. The three-dimensional image of this topographic distribution, along with the centre of NoGo focus observed by Konishi *et al*. [55], is shown in Fig. 6. Those brain regions for which the SnPM *t*-scores for independent groups were significant are listed, along with the MNI coordinates, in Table 4.

DISCUSSION

By measuring ERPs, the present study examined possible anomalies in prefrontal activity in young BDs during performance of a Go/NoGo task. Although there were no behavioural differences between BD and control groups, statistical analysis of the Go and NoGo-P3 components revealed that: (i) the BDs displayed a significantly larger NoGo-P3 amplitude than the controls in the second evaluation as well as a significantly larger Go-P3 amplitude in both first and second evaluations; and (ii) the rIFC was significantly more active during successful inhibition in BDs than in controls in the second evaluation.

Neurocognitive impairments in adolescents and young people derived from alcohol abuse have been observed repeatedly [56]. However, studies of adolescent and young BDs are scarce and the consequences of this pattern are somewhat unclear. Studies focusing on this issue show that BDs perform poorly in tasks involving prefrontal and hippocampal activity [19–26]. In particular, with regard to inhibitory control processes, Townshend & Duka observed that young female BDs were unable to inhibit their response to alerting stimuli in a vigilance task, which was interpreted as a sign of deficit in frontal inhibitory control [21]. Nevertheless, it remains unclear whether these abnormalities in performance reflect underlying neural impairments.

In this sense the present results suggest that, in addition to the dysfunctions observed in neuropsychological tests in other studies, BDs also show neural anomalies liable to be observed by ERPs. The main anomaly identified in this study was the increased amplitude of the P3 component in both conditions (Go and NoGo). Taking into account that the total amount of P3 activity represents the sum of the outputs derived from different sources or generators [57], the larger P3 amplitude in the BDs may be due to additional neural recruitment (or

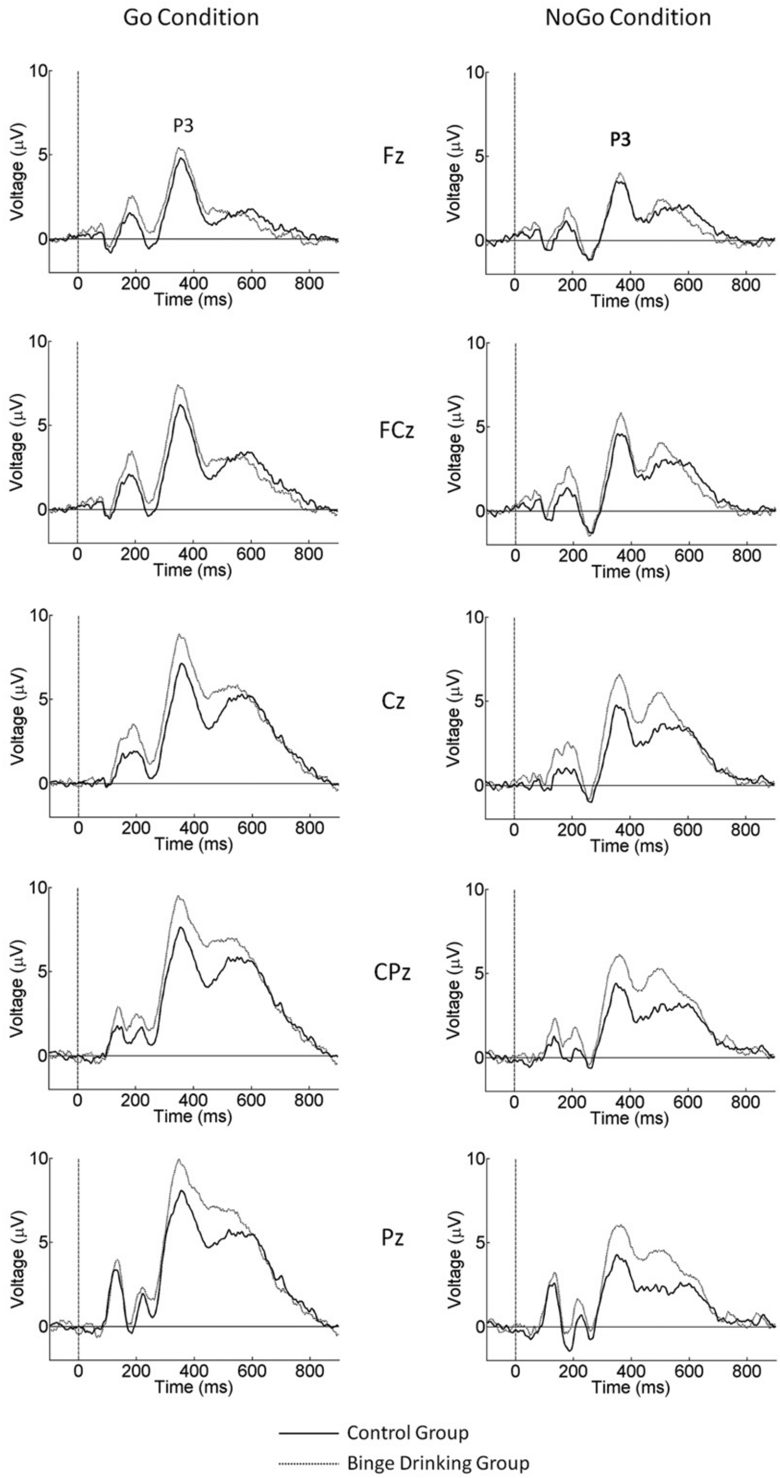

Figure 3 Grand averages of event-related potentials from the control (solid line) and binge drinking (dashed line) group, derived from Go and NoGo trials during the first evaluation. Averages are presented for Fz, FCz, Cz, CPz and Pz electrodes

greater activation of the engaged neural groups) required to resolve the task efficiently.

These results suggest that BD during adolescence and youth may induce disturbances in neural activity. Furthermore, they show that some disturbances may persist (increase in Go-P3 amplitude), whereas others may emerge (increase in NoGo-P3 amplitude) if consumption continues for a period of more than 2 years.

The involvement of the rIFC in the neural circuitry of response inhibition has been documented widely in neuroimaging studies with Go/NoGo and other tasks [58–61], and verified in lesion, TMS and animal studies [62–66]. Similarly, the eLORETA results also showed a clear relation between rIFC and inhibitory control (Fig. 6). Specifically, greater activation of this region during successful inhibition was observed in youths who

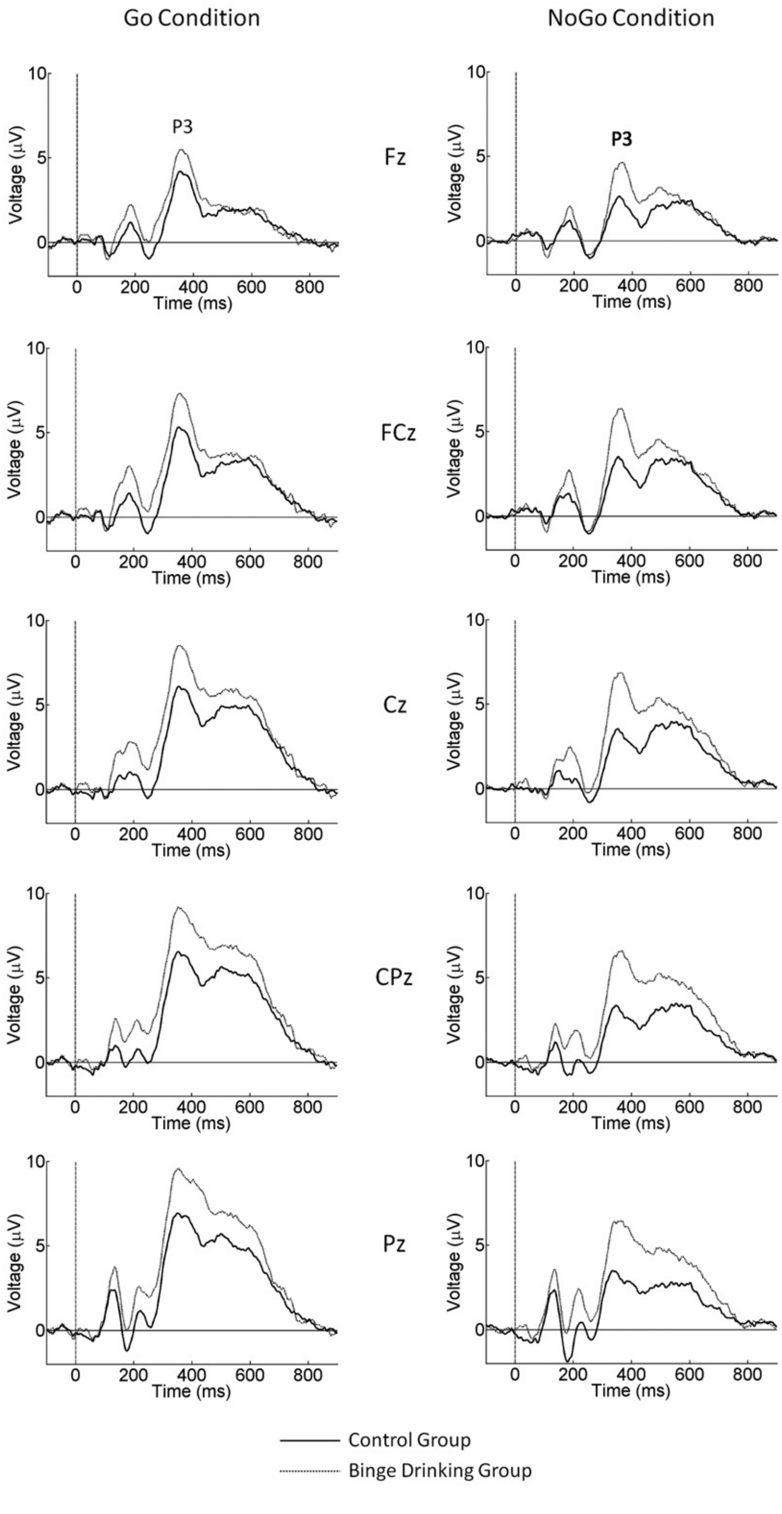

Figure 4 Grand averages of event-related potentials from the control (solid line) and binge drinking (dashed line) group, derived from Go and NoGo trials during the second evaluation. Averages are presented for Fz, FCz, Cz, CPz and Pz electrodes

engaged in BD for at least 2 years, relative to aged-matched controls. This greater neural activation may reflect a compensatory neurofunctional mechanism which would allow BDs to maintain similar task performance as controls, even though the neural system responsible for implementing such action may be compromised.

The greater neural activity in certain areas of the cortex in alcohol-using youths is not a new phenomenon, as has been reported in fMRI studies of BD and AUD sufferers [67–70]. Regarding BD, the only two studies which, to our knowledge, have used this technique showed that the adolescent BDs exhibited over-activation of frontoparietal systems, as well as hypoactivation of several areas

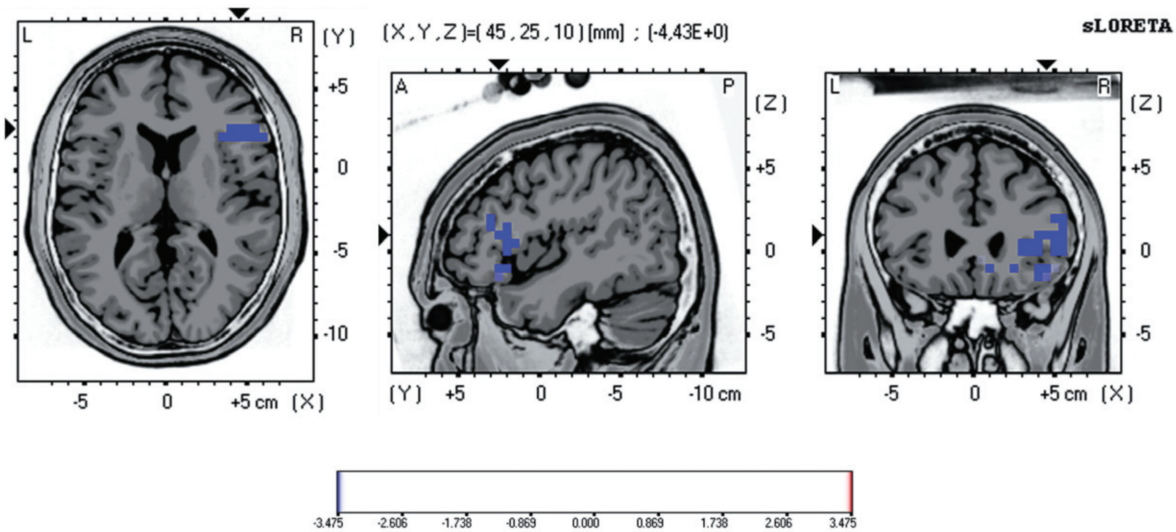

Figure 5 Exact low-resolution tomography analysis (eLORETA)-based statistical non-parametric maps (SnPM), comparing the exact current density values between control and binge drinking subjects during response inhibition for the NoGo-P3 component. Significantly greater activation (corrected $P < 0.05$) in binge drinkers relative to controls is shown in blue. L: left; R: right; A: anterior; P: posterior

of the frontal and occipital cortex during the learning of new word pairs [69,70]. The authors proposed that these findings were suggestive of the use by BDs of alternative memory systems during verbal learning and, more specifically, that the increased right prefrontal activation may partly reflect an increased effort to suppress irrelevant information [69].

Similar results have been reported in a recent ERP study by our research group, in which a larger N2 amplitude was observed in adolescent BDs during a visual identical-pairs continuous performance task [71]. The increased amplitude was also interpreted as indicative of greater attentional effort to perform the task adequately.

Similarly, an fMRI study conducted by Pfefferbaum and colleagues reported that chronic alcoholic adults showed increased activity in the rIFC during performance of a spatial working memory task; the authors interpreted this as reflecting a greater effort in invoking response inhibition by the alcoholics when suppressing non-relevant information [72].

Together, these results suggest that: (a) BDs may be vulnerable to neurofunctional impairments related specifically to the PFC (a class of impairment largely reported in chronic alcoholics [73,74]), and (b) hyperactivation of certain cortical areas may reflect a compensatory mechanism activated in the BDs' brains to perform efficient inhibitory control.

Nevertheless, some aspects of this interpretation must be considered further. On one hand, chronic abstinent alcoholics have been reported frequently to display decreased P3a and P3b amplitudes during performance of auditory and visual tasks [75–77]. However, the fact that these abnormalities do not recover to normal values after long periods of abstinence [78,79], along with the finding that low P3 is also observed in children of alcoholics prior to any alcohol exposure [76,80], have led to the hypothesis that the P3 deficits may precede development of alcoholism, rather than being a consequence of it [81,82]. Considering P3 reduction as a genetic risk marker for alcoholism may explain why an ERP study of young BDs, which included subjects with FHA, reported reduced P3 amplitude [83]. In the present study, in which subjects with FHA were excluded and participants did not display any signs of AUD, no anomalous ERP prior to consumption was expected. Therefore, there is no strong support for the possibility that the BDs consume alcohol to compensate a neurophysiological anomaly and that the increased Go and NoGo-P3 is a transient effect of this alcohol consumption.

Another important issue is the possibility that the anomalous activation observed in the BDs is related to working memory (WM) rather than to inhibition. It is well known that WM involves rIFC activation [84,85], and it is also true that the Go/NoGo task used in the present study involves an important WM load to discriminate between Go and NoGo trials. None the less, if the anomalous increased activity found in rIFC in BDs were related to WM, it would be expected to be present for both the Go and the NoGo stimuli, so that both involve the same WM effort. The e-LORETA results, indicating that the difference from control subjects emerge only for the NoGo stimuli, led us to interpret this in terms of inhibition, and not as a WM process.

On the other hand, one noteworthy aspect of the present study is the fact that the maintenance of a BD pattern for several years appears to lead to an increase in

Table 4 Summary of the brain areas associated with the NoGo-P3 component with significantly higher activation in the binge drinkers relative to controls in second evaluation.

Anatomical region[a]	*Brodmann area*	*MNI coordinates (x, y, z)*	*t-score*
Inferior frontal gyrus	13	45, 25, 10	−4.43213**
		45, 25, 10	−4.41871**
	45	50, 25, 10	−4.38060**
		40, 20, 5	−4.36656**
		55, 25, 10	−4.29541**
		35, 25, 5	−4.27748**
		45, 20, 5	−4.26735**
		40, 20, 10	−4.18929**
		45, 20, 10	−4.17791**
		55, 30, 15	−4.15459**
		50, 20, 10	−4.13146**
		55, 25, 15	−4.12537**
		50, 20, 5	−4.12045**
		55, 25, 5	−4.11050**
		55, 20, 10	−4.05311**
		55, 20, 5	−3.94199*
		60, 20, 15	−3.92404*
		55, 20, 15	−3.85419*
		55, 30, 20	−3.84672*
		55, 30, 5	−3.83728*
		50, 20, 15	−3.75153*
		55, 25, 20	−3.71946*
		45, 20, 15	−3.60448*
		50, 25, 20	−3.58256*
		60, 20, 20	−3.54531*
	46	45, 30, 15	−4.04154**
		50, 30, 20	−3.76249*
	47	40, 20, 5	−4.31148**
		50, 25, 5	−4.22008**
		40, 20, 0	−4.15372**
		45, 20, 0	−4.04818**
		35, 25, 0	−4.02981**
		40, 25, 0	−4.02835**
		35, 20, −5	−3.90584*
		50, 25, 0	−3.88982*
		50, 20, 0	−3.88787*
		30, 20, −5	−3.87844*
		55, 25, 0	−3.74679*
		55, 20, 0	−3.63869*
		35, 20, −10	−3.63495*
		40, 25, −10	−3.63442*
		50, 20, −5	−3.63411*
		30, 20, −10	−3.58839*
		45, 25, −10	−3.57927*
		45, 20, −10	−3.53804*
		25, 25, −10	−3.52889*
		40, 25, −15	−3.50970*
Insula	13	35, 20, 5	−4.40223**
		35, 20, 10	−4.14922**
		30, 25, 0	−4.00446**
		40, 15, 5	−3.62331*
		35, 15, 0	−3.59755*
		45, 15, 5	−3.52917*
		40, 15, 0	−3.50679*
	45	30, 25, 5	−4.19978**
Extra-nuclear	47	35, 20, 0	−4.19772**
Precentral gyrus	44	60, 20, 10	−4.05834**
Middle frontal gyrus	46	45, 30, 20	−3.64288*
Subcallosal gyrus	11	10, 25, −10	−3.49176*

[a]All the anatomical regions are located in the right cortex. *Corrected $P < 0.05$; **corrected $P < 0.01$. MNI: Montreal Neurological Institute.

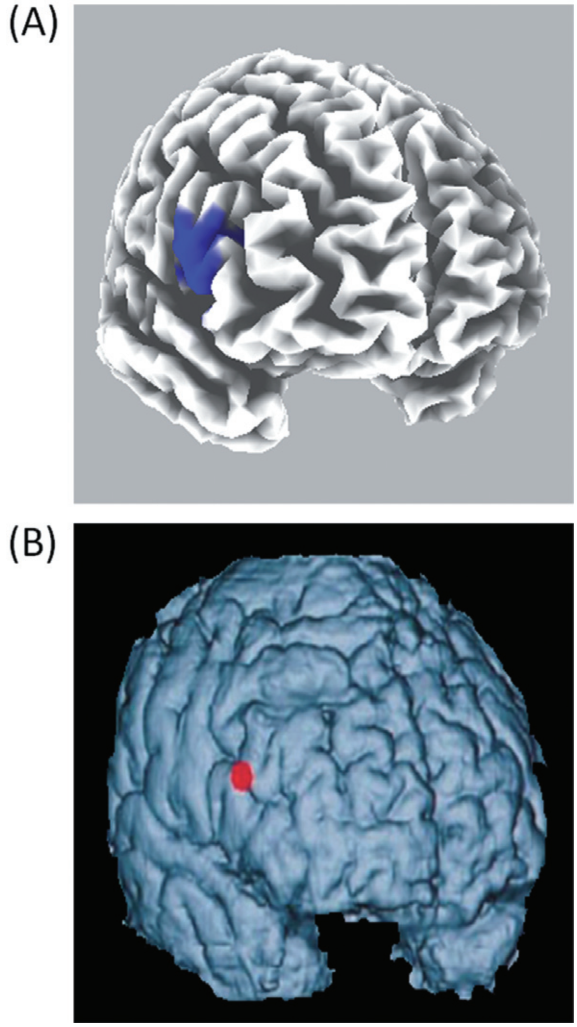

Figure 6 A) Three-dimensional eLORETA image relating to the NoGo-P3 component showing significantly higher activation in the right inferior frontal cortex (rIFC) in binge drinkers relative to controls during response inhibition. (B) Brain activity focus registered by fMRI in Konishi's study [58] while the response was avoided. Note that the coloured regions are similar in both cases. Figure reproduced from [58] with permission from Oxford University Press

neural anomalies in youths. To our knowledge, only one other study has assessed the effects of the duration of BD [86]. In that study, Maurage and colleagues found that, after 9 months of BD, youths presented delayed latencies in P1, N2 and P3 components elicited by emotional auditory stimuli, without any behavioural differences from controls. The authors interpreted these results as indicating slowed cerebral activity in the BDs after several months of consumption. In addition, neuropsychological studies with alcohol-dependent adolescents have reported a positive relation between life-time alcohol episodes and the magnitude of neurocognitive deficits [87]. As in these studies, the present results appear to show that the longer the BD pattern of consumption is maintained, the greater the expression of neurophysiological anomalies.

Finally, inhibitory control impairment has been indicated as a risk factor for substance abuse [88,89]. Thus, the anomalies in the rIFC reported here may represent a neural antecedent of posterior difficulties in impulse control (and therefore in control of alcohol consumption) in youths who have maintained a BD pattern for several years. However, this possibility must be tested in more extensive follow-up studies.

In summary, the present results indicate that, despite similar levels of behavioural performance in the groups, young BDs manifest anomalous neural activity, as demonstrated by increased P3 amplitude during response execution and inhibition in a Go/NoGo paradigm. The electrophysiological anomalies during response inhibition appear only after the subjects engage in a BD pattern for at least 2 years, and are associated with hyperactivation of the rIFC, which may suggest activation of additional neural mechanisms to compensate emerging functional alterations in the regions engaged in inhibitory control.

Declarations of interest

All authors reported no biomedical interests or potential conflicts of interest.

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