

# Alcohol-related stimuli modulate functional connectivity during response inhibition in young binge drinkers

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## Abstract

Binge drinking is a pattern of intermittent excessive alcohol consumption that is highly prevalent in young people. Neurocognitive dual-process models have described substance abuse and adolescence risk behaviours as the result of an imbalance between an overactivated affective-automatic system (related to motivational processing) and damaged and/or immature reflective system (related to cognitive control abilities). Previous studies have evaluated the reflective system of binge drinkers (BDs) through neutral response inhibition tasks and have reported anomalies in theta (4–8 Hz) and beta (12–30 Hz) bands. The present study aimed to investigate the influence of the motivational value of alcohol-related stimuli on brain functional networks devoted to response inhibition in young BDs. Sixty eight BDs and 78 control participants performed a beverage Go/NoGo task while undergoing electrophysiological recording. Whole cortical brain functional connectivity (FC) was evaluated during successful response inhibition trials (NoGo). BDs exhibited fast-beta and theta hyperconnectivity in regions related to cognitive control. These responses were modulated differently depending on the motivational content of the stimuli. The increased salience of alcohol-related stimuli may lead to overactivation of the affective-automatic system in BDs, and compensatory neural resources of the reflective system will thus be required during response inhibition. In BDs, inhibition of the response to alcohol stimuli may require higher theta FC to facilitate integration of information related to the task goal (withholding a response), while during inhibition of the response to no-alcoholic stimuli, higher fast-beta FC would allow to apply top-down inhibitory control of the information related to the prepotent response.

## KEYWORDS

adolescence, binge drinking, dual-process model, electroencephalography, functional connectivity, response inhibition

## 1 | INTRODUCTION

Binge drinking (BD) is a pattern of alcohol consumption in which intense episodes of intake that lead to intoxication (with blood alcohol

concentration levels reaching 0.08 g/dl in a short time interval<sup>1</sup>) alternate with periods of abstinence. This drinking pattern becomes problematic during adolescence and young adulthood, when intoxication at weekends alternates with abstinence during working days.<sup>2</sup>

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The neurocognitive consequences of BD have been explored within the framework of dual-process models. These models propose that most complex human behaviours, such as decision-making, are the result of the interplay between affective-automatic and reflective-executive systems.<sup>3</sup> Previous research has shown an imbalance between these systems in adolescence<sup>4</sup> and that this imbalance is exacerbated by drug abuse.<sup>5</sup> An imbalance between a dominant affective-automatic system and an immature or damaged reflective system would explain nonadaptive decision-making driven by short-term goals.

Although the mechanisms underlying this imbalance are different in adolescence and addiction models, they may complement each other in substance use during adolescence.<sup>6</sup> As the reflective system of the adolescent brain is still developing, the neurotoxic effects of alcohol may be especially deleterious during adolescence.<sup>7</sup> By impairing normal neurodevelopment, alcohol consumption could lead to perpetuation of the dominant short-term decision-making phenotype that manifests in adolescence, which could finally lead to substance use disorders and other types of behavioural dysregulation.<sup>8</sup>

Response inhibition (controlling prepotent or inappropriate responses) is one of the executive functions consistently found to be disrupted in young/adolescent binge drinkers.<sup>9</sup> According to dual-process models, Go/NoGo tasks with alcoholic cues enable exploration of the influence of the motivational characteristics of stimuli on the capacity to inhibit responses. Event-related potential (ERP) studies with alcohol cued Go/NoGo tasks report anomalies in binge drinkers while they are responding to motivational cues. These anomalies include delayed latency of P3-NoGo<sup>10</sup> and most consistently altered N2-NoGo amplitudes.<sup>11–13</sup>

According to conflict monitoring theory,<sup>14</sup> alcohol-related cues may increase the conflict between the prepotent Go response and inhibition of the response during NoGo trials. Attentional bias in response to alcohol-related images may disrupt task performance in binge drinkers,<sup>15,16</sup> unless compensatory cognitive control resources are recruited.<sup>11,12</sup> This compensatory activity has also been examined using functional magnetic resonance imaging (fMRI) analysis. Thus, fMRI studies have revealed increased activity during successful inhibition of the motor response to alcohol-related pictures in binge drinkers in brain structures related to cognitive control, such as the right dorsolateral prefrontal cortex, anterior cingulate cortex (ACC) and right anterior insula extending to the inferior frontal gyrus (IFG).<sup>17,18</sup>

Brain functioning in BDs during Go/NoGo tasks can also be studied by neuro-oscillatory activity. According to communication through coherence theory, only coherently oscillating neuronal groups (phase-locked) can communicate effectively. These oscillations have been described in different frequency bands both during resting and active experimental conditions, subserving diverse neural processes. Response inhibition has been related to theta (4–8 Hz) and beta (12–30 Hz) electroencephalographic activity (EEG). Specifically, during response inhibition tasks, frontal theta activity might work as a mechanism to facilitate the integration of information related to current goals during decisional stages of the task, whereas beta band activity could be subserving top-down inhibitory mechanisms.<sup>19,20</sup> Some BD studies have reported anomalies in these frequency bands in

Go/NoGo tasks with neutral stimuli, that is, an overall decrease in beta band power during the early stages of response inhibition<sup>21</sup> and reduced theta band activity during NoGo trials that was correlated with the number of BD episodes.<sup>21,22</sup>

Two magnetoencephalography (MEG) studies have analysed functional connectivity (FC) during Go/NoGo tasks. FC is defined as the statistical and temporal dependence between the activities of two or more brain regions.<sup>23</sup> In this vein, Correas et al.<sup>24</sup> reported that binge drinkers exhibited lower theta band connectivity than controls in the prefrontal network during the allocation of attentional resources and selection and execution of Go responses. Antón-Toro et al.<sup>25</sup> detected anomalies in alcohol-naïve adolescents 2 years before they became BDs: During NoGo trials, the future binge drinkers exhibited a wide pattern of beta band hyperconnectivity in a 250- to 350-ms time window in inhibitory control networks (supplementary motor area -SMA-, ACC, right IFG and left hippocampus).

In the present study, we aimed to explore EEG FC during response inhibition in a Go/NoGo task with alcohol-related stimuli in BD university students. This task has already enabled us to identify anomalies in BDs in ERP components related to conflict monitoring (N2-NoGo amplitude)<sup>11</sup> as well as anomalies in frontal BOLD activity recorded by fMRI.<sup>18</sup> From the perspective of dual-process models, these findings suggest that binge drinkers may need to recruit extra neural resources from the reflective system to overcome an affective-automatic system overactivated by the motivational salience of alcohol-related pictures.

Analysis of FC networks in the same sample and task will provide further information, characterising the functioning of inhibitory control networks and how these are modulated by the motivational value of stimuli. In line with previous findings,<sup>21,22,24</sup> we expected to observe anomalies related to inhibitory activity in theta and beta band connectivity.<sup>19,20</sup> According to the compensatory hypothesis and our previous findings,<sup>11,18</sup> we postulate that binge drinkers will exhibit increased connectivity in these EEG bands in functional networks related to inhibitory control. The increased activity of the reflective system would compensate for overactivation of the affective-automatic system in the presence of alcohol-related stimuli.

## 2 | MATERIALS AND METHODS

### 2.1 | Sample

The final sample comprised 146 subjects: 78 controls (38 women) and 68 binge drinkers (43 women). The participants were selected within the framework of a broader research project on BD among university students. The sample selection process, instruments and exclusion criteria are described in our previous study.<sup>11</sup> Subjects were classified according to the number of binge drinking episodes (BDEs) in the last 180 days. A BDE was defined as the consumption of five standard drinking units (SDUs, one Spanish SDU = 10 g of alcohol) for females and seven SDUs for males. Subjects who reported fewer than six BDEs in the last 180 days were included in the control (CN) group,

while subjects who reported six or more BDEs in this period were included in the BD group.

Of the 159 subjects who met inclusion criteria and completed the psychophysiological assessment, 13 were excluded from the study: 3 subjects because of low task performance and 10 subjects because of artefacts in the EEG recordings (according to a quality criterion of at least 60% preserved segments for correct Go trials or 20 segments for correct NoGo trials). The sociodemographic characteristics of the final sample are summarised in Table 1. None of the participants met the criteria for nicotine dependence, according to the Nicotine Dependence Syndrome Scale, short version (NDSS-S) scores.<sup>26</sup> None of the subjects had problematic cannabis use according to the *Observatorio Español de las Drogas y las Adicciones* (OEDA) criteria based on the Cannabis Abuse Screening Test scores.<sup>27</sup>

All participants gave written informed consent and received monetary compensation for their participation. The study was approved by the Bioethics Committee of the University of Santiago de Compostela.

## 2.2 | Procedure and task

The subjects performed a beverage Go/NoGo task (Figure 1), as previously described.<sup>11</sup> The task comprised two conditions: In one of them, Go stimuli were pictures of alcoholic (Al) drinks and NoGo stimuli were pictures of nonalcoholic (NoAl) drinks (Go-Al vs. NoGo-NoAl). In the other condition, the stimuli were reversed, that is, Go-NoAl versus NoGo-Al. Behavioural data analysis and results can be consulted in the supporting information.

**TABLE 1** Sociodemographic and consumption characteristics of the CN and BD groups

Sociodemographic/substance use variables	CN	BD
<i>n</i>	78	68
Sex (male/female <i>n</i> )	40/38	25/43
Age (range)	18–19	18–19
Tobacco consumption ( <i>n</i> > 2 cigarettes/day)	0	4
Cannabis consumption ( <i>n</i> with >3 and <12, in the last 90 days)	1	11
SCL-90-R: GSI (percentile scores)*	44.0 (26.89)	57.01 (23.78)
Age of onset of drinking**	16.25 (1.14)	15.43 (1.16)
BDEs (last 180 days)**	0.76 (1.67)	22.60 (11.87)
No drinks during peak consumption (2-h lapse)**	2.26 (1.30)	5.03 (1.36)
AUDIT**	1.96 (2.69)	9.35 (4.55)

Note: Mean values (standard deviation) for CN and BD groups. Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; BD, binge drinker; BDEs, binge drinking episodes; CN, control; SCL-90-R, GSI, Symptom Checklist-90-Revised, Global Severity Index.

\**p* < 0.05. \*\**p* < 0.001.

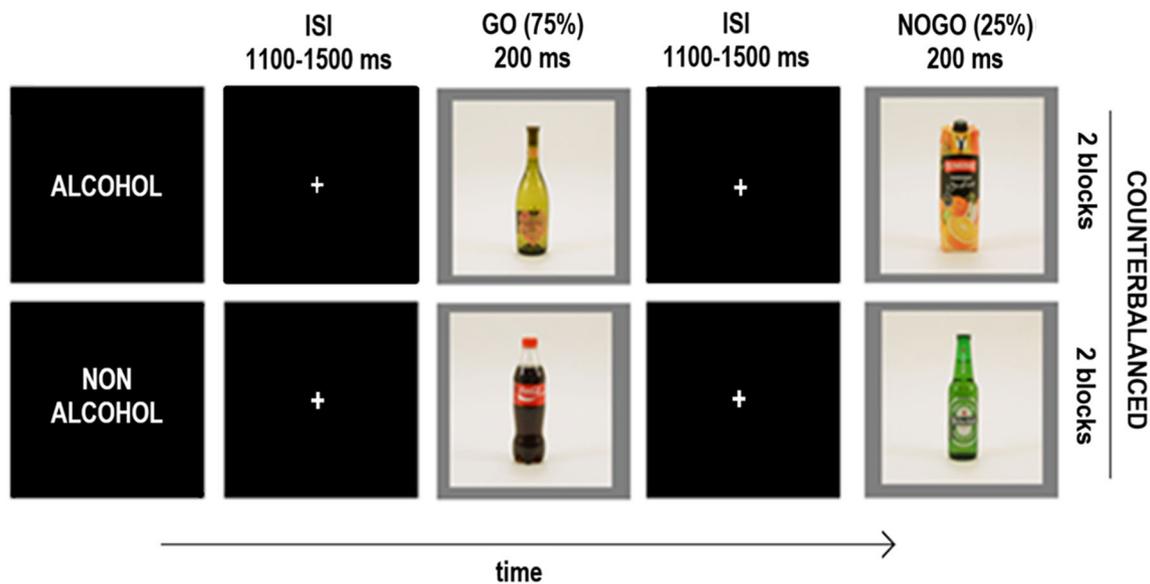
## 2.3 | EEG recording and processing

EEGs were recorded from 64 electrodes located according to the extended 10-20 International System,<sup>28</sup> using an Acticap System (Brain Products, Munich, Germany). The reference electrode was placed at the tip of the nose, and the ground electrode was at Fpz. To control ocular artefacts, horizontal (HEOG) and vertical (VEOG) electrooculograms were recorded. Impedances were kept below 20 kΩ. The EEG signal was amplified with BrainAmp DC amplifiers and filtered online with a 0.01- to 100-Hz band-pass filter and a notch filter of 50 Hz. Sampling rate was set at 500 points/s.

Raw EEG recordings were processed in the first phase with BrainVision Analyzer software (v. 2.1) (Brain Products GmbH, Scientific Support, Gilching, Germany). Failed EEG channels (due to partial or total lack of EEG activity) were disabled. The signal was off-line filtered at 0.1–47 Hz (12 dB/oct), and EOG, EKG and EMG artefacts were removed by Independent Component Analysis (ICA). Finally, EEG recordings were re-referenced to the average of all the scalp channels. EEG was segmented with a –1300- to 1900-ms stimulus-locked epoch, which included a padding of 900 ms before and after the segment of interest (–400 to 1000 ms), necessary for a subsequent processing phase. Baseline was corrected (adjusted to 0 μV in the –400- to 0-ms interval), and segments including artefacts exceeding ±100 μV were rejected. Only NoGo trials with correct performance were considered (NoGo trials no-followed by a response) for evaluation of the hypothesis. The resulting data for each subject and trial category were exported for processing and analysis with *FieldTrip*, the MATLAB toolbox for EEG analysis.<sup>29</sup> Although evaluation of Go trials was outside the scope of the study, we analysed them to facilitate data interpretation. Data processing and analysis of Go trials followed the same rationale depicted below for NoGo trials and can be consulted in the supporting information.

## 2.4 | Source reconstruction

Source reconstruction from the EEG activity recorded at the scalp requires resolution of the forward problem and the inverse problem. To solve the forward problem, we used the boundary element method (BEM).<sup>30</sup> The BEM requires specifying the position of the electrodes, a head model and a source model. We used a standardised template of 346 electrodes, in which the 60 scalp channels positions are defined. The Montreal Neurological Institute (MNI) brain atlas was used as the head model. This information was used to generate the source model in MATLAB, that is, a homogeneous three-dimensional template of the brain (with a separation of 1 mm between sources), resulting in 2459 sources located within the cranial cavity. According to the Automated Anatomical Labeling (AAL) atlas,<sup>31</sup> we selected 76 cortical regions of interest (ROIs) for further analysis, encompassing a total of 1,188 source positions. For the inverse problem, we calculated a linear constrained minimum variance (LCMV) beamformer as a spatial filter.<sup>32</sup> To eliminate possible phase



**FIGURE 1** Beverage Go/NoGo task: Subjects had to press the left-hand button of the mouse only in response to the Go stimuli (pictures of alcoholic or nonalcoholic beverages according to the condition)

distortions, we implemented a digital FIR (Finite Impulse Response) filter of order 400 through a Hamming window applied in two steps.

We calculated source-space electrophysiological activity for the frequency bands related to the hypothesis: theta (4 to 8 Hz), slow-beta (12 to 20 Hz), fast-beta (20 to 30 Hz) and whole beta (12 to 30 Hz). We selected an early time window from 100- to 550-ms post-stimulus, in order to encompass the ERP components identified in our previous study (P1, N2-NoGo and P3-NoGo).<sup>11</sup> Additionally, we calculated the p100 visual component using the spatial filter beamformer, in order to check the robustness of source-space signal reconstruction (see the supporting information, Figure S1).<sup>25</sup>

## 2.5 | Functional connectivity

FC was calculated under the hypothesis of phase synchronisation,<sup>33</sup> through the phase locking value (PLV).<sup>34</sup> Thus, FC was calculated from the distribution of the differences in the instantaneous phase of two time-dependent signals. In the present study, the instantaneous phase of the signals was estimated using the Hilbert transform (for a detailed description, see Bruña et al<sup>35</sup>).

According to the aim of the study, in order to explore the FC patterns associated with response inhibition in relation to the motivational content of the stimuli, we computed the PLVs associated with NoGo trials (NoGo-Al, NoGo-NoAl). Within each type of stimulus, we obtained a matrix of PLVs for each previously defined frequency band in the selected time window. First, we calculated PLV value for each pair of cortical sources, resulting in a FC matrix of  $1188 \times 1188$  elements for each subject and frequency band. Secondly, we averaged PLV values of cortical sources within each of 76 predefined ROIs, obtaining a  $76 \times 76$  connectivity matrix per subject, frequency band and condition.

## 2.6 | Statistical analysis

Within-group comparisons were made between type of stimuli (NoAl vs. Al) for each group and frequency band. Between-group (BD vs. CN) comparisons were made for each type of stimulus and frequency band. For each comparison (within and between groups), we performed a permutation-based ANOVA between each pair of cortical ROIs. We also corrected the resulting *p*-values by multiple comparisons using the false discovery rate (FDR) method at 0.1. Only connectivity links with *p*-values below FDR threshold were considered significant. In order to suppress potential source leakage and volume conduction bias over our results, we performed an additional correction of these effects by using spatial filter correlations. We introduced significant results in an ANCOVA model with the beamformer correlation as a covariate, as reported in previous studies.<sup>25,36</sup> This method is described in greater detail in the supporting information.

## 3 | RESULTS

### 3.1 | Within-group effects (NoAl vs. Al)

#### 3.1.1 | Binge drinkers

The BD group exhibited higher theta (4–8 Hz) FC in 35 links during correct response inhibition to Al stimuli than NoAl stimuli ( $p < 0.0013$ , FDR = 0.1). The significant links were mainly located within right hemisphere regions. The connectivity between orbitofrontal (bilateral rectus gyri, orbital parts of bilateral superior frontal gyri [SFG], right middle frontal gyrus [MFG] and right IFG) right parietal regions (angular gyrus, postcentral gyrus, superior, middle and inferior parietal gyri) and right temporal regions was particularly notable. Orbital parts

of right SFG and right MFG also showed higher FC with bilateral SMA. Figure 2 shows a topographical representation of the distribution of connectivity links.

In addition, the BD group exhibited lower fast-beta (20–30 Hz) FC during correct response inhibition to AI stimuli than to NoAI stimuli. A pattern of hypoconnectivity between the right IFG and the right calcarine fissure was detected ( $p < 0.00006$ , FDR = 0.1). Figure 3 represents the cortical distribution of significant links.

No other significant within-group differences were observed in the BD group.

### 3.1.2 | Controls

Regarding CN group, we did not find any significant within-group differences in FC between AI and NoAI stimuli during response inhibition.

## 3.2 | Between-group effects (BD vs. CN)

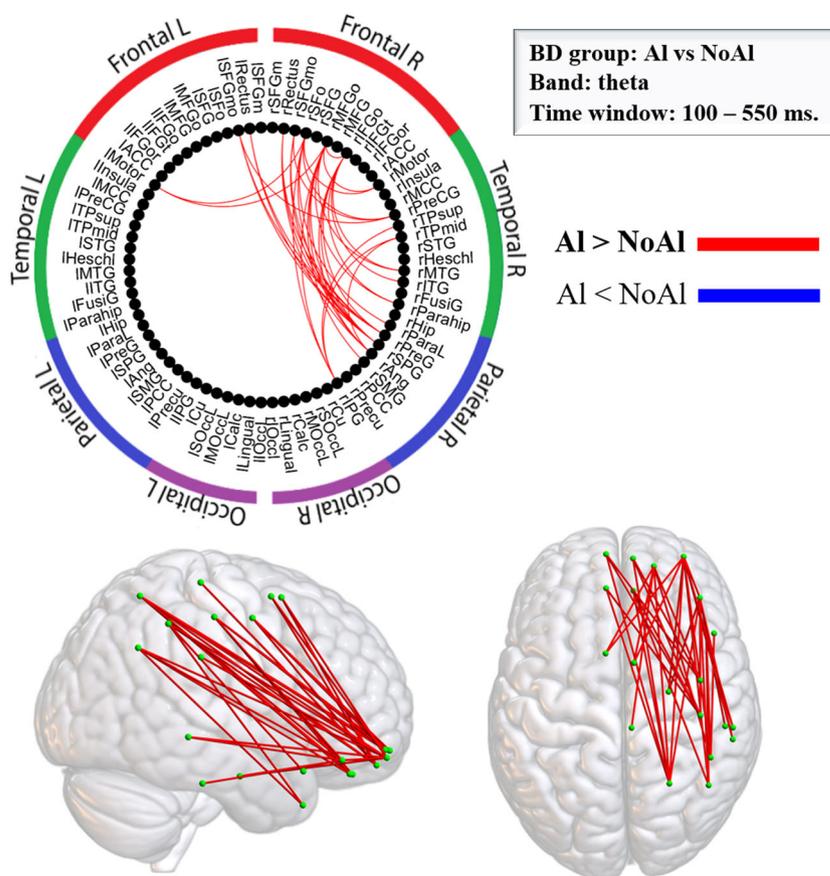
### 3.2.1 | AI stimuli

During correct response inhibition to AI stimuli, the BD group exhibited higher theta FC than CNs in 44 links, which mainly involved right hemisphere regions ( $p < 0.001$ , FDR = 0.1). The observed

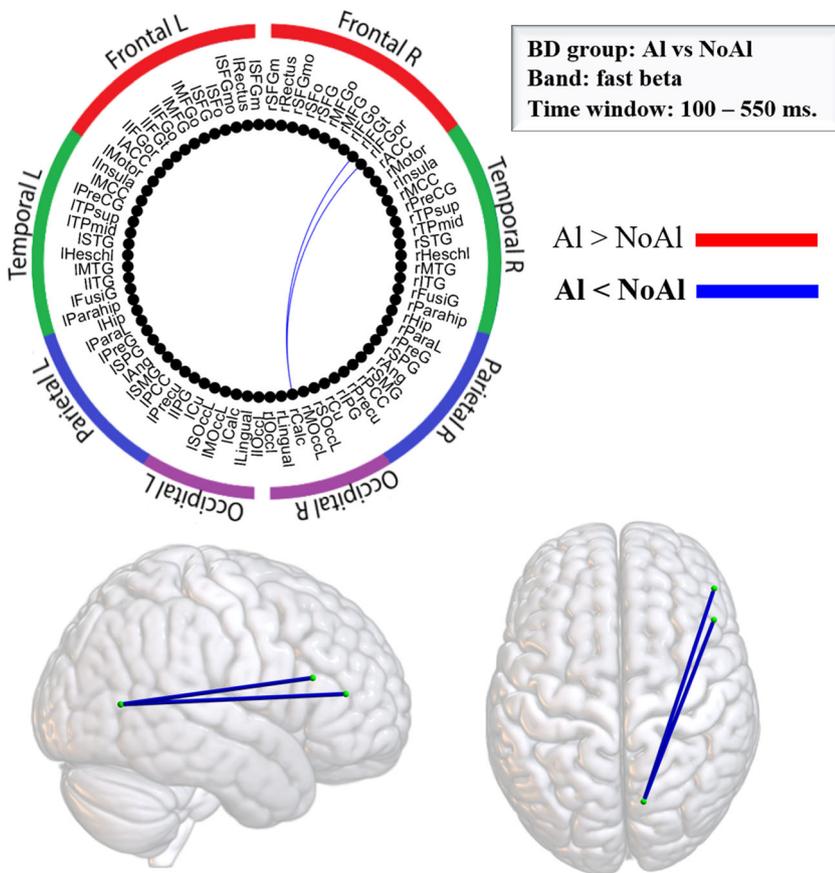
pattern highlighted the connectivity between orbitofrontal regions and specific regions of the right parietal cortex (superior parietal gyrus, angular gyrus and postcentral gyrus) and, to a lesser extent, right occipital regions. In addition, in specific regions such as the right insula, bilateral ACC showed higher FC with the mentioned right parietal and occipital regions. The cortical distribution of significant connectivity links is shown in Figure 4.

### 3.2.2 | NoAI stimuli

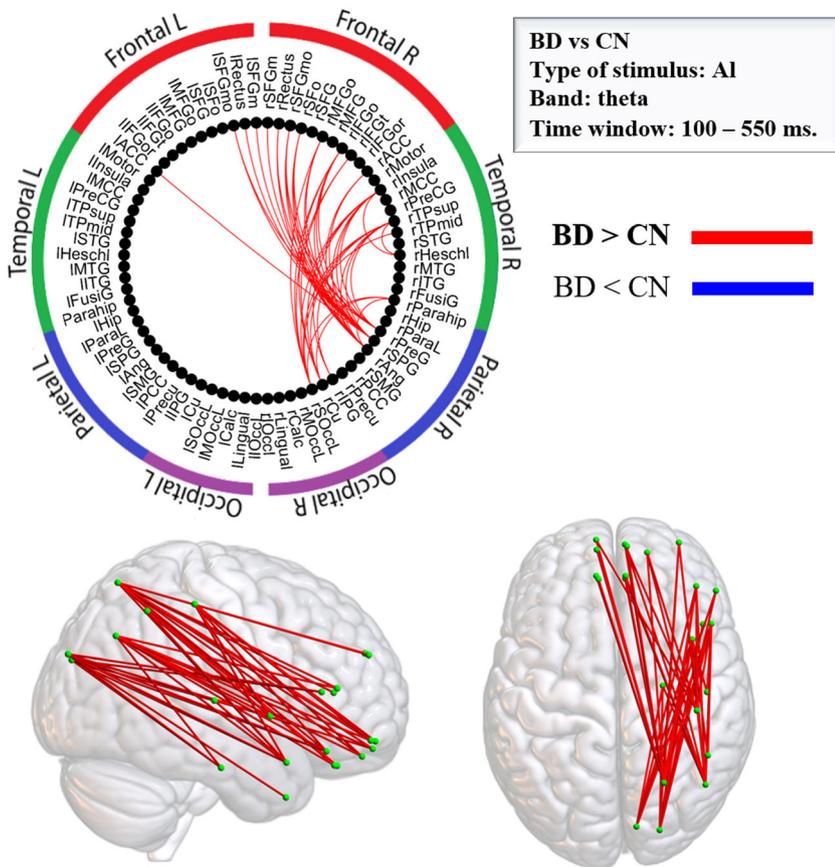
During correct response inhibition to NoAI stimuli, the BD group exhibited higher fast-beta FC than CNs in 24 links ( $p < 0.001$ , FDR = 0.1). The results highlighted the FC patterns related to the bilateral parahippocampal gyri and the left IFG. The left parahippocampal gyrus showed higher connectivity with other left hemisphere regions (IFG, temporal pole, posterior cingulate cortex [PCC] and lingual gyrus), whereas the right parahippocampal gyrus showed higher connectivity, mainly with left hemisphere regions (temporal pole, fusiform gyrus, parahippocampal gyrus and hippocampus) together with right calcarine fissure and right lingual gyrus. The left IFG showed higher FC with the same hemisphere regions (insula, temporal pole, Heschl's gyrus and parahippocampal gyrus). In addition, higher fast-beta FC was observed between specific right frontal regions (insula and IFG) and right occipital regions. The topographical distributions of significant links are shown in Figure 5.



**FIGURE 2** Functional connectivity in theta band (4–8 Hz). Significant functional connectivity (FC) links in type of stimulus comparison (AI > NoAI) of NoGo trials in the BD group. Schematic representation of significant FC links in the 76 Automated Anatomical Labeling (AAL) cortical regions. Significant FC links in sagittal and axial planes

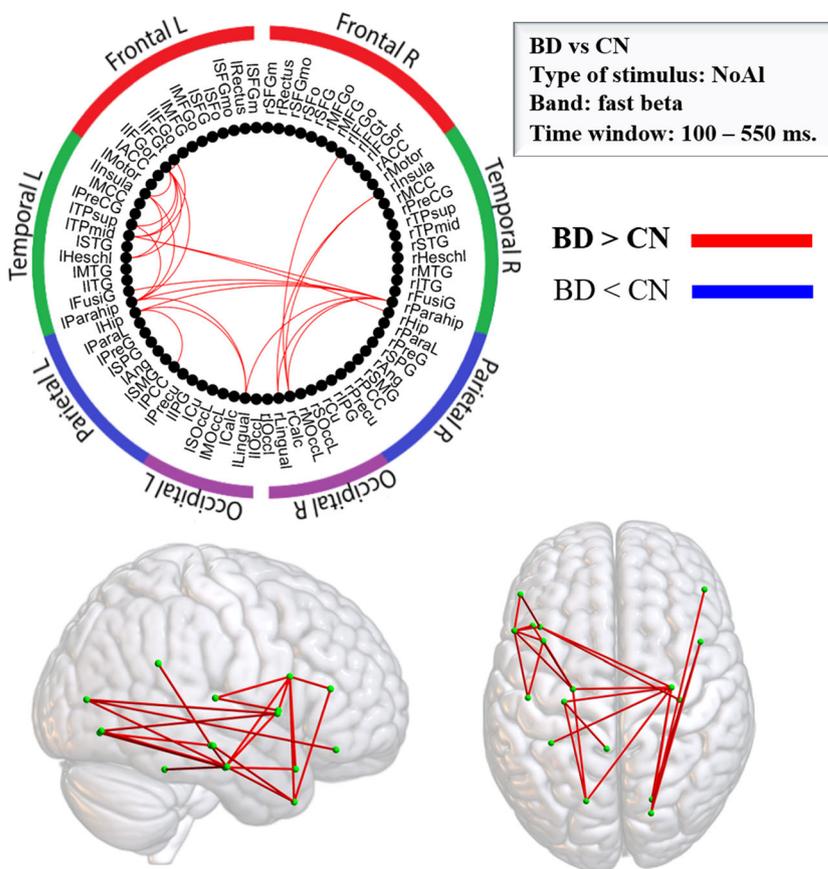


**FIGURE 3** Functional connectivity in fast-beta band (20–30 Hz). Significant functional connectivity (FC) links in type of stimulus comparison (AL < NoAI) of NoGo trials in the BD group. Schematic representation of significant FC links in the 76 Automated Anatomical Labeling (AAL) cortical regions. Significant FC links in sagittal and axial planes



**FIGURE 4** Functional connectivity in theta band (4–8 Hz). Significant functional connectivity (FC) links in group comparison (BD > CN) for NoGo trials to AI stimuli. Schematic representation of significant FC links in the 76 Automated Anatomical Labeling (AAL) cortical regions. Significant FC links in sagittal and axial planes

**FIGURE 5** Functional connectivity in fast-beta band (20–30 Hz). Significant functional connectivity (FC) links in group comparison (BD > CN) for NoGo trials to NoAI stimuli. Schematic representation of significant FC links in the 76 Automated Anatomical Labeling (AAL) cortical regions. Significant FC links in sagittal and axial planes



No significant between-group differences were found in response to NoAI stimuli in the other frequency bands.

### 3.3 | Go trials results

Between-group analysis showed that, during correct Go responses to AI stimuli, the BDs exhibited higher theta and fast-beta FC than CNs (for a detailed description, see the supporting information). No significant between-group effects were found for NoAI stimuli. No significant within-group effects were found.

## 4 | DISCUSSION

The present study aimed to investigate, in a sample of young binge drinkers and from the perspective of dual-process models, the neural FC patterns associated with response inhibition and modulation of the inhibition by the motivational value of alcoholic stimuli.

The main findings revealed the presence of different patterns of increased FC in the BD group in the theta and fast-beta bands. In terms of the dual-process model, the reflective system of the BD group seems to recruit more attentional and inhibitory resources than the CN group in the presence of alcohol pictures. This may represent a compensatory mechanism to overcome overactivation of the affective-automatic system provoked by the motivational value of

these pictures. Consistently, between-group comparisons enabled detection of FC differences, characterised by higher theta antero-posterior FC in BDs during inhibition of AI stimuli, together with higher fast-beta FC during inhibition of NoAI stimuli (in a context of prepotent response to AI stimuli).

### 4.1 | Higher theta FC in binge drinkers during response inhibition to AI stimuli

The BD group presented higher theta FC during inhibition of a motor response to AI than to NoAI stimuli. This pattern was mainly observed in the right hemisphere and highlighted the connectivity of orbitofrontal regions with parietal regions and, to a lesser extent, with temporal regions (Figure 2). This result was consistent with between-group analysis in the theta band, as BDs exhibited higher theta FC than CNs during successful inhibition of the response to AI stimuli. The FC pattern also highlighted the presence of orbitofrontal regions (as well as bilateral ACC, SFG and right insula) and its synchronisation with right parietal regions and, to a lesser extent, with temporal and occipital regions (Figure 4).

The increased activity in the theta band has been shown to be sensitive to task difficulty, reflecting cognitive effort. More specifically, frontal theta activity may reflect synchronisation of information relevant to the current goals around critical points in the decision-making process, such as the selection of one action over another.<sup>19</sup>

This selection process is more likely to be executed when election-relevant related information sources (such as context, working memory or rewards) are correctly integrated by the reflective system.<sup>37</sup>

In our task, both between-group and within-group analyses of theta band FC highlight the presence of orbitofrontal connections with other right hemisphere structures. The orbitofrontal cortex (OFC) plays an important role in decision-making and learning, as it may represent a 'cognitive map' of the environment in relation to current goals, signalling when it is appropriate to make a given choice (e.g. to make a motor response or to withhold it).<sup>38</sup> The OFC receives highly processed information from other regions, encoding and integrating associations between external sensory stimuli and internal states. In our task, these networks included regions involved in perceptual processing (occipital regions), sensorimotor integration (parietal regions), attentional salience (insula) and processes related to inhibitory control, such as conflict monitoring (ACC) and response inhibition (IFG, SMA).<sup>39,40</sup> The involvement of these regions has consistently been reported during inhibitory trials of Go/NoGo tasks and has been attributed to attentional and cognitive control processes.<sup>41</sup> The presence of the parahippocampal gyrus, which is not typically related to response inhibition tasks,<sup>42</sup> has recently been proposed as part of an inhibitory network when there is a high level of feature overlapping between Go and NoGo stimuli,<sup>43</sup> as may be the case in our task.

The oscillatory activity in the theta band has also been proposed as the origin of the N2-NoGo ERP component.<sup>19</sup> The N2-NoGo component is considered an index of conflict monitoring between incompatible responses, and its neural origins have been located in ACC and IFG.<sup>42</sup> Electrophysiological studies with beverage Go/NoGo paradigms have detected N2-NoGo anomalies in BDs related to the motivational content of the NoGo stimuli.<sup>11-13</sup> Altogether, these results suggest that BDs may experience greater conflict when alcohol-related content is present in the Go/NoGo task. Depending on their history of alcohol consumption, BDs may be able to recruit compensatory resources to successfully<sup>11</sup> or unsuccessfully<sup>12</sup> overcome the conflict and withhold the prepotent response. When there is a history of more intensive alcohol consumption, these compensatory resources may no longer be available.<sup>13</sup>

Previous electrophysiological studies in young BDs have also examined resting and task-related theta band oscillatory activity. Resting state studies reported greater spectral power and connectivity measures in the theta band in BDs, relative to CNs,<sup>44-47</sup> although no differences were reported in one study.<sup>48</sup> In contrast to our findings, studies with Go/NoGo neutral tasks observed lower power and/or connectivity in the frontal theta band (relative to CNs).<sup>21,22,24</sup> These discrepancies may be related to task design, as neutral Go/NoGo tasks may only be able to capture reflective system activity in the absence of any influence of the affective-automatic system, and thus, no compensatory resources are required to achieve a balance between systems, as may be the case with our task.

Our findings are consistent with those of fMRI studies within the framework of dual-process models.<sup>17,18</sup> BDs exhibited greater activation than CNs in the right IFG and the right insula during the

successful inhibition of a motor response to AI pictures. These fMRI findings highlight the importance of the IFG and the right insula in suppressing responses to motivational stimuli associated with alcohol consumption.

## 4.2 | Higher fast-beta FC in BDs during response inhibition to NoAI stimuli

The BD group exhibited higher fast-beta band FC during successful inhibition of the response to NoAI stimuli than during successful inhibition of the response to AI stimuli, a pattern that involved only two links between the right visual cortex (calcarine fissure and surrounding cortex) and the right IFG (Figure 3). More extensive differences in fast-beta FC (24 links) were found in the between-group comparisons during inhibition of the response to NoAI stimuli. The BD group exhibited higher FC than CNs, mainly related to the bilateral parahippocampal gyri and the left IFG (Figure 5). In terms of dual-process models, the reflective system of binge drinkers may be more active at the inhibitory level in the Go-AI/NoGo-NoAI condition than in the alternative condition, a result that was not observed in the CN group.

Beta band oscillatory activity has been extensively studied in response inhibition tasks, such as Go/NoGo tasks. Modulation in beta activity during these tasks seems to be related to facilitation (Go) or inhibition (NoGo) of movement. Beyond the motor component, Schmidt et al.<sup>20</sup> proposed that frontal beta activity may act as a general sign of suppression, as it has been observed in different cognitive domains (e.g. suppression of a motor response, working memory content, or distracting stimuli not relevant to goals). Such top-down activity has been detected from early time windows (100-ms poststimulus), indicating that inhibition may be implemented quickly to mitigate the incompatible but prepotent response that competes with the infrequent but task-relevant response.<sup>49</sup>

According to this global suppression mechanism, binge drinkers may apply (through IFG activity) more top-down control resources than CNs over a set of regions (Figure 5) related to motivational (insula), semantic (temporal pole) and perceptual (occipital) processing. Moreover, as described above, the involvement of parahippocampal gyri during response inhibition tasks may be related to the high degree of feature overlapping between Go and NoGo stimuli.<sup>43</sup> Thus, the higher fast-beta connectivity between the described regions would facilitate selection of the task-relevant response (withholding the response to infrequent NoGo-NoAI stimuli) by suppressing information related to the prepotent response (frequent Go-AI stimuli).

These results are not consistent with those of previous cross-sectional EEG studies. One study described lower beta band activity in BDs than in CNs,<sup>21</sup> while another study did not report any differences in this frequency band.<sup>22</sup> The discrepancies in findings may be due to task design, as both of these previous studies used neutral stimuli. However, our findings are consistent with a previous longitudinal MEG study, as future BDs exhibited a pattern of hyperconnectivity in the beta band during the 250- to 350-ms window.

This pattern also affected regions involved in inhibitory control networks, such as SMA, ACC and right IFG.<sup>25</sup>

In conclusion, the present study revealed the presence of FC anomalies related to the motivational content of the stimuli during the successful inhibition of a prepotent response in binge drinkers. The results suggest that the presence of alcohol stimuli in the Go/NoGo task may hinder the ability of BDs to inhibit a prepotent response, so that compensatory cognitive control resources are required for successful task execution. These compensatory resources may appear in different ways depending on whether AI pictures act as Go or NoGo stimuli. When facing NoGo-AI stimuli, BDs may have recruited higher frontal theta oscillatory activity as a mechanism to facilitate integration of information related to the task goals (withholding a response). As regards response inhibition to NoGo-NoAI stimuli, increased fast-beta oscillatory activity may act as a compensatory top-down mechanism to suppress the information related to the frequent and motivationally salient Go-AI response.

Considered together, these findings support the value of the dual-process model approach to exploring the neurocognitive correlates in BD. In summary, our results suggest that AI stimuli, due to its motivational value, may provoke the overactivation of the affective-automatic system of BDs. As a consequence, different compensatory resources in cognitive control may be recruited by the reflective system to overcome the prepotent tendency to respond. Specifically, higher theta oscillatory activity might facilitate integration of information related to current task goals, whereas higher fast-beta oscillatory activity may work as a compensatory top-down mechanism.

Studying the EEG FC via the PLV metrics is postulated as a promising and sensitive method for disentangling possible anomalies in functional networks in young binge drinkers. Future lines of research should replicate and extend these results from a longitudinal approach, including study of FC vulnerability prior to initiation of the BD pattern of consumption.

We recognise some limitations of the study. Most importantly, the cross-sectional design prevents conclusion of whether the observed anomalies arise as a consequence of BD or a prior vulnerability. In addition, future research should consider updated versions of the AAL, such as the recently published AAL3.<sup>50</sup> Other limitations include the highly specific characteristic of the sample, which does not allow generalisation of the results to other populations. Aspects such as the potential motivational value of nonalcoholic stimuli or the possible influence of individual preferences for specific alcohol beverages should also be considered. Finally, the lack of similar studies in the existing literature on BD led us to select an exploratory approach, based on the voltage analysis of the ERP components described in a previous study.<sup>11</sup> Thus, the study findings should be considered preliminary, and the interpretation and conclusions should be regarded with caution.

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## CONFLICT OF INTEREST

All the authors declare no conflicts of interest in the current study.

## AUTHOR CONTRIBUTION

FC, SRH and SD designed the study. SRH, SSS and JBR collected the data. JBR, LFAT, SRH analysed and interpreted data. JBR wrote the manuscript, which was reviewed by all authors.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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