

## **Electrophysiological correlates of alcohol- and non-alcohol-related stimuli processing in binge drinkers: A follow-up study**

Géraldine Petit, Charles Kornreich, Bernard Dan, Paul Verbanck and Salvatore Campanella

*J Psychopharmacol* published online 13 August 2014

DOI: 10.1177/0269881114545663

The online version of this article can be found at:

<http://jop.sagepub.com/content/early/2014/07/31/0269881114545663>

---

Published by:



<http://www.sagepublications.com>

On behalf of:



[British Association for Psychopharmacology](#)

**Additional services and information for *Journal of Psychopharmacology* can be found at:**

**Email Alerts:** <http://jop.sagepub.com/cgi/alerts>

**Subscriptions:** <http://jop.sagepub.com/subscriptions>

**Reprints:** <http://www.sagepub.com/journalsReprints.nav>

**Permissions:** <http://www.sagepub.com/journalsPermissions.nav>

>> [OnlineFirst Version of Record](#) - Aug 13, 2014

[What is This?](#)

# Electrophysiological correlates of alcohol- and non-alcohol-related stimuli processing in binge drinkers: A follow-up study

Géraldine Petit, Charles Kornreich, Bernard Dan, Paul Verbanck and Salvatore Campanella

*Journal of Psychopharmacology*  
1–12

© The Author(s) 2014  
Reprints and permissions:  
sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/0269881114545663  
jop.sagepub.com



## Abstract

**Background:** The continuation of binge drinking is associated with the development of neurocognitive brain abnormalities similar to those observed in patients with alcohol dependence. Alcohol cue reactivity constitutes a risk marker for alcohol dependence. Through event-related potentials (ERPs), we aimed to examine its potential presence as well as its evolution over time in binge drinkers in a one-year period.

**Methods:** ERPs were recorded during a visual oddball task in which controls ( $n=15$ ) and binge drinkers ( $n=15$ ) had to detect infrequent deviant stimuli (related or unrelated to alcohol) among frequent standard stimuli. The test was performed twice with a one-year interval in order to explore the long-lasting influence of drinking habits.

**Results:** Contrary to the controls, binge drinkers showed significantly reduced amplitudes of the P1 component for both alcohol and non-alcohol-related cues and of the P3 component only for neutral cues in the second assessment compared with the first.

**Conclusion:** The continuation of binge drinking over one year is associated with the development of brain functional abnormalities (indexed by the P1 component) as well as a higher reactivity to alcohol-related stimuli and/or a decreased reactivity to non-alcohol-related stimuli (indexed by the P3 component).

## Keywords

Binge drinking, alcohol, cue reactivity, longitudinal, event-related potentials, P1, P3

## Introduction

Binge drinking is defined as the alternation between periods of heavy drinking and abstinence. The most accepted definition of binge drinking is the consumption of at least four (for women)/five (for men) alcoholic drinks on one occasion within a two-hour interval (Courtney and Polich, 2010). In Europe, binge drinking peaks in late adolescence or early adulthood with 40% of people aged 18–24 years meeting the diagnostic criteria (Kuntsche et al., 2004). University students are particularly affected (Lang et al., 1996).

Young adulthood represents a critical period for deep cortical development and remodelling (e.g. Paus, 2001) that ends at around the age of 25 years old (Giedd et al., 1992). These aspects of brain maturation allow cognitive functions such as attention, working memory and inhibitory control to become fully developed and efficient (Luna and Sweeney, 2004). Heavy alcohol exposure during this period may unfavourably affect a large variety of neuromaturation processes and lead to neurophysiological dysfunction and cognitive impairment (Hingson et al., 2006). In this context, anatomical (Courtney and Polich, 2010; McQueeney et al., 2009; Squeglia et al., 2012), physiological (Crego et al., 2009, 2010; Ehlers et al., 2007; Lopez-Caneda et al., 2012, 2013; Maurage et al., 2009, 2012; Petit et al., 2012a, 2012b, 2013a; Schweinsburg et al., 2010) and neuropsychological (Goudriaan et al., 2007; Hanson et al., 2011; Hartley et al., 2004; Heffernan et al., 2010; Johnson et al., 2008; Mota et al., 2013; Parada et al., 2011, 2012) abnormalities have been increasingly documented in relation to binge drinking.

Despite the fact that adolescent binge drinkers show neurocognitive difficulties in population-based cross-sectional studies, little is known about the evolution of these impairments in relation to their binge drinking trajectories. Longitudinal studies providing repeated observations at an individual level of both alcohol consumption and neurophysiological performance are more suitable to elucidate causal relationships: in other words, to clarify whether neurophysiological deficits are a consequence of heavy episodic drinking during adolescence. Considering the evolution of these deficits in parallel with the continuation of binge drinking is a major current concern. At the neuropsychological level, Mota et al. (2013) showed that persistent binge drinking is associated with deficits in verbal memory and monitoring: cognitive functions that rely on the temporomesial and dorsolateral prefrontal cortex. The expression of dysfunctions in sub-clinical populations such as non-dependent binge drinkers is often less serious than those observed in dependent populations, and thus not always obvious on the behavioural

Laboratory of Psychological Medicine and Addictology, Université Libre de Bruxelles (ULB), Brussels, Belgium

## Corresponding author:

Salvatore Campanella, The Belgian Fund for Scientific Research (FNRS), CHU Brugmann, Psychiatry Department, 4, Place Vangehuchten, Brussels, B-1020, Belgium.

Email: salvatore.campanella@chu-brugmann.be

(neuropsychological) level (for a review, see Petit et al., 2013b). In this context, due to their higher sensitivity compared to behavioural measures and their ability to highlight more latent deficits (Wilkinson and Halligan, 2004), neuroimaging tools such as electrophysiological assessment have been shown to be very informative (e.g. Fehr et al., 2007; Field and Quigley, 2009; Maurage et al., 2009).

To date, three electrophysiological studies have focused on the cerebral anomalies associated with the persistence of binge drinking by using a follow-up procedure. Maurage et al. (2009) found that after nine months, young people who had been 'binging' showed delayed event-related potentials (ERPs) latencies in an emotional auditory task. López-Caneda et al. (2012) showed an increase in the abnormal electrophysiological activity related to impulse control in a group of drinkers who had been bingeing for two years. More recently, the same group showed an increase in aberrant P3b amplitudes in a visual oddball task after two years of binge drinking (López-Caneda et al., 2013). Overall, these follow-up results suggest that the emergence/continuation of a binge drinking pattern leads to the expression/amplification of neurophysiological anomalies that are similar to the long-term neurotoxic effect consistently documented in chronic alcoholism (e.g. see Campanella et al. (2009) for a review).

Moreover, it has been hypothesised that some of the deficits and/or neurobiological changes caused by binge drinking play a role in the subsequent continuation of alcohol use and abuse (Haller et al., 2010). This might explain the epidemiological data linking binge drinking patterns to alcohol dependence (e.g. Bonomo et al., 2004; Li et al., 2007). This raises the important clinical question of risk factors for drinking continuation and chronic consumption in young drinkers. In this context, the study of neurocognitive abnormalities that have been shown to play a key role in the emergence and/or continuation of drinking habits in chronic alcoholics may prove particularly relevant.

Repeated alcohol consumption leads to alterations in dopamine levels and mesocorticolimbic sensitisation, resulting in heightened incentive salience of stimuli associated with drinking (Robinson and Berridge, 1993). Notably, studies of dual processes (e.g. Stacy and Wiers, 2010; Wiers et al., 2007) have demonstrated a cognitive processing bias for alcohol-related stimuli in alcohol dependence (for reviews see Franken, 2003; Field et al., 2006; Field and Cox, 2008) which is believed to play a central role in the occurrence of alcohol consumption disorders (Goldstein and Volkow, 2002; Lubman et al., 2004). Accordingly, visual ERP studies have shown that the P3 component in response to alcohol-related stimuli is heightened in alcohol abusers compared to controls (Herrmann et al., 2000; Namkoong et al., 2004). Increased P3 amplitude has been correlated with motivational engagement, motivated attention, and the activation of arousal systems in the brain (Cuthbert et al., 2000; Lang et al., 1997). Therefore, P3 enhancement could indicate the high 'motivational' value of alcohol-related stimuli and reflect the allocation of attentional resources to stimuli corresponding to alcohol-dependent subjects' motivational states. Moreover, enhanced P3 cue reactivity may precede the onset of alcohol use disorders (and not be a consequence of it), and could perhaps be a predictor of future alcohol use (Bartholow et al., 2007, 2010; Fleming and Bartholow, 2014; Shin et al., 2010). Previous studies showed that higher reactivity to alcohol cues is not specific to adults with alcohol dependence, but may be found in heavy social drinkers

and binge drinkers (Ceballos et al., 2012; Dickter et al., 2013; Petit et al., 2012b, 2013a).

In the present study, we aimed to gain further insights into both alcohol reactivity and general stimuli processing indexed by ERP parameters in binge drinkers and assess how this evolves over time. We therefore chose to use an oddball paradigm in which participants had to detect deviant stimuli from a series of frequent standard stimuli. This experimental design has been shown to be highly informative in the investigation of neurophysiological anomalies associated with many psychopathological states such as alcoholism (e.g. Maurage et al., 2007), but also in non-dependent binge drinkers (e.g. Crego et al., 2012; Ehlers et al., 2007; Lopez-Caneda et al., 2013; Maurage et al., 2009, 2012). Moreover, in the current study, deviant stimuli were or were not related to alcohol, which allowed processing of both categories of stimuli to be investigated. Finally, the study was longitudinal, with the paradigm being administered twice to university students with a one-year interval.

We focused on two ERP components. Indeed, deviant stimuli classically elicit two consecutive effects reflecting two steps of the orienting response (Öhman, 1979). The first one consists of the capture of automatic attention and is reflected by several components, among which in the specific case of visual stimulation, P1, an early sensory component peaking around 100 ms and constituting an index of mobilisation of automatic attentional resources, which has been reported many times (see Hopfinger and Mangun (2001) for a review). The second, P3b (referred to here as P3) peaks at parietal sites at around 450 ms and reflects different higher level mechanisms, such as inhibition, cognitive closure, decision making and pre-motor response-related stages (see Polich (2007) for a review). P3 is considered as an important biological marker of alcohol abuse (e.g. Euser et al., 2012) and its alterations have also been observed in several oddball paradigms in binge drinking populations (Crego et al., 2009, 2012; Lopez-Caneda et al., 2013; Maurage et al., 2009, 2012). However, a high positive correlation between P1 and P3 values has been shown both in alcoholism and in sub-clinical populations (e.g. Maurage et al., 2007, 2009, 2012), suggesting that late P3 impairments can be linked to earlier visuo-spatial deficits indexed by the P1 values rather than being an impairment of the specific processes linked to P3. The use of electrophysiological (EEG) recordings in the task will therefore allow for the more precise definition of the level of the information processing stream at which the potential differences between control participants and binge drinkers originate.

As far as cue reactivity is concerned, P3 amplitude has been shown to be larger for emotional than for neutral stimuli (e.g. Schupp et al., 2004), which reflects preferential emotion processing. This effect has been especially observed in the addiction field in studies using oddball paradigms based on substance-related cues (e.g. Henry et al., 2013; Sokhadze et al., 2008).

On this basis, our hypotheses were that binge drinkers would show (a) general alterations in the processing of stimuli, and (b) differential processing between alcohol-related and non-alcohol-related stimuli and that these deficits and/or processing bias would be enhanced over time. In particular, we hypothesised that binge drinking and/or its continuation would lead to (a) alterations affecting P3 latencies and/or amplitudes and that these deficits would originate from alterations in latencies and/or amplitudes of the earlier P1 component, and (b) enhanced

responses to alcohol-related stimuli which would be indexed by an increased P3 in response to alcohol-related pictures compared to non-alcohol-related ones.

## Methods and materials

### Participants

A general screening was first conducted among 150 students from the Faculty of Psychology in the University of Brussels (ULB, Belgium). According to the definition of binge drinking used in European countries, participants who drank six or more standard alcoholic drinks (10 g of alcohol) on the same occasion at a speed of at least three drinks per hour and at most three or four times per week were selected and classified as binge drinkers. Those who drank one to 30 days a month, but never more than five standard alcoholic drinks on the same occasion and at a maximum speed of two drinks per hour, were classified as controls. Exclusion criteria were major medical problems, conditions of the central nervous system (including epilepsy and history of brain injury), past or current drug consumption other than alcohol, cannabis and tobacco, and alcohol abstinence. All participants were assessed for the following psychological measures: State and Trait Anxiety (STAI A and B, Spielberger and Gorsuch, 1983) and depression (Beck Depression Inventory (BDI), Beck et al., 1998). Earlier studies on binge drinking chose to exclude participants with tobacco and/or cannabis consumption as well as those reporting a family history of alcoholism as these characteristics modify cerebral functioning (e.g. Jacobsen et al., 2004). However, a high co-occurrence of binge drinking and other substance use such as cannabis and cigarettes as well as a family history of problematic drinking has been reported (Kuntsche et al., 2004). For the purpose of selecting a sample that is representative of the binge drinking population, we chose in this study not to exclude participants reporting tobacco and/or cannabis consumption or a family history of alcoholism but rather to control these variables by first making sure that they did not differ between the groups. In this way, the potential differences observed between groups could not be explained partially by these co-morbidities rather than by binge drinking itself. A family history of alcoholism is of particular interest in relation to the current topic as it is known that individuals with a family history of alcoholism show differential ERP components (e.g. Begleiter et al, 1984) and especially brain responses to stimuli associated with alcohol (Kareken et al., 2010). The students were evaluated twice, at an approximate one-year interval. Importantly, to be selected for the follow-up session, students had to continue the same drinking patterns from the first to the second assessment. Out of the 42 selected students, 20 were classified as controls and 22 as binge drinkers. Three out of the 22 binge drinkers did not continue their drinking pattern, and nine out of the 42 participants did not come to the follow-up session: four binge drinkers and five controls. Thus, each final group included 15 binge drinkers and 15 controls. The mean interval between T1 and T2 was 53 ( $\pm 11$ ) weeks.

### Visual stimuli

Alcohol-related and non-alcohol-related pictures were used as target deviant stimuli alongside frequent non-alcohol-related

**Table 1.** Mean scores obtained in terms of valence (1: negative; 9: positive) and alcohol specificity (1: non-alcohol; 5: alcohol) for the deviant stimuli.

Picture	Valence	Alcohol-related
A-picture 1 (beer)	6	4.05
A-picture 2 (bottles)	5.25	4.05
A-picture 3 (7280) (wine)	5	4.65
NA-picture 1 (7004) (spoon)	4.9	1
NA-picture 2 (7175) (lamp)	4.8	1.25
NA-picture 3 (7080) (fork)	4.95	1

A: alcohol-related pictures; NA: non-alcohol related pictures. International Affective Picture System (IAPS) picture numbers are indicated in parentheses.

stimuli. To construct the set of two types of pictures (alcohol-related and non-alcohol-related), we selected 14 pictures from the Internet or the International Affective Picture System (IAPS) (Lang et al., 2005). All pictures were standardised for brightness and colour with Photoshop 6.0 and resized to 12×12 cm. To appoint the task stimuli, 40 students who did not take part in the electrophysiological study rated the 14 pictures for alcohol specificity on a Likert scale from 0 (not related to alcohol at all) to 5 (extremely related to alcohol) and emotionality on a Likert scale from 0 (very unpleasant) to 9 (very pleasant). Based on the results of this rating, two categories of pictures were created. The seven images with the lowest alcohol specificity and the most neutral emotionality were selected and constituted the four frequent non-alcohol-related (frequent NA) stimuli (one of them was an IAPS image: no. 7006, a plate, the second pictured a pen, the third pictured a bulb and the fourth pictured a folder) and the three deviant non-alcohol-related (deviant NA) stimuli (these were all IAPS images: no. 7004, a spoon, 7175, a lamp, 7080, a fork). The three pictures with the highest alcohol specificity and the most neutral emotionality were selected as deviant alcohol-related (deviant A) stimuli (one of them was an IAPS image: no. 7280, glasses of wine and a picnic hamper, the second image pictured someone drinking a beer and the third pictured various bottles of alcohol). The mean scores of valence and alcohol specificity evaluations for each deviant stimulus are reported in Table 1.

### Procedure

The two assessments were conducted following the same procedure. After test results confidentiality was promised, all participants were first re-assessed with the questionnaire on alcohol and drug consumption used for participants' initial selection, the BDI (Beck et al., 1998) and the state and trait anxiety inventories (STAI A and B; Spielberger, 1983). The participants were instructed to abstain from consuming drugs (other than tobacco) or alcohol 24 h before the tests. Alcohol abstinence before the test was verified using Alco-Sensor III breathanalysers Alcometer (Alert J5, Alcohol Countermeasure Systems Corp, 2006) and urine screening was carried out for Tetrahydrocannabinol (Instant-View MultiDrug Screen Urine Test (Alfa Scientific Designs, Inc.). No participants were positive in these tests. If one of these tests had been positive for one of the students, the testing would have been rescheduled. No formal instruction was given to



subjects regarding abstinence from smoking prior to the ERP testing. However, as previous ERP studies (e.g. Houlihan et al., 1996) have shown that acute smoking has stimulant effects on mood and performance (improving them), we ensured participants abstained within the hour prior to testing by managing to occupy this time with the setting up of EEG installation and filling in of questionnaires. The task and EEG recording were then started. The participants sat in a dark room on a chair placed 1 m from the screen. The task was a visual oddball paradigm consisting of four blocks. In each block, the participants were confronted with one regularly repeated standard stimulus (frequent NA) and deviant ones (deviant A and NA). The frequent NA stimulus was different in each block. In each block 100 stimuli were presented: the same NA frequent stimulus appeared 70 times (70%), and the three deviant pictures for each condition (A and NA) each appeared five times (30%), for a total of 15 deviant A and 15 deviant NA stimuli. Participants were told that each new block would begin with the presentation of the frequent stimulus, which was repeated at least three times before a deviant stimulus would appear. A practice block of pictures (not included in the four experimental blocks or in the data analysis) was firstly shown to train the subjects for the tasks ahead. Each picture was presented for 800 ms. A black screen was displayed between pictures for a random duration of 600–1000 ms. The participants had 1200 ms to answer from the onset of the stimulus. They were instructed to indicate as quickly as possible the occurrence of any deviant stimulus with a right finger tap. The order of presentation of the four blocks varied across participants. Subjects were informed of the end of each block by a closing message. The response times and percentages of correct answers were recorded. The participants were told that speed was important, but not at the cost of accuracy. After completing the task, each participant was asked to evaluate each picture for alcohol-relatedness, valence and level of arousal. The Brugmann Hospital local ethics committee approved the study.

### EEG recording and analysis

During the testing phase, EEG activity was recorded with 32 electrodes mounted on a Quik-Cap and placed in standard (based on the 10–20 system) and intermediate positions (Jasper, 1958). Recordings were made with a linked mastoid physical reference but re-referenced off-line using a common average, based on the principle that the integral surface of the potential on a surface that completely encompasses all the active sources should be zero (Bertrand et al., 1985). The EEG was amplified with battery-operated ANT amplifiers with a gain of 30000 and a bandpass of 0.01–100 Hz. The impedance of all electrodes was maintained below 5 k $\Omega$ . EEG was recorded continuously at a sampling rate of 1024 Hz with ANT EProbe software. Of the participants' responses, 98.65% and 98.357% were correct at T1 and T2 respectively (i.e. a finger tap given for deviant stimuli). Only correct answers were considered for analysis of reaction times and EEG activity. The trials contaminated by eye movements or muscular artifacts were manually eliminated offline. A 2 $\times$ 2 analysis of variance (ANOVA) was conducted on the remaining non-biased trials, including group (control; binge) as a between-subject variable, and time of evaluation (T1, T2) as a within-subject variable. The results did not reveal any difference between controls and binge drinkers (9% vs 8%;  $p > 0.05$ ), nor

between T1 and T2 (9% vs 8%;  $p > 0.05$ ) for the rejected trials. Epochs starting 200 ms before the onset of the stimulus and lasting for 800 ms were created. The data were filtered with a 30 Hz lowpass filter. To compute averages of different ERP target stimuli for each subject, two parameters were coded for each stimulus: (A) the type of stimulus (A; NA); and (b) the type of response (key press for deviant stimulus, no key press for frequent stimulus). A general time window was first determined globally for the identification of each ERP component based on the literature: 90–160 ms for P1 (Hillyard et al., 1996) and 350–650 ms for P3 (Polich, 2004). The peak selection was then conducted as follows: for each participant individual peak amplitudes and maximum peak latencies were obtained for the ERPs from the waveforms evoked by the deviant stimuli, separately from the classical electrodes used to define the P1 and P3 components and from which the maximum amplitudes had been recorded for these components - Oz, O1, O2, P7, P8 and POz for P1 and Pz, P3, P4, CP1, CP2, POz for P3 (Polich, 2004).

## Results

### Participants' characteristics

Separate 2 $\times$ 2 ANOVAs were conducted for each characteristic variable, including group (control vs binge) as a between-subject variable, and time of evaluation (T1 vs T2) as a within-subject variable. The results showed that the mean number of drinking occasions per week (DOW) did not differ significantly between T1 and T2 in both groups (interaction group $\times$ time:  $p = 0.588$ ). Main time effects were found for the mean number of alcohol doses ingested per hour (ADH;  $p < 0.001$ ), the mean number of alcohol doses ingested per drinking occasion (ADO;  $p = 0.002$ ), and the mean number of alcohol doses ingested per week (ADW;  $p = 0.001$ ): these variables decreased between T1 and T2 in both groups, especially in the group of binge drinkers. However, as all these drinking characteristics differed between the two groups in both T1 and T2, the drinking patterns were maintained in both groups between the first and second assessments. Neither interaction nor main effect were found to be significant for the psychological measures of depression and anxiety, indicating that these measures did not differ between groups and between T1 and T2, except for trait anxiety, which showed a time main effect ( $p = 0.013$ ). This indicates that this variable increased between T1 and T2 in both groups. In addition, neither interaction nor main effect was found for age, family history of alcoholism (FHA), tobacco consumption, cannabis consumption, and body mass index (BMI). The groups were also similar in terms of duration of drinking habits before T1, number of weeks between T1 and T2, and duration of drinking habits at T2. Not surprisingly, as binge drinking is much more common among men than women (Kuntsche et al., 2004), the two groups differed in terms of sex ( $X^2(1) = 6.533$ ;  $p = 0.011$ ). However, in order to control for the influence of this variable, it will be added as a between-subject variable in subsequent analyses. The characteristics of the study population at the time of the first (T1) and second (T2) assessments are summarised in Table 2.

### Behavioural data

To investigate whether the group variable affected the reaction times (RTs) for correct answers while controlling for sex effect, a

**Table 2.** Characteristics of the study population.

		Binge drinkers ( <i>n</i> =15)	Controls ( <i>n</i> =15)
<b>Gender</b> (male: female)		11(73%): 4(27%) <sup>a</sup>	4(27%): 11(73%) <sup>a</sup>
<b>Tobacco (daily smoking)</b> (no: yes)		10(67%): 5(33%)	13(87%):2(13%)
<b>Family history of alcoholism</b> (no: yes)		9(60%): 6(40%)	10(67%): 5(33%)
<b>Cannabis</b> (no: yes)		11(73%): 4(27%)	13(87%): 2(13%)
<b>Body mass index</b>		22±2.6	23±1.94
<b>Number of weeks between T1 and T2</b>		51±8	53±13
<b>Age (year)</b>	T1	22±1.72	22±2.13
	T2	23±1.63	23±2.23
<b>Number of alcohol doses per week (ADW)</b>	T1	32.06±21.15 <sup>b,c</sup>	4.5±3.31 <sup>b</sup>
	T2	23.06±17.7 <sup>b,c</sup>	4.8±2.6 <sup>b</sup>
<b>Number of drinking occasions per week (DOW)</b>	T1	3.2±1.6 <sup>a</sup>	1.6±1.28 <sup>a</sup>
	T2	2.7±1.6 <sup>a</sup>	1.4±1.04 <sup>a</sup>
<b>Number of alcohol doses per hour (ADH)</b>	T1	3.3±1.61 <sup>b,c</sup>	1.5±0.77 <sup>b,c</sup>
	T2	2.3±0.69 <sup>b,c</sup>	1.0±0.58 <sup>b,c</sup>
<b>Number of alcohol doses per drinking occasion (ADO)</b>	T1	10.7±3.85 <sup>b,c</sup>	3.3±1.61 <sup>b</sup>
	T2	8.2±3.2 <sup>b,c</sup>	3.3±1.4 <sup>b,c</sup>
<b>Duration of alcohol drinking habits (in weeks)</b>	(before) T1	205±112	176±88
	T2	257±111	230±87
<b>BDI</b>	T1	2.6±2.1	2.8±2.6
	T2	3.0±2.9	2.8±3.1
<b>STAI trait</b>	T1	47±8.13 <sup>c</sup>	43±9.91 <sup>c</sup>
	T2	49±8.24 <sup>c</sup>	46±10.86 <sup>c</sup>
<b>STAI state</b>	T1	46±7.26	46±9.32
	T2	48±8.93	48±12.55

BDI: Beck Depression Inventory; STAI: State and Trait Anxiety Inventory.

The results are expressed as number, or mean±standard deviation (SD). One dose represents 10 g of alcohol.

<sup>a</sup>Statistically significant difference between groups at  $p<0.05$ .

<sup>b</sup>Statistically significant difference between groups at  $p<0.001$ .

<sup>c</sup>Statistically significant difference between the times of evaluation at  $p<0.001$ .

2×2×2 ANOVA was performed including group (control vs binge) and sex (male vs female) as between-subject variables, and time of evaluation (T1 vs T2) and type of stimulus (A vs NA) as within-subject variables. No significant effect was noted for the group variable, or for the sex variable ( $p>0.1$ ). However, an effect for the type of stimulus was found ( $F(1,26)=24.311$ ,  $p<0.001$ ,  $\eta^2=0.483$ , observed power=0.997), suggesting that all participants had faster reaction times in response to the A than to the NA stimuli at both times of evaluation (394±41 ms vs 415±37 ms).

## ERP

To investigate whether the group variable affected the components of interest (P1 and P3), while controlling for sex effect, 2×2×2 ANOVAs were performed separately for latencies and amplitudes for both components, including group (control vs binge) and sex (male vs female) as between-subject variables, and time of evaluation (T1 vs T2) and type of stimulus (A vs NA) as within-subject variables.

**P1 component.** *P1 amplitude.* No significant effect for either the group variable, or of the sex variable was noted ( $p>0.6$ ). However, a time×group interaction was detected ( $F(1,26)=4.52$ ,

$p=0.043$ ,  $\eta^2=0.148$ , observed power=0.535), which indicated that P1 amplitudes were smaller for both stimuli in T2 than T1 in the group of binge drinkers (4.8±2.9  $\mu$ V vs 2.4±1.7  $\mu$ V;  $p=0.002$ ), whereas no difference was found between the two evaluation times in the control group (5.2±3.5  $\mu$ V vs 5.6±2.8  $\mu$ V;  $p=0.654$ ). The results are shown in Table 3 and Figure 1.

*P1 latency.* No significant effect for the group variable, or the sex variable was noted ( $p>0.1$ ). However, an effect for the time of evaluation was found ( $F(1,26)=6.58$ ,  $p=0.016$ ,  $\eta^2=0.202$ , observed power=0.695), which suggested that in all participants and for all stimuli, P1 latency was shorter at T2 than at T1 (114±7 ms vs 124±16 ms).

**P3 component.** *P3 amplitude.* No significant effect for the group variable, or of the sex variable was noted ( $p>0.4$ ). However, a time of evaluation×type of stimulus×group interaction was found ( $F(1,26)=5.988$ ,  $p=0.021$ ,  $\eta^2=0.187$ , observed power=0.654), which indicated that, for the NA stimuli, P3 amplitudes were significantly smaller at T2 than T1 in the group of binge drinkers (7.5±4.4  $\mu$ V vs 10.8±4.6  $\mu$ V;  $p=0.006$ ), whereas no significant difference was detected between T1 and T2 for A stimuli ( $p=0.21$ ), or for both types of stimuli between the two times of evaluation in the control group (A:  $p=0.908$ ; NA:  $p=0.369$ ). The results are shown in Table 4 and Figure 2.

**Table 3.** The means and standard deviations (in parentheses) of P100 amplitudes ( $\mu\text{V}$ ) for deviant stimuli detection as a function of group (controls, binge drinkers) and time of evaluation (Time 1; Time 2).

	P100 amplitude mean (SD)	
<b>Controls</b>	T1	5.2 (3.5)
	T2	5.6 (2.8)
	<b>Difference<sup>a</sup></b>	<b>-0.4 (0.7)</b>
<b>Binge drinkers</b>	T1	4.8 (2.9) <sup>b</sup>
	T2	2.4 (1.7) <sup>b</sup>
	<b>Difference<sup>a</sup></b>	<b>2.4 (1.2)</b>

SD: standard deviation.

<sup>a</sup>Results represent the mean variation of amplitude values between times of evaluation 1 and 2 (Time 2–Time 1). The positive differences for amplitudes illustrate amplitudes decreases at Time 2 and the negative differences illustrate increases at Time 2.

<sup>b</sup>Difference between times of evaluation statistically significant at  $p < 0.05$ .

**P3 latency.** No significant effect for the group variable or for the sex variable was noted ( $p > 0.7$ ). However, an effect of the time was observed ( $F(1,26) = 23.262, p < 0.001, \eta^2 = 0.472$ , observed power = 0.996), which indicated that in both groups and no matter the type of stimulus, participants showed shorter P3 latencies in T1 compared to T2 ( $371 \pm 20.3$  ms vs  $397 \pm 27.5$  ms).

### Picture evaluations

Separate  $2 \times 2 \times 2$  ANOVAs were conducted for each picture evaluation criterion (alcohol relatedness, valence and arousal), including group (control vs binge) and sex (male vs female) as a between-subject variable and time of evaluation (T1 vs T2) and type of stimulus (A vs NA) as a within-subject variable. Not surprisingly, the results showed that all participants rated A pictures as more alcohol-related than NA pictures ( $4.4 \pm 0.37$  vs  $1.0 \pm 0.18$ ;  $t(29) = 39.151; p < 0.001$ ). The sex, the group and the time of evaluation variables had no effect on alcohol relatedness ratings ( $p > 0.29$ ). Valence and arousal ratings did not differ for any type of pictures, or according to group, sex or time of evaluation variables ( $p > 0.21$ ).

### Complementary analyses

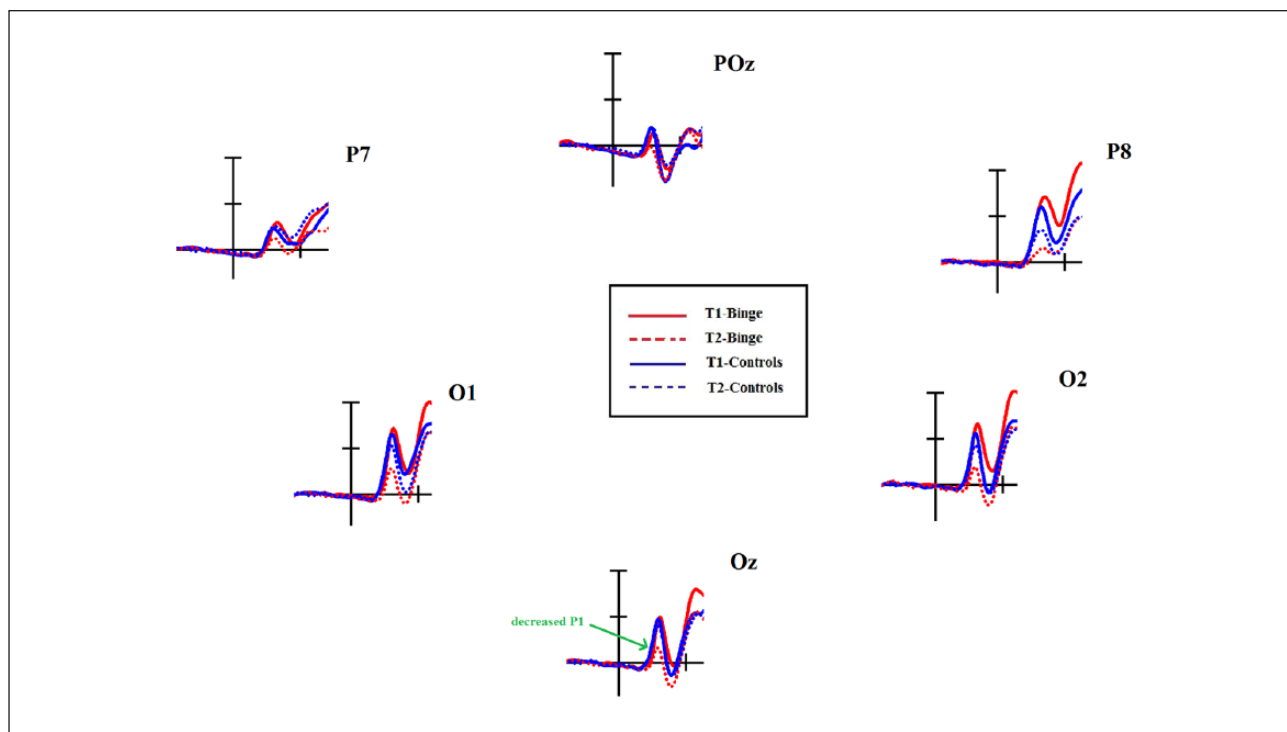
After excluding the possibility that other variables could influence ERP data (i.e. differences between groups in terms of depression, anxiety, age, FHA, tobacco and cannabis consumption, BMI, duration of drinking habits, number of weeks between T1 and T2, duration of drinking habits), and after controlling for the influence of sex, in order to get more insights into how group attachment (i.e. what drinking characteristics specifically in binge drinkers) is associated with the differences in P3 amplitude for NA cues observed at T2, we performed a multivariate linear regression analysis using the backward method. This procedure involves starting with a model including all independent variables, testing them for statistical significance, and deleting the least significant, one by one. We included all drinking-related variables that differed between groups in the model (i.e. DOW, ADO, ADH and ADW). In backward elimination, all independent variables are added together and removed one at a time based on the removal criteria. The significance threshold was set at 0.05

and the out threshold ( $p$ -value for removing a variable) was set at 0.1. Backward stepwise regression is the preferred method of exploratory analyses, where the analysis begins with a full or saturated model and variables are eliminated from the model in an iterative process (Kleinbaum et al., 2010). We found that the ADO variable was the best predictor of P3 amplitudes to NA stimuli in T2 (explained variance of 16%;  $p = 0.029$ ). These results are summarised in Table 5.

## Discussion

This study shows that perpetuation of binge drinking over one year is associated with the emergence of electrophysiological abnormalities characterised by the altered processing of deviant stimuli in the second evaluation compared to the first one. These electrophysiological abnormalities may provide an electrophysiological marker of the emergence of impaired cognitive processing of visual stimuli. This adds to previous documentation of other electrophysiological abnormalities in binge drinkers (Lopez-Caneda et al., 2012, 2013; Maurage et al., 2009). We found amplitude reductions both in the P1 component of ERP, which is mainly associated with early primary perceptual processing of information and highly sensitive to top-down processes (e.g. Heinze and Mangun, 1995), and in P3 for non alcohol-related cues, which is related to complex response-related stages of the information processing stream, such as the decisional and executive processing of relevant cues (Polich, 2004). The deficits thus appear to start very early along the processing stream as it affects the basic step of visual processing (i.e. P1) before extending to a more decisional stage for non alcohol-related cues (i.e. P3). The early appearance and spreading of this deficit later along the cognitive stream, which had already been observed in earlier studies (Maurage et al., 2009, 2012), further strengthens the notion of similarity between binge drinkers and alcohol dependent patients. Studies on chronic alcohol dependent patients also showed amplitude abnormalities affecting early components associated with visuo-spatial and perceptual abilities (e.g. Maurage et al., 2007; Nicolas et al., 1997) as well as marked P3 amplitude impairments (see Hansenne (2006), Porjesz and Begleiter (1996) for reviews). This may be consistent with the ‘continuum hypothesis’ suggesting that cerebral impairments linked with binge drinking show some similarities with those of alcohol dependence and could be considered as a first step to this pathological state (e.g. Courtney and Polich, 2010; Wagner and Anthony, 2002).

P3 amplitude reduction observed in binge drinkers only occurred with NA pictures. Whereas like P1 amplitudes, P3 amplitudes to non-alcohol-related pictures are reduced in the second compared to the first evaluation, P3 amplitudes in response to alcohol-related pictures remain statistically identical from the first evaluation to the second one. Enhancement of the P3 component has been proposed to reflect the amount of attention allocated to picture processing and engagement of the brain’s motivational systems (Cuthbert et al., 2000; Lang et al., 1997). The non-reduction of P3 amplitudes to A stimuli would therefore reflect the emergence of a bias in the processing of alcohol-related stimuli from Time 1 to Time 2. Similar biases that facilitate the detection and selection of substance cues have been suggested to play a causal or perpetrating role in substance-related behaviours (Garland et al., 2012; Goldstein and Volkow,



**Figure 1.** P1 component on six posterior electrodes (P7, O1, POz, Oz, P8, O2) for deviant stimuli in T1 and T2 in the control and binge drinkers groups.

**Table 4.** The mean and standard deviation (SD) (in parentheses) of P3 amplitudes (µV) for deviant stimuli detection as a function of group (controls, binge drinkers), time of evaluation (Time 1; Time 2) and type of stimulus (Alcohol, Non-alcohol).

		P3 amplitude mean (SD)	
		Alcohol	Non-alcohol
<b>Controls</b>	T1	9.6 (3.8)	8.7 (5.1)
	T2	9.5 (4.6)	9.5 (4.6)
	<b>Difference<sup>a</sup></b>	<b>0.1 (-0.8)</b>	<b>-0.8 (0.5)</b>
<b>Binge drinkers</b>	T1	11.0 (5.1)	10.8 (4.6) <sup>b</sup>
	T2	10.0 (4.8)	7.5 (4.4) <sup>b</sup>
	<b>Difference<sup>a</sup></b>	<b>1.0 (0.3)</b>	<b>3.3 (0.1)</b>

<sup>a</sup>Results represent the mean variation of amplitude values between times of evaluation 1 and 2 (Time 2-Time 1). The positive differences for amplitudes illustrate amplitudes decreases at Time 2 and the negative differences illustrate increases at Time 2.

<sup>b</sup>Difference between times of evaluation statistically significant at  $p < 0.05$ .

2002; Lubman et al., 2004; Robinson and Berridge, 1993; Zironi et al., 2006;).

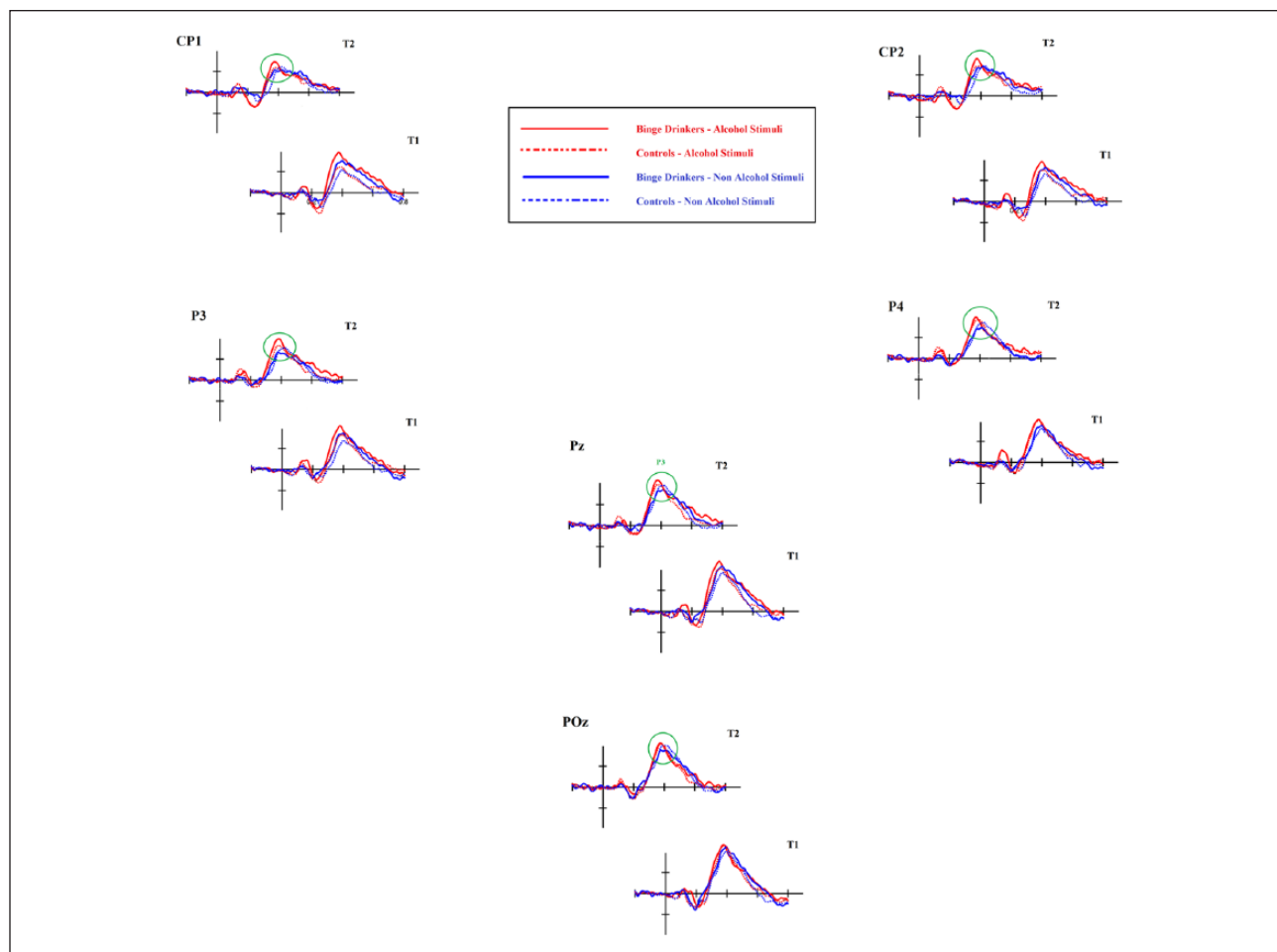
Binge drinkers also show inhibition impairments that increase with years of consumption (Lopez-Caneda et al., 2012), leading to a neurocognitive profile characterised by preferential processing of alcohol-related cues and a lack of inhibition resources, in a moderate but increasing way with the duration of drinking habits, consistent with the dual process model theories associated with chronic drinking behaviours (Stacy and Wiers, 2010).

Alternatively, the decrease specifically affecting NA cues between T1 and T2 could be due to reduced sensitivity to NA

cues. In other words, binge drinkers could actually allocate less attention to NA cues. Actually, both explanations could also be true: the different fates between responses to alcohol and non-alcohol-related stimuli over time in binge drinkers could be interpreted as an increased motivation for drug cues in addition to a decreased motivation for NA cues. A way to disentangle this issue could be to add rewarding stimuli in our paradigm. These being known to be associated with larger P3 than emotionally neutral stimuli (Johnston et al., 1986; Keil et al., 2002), observation of abnormally likened alcohol-related cues to rewarding cues in binge drinkers in T2 would confirm our hypothesis of an increased motivation for A cues, while a decreased response to NA cues compared to alcohol cues, but still smaller than rewarding cues, would advocate for a ‘simple’ decreased reactivity to neutral cues. Moreover, as it has been proven that addiction is characterised not only by an increased motivation for drugs, but also by a decreased motivation for natural rewards (Goldstein and Volkow, 2002), a higher P3 response to alcohol-related cues compared to NA cues, but also compared to rewarding cues, would speak in favour of the appearance of the combination of two features characteristic of the alcohol-dependent population in binge drinkers (i.e. cue reactivity for alcohol cues and increased sensitivity threshold to NA reward cues, i.e. decreased sensitivity for NA cues). Further studies would thus be useful to test these alternative options.

The fact that no differential processing between A and NA cues was observed in T1 between both groups could be surprising at first as other similar previous studies based on a single evaluation already showed a difference between heavy and light drinkers (e.g. Herrmann et al., 2001; Petit et al., 2013a). These findings may be explained if we carefully consider the length of heavy drinking habits in the different studies. In our previous study





**Figure 2.** P3 component on six parietal and centro-parietal electrodes (CP1, CP2, P3, Pz, P4, POz) for alcohol- and non-alcohol-related stimuli in the control and binge drinkers groups at T2 and T1.

(Petit et al., 2013a) showing differences in P3 amplitudes for A cues in binge drinkers at first (and unique) evaluation, students had already binge drunk for four and a half years, while binge drinkers in the present study had only been binge drinking for three years. In the second evaluation, they were then comparable to students in the study of Petit et al. (2013a) in terms of duration of drinking habits. In the same manner, in the study of Herrmann et al. (2001), the heavy drinkers sample was on average 36.5 years old and therefore presented a longer drinking history than the 21-year-old students in this study. Although no causal link can of course be thrown out here, these observations support our present hypothesis of time duration as the responsible factor for the appearance of differential processing of A and NA cues. The occurrence of a difference needs a beginning point. It looks like changes have been occurring within the year of our investigation. One could expect that differences will strengthen with the persistence of drinking habits. Also, the fact that no difference was seen in T1 between groups pleads for the rejection of alcohol cue reactivity as a hereditary trait in this sample.

In any case, precaution should be taken when evoking the popular continuum hypothesis. Indeed, just because data show a link between binge drinking and alcoholic disease does not mean

that (a) all binge drinkers will become dependent drinkers and (b) for those who will, that this will operate through the appearance of cognitive process modulations. On the one hand, statistics suggest that for many, drinking during adolescence and young adulthood is just a phase, most of them finally coming out of alcohol interest as they begin to take on adult responsibilities such as employment, marriage and parenthood (e.g. Muthen and Muthen, 2000; Wood et al., 2000). On the other hand, it is known that other factors such as genetic, environmental and personality aspects are also candidates for alcohol dependence risk (for a review, see Petit et al. (2013c)). Binge drinkers may, similarly to alcohol dependent patients, be vulnerable to and present some altered cognitive processes without these being the cause of the development of possible future alcoholic disease.

Finally, besides our main amplitudes-related results, latency-related results showed that in both groups and for both evaluation times, alcohol-related cues elicited shorter P3 latencies than non-alcohol-related cues. This aligns behavioural results showing faster reaction times in response to A compared to NA stimuli and suggests that all subjects were more vigilant in relation to alcohol-related cues leading to the more rapid processing of these. This difference in electrophysiological response for both

**Table 5.** *F* and *p*-values obtained from the linear regression computed on P3 amplitudes in response to non-alcohol-related (NA) stimuli in T2 using a backward procedure. Number of alcohol doses per drinking occasion (ADO) was the best predictor of P3 amplitudes to NA stimuli in T2.

Model P3	Variables entered	Variables excluded	R square	F	Significance
1	ADW, ADH, DOW, ADO	/	20.1	1.577	0.211
2	ADH, DOW, ADO	ADW $t = -0.333$ , $p = 0.742$	19.8	2.138	0.120
3	ADH, ADO	ADW $t = -0.549$ , $p = 0.588$ ADH $t = 0.898$ , $p = 0.377$	17.3	2.824	0.077
4	ADO	ADW $t = -0.078$ , $p = 0.938$ ADH $t = 0.552$ , $p = 0.585$ DOW $t = 0.656$ , $p = 0.518$	16.0	5.328	<b>0.029</b>

ADH: number of alcohol doses per hour; ADW: number of alcohol doses per week; DOW: number of drinking occasions per week.

stimuli types is consistent with an increasing body of findings in studies including light/social drinkers and also showing alcohol-related attentional bias in these populations (Bauer and Cox, 1998; George et al., 2001; Herrmann et al., 2001; Petit et al., 2012a, 2013a; Ryan, 2002; Stetter et al., 1994; Tapert et al., 2004; Vollstädt-Klein et al., 2009). This could appear surprising at first sight. However, it is not difficult to consider that alcohol-related items could draw more attention than household ones and, as alcohol cues are often associated with agreeable situations in social and light drinkers, it appears plausible that these recreational drinkers are more vigilant to alcohol-related cues (Vollstädt-Klein et al., 2009).

In summary, our results provide some answers to the issues raised above: (a) binge drinking patterns are associated over time with impairments in the processing of visual stimuli (P1 component); (b) the exploration of electrophysiological reactions to both alcohol- and non-alcohol-related stimuli shows evidence of differential processing of alcohol- and non-alcohol-related cues in binge drinkers (P3 component); and (c) time is linked to the appearance of brain functioning alterations as the differences observed between the two groups only appeared in Time 2 (P1 and P3 components).

Besides these questions, our regression analysis highlighted another important observation. It suggested that among the different drinking variables used to characterise binge drinking, the best predictor of P3 amplitudes to non-alcohol-related stimuli in T2 was the number of alcohol doses per occasion, which means the intensity of drinking, i.e. the specific binge drinking pattern. This result is very important as it supports an observation made in Muraige et al.'s (2012) study, which examined and revealed the specific effect of binge drinking patterns on cerebral dysfunction, regardless of the total weekly alcohol intake. Our present results thus confirmed that the specific consumption pattern of binge drinking, more than global heavy alcohol consumption, is associated with the onset of differential cue reactivity over time.

Our study clearly suffers from some limitations that should be noted. A first weakness is linked to gender composition in our sample, which showed a very large difference between the binge drinking and control groups. However, it has been previously shown that this variable is important as far as the dopaminergic response to alcohol and alcohol cue reactivity are concerned (Petit et al., 2013a; Urban et al., 2010). Replication of this study will have to carefully select a sufficient amount of participants of each sex to properly control for this variable. The second main limitation is linked to one of our selection

criterion, which was, for participants, to show the same consumption pattern from Time 1 to Time 2, i.e. binge drinkers all remained binge drinkers and controls all remained controls. Nothing is known therefore about what would have been observed in students who would have withdrawn from binge drinking habits from Time 1 to Time 2. Would ERP anomalies and cue reactivity also have been observed? Further follow-up studies should be more precise by choosing participants with no drinking history as of yet, and be more extensive, i.e. focus on both binge drinking 'withdrawers' and 'continuers' and follow participants over a longer period of time. They should also carefully control for family history of depression and antisocial personality, two variables known to influence the P3 component (O'Connor et al., 1994). Even though the centro-parietal P3 (P3b) component studied here is the most widely used ERP measure in psychiatric and other clinical applications (e.g. Polich and Herbst, 2000), another P3 component can be recorded at the anterior scalp locations, the P3a which reflects frontal lobe activity (Friedman et al., 1993; Knight, 1984). As frontal lobe functioning has been shown to be involved in cue reactivity, it would be worth investigating this P3a component in further studies in a modified oddball task using a third, also rare stimulus (distracter) along with standard and target stimuli. Finally, our sample size was limited which could have lowered the power of our results; further studies on larger samples should therefore be conducted.

Despite these limitations, we suggest that in regard to our data, there is an urgent need to (a) develop adapted information and prevention programmes putting across the message that binge drinking is not just inoffensive social fun but, if continued, promotes the onset of cerebral disturbances that may lead to alcohol dependence later in life and (b) develop appropriate interventions to be delivered before those drinking habits change into embedded practice.

### Conflict of interest

The authors declare that there is no conflict of interest.

### Funding

Géraldine Petit and Salvatore Campanella are Research Fellow and Research Associate, respectively, at the Belgian Fund of Scientific Research. This research was funded by the Belgian Fund for Scientific Research, but this did not exert any editorial steering or censorship on any part of this article.

## References

- Bartholow BD, Henry EA and Lust SA (2007) Effects of alcohol sensitivity on P3 event-related potential reactivity to alcohol cues. *Psychol Addict Behav* 21: 555–563.
- Bartholow BD, Lust SA and Tragesser SL (2010) Specificity of P3 event-related potential reactivity to alcohol cues in individuals low in alcohol sensitivity. *Psychol Addict Behav* 24: 220–228.
- Bauer D and Cox WM (1998) Alcohol-related words are distracting to both alcohol abusers and non-abusers in the Stroop colour-naming task. *Addiction* 93: 1539–1542.
- Beck AT, Steer RA and Brown GK (1998) *BDI-II, Inventaire de dépression de Beck: Manuel*. Toronto, Canada: Les Éd. du Centre de Psychologie Appliquée (ECPA), The Psychological Corporation.
- Begleiter H, Porjesz B, Bihari B, et al. (1984) Event-related brain potentials in boys at risk for alcoholism. *Science* 225: 1493–1496.
- Bertrand O, Perrin F and Pernier J (1985) A theoretical justification of the average reference in topographic evoked potential studies. *Electroencephalogr Clin Neurophysiol* 62: 462–464.
- Bonomo YA, Bowes G, Coffey C, et al. (2004) Teenage drinking and the onset of alcohol dependence: A cohort study over seven years. *Addiction* 99: 1520–1528.
- Campanella S, Petit G and Maurage P (2009) Chronic alcoholism: Insights from neurophysiology. *Neurophysiol Clin* 39: 191–207.
- Ceballos NA, Giuliano RJ, Wicha NY, et al. (2012) Acute stress and event related potential correlates of attention to alcohol images in social drinkers. *J Stud Alc Drugs* 73: 761–771.
- Courtney KE and Polich J (2010) Binge drinking effects on EEG in young adult humans. *Int J Environ Res Pub Health* 7: 2325–2336.
- Crego A, Cadaveira F, Parada M, et al. (2012) Increased amplitude of P3 event-related potential in young binge drinkers. *Alcohol* 46: 415–425.
- Crego A, Holguín SR, Parada M, et al. (2009) Binge drinking affects attentional and visual working memory processing in young university students. *Alcohol Clin Exp Res* 33: 1870–1879.
- Crego A, Rodriguez-Holguín S, Parada M, et al. (2010) Reduced anterior prefrontal cortex activation in young binge drinkers during a visual working memory task. *Drug Alcohol Depend* 109: 45–56.
- Cuthbert BN, Schupp HT, Bradley MM, et al. (2000) Brain potentials in affective picture processing: Covariation with autonomic arousal and affective report. *Biol Psychol* 52: 95–111.
- Dickter CL, Forestell CA, Hammett PJ, et al. (2014) Relationship between alcohol dependence, escape drinking, and early neural attention to alcohol-related cues. *Psychopharmacol* 231: 2031–2041.
- Ehlers CL, Phillips E, Finnerman G, et al. (2007) P3 components and adolescent binge drinking in Southwest California Indians. *Neurotoxicol Teratol* 29: 153–163.
- Euser AS, Arends LR, Evans BE, et al. (2012) The P300 event-related brain potential as a neurobiological endophenotype for substance use disorders: A meta-analytic investigation. *Neurosci Biobehav Rev* 36: 572–603.
- Fehr T, Wiedenmann P and Herrmann M (2007) Differences in ERP topographies during color matching of smoking-related and neutral pictures in smokers and nonsmokers. *Int J Psychophysiol* 65: 284–293.
- Field M and Cox WM (2008) Attentional bias in addictive behaviors: A review of its development, causes, and consequences. *Drug Alcohol Depend* 97: 1–20.
- Field M, Eastwood B, Bradley BP, et al. (2006) Selective processing of cannabis cues in regular cannabis users. *Drug Alcohol Depend* 85: 75–82.
- Field M and Quigley M (2009) Mild stress increases attentional bias in social drinkers who drink to cope: A replication and extension. *Exp Clin Psychopharmacol* 17: 312–319.
- Fleming KA and Bartholow BD (2014) Alcohol cues, approach bias, and inhibitory control: Applying a dual process model of addiction to alcohol sensitivity. *Psychol Addict Behav* 28: 85–96.
- Franken IHA (2003) Drug craving and addiction: Integrating psychological and neuropsychopharmacological approaches. *Prog Neuropsychopharmacol Biol Psychiatry* 27: 563–579.
- Friedman D, Simpson GV and Hamberger M (1993) Age-related changes in scalp topography to novel and target stimuli. *Psychophysiology* 30: 383–396.
- Garland EL, Franken IHA and Howard MO (2012) Cue-elicited heart rate variability and attentional bias predict alcohol relapse following treatment. *Psychopharmacology* 222: 17–26.
- George MS, Anton RF, Bloomer C, et al. (2001) Activation of prefrontal cortex and anterior thalamus in alcoholic subjects on exposure to alcohol-specific cues. *Arch Gen Psychiatry* 58: 345–52.
- Giedd JN, Blumenthal J, Jeffries NO, et al. (1992) Brain development during childhood and adolescence: A longitudinal MRI study. *Nat Neurosci* 2: 861–863.
- Goldstein RZ and Volkow ND (2002) Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. *Am J Psychiatry* 159: 1642–1652.
- Goudriaan AE, Grekin ER and Sher KJ (2007) Decision making and binge drinking: A longitudinal study. *Alcohol Clin Exp Res* 31: 928–938.
- Haller M, Handley E, Chassin L, et al. (2010) Developmental cascades: Linking adolescent substance use, affiliation with substance use promoting peers, and academic achievement to adult substance use disorders. *Dev Psychopathol* 22: 899–916.
- Hansenne M (2006) Event-related brain potentials in psychopathology: Clinical and cognitive perspectives. *Psychol Belg* 46: 5–36.
- Hanson KL, Medina KL, Padula CB, et al. (2011) Impact of adolescent alcohol and drug use on neuropsychological functioning in young adulthood: 10-Year outcomes. *J Child Adolesc Subst Abuse* 20: 135–154.
- Hartley DE, Elsabagh S and File SE (2004) Binge drinking and sex: Effects on mood and cognitive function in healthy young volunteers. *Pharmacol Biochem Behav* 78: 611–619.
- Heffernan T, Clark R, Bartholomew J, et al. (2010) Does binge drinking in teenagers affect their everyday prospective memory? *Drug Alcohol Depend* 109: 73–78.
- Heinze HJ and Mangun GR (1995) Electrophysiological signs of sustained and transient attention to spatial locations. *Neuropsychologia* 33: 889–908.
- Henry EA, Kaye JT, Bryan AD, et al. (2013) Cannabis cue reactivity and craving among never, infrequent and heavy cannabis users. *Neuropsychopharmacology* 39: 1214–1221.
- Herrmann MJ, Weijers HG, Wiesbeck GA, et al. (2000) Event-related potentials and cue-reactivity in alcoholism. *Alcohol Clin Exp Res* 24: 1724–1729.
- Herrmann MJ, Weijers HG, Wiesbeck GA, et al. (2001) Alcohol cue-reactivity in heavy and light social drinkers as revealed by event-related potentials. *Alcohol Alcohol* 36: 588–593.
- Hillyard SA, Anillo-Vento L, Clark VP, et al. (1996) Neuroimaging approaches to the study of visual attention: A tutorial. In: Kramer AF, Coles MGH and Logan GD (eds) *Converging Operations in the Study of Visual Selective Attention*. Washington, DC: American Psychological Association, pp.107–138.
- Hingson RW, Heeren T and Winter MR (2006) Age at drinking onset and alcohol dependence: Age at onset, duration, and severity. *Arch Pediatr Adolesc Med* 160: 739–746.
- Hopfinger JB and Mangun GR (2001) Electrophysiological studies of reflexive attention. In: Folk C and Gibson B (eds) *Attraction, Distraction, and Action: Multiple Perspectives on Attentional Capture*. Amsterdam: Elsevier, pp.3–26.
- Houlihan ME, Pritchard WS and Robinson JH (1996) Faster P300 latency after smoking in visual but not auditory oddball tasks. *Psychopharmacology* 123: 231–238.
- Jacobsen LK, Mencl WE, Westerveld M, et al. (2004) Impact of cannabis use on brain function in adolescents. *Ann N Y Acad Sci* 1021: 384–390.

- Jasper H (1958) Report of committee on methods of clinical exam in EEG. *Electroencephalogr Clin Neurophysiol* 10: 370–375.
- Johnson CA, Xiao L, Palmer P, et al. (2008) Affective decision-making deficits, linked to adysfunctional ventromedial prefrontal cortex, revealed in 10th grade Chinese adolescent binge drinkers. *Neuropsychologia* 46: 714–726.
- Johnston VS, Miller DR and Bursleson MH (1986) Multiple P3s to emotional stimuli and their theoretical significance. *Psychophysiology* 23: 684–694.
- Kareken DA, Bragulat V, Dziedzic M, et al. (2010) Family history of alcoholism mediates the frontal response to alcoholic drink odors and alcohol in at-risk drinkers. *NeuroImage* 50: 267.
- Keil A, Bradley MM, Hauk O, et al. (2002) Large-scale neural correlates of affective picture processing. *Psychophysiology* 39: 641–649.
- Kleinbaum D, Kupper L, Nizam A, et al. (2013) Applied Regression Analysis and Other Multivariable Methods. Boston, MA: Cengage Learning, pp. 1074.
- Knight RT (1984) Decreased response to novel stimuli after prefrontal lesions in man. *Electroencephalogr Clin Neurophysiology* 59: 9–20.
- Kuntsche E, Rehm J and Gmel G (2004) Characteristics of binge drinkers in Europe. *Soc Sci Med* 59: 113–127.
- Lang PJ, Bradley MM and Cuthbert BN (1997) Motivated attention: Affect, activation, and action. In: *Attention and Orienting: Sensory and Motivational Processes*. Hillsdale, NJ: Erlbaum, pp.97–135.
- Lang PJ, Bradley MM, Cuthbert BN (2005) *International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-6*. Gainesville, FL: University of Florida.
- Lang SW, Waller PF and Shope JT (1996) Adolescent driving: Characteristics associated with single-vehicle and injury crashes. *J Saf Res* 27: 241–257.
- Li T-K, Hewitt BG and Grant BF (2007) Is there a future for quantifying drinking in the diagnosis, treatment, and prevention of alcohol use disorders? *Alcohol Alcohol* 42: 57–63.
- López-Caneda E, Cadaveira F, Crego A, et al. (2012) Hyperactivation of right inferior frontal cortex in young binge drinkers during response inhibition: A follow-up study. *Addiction* 107: 1796–1808.
- López-Caneda E, Cadaveira F, Crego A, et al. (2013) Effects of a persistent binge drinking pattern of alcohol consumption in young people: A follow-up study using event-related potentials. *Alcohol Alcohol* 48: 464–471.
- Lubman DI, Yücel M and Pantelis C (2004) Addiction, a condition of compulsive behaviour? Neuroimaging and neuropsychological evidence of inhibitory dysregulation. *Addiction* 99: 1491–1502.
- Luna B and Sweeney JA (2004) The emergence of collaborative brain function: FMRI studies of the development of response inhibition. *Ann N Y Acad Sci* 1021: 296–309.
- McQueeney T, Schweinsburg BC, Schweinsburg AD, et al. (2009) Altered white matter integrity in adolescent binge drinkers. *Alcohol Clin Exp Res* 33: 1278–1285.
- Maurage P, Grynberg D, Noël X, et al. (2011) Dissociation between affective and cognitive empathy in alcoholism: A specific deficit for the emotional dimension. *Alcohol Clin Exp Res* 35: 1662–1668.
- Maurage P, Joassin F, Speth A, et al. (2012) Cerebral effects of binge drinking: Respective influences of global alcohol intake and consumption pattern. *Clin Neurophysiol* 123: 892–901.
- Maurage P, Pesenti M, Philippot P, et al. (2009) Latent deleterious effects of binge drinking over a short period of time revealed only by electrophysiological measures. *J Psychiatry Neurosci* 34: 111–118.
- Maurage P, Philippot P, Verbanck P, et al. (2007) Is the P300 deficit in alcoholism associated with early visual impairments (P100, N170)? An oddball paradigm. *Clin Neurophysiol* 118: 633–644.
- Mota N, Parada M, Crego A, et al. (2013) Binge drinking trajectory and neuropsychological functioning among university students: A longitudinal study. *Drug Alc Depend* 133: 108–114.
- Muthen BO and Muthen LK (2000) The development of heavy drinking and alcohol-related problems from ages 18 to 37 in a U.S. national sample. *J Stud Alcohol* 61: 290–300.
- Namkoong K, Lee E, Lee CH, et al. (2004) Increased P3 amplitudes induced by alcohol-related pictures in patients with alcohol dependence. *Alcohol Clin Exp Res* 28: 1317–1323.
- Nicolás JM, Estruch R, Salamero M, et al. (1997) Brain impairment in well-nourished chronic alcoholics is related to ethanol intake. *Ann Neurol* 41: 590–598.
- O'Connor S, Bauer L, Tasman A, et al. (1994) Reduced P3 amplitudes are associated with both a family history of alcoholism and antisocial personality disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 18: 1307–1321.
- Öhman A (1979) The orienting response, attention, and learning: An information processing perspective. In: Kimmel HD, van Olst EH and Orlebeke JF (eds) *The Orienting Reflex in Humans*. Hillsdale, New Jersey: LEA, pp.443–471.
- Parada M, Corral M, Caamano-Isorna F, et al. (2011) Binge drinking and declarative memory in university students. *Alcohol Clin Exp Res* 35: 1–10.
- Parada M, Corral M, Mota N, et al. (2012) Executive functioning and alcohol binge drinking in university students. *Addict Behav* 37: 167–172.
- Paus T (2001) Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nat Rev Neurosci* 2: 417–424.
- Petit G, Kornreich C, Maurage P, et al. (2012a) Early attentional modulation by alcohol-related cues in young binge drinkers: An event-related potentials study. *Clin Neurophysiol* 123: 925–936.
- Petit G, Kornreich C, Noël X, et al. (2012b) Alcohol-related context modulates performance of social drinkers in a visual go/no-go task: A preliminary assessment of event-related potentials. *PLoS One* 7: e37466.
- Petit G, Kornreich C, Verbanck P, et al. (2013a) Gender differences in reactivity to alcohol cues in binge drinkers: A preliminary assessment of event-related potentials. *Psychiatry Res* 209: 494–503.
- Petit G, Kornreich C, Verbanck P, et al. (2013c) Why is adolescence a key period to initiate drinking? Which adolescents are prone to develop long-term problem use? A review of current available data. *Soc Neurosci Psychol* 3: 21890: 1–14.
- Petit G, Maurage P, Kornreich C, et al. (2013b) Binge drinking in adolescents: A review of neurophysiological and neuroimaging research. *Alcohol Alcohol* 49: 198–206.
- Polich J (2004) Clinical application of the P300 event-related brain potential. *Phys Med Rehabil Clin N Am* 15: 133–161.
- Polich J (2007) Updating P300: An integrative theory of P3a and P3b. *Clin Neurophysiol* 118: 2128–2148.
- Polich J and Herbst KL (2000) P300 as a clinical assay: Rationale, evaluation and findings. *Int J Psychophysiol* 38: 3–19.
- Porjesz B and Begleiter H (1996) Effects of alcohol on electrophysiological activity of the brain. In Begleiter H and Kissin B (eds) *The Pharmacology of Alcohol and Alcohol Dependence*. New York: Oxford University Press, pp.207–247.
- Robinson TE and Berridge KC (1993) The neural basis of drug craving: An incentive sensitization theory of addiction. *Brain Res Brain Res Rev* 18: 247–291.
- Ryan F (2002) Attentional bias and alcohol dependence: A controlled study using the modified Stroop paradigm. *Addict Behav* 27: 471–82.
- Schupp HT, Ohman A, Junghofer M, et al. (2004) The facilitated processing of threatening faces: An ERP analysis. *Emotion* 4: 189–200.
- Schweinsburg AD, McQueeney T, Nagel BJ, et al. (2010) A preliminary study of functional magnetic resonance imaging response during verbal encoding among adolescent binge drinkers. *Alcohol* 44: 111–117.
- Shin E, Hopfinger JB, Lust SA, et al. (2010) Electrophysiological evidence of alcohol-related attentional bias in social drinkers low in alcohol sensitivity. *Psychol Addict Behav* 24: 508–515.
- Sokhadze E, Stewart C, Hollifield M, et al. (2008) Event-related potential study of executive dysfunctions in a speeded reaction task in cocaine addiction. *J Neurother* 12: 185–204.



- Spielberger CD and Gorsuch RL (1983) *Manual for the State-Trait Anxiety Inventory (Form Y) (Self-Evaluation Questionnaire)*. Palo Alto, CA: Consulting Psychologists Press.
- Squeglia LM, Sorg SF, Schweinsburg AD, et al. (2012) Binge drinking differentially affects adolescent male and female brain morphometry. *Psychopharmacology* 220: 529–39.
- Stacy AW and Wiers RW (2010) Implicit cognition and addiction: A tool for explaining paradoxical behavior. *Annu Rev Clin Psychol* 6: 551–575.
- Stetter F, Chaluppa C, Ackermann K, et al. (1994) Alcoholics' selective processing of alcohol related words and cognitive performance on a Stroop task. *Eur Psychiatry* 9: 71–76.
- Tapert SF, Schweinsburg AD, Barlett VC, et al. (2004) Blood oxygen level dependent response and spatial working memory in adolescents with alcohol use disorders. *Alc Clin Exp Res* 28:1577–1586.
- Urban NBL, Kegeles LS, Slifstein M, et al. (2010) Sex differences in striatal dopamine release in young adults after oral alcohol challenge: A positron emission tomography imaging study with [<sup>11</sup>C]raclopride. *Biol Psychiatry* 68: 689–696.
- Vollstädt-Klein S, Loeber S, von der Goltz C, et al. (2009) Avoidance of alcohol-related stimuli increases during the early stage of abstinence in alcohol-dependent patients. *Alcohol Alcohol* 44: 458–463.
- Wagner FA and Anthony JC (2002) From first drug use to drug dependence. Developmental periods of risk for dependence upon marijuana cocaine and alcohol. *Neuropsychopharmacol* 26: 479–88.
- Wiers RW, Bartholow BD, van den Wildenberg E, et al. (2007) Automatic and controlled processes and the development of addictive behaviors in adolescents: A review and a model. *Pharmacol Biochem Behav* 86: 263–283.
- Wilkinson D and Halligan P (2004) The relevance of behavioural measures for functional imaging studies of cognition. *Nat Rev Neurosci* 5: 67–73.
- Wood MD, Sher KJ and McGowan AK (2000) Collegiate alcohol involvement and role attainment in early adulthood: Findings from a prospective high-risk study. *J Stud Alcohol* 61: 278–289.
- Zironi I, Burattini C, Aicardi G, et al. (2006) Context is a trigger for relapse to alcohol. *Behav Brain Res* 167: 150–155.