Universidade do Minho
Escola de Psicologia

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The Hangover Effects on the Attentional Bias for Alcohol-related cues: an electroencephalographic study

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The Hangover Effects on the Attentional Bias for Alcohol-relates cues: An Electroencephalographic study

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Doutor Eduardo López-Caneda
e do
Doutor Alberto Crego

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DIREITOS DE AUTOR E CONDIÇÕES DE UTILIZAÇÃO DO TRABALHO POR TERCEIROS

Universidade do Minho, janeiro 2021

Mariana Rebelo Miranda

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"Para ser grande, sê inteiro: nada
Teu exagera ou exclui.
Sê todo em cada coisa. Põe quanto és
No mínimo que fazes.
Assim em cada lago a lua toda
Brilha, porque alta vive."
Ricardo Reis

DECLARAÇÃO DE INTEGRIDADE

Declaro ter atuado com integridade na elaboração do presente trabalho académico e confirmo que não recorri à prática de plágio nem a qualquer forma de utilização indevida ou falsificação de informações ou resultados em nenhuma das etapas conducente à sua elaboração.
Mais declaro que conheço e que respeitei o Código de Conduta Ética da Universidade do Minho.

Universidade do Minho, janeiro 2021

Adriana Rebela Miranda

Contents

Index of Tables

List of Illustrations

Os efeitos da ressaca no viés atencional para pistas relacionadas com o álcool: um estudo electroencafalográfico

Resumo

O *binge drinking* (BD) é um padrão de consumo caracterizado pela ingestão excessiva de álcool num curto período de tempo, seguido de abstinência. Especificamente, este padrão é definido como o consumo de 4 bebidas em duas horas para mulheres (5 bebidas para homens), sendo uma forma de consumo muito comum entre os jovens e adolescentes. Uma das consequências mais experienciadas a curto-prazo envolve a experiência da ressaca, que causa uma série de sintomas físicos e mentais desagradáveis quando o nível de concentração de álcool no sangue se aproxima de zero. Para explorar se a ressaca produz algum efeito no viés atencional para pistas relacionadas com o álcool, utilizou-se a metodologia dos potenciais evocados (ERPs) durante a realização de uma tarefa visual *oddball* com pistas relacionadas com o álcool. Assim, foram analisadas as amplitudes dos componentes P2, N2/P3a e P3b, bem como variáveis comportamentais (i.e., tempos de reação, percentagem de respostas corretas e percentagem de respostas incorretas) em 11 participantes, tanto num dia típico de ressaca como num dia normal sem consumo de álcool. Resultados não revelaram efeitos da ressaca a nível comportamental, nem aumentaram o viés atencional para pistas relacionadas com o álcool. No entanto, maiores amplitudes da P2 e da P3b foram observadas no momento de ressaca, sugerindo que causa o recrutamento adicional de recursos atencionais para realizar tarefas simples.

Palavras-chave: binge drinking, ressaca, vies atencional, ERPs, estudantes universitários

The hangover effects on the attentional bias for alcohol-related cues: an electroencephalographic study

Abstract

Binge drinking (BD) is a consumption pattern characterized by an excessive alcohol intake over a short period of time, followed by abstinence. Specifically, BD is defined as the ingestion of 4 drinks in two hours for women (5 drinks for men), being a very common drinking pattern among adolescents and young people. One of the most experienced short-term consequences of BD is the hangover, which causes a series of unpleasant physical and mental symptoms when the blood alcohol concentration starts approaching zero. To explore if the hangover state may affect the attentional bias for alcohol-related cues, the event-related potentials (ERP) approach was employed during the performance of a visual novelty oddball task. Amplitudes of P2, N2/P3a and P3b components and behavioral performance (i.e., reaction times and percentage of correct responses) were analyzed in 11 participants, both during hangover and during a normal day without alcohol consumption. Results revealed that hangover had no effects at the behavioral level neither did increase the attentional bias for alcohol-related cues. Nevertheless, increased P2 and P3b amplitudes were observed during hangover, suggesting the recruitment of additional attentional resources to perform simple tasks.

Keywords: binge drinking, hangover, attentional bias, ERPs, university students

Introduction

Alcohol is the most used psychoactive substance in the world, having been used for centuries in many cultural, religious, and socialization practices (World Health Organization (WHO), 2018). Its ingestion can cause perceived happiness and feelings of joy among individuals; however, the continued and harmful use of the substance can bring negative consequences to the social and health context of the individuals.

Alcohol abuse has been related to major non-communicable diseases (such as cardiovascular, cancers, and liver diseases), infectious diseases (as sexually transmitted infections, viral hepatitis, tuberculosis), mental disorders, and injuries (being either intentional or non-intentional) such as violence, crimes, poisonings, falls or road traffic accidents; overall contributing to a large scale for the disease burden worldwide (WHO, 2018). Accordingly, alcohol has a great expression in mortality rates, being estimated to be responsible for 3 million deaths worldwide (5.3% of all deaths) every year, counting for more mortality than the one caused by diseases such as HIV/AIDS, tuberculosis, and diabetes (WHO, 2018). This way, alcohol use end-up impacting far more than the individual alone, concerning also their families, the community, and the economy, as it appears related to several multi-contextual problems (eg. occupational and familiar neglect, vandalism and property damage, victimization by physical and sexual assault) (Karriker-Jaffe et al., 2018).

Although a slight decline tendency has been observed since 2000 in the number of drinkers worldwide, alcohol is still consumed by half of the world's population, being Europe the place with the highest per capita consumption (WHO, 2018). Namely, in Portugal, where alcohol is the preferred intoxicant by the population, prevalence rates point to approximately 85% of experimental use in total population, being responsible for a large part of hospitalizations, road traffic accidents, domestic violence, crimes against society and mortality (Balsa, Vital, & Urbano, 2018).

Over the last decades, excessive and regular alcohol drinking gave place to a new kind of drinking pattern widely spread in high-income countries (such as Portugal), characterized by excessive drinking episodes with abstinence periods between drinking sessions. This pattern of alcohol consumption is named Binge Drinking (BD), and is quantitatively defined as the ingestion of a minimum of four (five for men) alcoholic beverages in about two hours, bringing the level of blood alcohol concentration (BAC) to 0.08 g/dL (National Institute of Alcohol Abuse and Alcoholism (NIAAA), 2004). Moreover, these heavy drinking episodes must occur with a periodicity of at least once in two weeks, or once a month (Courtney & Polich, 2009).

Regarding this type of alcohol consumption, global epidemiological reports indicate that 42.6%

of drinkers engage in heavy drinking episodes, suggesting that most alcohol is consumed in heavy drinking sessions (WHO, 2018). More importantly, this type of drinking appears to be very famous in younger generations, with numbers suggesting that one-third of young Europeans and Americans (aged between 16-18 years) are binge drinkers (BDs)(Kraus et al., 2016; SAMHSA, 2016). Furthermore, reports indicate BD peaks at the ages of 20-24 years, persisting throughout university academic years, by when it becomes higher than in the total population (WHO, 2018). Accordingly, prevalence rates regarding national territory suggest that 11,8% Portuguese youngsters aged from 15-24 years engaged in BD in the previous 12 months, with further 51,9% of binge prevalence among youngsters aged 18 years old within the same period (Balsa et al., 2018).

These numbers come out as very worrying since this type of drinking is associated with higher risks for ischemic heart disease, sudden death, use of other drugs, injuries, car crashes and risky sexual behavior (WHO, 2012). Moreover, given the particularly vulnerable neurodevelopmental window this age-range represents, alcohol use by these developmental years could impair the maturation processes ongoing (Bava & Tapert, 2010), creating cognitive deficits and being able to influence the development of alcoholism into adulthood.

Alcohol in the adolescent and young brain

Adolescence and young adulthood are periods of critical importance for the development of the brain, for it is when major structural and functional changes take place (Bava & Tapert, 2010). In general terms, there is a non-linear decrease in the gray matter volume and an increase in the white matter volume as a result of synaptic pruning and myelination processes, which are meant to bring more efficacy and velocity to neuronal communication (Bava & Tapert, 2010). Thus, while primary sensory areas mature earlier in life, during adolescence and entering adulthood these maturation processes take place in high order association areas, like the prefrontal cortex and hippocampus, allowing the individuals the development of a more complex set of cognitive and affective functions (Bava & Tapert, 2010). By this, one could agree that changes in the brain morphology (e.g. synaptic pruning, myelination) end-up modulating the development of crucial executive functions, as inhibitory control, working memory, or decision making (Fuster, 2000), meaning that substance use by these developmental years could alter the normal course of maturation and reflect itself in functional consequences over time (Jacobus & Tapert, 2013).

Studies using different neuroscience techniques have been conducted in the last decades, suggesting this drinking pattern may cause functional brain impairments and poor cognitive

performance. More specifically, neuropsychological studies with adolescent and young adults suggest that BDs show weaker cognitive flexibility, abnormal functional activity in working memory tasks, impairments regarding prospective memory and poor performance in tasks of inhibitory control, among others (for a review see Carbia et al., 2018). These deficits, in turn, seem to heighten individuals' loss of control over drinking behavior (Lopez-Caneda et al., 2014), possibly favoring more ingestion and, therefore, more probable impairment.

Moreover, at neural level, studies using electroencephalographic (EEG) and event-related potentials (ERPs) techniques have shown that alcoholics display abnormal neural processing when compared to control subjects. To clarify, ERPs are a non-invasive technique that allows the study of individuals' cerebral activity associated with the sensory and cognitive processes through the placing of electrodes in the scalp. Due to its fine temporal resolution (by the millisecond) this technique enables the understanding of what a "normal" brain activity looks like versus an altered brain function of, for example, an alcoholic patient (Kamarajan & Porjesz, 2015).

In general, ERPs studies with BDs report alterations in several components associated with different cognitive functions, namely in early perceptual components (P1), and in later ones associated with attentional (N2) and decisional (P3) stages of the cognitive information stream (Petit et al., 2012; Crego et al., 2009, 2012; López-Caneda et al., 2012). Despite the alterations found in the neurocognitive functioning of individuals during their performance in tasks of attention, working-memory, and inhibitory control, most of the ERPs studies report no alterations at the behavioral level, being these interpreted as compensatory mechanisms that allow the individuals to perform the task adequately (e.g., Crego et al., 2012; López-Caneda et al, 2013).

Hangover

While many studies have focused on the effects of alcohol consumption and binge drinking neurocognitive processes of individuals in medium to long term effects, there is an important immediate consequence of heavy drinking episodes that has not been much explored, as it is the case of alcohol hangover. Although some questions exist regarding its definition, alcohol hangover have been commonly defined as "a combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when BAC approaches zero" (Van Schrojenstein Lantman et al., 2017). The symptoms might include fatigue, nausea, and headache, being also referred in literature other complaints of drowsiness and effects on cognition (Penning, McKinney, & Verster, 2012; Van Schrojenstein Lantman et al., 2017).

Although hangover causes seem to remain unclear, the literature suggests that it can differently affect individuals, with some claiming to be hangover resistant (Kruisselbrink et al., 2017). To date, various factors seem to influence its emergence and severity, being highlighted dehydration (van Schrojenstein Lantman et al., 2017) and sleep deprivation (Penning et al., 2012), as well as genetic predisposition, additives of alcoholic beverages (Rohsenow et al., 2010), or the effects of alcohol metabolites as acetaldehyde (AcH)(Stephens et al., 2008).

It is suggested that hangover produces consequences short- and long-term memory, sustained attention, and psychomotor speed, as well as it is related to potentially dangerous daily activities such as car driving, flying an airplane or surgery (for review see Gunn et al., 2018). In addition, a recent study on the hangover effects in memory and attentional processes has also suggested impaired reaction times in tasks of spatial and dimensional selective attention, highlighting its results differences compared to other previously existing studies (Devenney, Coyle, & Verster, 2019).

Attentional bias for alcohol-related cues

One of the things that characterizes substance use and abuse is the existence of biases in the attentional processing of substance-related stimuli in the environment (Field & Cox, 2008). Various theories have tried to explain how it develops but in sum, the idea is that when individuals make regular use of a substance - for example, excessive drinking - the stimuli associated with that substance gains strength, being flagged as a priority in attentional processes, and therefore is processed first (Field & Cox, 2008). Evidence suggests attentional bias (AB) could be determinant in the maintenance of BD pattern, or even to escalate individuals' behavior towards compulsive use (Langbridge et al., 2019).

These assumptions have been finding support in many studies (e.g., Fernie et al., 2012; Field and Eastwood, 2005; Field et al., 2004), inclusively in neurophysiological studies like the one of Petit and colleagues (2012) where a visual oddball task with alcohol-related pictures was used. Their experiment consisted in presenting a series of images to the participants, being asked of them to respond if deviant stimuli appeared. This "deviant stimuli" category included images related and not related to alcohol, so that it could be understood if BDs differed from controls in the cognitive processing of these images. More specifically, they analyzed ERP components that were related to early sensory processing (P1), to attentional orienting mechanisms (N2b), and to decision-making processes (P3b). Results suggested BDs display altered neurofunctional activity when compared to controls, as was expressed in larger amplitudes in the P1 ERP component to alcohol-related images, indicating these individuals display unconscious attentional bias towards these images.

Another thing that also has much relevance in the AB literature is the assumption that it shares a relationship of reciprocal effects with craving, being that if AB to substance-related cues increases, so does the experience of subjective craving, and so on, as in a mutually excitatory positive feedback relation: if one increases, so does the other (Field & Cox, 2008). This is important because craving is suggested to play a role in substance-seeking behavior, and to be modulated by individuals' impulsivity traits and impaired inhibitory control (Dicker et al, 2014; Field & Jones, 2017; Carbia et al., 2018).

Therefore, in sum, if inhibitory control deficits appear as related to craving, which in turn is reported to have a mutual excitatory relationship with AB, then it is believed to be important to understand how AB unfolds over time. Despite this being a relatively common topic in research, to date no studies have used the EEG/ERPs techniques to explore the possible neurocognitive consequences of hangover, nor how it could affect attentional bias for alcohol-related cues.

Aims

The present study aims to understand how hangover may affect attentional bias to alcohol-related cues in a population of BDs university students. Therefore, our specific objectives are 1) to analyze hangover effects in BDs at a neural level, comparing by ERPs methodology the neurofunctional activity associated with attentional bias to alcohol-related cues during the performance of a visual attentional task in a normal day and during hangover state; 2) to analyze the hangover effects at a behavioral level, measuring the percentage of correct responses as well as the reaction times during the performance of a visual attentional task in a normal day and during hangover state; 3) to explore the extent to which psychological and alcohol use variables can be correlated to attentional bias.

Following these objectives, it is hypothesized that (1) BDs will display abnormal functional activity in the perceptual and cognitive ERP components typically related to attentional bias in hangover state vs normal state, specifically larger amplitudes in P2 and P3b components in occipital regions, and in N2-P3a components in frontal region; (2) BDs will show larger reactions times in hangover state; and (3) that psychological measures, such as impulsiveness, will correlate positively with the frequency of BD episodes, and imply more pronounced attentional bias.

Method

Participants

The recruitment of participants was through a convenience sampling in which researchers tried to collect participants from the University of Minho (UM) or Católica University of Braga. To do so, the experiment became available on an online platform of the Psychology School (EPsi) of UM, where psychology students could register to participate. Their participation would be rewarded with 1.6 credits they could posteriorly distribute to their grades at the end of the semester. Students from other courses and Católica University were contacted by the researchers to participate. Potential participants performed a clinical interview and different tests aimed at obtaining information regarding alcohol and drug use, personality characteristics and medical history.

To be included in the study, participants had to 1) age between 18 and 24 years; 2) fulfill the criteria for BD, according to NIAAA, i.e., drink a minimum of four drinks (five for men) on one occasion (in about two hours), at least once a month during the last month. After being acknowledged as BDs, participants still had to not be excluded by any of the following criteria: loss of consciousness for more than 20 minutes; personal history of psychopathological disorders (according to DSM-5); family history of major psychological disorders (major depressive disorder, schizophrenia or anxiety); family history of alcoholism or substance abuse; personal history of illegal substance use (opiates, hallucinogens, cocaine, amphetamine compounds); regular cannabis consumption (more than once a week); diagnosed alcohol use disorder (AUD) or scoring higher than 20 in the Alcohol Use Disorders Identification Test (AUDIT) (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001; Portuguese version: Cunha, 2002).

The final sample was composed of 11 university students (6 females), with ages between 19 and 24.

Instruments

(1) Alcohol Use Disorder Identification Test (AUDIT; Saunders, Aasland, Babor, De la Fuente, & Grant, 1993; Portuguese version: Gomes, 2004). AUDIT is a screening tool used to assess alcohol consumption, drinking behaviors, and alcohol-related problems. In the present study, this instrument was used to determine whether the participants fulfilled the BD criteria (question 3: “How often do you have six or more drinks on the same occasion?”; one of the following answers was required: “At least once a month”; “At least once a week”; or “Daily or almost daily”).

(2) Clinical History Interview. This interview was conducted to gather information about the medical history of the participants and their close relatives (first and second-degree). The answers

provided in this interview could be enough to exclude possible participants.

(3) Drugs Use Disorder Identification Test Extended (DUDIT-E; Berman, Palmstierna, Källmén, & Bergman, 2007). This test is an assessment tool to determine frequency, positive and negative aspects of use of illicit drug use, and treatment readiness. In the present study this instrument was used to identify the possible use of drugs other than alcohol.

(4) Penn Alcohol Craving Scale (PACS; Flannery, Volpicelli & Pettinati, 1999; Portuguese version: Pombo, Ismail, & Cardoso, 2008). It's a self-report measure with five items to assess individuals' craving for alcohol during the previous week.

(5) Edinburgh Handedness Inventory (Oldfield, 1971; Portuguese version: Espírito-Santo, Pires, Garcia, Daniel, Silva & Fazio, 2017). It is an inventory with 10 items which evaluates handedness.

(6) Barratt Impulsivity Scale-11 (BIS-11; Patton, Stanford e Barratt, 1995; Portuguese version: Cruz & Barbosa, 2012). It is a self-reported questionnaire designed to assess the personality/behavioral construct of impulsiveness.

(7) Symptom Checklist-90-Revised (SCL-90-R; Franke, 1995; Portuguese version: Laloni, 2001). It is a self-reported measure designed to evaluate psychological problems and psychopathological symptoms.

(8) Alcohol Hangover Severity Scale (AHSS; Penning, McKinney, Bus, Olivier, Slot, & Verster, 2013). It is a scale composed of 12 items designed to assess the overall hangover severity.

Other instruments:

- Breathalyzer test. This test measures the breath alcohol level before de EEG sessions.

- EEG Session Checklist. It is a checklist used in this study to confirm if all criteria for conducting to EEG session was fulfilled, for number of sleeping hours, time since last meal, last day they drank alcohol, among others.

- AlcoDroid Application. It is a mobile application that allowed the monitoring of the quantity of alcohol participants ingestion during the BD episode, as well as for the time span in which they did it.

Procedure

The present study was divided into three moments, one first clinical interview and two EEG assessments. The participant would only proceed to the EEG assessments phase if he/she fulfilled the inclusion criteria, and if did not met any of the exclusion criteria.

The experiment began with a consent form as it is required by the Subcomissão de Ética para as Ciências Sociais e Humanas of the University of Minho, which follows the guidelines of the Code of Ethical Principles for Medical Research Involving Humans Subjects aligned with the declaration of Helsinki. Once the consent was signed and all the doubts clarified, the clinical interview would start. This interview was conducted with the purpose of understanding if the participant would be eligible for the study, therefore some socio-demographic and substance use questionnaires were administered (instruments 1 to 3). If none of the exclusion criteria was met and the inclusion ones fulfilled, the participants were then included in the study, and some more information would be gathered through the administration of instruments 4 to 7. The total duration of this first moment was of approximately 30 minutes, and it ended with the scheduling of the first EEG assessment.

As it was previously said, the EEG assessments postulated two different moments for each participant. One of the EEGs would be recorded on a regular day, that is a day without alcohol consumption, whereas the other would be recorded on a day after a BD episode and, therefore, in a hangover state. As each participant had to do both assessment sessions, the sample was divided into two groups to secure counterbalance. This way, one group would perform firstly the EEG on a regular day and then the hangover state assessment, while the other would perform it in the reverse order, firstly the hangover state assessment, and secondly the regular day one.

When the assessment was performed on a regular day, participants were instructed to not engage in BD episodes during the three days before the assessment, nor to consume alcohol (or cannabis) in the day of the EGG. Furthermore, instructions were also given so that participants would not consume tobacco, tea, or coffee in the three hours before the assessment.

Regarding only the hangover state assessment, the procedure was a little more complex. Previously to the binge night, the participants would install the AlcoDroid mobile application with the help of the researchers, as well as to configurate their weight and height in their profile. This way, when in the BD episode, they could insert the type of beverage they ingested, as well as the duration they took to drink it, so that an estimation of the BAC could be provided. This way, at the end of the night, participants could export the AlcoDroid data to the researchers, so that the qualification as a BD episode could be confirmed. Afterwards, participants were instructed to sleep between six to nine hours

before the assessment, which postulated an additional instruction to the general ones mentioned above.

Before both EEG assessments, participants were asked to respond to PACS and to do a Breathalyzer test to confirm that BAC was at zero; and on the hangover state EEG, they were also asked to respond to AHSS.

Additionally, and despite it was not analyzed for the present study, 3ml of participants' saliva was collected for biochemical analysis, before the EEG assessments.

Task

To assess the attentional bias participants had to perform a visual novelty oddball task with alcohol cues as distractors. This way, participants were sited at a 100cm distance from an LCD computer monitor and had a computer mouse predisposed to their predominant hand. On the monitor, they were presented with three types of stimuli that appeared in the center of the screen with a duration of 70ms and an interstimulus interval of 1000-1200ms. The stimuli were horizontal stripes, vertical stripes, and alcohol-related pictures. The target stimuli were the white horizontal stripes, which appeared with 10% of probability and requested a physical response of the participant by clicking the mouse key. White vertical stripes were the standard stimuli, with 80% of probability of appearance, and the alcohol-related pictures that served as distractors appeared with 10% of probability; both standard and distractors did not require the answer of the participant.

EEG Recording

For EEG recordings, the participants' head was measured first, so that the right headcap size was used. Afterwards, 64 electrodes of ActiveTwo Biosemi system were set, organized according to 10/10 system. Vertical and horizontal electrooculogram activity was recorded to control for blinks and eye movements. All active electrodes were referred to bilateral electrodes placed in the mastoids. Electrode impedances were kept below 20kΩ. EEG signals were continuously amplified and digitized at a rate of 500 Hz and filtered on-line with a 0.01-100 Hz band pass filter.

Data Analysis

Concerning the demographic and drinking characteristics, a paired samples t-test was used to explore the differences in the PACS score regarding the two moments of the assessment, as well as the differences regarding the sleeping hours before the two moments. Bivariate Pearson correlations were also used to explore relations between psychological, electrophysiological and alcohol use variables

(impulsiveness, craving, AUDIT scores and hangover severity scores).

The behavioral data, which included the reaction times and the percentage of both correct and incorrect responses, were analyzed by a t-student test being the moment of assessment (normal day/hangover) the independent variable.

For ERP analysis, data were processed by the BrainVision Analyzer software (Version 2.1). To avoid eye movement and other artifacts, EEG signal was corrected by the procedure developed by Gratton et al. (1983). Afterwards, data was digitally filtered off-line with a 0.1-30 Hz band-pass filter and segmented into epochs of 1000 ms (from -100 to 900 ms). Baseline correction was applied; epochs exceeding ±80 μV at any scalp electrode were rejected and EEG epochs corresponding to incorrect responses (false alarms) were excluded.

For the calculation of the ERPs, waveforms were averaged and EEG epochs corresponding to standard, target and novel or distractors (alcohol-related pictures) trials were separated by normal state and hangover state. The components of different conditions were identified through the average waveforms (elicited by all stimuli conditions: standard, target and novel) as the largest peak between 110 and 180 ms (P2), 200 and 300 ms (N2-P3a), 270 and 370 ms (P3b), post-stimulus onset. Amplitude (mV) and latency (ms) values of the three components were obtained from specific electrodes: F1, Fz, F2, FC1, FCz and FC2 for the N2 component; PO3, POz, PO4, O1, Oz and O2 for the P2 component; and PO3, POz, PO4, O1, Oz and O2 for the P3b component.

To analyze ERPs data, a repeated-measures analysis of variance (ANOVA) with three within-subject factors (“Moment”; “Region”; “Electrode”) was used to explore each component separately (alpha level ≤.05). Whenever appropriate, degrees of freedom were corrected by the conservative Greenhouse-Geisser estimate. All post hoc comparisons were performed with the Bonferroni adjustment for multiple comparisons, also with an alpha level ≤.05.

Results

Demographic and drinking characteristics

Table 1. *Demographic and drinking characteristics of the participants.*

	Participants
N (females)	11(6)
Age	21±1.8
Handedness (right/left)	9/2
Regular tobacco smokers	5
Regular use of cannabis	2
Age of onset of regular drinking	16.09±1.57
Number of times consuming 6 or more drinks in a day per month	3±2.18
Number of drinks consumed per hour (speed of consumption)	2.45±.52
Number of drinks consumed in the BD night before the assessment	11.6±3.43
Sleep hours before the assessment on normal day	
Sleep hours before the assessment on hangover	
PACS score normal day	2.3±1.77*
PACS score hangover state	4.8±4.98*
AHSS score	51.9±16.34
BIS-11 total score	55.09±6.19*
Global Symptom Index (GSI) score (SCL-90-R)	21±22.02
Total AUDIT score	11.82±3.60

* $p < .05$

To understand if there were differences in the craving scores depending on the moment of assessment, a paired samples t-test was conducted. Significant differences were found [t(10)= -2.32, p= .043], being the craving score higher during hangover (M= 5, SD= 4.78) than during the normal state assessment (M= 2.27, SD= 1.68).

The number of hours slept before the assessments were also compared by means of a paired samples t-test, and significant differences were also observed [t(11)= 4.02, p= .002]. Accordingly, analysis revealed that participants slept more hours in the night before the normal day without alcohol consumption assessment (M= 7.42, SD= .669), than in the night after binge, before the hangover state assessment (M= 6.58, SD= .996).

Furthermore, to explore possible relations between psychological and alcohol use variables a Pearson's Bilateral correlation was used, which revealed a positive correlation between impulsivity scores (i.e., BIS-11 total score) and the percentage of drinking events that result in intoxication (r= .591, p= .043), suggesting that the higher the impulsivity score, the more probable chance of losing control over drinking behavior. No other significant correlations were found among ERP components, behavioral measures or demographic and drinking variables.

Behavioral performance

The analysis revealed no significant differences between the normal and hangover day assessments for all the behavioral parameters: reaction times, percentage of correct responses and percentage of incorrect responses. Nevertheless, despite no significant values found, the hangover moment reflected larger reaction times, more percentage of incorrect responses and less percentage of correct ones as compared to the normal day. These results are summarized in the table below.

Table 2. *Behavioral data from Normal and Hangover days (Mean ± SD)*

	Normal day	**Hangover day**
Reaction times (ms)	444.41 ± 46.17	460.18 ± 55.25
Correct answers (%)	98.02 ± 3.45	95.39 ± 8.81
Incorrect answers (%)	1.98 ± 3.45	4.62 ± 8.81

Amplitudes

P2 component. The analysis of P2 amplitudes showed significant effects for only one within-subject factor, the Region factor [F(1, 10)= 68.006, p= .000]. This result allowed the understanding that the occipital region (M = 6.202, SD = 1.025) produced larger amplitudes than the parieto-occipital region (M = 3.405, SD = .795).

Still regarding P2 amplitudes, results concerning the Moment factor also appeared as relevant as comparisons revealed a non-significant trend toward differences between the two moments (p= .068). Thus, another ANOVA repeated-measures was conducted, this time with only two within-subject factors ("Moment" and "Electrodes") contemplating the occipital area only. From that analysis, significant results emerged, namely for the Moment factor [F(1, 10)= 5.018, p= .049], revealing that amplitudes were larger during the hangover state (M= 6.845, SD= 1.109) than during the normal one (M= 5.559, SD= 1.020).

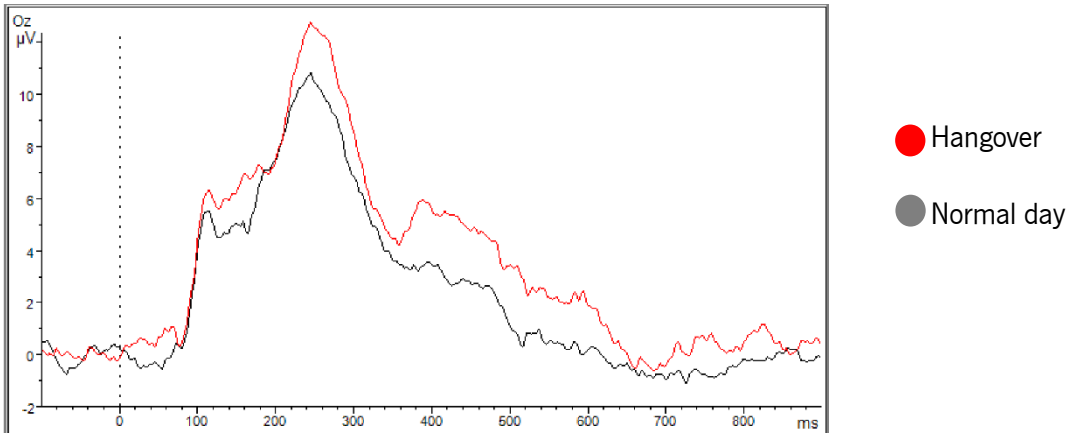

Figure 1. Representation of P2 in the Oz electrode – Moment comparison

N2-P3a components. The analysis revealed no significant main effects or interactions regarding the amplitudes of these components.

P3b amplitudes. The analysis of the P3b amplitudes revealed significant differences in the Region factor [F (1, 10)= 20.385, p= .001], and post hoc Bonferroni corrections showed significant differences in the amplitudes of parieto-occipital region (M= 2.515, SD= .433) and occipital region (M= -.155, SD= .855), revealing larger amplitudes in the parieto-occipital region. s. Lastly, significant differences regarding the Moment x Region x Electrode interaction were found [F(2, 20)= 49.746, p= .000]. Post hoc Bonferroni tests showed that during hangover state amplitudes were larger (4.89 µV) than in normal state (0.79 µV).

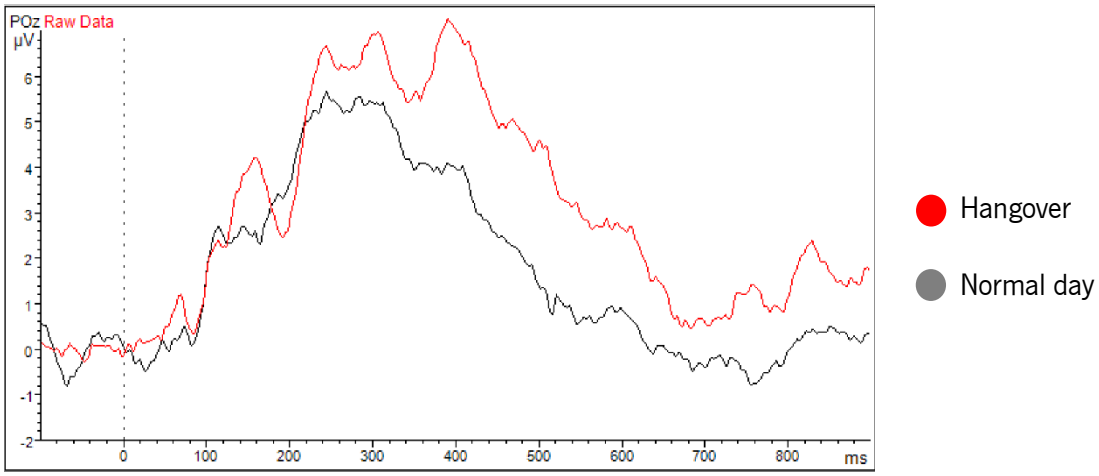

Figure 2. Representation of P3b in the POz electrode – Moment comparison

Discussion

This study was conducted to explore the effects of alcohol hangover in the attentional bias of young BDs, during a novelty oddball task with alcohol-related pictures as distractors. It was expected that, during hangover, BDs would perform the task with slower reaction times and would demonstrate larger amplitudes in occipital regions for P2 and P3b component, as well as larger frontal N2/P3a amplitudes during hangover. This study observed that hangover had no effect in the attentional bias for alcohol-related pictures, neither did it affect the participants' reaction times. Nevertheless, the study showed that hangover was linked to enhanced amplitudes of P2 and P3b components in occipital sites, in accordance with what was expected.

At the neurofunctional level, overall, this study demonstrated that hangover significantly alters the electrical activity of the brain, at least in part, given that P2 and P3b components exhibited significantly larger amplitudes during hangover than during a normal day without alcohol consumption. Regarding the P2, this is a component thought to reflect high-order perceptual processing, being modulated by attention, and linked to memory (Almeida-Antunes et al., 2020). Functionally, this component has been associated with attention modulation of non-target stimuli and stimulus classification (Key, Dove, & Maguire, 2005; Almeida-Antunes et al., 2020). Previous studies trying to understand alcohol effects on P2 amplitudes have reported that moderate doses of alcohol attenuate P2 amplitudes (Hernandez, Garcia-Martinez, & Monteón, 2014), which is interesting since the present study observed larger amplitudes after a night of heavy drinking, during hangover state. In this sense, while literature suggests that during alcohol intake and intoxication P2 amplitudes seem to diminish, the present study' results might indicate that, when experiencing hangover, BDs need to recruit additional attentional resources to perform the task adequately (since no behavioral differences were observed). Nevertheless, to the extent of our knowledge, this is the first study assessing hangover effects in the attentional bias using ERP measures, therefore these results should be interpreted with caution and more evidence would be needed to validate these assumptions.

Concerning P3b, accordingly to what was hypothesized, the present study observed increased amplitudes of this P3b component during hangover moment, being more pronounced in occipital regions. It is important to note that this component has been associated with the (voluntary) allocation of attentional resources to relevant stimuli, contributing to the updating of the stimulus classification in the working memory (Crego et al., 2012; Polich, 2007). The P3b is also considered to reflect decisional processes, emerging in tasks where a response (e.g., mouse click) is necessary to the target stimuli (Maurage et al., 2012). Bearing this in mind, the increased amplitudes observed during hangover are

perhaps a reflection of more attentional and working memory resources employed by the individuals to perform the task at the same level as they did in normal day (without alcohol consumption). Literature regarding young BDs support this idea, once it has been observed that BDs display larger P3b amplitudes in comparison with non-BDs (Crego et al., 20012); amplitudes that tend to increase even more if the engagement in BD pattern continues throughout the years (López-Caneda et al., 2013). The authors proposed those results reflected an increased attentional effort that BDs needed to employ in order to perform the task at the same level as controls (i.e., more attentional resources to correctly identify relevant/target stimuli), suggesting that engaging in BD leads to impairments at the neurocognitive level. Furthermore, other works have also revealed that BDs displayed increased P3b amplitudes in relation to alcohol-related cues (Petit et al., 2013), which were also observed to have increased even further after one year of continued engagement in BD (Petit et al., 2014). The same study also revealed that not only did the individuals demonstrated increased amplitudes to alcohol-related cues, but as diminished amplitudes were also observed (compared to previous values recorded) to stimuli not alcohol-related, suggesting the development of attentional bias after one year of BD.

In sum, all these results seem to point to the existence of increased P3b amplitudes in young BDs, as it was observed from several studies using a series of paradigms which involved different cognitive processes (i.e., attentional, working memory and inhibitory control), being proposed that increased P3 amplitude is an early biomarker of BD (for a recent review, see Almeida-Antunes et al., 2020). As the present study is a pioneer, as far as our knowledge goes, in assessing the hangover effects in attentional processes through electrophysiological markers, despite no solid conclusions being possible to extract, the increased P3b amplitudes observed might be indicative of a marked overactivation of the brain to perform the task successfully (i.e., at the same level as they do in normal day basis).

The absence of electrophysiological differences regard to the N2/P3a complex should also be mentioned. This complex is commonly observed in novelty oddball paradigms, being elicited by rare non-relevant stimuli in tasks with three stimuli: frequent standard, rare target and rare nontarget (Folstein and Petten, 2008). Being so, the N2/P3a is thought to reflect the individuals' initial orienting response and the subsequent intentional shift of attention towards the novel stimulus (Polich, 2007; Wienke et al., 2018). In this line of thought, as this study used a visual novelty oddball task with three stimuli type – standard, target and distractor – a frontal N2 and P3a was expected (Folstein and Petten, 2008) in response to alcohol-related pictures.

Going through behavioral results, contrary to the initial hypothesis, no significant differences

were found in the reaction times of the two assessment moments. Initially it was hypothesized that hangover would cause the individuals to perform with larger reaction times, as it was observed in previous studies with student populations (Howland et al., 2010; McKinney et al., 2012). However, that was not the case in the present study. As such, some considerations should be noted. On one hand, despite not reaching significance levels, reaction times were in fact larger during hangover moment. Thus, it is possible that with a larger sample size significant differences might arise. From another point of view, as significant differences in the percentage of both correct and incorrect responses were not expected due to the low task complexity, the same motive could justify the absence of larger reaction times. In either way, future research should be conducted to better understand how hangover can affect these behavioral parameters.

Finally, regarding the results obtained from questionnaires administered, there are three relevant results that should be acknowledged. On one hand, a positive correlation was identified between the impulsivity questionnaire (BIS-11 total score) and the question "what percentage of drinking events result in intoxication?", suggesting that BDs with higher impulsivity scores have more probability of losing control over drinking behavior. This assumption is supported by previous works with ERP correlates other than self-reported measures as BIS and AUDIT (e.g., López-Caneda et al., 2014), which emphasizes the continuum hypothesis that suggests that BD and alcohol use disorders may constitute two successive steps of the same phenomenon (Almeida-Antunes et al., 2020). On another hand, the scores obtained for alcohol craving (PACS total score) were greater during hangover than during the normal day without alcohol consumption, suggesting that hangover may result in increased alcohol craving levels. The relevance of this analysis resides in the importance that craving has in substance-seeking behavior (Flaudias et al., 2019), because if hangover produces increasing in craving, and in turn if craving motivates the individual to pursuit alcohol administration, then perhaps craving could be an important variable to further explore the continuum hypothesis. Lastly, significant differences were also found in the number of sleeping hours before the assessments, having participants slept less time in the night before the hangover assessment. This in fact an important limitation of the present study once the sleeping hours could affect individuals on both behavioral level and electrical activity of the brain.

Bearing the study limitations in mind, although this study accomplished the purpose of filling literature gap regarding the effects of hangover in attentional processing of young BDs, the present study displays a few features that deserve consideration. Other than the number of sleeping hours, the sample size of the study is too small to secure the reliability of the results. Additionally, the number of

participants performing the normal day assessment first (n=7) was not the same as the one of those who performed the hangover state assessment in the first place (n=4), which means that the test-retest effect was not fully controlled. Other important limitation is the absence of a control group (e.g., non-BDs university students), because otherwise it is not possible to attribute the present findings only to the experience of hangover by itself given that previous impairments resulting from the BD pattern could already exist. Lastly, although data was indeed collected concerning the type of beverage that participants ingested (by means of the AlcoDroid mobile app), that information was not analysed, and it might have played a role in the absence of results regarding hangover severity symptoms.

For future research, it would be interesting to increase sample size and to control for training effect and sleeping hours. Moreover, the analysis of the type of beverages (e.g. beer, wine, vodka) consumed should be interesting to understand what kind of beverage contribute to more severe hangover symptoms, as well as if that severity has a different impact in the alcohol attentional bias in BDs. Similarly, it would also be very interesting to try to understand in what way the "kindling effect" resulting from alcohol use might be present in young BDs experiencing hangover. Specifically, alcohol is known to have a suppressive effect on the central nervous system (CNS): that is, it reduces the activity of excitatory neurotransmitters and, in turn, increases the inhibitory neurotransmitters activity, consequently causing the previously mentioned "suppressive effect" on the CNS. Thus, in order to reestablish the CNS activity, a series of compensatory mechanisms are set into place, namely the promotion of excitatory neurotransmitter systems and, the suppression of inhibitory neurotransmitters systems (Abrahao et al., 2017; Roberto and Varodayan,2017). Thus, when a heavy drinking episode takes place, as it is the case of a typical BD night, these compensatory mechanisms come into play aiming at reestablishing the inhibitory/excitatory balance while the individual is suffering from alcohols' effects in the body and brain. However, when alcohol leaves the body, a state of hyperexcitability is established: the kindling effect (for review see Becker, 1998) that is normally manifested along with alcohol withdrawal symptoms. Therefore, as BD is characterized by frequent intoxications and subsequent abstinence periods, a certain degree of withdrawal-induced neuronal excitability might also occur (Stephens & Duka, 2008), being that a state of increased neural activity could thereby be stablished. Accordingly, the results of the present study might reflect increased neuronal activity resulting from several recurrent episodes of heavy alcohol drinking and abstinence, just as is the case for the BD pattern. In any case, future research is warranted to verify or refute these assumptions.

In conclusion, the present study analyzed the electrical activity of the brain before and after a BD night and results suggest that hangover did not seem to produce an effect in the attentional bias for

alcohol-related pictures, neither at the behavioral nor at the electrophysiological level. Nevertheless, the present findings revealed that hangover states in young BDs are associated with increased P2 and P3b amplitudes. This suggests that, during the experience of hangover, BDs need to recruit additional attentional resources to be able to perform simple attentional tasks adequately. Due to the limitations exposed above, caution is needed in the interpretation of these results, as well as future research is necessary to validate or refute the assumptions made in the present study.

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