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Alcohol-specific Memory Inhibition Training in Binge Drinkers: a double-blind randomized controlled trial examining alcohol use and craving levels

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Statement Of Integrity

I hereby declare having conducted this academic work with integrity. I confirm that I have not used plagiarism or any form of undue use of information or falsification of results along the process leading to its elaboration. I further declare that I have fully acknowledged the Code of Ethical Conduct of the University of Minho.

Francisca Batalha Reis

Alcohol-specific Memory Inhibition Training in Binge Drinkers: a double-blind randomized controlled trial examining alcohol use and craving levels

Resumo

Memórias persistentes relacionadas com álcool podem ser maladaptativas, levando a *craving* intenso e padrões de consumo perigosos. Assim, fortalecer o controlo cognitivo sob memórias pode beneficiar a redução do abuso de álcool. O presente trabalho avaliou a capacidade de inibição de memórias (IM) em indivíduos com padrões de consumo excessivo de álcool (CEA) e procurou determinar o efeito de um protocolo de intervenção de inibição de memórias relacionadas com álcool no nível de consumo e *craving*. 53 jovens sem CEA (NCEAs; 57% feminino; M_{idade}=19.74) e 47 jovens com CEA (CEAs; 47% feminino; M_{idade}=20.02) participaram neste estudo. Depois de realizarem a tarefa *Think/No-Think Alcohol* (TNTA), os CEAs foram aleatoriamente atribuídos a um grupo de intervenção: Intervenção Combinada [(IC); Treino Cognitivo (TC) e estimulação transcraniana por corrente contínua (ETCC) *verum* aplicada sob o córtex prefrontal dorsolateral (CPFDL); *N*=17], Treino Cognitivo (TC e ETCC *sham*; *N*=15), ou Grupo Controlo (TC *sham* e ETCC *sham*; *N*=15). A capacidade de IM dos CEAs foi avaliada antes e após três sessões diárias, e o *craving* e consumo de álcool foi medido 10 dias e três meses após a intervenção. Os resultados não apoiaram um efeito da intervenção em IM relacionadas com álcool, no entanto, sugeriram um potencial papel na redução do consumo de álcool regular (grupo TC) e irregular (grupo IC), três meses após intervenção. Apesar de algumas limitações, estes resultados podem ter implicações relevantes na literatura sobre a IM em padrões de CEA, bem como em futuros tratamentos para a Perturbação de Uso de álcool.

Palavras-chave: consumo excessivo de álcool, inibição de memórias, ETCC, treino cognitivo, *craving*

Alcohol-specific Memory Inhibition Training in Binge Drinkers: a double-blind randomized controlled trial examining alcohol use and craving levels

Abstract

Alcohol-related persistent memories can be maladaptive, leading to intense craving and to hazardous drinking patterns. Thus, strengthening cognitive control over memories might be beneficial in reducing alcohol misuse. Bearing this in mind, the present work assessed memory inhibition (MI) in individuals with a binge drinking pattern of alcohol use and sought to determine the effect of an alcohol-specific MI intervention protocol on the levels of alcohol use and craving. Accordingly, 53 non-binge drinkers (NBDs; 57% female; M_{age} = 19.74) and 47 binge drinkers (BDs; 47% female; M_{age} = 20.02) were part of the study. After completing the Think/No-Think Alcohol (TNTA) task, BDs were randomly assigned to an intervention group: Combined Intervention [(CI); Cognitive training (CT) and *verum* transcranial direct current stimulation (tDCS) applied over the right dorsolateral prefrontal cortex; N = 17], Cognitive Training (CT and *sham* tDCS; N = 15), or Control (*sham* CT and *sham* tDCS; N = 15). BDs' MI performance was assessed before and after three daily intervention sessions, and alcohol craving and consumption were measured 10 days and three months after intervention. Results did not endorse an effect of intervention on alcohol-related MI performance; however, findings suggest a potential role in the decrease of regular (in the CT group) and irregular (in the CI group) alcohol consumption three months after training. Besides some limitations, these findings may hold relevant implications for the knowledge on MI role on BD patterns, as well as for future alcohol abuse treatment interventions.

Key Words: binge drinking, memory inhibition, tDCS, cognitive training, craving

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Abbreviations

BD: Binge Drinking

NBD: Non-Binge Drinking

BDs: Binge Drinkers

NBDs: Non-Binge Drinkers

AUD: Alcohol Use Disorder

AAB: Alcohol-Attention Bias

IC: Inhibitory Control

MI: Memory Inhibition

TNT: Think/No-Think

DLPFC: Dorsolateral Prefrontal Cortex

tDCS: Transcranial Direct Current Stimulation

TNTA: Think/No-Think Alcohol

AUDIT: Alcohol Use Disorder Identification Test

ACQ-SF-R: Alcohol Craving Questionnaire-Short Form Revised

PACS: Penn Alcohol Craving Scale

FU: Follow-up

ms: milliseconds

mA: milliamperes

cm: centimetres

CG: Control Group

CT: Cognitive Training

CI: Combined Intervention

NT: No-Think

TH: Think

BL: Baseline

Introduction

Alcohol misuse is a public health matter responsible for three million fatalities every year, worldwide (World Health Organization, WHO, 2018), the third leading risk factor for premature death (Marinho et al., 2015). Excessive drinking is associated with several conditions, ranging from traumatic brain injuries (Rogan et al., 2021), road accidents, liver disease (Telles-Correia & Mega, 2015), cardiovascular (Day & Rudd, 2019) and respiratory diseases (Mehta, 2016), cancer (Rumgay et al., 2021), sexually transmitted infections (George, 2019), to mental health disorders (Cortez-Pinto et al., 2010), and even homicide (Trangenstein et al., 2021) and suicide (Brady, 2006) cases. Beyond health consequences, excessive alcohol consumption can have deep effects on social behaviour (Steele & Southwick, 1985), being related to sexual risk behaviours (George, 2019; Palfai & Luehring-Jones, 2021), poor academic performance (An et al., 2017) and reduced quality of life (Dormal et al., 2018). Moreover, economic costs associated with harmful alcohol use are heavy, accounting for more than 1% of the gross national product (Rehm et al., 2009). In 2010, excessive drinking is estimated to have cost the United States around 250 billion dollars, 40% of which was due to binge drinking ([BD]; Sacks et al., 2015).

BD is characterized by episodes of excessive drinking that bring blood alcohol concentration to 0.08g/dL, which typically occurs after four or more standard alcoholic drinks for females and five or more drinks for males, over two hours (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2004). It constitutes a common drinking pattern among adolescents and young adults, as 35% to 40% of college students state they had at least one BD episode in the last month (Substance Abuse and Mental Health Services Administration, 2018). Importantly, several aspects seen in BD conditions are very well-established characteristics of alcohol use disorder ([AUD]; Almeida-Antunes et al., 2022a; Jones et al., 2018; Loheswaran et al., 2016; Maksimovskiy et al., 2019; Pascual et al., 2007; Powell et al., 2021), highlighting the need to further study this phenomenon.

An additional aspect that emphasises the urgency to expand the understanding of this heavy alcohol use is the fact that adolescence and young adulthood are vital in terms of neurodevelopment, characterized by major structure, functional and neurochemical brain changes (Morris et al., 2018; Zhao et al., 2021), as well as considerable cognitive, emotional, social, and behavioural modifications (Lees et al., 2020).

The second decade of an individual's life portrays reductions in cortical gray-matter volume and thickness accompanied by increases in white-matter volume and integrity (Jones et al., 2018). Importantly, there is evidence of asynchrony between the maturation of sensorimotor and prefrontal cortices, as the latter – central to executive control – is one of the last brain regions to fully mature (Jones et al., 2018; Kolk & Rakic, 2022). This imbalance may not only render the brain particularly susceptible to the neurotoxic effects of alcohol, but is also thought to be related to increased reward sensitivity, sensation seeking, and low inhibitory control ([IC] Casey & Jones, 2010; Galvan et al., 2006) – which can increase the drive to engage in high-risk behaviours (Jones et al., 2018; Steinberg, 2005), namely the initiation or escalation of alcohol consumption, and increase of potentially serious and long-lasting consequences (Lees et al., 2020).

Not surprisingly, evidence has shown that BD interacts with this vital phase, altering neurodevelopmental trajectories (Lees et al., 2020), both through excessive drinking episodes – which increase the vulnerability to alcohol's neurotoxic effects (Bava & Tapert, 2010; Mota et al., 2013) – as well as through the following withdrawal periods – significantly harmful to brain functioning (Bava & Tapert, 2010; Pascual et al., 2007).

Atypical developmental trajectories of gray and white matter maturation during adolescence have also been documented in BD (for a review see Cservenka & Brumback, 2017). Specifically, there is evidence of accelerated decreases in gray matter volume in frontal and temporal lobes (Lees et al., 2019; Pfefferbaum et al., 2016; Squeglia et al., 2014; Howell et al., 2013; Doallo et al., 2014; Sousa et al., 2017), attenuated white matter growth (Jones et al., 2018; Squeglia et al., 2015), as well as poorer white matter integrity (Bava & Tapert, 2010; Jones et al., 2018; Lees et al., 2019; Zhao et al., 2021). Relevantly, abnormal volumes have been documented in the dorsolateral prefrontal cortex ([DLPFC]; Morris et al., 2018) and in the insula (Pérez-García et al., 2022), both very relevant structures, known as a gate for the interoceptive effects in addiction, affecting motivated behaviour (Naqvi & Bechara, 2010).

Neuronal anomalies related to BD patterns are not limited to volumetric measures, as multiple functional disruptions have been documented. Firstly, several studies have shown abnormal resting state functional connectivity in this population (Almeida-Antunes et al., 2022a; Sousa et al., 2019). Evidence on BD also shows significant

alterations in brain functioning/connectivity during basic and high-level cognitive domains (Folgueira-Ares et al., 2017; Lannoy et al., 2020; Lees et al., 2020; Loheswaran et al., 2017; Tong et al., 2021).

Altogether, it is not surprising that alcohol's neurotoxic effect during such a critical period might lead to cognitive deficits. Indeed, burgeoning neuropsychological studies have reported that binge drinkers (BDs) display difficulties in several cognitive domains, including attention, memory and IC (for reviews, see Carbia et al., 2018; Lees et al., 2020). Additionally, BD patterns have been associated with alcohol attention bias (AAB), which may also affect excessive use, perpetuation as well as craving levels (Fahardi & Cox, 2009; Field et al., 2008b; Langbridge et al., 2019; Pennington et al., 2020; Townshend & Duka, 2001). In fact, AAB has been found to be positively correlated with the amount of alcohol consumed (Fahardi & Cox, 2009; Simon et al., 2022), which highlights its association with craving and its role in alcohol use. Tong and colleagues (2021) found that abnormalities in attention networks have implications for rumination, craving, and relapse. Importantly, the reduction of this cognitive bias has been associated with reductions in alcohol use – sustained at follow-up three months later (Fahardi & Cox, 2009). The AAB is thought to arise from an attentional system very sensitized to alcohol, thus, when alcohol-related reminders take place, cognitive, emotional, and behavioural responses occur (even if they are not in line with the individual's rational decisions; Fahardi & Cox, 2009).

IC – a fundamental component of human behaviour – is the ability to override a prepotent response (Anderson & Hulbert, 2021). Deficiencies in this domain have been reported in BD (Carbia et al., 2018; Field et al., 2008b; Holcomb et al., 2019; Powell et al., 2021). In Carbia and colleagues' (2018) review, seven – out of the eleven studies on IC – reported differences in this function between BDs and controls. Relevantly, although some studies did not find behavioural differences (e.g., Bensmann et al., 2019), several authors have found neurophysiological differences associated with IC impairments in BD (e.g., Holcomb et al., 2019; Lannoy et al., 2020; López-Caneda et al., 2012, 2017). Evidence shows a hyperactivation profile associated with IC networks in BDs (López-Caneda et al., 2014a) which more recently was proved to exist prior to alcohol consumption initiation, highlighting the role of damaged executive control networks and its role in increasing the vulnerability to BD initiation (Antón-Toro et al., 2021). Interestingly, even with these

deficits' consistency, there is evidence that the termination of BD could stop the damage to IC domains (López-Caneda et al., 2014c).

Importantly, research has focused almost exclusively on the motor aspect of IC – usually assessed with Go/NoGo or Stop Signal tasks. However, IC is a heterogeneous construct that extends past the motor component into the cognitive domain. A pertinent cognitive function regulated by IC, which has been neglected in alcohol research, is memory inhibition (MI). MI is characterized by an intentional effort to keep a memory from entering consciousness, involving a deliberate interruption of the retrieval process, which, consequentially, diminishes the memory's accessibility later on (Anderson & Green, 2001; Anderson & Hanslmayr, 2014; Anderson & Hulbert, 2021; Lin et al., 2021; López-Caneda et al., 2014b). MI is an active, effortful, and cognitively demanding mechanism that strongly relies on IC (Anderson & Green 2001; Benoit et al., 2015; Catarino et al., 2015) – both on its rapid deployment, as well as on the capacity to sustain it (Lin et al., 2021) –, and on attentional processes (Anderson & Hulbert, 2021).

Despite the common negative connotation of forgetting, not remembering certain episodes can be adaptive and prevent distress and anxiety (Anderson & Hulbert, 2021; Fawcett & Hulbert, 2020; Hu et al., 2017). Thus, having the ability to control unwanted memories, namely keeping them out of consciousness (i.e., inhibiting them) can have emotional benefits and promote well-being (Anderson & Hulbert, 2021; Chen et al., 2022; Lin et al., 2021).

The exact way MI modulates brain functioning supporting memory is not fully comprehended yet (Anderson & Hulbert, 2021; Lin et al., 2021). Still, several brain regions associated with executive control (e.g., inferior frontal gyrus, ventrolateral prefrontal cortex, DLPFC, medial prefrontal cortex) have been found to be significantly active during MI, accompanied by a reduced hippocampal (and adjacent areas) activity (Anderson et al., 2004; Anderson & Hulbert, 2021; Depue et al., 2007; Hulbert et al., 2016). More specifically, research suggests that the DLPFC might be able to globally downregulate hippocampal functions, disrupting the encoding, retrieval, and stabilization of memories (Anderson & Hanslmayr, 2014; Benoit et al., 2015; Gagnepain et al., 2014; Levy & Anderson, 2012).

The Think/No-Think (TNT) task (Anderson & Green, 2001) is commonly used to study MI (Benoit et al., 2015; Catarino et al., 2015; Chen et al., 2022; Depue et al., 2010; 2013; 2016; Detre et al., 2013; Hertel & McDaniel, 2010; Salvador et al., 2018), as it involves the executive control over the memory retrieval process (Anderson & Green, 2001) and measures the ability to inhibit unwanted memories (Anderson & Levi, 2009). More recently, López-Caneda and colleagues (2019) created the Think/No-Think Alcohol Task – an adaptation of the TNT task with alcohol-related content –, which has been used to study MI in alcohol-related populations (Almeida-Antunes et al., 2022b; Simeonov et al., 2022).

Work conducted on this subject has supported the notion that MI can contribute to the perseverance of psychological well-being (Anderson & Hanslmayr, 2014; Lin et al., 2021; Harrington et al., 2021; Hu et al., 2017). Concordantly, involuntary, and intrusive thoughts (i.e., instances of involuntary memory retrieval that do not follow a purposeful retrieval effort) integrate several mental disorders (Brewin et al., 2010; Hirsch & Holmes, 2007) and deficits in the brain mechanisms that serve MI have been documented in several psychopathological disorders (e.g., Anderson & Levi, 2009; Sacchet et al., 2017; for a review, see Costanzi et al., 2021). Specifically, MI deficits have been observed in major depressive disorder (Hertel & Gerstle, 2003; Joormann et al., 2005; Zhang et al., 2016), posttraumatic stress disorder (Catarino et al., 2015; Mary et al., 2020; Sullivan et al., 2019), and schizophrenia (Racsmány et al., 2008; Soriano et al., 2009; Waters et al., 2006). Importantly, it has been suggested that strengthening this cognitive ability might be clinically effective (Gagnepain et al., 2017).

In this sense, a growing number of studies have tried to increase cognitive control through cognitive training (CT). Specifically, there is evidence that supports the beneficial role of CT in the reduction of alcohol consumption (Liu et al., 2019; Houben et al., 2011; Manning et al., 2016; Stein et al., 2023). However, other authors did not find a significant effect of CT on cognitive performance (Claus et al., 2019), drinking patterns (Reichl et al., 2023), or self-control when drinking (Reichl et al., 2023; Stein et al., 2023). Also, its efficacy regarding craving experience is scarce (Garfield et al., 2022).

Relevantly, evidence shows that CT effects can be potentiated through neurostimulation, namely transcranial direct current stimulation ([tDCS] Martin et al., 2013; Park et al., 2014). Despite the literature being conflicting regarding the

effectiveness of tDCS on improving executive functioning, alcohol use, and craving levels – with evidence showing no significant effects (den Uyl et al., 2017; 2018; Klauss et al., 2014; for a review see Mostafavi et al., 2020) and other defending its efficacy (Boggio et al., 2008; den Uyl et al., 2015; for a review see Kim & Kang, 2021) –, a combination of both CT and tDCS might enhance their potential beneficial effects. Particularly, this combination may have a beneficial role regarding IC (Ditye et al., 2012). Specifically, there is inconsistent data in terms of the efficacy of the combination of CT and tDCS in impacting alcohol consumption, with evidence supporting it (Dubuson et al., 2021), and other stating its limited utility (Claus et al., 2019).

The present work aims to assess MI in BDs, implementing a protocol created by Almeida and colleagues (2022b) which targets the examination of the effect of MI training by CT or CT combined with tDCS in such cognitive ability, as well as on consumption patterns and alcohol craving levels. We hypothesize that individuals who receive CT or CT combined with tDCS will improve MI and that this improvement will be associated with a decrease on alcohol consumption and craving. Secondarily, we will assess the existence of differences in MI between BD and non-binge drinking (NBD) groups.

Method

Participants

One hundred individuals (52% female, M_{age} = 19.87, SD_{age} = 1.66) from the University of Minho participated in this study. Of these, 53 were non-binge drinkers ([NBDs] 57% female, M_{age} = 19.74, SD_{age} = 1.68), and 47 were BDs (47% female, M_{age} = 20.02, SD_{age} = 1.65). BDs were divided into three intervention groups. The Cognitive Training (CT) group included 15 individuals (47% female, M_{age} = 19.27, SD_{age} = .96); the Control group (CG) also comprised 15 participants (53% female, M_{age} = 20.40, SD_{age} = 2.13); and the Combined Intervention (CI) group was composed by 17 subjects (41% female, M_{age} = 20.35, SD_{age} = 1.50).

In order to participate in the study, all individuals must meet certain criteria. These included to be considered BDs – drinking five or more drinks on one occasion, at least once a month, and drinking at a rate of at least two drinks per hour during these episodes (increasing blood alcohol concentration to at least 0.08 grams percent; NIAAA,

2004) – or to be classified as NBDs – never drinking five or more drinks on each occasion and having an Alcohol Use Disorder Identification Test (AUDIT) score below four points. Those who fulfilled these criteria were interviewed to evaluate the following exclusion criteria: use of illegal drugs – with the exception of cannabis (determined by the Drug Use Disorders Identification Test-Extended, Berman et al., 2007); alcohol abuse (i.e., AUDIT ≥ 20); use of psychoactive medical drugs (e.g., sedatives or anxiolytics) during the two weeks prior to the experiment; having a history of psychopathological disorders (DSM-V, APA, 2013), of traumatic brain injury or neurological disease; having a family history of AUD or other substance abuse disorder; having had one or more episodes of loss of consciousness lasting more than 20 minutes; non-corrected sensory deficits; a score of the Global Severity Index higher than 90 (Symptom Checklist-90-Revised questionnaire, Derogatis, 1983) or a score above 90 in at least two of the symptomatic dimensions. Prior the interview, we provided information about the study and its objectives, and participants signed an informed consent form in compliance with the Code of Ethical Principles for Medical Research Involving Human Subjects described in the Declaration of Helsinki (Brazil, 2013). This study was approved by the Ethics Subcommittee of the Social Sciences and Humanities of the University of Minho (CS.CSH 078/2018). Data collection took place at the School of Psychology.

Materials

Questionnaires

Assessment of Alcohol Use, Craving, and BD. We used the AUDIT (Babor et al., 2001) to examine drinking consumption patterns, as this instrument assesses alcohol consumption frequency and its negative consequences, as well as alcohol dependency. We also used the Typical and Atypical Drinking Diary to measure the number of drinks participants had in a typical and atypical week (e.g., holiday with friends; college party week) in the three months prior. We used the Alcohol Craving Questionnaire-Short Form Revised (ACQ-SF-R; Rodrigues et al., 2021) to assess acute alcohol craving in three dimensions (compulsivity, purposefulness, and emotionality). This instrument provides four variables (total score and three subscale scores). The Penn Alcohol Craving Scale

(PACS; Pombo et al., 2008) was also used to measure alcohol craving levels – namely regarding frequency, duration, and intensity of alcohol-related thoughts.

Assessment of Psychological Aspects. The Symptom Checklist-90-Revised was used to assess the existence of psychopathological traits. Also, the Urgency-Premeditation-Perseverance-Sensation Seeking-Positive Urgency (Cyders et al., 2014) impulsive behaviour scale and the Barratt Impulsivity Scale-11 (Cruz and Barbosa, 2012) were used to evaluate impulsivity traits. Finally, the Edinburgh Handedness Inventory (Espírito-Santo et al., 2017) was used to evaluate participants' handedness.

Experimental Task

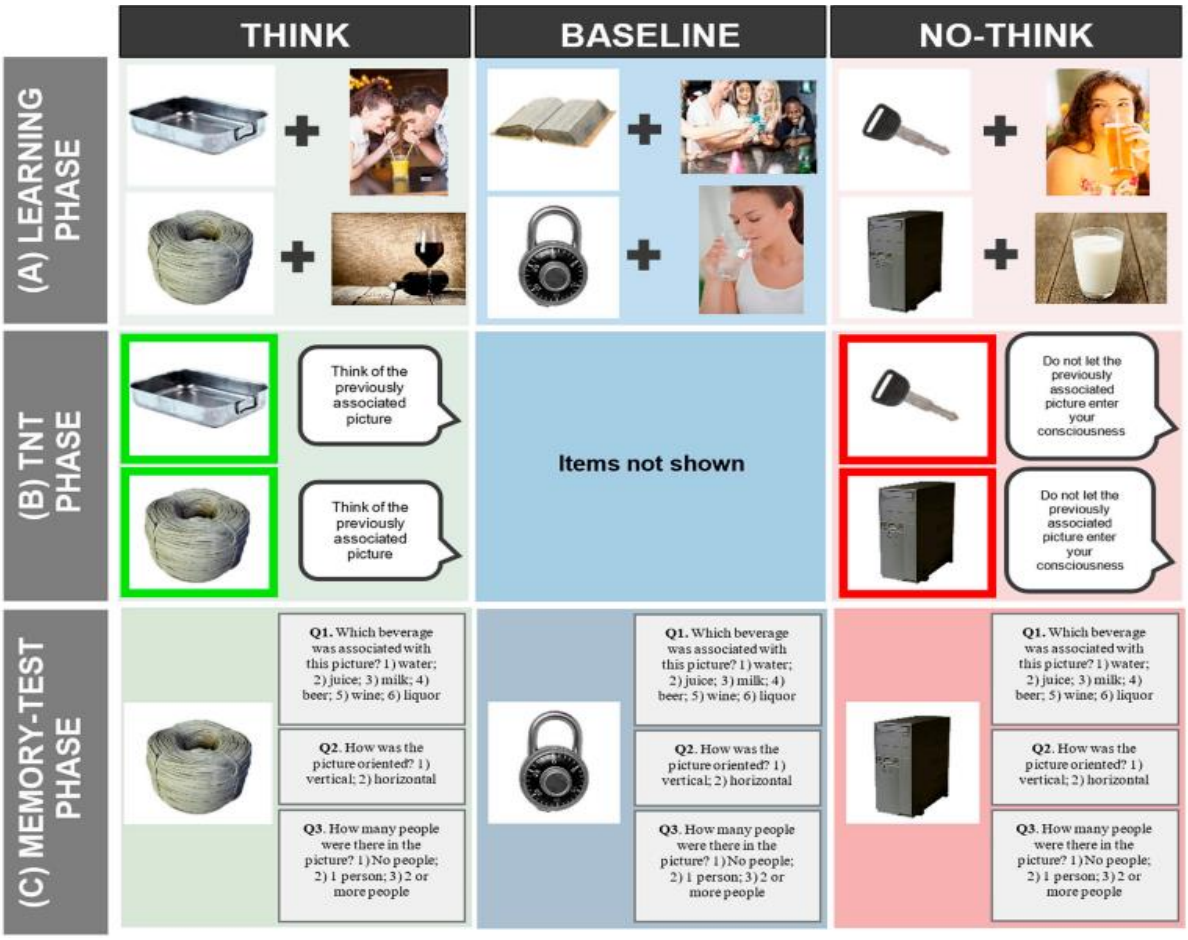
The experimental task used was the Think/No-Think Alcohol (TNTA) Task (López-Caneda et al., 2019) that examines the intentional process of inhibiting alcohol-related memories and comprises three phases (see Figure 1).

In the learning phase, individuals are asked to memorize three series of 12 pairs of images (shown for 4000 ms in a randomized order and with an inter-stimuli interval of 1100 to 1300 ms, with a rest of 4000 ms every 4 pairs): one is a neutral object and the other is either an alcoholic or a non-alcoholic beverage. After each series, each of the neutral images is presented for 2000 ms, and participants answer three questions regarding the learnt material: "Which beverage was associated with this picture?" (Answers: 1. water; 2. juice; 3. milk; 4. beer; 5. wine; 6. liquor); "How was the picture oriented?" (Answers: 1. portrait; 2. landscape); "How many people were there in the picture?" (Answers: 1. Nobody; 2. 1 person; 3. 2 or more people). The recall is considered correct only if the individual answered all questions accurately. The series of 12 pairs of images are presented at least twice – more, if needed – until participants correctly recall the target pairs with a minimum of 60% accuracy, to ensure the material was learnt. In the Think/No-Think phase, only the cue (i.e., the neutral object) is presented to participants, as they are asked to either recall (Think trials) or to inhibit (No Think trials) the associated target picture (i.e., the alcoholic or non-alcoholic beverage). In this phase, 12 neutral object images are used as Think (TH) trials, 12 others as No Think (NT) trials, and the remaining 12 are not included, to create a baseline (BL). The TH condition is represented by a green frame on the neutral picture, and participants are asked to "think of the previously learned picture and keep it in mind during the entire presentation".

Contrarily, the NT trials include a red frame, and the instruction is "not to let the previously associated picture enter consciousness", and subjects are advised not to generate other associations to the cue object. Importantly, the sequence of cue images is pseudorandomized, and the same condition does not occur more than three times in a row. The last phase – the Memory Test – includes the presentation of all 36 neutral pictures (TH, NT, and BL) and participants are asked to recall the initially associated target picture. Three versions of the task were created and counterbalanced across the subjects, to ensure that all the pictures were included in all three conditions.

Figure 1

Illustration of the Think/No-Think Alcohol (TNTA) Task.



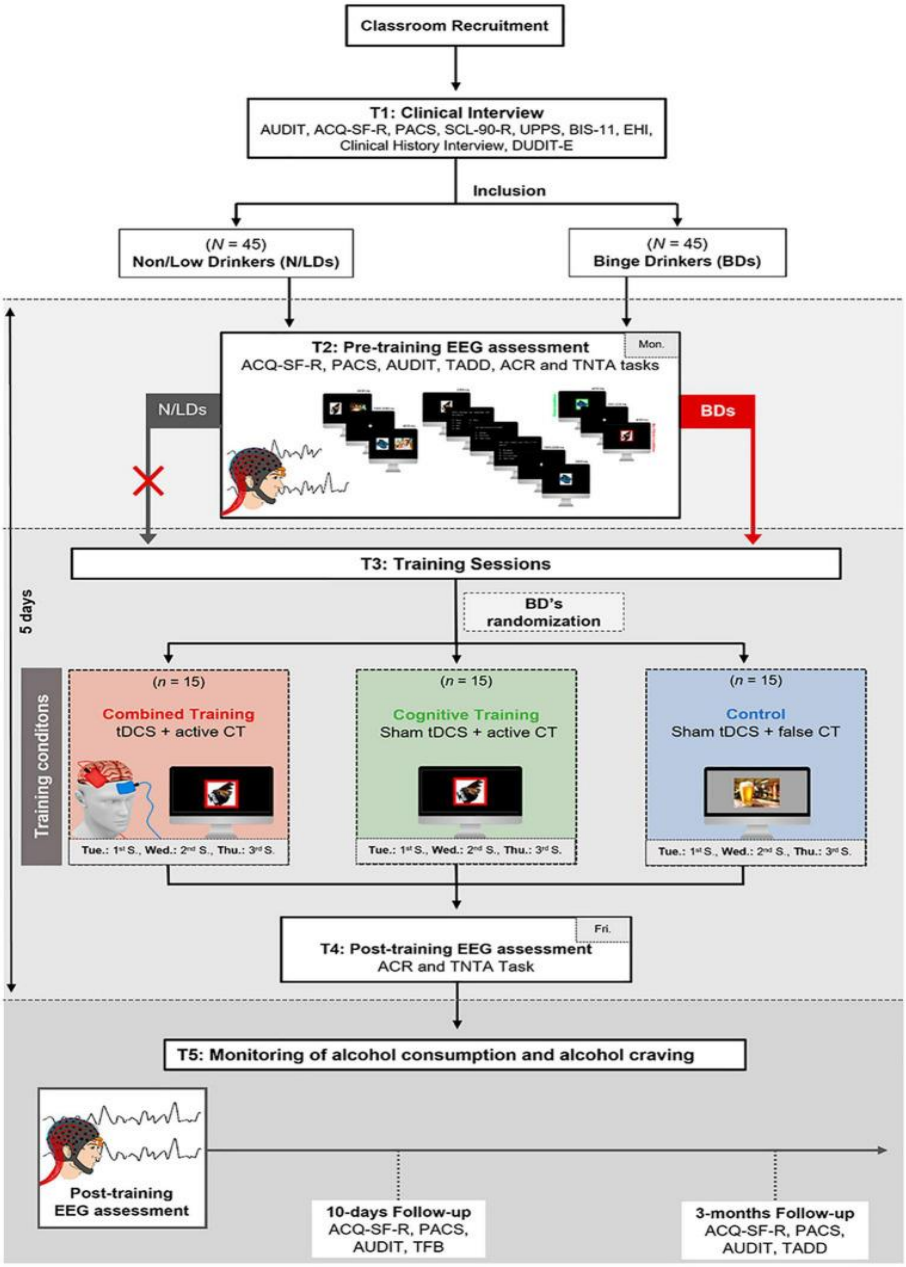
Note. Overall depiction of the Think/No-Think Alcohol (TNTA) task. From "Forgetting Alcohol: A Double-Blind, Randomized Controlled Trial Investigating Memory Inhibition Training in Young Binge Drinkers" by N. A. Antunes-Almeida et al., 2022, June 29, Frontiers in Neuroscience, 16, p. 7. Copyright 2022 by Frontiers in Neuroscience.

Procedure

The procedure followed in the present work was validated by Almeida-Antunes and colleagues (2022b; see Figure 2).

Figure 2

Schematics of the Intervention Protocol Procedure



Note. Graphic representation of the procedure. From "Forgetting Alcohol: A Double-Blind, Randomized Controlled Trial Investigating Memory Inhibition Training in Young Binge Drinkers" by N. A. Antunes-

Almeida et al., 2022, June 29, Frontiers in Neuroscience, 16, p. 5. Copyright 2022 by Frontiers in Neuroscience.

Firstly, participants underwent a clinical interview to determine if they fulfilled the BD criteria, to assess the baseline levels of some concepts (e.g., drinking patterns, craving levels), and to ensure the absence of relevant medical history (e.g., neurological or psychiatric family history) – through the instruments mentioned in the Questionnaires sub-section. Secondly, participants underwent a pre-training electroencephalographic assessment, in which psychological (i.e., craving levels), behavioural (i.e., alcohol consumption levels and task performance) and neurofunctional (e.g., event-related potentials, brain functional connectivity) outcomes were measured. Participants performed an alcohol reactivity task and the TNTA task, while electroencephalography data was being collected. Despite the collection of this information, data from the alcohol reactivity task and from the electroencephalogram will not be analysed or discussed in the present work. Before the TNTA task, participants performed a breathalyser test, with Alcoscan ALC-1, to confirm that the blood alcohol concentration was 0.0%. This procedure took about two hours to be completed.

In the third phase of the present study, subjects were randomly assigned – by an independent researcher, who oversaw the programming of the tDCS parameters – to one of the three training subgroups: Cognitive Training (CT), Control Group (CG) or Combined Intervention (CI). During this phase, participants performed the alternative version of the TNTA task corresponding to the group they were assigned to. After the initial learning phase of the task, subjects underwent (active or sham) neuromodulation with tDCS – using a Eldith DC Stimulator Plus (Neuroconn, Germany) – which released a direct current of 2 mA for 20 minutes to the scalp, through two saline-soaked 35 cm^2 surface sponge electrodes. The anodal electrode was placed over F4 to stimulate the right DLPFC – according to the 10–20 international system for electroencephalography electrode placement – and the cathode electrode was placed over the contralateral supraorbital area. Both active and sham stimulation were indistinguishable for the participants, as during the active simulation, the current faded in for 15 s, remained constant at 2 mA for 20 min, and faded out for 15s, and during sham stimulation, the electric current faded in for 15 s, remained constant at 2 mA for 15 s and faded out for 15 s. Before and after the

stimulation, participants answered to a continuous Visual Analog Scale to check for potential secondary effects of the electrical stimulation.

Afterwards, participants performed the TNTA task as they did in the second phase. Ten days after this, craving levels and consumption patterns were assessed again, using once more the following questionnaires: AUDIT, PACS, and ACQ-SF-R. Three months after the intervention, the same procedure took place – using the same instruments, as well as the TADD, to assess potential effects of the intervention.

Statistical Analyses

All statistical analyses were conducted using IBM SPSS Statistics version 27 software package (IBM Corp., Armonk, NY, USA, 2020.). An Independent-Samples T Test was conducted to assess the absence of differences in age, between BD and NDB groups, as well as to verify the differences in alcohol craving and consumption levels (i.e., PACS, ACQ subscales, ACQ total scores, AUDIT, number of drinks had in typical and atypical weeks).

MI was firstly analysed recurring to two Mixed Repeated Measures ANOVAs. The first one included one between-subject factor (Group: NBD and BD) and two within-subject factors (Condition: NT, TH, and BL; and Content: alcohol or non-alcohol). The second one was performed with one between-subject factor (tDCS Group: CT, CG, or CI) and three within-subject factors (Moment: pre- or post-intervention; Condition: NT, TH, and BL; Content: alcohol or non-alcohol). Analyses were corrected for non-sphericity using the Greenhouse–Geisser method. Main effects were followed with pairwise comparisons between conditions, using the Bonferroni adjustment for multiple comparisons. All significance levels are two-tailed with the present significance alpha level of $p < 0.05$.

Secondly, specific inhibition rates – concerning alcohol- and non-alcohol-related stimuli – were compared between evaluation moments (i.e., pre- and post-intervention) for each BD intervention group, with planned sample comparisons in the form of paired-sample t-test. The same analysis was used to compare the inhibition of alcohol and non-alcohol related stimuli after intervention.

Alcohol consumption (i.e., AUDIT, number of drinks in typical and atypical weeks) and craving (i.e., ACQ Factors, ACQ Total scores, and PACS) levels were firstly assessed

for differences between groups – in each of the moments – through a One-Way ANOVA. Secondly, these variables were analysed with a Mixed Repeated Measures ANOVA, and with planned sample comparisons in the form of paired-sample t-test, in order to assess – in each intervention group – the role of each intervention on each measure, in the different moments of evaluation.

Results

Demographic data and alcohol consumption and craving levels before intervention are summarized in Table 1.

BD and NBD groups did not differ significantly in age (p = .394). Contrarily, the two groups showed significant differences in alcohol consumption levels – AUDIT scores (p < .001), number of drinks had in typical (p < .001) and atypical (p < .001) weeks – and craving measures – PACS (p < .001), ACQ Purposefulness (p < .001), Compulsivity (p < .001) and Emotionality (p < .001) subscales, and ACQ total score (p < .001; see Table 1).

Memory Inhibition

The mixed ANOVA for Repeated Measures that compared BD and NBD groups showed a significant interaction effect between group and condition, $F_{(6,192)}$ = 2.262, p = .039, η^2 = .066. NBDs inhibited significantly more NT (M = 1.68) items than TH (M = 1.18), p = .008, and BL (M = .89) items, p < .001 (see Figure 3). Also, NBDs (M = 1.68) inhibited significantly more NT items, compared to those who received CI (M = .71), p = .007. There were no significant differences in the inhibition rate of NT items between the NBD and the CT group, p = .076, nor between the NBD and the CG, p = .226.

The mixed ANOVA for Repeated Measures that compared the three BD groups – which included condition (NT, TH, and BL), content (alcoholic or non-alcoholic), and moment (pre- or post-intervention) – showed a significant effect of condition, $F_{(2,88)}$ = 7.745, p = .001, η^2 = .150. BDs inhibited significantly more NT (M = 1.07) than BL (M = .69) items, p = .007, and remembered more BL (M = .69) than TH (M = 1.15) items, p = .003. There were no differences in the inhibition rate of NT and TH items, p = 1.000.

Table 1.

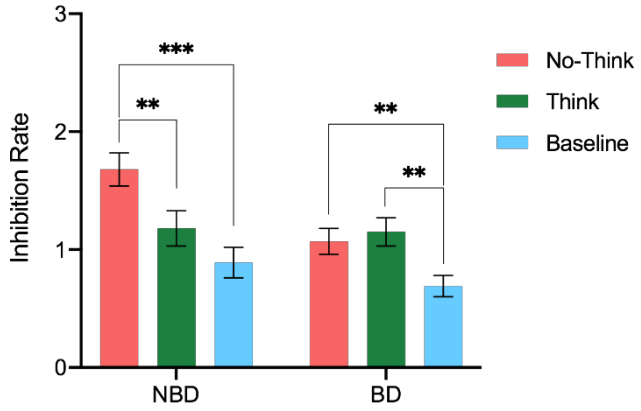
Sociodemographic Characteristics, Alcohol Consumption and Craving Measures of BDs and NBDs Before Intervention (M[SD])

Variables	BDs				NBDs
	All	CT	CG	CI	
N	47	15	15	17	53
Gender (%Female)	47	47	53	41	57
Age (years)	20.02 (1.65)	19.27 (.96)	20.40 (2.13)	20.35 (1.50)	19.74 (1.68)
Alcohol Consumption					
AUDIT	7.55 (2.80)	6.60 (1.92)	7.47 (2.90)	8.47 (3.20)	.96 (.85)
Total Drinks Typical Week	8.66 (5.68)	7.60 (3.81)	9.53 (6.82)	8.82 (6.12)	.25 (.88)
Total Drinks Atypical Week	20.77 (16.33)	20.13 (13.84)	20.13 (14.52)	21.88 (20.32)	1.50 (1.96)
Alcohol Craving					
PACS	3.81 (3.28)	3.87 (3.34)	3.60 (3.09)	3.94 (3.58)	.74 (2.02)
ACQ-SF-R Total Score	2.18 (.76)	2.21 (.68)	2.03 (.69)	2.29 (.88)	1.38 (.53)
ACQ-SF-R Purposefulness	3.14 (1.41)	3.17 (1.01)	3.31 (1.37)	2.98 (1.76)	1.69 (1.00)
ACQ-SF-R Compulsivity	1.46 (.53)	1.55 (.61)	1.38 (.45)	1.46 (.55)	1.05 (.12)
ACQ-SR-R Emotionality	2.18 (1.01)	2.17 (1.01)	1.77 (.68)	2.55 (1.19)	1.45 (.89)

Note. BDs = Binge Drinkers; NBDs = Non-Binge Drinkers; CT = Cognitive Training; CG = Control group; CI = Combined Intervention; AUDIT = Alcohol Use Disorder Identification Test; PACS = Penn Alcohol Craving Scale; ACQ-SF-R = Alcohol Craving Questionnaire-Short Form-Revised.

Figure 3

TNTA Performance Before Intervention in NBD and BD Groups



Note. NBD = Non-Binge Drinking Group; BD = Binge Drinking Group;

*** $p < .001$; ** $p < .01$.

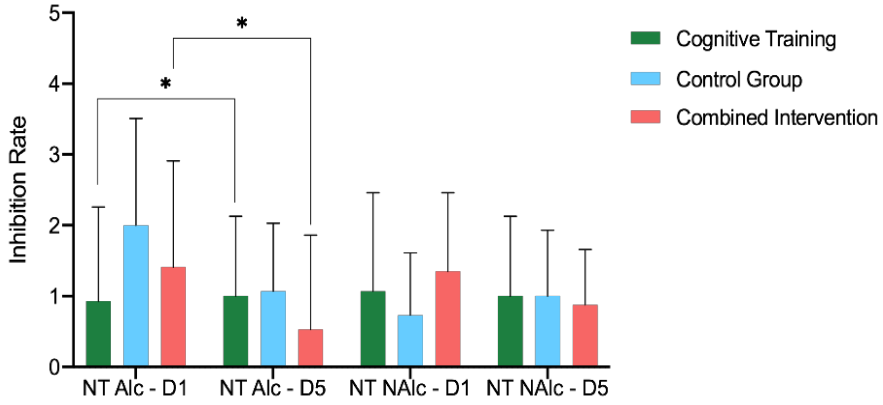
This analysis showed a marginally significant interaction effect between moment and condition, $F_{(2,88)} = 2.911$, $p = .060$, $\eta^2 = .062$. Before intervention, BDs retained more BL ($M = .59$) items, compared to both TH ($M = 1.18$), $p = .011$, and NT items ($M = 1.25$), $p = .002$ (see Figure 3). Also, BDs inhibited less NT items in the post-intervention moment ($M = .88$), compared to the pre-intervention moment ($M = 1.25$), $p = .033$. There was also a marginally significant interaction effect between moment and intervention group, $F_{(2,44)} = 2.891$, $p = .066$, $\eta^2 = .116$. Participants who received CI inhibited less items in the post-intervention moment ($M = .85$), compared to the pre-intervention moment ($M = 1.31$), $p = .022$. Planned sample comparisons in the form of paired-sample t-test were conducted individually for each group in order to assess potential differences concerning the inhibition of alcohol-related stimuli during both pre- and post-intervention moments (see Figure 4). Results showed that individuals from the CG inhibited less NT alcohol items in the post-intervention moment ($M = 1.07$), compared to the initial evaluation ($M = 2.00$), $t(14) = 2.514$, $p = .025$. Also, the CI group inhibited less NT-alcohol items in the post-intervention moment ($M = .53$), compared to the first assessment ($M = 1.41$), $t(16) = 2.504$, $p = .023$. Subjects who received CT showed no significant differences in the inhibition of alcohol-related stimuli before and after intervention, $p = .900$ (see Figure 4).

The same planned sample comparisons – in the form of paired-sample t-test – were conducted individually for each group in order to assess potential differences

concerning the inhibition of non-alcohol-related stimuli during both pre- and post-intervention moments (see Figure 4). Results showed no significant differences in any of the intervention groups (CT, p = .589; CG, p = .433; CI, p = .134).

Figure 4

BDs' Inhibition Performance Before and After Intervention



Note. NT Alc = Alcohol-related No-Think; NT NAlc = Non-alcohol-related No-Think; D1 = pre-intervention moment; D5 = post-intervention moment; * p < .05.

Lastly, we also used planned sample comparisons in the form of paired-sample t-test to evaluate potential differences in the inhibition of alcohol and non-alcohol-related stimuli, in the post-intervention moment. Results showed no significant differences in any of the intervention groups (CT, p = .629; CG, p = .818; CI, p = .318).

Intervention and Alcohol Craving Measures

Alcohol craving scores from each BD intervention group are displayed in Table 2. The One-Way ANOVA did not reveal any significant differences before intervention – between the three intervention groups – in the PACS score (p = .956), ACQ Purposefulness subscale (p = .809), ACQ Compulsivity subscale (p = .701), ACQ Emotionality subscale (p = .092), and ACQ total score (p = .609). This analysis also showed no differences at the 10-day follow-up (FU) between groups in the PACS score (p = .687), ACQ Purposefulness subscale (p = .762), ACQ Compulsivity subscale (p = .513), ACQ Emotionality subscale (p

= .193), and ACQ total score (p = .690). At the three-month FU, results still did not reveal differences between the three intervention BD groups in any of the four measures (see Table 2): PACS score (p = .187), ACQ Purposefulness subscale (p = .772), ACQ Compulsivity subscale (p = .251), ACQ Emotionality subscale (p = .224), and ACQ total score (p = .205).

Alcohol consumption scores from each BD intervention group are displayed in Table 2. The mixed ANOVA for Repeated Measures comparing the PACS and ACQ scores between the intervention groups throughout the different moments of evaluation (before intervention, 10-day FU, and three-month FU), showed a marginally significant main effect of moment, $F_{(2,80)} = 2.962$, $p = .057$, $\eta^2 = .069$, in the ACQ's Compulsivity subscale. BDs had higher scores on ACQ's Compulsivity subscale in pre-intervention moment (M = 1.43) compared to the 10-day FU (M = 1.67), p = .027.

Planned sample comparisons in the form of paired-sample t-test were conducted individually for each group in order to assess potential differences in the ACQ's Compulsivity subscale scores in the different moments of evaluation. Results showed a significant difference, $t(12) = -2.422$, p = .032, between the 10-day FU (M = 1.31) and the three-month FU (M = 1.87). Regarding the CI group, there was a significant difference in the ACQ's Compulsivity subscale scores, $t(16) = -2.209$, p = .042, from the pre-intervention moment (M = 1.46) to the three-month FU (M = 1.76).

The mixed ANOVA for Repeated Measures that compared ACQ's Emotionality subscale scores between moment (pre-intervention, 10-day FU, and three-month FU) and intervention groups, showed a marginally significant main effect of moment, $F_{(2,78)} = 2.962$, $p = .058$, $\eta^2 = .071$. BDs had higher scores on ACQ's Emotionality subscale 10 days post-intervention (M = 2.49) compared to pre-intervention moment (M = 2.14), p = .064.

Planned sample comparisons in the form of paired-sample t-test were conducted individually for each group in order to assess potential differences in the ACQ Total scores in the different evaluation moments. Results showed a marginally significant difference, $t(11) = -1.951$, p = .077, in the CT group. BDs who received CT had higher scores at the three-month FU (M = 2.50), compared to before intervention (M = 2.23).

No differences were found in PACS scores between moments of evaluation.

Table 2.

Alcohol Consumption and Craving Measures of BDs on 10-day and 3-month Follow-Ups

Variables	BDs							
	All (*N* = 47)		CT (*N* = 15)		CG (*N* = 15)		CI (*N* = 17)	
	10-days *M* (*SD*)	3-months *M* (*SD*)	10-days *M* (*SD*)	3-months *M* (*SD*)	10-days *M* (*SD*)	3-months *M* (*SD*)	10-days *M* (*SD*)	3-months *M* (*SD*)
Alcohol Consumption								
AUDIT	7.70 (3.13)	7.27 (3.31)	7.13 (2.90)	6.85 (3.26)	6.80 (2.11)	6.93 (2.56)	9.00 (3.76)	7.88 (3.94)
Total Drinks Typical Week		6.86 (6.41)		5.62 (4.94)		9.29 (7.07)		5.82 (6.64)
Total Drinks Atypical Week		15.74 (13.74)		16.15 (9.92)		20.79 (20.08)		11.26 (7.89)
Alcohol Craving								
PACS	4.23 (4.12)	3.67 (3.25)	4.60 (4.76)	4.85 (4.34)	4.67 (4.15)	3.79 (3.19)	3.53 (3.62)	2.63 (1.82)
ACQ-SF-R Total Score	2.31 (.90)	2.38 (.90)	2.36 (.86)	2.57 (1.02)	2.15 (.84)	2.01 (.65)	2.42 (1.02)	2.52 (.95)
ACQ-SF-R Purposefulness	3.31 (1.42)	3.45 (1.49)	3.42 (1.16)	3.62 (1.56)	3.42 (1.58)	3.21 (1.52)	3.10 (1.54)	3.51 (1.48)
ACQ-SF-R Compulsivity	1.48 (.73)	1.68 (.75)	1.30 (.37)	1.87 (.89)	1.53 (.86)	1.41 (.43)	1.59 (.84)	1.76 (.82)
ACQ-SR-R Emotionality	2.39 (1.32)	2.31 (1.19)	2.56 (1.50)	2.51 (1.58)	1.88 (.69)	1.83 (.58)	2.68 (1.51)	2.53 (1.16)

Note. BDs = Binge Drinkers; CT = Cognitive Training; CG = Control group; CI = Combined Intervention; AUDIT = Alcohol Use Disorder Identification Test; PACS = Penn Alcohol Craving Scale; ACQ-SF-R = Alcohol Craving Questionnaire-Short Form-Revised.

Intervention and Alcohol Use Patterns

The One-Way ANOVA did not reveal any significant differences before intervention – between the three intervention groups – in the AUDIT (p = .169), number of drinks in typical (p = .650) or atypical (p = .942) weeks. At the 10-day FU, there were no significant differences in the AUDIT score (p = .096) between the three groups. At the three-month FU, there were no significant differences in the AUDIT (p = .634), number of drinks in typical (p = .234) or atypical (p = .212) weeks.

The mixed ANOVA for Repeated Measures that compared the number of drinks BDs had in a typical week, before intervention and at the three-month FU, showed a main effect of moment, $F_{(1,41)} = 5.701$, p = .022, η^2 = .122. Subjects consumed significantly less drinks in a typical week after intervention (M = 8.82), compared to before intervention (M = 6.91), p = .022.

Planned sample comparisons in the form of paired-sample t-tests were conducted individually for each group in order to assess potential differences in the number of drinks participants had in a typical week, between the pre-intervention moment and the three-month FU. Results showed a significant difference between the number of drinks participants who received CT had in a typical week before intervention (M = 7.92) and at the three-month FU (M = 5.62), $t(12) = 2.739$, p = .018. In the CI group, there was a marginally significant difference between the number of drinks had in a typical week before intervention (M = 8.82) and at the three-month FU (M = 5.82), $t(16) = 1.859$, p = .081. There were no significant differences regarding the CG, p = .753.

Regarding the alcohol consumption pattern in an atypical week, the mixed ANOVA for Repeated Measures that compared the number of drinks BDs before intervention and at the three-month FU, between groups, showed a marginally significant main effect of moment, $F_{(1,40)} = 3.421$, p = .072, η^2 = .079. Subjects had less drinks in atypical weeks after intervention (M = 16.28), compared to before intervention (M = 20.53), p = .072. Planned sample comparisons revealed a significant difference between the number of drinks BDs who received CI had in an atypical week before intervention (M = 22.94) and at the three-month FU (M = 11.91), $t(15) = 2.274$, p = .038.

The same planned sample comparisons – in the form of paired-sample t-test – were conducted individually for each group in order to assess potential differences

concerning the AUDIT scores in the three moments of evaluation (i.e., before intervention, 10-day FU and three-month FU). Results showed a significant difference in the AUDIT score for the BDs who received CI, $t(16) = 3.379$, $p = .004$., with this group showing higher AUDIT scores at the 10-day FU ($M = 9.00$), compared to the three-month FU ($M = 7.88$).

Discussion

The present work aimed to assess the role of MI training – through CT alone or combined with tDCS over the right DLPFC – on MI ability, and, consequently, on alcohol craving and consumption levels. We hypothesized that BDs from the CT and CI groups would show an improvement in MI – namely, alcohol-related MI – and, consequently, would present a decrease in alcohol consumption and craving levels.

Using an adaptation of the TNT paradigm (Anderson & Green, 2001) involving alcoholic and non-alcoholic contexts (the TNTA task; López-Caneda et al., 2019), we were able to replicate the main behavioural finding obtained from the original procedure, i.e., recall for items instructed to be suppressed (NT images) was significantly diminished as compared to BL items. However, only the NBD group showed significant differences between items instructed to be suppressed and those instructed to be recalled (TH images).

One of the possibilities for the absence of differences between items that were to be remembered and those to be inhibited in the BD group may be related to the "White Bear effect" (Wegner et al., 1987). This paradoxical effect of MI regards the attention bias to the inhibition target, upon inhibition instructions (Muhl-Richardson et al., 2022), responsible for the intrusion of the unwanted thought (Wenzlaff & Wegner, 2000). It is argued that the instruction to inhibit a determined object or image leads to an attentional bias towards such object or image (Muhl-Richardson et al., 2022). In this context, the instruction given to inhibit acts as a reminder of the to-be-inhibited item, perhaps cueing individuals to think more about the target than they initially would have (Wenzlaff et al., 2000). Bearing this in mind, the absence of differences in the BD group could be explained by this role of the instruction to inhibit on attention bias – leading to higher retention, instead of inhibition –, associated with reduced executive control over memories. This type of strategic control is activated by executive control networks that seem to be altered

in subjects with history of BD (Cservenka & Brumback, 2017; Sousa et al., 2019). Therefore, we hypothesize that due to reduced executive control, BDs fail to decrease the accessibility of unwanted memories, which results in similar recalling rate for NT comparatively to TH items. Moreover, the fact that TH images were less recalled than BL images in BDs, leads us to suggest that BDs actually have a reduced ability to retain information voluntarily. In this sense, burgeoning studies have revealed memory impairments in BDs (Carbia et al., 2017; Heffernan et al., 2010; Nguyen-Louie et al., 2016; Parada et al., 2011), which could have led BDs not to be able to voluntarily retain the information long enough and thus performance in the TH condition would be similar to the NT condition.

On the other hand, our main hypothesis was refuted, as neither CT nor CT combined with tDCS applied over the right DLPFC showed an effect on improving MI ability. Specifically, results showed that BDs – in general – displayed reduced MI ability in the post-training, relative to the pre-training session. Particularly, participants who received CT combined with tDCS significantly decreased the inhibition rate, namely of alcohol-related items, which supports evidence showing no effects of tDCS in enhancing CT effects (den Uyl et al., 2016), but contradicts other which stand by its effect on improving cognitive function, namely IC (Ditye et al., 2012). Individuals who received CT showed no significant differences in the inhibition of alcohol-related stimuli before and after the intervention.

Several possibilities were discussed when interpreting these results, namely the absence of apparent intervention effect on MI. Firstly, taking a critical point of view on the TNTA task, it is relevant to mention that several authors (for a review, see Otgaar et al., 2019) have failed to verify the expected results of the TNT paradigm (i.e., higher retention of TH, followed by BL and, finally, NT items; Anderson & Green, 2001). Another aspect that is relevant to consider, raised in Reichl and colleagues' (2022) work, is the possibility that the exposure to alcohol-related stimuli during training could have induced alcohol craving and, consequently, affected BDs' ability to inhibit alcohol-related stimuli. Evidence states the existence of a positive relationship between alcohol consumption and reactivity levels to alcohol-related cues (Cofresí et al., 2019; Robinson & Berridge, 2001). Moreover, research shows that exposure to alcohol-related cues can elicit alcohol-seeking reactions, such as craving (Jones et al., 2013). Particularly, repeated

alcohol consumption leads to hypersensitivity to alcohol-related stimuli, which, in turn, causes an excessive attribution of incentive salience to such stimuli, instigating the craving experience (Robinson & Berridge, 1993). Focusing on BDs, it is known that their approach bias to alcohol-related cues is associated with alcohol consumption and craving (Field et al., 2008a). Based on this, it could be possible that the exposure to alcohol-related stimuli during CT could have elicited these processes, increasing craving levels and negatively affecting the ability to inhibit alcohol-related memories. Perhaps, in future studies, craving levels after exposure should be collected in order to try to control this possibility.

One additional issue we must also consider when discussing these results is the possibility that participants were not inhibiting the cue-associated memory. A factor that could play a role in this premise is the fact that individuals knew *a priori* that the task ended with a memory test and wanted to perform well. As in the learning phase they were expected to answer correctly to the questions – namely the one concerning the type of beverage associated with the neutral cue –, and only proceeded to the next trial when they got most of the questions right, in the memory test phase there could have been a similar (un)conscious will to achieve a high correct answer rate. If this were the case, participants would learn not to employ the cognitive effort necessary to inhibit NT items. As such, assuring participants do not know about the final memory test could eliminate this possibility and thus, improve the effectiveness of training. Indeed, a recent work by Mamat and Anderson (2023) showed reduced memory for suppressed events after a three-day training in which there were no daily memory tests. Further studies are needed to clarify the possible impact of each possibility explored above.

Nevertheless, and very importantly, CT appeared to have a significant effect on alcohol use, as BDs significantly decreased typical and atypical alcohol consumption. Specifically, individuals who received CT significantly decreased typical alcohol consumption three months after the intervention. This supports some previous work, that also found a role of CT in reducing alcohol consumption in young adults (Liu et al., 2019). In addition, we also found that participants who received CT combined with tDCS showed a tendency to decrease typical consumption, and significantly decreased atypical consumption, as well as the AUDIT scores, supporting previous work (Dubuson et al.,

2021). Notably, this reduction in alcohol use was not observed in the BD group who did not receive the MI training.

The presence of a decrease in alcohol consumption upon the absence of a behavioural outcome (i.e., an improvement in alcohol-related MI), leads us to hypothesize that the intervention might have had an *implicit* effect on alcohol consumption. That is, even though the intervention did not reflect behavioural results, it did impact alcohol use. In this sense, evidence shows that deviant behaviour – such as BD – may be regulated by both an explicit, slow, reflexive system and a faster, implicit, impulsive one (Evans, 2003; Wiers et al., 2007). The first involves conscious knowledge-based deliberations, as the latter includes automatic evaluation of stimuli through associative links and motivational orientations (Strack & Deutsch, 2004; Wiers et al., 2007). These dual-processes models state that even though the implicit system can be regulated by controlled processing, cognitive resources and motivational aspects might not be accessible (Wiers et al., 2007). Focusing on alcohol consumption behaviour, when cognitive resources – namely IC – are not available, drinking is predicted by the impulsive system, specifically by implicit alcohol associations that exist in this system (Houben & Wiers, 2009). Research has frequently shown that executive functions, such as working memory (Thush et al., 2008) and IC (Houben & Wiers, 2009) moderate the degree to which alcohol consumption is determined by implicit alcohol associations – and not by the reflexive system. Moreover, the impulsive system gets sensitized through frequent and repetitive alcohol consumption, increasing the strength of automatic appetitive alcohol cognitions, as well as the motivation to engage in such behaviour (Field et al., 2010; Wiers et al., 2007). Importantly, the IC observed in the BD population (e.g., Holcomb et al., 2019; López-Caneda et al., 2012, 2017) may contribute to the enhancement of automatic alcohol-related cognitions, leading to a priming effect of alcohol (Field et al., 2010).

Considering the role of IC in delineating the degree to which drinking is determined by the impulsive system, and knowing that MI is regulated by IC, we hypothesize that the intervention might have had an effect on the regulation of the impulsive system, leading to an adequate balance between both reflexive and impulsive systems, thereby readjusting the imbalance typical of individuals with alcohol misuse (Noël et al., 2013). Accordingly, there is evidence that supports the role of CT in changing the approach bias towards alcohol into an avoidance bias (Wiers et al., 2011), leading to

better treatment outcomes a year later in the CT group. Thus, our results suggest that MI training may have a role on reducing alcohol use, perhaps by decreasing the salience of alcohol-related cues and/or by enhancing the reflective or controlled processes.

Despite the decrease in alcohol consumption after the intervention, BDs showed an increase in the compulsivity to drink at the 10-day FU. Particularly, BDs from the CT group displayed a tendency to decrease the urge to consume alcohol from before intervention to the 10-day FU, but increased compulsivity levels from the 10-day FU to the three-month FU, whereas the CI group presented higher compulsivity scores at the three-month FU. Nonetheless, this could point to a short-term beneficial role of CT on craving, which leads us to an important aspect regarding the possibility of the need for additional sessions of training to consolidate the effect. Another possibility for these results is the influence of the COVID-19 pandemic, as a significant portion of FUs were conducted during confinement or periods in which restrictive measures were in place (e.g., bars closed), which could have moderated alcohol craving, leading to these little consistent results (see limitations section below).

Finally, literature is conflicting regarding the effectiveness of tDCS over the DLPFC on improving executive functioning and craving levels (for a review see Mostafavi et al., 2020), with some authors finding no significant effects (den Uyl et al., 2017, den Uyl et al., 2018, Klauss et al., 2014), while others defend its positive effects (for a review, see Kim & Kang, 2021).

Importantly, even considering the evidence supporting a downregulation of the hippocampal functions, which disrupts the encoding, retrieval, and stabilization of memories (Anderson & Hanslmayr, 2014; Levy & Anderson, 2012), the pathways through which the DLPFC modulates the hippocampus and cortex are not well known yet (Anderson & Hulbert, 2021). Bearing this in mind, there is growing evidence of the role of other cortical regions that somehow contribute to the MI processes – such as the anterior cingulate (Anderson et al., 2004) and the inferior frontal cortex (Depue et al., 2007). Relevantly, a recent review showed that bilateral tDCS has beneficial effects on craving levels, highlighting the possibility that cathodal tDCS on the left DLPFC and anodal tDCS on the right DLPFC, could improve dysfunctions in the anterior cingulate cortex (Kim & Kang, 2021) and thus might be a target for future interventions trying to improve MI abilities.

Limitations

Despite having an adequate sample – at least in compliance the standards of electroencephalography studies – of BDs and NBDs counterparts, statistical power was significantly reduced when the BD groups were split into the three subsamples that received each intervention, which could have affected our results. Furthermore, the present work did not include data regarding individual characteristics such as intrinsic motivation, effort put into the training sessions, and we also lacked the collection of information regarding the strategy participants used upon instructions to inhibit the cue-associated memory, which may significantly moderate performance in the TNT task (Nardo & Anderson, 2023). Similarly, information regarding the existence of intrusions during the individual's inhibition performance should have also been accounted for. All of this would have given us a better understanding of the subjects' experience during task performance, as well as during CT sessions.

The COVID-19 pandemic might also have had a role in the present results, as several participants performed the FU evaluations (i.e., assessment of consumption and craving levels) during – or in between – confinements, periods in which several restrictions were imposed that could have impacted alcohol consumption associated factors (e.g., bars closed, mandatory isolation, quarantines). Given the fact that we assessed variables such as typical and atypical alcohol consumption, it is relevant to reflect on the possible effect that social isolation might have had on these results, as BD is highly prevalent among social encounters. Vasconcelos and colleagues (2021) conducted a longitudinal study on the impact of the COVID-19 pandemic on alcohol consumption in BDs and showed that they decreased alcohol intake during confinement, a shift which was even more pronounced after lockdown – even though craving levels increased in the latter moment. During the pandemic (i.e., confinement and in-between confinement periods), the alcohol consumption levels steadied, staying significantly lower than usual (i.e., pre-COVID-19). The authors highlight the social nature of BD in college students, based on the reduction/extinction of BD patterns even when isolation was no longer mandatory – but measures that prevented/disrupted social gatherings (e.g., concerts, college parties) were in place (Vasconcelos et al., 2021). Given that BD is most prevalent in college students, the aforementioned aspects are crucial to consider when interpreting the present results.

Conclusion

In conclusion, the present work showed an absence of effects of MI training on BDs. Before the intervention, BDs showed no differences between the retention of to-be-retained and to-be-inhibited items. We discussed several possibilities for this, beginning with the "White Bear effect", and the role of anomalies in executive control networks that prevent strategic control over memory (i.e., reduced executive control and, consequently, altered accessibility of inhibited memories). We also considered if this result could have been verified due to a post-suppression rebound effect, which relates to a higher retention of a previously inhibited item. Moreover, we discussed if BD-associated deficits could be the origin of this absence of differences, namely memory impairments – as BDs might not have had the ability to voluntarily retain the instructions long enough, leading to a similar performance on TH and NT conditions. Our main hypothesis was refuted, as neither CT nor CI supported an improvement of MI. BDs' MI performance decreased from before to after intervention. Specifically, the CI group diminished the MI ability, as the CT group showed no significant differences. Based on the idea that frequent alcohol consumption increases alcohol-related cues' salience and reactivity, we reflected on the possibility of having increased BDs' craving levels upon exposing them to alcohol-related items. This craving raise could have harmed MI abilities, explaining the absence of the effect of MI training. The other possibility assessed was that participants were not inhibiting the cue-associated memory. As subjects knew the task ended with a memory test, there could have been an (un)conscious will to achieve a high correct answer rate.

Prominently, BDs from the CT and CI groups showed a decrease in alcohol consumption, supporting previous research (Dubuson et al., 2021; Houben et al., 2011; Liu et al., 2019; Manning et al., 2016; Stein et al., 2023). These results led us to reflect on a possible implicit effect of the intervention, that is, that MI training influenced a more balanced reflexive/impulsive duality of systems, which could have led to a decrease in alcohol use. Additionally, BDs increased the urge to consume alcohol after the intervention. Specifically, the CT initially tended to decrease compulsivity levels, but increased it after three months, as occurred in the CI group. Even so, this could indicate a short-term benefit of CT on craving, perhaps pointing to a need for additional sessions of training to consolidate the effect. Another possibility for these results is the COVID-19

pandemic, as several FUs were performed during periods in which restrictive measures that impacted BDs social lives and consumption habits were in place (e.g., bars closed).

Further investigation is needed to examine the effect of MI intervention in BDs. CT is a valuable tool, the effect of which could be potentiated if computerized or turned into a game, with the possibility of individualization (Dubuson et al., 2021, Reichl et al., 2023). It would also be relevant to take a closer look at the progress during the training itself, instead of just focusing on the outcome, as this could help to better understand what factors could be moderating or mediating the process (Reich et al., 2023). Additionally, it is important to assess the need for methodological refinements in the training format (Liu et al., 2019). Relevantly, considering another type of training should be explored in the future, as there is evidence of the benefits of working memory training in IC (Maraver et al., 2016). Resourcing to low-cost and easily available techniques, such as tDCS, might be advantageous, and could potentiate CT (Ditye et al., 2012). However, future research should contribute to define the most adequate number of sessions and FUs, as well as consider different montages – such as bilateral DLPFC (Boggio et al., 2008). Additionally, further studies should include a commonly overlooked aspect of BD – the emotional factor, as it is relevant and very often erased from the conceptual bridges regarding this pattern in young adults (for a review see Lannoy et al., 2021). Additionally, motivational variables should be considered, as there is evidence of the role of participants' motivation on training improvement potential (Maraver et al., 2016).

Given the high prevalence of BD in young adults, particularly in college students, and attending to the possible effect that the BD pattern might have on academic achievement, as well as on general cognitive function, it is urgent to continue investigating this scarcely explored area. Moreover, deepening our knowledge on this subject can lead us to approaches to prevent hazardous patterns – such as BD. There is evidence that such interventions can have a beneficial impact on young adults (Wolfson et al., 2012). Finally, these results are relevant in the field of alcohol misuse research and may provide valuable insights into IC over alcohol-related intrusions that can increase craving levels and escalate and/or perpetuate consumption patterns.

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INFORMED CONSENT FORMS

Official Title of the Study:

Forgetting Alcohol: A Double-blind, Randomized Controlled Trial Investigating Memory Inhibition Training in Young Binge Drinkers

NCT ID: not yet assigned

Date: February 5, 2019

University of Minho
School of Psychology
Research Center in Psychology
(CIPsi) Psychological Neuroscience
LaboratoryCampus de Gualtar
4710-057 Braga
Tel: +351 253 601 398

Research Project reference: NORTE-01-0145-FEDER-028672

Principal Investigator (PI) and Research Team: Dr. Eduardo López Caned (PI); Dra. AdrianaSampaio e Dr. Alberto Crego

INFORMED CONSENT FORM

COPY FOR THE PARTICIPANT

☐1) I confirm I have read and understood the informative document that was delivered to me, with all the information regarding the study in which I am participating, and that I had the opportunity to raise questions and doubts about it.

☐2) I confirm the research team had provide me clear answers to all my questions and doubts.

☐3) I understand that I am free to leave the study at every moment, without justification, and without any consequences.

☐4) I understand and agree that my personal identification data and the data obtained through the course of the research study will be kept in separate archives, therefore guaranteeing its safety, and that the team members with access to the data will respect their confidentiality.

☐5) I, therefore, consent that my data are stored and/or exported to external databases in order to be analysed, understanding that, in any circumstance, information regarding my identity will not be disclosed.

☐6) I understand that the present study does not have a diagnostic purpose and, consequently, I will not receive an individual report with my data/results.

☐7) I consent to participate in the above-mentioned study.

Participant name: .....

Researcher name: .....

Name of the person responsible for collecting this consent (if different from the researcher):

.....

Date: ..... **Participant Code:** .....

University of Minho
School of Psychology
Research Center in Psychology
(CIPsi) Psychological Neuroscience
LaboratoryCampus de Gualtar
4710-057 Braga
Tel: +351 253 601 398

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INFORMED CONSENT FORM

COPY FOR THE RESEARCHER

☐1) I confirm I have read and understood the informative document that was delivered to me, with all the information regarding the study in which I am participating, and that I had the opportunity to raise questions and doubts about it.

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Date: ..... **Participant Code:** .....

Annex B – Ethics Committee Approval

Universidade do Minho

Conselho de Ética

Conselho de Ética - Ciências Sociais e Humanas

Identificação do documento: CE.CSH 078/2018

Título do projeto: *To think or not think of alcohol, that is the question: Memory suppression in young binge drinkers*

Investigador(a) Responsável: Eduardo López Caneda (PhD), Escola de Psicologia, Universidade do Minho

PARECER

O Conselho de Ética analisou o processo relativo ao projeto de investigação acima identificado, intitulado *To think or not think of alcohol, that is the question: Memory suppression in young binge drinkers.*

Os documentos apresentados revelam que o projeto obedece aos requisitos exigidos para as boas práticas na investigação com humanos, em conformidade com as normas nacionais e internacionais que regulam a investigação em Ciências Sociais e Humanas.

Face ao exposto, o Conselho de Ética nada tem a opor à realização do projeto, emitindo o seu parecer favorável.

Braga, 29 de novembro de 2018.

A Presidente do CEUMinho

Assinado por : **GRACIETTE TAVARES DIAS**
Num. de Identificação Civil: BI071230157
Data: 2018.12.07 10:18:57 GMT Standard Time

CARTÃO DE CIDADÃO

Anexo: Formulário de identificação e caracterização do projeto