Universidade do Minho
Escola de Psicologia

Filipa Azevedo Dantas

Effects of Transcranial Direct Current Stimulation (tDCS) over dlPFC and over vmPFC in the Behavior in a Risky Decision-Making Task

outubro de 2022

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Professor Doutor Pedro Moreira
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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.

Braga, 17th October de 2022

(Filipa Azevedo Dantas)

Efeitos da Estimulação por Corrente Direta Transcraniana (tDCS) sobre o dlPFC e sobre o vmPFC no Comportamento numa Tarefa de Tomada de Decisão de Risco

Resumo

A tomada de decisão é um comportamento complexo, que compreende múltiplos componentes. A tomada de decisão arriscada tem ganho particular atenção, porque diariamente tomamos decisões sob algum grau de risco e conhecer o que nos torna propensos ao risco pode ajudar a prever essas decisões. As emoções influenciam a tomada de decisão de uma forma regular e previsível (Keltner & Lerner, 2010), portanto é pertinente explorar a capacidade de a modular. Estando os córtices pré-frontal dorsolateral e ventromedial implicados neste processo (Nejati et al., 2021), uma estratégia seria aplicar tDCS sobre estas regiões. Avaliámos os efeitos da tDCS anodal sobre os córtices pré-frontal dorsolateral e ventromedial na modulação da tomada de decisão arriscada, durante uma Balloon Analogue Risk Task (BART Automática e BART Manual) em 32 voluntários saudáveis (idades entre 18 e 25 anos). Hipotetizámos que todos os indivíduos manifestariam uma preferência por decisões pouco arriscadas, na sessão ativa comparativamente com a sham. Foi realizada uma ANOVA mista para cada uma das métricas da BART, seguida de testes-t amostras-emparelhadas (ou testes de Wilcoxon) para diferenças entre grupos. Os resultados não revelaram diferenças estatisticamente significativas entre as sessões sham e activa em nenhuma das métricas da BART.

Palavras-Chave: Tomada de Decisão de Risco, Córtex Pré-frontal Dorsolateral, Córtex Pré-frontal Ventromedial, Estimulação por Corrente Direta Transcraniana, Balloon Analogue Risk Task

Effects of Transcranial Direct Current Stimulation (tDCS) over dlPFC and over vmPFC in the Behavior in a Risky Decision-Making Task

Abstract

Decision-making is a complex behavior that comprises multiple component processes. Risky decision-making has been gaining particular attention as daily we need to make decisions under some degree of risk and knowing what makes us prone to risk may help us predict our decisions. As individuals make decisions in a regular and predictable manner when driven by emotions (Keltner & Lerner, 2010), it is pertinent to explore the capability of modulating decision-making. Since the dorsolateral and the ventromedial prefrontal cortices have been implicated in decision-making (Nejati et al., 2021), a useful strategy would be to apply tDCS over these regions. We aimed to evaluate the effects of anodal tDCS over vmPFC and over dlPFC on the modulation of risky decision-making during a Balloon Analogue Risk Task (BART; Automatic BART and Manual BART) in 32 healthy volunteers (ages between 18 and 25). We hypothesized that all individuals would reveal a preference for low-risk decisions in the active comparatively to the sham session. A mixed-design ANOVA was run for both BART metrics, followed by paired-samples t-tests (or Wilcoxon test) to analyze differences between groups. Results revealed no statistically significant differences between the sham and active sessions in none of the BART metrics.

Keywords: Risky Decision-Making, Dorsolateral Prefrontal Cortex, Ventromedial Prefrontal Cortex, Transcranial Direct Current Stimulation, Balloon Analogue Risk Task

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Effects of Transcranial Direct Current Stimulation (tDCS) over dlPFC and over vmPFC in Behavior in a Risky Decision-Making Task

Introduction

1. State of the art

1.1. Decision-Making

Decision-making has been comprehensively studied across diverse fields, such as Psychology, Economics, Medicine and Law. Reaching a precise and accurate definition has been quite difficult but it undoubtedly constitutes a complex behavior that comprises multiple component processes (Rangel et al., 2008).

Through the study of decision-making, we can improve our understanding of the processes by which individuals make a particular choice, in detriment of another; basically, why the individual chooses to act the way it does. Knowledge of the neurobiological correlates of decision-making processes may guide us in designing ways to overcome possible handicaps, yielding a great impact on an individual's quality of life.

For many years, normative theories of decision-making have claimed that individuals must act as rational agents that accurately and coherently understand their goals, stable preferences and self-interests and use directed behavior accordingly (Baron, 2000). Notwithstanding, a new perspective has arisen recently with the demonstration of the extent to which decision-makers deviate from rationality. Behavioral research has shown that people often do not behave rationally, that judgment can be biased, and it often is in reliable and systematic ways. Accordingly, individuals make decisions based on their subjective experience of reality, generating significant tendencies and biases (Kahneman, 2003).

1.2. Risky Decision-Making

It has already been well documented the influence that emotional states exert on cognitive processes (Bell & Wolfe, 2004). The psychological field of emotion science has revolutionized theories of decision-making. Now we know that emotions constitute a potent and predictable driver of most decisions. Also, there are important regularities in the underlying mechanisms through which emotions influence judgment and choice (Lerner et al., 2015).

A specific type of decision-making that has been gaining attention for a couple of decades now is risky decision-making. Daily, we are confronted with the need to make decisions under some degree of risk and gaining insight into the conditions in which people are more likely to be prone to risk may be useful in predicting their decisions.

1.3. Decision-Making in the Brain

The dorsolateral prefrontal cortex (dlPFC) and the ventromedial prefrontal cortex (vmPFC) are part of the distributed network of brain regions underlies the processes of decision-making (Brunyé et al., 2021; Rushworth et al., 2011).

Evidence from neuroimaging studies showed that the dlPFC, plays a crucial role in decision-making processes (Rorie et al., 2005). Weighting risks and benefits associated with each decision involves a complex neural network that includes the dlPFC (e.g. Rao et al., 2008). It has also been implicated in the modification of risk-taking, with reduced scores in risky decision-making tasks (e.g. Fecteau et al., 2007) and in stress regulation by limiting its biological and behavioural pejorative consequences (Brunelin & Fecteau, 2021).

Individuals suffering from Substance Use Disorder (SUD) presented impaired decision-making and elevated-risk taking behavior (Gowin et al., 2013) and reduced activity in the dlPFC (Eldreth et al., 2004). The reported elevated risk-taking in substance users may be interpreted as a consequence from dlPFC impairments on their ability to shift choices away from disadvantageous options, which seems a plausible proposal, considering dlPFC's active role in the maintenance and regulation of top-down control for driving appropriate behavior.

The comprehensive study of risk-taking involving reward processing has also implicated the ventromedial prefrontal cortex (vmPFC) in these processes. This region has been shown to be crucial for rational decision-making, as dysfunctions in this region have been linked to cognitive biases, impulsive behavior, and gambling addiction (Kroker et al., 2022). Lesion studies have associated damage to vmPFC with impaired performance on laboratory tasks of decision-making under ambiguity and risk (Bechara et al., 2000), supporting a role of vmPFC in biasing healthy individuals towards choosing more conservative options under risk.

Evidence from fMRI studies also points to the vmPFC being important for effective value-based decision-making (Juechems et al., 2017) and evidence from vmPFC lesions have been associated with

impairments in adaptive decision-making under affect-rich conditions, which suggests a role of vmPFC in the generation of affective meaning (Spaniol et al., 2019).

Functionally, dlPFC has a crucial role in executive processing and cognitive control, while the vmPFC appears to be associated with processing reward and the value of stimuli and it is assumed to have a major role in emotional processing. Results of a study suggested that the dlPFC is associated with processing the value of emotions, while the vmPFC is a key region activated in response to the arousal aspect of emotional stimuli (Kahnt et al., 2011; Nejati et al., 2021).

Notwithstanding, research using functional imaging techniques reveals a gradual transition between the ventromedial and dorsolateral prefrontal areas regarding emotion processing (Nejati et al., 2021). All in all, the best way to put may be to say that vmPFC and dlPFC interact in determining behavior.

1.4. Neuromodulation Decision-Making

Given that processes involved in risky decision-making are part of the individual human's emotional and social functioning, it is pertinent to explore the capability of modulating them. Findings from neuromodulation studies yield a particular clinical relevance for patients with abnormal risk-taking behaviors, such as in drug abuse, overeating, and pathological gambling, if translated into therapeutic interventions (e.g., Fecteau et al., 2010). Considering the above-mentioned literature about the involvement of vmPFC and dlPFC in risky decision-making, these regions are good candidates for modulation using strategies such as tDCS.

The most common area targeted with tDCS is the dorsolateral prefrontal cortex (dlPFC), probably due to its well-demonstrated role in decision-making, working memory, and emotion, and to the fact that it is positioned right under the scalp, facilitating the montage. A systematic review of 16 clinical trials and a handful of other studies (Lupi et al., 2017) investigating tDCS of the dlPFC synthesized evidence of reduced drug craving, cue reactivity, risky decision-making, and substance use, after stimulation.

A range of studies using stimulation techniques provides evidence that modulating activity in the dlPFC using transcranial direct current stimulation (tDCS) can, indeed, alter people's decisions in uncertainty' situations (Khaleghi et al., 2020). Khaleghi et al. (2020) demonstrated that tDCS over the dlPFC modulates risk-taking behavior to a more cautious performance traduced in lower scores on the Balloon Analogue Risk Task (BART).

Despite the vast literature addressing the use of tDCS on vmPFC in emotional processing paradigms (e.g., Winker et al., 2018), recent studies have used this methodology to study the role of modulating this region in the context of decision-making involving delay discounting (Manuel et al., 2019). A study that applied tDCS over the vmPFC in healthy individuals performing a delay discounting task following an emotional or neutral induction provided evidence that the vmPFC integrates reward and emotion in situations of high impulsivity (which imply an emotion-laden charge).

There is, however, a lack of studies investigating the impact of modulating the activity of vmPFC via tDCS in the behavior in a risky decision-making task, and the present study intends to bridge this gap.

2. Goals

As mentioned earlier, numerous findings point to an involvement of vmPFC and dlPFC in decision-making processes, which assume undeniable importance in people's daily life and can be particularly critical for pathological risk-taking behavior. It would be relevant to comprehend in what way it is possible to interfere in the decision-making behavior style of these individuals. A useful strategy would be to apply tDCS, particularly over vmPFC and dlPFC.

The aim of this study was to evaluate the effects of anodal tDCS over vmPFC and over dlPFC, as compared to sham, on the modulation of risky decision-making during a Balloon Analogue Risk Task (BART) in healthy volunteers.

Considering that both regions are already known to play a role in decision-making processes, specifically in risky decision-making, we hypothesized that both individuals receiving anodal tDCS over vmPFC and those receiving over dlPFC would reveal a preference for low-risk decisions - i.e., they would opt significantly more frequently for a smaller number of pumps per trial -, comparatively to sham control.

Considering vmPFC and dlPFC typically play a clear role in inhibitory control processes, impulsiveness tendencies, processing of emotional content and modifications in affect, a series of self-report control questionnaires were included in the procedure to understand if the effects of modulating these regions are reflected in other processes in which these regions are involved, i.e., if the efficacy of the modulation was related to external variables that are specific to the subject.

Method

1. Sample

Recruitment was carried out from the body of Psychology students at the University of Minho through their voluntary enrollment in the study, post divulgation of it on the SONA credit platform, and by institutional email.

Exclusion criteria were: the presence of a diagnosis of mental or physical disease, that could interfere with the aim of generalizing the possible encountered effects to the healthy population; a score above 70 on Edinburgh Handedness Inventory. Considering an estimate of Cohen's *d* of 0.5 (medium effect size) and an estimated power of 0.8, we determined a minimum sample size of 34 participants, between 18 and 25 years old, for each group (n=68). However, due to some exclusion of participants and to the late start of the data collection which shortened the data collection period, we could not achieve the sample size established. Thus, instead of the aimed sample size of 68, we were only able to recruit 32 participants. Considering this is the first study aiming to evaluate the effect of tDCS over dlPFC and over vmPFC (inter-subject variable) on the behavior in a decision-making task, that will compare two metrics between an active and a sham session (intra-subject variable), we will consider this a pilot study.

Procedures were approved by Ethics Committee for Research in Human and Social Sciences (CEICSH), at Minho University, and were performed accordingly with the Declaration of Helsinki (1964).

2. Instruments

2.1. Balloon Analogue Risk Task (BART)

The Balloon Analogue Risk Task is a laboratory-based behavioral measure for the assessment of risk-taking. Results of the original study showed that the average number of pumps on unexploded balloons, also referred to as average adjusted pumps, was associated with some real-world risky behaviors occurring outside the laboratory (Lejuez et al., 2002). Lauriola et al. (2014) demonstrated that the riskiness of the BART was significantly correlated with self-report measures of personality traits, namely impulsivity and sensation seeking, as well as with deficiencies in behavioral constraint.

The presentation of the BART required the use of a computer. On a computer screen was presented: the simulation of a small balloon, a display of the money already earned, and a display showing the money earned on the last balloon. Each click on "Space" key button inflates the balloon by 1◦ and increments the amount of money in a temporary bank by 5 cents. Participants can stop pumping the balloon at any point and click on "Enter" key to transfer all the money from the temporary bank to the

permanent bank (represented to the participant through a slot machine payoff sound effect). However, if a balloon is pumped after its individual explosion point, participants hear a "pop" sound, meaning it exploded, the amount of money on the temporary bank resets and a new uninflated balloon appears. Each appearance of a new balloon is preceded by an explosion of a balloon or a click on the button "Collect" and this process continues for 90 trials. The balloons have different probabilities of exploding, and participants only knew that a balloon could explode at any time and had a maximum number of pumps ranging between 1 and 128.

However, a limitation of this format has been pointed out by Pleskac et al. (2008), who presented formal proof that a bias exists in the measure of Adjusted Scores produced by the BART.

Participants have the indication that they must try to win as much money as possible by inflating the balloons that appear trial by trial. Therefore, when confronted with a balloon, they are constantly exposed to the need to make a choice between pumping the balloon (and risking its explosion and loss of all the money accumulated in the temporary bank) or stop pumping the balloon, by clicking on the button "Collect" (and saving all the money on the temporary bank). The Adjusted Score is the mean number of "Pump"'s some participant gives to a certain balloon on trials that do not end in an explosion. By using this measure, in our assessment of participants' risk-taking tendencies, we are only considering the number of "Pump"'s they gave in trials in which they chose to stop pumping (which is the safe option) – biasing the score obtained towards a lower value. The authors also pointed out that the Unadjusted Score, which is the mean number of "Pump"s on all trials (the ones that end in an explosion and the ones in which the participant chooses to stop pumping) is also a poor index of risk-taking behavior as it includes trials that have ended before the participant actually chooses to stop pumping.

In order to overcome the abovementioned limitations, Pleskac et al. (2008) presented an alternative format of the experience – Automatic BART. They proposed that, instead of asking the participants to pump the balloon by clicking on some button, we ask the participants to type the desired number of "Pump"'s they would like to give to the balloon. Then, they would either watch the balloon inflate the number of times they typed (if the number of "Pump"'s typed does not exceed the maximum number of "Pump" of that specific balloon) or watch it inflate until it reaches its explosion point and explodes. The main advantage of the Automatic BART is that the number of "Pump"'s participants want to give to the balloons is not restricted, allowing them to take as much risk as they want. This way we can assess the exact number of "Pump"'s participants would like to give on each trial, not excluding the ones that would result in an explosion, and not biasing the assessment of risk-taking towards a lower value.

The instructions given to the participants were the same as in the other format of the experience except for the explanation of how they should respond to pump the balloons.

As we intended to reduce any bias that we could predict to the minimum, we used two formats of the BART – the original format from Lejuez et al. (2002), or Manual BART, and the one proposed by Pleskac et al. (2008), or Automatic BART. Both formats of the task were created using PsychoPy (3.0). Illustrations of both formats used are presented in Figures 1 and 2 below.

Figure 1

Schema of the Manual BART

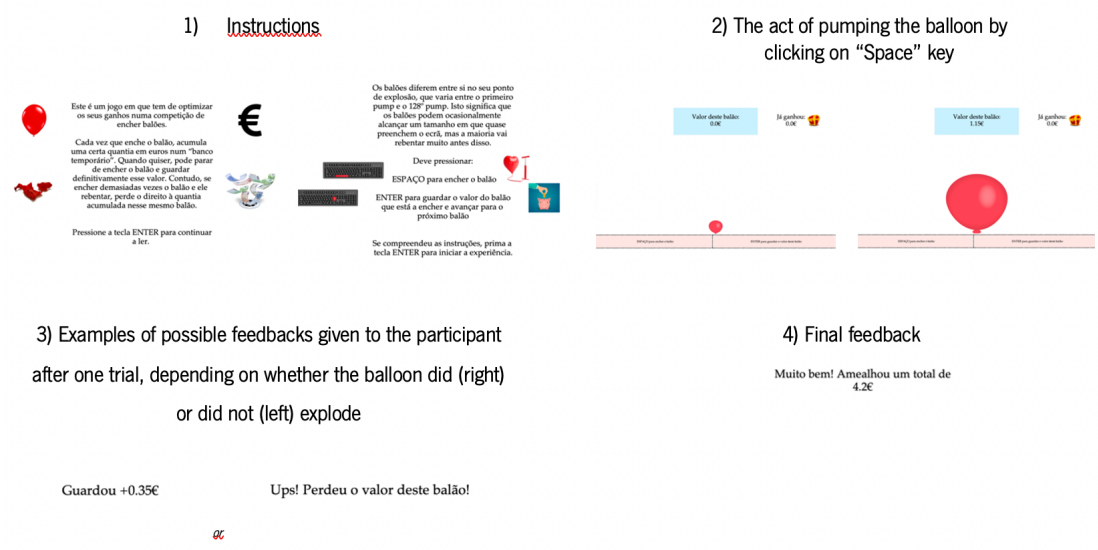
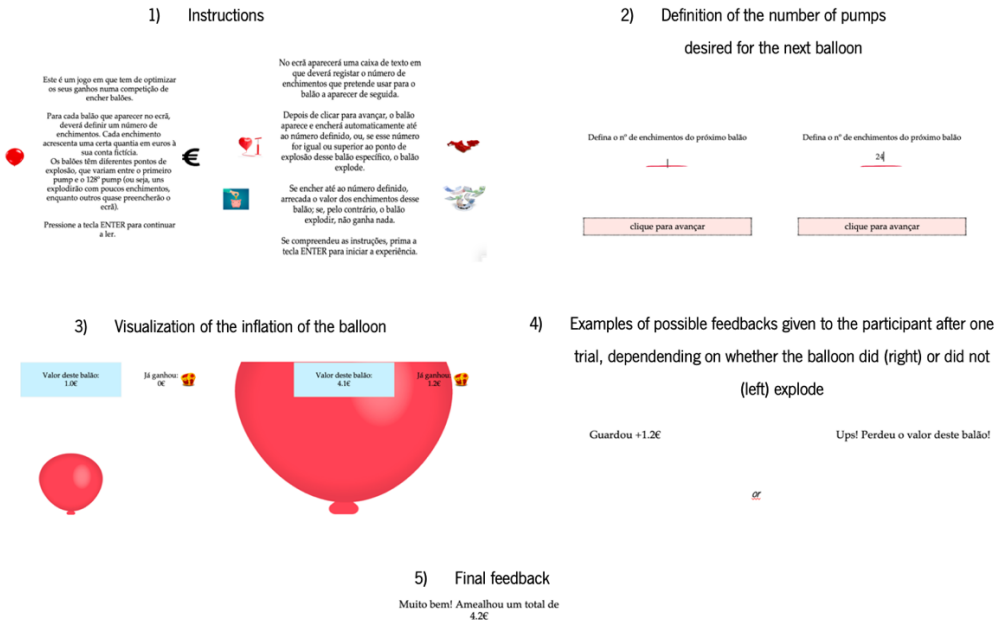


Figure 2

Schema of the Automatic BART



2.2. Self-report questionnaires

Considering the role of impulsivity in risky decision-making (Megías-Robles et al., 2022) and its association with dlPFC and vmPFC functioning, participants will be characterized with a widely used measure of impulsivity - Barratt Impulsivity Scale. Peculiarities in inhibitory control processes of individuals were assessed through the application of the BIS/BAS, which measures the reactivity of inhibition and activation systems. The SAM scale provided information about the emotional processing component of the decision. In similar logic, the PANAS was applied to assess changes in mood associated either with tDCS active stimulation or with the performance of the BART.

Behavioral Inhibition System and Behavioral Approach System Scale (BIS/BAS) The BIS/BAS has four scales: one for the Behavioural Inhibition System and three for the Behavioural Approach System (BAS-D, BAS-RR, BAS-FS). Internal consistencies of the subscales are satisfactory – Cronbach's alpha is .83 for the BIS subscale and .082 for the BAS composite.

Barratt's Impulsivity Scale (BIS-11) The BIS-11 is a 30-item self-report instrument with a four-point scale that appears to be the gold standard for measuring impulsivity. It has been used to explore the social consequences and behavioral correlates of individual differences in impulsivity (Carlson, Johnson, & Jacobs, 2010). In this investigation, Cronbach's alpha for the 2nd order factors is: .73 for the Attentional, .77 for Motor and .81 for Nonplanning.

Impulsive Behavior Scale – Portuguese Version (UPPS-P) UPPS-P is a 59-item self-report scale (Lynam et al., 2006) that assesses impulsivity as a multi-dimensional construct. It comprises the dimensions: Negative Urgency (i.e., the tendency to act rashly under extreme negative emotions); Lack of Premeditation (i.e., the tendency to act without thinking); Lack of Perseverance (i.e., the inability to remain focused on a task); Sensation Seeking (i.e., a tendency to seek out novel and thrilling experiences); Positive Urgency (i.e., the tendency to act rashly under extreme positive emotions; Whiteside & Lynam, 2001). In this investigation, Cronbach's alpha of UPPS' dimensions ranges from .84 to .94.

Self-Assessment Manikin Scale (SAM) SAM is a non-verbal picture-oriented questionnaire containing three single-item scales that directly measure: the valence of the response (from positive to negative), arousal (from high to low), and perceptions of dominance/control (from high to low) associated a person's affective reaction to a wide variety of stimuli. Cronbach's alpha ranges from .63 to .98.

Positive Affect and Negative Affect Scale (PANAS) The adapted version of PANAS for the Portuguese population is a scale formed of 10 items about positive affect plus 10 items about negative affect. To fill it, participants must rate the extent to which they experience each within a specified period on a five-point scale, with higher scores indicating higher PA or NA levels. Cronbach's alpha is .86 for the PA subscale and .89 for the NA one.

Three additional questionnaires will be applied. The Edinburgh Handedness Inventory (EHI) will be completed at the beginning of the first session to assess participants' laterality and bridge the need for homogeneity between participants in this feature. The Visual Analog Scale (VAS) will be completed pre- and post-stimulation to control for potential adverse effects of the stimulation. Moreover, a blinding questionnaire will be completed at the end of each session to assess the blinding procedure's efficacy.

Edinburgh Handedness Inventory (EHI) EHI measures hand preference for common manual tasks. To accomplish this, participants must rate 10 statements on the use of the right or left hand when performing a specific action. Scores range from -100 to +100 for left and right-handed, respectively. To be included, participants had to punctuate above 70.

Visual Analogue Scale (VAS) The VAS is a 10-item continuous scale that measures potential adverse effects of tDCS. Participants are screened for: tiredness, anxiety, sadness, restlessness, drowsiness, itch, headache, another pain, tingle, and metallic taste.

Blinding Questionnaire A blinding questionnaire asks participants to indicate if they think tDCS intervention was active, sham, or do not know the answer, and to mention how confident they feel about their response.

2.3.Go/No-Go

In order to do a manipulation check of the effect of the stimulation from tDCS participants also completed a control task at the end of the main task (BART) and before the post-stimulation questionnaires in both experimental sessions.

Inhibitory control refers to the capacity of interrupting a tendency action. A recent meta-analysis (Schroeder et al., 2020) that explored the effects of tDCS on inhibitory control demonstrated the existence of a small but significant moderating effect of tDCS on inhibitory control in single-session studies. Once we applied tDCS to increase the neural activity in dlPFC and in vmPFC, which, as we have seen, play

roles in impulsivity, application of a task that assesses inhibitory control seemed optimal for manipulation check purposes. The Go/No-Go paradigm is one of the most used (Wessel, 2018).

The Go/No-Go task we used here consisted of the sequential presentation of 120 trials represented by black tell screens with only a draw of a white square (30/120) or circumference (90/120) in it. Participants were instructed to click on the "Space" key if they saw a circle on the black screen and not to click on any key and just wait for the experience to move on to the next trial if they saw a square. Each trial was preceded by a cross fixation cross with variable durations and had a duration of 2000 milliseconds, except the ones in which the participant clicked on the "Space" key, which terminated that trial immediately and moved on to the next one.

The task was created and presented using E-Prime 3.0 software (Psychology Software Tools, Pittsburgh, PA).

3. Experimental design

Since the goal of this study is to analyze and compare the impact of anodal tDCS over vmPFC and dlPFC to sham stimulation, there will be two groups: one will receive anodal tDCS stimulation over vmPFC in one session and sham stimulation in another, and the other will receive anodal tDCS over dlPFC in one session and sham in the other.

Each participant will complete two sessions, separated by a minimum of two days washout period – in one session they will receive anodal stimulation, and, in the other, they will receive sham (intra-subject variable). Participants will differ by stimulation condition, i.e., by the fact that they will be stimulated on the vmPFC or the dlPFC (inter-subject variable). In the end, each participant will receive anodal stimulation in one session (either on vmPFC or on dlPFC) and sham stimulation in another.

4. Procedure

Participants were contacted by e-mail, requisites for participation were confirmed, study procedures were explained, and the experimental sessions were scheduled. Participants completed some of the self-report questionnaires (EHI, tDCS Feasibility, BIS/BAS, BIS-11) before the first session to accelerate the process. On the first session, participants signed the informed consent form, completed the rest of the self-report questionnaires, and were attributed to one of the two conditions, using Simple Random Sampling.

Direct electrical current was delivered using a Magstim Eldith DC Stimulator Plus (Neuroconn, DE) using two rubber electrodes enclosed in saline-soaked sponges. tDCS montage followed the 10-20 EEG system.
In the active session of dlPFC group, participants received left anodal/ right cathodal or right anodal/ left cathodal dlPFC tDCS (randomized). To stimulate the left dlPFC, the anode electrode was placed over F3 and the cathode over F4; to stimulate the right dlPFC, polarity was reversed. In the active session of the vmPFC stimulation condition, the anode was placed over Fpz and the cathode over Cz. In the sham session of both conditions, montage was the same as in the respective active condition.

A typical and safe stimulation protocol of 2mA with a 30ms ramp-in and ramp-out period was delivered. Stimulation began 5 minutes prior to the BART and lasted for the remaining 20 minutes for active sessions. For sham sessions, the current had an intensity of 2mA as well, but it was turned off after 30 seconds. Participants felt an initial itching but did not receive active current for the rest of the stimulation period. All subjects were blind to tDCS intervention.

While the BIS and the BIS/BAS instruments measure trait characteristics, and thus are stable and not prone to fluctuation as a function of one active session of tDCS, the SAM and the PANAS assess states, they are relatively volatile, and therefore susceptible to observable changes in their scores derived from stimulation. As such, these questionnaires were completed again at the end of each session. Also, in the pre- and post-stimulation assessments, participants were screened for potential adverse effects of tDCS using a continuous VAS. At the end of each session, the blinding procedure's efficacy was assessed with a blinding questionnaire.

5. Data analysis strategy

All statistical analyses were done using software JASP (0.16.03).

5.1. BART data

Risk-taking behavior was measured through the average number of adjusted pumps from the Manual BART (which considers only the trials in which the balloon did not explode) and the average number of pumps from the Automatic BART (which allows us to consider all trials without a bias towards lower numbers of pumps).

In order to scan for possible statistically significant (SS) differences in the BART metrics between the sham session and the active session in both groups, we first ran a mixed-design analysis of variance model, i.e., a mixed-design ANOVA model. In statistics, this model is used to test for differences between two or more independent groups whilst subjecting participants to repeated measures. In this case, the between-subjects variable is the stimulation site (vmPFC or dlPFC) and the within-subjects variable is the stimulation type (sham and active).

Then, to specifically evaluate the impact of modulating vmPFC and modulating dlPFC on the BART metrics, we needed to compare BART metrics from active tDCS with those resulting from sham tDCS, in a within-subject design, using paired samples t-tests (active vmPFC versus sham and active dlPFC versus sham). In cases where the normality of the distribution did not verify, we used a non-parametric alternative, the Wilcoxon test. The statistical analyses considered the Adjusted Mean Score from the Manual BART and the Average Number of Pumps from the Automatic BART.

5.2. Go/No-Go data

Analysis of the results of the Go/No-Go task was done through the computation of the D'Prime, a variable derived from signal detection theory and is thought to represent a person's ability to detect a target from among distracters, thus considering the proportion of targets to nontargets (Bodnar et al., 2007). A higher D' means a better performance at the task; in this case: a higher accuracy, with a reduced proportion of misses and false alarms.

To analyze the impact of stimulation by tDCS in inhibitory control, we ran a Pearson's correlation test for the D'Prime score between the sham session and the active session, for both stimulation groups (distributions' normality verified).

5.3. Self-report questionnaires data

The VAS informed about possible negative outcomes from tDCS (descriptive statistical data at Appendix A). For the Blinding Questionnaire, responses' frequency for "the guessing item", i.e., indicating whether they thought that session had been active, sham or if they did not know, was calculated, per group, and per session (Appendix B).

The BIS/BAS, BIS-11 and UPPS-P were applied once, and the SAM and PANAS were applied at the beginning and at the end of each session. Considering that the tDCS montages used are thought to

modulate impulsivity and inhibitory control processes, as well as to interfere with emotional and rational factors of decision-making, it seemed pertinent to investigate possible associations between participants' performance on both formats of the BART, in the active and/or sham sessions and their scores on the self-report questionnaires that aimed to access these precise constructs.

As such, Pearson or Spearman correlation tests (depending on whether normality of the distributions was verified or not, respectively) were run for the scores on the BIS/BAS, BIS-11, and UPPS-P and the four metrics obtained from the BART – MANUAL_Sham, AUTO_Sham, MANUAL_Active, AUTO_Active. Pearson's or Spearman's correlation tests were also run for the scores on the Sam and the PANAS in the sham and active sessions and participants' performance on the BART metrics.

Paired-samples t-tests, or the Wilcoxon test (when normality assumption did not verify), were run to detect SS differences between scores on the self-report questionnaires pre and post stimulation in both sessions.

Results

1. *Behavioral results: BART*

Descriptive statistics of the main metrics of the study, i.e., the metrics produced by the BART, in the active and in the sham session of both groups are presented in Table 1.

The mixed-design ANOVA model ran for the average number of pumps from the Automatic BART revealed no significant main effect of Stimulation Type ($F_{(1, 30)}$=0.319, p=0.576, η^2=0.003) and no SS interaction effect Stimulation Type*Stimulation Site ($F_{(1, 30)}$=0.222, p=0.641, η^2=0.002). A SS main effect of Stimulation Site was not found either ($F_{(1, 30)}$=0.103, p=0.751, η^2=0.003).

Although no SS results were found by the mixed-design ANOVA for the average number of pumps from the Automatic BART, the descriptive plot seems to suggest a tendency (Figure 1). While in the sham session the average number of pumps is evidently lower in the dlPFC stimulation group than in the vmPFC one, in the active session there is an accentuated decrease in the average number of pumps in the vmPFC stimulation group whereas in the dlPFC it remains almost the same.

In order to assess the SS of this difference in the average number of pumps between the sham and active sessions in the vmPFC group, a paired-samples t-test was applied. The results yielded no SS differences ($W_{(1, 16)}$=83.000, p=0.782, r_{rb}=0.085).

The mixed-design ANOVA ran on the adjusted mean score from the Manual BART revealed no SS main effect of Stimulation Type ($F_{(1, 30)}$=0.199, p=0.659, η^2<0.001) and no SS interaction effect Stimulation Type*Stimulation Site ($F_{(1, 30)}$=1.069, p=0.309, η^2=0.003). An SS main effect of Stimulation Site was not found either ($F_{(1, 30)}$=0.009, p=0.923, η^2<0.001).

Once again, despite the non-SS results obtained on the mixed-design ANOVA for the adjusted mean score from the Manual BART, a tendency is evidenced by the descriptive plot (Figure 2). The adjusted mean score is lower on the sham session for the vmPFC stimulation group than for the dlPFC stimulation group. On the other hand, on the active session, the adjusted mean score decreases for the dlPFC stimulation group whereas the one for the vmPFC stimulation group notably increases. Thus, in the active session, contrary to what is seen in the sham session, the adjusted mean score is higher for the vmPFC stimulation group than for the dlPFC one.

To evaluate the statistical significance of this change in the adjusted mean score for the active compared to the sham session, in the vmPFC stimulation group, a paired-samples t-test was further applied. No SS differences were found ($t_{(1, 16)}$=-1.108, p=0.284, Cohen's *d* = -0.269).

Similarly, a paired-samples t-test was run for the adjusted mean score in the active and in the sham session for the dlPFC stimulation group and, once more, no SS differences were encountered ($t_{(1, 14)}$=0.392, p=0.701, Cohen's *d* = 0.101).

Table 1

Descriptive Statistics of the Main Metrics of the BART, in the Sham and the Active Sessions of the dlPFC and the vmPFC Groups

	N	Mean	Std. Deviation	Shapiro-Wilk	P-value of Shapiro-Wilk
AUTO_Sham_dlPFC	15	42.033	12.167	0.978	0.954
AUTO_Sham_vmPFC	17	44.271	12.954	0.973	0.873
AUTO_Active_dlPFC	15	41.827	13.057	0.968	0.834
AUTO_Active_vmPFC	17	41.976	10.720	0.972	0.853
MANUAL_Sham_dlPFC	15	41.487	12.535	0.980	0.969
MANUAL_Sham_vmPFC	17	39.851	11.979	0.954	0.528
MANUAL_Active_dlPFC	15	40.788	12.828	0.961	0.713
MANUAL_Active_vmPFC	17	41.609	12.063	0.953	0.498

Figure 3

Descriptive plots of the Automatic BART

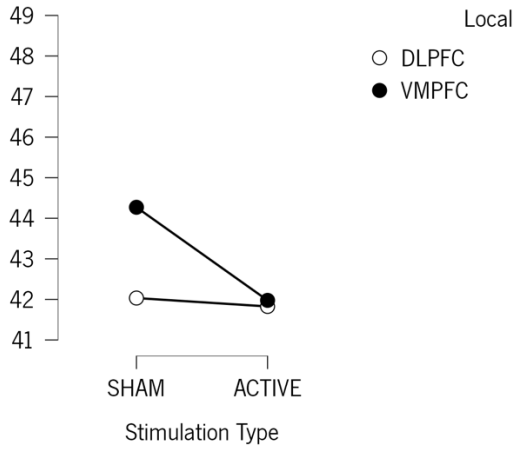
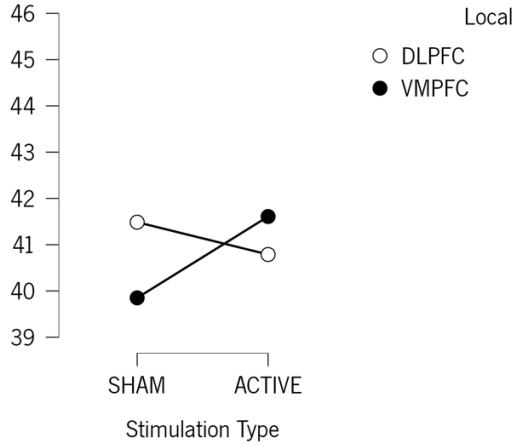


Figure 4

Descriptive plots of the Manual BART



2. Manipulation Check: Go/No-Go Task

tDCS effects on inhibitory control were analyzed through the D'Prime metric of the Go/No-Go task. The descriptive statistics of this metric can be found in Tables 2 and 3.

Normality test of Shapiro-Wilk ran for the dlPFC group did not indicate a deviation from normality (p=0.989). The paired-samples t-test ran for the D'Prime metric of the sham sessions and for the D'Prime metric of the active sessions, in the dlPFC stimulation group revealed no statistically significant differences *(*$t_{(1, 14)}$=-0.033, p=0.974*,* Cohen's *d* = 0.133*).* The test of normality of Shapiro-Wilk ran for the vmPFC

stimulation group did not suggest a deviation from normality (p=0.929). The paired-samples t-test ran for the D'Prime metric in this group yielded no SS results either ($t_{(1, 16)}$=1.139, p=0.276, Cohen's d = 0.276).

Although no SS differences were found between the D'Prime of the active and D'Prime of the sham session, in both groups, the correspondent descriptive plots seem to present a trend. While a tendency towards a decrease in the D'Prime metric from the sham to the active session in the vmPFC group can be observed (Figure 6), there does not seem to be a difference in the dlPFC group (Figure 5).

Table 2

Descriptive Statistics of the Metrics Extracted from the Go/No-Go Task, in the dlPFC Stimulation Group, in the Sham and in the Active Session

	Mean	Std. Deviation	Shapiro-Wilk	P-value of Shapiro-Wilk
Acc (NoGo)_Sham	0.831	0.155	0.909	0.132
ACC (Go)_Sham	0.996	0.007	0.608	< .001
Acc (NoGo corrected: 1-1/2*N = 0,983)_Sham	0.827	0.151	0.893	0.075
Omission errors (1 - Acc Go)_Sham	0.004	0.007	0.611	< .001
Omission errors (corrected 1/2*N = 0,005)_Sham	0.008	0.005	0.580	< .001
d'_Sham	3.625	0.792	0.940	0.386
Acc (NoGo)_Active	0.820	0.159	0.865	0.029
ACC (Go)_Active	0.997	0.009	0.398	< .001
Acc (NoGo corrected: 1-1/2*N = 0,983)_Active	0.823	0.161	0.848	0.016
Omission errors (1 - Acc Go)_Active	0.003	0.009	0.385	< .001
Omission errors (corrected 1/2*N = 0,005)_Active	0.007	0.008	0.370	< .001
d'_Active	3.629	0.839	0.915	0.159

Table 3

Descriptive Statistics of the Metrics Extracted from the Go/No-Go Task, in the vmPFC Stimulation Group, in the Sham and in the Active Session

	Mean	Std. Deviation	Shapiro-Wilk	P-value of Shapiro-Wilk
Acc (NoGo)_Sham	0.831	0.121	0.947	0.406
ACC (Go)_Sham	0.997	0.007	0.571	< .001
Acc (NoGo corrected: 1-1/2*N = 0,983)_Sham	0.829	0.118	0.935	0.264
Omission errors (1 - Acc Go)_Sham	0.003	0.007	0.569	< .001
Omission errors (corrected 1/2*N = 0,005)_Sham	0.007	0.005	0.543	< .001
d'_Sham	3.572	0.596	0.978	0.934

Descriptive Statistics of the Metrics Extracted from the Go/No-Go Task, in the vmPFC Stimulation Group, in the Sham and in the Active Session

	Mean	Std. Deviation	Shapiro-Wilk	P-value of Shapiro-Wilk
Acc (NoGo)_Active	0.794	0.157	0.932	0.236
ACC (Go)_Active	0.997	0.008	0.482	< .001
Acc (NoGo corrected: 1-1/2*N = 0,983)_Active	0.792	0.154	0.921	0.154
Omission errors (1 - Acc Go)_Active	0.003	0.007	0.486	< .001
Omission errors (corrected 1/2*N = 0,005)_Active	0.008	0.006	0.469	< .001
d'_Active	3.462	0.726	0.975	0.892

Figure 5

Descriptive Plot of D'Prime Metrics in the dlPFC Stimulation Group

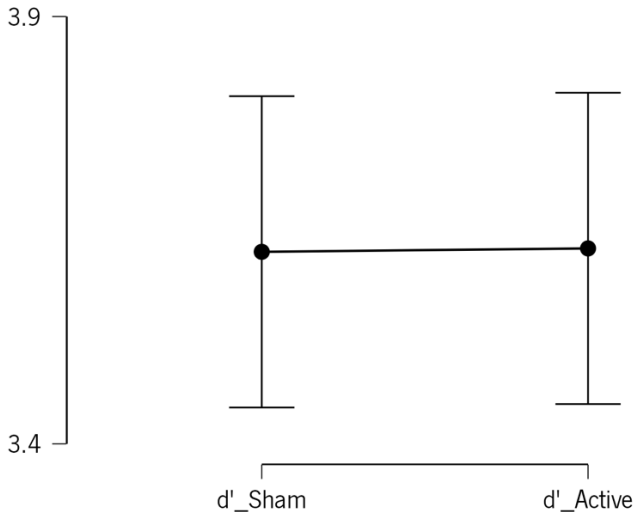
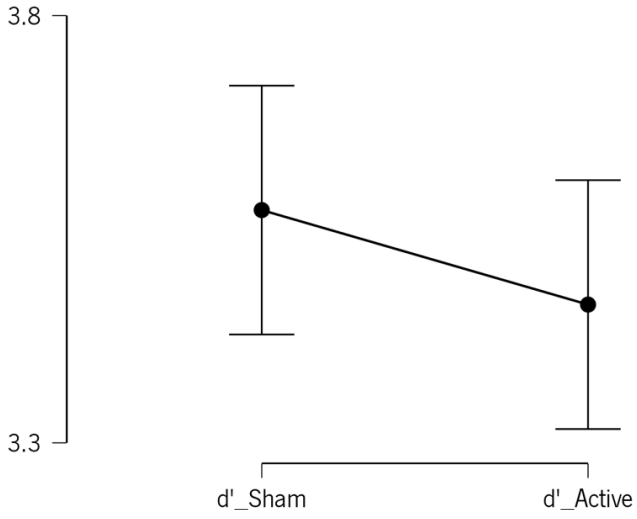


Figure 6

Descriptive Plot of D'Prime Metrics in the vmPFC Stimulation Group



3. Self-report questionnaires data

The p-values obtained from the correlation tests ran between the BIS_score, the BAS_score, the BIS-11 and the performance as measured by BART metrics in each session were not SS (all p-values>0.05; Table 7). The correlation tests ran for participant's score on each UPPS dimension and their performance as measured by metrics of the BART in both experimental sessions yielded no SS results (all p-values>0.05), except for Spearman's correlation test ran between the UPPS_PM and score on the Automatic BART in the sham session (p=0.018; ρ=-0.422).

The correlation tests ran for the SAM score in both sessions, pre and post stimulation, and participant's performance as measured by BART metrics revealed no SS results (all p-values>0.05; Table 7). No SS results were found by the correlation tests ran between PANAS_PA and PANAS_NA scores, pre and post stimulation, and participant's performance on both metrics of the BART, in the sham session, neither, in the active session, by the correlation analyses ran for the PANAS_PA and PANAS_NA pre stimulation scores and the BART metrics (all p-values>0.05; Table 7). Nonetheless, a positive correlation was found between score on the Manual BART and PANAS_PA post stimulation score (p=0.043; ρ=0.359).

In the dlPFC group, the paired-samples t-test ran for the SAM score pre and post sham stimulation yielded no SS differences ($t_{(1, 14)}$=-1.027, p=0.322, Cohen's *d* = -0.265) as well as the one ran for the SAM scores on the active session ($t_{(1, 14)}$=-1.843, p=0.087, Cohen's *d* = -0.476). The paired samples t-tests ran for the PANAS_PA ($t_{(1, 14)}$=0.848, p=0.411, Cohen's *d* = 0.219) and PANAS_NA ($t_{(1, 14)}$=0.863, p=0.403, Cohen's *d* = 0.223) scores pre and post sham stimulation revealed no SS differences either. Likewise, neither the paired-samples t-test ran for the PANAS_PA score ($t_{(1, 14)}$=0.244, p=0.811, Cohen's *d* = 0.063) neither the Wilcoxon one ran for the PANAS_NA score ($W_{(1, 14)}$=19.000, p=0.943, r_{rb}=0.056) pre and post active stimulation revealed SS differences.

In the vmPFC group, the paired-samples t-test ran for the SAM score pre and post sham stimulation yielded no SS differences ($t_{(1, 16)}$=-0.180, p=0.859, Cohen's *d* = -0.044) as well as the one ran for the SAM scores on the active session ($t_{(1, 16)}$=-0.832, p=0.418, Cohen's *d* = -0.202). The paired samples t-test ran for the PANAS_PA score ($t_{(1, 16)}$=3.403, p=0.004, Cohen's *d* = 0.825) and the Wilcoxon one ran for the PANAS_NA score ($W_{(1, 16)}$=45.000, p=0.082, r_{rb}=0.636) pre and post sham stimulation revealed no SS differences either. Likewise, neither the paired-samples t-test ran for the PANAS_PA score ($t_{(1, 16)}$=-

0.069, p=0.946, Cohen's *d* = -0.017) neither the one ran for the PANAS_NA score ($t_{(1, 16)}$=1.396, p=0.182, Cohen's *d* =0.339) pre and post active stimulation revealed SS differences.

Table 4

Correlations Table

		AUTO_Sham	MANUAL_Sham	AUTO_Active	MANUAL_Active
1. BIS/BAS	BIS	r=-0.074	r=0.191	r=0.023	r=-0.021
	BAS	r=-0.197	r=-0.032	r=-0.117	r=-0.195
2. BIS-11	Total Score	r=-0.012	r=0.055	r=0.172	r=0.041
3. UPPS-P	PM	ρ=-0.422*	ρ=-0.298	r=-0.148	ρ=-0.198
	OS	r=-0.325	r=-0.377	r=-0.095	r=-0.252
	NU	r=-0.189	r=-0.107	r=0.153	r=0.005
	PU	r=-0.174	r=-0.114	r=0.107	r=-0.075
	SS	r=-0.198	r=-0.346	r=-0.142	r=-0.231
3. SAM	Pre_Active	-	-	r=0.219	ρ=0.294
	Post_Active	-	-	ρ=-0.088	r=0.104
	Pre_Sham	r=-0.154	r=-0.05	-	-
	Post_Sham	r=0.073	r=0.035	-	-
4. PANAS_PA	Pre_Active	-	-	r=0.173	r=0.225
	Post_Active	-	-	r=0.061	r=0.127
	Pre_Sham	r=-0.180	r=-0.132	-	-
	Post_Sham	r=-0.157	r=-0.199	-	-
5. PANAS_NA	Pre_Active	-	-	ρ=0.071	ρ=0.210
	Post_Active	-	-	ρ=0.046	ρ=0.359*
	Pre_Sham	r=-0.139	r=0.130	-	-
	Post_Sham	ρ=-0.102	r=0.098	-	-

Note. *p-value<0.05

Discussion

This study aimed to analyze the role that neural activity in dlPFC and in vmPFC play in determining behavior in risky decision-making. Despite a series of works describing the way each of them may contribute differently to this process, it is agreed that their roles are not completely dissociable (Kahnt et al., 2011; Nejati et al., 2021). Thus, our hypothesis for this study considered this notion and transcribed in an expectation that anodal tDCS over both regions would result in a preference for low-risk decisions, traduced in lower scores on the average number of pumps in the Automatic BART and on the adjusted mean score in the Manual BART. We expected, then, to obtain significantly smaller scores on the BART metrics in the active session than in the sham session.

However, as we have seen, no statistically significant differences were found between the sham and the active sessions in both groups, on both BART metrics. This can be interpreted as not finding significantly smaller scores on the BART in the active compared to the sham session.

Nevertheless, the plot of the ANOVA for the Automatic BART score suggested an accentuated decrease from the sham to the active session in the vmPFC group. This can be interpreted as a tendency for participants stimulated on the vmPFC to score lower in the active than on the sham session, which is the precise effect of stimulation we initially predicted. On the other hand, the plot shows that for the dlPFC group the score remained approximately the same, suffering only a slight and almost imperceptible decrease.

The plot of the ANOVA for the Manual BART score revealed a tendency towards a decrease from the sham to the active session in the dlPFC group. Also, in this plot, the tendency for the vmPFC group inverted: lower scores in the sham session and evidently higher scores in the active session.

Considering the theoretical basis for our hypothesis is solid, we can interpret the results obtained for the dlPFC group in one of two ways: either stimulation of dlPFC by tDCS failed or the stimulation was effective yet not capable of significantly altering participant's behavior on the task in a consistent manner.

The results for the manipulation check ran through the application of the Go/No-Go task appear to corroborate the first possible explanation. Despite no statistically significant differences having been found between the D'Prime calculated for the sham and the one calculated for the active session in none of the groups, once again the plots present us a closer view of a difference. While, in the vmPFC group,

it seems that D'Prime is evidently higher in the sham session than in the active session, for the dlPFC group D'Prime does not present a visible difference from one session to another. As with what was observed on the BART metrics, the Go/No-Go metric also appears to present a tendency for a difference in the vmPFC group from the sham to the active session but not on the dlPFC group. This consistent contrast across tasks may suggest that, while stimulation over vmPFC might have been successful, stimulation over dlPFC probably was not.

Also, considering that, as we know, tDCS presents the disadvantage of having poor spatial resolution, as the montage is usually based on a cortical region (Datta et al., 2009), it is not a bold move to say that there is a possibility that tDCS current did not reach dlPFC and as such dlPFC stimulation may not have been successful.

A possible explanation for the absence of significant results also for the vmPFC group may be that the sample size was not big enough to allow the expression of statistically significant differences between the sham and active sessions. We initially calculated a minimum sample size of 68 participants in order to obtain statistically significant effects. This number contrasts with the 32 participants that we were able to recruit.

Considering an estimate of Cohen's *d* of 0.5 (medium effect size) and an estimated power of 0.8, we determined a minimum sample size of 34 participants, between 18 and 25 years old, for each group (n=68), in order to be able to detect significant differences between groups.

The second possible explanation attributable to the results obtained for the dlPFC group can underlie two possible ideas: 1) once more, the sample size was insufficient (an estimated Cohen's d of 0.5 and an estimated power of 0.8 had determined a minimum sample size of 68) to allow for SS effects of tDCS over dlPFC to be expressed on BART metrics, and 2) the choice to do an anodal bilateral stimulation as a unique tDCS protocol was not probably the best one.

dlPFC was chosen as modulation target due to consistent evidence that noninvasive brain stimulation targeting dlPFC exerts an influence on behavior in risky decision-making (Brunelin et al., 2021; Brunyé et al., 2021). A great deal of recent studies investigating how tDCS over dlPFC modulates risk-taking point to an effect of biasing individuals towards more conservative choices when confronted with the need to make decisions (Khaleghi et al., 2020).

However, if there is an agreement in that dlPFC plays a critical role in the modulation of risk-taking, the direction of this influence as well as the parameters of the stimulation that are associated with a decrease in risk-taking behavior has not yet been established (e.g., Brunelin et al., 2021; De La Torre et al., 2022; Mattavelli et al., 2022; Xiong et al., 2022). Due to this inconsistency, an investigation paradigm including more experimental conditions, for different protocols of stimulation for the dlPFC, would be of interest here, as it would help to discriminate the ones that are more effective in modulating risk-taking on the BART.

There is an agreement in that dlPFC plays a crucial role in top-down control and goal-directed behavior (Kelley et al., 2019; Tang et al., 2022). As such, anode stimulation of these region would improve inhibitory control and, by corollary, reduce impulsivity (Gilmore et al., 2018). Considering the reported link between higher risk-taking behavior and high levels of impulsivity (Megías-Robles et al., 2022) and that our goal was to modulate risk-taking behavior, the Go/No-Go task, which evaluates inhibitory control, would be a reasonable option for manipulation check.

Notwithstanding, the path that links the modulation of activity in the dlPFC with changes in behavior in a Go/No-Go paradigm, may not be that direct. Thus, it is possible that the construct tackled by stimulation over dlPFC may not be exactly the same that underlies performance on a Go/No-Go task. On this matter, a meta-analysis from Schroeder et al. (2020) about the effects of tDCS on inhibitory control produced a relevant finding here: the effect size of tDCS in the Stop-Signal Task (g=0.32) was significantly larger than the one in the Go/No-Go (g=0.10). As such, a Stop-Signal paradigm would be a potential option.

It is also worth noting that decision-making can be influenced by various internal and external individual variables (e.g., Doya, 2008), such as impulsivity levels of the participants. However, once almost none statistically significant correlations were found between the scores on the self-report questionnaires and the scores on the BART, no conclusions can be drawn about the possible influence of stable individual variables on participant's performance nor susceptibility to have its behavior altered by a single tDCS session.

1. *Future directions*

Considering all the above, we consider that a replication of this experimental design with a bigger sample would be relevant to further explore the trends observed for the vmPFC stimulation group. Future

investigations trying to accomplish what we tried to accomplish here could add experimental condition with different protocols for the stimulation of the dlPFC (unilateral dlPFC, bilateral, right cathode/left anode and left cathode/right anode); this way, the ideal protocol for modulating risk-taking behavior could be discriminated. It would also be also worth adding neuromodulation techniques with a higher spatial precision, such as High-Definition tDCS, in order to avoid shunting effects.

2. *Conclusion*

The results obtained did not allow us to confirm our hypotheses, but there are some relevant conclusions to be drawn.

Attending to the sample size setback we had, vmPFC remains, in our view, a good candidate for a region to modulate using tDCS.

Regarding dlPFC-related results, they sure are congruent with the previous literature insofar as they added to the existent notion that there is still no consistent evidence about the precise way in which this region's activity affects the process of decision-making under risk.

First, it is imperative that an investigation that compiles different stimulation protocols into different experimental conditions is developed in order to clarify dlPFC's role on these processes, as well as the optimal stimulation parameters to use when aiming to modulate them. Exploring more spatially precise neuromodulation techniques should be considered. Only afterwards can we know how therapies and treatments for increased impulsivity or deficits in inhibitory control should be designed.

Scientific investigation is increasingly valuing basic studies that focus on unraveling and modulating networks underlying circumscribed cognitive processes, yielding a huge potential for designing specific therapies and improving assessment.

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Appendix A

Table A1

Means and Standard Deviations of the VAS items, per session, in the dlPFC stimulation group

Session	Sham				Active			
	Pre		Post		Pre		Post	
	M	SD	M	SD	M	SD	M	SD
Tiredness	4,267	2,154	3,667	2,059	3,667	2,35	2,6	1,999
Anxiety	2,333	2,257	1,533	1,959	2,133	2,2	1,733	1,831
Sadness	1,533	1,552	0,867	1,187	1,933	2,344	1,2	1,612
Restlessness	2,2	2,274	1,6	2,098	2,067	1,751	1,733	2,187
Drowsiness	3,467	2,8	4	2,673	3,533	2,446	2,4	2,501
Itch	0,4	0,828	1	1,254	0,533	0,99	2,533	2,475
Headache	0,6	1,404	0,933	1,668	0,667	1,589	0,8	1,146
Another Pain	0,533	1,356	0,467	1,06	0,467	1,246	0,333	0,816
Tingle	0,467	1,302	0,533	1,125	0,267	0,799	1,6	1,805
Metallic Taste	0	0	0	0	0,067	0,258	0	0

Table A2

Means and Standard Deviations of the VAS items, per session, in the vmPFC stimulation group

Session	Sham				Active			
	Pre		Post		Pre		Post	
	M	SD	M	SD	M	SD	M	SD
Tiredness	5,235	2,796	4,529	2,478	4,353	103,882	4,412	152,118
Anxiety	1,882	1,833	2,118	2,421	2,353	51,882	0,941	32,941
Sadness	0,765	0,97	0,176	0,529	0,706	13,529	0,118	1,765
Restlessness	1,118	1,576	1,941	2,561	2,706	109,529	1,706	85,529
Drowsiness	4,765	2,884	3,941	2,926	4,059	168,941	4,235	211,059
Itch	0,353	0,862	1,176	2,007	0,471	18,235	2,353	151,882
Headache	0,412	1,064	0,647	1,115	1,059	30,941	1,412	46,118
Another Pain	1,118	1,996	0,706	1,532	0,706	21,529	0,529	14,235
Tingle	0	0	0,412	0,87	0,235	15,059	2,353	149,882
Metallic Taste	0,059	0,243	0	0	0	0	0,176	8,471

Appendix B

Frequencies of "Sham", "Active" and "I don't know" answers, per stimulation group, and per session

Stimulation Group	dlPFC		vmPFC	
	Sham	Active	Sham	Active
"Sham" answers	0.2	0.133	0.294	0.294
"Active" answers	0.8	0.866	0.588	0.647
"I don't know" answers	0	0	0.118	0.059

Universidade do Minho

Conselho de Ética

Comissão de Ética para a Investigação em Ciências Sociais e Humanas

Identificação do documento: CEICSH 119/2021

Relatores: Emanuel Pedro Viana Barbas Albuquerque e Marlene Alexandra Veloso Matos

Título do projeto: *The effects of dlPFC versus vmPFC tDCS stimulation on a risky decision-making task*

Equipa de Investigação: Pedro Miguel Silva Moreira, Centro de Investigação em Psicologia (CIPsi), Escola de Psicologia, Universidade do Minho; Sandra da Conceição Ribeiro de Carvalho, Escola de Psicologia, Universidade do Minho

PARECER

A Comissão de Ética para a Investigação em Ciências Sociais e Humanas (CEICSH) analisou o processo relativo ao projeto de investigação acima identificado, intitulado *The effects of dlPFC versus vmPFC tDCS stimulation on a risky decision-making task.*

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, a Comissão de Ética para a Investigação em Ciências Sociais e Humanas (CEICSH) nada tem a opor à realização do projeto nos termos apresentados no Formulário de Identificação e Caracterização do Projeto, que se anexa, emitindo o seu parecer favorável, que foi aprovado por unanimidade pelos seus membros.

Braga, 11 de janeiro de 2022.

O Presidente da CEICSH

(Acílio Estanqueiro Rocha)

Anexo: Formulário de identificação e caracterização do projeto

Comissão de Ética para a Investigação em Ciências Sociais e Humanas (CEICSH)

Universidade do Minho

Formulário de identificação e caracterização do projeto

Identificação do projeto

Título do projeto	The effects of dlPFC versus vmPFC tDCS stimulation on a risky decision-making task		
Data prevista de início	**November, 2021**	**Data prevista fim**	**July, 2021**

Investigador principal e filiação	Pedro Miguel Silva Moreira - Research Centre on Psychology (CIPsi), School of Psychology, University of Minho
Orientador(es) e filiação	Pedro Miguel Silva Moreira - School of Psychology, University of Minho Sandra da Conceição Ribeiro de Carvalho - School of Psychology, University of Minho

Nota: No caso de projetos de mestrado ou doutoramento deve ser indicado o estudante como investigador principal e o nome do mestrado ou doutoramento

Instituição proponente	Research Centre on Psychology (CIPsi), School of Psychology, University of Minho
Instituição(ões) onde se realiza a investigação	Research Centre on Psychology (CIPsi), School of Psychology, University of Minho

Entidades financiadoras	Not applicable

Questões relativas ao envolvimento de investigadores exteriores		
Estão envolvidos no projeto, colegas de outra (s) Escola(s)/Instituição(ões)?	S	N
Se sim, este pedido de parecer cobre o seu envolvimento?	S	N

Qualificação dos investigadores

The research team will be comprised by the main researcher (Pedro Silva Moreira, PhD), Sandra Carvalho (PhD) and Filipa Dantas (student of the 5th year of the Integrated Master's Degree in Psychology at the University of Minho). The research team has relevant expertise in the domains of neuroscience (Pedro Silva Moreira, Filipa Dantas and

Sandra Carvalho) and decision-making (Pedro Silva Moreira). The team (Sandra Carvalho) has also expertise on the use of neuromodulation and, more specifically, transcranial direct current stimulation (tDCS).

Caracterização do projeto e questões de carácter ético relativas à sua execução

Introdução justificativa do projeto e sumário dos seus objetivos

Decision-making is a complex behavior that comprises multiple component processes. Risky decision-making has been gaining particular attention from investigation, as daily we are confronted with the need to make decisions under some degree of risk and knowing what makes us prone to risk may be useful in predicting our decisions (Ahlbrecht & Weber, 1997).
It is already clear that emotions exert a great influence on cognitive processes, as individuals make decisions in a regular and predictable manner when driven by emotions (Keltner & Lerner, 2010). Given that processes involved in risky decision-making are part of the functioning and dysfunctioning of the individual, it is pertinent to explore the capability of modulating them.
Numerous findings clearly point to an involvement of vmPFC and dlPFC in decision-making processes, which, beyond assuming an undeniable importance in people's daily life, can be particularly critical for pathological risk-taking behavior. It would be relevant to comprehend in what way it is possible to interfere in the decision-making behavior style of these individuals. A useful strategy would be to apply tDCS particularly over vmPFC and dlPFC.
The main objective of the present study is to evaluate the effects of anodal tDCS over vmPFC and over dlPFC, as compared to sham, on the modulation of risky decision-making during a Balloon Analogue Risk Task (BART) in healthy volunteers.
Considering that both regions are already well documented to play a role in decision-making processes, and specifically in risky decision-making, we hypothesize that both individuals receiving anodal tDCS over vmPFC and those receiving over dlPFC will reveal a preference for low-risk decisions - i.e. they will opt significantly more frequently for a smaller number of pumps per trial -, comparatively to sham control.

Participantes

The target population of this study are healthy young adults (aged between 18 and 25 years), from both genders, portuguese, students at Minho University. Considering an estimate of Cohen's d of 0.5 (medium effect size) and an estimated power of 0.8, we will recruit a sample of 34 participants for each group (n=68).

Recrutamento e triagem

Recruitment of participants will take place across the first two months of the semester and will be carried out, by the main responsible researcher, from the body of students at the University of Minho through their voluntary enrolment in the study, post divulgation of it in the credit platform and by the institutional email.
Exclusion criteria in the study is the presence of a diagnosis of any disease, mental or physical, that could interfere with the aim of generalizing the effects encountered to the healthy population (healthy participants) and a score below 80 on Edinburgh Handedness Inventory.
All procedures will be approved by the local ethics committee, Ethics Committee for Research in Human and Social Sciences (CEICSH), at Minho University, and will be performed accordingly with the Declaration of Helsinki (1964).
Participants obtained through volunteering entry will be contacted by telephone or e-mail, requisites for participation in the study will be confirmed and the first experimental session will be scheduled. On the day of the first session, each participant will be randomly attributed to one of the two conditions, using a random number generator (available at https://www.randomizer.org/).

Compensação e custos

As compensation for participating in the study, an amount of credits (to be determined) will be attributed to the participants who were recruited through the credit platform SONA (Psychology students at Minho University). They will be able to distribute these credits for the CUs they are carrying out to improve their classifications. Participation in this study involves no costs to participants.

Procedimento

Since the goal of this study is to analyse and compare the impact of anodal tDCS over vmPFC and over dlPFC to sham stimulation, there will be needed two conditions and, subsequently, groups: one will receive anodal tDCS stimulation over vmPFC in one session and sham stimulation in another, the other will receive anodal tDCS stimulation over dlPFC in one session and sham stimulation in the other.
Each participant will complete two sessions of approximately 60 minutes each, differing by stimulation condition (vmPFC anodal stimulation/dlPFC anodal stimulation and sham; randomized), separated by a minimum of two days washout period. All procedures will take place in a laboratory room at the Psychology School of Minho University, during the first three months of the next academic year, and will be conducted
by the main responsible researcher.
Participants obtained through volunteering entry will be contacted by telephone or e-mail, requisites for participation in the study will be confirmed, study procedures will be explained, and the first experimental session will be scheduled. On the day of the first session, each participant will fill out the informed consent form before initiating its participation in the study. Then, all of the self-report control questionnaires will be administered in a private waiting room. The participants will, then, be randomly attributed to one of the two conditions, using a random number generator (available at https://www.randomizer.org/). The procedure will again be explained to the participant before initiating the tDCS montage.
Direct electrical current will be delivered using a Magstim Eldith DC Stimulator Plus (Neuroconn, DE) using two rubber electrodes enclosed in saline-soaked sponges. tDCS montage will follow the 10-20 EEG system.
In the active session of vmPFC stimulation condition, participants will receive either left anodal/ right cathodal or right anodal/ left cathodal vmPFC tDCS (randomized). To stimulate the left vmPFC, the anode electrode will be placed over F7 and the cathode over F8; to stimulate the right vmPFC, polarity will be reversed: the anode will be placed over F8 and the cathode over F7. In the active session of dlPFC stimulation condition, the procedure will be the same, but the electrodes will be placed over F3 and over F4. In the sham session of both conditions, the montage will be the same as in the respective active condition.
A typical and safe stimulation protocol of 2mA with a 30ms ramp-in and ramp-out period will be delivered to participants in experimental sessions. Stimulation will begin 5 minutes prior to the Balloon Analogue Risk Task and last for the remaining 20 minutes of the experiment for active sessions (vmPFC stimulation or dlPFC stimulation). For the sham session, the current will have an intensity of 2mA as well, but it will be turned off after 30 seconds. Participants will feel the initial itching sensation associated with tDCS, but will receive no active current for the rest of the stimulation period.
Inhibitory control processes will be assessed through the application of the BIS/BAS, that measures reactivity of inhibition and activation systems. It is expected that individuals that score higher on the BIS will reveal some resistance to the tDCS stimulation, since these regions are crucial for top-down control. The SAM scale will be used to provide information regarding the emotional processing component of the decision (e.g. knowing if the subject was aroused, and what valence was associated with its emotional response). It is expected that individuals that have received active tDCS will show altered scores in SAM' s dimensions, as the task implicates the need to make decisions in a context of risk and these regions are known to integrate emotion and cognition (Nejati et al., 2021). In a similar logic, the PANAS will be applied to assess changes in mood associated either with tDCS active stimulation or with performance of the BART. While the BIS and the BIS/BAS are instruments that measure trait characteristics, and thus are stable and not prone to fluctuation as a function of one active session of tDCS, the SAM and the PANAS assess states, they are relatively volatile, and therefore susceptible to observable changes in their scores as a result from stimulation. As such, these questionnaires will be completed again at the end of each session, to perceive possible changes in their scores as a result of effects from tDCS. In pre- and post-stimulation assessments, participants will be screened about discomfort, fatigue, pain, itching, humor, tingling, burning, headache and sleepiness (among others) using a continuous Visual Analog Scale (VAS). At the end of each session, we will assess the blinding procedure's efficacy with a blinding questionnaire.
All participants will be blinded to experimental condition and to tDCS intervention, to avoid bias effects in performance on the BART derived from knowing they are being stimulated in some brain region. At the end of

the second session, participants will be debriefed about the experimental condition they were attributed to and the order of tDCS interventions, along with the explanation of the reason for the use of that blinding procedure (already above mentioned). No video nor audio recordings will be made of participants' sessions.

Benefícios, Riscos e Desconforto

An amount of credits (to be determined) is predicted to be attributed to the participants who are Psychology students at Minho University and have enrolled in the study through the credit platform SONA.
This study does not anticipate more than minimal risk for those who participate in it. Stimulation itself is a completely safe procedure, which does not cause any physical or mental damage in the long term, as it will be used a safe and typical stimulation protocol of 2mA with a 30ms ramp-in and ramp-out period. However, some discomfort and/or temporary adverse effects (itching, tingling, headache, among others) may be experienced and this information will be provided to the participant in the informed consent, as well as the possibility to express any discomfort or symptoms they feel during and after the session so that measures can be taken to minimize them. In addition, potential adverse effects of stimulation will be assessed in each session through administration of the Visual Analogue Scale (VAS).

Confidencialidade

To ensure participant's privacy and confidentiality of the data, a code will be assigned to each participant and to his/her respective questionnaires/data records on the moment of their attribution to a study condition. Likewise, after data collection, all records will be encoded, safeguarding the identity of the participants, and kept in a locked cabinet in the research laboratory room, at Minho University. Thus, the only means to associate a participant to his/her data is through the respective code. Only the researchers responsible for the project will have access to the data. Data collected from the participants will only be kept until the end of this study (after completion of it - at the end of the next academic year -, they will be deleted) and they will be used solely for academic/scientific purposes.

Conflito de interesses

No conflict of interests to report.

Consentimento Informado

A investigação envolve apenas voluntários saudáveis?	S	N
A investigação envolve grupos vulneráveis: crianças, menores, idosos ou outras pessoas com incapacidade temporária ou permanente?	S	N
O pedido de parecer inclui a declaração de consentimento informado, livre e esclarecido?	S	N

Aqui tem de escolher o formato de consentimento informado

[x] Consentimento informado, livre e esclarecido para participação em investigação - de acordo com a Declaração de Helsínquia e a Convenção de Oviedo
[ ] Consentimento informado não assinado - E.g. formulário para questionários preenchidos online. Deverá adicionar a informação incluída e o modo de os participantes concordarem em participar
[ ] Consentimento informado alterado - Um formulário de consentimento informado que omite informação requerida. E.g., se não indica o objetivo do estudo para evitar o viés na resposta dos participantes. Deve explicar o racional no procedimento e os processos de *debriefing*
[ ] Isenção de consentimento – quando não é obtido consentimento informado – esta opção pode ser apropriada para utilização de dados já disponíveis. Justifique

Anexe o formulário de consentimento informado e outro material informativo relevante quando adequado, ou justifique a isenção de consentimento

Assinatura do Investigador Responsável

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Documentação a anexar

i. Cópia dos questionários ou formulários de recolha de dados a utilizar, quando aplicável;
ii. Modelo de consentimento informado, de acordo com as declarações, diretivas e regulamentos internacionais, europeus e nacionais, se aplicável, devidamente ajustado linguística e culturalmente às populações a que é dirigido;
iii. Declaração do(s) responsável(eis) pelo projeto, explicitando que os dados obtidos são confidenciais e usados apenas no âmbito do estudo em questão;
iv. Modelo de declaração de compromisso para outros investigadores ou colaboradores na investigação, se aplicável, destinada a documentar o seu envolvimento nas garantias de confidencialidade dadas pelo(s) responsável(eis) do projeto no âmbito do processo apresentado;
v. Informação a que se refere o número 3 do artigo 4.º das normas orientadoras da CEICSH, sobre o enquadramento, apoio e viabilidade do projeto, facultada pelo responsável da unidade/subunidade orgânica e/ou serviço onde se vai desenvolver o projeto e/ou onde serão recolhidos os dados;
vi. Declaração do(s) orientador(es) científico(s) do estudo, se aplicável, de acordo com o estabelecido no número 4 do artigo 4.º das normas orientadoras da CEICSH;
vii. Cópia de notificações a autoridades nacionais (e.g., Direção-Geral da Educação, no caso dos inquéritos em ambiente escolar) europeias ou internacionais competentes, se aplicável, juntamente com o parecer/autorização das mesmas, se emitido;
viii. Curriculum vitae resumido do(s) responsável(eis) pelo projeto e dos restantes membros da equipa de investigação.

Deverá ser seguido o Regulamento Geral de Proteção de Dados (RGPD), com entrada em vigor em 25 de Maio de 2018, - REGULAMENTO (UE) 2016/679 DO PARLAMENTO EUROPEU E DO CONSELHO, de 27 de abril de 2016, relativo à proteção das pessoas singulares no que diz respeito ao tratamento de dados pessoais e à livre circulação desses dados, que revoga a Diretiva 95/46/CE (Regulamento Geral sobre a Proteção de Dados).