Transcranial Direct Current Stimulation Decreases P3 Amplitude and Inherent Delta Activity During a Waiting Impulsivity Paradigm

Augusto J. Mendes
University of Minho
Santiago Galdo-Álvarez
Universidade de Santiago de Compostela
Alberto Lema
University of Minho
Sandra Carvalho
University of Minho
Jorge Leite (jorgel@upt.pt)
University Portucalense, Portucalense Institute for Human Development – INPP

Article

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Abstract

Background

One of the main features of addictive behaviors is the inability to wait for an action, that is, the waiting impulsivity. It has been suggested that potential therapeutic tools for addiction, such as transcranial Direct Current Stimulation (tDCS), might focus on this inability. Nonetheless, whereas there is consensus about the role of prefrontal cortex on impulsivity behavior, the effects of tDCS in waiting impulsivity and underlying electrophysiological (EEG) markers are still not clear.

Objective

The study aimed the neuromodulation of right inferior frontal gyrus during a task designed to elicit premature responses, while EEG markers important in reward anticipation (i.e., cue and target-P3 and underlying delta/theta activity) were studied.

Methods

Forty healthy subjects participated in two experimental sessions, where they received active and sham tDCS while performing a premature responding task and the EEG was recorded. At next, participants performed two control tasks to evaluate transfer effects for delay discounting and motor inhibition abilities.

Results

Active tDCS decreased amplitude in cue-P3, target-P3, and delta activity during target-P3. On the other hand, active tDCS increased the discounting of future rewards in small values in comparison with sham, while no tDCS effects were found in motor inhibition.

Conclusion

These findings suggest tDCS-induced modulation of the P3 component and underlying oscillatory activity during waiting impulsivity. Moreover, these changes were associated with differences in the discounting of future rewards. Thus, the current study suggests the usefulness of tDCS in modulating impulsive processes and the relationship between P3, the inherent delta activity, and reward processing.

Introduction

tDCS over the prefrontal areas has shown promising therapeutic effects in addiction [1], craving [2], and reward responsiveness [3]. Previous studies applied tDCS over the cortical regions associated with impulsive processes, such as the right inferior frontal gyrus (rIFG) related with response inhibition [4] and the dorsolateral prefrontal cortex (DLPFC) to enhance delay discounting [5]. Although both processes are framed within impulsivity (i.e., stopping vs waiting), they diverge in their cognitive procedures and neuronal networks. Moreover, waiting impulsivity relies on top-down regulation of the prefrontal cortex with subcortical structures such as the ventral striatum, amygdala, and hippocampus [6]. On the other hand, stopping requires interactions between the right inferior frontal gyrus (rIFG) and the pre-supplementary motor area (SMA), with the dorsal striatum and the subthalamic nucleus (STN) [7].

Nonetheless, waiting impulsivity can be divided into two main dimensions, namely the impulsive action measured by premature responses and impulsive choice assessed in delay discounting tasks. This distinction highlights the role of impulsive action as a 'cold' process with less influence of affective processing, whilst impulsive choice is thought to be a 'hot' process relying on reward processing (Reynolds et al., 2006). Premature responses have been associated with proactive stopping evaluated in Go/No-Go (GNG) paradigms, given that inhibitory processes may be prior to response selection [8]. On the other hand, reactive inhibition paradigms, such as the Stop Signal Reaction Time task (SSRTT), have not been associated to premature responses, given that the inhibitory processes act after response has started [9].

Furthermore, attentional and inhibitory processes have been studied using event-related potentials (ERPs), mainly through the P3 component. P3 is characterized by a peak between 250 and 600 ms after a task-relevant stimulus at parietal sites [10]. In the context of anticipating rewards/punishments, the anticipatory or cue-P3 is elicited after the cue onset and it has been interpreted as the motivated attention to a subsequent task-relevant stimulus (Pfabigan et al., 2014). On the other hand, the consummatory or target-P3 is the actual response towards the motivational stimulus predicted by the cue [12]. These components have been tested in the Monetary Incentive Delay (MID) task, in which participants are rewarded or punished accordingly to the response time towards a cued target stimulus [12]. The cue indicates the type of trial (i.e., win or loss), followed with a variable delay by a target, and followed with the feedback about its performance. Thus, the cue-P3 is elicited following the cue-onset that predicts the oncoming of the target and the type of feedback (i.e., reward/punishment), whilst the target-P3 is elicited following the onset of a stimulus implied in the subsequent reward or punishment. The target-P3 amplitude is increased after cues that predict gains and losses [12], whilst the effects of the valence of reward are still not clear in the cue-P3 [13–15].

Assuming that ERPs are representations of specific brain activations in the time domain, they co-occur with the synchronization of oscillatory activity in the time-frequency domain, i.e., the event-related oscillations (ERO) [16]. Regarding the EROs, the P3 elicited during oddball paradigm is accompanied by a transient increase in delta (0–4 Hz) and theta (4–7 Hz) activity at the same latency and scalp distribution of P3 [17]. These findings suggest that both oscillatory frequencies might represent the mechanism of

generation of the P3 component [18]. Also, an increase in parietal delta activity after a reward-laden stimulus has been shown, suggesting that the association between P3 and delta might occur also during the anticipation of rewards [19]. Nevertheless, this concurrent activity between both EEG markers in parietal regions was not tested yet in MID tasks or other reward processing paradigm.

In a recent meta-analysis about the modulatory effects of tDCS in the P3 component during cognitive tasks we were able to show an increase in the parietal P3 in attentional and working memory tasks after frontal tDCS [20]. On the other hand, no tDCS effects were found in the P3 elicited during response inhibition, given some studies demonstrate an increase in P3 amplitude [21], whilst others a decrease [22,23].

Even though previous tDCS studies have targeted addictive/impulsive behavior, the available knowledge about neural correlates of impulsivity highlights the importance of understanding how tDCS impacts not only cognition, but also the underlying neuronal activity. For that, a recent approach tested the adjustment of tDCS stimulation during the performance of a cognitive task through the data collected concurrently from an EEG [24]. This methodology aimed the enhancement of tDCS effects, however also emphasized the importance of ascertaining the neuro-markers of cognition and how tDCS might impact them.

In this sense, the aim of the current study was to assess the effects of tDCS over rIFG on (i) premature responses, and in the (ii) anticipatory and consummatory ERPs and EROs of waiting impulsivity. For this purpose, we developed a computerized task to test the anticipatory and consummatory neural response towards a salient-stimulus involved in reward-seeking tailored to each participant performance. We hypothesized that active tDCS would lead to a reduction in the number of premature responses and a potential transfer effect for delay discounting and inhibitory control. Likewise, the behavioral modulation is expected to be combined with an increase of P3 amplitude and consequently delta/theta activity.

Results

Behavioral analysis

Cued Premature Response Task

No significant effects of tDCS were observed in premature responses ($t(35) = -0.79$, $p = 0.438$), monetary amount earned ($t(37) = 0.78$, $p = 0.438$), and release time ($t(37) = -0.87$, $p = 0.438$) (Table 1). However, there was a significant correlation between the number of premature responses and the average release time of the baseline block ($R = -0.25$, $p = 0.028$), suggesting that the reward/punishment system was associated with the posterior number of premature responses (Figure 1).

<INSERT HERE FIGURE 1>

Stop Signal Reaction Time Task

The t-tests did not reveal any significant effect, namely in Go trials accuracy (t(30) = -2.11, p = 0.215), Go trials response time (t(30) = 1.09, p = 0.707), p(respond|signal) (t(30) = -0.38, p = 0.71), SSD (t(30) = -0.52, p = 0.71), SSRT (t(30) = 0.73, p = 0.71) (Table 1).

27-item Monetary Choice Questionnaires

There was a significant effect in the Small k (V(39) = 199, p = 0.016), suggesting a higher k in small amounts of money in the active tDCS session in comparison with sham. However, t-tests did not reveal significant effects in the other outcomes from the 27-MCQ, namely Overall k (V(39) = 344, p = 0.12), Medium k (V(39) = 134, p = 0.12), and Large k (V(39) = 223, p = 0.12) (Table 1).

<INSERT HERE TABLE 1>

EEG analysis

Event-related Potentials

The Wilcoxon signed rank test revealed a significant difference between active and sham session in target-P3 amplitude (V(32) = 106, p = 0.003) and cue-P3 (V(32) = 142, p = 0.036). The target and cue-P3 amplitude was significantly lower in active session in comparison with sham (Figure 2.B and 3.B; Table 2).

<INSERT HERE FIGURE 2>

<INSERT HERE FIGURE 3>

Event-related Oscillations

During the target-P3 time-window, the event-related synchronization in delta band during target-P3 was significantly higher during sham when comparing with active tDCS (t(32) = -2.29, p = 0.03) (Figure 2.C and 3.C). However no differences were found for theta band activity (t(32) = -0.66, p = 0.805). Regarding the cue-P3 time-window, t-tests did not reveal any significant effect in both oscillatory activities, namely in delta (t(32) = -0.24, p = 0.847) and theta bands (t(32) = -0.19, p = 0.847) (Table 2).

<INSERT HERE TABLE 2>

Discussion

The current study provides evidence of the neuromodulatory effects of tDCS to the right inferior frontal gyrus on the P3 component and underlying oscillatory activity during a waiting impulsivity task (CPRT). A decrease of target and cue-P3 amplitude elicited in CPRT during tDCS over rIFG was found. Moreover, the reduction in target-P3 amplitude during active stimulation was combined with a simultaneous reduction in delta activity for the same time-window. Regarding behavioral analysis, there was a significantly higher

k in the small amounts condition after active tDCS in comparison with sham. However, no modulatory effects of tDCS over rIFG in waiting impulsivity measures from CPRT were found.

Electrophysiological correlates

In the present study, anodal tDCS to the rIFG decreased the target-P3 amplitude and underlying oscillatory activity (namely delta activity) during waiting impulsivity response. However, there is a growing body of evidence suggesting that anodal tDCS in frontal areas increases P3 amplitude during performance of cognitive paradigms involving attentional and working memory processes [20], and, a decrease in P3 amplitude during inhibitory control paradigms [22,23]. Thus, the differential effects of tDCS on P3 is related to the functional role of each cognitive task and its underlying neuronal substrates [20].

Furthermore, these findings underpin the relationship between P3 and the delta/theta activity at the same time-window observed in several cognitive tasks [18,36] (Inter-Trial Phase Coherence (ITPC) analysis and additional discussion about cue-P3 in Supplementary Materials). In fact, a recent study showed an enhancement of P3 amplitude during a visual oddball paradigm after the entrainment of delta/theta frequency bands through the application of transcranial Alternating Current Stimulation (tACS) [37]. However, contrarily to our hypothesis, theta activity was not modulated concurrently to both cue and target-P3 amplitude. On the other hand, tDCS modulated delta activity concurrently with the target-P3 amplitude, suggesting a potential inter-dependency between both electrophysiological markers and its importance during impulsive behaviors. For instance, a study decreased impulsive eating behavior in rats through a closed-loop system that triggered a responsive neurostimulation in the nucleus accumbens every time delta activity was excessively increased during reward anticipation [38]. Likewise, delta activity and P3 amplitude in parietal region are also enhanced during the anticipation of rewards when compared to neutral trials [19]. This is of particular interest because it was showed before a positive correlation between the cue-P3 amplitude and the activity in the ventral striatum (including nucleus accumbens), which is a core structure for reward processing and impulsive choice [11]. Similarly, neuronal activity observed left ventral striatum activity during an inhibitory control task was negatively correlated with the rIFG [39]. Thus, this might suggest that tDCS over rIFG might not only result in the reduction of P3 amplitude and delta activity, but also in the decrease of ventral striatum activity. This is in accordance with the behavioral results as well, given that tDCS over rIFG increased the choice for immediate rewards, which, for its hand, it has been associated with reduced activity on ventral striatum [40].

Furthermore, the anticipatory (i.e., cue) and consummatory (i.e., target) P3 in paradigms with monetary incentives are strongly related with reward processing, although they show different patterns. The target-P3 amplitude is greater when preceded by cues that predict win and loss of monetary compensation, which suggests its involvement during reward and punishment processing [12]. On the other hand, mixed effects in relation to the cue-P3, such as an enhancement after reward cues [11–13], loss cues[15], or both [14] has been shown in literature. Similarly, as previously mentioned, cues that predict rewards elicited an enhancement of delta activity in parietal areas (and cue-P3 amplitude) when compared to neutral cues [19].

Although, most of previous studies did not show a significant relation between cue-delta activity and delay discounting, a recent study demonstrated that the increase of evoked delta after stimulus during delay discounting paradigm was associated with the choice of delayed and larger rewards [41]. Therefore, the decrease of P3 amplitude and delta activity might indicate a modulation in the impulsive choice identified in our delay discounting results (but not found in CPRT and SSRTT).

Behavioral Outcomes

tDCS over rIFG did not impact the CPRT outcomes, namely, the number of premature responses, release time, and total earned money. These findings suggest that, although previous studies suggested the involvement of the rIFG in inhibitory control abilities [22,42], it might not be critically involved in waiting impulsivity [8]. Specifically, we expected an increase in tonic inhibitory process, thus, less premature responses. Our results did not support this hypothesis. Nonetheless, several reasons might be pointed out to explain the lack of tDCS effects in waiting impulsivity. First, tDCS over rIFG might show greater effect in reactive inhibition than tonic inhibitory response involved in premature responses. Indeed, a recent meta-analysis exploring the effects of tDCS in both inhibitory processes showed a significantly larger effect size in reactive (e.g., SSRTT) than tonic inhibition (e.g., GNG task) [4]. Therefore, a smaller effect of tDCS over rIFG should be expected in premature response given their association with proactive stopping [8]. Additionally, the rIFG neural circuits involved in both reactive and proactive inhibition follow different pathways. An indirect pathway has been related to proactive inhibition, which connects the rIFG with globus pallidus through the dorsal striatum, whilst reactive inhibition is related with a hyperdirect pathway from the rIFG and pre-SMA to STN by-passing the striatum [43]. Consistent with this notion, the increase of premature responses was associated with lower connectivity within structures relevant for motor inhibition, such as the STN and ventral striatum [9]. Therefore, differences in neural pathways might influence how tDCS affects the rIFG based on the network-dependent activity related to the CPRT [44]. This is supported by the absence of transfer effects from the waiting impulsivity task to the motor inhibition performance evaluated in the SSRTT. Nonetheless, this hypothesis is not in line with previous literature, given that several studies targeting the same area showed an enhancement of proactive inhibitory processes [22,45–48].

Another explanation is that tDCS might increase the proactive inhibition, but without any consequence to premature responding, given that this dissociation was already observed in literature [9,49]. Waiting and stopping has been suggested to be different constructs within the impulsivity realm [6], given that they rely on different cortico-striatal connections between the DLPFC and ventral striatum for waiting processes and between the IFG and dorsal striatum for stopping [7,50]. Furthermore, the differences of reward/punishment system might undermine any conclusion about the tDCS effect on premature responses or other outcomes from CPRT as suggested in Pearson correlation. Specifically, when it was harder to gain money, participants incurred in more premature responses. The baseline block was performed in the beginning of each section and subsequently the system of reward/punishment was updated in each session (see Limitations).

Moreover, the preference for immediate and smaller rewards observed in the MCQ-27 might be explained by the activation of concurrent neuronal circuitries between waiting impulsive action and delay discounting [6]. This is of particular interest given that both processes depend on ventral striatum even though they share different pathways. Specifically, waiting impulsivity relies on the connectivity of STN with ventral striatum and subgenual cingulate cortex [9], whereas increased magnitudes of delayed rewards were associated with activation of mesolimbic pathways through the ventral striatum, medial prefrontal cortex, and posterior cingulate cortex [40]. In line with this, studies have shown an effect of tDCS over the DLPFC in the dopamine release in the ventral striatum [51,52], which might explain the transfer effect of tDCS to the delay discounting assessment. Similarly, a neuroimaging study showed that the activity observed in the rIFG was negatively correlated with the activity found in the left ventral striatum [39]. Therefore, the application of anodal stimulation over rIFG might result in lower activation in ventral striatum and consequently the increase of the *k* observed in the MCQ-27. Nonetheless, to the best of our knowledge, this study was the first to test the effect of tDCS over rIFG in delay discounting.

In general, the tDCS transfer effects were only observed in impulsive choice (i.e., delay discounting) that partially shares neuronal circuits with waiting impulsive action [6]. Therefore, the modulation of the neuronal circuits related with the waiting impulsivity is in line with the tDCS model of the network activity–dependent model [44]. On the other hand, the lack of transfer effect in the inhibitory control task (i.e., SSRTT) might suggest the dissociation between waiting and stopping impulsivity [53] or between impulsive choice and action [54].

Limitations

The individualized reward/punishment system revealed several problems in this experimental protocol as suggested by the Pearson correlation between premature responses and baseline release time. For some participants, the mean RT and SD were significantly different between sessions. This shift might misinterpret the effect of tDCS over the rIFG in the number of premature responses because the urge to prematurely release the button might be influenced by the reward/punishment system. Therefore, a larger sample size should be preferred to evaluate the neuromodulatory effects in CPRT, as observed in our EEG analysis. Furthermore, this limitation might also influence the SSRTT because the differential behavioral training (i.e., due to the distinct reward/punishment system) might result in distinct plastic changes induced by tDCS [44]. This limitation might have a strong impact on behavioral performance and therefore "mask" a potential tDCS effect in the CPRT outcomes.

Future Directions

The inter-dependency between impulsive subtypes is still not clear within premature response paradigms [8]. In fact, most of the evidence was observed from animal studies and it is occasionally contradictory when compared to human studies [6]. This highlights the importance of P3 as a surrogate marker for the cognitive processing of impulsivity and underlying clinical populations, such as, alcohol

use disorder [55] and attention-deficit/hyperactivity disorder (ADHD) [56]. Therefore, tDCS and EEG studies are important to understand the neural circuitries behind waiting impulsivity and consequently for the therapeutic use in the related clinical conditions [1].

In addition, other transcranial electrical stimulation techniques, such as tACS [37], or the application of closed-loop systems [24] in impulsive processes should be addressed in the future, given the strengthening of the association between P3 and oscillatory activity suggested by this study. However, although tDCS decreased concurrently P3 amplitude and delta after the target, this was not observed after the cue. This finding might raise some questions about the association between cue-P3 and delta/theta activity in the time-window suggested by Broyd and colleagues [12]. Therefore, cue-P3 should be re-examined according to its functional role and the related oscillatory activity during impulsive paradigms.

At last, in the current study, the cue did not predict the win or loss of money as in the studies previously mentioned [11–14], given that the reward or punishment could occur in each trial depending on the subject's performance (i.e., the only way of not winning/losing virtual money was the premature response). The difference between positive or negative reinforcement should be evaluated in the future to fully understand the dynamics of P3/delta and waiting impulsivity/reward processing.

Conclusion

Overall, the current study suggests the decrease of anticipatory and consummatory P3 amplitude and underlying oscillatory activity (i.e., decrease of delta activity during target-P3) after tDCS over rIFG. On the other hand, these variations were not accompanied with changes in behavioral outcomes during waiting impulsivity, although a difference in delay discounting ability was detected between tDCS conditions. These modulatory effects of tDCS are of particular interest due to the association between P3, delta activity, and reward processing. Moreover, these findings suggest the usefulness of studying tDCS-induced effects on ERPs and EROs as surrogate markers of cognitive processes. Therefore, considering the potential therapeutic purpose of tDCS on impulsive disorders such as addiction or ADHD, this study highlights the importance of future studies testing tDCS in waiting impulsivity and underlying EEG correlates.

Methods

Participants

A total of 40 healthy volunteers (31 females; mean age: 23.2 ± 3.52) participated in the study. All the participants were right-handed (Edinburgh Handedness Inventory > 40) and without recent history of neurological or psychiatric disorders. The volunteers were priorly assessed using the Beck Depression Inventory II [25], Alcohol Use Disorders Identification Test [26], and Drug Use Disorders Identification Test [27] to ensure the absence of depressive symptomatology and alcohol/drugs consumption. Moreover, participants that reported medication or psychotropic drugs consumption during the 4 weeks prior to the

study were not included. All participants gave their written informed consent preceding their enrollment. The study was in accordance with the Declaration of Helsinki and was approved by the local ethics committee (CEICVS 127/2019).

Study Design

The study comprised two sessions, one with active and another with sham stimulation, which were administered randomly to each participant in a counterbalanced order. Both sessions followed similar procedures, except for the screening, informed consent, and self-report questionnaires that were performed only in the first session. In each session, participants performed the Cued Premature Response Task (CPRT) (Figure 4) during tDCS and the EEG data collection. At last, participants performed the SSRTT [28] and the Monetary Choice Questionnaire – 27 (MCQ-27) [29] in a counterbalanced order to assess potential far-transfer effects for delay discounting and inhibitory control (methodological details in Supplementary Materials). At the end of the session, participants filled a blinding questionnaire about the tDCS condition and the side effects of tDCS using a Visual Analog Scale from 0 to 10 (see Table S1 and S2 in Supplementary Materials).

Cued Premature Response Task

The experimental task was developed to assess premature responding during monetary reinforcement and punishment. For that, CPRT was programmed based on an adaptation of the 4-Choice Serial Reaction Time Task [30] and the MID [12]. Participants were instructed to press the middle button of the E-Prime Chronos response box to start a trial and to release it as fast as possible when the target was displayed on the screen. The target was always preceded by a cue, which informs the participant that the target was about to be displayed. The cue and the target were always displayed with a random onset to minimize expectancy. Specifically, the interval between the trial onset and the cue ranged from 1250 to 1750 ms and the interval between the cue and the target ranged from 500 to 2500 ms (Figure 4.A). However, in the baseline block, these intervals were fixed at 1000 ms.

Participants were instructed to release the button after target appearance on the screen as fast as possible, thus favoring speedier responses instead of more accurate, however slower, responses. The participant's response was rewarded with virtual money if their response was faster, punished if their response was slower, or neither rewarded nor punished if they responded before target onset (i.e., premature response; Figure 4.B) [30]. The task comprised one training block with 20 trials and one test block with 180 trials. Participants started to perform the test block task after three minutes of the tDCS onset and the total duration of the task was approximately 15 minutes (details in Supplementary Materials).

<INSERT HERE FIGURE 4 >

Transcranial Direct Current Stimulation

Participants received both active and sham tDCS in distinct sessions through the Starstim R20 (Neuroelectrics, Barcelona, Spain). For the active tDCS condition, an electric current of 2 mA of intensity for 20 min (with 15 second of ramp up and ramp down) as applied while the participant performed the CPRT. Sham procedure was similar to the active stimulation, but with only 15 seconds of 2 mA tDCS intensity duration at the beginning (with 15 seconds of ramp up and ramp down: 45 seconds in total). For both stimulations, 25 cm2 round saline-soaked electrode sponges (~radius of 3 cm, current density: 0.08 mA/cm2) were placed over F8 (active electrode) and posterior to the left mastoid (return electrode) [31].

Electrophysiological acquisition and data analysis

The EEG data were collected with the Starstim R20 (Neuroelectrics, Barcelona, Spain) using 18 scalps electrodes and one earlobe electrode. Electrophysiological data were posteriorly preprocessed and analyzed offline in EEGLAB [32]. Data was sampled at a rate of 500Hz and FIR filtered with a bandpass between 0.5 and 40 Hz. The DC offset was removed as the line noise using a notch filter (i.e., 50 Hz). The artifacts in the continuous data were corrected and noisy channels removed using the Artifact Subspace Reconstruction in the *clean_rawdata* function. The parameters for the identification of noisy channels were the following: flatline with a maximum duration of 5 seconds and correlation between channels below 0.7. Then, the data were re-referenced without the pre-identified noisy channels and the rejected channels were interpolated using the spherical spline method [33]. An average of 1.85 channels were rejected (SD = 1.09) in datasets from the active sessions and 1.78 (SD = 0.92) from the sham.

The continuous data were segmented in epochs with a total length of four seconds (i.e., 2000 ms prior and post-stimulus onset) centered in the target and cue. The target-P3 (Figure 2.A) and cue-P3 (Figure 3.A) epochs were baselined to the 200 ms pre-stimulus interval. The epochs containing premature responses in the 1000ms post-cue onset were excluded. Moreover, due to the time window of cue-P3, it was only selected epochs with at least 800 ms of cue-target interval. The epochs that surpassed ±150 μV at non-frontal electrodes were rejected. All the epochs were visually inspected and manually removed in the plot window if artifacts were present. At last, an independent component analysis (ICA) was performed to detect and remove muscle and eye movement artifacts using the ICLabel [34]. For outliers' information see Supplementary Materials.

Event-Related Potentials

The ERPs analyzed were the cue-P3 and target-P3 in the Pz electrode. The time-windows selected for each ERP were based on the study by Broyd and colleagues (2012), and the data were averaged following those time-windows, namely: target-P3 was the average amplitude between 250 and 450 ms and the cue-P3 was between 350 and 600 ms.

Event-Related Oscillations

The ERO was analyzed in decibel (dB) units. For that, a time-frequency decomposition using 3 cycle Morlet wavelets with a frequency resolution of 0.25Hz and temporal resolution of 8 ms was applied. The

frequencies analyzed ranged from 1.5Hz to 20Hz in the cue and target epochs. The baseline normalization followed an unbiased single-trial baseline correction to minimize the sensitivity to noisy trials [35]. Therefore, at first each epoch was normalized according to each average activity of the entire epoch. Subsequently, these epochs were converted in dB units according to the baseline window (i.e., 1000 ms pre-cue or target) following the additive model suggested by Grandchamp and Delorme (2011). At last, the ERO was averaged following the same electrode and time-windows from the ERP analysis [12].

Statistical analysis

The analysis focused on the difference between the active and sham stimulation conditions. Therefore, paired t-tests were performed in the comparisons in which the difference between both conditions followed the normal distribution, as assessed by the Shapiro-Wilk test. On the other hand, in case of a non-normal distribution, Wilcoxon signed rank test on paired samples were performed instead. Holm-Bonferroni correction was also performed in each section of the statistical analysis for multiple comparisons. At last, to probe the association between the number of premature responses and the average release time on the Baseline block, Pearson correlations were performed to evaluate the association between the reward/punishment system in the number of premature responses. The statistical analysis was performed in R (R Development Core Team, 2018; Version 4.0.3).

Declarations

Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Author contributions: A.J.M., S.C. and J.L. designed the study. A.J.M. collected the data. A.J.M. performed the EEG preprocessing and analysis. A.J.M., S.G.A., S.C. and J.L. interpreted the data. A.J.M. and A.L.

worked on the figures. All authors participated in the writing of the manuscript, interpretation of all the results, and approved the final version of the manuscript.

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Tables

Table 1. Descriptive (mean and SD) and inferential statistics for each behavioral outcome

		tDCS		*df*			*Adjusted p-value (BH)*
		Active	Sham		*t* / V*	*p-value*	
Cued Premature Response Task	Premature Responses	27.78 (14.65)	29.75 (15.77)	35	-0.79	0.432	0.438
	Monetary Gain/Loss	41.82 (66.10)	31.50 (70.73)	37	0.78	0.438	0.438
	Release time *(ms)*	240.97 (34.19)	244.89 (42.14)	37	-0.87	0.388	0.438
Stop-Signal Reaction Time Task	Accuracy Go trials	97.1 (2)	96.2 (3)	30	2.11	**0.043**	0.215
	RT Go trials	456.49 (70.32)	443.34 (82.68)	30	1.09	0.283	0.707
	p(respond|signal)	44 (10)	45 (10)	30	-0.38	0.710	0.71
	SSD	207.71 (55.89)	212.25 (51.45)	30	-0.52	0.605	0.71
	SSRT	223.77 (46.38)	215.85 (61.63)	30	0.73	0.471	0.71
Monetary Choice Questionnaire - 27	Overall *k*	0.016 (0.02)	0.015 (0.03)	39	344*	0.061	0.12
	Small *k*	0.033 (0.04)	0.024 (0.04)	39	199*	**0.004**	**0.016**
	Medium *k*	0.016 (0.02)	0.015 (0.03)	39	134*	0.120	0.12
	Large *k*	0.012 (0.02)	0.010 (0.03)	39	223*	0.106	0.12

Table 2. Descriptive (mean and SD) and inferential statistics for each EEG outcome

		tDCS					
		Active	Sham	*df*	*t* / V*	*p-value*	*Adjusted p-value (BH)*
Target-P3 (250 – 450 *ms*)	ERP (µV)	0.99 (5.33 / 0.93)	3.58 (3.14 / 0.55)	32	106*	**0.001**	**0.003**
	Delta (dB)	2.49 (3.18 / 0.55)	5.01 (6.51 / 1.13)	32	-2.29	**0.015**	**0.03**
	Theta (dB)	3.28 (3.44 / 0.60)	3.77 (4.72 / 0.82)	32	-0.66	0.805	0.805
Cue-P3 (300 – 650 *ms*)	ERP (µV)	0.38 (1.97 / 0.34)	1.39 (1.65 / 0.28)	32	142*	**0.012**	**0.036**
	Delta (dB)	-0.17 (1.06 / 0.18)	-0.11 (1.04 / 0.18)	32	-0.24	0.808	0.847
	Theta (dB)	-0.12 (0.91 / 0.16)	-0.07 (1.17 / 0.20)	32	-0.19	0.847	0.847

Figures

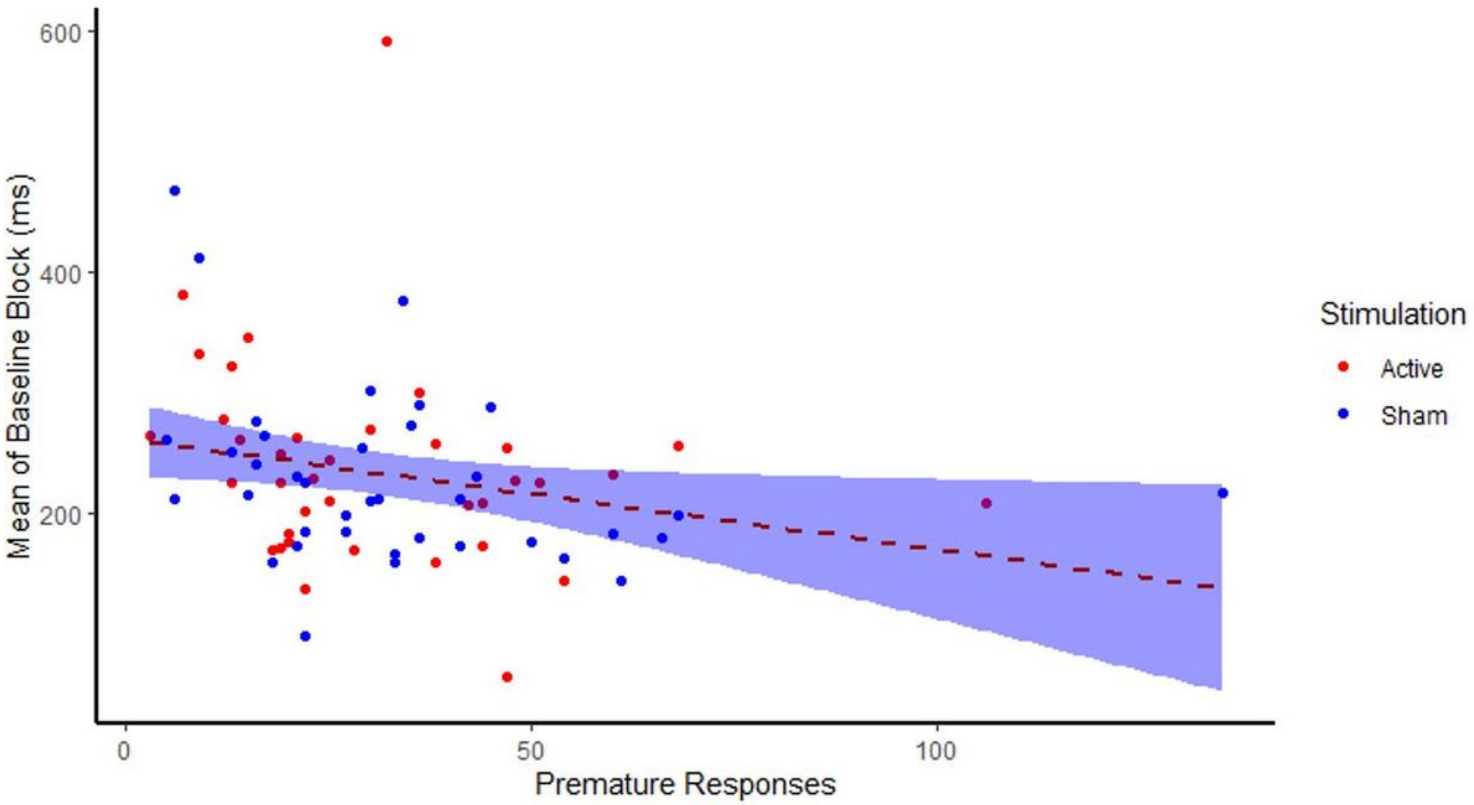

Figure 1

Correlation between the number of premature responses and the average of the release time in the baseline block.

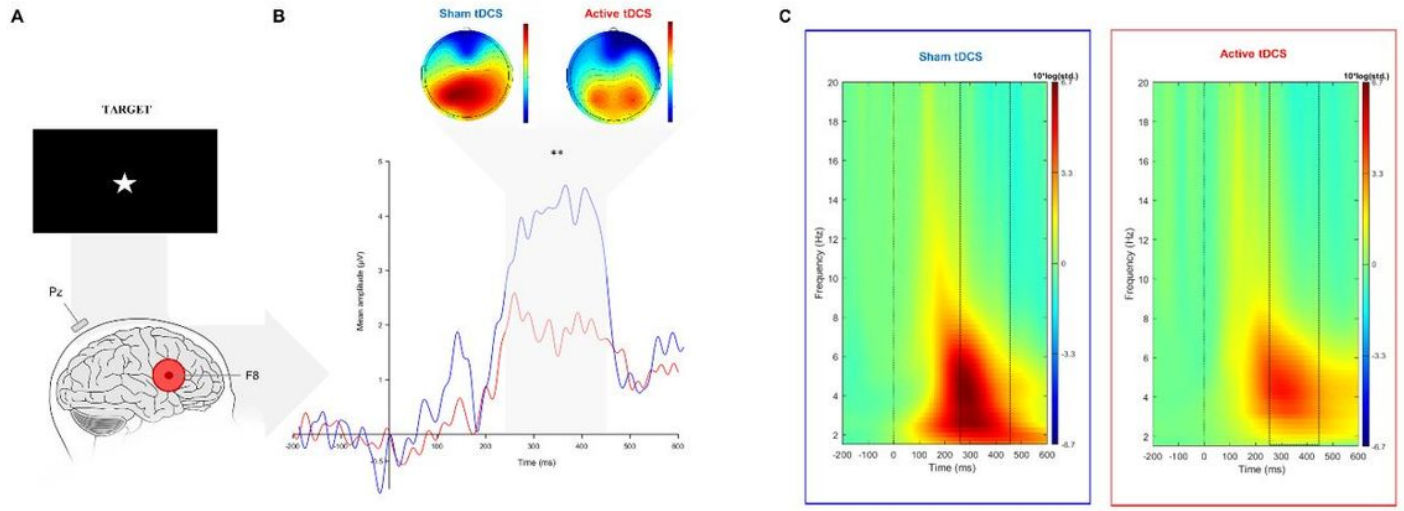

Figure 2

Grand average event-related target-P3 at Pz electrode (B) with topographical maps in the time-window of interest (represented in the gray area and dashed lines: 250 – 450 ms), and ERO results at Pz electrode (C) between both tDCS conditions.

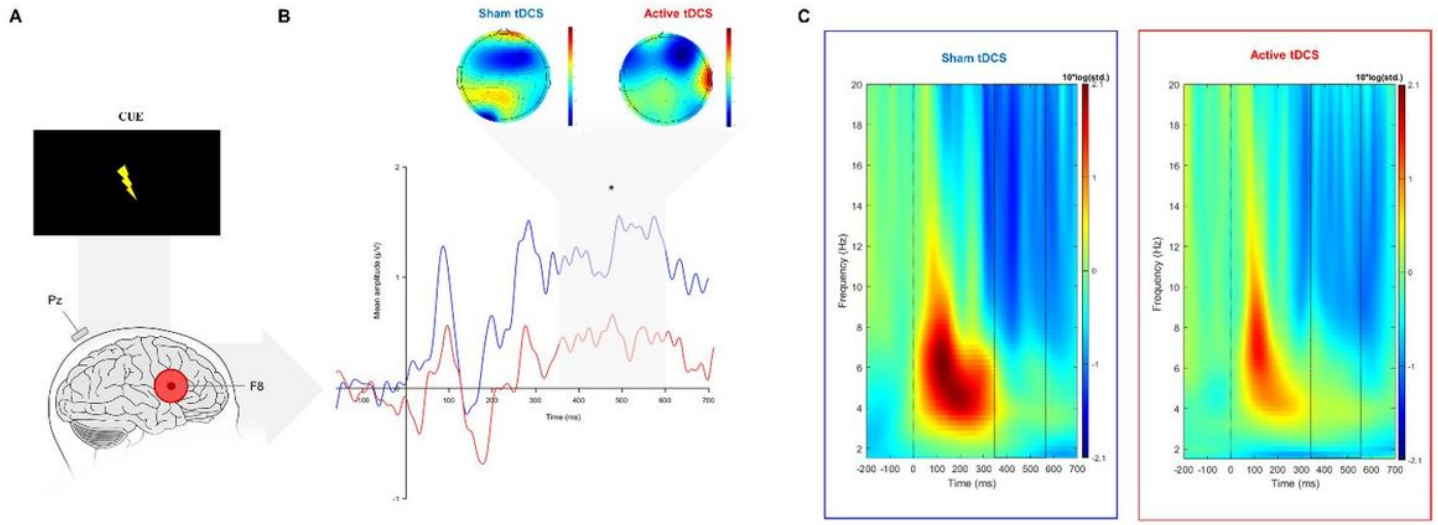

Figure 3

Grand average event-related cue-P3 at Pz electrode (B) with topographical maps in the time-window of interest (represented in the gray area and dashed lines: 350 – 600 ms), and ERO results at Pz electrode

(C) between both tDCS conditions.

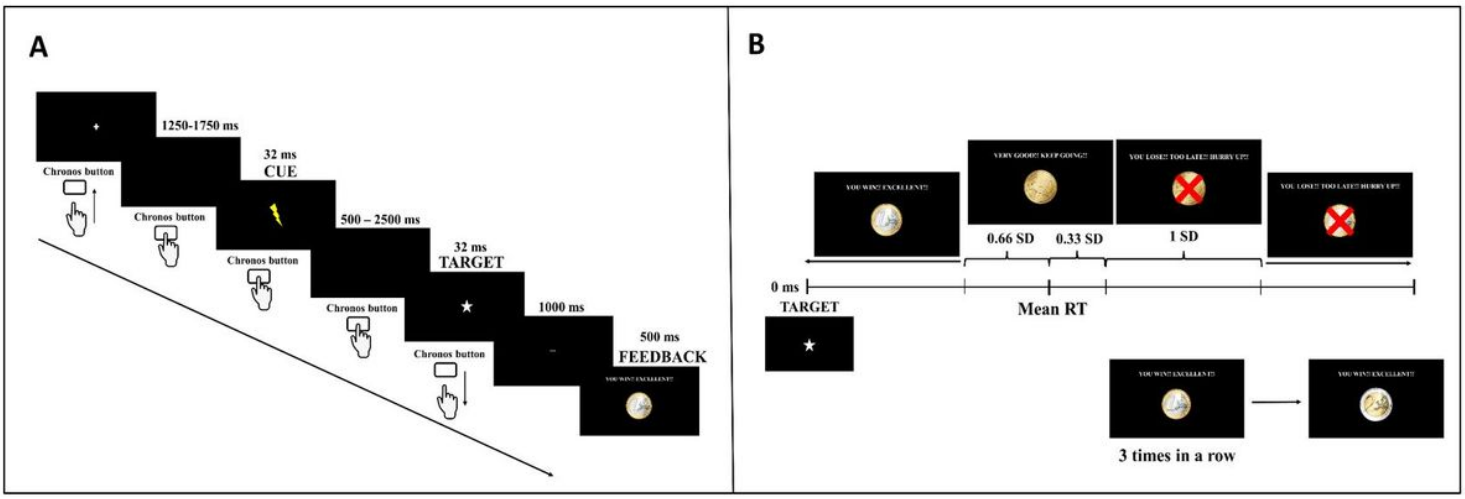

Figure 4

Overview of the experimental task (A) and the tailored reward/punishment system

Supplementary Files

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