Ambiguous tDCS: transcranial direct current stimulation effects on performance of monetary incentive delay task reinforcement learning

Anastasia Grigoreva[1], Aleksei Gorin[1], Valery Klyuchnikov[1], Anna Shestakova[1]

[1]*Institute for Cognitive Neuroscience*

Higher School of Economics, Moscow, Russia

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Abstract. The effects of transcranial direct current stimulation (tDCS) on cognitive function are not always predictable based on the direction of the current and therefore remain widely debated. Contrary to the optimism of studies using transcranial electrical stimulation (tES) over the motor cortex, cognitive domain research demonstrates great ambiguity and diversity of stimulation-related effects. Here, we investigated such a controversial impact of tDCS over the posterior medial prefrontal cortex in a monetary incentive delay (MID) task with which one can study reward-based learning or reward processing a. We found that in tMID) task where subject anticipated small or big losses in different monetary contexts, cathodal stimulation suppressed plastic changes in sensory auditory P2 event-related potential and increased feedback-related negativity (FRN) implicated in reward-prediction error processing thus revealing multidirectional effect of tDCS in the same subject group performing the same experimental task. Our finding of multidirectionality of tDCS compromise the use of tES as a ready-to-use method to test brain causality in the neurocognitive events of high complexity such as decision-making.

Key words: tES, cathodal tDCS, MID task, FRN, P2, decision making, reward anticipation.

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Introduction

The transcranial direct current stimulation (tDCS) is a non-invasive technique that can directly affect cortical excitability, enabling its selective modulation (Been et al., 2007; Hanley et al., 2016; Boroda et al., 2020). Still, effects of tDCS on brain function are multidirectional and often cannot be predicted (Boroda et al., 2020; Stagg et al., 2018). Contrary to the optimism of studies using transcranial electrical stimulation (tES) over the motor cortex (Nitsche & Paulus, 2000; 2001), cognitive domain research demonstrates great ambiguity and diversity of stimulation-related effects. Here, we investigated such a controversial tDCS effect on the medial prefrontal cortex (mPFC) in a widely used reward-processing task called monetary incentive delay task or MID (Knutson et al., 2001) paradigm.

The response to feedback is a crucial element of learning, and neural mechanisms involved in feedback processing have recently come to be the focus of research on human decision-making. The monetary incentive delay (MID) task is used to study neural mechanisms that provide stimulus-reinforcement association, including feedback response. FRN appears as the main candidate for neural correlate of reward prediction error (RPE) processing (Holroyd and Coles, 2002). According to the reinforcement learning explanation, better learning and adaptation are driven by RPE (Hauser et al., 2014; Rouhani & Niv, 2021).

In the previous MID experiment which was dedicated to study brain plasticity associated with anticipating losses in different context, we found that FRN differed as a results of magnitude of losses: dFRN as a difference between FRN in response to smaller and larger losses varied in different trial types: the dFRN was negative in the LL-trials and positive in the HL- and WL-trials. Our results indicate that in the context of losses, FRN is modulated by reference points and expectations (Gorin et al., 2020). Moreover, we found a correlation of the sensory auditory plasticity manifested in the MMN component with the reward-processing manifested in teh fRN. In a consecutive study (Gorin et al., 2020, we used cathodal tDCS to test whether medial prefrontal cortex known to drive the generation of FRN in the context specific manner, i.e. will

the effect of the cathodal tDCS which is known to drive an inhibitory response will be different depending on the context of the losses: widely varying losses vs. small losses vs. big losses. In this study, we found that FRN amplitude in the loss prevention version of the MID task (Gorin et al., 2022) was enhanced by cathodal tDCS, although suppression was expected according to previous results obtained by Reinhart and Woodman (2014). Following the main assumptions of the reinforcement learning theory, we hypothesized that there is also a change in the perception of sound in terms of changes in event-related potentials (ERPs), and particularly there are such effects mediated by electrical stimulation in P2, which is by some researchers considered as the 'biomarker of learning' (Tremblay, 2014).

We assumed that if FRN is enhanced by cathodal stimulation, this change could be reflected in the diurnal dynamics of P2.

Monetary incentive delay task to study reward processing and reinforcement learning

Capacity to learn, seek reward, and avoid punishment in an unknown environment is dependent on trial and error, according to reinforcement learning theory. Predicting and adapting behaviors based on experience (Noonan et al., 2012), individuals progressively change their internal perceptions of state-action values by measuring the difference between predicted results and external feedback (Sutton and Barto, 1998). The anterior prefrontal cortex (aPFC), the lateral orbitofrontal cortex (lOFC) and the ventromedial prefrontal cortex/medial orbitofrontal cortex (vmPFC/mOFC), are thought to greatly contribute to event value representation, reinforcement learning and decision making under uncertainty (Frank & Claus, 2006; Kringelback, 2005; Tsuchida et al., 2010). In addition, the process of learning with reinforcement is mediated by the striatal dopaminergic system, which forms the link between stimulus and response, as is known from studies of predictive coding and classical conditioning (Dayan & Balleine, 2007; Schultz, 2002).

The use of monetary incentives takes notable place in research of learning and decision making because the value of money can be positive or negative depending on the context in which it is presented (Delgado et al., 2006, 2011). One of the most used empirical traits to study mechanisms that provide the stimulus-reinforcement association is the monetary incentive delay (MID) task. It allows to examine prediction, anticipation, outcome processing and consumption in a variety of reward or punishment situations (Lutz and Widmer, 2014). The MID task incorporates stimuli that contain both the amount and likelihood of expected reinforcement, allowing to explore the impact of these expected value components on brain activity related with both stimulus and feedback processing (Knutson et al., 2005).

The difference between the actual and expected results forms the reward prediction error, which serves as a learning signal for choosing beneficial actions (Sutton and Barto, 1998). Feedback-related negativity (FRN) is considered as a main candidate neurophysiological correlate of the RPE signal, observed in both the money

loss and gain domains (Walsh and Anderson, 2012; Sambrook and Goslin, 2014). Earlier findings from our project reveal that the FRN magnitude is sensitive to both probability and size of the reward in the win-oriented version of the task and to the size of the money loss in the MID version of the task, which was aimed at preventing such loss (Krugliakova et al., 2018; Gorin et al., 2020).

In a series of studies previously conducted by the project group, it was established that the association of a previously neutral auditory stimuli with a particular loss value causes changes in ERP components observed in the oddball task (Näätänen et al., 2004), where participants do not respond to stimuli by passively listening to a series of auditory cues. As a result of the MID loss-avoidance task, the association between previously neutral auditory stimuli and a particular loss size led to plastic changes in the auditory cortex, reflected in an increase in mismatch negativity (MMN), a component of the auditory evoked potentials observed during the oddball task (Garrido et al., 2008; Näätänen et al., 2004). Furthermore, it was found that, at the individual level, such changes in the amplitude of the MMN correlate with the sensitivity of the FRN component to the magnitude of the loss (Krugliakova et al., 2019; Gorin et al., 2020). This correlation, however, cannot directly indicate a causal relationship between sensory cortex plasticity and the activity of feedback-processing areas.

Brain correlates of auditory plasticity associated with MID task

In the previous studies (Krugilakova et al., 2019; Gorin et al, 2020) we found that the effects of the MID performance affected memory traces to the sounds associated with gains or losses of different magnitudes in a separate oddball experiment. However, the questions remained as to whether in the two consequitive sessions of MID performance separated by the nocturnal sleep one could observe signature of the brain plasticity too and whether such plasticity can explain the counterintuitive effect of modulatory TES on FRN reported in the previous study (Gorin et al., 2022). We chose to study the TES on P2 component of the ERP evoked in the two consecutive MID session for the reasons explained bellow.

Training can cause observable alterations in neural systems that induce structural and functional plasticity (Galván, 2010). Neuronal plasticity mechanisms are essential for brain's capacity to acquire new information (Kania et al., 2017), adapt to a rapidly changing environment (Correia, 1998), as well as recover from trauma (Johnston, 2009), learn and make decisions (Ganguly & Poo, 2013). The plasticity resulting from training can lead to a temporary reorganization of cortical maps through the expansion of the representational region followed by the reversal of cortical expansion in parallel with the establishment of connections between specific cortical and subcortical regions (Xiong et al., 2015), according to studies in both animals (Kaas & Collins, 2001) and humans (Weinberger, 2015; Elias et al., 2015).

Like other sensory systems, the auditory system experiences plastic changes (Ponton et al., 2001; Purdy et all., 2001). Experience can alter performances in different listening tasks (Weinberger & Diamond, 1987; Wisniewski et al., 2020), such as increasing sound detection thresholds (Zwislocki et al., 1958; Leek et al., 1984), enhancing sensitivity to difference between simple (Delhommeau et al., 2005) and complex sounds (Tremblay et al., 2014). Auditory learning can alter neural activity in the human central auditory system (Tremblay et al., 2002).

Changes in neuronal activity associated with training can be examined using auditory ERPs (Näätänen et al., 1993). According to Tang et al. (2013), training with

auditory stimuli may increase the early components of auditory ERP along with a rapid improvement in frequency representation of the auditory cortex. In a study by Atienza et al. (2002), changes in neural activity associated with training preceded changes in auditory perception. Seppänen et al. (2012) states that auditory ERP, such as N1 and P2 (also known as N100 and P200) are useful to study auditory plasticity because, while emerge immediately after every audio signal is presented, they are also susceptible to training and different top-down influences including active attention and reinforcement (Seitz & Watanabe, 2005). N1-P2 complex reflected changes in neural activity associated with training (Tremblay et al., 1998, 2001, 2002). Tremblay et al. (2014) also argue that an increase in N1-P2 amplitude is consistent with an improvement in perception. In earlier studies N1-P2 is considered as the vertex potential complex having common generation origins: associative cortex, primary auditory cortex, and cingulate gyrus (Davis & Zerlin, 1966; Crowley and Colrain, 2004; Näätänen & Picton, 1987). Nevertheless, some authors claim that P200 is an independent component that can be dissociated from the N100 experimentally (Ford et al., 1999), developmentally (Ponton et al., 2000), and topographically (Ferreira-Santos et al., 2012).

N1 is often described as an exogenous response, sensitive to the physical characteristics of the sound used to trigger the response (Picton et al., 2013) and detect change (Näätänen and Picton, 1987). N1 activity has also been linked in studies to detection and orientation to changes in the auditory environment (Arnott et al., 2011) and selective attention (Wilkinson & Lee, 1972). N1 emerges between 60 and 150 ms after stimulus onset, followed by P2 (Paiva et al., 2016).

P2 is a positive deflection with a typical peak latency of 150-250 ms induced by auditory stimuli (Ferreira-Santos et al., 2012). Studies examining different auditory training have shown that P2 amplitude increases with training (Atienza et al., 2002; Hayes et al., 2003; Kuriki et al., 2007; Sheehan et al., 2005; Seppänen et al., 2012; Reinke et al., 2003; Kühnis et al., 2013) and represents the evaluation and classification of the stimulus (Tremblay et al., 2010). Wisniewski et al. (2020) observed a larger amplitude of auditory P2 accompanying trained sound detection rather than untrained

in passive exposure of sound. Reportedly, changes in P2 amplitude also may reflect the acquisition process during learning or other tasks (Tremblay, 2014). Studies on the role of P2 in learning are not always able to establish a direct relationship between changes in P2 amplitude and the size of perceptual change, according to Sheehan et al., (2005), although P2 amplitude increase correlate with frequency modulation rate, reaction time (Tong et al., 2009), and increased performance in various tasks (Orduña et al., 2012). Notably, increased P2 amplitude was concomitant with improved processing of random sounds without attention: in a study by Seppänen et al. (2012), increased fast N1 and P2 plasticity reflected faster auditory perceptual learning in musicians.

Source of P200 is located mainly near the auditory cortex in the temporal lobe (Hari et al., 1990, Perrault and Picton, 1984). Among newer studies, Ross and Tremblay (2009) suggested that the center of P2 activity may be located in the anterior part of the auditory cortex, the lateral part of Heschl's gyrus. In study by Crowley and Colrain (2004), the generation of P2 is dedicated to planum temporale, Brodmann's area 22, and auditory association cortices. Continuing the assumption of finding the source of P2 in the temporal lobe, there are reports that tissue loss in the frontal lobe also correlates with P2 amplitude in the attention task, but if the source of P2 generation is in the temporal cortex, other brain regions, such as the frontal cortex, may modulate this component (McCarley et al., 1989, 1991). Other reports suggest that the inferior parietal lobe can also modulate the P2 signal (Knight et al., 1988). In addition, this component may also take its origin from sources outside the cortex (Ferreira-Santos et al., 2012; Jacobson, 1994). MEG and Intracranial EEG data also suggest that P200 has different sources: the temporal plane and the auditory association complex in area 22 (Godey et al., 2001). Thus, most studies suggest that P2 originates from associative auditory temporal regions, although there may be non-temporal sources active in the same time window.

Recent advances in the use of non-invasive electrical and magnetic brain stimulation (TES and TMS) have demonstrated the usefulness in studying neural plasticity. For example, a study by May et al. (2007) showed that pTMS of the superior temporal cortex was able to induce macroscopic cortical changes in the auditory cortex

within 5 days of continuous intervention. Boroda and colleagues (2020) also claim that tDCS can modulate auditory cortex plasticity in an activity-dependent manner. Together with neuroimaging tools, brain stimulation presents itself as a useful tool to study changes in human brain plasticity.

tDCS as means to study brain causality in cognition

Transcranial direct current stimulation (tDCS) is a method of electrical stimulation that can directly affect cortical excitability (Been et al, 2007; Hanley et al., 2016; Boroda et al., 2020; Gordon et al., 2018; Matsushita et al., 2021) through subthreshold modulation of neuronal membrane potentials (Stagg et al., 2018). tDCS is mainly considered as one of the most safe and tolerable methods of brain stimulation (Woods et al., 2016). According to reports, this approach may raise and reduce the excitability of nerve cells beneath the anode and cathode electrodes (Nitsche et al., 2001; Fecteau et al., 2007; Stagg et al., 2018). Anodal stimulation is hypothesized to enhance the excitability of the stimulated regions owing to cell depolarization (Batsikadze et al., 2013; Stagg et al., 2018). Cathodal stimulation is predicted to reduce excitability by hyperpolarizing the activated neurons (Batsikadze et al., 2013; Stagg et al., 2018; Nitsche et al., 2008).

tDCS was reported to modulate perceptual behavior, such as visual function (Antal et al., 2011; Costa et al., 2015), somatosensory function (Costa et al., 2015), and auditory stimulus processing (Tang et al., 2013). A meta-analytic evaluation found that the effects of stimulation are dependent on the research field, i.e. motor or cognitive (the authors' overall term including all non-motor studies), as well as the polarity of the active electrode (Jacobson et al., 2012). Increased excitability following anodal stimulation, and notably decreased excitability after cathodal stimulation, are more reliably seen in the motor domain, according to the research of Kunzelmann et al. (2018) and Reis et al. (2009). Furthermore, research of tDCS effects in the cognitive domain found that anodal stimulation causes a substantial rise in excitability, whereas cathodal stimulation causes no significant decrease in excitability (Jacobson et al., 2012).

tDCS to modulate plasticity

The effects of tDCS depend on the duration and strength of stimulation and can last more than 24 hours after exposure (Monte-Silva et al., 2010; Jamil et al., 2017). From animal models, it is recognized that tES can modulate synaptic plasticity,

learning, and memory by inducing LTP via increased expression of brain-derived neurotrophic factor (BDNF) (Podda et al., 2016).

According to pharmacological studies, blocking of NMDA receptors prevents tDCS-induced changes in excitability regardless of the active electrode, and NMDA receptor agonists enhance the anodal tDCS-induced increase in excitability (Nitsche et al, 2003, 2004). Since NMDA receptor activation causes an influx of calcium ions into the cell, which controls both LTP and LTD induction, it is also consistent with the fact that when calcium channels are blocked, tDCS-related plasticity induction is prevented (Nitsche et al., 2003). Based on the same premises, the nonlinearity of tDCS effects is explained both due to protocol and montage, as well as the brain state and individual differences (Antal et al., 2007; Knechtel et al., 2014).

At this point, results of tDCS in the cognitive domain remain controversial. There is no precise understanding of how tDCS modulates somatosensory and auditory processes, but it is known to be reflected in somatosensory and auditory ERP. Part of the heterogeneity in results can be explained by individual differences, stimulation protocols (Stagg et al., 2018) and diverse impact of tDCS on various types of neurons located in different layers of cortex (Radman et al., 2009).

tDCS is currently seen as a tool enabling the investigation of the causal relationships between brain activity and behavior (Tanaka & Watanabe, 2009). It was established that learning processes can be causally controlled by transcranial direct current stimulation of medial-frontal cortex (MFC), (Reinhart & Woodman, 2014). By Reinhart and Woodman (2014), cathodal stimulation of MFC may decrease FRN and ERN compared to placebo due to MFC being responsible for the task performance monitoring.

According to To and colleagues (To, et.al., 2018) high definition tDCS (HD-tDCS) also affects anterior cingulate cortex (dACC): anodal stimulation in this study led to significant rise in beta-frequency band activity in dACC, while cathodal HD-tDCS led to increased activation of theta frequency band in dorsal and rostral ACC. Essentially, the study demonstrated the reliability of tDCS for dACC activity

modulation. Remarkably, in this work authors employed the offline effects of tDCS. Monte-Silva and colleagues (2010) proposed another stimulation paradigm, causing offline effects: 9+3+9 min (stimulation, rest, stimulation) of 1 mA stimulation was used. In their paper it is shown that such a paradigm provides the effect lasting more up to 120 min which is quite enough for the MID task. The lower current was applied in order to restrict the area stimulated and ensure that there are no overnight consolidation effects.

To investigate cathodal tDCS effects on reinforcement learning-related cortical plasticity, a sham-controlled study was conducted. Montage as in Reinhart and Woodman (2014) over the posterior medial prefrontal cortex was used. The paradigm involved MID task. Monetary losses, coded by sounds, were used as negative reinforcement. Cathodal stimulation was initially expected to inhibit FRN, but, contrary to the hypothesis, the value of the component in the stimulation group was significantly higher than in the control group (Gorin et al., 2022).

We decided to analyze how this effect on FRN is reflected in the perception of sound in terms of changes in ERP, and particularly in dynamics of auditory P2, by some researchers considered as the 'biomarker of learning' (Tremblay, 2014). We analyzed both evoked and induced activity to get the most complex picture of tDCS effects.

Methodology

Participants

30 healthy right-handed participants (18 women aged 23+-2 years) took part in the study. Half of the participants formed a cathodal stimulation group (Reinhart and Woodman (2014) montage), while the other half received sham (placebo stimulation) just before the economic game.

Procedure

The experiment consisted of 2 day-by-day sessions, including stimulation (sham or cathodal) for control and experimental group respectively, and the MID task (Figure 1).

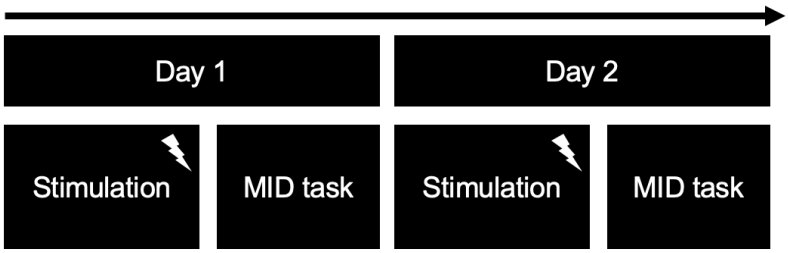

Figure 1. Structure of the present study

Participants got a quantity of money in the amount of 4’000 rubles before the MID session. They were told that throughout the economic game, they may lose some of the money, and that their reward for participating would be based on the remaining amount. A modified version of the MID task was used for the experiment as in Gorin (2020).

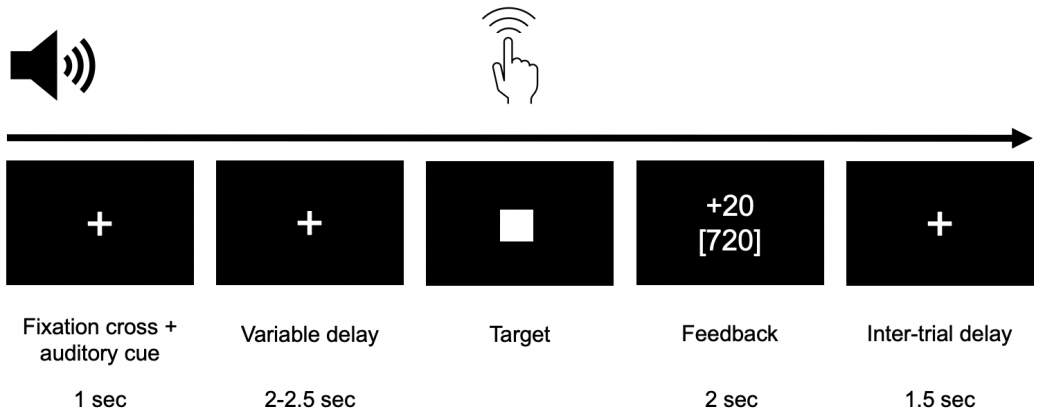

Figure 2. Procedure scheme

The monetary reinforcement was encoded by a sound signal that appeared 2000-2500 milliseconds before the target. If the subject failed to press the key before the square disappeared, they lost the amount of money encoded by the audible cue. If the button was pushed before the target faded, the trial was declared acceptable. The length of the target stimulus presentation was adjusted to influence the outcome probability using an adaptive algorithm that followed participants' performance so that for each type of trial, when they succeeded 60% of the time. Losses were determined in three contexts to detect changes in cortical responses associated with the expected value: low, high, and distinct losses (LL, HL, and DL, respectively), where a participant may lose 1 or 2, 50 or 51, and 1 or 50 rubles, respectively.

The task was split into different sections, two for each setting. Only two stimuli and two monetary rewards were employed in each block. If the participant pressed the button more than once or pressed the button before the target appeared, the feedback screen returned an image of three exclamation marks "!!!" in red, showing an error in the task. Subsequently, this trial was not considered completed and was repeated during the game to maintain the ratio of 50 trials per stimulus.

The average response time in a brief pretest, in which participants replied fast to the identical target that appeared in the middle of the screen for 400 ms, was used to determine the duration of display of the first target stimulus in the main experiment. Each block was preceded by a training portion, where participants associated auditory

cues with monetary results. Two numbers were displayed on the screen, denoting the amount of loss in a block. After the beep, participants used one of the two buttons (left and right arrows) to pick the correct amount and received feedback. The training ended when the subject completed 8 out of 10 trials successfully, and the MID task began.

Six auditory stimuli (325, 381, 440, 502, 568, and 637 Hz) constituted three pairs of stimulus signals that predicted low and high losses: -1 or -2, -50 or -51, -1 or -50 rubles (LL, HL, DL, respectively). Thus, the 1-ruble difference between the outcomes in the LL and HL settings did not matter considering the beginning sum of 4,000 rubles, while the 49-ruble difference between the outcomes in the DL context mattered. Participants were therefore more driven to recognize signals in the DL setting to enhance monetary outcomes.

Each pair of auditory money signals was randomly presented in mini blocks of 50 trials. In total, each session of the MID task consisted of six mini blocks, so that each of the three context types appeared twice during the experiment. The sample size was too small for full randomization; therefore, the acoustic match between stimulus and outcome using six main combinations was counterbalanced. Thus, the signal-result match between lower/higher frequency and lower/higher outcome values was counterbalanced among participants.

Equipment

tDCS was performed using a StarStim electrostimulator and two conductive rubber electrodes. Rectangular electrodes were placed in saline-soaked synthetic sponges (active electrode, 19.25 cm^2; reference electrode, 52 cm^2) and fixed in proper positions using a cap and bandage. The electrode positions were like in the work of Reinhart and Woodman (2014). Cathodal tDCS was expected to deliver the current to MFC and ACC. The active electrode was positioned in the FCz position using the 10-10 system, and the referent was put on the cheek, left or right (equally in each group). The current strength was 1 mA; the duration of the effect was extended using a customized stimulation pattern: 9 minutes of stimulation, followed by 3 minutes of rest,

and then another 9 minutes of stimulation, which ensured (Monte-Silva et al., 2010) that the post-stimulation effect would last throughout the MID task session.

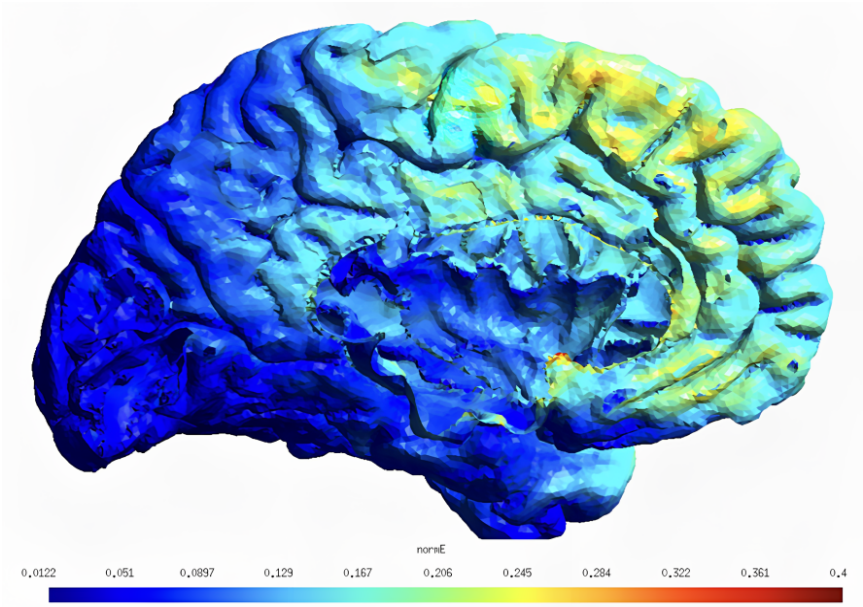

Figure 3. Model of current distribution in the stimulating electrode assembly used. Performed in the SimNIBS environment

During playing the game, EEG and EOG have been recorded. EEG recording was performed using the BrainProducts ActiChamp system with 60 active electrodes arranged according to an extended version of the 10-20 system. The signal was abstracted to the average signal from a pair of electrodes on the mastoid processes. An electrooculogram (EOG) was recorded using electrodes placed under the right eye and on the left cheekbone. The grounding electrode was placed in the Fpz position. The impedance of the electrodes was maintained below 5 kOhm before recording.

Data analysis

EEG preprocessing and ERP analysis

Data analysis has been performed using Brainstorm software (Tadel et al., 2004) in MatLab. The raw data of all participants for both days was checked and then eradicated of artifacts, labeled relative to *auditory stimuli* (coded loss amount), *context of playing* and *trial*; averaged within each group, computing both subject and grand averages. EEG data was filtered in the range from 1 to 40 Hz, Eye movement artifacts have been removed according to their topography and correlation with the EOG. Noisy

segments were marked as bad in the recordings during preprocessing and were excluded from further analysis.

After the preprocessing, epochs relevant to each stimulus in range of -200 and 800 ms with preprocessing of removing DC onset and selecting baseline definition in time range of -100.0 and -2.0 ms were imported to the database. Time window of 250-350 ms relative to the auditory stimulus, as in a previously published study (Krugliakova et al., 2018) has been analyzed. To correct eye movement artifacts, an independent component analysis of JADE (ICA) was used.

Statistical analysis

The periods obtained were averaged in the experimental (cathode) and control (sham) groups for each day. These data were also averaged across trials (day), game context, and loss size (e.g., DL context win records were averaged with a loss size of 50 rubles in the experimental group on 1 trial) in channel Cz.

To test the main hypothesis, we used permutation tests. We performed paired permutation tests between data recorded on days 1 and 2 for the control and experimental groups and with different losses. Precisely, we performed paired permutation tests for each group's data (sham and cathode) within the same contexts with the same amount of loss on each day. Thus, for example, we did pairwise permutation test between data recorded in the *cathode* group on *day **1*** and containing *1-ruble* losses for the *DL context* and those recorded in the *cathode* group on *day **2*** and containing *1-ruble* losses for the *DL context*, and so for each loss size of their respective contexts. We performed similar tests for the experimental group. In addition, we performed permutation tests for independent samples within the **same** *loss size* and *day* among the control and experimental groups. For example, we did a test between data obtained from the ***cathode*** group on *day 1* and containing *1-ruble* losses for the *LL context* and those recorded in the ***sham*** group on *day 1* and containing *1 ruble* losses for the *LL context.* Results of permutation tests were adjusted for multiple comparisons using the FDR (false discovery rate). Subsequently, we obtained permutation test results by day, within group, and between the two groups for each loss size and game

context and thus compared how the responses to signals of different losses in the same context differ in the same group and how the response to a signal of the same amount of possible loss in the same context changes between the two groups.

Basing on results of permutation tests, we also performed repeated-measures analysis of variance (RM ANOVA) with stimulation factors (cathode, sham), and stimulus context (LL, HL, DL) and day (1, 2) in STATISTIKA 12 software for the N1 and P2 amplitude. This test was accompanied by effect size calculations. Level of significance for all calculations was set to 0.05. Next, we interpreted the results based on a review of the literature, suggesting questions for further research on this project.

EEG induced activity analysis

The study also examined the dynamics of the oscillatory response to sound cues in the monetary game. For this purpose, the raw data were referenced against the averaged potential, then sliced into epochs of -1000 to 2000 ms to compensate for edge effects. The epochs were then subjected to a time-frequency transformation using the Morlet wavelet function. In our TFA, we focused the analysis on the frequency range of 4-20 Hz, thus overlapping the alpha, beta, and theta bands. The phase-linked component was subtracted from the data obtained, after which the data was standardized into an event-related synchronization-desynchronization view, where the reference period served as a range of -500 to -2 ms. Using pairwise permutation tests as part of the exploratory study, we compared the frequency-time dynamics between sessions of the experiment.

Results

The effect of cathodal tDCS on P2

We recorded EEG before and after two day-by-day MID task sessions. Fig. 4 shows the ERP curves for the two groups, averaged over the stimulation conditions, the size of the encoded loss, and the day. Noticeably, the amplitude of the N1-P2 complex was significantly larger in the control group that received sham stimulation compared to the stimulation group, and particularly for the second day. Then we performed an unpaired permutation test comparing ERPs on each channel in cathode condition vs sham condition on the first day. The permutation test revealed a significant effect of the group on the amplitude of the P2 component: in the *sham* condition, the P2 component showed enhanced magnitude, while *no P2 amplitude increase in stimulation group was observed while significant P2 amplitude increase in sham group*.

P2 as a correlate of neuroplasticity caused by the two-days training of MID

Next, we compared the difference ERPs (day two – day one) in the control group pairwise for each type of money loss, focusing on a time window of 100-300 ms. Results were adjusted for multiple comparisons using the FDR (false discovery rate) method. A pairwise permutation test showed significant differences (Fig. 6) at the 95% confidence level of 2 vs. 1 day in all game contexts in the following time intervals: for DL context -1 R 180-212 ms – smaller amount; for DL context -50 R 174-204 ms and 258-284 ms – larger amount; for HL context -50 R 166-212 ms and 260-292 ms – smaller amount; for HL context -51 R 170-212 ms and 272-278 ms – larger amount; for LL context -1 RR 188-212 ms – smaller amount; for LL context -2 RR 170-214 ms and 272-284 ms – larger amount.

Since significant differences were found for all loss contexts played ($p<0.05$), we extracted N1-P2 values for the difference between 2nd and 1st day and got repeated measures analysis of variance. To test the significance of the P2 differences, we averaged the signal observed on the Cz channel in the 180-260 ms time window

(Magnée et al., 2008) and performed RM ANOVA with the factors: day, context, and loss size (Table 2 and Figure 7). The analysis of variance of the amplitude of the P2 component revealed the significance of the factor Day ($F(1, 13) = 11{,}182$, $p = 0{,}002$, $\eta_p^2 = 0{,}493645$).

Induced activity analysis

Oscillatory activity statistical analysis (correction for multiple comparisons by the FDR method) revealed significantly higher alpha-band synchronization in the second session of the experiment on centroparietal electrodes with lateralization to the left for the group that received placebo (Figure 8). Such activity may reflect changes in sensorimotor rhythm in the brain regions that project to the right hand that subjects used to respond to stimuli. This may be due to learning the delay between the sound stimulus and the appearance of the target, that is, no motor response was required in the early post-stimulus period, and the synchronization of the sensorimotor rhythm may reflect the resting period. The latency of the oscillatory response was 300 ms and lasted up to 1050 ms (lead FC3), which is consistent with an increase in the probability of the target appearing 1000 ms after the presentation of the sound cue. At the same time, there were no statistically significant differences from session to session in the group that received cathodal stimulation. This finding is consistent with the observed suppression in the changes in the amplitude of the P2 component observed in the placebo group.

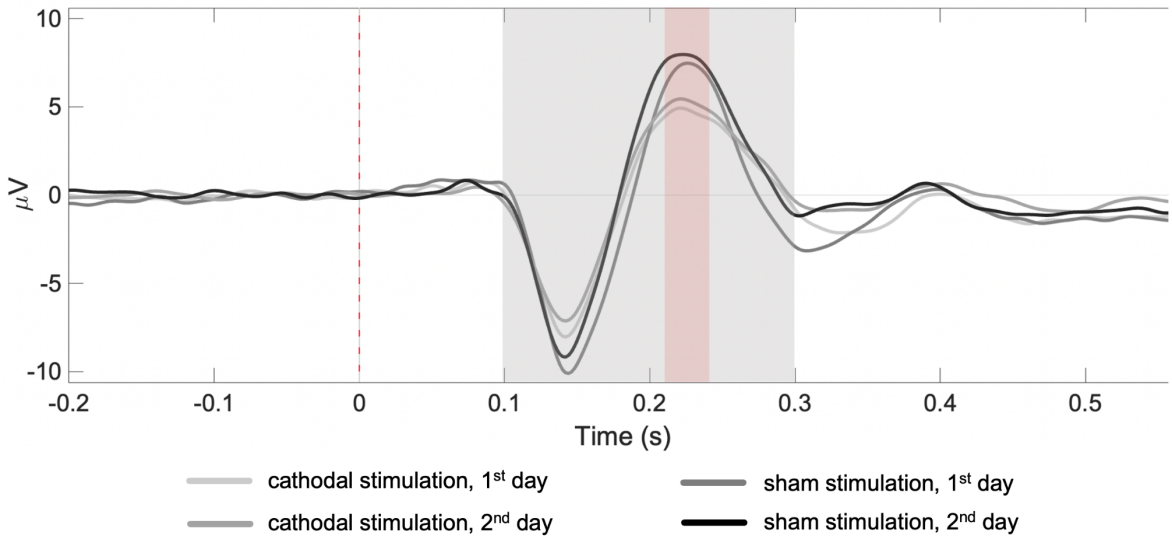

Figure 4. General average on all contexts for the 1st and 2nd day. Cz electrode. P2 amplitude is significantly higher in the control group (received sham stimulation), both on the first and the second day ($p<0.05$)

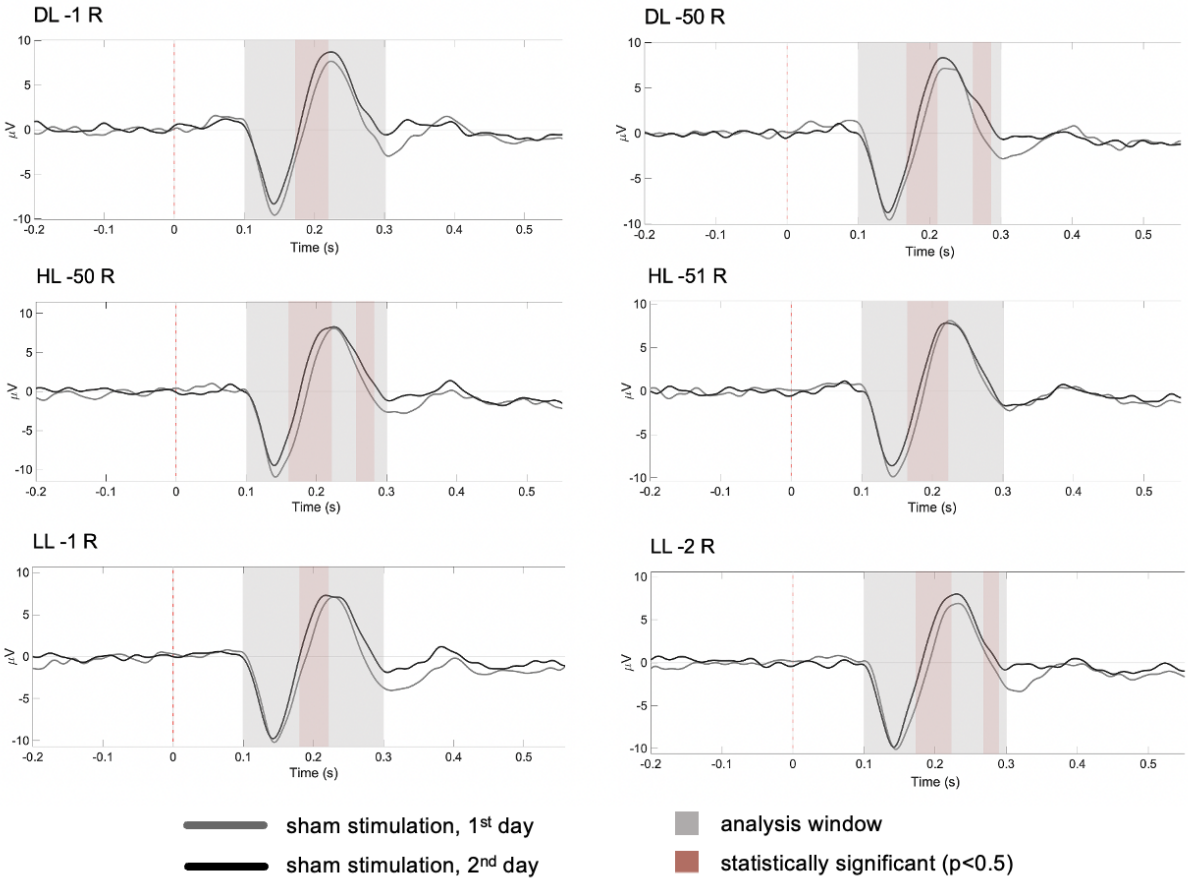

Figure 6. EP curves for sham group according to day, Cz electrode. The difference between the EPs is pronounced all contexts of play presented ($p<0.05$)

Table 2

Repeated Measures Analysis of Variance with Effect Sizes and Powers

	SS	DF	MS	*F*	*P*	*Partial eta-squared*	*Observed power*
Day	69,02	1	69,02	13,65	,002	**0,494***	**0,929***
Context	15,28	2	7,64	2,01	0,153	0,126	0,380
Value	3,31	1	3,31	1,24	0,284	0,081	0,180
*Day*context*	1,13	2	0,56	0,27	0,762	0,019	0,089
*Day*value*	0,11	1	0,11	0,09	0,764	0,007	0,059
*Context*value*	1,35	2	0,68	0,52	0,599	0,036	0,127
*Day*context*value*	2,55	2	1,28	0,7	0,505	0,048	0,156

Notes. * $p<0.05$

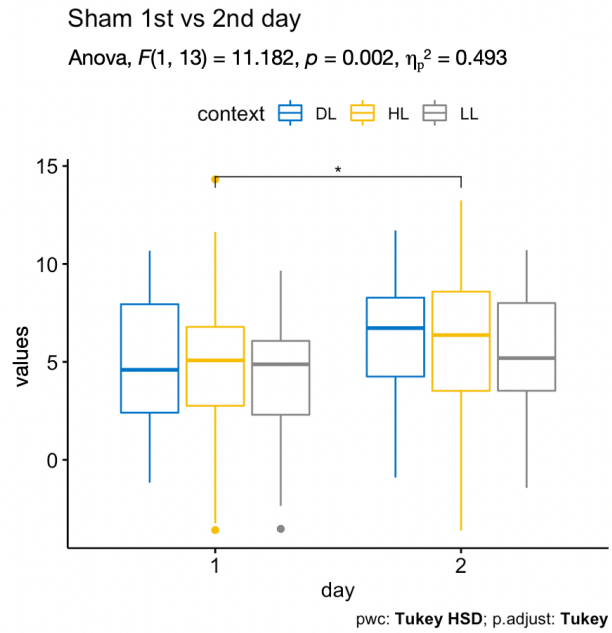

Figure 7. Results of analysis of variance by the factor *Day* in sham group. The magnitude of P2 was significantly higher on the second day, p = 0,002. *Averages: Day 1: 4,7 uV, Day 2: 6,0 uV.*

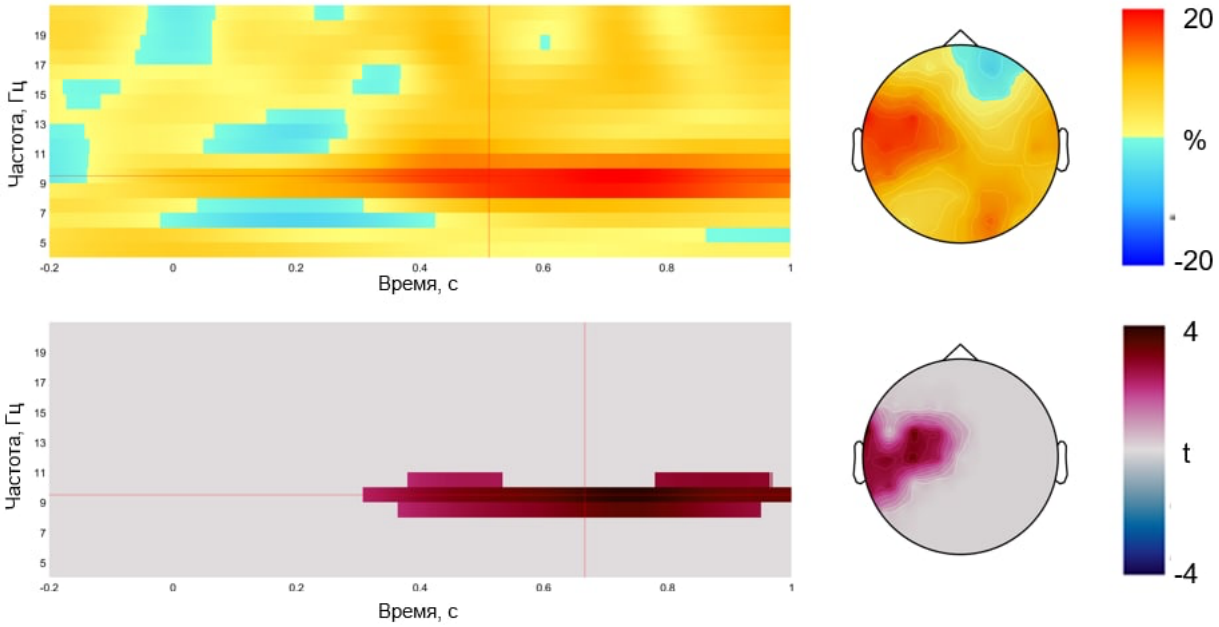

Figure 8. Topography of t-statistics, placebo group, 500 ms after audio cue, 10 Hz. Comparison of session 2 and session 1. In session 2, the amplitude of responses in the alpha range is significantly higher.

Summary and Discussion

In this study employing two sessions of MID task, we focused on the effect of cathodal tDCS on the brain plasticity manifested in the P2 component changes from one day of MID task performance to another. In our previous study, we found that FRN response in the MID task was significantly higher in the group which obtained stimulation than in the control group (Gorin et al., 2022). The FRN response is calculated as a difference between no-losses and losses trials at the time of the feedback given to the participant. FRN seems to represent the computation of RPE, indicating outcome and prediction inconsistency (Holroyd et al., 2004; Sambrook and Goslin, 2014; Walsh and Anderson, 2012). According to the reinforcement learning explanation, larger RPE provides better learning (Rouhani & Niv, 2021). The P2 component is an exogenous response calculated separately for all types of anticipated reward in all possible contexts. So, the two components reflect different processing associated with the repeated performance of the MID task and possibly activate different networks. We used tDCS to trace the plasticity of the two mechanisms and how they intertwined in the MID task performance.

In all permutation tests in the intervals that refer to the P2 component in the group that received the placebo stimulation, we observed an increase in the amplitude of the P2, which many studies (Atienza et al., 2002; Sheehan et al., 2005; Tremblay et al., 2001; Reinke et al., 2003; Hayes et al., 2003) attributes to plastic changes in the brain. On the contrary, in the group that received cathodal stimulation, we found no significant difference in amplitude between the experiment's first and second days. This observation is correct for each of the six monetary loss conditions: -1 and -2, -50 and -51, -1 and -50 rubles. Since the P2 amplitude on the first day is significantly higher in the control group, we assume that cathodal stimulation suppressed the P2 amplitude for both days of the experiment. The oscillatory data is consistent with the observed P2 inhibition. Thus, we can assume that cathodal stimulation influences the changes in the electrical activity of the brain, at least by slowing down their appearance (Holroyd et.al., 2008; Stagg et al., 2018).

This result, however, should be considered together with the suppression of FRN in the cathodal stimulation group demonstrated earlier (Gorin et al., 2022), where it was found that cathodal stimulation was initially expected to inhibit FRN, but, contrary to the hypothesis, the value of the component in the stimulation group was significantly higher than in the control group (Gorin et al., 2022).

Our findings demonstrate the inconsistency of FRN and P2 amplitudes to this assumption, which we attribute to the multidirectional stimulation effect on higher-order neural networks. Such results could be due to the anatomical features of the structures responsible for decision-making: the sources of the FRN are located in the dorsal ACC, while main sources of P2 are in the anterior part of the auditory cortex, the lateral part of Heschl's gyrus (Ross & Tremblay, 2009). Concurrently, some researchers propose that the sources of P2 are widespread (Ferreira-Santos et al., 2012). Recent EEG-fMRI study (Mayhew et al., 2010) also demonstrated that one of the P2 sources might be the dorsolateral prefrontal cortex (dlPFC). Because of the irregular distribution of tDCS current, these cortical areas may be directly exposed to electrical current.

We suppose that the posterior medial prefrontal cortex, which we stimulated, may overlap with one of the sources of P2, and fall under the direct influence of the electric current. This may also be due to the difficult predictability of tDCS-induced current propagation in an anisotropic environment (Datta et al., 2009). Perhaps our results can add evidence to the arguments that P2 consists of subcomponents (García-Larrea et al., 1992; Silva et al., 2020). Whether this is correct, and whether we affected an early subcomponent of P2, which is the source of the observed plastic changes, remains to be studied in the future experiment, using the multichannel tDCS.

Since anodal and cathodal stimulation are associated with LTP- and LTD-type plastic changes (Pelletier & Cicchetti, 2015; Stagg et al., 2018), we suggest that in our study cathodal tDCS has inhibited P2 source and led to the suppression of LTP, which is probably responsible for the plastic changes in the potential that we observe in the control group. Our results may add evidence in favor of the fact that tES does affect

plastic reorganization in the cerebral cortex due to changes not in the potential itself, but in its temporal dynamics.

Limitations and perspectives

Initially, tDCS does not provide full anatomic targeting (Datta et al., 2009). Current propagation is heterogeneous, which may spread effects beyond the primary target, consequently distorting both data and interpretation. Considering the apparent complexity of high-order neuronal networks, we suggest using imaging techniques to detect off-target effects. With all limitations acknowledged, brain stimulation techniques show great potential.

In future studies, we suggest using other types of electric and magnetic stimulation, particularly anodal tES, tACS, and other types of montage in similar paradigms. For example, one could concentrate specifically on the N1-P2 complex sources, placing the referent on the temporal region and the active electrode as in the work by Reinhart and Woodman (2014). We propose using a source analysis (via MEG or fNIRS) to confirm or reject the suppression of the N1-P2 sources that we target with stimulation. We also state the significance of a set of equally filled cathodal, anodal, and sham stimulation groups to study the effects of such stimulation as broadly as possible to get more complex results.

With regards to the paradigm, in this work we used only negative reinforcement, respondents tried to avoid monetary losses. A more comprehensive view requires paradigms that would include other types of reinforcement.

Conclusion

The present work demonstrates that cathodal tDCS can affect both FRN and P2, illustrating the multidirectional effect of tES in the nonmotor domain. In addition, of the P2 component. Since the study employed a monetary task, we observed a change in the component magnitude concerning both the sound and the feedback.

The FRN in the cathodal group increased, contrary to the initial hypothesis, so the plastic effects could have been enhanced by a stronger feedback signal, but the P2 amplitude showed no change, which may indicate the inhibitory effect of the tDCS on the P2 component of plastic changes. Our study brings more evidence of an unconventional cathodal effect of tDCS, namely increase, and not decrease of excitability for one component of the ERPs and no effect for the other obtained in the same experimental task – monetary incentive delay (MID). Our observations call for future studies using tDCS and suggest more cautious interpretations of tDCS effects in the absence of proper psychophysiological control.

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