No Evidence of Transcranial Direct Current Stimulation on Frontal Brain Asymmetry and Inhibitory Control: A Randomized Controlled Trial

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Abstract

Studies suggested a relationship between frontal brain activity asymmetry and self-regulation; however, these measures are regarded as indirect despite their relevance, and the underlying brain mechanisms are still unknown. Our preregistered study investigated the link between frontal alpha asymmetry as a potential neuromarker of self-regulation and behavioral and brain activity components of inhibitory control. We utilized a randomized controlled sham-feedback design involving 65 individuals (46 females). Prior to and following non-invasive brain stimulation, resting-state EEG data were collected to assess frontal alpha asymmetry scores, and participants completed a stop signal task, including neutral and reward conditions. During transcranial direct current stimulation, a 2 mA current was administered with the anode placed on the right frontal site and the cathode on the left frontal site. Results showed no effect of the intervention on frontal alpha asymmetry or any of the behavioral or neural indices related to inhibitory control. However, event-related potential analyses showed that inhibitory brain activity in the reward condition correlates with resting-state asymmetry of frontal brain activity, indexed by frontal alpha asymmetry. Specifically, higher right relative to left frontal brain activity was associated with lower early-onset inhibitory activity, presumably originating from the inferior Frontal Gyrus, but correlated with higher late onset inhibitory control, presumably originating from the superior Frontal Gyrus. The results suggest a functional dissociation regarding the lateralization of frontal brain activity and early and late onset inhibitory brain activity.

Significance statement

By investigating the connection between frontal alpha asymmetry, a candidate biomarker for self-regulation, and inhibitory control, we unveil a deeper understanding of human cognitive and behavioral processes. While transcranial direct current stimulation yielded unexpected outcomes in frontal alpha asymmetry and inhibitory control metrics, surprisingly, we found an interesting dissociation between inherent frontal alpha asymmetry and brain activity indices of inhibitory control in reward contexts. This dissociation might reflect a dynamic interaction among brain regions aimed at achieving optimal inhibitory control. Furthermore, heightened activity in the frontal brain's right hemisphere could imply a compensatory mechanism at this interaction. Our findings emphasize the complex relationship between non-invasive brain stimulation, frontal brain asymmetry, and behavioral/brain activity indices of inhibitory control in reward contexts.

1. Introduction

Self-regulation is “the self’s ability to control its own thoughts, emotions, and actions” (Baumeister et al., 1994), and its failure has been linked with various mental health problems such as depressive and addictive disorders (Heatherton and Wagner, 2011; Johnstone et al., 2007). It is understood that self-regulation is driven by two main motivations, both of which are influenced by environmental factors (Giorgio Vallortigara, 2005; Kelley et al., 2017). Environmental cues that indicate potential rewards trigger approach motivation, whereas cues signaling threat activate withdrawal/inhibitory motivation. Previous research found that these two tendencies may be associated with the asymmetry of frontal cortical activity (Coan et al., 2006; Harmon-Jones et al., 2010; Kelley et al., 2017): Relative left frontal cortical activity dominance is linked with approach tendency while right frontal cortical activity dominance is associated with inhibitory control. Particularly, frontal alpha asymmetry (FAA), which is an electrophysiological (EEG) measure of the difference in alpha power (8-12 Hz) between the left and right dorsolateral prefrontal cortex (dLPFC), can potentially be a biomarker for self-regulation and a treatment target for relevant clinical conditions. Here, our aim is to overcome the limitation of correlational studies by utilizing non-invasive brain stimulation to modulate FAA and inhibitory functions.

Transcranial direct current stimulation is a non-invasive neuromodulation technique that delivers electrical currents to the brain through electrodes placed on the scalp to modulate specific brain activities (Schestatsky et al., 2013). In the context of our interests, promisingly, various studies found that tDCS over dLPFC reduces craving, desire to binge eating, and total food intake (Burgess et al., 2016; Kekic et al., 2017; Lapenta et al., 2014). However, even though there is evidence regarding the effects of tDCS of dLPFC on self-regulation, these measures are indirect, and to the best of our knowledge, it is still unknown whether these tDCS-associated effects are mediated by the effect of tDCS on the modulation of FAA.

Inhibitory control, the ability to suppress an intended response, stands as a fundamental facet of self-regulation (de Jong et al., 1990) and its insufficiency can lead to various disorders (e.g., obesity, nicotine dependence, internet addiction) (Bartholdy et al., 2016; Charles-Walsh et al., 2014; Lavagnino et al., 2016; Lawrence et al., 2009; Luijten et al., 2011; Smith et al., 2014). Individual differences in inhibitory control are frequently assessed using the Stop Signal Task (SST) (Schmajuk et al., 2006). In this task, participants are presented with "go" stimuli (typically symbols in visual tasks) at the center of the screen, requiring a button-press response. Occasionally, these go stimuli are followed by a "stop" stimulus (a specific symbol), signaling participants to withhold their response. The stop-signal reaction time (SSRT), a widely accepted measure of inhibitory control (de Jong et al., 1990; De Jong et al., 1995), is derived from this task.

To explore brain mechanisms underlying inhibitory control, prior studies have utilized a combination of the SST and event-related potential (ERP) analyses (Kenemans et al., 2023; Logemann et al., 2013). ERPs reflect the synchronous activation of large groups of neurons time-locked to an event (Kappenman and Luck, 2012). The Stop N2, occurring around 200 ms latency, exhibits significantly more negative amplitudes during successful stop trials than unsuccessful ones (Schmajuk et al., 2006). Furthermore, it has been implicated that the neurobiological correlate of the Stop N2 is the right inferior frontal gyrus (Schmajuk et al., 2006). The Stop P3 is influenced by stopping success, showing larger amplitudes for successful inhibitions compared to failed ones (Schmajuk et al., 2006). Indeed, the Stop P3 has been thought to represent inhibitory control (Lansbergen et al., 2007) and to originate from the superior frontal gyrus (Kenemans and Kähkönen, 2010). Despite these presumed associations, inhibitory control's behavioral and electrophysiological indices have not been extensively explored in the context of state FAA and self-regulation.

In this preregistered study, our aim was to investigate the effect of FAA changes, through tDCS, on behavioral and brain activity indices of inhibitory control in exposure to palatable food pictures. We utilized food images, drawing from a previous study that found a divergence between the processing of intrinsic stimuli (like food) and learned rewards (such as money) concerning inhibitory control. First, we hypothesized that an active tDCS (anode over right dLPFC/cathode over left dLPFC) would result in an increase in right relative to left frontal brain activity. Secondly, this neural stimulation would improve inhibitory control as operationalized by both behavioral and ERPs indices in the food condition, relative to the neutral condition.

2. Materials and Methods

2.1. Participants

Our pilot study (N = 10) regarding the main effect of tDCS on the primary outcome FAA served as the foundation of the sample size rationale. More specifically, the expected effect (f >0.237; η2partial > 0.053) was estimated to be detectable with the a priori intended sample size of 30 for the active intervention group using G*Power (Faul et al., 2009, 2007), with a defined power of 80 percent, alpha at .05, and estimated FAA test-retest correlation of 0.6. Sixty-five individuals (46 females), ranging in age from 18 to 58 (M_{age} = 23.93; SD_{age} = 6.08), were ultimately recruited via social media and university courses for the study after several participants terminated the experiment for a variety of reasons, such as boredom and fatigue. Please consider each analysis for the numbers of excluded participants. Each participant was given a voucher or course credit for their participation. In order to participate in the study, individuals needed to meet certain eligibility criteria. Specifically, they had to be at least 18 years of age. Additionally, participants were screened for certain exclusion criteria, which included the presence of psychological or psychiatric disorders, frequent headaches or migraines, metallic implants, epilepsy, significant head trauma in the past, recent head trauma, pacemaker usage, chronic skin conditions, and current drug use. Participants were also required to self-assess their proficiency in English using the Common European Framework of Reference for Languages - Self-assessment Grid (*Common European Framework of Reference for Languages: Learning, Teaching, Assessment*, 2001), and a minimum of B1 level English proficiency was necessary for inclusion in the analyses. Psytoolkit was used for self-report assessments (Stoet, 2017, 2010). Before any procedures took place, all participants provided their written informed consent. The research was conducted following the ethical guidelines outlined in the Declaration of Helsinki and its later amendments. The study was approved by our research ethics committee.

2.2. Stop signal task (SST)

The SST was developed using OpenSesame (Mathôt et al., 2012). It was adapted from the original version (Schmajuk et al., 2006) and included an intrinsic reward condition (food) based on previous studies (Houben et al., 2014; Tsegaye et al., 2022). The task consisted of 10 blocks in total, with one practice and four main blocks for each condition (neutral/reward) separately. Participants were seated approximately 65 cm. from the screen. At the beginning of the task, participants were instructed with an understandable text, and it was also explained orally in case it was needed. First, a fixation dot is displayed in the middle of the screen to engage attention and eye fixation for 2000 ms. Slightly above the dot, in the reward condition, palatable food pictures, i.e., cookies, chips, chocolate, and nuts (115 px width (2.9°) x 200 px height (5.1°)), which require a key response were presented

randomly in horizontal or vertical orientation for 150 ms (Figure 1). Therefore, the reward condition had two dimensions (horizontal/vertical). On the other hand, in the neutral condition, instead of the palatable food pictures, the letters "X" or "O" (200 px width (5.1°) x 200 px height (5.1°)) were presented for 150 ms, which also requires a response depending on the letter presented. Either a left-button press or a right-button press with the left and right index fingers based on a stimulus was used for responses. In stop trials, go stimuli (either palatable food pictures in horizontal or vertical position or letters X or O depending on the condition) were infrequently followed by the letter "S" (200 px width (5.1°) x 200 px height (5.1°)) for 150 ms representing "stop" and participants were supposed to withhold their response in that case. The go-stop Stimulus Onset Asynchrony (SOA) was fixed at 350 ms, but when participants could not withold their response, the timing was arranged after each stop trial via algorithm; the go-stop interval was decreased 50 ms. In case of a successful inhibition, the interval increased 50 ms. The tracking algorithm yields an approximate 50% inhibit rate, increasing the reliability of the estimation of the SSRT (Verbruggen et al., 2013). In total, a session of the task took approximately 45 minutes. The main outcome of the SST was the SSRT. By following Verbruggen et al. (Verbruggen et al., 2013), omissions were replaced with maximum RTs (1500 ms).

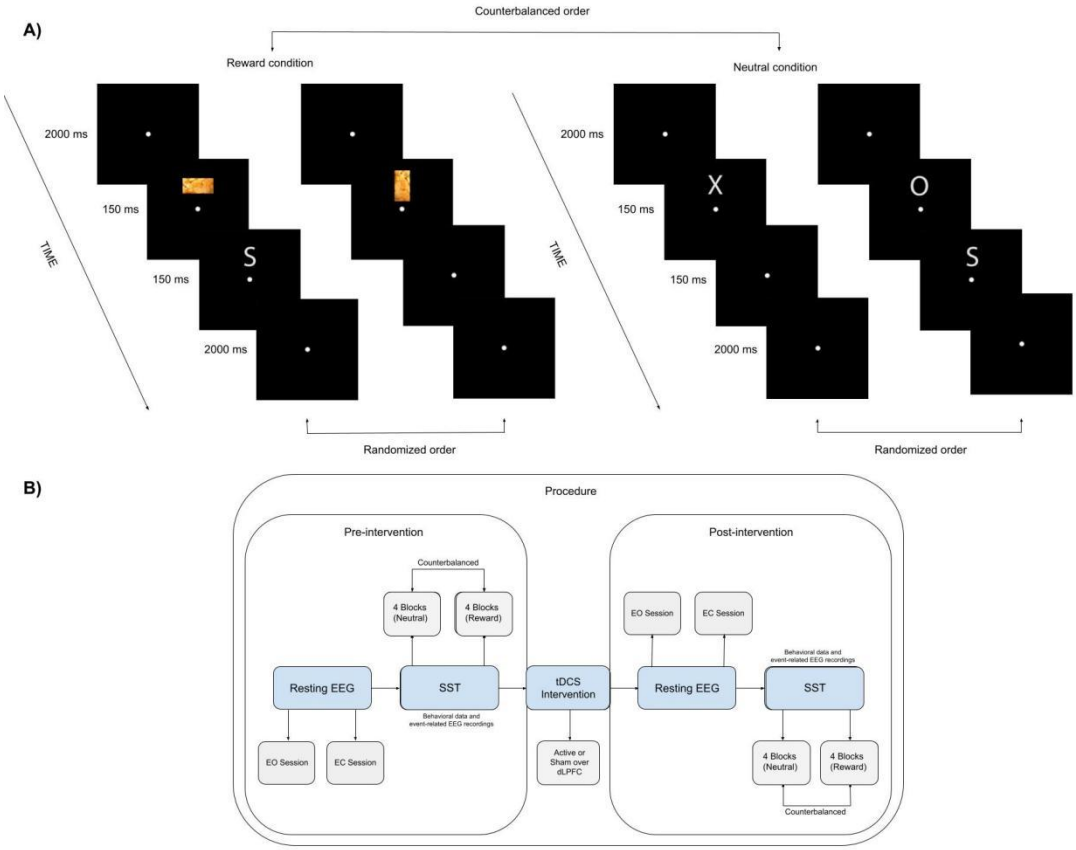

Figure 1. A) Based on the counterbalanced order, participants started the Stop Signal Task under either the neutral or reward condition. The initial two trials (on the left) represent the reward condition, where the target dimension (horizontal/vertical) and the palatable food pictures (such as chips, chocolate, cookies, nuts, etc.) were randomly presented. The final two trials (on the right) represent the neutral condition, where the letters “X” and “O” were

randomly presented. These trials were sometimes followed by the letter "S" indicating stop trials, where participants should withdraw their initiated responses to non-stop stimuli displayed beforehand. B) The process begins by gathering pre-intervention resting-state EEG data in order to measure frontal alpha asymmetry, which was conducted in two sessions: one with a 5-minute period of eyes open and another with 5 minutes of eyes closed conditions. Subsequently, participants performed the Stop Signal Task, where both the neutral and reward conditions were presented in a counterbalanced order. Following this, either sham or active transcranial direct current stimulation was administered. More details on the intervention can be found in Figure 2. After the stimulation, the same procedure was repeated for the post-modulation assessment, including the resting-state EEG and the Stop Signal Task.

2.3. EEG acquisition

Scalp voltages were captured using a 21-channel cap Ag/AgCl electrodes set according to the 10-20 system ("Nexus-32," n.d.). The vertical electrooculography (VEOG) was recorded above and below the left eye, and the horizontal EOG (HEOG) was recorded bipolarly from the outer canthi of both eyes. Sampling rate was set at 512 Hz. EEG was continually recorded aside from when tDCS was applied because switching from the EEG cap to the tDCS cap was necessary.

2.4. Frontal alpha asymmetry (FAA)

Frontal alpha asymmetry scores were derived from EEG data recorded during two separate 5-minute resting-state sessions: one with eyes open (EO) and another with eyes closed (EC) both before and after the intervention. Using BrainVision Analyzer 2 (www.brainproducts.com), FAA was calculated based on previous reports (Johnstone et al., 2007). First, a high-pass filter of 0.5 Hz, low-pass filter of 40 Hz, and 50 Hz notch filter were applied. Subsequently, the first and last 10 seconds of the EEG data was excluded due to artifacts. The data was then segmented into 2-second epochs. Based on VEOG and HEOG electrodes, the epochs for the EO condition were adjusted for ocular artifacts using independent component analysis (ICA). Epochs that still contained artifacts, determined by a 75 µV maximum amplitude +/- relative to the baseline criterion, were excluded. The Power Spectral Density (PSD) was determined using FFT with a 10% Hanning window for the remaining epochs after whole-segment baseline correction. Next, the epochs were averaged, and the mean activity in the alpha frequency band (8-13 Hz) was calculated. Values for the relevant electrodes were exported. Using SPSS 22 (IBM Corporation, n.d.), alpha power was corrected for skew via natural log transform (Smith et al., 2017). Lastly, frontal asymmetry was calculated by subtracting the log transformed alpha at lateral left electrode sites from right electrode sites (i.e., F4-F3 and F8-F7).

2.5. Event-related potentials (ERPs)

First, signals were referenced to linked mastoids. Subsequently, EEG data were filtered (offline) using a high cutoff 30 Hz, low cutoff 0.5 Hz, and notch filter of 50 Hz.

Data were segmented into epochs ranging from -100 ms to 2600 ms. Ocular corrections were conducted using Independent Component Analysis. Following that, epochs were segmented and they were baseline-corrected with the baseline set at -100 to 0 ms. We conducted a go-signal locked segmentation, then baseline correction followed by artifact rejection (using minimal/maximal allowed amplitude -75 µV/75 µV and marking 200 ms before and after events as bad). We employed a stop-signal locked segmentation, and baseline correction. Next, we computed separate averages for segments corresponding to failed stops and successful stops. The inhibitory ERPs were computed by subtracting the average stop-signal locked activity for failed stops from successful ones. Following a thorough examination of the grand average waveforms, we have identified specific latency intervals for further analysis. For the Stop N2 component, we extracted data from the time window of 166-286 ms, while for the Stop P3 component, data from the 211-271 ms time window was selected for export.

2.6. Transcranial direct current stimulation (tDCS)

The aim of brain modulation was to increase the relative activity of the right frontal cortex, which is linked with inhibitory control. A pair of circular sponges (25 cm2) soaked in saline solution, were used to deliver direct electrical current using STARSTIM-8, Neuroelectrics (www.neuroelectrics.com). According to the 10-20 system, the anode was positioned on the right dLPFC (F4) and the cathode on the left dLPC (F3). Unless it is a sham condition, a steady current of 2 mA was applied for 20 minutes (Kelley et al., 2017) (Fig. 2). The safety of this parameter has been shown in healthy subjects (Iyer et al., 2005).

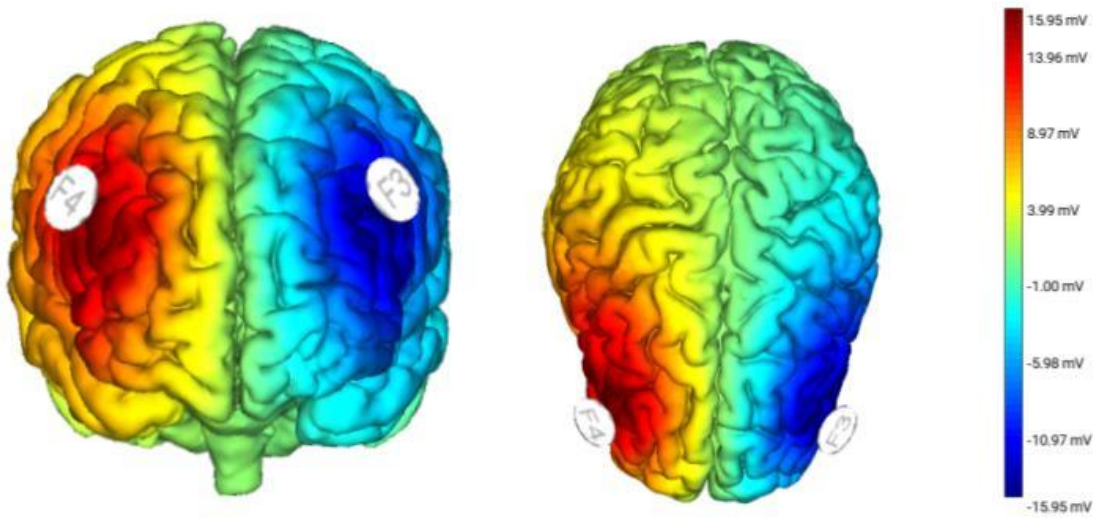

Figure 2. This illustration displays the positioning of the transcranial direct current stimulation electrodes and the measured electric fields viewed from the front and top perspectives. To administer transcranial direct current stimulation, a steady current of 2 mA was passed through two circular sponge electrodes (25 cm2 each), positioned on the scalp

over locations F4 (anode) and F3 (cathode) with the use of a saline solution. The maximum strength of the electric field reached 15.95 µV at the anodal electrode.

2.7. Procedure

This study was preregistered on Open Science Framework (https://osf.io/6k8up/?view_only=0cfdcc8e92f441e0905a456611a78762). A randomized, triple-blind, sham-controlled design was used in this research, with within-subject (time: pre-/post-assessment, condition: neutral/reward) and between-subject (group: active/sham tDCS) factors. Before and after the neural modulation session, the SST was completed. Participants were seated in a comfortable chair in a dimly lit testing room for the placement of EEG electrodes on the scalp sites after reading the information letter, verifying the inclusion and exclusion criteria, and completing the informed consent form when they arrived at our lab. Subsequently, resting-state EEG data was collected. It was recorded for 10 minutes in total with two blocks of five minutes sessions (EO/EC). They finished the questionnaires after recording the resting-state EEG. They then completed the first phase of the SST prior to the tDCS. Following that, individuals were assigned to either an active or sham tDCS. During the post-modulation evaluation, the same steps—resting-state EEG and the SST—were repeated. The intervention and pre-/post- assessments were conducted on the same day and lasted approximately five hours.

2.8. Statistical analyses

The analyses were conducted using SPSS 22 (IBM Corporation, n.d.) and R ("R software: a tool analysing experimental data," 2016). In addition to employing frequentist statistics, we also conducted Bayesian analyses for the main target of the study, which is FAA, using JASP (Team, 2023). Upon completing the calculations of the main variables, participants with missing values and outliers beyond 3 standard deviations (SD) from the mean were excluded in case of apparent erroneous data. Subsequently, a repeated measures ANOVA (2x2x2) was employed to examine the hypotheses. The electrophysiological variables investigated included FAA (EO/EC), the Stop P3, the Stop N2, in addition to the behavioral indices of inhibitory control. We also examined the correlation between baseline FAA and behavioral and brain activity indices of inhibitory control. For all frequentist statistical analyses, significance level was set at 0.05.

3. Results

3.1. Did the tDCS have an effect on resting-state frontal alpha asymmetry?

In order to examine the impact of the tDCS intervention on resting-state FAA scores, a repeated measures ANOVA with time (pre-/post-intervention) as the within-subjects factor and group (active/sham tDCS) as the between-subject factor was conducted. The results of the analysis revealed no significant interaction between the time and group factors concerning FAA, previously reported by Akil et. al (Akil et al., 2023). These results were also supported by Bayesian statistics (please see Table 4, 5, 6, and 7 in the supplementary materials).

We also conducted a correlation analysis to further explore the relationship between trait FAA and both behavioral and brain activity indicators of inhibitory control. In the reward condition, we observed a significant negative correlation between trait FAA F4-F3 (EO) and two key brain activity indices of inhibitory control, namely the Stop N2 ($r = -0.46$, $p < 0.01$) and P3 ($r = -0.30$, $p < 0.05$). For further information, refer to Table 1.

Table 1. Correlations between baseline FAA, SSRT, Stop N2, and Stop P3

Variable(s)		1	2	3	4	5	6	7	8	9
FAA F4-F3 (EO)										
FAA F4-F3 (EC)		0.32*								
	p value	0.009								
	N	65								
FAA F8-F7 (EO)		0.99	0.25*							
	p value	0.432	0.037							
	N	65	65							
FAA F8-F7 (EC)		0.13	0.65*	0.32*						
	p value	0.229	<0.001	0.007						
	N	65	65	65						
SSRT neutral		0.01	0.09	-0.01	-0.30*					
	p value	0.923	0.439	0.914	0.015					

	N	64	64	64	64					
SSRT reward		-0.01	0.13	0.01	-0.19	0.50*				
	p value	0.925	0.284	0.844	0.134	<0.001				
	N	64	64	64	64	64				
Stop N2 neutral		0.11	0.14	0.14	0.07	0.04	0.13			
	p value	0.396	0.275	0.288	0.578	0.739	0.322			
	N	59	59	59	59	59	59			
Stop N2 reward		-0.46*	0.07	0.22	0.26*	-0.04	0.18	0.88		
	p value	<0.001	0.600	0.084	0.045	0.761	0.157	0.507		
	N	59	59	59	59	59	59	59		
Stop P3 neutral		0.02	0.04	0.02	-0.02	-0.00	0.11	0.31*	0.52	
	p value	0.875	0.711	0.845	0.865	0.993	0.368	0.016	0.695	
	N	59	59	59	59	59	59	59	59	
Stop P3 reward		-0.30*	0.14	0.17	0.25	-0.13	0.22	0.11	0.71*	0.32*
	p value	0.019	0.269	0.192	0.055	0.307	0.081	0.398	<0.001	0.012
	N	59	59	59	59	59	59	59	59	59

3.2. Did the tDCS have an effect on the behavioral indices of inhibitory control?

To assess the effects of the tDCS intervention on inhibitory control, we conducted a repeated measures ANOVA using time (pre-/post-intervention) and condition (neutral/reward) as within-subjects factors, and group (active/sham tDCS) as the between-subject factor on SSRT scores. The results were presented in Figure 3, and inferential statistics are shown in Table 2. We found no significant effect of tDCS on the SSRT. However, there was a significant main effect of time on the SSRT ($F(1, 232) = 6.52$, $p = 0.011$, $\eta_p^2 = 0.004$). These findings indicate that inhibitory control decreases as time progresses, irrespective of the condition or group.

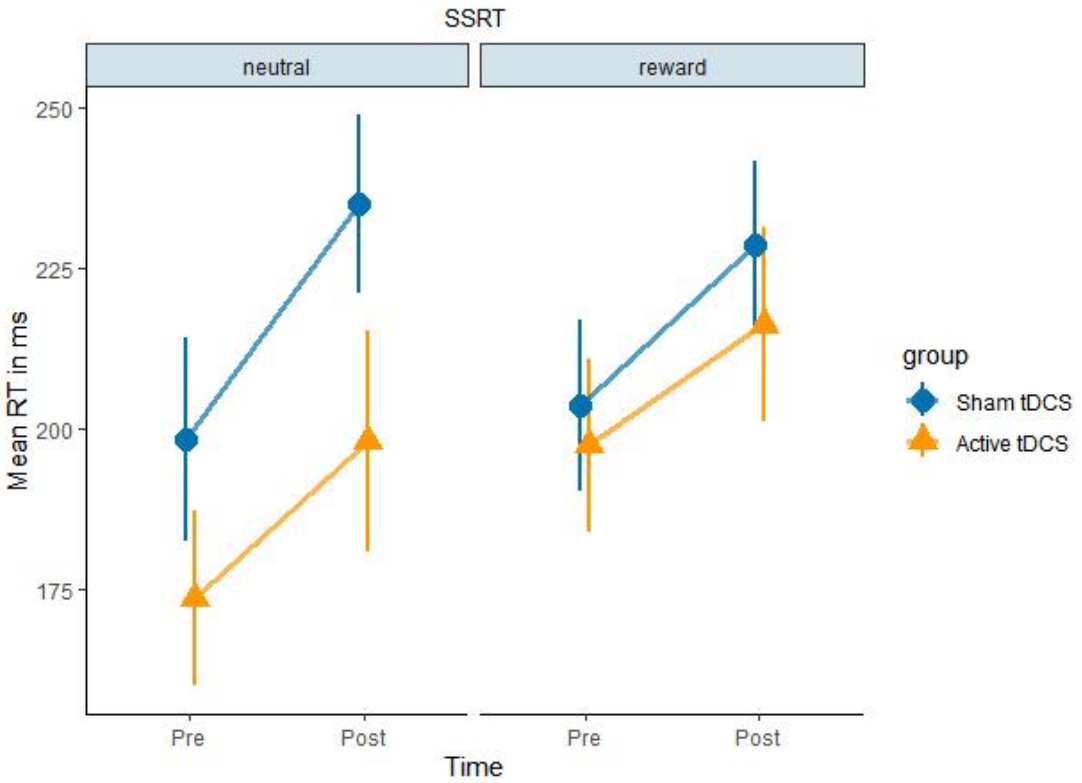

Figure 3. This figure displays the average stop-signal reaction times, considering the factors of time (pre-/post-intervention), condition (neutral/reward), and group (sham/active transcranial direct current stimulation). The error bars indicate standard errors. It illustrates that inhibitory control decreased from pre-assessment to post-assessment, regardless of condition and group factors. It is important to note that longer stop-signal reaction times represent decreased inhibitory control.

Table 2. Results of the SST

Variable(s) (N = 58)	Df	F	p	η_p^2
SSRT				
Time	1	6.52	0.011*	0.028
Condition	1	0.99	0.319	0.004
Group	1	3.82	0.051	0.016
Time x Condition	1	0.18	0.657	<0.001
Time x Group	1	0.19	0.670	<0.001
Condition x Group	1	1.10	0.294	0.004
Time x Condition x Group	1	0.02	0.883	<0.001
Error	232			

Note: Participants with missing values and erroneous data were excluded from the analyses.

3.3. Did the tDCS have an effect on the brain activity indices of inhibitory control?

In order to evaluate the impact of the tDCS intervention on the brain activity measures of inhibitory control, we performed a repeated measures ANOVA. This analysis included time (pre-/post-intervention) and condition (neutral/reward) as within-subjects factors, while group (sham/active tDCS) was the between-subject factor. The focus was on the Stop N2 and Stop P3 components. The interaction effect of time, condition, and group on the indices was found to be insignificant. They were displayed in Figure 4 and Figure 5, respectively. However, there is a statistically significant effect of the interaction between time and group on the Stop P3: $F(1, 57) = 7.18$, $p = 0.010$, $\eta_p^2 = 0.112$, as illustrated in Figure 6. More detailed results can be found in Table 3.

Table 3. Results of ERP models

Variable(s)	Df	F	p	η_p^2
Stop N2 at 166-188 ms. (F4) (N = 59)				
Time	1	1.58	0.214	0.027
Condition	1	0.27	0.602	0.005
Group	1	1.46	0.231	0.025
Time x Condition	1	1.75	0.191	0.030
Time x Group	1	0.25	0.613	0.005
Condition x Group	1	0.14	0.704	0.003
Time x Condition x Group	1	0.42	0.517	0.007
Error	57			
Stop P3 at 211-271 ms. (Cz) (N = 59)				
Time	1	0.97	0.327	0.017
Condition	1	1.44	0.234	0.025
Group	1	3.05	0.086	0.051
Time x Condition	1	7.18	0.010*	0.112
Time x Group	1	0.12	0.726	0.002
Condition x Group	1	0.05	0.818	0.001

Time x Condition x Group	1	0.08	0.775	0.001
Error	57			

Note: Participants with missing values and erroneous data were excluded from the analyses.

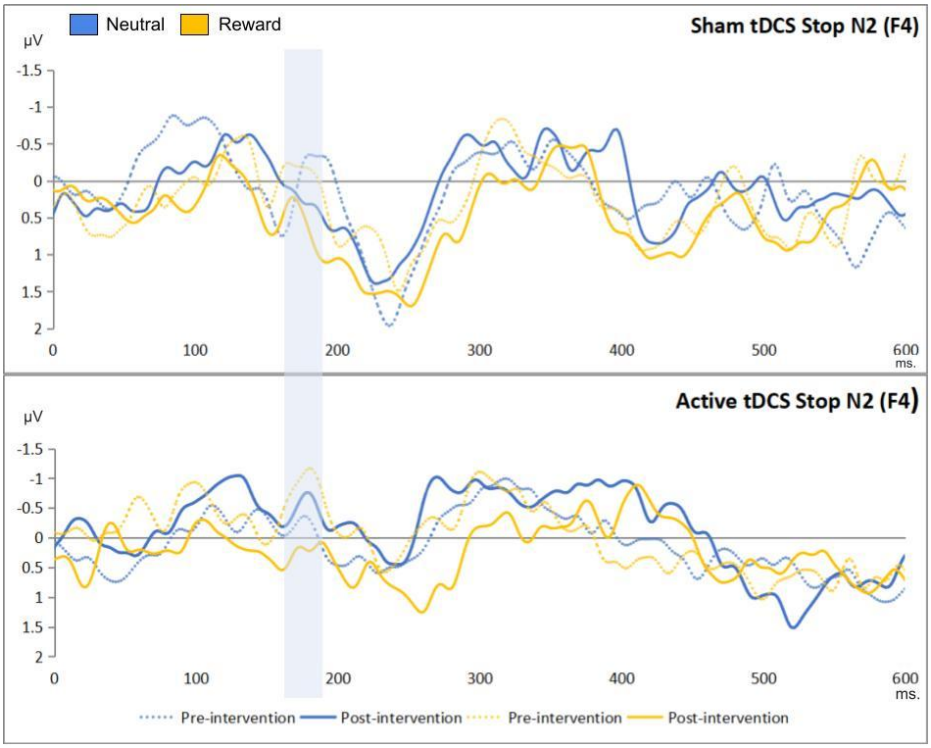

Figure 4. This figure shows the stop-signal locked event-related potentials during the stop signal task, effects of time, condition, and group on the Stop N2 (166-286 ms), based on successful inhibitions minus failed ones. The x-axes represent the time in milliseconds; the y-axes represent the Stop N2 scores in microvolts.

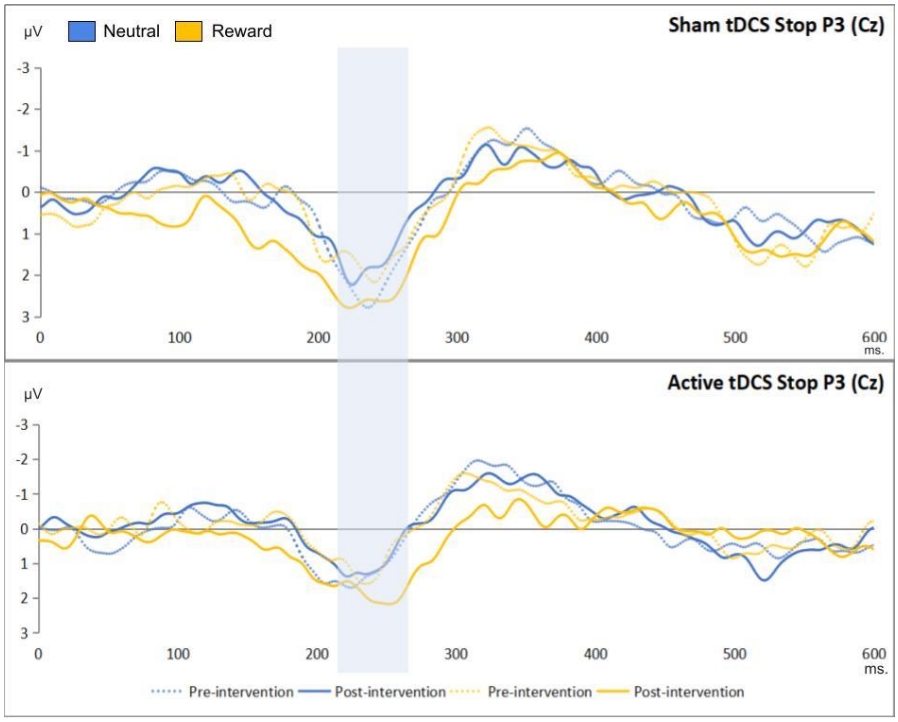

Figure 5. This figure shows the stop-signal locked event-related potentials during the stop signal task, the effects of time, condition, and group on the Stop P3 (211-271 ms), based on successful inhibitions minus failed ones. The x-axes represent the time in milliseconds; the y-axes represents the Stop P3 scores in microvolts.

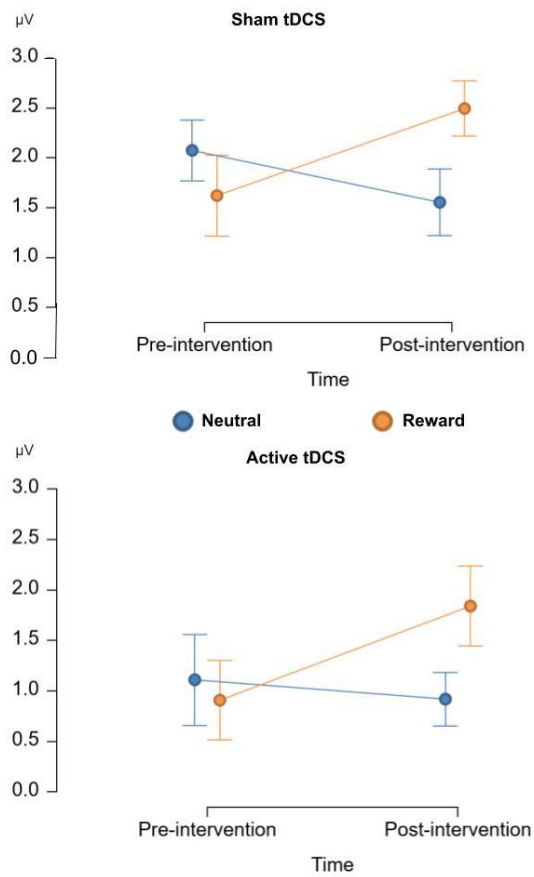

Figure 6. The figure shows the exact effect of time and group interaction on the Stop P3. The x-axes represent the time factor; the y-axes represent the Stop P3 in microvolts. The error bars illustrates standard errors. It indicates a higher inhibitory activity in the reward condition compared to the neutral condition.

4. Discussion

Our preregistered study aimed to explore the potential effect of tDCS on resting-state FAA, a promising transdiagnostic neuromarker for inhibition-related clinical conditions, and to investigate whether the effect of tDCS on inhibitory control is mediated by its influence on FAA. Contrary to our initial hypothesis, we did not observe any significant connections between tDCS and FAA, and there were no noticeable impacts on the behavioral and brain activity indicators of inhibitory control. Interestingly, greater right frontal brain activity compared to the left (indicating lower frontal alpha asymmetry) was found to be correlated with reduced early-onset inhibition (as evidenced by Stop N2), yet it was associated with heightened late onset inhibitory activity (as indicated by Stop P3). Furthermore, a noteworthy trend emerged wherein participants' SSRT showed a decline across all conditions and groups, with the concurrent rise in inhibitory brain activity, particularly prominent in the reward condition, as indicated by the stop-signal locked P3 component.

Previous research has suggested a potential influence of tDCS on the asymmetry of frontal brain activity (Kekic et al., 2017). However, these measures could be considered indirect due to the absence of comprehensive research into the direct impact of tDCS on the primary target, frontal asymmetry. One candidate measure for frontal asymmetry is the FAA. Nevertheless, our study did not find any support for the effect of tDCS on FAA, with direct measurement of resting states. The intricate nature of tDCS effects on brain activity, combined with the inherent individual variability in brain anatomy, may have contributed to the absence of significant findings in our research. More specifically, the path of electric currents during tDCS involves a multifaceted journey through different tissues and layers, with varying degrees of resistance and susceptibility to neural alteration. Each participant's unique brain structure, including factors like skull thickness and sulcal depth, could have resulted in divergent responses to tDCS (Laakso et al., 2015; Truong et al., 2013) (Opitz et al., 2015). Moreover, factors related to electrode positioning and properties may have played a role in shaping the outcomes. The size, shape, and conductivities of the electrodes, as well as the use of gels and saline solutions, may have influenced the distribution and intensity of the electric field (Saturnino et al., 2015). Furthermore, frontal tDCS is known to produce more variable electric fields compared to other types of tDCS (Laakso et al., 2016), adding further complexity to the neural adjustment processes. While our findings challenge the direct impact of tDCS on FAA, they underscore the importance of considering individual differences and optimizing stimulation protocols in future research.

Similarly, our investigation into the effect of tDCS on the various indices of inhibitory control yielded no significant results. The impact of tDCS on cognition and behavior

is notably variable, challenging the notion of a polarity-specific influence. While tDCS is theoretically expected to increase excitability under the anode and decrease it under the cathode, the actual cognitive and behavioral effects are far more complicated. Interestingly, some studies have even reported facilitatory effects associated with stimulation under the cathode, possibly attributed to noise reduction in specific networks, leading to improved performance (Jacobson et al., 2012). Alternatively, cathodal tDCS might inhibit a particular function as well, leading to enhanced performance in specific tasks, like faster reaction times (Tremblay et al., 2014). Numerous factors contribute to these contradictory outcomes. For example, the effects of prefrontal tDCS heavily depend on the state of the targeted neural network (Janacsek et al., 2015). In the online paradigm, tDCS influences networks already engaged in the task, while in the offline paradigm, it modifies neural activity beyond the stimulation period. Understanding these state-dependent effects is crucial for cognitive and behavioral studies, as factors like fatigue, task knowledge, and network connectivity can significantly influence the baseline neural state. Moreover, a recent meta-analysis (Schroeder et al., 2020) extensively examined the effects of tDCS on go/no-go and SST performance measures of inhibitory control in single-session designs. The findings revealed that the placement of electrodes significantly influences the outcomes. Specifically, tDCS targeting the right inferior frontal gyrus demonstrated a medium effect size, whereas a stimulation site over the dLPFC region showed an overall null effect. Variation in results was attributed to the positioning of the return electrode, with extracephalic placement differing from various positions across the head. These results underscore the critical importance of precisely targeting specific brain regions in tDCS research to achieve desired and consistent outcomes. Another plausible explanation could be attributed to the sample characteristics. Research on binge eating (Burgess et al., 2016; Kekic et al., 2017; Lapenta et al., 2014) suggests that tDCS primarily affects inhibitory control in samples with considerable room for improvement. This hypothesis proposes that individuals with relatively weaker inhibitory control at baseline may experience more pronounced enhancements following tDCS intervention. Conversely, in healthy individuals, the influence of tDCS may not predominantly target inhibitory activity but rather attentional bias (Akil et al., 2023).

Our correlation analysis revealed a significant connection between inhibitory brain activity during reward conditions and trait frontal brain asymmetry, as indexed by resting-state FAA before the neurostimulation. Precisely, greater right-sided frontal brain activity compared to the left side was linked to reduced initial inhibitory activity (Stop N2), likely emanating from the inferior frontal gyrus. However, it was also associated with heightened subsequent inhibitory control (Stop P3), which is thought to originate from the superior frontal gyrus. The brain is organized into functional networks, and the interaction between different regions is crucial for complex processes. The observed correlation might suggest a dynamic interplay between the inferior and superior frontal gyri in managing inhibitory control. Higher activity in one region may trigger or facilitate inhibitory control processes in another region. Furthermore, the higher right frontal brain activity might signify a compensatory mechanism. When early-onset inhibitory activity originating from the inferior frontal gyrus is compromised, the brain might engage the superior frontal

gyrus to enhance inhibitory control at a later stage. Alternatively, the nature and demands of the task being performed could influence how inhibitory control is exerted. Based on that, the brain's inhibitory processes might operate differently at different stages of a task such as at early-onset inhibitory activity, associated with the inferior frontal gyrus, and late onset inhibitory control involving the superior frontal gyrus to achieve optimal inhibitory control. It is important to note that the interpretation provided is speculative and would need to be validated through empirical research and neuroimaging studies. The brain is very complex, and multiple factors could contribute to the observed dissociation between brain activity and inhibitory control.

Lastly, based on the SST results, a notable reduction in inhibitory control was observed as time progressed, which aligns with expectations due to factors like tiredness and fatigue. However, the ERP results revealed an intriguing pattern in the reward context, where enhanced inhibitory activity in the brain (indexed by the stop P3) was observed as time progressed, relative to the neutral context. These results suggest that despite the absence of a significant time and condition interaction concerning SSRTs, the post-test reward block posed a stronger inhibitory challenge. As a consequence, participants displayed an adapted response marked by increased inhibition-related activity in the brain. This adaptive neurophysiological response may reflect the brain's capacity to dynamically adjust and allocate cognitive resources in response to varying levels of inhibitory demand. Consistent with our findings, prior studies have also observed increased N2 and P3 amplitudes during food-specific trials (Chami et al., 2019). In contrast, another study demonstrated that P3, but not N2, significantly decreased in obese participants across all Go/No-go task conditions compared to normal-weight controls, suggesting that P3 might serve as a more critical biomarker of inhibitory control deficits (Wang et al., 2022). However, it is important to note that variations in stimuli, paradigms, component timescales, and ERP analyses present challenges in synthesizing results across the existing literature. The diversity in methodologies utilized calls for caution in drawing definitive conclusions from the available evidence. Future research could benefit from standardized protocols and methodologies to address these complexities, enabling more robust comparisons and a deeper understanding of the neurophysiological underpinnings of inhibitory control in various populations.

Despite the valuable insights obtained from this research, several limitations require careful consideration. It is important to acknowledge that individual variations in brain anatomy might have contributed to the lack of significant effects observed. Additionally, the effectiveness of tDCS depends on various factors, including stimulation parameters (such as duration, intensity, and electrode placement) and target locations, as discussed. Although the chosen intervention parameters were based on existing literature and logical reasoning, alternative stimulation settings might have yielded different outcomes. Using neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), could provide valuable insights into the neural changes induced by tDCS. To gain a deeper comprehension of the impact of tDCS on FAA in relation to inhibitory control, it would be beneficial to carry out studies involving more diverse participant samples. Therefore, by carefully

considering individual brain differences, electrode-related factors, and tDCS parameters, researchers can enhance the reproducibility and reliability of tDCS studies on prefrontal cortex and inhibitory control.

Conclusion

In our study, we aimed to explore the effects of transcranial direct current stimulation on frontal brain asymmetry and whether the effects of the transcranial direct current stimulation intervention on inhibitory control-related indices could be attributed to changes in frontal alpha asymmetry. The results indicated that transcranial direct current stimulation did not yield significant effects on frontal alpha asymmetry. However, we made a notable discovery: there was a dissociation between baseline frontal alpha asymmetry and brain activity indices of inhibitory control. Furthermore, the stop signal reaction times consistently increased over time, suggesting reduced inhibitory control. Intriguingly, we also observed a simultaneous increase in inhibitory control-related brain activity, particularly in the post-stimulation reward condition. This finding probably indicates a dynamically adaptive response in the presence of food stimuli. Consequently, although the tDCS yielded negative outcomes, our study reveals that frontal alpha asymmetry still holds the potential to predict neural responses associated with within-task events. This intricate interplay underscores the dynamic relationship between frontal alpha asymmetry and inhibitory processes.

Data Availability Statement

All data and codes can be found on our online public repository.

Ethics Statement

The study received approval from the Research Ethics Committee at Eötvös Loránd University (project number: 2020/403) and was conducted following the principles of the Declaration of Helsinki and its later amendments.

Authorship Statement

AMA, RC, TN, ZD, DN, and AL Designed research; AMA Performed research; AMA and AL Analyzed data; AMA Wrote the paper

Funding

This research was funded by the Hungarian National Research, Development, and Innovation Office (https://nkfih.gov.hu; grant no. K131635).

Conflict of Interest

Authors report no conflict of interest.

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