Heliyon 9 (2023) e21074

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Modulation of smoker brain activity and functional connectivity by tDCS: A go/no-go task-state fMRI study

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ARTICLE INFO

Keywords:
Addiction
Behaviour control
Functional connectivity
Functional neuroimaging
Nicotine dependence
Seed-based analysis
Transcranial direct current stimulation

ABSTRACT

Background: Transcranial direct current stimulation (tDCS) applied to particular brain areas may reduce a smoker's smoking cravings. Most studies on tDCS mechanisms are performed on brains in the resting state. Therefore, brain activity changes induced by tDCS during tasks need to be further studied.

Methods: Forty-six male smokers were randomised to receive anodal tDCS of the left/right dorsolateral prefrontal cortex (DLPFC) or sham tDCS. A go/no-go task was performed before and after stimulation, respectively. Brain activity and functional connectivity (FC) changes during the task state before and after tDCS were used for comparison.

Results: This study revealed that the anodal stimulation over one DLPFC area caused decreased activity in the ipsilateral precuneus during the go task state. Right DLPFC stimulation increased the FC between the bilateral DLPFCs and the right anterior cingulate cortex (ACC), which is closely associated with cognition and inhibition of executive functions. Additionally, the study showed variations in brain activity depending on whether the anode was positioned over the right or left DLPFC (R-DLPFC or L-DLPFC).

Conclusion: During the go task, tDCS might exert a suppressive effect on some brain areas, such as the precuneus. Stimulation on the R-DLPFC might strengthen the FC between the right ACC and the bilateral DLPFCs, which could enhance the ability of behavioural decision-making and inhibition to solve conflicts effectively. Stimulating the L-DLPFC alone could increase the FC of bilateral DLPFCs with some brain regions associated with response inhibition.

1. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation (NIBS) that administers weak currents to modulate the activity of neurons in the cerebral cortex through scalp electrodes [1]. Transcranial direct current stimulation is a safe and harmless technology, and there is only a slight pain sensation. It is beneficial to basic and applied research as it ameliorates certain neuropsychiatric dysfunctions. Previous experiments have indicated that tDCS is useful in the treatment of substance use disorders (SUDs), such as drug [2], nicotine [3], alcohol [4] and food addiction [5]. The mechanism of tDCS reducing cravings is still being explored.

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https://doi.org/10.1016/j.heliyon.2023.e21074
Received 21 November 2022; Received in revised form 8 August 2023; Accepted 13 October 2023
Available online 17 October 2023

Chronic exposure to abusive drugs could induce reward circuit neuronal plasticity, which presents as changes in gene transcription, membrane excitability and neuronal morphology [6]. Plasticity may also be triggered by the after-effects of tDCS, such as long-term potentiation (LTP) and long-term depression (LTD), to correct abnormal plasticity changes [7]. Neuroimaging evidence further demonstrates that neuronal circuits involved in reward, incentive motivation and inhibitory control would undergo reprogramming during the addiction process [8]. After stimulation, increased cortical excitability might promote the reconfiguration of functional brain networks, potentially contributing to improving cognitive function [9] to reduce the craving for an addictive substance. The effects of tDCS on the local and overall human brain networks are not well understood yet [10], and much speculation for mechanism remains to be verified by neuroimaging.

In addiction-related studies of tDCS, the dorsolateral prefrontal cortex (DLPFC) has been frequently studied as a stimuli target [2–4]. DLPFC is an advanced function brain region responsible for social cognition functioning of self-control, which participants in some advanced cognition behaviours processing, including craving, motivation and action. Additionally, DLPFC is a critical area of the mesocorticolimbic system, providing top-down signals [11].

Integration of tDCS with magnetic resonance imaging (MRI) techniques provides a tool to directly visualise neuronal function while monitoring brain state [12]. Therefore, it enables researchers to study how stimulation modulates targeted brain regions and how tDCS regulates activity throughout the brain in the context of anatomical and functional connectivity (FC). Blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) depicts changes in deoxyhemoglobin concentration with task-induced or spontaneous modulation of neural metabolism; it has been commonly used to make inferences about FC [13]. Seed-based connectivity analysis is a method for examining the presence and degree of FC between brain regions after processing fMRI data, allowing for focus on brain regions of interest.

Most of the previous functional magnetic resonance imaging fMRI experiments about tDCS are conducted when the brain is resting. However, this study introduced a classic go/no-go paradigm. Go/no-go tasks are frequently used to assess behavioural inhibition [14]. It has been suggested that human brain functional networks in rest and task states are roughly similar, but relatively small differences exist [15,16]. Some scholars have argued that task-state FC can better characterise an active flow network than FC in a resting state [15]. Human cognitive activities are highly dynamic, so there is a need to reveal the effects of tDCS on brain activity more comprehensively by utilising task-related experiments. In addition, it is suggested that outcomes of the left and the right anodal stimulation are not the same. Generally, anodal stimulation leads to an increase in cortical excitability, whereas cathodal stimulation reduces cortical excitability. If left and right DLPFC (L-DLPFC and R-DLPFC) receive stimulation simultaneously, there is a high possibility of obtaining a mixed bilateral stimulation result. Therefore, this study aimed to explore the differences in FC between bilateral DLPFCs and the whole brain after stimulation using the seed-based analysis.

2. Materials and methods

2.1. Participants

All 46 recruitment participants were right-handed adult male smokers. The participants were randomly assigned to one of three groups: LEFT (n = 17), RIGHT (n = 16), SHAM (n = 13), and demographical characteristics are presented in Table 1. The inclusion criteria were as follows: 1) healthy men with no underlying diseases; 2) aged 18–55 years; 3) at least 2 years of smoking history and 4) currently or previously smoked five cigarettes or more per day. Exclusion criteria were as follows: 1) history of major neurological disorders (e.g., brain tumour, seizure, dementia, Parkinson's disease and depression); 2) history of head trauma or surgery; 3) use of nicotine products (except cigarettes) or psychotropic drugs; 4) history of other substance addiction and 5) contraindications discovered during the MRI examination. The severity of nicotine dependence was assessed using the Fagerström Test for Nicotine Dependence [17] during the recruitment phase, and the pack–year number of cigarette smoking (pack–year = the number of packs per day × duration of smoking) was calculated.

This study was conducted at China's First Affiliated Hospital of the University of Science and Technology (USTC). The informed consent was signed by all study participants before the experiment, and a certain monetary reward was delivered after the experiment. Ethical approval was obtained from the Hospital Ethic Committee (number 2020-KY671), and research procedures followed the principles of the Declaration of Helsinki.

Table 1
Demographical characteristics.

	LEFT	RIGHT	SHAM	All	*v*	*F*	*p*
Age(years)	33.7 ± 10.7	33.4 ± 9.5	29.5 ± 5.8	32.4 ± 9.1	2	0.941	0.398
Duration (years)	11.1 ± 8.4	13.1 ± 9.2	10.2 ± 5.3	11.5 ± 7.9	2	0.511	0.603
PY	10.8 ± 12.8	12.1 ± 15.1	7.8 ± 9.7	10.4 ± 12.7	2	0.408	0.668
FTND	3.5 ± 2.4	3.4 ± 2.4	3.8 ± 2.8	3.6 ± 2.5	2	0.064	0.938

± : mean ± S.D.; PY: pack-year of cigarette smoking = the number of packs per day × cigarette usage; FTND: Fagerstrom Test for Nicotine Dependence; v, F, p: the v, F, p value of Analysis of Variance (ANOVA) among three groups.

2.2. Procedures

This study was a double-blind, randomised, sham-controlled trial. The study flow is outlined in Fig. 1a. The participants were instructed to refrain from smoking 2 hours before the experiment, and then they practiced the go/no-go task to proficiency outside of the MRI examination room. Following these preparations, participants entered the examination room and were examined by routine cranial MRI sequences to visualise their brain's health state at the beginning of the experiment. When a participant laid on the scanning bed, they were handed a keypress and were required to respond to the pictures in the reflective mirror as quickly as possible with the keypress; a computer measured the reaction time (RT) and error rate. This task was also performed concurrently with MRI scanning. Participants received either tDCS or sham stimulation for 20 minutes after the go/no-go task (G_1). During stimulation, participants were asked to keep their eyes closed, sit calmly, not think of anything and not fall asleep. Participants returned to the scanning bed and completed the go/no-go task (G_2) again. The go/no-go task was performed in the same manner as previously, and each go/no-go task lasted approximately 8 minutes. The indicators included DLPFC, whole-brain voxels, brain MRI characteristics and go RT or no-go error rate.

2.3. Transcranial direct current stimulation

Transcranial direct current stimulation was delivered by the Soterix 1 × 1 stimulator (Soterix Medical Inc., NY, USA). The tDCS applied a weak direct current to the scalp via two 5 × 7 cm saline-soaked surface sponge electrodes. In active and sham stimulation conditions, the cathode was placed over the contralateral supraorbital area [16]. It has previously been demonstrated that supraorbital region cathodal stimulation did not cause a noticeable effect on experimental results [18]. The anodal electrode was placed over the L-DLPFC (F3, 10–20 electroencephalography (EEG) system) in the LEFT group. In the RIGHT group, the anodal was placed over the R-DLPFC (F4, 10–20 EEG system). In the SHAM group, the anodal was placed over F3 or F4. For the LEFT and RIGHT groups, a constant current of 2 mA intensity was applied for 20 minutes. However, for the sham treatment, a current of 2 mA faded in over 30 s and then switched off.

2.4. Image acquisition

Imaging was performed by a GE 3T Discovery 750w scanner using an eight-channel head coil. Individual high-resolution structural images were obtained at the beginning. Functional blood oxygen level-dependent (BOLD) images in each task scan were acquired using the T2 weighted echo planar imaging sequence (40 axial slices, slice thickness = 4 mm, TR = 2000 ms, TE = 30 ms, FA = 90°, Matrix = 64 × 64, FOV = 240 × 240).

2.5. Go/no-go task

During the entire MRI session, participants were asked to focus on a screen by a head coil using a reflective mirror. A white letter 'X' or 'K' appeared randomly on a black screen with the same frequency, shown in Fig. 1b. Participants were instructed to press the button as soon as they saw the letter 'X' and not to press the button when they saw the letter 'K'. Each word appeared on the screen for 1

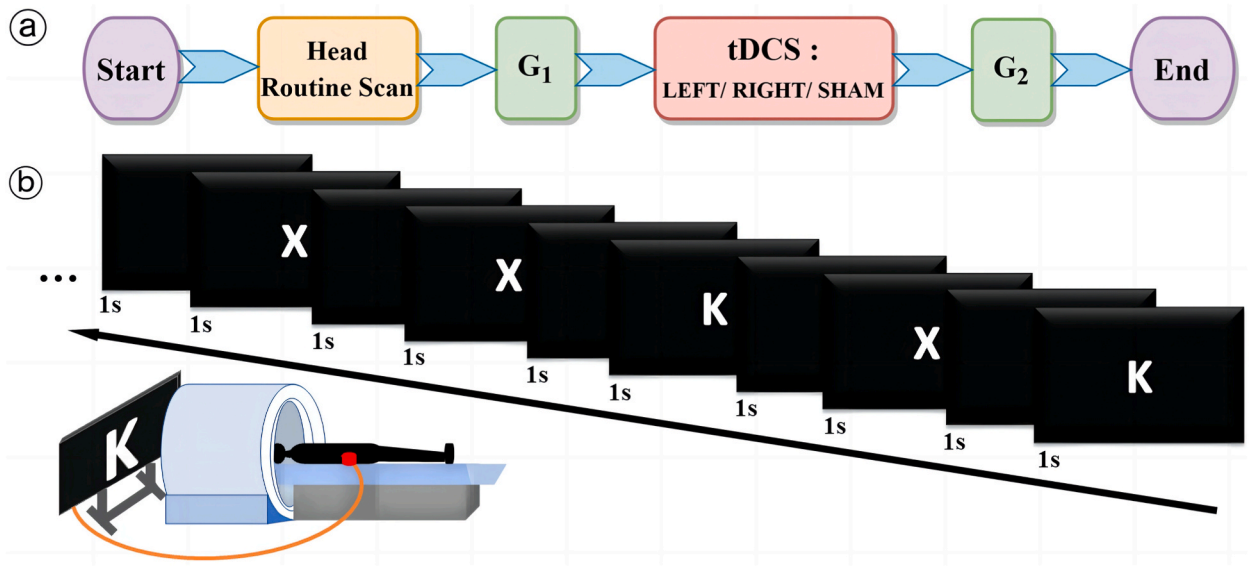

Fig. 1. The experimental design of this study a. The experiment flow diagram ($G_{1,2}$: Go/No Go task). b. Schematic of the Go/No Go task operation.

Table 2
Seed based connectivity analysis of No-Go task (voxel-lever).

Decreased
a. L-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Cingulate_Mid	R	5.16	0.000	6	-6	42
Temporal_Pole_Sup	L	5.04	0.000	-36	6	-24
Parietal_Inf	L	3.98	0.001	-36	-42	45
Postcentral	R	3.66	0.001	48	-27	45
RIGHT group G2(compared with intragroup G1)						
Temporal_Sup	L	5.18	0.000	-51	-9	0
Supp_Motor_Area	L	4.35	0.000	0	3	48

b. R-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Temporal_Pole_Sup	L	6.48	0.000	-36	6	-24
Temporal_Mid	R	4.82	0.000	57	-45	3
Supp_Motor_Area	R	4.76	0.000	12	-15	66
Postcentral	L	4.74	0.000	-30	-33	63
Temporal_Sup	R	4.5	0.000	48	-27	3
Parietal_Sup	R	4.21	0.000	18	-54	60
RIGHT group G2(compared with intragroup G1)						
Caudate	L	7.53	0.000	-12	3	9
Temporal_Pole_Sup	L	5.21	0.000	-36	27	-33
RIGHT group G2(compared with SHAM group G2)						
Temporal_Mid	L	2.7	0.005	-45	-12	-21
Temporal_Mid	R	2.39	0.011	69	-9	-12
Precentral	L	2.36	0.012	-60	0	33
Frontal_Sup_ Medial	L	2.34	0.012	-3	66	15

Increased
a. L-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Frontal_Med_Orb	R	5.25	0.000	9	57	-15
OFCmed	L	4.57	0.000	-18	36	-27
Frontal_Sup_Medial	R	4.33	0.000	12	27	54
Lingual	L	4.20	0.000	-12	-48	-9
RIGHT group G2(compared with intragroup G1)						
Thalamus	L	5.08	0.000	-3	-21	-3
Cingulate_Ant	R	4.31	0.000	15	36	12
LEFT group G2(compared with SHAM group G2)						
Temporal_Pole_Mid	R	3.90	0.000	24	9	-39
Cerebelum_4_5	L	3.56	0.001	-15	-30	-27
OFCmed	L	3.31	0.001	-15	33	-24

b. R-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Cerebelum_7b	L	8.38	0.000	-39	-69	-57
Frontal_Sup_2	R	4.50	0.000	33	60	-6
Cerebelum_Crus1	L	4.28	0.000	-36	-66	-27
RIGHT group G2(compared with intragroup G1)						
Precentral	R	6.05	0.000	30	-18	48
Cingulate_Ant	R	4.03	0.001	18	39	9
RIGHT group G2(compared with SHAM group G2)						
Cerebelum_Crus1	L	3.49	0.001	-54	-48	-39

AAL: Automated Anatomical Labeling; H: left (L) or right (R) hemisphere; t, p: t and p values(corrected) from a *t*-test of the peak voxel; MNI: Montreal Neurological Institute.

second, followed by a black screen for 1 second. In the go/no-go task, the inhibitory ability was measured by the error rate of no-go trials and the median RT of go trials [19], as shown in Fig. 1.

2.6. MRI data processing

Pre-processing. Raw fMRI data was established using SPM12 and Matlab2018b software. For the fMRI images of each subject, the time layer corrections and head movement corrections were conducted. Exclusion criteria included a head motion larger than 1.5 mm maximum displacement in any direction or an angular rotation greater than 1.5 throughout the scan (no participant was excluded). The corrected images were registered with the standard EPI template imaging provided by the SPM software. The images were spatially normalised to the MNI template, and their resampled voxel size as $3 \times 3 \times 4$ mm^3 voxels. Normalised images were spatially smoothed with a 6 mm full-width-at-half-maximum Gaussian kernel to decrease spatial noise.

Blood oxygen level-dependent analysis. The images after pre-processing were estimated with the model using SPM12, including 1-level and 2-level. In the 1-level parameters model, which included G1 and G2, we regarded head-movement parameters produced by head-movement correction as a regressor and put it into the model. Multiple regressions design matrix of all conditions (G1 and G2) of each subject was constructed using a linear basic regression model. In the 2-level, a flexible factorial design was utilised to build the parameters model on the based on the 1-level. After the model estimation, we performed a *t*-test with a false discovery rate (FDR) correction. Statistical thresholds for correlation analyses were set at $p < 0.05$ (two-tailed) after FDR correction (voxel-level significance was defined as $p < 0.05$). Finally, nuisance variables were regressed out, including head motions, global mean signals, white matter signals and cerebrospinal fluid signals. T-values of statistically significant brain regions (larger than 50 voxels) were recorded according to the AAL partition template.

Seed-based connectivity analysis. Seed-based analysis of task-state FC was conducted using SPM12 and CONN21 software. The L-/R-DLPFC was defined as a seed, a spherical region of interest (ROI) (10 mm radius) centred on the point of origin for L-/R-DLPFC within the MNI space. Pre-processing images were imported into CONN to set conditions, including G1 and G2. Seed-to-voxel analysis was performed to assess FC in the multivariate regression method, and the mean time series between the seed point and the whole-brain voxel was obtained. Pearson's correlation coefficients were computed between the mean time series of the seed region and the time series of each whole-brain voxel. The correlation coefficients were converted into z-values using Fisher's r-to-z transformation to improve their normality. One-sample t-tests analyzed the z-values to identify brain regions that exhibited significant positive or negative correlations with the seed region within each group. The significance level of one-sample t-tests was determined by the cluster-forming threshold of p voxel <0.001 with a family-wise error rate (FEW) corrected cluster of $p < 0.05$.

2.7. Behavioural assessment

In the go/no-go task, the RT of each go stimuli and the error rate of no-go stimuli were recorded by a computer. Intragroup differences before and after intervention were evaluated. In addition, participants' discomfort reactions and effect feedback were also documented after stimulation.

2.8. Statistical analysis

All statistical analysis was performed using the SPSS version 25.0 software (IBM Corp. Silicon Valley, CA, USA). Continuous variables were expressed as mean ± deviation and were compared using the paired *t*-test or analysis of variance (ANOVA) as appropriate. For the go RT and the no-go error rate, post hoc pairwise comparisons were utilised to test for pairwise differences and were Bonferroni corrected. The p-value of <0.05 was considered statistically significant. Categorical variables were expressed as counts (percentages) and were compared using the chi-square test. A two-tailed p-value of <0.05 was considered statistically significant.

3. Results

3.1. Correlation between DLPFC and whole-brain voxels

The variations in brain areas activated and seed-based analyses between, before and after sham stimulation in the SHAM group's go/no-go test were not statistically significant ($p > 0.05$). In the no-go task of the RIGHT group during G2, compared with G1, FC substantially increased between L-DLPFC and two brain regions, including the thalamus (corrected $p = 0.000$) and anterior cingulate (corrected $p = 0.000$). The FC significantly decreased between L-DLPFC and two brain regions, including the superior temporal (corrected $p = 0.000$) and supplementary motor areas(corrected $p = 0.000$). Furthermore, FC substantially increased between R-DLPFC and two brain regions, including precentral (corrected $p = 0.000$) and anterior cingulate (corrected $p = 0.001$), and FC significantly decreased between R-DLPFC and two brain regions, including caudate (corrected $p = 0.000$) and superior temporal pole (corrected $p = 0.000$) (Table 2). In the no-go task of the LEFT group during G2, compared with G1, FC substantially increased between L-DLPFC and four brain regions (corrected $p < 0.05$) and between R-DLPFC and three brain regions (corrected $p < 0.05$). The FC significantly decreased between L-DLPFC and three brain regions (corrected $p < 0.05$) and between R-DLPFC and six brain regions (corrected $p < 0.05$) (Table 2).

After stimulation treatment, FC was significantly increased between L-DLPFC and three brain regions (corrected $p < 0.05$) in the

no-go task of the LEFT group compared to that of the SHAM group. FC was significantly increased between R-DLPFC and Cerebelum_Crus1 (corrected $p < 0.05$) in the no-go task of the RIGHT group compared to that of the SHAM group. Moreover, FC was significantly decreased between R-DLPFC and four brain regions (corrected $p < 0.05$) in the no-go task of the RIGHT group compared to that of the SHAM group (Table 2).

In the go task of the RIGHT group during G2, compared with G1, FC substantially increased between L-DLPFC and four brain regions and between R-DLPFC and three brain regions. Additionally, the FC significantly decreased between L-DLPFC and one brain region and between R-DLPFC and one brain region (Table 3). However, in the go task of the LEFT group during G2, compared with G1, there was no substantial improvement of FC between R-DLPFC and whole-brain voxels (Table 3).

Table 3
Seed based connectivity analysis of Go task (voxel-lever).

Decreased
a. L-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Cerebelum_8	R	3.99	0.001	9	-69	-33
Calcarine	R	3.52	0.002	15	-72	3
RIGHT group G2(compared with intragroup G1)						
Temporal_Pole_Sup	R	4.43	0.000	45	12	-18
LEFT group G2(compared with SHAM group G2)						
Occipital_Sup	L	3.21	0.001	-6	-105	9
Parietal_Sup	L	3.18	0.001	24	-69	66
Vermis_8	/	2.41	0.010	-39	-75	-9
Occipital_Inf	L	2.29	0.014	-18	21	21

b. R-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Supp_Motor_Area	R	5.08	0.000	12	-3	54
Occipital_Sup	R	4.84	0.000	18	-93	21
RIGHT group G2(compared with intragroup G1)						
Frontal_Inf_Tri	R	4.99	0.000	57	36	9
RIGHT group G2(compared with SHAM group G2)						
Temporal_Pole_Mid	R	2.77	0.004	33	15	-36
Frontal_Sup_2	L	2.49	0.009	-18	24	66

Increased
a. L-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
LEFT group G2(compared with intragroup G1)						
Frontal_Sup_2	R	4.69	0.000	21	21	54
Cingulate_Mid	R	4.10	0.000	3	-42	39
RIGHT group G2(compared with intragroup G1)						
Occipital_Sup	R	9.97	0.000	18	-93	6
Occipital_Inf	L	5.33	0.000	-42	-66	-6
Precentral	R	5.15	0.000	18	-21	78
Cerebelum_Crus1	L	4.43	0.000	-30	-84	-21

b. R-DLPFC as the seed

Region Label (AAL Atlas)	H	*t*	*p*	MNI coordinates		
				x	y	z
RIGHT group G2(compared with intragroup G1)						
Frontal_Med_Orb	L	4.40	0.000	0	48	-15
Paracentral_Lobule	L	3.91	0.001	-6	-24	78
Calcarine	R	3.80	0.001	9	-66	15
RIGHT group G2(compared with SHAM group G2)						
Parietal_Inf	L	3.10	0.002	-60	-36	42
Frontal_Inf_Tri	L	2.56	0.007	-36	21	9
Occipital_Mid	L	2.39	0.011	-27	-69	27
Cuneus	R	2.35	0.012	15	-78	30

AAL: Automated Anatomical Labeling; H: left (L) or right (R) hemisphere; t, p: t and p values(corrected) from a *t*-test of the peak voxel; MNI: Montreal Neurological Institute.

After stimulation treatment, FC was significantly increased between R-DLPFC and four brain regions (corrected $p < 0.05$) in the Go task of the RIGHT group compared to that of the SHAM group, and FC was significantly decreased between R-DLPFC and two brain regions (corrected $p < 0.05$). In addition, FC was significantly decreased between L-DLPFC and four brain regions (corrected $p < 0.05$) in the Go task of the LEFT group compared to that of the SHAM group (Table 3).

3.2. Brain MRI characteristics

LEFT group. Some brain areas, such as the left middle occipital gyrus, left precuneus and left crus I of the cerebellar hemisphere, did exhibit a lower BOLD signal (corrected $p < 0.05$) in the go trials during G2 than G1, as shown in Fig. 2a. In the no-go trials of the LEFT group, compared with G1, there was no significant change in the BOLD signal in the brain area during G2.

RIGHT group. Some brain regions exhibited a lower BOLD signal during the go trials, including the right precuneus and the left middle occipital gyrus (corrected $p < 0.05$) (see Fig. 2b). The BOLD signal increased during the RIGHT group's no-go trials, including the left superior temporal gyrus and lobule IV and V of the cerebellar hemisphere (corrected $p < 0.05$) during G2 instead of G1.

After stimulation treatment, compared to SHAM group, the region where the BOLD signal decreases were right thalamus, right lingual gyru, left lobule IV, V of cerebellar hemisphere and left crus I of the cerebellar hemisphere in LEFT group (corrected $p < 0.05$), and the region where the BOLD signal increases were right parahippocampal gyrus and left middle occipital gyrus (corrected $p < 0.001$) (Fig. 2c). The region where the BOLD signal decreases were left superior temporal gyrus, right lobule III of cerebellar hemisphere in RIGHT group compared to SHAM group (corrected $p < 0.001$) (Fig. 2d).

3.3. Go RT or no-go error rate

There was no statistically difference in the go RT ($F(2,43) = 1.188$, $p = 0.315 > 0.05$) and the no-go error rate ($F(2,41) = 1.284$, p

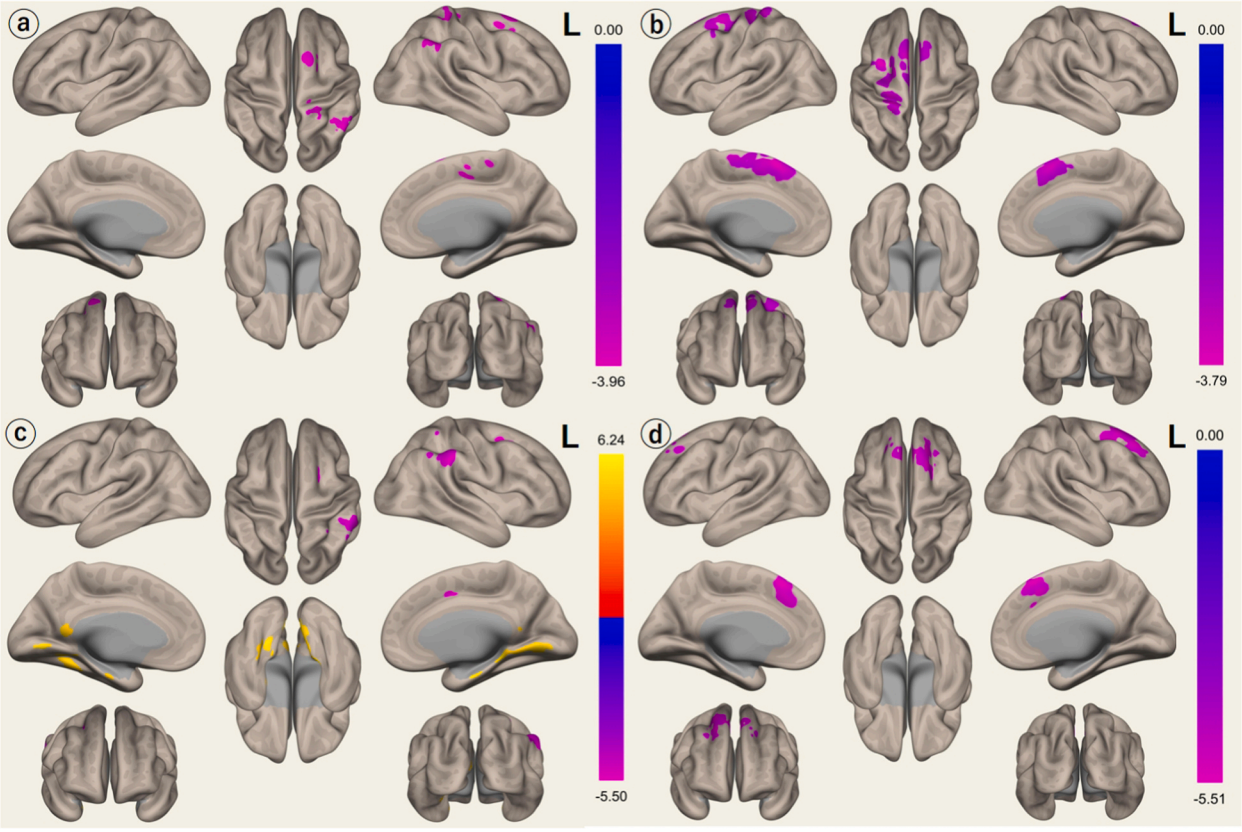

Fig. 2. Brain MRI characteristics a. LEFT group (corrected $p < 0.05$); The region where the BOLD signal decreases were left middle occipital gyrus, left precuneus, and left crus I of the cerebellar hemisphere; b. RIGHT group (corrected $p < 0.05$); The region where the BOLD signal decreases were the right precuneus and left middle occipital gyrus. **c.** Comparison of LEFT group and SHAM group after stimulation; The region where the BOLD signal decreases were right thalamus, right lingual gyru, left lobule IV, V of cerebellar hemisphere and left crus I of the cerebellar hemisphere (corrected $p < 0.05$); The region where the BOLD signal increases were right parahippocampal gyrus and left middle occipital gyrus (corrected $p < 0.001$); **d.** Comparison of RIGHT group and SHAM group after stimulation; The region where the BOLD signal decreases were left superior temporal gyrus, right lobule III of cerebellar hemisphere (corrected $p < 0.001$).

$= 0.288 > 0.05$) among the three groups before stimulation. There was a difference in RT between the three groups after stimulation ($F(2,43) = 3.847$, $p = 0.029 > 0.05$). And the further pairwise comparisons showed that there was a difference between RIGHT group and SHAM group ($p = 0.008 < 0.05$), but there was no significant difference between LEFT group and SHAM group ($p = 0.106 > 0.05$). There was no difference in error rate among the three groups after stimulation ($F(2,41) = 1.301$, $p = 0.283 > 0.05$). (see Fig. 3).

3.4. Assessment of participant satisfaction

All participants recorded their physiological experiences after the experiment. The findings showed that 39.4 % of participants had no feeling, 33.3 % had stinging, 21.2 % had itching and a few had burning, discomfort, tiredness or exhaustion on their scalp. A total of 94.1 % (16/17) of the LEFT group participants, 62.5 % (10/16) of RIGHT group participants and 30.8 % (4/13) of SHAM group participants believed that the microcurrent had momentarily suppressed their desire to smoke (LEFT group vs SHAM group, $p < 0.05$; RIGHT group vs SHAM group, $p < 0.05$; RIGHT group vs LEFT group, $p > 0.05$). The current's stimulation intensity was rated as satisfactory by all participants.

4. Discussion

Blood oxygen signals were reduced significantly in some brain areas post-stimulation compared with pre-stimulation, irrespective of the LEFT or RIGHT group's go task. The results indicated that tDCS over the DLPFC has a negative regulatory role in activating certain ipsilateral brain regions during the go task, such as the precuneus. The precuneus is one of the critical regions of the Default Mode Network (DMN) and may play an essential role in social cognition and introspective processing [20]. Spontaneous intrinsic activity in the DMN is often attenuated during attention-demanding cognitive tasks [21]. However, in this experiment, the reason for the decreased BOLD signal in the precuneus region is not the task itself but the applied current. Regardless of the resting state or task state, the anti-correlated networks (AN) have a significant negative relation with DMN [9]. The DLPFC is an important hub of the AN, so the anodal stimulation over the DLPFC could modulate the activation of DLPFC positively and DMN negatively. Additionally, this study also validated that there were differences in brain activity when the anode was placed alone over left or right DLPFC.

Behavioural inhibition is one of the executive functioning basics. The go/no-go paradigm often focuses on the result of no-go stimuli, which embodies the inhibitory effort necessary for brain responses to forbidden stimuli [22]. It is similar to the process that the brain utilises to inhibit smoking urges. According to previous studies, no-go signal processing would activate mostly the right network, which involves the dorsolateral and inferior frontal cortex, inferior parietal lobule, sensory-motor cortex (SMC), anterior cingulate cortex (ACC) and insula cortex [22]. Among patients with SUD, imaging studies consistently reported hypoactivation in frontal cortical areas associated with cognitive control [23], notably the dorsal anterior cingulate cortex (dACC), DLPFC and right inferior frontal gyrus [24]. This study's findings agree with previously reported experimental observations. It was observed that there were more connections between right ACC and bilateral DLPFC in the second no-go experiment of the RIGHT group than before, and networks of related information pathways were strengthened.

One highly influential study proposed that when ACC monitors or detects the presence of conflict, it conveys this information to areas such as the DLPFC, which adjusts the level of cognitive control accordingly [25]. In this model, the adjustments in the level of cognitive control led to better resolution of the conflict and could enhance performance should participants face conflict again [25]. Go/no-go tasks, as a means to assess behavioural inhibition, participants are required to respond to 'go' stimuli but have to withhold responses to 'no-go' stimuli, which triggers a 'conflict'. Among the smoking population, ACC is often in a hypoactivation state. Transcranial direct stimulation could strengthen connections of ACC with DLPFC. Therefore, the conflict signals are sent to the DLPFC constantly and behavioural decision and inhibition capabilities are enhanced more effectively by the DLPFCs constant integration and processing. Moreover, it is possible that tDCS can regulate the FC of contralateral brain regions.

Similarly, FCs of right superior frontal gyrus (SFG) with both DLPFC were increased after stimulus in the LEFT group's No-Go task. It is reported that activation of the right SFG was associated with more efficient response inhibition and less motor urgency [26].

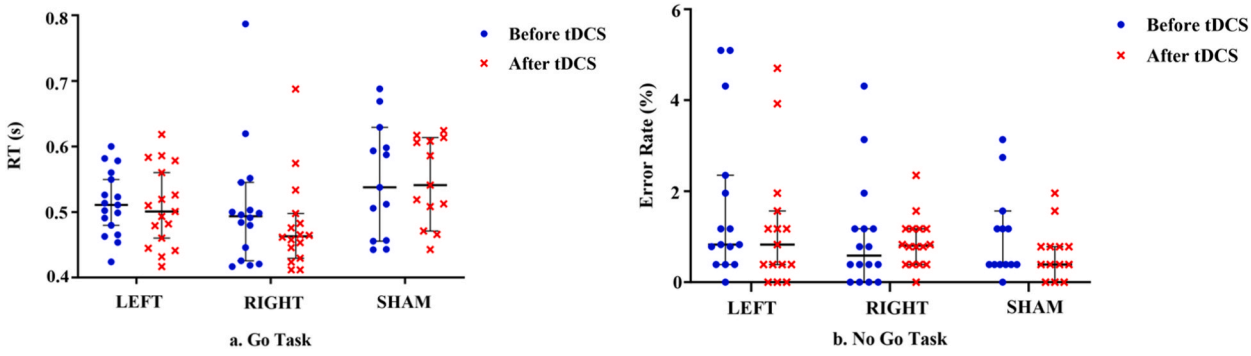

Fig. 3. Go RT or No-Go error rate. a. Within group comparison of RT. b. Within group comparison of error rate (For each group, $p > 0.05$). Error bars indicates 95 % confidence interval. RT: reaction time; tDCS: Transcranial direct current stimulation.

Over the past dozen years, neuroimaging studies that used other types of tasks have been studying the effects of tDCS on brain activity. In a tDCS-related experiment, Balloon Analog Risk Task experiment, task-related activity in the right DLPFC and ACC was also observed to increase after stimulation [27]. A smoking cue reactivity task revealed that tDCS could reduce smoking cravings, which is more likely because of increased FC between the left dorsal lateral prefrontal cortex and the right parahippocampal gyrus [28]. In this experiment, alterations in FC between DLPFC and PHG were not observed. Differences in these studies' results were related to the types of tasks and stimulation parameters. A brain perpetually resides in an active stance, so more task-state experiments are needed to investigate the impact of tDCS on the human brain's reward, behavioural inhibition, decision-making and cognition systems.

4.1. Limitations

There were some limitations in this study. Working memory processes, error detection and behavioural correction are additional executive function tasks that may be perplexed by the go/no-go paradigm's complex trial design. Therefore, we used a traditional experimental design involving only two stimuli. It can be possible to evaluate behavioural inhibition in its purest form. However, there were no significant changes in the intra-group or inter-group mistake rates due to a lack of difficulty or an absence of stimuli. Due to a lack of significant samples of left-handed men and women, all of our participants were right-handed male smokers. Even though we used FDR corrections, the final findings did not meet our expectations.

4.2. Summary

Several brain regions, including the precuneus, may have a suppressive impact from tDCS during the go task. The outcome of the smoking seed-based study in the no-go task was comparable to other research on task-state regarding tDCS. Smokers often have reduced activity levels in their ACCs. The R-DLPFC stimulation alone could improve the FC between bilateral DLPFCs and right ACC, which amplifies conflict signals over time. The DLPFC's executive function, including decision-making and reward processing, might be increased with this approach. The L-DLPFC stimulations alone may increase the FC of bilateral DLPFCs with specific brain areas linked to response inhibition. Additionally, there were variations in the outcomes of L- or R-DLPFC stimulation alone, which can be useful for future tDCS-related trial designs and parameter selections.

Author contribution statement

Jingya Lu: Zhifa Wu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Feiyan Zeng: Bin Shi: Performed the experiments. Mengqiu Liu: Jiaoyan Wu: Analyzed and interpreted the data. Ying Liu: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data will be made available on request.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The First Affiliated Hospital of University of Science and Technology of China and informed consent was obtained from all participants.

Consent for publication

N/A.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors appreciatively acknowledge grants from Bethune Charitable Foundation [bqe-tzb-2019-007]. We also thank the Department of Life Sciences and Medicine of USTC providing help.

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