POSTER NUMBER HERE

Neuromodulation of Impulsivity in Individuals with Substance-Use Disorder

Blake Andreou, Asif Jamil, Hitoshi Sakurai, Joan Camprodon

Department of Psychiatry, Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Charlestown, USA

INTRODUCTION

- Transcranial Direct Current Stimulation (tDCS) is a neuromodulatory technique commonly utilized to both improve and diminish a variety of cognitive functions.[1] These effects are dependent on the cortical areas that are modulated by the electric fields produced by the specific tDCS montage. [2]
- Individuals with substance use disorder (SUD) commonly experience deficiencies in the cognitive domain of response inhibition.[3]
- Our goal in this study was to target two cortical areas with tDCS to modulate the cognitive deficiencies associated with inhibitory control and cognitive impulsivity seen in the SUD population: the dorsolateral prefrontal cortex (DLPFC) and the ventrolateral prefrontal cortex (VLPFC)[4,5]
- Electroencephalography (EEG) was used to track for tDCS-induced neurophysiological changes during performance of a classic response inhibition task: the stop signal task (SST).

METHODS

Subjects: We recruited 24 volunteers between the ages of 18 and 56 that met criteria for substance-use disorder – specifically tobacco-use disorder and cannabis-use disorder. Exclusion criteria include a history of epilepsy, metallic implants in the head or neck, and comorbid psychiatric disorders considered the primary diagnosis.

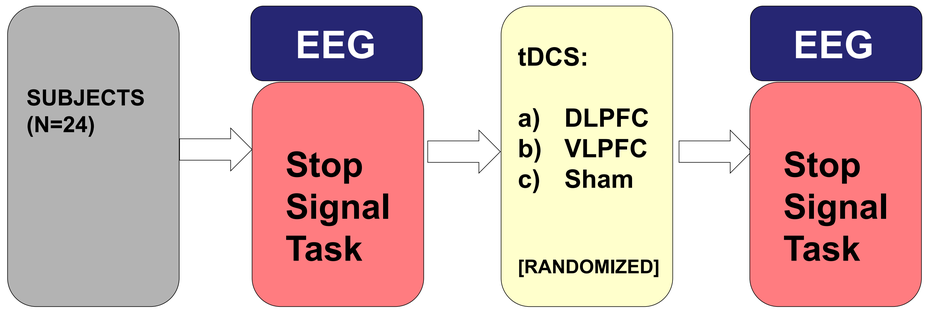
Study parameters: Each volunteer participated in three tDCS sessions. Within each tDCS session, volunteers participated in the Stop Signal Task (SST) before and after receiving tDCS. Electroencephalography (EEG) data was collected during computer tasks. Each participant received one of three stimulation types throughout their three tDCS sessions: anodal tDCS to the F3 site to target the DLPFC (according to the international 10-20 EEG coordinate system), anodal tDCS to the F8 site to target the VLPFC, and sham tDCS to the F3 site. For each montage, the cathodal electrode was placed on the contralateral supraorbital region. The order in which the participants received each stimulation type was randomized between participants. Regardless of stimulation type, the tDCS sessions were conducted using Ag/AgCl electrodes with a contact area of 3.14cm^2 and consisted of a 30sec ramp up to a full dose of 2mA for 30min, following by a 30sec ramp down. For the sham condition, the ramp up/down periods remained the same, but the device did not transmit current during the 30-minute stimulation period.

Measures: For each run of the SST, accuracy, measured by a d-prime score, as well as reaction time were collected and averaged. The stop-signal reaction-time (SSRT) was obtained from the reaction times of correct Go and No-Go responses and is a composite measure of inhibition that relates to impulsivity. EEG collection was performed using a 32-channel tDCS-EEG device (Starstim, manufactured by Neuroelectrics Barcelona). From this raw EEG data, event-related spectral perturbations (ERSPs) were generated. For group-level analysis, we averaged ERSPs between **200 and 400 ms** following the onset of the target stimulus, between **4-8 Hz** (theta range) and **9-12 Hz** (alpha range), and within a prefrontal region-of-interest (EEG channels **F3, Fz, and F4**).

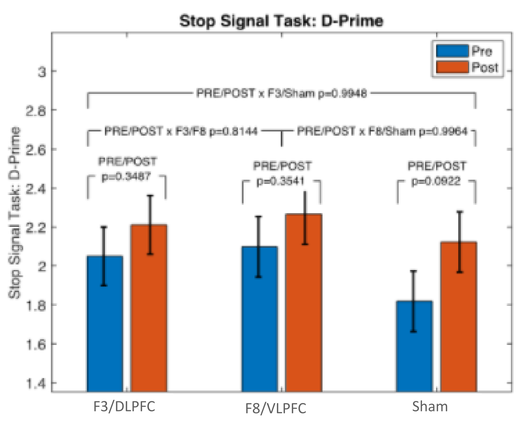
REFERENCES

1. Jacobson L., Koslowsky M., Lavidor M. (2012). tDCS polarity effects in motor and cognitive domains: a meta-analytical review. Exp Brain Res., 216(1),1-10.
2. Penolazzi B., Pastore M., Mondini S. (2013). Electrode montage dependent effects of transcranial direct current stimulation on semantic fluency. Behavioural Brain Res., 248,129-135
3. Heitzeg, M. M., Cope, L. M., Martz, M. E., & Hardee, J. E. (2015). Neuroimaging risk markers for substance abuse: Recent findings on inhibitory control and reward system functioning. Current Addiction Reports, 2(2), 91–103.
4. Shen, B., Yin, Y., Wang, J., Zhou, X., McClure, S. M., & Li, J. (2016). High-definition tDCS alters impulsivity in a baseline-dependent manner. NeuroImage, 143, 343–352.
5. Goya-Maldonado, R., Walther, S., Simon, J., Stippich, C., Weisbrod, M., & Kaiser, S. (2010). Motor impulsivity and the ventrolateral prefrontal cortex. Psychiatry Research: Neuroimaging, 183(1), 89–91.
6. Ray Li, C.-s., Cong Huang R., Constable T., Sinha R. (2006). Imaging response inhibition in a stop-signal task: Neural correlates independent of signal monitoring and post-response processing. Journal of Neuroscience, 26(1), 186–192.
7. Eagle DM, Baunez C, Hutcheson DM, Lehmann O, Shah AP, Robbins TW (2008): Stop-Signal Reaction-Time Task Performance: Role of Prefrontal Cortex and Subthalamic Nucleus. Cerebral Cortex, 18:178-188.
8. Friehs MA, Frings C. Cathodal tDCS increases stop-signal reaction time. Cogn Affect Behav Neurosci. 2019 Oct;19(5):1129-1142.

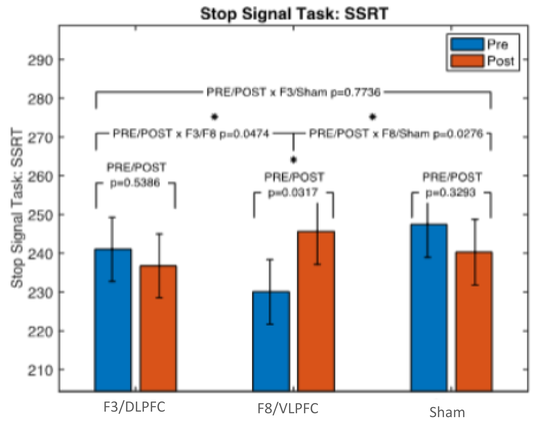
tDCS Protocol Schema



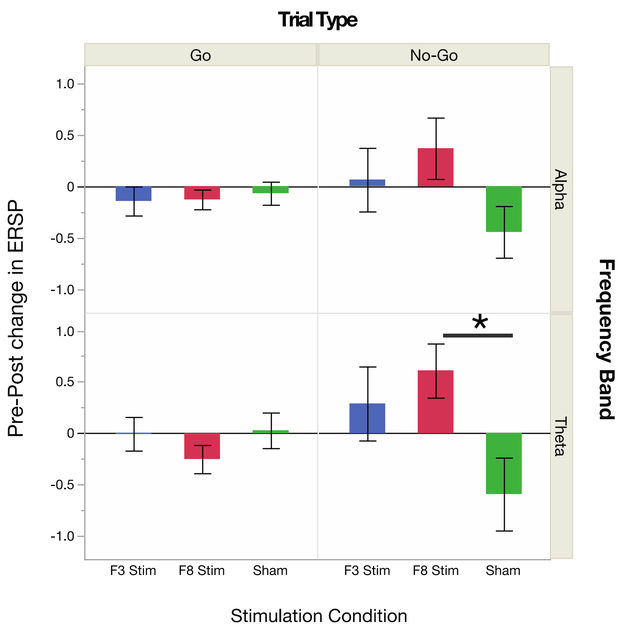
Stop Signal Accuracy (D-Prime) by Stimulation Site



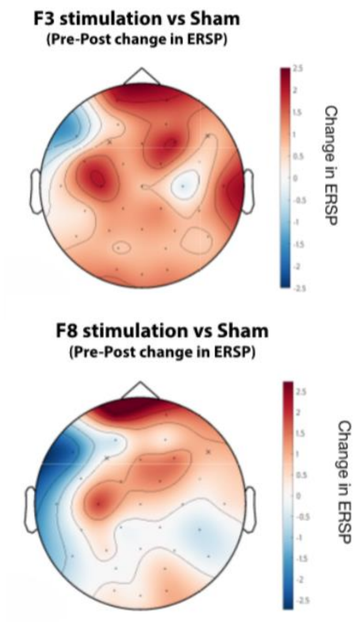
Stop Signal Task Reaction Times (SSRT) by Stimulation Site



Event-related spectral perturbation (ERSP): pre-post difference means by stimulation site



Topographical map of ERSPs in no-go trials in theta (4-8Hz) frequency range: F3/DLPFC v. F8/VLPFC



Stop Signal Task: Description

The Stop Signal Task (SST) has been repeatedly utilized as a reliable measure of impulsivity, specifically response inhibition[6]. In this task, participants must indicate which letter they see by pressing an associated computer key. However, if a red 'X' appears soon after the target letter, the participant should not press any button, and should wait for the next trial. Outcome measures of interest include a composite measure of accuracy (the d-prime index), and reaction time for both disinhibited (go) trials, as well as inhibited (no-go) trials.

DATA ANALYSIS

Behavioral: Accuracy scores were calculated using a d-prime score. This was done by subtracting the normalized proportion of correct responses to go trials from the normalized proportion of incorrect responses to no-go trials (i.e., false alarms). Stop Signal reaction times (SSRT) were generated for each experimental run by first subtracting the mean stop signal (red X) presentation time from the mean reaction time for the go trials. These differences were then utilized to approximate the SSRT using a horse race model.[7]

EEG: Raw EEG was first processed using standard band-pass filtering (0.1-40 Hz) and an average re-referencing. Then, independent component analysis (ICA) was used to identify and remove artifacts due to electrical and physiological noise. Next, the data was synchronized with the behavioral task markers and the event-related spectral perturbation (ERSP) was calculated on a trial-by-trial basis. These data were then divided by go and no-go trials and then by stimulation site.

SUMMARY RESULTS

- SSRT significantly increased (p=0.0317) after anodal F8 stimulation compared to before stimulation, indicating an increase in the impulsivity to stop. This pre-post difference was also significantly greater than the pre-post difference in the anodal F3 stimulation trials (p=0.0474) and sham stimulation trials (p=0.0276).
- There were no significant differences in task accuracy as defined by d-prime, either within or between stimulation conditions.
- ERSP results indicated an increase in theta band activity in the anodal F8 group that was significantly greater than the change in theta band activity noted in the sham stimulation group (p=0.0170)

CONCLUSIONS & FUTURE DIRECTIONS

•Our results demonstrate anodal tDCS targeting the VLPFC is associated with an increase in event-related frontal theta band activity during response-inhibition tasks

•The anodal VLPFC protocol also resulted in an increase in SSRT, suggesting an increase an impulsivity. This was not present in the overall accuracy, as the d-prime score was not negatively influenced.

•Our findings indicate an interesting yet counter-intuitive finding whereby greater impulsivity was observed with right-VLPFC stimulation. We hypothesized that increasing activity of the VLPFC would increase inhibition in the No-Go circuit, resulting in lower impulsivity and a better ability to withhold response.[8] However, our finding of reduced inhibition with anodal tDCS may indicate pathology-related differences in the prefrontal-motor inhibitory circuit, including the possibility of counter-regulation from homeostatic mechanisms. This could explain the increased activation (theta ERSP) in the frontal cortex of SUD patients which may be compensatory in order to account for the decline in inhibitory control. This is speculative, however, and further research would be needed to clarify this finding.

•Limitations of this study include the combination of individuals with tobacco and cannabis-use disorders to create the SUD cohort.