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Does Anodal tDCS Over the Left Prefrontal Cortex Using the F3-RSO Montage Improve Cognitive Control?

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Abstract:

Cognitive control is the ability to focus on relevant stimuli while disregarding irrelevant stimuli and is thought to be supported by the prefrontal cortex (see Miller & Cohen, 2001). Transcranial Direct Current Stimulation (tDCS) is a noninvasive brain stimulation technique that modulates the activity of underlying cortex regions through an electric current provided by two or more electrodes on the scalp. This study looks to determine whether anodal tDCS over the left prefrontal cortex can be used to increase cognitive control in healthy participants. Using an F3-RSO montage in a mixed between and within subjects design (with sham vs. anodal stimulation as the between factor, and pre- vs. post-stimulation as the within factor), we observed no increase in cognitive control as measured via comparing pre- and post-test Flanker and Stroop task congruency effects. However, there was substantial variability across our sham vs anodal participants in pre-test congruency effects, which persisted to the post-test. . Although there was no effect with this particular montage and stimulation parameters, it remains possible that with a different montage, anodal tDCS over the prefrontal cortex could increase cognitive control in participants. This study demonstrates the importance of considering baseline differences in cognitive control.

Introduction:

Executive function is a process that allows us to control our behavior in order to achieve a goal. There are many different aspects to executive function, one of which is cognitive control, which is the ability to inhibit irrelevant stimuli and focus on the relevant stimuli to a task. Executive function and cognitive control are thought to be supported by the frontal lobe. This is

supported by studies examining patients who have damage to the prefrontal cortex and exhibit impaired cognitive control (for review, see Banich, 2009). Neuroimaging studies have shown that the dorsolateral prefrontal cortex is the center for executive function (for review, see Miller & Cohen 2001). The prefrontal cortex is an association area which is a collection of interconnected neural circuits that receives signals from sensory, motor, and subcortical structures (see Miller & Cohen, 2001). Therefore, the prefrontal cortex has a role in integrating signals and regulating the functions of other brain regions. One of these functions supported by the prefrontal cortex is executive functions including cognitive control. Specifically, this study will look to alter the excitability of the prefrontal cortex to see if there is an effect on cognitive control.

Many studies testing executive function use the Stroop task (Stroop, 1935) in which participants are asked to respond to the color of ink used instead of the word written. For example, if the word "blue" were written in red ink, the participant would be asked to respond to the red ink instead of the word blue. This is a test of cognitive control because participants must respond to the relevant information for the task (ink color) in the presence of irrelevant stimuli (word). Word reading is a more automatic process than naming the color of ink used, which is why cognitive control is needed to inhibit the reflexive response of responding based on the word. This is demonstrated in the slower responses seen in incongruent trials where the ink color is not the same as the word when compared to congruent trials where the ink color and word are the same. In this study, the Stroop task will be used as a measure of cognitive control.

Another task used to test cognitive control is the Flanker task (Eriksen & Eriksen, 1974). In the version of the task we used, participants are presented with five arrows and are asked to respond to the direction of the central arrow. Trials consist of congruent, incongruent, and neutral

trials. In a congruent trial, all arrows face the same direction. However, in an incongruent trial, the central arrow faces an opposite direction from the other arrows, which requires cognitive control in order to inhibit the response to the outside arrows and only focus on the central arrow. In a neutral trial, there is only one arrow, surrounded by four crosses that the participant must disregard. This is a neutral trial because there is only one arrow in the center so the participant does not need to inhibit arrows going in opposite directions. The Flanker task will also be used in this study as a test of cognitive control.

Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that provides an electric current to the scalp through the use of (at least) two electrodes: an anode and a cathode. tDCS is thought to work by temporarily shifting the threshold for action potential firing in cortical neurons, thereby modulating neural firing in targeted regions (see Imburgio & Orr, 2018). It has been suggested that anodal tDCS may work by opening voltage-gated ion channels resulting in depolarization and excitability (Purpura & McMurtry, 1965; Nitsche et al., 2003). tDCS can increase or decrease brain activity depending on the direction of current flow (from anode to cathode vs cathode to anode). Anodal direct current increases the excitability of the neurons in the underlying cortical regions while cathodal stimulation decreases excitability (Priori et al., 1998; Nitsche & Paulus, 2000). In this study, we will use anodal tDCS to activate the left prefrontal cortex to test its effect on cognitive control.

Transcranial Direct Current Stimulation has many benefits when compared to other therapies, including its ability to be used on patients who experience adverse side effects from certain medications, and it could also be used alongside medications without having negative interactions (for review, see Brunoni et al. 2012), in addition to the fact that it is relatively inexpensive. tDCS is already thought to have beneficial effects for patients with

neuropsychiatric disorders such as major depressive disorder or drug additions (For review see, Brunoni et al., 2012), and its use for cognitive control seems promising. tDCS has already been shown to be effective in a clinical setting and it is the goal of this study to test its use on cognitive function.

As opposed to other types of noninvasive brain stimulation, such as transcranial magnetic stimulation, tDCS provides advantages such as the ability to have a stronger effect on modulating brain activation thresholds (Nitsche & Paulus, 2001) and allows for a reliable sham condition (Gandiga et al., 2006). In the sham condition, participants experience a brief tingling sensation at the beginning of stimulation to simulate the experience of receiving the treatment so the participants are unaware that they are not receiving stimulation.

By using anodal tDCS over the left prefrontal cortex, it is expected that the underlying cortex region will be more active due to the excitatory effects of anodal stimulation. By increasing the activity of the left prefrontal cortex, which is suspected to have a role in cognitive control, it is thought that participants in the anodal tDCS group will show an increase in cognitive control after stimulation compared to participants in the sham condition. Due to the between-subject design used, individual differences in cognitive control are accounted for by testing participants' pre and post-stimulation performance on the Flanker and Stroop Tasks. An improvement is expected in both the anodal stimulation group and sham group due to the practice effect which is the phenomenon that describes how individuals will perform better the second time they complete the task. However, we are looking to see if there will be a decrease in congruency effect from pre- to post-test in the stimulation group versus the sham group.

Certain stimulation parameters are used in tDCS studies to optimize the activation of the brain region of interest. These parameters include electrode size and position as well as intensity

and duration of stimulation. The size of the electrodes used has an effect on the current density delivered to the scalp such that increasing the size of the electrode decreases current density (Nitsche et al., 2007). During stimulation using tDCS, a current is generated across the brain, and changing the position of the electrodes, or the montage, allows for the current to stimulate different brain regions. Although tDCS is not extremely precise, electrode positioning still changes which brain regions are stimulated, as regions receiving a higher current flow will more likely be affected by stimulation (for review, see Brunoni et al., 2012). The position of the electrodes in studies using tDCS varies based on the brain region of interest.

The tDCS montage describes the placement of the electrodes used in stimulation. Each montage uses an anode (positive electrode) and cathode (negative electrode). However, the placement of the electrodes varies between studies depending on the brain area being targeted. In this study, the anode was placed on the F3 position to target the left prefrontal cortex and the cathode was placed on the RSO. The current flowed from the anode to the cathode. Although the existing literature has shown that this montage may not be ideal for targeting the left prefrontal cortex, we used it to connect to the existing literature with the plan of following this with another experiment using a different montage that is more appropriate.

Studies using tDCS in the past have used either online or offline designs. In an online design, participants perform a task while the stimulation is occurring. This is contrasted with an off-line design where participants perform a cognitive task following stimulation because the effects of stimulation on brain regions are thought to persist for up to an hour following a single session of tDCS (for review, see Berryhill & Martin, 2018). This study used an online design where participants completed the tasks while stimulation was being delivered. Online tDCS has been shown to have greater effects on executive function. This is consistent with studies using

magnetic resonance spectroscopy (MRS) during stimulation which showed an increase in neurotransmitter levels during stimulation as opposed to post-stimulation (Hone-Blanchet et al., 2016), indicating the fast and short-lived effects of tDCS. This was further shown in a study using whole-brain arterial spin labeling (ASL) to measure brain perfusion during tDCS that showed higher perfusion during stimulation than after (Stagg et al., 2013). Therefore, the effects of tDCS seem to be greatest during stimulation.

The dosage of tDCS is affected by the current dosage (amperes), duration of stimulation, and the size and position of the electrodes (for review, see Brunoni et al., 2012). It has been shown that higher current density is associated with a greater positive effect on executive function (for review, see Imburgio & Orr, 2018). The most common montages use electrodes that are 25-35 cm^2 with currents of 1-2mA for 20-40 minutes (for review, see Brunoni et al., 2012). There is evidence that smaller electrodes (less than $25cm^2$) are more efficient in causing excitatory effects of underlying, due to the ability to more precisely target a brain region (For review, see Imburgio & Orr., 2018). In reality, the current that actually reaches the neurons is smaller than this due to variables such as skin conductance, skull resistance, and resistance of the brain tissue (For review, see Brunoni et al., 2012). Although, this variability can be diminished by using saline-soaked sponges which minimize skin resistance and excluding patients on medications who may have varying resistance of brain tissue (for review, see Brunoni et al., 2012).

Additionally, there is reason to believe that individual differences in brain structure are responsible for the differential effects of tDCS. For example, effects may not be consistent due to the arrangement of gyri and sulci which concentrate the current on the gyri, according to recent modeling (Datta et al., 2009). Other differences between individuals that should be taken into

consideration are baseline neurotransmitter levels, genetics, and anatomical differences that can account for differences in the degree of stimulation (For review, see Imburgio & Orr, 2018). Therefore, due to differences in individual physiology tDCS may not target the same brain regions in different individuals. However, this is not something accounted for in this study.

It is our hypothesis that transcranial direct current stimulation over the left-prefrontal cortex will augment cognitive control when comparing pre- and post- Flanker and Stroop tasks. Specifically, the incongruency effect will decrease between pre- and post-test task scores in the anodal condition compared to the sham condition.

Methods:

Participants were drawn from the University of Connecticut Psychological Sciences participant pool. 52 healthy participants (23 male and 29 female) between the ages of 18 and 21 (mean age=19) were assigned randomly to one of two conditions: sham stimulation or anodal tDCS. 25 (13 female, mean age=19) participants received sham stimulation and 27 (16 female, mean age=19) participants received anodal stimulation.

Upon arrival, participants were asked to fill out questionnaires that provided demographic information and ensured it was safe for them to receive stimulation before the experiment began. The procedure and possible side effects of stimulation were explained to participants before signing a consent form. A Transcranial Direct Current Stimulation (tDCS) Adult Safety Screen was given that asked about brain injuries, history of seizures, medications, metal implants, and pregnancy to ensure eligibility in the study. If a participant had positive indicators on any of these questions, they were removed from the study and did not receive stimulation. We then administered two questionnaires for exploratory purposes (a participant information form which

asked about sex, age, and languages they speak fluently and the Edinburgh Handedness Inventory which asked about the degree to which the participant was left-handed or right-handed). We have not yet evaluated them and they will not be discussed further. Additionally, participants were asked to remove any metal such as piercings and jewelry and were also asked to remove any electronic devices from their person. Participants were also informed of possible side effects from stimulation which include itching, burning, and redness at the sight of the electrode.

Next, participants in both conditions were asked to complete the Flanker task which lasted six minutes. The Flanker task asks participants to respond to the middle arrow in a row of five arrows and trials consisted of congruent trials (all arrows facing the same direction), incongruent trials (the central arrow faces a different direction), and neutral trials (a central arrow surrounded by crosses). Participants then completed the Stroop task which lasted for five minutes. During the Stroop task, participants were presented with text and asked to respond to the ink color used instead of the word. Fifty percent of the trials were congruent where the ink color and word were the same while the remaining half were incongruent trials in which the ink color and word did not describe the same color.

Following these tasks, the participants' heads were measured in order to determine the correct size cap to use. Using this cap, the spots where the electrodes went were marked on the participant’s skull using a washable pen, to ensure proper placement of electrodes. The montage used was F3-RSO, in which the anode was placed over the left prefrontal cortex and the cathode was placed over the right supraorbital region. The electrodes were placed in 5x7cm saline-soaked sponges and then put on the participant’s scalp. These were held in place with two plastic straps.

Next, stimulation began. In both conditions, the ramp-up to 1.5mA happened over the course of 30 seconds. Following this, participants in the anodal tDCS condition received stimulation while in the sham condition, the stimulation was turned off. After the 30 second ramp up, participants in both conditions watched a nature video for three minutes to allow the stimulation to begin having effects before the tasks were repeated.

Next, participants repeated both the Flanker and Stroop tasks post-stimulation. We used a pre- and post-test design in order to take into account baseline differences in cognitive control in the stimulation vs sham groups. Additionally, participants completed an animal judgment task where they were asked to identify whether an object was an animal or not. This animal judgment task took 10 minutes. The data from this exploratory task has not been analyzed and will not be discussed further.

Following the last task, the tDCS machine ramped down for 30 seconds and then the plastic straps and electrodes were taken off of the participant. Before leaving, participants completed forms asking them about any side effects experienced and if they had any inclination about what was being tested in the study.

Results:

This analysis focused on the Flanker Task as the Stroop task showed no significant pre-test score difference between conditions and no pre- vs post- difference between sham and anodal groups.

Two pieces of information were collected from the Flanker Task. The first was accuracy which was not included in this analysis because participants are consistently very accurate when doing this task. The most important information collected from this task is reaction time. Specifically, we are interested in looking at the reaction time differences between congruent and

incongruent trials in the pre- and post-tests in both the sham and anodal conditions --i.e., the "congruency effect". To look at the congruency effect, the average reaction time for congruent trials was subtracted from the average reaction time for incongruent trials for each participant in both pre- and post-test flanker tasks.

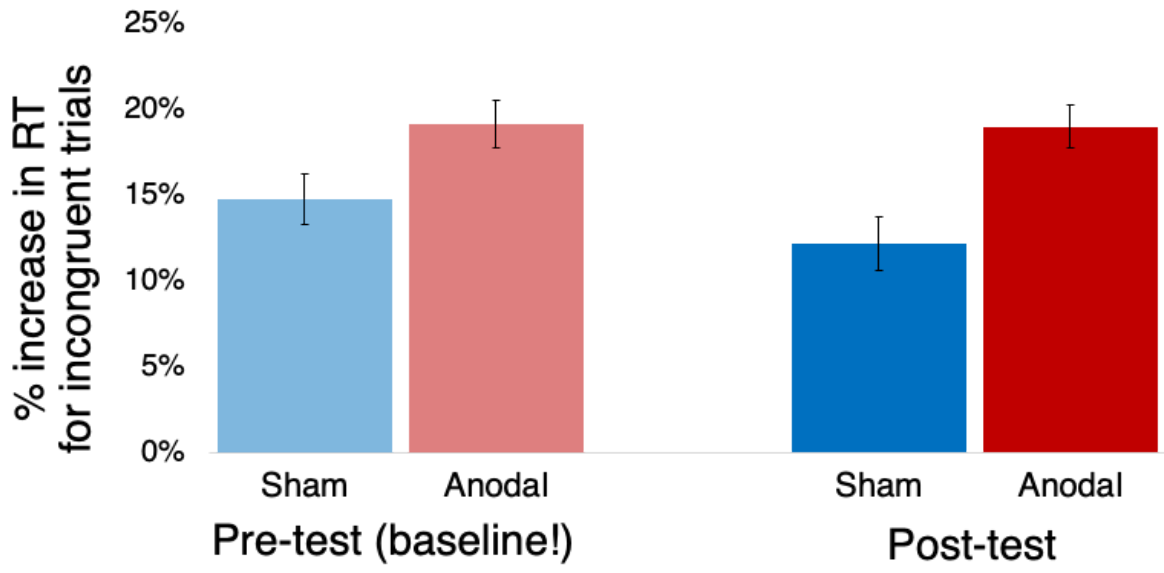

Figure 1: *The percent increase in reaction time for incongruent vs congruent trials in both pre-test and post-test flanker tasks in the anodal and sham conditions.*

When examining this congruency effect, we observed that the participants in the sham condition showed a smaller congruency effect in the pre-test condition than the participants in anodal stimulation group. This baseline difference accounts for the difference in congruency effect seen in the post-test condition. A direct comparison of the effect of stimulation on the congruency effect in the Flanker task, indicating no effect on cognitive control (t = -0.03, p = 0.98).

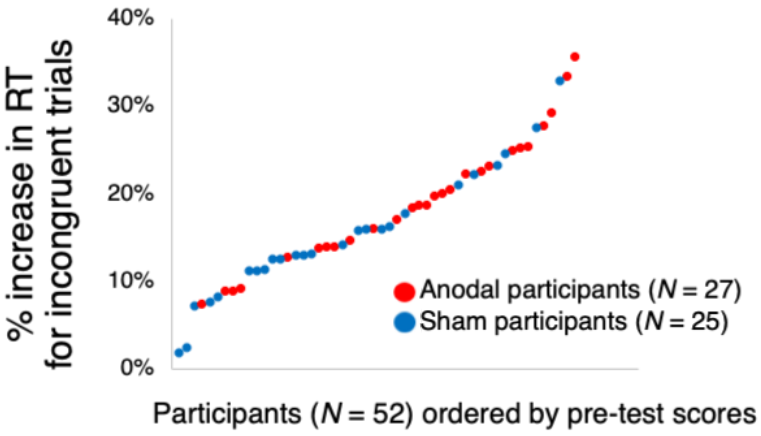

Figure 2: *Pre-test scores for each participant show the Sham group, on average, had faster baseline reaction times for incongruent trials. Since this group already demonstrated lower increase in reaction time for incongruent trials in the pre-test, the difference in congruency effect in the post-test condition was due to baseline differences between the two groups and not the stimulation condition.*

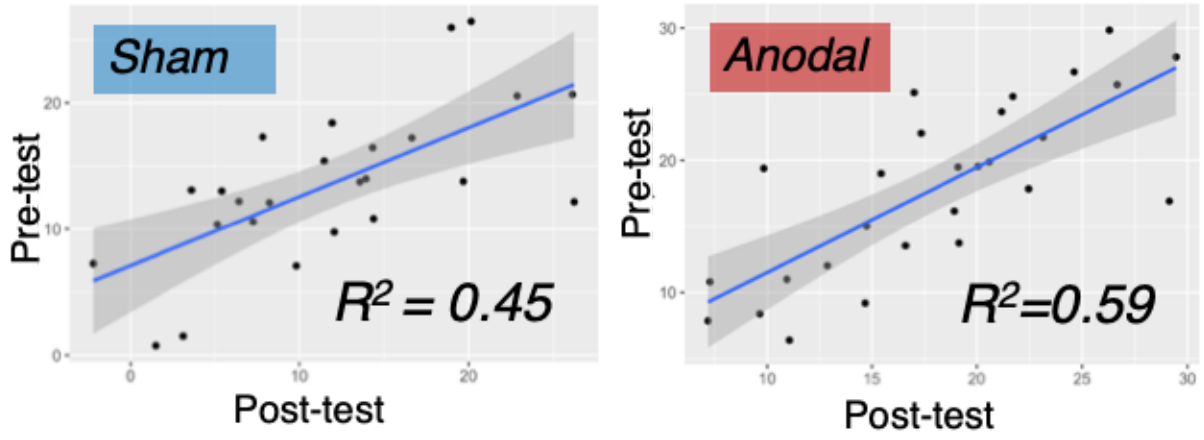

Figure 3: *Scatter plot of pre-test Flanker scores in the Anodal and Sham conditions. Despite a wide range of variability among participants, the correlation shows a significant test-retest*

reliability. Therefore, had anodal tDCS had an effect on the Flanker effect it would likely have been detectable after controlling for baseline differences, which had not been seen in the Stroop task.

After controlling for baseline differences in cognitive control in the Flanker Task, it is clear that anodal tDCS with this particular montage over the left prefrontal cortex had no effect on cognitive performance. If this had not been within subject design, the post-test scores on the flanker task would have indicated that anodal tDCS caused a *detriment* to cognitive control as indicated by a larger congruency effect. However, when comparing pre-test and post-test scores, this difference is due to the baseline differences in cognitive control that already existed and was not due to stimulation conditions.

Discussion:

The results of the study indicate that anodal tDCS over the left prefrontal cortex caused no significant effects on cognitive control. Looking at the baseline increases in reaction time for incongruent trials, the two groups differed in cognitive control, with the anodal condition showing increased reaction time for incongruent trials which is also seen in post-test trials.

Therefore, there was no effect of anodal tDCS over the prefrontal cortex with this specific montage and stimulation parameters used. However, this montage may not be best for increasing cognitive control. In the future, other stimulation parameters should be used to better target the prefrontal cortex.

One possible limitation to the use of Transcranial Direct Current Stimulation is that there is evidence that sham stimulation may produce similar results to the anodal stimulation condition. This is because, during sham stimulation, the tDCS machine is left on so that

participants are unaware that they are not receiving active stimulation, however, the electrodes still transmit a small current to the scalp and could elicit similar effects to active stimulation (Nikolin et al., 2018). Therefore, there it is possible that both groups could have received the treatment and sham stimulation is not reliable for comparison.

Additionally, the number of sessions and time interval between stimulation sessions can affect the duration of the effects of stimulation. If a participant received regular sessions of tDCS they could see cumulative effects (Monte-Silva et al., 2010). Some studies have shown that tDCS can have effects lasting up to one hour after a single session of stimulation lasting over 10 minutes (Ardolino et al., 2005; Nitsche & Paulus, 2000). When participants receive stimulation daily, the effects of stimulation are additive, and therefore last for longer periods of time (Nitsche et al., 2003; Nitsche & Paulus, 2001). This provides evidence that tDCS could be used as a therapy for participants who have lower baseline cognitive control if they receive stimulation more frequently.

There is evidence that anodal-tDCS of the dorsolateral prefrontal cortex may be an effective treatment for patients with Major Depressive Disorder (Fregni et al., 2006) and Schizophrenia (Brunelin et al., 2012) because these patients often experience impairment to executive function. Although this particular study did not show an increase in cognitive control with this particular montage, a different montage could have the potential to increase cognitive control and potentially be used as a treatment for populations experiencing decreased cognitive function. For example, moving the position of the cathode in our current study from the RSO to an extracranial sight (right neck site) could decrease unintended inhibition of other regions in the prefrontal cortex (For review, see Imburgio & Orr, 2018). In future studies, a different montage could be used to augment cognitive control.

Overall, this study showed no effect of anodal tDCS over the prefrontal cortex on cognitive control with this particular montage and stimulation parameters. In the future, a different montage could be used to better stimulate the prefrontal cortex. Additionally, it would be the goal to have a larger sample size as the original target was 60 participants per condition.

These results show the importance of considering individual differences in cognitive control. If only post-test performance on the Flanker task were taken into account, it would have been concluded that anodal tDCS had a detrimental effect on cognitive control based on the results of the Flanker task. However, there was a significant baseline difference in cognitive control between the sham and anodal tDCS groups. Therefore, our results suggest the importance of taking individual differences into account.

References:

Ardolino, G., Bossi, B., Barbieri, S., & Priori, A. (2005). Non-synaptic mechanisms underlie the after-effects of cathodal transcutaneous direct current stimulation of the human brain. *The Journal of physiology*, *568*(Pt 2), 653–663. https://doi.org/10.1113/jphysiol.2005.088310

Banich, M. T. (2009). Executive Function: The Search for an Integrated Account. *Current Directions in Psychological Science*, *18*(2), 89–94. https://doi.org/10.1111/j.1467-8721.2009.01615.x

Berryhill, M. E., & Martin, D. (2018). Cognitive Effects of Transcranial Direct Current Stimulation in Healthy and Clinical Populations: An Overview. *The journal of ECT*, *34*(3), e25–e35. https://doi.org/10.1097/YCT.0000000000000534

Brunelin, J., Mondino, M., Gassab, L., Haesebaert, F., Gaha, L., Suaud-Chagny, M. F., Saoud, M., Mechri, A., & Poulet, E. (2012). Examining transcranial direct-current stimulation (tDCS) as a treatment for hallucinations in schizophrenia. *The American journal of psychiatry*, *169*(7), 719–724. https://doi.org/10.1176/appi.ajp.2012.11071091

Brunoni, A. R., Nitsche, M. A., Bolognini, N., Bikson, M., Wagner, T., Merabet, L., Edwards, D. J., Valero-Cabre, A., Rotenberg, A., Pascual-Leone, A., Ferrucci, R., Priori, A., Boggio, P. S., & Fregni, F. (2012). Clinical research with transcranial direct current stimulation (tDCS): challenges and future directions. *Brain stimulation*, *5*(3), 175–195. https://doi.org/10.1016/j.brs.2011.03.002

Datta, A., Bansal, V., Diaz, J., Patel, J., Reato, D., & Bikson, M. (2009). Gyri-precise head model of transcranial direct current stimulation: improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain stimulation*, *2*(4), 201–207.e1. https://doi.org/10.1016/j.brs.2009.03.005

Eriksen, B.A., Eriksen, C.W. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics* 16, 143–149 (1974). https://doi.org/10.3758/BF03203267

Fregni, F., Boggio, P. S., Nitsche, M. A., Marcolin, M. A., Rigonatti, S. P., & Pascual-Leone, A. (2006). Treatment of major depression with transcranial direct current stimulation. *Bipolar disorders*, *8*(2), 203–204. https://doi.org/10.1111/j.1399-5618.2006.00291.x

Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical*

neurophysiology : official journal of the International Federation of Clinical Neurophysiology, *117*(4), 845–850. https://doi.org/10.1016/j.clinph.2005.12.003

Hone-Blanchet, A., Edden, R. A., & Fecteau, S. (2016). Online Effects of Transcranial Direct Current Stimulation in Real Time on Human Prefrontal and Striatal Metabolites. *Biological psychiatry*, *80*(6), 432–438. https://doi.org/10.1016/j.biopsych.2015.11.008

Imburgio, M. J., & Orr, J. M. (2018). Effects of prefrontal tDCS on executive function: Methodological considerations revealed by meta-analysis. *Neuropsychologia*, *117*, 156–166. https://doi.org/10.1016/j.neuropsychologia.2018.04.022

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual review of neuroscience*, *24*, 167–202. https://doi.org/10.1146/annurev.neuro.24.1.167

Monte-Silva, K., Kuo, M. F., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2010). Shaping the optimal repetition interval for cathodal transcranial direct current stimulation (tDCS). *Journal of neurophysiology*, *103*(4), 1735–1740. https://doi.org/10.1152/jn.00924.2009

Nikolin, S., Martin, D., Loo, C. K., & Boonstra, T. W. (2018). Effects of TDCS dosage on working memory in healthy participants. *Brain stimulation*, *11*(3), 518–527. https://doi.org/10.1016/j.brs.2018.01.003

Nitsche, M. A., Doemkes, S., Karaköse, T., Antal, A., Liebetanz, D., Lang, N., Tergau, F., & Paulus, W. (2007). Shaping the effects of transcranial direct current stimulation of the human motor cortex. *Journal of neurophysiology*, *97*(4), 3109–3117. https://doi.org/10.1152/jn.01312.2006

Nitsche, M. A., Liebetanz, D., Antal, A., Lang, N., Tergau, F., & Paulus, W. (2003). Modulation of cortical excitability by weak direct current stimulation--technical, safety and functional aspects. *Supplements to Clinical neurophysiology*, *56*, 255–276. https://doi.org/10.1016/s1567-424x(09)70230-2

Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of physiology*, *527 Pt 3*(Pt 3), 633–639. https://doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x

Nitsche, M. A., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology*, *57*(10), 1899–1901. https://doi.org/10.1212/wnl.57.10.1899

Priori, A., Berardelli, A., Rona, S., Accornero, N., & Manfredi, M. (1998). Polarization of the human motor cortex through the scalp. *Neuroreport*, *9*(10), 2257–2260. https://doi.org/10.1097/00001756-199807130-00020

Purpura, D. P., & McMurtry, J. G. (1965). Intracellular Activities And Evoked Potential Changes During Polarization of Motor Cortex. *Journal of neurophysiology, 28*, 166–185. https://doi.org/10.1152/jn.1965.28.1.166

Stagg, C. J., Lin, R. L., Mezue, M., Segerdahl, A., Kong, Y., Xie, J., & Tracey, I. (2013). Widespread modulation of cerebral perfusion induced during and after transcranial direct current stimulation applied to the left dorsolateral prefrontal cortex. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *33*(28), 11425–11431. https://doi.org/10.1523/JNEUROSCI.3887-12.2013

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. J*ournal of Experimental Psychology*, 18(6), 643–662. https://doi.org/10.1037/h0054651