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When you can, scale up: Large-scale study shows no effect of tDCS in an ambiguous risk-taking task

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ABSTRACT

Background: A wide range of neuroimaging and neuromodulation studies have shown that the dorsolateral prefrontal cortex (DLPFC) plays a pivotal role in decision-making. Of particular interest is the question of its role in decision-making when conditions are uncertain and whether manipulating this neural substrate through neuromodulation changes subsequent risk-taking behaviour. Previous work using the Balloon Analogue Risk Task (BART) suggests that bilateral tDCS stimulation of the DLPFC reduces risk-taking behaviour but unilateral stimulation has no effect. However, participant numbers have been limited and may have biased the estimate of the size of the effect of the stimulation on task performance.

Objectives/hypothesis: We aimed to test the robustness and generalizability of these previous findings by using a very similar methodology but with a much larger sample.

Methods: During both 20- and 30-min tDCS stimulation at 2 mA, we administered the BART to about 200 participants assigned to bilateral DLPFC stimulation of either right anodal/left cathodal, left anodal/right cathodal or sham (Study 1 and Study 2); and to unilateral stimulation conditions (Study 2): right anodal, left anodal or sham with the referent electrode over the contralateral supraorbital region.

Results: In the first bilateral study, we found that risk-taking was greater for participants in the right anodal/left cathodal stimulation group compared to those who received left anodal/right cathodal stimulation, but not compared to sham. The results obtained in the bilateral and unilateral stimulation protocols implemented in Study 2 yielded no evidence of any effect of stimulation. Combining the data from both studies, we found no statistically significant differences between mean performances of the nine stimulation groups. Indeed, all 95% confidence intervals for the nine means overlapped, suggesting that these randomly vary around a common population mean.

Conclusions: This study showed that there was no detectable effect of tDCS stimulation on risky decision-making under ambiguity, compared to sham stimulation. Hence, using a much larger sample, we did not replicate previous work reporting a reduction in risky decision-making by bilateral stimulation of the DLPFC compared to sham. When the results of our bilateral and unilateral stimulation studies were combined, it emerged that the most likely explanation for the apparent significant results in our bilateral stimulation study was random variation in performance. This outcome is a further reminder of the need for appropriately sized samples to potentially achieve reliable outcomes in brain modulation studies.

1. Introduction

Ernst and Paulus (2005, pg.1) define decision-making as "…the process of forming preferences, selecting and executing actions and evaluating outcomes". While research has consistently shown that decision-making involves the complex interplay between cognitive and emotional processes within the prefrontal cortex (PFC) and other closely interconnected neural networks, such as the limbic system (e.g. Ernst and Paulus, 2005; Slovic et al., 2004; Damasio, 1996), the extent to which particular neural substrates are engaged, varies depending on a range of factors. These include the stage of decision-making (e.g. forming preferences vs. executing actions) (Ernst and Paulus, 2005), whether the decision's outcome is certain, risky or simply ambiguous (Krain et al., 2006) and whether the outcome probabilities of a risky decision are unknown or calculable by the individual (Fecteau et al., 2007; Rao et al., 2008; Fukunaga et al., 2012).

Of particular interest is that, across a wide range of risk-based tasks combined with neuroimaging and/or neurostimulation, the dorsolateral

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prefrontal cortex (DLPFC) has been shown to be pivotal to the process of risky decision-making (Guo et al., 2013; Cho et al., 2012, 2010; Rao et al., 2008; Fecteau et al., 2007; Krain et al., 2006; Knoch et al., 2006a, 2006b; van 't Wout et al., 2005). For example, studies using transcranial magnetic stimulation (TMS) on healthy volunteers have found that disrupting right DLPFC activity leads to increased risk taking (Knoch et al., 2006a), and that this particular area of the prefrontal cortex plays an important role in strategy (van 't Wout et al., 2005) and cognitive control (Knoch et al., 2006a, b; Cho et al., 2012) in decision-making.

Fecteau et al. (2007) aimed to extend these findings by investigating whether modulating DLPFC activity using transcranial direct current stimulation (tDCS) would affect decision-making in ambiguous tasks (i.e. where the probability of the decision outcome is unknown). tDCS allows one to pass a mild current in the brain, and this technique creates a more subtle excitatory/inhibitory effect compared to TMS and has been shown to be effective in both clinical and healthy populations (for review see Brunoni et al., 2012). tDCS differs from TMS in that the current field applied is not sufficient to cause the rapid depolarisation required to trigger an action potential but instead modulates the spontaneous neuronal network by de/hyperpolarizing the resting membrane potential of the stimulated neurons based upon the polarity of the field applied. This means that anodal stimulation has the general effect of enhancing cortical excitability under the area of the electrode, whilst cathodal stimulation reduces cortical activity under this electrode (Nitsche and Paulus, 2000).

Fecteau et al. (2007) used the Balloon Analogue Risk Task (BART), a well-established measure of risk (Lejuez et al., 2002), in two experiments. In the first, participants underwent double-blind bilateral stimulation of the DLPFC: one group with the right anodal electrode positioned on F4 according to the 10/20 EEG positioning method (Jasper, 1958) and the left cathodal electrode on F3; the second group with a right cathodal/left anodal montage, and the third group receiving sham stimulation (i.e. the placebo control condition). Their second study aimed to assess whether unilateral stimulation of the DLPFC could impact on decision-making under ambiguity; two groups of participants received either only right (F4) or left (F3) anodal stimulation with the cathodal electrode positioned over the contralateral supraorbital region. In both experiments the current strength was 2 mA, delivered using 35 cm^2 electrodes. Participants performed a Stroop task prior to and following stimulation. The BART task was executed in an on-line neuromodulation mode following an initial 5-min 'warm-up' stimulation period where participants did not perform other tasks. The BART task was executed in less than 15 min. Participants were tested in a double-blind mode. In an overall analysis of their data, it emerged that both active bilateral stimulation groups (right anodal/left cathodal; left anodal/right cathodal), compared to sham, led to a significant reduction in risk-taking behaviour, while unilateral stimulation led to results equivalent to the sham condition, thus adding to the literature suggesting that neuromodulation of the DLPFC directly impacts on decision making tasks' performance. The obtained results led the authors to conclude that only when an excitatory effect applied to one side of the DLPFC (anodal stimulation) is coupled with an inhibitory effect (cathodal stimulation) applied to the contralateral side, cautious behaviour emerges. Furthermore, they speculated that this was a consequence of the tDCS changing the balance of activity between the left and right DLPFC.

While Fecteau et al. (2007) findings could potentially be relevant to refine our understanding of the role of DLPFC in decision-making, it is important to consider some potential caveats. Firstly, they tested a total of 47 participants across five conditions (reduced to 44 following the exclusion of three participants, whose performance fell outside two standard deviations from their group mean) in a between-groups design. Such a small sample size distributed over five conditions would increase the likelihood of obtaining a severely biased estimate of the effect size of a variable compared to the actual population parameter (e.g. Schönbrodt and Perugini, 2013). It is therefore unclear the extent to which the outcome of the study is reliable. Other studies assessing the impact of transcranial electrical stimulation on decision making tasks also appear to have used relatively small sample sizes, (e.g. Sela et al., 2012) thus they may also suffer from the same potential issue. While it is relevant to assess the robustness and generalizability of the findings of those studies based on small samples, we will confine ourselves in this study to try to assess the robustness and generalizability of the finding of Fecteau et al. (2007), since this is one of the first and more influential studies on the impact of transcranial electrical stimulation on decision making.

To this aim, we used a similar methodology to that employed by Fecteau et al. and we tested a much larger sample. Finally, we measured the correlation between the Sensation Seeking Scale (SSS) (Zuckerman et al., 1964), the Eysenck Impulsiveness Scale (Eysenck et al., 1985) and the performance in the BART. As found by Lejuez et al. (2002), we predicted that participants scoring higher on sensation seeking measures were likely to score higher on the BART (i.e. to take a greater risk).

2. Study 1

2.1. Methods and materials

2.1.1. Participants

One hundred and seventeen healthy students (68 females) aged 18–30 years (M 21.14, SD 2.7; 5 left-handed) participated in Study 1 (bilateral stimulation). Using the data available in the Fecteau et al. study we tried to estimate the effect size (measured as Phi) for the main effect of the stimulation condition in their bilateral study, which appeared to be about 1. Assuming that this value provides a fair reflection of the size of the effect of the stimulation protocol on the BART at population level, our study would have a power greater than .95 (indeed a total sample of at least thirty-three participants would suffice to achieve this level of statistical power).

All participants confirmed that they did not have any mental health or neurological disorders, were not taking medications affecting the central nervous system and were naïve to the BART task. All participants gave written informed consent and received either a course credit or small payment for attending. No performance task related payments were given to participants. This study was approved by the University of Essex Faculty of Science and Engineering Ethics Committee.

2.1.2. tDCS stimulation

We used a DC-Stimulator Plus (Neuroconn, Germany) with two 35 cm^2 (5 × 7 cm) conductive rubber electrodes inside saline-soaked sponges (NaCl concentration: 100 mM dissolved in distilled water). Due to an error, 20 participants in Study 1 were tested with 5 × 5 cm electrodes. As shown later the different sizes did not impact on the study outcome. The electrodes were secured using rubber straps and positioned over the DLPFC according to the International 10–20 system. In Study 1, participants were randomly assigned to one of three bilateral stimulation conditions: F4 right anodal/F3 left cathodal (n = 41); F3 left anodal/F4 right cathodal (n = 43) and sham (n = 33). Double-blinding was achieved using the "study mode" of the tDCS device. The sham setting aimed to produce similar sensory experiences as in those experienced in the verum conditions in order to mask the stimulation condition administered. In the active stimulation conditions, a current strength of 2 mA was applied for a total of 30 min with a ramp-up and ramp-down phase of 30 s. In the sham condition, ramp-up duration was 30 s followed by 1 min of 2 mA stimulation then a 30 s ramp-down. The duration of active stimulation during the sham period is automatically calculated by the DC-Stimulator Plus software: the active stimulation period (in seconds) is divided by 30 (i.e. 1800 s/30 = 60 s). Participants were told that they would be administered active stimulation. During stimulation, prior to completing any tasks, participants watched a nature video for 5 min to habituate to the stimulation.