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Research report

Polarity-specific transcranial direct current stimulation effects on object-selective neural responses in the inferior parietal lobe

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ABSTRACT

Neuromodulation techniques such as transcranial direct current stimulation (tDCS) are routinely used for treating neurological and neuropsychiatric disorders, and for enhancement of cognitive abilities. Recently, their effectiveness in modulating behavioral and neural responses has been questioned. Here we use excitatory and inhibitory tDCS prior to a functional magnetic resonance imaging (fMRI) experiment to show that neural responses for an area's preferred stimuli depend on the polarity of stimulation. This is an important, yet overlooked, data point in demonstrating the effectiveness of these stimulation techniques. Our results show that response preferences in the target area are dependent on the polarity of the tDCS session preceding the fMRI experiment – these preferences are less distinct in the cathodal than in the anodal session. As such, we show unequivocally that tDCS modulates neural responses. This result is of the utmost importance in demonstrating the effectiveness of tDCS for clinical and experimental purposes.

1. Introduction

Non-invasive neuromodulation techniques such as transcranial direct current stimulation (tDCS) have enjoyed a revival in the last few decades because of their putative effectiveness and their non-invasive nature. Specifically, these techniques have been shown to 1) be effective in the treatment of major depressive syndromes (e.g., Nitsche, Boggio, Fregni, & Pascual-Leone, 2009), as well as other psychiatric disorders (e.g., Senco et al., 2015); 2) improve neurorehabilitation of brain-lesioned patients (e.g., Fregni et al., 2005); and 3) affect the processing of different types of information in normal participants (e.g., Lupyan, Mirman,

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Hamilton, & Thompson-Schill, 2012). Importantly, this effectiveness has been achieved without compromising safety, and non-invasiveness.

But their neural and behavioral efficacy has recently been challenged (e.g., Buzsáki, 2016; Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016; Horvath, Forte, & Carter, 2015b; but see, 2015a,; Antal, Keeser, Priori, Padberg, & Nitsche, 2015; Joyal & Fecteau, 2016; Kekic, Boysen, Campbell, & Schmidt, 2016; Shin, Foerster, & Nitsche, 2015). Specifically, Buzsáki has suggested that the typical tDCS stimulation parameters used in neuroscientific research are underpowered, as the application of an electric current to the skull of a cadaver, following such parameters, fails to elicit any neural firing in adjacent brain cells (Buzsáki, 2016). Thus, tDCS should not modulate neuronal activity, and consequently affect cognitive and behavioral responses. Moreover, Horvath, Forte, and Carter (2015a, 2015b) performed a series of meta-analyses and failed to find effects of tDCS on the majority of neural and behavioral measures they tested. This further puts into question the effectiveness of these techniques in restoring function and treating neuropsychiatric disorders.

Because of the potential role of these techniques in bringing innovation and advances in our understanding of neural and cognitive processing, as well as in the betterment of our tools to intervene and rehabilitate neuropsychiatric disorders, it becomes crucial to unequivocally show that they can modulate neural responses. Here we measured object-selective neural responses while participants took part in an experiment where we coupled offline tDCS stimulation with a typical object processing fMRI experiment. Importantly, we manipulated the polarity of tDCS stimulation (i.e, we used excitatory and inhibitory tDCS), because demonstrating that neural responses change as a reflection of the polarity of stimulation is central in attesting the effectiveness of these non-invasive stimulation techniques.

1.1. *Experiment*

In our experiment, each participant went through 3 experimental sessions that were separated by at least one week. In the first session, participants went through the fMRI experiment (i.e., the control session), whereas in the second and third sessions participants were first subject to tDCS stimulation outside the MR scanner, and then immediately started the fMRI experiment. The order of the tDCS sessions was counterbalanced across participants. The fMRI experiment consisted of the presentation of a series of visual stimuli belonging to different object categories (e.g., tools, faces). tDCS sessions consisted of anodal (typically thought to increase neuronal excitability) or cathodal (typically thought to decrease neuronal excitability; Nitsche et al., 2009; Senco et al., 2015; Stagg & Nitsche, 2011) stimulation to the left Inferior Parietal Lobule (IPL).

The left IPL was chosen as the target area because it is highly accessible to these non-invasive neuromodulation techniques, and because it is known to respond more to images of tools than images of stimuli from other categories (e.g., Almeida, Fintzi, & Mahon, 2013; Chao & Martin, 2000; Garcea, Kristensen, Almeida, & Mahon, 2016; Kristensen, Garcea, Mahon, & Almeida, 2016; Mahon, Kumar, & Almeida, 2013).

The current understanding of how tDCS works assumes that tDCS modulates the polarity of the resting membrane and the synaptic strength of neurons (e.g., Fertonani & Miniussi, 2016; Stagg & Nitsche, 2011), but does not, in and of itself, elicit action potentials. By virtue of this mechanistic understanding of tDCS, we expect there to be modulation of the responses of those neurons already engaged in (cognitive) processing. As such, because in our experiment neurons within the left IPL will be engaged in processing tool stimuli, we will be able to test whether tDCS can modulate neural responses, and in particular tool-preferences, in IPL.

Importantly, if the stimulation parameters used in our sessions, which are similar to those typically used in regular tDCS experiments, are sufficient for modulating neural activity, then, activity in the left IPL for tools, when compared to activity for a control category (e.g., faces; henceforth tool-specificity), should be dependent on the polarity of the tDCS stimulation. Specifically, there should be a decrement of tool-specific responses in the left IPL when we inhibit this area (i.e., in the sessions in which we apply cathodal tDCS), when compared to when we excite it (i.e., in the sessions in which we apply anodal tDCS). That is, BOLD signal coming from the left IPL as a response to the presentation of tool images should be modulated by whether we excite or inhibit this area before the fMRI session.

2. Material and methods

2.1. *Participants*

Ten healthy right-handed adults (mean age = 23.0 years, SD = 4.5 years, range = 18–33 years; five females, and five males) participated in the experiment. Participants were part of the student population of the Faculty of Psychology and Educational Sciences of the University of Coimbra, and received course credit for their participation. The study adhered to the Declaration of Helsinki and was approved by the Ethical Committee of the Faculty of Psychology and Educational Sciences of the University of Coimbra. All participants gave written informed consent after a detailed description of the complete study. Because of the use of tDCS, and the collection of fMRI data, there were clear exclusion criteria that included cardiovascular or neurological disorders, brain injury, pregnancy, lifetime and current substance abuse or dependence, any mental disorder, and metallic implants.

2.2. *Procedure*

2.2.1. *fMRI experiment*

In the fMRI experiment we used grayscale photographs of tools, animals, famous faces, and famous places, plus phase-scrambled versions of these stimuli as experimental stimuli (for more details on materials, see Fintzi & Mahon, 2014). Stimuli were 400 × 400 pixels in size and were presented on a gray background using an Avotec projector with 60 Hz refresh rate. To control stimulus presentation we used "A Simple Framework" (Schwarzbach, 2011) under MATLAB R2014a (The MathWorks Inc., Natick, MA, USA). Stimuli were back-projected on a screen that participants viewed with a mirror