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Short communication

Modulating the interhemispheric balance in healthy participants with transcranial direct current stimulation: No significant effects on word or sentence processing

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A B S T R A C T

Patient studies and brain stimulation evidence suggest that language processing can be enhanced by altering the interhemispheric balance: namely, preferentially enhancing left-hemisphere activity while suppressing right-hemisphere activity. To our knowledge, no study has yet compared the effects of such bilateral brain stimulation to both logically necessary control conditions (separate left- and right-hemisphere stimulation). This study did so in a between-group sham-controlled design, applying transcranial direct current stimulation over Broca's area and/or its homologue in 72 healthy participants. The effects were measured not only in a single-word-level task but also in a sentence-level task, rarely tested previously. We did not find either any significant overall effects of stimulation or greater stimulation effects in the bilateral compared to control groups. This null result, obtained in a large sample, contributes to the debate on whether tDCS can modulate language processing in healthy individuals.

1. Introduction

Although patients with aphasia greatly benefit from behavioral language therapy (Brady, Kelly, Godwin, Enderby, & Campbell, 2016), the degree and rate of improvement vary across individuals. Lately, brain stimulation, and particularly transcranial direct current stimulation (tDCS) as a safe and tolerable method, has been discussed as a promising tool to enhance language therapy (Galletta, Conner, Vogel-Eyny, & Marangolo, 2016). Still, little is known about the most effective tDCS settings in terms of target areas, electrode montages, stimulation regimen and dosage, and their individual tailoring. Systematic investigation of these choices, similar to recent endeavors in the motor domain (Tremblay et al., 2016), is crucial before tDCS can be used clinically for language rehabilitation.

The choice of stimulation targets can be informed by current theories on the neural correlates of successful aphasia recovery. One of them, the interhemispheric competition hypothesis, states that successful recovery of aphasia following left-hemisphere damage is mediated by activation of perilesional left-hemisphere areas, whereas right-hemisphere activity is maladaptive and, via transcallosal inhibition, prevents the left hemisphere from restoring its functions (Hamilton, Chrysikou, & Coslett, 2011). The evidence comes from neuroimaging studies where increased involvement of the right hemisphere in language processing was associated with lower scores on language assessment (Szaflarski, Allendorfer, Banks, Vannest, & Holland, 2013), weaker improvement following therapy (Breier, Randle, Maher, & Papanicolaou, 2010; Marcotte et al., 2012; Saur et al., 2006 for chronic stage), or errors in single-trial analyses (Postman-Caucheteux et al., 2010). On the other hand, some studies demonstrated positive correlations between right-hemisphere involvement and language improvement in aphasia (Menke et al., 2009; Pulvermüller, Hauk, Zohsel, Neininger, & Mohr, 2005; see Cocquyt, De Ley, Santens, Van Borsel, & De Letter, 2017, for a review), particularly in the (sub)acute stage (Saur et al., 2006).

Despite conflicting evidence from neuroimaging, the interhemispheric competition hypothesis is further supported by brain stimulation studies that enhanced language processing by altering the "interhemispheric balance". Transcranial magnetic stimulation (TMS) studies have inhibited right-hemisphere areas and found positive effects on language processing (Naeser, Martin, & Ho, Treglia, Kaplan, Bhashir, & Pascual-Leone, 2012; for a review, see Otal, Olma, Flöel, & Wellwood, 2015). tDCS studies have, furthermore, used bilateral montages that

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apply anodal (supposedly excitatory) stimulation over the left hemisphere simultaneously with cathodal (supposedly inhibitory) stimulation over the right hemisphere. Studies using bilateral montages are limited in number but promising: bilateral temporal tDCS has enhanced verbal learning in healthy older adults (Fiori et al., 2017), bilateral frontal tDCS has improved articulation accuracy in non-fluent aphasia (Marangolo et al., 2016) and naming speed and accuracy in a mixed group of patients with aphasia (Lee, Cheon, Yoon, Chang, & Kim, 2013). However, to the best of our knowledge, no tDCS study has yet formally tested whether bilateral stimulation has a greater effect on language processing than its individual "components": i.e., separate anodal stimulation of the left hemisphere or cathodal stimulation of the right hemisphere. Lee et al. (2013) and Fiori et al. (2017) included only left anodal control stimulation as a control condition and showed it to be effective but inferior to the bilateral condition. The second necessary control condition, right cathodal stimulation, has not been tested.

Notably, many tDCS montages reported as left anodal or right cathodal in fact had bipolar montages. Conventionally, tDCS electrode montages are described by their target area. However, the positioning of the "reference" electrode is crucial (Garnett, Malyutina, Datta, & Den Ouden, 2015) because it critically modulates the orientation of the current flow relative to the target neuronal populations (Rawji et al., 2018). So, if the "reference" cathode in a "left anodal" montage is placed over the right hemisphere, or the "reference" anode in a "right cathodal" montage is placed over the left hemisphere, the montage in fact affects both hemispheres (see also De Aguiar, Paolazzi, & Miceli, 2015). Even if "reference" electrodes are not placed over cortical areas, the electric field can still spread there due to low focality of tDCS. For example, if using a right supraorbital "reference" electrode, some electric field must spread to the right frontal cortex. Such bipolar montages have been used among both right cathodal (for example, Flöel et al., 2011, Kang, Kim, Sohn, Cohen, & Paik, 2011, Rosso et al., 2014, You, Kim, Chun, Jung, & Park, 2011, with left supraorbital "reference" anodes) and left anodal montages (for example, Fridriksson, Richardson, Baker, & Rorden, 2011, "reference" cathode on right forehead; Saidmanesh, Pouretemad, Amini, Nilipor, & Ekhtiari, 2012, "reference" cathode over right dorsolateral prefrontal cortex; Fiori et al., 2011, and Marangolo et al., 2013, contralateral frontopolar "reference" cathodes). Again, the findings with these "implicitly bilateral" montages seem promising, but it was never controlled whether their effects are superior to pure anodal stimulation of the left hemisphere or cathodal stimulation of the right hemisphere.

To the best of our knowledge, the present study is the first to test the effects of bilateral tDCS (over Broca's area and its right-hemisphere homologue) against both logically necessary control conditions: separate anodal stimulation of the left Broca's area and cathodal stimulation of its right-hemisphere homologue. Although the ultimate purpose is to inform the choice of tDCS montages in aphasia therapy, here we opt for a large sample of neurologically healthy young control participants, ensuring better statistical power for comparing the stimulation conditions. Certainly, the very idea of interhemispheric competition has limited applicability to language processing in healthy individuals: presumably, they normally demonstrate optimal lateralization of language processing, without excessive activation of the right hemisphere. However, we are not introducing any novel electrode montages guided by the interhemispheric competition theory: rather, we compare the effectiveness of three montages widely used in healthy individuals, as discussed above, and hope that this comparison provides implications for a well-informed choice of bilateral versus unilateral montages also in clinical populations. A secondary goal of the study is to contribute to the general debate on whether tDCS can modulate language processing in healthy individuals: some consider it effective (Gauvin, Meinzer, & de Zubicaray, 2017; Price, McAdams, Grossman, & Hamilton, 2015), while others argue for lack of effects (Westwood, Olson, Miall, Nappo, & Romani, 2017). This study can make a special contribution to the debate due to its large sample size (n = 72, cf. n = 73 total in the four experiments by Westwood et al., 2017).

Besides the use of two unilateral control conditions, another novel contribution of this study is including a sentence-level task. So far, most tDCS studies have used single-word tasks such as naming or verbal fluency (for review, see Klaus & Schutter, 2018). Only a recent study by Giustolisi, Vergallito, Cecchetto, Varoli, & Romero Lauro (2018) showed improved sentence comprehension in healthy speakers following anodal tDCS over left Broca's area (in a bipolar montage with the the right supraorbital cathode). To add to this first evidence on sentence-level effects of tDCS in healthy speakers, we include both a single-word-level and a sentence-level task. The Broca's area has been implicated both in syntactic and semantic processing (Vigliocco, 2000) so its stimulation has a potential to enhance both levels, which is highly relevant clinically.

2. Methods

2.1. Participants

The participants were 72 young volunteers (49 females; mean age 22.9, SD 3.8, range 18–32 years), all self-reportedly right-handed (scores on the 11-item Edinburgh Handedness Inventory (Oldfield, 1971): mean 65.7, SD 19.0, range 22.7–100.0), monolingual native speakers of Russian, with normal or corrected-to-normal vision and no reported history of neurological, psychiatric, or speech-language disorders. Participants completed a tDCS safety questionnaire before the study to rule out any contraindications. Participants were blind to their experimental assignment and to the experimental design. The study protocol conformed to the Declaration of Helsinki and was approved by the local University Research Ethics committee.

2.2. tDCS

tDCS was delivered at 1.5 mA for 20 min using a battery-driven Starstim® stimulator (Neuroelectrics), via round 25 cm^2 rubber-sponge electrodes, soaked in saline and positioned in the supplied neoprene headcap, resulting in the current density of 0.06 mA/cm^2. In a between-group design, participants were randomly assigned to three stimulation conditions (n = 24 per condition) using a sealed-envelope approach. Participants in the bilateral condition received a combination of anodal stimulation over the left inferior frontal gyrus (IFG) and cathodal stimulation over the right IFG (anode at F7, cathode at F8; see Fig. 1). Participants in the left anodal condition received anodal stimulation over the left posterior IFG, corresponding to Broca's area (anode at F7, cathode at Pz). Participants in the right cathodal condition received cathodal stimulation over right IFG (cathode at F8, anode at Pz). The "reference" electrodes were positioned at the midline (as opposed to, for example, contralateral cheek) to ensure a unilateral electric field with minimal current spread to the contralateral hemisphere (based on modelling of the electric field in the Neuroelectrics Instrument Controller 1.4 software, see Supplementary Fig. S1) and to ensure the same amount of electric current over the scalp as in the bilateral condition. Specifically Pz was chosen because stimulation over the parietal area appeared less relevant to our tasks compared to prefrontal, temporal or occipital positioning of "reference" electrodes. Every participant was administered real and sham stimulation on different days; session order was counterbalanced across participants. For sham stimulation, current intensity was also ramped up to 1.5 mA but then ramped down in 50 s. The interval between sessions was 6.33 days on average (range 1–26 days) and did not differ between groups, $F(2,69) = 1.05$, $p = 0.35$.

2.3. Procedure and tasks

Participants performed a single-word-level task (lexical decision) and a sentence-level task (sentence comprehension). They received