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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 R T I C L E I N F O

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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

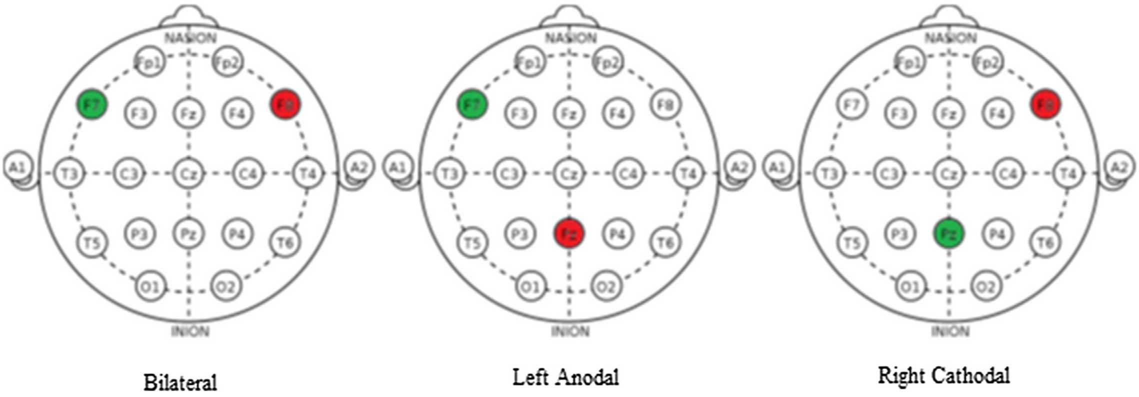

Fig. 1. Electrode placement across experimental conditions. Color-coding: anode – green, cathode – red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

instructions and short training before the stimulation start on their first day. On both days, participants practiced both tasks online (during stimulation) and were tested on them offline immediately after the stimulation. Task order was counterbalanced within each experimental group and was identical offline and online. Online, tasks were alternated twice with short breaks to prevent fatigue (tasks were terminated based on timing rather than completion: both online blocks included 3.5 min of sentence comprehension and 2.5 min of lexical decision, with 1.5-min breaks between tasks and blocks). The design included online practice because tDCS appears to preferentially modulate active neuronal networks (Bikson & Rahman, 2013). The mean duration of offline tasks was 13.5 min (SD 2.3 min, range 10.5–25.5 min), including on average 4.8 min of lexical decision (SD 0.6 min, range 4.4–7.7 min) and 8.7 min of sentence comprehension (SD 2.3 min, range 5.9–21.0 min).

In the lexical decision task, participants saw a string of letters in the center of the screen and pressed a button to respond whether it was a real Russian word. Each stimulus was presented for 1200 ms, followed by a 800 ms fixation cross. In the sentence comprehension task, participants read sentences in a self-paced mode; words appeared in the center of the screen one at a time. After each sentence, participants saw a comprehension question with two possible responses in the lower left and right corners of the screen and responded by button press, followed by a fixation cross (800 ms) and the start of the next sentence. All experimental paradigms were programmed with E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA).

In 1 min and 19 min after stimulation start, participants completed a tolerability questionnaire: they rated tDCS-related pain and unpleasantness on a scale from 1 (no pain/unpleasantness) to 10. After the end of the study, participants were informed that one session provided sham stimulation and were asked to guess which session it was.

2.4. Stimuli

No stimuli were repeated across any online or offline sessions. In lexical decision, each offline list included 60 Russian words and 60 pronounceable non-words, matched for length in letters and syllables. The two offline lists were matched for stimuli length in letters and syllables, lexical frequency (Lyashevskaya & Sharov, 2009) and orthographic neighborhood (Alexeeva et al., in press) of real words, and mean reaction time (RT) from a pilot study with 24 neurologically healthy young participants (none of whom participated in this tDCS study). Each online list included 75 words and 75 non-words, split into two blocks; the online lists were matched for stimuli length in letters and syllables.

In sentence comprehension, each list included 60 Russian sentences: grammatically complex sentences (44 in each offline and 28 in each online list) and fillers with simpler syntactic structure (16 in each offline and 32 in each online list). Grammatically complex sentences were designed to avoid ceiling effects and included syntactic structures shown to present a difficulty even for individuals without language deficits: a non-finite (participial) clause attached to one of the two nouns in the genitive noun phrase (Chernova & Slioussar, 2016); sentences with semantically reversible subject and object (including those with non-canonical object-verb-subject word order; Slobin, 1966); subject- and object-relative clauses (Wanner & Maratsos, 1978); and object-relative clauses with reflexive pronouns (Laurinavichyute, Jäger, Akinina, Roß, & Dragoy, 2017). Proportions of sentence types in offline versus online lists were different to minimize practice and strategy effects. Every sentence was followed by a comprehension question with two response options. For grammatically complex sentences, the incorrect response was a noun also mentioned in the sentence (e.g., *The judge, who the attorney waited for in the office, never came. – Who waited in the office? – Judge / Attorney*), requiring grammatical rather than superficial lexical analysis of sentences. Questions to fillers could refer to any part of speech and the incorrect response option was not mentioned in the sentence (e.g., *The graduating student was wearing a beautiful beige knee-long dress. – What color dress was the graduating student wearing? – Beige/Blue*). Across offline and across online lists, the stimuli were matched for sentence and question length in words and syllables, as well as for length in syllables and grammatical gender of responses; offline lists were also matched for log-transformed frequency of responses and all content words in sentences (Lyashevskaya & Sharov, 2009). In both tasks, the assignment of both online and offline lists to real and sham stimulation was counterbalanced across participants, and the stimuli order was randomized.

2.5. Data analysis

In lexical decision, the outcome measure were RTs (only from correct-response trials); accuracy was not analyzed due to ceiling effects. In sentence comprehension, the outcome measures were RTs (only from correct-response trials), accuracy, and self-paced reading time (mean speed per word in each sentence). RTs and reading time were log-transformed. Our primary analysis was performed on offline data. The online paradigms were originally designed solely to ensure online engagement into a linguistic task and thus had limitations in balancing (in both tasks, online lists were not matched for lexical frequency; besides, each online list was randomly split into two unbalanced blocks). Still, since linear mixed-effect models account for inter-item variability, we analyzed the online data using the same statistical models as for offline data.

We applied linear mixed-effect models (in case of accuracy, generalized linear mixed-effect models) using lme4 package, version 1.1–13 (Bates, Maechler, Bolker, & Walker, 2015) in R (R Core Team, 2017). The fixed factors were stimulation (real vs. sham), stimulation group (left anodal vs. right cathodal vs. bilateral), linguistic condition (word/non-word or sentence type), session (participant's day 1 or 2). The models included by-participant and by-item random intercepts, as well as by-participant random slopes for stimulation. *P*-values were obtained via likelihood ratio tests.

Since bilateral stimulation aimed to alter the interhemispheric balance, its effect could depend on individual language lateralization. Using participants' handedness scores on the Edinburgh Handedness Inventory (Oldfield, 1971) as a proxy for language lateralization, we performed an exploratory analysis where handedness scores were added as a covariate to the above-described linear mixed-effect models.

3. Results

3.1. Safety and tolerability

No participants reported any side effects during or after stimulation. Tolerability was high: on a 1–10 scale, mean (SD) ratings for pain and unpleasantness respectively in 1 min after stimulation start were 2.1(1.6) and 3.5(1.9) for real stimulation and 1.8(1.3) and 2.9(1.7) for sham; in 19 min after stimulation start, these were 1.3(0.8) and 1.9(1.3) for real stimulation and 1.2(0.8) and 1.8(1.6) for sham. Forty-one (57.8%) participants correctly guessed which session corresponded to sham, indicating valid blinding.

3.2. Lexical decision

For technical reasons, data from one participant's online block (0.35% of all online data) are missing. Mean accuracy and RTs are presented in Table 1. In the linear mixed-effect model on RT data, there was neither a significant main effect of stimulation (offline: $\chi^2(2) = 0.18$, $p = 0.67$; online: $\chi^2(2) = 0.94$, $p = 0.33$), nor a Stimulation by Group interaction (offline: $\chi^2(2) = 1.62$, $p = 0.45$; online: $\chi^2(2) = 1.02$, $p = 0.60$), nor a Stimulation by Session interaction (offline: $\chi^2(1) = 1.83$, $p = 0.18$; online: $\chi^2(1) = 1.47$, $p = 0.22$). Responses were faster for words than non-words (offline: $\chi^2(1) = 92.81$, $p < 0.001$; online: $\chi^2(1) = 80.93$, $p < 0.001$), and in second than first session (offline: $\chi^2(1) = 20.20$, $p < 0.001$; online: $\chi^2(1) = 76.52$, $p < 0.001$); there was no significant main effect of group (left anodal, right cathodal, bilateral) (offline: $\chi^2(2) = 0.31$, $p = 0.86$, online: $\chi^2(2) = 0.19$, $p = 0.91$).

3.3. Sentence comprehension

For technical reasons, some online data are missing: these are data from one participant's two online blocks (0.7% of all online data) and self-paced reading speed from one online block (25% of self-paced reading speed data, in balanced order across sessions and stimulation conditions; other measures from these blocks are fully available). Mean self-paced reading time (mean time per word within each sentence) and question RT and accuracy are presented in Table 1. Linear mixed-effect models revealed the same pattern for all three outcome measures. Namely, there was neither a significant effect of Stimulation (offline: reading time: $\chi^2(2) = 0.16$, $p = 0.69$, RT: $\chi^2(2) = 0.10$, $p = 0.76$, response accuracy: $\chi^2(2) = 1.96$, $p = 0.16$; online: reading time: $\chi^2(2) = 0.03$, $p = 0.86$, RT: $\chi^2(2) = 0.19$, $p = 0.66$, response accuracy: $\chi^2(2) = 0.81$, $p = 0.37$), nor a Stimulation by Group interaction (offline: reading time: $\chi^2(2) = 0.13$, $p = 0.94$, RT: $\chi^2(2) = 0.31$, $p = 0.86$, response accuracy: $\chi^2(2) = 3.36$, $p = 0.34$; online: reading time: $\chi^2(2) = 1.45$, $p = 0.48$, RT: $\chi^2(2) = 2.42$, $p = 0.30$, response accuracy: $\chi^2(2) = 1.97$, $p = 0.58$), nor a Stimulation by Session interaction (offline: reading time: $\chi^2(2) = 2.65$, $p = 0.10$, RT: $\chi^2(2) = 1.06$, $p = 0.30$, response accuracy: $\chi^2(2) = 1.96$, $p = 0.38$; online: reading time: $\chi^2(2) = 0.36$, $p = 0.55$, RT: $\chi^2(2) = 1.31$, $p = 0.25$, response accuracy: $\chi^2(2) = 1.10$, $p = 0.58$). Performance was affected by sentence structure (offline: reading time: $\chi^2(4) = 26.81$, $p < 0.001$, RT: $\chi^2(4) = 57.21$, $p < 0.001$, response accuracy: $\chi^2(4) = 40.92$, $p < 0.001$; online: reading time: $\chi^2(4) = 9.00$, $p = 0.06$, RT: $\chi^2(4) = 68.6$, $p < 0.001$, response accuracy: $\chi^2(4) = 26.87$, $p < 0.001$), but not by experimental group (offline: reading time: $\chi^2(2) = 1.09$, $p = 0.58$, RT: $\chi^2(2) = 0.90$, $p = 0.64$, response accuracy: $\chi^2(2) = 0.13$, $p = 0.94$; online: reading time: $\chi^2(2) = 1.03$, $p = 0.60$, RT: $\chi^2(2) = 1.06$, $p = 0.59$, response accuracy: $\chi^2(2) = 0.38$, $p = 0.83$). Session only affected online performance (offline: reading time: $\chi^2(1) = 0.03$, $p = 0.86$, RT: $\chi^2(1) = 0.33$, $p = 0.57$, response accuracy: $\chi^2(1) = 0.51$, $p = 0.47$; online: reading time: $\chi^2(1) = 77.82$, $p < 0.001$, RT: $\chi^2(1) = 17.02$, $p < 0.001$, response accuracy: $\chi^2(1) = 4.85$, $p = 0.03$).

3.4. Effects of handedness scores

In the additional linear mixed-effect models with handedness scores added as a covariate, the significance or non-significance of all factors and interactions remained the same as described in Sections 3.2 and 3.3. Handedness scores did not significantly modulate the effect of stimulation across experimental groups (Handedness x Stimulation, offline: lexical decision reaction times: $\chi^2(1) = 0.99$, $p = 0.32$; sentence reading time: $\chi^2(1) = 0.06$, $p = 0.80$, question reaction time: $\chi^2(1) = 0.20$, $p = 0.65$, question response accuracy: $\chi^2(1) = 1.84$, $p = 0.17$). Neither did the experimental groups significantly differ on how handedness scores modulated the effect of stimulation (Handedness x Stimulation x Group, offline: lexical decision reaction times: $\chi^2(2) = 0.81$, $p = 0.67$; sentence reading time: $\chi^2(2) = 1.68$, $p = 0.43$, question reaction time: $\chi^2(2) = 1.84$, $p = 0.87$, question response accuracy: $\chi^2(2) = 8.02$, $p = 0.16$). The main effect of handedness was not significant either (offline: lexical decision reaction times: $\chi^2(1) = 2.98$, $p = 0.08$; sentence reading time: $\chi^2(1) = 0.60$, $p = 0.44$, question reaction time: $\chi^2(1) = 0.21$, $p = 0.64$, question response accuracy: $\chi^2(1) = 0.01$, $p = 0.91$).

4. Discussion

This study tested whether language processing in healthy young adults can be modulated by altering the interhemispheric balance with tDCS. We applied bilateral tDCS combining anodal (supposedly excitatory) stimulation of the Broca's area and cathodal (supposedly inhibitory) stimulation of its right-hemisphere homologue. To our knowledge, this was the first study where bilateral tDCS was tested against both logically necessary control conditions: separate anodal stimulation of the left Broca's area and cathodal stimulation of the contralateral area. The effects were tested not only in a single-word task but also in a sentence-level task, previously reported only by Giustolisi et al. (2018).

We found no significant effects of tDCS on either speed or accuracy of either single-word or sentence-level processing (no significant effects of stimulation across the experimental groups). The effects of bilateral tDCS were not superior to those of control conditions: there were no significant interactions between stimulation (real versus sham) and experimental group (bilateral versus left anodal versus right cathodal). The null results held in both offline and online performance. Given our large sample size (n = 72; cf. typical sample sizes of ca. 20 participants, Klaus & Schutter, 2018), the study contributes to the debate on whether tDCS can modulate language processing in healthy speakers. While some argue that it can (Gauvin et al., 2017; Price et al., 2015), others pinpoint that positive effects in the published literature can be due to regression-to-the-mean in low-powered studies and/or publication bias (Westwood & Romani, 2017; Westwood et al., 2017). Our null results provide a contribution to future meta-analyses.

Null results in lexical decision have already been demonstrated following tDCS over Broca's area in healthy young participants (Malyutina & Den Ouden, 2015; although see significant effects following temporal tDCS: Brückner & Kammer, 2017; Weltman & Lavidor, 2013). In our sentence-level task, we did not replicate the positive effect

Table 1
Task performance across stimulation conditions, mean (SD).

Group	Session	Stimulation	Lexical decision		Sentence comprehension		
			Accuracy, %	Reaction time, ms	Question reaction time, ms	Question response accuracy, %	Mean self-paced reading time per word, ms
Online performance							
Bilateral	Session 1	Real	95.9 (2.1)	714 (68)	88.2 (4.3)	2006 (552)	522 (85)
		Sham	96.9 (3.0)	676 (61)	89.4 (3.6)	1802 (283)	526 (113)
	Session 2	Real	97.4 (2.0)	626 (41)	89.8 (5.0)	1681 (285)	427 (125)
		Sham	97.0 (1.2)	671 (79)	88.9 (2.9)	1874 (470)	423 (69)
	Across sessions	Real	96.6 (2.1)	670 (71)	89.0 (4.6)	1844 (461)	474 (115)
		Sham	97.0 (2.3)	674 (69)	89.1 (3.2)	1838 (381)	474 (106)
Left anodal	Session 1	Real	95.9 (2.1)	677 (65)	90.4 (3.5)	1880 (396)	507 (136)
		Sham	95.6 (3.9)	700 (71)	89.2 (4.4)	1893 (369)	574 (109)
	Session 2	Real	97.5 (1.3)	652 (65)	90.9 (5.1)	1759 (391)	494 (99)
		Sham	96.8 (2.1)	653 (88)	89.9 (5.0)	1857 (395)	462 (139)
	Across sessions	Real	96.7 (1.9)	665 (64)	90.7 (4.3)	1819 (390)	501 (117)
		Sham	96.2 (3.1)	676 (82)	89.6 (4.6)	1875 (374)	515 (135)
Right cathodal	Session 1	Real	96.9 (1.3)	718 (80)	89.4 (5.8)	2097 (524)	542 (125)
		Sham	97.3 (1.8)	691 (67)	89.9 (2.8)	1936 (523)	516 (108)
	Session 2	Real	97.4 (2.1)	632 (52)	90.5 (5.0)	1777 (321)	452 (90)
		Sham	96.9 (1.8)	653 (52)	90.8 (5.0)	1895 (547)	452 (115)
	Across sessions	Real	97.1 (1.7)	675 (79)	90.0 (5.3)	1937 (455)	497 (116)
		Sham	97.1 (1.8)	672 (62)	90.3 (4.0)	1916 (524)	484 (114)
Offline performance							
Bilateral	Session 1	Real	96.7 (2.5)	670 (57)	87.4 (5.6)	2377 (663)	391 (83)
		Sham	96.8 (4.5)	639 (54)	91.0 (5.8)	2142 (404)	400 (104)
	Session 2	Real	98.6 (1.0)	617 (37)	88.9 (6.6)	2059 (353)	362 (108)
		Sham	96.4 (2.3)	662 (66)	85.8 (4.7)	2318 (700)	348 (72)
	Across sessions	Real	97.7 (2.1)	643 (54)	88.2 (6.1)	2218 (544)	378 (95)
		Sham	96.6 (3.5)	650 (60)	88.4 (5.8)	2230 (566)	374 (91)
Left anodal	Session 1	Real	97.3 (2.8)	652 (77)	90.3 (4.7)	2224 (557)	417 (139)
		Sham	97.0 (2.6)	644 (65)	88.5 (6.0)	2141 (505)	433 (100)
	Session 2	Real	97.6 (1.6)	634 (77)	86.8 (4.3)	2115 (493)	405 (98)
		Sham	97.4 (2.5)	632 (69)	89.4 (5.8)	2115 (595)	373 (119)
	Across sessions	Real	97.4 (2.2)	643 (76)	88.6 (4.8)	2170 (517)	411 (118)
		Sham	97.2 (2.5)	638 (66)	89.0 (5.8)	2128 (540)	403 (112)
Right cathodal	Session 1	Real	97.2 (2.1)	676 (60)	89.7 (5.9)	2572 (1115)	430 (130)
		Sham	97.5 (1.8)	658 (60)	91.0 (5.5)	2270 (531)	431 (122)
	Session 2	Real	98.1 (1.6)	619 (47)	86.4 (6.9)	2101 (628)	390 (118)
		Sham	98.0 (1.6)	639 (66)	88.8 (6.0)	2272 (793)	384 (118)
	Across sessions	Real	97.6 (1.9)	648 (60)	88.1 (6.5	2336 (917)	410 (123)
		Sham	97.7 (1.7)	649 (62)	90.0 (5.7)	2271 (660)	407 (119)

of tDCS over Broca's area on sentence comprehension in healthy individuals recently found by Giustolisi et al. (2018). One possible reason is different stimulation dosage (0.75 mA for 30 min in their study versus 1.5 mA for 20 min here): possibly, longer and/or lower-intensity stimulation may have greater effects (Hoy et al., 2013). On the other hand, higher intensities such as 2 mA have also been effective in previous research (see reviews by Monti et al., 2013; Klaus & Schutter, 2018), although typically using larger electrode sizes and thus lower current densities than here. Given potentially non-linear effects of tDCS parameters (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013), it remains to be discovered which current density is appropriate to modulate language processing. Another possible reason for the discrepancy with Giustolisi et al. (2018) is experimental design: in our study, each participant received real and sham stimulation on different days, whereas Giustolisi et al. (2018) used a between-subject design (n = 22 each in real and sham stimulation), so between-group differences could be due to random individual variability. Then, both studies tapped into sentence comprehension but used different tasks. We used a purely verbal task in the written modality (self-paced reading with binary-choice comprehension questions). Giustolisi et al. (2018) used sentence-picture matching with auditory sentence presentation. It required retaining the sentence in auditory working memory and matching it with the visual modality. The positive effect of tDCS on sentence-picture matching could be mediated by enhancement of these processes. Lastly, unlike Giustolisi et al. (2018), we used two different tasks. This reduced the time during which the participants were enrolled in each individual task online. As tDCS is assumed to modulate active neuronal networks (Bikson & Rahman, 2013), the time of association between stimulation and task engagement could be insufficient to yield effects.

Besides, lack of significant tDCS effects in the language domain is often linked to ceiling effects in healthy young speakers (Westwood et al., 2017), whereas older adults and lower performers do demonstrate sensitivity to stimulation (Fiori et al., 2017; Habich et al., 2017, in the memory domain). According to Miniussi, Harris and Ruzzoli (2013), stimulation effects are contingent upon task demands because transcranial electrical stimulation modulates the amount of noise in the neural system. If an easy task provides strong input (corresponding to the flat part of the sigmoid input-response function), the neuronal response begins to saturate and thus becomes less sensitive to modulations of the signal-to-noise ratio by brain stimulation. In our lexical decision task, participants obviously performed largely at ceiling. In our sentence comprehension task, the mean accuracy (88.6%) appeared to leave room for improvement with tDCS. As a post-hoc speculation, we suggest that this imperfect accuracy rate in healthy young adults may originate from incomplete ("good-enough") processing strategies that are inherent to normal language processing (Ferreira, Bailey, & Ferraro, 2002) and thus, in a way, also reflect at-ceiling performance. In other words, imperfect accuracy in sentence comprehension in healthy young adults may be observed for strategic reasons and thus have different nature than low language performance in older adults or low memory/attention performance, which are likely due to shortage of resources such as working memory span, processing speed or sustained attention span, and thus more likely to be boosted by neurophysiological methods.

Importantly, we by no means argue for general inefficiency of tDCS. Rather, it appears that tDCS can modulate language processing under *some* conditions, which remain to be specified. Individual factors such as initial performance level or language lateralization may play a role, although our study did not reveal a dependency of stimulation effects on handedness scores used as a proxy for language lateralization. In addition to individual factors, an ever-important factor are stimulation parameters and electrode montages, including the positioning of the "reference" electrode. Here, for example, the "reference" electrodes in the left anodal and right cathodal conditions were positioned over the midline parietal region, thus introducing "implicit" parietal stimulation. Even though, as discussed in Section 2.2, this positioning appeared to minimize confounding in our design, tDCS effects could differ with a different positioning of "reference" electrodes. Careful consideration of electrode montages is crucial for further reports and meta-analyses of tDCS setup efficacy.

Ultimately, the purpose of the study was to inform tDCS applications in aphasia. Due to lack of effects in our control sample, the study did not provide clinical implications. It remains to be directly investigated in the population with aphasia whether bilateral stimulation, altering the interhemispheric balance, has a greater effect on language processing than separate application of its components (left anodal stimulation or right cathodal stimulation). Alternatively, in any future research with the healthy population, it would be worthwhile to follow the approach of Hartwigsen et al. (2013) and "model" perturbation of language network by downregulating the left-hemisphere activity with TMS, making it more relevant to subsequently alter the interhemispheric balance with tDCS. Based on previous neuroimaging and brain stimulation research, altering the interhemispheric balance promises a positive effect on language recovery in aphasia and thus deserves further experimental testing.

Conflict of interest

The authors declare no conflict of interest.

Statement of significance to the neurobiology of language

The study tested whether language processing in healthy participants can be boosted by altering the interhemispheric balance with tDCS, which is relevant for understanding the relative role of left and right hemisphere in language processing. The null results contribute to methodological debates on tDCS effects in healthy individuals.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bandl.2018.09.004.

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