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TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) OVER THE RIGHT DORSOLATERAL PREFRONTAL CORTEX AFFECTS STIMULUS CONFLICT BUT NOT RESPONSE CONFLICT

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Abstract—When the human brain encounters a conflict, performance is often impaired. Two tasks that are widely used to induce and measure conflict-related interference are the Eriksen flanker task, whereby the visual target stimulus is flanked by congruent or incongruent distractors, and the Simon task, where the location of the required spatial response is either congruent or incongruent with the location of the target stimulus. Interestingly, both tasks share the characteristic of inducing response conflict but only the flanker task induces stimulus conflict. We used a non-invasive brain stimulation technique to explore the role of the right dorsolateral prefrontal cortex (DLPFC) in dealing with conflict in the Eriksen flanker and Simon tasks. In different sessions, participants received anodal, cathodal, or sham transcranial direct current stimulation (tDCS) (2 mA, 20 min) on the right DLPFC while performing these tasks. The results indicate that cathodal tDCS over the right DLPFC increased the flanker interference effect while having no impact on the Simon effect. This finding provides empirical support for the role of the right DLPFC in stimulus–stimulus rather than stimulus–response conflict, which suggests the existence of multiple, domain-specific control mechanisms underlying conflict resolution. In addition, methodologically, the study also demonstrates the way in which brain stimulation techniques can reveal subtle yet important differences between experimental paradigms that are often assumed to tap into a single process. © 2016 Published by Elsevier Ltd. on behalf of IBRO.

Key words: brain stimulation, tDCS, Eriksen flanker effect, Simon effect, DLPFC, cognitive control.

INTRODUCTION

A robust finding from experimental psychology is that when the human brain encounters a conflict, the efficiency of its performance suffers noticeably. Various experimental conflict paradigms have provided ample evidence demonstrating that irrelevant, incongruent information affects individuals' response time and accuracy. This is evident in the flanker task introduced by Eriksen and Eriksen (1974), which shows slow and less accurate response to central visual target stimuli when these are flanked by stimuli that are incongruent with the target. Systematic experimentation has revealed two sources of conflict in this task, one related to the incongruence between the flankers and the target and one related to the incongruence between the response signaled by the flankers and the response signaled by the target (Wendt et al., 2007). Hence, the flanker effect reflects stimulus conflict and response conflict. Another extensively studied paradigm is the Simon task (Simon and Small, 1969), where responses to a non-spatial stimulus feature are slower and more error-prone when the location of the response is spatially incongruent to the location of the stimulus. Given the non-spatial nature of the relevant stimulus feature, this effect does not rely on stimulus conflict but on response conflict only (Hommel, 2011; Kornblum, 1992).

It has been suggested that when conflict (in incongruent trials) is detected, a cognitive control mechanism is engaged so to reduce and deal with the conflict according to the task's requirements (Botvinick et al., 2001). While the flanker task and the Simon task have often been used to explore conflict-related cognitive control mechanisms, the fact that they show comparable behavioral outcomes does not necessarily imply the same neural mechanisms. Previous imaging studies have associated conflict resolution with the dorsolateral prefrontal cortex (DLPFC; Durston et al., 2003) and specifically in the right hemisphere (Egner, 2008, 2011; Egner and Hirsch, 2005; Kerns et al., 2004). However, imaging studies provide only correlational evidence for associations between cognitive functions and brain regions, which calls for additional evidence from studies using methods that allow for causal inferences. A non-invasive, safe method that allows for such inferences is transcranial direct current stimulation (tDCS). By inducing either positive (anodal) or negative (cathodal) intracranial current flow on a specific brain region, and thus affecting its excitability, brain functions can be temporarily and reversibly modulated (Nitsche and Paulus, 2001). A number of tDCS studies have provided evidence for a role of the right DLPFC in cognitive

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Abbreviations: DLPFC, dorsolateral prefrontal cortex; PPC, posterior parietal cortex; RTs, reaction times; tDCS, transcranial direct current stimulation.

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control mechanisms; for instance, tDCS stimulation over the right rather than the left DLPFC reduced cognitive control of stimulus–response binding (Zmigrod et al., 2014). In addition, modulation of performances in a Go/NoGo task after stimulation over the right DLPFC was reported by Beeli et al. (2008). These observations suggest an involvement of the right DLPFC in cognitive control functions.

The aim of the present study was to examine the role of the right prefrontal cortex in the cognitive control of conflict by means of tDCS. We were particularly interested in testing whether the flanker task and the Simon task would be equally affected. Comparable effects on both tasks would indicate a role of the right DLPFC in dealing with response conflict while a selective effect on the flanker task would indicate a role in dealing with stimulus conflict.

EXPERIMENTAL PROCEDURES

Experimental design

A randomized sham-controlled within-subject design experiment was conducted on healthy volunteers. The experiment comprised of three sessions of tDCS (anodal, cathodal, and sham) over the right DLPFC with the order of the sessions being counterbalanced across participants. The interval between the different sessions was at least 48 h, in order to minimize carryover effects. The study conformed to the ethical standards of the declaration of Helsinki and was approved by the Ethics Committee of Leiden University.

Participants

Fourteen Leiden University students (eight women; mean age = 20 years; age range: 18–24 years) took part in the experiment for course credits or a financial reward. The participants were naïve to the experimental procedure and method as well as to the purpose of the study. All participants were right handed as assessed by the Edinburgh Inventory (Oldfield, 1971) with normal or corrected-to-normal vision. Exclusion criteria included: history of psychiatric disorders, drug abuse, active medication, pregnancy, or susceptibility to seizures. Participants gave their written informed consent to participate in the study.

Stimuli and procedure

Eriksen flanker task. An extended version of the flanker task was adapted from Davelaar (2008). The stimuli were composed of seven characters; the middle character was a right or a left arrow. There were four types of stimuli: congruent (> > > > > > >, all the characters are pointing to the same direction); incongruent (< < < > < < <, the flanker characters are pointing to the one direction and the target middle one is pointing to the other direction); neutral (= = = > = = =); and no-go (xxx > xxx). The participants were asked to respond to the middle character of the stimulus with "z" or "/" to the left or right arrow with the index finger in each hand respectively, however, they had to withhold their response when a no-go trial appeared. In each trial, after a blank fixation of 1000 ms, the stimulus appeared for up to 2000 ms, and in the case of a missing or incorrect response a feedback tone was played for 500 ms.

Simon task. The Simon task was performed during a 10-min session in which participants were asked to discriminate the color of a circular stimulus (blue or green) which was presented to the left or right of a central fixation point. Both colors and locations appeared with equal frequency across the experiment, and the color and location of the circle varied randomly throughout. The participants were instructed to respond to the color of the stimulus regardless of its spatial location with the index finger of each hand, where the response keys were "*p*" and "*q*". The mapping between color and response key was counterbalanced across participants. Each trial began with a fixation point (lasting 1000 ms) followed by the stimulus (1500 ms), and in the case of an error or lack of response, a feedback error tone was played.

Procedure

After reading and signing the informed consent form, each session started with tDCS stimulation lasting for 5 min, followed by the participants' completion of the Erikson flanker task and the Simon task in a counterbalanced fashion (see Fig. 1). Before each task, instructions and a practice session were given. The flanker task contained 16 practice trials followed by 192 experimental trials. In the Simon task, there were eight training trials and 120 experimental trials. At the end of the last session, the participants answered a questionnaire (Adverse Effects Questionnaire (Brunoni et al., 2011)) regarding their experience during and after the tDCS sessions.

Transcranial direct current stimulation. tDCS was delivered by means of a DC Brain Stimulator Plus (NeuroConn, Ilmenau, Germany) and was applied through a saline-soaked pair of surface sponge electrodes (5 × 7 cm). The active electrode was placed over F4, a location atop the right DLPFC, according to the international 10–20 system for EEG electrode placement; the reference electrode was placed over the contralateral supraorbital area. The stimulation lasted 20 min with a constant current of 2 mA and with a 15-s fade-in and fade-out. For sham stimulation, the electrodes were placed at the same position but the stimulator was automatically turned off after 15 s of stimulation.

RESULTS

All participants completed the three sessions without major complaints or discomfort as measured by the tDCS Adverse Effects Questionnaire (Brunoni et al., 2011). To compare the effect of the stimulation over the right DLPFC across the two tasks, mean reaction times (RTs) of correct responses and percentage of accuracy

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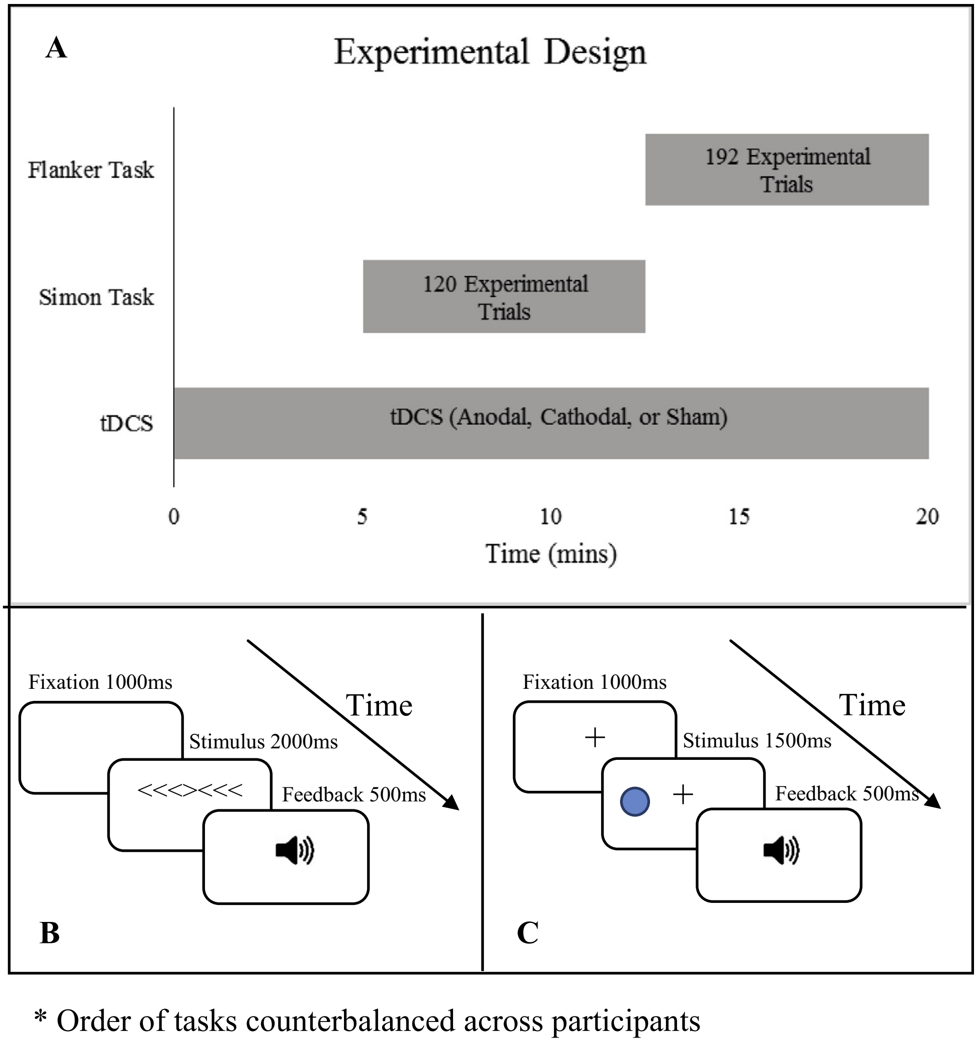

Fig. 1. Overall experimental design (A), Eriksen flanker task paradigm (B), and Simon task paradigm (C). Each session started with tDCS stimulation (anodal, cathodal or sham) after 5 min participants performed the flanker task and the Simon task in a counterbalanced fashion. Before each task, instructions and a practice session were given. On both tasks an auditory feedback was presented to incorrect responses.

Table 1. Means reaction time in millisecond and percentage of accuracy in flanker task and Simon task as a function of brain stimulation and congruency. Standard errors are shown in parentheses

			Brain stimulation		
			Anodal	Cathodal	Sham
Flanker trials	Reaction time	Congruent	548 (20)	546 (19)	516 (15)
		Incongruent	702 (31)	726 (35)	660 (20)
	Accuracy	Congruent	0.99 (.001)	0.99 (.004)	0.99 (.002)
		Incongruent	0.96 (.009)	0.93 (.017)	0.94 (.014)
Simon trials	Reaction time	Congruent	448 (16)	453 (11)	444 (11)
		Incongruent	487 (16)	486 (11)	466 (11)
	Accuracy	Congruent	0.97 (.008)	0.96 (.010)	0.97 (.008)
		Incongruent	0.95 (.012)	0.95 (.009)	0.95 (.008)

were analyzed per participant for congruent and incongruent trials in each task for each stimulation session. Repeated measures ANOVAs were performed on flanker trials and Simon trials, both on RTs and accuracy rate with stimulation type (anodal, cathodal, or sham) and congruency (congruent, vs. incongruent) as within-subject factors (Table 1).

As expected, main effects of congruency were observed for flanker trials in terms of RTs, $F(1,13) = 102.355$, $p < .0001$, $\eta_p^2 = .887$, and accuracy, F

$(1,13) = 26.278$, $p < .0001$, $\eta_p^2 = .768$, replicating the Eriksen flanker effect. Similar main effects of congruency were observed for Simon trials in RTs, $F(1,13) = 43.051$, $p < .0001$, $\eta_p^2 = .768$, and accuracy, $F(1,13) = 15.097$, $p < .005$, $\eta_p^2 = .537$, replicating the Simon effect. Moreover, there was a main effect of stimulation in the performance of flanker trials in terms of RTs, $F(2,26) = 3.747$, $p < .05$, $\eta_p^2 = .224$. A multiple comparisons Bonferroni test showed a significant difference ($p = .014$) between the performance in cathodal stimulation ($M = 625$ ms) and sham stimulation ($M = 588$ ms), suggesting a modulating effect during cathodal stimulation of the right DLPFC in the flanker task. No significant stimulation effect was found in accuracy. In addition, there was a close to significant interaction between stimulation and congruency in the performance of flanker trials in terms of RTs, $F(2,26) = 3.262$, $p = .054$, $\eta_p^2 = .201$. As revealed by further analyses, split by congruency, a significant main effect of stimulation was observed only in the incongruent trials, $F(2,26) = 4.12$, $p < .05$, $\eta_p^2 = .241$. Multiple comparisons Bonferroni tests showed a significant difference ($p = .012$) between cathodal stimulation and sham (see Fig. 2), suggesting a stimulation effect during cathodal tDCS over the right DLPFC on the incongruent trials in the Erikson flanker task.

In order to assess the effect of brain stimulation on the interference effects in both tasks, we calculated these effects by subtracting RT during congruent trials from those of incongruent trials (RTs of incongruent – RTs of congruent trials). Repeated measures ANOVAs were performed on the interference effect with stimulation type (anodal, cathodal, or sham) and task (Flanker, vs. Simon) as within-subject factors. As expected, a main effect of task was observed, $F(1,13) = 74.364$, $p < .0001$, $\eta_p^2 = .851$; the flanker effect was larger than Simon effect. In addition, there was a main effect of stimulation, $F(2,26) = 4.442$, $p < .05$, $\eta_p^2 = .255$. A multiple comparisons Bonferroni test showed a significant difference ($p = .33$) in the interference effect between cathodal and sham stimulation. Moreover, there was a significant interaction between task and stimulation: $F(2,26) = 3.653$, $p < .05$, $\eta_p^2 = .219$. Further analyses, split by task, revealed a significant difference in the flanker task, $F(2,26) = 5.267$, $p < .05$, $\eta_p^2 = .288$, but not in the Simon task, $F(2,26) = 1.55$, NS. A multiple comparisons Bonferroni test in flanker task showed a significant difference ($p = .035$) between cathodal and sham stimulation (see Fig. 3). From a methodological perspective, as suggested by Nieuwenhuis and colleagues (2011), this interaction demonstrates that indeed the cathodal stimulation over the right DLPFC affects only the performance on the flanker task and not the performance on the Simon task.

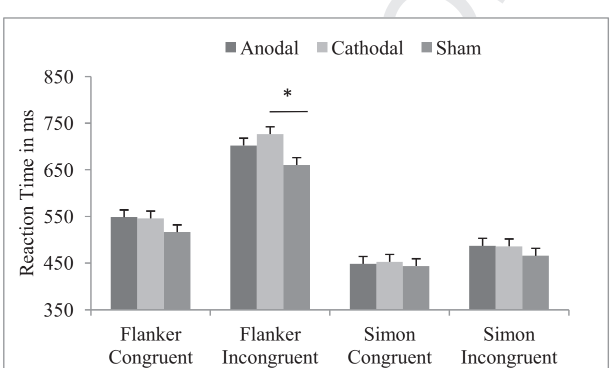

Fig. 2. Mean reaction time in millisecond with error bars for congruent trials and incongruent trials in Eriksen flanker and Simon task as a function of tDCS stimulation (anodal, cathodal, & sham) over the right DLPFC. *$p < .05$.

DISCUSSION

The aim of this study was to examine the involvement of the right DLPFC in conflict situations, either in the case of combined stimulus and response conflict (Eriksen flanker task) or in the case of response conflict only (Simon task). The results are clear: while the flanker effect was mediated by cathodal stimulation over the right DLPFC (reflected in a larger flanker effect), there was no stimulation effect on performance in the Simon task (Fig. 3), which was further confirmed by a significant interaction between task and stimulation. This suggests that the right DLPFC is involved in conflict situations arising mainly from stimulus–stimulus incompatibility rather than conflict in stimulus–response incompatibility, to the degree to which DLPFC activity was affected by our method and montage.

The observation that cathodal simulation over the right DLPFC increased, rather than decreased, the flanker interference effect (see Fig. 3) suggests that cathodal stimulation impaired the efficiency of conflict resolution induced by stimulus–stimulus incompatibility. Moreover, it was found that cathodal stimulation affects the incongruent trials more so than the congruent trials (see Fig. 2), indicating that to a large extent the cathodal tDCS was specifically influencing trials requiring attentional inhibition of task-irrelevant features. Hence, reducing cortical excitability by means of cathodal stimulation led to inefficient inhibition of irrelevant stimuli. The prefrontal cortex has long been implicated with cognitive control functions (Miller, 2000; Miller and Cohen, 2001) with different sub-regions involved in distinct aspects of cognitive control (Ridderinkhof et al., 2004). In particular, it has been suggested that the DLPFC plays a key role in inhibitory control over sensory processing by suppressing irrelevant information, as captured by the distractibility hypothesis of prefrontal function (Bartus and Levere, 1977; Knight et al., 1989, 1999). Empirical evidence can be found in numerous methodologies, including animal studies (Bartus and Levere, 1977), neurophysiological studies with patients who suffer from damage to the DLPFC (Knight et al., 1989, 1999; Yamaguchi and Knight, 1990), as well as in schizophrenic patients (Freedman et al., 1983) who exhibit altered DLPFC function (Weinberger et al., 1986, 1992). In a similar vein, it can be postulated that the cathodal stimulation over the DLPFC disrupts the suppression of the irrelevant information, which contributes to a slower performance in

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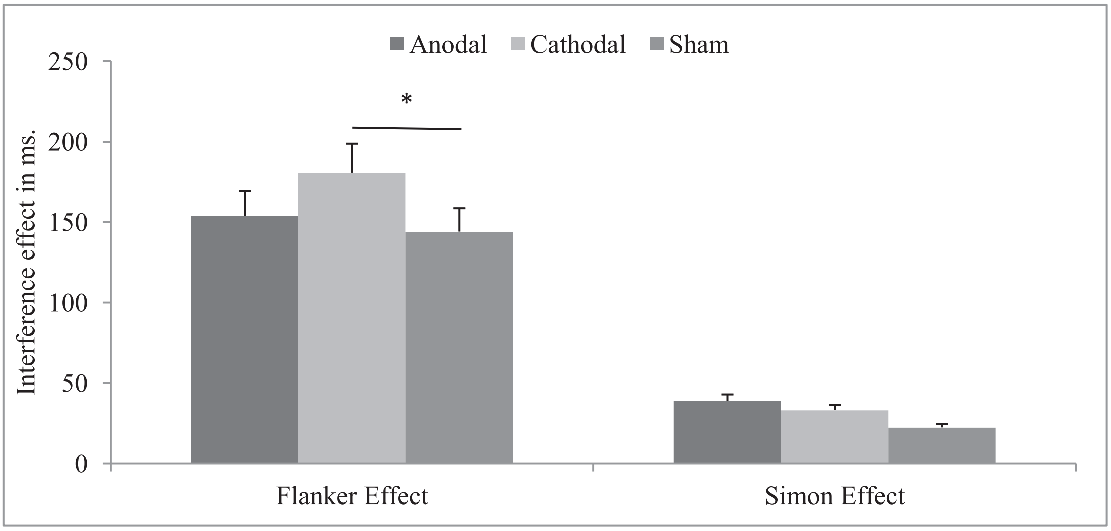

Fig. 3. Interference effect (RTs incongruent trials minus RTS congruent trials) with error bars for Eriksen flanker and Simon task as a function of tDCS stimulation (anodal, cathodal, & sham) over the right DLPFC.

the incongruent flanker trials. This finding thereby provides additional support to the distractibility hypothesis in the context of a healthy population experiencing a temporary, non-invasive reversible lesion in the form of tDCS.

In comparison to other brain stimulation studies, this finding is in line with previous research underscoring the importance of cathodal stimulation for cognitive functions. It complements the work of Bellaïche et al. (2013), who found that cathodal, but not anodal or sham, stimulation over the medial prefrontal cortex in the Eriksen flanker task affects the error monitoring system. In addition, stimulating the right posterior parietal cortex (PPC) with cathodal rather than anodal tDCS modulates the flanker effect both in low and high-loaded scenes (Weiss and Lavidor, 2012). Interestingly, it was found that that cathodal PPC stimulation facilitated flanker processing, implying that cathodal stimulation over the PPC can enhance attentional resources. In relation to the present study, this might indicate the relevance of frontal-parietal networks, and their responsiveness to cathodal stimulation, to cognitive control in stimulus–stimulus incompatibility contexts. Furthermore, Beeli and colleagues (2008) reported a greater number of false alarms in a Go/NoGo task after cathodal stimulation over the right DLPFC, highlighting the importance of cathodal stimulation in brain stimulation protocols that examine cognitive control functions. A recent review by Olk and colleagues (2015) of TMS studies that investigate cognitive control demonstrated that different frontal and parietal cortical regions are implicated in attentional control and response selection in the Eriksen flanker and Simon tasks. This is in accordance with the present tDCS results, as well as with Keye and colleagues' (2009) finding that individual differences in cognitive control are task-specific rather than representing a domain-general control mechanism. This provides support to Egner and colleagues' (2007, 2008) claim that there are multiple conflict-specific control mechanisms underlying these paradigms rather than a unitary, domain-general mechanism as sometimes assumed (e.g. Botvinick et al., 2001; Freitas et al., 2007; Niendam et al., 2012; Verbruggen et al., 2005).

To summarize, the present findings suggest three conclusions: First, conflict paradigms such as the Eriksen flanker and Simon tasks are tapping into multiple cognitive control mechanisms rather than one unitary domain-general system. Second, the DLPFC seems to play an important role in resolving stimulus–stimulus conflict, possibly through suppression of the irrelevant sensory information. And third, from a more methodological perspective, cathodal stimulation over the right DLPFC appears to impede the inhibitory modulation of sensory processing in healthy participants otherwise observed with prefrontal patients or people with schizophrenia, suggesting a useful non-invasive method that creates a temporary reversible lesion to study prefrontal functions and brain mechanisms. Continuing investigations along these lines will facilitate better understandings of the appropriate conceptual fractionation of these cognitive control mechanisms as well as their neural underpinnings and plasticity in response to interventional techniques and brain stimulation.

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We have no relevant financial or non-financial relationship or potential conflicts of interest to disclose.

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