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Modulating the interference effect on spatial working memory by applying transcranial direct current stimulation over the right dorsolateral prefrontal cortex

Yi-Jen Wu [a,b,c], Philip Tseng [d,e], Chi-Fu Chang [d], Ming-Chyi Pai [c], Kuei-Sen Hsu [f], Chou-Ching Lin [c,*], Chi-Hung Juan [d,*]

[a] Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, #138 Sheng Li Road, Tainan 701, Taiwan
[b] Department of Neurology, National Cheng Kung University College of Medicine and Hospital, Dou-Liou Branch, Yunlin, Taiwan
[c] Department of Neurology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, #138 Sheng Li Road, Tainan 701, Taiwan
[d] Institute of Cognitive Neuroscience, National Central University, #300, Jhongda Road, Jhongli City 320, Taiwan
[e] Taipei Medical University - Shuang Ho Hospital, Brain and Consciousness Research Center, New Taipei City, Taiwan
[f] Department of Pharmacology, College of Medicine, National Cheng Kung University, #1, University Road, Tainan 701, Taiwan

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ABSTRACT

Spatial working memory (SWM) is the ability to temporarily store and manipulate spatial information. It has a limited capacity and is quite vulnerable to interference. Dorsolateral prefrontal cortex (DLPFC) has been shown to be a part of the SWM network but its specific functional role still remains unknown. Here we applied transcranial direct current stimulation (tDCS), a noninvasive brain stimulation technique that provides polarity-specific stimulation over the targeted region, to investigate the specific role of the right DLPFC in resolving interference in SWM. A forward- and backward-recall computerized Corsi Block Tapping task (CBT), both with and without a concurrent motor interference task (the modified Luria manual sequencing task) was used to measure SWM capacity and reaction time. The results showed that motor interference impeded accuracy and prolonged reaction time in forward and backward recall for SWM. Anodal tDCS over right DLPFC yielded the tendency to shorten participants' reaction time in the conditions with interference (forward with interference, and backward with interference). Most importantly, anodal tDCS significantly improved participants' SWM span when cognitive demand was the highest (the "backward-recall with motor interference" condition). These results suggest that (1) the right DLPFC plays a crucial role in dealing with the cross-domain motor interference for spatial working memory and (2) the anodal tDCS over right DLPFC improved SWM capacity particularly when task difficulty demands more complex mental manipulations that could be due to the facilitatory effect of anodal tDCS which enhanced the DLPFC function within central executive system at the top-down attentional level.

1. Introduction

Spatial working memory (SWM), the ability to temporarily store and manipulate spatial information for further goal-directed behavior, is a fundamental cognitive component of human intelligence (McAfoose & Baune, 2009). The idea of working memory (WM), in contrast to short-term memory, is that WM not only stores but also manipulates the processed information based on available cognitive resources in the central executive system (Baddeley, 2001). Thus, the capacity of the WM is therefore quite constrained, due to the limited cognitive resources that its operation is dependent on. This attention-dependent nature of the WM may also cause the WM to be more vulnerable to interference during the maintenance or manipulation process. Indeed, several studies have already shown that WM capacity or the performance of recall in WM tasks are strongly correlated with the ability to ignore or suppress distraction when temporarily holding target information (de Fockert, Rees, Frith, & Lavie, 2001; Lavie, Hirst, de Fockert, & Viding, 2004; McNab & Klingberg, 2008; Sakai, Rowe, & Passingham, 2002; Schleepen & Jonkman, 2010; Vogel,

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Abbreviations: DLPFC, dorsolateral prefrontal cortex; SWM, spatial working memory.

* Corresponding authors. Fax: +886 3 426 3502 (C.-H. Juan).

E-mail addresses: cxl45@mail.ncku.edu.tw (C.-C. Lin), chijuan@cc.ncu.edu.tw (C.-H. Juan).

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McCollough, & Machizawa, 2005). Thus, the well-documented limit to visuospatial WM capacity may be, in part, due to memory interference.

Visuospatial working memory involves a network of multiple brain regions, and most imaging studies point to the activation of the dorsal stream, including DLPFC, PPC, and frontal eye field (FEF) to be highly relevant (Curtis, 2006; Vogel & Machizawa, 2004; Todd & Marois, 2004; Tseng et al., 2012). From the aspect of visuospatial processing, object recognition is associated with the ventral stream involving inferior temporal lobe and terminated in ventrolateral prefrontal cortex (VLPFC) while spatial location depends on the dorsal stream, consisting of the posterior parietal cortex (PPC) and projection to dorsolateral prefrontal cortex (DLPFC) (Ungerleider, Courtney, & Haxby, 1998). For the dorsal stream, DLPFC, PPC, and FEF show sustained delay period activity during a delayed-saccade SWM task, indicating that they are involved in the maintenance-related activities during the retention interval, separated from the visual cue and the motor response, at the SWM processing (Curtis, 2006; Tseng et al., 2012; Vogel & Machizawa, 2004). In a human electroencephalogram (EEG) study (Sauseng et al., 2009), cross-frequency phase synchronization between theta and gamma oscillations at bilateral PPC is associated with the successful maintenance of relevant objects in SWM, and ipsilateral hemispheric alpha activity amplitude is related to the efficient suppression of irrelevant information. Beyond parietal sites, prefrontal cortex (PFC) has been implicated as a critical area for more general WM beyond visual modality from lesional (Van Asselen et al., 2006), electrophysiological (Chafee & Goldman-Rakic, 1998), and functional neuroimaging studies (D'Esposito, Postle, Ballard, & Lease, 1999; D'Esposito, Postle, & Rypma, 2000; Fletcher & Henson, 2001). One notable fMRI study showed heightened activation in DLPFC and VLPFC during the maintenance phase of a delayed-response WM task, with DLPFC activation being greater in the manipulation trials (D'Esposito et al., 1999). Consistent findings from Toepper et al. (2010) pointed out functional dissociation of DLPFC and VLPFC in SWM using fMRI and Corsi Block Tapping (CBT) task. They reported only DLPFC was activated when the SWM processing required additional suppression for visual distraction at the encoding phase, while both of regions were involved in the encoding phase of CBT without distraction. They proposed that in the network of SWM, VLPFC contributed to the maintenance of spatial information while DLPFC performed higher-level executive processing like updating information and suppression distraction, and PPC was associated with the passive storage of spatial information related to WM load. Premotor area might reflect a general, task-independent processing for SWM (Toepper et al., 2010). At the cellular-level investigation for SWM, a study revealed *N*-methyl-D-aspartate (NMDA) receptors subserved the persistent neuronal firing in primates' DLPFC during performing SWM task using combined methods of single unit recoding and iontophoresis (Wang et al., 2013). Similarly, a human study with the combined use of pharmacology and fMRI showed NMDA receptor blockade decreased the activation and network connectivity of DLPFC and resulted in impaired SWM performance (Driesen et al., 2013).

Transcranial direct current stimulation (tDCS) is not a new technology, but it has seen a surge in usage in the field of neuroscience in the recent decade (Nitsche & Paulus, 2001). The neurophysiology of tDCS, in short, is that anodal (positively charged) stimulation should selectively increase cortical excitability beyond baseline activity by modulating NMDA activity (Nitsche et al., 2005), and induce a NMDA-mediated long term potentiation (LTP) like neural plasticity (Monte-Silva et al., 2013). A motor evoked potential study with transcranial magnetic stimulation showed anodal tDCS increased intracortical facilitation and decreased intracortical inhibition after stimulation while cathodal tDCS decreased facilitation and increased inhibition (Nitsche et al., 2005). Thus, anodal and cathodal stimulation usually elicits improved or impaired behavioral performance, respectively, at least in the motor cortex. Similar trends have also been reported in cognitive tasks such as inhibitory control (e.g., Hsu et al., 2011), although the directionality of the effect of anodal stimulation has been suggested to be more consistent in affecting cognitive function than cathodal stimulation, whose effect seems less consistent (excitatory or inhibitory) when moving outside the motor cortex (for a review, see Jacobson, Koslowsky, & Lavidor, 2012). Anodal tDCS has been used to investigate verbal working memory by stimulating the DLPFC with an electrical current of 1–2 mA for 10–30 min pre- or during the working memory task in different studies for healthy subjects, among which the *n*-back task is the most commonly used paradigm. In this task, participants are presented with a string of letters in sequence, and they are to respond whenever the current letter matches the letter that was presented either one, two, or *n*-items before the current letter (Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Elmer, Burkard, Renz, Meyer, & Jancke, 2009; Fregni et al., 2005; Mulquiney, Hoy, Daskalakis, & Fitzgerald, 2011; Ohn et al., 2008; Zaehle, Sandmann, Thorne, Jancke, & Herrmann, 2011). The *n*-back task is effective in testing participants' memory because its difficulty level can be manipulated (i.e., smaller n means less item needs to be held in memory), and there has been evidence suggesting that anodal tDCS over left DLPFC can improve such task performance. However, compared with studies using letter *n*-back to investigate left DLPFC for verbal WM, there is less literature looking into the role of right DLPFC in spatial WM (Driesen et al., 2013; Toepper et al., 2010; Wang et al., 2013). In light of this, in the present study we used tDCS to investigate the role of DLPFC in the context of SWM. Since visuospatial information processing depends more on the right hemisphere than the left side (Beck, Muggleton, Walsh, & Lavie, 2006; Tseng et al., 2010), here we specifically test whether the right DLPFC may play a crucial role in supporting SWM, with or without attentional interference, by using Corsi Block Tapping task and tDCS.

Together, recent studies suggest that several brain regions work together within the frontal–parietal network to support SWM. However, since SWM is highly vulnerable to interference (Toepper et al., 2010; Vogel et al., 2005; see Logie, Zucco, & Baddeley, 1990 for a distinction between general and mode-specific interference), the roles of these frontoparietal areas remain to be investigated in situations where high interference is involved. Therefore in this study, we specifically target DLPFC due to its involvement in the dorsal stream of spatial information processing (Ungerleider et al., 1998), SWM maintenance and manipulation (Curtis, 2006; D'Esposito et al., 1999), attentional control and shifting (Vanderhasselt, De Raedt, & Baeken, 2009), and suppression of distraction and updating information (Anderson et al., 2004; Toepper et al., 2010), to investigate whether the involvement of DLPFC in SWM is critical when interference is present. Furthermore, since NMDA was reported to be underlying the neurophysiological function of DLPFC in SWM (Wang et al., 2013) and tDCS can provide a NMDA-mediated facilitatory effect of cortical excitability (Monte-Silva et al., 2013; Nitsche et al., 2005), with the strength of tDCS over DLPFC, SWM could hopefully to be improved. tDCS will be applied over DLPFC and SWM will be evaluated pre- and post-tDCS to establish a causal relationship, if any, between DLPFC and SWM performance. The rationale is that if DLPFC is causally involved in the processes supporting SWM, tools such as brain stimulation that directly modulate the level of activity in DLPFC should create an observable impact in SWM performance. In contrast, if DLPFC is not directly involved in the processes behind SWM, or if its activation is a product and not the cause of SWM, then no change in behavioral performance should be observed in this study.

2. Material and methods

2.1. Participants

Twenty healthy postgraduate students from the National Central University participated in the present study (8 female, 12 male, age range: 24–31, mean age = 26, all right-handed). All participants had normal or corrected-to-normal vision, and all were examined by a neurologist prior to the experimental session to exclude the neurological or mental health problems. All participants provided informed consent before participation. All experimental and tDCS procedures were approved by the Institutional Review Board of the Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan.

2.2. Computerized Corsi Block Tapping task

The Corsi Block Tapping task (CBT) has been used to measure the spatial working memory (SWM) since 1972. By displaying the visual targets in sequence, participants are asked to memorize the location of the targets and the sequence of their presentation, and then recall the location and the sequence of the targets either in the forward manner, as the same sequence of the target presentation, or in the backward manner, as the reverse sequence (Fischer, 2001). This task required accurate encoding, maintenance, and recall processes of spatial information in and out of one's SWM, and the manipulation of forward and backward recall creates at least 2 levels of difficulty in the CBT task. Our CBT task was programmed using Microsoft Visual Studio 2010 in C++ code. In the beginning, 9 placeholders, in the form of 9 blue squares, were displayed in randomly locations on the screen as background (Fig. 1a). During the encoding phase (Fig. 1b), the yellow target square appeared in each of the placeholder locations, for 500 ms, in random sequence. The randomized positions of the nine squares and the stimulus were based on Donald E. Knuth's subtractive random number generator algorithm (Knuth, 1981). Participants were asked to memorize the squares that changed color for their locations and sequence. During the 5-s delay phase (Fig. 1c), a cross

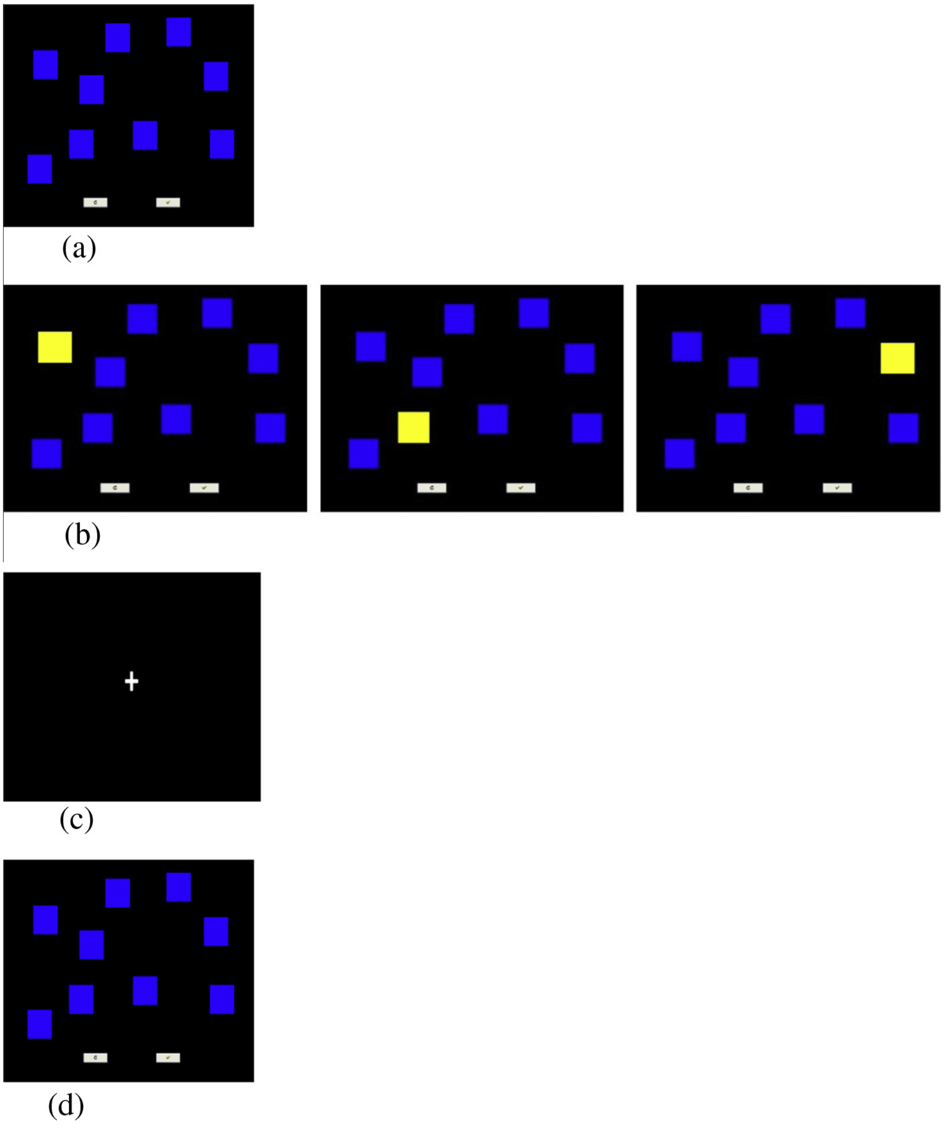

Fig. 1. Computerized Corsi Block Tapping task (CBT). The background displayed nine blue squares randomly placed on the screen (a). At the encoding phase, some of the squares changed color from blue to yellow when participants were asked to memorize the location and the sequence of the squares that changed color (b). During the 5-s delay phase, participants in the interference condition performed the modified Luria manual sequencing task (c). At the recall phase, participants clicked the squares that changed color in their location and sequence either forward or backward on the same display as the background (d). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

(+) was displayed at the center of the screen, and participants were asked to do either nothing (for non-interference condition) or the modified Luria manual sequencing task (for interference condition) (Christenson, 1975; Luria, 1969). Performing modified Luria manual sequencing task, participants tapped the table with a fist, the edge of an open hand, and an open palm, and then all over again in reverse order. Both sequences were performed from right hand then shifting to left hand, repeatedly. After the cross disappears, it was the recall phase (Fig. 1d), where participants were presented with the initial nine-blue-block background and were asked to point out the squares that changed color, in their corresponding location and sequence as originally presented (forward condition), or in the same location but with reversed sequence (backward condition). The paradigm was computer-adaptive, and thus the set size would only increase if the participant passed consecutive two trials of the same span. The lowest span level started from 2 (2 squares that change color) and up to 9 as maximum. If the participant failed two consecutive trials at one specific span, the session was terminated at that particular span level, which was defined as the individual's highest SWM span level. Each CBT session was composed of four conditions (forward, backward, forward with interference, and backward with interference) which were counterbalanced across all participants. Participants were instructed to respond as accurately and as fast as they can. The stimuli were displayed on a 19-in. personal computer screen. The responses were obtained through a computer mouse.

2.3. tDCS protocol

Right DLPC was located as F4 according to the international 10–20 EEG system. Anodal tDCS (NeuroConn Eldith DC-Stimulator) was delivered with the anodal pole on the right DLPFC (F4) and the cathodal pole on the left cheek of the participant to avoid contaminating other brain regions during electrical stimulation (Berryhill, Wencil, Branch Coslett, & Olson, 2010; Hsu et al., 2011) via a pair of rubber electrodes ($4 \times 4\ \text{cm}^2$) housed in saline-soaked sponge coverings ($5 \times 5\ \text{cm}^2$). The direct current was applied with 1.5 mA for 15 min which can facilitate visual short-term memory (Tseng et al., 2012) and create an excitatory effect for up to 90 min (Nitsche & Paulus, 2001). The anodal tDCS stimulated the right DLPC for 15 min with 1.5 mA in active tDCS condition. The sham tDCS condition followed identical tDCS protocol and same 15-min duration except the stimulation time only lasted for the initial 30 s so that the participants felt the same initial tingling sensation (if any, only in some participants) but without the actual stimulation. Questions regarding the different sensations between the sham and active session (if any), if raised, were explained with differences in individual perception or skin moisture across different days to eliminate any possible psychological anticipation.

2.4. Experiment design

The study used a within-subject design, thus each person participated in two different CBT sessions, one for active tDCS and the other for sham tDCS. The sham-tDCS crossover design was adopted to minimize the practice effect. To avoid any possible carry-over effect of tDCS, the sham and tDCS conditions took part on 2 different days at least 24 h apart. The order of the two sessions (sham and tDCS) was counterbalanced across participants, and CBT was always performed immediately after stimulation session. The order of the four conditions in one CBT session (forward, backward, forward with interference, and backward with interference) was the same for each individual, but randomized across all participants. Each participant had the introduction and full practice for the four conditions of CBT prior to the formal experimental session. The familiarization period was designed to be the longest session of the entire experimental session in order to give participants maximum amount of time to practice and familiarize themselves with the task to avoid any operation errors or practice effect that may overshadow the effect of stimulation. Once the familiarization period was over, participants whose scores did not fluctuate (+2 or −2) in memory span in all four conditions were considered as well-practiced. All participants were able to hit a plateau performance in all four conditions after the familiarization period, and thus the practice time was held constant across all individuals.

3. Results

3.1. Memory span

A three-way repeated-measures ANOVA was used to analyze the main effects and interactions between tDCS (sham vs. tDCS), CBT recall sequence (forward vs. backward), and interference (with vs. without) (Table 1a). There was a significant main effect of interference ($F(1,19) = 75.625$, $p < .001$) (Table 3), significant interaction between tDCS and interference ($F(1,19) = 4.412$, $p = .049$), and importantly, a significant 3-way interaction between tDCS, recall sequence, and interference ($F(1,19) = 4.824$, $p = .041$) (Fig. 2).

To investigate the 3-way interaction, we ran a 2×2 ANOVA with the factors of tDCS and interference (Table 1c). The analysis showed a significant main effect for interference ($F(1,19) = 41.201$, $p < .001$) and, again, a significant 2-way interaction between tDCS and interference ($F(1,19) = 4.412$, $p = .049$). The effect of interference is quite pronounced (from span of 6.4 and 6.3 to 4.8 and 5.1), whereas the interaction seemed to be driven in part

Table 1a
Memory span ANOVA table.

Source of variance	*F*	*df*	Sig.
Memory span			
tDCS	0.4	1	0.527
Interference	41.2	1	<.001
Directionality (forward vs. backward)	2.3	1	0.149
tDCS * interference	4.4	1	0.049
tDCS * directionality	0.1	1	0.821
Interference * directionality	0.4	1	0.536
tDCS * interference * directionality	4.8	1	0.041

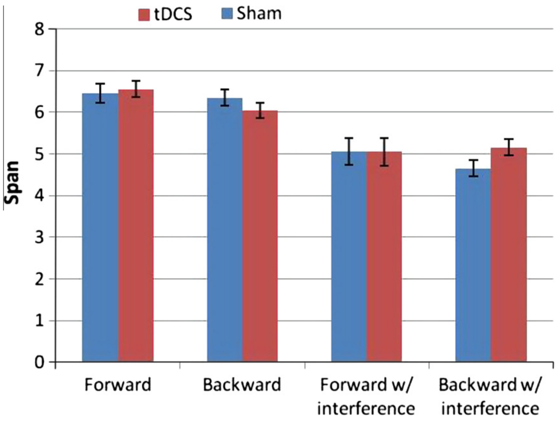

Fig. 2. The effect of interference and anodal tDCS on SWM span. There was a main effect of interference on SWM span ($p < .001$), as well as an interaction between interference and tDCS ($p = .049$) and 3-way interaction ($p = .041$). SWM span decreased under the conditions with interference. The interaction was driven by the fact that SWM span was improved significantly by tDCS at the backward recall with interference condition. The error bars represent standard error of the mean.

because the application of DLPFC tDCS was able to improve participants' memory span only when Luria's manual interference task was involved (from span of 4.8 to 5.1), and not when there was no interference (from span of 6.4 to 6.3). Indeed, when we compare the effect of tDCS separately within each interference and recall sequence combinations, the effect of tDCS was not effective in the forward-without-interference ($t = .462$, $p = .649$), backward-without-interference ($t = -1.552$, $p = .137$), and forward-with-interference ($t = 0$, $p = 1.0$) conditions, but was highly significant in elevating people's memory span in the most difficult memory condition – the backward-with-interference condition ($t = 3.249$, $p = .004$) (Table 1b). The results here showed that right DLPFC-anodal tDCS improved the SWM span in the backward recall within the interference condition. This interesting interaction between the effect of DLPFC tDCS and task difficulty will be discussed below.

3.2. Reaction time

A three-way repeated-measures ANOVA was also used to analyze the RT data between the 3 variables (Table 2a). All main effects were statistically significant, namely tDCS ($F(1,19) = 14.233$, $p = .001$), interference ($F(1,19) = 116.452$, $p < .001$), and CBT recall sequence ($F(1,19) = 12.634$, $p = .002$) (Fig. 3). None of the interactions were statistically significant.

Separate comparisons were performed for each factor (Table 3). For tDCS, participants performed faster on average, per square in the CBT task, with DLPFC tDCS (1197.3 ms) than their sham RT (1289.1 ms), suggesting an improvement of approximately 92 ms per square on the CBT task ($p = .001$). For Luria's manual interference effect on RT, participants responded slower with interference (1456.2 ms) than without (1030.3 ms) – a difference of 426 ms in RT ($p < .001$) with interference alone during the memory maintenance period. Lastly, for the CBT recall sequence, participants recalled faster in the forward condition (1185.9 ms) than the backward condition (1300.5 ms) ($p = .002$). All these results were additive since no significant interaction between these variables was observed.

Table 1b
Memory span pairwise comparisons (mean, std. err., and *t*-test *p*-value).

Conditions	Sham	tDCS	Sig.
Memory span			
Forward	6.5 ± .22	6.6 ± .20	0.649
Backward	6.4 ± .19	6.1 ± .19	0.137
Forward w/interference	5.1 ± .32	5.1 ± .33	1.000
Backward w/interference	4.7 ± .20	5.2 ± .20	0.004

Table 1c
Interaction of tDCS and interference on span (mean, std. err., and $p = 0.049$).

Conditions	With tDCS	Without tDCS
Memory span		
With interference	5.1 ± .24	4.8 ± .22
Without interference	6.3 ± .16	6.4 ± .17

Table 2a
Reaction time ANOVA table.

Source of variance	*F*	df	Sig.
Reaction time			
tDCS	14.2	1	0.001
Interference	116.5	1	<.001
Directionality (forward vs. backward)	12.6	1	0.002
tDCS ∗ interference	2.8	1	0.109
tDCS ∗ directionality	0.2	1	0.624
Interference ∗ directionality	0.1	1	0.790
tDCS ∗ interference ∗ directionality	0.0	1	0.903

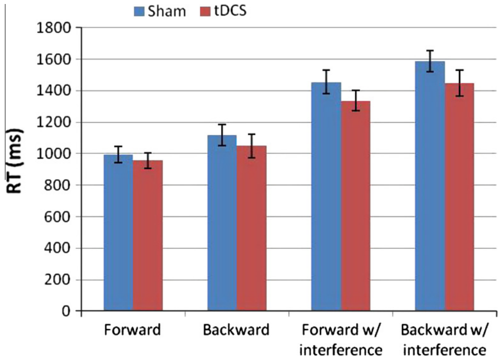

Fig. 3. Reaction time results. There was a main effect of CBT sequence (forward vs. backward; $p = .002$), interference (with vs. without; $p < .001$), and tDCS (sham vs. tDCS; $p = .001$) on the reaction time (RT) of SWM recall. The RT was shorter with forward recall (vs. backward recall), without interference (vs. with interference condition), and with tDCS (vs. sham). No interactions were observed. The error bars represent standard error of the mean.

Table 2b
Reaction time pairwise comparisons (mean, std. err., and *t*-test *p*-value).

Conditions	Sham (ms)	tDCS (ms)	Sig.
Reaction time			
Forward	996.0 ± 50.9	957.3 ± 49.3	0.127
Backward	1119.1 ± 66.8	1048.9 ± 75.1	0.139
Forward w/interference	1454.9 ± 74.0	1335.7 ± 64.2	0.005
Backward w/interference	1586.8 ± 65.8	1447.6 ± 80.3	0.067

To compare the RT effects here with our span results above, we also performed paired-sample *t*-test to see whether tDCS was facilitative across the board or only in a few selected conditions (Table 2b). These comparisons showed that tDCS only improved participants' RT over the interference condition, to some extent, when Luria's manual interference was involved (forward with interference: $p = .005$; backward with interference: $p = .067$), and was not effective when participants did not have to deal with the interference effect during memory maintenance (forward without interference: $p = .127$; backward without interference: $p = .139$). The results here revealed a trend that right DLPFC-anodal tDCS perhaps shortened the RT for SWM recall when the participants were dealing with concurrent motor interference at the maintenance phase. This observation is somewhat consistent with the findings from memory span in the sense that DLPFC tDCS could improve the SWM performance particularly when the task was more complex with interference. The tDCS effect was predominantly improving span level at the backward with interference condition while improving RT significantly at forward and marginally at backward recall with interference.

Table 3
Main effect analysis, from 3 way ANOVA (mean, std. err., and *p*-value).

Source of variance	With variance	Without variance	Sig.
Main effect analysis			
tDCS_span	5.7 ± .16	5.6 ± .16	0.527
Interference_span	4.9 ± .21	6.3 ± .16	<.001
Backward recall _span	5.5 ± .13	5.7 ± .20	0.149
tDCS_RT (ms)	1197.3 ± 60.2	1289.1 ± 52.3	0.001
Interference_RT (ms)	1456.2 ± 60.6	1030.3 ± 56.3	<.001
Backward recall _RT (ms)	1300.5 ± 62.3	1185.9 ± 52.0	0.002

4. Discussion

In this study we investigated the role of DLPFC using a SWM recall task by applying anodal tDCS over the right DLPFC while manipulating task difficulty (forward and backward recall) and cross-domain motor interference (with or without modified Luria's manual sequencing task). Our main findings are two-fold: (1) motor interference impairs SWM (Figs. 2 and 3) and (2) tDCS only improves SWM span when task demand is highest (motor interference plus backward recall) (Fig. 2).

Although it is not surprising that distraction can impair SWM, it is quite interesting that a motor task such as the Luria's task, as a cross-domain interference, can also be distracting and even detrimental to SWM performance. Evidence has shown that contents which share overlapping features within the same domain and are processed concurrently can interfere WM performance (Lange & Oberauer, 2005). For SWM, the concurrent appearance of visual distraction with the target presentation at the encoding phase prolonged the response time to recall the target and that additional activation of DLPFC corresponded with distraction suppression (Toepper et al., 2010). In terms of visual distraction at the maintenance phase, it has been shown that performing an attentionally-demanding visual search task in the middle of the memory maintenance period can impair subsequent memory recognition performance (Johnson, Hollingworth, & Luck, 2008). Distractions sharing the same-domain features impede WM at encoding and maintenance periods among which DLPFC seems to play a crucial role in dealing with the interference. However, there is less literature documenting a cross-domain interference effect in SWM, which in our opinion actually occurs more often in one's daily life (e.g., trying to remember some visuospatial information while performing an action). In this sense, Luria manual sequencing task is a kind of motor sequencing task that may demand the prefrontal lobe function for shifting the exact manual sequence. To ensure that the task was achieving the effective threshold of motor interference so that DLPFC involvement is critical, we modified the Luria task by additionally designing the sequence in reverse and then shifting from one hand to the other repeatedly. Although visuospatial sequence information and the motor sequence task can be processed via different downstream systems, cross-domain motor interference may still occur at the top-down control level where all information from different resources is supposed to interact and integrate. Thus, DLPFC is likely the corresponding functional neuroanatomy of the central executive system for maintaining visuospatial information while concurrently performing a cross-domain task that demands attentional shifts between forward and backward sequence manipulation. This would be consistent with the role of DLPFC in managing dual-task situations (Jaeggi et al., 2003; Szameitat, Schubert, Müller, & Von Cramon, 2002). Consequently, because the limited capacity of the central executive system was divided when participants attempted to simultaneously process a cross-domain dual task, the accuracy and response time of the SWM were compromised with concurrent motor interference. Thus, the modified Luria manual sequencing task could impair SWM and result in prolonged RT and decreased memory span. Our findings provide evidence of a cross-domain interference effect in SWM.

4.1. DLPFC and top-down control in SWM

In this study we observed a facilitating effect of anodal tDCS over right DLPFC in memory span and the tendency to see beneficial effects in RT. Interestingly, this effect in memory span was only observed in the backward-recall-with-interference condition, and the trend of effect in RT was only observed in the interference condition (forward and backward). Since memory span is the measure of interest here, we focus on this point in the discussion below. It is reasonable that DLPFC tDCS effect is only apparent in the interference condition because our source of interference, Luria motor sequencing task, was designed to recruit DLPFC involvement. DLPFC, as a possible locus of the central executive system for SWM, is activated particularly when distraction occurs or when tasks require higher level of attention shifting, information updating, monitoring and manipulation or coordinating with dual-task conditions (e.g., Toepper et al., 2010). In our study, right DLPFC could possibly be the main functional localization for manipulating reverse sequence, both spatial and motor, and handles concurrent cross-domain tasks. Thus, anodal tDCS enhanced DLPFC functioning and resulted in the tendency to shorten recall RT when dealt with the motor interference. Furthermore, backward recall, compared with the forward recall, demanded more sequencing manipulation that required advanced involvement of DLPFC. Therefore, the combination of the backward-recall condition and interference (spatial sequencing plus motor sequencing), called for the highest involvement of DLPFC among the four test conditions and reflected the highest (and only) level of facilitating effect of DLPFC tDCS in SWM span. The finding that tDCS improved memory span only in the backward recall with interference condition may suggest that task difficulty also plays an important role in determining the effectiveness of tDCS. That is, the more difficult the task is (i.e., backward recall with interference), the more ability is required, for which the participants could really use the facilitation brought forth by anodal tDCS. In support of this idea, some tDCS studies have already demonstrated that the effect of tDCS, specifically anodal, can often interact with task difficulty or participants' innate ability (Jones & Berryhill, 2012; Tseng et al., 2012). Specifically, Tseng et al. (2012) reported that tDCS over the right parietal cortex can improve SWM recognition performance, but only in participants whose memory span was lower than average to begin with. Since the Tseng et al. (2012) study did not manipulate levels of difficulty in their SWM task, their results could not conclude whether the high-performers could also improve their performance with tDCS, if they were properly challenged with a difficult task. Indeed, in another study where SWM task difficulty was manipulated, the authors found that high-performers can improve SWM performance via anodal tDCS in the memory condition with the highest level of difficulty (Jones & Berryhill, 2012). Those results would be consistent with the results in the present study. Note that those studies only applied tDCS over the posterior cortex, and did so without any manipulation on the level of interference. Thus, the present findings on the role of the right DLPFC in dealing with interference for SWM, as well as how SWM span can be improved via anodal tDCS when faced with such interference, provide an important piece of evidence to the current literature on SWM and tDCS. To contextualize our findings within the general framework of attention and SWM, it is plausible that the right DLPFC plays a role in top-down control for SWM, which belongs to the central executive for managing concurrent interference rather than the bottom-up slave systems (i.e., memory storage). This would explain why DLPFC has not been implicated much in the SWM literature, although its involvement in top-down attention has been suggested as a critical component in the process of SWM (Yang, Tseng, Huang, & Yeh, 2012). Therefore, the motor interference may impair SWM performance at the central executive level that could take place at the right DLPFC.

4.2. tDCS focality and network effect

It is worth mentioning that, in most tDCS studies, the size of the tDCS sponge coverings ($5 \times 5\ \text{cm}^2$) can often be larger than the exact size of the region of interest. Therefore, the lack of precise focality in the present study cannot rule out the possibility that perhaps areas adjacent to DLPFC may also have received increased activity. Furthermore, it is important to note that in this study we are not trying to argue for a DLPFC-exclusive effect that is induced by anodal tDCS. In fact, recent studies combining tDCS and neuroimaging techniques are beginning to suggest that such network effect seems to be what is going on after stimulation, with increased focal brain perfusion, over which directly received tDCS during the stimulation period (Stagg et al., 2013), and the coactivated adjacent frontal–parietal networks along with the enhanced connectivity within the network after stimulation (Keeser et al., 2011). Therefore, areas within the SWM network such as PFC, PPC, and the premotor cortex (e.g., Toepper et al., 2010) are likely to have been involved in the network under tDCS effect and resulted in SWM improvement in the present study.

5. Conclusion

This study provides evidence that motor interference can impede accuracy and prolong reaction time in forward and backward recall for SWM. Most importantly, applying anodal tDCS over right DLPFC improved memory span only in the backward-recall-with-motor-interference condition. These findings suggest that the right DLPFC may play a crucial role in dealing with cross-domain interference for SWM, particularly when task difficulty demands more complex mental manipulations at the top-down attentional level.

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