Assessing the role of the left dorsal frontal cortex in working memory guidance: attentional or mnemonic? A neurostimulation study

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Abstract

Perceptual selection can be guided by the contents of working memory (WM). Neuroimaging and neuropsychological data points to a role of a fronto-parietal and fronto-thalamic networks in WM guidance. Here we assessed the effect of transcranial direct current stimulation of the left dorsal frontal cortex (lDFC) in a combined WM/attention paradigm. We asked the extent to which the lDFC is implicated in mnemonic and selective attention functions during WM guidance of behaviour. Observers were asked to keep information in memory while searching for a visual target, while the validity of WM contents for the search task varied. We tested the effects of lDFC-tDCS on the strength of WM guidance of search, whether any tDCS effect is dependent on the amount of WM load, and whether lDFC-tDCS primarily influences how WM contents are retained, the process of selective attention in search task, or both. Consistent with prior behavioural findings, we found that (i) selection of items that matched the contents of WM was facilitated relative to non-matching items and (ii) this WM guidance effect was reduced when the level processing/cognitive load in WM was higher. Notably, across two experiments we found that lDFC-tDCS modulated WM guidance of visual selection in the context of high processing loads in WM. No effects of tDCS were observed in WM accuracy. These findings demonstrate that the role of the left dorsal frontal cortex in WM guidance is associated with selective attentional control rather than mnemonic processing.
Introduction

Working memory (WM) and attention interact. The way we direct our perceptual attention determines which information is more likely to be encoded in memory and later remembered. Likewise, the information that is kept active in mind can also influence the way attention is deployed, so that perceptual items that match the WM contents can be selected more easily. The influence of WM contents on selective attention has proven to occur automatically in most contexts, even when the WM contents are not relevant for our attention goals (Soto, Hodson, Rotshtein, & Humphreys, 2008; Kiyonaga & Egner, 2013). Understanding the factors that control the expression of WM-driven biases of perceptual selection remains a subject of active research: the mnemonic demands of the task, experience-dependent learning and strategic control factors are known to play an important role (Han & Kim, 2009; Gunesi, Olivers, & Meeter, 2016; Tas, Luck, & Hollingworth, 2016; Soto et al., 2008; Kiyonaga & Egner, 2013; Olivers, Peters, Houtkamp, & Roelfsema, 2011).

In the combined WM/attention paradigm that is used to assess WM guidance of attention, participants are asked to keep an item in WM while search concurrently for a different target object (i.e. a tilted line). In valid trials the WM cue reappears in search containing the target, while in invalid trials the WM cue matches a search distracter. A recognition memory test for the initial WM cue follows after the search task. The canonical finding is that search performance impairs in invalid trials relative to valid and neutral trials in which the WM cue is absent from the search display, despite the cue was no more likely to be valid, invalid or neutral. WM biases of attention also occur when the WM cues are always invalid for the attention goal (Downing, 2000; Soto, Heinke, Humphreys, & Blanco, 2005; Olivers, Meijer, & Theeuwes, 2006; Olivers et al., 2011; Hollingworth & Beck, 2016). Pan, Luo, & Cheng (2016). The findings from this combined WM/attention paradigm indicate that the contents of WM can guide attention in a rather automatic fashion, however, this effect is dependent on the availability of WM capacity: WM guidance of attention is impaired by high loads in WM (van Moorselaar et al., 2017; Zhang, Zhang, Huang, Kong, & Wang, 2011; Soto & Humphreys, 2008).

Previous human neuroimaging evidence has demonstrated the role of frontoparietal networks in controlling goal-directed behaviour; for instance, activity in the superior frontal gyrus and the intraparietal sulcus increases when attention is directed towards relevant spatial locations or when attention is precued to select specific object features (Posner, 1980; Corbetta & Shulman, 2002; Egner et al., 2008). Vossel, Geng, & Fink (2014). The influence of WM contents on selective attention may be based on top-down feedback from frontal substrates that bias neural activity in striate and extrastriate cortex (Ruff et al., 2006; Motter, 1993; Chelazzi, Miller, Duncan, & Desimone, 1993). Functional MRI studies using the combined WM/attention paradigm found increased hemodynamic responses to the mere re-appearance of search-irrelevant WM contents during a search task in superior frontal, dorsolateral prefrontal and also in visual areas (Soto, Humphreys, & Rotshtein, 2007; Soto, Rotshtein, Hod-
soll, Mevorach, & Humphreys, 2012), while the functional connectivity between prefrontal and visual cortex attenuated in the same conditions when the level of WM load was high (Soto, Greene, Chaudhary, & Rotshtein, 2011). This indicates that top-down frontal biasing signals may occur irrespective of the relevance of the contents held in WM for attentional selection. Other studies also point out to a role of subcortical areas in WM/attention interactions beyond those fronto-parietal networks, in particular, the thalamus (de Bourbon-Teles et al., 2014; Leszczynski & Staudigl, 2016), which is consistent with an integrative functional role across multiple neurocognitive functions (Hwang, Bertolero, Liu, & D’Esposito, 2017), such as memory and attention control.

The studies reviewed so far indicate that the superior frontal and dorsolateral prefrontal areas are implicated in both top-down attention and also in the maintenance of information in WM, but this has been tested mainly using paradigms that tap separately onto memory maintenance or top-down attention processes (Corbetta & Shulman, 2002; Egner et al., 2008; Pessoa, Gutierrez, Bandettini, & Ungerleider, 2002). A key unresolved question with regard to the interplay between WM and attention is whether these frontal regions play a more significant role in the maintenance/recall of the WM items in the combined WM and attention paradigm or whether frontal substrates are more implicated in the control of attention when WM and attention are concurrently manipulated.

The present transcranial direct current stimulation (tDCS) study employed the combined WM/attention paradigm from Soto et al. (2007) with the goals of (i) investigating the functional contribution of the lDPC for WM and attention interactions across different levels of cognitive load, (ii) examine whether lDPC-tDCS influences the retention of items in WM (i.e. the WM accuracy. As such this study represents an attempt to characterise the nature of the functional contribution of the lDPC in WM guidance of attention, namely, whether its role predominantly attentional in nature or whether it further contributes to mnemonic processes.

We elected to stimulate the lDPC following the prior neuroimaging studies using the combined WM/attention paradigm noted above (Soto et al., 2007; Soto, Greene, et al., 2011; Soto, Mok, et al., 2011), and also following prior studies that measured the effect of DPC-tDCS separately on attention and working memory tasks. Prior studies indicate that anodal tDCS (relative to cathodal or sham tDCS) over the dorsolateral prefrontal, superior frontal and parietal cortex can improve WM performance in a different range of tasks using both verbal and visual materials (Fregni et al., 2005; Boggio et al., 2006; Ohn et al., 2008; Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Jeon & Han, 2012; Pope, Brenton, & Miall, 2015; Arciniega, Gözenman, Jones, Stephens, & Berryhill, 2015; Heinen et al., 2016; Tseng et al., 2012) and also attention performance, namely, the generation of saccades and attentional orientation to visual targets (Kanai, Muggleton, & Walsh, 2012; Nelson, McKinley, Golob, Warm, & Parasuraman, 2014). It is therefore hypothesised that tDCS over the lDPC may influence WM guidance of visual attention. We ask whether this effect may also be dependent on the processing load in WM (i.e. as participants retain more items in WM).
We hypothesized that if the IDFC is causally involved in WM guidance of visual selection, then the application of anodal vs. cathodal stimulation should lead to a global change in the expression of the WM bias of attention in search (i.e. the difference in performance between valid and invalid WM-cues for search). In addition, if the IDFC is involved in the maintenance of the relevant memorandum then differential effects of anodal vs. cathodal stimulation should also be observed in WM accuracy. Increasing the amount of items in WM may facilitate the detection of tDCS on WM accuracy since tDCS effects on performance have been shown to be dependent on the level of task load (Jones & Berryhill, 2012; Roe et al., 2016).

Methods

Participants

Two separate experiments were conducted with independent samples. In Experiment 1, eight healthy volunteers (5 Males, 3 Females; aged between 21-29) were recruited to take part in the experiment. This sample size was selected based on the sample of our prior neurostimulation study of the superior frontal gyrus (Soto et al., 2012).

A total of new twelve healthy volunteers in Experiment 2 (8 Males, 4 Females, age range: 22-29) were recruited. Since the level of working memory load was higher than in Experiment 1, the sample size was increased following our prior study that examined the effects of increasing cognitive load on WM guidance (Soto & Humphreys, 2008).

None of the participants had prior history of neurological or psychiatric disorders. All participants provided written informed consent and were economically rewarded for their participation. This study was approved by the local Research Ethics committee.

Experimental procedure

Participants were given clear instructions about the task and performed a few training trials until they felt comfortable with the task (Figure 1). Each trial started with an instruction on the computer screen (i.e. ‘Remember 1 item’ or ‘Remember 2 items’) for 1000 ms. This was followed by a fixation dot for 500 ms and by a cue display displayed for 200 ms which contained either one colored shape (low load condition) or two-colored shapes (high load condition) to keep in WM. Each of the presented stimuli had a unique color (i.e. either red, blue, green, yellow, or pink) and shape (i.e. either a square, triangle, diamond, circle, or hexagon). After the cue display, there followed a delay of 500 ms which was followed by the search display. The search display was composed by 2 colored shapes: one of the shapes contained a vertical distracter line and the other shape contained a tilted line either to the left or the right (i.e. the search target). The size of the objects was the following: 1.80 x 1.80° of visual angle for the circle,
1.91 x 1.91° for diamond, 1.50 x 1.80° for the square 2 x 1.50° for the triangle, or 2.38 x 0.95° for the hexagon. The length of the lines was 0.57°.

There were two types of trials in which the validity of the memory cues for search varied: in valid trials, the target (tilted line) was surrounded by one of the 2 items held in WM (high load condition) or by the single item held in WM (low load condition). In invalid trials the cued object reappeared in the search display but now contained a vertical distracter line instead of the search target (Figure 1). The search display remained onscreen for 500 ms. Participants indicated the orientation of the target (right tilted or left tilted) by means of button pressing during a time window of 1.5 seconds since the onset of the search display.

A memory test followed the search response. A single colour shape was presented and participants were required to match it to the cue display. In responding to the memory item, participants had to indicate (via button press) whether or not the memory item matched both the colour and the shape of any of items held in memory. Hence, ‘same’ responses were requested when the test item matched the WM cue both in color and shape. Participants were instructed to respond ‘different’ whenever the item in WM was different in color, in shape or both, relative to the cue. Participants had an unlimited time window to respond in the memory test and they were instructed to try to be as accurate as possible in the memory test. Each participant completed a single block of 128 trials lasting for about 10 minutes, in which validity and load factors were varied randomly on each trial.

The task employed in Experiment 1 is depicted in Figure 1.

Experiment 2 was similar to Experiment 1. The main difference is that the level of working memory load was higher in Experiment 2 (i.e., 3 objects had to be remembered). Each trial started with a fixation display for 500 ms, which was followed by the presentation of three items for 200 ms. Participants were instructed to keep the particular color and shape of each of the objects in memory. Each of the stimuli was unique in colour and shape and appeared in 1 of 5 possible shapes (square, triangle, diamond, circle, or hexagon) and 1 of 5 possible colours (red, blue, green, yellow, or pink). After the cue display, there was a delay of 500 ms which was followed by a search display presented for another 500 ms. The search display remained onscreen for 500 ms and was followed by a further 1.5 seconds response period during which a blank screen was presented. Critically, on some trials the search display was not presented and instead a memory test appeared. Because participants could not predict whether a search display or a memory test would follow fixation, they were always required to keep the three items in memory. During the memory test, a single coloured shape was presented and participants were required to match it to the memory cue display. In responding to the memory item, participants had to indicate (via button press) whether or not the memory item matched both the colour and the shape of any of items held in memory. Hence, ‘same’ responses were requested when the test item matched the WM cue both in color and shape. Participants were instructed to respond ‘different’ whenever the item in WM was different in color, in shape or both relative to the cue. The
Figure 1: Illustration of the combined WM/attention paradigm used in Experiment 1. Two levels of WM load were included: low (1 item) and high (2 items). Note that in the low load condition the memory test item is 'new' (i.e. different) relative to the cue, while in the high load case the memory test item is 'old' (i.e. same as the cue).

Like in Experiment 1, the search display was composed of 2 coloured shapes, each containing a black line which could either be tilted (i.e. the target) or a vertical distracter. There were two conditions of cue validity, namely, valid and invalid similar to Experiment 1. The 2 trial types happened randomly and with equal probability. There were 96 trials in total (64 trials were search trials only and 32 trials were WM trials only).

In both Experiment 1 and 2, participants performed the task following a period of 10 minutes of neurostimulation (see below).

tDCS protocol

tDCS was applied to the scalp by a pair of 4 x 4 cm rubber electrodes, which were housed in 5 x 5 cm sponges soaked in saline solution. The site of stimulation was localized based on the 20-30 EEG system. We first determined the location of cortical area F3 which is known to correspond well to the left dorsolateral prefrontal cortex (Herwig, Satrapi, & Schönfeldt-Lecuona, 2003). The anterior end of the stimulating electrode was placed in the F3 region so that the stimulated area also extended posteriorly towards the left superior frontal gyrus. The reference electrode was located in the right arm contralateral to the site of stimulation with a current of 1.5 mA. The order of stimulation was counterbalanced across participants.

We elected to assess performance in the combined WM/attention paradigm
Figure 2: Example of the sequence of events during a trial in Experiment 2.

following two active tDCS conditions - anodal vs cathodal-. Participants were required to perform the task following each tDCS condition with the order counterbalanced across participants and separated by at least 24 hours. The observation of performance differences following two active tDCS conditions (i.e. anodal vs cathodal) is sufficient to establish the causal role of the lDFC in the combined WM and attention task, thus allowing us investigate how this is shaped by the level of cognitive load in WM and further explore whether its functional role is more ‘attentional’ or ‘mnemonic’ in nature.

During each session, participants were stimulated with either anodal or cathodal stimulation for 15 minutes. Although there was no sham tDCS condition, there were different task conditions (e.g., low vs high cognitive load) and task performance measures (i.e. search and memory scores), that allowed to test the effect of IDFC polarization. Importantly, tDCS effects on cognitive performance are both state- and task-dependent (Heinen et al., 2016; Jones & Berryhill, 2012; Wu et al., 2014) which is to say that tDCS effects may not be strictly fixed for a given cognitive process but rather be task-dependent or related to participants’ state prior to performing the task (Gözenman & Berryhill, 2016; Heinen et al., 2016). Accordingly, we assess the effects of anodal vs cathodal tDCS across different task contexts of WM load and WM validity and also on different performance measures (response latencies and accuracy in the memory and attention tests). The expected state-dependent nature of the tDCS effects allows to assess the causal role of IDFC stimulation even with the absence of a sham tDCS condition. Finding performance differences between these anodal and cathodal tDCS conditions is sufficient in the context of the present study to examine the nature of the functional contribution of the IDFC in WM and attention processes. We also note that the use of sham stimulation as a control may be a suboptimal comparison relative to two active tDCS conditions because
the subjective experiences during stimulation are significantly different between sham and active tDCS (Kessler, Turkeltaub, Benson, & Hamilton, 2012). During active tDCS tactile sensations are more frequent and more intense during the stimulation period, while sham tDCS is only associated with this type of experiences during the initial seconds of the protocol. This may have consequences for the blinding of participants. Hence, we elected to compare anodal vs cathodal tDCS of the lDFC, and assess the tDCS on behaviour across different task contexts and behavioural measures. This approach has been used in different tDCS studies investigating attention (Kanai et al., 2012; Sikström et al., 2016) and memory (Dutta, Shah, Silvanto, & Soto, 2014; London & Slagter, 2015; Marceglia et al., 2016).

Statistical approach

Shapiro-Wilk tests were used to check that our data conformed to the normal distribution. Reaction time data in both search and WM tasks in Experiment 1 conformed to normality assumptions. This held also in Experiment 2 except for the WM task data, in which case we used non-parametric statistics to verify the results and discard that the results obtained from the parametric tests were sensitive to the normality assumption.

Results

Experiment 1

We conducted a 2 (WM load: high load, low load) x 2 (validity: valid, invalid) x 2 (type of stimulation: anodal, cathodal) repeated measures ANOVA on the median search RTs, mean search accuracy and mean memory accuracy.

Only trials with correct responses in the search task and memory test were included in the analysis of search RTs. Figure 3 illustrates the pattern of search RTs across the different conditions. There was an effect of validity ($F (1, 7) = 18.5, p<0.004, \eta^2 = 0.73$) such that RTs were faster in valid relative to invalid conditions (Figure 2A). There was also an interaction between load and validity ($F (1, 7) = 17.2, p= 0.004, \eta^2 = 0.71$), showing that the size of the validity effect (Invalid RT minus Valid RT) was bigger in the low than in the high load condition. In other words, the validity effect decreased as load increased (see Figure 4). This was confirmed by means of additional t-tests that compared the size of the validity effect (invalid RT – valid RT) across WM load conditions. WM-validity effects were lower in the high WM load compared to the low WM load case, in both tDCS conditions ($t(7)=2.782, p=0.027$ for anodal, and $t(7)=4.731, p=0.002$, for cathodal). This result is in keeping with previous studies (van Moorselaar et al., 2017; Zhang et al., 2011; Soto & Humphreys, 2008).

Critically, for the purpose of this study, there was a significant interaction between load, validity and tDCS ($F (1, 7) = 6.24, p= 0.039, \eta^2 = 0.48$). Accord-
ingly, to unravel the source of this interaction, we performed t-tests to assess whether IDFC-tDCS moderated the detrimental effect of WM load on WM guidance. We first computed a score reflecting the reduction in validity effect from the low load to the high load condition (validity effect in low WM-load minus validity effect in high load) and assessed whether it was affected by the type of stimulation (cathodal vs. anodal). A two-tailed paired t-test showed a significant difference ($t(7) = 2.5, p<0.039$): following anodal stimulation the validity effects decreased 39.06 ms from the low load to the high load condition; however, cue validity effect decreased by 69.4 ms following cathodal stimulation (Figure 4). This suggests that although increasing WM load (i.e. from 1 item to 2 items) resulted in a cost in the strength of the validity effects, this cost was reduced after anodal stimulation relative to cathodal stimulation.

Finally, we also conducted a Bayesian paired t-test to provide another estimate of the strength of the evidence in favor of a tDCS effect. This Bayesian t-test compared the load-induced cost in the validity effect following anodal vs cathodal tDCS, as above. The results showed that the alternative hypothesis was 2.289 times more likely than the null hypothesis, hence constituting a form of weak or anecdotal evidence (Jeffreys, 1998).

Analysis of the search accuracy only showed an effect on validity ($F(1,7)=12.4, p=0.01, \eta^2 = 0.64$) showing that accuracy during search was higher in valid conditions (98 per cent correct) in comparison to invalid conditions (94 per cent correct). The pattern of search accuracy across conditions is depicted in Figure 5. There were no effects of load ($F(1,7)=1.15, p=0.32$) and tDCS ($F(1,7) = 0.13, p= 0.73$). Also, there were no two-way interactions between load and validity ($F(1,7) = 0.26, p=0.62$), validity and tDCS ($F(1,7) = 0.085, p=0.78$), load and tDCS ($F(1,7)=2.32, p=0.17$) on mean search accuracy. The
Figure 4: Validity effects (invalid RTs minus valid RTs) as a function of load and type of stimulation (error bars depict standard error of the mean).

three-way interaction between load, validity and tDCS was also non-significant (F(1,7)=0.14, p=0.72). Search accuracy did not meet the normality assumption. A non-parametric Durbin test with WM load, validity, and tDCS as factors only revealed an effect of validity on search accuracy (F(7,55)=8.985, p<0.001), while the effect of WM load and tDCS were not reliable (F<0.25, p>0.97) which is in keeping with the parametric ANOVA presented above.

Analyses of memory accuracy showed an effect of load (F(1,7)=25.7, p<0.001, \( \eta^2 = 0.79 \)) showing that participants were more accurate in the low load condition (94 percent correct) in comparison to the high load condition (81 percent correct). There were no effects of validity (F(1,7) = 4.0, p= 0.084) and tDCS (F(1,7)=0.021, p=0.88). Also, there were no two-way interactions between load and validity (F(1,7)=0.04, p=0.851), validity and tDCS (F(1,7)=0.37, p=0.562), load and tDCS (F(1,7)=0.233, p=0.64) on mean memory accuracy. The three-way interaction was also non-significant (F(1,7)=1.75, p=0.23). WM accuracy did not meet the normality assumption. A non-parametric Durbin test with WM load, validity, and tDCS as factors only revealed an effect of WM load on WM accuracy (F(7,55)=20.613, p<0.001), while the effect of validity and tDCS were not reliable (F <0.5, p>0.83) which is in keeping with the parametric ANOVA presented above.

Finally, analyses of memory RTs of trials with correct responses in both search and memory tasks showed an effect of load (F(1,7)=21.38, p<0.002, \( \eta^2 = 0.75 \)) with faster memory decisions in the low load condition. There was no effect of cue validity on subsequent memory RTs (F(1,7)=2.21, p=0.181) and no effect of stimulation condition (F(1,7)=1.96, p=0.204). Memory reaction times did not show an interaction between load and validity (F(1, 7)=0.139, p=0.72), validity and tDCS (F(1,7)=0.203, p=0.666) or load and tDCS (F(1,7)=0.593, p=0.466). The three-way interaction was also non-significant (F(1,7)=.492, p=0.506).

Table 1 illustrates the pattern of memory RTs and accuracy across the different experimental conditions (the scores in brackets depict the standard error
We found that search performance was better in valid relative to invalid WM cues, which is in keeping with previous demonstrations of WM biases of attention (Downing, 2000; Olivers et al., 2006, 2011; Hollingworth & Beck, 2016; Pan et al., 2016). WM biases of search performance were attenuated in the high WM-load relative to the low WM-load condition (Soto & Humphreys, 2008; Zhang et al., 2011; van Moorselaar, Theeuwes, & Olivers, 2014). LDFC-tDCS modulated the WM bias of selection and the influence of WM load on the expression of this bias. We argue that frontal tDCS modulated the scope of attentional control towards task irrelevant features and accordingly moderated the influence of the invalid WM distracters on search performance.

There was no evidence that tDCS influenced memory behaviour; both memory decision latencies and memory accuracy were not affected by tDCS. While it is always hard to make inferences based on null effects, it is tempting to suggest that frontal tDCS primarily affected processes related to selective attention rather than mnemonic processes per se. However, it may have been that a WM load of 2 items was not sensitive enough to detect tDCS effects in memory performance. Hence, the possibility that tDCS influenced memory accuracy was further explored in Experiment 2, in which WM load was further increased from two to three items. This also allowed to provide another test of tDCS effects on WM guidance at even higher levels of WM loads.

**Experiment 2**

Only trials with correct responses in the search task were included in the analyses. A 2 x 2 repeated measures ANOVA was conducted to assess the effect of validity and tDCS factors on the median search RTs and also on search accu-
Table 1: Memory RTs and memory accuracy (Acc) across validity, load and tDCS condition. The scores in brackets depict the standard error of the mean.

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<thead>
<tr>
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<th>Anodal</th>
<th>Cathodal</th>
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<tbody>
<tr>
<td>WM1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTs</td>
<td>548 (63)</td>
<td>527 (55)</td>
</tr>
<tr>
<td>Acc</td>
<td>0.93 (0.02)</td>
<td>0.96 (0.01)</td>
</tr>
<tr>
<td>WM2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTs</td>
<td>690 (75)</td>
<td>695 (77)</td>
</tr>
<tr>
<td>Acc</td>
<td>0.81 (0.03)</td>
<td>0.81 (0.04)</td>
</tr>
</tbody>
</table>

There was an effect of validity (F(1, 11)=14.46, p<0.003, \( \eta^2 =0.57 \)) such that median search RTs were faster in valid relative to invalid conditions (Figure 6). No effect of tDCS (F(1, 11)=1.7, p=0.21) and no interaction between validity and tDCS (F(1, 11)=0.22, p=0.65) were found on search RTs.

Analyses of search accuracy showed an effect of validity (F(1, 11)=13.57, p<0.004, \( \eta^2 =.55 \)), with higher accuracy in valid relative to invalid trials. An effect of tDCS was also present (F(1, 11) = 4.82, p<0.05, \( \eta^2 =0.31 \)) such that search accuracy was higher after cathodal relative to anodal stimulation. It seems that this effect was driven by differences in the invalid condition as indicated by a trend towards an interaction between validity and tDCS (F (1, 11) = 4.77, p=0.052, \( \eta^2 = 0.3 \))(see Figures 7). Post-hoc anodal tDCS impaired search accuracy in the invalid condition relative to cathodal tDCS (t(11)=2.702, p<0.042, two-tailed, Bonferroni corrected for multiple comparisons in both valid and invalid cases). Additional Bayesian t-tests indicated that the alternative hypothesis was 3.314 times more likely than the null, hence constituting a form of substantial evidence [Jeffreys 1998]. No such pattern of results was observed in the valid case (t(11)=.248, p=.809). Search accuracy did not meet the normality assumption. A non-parametric Durbin test with WM validity, and tDCS as factors revealed main effects of validity (F(3,35)=7.641, p<0.001) and tDCS (F(3,35)=3.323, p<0.031) on search accuracy, which is in keeping with the parametric ANOVA presented above.

Analysis of memory accuracy showed no effect of tDCS (t(11)=1.146, p=0.276; mean accuracy anodal = 0.808; cathodal = 0.767). A non-parametric test of the influence of tDCS on WM accuracy in Experiment 2 also revealed no significant modulation (Friedman test p = 0.366). To find out the evidence for
Figure 6: Median search RTs across validity and tDCS conditions. The colored lines illustrate the individual performance, while the thick black horizontal line illustrates the mean of the individual median RTs.

Figure 7: Mean search accuracy across validity and tDCS conditions. The colored lines illustrate the individual performance, while the thick black horizontal line illustrates the mean accuracy across participants.
the null hypothesis, we conducted a Bayes factor analysis. A Bayesian t-test showed anecdotal evidence for the null hypothesis (BF=0.494). Also, no effect of tDCS was observed on RTs of the correct memory decisions (t(11) = 1.115, p=0.289). A Bayesian t-test however showed only anecdotal evidence for the null hypothesis (BF=0.481). Since the RT data in the WM task did not meet the normality assumption we conducted a non-parametric test to assess the influence of tDCS on WM response latencies but we did not find any effect (Friedman test, p=0.366). These results are depicted in Table 2.

Like in Experiment 1, search RTs were faster in valid relative to invalid trials, suggesting that attention was guided by the WM contents. The effect of tDCS on WM guidance was however observed in search accuracy rather than search RTs in Experiment 1; following the presentation of an invalid WM item, search accuracy decreased after anodal stimulation in comparison to cathodal stimulation. The pattern of results in Experiment 1 and 2 are nevertheless compatible, both showing that IDFC-tDCS impacts the expression of the WM bias in search. Search accuracy in the valid condition was similar across tDCS conditions. This pattern of results found in accuracy in Experiment 2 resemble the pattern of results found in Experiment 1 in search RTs; anodal tDCS was associated with slower RTs in the invalid trials relative to the cathodal condition, while no differences were apparent in valid trials.

One explanation for why IDFC-tDCS influenced WM biases in search RTs in Experiment 1 and WM biases in search accuracy in Experiment 2 may relate to the different levels of task difficulty in Experiment 1 and Experiment 2. Indeed, visual inspection of the Figures that illustrate the search latencies in both experiments suggest that the higher WM load in Experiment 2 may have impaired overall search efficiency. An ANOVA of search RT latencies across Experiments using data from the WM load of two items (Experiment 1) and WM load of three items (Experiment 2) confirmed the existence of a main effect of Experiment; search latencies were indeed slower with three WM items relative to two WM items (F (1,18) = 11.435, p < 0.003, WM2 = 504.5; WM3 = 658.28). Given that search was overall slower with the increased WM load in Experiment 2 it follows that the disengagement of attention from the invalid WM distracter

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<tr>
<th>Memory</th>
<th>Anodal</th>
<th>Cathodal</th>
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<tr>
<td>RTs</td>
<td>809 (51)</td>
<td>855 (78)</td>
</tr>
<tr>
<td>Acc</td>
<td>0.81 (0.02)</td>
<td>0.77 (0.02)</td>
</tr>
</tbody>
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Table 2: Memory RTs and memory accuracy (Acc) across the tDCS conditions. The scores in brackets depict the standard error of the mean.
in search was very likely to occur later in time. Delayed disengagement in Experiment 2 meant that attention was more likely to be engaged in the invalid WM item by the time of search display is offset (i.e. at 500 ms), leading to an increase in error rate at identifying the search target.

General Discussion

We tested the effect of neurostimulation of the lDFC by means of tDCS on WM biases of selective attention in search and the maintenance of information in WM. Across two different Experiments we showed that the contents of WM biased the allocation of selective attention in the visual search display towards memory-matching items, leading to improved search on valid relative to invalid trials. This result is in keeping with a large-body of studies (for reviews see (Soto et al., 2008; Kiyonaga & Egner, 2013)). Also in keeping with previous evidence we found that WM effects on attention performance were attenuated when the processing load of WM is stressed ((van Moorselaar et al., 2017; Soto & Humphreys, 2008; Zhang et al., 2011; Soto et al., 2012; van Moorselaar et al., 2014)), leading to weaker effects of the WM content on attention when the amount of cognitive load in WM was higher, namely, when multiple items were held in WM (Experiment 1). At the same time, we found that memory accuracy was also affected by the number of items held in WM (Experiment 1). Thus this paradigm allowed us to test the influence of frontal neurostimulation both on the bias of attention by the WM content and also on the level of WM accuracy, within the same experimental procedure. Notably, we found that LDFC-tDCS modulated the influence of the WM content on attention performance, in particular when the number of items held in WM (i.e. the WM load) increased (Experiment 1 and Experiment 2). However, memory accuracy was not affected by lDFC-tDCS, which would be expected if neurostimulation modulated the maintenance of the WM content or the fidelity of the specific memorandum.

These pattern of results have a series of theoretical implications for understanding the role of the lDFC in visual cognition. First, the results suggest that in the context of the combined WM and attention paradigm, neurostimulation of the lDFC may predominantly influence attention control while any modulation of memory performance is weaker by comparison. This effect of lDFC-tDCS on WM biasing of attention in search is in keeping with a previous transcranial magnetic stimulation (TMS) study of the left superior frontal gyrus also performed in the context of the combined WM and attention paradigm (Soto et al., 2012), though this TMS study only employed a low WM-load and memory performance was close to ceiling. LDFC-tDCS appeared to have an effect mainly when the WM content was invalid for the attention task, while performance on valid trials did not differ between anodal and cathodal stimulation (see Figure 2 - Experiment 1- and Figure 7 -Experiment 2). We suggest that frontal tDCS modulated attentional control by broadening the scope of the focus of selection, thereby enhancing the influence of invalid WM distracters that turn out to be
misleading for search.

One potential limitation of the present study is the reduced sample sizes. We are mindful that tDCS-effects in behavioural performance can vary across subjects. This variability can lead to replicability issues that have recently been raised in tDCS research, which are more likely to occur with reduced and heterogeneous sample sizes (Chrysikou, Berryhill, Bikson, & Coslett, 2017). However in the context of this study, despite the low sample size, the influence of lDFC-tDCS on search was replicated across two different experiments with independent samples.

Another limitation of the present work is that while there was no evidence for an effect of tDCS on WM performance, it cannot be ruled out that an effect of lDFC-tDCS on WM performance may be found by increasing the sample size. However, based on the evidence available it is likely that lDFC-tDCS on visual selection biases are stronger than on WM performance. Notably, in Experiment 2, the level of task difficulty was if anything harder in the WM task relative to the search task in terms of accuracy. Despite this, tDCS has an effect on the WM bias in search but did not affect WM accuracy. Furthermore, the present study highlights an experimental framework to isolate attention from mnemonic control effects of frontal tDCS within the same task. Future studies could further exploit and further this protocol to understand the role of frontal substrates in mnemonic and attention control functions within a single experimental paradigm. Notably, it will be important to match the level of performance of WM and attention tasks in both response latencies and accuracy so that the influence of tDCS on both can be directly compared. This present study provides the foundation for future studies using high-powered samples and direct comparisons between WM and attention performance to establish whether the lDFC’s role is more attentional or mnemonic in nature.

A second implication of this study is that the effects of lDFC on the control of attention from the contents of WM are task-dependent, in that they are modulated by the amount of cognitive load in the WM system. Prior studies indicate that tDCS effects on performance may be dependent on the level of task difficulty (Jones & Berryhill, 2012) and a recent study showed that tDCS can impair attention performance when the level of cognitive load is high (Roe et al., 2016). We argue that the different task difficulty/cognitive load levels in the present study may well relate to the effects of tDCS we report (i.e. differential tDCS effects from low to high WM load).

It could be argued that the present study can not to determine the extent to which anodal and cathodal lDFC-tDCS stimulation promoted or attenuated the expression of the WM bias of selection. We note that our goal study was to provide insights into the role of the lDFC in the interaction between WM and attention. Although our design did not include a baseline tDCS condition (e.g. sham), it included various task manipulations (i.e., low vs high cognitive load, valid vs invalid trials) and, critically, tDCS effects on search and memory performance were contingent and dissociated across the different task states.

Accordingly, here we suggest that the role of the lDFC in WM biasing is more attentional than mnemonic in nature. We realise this may appear at
odds with several reports of tDCS effects on WM performance (Fregni et al., 2005; Boggio et al., 2006; Ohn et al., 2008; Andrews et al., 2011; Jeon & Han, 2012; Pope et al., 2015; Arciniega et al., 2018). However, as noted above and demonstrated in the present study, neurostimulation effects are known to be task-dependent (Silvanto, Muggleton, & Walsh, 2008; Romei, Thut, & Silvanto, 2016). It has been shown that tDCS effects are not fixed for a given cognitive process but rather depend on task-states or even to participants’ baseline performance prior to performing the task (Gözenman & Berryhill, 2016; Heinen et al., 2016). Given that brain responses can flexibly adapt to the demands of a given task context, IDFC-tDCS effects may accordingly be dependent on the state of the network as determined by task context. That the IDFC-tDCS effect was predominantly manifested in attention rather than mnemonic performance is in agreement with functional neuroanatomical frameworks of WM (D’esposito & Postle, 2015) according to which the role of frontal substrates in WM-based behaviour is to set and control feedback signalling processes to posterior areas based on task rules and behavioural goals. However, in the context of a WM test, frontal biases may serve to strengthen the specific memorandum that are both encoded and maintained in early sensory substrates (Serences, Ester, Vogel, & Awh, 2009; Ester, Anderson, Serences, & Awh, 2013) by selectively deploying internal attention to relevant representations. Furthermore, tDCS studies using the retro-cue WM paradigm -in which participants are required to switch between representations in WM based on task-relevance-, indicates that frontal tDCS modulation of WM processes are in keeping with an involvement in shifting internal attention to memory representations (Tanoue, Jones, Peterson, & Berryhill, 2013). This notion is also consistent with neurophysiological evidence in primates showing that prefrontal neurons are more engaged during selective attention than mnemonic demands (Lebedev, Messinger, Kralik, & Wise, 2004). Likewise, electrical stimulation of the frontal eye fields neurons in macaques has been also shown to selectively modulate responses in extra-striate cortex (Moore & Armstrong, 2003).

Previous fMRI studies using the combined WM and attention paradigm indicated that functional connectivity between frontal and visual cortex is impaired when the capacity of WM is loaded (Soto, Greene, et al., 2011). Given that IDFC-tDCS modulatory effects we report tended to occur at higher WM loads, an interesting avenue of neuroimaging inquiry is to assess the IDFC-tDCS modulation of top-down signalling between frontal and sensory cortex and how it relates to the behavioural expression of the WM bias under different WM-loads. Furthermore, the present results represent a preliminary foundation to test the potential role of IDFC-tDCS in populations in which WM guidance of attention has been shown to be compromised, namely, in ageing (Wedmore, Musil, & Soto, 2017).
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