# Effects of Primed Anodal Transcranial Direct Current Stimulation on the Psychomotor Function of Older Adults

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*I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary educational institution.*

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*Angela Jane Hui Ling Tan*

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Abstract

Declines in cognitive and motor functions as a result of ageing have an adverse impact on the quality of life. One such decline takes the form of poorer psychomotor performance, which involves both cognitive and motor processes in terms of perceiving and processing external stimuli, and executing motor responses. Recent research using transcranial direct current stimulation (tDCS) has shown that priming the corticospinal system by lowering the threshold for the induction of long-term potentiation facilitates subsequent motor performance. Here we utilised this priming approach in a double-blind sham-controlled experiment to investigate the efficacy of the application of tDCS to the dorsolateral prefrontal cortex (DLPFC) in improving the psychomotor performance of older adults. A group of 10 healthy older individuals (mean age 71.60 years; 5 males and 5 females) participated in 2 sessions on separate days, with 1 session involving a 10-minute cathodal tDCS followed by a 20-minute anodal tDCS (C-A), and the other involving a 10-minute cathodal tDCS followed by sham stimulation (C-S) over the left DLPFC. Psychomotor performance was determined through the accuracy and response speeds on a task measuring sustained, selective, and divided attention. The accuracy scores for divided attention were significantly higher in the C-A condition compared with the C-S condition, suggesting that anodal tDCS primed with cathodal tDCS is effective in improving divided attention, and shows promise as a clinical intervention for improving psychomotor function in older adults.

*Keywords*: transcranial direct current stimulation, tDCS, dorsolateral prefrontal cortex, DLPFC, attention, psychomotor speed, ageing

# Effects of Primed Anodal Transcranial Direct Current Stimulation on the Psychomotor Function of Older Adults

With increases in life expectancies and declines in fertility rates, populations worldwide are ageing at a substantial rate: the United Nations estimates that the number of people in the world over the age of 60 will increase by 56% between 2015 and 2030 (United Nations Department of Economic and Social Affairs, 2015). The most prevailing consequence of ageing is the deterioration of functional capabilities (Yoshihara, 2012), which usually manifests in the decline of psychomotor performance (Ilamkar, 2014). Psychomotor performance involves both cognitive and motor processes in terms of perceiving and processing external stimuli, and the initiation and execution of motor responses (Ilamkar, 2014). An example of a psychomotor activity is driving, with cognitive processes such as paying attention to traffic signs and other vehicles, and motor responses such as applying the brakes and turning the steering wheel (Moskowitz & Burns, 1990). While declining psychomotor performance is an inevitable consequence of ageing, any way of alleviating or slowing this deterioration is advantageous as it can improve the quality of life for older adults. For example, improving the functional abilities of older individuals can reduce their need and dependence on intensive medical and clinical interventions (Harvey & Thurnwald, 2009). Age-related declines in psychomotor functions should also be addressed because they bring about potential dangers such as a higher risk of falls and accidents (Di Fabio et al., 2005; Shanmugaratnam, Kass & Arruda, 2010). Furthermore, research into finding ways of ameliorating age-related decline for healthy populations can contribute towards the development of potential interventions for the pathological psychomotor decline present in

conditions such as dementia (Bailon, Roussel, Boucart, Krystkowiak & Godefroy, 2010).

Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique, presents as an attractive treatment option for alleviating age-related deterioration. By inducing the transmembrane neuronal potential, tDCS influences the level of cortical excitability (Nitsche et al., 2008; Zaghi, Acar, Hultgren, Boggio & Fregni, 2010). It is thought that the neuronal changes associated with the persisting effects of tDCS are analogous to activity-dependent synaptic plasticity, i.e., long-term potentiation and long-term depression (Fritsch et al., 2010; Rroji, van Kuyck, Nuttin & Wenderoth, 2015). Recent reviews (Hsu, Ku, Zanto & Gazzaley, 2015; Summers, Kang & Cauraugh, 2016) have found tDCS to be effective for improving cognitive and motor functions in healthy older individuals. However, a problem facing many tDCS studies is the inter-individual variability of responses to tDCS (e.g., Strube, Bunse, Malchow & Hasan, 2015; Wiethoff, Hamada & Rothwell, 2014). The differences in individual response to stimulation, with some individuals not showing the expected effects of tDCS, must be addressed in order for tDCS to be a more viable option for clinical interventions (Wiethoff et al., 2014).

To address this problem, a novel tDCS priming technique was recently developed and demonstrated to reduce the inter-individual variability in responses to tDCS (Fujiyama et al., in press). Using a double-blind sham-controlled experiment, this thesis is a follow-up study to explore the effectiveness of this tDCS protocol on improving the psychomotor performance of older individuals.

The following sections will begin with an overview of the age-related deterioration in response speed and attention, which is an important component of psychomotor functioning. The use of tDCS as a way of alleviating age-related

declines, including its mechanisms and how it is conducted, will also be outlined. The involvement of the dorsolateral prefrontal cortex (DLPFC) in psychomotor performance, and previous research investigating the effects of tDCS to the DLPFC will also be reviewed. This is followed by an explanation of homeostatic metaplasticity, which is the underlying principle behind the novel tDCS protocol that would be used to reduce inter-individual variability in responses to tDCS.

**Age-related Declines in Psychomotor Performance**

Psychomotor performance involves both cognitive and motor processes (Ilamkar, 2014), and a cognitive function that plays an important role in psychomotor functioning is attention (Kallus, Schmitt & Benton, 2005). There are three attentional functions as proposed by Posner and Petersen (1990): sustained, selective, and divided. Sustained attention refers to the process of achieving and maintaining attention on a particular target, selective attention refers to the process of directing attention to sensory stimuli, and divided attention refers to the ability to task-shift and resolve conflict between multiple stimuli (Drag & Bieliauskas, 2010; Posner & Petersen, 1990). These three types of attention are important for daily activities and for ensuring safety. For instance, sustained and selective attention is crucial for being alert and vigilant to potential hazards when walking or driving. Divided attention is required when there are various stimuli to simultaneously attend to, such as driving safely while navigating and trying to locate a building in an unfamiliar place.

Sustained attention appears to be preserved or even improved with old age, with recent studies finding higher accuracy rates on sustained attention tasks for older participants when compared with younger participants (Brache, Scialfa & Hudson, 2010; Carriere, Cheyne, Solman & Smilek, 2010; Jackson & Balota, 2012;

Staub, Doignon-Camus, Bacon & Bonnefond, 2014). The research on the two other types of attention, on the other hand, largely show that selective and divided attention decline with age, with older adults having poorer performance than their younger counterparts (e.g., de Ribaupierre & Ludwig, 2003; Getzmann, Golob & Wascher, 2016; Maurits, Renken, Lorist, Saliasi & Geerligs, 2014).

Apart from declines in cognitive abilities, the psychomotor performance of older individuals is also affected by the slowing in response speeds (Forstmann et al., 2011; Ilamkar, 2014). With slower psychomotor speed being a significant predictor of falls (Chen, Peronto & Edwards, 2012), it is thus important for age-related psychomotor slowing to be addressed as well.

Much of age-related functional decline has been associated with cerebral ageing, such as through the decrease in synaptic connectivity (Morrison & Baxter, 2012), as well as through neuronal loss and changes in white matter (Jellinger & Attems, 2013). Notably, structural changes in brain regions such as the DLPFC have been shown to underlie age-related declines in psychomotor function (Fujiyama et al., in press).

However, the central nervous system is highly plastic and is able to reorganise its structure, function, and connections in response to environmental stimuli: a concept known as neuroplasticity (Cramer et al., 2011). The induction of neuroplasticity is seen as a key strategy in alleviating age-related declines in functional capabilities (Jellinger & Attems, 2013). Neuroplasticity in older individuals can be induced through the use of non-invasive brain stimulation such as tDCS (Nitsche & Paulus, 2011).

**Transcranial Direct Current Stimulation (tDCS)**

The application of tDCS involves placing electrodes on the scalp for the delivery of small currents that induce changes in cortical activity (Nitsche et al., 2008). Whether tDCS increases (upregulates) or inhibits (downregulates) cortical excitability depends on the placement of the electrodes (Nitsche et al., 2008). Anodal tDCS increases cortical excitability, and occurs when the anode (a positively-charged electrode) is placed over the intended brain region to be stimulated and the cathode (a negatively-charged electrode) on a reference site (Nitsche & Paulus, 2000). Cathodal tDCS has an inhibitory effect, and occurs with the cathode placed over the targeted brain region and the anode on a reference site (Nitsche & Paulus, 2000).

The effects of anodal and cathodal tDCS resemble that of long-term potentiation (LTP) and long-term depression (LTD) respectively (Fritsch et al., 2010; Rroji et al., 2015). LTP refers to the increase in the rate of neural firing (synaptic strength) as a result of experiences, and LTD refers to the converse situation when synaptic strength is weakened (Bliss, Collingridge & Morris, 2003; Bliss & Lomo, 1973). Both LTP and LTD are forms of synaptic plasticity: the ability of neuronal synapses to adapt to environmental changes and experiences (Abbott & Nelson, 2000).

While the underlying mechanisms of tDCS remain unclear, it is thought that the generated currents act to modulate cortical activity by altering neuronal resting membrane potential to change the likelihood that neurons will fire (Nitsche & Paulus, 2000). It was also suggested that tDCS also modifies the synaptic microenvironment, such as through changing the concentration of gamma-aminobutyric acid (GABA), a neurotransmitter that is involved in inhibiting and reducing neuronal activity (Stagg et al., 2009).

The effects of tDCS on cortical excitability persist beyond the stimulation duration (Nitsche & Paulus, 2000), and the duration of these after-effects depends on factors such as the current intensity, the number of sessions administered, the duration of stimulation, and the brain region that is being stimulated (Nitsche et al., 2008). Single sessions of tDCS have been found to induce changes in cortical excitability lasting up to an hour (Ardolino, Bossi, Barbieri & Priori, 2005; Nitsche et al., 2008). The well-documented safety and cost-effectiveness of tDCS makes it an attractive treatment option (Nitsche et al., 2008; Williams, Imamura & Fregni, 2009). The most commonly reported sensations associated with tDCS are tingling and itching that are usually experienced in the initial stage of stimulation (Brunoni et al., 2011), with other side-effects such as nausea and headaches being rare and minimal (Poreisz, Boros, Antal & Paulus, 2007). Moreover, an advantage of using tDCS over other forms of non-invasive brain stimulation such as transcranial magnetic stimulation (TMS) is that it allows for double-blinding through the use of sham stimulation (Gandiga, Hummel & Cohen, 2006; Nitsche et al., 2008).

During sham stimulation, electrodes are placed on the participant's head as in a real stimulation protocol, except that currents are passed through the electrodes for only a brief period of time, such as 30 seconds (Gandiga et al., 2006). This brief stimulation provides the tingling and itching sensations that are usually experienced at the beginning of real stimulations, and most individuals are unable to distinguish sham from real tDCS (Ambrus, Al-Moyed, Chaieb, Sarp, Antal & Paulus, 2012). Sham stimulation does not appear to alter brain function (Nitsche et al., 2008), and thus serves as an active control condition. If the tDCS device is programmed by another researcher not carrying out the stimulation, double-blinding can be carried out, with both the participant receiving tDCS and the researcher administering the

tDCS treatment effectively blinded to whether real or sham stimulation is occurring (Nitsche et al., 2008). This reduces confounds caused by experimenter and participant expectations (Whitley & Kite, 2013).

**The Dorsolateral Prefrontal Cortex (DLPFC) and Previous tDCS Studies**

Located on Brodmann areas 9 and 46 (refer to Figure 1; Berntson & Cacioppo, 2009; Brodmann, 1909), the DLPFC has been found to be involved in cognitive functions such as attention (Gladwin, den Uyl, Fregni & Wiers, 2012; Johnson, Strafella & Zatorre, 2007; MacDonald, Cohen, Stenger & Carter, 2000), working memory (Mottaghy et al., 2000; Sauseng et al., 2004), and decision-making (Cho et al., 2012). The DLPFC was also found to be recruited by older adults when performing complex motor coordination tasks that require the cognitive control of motor actions (Heuninckx, Wenderoth, Debaere, Peeters & Swinnen, 2005). Notably, age-related declines in psychomotor function have been associated with microstructural changes in the DLPFC (Fujiyama et al., 2016).

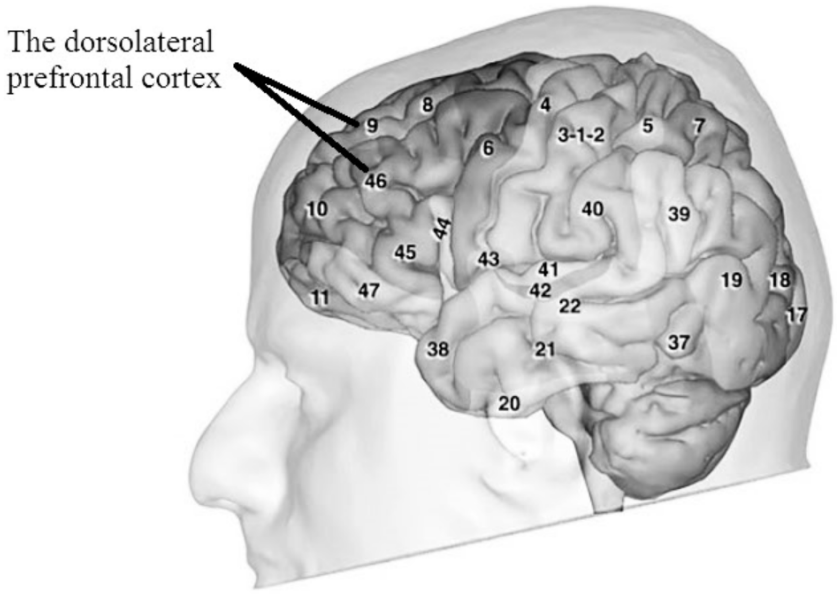


*Figure 1*. The DLPFC is located on Brodmann areas 9 and 46 (image adapted from Catani & de Schotten, 2012).

The application of anodal tDCS over the DLPFC has led to significant improvements in sustained attention (McIntire, McKinley, Goodyear & Nelson, 2014), selective attention (Gladwin et al., 2012), and psychomotor speed (McIntire et al., 2014). While no studies have yet investigated the effects of anodal tDCS to the DLPFC for divided attention, Johnson et al. (2007) found significant declines in the performance on a divided attention task when the DLPFC was temporarily disrupted with TMS. This not only demonstrates the involvement of the DLPFC in divided attention, but also presents the corollary that upregulating the cortical excitability of the DLPFC—such as with anodal tDCS—would lead to an improvement in divided attention.

**Homeostatic Metaplasticity and Inter-Individual Variability**

Despite the promise that tDCS shows, a major impediment to it becoming a truly effective treatment option is the inter-individual variability in responses to tDCS and other forms of non-invasive brain stimulation techniques (e.g., López-Alonso, Cheeran, Río-Rodríguez & Fernández-del-Olmo, 2014; Strube et al., 2015; Wiethoff et al., 2014). For instance, López-Alonso et al. (2014) found that only 45% of their participants had the expected increase in corticospinal excitability in response to anodal tDCS. Similarly, only 36% of participants in Wiethoff et al.'s (2014) study exhibited the expected facilitatory response to anodal stimulation and inhibitory response to cathodal stimulation.

It was posited that the inter-individual variability in responses to tDCS can be attributed to differences in the history of synaptic activity preceding stimulation (Ridding & Ziemann, 2010). This can be explained by homeostatic metaplasticity, which is based on the Bienenstock-Cooper-Munro (BCM) theory (Bienenstock, Cooper & Munro, 1982). The BCM theory proposes that synaptic plasticity is

bidirectional, and can result in either LTP or LTD (Bienenstock et al., 1982). The likelihood of an induction of LTP or LTD depends on the history of post-synaptic activity: low levels of previous post-synaptic activity lower the synaptic modification threshold, favouring the subsequent induction of LTP over LTD. The converse holds for high levels of post-synaptic activity, with an increase of the synaptic modification threshold to favour the induction of LTD over LTP (Bienenstock et al., 1982). Homeostatic metaplasticity thus serves to stabilise neural activity and prevents extreme neural states in the form of uncontrolled LTP or LTD in which excessive neural firing or complete inactivity might occur (Karabanov et al., 2015).

As aforementioned, non-invasive brain stimulation such as tDCS induces LTD- and LTP-like changes in the brain. Following the BCM theory of homeostatic metaplasticity, an individual's response to tDCS would depend on his/her history of post-synaptic activity (Fujiyama et al., in press; Ridding & Ziemann, 2010). An individual with low levels of previous post-synaptic activity is more likely to experience LTP-like activity in response to anodal tDCS compared with another individual with higher levels of post-synaptic activity (Ziemann & Siebner, 2008). As illustrated in Figure 2, low levels of previous post-synaptic activity (as represented by the gray ball) result in the lowering of the synaptic modification threshold, thus favouring the induction of subsequent LTP-like activity (as represented by the black ball) when anodal tDCS is applied.

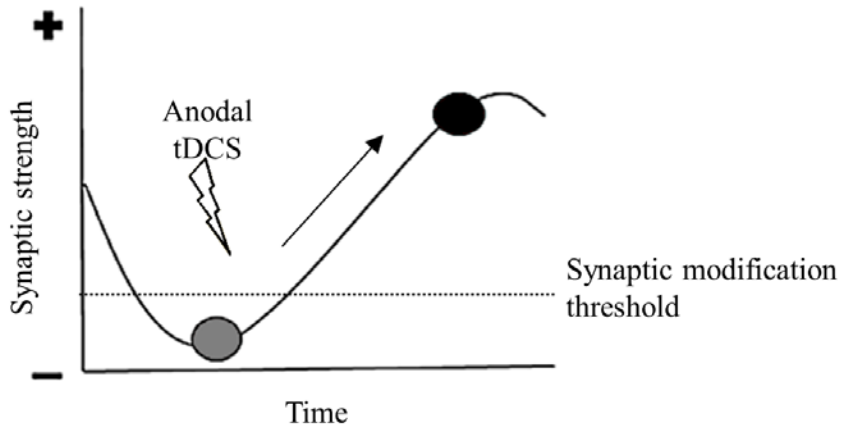


*Figure 2.* The synaptic modification threshold is lowered by a history of lower post-synaptic activity (presented by the gray ball) to favour the subsequent induction of LTP-like activity (presented by the black ball) upon the application of anodal tDCS.

**A Novel tDCS Priming Protocol**

Harnessing the principle of homeostatic metaplasticity, studies have shown that the use of a "priming" stimulation can increase responses to subsequent "test" stimulation if the priming stimulation has an opposite effect from the test stimulation (Karabanov et al., 2015). In other words, an inhibitory priming stimulation such as cathodal tDCS would boost the effect of an excitatory test stimulation such as anodal tDCS. The cathodal tDCS will downregulate post-synaptic activity, which lowers the synaptic modification threshold to favour the induction of subsequent LTP-like activity (Ziemann & Siebner, 2008). This increases the likelihood of higher cortical excitability resulting from a subsequent application of anodal tDCS, thus reducing inter-individual variability since more individuals will exhibit the expected response (higher cortical excitability to anodal tDCS).

To demonstrate this in the primary motor region (M1), Fujiyama et al. (in press) employed two experimental groups: one received cathodal tDCS as a priming stimulation while the other group was primed with sham tDCS. Both groups received anodal tDCS for the subsequent test stimulation, and their corticospinal

excitability and performance on a motor task was measured. Fujiyama et al. found that participants who had received cathodal tDCS as the priming stimulation had significantly greater corticospinal excitability and a greater improvement in task performance compared with those who received sham tDCS as the priming stimulation. The number of individuals exhibiting the expected increase in corticospinal excitability in response to anodal tDCS was significantly larger for the cathodal priming group compared with the sham priming group, and the inter-individual variability of responses was significantly lower when anodal tDCS was primed with cathodal tDCS than when it was primed with sham tDCS.

The current experiment aimed to investigate the effectiveness of this novel protocol—preceding anodal tDCS with a priming stimulation of cathodal tDCS—on improving psychomotor performance when applied to the DLPFC. It could be argued that the increase in excitability and task performance for Fujiyama et al.'s (in press) study was due entirely to the cathodal priming stimulation rather than due to the anodal tDCS applied. In view of this, the current experiment employed a control condition in which cathodal tDCS was also used for priming, but with a test stimulation of sham tDCS instead of anodal tDCS. This would examine if any effects that the experimental protocol might have on psychomotor performance could be attributable to the anodal tDCS applied instead of the priming cathodal tDCS.

**Aims and Hypotheses**

While the deterioration of psychomotor performance is an inevitable part of the ageing process, much can be done to alleviate this decline and improve the well-being and safety of older adults. Furthermore, research into the alleviation of age-related declines that are associated with normal and healthy ageing will contribute to

the development of potential interventions for age-related pathological conditions such as dementia.

Previous studies have found that the application of anodal tDCS over the DLPFC led to improvements in sustained attention, selective attention, and response speeds (Gladwin et al., 2012; McIntire et al., 2014). Moreover, the involvement of the DLPFC in divided attention indicated a likelihood that upregulating the DLPFC would improve divided attention as well (Johnson et al., 2007). In line with the BCM theory of homeostatic metaplasticity, the use of a cathodal priming stimulation to precede anodal tDCS was also demonstrated to boost the effect of the anodal stimulation (Fujiyama et al., in press). As such, it was hypothesised that compared with sham tDCS, the application of anodal tDCS to the DLPFC after priming it with cathodal tDCS will improve the psychomotor performance—specifically, the sustained attention, selective attention, divided attention, and psychomotor speed—for healthy older adults.

## Method

### Participants

Following the sample sizes used in previous research that investigated the effects of tDCS on older adults (e.g., Hummel et al., 2010; Zimerman et al., 2013), 10 right-handed participants (5 males and 5 females) were recruited through flyers (refer to Appendix A) placed at supermarkets, community centres, libraries, and retirement villages. Their demographic details are presented in Table 1. Thirteen participants were initially recruited, but one individual was not able to return for the second session due to personal reasons, and two left-handed participants had to be excluded because responses to tDCS have been found to be influenced by handedness (e.g., Vines, Cerruti & Schlaug, 2008). Handedness was determined

with the Edinburgh Inventory (refer to Appendix B): scores lower than -40 indicate left-handedness while scores above 40 indicate right-handedness (Oldfield, 1971).

Table 1

*Demographic Details of the Participants*

| | *M* | *SD* |
|---|---|---|
| Age (years) | 71.60 | 5.10 |
| Years of education received | 14.35 | 5.19 |
| Handedness score[a] | 89 | 14.49 |
| MoCA[b] score | 28.9 | 1.43 |

*Note.* [a]On the Edinburgh Inventory. [b]MoCA: Montreal Cognitive Assessment.

Potential participants were screened to determine their eligibility for participation, with exclusion criteria including a history of epilepsy or seizures, migraines, metal in the brain or skull, cardiac pacemakers, and the use of neuropsychoactive medications such as antidepressants (Nitsche et al., 2008). The screening questionnaire can be found in Appendix C. All the participants were cognitively healthy according to their scores on the Montreal Cognitive Assessment (MoCA; see Appendix D); a score of 26 points or more indicated normal cognition (Nasreddine et al., 2005).

Informed consent was obtained prior to participation, and participants were advised of their right to withdraw from the study. All participants were requested to attend two sessions; each session lasted around 2.5 hours. Each participant was involved in both experimental conditions: the C-A condition, in which anodal tDCS

was primed with cathodal tDCS, and the C-S condition, in which sham tDCS was primed with cathodal tDCS. A reimbursement of $15 was given for each session to cover time and travel costs.

The study was approved by the Murdoch University Human Research Ethics Committee (2016/021). The summary of project is presented in Appendix E.

**Materials and Apparatus**

**Transcranial direct current stimulation (tDCS).** Transcranial direct current stimulation was applied via two 4 x 6 cm conductive rubber electrodes that were connected to a battery-driven stimulator (Chattanooga Ionto™ Dual Channel Iontophoresis System; refer to Figure 3). The electrodes were placed in saline-soaked sponges applied with conductive gel before being secured with bandages on participants' heads as shown in Figure 3.

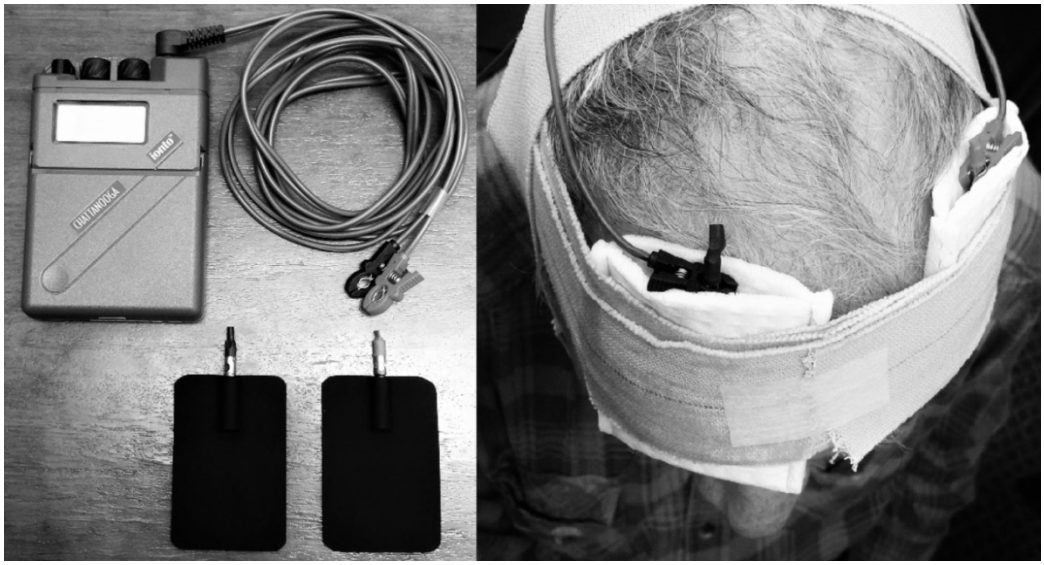

*Figure 3*. The tDCS was delivered using the Chattanooga Ionto™ Dual Channel Iontophoresis System and 4 x 6 cm conductive rubber electrodes as shown in the left image. The right image shows the electrodes placed in saline-soaked sponges and secured on participants' heads with bandages.

The tDCS device usually gives off a beeping alert at the end of stimulation, and the device used to deliver the test (sham or anodal) stimulation had its beeping

alert deactivated to ensure that participants and the researcher carrying out the experiment were blinded to whether anodal or sham stimulation was being applied.

A constant direct current of 1.5 mA was used for the cathodal, anodal, and sham stimulations. The stimulation durations were 10 minutes for cathodal tDCS, 20 minutes for anodal tDCS, and 30 seconds for sham tDCS. Each stimulation began with a ramp-up of the current from 0 to 1.5 mA and ended with a ramp-down from 1.5 to 0 mA; this ramp-up and down lasted 30 seconds. To ensure double-blinding, the tDCS device was calibrated for the sham and anodal stimulations by another researcher who was not directly involved in data collection and analysis.

**The Attention Network Test (ANT).** The Attention Network Test (ANT) is a choice reaction task that measures performance with regards to the three types of attention (Fan, McCandliss, Sommer, Raz & Posner, 2002), and a modified version was used in the current experiment as a measure of psychomotor performance.

The ANT in this experiment consisted of two blocks with 64 trials per block. Figure 4 shows an example of a trial. An initial screen with a fixation cross was presented for a variable duration of 0.4 to 1.6 seconds, and it was followed by a screen lasting 0.1 seconds with either no cue, a centre cue, double cues, or a spatial cue (see Figure 5 for these cue conditions). The screen with a fixation cross was presented again for 0.4 seconds, and it was succeeded by the target screen for which participants were required to respond to the direction of the central arrow in a row of arrows. The target screen was presented until the participant provided a response; a time limit of 1.7 seconds was given. Figure 6 shows the possible stimuli for the target screen. The left arrow key should be pressed if the central arrow pointed to the left, and the right arrow key should be pressed if it pointed to the right. The central arrow could be flanked by arrows that were in a direction congruent or

incongruent with that of the central arrow. In the example shown in Figure 4, the correct response would be to press the left arrow key. The stimuli could appear above or below the fixation cross. On certain trials, spatial cues would indicate the position of the stimuli. The example trial in Figure 4 contains a spatial cue to inform the test-taker that the stimuli will appear below the fixation cross in the target screen. Each ANT took around 4 minutes to complete.

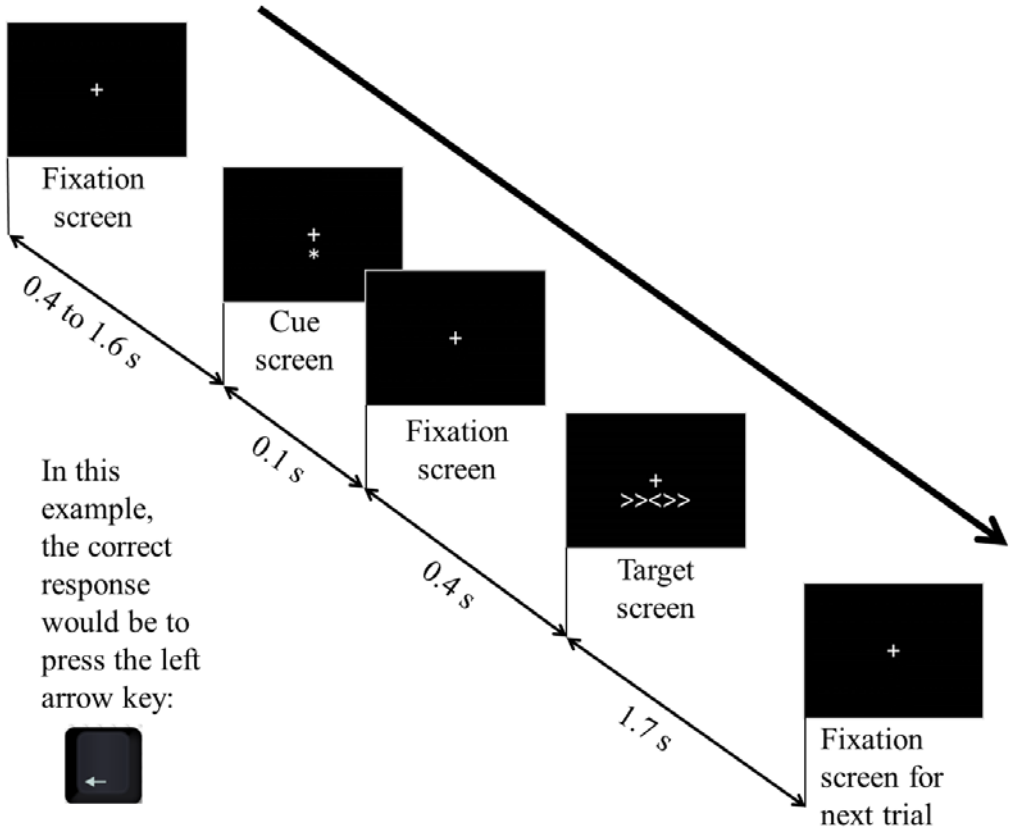


*Figure 4*. An example of an ANT trial. A spatial cue is shown on the cue screen as an asterisk below the fixation cross. This indicates that the stimuli (row of arrows) will appear below the fixation cross as shown on the target screen. Participants needed to respond to the central arrow by pressing the left or right arrow. Here, the central arrow is pointing towards the left, hence the correct response would be to press the left arrow key.

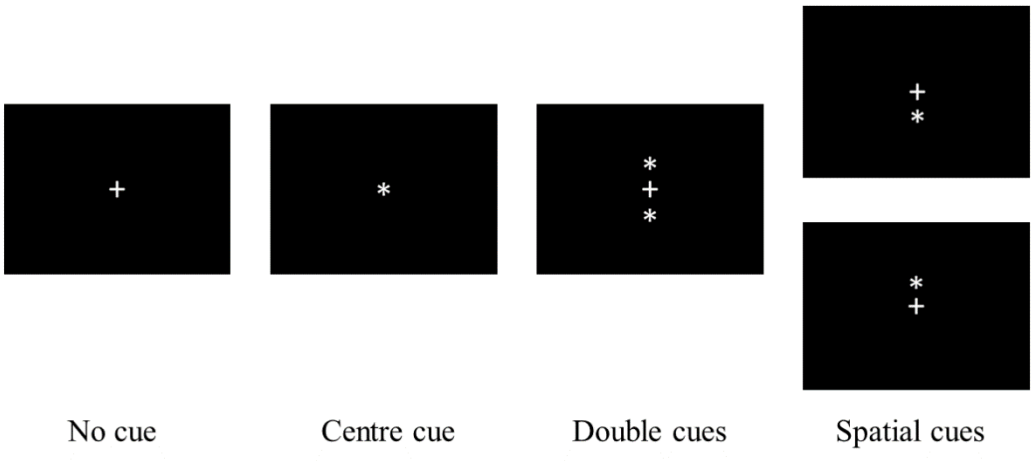


*Figure 5*. The four different cue conditions.

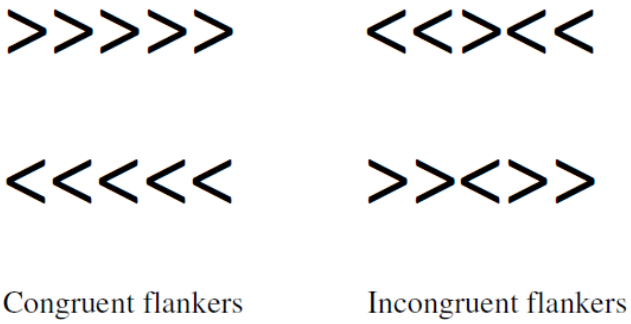


*Figure 6*. The four different stimuli. Flankers to the central arrow could be in a congruent or incongruent direction.

To enable direct comparison with previous relevant studies (e.g., Heinze et al., 2014), participants were to respond with only the right hand by pressing the left arrow key with the index finger and the right arrow key with the middle finger. They were also advised to keep their gaze directed at the fixation cross at all times, and to respond as quickly and as accurately as possible to the target stimuli.

Through the use of cues and flankers, the ANT enabled the assessment of each type of attention. As with Eriksen and Eriksen's (1974) flanker task, divided attention could be assessed by comparing the trials with congruent flankers with those that have incongruent flankers; this provided a measure of the ability to ignore

distractors and resolve conflict between competing stimuli (Fan et al., 2002). Selective attention could be assessed from trials with centre cues and trials with spatial cues: both of these cue conditions provided alerting cues for participants to direct their attention towards (Fan et al., 2002). Sustained attention could be assessed from the trials with double cues and those with no cues because these cue conditions kept attention diffused between two possible target locations before the presentation of the target stimuli (Fan et al., 2002).

***Measuring psychomotor speed.*** As designed by Fan et al. (2002), the divided attention reaction time (RT) index was calculated by subtracting the mean RT of all congruent conditions from that of all incongruent conditions. The selective attention RT index was derived by subtracting the mean RT of all spatial cue conditions from that of all centre cue conditions, and the sustained attention RT index was calculated by subtracting the mean RT of all double-cue conditions from that of all no cue conditions. These indices served as measures of psychomotor speed.

***Measuring accuracy for divided, selective, and sustained attention.*** The accuracy indices were calculated in a similar fashion, with the accuracy of responses used in place of RTs. The accuracy percentage was calculated as the percentage of correct responses for a specific condition out of the total number of trials with that condition. The divided attention accuracy index was calculated by subtracting the mean accuracy percentage of all congruent conditions from that of all incongruent conditions. The selective attention RT index was derived by subtracting the mean accuracy percentage of all spatial cue conditions from that of all centre cue conditions. The sustained attention accuracy index was derived by subtracting the mean accuracy percentage of all double-cue conditions from that of all conditions

with no cues. These indices served as measures of accuracy performance for each type of attention.

**Proof of principle: The 2-back task.** As the effectiveness of anodal tDCS applied to the DLPFC on improving working memory has been demonstrated in various studies (e.g., Berryhill & Jones, 2012; Fregni et al., 2005; Zaehle, Sandmann, Thorne, Jäncke & Herrmann, 2011), working memory was also assessed in the current experiment as a proof of principle for the effectiveness of anodal tDCS primed with cathodal tDCS. Assessment was conducted with the 2-back task, which is a form of n-back task. The n-back task is a valid and reliable assessment of working memory (Jacola et al., 2014; Kearney-Ramos et al., 2014). The n-back task is commonly used in tDCS studies to assess working memory (Jantz, Katz & Reuter-Lorenz, 2016), and it was hence used in this experiment to aid in the comparability of results across studies. During the task, a series of letters or images are presented one at time, and test-takers have to respond to any letter or image that has appeared "n" steps before the current letter or image presented (Jacola et al., 2014).

The 2-back task for this experiment consisted of a series of letters presented one letter at a time (refer to Figure 7). Participants were to respond by pressing the spacebar to any letter that was presented two letters before. In the example shown in Figure 7, the correct responses would be to press the spacebar during the presentation of the second "X" and the second "R". Each letter was presented for a maximum of 1.5 seconds during which participants had to decide if a response (pressing the spacebar) was required. Upon response or expiry of the 1.5 seconds of presentation, there was an interval of 0.5 seconds before the next letter was presented. Each 2-back task consisted of two trials with 24 letters presented for each

trial. It took around 2 minutes to complete a 2-back task. To ensure that participants do not

remember or memorise the sequence of letters in each trial, eight different sequences were developed and administered in a counterbalanced fashion.

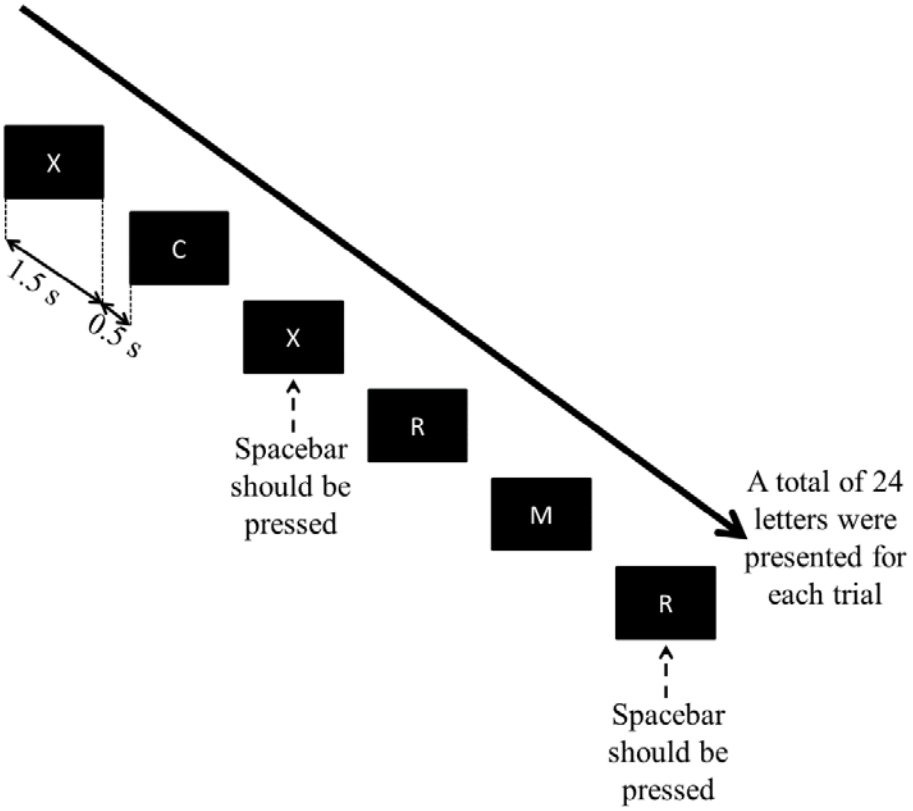


*Figure 7*. The 2-back task. The spacebar should be pressed upon the presentation of a letter that was presented two letters before. In this example, the spacebar should be pressed when the second "X" and the second "R" was presented.

Performance on the 2-back task was assessed through d prime (*d'*) scores, which were calculated as the *z*-scores for the false alarm rates subtracted from the *z*-scores for the hit rates (Macmillan & Creelman, 1991). A hit referred to a correct response: the spacebar was correctly pressed for a letter that had been presented two letters before. A false alarm was committed when the participant incorrectly pressed the spacebar for a letter that was not presented two letters before. The *d'* statistic was used because it provided a more accurate assessment of performance: for example, participants could achieve perfect hit rates just by pressing the space bar

for every single letter that was presented, but this would not take into account the high number of false alarms committed (Swets, Tanner & Birdsall, 1961). By taking into account both the hit rate and the false alarm rate, the *d'* statistic hence provided a more accurate assessment of performance on the 2-back task compared with just using the hit rate as a measure of performance (Swets et al., 1961).

Both the ANT and 2-back task were programmed using PsychoPy (version 1.83.04), and administered through a computer with the monitor elevated to eye-level.

**Control measures.** All participants had to complete a sleep questionnaire (see Appendix F) as used in Vancleef, Meesen, Swinnen and Fujiyama's (in press) study. It asked for the quality and amount of sleep they have had on the night prior to the experimental session. Sleep quality was rated on a scale of one to 10, with one being extremely poor and 10 being extremely well. The questionnaire also asked for the number of units of caffeine and alcohol consumed within the 12 hours prior to the experimental session. The purpose of such information was to assess if performance on the ANT and 2-back could have been influenced by variables other than the tDCS received.

As recommended by Brunoni et al. (2011), participants were asked to report any adverse sensations that they might have experienced during tDCS (refer to Appendix G for the questionnaire used). This also provided an indication of whether the participants were able to discern sham stimulations from anodal stimulations.

**Procedure**

All the experimental sessions were held at a quiet laboratory in Murdoch University. As neuroplasticity has been found to be influenced by circulating cortisol levels which vary according to the time of day (Sale, Ridding & Nordstrom,

2008), the timing of the day during which sessions were conducted were counterbalanced across C-A and C-S conditions. Participants were first briefed on the purpose of the study, potential risks and side-effects, as well as what participation would entail. These details were also included in the information letter (refer to Appendix H) provided to every participant before informed consent was obtained. They were also informed of their right to withdraw from the study at any point. The screening questionnaire was then administered to determine their eligibility before written informed consent was obtained (see Appendix I for the consent form). This was followed by practice sessions for the ANT and 2-back task to ensure that the participants understood the instructions and were familiar with the response formats.

Figure 8 shows the experimental protocol for each session. The ANT and 2-back task were administered before (Pre1) and after (Pre2) the 10-minute priming stimulation over the DLPFC using cathodal tDCS. A 20-minute test stimulation of either sham or anodal tDCS was then administered. Again, it should be noted that a direct current of 1.5 mA was only applied for 30 seconds for sham tDCS, and for the entire 20 minutes for anodal tDCS. The current strength and stimulation durations followed the parameters used in Fujiyama et al.'s (in press) study as the effectiveness of the test protocol was demonstrated based on these parameters.

Participants performed the ANT and 2-back task at three more times: immediately (Post0), 30 minutes (Post30), and 1 hour (Post60) after the cessation of the 20-minute test stimulation. The administration of the ANT and 2-back task was counterbalanced both within and between participants to prevent order effects. Assessment was conducted at several time points as the effects of anodal tDCS have been found to manifest over a longer time period for older individuals compared

with younger adults: in Fujiyama et al.'s (2014) study, older participants exhibited significant increases in corticospinal excitability only after 30 minutes post-

stimulation while younger participants exhibited significant potentiation immediately post-stimulation. Conducting assessments at various time points thus ensured that the effects of tDCS on the current sample of older adults do not go undetected.

The Edinburgh Inventory, sleep questionnaire, and tDCS questionnaire were completed in the interval between Post0 and Post30, and the MoCA was administered in the interval between Post30 and Post60.

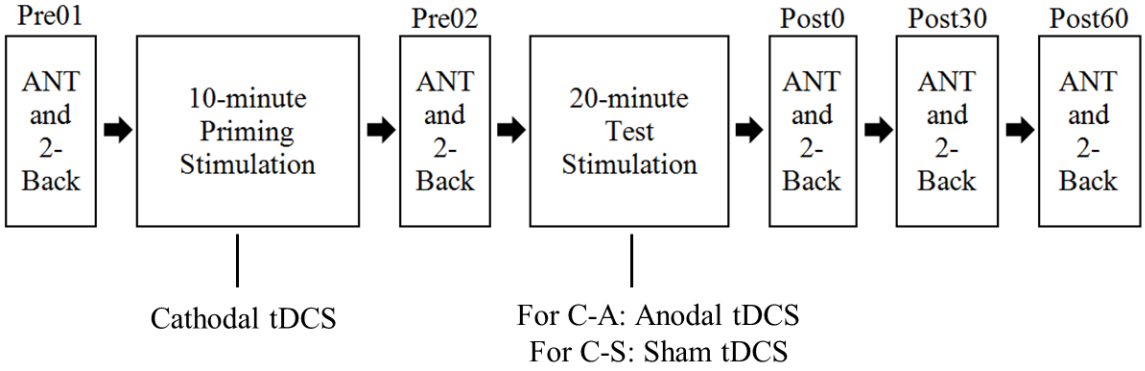


*Figure 8*. The experimental protocol. A 10-minute priming stimulation with cathodal tDCS was applied for both C-A and C-S conditions. For the C-A condition, participants underwent a 20-minute test stimulation with anodal tDCS. For the C-S condition, sham tDCS was applied for the test stimulation instead.

As most of the studies (e.g., Fregni et al., 2005; Gladwin et al., 2012; Nilsson, Lebedev & Lövdén, 2015; Zaehle et al., 2011) that have been conducted to examine the effects of anodal tDCS on DLPFC have focused on the left DLPFC, the current experiment has focused on the left DLPFC as well to aid in the comparability of research results across studies.

The left DLPFC is thought to be located on the F3 position on the International 10-20 system used for the standardised placement of electroencephalogram electrodes (Herwig, Satrapi & Schönfeldt-Lecuona, 2003). The F3 position for each participant was determined using the Beam F3 system, which only required three head measurements for the location of F3 (as shown in Figure 9; Beam, Borckardt, Reeves & George, 2009). The Beam F3 system has been found to be acceptably accurate in locating the left DLPFC when compared with neuroimaging techniques such as magnetic resonance imaging (Halper, Yagi, Manevitz, Nishimoto & Onishi, 2016; Mir-Moghtadaei et al., 2015).

*Figure 9.* Using the Beam F3 system, the location of the left DLPFC can be located using three head measurements. From left to right: the distance from tragus to tragus, the distance from nasion to inion, and head circumference (image adapted from Beam et al., 2009).

As shown in Figure 10, the cathode was placed over the left DLPFC and the anode was placed over the right (contralateral) supraorbital region for cathodal tDCS. The placement of the electrodes was reversed for sham and anodal tDCS (refer to Figure 10), with the anode placed over the left DLPFC and the cathode over the right supraorbital region. The supraorbital region is located above the eye socket, and is a common reference site in many tDCS studies targeting the DLPFC (Hsu et al., 2015).

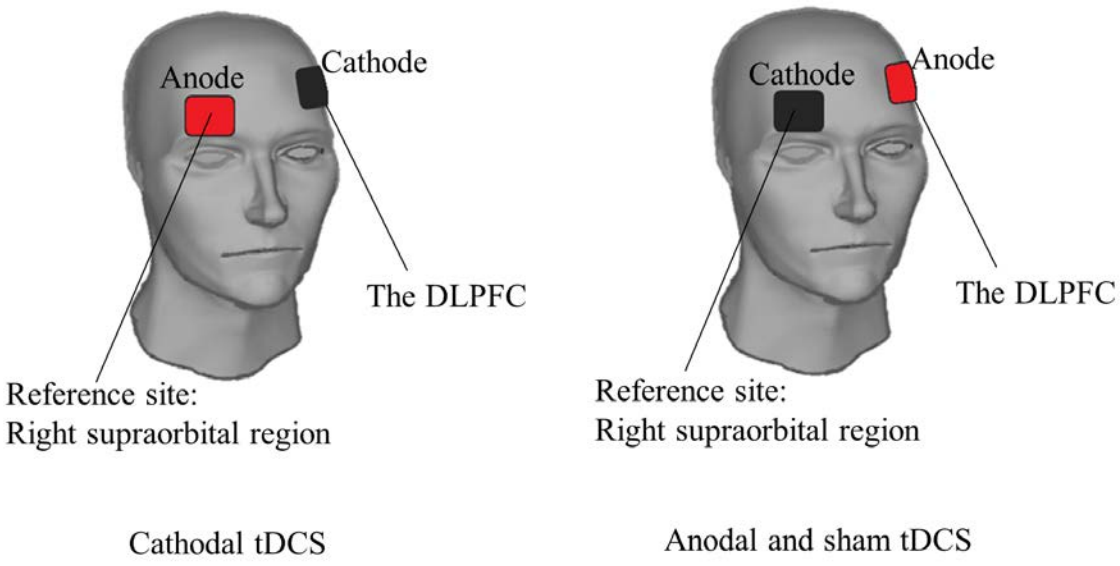


*Figure 10*. For cathodal tDCS, the cathode (black electrode) was placed over the left DLPFC and the anode (red electrode) over the right supraorbital region. The electrode placement is reversed for anodal and sham tDCS.

To ensure no carryover effects, particularly with regards to any lingering effects as a result of tDCS, the sessions for each participant were spaced at least a week apart (Nitsche et al, 2008). To minimise order effects, the administration of sham and anodal stimulation (i.e., whether a participant underwent the C-A or C-S condition for his or her first session) was counterbalanced across participants.

**Design and Analysis**

A 2 x 3 repeated-measures design was employed for each dependent variable. The two within-subject independent variables are stimulation condition (C-A and C-S) and time (Post0, Post30, and Post60). The data at each time point were normalised to Pre2 data (i.e., expressed as a ratio of Pre2 data) to provide a more accurate depiction of the changes in performance that have resulted from the application of the test stimulation (anodal or sham tDCS). This allowed the comparison of the effects of anodal tDCS with that of sham tDCS on the DLPFC, with both anodal and sham stimulations having been primed by cathodal tDCS.

Furthermore, normalisation also ensured that the data were not biased by differences in baseline performance before the application of sham or anodal tDCS (Hinder, Fujiyama & Summers, 2012). Normalised values exceeding 1 indicated improvements in performance relative to Pre2 levels (i.e., after the cathodal priming protocol), while values lower than 1 indicated decreases in performance levels that have occurred after the priming protocol.

The dependent variables were the accuracy and RT indices for the ANT, and *d'* scores on the 2-back task. Arcsine-root transformations were applied to the ANT accuracy data as they were calculated with accuracy percentages, and were hence proportions (Howell, 2009).

The data were analysed with repeated-measures factorial ANOVAs. The assumption of normality was assessed with the Shapiro-Wilk's test, as well as skewness and kurtosis of the data. Mauchly's test was used to test the assumption of sphericity. In cases when the assumption of sphericity was violated, degrees of freedom were adjusted using the Huynh-Feldt Epsilon. Where appropriate, significant main effects and interactions were further explored with simple effects analyses applying Bonferroni corrections. Partial eta-squared (partial $\eta^2$) values were provided as measures of effect sizes, with values of .01, .06, and .14 constituting small, medium, and large effects respectively (Cohen, 1988).

**The effect of priming cathodal tDCS on the dependent variables.** To investigate the effect of the cathodal priming stimulation, 2 x 2 (Stimulation [C-A, C-S] x Time [Pre1, Pre2]) repeated-measures factorial ANOVAs using non-normalised scores were conducted to compare the scores at Pre1 and Pre2 for each dependent variable.

**Analysis of control measures.** Paired-samples *t* tests were conducted to assess if the stimulation groups differed significantly on any of the control measures. Cohen's *d* was used to index effect sizes, with values of 0.20, 0.50, and 0.80 constituting small, medium, and large effects respectively (Cohen, 1988).

All data analyses were conducted using the Statistical Package for the Social Sciences (version 21), and significance was based on an alpha level of .05.

## Results

All analyses began with an examination of the data to ensure that the relevant underlying assumptions such as normality and sphericity were met.

### Control Measures

Table 2 shows the means and standard deviations for the units of caffeinated drinks consumed, sleep quality, sensations from tDCS, number of hours slept, and units of alcohol consumed.

Table 2

*Scores for Control Measures*

| | C-A | | C-S | |
|---|---|---|---|---|
| | *M* | *SD* | *M* | *SD* |
| Units of caffeinated drinks consumed | 1.80 | 1.14 | 2.40 | 1.65 |
| Sleep quality | 7.00 | 1.25 | 7.00 | 1.76 |
| Adverse sensations from tDCS | 2.45 | 1.17 | 2.70 | 1.25 |
| Number of hours slept | 6.50 | 1.25 | 6.50 | 1.08 |
| Units of alcohol consumed | 0.45 | 1.26 | 0.40 | 0.52 |

Data for the units of caffeinated drinks consumed, sleep quality, and sensations from tDCS were analysed using paired-sample *t* tests. There were no significant differences between the C-A and C-S sessions in terms of: (a) the units of caffeinated drinks consumed, $t(9) = 1.15$, $p = .279$, $d = 0.43$, 95% CI [-1.78, 0.58]; (b) sleep quality, $t(9) = 0.00$, $p = 1.000$, $d = 0.00$, 95% CI [-1.22, 1.22]; and (c) sensations from tDCS, $t(9) = 1.10$, $p = .299$, $d = 0.21$, 95% CI [-0.76, 0.26].

As the data for the number of hours slept and units of alcohol consumed were not normally distributed, Wilcoxon signed rank tests were conducted to examine these outcomes. C-A and C-S conditions did not differ significantly based on (a) the number of hours slept, $T = 9.5$, $z = -.211$ (corrected for ties), $N$ – Ties = 6, $p = .833$, two-tailed, $r = .09$; and (b) the units of alcohol consumed, $T = 6$, $z = -.368$ (corrected for ties), $N$ – Ties = 4, $p = .713$, two-tailed, $r = .26$.

Importantly, these results suggested that any differences in the dependent variables between C-A and C-S cannot be attributable to the above factors.

**The Effect of Priming Cathodal tDCS on the Dependent Variables**

To determine if the priming cathodal tDCS had any effect on the dependent variables, non-normalised data for each variable at Pre1 and Pre2 were analysed with 2 x 2 (Stimulation [C-A, C-S] x Time [Pre1, Pre2]) repeated-measures ANOVAs . The ANOVAs found no significant main effects and interaction effects for accuracy and RT indices for sustained, selective, and divided attention, $F$s < 4.57, $p$s > .061, partial $\eta^2$s < .34. No significant main effects and interactions were found for working memory as well, $F$s < 4.28, $p$s > .068, partial $\eta^2$s < .32.

The non-normalised scores for the dependent variables at Pre1 and Pre2 are presented in Table J1, and the ANOVA results in Table J2 (both tables are in Appendix J).

**Primary Outcomes**

Psychomotor performance was assessed using the accuracy and response times for sustained, selective, and divided attention on the ANT. As many of the variables deviated from a normal distribution, log transformation was applied to the data. For clarity, non-transformed data are reported in the tables and figures. The means and standard deviations of the scores at Post0, Post30, and Post60 for accuracy and RT indices for the ANT are presented in Table K1 in Appendix K.

The normalised (to Pre2 data) accuracy and RT indices were analysed with 2 x 3 (Stimulation [C-A, C-S] x Time [Post0, Post30, Post60]) repeated-measures ANOVAs.

**Accuracy indices.**

***Divided attention accuracy indices.*** There was a significant interaction between stimulation and time, $F$ (2, 18) = 6.41, $p$ = .008, with a large effect size of partial $\eta^2$ = .42. This interaction can be seen in Figure 11.

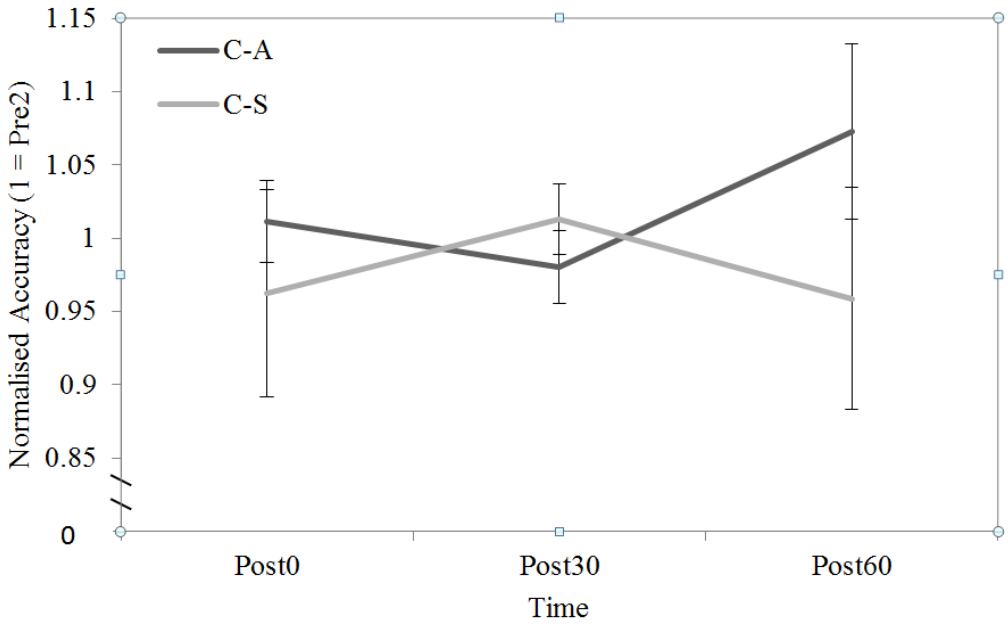


*Figure 11*. A line graph showing the significant interaction between stimulation (C-A, C-S) and time (Post0, Post30, Post60) for the accuracy indices for divided attention. Error bars indicate 95% CIs.

Simple effects analyses were conducted to examine the interaction. At Post60, accuracy for divided attention was significantly larger for C-A compared with C-S, $p$ = .014, with a large effect size of $d$ = 1.21, 95% CI [0.001, 0.01]. There were no significant differences in accuracy performance between C-A and C-S at Post0 and Post30, $p$ = .205, $d$ = 0.36, 95% CI [-0.001, 0.01], and $p$ = .112, $d$ = 0.95, 95% CI [0.00, 0.003], respectively. For the C-A condition, there were no significant changes in divided attention accuracy from Post0 to Post30, $p$ = .111, $d$ = 0.84, 95% CI [0.001, 0.003], with a significant increase from Post30 to Post60, $p$ = .017, with a large effect size of $d$ = 1.56, 95% CI [0.001, 0.01]. Divided attention accuracy for the C-A condition was also significantly higher at Post60 when compared with Post0, $p$ = .038, with a large effect size of $d$ = 1.00, 95% CI [0.00, 0.01]. There were no significant differences between all three points for the C-S condition: from Post0 to Post30, $p$ = .606, $d$ = 0.77, 95% CI [-0.002, 0.01], from Post30 to Post60, $p$ = .433, $d$ = 0.78, 95% CI [-0.002, 0.01], and from Post0 to Post60, $p$ = 1.000, $d$ = 0.03, 95% CI [-0.004, 0.01].

There was no significant main effect for stimulation, $F$ (1, 9) = 4.19, $p$ = .071, partial $\eta^2$ = .32. The main effect for time was not significant as well, $F$ (2, 18) = 0.93, $p$ = .421, partial $\eta^2$ = .09 respectively.

***Sustained attention accuracy indices.*** The interaction between stimulation and time was not significant for accuracy for sustained attention, $F$ (1.13, 10.14) = 1.07, $p$ = .335, partial $\eta^2$ = .11. There were also no significant main effects for stimulation, $F$ (1, 9) = 3.76, $p$ = .084, partial $\eta^2$ = .30, and for time, $F$ (1.07, 9.66) = 0.07, $p$ = .818, partial $\eta^2$ = .01.

***Selective attention accuracy indices.*** No significant interaction between stimulation and time was found for accuracy for selective attention, $F$ (1.36, 12.25) =

0.14, $p$ = .788, partial $\eta^2$ = .02. There were no significant main effects for stimulation, $F$ (1, 9) = 0.80, $p$ = .396, partial $\eta^2$ = .08, and for time, $F$ (1.20, 10.81) = 0.42, $p$ = .569, partial $\eta^2$ = .04.

**Reaction time (RT) indices.**

***Divided attention RT indices.*** There was no significant interaction between stimulation and time for divided attention RT, $F$ (1.07, 9.63) = 0.65, $p$ = .451, partial $\eta^2$ = .07. There were no significant main effects for stimulation, $F$ (1, 9) = 0.29, $p$ = .604, partial $\eta^2$ = .03, and for time, $F$ (1.10, 9.86) = 1.92, $p$ = .197, partial $\eta^2$ = .18.

***Sustained attention RT indices.*** Interaction between stimulation and time was not significant for sustained attention RT, $F$ (2, 18) = 1.45, $p$ = .260, partial $\eta^2$ = .14. There were no significant main effects for stimulation, $F$ (1, 9) = 0.10, $p$ = .756, partial $\eta^2$ = .01, and for time, $F$ (2, 18) = 0.88, $p$ = .434, partial $\eta^2$ = .09.

***Selective attention RT indices.*** No significant interaction was found between stimulation and time for selective attention RT, $F$ (1.03, 8.22) = 0.88, $p$ = .378, partial $\eta^2$ = .10. The main effect for stimulation was not significant, $F$ (1, 9) = 0.46, $p$ = .515, partial $\eta^2$ = .06. The main effect for time was not significant as well, $F$ (1.03, 8.21) = 0.92, $p$ = .367, partial $\eta^2$ = .10.

**Proof of Principle: 2-Back Task**

Performance on the 2-back task was assessed to establish a proof of principle. Log-transformation was applied as the data deviated from a normal distribution. A 2 x 3 (Stimulation [C-A, C-S] x Time [Post0, Post30, Post60]) repeated-measures ANOVA with normalised (to Pre2 data) *d'* scores found no significant interaction between stimulation and time, $F$ (1.07, 9.58) = 3.08, $p$ = .110, partial $\eta^2$ = .26. There were no significant main effects for stimulation, $F$ (1, 9) = 0.15, $p$ = .705, partial $\eta^2$

= .02, and for time, $F$ (2, 18) = 0.39, $p$ = .685, partial $\eta^2$ = .04. Table K1 in Appendix K presents the means and standard deviations of the *d'* scores.

## Discussion

It was hypothesised that when compared with sham tDCS, anodal tDCS to the DLPFC after it was primed by cathodal tDCS would improve the psychomotor function of older adults. Hence primed anodal stimulation was hypothesised to result in significantly higher accuracy and faster RT for the ANT for all three types of attention when compared with primed sham stimulation. Working memory was also assessed as a proof of principle for the effectiveness of primed anodal stimulation.

The results of the current experiment provided support for the hypothesised improvement in accuracy for divided attention. Accuracy indices for divided attention increased significantly between Post30 and Post60 when primed anodal tDCS was administered. By contrast, there were no significant changes in divided attention accuracy when primed sham tDCS was applied. Compared with primed sham stimulation, primed anodal tDCS resulted in significantly higher divided attention accuracy indices at 60 minutes post stimulation. Importantly, as there were no significant differences in RTs for divided attention, the improved accuracy associated with primed anodal tDCS was not because more time was spent on responses (Forstmann et al., 2011). This indicated that the ability to shift attention between conflicting stimuli for older individuals could be improved by applying anodal tDCS over the left DLPFC after a priming stimulation using cathodal tDCS. Deterioration in divided attention is associated with an increased risk of falls for older individuals (Chu, Tang, Peng & Chen, 2013), and the tDCS protocol therefore shows promise in boosting the safety and well-being of older adults.

There were no significant improvements in selective attention, sustained attention, psychomotor speed, and working memory, indicating that primed anodal tDCS of the DLPFC was not effective in improving these functions when compared with sham. As there were no significant differences in the sensations experienced by participants for the C-A and C-S sessions, the findings were unlikely to have been confounded by ineffective blinding. Both C-A and C-S conditions did not differ significantly with regards to the amount of alcohol and caffeinated drinks consumed, number of hours slept, and quality of sleep; it was thus improbable that the results were confounded by these factors. The absence of significant changes from Pre1 to Pre2 also indicated that the priming protocol using cathodal tDCS did not have an overt effect on the performance of participants before the administration of anodal or sham tDCS.

**Delayed Improvement in Divided Attention Accuracy**

It was notable that the significant improvements in divided attention accuracy only occurred after 30 minutes post anodal stimulation. This highlights the importance of assessing tDCS effects at several time points after stimulation, and not just immediately post stimulation. The improvement in performance would have been missed had the current experiment not conducted assessments up to 60 minutes after anodal stimulation.

It has been posited that the delayed response to tDCS exhibited by older adults could be due to age-related degradation in glial cells (Fujiyama et al., 2014). Glial cells are non-neuronal cells that interact with neurons to enable proper nervous system functioning (Barres, 2003). Astrocytes, a particular type of glial cells, regulate transmission among synapses, and are essential for synaptic plasticity (Ota, Zanetti & Hallock, 2013). A recent study found that tDCS-induced surges in

astrocytes play an important role in synaptic responses to tDCS (Monai et al., 2016). It is thus speculated that the degradation of glial cells as a result of ageing (Yu et al., 2002) might thus play a role in delaying the responses of older individuals to tDCS.

**The Limitations of Current tDCS Meta-Analyses**

Given that previous meta-analyses (e.g., Hsu et al., 2015; Summers et al., 2016) have found that the application of anodal tDCS to the DLPFC is effective in improving cognitive and motor functions, the lack of significant findings in most of the outcome measures for the current experiment, in particular for the 2-back task, was surprising. A possible explanation is that no thorough review of the effectiveness of tDCS with respect to any particular function or tDCS montage can yet be undertaken due to the relative shortage of research studies that have been conducted thus far. For example, Summers et al.'s (2016) meta-analysis of the efficacy of tDCS for older adults categorised cognitive functions into three broad categories, one of which is memory/working memory. Even after grouping working memory along with recall, visual memory, and long-term memory, this category only contains eight studies, four of which focused on working memory. Among the four, two studies included cognitive training along with tDCS, making it difficult to isolate the effects of tDCS from the effects of cognitive training on working memory. This left only two studies that explored the sole effects of anodal tDCS on the DLPFC. Even then, these two studies (Berryhill & Jones, 2012; Seo, Park, Seo, Kim & Ko, 2011) differed in terms of the current strength, electrode size used, reference site for cathode placement, and stimulation duration. Hence, despite Summers et al.'s conclusion that tDCS was effective in alleviating age-related declines in cognitive and motor functions, it is difficult to arrive at the same

conclusion if one wishes to examine that efficacy with regards to a specific cognitive function based

on a very small number of studies that might not be directly comparable due to differences in tDCS montage and protocol. Indeed, a very recent meta-analysis that specifically focused on the effects on working memory as a result of tDCS have concluded that current research findings are mixed with regards to tDCS's ability to improve working memory (Jantz et al., 2016).

**Generalising the Findings from Studies involving Younger Individuals**

It is also noted that much of the research involving tDCS has been done on samples of young and healthy individuals (Perceval, Flöel & Meinzer, 2016), hence raising the possibility that the effectiveness of tDCS as demonstrated in younger samples is less applicable for older individuals. For instance, the secretion of brain-derived neurotrophic factor (BDNF), a protein that helps to regulate synaptic plasticity (Genetics Home Reference, n.d.), has been shown to play an important role in tDCS effects (Chaieb, Antal, Ambrus & Paulus, 2014). BDNF levels have been found to significantly decrease with age (Lommatzsch et al., 2005). Furthermore, ageing is also associated with reductions in the connectivity of neural functional networks (Sala-Llonch et al., 2014), which can affect the effectiveness of tDCS (Summers et al., 2016). Such age-related neurophysiological changes might explain why there was no significant improvement in working memory for the current study when previous studies involving younger samples have found that anodal tDCS is effective in improving working memory (e.g., Fregni et al., 2005; Zaehle et al., 2011).

**The Cathodal Priming Procedure**

It is also possible that the cathodal tDCS priming procedure is not effective when applied to the DLPFC. The effectiveness of the priming procedure was demonstrated by Fujiyama et al. (in press) on the M1, and it has been suggested that the effects of tDCS on motor regions such as the M1 differ from that of non-motor regions such as the DLPFC (Jacobson, Koslowsky & Lavidor, 2012). The inhibitory effects of cathodal tDCS and the excitatory effects of anodal tDCS are largely based on the findings of early tDCS studies focusing on motor regions (Jacobson et al., 2012). While anodal tDCS of the DLPFC was generally associated with excitatory effects in terms of improved cognitive performance, Dedoncker, Brunoni, Baeken and Vanderhasselt's (2016) meta-analysis found that cathodal tDCS of the DLPFC tend to result in no significant changes in performance when compared with sham, rather than the expected inhibitory effect (poorer performance). It is thus uncertain if the deregulatory effect of cathodal tDCS on motor regions is also applicable to non-motor areas such as the DLPFC.

This has important implications for the effectiveness of the cathodal tDCS priming protocol that was used in the current study. If cathodal stimulation does not serve to downregulate post-synaptic activity in the DLPFC to favour the induction of subsequent LTP-like activity, then inter-variability of responses to the subsequent anodal tDCS would not have been reduced. The lack of significant improvements as a result of anodal stimulation might therefore have been due to high inter-variability in tDCS responses. The presence of high inter-variability might have also prevented divided attention from an even larger improvement resulting from anodal tDCS.

**Other Factors influencing Inter-Individual Differences**

Even if the priming procedure was effective in downregulating post-synaptic activity and lowering the synaptic modification threshold for subsequent

potentiation, it is acknowledged that inter-individual variability in tDCS responses can also result from other sources. For instance, differences in genetic variations (polymorphisms) at the BDNF gene have been shown to affect the responses of individuals to tDCS

(Puri et al., 2015). The level of regular exercise and activity can also lead to changes in cortical plasticity, hence influencing tDCS responses (Ridding & Ziemann, 2010). In addition, anatomical differences in terms of skull thickness, shape of brain, and cortical folding have been found to affect tDCS outcomes through differences in conduction current density values at the DLPFC (Kim et al., 2014).

**Different Cognitive Tests Used Across Studies**

Responses to tDCS can differ for different cognitive tests, even if these tests purportedly measure the same cognitive function (Zmigrod, Zmigrod & Hommel, 2016). This is possibly because different cognitive tests are likely to require different cognitive abilities, which would possibly require the activation of different neural networks. For example, although the Eriksen flanker task and the Simon task are both measures of conflict resolution, the former reflects both stimulus conflict and response conflict (Wendt, Heldmann, Münte & Kluwe, 2007), while the Simon task only relies on response conflict (Hommel, 2011). It is hence probable that different neural networks are activated during the performance of these tasks, even though they are purported to measure the same cognitive ability (Zmigrod et al., 2016). Such differences in neural activation can affect responses to tDCS, particularly if there are changes in activation to the region that is being stimulated (Zmigrod et al., 2016).

This might explain why the current experiment found no significant improvements in selective and sustained attention as a result of anodal tDCS, which

is contrary to the findings of Gladwin et al.'s (2012) study on selective attention and McIntire et al.'s (2014) study on sustained attention. While the ANT was used in the current study as measures of both selective and sustained attention, Gladwin et al. employed the Sternberg task to assess selective attention and McIntire et al. used the Mackworth clock test to measure sustained attention.

**The Relative Roles of Motor and Cognitive Processing in Psychomotor Speed**

The lack of significant changes in response speeds on the ANT could be due to the lack of improvements in cognitive processing speed. An alternative explanation is that motor processing simply plays a larger role than cognitive processing in psychomotor speed: hence there might have been an improvement in cognitive processing speed, but this was not translated into significantly faster psychomotor responses because motor processes have a greater influence over psychomotor speed.

If the latter explanation is true, then significant improvements in psychomotor speed might have resulted if anodal tDCS was administered to the motor cortex instead of the DLPFC. Indeed, Yordanova, Kolev, Hohnsbein and Falkenstein (2004) found that age-related psychomotor slowing was associated with a functional dysregulation of the motor cortex. Hence, even though the DLPFC was shown to be implicated in psychomotor functioning (Heuninckx et al., 2005), its role might not be as significant as that of motor regions with regards to response speed.

**Limitations of the Current Study**

It was likely that the current findings were affected by the small sample size used. For example, the main effects of stimulation for divided and sustained attention accuracy were found to approach significance ($p = .071$ and $p = .084$, respectively) with large effect sizes (partial $\eta^2 = .32$ and partial $\eta^2 = .30$, respectively), thus suggesting that the study was underpowered (Trout, Kaufmann &

Kallmes, 2007). Recruitment of participants was hampered by time constraints that were further exacerbated by the fact that each session required at least 2.5 hours to conduct. It was also difficult to find individuals from the wider community who were willing to participate and who also met the eligibility criteria.

The lack of a control group with young and healthy adults meant that the current findings cannot be interpreted as being unique to older individuals. However, due to the aforementioned time constraints, this study adopted an approach similar to that of Puri et al. (2015) and Puri, Hinder, Canty and Summers (2016), with the recruitment of only older adults.

**Future Perspectives**

In view of the significant improvement in divided attention accuracy that resulted from primed anodal tDCS, a replication of the current study should be conducted with a larger sample of participants. If proven to be efficacious in improving divided attention in healthy older adults, future research can explore its efficacy in clinical populations such as individuals with dementia.

Given that the performance for divided attention accuracy was the highest at the last assessment (60 minutes after the administration of anodal tDCS), it is unknown if the peak in performance has been reached, or if performance continued improving after the last assessment. Future studies are warranted to assess the performance for these cognitive functions at even longer periods after stimulation.

As the effectiveness of the cathodal priming procedure in alleviating inter-individual variability in tDCS responses was demonstrated over the M1 region in Fujiyama et al.'s (in press) study, future research should explore if this effectiveness is similarly applicable to non-motor regions such as the DLPFC. Further research is also required to verify the effects of cathodal tDCS on non-motor regions; the

physiological effects of cathodal tDCS can be monitored through techniques such as near-infrared spectroscopy (fNIRS) or functional magnetic resonance imaging (fMRI;
Nitsche & Paulus, 2011) to ascertain if the inhibitory effects of cathodal tDCS on motor regions are applicable to non-motor regions.

As also recommended by Jantz et al. (2016), more replication studies should be conducted in order for the efficacy of tDCS to be properly evaluated. The paucity of available research—particularly with regards to attention and age-related psychomotor slowing—currently prevents an informed evaluation of tDCS's effectiveness. As different cognitive tests can lead to differences in tDCS outcomes, there should also be more standardisation in terms of the tests used to assess cognitive functions; this allows findings across studies to be more comparable.

**Conclusion**

More research is clearly required to further explore the effects of anodal tDCS that has been primed with cathodal tDCS. For instance, future studies should investigate the effectiveness of the cathodal priming procedure in alleviating inter-individual variability in responses to tDCS when applied over non-motor cortical regions, such as the DLPFC. However, given that this study found the application of primed anodal tDCS over the left DLPFC to significantly improve the ability of older adults to task-shift and resolve conflict between multiple stimuli, primed anodal tDCS shows some promise as a potential clinical intervention for alleviating age-related declines in psychomotor performance.

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