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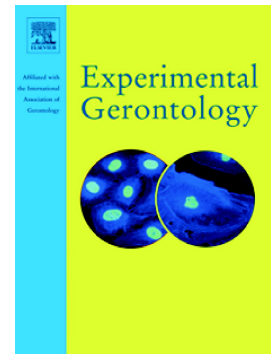
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Anodal tDCS improves attentional control in older adults.

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Abstract

Transcranial direct current stimulation (tDCS) facilitates cognitive enhancement by directly increasing neuroplasticity, and has shown promising results as an external intervention to attenuate age-related cognitive decline. However, stimulation protocols have failed to account for age-associated changes in brain structure and the present literature omits investigation of attentional control, despite the occurrence of substantial inhibitory processing deficits with age. To provide new insight into the benefits of tDCS, the objective of this study was to develop an age-optimised stimulation protocol in which key parameters (amplitude, duration, and electrode configuration) were selected in accordance with knowledge of stimulation effects, specific to the ageing brain. Participants (mean age 66.5 years) completed three sessions of double-blind, anodal or sham stimulation, in conjunction with a novel task switching paradigm, which was designed to reflect the complexities of simultaneously monitoring and updating stimulus representations. The results show that those who had anodal tDCS exhibited an acute, post-stimulation increase in task switching speed ($p < .01$, $d = 1.36$). Although the sham group were subject to the same task exposure, only the anodal stimulation group experienced a performance gain, thus emphasising the efficacy of active brain stimulation. For the first time, this study demonstrates the utility of stimulation protocols tailored specifically for use with older adults, targeted towards the modulation of attentional control. This

finding has critical implications for cognitive health and encourages the use of age-optimised tDCS as a viable method for enhancing executive function in later life.

Key words: healthy aging; neural plasticity; attentional control; task switching; transcranial direct current stimulation.

1. Introduction

Ageing is a complex process characterised by structural and functional changes in the brain, as well as associated declines in cognitive performance (Anderson et al., 1998; Gazzaley et al., 2008; Drag and Bieliauskas, 2010; Zanto et al., 2010; Erel and Levy, 2016). Considerable atrophy occurs as part of normal ageing (Raz et al., 2005) and this is accompanied by loss of excitatory and inhibitory neurochemicals that govern plasticity (Gao et al., 2013). Loss of structural integrity is particularly pronounced in anterior regions, such as dorsolateral prefrontal cortex (dlPFC), which exerts top-down control over attentional processes in a goal-oriented manner (Sylvester et al., 2003; Cieslik et al., 2015). However, to attempt to recruit sufficient resources to sustain such cognitive processes, the ageing brain adapts to these changes by undergoing substantial functional reorganisation (Reuter-Lorenz and Cappell, 2008). One empirical model proposes that this process fulfils a neuroprotective role thus preventing severe decline in cognition (Cabeza, 2002), whilst another account states that functional plasticity reflects the formation of alternative goal-oriented neural circuits (Reuter-Lorenz and Park, 2014). Such functional alterations are suggested to bolster existing task-relevant connections and compensate for losses in grey and white matter, corroborated by a recent approach designed to integrate structural and functional brain change (Marstaller et al., 2015).

In the absence of such compensation or where these mechanisms fail to provide adequate support, older adults show a marked decline in executive function (e.g. working memory, attentional control, task switching; Cabeza et al., 2002; Cabeza et al., 2004; Cappell et al., 2010; Hedden et al., 2011; Cona et al., 2013). Such cognitive deficits impact upon how an individual interacts with the environment and, as such, the efficiency of neural mechanisms supporting cognition is essential to life

satisfaction and adequate daily functioning (Wilkins et al., 2010). It is clear, therefore, that a gradual shift towards adaptive connectivity is advantageous in maintaining cognition, and also general well-being, throughout old age. This is an extremely pertinent issue given the projected growth of the ageing population and prevalence of cognitive impairment.

Accordingly, the success of interventions to prevent cognitive decline is likely to be highly dependent on their ability to aid adaptive neuroplasticity, by maintaining existing brain function and ensuring compensatory mechanisms are not over-recruited too early on. Current treatment options for cognitive impairment are largely ineffective at preventing further progression (Casey et al., 2010; Cotelli et al., 2012). Therefore, new methods are needed to support brain function prior to the onset of clinically observable decline. Such neuroenhancement has been made possible by the development of techniques that aid cognition by directly influencing the way the brain functions (Clark and Parasuraman, 2014). One such non-invasive brain stimulation method, transcranial direct current stimulation (tDCS), acts by modifying the action of glutamate and gamma-aminobutyric acid (GABA) receptors to alter plasticity (Bikson et al., 2004; Stagg and Nitsche, 2011; Rahman et al., 2013) and strengthen connections within specific functional networks (Polanía et al., 2011; Keeser et al., 2011; Hunter et al., 2015).

With advancing age, the presence of cells expressing the glutamic acid decarboxylase (GAD) enzyme, responsible for synthesising GABA from glutamate, is reduced in prefrontal cortex. The number of inhibitory interneurons and excitatory pyramidal cells, which alter the efficiency of neurochemical signalling, are also reduced (McQuail et al., 2015). This limits the potential for learning and cognitive flexibility as those with less frontal GABA have been shown to perform poorly on cognitive tasks (Porges et al., 2017). By selectively modulating prefrontal neurochemistry to regulate network activity and achieve the necessary balance of excitation and inhibition within each hemisphere, cognition may be improved in older adults. Consequently, the correspondence of neurochemical change as part of the ageing process, and the mechanisms underlying the neuromodulation technique, provide a highly compelling rationale for the use of tDCS to aid cognition in older adults.

The limited literature to date shows that tDCS is an effective tool for improving age-related cognitive deficits (Hsu et al., 2015). These studies utilise anodal tDCS, which has been shown to improve performance via depolarisation of resting membrane potential (Stagg and Nitsche, 2011). In turn, accompanying increases in glutamatergic transmission via N-methyl-D-aspartate (NMDA) receptors and decreases in GABA_A-mediated responses are generated under the anode (with the opposite expected under the cathode), which modulate plasticity and potential for learning (Liebetanz et al., 2002; Nitsche et al., 2003, 2004). However, previous work has largely been confined to aspects of memory (Berryhill and Jones, 2012; Park et al., 2014). Research relating to aspects of cognitive control with regard to attention and response inhibition is notably absent, with a recent meta-analysis (Summers et al., 2016) citing only 2 applicable studies that present a huge discrepancy in the ability of tDCS to improve executive function. Accordingly, Boggio et al. (2010) demonstrate that participants' ability to successfully complete a task designed to measure risk-taking behaviour declined following stimulation. While Harty et al. (2014) document the induction of a moderate enhancement in participants' awareness of incorrect responses during an error detection paradigm, thus highlighting the necessity for research in this field. Given the role of attentional control in our everyday lives and how it declines significantly with age (Campbell et al., 2012; Li et al., 2013), it is surprising that this domain has been overlooked.

Equally surprising is the lack of commentary on stimulation parameters in relation to their suitability for use with older participants. While the number of studies concerning older adults has risen in recent years, what we know of non-invasive brain stimulation is largely founded upon studies of young adults. Considering the ageing process from a neural perspective, advancing age is likely to have a profound result on the effects of stimulation (Laakso et al., 2015). The abundance of cerebrospinal fluid (CSF) in the ageing brain has been proposed to alter the resulting current distribution (Mahdavi and Towhidkhan, 2018), and such computational modelling work suggests that stimulation parameters need to be carefully considered to ensure effects are likely to emerge. Consequently, protocols used in conjunction with the ageing population are likely to benefit from attempts to make stimulation more focal, longer, and more intense than it typically is in studies of

young adults (e.g. 1 mA) (Lindenberg et al., 2013; Tatti et al., 2016). Choices related to individual parameters will, therefore, inherently influence the biological plausibility of associated research and potentially limit the validity of subsequent inferences (Bestmann et al., 2015).

To determine the potential for tDCS to aid adaptive neuroplasticity, the present research represents the first known attempt to enhance attentional control via a stimulation protocol tailored for use with older adults. Using a novel task switching paradigm, participants speed and accuracy was assessed following three applications of anodal or sham stimulation, which was administered via a bihemispheric electrode configuration (designed to regulate prefrontal recruitment demands via network-wide changes in the balance of excitation and inhibition). It was anticipated that anodal stimulation, in comparison to sham, would produce better performance on both measures.

2. Materials and methods

2.1. Subjects

24 subjects with corrected-to-normal vision were recruited to take part in the study, based on sample sizes cited in the corresponding literature (Summers et al., 2016). On entering the study, participants were assigned to one of two stimulation groups (anodal, sham) using a randomly generated sequence of the two possible outcomes. Subjects were allocated to the next available classification upon recruitment and received either anodal or sham stimulation for the duration of the three sessions. Participants were 54-75 years of age ($M=66.46$, $SD=5.34$; 16 female), representing an age range at the transition from middle age to older adulthood where interventions are well-placed to attenuate the progression of sub-clinical deficits. Upon expressing an interest in taking part in the study, subjects were screened to determine their eligibility to take part in tDCS research. Those with any contraindications were excluded from the study. Contraindications included history of neurological (e.g. seizures, stroke) and/or psychiatric conditions (e.g. anxiety, depression), head trauma/concussion, and certain surgical implants (e.g. neurostimulator, pacemaker, cochlear implant). Individuals were also excluded who had been prescribed medication designed to directly influence

cortical excitation/inhibition (e.g. gabapentin for nerve pain), that may interfere with the emergence of tDCS effects (McLaren et al., 2018). The Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was used to establish the cognitive health of all participants ($M=28.17$, $SD=1.61$), who gave written informed consent prior to taking part in the study. All procedures were carried out with the approval of the local ethics committee (Department of Psychology, Swansea University).

2.2. Task switching paradigm

The Swansea Test of Attentional Control (STAC; Carter, N. and Wood, R., unpublished) assesses task switching ability. Comprising of selective attention, task monitoring, and response inhibition components, STAC represents a complex task in terms of cognitive load (Sebastian et al., 2013). The stability and validity of the STAC task has previously been assessed, resulting in good test-retest reliability between two consecutive runs ($r(30)=.857$, $p=.000$) and strong correspondence between STAC final speed and reaction times (RT) from a standard Flanker task ($r(24)=-.650$, $p=.001$). The latter correlation indicates that as STAC final speed increases, Flanker RT decreases, thus signifying that performance improvement between the measures is aligned. Consequently, STAC performance is regarded as comparable to that of the widely used Flanker task but the novel task has several distinct advantages compared to such standard tests.

One advantage of the STAC paradigm relates to the integration of features from standard tasks of vigilance and executive processing. STAC combines the inhibitory control demands of a Flanker task, with the resource-intensive target identification of a visual search task, and also features continuous presentation of stimuli rather than being dependent on repeat presentation of single trials. Therefore, compared to use of other tasks in isolation, STAC has the benefit of being more holistic in relation to the demands of stimulus engagement in everyday life. Having been developed in such a manner, STAC represents an ideal task to use where a complex test of attentional control is required. Furthermore, task complexity is of particular importance with regard to tDCS research (where performance improvements have been more readily noted in relation to complex tasks; Suntrup et al., 2013, Berryhill et al., 2014). However, the issue of task difficulty is often problematic where older

adults are the focus of the research. Standard tasks such as Flanker require the researcher to set parameters (e.g. stimulus presentation speed) in advance and often lack flexibility because such values are fixed. This means that the participant is forced to struggle to respond or is not sufficiently challenged. Use of a flexible algorithm designed to track performance (Parameter Estimation by Sequential Testing, PEST; Taylor and Creelman, 1967), which calibrates speed on the basis of prior responses, facilitates completion of the task within the bounds of an individual's capabilities. The dynamic nature of STAC means the variation in ability often demonstrated in an older adult sample can be accommodated, ensuring participants are able to respond successfully while not compromising on task difficulty.

The task is to identify the target within a 3 x 3 matrix of symbols on the right and search for matching symbols amongst an array of three columns of symbols, which scroll up the left-hand side of the screen (Fig. 1). Participants respond when a matching symbol crosses behind the line. The target changes throughout the task such that participants must remain vigilant in order to consistently update their search criteria, while simultaneously monitoring the search array in order to identify matching items and inhibit the irrelevant symbols. Target changes take place every 12 s but are delayed if the current target appears in the search array. In such instances, the corresponding time lapse is added to the total run time. Speed (measured in symbols per minute per column; abbreviated to 'spm') is adjusted to maintain accuracy around a 75% correct criterion, using the PEST algorithm. After a minimum of 4 target changes, speed is calibrated on the basis of performance accuracy; increasing or decreasing with a step-size between 7 and 23 spm. The participants' threshold is the speed at which the task is performed at the end of the pre-defined duration. Higher speed thresholds, therefore, reflect performance capability under conditions of increased difficulty.

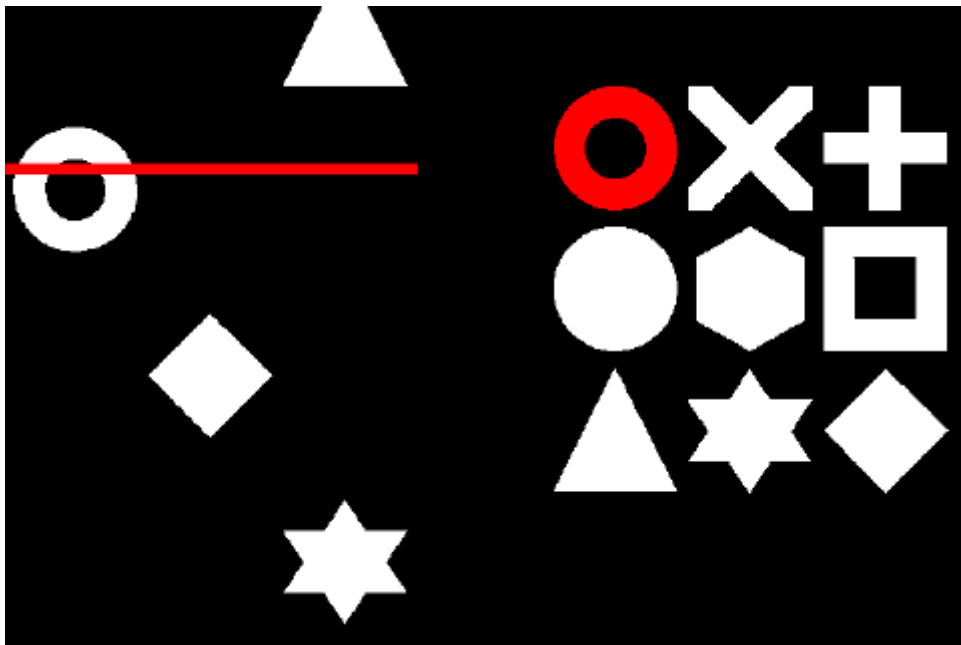


Fig. 1. STAC task. A target is identified within the 3 x 3 matrix of symbols (right). When a matching symbol appears amongst the three columns of the search array (left), participants press the spacebar as the symbol crosses behind the red line.

2.3. transcranial direct current stimulation

A DC-Stimulator Plus device (neuroConn, Germany) was used to deliver direct current stimulation. In line with studies outlining the interaction between age-related brain changes and the distribution of current (Lindenberg et al., 2013; Laakso et al., 2015; Tatti et al., 2016; Mahdavi and Towhidkhan, 2018), stimulation parameters were designed to be effective for use with older adults. Options with regard to electrode size and configuration, current duration, and amplitude were therefore cautiously reviewed as part of this study in an attempt to compensate for the inherent challenges posed by age-related atrophy (reflected in the stimulation protocol outlined below).

Rubber electrodes, measuring 5×5 cm (25 cm^2), were placed into sponge holders soaked in saline solution and positioned over dIPFC: F3 (anode) and F4 (cathode) (Fig. 2a; Chatrian et al., 1985). Although bihemispheric montages have been reported to lead to greater shunting of current through the scalp (Datta et al., 2008), Fig. 2b illustrates dIPFC is highly likely to be influenced given

the selected parameters. Stimulation was held constant for 20 minutes with an additional 30 s period at the beginning and end of the stimulation phase, during which the current was gradually increased to the pre-specified maximum and decreased to zero on termination. Anodal stimulation was delivered with a current of 1.5 mA (current density = 0.06 mA/cm²) to increase intensity from the standard 1 mA application, while maintaining participant comfort and the efficiency of the double-blind procedure (shown to be problematic at higher strengths; O’Connell et al., 2012). For sham stimulation, the neuroConn device initially ramped up the current to mimic the peripheral effects of active tDCS before ramping down.

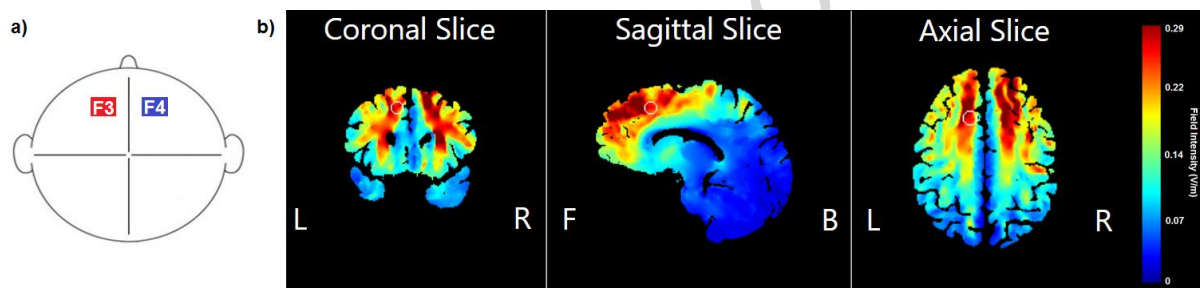


Fig. 2. Electrode configuration and current distribution. **a)** Bihemispheric stimulation was applied to F3/F4 in order to target dorsolateral prefrontal cortex (left hemisphere, anode; right hemisphere, cathode). **b)** The current distribution was modelled for the parameters used as part of the study, illustrating the anticipated stimulation of the target regions (HD-Explore; Soterixmedical Inc, New York).

2.4. Experimental procedure

Participants began each of the three sessions by completing consent and screening forms. During the first session, they were then seated in front of a computer monitor, at a distance of approximately 60 cm, to perform the STAC task. To gain experience with the paradigm, participants executed the task for approximately 5 target changes before baseline data was recorded (approximately 10 minutes into the first session). Acquisitions of task data were 5 minutes in length, resulting in approximately 25 target changes. The speed at which the task began was 41 spm, increasing or decreasing (to a minimum of 37 spm) in line with performance accuracy as the test

progressed. Participants indicated that they had identified that a symbol matching the target had passed behind the line by pressing the spacebar. Upon completing the task, subjects were prepared for tDCS (this process took 10 minutes, after which stimulation was administered as outlined above in section 2.3). Both the researcher and the participant were blind to the nature of the stimulation that took place during each session. Participants were instructed to rest and relax during this time while watching a nature documentary, and were not asked to complete the task during tDCS. Following stimulation, participants completed an Adverse Effects Questionnaire (AEQ) in order to determine the presence and severity of side-effects relating to tDCS. Subjects rated side-effects on a scale of 0-4; corresponding to absent, mild, moderate, strong, and severe. This process took 5 minutes, after which the STAC task was completed again. Subsequent sessions (administered 48 hours apart) were implemented such that further baseline measures were not acquired. During sessions 2 and 3, participants received a repeat of the tDCS procedure and were asked to complete the AEQ, before post-stimulation data from the task were recorded (Fig. 3).

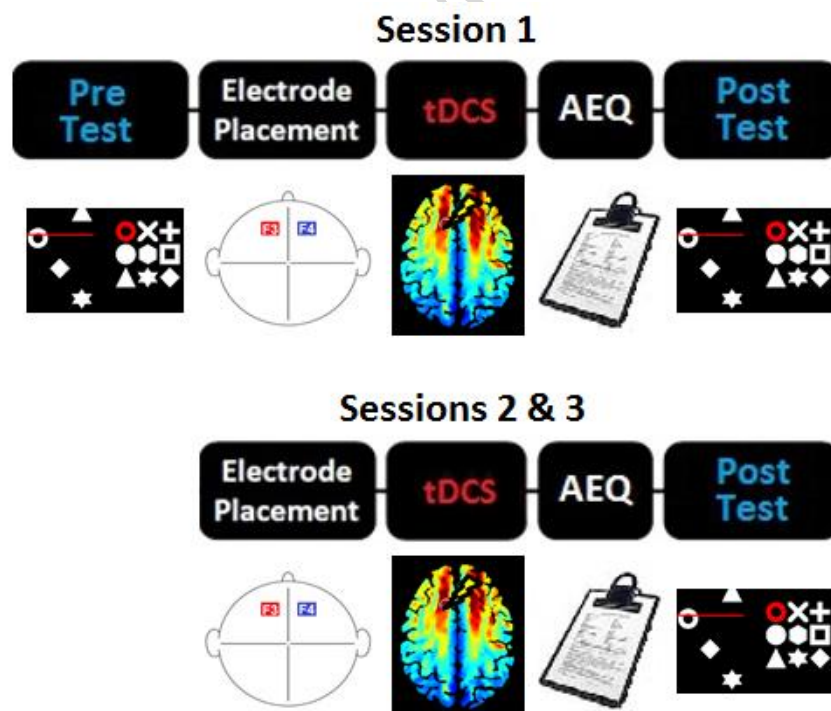


Fig. 3. Experimental procedure. During the first session, participants completed a baseline run of the attentional control task prior to stimulation. Post-stimulation, participants completed the Adverse

Effects Questionnaire (AEQ) and another run of the task. During the second and third sessions, participants repeated the tDCS procedure, followed by the AEQ, and then completed the task. Sessions took place 48 hours apart.

2.5. Data analysis

Of the 24 subjects tested, 2 were removed from the sample (1 from the anodal group due to incomplete data, and 1 from the sham group due to poor performance accuracy). Data from the remaining 22 participants (11 per group; 54-73 years of age ($M=66.50$, $SD=4.85$)) was entered into statistical analysis using SPSS for Windows software (version 22; IBM, New York). Prior to analysing the task data, independent samples t-tests were performed to test for group differences in age and performance on the MoCA. A one-way ANOVA featuring data from the AEQ (sessions 1, 2, 3) was used to assess group differences in the peripheral sensations experienced as a result of stimulation.

Pearson's correlation was used to assess the relationship of age and baseline data, whereby a significant result would signify the use of age as a covariate in the main analysis. Speed and accuracy measures resulting from the STAC task were entered into separate ANOVAs with the variables of Time (Baseline, Post Stim 1, Post Stim 2, Post Stim 3) and Group (Anodal, Sham). Further t-tests were conducted to investigate interactions. Greenhouse–Geisser correction was used for violations of sphericity. An alpha level of 0.05 was used to determine significance.

3. Results

3.1. Preliminary analyses (group differences)

No significant age difference was observed between groups ($t(20)=1.394$, $p=.179$), suggesting age could be ruled out as a contributing factor should differences arise as a result of stimulation.

No significant difference in MoCA score was found between groups ($t(20)=-1.934$, $p=.067$), indicating that each group was equally capable of performing the tasks.

Participants reported mild-moderate peripheral sensations (tingling/itching) under the electrode pads, largely towards the beginning of the stimulation period. These reports were consistent across each of the three sessions ($F(2,40)=1.637$, $p=.207$, $\eta^2=.076$) and between groups ($F(1,20)=2.778$, $p=.111$, $\eta^2=.122$), suggesting stimulation was experienced in a similar manner across the study.

3.2. STAC analyses

3.2.1. Speed threshold

No significant correlation was found between age and the speed of results at baseline ($r(22)=-.004$, $p=.986$), supporting the notion that the age of participants was not a contributing factor to performance.

No significant difference was found in the speed of baseline results between groups ($t(20)=-.183$, $p=.857$), indicating that there were no pre-existing distinctions in performance aptitude prior to stimulation.

The results of the ANOVA demonstrate no significant main effect of Time ($F(3,60)=2.398$, $p=.077$, $\eta^2=.107$) or Group ($F(1,20)=2.326$, $p=.143$, $\eta^2=.104$), but there was a significant Time*Group interaction ($F(3,60)=4.355$, $p=.008$, $\eta^2=.179$). Significant differences within the anodal group (Post Stim 1/Post Stim 3 ($t(10)=-3.133$, $p=.011$); baseline/Post Stim3 ($t(10)=-4.343$, $p=.001$, Cohen's $d=1.36$)), and between the anodal and sham stimulation conditions (Post Stim 3 ($t(20)=2.724$, $p=.013$)) account for the interaction effect (Fig. 4).

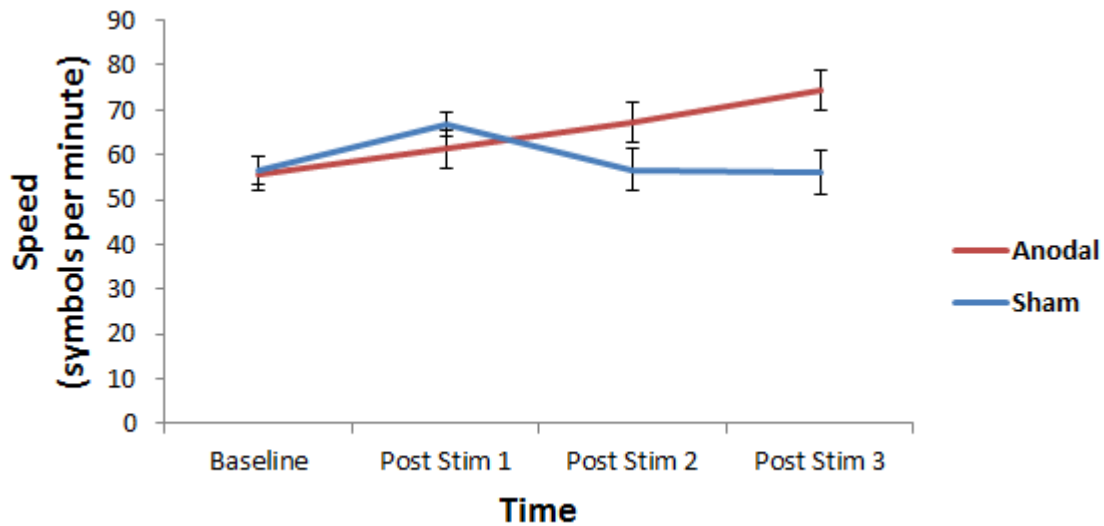


Fig. 4. STAC speed thresholds. Average speed values obtained at baseline and post-stimulation. Error bars represent ± 1 S.E.M.

3.2.2. Accuracy

As for speed threshold, no significant correlation was found between age and the accuracy of baseline performance ($r(22)=-.339$, $p=.123$). No significant difference in the accuracy of baseline results was observed between groups ($t(20)=-.334$, $p=.741$).

Both groups performed well, although accuracy within the sham group decreased during the final session (Fig. 5). Accordingly, the results of the ANOVA demonstrate no significant effect of Time ($F(3,60)=1.508$, $p=.222$, $\eta^2=.070$), Group ($F(1,20)=2.740$, $p=.113$, $\eta^2=.120$), or their interaction (Time*Group: $F(3,60)=1.975$, $p=.127$, $\eta^2=.090$).

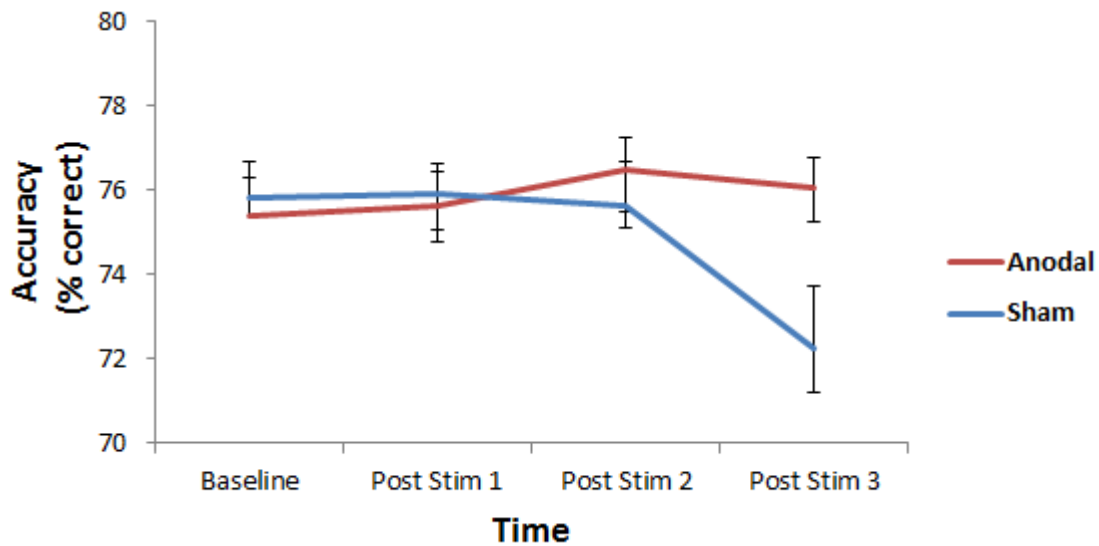


Fig. 5. STAC performance accuracy. Average accuracy values obtained at baseline and post-stimulation. Error bars represent ± 1 S.E.M.

In summary, anodal tDCS resulted in significantly better final speed thresholds, confined to the final stimulation session, whereas no significant differences in accuracy were evident.

4. Discussion

The aim of the study was to enhance attentional control in older adults, using tDCS optimised for use in the context of ageing. As predicted, anodal tDCS produced a significant increase in speed thresholds obtained as part of the STAC paradigm, whereas sham stimulation did not. However, this effect was restricted to the final session. The results, therefore, suggest that at this specific time point, those in the anodal stimulation group were more efficient at responding in line with task demands and inhibiting interference from irrelevant stimuli.

4.1. Improving attentional control in ageing

The results indicate that the observed increase in speed thresholds was unique to the anodal stimulation group. The lack of identical enhancement under sham control conditions suggests that task exposure (in the absence of active stimulation) was not sufficient to advance performance. The effect

emerged only at the third session, which suggests that the cognitive benefits of stimulation are not immediately observable in older adults (as found by Fujiyama et al., 2014). Such a delay is attributed to an age-related reduction in the efficiency of neurochemical signalling (McQuail et al., 2015), requiring additional exposure to stimulation to restore the mechanisms of plasticity and facilitate cognitive change. At present, it should be emphasised that the speed improvement is regarded as an acute, post-stimulation effect, as opposed to being sustained across the entire study. However, the present results highlight the potential benefits of non-invasive brain stimulation for older adults. To date, the literature has failed to demonstrate a robust effect of anodal tDCS on attention in general (Dedoncker et al., 2016; Reteig et al., 2017), and is lacking sufficient evidence with regard to attentional control in both younger and older adults. This study resulted in a large effect size (exceeding the 0.50 threshold required to be considered as clinically relevant; Sloan et al., 2005), thus making the results of the study particularly compelling. Nonetheless, further investigations are needed to clarify the extent to which tDCS can be regarded as beneficial in this context.

A task as simple as crossing the road requires consistent monitoring of the environment to update the surroundings, suppression of irrelevant distractions, and sufficient inhibitory signalling to acknowledge when it would not be safe to proceed. This signifies that cognitive control mechanisms are integral to everyday life (Wilkins et al., 2010). As such, tDCS-induced enhancements are an incredibly valuable prospect, which could potentially contribute to the attenuation of cognitive decline while also helping to sustain the independence and well-being of older adults. Plans for a large-scale intervention, featuring tasks of inhibitory control, were recently published, which will no doubt provide further insight into the benefits of tDCS, specific to the ageing population (Woods et al., 2018). Preliminary research suggests it is also possible to improve cognition via tDCS in those with Mild Cognitive Impairment (Meinzer et al., 2015) and early stage Alzheimer's disease (Boggio et al., 2012). However, improving severe impairment would be expected to be more difficult in light of advanced atrophy, as well as the loss of crucial neurochemicals that the stimulation method modulates. The greatest benefits of tDCS are, therefore, proposed to be apparent in supporting

existing plastic mechanisms and preventing cognitive decline, in advance of substantial neurodegeneration and related deficits.

4.2. Stimulating the ageing brain

The outcome of the current study highlights the importance of considering the neurobiological mechanisms of tDCS, and related issues of the chosen sample, as part of experimental design. As anticipated on the basis of computational modelling work (Laakso et al., 2015; Mahdavi and Towhidkhah, 2018), high intensity and long duration stimulation appears to be advantageous in the ageing population, contrary to findings in young adults (Batsikadze et al., 2013; Jamil et al., 2017; Esmailpour et al., 2018). Such protocols may also be crucial with respect to inducing sustained benefits because 2 mA stimulation has been reported as superior to 1 mA in this regard (Stephens and Berryhill, 2016), although blinding procedures may be compromised at such strengths (O'Connell et al., 2012). A systematic study of the effects of current intensity and duration in the ageing population has not been conducted but would certainly help to clarify the validity of this concept and its upper limits.

With advancing age, older adults have been shown to recruit the left and right hemispheres of frontal cortex to perform cognitive tasks, even at low levels of demand (compared to young adults who demonstrate lateralisation: Cabeza, 2002; Carp et al., 2010; Sala-Llonch et al., 2015). Accordingly, the electrode configuration implemented as part of the study was designed to balance the demands on resources across the prefrontal network (Lindenberg et al., 2013; Tatti et al., 2016). As such, an improvement in attentional control may not have been observed having utilised a unilateral montage (to target a single hub within the network). Therefore, the observed tDCS-induced improvement in task switching speed is attributed to the parameters used, which were selected on the basis of what is known of the ageing brain and how current distribution is altered as a result (Laakso et al., 2015; Mahdavi and Towhidkhah, 2018).

The complexity of the task switching paradigm may have also been integral to the present findings. Effects resulting from tDCS have been proposed to be more readily observed with difficult

tasks (Berryhill et al., 2014; Suntrup et al., 2013). Accordingly, the difficulty of the STAC task may have promoted engagement in order to elicit adequate performance. When coupled with the anticipated effects of tDCS on calcium transmission and the availability of glutamate (Nitsche et al., 2003; Stagg et al., 2009), synaptic activation and depolarisation of the post-synaptic membrane would be facilitated thus enabling LTP (Wigström et al., 1986). It can be inferred that optimal calcium levels resulted from the stimulation as excessive calcium influx triggers hyperpolarisation (Lisman, 2001), which would be predicted to result in poor task performance. The stimulation may have similarly regulated GABAergic neurotransmission (also integral to plasticity; Trepel and Racine, 2000) in frontal cortices. Consequently, tDCS effects are potentially most evident during complex top-down tasks, which would be of great benefit in restoring goal-oriented functions that suffer substantially as a result of age-related frontal declines (Bennett et al., 2012).

4.3. Optimising stimulation (study limitations and future developments)

In the absence of neuroimaging data, demonstrating structural, functional, and/or neurochemical change, the current study is unable to confirm the origin of the performance enhancement. However, on the basis of past literature, the findings suggest that anodal stimulation produced a strengthening of prefrontal information processing to support task performance under conditions of increased difficulty, by restoring more youth-like function and alleviating pressure on compensatory mechanisms (Meinzer et al., 2013). Investigation of prefrontal response patterns, functional connectivity, and changes in neurochemistry is needed to clarify the precise mechanism of action. Whether the stimulation produced a sustained, cumulative effect, or a more acute alteration in participants' response to stimulation, also remains to be determined. Such insight will be gained from incorporating baseline measures at each session. This will help to further characterise the nature of tDCS effects as research continues to support cognition in the context of ageing.

Where tDCS has been shown to be beneficial in older adult samples, participants typically attend 5-10 separate sessions (Jones et al., 2015; Stephens and Berryhill, 2016). Here, a significant improvement in attentional control was observed at the final session in a series of three. While the

observed effect suggests that fewer sessions of tDCS were required to support task switching performance (where the effect is inferred to have been due to a change in acute sensitivity to tDCS, developing post-stimulation with each subsequent exposure, as opposed to being sustained across the duration of the study), the results also imply that single-session approaches are unlikely to be effective in altering older adult performance (Fujiyama et al., 2014; Horvath et al., 2015). Moving forward, the key to enhancing plasticity may be to minimise sessions but to implement within-session repeats of tDCS (Monte-Silva et al., 2013; Bastani and Jaberzadeh, 2014; Au et al., 2016; Au et al., 2017). Such protocols are also likely to be more appealing to participants than more frequent attendance.

With regard to the precision of responses, in young adults, it is not uncommon for reaction time to improve but for anodal tDCS to result in a lack of benefits for performance accuracy (Brunoni and Vanderhasselt, 2014). In the context of the present study, it is also possible that no tDCS-induced improvement in accuracy was observed due to the nature of the task. The PEST algorithm attempts to maintain accuracy at 75% correct, whereas there was no ceiling level to the speed element of the task. Participants, therefore, had a far greater dynamic range for improvement with regard to speed. Adjusting the flexibility of the accuracy measure, may assist in determining whether improvements in the precision of task switching performance are also evident following anodal tDCS in older adult samples.

Finally, during future studies, a wider variety of tests will be implemented in a longitudinal manner, to offer perspective on sustained effects that this initial investigation could not accommodate. Firstly, subsequent work will incorporate the means to assess changes in motor function, alongside attentional control. Although it would be unlikely that the induction of improved response speed, for example, would sufficiently account for the present findings (where STAC is dependent on precision and vigilance, identifying the target as it crosses the line, as opposed to gross response time), it will be important to identify any contributions relating to enhanced motor function as the research develops. Use of additional tests of executive control will also be incorporated, similar to Jones et al. (2015) and Stephens and Berryhill (2016), to enable distinctions between local and global benefits of stimulation (using tasks that participants are highly familiar with, compared to those they will have minimal

exposure to). This approach will allow for inferences on the transfer of effects and more holistic outcomes that could potentially influence everyday aspects of function.

In conclusion, the study found that older adults' speed of processing in relation to attentional control can be improved, in an acute manner, using anodal tDCS. However, there is much scope for further optimisation. The findings are attributed to the implemented paradigm and stimulation parameters, which reflect knowledge of the ageing process and tDCS mechanisms from a neurobiological perspective. Ultimately, those seeking to enhance cognition in populations known to experience changes in brain structure and function are encouraged to adopt a similar approach, as opposed to relying on standard protocols reported in the literature. Future benefits of stimulation are far more likely in this context; particularly with regard to ageing, the maintenance of cognitive health, and subsequent well-being.

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Declaration of interest: none

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Anodal tDCS improves attentional control in older adults.

Dr Claire J. Hanley and Prof Andrea Tales

Highlights

Age-optimised stimulation parameters were used to increase attentional control.

The study featured a novel task-switching paradigm.

Anodal tDCS significantly improved task-switching speed in older adults.

tDCS represents a viable method for enhancing cognitive function in ageing.

ACCEPTED MANUSCRIPT

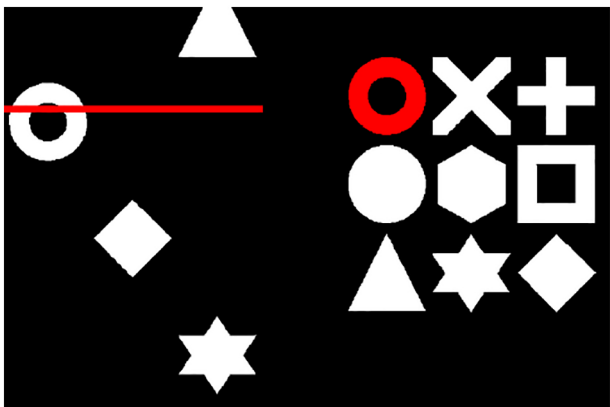


Figure 1

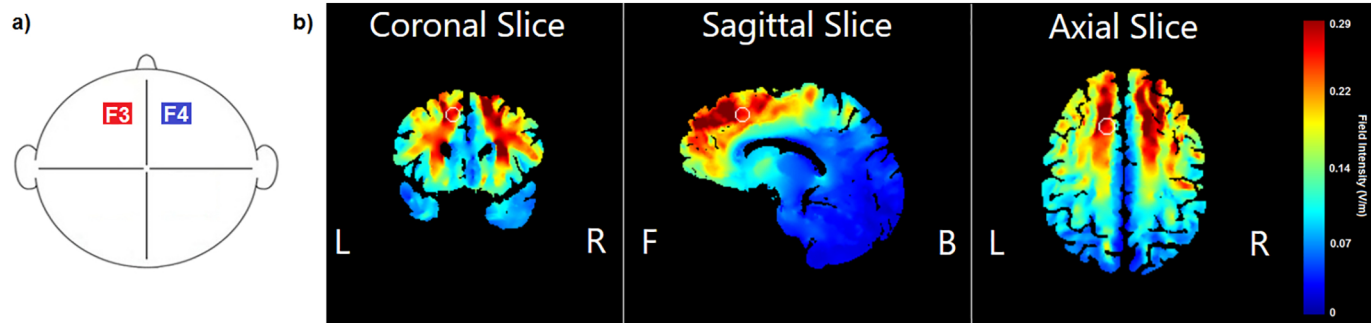
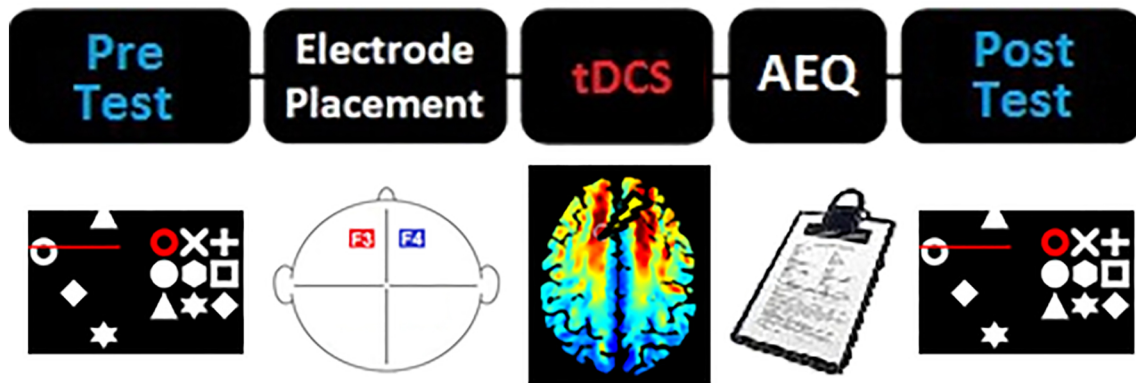


Figure 2

Session 1



Sessions 2 & 3



Figure 3

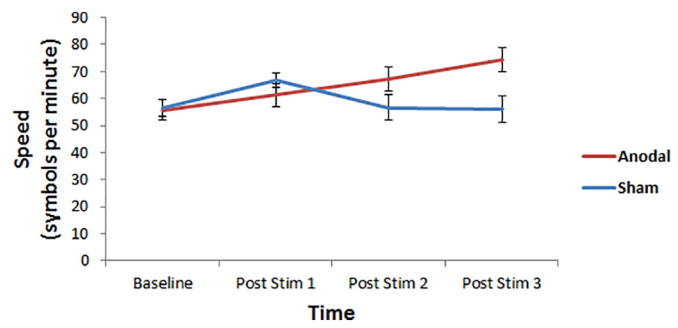


Figure 4

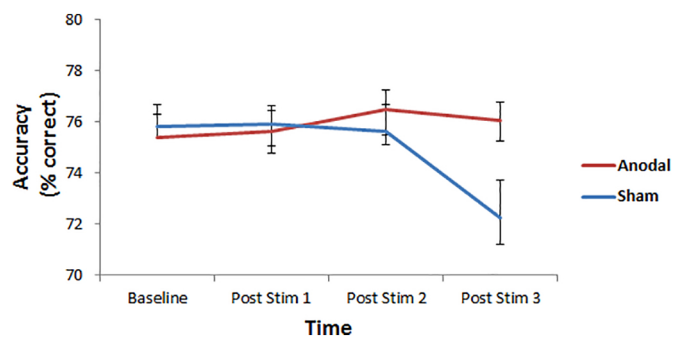


Figure 5