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# Prefrontal Modulation of Visual Processing and Sustained Attention in Aging, a Transcranial Direct Current Stimulation–Electroencephalogram Coregistration Approach

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## Abstract

■ The ability to sustain attention is integral to healthy cognition in aging. The right PFC (rPFC) is critical for maintaining high levels of attentional focus. Whether plasticity of this region can be harnessed to support sustained attention in older adults is unknown. We used transcranial direct current stimulation to increase cortical excitability of the rPFC, while monitoring behavioral and electrophysiological markers of sustained attention in older adults with suboptimal sustained attention capacity. During rPFC transcranial direct current stimulation, fewer lapses of attention occurred and electroencephalography signals of frontal

engagement and early visual attention were enhanced. To further verify these results, we repeated the experiment in an independent cohort of cognitively typical older adults using a different sustained attention paradigm. Again, prefrontal stimulation was associated with better sustained attention. These experiments suggest the rPFC can be manipulated in later years to increase top-down modulation over early sensory processing and improve sustained attention performance. This holds valuable information for the development of neurorehabilitation protocols to ameliorate age-related deficits in this capacity. ■

## INTRODUCTION

The integrity of the sustained attention system is a key constituent of healthy cognition in aging (Robertson, 2014). Deficits in this domain are associated with negative functional outcomes in both healthy older adults (O’Halloran, Finucane, Savva, Robertson, & Kenny, 2014; O’Halloran, Pénard, Galli, & Fan, 2011) and those experiencing pathological aging conditions (O’Keefe et al., 2007; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997).

The right-lateralized alertness network, the so-called locus-coeruleus-norepinephrine (LC-NE) system, has been proposed by several authors to contribute to nonspatial aspects of attention such as alertness (Robertson, 2014; Corbetta & Shulman, 2002, 2011; Posner & Petersen, 1990). Behavioral and pharmacological interventions targeting this system have shown promise at enhancing sustained attention performance in healthy aging (Milewski-Lopez et al., 2014) and stroke (Singh-Curry, Malhotra, Farmer, & Husain, 2011; Malhotra, Parton, Greenwood, & Husain, 2006).

Within the right-lateralized network supporting sustained attention capacity (Langner & Eickhoff, 2013; Singh-Curry & Husain, 2009; Rueckert & Grafman, 1996), PFC has been identified as particularly critical (O’Connor, Robertson, & Levine, 2011; Lawrence, Ross, & Hoffmann, 2003; Manly et al., 2003; Sturm & Willmes, 2001). Preliminary evidence suggests that manipulating activity within this region improves the maintenance of endogenous attention in young participants (deBettencourt, Cohen, Lee, Norman, & Turk-Browne, 2015; Nelson, McKinley, Golob, Warm, & Parasuraman, 2014). Moreover, recent work suggests that increasing excitability of right prefrontal activity in older adults enhances processing speed (Brosnan et al., 2018), an aspect of visual attention that is also closely linked to the right-lateralized alertness system (Matthias et al., 2009; Habekost & Rostrup, 2006; Duncan et al., 1999). However, to our knowledge, activity in the right PFC (rPFC) has never been directly targeted in older adults to manipulate sustained attention. It therefore remains to be seen whether plasticity of this region can be harnessed in later life to ameliorate deficits in this capacity.

The current article investigates, in two separate experiments, whether behavioral and electrophysiological markers of successful sustained attention could be modulated in older adults by increasing excitability of the rPFC using transcranial direct current stimulation (tDCS),

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a noninvasive method of brain stimulation. In the first experiment, a tDCS-electroencephalogram (EEG) coregistration approach was employed to assess how behavioral task performance and ERP markers of sustained attention would change during stimulation in an older adult sample who were cognitively healthy but exhibited relatively low sustained attention capacity. The second experiment assessed whether the tDCS-related behavioral effects observed in Experiment 1 (a) replicated using a separate sustained attention paradigm, such that the effects of stimulation could be attributed to the process of sustained attention and not the specific cognitive task, and (b) generalized to an independent sample of cognitively typical older adults, that is, older adults who were not preselected based on a relatively low ability to maintain attention.

## METHODS

### General Methods

This article describes two separate experiments exploring the effects of right prefrontal tDCS on sustained attention performance in older adults. Two independent cohorts ( $N = 56$  in total; see Table 1 for demographic information) were recruited for two distinct experiments. Experiment 1 was designed to explore whether sustained attention could be increased using right prefrontal tDCS in older adults who were cognitively healthy but vulnerable to sustained attention deficits. In this experiment, sustained attention was measured using the well-known Sustained Attention to Response Task (SART; Robertson, Manly, et al., 1997). This task correlates with attentional failures occurring in everyday life (Smilek, Carriere, & Cheyne, 2010) and has established electrophysiological markers of successful performance (Staub, Doignon-Camus, Marques-Carneiro, Bacon, & Bonnefond, 2015; O'Connell, Dockree, Bellgrove, et al., 2009; Dockree, Kelly, Robertson, & Reilly, 2005).

The second experiment (Experiment 2) assessed whether the tDCS-related behavioral effects observed in Experiment 1 generalized to an independent sample of healthy older adults. For this purpose, performance was assessed on a different sustained attention task, free from response inhibition requirements and known to be particularly sensitive to performance decrements over short time windows (3 min 5 sec; the Continuous Temporal Expectancy [O'Connell, Dockree, Robertson, et al., 2009]).

During both experiments, participants received active and sham tDCS over two sessions in a single-blind crossover design. The two tDCS sessions were separated by at least a 6-day period to minimize carryover effects. The order of sham and active tDCS was counterbalanced and randomized across participants. For both experiments, the rPFC was targeted using the F4-Cz tDCS montage employed by Harty et al. (2014; see tDCS protocol below). TDCS was always applied during performance of the tasks, and no stimulation was administered during break periods. All participants were right handed, had no history of neurological illness and/or no personal or family history of seizures, and scored 23 or higher on the cognitive screening tool (the Montreal Cognitive Assessment [MoCA]; Nasreddine et al., 2005). Both studies were approved by the Trinity College Dublin School of Psychology Ethics Committee, and written consent was obtained before participation.

### Experiment 1 Methods

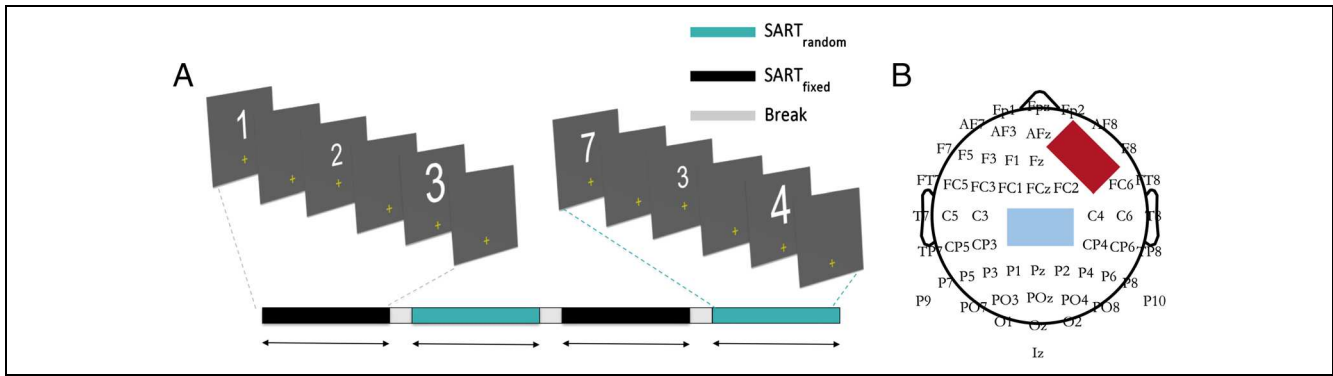
#### Participants

Experiment 1, the tDCS-EEG coregistration approach, explored the feasibility of using right prefrontal tDCS to improve sustained attention performance in older adults who were cognitively healthy (as assessed using the MoCA (Nasreddine et al., 2005) but whose capacity to sustain attention was relatively low (as assessed via their normative performance on a sustained attention assessment). For this purpose, 107 participants were prescreened for cognitive impairment using the MoCA, and their sustained attention capacity was assayed using the fixed version of the SART (SART<sub>fixed</sub>; O'Halloran et al., 2014; Robertson, Manly, et al., 1997; see task description below). A participant's sustained attention performance on the SART was classified with reference to normative data (from unpublished observations on 5,470 older adults who participated in The Irish Longitudinal Study of Aging [TILDA]), according to their age, gender, and level of education. All prescreened participants, scoring  $\geq 23$  on the MoCA cognitive screen (Coen, Cahill, & Lawlor, 2010; Luis, Keegan, & Mullan, 2009), were ranked based on their normative SART performance (with lower scores indicative of worse normative performance), and individuals were invited to participate in the tDCS-EEG coregistration study in ascending order based on these

**Table 1.** Demographic and Cognitive Characteristics of the Sample

	Age (years)	MoCA	Education (years)	PFS IQ
Experiment 1 ( $N = 26$ )	72.42 (5.43)	26.80 (2.28)	13.61 (4.62)	112.83 (7.99)
Experiment 2 ( $N = 23$ )	72.70 (5.93)	27.81 (1.63)	15.91 (3.66)	122.86 (3.86)

PFS IQ denotes predicted full-scale IQ as estimated from the National Adult Reading test (Nelson, 1982), a measure of premorbid intelligence. MoCA (Nasreddine et al., 2005) is a validated cognitive screening tool. Values denote means and standard deviations,  $M$  ( $SD$ ).



**Figure 1.** Outline of the task procedure for Experiment 1. (A) During both sham and real tDCS sessions, participants underwent interleaved blocks of the SART<sub>fixed</sub> and SART<sub>random</sub> and the order was counterbalanced across participants. tDCS was delivered for the duration of each task block (8 min 25 sec), and no tDCS was administered during the breaks between blocks. (B) tDCS was administered during simultaneous EEG recordings with the anode (in red) placed over F4 and the cathode (in blue) placed over Cz. Participants received sham and real stimulation separated by a minimum of 6 days. The same tDCS electrode montage was used for both stimulation sessions.

normative sustained attention percentile scores (as measured by commission errors).

During the initial testing session, participants who were subsequently included in Experiment 1 made an average of 5.99 ( $SD = 3.44$ ) commission errors, with 88.5% of the participants classified (via the TILDA norms) as performing in the 50th percentile or lower. The version of the SART used during the initial behavioral testing session was identical to that used for developing the normative TILDA data (see O’Halloran et al., 2014) except that 225 (as opposed to 223) iterations of the 1–9 sequence were administered.

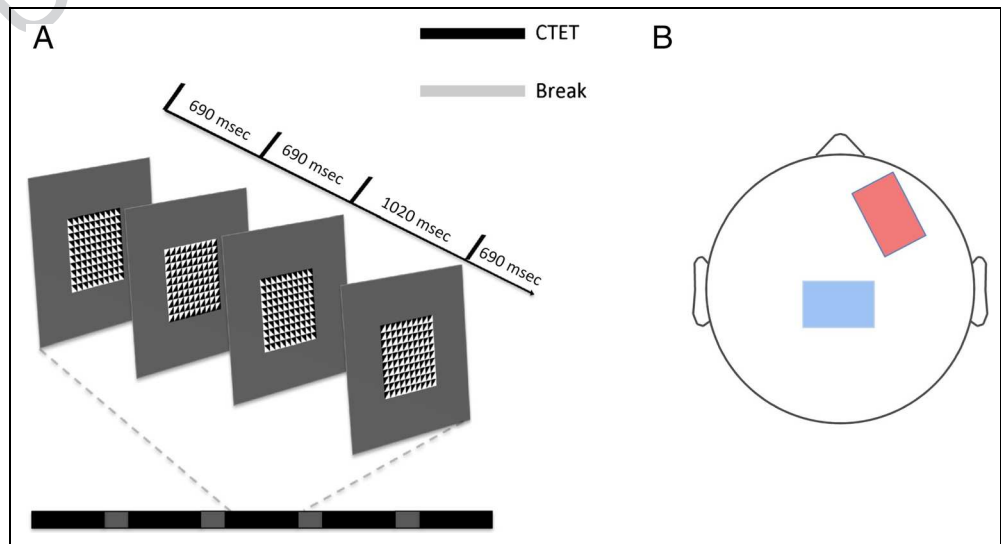
From the pool of 107 prescreened participants, 32 participants were recruited for Experiment 1. Five of these participants did not return for the second stimulation session, and one participant was excluded because of difficulty with coordinating timely responses to stimuli (resulting in 19.25% omission errors, which were more

than 3  $SDs$  from the mean). The final sample for Experiment 1 therefore consisted of 26 participants (seven men; see Table 1 for demographic information).

#### tDCS

tDCS was delivered using the F4–Cz tDCS montage utilized by Harty and colleagues (2014) to target the right dorsolateral PFC (DLPFC). Stimulation was administered using a battery-driven DC Brain Stimulator Plus (NeuroConn) with two  $5 \times 7$  cm electrodes, using high-chloride EEG electrode gel (Abralyt HiCl; EasyCap) as a conducting paste. The anodal electrode was placed over the right frontal cortex, and the reference electrode was placed over the vertex areas F4 and Cz, respectively, according to the 10–20 international system for EEG electrode placement; see Figures 1B and 2B). The same electrode montage was used for both sham and active stimulation.

**Figure 2.** Outline of the CTET and the tDCS procedure for Experiment 2. (A) During both sham and real tDCS sessions, participants underwent five blocks of CTET. (B) tDCS was delivered for the duration of each task block (approximately 3 min 5 sec), and no tDCS was administered during the break periods between blocks. The anodal electrode (in red) was placed over F4; and the cathode (in blue), over Cz. There were no simultaneous tDCS-EEG recordings during Experiment 2. Participants received sham and real stimulation separated by a minimum of 6 days. The same tDCS electrode montage was used for both stimulation sessions.



During active stimulation, tDCS was administered at 1 mA continuously during task performance with ramp-up/ramp-down periods of 20 sec, resulting in a current density of 0.02857 mA/cm<sup>2</sup> at the scalp. To minimize potential artifacts in the EEG signals at the beginning of stimulation, the current was administered and allowed to settle for 30 sec after the ramp-up period before the task began. The ramp-down began after performance of the task had finished. There was no stimulation during the rest periods in between the blocks. During sham stimulation, tDCS was administered at 1 mA for 15 sec at the beginning of each block with ramp-up/ramp-down periods of 20 sec. This is a frequently used sham protocol to ensure that the sensations often experienced with the onset of tDCS (such as a prickling sensation underneath the electrodes) are analogous across active and sham sessions (Gandiga, Hummel, & Cohen, 2006).

### *Monitoring Sustained Attention Performance*

*The SART.* During Experiment 1, a modified version of the SART was used to monitor performance during tDCS. In this task, a series of single digits from 1 to 9 are presented, and participants are required to make a response to each number (go trials) with the exception of the number 3 (no-go trial). Longer blocks were administered to participants during the tDCS sessions with 450 digits presented per block, representing 50 iterations of each 1–9 sequence, such that each block lasted 8 min 25 sec in duration (Figure 1A).

During the tDCS testing sessions, two blocks of the SART<sub>fixed</sub> were administered to assay sustained attention capacity. The task was slightly modified from the version used during the prescreening session. In the SART<sub>fixed</sub>, numbers are presented in a fixed, predictable order (1–9; see task description below). Sustained attention is considered the predominant cognitive process underlying successful performance on the SART<sub>fixed</sub> as an individual is required to continuously maintain intrinsic levels of alertness throughout the repeating, monotonous 1–9 sequence (O’Connell, Dockree, Bellgrove, et al., 2009; Dockree et al., 2005; Manly et al., 2003). The task necessitates that an individual successfully withholds his or her response to the critical no-go trial. However, given that this critical trial is embedded within the predictable, repeating sequence, the response inhibition requirements on the SART<sub>fixed</sub> are minimal.

Nevertheless, to confirm that any behavioral effects of tDCS could be attributed to changes in sustained attention, and not response inhibition, two blocks of the SART<sub>random</sub> were also administered to participants. In the SART<sub>random</sub>, stimulus characteristics and task requirements (withhold for digit “3”) were identical but the numbers were presented in a random unpredictable order, thus requiring the inhibition of a response to unpredicted, randomly presented targets. Although sustained attention is required for optimal performance of this task, inhibitory

control processes are considered predominant processes required for successful task performance on this task (O’Connell, Dockree, Bellgrove, et al., 2009; Fassbender et al., 2004), for example, as evidenced by an N2/P3 complex on the critical no-go trial during the SART<sub>random</sub> in young, healthy individuals, which is enhanced for correct withholds relative to errors and is absent during the SART<sub>fixed</sub> (O’Connell, Dockree, Bellgrove, et al., 2009). Participants performed four blocks of the SART during each experimental session. Blocks of the SART<sub>fixed</sub> and SART<sub>random</sub> were interleaved, and the order was pseudo-randomized across participants.

Five randomly assigned digit sizes (as described in O’Connell, Dockree, Bellgrove, et al., 2009) were used to increase the processing demands of the presented number and to minimize the likelihood that participants would search for some perceptual feature of the target digit (“3”). Digits were presented above a central yellow fixation cross on a gray background (Figure 1). The task was programmed, and stimuli were delivered using Presentation software (Neurobehavioural Systems). For each trial, the digit was presented for 300 msec, followed by an ISI of 800 msec. Participants were instructed to respond with a left mouse button press using their right forefinger when each digit (go target) was presented, with the exception of digit “3” (no-go target). Participants were asked to respond as quickly and accurately as possible but were cautioned to wait until the digit appeared on the screen before responding. The following error awareness component was added to the task: Participants were asked to indicate their awareness of commission errors with a right mouse button press using their right middle finger immediately after committing an aware error. To ensure that all participants fully understood the task requirements, practice trials were undertaken at the beginning of each session. All participants performed the task until three successful iterations of the sequence were completed (i.e., the participant clicked for all go-trials and successfully withheld on each no-go trial). Participants also demonstrated the error awareness button press.

Three performance measures were calculated to measure the effects of stimulation on the SART: commission errors, omission errors, and error awareness of commission errors. Any response occurring 1 sec after the stimulus onset was excluded from the analysis to exclude anticipatory responses for upcoming stimuli. Given the very low prevalence of omission errors in both the SART<sub>fixed</sub> ( $M = 0.3\%$ ,  $SD = 0.29\%$ ) and the SART<sub>random</sub> ( $M = 0.59\%$ ,  $SD = 0.82\%$ ), omission errors were excluded from further analyses. Commission errors were normalized as the percentage of commission errors divided by the total number of no-go trials. Error awareness was calculated as the percentage of commission errors that were followed by an error awareness click up to 1500 msec after the error took place. Evidently, error awareness was not calculated during blocks where “0” commission errors were made.

Outliers were defined using the interquartile range (IQR). The IQR is the third quartile (75th percentile) minus the first quartile (25th percentile). A value was identified as an outlier if either of the following conditions was met: if the value was  $<25\text{th percentile} - 1.5 * \text{IQR}$  or if the value was  $>75\text{th percentile} + 1.5 * \text{IQR}$ . These participants were then excluded on the given performance measure from further analyses, and the mean and *SD* were subsequently recalculated. Given the sensitivity of tDCS to timing parameters, particularly in older adults (Fertonani, Brambilla, Cotelli, & Miniussi, 2014), and given that elderly participants have been shown to improve their performance on the SART over longer durations (Staub et al., 2015), the effects of stimulation were investigated per block. Changes in performance during stimulation were therefore assessed using repeated-measures ANOVAs with Stimulation (active vs. sham tDCS) and Time (Block 1 vs. Block 2) as the within-subject factors. Significant main and interaction effects were followed up with simple effects analyses. All statistical analyses were performed using SPSS Statistics v21.0.0.1 (IBM), and all figures were designed using customized scripts in MATLAB R2014a 8.3.0.532 (The Mathworks). In all figures, the error bars indicate the standard error of the mean (*SEM*).

*Simultaneous tDCS-EEG recordings.* During Experiment 1, continuous EEG data were acquired during both tDCS sessions, concurrently with stimulation. The data were acquired using the ActiveTwo system (BioSemi) from 53 scalp electrodes, digitized at 512 Hz. EEG data were collected during all of the task blocks simultaneously with tDCS. Resting state data were also collected before and after stimulation and will not be discussed in the current article. A standard 64-channel system was used, but EEG was not recorded from the EEG scalp electrodes that were positioned at the tDCS electrode locations, namely, channels C1, Cz, C2, CP1, CPz, and CP2 under the cathodal tDCS electrode and channels F2, F4, F6, AF4, and FC4 under the anodal tDCS electrode (Figure 1B). EEG data were discarded for three participants on both tasks and for an additional four participants on the SART<sub>random</sub> because of issues during data collection and excessive movement artifacts, resulting in  $n = 23$  and  $n = 19$  participants for the SART<sub>fixed</sub> and SART<sub>random</sub> EEG analyses, respectively. Data were analyzed using custom scripts and EEGLAB functions (Delorme & Makeig, 2004) in MATLAB. EEG data were rereferenced offline to the average reference using the average of all available electrodes except electrodes over the left prefrontal regions (AF3, F1, F3, F5, and FC3), which were homologous to the missing right frontal EEG electrodes, and the corresponding parietal electrodes (CP3, P1, P3, P5, PO3, CP4, P2, P4, P6, and PO4). The data were high-pass filtered above 0.03 Hz and low-pass filtered below 35 Hz offline using an optimum Butterworth infinite impulse response filter. The “filtfilt” function in MATLAB was implemented to

allow for a noncausal zero-phase filtering approach to eliminate any nonlinear phase distortion associated with using an infinite impulse response filter.

For the ERP analysis, EEG data were segmented into epochs centered on stimulus onset using windows of  $-100$  to  $1100$  msec relative to the onset of each digit. The epochs were then baseline-corrected relative to the 100-msec interval before digit onset. Epochs were rejected if the changes in amplitude of any scalp channel exceeded an absolute value of  $100 \mu\text{V}$  during the epoch.

A notable strength of using the SART to measure the effects of tDCS is that electrophysiological signatures of successful performance have been established in both younger and older adults (Staub et al., 2015; O’Connell, Dockree, Bellgrove, et al., 2009; Dockree et al., 2005). Components of interest were therefore selected based on these prior studies (selection negativity [SN; comprising the visual evoked P1 and visual evoked N1], frontal P2 [fP2], and frontal P3 [fP3]).

To ensure that the selection of electrodes and time windows for each of these components was identified orthogonal to the effect of interest (active relative to sham tDCS), grand-averaged waveforms of the active and sham conditions during performance of the SART<sub>fixed</sub> were combined, collapsed across block and trial type (go and no-go). The electrode with the greatest peak amplitude for each of the components of interest was identified from these grand-averaged waveforms. For the visual evoked components (P1 and N1), peak amplitudes were observed over a right parieto-occipital scalp region, electrode PO8,  $6.52$  and  $-6.39 \mu\text{V}$ , respectively. Visual evoked ERP components in response to centrally presented stimuli are typically measured bilaterally (De Sanctis et al., 2008); therefore, the SN was measured using the average signal from electrode PO8 and the homologous PO7 electrode from the contralateral hemisphere. The P1 component peak amplitude was identified at  $96$  msec, which is within the time window of previous literature investigating this ERP in aging (Daffner et al., 2013; Zanto, Rubens, Thangavel, & Gazzaley, 2011; De Sanctis et al., 2008). The N1 component peak was identified at  $150$  msec, also in line with previous work on the N1 in aging (Wiegand et al., 2014; Daffner et al., 2013; De Sanctis et al., 2008). Previous work has shown that, during performance of the SART, these two components form a monophasic SN (Dockree et al., 2005). Accordingly, the SN was calculated as the mean amplitude of the signal between the peak of the P1 wave ( $96$  msec) and the peak of the N1 wave ( $150$  msec). The fP2 peak amplitude was identified at  $158$  msec ( $4.14 \mu\text{V}$ ), which is within the time window previously reported for this component in older adults performing the SART (Staub et al., 2015). Mean amplitude values for the fP2 were calculated over a 50-msec window, centred on this peak (i.e.,  $133$ – $183$  msec). The fP2 was preceded by an anterior, frontal N1 component, previously shown to be affected by aging and related to visual attention performance (Wiegand et al., 2014). To

ensure results from the fp2 could not be attributed to potential differences in the frontal N1, the mean signal between the peak anterior N1 to peak fp2 amplitude time windows was also extracted (Table 2).

For the P1, N1, and fp2, electrode selection was performed using the SART<sub>fixed</sub>, the task of predominant interest for this study. The fp3, however, was identified using the SART<sub>random</sub>, as previous work has shown that this common marker of response inhibition (Bekker, Kenemans, Hoeksma, Talsma, & Verbaten, 2005) is crucial to performance in the SART<sub>random</sub> and of minimal relevance to the SART<sub>fixed</sub> (O’Connell, Dockree, Bellgrove, et al., 2009; Dockree et al., 2005). Again, this component was selected using the grand-averaged waveforms of active and sham combined, collapsed across block and trial type. The fp3 component peak was at 488 msec (5.14  $\mu$ V), and the component was measured over a 100-msec window (438–538 msec), centred on this peak.

ERPs were computed separately for the go-trials (digits 1, 2, 4, 5, 6, 7, 8, and 9) and for the no-go trials (digit “3”). Only no-go trials for which responses were correctly withheld by the elderly participants were included in the analysis. Given that there was no interaction between Stimulation and Block in the behavioral analysis, ERP data were collated across blocks for the EEG analysis. Outliers were defined for each ERP component as described for the performance measures above. Separate repeated-measures ANOVAs were calculated for the SART<sub>fixed</sub> and SART<sub>random</sub> with Stimulation (active vs. sham tDCS) and Trial type (go vs. no-go trials) as the within-subject factors. To identify sources of significant main and interaction effects, follow-up ANOVAs were calculated where appropriate. In the text, the reported mean values are followed by standard error (i.e.,  $M \pm SE$ ).

Several analyses were conducted to explore inter-individual variability in responsiveness to tDCS. First, to elucidate the relationship between tDCS-induced changes in the frontal and visual evoked ERPs that were modulated during stimulation, Pearson’s product-moment correlations were conducted between the fp2 and SN (one-tailed, anodal > sham). To explore whether changes in behavioral performance were directly associated with changes in electrophysiology, Pearson’s product-moment correlations were employed between the changes in commission errors during tDCS and the ERPs that were

modulated by stimulation (again, one-tailed, anodal > sham). These change scores were calculated as the difference between active and sham and were conducted separately for go and no-go trials (e.g.,  $\Delta fp2_{GoTrials} = fp2_{amplitude_{GoTrials}} - fp2_{amplitude_{No-GoTrials}}$ ). Finally, to explore whether an individual’s baseline performance was predictive of tDCS-related improvements in sustained attention, Pearson’s correlations were conducted between performance during sham stimulation and the change in performance ( $\Delta$ commission errors, two-tailed).

## Experiment 2 Methods

### Participants

Experiment 2 was designed to further verify the role of the rPFC in sustained attention in aging by assessing the extent to which the tDCS-related behavioral effects generalized to an independent sample of older adults and a separate sustained attention task (described below). Twenty-four participants were recruited for this recapitulation experiment. Again, this cohort was prescreened using the MoCA. However, in contrast to Experiment 1, this sample was not preselected based on sustained attention capacity. This was to assess whether the effects of stimulating the rPFC on sustained attention generalized to a random sample of older adults with more typical sustained attention levels. One participant did not return for the second tDCS session; therefore, the final sample consisted of 23 older adults (11 men; see Table 1 for demographic information).

### tDCS

The tDCS procedure for Experiment 2 was identical to that used in Experiment 1 except that there were no simultaneous EEG recordings during Experiment 2. As there was no concurrent EEG, it was not necessary to allow the tDCS signal to settle after the ramp-up period; therefore, in Experiment 2, the task began immediately after the current ramp-up.

### Monitoring Sustained Attention Performance

*The continuous temporal expectancy task.* During Experiment 2, the Continuous Temporal Expectancy Task (CTET; O’Connell, Dockree, Bellgrove, et al., 2009) was employed to measure sustained attention. This is a temporal judgment task designed to elicit frequent lapses in attention. For example, O’Connell et al. reported average accuracy levels of 64% ( $SD = 15\%$ , range = 37–85%) in healthy, young participants. In this task, a patterned stimulus was presented centrally and was constantly rotated at 90° angles (see Figure 2). In the “standard” trials (~90% of trials), the stimuli were presented for a temporal duration of 690 msec. The participants’ task was to identify the infrequent “target” trials by a button press using their right index finger, where the stimulus was

**Table 2.** Summary of ERPs

ERP Component	Selected Region (Electrode)	Time Window (msec)
SN	Occipito-parietal (PO7/PO8)	96–150
fp2	Frontal (Fz)	133–183
fp3	Fronto-central (FCz)	438–538

presented for a longer temporal duration (1020 msec) as compared with the standard trials. In contrast to the SART, in this task, target detection was indicated by a button press, thus eliminating any response inhibition requirement. The CTET was designed such that these temporal judgments were perceptually undemanding for participants but challenging when asked to continuously perform the judgments over longer periods; thus, all participants were required to demonstrate 100% accuracy during an initial practice trial before advancing to the experimental blocks. For the practice block, three targets were randomly interspersed among 25 standard stimuli. Target stimuli were presented at the target duration of 1020 msec, that is, 330 msec/47.83% longer than standard trials. If participants missed one or more target stimuli, the practice was performed again. All participants demonstrated 100% accuracy on two consecutive blocks before commencing the experimental blocks. The pattern stimulus consisted of a single 8-cm<sup>2</sup> large square divided into a 10 × 10 grid of identical square tiles (0.8 mm<sup>2</sup>), each one diagonally split into black and white halves. The tile orientation shifted by 90° in a random direction (clockwise or counterclockwise) on each frame change, yielding four distinct patterns. All stimuli were presented on a gray background. Stimuli were pseudorandomly presented such that there were between 7 and 15 (average of 11) standard trials between each target presentation. A target response was accepted if the participant responded up to 2070 msec (the length of three standard trials) after target onset. A wide time window for responding was implemented to ensure that errors on the task, similar to the SART<sub>fixed</sub>, were due to failures of endogenous attention, rather than deficits in information processing speed, or delayed motor responses. Moreover, we would like this task to be directly applicable to assessing sustained attention deficits in clinical groups, including pathological aging conditions (such as stroke), where confounding factors such as processing speed and motor responses are more common. However, it must be noted that the cognitively healthy older adults in the current study did not demonstrate difficulties responding promptly. Mean RT on the CTET (collapsed across conditions) was 470.47 ± 16.98 msec (range = 248–823 msec), demonstrating that participants were able to promptly signal their response to the target stimuli. Participants completed five blocks of the task and were given a rest break in between each block. Each block consisted of 225 stimulus rotations, with a total duration of approximately 3 min 5 sec. The number of targets varied between 18 and 22 per block. After tDCS, participants performed three blocks of the error awareness task, which will not be discussed.

Sustained attention changes occurring during tDCS were assessed via accuracy (percentage of correctly identified targets) on the CTET. For three participants, there were technical difficulties recording data for one of the task blocks. For these participants, performance was calculated on the average of the remaining four blocks, and

to facilitate the analysis within and across blocks, the value for the missing block was filled in with the average of the other four blocks for that participant, for the session in question. Outliers were defined on a per-block basis, as described above. Changes in performance during stimulation were assessed using repeated-measures ANOVAs with Stimulation (active vs. sham tDCS), Block (across the five task blocks), and Quartile (each block subdivided into four quarters) as the within-subject factors. Significant main and interaction effects were followed up with simple effects analyses. Greenhouse–Geisser corrected degrees of freedom are reported in cases where the assumption of sphericity was violated.

## RESULTS

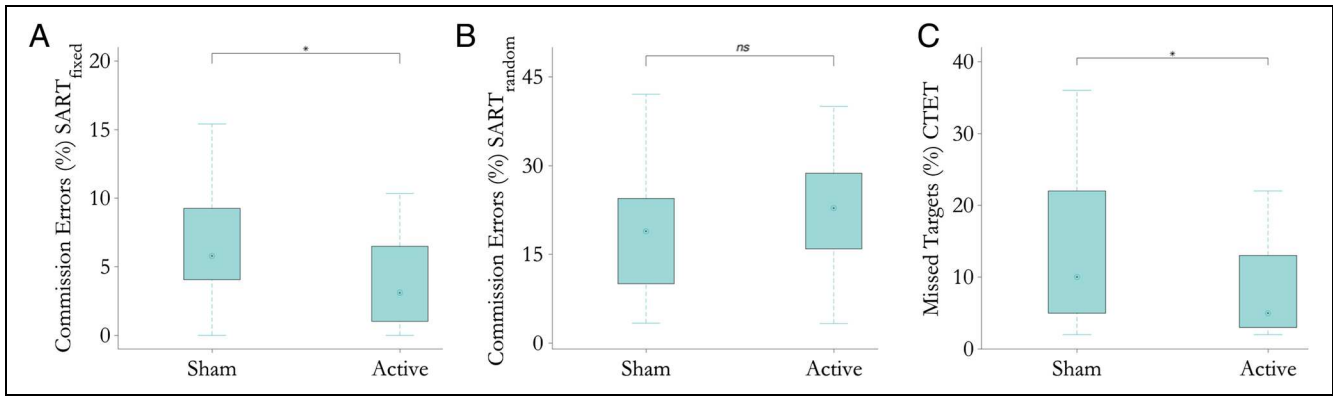
### Experiment 1 Results

#### *Behavioral Performance Changes during tDCS (SART)*

*Commission errors (SART<sub>fixed</sub>).* Consistent with our hypothesis that the rPFC would constitute a viable target region for supporting sustained attention in aging, there was a main effect of Stimulation,  $F(1, 21) = 5.1, p = .035, \eta_p^2 = .2$  (Figure 3A), on commission errors. Specifically, significantly fewer commission errors were made during the SART<sub>fixed</sub> during active ( $M = 4.06\%$   $SD = 3.36\%$ ) compared with sham ( $M = 6.20\%$ ,  $SD = 4.24\%$ ) stimulation. Baseline sustained attention was related to tDCS-related improvements in performance, such that worse performance at baseline predicted greater responsiveness to stimulation ( $r = .7, p < .0005$ ; Figure 4A). There was a trend toward a main effect of Time on the SART<sub>fixed</sub>,  $F(1, 21) = 4.00, p = .06, \eta_p^2 = .16$ , such that, regardless of stimulation, less errors were made during Block 2 ( $M = 4.47\%$ ,  $SD = 2.56\%$ ) as compared with Block 1 ( $M = 5.79\%$ ,  $SD = 4.19\%$ ). There was no interaction between Stimulation and Time for commission errors during the SART<sub>fixed</sub>,  $F(1, 21) = 0.82, p = .38$ .

*Error awareness (SART<sub>fixed</sub>).* There was no main effect of Stimulation (sham:  $M = 51.25, SD = 36.59$ ; active:  $M = 46.92, SD = 30.1$ ) or Time or any interaction effect on Error awareness during the SART<sub>fixed</sub>, all  $F_s(1, 11) < 0.5, p > .5$ . Note that the high accuracy levels of the SART<sub>fixed</sub> resulted in only 12 participants having sufficient error trials for inclusion in this error awareness calculation.

*Commission errors (SART<sub>random</sub>).* In contrast to the SART<sub>fixed</sub>, tDCS did not reduce the percentage of commission errors during the SART<sub>random</sub>,  $F(1, 25) = 0.02, p = .88$  (Figure 3B; sham:  $M = 20.27\%$ ,  $SD = 9.89\%$ ; active:  $M = 20.50\%$ ,  $SD = 10.35\%$ ). There was a main effect of Time on the SART<sub>random</sub>, whereby the percentage of commission errors made during Block 2 ( $M = 18.91\%$ ,  $SD = 10.25\%$ ) was less than that during Block 1 ( $M = 21.86\%$ ,  $SD = 9.71\%$ ),  $F(1, 25) = 4.43, p < .05$ ,



**Figure 3.** The effect of rPFC tDCS during the SART<sub>fixed</sub>, SART<sub>random</sub>, and CTET. Stimulation over the rPFC reduces commission errors during the SART<sub>fixed</sub> (A), reduces the amount of missed targets on the CTET (C), and does not alter accuracy during the SART<sub>random</sub> (B). Note that, for clarity, the CTET accuracy results were visualized here as the percentage of missed targets (100% accuracy); thus, for all tasks, higher values on the y axis denote worse performance (i.e., less accurate). \* $p \leq .05$ . "ns" denotes no significant difference between real and sham stimulation. Circular markers in the boxplots represent the median values.

$\eta_p^2 = .15$ . There was no interaction between Stimulation and Time for commission errors during the SART<sub>random</sub>,  $F(1, 25) = 0.07, p = .8$ .

**Error awareness (SART<sub>random</sub>).** There was no main effect of Stimulation (sham:  $M = 41.69, SD = 3.65$ ; active:  $M = 41.86, SD = 3.34$ ) or Time or any interaction effect on Error awareness during the SART<sub>random</sub>, all  $F_s(1, 20) < 2.9, p > .1$ .

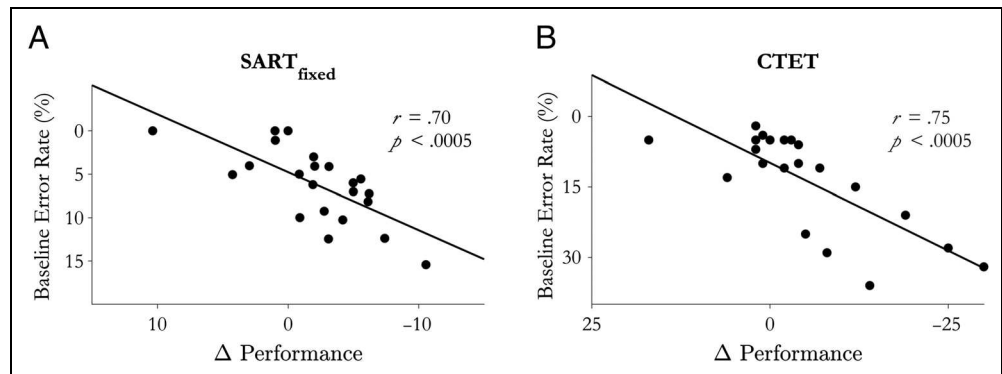
**Modulation of ERP Components during tDCS**

**The visual-evoked occipital SN.** The SN, composed of the visual evoked P1 and N1 components, is a sensitive electrophysiological marker of early visual attention engagement during performance of the SART (Dockree, Kelly, Robertson, Reilly, & Foxe, 2005). TDCS was associated with an enhanced SN amplitude during the

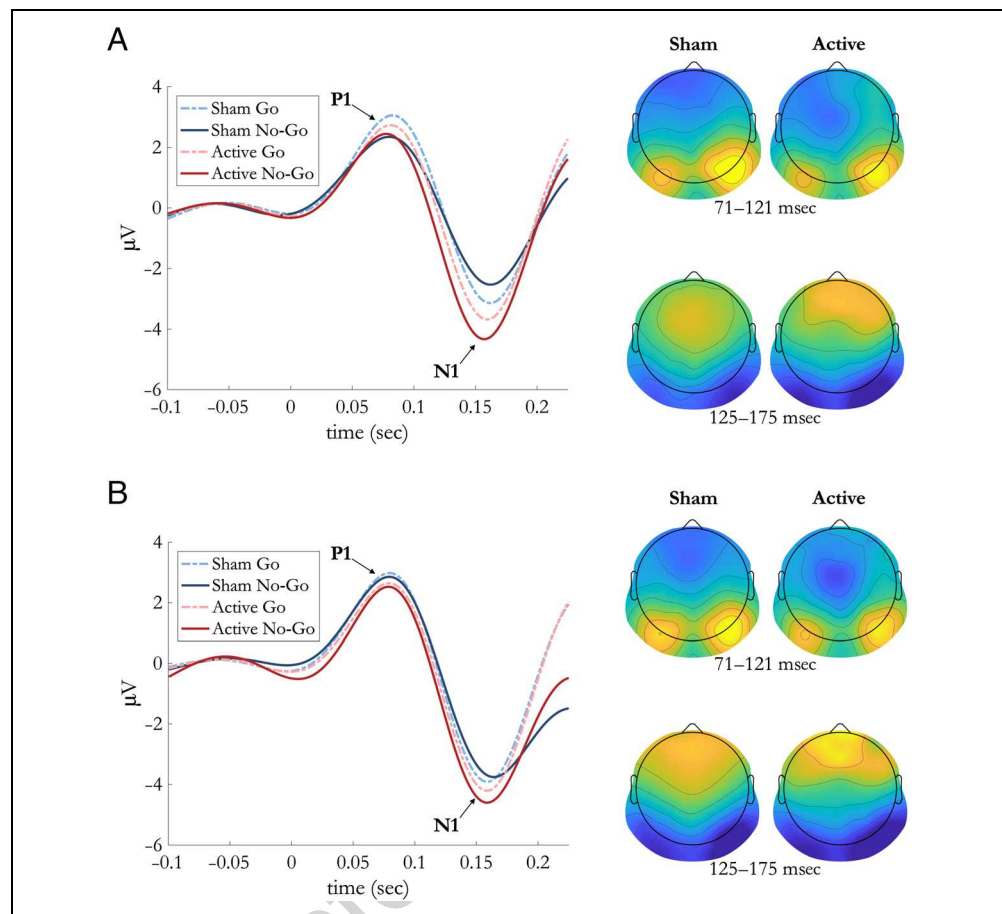
SART<sub>fixed</sub>, as evidenced by the main effect of Stimulation,  $F(1, 21) = 6.84, p = .02, \eta_p^2 = .25$ , such that the average SN amplitude was  $-1.9 (\pm 1.04) \mu V$  during active stimulation as compared with  $-0.11 (\pm 1.16) \mu V$  during sham stimulation (Figure 5A). There was a trend toward a significant main effect of Trial type,  $F(1, 21) = 4.14, p = .055, \eta_p^2 = .17$ , with slightly stronger SN amplitudes for no-go ( $-1.5 \pm 1.16 \mu V$ ) relative to go ( $-0.53 \pm 0.98 \mu V$ ) trials. There was no significant interaction between Stimulation and Trial type,  $F(1, 21) = 3.12, p = .09$ .

During the SART<sub>random</sub>, there was no difference in SN amplitude during tDCS as signified by no main effect of Stimulation,  $F(1, 16) = 0.76, p = .4$  (Figure 5B). Stronger mean SN amplitude was noted for no-go ( $-2.67 \pm 1.5 \mu V$ ) compared with go ( $-1.34 \pm 1.5 \mu V$ ) trials during the random version of the task, as illustrated by a main effect of Trial type,  $F(1, 16) = 8.9, p = .009, \eta_p^2 = .36$ .

**Figure 4.** The relationship between baseline performance and tDCS-related improvements per hemifield. There is a positive association between baseline performance and responsiveness to tDCS during both the SART<sub>fixed</sub> (A) and CTET (B), such that worse performance during sham stimulation (y axis) is predictive of greater tDCS-related improvements in sustained attention performance (x axis). Baseline error rate (%) denotes the percentage of commission errors during sham stimulation.  $\Delta \text{Performance} = \text{Active}_{\text{ErrorRate}(\%)} - \text{Sham}_{\text{ErrorRate}(\%)}$ .



**Figure 5.** (A) The effect of tDCS on the SN during the SART<sub>fixed</sub>. ERP plots (left) illustrating the effect of stimulation at electrodes PO7/PO8, and scalp plots (right) showing the topography of the components of interest (P1: 71–121 msec; N1: 125–175 msec) during both sham and active stimulation (collapsed across go and no-go trials). (B) The effect of tDCS on the SN during the SART<sub>random</sub>. ERP plots (left) illustrating the effect of stimulation at electrodes PO7/PO8, and scalp plots (right) showing the topography of the components of interest (P1: 71–121 msec; N1: 125–175 msec) during both sham and active stimulation (collapsed across go and no-go trials).



There was no interaction term for the SN amplitude during the SART<sub>random</sub>,  $F(1, 16) = 0.06, p = .81$ .

*The fp2 component.* The fp2 component is a frontal positivity, proposed to reflect greater allocation of attentional resources in older adults during performance of the SART (Staub et al., 2015; Staub, Doignon-Camus, Bacon, & Bonnefond, 2014). During the SART<sub>fixed</sub>, an enhanced fp2 amplitude was observed during active ( $3.85 \pm 0.40 \mu\text{V}$ ) versus sham ( $2.9 \pm 0.45 \mu\text{V}$ ) tDCS (Figure 6A), as evidenced by a main effect of Stimulation,  $F(1, 21) = 5.1, p = .035, \eta_p^2 = .2$ . There was no main effect of Trial type,  $F(1, 21) = 0.09, p = .77$ , or any interaction between Trial type and Stimulation on the SART<sub>fixed</sub>,  $F(1, 21) < 0.58, p > .45$ . Follow-up analyses conducted using the peak anterior N1 to peak fp2 time window revealed the same pattern of results; a significant main effect of Stimulation was observed,  $F(1, 21) = 5.82, p = .03, \eta_p^2 = .22$ , with a greater frontal positivity observed during active ( $1.44 \pm 0.34 \mu\text{V}$ ), relative to sham ( $0.59 \pm 0.38 \mu\text{V}$ ), tDCS. There was no main effect of Trial type,  $F(1, 21) = 0.17, p = .69$ , and no interaction term,  $F(1, 21) = 0.24, p = .63$ . These additional analyses indicate that the effect of tDCS on the fp2 could not be attributed to any stimulation-induced changes in the anterior N1.

There was no main effect of Stimulation,  $F(1, 16) = 3.72, p = .07$  (Figure 6B), or Trial type,  $F(1, 16) = 3.14, p = .1$ , or any interaction term during the SART<sub>random</sub>,  $F(1, 16) < 0.04, p > .8$ . Using the peak anterior N1 to peak fp2 approach, these results did not change; there was no main effect of Stimulation,  $F(1, 16) = 3.87, p = .07$ , or Trial type,  $F(1, 16) = 3, p = .1$ , or any interaction effect on the frontal positivity,  $F(1, 16) = 0.07, p = .79$ .

*The fp3 component.* The fp3 component is a frontal positivity with established links to response inhibition processes (O'Connell, Dockree, Bellgrove, et al., 2009; Bekker et al., 2005; Dockree et al., 2005). There was no effect of Stimulation,  $F(1, 21) = 1.66, p = .21$ , on the fp3 during the SART<sub>fixed</sub> (Figure 7A). There was a main effect of Trial type,  $F(1, 21) = 9.66, p = .005, \eta_p^2 = .32$ , with greater fp3 amplitudes for go ( $2.44 \pm 0.73 \mu\text{V}$ ) relative to no-go ( $0.73 \pm 0.58 \mu\text{V}$ ) trials. There was no interaction term,  $F(1, 21) < 0.44, p > .51$  (Figure 7A).

The fp3 was not modulated by tDCS during the SART<sub>random</sub> either, as evidenced by no main effect of Stimulation,  $F(1, 16) = 2.38, p = .14, \eta_p^2 = .13$  (Figure 7B). In direct contrast to the SART<sub>fixed</sub>, a main effect of Trial type,  $F(1, 16) = 10.61, p = .005, \eta_p^2 = .4$ , during performance of the SART<sub>random</sub> demonstrated an enhanced amplitude

of the fp3 marker of response inhibition during no-go ( $6.62 \pm 1.08 \mu\text{V}$ ), as compared with go ( $3.36 \pm 0.67 \mu\text{V}$ ), trials. There was no interaction effect,  $F(1, 176) < 0.02, p > .88$ .

*The relationship between electrophysiology and behavior.* Amplitude modulation of the fp2 component during right prefrontal tDCS compared with sham was correlated with amplitude modulation of the visual-evoked SN for both go ( $r = -.75, p < .0005$ ) and no-go ( $r = -.71, p < .0005$ ) trials. Neither stronger amplitude modulation of the fp2 component (go trials:  $r = -.26, p = .15$ ; no-go trials:  $r = -.03, p = .44$ ) nor the SN (go trials:  $r = .14, p = .29$ ; no-go trials:  $r = -.04, p = .44$ ) was associated with tDCS-related changes in commission errors.

### Interim Conclusion

In Experiment 1, it was observed that increasing excitability of the rPFC reduced the number of attention lapses on the SART<sub>fixed</sub> in older adults who were vulnerable to deficits in sustained attention. Concurrent tDCS-EEG recordings revealed that rPFC stimulation enhanced EEG markers of frontal engagement (the fp2) and early sensory processing (the SN), indicating that prefrontal stimulation enhanced top-down attention engagement over early stimulus processing.

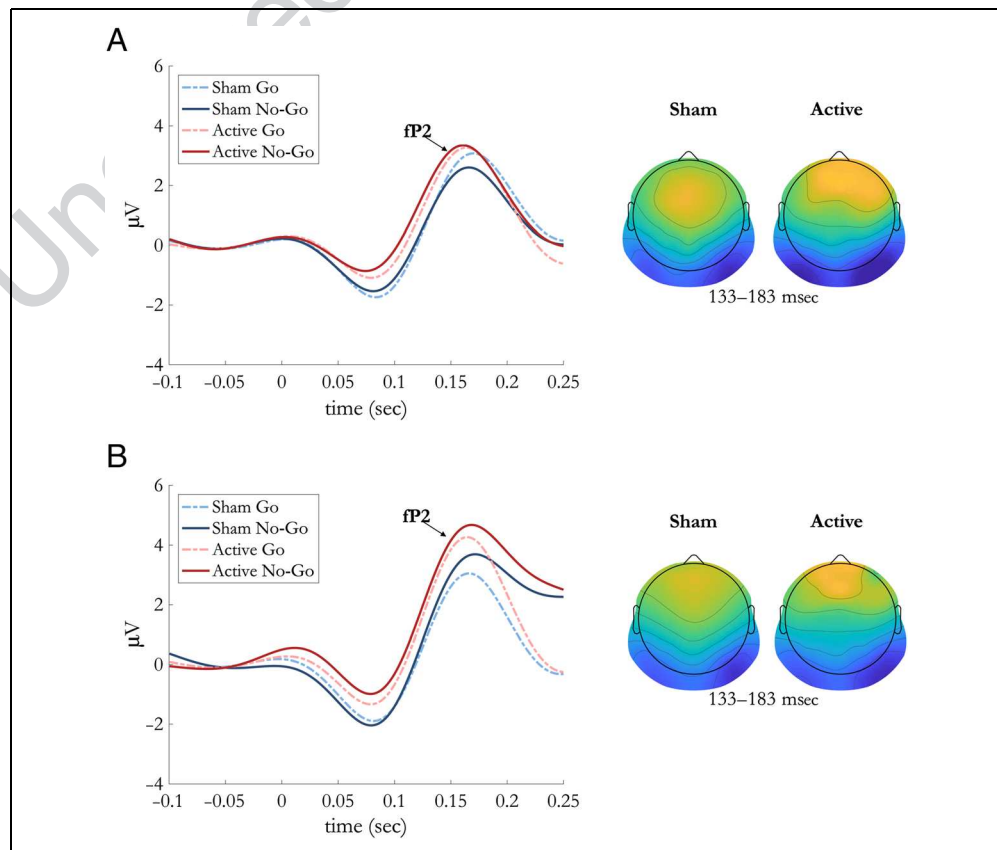
The first aim of Experiment 2 was to explore whether the benefits of rPFC tDCS on sustained attention performance would replicate in an independent cohort of older adults with more typical levels of sustained attention (i.e., not preselected based on low performance). The second aim of Experiment 2 was to verify that the effect of rPFC tDCS on performance could be specifically attributed to the process of sustained attention, as opposed to other task-specific requirements. Although the SART<sub>fixed</sub> is an established, sensitive measure of sustained attention (Smilek et al., 2010; Manly et al., 2003; Robertson, Manly, et al., 1997), successful performance on the task also necessitates both the capacity to inhibit a response to a no-go trial (albeit a predictably occurring number embedded within a continuous sequence) and the ability to effectively process and identify a visually presented target stimulus. As such, sustained attention performance during Experiment 2 was measured using a paradigm free from response inhibition demands and using a target stimulus that necessitates detecting a change within the temporal, as opposed to visual, domain.

### Experiment 2 Results

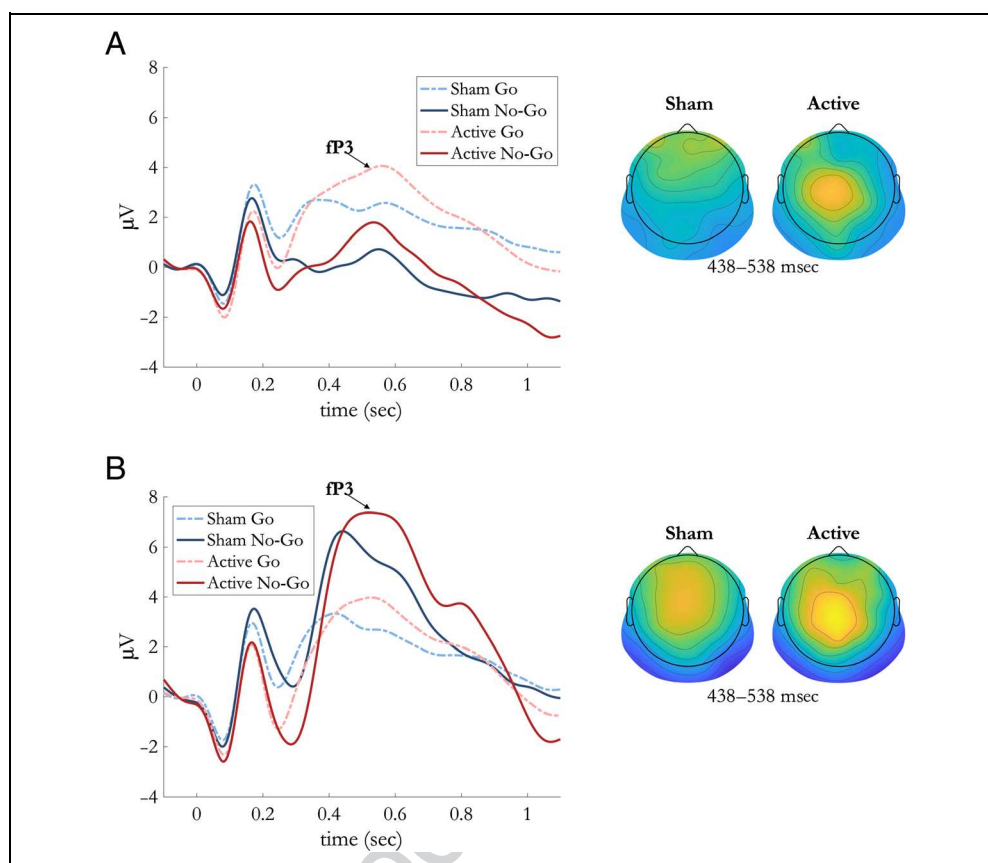
#### *Behavioral Performance Changes during tDCS (CTET)*

The rate of false alarms was low during the CTET ( $M = 2.64\%$ ,  $SD = 1.99\%$ , range = 1–9%) indicating that all participants were performing above chance level. A main

**Figure 6.** (A) The effect of tDCS on the fp2 component during the SART<sub>fixed</sub>. ERP plots (left) illustrating the effect of stimulation on the P2 component at electrode Fz, and scalp plots (right) showing the topography of the fp2 (133–183 msec) during both sham and active stimulation (collapsed across go and no-go trials). (B) The effect of tDCS on the fp2 component during the SART<sub>random</sub>. ERP plots (left) illustrating the effect of stimulation on the P2 component at electrode Fz, and scalp plots (right) showing the topography of the fp2 (133–183 msec) during both sham and active stimulation (collapsed across go and no-go trials).



**Figure 7.** (A) The effect of tDCS on the fp3 component during the SART<sub>fixed</sub>-ERP plots (left) illustrating the effect of stimulation on the fp3 component at electrode FCz, and scalp plots (right) showing the topography of the P3 (133–183 msec) during both sham and active stimulation (collapsed across go and no-go trials). (B) The effect of tDCS on the fp3 component during the SART<sub>random</sub>-ERP plots (left) illustrating the effect of stimulation on the fp3 component at electrode FCz, and scalp plots (right) showing the topography of the P3 (133–183 msec) during both sham and active stimulation (collapsed across go and no-go trials).



effect of Stimulation,  $F(1, 20) = 4.67, p = .043, \eta_p^2 = .19$  (Figure 3C), indicated that accuracy was significantly higher during active ( $M = 91.4\%, SD = 7.36\%$ ), compared with sham ( $M = 86.45\%, SD = 10.43\%$ ), stimulation. As observed in Experiment 1, worse performance at baseline (during sham stimulation) was associated with greater tDCS-related benefits to sustained attention performance ( $r = .75, p < .0005$ ; Figure 4B).

A main effect of Quartile demonstrated that, regardless of stimulation, accuracy levels decreased over time within each block,  $F(3, 60) = 6.51, p = .001, \eta_p^2 = .25$ , as evidenced by the significant linear contrast,  $F(1, 20) = 10.76, p = .004, \eta_p^2 = .350$ . More specifically, the older adults showed a significant drop in accuracy between the first and second,  $F(1, 20) = 6.49, p = .01, \eta_p^2 = .25$ ; second and third,  $F(1, 20) = 7.22, p = .014, \eta_p^2 = .27$ ; and third and fourth,  $F(1, 20) = 11.12, p = .003, \eta_p^2 = .36$ , quarters of the task blocks. A main effect of Block indicated that accuracy levels also changed significantly over time across the five task blocks,  $F(4, 80) = 5.61, p = .005, \eta_p^2 = .22$ . This effect was best fit to a cubic contrast,  $F(1, 20) = 9.86, p = .005, \eta_p^2 = .33$ ; a significant decrease in accuracy was noted between the first task block, and Block 2,  $F(1, 20) = 9.53, p = .006, \eta_p^2 = .32$ , Block 3,  $F(1, 20) = 10.34, p = .004, \eta_p^2 = .34$ , and Block 5,  $F(1, 20) = 7.63, p = .01, \eta_p^2 = .28$ , but not Block 4,  $F(1, 20) = 1.88, p = .19, \eta_p^2 = .09$ . There were no significant interaction terms (all  $ps > .07$ ).

## DISCUSSION

This study demonstrated in two separate cohorts of older adults that increasing activity in the rPFC improved sustained attention performance. These performance benefits were observed on two very different task paradigms, indicating that the effects of rPFC stimulation were not specific to a given sustained attention paradigm but rather to the process of sustained attention. Simultaneous tDCS-EEG recordings showed that tDCS was associated with an increased visual evoked SN component over parieto-occipital scalp regions as well as an enhanced frontally distributed P2 component. These findings suggest that tDCS induced an adaptive increase in attention and stimulus processing resources and modulated early frontal engagement in concert with greater deployment of visual attention.

### Right Prefrontal Contributions to Sustained Attention in Aging

The ability to sustain attention to the task at hand is fundamental to performance across a range of cognitive tasks (Taylor-Phillips et al., 2014; Smilek et al., 2010; Schwebel, Lindsay, & Simpson, 2007; Edkins & Pollock, 1997) and contributes to both cognitive and physical health in aging (O'Halloran et al., 2011, 2014; Robertson, 2014). Here, we provide empirical evidence that the rPFC

may be manipulated to improve the capacity to maintain attention in older adults.

In Experiment 1, we observed that increasing activity in this region was associated with improved sustained attention performance in a group of older adults with compromised sustained attention abilities. These performance benefits were specific to sustained attention and not observed for response inhibition processes necessitated during a modified version of the SART. To address the replicability of our results, which was of particular importance given that large interindividual variability in responsiveness to tDCS is a marked methodological concern for this technique (Li, Uehara, & Hanakawa, 2015; Wiethoff, Hamada, & Rothwell, 2014), we conducted a second behavioral experiment in an independent cohort of participants. Again, we observed that increasing excitability in the rPFC improved sustained attention performance in older adults. These results support indirect evidence from behavioral and pharmacological interventions that the rPFC might be a viable structure to support the remediation of sustained attention in aging (Milewski-Lopez et al., 2014; Singh-Curry et al., 2011; Malhotra et al., 2006).

### **Prefrontal Modulation of Early Visual Attention Processes**

Concurrent tDCS-EEG recordings identified two electrophysiological components that were modulated during tDCS. First, a stronger frontally distributed fp2 component was observed during stimulation. Stronger fp2 amplitudes during performance of the SART have been noted in older adults and interpreted as greater mobilization of top-down attentional resources (Staub et al., 2014, 2015). Our findings thus suggest that increasing right prefrontal activity heightened top-down frontal engagement during the task.

An enhanced SN was noted over occipito-parietal scalp regions during tDCS. Greater visual-evoked neural responses are typically considered an adaptive compensatory strategy of cognitively healthy older adults (Wiegand et al., 2014; De Sanctis et al., 2008; Daffner et al., 2006). Recent modeling work suggests that aging is associated with an increase in prefrontal inputs, which in turn drive stimulus-evoked EEG signals emanating from visual regions (Gilbert & Moran, 2016). Here, during tDCS over PFC, an increase in early frontal activity was observed that was strongly associated with enhanced early visual evoked responses, thus supporting the proposal that a functional pathway exists to support this top-down modulatory effect from prefrontal regions in older adults (Gilbert & Moran, 2016).

Early visual evoked electrophysiological responses in older adults are malleable in nature. Behavioral interventions, such as visual discrimination training protocols, have been shown to alter early visual ERPs with corresponding improvements in both early visual attention

processes and higher cognitive operations (Mishra, Rolle, & Gazzaley, 2015; Berry, Zanto, Clapp, Hardy, & Delahunt, 2010). The results presented in this article complement these earlier findings and show that increasing top-down control from PFC can potentiate electrophysiological markers of visual attention. This adds to evidence that the rPFC may support the efficiency at which visual information is processed in older adults (Brosnan et al., 2018).

### **Separate Neural Underpinnings for Sustained Attention and Response Inhibition**

The current study supports previous behavioral and neurophysiological evidence regarding a distinct role of response inhibition for successful performance of the SART<sub>random</sub> and not the SART<sub>fixed</sub> (O'Connell, Dockree, Bellgrove, et al., 2009; Dockree et al., 2005). Previous work has shown that, during response inhibition tasks with repeated stimulus-response mappings (as in a go/no-go paradigm like the SART), a shift toward bottom-up automated inhibition processes is progressively observed while top-down modulation from frontal control regions is gradually decreased (Verbruggen & Logan, 2008; Shiffrin & Schneider, 1977). Consistent with the automatic inhibition hypothesis where automatic processes develop over practice, in the current cohort of older adults, performance on the SART<sub>random</sub> was significantly better during the second block relative to the first block, irrespective of stimulation. Further evidence that response inhibition processes are predominating during performance of the SART<sub>random</sub> is the highly prevalent, frontally distributed P3 component that has been conceptualized by many as a marker of effective response inhibition (Bekker et al., 2005). In line with previous ERP investigations of the SART, this was more pronounced during no-go relative to go trials (O'Connell, Dockree, Bellgrove, et al., 2009). In support of different mechanisms governing performance during the two versions of the SART, the opposite pattern was observed during the SART<sub>fixed</sub>; that is, a more pronounced fp3 was elicited for go relative to no-go trials.

In the current set of experiments, tDCS targeting the right DLPFC reduced the number of attentional lapses on the two tasks (SART<sub>fixed</sub> and CTET), which heavily rely on the capacity for sustained attention. In contrast, lapses on the SART<sub>random</sub> were not altered by tDCS, and tDCS did not enhance any of the task-relevant electrophysiological signals. Moreover, tDCS did not modulate the fp3 component, a classic marker of response inhibition, during performance of the SART<sub>fixed</sub>. Thus, previous work outlining the contribution of the DLPFC to top-down attentional control (Brosnan & Wiegand, 2017; Gbadeyan, McMahon, Steinhäuser, & Meinzer, 2016), and not response inhibition, is supported (Manly et al., 2003).

## **The rPFC as a Target Region for Cognitive Interventions in Aging**

The right-lateralized LC-NE alertness system subserves a myriad of cognitive functions (Sara, 2009, 2015; Sara & Bouret, 2012; Hurley, Devilbiss, & Waterhouse, 2004) and, in the first neuroscientific theory of cognitive reserve, has been proposed to play an important contribution for healthy cognitive aging (Robertson, 2014). Our results demonstrate that increasing excitability of the rPFC in older adults improves sustained attention, a facet of cognition that is tightly linked with this system (Robertson, 2014; Singh-Curry et al., 2011; Malhotra, Coulthard, & Husain, 2009). Older adults with worse sustained attention capacity at baseline benefited most from stimulation, indicating that the rPFC might be a viable target region for neurorehabilitation interventions aimed at remediating sustained attention in individuals with compromised performance.

Visual processing speed and error awareness are cognitive processes that exhibit close ties with the right-lateralized LC-NE alertness network (Wiegand et al., 2017; Robertson, 2014; Matthias et al., 2009). Using an identical tDCS montage (current strength, electrode size, and placement), it has been shown that increasing excitability of the rPFC temporarily enhances both of these processes (Brosnan et al., 2018; Harty et al., 2014). Similar performance benefits were not observed in these aforementioned studies for anodal left PFC (Harty et al., 2014), anodal right parietal (Brosnan et al., 2018), or cathodal rPFC tDCS (Harty et al., 2014). The experiments presented in the current article further suggest that this tDCS montage is a promising protocol to increase excitability within the rPFC and modulate alertness-based cognitive functions in older adults. There is mounting evidence to suggest that the rPFC exerts a top-down modulatory role over noradrenergic activity emanating from the locus coeruleus (Carter et al., 2010; Raizada & Poldrack, 2008; Jodoj, Chiang, & Aston-Jones, 1998; Robinson & Coyle, 1980; Robinson, 1979). It is a question for future research to directly address using markers of noradrenergic activity (McGinley et al., 2015; Murphy, O'Connell, O'Sullivan, Robertson, & Balsters, 2014) whether rPFC tDCS improves cognitive performance by enhancing top-down modulation over LC-NE activity.

## **Limitations and Outlook**

In line with previous reports (Li et al., 2015; Wiethoff et al., 2014), we observed high levels of interindividual variability in responsiveness to tDCS. Several potential sources contributing to this variability have already been highlighted (Bestmann, de Berker, & Bonaiuto, 2015; Laakso, Tanaka, Koyama, De Santis, & Hirata, 2015; Opitz, Paulus, Will, Antunes, & Thielscher, 2015; de Berker, Bikson, & Bestmann, 2013; Bradnam, Stinear, Barber, &

Byblow, 2012), and as we further our understanding of this variability, it may be possible to deliver tDCS in a more precise and individualized manner. Nevertheless, it is important to note that the results presented in the current article are not an endorsement for the potential for tDCS, in its current form, as a rehabilitation tool to remediate attentional deficits in aging. Rather, the current results add to the growing evidence that the rPFC exhibits preserved levels of plasticity in older adults (Brosnan et al., 2018; Harty et al., 2014) and that this may be a promising structure to target to ameliorate alertness-based cognitive functions in older adults.

In the current study, we demonstrate that increasing cortical excitability in the rPFC using tDCS (a) reduces lapses in sustained attention and (b) strengthens the amplitude of frontal and visual-evoked ERPs. The effect of tDCS on the ERP signals was not related to the tDCS-related changes in behavior. Whether this represents an indirect relationship between the effect of prefrontal stimulation on early sensory processing and sustained attention performance, or whether this is due to a lack of signal to noise in our measurements, is a question subject to further investigation.

## **Conclusions**

This study suggests the rPFC is a viable brain area to support the remediation of age-related decrements in sustained attention. During rPFC stimulation, improvements in sustained attention were observed, both in a cohort of cognitively healthy older adults (Experiment 2) and in older adults who presented with suboptimal attention performance, relative to normative data based on over 5,000 individuals (Experiment 1). tDCS-Related performance changes were observed on two very different sustained attention tasks, suggesting that the behavioral changes associated with increasing rPFC excitability were process specific, not task specific. These findings therefore place the rPFC as a promising target region to improve sustained attention in clinical populations whose capacity for sustained attention is compromised, for example, after right-hemisphere stroke (Rueckert & Grafman, 1996, 1998; Robertson, Ridgeway, Greenfield, & Parr, 1997; Wilkins, Shallice, & McCarthy, 1987).

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Uncorrected Proof