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Multi-Session Anodal Prefrontal Transcranial Direct Current Stimulation does not Improve Executive Functions among Older Adults

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Abstract

Objective: Findings from single-session online studies highlighted the potential of using anodal prefrontal transcranial direct current stimulation (tDCS) to enhance executive functions (EF) in the context of aging. However, tDCS must be executed as a multi-session offline intervention to ascertain its viability in this context. Relatedly, findings from multi-session studies remained inconclusive. To this end, we examined the effects of multi-session anodal prefrontal tDCS on EF in an intervention. **Method:** The intervention consisted of 15 sessions; in each, healthy older participants ($Age_{mean} = 66.7$) received either 15 min of 1.5 mA tDCS ($N_{completed} = 35$) or sham stimulation ($N_{completed} = 33$) while performing EF training tasks. EF measures were assessed at baseline, post-intervention, and 1-month follow-up. Hierarchical linear models were used to examine the effect of tDCS on EF outcomes. **Results:** Both groups of participants did not differ significantly in side effect ratings and attendance. There were no significant tDCS-associated gains in any EF outcomes in the intervention. **Conclusions:** Multi-session prefrontal tDCS did not lead to any significant gains in EF in the current intervention. More research is needed to optimize the use of tDCS before it can be effectively used to enhance EF among older adults.

Keywords: tDCS, Intervention, Executive functions, Aging

INTRODUCTION

Executive function (EF) is a goal-directed, multi-component cognitive control process that enables one to override automatic or established thoughts and responses. It constitutes several cognitive abilities such as inhibition, mental flexibility, working memory (Diamond, 2013). EF, like most cognitive abilities in general, tends to decline with age (De Luca et al., 2003). To this end, there has been a growing interest in using transcranial direct current stimulation (tDCS) among healthy adults and geriatric populations to remediate EF impairments, delay subsequent EF decline, or even enhance one's baseline functioning (Cappon, Jahanshahi, & Bisiacchi, 2016). This noninvasive brain stimulation approach delivers weak current to the targeted areas via electrodes attached to the scalp. Typically, one of the electrodes (anode) is positioned over the dorsolateral prefrontal cortex (dlPFC) in studies targeting EF abilities (Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016); anodal tDCS alters the dlPFC-related functions by depolarizing the neuronal membrane and increasing its excitability, facilitating more spontaneous cell firing (Lefaucheur et al., 2017). Repeated stimulation induces a late-phase long-term potentiation, whereby the elevated neuronal excitability remains stable for more than 24 hr poststimulation, possibly leading to long-term changes in brain functioning (Monte-Silva et al., 2013).

According to two meta-analyses (Hsu, Ku, Zanto, & Gazzaley, 2015; Summers, Kang, & Cauraugh, 2016), tDCS on healthy older participants and those with Alzheimer's disease (AD) had resulted in significant improvements in cognitive outcomes as characterized by moderate to large effect sizes. Nevertheless, most of the studies included in these meta-analyses were those of single-session online design (cognitive assessments during the stimulation) which may not translate well to the real-life context. For instance, it would be impractical for one to carry a tDCS device with electrodes attached to his/her scalp and have it switched on all the time for the online effect. Furthermore, single-session stimulation, relative to multi-session stimulation, is unlikely to trigger a

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late-phase long-term potentiation that will result in long-term changes in brain functioning (Monte-Silva et al., 2013). Relatedly, a meta-analysis of single-session offline (poststimulation cognitive assessments) tDCS interventions did not reveal significant treatment effects in any cognitive domains (Horvath, Forte, & Carter, 2015).

For tDCS to be considered as a viable cognitive enhancement strategy, it has to produce sustainable offline gains in cognitive abilities. This is best demonstrated via multi-session offline intervention studies. Among those that carried out anodal prefrontal tDCS, some (Hanley & Tales, 2019; Jones, Stephens, Alam, Bikson, & Berryhill, 2015; Lawrence, Gasson, Johnson, Booth, & Loftus, 2018; Manenti et al., 2016; Park, Seo, Kim, & Ko, 2014; Stephens & Berryhill, 2016) found significant tDCS-associated gains in one or few of the EFs measured. However, the rest of these intervention studies (Cotelli et al., 2014; Fazeli, Woods, Pope, Vance, & Ball, 2019; Fileccia et al., 2019; Huo et al., 2018; Khedr et al., 2014; Manor et al., 2018; Nilsson, Lebedev, Rydström, & Lövdén, 2017; Ownby & Acevedo, 2016) did not observe significant tDCS-associated gains in any EF tests administered in their studies. One study even reported significant EF gains in the sham stimulation group, but not the tDCS group (Das et al., 2019). It should be noted that these studies had relatively small sample sizes ($N_{treatment\ group} \leq 21$), apart from a few exceptions ($N_{treatment\ group} \geq 30$; Huo et al., 2018; Nilsson et al., 2017; Stephens & Berryhill, 2016). Taken together, the current state of the evidence is inconclusive at best.

Most of these studies had paired stimulation with some kind of adjunctive cognitive training (CT), with a few exceptions (Hanley & Tales, 2019; Huo et al., 2018; Khedr et al., 2014; Manenti et al., 2016; Manor et al., 2018). Some researchers (Jones et al., 2015; Nilsson et al., 2017) suggest that tDCS would enhance transfer effects of such training to other cognitive domains. To this end, we paired tDCS with various EF training tasks in our study, so as to maximize intervention-related gains in cognitive functions.

In the current study, we sought to make a meaningful contribution to the existing pool of evidence, via our relatively large sampled intervention. We administered anodal prefrontal tDCS or sham stimulation, on top of an adjunctive EF training protocol, to older adults across 15 sessions. It should be noted that the current study is interested in the effects of the stimulation rather than that of the EF training protocol. In particular, we hypothesized that participants who received tDCS, relative to their sham stimulation counterparts, would experience significant gains in EF.

MATERIAL AND METHODS

Design

The consort flow diagram is shown in Figure 1. Due to the limited number of tDCS apparatus, the intervention study had to be carried out in batches of up to 15 participants. Within each batch, all participants were assigned to the same condition (either tDCS or sham); there would not be a mixed group of tDCS or sham condition participants in any batch. The assignment of the batches to either conditions was alternated periodically in a random manner. The recruitment and assignment of batches were carried out by the same team of research assistants. Baseline assessments were carried out prior to intervention. The intervention consisted of 15 one-hr sessions, spread across 3 weeks. Subsequently, post-intervention assessments and another round of assessments 1 month later were administered. This was a single-blind trial in which only the experimenter, and not the participants, was aware of which condition the latter was assigned to. Experimental procedures were implemented according to the declaration of Helsinki.

Intervention Protocol

As with most studies in this area, stimulation was paired with an adjunctive CT in the current study. Participants in both groups were administered the same computerized CT, which was designed for the current study. Briefly, this CT comprised of 10 different tasks and trained participants to react as quickly as possible to various stimuli, inhibit dominant responses and multitask. Each of these tasks is described in detail in the Supplementary Material. The trial items in these tasks consisted of visual and/or auditory stimuli; none of the stimuli used in the CT had any resemblance to those in our cognitive measures. Feedback was provided immediately after every trial. In each session, participants completed a different combination of four such tasks; each task took approximately 15 min to complete. Each of the 10 different tasks would have been repeated 6 times over the 15 sessions.

In both the tDCS and sham stimulation conditions, two 35 cm^2 rubber electrodes, enclosed in saline solution-soaked sponge pads, were placed on participant's scalp using adjustable rubber belts. The anode and cathode were located over the F3 and FP2, respectively, in accordance with the international 10–20 system for electrode placement (Herwig, Satrapi, & Schönfeldt-Lecuona, 2003). These positions were chosen because they were most commonly reported among studies targeting EF gains in a meta-analysis (Dedoncker et al., 2016). A previous study had modeled the current flow profile of this tDCS montage, using similar size of electrodes and magnitude of current; this tDCS setup resulted in a relatively high average current density (0.28 Am^{-2}) in the left dlPFC (Ramaraju, Roula, & McCarthy, 2018). In each session, participants in both groups were administered three doses of stimulation from a battery-driven tDCS device (NeuroConn, Germany), corresponding to the start of each of the first three tasks in the CT. The stimulation parameters of these doses differed between the tDCS and sham stimulation conditions. In the former, 1.5 mA current stimulation was delivered across a 5-min interval for each dose, with an additional 15 s of fade-in and 15 s of fade-out time. In the latter, 1.5 mA current stimulation was delivered across a 15-s interval for each dose without

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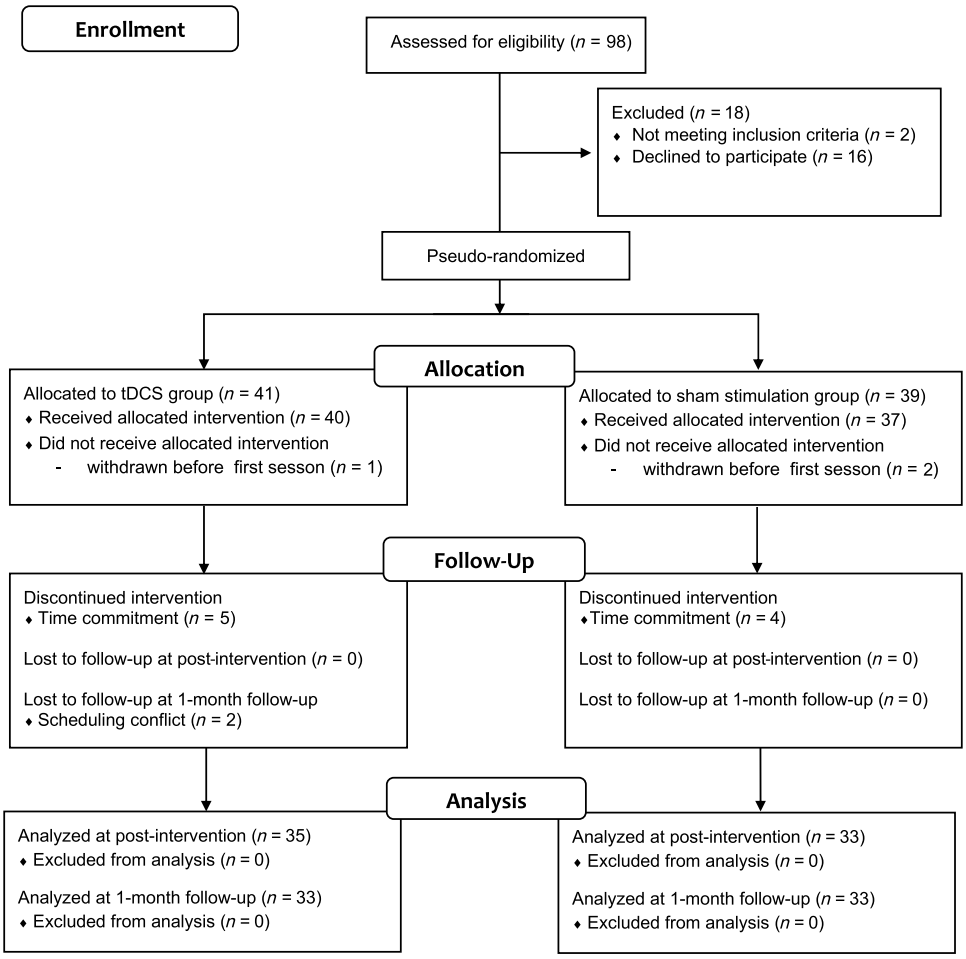

Fig. 1. Consort flow diagram. tDCS = transcranial direct current stimulation.

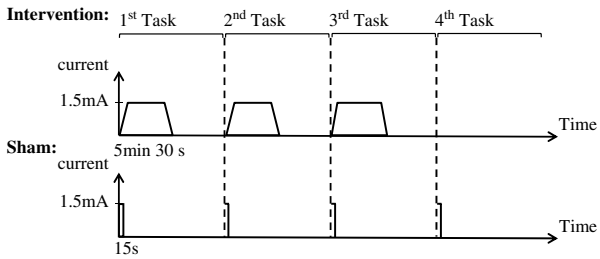

Fig. 2. Stimulation profiles in the tDCS and sham stimulation conditions.

any fade-in or fade-out. Figure 2 illustrates these stimulation profiles in tDCS and sham stimulation conditions.

Participants

Participants were recruited from the community via word of mouth and with the help of various nongovernmental organizations in Hong Kong. They were not given any financial incentives for their participation. The inclusion criteria were: (a) ages between 60 and 80 inclusive, (b) not cognitively impaired as defined by having a Montreal Cognitive Assessment score of 22 and above (Wong et al., 2009), (c) not depressed, as defined by having a geriatric depression scale (15-item) score of 7 and below (Boey & Chiu, 1998), (d) do not report having any present neurological and psychiatric conditions, and (e) do not have contraindications for tDCS, such as having a cerebral implant or history of seizures. Written informed consent was obtained from these participants prior to their participation. Ethical approval for the current study was granted by the Human Research Ethics Committee at the University of Hong Kong.

A total of 80 participants were pseudo-randomly assigned to the 2 treatment groups. Participants were deemed to have "completed" the intervention if they had attended at least 12

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Table 1. Participants' characteristics at baseline

	Conditions		Between-group comparison		
	tDCS ($N = 41$)	Sham ($N = 39$)	t	χ^2	p
Mean age in years (*SD*)	66.95 (4.53)	66.31 (4.43)	.64		.238
No. of males (%)	11 (26.8)	7 (17.9)		.90	.182
Mean years of education (*SD*)	11.17 (4.49)	13.15 (3.59)	2.17		.018
Mean GDS score (*SD*)	2.37 (2.00)	3.18 (2.20)	1.73		.125
Mean MoCA score (*SD*)	26.41 (2.44)	26.77 (2.32)	.67		.162

Note. tDCS = transcranial direct current stimulation; *SD* = standard deviation; GDS = geriatric depression scale; MoCA = Montreal cognitive assessment.

out of the 15 sessions. The characteristics of all participants included at baseline are presented in Table 1. Nonsignificant t and chi-square test statistics suggest that both groups were similar in terms of age, gender distribution, depression symptoms, and general cognitive ability. However, there was a significant but small difference between both groups in the years of education (Cohen's $d = .49$).

Measures

The Color Trails Tests (CTT) (D'Elia & Satz, 1996) was used to assess divided attention. The CTT consists of two parts. In the first, participants connected a series of numbers which were printed within colored circles, sequentially from 1 to 25. Subsequently, in the second part, participants alternated between choosing numbers in either pink or yellow circles while similarly connecting the numbers from 1 to 25. Divided attention was operationalized as the completion time for the second part and the interference effect, which is the difference in completion times of the first and second parts, divided by the former. A previous local validation study (Lee & Chan, 2000a) had found that completion time of the second part in the CTT correlated significantly ($r = .72$) with that of the trail making test.

A local Chinese adaptation (Lee & Chan, 2000b) of the Stroop Color-Word Test (Victoria version) (Spreen & Strauss, 1998) was used to measure selective attention/cognitive inhibition. The test stimuli consisted of three cards for the conditions of dot, word, and color-word. In each card, the items (appearing in blue, green, red, and yellow colors) were presented in a 4 × 6 matrix. The dot condition was administered first; participants were instructed to name the color of the dots as quickly as possible. Next, participants named the colors of Chinese characters, first in the word condition and then in the color-word condition. Frequently used Chinese characters, unrelated to color, were presented in the word condition, while lexicons of color terms were presented in the color-word condition. Selective attention was operationalized as the completion time for the color-word condition and the interference effect—the difference in completion times between the color-word and dot conditions. A local validation study reported the test–retest reliabilities, over a 1-month interval, of the completion times for the three tasks to range from .89 to .91 (Lee & Chan, 2000b).

The Ruff Figural Fluency Test (RFFT) (Ruff, Light, & Evans, 1987) is a measure of nonverbal fluency and flexibility. The test consisted of five parts. In each part, participants were given 60 s to draw as many unique designs as possible by connecting at least two out of the five dots in the box. In parts one to three, the dots were arranged in a pentagon, whereas in parts four and five the dots were scattered asymmetrically. Distractors such as diamond shapes and other lines were present in parts two and three. The total number of unique designs across all five parts was used as a measure of nonverbal fluency. This score was shown to correlate significantly with other tests of EFs ($r \geq .22$; Kuiper, Oude Voshaar, Verhoeven, Zuidema, & Smidt, 2017).

The DX second edition (Culbertson & Zillmer, 2005) of the Tower of London (ToL) was used to assess planning ability. The ToL consisted of a tower structure with three pegs and three colored beads which were placed in various starting positions. There were 15 trials, each with a different starting position for the 3 beads. The participant was instructed to move the beads on his or her tower structure to match the bead configuration on the examiner's tower structure using the fewest moves possible. The total correct score, that is, the number of trial items in which the participants had used the least amount of moves to replicate the examiner's tower bead configuration, was used to index planning ability. This version of the ToL was found to significantly predict left frontal cortical thickness in a healthy elderly sample ($r = .51$; Sánchez-Benavides et al., 2010).

The computerized version of the Halstead Category Test (HCT) (Hom, 2010) was used to assess problem-solving ability/abstract reasoning. It contains seven subtests; the first and second are practice subtests. In each item within a subtest, one or more figures were presented which, based on certain abstract reasoning rule (e.g., spatial reasoning and proportional reasoning), alluded to a number ranging from one to four, corresponding to four assigned keys participants pressed to indicate their response. Feedback was provided immediately after each response. The participant was informed that once they have figured out the rule in a subtest, they should continue to apply this rule to the rest of the items in the subtest and that this rule may change or remain the same between successive subtests. Participant's problem-solving ability was operationalized as the total number of errors. It was previously reported that participants with brain damage had significantly higher error scores than their matched controls (Loring & Larrabee, 2006).

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For the outcome variables of the RFFT and ToL, higher scores corresponded to better cognitive abilities whereas for CTT, Stroop test, and HCT, higher scores corresponded to worse cognitive abilities. The scores for the latter group of tests were reversed (multiply by -1) prior to the data analyses, such that higher scores for all tests corresponded to better cognitive abilities.

Additionally, participants also reported the intensity of stimulation side effects via a questionnaire administered to them at the end of each session. This questionnaire was designed by our team for the purpose of this study. In this questionnaire, participants rated on a scale from 0 (none) to 5 (very strong) for each of the six assessed side effects—itchiness, burning sensation, pain, headache, anxiety, and difficulty in concentration.

Statistical Analyses

Although we intended to examine the treatment effects using a hierarchical linear modeling (HLM) approach, the sample size calculations for such statistical models are complicated. As such, we determined the minimum sample size to detect a within-between interaction effect in a repeated measures analysis of variance (ANOVA) model, to approximate the sample size required to detect treatment effects in our hierarchical linear models. Assuming an effect size of 0.45, as reported in a meta-analysis (Summers et al., 2016), it was estimated using G*Power that a total sample size of 42 was required to detect a significant within-between interaction with a power of .80 (assuming $\alpha = .05$; correlation between repeated measures = .50; nonsphericity correction = 1). Given our valid sample ($N_{analyzed} = 68$) is much larger than 42, our sample size is more than adequate to detect an effect size of 0.45 or larger, at a power of .80 if such effect exists.

We assessed for baseline differences in sociodemographic, clinical, and cognitive variables between the tDCS and sham groups, and between completers and dropouts, using independent samples t tests and chi-square tests for continuous and categorical variables, respectively. Next, we assessed for between-group difference among completers in the number of sessions attended using independent samples t tests and self-reported side effects using hierarchical linear models (see Supplementary Material). Finally, to test our hypotheses, we modeled each of the EF outcome measures among completers using hierarchical linear models. The model is specified below:

Level 1:

$$y_{ij} = \beta_{i0} + \beta_{i1}(\text{baseline}) + \beta_{i2}(\text{education}) + \beta_{i3}(\text{stimulation}) + \beta_{i4}(\text{time}_{ij}) + e_{ij}$$

where

y_{ij} represents the test score for participant$_i$ at time$_j$ (j refers to the post-intervention or 1-month follow-up time points)

β_{i0} represents the random intercept for participant$_i$

β_{i1} represents the baseline test score as a fixed covariate for participant$_i$

β_{i2} represents the fixed effect of education for participant$_i$

β_{i3} represents the fixed effect of stimulation (tDCS = 1, sham = 0) for participant$_i$

β_{i4} represents the fixed effect of time of measurement (post-intervention = 1, 1-month follow-up = 2) for participant$_i$ at time$_j$

e_{ij} represents the residual

Level 2

$$\beta_{i0} = \gamma_{00} + u_{i0}$$

where γ_{00} represents the intercept for all participants

u_{i0} represents the residual.

A random intercept (β_{i0}) was included in the model. Education (β_{i2}) was included as a covariate in the model since there were significant baseline differences between groups. Baseline measurements (β_{i1}) were included as a fixed covariate to control for differences at baseline. A fixed effect of stimulation (β_{i3}) was assumed to account for the differences between both groups. Finally, the dependent variable (y_{ij}) at two time points (post-intervention and 1-month follow-up) was nested within each participant and a fixed effect (β_{i4}), presumably a practice effect, was assumed to account for the difference between both time points. p-Values for the βs were computed using Satterthwaite's degrees of freedom method. We decided on this approach as opposed to the conventional repeated measures ANOVA approach, because the former would effectively maximize the use of all available data from all time points to estimate a single stimulation effect (β_{i3}); participants with missing data either at post-intervention or 1-month follow-up need not be excluded. Furthermore, the HLM approach would better capture the nuances in the design in terms of discerning between practice effects and stimulation effects, which would be oversimplified in a repeated measures ANOVA. The HLM was carried out using the restricted maximum likelihood estimator in the R-package lmerTest (Kuznetsova, Brockhoff, & Christensen, 2017). All analyses are carried out in R 3.4.0. Statistical significance was set at $p < .05$.

RESULTS

Baseline Differences and Descriptive Statistics

The tDCS group, relative to sham, had significantly more errors on the HCT; $t(73) = 2.66$; Cohen's d = .62; $p = .010$. Apart from this, there were no other significant differences between both groups in any EF measures. There were no significant differences in any demographic characteristics or EF measures between completers ($N = 68$) and dropouts ($N = 8$); $ps > .265$. The descriptive statistics of all EF measures across all three time points are presented in the Supplementary Material (see Table s2 in the Supplementary Material).

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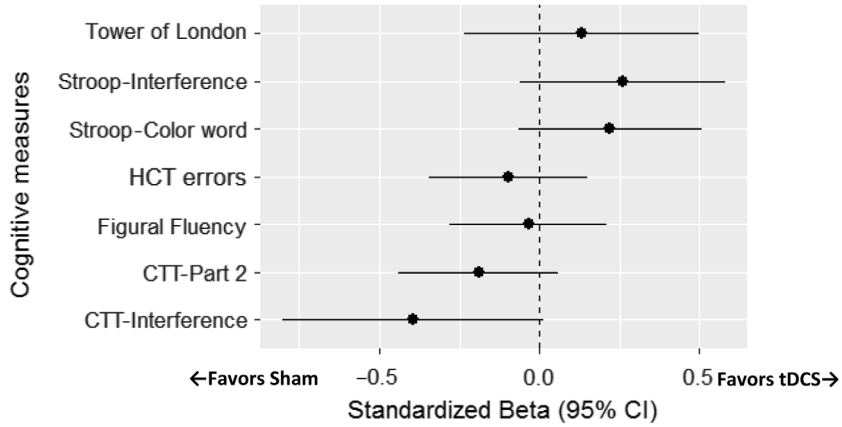

Fig. 3. Forest plots of tDCS treatment effect sizes across different EF measures. Effect sizes are presented as standardized betas within their 95% CIs. The effect size is not significantly different from 0 (i.e., $p > .05$) if their 95% CIs contained 0 (i.e., intersected with the dotted line). HCT = Halstead Category Test; CTT = Color Trails Test.

Attendance and Side Effects

Completers from both groups did not differ significantly in the number of sessions attended ($t(66) = 1.46$; $p = .150$; $M_{tDCS} = 14.2$, $SD_{tDCS} = .97$; $M_{Sham} = 13.85$, $SD_{tDCS} = 1.18$). Results from the hierarchical linear models (see Supplementary Material; Table s3) suggest that self-reported ratings of all assessed side effects were not significantly different between completers in both groups ($ps \geq .180$)

Effect of Stimulation

The forest plot of tDCS treatment effects (β_3) across all EF measures assessed in the intervention is presented in Figure 3. None of the β_3 for any of the EF measures was statistically significant ($ps \geq .064$). The full parameters (standardized coefficients, *df*, confidence intervals, *p*-values, and *t*-statistics) of β_0 to β_4 are presented in the Supplementary Material (see Table s4).

DISCUSSION

The current study sought to examine the effects of multi-session prefrontal tDCS on EF outcomes in an intervention. The results suggest that tDCS relative to sham did not significantly improve any EF outcomes, collectively at both post-intervention and 1-month follow-up. Participants in the tDCS and sham conditions did not differ significantly in terms of their side effects ratings and attendance. This would suggest that our sham stimulation condition was an effective control for the tDCS condition

Notwithstanding the fact tDCS did not lead to significant gains in any of the EF outcomes, we observed that the effect of tDCS differed across the different EF outcomes. For instance, the CTT outcomes appeared to have benefitted more from sham stimulation than tDCS. On the contrary, the Stroop outcomes seemed to benefit more from tDCS than sham stimulation. We speculate that such differences may relate to the possibility that both tests recruit upon different brain regions. For instance, a meta-analysis of functional magnetic resonance imaging (fMRI) studies on the Stroop task (Cieslik, Mueller, Eickhoff, Langner, & Eickhoff, 2015) revealed that its incongruent trial, relative to its congruent and neutral trials, consistently activated a network of regions that include the left inferior frontal junction. This left inferior frontal gyrus is located relatively close to the position of the anode (F3) in the current study, especially given that the surface area of the electrodes is relatively large. It is likely that repeated tDCS would increase the neuronal excitability in the left inferior frontal gyrus and thereby enhancing participants' ability to suppress a prepotent response as required in the Stroop task. On the other hand, an fMRI study on the trail making test (Jacobson, Blanchard, Connolly, Cannon, & Garavan, 2011) revealed that its part B trial (an analog to the CTT part 2), relative to its part A trial (an analog to the CTT part 1), significantly activate the right inferior middle frontal gyrus, right precentral gyrus, and middle temporal/angular gyri. None of these regions are remotely close to the anode position. Furthermore, the position of the cathode (FP2) would have been in the proximity of the right middle frontal gyrus. It is possible that the repeated cathodal stimulation of the right middle frontal gyrus would have decreased its neuronal excitability, and hence impairing participants' ability switch between the different sets in the CTT. As we compare the current study with previous similar interventions with significant findings, it is difficult to arrive at any consistent explanation for our negative findings. While it is easy to identify the differences between the current study and the six studies with significant findings (as alluded to in the introduction), these six studies had very little in common among themselves to begin with. They differed largely in terms of number of sessions (ranging from 3 to 10), stimulation duration (ranging from 15 to 30 min), population type (e.g., healthy, Parkinson's disease, and mild cognitive impairment), cathode sites (e.g., above left eye, supraorbital, cheek and nondominant arm), sham stimulation duration

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(i.e., ranging from 0 to 30 s), and type of adjunctive CT (if any at all). Furthermore, the domains of the significant tDCS-associated cognitive gains were not well replicated across these six studies. For instance, while Jones et al. (2015) reported significant tDCS-associated gains in working memory, Manenti et al. (2016) did not observe any significant tDCS-associated gains in their working memory outcomes.

Crucially, the two most salient intervention-related factors—amount of stimulation (current, duration, or sessions) and population type— could not explain the differences in tDCS-associated outcomes across studies. First, more stimulation is not necessarily better. One study utilizing a more intense stimulation protocol (i.e., 20 sessions × 25 min of 2 mA tDCS (Nilsson et al., 2017)) did not observe significant EF gains. On the contrary, another intervention with much fewer sessions (i.e., three sessions × 20 min of 1.5 mA tDCS (Hanley & Tales, 2019)) had achieved significant EF gains. Specifically, longer durations of stimulation does not translate to better outcomes as well. For instance, Huo et al. (2018) and Jones et al. (2015) had carried out 30-min and 10-min tDCS protocols, respectively. Counterintuitively, significant tDCS-associated gains were only observed in Jones et al. (2015). Although, the stimulation was not accompanied with any CT in Huo et al.'s study, both studies were similar in terms of number of sessions and population type. Future studies should verify this by varying stimulation durations among different groups of participants within study. Next, Hsu et al. (2015) previously suggested that participants with higher baseline cognitive abilities (such as our healthy participants) may benefit less from noninvasive brain stimulation as compared to those with lower baseline cognitive abilities. However, this may not account well for EF-related results—one tDCS intervention involving participants with AD (Cotelli et al., 2014) did not report significant EF gains, while another intervention with healthy participants had observed significant tDCS-associated EF gains (Hanley & Tales, 2019).

Given that these conventional intervention/stimulation parameters could not satisfactorily explain the differences in tDCS outcomes across studies, we should turn our attention to other factors which have been less studied. First, several studies, including the current, may have underestimated the effects of sham stimulation. Fonteneau et al. (2019) explained that sham stimulation protocols—typically configured as a short-duration (≤30 s) stimulation with or without ramp up/down— may produce not just transient tDCS-related side effects, but unintended neurobiological effects as well. These effects may have been further enhanced with repetitive stimulation. Hence, it is possible that our participants and those in other sham-controlled tDCS interventions might have benefitted from sham stimulation as well, thus obscuring the overall tDCS-associated gains. Future studies should consider including a third group of participants—one with the tDCS apparatus completely switched off, in addition to the tDCS and sham groups. This "switched off" group would not allow for effective blinding given the absence of side effects; nevertheless, by comparing between the three groups, one would be able to deduce the effects of the sham stimulation or blinding on the treatment outcomes. Second, findings from a meta-analysis of single-session studies (Imburgio & Orr, 2018) suggest that tDCS protocols with extracranial cathodes (e.g., cheek) tend to result in significant EF gains as compared to protocols with cranial cathodes (e.g., supraorbital). Imburgio and Orr (2018) explained using their current simulation model that cranial cathodes are likely to inhibit the functions of cortical regions within the proximity of these cathodes. Although such observations were derived from single-session studies, it appears that four out of the six multisession tDCS interventions that observed significant tDCS-associated EF gains had extracranial cathodes (Jones et al., 2015; Lawrence et al., 2018; Park et al., 2014; Stephens & Berryhill, 2016). Third, there is some evidence to suggest the manipulation of intervals between successive stimulation sessions may influence tDCS outcomes. For instance, Monte-Silva et al. (2013) showed that having a short interval (3–20 min) between two 13-min stimulation would more likely result in late-phase long-term potentiation, than longer intervals (≥3 hr) or if there were no intervals at all. Relatedly, Hurley and Machado (2017) reviewed tDCS studies with and without short intervals and concluded that having a short interval between successive stimulations may enhance tDCS-related outcomes. Finally, although the electrodes were attached to the scalp via rubber belts in the current and many other studies, there is a possibility that the electrodes' position may inadvertently shift during the stimulation duration as the participant fidgets. Consequently, this may influence the amount of stimulation received at the targeted regions. In fact, it has been demonstrated that the F3-Fp2 montage, which was used in the current study and in many other studies targeting EF gains, was highly susceptible to the effects of the electrodes' shift in positions. For instance, a 1 cm displacement of the anode can lead to a 38% change in average current density in the left frontal lobe (Ramaraju et al., 2018). In this regard, future studies should devise more reliable methods of affixing the electrodes to the scalp.

The implications of these negative findings cannot be overlooked. In comparison with other non-pharmacological cognitive enhancement strategies like CT (Hill et al., 2016; Kelly et al., 2014) and physical exercise (Groot et al., 2016) which have demonstrated robust improvements in cognitive abilities among healthy older adults and geriatric populations, tDCS appeared to have underperformed. Taken together with the fact that these two cognitive enhancement strategies are much cheaper and easier to execute, there are not a lot of justifications for using tDCS, except for populations afflicted with significant physical or motor-related impairments (e.g., those with Parkinson's disease).

The findings of the current study are subjected to some limitations. First, due to logistical and practical constraints, full random assignment and double blinding of the treatment groups could not be carried out. Relatedly, the presence of significant differences between both treatment groups in terms of education levels and baseline HCT errors may allude to the limitations of our pseudo-randomization procedures.

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Nevertheless, we have adequately accounted for such differences in our statistical models. Second, although we did show that depression levels were similar between the tDCS and sham groups, we did not account for other extraneous psychiatric variables, such as anxiety symptoms (Yochim, Mueller, & Segal, 2013) and sleep-related problems (Yaffe, Falvey, & Hoang, 2014), which may a confounding influence on the EF outcomes. Third, despite having one of the largest sample sizes among trials of its kind, it is possible that the tDCS effects were still too small for them to be detected with the current sample. Future research should attempt to pool similar studies together in a meta-analysis to obtain a more conclusive verdict on the use of tDCS for augmenting EF outcomes. Finally, the sham stimulation was not implemented with a fade-in/fade-out, unlike the tDCS condition. This presence of a fade-in/fade-out may act as an extraneous variable that differs between both treatment groups. Such differences might compromise participant blinding and influence participants' treatment expectancies in a confounding manner. Although our results are not as we hoped, it is important that these results are made public, to avoid a publication bias in favor of successful interventions and contribute to future meta-analytic research. In conclusion, the current intervention study did not observe any significant tDCS treatment effect on EF. More research is needed to optimize the use of tDCS for cognitive enhancement before it can be recommended as an effective strategy for enhancing EF in the context of aging

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CONFLICT OF INTEREST

The authors have no actual or potential conflicts of interest.

SUPPLEMENTARY MATERIALS

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