Effects of Multisession Prefrontal Transcranial Direct Current Stimulation on Long-term Memory and Working Memory in Older Adults

Jacky Au[1], Rachel N. Smith-Peirce[1], Elena Carbone[2], Austin Moon[3], Michelle Evans[4], John Jonides[4], and Susanne M. Jaeggi[1]

Abstract

■ Transcranial direct current stimulation (tDCS) is a noninvasive form of electrical brain stimulation popularly used to augment the effects of working memory (WM) training. Although success has been mixed, some studies report enhancements in WM performance persisting days, weeks, or even months that are actually more reminiscent of consolidation effects typically observed in the long-term memory (LTM) domain, rather than WM improvements per se. Although tDCS has been often reported to enhance both WM and LTM, these effects have never been directly compared within the same study. However, given their considerable neural and behavioral overlap, this is a timely comparison to make. This study reports results from a multisession intervention in older adults comparing active and sham tDCS over the left dorsolateral pFC during training on both an *n*-back WM task and a word learning LTM task. We found strong and robust effects on LTM, but mixed effects on WM that only emerged for those with lower baseline ability. Importantly, mediation analyses showed an indirect effect of tDCS on WM that was mediated by improvements in consolidation. We conclude that tDCS over the left dorsolateral pFC can be used as an effective intervention to foster long-term learning and memory consolidation in aging, which can manifest in performance improvements across multiple memory domains. ■

INTRODUCTION

Transcranial direct current stimulation (tDCS) is a noninvasive method of electrical brain stimulation that can influence cognitive functioning via modulation of cortical excitability. tDCS targeted over the dorsolateral pFC (DLPFC) has been shown to affect a variety of memory functions (Huo et al., 2021; Buch et al., 2017; Mancuso, Ilieva, Hamilton, & Farah, 2016; Brasil-Neto, 2012), which can be a critical boon for older adults looking for methods to mitigate age-related cognitive decline. For example, our previous work, although in younger adults, demonstrated sustained performance enhancements when administering DLPFC tDCS during an *n*-back working memory (WM) task over the course of a week-long intervention (Au et al., 2016), an effect that was replicated by an independent group in a similar experiment (Ruf, Fallgatter, & Plewnia, 2017). Other WM training studies have been similarly successful as well, both in younger (Ke et al., 2019; Richmond, Wolk, Chein, & Olson, 2014) as well as older adults (Stephens & Berryhill, 2016; Jones, Stephens, Alam, Bikson, & Berryhill, 2015).

Despite these initial successes, a follow-up study by our group failed to replicate our original training effects in younger adults (Au et al., 2021), and a large randomized controlled trial of 123 individuals also did not observe significant improvements in older adults (Nilsson, Lebedev, Rydström, & Lövdén, 2017). Furthermore, meta-analyses suggest that effects of tDCS on WM are small at best (Hill, Fitzgerald, & Hoy, 2016; Mancuso et al., 2016) or unreliable at worst (Horvath, Forte, & Carter, 2015). This is not to suggest that tDCS-enhanced WM is not a worthwhile pursuit, but rather to highlight the challenges in the field and the difficulty in understanding the specific conditions that will most likely elicit an effect. In contrast, tDCS effects on long-term memory (LTM) seem to be more promising, with stronger and more robust meta-analytic effects, especially among older adults (Huo et al., 2021; Galli, Vadillo, Sirota, Feurra, & Medvedeva, 2019; Summers, Kang, & Cauraugh, 2016). Moreover, there is accumulating evidence that tDCS can increase long-term potentiation (LTP; Kronberg, Bridi, Abel, Bikson, & Parra, 2017; Podda et al., 2016; Rohan, Carhuatanta, McInturf, Miklasevich, & Jankord, 2015; Ranieri et al., 2012) and LTP-like plasticity in the cortex (Frase et al., 2021; Agboada, Mosayebi-Samani, Kuo, & Nitsche, 2020; Monte-Silva et al., 2013), which may facilitate the consolidation and long-term retention of material learned during stimulation. In fact, even the WM training effects we originally reported (Au et al., 2016) displayed properties that were actually more reminiscent of LTM consolidation than WM per se, such as a spaced learning pattern in which gains were greater over a weekend compared with consecutive weekdays, as well as maintenance effects that persisted

[1]University of California, Irvine, [2]University of Padova, [3]University of California, Riverside, [4]University of Michigan

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up to a year later even in the absence of further stimulation (Katz et al., 2017). The main purpose of the current study, therefore, is to compare the relative effects of tDCS on both WM and LTM during a combined memory intervention in older adults who may be more susceptible to tDCS modulation and to investigate the extent to which improved LTM actually mediates any enhancements in WM performance.

In considering the effects of tDCS across memory domains, one important issue to recognize is that the processes that underlie WM and LTM are not completely distinct and have a bidirectional relationship (Bergmann, Rijpkema, Fernández, & Kessels, 2012; Cabeza, Dolcos, Graham, & Nyberg, 2002). WM processing relies on retrieval from LTM stores to contextualize incoming information, which in turn, with enough repetition or salience, can be re-encoded back into LTM (Miyake & Shah, 1999; van der Linden, 1998). Moreover, activity in the pFC during a WM task has been shown to predict LTM formation (Blumenfeld, 2006; Ranganath, Cohen, & Brozinsky, 2005), even of memoranda separate from those used in the WM task (Melrose et al., 2020). Conversely, activity in medial-temporal lobe structures such as the hippocampus typically thought to subserve LTM (Squire, Stark, & Clark, 2004) have also been implicated in the maintenance of WM (Bergmann et al., 2012; Nichols, Kao, Verfaellie, & Gabrieli, 2006; Cabeza et al., 2002). So, the two memory domains work together cooperatively, which is also reflected by their shared neural substrates (Nee & Jonides, 2008, 2013; Hannula & Ranganath, 2008). This is further underscored by findings of improvements in certain aspects of LTM measures after WM training (Rudebeck, Bor, Ormond, O'Reilly, & Lee, 2012; Richmond, Morrison, Chein, & Olson, 2011; Buschkuehl et al., 2008), as well as recent studies that show how WM performance can exhibit sleep-dependent enhancements reminiscent of LTM consolidation. Specifically, several studies have documented that training-related improvements on the *n*-back WM task were only observed if the interval between sessions included sleep or a nap, but not wake (Zinke, Noack, & Born, 2018; Lau, Wong, Lau, Hui, & Tseng, 2015). Furthermore, these performance improvements were associated with increased slow wave activity during sleep (Ferrarelli et al., 2019; Sattari, Whitehurst, Ahmadi, & Mednick, 2019; Pugin et al., 2015), which is a critical factor in the consolidation of perceptual and motor procedural skills (Määttä et al., 2010; Crupi et al., 2009; Huber, Felice Ghilardi, Massimini, & Tononi, 2004). Thus, we hypothesize that the long-term retention of performance benefits observed from the use of tDCS on WM tasks may arise from similar mechanisms as those observed on LTM tasks. These processes may relate to the consolidation of new cognitive routines (Gathercole, Dunning, Holmes, & Norris, 2019), which may include declarative components of WM training such as strategy learning or procedural components such as developing stimulus–response mappings or the proficiency of updating between shifting rules and goals (e.g., Sali & Egner, 2020; Oberauer, 2009).

Given the overlapping neural architecture between the two memory domains, it is perhaps not surprising that tDCS delivered over the same left DLPFC area can enhance both WM (reviewed in Mancuso et al., 2016) as well as LTM (Huo et al., 2021; Galli et al., 2019) performance. However, to our knowledge, a direct comparison between the two memory domains has never been made within a single study. Thus, the goal of the current study was to carry out this comparison in the context of a five-session intensive memory training intervention. Although we expected improvements in both memory domains based on previous literature (e.g., Perceval, Martin, Copland, Laine, & Meinzer, 2020; Au et al., 2016; Sandrini et al., 2016; Jones, Stephens, et al., 2015; Javadi & Cheng, 2013), we hypothesized stronger and more robust effects would emerge within the LTM domain because of the facilitatory effects of tDCS on memory consolidation (Au, Karsten, Buschkuehl, & Jaeggi, 2017; Podda et al., 2016). Moreover, if the long-term improvements in both memory domains arise from similar consolidation mechanisms, whether directly or indirectly, then we hypothesized that the strength of this consolidation, as measured by LTM retention, might mediate at least part of the relationship between tDCS and long-term WM performance.

Finally, we sought to build upon our previous work that has shown baseline WM performance and spaced training to be influential moderators of tDCS efficacy (Katz et al., 2017; Au et al., 2016). With respect to the former, we previously found that individuals with lower baseline ability benefitted more from tDCS, a finding generally corroborated by the literature (e.g., Perceval et al., 2020; McConathey et al., 2017; Looi et al., 2016; Tseng et al., 2012), although evidence for a high-baseline advantage also exists (Jones, Gözenman, & Berryhill, 2015; Jones & Berryhill, 2012). With respect to the spacing issue, we previously reported that spacing training sessions apart by a few days was associated with greater training gains compared with daily training, but only in the presence of tDCS (Au et al., 2016). It is known that varying the intersession interval between repeated bouts of tDCS can influence the size and direction of effects, although most studies to date have manipulated this interval on the order of minutes rather than days (Goldsworthy, Pitcher, & Ridding, 2015; Monte-Silva et al., 2013). With the higher-order learning involved in cognitive training protocols, we previously postulated that spacing tDCS sessions apart by days could facilitate consolidation processes that occur during that same time frame (Au et al., 2016, 2017). However, our previous study found this spacing effect with WM training gains, and it is important to replicate this phenomenon with memoranda encoded into LTM before endorsing an effect of spaced tDCS on consolidation.

Thus, the overarching goals of the current study are three. First, we seek to establish the efficacy of tDCS on improving WM and LTM in a sample of healthy older adults, both on trained and untrained measures. Second, we seek to compare the effects of tDCS between LTM and

WM and determine the degree to which LTM consolidation mediates long-term improvements on *n*-back training. Finally, we explore the possible moderating influences that baseline ability and intersession spacing interval have on the efficacy of tDCS. In tackling these goals, we included pretest and posttest measures of WM and LTM before and after the tDCS intervention, respectively, and we also randomly assigned older adult participants between the ages of 65 and 85 years to come into the lab either daily or every other day. Although there is no definitive evidence that tDCS is more or less effective in older compared with younger populations, there is some suggestion that lower-performing populations such as clinical and older adult populations may have a higher response rate to tDCS (Huo et al., 2021; Galli et al., 2019; Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016; Hill et al., 2016). Therefore, not only does testing older adults potentially increase our chances of finding a study effect, but it also affords us the opportunity to foster memory skills in a population that is susceptible to cognitive decline and is in great need of such interventions.

METHODS

Participants

In a joint collaboration between the University of California, Irvine, and the University of Michigan, 55 neurologically and psychologically healthy right-handed older adults (between ages of 65 and 85 years; mean age = 71.32 years, 73% women) were recruited from the local communities before the start of the COVID-19 global pandemic, which halted our recruitment. Of these 55, one scored above threshold on the Geriatric Depression Screener (Scogin, Rohen, & Bailey, 2000), and two others dropped out during the course of the study. Their data were excluded from all analyses. In the end, our analytic sample comprised 24 individuals randomized to receive active tDCS and 28 randomized to receive sham tDCS. Of the active tDCS group, 12 were randomized to train daily, and 12 were to train every other day. Of the sham group, 13 were randomized to train daily, and 15 were to train every other day. Rarely, a participant who could not make a certain training session was allowed to reschedule within 1 day, once during their training period. This only affected three of our participants (two sham/one active). All research procedures were approved by the institutional review boards at both universities, and each participant provided informed consent.

General Procedure

In our between-subject design, participants were randomly assigned to one of two stimulation conditions (active or sham tDCS) and one of two spacing conditions (daily or every-other-day training). In accordance with our previous procedure (Au et al., 2016), participants were not informed of the possibility of a sham condition. All participants were told they were receiving active stimulation and advised that the sensations associated with stimulation were generally subtle with considerable interindividual variability. Upon conclusion of study procedures, participants were debriefed about the sham procedure and asked to guess if they received active or sham stimulation.

The intervention itself consisted of five sessions of WM and LTM training, which occurred either within a calendar week for the daily training group or within two calendar weeks for the every-other-day group. Each training session lasted approximately an hour, including setup and cleanup, and started with word list learning, followed by *n*-back training. Stimulation was applied at the beginning of word learning and spilled over into part of *n*-back training, lasting for a fixed duration of 25 min regardless of how far along participants had progressed on the training. This was done to ensure a comparable stimulation duration across all participants and also to replicate our previous work, which showed 25 min of stimulation to be an effective dosage (Au et al., 2016). Furthermore, we aimed to avoid overstimulation, which has been observed to reverse the direction of tDCS effects (Monte-Silva et al., 2013). After *n*-back training, participants received a brief 5-min break during which the tDCS electrodes were removed. At the end of the session, participants were once again asked to recall as many words as they could remember from the beginning of that day's session. At the beginning of the next session, before learning the new word list for that day, participants were again asked to recall as many words as they could remember, but this time cumulatively from all previous sessions.

Pretests and posttests consisting of trained and untrained outcome measures took place within a few days before the first or after the last training sessions. A final follow-up appointment was scheduled 3 months after the last training session to repeat the outcome measures. Because of the unexpected COVID-19 global pandemic and the subsequent lockdown, the follow-up sessions were not completed by all participants and the data were not analyzed. However, descriptive data for the participants who did finish are provided in Appendix A (Table A1). A schematic of the study design is provided in Figure 1.

tDCS

Stimulation was administered via the Oasis Pro tDCS device by MIND Alive, Inc., using 5 × 7 cm sponge electrodes placed horizontally on the head. The anode was placed over the left DLPFC (corresponding to position F3 in the international 10–20 EEG system), and the cathode was placed over the contralateral supraorbital area (site Fp2). Electrode positions were identified using a BraiNet 10/20 placement cap (bio-medical.com), which was individually fitted to a participant's head based on their head circumference. Stimulation lasted 25 min with

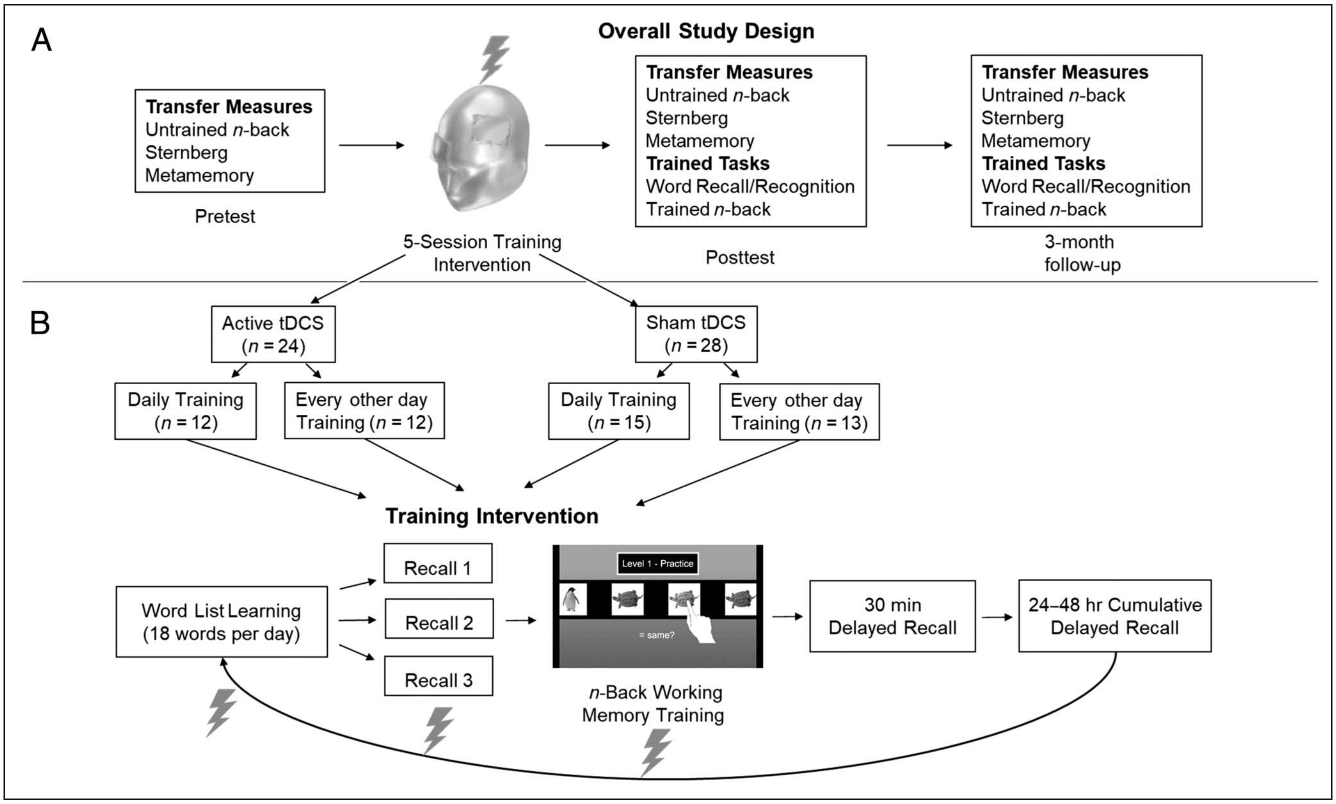

Figure 1. (A) Overall study design. General study procedures are depicted. Lightning bolts represents time period during which participants receive either active or sham stimulation. (B) Structure of a training session. A snapshot of the training intervention is portrayed, in which participants are randomized to train either daily or every other day under active or sham stimulation. The intervention itself consisted of both a word learning and *n*-back task under stimulation, followed by a delayed recall approximately 30 min later, and again at the beginning of the next session (either 24 or 48 hr later depending on the spacing condition) before repeating the training session all over again with a new set of words for the day. The 24–48 hr delayed recall is cumulative and consists of all words learned up to that point in training. Both delayed recalls are performed in the absence of stimulation.

a current intensity of 2 mA, which ramped up and down for the first and last 15 sec of stimulation. Sham tDCS was set up in the same way, except the current was shut off unknown to participants between the 15-sec ramping periods. The active and sham conditions were preprogrammed into the device using codes that only the first author knew. Thus, both the experimenters and participants were blind to the participants' conditions.

Word Generation Procedure

We used the same procedure to generate word lists for the LTM training task, metamemory outcome measure, and recognition outcome measure. We selected words from a variety of established databases (Brysbaert, Warriner, & Kuperman, 2014; Warriner, Kuperman, & Brysbaert, 2013; Reilly & Kean, 2007; Stadthagen-Gonzalez & Davis, 2006; Bird, Franklin, & Howard, 2001) to create separate word lists that were matched on key lexical features such as word length, familiarity, arousal and valence, concreteness, and imageability. For the training task, 150 words were selected and divided into five matched lists of 30. Eighteen of these 30 words were kept for use during each training session, whereas the remainder was retained for use as new, unstudied words for the recognition task, counterbalanced between posttest and follow-up.

A similar procedure was used to generate three lists of 60 words each for the metamemory outcome measure. A different list was used at pretest, posttest, and follow-up.

Training Tasks

LTM

The word-list learning task comprised a total of 90 words, which were separated into five lists of 18 words each. Each list was presented during one of the five training sessions. With the exception of the first training day, each subsequent session started with cumulative recall of all words learned during previous sessions. tDCS was not administered during cumulative recall. Following that, the tDCS device was set up in accordance with the participant's group assignment, and a new word list for the day was then visually presented on a computer screen at a rate of one every 3 sec. Participants verbally recalled as many words as they could remember immediately after the list while a researcher recorded their answers. The list was then repeated twice more, for a total of three rounds of immediate recall. After a delay of approximately 30 min, during which participants trained on the n-back task (see below), participants were once more asked to verbally recall as many words as possible.

The dependent variables of interest were the number of words recalled after three rounds of immediate recall, after a 30-min delay, and at cumulative recall at the beginning of the next session. Throughout the remainder of the article, these time points will be respectively referred to as immediate word learning (i.e., the third immediate recall), delayed recall, and cumulative recall.

At posttest and 3-month follow-up, a self-paced recognition test was administered in which participants were given 30 old words learned during training and 30 new words. Each word was displayed on a computer screen until participants made a response indicating whether the current word was old or new.

WM

Participants trained on a tablet-based version of an n-back task, identical to the training task used in the study of Jaeggi et al. (2020), which used pictures of everyday objects as stimuli and required indicating whether a presented picture was the same as that presented in trials previously. Stimuli were presented in a moving window that lasted for 1000 msec with an ISI of 2500 msec. The difficulty level continuously adapted to individual performance across sessions. Participants needed to achieve accuracy scores of 90% or greater to advance to the next round; scores of 70% or lower demoted them to the previous round. Each n-level comprised three rounds such that participants had to demonstrate 90% or greater accuracy three times before incrementing to the next n-level. This was done to encourage mastery of an n-back level before advancing to the next. The only exception was the 1-back level, which only contained one round. Each training session consisted of 10 rounds, and each round consisted of five target trials and approximately 20 nontarget trials.

A brief practice consisting of four rounds was given to participants at pretest to explain instructions and familiarize them with the upcoming training. At posttest and at 3-month follow-up, the training task was readministered but started over at 1-back instead of continuing adaptively from the last training day's n-level. This was done to ensure comparability across participants at posttest and 3-month follow-up. The dependent variable of interest for this task was the average n-level achieved during each session. Because of a combination of technical problems and experimenter error, posttest data from eight participants (four active/four sham) were not collected or were lost.

Incidental Memory

Embedded within the n-back WM task was an incidental memory task in which participants were unexpectedly asked to recall as many of the n-back stimuli as they could at the end of training. These stimuli consisted of everyday objects such as shoes, clocks, fruits, vegetables, animals, and so forth. Each session comprised a total of 16 unique objects, which rotated each training day for a total of 80 unique objects by Session 5. Participants were given a maximum of 2 min to recall these objects, and this was done at two time points—after their last training session as well as at the beginning of posttest and 3-month follow-up. Because of experimenter error, six participants (five active/one sham) were not administered the incidental memory test after their last training session and were therefore not included in the analyses. The dependent variable of interest was the total number of objects recalled per time point.

Untrained Outcome Measures

Number n-Back

The number n-back task was an untrained variant of the trained n-back task that used numbers instead of everyday objects as stimuli. Numbers were presented visually at the center of the screen at a rate of one every 3 sec. The task comprised one warm-up round of 1-back, followed by three rounds of 2-back and 3-back. Each round consisted of $20 + n$ trials, and the dependent variable was the accuracy rate, or the proportion of hits minus the proportion of false alarms for the 2- and 3-back rounds (Snodgrass & Corwin, 1988).

Sternberg Item Recognition

In the item recognition task (Sternberg, 1969), participants were shown 4–10 uppercase letters equidistant from a fixation cross located in the center of the computer screen. Set sizes varied between trials in a pseudorandom order that was unpredictable for the participant. Presentation time varied between set sizes. For set size 4, stimuli were displayed for 1300 msec, and this presentation time incremented up by 325 msec for each one-step increase in set size. A single, lower-case probe letter was displayed afterward, and participants had to indicate whether or not the probe was contained within the initial set of letters. There were three blocks of 20 trials each. Set sizes 4 and 5 were included primarily as a warm-up and were excluded from analyses because of near-ceiling performance for all participants. Thus, the dependent variable was the median RT for correct trials averaged across set sizes 6–10.

Metamemory

The metamemory task is a modified word list learning task modeled after that used in McGillivray and Castel (2011) and further described in Parlett-Pelleriti, Lin, Jones, Linstead, and Jaeggi (2019). It consisted of learning five 12-word lists presented one word at a time on a computer screen. However, after encoding each word, participants were additionally asked to give a confidence rating between 0 and 9, indicating their degree of confidence in their ability to subsequently recall that word. A flashing red box appeared around the word after 3 sec if participants had not yet responded. Participants were not penalized for slow responses, nor did the task move on without their response. This was merely done to encourage quick responses to ensure comparable encoding times among participants. At the end of each 12-word list, participants were asked to recall as many of the words from that list as they could recall. Participants gave all confidence and recall responses verbally while an experimenter typed in their responses. This was done to control for typing speed and ability between participants and allow participants to focus solely on the recall task at hand. Parallel test versions were administered at pretest, posttest, and follow-up (see Word Generation Procedure above). The dependent variable was the total number of correctly recalled words. Confidence ratings and other potential variables of interest (Parlett-Pelleriti et al., 2019) were not relevant to the present hypotheses and were not analyzed in the current article.

Analytical Approach

Statistical analyses were conducted using STATA Version 13 (StataCorp, 2013). To interrogate training and transfer effects, we used linear mixed-effects models, which are generalizations of ordinary least-squares linear regression, but allow for the inclusion of random deviations other than those associated with the overall error term. Specifically, our analyses accounted for participant-level random intercepts that shift the regression line up or down according to each participant's starting ability. The general equation used was as follows:

$$\begin{aligned}\text{Task}_{ij} = {} & \beta_0 + \beta_1\text{Session}_{ij} + \beta_2\text{Condition}_{ij} \\ & + \beta_3\text{Moderator} + \beta_{4-6}\text{Session XX Moderator}_{ij} \\ & + \mu_{0i} + \varepsilon_{ij}\end{aligned}$$

Task_{ij} represents the dependent measure for the ith participant for the jth session. β_0 represents the overall regression intercept. β_{1-2} represent vectors of fixed effect beta weight coefficients for the session and condition predictors. β_3 represents fixed effect beta weight coefficients for the baseline or spacing predictors, which are both used in separate models to assess the extent to which these variables moderate the results. β_{4-6} represents the fixed effect beta weight coefficients for all the double and triple interactions between the aforementioned predictors. The fixed effect coefficients from β_{1-6} are equivalent to those in a standard ordinary least squares regression. Finally, μ_{0i} represents the participant-level random intercept, and ε_{ij} represents a vector of error terms.

The predictor condition was coded as a dummy variable representing the tDCS group referenced to sham, whereas the predictor spacing was coded as a dummy variable representing more spacing (i.e., training every other day) referenced to less spacing (i.e., training daily). Baseline was a continuous predictor based on pretest performance on either the untrained number n-back task to index baseline WM performance or the metamemory task to index baseline LTM performance. Furthermore, baseline was mean-centered to zero so that interpretations of regression coefficients are made with respect to average baseline ability. In contrast, for the session predictor, zero was referenced to the last session rather than to the mean so that interpretations of regression coefficients can be made with respect to the end of training and not the middle. All variables were left unstandardized in their natural units, with the exception of baseline ability, as indicated in all the table legends in Appendix A.

Three separate models were run for each analysis, a main effects model and a separate interaction model for each moderator of interest (baseline and spacing). The main effects model was run because the interaction models alone do not include estimates of main effects, only partial effects and interactions. Separate interaction models were run for each moderator because we were not interested in interactions between baseline and spacing. Moreover, using separate models reduces the complexity of each model and avoids four-way interactions, which our analyses are underpowered to properly detect or interpret.

Mediation Model

To interrogate the potential mediating role of LTM consolidation on long-term WM performance, we conducted mediation analyses using ordinary least squares regression via the SEM builder in STATA using full information maximum likelihood. In the absence of complete 3-month follow-up data because of the COVID-19 lockdown, we used posttest performance on the trained n-back task as our dependent measure of long-term WM performance. The independent predictor variable was the dichotomous variable Condition (active/sham) and the mediator was the total number of n-back stimuli incidentally recalled (averaged between both time points at the end of training and at posttest). Baseline WM performance at pretest on the untrained n-back task was also put in the model as an independent variable to control for general relationships between LTM and WM performance. With the exception of the dummy variable, Condition, all variables in the model were standardized as z-scores, and effects are reported as standardized beta weights. Bias-corrected 95% confidence intervals were calculated for each direct and indirect effect based on 5000 bootstrap samples (Hayes, 2018).

As an additional sensitivity analysis, word learning retention was used as an alternate mediator. This was done to evaluate whether specific memory of n-back stimuli was necessary to manifest a mediation effect of LTM on WM performance or whether a more general measure of individual consolidation strength would also show the same effects. In this model, word learning retention was operationalized as a latent variable based on word retention at delayed recall, as well as at cumulative recall the next day. Here, retention was defined specifically as the total number of words recalled at each time point divided by the total number of words initially learned after three rounds of immediate recall, averaged across all five sessions. At the cumulative recall time point measured the next day, only words recalled from the previous session were counted. Thus, this is a measure of overnight consolidation, averaged over five sessions, rather than a cumulative measure as used in the main results. Retention scores were calculated in this way rather than simply using the total number of words recalled to isolate time-dependent consolidation processes from general cognitive ability. For example, a high-ability participant might initially learn 10 words and retain five, whereas a lower-ability participant might learn only eight words but retain four. Thus, controlling for general ability, both participants perform equally and retain half their learning.

RESULTS

Descriptive data for pretest, posttest, and follow-up are included in Table A1. Significant main and interaction effects involving tDCS are reported below. All other effects, significant or not, are not reported in the main text but are included in Tables A1–A11. Unless otherwise noted in the figures or table captions, the analytic sample size comprised 24 individuals who received active tDCS and 28 who received sham. Data at follow-up were unfortunately not completed because of research disruption by the COVID-19 pandemic. Although descriptive data on the partial sample collected are reported in Table A1, statistical analyses were not carried out and are not reported.

Debriefing

Forty participants (20 active, 20 sham) were debriefed about the existence of a sham group at the 3-month follow-up, 13 of whom were contacted by phone because of the lockdown restrictions imposed by the COVID-19 pandemic. Of the 20 active tDCS participants, only 10 successfully guessed their true condition. Of the 20 sham participants, only nine successfully guessed their true condition. There was no difference between groups in their guesses ($\chi^2_{1,n\,=\,40} = 0.10$, $p = .75$). Moreover, there was also no difference between groups in their confidence ratings concerning their guesses (mean active: 6.75/10; mean sham: 6.2/10), $t(38) = 0.69$, $p = .25$.

Training Effects

Intraday Immediate Word Learning

To measure intraday immediate word learning, we summed the total number of words participants were able to learn after three rounds of immediate word recall, across all five training sessions. We regressed this value on the following predictors: condition, baseline, and spacing. In two separate models, we also evaluated the interactions between condition and baseline as well as condition and spacing.

tDCS had little to no impact on intraday word learning as our analyses found no main or interaction effects of condition (ps > .19). See Table A2 for all regression coefficients.

Intraday Delayed Word Recall

To measure intraday delayed recall, we summed the total number of words participants were able to remember after a 30-min delay, across all five training sessions. Using this value as the dependent variable, the same analytic procedure was followed as described above for immediate word learning. Despite null effects on immediate word recall, tDCS was effective in boosting delayed recall (Figure 2). Our main effects model revealed a significant effect of Condition ($b = 6.56$, $z = 2.57$, $p = .01$, $d = 0.72$) showing greater performance in the tDCS group. Neither the interaction of Condition with Baseline nor Spacing was significant (ps > .095; Table A3).

Between-day Cumulative Word Recall

To test the effects of tDCS on cumulative word recall between days, we regressed the total number of previously learned words that participants were able to recall at the beginning of each session on the following predictors: Session, Condition, Baseline, and Spacing. In addition to testing the main effects, we also ran two separate models testing the interactions between Session, Condition, and Baseline as well as Session, Condition, and Spacing.

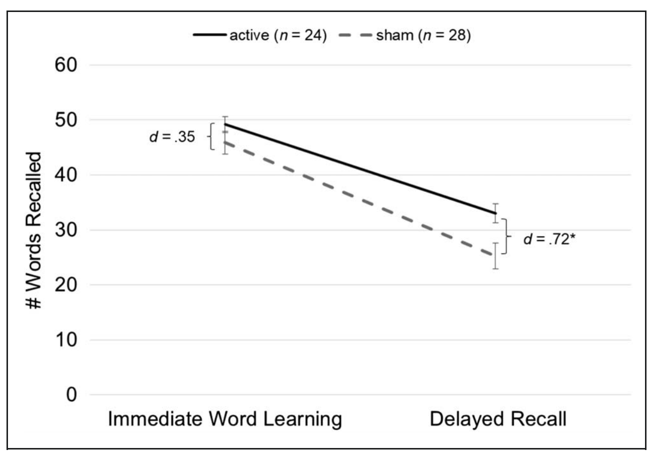

Figure 2. Intraday word recall. The total number of words recalled, summed across all five training sessions, is shown on the y-axis. Immediate word learning refers to the number of words recalled on the third (and final) round of immediate recall. No significant effects were observed, but the tDCS advantage approximately doubled and became significant 30 min later at delayed recall. Error bars represent *SEM*. * denotes significant Group effect ($p < .05$).

with no main or interaction effects involving Condition ($ps > .55$).

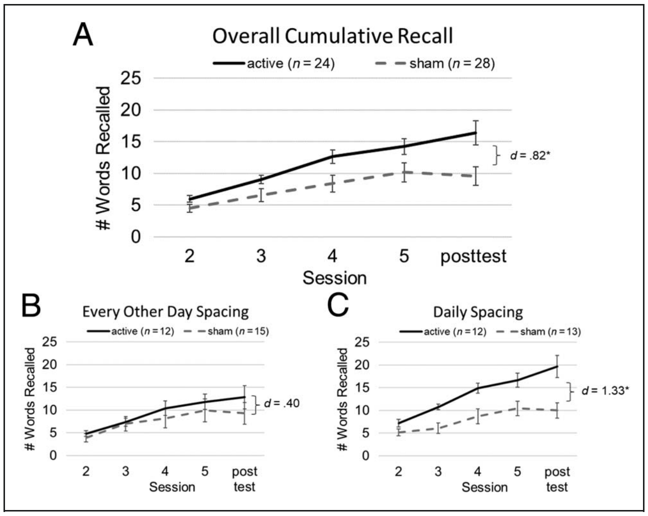

Figure 3. (A) Cumulative recall. The total number of words cumulatively recalled at the beginning of each session, including posttest, is shown on the y-axis. These words include all words learned since the beginning of training up until the current session (thus, Session 1 is excluded from this figure). The group receiving active tDCS consistently outperformed the sham group in each session, with the largest difference manifesting at posttest. (B) Every-other-day spacing condition. tDCS appeared less effective when training sessions were separated by 2 days, with a nonsignificant group difference by posttest ($d = 0.40$). (C) Daily spacing condition. tDCS was more effective when training sessions were only separated by 1 day, with a significant group difference by posttest ($d = 1.33$). Error bars represent *SEM*. * denotes significant Group effect ($p < .05$).

In addition to promoting delayed recall intraday, tDCS also improved cumulative recall throughout the training period (Figure 3). There was a main effect of Condition, showing a tDCS advantage across all sessions ($b = 3.187$, $z = 2.40$, $p = .016$). There were also significant Session × Condition interactions in both the baseline and spacing regression models ($ps < .001$), showing an increasing tDCS advantage over time, culminating in a large effect size difference by posttest ($d = 0.82$). Finally, despite the lack of a main effect of Spacing ($p = .15$), we observed both a Condition × Spacing interaction ($b = -6.47$, $z = -2.12$, $p = .034$) as well as a Condition × Session × Spacing interaction ($b = -1.17$, $z = -1.98$, $p = .048$), which indicate that every-other-day spacing significantly reduced the overall advantage of tDCS, as well as the marginal advantage per session. See Table A4 for all regression coefficients.

Word Recognition

In addition to free recall, we also tested the effects of tDCS on recognition memory at posttest (Table A5). We regressed recognition accuracy on the following predictors: Condition, Baseline, and Spacing. After running the main effects model, we tested for interactions between Condition and each of the other two predictors in two separate models. Our analyses found no evidence that tDCS influenced performance on recognition memory, with no main or interaction effects involving Condition ($ps > .55$).

n-Back WM Training

To evaluate the effects of tDCS during n-back training, our linear mixed-effects model regressed the average n-back level achieved each training day on the following predictors: Session, Condition, Baseline, and Spacing. Again, after running the main effects model, we then ran two separate interaction models testing first the interactions between Session, Condition, and Baseline and then the interactions between Session, Condition, and Spacing. Over the training period, tDCS had no observable effect on n-back performance (Figure 4), with no main or interaction effects ($ps > .54$). See Table A6 for all regression coefficients.

Posttest n-Back

We modeled n-back performance on the trained task separately at posttest because tDCS was not administered at this time point and also the n-back level was reset back to the beginning rather than continuing adaptively from the last training session; thus, it did not continue the same linear trend from training. The analytic model at this time point was the same as described above, except with the omission of the Session predictor. Additionally, the analytic sample was smaller ($n = 44$) because data from eight participants (four active/four sham) were lost or not collected because of a combination of technical glitches and experimenter error.

Although there was no significant main effect of Condition ($p = .17$), we did observe a trending interaction with

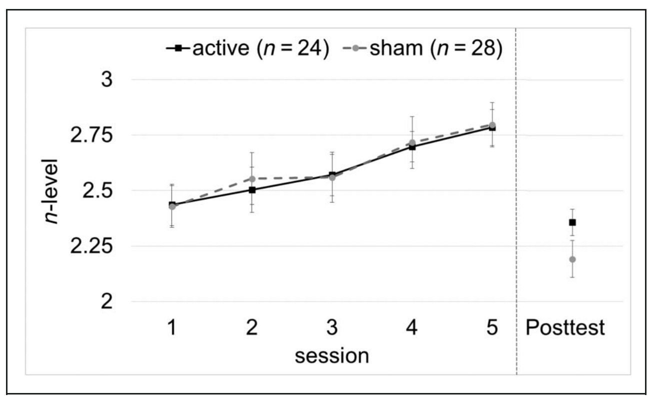

Figure 4. Trained n-back task. Training performance on the n-back task was very similar between groups across all five sessions and also was not significantly different at posttest. Posttest n-back was administered without stimulation and also without adaptively continuing from the previous session (i.e., all participants started over at 1-back). At pretest (not shown), participants were introduced to four rounds of n-back training to habituate them to the task before training and stimulation. The first training session continued adaptively from this pretest exposure, which explains why Session 1 performance is greater than at posttest.

Baseline ($b = -0.17, z = -1.93, p = .054$). Because of our a priori hypothesis and the robust literature support for a baseline-dependent effect of tDCS (Krebs, Peter, Wyss, Brem, & Klöppel, 2021; Perceval et al., 2020; Arciniega, Gözenman, Jones, Stephens, & Berryhill, 2018; Katz et al., 2017; Gözenman & Berryhill, 2016; Heinen et al., 2016; Looi et al., 2016; Minichino et al., 2015; Hsu, Tseng, Liang, Cheng, & Juan, 2014; Tseng et al., 2012), we conducted a post hoc analysis on this interaction, which revealed that lower-baseline tDCS participants (lowest 50th percentile) outperformed lower-baseline sham participants, $t(22) = 2.50$, $p = .02$, $d = 1.06$, whereas the same comparison among high-baseline performers yielded no difference, $t(18) = 0.74$, $p = .47$, $d = 0.33$. The overall group difference, irrespective of baseline performance, was $d = 0.47$. See Table A7 for all regression coefficients.

n-Back Stimuli Incidental Memory Recall

To evaluate incidental memory during *n*-back training, we regressed the total number of correctly recalled stimuli, both on the last training day and at posttest, on the following predictors: Session, Condition, Baseline (based on pretest metamemory performance), and spacing. Once again, interactions between Session, Condition, and Baseline as well as Session, Condition, and Spacing were tested in separate models after testing for main effects. Additionally, the analytic sample was smaller ($n = 46$) because data from six participants (five active/one sham) were not collected at the end of training because of experimenter error and were removed from the entire analysis.

We found that tDCS improved incidental memory recall of stimuli encountered throughout *n*-back training (Figure 5), with a main effect of Condition ($b = 4.89$, $z = 2.43$, $p = .015$) but no significant interactions (ps $> .21$). See Table A8 for all regression coefficients.

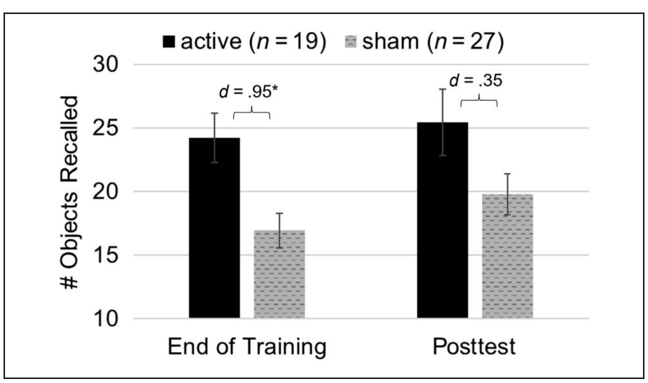

Figure 5. Incidental recall. Participants receiving tDCS demonstrated an advantage on incidental recall of *n*-back stimuli. Despite the lack of a significant group difference at the posttest time point alone, there is no interaction with Session, and this advantage is statistically significant overall. Error bars represent *SEM*. * denotes significant Group effect ($p < .05$).

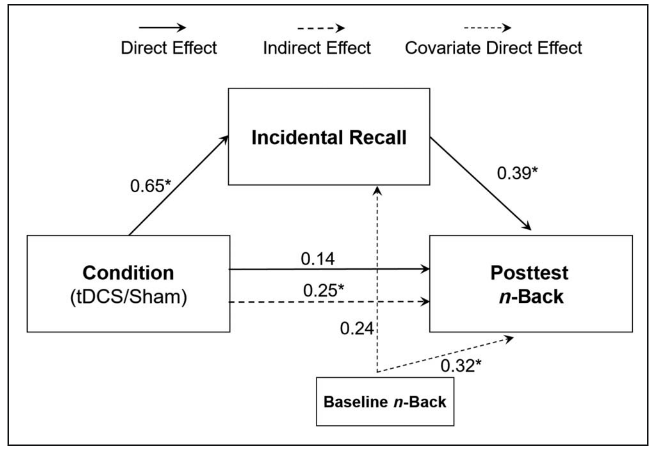

Figure 6. Mediation model. We found significant direct effects from condition to incidental recall and from incidental recall to posttest *n*-back, resulting in a significant indirect effect from condition to posttest *n*-back ($\beta = 0.25$). The bias-corrected confidence interval did not include zero (95% CI [0.03, 0.67]) after 5000 bootstrap samples. Baseline performance on the untrained *n*-back variant was included to control for general correlations between LTM and WM performance that may directly or indirectly influence posttest *n*-back scores.
* denotes significant path (bias-corrected confidence interval excludes zero).

Mediators of Long-term *n*-Back Improvements

To understand the relationship between tDCS and long-term WM improvements, we tested a mediation model evaluating the role of LTM as a mediating variable between condition (active/sham) and posttest *n*-back (Figure 6). All variables were standardized, and paths are reported as standardized beta weights, with the exception of condition, whose paths are unstandardized. Incidental memory of *n*-back stimuli was used as the mediator, and baseline scores on the untrained *n*-back variant were included in the model as a control. We found significant direct effects of Condition on incidental recall ($b = 0.65$, 95% bias-corrected CI [0.09, 1.21]) and incidental recall on posttest *n*-back ($\beta = 0.39$, 95% bias-corrected CI [0.09, 0.71]), resulting in a significant indirect effect of Condition on posttest *n*-back ($b = 0.25$, 95% bias-corrected CI [0.03, 0.67]). We also ran a sensitivity analysis with an alternate mediator, using a latent variable derived from word retention scores measured 30 min and 24 hr after initial word learning. A similar pattern of results emerged, with a significant direct effect of Condition on word retention ($b = 0.84$, 95% bias-corrected CI [0.37, 1.32]), a marginal direct effect of word retention on posttest *n*-back ($\beta = 0.45$, 95% bias-corrected CI [-0.06, 0.88]), and a significant indirect effect of Condition on posttest *n*-back ($b = 0.38$, 95% bias-corrected CI [0.05, 0.98])

Transfer Effects

For each of the transfer tasks, the untrained *n*-back, metamemory, and the Sternberg, we regressed the dependent variable of interest on the following predictors: condition and spacing. After running the main effects model, we tested for interactions between Condition and each of the other two predictors in two separate models. No transfer effects were detected on any task; specifically, there were no main effects of Condition nor any significant interactions (all *p*s > .23; Tables A10–A12). Baseline interaction models were not tested because baseline is colinear with pretest scores.

Power Analysis

Since the COVID-19 pandemic paused research activities and cut our recruitment short, we conducted a retrospective power analysis using the R package *pwr* to determine the level of power we had in detecting our main training effects. For LTM effects, we considered our effect size estimates derived from the average delayed recall over five sessions (d = 0.72) and the cumulative recall at posttest (d = 0.82), which were both within the confidence interval of meta-analytic estimates (d = 0.625, 95% CI [0.250, 0.999]) of tDCS-induced episodic memory improvement in older adults (Huo et al., 2021). Using sample sizes of 24 and 28 and a two-sided significance threshold of α = .05, we found that we had power ($1 - \beta$) between .60 and .82 to detect effect sizes ranging between meta-analytic and our own observed effects. Power for WM training effects were calculated with the same parameters, except we used the overall effect size at posttest of d = 0.47, which again was within the confidence interval of meta-analytic estimates (d = 0.28, 95% CI [0.06, 0.52]) of tDCS-induced improvements on WM training (Mancuso et al., 2016). Here, power ($1 - \beta$) ranged between .18 and .38, suggesting we may have been underpowered to detect a true effect if it existed. Sample sizes of approximately 72–188 participants per group would have been required to detect effects in this range with traditionally accepted statistical power ($1 - \beta$ = .80). Despite having our recruitment cut short from the pandemic and being underpowered in some of our analyses, we note that our sample size exceeded many other tDCS studies of WM training, which ranged from 10 to 21 per group (Mancuso et al., 2016), and was comparable to many other studies of LTM, which ranged from 10 to 48 per group (Huo et al., 2021; Galli et al., 2019).

DISCUSSION

The current study set out with three initial aims: to quantify the relative efficacy of tDCS on LTM and WM training in older adults over the course of five training sessions, to evaluate the extent to which LTM consolidation mediates WM improvements, and to identify potential moderators of the tDCS effect. With respect to the first aim, we found tDCS to be effective in boosting LTM performance, with effects about 1.5 times stronger (d = 0.72–0.82) than those observed after WM training (d = 0.47), which were not significant. The LTM improvements were observed in free recall but not recognition, in line with previous reports (Perceval et al., 2020; Galli et al., 2019; Leshikar et al., 2017; Matzen, Trumbo, Leach, & Leshikar, 2015), which collectively suggest that tDCS affects LTM by facilitating processes related to elaborate recollection rather than surface-level familiarity (cf. Yonelinas, 2002). Furthermore, these effects were time dependent in that no significant differences were observed between groups at immediate recall directly after word learning (d = 0.35; Figure 2), but a tDCS advantage started appearing at the 30-min delayed recall (d = 0.72; Figure 2), which persisted for the duration of the week-long intervention and was most pronounced at posttest (d = 0.82; Figure 3). This suggests that tDCS decreases the rate of forgetting or, put another way, increases the strength of consolidation. The lack of transfer to a novel word list at posttest rules out general improvements in strategies or processing ability, suggesting specificity to the words learned during stimulation. Importantly, benefits were observed both explicitly when participants were aware of the eventual word recall tasks, as well as incidentally when participants passively encoded a variety of stimuli during *n*-back training without being told of an eventual recall task (Figure 5). Overall, our results add to accumulating evidence demonstrating that prefrontal tDCS can enhance LTM consolidation in humans (Huo et al., 2021; Galli et al., 2019) and is consistent with animal work that shows that tDCS increases hippocampal LTP and levels of brain-derived neurotrophic factor, an important protein for learning and consolidation (Cocco, Podda, & Grassi, 2018; Podda et al., 2016). However, a critical difference between human and animal work is that the human hippocampus is too deep to be directly targeted by tDCS. Thus, to the extent that mechanisms of human tDCS are analogous to animal models, effects may derive from increased LTP-like plasticity in superficial cortical areas or may indirectly stem from hippocampal LTP via hippocampal-prefrontal circuitry (Sigurdsson & Duvarci, 2016; Blumenfeld & Ranganath, 2007).

Despite the robust effects of tDCS on LTM, there were no discernable effects on WM at the group level (Figure 4). Performance during the training period was virtually identical between groups, although see Moderation section further below for a discussion of possible baseline-dependent effects. In considering the reasons for this overall null effect, one advantage of the current study design is that we are able to rule out explanations related to an ineffective tDCS montage. Because of the black box nature of delivering a current through the scalp, where even small displacements in electrode positioning can dramatically alter current density over the desired cortical region (Ramaraju, Roula, & McCarthy, 2018), it is often difficult to ascertain the extent to which the experimental manipulation successfully targets the cortical ROI at an individual level. This can be one major source of variability between studies that can account for some of the unreliability in WM effects throughout the literature. However, because of the robust tDCS-related improvements in LTM, we can largely rule out this concern and focus on alternative explanations. For example, one possibility we cannot rule out is interference effects or neural competition between LTM and WM since participants perform the two tasks back-to-back during training. Interference between different memory domains, even with distinct memoranda, has been documented before (Brown & Robertson, 2007) and may have eclipsed any potential tDCS effects. This would be consistent with why we observe the greatest numeric difference at posttest (see Figure 4) where there is no LTM task administered before *n*-back, despite performance that is almost completely overlapping during training. Moreover, a recent article demonstrates that LTM consolidation during sleep diminishes the benefit of sleep toward improving WM training performance (Chen, Niknazar, Alaynick, Whitehurst, & Mednick, 2021). However, the extent to which these factors truly influence our results is beyond the ability of our study design to investigate, and a large randomized controlled trial of tDCS in older adults has also previously failed to observe benefits to WM training even in the absence of LTM tasks (Nilsson et al., 2017). Thus, we will refrain from further speculation here.

Mediation Effects

Regardless of the specific reason why we did not observe a significant effect of tDCS on WM training, our mediation analyses suggest that any effect that did exist may actually have been driven by LTM rather than any direct improvements in WM per se. Specifically, we observed that individuals assigned to the active tDCS condition performed an average of 0.65 *SD*s higher than their sham counterparts on the incidental recall task embedded in the *n*-back training (see Figure 6). In turn, each standard deviation increase in recall scores resulted in a 0.39-*SD* increase in *n*-back performance at posttest. The indirect effect of tDCS on posttest *n*-back scores was thus an average improvement of 0.33 *SD*s and was statistically significant. In other words, even though we found no evidence that tDCS directly improved the ability to manipulate items held in WM during the *n*-back task, it did improve the long-term retention of these items, which in turn predicted better WM performance at posttest. From this, one might be tempted to speculate that increased familiarity with the items in LTM facilitated WM performance involving those same items, as has been demonstrated before (Oberauer, Awh, & Sutterer, 2017). Although this may be true to some extent, especially given reciprocal interactions between the hippocampus and pFC in both LTM and WM (Jin & Maren, 2015), our sensitivity analysis revealed the same pattern of results even when using word retention as the mediator rather than *n*-back stimuli recall. Therefore, what these mediators may actually be measuring are individual differences in the ability to consolidate information more generally. This is in line with a body of research demonstrating that sleep-dependent consolidation augments WM training benefits (Ferrarelli et al., 2019; Sattari et al., 2019; Pugin et al., 2015). Although our study is unable to pinpoint what exactly is being consolidated that benefits WM training, there has been speculation in the literature that WM training benefits may arise from the acquisition of new cognitive routines, akin to the acquisition of new skill sets, rather than improvements in existing processes (Gathercole et al., 2019). Our current data fit within this framework.

Importantly, our mediation models controlled for a second independent variable, baseline *n*-back performance, which itself could have predictive value for both posttest *n*-back as well as LTM recall scores because of shared variance between WM and LTM task performance (Unsworth, 2010; Ranganath & Blumenfeld, 2005). Thus, controlling for baseline rules out alternative explanations that the mediation effect could simply be related to general correlations between WM and LTM. In fact, we did observe a small indirect effect (0.12 *SD*s) of baseline *n*-back performance on posttest *n*-back, suggesting that this shared variance does play a role in the interrelationships between LTM and WM performance (i.e., those who perform well on one memory task are likely to perform well on another memory task). Nevertheless, the indirect effect of tDCS on *n*-back performance remained significant above and beyond any confounding influences of these interrelationships.

Finally, a weakness to our mediation model is the lack of a preexisting relationship between tDCS and posttest *n*-back. This is not a statistical weakness, as such a relationship is not a necessary prerequisite for probing indirect effects in mediation analysis (Hayes, 2018; O'Rourke & MacKinnon, 2018; Rucker, Preacher, Tormala, & Petty, 2011), and in fact, it is in cases where a total effect is absent where mediation analyses can be especially informative by proposing an alternate causal chain other than the original independent-dependent variable relationship (Pieters, 2017). However, it does hamper our efforts to explain the long-term effects of tDCS on WM performance in other studies that "did" observe an overall effect on WM enhancement (e.g., Ruf et al., 2017; Au et al., 2016; Stephens & Berryhill, 2016; Jones, Stephens, et al., 2015; Park, Seo, Kim, & Ko, 2014; Martin et al., 2013), because the mechanisms of action in these studies may potentially differ. Although our current results suggest that the effect of tDCS on WM is fully mediated through its effect on consolidation, it would be important for future studies that do find a strong overall effect on WM to parcel out the relative contributions of the direct and indirect effects of tDCS. This understanding could serve to inform future studies and to increase the precision of training and transfer effects. For example, if a large portion of what is actually being modulated by tDCS actually pertains to processes related to LTM rather than WM per se, then training can be spaced appropriately to allow for consolidation to occur, and transfer can focus on the declarative and procedural components of the trained task rather than any WM-specific skills. The current study provides a prime example of this in that we found significant effects on the declarative recall of stimuli used during *n*-back training despite a lack of an overall effect on the WM portion of the task itself.

Moderation Effects

Although tDCS did not seem to enhance WM training at the group level, we found tentative evidence (p = .054) at posttest for a selective benefit in those who started with lower baseline WM performance. This is consistent with our previous work in young adults (Katz et al., 2017), as well as in a body of other tDCS work that also shows a low-baseline advantage across a variety of tasks (Krebs et al., 2021; Perceval et al., 2020; Arciniega et al., 2018; Gözenman & Berryhill, 2016; Heinen et al., 2016; Looi et al., 2016; Minichino et al., 2015; Hsu et al., 2014; Tseng et al., 2012). Thus, despite the marginal nature of the current findings, the cumulative evidence for a moderating influence of baseline ability is compelling and should be an important consideration in future studies for identifying potential responders and nonresponders to tDCS.

In addition to baseline, the spacing interval between sessions was also found to moderate the effects of tDCS. There was a selective tDCS advantage for the daily training subgroup in the cumulative word recall task (Figure 3B–C), which involved learning between days, but no effects on delayed or immediate word recall, which only involved intraday learning (and thus an effect of spacing would not be expected). Correspondingly, the daily training subgroup also outperformed the every-other-day group during *n*-back training as well, but there were no differential effects as a function of tDCS. Although these results should be interpreted with caution because of the small spacing subgroup sizes (between 12 and 15 per group; Figure 3B–3C), it is notable that the effect size of daily spacing was over three times greater than every-other-day spacing on the cumulative recall task by posttest (d = 1.33 vs. d = 0.40). It may be that training every other day left too much time for forgetting to occur in our cohort of older adults, which may have eclipsed any effect tDCS could have had on boosting between-session consolidation. A related issue to consider is that longer spacing intervals are generally optimized for longer retention intervals (Cepeda, Vul, Rohrer, Wixted, & Pashler, 2008). Thus, with the short retention interval (~1–2 weeks) of our current study, there may not have been enough passage of time to show any advantage of every-other-day spacing above and beyond the benefits of daily spacing. Although we did have a longer retention interval planned as a 3-month follow-up in our study, we were unable to complete data collection because of COVID-19 and unfortunately are unable to draw any meaningful conclusions. However, see Table A1 for descriptive data on the follow-up measures.

We note that this advantage of daily spacing stands in contrast with our previous study on young adults (Au et al., 2016), in which almost all of the tDCS benefit on *n*-back training appeared over a weekend (~72-hr spacing) rather than between consecutive weekdays. However, this contrast is not necessarily contradictory, as the two studies assessed different populations and different memory domains (LTM vs. WM). Unfortunately, we did not find an overall tDCS effect or a tDCS × Spacing interaction within the WM domain in the current study, which would have afforded a more direct comparison to our previous results. Once more, however, we reiterate that these subgroup analyses, both in our current and previous results, contain rather small sample sizes and should be interpreted cautiously when informing future study designs. So, although we do not advise overreliance on the specific spacing intervals reported in our studies, especially given that the optimal spacing and retention intervals will vary because of a variety of factors such as task selection, population, and study length, we do admonish that spacing is an important and underexplored moderator in the tDCS literature that has both theoretical and empirical basis to influence responsiveness to tDCS (Goldsworthy et al., 2015; Monte-Silva et al., 2013; Alonzo, Brassil, Taylor, Martin, & Loo, 2012; Monte-Silva, Kuo, Liebetanz, Paulus, & Nitsche, 2010) and should be considered when designing longitudinal tDCS studies meant to act upon between-session consolidation.

Conclusions

The current study found that tDCS is effective for improving memory performance among older adults. As we predicted, there were stronger and more robust effects on LTM than WM, presumably because of the role tDCS plays in enhancing consolidation processes. This is underscored by the observation that, despite the lack of an overall effect on *n*-back WM performance, we did observe a strong effect on the incidental recall of the stimuli used in the *n*-back task. In other words, even though the short-term relational characteristics of WM stimuli were not better encoded (i.e., their n position), their long-term semantic characteristics were. Moreover, our mediation model suggested that any influence tDCS did have on WM training at posttest was mediated through its effects on enhancing consolidation.

Additionally, both of our hypothesized moderators, baseline and spacing, were influential in different contexts. First, we found modest evidence that tDCS was selectively beneficial for individuals with low baseline WM abilities. Second, we also found that tDCS was selectively beneficial for LTM consolidation in older adults when applied daily rather than every other day. We posit that there is likely an optimal spacing interval for tDCS to act upon after enough time has passed for memory consolidation to reach a certain strength but before too much forgetting occurs. This optimal interval, however, can be variable for different tasks and different populations and is largely an unknown factor in most studies.

Overall, our results add to a line of existing literature that has documented an association between prefrontal activity and LTM (reviewed in Blumenfeld & Ranganath, 2007). Moreover, the use of tDCS in our study to modulate this prefrontal activity goes beyond these previous neuropsychological and neuroimaging studies by implicating a causal role of the pFC in LTM formation and consolidation. Given the ubiquity of age-related memory decline (Small, 2001) and its predictive value in everyday functioning in old age (Borella et al., 2017), it is imperative that we develop new treatments and interventions to mitigate this decline. The use of tDCS to enhance learning and consolidation in older adults is one step in that direction and can be used to facilitate the acquisition of new skills, knowledge, and hobbies that may help older adults maintain active and stimulating lives well into their golden years.

APPENDIX A

Table A1. Descriptive Data

	Active tDCS Group			*Sham Group*		
	Pre (n = 24)	*Post* (n = 24)	*Follow-up* (n = 13)	*Pre* (n = 28)	*Post* (n = 28)	*Follow-up* (n = 14)
Trained n-back[a] (n-level)	–	2.36 (0.27)	2.41 (0.39)	–	2.19 (0.41)	2.50 (0.61)
n-Back stimuli recall[b] (no. of objects)	24.21 (8.36)	25.42 (11.36)	20.18 (15.09)	16.93 (7.09)	19.78 (8.43)	11.92 (8.25)
Cumulative recall (no. of words)	–	16.39 (9.05)	8.15 (11.00)	–	9.63 (7.59)	2.07 (2.87)
Word recognition (% correct)	–	0.67 (0.09)	0.62 (0.07)	–	0.69 (0.08)	0.57 (0.08)
Untrained n-back (Pr)	0.62 (0.17)	0.67 (0.09)	0.62 (0.07)	0.61 (0.20)	0.76 (0.15)	0.73 (0.10)
Sternberg item recognition (sec)	1190.67 (136.40)	0.75 (0.17)	0.75 (0.13)	1195.53 (210.96)	1171.22 (183.23)	1138.92 (193.26)
Metamemory (% correct)	0.29 (0.14)	1147.98 (126.27)	1116.20 (102.54)	0.29 (0.15)	0.33 (0.15)	0.12 (0.17)

Descriptive data are provided for pretest, posttest, and follow-up. Values in parentheses are standard deviations. Pr values for the untrained n-back are measures of accuracy as described in the Methods.

[a] Because of experimenter error, the analytic sample for the trained n-back task at posttest comprised 20 active and 24 sham participants.

[b] For n-back stimuli recall, the pretest column refers to the first measurement after Training Session 5. Because of technical glitches and experimenter error, the analytic sample sizes for the active and sham groups were n = 19 and n = 27, respectively.

Table A2. Intraday Immediate Word Learning

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Condition	2.24	2.25	.32
	Baseline LTM	4.71	1.12	<.001*
	Spacing	−1.85	2.23	.41
Baseline	Condition	2.30	2.17	.29
	Baseline LTM	4.82	1.83	.008*
	Condition × Baseline	−0.14	2.15	.95
Spacing	Condition	4.78	3.61	.19
	Spacing	−0.99	4.16	.81
	Condition × Spacing	−3.02	4.98	.55

n = 52. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized.

* $p < .05$.

Table A3. Intraday Delayed Word Recall

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Condition	6.56	2.57	.011*
	Baseline LTM	4.87	1.28	<.001*
	Spacing	−3.25	2.55	.20
Baseline	Condition	6.66	2.51	.008*
	Baseline LTM	5.05	2.06	.014*
	Condition × Baseline	−0.18	2.50	.94
Spacing	Condition	12.26	3.93	.002*
	Spacing	0.39	4.63	.93
	Condition × Spacing	−9.06	5.42	.095

n = 52. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized.

* $p < .05$.

Table A4. Between-day Cumulative Recall

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	2.00	0.15	<.001*
	Condition	3.18	1.32	.016*
	Baseline LTM	2.07	0.66	.002*
	Spacing	−1.89	1.32	.15
Baseline	Session	1.54	0.20	<.001*
	Condition	5.17	1.46	<.001*
	Baseline LTM	2.56	0.97	.008*
	Session × Condition	0.97	0.29	<.001*
	Session × Baseline	0.47	0.19	.014*
	Condition × Baseline	1.79	1.46	.22
	Session × Condition × Baseline	0.33	0.29	.24
Spacing	Session	1.41	0.29	<.001*
	Condition	9.12	2.18	<.001*
	Spacing	0.10	2.07	.96
	Session × Condition	1.68	0.42	<.001*
	Session × Spacing	0.15	0.40	.70
	Condition × Spacing	−6.47	3.05	.034*
	Session × Condition × Spacing	−1.17	0.59	.048*

$n = 52$. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

Table A5. Word Recognition

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Condition	−0.03	0.02	.10
	Baseline LTM	0.05	0.01	.001*
	Spacing	−0.05	0.02	.012*
Baseline	Condition	−0.03	0.02	.14
	Baseline LTM	0.03	0.01	.015*
	Condition × Baseline	0.03	0.02	.10
Spacing	Condition	−0.02	0.03	.64
	Spacing	−0.05	0.03	.14
	Condition × Spacing	−0.01	0.04	.76

$n = 52$. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized.

* $p < .05$.

Table A6. *n*-Back WM Training

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	0.09	0.01	<.001*
	Condition	−0.03	0.11	.78
	Baseline WM	0.18	0.06	.002*
	Spacing	−0.07	0.12	.57
Baseline	Session	0.09	0.02	<.001*
	Condition	−0.03	0.15	.83
	Baseline WM	0.14	0.09	.14
	Session × Condition	0.001	0.02	.98
	Session × Baseline	0.01	0.02	.47
	Condition × Baseline	0.21	0.15	.18
	Session × Condition × Baseline	−0.05	0.03	.10
Spacing	Session	0.13	0.02	<.001*
	Condition	−0.09	0.19	.65
	Spacing	−0.29	0.18	.10
	Session × Condition	−0.05	0.03	.18
	Session × Spacing	−0.08	0.03	.013*
	Condition × Spacing	0.11	0.26	.67
	Session × Condition × Spacing	0.08	0.05	.10

n = 52. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

Table A7. Posttest *n*-Back

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Condition	0.13	0.09	.17
	Baseline WM	0.15	0.05	.003*
	Spacing	0.02	0.10	.82
Baseline	Condition	0.12	0.09	.17
	Baseline WM	0.20	0.06	.001*
	Condition × Baseline	−0.17	0.09	.054
Spacing	Condition	0.07	0.14	.62
	Spacing	−0.17	0.16	.28
	Condition × Spacing	0.19	0.20	.33

n = 44. Because of a combination of technical glitches and experimenter error, data were lost or not collected for eight participants. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized.

* $p < .05$.

Table A8. *n*-Back Stimuli Incidental Memory Recall

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	2.17	1.10	.05*
	Condition	4.89	2.02	.015*
	Baseline LTM	3.33	0.94	>.001*
	Spacing	−3.78	1.97	.054
Baseline	Session	3.13	1.31	.017*
	Condition	4.01	2.32	.084
	Baseline LTM	4.27	1.43	.003
	Session × Condition	−2.59	2.06	.21
	Session × Baseline	2.50	1.27	.049*
	Condition × Baseline	1.28	2.20	.56
	Session × Condition × Baseline	0.72	1.95	.71
Spacing	Session	2.92	2.11	.17
	Condition	2.98	3.45	.39
	Spacing	−5.35	3.20	.095
	Session × Condition	−3.10	3.05	.31
	Session × Spacing	−0.12	2.83	.97
	Condition × Spacing	4.62	5.00	.36
	Session × Condition × Spacing	3.42	4.42	.44

n = 46. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Baseline is a continuous variable mean-centered to zero and standardized. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

Table A9. Mediation Effects

Independent Variable	*Direct Effect ($a \rightarrow b$)*	*Direct Effect ($b \rightarrow c$)*	*Direct Effect ($a \rightarrow c$)*	*Indirect Effect ($a \rightarrow c$)*
		Mediator: *Incidental Recall*		
Condition	0.65 [0.09, 1.21]*	0.39 [0.09, 0.71]*	0.14 [−0.42, 0.61]	0.25 [0.03, 0.67]*
Baseline	0.24 [−0.07, 0.69]	0.39 [0.09, 0.71]*	0.32 [0.11, 0.60]*	0.12 [0.03, 0.29]*
		Mediator: *Word Retention*		
Condition	0.84 [0.37, 1.32]*	0.45 [−0.06, 0.88]	−0.09 [−0.89, 0.60]	0.38 [0.05, 0.98]*
Baseline	0.27 [−0.01, 0.52]	0.45 [−0.06, 0.88]	0.28 [−0.02, 0.71]	0.12 [0.01, 0.33]*

n = 52. Regression coefficients for direct and indirect effects are shown for both mediation models (incidental recall and word retention). The independent variable is represented by a, the mediator by b, and the dependent variable (posttest n-back) by c. All variables are standardized except for Condition, which is a dummy variable referenced to sham. 95% bias-corrected confidence intervals are included in brackets.

* $p < .05$

A1. Transfer Effects

Table A10. Untrained *n*-Back

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	0.14	0.02	<.001*
	Condition	0.004	0.04	.93
	Spacing	−0.01	0.04	.76
Interaction	Session	0.13	0.04	.001*
	Condition	0.04	0.11	.70
	Spacing	−0.05	0.11	.63
	Session × Condition	−0.04	0.06	.53
	Session × Spacing	0.01	0.06	.82
	Condition × Spacing	−0.07	0.16	.68
	Session × Condition × Spacing	0.06	0.08	.44

$n = 52$. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

Table A11. Sternberg Item Recognition

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	−38.56	16.70	.021*
	Condition	−9.61	42.96	.82
	Spacing	46.45	42.79	.28
Interaction	Session	−63.36	63.98	.32
	Condition	−16.04	146.64	.91
	Spacing	−61.77	138.58	.66
	Session × Condition	16.02	93.24	.86
	Session × Spacing	72.52	88.16	.41
	Condition × Spacing	53.92	205.43	.79
	Session × Condition × Spacing	−63.23	130.27	.63

$n = 52$. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

Table A12. Metamemory

Model	*Variable*	*B*	*SE B*	*p*
Main effects	Session	0.05	0.02	.033*
	Condition	0.03	0.04	.43
	Spacing	0.02	0.04	.65
Interaction	Session	−0.01	0.04	.82
	Condition	−0.01	0.11	.92
	Spacing	−0.04	0.10	.67
	Session × Condition	0.06	0.06	.31
	Session × Spacing	0.07	0.06	.23
	Condition × Spacing	−0.10	0.16	.54
	Session × Condition × Spacing	−0.01	0.09	.89

$n = 52$. Regression coefficients are displayed for each predictor. Condition and Spacing are both dummy variables referenced, respectively, to sham and daily spacing. Session is an unstandardized, continuous variable, referenced to the last session rather than the mean for ease of interpretation.

* $p < .05$.

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Reprint requests should be sent to Jacky Au, University of California, Irvine School of Education, 3200 Education Building, Irvine CA 92697, or via e-mail: jwau@uci.edu.

Author Contributions

Jacky Au: Conceptualization; Formal analysis; Methodology; Project administration; Writing—Original draft. Rachel N. Smith-Peirce: Project administration; Writing—Review & editing. Elena Carbone: Project administration; Writing—Review & editing. Austin Moon: Project administration; Writing—Review & editing. Michelle Evans: Project administration; Writing—Review & editing. John Jonides: Conceptualization; Funding acquisition; Resources; Software; Supervision; Writing—Review & editing. Susanne M. Jaeggi: Conceptualization; Funding acquisition; Resources; Software; Supervision; Writing—Review & editing.

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Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience* (*JoCN*) during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance. The authors of this article report its proportions of citations by gender category to be as follows: M/M = .541, W/M = .213, M/W = .098, and W/W = .148.

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