Transcranial Direct Current Stimulation Enhances Verbal Working Memory Training Performance over Time and Near Transfer Outcomes

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Abstract

■ Studies attempting to increase working memory (WM) capacity show promise in enhancing related cognitive functions but have also raised criticism in the broader scientific community given the inconsistent findings produced by these studies. Transcranial direct current stimulation (tDCS) has been shown to enhance WM performance in a single session [Fregni, F., Boggio, P., Nitsche, M., Bermpohl, F., Anatal, A., Feredoes, E., et al. Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research, 166,* 23–30, 2005]; however, the extent to which tDCS might enhance learning on a WM training regime and the extent to which learning gains might transfer outside the training task remains largely unknown. To this end, participants engaged in an adaptive WM training task [previously utilized in Richmond, L., Morrison, A., Chein, J., & Olson, I. Working memory training and transfer in older adults. *Psychology & Aging, 26,* 813–822, 2011; Chein, J., & Morrison, A. Expanding the mind's workspace: Training and transfer effects with a complex working memory span task. *Psychonomic Bulletin & Review, 17,* 193–199, 2010] for 10 sessions over 2 weeks, concurrent with either active or sham stimulation of dorsolateral pFC. Before and after training, a battery of tests tapping domains known to relate to WM abilities was administered. Results show that tDCS enhanced learning on the verbal portion of the training task by 3.65 items. Furthermore, tDCS was shown to enhance near transfer to other untrained WM tasks in comparison with a no-contact control group. These results lend support to the idea that tDCS might bolster training and transfer gains in populations with compromised WM abilities. ■

INTRODUCTION

Working memory (WM) training has been shown to produce broad benefits akin to those achieved by aerobic cross training; sustained, focused practice in the domain of WM has been shown to positively influence fluid intelligence (Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Jaeggi et al., 2010; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008), inhibition (Richmond, Morrison, Chein, & Olson, 2011; Chein & Morrison, 2010), and reading comprehension (Chein & Morrison, 2010; see Morrison & Chein, 2011, for a comprehensive review). It is for this reason that WM training, unlike other more focused memory training regimes (i.e., mnemonic training; see Verhaeghan, Marcoen, & Goossens, 1992), has become such an attractive intervention method in the public arena (Begley, 2012; Hurley, 2012).

WM training is based on the principle that an individual's WM capacity has been shown to predict abilities in reading (Daneman & Carpenter, 1980), fluid intelligence (Unsworth & Engle, 2007), long-term memory, attentional control (Unsworth & Spillers, 2010; Engle & Kane, 2004), and reasoning (Kyllonen & Christal, 1990). Because a large body of prior work demonstrates a strong link between WM capacity and these other areas of cognition, it might be expected that increasing WM capacity would exert a positive influence on ones' ability in these related cognitive domains as well. Indeed, this is the very basis for conducting training in the domain of WM (Morrison & Chein, 2011).

The controversy surrounding WM training centers on the fact that, although offering great promise, published work also suggests that these broad benefits are difficult to come by (Shipstead, Redick, & Engle, 2010). Far transfer can be difficult to demonstrate (Owen et al., 2010), and findings can be inconsistent across laboratories and participant populations (Redick et al., 2013; Jaeggi et al., 2008). Thus, methods that would enhance training and transfer gains and therefore provide more robust and reliable outcomes would increase the utility of WM training as well as confidence in the effectiveness of these regimes.

Noninvasive brain stimulation, which may modulate neural plasticity, offers promise as a tool to enhance learning and memory (Cramer et al., 2011; Reis et al., 2008), although it has not been tested as an adjuvant for WM training. Transcranial direct current stimulation (tDCS) has been shown to enhance learning (Floel et al., 2011; de Vries et al., 2009; Kobayashi, Théoret, & Pascual-Leone, 2009; Nitsche et al., 2003) as well as transiently improve

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verbal WM accuracy over a single session (Fregni et al., 2005). In one particularly compelling study in the domain of WM, Fregni and colleagues applied 1 mA of stimulation for 10 min to left dorsolateral pFC (DLPFC) with the reference electrode placed over the right supraorbital area in healthy, normal participants. A 3-back letter WM task was performed concurrently with the last 5 min of stimulation. Anodal stimulation of left DLPFC increased accuracy on this task compared with sham stimulation. Additionally, this study went on to apply anodal stimulation to motor cortex with no effect and cathodal stimulation to left DLPFC with no behavioral effect. These manipulations show the specificity for both stimulation site and polarity on WM task performance (Fregni et al., 2005). Other reported effects in the domain of WM and tDCS have used current strengths, return electrode placement, stimulation length, WM tasks, or a combination of these factors that differ from Fregni et al. (2005; see also Seo, Park, Seo, Kim, & Ko, 2011; Zaehle, Sandmann, Thorne, Jancke, & Herrmann, 2011; Jo et al., 2009; Boggio, Castro, et al., 2006) but have resulted in findings generally consistent with those reported by Fregni and colleagues (2005).

tDCS has also been used in a small number of training studies in an attempt to enhance performance over time. Notably, Reis and colleagues trained participants to perform a difficult motor task over 5 days. Participants either received anodal stimulation or sham stimulation over motor cortex (i.e., M1). After 5 days of training, the group that received anodal stimulation showed greater skill acquisition on the trained motor task than the group receiving sham tDCS (Reis et al., 2009). Furthermore, although the decrement in skill (i.e., the slope) was similar in both groups at 85 days posttraining, because the anodal group achieved a greater skill level than the sham group during the learning phase, the anodal group maintained their superior skill on the training task (Reis et al., 2009).

Perhaps more important than gains on the trained task in a WM training study is whether skill can be enhanced in related cognitive domains. Encouragingly, anodal stimulation over frontal regions in conjunction with a computerized anomia treatment in patients with aphasia found that stimulation enhanced naming of trained items as well as untrained items in comparison with the sham condition (Baker, Rorden, & Fridriksson, 2010). However, enthusiasm regarding these findings must be tempered in light of a report that tDCS might be better suited for improving learning within a relatively narrow range (Iuculano & Cohen Kadosh, 2013). In a line of research closely related to the present study, Martin and colleagues trained participants on a dual *n*-back training task in conjunction with tDCS and found enhanced learning within the training paradigm, but evidence of off-line near-transfer effects as a result of active tDCS was observed only at a 1-month follow-up, not directly after training (i.e., posttesting session; Martin et al., 2013). Given the variability of findings in the current literature, the extent to which tDCS enhances learning within a task and the subsequent associated gains or costs in terms of transfer task performance remains unclear.

The goal of this study was to test whether tDCS can enhance the gains associated with WM training and also whether it can enhance transfer. It has been reported that those participants exhibiting the largest training gains tend to show the strongest gains on transfer tasks (Chein & Morrison, 2010; Jaeggi et al., 2008). Thus, it is possible that tDCS may serve to enhance transfer via increasing training task gains. As such, we hypothesized that tDCS would enhance learning on the trained task and boost transfer outcomes compared with control conditions.

METHODS

Participants

Fifty-eight healthy college-aged individuals participated in this study; individual participants were assigned to one of the study groups via simple random assignment. Twenty participants received active tDCS (M age = 20.7; M years education = 14.0; 35% men), 20 received sham stimulation (M age = 20.7; M years education = 14.2; 35% men), and 18 were assigned to the no-contact control (NCC) group (M age = 21.6; M years education = 15; 25% men). There were no differences in pretest WM scores, age, gender, or years of education between groups.

Participants were recruited from Temple University, the University of Pennsylvania, and the surrounding communities. Qualification criteria included the following: aged 18–30 years, right-handed, and available to come into the lab for training every weekday for 12 consecutive weekdays. Participants had to agree to participate in a 2-hr pretesting session before beginning training and another posttesting session following training in addition to the longitudinal phase of the study. Exclusion criteria for tDCS included the following: previous adverse reaction to tDCS, personal history of seizure, personal or family history of epilepsy, personal history of neurological or psychiatric disorder, current consumption of medications known to alter neuronal membrane stability (SSRIs, tricyclics, buproprion [Wellbutrin], antipsychotics, anticonvulsants, sedative/hypnotics, or psychostimulants [amphetamines, cocaine, methylphenidate]) and pregnancy. All women were required to take a pregnancy test before the initiation of the tDCS/longitudinal phase of the experiment. In addition, for the duration of the tDCS phase of the study, participants could not participate in any other tDCS or TMS studies. All participants were qualified to receive tDCS regardless of group assignment. All participants provided informed consent before the initiation of the pretesting session.

Pretesting

All testing took place individually. The pretest battery included a number of tasks tapping distinct cognitive constructs. One criticism of the current WM training literature is that transfer effects have been identified with single measures (Shipstead et al., 2010); thus, it is unclear if the underlying domain is being influenced in a more general manner. Accordingly, multiple assessment tasks were utilized for each key construct. In addition, transfer tasks that have previously been tested in the context of this particular training regime were included (Richmond et al., 2011; Chein & Morrison, 2010). See Table 1 for latent construct and transfer type for each task. Pre- and posttesting were conducted on the workday immediately preceding (pretesting) or following (posttesting) the training phase.

Working Memory

To assess near transfer of the training task to other WM tasks, two complex span tasks were utilized: (1) Automated operation span (Unsworth, Heitz, Schrock, & Engle, 2005). This task involves making decisions about math problems while also remembering letters for later recall. Participants were asked to solve a math problem by reading the equation and calculating the correct answer. After the operation is carried out, a letter is displayed for later recall. Once the span for a given trial is reached, participants must recall the letters that they saw in the order that they saw them (Unsworth et al., 2005). (2) Automated symmetry span (Unsworth et al., 2005). In this task, participants make a decision about the vertical symmetry of a black and white grid; following that decision, another grid appears with a to-be-remembered spatial location cued in red. The decision portion (black and white grid) and storage portion are interleaved until the span for a given trial is reached. At the end of the trial, participants are required to recall the spatial locations in the order they were presented (Unsworth et al., 2005). The outcome of interest was WM span according to the absolute scoring method described in Unsworth et al. (2005, but see Conway et al., 2005, for a discussion of alternate scoring methods).

Cognitive Control

Because there is shared variance between WM capacity and cognitive control abilities (Kane et al., 2004), it is plausible that enhanced WM capacity might be accompanied by enhanced cognitive control (Chein & Morrison, 2010). Two measures were used to assess this: (1) Stroop (Stroop, 1935). In this task, participants should respond to the color of the font rather than reading the color word. Because word reading is more automatic than color-naming participants are expected to have greater interference on incongruent trials. (2) Antisaccade. In this task, participants are required to inhibit the prepotent response to look at a flashing stimulus. Performance on this task has previously been shown to correlate with WM capacity (Kane, Bleckley, Conway, & Engle, 2001; Roberts, Hager, & Heron, 1994). The outcomes of interest include cost scores on both accuracy (congruent − incongruent) and RT (incongruent − congruent). The smaller the cost score, the more efficiently the cognitive control system is thought to be dealing with increasingly difficult task demands.

Sustained Attention

The neural correlates of sustained attention are found predominantly in frontal and parietal regions (Sarter, Givens, & Bruno, 2001), overlapping with areas thought to support WM (Cabeza & Nyberg, 2000). We previously tested older adults and found that participants self-reported enhanced sustained attention following WM training (Richmond et al., 2011). To assess this more systematically, we included two sustained attention tasks: (1) Psychomotor Vigilance Task (Dinges & Powell, 1985). Participants see a row of zeros on the screen, and after a variable amount of time, the zeros begin to count up (much like a stopwatch). The task is to indicate as quickly as possible when the "stopwatch" has been turned on (Dinges & Powell, 1985). (2) Sustained Attention Response Task (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997).

Table 1. Pre- and Posttest Battery, Testing Time, and Latent Constructs

Task	*Latent Construct*	*Transfer Type*
Automated Operation Span	Working memory	Near
Automated Symmetry Span	Working memory	Near
Stroop	Cognitive control	Far
Antisaccade	Cognitive control	Far
Psychomotor Vigilance Task	Sustained attention	Far
Sustained Attention Response Task	Sustained attention	Far
Raven's Advanced Progressive Matrices		Far
California Verbal Learning Test		Far
Nelson–Denny Reading Test		Far

Total testing time for pre- and posttests was approximately 2 hr.

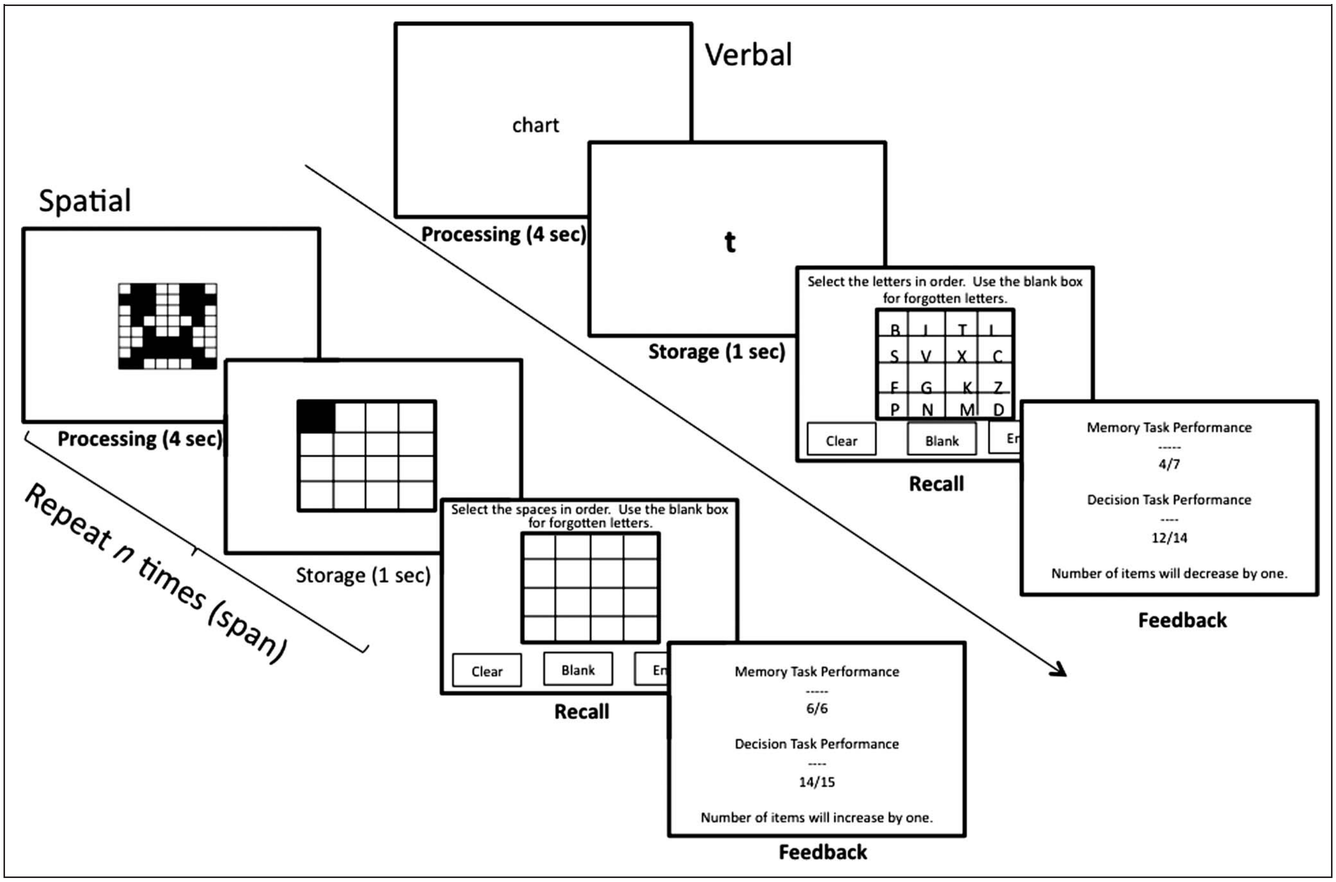

Figure 1. Schematic of the training task. Participants engaged in the adaptive complex WM span task for each of 10 training sessions. The task proceeded in the following way: Processing and storage portions of the task were interleaved until participants' individual span was reached. Participants made as many processing decisions as possible within a 4-sec window before receiving the to-be-remembered (storage) item. When span was reached, participants recalled the to-be-remembered items in the order that they were presented by clicking on boxes within the spatial array (spatial) or letters (verbal). Participants then received feedback regarding their performance before the subsequent trial was initiated.

Participants see 225 consecutive single digits (25 each of 0–9) displayed on the screen followed by an "X." Participants are instructed to respond to every presentation of an "X" except when the digit "3" is presented immediately prior; in this case, participants should not respond (Robertson et al., 1997). The outcome of interest was RT for correct trials only.

Additional Measures

Three additional measures were included in the transfer battery. All were chosen to make contact with prior WM training studies that in some instances showed transfer to these or similar measures (Richmond et al., 2011; Chein & Morrison, 2010; Jaeggi et al., 2008, 2010). (1) Raven's Advanced Progressive Matrices (Raven's; Raven, 1976), a test of nonverbal reasoning consisting of split-half forms 18 items[1] each; (2) *California Verbal Learning Test* (CVLT), a test of verbal long-term memory (Delis, Kramer, Kaplan, & Ober, 1987); and (3) Nelson–Denny Reading Test, a standardized test of reading comprehension (Brown, 1960). Alternate forms (or odd and even trials in the case of Raven's) were used for pre- and posttest assessment.

WM Training

An adaptive complex WM training task (Richmond et al., 2011; Chein & Morrison, 2010) was employed in this study. See Figure 1 for a schematic of the training task.

Training participants completed 10 approximately 30-min-long training sessions on a complex WM span task over a period of 2 weeks, with participants completing their sessions in a 5-day week (e.g., weekday) regimen. Training sessions were completed individually. This task is described in detail in Richmond et al. (2011) and Chein and Morrison (2010). In brief, approximately 15 min of each training session were devoted to spatial WM and approximately 15 min were devoted to verbal WM. The program was randomized with respect to order of presentation of verbal and spatial portions of the training task. The spatial subtest involved making symmetry decisions (symmetry) about a series of partially filled (black and white squares) matrices while intermittently encoding a sequence of highlighted locations for later recall in the order they were presented. Likewise, the verbal subtest required participants to make a series of word/nonword decisions (lexicality) while intermittently encoding a sequence of letters for later recall in the order they were presented. After each trial is completed, participants receive feedback regarding their performance.

All training participants began the program on Training Day 1 with a span of four recall items on both the verbal and spatial subtests, following the design of Chein and Morrison (2010). On all subsequent training days, starting span was determined by each individual's performance at the end of the prior session. The training task was adaptive to the participant's performance level, such that the number of recall items increased or decreased based on performance.

Brain Stimulation

During each training session, participants received either anodal or sham tDCS centered over left DLPFC, following prior tDCS studies in the domain of WM (i.e., Fregni et al., 2005). A Magstim Eldith 1 Channel DC Stimulator Plus (Carmarthenshire, UK) was used. The anode was placed over F3 (according to the international 10–20 system), and the cathode was placed over the right-sided analogue of F3 (i.e., F4).[2] Both the anodal and cathodal electrodes utilized in this study were 5×7 cm^2.

Active tDCS participants received 15 min of stimulation at 1.5 mA, with the last 5 min of stimulation occurring simultaneously with the initiation of task performance. During the first 10 min of stimulation, participants simply rested. As the physiological effects of tDCS have been shown to last up to 120 min after stimulation has ended (Fritsch et al., 2010), the effects of tDCS were thought to last throughout the entire training period. The same electrode montage was applied to sham participants, but these participants received 15 sec of "ramping up" of current followed by 15 sec of "ramping down" of current, after which time stimulation was discontinued. This sham method has been shown to be efficacious in blinding participants to their stimulation condition (Priori, Hallett, & Rothwell, 2009). Sensations associated with stimulation group were assessed at the end of each training session (see Richmond, Wolk, Coslett, Vyas, & Olson, 2013, for a detailed description of these data). In brief, participant blinding was not directly assessed; however, sensations associated with tDCS reported in Richmond et al. (2013) suggest that repeated exposure to stimulation is similar in terms of sensation profile to single-exposure studies (see Kessler, Turkeltaub, Benson, & Hamilton, 2012, as a point of comparison), providing evidence that the experience of the side effects associated with active tDCS in this study were in line with those observed in shorter-term studies.

NCC Group

In addition to the sham stimulation with training comparison group, to assess simple test–retest effects for assessment measures, we also included a group of control participants who received only pretesting and posttesting with no intervening longitudinal phase (i.e., an NCC group). Although this sort of control group has been sharply criticized in the past (Shipstead et al., 2010) as being poorly matched to the training group in terms of motivation, interest, and/or investment in the study, a recent effect size analysis from the published WM training literature found that effect sizes produced by active control and NCC groups for both near and far transfer were nearly identical (Chein, 2011), suggesting that previous critiques of the utilization of NCC groups in WM training studies may have been somewhat overstated. In addition, the inclusion of an NCC group allows us to explore simple test–retest benefits at the latent construct level.

Posttesting

Posttesting mirrored pretesting, using alternate forms when available (specifically, Nelson-Denny, Raven's, and CVLT). Stimuli for all other measures were presented in a randomized fashion such that first and second exposures to the task were not exact copies.

RESULTS

Training Results

Training data (i.e., final span from daily training sessions) were analyzed using mixed effects ANOVA examining the within-subject effects of Session (1, 10), Stimulus Modality (verbal, spatial), and the between-subject effect of Stimulation Group (active or sham). Comparing Sessions 1 and 10, WM span was found to increase with training in both groups, $F(1, 38) = 36.998$, $p < .001$. Performance on the verbal portion of the training task was significantly better than spatial span, $F(1, 38) = 73.976$, $p < .001$. Importantly, active tDCS participants exhibited higher WM spans compared with sham participants, $F(1, 38) = 4.975$, $p = .032$. No two- or three-way interactions reached significance (all ps $> .10$).

Visual inspection of the data suggested that the effect of tDCS was more robust in the verbal domain compared with the spatial domain. To that end, verbal and spatial performance was examined separately. Active stimulation, as compared with sham stimulation, enhanced verbal WM, $F(1, 38) = 27.613$, $p = .025$, and there was a trending interaction of Stimulation Group × Session, $F(1, 38) = 3.971$, $p = .054$, in the verbal domain. Although in absolute terms there appeared to be a benefit of active tDCS in the spatial task, this effect was not statistically reliable (group: $p = .136$; interaction: $p = .546$). Thus, tDCS significantly enhanced learning only in the verbal domain (see Figure 2).

To systematically explore the manner in which tDCS enhanced learning, a subsequent series of analyses were conducted. If tDCS acted as a catalyst for learning, we would expect the learning slope to differ in early versus late learning (and we would not expect this same pattern in

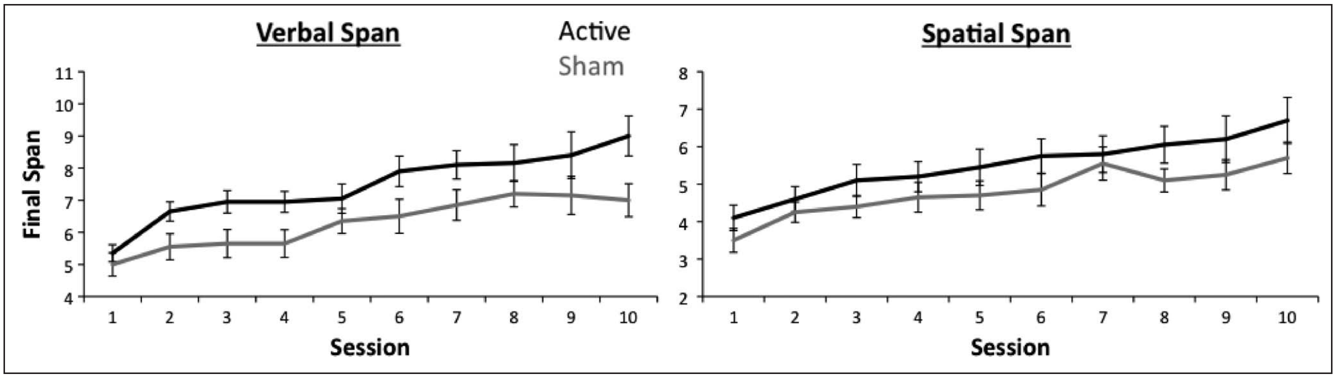

Figure 2. Daily training data for verbal and spatial variants of the training task. Active tDCS over left DLPFC significantly enhanced performance on the verbal WM task (left line graph). One active participant's data from Session 8 was excluded because of experimenter error.

the sham group). Alternatively, if tDCS were found to result in a consistent enhancement of performance over the training portion, we would expect that the learning curve would not differ early and late. Instead, we would observe that the training curve for the active group was simply shifted upwards of the sham group overall. To investigate these alternative hypotheses, a piecewise regression (McGee & Carleton, 1970) was conducted on active tDCS participants only. The regression line was split at Session 5, and a t test was used to compare the slopes of the learning curves early (Sessions 1–5) and late (Sessions 6–10) in training. tDCS was shown to globally enhance learning over all 10 sessions (comparison of regression slopes before and after Session 5 in the spatial domain: $t(198) = -0.480$, $p = .633$ and verbal domain: $t(198) = -0.570$, $p = .569$). In addition, the slopes and intercepts of the learning curves for the two groups were tested via ANCOVA (separate analyses were run for verbal and spatial portions). Beginning with the verbal portion of the training program, the slopes for active (0.3362) and sham (0.2467) performance over time were both significantly different from zero ($ps < .001$) but were not significantly different from one another, $F(1, 395) = 1.556$, $p = .213$. However, the active group's intercept was significantly elevated compared with the sham group (active intercept: 5.602, sham intercept: 4.933; $F(1, 396) = 31.637$, $p < .001$). Turning to the spatial portion of the training program, both slopes were found to be significantly different from 0 (active: 0.2514, sham: 0.2009, $ps < .001$) but did not differ significantly from one another, $F(1, 395) = 0.598$, $p = .440$. Again, the active group's intercept was found to be significantly higher than that of the sham group (active intercept: 4.113, sham intercept: 3.690; $F(1, 396) = 13.938$ m $p < .001$). Together, these results provide support for the idea that tDCS does not change the rate of learning over time (i.e., slope); rather, tDCS appears to shift the entire learning curve upwards (i.e., significantly different intercepts).

Near Transfer

Prior studies using this training regime have utilized 20 sessions of training (e.g., Richmond et al., 2011; Chein & Morrison, 2010), so we first examined the effect of our short-form training on transfer by comparing all participants who underwent WM training to the NCC group.

To assess near transfer, multiple measures (here, OSpan and SymSpan) indexing the same construct included in the transfer battery were z-scored separately for pre- and posttest sessions relative to overall pretest standard deviations. z scores from each individual measure were then averaged to create composite scores for pre- and posttest occasions. A 2 × 2 mixed effects ANOVA with the factors of testing occasion (pre, post) and training group (trained, untrained) was used to analyze z-score differences. Statistics of interest to the hypothesis are reported.

There was no main effect of Training Group ($p = .278$); however, the interaction of Testing Occasion and Group was significant, $F(1, 56) = 11.869$, $p = .001$: Participants in the training group (pretest mean: −0.044; posttest mean: 0.801)[3] showed significantly better pre- to posttest performance improvement than the NCC group (pretest mean: 0.097; posttest mean: 0.185). These data indicate that 10 sessions of training can lead to significant near transfer to other WM tasks and measures.

Next we examined the effect of tDCS on near-transfer outcomes. Here, three groups (i.e., active, sham, and NCC) were entered into the omnibus ANOVA.[4] In the event that significant two-way interactions were identified, planned follow-up comparisons (independent samples t tests) were conducted for pre- and posttest outcomes for each paired combination of data (i.e., active vs. sham, active vs. NCC, sham vs. NCC). Means and standard errors for both near and far transfer measures are reported in Table 2.

A significant interaction between Testing Occasion and Stimulation Group was observed, $F(2, 55) = 5.940$, $p = .005$. Follow-up planned comparisons were conducted for each combination of comparisons (active vs. sham, active vs. NCC, and sham vs. NCC) corrected for multiple comparisons (0.05/6 = 0.008 critical p value). No differences between groups were observed at pretest (active vs. NCC: $t(36)$[5] $= -0.211$, $p = .834$; sham vs. NCC: $t(36) = -0.753$, $p = .456$; active vs. sham: $t(38) = 0.553$, $p = .584$). At posttest, the active and NCC groups were statistically

Table 2. Mean (*SE*) of Performance on Transfer Tasks as a Function of Group and Session

Task	*Active*		*Sham*		*No-contact*	
	Pre	*Post*	*Pre*	*Post*	*Pre*	*Post*
Near Transfer						
OSpan	47.750 (4.067)	59.550 (2.512)	43.650 (4.831)	54.850 (3.442)	46.556 (4.814)	42.222 (4.374)
SymSpan	20.450 (1.884)	30.400 (1.939)	19.5 (1.997)	27.950 (2.342)	21.994 (1.807)	25.222 (2.166)
Far Transfer						
Anti-saccade RT cost ^	163.895 (36.314)	116.826 (22.492)	107.353 (17.454)	92.206 (17.603)	166.884 (28.890)	122.689 (30.968)
Anti-saccade ACC cost ^	0.296 (0.037)	0.283 (0.039)	0.217 (0.030)	0.217 (0.030)	0.306 (0.034)	0.263 (0.033)
Stroop RT cost ^	96.691 (12.695)	87.173 (14.916)	94.764 (14.586)	85.728 (13.855)	125.571 (23.667)	106.039 (16.596)
Stroop ACC cost ^	0.041 (0.016)	0.017 (0.010)	0.031 (0.010)	0.054 (0.047)	0.018 (0.008)	0.021 (0.008)
SART RT ^	393.274 (31.765)	361.533 (26.094)	343.332 (13.610)	318.145 (16.517)	399.232 (22.330)	349.558 (17.961)
PVT RT ^	347.154 (6.441)	394.664 (15.168)	358.203 (8.445)	372.336 (15.065)	386.320 (18.576)	424.204 (25.937)
Raven's	11.400 (0.947)	11.300 (0.818)	10.000 (0.707)	10.368 (0.766)	10.050 (0.716)	11.444 (0.764)
Nelson–Denny	34.450 (0.682)	34.05 (1.241)	34.550 (0.663)	34.947 (0.628)	32.167 (1.373)	33.000 (0.957)
CVLT Correct	87.750 (2.821)	87.700 (3.158)	81.250 (2.785)	83.053 (2.572)	87.889 (2.671)	91.333 (2.763)
CVLT Intrusions ^	1.05 (0.294)	1.650 (0.599)	2.100 (0.624)	2.842 (1.077)	1.389 (0.642)	2.333 (0.922)
CVLT Repetitions ^	4.850 (1.913)	2.450 (0.756)	3.800 (1.004)	3.526 (0.890)	2.889 (0.922)	1.889 (0.464)

Absolute scoring method for OSpan and SymSpan are reported. Antisaccade and Stroop ACC cost data are reported in terms of proportions. The tasks that have smaller scores associated with better performance are as follows: Anti-saccade RT cost, Anti-saccade ACC cost, Sart, PVT, CVLT Intrusions, CVLT Repetitions. These reversals (smaller scores = better performance) are denoted in the table with ^ to assist with clarity. For all other tasks (OSpan, SymSpan, Raven's, Nelson-Denny, CVLT correct), higher scores are associated with better performance.

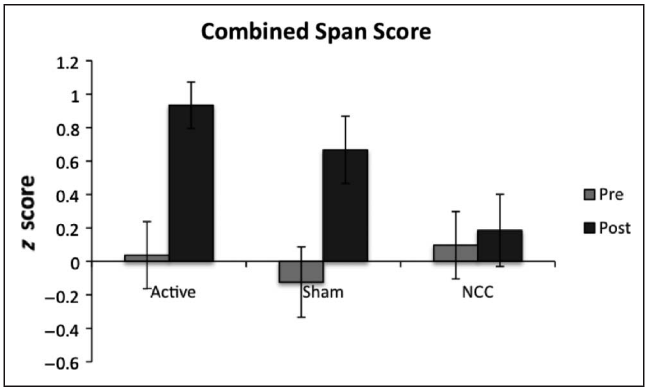

Figure 3. Near-transfer findings. Active tDCS participants achieved significantly better posttest outcomes on tasks indexing WM compared with the NCC group.

different, $t(36) = 2.980$, $p = .005$; however, the difference between active versus sham did not reach statistical significance, despite a numerical advantage for the former (active vs. sham: $t(33.741) = 1.092$, $p = .283$; sham vs. NCC: $t(36) = 1.639$, $p = .110$). See Figure 3 for a depiction of these data.

Far Transfer

There was no evidence of significant transfer from WM training itself (active and sham training groups collapsed) to any of the far transfer measures (i.e., cognitive control, sustained attention, CVLT, Raven's Advanced Progressive Matrices, Nelson–Denny Reading Test). In addition, there was no evidence that tDCS modulated transfer on any of the far transfer measures.

DISCUSSION

The present work examined the effect of tDCS on WM training and transfer. The addition of active tDCS during WM training enhanced learning in the verbal domain. Our findings support the claim that tDCS enhances practice effects (Iuculano & Cohen Kadosh, 2013; Baker et al., 2010; Reis et al., 2009). Additionally, we found evidence that the learning gains transferred to conceptually similar, but untrained, tasks.

Our findings are novel in three ways. This is one of the first studies of its kind to examine tDCS-enhanced multisession learning in the domain of WM. Previous research using tDCS in the domain of WM has focused specifically on single-session WM performance (Seo et al., 2011; Zaehle et al., 2011; Boggio, Ferrucci, et al., 2006; Fregni et al., 2005; Marshall, Molle, Seibner, & Born, 2005), providing "proof of concept" for the idea that tDCS can enhance WM performance, albeit transiently. Until recently, there was no evidence that tDCS could enhance WM over longer periods of time. A conceptually similar study to the one presented here was recently published by Martin and colleagues (2013). This work will be discussed in greater detail below.

In other literature, there are a small number of multisession tDCS studies showing positive effects on motor learning (Reis et al., 2009), verbal learning after stroke (Baker et al., 2010), and math learning (Iuculano & Cohen Kadosh, 2013).

Second, the effect of tDCS on complex span performance has not been examined. Prior studies of short-delay forms of memory coupled with tDCS have used *n*-back, Sternberg, or digit span paradigms (Seo et al., 2011; Zaehle et al., 2011; Boggio, Ferrucci, et al., 2006; Fregni et al., 2005; Marshall et al., 2005). Our study provides evidence that complex verbal WM span can be enhanced by active tDCS.

Third, we found near transfer after a limited number of training sessions—10—comparing performance of our tDCS + WM training group to an NCC group. Near transfer was indexed by multiple tasks to increase the reliability of transfer claims (see also Redick et al., 2013) following training. This finding supports the idea that the effect of tDCS in conjunction with WM training may serve to augment learning beyond the training paradigm to enhance the underlying cognitive operation. Importantly, the only comparison that resulted in statistical significance was the comparison of tDCS versus NCC (tDCS vs. training-only and training-only vs. NCC were not significant), suggesting the possibility of an additive effect of tDCS beyond training alone. Future research will serve to clarify the point at which tDCS may be found to have significant benefit to transfer effects above and beyond training itself.

Prior behavioral research found evidence of far transfer following 20 training sessions using the same training paradigm (Richmond et al., 2011; Chein & Morrison, 2010). As we found no evidence of far transfer following from either training + sham or training + active stimulation, it may be that more than 10 training sessions are needed to achieve far transfer gains. Visual inspection of the training data shows that learning had not yet plateaued. The finding of a possible dose-dependent response with the current paradigm is consistent with the work of other groups utilizing different training regimes (Jaeggi et al., 2008).

Additional analyses examined the way in which tDCS enhanced learning. tDCS was shown to enhance learning to the same degree during early and late training. The mechanism by which tDCS enhances learning, then, is not sensitive to cognitive changes that occur in the phase shifts from early to late learning (i.e., automaticity, task familiarity), at least over 10 sessions. These data provide preliminary support for the use of tDCS to improve learning in other training or intervention studies; in particular, to improve learning to a greater degree than simple practice. Importantly, the enhanced intercept for the active group but no differences in slope suggest that the active tDCS group performed the daily sessions at a higher level but did not necessarily extract more from the training task than the sham group. Future work could assess the extent to which the pattern of findings in relation to intercept and slope hold with additional sessions. Because it does not appear that learning in either domain, for either group, plateaued within 10 sessions, an interesting research question that remains unanswered surrounds the possibility that tDCS may help participants avoid a "leveling out" of learning.

There is some evidence, albeit limited, that we would have found similar effects had we used a different WM training regime. Martin and colleagues recently published a study in which they paired tDCS with a different WM training regime—the dual *n*-back—but the same number of training sessions (10 sessions) and reported somewhat similar findings. In short, they found evidence of enhanced training with active tDCS (main effect of Condition, active > sham) but only while stimulation was on. There was evidence of some near transfer, to digit span, but no evidence of far transfer.

Our study improves upon the design and extends the findings of Martin et al. (2013) in a number of ways. First, cognitive constructs were indexed by multiple transfer tasks. Therefore, evidence of transfer here speaks to enhancement of the underlying cognitive mechanism rather than single, task-specific transfer effects. In addition, both studies utilized left DLPFC as the region targeted by anodal stimulation, motivated by prior work. Importantly, we find stronger evidence of a tDCS effect on the verbal portion of our training regime. In the context of the dual *n*-back task, it may be difficult to understand the verbal/spatial distinction given the fact that the *n*-back level was the same for the visual and auditory streams (Martin et al., 2013). Despite these methodological differences, both we and Martin et al. (2013) find evidence that tDCS enhances learning in the domain of WM and this enhancement extends beyond a simple enhanced practice effect to conceptually similar tasks. In addition, both studies (current work; Martin et al., 2013) failed to find any evidence of far transfer effects following tDCS-enhanced WM training after exposure to a limited number of practice sessions, suggesting that additional training + tDCS may be needed to produce far transfer.

Limitations of the Current Work

One limitation of the current work is the inclusion of a test–retest control group. As previously discussed, a recent effect size analysis determined that the average effect sizes produced by test–retest and active control groups are nearly identical (Chein, 2011), suggesting that demand characteristics, while certainly different between these two types of control groups, may not influence transfer outcomes to the degree previously thought (Shipstead, Redick, & Engle, 2012; Shipstead et al., 2010). More convincingly, demand characteristics were identical between our active and sham tDCS groups, but only the active and NCC groups differed significantly at posttest. This suggests that differential demand characteristics cannot fully account for the pattern of results presented here. Instead, the inclusion of the sham training group and the subsequent lack of effect in comparison with the NCC group lend support to the interpretation that tDCS was an important addition to the training paradigm in inducing near-transfer effects, as training alone was not found to differ significantly from our test–retest control. Future work may be able to provide stronger evidence to this point by finding a stepwise pattern of transfer outcomes (tDCS + training > training alone > NCC).

An additional limitation of this research relates to the spatial resolution of tDCS. Frontal regions have been implicated in a wide variety of cognitive operations. As such, the application of tDCS to frontal sites has been reported to modulate performance in disparate operations such as inhibition (Ditye, Jacobson, Walsh, & Lavidor, 2012), planning abilities (Dockery, Hueckel-Weng, Birbaumr, & Plewnia, 2009), automaticity for newly learned material (Iuculano & Cohen Kadosh, 2013), declarative memory (Javadi & Walsh, 2012), and risk taking (Fecteau et al., 2007) in addition to WM. Because the swath of cortex affected by tDCS is relatively large, the specific portion of the DLPFC that was most influential in enhancing training gains is unknown. Future research with other methods, such as TMS, may help elucidate more specific neural underpinnings of tDCS-enhanced learning (see also Miniussi et al., 2008, for a review and discussion of the mechanisms of tDCS and TMS in cognitive neurorehabilitation).

One important limitation that should be noted with respect to the current set of findings relates to the lack of significant near-transfer differences between active and sham training participants. Although our interpretation of the findings here would have been strengthened had the comparison of active versus sham reached statistical significance, it is important to note that only the active tDCS + WM training compared with the NCC group resulted in a significant difference. Therefore, had the short-form WM training been conducted without tDCS (as in the sham group), these results would have provided no evidence for improvement in terms of transfer outcomes following WM training. We believe that these results provide preliminary evidence that tDCS enhances learning beyond the training domain. However, future research in this vein may pair tDCS with longer forms of WM training to observe greater divergence between the training groups with respect to transfer profiles.

Open Questions

Perhaps the most obvious question that follows from the pattern of results from this study is whether anodal stimulation of right DLPFC might enhance WM training and transfer outcomes, especially in tasks with a strong spatial component. It is possible that the effects of active tDCS on spatial WM did not bear out statistically (although there was a numerical effect) because the positive electrode was placed over the left DLPFC, a part of the cortex known to be relatively more important for verbal processing (Reuter-Lorenz et al., 2000). Thus, reversing the polarity of stimulation may lead to enhanced effects in the spatial domain. We note that the degree to which tDCS might modulate spatial WM abilities is not well understood because the existing literature has focused on verbal WM. Alternatively, spatial WM may require more training sessions than the small amount offered by the current study because of its relatively greater difficulty. Prior studies have related improvement in the spatial domain of training specifically with far transfer (Chein & Morrision, 2010), suggesting that enhancing this component of training may have more benefit in terms of far transfer outcomes. Applying positive stimulation over right DLPFC to enhance learning on spatial WM tasks and thereby attempting to increase transfer offers a tantalizing future direction.

It would also be fruitful to extend the training to 20 sessions, as was done in prior studies utilizing this regime (Richmond et al., 2011; Chein & Morrison, 2010), to enhance the transfer profile. Ten sessions of tDCS were well tolerated by our study participants, and no adverse effects were reported; we foresee no ethical or clinical reason why 20 sessions would not be tolerated as well (see also Richmond et al., 2013). Future researchers may wish to determine the point beyond which the benefit additional training is not evident in the transfer profile. Overall, the extent to which tDCS might modulate far transfer remains unknown, although we remain optimistic in light of the positive near transfer reported here.

By and large, the question of transfer has not been a focus of the tDCS literature. However, two contrasting reports have raised questions regarding the mechanism of tDCS-enhanced learning. Baker and colleagues (2010) found near transfer to the naming of untrained items after anomia treatment coupled with tDCS in aphasic patients. Conversely, Iuculano and Cohen Kadosh (2013) recently reported in a sample of healthy, college-aged participants, that those participants who showed enhanced magnitude symbol mapping on the training task with tDCS failed to show near-transfer benefits on an untrained task. Although our sample and design were in some ways similar to Iuculano and Cohen Kadosh's (2013), our findings stand in contrast to their reported effects; the study presented here supports the notion that performance outside the training task can be enhanced with the addition of tDCS in comparison with a test–retest control group.

One of the most interesting future directions for this research pertains to the possibility of conducting a WM training + tDCS study in populations with compromised WM, such as older adults. Research suggests that tDCS can potentiate LTP-like mechanisms (Fritsch et al., 2010). Furthermore, it has been suggested that older adults may exhibit lower levels of LTP in hippocampal regions compared with younger adults (Driscoll et al., 2003). If this is true in other brain regions of aging adults as well, older populations may benefit from tDCS to a greater degree than younger adults given that younger populations exhibit higher basal levels of LTP.

Conclusions

These data provide the first demonstration in the domain of WM that tDCS can enhance performance in verbal WM over time and that near transfer can be achieved after only 10 sessions of WM training when paired with tDCS (but not with 10 sessions of training alone) compared with a test–retest control group. However, there was no evidence of far transfer for either training group (active + training, sham + training) after only 10 sessions of training. Future research may investigate the effect of tDCS on spatial WM, as well as whether training gains in this domain may be related to transfer. Altogether, these data provide compelling preliminary evidence that tDCS is an effective, useful tool to enhance learning in normal, healthy adults. Furthermore, these findings provide theoretical support for the possible utility of adding tDCS to extant rehabilitation interventions to boost the efficacy of these regimes.

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Notes

1. A time limit of 22.5 min was imposed for Raven's (i.e., half of the standard 45-min limit for the 36-item version of the test). This resulted in the failure to complete all 18 items within the limit for three data points. These scores did not differ significantly from those scores obtained by participants completing all 18 items within the time limit ($p = .774$) and thus were included in further analyses.
2. Placement of the cathode over right DLPFC was based on a series of pilot studies suggesting that, in two sessions of stimulation, this placement resulted in larger effects than right supraorbital placement of the negative pole.
3. Means represent average combined z scores for pre- and posttest.
4. In addition, each near transfer task was assessed separately using a 2 × 3 ANOVA. The interaction term for OSpan ($p = .006$) was found to be relatively stronger than that for SymSpan ($p = .050$), suggesting that these results are not simply an artifact of the similarity between SymSpan and the spatial portion of the training program.

5. Equality of variances was checked using a Levene's test on all *t* tests. When the Levene's test revealed significant differences between variance equality, degrees of freedom representing the assumption of unequal variances were used.

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