COMBINING WORKING MEMORY TRAINING AND NON-INVASIVE BRAIN STIMULATION TO ENHANCE THE EFFECTS OF TRAINING AND TRANSFER

A Dissertation
Submitted to
The Temple University Graduate Board

In Partial Fulfillment
of the Requirements for the Degree
DOCTOR OF PHILOSOPHY

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August, 2013

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ABSTRACT

Studies attempting to increase working memory (WM) capacity show promise in enhancing related cognitive functions (see Morrison & Chein, 2011 for a recent review), but have also raised criticism in the broader scientific community given the scattered findings produced by these studies (Morrison & Chein, 2011; Shipstead, Redick, & Engle, 2010, 2012). Non-invasive brain stimulation, in particular transcranial direct current stimulation, has been shown to enhance WM performance in a single session (Fregni, et al., 2005) as well as learning over time in other cognitive domains (Iuculano & Cohen Kadosh, 2013; Reis, et al., 2009). However, the extent to which tDCS might enhance learning on a WM training regime, and the extent to which learning gains might transfer outside of the training task remain unknown. To this end, participants engaged in an adaptive WM training task (previously utilized in Chein & Morrison, 2010; Richmond, Morrison, Chein, & Olson, 2011) for 10 sessions over two weeks, concurrent with either active or sham stimulation of dorsolateral prefrontal cortex. Before and after training, a battery of tests tapping domains known to relate to WM abilities was administered. Results show that tDCS reliably enhanced learning on the training task, particularly in the verbal domain. Furthermore, tDCS was shown to enhance transfer to other untrained WM tasks. These results lend support to the idea that tDCS might bolster training and transfer gains in populations with compromised WM abilities.

ACKNOWLEDGEMENTS

I have been very lucky throughout my time in graduate school to be helped and supported by an incredible group of mentors, friends and family.

First, I would like to thank my committee members. *Ingrid*, I'm not sure there's space to properly thank you here. I have learned a great deal from you throughout my time as your student, not only about science, but also about career development and the intangibles of academia. In particular, your support of my interest in WM training from early on, although the lab was going in a different direction, was invaluable in allowing me to develop this line of work. *Tania*, thank you for always offering an interest in, and support of, my research. I also appreciate that you've always included me as a member of your lab although my interests don't necessarily 'fit in' to the everyday action world. *Jason*, thank you for taking me under your wing and sharing your interests in working memory training with me as a first-year graduate student- I'm not sure you knew you'd be stuck with me for so long, but I have certainly learned quite a bit as a result of our extended collaboration. *Roy*, I appreciate your willingness to share your resources, time and expertise on all things related to brain stimulation; had it not been for your guidance early on in my learning about tDCS this project would not be possible. To *Dave*- thank you for committing your time and resources to this big, risky project and for being on campus for every single tDCS session. Last, thank you *Nora* for agreeing to serve on my committee and your continued interest in WM training.

I would also be remiss if I didn't thank my friends and fellow graduate students. *Laura Skipper, Kinnari Atit, Vanessa Troiani* & *Alex Morrison*- thank you for talking through tough questions well before 9 am and after 5 pm, providing interesting suggestions and ideas when I was stuck, and always knowing when it was time to quit thinking about it and go out for coffee instead. Thank you also to my friends *Rachel Wainer*, *Kelly Estell* and *Liz Trost* for reminding me that there is life outside of science and encouraging me to visit it once in a while.

Finally, my family deserves a large portion of the credit for reaching this milestone. Thanks to my *dad* for the constant reminder to 'play the full 60 minutes' but never to let the work outweigh the enjoyment of anything that you do. To my sister, *Raquel*- what can I say? Thank you for always being ready with something to make me laugh- intentional or not. You remind me not to take it all so seriously. *Mom*- thank you for always holding me to the highest standard, academic and otherwise. You were never willing to accept anything less than my best effort. Because of your encouragement of my curiosity as a young girl about the hows and whys of almost everything, I grew to love learning. Thank you for that incredible gift. Finally, to *Adrian*- I don't even know where to begin. I couldn't have done this without your constant love and support. Thank you for encouraging me to follow my dreams even when that means putting physical distance between us. I couldn't imagine a better 'teammate.'

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CHAPTER 1

INTRODUCTION

In recent years, cognitive training has received a great deal of attention in the public arena (Begley, 2012; Hurley, 2012; Jonides, Jaeggi, Buschkuehl, & Shah, 2012) as well as criticism within the scientific community (Melby-Lervag & Hulme, 2012; Redick, et al., 2012; Shipstead, et al., 2010, 2012). The controversy surrounding cognitive training centers on the fact that, while offering promise as a tool to induce broad cognitive enhancement or remediate deficits associated with learning disabilities, aging and other conditions in which a number of cognitive domains are affected, much of the published work shows relatively weak evidence that cognitive training produces the expected benefits. This is particularly important as many for-profit companies are offering 'brain training' to the public (e.g. Nintendo's Brain Age, Lumosity.com) predicated on the idea that casually playing 'brain games' can enhance cognitive function to the same degree as more well-controlled laboratory based cognitive training regimes. Furthermore, the laboratory based effects are often presented to the public in a more positive light than they are generally viewed within the scientific community (Shipstead, et al., 2012).

Arguably, working memory (WM) training offers the greatest promise with regard to transfer of skills outside of the trained domain, although there has been some success associated with training the executive control system as well (i.e. task switching, see Karbach & Kray, 2009). While strategy training (Lustig & Flegal, 2008) is quite successful at increasing specific task performance, training of this sort has been shown to be limited in its ability to influence performance in disparate cognitive domains. In contrast, 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 (Engle & Kane, 2004; Unsworth & Spillers, 2010) and reasoning (Kyllonen & Christal, 1990). Theoretically, because previous literature has demonstrated a strong link between WM capacity and these other areas of cognition, increasing WM capacity could theoretically 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).

WM training studies, by and large, follow the format of a pre-test battery comprised of tasks tapping cognitive domains thought to rely on, or partially overlap with WM capacity. After the pre-test battery, participants are randomly assigned to the control group (typically a no-contact control, but see Klingberg, et al., 2005; Redick, et al., 2012; Richmond, et al., 2011) or the adaptive WM training group (discussed in greater detail below). At the end of the training, both groups are post-tested on a battery that mirrors the pre-test. Any gains exhibited by the control group are thought to reflect the benefit of previous exposure to the task (i.e. test-retest gains); gains in the training group above and beyond control group post-test performance is attributed to increased WM capacity as a result of practice with the training task (i.e. significant group x session interaction, with training group exhibiting superior post-test performance compared to control group). While this is a relatively young field of research, some research teams have published findings showing a positive influence of WM training on a number of cognitive domains (see Chein, Morrison, Richmond, & Olson, under review; Morrison & Chein, 2011 for recent reviews of this literature). Importantly, increased ability in the same cognitive domain as the training regime (for our purposes, WM) is termed 'near transfer'. Increased ability in the training group compared to the control group for cognitive domains outside the scope of WM are termed 'far transfer' (see Chein, et al., under review; Morrison & Chein, 2011 for an extended discussion of this distinction). While near transfer is important for demonstrating that increased ability on the training task over time doesn't simply represent task-specific learning or strategy implementation, the field as a whole is more interested in demonstrating benefits in far transfer (Shipstead, et al., 2010).

These sorts of training studies are difficult to conduct for a number of reasons. Subject attrition can be quite high (e.g. Owen, et al., 2010), likely due to both the longitudinal nature of the experimental design and the near-daily effort required by participants. These studies are also costly in terms of subject payment and staff required to oversee the project. In utilizing a no-contact control group, study cost and data management demands are kept to a minimum, but other issues arise. No-contact control groups can give information about the effect of previous exposure to a task on post-test scores, but cannot give insight into expectancy effects or motivation that might be differentially present in the training group (see Chein, et al., under review; Morrison & Chein, 2011; Shipstead, et al., 2010, 2012). Approaches that have been utilized in an attempt to ameliorate this concern include the utilization of a non-adaptive version of the training task (see Holmes, Gathercole, & Dunning, 2009; Klingberg, et al., 2005) or to ask control participants to engage in another type of cognitive task that is not thought to enhance cognitive function broadly (e.g. completing trivia quizzes, see Richmond, et al., 2011).

Turning to the training task itself, there are a number of important issues worthy of discussion. Training is typically either repetitive from day-to-day, albeit adaptive (see Chein & Morrison, 2010; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi, et al., 2010; Richmond, et al., 2011) or participants will engage in a number of different training tasks on a daily basis (see Klingberg, et al., 2005; Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009 for examples of this approach to training). Interventions with multiple training tasks may confer the advantage of increased day-to-day subject arousal, but it can be challenging to interpret transfer findings regarding which training task(s) give rise to any given transfer effect (Klingberg, et al., 2005; Thorell, et al., 2009). Additionally, it is largely unknown what constitutes the appropriate length of training.

Perhaps most importantly, it is difficult to get a read on the different transfer effects observed across training paradigms as there is no standard transfer task or sets of tasks in the literature (Morrison & Chein, 2011). A recent review of transfer findings across the lifespan reported effect sizes for transfer tasks (Chein, et al., under review), broadly defined in terms of 'near' and 'far'; this approach allows for a clearer overview of the literature as a whole. Admittedly, this approach glosses over important methodological differences between studies, especially in terms of far transfer, that might be informative. Nonetheless, the effect size analysis found overall larger effect sizes for near compared to far transfer. Furthermore, far transfer measures that have been included in testing batteries are relatively scattered, pointing to the idea that it is not yet well-understood what measures might be good indices of far transfer following from any given training regime (Chein, et al., under review). However, if researchers conducting this work aspire to advance beyond individual research teams reporting disparate findings using their specific training regime, the field should work towards a consensus regarding one or more appropriate transfer tasks to include in pre- and post-test assessment batteries. Another, possibly more fruitful, approach to this specific research question might be to conduct a study designed to assess the comparative efficacy of different WM training regimes.

Overview of transcranial direct current stimulation

Brain stimulation techniques offer promise as a possible tool to remediate or enhance learning and memory (Cramer, et al., 2011; Reis, et al., 2008). Transcranial direct current stimulation (tDCS) has previously been used in conjunction with training regimes, most notably in the motor domain (Reis, et al., 2009). In addition, tDCS has also been shown to effectively manipulate WM performance in a single stimulation session (Fregni, et al., 2005). Perhaps most importantly, tDCS has been used in stroke patients with chronic aphasia in conjunction with a standardized anomia treatment. This study showed generalization of learning to untrained items after stimulation (Baker, Rorden, & Fridriksson, 2010).

Technical Summary of tDCS

There are two polarities with which current can be applied to the scalp in tDCS. Anodal, or positive, stimulation delivers a small positive current and cathodal, or negative, stimulation delivers a small negative current. The net effect is to slightly depolarize (anodal) or hyperpolarize (cathodal) the resting potential of a given brain region. In general, the observed behavioral effect is that anodal stimulation facilitates behavioral performance and, conversely, cathodal stimulation degrades performance on a task (Poreisz, Boros, Anatal, & Paulus, 2007). However, this gross oversimplification does not take into account the excitatory or inhibitory effects of the cortical areas being affected by tDCS, such that anodal stimulation may increase excitability in inhibitory areas and lead to poorer performance compared to baseline and vice versa.

Stimulation is typically delivered in the strength range of 1-2 milliamps (mA) through electrodes encased in saline-soaked sponges (Minhas, Datta, & Bickson, 2011). The effects of a single application of tDCS are polarity-specific and can last up to 1 hour after stimulation (Nitsche & Paulus, 2000, 2001). The brain region to be stimulated is typically localized for each participant using the international 10-20 system (Jasper, 1958), although instances of localizing the to-be-stimulated region with TMS have been reported (Reis, et al., 2009).

With respect to safety, tDCS has quite a good record, with the most common complaint logged by participants being a mild tingling sensation during stimulation (Poreisz, et al., 2007). Slightly more serious adverse events, such as nausea, headache and sleep disturbance have been reported in a very small percentage of participants (Poreisz, et al., 2007). Isolated cases of minor skin burns have been reported, although it appears that when tDCS is applied according to the current safety guidelines significant adverse events can be avoided (Minhas, et al., 2011).

The area of cortex affected by tDCS is thought to be much more widely dispersed compared to TMS (Datta, et al., 2009). While for some research purposes the focality of TMS stimulation may make this methodology more attractive, the relative lack of specificity with respect to tDCS may make it a particularly useful method in fields such as rehabilitation (Brunoni, et al., 2011; Williams, Imamura, & Fregni, 2009).

Computer simulations have helped researchers get a handle on issues surrounding current dispersion, but are also limited with respect to their predictive power. One widely-used model is limited in its ability to take into account white matter conductance (Datta, et al., 2009). Other models that manage to take into account white matter do not include other important factors, such as head shape, that may influence current dispersion (Saidler, Vannorsdall, Schretlen, & Gordon, 2010). One of the difficulties in modeling current paths is that there are a number of individualized factors, such as age, head shape and ventricle size, that can influence the dispersion of current throughout brain tissue (Datta, et al., 2009).

However, these models have proven to be particularly useful in highlighting the importance of the placement of the reference electrode. The ‘active’ electrode must be placed somewhere over the scalp (either anodal or cathodal stimulation depending on the type of current one is interested in delivering to brain tissue) and the ‘return’ or ‘reference’ electrode must also be placed on the body in order to complete the circuit. In order to minimize the possibility that the opposite current is not affecting brain, one might think that it is best to put the reference as far away from the active electrode as possible. However, if the reference is placed on the shoulder, a placement that has been utilized in a few studies (e.g. Monti, et al., 2008), current may skip along the surface of the skin to get to the return electrode; as such, models predict little to no current entering cortical tissue (Bickson, 2011). At the very least, the placement of reference electrode influences the path that current travels through the brain as was elegantly demonstrated in a recent commentary by Bickson and colleagues (Bickson, Datta, & Rahman, 2010). Perhaps most important to note, computer models estimate that the region of brain tissue that may be maximally affected by stimulation do not necessarily lie directly beneath the 'active' electrode (Bickson, et al., 2010).

Plasticity and learning enhanced by non-invasive brain stimulation

It was recently demonstrated that tDCS induces long-lasting changes at the neural level. In this study, field excitatory post-synaptic potentials (fEPSPs) were recorded in slices of adult mouse motor (M1) cortex. Direct current stimulation (DCS) was applied at a strength estimated to be analogous to the lower range of tDCS current applied in human M1 cortex. The authors reported that anodal DCS potentiated the fEPSP in most slices of cortex beginning several minutes after stimulation was initiated and that this effect continued to increase for almost 60 minutes beyond the end of stimulation before reaching a plateau, indicating that long-term potentiation (LTP) mechanisms had been initiated (referred to as DCS-LTP; Fritsch, et al., 2010). In order to characterize DCS-LTP, M1 was treated with an NMDA-receptor antagonist and DCS-LTP was completely prevented, indicating that DCS-LTP is dependent on the activation of NMDA receptors (Fritsch, et al., 2010). Additionally, in mice with a forebrain specific deletion of the BDNF gene and in mice where TrkB kinase activity was inhibited the DCS-LTP was not observed, pointing to critical roles of BDNF in maintaining and TrkB receptors in initiating LTP processes induced by DCS (Fritsch, et al., 2010).

Subsequently, Fritsch and colleagues conducted a study in humans with and without the BDNF Met polymorphism, known to decrease BDNF levels in the range of 18-30% compared to Val/Val carriers. Val/Met carriers have previously been demonstrated to show a reduced response to brain stimulation techniques that alter neural excitability (Cheeran, et al., 2008). Using a motor training task, Met (meaning both Val/Met and Met/Met polymorphisms) carriers displayed reduced skill acquisition compared to Val/Val subjects (Fritsch, et al., 2010). However, it has also been reported that Val/Met carriers exhibited enhanced plasticity in response to both stimulation polarities of tDCS (Antal, et al., 2010), so effect of this polymorphism in human response to tDCS remains unclear.

In a similar vein, cathodal stimulation has been shown to lead to long-term depression-like (LTD-like) cortical plasticity (Hasan, et al., 2011). Modulation of NMDA receptors via pharmacologic interventions effects LTD-like plasticity initiated by cathodal tDCS (Nitsche, Fricke, et al., 2003), lending some backing to the claim that this process is similar to LTD as LTD is also NMDA-receptor dependent. In healthy human subjects, cathodal stimulation to the hand area in the motor strip (located via TMS) for 9 minutes at 1 mA reduced MEP amplitude (Hasan, et al., 2011). Furthermore, cortical silent period (CSP) is a marker of $GABA_B$-dependent inhibition; the CSP was prolonged in healthy controls after receiving cathodal stimulation (Hasan, et al., 2011).

On a more macroscopic level, it was recently reported that tDCS influences functional connections throughout a widespread cortical network. The default mode network (DMN) has been associated with rest states and is thought to reflect the ‘baseline’ activity the brain (Greicius, Krasnow, Reiss, & Menon, 2003; Racihle, et al., 2001). Conversely, activity in the anticorrelated network (AN) is associated with high task demands and focused attention (Fox, et al., 2005). Regions associated with the AN have been implicated in fMRI studies of WM task performance (Cabeza & Nyberg, 2000). These networks have been shown to fluctuate such that when the DMN is active, regions associated with the AN are relatively silent and vice versa (Hampson, Driesen, Skudlarski, Gore, & Constable, 2006). Using fMRI, researchers found that 20 minutes of anodal tDCS to both right and left DLPFC compared to sham increased connectivity between prefrontal and parietal regions (areas associated with the AN) and the connections between regions associated with the DMN were reduced (Pena-Gomez, et al., 2011). There was no difference between right and left DLPFC stimulation with respect to strength of functional connectivity (Pena-Gomez, et al., 2011). These results suggest that one possible mechanism for the behavioral after-effects of tDCS may stem from stimulation leading to increased functional connectivity in cortical areas associated with successful task performance.

Working Memory and tDCS

Studies influencing WM in a single session lend theoretical backing to the idea that tDCS can enhance WM task performance over time. In one particularly compelling study, Fregni and colleagues applied 1 mA of stimulation for 10 minutes to left dorsolateral prefrontal cortex (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 minutes of stimulation. Anodal stimulation of left DLPFC increased accuracy on this task compared to 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). However, there have been no reported attempts to directly replicate these findings to the author's knowledge.

Other reported effects in the domain of WM and tDCS have used current strengths, reference electrode placement, stimulation length, WM tasks or a combination of these factors that differ from Fregni, et al. (2005). A number of reports of verbal WM task improvement have been associated with anodal stimulation to left DLPFC, giving further support for site-specific and polarity-specific behavioral effects (Boggio, Castro, et al., 2006; Jo, et al., 2009; Seo, Park, Seo, Kim, & Ko, 2011; Zaehle, Sandmann, Thorne, Jancke, & Herrmann, 2011). The effect of anodal left DLPFC stimulation on WM has been found in older adults (Seo, et al., 2011), people with Parkinson's disease (Boggio, Castro, et al., 2006) and stroke patients (Jo, et al., 2009); as such, the effect of tDCS in the domain of verbal WM seems relatively robust. An important caveat is that the effect of anodal tDCS on spatial WM is not yet well understood.

tDCS and Learning

tDCS has also been shown to enhance the effects of learning in a number of domains, including object-location learning (Floel, et al., 2011), artificial language learning (de Vries, et al., 2009) and motor learning (e.g. Kobayashi, Théoret, & Pascual-Leone, 2009; Nitsche, Schauenburg, et al., 2003). 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, while the decrement in skill (i.e. the slope) was similar in both groups at 85 days post-training, 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 importantly with respect to WM training than gains on the trained task is whether skill can be increased 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 to the sham condition (Baker, et al., 2010).

On the other hand, it was recently reported that tDCS might be better suited for improving learning in a relatively narrow range, precluding transfer. In this experiment, participants trained for 6 days on a novel numerical system while receiving stimulation to either frontal or parietal regions. It was found that participants receiving stimulation to posterior parietal sites exhibited enhanced learning on the trained task but reduced automaticity for learned material (as indexed by another task). The opposite effect was found for frontal stimulation - reduced learning on the trained task but increased automaticity on the 'transfer' task, providing evidence for a double dissociation (Iuculano & Cohen Kadosh, 2013). Therefore, it remains unclear what the role of tDCS might be in inducing transfer beyond the training domain.

With respect to the training regime itself, it has been reported behaviorally that those participants who show the largest gains in terms of training effects tend to show the strongest gains on transfer tasks (Chein & Morrison, 2010). Therefore, it is possible that tDCS may serve to enhance transfer via increasing gains on the trained task. However, two recent reports call this hypothesis into question. Recently, Andrews and colleagues reported that n-back performance concurrent with tDCS was related to improved digit span forward accuracy following stimulation. However, there was no behavioral effect on n-back performance; furthermore, there was no evidence of post-stimulation improvement on digits backwards (Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011). In a related vein, a recent report by Iuculano & Cohen Kadosh failed to find strong evidence that tDCS-assisted learning lead to benefits beyond the learning task itself (2013). Thus, while the behavioral WM training findings suggest better training is related to improved transfer outcomes, it remains unclear if boosting learning with the application of tDCS might produce results that follow this pattern.

Specific Aims and Hypotheses

1. To investigate the effects of tDCS on training gains in a complex WM task. Understanding the role of tDCS in enhancing gains on a behavioral task with repeated exposures will aid in identifying other learning tasks that may be enhanced with the application of tDCS. As this task has previously been applied as a training regime (Chein & Morrison, 2010; Richmond, et al. 2011), practice-related improvement on the task over the training period is expected. Importantly, tDCS is predicted to enhance task-specific learning above and beyond practice with the task alone.

2. To investigate the role of tDCS as an adjuvant or a catalyst for learning. If tDCS is shown to enhance task-specific learning, it will be important to investigate whether tDCS acts as an *adjuvant* (i.e. leading to increased learning over all 10 sessions of training) or a *catalyst* (i.e. speeds up the rate of early learning, but after some time the effects taper off). More clearly, it will be important to assess if the anodal tDCS + WM training group shows better outcomes for the duration of the 10 session training regime, or if the anodal tDCS + WM training group shows an early burst in learning that tapers off, such that at the end of training no difference between anodal tDCS + WM training and sham tDCS + WM training can be detected.

If tDCS is shown to act as a catalyst for learning, tDCS could be applied to many training regimes to cut the number of practice sessions necessary to achieve a given outcome. If, instead, the effect of tDCS is to act as a global adjuvant, it may be better suited for applications in populations with learning deficits relevant to the training task.

3. To assess the efficacy of 10 WM training sessions in comparison to previous reports utilizing 20 sessions. In order to assess the transfer outcomes that follow from only 10 sessions of practice with this training regime (in contrast to previous research reports with this regime, i.e. Chein & Morrison, 2010; Chein, et al., under review; Richmond, et al., 2011), comparisons between all trained participants (sham and tDCS) vs. the NCC group will be conducted. Training is predicted to enhance transfer outcomes beyond test-retest effects.

4. To assess the extent to which tDCS in conjunction with WM training enhances transfer compared to training alone (WM training & sham). The ultimate goal of this study is to assess the extent to which cognitive domains separate from WM might be enhanced by the addition of tDCS. tDCS is predicted to boost transfer outcomes (either larger effect sizes or broader transfer profiles) compared to training alone (i.e. sham stimulation).

CHAPTER 2

WORKING MEMORY TRAINING AND NON-INVASIVE BRAIN STIMULATION

This study employed a similar design to that utilized in prior WM training studies (Chein & Morrison, 2010; Richmond, et al., 2011). The pre-and post-test assessments included tasks tapping a number of cognitive domains as well as an intervening longitudinal phase where participants were randomly assigned to WM training or an control condition. Each phase of the study is described in detail below.

Procedure

Pre-testing

The pre-test battery included a number of tasks that tap a single cognitive construct in order to create a composite score for that specific domain. A major criticism of the current WM training literature is that transfer effects have been found on single measures (Shipstead, et al., 2010); thus it is unclear if the underlying cognitive construct is truly being influenced or if there are task-specific effects that are being demonstrated by any given single-task transfer finding. As such, the pre-test battery for the current study included multiple measures that have been shown through previous latent variable analyses to tap the same underlying cognitive skill. In addition, single measures that have been utilized with this specific training regime were included to make contact with previous research (Chein & Morrison, 2010; Richmond, et al., 2011). See Table 1for latent construct and transfer type for each task.

Table 1

Pre- and post-test battery, testing time and latent constructs

Task	Latent Construct	Transfer Type	Estimated Testing Time
Automated Operation Span	Working Memory	Near	13 minutes
Automated Symmetry Span	Working Memory	Near	8 minutes
Stroop	Cognitive Control	Far	12 minutes
Antisaccade	Cognitive Control	Far	4 minutes
Psychomotor Vigilance Task	Sustained Attention	Far	10 minutes
Sustained Attention Response Task	Sustained Attention	Far	5 minutes
Raven's Advanced Progressive Matrices		Far	23 minutes
California Verbal Learning Test		Far	20 minutes
Nelson-Denny Reading Test		Far	20 minutes

Note: Total testing time estimated =1 hr, 54 minutes.

Working Memory

To assess near transfer of the training task to other tasks known to tap the construct of WM, two complex span tasks were utilized. This will ensure that the practice effects observed during training generalize outside of the training task itself. These tasks were chosen based on previous findings showing that these measures load strongly onto the construct of WM (Kane, et al., 2004).

Automated operation span (Unsworth, Heitz, Schrock, & Engle, 2005). This complex WM span 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. Once the correct answer has been computed, participants are instructed to click the mouse button. The following screen shows a number with a box marked 'true' and a box marked 'false.' If the number displayed on the screen matches the answer computed for the arithmetic problem, the participant should click 'true.' Otherwise, the participant should click 'false.' After this decision is made, 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. Next, they will receive feedback regarding their performance of both the arithmetic and recall portions of the task. Participants will complete spans of anywhere from 3-7 items. Participants will not know ahead of a given trial how many items they will have to recall (Unsworth, et al., 2005).

Automated symmetry span (Unsworth, et al., 2005). This complex WM span task is similar in structure to the spatial portion of the training task. In short, participants make a decision about the vertical symmetry of a black and white grid; following that decision, another grid appears with a spatial location cued in red. This highlighted spatial location is meant to be stored for later recall. The decision portion (black and white grid) and storage portion are interleaved until the span for a given trial (3-7 memory items) is reached. It differs from the training task in the following ways: participants only make one symmetry decision per item and participants receive trials at lengths anywhere from 3-5 items. Importantly, this task is not adaptive; all participants will be exposed to trials at lengths from 3-7 items regardless of performance on previous trials (Unsworth, et al., 2005). See Figure 1 for a depiction of both operation and symmetry span tasks.

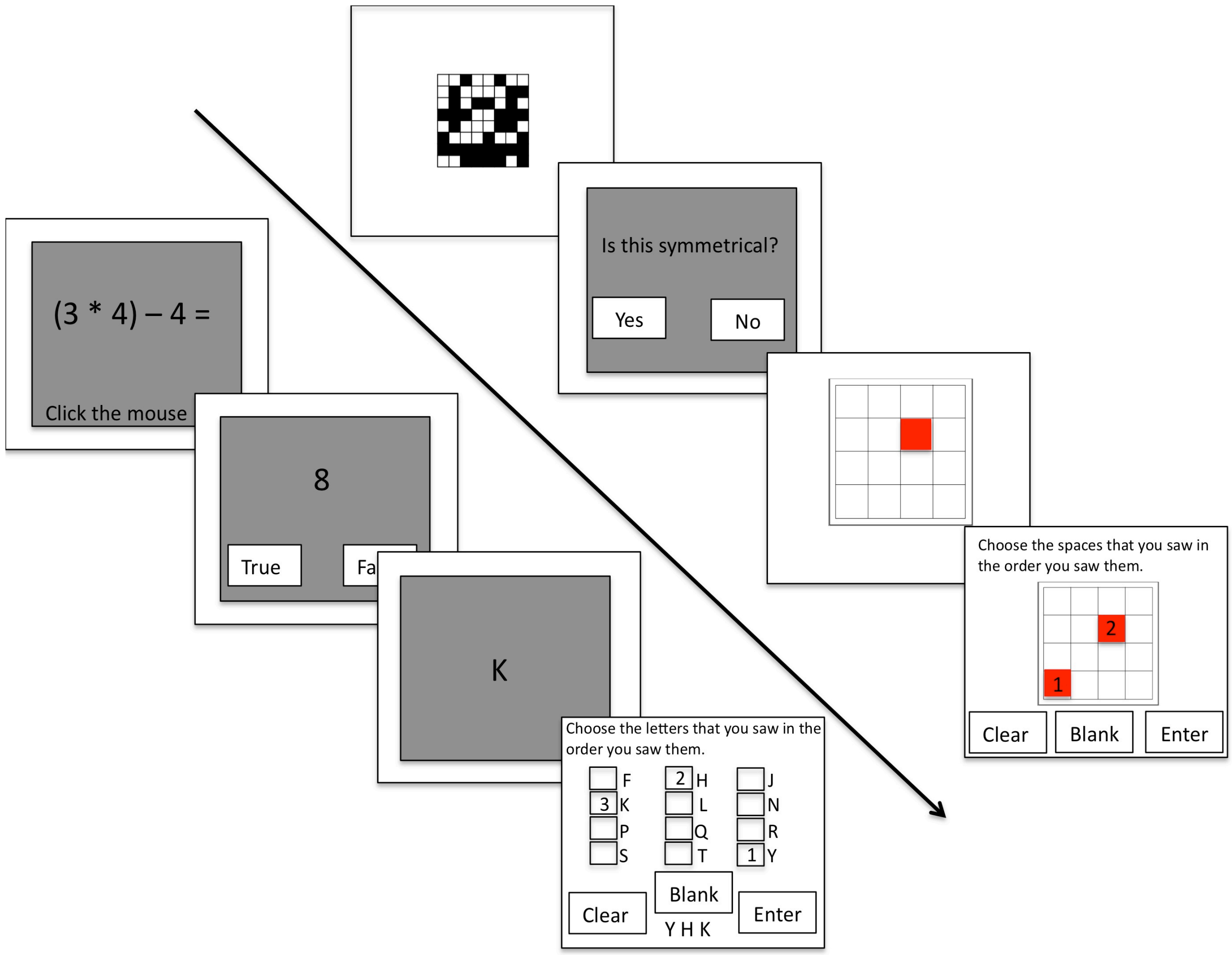

Figure 1. Operation and Symmetry Span Schematic

Cognitive Control

Cognitive control is an important component of executive functioning. It involves inhibition and biasing of goal-directed attention (Kane, Conway, Hambrick, & Engle, 2007). The rationale for including measures of cognitive control in our pre-test battery is that prior studies have reported that there is shared variance between WMC and cognitive control abilities (Kane, et al., 2004). As such, it is plausible that any enhancement in WM capacity should be accompanied by an enhancement in cognitive control. In support of this notion, inhibitory processes have previously been shown to improve in response to this specific training regime (Chein & Morrison, 2010), albeit at the single-task level (i.e., Stroop). Transfer to cognitive control will thus be assessed at the level of the latent construct.

Stroop. The Stroop task has been used previously in conjunction with this training regime (Chein & Morrison, 2010). Performance on the Stroop task has previously been associated with WMC (Kane & Engle, 2003). In this task, participants are meant to respond to the color of the font rather than to the printed color word. Participants respond by key press; colored stickers placed on the keyboard indicated key mapping. Because word-reading is considered more automatic than color-naming (Stroop, 1935), participants are expected to have greater interference on trials when the printed color word and the font color do not match (incongruent trial) compared to trials when the printed word and font color are the same (congruent trial). The variables of interest include cost data 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 (Stroop, 1935).

Antisaccade. In the antisaccade task, participants are required to inhibit the prepotent response to look at a flashing stimulus and instead look away. In order to successfully complete this task, participants must activate and utilize the task goals to direct behavior. Performance on this task has previously been shown to correlate with working memory capacity (Kane, Bleckley, Conway, & Engle, 2001; Roberts, Hager, & Heron, 1994). Participants will also complete pro-saccade trials in order to compute a 'cost' score (again, both RT and accuracy) associated with performing antisaccade trials in particular. See Figure 2 for a depiction of the two cognitive control tasks.

Sustained Attention

The cognitive construct of sustained attention is quite important for normal everyday functioning, and is thought to be compromised in disorders such as attention deficit hyperactivity disorder (Barkley, 1997), bipolar disorder (Clark, Iversen, & Goodwin, 2002) and in patients with frontal lesions (Wilkins, Shallice, & McCarthy, 1987). Functional neuroimaging research in humans has localized the neural correlates of sustained attention to predominantly right frontal and parietal regions (Sarter, Givens, & Bruno, 2001), overlapping with cortical areas thought to support working memory performance (Cabeza & Nyberg, 2000).

The rationale for including the construct of sustained attention as a transfer outcome comes from the previously identified relation between sustained attention and WMC (McVay & Kane, 2009). Previous research indicates that people with low WMC report mind-wandering more often than those with a high WMC in both thought-sampling methods (McVay, Kane, & Kwapil, 2009) as well as laboratory-based tasks (McVay & Kane, 2009; McVay, et al., 2009). As a result, increasing WMC via training may result in greater ability to sustain attention over time.

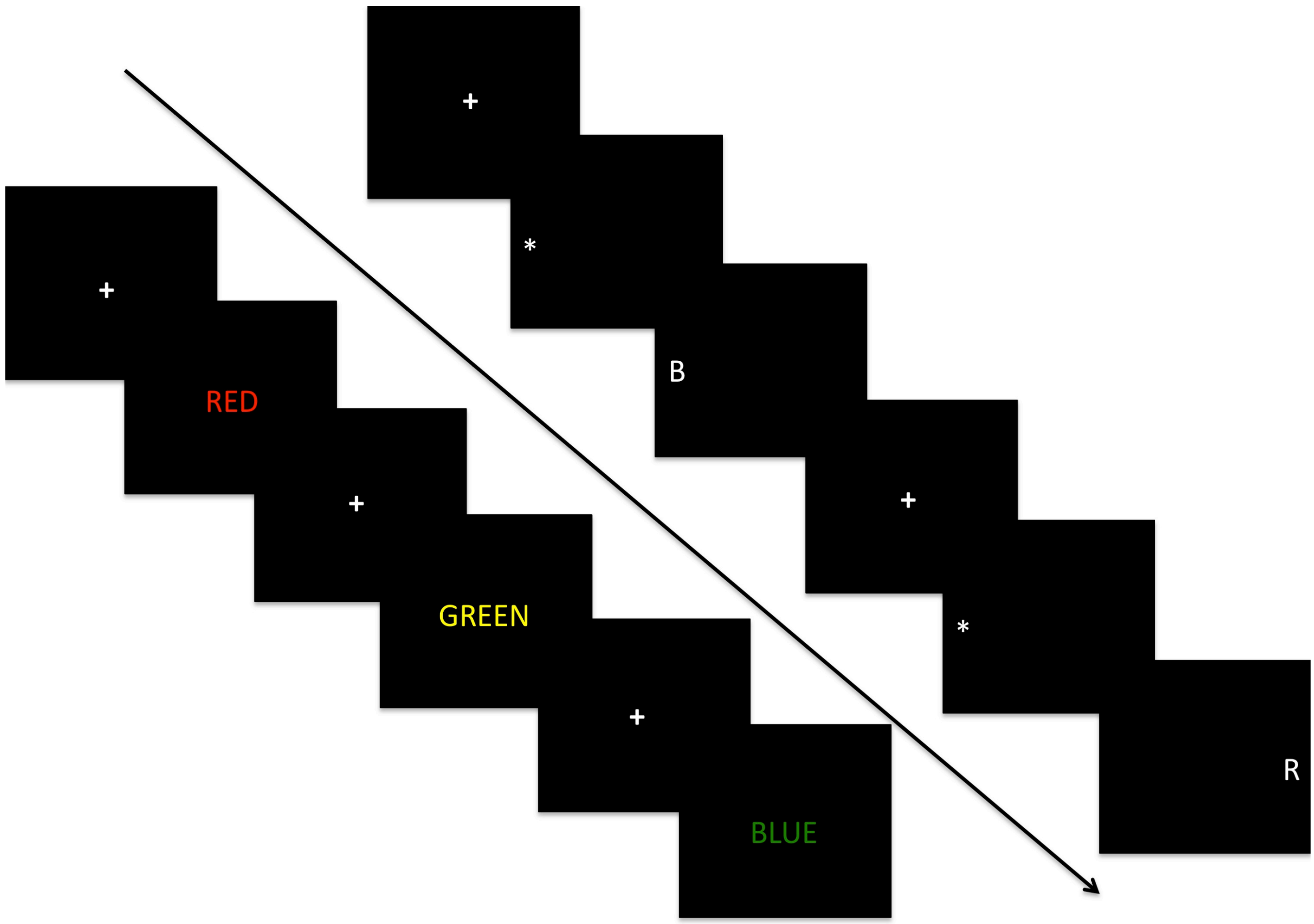

Figure 2. Stroop and Anti-saccade Schematic

In addition, in our previous study in older adults, a number of different attentional processes were investigated as a potential transfer outcome via the Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). Unfortunately, our sample of healthy older adults performed quite well on this neuropsychological test even at pre-test, limiting our ability to detect transfer to attentional abilities (Richmond, et al., 2011). In addition, both the active control group and the training group were administered a post-test questionnaire in which they were asked whether they thought the training (or trivia games for the control group) improved their cognitive functions. Both groups responded to this question in the affirmative. However, when probed for what specific aspects of their cognition were affected, a greater portion of the training group than would be expected by chance indicated that their attention span was improved (Richmond, et al., 2011). To follow up on this subjective report, sustained attention measures were included in our transfer battery.

Psychomotor Vigilance Task (Dinges & Powell, 1985). In this task participants observed a row of zeros that appear on the screen, and after a variable amount of time, the zeros began to count upwards (much like a stopwatch). Participants were instructed to press a key as quickly as possible once the zeros began counting up. Feedback is provided in the form of a visual display of speed (=RT). The dependent variable in this task is the average reaction time (Dinges & Powell, 1985). Task performance has previously been shown to relate to working memory capacity (Unsworth & Spillers, 2010) and executive control (Unsworth, Redick, Lakey, & Young, 2010).

Sustained Attention Response Task (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). This task has been widely utilized in healthy (McVay & Kane, 2009) and clinical populations (Robertson, et al., 1997). Participants observed 225 single digits (25 each of 0-9) for 250 ms followed by an "X". Participants are instructed to respond to every presentation of "X" with a key press except when the digit "3" is presented directly prior; in this case, participants must withhold a response (Robertson, et al., 1997). Participants are told that speed and accuracy are equally important and not to emphasize one over the other. Average RT on correct trials will be analyzed. See Figure 3 for a graphic depiction of the two sustained attention tasks.

Single Measures

Raven's Advanced Progressive Matrices. One of the most hotly contested findings in the WM training literature involves transfer to fluid intelligence (Jaeggi, et al., 2008; Jaeggi, et al., 2010; Moody, 2009). In addition, fluid intelligence is one of the most consistently tested measures of far transfer (Chein, et al., under review). In order to further extend the finding that this training regime does not show evidence of transfer to this particular measure of fluid intelligence (Chein & Morrison, 2010; Richmond, et al., 2011), as well as to make contact with previous literature, Raven's Advanced Progressive Matrices (Raven's; Raven, 1976) was assessed. This task was administered similarly to past administration: even and odd trials were separated into two batteries in order to create alternate forms. The outcome of interest is the number of items correct on the split-half form.

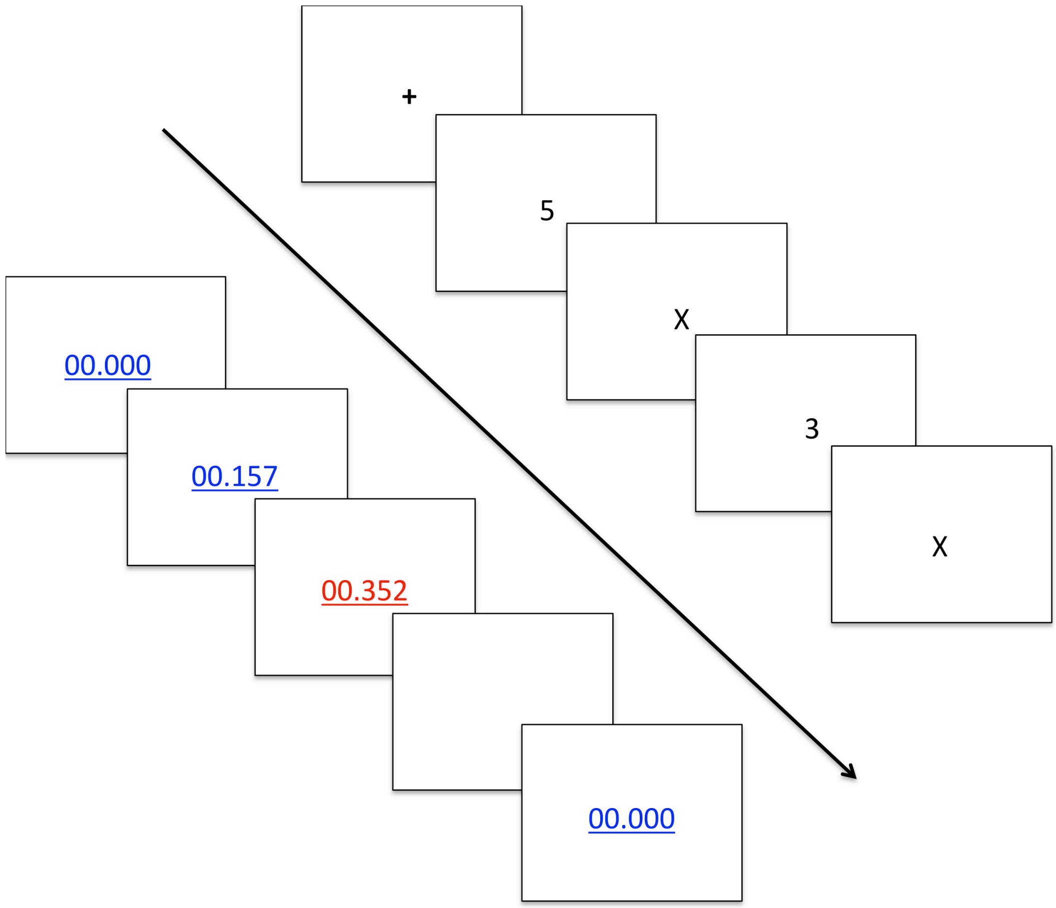

Figure 3. Sustained Attention Response Task and Psychomotor Vigilance Task Schematic

California Verbal Learning Test (CVLT). Again, inclusion of this task is meant to make contact with previous reports of transfer in relation to this training regime (Richmond, et al., 2011). Participants were read a list of 16 items, grouped into 4 semantic categories (i.e. list A). After five trials of immediate recall, participants received another list (distracter; i.e. list B). They were then asked to recall this list, and then, immediately following, recall the first list (list A). Participants were then cued to the semantic categories present in list A. After a 20-minute delay, participants were again asked to freely recall the first list (list A) and then completed a cued semantic trial. Lastly, participants engaged in a recognition trial where they were meant only to endorse items on the original list, responding in the negative to both semantically related items and items from the distracter list. Alternate forms were available for pre- and post-testing (Delis, Kramer, Kaplan, & Ober, 1987). Outcomes of interest on this measure include correct free recall for List A trials, as well as intrusions and repetitions on List A trials.

Nelson-Denny Reading Test. In order to follow up on previously reported findings that practice with the proposed WM training task influences performance on the Nelson-Denny (Chein & Morrison, 2010), this task was administered. The Nelson-Denny is thought to be an assessments of reading comprehension (Brown, 1960). Participants were asked to read seven passages and answer questions about each passage (38 comprehension questions in total). Participants were given up to 20 minutes to complete the entire test (Brown, 1960). Here, the outcome of interest was the number of correct responses on the comprehension questions. Alternate forms of this task were available for pre- and post-test occasions.

Working Memory Training

An adaptive complex WM training task (Chein & Morrison, 2010; Richmond, et al., 2011) was employed in this study. See Figure 4 for a schematic of the training task.

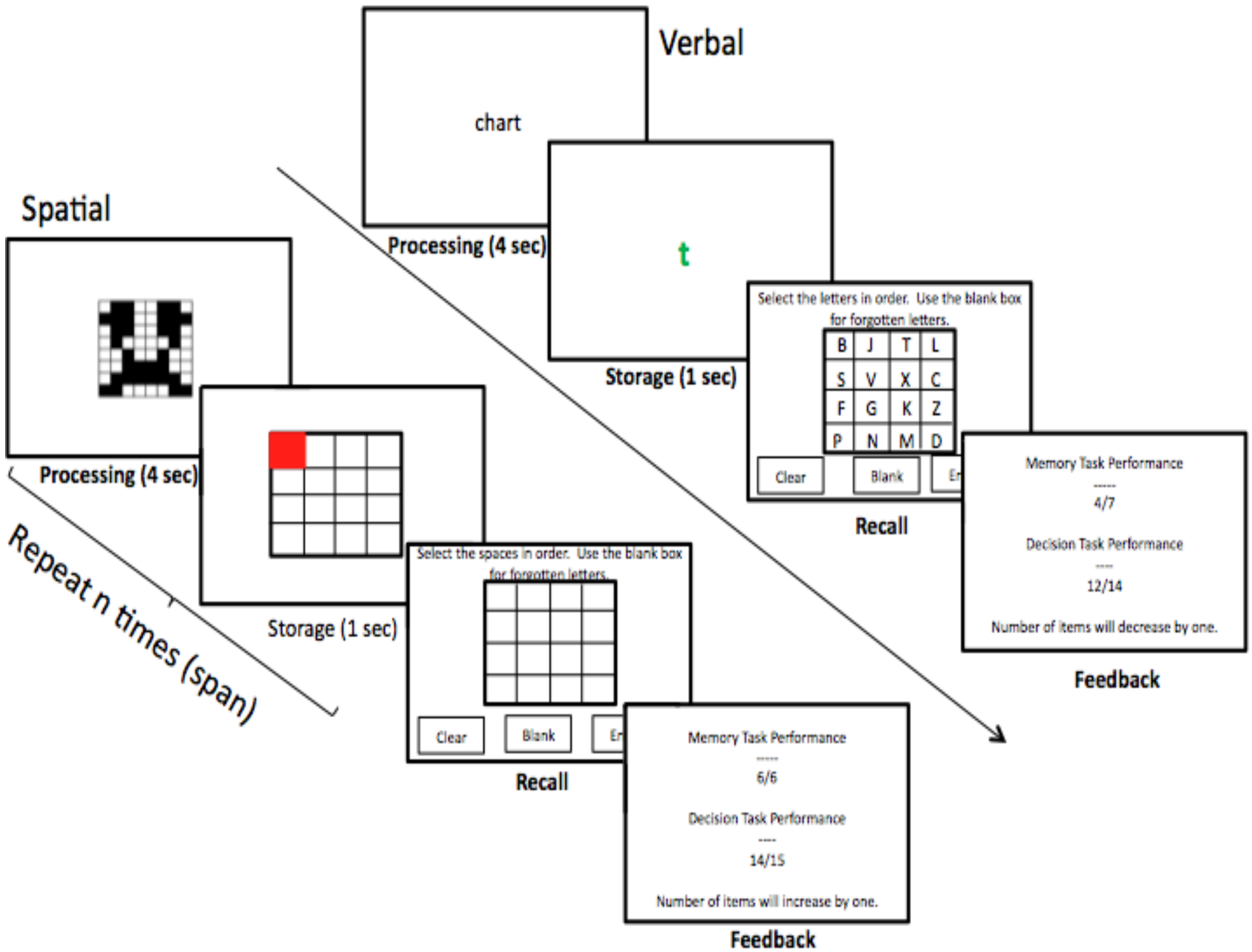

Figure 4. Training Task Schematic

Training participants completed ten (10) approximately 30-min. long training sessions on a complex WM span task over a span of 2 weeks, with participants completing their sessions in a 5-day a week (e.g., weekday) regimen. Within each training session, approximately 15 minutes of training were devoted to a spatial WM task and approximately 15 minutes were devoted to a verbal WM task. Trials are blocked by material type, but randomly sampled each day so that there is an equal likelihood of beginning each training session with the spatial or verbal subtest. The spatial subtest involves making symmetry decisions (symmetry) about a series of partially filled (black and white squares) matrices while intermittently encoding a sequence of highlighted locations on a 4 x 4 grid for later recall. Locations were recalled by mouse clicking on locations within the 4 x 4 grid in the order that they were seen. The verbal subtest requires participants to make a series of word/non-word decisions (lexicality) while intermittently encoding a sequence of letters for later recall. The letters were sampled from a pool of 16 consonants, evenly sampled throughout the task. The probe screen consisted of a 4 x 4 grid containing all of the possible letters. The letter sequence is recalled by mouse clicking on the appropriate letters (shown in shifted positions from trial to trial) in the order that they are seen. After each trial is completed, correct/incorrect feedback for both the decision and recall portions are presented on the computer screen. Successive trials are initiated by participant key press. In addition, participants were asked at the beginning of each session to assess their level of motivation to complete the daily training session. At the end of each session participants were probed as to their level of effort throughout the session. Participants responded to both questions on a 5-point likert-type scale.

All training participants began the program on training day 1 with a span of 4 recall items on both the verbal and spatial subtests, following the design of Chein & Morrison (2010). On all subsequent training days, verbal and spatial beginning span was determined by each individual’s performance on the previous session. Participants were told to work as quickly and as accurately as possible, and that both the decision and recall portions of the task were of equal importance. The training task is adaptive to the participant's performance level such that the number of recall items increases or decreases based on performance. If all items are correctly recalled for two trials in a row and at least 75% of the lexicality or symmetry decisions are correct, the list length will increase by one item, and so on. Likewise, two successive incorrect trials cause the set size to be reduced by one item.

Brain Stimulation

During each training session, participants received either anodal or sham stimulation centered over left dorsolateral prefrontal cortex. 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). Active tDCS participant received 15 minutes of stimulation at 1.5 mA, with the last 5 minutes of stimulation occurring simultaneously to task performance. The same electrode montage was applied to sham participants, but these participants received 15 seconds of "ramping up" of current followed by 15 seconds of "ramping down" current after which stimulation was discontinued. This method of applying sham stimulation has previously been shown to be efficacious in blinding participants to their stimulation condition (Priori, Hallett, & Rothwell, 2009).

No-contact Control Group

Participants in the control condition received only pre-testing and post-testing with no intervening longitudinal phase in order to assess test-retest effects (i.e. a 'no contact control' group, or NCC). While this sort of control group has been harshly criticized in the past (Shipstead, et al., 2010), there are a number of reasons why this control group has been chosen.

Importantly, as tDCS is a novel addition to the extant WM training literature, this control group served as a basic baseline against which to judge the efficacy of these new approaches. As the comparison between WM training + anodal tDCS and WM training + sham tDCS is of upmost importance to this particular study, and demand characteristics in these groups are thought to be equal, differential gains by training group cannot be explained simply on the basis of investment, interest, or other non-specific effects not accounted for by the inclusion of only a NCC control group (Shipstead, et al., 2010). Furthermore, because both tDCS training groups engaged in a training regime previously shown to induce benefit at post-testing (Chein & Morrison, 2010; Richmond, et al., 2011), understanding the benefit of multiple exposures to the pre- and post-test battery at the latent variable level will provide a useful benchmark against which both WM training groups can be assessed. The latent-variable approach to pre- and post-testing has only been utilized once before (Redick, et al., 2012). Practically, this sort of control group served to keep data collection, subject recruitment and study cost to a reasonable level. Perhaps the most convincing argument for the inclusion of a no-contact control group comes from a recent effect-size analysis of the published WM training literature that revealed nearly identical average effect sizes produced by active and NCC groups for both near and far transfer (Chein, et al., under review). This finding suggests that previous critiques of the utilization of NCC groups in WM training studies may have been somewhat overstated (i.e. Shipstead, et al., 2010, 2012).

Post-testing

Post-testing mirrored pre-testing, using alternate forms when available (specifically, Nelson-Denny, Raven's and CVLT).

Statistical Analysis

Training Data

In order to investigate the effect of tDCS on learning, a 2x2x2 mixed ANOVA was performed with session (1, 10) and task type (verbal, spatial) as the within-subjects factors and group (active, sham) as the between subjects factor. The inclusion of task type in this model allowed us to discern if the effect of left DLPFC stimulation is specific to verbal or spatial WM, or if both domains are affected to a similar degree. A significant main effect of stimulation will serve to demonstrate that tDCS enhanced learning on the trained task.

Furthermore, in order to investigate the mechanism of the active tDCS effect, the slopes of the learning curves were compared. In order to investigate if tDCS acts as a catalyst (i.e. the effect of tDCS drops off after a number of sessions) or a global adjuvant to learning, split-plot regression was used.

Transfer Analyses

Outcomes for latent variables were standardized (z-scored) and averaged to form a composite score. Pre- and post-test z-scores were normalized to pre-test performance, following Chein & Morrison (2010). For cognitive control and sustained attention z-scores, smaller values indicate better performance. Transfer from 10 sessions of training was first examined without taking into account any effects of tDCS. As such, a series of 2x2 mixed ANOVAs were conducted (within-subject factor: testing occasion- pre or post; between subjects factor: training group- training or NCC). Because this training regime has never been shortened to 10 sessions before, this analysis is important in exploring the potential dose-dependent response of training that has been reported in other regimes (Jaeggi, et al., 2008).

To examine the effect of tDCS on transfer, 2x3 mixed ANOVAs were then conducted with the within-subjects factor of testing occasion (pre- or post-testing) and the between-subjects factor of group (WM training + tDCS, WM training + sham, no-contact control group). A significant 2-way interaction is taken as evidence of positive transfer to a given construct (hinging on means in WM training + tDCS being higher than the other groups). If significant two-way interactions emerge, planned comparisons between each group will be conducted in a pairwise manner (i.e. active vs. sham, active vs. NCC, sham vs. NCC at pre- and post-test) to elucidate the group differences driving the interaction. The critical *p* value for each set of pairwise planned comparisons was adjusted to correct for multiple comparisons within each model (.05/6 comparisons = .008 critical *p* value).

Results

Participants

Subjects were recruited from Temple University, the University of Pennsylvania and the surrounding communities. Qualification criteria included: aged 18-30, 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-hour pre-testing session before beginning training and another post-testing session following training in addition to the longitudinal phase of the study. Exclusion criteria for tDCS included: 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, anti-convulsants, sedative/hypnotics, or psychostimulants [amphetamines, cocaine, methylphenidate]) and pregnancy. All females 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 subjects were qualified to receive tDCS regardless of group assignment.

In total, 58 subjects participated in this study (1 additional participant voluntarily withdrew from the study on training day 1); group assignment was random. Twenty participants received active tDCS, 20 received sham stimulation, and 18 participants were assigned to the NCC group. Demographic information can be found in Table 2.

Table 2

Demographics

Group	Age (SD)	Education (SD)	% Male
Active (n=20)	20.650 (2.996)	14.000 (1.892)	35 %
Sham (n=20)	20.750 (2.693)	14.150 (1.723)	35 %
No-contact (n=18)	21.556 (2.995)	14.611 (1.290)	28 %

Note: No significant differences were observed between groups.

Training Results

Training data (i.e. final span from daily practice with the adaptive complex span task) were analyzed using a 2x2x2 repeated measures ANOVA examining the within-subjects effects of session (1, 10), stimulus modality (verbal, spatial), and the between-subjects effect of stimulation group (active or sham)[1]. Comparing sessions 1 and 10, span was found to increase significantly (session 10 > session 1; $F(1, 38) = 36.998$, $p < .001$). In addition, verbal span performance was superior to spatial span ($F(1, 38) = 73.976$, $p < .001$). Last, active tDCS participants exhibited higher WM spans compared to sham participants ((1, 38) = 4.975,

[1] One active subject's data from session 8 was excluded due to experimenter error.

$p = .032$). No two- or three-way interactions reached significance (session x stimulation group: $F(1, 38) = .516$, $p = .477$; stimulus modality x stimulation group: $F(1, 38) = 2.847$, $p = .100$; session x stimulus type: $F(1, 38) = .953$, $p = .335$; session x stimulus modality x stimulation group: $F(1, 38) = 2.061$, $p = .159$).

In addition, separate mixed-effects ANOVAs were run on the training data in the verbal and spatial domains to further investigate the main effect of stimulus modality observed in the ANOVA conducted above. In the 2x2 ANOVA (within-subjects factor: session, between-subjects factor: stimulation group) in the verbal domain only, there was a main effect of session (session 10 > session 1; $F(1, 38) = 46.557$, $p < .001$) and a main effect of stimulation group (active > sham; $F(1, 38) = 27.613$, $p = .025$) and a marginally significant interaction of stimulation group x session ($F(1, 38) = 3.971$, $p = .054$). This interaction indicates that tDCS enhanced learning in the verbal domain above and beyond practice alone.

In the 2x2 ANOVA conducted in the spatial domain, again there was a main effect of session (session 10 > session 1; $F(1, 38) = 53.385$, $p < .001$). Unlike the findings in the verbal domain, there was no main effect of stimulation group ($F(1, 38) = 2.325$, $p = .136$). In addition, the interaction between session and stimulation group was not significant ($F(1, 38) = .371$, $p = .546$). Therefore, tDCS did not enhance learning in the spatial domain beyond simple practice effects. Data are depicted separately for the verbal and spatial domains in Figure 5.

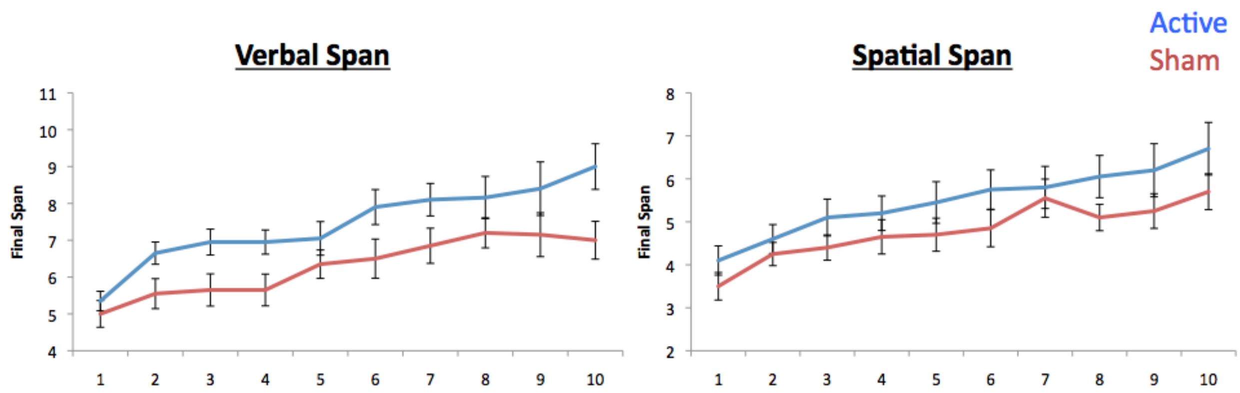

Figure 5. Daily Training Data

Power to detect an effect of tDCS in both the spatial domain (1-ß = .260) and the verbal domain (1-ß = .678) using a two-tailed test was found to be relatively low. Sample sizes reported here are based on average samples in previously reported studies of WM training and tDCS single-exposure studies. Because the approach of using WM training in conjunction with tDCS is novel, the effect size was difficult to determine prior to beginning data collection. In order to increase power in the verbal domain to 80%, 14 subjects would need to be added to the sample (7 in each group). To increase power to 80% in the spatial domain, 68 additional subjects should be added to each group.

In order to test whether tDCS acted as a catalyst for learning or a global adjuvant (i.e. boosted learning over all 10 training sessions) a piecewise regression was conducted on active tDCS subjects only. The regression line was split at session 5. This analysis revealed that tDCS acted as a global adjuvant, rather than speeding up early learning, given that there was no significant difference in slopes for the first and second halves of training (comparison of regression slopes before and after session 5 in the spatial domain: $t(198) = -0.480$, $p = .633$ and verbal domain: $t(198) = -0.570$, $p = .569$). See Figure 6 for split-plot regression lines for verbal and spatial data.

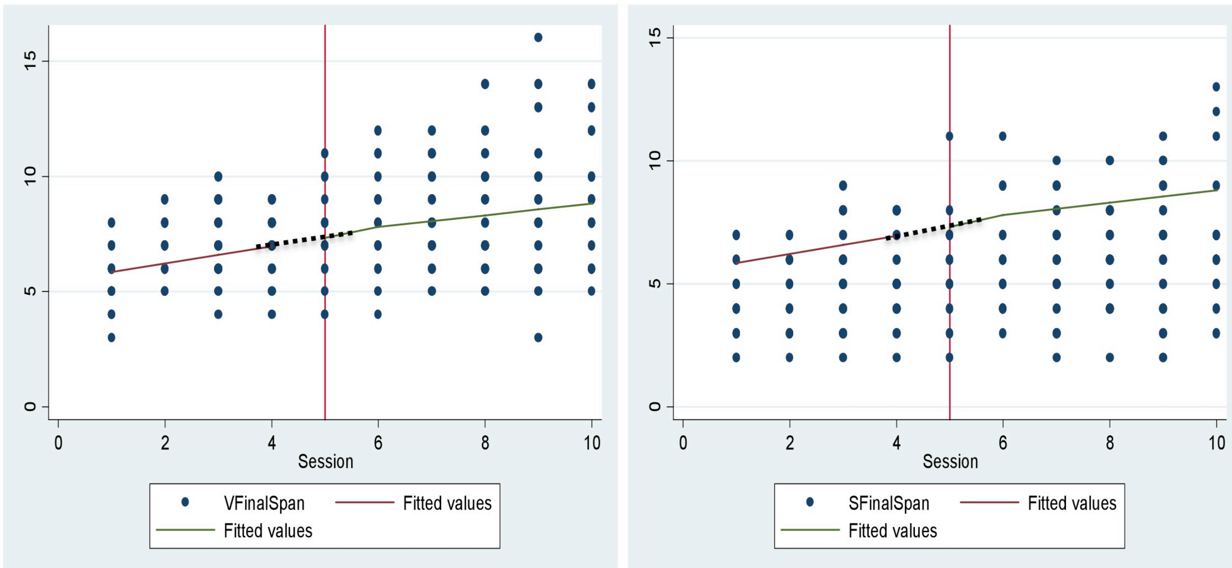

Figure 6. Piecewise Regression Scatterplots

Discussion

Results from the training data suggest that tDCS enhances the efficacy of WM training over and above the effect of practice alone. This effect was driven by improvements in verbal, but not spatial, WM. This is a novel finding for two reasons. First, the relation between complex span performance and tDCS has not been previously examined. Second, to the author's knowledge, tDCS-enhanced multi-session learning in the domain of WM (with a different training paradigm) has only been demonstrated once before (Martin, et al., under review). Thus, our data support and extend the findings presented in Martin, et al. (under review).

Given that the positive electrode was placed over the left DLPFC, a part of the cortex known to be relatively more important for verbal processing than spatial (especially in younger subjects, see Reuter-Lorenz, et al., 2000), this finding was not all that surprising. An interesting possibility that follows from this pattern of results is that reversing the polarity of stimulation may lead to enhanced effects in the spatial domain.

Stimulation was also found to influence learning by boosting the learning rate in the active tDCS group to a similar degree over all ten sessions. Due to the fact that tDCS was not found to speed up early learning or exert a relatively stronger influence in late phase learning, these data provide support for the use of tDCS in lengthy training regimes to improve learning to a greater degree than training alone, and may be of use particularly in compromised populations. The mechanism by which tDCS enhances learning, then, is not sensitive to cognitive changes that occur in the phase shift from early to late learning (i.e. automaticity, task familiarity) at least over 10 sessions.

Transfer Results

Effect of Training on Transfer

Prior studies using this, or similar, training regimes have utilized 20 sessions of training (Chein & Morrison, 2010; Chein, et al., under review; Richmond, et al., 2011). Due to the fact that only 10 sessions were used in the design reported here, we will first explore the effect of 10 sessions of complex WM span training on transfer. To be clear, these analyses collapsed across stimulation group (active and sham combined) to increase power and to examine specifically the effect of 10 sessions of training on transfer.

Working memory. Using a 2x2 mixed effects ANOVA (with between-subjects factor of group and the within-subjects factor of testing occasion), the effect of training on WM capacity was analyzed. Scores from the two complex span tasks included in the transfer battery (Operation Span and Symmetry Span) were z-scored separately for pre- and post-test session relative to pre-test performance for each individual. Z-scores from each individual measure were then averaged to create composite span scores for pre- and post-test occasions. Scoring was conducted according to the absolute scoring method described in (Unsworth, et al., 2005).

Overall, participants were found to benefit from previous exposure to the transfer tasks (main effect of testing occasion; post > pre: $F(1, 56) = 18.066$, $p < .001$). There were no significant differences in performance by training group (participants engaging in the training regime vs. NCC; ($F(1, 56) = 1.199$, $p = .278$). However, the interaction of testing occasion and group was significant ($F(1, 56) = 11.869$, $p = .001$), indicating that participants in the training group (pre-test mean: -.044; post-test mean: .801)[2] showed significantly better pre- to post-test performance improvement than the test-retest control group (pre-test mean: .097; post-test mean: .185). These data indicate that 10 sessions of training with this regime can lead to significant benefit in the domain of WM.

Cognitive Control. A 2x2 mixed effects ANOVA (with between-subjects factor of group and the within-subjects factor of testing occasion) was conducted to assess the effect of training on these inhibitory operations. Both accuracy and RT were analyzed, as there has recently been some evidence to suggest that WM training may make the trained group more conservative in their response style (i.e. slowed RTs coupled with greater accuracy; (Jaeggi, Buschkuehl, Jonides, & Shah, 2011). First examining RTs, there was no significant pre- to post-test improvement (main effect of testing occasion: $F(1, 54) = .145$, $p = .705$)[3] and no significant differences between groups (training vs. control; $F(1, 54) = .428$, $p = .516$). In addition, there was no significant interaction term ($F(1, 54) = .586$, $p = .447$). Examining costs for accuracy revealed a non-significant effect of testing occasion ($F(1, 54) = .714$, $p = .402$), a non-significant effect of

[2] Means represent average combined z-scores for pre- and post-test.
[3] Two anti-saccade datasets for subjects in the NCC group (pre-test) were lost due to computer error.

training group ($F(1, 54) = .997$, $p = .322$) as well as a non-significant interaction ($F(1, 54) = 1.346$, $p = .251$).

In short, inhibition effects were not modulated by previous exposure to the task (no main effect of session) or training (no main effect of group). Furthermore, no evidence of training on a complex span WM task enhancing transfer to these outcomes above and beyond those gains exhibited by our test-retest control group was identified (no significant interaction).

Sustained attention. Again, a 2x2 mixed effects ANOVA was conducted with training group as the between-subjects factor and testing occasion as the within-subjects factor with reaction time being the main variable of interest. No significant effects of testing occasion ($F(1, 56) = 1.935$, $p = .170$) or testing occasion x training group ($F(1, 56) = .030$, $p = .863$) were observed. However, there was a marginally significant effect of training group ($F(1, 56) = 3.890$, $p = .054$), such that the training group (pre-test mean: -.143; post-test mean: .011) exhibited superior performance to the control group (pre-test mean: .317; post-test mean: .437) at both pre- and post-test (smaller z-scores indicate shorter RTs).

Fluid intelligence. Turning to the Raven's task, we replicate prior findings concerning transfer from this training regime to Raven's performance. We do find a significant main effect of testing occasion, with post-test scores outperforming pre-test ($F(1, 55)$[4] $= 4.077$, $p = .048$). However, no other significant effects were observed (training group: $F(1, 55) = .001$, $p = .972$; testing occasion x training group: $F(1, 55) = 1.932$, $p = .170$).

Reading comprehension. In order to make contact with previous findings reported with this training regime, the effect of training on reading comprehension was examined. Neither benefit from previous exposure to the task nor differential effects by training group were

[4] One subject's data in the training group (sham stimulation) was excluded due to experimenter error. Alternate forms of paper-and-pencil measures were not administered at post-test.

identified (testing occasion: $F(1, 55) = .484$, $p = .489$; testing occasion x training group: $F(1, 55) = .379$, $p = .541$). However, a marginally significant main effect of training group was identified ($F(1, 55) = 3.477$, $p = .068$) with the training group (mean pre: 34.500; mean post: 34.487) exhibiting superior performance relative to the control group (mean pre: 32.167; mean post: 33.000) at both testing occasions.

California Verbal Learning Test. 2x2 ANOVAs were carried out on overall free recall of list A (interference list performance was not analyzed), overall intrusions on list A trials and overall repetition of items on list A trials. Recall on cued trials was not included due to overall high accuracy on these trials (overall accuracy pre-test cued trials: 27.507 out of a possible 32; overall post-test accuracy on cued trials: 28.053 out of a possible 32). First turning to free recall, there was a marginally significant main effect of testing occasion ($F(1, 55) = 3.488$, $p = .067$) with a larger number of correct freely-recalled items at post-test compared to pre-test. No other effects were identified (training group: $F(1, 55) = 2.722$, $p = .105$; testing occasion x training group: $F(1, 55) = .176$, $p = .676$). Examination of intrusions revealed no significant findings (testing occasion: $F(1, 55) = 2.728$, $p = .104$; training group: $F(1, 55) = .006$, $p = .940$; testing occasion x training group: $F(1, 55) = .008$, $p = .928$). Similar null findings were identified with respect to repetitions (testing occasion: $F(1, 55) = 2.805$, $p = .100$; training group: $F(1, 55) = 1.155$, $p = .287$; testing occasion x group: $F(1, 55) = .057$, $p = .812$).

Discussion

Overall, these data suggest that 10 sessions of training with this regime, unlike previous findings using 20 sessions of training (Chein & Morrison, 2010; Richmond, et al., 2011) do not lead to significant far transfer. However, there is evidence of near transfer to a latent variable of WM after 10 sessions of training. Dose-dependency has been reported with other WM training regimes (Jaeggi, et al., 2008). It is plausible that the lack of far transfer in our data reflects dose-dependency as well, such that 10 sessions of training is simply not enough training to evince far transfer.

Effect of tDCS on Transfer

To specifically examine the effect of stimulation on transfer outcomes, the next series of analyses were conducted. Here, three groups (i.e. active, sham and NCC) were entered into the omnibus ANOVA. In the event that a significant two-way interaction was identified, planned follow-up comparisons (independent samples t-tests) were conducted for pre- and post-test outcomes for each paired combination of data (i.e. active vs. sham, active vs. NCC, sham vs. NCC). Means and standard errors for performance on each individual task, separated by group and time, can be seen in Table 3.

Working memory. A 2x3 mixed effects ANOVA was performed with the within-subjects factor of testing occasion and the between-subjects factor of stimulation group (active, sham or NCC). A main effect of testing occasion (post-test z-scores > pre-test; $F(1, 55) = 33.467$, $p < .001$) was identified; however, there was no significant main effect of stimulation group ($F(2, 55) = .985$, $p = .380$). A significant interaction between testing occasion x stimulation group was observed ($F(2, 55) = 5.940$, $p = .005$).

Table 3

Mean and standard error of performance on transfer tasks

	Active		**Sham**		**No-contact**	
Task	Pre	Post	Pre	Post	Pre	Post
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)
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	.296 (.037)	.283 (.039)	.217 (.030)	.217 (.030)	.306 (.034)	.263 (.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	.041 (.016)	.017 (.010)	.031 (.010)	.054 (.047)	.018 (.008)	.021 (.008)
SART	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	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 (.947)	11.300 (.818)	10.000 (.707)	10.368 (.766)	10.050 (.716)	11.444 (.764)
Nelson-Denny	34.450 (.682)	34.05 (1.241)	34.550 (.663)	34.947 (.628)	32.167 (1.373)	33.000 (.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 (.294)	1.650 (.599)	2.100 (.624)	2.842 (1.077)	1.389 (.642)	2.333 (.922)
CVLT Repetitions	4.850 (1.913)	2.450 (.756)	3.800 (1.004)	3.526 (.890)	2.889 (.922)	1.889 (.464)

Note: Absolute scoring method for OSpan and SymSpan (span score) are reported. Anti-saccade and Stroop ACC cost data are reported in terms of proportions.

Due to the identification of this significant interaction term, follow-up planned comparisons were conducted using independent samples t-tests on pre- and post-test data for each combination of comparisons (active vs. sham, active vs. NCC and sham vs. NCC) corrected for multiple comparisons, setting the critical p value to less than or equal to .008. Based on this significance criterion, no differences between groups were observed at pre-test (active vs. NCC: $t(36) = -.211$, $p = .834$; sham vs. NCC: $t(36) = -.753$, $p = .456$; active vs. sham: $t(38) = .553$, $p = .584$). Correction for multiple comparisons revealed that post-test differences emerged only between the active and NCC groups ($t(36) = 2.980$, $p = .005$; sham vs. NCC: $t(36) = 1.639$, $p = .110$; active vs. sham: $t(33.741)$ [5] $= 1.092$, $p = .283$). See Table 3 for means and standard errors for each group at pre- and post-test. See Figure 7 for a depiction of these data.

Inhibition. 2x3 mixed effects ANOVAs were conducted on both accuracy and RT data for the inhibition measures, following the same logic as outlined in the training-only analyses presented above. First investigating RTs, we see a non-significant main effect of testing occasion ($F(1, 53) = .019$, $p = .891$) and stimulation group ($F(2, 53) = .226$, $p = .799$), as well as a non-significant interaction of testing occasion and stimulation group ($F(2, 53) = .546$, $p = .582$). In terms of accuracy, no significant effects were observed (testing occasion: $F(1, 53) = 1.829$, $p = .182$; stimulation group: $F(2, 53) = 1.413$, $p = .252$; testing occasion x stimulation group: $F(2, 53) = 1.028$, $p = .365$). Because no significant interactions of occasion x group were identified, planned comparisons were not performed. Overall, there was no evidence that tDCS modulated performance on the inhibition tasks in terms of costs on either accuracy or reaction time.

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[5] Equality of variances were 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.

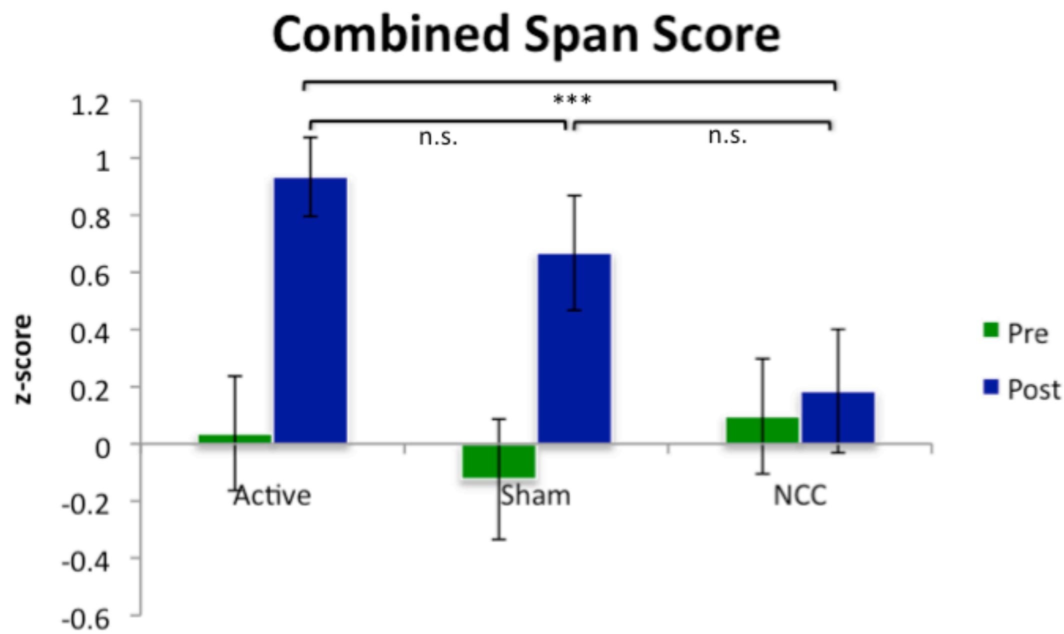

Figure 7. Near Transfer Data

Sustained attention. A 2x3 ANOVA was conducted on average RTs from the sustained attention tasks. No significant effects were found (testing occasion: $F(1, 55) = 2.474$, $p = .121$; stimulation group: $F(2, 55) = 3.171$, $p = .088$; testing occasion x stimulation group: $F(2, 55) = .847$, $p = .434$), although the main effect of stimulation group was marginally significant with sham group exhibiting the best performance overall with smaller z-scores indicating better performance (sham pre: -.209, sham post: -.195; active pre: .077. active post: .217; NCC pre: .317, NCC post: .437).

Fluid intelligence. The 2x3 mixed-effects ANOVA on Raven's performance revealed a marginally significant main effect of testing occasion (post-test > pre-test; $F(1, 54) = 2.832$, $p = .098$). No other effects were identified (stimulation group: $F(2, 54) = .827$, $p = .423$; testing occasion x stimulation group: $F(2, 54) = 1.276$, $p = .287$).

Reading comprehension. No significant effects were found on Nelson-Denny performance using a 2x3 mixed effects ANOVA (testing occasion: $F(1, 54) = .289$, $p = .593$; stimulation group: $F(2, 54) = 1.784$, $p = .178$; testing occasion x stimulation group: $F(2, 54) = .395$, $p = .676$).

California Verbal Learning Test. Separate ANOVAs were conducted on free recall, intrusions and repetitions on list A trials. Examination of free recall revealed a marginally significant main effect of testing occasion (post-test > pre-test; $F(1, 54) = 3.396$, $p = .071$). No other main effects or interactions reached significance (stimulation group: $F(2, 54) = 2.324$, $p = .108$; testing occasion x stimulation group: $F(2, 54) = .096$, $p = .908$). Turning next to intrusions, only a marginally significant effect of testing occasion was observed such that pre-test performance was superior to post-test performance (again smaller values indicate better performance; mean pre: 1.517, mean post: 2.263; $F(1, 54) = 3.020$, $p = .088$). No other significant effects were observed (stimulation group: $F(2, 54) = .714$, $p = .494$; testing occasion x stimulation group: $F(2, 54) = .089$, $p = .915$). Last, examination of repetition effects again revealed a marginally significant main effect of testing occasion (post-test performance > pre-test performance; $F(1, 54) = 3.510$, $p = .066$). No other significant main effects (stimulation group: $F(2, 54) = .567$, $p = .591$) or interactions (testing occasion x group: $F(2, 54) = 1.024$, $p = .366$).

Discussion

Overall, these data provide preliminary evidence that tDCS may be useful for enhancing near-transfer outcomes (i.e. significant post-test difference between active and NCC) but may not induce broad benefits in terms of far transfer. The training data presented here are largely consistent with two recent reports suggesting that tDCS may enhance learning but the effects may not extend beyond the practice domain (Iuculano & Cohen Kadosh, 2013; Martin, et al., under review). However, our near-transfer findings with respect to an effect of tDCS stand in contrast to these reports, providing initial evidence of enhanced learning beyond the training regime (see also Baker, et al., 2010). Both the Martin, et al. (under review), and Iuculano & Cohen Kadosh (2013) reports do not show evidence of near transfer of learning in the face of enhanced learning on the trained task. Taken together, these reports (Iuculano & Cohen Kadosh, 2013; Martin, et al., under review) along with our null findings with respect to far-transfer outcomes suggest that tDCS may be more well-suited to enhance learning within a relatively narrow range.

Correlations between Training Gains and Transfer Outcomes

Previous work with this paradigm examined individual differences in the amount of learning and found that enhanced learning on the training regime, specifically in the spatial WM task, was related to enhanced transfer outcomes (Chein & Morrison, 2010).

To investigate this possibility in my dataset, bivariate correlations were conducted on the relation between improvement in both the spatial and verbal domains of the training regime (session 10 performance-session 1 performance) and post-test transfer measures. These results can be seen in Table 4. Transfer outcomes on the Raven's were related to improvement on the spatial WM training task. Interestingly, improvement on the verbal portion of the training task was not significantly related to any of the outcome measures.

Table 4

Correlation matrix for training gains and transfer outcomes

	Spatial Gain	Verbal Gain
Span Score	.165	.188
Inhibition RT	-.100	-.056
Inhibition ACC	.205	-.021
Sustained Attention RT	.-.054	-.044
Raven's	**.315**^	.235
Nelson-Denny	-.027	-.056
CVLT Free Recall	.043	.119
CVLT Intrusions	.218	-.059
CVLT Repetitions	-.215	-.146

Note: The left column lists transfer measures, the middle column lists correlations with training gains on the Spatial WM task; the right column lists correlations with training gains on the Verbal WM task. Data shown here represent post-test performance; z-scores for composite measures were utilized. ^ $p < .10$

Discussion

These results provide some converging evidence with Chein and Morrison's (2010) finding regarding improvement on the spatial portion of the training task relating more strongly to transfer outcomes than verbal. Here, improvement on the spatial variant of the training task was found to be marginally correlated with improvements on Raven's (p = .051). Given our small sample size, these correlations provide additional support for the idea that improvements on the training regime in the spatial domain are related to a greater incidence of transfer. Because tDCS was found to enhance learning in the verbal domain to a greater degree than spatial, is it possible that the far-transfer effects we observed in relation to tDCS were limited by this modality-specific training effect.

CHAPTER 3

GENERAL DISCUSSION

The present work examined (a) the extent to which tDCS enhanced learning on an adaptive WM span task, (b) the manner in which tDCS enhanced learning (c) the transfer profile resulting from a shortened training regime and (d) the effect of tDCS on transfer. The work presented here makes a number of novel contributions to the extant WM training literature, including examination of the transfer profile resulting from this training regime with half the number of sessions typically used (Chein & Morrison, 2010; Richmond, et al., 2011) and the addition of tDCS to an adaptive WM training regime. These data also contribute novel findings to the tDCS literature by extending previous work in the domain of WM to a complex span task. Furthermore, this experiment extends findings from previous learning paradigms to the domain of WM. Possibly the most interesting novel contribution of this work to the existing tDCS-learning literature lies in providing evidence that tDCS can enhance learning beyond the training task (i.e. near transfer of learning).

This study yielded several findings worthy of review here. First, analyses on the training task itself showed that anodal tDCS over left DLPFC, over and above training plus sham stimulation, enhanced learning on a complex WM task particularly in the verbal domain. One interesting piece of correlational evidence - that training gains on the spatial task correlate with gains on the Raven's - supports the idea that enhanced training gains may lead to enhanced transfer outcomes (see also Chein & Morrison, 2010). However, the correlations were found in the spatial domain, not the verbal domain. Because the effect of tDCS was stronger in the verbal domain, future research in this vein should focus on applying tDCS in such a way that spatial gains are maximized in order to more directly modulate the transfer profile.

Second, the way in which tDCS enhanced learning on the training task was examined. Split-plot regressions centered midway through the training regime (session 5) did not show evidence that differential rates of learning were present in the first and second halves of training. Instead, these findings suggest that tDCS served to enhance learning to the same degree throughout all 10 training sessions. Future work related to this finding may help to elucidate if there is an asymptote for tDCS to enhance learning, or if the 'global adjuvant' description of the way in which tDCS enhances learning is applicable to longer training regimes.

In addition, the data presented here suggest that near transfer can be achieved with as little as 10 sessions of training. Importantly, near transfer was indexed by multiple tasks to increase the reliability of claims regarding enhancement of the WM store (see also Redick, et al., 2012) following WM training. Encouragingly, the near transfer effect of training was driven by a significant difference between the active tDCS group and the NCC (no significant difference between sham and NCC), lending support to the idea that the effect of tDCS extends beyond the training paradigm alone. Because no evidence of far transfer followed from either training or tDCS, it appears as though greater than 10 sessions are needed in order to achieve far transfer gains. In this experiment training itself did not lead to far transfer, therefore, the extent to which tDCS might modulate these effects remain unknown.

Limitations of the current work

There are a number of limitations of the current study that should be addressed. First, post-hoc power analyses suggest that power was relatively low in this study especially in the spatial domain. Because this is the first study of its kind, the effect size was difficult to predict *a priori*; thus, sample sizes were based on those previously reported in the WM training literature. As such, it is possible that the relatively low power in our study lead to type II error.

Second, an obvious criticism of the current work involves the inclusion of a test-retest control group rather than an active control group. Given that the near-transfer finding resulted in a difference only between the active tDCS group and the NCC, this is a particularly important limitation to consider. 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, et al., under review), suggesting that demand characteristics, while certainly different between these two types of control groups, may not affect transfer outcomes to the degree previously thought (Shipstead, et al., 2010, 2012). More convincingly, demand characteristics were identical between our active and sham tDCS groups, but only the active and NCC groups were significantly different at post-test. 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 to the NCC group, lends a great deal of support to the interpretation that tDCS enhanced WMC above and beyond training alone.

Third, it is both a boon and a limitation of the current study that only 10 sessions of training were undertaken by our sample. On the downside, it is difficult to compare the outcomes of this study to other previously published reports with twice as many training sessions. To that end, the effect of tDCS on far transfer remains unknown. Towards a more positive interpretation of this design decision, the basic comparison of 10 to 20 training sessions is informative for the behavioral WM training literature in that neither the tDCS nor the sham group exhibited far transfer in this study (converse to previous findings; Chein & Morrison, 2010; Richmond, et al., 2011). This basic comparison is the first demonstration of a dose-dependent response with this particular WM training regime. Due to the fact that others, utilizing different training regimes, have reported similar dose-dependent findings with respect to far transfer in particular (Jaeggi, et al., 2008), future researchers may wish to uncover the point at which dose-dependent transfer effects asymptote (i.e. the point beyond which more training doesn't lead to better/broader transfer).

Last, an additional limitation of this study relates specifically to the null finding on the sustained attention construct. This piece of the transfer battery was the most novel, and was predicated on self-report data from our older adult study (Richmond, et al., 2011). In the context of null findings on other measures of far transfer we have previously observed with this training regime, the effect of this training task on sustained attention was not uncovered. Specifically, it would be a clearer interpretation of a null finding with respect to sustained attention in the face of other, expected, far transfer outcomes. As it stands, the way in which to understand the null finding on sustained attention is murky. Two plausible interpretations can be offered: (a) this training regime does not lead to far transfer on indices of sustained attention; or (b) 10 sessions of training is simply not enough to obtain evidence of far transfer to sustained attention. The second interpretation is clearer for other far transfer measures, such as Nelson-Denny, CVLT and inhibition, because boosts in performance have been reported after 20 sessions of training. The current data cannot adjudicate between interpretations (a) and (b) for the sustained attention outcome. Future researchers may wish to include sustained attention measures in a transfer battery for a training regime lasting 20+ sessions to evaluate which of these interpretations may be most appropriate.

Open Questions

The findings of this study raise a number of interesting questions and opportunities for further research in a similar vein. Perhaps the most obvious question that follows from the pattern of results from this study is what effect anodal stimulation of right DLPFC might exert on

WM training and transfer outcomes. Because of the previously identified association between transfer and improvement on the spatial portion of the training regime (Chein & Morrison, 2010), as well as the additional support provided for this idea in these data, it stands to reason that improving training outcomes in the spatial domain may boost transfer to a greater degree than was observed here. Previous research using tDCS in the domain of WM have focused specifically on verbal variants of WM tasks (Boggio, Ferrucci, et al., 2006; Fregni, et al., 2005; Marshall, Molle, Seibner, & Born, 2005; Seo, et al., 2011; Zaehle, et al., 2011). Our finding of a main effect of stimulation (active > sham) on the training task suggests that tDCS enhanced learning in both the verbal and spatial domains. However, this main effect was driven by the strong effect of stimulation in the verbal domain only. In short, the degree to which tDCS might modulate spatial WM abilities is not well understood. Nonetheless, applying positive stimulation over rDLPFC in order to enhance learning in the spatial domain, thereby attempting to increase transfer, offers a tantalizing future direction.

It would also be fruitful is to extend the training out to 20 sessions. Visual inspection of the training curves shows that learning had not plateaued by session 10 and importantly, there was no evidence of far transfer. The literature on tDCS and 'transfer' is quite sparse and somewhat mixed (Baker, et al., 2010; Iuculano & Cohen Kadosh, 2013; Martin, et al., under review). Because previous research with this paradigm using 20 sessions provides surer footing with respect to the effect sizes and transfer profile that can be expected, extending the training by 10 additional sessions with tDCS would provide stronger evidence for the role of tDCS in far transfer than the current data can provide.

One of the most interesting future directions for this research involves conducting a WM training + tDCS study in populations with compromised WM abilities, such as older adults.

Research suggests that tDC stimulation can initiate LTP-like mechanisms (Fritsch, et al., 2010). Furthermore, it has been suggested that older adults may exhibit lower levels of LTP, at least in hippocampal regions, compared to 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 relatively higher levels of LTP normally.

Conclusions

Our findings suggest that tDCS is an effective tool to enhance learning over time. Furthermore, these data provide the first demonstration in the domain of WM that the effects of tDCS extend beyond the training task itself (i.e. near transfer); however, there was no evidence of far transfer after only 10 sessions of training. Future research may investigate the effect of tDCS on spatial WM, as training gains in this domain were related specifically to transfer outcomes. Altogether, these data provide strong evidence that tDCS is an effective, useful tool to enhance learning in normal, healthy adults. These findings provide support for the use of tDCS in rehabilitation settings as well.

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APPENDIX A: TASK SPECIFIC ANALYSES

To investigate any task-specific effects that may have been affected by training within the composite cognitive factors, a series of 2x2 ANOVAs were conducted on individual task performance (within-subjects effect of testing occasion, between-subjects effect of training group- training or NCC). These data can be seen in Table A1. To investigate the potential effects of tDCS on task-specific performance, 2x3 ANOVAs were conducted (within subjects effect of testing occasion, between subjects effect of stimulation group- active, sham or NCC). Results of these analyses are displayed in Table A2.

Table A1. Task-Specific Effect of Training

	Testing occasion		Training group		Interaction term	
	F value	*p* value	*F* value	*p* value	*F* value	*p* value
OSpan Score	2.357	.130	2.492	.120	11.503	.001
SymSpan Score	27.018	<.001	.199	.657	6.086	.017
Stroop RT Cost	1.579	.214	2.279	.137	.200	.656
Stroop ACC Cost	.005	.945	.669	.417	.013	.911
AntiSaccade RT Cost	2.306	.135	1.283	.262	.002	.966
Antisaccade ACC Cost	.158	.693	.133	.717	.003	.957
SART	22.692	<.001	.564	.456	1.672	.201
PVT	16.495	<.001	4.420	.040	.174	.678

Table A2. Task-Specific Effect of tDCS

	Testing occasion		Stimulation group		Interaction term	
	F value	*p* value	*F* value	*p* value	*F* value	*p* value
OSpan Score	8.134	.006	1.629	.205	5.657	.006
SymSpan Score	41.710	<.001	.332	.719	3.161	.050
Stroop RT Cost	1.404	.241	1.124	.332	.098	.906
Stroop ACC Cost	.001	.973	.520	.597	.583	.562
AntiSaccade RT Cost	2.716	.105	1.676	.197	.249	.780
Antisaccade ACC Cost	.165	.687	1.500	.232	.050	.951
SART	21.531	<.001	1.519	.228	.886	.418
PVT	18.649	<.001	2.214	.119	1.722	.188

APPENDIX B: SENSATION QUESTIONNAIRE & DATA

During each day of training, subjects in both the active and sham tDCS groups filled out a questionnaire asking about potential side effects of stimulation. The questionnaire is as below:

Post-Study Questionnaire

Transcranial Direct Current Stimulation Investigations of Cognition: Training Study

Protocol #815608

Subject Name: ________________________
Testing Date: _________________________

To what extent did you experience the following symptoms *during* tDCS:

Headache:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Difficulty concentrating:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Acute mood changes:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Changes in visual perception:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Tingling:

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Itching sensation:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Burning sensation:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Pain:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Fatigue:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Nervousness:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Visual sensation, associated with the start/end of the stimulation:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

<u>Other adverse effects:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

To what extent did you experience the following symptoms *after* receiving tDCS:
<u>Headache:</u>

1	2	3	4	5
Very mildly or not at all				To a significant degree

Difficulties concentrating:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Acute mood changes:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Changes in visual perception:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Tingling:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Itching sensation:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Burning sensation:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Pain:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Fatigue:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Nervousness:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Unpleasant sensation:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Nausea:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Sleep disturbance:

1	2	3	4	5
Very mildly or not at all				To a significant degree

Other adverse effects:

1	2	3	4	5
Very mildly or not at all				To a significant degree

In order to determine if active vs. sham tDCS generally resulted in a given side effect for each participant, scores over all 10 training sessions were averaged for each of the above questions. Following the logic of analyses presented in (Kessler, Turkeltaub, Benson, & Hamilton, 2011), distributions of (average) severity ratings were tested using a Mann-Whitney U test. Only the distributions for tingling (mean, active: 1.764; mean, sham: 1.364; $p = .014$), itching (mean, active: 1.768; mean, sham: 1.271; $p = .010$), burning (mean, active: 1.587; mean, sham: 1.121; $p < .001$) and pain (mean, active: 1.313; mean, sham: 1.056; $p = .015$) during stimulation were found to be significantly different between groups. These differences did not persist after stimulation was over (tingling after: $p = .602$, itching after: $p = .327$, burning after: $p = .478$, pain after: $p = .102$). To visualize the sensation ratings over time, see Figure B1.

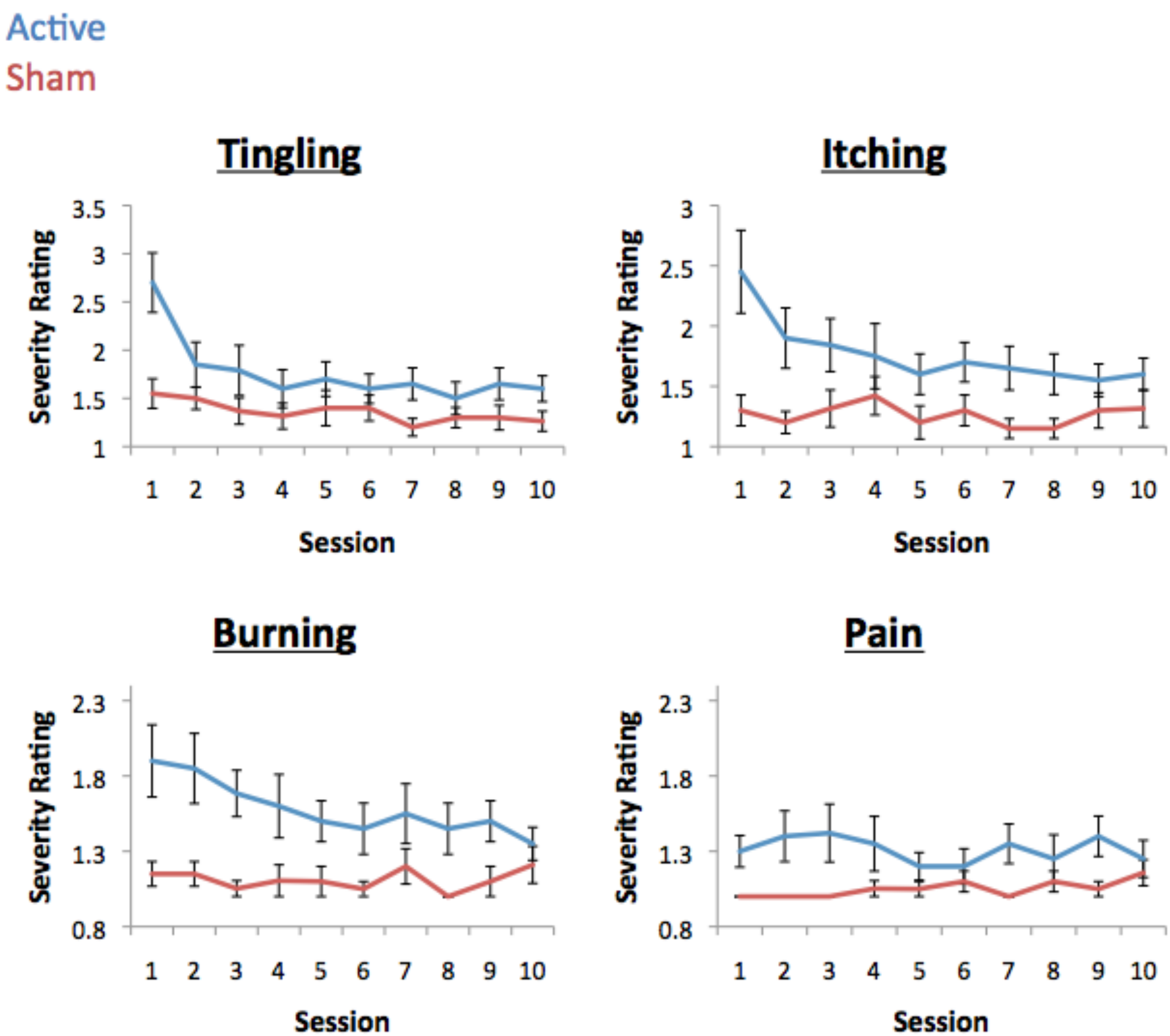

Figure B1. Symptom ratings over 10 sessions

APPENDIX C: EFFORT AND MOTIVATON SELF-REPORT DATA

At the beginning of each training session, participants were asked "How motivated are you to complete today's study?" Participants responded to the question using a 1-5 scale, with 1 being 'not at all motivated' and 5 being 'extremely motivated.' Likewise, at the end of each session, participants were asked how much effort they put into completing the training, with a similar response scale. In order to explore if motivation or effort on the daily training sessions differed by group, 2x2 ANOVAs were preformed with group as the between subjects factor (active or sham) and session (1, 10) as the within subjects factor. Statistics were performed separately for effort and motivation questions.

Turning first to motivation, no significant effects were identified (main effect of session: $F(1, 38) = .000$, $p = 1.00$; main effect of stimulation group: $F(1, 38) = .321$, $p = .575$; session x stimulation group: $F(1, 38) = .100$, $p = .753$). The investigation of effort yielded similar findings (main effect of session: $F(1, 38) = .018$, $p = .894$; main effect of stimulation group: $F(1, 38) = .437$, $p = .513$; session x stimulation group: $F(1, 38) = .162$, $p = .689$). These findings suggest that enhanced learning in the active stimulation group did not result simply from increased interest in training or effort expended on completing the training task. See Figure C1 for depiction of motivation and effort data.

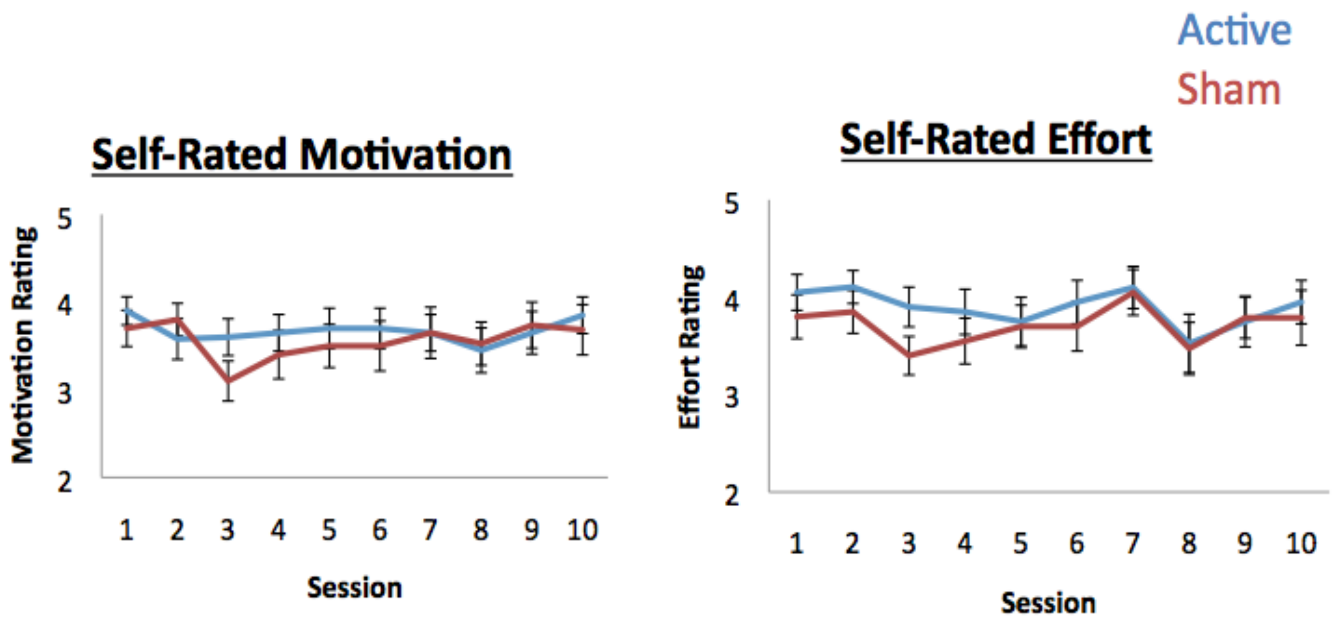

Figure C1. Daily Motivation and Effort Ratings