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SAND2014-18616
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September 2014

Effects of Transcranial Direct Current Stimulation (tDCS) on Human Memory

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Abstract

Training a person in a new knowledge base or skill set is extremely time consuming and costly, particularly in highly specialized domains such as the military and the intelligence community. Recent research in cognitive neuroscience has suggested that a technique called transcranial direct current stimulation (tDCS) has the potential to revolutionize training by enabling learners to acquire new skills faster, more efficiently, and more robustly (Bullard et al., 2011). In this project, we tested the effects of tDCS on two types of memory performance that are critical for learning new skills: associative memory and working memory. Associative memory is memory for the relationship between two items or events. It forms the foundation of all episodic memories, so enhancing associative memory could provide substantial benefits to the speed and robustness of learning new information. We tested the effects of tDCS on associative memory, using a real-world associative memory task: remembering the links between faces and names. Working memory refers to the amount of information that can be held in mind and processed at one time, and it forms the basis for all higher-level cognitive processing. We investigated the degree of transfer between various working memory tasks (the N-back task as a measure of verbal working memory, the rotation-span task as a measure of visuospatial working memory, and Raven's progressive matrices as a measure of fluid intelligence) in order to determine if tDCS-induced facilitation of performance is task-specific or general.

ACKNOWLEDGMENTS

This work was funded under LDRD Project Number 165715 and Title "Testing the Effects of Transcranial Direct Current Stimulation on Human Learning.” This project was conducted in collaboration with Dr. Vince Clark’s lab at the University of New Mexico and Dr. Eric Leshikar’s lab at the University of Illinois at Chicago.

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NOMENCLATURE

EEG	Electroencephalography
DLPFC	Dorsolateral Prefrontal Cortex
DOE	Department of Energy
fMRI	Functional Magnetic Resonance Imaging
SNL	Sandia National Laboratories
tDCS	Transcranial Direct Current Stimulation
VLPFC	Ventrolateral Prefrontal Cortex
WM	Working Memory

1. INTRODUCTION

Training a person in a new knowledge base or skill set is extremely time consuming and costly, particularly in highly specialized domains such as the military and the intelligence community. Recent research in cognitive neuroscience has suggested that a technique called transcranial direct current stimulation (tDCS) has the potential to revolutionize training by enabling learners to acquire new skills faster, more efficiently, and more robustly (Bullard et al., 2011). In tDCS, a small region of the brain is stimulated with a weak electrical current (1-2 milliamps) via an electrode placed on the scalp. This current makes the neurons in the vicinity of the stimulation either more or less likely to fire, depending on the polarity of the electrical field. Although tDCS has been used for over 50 years, recent advances in technology have created a surge of new applications (Utz et al., 2010). Some researchers suggest that tDCS devices will be widely available to the public in the near future. Most of the research in this rapidly developing field has been focused on medical applications, such as treating migraines or assisting with rehabilitation of brain injuries. However, tDCS has many potential applications with implications for national security and many of those applications have received little attention to date.

In this project, we tested the effects of tDCS on two different types of memory performance: associative memory and working memory. Associative memory refers to memory for the relationships between multiple pieces of information and working memory refers to the amount of information that can be held in mind and processed at one time. Both types of memory are vitally important for education and training. Associative memory is necessary for learning new information and forms the foundation for all episodic memories. Working memory capacity is crucial for basic information processing capabilities. It forms the basis for all higher-level cognitive processing and is one of the key cognitive abilities assessed in intelligence tests. If tDCS can improve an individual's memory performance in one or both of these areas, it could have a dramatic impact on training and learning performance. Recent research has shown that tDCS can have a substantial impact on procedural learning (Bullard et al., 2011) and our goal is to extend this research to encompass other types of learning and memory where the effects of tDCS on performance are currently unknown.

To test the effects of tDCS on associative memory and working memory, we carried out two experiments using the methods that are accepted as best practices for tDCS research (c.f. Gandiga et al., 2006; Nitsche et al., 2008). Both experiments used a double-blind, sham-controlled experimental design. This means that half of the participants received active tDCS stimulation and half of the participants received sham stimulation, which mimics the sensation of tDCS but does not influence brain activity. The tDCS stimulation was delivered in a double-blind manner so that neither the participant nor the experimenter knew whether the participant was receiving active or sham stimulation. In both the associative memory experiment (Experiment 1) and the working memory experiment (Experiment 2), the participants' memory performance in the active stimulation condition was compared to memory performance in the sham stimulation to determine what effects the stimulation has on memory performance.

Our findings, described below, indicate that tDCS can improve both associative memory and working memory performance. These findings indicate that tDCS could be a powerful tool for enhancing training, enabling trainees to encode and recall information more effectively.

2. EXPERIMENT 1: EFFECTS OF TDCS ON ASSOCIATIVE MEMORY

2.1. Methods

2.1.1. Participants

Twenty-six people, 13 male and 13 female, participated in the study and were paid for their time. The participants were student interns working at Sandia National Laboratories. Their average age was 22.25 (range 19-30). All of the participants were right handed, native English speakers with no history of neurological or psychiatric disorders, head injuries, or vision or hearing problems. None of the participants had surgical or other metal implants in their head, neck, shoulders, or arms, and none were taking any psychoactive medications at the time of the study. In addition, none of the participants had prior experience with tDCS. Half of the participants were assigned to the active stimulation group and half were assigned to the sham stimulation group in a double-blind manner. Two of the participants (one male and one female) were excluded from data analysis due to failure to follow task instructions. This left 12 participants (6 male and 6 female) in each of the tDCS conditions.

2.1.2. Materials

The images used in this study were drawn from the neutral emotion photographs in the FACES database (Ebner, Riediger & Lindenberger, 2010). Each person pictured in the database was assigned a first name. The names were drawn from the Social Security Administration's lists of the most common male and female names in each decade. Based on the age and gender of each person in the images, a name was selected from among the 60 most common names of the decade in which that person was born. No names were repeated and names that were popular for both males and females were excluded. The images were divided into three sets containing equal numbers of males and females and equal numbers of people from each age group (young, middle aged, and elderly). Each list included nine young women, nine young men, nine middle aged women, nine middle aged men, nine older women and nine older men. Nine additional image sets were used for the practice list.

Previous research has indicated that stimulation near regions homologous to those targeted in this study may impact mood and affect (Barrett et al., 2004). While the specific stimulation parameters in this study differ somewhat (e.g., along the dimensions of current strength, electrode size, and exact electrode location), we compared mood data obtained at the start of the experiment (following consent and collection of demographic information) and at the end (final item) in order to investigate the potential of tDCS administered as in the current work to influence participant mood. Mood was assessed via self-report questionnaire in which participants were prompted to indicate their level of agreement with 10 statements, such as "I feel nervous" and "I feel unable to concentrate or pay attention" on a six point Likert scale, ranging from 0 ("not at all") to 5 ("very much").

Participants were prompted to report their physical sensations at 8 time points during tDCS; at the one minute mark, and at each 4 minute mark thereafter (i.e., at 1, 5, 9, 13, 17, 21, 25, and 29 minutes following initiation of stimulation). For each time point, participants were asked to complete an 11-point Likert scale ranging from 0 ("none") to 10 ("excessive") for each of three sensations – tingling, itching, and heat/burning.

2.1.3. Procedure

After completing the informed consent process and passing a verbal screening of all inclusion and exclusion criteria, participants filled out questionnaires about demographic and handedness information. They also completed baseline mood and sensation questionnaires. Next, the participants completed a practice session that provided an overview of the memory tests and instructions for each section. They practiced the study phase, recognition test, and recall test with a set of nine face-name pairs. During the study phase, a picture appeared in the center of the screen with a name directly below it. Each face-name pair stayed on the screen for seven seconds. Participants were asked to study each face while it was on the screen and to try to memorize that person's name. After each face-name pair disappeared, the participants were asked "Does this name fit the person's face?" They responded yes or no with a button press. The question remained on the screen for two seconds. In the recognition memory test, participants were again shown face-name pairs, half of which were correct pairings and half of which were recombined pairs in which a previously studied picture was paired with a name that had been studied with a picture of a different person of the same gender and age group. Below the face-name pair, participants saw the question "Is this the correct name?" They responded using a 1-4 scale, with "1" indicating that they were sure it was not the correct name, "2" indicating that they didn't think it was the right name, but were unsure, "3" indicating that they thought it was the correct name, and "4" indicating that they were sure it was the correct name. Each face-name pair remained on the screen until the participant responded with a key press. The recognition test was followed by a recall test. In the recall test, participants were shown all of the faces from the study list, one at a time, and were asked to type in each person's name. They were encouraged to guess if they could not remember the name, or to type "no" if they did not have a guess. Each picture stayed on the screen until the participant hit the "enter" key.

Following the practice session, the participants completed a baseline memory test in which they studied 36 face-name pairs and completed the recognition and recall tests. The baseline test took approximately 5 minutes to complete.

After the baseline memory test, the tDCS equipment was set up. TDCS was delivered using the ActivaTek ActivaDose II system. The cathode was placed on the upper right arm of the participant, on a fleshy area near the bicep between the elbow and the shoulder. The anode was placed over the left sphenoid bone, near location F9 on the international 10-20 EEG system, targeting the left inferior frontal cortex. Functional magnetic resonance imaging (fMRI) has implicated this brain area in the successful encoding of face-name associations (Sperling et al., 2003). Current was delivered for 30 minutes at either 0.1 mA (sham) or 2.0 mA (active) via 3 cm x 3 cm (11 cm^2) sponge electrodes saturated with saline (6.25 mL of 140 mM concentration NaCl solution per sponge) and secured using Coban self-adherent wrap.

A current strength of 0.1 mA was chosen as the sham stimulation condition in order to induce physical sensations typically associated with tDCS by stimulating the skin/scalp without stimulating the brain areas beneath the electrode. Traditional methods of ramping up the current near the start of stimulation then ramping it down (typically after 30 seconds) may not be effective in blinding participants to stimulation condition, as under active stimulation conditions sensations may persist beyond this 30 second window (Dundas, Thickbroom, & Mastaglia, 2007; Poreisz, Boros, Antal, & Paulus, 2007). Additionally, current modeling studies suggest that current strength less than 0.5 mA at the electrode size used in the current research have no impact on brain activity in neural tissue 12 mm beneath the surface of the skin (Miranda, Faria, & Hallett, 2009). In our sham condition, participants received 20% of this current strength, making it unlikely that the 0.1 mA administered would have a meaningful impact on brain function.

Experimenter blinding was accomplished via a coded switch box outfitted with inputs for positive and negative leads from two current generators and output for just two electrodes – one anode and one cathode. One current generator was set to 0.1 mA while the other was set to 2.0 mA. A six-way switch was implemented to interrupt the circuit, with three settings allowing current to flow from one generator to the output leads and the other three supplying current from the second generator. In order to maintain the activity of the current generator that was not providing current to the output leads, the inputs not actively supplying current to the outputs were routed through a circuit loop in order to maintain the functioning of the inactive generator. The six-way switch was coded via a third party, with the coding released to the experimenters following completion of data collection.

During tDCS stimulation, all participants studied the same list, which consisted of 108 face-name pairs. The pairs were presented in a pseudorandom order such that no more than four faces of the same gender or age group appeared in a row. They were divided into six blocks containing 18 pairs each. After each block, participants took a short break and filled out the sensation questionnaire. The study session ended a few minutes before the end of the tDCS stimulation, which lasted for 30 minutes. Following cessation of stimulation, electrodes were removed and participants were provided with a recognition test.

In the recognition test, participants saw one of three test lists that contained 36 old face-name pairs and 36 recombined face-name pairs. The recombined pairs drew from faces and names of the same gender and age group so that the old and recombined pairings were equally plausible. The pairs were counterbalanced across lists so that the items were tested equally often in old and recombined pairs. For example, all participants studied the pairs FaceA-NameA, FaceB-NameB, and FaceC-NameC at study, where FaceA, FaceB and FaceC were all people of the same gender and age group. One-third of the participants were then tested on the pairs FaceA-NameA (old) and FaceB-NameC (recombined), one-third were tested on the pairs FaceB-NameB (old) and FaceC-NameA (recombined), and one-third were tested on the pairs FaceC-NameC (old) and FaceA-NameB (recombined). The pictures were not identical to the original pictures, but were of the same people with the same neutral expression. The FACES database contains two pictures of each person in each emotion condition, so if picture A was studied, picture B was used in the memory tests, and vice versa. This was done to make the task slightly more difficult and to ensure that the participants were remembering the faces and not some esoteric detail about a particular photograph of that face.

In the recall test, participants saw all of the 108 face that were studied in the study session and were asked to type in each person's name. Of those 108 faces, 36 had been tested as old pairs in the recognition memory test, 36 had been tested as part of recombined pairs in the recognition test, and 36 were not used in the recognition memory test (these were the studied faces whose names were re-paired with different faces to create the lures on the recognition memory test). Across participants, each face fell into each of these conditions an equal number of times. The participants' responses were corrected for spelling errors before the data were analyzed.

At the end of the experiment session, participants were asked to guess whether they were in the active or sham condition and to indicate why they thought so. They were also asked to complete a questionnaire describing any memory strategies that they used to complete the task.

2.2. Results

2.2.1. Baseline

On the baseline memory test, there were no significant differences in performance between the active and sham groups. For the recognition memory test, the active group responded correctly to 79.5% of the trials, on average, while the sham group responded correctly to 75.3% ($t(1,22) = 0.85$). On the recall test, the participants in the active group correctly recalled 42.4% of the names, on average, while the sham group correctly recalled 36.3% ($t(1,22) = 0.81$).

2.2.2. Study Phase

The participants generally responded that the names fit the faces across all of the age and gender groups. The participants in the active stimulation group were slightly more likely to say that the names fit the faces than the participants in the sham stimulation group (73.7% versus 69.4%), but this difference was not significant ($t(1,21) = 0.24$). Table 1 shows the breakdown of responses based on stimulation condition, gender of the participants, and the age group and gender of the face stimuli.

Table 1. Average Fit Response for Each Condition

Stimulation Condition	Participant Gender	Young Faces	Middle-Aged Faces	Old Faces	Male Faces	Female Faces	Overall
Active	Male	85.4%	74.6%	77.7%	82.2%	76.4%	79.3%
	Female	71.7%	57.9%	75.1%	68.8%	67.6%	68.2%
Sham	Male	70.5%	65.1%	71.3%	72.5%	65.3%	69.1%
	Female	68.8%	62.3%	78.1%	71.1%	68.4%	69.8%

2.2.3. Recognition Test

The performance of the two groups of participants was quite similar on the recognition memory test. On average, the participants in the active stimulation group had a 77% hit rate (a response of "1" or "2") for the old face-name pairs and a 23% rate of misses (a response of "3" or "4"). The participants in the sham group had a 76% hit rate and missed 24% of the old pairs. For the recombined pairs, the active group correctly rejected 70% of the lures and had false alarms to 30% of the lures. Similarly, the sham group correctly rejected 67% of the lures and had false alarms to 33%. None of the performance differences between the two groups were significant (all ts < 0.40). The proportions of each response type for each condition are shown in Figure 1. The recognition memory responses were broken down based on the participants' ratings of the fit between the face and the name at study. There were no significant differences in hit or false alarm rates between the good fits and the poor fits for either the active or sham stimulation groups (all ts < 0.66, all ps > 0.26).

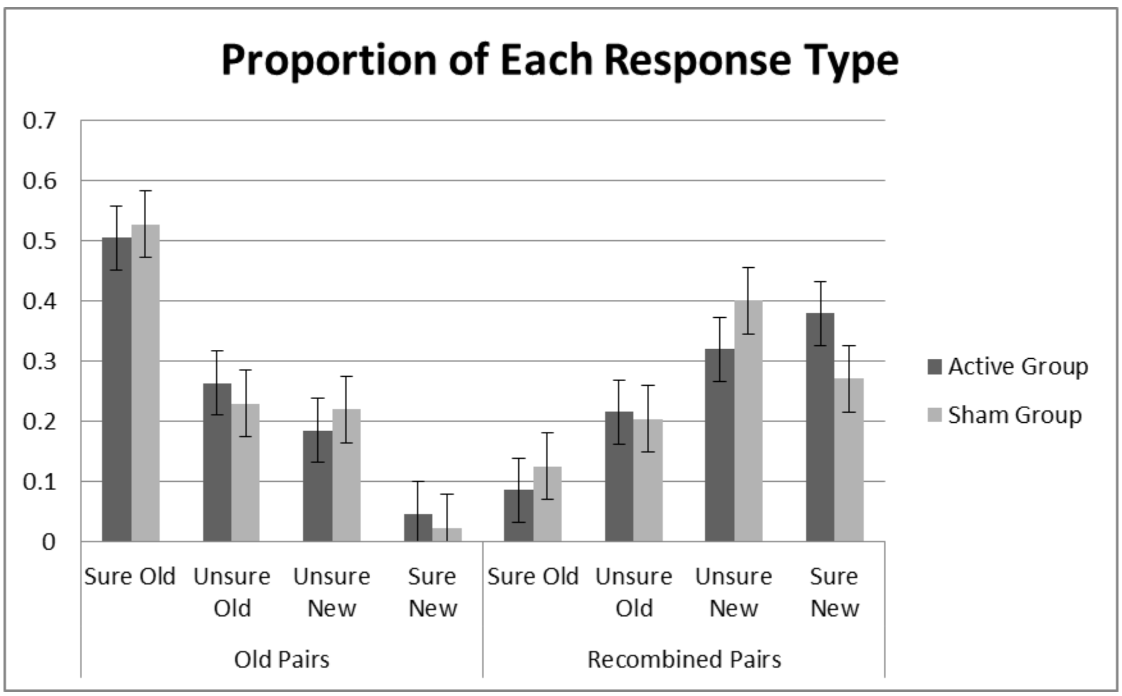

Figure 1. Proportion of Each Response Type for Each Condition

To determine whether or not the two groups differed in their ability to discriminate between old pairs and recombined pairs, the participants' responses were used to calculate d_a. The d_a scores were calculated using RSCORE+ (reference). There was not a significant difference between the two groups' recognition memory discrimination performance, as measured by d_a. The participants in the active stimulation group had an average d_a score of 1.42 while the participants in the sham group had an average d_a score of 1.28 (t(1,22) = 0.58).

2.2.4. Recall Test

In general, participants found the recall task to be quite difficult. There was a broad range of performance, with performance for participants in the active group ranging from 10 to 41 correct recollections and performance for participants in the sham group ranging from 5 to 34 correct recollections. On average, the participants in the active group recalled an average of 26% of the studied names, while the participants in the sham group recalled an average of 17%. The active participants' recall performance was significantly better than that of the sham participants ($t(1,22) = 1.93$, p = 0.03). The recall results are shown in Figure 2.

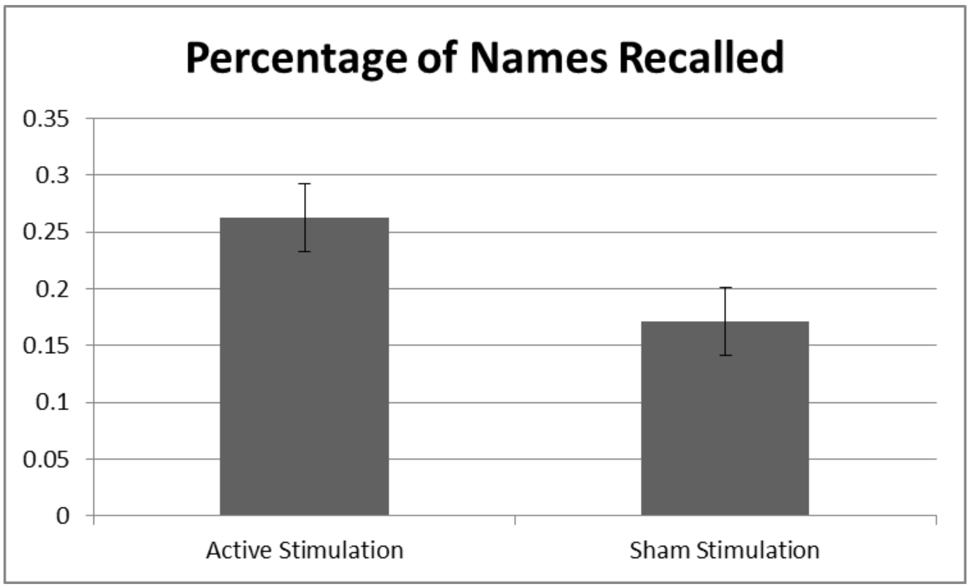

Figure 2. Average Percentage of Names Recalled Correctly

The participants' errors were broken into five categories: no response, recalling the mis-paired name from the recognition test (a source error), recalling a name that was studied with a different face from the same age group, recalling a name that was studied with a face from a different age group, and recalling a name that was never studied. The participants in the active group failed to enter a name for an average of 38.7% of the trials on the recognition test, while the participants in the sham group failed to enter a name for 40.0% of the trials. The difference between the two groups was not significant ($t(1,22) = 0.19$). The participants in the sham group were significantly more likely to enter a name that had never been studied than the active group (23.6% of trials versus 15.6% of trials, $t(1,22) = -2.08$, $p = 0.02$). However, the two groups were equally likely to recall names that had been studied with other faces. The participants in the active group entered names that were studied with a different face in the same age group on an average of 9.5% of trials, and names that were studied with a face from a different age group on 7.4% of trials. Participants in the sham group made the same types of errors on 11.3% and 6.0% of trials, respectively ($t(1,22) = -0.84$ for same age group errors and $t(1,22) = 0.59$ for different age group errors). In addition, the two groups did not differ significantly in their number of source errors (face-name pairings recalled from the recognition memory test rather than the study list, $t(1,22) = 0.73$). The participants in the active group made a total of 22 such errors (an average of 2.5% of trials) while participants in the sham group made a total of 16 errors (an average of 1.8% of trials across participants). These results indicate that active tDCS stimulation improved recall performance and did not increase the participants' chances of memory errors.

In addition to the overall differences between the active and sham groups, there were unexpected differences in recall performance based on the gender of the participants, as shown in Figure 3. A 2x2x2 ANOVA (stimulation condition x participant gender x face stimulus gender) showed that there was a significant main effect of stimulation condition ($F(1,40) = 7.59$, $p < 0.01$) and a significant main effect of participant gender ($F(1,40) = 11.60$, $p < 0.01$). Post-hoc t-tests showed that the female participants recalled significantly more names than the male participants in both the sham ($t(1,10) = 1.83$, $p < 0.05$) and active conditions ($t(1,10) = 1.98$, $p < 0.04$). Interestingly, there were also gender differences in terms of which names participants recalled. Paired t-tests showed that male participants in the sham condition were significantly better at recalling male names than female names ($t(1,5) = -3.04$, $p < 0.02$). There was not a significant difference in the ability of the female participants in the sham group to recall male versus female names ($t(1,5) = 1.21$, $p = 0.14$). However, numerically speaking, the female participants in the sham condition recalled a higher percentage of female names than of male names, and the lack of statistical significance may be due to the small sample size. In the active stimulation condition, the numeric difference in recall performance for same-gender and opposite-gender names was much smaller for both male and female participants. There were no significant differences in recall of same-gender or opposite-gender names for either male ($t(1,5) = 0.97$) or female ($t(1,5) = 0.38$) participants.

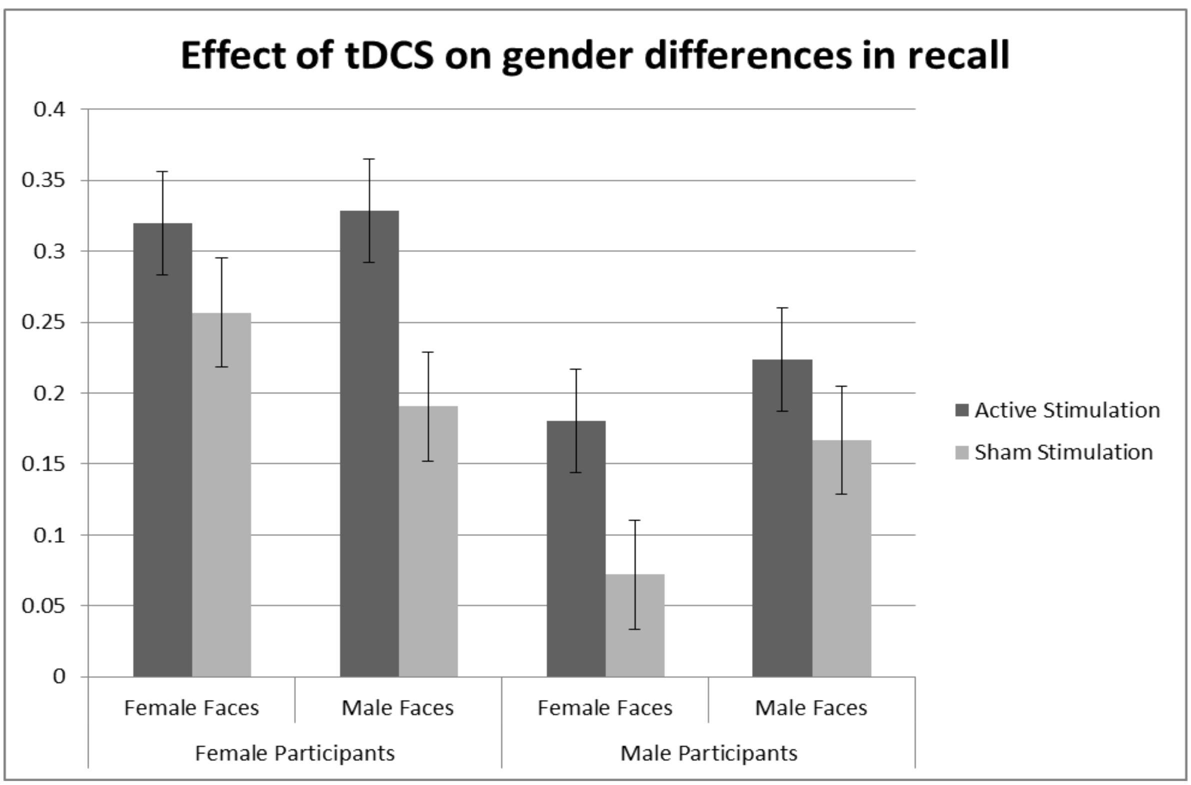

Figure 3. Gender Differences in Recall Performance

2.3. Discussion

The associative memory experiment showed that tDCS has a significant effect on recall performance, providing a particularly large benefit in cases where the task is most difficult. In addition, while improving recall performance, active tDCS did not increase the likelihood of memory errors. This indicates that it does not simply change a person's response threshold, increasing the likelihood of both correct and incorrect answers.

However, active tDCS did not improve recognition memory performance. It is unclear why there was a benefit to recall but not recognition. One possibility is that the stimulation was specifically activating neural circuits that are involved in recollection but not recognition memory. Another possibility is that performance on the recognition test was much higher overall, which could have obscured the effects of tDCS if participants were performing near ceiling even without active stimulation. The gender effects in the recall test results indicate that tDCS had the largest effect on the tasks that were most difficult for the participants. Recognition is far easier than recall in general, so perhaps the benefit from active stimulation was too small to be significant in the context of the participants' higher overall performance. In either case, it is clear that additional research in this area is warranted. These results suggest that tDCS could be used to test specific theories regarding memory encoding in the brain.

The substantial impact of tDCS on recall performance indicates that tDCS could be a very beneficial method for augmenting learning, particularly if it improves performance on the most difficult types of recollection. In Experiment 2, we sought to extend these findings to working memory in order to determine whether training effects augmented by tDCS can transfer to untrained tasks.

3. EXPERIMENT 2: EFFECTS OF TDCS ON WORKING MEMORY

Working memory (WM) refers to the system used for storage and manipulation of transitory information in the mind necessary for complex tasks such as learning, reasoning, and language comprehension (Becker & Morris, 1999). Working memory training refers to repeated completion of a working memory task (e.g., N-back) with the idea that improvement on the WM task will translate to improvement in other domains. For instance, some researchers (e.g., Klingberg, 2010; Sternberg, 2008) propose that computerized WM training is a promising way of increasing fluid aspects of intelligence (i.e., those aspects of intelligence that allow for adaptive reasoning and problem solving). Others (e.g., Conway & Getz, 2010; Morrison & Chein, 2011; Shipstead, Redick, & Engle, 2010) remain skeptical, concluding that WM training programs have limited efficacy regarding improvement of reasoning and intellect. This skepticism is in line with a long research history on cognitive training within psychological and educational science demonstrating that although task-specific performance commonly increases with training, transfer of this learning to other tasks or domains remains rare (Chase, & Ericsson, 1981; Ericsson & Delaney, 1998; Healy, Wohldmann, Sutton, & Bourne, 2006; Singley & Anderson, 1989).

Following a report by Jaeggi, Buschkuehl, Jonides, and Perrig (2008) in which the authors concluded that cognitive training utilizing an adaptive dual N-back task can improve fluid intelligence, commercial cognitive training programs (e.g., Brain Age, Brain Twister, CogMed, Jungle Memory, Lumosity, Mindsparke Brain Fitness Pro, Posit Science Brain Fitness, Posit, Science In Sight, WMPro) proliferated. However, the work by Jaeggi and colleagues has since failed to replicate (Chooi & Thompson, 2012) and a recent meta-analysis of WM training programs found no convincing evidence that WM training generalizes to other skills, including nonverbal and verbal ability, attention, word decoding, and arithmetic (Melby-Levag & Hulme, 2013). Rather, WM training programs typically produced short-term, specific training effects that do not generalize.

It is against this backdrop of WM training controversy that researchers have begun purportedly enhancing WM via tDCS (Andrews et al., 2011; Berryhill & Jones, 2012; Boggio et al., 2006; Fregni et al., 2005; Jo et al., 2009; Ohn et al., 2007; Zaehle et al., 2011). In light of the issues of task transfer in the WM training realm, it is critical to note that all of these studies used only an N-back task to assess working memory, a design which precludes investigation into task transfer and limits the conclusions that may drawn. In other words, claims that WM has been enhanced may be premature under such paradigms.

In Experiment 2, we sought to directly test transfer effects between different types of WM tasks and a fluid intelligence task. Participants completed a baseline session that included a verbal N-back task, a spatial N-back task, and an analogical reasoning test based on Raven's Progressive Matrices (Matzen et al., 2010). Then they trained on either a verbal or spatial N-back task while active or sham tDCS was applied to either the left or right dorsolateral prefrontal cortex (DLPFC; over electrode site F3 or F4, respectively, on the international 10-20 EEG system of electrode placement). Following the training session, the participants completed the baseline measures once again. The DLPFC has been used effectively as a target in tDCS investigations of WM (e.g., Andrews et al., 2011; Fregni et al., 2005) and is thought to play a crucial role in WM

(Curtis & D'Esposito, 2003). Additionally, there is thought to be hemispheric asymmetrical functioning of the DLPFC such that the left DLPFC is relatively more involved in verbal WM tasks, whereas the right DLPFC is relatively more involved in visuospatial WM tasks (Reuter-Lorenz et al., 2000; Smith & Jonides, 1998). This experimental design allowed us to test transfer of training effects and to evaluate the asymmetrical functioning hypothesis.

3.1. Methods

3.1.1. Participants

Thirty-six participants gave informed consent and participated in each working memory training task (verbal or spatial). The exclusion criteria were identical to those used in Experiment 1. No significant differences in age, gender, handedness [as measured by the Edinburgh handedness inventory (Oldfield, 1971)], or years of education were present between groups, as determined by individual independent-samples t-tests with $\alpha = 0.05$. A complete account of these participant demographics can be found in table 2.

Table 2 – Participant Demographics by Task and tDCS Group

		N	# Males	Age Mean ± SD	Education Mean ± SD	Handedness* Mean ± SD
Spatial WM Training	Left Frontal tDCS	12	6	18.75 ± 0.87	13.17 ± 0.52	76.78 ± 1.05
	Right Frontal tDCS	12	6	21.42 ± 5.33	14.04 ± 0.52	85.05 ± 1.29
	Sham tDCS	12	6	20.00 ± 2.09	13.63 ± 0.52	84.63 ± 1.64
	Total	36	18	20.06 ± 3.43	13.61 ± 0.51	82.15 ± 1.36
Verbal WM Training	Left Frontal tDCS	12	6	22.25 ± 5.76	13.54 ± 0.51	77.35 ± 1.27
	Right Frontal tDCS	12	6	18.92 ± 0.67	12.88 ± 0.52	68.41 ± 1.52
	Sham tDCS	12	6	21.50 ± 6.40	14.17 ± 0.52	70.31 ± 1.48
	Total	36	18	20.89 ± 5.08	13.53 ± 0.51	72.02 ± 1.44

*Handedness quotient: 100 = right hand dominant, -100 = left hand dominant, 0 = ambidextrous.

3.1.2. Materials

The experimental tasks consisted of a verbal N-back task, a spatial N-back task, and an analogical reasoning task based on the Raven's Progressive Matrices task (the Sandia Matrices, Matzen et al., 2010). In the verbal N-back paradigm, stimuli consist of a sequence of letters presented one at a time. Participants are tasked with evaluating each stimulus to determine whether it matches another stimulus that was presented previously in the sequence, with a certain lag, set by the value of "N". For example, when N=3 (a 3-back task) participants are asked to decide if each letter matches the one that was presented three letters previously. The present study used an N of 3 because prior studies have found ceiling effects for 1- and 2-back tasks, making the results difficult to interpret (Mulquiney, Hoy, Daskalakis, & Fitzgerald, 2011).

The verbal N-back task used in the present study had eight possible letters (B, F, H, K, M, Q, R, and X) that appeared in both upper and lower case. This ensured that participants had to verbalize the letters rather than performing a simple perceptual mapping between the shapes. The N-back task had six blocks containing 100 trials each. Within each block, 35 of the trials were targets (matching the letter presented three trials previously), 10 were N+1 lures (matching the letter presented four trials previously), 10 were N-1 lures (matching the letter presented two trials previously), and 45 were fillers that did not match any of the four previous trials. The lures were included to make the task more difficult. Each trial began with a fixation point that was presented for 500 ms. Then the letter appeared directly above the fixation point for 500 ms, followed by a blank screen presented for 1500 ms. Participants had two seconds to respond to each trial (the duration of the letter and the subsequent blank screen) by pressing keys marked "yes" or "no" on the keyboard.

The structure of the spatial N-back task was identical to that of the verbal N-back task. An array of eight box outlines (white on a black background) was presented around the fixation point, with two boxes above the fixation point, two below, two to the left, and two to the right. Participants saw the fixation point and the array of boxes for 500 ms, then one of the boxes turned white for 500 ms. Participants had to indicate whether or not the location of the white box was the same as it was three trials previously.

The Sandia Matrix test was based on the Raven's Progressive Matrices, which is a measure of fluid intelligence in which participants are asked to identify a missing element that completes a pattern (Raven, Raven, & Court, 1998). The Sandia Matrix test expands upon the Raven's test by using similar problem structures to generate a much larger set of matrix problems. These problems have been normed against the Raven's problems and are of equivalent difficulty (Matzen et al., 2010). Two sets of matrices were created, containing nine problems each. The matrices in the two sets had equivalent structures, making the two sets equally difficult. The order in which participants completed the two sets was counterbalanced across participants.

3.1.3. Procedure

Prior to tDCS, all participants completed a practice session in which they received instructions and practice for both N-back tasks. Then they completed a baseline memory test consisting of one block of the verbal WM task, one block of the spatial WM task, and one block of the matrix reasoning task. Following the baseline session, the tDCS electrodes were applied to either F3 or F4, using the same procedure described for Experiment 1. During stimulation, participants completed four blocks of the verbal or spatial WM task, depending on the experimental group to which they were assigned. Participants took short breaks between blocks and filled out sensation questionnaires. Following stimulation, all participants repeated the baseline tasks once again, but with different blocks of stimuli.

3.1.4. Data Analysis

Effects of tDCS on accuracy and reaction time measures were compared separately for each working memory training task (spatial and verbal) and for each stimulation target (left or right DLPFC) using split-plot multivariate analysis of covariance (MANCOVA). Baseline-subtracted difference scores (post-training minus pre-training) were first computed for each of the three cognitive tests used here to remove differences present prior to tDCS. Independent variables included tDCS condition (active and sham) and cognitive test (spatial working memory, verbal working memory, and matrix reasoning problems), factorially combined. Gender and handedness were included as covariates. Gender is a known factor in working memory experiments and correlations between gender and working memory training were found in the present experiment. Handedness is a known factor in cortical lateralization of working memory function and correlations between handedness and working memory training were also found. Follow-up univariate tests were used to further examine significant effects, as appropriate.

To assess the degree to which effects reported here were related to physical sensation associated with tDCS, mean sensation levels for each of the three measures collected (itching, heat, and tingling) and were compared between tDCS groups for each experiment, cognitive test, and stimulation target using multivariate ANOVA. Additionally, relationships between sensation and demographic variables were examined with Pearson correlation in an attempt to characterize parameters which lead to physical sensation of tDCS current. These variables included measures of head size (width, length, and circumference), gender, age, handedness, and the ratio of amount of sleep on the previous night to the amount of sleep on a normal night. Pearson correlation was performed separately for participants receiving active and sham tDCS.

Prior to inferential statistical analysis, the data were checked for outliers and assumptions of univariate analyses were tested. Two outliers existed due to lapse in performance for only one post-tDCS testing run, with accuracy values of 25% and 2%. These two data points were interpolated based on baseline performance and participant group. Strong correlation between baseline and post-tDCS scores was confirmed prior to interpolation ($r > 0.8$ in all cases). Data were additionally analyzed with and without these two participants, and no substantive differences were found in results of the two analyses. All variables tested met assumptions of normality (using The Shapiro–Wilk test, $p>0.01$) and multicolinearity, and pairwise linearity between groups was confirmed by visual assessment of scatterplots. All analyses were performed using IBM SPSS 21.

3.2. Results

3.2.1. Spatial Working Memory Training

No significant effects of tDCS or task were found for the participants who were trained on the spatial N-back task (p's > 0.1), indicating no effects of tDCS, and no difference in effects of spatial working memory training on performance across the three cognitive tests examined here. To investigate whether null effects of cognitive test were due to null effects of spatial working memory training, in general, or transfer of spatial working memory training to the other cognitive assessment types, one-sample t-tests were used to assess change from baseline in each of the three cognitive assessments, collapsing across tDCS groups (N=36). Interestingly, significant differences from zero were found only for difference scores pertaining to verbal working memory testing (mean ± SEM = 8.5% ± 8.5%; $t(35) = 6.02$, $p < 0.001$. No effects of tDCS, cognitive assessment type, or spatial working memory training were found for reaction time measures (p's > 0.1).

3.2.2. Verbal Working Memory Training

3.2.2.1. Effects of Left Frontal tDCS

A significant interaction was found between tDCS condition and cognitive assessment type [Wilks' Λ =0.72, $F(2,19) = 3.70$, $p < 0.05$, η^2=0.280] indicating significantly different effects of tDCS during verbal working memory training on each of the three cognitive tests (Figure 4). Further investigation of these effects revealed significant differences between active and sham tDCS groups only for the verbal working memory assessment type (Active = 7.8% ± 1.7%; Sham = 0.8% ± 1.7%; $F(1,20) = 8.81$, $p < 0.01$), and not spatial working memory or fluid intelligence (matrix problems), indicating enhancement of verbal working memory training with tDCS, which did not transfer to other assessment types. No effects of tDCS, cognitive assessment type, or spatial working memory training were found for reaction time measures (p's > 0.1).

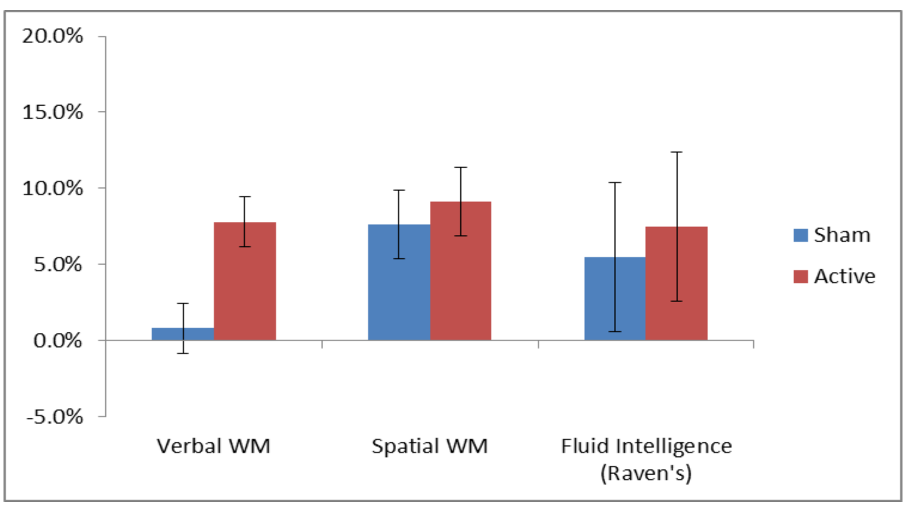

Figure 4 - Effects of left frontal tDCS on verbal working memory training and task transfer. Difference scores for active (red) and sham (blue) left frontal tDCS groups are shown, for each of the three cognitive tests. Significant effects of tDCS were found only for the assessment type which was trained (verbal working memory). Error bars denote SEM.

3.2.1.2. Effects of Right Frontal tDCS

A significant main effect of tDCS condition was found [$F(1,20) = 4.64$, $p < 0.05$, $\eta^2=0.168$] indicating similar effects of tDCS during verbal working memory training for each of the three cognitive tests (Figure 5).

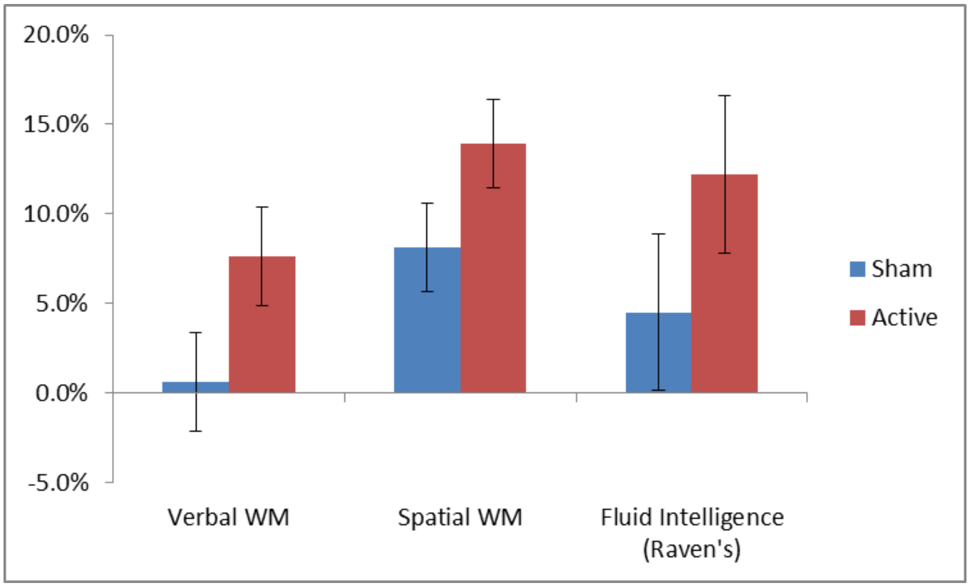

Figure 5 – Effects of right frontal tDCS on verbal working memory training and task transfer. Difference scores for active (red) and sham (blue) right frontal tDCS groups are shown, for each of the three cognitive tests. Significant effects of tDCS were found only for the assessment type which was trained (verbal working memory). Error bars denote SEM.

3.2.1.3. Physical Sensation associated with tDCS

Physical sensations did not differ significantly between tDCS groups (p's > 0.05). Interestingly, sensation during active tDCS was not correlated with any of the measures examined; however, sensation during sham tDCS was significantly correlated with handedness and head size measures. These correlation statistics can be found in table X.

Table 3 – Pearson correlation statistics comparing tDCS sensation and participant demographics for sham tDCS participants

	Itching	Heat	Tingling
Itching	1	.144	.546**
Heat	.144	1	.634**
Tingling	.546**	.634**	1
Handedness	-.612**	-.226	-.681**
Sleep Ratio	-.003	-.133	-.281
Extraversion	-.244	-.005	-.192
Head Width	-.582**	-.329	-.425*
Head Length	-.401	-.410*	-.519**

Head Circumference	-.527**	-.307	-.539**
Gender	-.390	-.185	-.315

*$p < 0.05$ ** $p < 0.01$

3.3. Discussion

The results of Experiment 2 indicate that, under certain conditions, tDCS can improve working memory and that improvement can transfer to untrained tasks. In particular, tDCS applied to the right DLPFC while participants practiced a verbal WM task enhanced verbal and spatial WM performance, in addition to improving performance on a test of fluid intelligence. These findings address one of the key unknowns in the existing literature on enhancing cognitive function with tDCS. They suggest that specific combinations of training task and stimulation location can indeed enhance underlying cognitive processing in a way that benefits multiple tasks, enabling transfer to untrained tasks. It is likely that other researchers investigating the effects of tDCS on WM have not found task transfer because they did not test multiple tasks and multiple stimulation locations. The design of the present study allowed us to identify combinations that did produce task transfer.

This finding has profound implications for training applications of tDCS. If tDCS can be used to improve general cognitive abilities, such as working memory capacity and fluid intelligence, it could have a dramatic impact on the speed at which people are able to learn new information or skills, or on their overall cognitive performance for tasks that place a high burden on working memory or adaptive reasoning. Additional research in this area, particularly research focused on real-world training domains, will be needed in the future to understand the best applications and methods for tDCS augmentation.

Taken together, the two experiments in this project provide strong support for the idea that tDCS can improve cognitive performance in healthy individuals. While much of the research to date has focused on clinical applications of tDCS, it is clear that this technology can also improve memory performance for people without brain injuries or other illnesses that could impact cognitive abilities. This has potential applications in numerous national security domains. Most national security problems involve an element of human performance and human decision making, leaving open the possibility for human error. There are also many domains in which people must learn complex skills or how to use extremely complex tools, whether those tools are hardware, software, or systems. Our research, combined with other ongoing research in this area, indicates that tDCS has the potential to improve human cognitive performance and to help people learn information faster and remember it better. That can impact any number of real-world applications through improving human performance.

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