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The strategy and motivational influences on the beneficial effect of neurostimulation: a tDCS and fNIRS study

Kevin T. Jones[a,b], **Filiz Gözenman**[a], and **Marian E. Berryhill**[a]

[a]Department of Psychology, Program in Cognitive and Brain Sciences, University of Nevada, Reno, 1664 North Virginia Street, Nevada, USA, 89557

[b]Department of Neurology, Center for Aphasia Research and Rehabilitation, Georgetown University Medical Center, 4000 Reservoir Road NW, Washington D.C., USA, 20057

Abstract

Working memory (WM) capacity falls along a spectrum with some people demonstrating higher and others lower WM capacity. Efforts to improve WM include applying transcranial direct current stimulation (tDCS), in which small amounts of current modulate the activity of underlying neurons and enhance cognitive function. However, not everyone benefits equally from a given tDCS protocol. Recent findings revealed tDCS-related WM benefits for individuals with higher working memory (WM) capacity. Here, we test two hypotheses regarding those with low WM capacity to see if they too would benefit under more optimal conditions. We tested whether supplying a WM strategy (Experiment 1) or providing greater extrinsic motivation through incentives (Experiment 2) would restore tDCS benefit to the low WM capacity group. We also employed functional near infrared spectroscopy to monitor tDCS-induced changes in neural activity. Experiment 1 demonstrated that supplying a WM strategy improved the high WM capacity participants' accuracy and the amount of oxygenated blood levels following anodal tDCS, but it did not restore tDCS-linked WM benefits to the low WM capacity group. Experiment 2 demonstrated that financial motivation enhanced performance in both low and high WM capacity groups, especially after anodal tDCS. Here, only the low WM capacity participants showed a generalized increase in oxygenated blood flow across both low and high motivation conditions. These results indicate that ensuring that participants' incentives are high may expand cognitive benefits associated with tDCS. This finding is relevant for translational work using tDCS in clinical populations, in which motivation can be a concern.

Address correspondence to: Kevin T. Jones, 4000 Reservoir Road NW, Building D, Suite 207, Washington, DC 20057, Tel: 202-687-2721, Fax: 202-687-7378, ktj9@georgetown.edu.

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Keywords

transcranial direct current stimulation; functional near infrared spectroscopy; working memory; working memory capacity

1.1. Introduction

The ability to hold and manipulate items in our conscious awareness is called working memory (WM). This ability is crucial for almost every cognitive task, yet WM is capacity limited to ~4 items (Cowan, 2001). This central role for WM in cognition has prompted serious efforts to expand WM capacity through training (recently reviewed in (Chein & Morrison, 2010; Harrison et al., 2013). One emerging way researchers are investigating WM and WM improvement is by applying transcranial direct current stimulation (tDCS) (Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Berryhill & Jones, 2012; Berryhill, Wencil, Branch Coslett, & Olson, 2010; Boggio et al., 2006; Fregni et al., 2005; Hoy et al., 2013; Jo et al., 2009; Jones & Berryhill, 2012; Lally, Nord, Walsh, & Roiser, 2013; Marshall, Molle, Siebner, & Born, 2005; Mulquiney, Hoy, Daskalakis, & Fitzgerald, 2011; Mylius et al., 2012; Oliveira et al., 2013; Saunders et al., 2014; Teo, Hoy, Daskalakis, & Fitzgerald, 2011).

TDCS involves the application of small amounts of electric current through scalp electrodes to modulate the excitability of underlying neural populations (Nitsche & Paulus, 2000, 2001; Stagg & Nitsche, 2011). This technique is appealing because it is well tolerated, safe, and more affordable than other techniques (Bikson, Datta, & Elwassif, 2009; Nitsche et al., 2003). However, several observations suggest that a single tDCS protocol does not work equally well in all individuals. For example, we paired anodal tDCS to the left or right PFC in healthy older adults performing a WM task, but found that only the more educated participants benefited from tDCS (Berryhill & Jones, 2012). Secondly, in young adults, we applied tDCS to the right PPC during verbal and visual WM tasks and found that only participants with high WM capacity showed improved performance after tDCS (either anodal or cathodal) (Jones & Berryhill, 2012). Other groups have begun to note heterogeneity in tDCS outcomes, particularly in the cognitive domain compared to the motor domain (Jacobson, Koslowsky, & Lavidor, 2012).

The question thus emerges as to why group differences predict tDCS benefits. One possibility is anatomical, such that different participants' brains are morphologically different and only the electrodes precisely positioned elicit the desired tDCS-linked cognitive benefit (Kim et al., 2014). However, this important factor is unlikely to explain the kinds of group differences we described because there would need to be something systematically and collectively different about participants' brains on a between-groups level. An alternative hypothesis is that our previous work tapped into differences in the way participants approached WM tasks along two domains: WM strategy and motivation.

There is reason to suspect differential WM strategy use in high and low WM capacity participants. There is considerable work demonstrating that WM strategy use differs across individuals with different WM capacities (Bailey, Dunlosky, & Kane, 2008; Baldwin &

Reagan, 2009; Cokely, Kelley, & Gilchrist, 2006; Imbo & Vandierendonck, 2007; Unsworth & Spillers, 2010). This difference in the innate strategy use may be due to the low WM capacity individuals being more susceptible to distraction (Unsworth, 2007), and/or having fewer attentional resources (Conway & Engle, 1996; Kane, Bleckley, Conway, & Engle, 2001; Unsworth & Spillers, 2010). In contrast, high WM capacity participants adopt more efficent strategies (Schelble, Therriault, & Miller, 2012). For example, in a category fluency task, the more effective classification strategy was more likely to be used by high WM capacity individuals (Schelble et al., 2012). This finding is further supported by research demonstrating that while under high cognitive load, high WM capacity participants' performance will suffer more than low WM capacity participants (Cokely et al., 2006; Conway & Engle, 1996). This is due to less of a reliance on more complex, active strategy use in low WM capacity individuals. One promising observation in the above findings is that when provided instruction regarding strategy use, performance was rescued in low WM capacity participants. This suggests that low WM capacity participants fail to *spontaneously* apply an effective WM strategy. If true, then providing specific strategy-related instructions might expand tDCS-linked WM benefits to low WM capacity participants.

Alternatively, low WM capacity participants may simply be less motivated. Not surprisingly, high motivation enhances performance (Brose, Schmiedek, Lovden, & Lindenberger, 2012; Krawczyk & D'Esposito, 2013; Roets, Van Hiel, & Kruglanski, 2013; Sanada, Ikeda, Kimura, & Hasegawa, 2013; Unsworth & McMillan, 2013). Neuroimaging data demonstrate differential processing when participants are extrinsically motivated through financial incentives. For instance, high reward WM trials significantly improved behavioral performance and modulated late-trial components of the event-related potential (ERP) (Sanada et al., 2013). Furthermore, extrinsic motivation differentially activates regions in the PFC and visual association regions (Krawczyk & D'Esposito, 2013). In addition, the burgeoning neuroeconomics literature reliably reports differential processing in the ventromedial PFC that appears to track the current motivational significance (Kringelbach & Rolls, 2004). However, others find that financial motivations alone cannot expand WM capacity (Zhang & Luck, 2011). In other words, we suspect that an inattentive, disengaged participant is less likely to benefit from tDCS due to either low intrinsic or extrinsic motivation. The possibility remains, though, that increasing motivation will extend tDCS-linked WM benefits to a greater number of participants.

An additional concern receiving growing attention is the fact that the mechanism of tDCS in functional changes remains unclear. One way to measure cortical changes in activity is through functional Near-Infrared Spectroscopy (fNIRS). FNIRS, like fMRI, provides a proxy measure of neural activity by assessing hemodynamic changes by measuring differential absorption of near-infrared light by oxygenated and deoxygenated hemoglobin. FNIRS has been used in a number of studies of cognitive performance and attention (e.g. (Cutini et al., 2008; Fallgatter & Strik, 1997; Herrmann, Ehlis, & Fallgatter, 2003; Honma, Soshi, Kim, & Kuriyama, 2010; Horovitz & Gore, 2004; Kubota et al., 2006; Leon-Carrion et al., 2006; Schroeter, Zysset, Kupka, Kruggel, & Cramon, 2002; Tian, Sharma, Kozel, & Liu, 2009); reviewed in: (Ehlis, Schneider, Dresler, & Fallgatter, 2014; Homae, 2014; Obrig, 2014; Shalinsky, Kovelman, Berens, & Petitto, 2009). Importantly, one recent study found

that fNIRS recordings from the PFC found a positive linear relationship between the hemodynamic response and cognitive load during n-back WM tasks (Fishburn, Norr, Medvedev, & Vaidya, 2014). Thus, there is precedence for using fNIRS to study PFC activity during WM tasks.

There is some evidence to suggest that fNIRS can be paired with tDCS. Three studies measured neural changes using fNIRS after tDCS. First, fNIRS detected temporary increases in oxygenated hemoglobin (HbO) induced by anodal tDCS to the PFC (Merzagora et al., 2010). Secondly, two studies used fNIRS to measure changes in motor cortex activity following tDCS to primary motor cortex (Khan et al., 2013; Muthalib, Kan, Nosaka, & Perrey, 2013). The results showed modulation in the rate of motor movements and increased HbO levels at the stimulation site (Khan et al., 2013). These findings confirm the feasibility of combining fNIRS with tDCS and extending them into cognitive tasks to gain insight regarding underlying neural changes.

The following experiments address two questions with the goal of expanding tDCS benefits to a larger proportion of participants. First, can instruction in WM strategy extend tDCS-linked WM benefits to low WM capacity participants? Second, can increasing motivation extend tDCS linked WM benefits in low WM capacity participants? We hypothesized that in both cases participant groups who previously did not benefit from tDCS will show a significant tDCS-linked improvement in WM performance. We also predicted that fNIRS over the stimulated left PFC would reveal increases in activity changes corresponding to behavioral benefits afforded by tDCS.

2.1. Experiment 1: The Role of Strategy Use in the tDCS Benefit

Here, we provided participants with an explicit active verbal rehearsal strategy during some WM trial blocks. We predicted that this would improve the performance of low WM capacity participants, but not have a significant effect on the high WM capacity group. We also predicted that when strategies were used, we would see more similar PFC activity between the low and the high WM capacity groups. We targeted the left PFC for tDCS due to previous tDCS and fNIRS research showing successful application of both techniques to modulate and measure WM performance.

2.2. Experiment 1 Methods

24 neurotypical right-handed University of Nevada students (mean age: 23.83, standard deviation (SD): 3.67, 12 females) participated for $15/hour. Participants reported no history of neurological or psychiatric symptoms or head injuries and no use of neuroleptic, hypnotic, or anti-seizure medications. All procedures were conducted in accordance with the University of Nevada Institutional Review Board and participants signed informed consent documents.

2.2.1. Transcranial Direct Current Stimulation

Stimulation consisted of a single continuous direct current delivered by a battery-driven stimulator (Eldith MagStim, GmbH, Ilmenau, Germany). There were 2 counterbalanced

sessions on different days where participants received only 1 type of stimulation: anodal tDCS (active) and sham (control). Anodal tDCS (1.5 mA, 10 minutes) was delivered through two 5 x 7 cm^2 electrodes housed in saline-soaked sponges. Sham stimulation included 20 seconds of ramping up and down stimulation at the beginning and end of to give the participant a physical sense of stimulation associated with current change (Gandiga, Hummel, & Cohen, 2006). In both conditions, the anode was placed over the left PFC directly between F3 and F7 (International 10–20 EEG system) and the reference electrode (cathode) was placed on the contralateral cheek; see Figure 1c (Berryhill & Jones, 2012; Berryhill et al., 2010; Elmer, Burkard, Renz, Meyer, & Jancke, 2009; Hsu et al., 2011; Jones & Berryhill, 2012; Marshall et al., 2005; Tanoue, Jones, Peterson, & Berryhill, 2012; Tseng et al., 2012; Zaehle, Sandmann, Thorne, Jancke, & Herrmann, 2011). After stimulation, the electrodes were removed and the fNIRS setup began. All sessions included a washout period of at least 24 hours.

2.2.2. Functional Near-Infrared Spectroscopy

Neurovascular recordings used a continuous wave fNIRS system (TechEn CW6 fNIRS System, Milford, MA), measuring two wavelengths (690, 830 nm), sampling at 50 Hz. There was a single emitting source surrounded by 3 detectors placed 2.6 cm apart from each other and from the emitter to measure the stimulated region of the PFC. The detectors and emitter were attached to a custom-made headband so that the configuration was constant between all participants; see Figure 1b. The emitter on the headband was placed intermediately between F7 and F3 (International 10–20 system) to measure the stimulated region targeting the left PFC (Friederici, Hahne, & von Cramon, 1998; Kang, Kim, Sohn, Cohen, & Paik, 2011; W. J. Kim, Min, Yang, & Paik, 2014; Okamoto et al., 2004). To ensure consistent placement of the headband between sessions, a photograph was taken of the head with the emitter and detector areas marked on the scalp (Figure 1a). During fNIRS set up, channels were screened to ensure that all showed a clear respiratory pattern at 690 and 830 nm. Signals were clear enough that we were able to see the respiratory pattern and cardiac pulsation. Set up was timed and took less than 5 minutes to ensure the effects of tDCS did not dissipate. If there were no concern as to the dissipating effects of tDCS, we would have employed a broader fNIRS setup in order to measure the right PFC and parietal regions.

2.3. Behavioral Tasks

2.3.1. The Automated Operation Span (OSpan)

To get an independent baseline measure of WM capacity, we conducted the computerized OSPAN task (Unsworth, Heitz, Schrock, & Engle, 2005). Before the first session (Figure 1), participants completed the OSpan; a task of divided attention in which participants must solve true/false arithmetic problems while simultaneously encoding and maintaining a letter sequence. Participants recall the letters after completing the arithmetic problems. The task lasted ~5 minutes. We measured performance by letter recall and math accuracy (scores range from 0 to 22). The OSPAN data were used to complete a median split to determine high and low WM capacity groups.

2.3.2. WM Change Blindness Task

Next, during the first session the participant completed a preliminary WM task. Participants viewed four novel geometric stimuli (different sets/session, 3° visual angle, 1000 ms) followed by a blank delay period (5000 ms). Next, a single probe item appeared and participants made a speeded old/new recognition key press response (2000 ms). After each block of 3 trials there was a 15 second pause to allow for the BOLD response to return to baseline. Participants completed 8 blocks of 3 trials, lasting ~6 minutes. At the end of the preliminary task participants were asked to type a brief description of the WM strategy they employed and to judge their motivation (1–5, 5 being high). After the preliminary task, the fNIRS headband was removed from the participants' heads and tDCS was applied to the same location.

Following tDCS, the fNIRS headband was reapplied in the same location. We marked the locations on the scalp and took a photograph during the preliminary task to ensure exact fNIRS placement on later tasks. Participants then completed the WM task again, however they were given explicit strategy instructions. For active strategy blocks, participants were instructed to employ an active, verbal rehearsal strategy (internal) that required naming and rehearsal of the geometric stimuli during the delay period. During the passive blocks, participants were instructed to passively view the stimuli, and to refrain from internal verbal rehearsal. Participants completed active and passive WM task performance blocks, 15 each. Each block of trials lasted exactly 25 seconds followed by a 15 second rest period. At the end of the session, participants were asked to rate their adherence to the given strategy condition (1–5, 5 being high) as well as their motivation during the task (1–5, 5 being high).

2.4. Experiment 1 Analysis

For each participant, we calculated WM performance using normalized difference scores for each session (anodal, sham) and strategy (active, passive) as follows: [(session accuracy − preliminary accuracy)/(session accuracy + preliminary accuracy)]. High and low WM capacity groups were determined by a median split on the OSpan scores (paired t-test between each group's OSpan score: high WM capacity group mean (M): 19.90 (SD: 1.52), low WM capacity group M: 13.4 (SD: 3.50), $t_{11} = 5.38$, $p < .001$).

To examine the changes in cortical activity in the PFC we focused on the mean oxygenation value (HbO) per condition where the greatest response changes were evident. We calculated the average HbO level change from the resting state for the final 20 seconds of each 25-second block per channel. The first five seconds were removed to account for the rise of the hemodynamic response from resting levels. The changes in oxygenation from the preliminary task were obtained from the raw optical density signals using the modified Beer–Lambert law (Chance et al., 1998) and analyzed using HomER2 software (Huppert, Diamond, Franceschini, & Boas, 2009). The raw fNIRS data were low pass filtered (0.5 Hz cut-off) to eliminate high frequency noise due to physiologically irrelevant data (such as respiration, cardiac cycle and heart pulsation effects) and equipment noise. For each channel, we calculated normalized HbO difference scores for each session (anodal, sham), and strategy (active, passive) as follows: [(session HbO level − preliminary HbO level)/

(session HbO level + preliminary HbO level)]. The means per each condition were subjected to statistical analysis.

2.5. Experiment 1 Results

2.5.1. Behavioral Effects

First, we compared baseline behavioral performance between the high and low WM capacity groups on the change blindness WM task and found a non-significant trend (low WM M: .64 (SD: .09), high WM M: .69 (SD: .09), $t_{11} = 1.39$, $p = .19$). One likely explanation for the trend rather than a significant between-groups difference is that this task is not as challenging for participants compared to the OSpan task. Next, we were interested in testing whether use of a beneficial WM strategy could provide a tDCS-linked WM benefit to low WM capacity participants. Thus, we subjected the normalized difference scores to a 2 session (anodal, sham tDCS) x 2 strategy condition (active, passive) repeated-measures ANOVA with the between group factor of WM capacity (high, low). There was no significant main effect of tDCS session ($F_{1, 22} = 1.00$, $p = .33$, partial $\eta^2 = .04$). However, there was a main effect of strategy condition ($F_{1, 22} = 8.40$, $p < .01$, partial $\eta^2 = .28$) such that an active WM strategy improved WM performance for both the high and low WM groups. There was also a main effect of WM capacity ($F_{1, 22} = 4.43$, $p = .04$, partial $\eta^2 = .17$), such that the high WM capacity group had greater improvements in accuracy as compared to baseline. The interaction between strategy x WM capacity reached borderline significance ($F_{1, 22} = 3.24$, $p = .08$, partial $\eta^2 = .13$). Importantly, the 3-way interaction between tDCS session x strategy x WM capacity was significant ($F_{1, 22} = 8.12$, $p < .01$, partial $\eta^2 = .27$). This complex interaction can be understood as follows: the high WM capacity participants benefited from the anodal tDCS *and* the active rehearsal strategy (raw accuracy data: anodal *active* strategy M: .81 (SD: .07), anodal *passive* strategy M: .70 (SD: .09), sham *active* strategy M: .76 (SD: .07), sham *passive* strategy M: .71 (SD: .07)) whereas the low WM capacity group showed little benefit of either tDCS or strategy (anodal *active* strategy M: .69 (SD: .11), anodal *passive* strategy M: .69 (SD: .06), sham *active* strategy M: .70 (SD: .11), sham *passive* strategy M: .66 (SD: .07)); see Figure 2. No other interaction reached significance (all p's > .72).

To better understand these data we next determined whether there were significant between-group differences in *self-reported* intrinsic motivation or adherence to the instructed strategy. The low WM capacity group reported higher levels of motivation during the preliminary task (high WM M: 4.00 (SD: .42), low WM M: 4.58 (SD: .52); $t_{11} = 3.02$, $p = .01$), furthermore the low WM capacity group also reported higher levels of motivation after anodal tDCS (high WM M: 4.25 (SD: .62), low WM M: 4.41 (SD: .90), $t_{11} = .52$, $p = .62$), and there was no difference following sham stimulation (high WM M: 4.33 (SD: .65), low WM M: 4.33 (SD: .78), $t_{11} < .01$, $p = 1.00$). Next, we compared the reported motivation level following each session (during anodal, sham tDCS) with the between group factor of WM capacity. There was no main effect of tDCS ($F_{1, 22} < .01$, $p = 1.00$, partial $\eta^2 < .01$) and no interaction of tDCS and WM capacity ($F_{1, 22} = .19$, $p = .67$, partial $\eta^2 = .01$).

The high WM capacity group reported slightly higher levels of adherence to the given strategy instructions following anodal stimulation (high WM M: 4.33 (SD: .49), low WM

M: 4.16 (SD: .83), $t_{11} = .62$, $p = .55$), but not during sham stimulation (high WM M: 4.25 (SD: .45), low WM M: 4.25 (SD: .87), $t_{11} < .01$, $p = 1.00$). Next, we conducted the same analysis as above, for participants' self-reported adherence to strategy. There was no main effect of tDCS ($F_{1, 22} < .01$, $p = 1.00$, partial $\eta^2 < .01$) and no interaction of tDCS and WM capacity ($F_{1, 22} = .63$, $p = .44$, partial $\eta^2 = .03$). Thus, the interaction could not be attributed to differences in motivation or adherence to WM strategy. There was no significant difference in reported WM strategy use, as 6 low WM capacity and 4 high WM capacity participants reported using an active strategy in the preliminary WM task. This prediction was based on previous research showing that high WM capacity participants spontaneously employed more effective strategies (Bailey et al., 2008; Baldwin & Reagan, 2009; Cokely et al., 2006; Imbo & Vandierendonck, 2007; Unsworth & Spillers, 2010).

2.5.2. fNIRS

Despite instructions to remain still during the task, one low WM capacity participant was excluded due to excessive motion artifact in the fNIRS data. We used the HomER2 software for removing motion artifact. If the signal increased more than 50 standard deviations within a window of 500 ms, then this period, and the following 1000 ms is defined as motion artifact. Those time windows were excluded from the analyses. We were interested in assessing how tDCS altered the BOLD signal in the left PFC. Furthermore; we were interested in understanding group differences in the fNIRS difference scores between tDCS and strategy conditions. To answer these questions, we conducted a 2 session (anodal, sham) x 2 strategy condition (active, passive) x 3 channel repeated-measures ANOVA with the between group factor of WM capacity for the normalized HbO difference scores for only the final 20 seconds of data in each block. There was a significant main effect of tDCS ($F_{1, 21} = 4.45$, $p = .04$, partial $\eta^2 = .18$), such that anodal tDCS led to a significant increase in HbO levels. The main effects of fNIRS channel ($F_{2, 42} = 2.52$, $p = .09$, partial $\eta^2 = .11$), strategy ($F_{1, 21} = 1.70$, $p = .20$, partial $\eta^2 = .08$), and WM capacity ($F_{1, 21} = 0.21$, $p = .65$, partial $\eta^2 = .01$) failed to reach significance. The interaction of strategy and fNIRS channel was significant ($F_{2, 42} = 3.05$, $p = .05$, partial $\eta^2 = .13$), such that greater strategy-related HbO increases were apparent at channels 1 and 3 compared to channel 2. The interaction of tDCS condition and strategy neared significance ($F_{1, 21} = 3.21$, $p = .08$, partial $\eta^2 = .13$), as did the interaction of tDCS and fNIRS channel ($F_{2, 42} = 2.63$, $p = .08$, partial $\eta^2 = .11$). Of greatest importance, the three-way interaction of tDCS, strategy, and fNIRS channel was significant ($F_{2, 42} = 3.24$, $p = .05$, partial $\eta^2 = .13$; Figure 3), such that the greatest increase in HbO was apparent following anodal tDCS and active strategy use, especially at channels 1 and 3. No other interactions reached significance (all p's > .36).

2.6. Experiment 1 Discussion

We were interested in extending tDCS-linked WM benefits to low WM capacity participants by supplying a beneficial WM strategy. However, the low WM capacity participants received no benefit of anodal tDCS to the PFC and showed no modulation in HbO. In contrast, the high WM capacity group unexpectedly showed improvement from the reminder to use an active WM strategy. These behavioral results extended our previous finding that low WM capacity participants do not benefit from anodal tDCS to parietal cortex (Jones &

Berryhill, 2012). In conclusion, group differences in spontaneous use of WM strategy did not provide a strong explanation for why low WM capacity participants do not benefit as much as high WM capacity participants from tDCS. Furthermore, supplying a WM strategy did not provide the low WM capacity group with tDCS-linked WM benefits.

3.1. Experiment 2: Motivational Factors in the Beneficial Effect of tDCS

We next investigated how extrinsic motivation modulates tDCS-linked WM performance and neurovascular patterns at the stimulated left PFC site. If the low WM capacity group were less engaged by the task, we predicted that increasing extrinsic motivation with financial incentives should restore the tDCS-linked WM benefit. If not, then we should see no tDCS-linked WM benefit in the low WM capacity group. We also predict that high motivation should lead to greater PFC activity, as measured by a greater level of HbO levels than low motivation conditions. If low response to extrinsic motivation is responsible for previous null tDCS findings in low WM capacity participants, we expect to see increases in HbO levels during high motivation/anodal tDCS conditions across groups.

3.2. Experiment 2 Methods

20 new neurotypical right-handed University of Nevada students (mean age: 21.95, SD: 3.28, 12 females) participated. Participants reported no history of neurological or psychiatric symptoms or head injuries and no use of neuroleptic, hypnotic, or seizure medications. All procedures were conducted in accordance with the University of Nevada Institutional Review Board and participants signed informed consent documents.

The experiment followed the methods described in Experiment 1 with the following modifications. First, the blocks varied by extrinsic motivational value rather than strategy instruction. Similar to Experiment 1, participants completed 15 blocks of 3 trials with low ($.01/correct response) and high ($.25/correct response) financial incentive in a counterbalanced order. Before each block of trials, participants were instructed on the screen as to whether the block rewarded $.25 or $.01 per correct trial. Second, participants received performance feedback after each trial. Participants were not penalized for incorrect answers. At the end of the experiment, participants were asked to report their level of intrinsic motivation and what WM strategy they employed (1–5 as in Experiment 1). Trial blocks were extended an additional 3 seconds (28 seconds) due to feedback after each response, which included monetary gain values per trial.

3.3. Experiment 2 Analysis

High and low WM capacity groups were determined by a median split on the performance on the OSpan (paired t-test between each group's OSpan score: high WM capacity group M: 19.90 (SD: 1.60), low WM capacity group M: 12.30 (SD: 4.89), $t_9 = 4.72$, $p < .01$). As in Experiment 1, for each participant, we calculated normalized difference scores for each session (anodal, sham) and strategy (active, passive) as follows: [(session accuracy − preliminary accuracy)/(session accuracy + preliminary accuracy)]. The fNIRS data were normalized and analyzed as described above.

3.4. Experiment 2 Results

3.4.1. Behavioral Effects

First, we compared baseline performance between the high and low WM capacity groups on the preliminary task. There was a non-significant between-groups difference in accuracy ((high WM M: .67 (SD: .13), low WM M: .61 (SD: .10)), $t_9 = 1.52$, $p = .16$). Again, we suspect that this is because this task is easier than the OSpan task used to form the low and high WM capacity groups. Experiment 2 tested whether increasing motivation might reveal tDCS-linked WM benefits in low WM capacity participants. Therefore, we subjected the normalized difference scores to a 2 session (anodal, sham) x 2 motivation condition (high, low) repeated-measures ANOVA with the between group factor of WM capacity (high, low). There were no significant main effects of tDCS session ($F_{1, 18} = 1.73$, $p = .21$, partial $\eta^2 = .09$), motivation condition ($F_{1, 18} = 3.12$, $p = .09$, partial $\eta^2 = .15$), or WM capacity ($F_{1, 18} = 0.20$, $p = .66$, partial $\eta^2 = .01$). However, the interaction between tDCS condition and motivation reached significance ($F_{1, 18} = 4.81$, $p = .04$, partial $\eta^2 = .21$), such that all participants performed best after anodal tDCS and under high extrinsic motivation (Figure 4). Although the high WM capacity group showed a numerically stronger benefit (raw accuracy data: anodal *high* motivation M: .81 (SD: .08), anodal *low* motivation M: .76 (SD: . 09), sham *high* motivation M: .76 (SD: .06), sham *low* motivation M: .76 (SD: .07)) than the low WM capacity group (raw accuracy data: anodal *high* motivation M: .68 (SD: .12), anodal *low* motivation M: .66 (SD: .10), sham *high* motivation M: .66 (SD: .11), sham *low* motivation M: .66 (SD: .13)), the three-way interaction of tDCS condition x motivation level x WM capacity group did not reach significance ($F_{1, 18} = .02$, $p = .89$, partial $\eta^2 < .01$). No other interaction approached significance (all p's > .66).

The high WM capacity group provided numerically higher self-report ratings of intrinsic motivation during the preliminary task (high WM M: 4.50 (SD: .52), low WM M: 4.22 (SD: .67); $t_9 = 1.15$, $p = .28$). Next, to determine whether tDCS or WM capacity had any effect on self-reports of intrinsic motivation we conducted an ANOVA comparing self-reported motivation for each tDCS session (anodal, sham) with the between group factor of WM capacity. There was no main effect of tDCS ($F_{1, 18} = .24$, $p = .63$, partial $\eta^2 = .01$). However there was an interaction of tDCS and WM capacity group ($F_{1, 18} = 6.08$, $p = .02$, partial $\eta^2 = .25$), such that the low WM capacity participants' self-reports regarding intrinsic motivation were higher following the sham tDCS (high WM M: 4.50 (SD: .71), low WM M: 4.66 (SD: .50)) whereas the high WM capacity participants reported a higher level of intrinsic motivation following anodal tDCS (high WM M: 4.70 (SD: .48), low WM M: 4.33 (SD: .71)).

3.4.2. Functional Near-Infrared Spectroscopy Results

To assess changes in cortical activity, we subjected the normalized HbO mean amplitudes to a 2 session (anodal, sham) x 2 motivation condition (high, low) x 3 channel repeated-measures ANOVA with the between group factor of WM capacity (high, low). There was a main effect of WM capacity ($F_{1, 18} = 4.80$, $p = .04$, partial $\eta^2 = .21$), such that the low WM capacity participants had a greater increase in HbO following anodal tDCS across all channels as compared to the high WW capacity participants. There was a borderline

significant main effect of tDCS ($F_{1, 18} = 3.37$, p = .08, partial $\eta^2 = .16$), but no main effect of motivation condition ($F_{1, 18} = 2.70$, p = .11, partial $\eta^2 = .13$), or fNIRS channel ($F_{2, 36} = 0.11$, p = .90, partial $\eta^2 = .01$). However, the 4-way interaction of tDCS (anodal, sham) x motivation (high, low) x fNIRS channel x WM capacity (high, low) was significant ($F_{2, 36} = 3.66$, p = .03, partial $\eta^2 = .17$), such that the low WM capacity group showed sustained elevated blood flow across all conditions and channels (Figure 5). The high WM capacity group showed little change, but there was a pattern of decreased HbO under high motivation in the sham condition. No other interactions reached significance (all p's > .20).

3.5. Experiment 2 Discussion

The extrinsic motivation manipulation improved WM performance for both the low and high WM capacity groups. Importantly, there appeared to be a 'double-boost' benefit of anodal tDCS and high motivation as performance was best in this condition. Furthermore, the behavioral improvement observed in the low WM capacity group matched that of the high WM capacity participants.

The fNIRS data added nuance to these data. These data demonstrated that the low WM capacity group showed a significant and consistent increase from the preliminary session in HbO levels across all tDCS and motivation conditions. The PFC activity appeared to be sensitive to the presence of externally provided motivation, regardless of the magnitude of incentive. The data for the high WM capacity participants revealed no modulation of HbO at any channel for any condition. The high WM capacity group did not show much of a change in HbO as a function of this external motivation manipulation, speculatively because they had slightly higher intrinsic motivation during this task. More importantly, these data provide evidence that low WM capacity participants can improve WM performance after anodal tDCS to the PFC, given certain conditions are in place.

4.1. General Discussion

TDCS shows promise in enhancing, remediating and stabilizing cognition in healthy, clinical and aging populations. However, we previously found that tDCS-linked WM protocols did not benefit everyone, and unfortunately, those with the greatest to gain (e.g. low WM capacity) showed no WM improvement (Jones & Berryhill, 2012). Here, we tested whether two manipulations involving WM strategy and financial motivation could promote tDCS-related WM benefits in low WM capacity participants. Experiment 1 revealed that supplying a beneficial verbal rehearsal WM strategy provided an added performance benefit to the high WM capacity participants, but it did not help the low WM capacity participants. Furthermore, changes in cortical blood flow before and after tDCS followed a similar pattern. Only the high WM capacity participants showed an increase in HbO levels following anodal tDCS, regardless of strategy condition. Experiment 2 showed that providing increased incentive sufficiently raised performance across WM capacity groups. All participants improved following tDCS regardless of financial incentive or stimulation type. Both the high and low WM capacity groups improved in the high motivation condition following anodal tDCS. The fNIRS data showed that the high WM capacity participants showed little to no change from the preliminary task following tDCS regardless of

motivation condition, despite the behavioral improvements. However, the low WM capacity participants showed a significant increase in HbO levels following tDCS. In short: increasing external motivation restored tDCS-related WM benefits to the low WM capacity group.

An intriguing experimental finding from the present research is the generalized impact financial incentive had on low WM capacity participants. We observed a global improvement that was apparent in behavior and increased HbO levels in the low WM capacity participants. The high WM capacity participants had a slightly higher level of motivation during the preliminary task. However, self-reported levels of motivation did not significantly differ between WM capacity groups during the preliminary session. Thus, we return to the conclusion that explicitly providing per-trial external incentives extended tDCS benefits to the low WM capacity group in a general fashion. We suspect that they responded more strongly to the extrinsic motivation manipulation and that it heightened their arousal throughout the experiment. There are data confirming that high arousal/incentive increases PFC activity (Chib, Rangel, Shimojo, & O'Doherty, 2009; H. Kim, Shimojo, & O'Doherty, 2011; Lim, O'Doherty, & Rangel, 2011; McClure, Laibson, Loewenstein, & Cohen, 2004; O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001). Furthermore, TMS to the left, but not right PFC increased preference for immediate rewards rather than delayed rewards (Figner et al., 2010). These findings may suggest differences in how the PFC responds to monetary rewards based on WM capacity limits between participants. Certainly, future work is needed to assess whether these effects are durable, what the optimal and minimal motivation tool could be, and whether longitudinal training could facilitate internally produced motivation levels in the low WM capacity group.

4.2. The Mechanism of tDCS Benefits

One open question is the mechanism responsible for differential WM benefits following tDCS. One possibility is that groups defined by behavioral performance tap into underlying differences in receptor subtypes that are more or less responsive to electrical stimulation via tDCS. More likely, we expect that tDCS is not a 'one-size fits all' technique. In other words, the optimal tDCS protocol for a particular person is likely to depend on both physiology and other factors, including attention, alertness, interest (motivation), affect, etc. This is a considerably more positive interpretation than indicating that some people are contraindicated from tDCS. Our previous finding demonstrated that greater task difficulty predicted tDCS-related WM benefits in the high WM capacity participants (Jones & Berryhill, 2012). This raises a concern regarding WM task difficulty. In this case, neither group approached ceiling (performance across groups 66–81%). Thus, we are confident that this WM task was sufficiently challenging to elicit tDCS-related WM benefits. However, certainly, a staircase approach would ensure that task difficulty was titrated to match each participant's abilities. The current data demonstrate that refining the tDCS technique to incorporate, even crudely, some of these other factors will provide tDCS-linked cognitive benefits to a wider pool.

It is also important to note that included in this broad set of relevant factors is the tDCS current flow itself. Current modeling techniques show that current flows below the PFC

sites, but it also reaches orbitofrontal and ventral temporal regions (Brunoni et al., 2014; Truong, Magerowski, Blackburn, Bikson, & Alonso-Alonso, 2013). Orbitofrontal regions contribute to motivational engagement and performance (Arana et al., 2003; Klein-Flugge, Barron, Brodersen, Dolan, & Behrens, 2013; Szatkowska, Bogorodzki, Wolak, Marchewka, & Szeszkowski, 2008; Tobler, O'Doherty, Dolan, & Schultz, 2007). However, if anodal tDCS is indirectly, through PFC connections, affecting subcortical regions involved in WM and reward, such as the basal ganglia, then this may explain some of the behavioral effects we find in our current and previous tDCS experiments. The strong connections between the PFC and the basal ganglia as seen in animal (Maurice, Deniau, Glowinski, & Thierry, 1998, 1999; Middleton & Strick, 2002) and human studies (Voytek & Knight, 2010) may be responsible for activation in these deeper regions of cortex following PFC stimulation. In addition to this, fMRI research has demonstrated that the basal ganglia modulates connectivity between frontal regions as well as asserts control on attentional resources (van Schouwenburg, den Ouden, & Cools, 2010). Furthermore, the basal ganglia are known to have strong modulatory interactions in the cortex due to dopamine (Foerde & Shohamy, 2011; Shohamy, Myers, Kalanithi, & Gluck, 2008), a neurotransmitter that also is implicated in the effectiveness of tDCS through an inverted u-shaped function of the amount of dopamine available (Boggio et al., 2006; Nitsche & Paulus, 2000). Lastly, the basal ganglia are associated with reward processing (Frank, Loughry, & O'Reilly, 2001; Sesack & Grace, 2010; Tanaka et al., 2004; Vitay & Hamker, 2014), which further accentuates the possibility of anodal tDCS impacting WM tasks that have monetary rewards. In summary, we would argue that a full understanding of the relevant physiological, neurological and emotional factors at play would ultimately succeed at extending tDCS-linked cognitive benefits to all participants for all tasks and all stimulation sites. Future work pairing fMRI with tDCS and current modeling will be helpful in elucidating these distal effects.

4.3. Limitations

This article reflects our initial application of fNIRS and we employed a simple montage to record activity. In spite of the few numbers of channels, we are encouraged that the pairing of tDCS with fNIRS can begin to address mechanistic changes both at the tDCS sites and more broadly throughout the cortex. FNIRS has the advantage of being appropriate for use in all ages and conditions, unlike fMRI. With the expanding use of tDCS in special populations this becomes a greater selling point for pairing tDCS with fNIRS. Future work in our lab will use broader fNIRS montages that will allow us to record from more cortical areas, including bilateral recordings. This expansion is dependent on streamlining set-up time to maximize recording coverage without missing the effects of tDCS.

Secondly, we found no distinction between the high and low monetary incentives in Experiment 2. One possibility is that any amount of extrinsic motivation would have succeeded at enhancing arousal and improving performance throughout the session. In other words, potentially simple feedback would restore benefits to the low WM capacity group. Alternatively, the two incentive values may not have been sufficiently different in magnitude to expose differences due to high and low extrinsic motivation. However, previous research has observed enhanced PFC and visual association cortex activity in the presence of an imaginary point system (no monetary reward) as compared to non-incentive

trials (Krawczyk, Gazzaley, & D'Esposito, 2007). In essence, a much larger differential in value might be necessary to identify results associated with high and low extrinsic motivation.

4.4. Conclusion

We tested whether WM strategy or motivation could restore a benefit of tDCS to low WM capacity participants. The present data showed that raising incentives could indeed, provide a tDCS benefit to the low WM capacity participants of equal magnitude as that garnered by the high WM capacity group. Thus, tDCS applicability is likely to be able to improve cognitive performance broadly – but the setting and circumstances deserve careful attention to avoid null findings (e.g. (Jacobson et al., 2012). For example, some people (e.g. those with low WM capacity) may need more stimulation for longer periods of time to achieve the same benefits. Extensive research is now needed to predict the ideal tDCS parameters and experimental demands for eliciting tDCS-linked cognitive improvement in healthy and clinical populations.

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Highlights

- We investigate individual differences previously found in tDCS studies.
- We test whether strategy or motivation can restore benefits from tDCS in those with low WM capacity.
- We also collected fNIRS data to monitor tDCS-induced changes in cortical activity.
- Strategy had no impact on low WM capacity participants, but motivation did improve performance.
- Only the low WM capacity participants showed an increase in neural activity across motivation conditions.

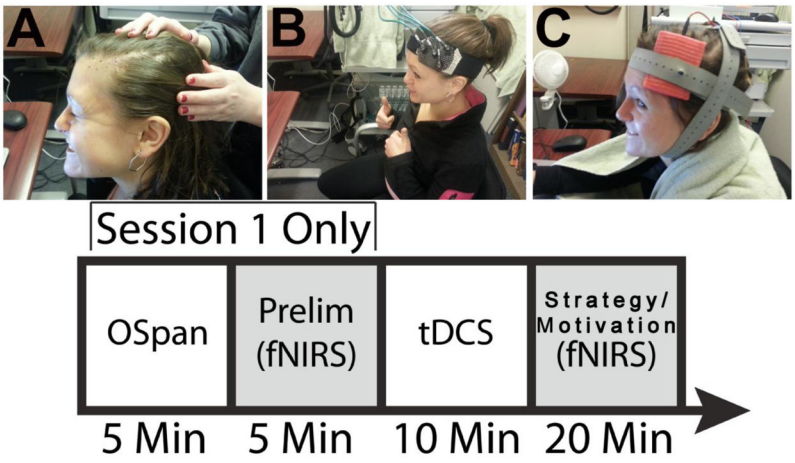

Figure 1. Applying Functional Near-Infrared Spectroscopy and Transcranial Direct Current Stimulation

Top: A) The participant had their head marked to correspond with the fNIRS headband. Next the participants' hair was parted to ensure good scalp contact. B) The fNIRS headband was strapped to the participant and the signal was checked at 690 and 830 nm to ensure good signal. C) The fNIRS headband was removed and the participant receives 10 minutes of tDCS to the same location.

Bottom: The sequence order of the tasks in Experiment 1. First, during the first session only the participant completed the OSpan task. Next, the participant has their head marked for the location of the emitter and detectors (Figure 1 A) and the fNIRS system is placed on the head. Once a good signal was obtained, the participant completed the preliminary WM recognition task, again, only during the first session. In both sessions, the tDCS electrodes were applied for 10 minutes of active or sham stimulation. Next, the tDCS electrodes were removed and the fNIRS montage was reapplied to the marked location. The participant then completed the WM task.

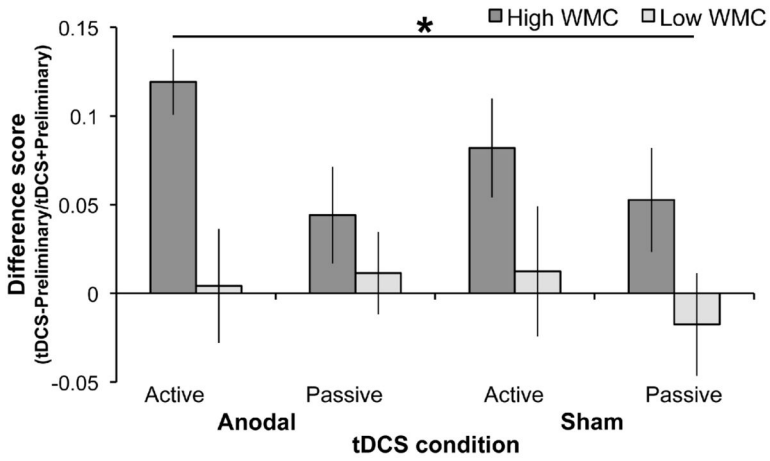

Figure 2. The Accuracy Difference Scores in Experiment 1

Bars represent the accuracy difference score from preliminary task for each condition. The terms ‘active’ and ‘passive’ refer to the different strategy conditions. The active strategy did not change performance in the low WM capacity participants. Anodal tDCS benefited the high WM capacity group more during anodal tDCS than during sham tDCS.

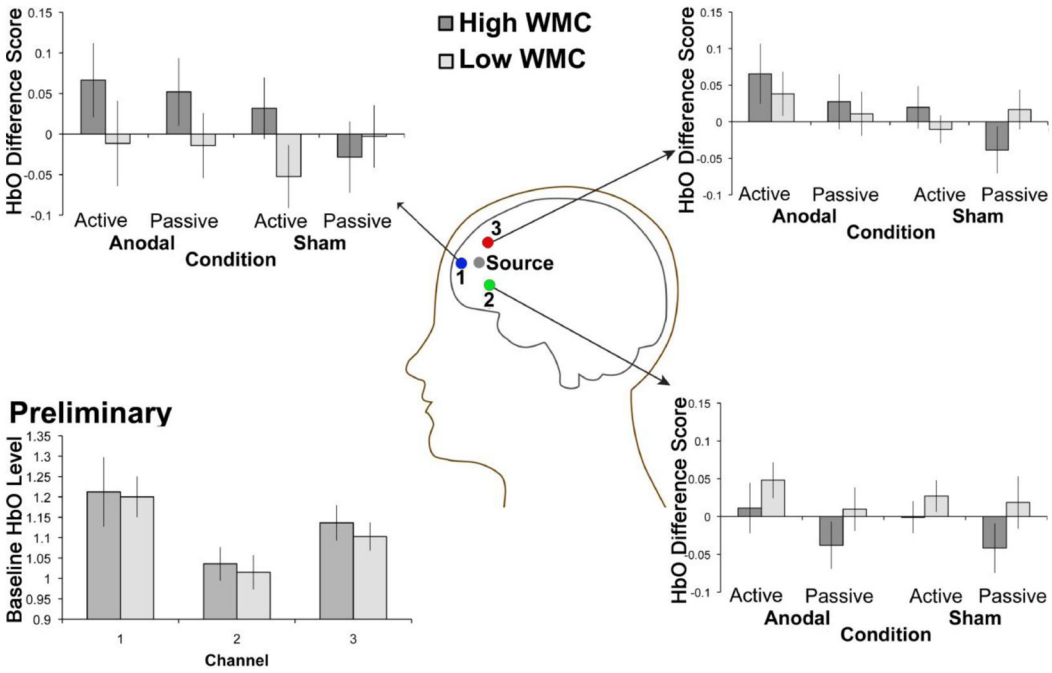

Figure 3. The Functional Near-Infrared Spectroscopy Difference Scores in Experiment 1

The normalized HbO difference scores derived from the preliminary task and each of the tDCS and strategy conditions for the high and low WM capacity groups at channels 1–3. At channel 1, the high WM capacity group showed an increase in HbO levels as compared to the preliminary task during both active conditions. The low WM capacity participants showed more subtle changes in HbO levels. Bottom Left. The raw HbO levels during the preliminary task. Both the high and low WM capacity group had similar baseline levels of oxygenated blood during the preliminary task prior to both tDCS and strategy instructions. The values plotted in the preliminary bar graph in represent the activation at each of the 3 channels. Positive values represent an increase as compared to the preliminary task.

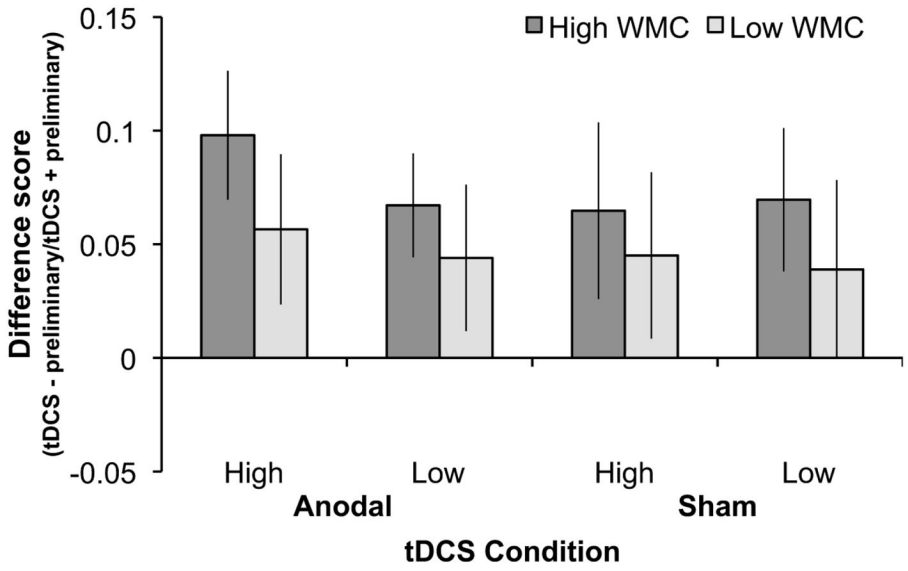

Figure 4. The Accuracy Difference Scores in Experiment 2

The normalized difference scores from preliminary task for each tDCS and motivation condition for high and low WM capacity groups' accuracy. Both WM capacity groups showed improved performance across all conditions. The high WM capacity group had the greatest increase in performance in the anodal tDCS and high motivation session, however this improvement was no significantly different from the low WM capacity group. High = high motivation condition, Low = low motivation condition.

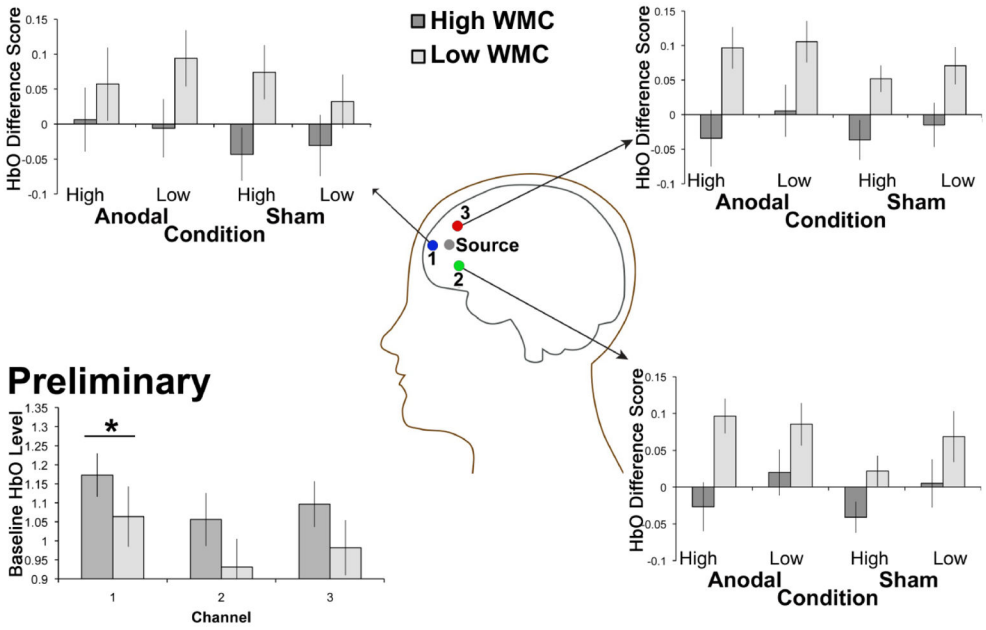

Figure 5. The Functional Near-Infrared Spectroscopy Difference Scores in Experiment 2

The difference scores for HbO levels between the preliminary task and each of the tDCS and motivation conditions for the high and low WM capacity groups at channel 1, 2, and 3. Across all channels, the high WM capacity group showed little to no change in HbO levels from preliminary across both tDCS and motivation conditions. The low WM capacity group showed in increase across both tDCS and motivation conditions at each of the three channels. Bottom Left) The raw HbO levels during the preliminary task. The high and low WM capacity group had significantly different HbO levels at channel 1 during the preliminary task ($t_9 = 2.23$, $p = .05$, $r^2 = .36$), however not at channels 2 ($p = .20$) and 3 ($p = .17$). The values plotted in the preliminary bar graph in represent the activation at each of the 3 channels. Positive values represent an increase as compared to the preliminary task.