Measuring Placebo Effects of Transcranial Direct Current Stimulation (tDCS) on Motor Learning

by

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A Thesis Presented in Partial Fulfillment
of the Requirements for the Degree
Master of Science

Approved July 2022 by the
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ARIZONA STATE UNIVERSITY

August 2022

ABSTRACT

Studies using transcranial direct current stimulation (tDCS) to enhance motor training are often irreproducible. This may be partly due to differences in stimulation parameters across studies, but it is also plausible that uncontrolled placebo effects may interact with the true 'treatment' effect of tDCS. Thus, the purpose of this study was to test whether there was a placebo effect of tDCS on motor training and to identify possible mechanisms of such an effect. Fifty-one participants (age: 22.2 ± 4.16; 26 F) were randomly assigned to one of three groups: active anodal tDCS (n=18), sham tDCS (n=18), or no stimulation control (n=15). Participant expectations about how much tDCS could enhance motor function and their general suggestibility were assessed. Participants then completed 30 trials of functional upper extremity motor training with or without online tDCS. Stimulation (20-min, 2mA) was applied to the right primary motor cortex (C4) in a double-blind, sham-controlled fashion, while the control group was unblinded and not exposed to any stimulation. Following motor training, expectations about how much tDCS could enhance motor function were assessed again for participants in the sham and active tDCS groups only. Results showed no effect of active tDCS on motor training (p=.67). However, there was a significant placebo effect, such that the collapsed sham and active tDCS groups improved more during motor training than the control group (p=.02). This placebo effect was significantly influenced by post-training expectations about tDCS (p=.0004). Thus, this exploratory study showed that there is a measurable placebo effect of tDCS on motor training, likely driven by participants' perceptions of whether they received stimulation. Future studies should consider placebo effects of tDCS and identify their underlying mechanisms in order to leverage them in clinical care.

ACKNOWLEDGMENTS

1. As a student of ASU, I acknowledge that the Tempe campus sits on the ancestral homelands of those American Indian tribes that have inhabited this place for centuries, including the Akimel O'odham (Pima) and Pee Posh (Maricopa) peoples.

2. I would like to express my immense gratitude to my advisor for the opportunity to work on my research project and for their guidance and support throughout my journey toward becoming a scientist. I would also like to sincerely thank my committee members for helping me develop my research and for providing valuable guidance and encouragement throughout my studies.

3. Finally, I would like to thank my loved ones for their unwavering support and limitless inspiration. When I was not strong enough to believe in myself, you did. Thank you to every single one of you, especially to my mom, sister, and partner.

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CHAPTER 1

INTRODUCTION

Placebo effects are the psychophysiological responses to perceived medical treatments, regardless of whether the treatment was active or inactive (Colloca, 2018; Evers et al., 2018). There are many intrinsic and extrinsic factors that are involved in placebo effects, including expectations, classical conditioning, social learning, affected neural pathways, perceptions, personality traits, genetics, experiences, and contextual factors (Friesen, 2019; Colloca & Barksy, 2020; Haas et al., 2022). It has been suggested that one of the strongest components of placebo effects is people's expectations (Anderson & Stebbins, 2020; Rabipour et al., 2019). Thus, if people expect that the treatment will be effective, they will likely experience a larger placebo effect. This may be why placebo and expectancy effects are susceptible to positive and negative priming (Rabipour et al., 2018), memory cues (Weik et al., 2022), and verbal suggestion (Villa-Sánchez et al., 2021; Frisaldi et al., 2021). Similarly, people's overall suggestibility (likely a trait) can predict the magnitude of placebo effects (Kotov et al., 2004; Parsons et al., 2021; Horing et al., 2014).

To be more specific, people with higher expectations of a treatment may have larger placebo effects. Benedetti (2013) regarded placebo effects as a valuable and untapped source of neuroscientific discovery. Unfortunately, the majority of placebo effect research has revolved around pain pharmacology (Meissner et al., 2011; Weimer et al., 2020;), leaving a large gap in research on placebo effects of neurostimulation in general and for enhancing motor learning specifically.

A valuable, inexpensive, and easy-to-use non-invasive brain stimulation technique is transcranial direct current stimulation (tDCS) (Utz et al., 2012). tDCS can be used to safely modulate cerebral excitability of the motor system (Nitsche & Paulus, 2000; Thair et al., 2017; Woods et al., 2016; Muller et al., 2021), affecting motor function and learning. This stimulation is widely viewed as a potential tool to enhance motor rehabilitation due to its ability to induce

neuroplasticity within the motor system (Gandiga et al., 2006; Reis and Fritsch, 2011). Furthermore, there is evidence that tDCS can reinforce brain networks activated by the expectation of benefiting from treatment, thus fortifying the placebo effect (Schambra et al., 2014; DosSantos et al., 2012). Even though tDCS is emerging as a treatment to enhance motor performance and learning, there are virtually no studies of its placebo effects and whether expectations about tDCS are critical for enhancing motor performance/learning. Only one study has tested for expectation-dependent placebo effects of tDCS on motor training (Rabipour et al., 2019) but failed to show significant effects due to the selected motor task (serial reaction time test) being too simple and having a ceiling effect (i.e., there was no room for improvement due to placebo effects). New data from our laboratory showed a significant placebo effect of tDCS on cognitive training (manuscript in preparation). For that study, stimulation was applied to the right posterior parietal cortex during 20 minutes of cognitive training. This study aimed to address the knowledge gap regarding expectation-dependent placebo effects (i.e., tDCS expectancy effects) on motor learning.

Exploring the potential impact of placebo effects of tDCS on motor learning is critical to the field. A large percentage of published tDCS studies on motor learning report null findings, whereby no significant effect of active tDCS is found. For example, according to PubMed, in 2020 alone, there were 38 studies investigating the effects of anodal tDCS on motor learning, with 16 (42%) reporting negative or inconclusive findings. We argue that a potential explanation for null findings is that participants' expectations about the efficacy of tDCS have been largely unaccounted for in previous tDCS research (Wang et al., 2021). To test this hypothesis, this study aimed to 1) determine whether there is a significant placebo effect of tDCS on motor learning and 2) test whether the placebo effect is due to participants' expectations about tDCS (i.e., an expectancy effect).

In this study, participants were randomly assigned to either sham tDCS (fake), active tDCS (real), or control (no-tDCS) groups. They completed a Short Suggestibility Survey (SSS)

prior to tDCS, which was a modified Multidimensional Iowa Suggestibility Scale (Kotov et al., 2004). Participants completed a brief expectancy questionnaire before and after receiving tDCS stimulation (active and sham). This questionnaire was adapted from the Credibility and Expectancy Questionnaire (CEQ) (Devilly & Borkovec, 2000) and has been used and validated (Rabipour et al., 2019). The study used an upper extremity motor task training paradigm that has been used previously to simulate activities of daily living (ADL) (Hooyman et al., 2021; Schaefer et al., 2020; Schaefer & Lang, 2012). Active or sham tDCS was applied during motor training. In addition, this study had a control group who wore the device (to control for scalp tactile sensation and pressure) but were told and shown that the device was not connected. Identifying a significant placebo effect of tDCS would provide exciting new avenues for patient healthcare or complementary methods to improve current medicine centered around patient mindset.

CHAPTER 2

MATERIALS AND METHODS

PARTICIPANTS

This study recruited fifty-one right-handed participants over the age of 18 (mean age: 22.2 ± 4.16; 26 F) that were randomly assigned to one of three groups: control, active tDCS, and sham tDCS. Right-handedness was determined using a modified Edinburgh Handedness Inventory (Oldfield, 1971; Veale, 2014). There were 18 participants in the sham and active tDCS groups each and 15 participants in the control group. To uphold all safety measures, all participants completed a Covid-19 pre-screening; additionally, all participants randomly assigned to either the active or sham tDCS groups also passed a tDCS safety screening to participate (described below). The protocol was as follows: Pre-Study Screenings, Pre-Training surveys, and Motor Training (with or without tDCS). The active and sham tDCS groups also completed an additional Post-Training Survey. The protocol used is summarized in Figure 1. To safeguard against experimenter errors during the motor task (e.g., incorrect explanation, failure to note a participant error, etc.) and/or during the tDCS (e.g., incorrect electrode placement, etc.), all research assistants were trained extensively and followed a uniform script for data collection

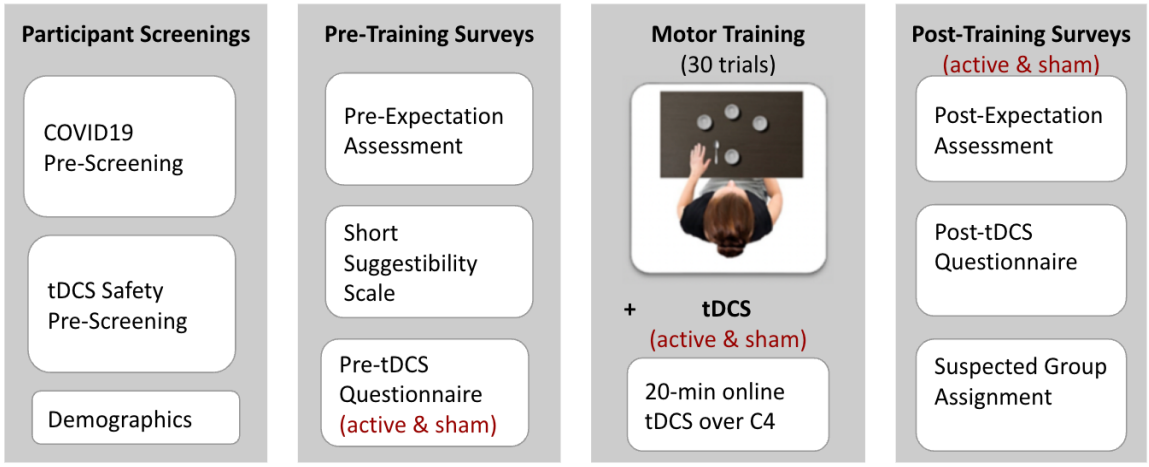

Figure 1. Experiment Protocol

accordingly. We also note that for the sake of the thesis, more variables were collected than what

was reported and analyzed for testing our aims. Exploratory analyses of these additional variables will be discussed outside of the scope of my formal thesis presentation.

PROTOCOL

Participant screenings.

Covid-19 pre-screening. The purpose of this was to screen for any signs/symptoms of or exposures to COVID19. The test includes taking their temperature and asking questions about new symptoms in the past 48 hours, close contact with anyone diagnosed with COVID19, recent travel, and a recent diagnosis of COVID19. If a participant did not pass this pre-screening, they were not invited into the lab space and rescheduled for another date.

tDCS pre-screening. The purpose of this was to screen for factors that disqualify a participant for tDCS stimulation. The screening entailed 11 questions asking about medical history (e.g., seizure, head injury, migraines, psychological/neurological condition, metal in the head, implanted devices, skin conditions, head wound that has not healed completely, adverse reaction to brain stimulation, possibility of pregnancy, and prescription medicines). If participants did not pass the screening, they were not eligible for either the sham or active tDCS groups.

Demographics. Demographic information (race, biological sex, gender, age) was collected from participants. Recent work has shown that racial differences do exist within placebo effects such that white participants are more likely to experience placebo effects, especially involving conditioning and expectancy effect (Okusogu et al., 2020). These measures are not included in our primary analysis (see 2.3.2) but may potentially be explored in future analysis.

Pre-training surveys.

Measuring participants' expectations about the efficacy of tDCS for improving motor function. Because expectations about a given treatment are one of the strongest sources of placebo effects in general (Anderson & Stebbins, 2020; Rabipour et al., 2019), we aimed to quantify participants' expectations about the effect of tDCS on motor function here by assessing

them on the Expectation Assessment Scale prior to the tDCS treatment. To do so, participants were asked, “Do you think tDCS can improve your motor performance on the study task? (i.e., Do you think it will work?)”. Participants responded using a Likert scale of 0 to 8, with 0 indicating “No not at all” and 8 indicating “Yes very much.” This was the primary measure of participants’ tDCS pre-expectations. We also asked participants to respond with the same Likert Scale to the question: “In general, would you like to improve your motor performance?”. These two questions were adapted from the Credibility and Expectancy Questionnaire (CEQ) and previous tDCS research investigating participants’ expectations of tDCS (Rabipour et al., 2019; Devilly & Borkovec, 2000) (See Appendix A). For the pre-training survey only, we also asked participants about their prior experience with tDCS (i.e., “Have you heard of transcranial direct current stimulation before (before you signed up for this study)?” and “Have you previously participated in any tDCS studies before?”). Participants answered these questions with either a “yes” or a “no” (see Appendix B). Answering “yes” to either of these questions was scored as the participant having prior experience with tDCS.

Measuring participants’ suggestibility. Given the extent of media coverage on the benefits of tDCS for improving motor function in addition to multiple research papers suggesting general suggestibility may predict placebo effects (Kotov et al., 2004; Parsons et al., 2021; Horing et al., 2014; Ray et al., 2019). To quantify participants’ suggestibility overall, we used the Short Suggestibility Scale (SSS), which has been validated previously (Kotov et al., 2004). The SSS included 21 statements related to how likely a person is to accept suggestion (e.g., “I am easily influenced by others’ opinions”; “Imagining a refreshing drink can make me thirsty”; “It is important for me to fit in”). The questionnaire asked the participant to indicate to what extent each statement applies. It was scored on a Likert scale of 1 to 5, where 1 indicated “Not at all or very slightly” and 5 indicated “A lot” (see Appendix C). This measure was not included in our primary analysis.

Pre-tDCS questionnaire. Participants completed a pre-tDCS questionnaire that asked 14 questions about possible medical symptoms prior to the tDCS stimulation (e.g., headaches, neck pain, back pain, blurred vision, scalp irritation, tingling, itching, increased heart rate, burning sensation, hot flush, dizziness, acute mood change, fatigue, and anxiety) and to what severity. The questionnaire was scored on a Likert scale of 1 to 10, where 1 indicated absent and 10 indicated most severe (see Appendix F). If the participant scored above 5 on any symptom before tDCS, they were not eligible for participating on that day and were re-scheduled for at least 48 hours later. Likewise, if they scored above 5 after tDCS, they were instructed to remain in the lab until symptoms subsided or until the participant and researcher were both satisfied for them to leave. However, they were clearly notified that if their symptoms persisted for more than 24 hours, then the researcher should be contacted, and an adverse event would be reported to the ASU IRB. This questionnaire has been validated and used in previous tDCS research (Thair et al., 2017; Brunoni et al., 2011). The purpose of this was to confirm that the participant was not experiencing any symptoms that could potentially be worsened because of tDCS stimulation and to provide a baseline to compare to the post-tDCS questionnaire to monitor for any potential adverse side effects from undergoing tDCS stimulation (or perception of undergoing stimulation) (described below).

Motor training and tDCS.

Following the initial questionnaires, participants completed a single session of motor training. This motor training involved the repetitive practice of a functional upper-extremity task which involved functional tool use and center-out reaching. This simulated feeding task paradigm has been validated against other center-out reaching tasks (Schaefer & Hengge, 2016) and is associated with activities of daily living (Schaefer et al., 2020). Importantly, it was also used to study motor learning in various populations, including young adults (Schaefer and Lang, 2012). The task involved the use of a tool (plastic spoon, 5.21g) to move items (raw pinto beans) between a “home” plastic cup (9.5cm diameter, 5.8cm height) and 3 identical cups placed radially at +40˚, 0˚, and -40˚ relative to the home cup at a distance of 16cm each (Figure 2). All cups were adhered to a thin board (60.5 cm x 40.0 cm).

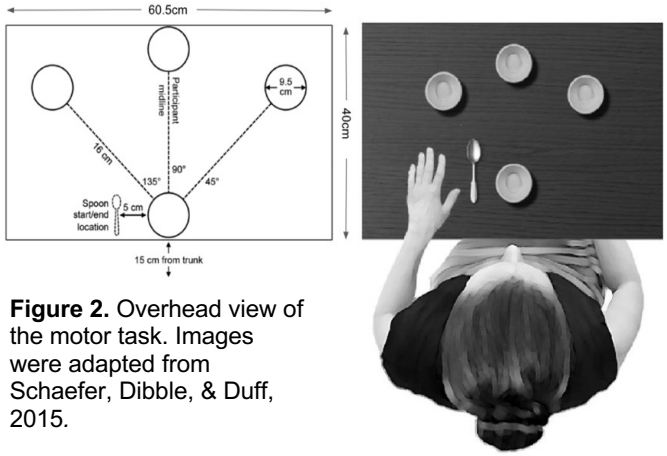

Figure 2. Overhead view of the motor task. Images were adapted from Schaefer, Dibble, & Duff, 2015.

Participants were required to use their non-dominant hand to allow for improvement with practice and avoid ceiling effects; as the MRL lab has shown that prior to practice, the non-dominant hand is significantly slower than the dominant hand (Schaefer, 2015). At the start of each trial, the plastic “home” cup was centered in front of the participant and contained 30 beans. Participants were given a standard-sized plastic spoon and instructed to use it to move 2 beans at a time from the home cup to one of three radial cups, starting with the leftmost cup at 40˚, then return to the home cup to pick up 2 more beans with the spoon and transport them to the middle cup, then the rightmost cup. They continued this sequence (left, middle, right) until the home cup

was empty. As such, each trial had 15 repetitions. For this study, motor training consisted of 30 total trials. This dose of motor training was chosen to prevent over-learning of the task and (theoretically) allow room for additional improvements due to placebo and tDCS effects (Kantak & Winstein, 2012). Our primary dependent variable was trial time (i.e., the total time to complete each trial). Each trial began when the participant picked up the spoon and ended when the last two beans were dropped into the final cup; thus, faster (lower) trial times indicated better performance.

Participants were randomly assigned to one of three groups using a random number generator. Participants in the control group underwent motor training only and had the tDCS electrodes applied without the electrodes plugged into the tDCS device. They were informed that they were assigned to the control group and shown that the electrodes were not plugged in, eliminating the possibility of active stimulation. This was done so that we could differentiate any tDCS effect from any placebo effect that occurred in the absence of any active stimulation. The two remaining groups received (either sham or active) online tDCS during motor training. The target area for stimulation was the right primary motor cortex (right M1), contralateral to the non-dominant hand. Thus, the active electrode (anode) was placed over the C4 location, according to the International Federation of Clinical Neurophysiology's 10-20 electrode system (Klem et al., 1999); the return electrode (cathode) was placed on the contralateral supraorbital area (left forehead). Previous research has demonstrated an effect of online stimulation of the right primary motor cortex (right M1) on learning complex upper-extremity motor tasks like the one used here (Hummel et al., 2005).

A 1X1 tDCS machine (Soterix Medical Inc) was used in this study. The tDCS stimulation parameters for the active tDCS group include a 30 second onramp (0mA to 2mA), 19 minute stimulation at 2mA, and a 30 second offramp (2mA to 0mA) (total stimulation = 20 minutes). This has been further illustrated in Figure 3. tDCS stimulation parameters for the sham tDCS group included a 30-second onramp (0mA to 2mA), followed by 30 seconds to go back down to 0mA from 2mA, and ended with 19 minutes of perceived "stimulation" at 0mA (total perceived stimulation = 20 minutes). This has been further illustrated in Figure 4. The sham parameters (gradual initial stimulation and decreased slowly back down to 0mA) were chosen to ensure the participant perceived they were receiving active tDCS treatment. While it was not likely that participants would notice an interruption of stimulation, we took precautions by telling all

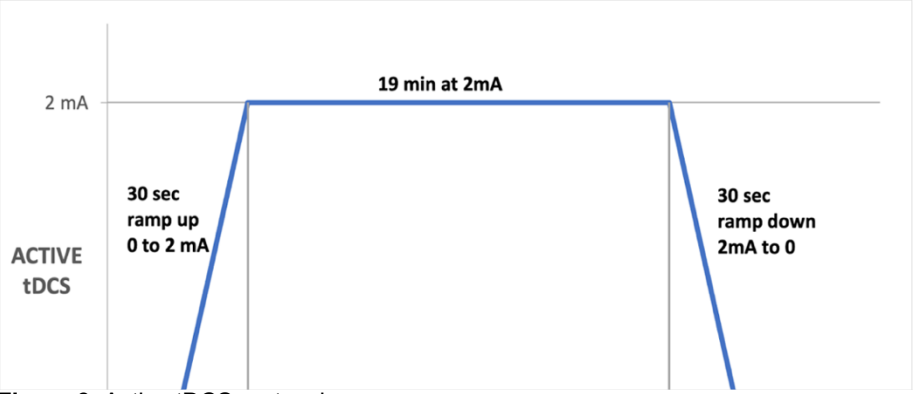

Figure 3. Active tDCS protocol.

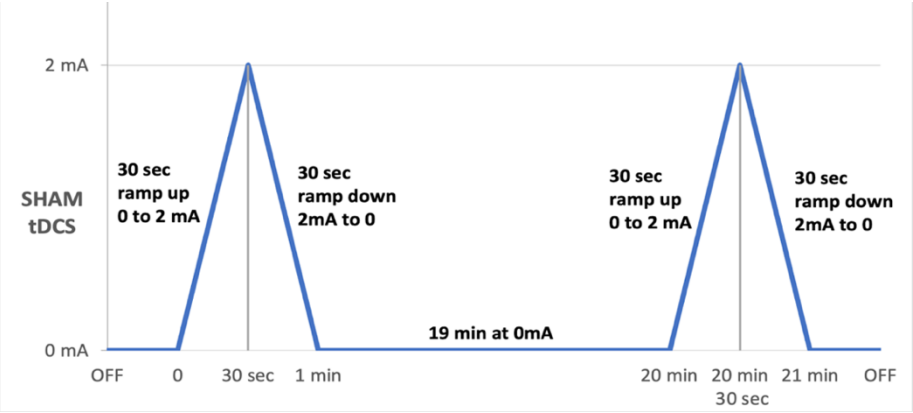

Figure 4. Sham tDCS protocol.

participants in the tDCS groups that they may become accustomed to stimulation over time (Fertonani et al., 2015).

Post-training surveys (administered to the active and sham tDCS groups only).

Following training, participants were asked to report their expectations of tDCS again using the same 0 to 8 scale as before, this time specified to their study experience (i.e., “After completing the study”…“Do you think your motor performance on the study task improved?”, “Do you think the tDCS you received improved your motor performance on the study task?”) (see Appendix E). The second question above was used to determine the participants' tDCS post-expectations score. Likewise, they were also asked which type of stimulation they thought they received (active vs. sham) (see Appendix E). Lastly, participants were asked to complete the same tDCS questionnaire of symptoms they were given just before tDCS stimulation. If the participant scored above 5 on any symptom before tDCS, they were not eligible for participation. Likewise, if they scored above 5 after tDCS, they were instructed to remain in the lab until symptoms subsided or until the participant and researcher were both satisfied for them to leave. However, they should be clearly notified that if their symptoms persisted for more than 24 hours, then the researcher needed to be contacted and appropriate medical attention sought.

STATISTICAL ANALYSES

All analyses were conducted using R, Version 4.0.0 (RCore Team 2019). To test Aim 1, a linear mixed-effects model was used to determine the presence of any placebo or tDCS effects by examining the effect of group (control vs. sham tDCS vs. active tDCS) on task performance. Specifically, we modeled group, (the logarithm of) trial, and a group-by-trial interaction as fixed effects, and participant as a random effect on motor performance. This approach allowed us to differentiate between placebo and tDCS effects on motor learning and control for potential differences in baseline motor performance. The logarithm of trial was used because, as is

common with motor learning research (Bosch et al., 2018; Perry et al., 2020), our motor performance data better fit a logarithmic function than a linear one. To further test the underlying nature of any placebo effect (Aim 2), a linear mixed-effects model was used where expectation score, (the logarithm of) trial, and a trial-by-expectation interaction were modeled as fixed effects and participant as a random effect on motor performance. In this analysis, we used participants' post-training expectation scores. This analysis tested how expectations about tDCS influenced motor task performance.

CHAPTER 3

RESULTS

Evidence of a placebo effect, but not a treatment effect, of tDCS on motor learning

A main effect of trial on motor performance ($F=40.13$, $p<.0001$) was observed, such that compared to the control, participants performed 2.5s faster per (log of) trial. As expected, this indicated a practice effect from our feeding motor task paradigm. When three groups were considered (control, sham, and active), there was no significant interaction between trial and group on motor performance ($F=5.63$, $p=.06$). However, when we collapsed across the sham and active tDCS groups (since both were blinded) and compared this new grouping to the control group, there was a significant interaction between trial and group ($F=5.47$; $p=.02$), such that the control group performed on average 1.1s slower per (log of) trial than the combined tDCS groups. When comparing just the active and sham tDCS groups, there was no significant interaction between trial and group on motor performance ($p=.7$).

Using the regression models to predict motor performance for each trial, data showed that the control group experienced an average change in performance of 9s from trial 1 to trial 30. In contrast, the tDCS group experienced an average change in performance of 15s. Thus, the tDCS group (collapsed across the sham and active tDCS groups) experienced, on average, a 6-second advantage over the control group by the end of training. Figure 5 shows the average motor performance by trial for each group.

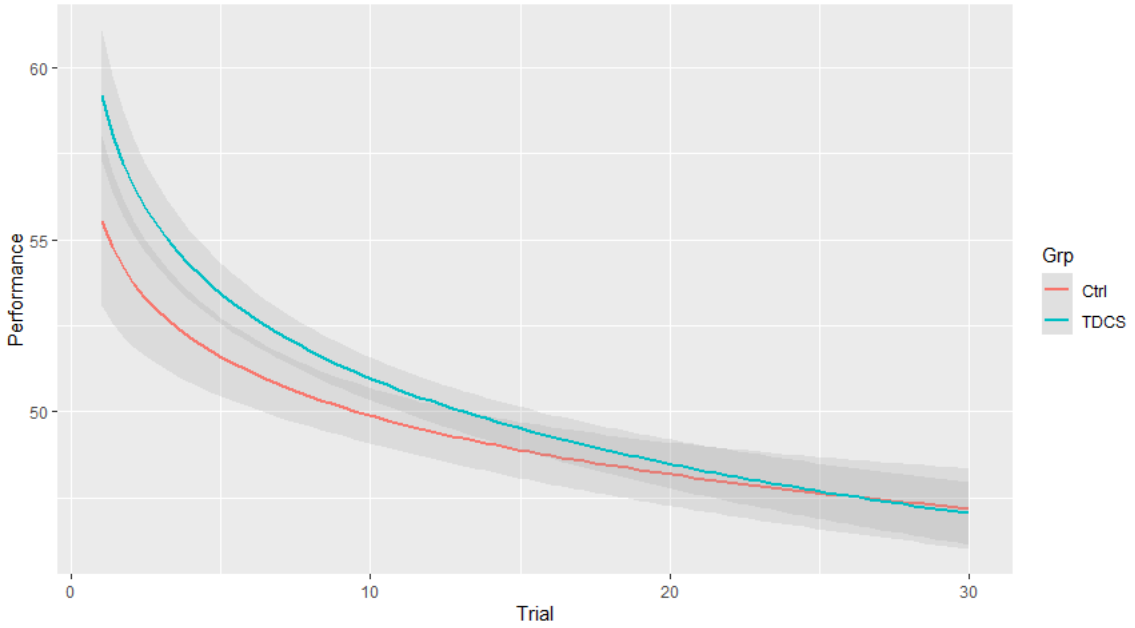

Figure 5. Average motor performance (shown on a logarithmic scale) by trial for groups. Lower values indicate better performance. Ctrl=control; TDCS=collapsed sham and active tDCS groups

Effects of participant expectations of tDCS

Although we were not expecting expectations to change, we assessed expectations of tDCS before and after training to investigate whether simply participating in the study significantly changed expectations. As such, our data showed that regardless of group, expectations about tDCS tended to decrease over the course of training. Prior to training, all but one participant reported neutral or positive expectations of tDCS (4 or higher; median = 6), such that the average pre-expectancy score was 5.2. But after training, the average expectation score was 3.65. Using a standard least square equation, we found a significant effect of time (pre- vs. post-tDCS) on expectations (p=.0074), such that expectation scores decreased on average 0.625 points (out of 8) after stimulation regardless of group.

However, pre-training expectation scores were unrelated to motor learning (p=.78), whereas post-training expectation scores were when collapsed across groups (p=.0004). Figure 6 illustrates this interaction, where the solid lines indicate the average motor performance

(predicted by the mixed-effects model) for the control group (shown in red) and the tDCS group (shown in blue). (Note: the red curve in Figure 6 is the same red curve in Figure 5, just for comparison.) The dotted curves indicate predicted motor performance for each level of expectation (0 to 8). In other words, participants with higher expectations of tDCS at the end of training showed more improvement over the course of training than those with lower expectations.

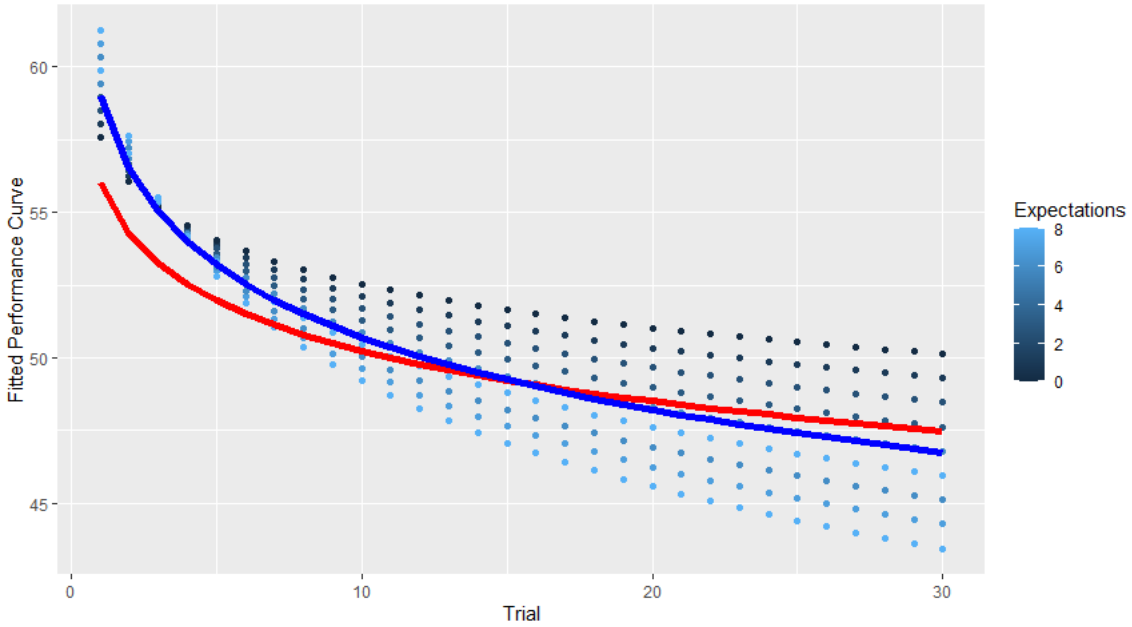

Figure 6. Average predicted motor performance over the course of training as a function of tDCS expectations and trial for the tDCS group (collapsed across sham and active groups, shown in blue). The red curve is for the control group, which is copied from Figure 5. Individual dotted curves show predicted performance for each level of expectation.

CHAPTER 4

DISCUSSION

The overall purpose of this study was to 1) determine whether there is a significant placebo effect of tDCS on motor learning and 2) test whether the placebo effect is due to participants' expectations about tDCS (i.e., an expectancy effect). Aim 1 was supported by results showing that the tDCS (collapsed sham and active) group was faster at the end of training than the control group (i.e., a placebo effect). Aim 2 was also supported, given that higher expectations of tDCS were associated with more improvement over the course of motor training, regardless of whether active or sham tDCS was administered. The effect of expectations aligns with previous research (Horing et al., 2014; Ray et al., 2019; Evers et al., 2018; Rabipour et al., 2018; Colloca, 2018; Colloca & Barksy, 2020; Friesen, 2019); however, we also found that expectations were malleable, changing substantially over the course of training (Anderson & Stebbins, 2020; Arandia & Di Paolo, 2021)

There are several limitations to this study. First, no treatment effect was detected, meaning there was no significant difference in motor learning between the sham and active tDCS groups. This could have been due to between-subject variability in our electrode placement which was based on the 10-20 EEG system. Future studies could use magnetic resonance imaging (MRI) to guide neuronavigation to ensure accurate stimulation location (De Witte et al., 2018) and/or use a high-definition system (HD-tDCS) to diffuse the electric field over a smaller and more precise area of the head (Masina et al., 2021; Villamar et al., 2013; Kuo et al., 2013; Elyssa Kok et al., 2021; Luna et al., 2020). The lack of treatment effect could also be due to a lack of statistical power, given that we were unable to achieve our target recruitment in our short timeframe. As noted in my thesis proposal, our power analysis was designed to detect a significant treatment effect (i.e., a difference between the sham and active tDCS groups) based on previous literature (Hummel et al., 2005). However, our sample size was sufficient to detect a

significant placebo effect (i.e., a difference between the control and sham groups), suggesting that the placebo effect is stronger and more robust than a treatment effect.

This study can therefore help future tDCS studies in motor learning to estimate the effect sizes for both a placebo and treatment effect. Future research is needed, however, to compare the relative magnitudes of both effects side-by-side. Second, we also note that expectations of tDCS prior to motor training were unrelated to motor learning. Although this finding could also be due to a lack of statistical power, we interpret our findings as expectations of tDCS after motor training (and after experiencing/perceiving tDCS) being more relevant to a placebo effect. Third, participants only received a single session of tDCS and were not re-evaluated on the motor task after any consolidation period (i.e., 24 hours later) to determine the extent of learning. Previous research has shown that tDCS is maximized by repetitive sessions over time (Dos Santos et al., 2012; DaSilva et al., 2011). Future studies will therefore explore longer training sessions and retention periods.

This study demonstrated a significant placebo effect of tDCS and identified a possible mechanism of this placebo effect: participants' expectations of the treatment. Our next steps will be to prime participants' expectations using positive or negative information about the effects of tDCS on motor learning to test whether the magnitude of the placebo effect can be manipulated (Rabipour et al., 2018; Villa-Sánchez et al., 2021; Frisaldi et al., 2021; Horing et al., 2014). Additional next steps are to begin advocating for the inclusion of person-specific factors, namely treatment expectation, as a best practice in studies using tDCS and other non-invasive brain stimulation to control for placebo effects (Weik et al., 2022). We expect that doing so would improve the rigor and reproducibility of such research in the future.

There is an overwhelming application of tDCS in the clinical setting (Luna et al., 2020; Reis & Fritsch, 2011; Muller et al., 2021; Gandiga et al., 2006; Hahn et al., 2022), in addition to widespread commercial use among the general public for a variety of things like sports recovery/endurance and mental performance. Outside the field of non-invasive brain stimulation,

evidence showing the placebo effect as a real neurobiological phenomenon has been developing for years (Meissner et al., 2011; Boussageon et al., 2022). Placebo effects offer a vastly unexplored method to improve the efficacy of medical treatments and enhance patient quality of life (Benedetti, 2013). A better understanding of the mechanism behind placebo effects of tDCS specifically will allow clinicians to leverage patients' mindsets in addition to a treatment's biological mechanisms of action to improve outcomes.

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APPENDIX A

tDCS PRE-EXPECTATIONS SURVEY

Thoughts about tDCS Questionnaire

Please indicate to what extent the following statements apply to you. Use the following scale to record your answers:
0 = No not at all
...
4 = neutral
...
8 = Yes very much

In general, would you like to improve your motor performance? *

	0	1	2	3	4	5	6	7	8	
No, not at all	○	○	○	○	○	○	○	○	○	Yes, very much

Do you think brain stimulation would improve your motor performance? (i.e., Do you think it will work?) *

	0	1	2	3	4	5	6	7	8	
No, not at all	○	○	○	○	○	○	○	○	○	Yes, very much

APPENDIX B

EXPERIENCE WITH BRAIN STIMULATION SURVEY

Experience with Brain Stimulation Questionnaire

In this section we will ask for your experience in this experiment.

Have you heard of transcranial direct current stimulation before (before you signed up for this study)? *

- ◯ Yes
- ◯ No

Have you previously participated in any tDCS studies before? *

- ◯ Yes
- ◯ No

APPENDIX C

SUGGESTIBILITY SURVEY

Suggestibility Questionnaire

Please indicate to what extent the following statements apply to you. Use the following scale to record your answers:
1: Not at all or very slightly
2: A little
3: Somewhat
4: Quite a bit
5: A lot

I am easily influenced by other people's opinions *

1	2	3	4	5
○	○	○	○	○

I can be influenced by a good commercial *

1	2	3	4	5
○	○	○	○	○

When someone coughs or sneezes, I usually feel the urge to do the same *

1	2	3	4	5
○	○	○	○	○

Imagining a refreshing drink can make me thirsty *

1	2	3	4	5
○	○	○	○	○

A good salesperson can really make me want their product *

1	2	3	4	5
○	○	○	○	○

I get a lot of good practical advice from magazines or TV *

1	2	3	4	5
○	○	○	○	○

If a product is nicely displayed, I usually want to buy it *

1	2	3	4	5
○	○	○	○	○

When I see someone shiver, I often feel a chill myself *

1	2	3	4	5
○	○	○	○	○

I get my style from certain celebrities *

1	2	3	4	5
○	○	○	○	○

When people tell me how they feel, I often notice that I feel the same way *

1	2	3	4	5
○	○	○	○	○

When making a decision, I often follow other people's advice *

1	2	3	4	5
○	○	○	○	○

Reading descriptions of tasty dishes can make my mouth water *

1	2	3	4	5
○	○	○	○	○

I get many good ideas from others *

1	2	3	4	5
○	○	○	○	○

I frequently change my opinion after talking with others *

1	2	3	4	5
○	○	○	○	○

After I see a commercial for lotion, sometimes my skin feels dry *

1	2	3	4	5
○	○	○	○	○

I discovered many of my favorite things through my friends *

1	2	3	4	5
○	○	○	○	○

I follow current fashion trends *

1	2	3	4	5
○	○	○	○	○

Thinking about something scary can make my heart pound *

1	2	3	4	5
○	○	○	○	○

I have picked-up many habits from my friends *

1	2	3	4	5
○	○	○	○	○

If I am told I don't look well, I start feeling ill *

1	2	3	4	5
○	○	○	○	○

It is important for me to fit in *

1	2	3	4	5
○	○	○	○	○

APPENDIX D

tDCS POST-EXPECTATIONS SURVEY

Section 2 of 3

Thoughts about tDCS

Please indicate to what extent the following statements apply to you. Use the following scale to record your answers:
0 = No not at all
...
4 = neutral
...
8 = Yes very much

After completing this study, do you think your motor performance on the study task improved? *

	0	1	2	3	4	5	6	7	8	
No, not at all	○	○	○	○	○	○	○	○	○	Yes, very much

After completing this study, do you think the tDCS you received improved your motor performance on the study task? *

	0	1	2	3	4	5	6	7	8	
No, not at all	○	○	○	○	○	○	○	○	○	Yes, very much

APPENDIX E

PERCEIVED GROUP SURVEY

Section 3 of 3

Questions about tDCS

In this section we will ask for your experience in this experiment.

Do you think you received active tDCS? *

- ○ Yes
- ○ No

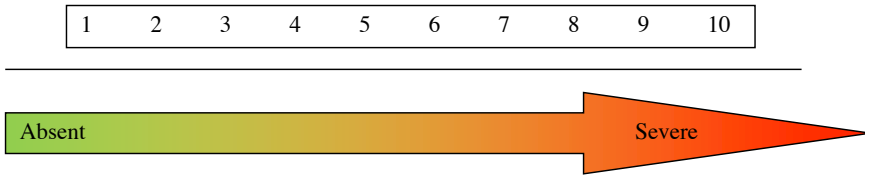
Please summarize your experiences with the experiment with 3 words (adjectives), separated by comma. For example: "fun, interesting, engaging", or "boring", etc. *

Long answer text

APPENDIX F

PRE- AND POST-tDCS SYMPTOM SURVEY

This questionnaire will be filled in before and after receiving tDCS. Please enter a value from 1-10, ranging from absent to severe, in the 'Rating' space below in response to the question: "Do any of these statements currently apply to you?" It is important that you answer all questions truthfully.



Do any of these statements currently apply to you?	Rating		Notes
	Before tDCS	**After** tDCS	
1. Headache			
2. Neck pain			
3. Back pain			
4. Blurred vision			
5. Scalp irritation			
6. Tingling			
7. Itching			
8. Increased heart rate			
9. Burning sensation			

10. Hot flush			
11. Dizziness			
12. Acute mood change			
13. Fatigue			
14. Anxiety			
Others:			

Instructions for application

Before: If participants score '5' or above for any of the statements*, they should not participate on the day. This is for their own safety and comfort as tDCS has been shown to temporarily aggravate some of these conditions.

After: If participants have scored '5' or above for any of the statements*, they should stay in the laboratory until symptoms have subsided or until they and the researcher are satisfied for them to leave. If their symptoms persist for more than 24 hours then the researcher should be contacted and appropriate medical attention should be sought.

*Apart from questions 3, 8, 10 and 11 as these are pseudo items

APPENDIX G

IRB APPROVAL

APPROVAL: MODIFICATION

Sydney Schaefer
BHSE: Biological and Health Systems Engineering, School of
480/727-6651
Sydney.Schaefer@asu.edu

Dear Sydney Schaefer:

On 2/19/2022 the ASU IRB reviewed the following protocol:

Type of Review:	Modification / Update
Title:	Investigation of the relationship between visuospatial function and motor learning through noninvasive brain stimulation
Investigator:	Sydney Schaefer
IRB ID:	STUDY00009764
Funding:	Name: North American Society for the Psychology of Sport and Physical Activity (NASPSPA), Grant Office ID: FP00024305 ; Name: BHSE: Biological and Health Systems Engineering, School of, Grant Office ID: Program PG08347
Grant Title:	None
Grant ID:	None
Documents Reviewed:	• 1 COVID-19 Screening Form_update.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • 4 Thair et al. 2017_sheet 2 screening.pdf, Category: Screening forms; • 5 Entrance Questionnaire tDCS C4 - Google Forms.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • 6 Thair et al. 2017_sheet 1 questionnaire.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • 7 Exit Questionnaire tDCS C4 - Google Forms.pdf, Category: Measures (Survey questions/Interview

	questions /interview guides/focus group questions); • 8 scripts_tDCS_C4_clean.pdf, Category: Recruitment materials/advertisements /verbal scripts/phone scripts; • Data Collection sheet, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Protocol_022120 covid update_Revised_SONA verbiage_m1_NEW 11.docx, Category: IRB Protocol; • Reminder Email - SONA, Category: Recruitment Materials; • Scheduling Email - SONA, Category: Recruitment Materials; • Screening Email - SONA, Category: Recruitment Materials; • SONA Study Advertisement.pdf, Category: Recruitment Materials; • Subject Pool Approval SP22-09.pdf, Category: Other;

The IRB approved the modification.

When consent is appropriate, you must use final, watermarked versions available under the "Documents" tab in ERA-IRB.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

REMINDER - Effective January 12, 2022, in-person interactions with human subjects require adherence to all current policies for ASU faculty, staff, students and visitors. Up-to-date information regarding ASU's COVID-19 Management Strategy can be found here. IRB approval is related to the research activity involving human subjects, all other protocols related to COVID-19 management including face coverings, health checks, facility access, etc. are governed by current ASU policy.

Sincerely,

IRB Administrator

cc: Jessica Trevino
Richard Yan
Lalaine Dungca
Alexis Torres
Hitesh Gurram
Andrew Hooyman

Jennapher Lingo Vangilder
Afzal Ariff
Mckenna Godman
Schuyler Vink
Nicole Haikalis
Keenan Woodburn
Randy Essikpe
Britney Hill
Sydney Schaefer
Alexandra Lewis
Jessica Trevino
Peiyuan Wang
Shreyas Jejurkar
Ayoub Daliri
Gene Brewer
Hailey Dziendziel

BIOGRAPHICAL SKETCH

Nicole Kallima Haikalis Aguilar was born and raised in San Diego, CA. She learned the value and importance of education and research from her mom, who raised her and her older sister alone. Before college, Nicole served in the United States Marine Corps. Nicole graduated from ASU in 2021 with a B.S.E in Biomedical Engineering, a B.S. in Neuroscience, and a minor in Psychology. She is a dedicated advocate for equality, especially within science and research, and serves in several organizations dedicated to advocacy within STEM, people with disabilities, sexual violence survivors, LGBTQIA+, Hispanics, and other minorities. Her overarching research goal is to use science in accordance with respect, empathy, and inclusion to discover how best to optimize medical care to relieve patient suffering and improve people's daily lives. By reflecting on her own value of respect and body autonomy, she began wondering why transcranial direct current stimulation (tDCS) research by and large has failed to consider people's expectations and perceptions of non-invasive brain stimulation itself as important, and how placebo effect could play a role in treatment. Her research attempts to merge psychology, neuroscience, and biomedical engineering, and advance knowledge within and across these fields to explore new ways that tDCS (and other types of non-invasive brain stimulation) can enhance motor learning as well as other targeted behaviors. Her goal is for placebo effects of tDCS to be used as a tool, rather than a nuisance, to promote and strengthen patient recovery. She will continue her studies by beginning a Ph.D. in Biomedical Engineering at ASU in the fall of 2022.