

Priming Expectations and Motor Learning With tDCS

This title should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied.

Unique Protocol Identification Number: STUDY00015655

National Clinical Trial (NCT) Identified Number: NCT06039605

Principal Investigator: Sydney Schaefer

Sponsor:

"Sponsor" indicates an institution, foundation, or individual who takes responsibility for and initiates a clinical investigation; often times this is the university with which the Principal Investigator is affiliated.

Grant Title: Measuring Expectancy Effects of Transcranial Direct Current

Stimulation on Motor Learning

Grant Number: 1R21AT012088-01A1

Funded by: NCCIH

Version Number: v.0.074

27 April 2026

All versions should have a version number and a date. Use an international date format (e.g., YYYY-MM-DD [2017-12-21] or write out the month (e.g., 21 December 2017).

For the initial submission of a protocol to the IRB, indicate "Not applicable; this is the first version of the protocol." in the table below. For any subsequent amendment being submitted to the IRB, add details of the specific changes that are being implemented in the amendment. Please note that Section 10.4 is a high-level summary of all formal protocol versions/amendments.

Summary of Changes from Previous Version: N/A

Affected Section(s)	Summary of Revisions Made	Rationale

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STATEMENT OF COMPLIANCE

*Provide a statement that the trial will be conducted in compliance with the protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP) and applicable state, local and federal regulatory requirements. Each engaged institution must have a current Federal-Wide Assurance (FWA) issued by the Office for Human Research Protections (OHRP) and must provide this protocol and the associated informed consent documents and recruitment materials for review and approval by an appropriate Institutional Review Board (IRB) or Ethics Committee (EC) registered with OHRP. Any amendments to the protocol or consent materials must also be approved before implementation. Select one of the two statements below. If the study is an **intramural** NIH study, use the second statement below:*

1. The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:
 - United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

OR

2. The trial will be conducted in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the [specify NIH Institute or Center (IC)] Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), and the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor, if applicable, except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

For either option above, the following paragraph would be included:

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

Principal Investigator or Clinical Site Investigator:

Signed:

Date: 4/21/2026

Name*: Sydney Schaefer, PhD

Title*: Associate Professor

Investigator Contact Information:

Affiliation*: Arizona State University

Address:

Telephone:

Email: sydney.schaefer@asu.edu

For multi-site studies, the protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site:

Signed:

Date:

Name:

Title:

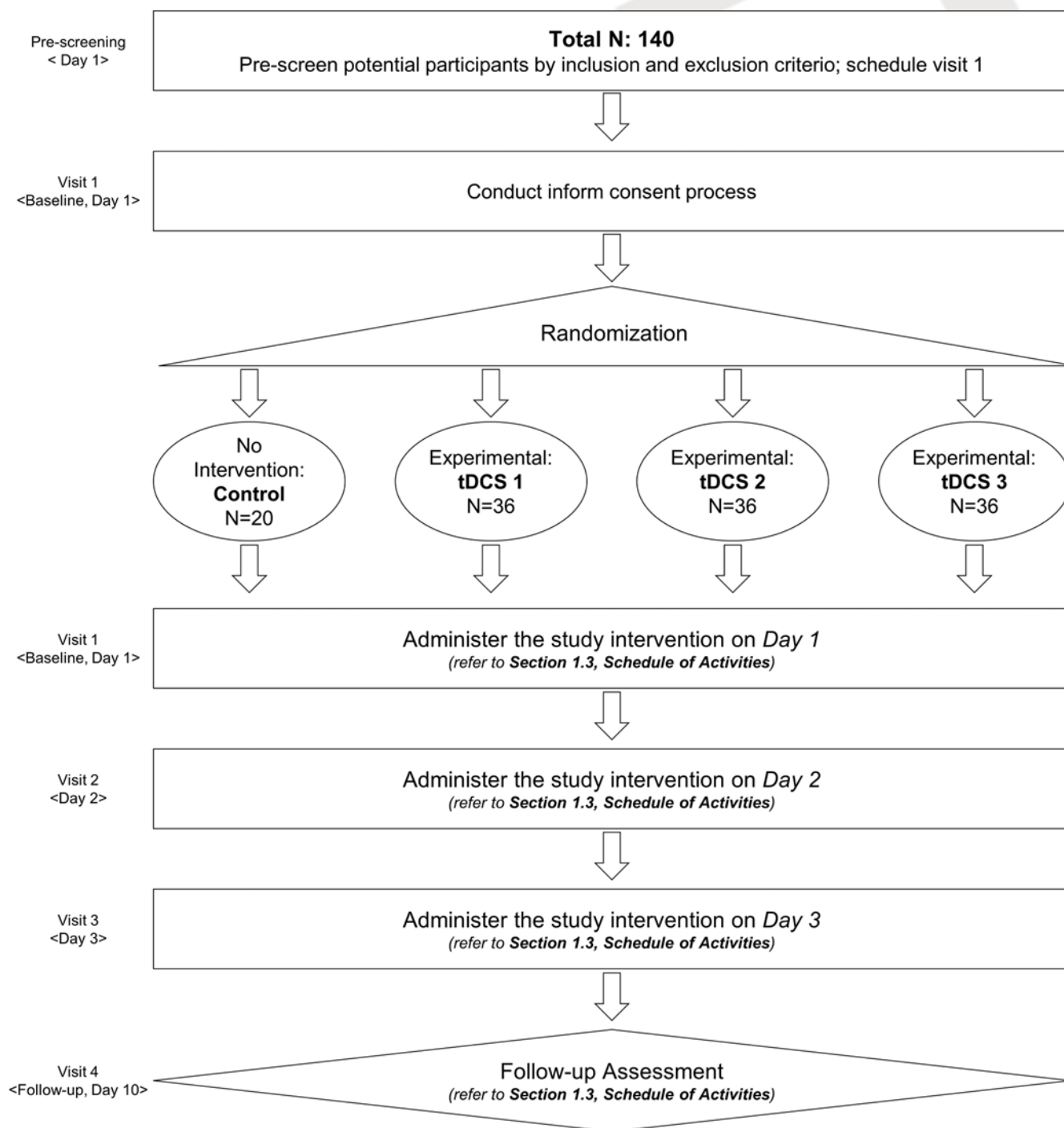
Affiliation:

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Priming Expectations and Motor Learning With tDCS
Grant Number:	1R21AT012088-01A1
Study Description:	
Objectives*:	Primary Objective: Determine the extent to which priming expectations of tDCS will modulate motor skill learning.
	Secondary Objectives: Determine the extent to which sham tDCS improves motor skill learning.
Endpoints*:	Primary Endpoint: Motor task performance at one-week follow-up (Day 10)
	Secondary Endpoints: Change in task performance over three days of training (Day 3)
Study Population:	Adults age 18+ with no self-reported neurological or physical condition or conditions contraindicated for transcranial direct current stimulation
Phase* or Stage:	Phase I
Description of Sites/Facilities Enrolling Participants:	
Description of Study Intervention/Experimental Manipulation:	
Study Duration*:	2 years
Participant Duration:	10 days

1.2 SCHEMA



1.3 SCHEDULE OF ACTIVITIES

	Pre- screening (Pre- consent)	Day 1 (Baseline)	Day 2	Day 3	Day 10 (Follow-Up)
Screening Eligibility	X				
Informed Consent		X			
Randomization		X			
Demographics		X			
Priming tDCS Information (Skip for Group 1: Control and Group 2: tDCS1)		X	X	X	
Expectation Assessment Scale (Skip for Group 1: Control)		X	X	X	
Pre-tDCS Side effects questionnaire (Skip for Group 1: Control)		X	X	X	
Intervention Sham (double-blinded) tDCS intervention + Motor training (10 trials) (Skip TDCS intervention for Group 1: Control)		X	X	X	
Post-tDCS Side Effects Questionnaire (Skip for Group 1: Control)		X	X	X	
Motor training (2 trials)					X
Exit Questionnaires (Short Suggestibility Scale, Previous knowledge of tDCS, Post-Expectation Assessment (Skip for Group 1: Control), Participants' experience)					X
Adverse Events Reporting (Skip for Group 1: Control)					X

2 INTRODUCTION

2.1 STUDY RATIONALE

Transcranial direct current stimulation (tDCS) is currently being investigated by the scientific community as an intervention to improve motor learning in the context of neurorehabilitation (e.g., recover lost motor function after stroke) and performance enhancement (e.g., improve sports or technical skill training). More importantly, consumers believe that tDCS works. The expectation surrounding the benefits of tDCS for skill enhancement is so pervasive that the technology is sold for less than \$200 and highly rated by the general public on Amazon.com. At the same time, there is considerable skepticism within the motor control field regarding the efficacy and mechanism of action of tDCS on motor learning, driven by highly irreproducible and equivocal findings between and even within laboratories. How effective is tDCS, and could the positive effects of tDCS be attributable in part to a strong placebo effect? Placebo effects (i.e., a positive expectation associated with positive treatment outcomes), are well documented in other interventions like surgeries and pharmaceuticals, but have not been investigated in detail for tDCS, particularly in the motor domain. The lack of knowledge or consideration of the placebo effect may therefore explain why tDCS findings are so inconsistent within motor learning. Thus, the overall aim of this project is to determine whether people's expectations about tDCS change as a function of information about tDCS itself, and whether these changed expectations modulate the effects of tDCS on motor learning.

2.2 BACKGROUND

Transcranial direct current stimulation (tDCS) is a noninvasive, safe cortical stimulation technique that has been effectively used for enhancing and inhibiting sensory and motor performance when applied to the responsible cortical areas in healthy adults. For instance, anodal tDCS of the primary motor area can improve motor execution. More specifically, online tDCS (i.e., stimulation during task performance) has been considered a potential non-pharmacological approach to augment motor skill learning, as demonstrated by faster skill acquisition and greater motor retention compared to motor practice alone. As such, tDCS may be used in neurorehabilitation to promote motor recovery following neural injury and to enhance motor performance.

Many tDCS studies have shown inconclusive results in motor learning, failing to replicate previous findings and revealing significant variability in individual responses. Indeed, recent research has investigated whether it is the expectation of receiving tDCS that has a greater impact on behavioral outcomes compared to the actual application of tDCS and the reason of the high variability. These studies focused on a single motor practice session without a consolidation period, leaving it unclear if the observed expectation-driven placebo effect is temporary or lasts over longer training durations typical in clinical neurorehabilitation trials. This is important as many domains of science are challenged to reproduce previous research demonstrating a positive effect of tDCS on behavior. Thus, to decipher legitimate effects

of tDCS on behavior it is important to quantify and compare how changes in behavior are related to tDCS, a key metric related to strength of the placebo effect, and how malleable these placebo effects are.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Transcranial Direct Current Stimulation (tDCS) is a minimal risk, non-invasive, neuromodulatory technique that involves the emission of a weak electrical current, traditionally via the placement of two electrodes attached to the scalp of a participant. TDCS is widely used for research purposes, the US FDA considers trials of tDCS as non-significant-risk. There are several review articles supporting the safety of tDCS usage in controlled human trials (Brunoni et al, 2012, doi:10.1016/j.brs.2011.03.002; Bikson et al. 2016, doi:10.1016/j.brs.2016.06.004). According to a meta-analysis by Bikson et al (2016, doi:10.1016/j.brs.2016.06.004), the use of conventional tDCS protocols in human trials (≤ 40 min, ≤ 4 mA) has not produced any reports of a Serious Adverse Effect or irreversible injury across over 33,200 sessions.

There is a low-risk for some minor side-effects or adverse reactions. Subjects with sensitive skin may experience skin irritation in the area where electrodes are applied. Mild redness has been reported at the site of electrode placement, but this is an acute effect of vasodilation as opposed to inflammation. Skin sensations, such as itching, tingling, heat or mild pain during tDCS are transient. To minimize these sensations, we are using saline-soaked sponges attached to conductive rubber electrodes to distribute current across the electrode-skin interface. Participants might feel anxious due to stimulation-related discomfort, even with Sham tDCS. We will accommodate anxious Participants by manually decreasing current density to a more comfortable level and then slowly increase current density to the experimental level. In addition, participants will be able to abort the stimulation paradigm if they become uncomfortable at any time.

Other foreseeable risks and discomforts include boredom and within-session fatigue of arm and hand. If participants express fatigue, they will be offered a brief break (1-5 minutes) for refreshment or toileting. Participants may experience minor discomfort from the placement or positioning of the electrode on the scalp or skin of the forehead, but we will work with participants to ensure the most comfortable fit. Participants may also experience a loss of confidentiality.

Pregnancy is an exclusion criterion of the study; thus, embryonic or fetal risk is not applicable.

2.3.2 KNOWN POTENTIAL BENEFITS

It is unlikely that participants in this study will immediately benefit from research procedures. However, their participation is critical to better understanding the nature of placebo effects of tDCS on motor learning that arise from people's expectations of the technology. Due to the potential for these so-called

‘expectancy effects’ to enhance motor learning independently of the stimulation itself, and the minimal risks of this protocol, the benefit to the field of motor rehabilitation and beyond outweighs the risks to participants associated with taking part in the study.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

General safety guidelines:

Safety of the participants is a primary concern. During all testing procedures, subjects will be continuously monitored and protocol will be immediately ceased if deemed necessary by the subject or researcher. Risks associated with research procedures will be minimized by using qualified personnel as well as performing thorough screening prior to data collections. All protocols will be fully approved through the Arizona State University before data collection begins.

Protection against the potential risks noted above:

1. tDCS: Even if participants are initially eligible, they are further screened for tDCS eligibility by answering the following tDCS Screening (Thair et al., 2017. doi:10.3389/fnins.2017.00641).

1. Have you ever had a seizure?
2. Have you ever had a head injury resulting in a loss of consciousness that has required further investigation (including neurosurgery)?
3. Do you suffer from migraines?
4. Do you currently have a medical diagnosis of a psychological or neurological condition?
5. Do you have any metal in your head (outside of the mouth) such as shrapnel or surgical clips?
6. Do you have any implanted devices (e.g. cardiac pacemaker, brain stimulator)?
7. Do you have a skin condition on your scalp? (e.g. psoriasis)
8. Do you have a head wound that has not completely healed?
9. Have you ever had an adverse reaction to tDCS, or any other brain stimulation technique (e.g. TMS, tRNS)?
10. For female participants: Is there the possibility that you might be pregnant?
11. Are you currently taking any prescribed medications or are self-medicating (including recreational drug use), other than the contraceptive pill?

If a potential participant verbally answers “no” to all of these questions, then he or she will be recruited to participate. Once a participant is enrolled following informed consent, on the day of the experiment, participants will answer a tDCS safety questionnaire in the lab which asks for levels of the following conditions (1 - 10, 1 being absent and 10 being severe):

1. Headache

2. Neck pain
3. Blurred vision
4. Scalp irritation
5. Tingling
6. Itching
7. Burning sensation
8. Acute mood change
9. Fatigue
10. Anxiety

If participants score '5' or above for any of the conditions, they will not participate on that day and will be rescheduled for a different day.

To minimize the transient skin sensations of itching, tingling, heat or mild pain during tDCS, we will use saline-soaked sponges attached to conductive rubber electrodes to distribute current across the electrode-skin interface. In addition, participants will be able to abort the stimulation paradigm if they become uncomfortable at any time. We also note that the tDCS Questionnaire (Thair et al., 2017. doi: 10.3389/fnins.2017.00641; see questions above) is used prior to initiating any tDCS to ensure participants are not experiencing any symptoms beforehand.

2. Loss of confidentiality: All consenting, screening, and research procedures will be performed at Arizona State University in private to maintain the participant's privacy. Eligible participants will be assigned non-identifiable codes that will be associated with all data. Paper records, when necessary, will be maintained in locked filing cabinets in locked rooms. All other data will be stored on ASU servers behind firewalls with access only provided to members of the research study team. Data safety will be ensured by saving all electronic data to our research folder that is accessible only to the PIs and research team.

3. Fatigue during motor training: Participants will be given rest periods. Furthermore, the motor task is performed while seated, thereby eliminating any standing balance demands and associated fall risk.

Important of knowledge to be gained

The proposed research is expected to demonstrate that participant expectations about tDCS can and should be exploited in real-world uses of tDCS (e.g., motor rehabilitation, military training, at-home personal use) to maximize motor outcomes (e.g., dexterity or speed), particularly in cases where true stimulation is contraindicated, unsafe, or not feasible.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
To determine how much expectations about transcranial direct current stimulation (tDCS) enhance motor learning (independent of active stimulation)	Motor task performance at day 10 (one week after training)	The definition of motor learning is a relatively permanent change in motor performance in response to practice (Schmidt & Lee, 1999). Thus, the 10-day endpoint reflects relative permanence of performance on the task after three days of practice.	N/A
Secondary			
To determine how much expectations about transcranial direct current stimulation (tDCS) enhance motor acquisition (independent of active stimulation)	Motor task performance for day 3 (average trial time)	While motor learning is defined by a relative permanence in performance change, motor acquisition is a change in performance over the course of practice (Schmidt & Lee, 1999). This change may not, however, persist over a period of no practice, but may still provide insights into drivers of behavioral change.	N/A
Tertiary/Exploratory			
N/A	N/A	N/A	N/A

4 STUDY DESIGN

4.1 OVERALL DESIGN

This study will employ a four-group, parallel, double-blind, randomized controlled trial design. The study will adhere to CONSORT guidelines. Participants provided written informed consent before enrolling in the study.

A planned sample size will be determined (see Section 9.2) before enrollment to ensure adequate statistical power for the primary outcome. Participants will be 18 years old or older, have no self-reported motor impairment, be right-handed, have no contraindications to tDCS (Thair et al., 2017, doi:10.3389/fnins.2017.00641), not be actively taking any medication (except for oral contraception), and not report having a diagnosis of a psychiatric or neurological condition by a physician. Participants were randomly assigned to one of four groups: Group 1: Control (unblinded), Group 2: tDCS1 (unprimed tDCS), Group 3: tDCS2 (primed tDCS), Group 4: tDCS3 (primed tDCS) (see Section 6 for Experimental Manipulation).

The study will consist of 4 days to perform a motor training task. The non-clinical sample of participants will complete three daily motor training sessions with no tDCS (unblinded Control group) or with double-blind tDCS. The tDCS (active or sham) will be applied for 20 minutes. Before the tDCS application, participants from Groups 3 and 4 will first read some information about tDCS based on cited studies. Participants' expectations about the efficacy of tDCS will be measured before each training session. Follow-up motor performance will be measured one-week post-training (day 10).

The study is single-site and will be developed and conducted at Arizona State University.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The rationale is to isolate the expectancy effect from the physical stimulation effect by manipulating participants' beliefs about the efficacy of tDCS. The unblinded non-tDCS exposure Control group is critical as it serves as a "true" baseline. It is critical for testing the expectancy effect, as all other groups may expect to receive stimulation because the device will be placed on their heads and sham stimulation will be applied. The tDCS1 group, receiving only tDCS without information, allows to control and test the expectancy effect based solely on the montage and application of the intervention.

4.3 JUSTIFICATION FOR INTERVENTION

The montage for the tDCS intervention will follow a gold-standard approach to enhance motor learning by stimulating the primary motor cortex (Reis et al., 2008, doi:10.1016/j.brs.2008.08.001). Specifically, the electrodes will be placed over the right primary motor cortex (anode), with the return electrode on

the left supraorbital region (cathode). To maintain participants' blindness, the sham stimulation will include a 30-second ramp-up and ramp-down at the start and end of the training. Both participants and interventionists will also be unable to know the type of stimulation (active or sham) applied, although sham tDCS will be always applied. The 20-minute stimulation is a standard protocol for tDCS intervention.

Multiple sessions are typically used to enhance motor learning, with a one-week follow-up session to test for retention.

The minimum-acceptable participation requires completing the four days (3 motor training + 1 motor training follow-up).

4.4 END-OF-STUDY DEFINITION

The end of the study is defined as completion of the 4 days (3 consecutive motor training + 1 motor training follow-up session)

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

Inclusion criteria are: being 18 years or older and being right-handed.

5.2 EXCLUSION CRITERIA

Exclusion criteria are: Failure to meet the eligibility criteria outlined by the tDCS screening form (Thair et al., 2017, doi:10.3389/fnins.2017.00641): a history of seizure, loss of consciousness due to head injury, migraines, psychological or neurological condition, metal in the head, implanted devices, skin condition, unhealed head wound, previous adverse reaction to brain stimulation, or be pregnancy. Participants will also be excluded if they verbally report taking any prescribed medications other than oral contraception, or are self-medicating (including recreational drug use). Participants will also be excluded if they report any diagnosed current psychiatric condition, such as clinical depression or bipolar disorder.

To ensure no potential coercion of students, no participants who express interest in the study based on posted flyers or word-of-mouth will be allowed to participate if they are actively enrolled in a course taught by the PI, and they will only be allowed to do so until after the semester ends and grades have been submitted.

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Individuals who do not meet the criteria for participation in this trial are excluded (consider screen failures) because they meet one or more exclusion criteria.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We will recruit students enrolled in Biomedical Engineering at the Arizona State University (ASU). The College of Liberal Arts and Sciences (which houses the Psychology department at ASU) and the College of Engineering alone at ASU have 32,029 total undergraduate students enrolled. In addition to traditional recruitment methods (approved posting of IRB-approved flyers on campus and in the local community), we will be approved to post this study on the SONA site at ASU, which makes the study visible and eligible to all students currently enrolled in psychology, and allows them to earn credit towards this class.

We will also advertise to the broader Maricopa County community, with 4.4 million residents, >75% of whom are ages 18 and older. This, along with dedicated staff (a project coordinator and a graduate research assistant), will ensure sufficient recruitment for this project.

To further ensure no potential coercion of students in this study specifically, no participants who express interest in the study based on posted flyers or word-of-mouth will be allowed to participate if they are actively enrolled in a course taught by the PI, and they will only be allowed to do so until after the semester ends and grades have been submitted.

We acknowledge that an important factor in this project is continued engagement with our enrolled participants to decrease the likelihood of dropout across days.

Our proposed engagement strategies include:

- Project coordinator to schedule all days with the participant at enrollment
- Project coordinator to send reminder emails (also through REDCap) and make phone calls the afternoon prior to next appointment
- Project coordinator to maintain communication with enrolled participants through an email newsletter and small tokens of appreciation that will remind them of the study (e.g., refrigerator magnets, pens, etc.)
- Provision of free parking immediately outside of our laboratory
- Provision of transportation to/from testing sessions
- Provision of water and snacks
- Participant compensation

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Motor training

All groups will perform the same motor training intervention. Motor training will consist of 10 practice trials per day (150 repetitions) over 20 minutes for 3 consecutive days (Days 1, 2, 3) on a functional upper-extremity task. Two additional trials will be measured at one-week follow-up (Day 10). Details about the task and outcomes are describes in section 8.1

Transcranial Direct Current Stimulation (tDCS)

The three tDCS groups will undergo the same tDCS protocol, which will be applied concurrently with the motor training task ('online' tDCS). A traditional 1x1 transcranial direct current stimulation (tDCS) device will be used (Soterix Medical Inc., New York, NY) with two conducting 5 cmx7 cm saline-soaked sponge-encased rubber electrodes (8 mL of saline injection). The anodal electrode will be placed on the right primary motor cortex, with its center covering the C4 site on the International 10-20 Electrode Placement System. The return electrode will be placed on the contralateral supraorbital area (left forehead). Sham stimulation will be delivered as a 30-second ramp-up to 2 mA and a 30-second ramp-down at the beginning and end of the 20-minute motor training period (i.e., sham stimulation will be administered as online stimulation during motor training).

Priming tDCS information

Only participants from tDCS2 and tDCS3 groups will be primed with specific information about tDCS before the intervention. Specifically, these groups will read either a positive or a negative prime as reported in a previous experiment (Rabipour et al., 2018, doi:10.3389/fnins.2018.00999). We have selected a negative prime instead of a neutral prime to minimize participant bias, since participants tend to have more positive expectations initially, skewing EAS scores higher. Including a negative prime should provide a more normal distribution and broader range of expectation scores, at least pre-stimulation. The tDCS1 group will receive no prime information about tDCS (i.e., unprimed Sham tDCS).

6.1.2 ADMINISTRATION AND/OR DOSING

The study intervention and experimental manipulations will be administered by a research team in a controlled laboratory setting. Participants from the tDCS2 and tDCS3 group will read their respective priming information about tDCS's efficacy before each tDCS application (during the three continuous motor training interventions) and fill out the EAS before the tDCS + Motor training intervention. The tDCS will then be set up in the same configuration for all tDCS groups (tDCS1, tDCS2, tDCS3), as described in section 6.1.1. During each training session, interventionists will place saline-soaked electrodes on the participant's head to deliver sham stimulation (interventionist and participant does not know the real type of stimulation, actually sham) while the participant simultaneously performs a

simulated feeding task using their nondominant hand. The type of stimulation will be double-blind for both the participants and the interventionist.

A "full-dose" intervention consists of four total sessions: three consecutive daily training days performing the motor training (Days 1,2,3), followed by a one-week follow-up (Day 10).

Participants from the Control group will perform only the motor training and follow-up motor task.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

All members of the research team will have completed the Human Research Curriculum Group (Course Learner Group 1: IRB - Biomedical Research, Stage 1 – Basic Course) and the Good Clinical Practices course from the Collaborative Institutional Training Initiative (CITI) program. Interventionists will also be trained on administering all cognitive and physical assessments in compliance with test standards (rehabmeasures.org). As for the laboratory motor tasks, the PI has developed a training handbook to ensure proper administration of the motor training.

Lab personnel (interventionists) who will conduct the stimulation experiment have been trained through a specialized tDCS workshop and by experienced researchers in the department. Any new interventionist will be trained by the lab personnel.

The suite of research labs are wheelchair and handicap accessible, and is near restrooms and water fountains in the event that subjects need breaks.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

After signing the informed consent, the participant will be randomly assigned to one of the four groups and will receive either sham or active stimulation. However, all participants will receive sham stimulation.

The study will use a double-blind design to minimize experimenter/interventionist bias and cues.

Double-blind design is needed because expectations regarding the efficacy of tDCS may be dependent on stimulation awareness; research has shown that placebo-associated expectancy effects tend to be smaller under unblinded conditions. To maintain blindness, participants will be presented with materials, including the consent form, which will state that participants may receive a sham or active stimulation, even though all participants will receive a sham. Additionally, interventionists will utilize a device that conceals whether the stimulation is active or sham during application.

Participants' tDCS blinding will assess whether the study was sufficiently blinded for all participants in the tDCS groups. Participants will be asked at the end of the follow-up session (day 10) whether they believed they had received active or sham stimulation. This question will be administered only to the tDCS groups.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

For specific details about adherence, see Section 5.5. Additionally, a specific log file will be used to track the day and time participants arrive at the lab using anonymized codes.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Participation is entirely voluntary. Participants may request a small break within a session or withdraw from the study at any time without penalty. They may also be removed from the study intervention by the PI or main research manager if they do not follow protocol, particularly regarding day timing, frequency, and safety reasons regarding the tDCS application. Exceptions are made for specific timing. Once participants withdraw from the intervention, they cannot continue with the study.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants will be free to withdraw from participation in the study at any time without penalty and for any reason. An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance.
- Unable to contact subject.
- Unable to follow the three consecutive motor training (Day 1, 2, 3).
- Unable to perform the follow-up session (Day 10)
- Any event, medical condition, or situation that occurs during the intervention and does not allow the participant to continue with the study.
- Any medical or physical event that does not allow to continue with the tDCS application (skip for Control Group).
- The participant meets an exclusion criterion that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded on a Master Data file. Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, are randomized and receive the study intervention, and subsequently withdraw or are discontinued from the study, will be replaced. Data from participants who withdraw from the study will not be used.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to return for any of the expected 4 scheduled visits or if the study staff is unable to contact the participant. The following actions must be taken if a participant fails to return to the laboratory for the required study day:

- The site will attempt to contact the participant, reschedule the missed day as soon as possible (the next day), counsel the participant on the importance of maintaining the assigned day schedule, and ascertain if the participant wishes to and/or should continue in the study. The data and time for each day will be recorded in the Master Data file.
- Before a participant is deemed lost to follow-up, the investigator or the main research manager will make every effort to regain contact with the participant. The contact
- If the participant continues to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Demographic information assessment

We will collect participants' age, gender, education level, race, and ethnicity at the start of the study (Day 1), independently of the group to which they are assigned.

Participants' expectations of tDCS assessment

The tDCS expectation scores will be assessed using a 1-item survey adapted from the Expectation Assessment Scale (Rabipour et al., 2015, doi:10.1016/j.bbr.2015.01.002) for tDCS research. The scores range from 0 (no expectation) to 8 (high expectations); a score of 4 is considered neutral. Only participants from the Groups tDCS1, tDCS2, and tDCS3 will rate their expectations of tDCS's effect on their motor learning at the beginning of 3 days of motor training, and after the Follow-up Session (Day 10). We will measure the change in tDCS expectations from Day 1 to Day 10 and the variability in tDCS expectations (i.e., the coefficient of variation for tDCS expectation scores across the 4 days). Day 1 tDCS expectation score will also be considered as the baseline expectation of tDCS. Expectation of tDCS assessment will be evaluated only to participants assigned to the experimental tDCS groups (tDCS1, tDCS2, tDCS3)

Motor performance assessment

The task apparatus has three target cups placed radially around a central start cup, spaced 16 cm apart; each cup is 9.5 cm in diameter and 5.8 cm in height. Participants will use their nondominant (left) hand to acquire and transport two raw kidney beans at a time from the start location to one of the three target locations with a spoon, as quickly and accurately as possible. Using the nondominant left hand will maximize the likelihood of a learning effect, as our previous research has shown a ceiling effect on the dominant hand while the nondominant hand improves substantially with practice (Schaefer et al., 2017, doi:10.1080/13803395.2016.1236905). Each trial will begin with 30 raw kidney beans located in the start cup. At the start of each trial, participants will be instructed to reach for and use the spoon to acquire and transport beans first to the left target cup, then to the center target cup, then to the right target cup, and then repeat this sequence until the last two kidney beans are deposited in the final cup. Thus, each trial comprises 15 repetitions, five reaches to each target. We collect trial time and error (beans drop). Kinematic data will be collected using a non-invasive computer measurement system. Specifically, subjects' arm and hand movements will be collected using an electromagnetic tracking system (Flock of Birds®, Ascension Technology Corp, Shelburne, VT). Kinematic data will be collected through a sensor that is placed at the center of mass on the underside of a conventional plastic spoon, at 100 Hz and filtered at 8 Hz using a second-order Butterworth filter, which allows us to quantify quality of movement by resultant velocity, and acceleration. The primary outcome will be performance on motor task one week after final training session (Follow-up; Day 4). This will be calculated as the average of two motor task trials completed one week after the last training session (Day 4), after controlling for baseline (Day 1). We will also assess other secondary outcomes: 1) Change in motor performance over

the course of training: average time of trials per training day (Day 1, 2, 3); 2) Average dwell time: the average amount of time spent in the home cup for each repetition, averaged across the two follow-up trials (Day 4), controlling for baseline (Day 1); 3) Average peak reach velocity: the average peak velocity for the outward portion of each repetition, averaged across the two follow-up trials, controlling for baseline. These assessments will be collected for all participants.

tDCS Blinding

Blinding integrity was assessed across all experimental groups (tDCS1, tDCS2, and tDCS3) to determine the effectiveness of the sham-control protocol. Specifically, at the end of the follow-up session (day 4), participants were required to guess whether they had received active or sham stimulation.

Exit Questionnaires

We will also administer the Short Suggestibility Scale, a 21-item shortened version of the Multidimensional Iowa Suggestibility Scale that measures a reliable general suggestibility trait (Kotov et al., 2004, <https://renaissance.stonybrookmedicine.edu/sites/default/files/MISSBriefManual.pdf>). Participants will be asked to respond to each item on a 5-point Likert scale, where 1 represents "not at all" and 5 represents "a lot." There will also be additional free-response questions to assess participants' experience with the session. These assessments will be administered to all participants at the end of the study (Day 4). Furthermore, we will assess prior knowledge of tDCS stimulation among the experimental groups (tDCS1, tDCS2, and tDCS3) using a binary (yes/no) question.

8.2 SAFETY ASSESSMENTS

Safety criteria for inclusion in a tDCS study.

Only participants who positively pass the tDCS screening form (Thair et al., 2017) will be included in the study.

Safety tDCS assessment

Once randomly assigned to one of the Groups, those belonging to the experimental tDCS groups (tDCS1, tDCS2, tDCS3) will have to complete the tDCS safety questionnaire (Thair et al., 2017, doi:10.3389/fnins.2017.00641) prior to the application of the tDCS concurrent with motor training (Pre-tDCS Side effects questionnaire). The tDCS safety questionnaire consists of a 14-symptom scale (e.g., headache, fatigue), which will have to be self-rated from 1 ("absent") to 10 ("severe"). A score <5 on each symptom will be necessary to proceed with the intervention. Moreover, at the end of each tDCS and motor training session, the presence and severity of negative symptoms associated with tDCS will again be quantified with the same 14-symptom safety questionnaire (Post-tDCS Side effects questionnaire). Participants with a score of ≥5 for any symptom will be asked to remain in the laboratory until those symptoms had diminished or until both the participant and the experimenter felt satisfied that they could leave. Participants in the Control group will be excluded from these assessments.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

This protocol uses the definition of adverse event from the [*OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events*](#) (2007): Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Any adverse event that:

- Results in death
- Is life-threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition that investigators judge to represent significant hazards

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol-defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will be evaluated by the Principal Investigator to determine their potential link to the tDCS or motor training procedures. Causality will be classified according to the following criteria:

- **Related:** The event occurs in a clear temporal order following the intervention and is a recognized side effect of tDCS (such as scalp redness, tingling, or itching at the electrode site) or the posture use during the motor training.
- **Possibly Related:** The event occurs after the intervention but could also be explained by the participant's health condition or other environmental factors (like headache or fatigue).
- **Unrelated:** The event is caused by external factors unrelated to the study (for example, a pre-existing injury or seasonal illness) and does not follow a temporal relationship with the study procedures.

8.3.3.3 EXPECTEDNESS

An expert in tDCS application will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The clinical course of each AE will be followed until resolution, stabilization, or until it has been ultimately determined that the study treatment or participation is not the probable cause. The PI or research manager will evaluate all apparent AEs and determine the necessary follow-up and reporting required.

8.3.5 ADVERSE EVENT REPORTING

Assessment of AEs (including Unanticipated Problems) will be performed continuously during the study period. Possible AEs will be detected through spontaneous reports from the subject, direct questioning, or direct examination during study days (e.g., tDCS safety questionnaire). When an AE has been identified, the study team will take the necessary action to protect the study participant, then complete the Study Adverse Event Worksheet and/or log. Any SAE will be reported immediately, i.e., within 24 hours to the PI; all others will be reported within 48 hours. The PI will consult with the DSMB as appropriate and will determine if any action is required to resolve the AE. The PI will also report any such AE to ASU IRB.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

In consultation with the PI, a trained member of the study team will be responsible for conducting an evaluation of a serious adverse event and shall report the results of such evaluation to the NIH and the reviewing Institutional Review Board (IRB) as soon as possible. Any SAE (serious or not) will be reported immediately, i.e., within 24 hours to the PI; all others will be reported within 48 hours.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

The application of the tDCS safety questionnaire before tDCS will help reduce unanticipated problems associated with the stimulation.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

Similar to the AE, see Section 8.3.5.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- **Primary Efficacy Endpoint(s):** Based on pilot data, we predict that the group receiving positive information about the efficacy of tDCS (n=36) prior to each stimulation session will show more motor learning, while the group receiving negative information (n=36) will show less motor learning, relative to the group receiving unprimed sham tDCS (n=36), controlling for multiple comparisons. The primary outcome will be motor performance (measured as trial time) at one-week post-training (primary timepoint).
- **Secondary Efficacy Endpoint(s):**

Secondary analyses will consider how the level of expectation (quantified on a 1-item of the scale from 0-8 on the Expectation Assessment Scale) affects the primary endpoint, as well as the secondary endpoint.

9.2 SAMPLE SIZE DETERMINATION

By a priori defining average trial time at follow up as our primary outcome, we estimate the necessary sample size to detect a significant expectancy effect to be n/group=36 for 80% statistical power, assuming a standardized mean difference of $d=0.6$ at $\alpha=0.05$. We note that $d=0.6$ is smaller than our pilot data suggest (i.e., faster trial times at retention in the sham tDCS group than the control group, indicating more learning), making this a conservative estimate of the true effect size. To allow for 10% attrition, we will enroll n/group=40, which is very feasible given the lab's history for recruitment in tDCS studies and other motor training studies. Our preliminary data suggest that the relationship between tDCS expectation scores and learning is relatively strong ($r^2 > 0.3$). Conservatively, if we estimate the true r^2 to be 0.2, then n/group=36 would yield 80% statistical power to detect an $r^2 \geq 0.2$ ($\alpha=0.05$) for the relationship between expectations and learning (β_4) in the sham group by itself, $y_i = \beta_3 + \beta_4$ (Expectation) + ϵ_i . Expectations will be quantified from EAS on day one in this aim.

When appropriate, we will implement Bonferroni corrections within families of related tests to control the family-wise Type 1 error rate. Further, all analysis plans will be pre-registered prior to the analysis being undertaken, all analyses will be reported, and all code/data will be made available to increase the reproducibility of the results.

9.3 POPULATIONS FOR ANALYSES

Per-Protocol Analysis Dataset: Participants who completed 100% of study intervention for 100% of the days within the maintenance period.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

- Descriptive statistics: Continuous data will be presented as Mean $\pm$ Standard Deviation; categorical data will be presented as Frequencies (n) and group percentages (%).
- Inferential tests: p-value = .05, confidence intervals = 95%, one-tailed
- Covariates will be pre-specified.
- Checks of normality will be performed and corrective procedures will be applied using log-transformations or nonparametric tests.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

To test our primary endpoint, multivariable linear regression models will test the effect of group on motor learning (task performance on Day 10), while controlling for baseline motor performance (i.e., the average of the 10 trials on Day 1). A directional hypothesis will be used (one-tailed) with $\beta_{\text{tDCS Groups}}$. Task performance is a continuous variable, measured as time. Beta values, 95% CI, and effect sizes (either as Cohen's d or partial R-squared) will be reported. Analysis will include those who completed the full study protocol (per-protocol analysis dataset). Thus, we do not expect any missing data nor loss to follow-up.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Secondary endpoint will be analyzed and reported like the primary endpoint.

9.4.4 SAFETY ANALYSES

There are no safety endpoints. For more information about Safety Assessments, please see Section 8.2.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Demographic characteristics between study arms (groups) will be compared using nonparametric tests and chi-squared tests to determine whether groups are balanced for age, sex, education, ethnicity, race, and knowledge of tDCS.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

Age, sex, education and race/ethnicity will be considered as co-variates in the proposed regression models in both primary and secondary endpoints.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be posted upon study completion by measure and time point with no identifiers.

9.4.9 EXPLORATORY ANALYSES

N/A

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant, and written documentation of informed consent will be completed prior to starting the study intervention and after the approval of the ASU's Institutional Review Board (IRB)

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The PI or research assistant will be responsible for consenting subjects. The consent process will occur in the laboratory. The PI or research assistant will verbally describe in lay language the nature and risks of the study as outlined in the informed consent form. The PI or research assistant will answer any questions that the potential subject may have. Once the subject has been informed, he or she will be asked to sign a copy of the informed consent form. The subject will also be given another copy of the consent form for his or her own records. For participants who do not speak or read English, a translated form of the consent form can be provided. Based on previous studies in SBHSE with similar subject criteria, we anticipate that having consent forms printed in Spanish may be helpful. We acknowledge that such translated consent forms will be submitted after the English version is approved.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to investigator and funding agency. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study day schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (ie, significant protocol violations)
- Data that are not sufficiently complete and/or evaluable

- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

To ensure the protection of human subjects and the integrity of research data, all members of the research team will complete CITI training, with the PI (Dr. Sydney Schaefer) maintaining up-to-date completion records. Once informed consent is provided, participants are assigned a unique subject identification number (e.g., tDCS_01) to which all research data is linked. A single, password-protected spreadsheet—filed separately from data collection sheets—serves as the exclusive "key" for identifying subjects. Physical records, including signed consent forms, are stored in a locked file cabinet within a secured laboratory room accessible only via key or key-card. Contact information is stored securely at the clinical site for internal study use, while research data for statistical analysis and scientific reporting is transmitted to the Data Coordinating Center identified only by the unique study ID. All study databases and management systems are password-protected, and at the end of the study, records will be de-identified and archived in accordance with IRB, institutional, and sponsor requirements.

In compliance with NIH Data Sharing Policies, the PI will implement proper safeguards for data dissemination and reuse, ensuring that all shared results are thoroughly de-identified and untraceable to specific participants. To further protect privacy, this research is covered by a Certificate of Confidentiality (CoC) issued by the Secretary of Health and Human Services (HHS). Per NIH policy and federal regulations (45 CFR Part 75.303(a)), the research team will establish effective internal controls to protect identifiable information from forced disclosure, except where the participant consents or where federal, state, or local law requires disclosure. Additionally, the clinical site will permit authorized representatives of the sponsor, funding agency, IRB, or regulatory agencies to inspect all required documents and records, including medical or pharmacy records, to ensure compliance and study oversight.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see <https://humansubjects.nih.gov/coc/index>). As set forth in [45 CFR Part 75.303\(a\)](#) and [NIHGPS Chapter 8.3](#), recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to

inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Before publication, only specific personnel will have direct access to the data and the analyses. After publication, de-identified, aggregated, final data will be made available at online data repositories so that other investigators can verify or follow-up on the reported analyses. Data analyzing scripts will also be made available at online repositories. Candidate online repositories include Open Science Framework (osf.io), sportrxiv.org, github.com, and/or zenodo.org. De-identified data of this research study may also be used in reports, presentations, and publications. After publication, de-identified, aggregated data may also be made publicly available at Open Science Framework (osf.io), sportrxiv.org, GitHub (github.com), and/or Zenodo (zenodo.org), so that other investigators can verify or follow up on the reported analyses.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

The purpose of this plan is to define the responsibilities of the Data Safety Monitoring Board (DSMB), detail membership requirements, describe the data to be reviewed, delineate the meeting process, and outline the considerations and policies of the DSMB. The DSMB will act in an expert, independent advisory capacity to monitor participant safety and evaluate the efficacy and conduct of the study. For the purposes of study oversight, the PI (Dr. Sydney Schaefer), will serve as an Executive Committee member

The DSMB members were selected by the principal investigators, as Executive Committee members, and met the following requirements:

- willing to serve as a DSMB member for the duration of the study
- able to comply with the conflict of interest policy specified in this charter

Although DSMB members are expected to serve for the duration of the study, in the unlikely event that a member is unable to continue participation, the reason will be documented and a replacement member will be selected by the principal investigators. The new member must have comparable expertise and qualifications to the DSMB member he/she is replacing.

Principal Investigator

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DSMB Responsibilities

The DSMB's responsibilities are to:

- Review the research protocol, informed consent documents, and plans for data safety and monitoring periodically during the study, and at the conclusion of the study.
- Evaluate the progress of the study, including participant recruitment, accrual and retention, participant risk versus benefit, performance of the study site, and other factors that may affect study outcome.
- Review participant safety, protocol violations, medication use, adverse events, and any other relevant topics in order to assure patient safety and study integrity.
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on participant safety, scientific integrity, or the ethics of conducting the study.
- Review and evaluate ad hoc safety issues concerning the study at the request of the investigators as Executive Committee members.
- Make recommendations to the investigators concerning continuation, termination, or other modifications of the study based on the observed beneficial or adverse effects of the study.
- Operate according to the procedures described in this plan and all procedures of the DSMB

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of the Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including physical therapy, psychology, or bioengineering.

Conflict of interest

DSMB members should have no other relationship with the investigators that could impair the members' ability to objectively review study data as set forth below:

- DSMB members must not have any real or perceived scientific, financial, professional, personal, proprietary, or other conflict of interest related to the conduct, outcome, or impact of the study. This may include having been or being employed by the investigators, having a fiduciary interest in the sponsor, conducting and/or managing the study, and/or having contact with participants during the course of regular clinical care
- DSMB members must not be engaged in any simultaneously occurring competitive studies in any role that could pose a conflict of interest. DSMB members must also identify and disclose any concurrent service on other DSMBs of the same, related, or competing products
- DSMB members must be independent from IRBs, regulatory agencies, principal investigators All DSMB members must disclose all possible conflicts of interest in writing prior to beginning service as a

Projected Schedule of Meetings

An initial meeting of the DSMB will be held within one month of the study initiation visit in order for the members to review the charter, form an understanding of the protocol and definitions being used, establish a distribution and meeting schedule, review the study modification and/or termination

guidelines, and finalize format and protocol-specified statistical methods to be used in reports to be considered by the DSMB. The DSMB will review, discuss and provide its input to adverse events, protocol violations, enrollment summary, review of medication preparation, distribution protocol and management, data integrity and medication issues.

10.1.7 CLINICAL MONITORING

If any concern or unexpected issue is identified by the DSMB at either site with any subject that could be of potential risk or concern to other subjects, action will be taken to address, mitigate, and/or eliminate such risk from the study. Any serious adverse events (AE) will be reported immediately, i.e., within 24 hours, to the study coordinator and site PI. The site PI and DSMB will determine if any action is required to resolve the AE. The site PI will also report the AE to the IRB, and to the lead site study coordinator and PI.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

Informed consent: Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents.

Source documents and the electronic data: Data will be initially captured on specific documents (see Section 10.1.9) and will ultimately be entered into the study database.

Intervention Fidelity: Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in Section 6.2.1.

If independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

All physical data forms will be completed during data collection, and will be filed in a file folder labeled with only with ID numbers. Cleared lab personnel will manually enter any hard copy data (e.g. clinical tests, trial times) into password protected spreadsheets. All electronic records and data will be managed as data spreadsheets in .jmp, .xlsx, .csv, or .mat format for reading and analyzing in JMP, Microsoft Excel, R, or MATLAB. Spreadsheets will then be accessed via a password-protected Dropbox folder by cleared members of the research team only. Hard copies of any data collection sheets will be locked in a different file cabinet drawer than the signed consent forms in the secured lab space.

10.1.9.2 STUDY RECORDS RETENTION

All data will be stored for 7 years after completion of the study. Hard copies will remain in the locked file cabinets, and electronic copies will be written to DVD and stored there as well. Two copies of DVDs will be made, with one stored in the laboratory and the other in the PI's locked office.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 7 working days of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the National Center for Complementary and Integrative Health Program Official. Protocol deviations must be sent to the reviewing IRB per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals.

Before publication, only the personnel listed on this document will have direct access to the data and the analyses. After publication, de-identified, aggregated, final data will be made available at online data repositories so that other investigators can verify or follow-up on the reported analyses. We expect the final research data of this study to be a computerized dataset with computed variables, not including any information that would allow reverse engineering of an identity (e.g., names, birthdates, and zip codes). We might include raw kinematic data, which is not identifiable due to the nature of the data (the position and orientation of subjects' arms and hands during performing the motor tasks). Data analyzing scripts will also be made available at online repositories. Candidate online repositories include Open Science Framework (osf.io), sportrxiv.org, github.com, and/or zenodo.org.

After publication, de-identified, aggregated data can also be made publicly available at Open Science Framework (osf.io), sportrxiv.org, GitHub (github.com) or Zenodo (Zenodo.org), so that other investigators can verify or follow up on the reported analyses. De-identified data of this research study may also be used in reports, presentations, and publications.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Center for Complementary and Integrative Health as established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
ASU	Arizona State University
CFR	Code of Federal Regulations
CITI	Collaborative Institutional Training Initiative
CoC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
DSMB	Data Safety Monitoring Board
EAS	Expectation Assessment Scale
FDA	US Food and Drug Administration
GCP	Good Clinical Practices
HHS	Health and Human Services
Hz	Hertz (Frequency)
IRB	Institutional Review Board
mA	Milliamps (Current)

N/A	Not Applicable
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
QC	Quality Control
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SONA	Participant Recruitment System
tDCS	Transcranial Direct Current Stimulation
TMS	Transcranial Magnetic Stimulation
tRNS	Transcutaneous Random Noise Stimulation

10.4 PROTOCOL AMENDMENT HISTORY

N/A

11 REFERENCES