Naval Medical Center San Diego
CONSENT TO PARTICIPATE IN RESEARCH
Title: Transcranial Direct Current Stimulation (tDCS) and Cognitive Training to Improve Concentration and Working Memory in Active Duty Service Members Following Mild Traumatic Brain Injury (mTBI): A Pilot Study
Principal Investigator: Lars Hungerford, PhD, ABPP-CN

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to carefully review this information. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION:

The proposed study will evaluate a new approach to cognitive rehabilitation of mild traumatic brain injury (mTBI) using a non-invasive brain stimulation technique called transcranial Direct Current Stimulation (tDCS). We will investigate how tDCS combined with cognitive training influences attention and working memory in Active Duty Service Members with a history of mild traumatic brain injury (TBI). Specifically, we want to test whether any neurocognitive complaints you may be experiencing, like attention, concentration, memory or other related thinking difficulties, are improved by tDCS and cognitive training. By doing this study, we hope to find a reliable method of treating mild TBI cognitive symptoms.

You will be asked to complete baseline and post-treatment evaluations which consist of self-reported symptom questionnaires, an evaluation of your cognitive abilities, and evaluation of brain function by electroencephalogram (EEG), eye tracking, and optional magnetic resonance imaging (MRI). After baseline, you will complete 5 daily sessions of tDCS and computerized cognitive training. Following the 5-day treatment, you will have a post-treatment evaluation that is exactly the same as the one at baseline. There will be one 6-week follow-up visit where you will again be asked to fill out symptom questionnaires and undergo a brief evaluation of your cognitive functioning, and have your brain function assessed by EEG. Overall, your participation in this research will last 11-12 hours in total, with the main intervention lasting for one week, followed by a six-week follow-up appointment.

Your participation in this research project may or may not be of direct benefit to you personally. However, the treatments used in this study are designed to help people with a history of mild TBI. Also, results of this study may help the investigators develop tools for the improved treatment of mild TBI symptoms.

Participation in this study may involve some added discomforts. The procedures used may cause:
A. Fatigue, boredom, or stress while completing the assessments.
B. Low-risk discomfort from initial application of the brain stimulation procedure, including light itching, burning, or tingling under the electrode, headache, fatigue and/or nausea.
C. Fatigue and discomfort due to sitting motionless while in the MRI scan. The MRI scan could also make you feel claustrophobic.
D. As with any research study, the possibility of breach of confidentiality exists.

A complete description of risks is included in the Research Details Study Risks section.

Participation is voluntary. If you choose not to take part in the study, you may already be eligible to receive other treatments from your medical providers. Talk to your doctor if you have any questions about other treatments that may be available to you. Your decision to participate will not affect your future care at Naval Medical Center San Diego.

If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about in all sections of the consent form, including the risks and possible benefits to you.

Please tell the researchers if you are taking part in another research study.

NOTE: If you are providing consent as a legally authorized representative (LAR), "you" or "your" refers to the research participant.

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you are an Active Duty Service Member who sustained a mild TBI and are currently experiencing symptoms related to attention, concentration, or other related thinking processes. The purpose of this research study is to test new methods for treatment of cognitive symptoms related to mild TBI.

Your individual participation will take place at NMCSD over the course of eight total visits, which will occur over a 7 week period. The first visit will be a baseline session that will include interview assessments, paper questionnaires, EEG, and an optional MRI, lasting approximately 3.5 hours (2.5 hours without MRI). Sessions 2-6 will occur Monday through Friday of the following week, where you will complete the tDCS and cognitive training intervention that will last approximately 1 hour per session. The post-intervention assessment (Session 7) will include interview assessments, paper questionnaires, EEG, and another optional MRI, lasting approximately 2.5 hours (1.5 hours without MRI). Finally, you will complete a follow-up visit six weeks later that will include interview assessments, paper questionnaires only, and an EEG, lasting approximately 1.25 hours. Overall, your participation will last no more than 11-12 hours in total.

Table 1. Schedule of Assessments

Task Name	Task Type	Visit #1	Visit #2-6	Visit # 7	6-week follow-up	Length
Informed Consent, HIPAA	Regulatory	X				20 min
OSU-TBI-ID	Structured interview to assess past head trauma (staff-administered)	X				25 min
MRI Brain w/out Contrast (optional)		X		X		45 min
Pre and Post tDCS Symptom Rating Questionnaire (SRQ)	Questionnaire to assess symptoms pre and post stimulation		X			5 min
NIH Toolbox Quality of Life assessment	Questionnaire to assess quality of life with regard to cognitive, social, emotional, and behavioral abilities (49 questions)	X		X	X	20 min
Neurobehavioral Symptom Inventory	Measure of common post-concussive symptoms	X		X	X	5 min
Insomnia Severity Index	Measure of insomnia severity	X		X	X	5 min
Symbol Digit Modalities Test	Measure of visual attention and working memory	X		X	X	10 min
NAB Attention Module	4 subtests to assess visual and auditory attention, working memory, and scanning.	X		X	X	10 min
Fusion Task	Multi-modal assessment of brain function including EEG and eye tracking	X		X	X	20 min
tDCS/Sham	Intervention		X			50 min

EEG (set up and resting)	EEG will be collected to assess neural dynamics during rest and during performance of generalization tasks.	X		X	X	(30 min set up-done during questionnaires) + 6 minutes resting
Cognitive Training Protocol (BrainHQ Tasks)	Computerized cognitive training tasks (see Table 2 for details)		X			46 min (completed during tDCS)
Total Length (minutes)		**190**	**275**	**145**	**70**	**680**

After completing the baseline assessment, you will receive verbal feedback regarding your baseline testing results. You will be notified if any important new information is found that may affect your willingness to continue.

All assessments are done for research only. At the end of this research study the clinical results, which includes research results about you, may be shared with you upon your request. The study results will include a summary document that describes the evaluations performed, including cognitive tests and symptom questionnaires, and descriptions of the findings of these evaluations. If the results of this research might influence your medical care after you complete participation, the investigators will contact you to let you know these results.

Overall, there will be about 60 people taking part in the study. All volunteering participants for this study will be Active Duty Service Members recruited from Naval Medical Center San Diego, over a period of two years.

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you will need to have some tests and provide some information so that the Investigator can confirm that you qualify for the study. This is called the "Screening Process". These tests may have been done or this information collected as a part of your regular medical care. The information collected from the screening process will be used for the purpose of confirming study eligibility related to mild TBI and other inclusion/exclusion criteria.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

- You will complete tasks and answer questions to measure your thinking abilities. You will also answer questions about your thoughts and feelings and symptoms you may be experiencing.
- You will do tasks on a computer while your eye movements and brain activity (EEG) are recorded.
- You will give us information about yourself such as military, Veteran, and employment status, medical and educational history, date of birth, and contact information.

- We will review your medical history to confirm possible history of brain injuries and other information used to determine whether you are eligible to participate.
- You will complete one baseline assessment, five tDCS (stimulation) sessions, and two follow-up visits.
    - tDCS involves applying a weak electrical current to the scalp. We will be using the Neuroelectrics StarStim 8 device to apply the stimulation. This device is experimental.
    - The experimental part of this study is the use of ***active*** transcranial Direct Current Stimulation (tDCS) to treat the cognitive effects of mild TBI. Participants in the study will be divided into two groups based on randomization, a process similar to flipping a coin. Neither you nor the study investigator will choose, or know, which group you are in.
        - The experimental group will receive active tCDS while completing computerized cognitive training on BrainHQ.
        - The control group will receive sham tCDS while completing computerized cognitive training on BrainHQ.
- You have the option to complete two 3T Magnetic Resonance Imaging (MRI) scans; these will occur at your baseline session (Visit 1) and your post-intervention session (Visit 7). The MRI scans will result in pictures of your brain that are similar to x-rays without exposure to radiation. These pictures will be used to measure the structure and activity of certain brain regions. During the MRI scans, you will be asked to lie down on a bed, and the bed will slide into the scanner, which is a tunnel that is open on both ends. You will be asked to either simply lie still while the scan is taking place or perform a task in which you must pay attention and respond to certain stimuli by pressing buttons.
- The research office visits will be conducted at the Naval Medical Center San Diego and the MRI scans will take place at the NMCSD Radiology Department.

While participating in this research study, please do not take part in any other intervention research studies or cognitive treatments without approval from the investigators. Taking part in other research studies would make it difficult for the researchers to know which treatment affected the outcomes.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there is a risk of:

There is currently no evidence of serious side-effects related to transcranial Direct Current Stimulation (tDCS). Listed below are mild side effects that typically go away after stopping tDCS:

- Light itching, burning, or tingling under the electrode (68 out of 100 people)
- Headache (13 out of 100 people)
- Fatigue (20 out of 100 people)
- Nausea (2 out of 100 people)

You may choose to discontinue stimulation at any time during the session if you are experiencing excessive discomfort or side effects.

Some subjects may find the EEG cap uncomfortable. You may choose to discontinue the EEG at any time during the session if you are experiencing excessive discomfort or side effects. If necessary, the EEG cap can be removed to relieve discomfort.

The risks associated with MRI scans are:

- Projectiles: Objects with magnetic properties can be pulled into the magnet and turn into projectiles. To minimize this risk, we ask that subjects remove all metallic items (watches, cell phones, hair pins, etc.) prior to entering the scanner and by controlling access to the scanner.
- Claustrophobia: The scanner is a long narrow tube that may cause some people to feel uncomfortable due to a fear of small enclosed spaces.
- Hearing Damage: The noise generated by the operation of the scanner during the study is loud enough to cause hearing damage if you do not wear hearing protection. Hearing protection is required and is provided by the investigator.
- Nerve Stimulation: Some people experience localized tingling, twitching, or muscle contractions during MRI scans. This is expected, but if it is uncomfortable please notify the investigator.
- Disruption of Devices: Some devices can be damaged by magnetic fields and should not be brought into the scanner room. This includes some implanted devices such as pacemakers, cochlear implants, insulin pumps, nerve stimulators, etc. If you have any implanted device, notify the investigator.
- Heating of Devices: The radiofrequency waves used in MRI can heat conductive materials such as metal implants (screws, plates, rods, wires, artificial joints, etc.), certain tattoo inks, certain clothing fabrics, jewelry, medication patches, wigs, etc. You will be asked to remove these items if possible. If they cannot be removed, you will be asked to provide more information to allow MRI staff to be able to make determination about the safety of proceeding with the scan.

If we feel it is needed or you request it, we will provide you with referrals to a mental health care provider for evaluation or treatment at your option if a licensed member of the study team judges that you may benefit from these services based upon evidence of mental health difficulties. However, this study is not intended to diagnose or treat any mental health conditions. Non-referral does not imply the absence of a mental health condition.

Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?:

Your participation in this research may or may not be of direct benefit to you personally. However, others may benefit in the future from the information learned during this study. The treatments used in this study are designed to help people with mild TBI. Also, results of this study may help the investigator develop tools for the improved treatment of mild TBI.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

If you choose to take part in the study, you will be asked not to partake in other cognitive training until the study is over. You can keep taking part in other treatments that do not involve cognitive training. You can withdraw from the study if you change your mind.
Choosing not to participate in this research study is also an option. If you choose not to take part in this study, you may already be eligible to receive other cognitive treatments from your medical providers. Talk to your doctor if you have any questions about other cognitive treatments that may be available to you.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

No, you will not receive any compensation for participating in this study. If you choose to do so, a letter of appreciation can be issued to you at the end of your participation in the study.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

10. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

Lars Hungerford, Ph.D., ABPP-CN
Senior Clinical Research Director, TBICoE
Naval Medical Center San Diego
Email: lars.d.hungerford.ctr@mail.mil

11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

The present study is supported by salaried scientific staff of The Defense and Veterans Brain Injury Center (DVBIC).

12. SOURCE OF FUNDING:

This is an unfunded study utilizing salaried scientific staff of the Defense and Veterans Brain Injury Center (DVBIC).

13. LOCATION OF THE RESEARCH:

Research will be conducted at Naval Medical Center San Diego.

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

No study personnel have any personal or financial interests associated with the conduct or outcomes of this research study.

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at: http://www.dtic.mil/whs/directives/infomgt/forms/eforms/dd2005.pdf.

The research team will keep your research records. These records may be looked at by staff from the NMCSD IRB, DVBIC, General Dynamics Information Technology (GDIT), Defense Health Agency (DHA), the Institutional Review Board (IRB), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to: Your research records will be labeled with a code number. The list that matches your name with the code number will be kept in a locked file in the research team's office. Any research records that identify you will be kept only as paper records in a secure location, or as files behind the secure computer firewall. Identifiers might be removed from the identifiable private information that are collected. After that removal, the information could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

Your data will be sent to the Federal Interagency Traumatic Brain Injury Research Informatics System (FITBIR). All data that is sent to FITBIR will be completely free of any identifying information such as names and unique subject identification numbers.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

By signing this document, you give your permission for information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

Research Staff, DVBIC, GDIT, DHA, IRB, and the DoD will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

16. INCIDENTAL FINDINGS

There is a possibility that while reviewing your test results we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away.

You do not have an option to decline receiving information about an incidental finding. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding.

We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

17. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part which means you do not have to take part if you do not want to. Participation or declination by active duty participants will not affect duty status or eligibility for advancement. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty or loss of benefits to which you are otherwise entitled.

You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

18. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

You may withdraw your consent at any time and stop participating in this research study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must notify Dr. Lars Hungerford at (619) 532-6711 to ensure timely

removal from the study. If you do not follow these procedures, you may not have your data withdrawn from the study efficiently and you will be continued to be contacted by research staff.

If you are receiving treatment as part of this research study, you will no longer be eligible for such research-related treatment. Contact your personal physician to discuss medical treatment for your condition.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

The principal investigator of this research study may terminate your participation in this research study at any time if he determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

19. CONTACT INFORMATION:

Principal Investigator (PI)
The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Lars Hungerford, PhD, ABPP-CN
Phone: (619) 532-5715
Mailing Address: 34800 Bob Wilson Drive, San Diego, CA 92134

NMCSD Human Research Protection Program (HRPP) Office
The Human Research Protection Program Office Point of Contact will be available to answer questions or discuss concerns you may have about this research study.

Human Protections Administrator/HRPP POC: Mitchell Dukovich, Ph.D.
Phone: (619) 532-5524

Institutional Review Board (IRB) Office
If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:

Institutional Review Board	or	Clinical Investigation Department
(619) 532-9927		(619) 532-6099

California Experimental Subject's Bill of Rights

(a) Be informed of the nature and purpose of the experiment.

(b) Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

(c) Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

(d) Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

(e) Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

(f) Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

(g) Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

(h) Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

(i) Be given a copy of the signed and dated written consent form as provided for by Section 24173 or 24178.

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

SIGNATURE OF PARTICIPANT

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT
(Can only be signed by an investigator or staff approved to administer consent)

_____
Printed Name of Administering Individual

_____ _____
Signature of Administering Individual Date