Combined Transcranial Direct Current Stimulation and Virtual Reality for PTSD

NCT03372460

Informed Consent Form

Document Date: 07/13/2022

Subject Name: **Date:**

Title of Study: Combined Transcranial Direct Current Stimulation and Virtual Reality for PTSD

Principal Investigators: Noah S. Philip, M.D. and Mascha Frank, Ph.D.

1. Purpose of study and how long it will last:

The goal of this research study is to find out if the use of a low level electrical current on the scalp, called transcranial direct current stimulation or tDCS, makes it easier for Veterans with posttraumatic stress disorder (PTSD) to watch deployment scenes (e.g. Iraq, Afghanistan) using virtual reality (VR). We will call this combination of tDCS and virtual reality, tDCS+VR. The purpose behind this study is to test whether tDCS+VR could be an effective non-medication treatment for Veterans with PTSD. Ultimately, results from this study are intended to develop a possible new treatment for PTSD.

If you decide to participate, involvement after you sign this consent form consists of up to thirteen study visits. The first visit will include screening assessments. On the second visit you will get a scan of your brain (MRI). Visits three through eight will include tDCS+VR sessions and will occur over the course of 2-3 weeks. On the ninth visit you will get a second MRI. Visits ten and eleven are follow-up appointments that will occur 1 and 3 months after the last tDCS+VR session. The twelfth visit is an optional visit where you will undergo an EEG, if you choose to participate, this visit will occur before the tDCS+VR sessions. Visit thirteen is an optional visit where you will undergo a follow-up MRI. All screening, tDCS+VR sessions, optional EEG visit and follow-up visits will occur at the Providence VA Medical Center (PVAMC). If the study Principal Investigators (PIs) deem it appropriate or necessary, study visits/session may occur virtually, via video or telephone. The MRIs will occur at either the PVAMC or the Brown University MRI Research Facility. The researchers plan for ninety people to be part of this study.

2. Description of the study including procedures to be used:

Screening: If you agree to participate, you will first undergo measures to see if you are eligible. These will include questionnaires to fill out and an interview with trained study personnel. Study investigators will review your current health history and medications. You will also be asked to answer questions about your military experience, symptoms related to PTSD/depression/anxiety, and prior or current drug/alcohol use. If you are a woman of childbearing age you will be asked about the likelihood of pregnancy. When it is appropriate you will be asked to complete a pregnancy test or urine drug test prior to study procedures. You may refuse to answer any of the questions. This first visit will last approximately 3-3.5 hours.

MRI: MRIs will take place before and after you have done all tDCS+VR sessions. When you arrive for the scan, you will receive a brief orientation to the facility and will be asked to review safety forms, remove all metal/jewelry, and to make sure there is no metal in your body. After completion of the safety form(s), you will have a scan done on your brain. You will be asked to lie in the scanner for about 45 minutes and complete a task. You will be able to hear and speak to the MRI personnel/research staff. The scanner makes loud noises during imaging. Ear protection will be provided to reduce the noise level. The first MRI scan, will take place before the virtual reality sessions. A second MRI scan will be done after the last virtual reality session. All of the scans will take about 1 hour. There is the possibility of additional MRIs in

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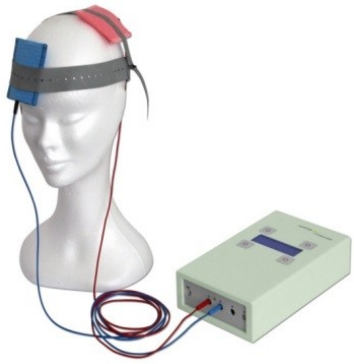
the case of scanning related failures. Participants may also choose to participate in an optional MRI during the follow-up period.

Follow-Up MRI (*Optional*): This MRI will follow the same procedures and take the same amount of time as the pre and post tDCS+VR scans. It will take place during the follow-up period, approximately 1-month after your last tDCS+VR session. This visit is optional and will not affect your participation in the previous study procedures.

_____ (initial) I consent to participating in the follow-up MRI portion of this study.

_____ (initial) I do not consent to participating in the follow-up MRI portion of this study



tDCS+Virtual Reality: Visits 3-8 include the virtual reality sessions. Appointments for these visits will be made within a 2-3 week period, amounting to about 2-3 visits per week. These visits will take about 1 hour each. You will also be asked to complete some of the same questionnaires and interviews from the screening visit after some of these sessions. Visits that include questionnaires and/or interviews will be slightly longer (up to 2 hours).

During each of the visits you will be watching deployment scenes through virtual reality. You will wear a pair of goggles and headphones. We will also measure your heart rate and the amount of sweat on your hands. We will do this by placing one sensor on your upper chest and one sensor on your lower belly. Another pair of sensors will be attached to your palm to measure the amount of sweat on your hand. Each virtual reality deployment scene will be about 8 minutes long and repeated about three times, with breaks in between. The virtual reality scenes will get more intense with each scene and will include smells and sounds related to each situation. You can stop the experiment at any time.

Participants will be randomly, like a flip of a coin, placed into 1 of 2 groups. One group will receive small amounts of electricity, while the other group will not receive active electrical brain stimulation. There is a 50% chance of being placed in either group. Other than whether the brain stimulation is on or not, there is no difference between the groups.

While you watch the virtual reality deployment scenes you will receive a small amount of electricity (tDCS) through small rubber pieces covered with sponges (electrodes) that will be against the skin of your head and held in place with a flexible headband. The skin on your head will be checked by research staff to make sure there are no cuts, lesions or other skin problems. This skin area will be cleaned with an alcohol pad. The electrodes on your head will be connected to the small battery operated stimulator machine. We will not shave any hair and you will not feel any electric shocks, only a tingling or itchy sensation under the electrodes. This is what the tDCS machine and sponge-covered electrodes look like:

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Follow-up: Approximately one and three months after your last tDCS+VR session, you will return for a set of follow-up questionnaires and interviews. The 1- and 3-month follow-up sessions will take about 1-1.5 hours each. At the discretion of the study PIs, follow-up sessions may be provided via phone or video (VA approved VA Video Connect). If this happens, you will be asked to find a private space for phone/video sessions to keep your sessions private.

In the event that we are unable to contact you, we ask that you provide the research team with the name and phone number of a close relative, friend, or other person who is likely to stay in contact with you during the time you are participating in this study.

EEG (Optional): An EEG measures your brain's activity. To do this a stretchy cap will be placed on your head. This cap includes small electrodes in which a small amount of gel is placed. Once you are wearing the cap, you will be asked to sit quietly for a recording session and will either be instructed to close your eyes or keep your eyes open. The total time for the EEG visit will be about 1 hour; this includes the set-up, orientation, and recording session. This visit is optional and will not affect your participation in the previous study procedures. If you choose to participate this visit will take place after the screening visit and before the first tDCS+VR session.

_____ (initial) I consent to participating in the EEG portion of this study.
_____ (initial) I do not consent to participating in the EEG portion of this study.

3. Description of any procedures that may result in discomfort or inconvenience:
Psychological Discomfort: You may feel uncomfortable discussing mental health symptoms with study staff. We encourage you to discuss any discomfort with a research staff member. You may refuse to answer any questions. The VR scenario may remind you of difficult things you have experienced. If this becomes too much, you may stop the task at any time. Licensed professionals will be available to help you talk about and work through these memories.

Physical Discomfort: The electrical stimulation might feel uncomfortable. You might find the VR sessions too much to bear, and we will stop these as soon as you tell us to. It is important that you tell the research team about any discomfort and we will stop the study procedures at your request.

4. Expected risks of study:
Physical Risks: Mild electrical stimulation on the head has been done in this way in humans and animals for many years, and there is no evidence that it is harmful. The most common side effect is a slightly itchy and tingling feeling of the skin under the electrodes. The most serious side effect is the possibility of small burns on the skin. We will do everything possible to avoid this, including checking the electrodes carefully and making sure they are not placed over cuts, scratches, moles or other abnormal skin areas. However, there is still a small possibility that this will happen to you. Therefore, it is very important that you tell us immediately if you feel any pain or burning sensations under one of the electrodes. This is different from the mild tingling or itching that the electricity often causes. Under normal conditions, there may be

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some skin redness under the electrodes that goes away within several hours. We will monitor you throughout each session. If you develop any problem that affects your safety we will stop the session immediately. We expect any effects caused by this electrical stimulation to wear off within an hour after the current is stopped. There may be other risks and side effects that are not known at this time. A small percentage of people experience lightheadedness, dizziness, upset stomach, or visual symptoms, like eyestrain and/or blurred vision, when experiencing a VR environment. If you experience any of these, please let the research staff know immediately.

Psychological Risks: You may feel upset answering questions about your current health and symptom severity. Mental health symptoms may temporarily worsen as a result of these questions. You may discuss any discomfort with one of the researchers. If you become distressed and require additional support, a study staff member will put you in touch with your mental health care provider.

Risk of loss of confidentiality: While every effort will be made to maintain your confidentiality, it is possible that complete confidentiality will not be maintained. However, safeguards are in place to protect your confidentiality. All identifiable and non-identifiable paper data will be stored in a locked office in a locked cabinet at the VA and will only be seen by the study team. All identifiable and non-identifiable electronic data will be stored in a restricted file on the VA computer system. Information that might possibly allow you to be identified will not be allowed in any publications or reports sent to individuals outside the study. All employees who are to handle data will be trained in confidentiality policies and procedures.

If the study PIs determine it to be necessary, you may need to complete study visits via phone or video. If this happens, you will be asked to find a private space for phone/video sessions to help keep your information private. It is still possible that others may overhear your sessions. The research staff will work with you to try to find a private space for you to complete your sessions, to minimize the risk that you will be overheard.

Risks of MRI: MR imaging is generally considered to be safe; but accidents, injuries, and even deaths have occurred during MRI procedures. Such adverse events are extremely rare if appropriate safety precautions are followed. Serious complications can occur in people who have metal pacemakers, metallic dust in the eyes, or certain types of metal prostheses, implants, or surgical clips. MRI is also dangerous for anyone wearing any metal objects, including jewelry, watches, hair holders, eyeglasses or metal on clothing, as well as eye shadow, which sometimes contains metallic substances. In addition, if you enter the MRI room with any magnetic cards, such as ATM and credit cards, you will risk having the data on the cards erased by the MRI machine. For these reasons, a researcher or technician will review safety information with you before the scan. In order to determine whether it is safe for you to go into the scanner, it will be important that you tell study personnel and the MRI technician about any metallic objects or devices in, or on, your body.

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Some people experience a sensation of claustrophobia when lying in the MRI machine. If you think this may happen to you, please tell the researchers before you have the scan. The scanner also makes loud noises during imaging. Ear protection will be provided to reduce the noise level. If you feel uncomfortable for any reason before or during the procedure, please tell the researchers. If for any reason during the procedure you want to stop, you may do so at any time. There is a risk of heating during MRI scanning. Please report any heating/burning sensation immediately. You are encouraged to signal to have the scan stopped at any time if this occurs.

CAUTION: This study is neither designed nor intended to detect health problems in participants. The MRI scans that you will undergo do not substitute for an appropriate medical examination by a qualified health care provider. The investigators for this project are not trained to do diagnosis based on the MRI, and the MRI scans performed in this study are not designed to find abnormalities. The investigators and the Providence VA Medical Center are not responsible for failure to find existing abnormalities in your MRI scans. However, on occasion the investigator may notice an MRI image that seems abnormal. In these cases a radiologist at the Providence VA Medical Center will be asked to examine the images to determine if an abnormality is present and if it requires medical attention. A member of the study staff will then inform you of the abnormality and whether or not it needs medical attention. If medical attention is advised, the study staff will encourage you to contact your physician. You may choose for the study staff to discuss such an abnormality with your physician. If your physician is not a member of the Providence VA Medical Center, you will be asked to sign a release of information for us to contact him or her.

The decision whether to proceed with further examination or treatment lies solely with you and your physician. The investigators are not responsible for any examination or treatment that you undertake based upon these findings. Because the images collected in this study are not labeled with your identifying information, they will not be entered into the VA electronic medical record system (Computerized Patient Care System or CPRS). However, to facilitate your care in the event an abnormality is found, we will provide your PVAMC provider (possibly including a PVAMC MRI radiologist) with a copy of the images on CD or DVD if they request it. Also, we may provide a non-VA provider with the images in which case the images may be given to you to bring to your non-VA Provider. You will be asked to sign appropriate release of information documents before we release images to you or your provider(s).

***Risks of EEG*:** EEGs are considered to be very safe, although the cap can be tight at times, and gel will be put on your head to improve the recording. You may feel areas of pressure on your scalp at the location of the recording electrodes. Adjustments may be possible to reduce this sensation if it is uncomfortable. It may be difficult to remove the gel from your hair but it should come out of your hair with a few washings with regular shampoo.

Other risks: The effect of tDCS on pregnant women and on a developing fetus is unknown, therefore pregnant women are not allowed in this study. If you are a woman of childbearing age, you will be asked to complete a pregnancy test, when appropriate, before you begin the

investigational study. If it is confirmed that you are pregnant you will be immediately excluded from this study.

If there are any medical problems as a result of your participation in this study, we will refer you to the VA Medical Center, as the VA will provide you with emergency services. If you would like to go get treatment outside the VA Medical Center, you may be responsible for the costs of your own treatment.

Since you will be receiving compensation for your participation, there is a risk that your bank account information or social security number can be stolen or misused. If you elect to receive compensation by electronic funds transfer (EFT), there is a risk that any individuals with access to your account, would be made aware of your participation in PVAMC research.

5. Expected benefits of study:
You will not benefit directly from taking part in this study. The information collected in this study may help determine whether the use of mild electrical current can be a treatment that is helpful for military personnel who experience PTSD following service in warzone deployments.

6. Other treatment(s) available:
Other treatments available include continuing previous treatment or starting new trials of standard treatments that have been proven to work for PTSD given by a clinician or prescribed by a physician or nurse outside of this research study.

7. Costs to participants and compensation:
Costs to Participants: You will be responsible for the cost of round-trip transportation to study visits. You will not be required to pay for care and services (treatment) received as a participant in this VA research project.

Compensation Offered for Participation: You will be compensated up to $425 using electronic funds transfer (EFT). To receive funds by EFT, you will have to provide your bank account number, bank routing number, and social security number on the form provided, so the funds can be sent directly to your bank account. This usually takes less than a week after we have asked the funds to be sent to you. When using EFT, all payments will be reported directly to the Internal Revenue Service. Deposited funds, via EFT, may be affected if you have any unpaid debts or liens on the account. Additionally, if you elect to receive compensation by EFT, deposited funds may be seen by anyone with access your bank account (e.g., joint/shared account, authorized users, etc.). If you do not wish to use EFT and would prefer to receive gift cards (e.g. CVS) of the same amount, please discuss this with study staff. You will be paid $75 when you complete the first study visit, $75 after you complete tDCS + VR sessions, $75 when you return for the 1 month follow-up, and another $75 when you complete the final visit 3 months later. If you do not finish the study completely, you will still be paid for your time based on the amount of study completed. *Optional – If you choose to participate in the EEG portion of this study, you will be compensated $50 for your time and participation. If*

you are eligible and choose to participate in the follow-up MRI portion of this study, you will be compensated $75 for your time and participation.

8. Use of research results:
All information will be confidential to the extent of the law. Access to data will be limited to study investigators and staff. Data will be stored in a locked file cabinet and on password protected computers in the study office. It will be identified by a code number and kept separately from your personal information. As a VA patient, you have a computerized medical record and we will put notes in your record about your participation in this research study. A copy of this consent form will be scanned into the record. Research results will not be placed in your medical record unless you specifically request it and sign an authorization form. We will need access to your medical record for this purpose until you finish the study. You will not be able to view records related to your participation in this study until your participation has ended. Only the investigators and their staff will have access to the study records. No information will be shared outside of the VA. Information that does not identify you may be used for medical and scientific purposes including teaching and/or publication.

9. Right of investigator to terminate participation:
The investigator or a study staff member may end your participation if he/she feels it is in your best interest or believes you are not following study procedures.

10. Participant Withdrawal
Participation in the study is voluntary so you have the right to withdraw at any time. Participant withdrawal will not affect your social, financial, or medical standing.

11. FDA related studies involving drugs, biomedical drugs and medical devices
A description of this clinical trial will be available on http://www.clinicaltrials.gov/, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

RESEARCH PARTICIPANT'S RIGHTS: I have read or have had read to me all of the above. Dr. Mascha Frank, Ph.D., Dr. Noah S. Philip, M.D. or a member of their research team has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I have been told that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law. The Institutional Review Board at the Providence VA Medical Center or other federal oversight offices may monitor my records for quality assurance purposes. Federal agencies including, but not limited to, the Food and Drug Administration (FDA), the Office for Human

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Research Protection (OHRP), the Office for Research Oversight (ORO), the Office of the Inspector General (OIG) and the Government Accounting Office (GAO) may have access to the records as allowed by law. If an FDA-regulated test article is part of this study, the FDA may choose to inspect research records that include research subject's individual medical records. Records will be maintained in accordance with the Department of Veterans Affairs Record Control Schedule 10-1.

If I experience a side effect or adverse (bad or unexpected) reaction as a result of my involvement in this study, I will report these to the study investigator Dr. Mascha Frank at 401-273-7100 x16256 or Dr. Noah S. Philip at 401-273-7100 x16235 who will arrange for any medical treatment that is necessary. After hours, I will call 401-273-7100 and ask the operator to page the psychiatrist on call.

In case there are medical problems or questions, I have been told I can call Dr. Mascha Frank at 401-273-7100 x16256 or Dr. Noah S. Philip at 401-273-7100 x16235 during the day and afterhours call 401-273-7100 and ask the operator to page the psychiatrist on call. If any medical problems occur in connection with this study the VA will provide emergency care.

The VA has the authority to provide medical treatment to participants (veterans and non-veterans) injured by participation in a VA study. If you are injured as a result of being in this study, the VA will provide the necessary medical treatment in accordance with federal law. If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document you are not giving up your right to make a legal claim against the United States.

I can call the IRB Coordinator at (401) 273-7100 ext. 13470, the Research Administrative Officer at (401) 273-7100 ext. 13066 or the Providence VAMC Patient Advocate at (401) 273-7100 ext. 13093 while I am a participant or after my participation is over for the following: 1) concerns, 2) complaints, 3) problems, 4) suggestions, 5) more information, 6) questions about my rights as a research participant or 7) verifying the validity of the study and authorized contacts.

I voluntarily consent to participate in this study. I confirm that I have read this consent form or it has been read to me, and I agree it explains what this study is about and how and why it is being done. I will receive a signed copy of the consent form document after I sign it.

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_____	_____	_____
Participant's Signature	Participant (printed)	Date
_____	_____	_____
Signature of Person Obtaining Consent	Person Obtaining Consent (printed)	Date

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