COVER PAGE – MAIN CONSENT

Title: Effect of tDCS timing on safety memory in PTSD

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BUTLER HOSPITAL CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

Effect of tDCS timing on safety memory in PTSD

Sponsorship
This study is being paid for by a grant from the National Institute of General Medical Sciences (NIGMS).

Research Project Summary
You are being invited to participate in a study designed to test whether electrical brain stimulation during or after emotional learning changes emotional memory. You are being asked to participate because you are between the ages of 18 and 70 years and have received a diagnosis of posttraumatic stress disorder (PTSD). Your participation in the study will involve four to five visits over approximately two weeks and approximately 7 hours total. The first visit will take about three hours at Butler Hospital or remotely through phone/videoconferencing. Visits 2-5 will each take about one hour per visit and will take place either on Brown University campus at the MRI Facility or at Butler Hospital. During the visits you will be asked to complete interviews and questionnaires, may get one to two brain scans, and perform a computer task during which you will receive an annoying (but not painful) electrical shock to your fingers. In addition, you may or may not receive electrical brain stimulation, called transcranial direct current stimulation (tDCS) at some point during one of these visits. Whether and when you will receive tDCS is random, like a roll of a dice. You will be paid for taking part in this study (details can be found below). The main risks of participating in this study are related to the tDCS. Most people feel this as an itchy, prickly or tingling feeling of the skin under the stimulation electrodes.

In order to decide whether or not you wish to be a part of this research study, you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, risks associated with the procedures, possible benefits of participation, and possible alternatives. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form. This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.

Description of Procedures
If you decide to participate, and after you sign this form, you will be asked to do the following:

Visit Day 1 (Butler Hospital or remotely through phone/videoconferencing)
At your first visit, we will ask you to complete two interviews with one or two of our study team members. During these interviews, the interviewer will ask you about mental health symptoms and about your past experiences. You will be asked to provide information on traumatic experiences that you may have experienced, and complete questionnaires about your sleep, feelings of anxiety and mood, and other emotions. We will also ask you some questions about your physical health. The information you provide at this visit will help us decide whether this study is a good fit for you. In total, this visit will take about 3 hours.

Visit Day 2 (Brown University MRI Facility)
You may be asked to complete an MRI scan after your first visit. If asked to complete this scan, this visit will take about 1 hour and will take place at the brain imaging facility at Brown University. During this visit you will get a scan of your brain.

Visit Day 3 (Brown University MRI Facility or Butler Hospital)
On your third visit we will ask you to complete a task that tests your brain's processes for making new associations between things that you hear, see or smell, and emotional events, like a wedding or a bad

accident. For example, the smell of vanilla may be very strong at a friend's wedding. Days, or even weeks after the event, exposure to the smell of vanilla may remind you of the wedding and your positive or negative experience at that event.

Two small electrodes will be attached to two fingers. The electrodes are made of a small piece of metal that is attached to a cable. The cable is connected to a stimulator. While you do the task, we will apply an annoying but not painful electric shock to your fingers that lasts half of one second. To most people, the finger shock feels like an annoying tingling sensation. The first part of this experiment will be to find the level of finger shock that you find is very annoying, but not painful. To do this, we will begin at a low level that you will not be able to feel. We will slowly increase the intensity level of the shock with your permission. We will ask you to tell us when you find the level of the finger shock very annoying, but not painful. During the rest of the experiment, the level of shock intensity that you experience will not be higher than this very annoying level. The purpose of the electric finger shock is to create a situation in which emotional learning may occur. During the task, you will learn that the finger shocks may always follow a specific picture. When we thereafter show you the picture, you may become a bit nervous because you have now learned that this particular picture predicts the occurrence of the finger shocks. We will then show you a series of pictures of different rooms. After you see some of the pictures, you will receive the half-second shock to your fingers at the very annoying level that was selected earlier. Small stick-on pads that are attached to the surface of your hands will measure your body's responses to the pictures that you see. The stick-on pads attached to your hands have wires that connect to a computer to detect how nervous you are by measuring the amount of sweat on your hands. If your visit happens at the Brown University MRI Facility, you will be doing this task while lying in a device that looks and feels like the MRI scanner used in visit 2, but a brain scan is not really happening during the task at this visit 3. The device is a "simulation" scanner and is used to help people get used to the appearance and feel of the real MRI scanner environment. This visit will take about one hour.

Visit Day 4 (Brown University MRI Facility or Butler Hospital)
This visit will need to happen the next day (20-28 hours after visit 3). If you are not able to schedule visit 4 within this time, you are not eligible to participate in this study. If your visit happens at the Brown University MRI Facility, you will again be doing the task in the simulation scanner device. You may also receive tDCS during or after the task. This means we will apply a low level of electrical current through two electrodes placed in wet sponges that will be held in place on your head by rubber bands wrapped around your head (we will not shave any hair). The electrodes on your scalp will be connected to a battery-operated stimulator which will deliver a low constant direct current which you might feel as a slight tingling, itchy, or prickly feeling under the electrodes. Not everyone in this experiment will get the actual tDCS. Some people will be randomly (like a roll of a dice) assigned to have the electrodes placed on their scalp without current, which might feel similar to stimulation (this is called a "sham" procedure). You will not know whether you received actual stimulation or not. We will ask you afterwards whether you thought you received actual stimulation or not. This visit will take about one hour.

Visit Day 5 (Brown University MRI Facility or Butler Hospital)
This visit will need to happen the day after your fourth visit (20-28 hours after visit 4). If you are not able to schedule visit 5 within this time, you are not eligible to participate in this study. Once again, we will ask you to do the same task as in visits 3 and 4. In addition, you may or may not be asked to complete a second MRI scan. If so, you will complete the task while lying in the real MRI brain scanner and we will make a scan of your brain. This visit will take about one hour.

Risks and Inconveniences

Participating in this study may include several risks. It is important that you understand these risks in order to make an informed decision about whether or not you wish to participate. First, during this study you may be asked about personal things, such as your health history, whether you might be pregnant if you are female, and how you are feeling, which may make you uncomfortable. You are free to not answer any questions which make you uncomfortable. While we protect your information in line with hospital policies

and state and federal laws, there is always the possibility that this information could be compromised, despite our best efforts, resulting in loss of privacy or confidentiality. There is the possibility that you may experience minor physical discomfort during the task from the shocks to your fingers. Please remember that the finger shocks should not be painful or intolerable, and that we want you to report any discomfort to the research team. You should feel free to request the procedure be stopped at any point if you are uncomfortable.

Finally, there are some possible risks associated with tDCS and MRI. tDCS has been done in humans and animals for many years, and there is no known evidence that it has lasting harmful effects. In recent studies on humans, no serious side effects have been observed. The most common side effect that most people feel is an itchy, prickly or tingling feeling of the skin under the stimulation electrodes. Also, sometimes people report headaches, feeling tired, or a brief feeling of dizziness after the stimulation session. Another more serious side effect is the possibility of small burns on the skin or scalp, which are rare. For example, this has happened after the skin was vigorously rubbed before tDCS. We will do everything possible to avoid this, by not rubbing the skin (we will wipe your skin clean under the electrodes with a small alcohol wipe); checking the electrodes carefully and making sure they are not placed over cuts, scratches, moles or other abnormal skin areas, as well as using normal saline to wet the sponges in which the electrodes are placed. However, there is still a small chance that this could happen. This is why it is very important that you tell us immediately if you feel any pain or burning sensations under one of the electrodes. This feeling is different from the mild tingling or itching that the current often causes. Under normal conditions, there may be some skin redness under the electrodes that goes away within a few hours. Another side effect which may be possible with tDCS is the risk of hypomania, or feeling too good or abnormally energetic. This has been reported in some people receiving repeated, daily tDCS targeting a different brain area. We will monitor you throughout the session. If you develop any problem that affects your safety we will stop the session immediately. We expect any effects caused by the tDCS to wear off within a short time after the current is stopped.

MRI scans are 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 undergo the scanning procedure, it will be important that you tell study personnel and the MRI technician about any metallic objects or devices in, or on, your body. There is a risk of heating too much from some of the coils and cables in the MRI, which can result in burns if there is any metal on or in you (such as from certain older tattoos, some permanent eye makeup or metal pins). The scanner also makes loud noises during imaging. Ear protection will be provided to reduce the noise level. You could become anxious during the scan if you have difficulty being in small spaces. If for any reason during the procedure you want to stop, you may do so at any time by telling the technician through the intercom or by squeezing a ball that we will place in your hand. You will be asked to sign a separate MRI consent form that provides details about these risks.

It is your responsibility to inform study staff of your current medical conditions. The MRI scans obtained in this study will not be read by a radiologist and are not the type used for diagnosing any medical problems. However, if it is discovered by the researchers that your brain appears abnormal, study personnel will provide a referral for you to have an evaluation by a neurologist.

Any medical treatment or procedure may have unforeseen side effects. You should know that the prediction of effects from a treatment or procedure for any individual cannot be done with certainty, and unexpected

potentially harmful effects occasionally occur with the administration of any type of treatment. If you have questions about investigational procedures or treatments, or if you experience any disturbing side effects during participation in this study, inform study personnel. In the event of any unexpected, potentially harmful effects of any treatment or procedure administered in this study, we will monitor your condition closely and institute appropriate treatment. If significant new knowledge is obtained through the course of the research which may impact your willingness to continue participation, you will be informed of this knowledge.

Video Communication

With your permission, we will contact you via phone/video to complete study measures. If necessary, video conferencing for the study will done via HIPAA compliant software. Using this secure video conferencing system will help reduce the chance that you will experience loss of confidentiality when using video conferencing When using any public computer you should be careful to protect your username and password, and make sure you log-out before getting up from the computer.

Text Message Communication

If you agree, we may send you text messages to make appointments or remind you of appointments you have with us. These text messages will be sent from a phone that is only used by staff on this study and for this study only. The phone will not be monitored for return messages constantly, but it will be checked periodically during regular office hours. You can reply to messages from study staff by sending text messages back, but there are only certain things you should communicate via text message.

Risks related to text communication

Your participation in this research may be considered health information that should be kept confidential. There are risks associated with sending messages related to your health information via text. We will only communicate by text to schedule or confirm study appointments. We will not send text messages to a group of people. If you share your mobile phone or messages with others, it is possible that others might see you take part in this study and that they might find out health information about you. You should make sure to protect your phone with a password if you send or receive text messages during participation in this study.

It is possible that a message you send will go unnoticed, or will not be read by the research team for days or weeks. Therefore, you should use the telephone to contact the research team for any urgent matters. Medical issues (symptoms, side effects, injuries, questions about medications, concerns about effects of study procedures, etc.) should NOT be communicated by text. These should be directed to the research staff by telephone or in person. To discuss medical issues, please contact our office at XXX-XXX-XXXX.

Do you give permission for research staff to send you text messages, as described above? (Indicate your answer below.)

YES / NO

_____
(Initial here)

Remote Consent

This consent form can be signed electronically through REDCap. You will receive an e-mail from a study email address containing a link, which will securely connect you directly to the REDCap system. Your email survey link is associated only with your e-mail address. After electronically signing the informed consent form, a copy will be sent to your email. At the time of the first in-person visit, the consent form will be reviewed again before beginning study procedures.

Women Please Note:
The effects of tDCS and MRI during pregnancy are not known, and thus, tDCS and MRI is not recommended for use during pregnancy. tDCS and MRI may be harmful to a developing fetus. Therefore, you may be asked about pregnancy at the time of your admission to the study and before the MRI and tDCS. We will specifically ask you to let us know if you change your mind and decide to become pregnant during the study. If you are currently pregnant, or if there is any chance you may be pregnant, you are not eligible to participate.

Benefits
You may not benefit directly from participation in this study. The main benefits of this study are to help researchers and clinicians develop future interventions that improve care for individuals with posttraumatic stress disorder.

Economic Considerations
You will receive $170 in checks or gift cards for completing the entire study. You will receive an additional $50 for each MRI you complete. If you are asked to complete one MRI scan (on Day 2 *or* Day 5), you will receive a total of $220 for study completion. If asked to complete two MRI scans (on Day 2 *and* Day 5), you will receive a total of $270 for study completion. If it turns out that after screening, that is after you complete the interviews and other questions, you are not a good fit for this study, you will receive $50 in checks or gift cards for completing the screening portion of the study. If you do not complete the entire study for other reasons – for example you don't want to participate anymore or the research team decides it is not a good idea for you to continue, you will be paid up until what was completed. This will be at minimum $50 in checks or gift cards for the screening of Visit Day 1, plus $10 in checks or gift cards for each half hour (30 minutes) of the study that you did take part in.

Depending on the amount of payment you might receive for your participation in this study, you might have to provide your name, address, and taxpayer ID or Social Security number to the Butler/CNE Research Accounting Department. In order to receive payment of $300 or more for participation in this research, you will have to complete and sign a W-9 form. If you are paid $600 or more in any calendar year for research participation, the IRS will be notified of the total amount you were paid, in accordance with federal regulations. You should ask the researcher for more information if you have questions about this process.

In Case of Injury
We will offer you services in Care New England facilities as needed to treat any injury that results directly from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for any injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed on the last page of this consent form.

In the case of procedures occurring over phone/videoconference, research staff will ask you questions about your current location to verify your safety. The research team reserves the right to report your current location and state to a clinician and/or emergency services if we feel as though there is the danger of substantial and imminent harm to yourself and/or others.

Alternative Treatments/Alternative to Participation
No treatments are being offered in this study.

Financial Disclosure
None.

Voluntary Participation
You are free to decide whether or not to participate in this study, and you are free to withdraw from the study at any time. A decision not to participate or to withdraw from the study will not adversely affect your current or future interactions with Butler Hospital or Care New England. Your participation in the study may be terminated by the researchers without regard to your consent; in that case, you are entitled to an explanation of the circumstances leading to that decision.

Confidentiality
Personal identifiers will be removed from any identifiable private information about you in the final research dataset created by this study. The de-identified information may be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you (or the legally authorized representative).

You will not be personally identified in any reports or publications that may result from this study. The confidentiality of the information you provide to us will be maintained in accordance with state and federal laws. If you tell us something that makes us believe that you or others have been or may be physically harmed, we may report that information to the appropriate agencies.

Clinically relevant research results, including individual research results, will not be disclosed to you. To keep your information safe, demographic information that is collected about you and that can be used to identify you, such as name and date of birth, will be stored separate from other research data that will be collected in a password protected file on a secure research server and/or in a secure web application (REDCap)All other research data collected in this study, such as answers to the interview, questionnaires and decisions you make in the decision-making task, will be identified with only a unique code that is given to each person who takes part in this study and will contain no identifying information. Electronic research data will be stored on a secure research server and paper forms will be stored in locked file cabinets at Butler Hospital. Research data will be destroyed 6 years after research study activities have been concluded.

General information about this study has been or will be submitted to the federal clinical trial registry databank, which can be accessed on the Internet at www.ClinicalTrials.gov.

This research is covered by a Certificate of Confidentiality. Unless you give special written permission, the researchers and Butler Hospital cannot give out any information about you that could potentially identify you or be used as evidence in a legal case (including any federal, state, or local civil, criminal, administrative, or legislative case).

The only situations where researchers would share your information with others are:
(1) when a specific law (federal, state, or local) requires that potentially harmful things be reported to the authorities (such as reporting child abuse, elder abuse or spread of communicable diseases);
(2) when you have given permission (consent) for the information to be shared in order to help your medical treatment; or
(3) when your information will be used for other scientific research, as allowed by federal regulations protecting research subjects.

Authorization for use/disclosure of Health Information that Identifies you for a Research Study

If you sign this document, you give permission to this study's research team at Butler Hospital to use your health information that identifies you, for the purpose of conducting the research study described above. Your health information related to this study may also be shared with and used by individuals outside of Butler Hospital, including our study collaborators at the Providence VA Medical Center, Brown University including the Brown MRI facility staff, individuals on the data safety monitoring board of this study, or the Butler Hospital Institutional Review Board who may need the information to make sure that the study is done is a safe and proper manner. The health information that we may use or share with others for research purposes includes information gathered as part of your study visits.

You should also know that if you do not yet have a medical record at Butler Hospital, one will be made for the purpose of this study. If you do not want to have a medical record at Butler Hospital, you should not participate in this study.

Your health information may also be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions. The U.S. Food and Drug Administration (FDA) may inspect all study records to ensure that the study is being conducted in accordance with FDA regulations.

Butler Hospital is required by law to protect your health information. Individuals outside of Butler Hospital that receive your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it, so we cannot guarantee that they will not share it without your permission.

Please note that:

- You do not have to sign this consent form, but if you do not, you may not participate in this study.
- Butler Hospital may not withhold treatment or refuse to treat you, based on whether you sign this consent form.
- You may change your mind and revoke (take back) this consent and authorization at any time. If you no longer want to give us permission to use your health information for this research study, you must contact the Principal Investigator, Mascha van ’t Wout-Frank, PhD, and you will be instructed to provide a written statement.
- Even if you revoke (take back) this consent and authorization, Butler Hospital researchers may still use or share health information about you that they already have obtained, when doing so is necessary to maintain the integrity or reliability of the current research.
- You generally will not have access to your personal health information related to this research until the study is completed. At the conclusion of the research and at your request, you will have access to your health information that Butler Hospital maintains in a designated record set, according to the Notice of Privacy Practices provided to you by Butler Hospital. The designated record set includes medical information or billing records used by doctors or other health care providers at Butler Hospital to make decisions about individuals.
- Your health information will be provided to you or to your physician if it is necessary for your care.
- If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

This Authorization does not have an expiration date.

Questions

Taking part in this study is entirely voluntary. We urge you to discuss any questions about this study with our staff members. You should take as much time as you need to make your decision. If you decide to participate, you must sign this form to show that you want to take part.

Authorization:
I have read this form and decided that _____
(printed name of participant)
will participate in the project described above. Its general purposes, the nature of my involvement, and possible hazards and inconveniences have been explained to my satisfaction. I have received a copy of this consent form.

_____ _____
Signature Date

_____ _____
Signature of Principal Investigator Date

~or~

_____ _____
Signature of Person Obtaining Consent Date

Telephone Number of Principal Investigator or Person Obtaining Consent_____

If you have further questions about this project or about research-related injuries, please contact XXXX, PhD, at Butler Hospital XXX-XXX-XXXX. If you have questions about your rights as a research subject, please contact XXXX, M.D., Chair, Butler Hospital Institutional Review Board, at XXX-XXX-XXXX.

THIS FORM IS NOT VALID UNLESS THE FOLLOWING BOX HAS BEEN COMPLETED BY THE IRB OFFICE

THIS FORM IS VALID UNTIL

DATE: December 31, 2023

IRBNET ID# 1346426

BUTLER IRB REFERENCE# 1901-002

BY (ADMINISTRATOR): [redacted]