Title of Study: Safety, feasibility, and benefits of transcranial direct current stimulation (tDCS) in human subjects with PTSD receiving an exposure-based, behavioral therapy

Concise Summary

Important Information

This information gives you an overview of the research. More information about these topics may be found in the pages that follow. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with us.

1. What problem is this study trying to solve?

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future**.** In this study, we are evaluating whether transcranial direct current stimulation (tDCS), a brain stimulation technique, can be combined with Written Exposure Therapy (WET), an evidence-based, gold standard talk therapy for posttraumatic stress disorder (PTSD) to improve treatment response. For more information, please see the *Why is this Study being Done* section below.

2. What will happen to me during the study and how is this different from continuing with usual care? What are all my options for treatment, including the pros and cons?

After consenting to be in the study, you will be asked to complete a baseline assessment of your psychological and physical health that will determine whether you are able to participate in the study. Following the baseline, you will be randomly assigned to receive tDCS or a sham/placebo. Everyone will also participate in 5 weekly WET psychotherapy sessions for 5 consecutive weeks. The first appointment will be 90 minutes and the subsequent appointments will be 60 minutes. tDCS or sham/placebo will occur during the writing portion of the session. Prior to each treatment session, you will be asked to complete additional assessments. Finally, you will be asked to complete a follow-up assessment 1-month after you finish with treatment. In addition to questionnaires and interviews, you will be asked to wear a device during the writing portion of sessions to monitor your heartrate and your galvanic skin (sweating palms) response. Not all assessments will be done at every assessment time.

Comparison to Usual Care: WET is care typically provided to treat PTSD and is considered a standard treatment. Other treatments for PTSD can include other talk therapies, medications, or other brain stimulation techniques (e.g., transcranial magnetic stimulation) that may help manage PTSD symptoms. It may be possible that a community physician will prescribe tDCS, but this is not currently a usual practice. Additionally, there may be other research studies that treat PTSD. For more information, see the What will be done if you decide to be in the research section in the next pages.

3. How much time will I spend on the study?

You will be asked to complete a total of 7 visits, which includes 2 assessment visits (up to 4 hours each) and 5 WET treatment visits (60-90 minutes each). Prior to each treatment session you will also be asked to complete some brief, self-report assessments that will take you up to 30 minutes to complete. Altogether, you will spend up to 16 hours in this study over the next two to three months.

4. Could taking part in the study help me and are there risks?

Participating in this study may help you reduce your PTSD symptoms. Research on tDCS has found that it is safe and well-tolerated by most individuals. Common risks of tDCS may include mild itching sensation and skin irritation at the point of contact with the electrode. Other side effects that can occur are mild headaches, nausea, fatigue, and mild burning sensation at point of electrode contact. Risks of WET talk therapy may include temporary increases in emotional distress, PTSD, depression, or anxiety symptoms. For more information, please *see **How could you or others benefit from your taking part in this study*** section below. For details and a list of risks you should know about, please see the ***What are the risks of participation in the research*** section below.

5. What else should I consider before I make my decision?

Participation in weekly sessions over a five-week period is a time commitment. It is helpful to review your calendar and make sure that you can minimize other appointments and obligations over the next five weeks and attend weekly appointments during this study.

Please review the rest of this document for additional details about these topics and other information you should know before making a decision about participating in this research.

Title of Study: Safety, feasibility, and benefits of transcranial direct current stimulation (tDCS) in human subjects with PTSD receiving an exposure-based, behavioral therapy

Consent to be part of a Research Study
To be conducted at
University of Texas Health Science Center at San Antonio (UT Health San Antonio)

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study. Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you. Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are entitled.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety, and welfare as a participant in the research. The PI for this study is Casey Straud, PsyD, a board-certified psychologist and Assistant Professor in the Department of Psychiatry and Behavioral Sciences, UT Health San Antonio.

Study Physician/Co-Investigator
The Attending Physician on this study is Melissa Martinez, MD, a psychiatrist and Professor in the Department of Psychiatry and Behavioral Sciences, UT Health San Antonio. Dr. Martinez will oversee all medical aspects of this study.

Funding
This project is funded as part of a program award titled "Transcranial direct current stimulation for the treatment of post-traumatic stress disorder – from rodent models to clinical studies" through Center for Biomedical Neurosciences at UT Health San Antonio (Co-PIs: Casey Straud, PsyD, ABPP; Daniel Lodge, PhD; Flavia Carreno, PhD).

Purpose of this study – "Why is this study being done?"

This study is being done to see if transcranial direct current stimulation (tDCS), a low electrical current brain stimulation technique, can be combined with Written Exposure Therapy (WET), an evidence-based, gold standard talk therapy for posttraumatic stress disorder (PTSD) to improve treatment response. tDCS is a brain stimulation technique that involves the use of a low grade, consistent electrical current (1-2 mA) delivered through electrodes placed on the scalp. This amount of electrical current generally only causes a faint tingling sensation. For this study, tDCS will be administered using the Soterix 1 x 1 Transcranial Direct Current Stimulator Mini-Clinical Trials device. The use of tDCS in combination with WET may help process the traumatic event more effectively during therapy.

The researchers hope to learn if the combination of tDCS+WET is safe and effective in reducing PTSD symptoms and physiological outcomes associated with the fear response (heart rate and galvanic skin response [sweating palms]).

Investigational Use of Procedures & Device for PTSD: This study involves the use of an investigational device (Soterix 1 x 1 Transcranial Direct Current Stimulator Mini-Clinical Trials) for tDCS brain stimulation to augment treatment for PTSD. "Investigational" means that this device has not yet been approved by the U.S. Food & Drug Administration (FDA) for treating PTSD. However, tDCS has been tested in human trials and to date has not produced any reports of serious adverse events or irreversible injury across over 33,000 sessions and 1,000 subjects with repeated sessions. The amount of benefit of tDCS to treat PTSD above and beyond sham (placebo) in combination with WET therapy has not been determined.

This trial will be registered on www.ClinicalTrials.gov, a publicly available registry of clinical trials. This web site will not include information that can identify you. At most, the web site will include a summary of the study results. You can search this web site at any time.

Information about Study Participants – "Who is participating in this research?"

You are being asked to take part in this research study because you are an individual who is experiencing trauma-related symptoms consistent with posttraumatic stress disorder (PTSD). This study will enroll up to 50 study participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 7 visits (a baseline assessment, five treatment sessions, and a one-month follow-up assessment) with the researchers or study staff. We will ask that you return to the clinic once a week for five consecutive weeks for treatment sessions. All therapy sessions will need to be face-to-face to receive the tDCS intervention. The preferred method of assessment is also face-to-face. However, there may be circumstances when you can complete some of the assessments electronically or over the telephone. Decisions will be made on a case-by-case basis as issues arise for individuals (e.g., childcare) and in discussion with the treatment team. Participants who do not have internet access will need to complete assessments in person.

Screening Procedures: After you sign this consent to participate, you will be asked to complete a series of questionnaires and then meet with an evaluator who will assess your mental and physical health. Females who can become pregnant will complete a urine pregnancy test. You cannot take part in this study if you are pregnant or breastfeeding. The baseline/screening process will take approximately 3-4 hours. The results of these screening procedures will be reviewed to determine whether it is appropriate for you to continue in the study. If at any point during the baseline process it is determined that *it would not* be appropriate for you to continue in the study OR if you choose not to enroll, then the researcher will discuss the reasons with you and coordinate appropriate follow-up outside of this study.

You have my permission to use assessments collected as part of the screening for another UT Health San Antonio STRONG STAR study or program as baseline data for my participation in this study.

Circle one: N/A YES NO _____ _____
Initials of Participant Date

Study Procedures: As a participant, you will be asked to:

- Meet with a member of the research team to review your assessment findings and discuss treatment.
- Participate in five weekly WET sessions on weekdays over 5 consecutive weeks. Session 1 will last approximately 90 minutes. Sessions 2 through 4 will last approximately 60 minutes. All WET sessions will include a 30 minute writing portion where you will be asked to write out about your traumatic event. During the writing portion of WET sessions you will simultaneously receive tDCS or sham (placebo).
- Wear an additional device on your non-writing hand during the writing portion of sessions 1, 3, and 5 to monitor your heart rate and galvanic skin response (which is a measure of changes in your sweat gland activity associated with your emotional state: sweating palms).
- Complete self-report assessments prior to each treatment session.
- Refrain from or postpone changing your medications or working with another provider on problems related to PTSD while you are in the study. This will help us better understand how the treatment in this study impacts you. However, if you feel that you do need to work with another provider on your PTSD, please be sure to let us know so that we can coordinate your care accordingly. Also, if you and your prescriber feels that a change in your medication is needed please let a member of the research team know so that we can record the change in your research file.

Since the study is examining an outpatient treatment for PTSD, you have the option of having the study team coordinate with you and your employer to ensure you have the time to attend all of the treatment and assessment sessions. With your permission, one of the members of the research team will contact your supervisor to get his or her support for you to participate in this study. If you choose to have the research team contact your supervisor, supervisor will be told that you have agreed to participate in a research study and will be given your treatment and assessment schedule.

Assignment to Study Groups: If it is determined that you are eligible for the study, you will be assigned by chance (like flipping a coin) to receive five (30 minute) treatments of tDCS or a sham (placebo) condition. You will have a 50% chance of being in the sham (placebo) group. The sham (placebo) will be an inactive procedure that looks and feels like the tDCS procedure. Randomization will be partially double blinded which means that neither you or the clinical team will know whether you are receiving the tDCS or sham/placebo. A non-clinical team member will be aware of randomization, so that the PI and research team can be quickly made aware of which treatment you are receiving in the event of an emergency. All participants will receive 5 WET sessions regardless of which group they are randomized to for the study.

Assessments: In addition to the treatment sessions, you will be asked to complete self-report assessments prior to each WET session. These questionnaires will add up to 30 minutes to your therapy appointment to complete. Additionally, you will be asked to wear a heart rate monitor watch and galvanic skin response (sweating palms) device on your non-writing hand during the writing portion of sessions 1, 3, and 5. One month after you have completed treatment, you will be asked to complete a longer, more comprehensive assessment.

Even if you choose to stop treatment, we will ask that you complete the one-month assessment visit. This will help us understand how the treatment works even if you do not receive the full dose. Your participation in all parts of this study is very important However, your participation in the follow-up assessments is completely your choice. There is no risk to you if you do not complete the final withdrawal procedures, and you can choose not to participate in them.

Recordings: Select assessment interview measures will be audio recorded to make sure that the study staff members are correctly following study procedures. These recordings may be reviewed by research experts who are a part of the research team.

Time Commitment: While you are taking part in this study, you will be asked to attend approximately 7 visits, which includes 2 assessment visits (up to 4 hours each) and 5 weekly tDCS/sham + WET treatment visits (session 1 will last 90 minutes and sessions 2-4 will last 60 minutes). You will also complete self-report questionnaires prior to each session that will add up to 30 minutes to each appointment. Altogether, you will spend up to 16 hours in this study over the next two to three months.

Future Use of Your Information Collected as Part of Your Participation

The researchers will be asking your permission to store your questionnaire answers and physiological data with your personal identifying information after this study is completed in the STRONG STAR Repository. The Repository is designed to be used for research investigating the causes, consequences, and treatment of PTSD and related conditions. Your consent to allow us to store your information will be given in a separate consent document. Your participation in the current study does not depend on your decision to participate or not in the Repository. Please note however that if you decide not to participate in the Repository, the researchers intend to keep and use the information collected as part of this study, but your personal identifiers (such as name, SSN, and contact information) will be permanently destroyed so that it can never be linked to you again. No biospecimen data is being collected in this study.

The de-identified 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.

Information about Optional Procedures – "What are other research activities that may be done but are not required for your participation?"

E-mail Authorization Agreement
The research team would like to communicate with you regarding your research visits via email. If you agree to receive emails about your research visits, we will ask that you sign a separate Email Authorization Agreement. You do not have to consent to receive emails.

Ending Participation Early - **Could your participation end early?** There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.

- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

Risks – "What are the risks of participation in the research?"

Risks from the research
There are risks to taking part in this research study. One risk is that you may have side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. However, the study staff do not know all of the side effects that may happen. Be sure to tell your study therapist immediately about any side effects that you have while taking part in the study. The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

The following section will describe the risks related to your participation in this research study, including your participation in tDCS, WET, and psychological assessments. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Risks related to tDCS:
Likely, but Not Serious Risks (expected to occur in 15-30 out of 100 participants):
- The most common side effect of tDCS is mild itching sensation at the point of contact with the electrodes.

Less Likely, some may be Serious (expected to occur in 10-18 out of 100 participants):
- Transient minor discomfort can occur in about 10-18% of participants, such as mild headaches, nausea, mild burning sensation at the point of electrode contact, and fatigue.

Rare and Serious (expected to occur in <1 out of 100 participants):
- A rare but serious side effect of tDCS can be skin lesions following repeated tDCS.
- Another potentially serious AE that has been discussed in the literature is seizures. There is also a theoretical rationale that brain stimulation can increase the risk of seizures. However, to date, there is no documented evidence that tDCS has resulted in a seizure.

Risks related to WET:
Likely, but Not Serious Risks (expected to occur in 15-30 out of 100 participants):
- Temporary increases in psychological distress can occur among individuals engaged in WET for PTSD.

Risks to Confidentiality:
With the handling of medical and research records there is always the possibility of a breach of confidentiality. We will maintain participant's names, contact information (i.e. Identifiers), and all PHI (protected health information) in an encrypted computer database and all PHI identifiers will be removed in the database during data analysis. Every member of the Research Team is carefully trained and monitored about how to store, handle, and protect participant records.

Risks of PTSD Diagnosis regardless of Treatment:
One of the risks of PTSD both in and out of treatment is attempted suicide, which can result in death. Increased suicidality is possible during study participation.

Are there Risks related to withdrawing from the study?
If you decide to withdraw from this study early, please discuss your decision with the research team. If you decide to withdraw, we may ask you if you are willing to participate in a brief assessment with a study clinician either in-person or by phone just to assess your condition and make appropriate referrals if necessary. We are also interested in following up with you at the times you would have been assessed if you had completed all of the sessions to answer some questionnaires. However, your participation in the follow-up assessments is completely your choice. There is no risk to you if you do not complete the final withdrawal procedures, and you can choose not to participate in them.

Reproductive Risks

Concerns for sexually active men and women: Women should not become pregnant and men should not father a baby while taking part in this study because we do not know how tDCS could affect a man's sperm or a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant or if you believe your female partner has become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed.

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how tDCS might affect a developing fetus. We will do a pregnancy test before you start treatment to make sure you are not pregnant.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect tDCS might have on their breast milk.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time may affect the results of the studies. You should not take part in more than one study without discussing it with the researchers of both studies.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section “Contact Information” for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – “How could you or others benefit from your taking part in this study?”

The possible benefit of your participating in this study is a potential reduction in your symptoms associated with PTSD, which may positively affect your overall health and well-being. There is no guarantee or promise that you will receive any benefit from this study. We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – “What other options are there to participation in this study?”

There are other options available to you for study participant. Your other choices may include:

- Not participating in the study.
- Receiving another form of psychotherapy (talk therapy) from another therapist.
- Medications, such as antidepressants.
- A community physician may be willing to prescribe you tDCS, but this is not a usual practice for PTSD at this time.
- There may be other research studies involving experimental treatments that could be helpful for your conditions.

Payments – Will there be any payments for participation?

Participants will be paid $25 at sessions 1, 3, and 5 for physiological assessment participation for up to $75. The researchers will provide you with a MasterCard®. Compensation will be automatically credited after completion of sessions 1, 3, and 5. Your name, address, and date of birth will be shared with a third-party solely for the purposes of compensation processing. This information will only be used for the administration of the compensation (ClinCard) and will be kept strictly confidential.

In addition to the compensation on the card, you may also elect to receive messages (text and/or email) that money has been loaded onto your card. Please indicate your willingness to receive these messages:

- □ **Yes,** I would like to participate (please select the best method(s) for communication)
  - Cell Phone (text messages)
  - Email
- □ **No,** I choose not to participate

Costs – Will taking part in this study cost anything?

tDCS and WET will be provided free of charge during this study.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out who it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include: name, address, phone numbers, and email address to be able to contact you and make follow-up appointments; and questionnaire answers that you provide us as part of this study. We will get this information by asking you.

How will your PHI be shared?
Because this is a research study, we will be unable keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- Members of the STRONG STAR research team at UT Health San Antonio
- The STRONG STAR Data & Safety Monitoring Board, which is a committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason.
- The Institutional Review Board and the Compliance Office of the University of Texas Health Science Center at San Antonio, and other groups that oversee how research studies are carried out.
- The Food and Drug Administration (FDA) and other U.S. State and Federal Government agencies when required by law.

If you decide to participate in this study, you will be giving your permission for the groups named above to collect, use and share your health information within the limits of the law. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. You need to be aware that some parties receiving your protected health information may not have the same obligations to protect your protected health information and may re-disclose your protected health information to parties not named here. If your protected health information is re-disclosed, it may no longer be protected by state or federal privacy laws.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name to identify your health information. These code numbers will be used on any copy of our study records and other study materials containing health information. If the results of the study are reported in medical journals or meetings, you will not be identified.

STRONG STAR strictly controls access to study data only allowing researchers associated with this study to review your data. However, complete confidentiality cannot be promised because information regarding your health may be required to be reported to appropriate medical authorities. For example, if you indicate you have thoughts of harming yourself of others the research team will want to immediately work with you to get you help.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study.

After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to:

Dr. Casey Straud
University of Texas Health Science Center at San Antonio
Department of Psychiatry and Behavioral Sciences – Mail Code 7747
7550 IH10 West, Suite 1325, San Antonio, Texas 78229

How long will your PHI be used?
By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends and all required study monitoring is over. If you also decide to participate in the STRONG STAR Repository with a separate consent, you will agree to let us use and disclose your health information in accordance with the Repository's authorization.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:
Principal Investigator: Casey Straud, PsyD, ABPP who can be reached at 210-562-6742.

If primary is not available, contact
Study Coordinator: Amanda Flores, BS, who can be reached at 210-562-6726

The University of Texas Health Science Center committee that reviews research on human subjects (Institutional Review Board) will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the IRB by calling 210-567-8250, or by mail to IRB, UT Health San Antonio, Mail Code 7830, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.

Title of Study: Safety, feasibility, and benefits of transcranial direct current stimulation (tDCS) in human subjects with PTSD receiving an exposure-based, behavioral therapy

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE

- You have read the above information.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.

Adult Signature Section

- You have voluntarily decided to take part in this research study.
- You authorize the collection, use and sharing of your protected health information as described in this form.

Printed Name of Subject	Signature of Subject	Date	AM PM

Printed Name of Person Obtaining Consent and Authorization	Signature of Person Obtaining Consent and Authorization	Date	AM PM Time

☐Consent and authorization was obtained from this individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. The method used for communication with the subject was: _____.

The specific means by which the subject communicated agreement to participate was: _____