

UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT FORM AND HIPAA AUTHORIZATION FORM

Protocol Title: Accelerated TMS to a novel brain target in MDD and PTSD

Study Sponsors: CureAccelerator (Cures Within Reach and The Kahlert Foundation)
University of Pennsylvania School of Medicine

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Emergency Contact: If you have a study related medical emergency,
please contact the study staff or call 911

Why am I being asked to volunteer?

You are being asked to voluntarily participate in a research study because you are between the ages of 18-60, you are experiencing post-traumatic stress disorder (PTSD) and/or depression, and you expressed an interest in participating. In order to participate in the present study, you must not be currently taking any psychiatric medications. Your participation is voluntary, which means you can choose whether or not you want to participate.

If you choose not to participate, there will be no loss of benefits to which you are

otherwise entitled. We will be recruiting 40 subjects to complete this study.

This consent form describes what this study is about, the possible risks and benefits of being in this study, and what we will ask you to do. The research team will explain the study and answer any questions you may have. You may also discuss it with your family, friends, or doctor. You may find some of the medical language difficult to understand, so please ask the research team about anything you would like to know. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

This is a Phase I Clinical Trial designed to evaluate novel transcranial magnetic stimulation (TMS) methods for treating depression/PTSD. TMS is an FDA- approved procedure for treatment-resistant depression. The use of the stimulation in this current study is considered experimental. The purpose of this research study is to compare the effects of TMS at two different brain regions. This information will help us to determine which treatment strategies provide the greatest clinical benefit to patients. Results of the study will provide brain and behavior measures for future work, which may be critical to developing effective disease markers and novel treatments for psychiatric conditions.

How long will I be in the study?

If you agree to take part in this study, your involvement will take place over approximately 8 months, with actual, in-person study visits finishing after 2 months. Participation will involve:

- One screening session, which includes a series of questions about your medical history, psychiatric symptoms, and a demonstration of the TMS procedures. This screening visit will last approximately 2-3 hours.
- One MRI scan, which will take place over a single 1-hour session. In some instances, if you are also participating in one of our other studies at the CNDS, then the same MRI scan may be used for both studies. In this case, the MRI session would not need to be repeated.
- 10 initial TMS treatment visits (every weekday for 2 weeks). We will spend 20 minutes marking sites on a swim cap to target areas of your brain for stimulation, and then we will administer TMS over the course of approximately 1 hour.
- A psychological assessments, conducted during your TMS visits. This will include questions about your current mood, history of symptoms, and memory.
- A 3-week break from TMS treatment; this break will include two phone visits that will take approximately 30-60 minutes.
- 10 additional TMS treatment visits (every weekday for 2 weeks). We will spend 20 minutes marking sites on a swim cap to target areas of your brain for stimulation, and then we will administer TMS over the course of approximately 1 hour.
- Monthly phone and/or survey visits for follow up assessments of symptoms for an additional 6 months concluding your 8 month study participation.

Procedure	Screening (2-3 Hours)	Baseline (2- 3 Hours)	TMS Treatment (1 ½ hours)	*3 week break* 2 Phone calls (30-60 minutes)	TMS Treatment (1 ½ hours)	Follow-Up Calls (30-60 minutes)
Visit Number	0	1	2-11	N/A	13-22	N/A
Visit Type	In-person	In-person	In-person	Phone	In-person	Phone/ Surveys
Informed Consent	X					
Clinical Assessments	X	X	X	X	X	X
Neurocognitive Assessments		X	X (Visit 11 Only)		X (Visit 22 Only)	
MRI		X				
TMS	X (Demonstration Only)		X		X	
Behavioral Tasks			X		X	
EEG and eyetracking		X	X (Visit 11 Only)		X (Visit 22 Only)	

What am I being asked to do?

Medical History

We will also ask you questions about your medical and psychological history. Because we require participants to abstain from drug use for the duration of the study, we may ask you to complete a urine drug screen to confirm adherence to this policy. This is to ensure patient safety and data quality. For this drug screen, we will use a secure urine analysis. The test will be collected by study staff and results are available within approximately five minutes of collection. We will record the test results in our secure online database, which only team members have access to. The test will be destroyed immediately after.

Neurocognitive testing and symptom interview

We will conduct neurocognitive tests to assess your attention, concentration, and memory. These tests will involve a combination of oral and written procedures.

EEG and eyetracking

During the neurocognitive tasks we may ask you to wear an EEG headset. We may also record the location of your gaze at any particular time during these tasks using a passive eye-tracking device.

Behavioral Tasks

We will ask you to view peaceful videos of nature scenes or to view and remember images on a screen. You will be randomly assigned the order in which you complete these tasks by a random number generator. You will also be asked to repeat some of the neurocognitive tests completed during your initial screening interview.

MRI scan

We will ask you to undergo one MRI scan of your brain. For the MRI, you will be asked to lie still on a padded table in the scanner while images of your brain are obtained. The scanner produces loud repetitive knocking noises during the study that some people find bothersome. Earplugs will be provided to lessen the noise.

TMS sessions

Visits 2-11 and 13-22 will use TMS. We will ask you to sit still for approximately seven minutes at a time when TMS is administered. TMS will be administered twice per session, with approximately a 20 minute break between each round of TMS. The TMS, itself, feels like someone is tapping or flicking you on the side of the head. It can sometimes feel uncomfortable and produce a localized headache or tenderness, but that should go away within an hour or less.

What are the possible risks or discomforts?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Clinical interview and assessment

Some discomfort may be associated with the clinical assessments conducted in this study. You may experience emotional discomfort when answering some questions related to past or current symptoms, traumatic experiences, and/or stressful events. Our study staff will accommodate requests to facilitate the interview process. You may choose not to answer any of the questions and to terminate your participation.

Behavioral Tasks

There are no known risks to these standardized assessments.

MRI scan

An MRI scan requires you to be in a partially enclosed space inside the scanner. Some people find this uncomfortable and claustrophobic. You need to inform the doctor ordering the scan, or the study staff, if you suffer from claustrophobia (fear of enclosed spaces or anxious feelings accompanied by rapid heart rate or shortness of breath). The MRI scanner produces different types of noises during a scan. Since the noises can be loud, you will be given earplugs. The MRI scanner has an intercom which allows the technologist to talk to you and to hear you during the scan. You will be able to hear the technologist talking to you during the scan even if you wear earplugs.

- An MRI scanner has a strong magnet which attracts certain metals. If anyone has these types of metal in their body, the MRI's strong magnetic field can cause metal to move, resulting in injury. To prevent an injury, you will be asked questions or given a form requesting information about any metal in your body, including implanted medical devices, and asking if you work with metals. If you have metallic devices or fragments in your body, you will not be able to participate in this study.
- Some dyes in tattoos and permanent eyeliner contain metals which may heat up

during the MRI scan, causing the area with the tattoo to become irritated and swollen.

- No metal objects can be brought into the MRI scan room at any time, because the MRI magnet will quickly and strongly pull those items into the scanner. To prevent any injury to patients and staff and any damage to the MRI scanner, you will be asked to remove all jewelry and clothing containing metal before you enter the MRI scan room. Also, since the MRI magnet will erase credit cards, they must not be taken into the scan room. Once you are positioned in the scanner, the door to the room will be closed to prevent anyone with any metal object entering the scanroom.
- It is possible that during the course of the research study, the research staff may notice unexpected findings on an MRI scan. Should this occur, the findings will be considered by the appropriate personnel and the study doctor will inform you. This information may or may not be significant and may lead to anxiety about your condition and to further evaluation by your physician.
- Although there are no known risks related to MRI in pregnancy, there is a possibility of undiscovered risks. Since there is no possible benefit from participating in this study for a pregnant woman, we will exclude pregnant women. Likewise, women of childbearing potential should use an acceptable method of contraception for the duration of the study (condoms with spermicide, intrauterine device, oral contraceptive pills, sterilization, or abstinence). Implantable contraceptives are generally very safe for MRI, but the MRI technician may ask you additional questions before entering the MRI suite to ensure your safety.

TMS

The most common side effect of TMS (approximately 25% of patients) is a mild headache. There are no known long-term adverse effects reported with the use of this device. Rarely, device malfunction could result in a scalp burn (fewer than 1% of patients). There may be long-term risks that are currently unknown.

- Risk with TMS is considered low because the magnetic fields produced at the stimulation intensity used are thought to be without harm. The exception is if you have a cardiac pacemaker, or a certain type of metallic clip in your body (i.e., an aneurysm clip in your brain). Participants with these devices will be excluded from this study, as TMS could cause these object to heat up, move, or malfunction.
- In patients with epilepsy, activation of the brain by TMS could also activate a seizure. Patients with stroke may be at increased risk for a seizure due to the brain scar. Therefore those with history of epilepsy or stroke will be excluded from the study. For a typical physically healthy person, a TMS- induced seizure in this experiment is very unlikely.
- The TMS device produces a clicking sound. Although studies have found no hearing impairments as a result of this sound, some subjects experience a mild temporary effect on their hearing. To minimize this possibility, you

will be given protective earplugs or headphones.

- Although it is uncommon, approximately 5% of subjects have experienced nausea during the experiment. You can discontinue the experiment if you experience any discomfort during the study.
- Objects such as watches and credit cards should also be removed as these could be damaged.
- Some subjects experience a minor headache or local pain or swelling as a result of the TMS procedure; you may discontinue the experiment at any time.
- You may also experience temporary and local bruising, swelling, or pain from the swim cap and/or muscle activation by TMS.

EEG

EEG procedures are safe and have been in use for decades in both clinical and basic research settings. There are no known major risks associated with this procedure. Some people may experience a mild headache or discomfort when wearing the headset and completing the computerized tasks. Very rarely, seizures have been reported during EEG recordings for individuals with a preexisting condition of seizure disorder.

Eyetracking device

The eyetracking glasses feels just like regular eye glasses, and you will be able move your eyes, head, and body as normal. No discomfort is expected during the procedure.

Risk to confidentiality

There is a rare risk that confidentiality could be breached in this study. Breaches in confidentiality could impact your future insurability and/or employability.

Our research office is not equipped to provide clinical support or counseling beyond the study visits and your participation in our projects. Therefore, if during the course of this investigation, your symptoms worsen to the point where you feel you need psychological or medical support, we ask that you contact the advice nurse / primary care doctor / or relevant agent representing your medical coverage for help.

If you begin a new course of treatment during the course of your participation with us, it may disqualify you from further participation in our study. We ask you to notify us to discuss this possibility if you begin a new treatment or are hospitalized for any condition during your participation in this study.

For suicide or crisis intervention, you are invited to call Philadelphia Behavioral Health which accepts calls 24 hours / day and 7 days / week at: [\(215\) 686- 4420](tel:2156864420). For similar hotlines outside of the Philadelphia area, please consult www.suicide.org

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You will be participating in an experimental treatment that may or may not help to alleviate your symptoms. Thus, there may be no direct benefits to you for your participation in this study. One potential benefit of participation includes the advancement of science.

What other choices do I have if I do not participate?

This is a voluntary study. If you choose not to participate, you may seek information about other alternatives and treatments available by discussing options with your personal physician. You are still eligible to receive the standard of care treatment if you do not participate in the research. You may discuss these options with your personal physician.

Will I be paid for being in this study?

You will receive \$30.00 compensation for completing the MRI procedure, and all TMS treatment is included as a part of the study. For participants who wish to complete the EEG/eyetracking procedure during the Baseline Visit, Visit #11, and Visit #23, they will receive a total of 75\$ (25\$ per visit) at the end of the study. Therefore, subjects will receive a grand total of \$105 if they participate in the EEG/eyetracking procedures and complete the MRI. If subjects prefer to not complete the EEG/eyetracking recordings, they will receive \$30 for completing the MRI.

If you have already completed an MRI as a part of another study at our center, this MRI may be able to be used for this this study and may not need to be repeated. In this case, you would not be compensated for the MRI scan.

Your payments will be given to you in the form of a Greenphire ClinCard. This is a reloadable prepaid card (similar to a debit/ credit card) which allows funds to be available immediately. You can use it for in-store or online purchases by selecting the “Credit” option at check-out, or it can be cashed out by presenting to a teller at any MasterCard member bank (look for a MC logo on the bank window). Study staff will provide you with a “ClinCard Cardholder FAQ: US” document to help answer any additional questions you may have. You will receive this card on the day you complete the MRI.

Please note: In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of \$600 in a calendar year.

Will I have to pay for anything?

You will not have any costs for participating in this research study. The costs of all procedures will be covered by the study.

What happens if I am injured from being in the study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. If you are injured, you should inform the physician who treats you that you are participating in this study.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

This research may involve risks that are currently unforeseeable. University of Pennsylvania investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator, Dr. Desmond Oathes at (215)-573-9390.

When is the study over? Can I leave the study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. Your personal participation in the study will last approximately 8 months. This study may be stopped by you at any time. It may also be stopped by the Principal Investigator, the study Sponsor, or the Food and Drug Administration (FDA) without your consent if:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor or the study Principal Investigator has decided to stop the study.
- Other administrative reasons
- Unanticipated circumstances

If you decide to participate, you are free to leave the study at any time. There are no medical risks involved in the early termination of this study.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy.

An exception to confidentiality is if you report child abuse or neglect or if you report current suicidal or homicidal ideation of concern to the research team. Any information about child abuse or imminent intent to harm yourself or others will be reported to authorities, as required by law.

We will keep your participation in this research study confidential to the extent

permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research.

Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives, to complete Hospital or University responsibilities
- University Pennsylvania's Institutional Review Board (a committee that oversees the conduct of research involving human participants).

Once all hard copy records are collected, they will be kept in a double-locked environment. Data collected during the study will be entered and stored in a password-protected database, accessible only to engaged study members. All electronic data will be coded and assigned a randomly generated research identification number. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you; that is, the information will be de-identified. Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form.

What information about me may be collected, used or shared with others?

During your participation, you will be asked to provide your name, address, telephone number, email address, date of birth, and your social security number (so that we may issue you a check to compensate you for participation). This identifiable information will be held in strict confidence and will be kept in password protected files behind locked doors. Your personally identifying information will not be linked to any of the data that is analyzed and reported. All data will be de-identified when reported.

You will also be asked to answer questions about your medical history including questions about your physical and mental health. Results from physical exams and cognitive assessments will be part of the research record.

All research data will be de-identified and assigned a randomly generated research identification number.

All information obtained will be kept completely confidential and will be in locked files behind locked doors. Electronic data will be encrypted and password protected.

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures also are used to:

- Do the research
- Oversee the research
- To see if the research was done correctly.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Subject Informed Consent Form and HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above. If you do not sign this form, you will not be able to participate in the study.

If you decide not to participate, it will not affect

- Your treatment or the care given by your health provider
- Your insurance payment or enrollment in any health plans.
- Any benefits to which you are entitled.

If you sign this form:

- You authorize the use of your PHI for this research.
- Your signature and this form will not expire as long as you wish to participate.
- You may later change your mind and not let the research team use or share your information.

If you revoke your authorization:

- The research team may only use and share information already collected for the study.
- Your information may still be used and shared if necessary for safety reasons.
- You will not be allowed to continue to participate in the study.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

For general questions or for scheduling, please call the Center for Neuroscience of Depression and Stress at 215-746-2637. If you have concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, please call the study supervisor at 215- 746-2637. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

How will I be contacted?

We would like to contact you by phone, email, or mail in order to arrange your appointments. Some of these messages may contain information that identifies you. We will also be contacting you in the future, after the conclusion of the study, in order to follow up on your status. We will ask you to provide contact information for an additional individual who knows where to find you in the event that we cannot reach you.

May we contact you to invite you to participate in future studies if we determine that you may be eligible for them?

Yes

No

Would you like to participate in the EEG and eyetracking procedures of this study?
Participation is optional and not a requirement of the study.

Yes
No

If you choose to participate in future studies at the Center for Neuromodulation in Depression and Stress, may research staff have access to and use your data (including MRI scans) collected as a part of this study?

Yes
No
N/A

If you have previously participated in a study at the Center for Neuromodulation in Depression and Stress, may research staff have access to and use your data (including MRI scans) collected as a part of that study for the current study?

Yes
No
N/A

Do you agree to abstain from **substance use** (including marijuana and illicit drugs) **throughout the study duration** and **alcohol 24 hours prior** to your visits? Please note that we may use a drug screening to verify adherence to this policy and results may affect study eligibility.

Yes
No

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

Name of Subject (Please Print)

Signature of Subject

Date

Name of Person Obtaining Consent (Please Print)

Signature

Date