Intermittent Theta Burst for the Treatment of Alcohol Use Disorders in Veterans

NCT03291431

November 29, 2021

Informed Consent

Intermittent Theta Burst TMS for the Treatment of Alcohol Use Disorders in Veterans

Are you participating in any other research studies? _____ Yes _____No

PURPOSE OF RESEARCH: Why is this study being conducted?

You are invited to participate in a research study to determine the effectiveness of a type of transcranial magnetic stimulation for the treatment of alcohol use disorders. In this study, theta burst transcranial magnetic stimulation (TBS) will be used and involves periods of brief stimulation of a brain region under the left side of your forehead.

You were selected as a possible participant in this study because you have been diagnosed with an alcohol use disorder and are being treated for this disorder the VA Palo Alto. This study is being done together by researchers at VA Palo Alto and Stanford University and will include about 40 research participants.

You have already completed an in-person or telephone interview about joining this research study and were asked basic questions about your health, medications and psychological functioning determine if you are eligible to participate in the study. You are now receiving this consent form for you to read and think about before you participate further in the study. The study staff will review the consent form with you and answer any questions you may have.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care you are entitled to.

DURATION OF STUDY INVOLVEMENT: How long will I be in the study?

This research is expected to take approximately 5 years to study 40 participants. While in treatment at the Palo Alto VA, your participation will usually involve 12-14 study visits: Two Baseline Visits, 20 TBS Treatment sessions (2 or 3 per day over about 2 weeks, Monday-Friday), one Post-Treatment Visit. After your Post-Treatment Visit, we will contact you by phone each month for 1 year.

If you are eligible and agree to participate, you will be randomly assigned to receive *either* active/real TBS *or* inactive/placebo TBS. It is important to know that random assignment means you will have a 50% chance of receiving the active/real TBS treatment. In other words, 50 of 100 study participants will receive active/real TBS treatment.

PROCEDURES: What will happen if I participate in this study?

If you agree to take part in this study, you will be asked the following procedures, as indicated. You may be asked to repeat some procedures if the original data collected are not useable for some reason. Magnetic resonance imaging scans will take place at Stanford University and all other procedures will take place at the VA Palo Alto.

BASELINE VISIT (about 10 hours over 2 days)
The Baseline Visit will be completed over two days:

1) Psychiatric Interviews, Medical History, Drug/Alcohol/Pregnancy Screens, Cognitive Assessments, Motor Threshold, and Saliva Samples:
   - You will be complete written and/or computer interview/questionnaires that ask about your psychiatric history including questions about your alcohol and substance use, and any mood, anxiety, PTSD, pain symptoms.
   - We will ask you to provide demographic information (such as your age, your occupation, your level of education).
   - We will ask about your medical history and any medications that you are currently taking, or have taken in the past month, including vitamins or supplements, and record your height and weight. During the study, you cannot take any medications known to increase the risk of seizures.
   - If you are a woman capable of becoming pregnant, a urine sample will be used to test for pregnancy. A positive test will exclude you from participation in this study. Additionally, it is important for you to tell us if you think you trying to become pregnant or might be pregnant. The risks of TBS on a pregnancy are unknown.
   - You may be asked to submit a urine sample to screen for illegal/non-prescribed drug use and/or do a breathalyzer to screen for alcohol use.
   - You will be complete paper-and-pencil and computer test of your attention, memory, problem-solving and other thinking skills.
   - We will take measurements using the TBS machine to find your “motor threshold”. This is used to determine the settings that will be used for your study treatments.

- Saliva samples will be collected by study personnel. This involves you spitting into two or three collection tubes. You will be asked NOT to eat or drink anything, including water, 30 minutes prior to your saliva collection.
- Cells in your saliva will be used to see if we can identify biological markers of how well study participants respond to TBS. Uses of saliva samples in biological marker and genetic research are explained below in the GENETIC TESTING AND TISSUE BANKING FOR FUTURE RESEARCH section of this consent form.

2) Magnetic Resonance Imaging (MRI) scans of the brain:
MR scans will be conducted at Stanford Center for Cognitive and Neurobiological Imaging and will take about about 3 hours, including travel to and from Stanford (which we will provide). This scanner is an investigational system; it contains much of the same hardware and software as an FDA approved system but has improved performance due to a better performing gradient coil. The scanner has the same magnet strength, SAR limits, slew rates and noise characteristics consistent with the FDA approved scanners, so there is no additional risk. The MRI scan uses a strong magnet to take images/pictures of the brain and test other brain functions. The MRI scan involves lying on a table, then being slid into a large tunnel. Your head and shoulders lie in a plastic rounded tray which makes it more comfortable and easier to lie still. MR machines use a strong magnet and radiofrequency magnetic fields to make images of the body interior. The hardest part of the scan is the need to lie still for this amount of time. You might also be asked to return for additional scans at a future time.

During this time you will not be exposed to x-rays, but rather to a strong magnetic field and radiofrequency magnetic fields, which you will not feel. You will hear repetitive tapping noises from the scanner as it collects the data that makes the images. You will be required to wear earplugs or headphones that will be provided. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

If you are a woman who can become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

Risks: There are currently no known harmful side-effects associated with temporary exposure to the strong magnetic field used by MRI scanners. Some of

the images, words, and sounds presented will have an emotional content and so could be mildly upsetting to some individuals. Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body, including eyeliner and other permanent makeup. Tattoos could become warm and irritated during the scan and remain so for several days. If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is not unexpected and should not be painful. However, you may have the scan stopped at any time if this occurs. If you feel discomfort at any time, notify the operator and you can discontinue the scan at any time. Dizziness or nausea may occur if you move your head rapidly within the magnet. Some of the radio frequency imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Please report any heating sensation immediately. **If you feel discomfort at any time, notify the operator and you can stop the exam at any time.**

Some of the radio frequency imaging coils, the imaging software and other devices being used to perform scans are not approved by the FDA, thus are considered experimental in nature.

Incidental Findings:
The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. Our research scans do not qualify as a

clinical diagnostic scan. The investigators for this project may not be trained to perform medical diagnosis. The investigators are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. If this occurs, we will follow Stanford Center for Cognitive and Neurobiological Imaging protocol for incidental findings. In this case the research scans are referred to an approximately qualified individual. Because the images are taken using research settings they will not be made available for clinical purposes. Finding out that you may have a medical abnormality that you had not been aware of before could cause psychological stress to you or your family and possibly affect your health insurance coverage in the future.

TREATMENT PHASE (2 to 2.5 weeks)

The Treatment Phase will last up to 2.5 weeks and involves the following procedures:

Randomization to TBS Treatment:

- The study is a clinical trial, in which **you will be randomly assigned to receive *either* active/real TBS *or* inactive/placebo TBS. It is important to know that random assignment means you will have a 50% chance of receiving the active/real TBS treatment. In other words, 50 of 100 participants will receive active/real TBS treatment.**
- If you are assigned to the active/real TBS treatment group, brief pulses of magnetic energy will be used to stimulate your brain nerve cells (neurons).
- If you are assigned to the inactive/placebo TBS group, the exact same machine will be used; however, the magnetic energy reaching your brain will be greatly reduced and your brain cells will not be stimulated.
- You and the study staff will not know if you have been assigned to the active/real TBS or inactive/placebo TBS. The study staff will not know which study participants were assigned to the active/real TBS or inactive/placebo TBS until the entire study is completed. In case of an emergency, the study staff can find out which treatment you are receiving.

TBS Session Scheduling:

- You will have a total of 20 TBS sessions over about 2 weeks. TBS sessions will usually occur Monday through Friday, but a Saturday and/or Sunday session may be necessary.
- You will typically complete two (2) TBS sessions per day, usually immediately after breakfast and immediately after lunch. If a TBS session is missed, you may complete three (3) sessions per day.
- Each TBS session may take up to 30 minutes. The treatment (active/real TBS *or* inactive/placebo TBS) itself lasts about 3 minutes, plus another 20-25 minutes of preparation.

- You may walk or drive yourself to and from treatment visits and attend to your normal daily tasks before and after your TBS sessions.

Procedures for TBS Session:

- During treatment, you will sit in a reclined in a chair. You will be provided with ear plugs and headphones.
- You may close your eyes and rest while you sit still in the chair, but not sleep.
- At each TBS session, we will ask you about any changes in medications. We will also ask you about any changes in health or behavior since your last visit, which may or may not be related to the study treatment. We will ask you how many hours you slept the night before and if you have taken any drugs or alcohol between visits.
- You may be asked to submit a urine sample to screen for illegal/non-prescribed drug use and/or do a breathalyzer to screen for alcohol use.

Description of TBS Sessions:

- You will be awake and alert while you will recline in the chair.
- You will wear a cloth or plastic cap that is personalized for you, which has markings on it for correct placement of the TBS coil that delivers the magnetic pulses. Your head will be placed in a holder so that it is correctly positioned and does not move. You will have electrode pads placed on your forehead.
- The real/active or inactive/placebo TBS magnetic energy is delivered through metal coil in a plastic case. The coil will be held on the side of your head and positioned by the markings on your cloth or plastic cap.
- There will be a clicking noise as magnetic pulses are produced, but you will hear white noise through the headphones you will wear. You will also be given earplugs to protect your hearing from the clicking sound.
- You may feel a tingling sensation on your head. Study staff will ensure you are as comfortable as possible during the TBS sessions.

POST-TREATMENT VISIT (4 to 5 hours)

About 1 to 3 days after your last TBS session, you will repeat several of the tests you did at your baseline. The Post-Treatment Visit is very important, so that we can measure any changes in your memory, other thinking skills, and brain function following your TBS sessions. The Post-Treatment Visit will be completed over 1 or 2 days. At this visit will you will repeat:

- Written and/or computer interview/questionnaires that ask about your any mood, anxiety, PTSD and pain symptoms.
- Paper-and-pencil and computer test of your attention, memory, problem-solving and other thinking skills.

- An MRI brain scan at Stanford Center for Cognitive and Neurobiological Imaging.
- You may be asked to submit a urine sample to screen for illegal/non-prescribed drug use and/or do a breathalyzer to screen for alcohol use.
- Repeat collection of saliva samples.

FOLLOW-UP PHASE (15-20 minutes per contact or visit)

- After your Post-Treatment Visit, we will call you once per month, for 1 year. You may also meet with a study team member, in person, if it is convenient for you.
- During this follow-up contact we will ask you questions about any alcohol or substance use since your Post-Treatment Visit and questions about any mood, anxiety or PTSD symptoms.

WOMEN OF CHILDBEARING POTENTIAL

If you are a woman who can become pregnant, it is expected that you will use an effective method of birth control to prevent exposing a fetus to a potentially dangerous agent with unknown risk. If you are pregnant or currently breast feeding, you may not participate in this study. You understand that if you are pregnant, if you become pregnant, or if you are breast-feeding during this study, you or your child may be exposed to an unknown risk.

To confirm to the extent medically possible that you are not pregnant, you agree to have a pregnancy test done before beginning this research study. You must agree to avoid sexual intercourse or use a birth control method judged to be effective by the investigator and which will not interfere with the proposed investigation. You must accept the risk that pregnancy could still result despite the responsible use of reliable method of birth control. You agree to notify the investigator as soon as possible of any failure of proper use of your birth control method, or if you become pregnant, either of which may result in your being withdrawn from the study.

GENETIC TESTING AND TISSUE BANKING FOR FUTURE RESEARCH

As part of the analysis on your saliva samples, the investigators will do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. **In this study**, genetic tests on cells from your saliva may allow us to better understand: 1) How the code of your genes may influence study your response to TBS; 2) The code of

your genes relates to your brain function and behavior. This research will inform an understanding of how differences in genetic code influence in function in the nervous system, which may also be relevant to risk for psychiatric illness or response to treatments. **The genetic findings from your saliva samples collected for this project will be used for research purposes only, and you will not be told the results.**

Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include anxiety, other psychological distress, and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

We will protect the confidentiality of your samples and information about you. Your samples will be stored in a locked area and all information about you will be stored in a locked file cabinet or on a password protected secure computer.

As part of this research we would like to save any leftover saliva and/or genetic samples from the saliva for future research. Your saliva samples and any genetic material from these samples will be securely stored at the Palo Alto VA and may be used for future research on psychiatric problems, including alcohol and substance use disorders. Your samples will be stored and used for future research until the sample is all used up. Your sample and information about you will be labeled with a code that **does not** contain your name, initials, social security number, date of birth, or other ways that identify who you are. The research we conduct with your saliva is being done for research purposes only and we will not tell you or your doctor about the or results of any current or future the genetic research.

The research we conduct using your saliva samples may result in inventions or discoveries that could be used to make new products or diagnostic or therapeutic agents. These inventions and discoveries may become financially valuable. You

will not receive any money or other benefits from any commercial or other products that are made using your saliva samples.

You may withdraw your permission for us to use your saliva samples for future research at any time. Contact the Program Director, Dr. Timothy C. Durazzo at (650) 493-5000 x62982 to withdraw your permission. If you take back your permission, the research team can continue to use information about you collected before you decided to take back your permission, but they will not collect any information about you going forward and any remaining samples will be destroyed.

_____ Yes, I give permission for my samples to be saved for future research, as described above.

_____ No, I do not give permission for my samples to be saved for future research.

PARTICIPANT RESPONSIBILITIES

As a study participant, your responsibilities include:

- Following the instructions of the investigators and study staff.
- Keeping your study appointments. If it is necessary to miss an appointment, please contact the investigators or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigators or research study staff about any side effects, additional doctor visits, or hospitalizations that you may have.
- Tell the investigators or research staff if you stop using birth control or think you might be pregnant.
- It is important that you not give false, incomplete, or misleading information about your medical history, including past and present alcohol and drug use, because this could have serious consequences for your well-being. Active use of amphetamines, cocaine and alcohol can increase the risk of a seizure while receiving TBS. If the study staff is concerned about your use of alcohol and other substances during your participation in this study, you may be asked to stop the study.
- Ask the study staff questions as you think of them.
- Tell the Program Director/Principal Investigator (Dr. Timothy Durazzo or study staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you agree to participate and then you change your mind, you are **free to withdraw** your consent and stop your participation at any time. If you decide to withdraw from the study, you will not lose any benefits to which you would otherwise be entitled to receive at any VA facility or other health care organizations. If you want to stop being in this study, you should tell the investigators or study staff. You can do this by phone by calling the Program Director, Dr. Durazzo at 650-493-5000 ext.62482.

The study investigators, study institutional review board or study sponsor may also withdraw you from the study without your consent. Should this happen, research personnel will contact you to discuss the reason for your discontinuation in this study. You may be withdrawn without you consent for one or more of the following reasons:

- Failure to follow the instructions of the investigators and/or study staff.
- The researchers or study sponsor decides that continuing your participation could be harmful to you.
- Pregnancy (if applicable).
- You need treatment or medications not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

This study involves the following risks, discomforts, and possible inconveniences:

Risks of TBS:
A few individuals receiving different types of transcranial magnetic stimulation have had a seizure. The type of transcranial magnetic stimulation that is FDA approved to treat depression has a risk of seizure that is far below 1 out of 100 people (less than 1%). The TBS administered in this study has different settings and procedures that are thought to lower the risk of seizure even further. All the reported seizures associated any type of transcranial magnetic stimulation resolved quickly, on their own, and no one had any negative lasting effects or impact. In summary, the risk of a seizure is low when TBS is used the way it will be applied in this study.

In the unlikely event that a seizure does occur, you will be closely monitored and

treated for any medical or psychological consequences. Lab tests will be drawn and you will be seen by a neurologist as soon as possible. The VA Palo Alto facility where this and other TBS studies are being conducted is fully equipped to safely handle a seizure. You will be given a letter regarding the seizure to share with your primary health care provider. The letter will indicate that the seizure during TBS does not increase your risk for future seizures.

TBS treatment can result in mild to moderate headaches in as many as 30 out of 100 (30%) patients. Headaches and site discomfort readily respond to acetaminophen or ibuprofen. Discomfort may improve over time or go away. TBS treatment may produce movement or tingling of the arm, leg, face, or scalp. You may also experience a temporary feeling of numbness in the face. Rarely, people have fainted, particularly in the initial session of TBS due to the newness of the procedure to them. If you feel faint or dizzy, be sure to let the study staff know. Our study staff is experienced, and you will be reclining in a chair to protect you from falling if you feel faint or dizzy.

In some people, daily TBS caused them to have increased energy, decreased need for sleep, and rapid racing thoughts. This is called manic episode. If you notice these changes notify medical staff at your treatment clinic and this study team.

The possibility of long-term risks is unknown, but previous human and animal brains have shown no evidence of any kind of damage from TBS. As with any investigational treatment, there may be unforeseen risks associated with the TBS device. You will be informed of any new information that is developed during the study that might affect your willingness to continue your participation.

If you are taking any medications or substances that may increase the risk of having a seizure, you will need to be taken off those medications or substances before you can participate. You and your physician will need to discuss the feasibility of your discontinuing any such medications. Withdrawal from such medications may cause discomfort or illness.

The TBS operator will monitor you for ear protection, coil placement, and seizure activity during all TBS sessions. Study staff will monitor you for side effects, and it is important that you report any side effect to study staff promptly. If you believe, or the study investigator believes, that any TBS side effects are not well tolerated, treatment may be stopped altogether and you may be withdrawn from the study.

Risks of MRI:
Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. It is very important that you notify the researcher of any metal objects, devices or implants that are in or on your body before entering the magnet room. This includes biomedical devices such as pacemakers and aneurysm clips, prostheses, and any other metallic objects embedded in your body, such as bullets, buckshot, shrapnel, and any metal fragments from working around metal. All other metallic objects must also be removed from your person prior to entering the magnet room or approaching the magnet to prevent them from becoming a projectile or being pulled by the magnet. This includes keys, jewelry, body piercing, pocket knives, money clips, paper clips, safety pins, hair pins, and barrettes. In addition, objects such as watches, credit cards, and hearing aids could be damaged in the presence of the magnetic field. A locker will be provided for you to secure all your items and valuables.

Before you enter the scanner, we will ask you questions about whether you have any non-removable metal in your body. In addition, we may ask your permission to communicate with your physician to obtain information about your medical history if we need additional information to determine whether you should or should not have the MRI scan.

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator / investigator. You should also notify the operator/investigator if you have any tattoos on your body. There is a small risk that areas with tattoo(s) could become warm, irritated and painful, and remain so for several days due to exposure to the radiofrequency electromagnetic field. If you are or are trying to get pregnant, the effects of the scan on a fetus are unknown and, therefore, we will not perform the examination at this time.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is expected and should not be painful. Some of the radio frequency imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Please report any heating sensation immediately. Dizziness or nausea may occur if you move your head rapidly within the magnet. **IF YOU FEEL DISCOMFORT AT ANY TIME, NOTIFY THE OPERATOR AND YOU CAN DISCONTINUE THE EXAM AT ANY**

TIME.

Risks of Psychiatric Interviews, Medical History, Drug/Alcohol/Pregnancy Screens, Cognitive Assessments

Answering questions on some of the questionnaires and interviews used in this study may provoke mild feelings of frustration, fatigue, sadness or anxiety. A positive pregnancy test may be associated with anxiety. You have the right to refuse to answer any question that makes you feel uncomfortable on any of the interviews, questionnaires or tests. Information you provide will remain anonymous, confidential and will be used only for the purposes of the research study. However, by law, it is possible that information you provide for this study may require research staff to report to the appropriate authorities if you are currently a danger to yourself, danger to someone else, cannot adequately provide for your food, basic clothing or shelter. Additionally, if information is revealed about child abuse or neglect, elder abuse or neglect, or potentially dangerous future behavior to others or yourself, the law requires that this information be reported to the proper authorities.

Risks of Saliva Samples

There are no physical risks associated with collection of your saliva samples.

Risks of Urine Toxicology Screen or Alcohol Breathalyzer Test

There are no physical risks for these procedures. One possible risk is breach of confidentiality, which is very low as all data will only be used for research purposes and will be securely stored. If the drug screen were found positive for an illicit drug and in the unlikely event that it was subpoenaed by a court-of-law or somehow disclosed, it could be incriminating.

POTENTIAL BENEFITS

We cannot guarantee or promise that you will get any benefits from taking part in this study. However, possible benefits may include improvement in attention, memory, other thinking skills, and mood and/or decreased cravings for alcohol or other substances. The information obtained during this study is expected to help researchers learn more about how to more effectively treat alcohol and substance use disorders.

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY DIRECT BENEFITS FROM THIS STUDY.

ALTERNATIVES

The alternative to participating in this study is not to participate. Alternative choices include continuing in your current VA Palo Alto Addiction Treatment Service program.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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.

CONFIDENTIALITY

We will keep your name and all the information you tell us in this study as confidential as possible. We may publish the results of this study for others to read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier.

Other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information. Because this study involves an investigational device, the FDA may also have access to information about you collected in this study.

If you disclose that to study staff that: (a) You intend to harm yourself or someone else, (b) A child is currently or had been abused or neglected, or (c) An elder or dependent adult is currently, or had been abused, we are required by California law to notify the appropriate authorities.

We will keep your name and all the information about you used in this study as confidential as possible. We may publish the results of this study for others to

read about, but you will not be identified in any articles about the study by name, social security number, address, telephone number, or any other direct personal identifier. Also, other federal agencies as required, such as the VA Office of Research Oversight and the VA Office of the Inspector General may have access to your information.

FINANCIAL CONSIDERATIONS

Payments. Will I be paid for taking part in this study?
Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa.

You will receive a total of $240 for baseline, treatment phase and post-treatment visit study procedures. Participants who complete the MRI MID task may be offered additional minor compensation depending on their performance on the task. If you do not complete all baseline or post-treatment visit procedures, you will receive a pro-rated amount that is lower than $240, based on how many procedures you completed. You will receive $50 if you complete all six-monthly contacts after the Post-Treatment Visit. The maximum amount of compensation you can receive by completing all parts of the study over 1 year is $290.**You will be paid an equivalent dollar amount for your participation in Amazon gift cards. No cash or checks will be dispensed for your participation.**

Costs
There will be no costs to you for any of the treatment or testing done as part of this research study. However, medical care and services provided by the VA that are not part of this study (e.g., normal hospital and prescription expenses which are not part of the research study) may require co-payments if your VA-eligibility category requires co-payment for VA services.

Sponsor
The Stanford University Neurosciences Institute is providing financial support and/or material for this study.

COMPENSATION for Research Related Injury

If you are injured as a direct result of being in this study, medical treatment will be available. If you are eligible for veteran's benefits, the cost of such treatment will be covered by the VA. If not, the cost of such treatments may still be covered by the VA depending on several factors. In most circumstances, the treatment must be provided in a VA medical facility. No other form of compensation for

injuries is available. However, by signing this form you have not released the VA from liability for negligence. For further information, you may call the Human Protections Administrator at (650) 493-5000, ext. 67593 or the V.A. Regional Counsel at (415) 750-2288.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the principal investigator/program director Dr. Timothy C. Durazzo at (650) 493-5000 x62982.

Injury Notification: If you feel you have been hurt by being a part of this study, please contact the Protocol Director Dr. Timothy C. Durazzo at (650) 493-5000 x62982.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650) 723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to be:

- informed of the nature and purpose of the experiment;
- given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- given a description of any attendant discomforts and risks reasonably to be expected;
- given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- given an opportunity to ask questions concerning the experiment or the procedures involved;

- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- given a copy of the signed and dated consent form; and
- given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you (by phone or letter) about related studies that may be of interest to you?

_____ Yes, I would like to be contacted for future research opportunities.

_____ No, please do not contact me about future research opportunities.

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Participant Date

_____
Print Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

Person Obtaining Consent HIPAA Authorization confirmation:

_____

☐ Confirm the participant signed the VA HIPAA Authorization (VA 10-0493)

Department of Veterans Affairs

Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research

Subject Name (Last, First, Middle Initial):	**Subject SSN** (last 4 only):	**Date of Birth:**

VA Facility (Name and Address):
VA Palo Alto Health Care System
3801 Miranda Ave.
Palo Alto CA 94304

VA Principal Investigator (PI):
Timothy C. Durazzo, PhD

PI Contact Information:
VA Palo Alto Health Care System
Bldg. 5, C-441
3801 Miranda Ave .
Palo Alto CA 94304 Office:650-493-5000 x62982

Study Title:
Intermittent Theta Burst TMS for the Treatment of Alcohol Use Disorders in Veterans

Purpose of Study:

The purpose of this research study to determine the effectiveness of a type of transcranial magnetic stimulation, intermittent theta burst, for the treatment of alcohol use disorders.

USE OF YOUR INDIVIDUALLY IDENTIFIABLE HEALTH INFORMATION (IIHI):

Your individually identifiable health information is information about you that contains your health information and information that would identify you such as your name, date of birth, or other individual identifiers. VHA is asking you to allow the VA Principal Investigator (PI) and/or the VA research team members to access and use your past or present health information in addition to new health information they may collect for the study named above. The investigators of this study are committed to protecting your privacy and the confidentiality of information related to your health care.

Signing this authorization is completely voluntary. However, your authorization (permission) is necessary to participate in this study. Your treatment, payment, enrollment, or eligibility for VA benefits will not be affected, whether or not you sign this authorization.

Your individually identifiable health information used for this VA study includes the information marked below:

☒ Information from your VA Health Records such as diagnoses, progress notes, medications, lab or radiology findings

☒ Specific information concerning:

☒ alcohol abuse ☒ drug abuse ☒ sickle cell anemia ☐ HIV

☒ Demographic Information such as name, age, race

☐ Billing or Financial Records

☐ Photographs, Digital Images, Video, or Audio Recordings

☒ Questionnaire, Survey, and/or Subject Diary

☒ Other as described: Study MRI data

Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

Subject Name (Last, First, Middle Initial):	**Subject SSN** (last 4 only):	**Date of Birth:**

USE OF YOUR DATA OR SPECIMENS FOR OTHER RESEARCH: (Instruction: When banking or further analysis is an **optional** research activity, complete page 5 and leave this section blank. If banking is a required research activity to store "Data" and/or "Specimen" for future use or if "Not Applicable" is selected, remove page 5 in its entirety.)

☐ Not Applicable - No Data or Specimen Banking for Other Research

An important part of this research is to save your

☐ Data

☐ Specimen

in a secure repository/bank for other research studies in the future. If you do not agree to allow this use of your data and/or specimen for future studies approved by the required committees, such as the Institutional Review Board, you will not be able to participate in this study.

DISCLOSURE: The VA research team may need to disclose the information listed above to other people or institutions that are not part of VA. VA/VHA complies with the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA), Privacy Act of 1974 and all other applicable federal laws and regulations that protect your privacy. The VHA Notice of Privacy Practices (a separate document) provides more information on how we protect your information. If you do not have a copy of the Notice, the research team will provide one to you.

Giving your permission by signing this authorization allows us to disclose your information to other institutions or persons as noted below. Once your information has been disclosed outside VA/VHA, it may no longer be protected by federal laws and regulations and might be re-disclosed by the persons or institutions receiving the information.

☒ Non-VA Institutional Review Board (IRB) at Stanford University
who will monitor the study

☒ Study Sponsor/Funding Source: Stanford University Neuroscience Institute
VA or non-VA person or entity who takes responsibility for; initiates, or funds this study

☒ Academic Affiliate (institution/name/employee/department): Stanford University/Stanford Center for Cognitive and Neurobiological Imaging.
A relationship with VA in the performance of this study

☒ Compliance and Safety Monitors: Study Data Monitoring and Safety Board
Advises the Sponsor or PI regarding the continuing safety of this study

☒ Other Federal agencies required to monitor or oversee research (such as FDA, OHRP, GAO):
FDA and/or OHRP

☐ A Non-Profit Corporation (name and specific purpose):

☐ Other (e.g. name of contractor and specific purpose):

Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

Subject Name (Last, First, Middle Initial)**:**	**Subject SSN** (last 4 only)**:**	**Date of Birth:**

Note: *Offices within VA/VHA that are responsible for oversight of VA research such as the Office of Research Oversight (ORO), the Office of Research and Development (ORD), the VA Office of Inspector General, the VA Office of General Counsel, the VA IRB and Research and Development Committee may also have access to your information in the performance of their VA/VHA job duties.*

Access to your Individually Identifiable Health Information created or obtained in the course of this research: While this study is being conducted, you

☐ will have access to your research related health records

☒ will not have access to your research related health records

This will not affect your VA healthcare including your doctor's ability to see your records as part of your normal care and will not affect your right to have access to the research records after the study is completed.

REVOCATION: If you sign this authorization you may change your mind and revoke or take back your permission at any time. You must do this in writing and must send your written request to the Principal Investigator for this study at the following address:

Dr. Timothy C. Durazzo
VA Palo Alto Health Care System
Bldg. 5, C-441 (151Y)
3801 Miranda Ave .
Palo Alto CA 94304

If you revoke (take back) your permission, you will no longer be able to participate in this study but the benefits to which you are entitled will NOT be affected. If you revoke (take back) your permission, the research team may continue to use or disclose the information that it has already collected before you revoked (took back) your permission which the research team has relied upon for the research. Your written revocation is effective as soon as it is received by the study's Principal Investigator.

EXPIRATION: Unless you revoke (take back) your permission, your authorization to allow us to use and/or disclose your information will:

☐ Expire at the end of this research study

☐ Data use and collection will expire at the end of this research study. Any study information that has been placed into a repository to be used for future research will not expire.

☒ Expire on the following date or event: 12/31/2050

☐ Not expire

Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

Subject Name (Last, First, Middle Initial)**:**	**Subject SSN** (last 4 only)**:**	**Date of Birth:**

TO BE FILLED OUT BY THE SUBJECT

Research Subject Signature. This permission (authorization) has been explained to me and I have been given the opportunity to ask questions. If I believe that my privacy rights have been compromised, I may contact the VHA facility Privacy Officer to file a verbal or written complaint.

I give my authorization (permission) for the use and disclosure of my individually identifiable health information as described in this form. I will be given a signed copy of this form for my records.

_____ _____

Signature of Research Subject Date

_____ _____

Signature of Legal Representative (if applicable) Date

To Sign for Research Subject (Attach authority to sign: Health Care Power of Attorney, Legal Guardian appointment, or Next of Kin if authorized by State Law)

_____

Name of Legal Representative (please print)

Authorization for Use & Release of Individually Identifiable Health Information for Veterans Health Administration (VHA) Research

Subject Name (Last, First, Middle Initial):	**Subject SSN** (last 4 only):	**Date of Birth:**

VA Facility (Name and Address):
VA Palo Alto Health Care System
3801 Miranda Ave.
Palo Alto CA 94304

VA Principal Investigator (PI):	**PI Contact Information:**
Timothy C. Durazzo, PhD	VA Palo Alto Health Care System Bldg. 5, C-441 3801 Miranda Ave . Palo Alto CA 94304 Office:650-493-5000 x62982

Study Title:
Intermittent Theta Burst TMS for the Treatment of Alcohol Use Disorders in Veterans

Optional Authorization Supplement for Placing My Data or My Biological Specimens in a Repository or for Conducting Optional Analysis of My Specimens for Future Use in Research

Purpose. This supplement to the authorization is for either banking of data and/or biological specimens (for example blood, urine, tissue) collected during the study for future research or for conducting optional analysis for this study . You are not required to provide this permission and not providing this permission will have no impact on your participation in this study, i.e., granting this permission is not a condition of participating in this study.

Research Subject Signature. This additional permission (authorization) has been explained to me and I have been given the opportunity to ask questions about this activity. By signing below, I am giving my permission for VHA to:

☒ Store my health information in a research data repository at
VA Palo Alto Health Care System
and sponsored/run by Dr. Timothy C. Durazzo

☒ Store my biological specimens (blood, tissue, urine, etc.) in a research biological specimen/tissue repository at VA Palo Alto Health Care System
and sponsored/run by VA Palo Alto MIRECC and Dr. Timothy C. Durazzo

☐ Further optional analysis of my specimens for the current study occurring below:

Future research of data maintained within a research data repository will only occur after further Institutional Review Board and/or other applicable approvals of the new research to ensure the protection of your individual privacy. Future use of my biological specimens will only occur after the new research has been approved by all required committees.

Signature of Research Subject _____ Date _____

Signature of Legal Representative (if applicable) _____ Date _____

To Sign for Research Subject (Attach authority to sign: Health Care Power of Attorney, Legal Guardian appointment, or Next of Kin if authorized by State law)

Name of Legal Representative (please print) _____