Official Title: Brain Targets for Alcoholic Craving in Veterans with mTBI
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Participant Name: _____ **Date:** _____

Title of Study: **Brain Targets for Alcoholic Craving in Veterans with mTBI (Aim III)**

Principal Investigator: **Amy Herrold, PhD**

VAMC: **Edward Hines, Jr VA Hospital**

SUMMARY

The research is being conducted *to* examine safety, feasibility, and the behavioral and brain effects of a non-invasive treatment, repetitive transcranial magnetic stimulation (rTMS), for Veterans with Alcohol Use Disorder (AUD) and co-occurring Mild Traumatic Brain Injury (mTBI) and/or Post Traumatic Stress Disorder (PTSD). You are being asked to participate in this research study because you are a Veteran and may have symptoms of alcohol use disorder *or* may experience combined alcohol use disorder, mild traumatic brain injury and/or post-traumatic stress disorder symptoms. You also previously participated in the study Brain Targets for Alcohol Craving in Veterans with mTBI (Aim I and Aim II) or Alcohol Craving Treatment Development for Individuals with Co-occurring mTBI, PTSD and AUD (Aim I-Phase I). This study is a continuation to the study/studies you already completed.

If you agree to participate in the study, and you meet study criteria, you will be asked to complete the following research procedures: Informed consent, HIPAA Authorization, a urine sample for drug and nicotine screening, a breathalyzer for breath alcohol concentration screening, neurobehavioral interviews and questionnaires, a structured interview, EEG, 10 rTMS sessions and an MRI, conducted by the PI, Dr. Herrold, or a trained research team member. To find out the effects of rTMS, this study will provide half of the participants real rTMS and half of the participants placebo or fake rTMS. You will not know which group you are in because the placebo or fake rTMS is designed to look, sound and feel like the real rTMS.

Your participation will last for 12 in-person research Visits. A research team member will also call you at a preferred time one day, one week and one month after the 10th rTMS session to complete questionnaires about alcohol craving, mild TBI symptoms and PTSD symptoms over the phone.

During your participation in this study, treatment with real rTMS may improve alcohol craving. This may also improve your quality of life. However, neither of these benefits is guaranteed. <u>You may not personally benefit</u> from taking part in the research but the knowledge obtained may help the health professionals caring for you better understand the disease/condition and how to treat it.

The most common risks of participation are***:***

- Skin irritation from the use of electrodes
- You may experience unpleasant emotions, thoughts or memories during assessments
- Some people experience mild discomfort during the MRI because of tight spaces and keeping still
- *Magnetically Evoked Potentials, Motor Threshold Tests and rTMS Treatment:* the seizure risk for people with AUD, PTSD, mild TBI and combinations of these conditions is unknown, and this is why we are investigating safety in this study.
- Mild temporary headache and/or hearing loss is possible after each rTMS treatment session.

rTMS treatments will be stopped if you go into shock or have a seizure.

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Please note that there are other factors to consider before agreeing to participate, such as additional procedures, use of your personal information, costs, loss of confidentiality, rTMS, might involve risks to the embryo or fetus in pregnant women, which are currently unforeseeable. If you are interested in participating, a member of the study team will review the full information with you.
The alternative to participating in this study is to choose not to participate. You are free to elect this option at any time during or after the consenting process.

INTRODUCTION

You are being invited to participate in a research study that is being carried out at the Edward Hines Jr. VA Hospital. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. The sponsor of the study is VA Office of Research and Development Rehabilitation Research and Development (VA ORD RR&D). If you have any questions about your rights as a human research participant at any time before, during, or after participation, please contact the Institutional Review Board (IRB) at (708) 202-2811 for assistance. If you have questions about this study, you may contact the Principal Investigator, Dr. Amy Herrold at 708-202-5867.

Read the information below closely and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information below, and that you were able to discuss any questions and concerns you had with a member of the study team.

BACKGROUND AND PURPOSE

The **purpose** of this research study is to examine safety, feasibility, and the behavioral and brain effects of a non-invasive treatment, repetitive transcranial magnetic stimulation (rTMS), for Veterans with AUD and co-occurring mTBI and/or PTSD. The intended effect of rTMS is to reduce alcohol craving among Veterans experiencing combined mild traumatic brain injury, post-traumatic stress disorder and alcohol use disorder. The *objective* of Aim III is to compare safety, feasibility, and the behavioral and brain effects of a non-invasive treatment, repetitive transcranial magnetic stimulation for Veterans with AUD and co-occurring mTBI and/or PTSD that are given active rTMS relative to Veterans that are given placebo rTMS.

This study will be conducted by trained research staff at Hines VA Hospital and Northwestern University's Center for Translational Imaging (CTI) at 710 N. Fairbanks Ct, Chicago, IL.

You are being asked to participate in this research study because you are a Veteran and may have symptoms of alcohol use disorder *or* may experience combined alcohol use disorder, mild traumatic brain injury and post-traumatic stress disorder symptoms. You previously participated in the study Brain

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Targets for Alcohol Craving in Veterans with mTBI (Aim I and Aim II) or Alcohol Craving Treatment Development for Individuals with Co-occurring mTBI, PTSD and AUD (Aim I-Phase I). This study is a continuation to the study/studies you already completed.

The current study addresses specific research interest areas to the VA including chronic diseases, psychiatric disorders, neurological dysfunction, brain injury and rehabilitation outcomes. Current military conflicts in Iraq and Afghanistan have led to over 200,000 reported cases of mild traumatic brain injury (mTBI). Among Veterans, mTBI commonly co-occurs with chronic, psychiatric conditions including alcohol use disorder (AUD) and post-traumatic stress disorder (PTSD). In particular, AUD negatively affects rehabilitation outcomes in Veterans. Specifically, the completion of this study will provide essential knowledge that can be incorporated into therapeutic strategies targeted to reduce alcohol craving and subsequent relapse in Veterans returning from Iraq and Afghanistan with co-occurring mTBI, PTSD, and AUD.

Dr. Herrold has an FDA Investigational Device Exemption (IDE) approval (# G180292) for this study.

Our goal is for 40 veterans to complete this study.

DURATION OF THE RESEARCH

This research study will take two years. However, your participation will only require participation in 12 in-person visits. Ten of these 12 visits will take approximately 1 hour. The third and last research visit will take approximately 2 hours. After the last research visit, we ask that you complete 3 follow-up phone calls each lasting approximately 15min. The details of these visits and follow-up phone calls are described below.

STUDY PROCEDURES

If you are eligible to participate in this research study and you chose to continue, you will then complete research procedures over the course of 12 in-person research Visits, each described below. The research procedures including informed consent, HIPAA Authorization, urine sample for drug and nicotine screening, breathalyzer for breath alcohol concentration screen, neurobehavioral interviews and questionnaires, a structured interview, EEG, 10 rTMS sessions and an MRI will be conducted by the PI, Dr. Herrold, or a trained research team member.

Visit 1: *This visit will occur at Edward Hines Jr., VA Hospital (Hines VA) and will take approximately 1 hour.* You will complete a structured interview about alcohol, a medical evaluation form about alcohol withdrawal, a questionnaire about mental health symptoms and a 20-minute EEG.

The EEG will be conducted so that if a seizure occurs, and EEGs are ordered by your treating physician, there will be a pre-rTMS baseline for comparison. The 20min baseline EEGs will be evaluated by the study team epileptologist, Dr. Vijaya Patil, will complete a clinical read of all baseline EEGs.

You will be asked to complete a Breathalyzer to help the research team determine the amount of alcohol that may be in your bloodstream. During this alcohol screening, you will be asked to blow into a tube attached to a special hand-held machine. No results will be entered into your electronic medical

record.
You will be asked to provide a urine sample to allow the research team to determine if certain drugs are in your body. This includes pain medications like morphine and Vicodin; benzodiazepines such as Valium, Librium, Xanax and Ativan, that are usually used to treat anxiety or alcohol withdrawal; and substances like cocaine, marijuana/cannabis, heroin, amphetamine or speed and barbiturates. You will also be tested for the amount of nicotine in your system resulting from your use of nicotine gum, nicotine patches and tobacco products like cigarettes, cigars, pipes and chewing tobacco.

Visit 2: Visit 2 will occur at Northwestern University's Center for Translational Imaging (CTI) at 710 N. Fairbanks Ct, Chicago, IL and take approximately 1 hour.

Pre-MRI Assessments

- You will be asked to complete a Breathalyzer to help the research team determine the amount of alcohol that may be in your bloodstream. During this alcohol screening, you will be asked to blow into a tube attached to a special hand-held machine. No results will be entered into your electronic medical record.
- You will be asked to provide a urine sample to allow the research team to determine if certain drugs are in your body. This includes pain medications like morphine and Vicodin; benzodiazepines such as Valium, Librium, Xanax and Ativan, that are usually used to treat anxiety or alcohol withdrawal; and substances like cocaine, marijuana/cannabis, heroin, amphetamine or speed and barbiturates. You will also be tested for the amount of nicotine in your system resulting from your use of nicotine gum, nicotine patches and tobacco products like cigarettes, cigars, pipes and chewing tobacco.
- If you are female, you will be asked to complete a urine pregnancy test. If the pregnancy test is positive, then participation in the study will stop.
- You will ask to complete an MRI safety form.

MRI Scan

- You will also undergo a **magnetic resonance imaging scan (MRI)** to look at the brain. An MRI is a type of scan that uses magnetic fields and radio waves to take a picture of the brain. The MRI will last about 45 minutes.

In order to make sure the MRI procedure will be safe, you will be asked to fill out a screening form before starting the study. It is important that you tell the researchers in this study if you have any history of:

- Metal fragments in your eyes or face.
- Implantation of any electronic devices such as (but not limited to) cardiac pacemakers, cardiac defibrillators, cochlea implants or nerve stimulators.
- Surgery on the blood vessels of your brain or the valves of the heart
- Claustrophobia (fear of enclosed places)
- Body piercing or tattoos

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You will be asked to change into a hospital gown or surgical scrubs and remove any metal, such as earrings.

A MRI technician will give you instructions outside the MRI scanner about the scanning. Next, you will be asked to lie still on the MRI patient table and your head will be placed in a specially-designed head holder. Your head will be cushioned by a firm foam pillow. The table will then slide into the enclosed space of the MRI scanner.

During a portion of the scan, you will see pictures of alcoholic beverages or people drinking alcohol alternated with neutral pictures (e.g., of shapes or landscapes). During this time, you will also be shown a slide that asks you to rank your craving for alcohol on a scale of 1-10 and you will press a button that corresponds with your choice.

The MRI scanning session will take **up to 45 minutes** to complete once you are in the scanner.

The information from the MRI scanner is only useful if you are able to complete the whole imaging session, and hold your head very still the whole time. Therefore, you will be encouraged to hold as still as possible, and to let the investigators know if you are uncomfortable in any way as soon as possible after the imaging session begins.

The front of the head-holder will be open, which lets you look through a special mirror and see pictures presented to you on a projection screen near your feet. Sounds may also be presented to you using specially designed headphones. You will be asked to hold your head as still as possible and to respond to the pictures or sounds by pushing a button or thinking quietly to yourself.

The MRI scanner makes loud banging noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise. The researchers will be in communication with you through an intercom system to tell you how the study is going. The earplugs or headphones should not get in the way of communicating with the researchers. You can speak to the technician by talking out loud. If at any time or for any reason, you wish to stop the exam, you may do so by squeezing a rubber ball. This will signal the MRI technician to stop the scanner.

A copy of the TI/MPRAGE/structural scan will be made available to your physician on a CD/DVD with a viewing program upon your request. You will need to sign a medical release form and after you sign it the CD/DVD will be mailed to your doctor using a Courier mailing service. The fMRI pictures in this study will not be reviewed by a neuroradiologist, however, if an abnormality is detected during the processing of the scan you will be contacted and the information provided to the physician of your choice. You will be asked to provide us with the name and address of the doctor you want us to contact.

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Visits 3, rTMS Treatment Sessions #1: Visit 3 will occur at Hines VA and will take approximately 2 hours.

Because of potential pain (see POSSIBLE RISKS OR DISCOMFORTS below), we recommend that you bring acetaminophen (i.e., Tylenol) to take prior to each rTMS session.

Pre-rTMS Assessments

- You will be asked to complete a Breathalyzer to help the research team determine the amount of alcohol that may be in your bloodstream. During this alcohol screening, you will be asked to blow into a tube attached to a special hand-held machine. No results will be entered into your electronic medical record.
- You will be asked to provide a urine sample to allow the research team to determine if certain drugs are in your body. This includes pain medications like morphine and Vicodin; benzodiazepines such as Valium, Librium, Xanax and Ativan, that are usually used to treat anxiety or alcohol withdrawal; and substances like cocaine, marijuana/cannabis, heroin, amphetamine or speed and barbiturates. You will also be tested for the amount of nicotine in your system resulting from your use of nicotine gum, nicotine patches and tobacco products like cigarettes, cigars, pipes and chewing tobacco.
- You will complete a structured interview with a trained research team member about symptoms related to alcohol use.
- You will be asked to complete questionnaires about your alcohol use, alcohol craving and demographic information (such as age, race, sex, economic status, level of education, income level and employment, among others)
- A series of questionnaires will be used to monitor and measure changes in PTSD, mTBI and alcohol craving symptoms.
- During the assessments, interviews and completing of questionnaires, you are free to skip any questions if you become uncomfortable or you simply prefer not to answer.
- The PCL-5 will be used to track changes in PTSD symptoms. The Neurobehavioral Symptom Inventory (NSI) will be used to measure changes in mTBI symptoms and involved reporting the presence/absence of symptoms and how these symptoms impact overall function.
- If you are female, your urine sample will be used to test to see if you are pregnant (at Visit 7).
- It is important to know that any Breathalyzer or drug screening results are used to determine if you are eligible to continue in this research study and will **NOT** be entered into your medical record or reported to legal authorities.
- Results of urine tests, like all other data collected as a part of research procedures will not be entered in the electronic medical record.

- A process called Randomization will be used to assign you to a treatment group. This procedure is like flipping a coin, so that you will have a 1 in 2 chance of receiving active rTMS instead of placebo (a mock process that does not include the active rTMS treatment, but otherwise looks, sounds and feel like active rTMS). Neither you, nor the treatment team will know what your treatment group assignment is during your participation (this process is called blinding, and is used to maintain integrity and prevent manipulation of treatment groups).

Motor Cortex Excitability Threshold

This test will be done prior to starting rTMS. This test involves magnetic stimulation of the brain while recording muscle activity from the arm, wrist, hand, finger, leg and/or foot. The structural brain image collected during the MRI procedure described above will be used to help locate the correct site of stimulation.

Electrical activity from the arm, wrist, hand, finger, leg and/or foot muscles will be recorded using surface electrodes placed on the arm, wrist, hand, finger, leg and/or foot. These electrodes will be placed using a gel or sticky paste.

A researcher will hold a figure-of-eight (8) shaped magnetic coil on the top of your head at different points along the scalp and provide a pulse of magnetic stimulation to confirm magnet placement. The test will take about **1 hour**.

Repetitive Transcranial Magnetic Stimulation (rTMS) Treatment Session 1: Once all the tests listed above are complete, the experimental treatment will begin. Repetitive transcranial magnetic stimulation (rTMS) stimulates the brain using magnetic pulses. The magnetic pulses create electrical currents in the brain. The electrical currents may affect brain activity and function. The long-term effects of rTMS are not known. If you are randomized to the real rTMS group, then this is the treatment that will be provided to you.

During the real and placebo rTMS treatments, earplugs will be placed in your ears because the magnetic stimulator makes a loud clicking noise. Tape may be placed over the earplugs to make sure the earplugs stay in place.

During the real and placebo rTMS treatments, the researcher will hold a figure-of-eight shaped magnetic coil on the right side and toward the front of your head. It takes approximately 30-45 minutes to provide real or placebo rTMS during each treatment.

Each session will take about an hour to allow for set-up and take-down. The weekly schedule for real and placebo rTMS will be one session of rTMS every week day (Monday, Tuesday, Wednesday, Thursday, Friday) for two weeks. In order to monitor for safety, all rTMS sessions will be videotaped. All security procedures for data will apply. A separate consent for picture and video will be completed.

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A total of 10 rTMS sessions will be provided over two weeks (5 rTMS sessions per week). The only difference between real and placebo rTMS is that no stimulation is received during placebo rTMS.

Safety Measures:

You will participate in safety monitoring using the Data Safety Monitoring Scale (DSMS). This scale rates changes from baseline vital signs (temperature, blood pressure, heart rate, oxygen saturation levels), fatigue, tinnitus (ringing in the ears), sleep, dizziness, nausea, vomiting, confusion, seizure, syncope (fainting), headache, neck pain, skin integrity of the scalp, substance use, suicidal ideation, and PTSD symptoms.

The Beck Depression Inventory (BDI-II) will be administered at baseline (Visit 1), after the first week of treatment, and endpoint to monitor for symptoms of depression.

A pain scale will be administered before and after each rTMS session to track the amount of discomfort participants are feeling during the intervention.

Visits 4-11, rTMS Treatment Sessions #2-9:

These visits will all occur at Hines VA and last approximately 1 hour. You will be asked to complete a Breathalyzer to help the research team determine the amount of alcohol that may be in your bloodstream. During this alcohol screening, you will be asked to blow into a tube attached to a special hand-held machine. No results will be entered into your electronic medical record.

Procedures described above for rTMS Treatment Session #1 will be repeated. After the 5th rTMS session at the end of the first week, the depression (BDI-II) and PTSD symptoms (PCL-5) will be re-evaluated for safety purposes.

Visit 12, rTMS Treatment Session #10:

This visit will occur at Northwestern University's CTI for all participants. You will be asked to complete a Breathalyzer to help the research team determine the amount of alcohol that may be in your bloodstream. During this alcohol screening, you will be asked to blow into a tube attached to a special hand-held machine. No results will be entered into your electronic medical record.

Procedures described above for rTMS Treatment Session #1 will be repeated for the final rTMS session. The rTMS session will last approximately 1 hour.

You will then complete an MRI as described above that will last approximately 45 minutes.

You will be asked to complete questionnaires about your alcohol use, alcohol craving, and mental health symptoms. These questionnaires will take approximately 30 minutes to complete.

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Follow-Up, Telephone Assessments

A research team member will call you at a preferred time one day, one week and one month after the 10th rTMS session to complete questionnaires about alcohol craving, mild TBI symptoms and PTSD symptoms over the phone.

POSSIBLE RISKS OR DISCOMFORTS

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur.

Surface electrodes: The self-adhesive surface electrodes used to record muscle activity may produce minor irritation (redness) of the skin.

The possibility of irritation will be minimized by applying gel to the skin before electrode placement and by gently cleaning the skin before and after the use of electrodes.

There is also the possibility of an allergic reaction to the electrode gel or paste. If you are allergic to the gel or paste, then a different gel or paste will be used.

***Behavioral Assessments*:** You may experience unpleasant emotions, thoughts or memories due to the types of questions being asked. You do not have to answer all the questions. We will be asking you questions about alcohol use, alcohol craving, depression, anxiety and PTSD symptoms. If your overall answers to those questions are of concern, or you appear to be extremely upset by the procedures, we will encourage you to contact your primary care or mental health provider. If you choose, a member of our research team will contact them on your behalf. If it is determined you are an immediate threat to yourself or others, you will be escorted to Mental Health Intake at Hines VA or you will be accompanied to the Hines VA Emergency room. Signing this consent document gives us permission to contact your health care provider and/or escort you to Mental Health Intake or the Emergency room at Hines VAH as necessary.

***MRI*:** There are no known health risks associated with the MRI, although some people experience mild discomfort from trying to keep still during the study. Some participants also feel closed-in due to the small space in the scanner (claustrophobia) or anxious in the scanner. You will be able to squeeze a ball to sound an alarm at any time if you need to talk to the researchers during the MRI. This test does not use radiation.

Magnetically Evoked Potentials, Motor Threshold Tests and rTMS Treatment: TMS will be used in two tests. TMS will be used to magnetically evoke a motor action potential and to determine the most effective rTMS intensity level (motor threshold). rTMS, will also be provided as the experimental treatment.

The Food and Drug Administration has found that rTMS does not present a risk to the health, safety, or welfare of research participants without brain injuries, alcohol use disorder or PTSD and does not

cause seizures at the rate of stimulation used in this experiment for persons without brain injuries or PTSD.

The risk of causing a seizure in persons with alcohol use disorder, mild traumatic brain injuries and PTSD is not known, but it is possible that repeated rTMS would cause one or more seizures. If a seizure occurs, then emergency procedures will be followed in order to treat the seizures with medicine, if needed. If a seizure occurs, then you will no longer be eligible to participate in this study. You will be informed of this and encouraged to follow up with your primary care provider.

It is also possible that you may get a mild temporary headache after each rTMS treatment session. Most headaches resolve after taking acetaminophen (such as Tylenol).

There is a risk of a temporary hearing loss because the magnet is placed near the ear and the magnet makes a clicking noise. You will have earplugs placed in your ears during each rTMS session to reduce the risk of hearing loss. The earplugs are checked during the rTMS treatment to make sure they stay in place.

Additional risks of rTMS are:

- Damage to insulation of the coil, would create a remote possibility of electrocution during rTMS. The coils will be inspected before and after each rTMS session to ensure that the coil does not have any cracks or loss of integrity.
- Over-heating of the coil which may lead to scalp burns or damage to underlying tissue. The rTMS device has a sensor that alerts the researcher when the coil is beginning to overheat.
- Mechanical vibrations that occur within the coil while an rTMS pulse is being generated may result in discomfort or headache.
- Device failure due to overheating, electrical short-circuiting or mechanical breakdown from force on the device. All precautions will be taken to prevent device breakdown that may affect your welfare. The rTMS device will be inspected routinely and safety guidelines from the manufacturer will be followed.
- Contamination spread from one participant to another following treatment. The device will be disinfected after every use to prevent spread of germs between participants.
- Mania, depression, anxiety and suicidality, although rare and usually associated with underlying depression or bipolar depression.
- Physical discomfort, facial numbness, headache or dental pain.

rTMS treatments will be stopped if you go into shock or have a seizure.

Loss of Confidentiality: All individual health information is removed from data collected for this study except dates of injuries, procedures or interventions. This information is necessary in the analysis for the study. Names, social security numbers, dates of birth, addresses and phone numbers are kept in a separate file on a VA secured computer with limited research team access.

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Privacy: In order to protect your privacy, all data from the behavioral assessments, questionnaires, and MRI scans will be de-identified. All study data will be stored on a secure VA server as well as in a locked cabinet in a locked room at the Hines VA Hospital. The MRI data will be uploaded to the Northwestern University Research Image Processing System (NURIPS), which is a secure storage and computing environment for imaging data. The data will be password protected and only approved researchers will be provided access.

Other Risks: There may be other unknown side effects that could occur. Participation in this research may involve risks that are currently unforeseeable.

REPRODUCTIVE AND SEXUAL ACTIVITY INFORMATION:

All women who are enrolled in the study will be asked to take a urine pregnancy test prior to initiating study procedures (Visit 1) and at midpoint (Visit 7). If the test is positive, you will be withdrawn from the study. If the test is negative, you will continue with study participation. You will be asked before every treatment session if there is a chance you may be pregnant. If you become pregnant, the research procedure, rTMS, might involve risks to the embryo or fetus which are currently unforeseeable.

Risks of the usual care you receive are not risks of the research. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care. Participation in research may involve a loss of privacy. Your research records will be kept as confidential as possible.

POTENTIAL BENEFITS

1. Treatment with real rTMS may improve alcohol craving. This may provide also improve your quality of life. However, neither of these benefits is guaranteed.

2. You may not personally benefit from taking part in the research but the knowledge obtained may help the health professionals caring for you better understand the disease/condition and how to treat it.

CONFIDENTIALITY

Loss of confidentiality is a potential risk. This research study involves collection of self-report alcohol craving and alcohol use severity. Your response to self-report questionnaires will be documented. All hard copies of questionnaires and neuropsychological assessments as well as urine screens and breathalyzer screens will include a unique participant identification number and the date the assessment was completed. Thus, it will be de-identified.

As a part of advancing knowledge in the scientific process, we will be publishing and presenting data collected in this study. However, we will be presenting the data as a group. Therefore, any talks or papers about this study will not identify you.

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The information collected for this study will be kept confidential. There are times when we might have to show your records to other people. Only authorized persons will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration, (FDA), the Government Accounting Agency (GAO) or the Office for Human Research Protection (OHRP), Office of Research Oversight (ORO), as well as members of the Research Administration staff of CAVHS. The Department of Veterans Affairs (VA) requires some information to be recorded in the VA electronic medical record for all veteran and non-veteran research participants. The FDA may choose to inspect research records, including individual medical records due to the use of an FDA-regulated test article (rTMS). By signing this document, you consent to such inspection.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

This informed consent form does not give the study investigator permission to access, record, and use your private health information. You will be given a separate HIPAA form which provides more information about how your private health information will be used in this study, who will have access to your records, and how you can revoke (take back) your permission in the future. You will not be able to participate in this study if you do not sign the separate HIPAA authorization form.

COSTS TO PARTICIPANTS AND PAYMENT

Costs to Participants*:*

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study. You will not be required to pay for medical care or services received as a participant in a VA research project except as follows: some veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this study.

FINANCIAL COMPENSATION:

You will be compensated $225 for completing research procedures in this study. If you also complete the MRI at Visit 2, you will be compensated an additional $65 (total $290). You will also be reimbursed for parking at Northwestern. If the you did not drive to Northwestern then you will also be reimbursed the cost of the 6-hour parking voucher which is $5.75. If the you withdraw or the PI withdraw you from the study, you will receive a prorated amount based on how much of the study you completed. You will be reimbursed in cash from the agent cashier's office at Hines VA.

Payments will be disbursed by the Agent Cashier's office at Hines VA, and compensation for visits to Northwestern University's CTI will be dispensed at that location. An IRB 1099 form will be issued to all participants who receive payments. This information and the fact that the SSN of the participant will be used for this purpose must be included in the informed consent form.

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VAMC: **Edward Hines, Jr VA Hospital**

RESEARCH-RELATED INJURIES:

Per the federal regulations, (Title 38 Code of Federal Regulations (CFR) 17.85), The VA will provide necessary medical treatment to you as a research subject if you are injured by participation in this research project approved by the Research and Development Committee and conducted under the supervision of one or more VA employees. Except in limited circumstances, this care will be provided at this VA facility. This requirement does not apply to treatment for injuries that result from non-compliance by you with study procedures. The Department of Veterans Affairs does not normally provide any other form of compensation for injury. You have not released this institution from liability for negligence.

Participation in this research may involve risks that are currently unforeseeable.

You do not give up any of your legal rights and you do not release the VA from any liability by signing this form.

In case (If) there are any medical problems, complaints, concerns, or if you have questions about the research, you can call Dr. Amy Herrold at.

DURING THE DAY: Dr. Amy Herrold at 708-202-5867 and

AFTER HOURS: Please call 911 for medical emergencies. Emergency and ongoing medical treatment will be provided as needed. Veterans may also contact the crisis line at **1-800-273-8255** and Press 1 or chat online to receive confidential support 24 hours a day, 7 days a week, 365 days a year.

PARTICIPATION IS VOLUNTARY

Participation is voluntary and the participant (you) can withdraw from the study at any time.
You do not have to take part in this study and refusal to participate will involve no penalty, consequences or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty, consequences or loss of VA benefits. *If applicable, you may withdraw and still receive the same standard of care that you would otherwise have received. If you are a VA employee or student, refusal to take part in the study will in no way influence your employment, ratings, subsequent recommendations, or academic progress as applicable. The investigator may also continue to review the data already collected for the study but cannot collect further information, except from public records, such as survival data. Please be advised that specimens already used cannot be withdrawn.*

RESEARCH PARTICIPANT'S RIGHTS AND RESPONSIBILITIES:

You have read, or have had read to you all the above information. _____ explained the study to you and has answered all your questions. The risks or discomforts and possible benefits and the alternatives of the study have been explained to you.

Participant Name: _____ **Date:** _____

Title of Study: **Brain Targets for Alcoholic Craving in Veterans with mTBI (Aim III)**

Principal Investigator: **Amy Herrold, PhD**

VAMC: **Edward Hines, Jr VA Hospital**

Please keep your study appointments. Please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment. Also remember to:

- Tell the investigator or research staff if you believe you might be pregnant or might have gotten your partner pregnant.
- Ask questions as you think of them.
- Tell the investigator or research staff immediately if you change your mind about staying in the study.
- While participating in this research study, please inform the study investigator if you choose to participate in other research studies. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this research, as well as that of the other studies

The results of this study may be published but your identity and records will not be revealed unless required by law.

SIGNIFICANT NEW FINDINGS:

Sometimes during the course of a research study, new information becomes available about rTMS that is being studied that might change a person's decision to stay in the study. If any significant new findings develop during the research regarding the treatment of your condition or which may impact on your decision to continue to participate, the investigator will discuss them with you. If you decide to continue in the study, you might be asked to sign an updated informed consent form.

RIGHT OF INVESTIGATOR TO TERMINATE PARTICIPATION

The investigator has the right to terminate your participation in the research study if:

- Participant is uncooperative or unwilling to complete study tests
- Participant is experiencing undue stress from the study procedures
- Participant has a substance abuse, mental health, or medical problem that interferes with completion of the study tests.

FUTURE USE OF DATA AND RE-CONTACT

Any information obtained about you in this study will be treated as confidential and will be safeguarded in accordance with the Privacy Act of 1974. Information published or presented about the results of the study will be in a form that does not identify any particular participant. In order to comply with federal regulations, records identifying you may be reviewed by the members of the research team, the representatives of the sponsor or sponsors (identify) of this study, the Chicago

Participant Name: _____ **Date:** _____

Title of Study: **Brain Targets for Alcoholic Craving in Veterans with mTBI (Aim III)**

Principal Investigator: **Amy Herrold, PhD**

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Association for Research and Science in Education (CARES), authorized representatives of the Hines VA or Northwestern IRB, VA, a statement that Federal agencies such as the Food and Drug Administration (FDA), the Office for Human Research Protection (OHRP) and the Government Accounting Office (GAO) may have access to the records. If an FDA-regulated test article is involved, the FDA requires a statement that the FDA may choose to inspect research records that include the subject's individual medical records. By signing this document, you consent to such inspection.

During the conduct of this study, protected health information will be collected and reviewed for the purposes of obtaining medical history. Protected health information will also be released to necessary offices at Northwestern University and Northwestern Memorial Hospital in order to conduct research procedures at those sites.

All information collected during the conduct of this study will be stored and analyzed at the Hines VA in research areas accessible only to authorized research personnel for this study. Study related information will be stored in locked filing cabinets in a locked office. Electronic study related information will be stored on a VA server that is safeguarded and accessible only to authorized study personnel.

You may be eligible to participate in future research. Future studies may use some of the same information that you provide today, but may also involve additional assessments. In order to contact you for future research, your information will be placed in a TBI data repository. This TBI data repository is its own Edward Hines Jr., VA IRB-approved protocol (IRB#14-003). This data repository may be shared with other investigators in keeping with that IRB-approved protocol through a formalized process. Choosing or refusing to include your data in the TBI data repository will not affect your ability to participate in this research study as long as you meet study inclusion criteria. Additional clarification regarding the future use of data is included in the HIPAA Authorization that will be provided for your signature.

☐ I agree to have my data placed in the TBI data repository for future use._____(Initials)

☐ I do not wish to have my data placed in the TBI data repository_____(Initials)

You may be eligible to participate in future research. Future studies may use some of the same information that you provide today, but may also involve additional assessments. If you would be interested in hearing about future research opportunities, please indicate your interest below:

☐ I agree to be contacted for future research._____(Initials)

☐ I do not wish to be contacted about future research._____(Initials)

STUDY RESULTS:
The results of this study will not be shared with the participant.

ADDITIONAL CONTACT INFORMATION

Participant Name: _____ **Date:** _____

Title of Study: **Brain Targets for Alcoholic Craving in Veterans with mTBI (Aim III)**

Principal Investigator: **Amy Herrold, PhD**

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Additionally, if you have any questions about the research; **your rights as a research subject; you want to discuss problems with the research process; lodge a complaint; offer input or have other concerns;** you may contact/call the Chairperson of the Institutional Review Board (IRB) or the IRB Administrative Office at: 708-202-2811.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____ _____has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it.

_____ ___/___/_____

Signature of Participant Date Written by Participant

_____

Participant's Last Four of SSN