Official Title: Theta Burst Stimulation as a tool to decrease drinking in treatment-seeking alcohol users

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Wake Forest School of Medicine

Wake Forest School of Medicine

Department of Cancer Biology

THETA BURST STIMULATION AS A TOOL TO DECREASE DRINKING IN TREATMENT-SEEKING ALCOHOL USERS

Informed Consent Form to Participate in Research
Merideth Addicott, PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to develop transcranial magnetic stimulation (TMS), specifically TMS at a frequency known as theta burst stimulation (TBS), to see how it affects the brain and changes the brain's response to alcohol-related pictures. You are invited to be in this study because you are seeking treatment for alcohol use. Your participation in this research will involve 21 visits and last about 5 months.

Participation in this study will involve the following: a screening visit, 15 visits of TMS (real or placebo TMS, 2x/day, 3x/week), 2 functional magnetic resonance imaging (MRI) scans of your brain, and a follow-up visit every month for 3 months. All research studies involve some risks. A risk to this study that you should be aware of is TMS and MRI risks. For TMS, there are potential risks of seizure, headache, scalp discomfort, hearing loss, and fainting. For the MRI, there is potential risk to individuals with metallic implants or medical devices. Additionally, participants may feel restless or uncomfortable lying in the MRI scanner. The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments. There is the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include substance abuse treatment programs which can be referred to you clinically. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Dr. Merideth Addicott. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [redacted] or [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

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INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are an alcohol user that would like to seek treatment for alcohol use. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out what effects (good and bad) TMS has on you and your condition. TMS is a technique that uses magnetic pulses to temporarily stimulate specific brain areas in awake people (without the need for surgery, anesthetic, or other invasive procedures). This study will test whether TMS can be used as an alternative tool to reduce your desire to use alcohol and reducing your brain's response to alcohol-related pictures. TMS has been approved by the US Food and Drug Administration (FDA) as a treatment for depression, but it has not been approved as a treatment for alcohol use.

In this study real TMS will be compared to placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on your disease or condition. In this study you will either receive the active study medication, TMS or placebo which is not active. Placebos are used in research studies to see if the drug being studied really does have an effect.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

180 people will be enrolled at this research site. In order to identify the 180 subjects needed, we may need to screen as many as 215 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in any group.

Neither you nor the investigator will know which study treatment you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

If you take part in this study, you will have the following tests and procedures:

1. Baseline Screening Visit, Consent, Genetic Analysis): You will complete self-report screening measures (on paper and computer) designed to assess your alcohol use, your psychiatric history, and your mood. We will test your visual acuity. You will also be asked to track your daily alcohol consumption during the course of the study. You will be asked about your current height and weight, past medical history focusing on chronic

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(and current) medical problems, seizure history, medications, psychiatric disorders, and substance use. The research procedures, risks, and benefits will be explained. As part of this research study, you will be asked to provide a biological specimen (saliva sample) for genetic testing. Your saliva sample will be taken at your screening visit for genetic analysis of either brain derived neurotrophic factor gene variants or DNA methylation. Your information or biospecimen that will be collected as part of this research study, even if identifiers are removed, will not be used or distributed for future research.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information.

This law will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information that we get from this research when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and you **will not** share in this profit.

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading", every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research **will not** include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

2. (Urine screen/drinking assessments: All visits): If you qualify for the study and agree to continue, then you will do a urine screen. If you are a woman of childbearing age, you will first undergo a pregnancy test by providing a urine sample. The pregnancy test is important because the effects of TMS on the developing fetus in the first trimester of pregnancy are unknown. As such, if you are a pregnant female or lactating, you cannot participate and will be excluded from the study. If you are not pregnant, you must use a

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reliable method of birth control.

If you are not pregnant, you will have a urine drug screen to detect the presence of drugs in your urine. If you are a man, TMS is not known to affect the sperm and you are not required to use contraceptive measures. Magnetic stimulation is not allowed in people who have a pacemaker, an implanted medication pump, a metal plate in the skull, or metal objects inside the skull (for example, after brain surgery). You will complete a urine screen to detect recent use of alcohol (ETG) and drugs of abuse (cocaine, benzodiazepines, marijuana, opiates). A urine sample will be collected at the screening visit and visits 1, 2, 7, 12, 16, 17, 18, 19, and 20 for ETG testing. You will also complete a breath carbon monoxide (CO) sample to detect recent cigarette smoking, and a breath sample to test for recent alcohol use.

3. (MRI scanning - Visits 1 and 17): On visits 1 and 17 (before your first TMS session, and after your last TMS session), you will have a Magnetic Resonance Imaging (MRI) exam of your brain. This test will provide us with an image of your brain and brain activity during various tasks. You will lie still in the MRI machine for about 1 hour while this image is being made. The MRI does not use radiation, but it can be difficult for persons who have fear of being closed in small spaces because it can feel somewhat confining in the MRI scanner. The MRI utilizes magnetism so you will need to remove loose metal objects such as earrings and key chains prior to the procedure for your safety. If you have pieces of metal in your body, such as a pacemaker or aneurysm clip, you cannot have a MRI. These research MRI techniques are different from a MRI obtained for medical reasons. However, this is not a study for diagnostic purposes and will not be read by a radiologist. If, by chance, something abnormal is observed, you will be informed of this and counseled as to what clinical referral would be appropriate.

   (TMS overall – Visits 2-16): If you qualify for the study and agree to continue, you will be randomized to receive either the placebo TMS treatment or one of two real TMS treatments. The randomization process works like flipping a coin, and is pre- determined by a computer program and not by the researchers. The placebo TMS is an inactive treatment that is designed to mimic the sounds, feelings and appearance of the real thing. You will not be told which type of stimulation you are receiving during the treatment session. This improves our ability to determine how effective the treatment is. Previous studies have indicated that the real TMS and the placebo TMS feel the same, so you will not be able to determine which type of stimulation you are receiving during a treatment session. This is done so that we can be sure our active treatment is really having an effect. On each of these visits, you will fill out several questionnaires related to alcohol use, mood, and craving. These questionnaires will track your current urge to drink alcohol and assess your mood levels. You will complete these assessments throughout the course of the TMS sessions. We will try to schedule treatments at the same time of day for all of your treatments. We would prefer that you finished these sessions within 5 weeks. You may reschedule up to 3 sessions of TMS total, but all 15 TMS sessions must take place within 6 consecutive weeks.

4. (TMS motor threshold – Visit 2): Regardless of which treatment you receive during your

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visits (real or placebo TMS), the researchers will first determine your individual level of thumb muscle response to TMS pulses (called the resting motor threshold, rMT). This is done because everyone's response to TMS is a little different, and we want to make sure that we give you the right "dose" of TMS. The researcher will ask you to hold out your hand and fingers. He/she will then slowly and carefully move a magnetic coil over your head. The coil will send a single magnetic pulse every 3-4 seconds. The researcher will continue to move the coil until he/she finds the specific brain area that results in slight movement of your thumb. Once the researcher has your rMT, the researcher will measure your individual response level to TMS pulses.

5. (TMS treatment – Visits 2-16): You will receive either two real TMS sessions or two placebo TMS sessions during your treatment visits (2x/visit for 15 days, 3x/week for 5 weeks total). You will receive two sessions of discontinuous stimulation, with stimulation for 2 seconds followed by 8 seconds of rest for a total duration of 3 minutes. During the TMS sessions, we will ask you to think about alcohol related cues.

6. (Secondary assessments and self-report questionnaires: Visits 1, 6, 11, 15, and Follow-up visits): You will complete a set of computer based self-report questionnaires related to your alcohol use, cravings, and mood.

7. (Blood Draws – Visits 1, 17, 18-20): You will have about two teaspoons of blood withdrawn from a vein five times throughout the study. The total amount of blood withdrawn during the five months of the study will be about ten teaspoons.

   (Follow-up visits – Visits 18-20): You will have three in person follow-up visits once a month for 3 months following the last TMS session. At these follow-ups, you will be asked to complete the assessments rating your current alcohol use, mood, and craving on a computer. You will also undergo a urine screen as well as the alcohol assessments at these visits.

SHARING OF DATA

Data from this study will be submitted to the National Institute on Alcohol Abuse and Alcoholism Database ($NIAAA_{DA}$) at the National Institutes of Health (NIH). $NIAAA_{DA}$ is a large database where de-identified study data from many NIAAA studies is stored and managed. De-identified study data means that all personal information about you (such as name, city of birth, birthdate and phone number) is removed and replaced with a code number. Sharing your de-identified study data helps researchers learn new and important things about alcohol problems more quickly than before.

If you agree, during and after the study, the study researchers will send de-identified study data about your health and behavior to the $NIAAA_{DA}$. Other researchers across the world can then request your de-identified study data for other research. Every researcher (and institutions to which they belong) who requests your de-identified study data must keep your data safe and must not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have

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some risks, although these risks are rare. Risks include data breach and unintentional sharing with an unauthorized person, however the study researchers and the NIH will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with $NIAAA_{DA}$, but the study data provided to $NIAAA_{DA}$ may help researchers around the world learn more about alcohol problems and how to help others who have problems with alcohol. NIAAA will also report to Congress and on its website about the different studies using $NIAAA_{DA}$ data. You will not be contacted directly about the study data you contributed to $NIAAA_{DA}$.

You may decide now or later that you do not want your study data to be added to the $NIAAA_{DA}$. You can still participate in this research study even if you decide that you do not want your data to be added to the $NIAAA_{DA}$. If you know now that you do not want your data in the $NIAAA_{DA}$, please indicate this on the signature page of this consent form. If you decide any time after today that you do not want your data to be added to the $NIAAA_{DA}$, call or email the study staff who conducted this study, and they will stop sharing your study data with $NIAAA_{DA}$. Once your data is part of the $NIAAA_{DA}$, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about $NIAAA_{DA}$, this is available on-line at https://nda.nih.gov/niaaa.

How Long Will I Be in the Study?

You will be in the study for about 5 months.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the TMS device we are studying include:

1. Potential risk of a seizure: In designing this experiment, we have followed the latest safety guidelines for TMS. Despite these precautions, there is a chance of a seizure as a result of TMS. Eight seizures have been noted in previous studies, with six of them occurring in healthy volunteers without any history of seizures, brain tumors or traumatic brain injuries. All of these seizures have occurred during TMS with the participant in the treatment chair and a trained operator on hand. All seizures have stopped by themselves without any medication. No participants have had any problems after the seizures. Additionally, if a participant has a seizure an emergency response team will be called. Most seizures, including those caused by TMS, last less than 60 seconds and do not require any medication. Participants will be evaluated by a physician associated with the Research Laboratory following recovery from the seizure. Any participant who has a seizure cannot continue with the study.

   Following the adoption and widespread use of safety guidelines, 1 seizure has been reported since 1997 and it involved parameters of higher settings than the safe range. The TMS used in this study follows the published TMS safety guidelines.

   To further reduce this risk, we will ask a series of screening questions prior to TMS

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administration. You will be asked if you have ever had a seizure or if any member of your family has ever had a seizure. You will be asked if you have any known tumors or lesions or if you have ever had an abnormal MRI or CT scan. We will ask if you have ever had a severe head injury and/or have ever been unconscious for more than a few minutes. A positive response to any of these screening questions will warrant follow-up questions and may mean you are ineligible to participate.

2. Potential for scalp discomfort and headaches: You may report some mild discomfort when the magnetic pulses are applied over your scalp, and a small number of people (~1 in 20 people) report headache following TMS. However, the headaches are temporary, go away on their own within 60 minutes, and are manageable with common over-the-counter pain remedies.
3. Potential worsening of mood with TMS: Several studies have so far demonstrated the feasibility of TMS as a treatment for depression. However, there is a chance you may feel that your mood is worsened, though there is no evidence that this will occur.

4. Potential Worsening of Pain with TMS: To date, we have not seen any evidence that TMS is associated with increases in pain perception or worsening of pain conditions. Most of the available evidence of the effects of TMS on pain perception suggests that TMS provides temporary relief from pain, a temporary decrease in sensitivity to pain, or no effect at all.

5. Other potential effects of TMS on brain tissue: TMS is thought to be safe, with no brain damage, despite its large-scale use in humans and other animals. Within our laboratory, multiple safety studies have found no changes in the structure of the brain following TMS.

6. Potential hearing loss: The discharge of the TMS coil generates a high-energy click that may cause hearing damage. Foam earplugs can protect against these changes and will be given to you to wear during TMS sessions.

7. Potential changes in cognitive function: There have been no reports of long-term changes (more than a minute) in cognitive function (memory, attention, etc.) in TMS studies.

8. Safety in case of pregnancy: If you are pregnant, you will be excluded from this study. The risks of using TMS with pregnant women are currently largely unknown. All female participants will be required to be using an acceptable form of birth control (including abstinence) during the TMS visits in order to continue participation. If there is a chance you may be pregnant, a urine pregnancy test will be done. Further, while the risks of using TMS with pregnant women are unknown, there is no available evidence to date suggesting that TMS is harmful during pregnancy.

9. Potential for fainting event: Fainting or “passing out” is defined as a temporary loss of

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conscious. Although fainting episodes are very rare with TMS (less than 1 in 100 people), they typically occur before the TMS treatment, when the study members are finding your "dose" of TMS, known as the motor threshold. Individuals that are sleep deprived and have low or unstable blood pressure are at greater risk.

10. Unknown Risks: TMS is an experimental procedure that has not been approved by the FDA as a treatment for alcohol use disorder and it may have unknown side effects. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

In addition to TMS risks, there may also be risks related to the MRI device we are using. This includes:

1. The risk from magnetic resonance imaging (MRI) is low. No radiation or x-rays are used in making pictures of your brain during the MRIs. You cannot have an MRI scan if you have metal in the skull, metal implants, a cardiac or brain pacemaker, or old metal fragments in the eye or retina. If you have a question about metal in your body, you should inform the researchers and they will determine whether it is safe in a MRI scan.

2. Some discomfort may occur from having to remain still for the 1 hour that you will be in the scanner.

3. The MRI scanner is noisy, and there is a risk of hearing damage if you do not wear earplugs. To minimize this risk, you will be given earplugs to wear during each scan.

4. Although the MRI scanner is open on both ends, some people become anxious when entering the MRI scanner due to the feeling of being enclosed. If this has happened to you in the past, you should inform the study personnel. The researchers will work with you to keep this from happening by allowing you to view relaxing pictures on a screen above your head prior to the start of the research procedure (until any anxiety has passed). Also, the researchers can talk with you during the procedure through a microphone in the scanner to reduce your concern.

5. If you are female and of child-bearing potential, you must have a pregnancy test performed prior to the scanning procedures. This test must be negative for you to participate in the study. You must also practice an acceptable method of birth control during the course of the study. If you are pregnant, you will be excused from the study.

In addition, there are risks associated with blood draws. You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other risks that we cannot predict. You should

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tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks

Further risks include the following:

1. Randomization risk: The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.
2. Alcohol related cue risks: Given that you will be exposed to pictures of alcohol related cues throughout the duration of this experiment, there may be an added risk of relapse during the study. Contact study staff if this becomes a problem for you.
3. Security of confidentiality and privacy risk: Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.
4. Potential Risk of Psychiatric Interviewing (minimal risk): As part of this study, you will be asked questions about sensitive personal information. You may feel anxiety about disclosing your alcohol use history and reporting some aspects of your demographics. You will be asked about suicidal ideation. In the event that you endorse suicidal ideation, the staff present with you will be authorized to contact the PI or one of the Co-I's on the study who will then assess the situation to see whether further intervention is required. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

Reproductive Risks and Other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, OrthoEvra patch, NuvaRing, intrauterine devices (IUD), Nexplanon implant, DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a diaphragm with spermicide with Plan B used for any noticed condom or diaphragm failures. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Urine pregnancy tests will be conducted prior to each MRI and TMS session.

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ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be the following: the treatment you receive may prove to be more effective than the other study treatment or than other available treatments, although this cannot be guaranteed. From a biological perspective, you may benefit from the positive effects of real TMS if you are randomized to the active groups. From a psychological perspective you will likely benefit from the additional time you will spend in contact with the study team when you will be surrounded by educational materials and an environment that is generally supportive and encouraging despite your struggle with substance use disorders.

Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have a number of options. Most types of treatment for alcohol use disorder involve some form of counseling and medication. If you would like to receive additional information on substance abuse treatment, you will be referred clinically from the PI.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Neither you nor your insurance company will be billed for the investigational device.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of TMS; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or

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biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by Wake Forest University Health Sciences which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $580 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be compensated for each complete study visit.

Payment will be made using a pre-paid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card and each time you receive a payment for participation in this study, the money will be added to the card after each completed visit. You may use this card at any store that accepts MasterCard or you can use a bank machine to remove cash. However, there may be fees drawn against the balance of the card for cash withdrawals (ATM use) and inactivity (no use for 3 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The debit card system is administered by an outside company, Greenphire. Greenphire will not receive any information about your health status or the study in which you are participating.

On the day of the Screening Visit, you will receive $20 for completing baseline assessments to see if you meet study requirements. If you remain eligible, you will be scheduled to attend the scanning visits in which you will be paid $40 for completion of each of the two MRI scanning visits. You will receive $20 for completion of each of the 15 TMS visits. You will receive $40 for the first follow-up visit, $60 for the second follow-up visit, and $80 for the third follow-up visit. If you do not show up to your scheduled appointment time, or your urine screens are not

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consistent with the information you reported on the screening day, you will be given one opportunity to reschedule before you are no longer eligible to participate.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institutes of Health (NIH). The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied. Portions of Dr. Addicott and her research team's salaries will be paid by this grant.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call our lab team at [redacted] or email us at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected

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Health Information. The information we will collect for this research study includes**:** Names, all elements of date (except year) for dates directly related to an individual (DOB, admission date, discharge date), telephone numbers, electronic mail addresses, medical record number, medical records/physician notes/hospital discharge records, psychotherapy notes, and medical test results.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the

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research records will be kept for an indeterminate period of time. This authorization does not expire.

You can tell Dr. Merideth Addicott that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Merideth Addicott
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to participate in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

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FUTURE RESEARCH?

From time to time we have other research studies that you may be eligible to participate in. We are inviting you to allow us to contact you by phone, mail, or both to see if you would be interested in participating in any future studies. By initialing next to the "yes" box below, you are indicating that you would like to give us your phone number, any alternate phone numbers, and address so that we may contact you if another study becomes available that you might qualify for. **To maintain your confidentiality, we will not leave identifiable messages or any identifiable information on letters or envelopes that are mailed to you.** By initialing next to the "no" box below, you are indicating that you do not want study personnel to contact you for any future studies. You may still participate in the current study if you choose "no" and you will not suffer any adverse consequences in doing so.

☐ Yes. I would like to be re-contacted for future studies. I give permission for study personnel to contact me by phone or by mail to inform me of other available studies I may be eligible for.
☐ No. I do not wish to be re-contacted for any future studies.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study team at [redacted] or call [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

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SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

I agree to share my de-identified data in the NIAAA Database for use in future research.

___ YES ___ NO

Subject Name (Printed):_____

Subject Signature (Date/Time, am/pm): _____

Person Obtaining Consent (Printed):_____

Person Obtaining Consent (Date/Time, am/pm):_____

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