RESEARCH CONSENT FORM

Providence VA Medical Center

IRB # 00001402

Subject Name: **Date:**

Title of Study: Synchronized TMS for Posttraumatic Stress Disorder and Comorbid Depressive Symptoms

Principal Investigator: Noah S. Philip, M.D.

Study Sponsor (if applicable):

1. Purpose of study and how long it will last:

This is a research study that will evaluate how well a treatment called "Synchronized Transcranial Magnetic Stimulation" (abbreviate as "sTMS") works for patients who struggle with symptoms of both major depressive disorder (MDD) and posttraumatic stress disorder (PTSD). Synchronized TMS is being studied as a non-invasive, non-drug therapy to reduce symptoms of PTSD and major depression.

In sTMS therapy, a device first measures a patient's brain waves, using an electroencephalogram (EEG). Then, the device makes a weak magnetic field at the same rate as the brain waves. Magnetic fields can move easily through human tissues like skin, hair, and skull bone. During sTMS given, the device is placed gently on the forehead while patients lay back with their eyes closed, awake, on a table or recline on a chair.

The purpose of this current study is to assess whether sTMS can relieve symptoms of both depression and PTSD. This study will use the NeoSync sTMS device, which has been tested for its safety and effectiveness for relieving depression symptoms in people for whom standard antidepressant medications had not worked.

Participants who meet eligibility criteria will receive sTMS therapy added on to their psychiatric medications in this study. If you participate in this study, you will be asked to keep your psychiatric medications and doses unchanged while participating in this study. If you need to change your medications, let us know right away. The treatment course will be a total of 20 treatment sessions delivered once per weekday. Study personnel will then check your depression and PTSD symptoms after you finish sTMS, and then, and again 1 month after the final treatment. You may also undergo magnetic resonance imaging (MRI) scans during the course of this study.

You will be randomly placed in to 1 of 2 groups. This is like the flip of a coin. One group will receive the magnetic energy from the sTMS machine, while the other group will receive no magnetic energy from the sTMS machine (also called a "sham," or placebo). There is a 50% chance of being placed in either group. You will not be told before or during the study to which group you belong. After the study is finished you will be asked to guess in which group you were placed.

At the end of the first 4 weeks, you will be offered a 4 week continuation of real sTMS, meaning that you will receive magnetic energy. If you chose to participate in this part of the study, the study post-treatment assessment visit will occur 1 month after your last treatment session.

2. Description of the study including procedures to be used:

Screening Visit: If you agree to participate, you will first undergo measures to see if you are eligible. These will include questionnaires to fill out and an interview with trained study personnel. Study investigators will review your current health history and medications and help you determine whether it is medically appropriate for you to participate in this study. Women of child-bearing age may be given a pregnancy test. They will also assess whether your medications have been constant for at least 6 weeks before the screening visit. This visit will take up to two hours. At this appointment, you may also be scheduled for an MRI scan, which will occur at either the Providence VAMC or Brown University.

sTMS Treatment Visits:

Baseline/Treatment Days 1-20: If you meet the eligibility rules for the study, and agree to participate, you will first talk with research staff for about 2 hours. This visit is called the Baseline session, and during this visit research staff will measure your brain waves with an EEG and set the device to provide magnetic energy at this rate.. During your visits to the clinic, the trained sTMS operators will set up and administer treatments. You will be asked to complete questionnaires that evaluate mood, mental functioning, and quality of life before treatment, at the end of every week and

after treatment is done. Before each treatment, a research staff member will ask questions regarding changes in your medications, any medical events that have happened since your last visit, and how you have been feeling. You will remain awake and alert throughout the treatment, and lay back on a table or chair with your eyes closed for 30 minutes. You will be given sTMS daily for 20 sessions (either sham or real), and will then have the option to complete an additional 20 real sTMS sessions. At the end of each treatment session, you will be asked questions about any discomfort or unusual effects that you may have experienced during the treatment.

Post Treatment Visits: Post treatment assessments will be done on the last day of your treatment and on a follow-up date 1 month after your last treatment date. During these visits you will fill out questionnaires and meet with a study interviewer who will ask you questions about your mood, any medical events, review your current medications, and you may be scheduled for post-treatment MRI scans. You may also do another EEG. Each post treatment visit will be about an hour.

MRI Scans: You may undergo 3 MRI scans as a part of this study. Each MRI will take place at either the Providence VAMC or Brown University. You will be asked to remove all metal jewelry, clothing and/or accessories and research staff will make sure you are MRI safe and that there is no metal in your body. You will lie in an MRI scanner for about 45 minutes and complete a task. The MRI scanner will be taking pictures of your brain while you are doing the task.

3. Description of any procedures that may result in discomfort or inconvenience:

You may feel uncomfortable answering personal questions about your emotions and health. You are free not to answer any questions but you may not be able to continue in the study unless the researchers are able to get enough information about your medical and emotional history to make sure you are safe to have sTMS.

The sTMS coil makes a calm, humming noise. You will have the option to wear earplugs to keep the sound out. Some people find earplugs uncomfortable.

When you have the sTMS you may feel slight pressure on your forehead. This might be uncomfortable for some people.

Frequent visits to the Providence VAMC for the sTMS treatments (5 days per week) for up to 4 weeks may represent an inconvenience. If you participate in the second study this will require another 4 weeks, with sTMS given 5 days a week.

MRI Scans: MRI is generally considered to be safe; but accidents, injuries, and even deaths have occurred during MRI procedures. Such adverse events are extremely rate if appropriate safety precautions are followed. Serious complications can occur in people who have metal pacemakers, metallic dust in the eyes, or certain types of metal prostheses, implants or surgical clips. MRI is also dangerous for anyone wearing metal objects, including jewelry, watches, hair holders, eyeglasses or metal on closing, as well as eye shadow, which sometimes contains metallic substances. In addition, if you enter the MRI room with any magnetic cards, such as ATM and credit cards, you will risk having the data on the cards erased by the MRI machine. For these reasons, a researcher or technician will review safety information with you before each scan. In order to determine whether it is safe for you to go into the scanner, it will be important that you tell study personnel and the MRI technician about any metallic objects or devices in, or on, your body.

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4. Expected risks of study:

Risk of side effects from sTMS treatments: Synchronized TMS is considered to be safe. The U.S. Food and Drug Administration has designated this device as a "non-significant risk device" in previous trials regarding the treatment of depression. Nonsignificant risk devices do not pose a significant risk to the subjects. This device and therapy is considered investigational, meaning that sTMS has not been approved by the United States Food and Drug Administration (FDA).Therefore, serious complications could occur in people who have metal in their head, such as shrapnel (pieces of bullets or metal from explosions) or implanted metallic objects such as a metal clip put in your body during surgery (such as aneurysm clips).

You should not have sTMS if you have ever had a seizure (also known as convulsions, fits, or epilepsy), stroke, or hearing problems, suffer from severe frequent headaches, or have been knocked out for more than 10 minutes. Study staff will ask you about these and related conditions that may put you at greater risk during sTMS. It is important that you tell study staff if you have or have had any of these conditions.

Risk of Worsening PTSD/Depression Symptoms or Lack of Improvement: Risks associated with participation in this trial include possible lack of benefit from the sTMS treatment. Worsening of depression and/or PTSD symptoms is also a risk. There is no guarantee that the treatment will lead to improvement of your symptoms. During the course of sTMS treatments or after finishing the final session in a sTMS treatment series, your symptoms may worsen even if you do not change your ongoing medications. The research staff will ask you at every treatment session how you are doing and the study doctor will be available at all times during the study to ensure that participation in this research continues to be safe and reasonable for you.

Risk of Confidentiality: There is some risk to patient confidentiality associated with participation in research clinical trials. Steps will be taken to protect privacy of your health information. This study is also being conducted at the VA Hospital in White River Junction, Vermont. Data collected from White River Junction will be shared in a database together with data collected from subjects at the Providence VAMC for final analyses. No personally identifiable information (like your age, birthday, social security number, etc.) will be shared with the research scientists at White River Junction VAMC.

EEG data may be acquired, downloaded to and stored via NeoSync-provided utilities and recording equipment. De-Identified data may be shared with NeoSync, Inc., the device manufacturer. Subject confidentiality will be maintained.

Other Risks: There may be other risks that are currently unknown. Although sTMS has been used for several years, the long-term effects of sTMS on individuals are not completely known. The research team will let you know if anything new is learned about the safety of sTMS that might make you change your mind about participating in this study. If this happens, you will be told what is known about the safety of the treatment, so you can decide if you want to continue to be in this study or not.

sTMS is not recommended during pregnancy. The effect of sTMS on pregnant women and on a developing fetus is unknown, so pregnant women are not allowed in this study. This treatment may be harmful to the developing fetus. Women of child bearing potential must use a medically acceptable birth control method during the trial, and may be tested for pregnancy at the time of admission to the study and will be required to be tested for pregnancy again later in the study if pregnancy status becomes questionable. Before you begin the investigational treatment, we will discuss with you in more detail the importance of avoiding pregnancy during the entire period of study participation. We will specifically ask you to let us know if you change your mind and decide to become pregnant during the study, or if you are not consistently using an acceptable method of birth control. If, during this study, you become pregnant, you should notify

Dr. Philip as soon as possible. Confirmed pregnancy will lead to immediate withdrawal from the study (unless a later pregnancy test shows that you are not pregnant).

MRI: There is a risk of heating too much from some of the coils and cables, which can result in burns if there is any metal on or in you (such as from tattoos or eye makeup or pins). The scanner also makes loud noises during imaging. Ear protection will be provided to reduce the noise level. If for any reason during the procedure you want to stop, you may do so at any time by telling the technician or by squeezing a ball that we will place in your left hand.

5. Expected benefits of study:

There may or may not be any direct benefits to you as a result of your participation in this study. You might benefit from a thorough assessment of your symptoms and diagnosis, which takes place during the screening process. sTMS may relieve your depression or anxiety symptoms. sTMS has been shown in the past to help people with depression. However, your participation in this study may also benefit others in the community with depression by adding to the information available for new treatments, and specifically by adding information to the field of psychiatry and mental health care, about the safety and effectiveness of sTMS therapy done the way we do it for patients with both major depression and PTSD.

6. Other treatment(s) available:

The alternatives to participation in this study include continuing previous treatment or starting new trials of standard treatments that have been proven to work for depression and/or PTSD administered by a clinician or prescribed by a physician or nurse outside of this research study (including medications, talk therapy or electroconvulsive therapy (ECT).

7. Costs to participants and compensation:

You will receive a total of $100 in gift cards for your participation. You will receive a $25 gift card after completing the eligibility and baseline procedure, $25 after the first follow up visit, and $50 at the end of the study, for a total of $100. You will not be required to pay for care and services (treatment) received as a participant in this VA research project. If you participate in the continuation part of the study will receive an additional $25 for completing additional procedures, bringing the maximum total of $125.

You will receive additional payments if you undergo MRI scans. You will receive up to $150, $50 per MRI scanning session, using either gift cards or electronic funds transfer (EFT). To receive funds by EFT, you will have to provide your bank account number, bank routing number, and social security number on the form provided, so that the funds can be sent directly into your bank account. This usually takes less than a week. When using EFT, all payments will be reported directly to the Internal Revenue Service (IRS). If you do not wish to use EFT and would prefer to receive gift cards of the same amount, please discuss this with study staff.

If you do not finish the study completely, you will still be paid for your time based on what you have completed.

8. Use of research results:

Every effort to maintain confidentiality will be made. You will not be identified in any reports or publications that may result from this study. The confidentiality of the information you provide will be maintained on a secure research server. As a VA patient, you have a computerized medical record and we will put notes in your record about your participation in this research study. A copy of this consent form will be scanned into the record. Information gathered during the course of this study will not be shared outside study staff except where permitted by law. If we believe you are in danger or

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hurting yourself or someone else, or if there is reason to believe that you have committed child or elder abuse or neglect, the information will be shared with the proper authorities.

9. Right of investigator to terminate participation:

Your participation in the study may be ended by the researchers without your permission if you are a woman of childbearing age and become pregnant or if we discover a medical condition that makes sTMS unsafe for you. While there are no other specific foreseeable future situations for which your participation may be ended, your participation in the study may be ended by the researchers without your permission. If we do that, we will tell you why.

10. Special circumstances:

Significant New Findings: You will be informed of any new findings that may affect your participation. These may be changes needed to the devices used in this study, or new research on sTMS.

Participant Withdrawal: If you stop the study for any reason before the follow- up visit, Dr. Philip may ask you to have some end-of-study tests so the research team can learn about how you are doing at the time you stopped participating in the study and so we can find out about any side effects that you experienced. We might have you meet with a study member who will ask you questions about your mood, any medical events that have happened since your last visit and how you have been feeling, and review your current medication.

FDA related studies involving drugs, biomedical drugs and medical devices: 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.

RESEARCH PARTICIPANT'S RIGHTS: I have read or have had read to me all of the above.
Dr. Philip or his research staff has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I have been told that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law. The Institutional Review Board at the Providence VA Medical Center or other federal oversight offices may monitor my records for quality assurance purposes. Federal agencies including, but not limited to, the Food and Drug Administration (FDA), the Office for Human Research Protection (OHRP), the Office for Research Oversight (ORO), the Office of the Inspector General (OIG) and the Government Accounting Office (GAO) may have access to the records as allowed by law. If an FDA-regulated test article is part of this study, the FDA may choose to inspect research records that include research subject's individual medical records. Records will be maintained in accordance with the Department of Veterans Affairs Record Control Schedule 10-1.

If I experience a side effect or adverse (bad or unexpected) reaction as a result of my involvement in this study, I will report these to the study investigator Dr. Noah Philip at 401-273-7100 x6235 who will arrange for any medical treatment that is necessary. After hours, I will call Dr. Noah Philip at 401-632-6613.

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In case there are medical problems or questions, I have been told I can call Dr. Noah Philip at 401-273-7100 x6235 during the day and Dr. Noah Philip at 401-632-6613 after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

The VA has the authority to provide medical treatment to participants (veterans and non-veterans) injured by participation in a VA study. If you are injured as a result of being in this study, the VA will provide the necessary medical treatment in accordance with federal law. If you want to make a legal claim against the VA or anyone who works for the VA, special laws may apply. The Federal Tort Claims Act (28 U.S.C. 1346(b), 2671-2680) is a federal law that controls when and how a person can bring a claim against the U.S. Government. If you sign this document you are not giving up your right to make a legal claim against the United States.

I can call the IRB Coordinator at (401) 273-7100 ext. 3470, the Research Administrative Officer at (401) 273-7100 ext. 3478 or the Providence VAMC Patient Advocate at (401) 273-7100 ext. 3093 while I am a participant or after my participation is over for the following: 1) concerns, 2) complaints, 3) problems, 4) suggestions, 5) more information, 6) questions about my rights as a research participant or 7) verifying the validity of the study and authorized contacts.

I voluntarily consent to participate in this study. I confirm that I have read this consent form or it has been read to me, and I agree it explains what this study is about and how and why it is being done. I will receive a signed copy of the consent form document after I sign it.

Participant's Signature	Participant (printed)	Date
Signature of Person Obtaining Consent	Person Obtaining Consent (printed)	Date

Version Date: 3/14/16, 9/1/16, 10/15/16, 3/23/17, 5/3/17, 5/31/17