Form
M0345

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Neuromodulation Enhanced Cognitive Restructuring: A Proof Of Concept Study
Version Date: 6/11/2019

Concise Summary

We are doing this study to learn more about a form of therapy designed to help people who have difficulties calming down when they get upset.

People in this study will have a 1-day screening visit that includes sharing their difficulties and treatment history and questionnaires about stressful situations they have had in their lives.

Next, we will ask people in this study to return for an MRI scan, where we will look at what happens in their brains when they are reminded of a stressful situation.

Everyone who joins this study will come for a visit where they will learn how to do *cognitive restructuring* (learning to think differently about emotional situations) and then practice it on their personal stressors while having real or sham (fake) *neurostimulation*. Neurostimulation involves placement of a wire coil shaped like an 8 on the scalp that produces very small electric currents in the part of the brain that is closest to the coil.

Everyone in the study will get 8 brief calls/day for 7 days following the intervention to see how they are doing with use of cognitive restructuring and current distress. Everyone will complete questionnaires and will be asked to return for a repeat MRI scan at the end of that week.

Everyone in the study will return 1 month later to complete questionnaires, have an additional stressor task, and an exit interview.

Participation in the study takes 1-3 months and includes 5 total visits.

People in the study will be compensated for the parts of the study they finish.

About 2 out of 1000 people may have a seizure during the neurostimulation. The most common side effect is headache.

If you are interested in learning more about this study, please continue to read below.

We are asking you to take part in a research study as part of the Duke Cognitive Behavioral Research Program (CBRTP). The purpose of this consent form is to give you the information you will need to help you decide whether or not to be in the study. Please read the form carefully.
We are asking you to take part in this research study because you have said you have difficulties managing your emotions. You have also told us that you are not currently in active psychotherapy treatment. You may ask any questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this

form that is not clear. When all of your questions have been answered, you can decide if you want to be in the study or not. This process is called 'informed consent'. We will give you a copy of this signed and dated consent form for your records.

Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study staff if you are taking part in another research study.

Dr. Andrada D. Neacsiu will conduct the study that is paid for by the Duke CTSA Research Career Development Award Program funded by the National Institute of Health (NIH). The sponsors of this study will pay Duke University to perform this research, and these funds may reimburse part of Dr. Andrada Neacsiu's and her research team's salary.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Steven Szabo, MD will be your medical doctor for the study and will be in contact with your regular health care provider if needed during the study or after.

WHY IS THIS STUDY BEING DONE?
Repetitive transcranial magnetic stimulation (rTMS) involves placement of an electromagnetic coil over the scalp that produces very small electric currents in the part of the brain that is closest to the coil.

CR is a psychological skill that can be utilized to actively reduce emotional distress in a variety of situations. There are signs that it can reduce emotional distress and help people regulate their emotions better.

rTMS is a noninvasive and painless treatment that is approved by the Food and Drug Administration (FDA) for the treatment for depression only. In this study, we will use rTMS differently than what it has been approved for by the FDA but within safety guidelines. We will use rTMS together with cognitive restructuring (CR) in one session to test if it is helpful in reducing problems with dealing with emotions and mental distress.

Using rTMS in studies for conditions other than depression is investigational. The word "investigational" means the study device is still being tested in research studies and is not approved by the U.S. Food and Drug Administration (FDA) for this condition.

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The purpose of our research is to test whether combining CR and rTMS during one clinic session can help to reduce negative emotions and problems with dealing with emotions in both a laboratory setting and in a person's everyday life.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
About 105 people will take part in this study at Duke. We may enroll up to 200 people in order to have 105 people complete the study.

WHAT IS INVOLVED IN THE STUDY?

	Assessment Day	Pre – intervention MRI Day	Study Intervention Day	Follow-Up Week	Post-intervention MRI	Follow-Up Week 5
Consent discussion	▲					
Medical history	▲		▲			
Questionnaires	▲		▲		▲	▲
Computer tasks		▲	▲		▲	▲
Interview	▲					▲
Randomization to study group	▲					
Urine pregnancy test		▲	▲		▲	
CR Training Session			▲			
Emotion Regulation Tasks			▲			
rTMS or Sham TMS			▲			
Brain imaging		▲			▲	
Phone calls every 2 hours while awake				▲		

These activities are described in detail below.

First Appointment (Assessment Day):
If you choose to take part in this study, you will first be asked to sign and date this consent form. You have already completed the telephone or online screening, but we are not yet sure if you will be eligible for the study. Today's visit will last between 1 and 5 hours.
During your first study visit (today) you will talk with an assessor about your medical and mental health history. Questions will include how you cope with stress, ways in which you tend to think about yourself, and how you get along with others. We will also ask questions about your personality, intelligence, and specific psychological problems such as anxiety and depression.

We will ask you about your treatment history, including any medications you may be currently taking (for example, prescription medications, over-the-counter medications and vitamins).

During this visit, we will also ask you to complete a number of questionnaires that tell us about your difficulties managing emotions, general mental health and distress, functional impairment, anxiety, depression, and coping.

If you are enrolled in this study, you cannot also be in cognitive behavioral psychotherapy. You can be on medication for mental health problems as long as there have been no changes in your medication in the past month and you agree not make any changes in medication throughout the study (with the exception of a medical emergency).

If you have recently participated in other studies here in our clinic, you may not have to answer all of the interview questions that we normally ask during this visit. Instead, we will use the answers that you gave in your other recent visit when we review the data for this study. The study staff will review the results of the visit to decide if you continue to qualify for the study.

If after the initial interview, you do not qualify to stay in the study you will be paid for your time and your participation will be complete.

If you continue to qualify for the study, an interviewer will ask you to describe in detail several stressful experiences you have had during your lifetime as well as in the past few weeks. You will also be asked to write them down, review them with the interviewer, and rate how stressful each event is. We may also ask you to rate how distressed and how negative each of a list of 100 words makes you feel.

We will then schedule you for the next appointment. You may have to wait until the end of the study to be paid.

Sometimes the interviews and questionnaires can last longer than expected. If this first visit is lasting longer than planned, we may have to finish it on a second day. If that is the case, you will finish the interviews or the self-report scales before the intervention. We will only ask you to finish the visit and questionnaires on the second day if you qualify for the study.
We will video record or audio record you as part of this study to make sure the research staff are doing the study procedures correctly. If you are not willing to be video-or audio-recorded, please indicate so below (you will still be eligible to be in the study).

Recordings will be kept strictly confidential and will be directly recorded on Duke office computers using a web camera directly connected to the computer's hard drive. The recordings will then immediately transferred from the computer's hard drive to the Duke protected hard drive that is maintained and secured by Duke in the Department of Psychiatry and Behavioral Sciences. The folder that will contain these video/audio recordings is protected and only members of the study team who are listed as key study personnel can access them. The video/audio-recordings may be reviewed by the key research and clinical staff members in Dr. Neacsiu's team, and may also be used for training within Dr. Neacsiu's lab of new research staff, if you agree. At the end of the study you may review the recordings

and delete any portions you don't want us to save. You have the right to come in and erase any parts of the recording, but you do not have a right to copy our recordings or any of our research material. These recordings will be destroyed at least six years after the study is completed.

Please initial below whether or not you are willing to be audio or video-recorded as part of this research study.

_____ "I am willing to allow the researchers to audio or video-record the interviews to see if the experimenter is following the protocol correctly."

_____ "I am NOT willing to allow the researchers to audio or video-record the interviews to see if the experimenter is following the protocol correctly."

Treatment Groups:
If you qualify, before coming back for the intervention, you will be randomly assigned (like the flip of a coin) to get one of two research groups:

1) **Real left rTMS:** you will get active neurostimulation over the left side of your brain.
2) **Sham (fake) TMS:** you will not get active brain stimulation

You will not know whether you are getting real or sham brain stimulation until the end of the study. Throughout the study we will talk to you as if you have received real rTMS regardless of your group.

Thus, we may be telling you that you had real rTMS when in fact, you may have actually had sham TMS. This is to help you remain unbiased in your reporting of mood, distress levels and ability to manage emotions after undergoing a session of TMS with CR. This will help us to examine the true effects of brain stimulation. Regardless of whether you get real or sham rTMS, you will learn the cognitive restructuring skill and how to use it to reduce distressing emotions.

Brain Imaging Session:
Before the intervention, you will have a brain imaging session. We will meet here and walk together to the MRI building (5 minute walk). If you are a woman, we will ask you to provide a urine sample to check if you are pregnant during this visit. We will not continue with the MRI visit if the pregnancy test is positive for your own safety. The Magnetic Resonance Imaging (MRI) instrument being used in this study has a part that is not commercially available and is considered investigational and is being used for research purposes only.

At your MRI scan Brain Imaging Session appointment, you will first learn how to think differently in emotional situations. You will practice this strategy with an experimenter using 'fake' distressing memories.
We will also ask you to complete some questionnaires and an MRI safety screening form. You will also participate in a personalized computer task where you will have to indicate with key presses the color of words seen on a screen. The computer task lasts for about 5 minutes, and some of the words used come from the list of words rated during your first appointment.

If you have never had an MRI of the brain, we will ask you have a "mock scan" to familiarize you with the sights and sounds of the MRI scanner using a practice MRI machine. This part of the session will take about 1 hour.

During the MRI portion of the session, you will lie on your back upon a narrow bed that will be pushed into the MRI machine. The MRI technician will provide padding for your head and knees to make you more comfortable while lying down.

If you are uncomfortable or feel pain because of lying down, please tell the technician right away. The technician will also place a respiration belt on your chest and a clip on your finger so we can monitor your breathing and pulse during the scan.

The technician will position your head inside a head tube, and the platform will be pushed into the bore of the MRI machine. You will be able to communicate with the technician during the MRI using a microphone and speaker in the MRI machine.

While in the scanner, you will be asked to remember the negative memories you listed in the First Appointment. You will use the emotion management strategies you learned during the training session. You will also be asked to rate your mood after each memory. This portion of the study will take about 1 hour.

Study Intervention Session:
When you return to the lab for the study intervention we will go to a different building where training will happen.

First, if you are a woman we will ask you to provide a urine sample to check if you are pregnant. We do this to ensure your safety.

Next, we will check whether the study brain stimulation intervention we are planning is safe for you. The study team may review your medical history and some of the forms you completed during the assessment day and may ask you more questions. Based on the study team's review and the urine pregnancy test we will decide whether it is safe for you to continue with the study.

CR Training session:
First, we will teach you about the connection between thoughts and emotions and how thinking can affect how you feel. We will then introduce a few ways of thinking differently in emotional situations. We'll practice together on examples of how to think differently in order to feel emotions less intensely. You will work one on one with a study staff member for about 45 minutes to learn and practice this skill.

Baseline and pre-intervention assessments:
Before the study intervention, we will ask you about any changes in your medications, caffeine, alcohol, & nicotine use on that day, your sleep habits, and current pain, physical distress, and drowsiness levels.

You will sit in a chair in front of a computer and we will attach several electrodes that measure your body's physiological responses. Throughout this period and the intervention, we will study your body's stress level by measuring your "galvanic skin response" (GSR) and heart rate. The GSR is checked painlessly by placing two sensors on your fingers that measure small changes in sweat activity. Once you're set up, we will wait 5 minutes for your body to relax so we can collect your physiological baseline.

Establishing dose of brain stimulation and getting used to the TMS machine:
The rTMS equipment includes an electric stimulator and a wire coil. Turning the stimulator on and off produces brief electrical currents in the coil, and these currents create a magnetic field around that coil (also called a 'magnetic pulse').

The wire coil is shaped like an '8' and coated in plastic in order insulate the current and is a little larger than a piece of notebook paper. When the coil is held close to the head it generates a magnetic pulse which can induce very small electric currents in the part of the brain that is closest to the coil. These currents are similar to the currents that the neurons in the brain create when communicating with each other.

Before applying rTMS, the study doctors will need to decide what "dose" of stimulation to use for you by establishing your personal "motor threshold." The motor threshold is a measure of the excitability of the area of the human brain called the motor cortex.

To establish this threshold, we wil first place the stimulator over the part of your brain that controls the motor activity in your left or right hand. You will hear a clicking sound and feel a tapping sensation at your scalp. The stimulator will be adjusted to give just enough energy so that the motor region of the brain sends signals to your hand muscles, to make your hand twitch. The lowest amount of energy required to make your hand twitch is called the "motor threshold." Everyone has a different motor threshold. This will take about 15 minutes.

Next, we will apply the rTMS (or sham TMS) stimulation for 10 minutes so you can get used to the noise and sensations. The rTMS stimulation will be applied at a rate of 10 Hz (10 Hz means 10 stimulation pulses per second) over the right or left side of your head depending on your assigned group. The 10 Hz frequency is the FDA approved frequency for the treatment of depression.

The stimulation will be done in brief bursts of 4 seconds while you are sitting still. During this time, you will not be asked to do anything but your technician will check with you about how you are feeling. This period is to get you comfortable with the rTMS.

We may also need to identify the place for stimulation by using a system that involves head measurements. We will ask you to wear a swim cap and we will use a measuring tape to make several measurements.

<u>Emotion regulation session (2 hours)</u>:
Once we have found the right dose for you, we will move ahead with the emotion regulation stressor task. During this task, you will complete computer questionnaires that will ask you about your stress, dissociation, and emotional arousal levels.

After another 5-minute baseline, we will start the experimental task. The task includes:

(1) You will be given instructions to imagine as vividly as possible one of the recent stressful experiences that you previously described
(2) Your stressful experience will be played to you on headphones for 30-40 seconds, and
(3) You will continue to sit in silence imagining the event until you see and hear instructions to reduce your distress by thinking differently about what happened (10 min).

The rTMS or sham TMS will begin 10 s after these last instructions appear. Your GSR and heart rate will be measured while you're doing this task. Then you will be asked to report how you are feeling.

After completing the first task, there will be a 10-minute break. You will then go through a second and third version of the same task, but using a different stressful event that you talked about at your first appointment. At the end of the third task, if you continue to report high distress, the researcher will guide you through a 10-minute relaxation exercise.

After the computer experiment, you will be asked to complete a few questionnaires about your experience with the intervention, your current level of distress and emotions.

The study team member will then explain the upcoming week of phone self-report assessments and the follow up procedures.

We may record a video of your face to analyze your facial expressions during this portion of the study. This would be entirely optional.

_____ "<u>I am willing to allow the researchers to video-record my face during the intervention</u>"

_____"<u>I am NOT willing to allow the researchers to video-record my face during the intervention</u>."

<u>Follow up assessments</u>:
At the end of the intervention session, a staff member will explain how your cell phone will be used to collect data from you. We will not provide you with a study phone. Rather we will ask you to use your

own cellphone for this portion of the study.

You will be asked to carry your cell phone with you at all times for the following week. Over that week, you will get eight calls each day (about one call every two hours that you are awake), with each call lasting 30-60 seconds.

When you answer a call, you will hear a prerecorded voice that will ask you about your level of emotional distress at the time of the call and whether you have used the CR skill since the last phone call. On some calls, you may also hear a prompt to use CR if we think that your distress level is high.

If you miss a call, you can call back the missed call number to provide this information.

After one week the calls will stop. You may get a link by e-mail to an online set of questionnaires that are similar to the ones you completed at the beginning of the study. We will ask you to complete the questionnaires as soon as you can after the calls stop. They should not take longer than 30-45 minutes to finish.

If you have not finished the questionnaire within 2 days of getting the e-mail a staff member will call you to problem solve or to see if you want to do the questionnaires by phone. You can also inform the staff that you want to complete these questionnaires by phone at any point during the study.

You will also be invited back for a follow up MRI scan at the end of this week. You can complete the 1 week questionnaires at the MRI visit if you choose to do so.
At your follow up MRI scan appointment, you will complete a urine pregnancy test if you are a woman who can get pregnant. Next, you will review the strategy of how to think differently in emotional situations and practice with a few examples and then complete a 5-minute behavioral task where you indicate the colors of words on a computer using a keyboard. During the MRI part of the visit, you will lie on your back upon a narrow bed that will be pushed into the MRI machine with the same set up as described before. While in the scanner, you will be asked to remember the negative memories you listed in the First Appointment. You will use the emotion management strategies you practiced during the training session following the memories. You will also be asked to rate your mood after each memory. The follow up MRI session should take an additional 90 minutes.

One month later (about 5 weeks after intervention visit), you will to return to our office where you will complete a brief interview about treatment you received and answer questionnaires similar to the ones you did at the beginning of the study.

You will also participate in one additional stressor task. Like during the intervention visit you will be connected to physiological recording equipment but no TMS stimulation or machine will be used in the follow up task. After a 5-minute baseline, you will hear your fourth stressful event through headphones and be asked to try to lower your emotional arousal followed by silence for 5 minutes.

We may video-record your face during this task to analyze your facial expressions during the stressor and regulation periods.
You will complete a few questionnaires before, during and after the task that mirror the questions from the intervention day. You will also complete a computer task involving indicating colors of words with a keyboard.

We will then inform you about the group you were assigned to and debrief you about the study. We will provide you with additional treatment referrals as needed. This visit will last about 2 hours.

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HOW LONG WILL I BE IN THIS STUDY?
Your participation in the study will last up to 3 months. This includes the screening visit, the MRI sessions, the intervention day, the ambulatory assessment, the 1-week follow up and the 1 month follow up.
We will try to have all procedures completed within 6 weeks but may extend to 12 weeks if finding times for you to come in is difficult. You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to a staff member so we can best assist you and help you find additional services if needed.

WHAT ARE THE RISKS OF THE STUDY?
As a result of being in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

<u>Risks of rTMS</u>:
The most serious known risk of TMS is seizures. TMS procedures come with a very low risk of seizures. Out of over 10,000 people given various forms of TMS to date, 16 people (less than 0.2%) have had a seizure. TMS can produce a seizure when a series of pulses is given at high power and when repeated series of pulses are given extremely close together.

This study will use only levels of TMS that are within safety guidelines. Levels of TMS that fall within the safety guidelines have not been associated with seizures in people who have been evaluated medically and undergone the motor threshold test. No seizures have occurred in normal volunteers with the dosage of TMS used in this study.

To minimize this risk, we will medically screen you for any of medical reasons that could lead to seizures. For example, persons with epilepsy cannot be in this study. You will be watched carefully during the TMS for any signs of seizure or muscle twitching. In spite of these precautions, there is a chance that you will experience a seizure.

Should this occur, emergency facilities are available. If you have a seizure, you may require hospital admission and follow-up neurological evaluation. Having had a seizure may make it difficult for you to obtain medical insurance, future employment, and to drive. It is not known whether having had one seizure will make a person more prone to have future seizures. Should you have a seizure caused by TMS in this protocol, we will provide you with a letter stating the seizure was caused by a research procedure.

The most commonly reported side effect of TMS is a "muscle-tension" type headache. About three out of ten people may experience a headache with the types of TMS used in this study. We will make every effort to reduce any discomfort.

If a headache occurs, it usually starts during or immediately after the TMS and lasts from minutes to hours. The headache usually goes away with standard over-the-counter pain medications. You may also have neck pain. You may also experience some discomfort on your head where the coil is placed. This is due to contraction of scalp muscles.

Numbness of the face lasting for a short time has also been reported in rare instances and may last for several weeks after receiving the procedure. Fainting is considered a rare side effect of TMS and has been reported in people who faint during blood draws. If you experience fainting, you will be withdrawn from the study and have your blood pressure monitored until it returns to a healthy level.

The clicking noises produced by the TMS procedure are loud enough to be damaging to your ears. You will therefore be required to wear earphones and listen to white noise during the TMS procedures.

Additional rare side effects of TMS are dizziness, memory problems, trouble concentrating, and acute mood changes. If these happen they usually do not last long and will resolve without need for treatment.

There may be other risks that are currently unknown. The long-term effects of rTMS are not known.

Risks of behavioral intervention procedures and assessment:
It is possible that you may experience some unpleasant thoughts or emotions from the interviews, questionnaires and/or stressor tasks on the computer. However, we have no reason to believe that any unpleasant thoughts or emotions will last long after the experiment is over. Some of the questions we will ask you as part of this study may make you feel temporarily uncomfortable, as they have to do with psychological problems such as depression or anxiety.

You may refuse to answer any of the questions and you may take a break at any time during the study. If you are feeling very upset during an assessment interview or the stressor task, a trained staff member will be available to talk with you about these feelings.

If at any time during the interview or the procedures you have strong thoughts of suicide, you should notify the study staff and a trained professional will be available to talk. The trained study staff will work with you to address these suicidal thoughts and if you are at imminent risk of suicide after the conversation, you will be taken to the nearest hospital emergency room (for example: Duke ER).

There is also a potential risk of loss of confidentiality. Every effort will be made by the study staff to keep your information confidential; however, this cannot be guaranteed.

If you have any medical adverse events (a bad effect) after leaving the TMS laboratory, please contact the Duke operator at 919-684-8111 and have Dr. Steven Szabo paged. If you have any psychological adverse events, please have Dr. Andrada Neacsiu paged at the same number.

There are no known risks of cognitive restructuring, however, in case it is difficult to understand or use this technique using your stressful events, it's possible that you may feel frustrated or disappointed.

Risks of MRI Scan:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no bad effects reported from exposure to the magnet or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future.

A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you not be allowed to participate in this research study. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner.

The study involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 2 feet across. You will be asked to lie still for about one hour on this bed.

You will hear a loud machine-like banging noise. We will give you earplugs and/or headphones to protect your hearing. You may be asked to have a harmless monitoring device applied during the study.

Some people feel anxious when confined by the small space of the MRI machine. If you feel anxious or uncomfortable inside the MRI machine, you can tell the study staff over the intercom and you will be removed immediately from the MRI machine. You can also have voice contact and physical contact with someone in attendance if you desire.

Reproductive Risks:
For women of who can get pregnant:

Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unknown. Therefore, pregnant and breastfeeding women will be excluded from the study.

If you are a woman who can get pregnant, a urine pregnancy test will be done on the day of any MRI scan or TMS session, and it must be negative before you can continue in this study.

If you are sexually active we recommend that you use appropriate contraceptive measures until you have completed all MRI and TMS sessions. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD).
Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant during the study or if you have unprotected sex during the study, you must inform your study physician immediately.

There may be risks, discomforts, drug interactions, or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
This study may be of no direct benefit to you, but you will help improve our knowledge about which strategies are helpful or unhelpful for people who experience strong negative emotions.
A possible benefit is that the study could help develop personalized strategies for you to use to feel better when upset, but this cannot be guaranteed. We hope that in the future the information learned from this study will benefit other people with your condition.

WHAT IF WE LEARN ABOUT NEW FINDINGS OR INFORMATION DURING THE STUDY?
You will be given any new information gained during the course of the study that might affect your willingness to continue. If any unexpected abnormalities are found that might pose a significant health risk to you, Dr. Neacsiu will inform you so that you may seek follow up medical consultation with a doctor of your choosing.

POSSIBLE DISCOVERY OF FINDINGS RELATED TO MEDICAL IMAGING
It is possible that the MRI component of this study will identify information about you that was previously unknown, such as disease status or risk. This research scan is not a medical diagnostic test, nor a substitute for a medical test.
There are no plans to provide this information to you or your physician unless there is an unexpected finding on the scan that indicates a possible need for follow-up testing. This is rare, occurring in only about 3 of every 1000 people scanned. If this happens, your scan will be reviewed by a physician or the MRI technician, who may recommend further diagnostic testing. If this happens, the physician or MRI technician will discuss this with you and you will be asked for separate permission for the follow-up and

further testing outside of this research study. The possible costs associated with this follow-up and/or further testing will be discussed with you at that time.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
You do not have to participate in this study to get treatment for your mental health problems. Currently available treatments include many types of psychotherapy, medications, electroconvulsive therapy (ECT), and transcranial magnetic stimulation (TMS). Please talk to your doctor about these and perhaps other options.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS).

All paper data and research forms will be kept in a secure locked cabinet in Dr. Neacsiu's office and will only be made available to members of the research team for this study. Your name and other personal identifying information will not be stored in the computer system databases that store your ratings, and thus individuals who might gain unauthorized access to your ratings will not know your identity.

Video recordings which could contain identifiable information will be destroyed no more than 6 years after the study is completed.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include the representatives from the Duke University Health System Institutional Review Board. If your research record is reviewed by this group, they may also need to review your entire medical record (if you receive your medical care at DUHS).

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or
3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project (NIMH).

You should understand that a Confidentiality Certificate does not prevent you or a member of your family 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. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

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.

Your name and other personal identifying information will not be used in any scientific reports of this study, and will not be made available to representatives from the Brain and Behavior Foundation, PRIDe award, or CTSA KL2 award groups. Some people or groups who receive your health information might not have to follow the same privacy rules.

Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information
Your records may be reviewed in order to meet federal or state regulations. Reviewers may include the representatives from the Food and Drug Administration (FDA), and the Duke University Health System Institutional Review Board. If your research record is reviewed by either of these groups, they may also need to review your entire medical record (if you receive your medical care at DUHS).

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

The study results will be combined with results from other subjects and given to the FDA to support applications to use rTMS. All reasonable efforts will be made to keep your identity confidential. Because of the need to release safety information to third parties absolute confidentiality cannot be guaranteed. This information may be further disclosed by the sponsors of this study, the Brain and Behavior Foundation, Duke University, and NIH. If disclosed by the sponsor, the information is no longer covered by the federal privacy regulations.

During the week when we will call you several times per day, there is the risk that someone else may see the call from Duke University Medical Center on your phone, or may overhear the questions asked over the phone. These situations may put your confidentiality at risk. To mitigate this risk, we may add the phone line that makes the automatic calls temporarily to your contacts with a nickname of your choosing that can mask whom the call is coming from.

On the call, you may be asked for your study ID, current level of distress, and use of cognitive restructuring. No identifiable information will be asked of you over the phone and you will answer using key presses, which makes it less likely that someone else could overhear your answer.

Furthermore, if you are in a place where you can be overheard or where you are not comfortable taking the call, you can reject the call and call the study at a later time when it's more convenient or you can wait for the next automatic call.

Calls are automatically logged in a password- protected database on a password-protected local computer that is kept in a locked office at the CBRTP. Only a limited number of CBRTP staff has access to this computer. Should someone gain unauthorized access to this database they will have access to your cell phone number.

At the end of this week we will e-mail you a link to a questionnaire to complete. The questionnaire will not ask for your name, but will ask for your study id number, which will be given to you during the intervention day. Because of this, your answers to the questions will not be directly linked to you should someone intercept this data. There is the risk of breach in confidentiality if someone sees you answering the questions.
To protect you against this risk, we will ask that you complete the questionnaire in a private setting and will give you the option to complete the questionnaire over the phone with one of the study staff should you choose to do so.

Another risk to your confidentiality comes from someone intercepting the e-mail we send. We will keep the information in the e-mail brief, but an e-mail breach would get your e-mail address connected to a Duke study. No other information should be apparent if there is a breach. The link to the online survey is generic and does not "remember" your previous answers. Therefore, if someone else accesses the link from your e-mail they will not be able to see any answers that you have entered. We will use QUALTRICS, a Duke approved platform, to collect your information at this assessment.

WHAT ARE THE COSTS?
There will be no additional costs to you as a result of being in this study.

WHAT ABOUT COMPENSATION?
You will be compensated between $150 and $250 for your participation and will be given a parking pass or a bus pass to cover your travel to Duke during days when you have in person visits. All payments will be made via check by Duke University at the end of your participation.

When you finish the assessment day, and you are not eligible to participate in the full study, you will receive $10 plus a parking pass at the Duke Hospital parking garage or a bus pass (up to $3) to cover the cost of parking or bus fare.
If you complete the full day of assessments at the first visit and are eligible to participate in the full study, you will receive $25 plus a parking pass at the Duke Hospital parking garage or a bus pass (up to $3) to cover the cost of parking or bus fare.

After the initial screening day compensation for the study depends upon the procedures that you complete. You will be screened for the appropriateness of TMS. If TMS is not appropriate, you will be paid $10 and a parking pass/bus pass for the intervention day. If TMS is medically appropriate, you will be paid $75 for the intervention day.

You will get $50 for completing the pre-intervention imaging session. You will be paid $10 if you attempt to complete the MRI session but do not complete it (because of detected pregnancy or claustrophobia).
For each call you complete during the 1-week ambulatory assessment you will receive $.25, up to $2 per day. For completing the online assessment at the 1-week follow up you will be paid $10.
For completing the 1-month follow up you will be paid $26. For the follow up MRI session, you will get an additional $50.

For eligible participants, all payments will be done at the end of the study.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Neacsiu at 919-684-6714 during regular business. If outside regular business hours, please contact the Duke operator at 919-684-8111 and have Dr. Andrada Neacsiu paged.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke.

Nonparticipation or withdrawal from this study will not affect your job status if you are a Duke employee and will not affect your grades if you are a Duke student. If you do decide to withdraw, we ask that you contact Dr. Neacsiu in writing and let her know that you are withdrawing from the study. Her mailing address is Box 3026, Duke University Medical Center, Durham, NC 27710.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study. Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if the study team determines that it is no longer in your best interest to continue.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Andrada Neacsiu at 919-684-6714 during regular business hours, or the Duke operator outside of business hours at 919-684-8111 to have Dr. Neacsiu paged.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

Form
M0345

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Neuromodulation Enhanced Cognitive Restructuring: A Proof Of Concept Study
Version Date: 6/11/2019

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time