TITLE OF RESEARCH:

Tracking Brain Biomarkers and Renormalization Associated with Antidepressant TMS Therapy

SUMMARY

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Your participation is entirely voluntary. The purpose of this study is to take a picture your brain using magnetic resonance imaging (MRI) and then use an investigational way of imaging the brain, called Individualized Network-based Single-frame Coactivation Pattern Estimation ("INSCAPE") to capture your brain activity. This method uses a computer program to understand which parts of your brain communicate with each other and creates a map of the brain areas that are connected.

You are being asked to participate in this study either because you are planning to receive Transcranial Magnetic Stimulation ("TMS") for Major Depressive Disorder ("MDD"), or because you are a healthy volunteer. If you agree to participate, you will attend three experimental visits in which you will undergo MRI scans. The interval between each experimental visits is about 3 weeks.

During each experimental visit, we will conduct a brain scan for about 30 minutes in total. During the MRI scan, you will need to stay still, relax, and keep eyes open in the scanner.

Your participation is voluntary, and you may ask to stop procedures at any time. As a healthy volunteer, your alternative is to not participate in this trial. As a volunteer who is going to receive TMS for MDD, your alternative is to receive standard of care TMS for MDD without being enrolled in the study.

It is not expected that participants will benefit but researchers hope that what is learned will help us better understand how this investigational brain imaging method can track brain activities or help us understand how to improve transcranial magnetic stimulation (TMS) Therapy. If you are interested in learning more about this study, please continue reading below.

A. PURPOSE OF THE RESEARCH

The purpose of this study is to explore whether this investigational brain scan protocol, referred to as INSCAPE, can detect brain changes over the course of depression treatment while patients are receiving TMS. This method uses a computer program to understand which parts of your brain communicate with each other and creates a map of the brain areas that are connected.

TMS is an approved treatment for MDD, in which patients receive daily treatment sessions over 6 to 8 weeks. Each session involves an electromagnet being placed on the head over the front portion of the brain for 20 minutes. The treatment is highly effective in treating depression.

In this study, we will use MRI scans to collect your images of your brain. MRI is an FDA-approved medical imaging procedure for taking pictures of the internal structures of the body, and has been widely used in clinics and research. We will check in with you frequently to assess for any discomfort throughout the experiment. The collected pictures will then be analyzed using our INSCAPE program.

Images of the brain will be collected from both healthy people and depressed people. Depressed people in this study will have pictures taken before, during, and after a course of TMS.

Investigators will then look for changes found using the INSCAPE program by comparing pictures of depressed brains over the course of TMS treatment to non-depressed individuals.

The goal is to determine if there are depression symptoms related to specific brain states, and whether they can be used to descibe depression severity, and to track antidepressant treatment effect of clinical TMS therapy.

Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. You are being asked to participate in this study because you are/have interested in participating as a healthy volunteer, or because you are planning to receive TMS for MDD. The study is sponsored by MUSC Department of Psychiatry Chair's Research Development Fund (CRDF). The investigator in charge of this study at MUSC is Andrew Manett, MD. The study is being done at one site. Approximately 40 people will take part in this study (20 healthy volunteers and 20 depressed patients receiving TMS).

B. PROCEDURES

If you agree to be in this study, the following will happen:

Pregnancy Test

If you are an individual of childbearing potential, you will be asked to take a urine pregnancy test at the MUSC center for biomedical imaging right before each MRI scan. This test will be provided to you at no cost. Should the test present a positive result, you will no longer be eligible to participate in the study.

Experimental Visit 1 - Baseline

MRI Brain Scan - The study team will take pictures of your brain during this scan. This will be done at the MUSC center for biomedical imaging. A magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise. You will be asked to keep your eyes open during the scanning, though you may blink as needed.

Experimental Visit 2 – Week 3

MRI Brain Scan - The study team will take pictures of your brain during this scan. This will be done at the MUSC center for biomedical imaging. A magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise. You will be asked to keep your eyes open during the scanning, though you may blink as needed.

Experimental Visit 3 – Week 6

MRI Brain Scan - The study team will take pictures of your brain during this scan. This will be done at the MUSC center for biomedical imaging. A magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud machine-like noise. You will be asked to keep your eyes open during the scanning, though you may blink as needed.

Depression Assessments (Ongoing)

If you are a patient receiving TMS Therapy for depression, we will collect measurements that help us understand the severity of your depression. These assessments will be done at the beginning, middle, and end of the 6-week period. These will be done at the clinic where you are receiving TMS during your scheduled treatment visits. There will not be additional clinic visits required to complete these assessments.

Voluntary Withdrawal

Participation in this study is voluntary. You are free to withdraw your consent and discontinue participation in the study at any time throughout the study without negative consequences to your relationship with the Medical University of South Carolina.

Involuntary Withdrawal

You may be withdrawn from the study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

Withdrawal from study will not affect any routine care you would normally receive at MUSC.

C. DURATION

For Healthy volunteers, you will have 3 MRI scanning visits over a period of six weeks.

For patient with MDD receiving TMS, you will have 3 MRI scanning visits over a period of six weeks of treatment. You will also complete depression and anxiety assessments weekly during your TMS treatment session visits.

D. RISKS AND DISCOMFORTS

MRI Brain Scan: There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. 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 will be excluded from participation 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. Please inform the study staff if you have a history of claustrophobia (extreme anxiety in close spaces). This may also be a contraindication to participation in the study. You will be required to keep your eyes open during a roughly 30 minute scan period, though you may blink as needed.

This MRI scan will be used to answer research questions, not to examine your brain medically. This MRI scan is not a substitute for one a doctor would order. It may not show problems that would be picked up by a medical MRI scan. Nevertheless, a clinical neurologist or neuroradiologist will read your scan. If we find an abnormality, we will let you know, and will advise you to follow this up with your doctors. If you wish a copy of your MRI scan, we can provide it to you on a CD. The MRI scans will be stored on research computers for 7 years and then they will be destroyed. It is not possible to access them after you complete the study so please get a copy of your MRI on a CD if you think you might want it in the future.

Psychological Risks for participants with MDD receiving TMS: Some of the questions the researchers ask you may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you can skip it and go to the next question.

There is a risk of loss of confidentiality of your information that is used in this study.

E. MEDICAL RECORDS AND/OR CERTIFICATE OF CONFIDENTIALITY

Information about your study participation will not be in your medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record.

This research is covered by a Certificate of Confidentiality from the Federal government. This means that the researchers may not disclose information or biospecimens that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, nor can the information or biospecimens be used as evidence, unless you have consented to this disclosure. Information or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless you have consented to the disclosure. More specifically, identifiable information or biospecimens will not be shared with your medical providers who are not involved in this research unless you authorize the study to disclose information to them, or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Information about your study participation will not be in your MUSC medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record. 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 authorize the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law. Examples of required disclosure include: child abuse and neglect, or harm to self and others, but there could be others.

Finally, a Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating Federally funded projects or information needed by the FDA.

F. BENEFITS

There will be no direct benefit to you from participating in this study. However, it is hoped that the information gained from the study will help in the treatment of future patients with conditions like yours/will help the researcher learn more about antidepression therapy.

G. COSTS

There will be no cost to you as a result of participation in this study.

H. PAYMENT TO PARTICIPANTS

In return for your time and effort, you will be paid $15 for completing the first neuroimaging visit, and $15 for completing the second neuroimaging visit, and $20 for completing the third neuroimaging visit. Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment will be made using a Clincard, which is like a debit/credit card. Funds will be added to the Clincard after each MRI visit.

If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

If you wish a copy of your MRI scan, we can provide it to you on a CD.

I. ALTERNATIVES

As a healthy volunteer, your alternative is to not participate in this trial.

As a volunteer who is going to receive TMS for MDD, your alternative is to receive standard of care TMS for MDD without being enrolled in the study.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

Data collected and results will not be disclosed to participants in the study, however will be released for public dissemination in published manuscripts and conference presentations.

L. Authorization to Use and Disclose (Release) Medical Information

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information MUSC may use or disclose (release) for this research study includes information in your medical record, results of physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study whom may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and MUSC committees having authority over the study such as:
    - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study or, if you are participating in a study designed for the development of a drug or device, your authorization will remain in effect until the drug or device is approved by the FDA or until the company's application to study the drug/device is withdrawn. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact MUSC's Privacy Officer at (843) 792-8740.

M. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

N. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

O. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

P. CLINICAL TRIALS.GOV

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

Q. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

____Yes, I agree to be contacted

____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact **Andrew Manett (843-792-0192)**. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may

contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

_____ _____

Signature of Person Obtaining Consent Date *Name of Participant

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Signature of Participant Date