Theta Burst Stimulation of Reward Circuitry

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: Theta Burst Stimulation of Reward Circuitry in Young Adults with Depression

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If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

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Why is this research being done?
In this research study we are trying to learn more about the role of neural mechanisms in depression. We know that certain areas of the brain are involved in regulating emotion, which seems to be an important part of depression, but we want to find out to find out how changing function in these areas influences brain function, mood, and behavior. Eventually, the findings of this study might be useful for treatment.

What will happen in the study?
We will be asking 36 young adults (aged 18-25) with a diagnosis of depression (Major Depressive Disorder, Persistent Depressive Disorder (Dysthymia), Other Specified Depressive Disorder, or Other Unspecified Depressive Disorder) to participate in our research study. We will first need to determine if you are eligible for this study.

The screening process will include:

- An interview with questions about your emotions, mood, and behaviors, about how you get along with others at home and at school or work, and questions about your health. You will also be asked about your treatment history, including current medications. This interview will take approximately 1-2 hours. With your permission, interviews will be video recorded to facilitate training and supervision of study staff.
- Questions checking for certain types of metal in your body, because you cannot participate in the MRI if those metals cannot be removed.
- Providing a urine sample for pregnancy and drug screening.
- Completing a TMS Safety Screening.
- Completing a physical exam with a study physician. The physical exam will include assessment of your height, weight, blood pressure, pulse, respiration, and temperature.

If you are eligible to participate, then you will be asked to complete 5 visits in total:
VISIT 1: Questionnaires on the same day as your eligibility interview
VISIT 2: Questionnaires about your health and mood, a physical exam, safety screening, a procedure to measure the TBS setting that should be used for you, one 30-minute fMRI session to determine where to place the TBS on your scalp, and a computer task
VISIT 3: A 15-minute fMRI scan before TBS, the TBS procedure, a 20 minute fMRI scan after TBS, questionnaires and computer tasks
VISIT 4: A 15-minute fMRI scan before TBS, the TBS procedure, a 20 minute fMRI scan after TBS, questionnaires and computer tasks
VISIT 5: A 15-minute fMRI scan before TBS, the TBS procedure, a 20 minute fMRI scan after TBS, questionnaires and computer tasks

Each visit (1-5) will take approximately 3 hours to complete.

These 3 Theta Burst Stimulation (TBS), sessions will include:

- 1 with continuous TBS
- 1 with intermittent TBS
- 1 simulation of TBS, which means there is no real stimulation to your brain

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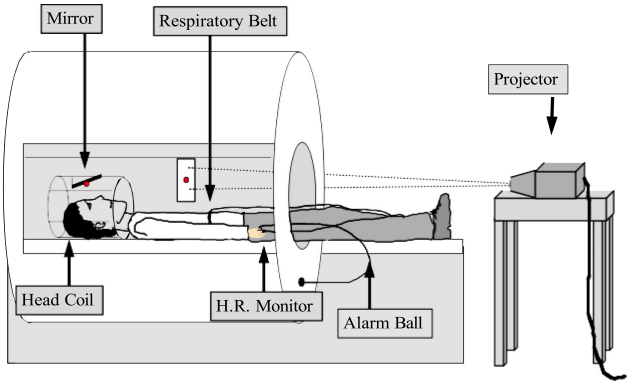
What is an fMRI?

fMRI is a type of brain scan that gets pictures of the brain while people are experiencing and doing different things. The pictures that the scan creates show the parts of the brain that are active and how they coordinate their activity. fMRI is a painless procedure that does not use radiation, but uses radio waves, a large magnet, and a computer to create images.



All of the fMRI scan sessions will take place at the Magnetic Resonance Research Center (MRRC) which is located at Presbyterian Hospital, part of the University of Pittsburgh Medical Center. At the MRRC, a staff person will help you fill out an MRI Safety Screening Form to make sure that there are no known risks (for example, metal fragments in your body) to your participation. Before beginning the real brain scans, you will be given a chance to practice the game you will be playing in the scanner and be able to lie in a realistic simulator to become comfortable with the scanning machine. While the scanner is recording, you will complete the task that you practiced earlier. The staff person will talk to you while you are in the scanner through a microphone; you should tell the technician if anything is uncomfortable. You can also choose to stop scanning at any time.

It is important in these studies that you remain still while in the scanner; movement in the head, arms and legs can make the brain pictures blurry. You should experience no physical discomfort, except that associated with remaining still for the actual scanning period. The initial scan for neuro-navigation is to see the shape and functioning of your individual brain, so that we can do TBS effectively. This will take approximately 30 minutes to complete. The fMRI scans that will happen before and after each TBS session will last approximately 15 minutes each.

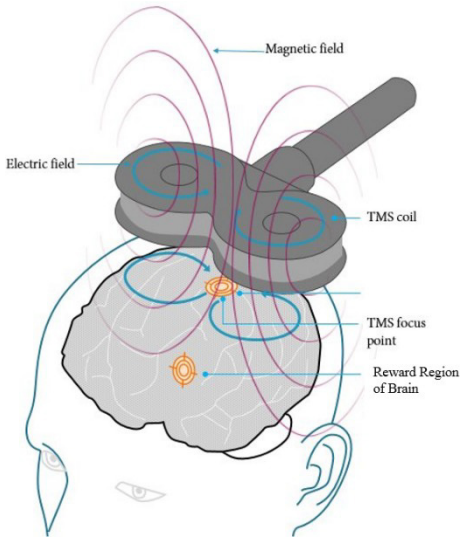
You will not be informed of the results of the brain imaging scans because the purpose of these MRI recordings is for research and this type of scan can't be used to get clinical information such as neurological health. However, if there is something unusual on the scans that requires further clinical evaluation (as judged by a radiologist) we will tell you this information and offer an appropriate referral to a medical facility.

What is Theta Burst Stimulation (TBS)?

Theta Burst Stimulation (TBS) describes the type of brain stimulation that we are using. You may also see or hear the term TMS— Transcranial Magnetic Stimulation –
Theta Burst Stimulation (TBS) is just a shorter version of TMS.

TBS is a technique to briefly stimulate a region of your brain with a magnetic field that passes through the scalp and the skull safely. We will use the MRI brain images to guide the TBS so that the stimulation is in the right place for our study. We will ask you to complete 3 sessions of TBS. Each time you get TBS, it will last approximately 3 minutes long, but each session will be slightly different. For some of them there will be small breaks in between the pulses of stimulation. In one of these sessions, you will hear and feel a similar sensation around your head,

but you will be getting a simulation of pulses, so nothing will be happening to stimulate your brain. In order to prevent any differences caused by personal expectations, we will not tell you which condition of TBS that you receive on which day.



The study staff will be available to talk to you before you start the procedure and will give you a chance to see the device that will be used and to ask any questions that you have before beginning the TBS process. The staff will also be standing by while you are receiving TBS and you should tell the research team if anything is uncomfortable. You can also choose to stop the procedure at any time.

What are the computer tasks?

The computer tasks are about winning money. The task you will complete in the scanner is a game that involves guessing numbers on cards for a chance to win money. The other task you will complete will happen outside of the scanner and will involve making button presses on a computer keyboard for the chance to win money.

What are the questionnaires going to ask?

We will be asking questions about your emotions, experiences, and behaviors. These will cover things related to your mental health, as well as your interactions with people, recent life events, and activities you do. We will also ask about your age, gender, race/ethnicity, and household income.

What are the risks in this study?

1) Some of the questions about your mood and emotions may cause you to feel anxious, embarrassed or sad for a short period of time. The session may be stopped at any time if you feel undue psychological or physical discomfort. It is also important that you express any concerns and/or ask any questions throughout the whole study.
2) The brain stimulation in this study comes with the risk of experiencing scalp discomfort and/or a mild headache during or immediately after the TBS procedure due to the activation of the scalp muscle near the device. There is also a less common risk with the TBS of a delayed onset headache (which can be helped with ibuprofen), and the very unlikely possibility of a seizure. There have been no reported seizures in anyone that has received the procedure that is used in this study. There is also the rare chance that a hypomanic mood state could result from the TMS procedure. Lastly, there is also a possibility that a TBS session will produce worsening of depression symptoms (a rare side effect in TMS) however, we do not anticipate that anyone will experience long-lasting mood change from a single session.
3) There are no known dangers of exposure to the magnetic fields used for the MRI imaging studies. The fMRI involves few physical risks, but you should be aware of the following:

    - The magnet used in the MRI machine is very powerful and may attract and may move

metal objects. If you have certain types of metal in your body, you cannot participate in the MRI part of this study. We will ask you questions before the MRI testing to make sure you are safe. Trained medical personnel are always present during these studies.

- Since the machine is loud, you will be given and must wear earplugs.
- Some people become uncomfortable while in the machine.
- Sometimes people worry about how well they do on tasks or become tired. To reduce these problems, scanning will not begin until you are comfortable.

4) Additionally, we will offer you the option of communicating with us over text-message during your time in this study, and although we will do everything within our power to protect your information text messages are not encrypted or secure during their transmission and it is possible they could be intercepted and used by others not associated with this study.

What are the benefits?
You will not benefit from this study. We hope to learn more about the brain response to theta burst stimulation, especially for depressed individuals. We are looking at this so that we can learn more for future treatment studies and to reduce health problems in the future.

What is the compensation?
You will be compensated for parking or bus fare that is needed to get to and from all visits to the laboratory. For your first visit to the lab, you will receive $30 for the interview to assess eligibility. If eligible, you will receive another $20 for completing the questionnaires and computer tasks.

That is up to $50 for your first visit.

For your second visit, you will receive *at least* $100.

For your third visit, you will receive *at least* $100.

For your fourth visit, you will receive *at least* $100.

For your fifth visit, you will receive *at least* $100.

Your total payment for each of these visits may include additional money that can be won during the computer tasks, which is why we say *at least* $100.

Will I be billed for study procedures?
Neither you, nor your insurance provider, will be charged for the costs performed only for the purposes of this research study.

Will this be confidential?
To protect your privacy and maintain the confidentiality of information we obtain, we will keep all information we obtain in a secure location and use a number rather than your name as

identification. All paper records that could identify you will be kept in a locked filing cabinet, and all electronic records will be stored in password-protected files. Although we will do everything in our power to protect your privacy and the confidentiality of research records, we cannot guarantee the confidentiality of research records. However, no third party, including relatives, personal physicians, employers, insurance companies or other researchers will be provided with names or other identifying information.

There are 3 exceptions to your confidentiality in this study. First, staff at the Magnetic Resonance Research Center at Presbyterian Hospital will have access to your identifiable information related to the eligibility screening for participants and for handling internal hospital operations. Second, Authorized representatives of the NIMH and the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable information for monitoring the appropriate conduct of this research study. Third, if the study staff learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies. In rare cases, identifiable records may be released in response to an order by a court of law.

Data from this study will be submitted to the National Institute of Mental Health Database (NDA) at the National Institutes of Health (NIH). NDA is a large database where deidentified study data from many National Institute of Mental Health (NIMH) studies is stored and managed. Deidentified study data means that all personal information about you (such as name, address, birthdate and phone number) is removed and replaced with a code number. Sharing your deidentified study data helps researchers learn new and important things about mental health and substance use more quickly than before.

During and after the study, the study researchers will send deidentified study data about your health and behavior to the NDA. Other researchers across the world can then request your deidentified study data for other research. Every researcher (and institutions to which they belong) who requests your deidentified study data must promise to keep your data safe and promise 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 some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about mental health and substance use and how to help others who have problems with mental health and substance use. NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA.

You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA. If you know now that you do not want your data in the NDA, please tell the study researcher before leaving the clinic today. If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff who conducted this study, and they will tell NDA to stop sharing your study data. Once your data is part of the NDA,

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 NDA, this is available on-line at http://nda.nih.gov.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

1) The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally-funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).
2) You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What else is important to know?

It is possible that we may use the information obtained from this study in other research studies examining TBS and its effects on mood and brain activity. This information may also be shared with other researchers here, and at other research centers, but those researchers will never be provided with any personal identifiers that would allow them to learn who you are.

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

Your participation in this study is completely voluntary, at all times.

Your decision to participate, or later withdraw, from this study will not affect your current or future relationship with the University of Pittsburgh, current or future medical care at a UPMC Health System hospital or affiliated health care provider, and current or future relationship with a health care insurance provider. If you decide you no longer want to continue to participate after you have signed the consent form, you should contact Dr. Forbes or her research staff with the information on the front of this form. You may withdraw from the study at any time. If you choose to withdraw, we will typically continue to use information already collected. However, if you prefer that we no longer use any information from your participation, you should provide a written and dated notice to Dr. Erika Forbes.

You may also be removed from the study by the study staff if you no longer meet the eligibility criteria (for example, if you are not safe to undergo an MRI scan or are found ineligible during the interview). Participants may also be removed from the study for failing to follow study procedures.

If you believe that the research procedures have resulted in a personal injury, immediately contact Dr. Forbes, the principal investigator of this study, who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation

in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions and voice concerns or complaints about any aspect of this research study during this study, and any future questions you ask will be answered by the researchers listed on the first page of this form at the telephone number(s) given.

By signing this form, I agree to participate in this research study.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

VIDEO RECORDING

By signing below, I agree to have my interview audio- or videotaped. Recordings are for training and supervision purposes.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____

Signature of Person Obtaining Consent Date, Time