Indiana University Informed Consent Statement for Research

Temporal interference methods for non-invasive deep brain stimulation
Aim 1 Brain Stimulation and Brain Activity

You are being asked to participate in a research study. This consent form will give you information about this study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

Important Things to Know:

- The project is research, and your participation is voluntary
- You will have your brain scanned in a MRI (magnetic resonance imaging) machine while receiving mild electrical current to electrodes on your scalp
- The study will take 2-3 hours, and you will be paid $35 for each hour you spend in the laboratory. Beyond that, there are no expected benefits to you.
- There is a risk of mild boredom from the procedure and tingling sensations on your scalp from the stimulation, as a well as a risk of loss of confidentiality.

Please review the rest of this document for more details about this study and the things you should know before deciding whether to participate.

Why is This Study Being Done?

The overall purpose of this research is to understand how gentle electrical stimulation on the scalp of your head affects brain activity and the ability to perform simple tasks. In this part of the research, we are studying the effects of applying this mild electrical current to the scalp on brain activity and sensations. In order to do this, you will have your brain scanned in a MRI (magnetic resonance imaging) machine while: (1) receiving mild electrical current to electrodes on your scalp using a new technique called non-invasive transcranial stimulation (TI-NDBS) or (2) you will have the four electrodes on your scalp and receive no stimulation.

This study involves stimulation through a device. Electrical stimulation has commonly been done in humans. For example, it has been used clinically to reduce pain and cigarette craving, and in research studies to improve depression and cognitive functions like working memory. However, this pattern of stimulation is relatively new. Thefore, the use of the device in this study is considered investigational because it is not approved by the Food and Drug Administration (FDA) to be used outside of research studies.

We are asking you if you want to be in this study because you are an adult between the ages of 18 and 50, weigh less than 440 pounds, and have at least a 6th grade education.

The study is being conducted by Dr. Joshua Brown (Department of Psychological and Brain Sciences). It is funded by the National Institutes of Health (NIH).

How Many People Will Be in the Study?

You will be one of 200 participants taking part in this study.

What Will Happen During the Study?

The study will take place at the IU Department of Psychological and Brain Sciences in Bloomington, Indiana.

Testing will take about 2-3 hours. The visit will include having different parts of your scalp

stimulated during brain imaging as well as some questionnaires to fill out. More information about each procedure is described below.

Complete Self-Report Measures:
You will complete a magnetic resonance imaging (MRI) screening questionnaire that asks about metal implants, the potential presence of metal objects under your skin, feelings of claustrophobia and other experiences. You must pass the MRI screening in order to be able to participate. You will also be asked demographic questions, a handedness questionnaire, discomfort scales, and quality of life questions. We will also use the information you provided as part of your screening interview.

Scalp Stimulation:

The imaging procedure will take approximately one to two hours.

Before entering the MRI magnet room, you will be required to complete an MRI screening checklist (described above), which ensures that it is safe for you to enter the scanner. We will also ask you to complete a questionnaire, which asks about your demographic information. We will use this information to help interpret the MRI data.

After completing the checklist, you will be asked to remove all metal objects from your person.

You will then be sitting in a chair and have the electrodes attached to your scalp with a tight-fitting hat. The skin beneath the electrodes will be cleaned prior to application, and a saline solution or gel will be used to help to attach the electrode to your scalp. You will then enter a magnetic resonance imaging (MRI) brain scanner.

For the MRI, you will lie on the patient bed, and be given instructions to just relax and lie still throughout the imaging procedures. For head/brain MRI, you will have an MR head coil surrounding your head. Your head will be supported with foam pads to make you more comfortable and to help you to keep your head still.

In the brain scanner you will have electrodes attached to your scalp and receive (1) active transcranial electrical stimulation (TI-NDBS), through these electrodes and (2) sham (fake) stimulation at different times, for a total stimulation period of approximately 60 minutes. There will be periods of no stimulation mixed in while you are inside the scanner. You will not be told which stimulation is active vs sham. The sham stimulation is designed to create mild sensations similar to the active stimulation, so that you will not be able to notice a difference between the active and sham stimulation.

The active stimulation will consist of a very small electric current applied to the brain through the scalp electrodes. A very small current of electricity (about 2 mA per electrode) will run through the electrodes while you sit. There will be a maximum of 2 mA per electrode pair and no single region will receive more than 2 mA because the currents will be administered to distinct regions. Some tingling under the electrodes may be felt.

After the procedure the experimenter will let you in the restroom so you may clean off any gel that remains on your skin. The gel washes away easily with water.

You will be in this study for about 2-3 hours.

Because we are doing an MRI, we may learn things about you that could be important to your

health or interesting to you. We will share the following information with you:

- We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you. The MRI scan may reveal an abnormality in your brain structure. Any findings that might be immediately critical to your health, such as a brain abnormality, will be reviewed by a neuroradiologist in a de-identified manner. If the neuroradiologist recommends further action, results will be shared with you. You might want or need to meet with a doctor or other professional to help you decide what to do with this information. We do not have money available to pay for any follow-up consultations, testing, or treatments.

What Are the Risks of Taking Part in the Study?

MRI screening interview:

- You may feel uncomfortable completing the interview. For instance, there are questions about whether you may be pregnant, your surgical history, and about the existence of tattoos and piercings on your body. You may choose not to answer any questions that make you uncomfortable, but if we cannot verify that it is safe for you to participate, then you may not be allowed to participate in the rest of the study.

MRI procedures

- This MRI scan is not a medical test. It is designed to address research questions and it is not a complete scan for any clinical purpose. If there is an abnormality, the scan, the MRI technician, or the researcher may not detect it.

- MR imager: MRI has not been shown to produce health problems in normal, healthy individuals. The imager DOES NOT produce ionizing radiation, which is radiation associated with conventional radioactive sources, such as x-rays, radioactive iodine, uranium, or other substances. No medication, needle stick, or injections of drug or contrast agents are involved. There are hundreds of imagers of this type used in the U.S. and abroad, both to assist doctors in clinical diagnoses and for research. To view a copy of the Food and Drug Administration safety guidelines for MR imagers, simply ask the MRI operator.

- Because of the strong magnetic fields used for MR imagers, persons who have magnetic life-support devices (e.g., pacemakers and aneurysm clips), metal prostheses or other metallic objects (e.g. cochlear implants, steel pins implanted to help repair and strengthen broken bones, metal fragments from previous injuries) cannot participate in this research.

- MRIs are known to blank out magnetic strips on credit cards, so you must leave your wallet as well as your watch and any other metallic object in the Imaging Research Facility (you can place it in a locked cabinet which we will provide to you).

- The radio frequency energy used in this exam has produced burns (most of them minor) in about one in a million cases. If you feel any burning sensation you will immediately inform the staff, so that the scan can be stopped.

- MRI may be harmful to an unborn child. If you are of childbearing potential (that is, if you are a woman with sexual partner(s) and do not use an adequate birth control method), you must be excluded. Reliable birth control (i.e. oral, implanted, or barrier methods)

should be used by all participants and/or their sexual partner to prevent pregnancy while participating in MR imaging. If you find that you were pregnant while participating and undergoing MRI, you should notify your physician immediately. If you use an IUD for birth control you will be excluded unless you can document the model of the IUD and we can verify its safety for the MRI environment. Pregnancy should be self-reported, and a pregnancy test will not be administered.

- While there is no evidence of increased risk with multiple scans, the risks associated with multiple scans are not known. The IUB imaging center is adopting an arbitrary maximum of 40 hours of scanning time per individual per year and the time involved in the present study is well below that limit.

- Though uncommon, there is also the risk that the imaging procedure may result in claustrophobia, nausea, dizziness, sweating, or headaches. Individuals who suffer from migraines may be more susceptible to these side effects as a result of the noise level inside the scanner. These symptoms are generally temporary, and the scan can be stopped at any time if you begin experiencing discomfort. If you feel uncomfortable or wish to end your participation, you may let the MRI operator know and the MRI will be stopped. When no scans are in progress, you can be heard in the control room on a speaker system. Also, you are provided with a squeeze bulb which you can squeeze during scanning sessions to let the MRI operator know that you need attention. If you signal that you wish to stop the imaging, the operator will immediately enter the magnet room and assist you in exiting the MRI and patient bed.

- The MRI takes hundreds of images and possibly as many as several thousand, which is necessary to measure brain activity accurately. When the MRI takes images, it makes loud buzzing and clicking noises. You will be given ear-protection to prevent the noise from making you uncomfortable.

Brain stimulation:

- Mild physical discomforts: Approximately 66% of participants who receive this kind of stimulation experience mild physical discomforts that are short-lived, such as tingling, itching, redness, or mild burning sensations on the skin under the pads. Some participants have also reported occasional mild headaches and fatigue. There is also a risk of seeing flashing lights. These effects are mild, short lived, and benign. The electric current is very mild and is approximately 1000 times smaller than the average static electric shock one might receive touching a door knob or light switch after walking on a carpet with socks. While it is rare, some participants may experience a stronger unpleasant sensation. If you experience any discomfort or wish to stop the experiment, please let the experimenter know and the procedure will be stopped immediately.

- Long term effects: Long term effects of exposure are largely unknown, though no long term adverse effects have been reported from any previous study. As a precaution, the stimulation will not last longer than 20 minutes continuously at one time.

- Medical precautions: Though a significant adverse event has never been reported with similar brain stimulation procedures, there theoretically may be a risk to persons with conductive metal (i.e. implants) in their head, and to persons who suffer from migraines, epilepsy, or other neurological syndromes. If you have any of these conditions you may be ineligible to participate in this study. Also, you may be ineligible to participate in the study if you have a history of seizure disorder, history of cognitive impairment, symptoms of psychosis or if you are taking medications for cancer, attention deficit hyperactivity disorder (ADHD), autoimmune deficiency syndrome (AIDS), or other mental illness.

These risks will be managed by trained researchers; at least one will always be present when the machine is operating. The researcher will stop the experiment if you experience discomfort that you do not wish to tolerate. Furthermore, the stimulator does not transfer current greater than 3 mA per electrode pair, which is still, relatively, a very small current.

Questionnaires:

- Some of the questions may make you uncomfortable or upset. You can skip any questions that you do not want to answer.
- There is a small risk of boredom during the session. You may decline to continue participating if you no longer wish to continue.
- There is also a small risk of loss of confidentiality. Your data will be stored in a secure location and separated from information that can identify you to minimize the risks of loss of confidentiality.

What Are the Benefits of Taking Part in the Study?

There may be no immediate benefits involved in participating in this research; however, we hope to find in the long term that TI-NDBS will help with treating clinical disorders such as addiction and psychosis. The results of this study are expected to contribute to a better scientific understanding of cognitive processes in the brain.

How Will My Information be Used?

The following individuals and organizations may receive or use your identifiable health information:

- The researchers and research staff conducting the study
- The Institutional Review Boards (IRB) or its designees that review this study
- Indiana University
- State and Federal government agencies as permitted by law including but not limited to:
    - Office for Human Research Protections (OHRP)
    - National Institutes of Health (NIH)
    - The United States Food and Drug Administration (FDA)
- Data safety monitoring boards and others authorized to monitor the conduct of the study

Information collected for this study may be used for other research studies or shared with other researchers who are conducting their own research studies. This may include sharing with researchers outside Indiana University and sharing with private companies. It may also include making the information available in public and private databases of research data so that other researchers can use the information to answer research questions.

If we share your information in this way, we will remove information that could identify you, such as your name and contact information, before any information are shared. Since identifying information will be removed, we will not ask for your additional consent for this sharing. It is possible that you may be re-identified. As mandated by U.S. law, your data will up uploaded to the National Institutes of Mental Health data archive (https://nda.nih.gov/), and other data you provide can be linked to this data.

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

How Will My Information be Protected?

We will do our best to keep your personal information private, but we cannot promise complete confidentiality. We won't share any information that we think could be used to identify you in publications about this study. However, your personal information may be shared outside the research study as described above and/or if required by law. Data will be coded using subject numbers and data will be stored separately from these informed consent forms and other study documents that collect identifiers to protect confidentiality. The researchers and their associates will have access to the data collected from this experiment, but your identity will not be revealed outside of the research group.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that information, documents, or specimens from this study that could identify you cannot be used in any legal action or lawsuit unless you say it is okay.

There are some types of sharing the Certificate does not apply to. The Certificate does not stop reporting required by federal, state, or local laws, such as reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate also does not stop sharing of information as described in the How Will My Information be Used section above.

Will I be Paid for Participating?

You will be paid $35 for each hour you spend in the laboratory. You will be reimbursed in cash immediately following the session or immediately upon withdrawal from a session. If you withdraw from the study prior to its completion, your payment will be prorated based on the amount of time you were in the session. For example, if you spend 2.5 hours, you will be paid $87.50. Your total payment will be between $70 and $105, depending on how much time you spend in the laboratory.

Who Will Pay for my Treatment if I am Injured?

If you have an injury or illness as a result of participating in the study, you will be responsible for seeking medical care and for the expenses associated with any care received. Any costs not covered by your medical insurance will be your responsibility. We don't have money set aside to pay for these types of injuries. However, signing this form won't take away any of your legal rights if you are injured.

Who Should I Call with Questions or Problems?

If you have questions at any time about the research or the procedures, (or you experience adverse effects as a result of participating in this research) you may contact the principal investigator, Dr. Joshua Brown at 1101 E Tenth St., Bloomington, IN 47405, phone (812) 855-9282, email jwmbrown@iu.edu.

In the event of an emergency, you may contact Dr. Joshua Brown at 812 716-2057.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

What if I Do Not Want to Participate or Change my Mind?

After reviewing this form and having your questions answered, you may decide to participate in the study. Or, you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your relationship with Indiana University.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw, we will remove any equipment from you that may be part of the research, such as electrical stimulation equipment, and remove you from any research equipment such as the MR scanner.

The researchers may stop your participation in the study even if you do not want to stop if we determine that you no longer meet the eligibility criteria or have a contraindication to the study procedures, or if we are unable to proceed with the experimental session due to equipment malfunction.

Agreement to be Contacted by Text and/or Email

We would like to communicate with you about this study by text message and/or email. We might use text or email to schedule your visit or communicate about your compensation for participating, or check on how you are doing.

Text messaging and email are not secure methods of communication. The information sent over text or email, which may include sensitive or personal information, such as protected health information, could be accessed or read by someone other than you. If you would like us to communicate with you via text or email, please initial the lines below and provide the phone number(s) and/or email address(es) you would like us to use.

_____ I authorize the researchers to send me emails related to this research study

Email address for this communication:

_____

_____ I authorize the researchers to send me text messages related to this research study

Phone number for this communication:

_____

You can still participate in this study even if you do not want us to contact you by text or email.

Participant's Consent

I agree to participate in this research study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____**Date**:_____