CAHBIR CENTER FOR ADVANCED HUMAN BRAIN IMAGING RESEARCH
RUTGERS Brain Health Institute

CONSENT TO TAKE PART IN A RESEARCH STUDY

Title of Study: Criticality and Working Memory
Principal Investigator: Andrew Westbrook, PhD

STUDY SUMMARY: This consent form is part of an informed consent process for a research study, and it will provide information that will help you decide whether you want to take part in this study. It is your choice to take part or not.

The **purpose of the research** is to: test how brain activity is related to your ability to perform mental tasks that require remembering items and responding to them flexibly. We will also test whether we can alter brain activity using transcranial magnetic stimulation (TMS) and whether this has any effects on your ability to perform the tasks during your study visits. If you take part in the research, you will be asked to perform memory and judgement tasks on a computer while we record your brain activity using electroencephalography (EEG). We will also use TMS while to test whether we can alter brain activity patterns. This study is purely experimental and will not have any lasting effects on the brain beyond your study visit. Your time in the study will take 4 sessions: one 1-hour session to take a picture of your brain with magnetic resonance imaging (MRI), and three 3 to 4-hour sessions using TMS and EEG.

Possible harms or burdens of taking part in the study may be mild discomfort, boredom, and a very minimal risk of headache or seizure. There are no direct benefits from taking part in the study.

An alternative to taking part in the research study: Your alternative to taking part in the research study is not to take part in it.

The information in this consent form will provide more details about the research study and what will be asked of you if you choose to take part in it. If you have any questions now or during the study, if you choose to take part, you should feel free to ask them and should expect to be given answers you completely understand. After your questions have been answered and you wish to take part in the research study, you will be asked to sign this consent form. You are not giving up any of your legal rights by agreeing to take part in this research or by signing this consent form.

Who is conducting this study?
Andrew Westbrook, PhD is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the research. However, there are often other individuals who are part of the research team.

Dr. Westbrook may be reached by phone at 919-360-5399 or email at andrew.westbrook@rutgers.edu or by mail at 119 RWJMS Staged Research Building, 661 Hoes Lane West, Piscataway, NJ 08854.

The Principal investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

Sponsor of the Study: This study is sponsored by the National Institute of Mental Health.

Why is this study being done?
This study is being done to understand whether there is a relationship between specific patterns of brain activity and people's ability to perform tasks that require short-term memory and to switch back and forth between mental tasks, flexibly. This study is also being done to determine whether brain dynamics can be altered – in the short term – using transcranial magnetic stimulation (TMS) and thereby affect ability to perform these tasks.

Who may take part in this study and who may not?
Before the TMS procedure, you will be interviewed to see if you are eligible to participate in the study. The interview questions that determine your eligibility are chosen for both scientific and safety reasons. The interview will include some personal questions, such as questions about your health history, and any drugs or medications you might be taking.

You are eligible to participate if you are a healthy young adult between the ages of 18 and 45 and can safely participate in an MRI scan and receive TMS. You are ineligible to participate if you have any metal implanted in your body that would interact with a magnet, have a history of seizure or fainting, have a history of mental illness, have ever had a concussion, or are taking any medications that would increase your chances of having a seizure. You are also ineligible to participate if you are pregnant or are potentially pregnant. If you are unsure, you may be asked to take a urine pregnancy test – the results of which will be kept private. Or, if you know that you are not, you can also sign a pregnancy test waiver.

Why have I been asked to take part in this study?
You are invited to be in this study because you are a healthy adult (18-45 years old) with no pre-existing conditions or medications that could put you at increased risk for seizure or other complications.

How long will the study take and how many subjects will take part?
Overall, goal is to recruit 65 participants to complete this study. Each individuals' participation will involve 4 sessions that are separated by between 1 and 4 weeks each, so your participation may range from between 4 and 16 weeks. We expect to finish enrollment and data collection for all participants in approximately 2 years.

What will I be asked to do if I take part in this study?
Before you consent to participating in this study, it is important you understand what this research study will involve. Please take the time to carefully read the following information. Ask the experimenter at any time if there is anything that is not clear or if you would like more information. Your participation is voluntary, and you may withdraw at any point.

In this study, you will be asked to participate in four sessions in which you will be asked to take part in a MRI session on one day, and three different EEG plus TMS sessions on different days.

☐ Use of Magnetic Resonance Imaging (MRI):
You will have an MRI in your first session.

- To capture images of the structure of your brain, we use Magnetic Resonance Imaging (MRI). This is a non-invasive method of imaging, which means there are no injections, drugs or radioactive tracers used while a person is in the scanner. The brain images collected so that we will have a map to help guide the orientation of TMS in a subsequent session.
- Before MRI, you will need to fill out a questionnaire about your health and handedness. You will be screened for "MR Safety" by answering questions about surgeries you had, and any medical devices or metal you may have on or in your body.
- The MRI session will last 1 hour which includes up to 30 minutes of screening, set-up, and training outside of the scanner and up to 20 minutes inside the MRI scanner.

☐ Use of Electroencephalography EEG:
During the second, third, and fourth sessions involving EEG, you will complete one or more computer-based tasks in which you will make decisions about images or text on the computer screen within a certain amount of time. You will be given the opportunity to take a break between tasks.

While you do these computerized tasks, we record electrical signals from your brain using EEG sensors placed on your scalp.

- Electroencephalography (EEG) is a non-invasive method of measuring brain activity which means there are no injections or drugs used. The EEG procedure requires putting on an "electrode cap," which looks similar to a swimmers cap. The electrodes do not deliver electrical shocks, but instead will measure brain activity. Your hair and face may get wet while you are wearing the cap. Conductive paste is applied to each sensor and your scalp may be rubbed gently with an instrument similar to a Q-tip to ensure there is good contact between your scalp and the electrode.
- The EEG paste is similar to the consistency of hair gel and can be washed out with water.

☐ Use of Transcranial Magnetic Stimulation (TMS):
During the second, third, and fourth sessions involving TMS, while you do computerized task and we record electrical signals using EEG sensors, we will also apply transcranial magnetic stimulation (TMS) before or after you complete tasks. TMS is a way of stimulating the brain, without injections, drugs or surgical procedures of any kind.

- During the course of the experiment, we may apply TMS using a hand-held device. The TMS feels like a light tapping sensation and will make a loud noise. We will require you to wear earplugs (which we will provide) and/or headphones playing white noise during the experiment in order to protect your hearing. You might feel discomfort as muscles in your scalp and/or face tense up temporarily during the experiment, or head/neck pain immediately following TMS.

How TMS works: TMS works by passing an electric current through a "TMS coil" that is held against your head. A TMS coil looks like a wand with either a circle or a figure 8 at the end of it. Inside the coil are loops of wire. When the electric current goes through the coil, it creates a magnetic field that can safely go through your skull and your brain to briefly affect the way the cells in your brain work for a short time (1 second to 1 hour depending on the kind of TMS – described in detail below). The effects can be minor, such as a brief twitch, or you may not notice them.

TMS coils are not always "on," so even if the coils are on your head, the experimenter needs to start the equipment. The procedures used in this study are described in detail below. You may or may not receive the real TMS in a given session.

Eligibility: Before the TMS procedure, you will be interviewed to see if you are eligible to participate in the study. The interview questions that determine your eligibility are chosen for both scientific and safety reasons. The interview will include some personal questions, such as questions about your health history, and any drugs or medications you might be taking. All your answers to our questions will be protected, as described in the "Confidentiality" section.

For Women: It is unknown if TMS is safe during pregnancy. If you are, or you think you might be, pregnant, you cannot take part in this study.

Location of TMS: The TMS coil will be put on your head. Before the formal study begins, a member of the research team will show you the place(s) we will put the coil. Example places are on your forehead above your eye, above your temple, or on the back of your head.

TMS Research Procedures: The TMS procedures below will be used in this study. All TMS procedures will last approximately 45 minutes out of the full 3.5-hour session. This includes time necessary to identify motor thresholds and one single train or two trains of theta-burst stimulation with a 5-20 minute break in between each train and single and paired-pulse stimulation. These stimulation protocols are described below.

☐ Motor Threshold
We will find your motor threshold (which is your baseline). This TMS procedure is used to customize the strength of stimulation specifically for you and your brain.

You will be asked to sit comfortably in the chair in the TMS testing room. Your muscle may twitch or move without you telling it to move (involuntarily) from this test. TMS feels like tapping on your head. Muscles on your eyes, head, or neck may also twitch, if the coils are on the side of your head near those muscles.

Finding your motor threshold will take about 20 minutes.

When finding your baseline, there will be occasional short, single pulses of TMS (lasting a fraction of a second) delivered through the coils while you complete the task(s). You will get no more than 1 pulse per second, and most pulses will have at least 1 second in between them.

☐ Offline Theta-burst Stimulation
You will be comfortably sitting up or reclining in the TMS chair and we will slowly stimulate your brain in one place with 50 pulses per second, in sets of 3 pulses at a time; sets will happen 5 times every second. This stimulation will last 40 seconds, and there will be two rounds of stimulation with a break in between.

TMS feels like tapping on your head. Muscles on your eyes, head, or neck may also twitch, if the coils are on the side of your head near those muscles. After the stimulation, you will be asked to do a task and then there will be a break.

This kind of TMS might change the way your brain works for up to 1 hour after the TMS ended, and you will stay in the lab during this time. If you finish the task before 1 hour has gone by, we will ask you to stay in the lab until 1 hour has passed.

☐ Single and Paired-Pulse Stimulation
We will apply single TMS pulses and two pulses in quick succession while we record EEG data. The purpose of this stimulation is to see how your brain responds to these pulses in terms of effects on brain activity as measured by EEG.

You will be asked to sit comfortably in the chair in the TMS testing room. Your muscle may twitch or move without you telling it to move (involuntarily) from this test. TMS feels like tapping on your head. Muscles on your eyes, head, or neck may also twitch, if the coils are on the side of your head near those muscles.

There will be occasional short, single pulses and paired pulses of TMS (lasting a fraction of a second) delivered through the coils while you sit still. All pulses will have at least 4 seconds in between them.

☐ Heart rate:
If we record your heart rate, we will attach three electrodes – two to your chest just below your collar bone and a third near the bottom of your rib cage. The electrodes do not deliver electrical shocks, but instead will measure heartbeats.

Today we are asking for your consent to participate in the following (please initial):

MRI _____

EEG with TMS _____

Heart Rate (ECG) _____

You may also be asked to complete questionnaires. The questionnaires may measure traits associated with mental/psychiatric conditions; however, the questionnaires will not be used as diagnostic tools. You will not be given the results of any of the questionnaires.

It should be understood that there may be certain aspects of the study session which will not be fully disclosed until after your participation is complete. Upon completion of the study session, you will be given a full debriefing describing all research procedures and contact information by the experimenter. Any questions you may have will also be addressed.

What are the risks of harm or discomforts I might experience if I take part in this study?
The possibility of a breach of confidentiality with regard any data collected from you during your participation (including EEG recordings, questionnaire responses, or your performance on the computer tasks) is minimal. To protect your confidentiality, any data we receive from you will only be labeled with a subject identification number and not your name or any other demographic information. Furthermore, any identifying information, such as your name, will be deleted permanently from files at the completion of data collection for the study.

You may read below for more details corresponding to each study procedure type:

Behavioral Tasks
The tasks involved may require some mental effort, and you may therefore experience some fatigue. For these kinds of tasks, you will receive ample time for reset periods and/or stretch breaks.

Eye-Tracking
You may experience some discomfort from a head and chin rest, but you may take breaks during the experiment to alleviate this discomfort.

Electromyography (EMG) and Electroencephalography (EEG)
There are minimal risks associated with the use of the EEG and EMG in this study. There is a small possibility that you may experience some tenderness or reddening of the skin where the electrodes are placed, as your head will be mildly scraped. This feels similar to scratching your head with your hand. You may also feel slight irritation from the gel solution, but the irritation commonly dissipates soon afterwards. The electrode cap may feel tight on your head.

Researchers will wear latex-free gloves and have received extensive procedural training to minimize the possibility of the reddening of skin while preparing participants for recording. All equipment in direct contact with you will be chemically sterilized with an FDA-approved solvent immediately after each use.

Magnetic Resonance Imaging (MRI)
There may be some discomfort from being in the MRI scanner because you will be asked to lie down and be very still for a long time. The research team will try to make you as comfortable as possible before the imaging begins. There are no known health risks associated with the magnetic field produced by the scanner in healthy adults. Exposure to high magnetic fields is associated with primary or secondary risks in certain patient populations (e.g., patients with pacemakers), therefore such patients are excluded. Subjects with aneurysm clips, neural stimulators, possible metal fragments in the eyes, cochlear implants, artificial cardiac valves, iron based facial tattoos, and body piercings that are not removable are also excluded from participation. The only other risks associated with scanning are claustrophobia while in the magnet, physical discomfort from lying still in the magnet, and the loud sound of the magnet. If you feel claustrophobic or anxiety, let the researcher know immediately. Screening interviews and the MRI screening questionnaire are used to rule out the presence of any medical or neurological problems that would cause a risk in the magnet.

Incidental findings: The MRI exam could reveal an abnormality in your brain. This finding may be distressing to you. Scans at CAHBIR are screened for abnormalities. If there is any sign of an abnormality, the scan data is reviewed by a certified neuroradiologist through a contract with University Radiology Group. The neuroradiologist provides a brief written evaluation that includes their recommendation as to whether any potential abnormality is clinically significant, and if it is, provides a recommendation for referral or further evaluation. The study PI, Dr. Westbrook, is responsible for communicating this finding to you if it is deemed clinically significant.

Transcranial Magnetic Stimulation (TMS)

- TMS carries a small risk of inducing a seizure. This is rare (estimates are 7 in 100,000 individuals). The stimulation parameters used have been chosen based on safety norms that minimize this risk. In addition, you will be screened for risk factors related to seizure, such as epilepsy, history of prior seizure or convulsions, or a family history of seizures/epilepsy. A seizure may be thought of as a convulsion where a person's body shakes. Many seizures are not like this. Some have very mild symptoms. Experiencing a seizure caused by TMS does not mean that you will have another seizure. The researcher is trained to manage the room and call for medical help in the unlikely event of a seizure.
- It is possible that you could faint during TMS. This does not happen often, but can happen if you are anxious, nervous, or have not eaten. You should immediately tell the research staff if you feel dizzy or lightheaded.

If you have the above symptoms, the TMS study procedure will be stopped. You will be monitored until you are feeling better.

- When current is passed through the TMS coil, it moves within its casing producing a loud "click." It is possible that you could experience a temporary ringing in your ears. You will wear earplugs during the TMS to reduce the noise to prevent the risk of hearing problems.

We will ask you to let us know immediately if your ear plugs loosen or fall out.

- The sensation of TMS is a tapping on the head at the site of stimulation. Depending on the site of stimulation, there can also be twitching in nearby muscles around the head, eyes and neck. The immediate effect of these sensations can range from mildly irritating to painful at high frequencies. Based on your feedback, we will adjust the stimulator output to a level that is not painful for you.
- Participants undergoing TMS sometimes experience headaches. The cause of headaches can relate to the procedure set-up (for example, neck tension) as much as the TMS stimulation itself. Headaches usually start after the session (about 20 mins. to 3 hours after TMS). If you feel a headache coming on, we will stop the session and allow you to cope with the headache in your preferred way.
- There is a risk of fatigue. We will give you regular breaks through the procedure.
- TMS for research is regulated by the FDA. Although TMS is an FDA regulated device, it is being used for research purposes and is considered an investigational device. There may be complications that are not yet known.

In order to minimize these risks, participants are in constant contact with an experimenter while seated in the recording room and while connected to the recording equipment. Experimenters will have received extensive procedural training to minimize risks.

Also, prior to the experiment, we will ask you to fill out a questionnaire that will allow us to make sure that (1) our study participant group is representative of the greater population, and (2) that TMS is safe for you. Some of the questions pertain to gender and ethnicity. These questions are included so that we can

properly interpret our study results at the population level, and to ensure that we are assessing a fair and representative group from the greater population. Other questions pertain to overall health, mental health status, medications and pregnancy. These questions are for your safety, and your answers will be subsequently anonymized and protected- we will not share this information with anyone other than necessary lab personnel. You may refuse to answer or skip any questions we ask.

You are free to stop at any point during the experiment, for any reason whatsoever. In the event of study-related injury, illness or distress, please contact the study PI, Andrew Westbrook at andrew.westbrook@rutgers.edu.

Reproductive Risks of Harm
There is no known risk of study procedures to fetuses or pregnant mothers. Nevertheless, out of extra caution, we are excluding any participants who are pregnant or potentially pregnant.

Are there any benefits to me if I choose to take part in this study?
You will not receive any direct benefit from taking part in this study.

What are my alternatives if I do not want to take part in this study?
Your alternative is not to take part in this study.

How will I know if new information is learned that may affect whether I am willing to stay in the study?
During the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will I receive the results of the research?
In general, we will not give you any individual results from the study. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence. For example, we might inform you if there are any unusual findings on an MRI report that we think you should discuss with your doctor. In that case, we will notify you by email after analysis of research data are concluded, which may take several weeks.

Will there be any cost to me to take part in this study?
There is no cost to you to take part in this study.

Will I be paid to take part in this study?
You will receive $ 20.00 per hour for taking part in this study, at the end of every session, based on the duration of each session. Payment will be prorated to the nearest 15 minutes. Also, you will be eligible for bonuses during each of the TMS-EEG sessions up to $4.00. So, if a session takes 3.5 hours, and you get a $3.00 bonus, you will be paid $73.00 at the end of that session.

How will information about me be kept private or confidential?
All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. We will store all study data, MR images, and EEG data on password-protected computers at Rutgers. Only study personnel will have access to these data. Also, these data will only be linked to a random participant ID number, and not to any identifying information.

The research team may use or share your information collected or created for this study with the following people and institutions:
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- The Food and Drug Administration

- The National Institutes of Health

A description of this Basic Experimental Study Involving Humans 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.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

What will happen to my information—data, recordings and/or images—collected for this research after the study is over?

- After information that could identify you has been removed, de-identified information collected for this research may be used for other research we conduct without obtaining additional informed consent from you.

What will happen if I am injured during this study?
Subjects in this study will be exposed to certain risks of personal injury as described above in the section entitled "*What are the risks of harm or discomforts I might experience if I take part in this study?*". In addition, it is possible that during the course of this study, new adverse effects of transcranial magnetic stimulation that result in personal injury may be discovered. The University will make appropriate referrals for medical treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or TRICARE/CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University. However, by signing this form, you are not giving up any legal rights to seek further compensation.

What will happen if I do not wish to take part in the study or if I later decide not to stay in the study?
It is your choice whether to take part in the research. You may choose to take part, not to take part or you may change your mind and withdraw from the study at any time. If you do not want to enter the study or decide to stop taking part, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

Any data that has already been collected cannot be withdrawn because there may not be any identifiers to link the data with you. We are required by the Food and Drug Administration to continue to report anything that is related to the safety of the devices used in the research.

Who can I contact if I have questions?
If you have questions, concerns or complaints about the research, wish more information or if you feel you may have suffered a research related injury, you can contact the Principal Investigator: Dr. Andrew Westbrook, Department of Psychiatry at (919) 360-5399.

If you have questions, concerns, problems, information or input about the research or would like to know your rights as a research subject, you can contact the Rutgers IRB or the Rutgers Human Subjects Protection Program via phone at (973) 972-3608 or (732) 235-2866 or (732) 235-9806 OR via email irboffice@research.rutgers.edu, or you can write us at 335 George Street, Liberty Plaza Suite 3200, New Brunswick, NJ 08901.

AGREEMENT TO TAKE PART IN RESEARCH

Subject Consent:

I have read this entire consent form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form and this study have been answered. I agree to take part in this study.

Subject Name (Print):_____

Subject Signature:_____ Date:_____

Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed all the important details about the study including all of the information contained in this consent form.

Investigator/Person Obtaining Consent (Print):_____

Signature:_____ Date: _____