Causal role of theta and alpha oscillations in output-gating

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants
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IRB Study # 21-0248
Title of Study: Causal role of theta and alpha oscillations in output-gating
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CONCISE SUMMARY

This study was designed to better understand the role of electrical brain activity in the control of memory. The current study has no immediate benefit to the participant. However, the results of this study may be used to develop novel tools for the treatment of psychiatric mood-disorders that involve a detriment in cognitive control.

The study requires approximately 15 hours of participation across five sessions. In the first session, you will do a computerized task and complete questionnaires about your mental health and personality. Based on your task performance, you may advance to the next stage of the experiment. In the next sessions, your brain activity will be recorded using electroencephalography (EEG), sensors on your scalp, and with magnetic resonance imaging (MRI). Finally, you will receive transcranial magnetic stimulation (TMS) during performance of a memory task.

There are no known health risks associated with EEG or MRI. For TMS, there is a rare risk of seizure and hearing loss. To reduce these risks, the TMS is calibrated to the sensitivity of your brain and you have been screened to reduce risk. In addition, you will wear ear plugs for hearing protection. Known side effects of TMS are headache, dizziness, muscle tightness or twitching, and the small space for the MRI could make you feel claustrophobic.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people

in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Healthy brain function includes rhythmic activity that is associated with cognitive functions. Non-invasive brain stimulation by magnetic fields applied to the scalp is an experimental technique to manipulate this activity. Transcranial magnetic stimulation (TMS) has been used without reports of any serious side effects. The purpose of this research is to investigate the effects of TMS on brain activity and behavior.

Are there any reasons you should not be in this study?

You should not be in this study if:

- You have been diagnosed with ADHD (currently under treatment)
- You have been diagnosed with neurological disorders and conditions, including, but not limited to:
    - History of epilepsy
    - Seizures (except childhood febrile seizures and ECT-induced seizures)
    - Dementia
    - History of stroke
    - Parkinson's disease
    - Multiple sclerosis
    - Cerebral aneurysm
    - Brain tumors
- You have been diagnosed with medical or neurological illness or are current receiving treatment for a medical disorder that could interfere with study participation (e.g., unstable cardiac disease, malignancy)
- You had any prior brain surgery
- You have any brain devices/implants, including cochlear implants, aneurysm clips, cardiac pacemaker, or other implanted electronic devices
- You have a history of or current traumatic brain injury
- You are pregnant or breast feeding (if you are female)
- You or your family members have a history of epilepsy
- You have been diagnosed with mental/psychiatric disorder (e.g., anxiety, major depressive disorder, schizophrenia, etc.)

How many people will take part in this study?
Approximately 200 people will take part in this study.

How long will your part in this study last?
This study will last approximately a total of 15 hours spread across 5 sessions. There will be no follow-up communication after the study is complete.

What will happen if you take part in the study?
Session 1 (Screening): In the first session, a pregnancy screening (if you are a female) will be administered. Then you will perform the cognitive task as practice from which performance will be assessed.

Session 2 (Baseline): You will be asked to fill out a series of questionnaires pertaining to handedness, affect, behavioral traits and personality. These may be completed remotely via an online web link before the session, or during the session upon arrival. You may refuse to answer any question for any reason. Next, the EEG net will be applied. You will be asked to relax with eyes open and eyes closed while EEG will be collected simultaneously. The muscle activity in your hand will be recorded with small electrodes. The electroencephalogram (EEG) net consists of 128 small (~20 mm diameter, ~15 mm deep) cups connected to each other through elastic netting. The EEG net will be attached to your head using elastic straps and is generally adjusted to be comfortable. We will use conductive electrode gel to fill the cups. The EEG net records your brain activity. You will then perform the cognitive task. Following the end of the session, electrodes and net will be removed, and you will be able to wash your hair and face.

Session 3: You will go to the Biomedical Research Imaging Center (BRIC) in Marsico Hall for magnetic resonance imaging. An anatomical image of your brain will be collected and you will be asked to stare at a point on a computer screen while your resting brain activity is collected. For this session, you will need to change into a medical gown and the session will be facilitated by the personnel at the BRIC.

Sessions 4 and 5 (Stimulation 1 and 2): The TMS coil will be held to your scalp during the session, and single pulse of TMS will be delivered to your motor cortex to generate muscle twitches in your hand muscle. This is used to calibrate the level of stimulation that you will receive. The EEG net will be applied. You will be asked to relax with eyes open and eyes closed while electrical brain activity is recorded. Next, transcranial magnetic stimulation (TMS) coil(s) will be held to your scalp during the session. You will then perform the cognitive task while receiving trains of TMS during performance of the cognitive task. Following the end of the session, electrodes and net will be removed, and you will be able to wash your hair and face.

Memory Task: You will see colored squares appear on the right and left side of the screen. Sometimes an arrow will point to either one or both sides of the screen, indicating which colors to remember. You will be presented with new colors indicate by pressing a button the initial colors you saw. You will have breaks to rest throughout the task as needed.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

While interventions that use TMS to treat depression do exist, these effects are dependent on the location and type of stimulation. You will not be receiving stimulation intended to create a change in mood. However, this is a theoretical and rare side effect.

What are the possible risks or discomforts involved from being in this study?

Transcranial magnetic stimulation (the application of a magnetic field to a focal brain region) has been used without reports of any serious side-effects. Some subjects report muscle twitching during stimulation and sometimes a headache, but no other side effects have been noted. The transcranial stimulator used in this was cleared by UNC Hospital Medical Engineering, the in-house engineering team of UNC hospitals that test the safety of medical devices. This TMS device has been cleared by the FDA for some indications, such as Major Depressive Disorder in some people, but it has not been evaluated by the FDA for this study. During the study, we will ask about your comfort, and the study will immediately be stopped if you are experiencing discomfort.

In theory, there is a possibility that application of magnetic fields could induce a seizure. However, this has never been reported as occurring in general. In the unlikely event of this occurring, trained medical professionals are on-site to respond. To reduce this risk, the TMS is calibrated to the sensitivity of your brain and you have been screened to reduce risk. In addition, there is a rare and theoretical risk that TMS could lead to hearing loss. In addition, you will wear ear plug for hearing protection. Known side effects of TMS are headache, dizziness, and muscle tightness or twitching. For the MRI, you will be placed in a small space and might feel claustrophobic, but you will be able to signal to the experimenter to be removed from the MRI in this scenario.

There are no known risks associated with the EEG. If you have sensitive skin, then there is a chance that the application of the EEG net or the movement of the TMS coil on your scalp may irritate your skin. The gel used for EEG is composed of water and salt, so there is no chemical agent that could lead to irritation. The TMS coil is placed on the scalp and held in place by an experimenter with assistance from an adjustable holder.

As with all research, there is the possibility for a breach of confidentiality. This will be minimized by only identifying your data with a number. The only code linking your identity and that number will be kept in a locked office.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study. The pregnancy test will be provided to you. On subsequent sessions, female participants will be asked if it is possible that they may have become pregnant since the previous session. If

the participant responds yes, or is unsure, then a pregnancy test will be administered. While there is no known risk to a fetus from transcranial magnetic stimulation, there is no study to our knowledge that has investigated possible negative effects. As such, participants that are pregnant will be excluded from participation.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

The imaging we are using in this research study is not the same quality as imaging that you may have as part of your health care. The images will not be reviewed by a doctor who normally reads such images (such as a radiologist). As a result, you may not be informed of any unexpected findings. The results will not be placed in your medical record. Occasionally the technologist or principal investigator may notice something abnormal on the imaging. If this does occur, the images will be reviewed by a qualified doctor to determine if there is anything of clinical importance. If something is found to be important then you, and/or your primary care provider will be notified. Any further follow up and costs associated with the incidental finding will be your responsibility. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate).

Do you wish to be informed in case of clinical/relevant unexpected findings? Please initial in the box below if you do not wish to be notified of clinical/relevant unexpected findings. If you do not initial in the box, you will be notified of any findings.

_____ I do not wish to be notified.

How will information about you be protected?

Your name will be recorded only in the master list and not on any data collected. Data will only be identified by a code number. The master list will contain the key connecting your name and code number and will be kept in a locked cabinet, accessible only by research personnel. All data will be stored and analyzed on password protected computers, also only accessible by research personnel. After completion of the study, this list will be destroyed and there will be no way to identify the data as yours.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This

is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you 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 will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal

Will you receive anything for being in this study?
You will be receiving $170 for taking part in this study. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

After the first session you will receive $20. After the second session, you will receive $30. After the third session, you will receive $20. After the fourth session, you will receive $40. After the fifth session, you will receive $60.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you are a UNC student?

You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?

Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?
This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form. A description of this clinical trial will be available on www.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.

National Institute of Mental Health Data Archive (NDA)

Data from this study will be submitted to the National Institute of Mental Health Data Archive (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.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you

would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent