Permission to Take Part in a Human Research Study
Do not sign this consent if today’s date is later than the stated expiration date above.

Title of Research Study: Functional MRI Study of Transcranial Electrical Stimulation in Chronic Tinnitus

Investigator: Amber M. Leaver, Ph.D.

Supported By: This research is supported by the National Institutes of Health.

Key Information:
The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?
We are asking you to take part in this research study because you have chronic tinnitus, and because you are interested in volunteering for our single-visit study.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?
The purpose of this research study is to understand how a kind of neuromodulation, called transcranial electrical stimulation (tES), affects brain function.

tES delivers low electrical current to the head, and is described as a “neuromodulation” or “neurostimulation” technique. Neuromodulation methods like tES have shown promise in improving performance on tests of thinking and sensory perception (like vision or hearing), as well as treating some brain disorders. However, it is unclear exactly how tES changes the brain. To better understand the effects of tES, we will use MRI (a type of brain scan) to measure brain function during tES in people with chronic tinnitus (a chronic ringing or buzzing “in the ear”).

There are no potential benefits to you or others should you choose to participate in this research study.

The use of tES and MRI in this research study is for investigational purposes only. The USFDA does not regulate and has not approved tES for use in research studies.

How long will the research last and what will I need to do?
We expect that you will be in this research study for 4-6 weeks. During this time, you will make one study visit to Northwestern Chicago Campus. This study visit will last five hours.

During the first study visit, you will be asked to fill out questionnaires asking about your medical history, complete simple tests of thinking and sensory perception (like vision and hearing), and have a brain scan (MRI).
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More detailed information about the timing and nature of study procedures can be found under the section What happens if I say “Yes, I want to be in this research”?

Is there any way being in this study could be bad for me?
MRI and tES may be uncomfortable. During tES, you may feel tingling or slight discomfort under the electrodes. During MRI, you will lay on your back in an enclosed space (the MRI scanner) and be exposed to loud noise (with hearing protection) for one hour. Filling out questionnaires regarding your medical history may cause emotional distress or embarrassment.

More detailed information about the risks of this study can be found under “Is there any way being in this study could be bad for me? (Detailed Risks)”

Will being in this study help me any way?
We cannot promise any benefits to you or others from your taking part in this research. Possible benefits to others include contributing to knowledge that may one day improve tES as a therapy for brain conditions.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You decide whether or not to participate. If you choose not to participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Who can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at (312) 694-2966 or inmri@northwestern.edu.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:
- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?
We expect about 35 people here will be in this research study out of 35 people in the entire study nationally.

What happens if I say “Yes, I want to be in this research”?
You will participate in one study visit at the Center for Translational Imaging at Northwestern University, located at the Olson Pavilion, 710 N Fairbanks Ct. During this study visit, you will
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interact with trained study staff, as well as trained MRI and administrative staff at the CTI. During the visit, you will also have a hearing test at Northwestern’s Audiology Clinic. You will also rate your tinnitus symptoms at home. The schedule of study procedures is described below.

Intake will last approximately 30 minutes and will be held via telephone or secure video conference. During this time, you will:
- Review and sign this consent form
- Review all study procedures with study staff, and ask any questions you have about study procedures at any time
- Complete questionnaires about your medical history on the following topics:
  - MRI safety
  - tES safety
  - Experiences and conditions that can affect brain function, including neurodevelopmental disorders, neurological injury and disorders, psychiatric and/or mood disorders, and overall health

For two weeks following Intake, you will rate your tinnitus symptoms at home. At the end of each week, you will report these ratings to study staff online or by phone. This will take about 5 minutes.

The in-person study visit will last approximately 5 hours. During this visit, you will:
- Complete a brief hearing test at Northwestern’s Audiology Clinic
- If you choose, you may complete a tES demonstration, where tES will be applied briefly to your arm as a demonstration of what to expect during tES-MRI and tES sessions
- Have tES electrodes covered in water-soluble gel placed on your head
- Have one MRI session lasting one hour. During this MRI session, tES will be applied for 5-10 minutes and changes in brain function will be recorded with functional MRI during two scans:
  - During one MRI scan, “active” tES will be applied, where the tES device will be turned on and will stay on for 5-10 minutes.
  - During one MRI scan, “sham” tES will be applied, where the tES device will be turned on for only approximately 60 seconds.
  “Sham” tES is meant to cause the same skin sensations as active tES, but is unlikely to change symptoms or brain activity (for example like a “placebo” or “sugar pill”). The order of these two runs will be chosen by chance, like flipping a coin. Neither you or study staff will choose the order. You will receive both active and sham tES scans during this MRI session. You will not be told whether active or sham tES will come first; however, study staff will know.
- Complete brief tests of perception and cognition at a computer

After this study visit, you will be asked to complete brief ratings of your tinnitus symptoms while at home. This will take about 5 minutes. At the end of each week, you will report these ratings to study staff online or by phone. These ratings will occur each week for 2 weeks after the study visit and once 30 days after the study visit.

Two devices are used during this study. Both are for experimental (investigational) use only in this study, and include:
- MRI scanner (manufactured by Siemens)
- tES device (manufactured by Soterix Medical)
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Please note that you will be asked to indicate at the end of this consent form whether you are interested in being contacted for future studies like this one. Your answer will not affect your ability to participate in this current study.

What are my responsibilities if I take part in this research?
If you take part in this research, you will be responsible to: arrive to study visits on time and follow study instructions.

What happens if I say “Yes”, but I change my mind later?
You can leave the research at any time; it will not be held against you. If you decide to leave the research, contact the investigator at (312) 694-2966 or inmri@northwestern.edu so that the investigator can cancel any remaining study visits.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment, your class standing (for students enrolled in a class at NU), or your present or future employment (for employees at NU or its affiliates).

Detailed Risks: Is there any way being in this study could be bad for me?
This research may hurt you in the following ways:

Physical risks
• tES might be uncomfortable. Potential risks and discomforts associated with tES include tingling, mild irritation, or a light itching sensation under the electrodes. This is a natural, non-painful sensation associated with the passing of electrical current through the skin, sometimes likened the flow of water on the skin. You may also experience redness under tES electrodes. For many people, these sensations lessen or disappear soon after the start of stimulation, and are rarely reported as unpleasant or painful. However, if you become uncomfortable, please inform the staff and tES can be terminated immediately.
  Alert study staff immediately if:
   o you feel uncomfortable tingling after the first 30-60 seconds of tES and wish to stop
   o you feel heating or burning under tES electrodes during tES-MRI at any time
   o you have skin condition, injury, or sensitivity on your scalp
Rarely, people have reported headache, fatigue, or trouble sleeping after tES. However, these were reported after both active and sham tES, and so it is unclear whether headache, fatigue, or trouble sleeping was related to tES in these studies. tES uses a low level of electrical current, and has been used with no significant injuries or other ill effects in clinical research laboratories worldwide for the last 30-40 years in healthy adults and for the treatment of tinnitus, depression, anxiety, chronic pain, and stroke. Established safety procedures for tES will be strictly followed in this study.
• MRI scans might be unsafe if you have metal or implants in your body. The MRI scanner uses magnetic fields to take pictures, and this can attract and influence certain metals. Therefore, people with metal in their body that cannot be removed (like pacemakers, infusion pumps, aneurysm clips, metal prostheses, metal joints, rods, plates, or other metallic objects) will be excluded from this study. You must tell study staff if you have any of these types of devices in your body. The metal used in dental fillings is less susceptible and is therefore

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allowed. You will be asked to change into a hospital gown and/or hospital “scrub” pants prior to your MRI scan.

- **MRI and pregnancy.** MRI is not known to pose risks to a pregnancy or fetus. However, having an MRI while pregnant may hurt a pregnancy or fetus in ways that are unknown. possible that there are risks about which the investigators are unaware or cannot foresee. Because of this, pregnant women and women who are trying to become pregnant are excluded from this study. If you are unsure whether you are pregnant, you should not volunteer for this study.

- **MRI is loud.** The sound of the MRI scanner can also be quite loud, and prolonged exposure has the potential to damage your hearing. So, you will be given special ear plugs and/or headphones to minimize this noise. For some people, certain noises can make their tinnitus worse. If the MRI scanner noise makes your tinnitus worse, we can stop the MRI at any time.

- **MRI scans might be uncomfortable.** Although some people find MRI to be a comfortable experience, others might become uncomfortable. You will be asked to lay on your back for the duration of the scan, and special padding or foam might be used to help keep your head still. Some people may feel claustrophobia or anxiety from being a tight, enclosed space. If you become uncomfortable for any reason, please inform the staff and the MRI can be terminated immediately.

- **Research MRI is not diagnostic.** The brain images obtained from this research cannot be used to screen for or diagnose medically significant brain abnormalities. Because these brain scans are not designed to detect all possible brain abnormalities, you should not assume, based on this research, that the scan of your brain was normal if this ever becomes an issue in your future medical care. However, if the investigators do identify an abnormality in your MRI that may be of potential medical significance, they will discuss this with you and suggest options for medical follow-up such as you talking with or seeing your regular medical doctor.

- **Paying attention to your tinnitus symptoms may worsen tinnitus.** During this study, you will be asked to rate your tinnitus symptoms, which may make you more aware of your tinnitus. For some people, being more aware of tinnitus may make it more intrusive or annoying. Remember that you can stop the study at any time.

**Psychological risks**

- **Completing questionnaires or perceptual/cognitive tests might be boring or uncomfortable.** During these tests, you will be sitting at a desk or table writing on paper or typing at a computer. Some people might find this part of the study boring or tedious, and others might be uncomfortable answering questions about their thoughts, feelings, or medical history. Otherwise, we do not expect these questionnaires or tests to pose any significant risks or discomforts.

- **Study visits may be cancelled or rescheduled in cases of unexpected staff illness, equipment maintenance, or other reasons.** Though not anticipated, study staff may need to cancel or reschedule your study visits if unforeseen circumstances interfere with study procedures, for example, should staff become ill or if study equipment is unavailable due to unscheduled maintenance. In these circumstances, you will be notified immediately, and we will make every effort to reschedule your study visit(s). Should this happen, this may cause distress or inconvenience.

**Privacy/Confidentiality risks**

- **Your privacy and confidentiality.** This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: “What happens to the information collected for the research?"
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**What do I need to know about reproductive health and/or sexual activity if I am in this study?**
The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You should not be or become pregnant while on this research study.

If you are unsure of your pregnancy status, you should not volunteer for this study.

**Will it cost me anything to participate in this research study?**
Taking part in this research study will not lead to any costs to you.

**Will being in this study help me in any way?**
There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include: contributing to knowledge that may one day improve tES as a therapy for brain conditions.

**What happens to the information collected for the research?**
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution, the sponsor.

Study data will be retained after the study for future research. These data will be de-identified, meaning that they will not be linked to any information that could identify you, like your name or phone number. These data will be stored in secure, password-protected computers located in the PI's laboratory in a secure suite only accessible by approved study staff. The data will be retained indefinitely for use in future research.

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

**Data Sharing**
De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

**Can I be removed from the research without my OK?**
The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include arriving late for study visits or not following study instructions.

**What else do I need to know?**
If you become ill or get injured as a result of this study (devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.
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The researchers will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study, we will pay you $100 for your time and effort at the end of the study. Should you choose to withdraw from the study, or if study staff should withdraw you from the study, before the study is complete, you will be paid $15 per hour you completed. You will also receive compensation for parking for each study visit, in the form of parking validation.

The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Name, address, phone number, and date of birth to be used to schedule hearing tests at Northwestern’s Audiology Clinic for this research study.
- Medical history and surgical records relevant to MRI safety
- Hearing tests

During this study, you may be coming to a Northwestern Memorial Healthcare corporation entity (for example, Northwestern Memorial Hospital, Prentice Women’s Hospital) for research appointments or to get clinical services, such as lab tests, needed for the study. When that happens, you will be scheduled for these services through the NMHC computer system. When a clinical exam or lab is done by NMHC or one of its employees for the purpose of this research study, that information will be kept in both NMHC’s clinical records and in the study records.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy.
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[except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator’s office].

The following entities may receive your health information:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board.
- Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children’s Hospital of Chicago (Lurie Children’s). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire at the end of the study.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

PI’s Name: Amber Leaver, PhD
Institution: Northwestern University
Department: Radiology
Address: 737 N Michigan Ave Ste 1600, Chicago IL 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

Optional Elements:
The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

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The researcher may contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

______________________________          __________________
Signature of Participant                                                               Date

______________________________
Printed Name of Participant

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____________________________________________            __________________
Signature of Person Obtaining Consent                                     Date

______________________________________________________
Printed Name of Person Obtaining Consent