

**Safety, tolerability and neurophysiological response of transauricular
vagus nerve stimulation in children without brain injury**

Principal Investigator: Alyssa Smith, MD

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INFORMED CONSENT DOCUMENT

Project Title: Safety, tolerability and neurophysiological response of transauricular vagus nerve stimulation in children without brain injury

Principal Investigator: Alyssa Smith, MD

Research Team Contact: Angela Sellitto (314) 273-2622

If you are the parent/guardian providing parental permission the word “you” refers to your child.

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant.

KEY INFORMATION

The first section of this document contains some key points that the research team thought you would find important. The research study is described in more detail after this section.

This is a research study conducted by Dr. Alyssa Smith having to do with your physical response to a small electrode attached to the ear which will stimulate a nerve in the ear (vagus nerve). You should carefully consider the information in this consent document and discuss it with the research team. Be sure you understand why you might want to participate, or why you might not want to participate. You may choose to participate or not. Before you decide whether to be in this study, you may wish to consider other options that are available to you. Instead of being in this study, you could receive the regular standard of care for spell characterization alone.

If you agree and sign this consent, you will be volunteering to participate in the research study. All of the information below will be explained and is listed in more detail in the consent document below. The research team must give you a copy of this signed consent document.

How will this study affect me?

- The purpose of this study is to evaluate the safety, tolerability, and physiological response of transauricular vagus nerve stimulation in children undergoing EEG and to further help determine the mechanism of vagus nerve stimulation (VNS) in the brain.
- As a voluntary participant, you will be asked to spend up to 90 minutes during your inpatient electroencephalography (EEG) session.
- You were selected because you are being admitted for spell characterization on the Epilepsy Monitoring Unit at St. Louis Children’s Hospital.
- You will be in this study for up to 1 day, including the 24-hour period that you are admitted on the Epilepsy Monitoring Unit.
- The main risks to you are skin irritation/redness at the site of stimulation. More detail about risks is provided below.

- You will not benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because it will help us understand how transauricular vagus nerve stimulation affects children.
- You will be paid \$100 for participating in this study. If you withdraw from the study, the research team may continue to use information already collected about you in this study.

The rest of this document provides more details about the study.

WHAT IS THE PURPOSE OF THIS STUDY?

Electroencephalography (EEG) may be a marker of VNS neuromodulation. To inform future use of taVNS in children with neurologic conditions we are studying how taVNS affects EEG after a short session in healthy children. VNS is thought to improve the rewiring of the brain after injury however it is unknown how to measure this function. EEG may be a marker that will allow us to evaluate VNS activity.

Transcutaneous auricular vagus nerve stimulation (taVNS) is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

WHAT WILL HAPPEN DURING THIS STUDY?

The device we use in this study is non-invasive, meaning that it does not require surgery. It has small electrodes that clip /or get taped to your ear, and wires that are connected to a remote controller box where your care provider can adjust the level of electrical impulse that you receive during the treatment. You might feel tingling or warmth while the device is on, or you may feel nothing. You will receive electrical stimulation for 30 minutes.

The procedure will take place during your admission to St. Louis Children's Hospital.

You will be asked to answer some questions to better understand the effect of taVNS stimulation. We will obtain measurements before, during and after taVNS stimulation. The participant is free to skip any questions that they would prefer not to answer.

The results of this study is not clinically relevant to your care during this admission. We do not have plans to give results to participants for this reason.

Your participation will end after the treatment and assessment is complete. There are no follow up visits after participation.

The data from your inpatient electroencephalography (EEG) will be collected from your medical record and used as part of this study. We will have access to this data until the study has ended.

Will you save my research information to use in future research studies?

The data we are obtaining in this study may be made available for studies going on right now as well as studies that are conducted in the future. These studies may be done by researchers at Washington University, other research centers and institutions, or private companies involved in research.

We may also share your research data with large data repositories (a repository is a database of information) for use by others, such as the research community, institutions, private companies and the general public. If your individual research data is placed in one of these repositories, your name and other identifying information will be removed. All reasonable precautions will be taken to protect your privacy and confidentiality. Necessary approvals will be obtained to use the data. Certain summary information may be available to the general public.

These future studies may provide additional information that will be helpful in understanding how transauricular vagus nerve stimulation affects children, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. Should this occur, there are no plans to provide financial compensation to you. There are no plans to provide financial compensation to you should use of your data occur. It is unlikely that what we learn from these studies will have a direct benefit to you. By allowing us to use your data you give up any property rights you may have in the data. We will protect the confidentiality of your information to the extent possible.

If you change your mind and do not want us to store and use your data for future research you should contact the research team member identified at the top of this document. The data will no longer be used for research purposes. However, if some research with your data has already been completed, the information from that research may still be used. Also, if the data has been shared with other researchers it might not be possible to withdraw the data to the extent it has been shared.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at Washington University.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Less Likely / Less Common

Mild

- Skin irritation/redness at the site of stimulation
- Cough/hoarseness

Rare

Serious

- Bradycardia (slow heart rate)

Mild

- Discomfort or pain during the stimulation period

Risk of Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled “*How will you keep my information confidential?*” for more information.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study.

You will be asked to provide your social security number (SSN). You may also need to provide your address if a check will be mailed to you. It should take approximately 2-3 weeks to receive your payment.

WHO IS FUNDING THIS STUDY?

NIH (National Institutes of Health) is funding this research study. This means that Washington University is receiving payments from NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIH for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at 314-454-6120 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration

- NIH
- The NIH may also inspect any part of your medical record for the purposes of auditing the conduct of the study.
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will store all paper questionnaires and paper records in a locked cabinet inside a locked office. Data entry will be done on password-protected computers and electronic data will be stored on secure servers.

A description of this clinical trial will be available on <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.

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others;
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

This Certificate may not be effective for information held in foreign countries.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, “How will you keep my information confidential?”

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University’s Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
 - To revoke your authorization, complete the withdrawal letter found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.
 - **If you revoke your authorization:**
 - The research team may only use and share information already collected for the study.
 - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant’s withdrawal from the research study or for safety reasons.
 - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found in the Participant section of the Human Research Protection Office website at hrpo.wustl.edu.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because it is considered unsafe for you to continue in the study or the study has ended.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: **Angela Sellitto (314) 273-2622**. If you experience a research-related injury, please contact: **Angela Sellitto (314) 273-2622**.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.

- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 08/13/24.

(Signature of Participant)

(Date)

(Participant's name – printed)

Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 08/13/24.

(Child's name – printed)

(Signature of Parent/Guardian)

(Date)

(Name of Parent/Guardian- printed)

(Relationship to participant – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

(Signature of Person who Obtained Consent)

(Date)

(Name of Person who Obtained Consent - printed)