Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) for the treatment of anxiety comorbid with autism spectrum disorder (ASD)

If participants include those under 18 years of age: 1) The subject's parent or legal guardian will be present when the informed consent form is provided. 2) The subject will be able to participate only if the parent or legal guardian provides permission and the adolescent provides his/her assent. 3) In statements below, the word "you" refers to your child or adolescent who is being asked to participate in the study.

SUMMARY

You are being asked to volunteer for a research study. Research studies are voluntary and include only people who choose to take part. Your participation is entirely voluntary. This is a research study to find out if mental health symptoms in patients with Autism Spectrum Disorder are affected by stimulation to the ear performed at home.

If you agree to participate, you will receive an ear stimulation device and, with the help of your parents, will performed ear stimulation daily at home. Ear stimulation will involve your parent applying small electrodes to your outer ear and giving small amounts of electrical stimulation that may cause you to feel a “tickling” sensation on your ear. Each treatment will last up to 30 minutes and there will be a break of at least 30 minutes in between treatments. The study team will ask you to complete a group of questionnaires at the beginning and end of the study, along with one test that asks you to think about other people’s emotions. In addition, there are some questionnaires that will be completed 2 weeks into the study, as well as the end of the study once you are done receiving ear stimulation. The questionnaires will ask questions about mental health symptoms that you may or may not be experiencing, including questions about your mood, anxiety, and sleep. The ear stimulation treatments will not interfere with the care you are receiving from the medical team.

There are risks to the technique being used in this study. Risks include: ear stimulation may result in redness and some discomfort, such as a “tickle” or “pricking” sensation. It is possible ear stimulation will not have any effect on the mental health symptoms you are currently experiencing, but researchers hope to learn more about the effects ear stimulation has on these symptoms.

If you are interested in learning more about this study, please continue reading below.

A. PURPOSE OF THE RESEARCH

The purpose of this study involves evaluation of the safety and efficacy of at-home ear stimulation in patients with Autism Spectrum Disorder (ASD) who also have anxiety. The type of ear stimulation used in this study is known as transcutaneous auricular vagus nerve stimulation (taVNS). taVNS is an easy way to study the effects of non-invasively stimulating the vagus nerve (i.e., delivering stimulation via small electrodes on the outer portion of the ear). The goal is to determine if ear stimulation can be safely given to patients with ASD at home, and if it helps improve any mental health symptoms. You are being asked to volunteer because of you have been diagnosed with ASD, have anxiety, and have expressed interest in participating.

This research involves an investigational treatment which is not currently U.S. Food and Drug Administration (FDA) approved and has not yet been approved for the use in children. The device being used to deliver ear stimulation is called the **Spark Sparrow Ascent taVNS System**, which is an FDA cleared medical device. FDA approval means that a device has been determined to have benefits that outweigh the risks for the intended use (intended for treatment). FDA clearance requires a manufacturer to demonstrate that their product is substantially equivalent to another (similar) legally marketed device (not intended for treatment), meaning that the device meets safety criteria determined by the FDA but is not currently approved as a treatment.

The study will be done mostly at your home, with occasional visits to the Neuro-X lab at MUSC. Approximately 10 people will take part in this study. The investigator in charge of this study at MUSC is Stewart Cox, MD, PhD.

B. PROCEDURES

If you agree to be in this study, the following will happen:

1. If you are a female and able to bear children, you will be asked to take a urine pregnancy test, because the risks of ear stimulation to a fetus are currently unknown. This test will be provided to you at no cost. Should the test present a positive result, you will no longer be eligible to participate in the study.

2. You will be asked to complete a set of questionnaires and one behavioral test prior to receiving any ear stimulation. The questions on these forms will ask you about certain mental health symptoms that you may or may not be experiencing currently. You will be asked to complete the same set of questionnaires once you have completed the study. The behavioral test asks you to look at pictures of people's faces and to think about the emotions the individuals may be feeling, and again you will be asked to repeat this test at the end of the trial.

3. Ear stimulation will take place mostly at your home. First, you and your parent will participate in a training session in the Neuro-X lab on the MUSC campus to see how it feels, how to set it up, and, with the help of the research team, to calculate your dose you will receive at home. While we practice together, the study team members will be monitoring your response to treatment, including heart rate and blood pressure, if you have any questions or are experiencing any side effects. After the training session, you will then take the device home where you, with the help of your parents or guardian, will complete 4 total weeks of stimulation at home, up to two times a day for 30 minutes per session.

4. At home and with the help of your parent or legal guardian, electrodes will be attached to your ear with a small sticker with the help of your parents, which will deliver mild stimulation. These electrodes will be plugged into the Spark Sparrow Ascent taVNS System, which is a device that delivers transcutaneous auricular vagus nerve stimulation, or taVNS. This device will be shown to you and your parent or legal guardian, and both of you will be taught how to adjust settings and start a session. You will be asked to remain sitting during while receiving ear stimulation so you can be monitored by a guardian as it occurs. You will receive twice daily stimulation for 4 weeks. Stimulation will be delivered to your tragus (the small cartilage knob before the ear canal) for up to 30 minutes per treatment session. At each session, you and your parents can work together to make sure the stickers are placed correctly, and they will monitor for any side effects, but these are very rare. During the study, the team will check in with you regularly via phone call or virtually about how you are tolerating stimulation, and if you are experiencing any discomfort, you will be given the option to stop stimulation. We will also have you come in after 2 weeks so we can talk to you about how the study has been so far. At that point, you may choose to continue up to the maximum number of sessions stated above (twice daily for 4 weeks), but you may choose not to continue with treatments at any time and for any reason. You can also choose to stop any session at any time if you are uncomfortable.

5. You can discontinue your participation of this study at any point without consequence. The study procedures are estimated to last 4 weeks. If at any time there are questions or concerns, you can contact our lab team to help.

C. DURATION

In this study, you will receive a total of 4 weeks of ear stimulation. You will receive up to two treatments a day for up to 7 days a week. Treatments will last 30 minutes per session, making total treatment time 1 hour per day. Of note, participants will receive a single treatment in the Neuro-X lab to practice using the device and assessing for threshold dose.

D. RISKS AND DISCOMFORTS

There are risks to the participation in this study.

Questionnaires/Multifaceted Empathy Test (MET): You may experience some mild discomfort while answering some of the questions in the questionnaire part of the study, as they ask about personal topics. You may feel strong emotions when looking at the images during the MET, as some of the images are of people's faces experiencing strong emotions.

Ear Stimulation: taVNS is not approved for anxiety or ASD, and not approved for use in children by the FDA. The ear stimulation delivered during the study is not invasive but includes risk. Others who have received ear stimulation state that it feels like a "tickle" or "pricking" sensation. Some report mild irritation or redness from the stimulation. This will likely be temporary. In extreme cases burns might occur. We will monitor any potential burns and will stop stimulation and offer subjects vitamin E cream which they can apply to the affected area. Tissue surrounding the ear may be sensitive, sore or feel slight numbness. Hopefully this will be temporary and will go away after stimulation is turned off. In addition, ear stimulation might cause headaches or face pain, which should resolve shortly after treatment. You are encouraged to inform the researcher about any discomfort during stimulation and may discontinue at any point.

The experimental treatments may have unknown side effects. The researchers will let you know if they learn anything during the course of the study that might make you change your mind about participating in the study.

Finally, there is also a risk of loss of confidentiality of your personal information as a result of participation in this study.

E. MEDICAL RECORDS AND CERTIFICATE OF CONFIDENTIALITY

Information about your study participation will not be in your medical record. This

means that neither your research participation nor any of your research results will be included in any MUSC medical record.

F. BENEFITS

It is possible ear stimulation will not have any effect on the mental health symptoms you are currently experiencing, but researchers hope to learn more about the effects ear stimulation has on these symptoms.

G. COSTS

There will be no cost to you as a result of participation in this study.

H. PAYMENT TO PARTICIPANTS

There will not be any monetary compensation for participating in this study.

I. ALTERNATIVES

This study does not ask you to change your current treatment. Therefore, your alternative is to not participate in this study and continue your current standard of care treatment, including, but not limited to, therapy and psychotropic medications for your symptoms.

J. DATA SHARING

Information about you (including your identifiable private information and/or any identifiable biospecimens) may have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you.

K. DISCLOSURE OF RESULTS

Research results will not be disclosed.

L. AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, your study doctor and his/her research team will keep records of your participation in this study.

The health information MUSC may use or disclose (release) for this research study includes information in your medical record, results of

physical exams, medical history, lab tests or certain health information indicating or relating to your condition.

Your study doctor and his/her research team will use and disclose (release) your health information to conduct this study. The health information listed above may be used by and/or disclosed (released) to the following, as applicable:

- The sponsor of the study including its agents such as data repositories or contract research organizations monitoring the study;
- Other institutions and investigators participating in the study;
- Data Safety Monitoring Boards;
- Accrediting agencies;
- Clinical staff not involved in the study who may become involved if it is relevant;
- Parents of minor children if less than 16 years old. Parents of children 16 years old or older require authorization from the child; or
- Health insurer or payer in order to secure payment for covered treatment;
- Federal and state agencies and MUSC committees having authority over the study such as:

    - The Institutional Review Board (IRB) overseeing this study; Committees with quality improvement responsibilities; Office of Human Research Protections; Food and Drug Administration; National Institutes of Health or Other governmental offices, such as a public health agency or as required by law.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You do not have to sign this consent form. If you choose not to sign, it will not affect your treatment, payment or enrollment in any health plan or affect your eligibility for benefits. However, you will not be allowed to be a participant in this research study.

You will be given a copy of this consent form. Your authorization will expire at the conclusion of this study or, if you are participating in a study designed for the development of a drug or device, your authorization will remain in effect until the drug or device is approved by the FDA or until the company's application to study the drug/device is withdrawn. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

Your health information will be used or disclosed when required by law. Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury or disability and for conducting public health surveillance, investigations or interventions. No publication or public presentation about the research study will reveal your identity without another signed authorization from you.

If you have questions or concerns about this Authorization or your privacy rights, please contact MUSC's Privacy Officer at (843) 792-8740.

M. SIGNIFICANT NEW FINDINGS

If there are significant new findings during the course of the study, you will be notified.

N. STUDENT PARTICIPATION

Your participation or discontinuance will not constitute an element of your academic performance, nor will it be a part of your academic record at this Institution.

O. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation, nor will it be a part of your personnel record at this Institution.

P. FUTURE CONTACT

The researcher in charge of this study might like to contact you in the future about other research opportunities. Please initial by your choice below:

____Yes, I agree to be contacted

____No, I do not agree to be contacted

Results of this research will be used for the purposes described in this study. This information may be published, but your child will not be identified. Information that is obtained concerning this research that can be identified with your child will remain confidential to the extent possible within State and Federal law. The sponsor and the Food and Drug Administration (FDA) will receive copies of the research records. The investigators associated with this study, employees of the sponsor, the FDA, and the

MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that your child is injured as a result of participation in this study, you should immediately take your child to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that your child is in a research study. They will call your child's study doctor who will make arrangements for your child's treatment. If the study sponsor does not pay for your child's treatment, the Medical University Hospital and the physicians who render treatment to your child will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to your child.

Your child's participation in this study is voluntary. Your child may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if your child decides to do this. Your child's decision not to take part in the study will not affect your child's current or future medical care or any benefits to which your child is entitled.

The investigators and/or the sponsor may stop your child's participation in this study at any time if they decide it is in your child's best interest. They may also do this if your child does not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my child's participation in this study or study related injury, I may contact ***STEWART COX at 843-243-7303***. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input about my child's rights as a research subject in this study, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, you should sign below.

_____ _____

Signature of Person Obtaining Consent Date *Name of Participant

Participant's Personal Representative (if applicable):

_____

Name of Personal Representative *(Please print)*

_____

Signature of Personal Representative Date

Relationship: ___ Spouse ___ Parent ___Next of Kin ___Legal Guardian* ____ DPOA for Healthcare*

**(If you are the health care agent or guardian, please provide proof of your authority to act on behalf of the patient)*

*12-17 years of age:

"My participation has been explained to me, and all of my questions have been answered. I am willing to participate."

Signature: _____