Official Title: Noninvasive VNS for Neuromotor Adaptations

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Informed Consent Form: 04/16/2021

**Georgia Institute of Technology**
**Noninvasive VNS for Neuromotor Adaptations**
**Principal Investigator: Minoru Shinohara, PhD (Georgia Institute of Technology)**

You are being asked to be a volunteer in a research study. Georgia Tech (GT) School of Biological Sciences is conducting a research study, led by Associate Professor Minoru Shinohara and the Human Neuromuscular Physiology Lab. We ask you to join this study as a research subject because you are a healthy young adult (ages 18-39 years). The study involves magnetic stimulation of the brain (TMS brain stimulation) from the skin surface. The study also involves electrical stimulation of a nerve (called vagus nerve) from skin surface at the outer ear (tVNS), independently. Brain stimulations of various intensities will be applied to the left side of your brain that controls your right upper limb. According to our safety questionnaire, you do not have risk factors that prevent from brain stimulation or tVNS.

**Purpose:**
The purpose of this study is to understand how electrical stimulation of the nerve at the ear (vagus nerve) from the skin surface during motor training influences a brain hormone (called norepinephrine), brain activity, and motor performance. The planned number of subject enrollment is 24.

**Procedures:**
We will conduct the study in the Human Neuromuscular Physiology Lab. The Lab is located in the Biological Sciences/Applied Physiology Building of the Georgia Tech campus, 555 14th St NW, Atlanta, GA 30318. This study consists of experiments and training to be performed for 5 days in 2 weeks. The experiments and training involve brain stimulation and tVNS independently. If you agree to participate in this study, we will ask you to read and sign this consent form. We will then ask you to go through the following procedures.

You will be randomly assigned to one of the 2 groups (tVNS and Sham), like flipping a coin. In either group, you will perform the following test and training. The duration in parentheses are approximate, including preparation.

Day 1 (3.75 hours): Motor Test, Brain Stimulation Test, Motor Training
Day 2 (1.5 hour): Motor Training
Day 3 (1.5 hour): Motor Training
Day 4 (1.5 hour): Motor Training
Day 5 (3.75 hours): Motor Test, Motor Training, Brain Stimulation Test

There will be 1-2 day intervals in between the experiment days. The total amount of time you will be in the lab is about 1.5 hours on each Day 2-4, and about 3.75 hours on each Day 1 and Day 5. The total hours of participation will be approximately 12 hours. Remember, you may stop at any time.

**1. Preparation**

First, you will wear an arm cuff on your right arm. The cuff will measure your blood pressure. Then you will complete a questionnaire (called Edinburgh handedness inventory). This questionnaire will ask you about your preferences in the use of left and/or right hands in several daily activities and determine your overall preference. We will then attach disposable surface electrodes to your chest. The electrodes will record your heart activity. We will clean your skin before attaching these electrodes. If there are hairs that cover the spot for electrodes, we will ask you to shave them.

Several disposable electrodes will also be attached to your left outer ear at the ear lobe and at the tragus. The tragus is the little nub at the center of your ear. The electrodes will be attached after cleaning the areas with the alcohol swab.

You will then comfortably sit in a chair. Your hands will be placed in a comfortable resting position. We will place small monitors (sets of small electrodes) on your left hand and arm with medical tape. These monitors will record the movement of your hand muscles. We will clean your skin before attaching the electrodes.

**2. Protocol**

After the preparation, you will relax your muscles or perform motor tasks. The motor tasks are light contractions of hand muscles. You will receive brain stimulations during these tasks on Day 1 and Day 5. In addition, you will receive electrical stimulations to either pair of electrodes at the ear and brain stimulation to your head.

**3. Motor task**

We will ask you to contract your left hand muscles. You will be asked to produce rapid and accurate muscle activity and finger forces. We will ask you to contract muscles several times. You will have resting intervals of 1 minute or longer. You will perform the motor task for testing and training.

**4. Electrical stimulation of the outer ear**

Weak electrical stimulation will be applied to either the tragus (tVNS group) or ear lobe (Sham group) at a time during the training. You will feel weak stimulation but it is not strong or painful. Your hearing will not be influenced by this stimulation. We will let you know when the stimulation is about to begin.

**5. Brain and motor nerve stimulations**

You will receive brain stimulation and nerve stimulation on Day 1 and Day 5. First, you will receive electrical stimulation of the nerve in the arm. You will feel weak stimulation but it is not strong or painful. The stimulation will contract your hand muscles. Next, we will place a light coil on the right side of your head for brain stimulation. We will tell you when the stimulation is about to begin. You will feel as if you were tapped with a finger in your head, and it is not painful. We will first find your brain areas that control the hand muscles. Then we will give you a series of stimulations (called magnetic pulses). This way, we will find the spot that controls your hand muscles. Next, we will find the lowest stimulation to activate the muscles. At this

point, we will be ready for testing muscle contractions with brain stimulation in various conditions. We will stimulate your brain at rest and during a motor task. The interval of brain stimulations will be 4-5 seconds.

**6. Measurements**

The activity of your hand muscles will be measured from the electrodes on your muscles. The activity of your heart will be measured from the electrodes on your chest. Concentration of a hormone (called norepinephrine) will also be measured from your saliva that will be sampled with strips on Day 3.

## Flow chart of each procedure

**Electrical stimulation of outer ear**
Attachment of surface electrodes to two sites of the outer ear → Electrical stimulation of either site of the ear

**Motor test**
Finger movement task without electrical stimulation of the ear

**Motor training**
Attachment of surface electrodes to two sites of the outer ear → Finger movement task with electrical stimulation of either site of the ear

**Brain stimulation**
Attachment of surface electrodes to the arm → Electrical stimulation of the arm → Magnetic stimulation of the head

**Risks or Discomforts:**

The amount of brain stimulation you will receive will be in a range that is considered low risk. Seven people out of several tens of thousands without epilepsy have been known to suffer a seizure after repetitive magnetic brain stimulation. You will receive magnetic stimulation of much shorter duration and lower intensity than the individuals who had seizures. No healthy people have ever had seizures with the amount of magnetic stimulation you will receive. In addition, to minimize any possible risk of seizure, you must certify that you, your parents or siblings, or your children have never suffered an epileptic seizure. There is a rare or < 1% chance of you having a seizure. Should a seizure occur, 911 will be called. Seizures induced during the brain stimulation do not represent epilepsy, have never been known to occur again, and should not affect driving or insurability.

The electrical stimulation to the ear is considered low risk in healthy adults who do not have heart disease. The intensity of electrical stimulation will not be high so you will not feel

uncomfortable or painful. We will monitor your blood pressure and heart beat. We will communicate with you and, if necessary, decrease the stimulation intensity to minimize your discomfort.

Other risks/discomforts, aside from brain stimulation and electrical stimulation, may be possible in rare cases: The tape used to attach electrodes (medical grade surgical tape) may cause irritation of the skin in a small percentage of people. This effect will last no longer than a day or so.

**Benefits:**

There are no direct benefits to participating in the study. However, this study has the potential to benefit society. We (doctors, researchers, and scientists) may learn new things that will help better the lives of individuals suffering from impaired motor function (e.g. elderly, stroke victims). You will learn information on how nerves work for controlling movement.

**Compensation to You:**

You will receive $180 at the completion of full participation. If you choose to withdraw your participation before full completion, you will receive prorated compensation for $15 per hour or portion thereof.

U.S. Tax Law requires that a 1099-misc be issued if U.S. tax residents receive $600 or more per calendar year. If non-U.S. tax residents receive more than $75, mandatory 30% withholding is required. Your address and Tax I.D. may be collected for compensation purposes only. This information will be shared only with the Georgia Tech department that issues compensation, if any, for your participation.

**Storing and Sharing your Information:**

Your participation in this study is gratefully acknowledged. It is possible that your information/data will be enormously valuable for other research purposes. By signing below, you consent for your de-identified information/data to be stored by the researcher and to be shared with other researchers in future studies. If you agree to allow such future sharing and use, your identity will be completely separated from your information/data. Future researchers will not have a way to identify you. Any future research must be approved by an ethics committee before being undertaken.

**Confidentiality:**

The following procedures will be followed to keep your personal information confidential in this study: We will comply with any applicable laws and regulations regarding confidentiality. To protect your privacy, your records will be kept under a code number rather than by name. Your records will be kept in locked files and unless you give specific consent otherwise, only study staff will be allowed to look at them. Your name and any other fact that might point to you will not appear when results of this study are presented or published. The Georgia Institute of Technology IRB, the Office of Human Research Protections, and/or the Food and Drug Administration may look over study records during required reviews.

We have obtained a Certificate of Confidentiality from the National Institutes of Health to help us keep your information confidential. This Certificate provides a way that researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). A Certificate of Confidentiality does not prevent you or a member of your family 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.

**Costs to You:**

There are no costs to you, other than your time, for being in this study. Parking will be provided at no charge.

**Questions about the Study:**

If you have any questions about the study, you may contact Dr. Minoru Shinohara at telephone (404) 894-1030 or shinohara@gatech.edu.

**In Case of Injury/Harm:**

If you are injured as a result of being in this study, please contact Dr. Minoru Shinohara at telephone (404) 894-1030. Neither the Principal Investigator nor Georgia Institute of Technology has made provision for payment of costs associated with any injury resulting from participation in this study.

**Questions about Your Rights as a Research Participant:**

- Your participation in this study is voluntary. You do not have to be in this study if you don't want to be.
- You have the right to change your mind and leave the study at any time without giving any reason and without penalty.
- Any new information that may make you change your mind about being in this study will be given to you.
- You will be given a copy of this consent form to keep.
- You do not waive any of your legal rights by signing this consent form.

If you have any questions about your rights as a research participant, you may contact

Ms. Melanie Clark, Georgia Institute of Technology
Office of Research Integrity Assurance, at (404) 894-6942.

*or*

Ms. Kelly Winn, Georgia Institute of Technology

Office of Research Integrity Assurance, at (404) 385- 2175.

If you sign below, it means that you have read (or have had read to you) the information given in this consent form, and you would like to be a volunteer in this study.

_____
Participant Name (printed)

_____ _____
Participant Signature Date Time

_____ _____
Signature of Person Obtaining Consent Date

**Consent to Store and Share your Information:**

*I agree that my de-identified information/data may be stored and shared for future, unspecified research.*

*SIGNATURE* _____

*I do not allow my de-identified information/data to be stored and shared for future, unspecified research. These may only be used for this specific study.*

*SIGNATURE* _____