Non-Invasive Vagal Nerve Stimulation in Veterans With Mild Traumatic Brain Injury (mTBI)

NCT04437498

6/4/2025

U.S. Department of Veterans Affairs
Atlanta VA Health Care System

Informed Consent Template Version 1/10/25

Consent to be a Research Subject

You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 100 people who are being studied at the Atlanta VA Health Care System.

Why is this study being done?

This study is being done to answer the question: what are the brain and body relationships of mild Traumatic Brain Injury (mTBI) and memories of traumatic events in veterans with mTBI and posttraumatic stress disorder (PTSD), and what are the effects of treatment with non-invasive Vagal Nerve Stimulation (nVNS)?. You are being asked to be in this research study because you are a veteran and you have mTBI and PTSD.

Do you have to be in the study?

It is your decision to be part of this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you make your decision, you should take time to learn about the study.

What do I have to do if I choose to participate in this study?

If you are eligible and want to be part of the study, you will participate for up to 12 study visits. The researchers will ask you to do the following: complete several psychiatric questionnaires/interviews, blood draws, physiological monitoring with several devices (explained below), nVNS, at home monitoring and undergo some brain imaging if possible. For the at home portion, you will be asked to undergo nVNS or sham twice daily for a period of 2-3 months. You will administer these to yourself. These will be done with and without trauma scripts. A research assistant may call or connect with you via video conference to check how you are doing these. After month 1 and month 2 in the study, you will be asked to repeat some assessments virtually (memory tasks, nVNS/sham, assessment for PTSD, blood draw, wearable sensing devices). After 3 months, you will return to repeat blood draws, physiological monitoring, and possibly a Positron Emission Tomography (PET) scan, if possible. We will give you an active nVNS device to take home and use for up to 3 months. At 6 months you will return to repeat the assessment for PTSD and memory tasks. All these procedures will be paid for by the study and are described in more detail below.

How is this study going to help you?

If you are in the study, you will be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?

The study will take time. The drug/device/procedure that is being tested may not work any better than regular care, and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious – for this study, these include an increase in PTSD symptoms and/or anxiety, skin irritation, radiation exposure, loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are in the RISKS section of this document.

gammaCore use warning: You must store the device in a secure location where others will not have easy access to the device. Additional warnings are listed in the consent Risks section.

The use of the vagus nerve stimulation device (gammaCore) is central to this study. You may not participate in this study if you have been diagnosed with or have any of the following conditions:

- Patients with an active implantable medical device, such as a pacemaker, hearing aid implant, or any implanted electronic device.
- Patients who are using another device at the same time (e.g., TENS Unit, muscle stimulator) or any portable electronic device (e.g., mobile phone)

Safety and efficacy of gammaCore have not been evaluated in the following patients:

- Patients with uncontrolled hypertension, hypotension, bradycardia, or tachycardia
- Patients with a history of baseline cardiac disease or atherosclerotic cardiovascular disease, including congestive heart failure, known severe coronary artery disease, or recent myocardial infarction (within 5 years)
- Patients with metallic device such as a stent, bone plate or bone screw implanted at or near their neck.
- Patients with a history of abnormal baseline electrocardiogram (ECG), prolonged QT interval or arrhythmia
- Patients who have had surgery to cut the vagus nerve in the neck (cervical vagotomy)
- Pregnant women
- Patients with active cancer or cancer in remission
- Patients with an abnormal cervical anatomy

- Patients with a history of brain tumor, aneurysm, bleed or head trauma
- Patients with a history of syncope or seizures

Alternatives to Joining This Study

Since this is not a treatment study, the alternative is not to participate.

What Should I Do Next?

Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions (e.g., about exact time commitment, about unfamiliar words, more details on specific procedures, etc.) Make sure you understand. Take time to consider this and talk about it with your family and friends.

U.S. Department of Veterans Affairs
Atlanta VA Health Care System

Informed Consent Template Version 1/10/25

TITLE: Non-invasive Vagal Nerve Stimulation in Veterans with Mild Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: J Douglas Bremner, MD

SPONSOR'S NAME: J Douglas Bremner, MD

PURPOSE:
You are being asked to volunteer in a research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. It is entirely your choice. If you decide to take part, you can change your mind later and withdraw from the research study. The decision to join or not join the research study will not cause you to lose any benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

The purpose of this study is to: look at mTBI, PTSD and Vagal Nerve Stimulation (VNS). PTSD is a condition that can follow exposure to a psychological trauma, like being in combat, being the victim of assault, being in a car accident, or being the victim of childhood abuse. mTBI occurs after being hit in the head or exposed to a blast or explosion that leaves you dazed and confused or seeing stars. VNS is a procedure where the vagus nerve, which is in the neck, is electrically stimulated. Much like a pacemaker is used to stimulate the heart. Branches of the vagus nerve travel throughout the brain and the body. Vagal nerve stimulation is felt to have positive effects on the brain and body by fighting the effects of stress, reducing pain (including headaches), and helping memory. A surgically implantable VNS device has been approved by the Food and Drug Administration (FDA) for the treatment of both epilepsy and severe depression. Studies have shown that VNS stimulation is helpful for both conditions. We are using a non-invasive hand-held VNS device made by a company called ElectroCore. It is applied directly to the neck and does not require surgery. It is approved in Europe for the treatments of epilepsy, anxiety, depression, headaches, and other conditions, and in the US by the FDA for the treatment of headaches. We have studied its use at Emory for PTSD and have found it to be well tolerated and there have been no

adverse events or untoward effects with the device. It has not been approved in the US by the FDA for the treatment of mTBI or PTSD and is considered investigational in this study.

You have been selected to participate in this study because you are a physically healthy veteran with the diagnosis of mTBI and PTSD. The main purpose of this study is to look at the effects of nVNS on behavior as well as on blood and the brain. Study procedures include a screening, mental health assessment, medical assessment, lab work, and brain imaging with exposure to neutral and personalized traumatic scripts and at rest. If possible, brain imaging may be done with PET. There will also be at-home monitoring after your initial visits. You will be asked to undergo twice daily nVNS or sham for a period of 2-3 months. You will administer these to yourself. These will be done with and without the personalized trauma scripts. We may also ask you to wear an ECG patch before and during some of your visits. This patch is waterproof and can be worn in the shower. A prepaid mailer may be used to send or return the devices. A research assistant may call or connect with you via video conference to check how you are doing with these. You will be asked to repeat some assessments (memory tasks, nVNS/sham, assessment for PTSD, blood draw, and wearable sensing devices). After 3 months, you will return to repeat blood draws, physiological monitoring which may include a PET scan if possible. We will then give you an active nVNS device to take home and use for up to 3 months. At 6 months you will return to repeat the assessment for PTSD and memory tasks. The study will be completed in up to 12 visits.

CLINICALTRIALS.GOV:.
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.

WHAT WILL I BE ASKED TO DO?: After signing the consent form, you will begin research procedures. All of the study procedures will take place at the Atlanta VA Medical Center (AVAMC), except for the PET scans, which will take place at the Emory Center for Systems Imaging (CSI). All procedures will be done for study purposes. Depending on circumstances, certain aspects of the study, including the consent process, might be conducted virtually via video conference or by phone.

Visit 1 (Screening): A study coordinator will go over the written consent form and obtain permission to complete research activities. If you agree, you will be screened for eligibility and contraindications to the brain imaging or other study procedures. You will be asked to complete a mental health assessment and medical assessment. This visit may take place via video conference or a phone call.

Visit 2 (Enrollment): If you qualify for the study and decide to participate, this visit may take place right after screening. You will undergo an initial group of tests, which include

questionnaires about your health behaviors such as smoking status, clinical events and procedures, medications, and medical history. This can be done virtually via video conference or in-person. We will also go over psychiatric questionnaires with you. These will either be collected in paper form or using a computer or tablet. You will be asked to prepare/write two scripts about traumatic events have happened to you with assistance from the study coordinator. The scripts will be transcribed, edited, and recorded by a research associate for playback during visit 3 and 10. This visit will take around 1-2 hours.
We may also ask if you are willing to be a backup participant. If you are, we may ask you to come in for an hour or two during visit 3. If the scheduled participant is not able to complete the study, then we would proceed for the full day with you. If the other participant is able to complete the study, then we would reschedule your visit for another day.

Visit 3 (Stimulation and Lab Flow, possible PET Imaging): If possible, during this visit you may undergo brain imaging using PET. We may ask you to hold all your morning medications on the day of your testing. You may take these medications once you are done with the testing. You will be asked not to eat or drink anything except water for two hours before your visit. If possible, ten brain scans sessions may be performed using PET during one study visit with neutral and personalized traumatic scripts. We will also ask questions about your mood and stress level. And we will go over psychiatric questionnaires with you. Blood and urine tests, including a urine pregnancy test if you are a woman of childbearing potential, will be done. **Women who are positive for pregnancy will not be eligible for participation in this study.** Blood vessel testing and heart monitoring will be performed. You may be fitted with a Biopac monitor that will measure things like heart rate and skin temperature at each visit. You may be given an activity monitor to wear on the wrist of either arm. If PET is possible, this visit will occur at the Emory Center for Systems Imaging (CSI) and will take around 3-4 hours. If PET is not possible, this visit will take place at the AVAMC.

PET scan: You may undergo PET scanning of your brain at the Emory Center for Systems Imaging (CSI). A PET scan is an imaging system which provides a picture of the functioning or activated areas of the brain. If you have severe claustrophobia, you might find it uncomfortable, or the enclosed space of the camera might trigger a traumatic memory. If needed the study will be stopped. You will also be wearing a set of noninvasive sensors on your body to measure physiological signals. These signals may include the following: brain activity, heart activity, blood vessel function, and skin activity and temperature. You will also be wearing the sensor on your finger for the Peripheral Arterial Tonometry (PAT) test during the scans. PAT measures blood vessels in your finger and is a marker of stress. A small needle (intravenous catheter or I.V) will be placed in a vein in your arm to allow for blood collection. If PET is possible, the I.V will also be used to administer radioactive water by a physician, nurse, or Nuclear Medicine Technologist. If a PET scan is possible, there will be 10 injections of radioactive water (one injection every 8 minutes or so). For the scan, after the

I.V. is in place, you will be asked to lie on a narrow table with your head inside of an open tunnel. The first scan will be to measure the position and size of your head. You might hear a very faint sound during scanning (most people don't hear anything). The scans will be done while you are listening on headphones or ear buds to the neutral and personalized traumatic scripts you prepared during visit 2. If a PET scan is not possible, you will still use headphones or ear buds to listen to the trauma and neutral scripts. These scripts will be used for research purposes and used by the research team. You will also receive either nVNS or sham stimulation. You will be randomly assigned the order by a computer program. You have a 50/50 chance of ending up in either group. Blood samples will be drawn to measure molecules in the blood that may be involved in the stress response (for example: cortisol and norepinephrine and other biomarkers) at various time points during the study visit (a total of around 8 tablespoons). The PET procedure will take about 90 minutes, plus about a half hour of preparation time.

Depending on the availability of the PET, the scheduling of visits may occur in a different order than described above. Secondly, the PET equipment will require a safety pre-screen at the time of visit and any safety concerns identified during these screenings may require the visit to be rescheduled or cancelled. It is possible that you may not have the brain imaging (PET) during the study.

Visit 4 (1 Day Post Visit 3): You will be asked to return to the AVAMC to complete another blood draw and some memory testing and surveys. If you are unable to come in person, the memory testing can be done virtually, and no blood would be collected.

Visit 5-7 (Memory Testing) You will undergo daily nVNS stimulation with a memory task for visits 5-7. This will be done with a research coordinator talking to you via telephone or a video conference. During this procedure you will be asked to remember things while getting nVNS or sham stimulation. You may also be wearing a set of noninvasive sensors on your body to measure physiological signals.

Daily VNS: You will next undergo twice daily VNS or sham for a period of 2-3 months. You will administer these to yourself. The VNS device should only be used on yourself and not anyone else. A research assistant may call or connect with you via video link to check how you are doing these. You may also be wearing a set of noninvasive sensors on your body to measure physiological signals. Once a month we may ask you to come in for repeat memory and psychiatric symptom testing and you may have a blood draw. After this time period you will undergo the PET scan session like you did before. After the 3-month visit, we will give you an active VNS device to keep that will last up to 3 months. We will follow-up up three months later in person or on the phone with memory and psychiatric questionnaires. Then the study will be over.

Visit 8 (Month 1): After 1 month you will be asked to complete some memory testing, paired with a nVNS session. You will also be asked to complete some questionnaires and surveys. You may also be asked to wear sensing devices to capture physiological test information.

Visit 9 (Month 2): After 2 months you will be asked to complete some memory testing, paired with a nVNS session. You will also be asked to complete some questionnaires and surveys and you may also be asked to wear sensing devices to capture physiological test information.

Visit 10 (Month 3, Stimulation and Lab Flow, possible PET Imaging): Prior to this visit, you will be asked to complete some memory testing and psychiatric questionnaires virtually. During your in-person follow up, you may undergo brain imaging using PET, if possible. We may ask you to hold all of your morning medications on the day of your testing. You may take these medications once you are done with the testing. You will be asked not to eat or drink anything except water for two hours before your visit. If possible ten brain scans sessions may be performed using PET during one study visit with neutral and personalized traumatic scripts. If PET is not possible, you will still use earbuds or headphones to listen to the neutral and personalized traumatic scripts. We will also ask questions about your mood and stress level. And we will go over psychiatric questionnaires with you. Blood, COVID-19, and a urine pregnancy test if you are a woman of childbearing potential, will be done. **Women who are positive for pregnancy will not be eligible for participation in this study.** Blood vessel testing and heart monitoring will be performed. You may be fitted with a Biopac monitor that will measure things like heart rate and skin temperature at each visit. You may be given an activity monitor to wear on your wrist of either arm. This visit will occur at the Emory Center for Systems Imaging (CSI) or the VAMC and will take around 3-4 hours if a PET scan is possible. After this visit is completed, we will give you an active tcVNS device to keep that will last up to 3 months.

Visit 11 (Month 3, 1 Day Post Visit 9): You will be asked to return to the AVAMC to complete another blood draw and some memory testing and psychiatric questionnaires. If you are unable to come in person, the memory testing can be done virtually, and no blood will be collected.

Visit 12 (Month 6): We will follow-up with you three months after Visit 11 either in person or virtually. We will repeat some of the psychiatric questionnaires. Then the study will be over.

RISKS:

There may be side effects from the study drug, device or procedures that are not known at this time.

The most common risks and discomforts expected in this study are:

1. Psychological questionnaires/interview/trauma scripts: Being asked questions about the stress in your life, traumatic events or your mood and anxiety may cause you to have unpleasant and/or upsetting feelings or have an increase in PTSD symptoms if you have PTSD. If this happens, then you can take a break from the interviews. You can also slow down and take longer to do the tests. Should you so desire, a referral for counseling will be made available.

2. Physiological monitors: (Biopac monitor, ECG patch, etc.) These monitors require you to have sensors attached to your skin which may represent an inconvenience to you e.g., when adhesives are removed. They may also cause mild skin irritation or itching. You may feel itchiness due to sensor hookups on hands (due to sticky electrodes and gels) and temporary numbness of the arm is possible since the subject will remain in the same position for half an hour.

3. Intravenous (IV) catheter and blood draw. The IV can result in infection, bruising of the skin, or a blood clot in the vein. These complications are not common when the catheter is inserted by a professional under clean conditions. Dizziness and fainting are rare risks of blood draws. There are no long-term side effects. You may have some discomfort from the blood drawing. The risk from blood drawing is minimal but may include bruising and infection. The use of sterile precautions will decrease the risk of infection. However, you may develop a bruise at the site of the puncture, but this will go away in two to three days.

4. VNS Testing. Sometimes, you may experience coughing, stomach discomfort, headache, hoarseness, shortness of breath, irregular heartbeat, metallic taste, nausea, local pain, or change in voice/taste during treatment. A tingling/pricking/twitching feeling where the device is applied is normal but should not cause major discomfort. These effects usually stop right away once the treatment is completed. Mild skin irritation/redness or dizziness are other possible side effects. Do not use the VNS device if you have any of the following conditions: an active implantable medical device, such as a pacemaker, hearing aid implant or any implanted electronic device or if you are using another device at the same time (e.g., TENS Unit, muscle stimulator) or any portable electronic device (e.g., mobile phone).

5. PET scan: This research study may involve exposure to radiation from a PET scan. This PET scan procedure is routinely used for medical purposes; however, radioactive water is investigational and not approved by the FDA. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in this study. The long-term risks of radioactive water are not known. If you have had any significant exposure to radiation over the past year or plan to participate in other research studies

involving radioactivity over the next year, please consult with the study team and Dr. Bremner first. Some people experience anxiety from the PET scan procedure. A nurse or technologist will be with you during the PET scan procedure. If you should become claustrophobic, anxious, or agitated in the PET scanner, the scan will be stopped. If you are not able to complete the first PET scan, you may not be able to continue in the study. This study will expose you to a small amount of radiation. The radiation dose that you will receive is equal to or less than the annual radiation exposure limit allowed for persons who are occupationally exposed to radiation (x-ray technicians, radiologist). The principal risk associated with a radiation does is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is minimal. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The risk from radiation exposure of this magnitude is considered to be comparable to other everyday risks.

6. Fasting: You will need to fast for 2 of the study visits in order to undergo PET scan testing, until the scans are complete. Some people may show discomfort from this prolonged fasting, although true hypoglycemia is rare. A sweetened beverage will be administered if patients complain of lightheadedness or other fasting-related symptoms.

7. **gammaCore use warnings:**

   - **You must store the device in a secure location where others will not have easy access to the device. Do not permit anyone else to use the device..**
   - **You should not use the device:**
     - **While driving, operating machinery, or during any activity that may put you at risk of injury.**
     - **You must inform your HCP of any planned surgeries that may involve implants.**
     - **Near Microwave rays, MR, X-Ray, RF surgical, or CAT machines.**
     - **gammaCore is not compatible for use in an MR field.**
     - **In an explosive atmosphere or in the presence of flammable gas mixtures.**
     - **If you have an open wound, rash, infection, swelling, cut, sore, drug patch, or surgical scar(s) on your neck at the treatment location.**
     - **If you have wet skin, are in the water, or just stepped out of the water (e.g., shower, bath, pool).**
     - **If you are using another device at the same time (e.g., TENS Unit, muscle stimulator) or any portable electronic device (e.g., mobile phone).**

REPRODUCTIVE RISKS:

Women of childbearing potential please note: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

BENEFITS: There is no direct benefit to you from taking part in this study. This study is designed to learn more about the effects of VNS on behavior as well as blood and brain responses to stress, however, this research study may help us learn new things that may help other people in the future.

COMPENSATION:

You will be compensated for your time, travel, and effort for participating in this study. This compensation will either come as a check through the mail or by using direct deposit. Compensation ranges from $25 to a total of up to $550 for the study. A breakdown of payments is listed below. Successful return of the devices will be included as a requirement for your study compensation. If used as a backup participant, you will receive $50.

Visit 1: Screening: $50
Visit 2: Baseline and enrollment $50
Visit 3: Labs, stimulation $50, PET Scan $50
Visit 4: Labs, memory testing $50
Visits 5: Memory testing Day 1 $25
Visits 6: Memory testing Day 2 $25
Visit 7: Memory testing Day 3 $25
Visit 8: 1 Month Follow-up $50
Visit 9: 2 Month Follow-up $50
Visit 10 & 11: 3 Month questionnaires, labs, stimulation $50, PET Scan $50
Visit 12: 6 Month Follow-up $25



You may be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options.

COSTS:

You or your insurance will not be charged for any treatments or procedures that are part of this study. However, some Veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services that are not part of this study.

You will get necessary medical treatment if you get injured from being in this study. This requirement does not apply to:

(1) Treatment for injuries due to non-compliance by a subject with study procedures;

Or

(2) Research conducted for VA under a contract with an individual or a non-VA institution.

If you believe you have been injured by this research, you should contact J Douglas Bremner, MD at 404-712-9569..

ALTERNATIVES:
Since this is not a treatment study, the alternative is not to participate.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED:

We will keep information about you, including any research records we create, strictly confidential to the extent required by law.
We may be required to release your record if we receive a subpoena or a court order. The study staff will keep your study files locked in a file cabinet in a private office. We will use [a study number*] rather than your name on study records when we can. Your name and other facts that might point to you will not appear when we present this study or publish its results." People other than those doing this research study may have access to your medical and study records including:

- **Sponsors, companies or agencies paying for the study**

- **The Office for Human Research Protections**
- **The Government Accountability Office (GAO)**
- **The Inspector General**
- **Emory University and its affiliate institutions**
- **Any appropriate state or federal government agencies that make rules and policy about how research is done that are not listed above**

All research records and/or identifiers will be destroyed in accordance with the VA record retention schedule.

If you are a veteran who is a patient at the Atlanta VA Health Care System, a copy of your signed and dated consent and HIPAA forms may be placed in your medical record(s). If you are a non-veteran receiving clinical services (i.e., use of the laboratory, radiology, audiology, etc.) as part of this study, you will have an electronic medical record created for you. You will also be given a VA Notice of Privacy Practices (NOPP) and we will ask you to sign a form saying that you have received this notice.

If you are participating in a study where a test and/or procedure may be performed at Emory and you are not and have never been an Emory patient, you do not have an electronic medical record. Please note that an Emory medical record will be created if you have any services or procedures done by an Emory provider or facility for this study.

RESULTS: In general, we will not give you any individual results from the study of the samples or information you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

BIOSPECIMENS: We will use your sample and data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

IDENTIFIABLE PRIVATE INFORMATION OR IDENTFIABLE SPECIMENS:
Identifiers might be removed from the identifiable private information or identifiable biospecimens that are collected. After that removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

CONFLICT OF INTEREST: *None.*



CONTACT PERSONS:
If you have any questions, concerns, or complaints about this study you can call a member of the study staff: Mykayla Jeter by cell: 404-295-9594. If you have been harmed from being in this study call: J Douglas Bremner, MD at 404-712-9569

If you have been harmed from being in this study call: J Douglas Bremner, MD at 404-712-9569**. If you want to speak to someone who is not a member of the study to discuss problems, ask questions or voice concerns, you can call:**

The Research Compliance Officer at (404) 895-3529 or the Clinical Studies Center Manager at (404) 321-6111 ext. 206933.

If you have any questions about your rights as a participant in this research study, call the Emory University Institutional Review Board at (404) 712-0720 or toll free at 1-877-503-9797.

VOLUNTARY PARTICIPATION AND WITHDRAWAL:

The study doctors have the right to end your participation in this study for any of the following reasons: If it would be dangerous for you to continue, if you do not follow study procedures as directed by the study doctors, or if the sponsor decides to end the study.

Your participation is voluntary and you have the right to refuse to be in this study. You can stop at any time after giving your consent. This decision will not affect in any way your current or future medical care or any other benefits to which you are otherwise entitled. For your safety, however, you should consider the study doctor's advice about how to go off the study treatment.

The study doctor, investigator, or sponsor may stop you from taking part in this study at any time if they decide it is in your best interest or if you do not follow study instructions.

We will give you a copy of this consent form to keep. If you are willing to volunteer for this research, please sign below.



RESEARCH PARTICIPANT'S SIGNATURE AND DATE:

_____
Research Participant's name

_____ _____
Research Participant's Signature Date

_____ _____
Participant's Legally Authorized Representative Date



U.S. Department of Veterans Affairs
Atlanta VA Health Care System

Informed Consent Template Version 1/10/25

Optional Study Information

Your data and/or specimens will be protected the same way as the data and/or specimens for the main study. There are no additional risks or costs for joining the optional study than the ones already described for the main study (see sections above).

What is the purpose of this study?
The purpose of this study is to see if VNS has an impact on the gut microbiome. The gut microbiome is the collection of all the microorganisms in your gut, and it plays a role in digestion, the healthy immune response, and possibly some aspects of mental health. Future research will be planned.

What will I be asked to do?
You will be asked to give two stool collections at different time points (one at the beginning of the study and the other before visit 8. Stool collection kits will be provided, and instructions will be included. If you join this substudy, you will be donating your samples and study information. We will use your sample and data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product. Identifiers might be removed from the identifiable private information or identifiable biospecimens that are collected. After that removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you. Your samples will be retained until the testing is completed.

Will I benefit directly from the study?
This substudy is not designed to benefit you directly. The study results may be used to help others in the future.

Will I be compensated for my time and effort?
You will get $25 for the first stool collection and $50 for the second, to compensate you for your time and effort. You will get up to $75 total if you complete both collections. You may be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, if joining the substudy increases your annual compensation over the taxable amount.

Risks?
There are no known risks at this time except for the potential loss of privacy.

What are my other options?

You can participate in the main study and not take part in this substudy.

Withdrawal from the Substudy
You have the right to leave this substudy at any time without penalty. You may stay in the main study even if you leave this substudy.

The researchers also have the right to stop your participation in this substudy without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

These are the expected reasons why the researchers may stop your participation:
Recruitment goal for the substudy has been reached.

Contact Information
See contact information for the main study, above.

RESEARCH PARTICIPANT'S SIGNATURE AND DATE:

Please initial beside your choice and sign below.

_____ Yes, I want to participate in the optional substudy.

_____ No, I do not want to participate in the optional substudy.

_____
Research Participant's name

_____ _____
Research Participant's Signature Date