A Feasibility Study to Evaluate the Safety and Effect of the Optimization of Vagus Nerve Stimulation in Epileptic Patients to Induce Cardioprotection

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NCT04387435

ICF Version: 11/21/2022

UNIVERSITY OF CALIFORNIA LOS ANGELES
CONSENT TO PARTICIPATE IN RESEARCH

A Feasibility Study to Evaluate the Safety and Effect of the Optimization of Vagus Nerve Stimulation in Epileptic Patients to Induce Cardioprotection

A study to evaluate vagal nerve stimulation in relation to heart function.

INTRODUCTION

Olujimi Ajijola, MD, PhD and associates at the University of California, Los Angeles are conducting a research study. You are being asked to participate in a research study that is funded by the National Institute of Health (NIH).

The researchers will explain this study to you. **Research studies are voluntary and include only people who choose to take part.** Please take your time about deciding whether to participate in this study. Before deciding:

- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor or request a second opinion.
- If you have any questions, you can ask the researchers for more information before deciding to participate.

Key Information:

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you have an implanted vagal nerve stimulator for epilepsy.

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 the study is to learn more about the vagus nerve.

How long will the research last and what will I need to do?

You will be in the study up to 9 weeks. More detailed information about the study procedures can be found under "What Will Happen If I Take Part in this Study?

Is there any way being in this study could be bad for me?

There are risks to taking part in a research study. Some of the known risks for this study may include a decrease in heart rate and blood pressure and an increase in the number of seizures. More detailed information about the risks of this study can be found under "What Kinds of Risks or Discomforts Can I Expect?

Will being in this study help me anyway? There is no direct benefit from participating in the research study.

What happens if I do not want to be in this research? Participation in research is completely voluntary. You can decide to participate or not to participate.

WHY IS THIS STUDY BEING DONE?

Your neurologist has determined that you may qualify for this study because you have a vagal nerve stimulator or are scheduled for a vagal nerve stimulator implant. This study is investigating if adjusting the parameters of your vagal nerve stimulator could protect your heart. Vagal nerve stimulation has been shown to be beneficial in several studies related to heart failure. The tests in this study will provide additional information about how stimulation relates to heart function and heart arrhythmias. The outcomes of this study will help researchers design new therapies for patients.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

The study will enroll 12 patients at UCLA.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

Screening

If you decide to take part in this study, your physician will review your medical history and seizure activity to determine if you qualify to participate. If you choose to participate, you will be asked to sign this consent form.

If you are enrolled in the study, your physician will review the research procedures with you in detail and answer any of your questions. The full schedule of events is on the last page of the consent form.

Baseline Visit (up to 4 hours): The study team will review your medications and seizure history. You will have an autonomic test and cardiopulmonary exercise test. The study neurologist will work with you to decide if you can do all of the testing or some of the testing. Your vagal nerve stimulator (VNS) parameters will be adjusted by the study physician during the testing. This adjustment will only take place if you tolerate the changes. You will also be asked to notify the study team know when the VNS goes on or goes off.

If you agreed to participate in baseline testing only this will be your one visit and the study has ended.

If you agree to participate in titration visits, you will continue in the study.

VNS Titration Visits (1 hour each, up to 5 visits): The study team will review your medications and seizure diary. The neurologist will adjust your VNS in a similar manner as if you were not in the study (based on your seizure frequency and how well you tolerate the adjustments). This phase may include up to 1-5 sessions during a 2-4 week timeframe.

Treatment phase (at home): After the final VNS study titration visit you will remain at home. You should contact the study's neurologist and/or study team with any problems or concerns during this phase. You will return to the clinic for your final visit after 4 weeks.

Final Visit (3 hours): The study team will review your medications and seizure history. You will have an autonomic test and cardiopulmonary exercise test. The study neurologist will work with you to decide if you can do all of the testing or some of the testing. You will also be asked to notify the study team when the VNS goes on or goes off.

Research Procedures:

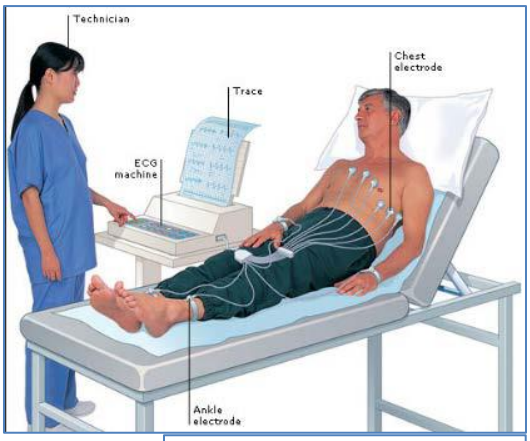
What is an Autonomic Test and what happens during this test?

This is a non-invasive test that measures how the nervous system works to control blood pressure and heart rate. They study team will review the preparation and research procedures with you in detail before starting the tests. You can not have alcohol or any caffeinated drinks 24 hours prior to testing. You cannot exercise 12 hours prior to testing.

The testing will take up to 2 hours.

Non-invasive neuro-physiologic testing
To record measurements, you will have the following monitors placed:

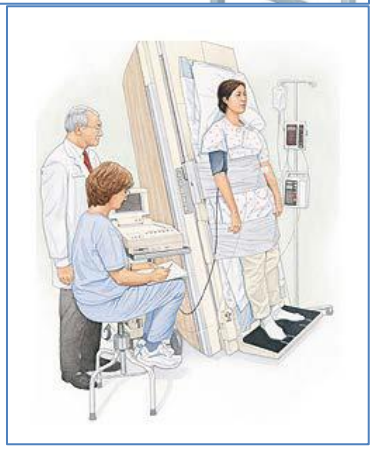
- Chest belt for respiration
- ECG pads for heart rate
- Finger monitor for blood pressure



Measurements recorded by the technician during the tests that may include:

- Continuous blood pressure
- Heart Rate
- Respirations

The following procedures will be performed to obtain the measurements:



Tilt Table Test
You will lie flat on the examination table for 5 minutes to collect baseline measurements. You will then be transitioned to a 70 degree angle and 10 minutes of measurements are recorded. You will be asked about lightheadedness and/or dizziness.

Deep Breathing
You will be asked to inhale for 5 seconds and exhale for 5 seconds. The cycle is repeated 6 times, or as tolerated.

Valsalva Maneuver
You will be asked to take a deep breath and blow hard into a mouthpiece. The Valsalva maneuver is performed 2-3 times.

Cold Pressor Test
You will be seated quietly in chair and the study team will record your heart rate and blood pressure. After 15 minutes, the study team will then place a cooling pad on your right arm that is attached to a cooling machine. You will then have 15 minutes with cooling pad turned on. The study team will record your heart rate and blood pressure with the cooling pad on your arm.

What is a Cardiopulmonary Exercise Test (CPX) and what happens during this test? (Bicycle)
This is a non-invasive test that tells your doctor how well your heart and lungs are working during exercise. The first thing that we will do is a breathing test called spirometry. This will measure the amount of air that you exhale when you are resting. We will then attach several monitoring devices including small pads with wires (electrodes) on your chest, a blood pressure cuff on your arm, a little clip on your finger to measure your oxygen level, a nose clip and a mouthpiece for you to breathe. You will then exercise on an exercise bike at different speeds until you reach the maximum that you can continue. Your heart rate and blood pressure measurements, ECG, and heart rate variability (HRV) will be evaluated during exercise and for 5 minutes after the exercise has stopped.

The testing will take approximately 45 minutes.

What happens during the VNS Titration Visits?
This is the part of the study that the physician will program your vagal nerve stimulator to treat your seizures and based on settings that the researchers believe could give additional protection to your heart. The settings will be approved by your neurologist and be performed using the same equipment used for your routine care.

These visits will take approximately 60 minutes.

HOW LONG WILL I BE IN THIS STUDY?

You will be in the research study for up to 9 weeks.

WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

Risk related to VNS parameter changes: You could experience coughing and hoarseness during the changes. If this occurs the parameters will be immediately reversed to your previously tolerated parameters. You could also experience a change in seizure frequency or a decrease in heart rate and blood pressure. If this occurs the parameters will be immediately reversed to your previously tolerated parameters.

Risks related to monitor pads and electrodes: Some people can have minor skin irritation or an allergic reaction from the sticky patches that are placed on the chest and limbs. The irritation should go away once the patches are removed.

Risks related to tilt table test, valsalva maneuver or deep breathing: Some people may report feeling dizzy or lightheaded from these tests. The technician can stop the test at any time if you feel uncomfortable.

Risks related to Cardiopulmonary Exercise Test (CPX): Some people may report feeling short of breath, fatigue, dizzy, or have an arrhythmia. The technician can stop the test at any time if you feel uncomfortable.

Risk related to Cold Pressor Test: Some people may be uncomfortable with having their arm cooled for 15 minutes. The technician can adjust the temperature or stop the test if this is reported.

Unknown risks and discomforts: The experimental treatments may have side effects that are currently not known. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

ARE THERE ANY BENEFITS IF I PARTICIPATE?

Possible benefits to me:
There is no direct benefit to you for participating in this study. The knowledge obtained from this study may advance medical science and have a future benefit to patients with ventricular arrhythmias.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

If you decide not to take part in this study, or if you withdraw from this study before it is completed, your doctor will discuss other options available to you. The alternatives to participation include not participating in the research study.

CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?

The researchers may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The researchers might also decide to stop the study at any time. The data collected about you up to the point of withdrawal will remain part of the study and may not be removed from the study database.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Identifiers will be removed from your study data, and, after such 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.

Though the confidentiality of your data is very important to us and we will use many safety measures to protect the confidentiality of your data, it is possible that it could be compromised. For example, although we would not put any personal identifying information about you in a shared database, someone in the future might find some way to link your medical information or other information collected for this study back to you even in the absence of your name or other personal identifying information. Alternatively, there could be violations to the security of the separate computer systems used to store the codes linking your information to you.

Use of personal information that can identify you:
Federal law requires that personal health information that is created or obtained during this research cannot be used without your permission. Therefore, you may not participate in this study unless you give permission to use and disclose your personal health information. You will be asked to sign a separate consent called a HIPPA authorization for this purpose.

How information about you will be stored:
If you decide to take part in this study, the study doctor and study staff will keep your medical records and personal health information private to the extent allowed by federal, state, and local law. A special code (number combination) and your initials will be used to identify your personal health information. No personal health information about you, your illness, or your treatment will be made public.

People and agencies that will have access to your information:
Your personal health information may be given to governmental agencies, for example: the Food and Drug Administration (FDA) or similar government agencies in other countries. Only information about your medical condition as it relates to this study will be provided. In order to verify study data, monitors from governmental agencies (for example: FDA) and the Institutional Review Board (IRB)/Medical Ethics Committee (MEC) will have the right to review your medical records as they relate to this study.

Publication(s) using data collected during the study will not include your name or any information that can identify you.

Certificate of Confidentiality
The information about you is protected by a federal Certificate of Confidentiality. This means that we can't be forced to release information about you for any legal proceeding, even if a court of law asks.

The Certificate allows us to use the information about you for purposes of this research, or to disclose it for other research when allowed by law. The Certificate requires other researchers to also protect the information we share with them.

There are limits to this protection. The Certificate does not protect your information when:

- You or your family voluntarily release information about yourselves.
- You consent to release of information (for example, the uses described in this form, or if you sign release forms for employment, insurance or medical care).
- A federal agency audits or evaluates research that it funds.
- Researchers are required to report possible intent to harm yourself or others, child abuse, elder abuse, or infectious disease cases.

ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?

The study will pay for the cost of supplying and administering the study device, and all required study items and services as described in this consent form.

WILL I BE PAID FOR MY PARTICIPATION?

You will receive a **parking voucher** for each research visit.

You will also receive a gift card when the study visits are completed. You will receive up to $200 for the entire study:

- Screening and Baseline: $100
- VNS Titration Visits (up to 5 visits): $50
- Final Visit: $50

WHAT OTHER THINGS SHOULD I CONSIDER BEFORE PARTICIPATION?

Your doctor may decide to withdraw you from the study at any time without your consent. If it is felt to be in your best interest, or if the study is stopped, your doctor may withdraw you from this research. If you have a problem as described in the risks section, or if you become ill during the research, you may have to stop participating in the study, even if you would like to continue. Your study doctor will make this decision. Your study doctor or designee will discuss with you what follow-up is required if you decide to withdraw, or are withdrawn from the study before the study is finished.

The information collected as part of this study is being obtained for research purposes only. The data are not being collected for clinical purposes and will not be provided to you unless there are clinically relevant findings which may be reviewed by a study physician or provided to you to take to your Primary Care Physician (PCP).

RESEARCH FINANCIAL INTERESTS IN THE STUDY

There are no researcher financial interests in this study.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:

You may contact any of the personnel below with any questions or concerns about the research or your participation in this study. You can also call the UCLA Page Operator at (310) 825-6301 to reach the below investigators 24 hours a day, 7 days week.

Principal Investigator:	Olujimi Ajijola, MD, PhD 100 Medical Plaza, Suite 660 Los Angeles, CA 90095 (310) 825-2235
Neurology Investigators:	Ausaf A. Bari MA MD PhD FAANS Raman Sankar, MD, Phd 300 Stein Plaza Driveway Suite 420 Los Angeles, CA 90095 (310) 825-5111
Electrophysiology Investigators:	Jeffrey L. Ardell, PhD Jason Bradfield, MD Kalyanam Shivkumar, MD, PhD Marmar Vaseghi, MD, Phd
Nurse Coordinators:	Julie M. Sorg, RN, MSN UCLA Cardiac Arrhythmia Center 100 Medical Plaza, Suite 660 (310) 206-2235

UCLA Office of the Human Research Protection Program (OHRPP):
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact UCLA OHRPP by phone: (310) 825-5344; by email: mirb@research.ucla.edu or U.S. mail: UCLA OHRPP, Box 951406, Los Angeles, CA 90095-1406.

WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed above. If you are injured as a result of being in this study, UCLA will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call the UCLA Office of the Human Research Protection Program at 310-825-5344 or send an email to mirb@research.ucla.edu.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA.
- If you decide to take part, you can leave the study at any time.
- If you decide to stop being in this study you should notify the research team right away.
- The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

If important information is learned during the course of this study, your doctor will be notified by the sponsor. You will be told of any important new information that is learned during the course of this research study that may affect your condition or your willingness to continue to take part in this study.

HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date

APPENDIX 1. SCHEDULE OF STUDY VISITS

	Screening and Baseline Visit[a]	**VNS TITRATION VISITS (UP TO 5 VISITS AT UCLA) (FOR PATIENTS THAT PARTICIPATE IN TITRATION VISITS)**	**FINAL VISIT (FOR PATIENTS THAT PARTICIPATE IN TITRATION VISITS)**	**EARLY STUDY WITHDRAW VISIT**
Informed Consent	**X**			
Medical History	**X**			
Seizure History	**X**	**X**	**X**	**X**
VNS Titration		**X**		
Autonomics Test: Tilt Table Test Deep Breathing Valsalva Maneuver Cold Pressor Test	**X**		**X**	
Cardiopulmonary Exercise Test	**X**		**X**	
Medication Review	**X**	**X**	**X**	**X**
Adverse Events		**X**	**X**	**X**

[a] ±2 days