Randomized Double-Blind Placebo-Controlled Trial: fMRI Assessment of Cranial Electrical Stimulation for Fibromyalgia in Veterans

NCT04115033

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

Informed Consent Template Version 7-1-20

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 50 people who are being studied at the Atlanta VA Health Care System.

Why is this study being done?
This study is being done to help determine the usefulness of auricular CES (Cranial Electrical Stimulation), commonly known as the "Alpha-Stim", in veterans with Fibromyalgia using MRI to measure outcomes. You are being asked to be in this research study because you have a diagnosis of Fibromyalgia.

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 weeks (3 study visits). The researchers will ask you to do the following: Answer Questionnaires, complete 3 fMRIs and be randomized to control or true CES.

How is this study going to help you?
If you are in the study, you will be helping the researchers determine the usefulness of CES in patients with Fibromyalgia.

What are the risks or discomforts I should know about before making a decision?
The study will take time. The 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 exposure to magnetic fields, possible feeling of claustrophobia, exposure to loud noise, dizziness, faintness or anxiety, 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.

Alternatives to Joining This Study
You do not have to be in this study to receive treatment for your condition. Your study doctor can discuss with you the alternative treatments.

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 which parts of the study are research and which are standard care that you would have even if you did not join the study. Take time to consider this and talk about it with your family and friends.

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TITLE: Randomized Double-Blind Placebo-Controlled Trial: fMRI Assessment of Cranial Electrical Stimulation for Fibromyalgia in Veterans

PRINCIPAL INVESTIGATOR: Anna Woodbury, MD

SPONSOR'S NAME: Department of Veteran Affairs

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 research study is to learn more about the usefulness of CES (Cranial Electrical Stimulation) in veterans with Fibromyalgia using magnetic resonance imaging (MRI) to measure outcomes. This research study aims to find out if MRI is useful in studying pain-related brain changes following the use of a device, called the Alpha-Stim, which uses electrical stimulation applied at the ear to treat pain. The Alpha-Stim device is FDA cleared for pain management due to its minimal risks. The study doctors want to find out if it is effective for pain control in those with fibromyalgia, and whether these improvements in pain can be seen on a special kind of MRI called functional MRI (fMRI). Testing will take place at the Atlanta VA Health Care System (VAHCS) and at Emory University.

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?:

Visit	Activity	Time	Location
1	Screening & Randomization fMRI Intervention	90 - 120 minutes	Emory Imaging Center
2	fMRI 4-6 week post-treatment follow-up	90-120 minutes	
3	fMRI 12-week post-treatment follow-up	90-120 minutes	

Screening and Randomization: At your first visit, study staff will assess you for eligibility to participate in the study. You will be given assessments using standardized forms (verbal and or pen and paper) for cognitive and psychological evaluation, eating, sleeping and drinking habits, and surveys of physical function, anxiety, depression, fatigue, sleep disturbance, social function, pain interference, health, and activity level. You will also be asked to perform fitness measures such as arm curls, 30-second chair stand, and handgrip strength tests. These tests will be repeated at the post-treatment follow-up visits. You will be randomly (like flipping a coin) placed into either a control group or a treatment group.

Control Group and Treatment Group Intervention: involves receiving a Alpha-Stim device (Sham Device for Control Group and True Device for Treatment Group). The stimulator device uses earclip electrodes to deliver a current to the ear. You will be trained how to power on and off the device, how to properly attach the earclip electrodes, and how to clean the earclip between uses.

For both the control group and the treatment group, you will run daily 60 minute treatments (either sham or true), then assessed for changes in pain and function at 2 weeks, 6 weeks and 12 weeks following the initial treatment.

Functional Magnetic Resonance Imaging (fMRI) scans will be collected within 2 weeks for both treatment groups prior to the start of treatment, at 4 weeks following treatment initiation, and again at 12 weeks near the end of the treatment series. To have the scan, you will need to go to an imaging center located on the Emory University campus, about a 3-mile drive from the VA Health Care System. You will be given directions to the facility at your first visit.

To be scanned, you will be asked to remove all jewelry and other metal containing objects (including credit cards). You will enter a large room where a powerful magnet is located. You will be asked to lie down on a narrow table and then you will be put into a small tunnel

approximately 6 feet long and 2 feet in diameter. In the scanner, you will then be asked to lie as still as possible during the scan for approximately 60 minutes. Cushions will be used to reduce head movement. You will have headphones and a microphone through which you will be able to communicate with the members of our team running the experiment. A small mirror will be positioned above your head so you will be able to see out of the end of the scanner. During scanning, you will hear a loud banging noise while the MRI machine takes pictures of your brain. This is normal. If needed, you will be given earplugs to make you more comfortable. Physiological data such as heart and breathing rate will be measured during the scan using an MR-compatible infrared pulse oximeter attached to the right middle finger and an MR-compatible respiratory rate monitor and plethysmograph.

RISKS:
There may be side effects from the study procedures that are not known at this time.

The most common risks and discomforts expected in this study are:
Behavioral assessments: It is possible that you will become frustrated or tired during these tests. If this occurs, you may request a break from the procedure(s).

Fitness assessments: You may experience muscle soreness or cramping from the fitness tests. These sensations should be mild and should lessen and/or completely go away in a few days.

The less common risks and discomforts expected in this study are:
Alpha-stim Device: Physical risks are minor and are unlikely. Rarely skin irritation or electrode burns, dizziness, and headaches could occur. Treatment immediately prior to going to sleep can cause difficulty sleeping.

Rare but possible risks include:
fMRI: A potential for physical risk related to MRI exposure exists, but there is not enough evidence to conclude that significant risks are posed with MRI exposure unless you have an implanted MRI-incompatible device, in which case you will be excluded from the study. Psychological risks include possibility of claustrophobia or PTSD related to a small space in the MRI scanner, so subjects with significant anxiety related to the MRI scanner will be excluded. Other considerations:

- The MRI machine is as loud as riding in a loud train—you will be given earplugs and headphones to lessen the noise.
- You may experience some muscle discomfort while lying in the scanner. You may also become too hot or too cold, in which case you may ask for an adjustment of room temperature or a blanket. Some people become nervous or claustrophobic (anxious or

afraid of closed spaces) in the scanner. If this happens to you, you may ask to be withdrawn immediately.

- In the 3 Tesla MRI used in this study, rarely, you may also experience a sense of dizziness in the magnet. This is due to the strong magnetic field, and if it disturbs you, you may ask to be withdrawn.
- Because the magnetic field will affect any metallic object, you should not participate if you have any type of metallic implant in your body, including pacemakers, aneurysm clips, shrapnel, metal fragments, orthopedic pins, screws, or plates, metallic IUD's, or piercings that you cannot remove. If you have any of these, there is a risk that the magnetic field could cause them to move or heat up. It is important that you inform the study personnel if you have any implants.
- Because the imaging center is not a hospital facility, there is no emergency personnel on site.
- This type of brain scan is not designed to detect problems of the brain. A radiologist will not be reading the scan. The study team will review the scan. If we determine that data from the scan suggest something that may be important clinically, we will share them with you so that you can discuss them with your own doctor.
- Because of the investigative nature of this study and the unknown effects of the magnetic field on the fetus, you should not participate if there is the possibility that you are pregnant.
- Measuring physiological state should not have any risks. Sometimes there is some discomfort when we remove the stickers holding the recording wires in place, but this is small. The wires are grounded and are only measuring your body's responses, so there is no danger of electric shock.

Research risks include possibility of a security breach and misuse of your data. Your data will be de-identified and protected according to HIPAA regulations.

REPRODUCTIVE RISKS: 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 the possibility of long-term pain control using a non-narcotic modality for pain, improving function and decreasing side effects related to drugs and other more invasive therapies. Another potential benefit is receiving fMRI analysis that may unearth underlying neurological disease processes leading to early diagnosis and referral to appropriate physicians for further treatment. Subjects will also be selected for early referral to the pain

clinic, where the pain therapies will be optimized under the guidance of Dr. Woodbury, independent of whether they are in control or treatment groups.

Taking part in this research study may not benefit you personally, but we, the doctors, researchers and scientists, may learn new things that will help others. Benefits to others may include understanding of the neural correlates for fibromyalgia and chronic pain processes and wider application to the general population for improving pain management and designing targeted therapies for pain and specifically fibromyalgia.

COMPENSATION: You will receive a total of $100 for your participation in the study. A check will be mailed to you 4 – 6 weeks after your completion in the study.

COSTS: You 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 Anna Woodbury, MD Principal Investigator.

ALTERNATIVES: You do not have to be in this study to receive treatment for your condition. Your study doctor can discuss with you the alternative treatments.

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 Office of Research Oversight (ORO)
- The Inspector General
- Emory University
- 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.

HEALTH INFORMATION PORTABILITY AND ACCOUNTABILITY ACT (HIPAA): There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, allergies, lab results, or mental health treatment.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), the Government Accountability (GAO), Emory University and the Emory Institutional Review Board and the Food and Drug Administration (FDA).

Your health information disclosed pursuant to this authorization may no longer be protected

by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Anna Woodbury, MD and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

RESULTS: The study team will give you your individual results from your participation in this study. You may ask for a picture of your brain to take with you that will not include clinical summary.

IDENTIFIABLE PRIVATE INFORMATION OR IDENTFIABLE SPECIMENS: Your information collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

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 Anna Woodbury, MD Principal Investigator.

If you have been harmed from being in this study call**:** Anna Woodbury, MD Principal Investigator.

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 or the Clinical Studies Center Manager.

If you have any questions about your rights as a participant in this research study, call the Emory University Institutional Review Board.

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