Graded Intensity Aerobic Exercise to Improve Cerebrovascular Function and Performance in Aged Veterans

NCT03803904

June 27, 2022

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 134 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: how does exercise influence cerebrovascular health. You are being asked to be in this research study because you're a relatively healthy adult, willing to participate in an MRI, and able to commit to exercise classes three days a week for three months.

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 3 months (40 visits including pre and post assessments). The researchers will ask you to do the following: cognitive, motor, and fitness assessments, an MRI, and exercise sessions 3x a week.

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. All studies have some risks. Some risks are relatively small, like being bored or losing time. 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

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 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: Graded Intensity Aerobic Exercise to Improve Cerebrovascular Function and Performance in Aged Veterans

PRINCIPAL INVESTIGATOR: Joe Nocera, PhD

SPONSOR'S NAME: Department of Veteran Affairs

PURPOSE:
You are being asked to volunteer for a research study. Please carefully read this consent form. Before you decide to take part, discuss any questions or concerns with the research staff. If you agree to be in this study, you will need to sign this consent form and a HIPAA form before starting in the study.

The purpose of this study is to look at the impact of aerobic exercise on cerebrovascular health. We will use brain imaging along with cognitive and behavioral tests to study the impact. We will recruit up to 134 healthy adult participants ages 18-80 years old. The results of this study should help improve our understanding of how exercise impacts brain health as we age.

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?:
This table is an overview of the study activities. A full description of the activities follows the table.

Study visits	Activity	Location	Time it will take
Assessment 1 (Baseline)			
Day 1	Consenting Study tests: Questionnaires, Behavioral tests, Physical Fitness Assessment, Motor Tests	Atlanta VA, GRECC, or through phone and video communication	2 hours
Day 2	MRI Finger stick	Emory University Hospital (EUH)	2 hours
Intervention 1			

Months 1-3	Aerobic Exercise **OR** Interval Training	Atlanta VA or GRECC	3 days a week, 60 minutes/session
Assessment 2			
Day 1	Study tests: Questionnaires, Behavioral tests, Physical Fitness Assessment, Motor Tests	Atlanta VA, GRECC, or through phone and video communication	2 hours
Day 2	MRI Finger stick	EUH	2 hours

ASSESSMENTS

Day 1: Questionnaires and Behavioral Tests

All the activities on Day 1 occur at the Atlanta VA or through phone and video communication and will take about two hours to complete.

- Questionnaires: We will conduct a review of your current health and medical history including potential exclusion criteria (e.g.: chronic illnesses, medications, and HIV Status), and ask questions about physical and cognitive (memory, attention, processing speed) functioning.
- Cognitive (thinking) tests: These tests are designed to examine your memory, planning and language abilities.
- Body Measurements: Height and body weight measurements will be taken.
- Hand movement tests: These test qualities of the neuromuscular system of your hand, such as dexterity, strength and coordination. You may request rest breaks between each task, and of course, may stop at any time.
- Physical fitness assessment: This assessment will be used to estimate your fitness level and will include the following:

    - 400 Meter Walk*:* You will be asked to walk at your usual pace, without overexerting. You can stop for up to 1 min for fatigue or other symptoms. You will be allowed to use a cane if you feel unsafe.

    - Walking and Walking While Talking*:* Participants will be asked to walk across an electronic walkway which captures walking speed and foot placement in a quiet well-lit hallway wearing comfortable footwear. You will be asked to recite alternating letters of the alphabet while walking.

- Short Physical Performance Battery (SPPB): The SPPB is based on a timed short distance walk, repeated chair stands and a balance test. The battery will be administered by a trained and certified examiner.

- The Activities-specific Balance Confidence (ABC) Scale*:* The questionnaire will ask you about perceived difficulties in general activities of daily living during the last month.

- Sit and Reach Test*:* This test assesses the flexibility of the lower back and hamstrings. Participants will sit on the floor and reach as far they can towards their toes. The test will be performed three times while measuring the distance reached.

- Functional Reach Test*:* This test will assess participants' balance and functional mobility by having them stand perpendicular to a wall and reach out as far as possible.

- Leg Press: An assessment of bilateral leg movement function will be completed using the Keiser Leg press.

- Maximal Treadmill Exercise Test: You will complete a maximal treadmill exercise test to determine peak oxygen uptake (VO2 max). You will wear a breathing apparatus to measure your oxygen, carbon dioxide, and ventilation. A registered nurse will be present for the entire test and manually monitor blood pressure at baseline and during each stage of exercise, as well as monitor continuous EKG recordings.

- Submaximal Treadmill Exercise Test*: (For participants unable to complete a maximal test)* This test will examine estimates VO2max using an "extrapolation" method. This test will provide an indication of aerobic capacity and will be used to set subjects' individual target training zone for exercise training. Heart rate monitors will be used to ensure subjects are maintaining their target heart rate and to prevent heart rate increases above levels that are considered safe.

You may be asked to complete cognitive, motor, and physical function (fitness) assessments. If you have participated in Dr. McGregor's study, "Effects of Acute Exercise on Functional Magnetic Resonance Spectroscopy Measures of GABA in Aging and Chronic Stroke" (IRB00001334) we may obtain your data from your assessments. We will only share this data to decrease participation burden.

Day 2: Magnetic Resonance Imaging (MRI)
The MRI test takes place at Emory University Hospital, 1364 Clifton Road, Atlanta, GA 30322. You will complete an MRI screening evaluation before you are put in the MRI scanner.

For the MRI, you lie down on a special table that slides inside the MRI scanner. You will be asked to stay very still during the scan. The space within the magnet is small. If you feel claustrophobic (uncomfortably confined), you can stop at any time. The MRI scanner makes loud repetitive tapping sounds when in use. You will be required to wear earplugs and protective ear coverings for hearing protection. You may be fitted for a bite bar in order to keep your head from moving during the scans.
During the MRI, you will be asked to do memory tests similar to those you will perform outside the MRI during the cognitive evaluation. These tests will examine your memory as well as your thinking and language ability. For a few minutes of scanning, we will ask participants to breath via a mask air richer in CO_2 than normal atmospheric air (5-8%). CO_2 will be administered by Center for Systems Imaging nursing staff.
We will do a simple finger stick for a drop of blood to measure your hematocrit level. Hematocrit level can impact flow which is what we are measuring with the MRI.

Blood Draws
Three times over the course of the study, you will be asked to come to the laboratory after an overnight fast and have your blood drawn. For each blood draw, using one venous port we will collect 10mL of blood (~1-2 teaspoons), for a total of 40mL (~4-8 Tablespoons). The following is a list of what happens at each of the blood draw visits.

Saliva Collection
We will ask you to provide 3mL of saliva. We will collect them in a 15mL sterilized tube and immediately placed on ice and stored at -80 degrees for subsequent analysis. We will collect saliva at week 1, week 6, and week 12 at the blood draw visit.

Week 1: Taken immediately prior to exercise, immediately post, 15 min post, 30 min post.

Week 6: Taken immediately prior to exercise, immediately post, 15 min post, 30 min post.

Week 12: Taken immediately prior to exercise, immediately post, 15 min post, 30 min post.

INTERVENTIONS

At the beginning of this study, you will be randomized (like the toss of a coin) to an exercise group for the study. The aerobic and stretch sessions will meet at the Exercise Lab of the Atlanta VA Rehab R&D Center or the Geriatric Research Education and Clinical Center (the

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GRECC), an Atlanta VA affiliate. You can also choose to have your sessions held remotely. You will wear the Polar Tracker heart rate tracker during each exercise session. The tracker will allow the team to track and record your heart rate throughout the exercise session.

Intervention Groups

Aerobic Exercise

You will participate in an aerobic exercise program using a stationary bicycle 3 times a week, for 12 weeks. Over the 12-week period, you will gradually progress in your exercise difficulty and time. Generally, you will start with about 20 minutes per session and increase to a maximum of 60 minutes per session. Trained staff members will give you instructions throughout each exercise session. Before each exercise session, you will do a warm-up activity for your legs. You may request rest breaks and you may stop at any time.

Interval Exercise Group

You will participate in an interval exercise group 3 times a week, for 12 weeks. Over the 12-week period you will do progressive whole body stretching, toning and balance exercises designed for individuals 60 years and older. You will start with 20 minutes per session and increase to a maximum of 60 minutes per session. Trained staff members will give you instructions throughout each exercise session. Before each exercise session, you will do a warm-up activity for your legs. You may request rest breaks and you may stop at any time.

Remote Exercise Monitoring

As an alternative, participants that are uncomfortable with receiving face-to-face training within the hospital will be given the option to continue their exercise intervention visits remotely. For participants that have been randomly assigned to the ‘spin’ exercise training program, will be provided a stationary cycle ergometer that has been sanitized properly to use during the 12-week period. All subjects will be monitored and trained through VA and Emory approved remote access sites.

Control Group

A random subset of participants will be in a 12-week wait-list control. These participants will undergo the same screening procedures as described above without cognitive or physical function testing. After 12 weeks you these participants will complete the pre-assessment and 12-week exercise intervention.

We will ask you to return after the exercise period to complete the final assessments for this study.

Apple Watch

Some study participants will be asked to wear an Apple Watch. Some individuals will also be loaned an iPhone. Before taking home the Apple Watch (and iPhone, if applicable), you will be asked to sign a form indicating that you understand the item(s) is/are being loaned to you and must be returned. A member of the study team will setup the Apple Watch for your use and will explain how to use the Watch. Setup will include entering your height, weight, and year of birth. The Watch will collect your daily total activity level. During Assessment 1 we will also schedule when you will return the Watch/iPhone to the study team. While you are in possession of the Watch, we ask that you wear it every day.

RISKS:

You may experience some frustration during the cognitive testing. You will be given breaks during testing and allowed to express any frustration.

Risks with Exercise

During any type of exercise, your heart rate and blood pressure will change. Because of these changes, there is a minimal risk of cardiac event or heart attack. Although any exercise program carries the possibility of a cardiac event, we minimized this risk by requiring you to be cleared by a doctor. We will instruct you in proper exercise procedure. While at the VAMC, you will be monitored throughout all exercise activity by research staff trained in cardiopulmonary resuscitation (CPR). Furthermore, when at the VA Medical Center, there is access to a full medical code response should an untoward event occur.

Risks with Magnetic Resonance Imaging (MRI)

An MRI scan exposes you to strong magnetic fields. There is no evidence that this is directly harmful to you. Strong magnetic fields are capable of moving metal objects. Therefore, if you have any metal objects or fragments in your body, other than dental work, or you have a cardiac pacemaker, you must let us know so we can cancel this test. The MRI scan is conducted like a CT scan but the area in which you lie is quite confining and some people experience claustrophobia, that is discomfort in enclosed spaces. If you are affected in this way, it will be important for you to let us know, as this could adversely affect the results of the study and would lead us to discontinue our research with you.

The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of individuals. You will be given hearing protection to reduce this risk. You may experience a temporary decrease in your hearing abilities accompanied by a ringing in the ears. This should stop within 48 hours from the time you were scanned. If this does not stop within 48 hours please contact Dr. Joe Nocera, Principal Investigator of this study at 404-321-6111, ext. 206354.

You should stay away from loud noise environments for 24 hours after you have been scanned. Examples of a loud noise environment include mowing the lawn, riding on a

motorcycle, and attending a music concert or sporting event. If you must be in a loud noise environment, you should use hearing protection. We will provide you with foam earplugs for this purpose and we will show you how to use them.

The reported potential side effects of the CO_2 mask may include a feeling of dizziness, faintness, or anxiety during CO_2 inhalation.

Risks with Blood Draw and Finger Stick

The risks of drawing blood from a vein include discomfort at the site of injection; possible bruising and swelling around the injection site; rarely an infection; and, uncommonly fainting from the procedure. A trained phlebotomist will collect all blood samples following standard protocol.

The finger stick for blood testing is a minimally invasive procedure that may result in slight discomfort that includes mild momentary pain at the skin site.

Risks with Apple Watch

People with skin sensitivities could experience skin irritation from wearing an Apple Watch. This risk can be reduced by keeping the watch band clean and dry. Anyone with a nickel or methacrylate allergy should confirm when first wearing an Apple Watch that it does not irritate his or her skin. Please stop wearing the Apple Watch if you experience any redness, itching, swelling, or other signs of skin irritation. Continuing to wear the Watch could worsen these symptoms.

Electromagnetic fields coming from the Apple Watch can interfere with pacemakers, defibrillators, and other medical devices. Please keep the Watch, band, and charger a safe distance from any medical devices (as specified by the medical device manufacturer), including others' medical devices. Stop using the Watch and its accessories if you suspect they are interfering with a medical device.

Information on safe handling of the Apple Watch can be found here:
http://help.apple.com/watch/#/apdcf2ff54e9

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 may be no direct benefit to you from taking part in this study. You will receive information on your physical fitness levels and the results will be discussed with you. You also will have the opportunity to participate in a physical activity program with professional supervision.

This research study will ultimately lead to a better understanding of how the brain works as well as the impact of exercise on brain function. We hope that one day this knowledge will in turn lead to improvement of rehabilitation techniques for older adults, neurological impairment, or after brain injury and spinal cord injury.

COMPENSATION:
You will be compensated $50 for your time after completion of the initial assessments (Assessment 1). You will receive $100 for your time after the follow-up testing sessions (Assessment 2). A check will be mailed to you 4 – 6 weeks after each assessment period.

You will get emergency medical care if you get injured from being in this study. Under Federal Law, you will qualify for follow-up treatment if the injury was related to the research study. You may or may not get further compensation if you are injured in this study. This rule would not apply if you do not follow study procedures. If you believe you have been injured by this research, you should contact **Dr. Joe Nocera, the Principal Investigator, at 404-321-6111, ext. 206354.**

COSTS:
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.

ALTERNATIVES: There are no alternative treatments to those offered in this research study.

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

- 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, HIV status, drug, alcohol or STD treatment, genetic test 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 Inspector General, the Government Accountability Office (GAO), and Emory University.

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

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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, Dr. Joe Nocera at the Atlanta VA, and his or 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: 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.

IDENTIFIABLE PRIVATE INFORMATION OR IDENTFIABLE SPECIMENS:
Identifiers might be removed from the identifiable private information that are collected. After that removal, the information 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 or if you have been harmed from being in this study, call **Dr. Joe Nocera at 404-321-6111, ext. 206354.**

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 Emory Institutional Review Board (404) 712-0720 or toll free at 1-877-503-9797, □ The VA Research Compliance Officer at (404) 321-6111 ext. 206964, or □ The VA Clinical Studies Center Director 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:
Participation in this study is voluntary. You have the right to refuse to be in this study. You can stop at any time after giving your consent. Whatever you decide, you will not lose any benefits to which you are entitled, nor are there any medical consequences associated with

your nonparticipation. The study investigator and/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. You may be withdrawn from the study for other reasons, for example: if you are unable to understand directions for the study

- if you are unable to fit into the MRI scanner
- if you show signs of significant discomfort from the procedures
- if your medical history indicates scanning is not safe for you
- if your performance on tasks administered outside the scanner does not meet established enrollment criteria

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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