Informed consent

ID: C1924-P Bridging Animal and Human Models of Exercise-induced Visual Rehabilitation NCT02911805

14 May 2017

ATLANTA VA HEALTH CARE SYSTEM

Consent to be a Research Subject

Title: Aerobic Exercise and Cognitive Training in Older Adults (parent project for *Bridging Animal and Human Models of Exercise-induced Visual Rehabilitation*)

Principal Investigators: Joe Nocera, PhD (MPI: Jeff Boatright, PhD (Atlanta VA Rehab R&D Center)

Sponsor's Name: Department of Veterans Affairs

Introduction/Purpose:
The purpose of this research study is to see if aerobic exercise can improve brain function and vision in older adults. Testing will take place at the Atlanta VA Health Care System or through phone or video communication.

You are being asked to be in this research study because you are an adult aged 18-89. The study will require visits for 14 months total; 1 week (2 days total) for pre-intervention assessment, 6 months of intervention (3 times per week), and 1 week (2 days total) for post-intervention assessment. There will be about 200 people volunteering for this study over a five-year period of time.

Procedures:
Before you may begin this study, we must receive written approval from a doctor that it is safe for you to participate in the exercise intervention and/or the fitness assessment. We will describe the study in writing to the doctor. Following receiving clearance and agreeing to participate in the study you will undergo a brief cognitive examination and questions about your how commonly you do physical activity. If it is revealed that you are not eligible or if it is not safe for you to participant in this study, we will not continue. However, we appreciate your interest and willingness to take part in the study.

If you are approved to continue, you will take part in 2 pre-intervention (before 6-month exercise) visits. The visits will be conducted at the Atlanta VA Health Care System, the Geriatric Research Education and Clinical Center (the GRECC, an Atlanta VA affiliate), or through phone or video communication. These 2 meetings will take place over the course of 2 weeks. Each session will be on a separate day and will last not more than 2 hours. Following this you will be randomly assigned (much like the flip of a coin) to either take part in 6-month aerobic exercise intervention or 6-month of stretch and balance. At the midpoint, the 3-month point, you'll engage in a short assessment visit including a blood draw, saliva collection and visual assessments. Following completion of your 6-month intervention you will take part in 2 post-intervention (after 6-month exercise) assessment days that will follow an identical format

as the 2 pre-intervention assessments described below.

Pre-intervention Assessment- Day 1: Cognitive and Visual Assessments
You will first complete questionnaires about your medical history, physical and cognitive (memory, attention, processing speed) functioning. Measurements of your height, body weight, blood pressure, and pulse rate will also be taken. We will also evaluate your vision and evaluate your knowledge of your spatial environment. These evaluations will take about 3-4 hours.

Cognitive Function Assessment
We will ask you to complete multiple cognitive (brain function) evaluations. These evaluations are designed to examine your memory as well as your cognitive and language ability. Some will be pencil and paper type tests, some will require you to verbally respond to a question and some will be conducted on a computer. A research assistant will be with you at all times. You may request rest breaks between each task, and of course, may stop at any time.

Visual Assessments
-Contrast Sensitivity-Visual Acuity, Amsler grid: You will look at an illuminated screen and/or chart, one eye at a time while wearing your normal eyeglasses/contacts. We will test how pale of a target you can see, how small a target you can see, and the appearance of a grid pattern. These tests will take about 1 1/2 hours.

-Low Luminance Questionnaire: You will be asked to complete a Low Luminance Questionnaire that asks several questions about your ability to see in various lighting conditions.

-Dark Adaptometry: Dark adaptation or night vision is known to be affected with increasing stages of age-related macular degeneration (AMD). This test will probe the ability of your eye to dark adapt, and it will require for your pupils to be dilated. You will be asked to place your head in a chin rest in front of the machine. Each eye will be tested individually, and the opposing eye will be covered with an eye patch. After dilation, while fixating on a light at the back of the machine, a bright flash will be presented to bleach the photoreceptors in your eye and then you will be presented a series of dimmer circular spots that you will be asked to identify whether you saw or not by pushing a response button. The duration of the test is about 5 minutes per eye. Corrective lenses may be put in the machine in front of your eye to correct for blur if necessary.

-Eye Photography: A series of photographs will be taken of your eyes. For this test, your pupils will be already dilated from the previous exam. You will be asked to place your head in a chin rest in front of a special camera called a scanning laser ophthalmoscope/optical coherence tomography machine (SLO/OCT). You will look at a point of light and the back of your eye will be imaged. The SLO/OCT is used routinely in eye doctor's offices and vision clinics. It is safe and requires no contact with your eye. The imaging will take no longer than 30 minutes.

Pre-intervention Assessment- Day 2: Physical Function Assessment
For the second pre-intervention assessment you will complete a treadmill test designed to assess your fitness level. Additionally, you will complete an evaluation of your balance and walking ability. The total time for the Day 2 assessment will be approximately 2 hours.

Fitness Assessment*:*

- 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.

Balance *&* ***Walking Ability****:* We will also ask you to walk for 400 meters (4 football fields) at your usual walking pace. The maximum time you will walk during this test will be 15 minutes. We will also ask you to walk for 30 seconds while talking or performing memory test, for example, counting backward by 3's. You will also be asked to rise up from a seated position for 1 minute. And lastly, you will be asked to perform a series of balance tests. A trained staff member will be next to you at all times in case you lose your balance.

Intervention Groups
Following the 2 days of pre-intervention assessment you will be randomly assigned (much like the flip of a coin) to either take part in 6-months aerobic exercise or a 6-month stretch and balance group. The aerobic and stretch sessions will meet at the Exercise Lab of the Atlanta VA Rehab R&D Center or the GRECC. 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.

Aerobic Exercise
If assigned to this group, you will participate in a 6-month, 3 times week aerobic program following the guidelines provided by the American College of Sports Medicine (ACSM) for optimizing cardiovascular fitness. Thus, exercise intensity will begin at low levels (50

percent of your resting heart rate) and increase to no greater than 80 percent of your resting heart rate. Exercise time will progress, depending on your progress, from an initial 20 minutes per session to a maximum of 60 minutes. Trained staff members will give you instructions throughout each exercise session. All sessions will meet at the Exercise Lab of the Atlanta VA Rehab R&D Center. Prior to beginning each exercise session you will be instructed on a warm-up focusing on preparing the legs for activity. You may request rest breaks and any time, and of course, you may stop at any time.

Balance and Stretch

If assigned to this group, you will participate in a 6-month, 3 times per week stretch and balance program that will take place in the Exercise Lab. This group will complete activities designed to increase flexibility and range of motion. Prior to beginning each exercise session, you will be instructed to warm-up. You may request rest breaks and any time, and of course, 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.

Blood Draws

During 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, 10mL of blood will be taken (~1-2 teaspoons), for a total of 40mL (~4-8 Tablespoons).

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.

Blood and saliva will be collected at three time points; prior to starting the intervention, at the 3-month (midpoint), and within the last week of the 6-month intervention completion date.

Risks:

Your eyes may get tired during testing. If you get tired, or your eyes get tired, you may stop and rest at any time. If you would like, you can stop the testing and continue at another time. The anesthetic eye-drops and dilating eye-drops for the dark adaptation and eye photography (SLO/OCT) are drops routinely used for eye exams when you go to the eye doctor (your

ophthalmologist or optometrist). The most common side effects include blurred vision, sensitivity to the bright lights, and mild stinging. Much less common side effects include dry mouth, tachycardia (fast heart rate), headache and allergic reaction.

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.

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.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform Joe Nocera (listed on page 7 of this consent form) or the person reviewing this consent with you before enrolling in this or any other research study or project.

There may also be risks or discomforts that are not yet known.

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 supervised 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.

Confidentiality:
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 study records including:

- The sponsor of the study: Department of Veterans Affairs
- The Office for Human Research Protections
- The Government Accountability Office (GAO)
- The Office of Research Oversight (ORO)
- The Inspector General
- The Emory University Institutional Review Board and other offices in Emory University that help run and/or oversee studies
- The Atlanta VA Research Compliance Officer
- VA research staff with the VA Hospital or at Emory University (when data is stored at Emory)
- Any appropriate state or federal government agencies that make rules and policy about how research is done that are not listed above

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.

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 you have received this notice.

If you are in an FDA sponsored clinical trial: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Compensation/Costs:

You will be compensated $50 at the conclusion of your pre-assessments, $50 after the 3-month blood draw, and $50 at the conclusion of your 6 month intervention-assessments.

Compensation will be provided in the form of checks, which will be mailed to you. There will be no cost to you. The Department of Veterans Affairs Rehabilitation Research and Development Service is funding all costs of this project.

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.

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.

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:

- Joe Nocera, PhD, the Principal Investigator, at (404) 321-6111, ext. 206354

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

  Or

- The Research Compliance Officer at (404) 321-6111 ext. 206964 or the 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. If you decide to be in the study and change your mind, you have the right to drop out at any time. Whatever you decide, you will not lose any benefits to which you are entitled nor are there any medical consequences associated with your non-participation. 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 the following reasons:

(1) if you are unable to understand directions for the study
(2) if you show signs of significant discomfort from the procedures
(3) if your performance on tasks does not meet established enrollment criteria

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** **Time**
(to be entered by Participant)

_____
Name of Approved Individual Obtaining Consent

_____ _____ _____
Signature of Approved Individual Obtaining Consent | Date | Time
(to be entered by Approved Individual)

An Approved individual is one who has completed HRPP training and is officially approved to consent subjects for this specific study. The signature and date of this individual certifies that this is the most current approved consent document for this study.