

Informed Consent Form

Title: Exercise for Brain Health with Increased Genetic Risk for Alzheimer's Disease

Clinical Trials.gov: *NCT03727360*

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Initials: _____ Date: _____

Institutional Review Board

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CONSENT TO PARTICIPATE

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| Project Title | Exercise for Brain Health in the Fight Against Alzheimer's Disease |
| Purpose of the Study | <p><i>This research is being conducted by J. Carson Smith, PhD, at the University of Maryland, College Park. We are inviting you to participate in this research project because you are a healthy older adult between the ages of 60 and 89.</i></p> <p><i>The purpose of this research project is to measure the effects of 6-months of exercise on your mental and physical abilities, and your brain function and brain structure using Magnetic Resonance Imaging (MRI).</i></p> |
| Involves | <input type="checkbox"/> Functional Magnetic Resonance Imaging (fMRI) |
| Procedures | <p><i>This study begins with three days of baseline testing within about one week, including a 4-hour visit on the first day, a 2-hour visit on the second day, and a 1-hour visit on the third day.</i></p> <p><i>After the baseline testing, you will participate in a 6-month exercise training program, starting with two 30-min sessions per week increasing to four 60-min sessions per week.</i></p> <p><i>Your participation will end with three days of 6-month follow-up visits, including a 4-hour visit on the first day, a 2-hour visit on the second day, and a 1-hour visit on the third day.</i></p> <p><i>This study involves the use of MRI, which will involve the following procedures:</i></p> <ol style="list-style-type: none"><i>1. The MRI scans usually last approximately 75 minutes and will never last longer than 2 hours. You will be asked to participate in two MRI sessions taking place on different days. If technical difficulties arise in these two sessions, you may be asked to participate in up to four sessions.</i><i>2. Before entering the MRI magnet room, you will be required to complete an MRI screening checklist, which ensures that it is safe for you to enter the machine.</i><i>3. After completing the checklist, you will be asked to remove all metal objects from your person. MRIs are known to blank out magnetic strips on credit cards, so you must leave your wallet as well as your watch and any other metallic object outside the magnet room (you can place it in a locked cabinet which we will provide to you).</i> |

4. *For the MRI scan, you will lie on the patient bed, and be given instructions either to just relax throughout the scanning procedures or, for example, to view or listen to stimuli, and in some cases, respond (e.g., using a response keypad or other equipment, or hand signals). For head/brain MRI, an MRI head coil will surround your head (a head coil is an apparatus that is used to measure signals emitted from your brain). Your head will be supported with foam pads to make you more comfortable and to help you to keep your head still. Pillows and other cushions may be used (e.g., under your knees) to make you more comfortable.*
5. *You can end your participation at any time. You can be heard in the control room on a speaker system. Also, you will be provided with a squeeze bulb which you can squeeze to let the MRI operator know that you need attention. If you signal that you wish to stop the scanning, the operator will immediately enter the magnet room and assist you in exiting the MRI and patient bed.*
6. *When the MRI takes images, it makes loud buzzing and clicking noises. You will be given ear-protection to make the noise tolerable.*
7. *For the study, you will be shown the names of people, and asked to identify names of famous people and not famous people during one of the scans. For another scan, you will be asked to press a button to indicate the direction of an arrow on the screen. Other times, your job will be to look at a cross on the screen, and to always do your best to keep your head still.*

If you are unable to receive an MRI scan due to safety concerns, you may still participate in the study without receiving an MRI.

Additional Cognitive, Physical, and Exercise Testing

1. *Today's visit, after you consent to participate, will take about one hour. You will complete a few brief questionnaires about your health and cognitive abilities, and if you have never walked on a treadmill, you will have the chance to practice walking at a slow pace for a few minutes. Next, we will ask you to provide a small saliva sample using a cotton swab. The saliva sample will be used to obtain a DNA sample. This will take about 5 minutes. We will use a sterile collection kit containing a cotton swab, which will be used to rub the inside of your cheek. You will not receive the results of the genetic tests because we are not an approved clinical testing facility. We will be testing your DNA for genes that are related to the risk for cognitive decline.*
2. *The next visit, baseline day 1 testing, which will last approximately 4 hours, will consist of several cognitive tests and questionnaires about your mood state, and also tests of your*

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| | <p><i>physical abilities and balance. The cognitive tests, for example, will involve remembering a list of words or a story. The mood tests will ask about how you have been feeling for the past week, and also about your perceived mental and physical health. The physical tests will include walking for 6 minutes, and other tests that involve walking and reaching. We will give you clear instructions about each test, and breaks will be provided as needed. Some of the tests will be audio recorded, but the audio recordings will not identify you by name.</i></p> <p>3. <i>Lastly on baseline day 1, you will complete an exercise stress test that involves walking on a treadmill. While you are walking, you will breathe through a tube that looks like a snorkel, while your nose is pinched close, and you will wear sensors that will measure your heart rate. The steepness of the treadmill will gradually increase as you walk until you reach 85% of your maximum heart rate, or until you tell us that you cannot continue to walk. We will also stop the test if we determine that you may be at risk for injury. We will ask you to rate your level of effort as you walk, and will monitor your heart rate and blood pressure. The exercise test usually takes less than 12 minutes, and no more than about 18 minutes.</i></p> <p>4. <i>The baseline day 2 testing, which occurs within one week after baseline day 1, will involve the MRI scan session, described above, and will take about 2 hours. You will be provided with an orientation to the MRI scanner, and practice with the tasks given during the scan.</i></p> <p><i>The baseline day 3 testing will consist of providing a blood sample and obtaining measurements of your blood vessel function. The blood sample will be stored for later analysis of additional genetic factors and blood proteins that may emerge as important predictors of brain health. You will be asked to arrive in a fasted state by not eating or drinking anything after midnight the night prior to your appointment. We will draw about 130 ml of blood, which is equal to about 9 tablespoons. The blood samples will be analyzed at UMD, and also sent to the Cleveland Clinic Biobank for processing and secure confidential storage. Your blood samples may be made available for future research, but your name or identity will never be shared. You will receive an additional payment of \$50 after each blood draw, at baseline and after 6 months of exercise.</i></p> <p><i>Please initial here to indicate your consent for the blood draw:</i></p> <p>_____</p> <p><i>Immediately after the blood draw, your vascular function will be tested using noninvasive ultrasound equipment. While laying on your back, an inflatable cuff will be placed on your forearm. An ultrasound probe will be used to find a blood vessel in your arm</i></p> |
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| | <p><i>(brachial artery) and measure its ability to enlarge (dilation). The cuff on your forearm will be inflated to 220mmHg for five minutes. Once the cuff is released, we will measure the size of your artery for another two and a half minutes. After this, the ultrasound machine will also be used to measure the size and blood pressure of a blood vessel in your neck (carotid artery). We will also be measuring how fast blood travels in your arteries using a small hand held pencil device. The recordings will be performed at the wrist, neck and the femoral (groin) artery. The femoral measurement is done in an automated manner using a leg cuff.</i></p> <p><i>Handgrip Exercise: You will be asked to squeeze a handgrip strength-measuring device at 30% of your maximal strength for several minutes. Immediately after you stop squeezing the device, we will inflate the cuff on your arm to 220mmHg for 90 seconds. If you experience pain or discomfort, please communicate with researchers so that we can pause or terminate the test.</i></p> <p><i>Heart rate and beat-to-beat blood pressure measurements will be taken through the duration of the visit by placing a small Velcro cuff around the top of your middle finger. The cuff is very sensitive to movement, so you will be asked to keep your hand/arm as still as possible. If you are feeling too uncomfortable with the finger cuff, we can remove it for you at any time.</i></p> <p><i>Four ECG electrodes will be placed under your shoulders and on each side of your stomach to record a single lead ECG tracing for 5 minutes during rest and throughout the isometric handgrip exercise test. During the 5 minutes of rest, the number of breaths will be counted by watching the rise and fall of your abdomen.</i></p> <p><i>5. The order of the exercise testing, MRI scans, and blood draws may vary. You will be contacted by phone or email by the study staff to schedule these three days of tests, and again after the 6-month exercise training program has ended. It may take between 30-90 days before we can schedule your first baseline test day. We will pay for your parking for all visits to the UMD campus.</i></p> |
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| | <p>Exercise Training for 6-months, 4 days per week</p> <ol style="list-style-type: none"> <i>1. You will be assigned to one of two possible exercise training programs, both of which are expected to have health benefits.</i> <i>2. If you are assigned to the first group, the sessions will end with 20-minutes of flexibility stretching. If you are assigned to the second group, the sessions will end with a 20-minute walk on the treadmill, at a pace tailored to your ability.</i> <i>3. Both programs begin with the same procedures; a warm-up and light stretching, followed by low intensity callisthenic types of arm and leg exercises in a seated or standing position.</i> <i>4. The sessions will start slow and easy (30 minutes 2 days per week) and gradually increase in duration and to a moderate intensity (60 minutes 4 days per week). The exercises will be supervised by one of the study staff, and will be conducted in small groups. We will monitor your heart rate and ask you about your feeling of effort during each session.</i> |
| <p>Potential Risks and Discomforts</p> | <p>There may be some risks from participating in this research study.</p> <p>Potential risks and discomforts related to MRI are as follows: MRI screening interview: You may be uncomfortable completing the interview. For instance, there are questions about the existence of tattoos and piercings on your body. You may choose to not answer questions that make you uncomfortable, but in that case you will not be able to participate in the experiment.</p> <p>The Maryland Neuroimaging Center (MNC) is not a medical facility, does not do clinical work, and an MRI scan at the MNC is not a medical test. It is designed to address research questions and it is not the kind of scan that can be used for any clinical purpose. In fact, if there is an unusual finding in the scan, the MRI technician, or the researcher may not even detect it. However, if the technician or researcher sees something in the scan that appears unusual, the scan will be sent without any personal identifiers to a certified neuroradiologist at the University of Maryland Baltimore School of Medicine (UMB) for further review. If the neuroradiologist concurs that this unusual finding should be investigated further by a physician, you will be notified by the principle investigator leading the study.</p> <p>MRI has not been shown to produce health problems in normal, healthy individuals. The scanner does not produce ionizing radiation. No medication, needle stick, or injections of drug or contrast agents are involved. There are hundreds of scanners of this type used in the U.S. and abroad, both to assist doctors in clinical diagnoses and for research.</p> <p>Because of the strong magnetic fields used for MRI scanners, persons who have magnetic life-support devices (e.g., pacemakers and aneurysm clips), metal prostheses or other metallic objects (e.g. cochlear implants, steel pins implanted to help repair and strengthen</p> |

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| | <p>broken bones, metal fragments from previous injuries) cannot participate in the fMRI, but can participate in all other parts of the study.</p> <p>If you have used an IUD for birth control you will be excluded unless you can document the model of the IUD and we can verify its safety for the MRI environment.</p> <p>The radio frequency energy used in the MRI scan has produced burns (most of them minor) in about one in a million cases. If you feel any burning sensation you should immediately inform the staff, so that the scan can be terminated. In rare instances, warming of the skin has also occurred. If you feel any warming sensation, please inform the staff immediately, so that the scan can be interrupted.</p> <p>While there is no evidence of increased risk with multiple scans, the risks associated with multiple scans are not known.</p> <p>There are inherent risks associated with moderate and strenuous intensity exercise, including injury and, in rare instances, death. We will require consent from your physician stating that you may participate in moderate intensity exercise, and complete the submaximal exercise stress test. You will also perform warm-up exercises each session, in order to minimize the risk for injury, and the exercise program will start slowly, at a low intensity.</p> <p>You may feel faint during the blood draw. We will have you seated in a chair to minimize this risk. There are risks of infection from the blood draw; however, we will use standard sterile techniques to minimize risk of infection. Blood draws will be conducted by a trained phlebotomist.</p> <p>Before the ultrasound testing of your vascular function, we will explain to you when and where we will be placing the testing instruments. You will be encouraged to notify the researchers at any time if you feel too uncomfortable with the probe on your neck or blood pressure cuff around your arm or thigh.</p> <p>There is a chance of minor discomfort with the finger cuffs but there are no additional risks expected. If you feel too uncomfortable with the cuff on your finger, researchers will remove it immediately.</p> <p>Flow-mediated dilation: Should you feel too uncomfortable or are experiencing pain when the cuff is inflated on your arm, you will be encouraged to ask the researcher to end the test. Cuff inflation to 220 mmHg around the upper forearm is not known to cause any risks after occlusion is released. A pillow and blanket will be offered to you to use for the duration of the test to help you feel more comfortable and/or for increased privacy.</p> |
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| | <p>Carotid Artery Stiffness: Before the administration of this test, we will explain when and where we will be placing the probe on your neck. This will feel similar to taking your pulse with two fingers on your neck, and will not take longer than one minute. If at any time you become too uncomfortable with the probe on your neck, researchers will remove it immediately.</p> <p>Isometric Handgrip Exercise: During this exercise bout, you may feel fatigue or soreness in your forearms or hands; however, any fatigue or soreness will quickly dissipate afterwards. No additional risks are expected.</p> <p>There are no additional risks associated with the 3-lead ECG or the breaths per minute measurements.</p> <p>Please note: There may be increased risk by coming to campus due to the state of the COVID-19 pandemic. We take a number of precautions to minimize this risk, including the use of face coverings, allowing the area to settle between participants, using air purification systems, and sanitizing all surfaces after each participant. We also sanitize the computer and other surfaces touched by the researcher between launching the experiment and the participant using the area. However, the risks cannot be entirely eliminated despite these precautions.</p> <p>If your BMI is greater than 30, you are at increased risk for severe symptoms if you become infected with COVID-19. We are following all of the current recommendations, and University policy, to protect you and our research staff from COVID-19. There is a very low risk that you will be exposed to COVID-19 during face-to-face interactions with the researchers.</p> |
| Potential Benefits | <p><i>This research is not designed to help you personally, but the results may help the investigator learn more about how exercise affects brain function in older adults. In addition, you will be provided with a supervised exercise training program for 6 months, and a picture of your brain.</i></p> |
| Confidentiality | <p><i>Any potential loss of confidentiality will be minimized by using a unique identifier, and not your name, for all of your forms, papers, and electronic data records. Your study files will be stored on password protected and firewalled computers, or within locked file cabinets within secured laboratory space. Your saliva and blood samples will be marked with a unique identifier, and will be stored in a secured laboratory at the Cleveland Clinic Biobank. The Cleveland Clinic will conduct genetic testing on your blood and saliva samples. Members of the study team, including researchers at the Cleveland Clinic, will have access to your blood and DNA samples. Your blood samples may also be made available for future research without your consent, but your name or identity will never be associated with your blood samples. We will store your blood forever, to be used for future analyses for markers that may be related to changes in brain function after exercise.</i></p> |

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| | <p><i>With your initials below, you acknowledge and agree that your blood samples will be kept and used for future research, and that you may request that your blood and DNA samples be destroyed when they are no longer needed. _____</i> (initials)</p> <p><i>I do not agree to have blood samples stored for future research.</i> _____ (initials)</p> <p>Concerning the MRI portion of this study, potential loss of confidentiality will be minimized by storing the screening form in a locked cabinet at the MNC, and by storing MRI data in password protected and firewalled computers during the length of the study. At the conclusion of the study, all materials will be given to the PI for inclusion in the study's safeguarded record.</p> <p>If we write a report or article about this research project, your identity will be protected to the maximum extent possible. Your information may be shared with representatives of the University of Maryland, College Park or governmental authorities if you or someone else is in danger or if we are required to do so by law.</p> |
| Medical Treatment | <p>The University of Maryland does not provide any medical, hospitalization or other insurance for participants in this research study, nor will the University of Maryland provide any medical treatment or compensation for any injury sustained as a result of participation in this research study, except as required by law.</p> |
| Compensation | <p><i>You will receive a total of \$400, paid at different stages of the study as each stage is completed. You will be responsible for any taxes assessed on the compensation.</i></p> <p><i>If you do not receive the MRI scan, you will be compensated a total of \$300, paid at different stages of the study as each stage is completed.</i></p> <p><input type="checkbox"/> <i>Check here if you expect to earn \$100 or more as a research participant in UMCP studies in this calendar year. You must provide your name, address and SSN to receive compensation.</i></p> <p><input type="checkbox"/> <i>Check here if you do not expect to earn \$100 or more as a research participant in UMCP studies in this calendar year. Your name, address, and SSN will not be collected to receive compensation.</i></p> |
| Participation in other studies | <p>If you do not qualify for this study, can we contact you to participate in other studies? <input type="checkbox"/> yes <input type="checkbox"/> No</p> <p>Please initial here to indicate your consent: _____</p> |

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| Right to Withdraw and Questions | <p>Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify.</p> <p>If you decide to stop taking part in the study, if you have questions, concerns, or complaints, or if you need to report an injury related to the research, please contact the investigator:</p> <p style="text-align: center;">J. Carson Smith, PhD 4200 Valley Dr., SPH Bldg #255 College Park, MD 20742 carson@umd.edu; 301-405-0344</p> | |
| Participant Rights | <p>If you have questions about your rights as a research participant or wish to report a research-related injury, please contact:</p> <p style="text-align: center;">University of Maryland College Park Institutional Review Board Office 1204 Marie Mount Hall College Park, Maryland, 20742 E-mail: irb@umd.edu Telephone: 301-405-0678</p> <p>This research has been reviewed according to the University of Maryland, College Park IRB procedures for research involving human subjects.</p> | |
| Statement of Consent | <p>Your signature indicates that you are at least 18 years of age; you have read this consent form or have had it read to you; your questions have been answered to your satisfaction and you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.</p> <p>If you agree to participate, please sign your name below.</p> | |
| Signature and Date | NAME OF SUBJECT [Please Print] | |
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