CONSENT FORM

Title of Research: Effects of Exercise Training on Learning and Memory Outcomes in MS

IRB Protocol #: XXX-XXXXXXXX

Principal Investigator: Brian M. Sandroff, Ph.D.

Purpose of the Research

We are asking you to take part in a research study. The purpose of this research study is to compare the effects of two different 12-week long exercise programs (treadmill walking or stretching-and-toning) on cognitive (thinking) performance in persons with multiple sclerosis (MS). The study principal investigator will discuss with you your responsibilities as a participant. As a participant, you will complete one of these 12-week long exercise programs. This is important because exercise has been identified as a possible way to improve thinking performance in people with MS. There will be 40 participants enrolled at UAB.

Explanation of Procedures

If you agree to participate, during the course of this study, the following research procedures will occur during 40 separate visits to the laboratory over the course of 3 months:

The first visit will last about 3 hours in total and will occur at the UAB/Lakeshore Collaborative Research Center, located at 3810 Ridgeway Drive, Birmingham, AL 35209.

- On the first visit, you will first take a paper-and-pencil thinking test of how well you can remember a list of words.
  - Depending on your score on this test, you may be ineligible to participate in this study.
    - If this is the case, you will be paid $50 in the form of a check for your time.

- If you are eligible to participate based on that test, you will then undergo a brief examination, where a researcher will measure your reflexes, how well you can feel a light touch, your muscle strength, vision, and ask you some questions concerning your bladder/bowel function and thinking ability.

- You will then complete a brief questionnaire on whether or not it would be safe for you to undergo an MRI scan.
  - If it is unsafe for you to undergo an MRI scan, you will be ineligible to participate in this study, but you will be paid $50 in the form of a check for your time.

- You will then have your blood pressure measured when you are seated comfortably in a chair using an automated blood pressure cuff in order to ensure your safety in participating in the study.
If your blood pressure is too high (i.e., greater than 200/110), you will be ineligible to participate in this study, but you will be paid $50 for your time.

- If your blood pressure is below 200/110 at rest, you will then complete several computerized and paper-and-pencil thinking tasks that will take approximately 1 hour and will include the following:
  - A test of how well you can remember a list of words that is read to you out loud
  - A test of how well you can draw shapes from memory
  - A test of how quickly you can match shapes with single-digit numbers
  - A test of how quickly and accurately you can add up 2 numbers in a row, out loud, for 10 minutes
  - A test of how quickly and accurately you can recognize complicated images on a computer
  - A test measuring how well you can tell the difference between several arrows that look alike
  - A test of how many words beginning with a certain letter that you can name

- You will then undergo a six-minute long walking test which will be performed indoors, on a flat surface with no obstacles.
  - You will be asked to walk laps around a circle of cones and continue for 6 minutes.
  - You will be allowed to stop and rest during the test; however, the clock will not stop.
  - For your safety, study staff will stay close to you during walking trials.

- You will then undergo a brief test measuring how fast you can place pegs in and out of holes on a plastic peg board with each hand.

- You will then complete a maximal exercise test to determine your aerobic fitness level.
  - This test will involve fitting you with a mouthpiece to monitor your breathing and a heart rate monitor to assess your heart rate during exercise.
  - The test will require you to walk on a motor-driven treadmill at zero incline (flat), and after a 3-minute warm-up, the incline will continually increase until you can no longer continue to exercise.
  - The test should take approximately 10-15 minutes.
  - For your safety, two researchers will be present within an arm’s reach at all times during this test.
  - The researcher will end the exercise session early if you begin to feel uncomfortable.

Three (3) days later, you will visit the Civitan Neuroimaging Laboratory in UAB Highlands Hospital (1201 11th Ave S, Birmingham, AL 35205) to complete more tests of your thinking ability, walking speed, physical function, and an MRI/fMRI scan. This visit will last approximately 3 hours.

- First, you will complete several computerized and paper-and-pencil thinking tasks that will take approximately 1 hour and will include the following:
  - A test examining your language skills
  - A test examining how many different ways you can sort a set of cards
A test examining how quickly and accurately you can draw a line between dots
A test examining how well you can purposely remember some information while ignoring distracting information
A test examining how quickly you can analyze patterns of shapes and letters

Then, you will complete a short walking test measuring how fast you can walk over a 25-foot distance.

You will then undertake a short series of tests measuring how fast you normally walk, your ability to stand up and sit down in a chair, and your ability to balance with your feet together.

This will be followed by a short test measuring how flexible you are when sitting down.

You will then undertake an MRI scan.
- Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the brain.
  - fMRI allows the researchers to see what parts of the brain are used when you perform certain thinking tasks.
  - The MRI scanner is a metal cylinder surrounded by a strong magnetic field.

- During the MRI, you will lie on a table that can slide in and out of the cylinder.
  - A device called a “coil” will be placed over your head.
  - Before the scan, you will be told about the thinking tasks that you will do during the scan and you may have the opportunity to practice.
  - There is a computer screen that you will be able to see when you are inside the scanner.
  - The screen will show you the thinking tasks that you will do in the scanner.
    - These tasks include matching shapes and single-digit numbers, remembering a list of words, and recognizing complicated shapes as quickly and accurately as possible.

- You will be in the scanner for about 60 minutes.

- During the scan, you will undertake the 3 thinking tasks.
  - You will respond by pressing a button on a button box that will be attached to your hand with a Velcro strap.

- You may be asked to do these tasks, or you may be asked to lie still for up to 10 minutes at a time.

- While in the scanner, you will hear loud knocking noises and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan and you may ask to be moved out of the machine at any time.
It is very important for the experiment that you do not move your head or body inside the scanner.

- Padding, a vacuum bag, or expanding foam will be placed around your head to help keep it in position.
- You may also be asked to bite down on a mouth bar to help keep your head still.

For the next 12 weeks (i.e., 3 months), you will then be randomly picked (like the flip of a coin) by a computer to participate in one of two exercise groups.

- One group will complete an in-person treadmill walking exercise program, and the other group will complete an in-person stretching-and-toning exercise program
  - Both programs are based on activity guidelines for people with MS and will be led by trained exercise leaders.
  - You will have a 50/50 chance of being placed in either group.

- No matter which group you are assigned to, you will be asked to complete 36 exercise training visits (treadmill walking or stretching-and-toning) that will take place at the UAB/Lakeshore Collaborative Research Center.
  - This facility is located at 3810 Ridgeway Drive, Birmingham, AL 35209.

These visits will take place 3 days per week for 12 weeks and will each last approximately 1 hour in total.

These will be individual visits led by a trained exercise leader and will initially consist of 15 minutes of actual exercise and progress up to 40 minutes of actual exercise.

- Each visit will begin and end with a 5-minute warm-up/cool-down period.

During the initial visit, you will learn how to safely perform the exercises.

- You will be given a log book to monitor and record your progress.

For each visit, you will also be given individualized feedback and changes will be made to your program if needed.

Before you begin the first training session, you will complete two additional tests of how well you can remember information, and you will also complete a number of questionnaires that ask you about your everyday functioning, how you feel about your life, and your mood.

- You will then complete the first exercise session of either treadmill walking or stretching-and-toning exercise.

At the end of your 12-week training program, you will return to the UAB/Lakeshore Collaborative Research Center for a follow-up visit.
o This visit will last 3 hours where you will repeat the tests you completed during your initial visit.

- Three (3) days later, you will return to UAB Highlands Hospital for a final follow-up visit.
  o This visit will also last 3 hours where you will repeat the tests you completed during your second overall visit, and will also involve another MRI/fMRI scan.

- We are performing imaging solely for the research purposes described above. It is not a clinical scan intended for diagnostic or therapeutic purposes. The MRI scans that will be performed in connection with the study you are participating in are not necessarily equivalent to the type of MRI scans more commonly used to diagnose medical problems. Many potentially serious medical problems may be undetectable on the scans performed in the study.

- Under no circumstance will the investigator, research staff, or imaging staff interpret the scan as normal or abnormal. They are unable to make any medical comments about your scan. The scan will not be looked at or read for any healthcare treatment or diagnostic purpose. If you are experiencing physical symptoms or otherwise have concerns about your health, you should see your primary care physician or specialist physician. If you want your scan to be reviewed by a physician so the physician can look for medical issues, you can request a copy of your scan. We will provide an electronic copy at no charge.

 **Risks and Discomforts**

The study described above may involve the following risks and/or discomforts:

**Exercise:**
- With the completion of the maximal exercise test and exercise training visits, there are always risks of death, heart attack, arrhythmia, difficulty breathing, and complications that require hospitalization.

- All lab personnel in attendance are trained in CPR, AED, and First Aid.

- Importantly, it is still possible that you will experience some fatigue, sprains, cramps, and muscle soreness after the completion of the maximal exercise test and exercise training visits. Those responses can be temporary (i.e., for a few hours afterwards).

- Any possible symptoms associated with an increase in body temperature will be reduced by controlling the room temperature with air conditioning and using multiple fans.

- There is a small risk of falling, injury, head trauma, and death when performing a walking exercise on a treadmill. To minimize this risk, you will be encouraged to hold on to the handrails on the treadmill, as well as having a gait belt (i.e., a belt with handles on it where
spotters can provide physical support in case of a slip) around your waist, and a research assistant within arm's reach to quickly assist if you lose your balance.

- During the maximal exercise test, there may be some discomfort when wearing the mouthpiece.

MRI:

- People are at risk for injury from the MRI magnet if they have:
  - Pacemakers or other implanted electrical devices
  - Brain stimulators
  - Particular types of dental implants
  - Aneurysm clips (metal clips on the wall of a large artery)
  - Metallic prostheses (including metal pins and rods, heart valves, and internal hearing aids [cochlear implants])
  - Permanent eyeliner
  - Implanted delivery pumps
  - Shrapnel fragments
  - Welders and metal workers are also at risk for injury because of possible small metal fragments in the eye of which they may be unaware.

- You will be screened for these conditions before having any scan, and if you have any, you will not receive an MRI scan.

- If you have a question about any metal objects being present in your body, you should inform the study personnel.

- In addition, all magnetic objects (for example, watches, coins, jewelry, and credit cards) must be removed before entering the MRI scanning room.

- People with fear of confined spaces may become anxious during an MRI.

- Those with back problems may have back pain or discomfort from lying in the scanner.

- Some may experience dizziness or paresthesia (tingling or numbness).

- The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss.
  - Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let the study personnel know right away.
  - You will notify the investigators if you have hearing or ear problems.
• You will be asked to complete an MRI screening form for each MRI scan you have. There are no known long-term risks of MRI scans.

• It is not known if MRI is completely safe for a developing fetus. If you are a woman, you will have a pregnancy test before the MRI scan. Therefore, if you are pregnant, you will not be eligible to participate in the study.

Thinking tasks:
• You may also feel tired or experience mild frustration during the tasks designed to measure your thinking ability. This is because the tasks are often difficult. You will be allowed to take short breaks as necessary.

Walking tests:
• There is also a small risk of falling or injury during the six-minute or 25-foot walking test as well as the Short Physical Performance Battery. For your safety, study staff will stay close to you during the walking trials.

• There is also a risk of dizziness or fatigue. You will be permitted to take breaks as needed to minimize these effects.

• All study procedures and testing will be performed under supervision of qualified personnel.

Questionnaires:
• There is a small psychosocial risk associated with the completion of questionnaires such as embarrassment or anxiety in responding to some questions.

You will be assigned to an exercise group by chance, which may prove to be less effective or slightly more fatiguing than the other exercise group.

There also may be risks and discomforts that cannot be foreseen. You will be given more information if other risks are found.

Benefits

You may not benefit directly from taking part in this study. However, the beneficial effects of exercise training on general health are very well known. Further, this study may help researchers better understand the effects of exercise in persons with MS. The results of this research may also lead to more effective ways to treat individuals with MS.

Alternatives

The study principal investigator will discuss with you the alternatives to participation and their risks and benefits. The alternative is to not participate in the study.
Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. However, research information that identifies you may be shared with people or organizations for quality assurance or data analysis, or with those responsible for ensuring compliance with laws and regulations related to research. They include:

- the UAB Institutional Review Board (IRB). An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- the Office for Human Research Protections (OHRP).

The information from the research may be published for scientific purposes; however, your identity will not be given out.

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.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact the Principal Investigator if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study or if the Principal Investigator decides it is not in the best interest of your health.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. All tests, exams, and exercise related to this study will be provided to you at no cost during the 3-month study period. However, attending visits can involve some transportation costs (i.e., the cost of gas). But, parking will be free for each of the 40 visits you attend. The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.
**Payment for Participation in Research**

You will receive the following compensation: $50 after the baseline evaluation and MRI scan (i.e., the first 2 study visits); up to $360 at the conclusion of the 3-month exercise program (i.e., $5 for attending each exercise visit [up to 36 visits] plus an additional $5 for travel expenses per exercise visit; and $50 for after completion of the follow-up evaluation and MRI scan. This will total up to $460. Please ask the study staff about the method of payment that will be used for this study (e.g., check). The payment is prorated per visit in the event that you stop participating in the study or the investigator terminates the study.

**Payment for Research-Related Injuries**

UAB and EMD Serono, Inc. have not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

**Significant New Findings**

You will be told by the Principal Investigator or the study staff if new information becomes available that might affect your choice to stay in the study.

**Questions**

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Prof. Brian Sandroff, PhD by phone at 205-934-5972 or by email at sandroff@uab.edu.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

**Legal Rights**

You are not waiving any of your legal rights by signing this consent form.

**Signatures**

Your signature below indicates that you have read (or been read) the information provided above, including your responsibilities as a participant, the alternatives to participation, and the approximate number of subjects involved in the trial. Your signature below further indicates that you agree to participate in this study. You will receive a copy of this signed consent form.
AUTHORIZATION FOR USE/DISCLOSURE OF PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Participant Name: ____________________________  UAB IRB Protocol Number: XXX-xxxxxxxxxx
Research Protocol: Effects of Exercise Training on Learning and Memory Outcomes in MS  Principal Investigator: Brian M. Sandroff, Ph.D.

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your protected health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your protected health information may be used for the research.

Why do the researchers want my protected health information? The researchers want to use your protected health information as part of the research protocol listed above and as described to you in the informed consent.

What protected health information do the researchers want to use? All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills, and any other information related to or collected for use in the research protocol, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes.

Who will disclose, use and/or receive my protected health information? All Individuals/entities listed in the informed consent documents, including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, Children’s of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees and agents, including any CRO; and any outside regulatory agencies, such as the Food and Drug Administration, providing oversight or performing other legal and/or regulatory functions for which access to participant information is required.

How will my protected health information be protected once it is given to others? Your protected health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel this Authorization? You may cancel this Authorization at any time by notifying the Principal Investigator, in writing, referencing the research protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the protected health information that was provided before you cancelled your authorization.

Can I see my protected health information? You have a right to request to see your protected health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: ____________________________  Date: __________
or participant’s legally authorized representative: ____________________________  Date: __________
Printed Name of participant’s representative: ____________________________
Relationship to the participant: ____________________________

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