Study Title: A Placebo-controlled Double Blind Crossover Trial of Acetylsalicylic Acid as a Pre-treatment for Exercise in Multiple Sclerosis

Unique Protocol ID: AAAQ1758

Document: Study Consent Form

Date of Document: 12/29/2016

Columbia University Consent Form

Protocol Information

Attached to Protocol: IRB-AAAQ1758
Principal Investigator: Victoria Leavitt (vl2337)
IRB Protocol Title: Aspirin in Multiple Sclerosis

General Information

Consent Number: CF-AAAV1017
Participation Duration: 2 hours
Anticipated Number of Subjects: 72
Research Purpose: You are participating in a research study for the Columbia University Multiple Sclerosis Clinical Care and Research Center.

The purpose of this study is to investigate the relationship between body temperature, fatigue and multiple sclerosis. This study examines the effect of aspirin on body temperature, and (if you are enrolled in the exercise condition) the effect of using aspirin before exercising in people with MS. Finally, if you are enrolled in the MRI scanning condition, this study will use magnetic resonance imaging (MRI) techniques to assess the relationship between brain temperature, body temperature, and fatigue.

Contacts

Contact	Title	Contact Information
Eva Gelernt	Coordinator	Phone: 212-305-1987 Email: erg2144@cumc.columbia.edu

Information on Research

You are being asked to join a research study funded by the National Multiple Sclerosis Society. This consent form explains the research study and your part in the study. Please read it carefully and take as much time as you need. Please ask questions at any time about anything you do not understand.

You are being asked to participate in this research study because you have multiple sclerosis. You are a volunteer. You can change your mind at any time during the evaluation and withdraw this consent. There will be no penalty or loss of benefits if you decide to quit the study.

Study Procedures: If you consent to participate, you will undergo the following during the study visit:

If you are in the scanning condition, you will participate in a brain scan (MRI). Prior to the scan, you will be administered a pregnancy test if you are female. If it is positive, you will NOT be able to participate in the scan and you will not be eligible for the study.

Although the purpose of this scan is research, there is a possibility of finding something in your brain scan that has medical implications for you. We refer to this as an incidental finding (IF) of clinical significance. Therefore, your scan will be read by study personnel for research purposes, and it will also be read by a trained radiologist to screen for the presence of any IFs. If the radiologist sees an IF on your scan, we will tell you. An IF could be something that is important for your health but is not life threatening, or it could be more serious. If we find an IF, we will immediately convey the information to you. If you wish, we will also alert your physician of the IF. If you do not have a private physician, we will refer you to an appropriate clinic. The decision to proceed with further examinations, tests, and/or treatment related to the IF will be yours, and you and/or your insurer will bear any costs related to further examinations, tests, or treatments related to the IF.

Your temperature will be taken with an ear thermometer before and after the scan. You will then be given a pill, either aspirin or placebo. You will answer questions related to how fatigued you feel, how much pain you are experiencing, and your mood. You will take a quick test of grip strength. Then you will receive a 1-hour scan. MRI involves lying on a bed which slides into a large cylindrical magnet. Radio waves are used to obtain images from the internal parts of your brain. Before beginning the imaging procedure, you will be asked to remove any metal or magnetized objects (such as keys, chains, hairpins, watches, belt buckles, coins, and credit cards). If you have a pacemaker or any permanent metal implants like hip prosthesis (other than tooth fillings) you will not be able to participate in this study. You will be asked to breathe quietly and not move during the scan time. There is no pain or discomfort associated the MRI scanning itself. However, you will hear a banging noise during the scan. This is a normal sound produced by the MRI scanner and does not indicate that anything is wrong.

If you do not participate in the scan condition, you will be randomized to receive either aspirin (standard dose, 650 mg), or a placebo pill. After having your ear temperature taken, completing the grip strength task, and completing brief questionnaires, you will be given a pill to take. Neither you nor the investigators will know which pill you have been given until after the study is completed. After being administered the pill, you will relax with magazines or an iPad for one hour (the estimated time to peak serum level for aspirin), before once again having ear temperature taken, and filling out brief questionnaires and doing the grip test again.

If you choose to participate in the exercise condition, you will be scheduled for two visits separated by approximately one week. You will be asked to refrain from eating for 2 hours prior to your scheduled visit. The same procedures will take place at both of your visits: upon arriving to our lab, you will have your temperature taken in your right ear. Then you will be given a single pill to take, it will either be aspirin or placebo and neither you nor the investigator will know which pill you are given. You will then fill out questionnaires related to mood, fatigue, and how you are feeling. We will

familiarize you with a scale that will be used during your exercise session to measure how tired you are feeling (your level of exertion). Once that has been completed, an exercise physiologist will give you an exercise test on a stationery cycle. You will wear a face mask so that we can measure your respiration during exercise. We will also continuously monitor your heart rate. Your blood pressure, ear temperature and feelings of exertion will be recorded every 60 seconds during exercise. After that, the exercise test will begin. This will involve cycling until you feel too tired to continue. For most people, this is not longer than about 8-12 minutes. After you finish, blood pressure, ear temperature, and exertion will be recorded again, and we will have you fill out some questionnaires on your current level of fatigue. At the end of each session, we will ask you whether you think you were given aspirin or a placebo.

Future Use of Data

We will use your data for the research described in this form and for other future research. We will label your data with a code instead of your name. The key to the code connects your name to your samples and health information. The Study Doctor will keep the key to the code in a password protected computer and locked file.

Risks

MRI uses a strong magnetic field to create images of your brain. There is no evidence that this causes any biological harm. Some subjects experience discomfort lying on their back for up to 45 minutes, or from being in a small space. Some subjects may be unable to complete the study because of these discomforts. If you should feel the need to leave the MRI scanner at any time for any reason, the study will be immediately stopped and you will be allowed to do so.

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy.Their plans for keeping your information private are described in the Confidentiality section of this consent form.

Exercise causes exertion. To ensure your safety if you participate in the exercise condition, we will consult with your physician before enrolling you to make sure you meet all study criteria. The one-on-one exercise sessions you take part in will be overseen by a certified exercise physiologist with experience working with patients who have a variety of medical condition. In addition to the exercise physiologist, a physician will be available throughout both of your sessions to ensure your safety.

Allergic Reaction

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or serious, and can even result in death in some cases. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing.

The risks of a single dose of aspirin are minimal, and because we will carefully screen for any/all conditions that may counter indicate the use of aspirin before enrollment, we do not expect any issues to arise as a result of aspirin use in this study. Furthermore, the dosage being given is the standard dose taken for, e.g., a headache (2 325-mg pills).

If you are unsure whether you have an aspirin allergy, please let the study team know immediately.

Benefits

You are not expected to benefit directly from participation in this study. The ultimate benefit of thisresearch is that we better understand how changes in body temperature affect fatigue associated with multiple sclerosis. Should we find any information of medical interest or clinical significance from these procedures (e.g., brain abnormalities in the MRI scan), you will be informed.

Alternative Procedures

The alternative is to not participate.

Confidentiality

Any information obtained during this study and identified with you will remain confidential. Any information that may be of value to your physician for your personal treatment will be shared with your physician, unless you object to this. All information will be stored in locked files and all information in computer data bases will not have your name or any other identifying information associated with it. The following individuals and/or agencies will be able to look at and copy your research records:

- The investigator, study staff and other medical professionals who may be evaluating the study
- Authorities from Columbia University and New York Presbyterian Hospital, including the Institutional Review Board ('IRB')
- The United States Food and Drug Administration ('FDA') and/or the Office of Human Research Protections ('OHRP')
- If this study is sponsored (money or supplies are being provided), the sponsor of this study, the National Multiple Sclerosis Society, including persons or organizations working with or owned by the sponsor
- Other government regulatory agencies (including agencies in other countries) if the sponsor is seeking marketing approval for new products resulting from this research.

Research Related Injuries

Taking part in this research study may result in injury or harm to you. In the event of an injury resulting from your participation in this study, you should seek appropriate medical care and inform the study doctor. In the event of an emergency you should go to an emergency room.

If you are injured or harmed as a result of participating in the study and receive medical care through the NewYork-Presbyterian Hospital (NYPH), a Columbia doctor, or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance.

Columbia University and NewYork-Presbyterian Hospital (NYPH) are not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in this study. However, you do not waive any of your legal rights in signing this form.

Compensation

There is no cost to you for participation in this study. You will be compensated $25 for your participation. If you participate in the exercise condition you will receive an additional $25, as that will require you to come for two visits.

Voluntary Participation

Your participation in this study is completely voluntary. You can refuse to participate or withdraw at any time and such a decision will not affect your medical care at New York Presbyterian Hospital, now or in the future. Signing this form does not waive any of your legal rights.

Additional Information

If you have any questions or concerns about the study, you may contact Dr. Victoria Leavitt at 212 342 1351. If you have any questions about your rights as a subject, you may contact the Institutional Review Board at (212) 305-5883 or by email at irboffice@columbia.edu. An Institutional Review Board is a committee organized to protect the rights and welfare of human subjects involved in research.

Statement of Consent

I have read the consent form and talked about this research study, including the purpose, procedures,risks, benefits and alternatives with the researcher. Any questions I had were answered to my satisfaction. I am aware that by signing below, I am agreeing to take part in this research study and that I can stop being in the study at any time. I am not waiving (giving up) any of my legal rights by signing this consent form. I will be given a copy of this consent form to

keep for my records.

Signatures

Participant Signature Lines

Study Participant

Print Name _____ Signature _____

Date _____

Research Signature Lines

Person Obtaining Consent

Print Name _____ Signature _____

Date _____