

Research Subject's Consent Form Cover Sheet
Dietary Modulation of Neuroinflammation in Age-Related Memory Disorders
PI IRB #7665

Overview

Below is a summary of the study that you are asked to participate in. This outline is meant to be a guide for you to use while considering the study and reading the consent form. It is not meant to replace the consent form, which you will have to sign if you decide to participate in the study. The consent form contains detailed information about the study and about the risks which you will need to consider before making your decision. Read the consent form carefully and discuss it with others before deciding to take part. And remember that, even if you agree to participate, you can change your mind at any time.

Purpose of Study

The purpose of this study is to examine the effect of dietary flavanols on brain activity. Flavanols represent a specific group of plant-derived nutrients that are found in cocoa beans, grapes, tea, berries and various other fruits and vegetables. The specific flavanols investigated in this study come from cocoa.

Participation is Voluntary

As with all research, this is a voluntary study, and you do not have to participate if you do not want to. You may stop participating at any time.

Procedures

- **Consent Appointment:** You will be asked to read and sign the informed consent form as well as complete some forms and evaluations.
- **Neuropsychological Testing Sessions:** You will complete a series of computer based and paper/pencil tests to assess your memory and attention.
- **Cocoa Flavanol Run-In Period:** You will be asked to consume two cocoa flavanol capsules twice per day with meals for two weeks.
- **Blood draw:** You will be asked to have fasting blood draws.
- **MRIs:** You will have two MRI scans of your brain using a contrast agent called Gadolinium.
- **Cocoa Flavanol Intake:** For 12 weeks, you will be asked to take three capsules once a day with a meal.

Risks

This study includes some risks and discomforts (please refer to the consent form for further details and explanations of these risks). These include: discomfort from blood draw, cocoa flavanol intake problems, and MRI contraindications and a Gadolinium contrast agent that will be administered to you intravenously (i.e., through the vein). Gadolinium dissolves in blood and is eliminated by the kidneys. The FDA has issued an announcement stating they are investigating a possible risk of adverse health effects from repeated use of gadolinium for MRI. Though the FDA has not reached a conclusion at this time, you will not be allowed to participate in this study if you have previously had more than one MRI scan with gadolinium.

Benefits

There are no direct benefits to participation in the study.

You may contact the Principal Investigator, Dr. Richard Sloan at 646-774-8940 with any questions. Please read and sign the attached consent form for a full description of the study.

Research Subject's Consent Form
Dietary Modulation of Neuroinflammation in Age-Related Memory Disorders
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Purpose of Study

The purpose of this study is to examine the effect of dietary flavanols on brain activity. Flavanols represent a specific group of plant-derived nutrients that are found in cocoa beans, grapes, tea, berries and various other fruits and vegetables. The specific flavanols investigated in this study come from cocoa. You are being asked to participate because you are a healthy subject between the age of 50 and 69 years old.

This research study is funded by the National Institutes of Health.

Voluntary

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University Medical Center.

Alternatives to Participation

This is not a treatment study. The information being collected is for research purposes only and is to learn more about the effects of dietary intervention on brain activity, not about you. The alternative to participating in this study is not to participate.

Procedures

Eligibility During the Study

Your eligibility is checked at multiple times over the course of the study through a series of evaluations and tests conducted during study meetings. These help to determine whether or not you are able to continue. Also, in the event that you are unable to follow the procedures required, you may be withdrawn from the study.

Consent Session

If you agree to participate, at your first meeting, you will be asked to read and sign the informed consent form and complete additional forms that will be needed for the study. A brief psychology test will also be used to see if you qualify for the study. Your height, weight and blood pressure also will be measured at this time. If you are eligible, you will be asked to come in for the first appointment which is the neuropsychological testing session.

Neuropsychological Testing & Run-In Period

You will complete tests that measure cognitive function. These are standardized pencil-and-paper or computerized tests of different thinking abilities, such as memory, reasoning, attention, and language. For example, some of these tests might require you to memorize a list of words. You will complete most of the testing in person, but we may contact you over the telephone to ask you some follow up questions. It will take about one hour to complete the testing session.

During this appointment, you will also be given a number of cocoa flavanol capsules which may contain 0mg or 650 mg of *Cocopro™* flavanols. You will be asked to take three capsules once a day with a meal for two weeks. If you successfully complete this two-week period by taking 90% of the capsules, you will be asked to come in for a set of appointments which consist of a neuropsychological testing session, blood draw, completion of questionnaires and an MRI scan, all of which can all be completed on the same visit. Your body composition (height, weight, body fat percentage) also will be measured at this time. If you cannot complete the two weeks of capsule consumption, you will discontinue the study.

You will receive the cocoa flavanol capsules in a sealed bottle, topped with an electronic Pillsy Cap. This Bluetooth-enabled smart cap tracks the date and time the bottle is opened and works in conjunction with a mobile app. After each flavanol intake the data from the cap will be synchronized via the app and it will be sent to a secure cloud-based server provided by Pillsy. The Pillsy accounts are anonymous and do not have any identifiable information contained within. Because the app may be downloaded on your phone, we will use randomly generated, lab-maintained email addresses, phone numbers and IDs for registering the app. All data containing personal identifiers, such as your name and telephone number, are kept on a password protected secure server at CUMC. At the end of this two-week period, you will return the bottle and the cap to the study research assistant.

Blood Draw

You will be asked to have an overnight fasting blood draw of 41mL of blood (less than 3 tablespoons). The blood will be used in several ways. First, it will be used to confirm that you have been taking the cocoa flavanols. Second, if you are female, it will also be used to confirm that you are in menopause. Third, it will be analyzed for certain blood markers that might be associated with brain function.

During the MRI section of the study, your blood will also be analyzed when it's drawn to screen for kidney problems that may exclude you from the MRI scans.

MRI Scan

The Magnetic Resonance Imaging (MRI) machine uses strong magnetic fields and radio waves to take pictures of your brain. The MRI scan uses a contrast agent called Gadolinium that will be administered through an intravenous injection. It dissolves in blood and is eliminated by the kidneys. You will receive an information sheet about Gadolinium including a description of the type we use and its possible side effects. On the day of the MRI, a research assistant will bring you to the Hatch center where a registered nurse will go over the details of the MRI consent form. This form contains a detailed description of the MRI procedure including the use of the contrast agent gadolinium, possible side effects, and contraindications. After the discussion of the MRI consent is completed, you will fill out the gadolinium quiz. The nurse then will review the

quiz and will provide feedback for the incorrect answers. At the end of the whole process, both you and the nurse and will sign the MRI consent form.

Immediately before the scan, we will determine that you do not have a pacemaker or any unsafe metallic implants such as an aneurysm clip or heart valve and certain tattoos. You will be asked to remove any metal or magnetized objects (such as keys, chains, jewelry, retainers, medication patches, hairpins or credit cards).

For the MRI scan, you will be asked to lie on your back on a bed that slides into a large magnet shaped like a cylinder for 45-60 minutes. You will be asked to remain as still as possible. You will not feel anything, but you will hear a knocking noise. This is a normal sound produced by the MRI scanner and does not indicate that anything is wrong. The total time required for scanning will be around 45-60 minutes. However, including preparation time, up to 2 hours may be needed.

Randomization

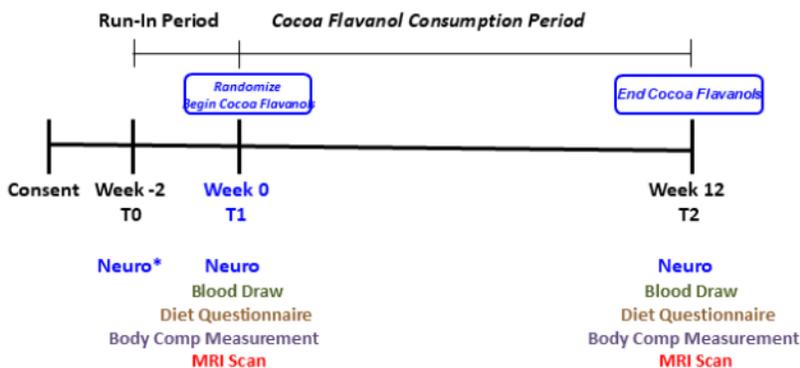
You will be randomly assigned (like flipping a coin) to one of two flavanol amounts, including: 0mg or 650 mg of Cocoapro™ flavanols per day. Everyone will receive 0mg of cocoa flavanols at some point in the study and some will receive 0mg throughout the study.

12-week Period: Cocoa Flavanol Capsules

You will begin a 12-week period during which you will be asked to consume three cocoa-flavanol-containing capsules once a day with a meal. You will receive the capsules in a sealed bottle topped with the Pillsy Cap you used during the two-week Run-In Period. You will take the capsules for 12 weeks and neither you nor the investigators will know which intake amount you are receiving. The cocoa flavanol capsules contain cocoa extract and other ingredients including theobromine and caffeine that are naturally found in chocolate. Some participants will consume capsules containing Cocoapro™ cocoa extract that may be beneficial to cognitive function while other participants will consume capsules that do not contain the Cocoapro™ cocoa extract.

End of 12-week period

After the end of the 12-week period, you will be asked to complete a second set of appointments including a blood draw and a neuropsychological testing and MRI scan which can all be completed on the same visit. You also will complete some questionnaires and your body composition (height, weight, body fat percentage) will be measured at this time.



Neuro* = Neuropsychological Testing Session

Risks and Inconveniences

Blood Draw Risks

During the blood draw, you may feel slight pain from the needle or experience some dizziness. You may also develop a temporary bruise where the needle was inserted. If there is any difficulty in obtaining the blood or if there is some medical reason why we cannot perform the blood test, you will be discontinued from the study.

Cocoa Flavanol Risks

Although we are currently unaware of any risks, there may be possible risks to the dietary intervention, such as previously unknown allergies.

MRI Risks

The MRI scan uses the contrast agent Gadolinium that will be administered through an intravenous injection. It dissolves in blood and is eliminated by the kidneys. Gadolinium is routinely used as a part of standard MRI tests around the world and it has rare side effects. The most commonly reported adverse reactions in adult subjects are headache and nausea. Participants who experience nausea in the MRI scanner should alert study staff immediately to remove them from the scanner. Less common reactions include vomiting, feeling hot, an allergic reaction at the injection site, distorted sense of taste, the sensation of tingling, pricking, or numbness, dizziness, rash, or increased blood pressure. Some patients with severe or acute kidney impairment have developed a condition called nephrogenic systemic fibrosis (NSF), a condition that may be fatal. In addition, people with allergies or known sensitivities to contrast agents such as gadolinium are at increased risk for more serious side effects, and therefore will not be injected with gadolinium. The form of gadolinium used in this study is designed to minimize these risks.

While there have been no reports of any harmful long-term effects caused by very strong magnets like the one used in the MRI scanner, the long-term effects of being placed in a magnet of this strength are unknown. Also, although there are no known risks of MRI scans associated with pregnancy, we will not scan someone who is pregnant. If you are a woman in your childbearing years, you will be asked to take a pregnancy test to ensure that you are not pregnant. Some people have reported sensations during MRI scans such as "tingling" or "twitching" (or, very rarely, a painful sensation), which are caused by changes in the magnetic field that can stimulate nerves in your body. With any MRI scan, on

occasion, some people experience nervousness or discomfort due to the scanner's small space and the need to lie still.

Except for pacemakers, some types of metallic implants, and medication patches, we are not aware of any other potentially dangerous interactions or hazards associated with the MRI scan. The MRI scanner produces a loud noise; earplugs will be provided to reduce this discomfort. If you experience any discomfort and wish to stop the scan, you can tell the MRI technologist, and he or she will stop the scan immediately. In our experience, no one has had sensations from the MRI that did not stop when the scanning stopped. If you are not able to complete the MRI scan, you will be not eligible to participate in the study.

Benefits

This study is not designed for your benefit. The primary benefit will be to increase understanding of how dietary interventions influence brain function. If examination discloses any abnormality, this information will be made available for evaluation by your physician.

MRI Results

While MRI scans are sometimes done for clinical purposes, the kind of MRI scan you will have as part of this study is for research purposes only. This means that the scans are not designed to provide clinical information that might be helpful to you or your doctor and they may not show problems that would normally be found in an MRI ordered to evaluate a specific medical problem. It is likely that the MRI scan will not have the same quality of those done for clinical purposes.

However, within a month of the MRI, the scan will be read by a neuroradiologist for evidence of any obvious irregularities requiring follow-up. You will receive a letter indicating the presence of no clinically significant findings or uncertain findings. If significant abnormalities are detected, you, or a physician whom you may designate, will be informed by a phone call from the responsible investigator, Dr. Scott Small. If no clinically significant findings or uncertain findings are detected, you may still opt to receive additional feedback about your MRI. Given the nature of the scan, the absence of a finding does not mean that one is not present.

Confidentiality

Your participation in this study will be confidential and if the results are published, your name will not be identified. Your records will be kept in locked files in locked offices and access will be allowed only to members of the research team or institutional personnel as part of a routine audit. Your name and other personal identifying information will be stored in an electronically secure database at Columbia University and if you download the phone app to record when the electronic pill bottle cap is opened, we will use randomly generated, lab-maintained email addresses, phone numbers and IDs for registering the app. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits). The study cannot be completed without this information. We will do everything we can to avoid disclosure about your participation in this study.

Your MRI will be interpreted and the results will be shared with you or a physician who you may designate. Your MRI report will be maintained as part of the clinical database at the New York State Psychiatric Institute along with your name and will be accessible to clinicians at the Columbia University Medical Center. A description of this clinical trial is 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 when the study has been completed. You can search this website at any time.

Study Compensation

You will be paid \$40 for each of the three neuropsychology testing sessions and \$70 for each of the two MRI scans. If you consume at least 90% of the total number of required capsules and complete all testing sessions, you will be paid an additional \$50 at the end of study for a possible total of \$310.

You will be compensated through a debit card, which will be provided to you. We will register you with the vendor of the debit cards, Bank of America (BOA), by providing your name, address, and phone number. These cards are "reloadable" which means you will receive one card, which will be "reloaded" within 2 weeks after each completed study visit. This card can be used as a credit card OR as an ATM card. You will be able to withdraw money from a bank either through a bank teller or an ATM. Please note that banks may charge a fee for using their ATM. If you lose the card, you can call BOA and have the card replaced. Please read the information sheet that comes with the card for more information.

Travel Reimbursement

You will receive a travel reimbursement of \$10 for each evaluation visit and this amount will be loaded onto your debit card.

Text Message Appointments Reminders

You can choose to receive text message reminders for study visits. If you opt-in to receive these reminders, our password-protected database will send text messages to your mobile phone one week and 1-2 days before the scheduled study appointments. The message will prompt you to reply indicating whether you confirm or need to reschedule the appointment. If you need to reschedule, a research assistant will contact you directly. The only information provided to the text messaging service provider is your mobile number and the message will not reveal any aspect of the study procedures. You may choose to opt in or opt out of the text message reminders at any time throughout the study.

Use and Storage of Biological Samples

Your name will not appear on any samples. They will be given unique study identification codes, and only the primary study investigators will have the code. This is important for us to link potential discoveries in this study to your past and future health and symptoms.

From your blood, different types of measures will be made in our laboratory. The results of these analyses are for research purpose and will not go in your clinical chart. The research will not include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Your private information or biospecimens could be used for future research studies completed in the division of Behavioral Medicine, department of Psychiatry. They will not be distributed to another investigator for future research studies, with or without identifiers. Your biospecimens (even if identifiers are removed) will not be used for commercial profit.

In Case of Injury

Federal regulations require that we inform participants about our institution's policy with regard to compensation and payment for treatment of research-related injuries.

Please be aware that:

The New York State Psychiatric Institute, Columbia University, and New York Presbyterian Hospital will furnish that emergency medical care determined to be necessary by the medical staff of this hospital.

You will be responsible for the cost of such care, either personally or through your medical insurance or other form of medical coverage.

No monetary compensation for wages lost as a result of injury will be paid to you by the New York State Psychiatric Institute, Columbia University or by New York Presbyterian Hospital.

By signing this consent form, you are not waiving any of your legal rights to seek compensation through the courts.

Questions

Research personnel will answer all current or future questions about the procedures and/or responses to the best of their ability. If you have any questions about this study in the future, you may reach the study's Principal Investigator, Dr. Richard Sloan at (646) 774-8940

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of human subjects in research studies). You may call the IRB Main Office at (646)774-7155 during regular office hours.

Documentation of Consent

I voluntarily agree to participate in the research study described above.

- I want to receive text message appointments reminders.
- I do not want to receive text appointments message reminders.

Print name: _____

Signed: _____ Date: _____

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____

Person Designated to Obtain Consent

Signed: _____ Date: _____