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Sedentary Behavior Interrupted: A Trial of Acute Effects on Biomarkers of Healthy Aging

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IRB Consent Form: 5/19/2021

University of California San Diego
Consent to Act as a Research Subject

Sedentary Behavior Interrupted - A randomized crossover trial of acute effects on biomarkers of healthy aging in the laboratory

Introduction

Dr. Dorothy Sears is conducting this research and asking for your consent to participate. This section provides a summary of important information. The rest of the form provides additional details.

- Research is voluntary - whether or not you join is your decision. You can discuss your decision with others (such as family or friends).
- You can say yes but change your mind later.
- If you say no, we will not hold your decision against you.
- Your decision will not affect your health care or any other benefits you may be entitled to.
- Please ask questions or mention concerns before, during or after the research.

The purpose of this study is to test if different interruptions of prolonged sitting improve metabolism. We are trying to find out if breaking up sitting with brief standing breaks can improve health. Participation in the study may or may not benefit you directly and may result in new knowledge that may help others.

You will first undergo several procedures at the Screening Visit to determine if you are eligible for the study. If you are eligible, you will wear a thigh worn device that measures your sitting and activity patterns for about one week. You will then participate in 3 study clinic visits that will occur within a 4–6-week time span. All 3 study visits will include about 30-60 minutes of set-up and about 30-60 minutes of wrap-up so, your total study visit time will be approximately 7 hours. During those clinic visits, you will provide urine samples, have your blood drawn and blood pressure takens, and complete blood vessel response tests. You will also complete some surveys. You will be asked to refrain from drinking alcohol, moderate-to-vigorous exercise, and smoking cigarettes (if you are an occasional smoker) for 48 hours before each clinic visit. You will be asked to fast for at least 10 hours before arriving in the morning for each clinic visit. You will be given

market-variety, prepared meals to eat the night before each study visit and provided with liquid meals during your clinic visits. You must also be willing to maintain your regular sedentary and physical activity behavior during the time you are enrolled in the study.

The most commonly expected risks of the study are infection, bruising, or pain from the blood draw, or pain or discomfort from sitting or standing during the 7-hour clinic visits.

The most serious risks of the study may include extremely high blood pressure if you take vasodilator medications, or deep vein thrombosis (blood clots in the legs) from extended periods of sitting. The longest you will be asked to sit without a break from sitting is about 2.5 hours. These risks are rare.

Additional, detailed information about this research is provided below. Please feel free to ask questions before signing this consent.

Why have you been asked to participate, how were you selected, and what is the approximate number of participants in the study?
Dr. Dorothy Sears is asking you to participate in this clinical research study because you are a postmenopausal woman. “Sedentary” means that you spend a large portion of the day sitting down There will be about 50 participants from UC San Diego and up to 86 participants at all sites.

Study Procedures
In addition to the information at the beginning of this form, here are some additional details about what will happen to you if you agree to be in this study.

Screening Visit: You will not be required to fast for this visit. The screening visit will take approximately 1 – 1.5 hours and will include the following procedures:

- Review and sign the informed consent document with UCSD staff.
- Complete a medical history, demographics, and physical activity questionnaire
- Test of your ability to safely and comfortably stand up and walk.
- Vital Sign measurements (blood pressure and heart rate.
- Height, weight, hip and waist measurements.
- Finger prick blood sample collection (a few drops).
- Your final eligibility will be determined from results from the various screening tests at the screening visit. You will be notified of your eligibility status at the end of the screening visit. If you are eligible for the study, you will:
    - be given an activPAL device that will be attached to the front of your thigh using adhesive tape. You can wear the device in the shower and underneath your clothing. The activPAL is the size of a thick credit card. It senses the position of your leg during standing and sitting and records your sitting, standing, and moving habits. You will wear this every day and night for about

5-7 days. During the days you wear the activPAL you will complete a sleep log to track when you wake up and go to sleep. You will bring the activPAL to study visit #1. You will not be financially responsible for lost or damaged activPALs.

Study Visits 1-3: The study visits will start in the early morning, **will require you to be fasting (no food or drinks other than water) for at least 10 hours prior to visit,** and will last approximately 7 hours. Most Study Visits will begin at 7:30a; exact start times and exact times of events noted below will depend on your Study Visit start time. To help with urine collection upon your arrival, you will be asked to drink a glass of water during or just before your travel to the clinic. You will be asked to wear loose, comfortable shorts, a dress or a skirt to the clinic so that we can conduct the study measurements on your thigh as described below. You will be seated in a comfortably cushioned but firm, straight-backed chair and will be instructed to minimize excessive movement while you are sitting. During the study visits you will be allowed to read, play games, or watch DVDs. A DVD player will be available during your visit. You will undergo several procedures during all 3 visits including the following:

- Your vital signs (blood pressure, temperature, pulse and respirations) will be collected. You will wear an automatic blood pressure monitor on one arm that will measure your blood pressure once per hour. We will take blood draws via an intravenous (I.V.) line inserted on the opposite arm of the blood pressure monitor. No more than three attempts will be made by trained staff to insert the I.V. line in your arm. Every 20-60 minutes throughout the study visit, you will have a small blood draw from the I.V. line so that we can measure the glucose (sugar), insulin, and other nutrients and proteins in your blood. You will have a total of 13 blood samples drawn via the I.V. line throughout each study visit. A total of ¼ cup of blood will be collected during the day.
- 3 urine samples will be collected during the day (4 tablespoons each) at the beginning (8:00am) in the middle (11-11:30am) and at the end (2:00pm) of each sitting protocol. You will be allowed additional bathroom breaks, if needed. Your bathroom breaks and urine collection will occur in a private restroom <20 feet from the study room chair.

- You will drink 2 liquid EnsurePlus® meals during the day (breakfast and lunch) so that we can measure your glucose and insulin response. At 9:00am, you will be asked to drink an EnsurePlus® shake "breakfast." Three hours later (12:00pm), you will drink another EnsurePlus® shake "lunch."
- We will draw small blood samples every 20 – 60 minutes and measure your blood pressure once per hour (7 times over the course of each study visit).
- Your blood vessel activity will be measured at the start of a 1-hr lead-in sitting time (8:00am) and at the end of each protocol (2:00pm). We will measure your blood vessel activity non-invasively using a method called "flow-mediated dilation" that includes a blood pressure cuff on your lower thigh and an ultrasound probe positioned just above that position. Your heartbeat will be monitored using electrocardiogram (ECG). The ultrasound probe will glide smoothly on your skin about 3-5 inches above the cuff on your thigh. The cuff will be inflated for 5 minutes then deflated, the ultrasound and ECG readings will be collected for 5 minutes after the cuff deflates. The cuff, ultrasound probe, and ECG wires will be removed after each of measurements.
- You will be allowed to drink moderate amounts of water throughout the protocols and given a granola bar-type snack at the end of each day before you leave the UCSD ACTRI Clinic.
- On each of the study visit days, you will complete one of the 5-hour sitting period protocols described below in random order (like the flip of a coin). As noted above, each of these protocols includes a bathroom break between 11 - 11:30am and after the protocol is over at 2:00pm. The different sitting period protocols are the following:

  A. Sitting quietly uninterrupted for the 5-hour study period. You will stand up once during this protocol for your middle bathroom break.

  B. Sitting quietly for the 5-hour study period during which you will interrupt that sitting every 15 minutes by standing up for 2 minutes and then sitting back down. One of these standing interruptions will include your middle bathroom break.

  C. Sitting quietly for the 5-hour study period during which you will interrupt that sitting 5 times by standing up in place for 8 minutes

and then sitting back down. One of these standing interruptions will include your middle bathroom break.

- You will wear an activPAL device. This is a small device that is worn on your thigh during the duration of the study visit. The activPAL measures time spent sitting and doing sit-stand transitions. You will not be financially responsible for lost or damaged activPALs.
- You will be asked to complete surveys during and after each study visit about your experience of the sitting protocol.
- You will be contacted by text, email, or regular mail for scheduling and appointment reminders and as needed. All study visits (Screening Visit, Study Visit 1, Study Visit 2, and Study Visit 3) will take place at UCSD's ACTRI Clinic located at 9452 Medical Center Drive in La Jolla.

COVID-19 TEST

You may be asked to complete a COVID-19 test 72 hours before Study Visit #1, Study Visit #2, and Study Visit #3. You will not have to pay for the test. You will be given instructions on where and when to get your test if you enroll in the study and if a COVID-19 test is needed. There are several location options for taking the test.

SUB-SAMPLE

Twenty participants will be asked to wear an accelerometer (small sensor) during the study visits. The accelerometer is a small device the size of a wristwatch that measures motion. If you are randomly assigned to the sub-sample you will be asked to wear this device on a belt around your waist (can be worn over or under your clothes) for the entire duration of the 3 study visits. You will not be financially responsible for lost or damaged accelerometers.

PRESCRIPTION MEDICATIONS

If you take oral prescription medications, you should take these at or near the normal time of day that you usually take them with a few exceptions. That can be in the morning during your fast if you can take them with water only. If you need to take them with food, you can bring them to the study clinic and take them after your breakfast meal (study visits 1-3). If you take vasodilator medication (for example, nitrates or ACE inhibitors) before 2:00pm each day, you will be asked

to delay your dose until after the last study measurement at 2:00pm. You should bring these study medications with you and will be asked to take your vasodilator medication immediately if your blood pressure rises above our safety limit at any time during your study visit. We will immediately stop all protocol activities and have you take your medication if your blood pressure rises above our safety limits (systolic pressure equal to or greater than 165 mmHg or diastolic pressure equal to or greater than 100 mmHg.

FUTURE USE
Your biospecimen samples (blood and urine) may also be used in additional research to be conducted by the University of California personnel or other researchers at other institutions. This blood and urine and its derivatives may have significant therapeutic or commercial value. You consent to such uses.

PARTICIPANT RESPONSIBILITIES
If you decide to take part in this research study, you will be expected to complete the study visits and other procedures and to follow the instructions of the study doctor and study staff. You will be advised not to donate blood during the study and to wait to donate blood for 56 days after completing the study. If you decide to stop participating in the study, or if you do not follow instructions, it is important that you notify the study doctor or study staff to help you make these decisions safely.

KNOWN RISKS: Participation in this study may involve some added risks or discomforts. In addition to the risks described at the beginning of the form, you may experience these risks:

1. **Embarrassment:** It may be difficult or uncomfortable to answer questionnaires about your health history even with assistance from study personnel. You may also feel embarrassment about your sitting behaviors. Increased knowledge of sedentary behavior may provide more information about your habits and behaviors than you would like the study investigators to know.
2. **Discomfort from wearing any of the devices during the study clinic visits**: You may be uncomfortable wearing the blood pressure cuff on your arm and the blood pressure cuff on your other thigh (during blood vessel activity assessments only).
3. **Loss of confidentiality:** The investigators have a plan to minimize the loss of confidentiality risk for your personalized information. As part of this plan, the study investigators will assign a study identifier to you and all of your data and samples.

4. **Boredom during prolonged sitting**: You may spend 5 hours sitting during each of the 5-hour sitting period protocols. You will have bathroom breaks and sitting interruption breaks during protocols B and C.
5. **Anemia**: We are withdrawing what is commonly a safe amount of your blood over a 4–6-week period. Nonetheless, you may experience anemia or low blood hemoglobin levels. You will be tested for anemia during screening, and you agree to refrain from donating blood for 56 days after completing this study.

PRIVACY AND CONFIDENTIALITY

As with all research, there is also the possibility of loss of confidentiality. Information from study participants will be identified by a study number and study files and database information will be kept locked in the study coordinator's office. We will keep your name and contact information for purposes of follow-up calls and mailings of study materials. Research records will be kept confidential to the extent provided by law. Every effort will be made to keep all information about you confidential. The UCSD Institutional Review Board, the Sponsor, the Sponsor's representative(s) or other regulatory authorities may need to review and/or copy the research-related records of individual participants. These individuals will take all precautionary means to protect your identity. On rare occasions, disclosure to a third party or parties may be required by law. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

You give your permission for your data to be:

1. Used for analyses that have not yet been specifically planned at this time by researchers at UCSD and other universities. Dr. Sears will be responsible for deciding how your data will be used. Even if you withdraw from the study or are removed from the study by study personnel, your data may still be used in analyses. There will be no direct benefit to you from future studies since you will not be provided with any results or information regarding research done with your data. Dr. Sears, her associates, or her successors in these studies will keep your data and the information derived from it for an indefinite period.

   If you decide later that the de-identified samples & data collected from you should not be used for future research, you may contact Dr. Sears, who will use her best efforts to stop any additional studies. However, in

some cases, it may be impossible to locate and stop future use once the materials have been shared with other researchers.

2. De-identified data will be uploaded to ClinicalTrials.gov, a web-based resource that provides the public with easy access to information on publicly and privately supported clinical studies.

3. Shared on a public website for use by others to better understand the health of postmenopausal women. Only de-identified data (i.e. data with no personal identifiers) will be shared on a public website. This means that it will not contain any information that would like that data back to you.

You consent to such uses.

COMPENSATION FOR PARTICIPATION

You will receive $10 compensation for your initial Screening Visit. If you are enrolled in the study, you can receive up to $260.00 in total for your time and travel associated with participating in this study. If you do not complete the entire study, your payment will be pro-rated after you have completed the following visits: $10.00 for Screening Visit, $50.00 for Study Visit 1, $50.00 for Study Visit 2, and $150.00 for Study Visit 3. You will also be provided with market-variety, dinner meals to eat the night before each of your 3 study visits.

COSTS OF PARTICIPATION

There will be no cost to you other than your time. You (and/or your insurance company) will not be expected to pay for any of the procedures or tests that are required for this research study. You will still be responsible for the cost of your usual ongoing medical care, including procedures and non-study medications that your study doctor or regular doctor requires during this study as part of your usual medical care. If you have any questions, please ask a member of the study staff.

ALTERNATIVE TREATMENTS

Your alternative is not to participate in this study, to continue receiving standard medical care as prescribed by your doctor, and to continue your regular behavior. For participants who do not wish to participate in this study, information about sedentary behavior is available on the internet and in books.

NEW FINDINGS/CHANGES IN PROCEDURES

Because this is a research study, there may be some unknown risks that are currently unforeseeable. Any significant or new findings developed during the course of this research that may relate to your willingness to continue participation in this study will be provided to you in writing in a timely manner.

WHOM TO CONTACT

Dr. Sears and/or _____ have explained this study to you. If you have any questions regarding the study, or have any adverse events or research-related injuries to report, contact Dr. Sears by telephone at (858) 534-8898 at any time. Do not sign this consent form unless you have had a chance to ask questions and have them sufficiently answered.

VOLUNTARY PARTICIPATION AND WITHDRAWAL/TERMINATION OF STUDY PARTICIPATION

Your participation in this study is voluntary. You have the right to refuse to participate or to stop being a part of this study at any time without any consequences. This means that there will be no penalty or loss of medical benefits to which you are entitled.

If you choose to stop participating this study, you must notify a member of the research team immediately.

The study doctor and study investigators can remove you from the study without your consent. Reasons for removal may include but are not limited to:

- If you have any change in your medical condition which might be harmful to you;
- If you have severe or unacceptable adverse effects;
- If you fail to follow the study instructions;
- If the study doctor feels that it is best for you not to participate or continue in the study;
- If the study is stopped for any reason,

You must agree to notify the study investigators if you change your medications while you are in this study. This includes both prescription drugs and drugs bought over the counter.

Future Contact: The investigator may want to contact you at some point in the future to get more information on your experience in this study or to let you know about other related studies that may be of interest. This information will be confidential and used to help make improvements to this study or future studies. You are not required to agree to future contact.

Do you agree to be contacted in the future by study staff?

___ Yes, I agree to be contacted in the future by study staff.

___ No, I do not agree to be contacted in the future by study staff.

WHAT IF YOU ARE INJURED AS DIRECT RESULT OF BEING IN THIS STUDY?

If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call (858) 246-4777 for more information about this, to inquire about your rights as a research participant, or to report research-related problems.

RESEARCH PARTICIPANTS' RIGHTS:

You have read or have had read to you all of the above. Dr. Sears or a member of the study staff has explained the study to you and answered all of your questions. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you.

You understand that you do not have to take part in this study, and your refusal to participate will involve no penalty or loss of rights to which you are entitled. You may withdraw from this study at any time without penalty or loss of other benefits to which you are entitled. Research records will be kept confidential to the extent provided by law. The results of this study may be published; however, you will not be identified in the published results.

By signing this consent form, you indicate that you have been informed of your rights as a research participant, and that you voluntarily consent to participate in this study. You have been informed what the study is about and how and why it is being done. You will receive a signed copy of this consent form. You will also receive a copy of the California Experimental Subjects Bill of Rights. Once you have signed this form, you will be considered as an enrolled study subject.

Participant's Signature	Date
Participant's Printed Name	Date
Study Staff Administering Consent	Date