Passive Heating as an Accessible and Tolerable Strategy to Improve the Inflammatory Profile and Cardiometabolic Health in People With Spinal Cord Injury

NCT04971408

December 5, 2023

Title of Study: Passive heating as an accessible and tolerable strategy to improve the inflammatory profile and cardiometabolic health in people with spinal cord injury

Consent to be part of a Research Study
To be conducted at
South Texas Veterans Health Care System

Concise Summary

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with us.

1. What problem is this study trying to solve?
You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. We know that persons with spinal cord injury (SCI) are at a greater risk for heart disease, inflammation throughout their body and diabetes than their able-bodied counterparts. There is evidence in persons without a spinal cord injury that repeated exposure to whole body heating (sauna, hot water, warm temperatures) decreases whole body inflammation which contributes to heart disease and diabetes. Repeated heat stress has never been studied in persons with SCI but has potential to be a fairly practical and non-invasive, non-pharmacologic (not requiring drugs) intervention to decrease inflammation in persons with SCI. This is what we are studying.

For more information, please see the ***Why is this Study being Done*** section below.

2. What will happen to me during the study and how is this different from continuing with usual care? What are all my options for treatment, including the pros and cons?
This study involves your participation for 16 weeks. You will be examined for 2 periods each lasting 8 weeks in one period you will not undergo heat stress. In another period, you will undergo heat stress by laying under some warm electrical heating blankets for about 1-hour 3x/week for 8 weeks. At 3 time points throughout the 16 weeks, we will do a blood draw (testing inflammation in the blood levels), an oral glucose tolerance test (where you drink sugar water then we measure your blood sugar levels) and a measure of blood vessel function by heating a small area of skin in your arm. All of these procedures are for research purposes only. There is currently no evidence that the interventions will improve your health. The goal is not to cure any underlying disease.
For more information, please see the ***What will be done if you decide to be in the research*** section below.

3. How much time will I spend on the study?
You will participate for a total of 16 weeks. During 8 of these weeks, you will undergo passive heat stress by lying on your back for an hour under warm electrical heating blankets 3x/week. At 3 time points you will also take 8 surveys on sleep, physical activity and mental health, have a blood draw, oral glucose tolerance test (Visit 1) and a skin heating exam (visit 2). Visit 1 will last 3 hours and visit 2 will last 1.5 hours.

UT Health
San Antonio
IRB
Approved
12-05-2023

4. Could taking part in the study help me and are there risks?
There are no known benefits to taking part in the study. The risks are minimal. Blood draws are the same as those done typically in a laboratory setting. The passive heat stress protocols have been performed over 100 times in our lab previously with persons with SCI and no one has had a burn or other adverse effect from the heating blankets.

For more information, please see **How could you or others benefit from your taking part in this study** section below. For details and a list of risks you should know about, please see the **What are the risks of participation in the research** section below.

5. What else should I consider before I make my decision?
Coming into the VA 3x/week for 8 weeks could be a burdensome time commitment for some persons.

Please review the rest of this document for additional details about these topics and other information you should know before making a decision about participating in this research.

Title of Study: Passive heating as an accessible and tolerable strategy to improve the inflammatory profile and cardiometabolic health in people with spinal cord injury

Consent to be part of a Research Study
To be conducted at
South Texas Veterans Health Care System

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are entitled.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety, and welfare as a participant in the research. The PI for this study is Michelle Trbovich, MD from the STVHCS, SCI Center and the UT Department of Rehabilitation Medicine, UT Health, San Antonio, TX.

Funding
VA Rehabilitation and Research Development, a federal agency that promotes scientific research, is funding this study. This organization is providing money to the Audie L Murphy VA, so that the researchers can conduct the study.

Purpose of this study – "Why is this study being done?"

You are asked to participate in this research study of persons with SCI.

SCI results in higher incidence of heart disease and diabetes and heart disease is the most common cause of death. Chronic inflammation, deleterious changes in vascular structure and impaired glucose metabolism are risk factors that contribute to both heart disease and diabetes. While exercise can help reduce these risk factors, paralysis and impaired accessibility often precludes exercise in persons with SCI. New research in able-bodied persons demonstrates that passive heating decreases inflammation and improves vascular function.

Similar studies in persons with SCI suggest they may also have the same health benefits however these. studies only investigated the impact of short term (one episode) passive heating (as opposed to repeated bouts). Repeated bouts of heat exposure will likely be required to impact chronic inflammation, but this has never been tested in persons with SCI. This study will test the impact of repeated bouts (3x/week) of passive heat stress over a longer term (8 weeks) on inflammation, metabolism and vascular function.

The researchers hope to determine if chronic heat exposure can decrease whole body inflammation that leads to heart disease and diabetes.

Title of Study: Passive heating as an accessible and tolerable strategy to improve the inflammatory profile and cardiometabolic health in people with spinal cord injury

This trial is registered on www.ClinicalTrials.gov, a publicly available registry of clinical trials. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you have a spinal cord injury.

How many people are expected to take part in this study?
This study will enroll approximately 15 study participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 30 visits with the researchers or study staff.

Study Procedures - as a participant, you will undergo the following procedures:

ALL PROCEDURES ARE SOLEY FOR RESEARCH PURPOSES – NONE ARE FOR CLINICAL CARE

The OGTT and blood collection for inflammatory and circulating vascular markers will occur in the Bartter Research Unit while all other procedures will be conducted in the SCI lab inside the gymnasium C002.

Visit 1: Two tests and one survey will be conducted in this visit (~ 3 hours):

1) Oral glucose tolerance test or OGTT: You will be asked to fast (no food or sugar intake) for ten (10) to twelve (12) hours prior to arriving for this visit/test. Once at the lab, you will drink a bottle containing sugar in water to see how your blood sugar responds to oral sugar intake. Just before (at -10 and -5 minutes) and after drinking the sugar-water, at 15, 30, 45, 60, 90, 120, 150 and 180 minutes, a blood sample will be collected through a catheter placed in a vein of the arm for the assessment of blood sugar and related outcome measures. The blood collected before the sugary drink will also be used to analyze a range of inflammatory and circulating vascular markers. In total, a maximum of 200 ml of blood will be drawn on this visit.
2) International Standards of Neurological Classification after SCI (INSCSCI) exam (Research only). The INSCSCI is an exam one of the Investigators/doctors will use to confirm your level of spinal cord injury. The doctor will use a small instrument to measure your sensitivity to light touch and a pinprick within certain areas (dermatomes) of your limbs. They will also test your limbs for functional strength (if you can move them and with which muscles). The exam typically only takes about five (5) minutes.
3) International Standards assessment to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) form. To complete this form, the doctor will want to ask you questions about how well different bodily functions are regulated by autonomic (involuntary/ unconscious) control. You will be asked questions about your heart and blood pressure function, sweating and body temperature control, bowel and bladder control, sexual function, and pulmonary (lung and breathing) issues. Most of the questions are simple "yes/no" responses and the entire form should take no more than five (5) to ten (10) minutes. This procedure is for research purposes only.
4) Seven surveys will be conducted regarding your mental health, sleep, physical activity, overall health and pain. You will also be asked to report all foods and drinks you have consumed in the 24 hours prior to the visit using a food diary.

Visit 2:

Maximal vasodilation (laser doppler flowmetry with heat): This will measure the maximal amount the blood vessels in the skin of your forearm are able to dilate/expand in response to local skin heating at 42 degrees Celsius. Skin blood flow will be measured via laser doppler flowmetry. The laser Doppler flow meter device sits on the skin, is only a few centimeters in size, and uses very low power laser light to measure skin blood flow; control of local (i.e., restricted to just around the probe) skin temperature is accomplished by placing the laser doppler flow probe in a metal sleeve which has an electric warmer

inside. A thermocouple (a tiny piece of wire) will be placed under the probe to measure the local skin temperature. Using this system, local skin temperatures can be held constant at temperatures from 34°C to 42°C (108°F). This skin heating will occur over a very small area of skin (<1cm2) and the procedure will take about 90 minutes to complete.

Visit 3: Passive heat stress (~1.5 hours)

1. Body/core temperature monitoring. Core temperature will be measured by an oral temperature probe that you will be asked to place under your tongue. We will also measure your aural temperature (with a sensor placed in your ear) at regular intervals (Braun Thermoscan Ear Thermometer). Additionally, you will be fitted with a 3M™ Bair Hugger™ Temperature Monitoring System, which is a non-invasive, accurate deep tissue temperature monitoring system that will continuously measure your temperature with a single-use sensor placed on your lateral thigh. The combined measures from these two devices will ensure accurate core temperature measures.
2. Passive Heat Stress test. You will lie flat on a bed for about 1 hour under soft warm electrical heating blankets and a water perfused suit. A temperature-controlled water perfusion suit will be placed on sensate skin areas (areas with feeling) and electrical heating blankets at a constant temperature on areas you cannot feel, to evoke heat stress. During whole body warming, temperature control is managed through the water perfused suit and monitored with a skin sensor. Water perfused through the suit will warm your skin temperature to 39°C (102.2°F) and will maintain it at that temperature for the duration of the 1-hour session. Please note, “skin temperature” and “core temperature” are not the same thing; a skin temperature of 102 degrees Fahrenheit does not mean you have a fever of 102 degrees. Most persons are comfortable during this protocol, but some feel quite warm and uncomfortable.
3. Physiologic Monitoring. Your skin temperature will be measured by small sensors (thermocouples) attached with adhesive on your forehead, chest, upper arm, upper and lower leg; blood pressure (BP) and heart rate (HR) will be measured via Portapres® (a finger cuff worn on your index finger); and perceived thermal pain responses will be measured on a 9-point Likert scale from 0-8. Skin blood flow will be measure at your lower arm and leg using a laser Doppler flowmeter. All such measures will be collected throughout the testing period to ensure your safe status and response to the heat stress.
4. Blood draw for inflammatory and metabolic markers. Blood will be drawn pre and post heat stress, from a vein in your arm to measure markers of inflammation. In total, no more than 40 ml will be drawn on this visit.

8 weeks of no interventions

Visit 4 - (8 weeks after Visit 2) Repeat procedures from Visit 1: Glucose tolerance test and blood draw for inflammatory and circulating vascular markers. Repeat surveys from Visit 1 and consume an identical diet in the 24 hours prior as that recorded prior to Visit 1.
Visit 5 – (within 1 week after V4) Repeat procedures from V2
Visit 6 – (within 1 week after V5) Repeat procedures from V3
Visit 7 thru 29 - Repeat procedures from Visit 3: heat stress monitoring test, Body/core temperature monitoring (with Bair Hugger only) and physiologic monitoring. Visits will be scheduled for three times per week, for eight weeks. There will be no blood draws during these visits.
Visit 30 - Repeat procedures from Visit 3: body/core temperature monitoring, heat stress test, physiologic monitoring.
Visit 31 – (within 1 week after V30) Repeat procedures from Visit 1: glucose tolerance test, and blood draw for inflammatory and circulating vascular markers. Repeat surveys from Visit 1 and consume an identical diet in the 24 hours prior as that recorded prior to Visit 1.
Visit 32 – (within 1 week after V31) Repeat procedures from V2

Ending Participation Early

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

Future Use of Your Information or Biospecimens Collected as Part of Your Participation

Identifiers may be removed and the de-identified information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

Your biospecimens, even if identifiers are removed, will not be used for commercial profit.

Risks – "What are the risks of participation in the research?"

Risks from the specific research procedures (drug(s), interventions, or procedures)

There are minimal risks to taking part in this research study.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Oral glucose tolerance test (after fasting):

Most people do not experience any side effects from glucose testing, and serious complications are rare. You will be monitored for symptoms and hypoglycemia in the lab by an RN and/or MD at all times during this test.

Less likely (non serious)

In 100 people approximately 1 may experience:

- Hypoglycemia (low blood sugar)
- Nausea
- Light-headedness
- Shortness of breath
- Sweating

Measuring body core temperature (Bair Hugger sensor)

Less likely (non serious)

In 100 people approximately 1 may have:

- Local skin irritation from adhesive used to hold the Bear Hugger sensor in place.

Skin Blood Flow measurements (laser doppler flowmetry with local skin temperature control):

The device to be used has been approved for human usage and is very low risk. Generally, no burn of any kind occurs at the temperatures used during this study. We have used this procedure on over 50 persons in our lab with no adverse events indicated or reported.

Less likely (non serious)

In 100 people approximately 1 may have:

- Local allergic reaction to the adhesive 0.6cm in diameter
- Skin redness at site of probe (usually dissipates within minutes of probe removal)

- Superficial skin burn over a 0.6 square centimeter area

Passive heat stress test (temperature-controlled water perfusion suit and electric blankets):
Risks associated with this procedure are minimal. However, we will monitor your skin and core temperature, heart rate and blood pressure throughout the entire study period. Should the temperature become intolerable the electric blankets will then be removed and/or the study stopped.

Less likely (non serious)

In 100 people approximately 2 may

- Feel uncomfortable/overheated to the point of being intolerable
- Skin redness
- Slight drop in blood pressure
- Slight Increase in heart rate

Venipuncture (blood draw): no greater risk than when collected for clinical purposes

- Bruising
- Pain
- Infection

For more information about risks and side effects, ask one of the researchers or study staff.

Are there Risks related to withdrawing from the study?

If you decide to withdraw from this study early, please discuss your decision with the principal investigator. The researcher may ask you to complete study withdrawal procedures at a final study visit. This involves a blood draw, oral glucose tolerance test and laser doppler flowmetry with skin heating. There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

Reproductive Risks

Concerns for sexually active women: You should not become pregnant while taking part in this study because we do not know how the study procedures could affect a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed.

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the repeated heat stress might affect a developing fetus. We will do a pregnancy test before you start treatment to make sure you are not pregnant.

Are there risks if you also participate in other research studies?

Being in more than one research study at the same time, may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?

The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section “Contact Information” for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more

information. If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – "How could you or others benefit from your taking part in this study?"

There is no guarantee or promise that you will receive any benefit from this study. We hope the information learned from this study will benefit other people with a spinal cord injury in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

You may choose not to participate in this study. There is no equivalent clinical treatment course. You may continue regular clinical care from your SCI primary care physician.

Payments – Will there be any payments for participation?

You will receive $50.00 per visit for a total of 29 visits. This payment will be deposited in your bank account within 6-8 weeks of each visit. The money you receive may be taxable. When the total payment is $600 or more in one calendar year, the institution must report the amount to the IRS. The IRS considers it earned income and treats it like any other income.

Please note that if you are on record as owing money to the State of Texas, such as for back child support or a delinquent student loan, the payment may be applied to that debt and you may not receive a check.

Costs – Will taking part in this study cost anything?

If you are enrolled at a VA site, please note that some veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by the VA that are ***not*** part of this study. There will be no cost to veterans or non-veterans for medical care and services provided by VA that are part of this study.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study. More information concerning confidentiality is described in the HIPAA Authorization to Use and Disclose Protected Health Information as part of a Research Study.

Limits of Confidentiality

Even without your consent, suspected or known abuse or neglect of a child, disabled, or elder abuse, threatened violence to self or others or other local health reporting requirements will be reported to appropriate authorities.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, allergies, or lab results.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the Institutional Review Board, Food and Drug

Administration (FDA), Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability (GAO).

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Release of Information Office at this facility, or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Michelle Trbovich, M.D. and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact Michelle Trbovich, M.D.

Primary contact:
Michelle Trbovich, MD, Principal Investigator can be reached at 210-392-2340.

If primary is not available, contact:
Research Lab can be reached reliably during normal work hours at (210) 617-5300 x16845.

The University of Texas Health Science Center committee that reviews research on human subjects (Institutional Review Board) will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the IRB by calling 210-567-8250, or by mail to IRB, UTHSA, Mail Code 7830, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.

Title of Study: Passive heating as an accessible and tolerable strategy to improve the inflammatory profile and cardiometabolic health in people with spinal cord injury

Research Consent & HIPAA Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE

- You have read the above information.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.

Adult Signature Section

- You have voluntarily decided to take part in this research study.
- You authorize the collection, use and sharing of your protected health information as described in this form.

Printed Name of Subject	Signature of Subject	Date	Time AM PM
Printed Name of Witness	Signature of Witness	Date	Time AM PM

☐ *Check if consent and authorization obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. Have witness initial below.*

Declaration of witness: I was present for the entire consent process. ←(initials of witness)

Printed Name of Person Obtaining Consent & Authorization	Signature of Person Obtaining Consent & Authorization	Date	Time AM PM