HypErthermia as an Additional Treatment for the Biology and Experience of Depression: Study 2

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UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: HypErthermia as an Additional Treatment for the Biology and Experience of Depression: The HEAT BED Study

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This is a research study testing active sauna sessions versus sham sauna sessions in combination with cognitive behavioral therapy (CBT) sessions in adults with clinical depression. The study researchers, Ashley Mason, PhD, and Frederick Hecht, MD, from the Departments of Psychiatry and General Internal Medicine, and the UCSF Osher Center for Integrative Health, or a member of the study team, will explain this study to you.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.
Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you have major depressive disorder.

Why is this study being done?

The purpose of this study is to test the feasibility and acceptability of 8 cognitive behavioral therapy (CBT) sessions and either 4 active sauna sessions that cause increases in body temperature or 4 sham sauna sessions that do not cause these increases in body temperature, in patients with major depressive disorder. The Clearlight Portable Sauna Dome used for the sauna sessions in this study is commercially available. It is not approved by the Food and Drug Administration (FDA) as a medical device. Its use in this study is considered experimental.

Who pays for this study?

This study is funded by the National Institutes of Health, the William H. Donner Foundation, Wilkinson Ventures, and the Aoki Foundation.

What is the usual care for my condition?

The usual care for your condition is psychotherapy and/or antidepressant medications.

How many people will take part in this study?

About 30 people will take part in this study.

What will happen if I take part in this research study?

If you agree, the following procedures will occur:

Study Procedures:

- **Study location:** All in-person procedures will be conducted at the UCSF Osher Center located at 1545 Divisadero Street, San Francisco, CA 94115. You will also complete online questionnaires from home.
- At the **baseline study visit,** you will complete screening procedures that include a study therapist interviewing you about your depression symptoms and study staff measuring your height, weight, hip and waist size, and blood pressure.
- Also at the **baseline study visit,** if you are eligible, you will complete online questionnaires (on an iPad). Study staff will also provide you with the app-enabled Oura ring to wear starting that day and will help you download the Oura ring app onto your smartphone. The Oura ring will measure your body temperature and heart rate while you sleep at night during your study participation. Study staff will also work with you to schedule your sauna and CBT sessions. This visit will take about 3.75 hours.
- Randomization: If you are eligible and complete required baseline assessments, **you will be randomized** to one of two different depression treatment groups. People in both treatment groups will receive 8 weekly cognitive behavioral therapy (CBT) sessions, which has been shown to be an effective treatment for clinical depression in clinical trials. A study therapist will provide the CBT sessions. One of the two groups will receive 4 active biweekly sauna sessions that cause increases in body temperature, which have shown promise in the treatment of depression in a few small clinical trials but have not been widely tested as a depression treatment. The other group will receive 4 sham biweekly sauna sessions that do not cause these increases in body temperature, which has been used as a control group in prior clinical trials. You will have an equal chance (like a flip of a coin) of being assigned to either of the treatment groups - the active sauna sessions treatment group or the sham sauna sessions treatment group. Neither study staff nor you will make the choice. Study staff will **not** tell you which treatment group you have been assigned to. If you have any concerns about participating in the study, you should speak with study staff before agreeing to be randomized. Once you are randomized, you cannot be replaced in the study. You should only complete this randomization step if you intend to: a) complete the assigned treatments (either the active sauna sessions or sham sauna sessions and the CBT sessions), and b) complete the study assessments. If you have any questions, concerns, or reservations about participating in the study and completing the study assessments, sauna sessions, and CBT sessions, please speak to the study team before proceeding with randomization.

- At your **cognitive behavioral therapy (CBT) study** visits, you will complete 50-minute CBT sessions with the study therapist and will answer brief questionnaires before and after each session. CBT has been shown to be an effective treatment for clinical depression in clinical trials. The therapist will follow a CBT protocol specifically designed to help people with clinical depression. A dedicated study therapist will provide the CBT sessions. Your sessions will be audio-recorded to ensure that the study therapist is providing the CBT treatment according to the protocol. Researchers may also use the recordings to study whether qualities from the session, particularly on the part of the therapist, are associated with study outcomes. All recordings will be stored on a secure, UCSF passcode-protected system and will be destroyed after the study. These visits will take about 1 hour.
- At your **first and fourth sauna study visits**, you will first complete COVID-19 screening procedures, which includes a rapid COVID-19 test, and then complete your first sauna session in a single-person

sauna device. During the sauna session, we will measure your temperature continuously using a rectal thermometer with a cover that you will insert using a water-soluble, non-staining jelly lubricant. Before and after entering the sauna device, you will complete brief online questionnaires (on an iPad) and staff will collect a saliva sample from you before and after the sauna session. At your first visit, a phlebotomist will collect blood samples from you before and after the sauna session; details below). At your fourth visit, depending on the time of day of the visit, you may be able to choose provide blood samples before and after the sauna session. We suggest wearing cotton underwear (briefs or boxers) and if female, a loose-fitting sports bra (optional) during the sauna sessions. Staff will remain with you during the entire sauna session. These visits will take about 4 hours each.

- Your **second and third sauna study visits** will be the same as your first and fourth sauna study visits, however, they will not include saliva and blood collection. These visits will take about 3.75 hours.
- At your **final study visit**, you will complete online questionnaires (on an iPad) and return the Oura ring. A study clinician will interview you about your depression symptoms. A phlebotomist will also collect a blood sample and a saliva sample from you. This visit will take about 1 hour.
- **Blood drawing (venipuncture):** At the two sauna study visits that include blood draws, a blood sample will be drawn before and after the sauna session by inserting a needle into a vein in your arm. Each sample will be approximately 4 teaspoons, for a total of about 8 teaspoons at these visits. A total of about 5.5 tablespoons will be drawn for the whole study. Researchers will use the blood samples to examine how immune factors and other blood markers may be altered in individuals with depression change over the course of treatment.
- **Saliva sampling:** At your first and fourth sauna study visits, we will collect a small amount of saliva from you. This will allow researchers to examine how the sauna sessions impact levels of the hormone cortisol, which may be altered in individuals with clinical depression.
- **Pregnancy testing:** If you are female, you will also complete a urine pregnancy test at the in-person screening visit and before sauna sessions.

How long will I be in the study?

Participation in the study takes place over about 10 weeks. Participating in the study will take a total of about 34 hours.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study team if you are thinking about stopping or decide to stop. They will tell you how to stop your participation safely.

It is important to tell the study team if you are thinking about stopping so any risks from the interventions can be evaluated by the study doctor. Another reason to telling the study team that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

If you withdraw from the study, any data or specimens we have already collected from you will remain part of the study records. The study researcher may stop you from taking part in this study at any time if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, the researchers don't know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop the sauna session.

You should talk to the study team about any side effects you experience while taking part in the study. Risks and side effects related to the study interventions and procedures include those which are:

Likely:

- Physical discomfort: You may feel discomfort related to feeling hot in the sauna, but we will place cool towels on your forehead as often as you wish and you will be able to stop the sauna session at any time. You may find the rectal thermometer uncomfortable, but it is made of silicone and is designed to fit in the rectum. It is unlikely, but possible, that you may experience increased heart rate or shortness of breath. It is also possible that you will experience dizziness, lightheadedness, and/or fainting when trying to stand up after the sauna session. Study staff will be available during the entire sauna session to help if you have these symptoms.
- Thirst: You may feel thirsty during the sauna session, but we will provide you with bottled water as often as you wish. Although unlikely, you may experience a decrease in electrolytes, and we will provide you with electrolyte replacement beverages, such as Pedialyte and others, as often as you wish.
- Emotional discomfort: You may feel emotionally uncomfortable at times during the cognitive behavioral therapy (CBT) sessions with the therapist. Like other types of psychotherapy, CBT can involve exploring difficult feelings, emotions, or experiences. However, our skilled study therapist will help you with this discomfort.

Less Likely:

- Claustrophobia: The sauna sessions can take up to 140 minutes, during which you will be in a relatively small space, but your head will be outside of the sauna the entire time.
- Tachycardia: It is possible that you will feel your heart rate increase during your sauna session, much like your heart rate increases during exercise like running.
- Confidentiality: Participating in research may involve a loss of privacy, but information about you will be handled as confidentially as possible.

Rare but Serious:

- There may also be risks that we do not know about. **Other Risks:**
- **Randomization risks:** You will be assigned to a sauna condition by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other sauna condition
- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and/or fainting.
- **Time:** Participating in this research study will use approximately 34 hours of your time over about 10 weeks, but we will schedule your study visits as conveniently for you as possible.
- **Unknown Risks:** The sauna sessions may have side effects that no one knows about yet. The researchers will let you know if they learn anything that could change your mind about participating in the study.
- **Reproductive risks:** The procedures in this study may affect an unborn baby or infant. You should not become pregnant or breastfeed during your participation. If you can become pregnant, you must have a pregnancy test before you enter this study. If you are female and you have sexual intercourse with males, you must use contraception the entire time you are in the study. If you think you may be pregnant at any time during the study, tell the study staff right away. Acceptable methods of contraception are:
    - Condoms (male or female) must be used with another method, other than spermicide
    - Intrauterine devices (IUDs)

- Hormone-based contraceptives (birth control pills)
- Complete abstinence from sexual activity that could result in pregnancy For more information about risks and side effects, ask one of the researchers.

Are there benefits to taking part in the study?

You may or may not benefit from participating in the study. Cognitive behavioral therapy (CBT) is an established effective treatment for clinical depression. The study will provide you with CBT without charge.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your depression without being in a study
- Taking part in another study
- Getting no treatment

Please talk to your doctor about your choices before deciding if you will take part in this study.

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study. Once the study is done using your specimens and information, we may use the remaining specimens and information collected for future research studies or share them with other researchers so they can use them for other studies in the future. We will not share your name or any other personal information. We cannot guarantee that this will prevent future researchers from determining who you are. We will not ask you for additional permission to share this deidentified information. ○ **Research results:** There may be times when researchers using your information and/or specimens may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

In this study, we collect information about depression and suicidal thoughts. If we determine that you are at high risk of harming yourself, we will conduct a risk assessment and may direct you to the nearest emergency room and/or to call 911. If you decline, we will call your local emergency services number to ensure your safety.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the University of California
- Representatives of the National Institutes of Health
- Representatives of the Food and Drug Administration (FDA)

Under California law, we must report information about known or reasonably suspected incidents of abuse or neglect of a child or elder including physical, sexual, emotional, and financial abuse or neglect. If you disclose actual or suspected abuse, neglect, or exploitation of a child or elder, members of the study staff may be required to report such information to appropriate authorities such as Child or Adult Protective Services.

Are there any costs to me for taking part in this study?

No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

Will I be paid for taking part in this study?

In return for your time and effort, you will be paid $15 for each sauna session, $15 for the baseline visit, and $15 for the final visit, for a total of up to $90. If you choose to do a blood draw at your fourth sauna study visit, you will be paid an additional $15, for a total of $105. You will be paid in cash at the end of each of these visits. There is no compensation for completing cognitive behavioral therapy (CBT) sessions.

Will I be reimbursed if I pay expenses related to my participation in this study?

You will be reimbursed for round trip Muni, BART, or other public transportation to study visits. If you drive to study visits, you will be given parking stickers for validation at the UCSF parking garage at Sutter Street.

What happens if I am injured because I took part in this study?

It is important that you tell the study doctor, Frederick Hecht, MD, if you feel that you have been injured because of taking part in this study. You can tell the study doctors, Ashley Mason, PhD and Rick Hecht, MD, by calling the study at 415-514-8445 or emailing Dr. Ashley Mason (ashley.mason@ucsf.edu) or Dr. Rick Hecht (rick.hecht@ucsf.edu).

Treatment and Compensation for Injury

If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can contact the research team with any questions, concerns or complaints you have about this study at heatbed@ucsf.edu or 415 514 8445.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. 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.
The National Clinical Trial (NCT) number for this study is not yet assigned.

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____	_____	_____
Date	Participant - Printed Name	Participant - Signature for Consent

_____	_____	_____
Date	Person Obtaining Consent - Printed Name	Person Obtaining Consent - Signature

Emergency Contact

We also request that participants provide an emergency contact. This can be a health care provider (like your primary care doctor, or a mental health professional) or a friend or family member. We may contact this person if your responses on a survey or interview suggest that you intend to kill yourself.

It is optional to provide an emergency contact. You can participate in the study either way. If you do not provide a contact, we may contact local emergency services to ensure your safety.

If your responses suggest that you intend to kill yourself, do we have your permission to contact this person?

□ No, I decline to provide an emergency contact.

□ Yes, you can contact the person below if you are unable to reach me:

Name: _____

Phone: _____

Email: _____

Relationship to you (e.g., primary care doctor, friend, sibling): _____