UNIVERSITY OF CALIFORNIA, SAN DIEGO
CONSENT TO PARTICIPATE IN RESEARCH

1. Study Title and Number

Title: Spaced Transcranial Direct Current Stimulation for Treatment-Resistant Depression: A Home-Based Feasibility and Safety Study
Study #812687

2. Principal Investigator

Dr. Jean-Philippe Miron, MD, PhD

3. Principal Investigator Phone Number, Research Team Number, and Emergency Contact Number

Research Team Phone Number: 858-249-2625
Emergency Contact Number: 858-534-5821

4. Study Overview

This research study is being conducted to evaluate the feasibility, safety, and tolerability of home-based spaced Transcranial Direct Current Stimulation (tDCS) in participants with treatment resistant depression (TRD).

We are inviting you to participate in a research study because you have been diagnosed with Major Depressive Disorder (MDD) that has been resistant to treatment.

This form explains the research so that you may make an informed decision about participating.

- Research is voluntary - whether or not you participate is your decision. You can discuss your decision with others (such as family, friends or another physician).
- You can say yes, but change your mind later.
- If you say no, we will not hold your decision against you.
- You can say no even if the person inviting you is part of your healthcare team.
- Your decision will not affect your health care or other benefits you may be entitled to.
- Please ask the study doctor or study team questions about anything that is not clear, and feel free to ask questions and mention concerns before, during, and after the research.
- You may consult with friends, family, a personal doctor, or anyone else before deciding whether or not to be in the study.
- You will be given a copy of this consent form and the Participant's Bill of Rights.

The purpose of this research study is to evaluate the effectiveness, safety, tolerability and feasibility of at-home transcranial direct current stimulation (tDCS) as a treatment for depression. The study aims to examine changes in mood, brain activity, and related clinical outcomes before, during, and after treatment, with the goal to provide more information that can be used for future studies

You will first undergo several procedures to determine if you are eligible for the study. You will attend an in person screening visit that will consist of clinical assessments and safety screenings at the clinic in 4S Ranch. If you are eligible, you will complete two weeks of weekday transcranial direct current stimulation (tDCS) treatment, beginning with an in-clinic training session and followed by 3 hour at-home treatment sessions consisting of five 20-minute stimulations with breaks in between. All treatment sessions will be remotely monitored by a study coordinator. You will also visit the clinic in 4S Ranch for additional baseline clinical assessments and transcranial magnetic stimulation (TMS) procedures a few days prior to your treatment

schedule, as well as one week after your treatment, and 4 weeks after your treatment. After treatment days 5 and 10, as well as 1, 2, 3, 4, 8 and 12 weeks after your treatment, we will assess your depression symptoms to measure how you responded to treatment. The estimated duration of study participation is 13-14 weeks.

The most common risks or discomforts of this study are tingling or burning sensations during stimulation, and temporary skin redness/irritation, headaches, and fatigue after stimulation.

The most serious risks include skin burns, which has only occurred in a few case reports in previous studies (7 total). Given that tDCS has been administered to hundreds of thousands of individuals over the last decades, the risk of such an incident is extremely low. Potential skin irritation from the treatment will be monitored at at the start of each treatment day by taking a photograph of the small area of skin that comes into contact with the tDCS electrodes.

A complete listing of possible risks and discomforts associated with this study can be found in Section 9 of this document.

We cannot promise any benefit to you or to others from participating in this research. However, possible benefits may include experiencing a positive change in mental health with repeat sessions. The investigators also may learn more about the nature and treatment of mental health conditions based on brain function.

Other alternatives to participation in this study are not to participate. Your decision to participate in the study will not affect your eligibility to receive standard of care through the Interventional Psychiatry clinic, which may include electroconvulsive therapy, ketamine, or other forms of treatment.

6. Whom can I talk to if I have questions?

If during your participation in the study you have questions or concerns, or if you think the research has hurt you, contact the research team at the numbers listed in Section 3 on the first page of this form. You should not agree to participate in this study until the research team has answered any questions you have about the study, including information contained in this form.

If before or during your participation in the study you have questions about your rights as a research participant, or you want to talk to someone outside the research team, please contact:

- UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu

7. How many people will take part?

We plan to study 10 people here.

8. What happens if I take part in the research?

As you read this form, please ask questions if something is not clear.

Here is what will happen to you if you agree to be in this study:

The study intervention will be administered with the Soterix Medical mini - CT device. The Soterix Medical mini - CT is an investigational device not yet approved by the Food and Drug Administration (FDA). The safety and effectiveness of the device is being tested. Participation in this study will span approximately 13-14 weeks and will include one week for screening and baseline assessments, two consecutive weeks of weekday treatment sessions, and follow-up assessments at weeks 1, 2, 3, 4, 8, and 12 post-treatment.

The treatment in this study may affect a baby, before or after the baby is born. As a result, those able to become pregnant should not be in this study if they are:

- pregnant,
- breast-feeding, or
- trying to become pregnant.

If you are able to become pregnant, you should use birth control for the entire time you are in the study. Hormonal methods (birth control pill, etc.), double-barrier methods (condoms with spermicidal, sponge with spermicidal, or diaphragm with spermicidal), or not having sex may be used. Your doctor will discuss these with you.

If you become pregnant or think you might be pregnant during study treatment, you must inform the Study Doctor immediately. Your Study Doctor will want to follow the pregnancy and collect information about the outcome of the pregnancy.

	Screening	Baseline assessment	Treatment Phase - 2 weeks	1-week post-treatment reassessment	2-week post-treatment reassessment	3-week post-treatment reassessment	4-week post-treatment reassessment	8-week post-treatment reassessment	12-week post-treatment reassessment
Informed consent form and ACE	X								
Demographics	X								
Medical history	X								
Pregnancy Test	X								
ATHF – current and lifetime medication history	X								
MINI: Psychiatric Interview	X								
TASS: TMS Safety Form	X								
MSSI: Suicidality Assessment	X								
Concomitant medications	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X
MADRS * Depression Interview	X	X	X	X	X	X	X	X	X
QIDS-SR – Depression Symptoms Survey	X	X	X	X	X	X	X	X	X
Neurophysiology (TMS-EEG, TMS-EMG, rsEEG)		X		X			X		

tDCS	X		X						

Screening: Visit 1

The screening visit should take approximately 2-3 hours. During this visit, we will do some tests and procedures to see if you qualify to participate in this research study. This visit will take place at one of the outpatient clinics (either La Jolla or 4S Ranch). This visit will first consist of reviewing and signing the consent form.

After consenting, you will complete forms, clinical questionnaires, and tests with a research coordinator. The study doctor will review the results of these tests and procedures to determine if you are eligible to participate.

At this visit, we will:

- Ask about your medical history and any medications you may be taking.
- Ask about your psychiatric history and review how you have recently felt.
- Review what antidepressant treatments you have tried and may currently be taking, including medications, psychotherapy, etc.
- Ask you to complete some questionnaires about your mood and memory.
- If you are of childbearing potential, we will have you take a pregnancy test that study personnel confirm negative. We will also ask you questions about your current method of birth control to ensure you have an adequate method to prevent pregnancy throughout the trial.
- At the end of the visit, you will also test the tDCS procedure at a standard intensity for up to 2 minutes to determine your tolerability of treatment stimulation.

Pre-Treatment Neurophysiology: Visit 2

This visit will take place at the UC San Diego Interventional Psychiatry Clinic and will include both clinical assessments and brain activity measurements. These measurements are being done to help researchers better understand how transcranial direct current stimulation (tDCS) affects the brain and how it may help with depression. You will complete a series of clinical questionnaires and interviews at either the start or end of this visit. Clinical assessment data are a series of questionnaires that will consist of questions regarding your current and past depression. These questionnaires will involve questions about your mental health, mood, and how you have been feeling in the previous days, weeks, or months. We will also be asking about your mental health and past treatments you have taken regarding your depression. For the TMS-EMG and TMS-EEG portion of the visit, we will perform a series of brain measurements using the following tools:

- **Transcranial Magnetic Stimulation (TMS):** A non-invasive technique that uses brief magnetic pulses to stimulate specific areas of the brain. These are called **TMS pulses**, and they feel like light tapping on your scalp.
- **Electromyography (EMG):** A way to measure small muscle movements. We use this to detect when a TMS pulse causes a twitch in your thumb, which helps us determine the correct stimulation level.
- **Electroencephalography (EEG):** A method of measuring brain wave activity using small sensors placed on the scalp with a stretchy cap. A small amount of gel is applied to improve signal quality. This allows us to see how the brain responds to TMS.

Resting motor threshold (RMT), will be determined by sending TMS pulses to evoke a twitch in the thumb muscle. This RMT procedure will be used to determine the stimulation intensity that will be used throughout the session. For the TMS-EMG portion of the visit, you will receive a series of pulses to your head while muscle activity in your thumb is measured. For the TMS-EEG procedure,

you will receive a series of pulses to your head with an electroencephalography cap on to measure your brain activity. The EEG cap will be fitted tight over the head, and electrode gel will be inserted on the surface of the scalp. Throughout the session, you will feel a twitch or light tapping on the surface of your scalp when the magnetic stimulation is applied. You will also hear a clicking noise. Earplugs will be provided prior to any magnetic stimulation for comfort and safety. All data collected will be de-identified.

This visit may be split between morning and afternoon or over two days, lasting approximately 2 to 2.5 hours. The clinical questionnaires will take approximately 30 minutes, with approximately 1 hour of TMS-EMG and 1 hour of TMS-EEG. The resting state electroencephalography (rsEEG) will consist of 10 minutes of measurements of brain activity with the EEG cap on. This helps us understand your brain's activity when it is not being actively stimulated.

Treatment: Visits 3-12

Transcranial Direct Current Stimulation (tDCS) is a non-invasive treatment that uses a weak electrical current applied to the scalp to help improve symptoms of depression. It works by gently stimulating specific areas of the brain that are involved in mood regulation, aiming to restore a healthier balance of activity. You will receive treatment daily on weekdays over two (2) consecutive weeks (10 days total). The first treatment will occur in-clinic to provide hands-on training on the safe use of the tDCS device. All subsequent sessions will be conducted at home under real-time remote supervision by a trained clinical research coordinator (CRC) via Microsoft Teams. Participants must remain in front of their computer for the full duration of the treatment session, just as they would be required to stay in the treatment room during in-clinic administration. While brief movements such as stretching or bathroom breaks are permitted, extended periods off-camera will not be allowed. Participants may engage in non-disruptive activities such as reading, watching videos, or working on their computer, but must not cook, clean, drive, or engage in any activity that could interfere with treatment. Failure to adhere to these requirements will result in removal from the study to ensure both safety and scientific validity.Monitoring of side effects, discomfort, skin irritation, and ongoing medication use will occur throughout the treatment phase. Total treatment time will be 3 hours per day, with five 20 minutes sessions of tDCS occurring with 20 minute breaks in between.

You can start your treatment on any weekday (preferably Monday) and will be asked to attend daily treatments until you have reached 10 treatment days. However, if you do miss treatment days, you will have up to 3 weeks to complete 10 treatment days with a minimum of 3 and a maximum of 5 treatment days per week.

Per-Treatment clinical assessments: Visits 7 and 12

This follow up will consist of the same clinical assessments conducted in the pre-treatment neurophysiology visit (visit 2), which will be questionnaires about your current and past depressive mood. These assessmentswill occur on the same day as your 5th and 10th day of treatment.

Post-Treatment Neurophysiology: Visits 13 and 16

Post treatment neurophysiology will be identical to the pre-treatment neurophysiology session and will occur approximately 1 week and 4 weeks after your last day of treatment.

Follow-ups: Visits 14, 15, 17 and 18

At approximately 2, 3, 8 and 12 weeks post-treatment, you will either come to one of our clinics or do these scales remotely via UCSD Health Zoom. During these assessments, you will be asked about the medications you are taking, and depression symptoms you may be experiencing.

8. What are the risks and possible discomforts?

Participation in this study may involve some potential risks or discomforts~~,~~ primarily associated with the tDCS treatment protocol. While tDCS is generally considered safe with no known long-term adverse effects reported, and has been utilized in hundreds of thousands of patients, there are still inherent risks, as outlined below:

- **tDCS-Related Risks**: **Itching, Tingling, or Burning Sensation during stimulation**: Nearly all participants may experience at least one of these sensations during the tDCS session.
- **Skin Redness**: Nearly all participants may experience temporary skin redness following tDCS.
- **Headache**: Approximately 30 out of 100 individuals may experience mild headaches after undergoing tDCS.
- **Fatigue**: About 20 out of 100 people might feel fatigued after a tDCS session.
- **Dizziness**: Up to 15 out of 100 participants may report feeling dizzy post-tDCS.
- **Insomnia**: Around 10 out of 100 individuals could experience insomnia following tDCS.
- **Skin Irritation**: Up to 10 out of 100 people may experience temporary skin irritation after tDCS. These side effects are typically mild and transient. The study team will monitor participants closely for any adverse effects and provide appropriate management as needed. Potential study participants must consider these possible side effects when deciding to participate in the study.

- **Worsening Mood and Suicidality**: As with any antidepressant treatment, there is a risk of worsening mood and increased suicidality. Should your mood deteriorate significantly or if there is an immediate threat of self-harm, our study team will provide emergency contact information and instruct you to call 911 to be taken to the emergency room for immediate care.
- **Emergency Care**: If at any point during the study you feel unsafe or experience severe depressive symptoms, you are advised to go to your nearest emergency room or call the national suicide hotline at (800)-273-8255 for support.

We will closely monitor you during the study and will treat any discomforts or side effects that you have the best we can. If your side effects are severe, we may stop the tDCS treatment.

***Neurophysiology Visit*:** Transcranial Magnetic Stimulation (TMS) coupled with EEG (TMS-EEG) and EMG (TMS-EMG) is generally safe and well-tolerated. However, participants should be aware of the risks and adverse effects associated with these procedures.

- **Seizure Risk**: The most serious adverse effect of TMS is the potential for a generalized seizure, although this is rare. The risk of a seizure is comparable to that of antidepressant treatments, occurring in less than 0.1 to 0.5 percent of patients when safety protocols are strictly followed. Seizures associated with TMS are typically self-limited and do not lead to chronic illness. This means that if a seizure were to occur during TMS, it usually ends by itself quickly. Seizures have mainly been described with a specific type of TMS called repetitive TMS (rTMS), which is another type of treatment for depression. It would be extremely unlikely for TMS used as a research tool and not as a treatment to provoke seizures.
- **Hearing Loss**: Extremely unlikely and can be prevented by the use of foam ear-plugs during the procedure.
- **Fainting**: Very rare, likely due to the intense sensory experience.
- **Headaches or Neck Stiffness**: Often accompanied by the unpleasant noise during stimulation.

Risks of Loss of Confidential Information: Study personnel will access your electronic medical record to collect information that will be used to determine your eligibility. There is also a risk that information about you could be released to an unauthorized party. To minimize this risk, we will deidentify data when possible and limit access of information about you to only necessary parties.

Risks Associated with Reproduction, and Pregnancy: Procedures involved in this research might be dangerous for pregnant individuals and/or fetuses. The risks of tDCS on pregnant individuals and/or fetuses are currently unknown. You should not become pregnant while in this research. Methods of birth control required for this study are described in Section 7 above. If you are breastfeeding, you should not breastfeed a baby while taking part in the study as the tDCS could harm the baby.

Risks of Collection of Sensitive Information: Some of the questions we will ask you are personal. You may feel embarrassed or stressed. You may ask to see the questions before deciding whether or not to take part in this study

Risks of Interviews/Questionnaires/Quality of Life Assessments that Discuss Sensitive Issues: Some of these questions may seem very personal or embarrassing. They may upset you. You may skip any

question that you do not want to answer. If the upset you, we will help you find a counselor, refer you to an appropriate clinic for follow-up, or you may contact the research manager at (858) 657-6152.

Possible Unknown Risks: In addition, there might be risks that we cannot predict at this time. These unknown risks may be temporary, mild, and last only while you are actively participating in the research, or they may be serious, long-lasting, and may even cause death. You will be informed of any new findings that might affect your health or welfare, or might affect your willingness to continue in the research.

9. How will information about me be protected?

While we cannot guarantee complete confidentiality, we will limit access to information about you. Only people who have a need to review your information, documents, or specimens will have access. These people might include:

- Members of the research team and other staff or representatives of UCSD whose work is related to the research or to protecting your rights and safety.
- Representatives of the study sponsor or product manufacturer
- Representatives of Federal and other regulatory agencies who make sure the study is done properly and that your rights and safety are protected.

Study information will be labeled with a code instead of your name or other information that can easily identify you. The record linking your identifying information (name, address, etc.) and the code will be kept separate from the rest of the study information.

The results of this study may be published once the study is completed. However, we will keep your name and other identifying information confidential. We expect this study will be completed in 5 years. This is only an estimate and the actual time to complete the study may be longer or shorter depending on a number of factors.

You will be asked to sign a separate UC Health Insurance Portability and Accountability Act (HIPAA) Research Authorization form to use and disclose (share) your health information that identifies you for the purposes of this research study (see the separate authorization form for more information). Your permission, as described in this informed consent and authorization form, does not have an automatic expiration date.

Under California law, we must report information about known or reasonably suspected incidents of abuse or neglect of a child, dependent adult, or elder, including physical, sexual, emotional, and financial abuse or neglect. In addition, if researchers are made aware that a subject has certain communicable diseases, including sexually transmitted diseases/infections (STDs/STIs), hepatitis, and

HIV, this must be reported. If any investigator has or is given such information, they may be required to report it to the appropriate authorities.

10. Will I need to pay to participate in the research?

The tDCS will be supplied at no cost while you take part in this study. The cost of getting the tDCS ready and giving it to you is also provided at no cost. It is possible that the tDCS may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options. You and/or your health plan/insurance company will need to pay for all costs of treating your condition while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no cost. Before you decide to be in the study, you should check with your health plan/insurance company to find out exactly what they will pay for

11. What if I agree to participate, but change my mind later?

You can stop participating at any time for any reason, and it will not be held against you. Your choice will not affect treatment relationship with healthcare providers at UC San Diego Health or any services you receive from them. No matter what you decide, there will be no penalty to you. You will not lose medical care or any legal rights.

If you stop early, please contact us immediately. We will ask you to complete some study termination tests. If you stop participating, we may not be able to remove the information we have already collected about you.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research. In addition, the study doctor or sponsor may stop the study or take you out of the study at any time, even if you would like to continue. This could happen for the following reasons:
• A study physician believes it is in your best interest not to continue the study.
• You begin to pose a serious threat to your life or another's life
• You feel unmanageable pain/discomfort at any point throughout the study.
• You no longer wish to participate in the remainder of the study in its entirety
• You may also be withdrawn from the study if you do not follow the instructions given to - you by the study personnel.
• Your clinical symptoms do not remain stable between screening and the start of treatment.

12. What will happen to information and/or biospecimens collected from me?

The data we collect with your identifiable information (for example, your name, medical record number, or date of birth) as a part of this study may be used to answer other research questions or may be shared with other investigators for other research. If we do so, we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask for your consent for the use or sharing of your data in other research. In addition, data that have been de-identified will be uploaded for other researchers to access and use. While your privacy and confidentiality are very important to us and we will use safety measures to protect it, we cannot guarantee that your identity will never become known.

13. What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for attending and completing all the research-required visits. You will also be responsible for the study-provided tDCS device and accessories while participating in this study. You will sign a responsibility agreement prior to being given the study equipment. This agreement ensures you understand the need to handle the equipment properly, prevent unauthorized use, and return the device upon study completion or early termination.

14. Will I be compensated for participating in the research?

If you agree to take part in this research, we will provide you with $20 for each neurophysiology visit, with a total potential study compensation of $60 for participation in both pre, 1-week post and 4-week post treatment neurophysiology visits. All compensation will be given as Vanilla Visa gift cards.

15. What else is important for me to know?

You will not be provided any clinically relevant information that may pertain to your physical health as no such information would be collected as part of your research participation. You will not be provided a summary of the research findings. This is because the study may still be ongoing, and individual results may not be meaningful outside of the full research context.

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 the Office of IRB Administration at 858-246-4777 or irb@ucsd.edu for more information about this, to inquire about your rights as a research participant, or to report research related problems.

A description of this clinical trial will be available on 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. You can search this Web site at any time

16. Additional Choices to Consider

The study team would like your permission to contact you about participating in future studies. You may still join this study even if you do not permit future contact. You may also change your mind about this choice. Please initial your choice below:

_____YES, you may contact me

_____NO, you may NOT contact me

UNIVERSITY OF CALIFORNIA, SAN DIEGO

CONSENT TO PARTICIPATE IN RESEARCH

Signature Block for Adults Able to Provide Consent

Participant

I have received a copy of this consent document and a copy of the "Experimental Participant's Bill of Rights" to keep. I agree to participate in the research described in this form.

Printed Name of Participant

Signature of Participant Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the participant.*
- *I have personally evaluated the participant's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the participant. The participant appears to have understood and freely given consent to join the research.

Printed Name of Witness

Signature of Witness Date

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CONSENT TO PARTICIPATE IN RESEARCH

Experimental Participant's Bill of Rights

Every individual asked to participate in a research study has the right to be:

1. Informed about the nature and purpose of the study.

2. Provided an explanation of the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. Given a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. Informed about any benefits that would reasonably be expected from the participation in the study, if applicable.

5. Informed about of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. Told of the types of medical treatment, if any, available if complications should arise.

7. Provided an opportunity to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. Informed that individuals can refuse to participate in the research study. Participation is voluntary. Research participants may refuse to answer any question or discontinue their involvement at any time without penalty or loss of benefits to which they might otherwise be entitled. Their decision will not affect their right to receive the care they would receive if they were not in the experiment.

9. Provided a copy of the signed and dated written consent form and a copy of this form.

10. Given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study contact the researchers listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research participant, please contact:

- UC San Diego Office of IRB Administration at irb@ucsd.edu or 858-246-4777