INFORMED CONSENT FORM

Sponsor / Study Title:	**National Institute on Drug Abuse (NIDA) / "Combining Neuro-Imaging and Non-Invasive Brain Stimulation for Clinical Intervention in Opioid Use Disorder"**
Protocol Number:	**26724 / 298**
Principal Investigator: (Study Doctor)	**Kelvin Lim, MD**
Telephone:	**(612) 626-6772 (24 hours)**
Address:	**University of Minnesota** **Center for Magnetic Resonance Research** **2021 6th ST SE** **Minneapolis, MN 55455** **Hennepin Healthcare** **701 Park Ave South** **Minneapolis, MN 55404** **The Berman Center for Outcomes and Clinical Research** **825 South Street Suite 440** **Minneapolis, MN 55404**

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

If your regular doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

If you have any questions regarding this research you may reach out to either PI involved in this research study, Dr. Kelvin Lim at 612-626-6772 (University of Minnesota) or Dr. Gavin Bart at 612 873-6901 (Hennepin County Medical Center).

Why am I being asked to take part in this research study?

I am asking you to take part in this research study because you have a current opioid use disorder (OUD) diagnosis, are between 18-60 years old, and are enrolled in a methadone or buprenorphine treatment program.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- The experimental treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what experimental treatment you get. You will have an equal chance of being given either experimental treatment.

Why is this research being done?

This study is being done to learn whether transcranial direct current stimulation (tDCS) can help current treatments become more effective in supporting abstinence in opioid use disorder. The information gained from this study will help us to understand how the brain works and whether tDCS could be used to improve brain function.

How long will the research last?

If you choose to participate, you will be in this research study for about 4 months. You will be asked to participate in study sessions that will be scheduled for up to 17 visits over 60 days, and up to 2 follow-up visits. You can expect 5 sessions of transcranial direct current stimulation (tDCS) over 2 weeks, with 1 session per visit. This would be followed by 5 more sessions of tDCS over 2 weeks, with 1 session per visit.

What will I need to do to participate?

Over the course of about 4 months, you will be asked to:

- Complete questionnaires
- Provide samples of urine or saliva for a drug screen
- Complete 3 magnetic resonance imaging scans (MRIs)
- Undergo tDCS or sham tDCS

- Attend up to 2 follow-up visits.

Study staff will work with you to schedule these appointments.

tDCS is considered to be a non-invasive investigational device that involves applying a weak electrical current to the scalp. This device has been labeled as a non-significant risk device by the FDA for investigational purposes. This small current is able to change the electrical activity inside the targeted areas of the brain. The tDCS device consists of two saline soaked sponges beneath small electrodes. Both sponges will be positioned on your forehead.

Half of the participants in this study will receive 10 sessions of active stimulation during the training session. The other half of the participants will receive 5 sessions of active stimulation and 5 sessions of sham stimulation. Sham stimulation will feel like active stimulation, but won't deliver meaningful electrical current during the whole training session.

If you decline a drug test, you will be asked to reschedule your visit.

If you decline a pregnancy test, and there is a chance you may be pregnant, you may be removed from the study.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

There is a slight risk you may feel uncomfortable or upset answering some sensitive questions asked in the questionnaires or forms. These questions are important for the study, but you can also skip any questions you feel uncomfortable or upset answering. Please make sure that you tell the study staff if you feel uncomfortable or upset while answering questions or completing tasks. You can choose to stop participating at any time.

You may also feel some itching or discomfort during the tDCS procedure.

There are some risks associated with MRIs.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research.

What happens if I do not want to be in this research?

You do not have to participate in this research if you do not want to.

Detailed Information About This Research Study

The following paragraphs have more detailed information about this study in addition to the information listed above.

How many people will be studied?

Up to 250 people will participate in this research study.

What happens if I say "*Yes, I want to be in this research*"?

If you agree to take part in this research study, you can expect the following procedures to take place:

Screening Visit/ Visit 1:

- You will be asked questions about mental health.
- You will complete questionnaires and tests of your thinking and memory.
- You may be asked to take a urine pregnancy test, if you are a female of childbearing potential.
- You will be randomly assigned to receive either active tDCS or half-active, half-sham tDCS. You have a 50% chance (like a flip of a coin) of receiving either active tDCS or half-active, half-sham tDCS during your study sessions.
- The study team will ask you about any medications you are taking.
- You may be asked to provide a saliva or urine sample for a drug screen test (for example: If there is a chance you may be under the influence of alcohol or drugs.

Assessments:

- You will complete questionnaires and tests of your thinking and memory.
- You may be asked to provide a saliva or urine sample for a drug screen test. (For example: if there is a chance you may be under the influence of alcohol or drugs).

MRI Scans:

- You will fill out an MRI safety form.
- You may be asked to take a urine pregnancy test, if you are a female of childbearing potential.
- You will have a 3T MRI scan. The MRI visit should last approximately 2 hours, and will take place at the Center for Magnetic Resonance Research at the University of Minnesota.
- You will be asked to provide a saliva or urine sample for a drug screen test.

tDCS Visits:

- You will receive 1 session of tDCS intervention per visit.
- You will have cognitive training during tDCS intervention for about 45 minutes. Video and audio may be recorded during the session to help the study team monitor your performance and engagement with the training.
- You will complete tDCS side-effect questionnaires before and after the intervention.
- You may be asked to provide a saliva or urine sample for a drug screen test (for example: if there is a chance you may be under the influence of alcohol or drugs.)

Follow-up Visit 1 and Visit 2:
The Follow-up Visits will last about 90 minutes each and will be scheduled 1 and 2 months after Visits 16-17.

- You will complete questionnaires and tests of your thinking and memory.
- You may be asked to provide a saliva or urine sample for a drug screen test (for example: if there is a chance you may be under the influence of alcohol or drugs).

Visit	**Procedures**	**Time**	**Compensation**
Visits 1, 2, and 3 (Baseline)	Assessment 1a Assessment 1b MRI Brain Scan 1	2 hours 2 hours 2 hours	$35 $25 $25
Visits 4-8	tDCS	1 hour	$15 each day *(up to $75)*
Visit 9 and 10 (Midpoint)	Assessment 2 MRI Brain Scan 2	2 hours 2 hours	$25 $25
Visits 11-15	tDCS	1 hour	$15 each day *(up to $75)*
Visit 16 and 17 (Endpoint)	Assessment 3 MRI Brain Scan 3	2 hours 2 hours	$25 $25
Follow-up 1	Assessment 4	1.5 hours	$50
Follow-up 2	Assessment 5	1.5 hours	$50

What are my responsibilities if I take part in this research?
If you take part in this research, you will be responsible for attending all study visits and following instructions given to you by study staff.

What happens if I say "Yes", but I change my mind later?
You can leave the research study at any time. You can leave the research study at any time and no one will be upset by your decision.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care.

If you stop being in the research, information about you that has already been collected may not be removed from the study database.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

tDCS is considered to be a non-invasive brain stimulation technique. During the stimulation, you may feel some itching underneath electrodes, and you may have a headache, fatigue, or nausea. These typically resolve when the stimulation stops.

MRI machines use a strong magnet and radiofrequency magnetic fields to take images of your body. The scanning process is similar to an x-ray or CT scan, but MRI does not use ionizing radiation (high-energy radiation that can potentially cause damage to DNA) like x-rays or CT scans.

The risks associated with MRI scans are:

Projectiles: Objects with magnetic properties can be pulled into the magnet and turn into projectiles. To minimize this risk we ask that subjects remove all metallic items (watches, cell phones, hair pins, etc.) prior to entering the scanner and by controlling access to the scanner.

Claustrophobia: The scanner is a long narrow tube that may cause some people to feel claustrophobic.

Hearing Damage: The noise generated by the operation of the scanner during a study is loud enough to cause hearing damage if you do not wear hearing protection. Hearing protection is required and is provided by the investigator.

Nerve Stimulation: Some people experience localized tingling, twitching, or muscle contractions during MRI scans. This is expected, but if it is uncomfortable please notify the research staff.

Disruption of Devices: Some devices can be damaged by magnetic fields and should not be brought into the scanner room. This includes some implanted devices such as pacemakers, cochlear implants, insulin pumps, nerve stimulators, etc. If you have any implanted device notify the research staff.

Heating of Devices: The radiofrequency waves used in MRI can heat conductive materials such as metal implants (screws, plates, rods, wires, artificial joints, etc.), certain tattoo inks, certain clothing fabrics, jewelry, medication patches, wigs, etc. You will be asked to remove these items if possible. If they cannot be removed you will be asked to provide more information to allow MRI staff to be able to make determination on the safety of proceeding with the scan.

A thorough pre-scan questionnaire will allow us to minimize the risk of device disruption and heating. You will be in constant contact with the research staff and should notify the research staff immediately, via the squeeze ball, if you notice anything unusual, become claustrophobic, think that your hearing protection is not adequate, or if you experience nerve stimulation that is uncomfortable.

In addition, there is a risk of unknown effects related to participation in MRI research. Long-term effects of exposure to high magnetic fields are unknown. Most people experience no short-term ill effects from the strong magnetic field, but some people report dizziness, mild nausea, headache, a metallic taste in their mouth, or sensations of flashing lights. These symptoms, if present, subside shortly after leaving

the magnet. If any sensations experienced during participation cause discomfort or pain, notify the research staff right away and your participation will stop and you will be taken out of the magnetic field.

Will I receive any imaging results after an MRI?
The pictures created during this study are for research purposes only and are not intended to provide health care to you. The investigator in charge of this study has decided that results from your scan will not be shared with you or your physician.

What do I need to know about reproductive health and/or sexual activity if I am in this study?
The risks of exposure to high magnetic fields are unknown for fetuses. Therefore, if you are a female who is capable of becoming pregnant, and you have any reason to believe that you might be pregnant, you should not participate in this study.

Confidentiality
During the study, you will be asked for personal information. This information will be stored securely to protect your privacy, but there is a risk that it could be accidentally shared with people who do not have access to this information.

Notification of Significant New Findings
You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

Are there any alternatives to being in this research study?
This research study is for research purposes only. The only alternative is to not participate in this study.

Will it cost me anything to participate in this research study?
There will be no cost to you for any of the study activities or procedures.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance, and Hennepin Healthcare. To comply with retention requirements, records including HIPAA and consent forms will be retained for at least six years after completion of the research.

The test results of your alcohol/drug screening will only be shared with the research team.

Data or Specimens Collected
If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The sponsor, monitors, auditors, the IRB, the University of Minnesota and representatives of this institution and its affiliates, including those that have responsibilities for monitoring or ensuring compliance, such as the Quality Assurance Program of the Human Research Protection Program, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing and dating this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential. If required by state law, the study doctor or study staff may report a positive test result to the local health department.

If we learn about current or ongoing child [or vulnerable adult] abuse or neglect, we may be required or permitted by law or policy to report this information to authorities.

Certificate of Confidentiality

To help protect your privacy, the National Institutes of Health has granted a Certificate of Confidentiality. The researchers can use this Certificate legally to refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate does not prevent a researcher from reporting information learned in research when required by other state or federal laws, such as mandatory reports to local health authorities for abuse or neglect of children/vulnerable adults, or information to the Food and Drug Administration (FDA) when required in an FDA audit. However, the Certificate limits the researcher from disclosing such information in follow up civil, criminal, legislative or administrative legal proceedings if the information was created or compiled for purposes of the research.

You also should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

Whom do I contact if I have questions, concerns or feedback about my experience?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study.

An institutional review board (IRB) is an independent committee established to protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll-free**: 877-922-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00037608.

To share feedback privately with the University of Minnesota Human Research Protection Program (HRPP) about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

The University of Minnesota HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous. If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the University of Minnesota HRPP.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the first page of this form for study team contact information and earlier in this section for HRPP contact information.

Can I be removed from the research?

The person in charge of the research study can remove you from the research study without your approval. Possible reasons for removal include:

- if the study staff feels it is unsafe for you to continue
- if you do not comply with study procedures (for example: drug or pregnancy tests)
- if you are unable to tolerate the tDCS
- if you are no longer able to provide your consent for research
- if you become pregnant and cannot do the MRI
- if you leave methadone or buprenorphine treatment prior to completion of all MRI scans

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary

manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

Will I be compensated for my participation?

If you agree to take part in this research study, we will pay you up to $435 for your time and effort. If you do not complete the study, you will be paid for the visits you complete.

Compensation will be provided according to the schedule below:

- Visit 1: $10 screening evaluation and $25 baseline questionnaires
- Visit 2-3: $25 pre-intervention assessment, $25 MRI scan
- Visits 4-8: $15 each day for tDCS interventions (up to $75)
- Visits 9-10: $25 midterm-intervention assessment; $25 MRI scan
- Visits 11-15: $15 each day for tDCS interventions (up to $75)
- Visit 16-17: $25 post-intervention assessment and $25 MRI scan
- Follow-up visit 1: $50
- Follow-up visit 2: $50

Payment will be made using a prepaid debit card called Greenphire ClinCard. It works like a bank debit card. We will give you a debit card and each time you receive a payment for participation in this study, the money will be added to the card after each completed visit.

You may use this card at any store that accepts MasterCard or you can use a bank machine to remove cash. However, there may be fees drawn against the balance of the card for cash withdrawals (ATM use) and inactivity (no use for 3 months). We will give you the ClinCard Frequently Asked Questions information sheet that answers common questions about the debit card. You will also receive letters with additional information on how you can use this card and who to call if you have any questions. Be sure to read these letters, including the cardholder agreement, for details about fees.

The debit card system is administered by an outside company. The company, Greenphire, will be given your name and social security number. They will use this information only as part of the payment system. Your information will not be used for any other purposes and will not be given or sold to any other company. Greenphire will not receive any information about your health status or the study in which you are participating.

Additionally, you will have the option to receive updates related to appointment reminders and payment reminders and updates via text message and email message (Standard text messaging rates will apply). You will have the opportunity to opt-in to receive these messages, you are not required to provide your cell phone or email address to be enrolled in the study or use a ClinCard. If you choose to receive messages and decide at a later date that you want to stop these messages, you will have the ability to opt-out.

Any demographic information collected and provided to Greenphire is stored in a secure fashion and will be kept confidential, except as required by law.

Payment you receive as compensation for participation in research is considered taxable income. If payment to an individual equals or exceeds $600 in any one calendar year, the University of Minnesota is required to report this information to the Internal Revenue Service (IRS). Research payments to study participants that equal or exceed $600 during any calendar year will result in a FORM 1099 (Miscellaneous Income) being issued to you and a copy sent to the IRS.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule or what you may know as "HIPAA") to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

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 when available. You can search this Web site at any time.

ClinicalTrials.gov Identifier: NCT04495673.

Optional Element:

The following research activity is optional, meaning that you do not have to agree to it in order to participate in the research study. Please indicate your willingness to participate in the optional activity by placing your initials next to the activity.

Yes, I agree	**No, I disagree**	
_____	_____	I would like to receive reminders using Greenphire.

If yes, provide the following contact information:

Email Address: _____

Phone Number: _____

Signatures:

Your signature and date documents your permission to take part in this research. You will be provided a copy of this signed and dated document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent