Consent to Participate in Research Study: Effects of Neuromodulation and Cognitive Training on Brain Networks Associated with Relapse in Alcohol Use Disorder

You are invited to participate in a study examining the effects of brain stimulation on alcohol use disorder using a device called transcranial direct current stimulation. This study is being done by Jazmin Camchong, PhD in the Psychiatry Department at the University of Minnesota.

Investigator Team Contact Information: *Jazmin Camchong, PhD*

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name: Jazmin Camchong, PhD **Departmental Affiliation:** Department of Psychiatry **Phone Number:** 612-842-8704 **Email Address:** camch002@umn.edu	**Study Staff:** Hannah Verdoorn **Phone Number:** 612-842-8704 **Email Address:** lnpiumn@umn.edu

Supported By: This research is supported by the National Institutes of Health (NIH).

Please read this form and ask any questions before agreeing to be in this study.

Introduction

The purpose of the study is to use transcranial direct current stimulation (tDCS) to explore the effects of neuromodulation in alcohol use disorder. Specifically, we want to examine whether your treatment outcome might be improved by the stimulation. 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. The intervention sessions will include administering transcranial direct current stimulation (tDCS) while you complete a task on a computer, in addition to completing paper questionnaires. Your participation is expected to last 8 days plus three follow-up visits over 8 months. Approximately 100 people will be enrolled in the study. If you are currently enrolled in the Lodging Plus treatment program, and an off-site research procedure interferes with a treatment program scheduled meal, we will provide a comparable meal.

Additionally, we are interested in whether genetic differences between people might affect how they respond to the tDCS and brain training. Some evidence suggests that genetic differences that affect the brain may play a role in how people respond to psychiatric treatments. If we can find genetic differences between individuals that have different responses to the treatment being used in this study, then we will be able to better "personalize" treatment in the future by providing people with a treatment plan based on their individual genetic make-up. Providing a genetic sample (saliva) is optional and takes about 5 minutes.

Procedures

If you agree to participate, you will be seen for eight days while in the treatment program.

BASELINE INTERVIEW: You will meet with a research staff member from the University of Minnesota either in person or through a video conference call. You will complete questionnaires relating to alcohol craving levels, expectancies of use, sensation seeking tendencies, and impulsivity levels. Baseline activities will take about 1.5 hours total. You may also be tested during a follow-up visit by the research staff for recent alcohol use, using a Breathalyzer. We will share the results with you. You will be asked to reschedule the visit if your alcohol level is higher than an acceptable level.

MRI GENERAL PROCEDURES: MRI screening assessment. You will be asked to remove all metallic objects and asked to wear a hospital gown. Females who could potentially be pregnant will be tested for pregnancy and, if positive, will not be allowed to participate. If testing is refused, participation will not be allowed. See below for additional procedures you will be asked to perform in this study while in the MRI scanner.

PRE-INTERVENTION MRI: You will undergo an MRI scan (3T), which takes about 75 to 80 minutes. MRI involves taking pictures of your brain, from which the properties of certain brain tissues can be measured. While sometimes MRI scans are done for clinical purposes, the scans you will receive are being done for research purposes. Since these scans are not designed for clinical or medical reading, your scans will not receive a clinical or medical interpretation. For the scan, you will be asked to lie down quietly on a bed, and the bed will slide into the scanner. Once you are inside the scanner, it will start to take the pictures. During the scan, you will simply lie quietly in the scanner with your eyes closed while it takes images of your brain. The MRI scan will be performed at the University of Minnesota's Center for Magnetic Resonance Research. Pre-intervention MRI assessments will take about 2.5 hours total.

INTERVENTION DAYS 1-5: Will involve reversal learning task training and daily tDCS intervention. We will first explain to you what the reversal learning task is, and you will perform one trial/practice run. During the reversal-learning task you will be presented with four identical stimuli. You will be required to choose the stimulus that is in the correct location (correct location is randomly determined and changes across trials). After you acknowledge full understanding of the task, you will be randomly assigned (with 50% chance) to receive either active tDCS or sham (placebo) tDCS while you perform the reversal-learning task. During tDCS intervention (active or sham) you will be seated in a reclining chair while you perform the reversal- learning task. There will be two tDCS intervention (13 minutes each intervention) sessions daily (for five days). The two daily interventions will be separated by a 20-minute break.

In addition, before and after completion of all tDCS interventions, you will play two computer tasks that assess decision-making: the computerized dimensional set shifting task and the risk task. During the computerized dimensional set shifting task, you will be required to determine the correct shape (correct shape is randomly determined and changes across trials). During the risk task, you will be required to choose between two options to gain points.

At the beginning and end of intervention days 1-5, you will fill out a form asking you about potential side effects of intervention. Total participation time for intervention days 1-5 will be about 2 hours each day.

POST-INTERVENTION MRI: You will be asked to fill out the same behavior, personality and substance use questionnaires as you did at the baseline interview. Alcohol craving will be re-assessed and a post-intervention MRI scan with same procedures as baseline will be collected. Total participation time for the

post-intervention MRI will be about 2.5 hours. If you need to pay for parking for this visit, we will reimburse you up to $7.

TELEPHONE FOLLOW-UP: Monthly follow-up phone interviews will be conducted for about 8 months after study completion to query relapse status. We will ask you to provide the phone number of a good friend or relative who will know your whereabouts to help us re-contact you if needed.

IN-PERSON OR REMOTE FOLLOW-UP VISITS: You will be asked to return 1, 4 and 8 months (in person or through a video conference call) after the post-intervention MRI to fill out the same behavior, personality and substance use questionnaires. In addition, we will conduct an interview on circumstances surrounding relapse if necessary (only if you have relapsed). At only the first follow-up, you will have a third MRI scan with the same procedure as the other two scans. The first follow-up will be about 2.5 hours and the 2nd and 3rd follow-up will be about 1.5 hours each. During the very last visit you will fill out an end of study questionnaire to give us your perception of the study. MISSED VISITS: In case a follow-up is missed, we will try to collect as much missing data as possible when we talk to you next. If your follow-up visits are in-person and you need to pay for parking for this visit, we will reimburse you up to $7 for each follow-up visit.

Of all the procedures described above, the following assessments may be completed remotely during the COVID19 crisis: (1) Baseline interview, (2) Follow-up timepoints at around 1, 4 and 8 months after the post-intervention.

OPTIONAL SALIVA SAMPLE:
If you choose to provide a genetic sample (saliva), we will ask you to not eat, drink, smoke, or chew gum for 30 minutes before giving the saliva sample. Then you will spit into a plastic container a few times to fill the container to a designated line. About 2 milliliters, or half a teaspoon, of saliva will be collected. It is an option to skip the genetic sample procedure and still take part in the rest of the study.

OPTIONAL IN-PERSON COMPUTERIZED TASK:
During this task, you will be asked to make a series of economic choices on a computer for about 30 minutes. You will be looking at different video clips. You will be paid $20 for finishing this task. You can complete this task up to 3 times during the study. The task may be completed at any in-person visit. This is optional; you do not have to take part in this activity to remain in the main part of this research study. Just let the study team know if you are interested in completing this task.

OPTIONAL MOMENTARY ASSESSMENT SURVEYS:
If you choose to participate in this portion of the study, you will fill out surveys asking you about current urge to drink, mood, and stress levels. You will fill out one daily survey while in Lodging Plus. You will fill out up to three surveys a day after you are discharged from Lodging Plus. Each survey will take about 5 minutes. You will receive $1 per survey completed (each takes about 5 minutes to complete). *Payment for this optional portion of the study will be given weekly and these payments will be processed on the business day following each 7-day window. At each weekly payment after leaving Lodging Plus, you will get a $5 bonus if you have completed at least 2 assessments per day in the past week.*

OPTIONAL WEARABLE ACTIVITY TRACKER:
You have the option to wear the Garmin VivoSmart4 around your wrist to track your activity levels during the 8-month follow-up period. This device will track your sleep, physical activity, heart rate, and

stress level. If you choose to wear the activity tracker, you will install the "Garmin Connect App" on your smartphone and authorize Garmin to transfer the data to our secured servers. We ask that you wear the activity tracker for the entire 8-month follow-up period. And at the end of this period, you can choose to return the device or keep it for personal use-- the study team will not collect data from the tracker after this period is over. You will be paid an additional $80 at your 8-month follow-up visit for wearing this device during the 8-month follow-up period.

Benefits of Study Participation
There is no direct benefit to you to participate in this study. Learning more about brain function in psychiatric disorders could aid in directing patient treatment in the future.

Should you desire photos from your brain MRI as souvenirs, we will request that you fill out a release of information allowing us to release a picture of your brain to you by mail or by secure, encrypted e-mail through the University of Minnesota's preferred encrypted email service. These photos have not been evaluated by a medical professional and are for souvenir purposes only.

What happens if I do not want to be in this research?
There are no known alternatives, other than deciding not to participate in this research study. Your decision to not participate will not affect any of your current treatment program in Lodging Plus and will have no impact on any medical care.

Risks of Study Participation
1) Saliva collection for genetic testing:
The collection of saliva for genetic material is painless with little risk to your health. If you choose to provide a saliva sample, you will not be allowed to eat, drink, smoke, or chew gum at least 30 minutes prior to the saliva collection. Some people may experience dry mouth after saliva collection. Water may be provided to you by the study staff member if you experience dry mouth or discomfort after the saliva sample collection.

2) Possible risks associated with use of the high field MRI system:
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 investigator.

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 investigator.

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 investigator and should notify the investigator 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 researcher right away and your participation will stop and you will be taken out of the magnetic field.

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.

3) TDCS is considered to be a non-invasive investigational device that involves applying a weak electrical current to the scalp. There is currently no evidence of serious side effects. Listed below are mild side effects that typically go away after stopping tDCS:

- Light itching under the electrode at the beginning of administration
- Headache
- Fatigue
- Nausea

You may choose to discontinue stimulation at any time during the session if experiencing excessive discomfort or side effects. While electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS) may induce seizures, the amount of current used to stimulate with tDCS is not enough to induce seizures. Although seizures are not a known risk of tDCS intervention, anyone with a history or a risk for seizures will be excluded from the study.

4) Some of the questions in the clinical interview may make you feel anxious or uncomfortable as they are of a personal nature. You may refuse to answer any of the questions that make you uncomfortable.

5) There are certain privacy risks that are also associated with the nature of this study. Confidential information is disclosed throughout the interview process. Therefore, a potential risk is the release of confidential information.

If at any time it is clear that you are too uncomfortable with the interview, the MRI scan, the tDCS

intervention, or the investigator becomes concerned about your physical and mental health, we will discontinue the study.

If at any time during these assessments you become excessively distressed or otherwise need access to mental health resources, the research staff and clinicians involved in the study with meet with you.

Research Related Injury

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, please let us know right away.

Study Costs/Compensation

There is no cost for you to participant in the study. You will be compensated at the end of each of each day you participate (8 potential days plus 3 follow-up visits). You will be compensated:

Baseline interview	**$25**
Pre-Intervention MRI	**$25**
Intervention Day 1	**$10**
Intervention Day 2	**$10**
Intervention Day 3	**$10**
Intervention Day 4	**$10**
Intervention Day 5	**$10**
Post-intervention questionnaires	**$25**
Post-intervention MRI	**$25**
1-month in-person follow-up with MRI	**$50**
MRI #3	**$50**
4-month follow-up	**$100**
8-month follow-up	**$100**
Total (assuming all visits are completed)	**$450**

If your follow-up visits are in-person and you need to pay for parking, you will be reimbursed up to $7 for each follow-up visit.

If you choose to participate in any of the following optional activities, you will receive additional compensation for your time and effort:

Optional In-Person Computerized Task: You will be paid an additional $20 for each in-person

computerized task you complete. You are allowed to complete the task 3 times for a total of $60.

Optional Momentary Assessment Surveys: You will be paid an additional $1 for each survey you complete. You could receive up to $118 if you complete every survey.

Optional Wearable Activity Tracker: If you wear the optional activity tracker during your entire 8-month follow-up period, you will be paid an additional $80 at your 8-month follow-up Visit.

Payment Method
You will be given a Greenphire ClinCard, which is a specially made debit card for clinical research payments. After you have completed a visit, the specific payment for that visit will be added onto your card. It can be used wherever MasterCards are accepted. You will be given additional information on how the card works.

Certain types of transactions made with your ClinCard may incur usage fees (similar to the fees you pay when using an ATM that is not your bank's). These fees are determined by Greenphire, and you will be responsible for them. A detailed notification of the potential fees will be given to you to assist you in assessing when you may be charged a fee. You will never be charged a fee for making in store or online purchases with your ClinCard.

Lost or Stolen ClinCards: If your card is lost or damaged, please contact the study coordinator for assistance. If the card is stolen, please call (866) 952-3795 for ClinCard's Customer Service immediately and also notify the study coordinator. Available funds on the card at the time of notification will be frozen and transferred to a new card. Customer Service will mark the card "stolen" and will assist you in contacting MasterCard to open a case.

If you receive more than $600 in compensation/stipends in a calendar year for participating in a research study, you will be required to fill out an IRS form W-9. Your name, address, and social security number will be collected as part of that form. You will receive an IRS form 1099-MISC and those monies will be taxed as income and reported to the IRS. You would be responsible for the payment of any tax that may be due.

Will I receive research test results?
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.

Genetic study results:
Information from these genetic studies or future studies using this data will not be made available to you or your doctors and will not affect you or your clinical care. The genetic analyses performed in this study are not for clinical use, therefore none of the genetic results from this study will be put in your medical records. We will not contact you about specific genetic results of this study, and you will not be contacted about results of future studies using this data. All study information, including genetic results, is stored under conditions that limit access in order to protect your privacy. Genetic results will be de-identified and stored separately from your contact and personal information. Individualized identifiable genetic results will not be published. Results obtained from this study or future genetic research studies will not provide any direct benefits to you.

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.

Confidentiality
The records of this study will be kept private. In any publications or presentations, we will not include any information that will make it possible to identify you as a subject. Your record for the study, however, may be reviewed by departments at the University with appropriate regulatory oversight. If you are enrolled in the Lodging Plus in-patient treatment program, research staff will notify Lodging Plus staff that you will be leaving the facilities on the days when MRI scans are completed (Days 2 and 8) and will let them know approximate time of return.

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, 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 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.

We are also required to report events regarding safety concerns (e.g. current abuse of a child or vulnerable adult, ingestion of certain drugs by a currently pregnant person, or suicidal tendencies). To these extents, confidentiality is not absolute and we may be required or permitted by law or policy to report this information to authorities.

Additionally, a risk of genetic research is loss of confidentiality. If your results were to get out, it could cause emotional distress for you and your family, or lead to discrimination against you by insurance companies or employers. To protect against these risks, we will not put any information from this study in your medical record. Any physical copies of your genetic results will be stored in a locked file cabinet within a secured office. Any electronic genetic results will be encrypted and stored on a password-protected computer according to current University of Minnesota policy for protection of confidentiality. Your donated saliva sample and genetic material will not be stored with your name or any other identifying information, but instead will be given a code number to protect your identity.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

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.

Protected Health Information (PHI)
Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Genetic Samples:
The saliva samples collected in this study can be stored for a long time, many years after the study is completed. This allows for the possibility of future genetic research beyond the current study, either by the researchers of the current study or by other researchers who may request access to this study's data in the future. Any future genetic research that is not a part of the current study will only be done after approval by a special committee (Institutional Review Board) that protects the interest of research participants. You may choose whether or not your genetic samples are stored for future research by indicating your choice at the end of this form. If you agree to allow your saliva and genetic material to be used for future genetic research, your sample will be stored with a number code and not with any identifiable information. This unique number code will be linked to your clinical research data by an encrypted and secure database. Only the study investigators will have access to this database. If you agree to allow your saliva and genetic material to be used for future genetic research, you will not be asked again for consent to use your sample in future genetic research studies. There is no limit to how long we will store your sample. We may keep using them for research studies until they are used up. If you choose to withdraw from the study, any genetic samples you have already provided to the study will be retained.

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. To comply with retention requirements, records including HIPAA and consent forms will be retained for at least six years after completion of the research.

Voluntary Nature of the Study
Participation in this study is voluntary. Your decision whether or not to participate in this study will not

affect your current or future relations with the University of Minnesota Medical Center or Fairview. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Whom do I contact if I have questions, concerns, or feedback about my experience?
This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the 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.

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.

Optional Elements:
The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by **placing your initials** next to each activity.

Yes, I agree (Initials)	**No, I disagree (Initials)**	
_____	_____	I give permission to collect saliva for the optional genetic study.
_____	_____	I give permission to store my saliva and genetic material after completion of this study for future genetic research. I understand that my stored sample will be kept in a non-identifiable form to prevent anyone from identifying me.
_____	_____	I agree to complete the optional decision-making task.
_____	_____	I agree to complete the daily momentary assessment surveys.
_____	_____	I agree to wear the activity tracker during the 8-month follow-up period.

You will be given a signed copy of this form to keep for your records. You are making a decision whether or not to participate. Your signature indicates that you have read the information provided above and have decided to participate.

_____

Name of Participant (PRINT)

Date: _____

_____ Time of day: _____

Signature of Participant

_____

Name of Person Obtaining Consent (PRINT)

Date: _____

_____ Time of day: _____

Signature of Person Obtaining Consent