Informed Consent

Frontal E/I balance mediation of tACS effects on behavioral flexibility

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

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IRB Study # 23-1702
Title of Study: Frontal E/I balance mediation of tACS effects on behavioral flexibility
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CONCISE SUMMARY

The purpose of this study is to better understand how alcohol use during adolescence affects the adult brain and behavior. We are testing whether alcohol use during adolescence changes the relationship between current alcohol use and certain measures of brain function and behavior, and whether non-invasive brain stimulation can change these behavior measures through changes to these brain function measures.

Participation in this study will involve three in-person sessions at the UNC Chapel Hill campus, each lasting between 2 and 5 hours. During the first session, you will be asked to complete some questionnaires to confirm eligibility, then you will be trained on a computer-based behavioral task, and we will collect saliva, urine, and blood samples. During the second session, you will come to the Biomedical Research Imaging Center (BRIC) at UNC to undergo a functional magnetic resonance imaging (fMRI) scan and complete another version of the computerized task. During the third (final) session, you will complete the computerized task again while receiving either sham or active non-invasive transcranial alternating current stimulation (tACS) on your scalp, and we will collect resting-state EEG data before and after brain stimulation. You will then return to the BRIC for a final fMRI scan. At the beginning of each session you will be asked to complete a urine drug screen and an alcohol breath test, and the detection of any drug use or a blood alcohol content (BAC) value above .000 will result in exclusion from participation.

The risks and benefits associated with participation are outlined below. If you are interested in participating in this study, please continue reading.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this study is to better understand how alcohol use during adolescence affects the brain and certain types of behavior during adulthood. We are interested in whether adolescent alcohol use shifts the balance of excitatory and inhibitory activity in a part of the brain (the prefrontal cortex), and whether there is a change in behavioral flexibility associated with this shift. We are also interested in whether non-invasive brain stimulation can improve behavioral flexibility by altering this balance of activity in the brain.

Are there any reasons you should not be in this study?

You should not be in this study if you:

- Are pregnant
- Have a diagnosis of any neurological disorder (e.g., Parkinson's, Multiple Sclerosis)
- Have a seizure disorder or any family history of Epilepsy
- Have a history of brain injury or brain surgery
- Are claustrophobic
- Have any brain implants or devices (e.g., aneurysm clips, cochlear implants)
- Have any history of Psychosis

How many people will take part in this study?

Approximately 66 people in the Chapel Hill area will take part in this study.

How long will your part in this study last?

This study will involve three visits to the UNC Chapel Hill campus, each lasting between 2 and 5 hours. The first two sessions should take approximately 2 hours, and the final session will be longer (lasting up to 5 hours). You will also be asked to complete an online survey on your own time at home, which is expected to take between 1 and 1.5 hours to complete. Over the course of the study you will be asked to give a saliva sample, which will be used to look for a certain gene, a urine sample, and a blood spot (finger stick) sample, all of which will be securely stored at

UNC Chapel Hill.

What will happen if you take part in the study?
During the first session, you will come to Howell Hall at UNC where you will be asked to complete some questionnaires to confirm eligibility. You will also be trained on our learning task, and will be asked to donate a saliva sample, a urine sample, and a small amount of blood. At the beginning of each session, you will also be asked to complete a urine drug screen and an alcohol breath test. Any drug use detected by the urine test or failure to blow a .000 BAC will result in exclusion from further participation.

During the second session, you will come to the BRIC at UNC, where you will be asked to complete a longer version of the learning task and will undergo a resting-state fMRI scan (a non-invasive procedure that looks at the function of the brain.)

During the third and final session, you will return to Howell Hall where you will complete the learning task again. Afterwards, your head will be measured and you will be outfitted with three electrodes connected to an apparatus designed to administer non-invasive brain stimulation. You will also have an EEG net placed on your scalp, over the stimulation electrodes. This net will be used to record your resting-state brain activity immediately prior to and after stimulation. You will either receive active stimulation or sham stimulation – neither you nor the researcher will know which type of stimulation you are receiving. You will be randomly assigned (like flipping a coin) to receive active or sham stimulation prior to your third session, and only the study PI, Charlotte Boettiger, will know which condition you have been assigned to. During active stimulation, a small amount of current will be delivered to the electrodes placed on your scalp for the duration of the stimulation period. During sham stimulation, the electrodes will be briefly charged up and then stimulation will be ceased. Some people report itching or tingling on the site of stimulation, while others feel nothing. If at any point you feel uncomfortable, the researcher can turn off the stimulation apparatus and disconnect the electrodes. During the stimulation period, you will complete another round of the learning task. Following the post-stimulation EEG recording, you will be escorted to the BRIC for the final fMRI scan.

Additionally, you will be asked to complete a series of online questionnaires prior to your final session. This is expected to take 1 to 1.5 hours to complete, and can be done wherever and whenever you please.

The saliva, urine, and blood samples collected during this study will be stored anonymously at UNC Chapel Hill for later analysis, and may be used for future re-analysis without obtaining additional consent.

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?
Some of the questions you will be asked during this study pertain to sensitive subjects and may

make you feel uncomfortable. You do not have to answer any questions we ask unless you want to.

Most people who undergo non-invasive brain stimulation report only itching or tingling during the ramp-up period. Some people feel nothing, and a small number of people report a burning feeling. If you feel uncomfortable with stimulation at any point, please tell your researcher and they can turn the machine off immediately. tACS is considered investigational and has not been authorized for clinical use by the FDA, however it has been approved for research purposes and has been approved for clinical use in the European Union. The Boettiger lab research team has completed hundreds of stimulation sessions with no adverse events reported.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

What are the risks to a pregnancy or to a nursing child?

If you are a woman and you are planning to get pregnant, you should not be in the study. While there is no research indicating that tACS poses a risk, there is also no research confirming that it does not. Given that the risk of tACS to pregnant women is unknown, if you are able to get pregnant, you will be given a urine pregnancy test prior to each session.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Will I receive any other clinical results?

The imaging we are using in this research study is not the same quality as imaging that you may have as part of your health care. The images will *not* be reviewed by a doctor who normally reads such images (such as a radiologist). As a result, you may not be informed of any unexpected findings. The results will *not* be placed in your medical record. Occasionally the technologist or principal investigator may notice something abnormal on the imaging. If this does occur, the images will be reviewed by a qualified doctor to determine if there is anything of clinical importance. If something is found to be important then you, and/or your primary care provider will be notified. Any further follow up and costs associated with the incidental finding will be your responsibility. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate).

Do you wish to be informed in case of clinical/relevant unexpected findings? Please initial in the box below if you do not wish to be notified of clinical/relevant unexpected findings. If you do not initial in the box, you will be notified of any findings.

_____ I do not wish to be notified.

How will information about you be protected?

Participating in research has inherent risks related to privacy and confidentiality. Your data will be stored separately from all identifying information, and you will be assigned a random study ID to keep your data anonymous. Your data will be stored securely and will only be accessible by the research team to minimize the risk of a breach of confidentiality.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

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

Will my genetic information be shared?

Your blood and tissue samples contain genes that are made of DNA unique to you. To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. If you agree to take part in this study,

some of your genetic and health information might be placed into one or more scientific databases. There are many different kinds of scientific databases; some are maintained by this institution, some are maintained by the federal government, and some are maintained by private companies. For example, the National Institutes of Health (an agency of the federal government) maintains a database called "dbGaP." A researcher who wants to study the information must apply to the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with information from many other people. Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small but may grow in the future as technology advances. Researchers will always have a duty to protect your privacy and to keep your information confidential.

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. GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Biospecimens collected for this study (blood, saliva, urine) may be de-identified and added to a database, where they may be used for commercial profit. You will not be entitled to any portion of this profit.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?

You will be receiving approximately $15/hour for taking part in this study. You will be paid according to bonuses related to performance on the learning task. You will also receive $30 for completing the online questionnaires and an additional $80 bonus for completing all study sessions. Any payment provided for participation in this study may be subject to applicable tax withholding obligations. Payment will be initiated via PayPal or a visa prepaid gift card at the end of your final session, or will be mailed to you if you withdraw from participation prior to the third session.

In order to process payments, the University may share certain identifiable information about you, such as name, contact information, and Social Security Number where required with third parties that the University retains to process payments on its behalf. If you do not want to agree with sharing your information with these third parties, then you will be unable to receive payment/compensation for participating in the study.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?

It will not cost you anything to be in this study. All tests and procedures are being done as part of this study and are paid for by the study, including the urine pregnancy tests.

What if you are a UNC student?

You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study
This research is funded by NIH National Institute on Alcohol Abuse and Alcoholism (NIAAA). This means that the research team is being paid by the sponsor for doing the study. UNC-Chapel Hill owns technology being used in this study and which is licensed to Pulvinar Neuro. Accordingly, the University has a financial interest in the outcome of this study. If this technology or approach is successful at some point in the future, UNC-Chapel Hill may receive financial benefits.

If you would like more information, please ask the researchers listed on the first page of this form

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

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 website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness if applicable; e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness