

Consent Form

Title: At-home Transcranial Alternating Current Stimulation During Multitasking

NCT#: NCT04231825

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

Study Title: Enhancing cognitive health via non-invasive neurostimulation

This is a research study assessing the utility of non-invasive neurostimulation to enhance cognitive abilities such as attention and memory. The study researcher Theodore Zanto, Ph.D. from the UCSF Department of Neurology, or a member of his laboratory, will explain this study to you. Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study researcher. You are being asked to take part in this study as a volunteer.

Why is this study being done?

The purpose of this study is to assess the utility of non-invasive neurostimulation to enhance cognitive abilities such as attention and memory and to understand the neural mechanisms that underlie alterations in cognitive ability following non-invasive neurostimulation. The National Science Foundation has provided funding to help understand the neural mechanisms that underlie alterations in cognitive ability following non-invasive neurostimulation whereas the National Institute on Aging has provided funding to assess the utility of non-invasive neurostimulation to enhance cognitive abilities such as attention and memory. The neurostimulation procedures that will be performed use the Chattanooga Ionto Dose Controller and/or the Neuroelectronics Starstim device, which are investigational devices only and have not been approved by the U.S. Food and Drug Administration (FDA).

How many people will take part in this study?

Approximately 450 people will take part in this study.

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

If you agree, the following procedures will occur:

First, you will participate in a prescreening where we will evaluate your attention and memory in order to determine your eligibility for the main part of the study. If the screening exam shows that you are eligible and you choose to continue, then you will be asked to participate in some or all of the procedures described below. By writing your initials, it means that you have been invited to participate in the corresponding part(s) of our research study and consent to the procedures. The corresponding part(s) that you will be invited to participate is based on a quasi-randomized process that assigns participants to particular subgroups. The quasi-randomization process limits who will be assigned to certain experimental procedures. For example, older adults will not be randomized to a group that receives neurostimulation at home, whereas younger adults will not be randomized to a group that receives positron emission tomography.

Study Procedures

Phases I and III: At-home or in-lab testing at UCSF (pre/post neurostimulation and follow-up)

You will be compensated for your total participation in the study. Your participation in phases I and III may include some or all of the following procedures:

Initials

Behavioral Assessment: You will take part in cognitive testing at UCSF Neuroscape. These behavioral testing measures will assess your attention, working memory, perceptive and motor abilities.

Initials

IQ Assessment: You may be asked to complete a standard intelligence quotient (IQ) assessment.

Initials

Survey Questionnaires: You will take part in completing online surveys through a secure web interface. Copies of these surveys will be available upon request. These surveys may assess the following: multimedia use, mood, socio-economic status, aspects of cognition (e.g., attention, memory, expectancy), daily habits and routines (e.g., sleep and stress) to better characterize individual differences. These surveys should last no more than ninety minutes.

Initials

EEG Cognitive Testing: You will take part in cognitive testing at UCSF Neuroscape, during which electrical activity from your scalp will be recorded through electroencephalography (EEG). You will perform computer based tasks while we record electrical activity from your scalp with EEG equipment. Upon arriving at the laboratory, we will train you on the tests first. You will be presented with images on a computer monitor and/or sounds through headphones and instructed how to engage in the task. You will be asked to press a button in response to certain stimuli. Following this training, you will perform these same cognitive tests while wearing a cap that contains multiple EEG electrodes applied to your scalp with a removable gel, or perform the cognitive tests without the EEG electrodes. The EEG measures electrical activity produced by your brain. There is also a possibility that you may wear an alternative “dry” electrode cap without any gel. An entire session should last no more than four hours.

Initials

fMRI/MRI Cognitive Testing: You will take part in a cognitive testing session at the Neuroscience Imaging Center (NIC) at UCSF Mission Bay. Upon arriving at the NIC, we will train you on a memory or attention test. Depending on the individual study, you will be presented with either pictures or words on a computer monitor or sounds through headphones. You will be asked to pay attention to and remember the different pictures, words, or sounds. You will be asked to press a button in response to certain stimuli. In the fMRI study, we will use a magnet to measure blood flow to your brain. We use the fMRI to study which parts of your brain are most active while you do different cognitive tasks. You will be asked to lie down on a platform that can be slid into the middle of a magnet. A plastic MRI imaging coil will be placed around your head. You will not come into contact with the coil during the experiment. Foam pads will be placed around your head to limit head movement during the experiment. We will then slide you into the magnet. At different points during the experiment, you will be asked to do the same tasks you did in the training session. The tasks will take about one to two hours. The entire session should last no more than four hours.

Initials

Saliva Sample Collection for Genetic Testing: You will be asked to spit into a small container until we have collected 1 tablespoon of specimen. Alternatively, we may perform a buccal cell sample collection. In which we will rub the inside of your cheek with an abrasive cotton swap, the abrasiveness of the swap might cause slight and brief discomfort. This part of the experiment will take less than one minute. The saliva sample will be used to conduct genetic testing. These results will not be shared with the participants. The samples will be banked at the UCSF DNA Genomics Core Bank for a minimum of 1 year and will be reassessed on a monthly basis thereafter. The DNA can be banked for up to 20 years maximum.

Initials

Physical Assessment: You will be asked to perform a series of physical assessments, demanding various cardiovascular and aerobic exercise activities. These assessments include the Timed Up and Go test as well as the 30-Second Chair Stand test and will measure how quickly you sit down, stand up and walk to/from a chair. The assessment duration will not exceed a total of 15 minutes, and all participants will be offered breaks, water and snacks throughout the duration of the assessment.

Initials

Fasting Blood Draw (venipuncture): You will be asked to participate in a blood draw. We will be drawing 200ml of blood total. Because we are measuring hormones related to metabolism, such as insulin, we must draw blood before you have eaten breakfast. Therefore, for each visit, you will be asked to not eat or drink anything (except water) after midnight before you come in for the blood draw. This blood will be analyzed for indices of stress, aging, vascular health, and metabolism (stress and metabolic hormones, markers related to immunology, and potential genetic markers for aging, stress, and depression). Some samples will be sent outside UCSF to Quest Diagnostics for testing. These samples will include your date of birth. Based on standard assays from the blood draw, if diabetes or any other clinically significant condition is detected, you will be informed after your visit, and advised to consult your doctor, and you will no longer be eligible to continue in the study.

Initials

Blood Bank: If you consent by initialing the adjacent box, we will bank extra blood for future assays, as new hypotheses are developed. Blood would be banked for 10 years. For example, we would assay for any new important genetic markers of vulnerability to stress or aging. All samples will be identified by ID only, and participants will not be told any results, given that we are only looking at experimental questions that have no diagnostic significance.

Initials

PET/CT Scan: You will have a small intravenous catheter (IV) placed in your forearm. About two teaspoons of the imaging agent florbetapir F 18 will be injected in to your bloodstream. After the injection of the florbetapir F 18, you will rest for approximately 50 minutes, then you will be taken to the positron emission tomography / computerized tomography (PET/CT) scanner. You will then be asked to lie flat on a gurney and then the bed will move you into the PET camera. You may be placed back in the PET scanner for a second imaging session (also 20 minutes) if the first imaging picture is not usable. During your time in the PET scanner you must hold your head as still as possible. You will be asked to lie still while the PET cameras detect the radioactivity in your body. A physician or technologist will be with you in the room, and you will be able to

communicate with them at any time. You will not feel anything during the imaging process. Most people do not find the scanner to be constricting or claustrophobic. If at any time you wish to stop the scan, this will be done immediately upon your request. You will also have a computerized x-ray (CT scan) to help align the positioning of your brain before each PET scan. After the scans are completed you will be asked to drink fluids and empty your bladder. You should not receive research PET scans if you are pregnant, have received radiation therapy, or have been in another research study involving radiation within the last year.

Phase II: At-home or in-lab neurostimulation (up to a 5 week period)

You will be quasi-randomized to one of two neurostimulation groups: experimental or control. The difference between the experimental and control groups is based on differing frequencies and/or duration of the neurostimulation applied. Because the study is double blinded, neither you, nor the experimenter will know which group you have been assigned. Regardless of the group you are assigned, the neurostimulation will occur either at-home or in-lab at UCSF Neuroscape. At-home and in-lab neurostimulation only differ in the way data is collected. At-home neurostimulation will involve being sent home and asked to complete neurostimulation from home. In-lab neurostimulation will involve coming into the UCSF Neuroscape lab for each day of neurostimulation. You will be compensated for your total participation in the study. Your participation in phase II will include some of the following training procedures:

Initials

tES Cognitive Testing: You will take part in cognitive testing either at home or at UCSF Neuroscape, while tES is applied. tES stands for Transcranial Electrical Stimulation, which is a form of non-invasive neurostimulation that uses a weak electrical current to stimulate the brain's nerve cells. An electrical stimulator will be placed so that the stimulators touch your scalp. An electrical current will be passed between the stimulators, causing a transient change in normal brain activity around the stimulation sites. The current being generated is approximately the same as that drawn by a hearing aid. tES will be applied using one of three types: direct current (tDCS), alternating current (tACS) or random noise (tRNS). When the current is being passed you may feel some itching or a small shock similar to that caused by static electricity. These sensations are not painful but can be bothersome or irritating. You may also see small, brief flashes of light — called phosphenes — due to the stimulation of optical nerve or visual brain regions. tCS will be applied for up to 30 minutes per day. During stimulation you will perform the cognitive tasks. The entire session should last no more than three hours. You may receive regular email reminders and check-in phone calls as reminders to your at-home or in-lab neurostimulation sessions. If you are in the at-home tES portion of the study, members of UCSF Neuroscape may visit your home to assist you in the initial set up of the equipment. Equipment set-up will be done by qualified research staff. Telephone and email support will be provided to you throughout your involvement.

Initials

Simultaneous tES-EEG Cognitive Testing: You will take part in cognitive testing either at home or at UCSF Neuroscape, during which both transcranial electrical stimulation (tES) is applied and electrical activity from your scalp will be recorded through electroencephalography (EEG). tES is a form of non-invasive neurostimulation

that uses a weak electrical current to stimulate the brain's nerve cells. An tES electrodes will be placed so that the electrodes touch your scalp. An electrical current will be passed between the electrodes, causing a transient change in normal brain activity around the stimulation sites. The current being generated is approximately the same as that drawn by a hearing aid. tES will be applied using one of three types: direct current (tDCS), alternating current (tACS) or random noise (tRNS). When the current is being passed you may feel some itching or a small shock similar to that caused by static electricity. These sensations are not painful but can be bothersome or irritating. You may also see small, brief flashes of light — called phosphenes — due to the stimulation of optical nerve or visual brain regions. tCS will be applied for up to 30 minutes per day. While you perform computer based tasks, tES will be applied and electrical activity from your scalp will be recorded with EEG equipment. Upon arriving at the laboratory, we will train you on the tests first. You will be presented with images on a computer monitor and/or sounds through headphones and instructed how to engage in the task. You will be asked to press a button in response to certain stimuli. Following this training, you will perform these same cognitive tests while wearing a cap that contains multiple EEG and tES electrodes applied to your scalp with a removable gel. The EEG measures electrical activity produced by your brain. There is also a possibility that you may wear an alternative “dry” EEG electrode cap without any gel. An entire session should last no more than three hours. You may receive regular email reminders and check-in phone calls as reminders to your at-home or in-lab neurostimulation sessions. If you are in the at-home tES portion of the study, members of UCSF Neuroscape may visit your home to assist you in the initial set up of the equipment. Equipment set-up will be done by qualified research staff. Telephone and email support will be provided to you throughout your involvement.

Once you consent to participating in this study, we ask that you do not change your interaction with technology (i.e., do not spend more time on your computer or expand the number/type of activities you use the computer for, upgrade your cellular phone to a smart phone, begin playing other video games, etc.) until you are no longer enrolled in this study. If any changes of this nature do occur, we ask that you let us know.

Further Information: Blood or Saliva Sample Collection – Genetic Testing:

Types of specimen kept, and where:

Blood or saliva samples will be collected from some participants for genetic testing. These will be housed at the UCSF DNA Genome Bank in Rock Hall at the Mission Bay Campus. This is a core facility of UCSF and accepts the clinical samples from projects that have been approved by the Institutional Review Board (IRB). Genomic DNA isolation is performed utilizing standardized and quality controlled Genra Systems' PureGene DNA isolation system or Qiagen Kits.

Types of research the specimens can be used for and duration of specimen retention:

The specimen will be used for genetic testing for genes associated with cognitive enhancement or decline in healthy aging and Alzheimer's disease. The samples will be banked at the UCSF DNA Genomics Core Bank for a minimum of 1 year and will be

reassessed on a monthly basis thereafter.

Types of data/medical information collected with the specimens and how long the information will be collected:

The information that will be collected with the specimen includes demographics, testing performance, and measures of brain activity. The information will be collected during a single visit or over a series of visits based on the project goals. The specimen will be collected during a single visit.

Who will have access to specimens and data:

Genetic information (also known as genotype data) and the medical record data (also known as phenotype data) may be shared broadly in a coded form for future genetic research or analysis. We may give certain medical information about you (for example, diagnosis, blood pressure, age if less than 85) to other scientists not at UCSF, including to a government health research database, but we will not give them your name, address, phone number, or any other identifiable information. Research results from these studies will not be returned to you. If you decide later that you do not want your information to be used for future research, you can notify Dr. Zanto in writing at 675 Nelson Rising Ln Box 0444, San Francisco, CA 94158 or email theodore.zanto@ucsf.edu, and any remaining data will be destroyed. However, we cannot retract any data has been shared with other researchers.

How long will I be in the study?

There are three phases to the study, which in total, will not exceed 15 experimental sessions over the course of one year.

Phase I: no more than 3 sessions.

Session length not to exceed: 4 hours.

Total time not to exceed: 12 hours.

Phase II: up to 5 weeks of at-home or in-lab testing, maximum of 9 sessions.

Sessions per week: not to exceed 5 sessions.

Maximum time per session: not to exceed 3 hours.

Total time not to exceed: 27 hours.

Phase III: no more than 3 sessions.

Session length not to exceed: 4 hours.

Total time not to exceed: 12 hours.

*You will be compensated for your active time in the study.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study. Also, the study researcher may stop you from taking part

in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

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

Cognitive Tasks: Depending on the nature of the cognitive tasks, mental fatigue or boredom are minor risks.

EEG: All of the EEG procedures have been used extensively in previous research. In some cases, EEG caps and gel may cause mild skin irritation/ discomfort. We try to remove all of the electrode paste from your scalp, but some may remain. You can easily remove this extra paste by shampooing. The pictures/sounds used in the studies are presented at a comfortable lighting/hearing level. The button presses require minimal effort.

fMRI/MRI: The levels of energy used to make fMRI measurements are far less than are used in a single X-ray, and many patients have been safely studied using MRI techniques. While there are no significant risks from fMRI as it is to be performed, the fMRI procedures can be risky for people with pacemakers or metal in their bodies. We will not ask you to participate in the fMRI if you have a pacemaker or any metal in your body that cannot be easily removed. Some people get claustrophobic in the MRI scanner. If you have a history of claustrophobia, we will not ask you to participate in the fMRI study. Because the fMRI scan makes loud noises, we will give you ear plugs to dampen the sound. You may also experience peripheral stimulation, which will feel like a gentle tap or sensation of mild electric shock. If you do not like being in the scanner for any reason, we will immediately stop the experiment.

We do not know if the fMRI procedure is associated with risks to an unborn fetus. We ask that all women of child-bearing age take a pregnancy test before participating. This is an “over-the-counter” pregnancy test that identifies pregnancy through a urine sample. We will give you the test kit for you to take by yourself, in private, in the bathroom. If you are pregnant, please tell the experimenter that you cannot participate in the fMRI scan.

tES: tES, as used in this experiment, has been found to be a very low-risk procedure. The potential concern with tES arises from the possibility for discomfort during the stimulation. The adverse effects that have been commonly reported are mild headache, tingling, itching, burning sensation, and skin redness in the area of stimulation. In addition, some participants have reported the feeling of shock during the beginning of the tES session. The shock has been described as similar to a shock from static electricity. Some individual characteristics such as type of skin and hair may make this more likely to occur. You should know that tES might result in acute mood or temporary thought changes and also cognitive side effects such as dizziness, disorientation, sleepiness, or confusion; if they do appear, these symptoms usually disappear shortly. Mood changes usually include a transient increase in the state of happiness or sadness. In addition other mood symptoms such as irritation or a slight feeling of euphoria may occur. Please inform the study personnel if you experience any of the discomforts described. tES could induce lasting changes in memory, attention and other cognitive functions. This is a theoretical risk but none of the safety studies conducted have found negative side effects.

Saliva Sample Collection-Genetic Testing: No adverse effects are associated with spitting into a container; however, some people might find it embarrassing to do so. Buccal cell sample collection might cause slight and transient discomfort due to the abrasiveness of the swab.

Physical Testing: The physical testing will be physically demanding, and there is a risk that you will perspire, feel exhausted, feel out of breath, and potentially feel dizzy. At any point in the testing if you begin experiencing any physical effect that exceeds your comfort level, you will be asked to please let us know immediately and testing will be either paused or discontinued, which will be at the participant's discretion.

Blood Draw: The risks of drawing blood and catheter insertion include temporary discomfort from the needle stick, localized bleeding and bruising, lightheadedness, and rarely, fainting or localized infection. A registered nurse or phlebotomist will do the blood draw in a sterile manner. Up to 200 mls of blood will be collected per visit, which amounts to around 14 tablespoons. To give you a sense of how much blood this is, it is a lot less than a typical blood donation, which is around 31 tablespoons.

Radiation Risks: This research study may involve exposure to radiation from F-18 florbetapir PET. This radiation exposure is not necessary for your medical care and is for research purposes only. The additional amount of radiation that you will receive as a result of participating in this study will be a maximum of approximately 16 mSv, or approximately 5 times the yearly natural background of radiation in the US, which is 3 mSv (a mSv, or milliSievert, is a measurement of radiation). This amount of radiation may involve a low, lifetime risk of cancer. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the primary investigator conducting the study.

Risks from florbetapir F 18: Florbetapir F 18 is an imaging agent that includes a small amount of radioactivity necessary to create the PET images. See radiation risks above. To date, florbetapir F 18 has been tested in approximately 3,500 people in completed and ongoing trials. The most common side effect involving 555 subjects was headache. Additional uncommon side effects reported were nausea, dysgeusia (bad taste in the mouth), flushing, pruritus (itching), urticaria (hives) and infusion site rash. Musculoskeletal (muscle and bone) pain in the neck, shoulder and back, fatigue, anxiety, claustrophobia (fear of being in closed or narrow spaces), insomnia (inability to sleep), dizziness, chills/feeling cold and hypertension (high blood pressure) were also reported. Florbetapir F 18 is approved in the United States for use in the clinical evaluation of patients who are being evaluated for Alzheimer's disease (AD) and other causes of cognitive decline.

PET/CT scan risks: Having a PET/CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the PET scanner, or by lying in one position for a long time. PET involves radiation, please see radiation section above.

For more information about potential risks and side effects, ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study or from allowing your data to be kept and used for future research. If you are currently undergoing medical treatment, these procedures will not benefit or adversely affect you. The test(s) we will perform on the saliva sample will not be shared with you, or anyone else, without exception. At the end of the experiments, we will explain what we expect to learn from the study (with the exception of the saliva sample collection). We hope that this knowledge will be useful in the future diagnosis and treatment of neurological patients. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

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

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you.

Will information about me be kept private?

We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Genetic data: Donating data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

Organizations that may look at and/or copy your research records for research, quality assurance, and data analysis include: The University of California, the National Institutes of Health and the National Science Foundation. Some blood samples will be sent outside UCSF to Quest Diagnostics for testing. The samples will include your date of birth and will be linked to your unique study ID.

Volunteers in research: UCSF volunteers are part of our research team and may assist on a research study that you are enrolled in. All volunteers receive HIPAA and CITI (Human Subjects Research) training and certification.

Obtaining study results: Participants may have the option to obtain study results, including MRI scans and basic behavioral analysis. These data were collected for research purposes and, therefore, should not be used for clinical decisions should you consult with your physician or

other healthcare provider. The results of the genetic testing will remain confidential and will not be released to the participant.

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

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

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you will be compensated \$20/hr for participating in the tES, EEG, behavioral testing (both in the lab and for the home training), blood / saliva samples, MRI/fMRI, and PET/CT testing. You will receive cash, check, or gift card. A check will be mailed to you about 6-8 weeks after you complete your participation in the study (thus requiring us to obtain your social security number).

If and only if ALL assigned tasks are completed during the study, you will earn a “**completion bonus**” of \$50, which will be added to your check at the end of the study. If you participate in the at-home research protocol and the equipment that is lent to you is either lost or damaged, we may retain some or all of your compensation to help offset losses.

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

It is important that you tell your study investigator, Theodore Zanto, Ph.D., if you feel that you have been injured because of taking part in this study. You can tell the researcher in person or call a member of the lab at 415-502-7321.

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

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

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you in any way. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do. We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to the researcher(s) about any questions or concerns you have about this study. Contact Dr. Zanto or a member of his lab at 415-502-7321. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

Date

Signature of Person Conducting Assent Discussion
with Participant with Mild Cognitive Impairment

Date

Legally Authorized Representative

Date

Person Obtaining Consent from Legally Authorized Representative