Date: 9th August, 2022

INFORMED CONSENT FORM

Study Title: Investigating if a stronger tDCS intensity is more effective for improving executive function in people living with Alzheimer's Disease

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Source of funding for the study: BrightFocus Foundation grant presented to Dr. Carlos Roncero

You are being recruited as a participant with mild to moderate Alzheimer's disease in the research study mentioned above. This form provides information about what participating would mean. Please read it carefully before deciding if you want to participate or not. If there is anything you do not understand, or if you want more information, please ask the researcher.

Clinicaltrials.gov ID: **NCT05508841**

A. PURPOSE

Transcranial Direct Current Stimulation (tDCS) is a form of stimulation where two electrodes are placed on the scalp to produce a mild electric current that passes through the brain. Previous studies have found results that suggest the administration of tDCS while people do a particular activity can lead to them being able to perform that activity better. In people with Alzheimer's Disease, for example, receiving tDCS while practicing the N-Back task seems to improve overall cognitive ability.

In the current project, you are being recruited into the study as a person with Alzheimer's disease. Our central goal is to examine if a higher tDCS intensity level will produce more benefit than the stimulation level that is usually given. tDCS stimulation is normally given at an intensity level of 2.0 mA, but higher intensities, such as 4.0 mA, can also be administered. In the current study, you will receive tDCS at 4.0 mA to observe if this produces more improvement than a lower intensity level (i.e., 2.0 mA) or the placebo condition (which is called SHAM stimulation and described later). However, before being formally enrolled, you will complete two meetings: a screening and pre-assessment. These initial meetings have two goals: 1) to ensure you fully understand the pros and cons of participating in the study; and 2) Verify that you are able do the tasks that you will be asked to do during the study. In this manner, we can verify you are fully informed and able to handle the study requirements.

In the screening, you will meet with Dr. Roncero who will go over this consent form with you, discuss what participation would require, explain the benefits and risks of tDCS, as well as answer any questions you may have. The screening is done to ensure you fully understand the pros and cons of participating in the study and type of stimulation you will be receiving. The screening with Dr. Roncero will be done over ZOOM or in person at Baycrest. You can state if you prefer having the screening be done in person or over ZOOM. Assuming you are still interested in participating in the study after attending the screening with Dr. Roncero, you will be scheduled to undergo an initial pre-assessment. This assessment is done to verify your eligibility for the study; specifically, that you have the capacity to complete the tasks that will be administered during the study. You will be asked to complete a practice version of the N-Back task, where you will be shown a series of visual stimuli in different categories. For each image, you will be asked to identify if the presented image is the SAME or DIFFERENT from the previous image. Assuming you are interested in participating in the study, have been fully informed, and demonstrated an ability to handle the study requirements, the next step will be a structural MRI in the week prior to starting your first round. However, if you are unable to complete a structural MRI due to an exclusion criteria specific to MRI, you will still be able to participate in the study.

- **What will happen during the Structural MRI?**

Magnetic resonance imaging performed in research gives images of the body and the brain as well as how they work. You will be asked to arrive 15 minutes prior to your scheduled appointment to review and fill out the consent and MR screening forms. You will then be escorted to the Interview Room to meet with a trained MR Personnel who will interview you with respect to the MR screening form and your medical history. Post the interview, you will be asked to change. You will have to remove all jewellery, metallic and electronic items, all clothing except for underwear. A hospital gown and a pair of PJ bottoms will be provided for you to change into. Afterwards, the MR Technologist will escort you into the room for a scan. During the MRI, you will lie on your back while breathing normally. The structural MRI will last approximately six minutes, and you can choose to keep your eyes closed or open. After the scan, the lab member accompanying you will monitor the change process and your exit from the suite. The total time in the scanner from entry to exit will be roughly 15-20 minutes. You will also sign another consent form with regards to the MRI.

B. PROCEDURES:

- **What will study participation be like in the following months?**

The study will require a significant time commitment on your part. Your participation in this study will require three rounds of tDCS stimulation where you will be asked to complete 11 sessions over the course of five weeks. There is a minimum six-week break between the rounds, therefore, it will take around 22 weeks (roughly 5 months) to complete all three rounds. Indeed, there are only two differences between the rounds: 1) A new version of the training task (N-Back) will be given in each round; and 2) The type of tDCS given will be different in each round (2mA, 4mA, or SHAM). SHAM is a placebo condition; it will feel as if stimulation is being administered, but no stimulation is being delivered; 2mA is the standard intensity in tDCS studies; and 4mA is an intensity we found to be safe and believe is possibly more effective. All sessions occur at our laboratory at:

Rotman Research Institute at Baycrest Health Sciences,
3560 Bathurst St, North York, ON M6A 2E1
Kimel Family Building, 3rd floor, Room 316

In the first week of each round, there is a baseline evaluation in the first week on Tuesday, followed by two stimulation sessions on Thursday and Friday where the N-Back is practiced while receiving stimulation. These stimulation sessions are repeated each day of the following week from Monday to Friday, as well as Monday and Tuesday of the third week. Finally, on Wednesday of the third week, another evaluation takes place while you receive stimulation. This final evaluation is repeated two weeks later, but without the administration of stimulation. While most sessions will last 60-90 minutes, sessions with evaluations will last roughly two hours. We display the structure of a round below:

Sequence of the Rounds (1,2 and 3)	
WEEK 1	Tuesday (Baseline Evaluation)
WEEK 1	Thursday (Training day)
WEEK 1	Friday (Training day)
WEEK 2	Monday (Training day)
WEEK 2	Tuesday (Training day)
WEEK 2	Wednesday (Training day)
WEEK 2	Thursday (Training day)
WEEK 2	Friday (Training day)

WEEK 3	Monday (Training day)
WEEK 3	Tuesday (Training day)
WEEK 3	EVALUATION DAY
WEEK 5	Two-week follow-up Evaluation without Stimulation

- **What will happen during the baseline evaluation session?**

During the first visit, you will be asked to complete two different versions of the N-back: one that will be subsequently trained that round, and a second list that will be left untrained. You will also complete a questionnaire that measures your mood in the past week and tasks that measure cognitive function. If it is the first round, you will also be asked to provide demographic information (age, sex, handedness).

- **What happens during the training sessions?**

During each tDCS session you will be asked to sit comfortably in a chair and the sponges will be placed upon your scalp to stimulate the brain with a certain intensity of tDCS stimulation (2mA, 4mA or SHAM). During tDCS stimulation, you can expect to feel an itching sensation, but it should not be painful, and typically will fade after 2 minutes. Each session should take 60-90 minutes. While receiving stimulation, you will be asked to practice the N-Back. Furthermore, you may be trained using tasks like those used during evaluation, but the exact items will be different from those used during evaluation.

- **What will happen during the final stimulation session and two weeks later?**

During the final stimulation session, you will receive tDCS stimulation in addition to being evaluated with the same set of tasks used in the baseline evaluation. This session will occur at the same location as the previous sessions, but last approximately two hours. The same evaluation will then also take place two weeks after this session, but without tDCS stimulation. In this manner, we can obtain a baseline measurement, check for post-stimulation changes, and if those changes have continued two-week's post-stimulation.

- **Will I know what stimulation I am receiving in each study round?**

As mentioned, each round has the same number of sessions and the same number of evaluations, but the stimulation given in each round is different. More specifically, you will receive stimulation in one of three orders (4 mA, 2 mA, SHAM), (2 mA, SHAM, 4 mA), or (SHAM, 2 mA, 4 mA). Therefore, you will receive one of the three stimulation orders presented below when completing the three rounds:

	(Order 1)	(Order 2)	(Order 3)
Round 1:	4 mA Stimulation	2 mA Stimulation	SHAM Stimulation
Round 2:	2 mA Stimulation	SHAM Stimulation	4 mA Stimulation
Round 3:	SHAM Stimulation	4 mA Stimulation	2 mA Stimulation

YOU WILL NOT BE TOLD which stimulation order has been assigned to you AND it is believed that you will be unable to determine in which round you are receiving real tDCS or placebo (i.e., SHAM stimulation).

Known Risks/Side-Effects:

The skin areas where electrodes are placed can become temporarily red, which dissipates after a few hours. When the machine is turned on, you will feel tingling sensations around the electrodes, which can also cause itchiness. These feelings are temporary and should disappear after a few minutes. Headaches have been occasionally reported by participants after receiving stimulation. We recommend you take Tylenol if you experience any headaches. The nature of the tasks in the study might be tedious but we ask that you do the tasks at the best of your abilities. Alternatively, you may find them difficult, but just try your best.

Possible Side-Effects:

Extremely rare, and never experienced in our own past tDCS studies, have been instances of drowsiness, nausea, or disorientation. If you ever experience these in your session, it would be immediately stopped. We would also give you a glass of water and allow you to rest for a period of time in the study room until you felt better. You may also choose to take a break from stimulation and redo the stimulation round at a later time if experienced. A 1st degree burn was once reported in the tDCS literature, but likely due to issues related to the administration of tDCS (e.g., using tap water). The chance of a burn in the current study is extremely unlikely because electrodes will be placed in sponges properly saturated with saline and we have never had a burn occur in any of our participants. Finally, there have been no known cases of seizure in past tDCS studies.

Advantages of participating in this study:

Your performance on the tasks in each stimulation session will be recorded to examine if performance was greater with 4 mA tDCS, or 2 mA tDCS, compared to the SHAM stimulation. Indeed, previous tDCS studies have found both older adults and people living with dementia often complete a given task better when it is done with tDCS. The stimulation may improve your naming abilities, at least temporarily. The project coordinator will also reach out to you after every round to ensure that there is no change in your ability to continue the study. You will also have the opportunity to ask questions pertaining to the study after every round. You will be debriefed of these results either by telephone or a zoom session once the data has been analyzed. You will also be told at that time the stimulation intensity that was delivered in each round.

Withdrawal from the study:

Your participation in this study is voluntary. You may refuse to participate or if you agree to participate, you may leave the study at any time without affecting your medical care. Any information relevant to the results of the study will be provided to you upon request. You will be notified if new information, which may affect your engagement, becomes available during your participation in the study. Data collected from your participation may be used for data analysis if a sufficient amount has been collected for analysis.

Discontinuation of the study by the investigator:

You will be able to continue to participate in the study as long as you are able to perform the evaluation tasks required for the study. As previously mentioned, at the beginning of the first session, you will be asked to complete assessments that measure your level of cognitive impairment. In this manner, we can verify you are able to properly answer the questions being asked in the session. For the N-Back task, a practice version will be administered to ensure that you can complete it in the upcoming rounds. If you are able to successfully complete this task, you will be enrolled in the study.

At the beginning of every session, the initial ramp-up to 4 mA will have an intensity level of 0.5 mA tDCS, which represents a very low intensity level. In our experience, all past participants have been able to tolerate

this intensity level. However, if you are unable to experience this low intensity level, for your own safety and to avoid any additional feelings of pain, you will be withdrawn from the study.

COSTS AND COMPENSATION:

There are no costs to you for participating in this study other than your time. You will also be compensated for your travel expenses. If you suffer an injury as a result of participating in the study, necessary medical treatment will be available at no additional cost to you. Unless required by law, compensation for such things as lost wages, disability or discomfort due to such an injury will not be offered. However, by signing this consent form you do not give up any of your legal rights (including the right to seek compensation for an injury resulting from your participation in the study) nor relieve the sponsor, institution and investigator from their professional and legal responsibilities.

CONFIDENTIALITY:

While you take part in this research study, the researcher in charge and study staff will collect and store personal identifiable information about you in a file for the purpose of the research study. Only information necessary for the research study will be collected. Dr. Chertkow will keep your study information for 10 years after the end of the study. All the information collected about you during the study will remain confidential within the limits of the Law. To protect your identity, your name and identifying information will be replaced with a code (containing numbers and/or letters), the link between the code and your identity will be held by the researcher in charge of the study. No information that discloses your identity will be allowed to leave the institution. The study information could be printed/published in medical journals or shared with other people at scientific meetings. Your identity will be replaced by a code and will not be revealed. For the purpose of monitoring this research, your research study file as well as your medical records identifying you could be checked by a person authorized by the Research Ethics Committee of the Baycrest Health Science. These people are obliged to respect your privacy.

You have the right to look at your study file in order to check the information gathered about you and to correct it, if necessary, as long as the study researcher or the institution keeps this information. However, we can only tell you which stimulation you received each round once the study is finished. We might use the data acquired from this study for additional studies conducted in the future. If you do not meet the eligibility criteria for the study after the initial screening, any information collected will be discarded in the confidential bin on the 7th floor of the Kimel Family building.

RESULTS OF THE RESEARCH:

Any relevant information regarding the results of the research will be communicated to you, upon your request. You will be informed if new information is available during your participation in this study, which could affect your willingness to continue the study. You will be allowed to continue participating in the study as long as you complete the tasks administered during the assessment sessions. To receive the results from the study, please contact the Project Coordinator of the study; Yashna Kochar at 416-785-2500 ext. 2522.

FOR MORE INFORMATION:

The following are the names, addresses and telephone numbers of the doctor and the researcher whom you may contact for questions about the research or any injuries or adverse reactions. For more information concerning this study, contact **Dr. Carlos Roncero at the Rotman Research Institute, Baycrest Health Sciences, 3560 Bathurst Street, Toronto, ON, North York, ON M6A 2E1, 438-399-4842.** The study coordinator, **Ms. Yashna Kochar** can be reached at **416-785-2500 ext. 2522**. If you experience a research-related problem or injury, contact: **Dr. Howard Chertkow , Tel. no.: 416-785-2500 ext. 2734**

If you wish to contact someone not connected with the project about your rights as a research participant, feel free to call: **Dr. Daphne Maurer, Chair of the Research Ethics Board at (416)785-2500 ext. 2440**

Date: 9th August, 2022

STATEMENT OF CONSENT:

Investigating if a stronger tDCS intensity is more effective for improving naming ability in people living with Alzheimer's Disease

I have reviewed the information and consent form. Both the research study and the information and consent form have been explained to me. My questions were answered, and I was given sufficient time to make a decision. After reflection, I consent to participate in this research study in accordance with the conditions stated above.

I authorize the research study team to have access to my medical record for the purposes of this study.

I do not give up any of my legal rights by signing this consent form.

I agree to take part in this study.

_____	_____	_____
Printed Name of Participant	Signature	Date

Signature of person obtaining consent

I have explained the research project ant the terms of this information and consent form to the research participant, and I answered all his/her questions.

_____	_____	_____
Printed Name of Participant	Signature	Date