EFFECTIVE

1/25/2021

MCW/FH IRB

Medical College of Wisconsin and Froedtert Hospital
INTRODUCTION TO THE INFORMED CONSENT

Name of Subject: _____

Effects of tDCS on Language

Principal Investigator: Sara Pillay, PhD
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You are invited to take part in this research. You can decide whether to take part in this project or not. You are free to say yes or no. If there is anything that you do not understand, please ask questions.

Definitions

Functional Magnetic Resonance Imaging (fMRI): Functional magnetic resonance imaging or functional MRI measures brain activity by detecting changes associated with blood flow.

Transcranial Direct Current Stimulation (tDCS): A form of neurostimulation that uses constant, low direct current delivered via electrodes on the head. This technique relies on the fact that cerebral blood flow and neuronal activation are coupled.

Phonologic-Focused Speech Therapy: a type of language therapy that focuses on practicing the sounds in a word.

Semantic-Focused Speech Therapy: a type of language therapy that focuses on practicing the meaning of a word.

Purpose

The purpose of this study is to assess whether phonologic-focused therapy vs. semantic-focused therapy with transcranial direct current stimulation (tDCS) is most beneficial for recovery.

Length

- You will be in this research project approximately seven months.

Procedures

List of visits:

- **Pre-assessment**
  - Total Number: 3-4
  - Total Time: 8 hours
- **Speech therapy**
  - Total Number: 10
  - Total Time: 1-2 hours each visit
- **Post-assessment A**
  - Total Number: 2-3
  - Total Time: 8 hours
- **Speech therapy**
  - Total Number: 10
  - Total Time: 1-2 hours each visit
- **Post-assessment B**
  - Total Number: 2-3
  - Total Time: 8 hours

You will undergo MRI at the Pre-assessment, Post-assessment A and Post-assessment B timepoints (3 times total).

Procedures that will occur at various visits:

Invasive Procedures

None

Non-invasive Procedures

- Medical history
- Language testing
- fMRI
- tDCS

Risks

This is a brief list of the most commonly seen side effects. The ***full consent form*** after this introduction contains a more complete list of potential research risks.

MRI risks:

- Potential hearing damage
- Feelings of anxiousness

tDCS risks:

- Mild Tingling
- Fatigue
- Itching or burning sensation

Benefits

We don't know if this project will help you. Your condition may get better but it could stay the same or even get worse.

My Other Options

You do not have to join this project. Your other options may include:

- Joining a different project
- Routine care for this condition
- Getting no treatment for this condition

If you have more questions about this project at any time, you can call Dr. Sara Pillay at 414-955-4482.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are invited to participate in this research study because you have a language deficit due to neurologic damage.

A total of about 150 people are expected to participate in this study all at the Medical College of Wisconsin/Froedtert Hospital.

The Principal Investigator for this study is Sara Pillay, PhD in the Department of Neurology. A study team works with Dr. Pillay. You can ask who these people are.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A research project is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the research procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS PROJECT BEING DONE?

The purpose of this study is to assess which of two targeted speech therapy interventions with transcranial direct current stimulation (tDCS) is most beneficial for recovery. We also want to examine the neural processes that are affected by tDCS.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

Eligibility

You will be asked questions about your medical history and condition to ensure that you meet the study criteria and can safely participate. You will also take several cognitive tests to determine whether or not you meet behavioral criteria for the study. If you are not eligible, you will not continue in the study.

Randomization

You will be “randomized” into one of two groups. Randomization means that you are put into a group by chance. You will have a one-in-two chance of being placed in any group. Neither you nor the research doctor can choose what group you will be in.

For the first treatment period, you will be randomly assigned to either targeted stimulation or an active control stimulation treatment with the HD-tDCS. The treatment in each group will look the same and neither the person delivering the treatment, nor you will know if it was targeted or active control stimulation. For the second treatment period, you will receive the

opposite treatment of what you received in the first period.

Language Test

Patients enrolled in the study will undergo an approximately 8-hour language battery which is spaced out over several sessions on separate days (maximum 6 hours of testing on any single day). The battery includes tests covering a broad range of language functions. Tests are administered using a computer display with a touch-sensitive screen to allow participants to indicate responses in a multiple-choice format. Headphones are used to present auditory stimuli, and a headset microphone is used to record spoken responses (audio recording). During the language testing, audio recordings will be made of your speech on some of the tests. The data collected will be stored on a password-protected computer that is kept in a locked office. The audio recordings will be used to analyze your speech ability. Signing this consent form indicates awareness and consent to having audio recordings made. Individual tests last between 2 and 25 minutes and are always followed by a brief rest break.

Neuronavigation

Patients will complete a cap fitting, and then wear a tracking device like a headband while a computer works to determine the best location for stimulation during therapy.

Transcranial Direct Stimulation (tDCS)

Patients will receive either anodal targeted or active control tDCS. TDCS involves a weak electrical current that is administered via scalp-attached electrodes. During tDCS, patients will concurrently receive a form of speech therapy. Patients will receive anodal tDCS during the course of the study, but will not be informed whether they are receiving targeted versus the active control stimulation.

Speech Therapy

Patients will receive either phonologic-focused speech therapy (practicing sounds) or a semantic-focused speech therapy (practicing meaning) intervention.

Magnetic Resonance Imaging (MRI) Procedure:

Patients will have a type of MRI procedure called functional magnetic resonance imaging (fMRI) performed. fMRI is a method for measuring brain activity. Your participation will involve lying still in the scanner and answering questions. The MRI procedures will last for about 1 hour. Padding is placed around your head and under your legs to make you as comfortable as possible. An intercom system in the scanner will be available through which you can be heard at all times, and the staff in the adjacent control room will use the intercom to talk to you throughout the procedure, and you will be asked to complete a series of tasks while being scanned. You will also be asked to hold your breath for a short period (about 16 seconds) during the scan. Participants would complete 3 fMRI sessions during

the entire study (one prior to starting therapy, one in the middle of therapy, and one at the completion of therapy).

B2. HOW LONG WILL I BE IN THE PROJECT?

Participants will be enrolled for approximately seven months.

B3. CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the research doctor.

The research doctor may take you out of this project at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the project rules.
- The whole project is stopped.

If this happens, the research doctor will tell you.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

There are risks to taking part in any research project. There is a risk that this treatment might not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from the device itself. If we learn about new important side effects, we will tell you.

We watch everyone in the project for problems (side effects). **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.**

C2. RISKS OF TRANSCRANIAL DIRECT STIMULATION AND MAGNETIC RESONANCE IMAGING

The research device intervention itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

<u>Transcranial Direct Stimulation</u>

Even though known safety precautions will be implemented, and even though we will use tDCS well within established safety parameters which has been found safe, we would like to point out the following potential side effects:

Mild Tingling: During the initial application of tDCS, the most common reported effect is a mild tingling sensation under the electrodes; however, this effect is short-lived and lasts only during the first few seconds of stimulation.

Fatigue: Moderate fatigue is the second most often reported effect and may relate to the behavioral portion of the experiment. Participants may find the behavioral therapy/assessment tiring and/or boring, remaining stationary during the experiment might

cause some physical discomfort, but not more than normally encountered in situations such as sitting in a lecture hall or a movie theater. The participants will also be encouraged to take frequent breaks.

Itching or burning sensations may occur under the electrodes.

Magnetic Resonance Imaging (MRI) Risks:

There is no exposure to x-rays or radioactivity during an MRI (Magnetic Resonance Imaging) scan, and the risk of injury is very low. However, MRI is not safe for everyone. Serious injury or death can result if you go into the scanner with certain metal objects in or attached to your body. For example, it is not safe to have an MRI scan if you have a cardiac pacemaker, defibrillator, certain metal or implants in your body or have metal in or near your eye.

The MRI scanner makes loud banging sounds that can cause hearing damage, but with earplugs properly worn, there is no known risk of permanent hearing damage. Rarely, your hearing may be less sensitive for several days after an MRI scan, but if this happens your hearing should return to normal within a few days. You may feel some discomfort because you are lying still for a long time, or because of the padding used to keep your head from moving.

The breath hold portion of the MRI could elevate pressure in the head for people with hypercapnia; however, this risk is considered to be minimal due to the short length of the breath hold.

Some people feel anxious being in closed or narrow spaces. The scanner operator will be in constant contact with you, and if you choose, you can be taken out of the scanner quickly. The safety of an MRI during pregnancy is unknown. Therefore, women who have the potential of becoming pregnant should be using some form of effective birth control. Any female, who is menstruating or is between the ages of 11 and 55 years with a uterus, tubes, and ovaries, has the potential to conceive a healthy pregnancy. Effective birth control is defined as any of the following: 1) Refraining from ALL acts of vaginal intercourse (abstinence); 2) Consistent use of birth control pills or birth control patches; 3) Injectable birth control methods (Depo-Provera, Norplant); 4) Tubal sterilization or male partner who has undergone vasectomy; 5) Placement of an IUD (intrauterine device); 6) Use, with every act of intercourse, of a diaphragm with contraceptive jelly and /or condoms with contraceptive foam.

MRI Pregnancy Statement. The MRI procedures used in this study has not been proven to be safe during pregnancy. Pregnant women will not be allowed to undergo an MRI in this study. Therefore, one of the following must be indicated if you are female: (Please initial one of the following.)

_____ I am not pregnant because I am using birth control methods to prevent pregnancy, or I am postmenopausal.

_____ I am pregnant; therefore, I cannot take part in this study.

_____ I don't know if I am pregnant and I agree to have a pregnancy test to see if I can take part in this study.

C3. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

Cognitive Improvement: Tests studying cognitive functions have revealed transient changes in performance, such as improved performance in verbal fluency, motor learning and memory tasks. Patients in the study may benefit from a better understanding of language deficits as provided by the language test battery. Test results can only be provided after all study activities are complete, but may also be released to your caregivers and physician if requested by you, which may help them better understand the nature of your communication difficulty

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

Activities that are part of the project will not be billed to you or your insurance company. These are speech therapy, MRI, and tDCS. Some insurers will not pay for drugs, tests or hospitalization that are part of research, so check with your insurer before you join this project. If you have questions regarding costs, please contact study coordinator Samantha Drane at 414-955-5891.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

Yes, you will be paid a one-time stipend of $150.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. If you do not join this project, your research doctor can discuss other healthcare choices with you.

The research doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about the device that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

When research images are collected and analyzed, there is the chance of finding something clinically relevant. 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 feeling worried about a finding for which no treatment is required or appropriate).

In this study, you will be informed of any findings of possible clinical significance that may be discovered during review of results from your research images. The results of your research images will not be placed in your medical record.

The results from the images we collect in this research study are not the same quality as what you would receive as part of your health care. The images will not be reviewed by a physician who normally reads such results. We will provide you with this information so that you may discuss it with your primary care physician.

Clinically relevant results, including individual results will not be disclosed to you unless all study activities are complete. Targeted or active-control stimulation results cannot be shared until the entire study closes to enrollment.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Dr. Sara Pillay (414) 955-4482.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Dr. Pillay at 414-955-4482
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this project is:
Medical records of the care you receive for this study such as MEG and MRI scans. Heath information collected during this research.
Past medical records supporting your eligibility for the study including MRI of Brain.

E2. Who will see the health information collected for this project?

The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the research team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information, the information may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information for 10 years after the research project ends in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Sara Pillay at:

Medical College of Wisconsin
8701 Watertown Plank Road
Milwaukee WI 53226

The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

E6. Access to records

If you join this project, you will be given one of two device interventions without knowing exactly which one (a “blinded” project). If you ask to see your health records during this “blinded” project, the research team cannot tell you which intervention you are being given. This is because the research team also remains “blinded” about which intervention the investigator has randomly assigned to you. You would have to wait until the time given below. We cannot do the project unless you agree. However, if the blinded information is needed to treat you, it will be provided to the research doctor.

- What are the blinded options? You will get one of these interventions: Targeted or active control transcranial Direct Current Stimulation (tDCS)
- When can you find out which device intervention you were given? You can find out at the completion of the study.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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. You can search this Web site at any time.

You can look up this project by referring to the ClinicalTrials.gov number (NCT04166513) or by asking the research team for a printed copy.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**
Name of Legally Authorized Representative (if applicable**)** *please print*	**Signature of Legally Authorized Representative**	**Date**
Name of Witness (if applicable**)** *please print* (for short form consent process, or consent of blind or illiterate subject)	**Signature of Witness**	**Date**

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*