Title: Effects of transcranial direct current stimulation (tDCS) in primary progressive aphasia (PPA).

NCT: NCT02606422

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If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. Plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Effects of transcranial direct current stimulation (tDCS) in primary progressive aphasia (PPA).

Application No.: NA_00071337

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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens may be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

2. Why is this research being done?

This research is being done to help us understand whether and how the application of transcranial direct current stimulation (tDCS) may affect spelling, naming, or working memory in people with Primary Progressive Aphasia (PPA) and Mild Cognitive Impairment (MCI).

tDCS is the application of a very weak electrical current on the surface of the scalp. One of our aims is to find out whether tDCS will increase the effects of language intervention on improving spelling, naming, or working memory performance Another goal (the MRI part of the study) is to investigate the particular concentration of certain molecules in the brains of people with PPA and MCI and how these may change after application of tDCS. This will enable us to better understand how the brains of people with PPA work and whether and how interventions with tDCS work. Not everyone in the study will participate in the MRI part of the study; some people will elect not to participate in this part and others will not be able to participate because that part of the study may be closed at the time of recruitment. A final aim is to investigate the predictive role of genetic information and how sex differences (male versus female) play a role in tDCS related outcomes. Collection and analysis of blood and saliva samples will allow us this research. Individuals may elect to not participate in the blood draw or saliva collection portion of the study.

Are there any investigational drugs/devices/procedures?

The use of tDCS in this research study is investigational. The word "investigational" means that tDCS is not approved for marketing by the Food and Drug Administration (FDA).

Who can join this study?

People diagnosed with primary progressive aphasia or mild cognitive impairment may join. An additional group of adults without PPA or MCI (controls) may also join.

How many people will be in this study?

About 150 people are expected to take part.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

All participants will serve as their own control by undergoing 1) no intervention, 2) active tDCS, and "3) sham" tDCS conditions. For the "sham" tDCS condition, the electrodes will be placed on your skin but no electrical current will be administered.

Quality of life assessment(s):

In the beginning and at follow-up intervals you will receive quality of life assessments as part of evaluation.

Cognitive and language tasks:

Before receiving intervention (with and without tDCS), you will be asked to complete a series of cognitive and language tasks. You may be asked to spell words, repeat words, name pictures, and discuss a pictured scene. This evaluation is typically completed over two sessions (approximately 6 hours each session).

You will also have an assessment of intervention materials (related to spelling, naming or working memory) to establish baseline performance. This assessment will be part of the two sessions mentioned above.

tDCS:

After you get familiar with the cognitive and language tasks, we will prepare you for the application of tDCS.

To do so, we will apply small sponge electrodes (metal disks) that have been soaked with water to your head: one electrode will be placed on your cheek and the other electrode will be placed on the side of the head.

Once the electrodes are in place, you will be asked to do a language (spelling, naming, or working memory) task while a small electrical current will be passed between the electrodes.

Most individuals do not find the procedure uncomfortable, and there are no known long-term risks of tDCS. When the tDCS current goes through the electrodes, you may feel an itching or tingling sensation under the electrodes or see slight light flashes, or you may not feel anything at all. If the sensation is unpleasant, please let us know immediately. If you find the procedure too uncomfortable, you may stop it at any time. Current will flow for approximately 20 minutes. Language intervention continues while current is on and for approximately 30 minutes after it is turned off.

You will receive this procedure for 3-5 days per week depending on your availability for 2-3 weeks total and 10-15 overall sessions Depending on availability, you may be asked to undergo 3 tDCS intervention sessions (involving different brain stimulation sites) with 2-week intervals in-between, before the start date of your treatment.

There will be a cognitive and language assessment 2 weeks after the end of intervention and then 2 months after the end of intervention for both periods (tDCS condition and sham condition). The 2-week evaluation may be done via video conferencing if you live long-distance and would otherwise have to fly into Baltimore.

Depending on availability, tDCS may be delivered using remote (i.e., at-home) tDCS devices. The remote devices follow the same procedures as the devices used during in-person sessions and all necessary equipment will be provided. Participants and their spouses/family members/friends will be trained by the clinician on how to place electrodes and deliver current during an initial in-person training session. All intervention sessions will be conducted virtually during which the clinician will ensure correct tDCS procedures and administer behavioral tasks. Participants may be asked to come for in-person visits before and after each intervention period, as well as for the final follow-up appointment to include imaging. Following each period, participants will mail back the tDCS device and accompanying equipment to prepare for the next period and/or participant.

Accelerometer:

We may ask you to wear an accelerometer, like a FitBit, on your wrist or ankle for 2-3 weeks. The accelerometer will measure your activity and sleep patterns.

Audio recordings:
As part of this research, we are requesting your permission to create and use audio recordings of the testing to help answer our behavioral research question. Any audio recordings will not be used for advertising or non-study related purposes.

You should know that:
- You may request that the audio recording be stopped at any time.
- If you agree to allow the audio recording and then change your mind, you may ask us to destroy that recording. If the recording has had all identifiers removed, we may not be able to do this.
- We will only use these recordings for the purposes of this research.

Please indicate your decision below by checking the appropriate statement:

_____I **agree** to allow the Principal Investigator and Johns Hopkins study team members to make and use audio recordings of me for the purpose of this study.

_____I **do not agree** to allow the Principal Investigator and Johns Hopkins study team members to make and use audio recordings of me for the purpose of this study.

_____ _____
Participant Signature Date

How long will you be in the study?
You will be in the main part of the study for about one year including follow-up testing intervals, depending on your availability. All participants receive language intervention in both periods, but only one period includes active tDCS. You will receive either tDCS and sham condition in a randomized order.

If resources are available, you will be given the option of participating in an extension period of the study. The purpose of this period is to see if any improvements you have made are maintained by continuing brief periods of intervention + tDCS periodically over the next 6 months. If you decide to participate in this period, you will receive tDCS + language intervention for 5 sessions every 2 months (all in the same week) for up to 6 months. Overall you will receive 15 additional sessions of intervention + tDCS. If you have not made any improvements in the first part of the study, we may still give you the option of participating in this part of the study.

As research develops, we may have future studies beyond the extension period of this study. Will you allow us to contact you for these future research studies?

YES _____
Signature of Participant

NO _____
Signature of Participant

4. What are the risks or discomforts of the study?

tDCS

tDCS has been used in humans and animals for many years. In recent studies that involved several hundred people, there were no side effects other than itching under the electrode that went away when the current was stopped, and slight light flashes with stimulation.

There is no danger of heat to the brain during tDCS. However, there is a slight risk of an electric burn. One patient without adequate protection had a small burn on the ear, which healed in several days. To eliminate this risk we will use insulated electrodes. If you develop any problem during any of the experiments, we will stop the stimulation immediately. Any effect on brain function will be brief.

Questions/Language Evaluation

You may get tired or bored when we are asking you questions or you are completing language evaluation. If you feel tired or frustrated, you may take a break. You do not have to answer any question you do not want to answer. If a language and cognitive evaluation makes you feeling extremely uncomfortable and distressed, the examiner may ask you to take a break. If this happens consistently and it begins to interfere with the evaluations. , the examiner may ask you to stop the study without any consequences to your regular medical care at Johns Hopkins.

Confidentiality:

There is the risk that information about you may become known to people outside this study.

5. Are there risks related to pregnancy?

If you are pregnant during your participation in this study, we will not do any MRI scans (see optional portion below), although there are no known risks of the procedures to the fetus. This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to being in the study?

There may or may not be a direct benefit to you from being in this study.

If you participate in this study it may help others in the future.

7. What are your options if you do not want to be in the study?

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet.

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

No.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.
- If you leave the study early, Johns Hopkins may use or give out your health information that it already has if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- You fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team who may be a part of Johns Hopkins Health System, Johns Hopkins University or the Johns Hopkins Applied Physics Laboratory will know your identity and that you are in the research study. Other people at Johns Hopkins, including your doctors, may also see or give out your

information. We make this information available to your doctors for your safety. If you think this study might affect your clinical care, please inform your doctor.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

14. What is a Certificate of Confidentiality?

Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

15. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

You will not give up your right to seek compensation for harm by signing this form.

16. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Kyrana Tsapkini at (410) 736-2940. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

Call Dr. Argye Hillis-Trupe at her beeper number available 24 hours per day: 410-283-3885 if you have an urgent medical problem related to your taking part in this study. **After the tone, enter the phone number where you can be called, press the # key, and hang up.**

Call Dr. Argye Hillis-Trupe, at 410-614-2381 or beeper 410-283-3885 if you think you are injured or ill because of this study.

d. What happens to Data that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The data you provide are important to this effort.

If you join this study, you should understand that you will not own your data, and should researchers use them to create a new product or idea, you will not benefit financially.

17. Optional Study Components

This part of the consent form is about optional component(s) of the study that you can choose to take part in or not. You can still take part in the main study even if you say "no" to this/these optional component(s).

Magnetic Resonance Imaging (MRI):

As part of your participation in this research study, you may also be asked to have a Magnetic Resonance Imaging (MRI) exam before and after each intervention period, as well as at the final 3-month follow-up for a total of 5 MRIs over the course of about a year. You may decline to have the MRI exam and still participate in the study. Only some participants will take part in the MRI portion of this study, so even if you agree, we may not ask you to have MRI exams.

MRI scans create images of the body using a magnet and radio waves. While the procedure is much like a computerized tomography (CT) scan, there is no radiation involved in an MRI exam. MRI exam(s) in this study will take about 60 minutes.

You may not take part in this study if you have any metal or device in your body which is not compatible with MRI. Examples include certain pacemakers, defibrillators, aneurysm clips, or other implanted electronic or metallic devices, shrapnel, or other metal. If you have a history of metal in your head or eyes, you cannot take part in this study.

The MRI machine periodically makes loud banging noises. We will provide earplugs or headphones for you to wear during the MRI exam.

Incidental Findings

As part of the MRI part of this research study, you will undergo an imaging procedure. A qualified professional will review your research imaging. This research imaging will not include the full diagnostic information that you would get if your primary doctor referred you for imaging.

There is a possibility that while reviewing your imaging we may see an unexpected abnormality. This is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by mail, email, or phone. In the case of a potential serious emergency, someone may go to your home.

A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding from an imaging procedure.

If you want, we will give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

What could happen if there is an incidental finding?

- An incidental finding may cause you to feel anxious.
- Since a report of the incidental finding will be part of your medical record, it will be available to those accessing your medical record for your clinical care and may affect your current or future life or health insurance coverage. This risk will vary depending on the type of insurance plan involved.

The costs for any care that may come from the incidental finding, such as the need to see a doctor to diagnose or treat an incidental finding, will not be paid for by this research study. These costs would be your or your insurance company's responsibility.

MRI risks
While no significant risks have been found from the use of MRI scans, you may be bothered by the noise made by the MRI scanner and by feelings of being closed in (claustrophobia). If you want to be removed from the MRI scanner, you can push a button that will be given to you, or simply say out loud that you want to stop, and you will be removed. You are not required to complete the MRI examination.

Please indicate your decision below by checking the appropriate statement:

_____I **agree** to participate in the MRI portion of this study.

_____I **do not agree** to participate in the MRI portion of this study.

_____ _____
Participant Signature Date

Biospecimen Collection:
As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could include other diseases.

We will also draw approximately 10-15mL (1 tablespoon) of blood for research purposes related to this study before, after and 6-months post intervention. Most biospecimens contain DNA, which is the genetic code for each person. Collection will take place in an outpatient lab at Johns Hopkins Bayview Medical Center by experienced staff, and all analyses will be conducted by members in the Department of Genetic Medicine and Geriatric Medicine and Gerontology. With your permission, we would like to store the samples for further research and testing. All samples will be deidentified and securely stored.

For saliva collection, we will send saliva tubes to your home with a paid return address at our lab.

What happens to Data that are collected in this optional component of the study?
See Section 16D. Additionally, with appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

This study plans to look at several genes that are associated with sex differences in PPA. Specifically, the genetic testing will look at variations in these genes in the people in this study.

This study involves genetic testing on samples that you provide. The Genetic Information Nondiscrimination Act (GINA) is a federal law that helps reduce the risk of discrimination by health insurers or employers based on your genetic information. GINA does not protect you from discrimination if you apply for other types of insurance (such as life, disability or long-term care). GINA

also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Genetic information is unique to you and your family. Even without your name or other personal identifiers, it may be possible to identify you or other members of your family with your genetic information.

Johns Hopkins follows procedures so that people who work with your DNA information for research cannot discover it belongs to you, unless you have given consent. However, new techniques will likely make it easier to link your genetic data to you in the future, so we cannot promise that your genetic information will never be linked to you.

Biospecimen risks
Participants may feel some pain and discomfort at the needle entry site where blood is drawn, and there is a slight risk of bleeding or bruising around that site. There is also a remote risk of fainting after having blood drawn. To reduce the risk of injury because of a faint-related fall, participants will be closely monitored and asked about symptoms before they are allowed to stand up. Infection at the site of blood draw may occur.

Please indicate your decision below by checking the appropriate statement:

_____I **agree** to allow the Principal Investigator and Johns Hopkins study team members to collect biospecimen and store it for further research for the purpose of this study.

_____I **do not agree** to allow the Principal Investigator and Johns Hopkins study team members to collect biospecimen and store it for further research for the purpose of this study.

_____ _____
Participant Signature Date

18. What does your signature on this consent form mean?

Your signature on this form means that:

- you understand the information given to you in this form
- you accept the provisions in the form
- you agree to join the study

You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).