KEY INFORMATION FOR STUDY OF NEUROSTIMULATION FOR COGNITIVE ENHANCEMENT IN ALZHEIMER'S DISEASE (NICE-AD).

We are asking you to choose whether or not to volunteer for a research study to test if low-risk neurostimulation called Transcranial Direct Current Stimulation (tDCS) at home can improve cognitive performance and symptoms in patients with mild to moderate Alzheimer's Disease.

This page is designed to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

After you read the consent form, we will ask you questions about your understanding of the study. You can ask questions about the study and refer to the consent form during this time.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn about the effectiveness of at-home tDCS to improve cognition and behavioral symptoms of mild to moderate Alzheimer's Disease.

Your participation in this research will last for about ten months.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

The study may or may not include a direct benefit to you. The possible benefits of taking part in this study include improved cognitive performance and improved quality of life. Some participants appreciate knowing that they have contributed to research that may benefit others in the future.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The risks associated with the tDCS are minimal and may include slight itching, tingling, and reddening of the skin under the stimulating pads. You may be embarrassed if you have some difficulties with some of the cognitive and mobility tests that you will be asked to perform. You also may experience discomfort or claustrophobia while undergoing the MRI. If you experience any distress, you will have the opportunity to have your questions answered by the investigators. For a complete description of risks, refer to the Consent Document below.

DO YOU HAVE TO TAKE PART IN THE STUDY?

No. If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Mirnova Ceïde. If you have questions, suggestions, or concerns regarding this study, or if you want to withdraw from the study, his contact information is:
1225 Morris Park Avenue, Van Etten Building # 316C
Bronx, NY 10461
Telephone #: 718-430-3808

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the Einstein Institutional Review Board (IRB) between the business hours of 9am and 5pm EST, Monday-Friday at 718-430-2253 or irb@einsteinmed.org

ALBERT EINSTEIN COLLEGE OF MEDICINE

DOCUMENTATION OF INFORMED CONSENT AND HIPAA AUTHORIZATION

If you are the surrogate decision maker of an adult who may take part in this study, consent from you and the assent (agreement) of the study participant will be required. When the word "you(r)" / "my" / "me" / "I" appears in this consent form, we mean the participant; "we" means the research study doctors and research staff.

Introduction

You are being asked to participate in a research study called **Neurostimulation for Cognitive Enhancement in Alzheimer's Disease (NICE-AD).** Your participation is voluntary—it is up to you whether you would like to participate. It is fine to say "no" now or at any time after you have started the study. If you say "no," your decision will not affect any of your rights or benefits.

The researcher in charge of this project is called the "Principal Investigator." His name is **Dr. Mirnova Ceïde.** You can reach Dr. Ceïde at:

1225 Morris Park Ave., Van Etten Bldg #316C
Bronx, NY 10461
Telephone #: 718-430-3978

For questions about the research study, or if you believe you have an injury, contact the Principal Investigator or the IRB.

The Institutional Review Board (IRB) of the Albert Einstein College of Medicine and Montefiore Medical Center has approved this research study. The IRB # is in the stamp in the upper right hand corner. If you have questions regarding your rights as a research subject you may contact the IRB office at 718-430-2253, by e-mail at irb@einsteinmed.org, or by mail:

Einstein IRB
Albert Einstein College of Medicine
1300 Morris Park Ave., Belfer Bldg #1002
Bronx, New York 10461

Support for this research study is provided by
The National Institute of Health
NIH # 1 R01 AG068167-01

Why is this study being done?

The goal of this study is to examine the use of an at-home neuromodulatory therapy called **transcranial direct current stimulation (tDCS)** to improve cognitive performance (thinking and memory) and behavioral symptoms (mood) in older adults with mild to moderate Alzheimer's Disease.

tDCS is a small minimal risk, non-invasive (no surgical procedure is needed) battery-operated device that provides painless stimulation of neural pathways. Previous research has shown that the stimulation may improve certain symptoms such as pain, worrying, feeling sad, or difficulty concentrating. People that use tDCS in research studies can continue taking their medications and receive their treatments as usual.
Transcranial direct current stimulation (tDCS) is not approved by the U.S. Food and Drug Administration (FDA). This means that tDCS can only be used in research studies.

This study will provide important information regarding the effectiveness and acceptance of the at-home tDCS device to improve cognitive performance and symptoms in patients with mild to moderate Alzheimer's Disease. If effective, this novel intervention can substantially enhance Alzheimer's Disease symptom management at home, improve quality of life of Alzheimer's Disease patients and their families, and reduce burden associated with this illness.

A description of this clinical trial will be available on www.ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT04404153) 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.

Why am I being asked to participate?

You are being asked to participate in this study because you are a community-dwelling adult age 60 and older, and a neurologist or geriatrician at one of our clinical sites has previously diagnosed you with mild to moderate Alzheimer's Disease.

How many people will take part in the research study?

You will be one of about 100 people who will be participating in this study.

How long will I take part in this research?

It will take you about **ten months** to complete the research study. During this time, we will ask you to complete six study appointments. One of these appointments will be conducted over video conference, and the other five appointments will take place in-person at the Albert Einstein College of Medicine. Today's appointment is the only appointment scheduled to take place remotely. After today's appointment, visits 2 and 3 will take place in the next 1 and 2 weeks, respectively. The six-month intervention where you use the device at home will begin after Visit 3. This is when we will ask you to use the device five times per week, for 30 minutes each time, for 26 weeks (**six months**). After the six-month time period is complete, we will ask you to complete three more study visits. Your first follow-up appointment will take place immediately after the 26 weeks are over. This visit is considered the "six month follow up." We have two follow-up visits after that, the 7-month and 9-month study visits. More detailed information regarding the visits and the study timeline can be found in the next section.

What will happen if I participate in the study?

If you agree to participate in this study you will be asked to complete six study visits over a ten month period and you will be **randomly assigned** into one of two 6-month tDCS programs. One group will complete the intervention with a tDCS device that emits low intensity electrical currents to the surface of the head. The other group will complete the intervention with an identical tDCS device that looks and feels the same but is a placebo (or fake) tDCS stimulation acting as a control. **It is important that you understand that by participating in this study there is a 50% chance of being assigned to the active tDCS group or the placebo tDCS group.** The research team will not know which group you are in, and neither will you, your caregiver, or your doctor.

During **three** of the study visits you will undergo **Magnetic Resonance Imaging (MRI)**. **The MRIs will take approximately 1.5 hours and will take place at Albert Einstein College of**

Medicine. MRI is a test that uses magnets and radio waves to make pictures of organs and structures inside the body. For an MRI test, the area of the body being studied is placed inside a special machine that contains a strong magnet. Pictures from an MRI scan are saved and stored on a computer for more study. Although the MRI you will have in this study is being done for research purposes only, it is possible that doctors may notice something that could be important to your health. If so, we will contact you to explain what was seen and tell you whether you should consult your doctor. We will make the MRI report available to your doctor, and if you want, we will talk with your private physician or refer you to someone for follow-up.

The **first study** visit will take place **over video conferencing technology** and will last about **120 minutes**. During this visit, we will do some questionnaires to see if you eligible to take part in this research study. At this visit we will:

- Conduct informed consent and review the study design with you
- Ask you about your medical history and lifestyle

Visit 2 will take place 1 week after visit 1 **at our research center** and will last about **140 minutes**. At this visit we will:

- Conduct tests that measure cognitive functions such as memory and attention
- Conduct tests that measure physical function such as walking speed.
- Conduct questionnaires
- Provide in-person trainings with the tDCS device
- Assess your ability to safely use the tDCS device

Visit 3 will take place 1 week after visit 2 **at our research center** and will last about **90 minutes**. At this visit we will:

- Ask you to undergo neuroimaging (an MRI)
- Assist you with the tDCS device and supervise your first session

Following **Visit 3**, we will ask you to apply the tDCS for **30 minutes per day, five days per week for the next 26 weeks (six months) at your home**. Study personnel will contact you to schedule the applications at a certain time when you, your informal caregiver (if he/she participates with you) and the study personnel are available. Remember, the study personnel will be in touch with you either by a video connection or by phone every time you use the device at home. They will assist you if you have any questions during preparation of the device or when the stimulation is ongoing. It is important to be ready for the applications at scheduled time. Notify study personnel in advance if you are not able to have the application at the scheduled time. Study personnel will assist you with rescheduling.

Visit 4 will take place **at our research center** within 1 week of your completing the six-month training period, and will last about **200 minutes.** At this visit we will:

- Conduct tests that measure cognitive functions such as memory and attention
- Conduct tests that measure physical function such as walking speed.
- Conduct questionnaires
- Ask you to return the tDCS equipment
- Ask you to complete an MRI
- Provide reimbursement for the intervention and this visit

Visit 5 will take place one month after Visit 4. It will take place at **our research center** and will last about **120 minutes**. At this visit we will:

- Conduct tests that measure cognitive functions such as memory and attention
- Conduct tests that measure physical function such as walking speed.
- Conduct questionnaires
- Provide reimbursement for this visit

Visit 6 will take place two months after Visit 5. It will take place at **our research center** and will last about **200 minutes**. At this visit we will:

- Conduct tests that measure cognitive functions such as memory and attention
- Conduct tests that measure physical function such as walking speed.
- Conduct questionnaires
- Ask you to complete an MRI
- Provide reimbursement for this visit

If you take place in all study visits and complete the intervention, you will have the **opportunity to use an active tDCS device at home for two months**, regardless of which group you were randomized into during the intervention. This is considered an "**open label**" extension study. If you do not complete the required on-study treatment you will not be able to participate in the open-label extension phase. For the open label extension study, all participants will receive an active tDCS device, and there will be no placebo control device. You do not have to participate in the open label extension, but it is your right to do so if you complete all baseline and post-intervention appointments. If you are interested in participating in this extension, you should ask the study team about it at your six-month appointment. We will provide more information about the opportunity during your six-month visit if you express an interest in it.

Will there be audio and/or video recording?

Your whole body including face may be video-taped while these evaluations are performed. The tapes will be used by the research team to score the evaluations and refine measurements already collected. You will not receive any monetary compensation for allowing yourself to be taped. The tapes will not be destroyed at the end of the study as they may be used as teaching tools to study personnel or other students who are not members of the research staff.

The study personnel will also be in touch with you either by a video connection or by phone every time you complete the tDCS application at your home to ensure that the tDCS application is being applied correctly and to provide the activation code for the session. Study personnel will also ask you about your health and experience with the tDCS device after every session. Protected Health Information (PHI) will NOT be collected at the video-contact.

Information Banking (Future Use and Storage)

We will store information about you in a "bank", which is a library of information from many studies. This information cannot be linked to you. In the future, researchers can apply for permission to use the information for new studies to prevent, diagnose or treat disease, including genetic research. If you agree to the future use, some of your de-identified genetic and health information (not linked to you) may be placed into one or more scientific databases. These may include databases maintained by the federal government. Your information may be kept for a long time, perhaps longer than 50 years. You may remove your consent for future research at any time by contacting the Principal Investigator named on the first page of the

consent or the IRB office at 718-430-2237. If you do, we will destroy the information in the bank but if the information was already shared with other researchers, we cannot get it back.

You can choose not to participate in the bank and still be part of the main study.

INITIAL ONE (1) OF THE FOLLOWING OPTIONS

_____ I consent to have my information used for future research studies.

_____ I do NOT consent to have my information used for future research studies. Information about me will be kept as long as required by regulations and institutional policy, but will not be used for future studies.

INITIAL YOUR CHOICE BELOW

_____ I consent to be contacted in the future to learn about:

_____ New research protocols that I may wish to join.

_____ General information about research findings.

_____ I do not want to be contacted at all.

Will I be paid for being in this research study?

You will be paid for your time associated with study procedures. For visits 3, 4, 5, and 6 you will be paid $50.00. During the six-month intervention you will be paid $2.00 per session (up to $10.00 per week) for 26 weeks. In total you may be paid up to $460.00 for your participation. If you choose to withdraw from the study before all three follow-up visits are completed, you will only be paid for the visits and tDCS sessions you completed.

Some researchers may develop tests, treatments or products that are worth money. You will not receive payment of any kind for your specimens and information or for any tests, treatments, products or other things of value that may result from the research.

Will it cost me anything to participate in this study?

There will be no cost to you to participate in the study.

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

If you are injured as a result of this research, only immediate, essential, short-term medical treatment as determined by the participating hospital, will be available for the injury without charge to you personally.

- No monetary compensation will be offered.

- You are not waiving any of your legal rights by signing this informed consent document.
- If additional treatment is required as a result of a physical injury related to the research, necessary medical treatment will be provided to you and billed to your insurance company or to you as part of your medical expenses.

Immediately report any discomforts, problems or injuries you experience during the course of your participation in the study to Dr. Ceïde (Telephone: 718-430-3808).

What else do I have to do?

- You must tell the research study doctor about any past and present diseases or allergies you are aware of and about all medications you are taking including "over-the-counter" remedies and nutritional supplements or herbs.
- You must provide the research study staff with accurate information about any surgeries, medical procedures, or conditions you have that may involve metal in your body. This will ensure that it is safe for you to take part in the neuroimaging (MRI) portion of the study.
- You must use the tDCS equipment as instructed, and you must return the device at study visit 4.
- If you do not feel well at any time, call your doctor or the research study doctor immediately.
- You may carry out all your normal daily activities.

Confidentiality

The researchers and study staff follow federal and state laws to protect your privacy. This part of the consent form tells you what information about you may be used and shared in the research described in this form. You do not have to sign this form but, if you do not, you may not participate in the research.

The health information that we may use or disclose for the research described in this form includes information from your entire medical record, such as your name, phone number, email, medical diagnoses, dates, test results, social security number, medical record numbers, etc.

Your information and research records will be kept confidential. Your study information will be kept as long as they are useful for the research described in this form.

The only people who can see your research records are:

- Researchers and other individuals who work with the researchers
- Organizations and institutions involved in this research, including those that fund the research, if applicable
- Groups that review research such as central reviewers, Institutional Review Boards, the Office for Human Research Protections, the US Food and Drug Administration, data coordinating centers, and domestic and foreign agencies that regulate research.

The purposes of these uses and disclosures are to (1) conduct the study and (2) make sure the study is being done correctly. The information covered under this form may no longer be

protected by federal privacy laws (such as HIPAA) once disclosed, and those persons who receive your health information may share your information with others without your additional permission. All of these groups have been asked to keep your information confidential.

To maintain the integrity of this research study, you generally will not have access to your research-related personal health information. If it is necessary for your care, your research-related health information will be provided to you or your physician.

Certificate of Confidentiality

As a way to protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health, which is funding this study. If information from this study were requested or subpoenaed by government agencies or the courts, we would use the Certificate to attempt to legally refuse to provide that information. These requests are rare – in only a few cases did researchers have to use the Certificate, and it was honored most of the time, but not every time. There are several kinds of situations to which the Certificate does not apply. For example, we are still required to report child abuse and some diseases, and we must make data available to the government for review or evaluation of our research. The Certificate does not prevent you or a member of your family from voluntarily sharing information. Similarly, if an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Are there any risks to me?

A risk of taking part in this study is the possibility of a loss of confidentiality or privacy. Loss of privacy means having your personal information shared with someone who is not on the study team and was not supposed to see or know about your information. The study team plans to protect your privacy – see the Confidentiality section above for details.

Questionnaire
You may feel uncomfortable answering questions about your health. You can choose not to answer questions that make you feel uncomfortable.

Risks of tDCS
The risks associated with the tDCS are minimal.

Common side effects:

Slight itching, tingling, and reddening of the skin under the stimulating pads. The itching or tingling sensations usually stop within 60 seconds of stimulation.

Less common side effects:

Transient headache
Headpiece could possibly cause skin irritation or friction resulting in slight itching, reddening or injury to the skin.

Uncommon side effects:

Transient dizziness
Transient nausea

These side effects are infrequent and typically resolve when the tDCS stops.

MRI
Some people are bothered by feelings of confinement (claustrophobia), and by the noise made by the machine during the test. You will be asked to wear earplugs and headphones while in the machine. You may not participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to tell the MRI staff if you have had brain surgery for a cerebral aneurysm, or if you have implanted medical or metallic devices, shrapnel or other metal, such as metal in your eye.

Unknown Risks
We have described all the risks we know. However, because this is research, there a possibility that you will have a reaction that we do not know about yet and is not expected. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

New Findings
If we learn any significant new findings during the study that might influence your decision to participate, we will contact you and explain them.

Are there possible benefits to me?

You may or may not receive personal, direct benefit from taking part in this study. The possible benefits of taking part in this study include improved cognitive performance and improved quality of life.

What choices do I have other than participating in this study?

You can refuse to participate in the study. If you decide not to participate, the medical care providers at this facility will still give you all of the standard care and treatment that is appropriate for you. This includes but is not limited to any newly FDA approved monoclonal antibody treatments for Alzheimer's Disease.

Are there any consequences to me if I decide to stop participating in this study?

No. If you decide to take part, you are free to stop participating at any time without giving a reason. However, some of the information may have already been entered into the study and that will not be removed. The researchers may continue to use and share the information they have already collected.

To revoke (take back) your consent and authorization, you must contact the Principal Investigator in writing at the address on page 1 of this form. However, you may first call or speak to the Principal Investigator and he will stop collecting new information about you. If you take back your consent and authorization, you will not be allowed to continue to participate in this research study.

Can the study end my participation early?

We will not let you participate in the study any more if **unanticipated serious adverse events determined to be possibly, probably or definitely related to study procedures occur.** In

addition, your participation will end if the investigator or study sponsor stops the study earlier than expected.

If you are a randomized participant and decide to start any monoclonal antibody treatment for Alzheimer's, your participation in the study will end.

CONSENT TO PARTICIPATE

I have read the consent form and I understand that it is up to me whether or not the individual named below participates. I know enough about the purpose, methods, risks and benefits of the research study to decide. I understand that I am not waiving any of his/her legal rights by signing this informed consent document. I will be given a signed copy of this consent form.

Printed name of participant	Signature of participant	Date	Time
Printed Name of Surrogate (when applicable)	Signature of Surrogate (when applicable)	Date	Time
Printed name of the person conducting the consent process	Signature	Date	Time