Official Title:	Transcranial Photobiomodulation for Alzheimer's Disease (TRAP-AD)
NCT Number:	NCT04784416
Study Number:	20-00865
Document Type:	Informed Consent Form
Date of the Document:	• April 15, 2025

Research Subject Informed Consent Form

Title of Study: Transcranial Photobiomodulation for Alzheimer's Disease (TRAP-AD) s20-00865

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1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called "subjects" or "research subjects". These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or this form, please ask us. If you decide to takepart in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

We are asking you to take part in this research study because you may have amnestic mild cognitive impairment (MCI) or early and mild Alzheimer's Disease (AD). People with MCI or early and mild AD have more memory problems than normal for people their age, but their symptoms are not as severe as those people with moderate to severe AD. They are able to carry out their normal daily activities and make important medical decisions.

Some, but not all, people with MCI or early and mild AD go on to develop moderate or severe AD. Because MCI and early and mild AD are sometimes related to moderate or severe AD we hope this study will also help us learn about AD, in addition to learning about MCI.

The primary purpose of this research study is to determine if application of near infrared energy to the forehead can help improve thinking and memory in people with MCI and early AD. Near infrared energy is like light but is not visible to the human eye.

This study will compare near infrared exposure with a placebo or sham procedure. The sham procedure will look and feel just like the near infrared procedure but won't include near infrared exposure. A sham procedure is used in research studies to compare the results and side effects of the treatment being studied to the results and side effects of receiving no treatment. This allows us to see if the treatment being studied works and what side effects it causes.

Will I undergo the near infrared or the sham procedure?

During the study you may get the sham procedure instead of the near infrared procedure.

This study is a randomized study. This means, like flipping a coin, you will be assigned to one of the groups and undergo either the near infrared procedure or the sham procedure. There are no special requirements or criteria to be in either group. You will have a 50% chance of undergoing the near infrared procedure and a 50% chance of undergoing the sham procedure.

This study is called "double blind" because neither you nor the study staff will know if you are undergoing the near infrared procedure or the sham procedure. A statistician keeps records of which procedure you are undergoing. The study staff can get this information if needed. In the remainder of this consent form, we refer to the near infrared and sham procedures as the study treatment.

Is the near infrared procedure approved to treat mild cognitive impairment?

No. The device that delivers the near infrared energy is Food and Drug Administration (FDA)-cleared for treating muscle aches and joint pains. It is not, however, FDA-cleared to treat mild cognitive impairment. For this reason, the near infrared procedures in this study are experimental.

3. How long will I be in the study? How many other people will be in the study?

Your participation in this study will take about five months and will involve about 31 visits with study staff. We will offer flexible visit options so the study could last up to seven months. Twenty-eight (28) visits include tests or procedures that will require that you come to the clinic. The rest may be conducted via video conference or telephone.

Over a total period of 5 years, about 200 study subjects between the ages of 65 and 85 are expected to participate in this study across three sites.

4. What will I be asked to do in the study?

If you choose to take part in the study, we will ask you to sign this consent form before you undergo any procedures with the study staff that are part of the study. We will also ask you to sign a separate Audio Consent form that will indicate your consent to being audio recorded during certain portions of the neuropsychological testing sessions (detailed on page 4 of this document under "Cognitive Testing").

The study has five phases.

1. **Screening:** We will do some tests and procedures to see if you meet the requirements to take part in the study. The study doctor will review the results of these tests and procedures. If you do not meet the requirements, the study doctor will tell you why.

2. **Baseline:** If you do qualify to take part in the study, we will scan your brain to help us understand how it is working at baseline (before the study treatment). We will also give you a single near infrared exposure session (i.e., open label t-PBM session) so that we can understand if and how it changes your brain function immediately (in the short term). This session is NOT part of the treatment you will receive, and you will receive near infrared exposure during this session regardless of your randomization status. We will also do additional tests and procedures to confirm your eligibility for the study.
3. **Treatments:** We will giveyou all of your study treatments in a regular office. We will try to schedule the treatments three times a week for 8 weeks.
4. **Primary Outcome:** After completing all treatments, we will ask you to return for another brain scan, neuropsychological testing, and an optional blood draw so we can see if and how all the treatments in combination changed your brain and your memory and thinking.
5. **Follow-up:** We will call you about one week after the primary outcome completion to check on your safety. Then, finally, we will invite you back for more neuropsychological testing 8 weeks after you finish the treatments to see if they had any lasting effects on your memory or thinking.

Optional Open Label t-PBM: After completing all the study procedures, if you still have memory problems during the neuropsychological testing, we will offer you the option to receive the open label t-PBM treatments 2 times a week for 6 weeks. When t-PBM treatment is “open label”, this means that you, as well as the study staff, all know that you are undergoing the near infrared procedure. There is no longer a chance that you could undergo the sham procedure. After completing all treatments, we will ask you to complete neuropsychological testing so we can see if and how all the treatments changed your memory and thinking. The completion of this neuropsychological testing is optional; you may choose to refuse to participate in this testing session.

Below, you will find more detailed descriptions of each phase of the study.

1) SCREENING:

The screening takes 4-6 hours. We can conduct most of the screening procedures over the telephone or using video conferencing.If we use video conferencing, you will use a device with a camera that can also connect to the internet such as a computer, tablet, or smart phone at home so that we can see you and you can see study staff.

Some popular video conferencing applications are Zoom, FaceTime, and Skype. We will use a similar application (WebEx), but one that is more secure so you can feel comfortable sharing personal information with us.

We will:

- Ask you about your medical history.
- Ask you what medications you take – including over-the-counter and prescription medications, vitamins or herbal supplements.
- Ask you to complete some forms and answer questions about your background, general health and well-being, quality of life (i.e., if you are happy about your life), mental health, mood and memory.
- Conduct tests of your memory and thinking (see section called cognitive testing).
- Ask you to identify a study partner: a close friend or family member to whom we will also ask questions about your history and symptoms.

You will then have to come into the clinic so we can:

- Give you a physical exam, including recording your height, weight and “vital signs” (blood pressure, temperature, heart, and breathing rates).

- Take a blood sample; we will insert a needle into your arm and take a few small tubes or vials of your blood (about 12 teaspoons).
- Take a urine sample; We will test your urine for:
    - Certain drugs including illegal drugs (see section called Urine Drug Screen).
    - Pregnancy (if applicable); you may not take part in this study if you are pregnant.
- Perform an ECG (electrocardiogram) to check the electrical activity of your heart.

Cognitive testing
The testing includes the assessment of your intellectual abilities including memory, perception, vigilance, concentration, language, reasoning, and comprehension. We will examine verbal, visual, working, and remote memory both immediately and after a timed delay. In addition, visual spatial skills, attention, and problem-solving skills will be examined. These tests may be given orally and by paper and pencil. We will audio-record some of your responses during the testing in order to ensure accuracy of capturing your responses.

Urine Drug Screen
We will test your urine for drugs, including illegal drugs like cocaine, amphetamines and others. If your urine shows you have taken any of these drugs, you cannot be in the study. The results of the urine test will NOT become part of your medical record.

Blood Testing
We will test your blood for evidence of common diseases that might make it unsafe for you to participate in the study, for the presence of certain proteins that scientists believe are abnormal inpeople with Alzheimer's Disease, for specific biomarkers that might show how your brain metabolizes energy, and obtain DNA for genotyping. We will ask you to do a fasting blood draw if possible (this would be an overnight fast, so you would go to sleep and then refrain from eating until after the blood draw in the morning), but if this is not feasible for you or if you prefer not to, we can do a normal non-fasting blood draw instead.

We plan to do genetic research on the DNA in your blood sample. DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work and determine physical characteristics such as hair and eye color. Genes are passed from parent to child. We will study the ApoE gene specifically because research shows that one form of this gene may increase risk for Alzheimer's Disease. This testing is being done for research only and is not used for diagnostic test. Therefore, the results of this test will not be released for you. If you are interested in knowing your ApoE type and understanding the implications of your genotype, we can provide information about certified laboratories and genetic counselors. However, clinical testing and genetic counseling are not provided by this study.

2) BASELINE:

If you qualify to participate in the study, we will ask you to return to NYU Langone Health for baseline brain scans. The baseline visit(s) will take 3-5 hours. You will:

- Report any medications you are taking or side effects that you experience.
- Have your "vital signs" (blood pressure, temperature, heart and breathing rates) recorded.
- Complete some forms and answer questions about your general health and well-being, quality of life (i.e., if you are happy about your life), mental health, and mood.
- Receive an injection of a radioactive substance that will help us detect the presence of tau proteins in your brain during the brain scan. Tau proteins are thought to contribute to the thinking and memory problems that people with Alzheimer's Disease experience.
- Have brain scans.
- Have an open label t-PBM session.

Brain Scans:

The brain scans will start about 1.5 hours after the injection. You will lie in two separate scanners for about 1.5 hours in total at NYU Center for Biomedical Imaging. During the scans, we will use three different types of “cameras” to get different types of information about your brain.

The first part of the scan will use Positron Emissions Tomography (PET) and Magnetic Resonance (MR) cameras at the same time.

The PET camera in this study needs a radioactive substance, or tracer, called ^{18}F MK-6240 to detect a specific protein (i.e., tau protein) in the brain, which has been shown to be elevated in people who have MCI and Alzheimer’s Disease. The tracer will show us specifically where these tau proteins are elevated and located in your brain on the PET scan. The ^{18}F MK-6240 tracer has been used in various research studies, but it is currently not approved by the FDA for use in clinical settings. For this reason, the tracer is being used experimentally, but it has been used safely and effectively in older individuals with MCI and Alzheimer’s Disease.

The MR camera uses magnetic fields and radio waves to produce images of the structure or anatomy of your brain.

Using both PET and MR cameras simultaneously provides more useful information while reducing the amount of radiation exposure compared to a standard PET scan.

The second part of the scan, done in a different scanner than PET, will use an MRS (Magnetic Resonance Spectroscopy) camera to produceimages that show us how the brain is getting energy.

During the 1.5 hours of scanning, it will be necessary for you to lie very still and to stay as still as possible. At times there will be a loud banging noise. This is a normal part of scanner functioning, but it may cause slight discomfort if you are sensitive to loud noises. You will be given noise-cancelling headphones and/or foam earplugs to help reduce the noise. You will be able to communicate with the person operating the scanner by intercom. If you feel uncomfortable, you may choose to stop the scan at any time.

Open label t-PBM fMRI session at NKI:

This session will last 1.5 hours.

This 1.5 hour brain scan will use both an MR camera to take pictures of the structure of your brain (as described above) and a functional magnetic resonance imaging (fMRI) camera to produce images that show us the flow of blood and cerebrospinal fluid in your brain as well as help us understand how your brain processes waste before, during, and after the study treatment. For you, the brain scan will feel a lot like the previous brain scans. However, you will wear the study device during the scan so we can give you a treatment, and there will be no injection before it begins.

Before you put on the study device, we will examine your forehead for any possible skin lesions (for example, any cuts or signs of swelling). If you have any lesions on your forehead, you cannot undergo the treatment. The study device includes both a special cap or headgear that you wear on your head, and protective goggles. The headgear will be connected, with a cord, to a laser device. The laser device is programmed to automatically deliver either near infrared energy or sham. The headgear will emit near infrared energy onto your forehead, through your skull, and into your brain. The near infrared treatment procedure may leave your forehead feeling warm.

During this session, you will receive actual near infrared energy from the treatment device. This session is not considered as part of the treatment procedures described below.

3) TREATMENTS:

Treatment visits 1-24 will last about one hour each.

For these treatments, you will first be randomized to either the active near infrared procedure or a sham procedure. Both the near infrared and sham treatment procedures may leave your forehead feeling warm. Therefore, and because near infrared energy cannot be seen by the human eye, you will not know whether or not you are being exposed to the near infrared energy.

These treatments will involve the same procedures as described above except for the brain scan (the brain scan during treatment is only during your open label t-PBM session). They will take place at NYU Langone Health. We will try to schedule them three times a week for eight weeks.

4) PRIMARY OUTCOME:

The primary outcome procedures will take place after you complete all the study treatments and will take 5-8 hours.

Some procedures will take place at NYU Center for Biomedical Imaging. There, you will:

- Report any medications you are taking or side effects that you experience.
- Have your “vital signs” (blood pressure, temperature, heart and breathing rates) recorded.
- Have a final brain scan.

Other procedures may be conducted at NYU Langone Health or using video conferencing or over the telephone. We may also ask you to complete some forms on the internet or in the office. Specifically, you will:

- Repeat the cognitive testing (as described in the “Screening” section).
- Complete some forms and answer questions about your general health and well-being, sleep, mental health, and mood.
- Take a blood sample; we will insert a needle into your arm and take a few small tubes or vials of your blood (about 8 teaspoons).

Final brain scan: For you, the final brain scan will feel very similar to the others though you will not have an injection before it begins, and you will not wear the study device. It will use an MR camera to take pictures of the structure of your brain and an MRS camera to produce images that show us how the brain is getting energy.

5) FOLLOW-UP:

We will schedule a ***short-term follow-up visit*** lasting about 1 hour to take place within two weeks of primary outcome completion. We may conduct it via videoconference or telephone. We may also ask you to complete some forms on the internet.

You will:

- Complete some forms and answer questions about your general health and well-being, sleep, mental health, and mood.
- Report any medications you are taking or side effects that you experience.

We will schedule a ***long-term follow-up visit*** lasting about 3 hours to take place about eight weeks after primary outcome completion (six to seven weeks after the short-term follow-up visit). We may conduct it via video conference or telephone or at NYU Langone Health. We may also ask you to complete some forms on the internet.

You will:

- Complete some forms and answer questions about your general health and well-being, sleep, mental health, and mood.
- Report any medications you are taking or side effects that you experience.
- Repeat the cognitive testing (as described in the Screening section)

Optional Open Label t-PBM:

We will offer the open label t-PBM treatment to participants who have completed the study *and* still show some memory impairment during the primary outcome neuropsychological testing. The open label phase will include 12 treatments over the course of 6 weeks. We will also ask you to complete neuropsychological testing upon completion of the treatments.

5. What are the possible risks or discomforts?

Risk of Study Treatment

The near infrared and sham procedures may cause you to have one or more of the side effects listed below. Because the near infrared procedure is experimental, not all side effects are known. There may be rare and unknown side effects.

It is important for you to tell the study staff about any changes you notice from the study procedures. You can tell the study staff at your scheduled visits or by calling the staff and telling them how you are feeling different from before the study procedures. If you are not honest with the study staff during this study, it may not be safe for you to stay in the study.

The **most common side effects** of the near infrared procedure are:

- Disturbed sleep, including restless or erratic sleep, or early morning awakenings
- Irritability, and
- Seeing vivid colors.

Rare side effects of the near infrared procedure are:

- Abdominal bloating
- Amnesia (memory loss)
- Reddening of the skin at the application site
- Skin peeling and chafing at the application site
- Application Site Pain
- Application Site Reactions such as warming sensations and thermal pain
- Abnormal taste
- Decreased heart rate
- Abnormal hair growth
- In patients who have a history of stroke, t-PBM treatments may cause blood clots leading to oxygen deprivation of the brain. This may cause swelling or bleeding of the brain as well as cell damage or death.
- Nausea
- Neck Pain
- “Out-of-body” experiences
- Itchy Skin
- Rash
- Skin Laceration (cut)
- Skin Lesion (bruise, scrape)
- Skin burn if the device is not used as intended
- Vivid dreams
- Vomiting, and
- Word finding difficulties

Other risks of the study treatment:

Risk of Eye Damage: There is a risk of damage to your eyes (retina) due to accidental exposure to the laser. There are multiple precautions made to prevent such an accident. You will need to wear protective goggles at all times during the procedure.

Risk of Allergic Reaction: As with any treatment, an allergic reaction can occur. Allergic reactions can be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away at the phone number at the top of page 1 of this consent form. If you are having trouble breathing, call 911 immediately.

Risk of Receiving Sham Procedure: As described before, there a chance you will not actually undergo the near infrared procedures, but only the sham procedures, during the 24 study treatment visits. In this case, your condition might not improve or could get worse. You could miss the benefits or harms (if any) of the near infrared treatment. All participants who still have memory problems after completing the study, however, can opt to receive active treatment for six weeks.

Other Risks

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk. For instance, brain scan data, questionnaire responses, and health and symptom information obtained from this research are stored with a code number and not your name. A tracking file will link the codes with identifying information, such as your name and contact information, but this file will be password-protected and located on a computer that can only be accessed with a password. Paper consent forms and payment forms that contain subject names will be kept in a locked cabinet located in a locked room, to which only authorized research personnel have access.

Side Effects of Having Blood Taken include fainting or feeling faint. Tell the study staff right away if you feel faint. Redness, pain, bruising, bleeding or infection at the needle site may occur.

Electrocardiogram (ECG)
The ECG test is a recording of the electrical activity of your heart and an ECG is harmless. The sticky pads (electrodes) that are placed on your chest can sometimes cause discomfort such as redness or itching. We may need to shave your chest before we attach these pads. Irritation from shaving also may occur.

Magnetic Field Risk
All the brain scans in this study use strong magnetic fields and radiowaves to make images of the inside of your body. The brain scans do NOT involve high-energy radiation (like x-rays). For most people the brain scans are very safe. However, if you have anything made of metal on your skin or inside your body, the brain scans may not be safe for you, and you must tell study personnel before your scan. Also, if you have any electronic devices on the outside or inside of your body, you must tell study personnel about those too. Some things, like tattoos, may have metal materials in them even though you might not realize it. For this reason, study personnel will give you a checklist of things that have metal or electronic parts in them. You must read the list carefully before your scan and put a checkmark next to everything that applies to you.

The following paragraphs will describe the possible risks of the brain scans. To reduce many of these risks, you will be given an emergency squeeze ball to hold in your hand during the scan. If you feel any discomfort you should squeeze the ball. This sets off an alarm that the technologist can hear. The technologist will then talk to you and will stop the scan if you want. There is a microphone in the scanner so that you can communicate with the technologist. However, the scanner makes a lot of noise when it is running and the technologist may not always hear what you say. If you need to get the technologist's

attention, you should squeeze the ball.

Remember, if at any point you feel uncomfortable and want to stop the scan, just squeeze the ball and tell the technologist.

Risks from metal
The strong magnetic field in the scanners will pull on things that contain certain types of metal. If someone takes a metal object into a scan room, it might fly towards the scanner and hurt you. For this reason, everyone (including you) must remove everything metal from their clothes and pockets before going into a scan room. Also, the door to the scan rooms will be kept closed during the scans to prevent unauthorized people from walking in.

If you have something metal inside your body, the scanners might pull on it and make it move. You must tell study personnel before your scan if you have anything metal inside your body. Some types of metal might heat up when a scanner is running. If you feel any burning sensation during the scans, you should squeeze the emergency ball and the technologist will stop the scan.

Risks from electronic devices
If you have any electronic devices on the inside or outside of your body, the scanners might make them stop working properly. For this reason, you must tell study personnel before your scans if you have anything electronic on or in your body.

Burns
Metal is not the only thing that can cause burns during a brain scan. It's possible (although very rare) to get burned by touching the inside walls of the scanner or by making skin-to-skin contact. The technologist will give you a blanket or cushions so that you don't touch the inside walls of the scanner. You should also avoid letting your hands or legs touch each other. Remember, if you feel any burning sensation during the scan, you should squeeze the emergency ball and the technologist will stop the scan.

Tinnitus (ringing in the ears) and hearing loss
A scanner makes very loud sounds while it is running. You will be given earplugs or headphones to wear during the scans. Make sure you roll the earplugs tightly and let them expand in your ears so that they work properly. If the sound of a scanner is still so loud that it causes you discomfort, squeeze the emergency ball and tell the technologist. This is important because very loud sounds can cause ringing in the ears or even hearing loss.

Feeling warm or hot
The radiowaves used in brain scans are like those your cellphone uses, but much stronger. Sometimes they are strong enough to make you feel warm (just like standing in bright sunshine makes you feel warm). Brain scanners are designed to try to avoid you getting too hot. However, if you start to feel uncomfortable, squeeze the ball.

Peripheral nerve stimulation (tingling or twitching)
The magnetic field inside the scanner changes very quickly while the scanner is running. If it changes too quickly, it can give you tingling sensations or make you twitch. Brain scanners are designed to try to avoid this. However, if you experience tingling or twitching, squeeze the emergency ball and tell the technologist.

Claustrophobia (discomfort in enclosed spaces)
Some people get panic attacks inside enclosed spaces. This is called 'claustrophobia', which means 'fear of confined spaces'. If you know that you are claustrophobic, tell study personnel before your scans. Some people only find out they are claustrophobic when they have a scan for the first time. If you feel anxious or panicky inside a scanner, squeeze the emergency ball and the technologist will get you out.

Quench
In very rare circumstances, a scanner can lose its magnetic field. This happens very suddenly and is known as a 'quench'. The helium that helps keep the magnetic field strong will then escape from the scanner. The scanner is connected to a vent so that the helium will go outside the building. However, if for some reason the vent doesn't work properly, helium might fill the scan room, making it difficult to breathe. In the very unlikely event of a quench, the technologists will get you out of the scanner immediately.

Risks of exposure to radioactive PET tracer:
Your participation in this study will involve exposure to radiation from 1 PET scan with ^{18}F MK-6240 at your baseline visit. This exposure is not necessary for your medical care, is for research purposes only and is necessary to obtain the desired medical information.

The effective radiation dose you will receive from these research scans is approximately 5.4 mSv which is approximately 1.74 times, your yearly dose from natural environmental radiation in the US (3.1 mSv) and less than the limits set by the FDA for individuals participating in basic research studies, which is 50 mSV. According to the International Commission on Radiological Protection (ICRP), the increased risk of health effects, such as cancer, from radiation doses of this amount is either too small to be observed or nonexistent.

It is also possible that the tracer injection will cause an allergic reaction such as nausea, vomiting, and hives. These are usually limited. Very infrequently, there is difficulty in breathing, low blood pressure and dizziness that requires appropriate treatment. Severe reactions are extremely rare where death has occurred. If you have allergies, the possibility of reaction is higher than a patient without allergies. If applicable, in consultation with your doctor, it may be needed to have pre-medication to decrease the possibility of these complications.

Risks of genetic testing: There are potential dangers in obtaining DNA information. Genetic testing can generate information about your personal health risks and can cause or increase anxiety, damage family relationships, and/or compromise insurability and lead to social discrimination. To greatly reduce these risks, all identifiers will be removed from your samples and genetic data.

Since the genetic information gained is for research purposes only, the results will not be made available to anyone (including you and your physician). However, if you wish to learn your ApoE type, we can arrange for your genotyping and genetic counseling to be determined by an outside certified clinical laboratory. If you decide to do this privately, it is not part of this study and the costs of this service or the recommended counseling will be your responsibility.

Although every effort will be made to ensure that you do not learn the results of this test, there is the very unlikely risk that you may inadvertently gain this information. In this case, the primary risk of the genotyping would be a risk of social and psychological harm rather than a risk of physical injury. To minimize this risk, if you inadvertently learn the results of this genotyping you will be given the opportunity to discuss the test results, with a study physician. There is evidence that one type of the ApoE gene may be a risk factor for Alzheimer's disease. However, ApoE genotyping is not a diagnostic test and is not part of the recommended diagnostic evaluation for Alzheimer's disease.

There is no possibility of obtaining incidental (accidental) findings, such as paternity (parental origin) or information about diseases or conditions other than the ones in this study. It is highly unlikely that any genetic information we receive could cause embarrassment to you or your family members. If you experience discrimination because of the release of DNA related information you may contact the New York State Division of Human Rights at (212) 870-8624 or the New York City Commission of Human Rights at (212) 566-5493. These agencies are responsible for protecting your rights.

There is a risk that someone could get access to the data we have stored about you. If those data

suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. There are laws against this kind of misuse, but they may not give full protection. There may be other unforeseen privacy risks.

We believe the chance these things will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us and we will make every effort to protect them by coding your samples, limiting access to the samples and the information collected during your participation in the study, etc.

Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes.

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

OPTIONAL SAMPLE BANKING AND GENETICS RESEARCH

With your permission, the blood and DNA samples collected in this study will be stored indefinitely at the NYU Grossman School of Medicine Center for Sleep and Brain Health (CSBH) for future research on MCI, Alzheimer's Disease, and/or mechanisms change in the brain with aging. Testing on your DNA associated with these areas of research will not be used for clinical or individual purposes and results will not be shared with you. Science and medicine are continually advancing. New discoveries, experimental tests and ways of looking at your blood and genes might be developed in the future to provide valuable information associated with this research.

We can't predict what specific tests will be done or what the results will mean for your health or when they will be done. All this future information will be experimental and we therefore will not be able to share it with you.

Your name and other information that could directly identify you (such as address or social security number) are called identifiers. If you agree to let us store your samples, identifiers will be removed from your blood and DNA samples. After such removal, the samples may be used for future research studies or shared with other researchers and we will not request additional informed consent from you to use these specimens as we have noted here. The other researchers may be at NYU, or they could be at other institutions. Only the study team here at NYU will be able to link your samples back to you.

Though your identifiers will never be shared, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

If you agree now, but later decide you don't want your samples to be stored for future research, we ask that you contact Dr. Dan Iosifescu in writing and let him know you are withdrawing your permission for yoursamples to be used for future research. His mailing address is:

Dan Iosifescu, MD
Department of Psychiatry
New York University Grossman School of Medicine
One Park Ave, 8th Floor

New York, NY 10016

Any unused samples will be destroyed.

Please choose one option below by writing your initials next to your decision:

OPTIONS TO CHOOSE

1. The investigator may wish to contact you in the future to obtain follow-up information. Is it okay to contact you for additional information in the future?

YES_____NO _____

Subject initials: _____

2. Are you willing to have your samples and data released to other investigators doing studies of the genetics of human disease?

YES_____NO _____

Subject initials: _____

3.Can the investigator store your samples for current and future research projects?

YES_____NO _____

Subject initials: _____

6. Can I be in the study if I am pregnant or breastfeeding?

We do not know how taking part in this study would affect an embryo, fetus, or breastfeeding baby. Therefore, you should not become pregnant, breastfeed a baby, or father a child while participating in this study. Other risks may not yet be known.

If you are currently pregnant, you will not be able participate in the study. You should not become pregnant while you are participating in this study. If you are able to become pregnant, you will be required to use a medically accepted method of birth control while you participate in the study:

- Hormonal methods like birth control pills, patches, vaginal rings or implants
- Barrier methods such as condoms or a diaphragm used with spermicide (a foam, cream or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

If you become or you think you have become pregnant during the study, you must tell the principal investigator right away and must tell your obstetrician or other health care provider caring for you during your pregnancy that you took part in this study. If you become pregnant, you will have to stop taking part in the study for safety reasons. The principal investigator may ask you to provide information about the outcome of your pregnancy and the health of your baby.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

In some cases, a brain scan will reveal an abnormality with or without a clinical significance. Every scan performed in this study is saved and handled under standard private health information confidentiality restrictions and regulations employed for patients' information. Each MRI scan is additionally reviewed by a radiologist, who might then detect an abnormality. If clinically useful information is uncovered, either the Principal Investigator or another clinician on the study will speak to you in person or on the telephone regarding the new information. A copy of the original MRI report will be provided to you and you will be encouraged to follow up on the discovery with your treating physician. Results of the brain scans which are strictly investigational and not used in clinical practice (i.e., PET, 31-P-MRS) will not be provided to you.

8. What are the possible benefits of the study?

It is possible that some subjects may experience an improvement in their thinking or memory after the near infrared procedures during the study. However, if you receive such benefit, because near infrared exposure is not FDA-approved for MCI, your doctor cannot prescribe it after you finish the study. You may not benefit personally from being in this study. However, we hope that, in the future, other people might benefit from this study because of what we learn about MCI. Others MCI or Alzheimer's Disease may benefit in the future from what we learn in this study.

9. What other choices do I have if I do not participate?

You do not have to take part in this research study. If you decide not to participate, your decision will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

There currently is no standard treatment for MCI, but there are things a person can do that may help them stay healthy and deal with changes in their thinking such as: staying involved in mental and physical activities, sleeping and eating well, and avoiding alcohol. You discuss these and other options with your personal doctor. You may also continue them during the study.

10. Will I be paid for being in this study?

Biospecimens collected for the purposes of this research (even if identifiers are removed) may be used for commercial profit. If your biospecimens are or become commercially profitable, you will not share in this commercial profit.

You will be paid per completed procedure according to the following schedule:

- Screening procedures: $50
- Baseline procedures (includes brain scan and open label t-PBM session): $100
- Study treatments 1-24: $50 per treatment.
- Primary outcome procedures (includes brain scan): $75
- Follow up procedures: $50 each for short-term and long-term follow-up.
- Optional Neuropsychological testing post open-label treatments: $25

If you chose to leave or are withdrawn from the study for any reason before finishing the entire study, you will be paid for each visit completed at the time you leave or are withdrawn. You will not be compensated for the open label t-PBM treatments offered post- study completion. You will be compensated for the neuropsychological testing completed post- optional open label treatments, if you decide to undergo this testing. If any of the study procedures were repeated due to technical difficulties, you will be compensated for the repeated procedures in accordance with the payment schedules listed above.

If you complete all the study visits without repeats, plus the optional neuropsychological testing after you complete all post-study optional open-label treatments, you will receive **$1550** for being in this study.

As is required by the laws that apply to NYU Langone Health, in order for you to receive a payment, you need to give the study staff either your Social Security number or your Alien Registration number and will be asked to complete a IRS W9. If you do not have either of these numbers or are not willing to complete the IRS, you may be in the study but will not receive any payment.

You are required to track all payments made to you by NYU Langone Health for your participation in any research for this calendar year. You must let us know immediately if/when the total research payments presently equal or is likely to exceed $600.00 total (not including travel reimbursements) for this calendar year. If your total payments (for one or more studies) reach $600.00, please advise the study coordinator, Anna Peterson (646-754-2260) or Zamfira Parincu (646-754-2211)

In order to receive payments for your participation in research, you may need to provide your Social Security number. This is because NYU Langone Health is required to report to the Internal Revenue Service (IRS) any amounts that are paid to research participants that are equal to or greater than $600.00, andyou may be taxed on these research payments above $600.00. If you will receive payments in any amount by a check, you will need to provide your Social Security number or Alien Registration Number and will be asked to complete an IRS W9. If you do not have either of these numbers or are notwilling to complete the IRS, you may be in the study but will not receive any payment.

We will pay you back for travel costs up to $50 per visit to and from the study. In order to be paid, you must give the receipts to the study staff. However, if you choose to let the study staff coordinate transportation for you (i.e., arranging a taxi service to take you to and from study visits), you will not be charged and will not need to worry about reimbursement. Note that we will be unable to pay you back for travel costs or coordinate transportation during the open label t-PBM treatments offered post-study completion.

11. Will I have to pay for anything?

You will not have to pay for any tests or procedures as they are all covered by the study.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator’s name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for NYU Grossman School of Medicine or NYU Langone Health to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

13. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician, the study sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study sponsor, the principal investigator, the Food and Drug Administration (FDA) or other

body responsible for monitoring the safety of the study has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

14. How will you protect my confidentiality?

Your medical information is protected health information, or “PHI”, and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

Certificate of Confidentiality
To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research, without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases).

The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight. The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.
By agreeing to be in this research and signing below, you are giving your consent to share research information with others at NYU Langone Health. This means that your research information, including lab results, brain scans, information about the investigational drug used in this study, may be included in your NYU Langone Health electronic medical record.

15. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your

permission (authorization) to use and share your health information with others in connection with this study- in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?
All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, procedures, questionnaires, and diaries.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- The study sponsor: National Institutes of Health & the Alzheimer's Association
- Governmental agencies responsible for research oversight (e.g., the Food and Drug Administration or FDA).
- Health care providers, including your doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.
- Other study sites involved in the research (Nathan Kline Institute for Psychiatric Research and Massachusetts General Hospital)
- Anonymized MRI data will be shared with our collaborator and co-investigator, Jacek Dmochowski, PhD, of CUNY, such that he will analyze the imaging data we collect Data and Safety Monitoring Board

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?
Signing this form is voluntary. You do not have to give us permission to use and share your information,but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?
Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

Study staff may review each participant's medical record for laboratory tests. If any of the above laboratory tests have been performed and found within normal ranges within the past 6 months of study enrollment, those tests do not need to be repeated and results from previous tests may be used, under the discretion of site PI.

Optional permission for future use:

NYU Langone Medical Center (NYULMC) would also like to store, use, and share your health information from this study in research databases or registries for future research conducted by NYULMC or its research partners. Such healthinformation may include biological samples from the study. If you are concurrently enrolled in another study with the same PI(s), where the same cognitive, blood biomarker, or imaging data are being collected, then this data will only be collected once and will be shared between studies. This will eliminate the need to complete additional procedures that are identical and that may increase exposure to any risk, or make you uncomfortable. To give this additional permission, check the box below and write your initials where indicated. You may still participate in this study even if you do notgive us this additional permission. NYULMC will continue to protect the confidentiality and privacy of this information as required by law and our institutional polices. If you give this additional permission, youwill continue to have the rights described in this form. You have the right to take back this additional permission at any time.

☐ Checking this box indicates my permission to store, use, and share my health information from this study in research databases or registries for future research conducted by NYULMC or its research partners.

Subject Initials:_____

16. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU Langone Health IRB Office number is (212) 263-4110. The NYU Langone Health IRB is made up of doctors, nurses, non-scientists, and people from the Community.

17. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the NYU Langone Health IRB at (212) 263-4110.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this web site at any time.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject	Date

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

Informant Contact Information

Name of Informant (Print)	Relationship to Subject	Phone Number