CONSENT FORM COVER PAGE

STUDY TITLE: Dopaminergic Dysfunction in Late-Life Depression

NCT Identification Number: NCT04469959

Date of document: 12/11/2025

Institutional Review Board
Informed Consent Document for Research
MASTER CONSENT

Study Title: Dopaminergic Dysfunction In Late Life Depression (D3 Study)
Version Date: 12/11/2025

Part 1 of 2: MASTER CONSENT
Control Participants

Name of participant: _____ Age: _____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

What is the purpose of this study?

The purpose of this research study is to better understand how the brain's dopamine system may contribute to depression in older adults. Dopamine is a neurotransmitter, a chemical messenger released by nerve cells. Some medications used to treat depression affect dopamine but most do not.

This study is being conducted at Vanderbilt University Medical Center (VUMC) and the University of Pittsburgh Medical Center (UPMC). Across both sites, we plan to enroll up to 100 eligible participants with depression and 70 eligible participants with no history of depression for this study over five years.

In this study you will have tests of your memory, concentration, thinking, and walking. You will have a brain scan using magnetic resonance imaging (MRI). If you are a participant at Vanderbilt University Medical Center (VUMC) you will also complete a positron emission tomography (PET) scan. We are performing these scans to understand more about how the brain's dopamine system may be different in older adults who are depressed.

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What will happen and how long will you be in the study?

If you agree to be in this study, you will first be asked to sign and date this consent form. The study involves an initial screening visit and a baseline period. The screening visit is an initial visit to determine if you are eligible for the study. Over the course of the study, you can expect to spend 14 hours completing all study related procedures.

If you are eligible for the study and decide to participate, you will enter a baseline period. During the baseline period, we administer tests of your memory, concentration, and thinking. How you walk will be measured using a special mat. You will also complete one MRI scan and a blood draw. These baseline tasks, procedures, and assessments will be spread out over at least 2 visits over a period of up to 4 weeks. You can expect to spend about 10-12 hours total to complete them.

While not necessary for many people, to confirm it is safe for you to have an MRI we may ask you to have an x-ray, which does use radiation, to see if there is metal in your body.

If you are a participant at VUMC, you will also complete a PET scan. The PET scan will likely happen after your first MRI scan, but on a different day. The PET scan will be discussed in the Vanderbilt-specific section of this consent form. If you are a participant at UPMC, you will not complete a PET scan.

During parts of the MRI scan, you will be asked to look at a screen and accomplish tasks by pressing buttons.

There is no cost to you for taking part in this research study. You will not have to pay for the brain scan(s) or the tests and treatments that are being done only for research. The study medications will be free of cost throughout the study. You are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This will be discussed in more detail later in this document.

All study visits will be discussed in more detail later in this document.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Study Title: Dopaminergic Dysfunction In Late Life Depression (D3 Study)
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You are being asked to take part in this research study because you are 60 years or older and you are healthy individual with no history of depression or other mental illness.

You are participating as a never-depressed comparison participant, which means your results will be compared with results from participants with depression to learn more about what brain changes are associated with depression.

You do not have to be in this research study. You may choose not to be in this study and get treatment without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

Side effects and risks that you can expect if you take part in this study:

Diagnostic, Memory, and Motor Testing: We will ask you to complete some tasks that measure your memory, concentration, and your walking speed. Some of these will be done using pencil-and-paper while other tests will be done on a computer or iPad. It may take up to 4 hours to complete these tests.

You may experience boredom or discomfort during the clinical interview and evaluations when discussing symptoms and recent life events. You may also experience frustration with some tasks. Should you wish to stop or take a break, the study staff will allow it.

Walking Assessment: The walking assessment is done using a special mat. During the walking speed assessment or other physical movement measure you may feel unsteady and there is a risk of fall. During each performance-based assessment study personnel will be there to accompany you to ensure safety and provide support in case of a fall or if you are unsteady.

Risks of Magnetic Resonance Imaging (MRI): You will have one MRI scan during the baseline period.

There are no known major risks with an MRI scan. But it is possible that harmful effects could be found out in the future. The tunnel is closed. It may bother you to be placed in a tight space (claustrophobia), and to hear the noise made by the magnet during the scan. You will be given earplugs to reduce the noise. You may also feel the table vibrate and/or move slightly during the scan. It may be hard to lie on the table during the scan. If you have any metal pieces in your body, they could move during the scan and damage nearby tissues or organs.

If you use a transdermal patch (medicated patches applied to the skin), you may need to take it off during the MRI scan. Transdermal patches slowly deliver medicines through the skin. Some patches have metal in the layer of the patch that is not in contact with the skin (the backing). You may not be able to

see the metal in the backing of these patches. Patches that contain metal can overheat during an MRI scan and cause skin burns in the immediate area of the patch. Tell the study staff that you are using a patch and why you are using it (such as, for pain, smoking cessation, hormones). Ask your doctor for guidance about removing and disposing of the patch before having an MRI scan and replacing it after the procedure. Tell the MRI facility that you are using a patch. You should do this when making your appointment and during the health history questions you are asked when you arrive for your appointment.

Loss of Confidentiality: There is also the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential, however this cannot be guaranteed.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study: You will be adding to the understanding of whether treatments that target dopamine may help treat depression in older adults, as well as the effects of carbidopa/levodopa on memory performance and movement. This information will help us determine if carbidopa/levodopa may be a useful approach to treating depression or mobility problems.

The benefits you might get from being in this study: As a non-depressed comparison participant, you will not directly benefit from participating in this study.

Procedures to be followed:
Screening Visit (Total Time: 2-3 hours):

The initial visit is called the screening visit. Your medical and psychiatric history will be carefully reviewed to make sure that you are eligible for the study. Additionally, we will assess your current depressive symptoms and your current and past medication use. You do not have to answer any questions you do not feel comfortable answering.

For your safety, you must tell study staff about all the medications you are taking, including over-the-counter drugs and herbals, before you start the study and before taking any new medications. If there is a problem where you cannot be in the study because of one of the medications you are taking, study staff will discuss that with you.

As part of this visit, we will carefully evaluate you to determine if you have any metal in your body that could stop you from having the MRI. If you have had any surgeries that may have used implanted metal objects, we may need to request medical records to assure your safety before you could proceed to MRI.

At the end of the screening visit, or during the baseline period, you will be asked to complete a series of questionnaires. These questionnaires can be completed in several ways.

1. We can email you a link that will allow you to complete the questionnaires on a device with internet access, such as a computer or smartphone. These questionnaires will be completed in a secure database in REDCap. REDCap is a secure web platform created for researchers where data for this study are collected and stored. VUMC is managing the REDCap database for this study.
2. If you do not have an email address, or if you prefer to complete the questionnaires on paper, you can be given a take-home packet of questionnaires to complete. We will ask you to complete them as soon as possible. If you are given paper questionnaires to complete at home, you will return them to us via the addressed, stamped envelope we will provide, or you can return them at your next in-person visit.
3. You can also complete the questionnaires during a study visit, using a study iPad or computer. This will not require your email address to be entered in the REDCap study database.

If you have any questions, you can contact us at any time.

Baseline Period (Total time varies by site):

If you are eligible and would like to participate, you will be scheduled for the baseline period. The baseline period will last up to 4 weeks. You will meet with study staff who will again assess your depressive symptoms. You will also complete neuropsychological (memory) testing, a gait (walking) assessment, and one MRI scan. Participants at VUMC will also complete one PET scan. This will be discussed in the Vanderbilt-specific part of this consent document.

These baseline study procedures will be done over 2-4 separate visits. The symptom assessment portion of the baseline period may be done in-person or remotely using HIPAA compliant video conferencing (for example, Zoom). All other baseline assessments will be completed in-person.

Neuropsychological (Memory) Testing: We will ask you to complete some tasks that measure your memory, concentration, and problem-solving abilities. Some of these will be done using pencil-and-paper while other tests will be done on a computer or iPad. The memory testing will take about two hours. Memory testing can be on the same day when you have the MRI scan, or on a separate day.

The memory tests are completed for research purposes only. They are not administered by a licensed clinical psychologist and thus, we are not able to provide a clinical interpretation of the results.

MRI: You will have one MRI scan during the baseline period. The MRI scan will take about 90 minutes. An MRI scan is taken in a large machine that is shaped like a tunnel. This scan does not use x-rays. Instead, they use a strong magnet and radio waves, like those used in an AM/FM radio to make pictures of your body.

During the MRI scan you will be asked to complete two tasks measuring your attention and decision-making abilities. You will see images on a screen and you will press buttons with your fingers to complete the tasks. You will be able to practice the tasks before entering the MRI scanner. Both tasks involve you responding to images on-screen to examine how people make decisions about rewards, such as choosing a high reward with a low chance of receiving it or choosing a low reward with a high chance of receiving it. Your performance on the tasks will determine how much compensation you receive for completing the MRI scan.

You may not be able to have this scan if you have a device in your body, such as aneurysm clips in your brain, heart pacemakers or defibrillators, or cochlear (inner ear) implants. Also, you may not be able to have this scan if you have iron-based tattoos or pieces of metal (bullet, BB, shrapnel) close to or in an important organ (such as the eye). If we determine that you cannot safely complete the MRI, we will withdraw you from the study.

Certain metal objects like watches, credit cards, hairpins, writing pens, etc. may be damaged by the machine or may be pulled away from the body when you are getting the scan. Also, metal can sometimes cause poor pictures if it is close to the part of the body being scanned. For these reasons, you will be asked to remove these objects before going into the room for the scan.

You will hear "hammering," clicking, or squealing noises during the scan. You will be given earplugs to reduce the noise. You will also be told how to alert the staff if you need them.

During the scan, the MRI staff is able to hear and talk to you in between scans. You will also be able to hear the staff in between scans. They will be talking to you during your scan and may ask you to not move or other simple tasks. You may be asked to lie very still throughout the scan.

Reasons why the study doctor may take you out of this study:

Your study clinician may withdraw you from study participation if he or she determines that, based on the initial study interview, you are not eligible to continue the study. He or she may also withdraw you if you are having difficulty completing study procedures, if you need an immediate referral for clinical care, or if he/she decides that it is not in your best interest to continue in the study. If you are taken out of the study, you will be told the reason.

What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study clinician or study staff. We may ask you to come in for a final study visit. If you withdraw or are withdrawn from the study early, you will be compensated for the parts of the study you have completed.

All participation in the study is voluntary, and there is no penalty for refusing to participate or for early withdrawal. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:

A description of this clinical trial will be available on 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.

Confidentiality:

All reasonable efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. Your information may be shared with institutional and/or governmental authorities, such as the Institutional Review Boards for the University of Pittsburgh Medical Center or Vanderbilt University Medical Center. It may also be shared if you or someone else is in danger or if we are required to do so by law.

All data are labeled and coded for protection and confidentiality. Data are kept on secure, password protected networked computers, in secure REDCap database, and in locked offices. Identification numbers are used instead of names for additional protection. Only research staff will have access to participant data. Source materials will be labeled and coded with an identification number that is not linked in any way to participant personal identifying information for purposes of additional protections and confidentiality. This number will be used to identify participants' self-reported questionnaires, memory test results, brain scans, and other data. Other than your date of birth, no other direct identifiers will be shared with our collaborators.

A list linking names to identification numbers will be available only to authorized personnel and will be kept separately from research charts. Only research personnel authorized by the Principal Investigator will have access to these records. The link between your identity and your identification number will not be shared with researchers in other institutions and will not leave your study site.

During the study, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include:

- working with you to contact your doctor,
- contact a trusted family member, or a therapist to discuss your thoughts,
- or work with you on a plan that may include getting you to a hospital for safety.

In these cases, the research team may share information about your condition with other health care providers.

Investigators may share your information, without identifiers, to others or use it for other research projects not listed in this form. We will be sharing de-identified data with the University of Pittsburgh Medical Center, Vanderbilt University Medical Center, Emory University, Rutgers University, and University of North Carolina. We will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

This study is supported by the National Institutes of Health (NIH) and 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.

Privacy:

Any samples and information about you may be made available to others to use for research. Study information about you will be shared with study investigators across both sites, including Vanderbilt University Medical Center and the University of Pittsburgh Medical Center. To protect your privacy, other than your date of birth, we will not release your name or other direct identifiers.

De-identified data will also be shared with the University of North Carolina, Emory University, and Rutgers University.

You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Data from this study will be submitted to the National Institute of Mental Health Database (NDA) at the National Institutes of Health (NIH). NDA is a large database where deidentified study data from many National Institute of Mental Health (NIMH) studies is stored and managed. Deidentified study

data means that all personal information about you (such as name, address, birthdate and phone number) is removed and replaced with a code number. Sharing your deidentified study data helps researchers learn new and important things about mental health and substance use more quickly than before.

During and after the study, the study researchers will send deidentified study data about your health and behavior to the NDA. Other researchers across the world can then request your deidentified study data for other research.

Every researcher (and institutions to which they belong) who requests your deidentified study data must promise to keep your data safe and promise not to try to learn your identity. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about mental health and substance use and how to help others who have problems with mental health and substance use. NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA.

You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA. If you know now that you do not want your data in the NDA, please tell the study researcher before leaving the clinic today. If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff who conducted this study, and they will tell NDA to stop sharing your study data. Once your data is part of the NDA, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about NDA, this is available on-line at http://nda.nih.gov.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, Vanderbilt University Medical Center, and/or others. If this happens, there are no plans to provide money to you.

While you are participating in this study, we may want to discuss with you about possibly participating in other research studies at your study site. Please indicate below if you are willing to be

contacted about other research studies. We will not contact you about future research studies once your participation in this study is complete.

O Yes, I agree to be contacted about other research studies.

O No, I do not want to be contacted about other research studies.

Study Results:

Study records will be maintained for at least seven years after all study procedures are complete, all subject contact has ended, and the study is closed with the IRB. After that time, study data may be destroyed or anonymized, meaning all links to direct identifiers will be destroyed. Any study data in the medical record will be kept indefinitely.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

Institutional Review Board
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STUDY SITE INFORMATION

Study Title: Dopaminergic Dysfunction In Late Life Depression (D3 Study)
Version Date: 12/11/2025

Part 2 of 2: STUDY SITE INFORMATION
Control Participants

Site Name:	Vanderbilt University Medical Center
Site Principal Investigator:	Alexander Conley, Ph.D.
Site Principal Investigator Contact:	(615) 322-1073
Site Study Coordinator *(if applicable)*:	Carrie Williams
Site Study Coordinator Contact *(if applicable)*:	(615) 936-2162

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Site specific key information:

In addition to the baseline period procedures described in Part 1 of this consent form, you will also complete one Positron Emission Tomography (PET) scan during the Baseline Period.

To make sure it is safe for you to have the PET scan, you will have approximately 1 tablespoon of blood drawn for a blood count and to measure electrolyte levels (sodium, potassium, and an estimation of your kidney functions). We will also perform a test called an "EKG", which measures your heart rate and regularity of your heartbeat. If you have had these tests performed within 3 months prior to your screening visit, we will ask for your permission to obtain these records and may not need to repeat the EKG or safety blood samples for this study.

The PET scan requires placement of an IV catheter (placed in a vein) and injection of a short lived investigational radioactive dye (a "radiotracer").

You will receive one radiotracer during the scan, [[^{18}F]FDOPA. [^{18}F]FDOPA is a non-FDA approved investigational drug. This radiotracer helps measure dopamine in the brain. Dopamine is an important chemical within the brain that helps brain cells function properly and may contribute to depression.

You will also be asked to take two medications, carbidopa and entacapone, one time prior to the PET scan. These medicines help improve the images obtained on the PET scan.

Site specific procedures and risks:

Blood sampling: We will draw up to 25mL (about 5 teaspoons) of blood one time. 15mL (about 3 teaspoons) of blood will be used to assure PET scan safety. 10mL (about 2 teaspoons) of blood will be used to measure inflammation. Pain, redness, soreness, bruising, or infection may occur at the needle stick site. However, this risk is low. Blood will be drawn by a phlebotomist using sterile technique. Rarely some people faint. The study staff may put some cream (called EMLA) on your skin to numb the area so you will not feel the needle stick as much. The numbing cream may make your skin have a change in skin color, but this is rare.

Risks of Positron Emission Tomography Imaging (PET scan): You will be asked to have one PET scan that includes radiation exposure. During PET imaging, you will be exposed to radiation from x-rays and radioactive materials. This research study involves exposure to radiation from the administration of [^{18}F]FDOPA. You should not have a PET scan for this study if you routinely work around radiation.

Radiation:

Radiation: This research study may involve exposure to radiation from up to 1 X-ray and 1 PET/CT scan. This radiation exposure may not be necessary for your medical care and may be for research purposes only. The total amount of radiation that you will receive by participating in this study is equal to your body receiving 56 months (4.7 years) of radiation from your natural surroundings, or about 28% of the amount allowed in a year for people who are exposed to radiation as part of their work. To protect your bladder from the effects of the injected radioactive substances, you should drink plenty of fluids and empty your bladder every two hours for at least the first six hours after you have each PET/CT scan.

X-ray Radiation exposure (if needed): If you possibly have metal in your body, to determine if it is safe for you to have an MRI we may ask you to have an x-ray before the MRI scan. This involves exposure to radiation from the x-ray. This radiation exposure is not necessary for your medical care and is for research purposes only.

PET Compound: The radioactive mixture will be injected in a vein (intravenous). This can result in a risk of pain or bruising or infection at the site of the needle stick. As with any medication or substance, allergic reactions are a possibility. This reaction may be mild, such as a skin rash, or you

may have more severe symptoms like throat tightness, low blood pressure, and it may be hard to breathe. In rare cases, a severe reaction could cause death.

FDOPA: This radioactive compound has been used for decades and has not indicated any bad effects. Animal studies have shown no bad effects from much larger doses of this compound than those used for human PET scanning. Entacapone and carbidopa are given one time before the FDOPA PET scan. These medications are clinically used to treat Parkinson's disease. We are using them in this study as they help slow the breakdown of dopamine and will improve the pictures of the brain. The risks and side effects related to using entacapone and carbidopa include nausea, dizziness, vomiting, diarrhea, unwanted/uncontrolled movements, increased sweating, drowsiness, tiredness, dry mouth, gas and abdominal pain.

Discomforts associated with PET scanning: Minor discomfort may occur during the PET scan. This includes discomfort from having to lie still in the scanner for a long period of time. A PET scan may cause you to feel "closed in" while lying in the scanner. However, the scanner is cylinder open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort, or the scanning will be stopped. We will provide pillows.

Injection-Site Reactions: We will use a needle to inject FDOPA into a vein in your arm. Putting in the needle may cause pain or stinging, and you may feel dizzy. On rare occasions, the needle can cause bleeding, bruising, swelling, or infection at the place where the needle is inserted. A small amount of bleeding may occur when an intravenous line is inserted or removed. While there is the possibility of infection, this is very unlikely.

Risks of drug interactions: It is possible that receiving FDOPA, carbidopa, or entacapone may change how your regular medications, vaccines, or supplements work. It is important that you tell the study staff about any medications, supplements, or vaccines before you take them during the study.

Risks that are not known: As with any research, there may be risks of participation or from the study medication that we cannot predict. Because the FDOPA is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time. If you experience any unpleasant effects during this study not mentioned in this consent form, please contact a study staff member or study doctor as soon as possible.

Site specific detailed Information

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Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

We are requesting that you provide the name and contact information of your primary care provider. If any clinically significant health findings arise from study procedures, we would like to inform you and your health provider of these findings. We ask that you designate your health care provider:

Name of health care provider _____

Phone number of health care provider_____

_____ I do not have a healthcare provider or do not want any information shared with my healthcare provider. If results are shared with me, I am encouraged to share them with a healthcare provider.

At the beginning of each virtual visit, you will be asked to confirm your location. Virtual study visits will need to occur when you are in a residence or work location. We ask that you keep your camera on for the duration of the visit. If you are unable to stay in one location for the entire visit, your visit may be rescheduled. If you are unable/unwilling to provide your location and keep your camera turned on for the entire visit, your visit will need to be rescheduled to a different time, rescheduled to an in person visit, or you may need to be withdrawn from the study.

Screening Visit:
During the screening visit, we will carefully inquire about your radiation exposure in the past to evaluate you for the PET scan. Since the radioactive drug FDOPA will be administered for PET scan, we will obtain a detailed history of allergic reactions, current medications, supplements and vaccines to avoid the risk of any drug interaction.

Please inform your study doctor or study staff if you have taken part in other procedures or research studies that used radiation, this way we can make sure that you will not receive too much radiation. You should consider x-rays, cardiac catheterization and fluoroscopy as well as nuclear medicine scans in which radioactive material were injected into your body. You may be asked to complete an EKG, a brief physical exam, and a blood sample may be collected. These assessments can be done during the baseline period if they are not completed at the screening visit. The blood sample will be discussed later in this document.

Baseline Period (Total Time: about 10 hours)
In addition to the procedures described in Part 1 of this consent form, during the baseline period you will complete a physical exam, a blood draw, and an EKG if they were not completed at the screening visit.

PET Scan: You will also have one PET scan during the baseline period. A PET scanner is a large machine, shaped like a tunnel. It is similar to the shape of an MRI scanner. For the PET scan, we will ask you to lie on a narrow table. We will also position your head with a chin strap or a polyurethane head holder that we will mold around your head to reduce head movement during the scan. Right before each PET scan we will perform a very short (~10-15 second) computerized tomography (CT, or "CAT") scan of the brain which helps us make sure the PET scan is positioned correctly. The CT scan is a special x-ray test that will allow us to collect more accurate data from the PET scan.

The PET scan will likely happen after your first MRI scan and on a different day. The PET scan will usually begin in the late morning or early afternoon. On the day your PET scan is scheduled, we will provide a moderate lunch with no more than a single cup of coffee or tea.

The PET scan involves the use of a radioactive investigational drug, [^{18}F]FDOPA. It is an investigational drug that binds to parts of your brain that process dopamine. It contains a small radiotracer that can be "seen" by the PET camera. The PET camera then takes "pictures" of the chemical activity in the brain by detecting the radioactive signal of the FDOPA.

To administer the radiotracer, we will need to place an intravenous (IV) catheter in one of your veins. After the catheter is inserted and the radiotracer is injected, we will begin the PET scan.

If you complete the FDOPA PET scan, you will receive a dose of entacapone (400mg) and carbidopa (200mg) 30-45 minutes prior to the start of the PET scan. These medications reduce the metabolism of the radiotracer in your body. This will allow most of the metabolism to occur in the brain and increase the signal seen in the PET scan. The scan session, in combination with the medication, will show where dopamine is being stored and produced. The FDOPA scan will take about one hour and 45 minutes. [^{18}F]FDOPA is a radioactive compound because the [^{18}F] part of the compound breaks down quickly, making radiation that can be measured with the PET scanner. FDOPA has been developed at other institutions to study how dopamine production occurs in the brain.

[^{18}F]FDOPA is an investigational drug and has not been approved by the

Food and Drug Administration for general clinical use. Vanderbilt has approval from the Food and Drug Administration to use [^{18}F]FDOPA as an investigational drug for research.

If you move your head during the PET scan, we may do an additional CT position scan at the end of the PET scan. If you feel nauseated during scanning, please immediately alert the PET staff member. It could be dangerous to vomit while in the scanner due to a risk of aspiration. After the end of the last scan, we will remove the catheter and you will be evaluated for safety.

Blood Sample: We will collect up to 25 mL (about 5 tsp) of blood for one time during the study. The blood draw will occur either at an in-person screening visit or during the baseline period, prior to the PET scan. You will not need to fast prior to the blood draw.

If you have had blood drawn for a complete blood count and electrolyte levels within 3 months prior to your screening visit, we are able to obtain records, and your results were normal, we may not need to repeat these tests. If these tests don't need to be completed, we will still collect up to a 10 mL (about 2 tsp) blood sample for inflammatory markers.

Additional Information about MRI: The MRI scan is being done for research purposes rather than for diagnosis. The scan will not be routinely examined by health professionals for potential abnormalities. However, in the event an abnormality is detected by the investigators or the MRI technologist, the scan will be further examined by a radiologist and the investigator may encourage you to consult your physician or provider referrals for further evaluations. If your healthcare provider would like to use the MRI for comparison with another clinical scan that has already been obtained or may obtain in the future, they may request a copy of the research scan if they are still available.

If you have had surgeries where records are not available, or you have a history of one or more injuries involving metal fragments, we may ask you to have an x-ray of that part of your body to make sure there is no metal in that site. If it is deemed necessary for you to have an x-ray, this will take place before your next visit.

During the screening visit, you will have an option to complete a "mock" MRI scan. Although no actual scan is taken, you will be able to experience the process (getting on and off the table, being inside the scanning tube, hearing the sounds the machine produces during the scan) to make sure you are comfortable with having an MRI scan. Completing the "mock" MRI scan will take about 30-45 additional minutes.

This MRI scanner has been used with research animals. For your safety, we clean the scanner with bleach before and after your scan as we do with scanners used only for patients.

Additional Information about your Medical Record: Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Payments for your time spent taking part in this study or expenses:

You will be compensated for your participation and time based on how many visits/assessments you attend as well as your performance on the MRI tasks. You can receive up to $625. The table below shows how much you will receive for completing each visit:

Visit	Amount
Screening Visit	$25.00
Baseline Period	
Memory & Walk Testing	$75.00
MRI	Up to $150.00
PET	$350.00
Blood draw	$25.00
Total:	**Up to $625**

You will receive up to $150 for completing the MRI scan. You will receive at least $90 as base pay for completing the MRI scan. You can receive an additional $60 bonus based on your performance.

For one task, you will receive 20% of the total amount you earned while completing the task (for example, if you won $80 during the task, you will receive 20% of that amount, which is $16). For the second task, you will complete several trials of the task that each contain several rounds. We will select three rounds from each trial and pay you the amount you won during those trials. Your total bonus payment of up to $60 will be given to you in cash immediately after the scan. The $90 base pay will be included in a check with the rest of your reimbursement.

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The table below shows how much you will receive for completing the MRI scan:

Task	Amount
Base Pay	$90.00
Task Performance	Up to $60.00
Total:	**Up to $150 per MRI**

We will ask for your Social Security number and address before you are compensated for taking part in this study. You may receive up to $625 for taking part in this study. This amount may be taxable and will be reported to the Internal Revenue Service (IRS).

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided at Vanderbilt to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact the study coordinator, Carrie Williams, at (615) 936-2162 or the principal investigator, Dr. Alexander Conley, at (615) 936-1552. If you cannot reach the research staff, please call the study doctor, Dr. Patricia Andrews, at (615) 875-3722.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Medical Center Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Confidentiality:

Your paper research records will be kept in locked filing cabinets within locked rooms, and only the site research team will have access.

Blood samples will be leaving Vanderbilt University Medical Center for analyses of levels of inflammatory markers. They will be sent to Emory University to measure inflammation markers. These samples will be deidentified. This means they will only include your study-created identification number, the type of blood sample, and the date of blood collection.

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.

Authorization to Use/Disclose Protected Health Information:

What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

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Who will see, use or share the information?

The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

What if you change your mind?

Unless told otherwise, your consent to use or share your PHI does not expire. You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know. The mailing address is 1601 23rd Avenue South, Nashville, TN 37212. At that time, we will stop getting any more data about you. Your cancellation will not affect information already collected in the study, or information that has already been shared with

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others before you cancelled your authorization. The health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

Time: _____