Study Title: Vestibulopathy, imbalance and gait disturbances in Parkinson disease

PI: Fay Pongmala, PhD

Study ID: HUM00192613

NCT#: NCT05446194

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UNIVERSITY OF MICHIGAN

CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title:

Vestibulopathy, Imbalance, and Gait Disturbances in Parkinson Disease

Company or agency sponsoring the study:

Ann Arbor VA

Names, degrees, and affiliations of the principal investigator:

Fay Pongmala PhD, University of Michigan, Departments of Radiology and Neurology PhD, University of Michigan, Departments of Radiology and Neurology

Co-Investigator: Nicolaas Bohnen, MD, PhD, University of Michigan, Ann Arbor VA, Departments of Radiology and Neurology

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start any study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This study investigates whether vestibular (inner ear) dysfunction is a cause for poor balance in Parkinson Disease (PD). This study will involve clinical testing and brain imaging. The study will require you to withhold your Parkinson Disease (PD) medications the night before, and the morning of, motor testing and imaging. You will be asked to bring your PD medications with you, and you will be able to take your PD medications once certain testing is completed.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of the risks may include “freezing” symptoms when you do not take your dopaminergic medications, physical fatigue during testing, risk for falls or near falls during motor testing, and discomfort or anxiety from being in the confined space of the MRI scanner. More detailed information will be provided later in this document.

Participation in this study may provide important new insights into Parkinson disease and balance. More information will be provided later in this document.

We expect the minimum amount of time you will participate in the study will be 2 – 3 days.

You can decide not to be in this study. Alternatives to joining this study include current standards of care or there may be other studies with experimental treatments available.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues below.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

Balance and gait problems, including freezing of gait (FoG), cause severe impairments for people with Parkinson disease (PD) and significantly affect their quality of life. This study is looking at performing detailed clinical assessments and brain imaging in subjects with PD, especially FoG and imbalance, and how this may relate to vestibular (inner ear balance) changes. This study is being funded by the Ann Arbor VA. By doing this study, we hope to learn more about PD and balance issues.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Men and women who are at least 45 years of age who have had PD with a duration of disease > 5 years and/or Hoehn & Yahr states 1.5-4 and can walk independently can participate in this study. Participants should be willing and able to comply with study requirements.

Subjects with dementia, Meniere's disease (a rare disorder of the inner ear that causes episodes of a sense of whirling, loss of balance, vomiting, loss of hearing, or fullness in the ear), or acute vestibular dysfunction, history of stroke or mass on brain MRI, other neurological disorders that resemble PD, or unstable medical conditions may be excluded. In addition, subjects who, in the opinion of the investigators, would be at increased risk or who are unable to perform or tolerate the research procedures will be excluded. People who have any contraindication for MRI imaging such as a pacemaker, metal fragment(s) in their body, or severe claustrophobia may not be eligible, as well as subjects with any contraindication for Positron Emission Tomography (PET) imaging, including significant prior participation in research procedures involving ionizing radiation.

3.2 How many people are expected to take part in this study?

A total of 64 people are expected to participate in this study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

After having passed the initial screening process, and if you agree to take part in this study, you will be asked to sign this informed consent form before testing will begin. During the screening process we will ask questions to determine if you are eligible to participate in this study.

Screening Assessment (Visit 1)

Physical exam: You will receive a physical and neurological examination ("medical check-up") including the measurements of your weight, height, pulse and blood pressure as well as an evaluation of your ability to move and walk. We will ask you questions about your health and medications, and screen your cognitive abilities. We will also ask questions to see if you're eligible to undergo both MRI and PET scans. In addition, we will ask you for some general demographic and clinical information.

Motor tests: We will place small sensors on your wrist, ankles, and around your chest to measure your body movements while you perform different balance and walking tasks. Some of the walking may be tested while on

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an electronic gait mat. All of these assessments will be performed while you are "off" and "on" your dopaminergic (PD) medications. You will be asked to hold specific medication(s) prior to this testing. After motor testing is completed, you can take your medication.

Vestibular tests: These assessments will involve evaluating your inner ear system called the vestibular system. This may involve using multiple pieces of equipment. You may wear goggles and follow some lights with your eyes. Also, you may be put into a chair that will spin. You may perform multiple tasks during the spinning. There may also be additional assessments involving your inner ear system, including putting warm and cold water in your outer ear canal.

You will also be asked to sit in a comfortable chair and wear virtual reality goggles connected to a laptop computer controlled by the test administrator. When wearing the goggles, you will see one or more dots of light moving in different directions. You will be asked to follow these dots with your eyes in a specific way by a computer-generated voice. The test administrator will monitor your progress on a laptop computer and will ensure that you understand the directions for each test. These tests are designed to evaluate eye tracking, balance, reaction times, attention, and memory abilities. This will take approximately 20 minutes, including instructions and calibration.

Thinking and memory tests: The tests are designed to get an overall estimate of your memory, concentration, and ability to think. These functions will be measured with standard tests. We will also ask you questions about mood, sleep, and fatigue.

Screening imaging day (Part of Visit 1)

MRI scan: MRI scans allow the investigators to visualize all the structures in the brain in great detail by using a large magnet. An MRI scan of the brain involves lying on a table which slides into a scanner. You will be instructed to remove all jewelry and other metal-containing objects for the MRI scan. During the MRI scan loud noises may be heard. The MRI scan will be performed in an FDA-approved MRI scanner at the Department of Radiology at the University of Michigan Hospital.

PET scan: The PET scan will allow the investigators to "see" the specific marker of dopamine transportation in the brain. To establish this a chemical tracer will be injected into your vein through an i.v. (intravenous line or plastic "tube" inserted in an arm vein). A tracer refers to a small amount of a radioactive substance that does not alter body function, but that can be detected (imaged) in the PET scanner. The tracer will be injected as you lie on a table, which will move into a hollow machine resembling an X-ray scanner (CT or CAT). Images of your brain will be obtained over a period of time. Women of childbearing potential may be required to provide a urine sample for a urine pregnancy test within 48 hours prior to the PET scan. For the PET scans you will be asked to withhold taking your dopaminergic medications, such as Sinemet (levodopa) or Mirapex (pramipexole), on the morning of your testing.

DEXA scan: You will also undergo a DEXA scan to measure bone mineral density in the bones as well as soft tissue composition in the body. The DEXA scan will be performed in the Neuroimaging, Cognitive & Mobility Laboratory at Domino's Farms. You will lie down on a soft scanner bed mattress while the camera head moves over your body. The exam will take about 6-10 minutes.

If you are a woman who is sexually active and have not yet gone through menopause, you will need to assure the study team that you will avoid pregnancy through using abstinence or an effective family planning method. You will be required to provide a urine sample for a urine pregnancy test within 48 hours prior to the PET scan.

Optional Follow-Up Visits (Visits 2 and 3)

You will be asked to return for two follow-up visits. The first follow-up visit will occur 3 years (± 1 year) after your first visit. The second follow-up visit will take place 2 years (± 1 year) from the first follow-up visit. These visits will include:

Physical exam: You will receive a physical and neurological examination ("medical check-up") including the measurements of your weight, height, pulse and blood pressure as well as an evaluation of your ability to move

and walk. We will ask you questions about your health and medications. In addition, we will ask you for some general demographic and clinical information.

Motor tests: We may place small sensors on your wrist, ankles, and around your chest to measure your body movements while you perform different balance and walking tasks. Some of the walking may be tested while on an electronic gait mat. All of these assessments will be performed while you are "off" your dopaminergic (PD) medications. You will be asked to hold specific medication(s) prior to this testing. After "off' state testing is completed, you can take your medication.

Vestibular tests: You will also be asked to sit in a comfortable chair and wear virtual reality goggles connected to a laptop computer controlled by the test administrator. When wearing the goggles, you will see one or more dots of light moving in different directions. You will be asked to follow these dots with your eyes in a specific way by a computer-generated voice. The test administrator will monitor your progress on a laptop computer and will ensure that you understand the directions for each test. These tests are designed to evaluate eye tracking, balance, reaction times, attention, and memory abilities. This will take approximately 20 minutes, including instructions and calibration.

ADDITIONAL TESTING AT HOME

Diary study: You will be asked to fill out a monthly diary to document any falls or near falls you might have experienced, and the circumstances and possible consequences of the falls. You will be asked to send a completed diary by mail to the investigators for each month during a 6-month period. We will contact you on a regular basis to see how you are doing.

_____(initials) I discussed participating in the study and agree to participate.

Optional video and photo recording:

We would also like your permission to video record some of the assessments. This may be used for presentation or educational purposes. Video recording is optional and you do not have to agree in order to participate in this study. Your name or personal information will not be identified on the videos and confidentiality will be strictly maintained. However, when these videos are shown others may be able to identify you. Please initial below whether you agree to have a video of you performing some of the assessments recorded.

_____(initials) I discussed the video recordings and **agree** to participate in the video recording.

_____(initials) I discussed the video recording and **do not agree** to participate in the video recording.

We would like to ask your permission to take photographs of your torso from your sides and back. These photos would be taken with your shirt removed to accurately see your posture. If you are not comfortable with removing your shirt, we would still ask for your permission to take the photos with your shirt on. Photographs would be taken on a camera and would be used for scoring or educational purposes with your permission. Your name or personal information will not be identified on the photographs and confidentiality will be strictly maintained. However, when these photograph(s), are shown others may be able to identify you.

_____(initials) I discussed the posture photos and **agree** to participate in the photographs remaining in my shirt for the purpose of the study.

_____(initials) I discussed the posture photos and **agree** to participate in the photographs and removing my shirt for the purpose of the study.

_____(initials) I discussed the posture photos and **do not agree** to participate in the posture photographs.

Data Sharing permissions for photographs:

_____(initials) I discussed the posture photos and **agree** to participate in the video recording for scoring purposes only.

_____(initials) I discussed the posture photos and **agree** to participate in the photographs for scoring. and for the purposes of education at the University of Michigan. The PI may keep the following for an indefinite period of time in a locked file, in a password protected computer server drive, or as an encrypted electronic file.

_____initials) I discussed the posture photos and **agree** to participate in the photographs for scoring and educational purposes for the purposes of education at the University of Michigan; and for presentations at scientific meetings outside the University. The PI may keep the following for an indefinite period of time in a locked file, in a password protected computer server drive, or as an encrypted electronic file.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive at all of your scheduled appointments and that you report unexpected (mild or severe) side effects to the study team.

Some assessments throughout this protocol may be performed remotely using Zoom for Health at U of M.

4.2 How much of my time will be needed to take part in this study?

Most of the testing for this study will take place at the Functional Neuroimaging, Cognitive and Mobility Laboratory located at Domino's Farms, Suite B1000 in Ann Arbor. PET and MRI imaging will take place at the University of Michigan Health System Hospital (University Hospital).

The clinical part of the study at the Domino's Farms laboratory will require 6-8 hours of testing. If all the study procedures cannot be completed in one visit, you may be asked to return to complete the procedures or, if possible, to conduct them by phone.

The brain imaging part of this study at the University Hospital will be performed over 1 or 2 or more days, depending on scheduling availability and to account for unforeseen circumstances. The dopamine PET scan will take approximately 1 hour. The MRI scan will take approximately 75 minutes.

The fall diary portion of this study will last for 6 months.

4.3 When will my participation in the study be over?

Study participation will end after all testing has been completed.

4.4 What will happen with my information and/or biospecimens used in this study?

With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks will be defined as:

Likely - occurring in more than 25% of people (more than 25 out of 100 persons);

Common – occurring in 10% - 25% of people (in 10 to 25 out of 100 persons);

Infrequent - occurring in 1 - 10% of people (1 to 10 out of 100 people);

Rare - occurring in less than 1% of people (fewer than 1 out of 100 persons);

Very Rare - occurring in less than 0.1% of people (fewer than 1 in 1,000 persons).

The known or expected risks will be described in normal script.

The actions that the researchers take to minimize these risks will be described in italic script, as demonstrated in this paragraph.

General risks:

- There is a **very rare** risk of breach of confidentiality, which may affect privacy, self-esteem, social standing, employability, and insurability.

Section 9.1 will provide more detailed information on how we protect your privacy. In general, study records will be kept in databases maintained by the investigators. These databases are kept separate from medical records, are protected by passwords, and can only be accessed by personnel involved in the study. If you withdraw from the study at any time, a record of the withdrawal and the reasons given for withdrawing may be kept as part of the study record. The original video recorded on the video camera will be transferred off the camera to a secure server, which can only be accessed by personnel involved in the study. The original copy on the recording device will be deleted. Your face and identifying features will not be included in the video recording, or will be obscured ('pixilated') prior to use in the presentation.

- There is a **rare** risk that you may experience some minor anxiety ('test anxiety'), become worried, or have an anxiety reaction in response to any of these tests and procedures. For example, you may become worried about your health, or you may experience a sudden fear of the confined space while in the scanner.

Trained research staff will conduct all tests and procedures. The staff will be prepared to respond to your anxiety, concerns, and behavioral changes by temporarily suspending testing, breaking up testing sessions into several brief visits if needed, and/or answering your questions. During the PET and MRI scans you will be able to talk to technologists throughout the scan and indicate right away if you wish to stop the study and leave the scanner. At the option of your personal physician, (s)he may prescribe sedation with lorazepam (Ativan) or diazepam (Valium) to be taken before the scan in accordance with the prescription directions.

- In most patients, temporary withdrawal of dopaminergic medication can be accomplished safely on an outpatient basis and may result in inconvenient reduction in functional abilities, but not result in inability to conduct essential activity of daily living. There is an **infrequent** chance that you may develop "freezing" symptoms when you do not take your dopaminergic medication, which is caused by stiffening of your muscles making movements more difficult. You may require additional assistance from your caretaker during this time.

Any risk of adverse effects will be minimized by careful supervision during test procedures that are being conducted when you are off of your dopaminergic medications. You will be instructed to resume taking your dopaminergic medications after the completion of the testing. If the withdrawal of medication is intolerable, you may resume taking medication and withdraw from this study at any time.

- During the course of the study you will receive an injection for the PET tracer. There is an **infrequent** risk of bruising, bleeding, infection, or soreness at the injection site. There is a **very rare** risk for infection. There is a **rare** risk that you may feel dizzy, lightheaded, or faint after an injection.

Injections will be performed by a certified and experienced research technician or other health care professional who is also trained in blood borne pathogens control. Aseptic technique will be used in accordance with University of Michigan guidelines. You can lie down if you feel dizzy, lightheaded or faint after an injection.

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- None of the test results, brain images, and procedures in this study will be reviewed or interpreted for making a medical diagnosis. For example, there is the potential that the MRI scan may reveal an abnormality that is already in your body, such as a cyst or tumor. Any result or abnormality that would be indicative of current or future disease will most likely not be discovered. Many such abnormalities are not clinically significant, but you may need or want to investigate them further. Such a finding might require additional studies, and maybe even treatment, which would not be paid for by the investigators, the sponsor, or the University of Michigan. The research results of the brain images and genetic testing will NOT be communicated back to you.

You should consult your personal doctor if you have any health concerns.

Clinical tests:

- There is an **infrequent** risk of physical fatigue during the clinical examination.

Trained research staff will conduct all the tests and administer all the questionnaires. The staff will be prepared to respond to your concerns by temporarily suspending testing and/or breaking up testing sessions into several brief visits if needed.

Motor testing:

- Many of the tests are comparable to normal standing and walking conditions that you may experience in everyday-life. Nonetheless, there is an **infrequent** risk of falling or near falling during these tests which may result in fall-related injuries.

Trained research staff will remain in close proximity to you at all times, and observe ('spot') you to prevent you from falling.

- There is a **very rare** risk that the sensors to measure overall movement and balance may become detached and that you may trip. You may also trip on the pressure sensitive mat.

We will regularly check the sensors for appropriate attachment and you will be closely monitored.

Eye movements will be measured with video eye goggles (videonystagmography or VNG) while you are making small eye movements. There is **rare** risk that this may cause some eye strain or discomfort. There is a **very rare** risk that you may experience some minor eye strain when doing the visual tracking tests.

Rest breaks will be provided if needed. Any minor eye strain will disappear shortly after the test.

Vestibular testing:

There is an **infrequent** risk that you may experience dizziness, nausea, headache, feeling off balance, feeling unsteady on feet, blurry vision or having a warm or cold feeling in the ear, and there is a **rare** risk of vomiting.

- *Rest breaks will be provided if needed. Any dizziness, nausea, headache, feeling off balance, feeling unsteady on feet, blurry vision or having a warm or cold feeling in the ear will disappear shortly after the test.*

There is an **infrequent** risk that during the vestibular testing, a piece of ear wax may become loose and may plug up the ear that could result in hearing and balance changes.

- *This typically resolves within days but when persistent may require ear cleansing by your physician.*

Subjects with a history of Meniere disease or recent onset of acute vestibular dysfunction should not participate in this study.

Cognitive, visual, and neurobehavioral tests:

There is an **infrequent** risk of boredom, frustration, and/or mental and physical fatigue during the neuropsychological and neurobehavioral testing.

- *Trained research staff will conduct all the tests and administer all the questionnaires. The staff will be prepared to respond to your concerns by temporarily suspending testing and/or breaking up testing sessions into several brief visits if needed.*

Fall diary study:

- There is a **very rare** risk that confidentiality will be breached when the diary, fall-event information sheet, or the activity questionnaire are returned to us by mail.

You will be asked not to write your name on neither the envelope nor on any of these test materials. We will write a code on the test materials that will allow us to connect these test materials with your name. This code is securely monitored and behind lock and key, only accessible by the investigators of this study (see also 9.1).

MRI scan:

- There is an **infrequent** risk of discomfort or anxiety from being in the confined space of the MRI scanner.

We will provide pads and blankets to make you as comfortable as possible. You will be able to talk to a technician throughout the study, and you will be able let him/her know right away if you want to stop the study and get out of the scanner. At your request, you may be provided with a mild sedative, however, you must have made prior arrangements to be driven home by an accompanying adult.

- The MRI scanner makes loud, vibrating noises.

You will wear foam earplugs to reduce the loud noises made by the scanner and prevent any hearing damage.

- Some studies, like this one, have the potential to cause "peripheral nerve stimulation" (PNS). PNS is a light touching sensation on the skin surface, lasting only for a few seconds. It may cause mild discomfort, but is not harmful to you.

The MRI machine is operated within FDA guidelines so the potential for inducing PNS is low.

- Sometimes, subjects report a temporary, slight dizziness, light-headedness or nausea during or immediately after the scanning session.

If you feel dizzy or light-headed, we will have you get up slowly from the scanner.

- Because the strong electromagnetic fields can move metal objects and cause heating, there is a risk that loose objects (jewelry, keys) outside your body could be accelerated by the magnetic field and strike you, causing you injury. There is also a risk that the magnetic fields could disturb a metal fragment in your body, interfere with an implanted device, such as a pacemaker or neurostimulator, or cause metal (including foil-backed medication patches) on or in your body to heat up, causing you harm.

We keep the environment around the MRI scanner completely free of loose metal objects that could be moved by the magnetic field, and we will make sure that you have no metal on your body that could be affected by the MRI scanner. We will also ask you questions and have you complete an MRI screening form to make sure that you have no metal inside your body that would cause you harm during the MRI scan. The radiologist may order an X-ray to make sure there are no metallic fragments in your eyes.

Subjects with evidence of stroke or mass lesion on MRI should not participate in this study.

PET scan:

- There is a **very rare** risk that you could experience an allergic reaction to the PET tracer. This could involve itching, skin rash or shortness of breath shortly after injection. However, because of the very small tracer amounts used in PET imaging, the risk is very rare.

The use of [^{11}C]PE21 is considered to be generally safe and effective as approved by the University of Michigan Radioactive Drug Research Committee in accordance with Food and Drug Administration regulations (21 CFR 361.1). Adverse reactions to [^{11}C]PE21 PET radiotracer doses used in this study have not been reported. Certified

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staff will be in attendance at all times during the study. A physician will be available and an emergency cart is located in the PET Facility for treatment of any adverse reactions that may occur.

- During the course of this study, you will be exposed to radiation from the PET scan and the [^{11}C]PE21 PET radiotracer and DEXA scan. The risks associated with the amount of radiation exposure participants receive in this study are considered very rare and comparable to every day radiation exposure risks. **Please inform the investigators if you have had any major radiation exposure in the past, particularly in the past year, such as medical treatment with X-rays or radioactivity, or diagnostic X-rays, CT-scans or nuclear medicine scans.**

The biological effect of radiation in humans is measured in terms of Sieverts (Sv) or mSv (1/1000 Sv), which is a unit of uniform whole body exposure. All subjects will undergo a [^{11}C]PE2I scan. The exposure for a single [^{11}C] PE2I PET scan is 3.6 mSv. Each scan will also require a head CT scan which adds 0.17 mSv per scan. The DEXA scan will have minimal radiation exposure. Thus you will be exposed to a total of about 3.8 mSv for the PET-CT scan. Your life-time radiation risk includes the background radiation you are exposed to naturally like everyone else living on this planet, which is on the average 3 mSv per year. The exposure resulting from this PET scan in a single year is about 1.3 times higher than the natural background exposure. You will be instructed to use the bathroom and urinate as soon as possible after the PET scan in order to minimize bladder exposure. In case of a technical failure of the scan, you may be asked to undergo a repeat [^{11}C]PE2I PET scan and/or DEXA scan. Due to the possible repeat scans, your total exposure may be 7.6 mSV or less. The effects on the body of this radiation exposure will be added to your overall lifetime radiation risk. The US Federal Government requires that the annual amount of radiation exposure of radiation workers does not exceed 50 mSv per year; the radiation you will be exposed to in this study is a maximum of about 15% of this amount.

Your lifetime radiation risk also includes any radiation you may have received in the past for diagnosis or treatment, and any such radiation you may be exposed to in the future.

Please inform the investigators if you have had any major radiation exposure in the past, particularly in the past year, such as medical treatment with X-rays or radioactivity, or diagnostic X-rays, CT scans or nuclear medicine scans.

- No PET scan will be performed on pregnant, nursing, or potentially pregnant women.

A urine pregnancy test will be performed on all women of childbearing potential within 48 hours prior to the PET scanning session.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

Participation in this study may provide important new insights into Parkinson disease.

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5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

You do not have to participate in this study. You may drop out of the study at any time without penalty.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

There is no harm in leaving the study before it is finished. However, if you decide to leave the study during some of the procedures we may ask you to stay until it is deemed safe to leave.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems

- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

There is the potential that the research evaluations may have caused you anxiety or worries about your health. You may need or want to investigate these health concerns further for an appropriate diagnosis. However, any procedures or tests, including the MRI and PET scan, should be obtained separately if your doctor believes that you require those tests for your diagnosis. These additional studies and appropriate treatment, if necessary, will not be paid for by this study.

8.2 Will I be paid or given anything for taking part in this study?

Visit #	Activities			$30 Travel per day	Total Compensation
1. Screening / Baseline (over 2-3 days)	PET Scan	MRI Scan	History, physical exam, motor tests, vestibular tests, surveys		
Compensation	$100	$100	$200	$60-90	$460-490
2. Optional Follow-Up #1			Physical exam, motor tests, vestibular tests, surveys		
Compensation			$25		$25
3. Optional Follow-Up #2			Physical exam, motor tests, vestibular tests, surveys		
Compensation			$25		$25

Compensation for your time and effort after full study completion may total a maximum of $540

Overnight accommodations may be provided depending on personal circumstances or if you live far away. We will discuss with you the need for these accommodations as the research appointment(s) are being arranged. If eligible, overnight lodging can be arranged through the UMHS Patient and Visitor Accommodations Program either by a study team member or by you. However, you may decide to make alternative arrangements. In that case, please discuss with the study team first if you are eligible for reimbursement prior to making any reservations. We can only reimburse for expenses that have been approved in advance by the study team. You will need to provide receipts to the study team before expenses can be reimbursed. We will reimburse to a maximum of $280 for lodging and meals. You will receive a voucher for valet parking at the University Hospital. Parking at Domino's Farms is free.

You will be paid after your last study visit or, in case you decide to withdraw from the study, you will be paid for the parts that you have completed. You will be paid by check, which will be sent to your home address. Alternatively, you may request a payment coupon for cash payment at the University Hospital. We do not keep cash for immediate payment.

If you receive any payments for taking part in this study through the University of Michigan, the University of Michigan finance department will need your name and address for tax reporting purposes. In a calendar year if: 1) your payments total greater than $400 for this study or 2) if you receive payments of greater than $400 for being in more than one study, the University of Michigan finance department will also require your Social Security Number for tax reporting purposes. If you do not wish to provide your Social Security Number, you may continue to participate in research studies, but you will not be able to receive payment for the remainder of the calendar year.

8.3 Who could profit or financially benefit from the study results?

Researchers conducting the study, the University of Michigan, and other researchers that obtain your de-identified clinical data will not profit directly from the study results.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?

Your research records will be stored in a secure location to which only the investigators have access. All research records will be stored under code numbers, without attached names or other identifying information. The "key" linking these records to subject names will be stored in a separate, locked (electronic) file. The storage locations for the MRI and PET brain scans will be in protected computer files that are accessible only to investigators within the University who are participating in the research project. If the radiologist orders any X-rays for MRI screening purposes or a urine pregnancy test is ordered, the order requisition and test results may become part of your regular medical record.

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

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Demographic information
- Personal information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly

  - Learn more about side effects
  - Analyze the results of the study

- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan and Ann Arbor VA accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 Will I be contacted for other studies?

No, unless you indicate by initialing below that you may be contacted by researchers at the University of Michigan for studies for which you may be eligible. If you agree to be contacted for other studies, we will keep your name and contact information in a separate password-protected database.

_____(initials) I agree to be contacted about other research studies for which I may qualify. If I cancel my permission for this study, I will not be contacted for other studies.

9.4 What will happen with my research data?

The observational research data and brain images collected in this study (collectively referred to as "research data") may be shared with University of Michigan investigators, investigators from outside of the University of Michigan, or may be submitted to data repositories. When we share this research data we will completely de-identify it. This means that other investigators will not know your name or anything else that could let others know who you are. We will only use a code (for example SUBJECT01, SUBJECT02, etc.). This code will not be connected to your name or any other identifiable data. Researchers from all over the world can apply to these data-repositories and take information from the repository for use in their research. Their studies may be similar to this one, or may be completely different. The accompanying information may be used for studying many disorders, not just Parkinson disease. The de-identified research data in the data repositories and/or research data that are shared with other investigators may be maintained indefinitely. If you request to have your research data removed or not used, a reasonable effort will be made to do so; however, it might not be entirely possible because of distribution and coding of samples and data.

_____(initials) I agree that my de-identified research data may be submitted to data-repositories and/or may be shared with other researchers from inside or outside of the University of Michigan.

_____(initials) I agree that my de-identified research data may be shared with University of Michigan investigators.

_____(initials) I understand that if I withdraw my permission, a reasonable effort will be made by the investigators to remove the research data or prevent it from being used; however, this may not always be possible.

_____(initials) I do not agree that my de-identified research data may be submitted to data repositories and/or shared with other researchers from inside or outside of the University of Michigan.

It may be that you have participated in previous studies or are currently participating in one of the studies by the investigators. The research data of those studies may be combined with the research data of the current study. This will allow for a more complete analysis of Parkinson disease symptoms and also allows the investigators to more comprehensively study the progression of Parkinson disease symptoms. This research data may be maintained indefinitely.

_____(initials) I understand that any existing research data from previous or current research studies that I participated in may be combined and used in the current research study.

9.5 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission, or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.6 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Fay Pongmala, PhD
Mailing Address: UM Functional Neuroimaging, Cognitive, and Mobility Laboratory
24 Frank Lloyd Wright Dr., Suite B1000, Box #362, Ann Arbor MI 48105
Telephone: 734-998-8400

Study Coordinator: Jaimie Barr
Mailing Address: UM Functional Neuroimaging, Cognitive, and Mobility Laboratory
24 Frank Lloyd Wright Dr., Suite B1000, Box #362, Ann Arbor MI 48105
Telephone: 734-998-6894

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This signed and dated informed consent document, "Consent to be Part of a Research Study"). (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent Subtitle: _____
Consent Version: _____