PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

Welcome from Michael J. Fox

Dear Friend,

I wanted to personally welcome you to the Parkinson's Progression Markers Initiative (PPMI). Whether you're still weighing the possibility of joining, or you've already enrolled, you have my deepest thanks for being part of our mission to speed breakthrough treatments for Parkinson's disease.

I'm grateful you're here because, if there's one thing I know for sure, it's that better treatments aren't going to fall from the sky. Real challenges stand in the way of the results we need, and it's up to all of us to get involved and meet those challenges however we can. By participating in PPMI, you can do just that.

Our Foundation has been funding various biomarker projects for years. Now the time has come for a concerted, unified effort that will optimize our chances for results. With your help, we're ready to roll up our sleeves and get it done. Everything we've learned up to now has put us in position to work with the hundreds of partners — study volunteers, scientists, clinicians, funders — who are coming together to make PPMI a reality.

At our Foundation, we don't like to pat ourselves on the back. But I hope you'll give yourself one for raising your hand to be part of this effort. The thoughtful engagement of people like you is the only thing that can help meet a major need for participants in clinical research. Across all diseases, 85 percent of trials finish late because of difficulty with enrollment. That is being felt by all of us in the form of slower progress toward cures.
Today, you are part of the solution.

I have experienced profound benefits — some of the richest of my life — from taking action to meet challenges I never even saw coming. Parkinson's was a choice that was made for me, but once I accepted that, I found a freedom to do incredible things that I would never have known about under other circumstances. It's amazing; it's a gift. And I believe we all have that freedom.

Thank you again for being part of something that could change everything for the five million Parkinson's patients worldwide.

All my best,

Michael J. Fox

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Study Overview

ABOUT PPMI

The Parkinson's Progression Markers Initiative (PPMI) is an observational research study to identify biomarkers of Parkinson's disease (PD) progression. A biomarker is a substance or characteristic in our bodies that is associated with the presence of disease, or that changes over time in a way that can be linked to the progression of disease. An observational study means that study participants will undergo numerous tests and assessments of bodily processes related to PD, but will not receive an experimental drug or treatment. This study will use a combination of imaging techniques, collection of blood, urine, and spinal fluid, and clinical tests.

The information gathered from these procedures is critical to the future development of new and better treatments for Parkinson's disease. PPMI is the first clinical study to assemble a population of sufficient size to collect this information, draw meaningful scientific conclusions over time, and try to develop better ways to measure the progression of PD.

The study will be conducted in the United States and Europe. It is expected to take about five years. It is being sponsored by The Michael J. Fox Foundation for Parkinson's Research and will be made possible through the efforts of agencies interested in PD drug development. The study team includes many clinicians and scientists who conduct research in Parkinson's disease. It will be led by principal investigator Ken Marek, MD, President and Senior Scientist of the Institute for Neurodegenerative Disease, New Haven, Connecticut.

PURPOSE OF THE RESEARCH

The goal of the PPMI study is to identify one or more biomarkers of Parkinson's disease. The discovery of a biomarker of Parkinson's disease is critical to the development of new and better treatments for PD, particularly treatments that could slow or stop the progression of the disease, something no currently available treatment can do.

WHO IS ELIGIBLE TO ENROLL?

PPMI requires the participation of 400 Parkinson's patients who are newly diagnosed and are not currently taking standard PD medications and 200 individuals who do not have PD. Participants must be at least 30 years of age. They will be enrolled at about 18 Parkinson's disease centers — 14 across the United States and 4 in Europe — over approximately two years.

WHAT IS THE VISIT SCHEDULE?

Interested participants will be provided with detailed information by the study team. Those who consent will be screened for eligibility. If enrolled, participants will undergo four patient visits in their first year, with visits twice a year thereafter.

HOW TO LEARN MORE

Contact Cathi A. Thomas, RN, MS, CNRN, (617) 638-7737 or neurocat@bu.edu or Raymond C. James, RN, BS, (617) 638-7745 or rcjames@bu.edu

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Frequently Asked Questions

AM I ELIGIBLE TO PARTICIPATE IN PPMI?
Your eligibility will be determined by staff at the study site during your screening visit. We are seeking 400 PD participants — recently diagnosed Parkinson's patients who are not currently taking standard medications for Parkinson's disease — and 200 control participants — adults who do not have PD who are at least 30 years old and who do not have a first-degree relative (parent, child or sibling) with PD. Interested volunteers should contact Cathi A. Thomas, RN, MS, CNRN, (617) 638-7737 or neurocat@bu.edu or Raymond C. James, RN, BS, (617) 638-7745 or rcjames@bu.edu.

HOW LONG WILL THE STUDY LAST?
PPMI will be conducted over the course of about five years. For individual participants, the duration will range from three to five years depending on their particular study entry date during an initial two-year enrollment period.

WHAT WILL HAPPEN AT THE FIRST VISIT?
The first, or screening, visit will be conducted by the study coordinator and investigator. The screening visit is expected to last three to four hours and includes two parts:

1. First there will be a comprehensive review of study details and consent form. The consent form is a document you will be asked to sign if you are interested in participating in the study. This review is an opportunity to ask questions and address any concerns about participating. You may want to take the consent form home to review it and come back for the screening activities once you decide to join PPMI
2. Once you provide consent, evaluations and assessments will be conducted to determine your eligibility to participate in PPMI. This includes a medical history, neurological exam, physical exam, assessment of your vital signs, blood collection and cognitive assessments, medication review and DaTSCAN™. Consult the PPMI Imaging Procedures and Blood Sampling Overview/FAQs for more information about these procedures.

HOW OFTEN WILL STUDY VISITS TAKE PLACE?
After the first (screening) visit, you will visit the site upon enrolling and again at 3, 6, 9 and 12 months. Visits will then occur every 6 months until the study is over.

HOW LONG WILL EACH VISIT TAKE?
The study has been designed with a schedule of shorter and longer visits. Shorter visits are expected to take 1–3 hours and will include assessment of vital signs, medication review, motor testing and blood collection. Longer visits include a more comprehensive set of assessments and sampling, including motor, neuropsychiatric and cognitive assessments; DaTSCAN™ and MRI imaging; and blood, spinal fluid, urine and DNA sampling. These visits are expected to take 6–8 hours, and can be spread over 2 days if more convenient. Please consult the Schedule of Study Activities for Year 1 to learn more about the procedures required at each visit.

THE NEAREST PPMI SITE IS FAR FROM WHERE I LIVE. CAN I BE PART OF THE STUDY BUT DO MY VISITS AT A MEDICAL FACILITY CLOSER TO MY HOME?
Unfortunately, no. Every PPMI site has been carefully selected for its ability to adhere to strict processes and procedures. This is because sample acquisition, handling and storage must be stan-dardized so that results from all sites can be compared — critical for maximizing what researchers are able to learn from this and other studies.

WILL I BE PAID FOR MY TIME AND TRAVEL?
Participants will be compensated upon completion of each visit — $50/€38 for each short visit and $200/€150 for each long visit. Additionally, all travel expenses will be reimbursed.

CAN I CHOOSE TO DO ONLY SOME OF THE STUDY ACTIVITIES?
As a PPMI participant, you will be expected to complete all study activities and assessments. Park-inson's disease involves multiple systems and processes in the body, and researchers have designed the study for the greatest chances of success.

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WILL MY PERSONAL INFORMATION AND MEDICAL DATA BE KEPT CONFIDENTIAL?
Your privacy is very important. All data collected in PPMI will remain anonymous. Significant measures have been taken in designing the study to ensure that your identity remains completely private. Additional information on privacy policies and procedures can be found in the Informed Consent Form.

WHAT WILL HAPPEN TO THE BIOLOGICAL SAMPLES YOU COLLECT?
The samples collected in PPMI will be "de-identified" (stripped of your personal information to ensure your privacy) and sent to a central storage facility. De-identified samples will be analyzed for study-relevant characteristics using state-of-the-art lab procedures. The data from this analysis will be entered in a database maintained by the PPMI bioinformatics core at the Laboratory of NeuroImaging (LONI) at the University of California, Los Angeles. Samples will be banked in a central repository. The data, and the samples themselves, will be available to qualified Parkinson's researchers on request for use in other studies.

CAN I PARTICIPATE IN OTHER TRIALS WHILE I AM ENROLLED IN PPMI?
Yes, but we ask that you wait one year. After you have been enrolled in the study for a year, you may enroll in any other study you wish at the same time as you are participating in PPMI.

IF I ENROLL, DO I HAVE TO STOP SEEING MY CURRENT PHYSICIAN?
No, you are encouraged to maintain your relationship with your doctor. When you come for study visits as a PPMI participant you will be evaluated by an experienced clinical research team. All other decisions about your medical care outside of the study are up to you. PD patients who enroll in PPMI may elect to have the PPMI study site share test results and clinically relevant findings with their personal physician.

WHAT IF MY DOCTOR SUGGESTS THAT I TAKE MEDICATION FOR MY PARKINSON'S AFTER I ENROLL?
Your health is of the utmost importance. While our hope is that participants will not begin taking Parkinson's disease medications for the first 6 to 12 months, physicians and patients should make the decision to begin a new medication regimen independent of participation in PPMI.

WHAT IF A PPMI TEST REVEALS THAT I HAVE AN UNEXPECTED ILLNESS OR MEDICAL PROBLEM?
The PPMI clinical team will report any unexpected results of this nature to you and, if given your permission, share this information with your physician.

WHERE IS PPMI BEING CONDUCTED?
PPMI is occurring at 18 sites across the United States and in Europe in the following locations:

- Atlanta, GA
- Baltimore, MD
- Birmingham, AL
- Boston, MA
- Chicago, IL
- Houston, TX
- Innsbruck, Austria
- Kassel and Marburg,Germay
- Naples, Italy
- New Haven, CT
- Philadelphia, PA
- Portland, OR
- Rochester, NY
- Sun City, AZ
- Sunnyvale, CA
- Tampa, FL
- Tübingen,Germany
- Seattle, WA

WHO IS SPONSORING THIS RESEARCH?
PPMI is sponsored by The Michael J. Fox Foundation for Parkinson's Research.

WHERE CAN I LEARN MORE ABOUT PPMI?
Visit http://www.michaeljfox.org/PPMI to learn more about the study. For more information about PPMI at UAB, contact Cathi A. Thomas, RN, MS, CNRN, (617) 638-7737 or neurocat@bu.edu or Raymond C. James, RN, BS, (617) 638-7745 or rcjames@bu.edu.

I DON'T QUALIFY FOR PPMI, BUT I STILL WANT TO HELP. WHAT CAN I DO?
Please help us spread the word to people who might be interested in participating. If you know someone recently diagnosed with PD, or someone who does not have PD and is not a first-degree relative (parent, child, sibling) of a PD patient, please refer them to http://www.michaeljfox.org/PPMI.

You should also contact your nearest study site as they very likely are conducting other trials for which you may be eligible.

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Lumbar Puncture Overview/FAQs

WHAT IS A LUMBAR PUNCTURE (LP)?
An LP is an outpatient procedure where a small needle is inserted between the vertebrae (bones) of the lower back at a level well below the spinal cord.

WHAT IS THE PURPOSE OF THE LP IN THIS STUDY?
The purpose of obtaining spinal fluid is to learn as much as possible about the proteins and other
neurochemical changes that may occur in individuals with neurological conditions, like Parkinson's disease. Spinal fluid is useful because it bathes the brain and spinal cord, making it the best source of information about neurochemical changes that may be occurring in the brain. Scientists pre-dict that spinal fluid is where they are most likely to find a biomarker of Parkinson's progression. Being able to measure changes in specific proteins or neurochemicals in spinal fluid may provide a way to measure progression of Parkinson's disease or monitor whether medications are slowing progression of the disease.

AS A CONTROL PARTICIPANT, WHY DO I NEED AN LP?
In addition to what we can learn from spinal fluid from PD patients, we can learn a lot from the spinal fluid of control participants who are about the same age, and the same gender, as PD patients in the study. By comparing these samples, researchers can determine which changes are unique to Parkinson's disease and which are associated with normal aging.

IS AN LP PAINFUL?
The only part of the LP that is likely to cause pain is the administration of the anesthetic, which typically stings or burns for a few seconds when injected. (In some centers, anesthetics are not typically used for an LP.) You will feel a pressure sensation when the needle is inserted, and there is usually some brief pain when the needle goes through the tissue surrounding the spinal cord. This pain should stop in a few seconds. Overall, discomfort is minimal to moderate.

WHAT ARE THE RISKS OF LP?
When performed by an experienced doctor, as in PPMI, LP is safe and involves minimal discomfort. LPs for PPMI will be performed using a special needle designed especially for this procedure. This needle causes less pain at the site where the needle goes in and brings less risk for headache after the LP. There is a small chance of developing a headache after the procedure. This usually gets better with rest and drinking plenty of fluids. Rarely, the headache may continue for more than 24 hours after the procedure and require additional treatment. There is no risk of paralysis.

WILL I GET RESULTS FROM THE SPINAL FLUID TESTING?
Spinal fluid collected during the LP will be tested using standard clinical tests. You will be notified by the principal investigator at your study site if there is any reason for concern from the results of these tests. Otherwise, you will not learn anything directly about the results of spinal fluid testing.

WILL THE RESEARCHERS ANALYZING MY SPINAL FLUID KNOW THAT IT IS MINE?
No. Like all samples in this trial, spinal fluid samples will be de-identified, which means that it will be stripped of any information that could link the sample to you as an individual.

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Imaging Procedures Overview/FAQs

WHAT IS MRI?
MRI is short for Magnetic Resonance Imaging. An MRI machine uses a magnetic field and radio waves to create detailed images of structures inside the body.

WHY IS A BRAIN MRI IMPORTANT FOR THIS STUDY?
An MRI enables us to take pictures of basic brain structures. For PPMI, this is important for both PD participants and control participants:

- In early Parkinson's disease (PD), MRI of the brain is usually normal so we would like to check there is no other reason for your symptoms. Using special analysis techniques researchers may also obtain useful information about PD and assess how MRI results in individuals with Parkinson's disease change over time.
- It is also important that researchers obtain similar imaging data from control participants so that we can learn which changes are unique to Parkinson's disease and which are associated with normal aging.

WILL I BE EXPOSED TO RADIATION DURING THE MRI?
No. There is no radiation exposure in an MRI.

WILL I GET CLAUSTROPHOBIA DURING THE MRI?
Brain MRIs are very common, and most individuals tolerate the procedure quite well. If you are concerned about claustrophobia, speak to your study doctor before the procedure. The study team will make their best effort to make the process as comfortable for you as possible.
What should I do to prepare for an MRI?

Little to no preparation is required before an MRI. When you arrive at the clinic you will be asked to remove all accessories such as jewelry, credit cards, and any metallic objects. This is because MRIs involve magnets, which may interact with objects in your possession and could affect the image quality.

WHAT IS DATSCAN™ IMAGING?
DaTSCAN™ is a specialized imaging technique that allows doctors to capture detailed pictures of the dopamine neurons in your brain. This technique involves the use of a radiopharmaceutical agent (a chemical compound containing an isotope, or radioactive element). The radiopharmaceutical agent is injected into a vein and taken up by the brain's dopamine cells. The cells can then be detected through SPECT (single photon emission computed tomography) scanning. In this way it is possible to determine whether there is a reduction in dopamine cells, which usually occurs in the presence of Parkinson's disease.

WHY IS DATSCAN™ IMPORTANT FOR THIS STUDY?
DaTSCAN™ allows researchers to take detailed pictures of activity in the brain and measure dopamine cells. This is important for two reasons in PPMI:

- For Parkinson's patients volunteering for the study, the DaTSCAN™ data will be crucial to understanding the neurologic changes associated with PD. It is also a required element to determine your eligibility for enrollment.
- For control participants volunteering for the study, the data ensure that brain function is normal, which is a required element to confirm your eligibility for enrollment. This scan also provides researchers with an age- and gender-matched image that can be compared to images of PD patients enrolled in the study.

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WHAT DOES DATSCAN™ OFFER THAT MRI DOES NOT?
A DaTSCAN™ provides a more detailed picture of the dopamine system of the brain and richer in-
formation about how the brain is functioning. This is critical because degeneration of the dopamine system is the pathological hallmark of Parkinson's disease.

WILL I BE EXPOSED TO RADIATION DURING THE DATSCAN™?
There is a small amount of radiation exposure from the chemical substance injected prior to SPECT scanning. The amount of radiation exposure is in the range between a chest X-ray and a chest and abdominal CT scan. This kind of radioactivity is also used routinely in other common procedures, such as imaging of the thyroid gland. The level of exposure from this study is well within the limits specified by the United States Food and Drug Administration (FDA) in its guide-lines for acceptable radiation exposure for research participants.

WHY HAVEN'T I HAD A DATSCAN™ BEFORE?
DaTSCAN™ is a new procedure in the United States and is currently in the FDA approval process.
While PPMI is one of the first trials to use DaTSCAN™ in the United States, DaTSCAN™ is widely used internationally. To date, more than 180,000 people worldwide have undergone DaTSCAN™,
and the procedure has posed no significant safety issues.

DaTSCAN™ has been in use for quite some time in Europe, but it remains relatively expensive and
is not broadly available.

WHAT IF THE DATSCAN™ SHOWS SOMETHING UNEXPECTED?
The information obtained in this procedure will be used primarily for the purposes of research. If a
medically significant abnormality is observed on your scan, study personnel will be in contact with
you. If given your permission, your study doctor will contact your primary physician to recommend that you receive additional medical attention.

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Blood Sampling Overview/FAQs

BLOOD COLLECTION FOR ANALYSIS
What is the purpose of collecting blood in this study?
Blood will be obtained from each participant at regular intervals over the course of their participation in PPMI. The blood will be analyzed to test for proteins or other chemicals that may differ in amount or change at different rates in PD participants and control participants. Blood will also be taken to identify genes that may be related to Parkinson's disease.

ARE THERE ANY SIDE EFFECTS FROM BLOOD SAMPLING?
You may experience bruising at the site where the blood was withdrawn, which is usually minor. In addition, you may feel lightheaded during or following the procedure. Drinking fluids and lying down for a few minutes usually reverses this sensation.

WILL I GET RESULTS FROM THE BLOOD SAMPLE COLLECTION?
No, you will not learn anything directly about your personal health from the blood testing. The purpose of obtaining blood samples in PPMI is to learn as much as possible about the proteins and other neurochemical changes that may occur in the blood of people with Parkinson's disease.

WILL I LEARN ABOUT MY GENETIC PROFILE?
No. Neither you nor the site staff, including your study doctor, will have access to the genetic testing information.

WILL THE RESEARCHERS ANALYZING MY BLOOD KNOW THAT IT IS MINE?
No. As with all samples in the trial, your personal information will be removed to "de-identify" the sample. Any analysis will not be associated with you as an individual. Any results from the testing, including genetic findings, will not be able to be linked back to you as an individual.

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Schedule of Study Activities for Year 1

Study Activity	Screening Visit *	Baseline Visit	3 Months	6 Months	9 Months	1 Year
Medical and Family History/Demographics	●					
Physical Exam	●					
Neurological Exam	●					●
Vital Signs	●	●	●	●	●	●
Clinical Lab Tests	●					●
Blood Sample	●	●	●	●	●	●
Smell Testing		●				
Questionnaires to measure your thinking, memory, moods and behaviors	●^	●		●^		●
Questions about your ability to perform daily activities and an exam to measure your movement	●	●	●	●	●	●
Urine Sample		●		●		●
MRI Scan		●				●U
DAT Scan	●					●^
Lumbar puncture (CSF collection)		●		●		●
Review of your health and medications	●	●	●	●	●	●
Approximate time commitment	**1.5 days**	**1–1.5 days**	**3–4 hours**	**1–1.5 days**	**3–4 hours**	**1–1.5 days**

* Screening visit will take place at least one month before the Baseline visit.

^ PD Participants only

U At select sites participating in MRI-DTI