On the Heels of Early Success, PPMI Expands to Include New Cohort

The search for a Parkinson’s disease (PD) biomarker is a complex one, so a large-scale effort like PPMI is critical to making potential breakthroughs. In 2010, PPMI was launched to be the kind of collaborative solution that could support the PD research community and accelerate this search. When the study began, many were skeptical that PPMI could overcome the challenges of building the infrastructure to enroll enough participants and orchestrate the logistics to carry out the multi-year investigation. Now, less than three years later, with $45 million invested thus far, it’s evident that PPMI is not only possible, but becoming a new model for research. None of our progress would be possible without the loyal and willing volunteers who keep coming back for study visits to add more data and samples to the initiative. As a result of the dedication of PPMI participants, the study is already reaching critical benchmarks. Recruitment of the original study has been successfully completed: 400 people with Parkinson’s and 200 age-matched controls are now actively participating in PPMI at 24 sites around the globe.

The study’s robust infrastructure has inspired intricate collaboration across nine PPMI “Study Cores” — groups behind the scenes that do everything from developing and managing the study data entry system, to receiving and processing samples and conducting quality control analyses. This infrastructure is responsible for taking the information gathered from participants at a site one day, and making it de-identified and available online to the research community at large, the next.

Study cores and researchers alike have begun to analyze PPMI data and publish preliminary findings. Scientists are taking advantage of the immense biorepository, and conducting research in their own labs across the globe: More than 40,000 data downloads have been made and shared by scientists in 30 different countries. (See “PPMI Publishes First Paper” on page 2 for more information.) Participants like you are making all of this possible.

Rather than rest on its laurels, the PPMI study leadership is examining ways to leverage the immense infrastructure of the study. Recently, they decided to continue to grow PPMI by launching a new arm, including a new group of participants focused on the same mission of identifying progression markers, but potentially enabling researchers to do so earlier in the disease process. As the first group of participants enrolled in the study, you have not only proved PPMI’s success, but are paving the way for new groups to join to make PPMI an even more valuable resource.

The PPMI “pre-motor” cohort will help scientists better understand what’s happening in the body prior to the onset of PD’s motor symptoms. This new arm of PPMI focuses on three of the most researched early symptoms of PD: people who suffer from a reduced sense of smell; those with rapid eye movement sleep behavior disorder (RBD); and individuals with a mutation in the LRRK2 gene (the single greatest genetic contributor to PD known to date). Conducting similar tests and collecting the same biospecimens in these individuals (as is currently done in PPMI) could lead scientists to detect the presence of Parkinson’s earlier, and to develop treatments for patients that more holistically address the disease.

About PPMI The Parkinson’s Progression Markers Initiative (PPMI) is a landmark, five-year international clinical study that aims to find reliable and consistent biomarkers of Parkinson’s disease (PD) progression. The study is testing today’s most promising biomarker candidates through neuroimaging, the collection of blood, urine, and spinal fluid, and clinical and behavioral tests. Valid measures could allow scientists to predict, objectively diagnose and monitor diseases as well as definitively determine which medications work and which will not. PPMI is sponsored by The Michael J. Fox Foundation for Parkinson’s Research and funded by a consortium of industry partners and individual donors. To learn more or volunteer to participate in the study, visit www.michaeljfox.org/PPMI or call (877) 525-PPMI.
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“If scientists can learn more about the biological processes taking place in people with any of these three conditions, they may be able to define biomarkers at an even earlier stage,” says Ken Marek, MD, principal investigator of PPMI and president and senior scientist at the Institute for Neurodegenerative Disorders in New Haven, Connecticut. “This type of information could be vital for Parkinson’s drug development, while leading to new targets for drugs to attack the disease before it starts.”

Collectively, across the pre-motor volunteers who will enroll this year and PD volunteers who have already enrolled in PPMI, the study will gain a unique and in-depth view into what happens before someone develops PD and at the earliest stages of the disease. The control volunteers already recruited will inadvertently become controls for this new group of pre-motor participants as well—doubling their value in the study.

As PPMI continues to expand, opportunities for additional new cohorts could inevitably follow. With the initial investment of time, money, and expertise already made, it is exciting to think about new populations that can be incorporated into the initiative to deepen our understanding and move the field forward. But we wouldn’t be where we are today without those of you who have so courageously volunteered to prove that this is possible. Thank you for being a part of PPMI and especially for being the founding participants of the study. It truly is people like you who are making all of this progress possible.

The pre-motor cohort of PPMI is recruiting. Specifically, help PPMI identify people without Parkinson’s who are 60 years or older who are willing to take an online smell survey. Share this new call for participants with family and friends by visiting www.michaeljfox.org/ppmi/smell.

PPMI Publishes First Paper

In early 2013, an important milestone was reached: researchers from the University of Pennsylvania published the first paper using PPMI data. The published findings, in the journal Neurology, showed that Parkinson’s itself does not confer a higher risk for Impulse Control Disorders (ICD), supporting other research that suggests the high prevalence of ICDs in people with PD is related to Parkinson’s medications, and not the disease itself. This paper relied on data collected from PD participants, all of whom enrolled in PPMI before they began taking medication. Being able to analyze data from such a large group of patients prior to initiating medication has enabled researchers to conclude that the prevalence of ICDs in unmedicated PD volunteers is not different than the prevalence in controls.

The Parkinson’s Minute Highlights LRRK2 Genetics

To learn more about how LRRK2 genetics are having an impact on PD research in the here and now, watch the latest edition of The Parkinson’s Minute, which delves into the story of one person with Parkinson’s, Genia Brin: http://bit.ly/V5ypFz.

View the entire video series on YouTube: http://www.youtube.com/user/michaeljfox

PPMI Data Usage Stats

Researchers from all over the world are downloading and analyzing data collected in PPMI. Here are some of the most interesting facts:

- 45,372 individual data downloads
- These downloads have been made by 433 individuals
- Data has been downloaded by researchers in 30 countries
- Downloads by sector:
  - 87% University/Research
  - 9% Other/Unknown
  - 2% Biotech Companies
Rationale for Inclusion of the Pre-Motor Cohort

Hyposmia (a.k.a. Smell Deficit):
While most people with a reduced sense of smell will not develop Parkinson’s, the majority of PD patients do have reduced sense of smell.

Little is confirmed about what causes the early, pre-motor symptoms of Parkinson’s, such as hyposmia, this loss of smell, says Maurizio Facheris, MD, MSc, of the Michael J. Fox Foundation. But one prevalent theory in Parkinson’s research about disease progression that is gaining some traction has to do with the protein alpha-synuclein, whose clumping is found in all people with the disease.

This theory, based on the research of Heiko Braak, MD suggests that the disease may start not in the substantia nigra (the region of the brain where loss of nerve cells leads to the dopamine deficit experienced by people with PD) but in the gastrointestinal system and the olfactory bulb, the part of the brain that controls sense of smell. Researchers have hypothesized that the alpha-synuclein clumps found in all people with Parkinson’s may form in these parts of the body first, before migrating to other parts of the brain. “Should this turn out to be true, and if researchers can find the clumps and break them up before they reach the brain,” says Facheris, “it may become possible to treat Parkinson’s before major neurological damage occurs.”

PPMI is focusing its resources on the olfactory bulb to determine if down the road a reduced sense of smell could serve as a Parkinson’s biomarker. For this study, PPMI seeks people over the age of 60 who believe they may have a smell deficit, who do not have Parkinson’s, and who have no history of nasal trauma. PPMI will need 20,000 people who meet these criteria to take a simple smell survey online.

Please encourage family and friends to visit www.michaeljfox.org/PPMI/smell or call (877) 525-PPMI to learn more.

LRRK2 Genetic Mutation:
“By analogy, the role of genetic discovery in developing treatments for diseases like PD is rather like trying to fix a car when the engine refuses to start,” explains Matt Farrer, PhD, of the University of British Columbia, and an MJFF Scientific Advisory Board member. “The first step to getting it running is to have a rudimentary understanding of what the different components of the engine do — the battery, distributor, spark plugs, valves, pistons etc. — and how these components work together. While susceptibility to PD may vary according to individual —whether it’s the battery or spark plugs — the overall system perturbed, the engine, is likely to be similar in all patients. The ‘molecular machinery’ discovered through human genetics provides novel targets for new, more effective treatments.”

Most progress in genetic research related to PD has been made through large-scale studies of familial populations with similar genetics: By analyzing large pools of similar data, researchers can home in on shared characteristics that play a role in disease. Genetics cohorts are designed to bring research groups together early on — sharing resources, troubleshooting common problems and identifying best resources — to speed collective efforts into better understanding how genetic targets could have practical therapeutic relevance for patients.

PPMI is assembling its own genetics cohort, and looking specifically at mutations in the LRRK2 gene, the most common genetic contributor to PD discovered to date, to determine if the changes taking place in its ‘molecular machinery’ could provide a Parkinson’s biomarker.

People who are 60 or older who do not have PD and know they have a LRRK2 mutation are invited to learn more at www.michaeljfox.org/PPMI/genetics.

Individuals who are able to travel to the Boca Raton area and who are of Eastern European (Ashkenazi) Jewish descent are invited to receive genetic testing and counseling at the PPMI site in Boca Raton, FL.

REM Sleep Behavior Disorder (RBD):
Many people with Parkinson’s have trouble sleeping. In addition to a general difficulty falling and then staying asleep, some deal with restless leg syndrome (an uncontrollable urge to move the legs during sleep). Others experience intense nightmares.

One particular sleep disorder that is associated with PD called REM Sleep Behavior Disorder (RBD) may hold critical clues to what’s taking place in the course of the disease before the motor symptoms occur, explains Aleksander Videnovic, MD, of Northwestern University. “We know that up to 60 percent of people with PD experience RBD,” he says. And of those diagnosed with RBD, but who are not yet diagnosed with a movement disorder, as many as 50% will develop a neurodegenerative disorder one decade after the diagnosis of RBD was established.

“It is becoming increasingly clear that there is a definitive link between difficulty sleeping and movement disorders such as PD. If we can learn more about the biological processes that link these conditions, we could also potentially develop treatments to slow their progression, before the motor symptoms that are usually associated with the disease, occur.”

Videnovic cautions that many people with PD won’t ever go on to develop RBD, or other sleep conditions, and for those that do have them, there are certainly other potential causes. By and large, he says, patients who struggle with difficulty sleeping tend to under-report their conditions, while physicians also tend to under diagnose. So the best thing one can do is to visit one’s clinician and work to evaluate what might be going on.

Individuals with RBD who are at least 60 years of age, and who have not been diagnosed with PD, are being considered for PPMI at select sites.
Recruitment has officially begun for the three new cohorts of PPMI. This arm of the study could help researchers detect, and ultimately treat, PD in patients before the onset of motor symptoms. There is no better advocate for PPMI than those of you who are already participating in the study. PPMI participants can play a critical role in helping us to spread the word about this new group being added.

Who is eligible to enroll in the new arm of PPMI?
People over 60 who do not have Parkinson’s are needed for this study, which is being conducted at 22 centers across the United States and in Europe. Participants in the RBD and LRRK2 cohorts will largely be enrolled via sleep centers and clinical research centers, respectively. This means that PPMI needs the most help recruiting people who may qualify for the part of this new effort that is studying the sense of smell.

How can I help spread the word?
Ask your friends and family who are over 60 and have not been diagnosed with PD to visit www.michaeljfox.org/PPMI/smell for more information about this arm of the study and encourage them to take our smell survey at www.michaeljfox.org/takethesmellsurvey.

PPMI will need 10,000 people total to take the smell survey. Ask your friends and family who are over 60 and do not have PD to follow their noses to Parkinson’s research by learning more at www.michaeljfox.org/PPMI/smell or by calling (877) 525-PPMI.

Want to stay informed of the latest scientific developments in PPMI? Visit www.PPMI-info.org. This is the portal for the scientific community to learn more about PPMI and to access the data and samples coming out of the study.