After Meeting Initial Milestones, PPMI Takes Next Steps toward a Cure

The process of achieving a medical breakthrough is a series of incremental goals where meeting one milestone tees up a next challenge until the end goal is met. With every completed task, the field is one step closer to our larger goal: better therapies and eventually a cure for Parkinson’s disease (PD).

Another baseline assessment that is underway is based on a pilot study looking at cerebrospinal fluid samples from 100 PPMI participants for proteins associated with PD. This first analysis indicates that these proteins are reduced in PD volunteers compared to controls. Information on analysis of the same protein levels among the full group of PPMI volunteers will be featured in the upcoming baseline paper. Read more about early PPMI findings on page 3.

Identifying New Research Possibilities

PPMI initial research is providing insight into new avenues to explore. One area of interest is the overlap in the pathology of Parkinson’s and Alzheimer’s diseases. Analysis of a small number of samples suggests that the lower protein levels in spinal fluid of PD patients were similar to the levels seen in Alzheimer’s patients in another study. While this is only one similar biological feature among many differences between the two diseases, it does open the possibility of further research to examine what these protein levels mean and promotes collaboration with Alzheimer’s researchers to leverage our work and findings toward discovery. We’re extending our analysis to more samples to confirm these findings.

Progressing and Expanding Pre-Motor PPMI

Our last newsletter featured the launch of the PPMI pre-motor cohort, which aims to help scientists better understand what’s happening in the body prior to the onset of PD motor symptoms. Recruitment is now in full-swing for this new arm, with a heavy focus on identifying people age 60 and older who do not have Parkinson’s to take our smell survey online.

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VIDEO: PPMI in the News!

Philadelphia’s ABC6 Action News interviewed Dr. Matthew Stern, an investigator for the Parkinson’s Progression Markers Initiative (PPMI), about the link between loss of sense of smell and Parkinson’s disease.

Watch the ABC6 video on the MJFF FoxFeed blog: bit.ly/17REIp2.

Be a PPMI Ambassador

Recruitment is under way for the pre-motor arm of PPMI. 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 spreading the word about this new effort.

Who is eligible to enroll?
People over 60 who do not have Parkinson’s are needed for this study, which is being conducted at 24 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 this new effort 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 or call (877) 525-PPMI for more information about this arm of the study and encourage them to take our smell survey.

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:

- 85,765 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

Next Steps for PPMI

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Since about 70 percent of people who have smell loss don’t know it, we’re casting a wide net to ask people over 60 without PD to take a smell test to then determine who might be able to participate. We hope you will share the smell survey with family and friends by directing them to www.michaeljfox.org/takethesmellsurvey.

“In previous studies, individuals without a diagnosis of PD, with and without smell loss underwent a specialized scan to look at dopamine levels in the brain. The people who developed PD in the few years after the scan were among those with the lowest smell test scores and low dopamine levels. Thus, smell loss may be an early indicator of PD risk,” said Dr. David Russell, associate director for clinical research at the Institute for Neurodegenerative Disorders in New Haven, Connecticut – one of the 24 PPMI clinical sites around the world.

As of September, more than 5,000 people over 60 without PD have completed the online smell survey. The first pre-motor PPMI volunteer enrolled in July, and we’re working to see that number climb. Our goal is to complete recruitment next year.

We are proud to already be passing these important PPMI milestones and excited for what the future holds. Of course, we realize that we couldn’t have gotten here without you—our partners in research. Your continued study visits are enabling us to focus on what might be possible as we take these next steps. Thank you for continuing to remain committed to PPMI.
Scientific Results Coming Out of PPMI

Researchers share their findings with peers in different ways, but the major vehicles are published articles in “peer-reviewed” journals (professional publications where experts who are not involved in the research review and select the best research to publish) and presentations at professional conferences. Below we review recent articles and presentations using PPMI data and specimens to give you a sense of what the field is learning from PPMI.

Baseline Data and Engagement Report

The PPMI Steering Committee submitted an abstract (a research overview) to the Movement Disorders Society International Congress meeting in Sydney, Australia in June 2013 on the initial analysis of PPMI data collected at baseline (the first study visit).

Baseline Results:

- Researchers verified that PPMI Parkinson’s participants demonstrate motor symptoms and severity of disease consistent with PD enrolled in other clinical trials. It is important that results among this population are comparable to PD patients in past studies to ensure accurate analysis of the disease and the potential to develop treatments to help a large number of people based on PPMI outcomes.
- Cognitive and neurobehavioral scores of early-stage PD participants differ from scores of control volunteers.
- SWEDD participants may demonstrate increased mood, anxiety and autonomic scores compared to PD and control participants, according to the baseline data.
- A pilot study looking at proteins associated with PD in cerebrospinal fluid indicates that these proteins are reduced in PD volunteers compared to controls. Read more about those findings in the next column.

PPMI aims to collect longitudinal data (several snapshots over time), but data collected from a single or few volunteers visits so far is already being used widely by the research community. To date, researchers from almost 30 countries have downloaded PPMI data more than 84,000 times. And the study has received 26 requests for use of the collected biosamples.

Protein Levels Compared with Clinical Features

An article by PPMI investigators was published online in JAMA Neurology on August 26. The paper is titled “Association of Cerebrospinal Fluid β-Amyloid 1-42, T-tau, P-tau181, and α-Synuclein Levels With Clinical Features of Drug-Naive Patients With Early Parkinson Disease.”

Among the first 102 PPMI volunteers (63 PD patients and 39 controls), researchers observed that levels of some proteins associated with PD (beta amyloid, tau proteins and alpha-synuclein) in cerebrospinal fluid (CSF) were slightly, but significantly, lower in PD patients than in healthy controls.

The scientists’ next step was to compare these outcomes to clinical features among these PPMI volunteers. Researchers reviewed demographic characteristics; motor, neuropsychiatric, and cognitive assessments; and DaTscan results. Researchers found that lower levels of two of the proteins (beta-amyloid and phosphorylated tau) were associated with PD volunteers who experience postural instability and gait disturbances. These proteins were interestingly not associated with the tremor-dominant PD.

Differences in these protein levels among PD patients and controls indicate that they may be potential biomarkers to diagnose and measure Parkinson’s. Only a subset of volunteer samples were looked at, so this analysis needs to be reproduced using samples from all volunteers to further validate these findings. It will also be important to continue to look at these proteins throughout the study to see if differences in these protein levels change over the course of the disease.

DaTscan Results at Baseline and One-Year

At the International Parkinson and Movement Disorder meeting, PPMI investigators presented a poster on results of DaTscan imaging from a selection of PPMI volunteers at baseline and one-year after baseline.

Researchers analyzed images of various parts of the brain of 117 PD patients enrolled in PPMI for this study at two different points in time. The comparison of individuals’ scans at baseline and one year later demonstrate that changes in the brain happen faster on one side versus the other (right versus left varied by individual) Dopamine levels in PD patients studied dropped an average of 13.3 percent in the year between scans. The average loss in normal aging is 0.6 percent, showing this PD population experienced dopamine degeneration at a rate 20 times faster than the normal population. That said, there was significant variability in dopamine level degeneration amongst individuals with PD.

The observation that changes happen faster on one side of the brain reflects the fact that PD onset usually begins on one side of the body. The variability in the participants’ rate of dopamine degeneration reflects the variability in individuals’ PD progression.

The ability to see differences in an individual’s time-lapsed scans confirms that researchers can track changes in PD using DaTscan, which, in the future, could serve as a useful marker of PD progression. As with all other aspects of the PPMI study, only time will tell—continuing to track these changes over time and comparing annual DaTscans will be important.
Why Do We Care About Smell?

Dr. David Russell is associate director for clinical research at the Institute for Neurodegenerative Disorders in New Haven, Connecticut, one of 24 PPMI sites worldwide. Dr. Russell answered some questions on smell loss as a biomarker and what researchers hope to accomplish in the new pre-motor PPMI study.

**Why are you focusing on smell loss?**

DR: Smell loss is a biomarker for PD. Biomarkers are biological features of disease, such as a chemical or molecular change, a brain scan finding or even a behavior. Biomarkers show us a pattern that results from an underlying problem. Identifying biomarkers can help us delve deeper to pinpoint that underlying problem. When we know the problem, we can develop solutions.

**If you know it is a biomarker, why do you need to do more research?**

DR: We need to validate and identify the parameters of smell loss as it relates to PD. When we have more data and more biomarkers, then we can go to academic research partners and ask them to identify the underlying problem. We can also approach the pharmaceutical industry and ask them to begin drug development to address that problem.

Smell loss may be a precursor to PD development. If we can correct the underlying problem before it progresses to the point of expressing PD symptoms, we should be able to prevent disease. The way I see it, that’s the greatest cure - not to treat the disease once you already have it, but to prevent it in the first place.

**Want to stay informed of the latest scientific developments in PPMI? Visit [www.PPMI-info.org](http://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.**

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**Fox Trial Finder**

Know someone who is interested in participating in PD clinical research but does not qualify for PPMI?

Fox Trial Finder is a user-friendly online tool that helps both patients and their loved ones get involved in the research nearby that needs them. By taking into account personal information and medical history, Fox Trial Finder generates a list of trial matches and allows volunteers to connect with trial teams anonymously before deciding to participate.

Visit [www.foxtrialfinder.org](http://www.foxtrialfinder.org) or email support@foxtrialfinder.org to learn more and get started.

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