# PROTOCOL

**Title:** Parkinson's Progression Markers Initiative Cognitive Activities (PPMI Cognitive Activities)

**Sponsor:** The Michael J. Fox Foundation for Parkinson's Research (MJFF)

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# PROTOCOL APPROVAL

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## The Parkinson's Progression Markers Initiative Cognitive Activities Study (PPMI Cognitive Activities)

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# 1. PURPOSE OF STUDY

This protocol is a web-based study being launched under the myPPMI platform as a sub-study for participants enrolled in an active PPMI protocol and registered in the myPPMI platform. PPMI is a broad program that is expanding the goals of the original PPMI study[1], and will include this PPMI Cognitive Activities protocol.

The Parkinson Progression Marker Initiative (PPMI) is a longitudinal, observational, multi-center natural history study to assess progression of clinical features, digital outcomes, and imaging, biologic and genetic markers of Parkinson's disease (PD) progression in study participants with manifest PD, Prodromal PD, and Healthy Controls. The overall goal of PPMI is to identify markers of disease progression for use in clinical trials of therapies to reduce progression of PD disability.

## 1.1 PRIMARY OBJECTIVE

The primary objective of PPMI Cognitive Activities is to assess the feasibility of web-based cognitive testing in people with and without PD and how the results relate to other data collected in the PPMI program.

## 1.2 SECONDARY OBJECTIVE

Secondary objectives include:

1. Describing the feasibility, test-retest, completeness of data, completion time, retention, sensitivity, concurrent validity compared to other cognitive measures and tests in PPMI.
2. Among those with PD, describing patterns of cognition that may be associated with PD severity and/or disease progression.
3. Among those without PD, comparing cognitive testing scores in groups defined by the presence or absence of certain characteristics including for example endorsing cognitive change, REM sleep Behavior Disorder (RBD) diagnosis, hyposmia, demographic characteristics, etc.

# 2. STUDY OUTCOMES

The primary outcome measures are measures of cognitive assessments collected using web-based cognitive research software and may include:

- tests of working memory, learning and executive function; visual, verbal and episodic memory; attention, information processing and reaction time; social and emotion recognition, decision making and response control.

# 3. BACKGROUND AND RATIONALE

Cognitive impairment is one of the important functional changes experienced by some people with Parkinson's disease. Detecting cognitive change using web-based testing may be a useful way to identify this dysfunction.

Web-based cognitive testing batteries are language independent making them suitable for cross-cultural studies. They do not require participants to be seen in-person, thus reducing participant burden.

## 4. STUDY DESIGN

This protocol involves the indefinite, web-based collection of cross-sectional and longitudinal cognitive information from people with and without PD. The cognitive data will be collected through web-based cognitive software platforms that can be continually modified to accommodate study objectives over time. Cognitive testing opportunities will be presented to eligible participants through the myPPMI portal, a PPMI program specific web-based portal for participants to learn about PPMI study related activities and new information. Eligible participants will be presented with a tile (or button), which will contain a link to learn more about this study. Participants will be required to consent prior to being connected to web-based cognitive testing. Following consent, participants will provide demographic information before being connected to the web-based cognitive testing software via a secure link in myPPMI. Participants will be directed to web-based portals to access cognitive testing software such as Cogstate Brief Battery, CANTAB Connect or other cognitive tests. Once a participant agrees to participate, he/she may be asked to do some or all of the following at least one-time per year and up to 4 times per year for select participants:

- Provide demographic information required for normative scoring (e.g., Date of Birth, sex, level of education etc.).
- Complete web-based cognitive tests and activities.
- Complete health-related questionnaires, (e.g., questions related to PD and PD risk, daily activities, and quality of life, etc.)
- Complete questionnaires related to participant motivation for study participation, as well as the participant experience, may also be administered throughout the study period. These questionnaires will be established following initial launch. These may be administered via a web-based platform or sometimes supplemented with telephone or USPS mailings.

## 5. STUDY POPULATION

This study will include people with and without PD who are also participating in PPMI. During the course of this study, we expect to enroll up to 100,000 participants globally, starting with the US for the initial phase.

## 6. RECRUITMENT METHODS

Participants in PPMI related studies will be invited to cognitive activities via emails, myPPMI opportunity tiles, PPMI site invitations and other PPMI recruitment and outreach campaigns.

## 7. PARTICIPANT ELIGIBILITY

Participants must meet the following criteria to enroll in PPMI Cognitive Activities:

- Age 18 years or older
- Participating in PPMI
- Access to appropriate hardware and/or software such a laptop, desktop computer, tablet, or updated operating systems, etc.

## 8. OBTAINING INFORMED CONSENT

Potential participants will already have a PPMI ID, as well as a username and password for myPPMI as they will already have been registered with PPMI. Once a potential participant is participating in PPMI, eligible individuals will be invited to participate in PPMI Cognitive Activities Study via a "tile" surfaced on myPPMI. Prior to viewing the informed consent, eligible individuals can read more about the Cognitive Activities study. If interested, they will be required to read the consent. If the individual agrees to participate, consent will be acknowledged electronically. Participants will have the opportunity to save a digital copy of the signed informed consent, GDPR Addendum (as applicable), and privacy notice (as applicable) for their records.

## 9. PARTICIPANT ID ASSIGNMENT

All PPMI Cognitive Activities Study participants will already have a PPMI Participant ID. Only this participant number will be utilized to identify the participant on all study-related documentation.

## 10. STUDY PROCEDURES

PPMI Cognitive Activities will incorporate a variety of web-based cognitive tests and activities throughout the study period. Eligible PPMI participants will be directed to log into myPPMI where the cognitive testing opportunities will be surfaced. Participants will connect to the web-based cognitive testing software via a secure link. Participants will be presented with web-based tests of cognitive functioning involving, but not limited to, reaction time, executive functioning, planning, episodic memory, short-term memory, sustained attention, and working memory. Participants may also be asked to complete other questionnaires electronically, on paper and/or via telephone.

## 11. RISKS TO PARTICIPANTS

The most common risk associated with web-based cognitive data collection is that study participants may feel anxious about completing the study tasks. There is a risk of disclosure of private information by participating in this study. However, safeguards are in place to reduce the risk of this happening. In addition, participants are provided with a link to the privacy policy which further describes how their study information is kept private. Data will be securely transferred between cognitive research software providers and PPMI cores (designated study teams who collect, store, and handle study information) for the required workflows under the PPMI program. Any study data that is made available to researchers external to PPMI will be coded and will not contain identifiers. While every effort will be made to maintain confidentiality, there is a small risk that information may be disclosed. There may be other privacy risks that the study team may not have foreseen.

## 12. POTENTIAL BENEFITS TO PARTICIPANTS

There are no direct anticipated benefits to study participants in this study. However, new information may be generated by the study to support development of better treatments for Parkinson's disease.

## 13. COSTS FOR PARTICIPATION

There will be no cost to the study participant for participating in this study.

## 14. PARTICIPANT WITHDRAWALS

Study participants will be informed during the consent process that they have the right to withdraw from the study at any time without prejudice. Withdrawal from this study will not affect the study participant's continued participation in other PPMI protocols. Any information that has already been collected prior to the study participant's withdrawal will not be removed.

## 15. ADVERSE EVENTS

There will be no adverse event reporting as part of this web-based cognitive activities study. All data collected as part of this study are for research purposes only and not for clinical care purposes. There will not be any routine medical monitoring of the data collected nor any reports run looking at trends and/or worsening of a participant's condition requiring medical intervention.

## 16. PRIVACY AND CONFIDENTIALITY

The privacy of participants will be protected in that each person will have the option to voluntarily choose whether to participate in this study and where assessments are completed. The information being collected will be outlined during the consent process.

## 17. DATA SHARING AND STORAGE FOR FUTURE USE

Cognitive research software providers will be required to meet the same data security standards as the PPMI Cores who collect, store, and handle study information.

Participant data collected for this study will be maintained and stored for up to fifteen years on the cognitive research software provider servers and indefinitely at the PPMI study cores. All identifiable study data will be accessed only by those who require access as pertains to the individual's role in the study. All organizations responsible for data storage and review will observe the highest precautions to ensure data integrity and security.

Data collected for this study will be maintained and stored indefinitely at the study cores and may be transferred and shared across participating PPMI cores for conducting analyses as pertains to the study including, but not limited to, enrollment, compliance, study outcomes. Data collected for this study will be incorporated into the PPMI database to create a fully harmonized PPMI database.

Study information will be accessed only by those who require access as pertains to the individual's role in the study. All organizations responsible for data storage and review will observe the highest precautions to ensure data integrity and security.

Data obtained during the conduct of this study will be sent to the Laboratory of Neuro Imaging (LONI) in Los Angeles, California, to be stored indefinitely for research purposes. Research data will be made available to researchers to conduct analyses related to PD and other disorders. Researchers will be required to comply with the PPMI data

agreement to receive data. All personally identifiable information will be removed before it is shared outside the study.

## 18. ANALYSIS PLAN

On a regular basis, summary data will be reviewed to verify the completeness of the collected data. Based on this regular review recommendations may be made regarding modifications to the type of data collected and/or the data collection process.

Cognitive test data will be used for analyses in line with the study objectives. This will include but is not restricted to analyses of test-retest reliability, cross-sectional and longitudinal correlations between relevant web-based cognitive testing and clinical data, known-group comparisons, sensitivity to change, predictivity of future change in disease status.

Recruitment and retention metrics will be regularly assessed by demographics characteristics overall and by cohort.

## 19. REFERENCES

1. Parkinson Progression Marker Initiative. The Parkinson Progression Marker Initiative (PPMI). Prog Neurobiol 2011;95(4):629-635