Molecular Integration in Neurological Diagnosis (MIND) Parkinson's Disease Inception Cohort Study Protocol

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Abstract

This is an inception cohort study protocol to enroll people with Parkinson's disease into a biobanking protocol at the clinic-wide level collecting clinical information and blood for future research use. The informed consent process includes optional recontact for future research studies, access to the medical record, and use of samples for future studies. Blood products (plasma and genomic DNA) are banked for future use. Clinical data is obtained through a questionnaire. Each visit lasts between 10-20 min between a clinical research coordinator and patient at the time of their return visit to the medical office. The strength of this protocol is the broad research enrollment across a whole clinic target for recruitment, optional consents for future research and access to the medical record. Weakness include the time needed for enrollment and limited clinical information collected.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease affecting 0.3% of the U.S. population, 1% of people over age 65,1–3 and nearly 2% over the age of 80.4 The incidence is estimated at 8 -18 per 100,000-person years (reviewed in3). PD is a progressive multisystem disorder, characterized by motor symptoms including bradykinesia, tremor, and rigidity,5 and other non-motor features affecting mood, cognition, sleep, and autonomic function.6 The defining pathology of PD is the degradation of nigrostriatal dopaminergic neurons and aggregation of misfolded alpha-synuclein in neurons,7–9 known as Lewy bodies. There is no cure for PD, although many symptomatic therapies are available that mainly target the dopamine system.

PD was thought to be a sporadic disorder until the late 1990s when mutations responsible for the disease were identified in the synuclein gene (SNCA).10 Since that time significant progress has been made in understanding the genetics of PD. A number of rare monogenic forms of PD associated with highly penetrant mutations have been identified including the genes Parkin, DJ-1, Pink1 and SNCA.10–13 Additionally, variants with incomplete penetrance have been shown to increase risk of PD in certain populations, including glucocerebrosidase (GBA).14 Additionally, at least 28 independent disease-associated risk loci have been identified through genome-wide association, each conferring a small, but significant risk of developing PD.15 Genetic variants associated with disease complications such as impulse control disorders,16 and dementia17 have expanded our understanding of these complex traits and provide a unique opportunity to identify high risk groups prior to the development of these complications. Additional studies are essential to expand our understanding of the impact of genetic variation on clinical symptoms and pathophysiology of PD and PD-related complications.
In this study we propose to develop a clinic-wide molecular and genetic biobank that will afford researchers at the University of Pennsylvania (UPenn) and collaborators the ability to expand our knowledge of PD genetics and genetic risk factors associated with PD-related complications. Additionally, this will support future research endeavors by creating a biobank of blood specimens, genetic material and clinical data to support research at UPenn as well as foster the development of collaboration.

**Reagents**

NA

**Equipment**

BD vacutainer K2 EDTA Blood collection tubes (367899)

BD vacutainer Blood collection kids (367344)

**Procedure**

1 **Investigational Plan**

1.1 **General Design**

This is an inception cohort study protocol. The study requires one in-person visit, generally associated with either a visit to the UPenn Parkinson's Disease and Movement Disorders Centier (PDMDC) for a clinical visit, another research visit, or a separately scheduled visit at an alternative time based on the discretion of the research coordinator and the patient. During this visit, the participant will give written informed consent and a research associate trained in phlebotomy will draw 50 mL of blood via venipuncture. The participants will be asked to complete a questionnaire, which can be completed after the blood draw or at home and returned by mail. If the participant gives permission in the informed consent, the medical record will be accessed, and participants may be contacted in the future for updated medical information, to perform additional clinical questionnaires, clinical examinations (rating scales) or may be asked to participate in future research studies.

1.2 **Study Measures**

A PDMDC Genetics Biobank Clinical Questionnaire (supplement) will be distributed to each participant. The questionnaire asks for contact information, demographic and medical information, and has a series of questions pertaining to Parkinson's disease and PD-related complications for which the participant has
to check the most appropriate box. Each participant will complete this form once at enrollment. Based on
the results of this questionnaire, participants may be asked to complete additional clinical questionnaires
or rating scales.

2 Study Population and Duration of Participation

Any patient over the age of 21, who has a diagnosis of Parkinson's disease or is at risk of PD, and
receives their medical care at the University of Pennsylvania PDMDC or has other appointments at the
PDMDC, is eligible for participation in this study.

2.1 Duration of Study Participation

Each participant will be asked to participate in a single study visit, lasting between 10-15 minutes.
Enrolled participants will be asked to complete a questionnaire that can be completed in the office or can
be returned via mail. We anticipate enrolling all PD patients currently seen at the PDMDC within 1.5 years
and will have ongoing enrollment for new patients to the PDMDC thereafter.

2.2 Total Number of Participants and Sites

It is expected that approximately 2500 participants will be offered enrollment at the University of
Pennsylvania. Enrollment will continue beyond the initial phase to capture any new patients to the
PDMDC.

2.3 Inclusion Criteria

· Males and Females;
· Over 21 years of age;
· Have a diagnosis of Parkinson's disease, another form of parkinsonism or are at risk of PD and come to
the PDMDC for appointments.
· Able to consent to research and must sign the consent form, or have an appropriate surrogate sign the
consent;

2.4 Exclusion Criteria
2.5 Participant Recruitment

All patients at the University of Pennsylvania PDMDC will be approached by a PDMDC research coordinator or the study principal investigators. This will occur in conjunction with their scheduled clinic visit with their movement disorders neurologist or other visit to the PDMDC.

2.6 Vulnerable Populations

Children, pregnant women, fetuses, neonates, or prisoners are not included in this research study. Pregnancy will be determined based on self-report from the patient. If, after the collection of blood specimen and clinical data at the single-office visit the patient learns they were pregnant, we would not discard their information.

3 Study Procedures

This study involves a single in-person visit that will occur in conjunction with a visit to the PDMDC, such as a clinical office visit, another scheduled research-related visit, or a visit scheduled separately at the discretion of the patient and the research coordinator. During this visit, participants will have the opportunity to review, discuss, and sign the consent form. If they agree to participate, they will have 50ml of blood drawn and they will complete a brief questionnaire about their Parkinson's disease (see Supplement). This questionnaire can be completed in the office or can be taken home to be completed and mailed back to the PDMDC. A stamped and addressed envelope will be provided for this purpose. Participants who give permission might be contacted in the future, while the study remains active, in order to obtain updated health information, perform additional clinical questionnaires, standardized clinical examinations, or potentially to participate in new, separate research protocols for which they may qualify.

3.1 Informed Consent and HIPAA Authorization

The investigators will obtain written informed consent and HIPAA Authorization from each participant enrolled in the study using a combined Informed Consent/HIPAA Authorization form (See Attachment). It is the responsibility of the investigator to ensure that the informed consent is obtained from the
participant or his/her guardian or legal representative before any activity is undertaken that is not part of routine care. All signed informed consent forms will be maintained in a locked file cabinet in the PDMDC.

3.2 Participant Withdrawal

Participants may withdraw from the study at any time without impact to their care. They may also be discontinued from the study at the discretion of the Investigator. In the event that someone does request to withdraw consent, their data will be removed from the database, their medical record will no longer be accessed for purposes pertaining to this research protocol, and they will not be contacted in the future about potential research trials for which they may be eligible.

3.3 Blood Collection

Up to fifty (50) mL of blood will be drawn into sterile vacutainer tubes. Blood will be used for the extraction of DNA and for preparation of aliquots of plasma and/or serum. All samples will be processed the same day and stored at -80 degrees C. Blood will be drawn by a researcher who is trained in phlebotomy or by the principal investigators.

This protocol and consent specifically covers the banking of biospecimens and their generic use for biomedical research in the future. Specific research studies that make use of the data collected in this protocol or derived from the biospecimens will require an update to this protocol, or the submission of a new protocol(s). However, reconsent of participants will not be required as the current protocol and consent form allow for the use of the data and biospecimens in a wide range of assays to be proposed in future amendments or protocols. For example, we anticipate that DNA extracted from these samples will be tested for specific genes associated with PD (ie: Glucocerebrosidase (GBA) or LRRK2) and genotyped for a large number of genetic markers using genechip microarray technology for more exploratory purposes in a research lab.

In the event that a patient is interested in participating in this research, but unwilling to have venipuncture performed to draw blood, they will be asked to provide a saliva sample or cheek swab to allow for isolation of DNA.

3.4 Parkinson’s Disease and Movement Disorder Center Biobank Questionnaire

The participant will be given a brief PDMDC Genetics Biobank Questionnaire (Supplement) to complete on a tablet or on paper. The paper form will be collected at the end of the visit or returned by the patient after the research visit using a stamped, self-addressed envelope provided. The tablet questionnaire responses will be uploaded automatically to a database in redcap. Paper responses will be entered into
redcap and then all data will be entered into the research database along with any additional protected health information collected from the electronic medical record. Original surveys will be stored in a locked file cabinet in the PDMDC.

3.5 Data obtained from the Electronic Medical Record

Data from the electronic medical record may be obtained directly via access through the electronic medical record or through the use of a clinical data warehouse. If participants agree to have future health information updated, then data from the electronic medical record may periodically be updated in the research database, while the study is active.

3.6 Genetic Testing

Although this protocol plans to collect and store genetic material, it does not propose to perform clinical genetic testing. In the future, amendments to this protocol or additional protocols may propose clinical genetic testing. The consent form allows for the collection and use of the data and biospecimens in a wide range of assays to be proposed in future amendments or protocols. If clinical genetic testing is proposed in the future, and testing is performed in a CLIA-approved facility, patients may be able to learn about their genetic testing results. Each participant, regardless of their genetic testing results, will be offered clinical genetic counseling as part of their medical care. The genetic counseling would be conducted in the same manner as any other genetic counseling referral, and additional studies may be recommended by the genetic counselor. They can then be offered the opportunity to learn about the results of their genetic testing that was performed in a CLIA-approved facility that meets standards for clinical genetic testing. However, genetic testing results that were not performed in a CLIA-approved manner will not be disclosed to participants. Genetic counseling may be performed in person or by phone at the discretion of the genetic counselor.

4 Statistical Plan

This protocol pertains to the collection and biobanking of specimens and clinical data. The data will be used to support additional research protocols, and statistical plans will be outlined for each of those protocols proposing to use biobank data.

Troubleshooting

Time Taken
Each enrollment should take 10-15 min.

**Anticipated Results**

**References**


**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- MINDICFv2.0PDMDCGeneticsBiobank18JUN201917JUN2020.pdf
- MINDQuestionnaireSupplemental.pdf