The Personalized Parkinson Project

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Ethical review	Approved WMO
Status	Completed
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON45667

Source
ToetsingOnline

Brief title
PPP

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Verily Life Sciences LLC,Verily Life Sciences LLC;Radboudumc;Radboud Universiteit;Topsector Life Sciences and Health;Province of Gelderland;City of Nijmegen

Intervention

Keyword: Big Data, Biomarkers, Parkinson's Disease, Wearable sensors

Outcome measures

Primary outcome

Clinimetrics (on site, by assessor):

- Motor Assessment Subset OFF Medication: Hoehn & Yahr stage; UPDRS-III (Including timed up-and-go tests to assess gait); UPDRS-IV; Standing leg / flamingo Test; Pirouette Test; Pegboard Test; Grip strength.
- Motor Assessment Subset ON Medication: Hoehn & Yahr stage; UPDRS-II; UPDRS-III (Including timed up-and-go tests to assess gait); UPDRS-IV; Freezing of Gait Questionnaire; Standing leg / flamingo Test; Pirouette Test; Pegboard Test; Grip strength.
- Neuropsychological Symptoms: UPDRS-I; Montreal Cognitive Assessment; Phonemic Fluency Semantic Fluency; 15 Words Test; Benton Judgment of Line Orientation; Letter Number Sequencing; Symbol Digit Modalities Test.

Vragenlijsten voor patiënt:

- Neuropsychological symptoms: Beck Depression Inventory; Quip- RS (impulsive compulsive disorder); Apathy scale; Trait Anxiety Inventory for Adults;
- Other UPDRS-II;: SCOPA- autonomic; SCOPA- sleep; RBD questionnaire; Epworth sleep questionnaire; SF-12; Wearing-off questionnaire; Radboud Oral Motor Inventory; Screening Questionnaire on Visual Impairment; Diet - 24h web based self-report (developed by Wageningen University)

Biomarkers

* Imaging

- MRI: volumetrics, DTI, resting state

- ECG: heart rate variability

* Biospecimens

- Blood: Plasma / PBMCs serum, EDTA plasma (DNA), PAXgene (RNA)

- CSF: Tau, urate

- Stool

Secondary outcome

Study Watch Data collection:

• Pulse rate

• Skin temperature, Electrodermal activity (sweat)

• Movement data (Accelerometer)

• Electrocardiogram (ECG)

• Altitude, pressure, relative humidity

• Environment temperature

• Ambient light level

• Sound pressure level

Study description

Background summary

Parkinson*s disease (PD) is the second most prevalent degenerative brain disease. Our understanding of the basic pathology, etiology, and progression of

PD has stagnated, partly due to the limited patient diversity captured in study cohorts. Additionally, we lack sufficient biological insight into the underlying etiologies and pathophysiological mechanisms to develop new interventions that can slow down or arrest disease progression. As a result, patients do not receive the best care they deserve, leading to unnecessary disability, and to mounting costs for society.

Currently biomarker studies have been especially valuable for the differential diagnostics (distinguishing PD patients from healthy controls, and to differentiate PD from the different forms of atypical parkinsonism). There are currently no reliable biomarkers that can help to predict the widely varying differences between patients in prognosis, rate of progression, time to development of important milestones (such as development of falls), or treatment response. Additionally, an important limitation of the ongoing research is that biomarkers are often investigated in isolation, for instance with one measurement per patient, and not combined with other disease-specific characteristics, and often not longitudinally. The few available longitudinal studies typically have had brief follow-up periods.

Furthermore, the clinical presentation of PD varies considerably within and across days. Patients perform paradoxically well when being observed in clinical or in research settings, so this offers a biased view of their real-life performance. Consequently, it has to date not been possible for researchers to capture a truly accurate picture of the diverse day-to-day experiences of people living with PD. Today, a new field of technology called *wearable devices* has the potential to revolutionize how we collect this critical information from patients.

Study objective

The primary objective of the study is to perform a set of hypothesis-driven analyses on the study data set, aiming to correlate established biomarkers (obtained clinically, from brain MRI, from CSF, from known genetic factors, and from monitoring of biosensors signals) to the rate of disease progression, and to responses to treatment (both pharmacological and behavioral, such as participation in exercise). Additionally, we aim to identify biomarkers that can assist in predicting differences in prognosis and treatment response between patients. Finally, by developing novel etiological and pathophysiological insights, we aim to improve existing treatments and to develop new therapeutic approaches, as a basis for development of a more precise and personalized disease management approach.

The secondary objective of the study is to evaluate the Verily Study Watch, to assess how these devices could provide information about the function of patients with PD.

The tertiary objective of this study is to create an extensive longitudinal

dataset describing the genetic, clinical, functional, and phenotypic characteristics of a representative Parkinson*s disease (PD) subject cohort (n = 520) to allow researchers to investigate important unanswered questions in PD.

Study design

Prospective, longitudinal, single-center cohort study.

Study burden and risks

Nature and extent of the burden to patients
Participants are invited to come to the study site in Nijmegen for a full (up to 1.5) day of data collection three times during the 2-year study duration. As is common practice in any clinical trial with PD patients, the initial assessments are performed in the OFF-medications state, i.e., after PD medications have been withheld for 12 hours. Subjects* Parkinson symptoms may temporarily worsen, but medications will be resumed immediately after the initial clinical assessments. This is a widely accepted and safe procedure in the Parkinson research field. All study assessments are routine exams done in standard clinical practice and are generally well tolerated. The noise in the MRI scanner, and lying in a small space for approximately 1 hour, may lead to minor discomfort; however, subjects with claustrophobia will be excluded from the study to avoid burden for the patients. The lumbar puncture to obtain CSF is optional, although based on our extensive prior experience in large Parkinson studies, we strive for a 75% acceptance rate of lumbar punctures by patients. The risks of the lumbar puncture are outlined In Section *Risks and Benefits* of the Protocol.

The Verily Study Watch will be worn daily for up to 23 hours. This small, unobtrusive electronic device is easily applied and poses no significant safety issues. Data collection does not require patient intervention, and data transfer does not require connection to a mobile phone or computer. The Study Watch requires minimum care (daily charge and sync, remove when near water).

Risks
There are limited risks for the patients during the data collection. The diagnostic measurements (MRI, Holter ECG) are standard non-invasive tests that are routinely performed in clinical practice.
Tests that may lead to discomfort / risk are the following:
• Local hematoma can occur related to the venipuncture for blood collection.
• The lumbar puncture is an optional assessment. It can be uncomfortable, although local anesthesia will be used. Radboudumc*s extensive experience shows that patients greatly value this, as it markedly diminishes local discomfort. A small percentage of patients may suffer from prolonged and severe headache after CSF collection. However, this risk will be further reduced by using

atraumatic needles.
• The Verily Study Watch is a low risk non-invasive device (class IIa) used as an adjunct tool and not to guide diagnosis or therapy, therefore it does not pose significant risks.

Benefits
Because data collection is not performed for immediate diagnostic or therapeutic purposes, there will be no direct benefits for the subjects enrolled in this study. As a service in return for their efforts for research, participants will be offered an educational program (voluntarily) on Parkinson*s disease and how to handle the disease in daily life. Moreover, patients will indirectly benefit from the study, as their data contribute to gain novel etiological insights for improvement of existing treatments, development of new therapeutic approaches, and more precise and personalized disease management. This will provide future benefit for all patients affected by the disease.

The Study Watch supplements and enhances the information available to the physician, providing continuous measurement and quantitative (rather than subjective) data. The device detects important physiologic parameters that are expected to change with disease conditions or behavioral patterns (e.g., electrodermal activity [EDA], physical movement of the body in three dimensions [acceleration], skin temperature, heart rhythm). As such, by wearing the Study Watch, patients are providing unprecedented insight into the evolution of PD and potentially allowing to identify better ways to treat the disease. In addition to collecting data, the device also functions as a wristwatch.

Contacts

Public
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6535 GC
NL
Scientific
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6535 GC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Prior to enrollment in this clinical investigation, candidates must meet ALL of the following criteria:* Subject has Parkinson*s disease of <=5 years duration, defined as time since diagnosis made by a neurologist.
* Subject is an adult, at least 18 years of age.
* Subject can read and understand Dutch.
* Subject has completed the CMO-approved Informed Consent.
* Subject is willing, competent, and able to comply with all aspects of the protocol, including follow-up schedule and biospecimen collection.
* Subject is not a current or previous employee or family member of employees of the institutions involved in the study, including Verily Life Sciences and Radboudumc.bjects

Exclusion criteria

Candidates must be excluded from this study if ANY of the following criteria are met:* Subject is pregnant or breastfeeding.
* Subject has co-morbidities that would hamper interpretation of parkinsonian disability, such as coincident musculoskeletal abnormalities, in the opinion of the Investigator.
* Contraindicated for MRI, e.g. claustrophobia, presence of an active implant, pacemaker, insulin pump, neurostimulator, ossicle prosthesis, and/or other medical device or other non-removable metal part incompatible with MRI.
* For lumbar puncture:
o Allergy to local anesthetic agents
o Medical history of compression of spinal cord, current local skin infection at the site of the lumbar puncture, developmental abnormalities in lower spine, blood coagulopathy, anticoagulant medication (Acenocoumarol, Warfarin,

Dabigatran).
o Clinical (or previous MRI) evidence of structural cerebral abnormalities that are not compatible with the performance of a lumbar puncture such as malignancies, abscess, or obstructive hydrocephalus.
ddress

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	31-10-2017
Enrollment:	520
Type:	Actual

Medical products/devices used

Generic name:	Verily Study Watch
Registration:	No

Ethics review

Approved WMO Date:	07-09-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-11-2017
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-06-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-04-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-03-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL59694.091.17