How Cerebral Plasticity Shapes Symptom Progression in Parkinson's Disease: A Longitudinal Neuroimaging Study

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To identify the cerebral mechanisms underlying clinical disease progression in PD. The current proposal aims to further specify: (1) differences in motor and limbic activity between patients and controls; (2) the effect of dopamine on motor and...

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

Summary

ID

NL-OMON46228

Source
ToetsingOnline

Brief title
Symptom Progression in PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Michael J Fox Foundation

Intervention

Keyword: Functional neuroimaging, Neuronal plasticity, Parkinson disease

Outcome measures

Primary outcome

For this study, we will assess 50 patients with PD once (OFF their dopaminergic medication) and 50 healthy volunteers twice (baseline and two-year follow up). We will use a subset of the protocols used in the PPP, in which 650 PD patients are assessed ON their dopaminergic medication. This protocol includes two functional MRI tasks (motor task in first half (n=325) of patients, reward task in second half (n=325) of patients) that quantify both (dysfunctional) processing in the basal ganglia and (compensatory) processing in the cortex (i.e. parietal cortex for the motor task, orbito-frontal cortex for the reward task). We will quantify clinical disease progression with clinical measures such as the MDS-UPDRS.

Secondary outcome

Secondary study parameters include participant characteristics (e.g. Age, Gender, Comorbidity, Medication use), clinical measures (e.g. severity of motor, cognitive and neuropsychiatric symptoms), and additional MRI-measures (Resting state functional connectivity, Diffusion tensor imaging, Quantitative susceptibility imaging and fluid-attenuated inversion recovery) to be used for thorough interpretation of primary outcomes.

Study description

Background summary

Parkinson*s Disease (PD) is the second most prevalent degenerative brain disease, with over 7 million people with PD worldwide. There is no cure, and current treatments are unable to slow down disease progression. This is largely caused by a lack of insight in the cerebral mechanisms underlying disease progression. The pathological hallmark of PD is dopaminergic dysfunction of the basal ganglia, but longitudinal studies show a surprisingly poor, if any, correlation between worsening dopaminergic dysfunction and disease progression. This suggests a key role for other, non-dopaminergic mechanisms outside the basal ganglia. More specifically, we hypothesize that cerebral changes in cortical regions inter-connected to the basal ganglia can compensate for progressive basal ganglia dysfunction, and that the degree of cerebral compensation is associated with inter-individual differences in disease progression. We will focus on longitudinal changes across two distinct cerebral circuits: the motor loop (associated with motoric symptoms) and the limbic loop (associated with neuropsychiatric symptoms such as depression and apathy). This study will build on the already approved and currently running Personalized Parkinson Project (PPP, NL59694.091.16). To answer our research question, we will add two crucial measurements to the existing PPP protocol: an additional measurement OFF dopaminergic medication in a subsample of 50 PPP participants, and two sessions (at baseline and after two years) in an additional group of 50 healthy controls.

Study objective

To identify the cerebral mechanisms underlying clinical disease progression in PD. The current proposal aims to further specify: (1) differences in motor and limbic activity between patients and controls; (2) the effect of dopamine on motor and limbic activity in PD.

Study design

Combined cross-sectional and longitudinal observational study.

Study burden and risks

The load on patients consists of the time spent on this project, and potentially a temporary worsening of symptoms caused by withholding medication. Patients will arrive in a practically defined OFF state, i.e. at least 12 hours after having taken their last dopaminergic medication. At the end of the measurement, they will resume their normal medication regime. All measurements are non-invasive, painless, and without nuclear radiation. Individual participants do not directly benefit from participation. However, we expect that this study will improve our knowledge about the cerebral mechanisms underlying clinical disease progression in Parkinson*s disease (PD), which may

lead to new ways of treating this debilitating disease.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

General:
1) *40 years old.
2) Able to read and understand Dutch.
3) Subject is willing, competent, and able to comply with all aspects of the protocol, including follow-up schedule.
Parkinson's Disease-specific:
1) Participation in motor and reward tasks Personalized Parkinson Project (NL59694.091.16)
2) Subject has Parkinson*s disease of *5 years* duration, defined as time since diagnosis made by a neurologist.

Exclusion criteria

1) Subject has co-morbidities that would hamper interpretation of parkinsonian disability or task performance, such as coincident musculoskeletal abnormalities, in the opinion of the investigator.
2) Contraindicated for MRI, e.g., claustrophobia, presence of an active implant, pacemaker, insulin pump, neurostimulator, ossicle prosthesis, pregnancy, and/or other medical device or other non-removable metal part incompatible with MRI.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-01-2019
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	06-12-2018
Application type:	First submission
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	NL67597.091.18