Longitudinal ultra-high field imaging in Parkinson*s Disease: Tracking the disease course

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

Summary

ID

NL-OMON54720

Source
ToetsingOnline

Brief title
TRACK-PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Stichting de Weijerhorst

Intervention

Keyword: MRI, Parkinson's disease, Subtypes, Ultra-high field

Outcome measures

Primary outcome

The main study endpoint will be the structural and functional changes of the PD brain as compared to HC, which will be assessed on 7T ultra-high field MR images. We will also use quantitative MRI approaches, since this enables us to detect small structural and anatomical differences which cannot be detected on qualitative MRI acquisitions. Our aim is to create a diagnostic tool, based on MRI characteristics, which can distinguish PD patients from HC.

Secondary outcome

A secondary study endpoint will be the detection of differences in imaging characteristics between clinically dissimilar subtypes of PD. We aim to correlate clinical phenotype, genetic characteristics and progression of symptoms to functional and structural MRI variations. This requires a longitudinal follow-up, which enables us to establish in what manner progression of clinical symptoms is related to certain neuroimaging characteristics. Furthermore, our aim is to develop a patient specific prognostic model based on MRI characteristics, which can (partially) predict the disease course for the individual patient.

Moreover, we aim to assess the potential of brain-enriched EV miRNAs in blood to distinguish PD from the healthy population.

Study description

Background summary

Parkinson*s disease (PD) is the second most common neurodegenerative disorder after Alzheimer*s disease. It is characterized by both motor symptoms and non-motor symptoms, such as neuropsychiatric disturbances and autonomic dysfunction. The diagnosis of PD is currently based on the assessment of clinical symptoms and monitoring these symptoms over time. But the early diagnosis of PD can be challenging and it is often not immediately recognised. During the past years it has become well-established that MR imaging may be able to serve as a valuable method in the diagnostic work-up of PD. Early MRI biomarkers have been discovered that suggest a possibility to distinguish PD patients from healthy controls based on ultra-high field neuroimaging. However, until now insufficient sensitivity and specificity is reached for the MRI characteristics in the performed studies to determine whether a single individual has PD.
Furthermore, over the last few years there has been growing interest in the heterogeneous nature of PD. A great variability exists not only in motor manifestations, but also in cognitive functions, autonomic complaints, prognosis and response to therapy. As a result, several attempts have been made to subdivide PD patients into different clinical subtypes, which might be influenced by a combination of environmetnal and genetic factors. However, the underlying aetiology of this clinical heterogeneity in PD is still not understood and at this moment we are not able to predict the individual disease course of a patient. Nevertheless, previous studies have suggested that different motor subtypes of PD may show dissimilar MR characteristics, especially in the substantia nigra. Unfortunately, most studies contain only small groups of subjects and results are not unambiguously. Until now it is still not clear to what extend changes on MR imaging in PD patients correlate to the clinical subtype of these patients and if certain MRI characteristics can predict the individual disease course.
With this longitudinal ultra-high field 7T study, which combines several different MRI techniques, we believe that we can make an important contribution to the development of a distinctive MRI pattern for PD. Furthermore, we expect different clinical subgroups of PD patients to show dissimilar MRI profiles.

Study objective

The primary objective of this study is to confirm early and subtle MRI changes in PD patients which distinguish them from the healthy population and to create a diagnostic tool for neurologists based on these differences. Secondary objectives are to detect whether different clinical phenotypes of PD patients also show different imaging characteristics and to correlate MRI characteristics to clinical phenotype, genetic characteristics and progression

of symptoms.

Study design

We will perform a longitudinal observational 7T MRI study in PD patients and healthy controls (HC). All subjects will undergo a 7T MRI scan of the brain at baseline and after 2 and 4 years. Moreover, a blood sample for genetic testing and the detection of brain-enriched microvesicle miRNAs will be collected at baseline and at the second follow-up visit. Furthermore, motor, psychological, cognitive and autonomic functions of the PD subjects will be assessed at each follow-up moment. During all test days, subjects will also be asked to wear 3 wearable sensors (one at each wrist and one at their chest) to assess motoric function. Based on these clinical parameters, PD patients will be subdivided into different clinical subgroups.

Study burden and risks

The burden for the subjects related to this study is limited. Patients will undergo an assessment at baseline, after 2 and after 4 years. For this MRI scan, medication does not have to be discontinued. The duration of the scan will be approximately 60 minutes, which is considered to be acceptable. Only patients without contra-indications for MRI will be included, therefore the procedure is safe. Furthermore, assessments of motor, psychological, cognitive and autonomic functions will be performed during the follow-up moments. During these assessments, participants are asked to wear three wearable sensors, which are not considered to be a risk or burden. Furthermore, we will ensure that sufficient moments of rest are scheduled between the tests. Finally, if patients give their permission for this, a sample of blood will be drawn from all subjects at baseline and during the second follow-up visit. There is a small risk for all participating subjects that incidental observations can be found within this study. Only subjects who give permission to inform their treating physician in case of an incidental observation will be included in the study.
There are no immediate benefits for the participants. However, PD patients can benefit from optimised treatment in the future, as will other PD patients not included in the study due to group-relatedness.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria for Parkinson's disease patients:
-18 years of age or older.
-Recently diagnosed idiopathic Parkinson's Disease according to the UK Brain Bank Criteria (<=3 year after diagnosis)., Inclusion criteria for healthy controls:
-The age and sex of healthy control subjects should not significantly differ from the age and sex of the PD patients

Exclusion criteria

Exclusion criteria for all subjects:
-Subjects with contra-indications for a MRI scan as defined in the MRI screenings form of Scannexus (Appendix E), such as claustrophobia or subjects carrying incompatible metallic devices such as pacemakers and certain mechanical valves.
-Advanced cognitive impairment (MoCA <24) or dementia according to the DSM V criteria at baseline.
-Subjects with other neurodegenerative diseases.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-07-2019
Enrollment:	190
Type:	Actual

Ethics review

Approved WMO Date:	20-12-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-11-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL67241.068.18