Atypical parkinsonism: Early diagnosis with quantitative MRI

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Primary Objective: To investigate whether a quantitative MRI protocol can detect the difference between atypical parkinsonism and patients with Parkinson*s disease, in an early phase of the diseases when the clinical diagnosis for either is not yet...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system infections and inflammations
Study type	Observational invasive

Summary

ID

NL-OMON52291

Source
ToetsingOnline

Brief title
APqMRI

Condition

- Central nervous system infections and inflammations

Synonym
Atypical parkinsonism; Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Parkinson Vereniging

Intervention

Keyword: Atypical parkinsonism, Early diagnosis, Quantitative MRI

Outcome measures

Primary outcome

The differentiations will be made based on the following measurements:

- Atrophy measurements will be made on a sagittal view of the T1-weighted images, without additional post-processing. This is done by measuring the surface and diameters of the midbrain, pons and superior and middle cerebral peduncle (8,9) for all the differentiations, and in addition for differentiating MSA-C from the rest can be improved by looking for a Hot-Cross-Bun Sign (HCBS) on a T2-weighted image in the pons (14,15).
- MT-weighted measurements are made in the Substantia Nigra and Locus Coeruleus
- Quantitative Susceptibility Mapping (QSM) will be done in the brain, including the basal ganglia (putamen and globus pallidus) (6,11) and the midbrain (nucleus ruber and substantia nigra) using, for example, the MEDI toolbox (16).
- Diffusion MRI measures, including Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) will be conducted in the brain, including the putamen, cerebellum and brainstem (12,17-20). This can, for example, be done using MRtrix (21).
- Neurological examination including a UPDRS score (movement disorder severity) and MOCA score (Cognitive test).
- Neurofilament quantification from a blood sample.

Secondary outcome

The same approaches as primary parameters will be applied, however each

atypical form will be grouped separately.

Study description

Background summary

Patients with atypical forms of parkinsonism are challenging to distinguish from Parkinson patients in the clinical workflow. Novel quantitative MRI techniques demonstrated differential diagnosis at a late-stage of disease. It is unknown how valuable such techniques are at an early-stage of the disease.

Study objective

Primary Objective: To investigate whether a quantitative MRI protocol can detect the difference between atypical parkinsonism and patients with Parkinson*s disease, in an early phase of the diseases when the clinical diagnosis for either is not yet certain.

Secondary Objective(s):
1. To investigate differences in the primary outcomes between patients with possible Parkinson*s disease, MSA-C, MSA-P and PSP.
2. To investigate the differences among early-stage, possible PD patients and near-certain PD patients.
3. To calculate the sensitivity and specificity of differential diagnoses using the differences in the primary objective as well as the first and second secondary objectives, and compare those to current published results for late-stage patients.

Study design

Observational pilot study

Study burden and risks

Patient participants in this study whom are already eligible for an MRI scan, will be burdened with additional MRI scan-time of 15-20 minutes. Patient participants who are not eligible for an MRI scan will be burdened with a new MRI scan of 45 minutes. Both will receive a physical follow up health check, which will take place approximately and at a maximum 1 year after the MRI,

during their control visits.

Healthy volunteers will be burdened with an MRI scan of 40-45 minutes and a 1 year follow-up with a phone call.

Patients participating in this study will not receive a benefit, in the form of an improved clinical treatment. The MRI scan is harmless as there is no use of ionizing radiation. However, they have to lie in a narrow bore for the examination which is not suitable for people with claustrophobia. The MRI scan is also loud and requires wearing ear-plugs. Volunteers participating in this study will experience the same burdens, however in addition the MRI was not required in the first place.
Both participant groups will be exposed to incidental findings, unrelated to parkinsonism. Any consequent health care fees are for the responsibility of the participants.

Patient participants will required to undergo a neurofilament test from their blood. Blood is typically already drawn from these patients on routine visits and no additional blood tests are needed. However in the case no blood has been taken, patients will be burdened with a new blood test. Additional blood tests are inconvenient.

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

Patients:
- Patients who present at the outpatient clinic of the department of neurology with symptoms consistent with degenerative parkinsonism.
- For possible PD patients: Diagnosis of Parkinson*s disease is unclear and an atypical form of parkinsonism is suspected.
- For near-certain PD patients: Patients for whom Parkinson*s disease is highly suspected.
- At least 50 years old
- Signed informed consent.

Healthy volunteers:
- Healthy subject (defined as a volunteer without and signs or symptoms of disease)
- At least 50 years old and not older than 75
- Signed informed consent

Exclusion criteria

- Patients with parkinsonism symptoms caused by medication or essential tremors.
In addition, both patients and healthy volunteers are excluded if they meet any of the following criteria:
- a history of another neurodegenerative disease.
- History of significant intracranial disease
- Contra-indication to an MRI exam
- Metal implants
- Women who are pregnant or lactating
- Having any physical or mental status that interferes with the informed consent procedure

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-05-2022
Enrollment:	55
Type:	Actual

Ethics review

Approved WMO Date:	14-01-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL78601.078.21