Longitudinal prediction of progression in MS: The PrograMS Cohort

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Demyelinating disorders
Study type	Observational invasive

Summary

ID

NL-OMON51918

Source
ToetsingOnline

Brief title
PrograMS

Condition

- Demyelinating disorders

Synonym
Disseminated sclerosis, MS

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Stichting MS Research (collectebusfonds)

Intervention

Keyword: longitudinal, multiple sclerosis, prediction, progression

Outcome measures

Primary outcome

Cognitive measures

• Neuropsychological test scores.

Neurological measures

• Clinical scales.

Blood serum measures

• (Changes in) blood biomarkers as defined in the MS biobank protocol.

Neuro-ophthalmological measures

• (Changes in) retinal layer integrity and eye movements.

Questionnaires

• (Changes in) mood and anxiety, fatigue, sleep disturbances, quality of life, coping style, personality, subjective motor function and cognitive complaints, work participation, stress, resilience.

Structural brain measures

• (Changes in) white and grey matter tissue integrity and volume, as well as lesions.

Functional brain measures

• (Changes in) functional activation as well as connectivity and network

changes, measured with fMRI and MEG.

Secondary outcome

We will identify (novel, clinical) measures and combinations of measures (e.g.

grey matter atrophy patterns, serum NfL levels, dynamic network changes,

structural network topology) to better understand the mechanism underlying

progression, as well as (combinations of) measures that are most predictive for

clinical progression.

Study description

Background summary

Multiple sclerosis (MS) is the most important cause of acquired disability in young adults with a significant impact on the lives of patients and their relatives and forms a major economic burden to society. Both internal (e.g. genetic) and external (e.g. environmental) factors are thought to play a role in the initiation and the evolution of the disease process. That being said, our understanding of the mechanisms involved in disease progression remains limited. This scarcity of knowledge on the mechanism and predictors of disease progression can lead to under- and overtreatment which can both negatively affect patient wellbeing and societal costs.
A growing body of predominantly cross-sectional evidence has shown that both conventional and advanced imaging and blood (bio)markers contain unique (predictive) information on the clinical status and outcomes of patients with MS. In the past decade, a number of studies have investigated the role of conventional MRI (i.e. lesions) in disease progression and have indicated that there is much to be gained in this field of research. The latest advancements in the field explore the relationship between disease progression and advanced imaging markers that are more sensitive to damage in the grey and white matter, as well as serum-based biomarkers of inflammation and degeneration such as Neurofilament Light (NfL). In addition, relative newcomers to the field with high potential are changes in brain functioning and brain networks, as well as neuro-ophthalmology.

Study objective

The main objective of this project is to build a comprehensive model for a better predictio n of progression in MS, as a first step to move towards personalized prediction. Secondary objectives aim to study specific aspects of underlying mechanisms of progression in MS. By investigating the evolution of grey and white matter damage (lesions, atrophy, microstructural myelin damage), changes is brain function and connectivity, and the relation of such measures with ophthalmologic measurements (OCT and eye movements) and blood biomarkers we aim to significantly improve our understanding of MS, its progression, and its clinical course.

Study design

The proposed study is a single center, observational, follow-up cohort study for which we aim to include all people with MS and all healthy controls (HC) who have previously participated in the Presto, GeneOCT, and LTD studies (collectively now known as *PrograMS*) and have not provided objection to be contacted for follow-up study. The inclusion of the previously followed HC groups associated with the three subcohorts is necessary as a reference to understand the longitudinal changes in patients i.e. to distinguish pathological change from normal variations over time and healthy aging .
Because of the large amount of persons to be included (around 240 patients and 60 controls) the total inclusion period and thereby duration of the acquisition of data for this cohort visit is estimated at 1,5 years. All included persons will be invited at the VUmc for a 1 day program in which all data will be collected, which is comparable to earlier visits of these subjects.
All subjects in this study will visit the Amsterdam University Medical Center, location VUmc. For patients the visit will consist of a neurological examination, a neuropsychological examination, blood sampling (8 vials of 42 ml), MR imaging (~60 minutes, without contrast), a magnetoencephalography (MEG) scan (~45 minutes) and retinal optical coherence tomography (OCT) and eye movement examination. Healthy control subjects will undergo a similar protocol, except for the neurological examination and blood sampling. All subjects will fill out questionnaires on anxiety and depression, fatigue, sleep disturbances, and subjective cognitive functioning. The entire protocol has been administered before to all subjects in the study.

Study burden and risks

For patients, duration of the study will be a visit of approximately 6 hours (including a 30-minute break halfway through the visit, and including 30 minutes of questionnaires which can optionally be completed at home). For controls, the visit will last approximately 4 hours and 30 minutes (due to exclusion of neurological examination and blood sampling). From previous

studies, the protocol is known to be well tolerated by patients.

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

All people with MS and all healthy controls (HC) who have previously participated in the Presto (2002/140), GeneOCT(2004/9), or LTD (2010/336) studies (collectively also known as *PrograMS*) and have not provided objection to be contacted for follow-up study, or have been enquired to join the cohort based on the Amsterdam MS Cohort (2020/269) protocol.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

MS patients:
- Persons unable to undergo the minimal data collection (as described in Methods section)

Controls:
- Comorbidity that interferes with participation in this study

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):	25-05-2021
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Date:	10-03-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL74887.029.20