The importance of early brain changes in patients with MS with regard to cognitive and physical outcome

Published: 30-07-2020
Last updated: 11-06-2024

The main objective of this project is to identify the early brain changes in MS (i.e. patients that are recently diagnosed with MS) that can be measured by advanced structural and functional (network) imaging measures. Additionally, we will...

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

Summary

ID

NL-OMON52939

Source
ToetsingOnline

Brief title
The importance of early brain changes in MS

Condition

- Demyelinating disorders

Synonym
MS, Multiple Sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Celgene B.V.,Farmaceutisch bedrijf

Intervention

Keyword: Advanced MRI, Biomarkers, Cognition, Multiple Sclerosis

Outcome measures

Primary outcome

Changes in structural MRI (i.e. atrophy and (grey matter) lesions) will serve as primary outcome measures, such as atrophy in the cortex and deep grey matter, changes in white matter damage in specific tracts and white matter and cortical lesions.

Next, changes in functional brain measures will be included, measuring for instance functional connectivity, eigenvector centrality mapping and functional brain adaptation.

Secondary outcome

Changes in cognitive performance (as measured with the neuropsychological examination) and clinical performance (as measured with the neurological examination) will serve as secundary parameters. Additionally, changes on questionnaires (e.g. arm and walk function, fatigue, anxiety and depression, subjective cognitive perfor-mance, coping style, mastery, stress, work participation and quality of life) will be included.

Molecular brain changes will also be investigated, addressing for example changes in GABA/glutamate and serum biomarkers NfL and GFAP.

Study description

Background summary

Within five years after diagnosis, approximately 50% of the patients with multiple sclerosis (MS) develop cognitive decline and 65% of the patients become unemployed, negatively impacting the quality of life. To be able to postpone or ultimately prevent these negative effects of MS, we urgently need to understand which underlying mechanism(s) lead to such a rapid decline in daily functioning and whether we can predict such an early clinical and cognitive decline. It is expected that especially in this early phase of the disease a window of opportunity for neuroplasticity exists (functional reorganization, brain and cognitive reserve), which is not yet exhausted due to a relatively limited amount of brain tissue damage. Understanding these early changes is key to develop new treatment targets in order to halt the disease, i.e. to identify a window-of-opportunity for early intervention. Until now, these very early changes, measured with advanced imaging and biomarkers, remain unknown.

Study objective

The main objective of this project is to identify the early brain changes in MS (i.e. patients that are recently diagnosed with MS) that can be measured by advanced structural and functional (network) imaging measures. Additionally, we will determine how and when these changes relate to clinical and cognitive decline and serum biomarkers. Finally, we will determine which of the measures is most predictive for clinical and cognitive decline in patients recently diagnosed with relapsing-remitting MS (RRMS). Ultimately we would like to introduce (a) new biomarker(s) (or combinations of biomarkers) to detect the first pathological changes in patients with MS. The detected outcome measures can serve as novel outcomes in clinical trials and may open a new road towards precision medicine.

Study design

This 2-year prospective, longitudinal, single center, observational cohort study will be performed at the Amsterdam UMC, in which recently diagnosed MS patients will be followed over time with regard to cognitive and clinical performance, and structural and functional (imaging) measures.

Study burden and risks

All subjects in this study will visit the Amsterdam UMC, location AMC three times: at baseline, after 1 year and after 2 years. For the patients the visits will consist of a neurological examination, a neuropsychological examination, blood sampling (6 mL) and MR imaging (structural and functional). At home, patients will fill out several questionnaires on arm and walkfunction, fatigue, anxiety and depression, subjective cognitive performance, coping style, mastery, stress, work participation and quality of life. Additional blood samples (6 mL) will be drawn at month 3, month 6, month 9, month 15, month 18

and month 21.

Healthy control subjects will undergo a similar protocol, except for the neuropsychological examination.

The burden will be mainly the time-investment in the study. Risks are limited due to the observational character of the study. However, it is possible that coincidental findings will be shown via the MRI-scans. In case of coincidental findings by participants the researcher will ask the radiologist to review the scans. In case of coincidental findings in patients, their neurologist will be informed. In case of coincidental findings in healthy controls, their general practitioner will be informed.

Contacts

Public
Vrije Universiteit Medisch Centrum

De boelelaan 1108
Amsterdam 1081 HZ
NL
Scientific
Vrije Universiteit Medisch Centrum

De boelelaan 1108
Amsterdam 1081 HZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the following eligibility criteria at baseline:

1. Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (PHI) in accordance with national and local subject privacy regulations;
2. All participants should be 18-65 years of age;
3. Sufficient Dutch proficiency to be able to comprehend and to perform the neuropsychological examination;
4. All participants need to meet the safety criteria to undergo an MRI examination;

For the patients specifically:
5. Only patients that are recently (between 6 up to 12 months) diagnosed with clinically definite MS according to the 2017 revision of the McDonald MS criteria will be included (a range of one month before and after this window was applied; thus 5-13 months);
6. Only patients with (active) relapsing-remitting disease course will be included;
7. All types of disease modifying treatment for MS are allowed.

Exclusion criteria

Subjects will be excluded from study entry if any of the following exclusion criteria exist at baseline:
1. Unable or unwilling to provide informed consent;
2. Presence or history of alcohol or drug abuse;
3. Presence or history of psychiatric or neurological disease of the CNS (for patients: neurological disease other than MS) that is expected to affect any of the outcome measures (will be discussed with the principal investigator and neurologist);
4. Presence of contra-indications for MRI;
5. Participation in other (scientific) studies using cognitive or physical training programs (interventions other than standard care) at baseline to avoid noise.

For the patient groups specifically:
6. Patients with disease categorized as clinically isolated syndrome, primary progressive, secondary progressive or progressive relapsing;
7. Relapses or steroid treatment less than four weeks prior to the visits.
Visits of included patients experiencing a relapse will be postponed if

possible;
8. Patients undergoing a cognitive relapse. Visits of included patients experiencing a cognitive relapse will be postponed if possible.

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):	28-02-2021
Enrollment:	180
Type:	Actual

Ethics review

Approved WMO Date:	30-07-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2021
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2024
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	NL72064.029.20