Does MS grey matter atrophy progress faster in regions with more damage in connected white matter?

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To determine whether damage in the cortical and/or subcortical GM in patients with early RRMS increases in regions connected to more damaged WM tracts, i.e. WM tracts with larger lesion volume, WM tracts with more severe damage inside lesions, and/...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Observational non invasive

Summary

ID

NL-OMON43307

Source
ToetsingOnline

Brief title
Rate of GM atrophy in MS

Condition

- Demyelinating disorders

Synonym
multiple sclerosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: grey matter atrophy, multiple sclerosis, neurodegeneration, white matter tract damage

Outcome measures

Primary outcome

Three measures for WM damage will be assessed, i.e. lesion volume, lesion fractional anisotropy (FA) and NAWM FA, from which a composite WM damage score will be computed. High versus low WM damage scores will then be compared to the atrophy rates in the GM, based on subcortical volume and cortical thickness measures. From this, we can compare atrophy rates of each GM structure from baseline to follow-up 1 between the group of patients with higher damage in the WM tracts connected to that GM structure on the one hand, and the group of patients with lower damage in those WM tracts on the other.
Similar calculations will be performed between follow-up 1 and follow-up 2 in order to determine whether a larger increase of WM damage over the first study year is predictive of faster subsequent GM atrophy in the second year.

Secondary outcome

Next to the measures for GM and WM damage, resting state functional connectivity measurements will be used to assess whether GM and WM damage patterns effect the functional organization of the brain at rest, either prior to GM/WM damage, or following the damage patterns observed.
Furthermore, clinical measurements will be taken into account, in order to link the structural data to functionality of the brain in the RRMS patients.

Study description

Background summary

It is currently unclear whether and how atrophy of the brain*s grey matter (GM) in multiple sclerosis (MS) is related to pathological changes in white matter (WM). This knowledge is needed to determine whether treatment efforts aimed at the neurodegenerative component of MS are targeting a primary disease mechanism, or in fact merely treating secondary symptoms. Atrophy of the connected (sub)cortical GM, i.e., the change of volumes of deep GM structures and change of cortical thickness of cortical GM regions, can thus be related to location and severity of WM damage. We will analyze local rates of atrophy in distinct cortical and subcortical GM regions in early relapsing-remitting MS (RRMS) patients at three time points (baseline, follow-up 1 [baseline + 1 jaar ± 3 months] and follow-up 2 [follow-up 1 + 1 jaar ± 3 months]) to determine whether the rate of GM atrophy of a specific region is related to the amount of pre-existing WM damage and/or its early rate of change. In this way, this project will deliver valuable quantitative longitudinal data on RRMS patients to understand the relations between WM pathology and subsequent GM atrophy in early RRMS patients.

Study objective

To determine whether damage in the cortical and/or subcortical GM in patients with early RRMS increases in regions connected to more damaged WM tracts, i.e. WM tracts with larger lesion volume, WM tracts with more severe damage inside lesions, and/or more severe NAWM damage, and to see whether a larger increase of damage over the first study year is predictive of faster subsequent GM atrophy in the second year.
Second, to determine how the structural changes in early RRMS patients effect the functionality of the brain, as measured by i.e. functional connectivity and several clinical parameters.

Study design

The study proposed here is a follow-up study in which GM atrophy rates and changes of WM tract damage are quantified over two consecutive ±1-year intervals. For this, 40 MS patients and 15 healthy controls will be included, taking the inclusion criteria in consideration. At baseline, follow-up 1 and follow-up 2, MRI measurements will be performed to study brain volume, functional connectivity, lesion load, tract damage and WM integrity. Furthermore, clinical parameters are measured as well to relate the MRI measurements to functionality.
At each time point, measurements of GM atrophy, WM damage and functionality (i.e. fMRI and clinical parameters) will be performed. Per time point, GM

atrophy is related to WM tract damage to identify WM tracts connected to each GM region and to quantify damage therein, which will be related to functional parameters. Over two consecutive ±1-year intervals, the measured GM atrophy rates will be compared between patient groups with high WM damage and low WM damage in order to determine whether the rate of GM atrophy is predictive of later WM tract damage, and/or vice versa.

Study burden and risks

No risks are associated with MRI acquisition and no direct benefits are expected for the 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

Patient group:
1. Minimum age 18 years
2. Clinical definite relapsing remitting MS for < 5 years
3. Either receiving no treatment , or receiving first line treatment for at least 6 months
4. Expanded Disability Status Score (EDSS) * 5.0
5. Written informed consent ;Control group:
1. Minimum age 18 years
2. Written informed consent

Exclusion criteria

1. Past or current clinical relevant non-MS neurological or psychiatric disorder(s)
2. Past or current clinical relevant (auto)immune disorder(s)
3. Treatment with first line therapy for less than 6 months
4. Treatment with second line therapy
5. Relapse and/or steroid treatment in past 3 months
6. Pregnancy
7. MRI incompatibility, e.g. metal objects in or around the body, claustrophobia or inability to lie still in the scanner

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2016
Enrollment:	55
Type:	Actual

Ethics review

Approved WMO Date:	07-09-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-02-2018
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	NL57713.029.16