Quantitative MRI of extra-ocular muscles in myasthenia gravis

Published: 25-06-2019
Last updated: 15-05-2024

1. Explore the diagnostic value by comparing muscle volume, fatty infiltration and oedema/inflammation using qMRI in MG patients, healthy controls and MG mimics (other neuromuscular diseases and Graves* ophthalmopathy (GO) patients).2. Explore the...

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

Summary

ID

NL-OMON48436

Source
ToetsingOnline

Brief title
Quantitative MRI of extra-ocular muscles in myasthenia gravis

Condition

- Ocular neuromuscular disorders
- Muscle disorders
- Neuromuscular disorders

Synonym
Myasthenia gravis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Extraocular muscles, MRI, Myasthenia gravis, qMRI

Outcome measures

Primary outcome

(1) QMRI parameters (muscle fat fraction, muscle inflammation, muscle volume) which are hypothesized to differ between MG patients and the healthy/disease controls for diagnostic value.

(2) For the second objective comparing recently diagnosed and chronic MG patients for exploring the pathophysiology

Secondary outcome

(3) For the third objective comparing the qMRI parameters in time in the recently diagnosed MG group to measures of severity of disease to assess the predictive value for treatment response.

(4) For the fourth objective comparing qMRI parameters to functional measures in all groups for exploring the relationship with the symptoms

Study description

Background summary

The auto-immune disease myasthenia gravis (MG) affects the neuromuscular junction (NMJ) and commonly starts with weakness of the extra-ocular muscles (EOM). In patients with pure EOM symptoms and no acetylcholine receptor (AChR) antibodies, diagnosis is difficult and time-consuming. This causes significant burden for patients, delays effective treatment, and possibly increases the chance of developing generalized MG.

Furthermore, treatment usually consists of immune suppressant medication, of which corticosteroids are the most commonly prescribed. Unfortunately, long term steroid use carries a considerable risk of unacceptable side effects.

While immune suppressant treatment leads to a significant improvement in the majority of patients, 15% show only a moderate improvement or no improvement at all after treatment with corticosteroids.

In this study, we aim to assess inflammatory and structural changes of EOM with magnetic resonance imaging (MRI). Our pilot data using quantitative MRI (qMRI) show structural degenerative changes in the EOM of chronic MG patients, which has not been described in literature before. We aim to develop a novel diagnostic paradigm for AChR negative MG and a predictor for treatment efficacy in all MG patients by systematically comparing qMRI parameters of the EOM in clearly defined clinical groups of MG patients to healthy and disease controls (other neuromuscular diseases and Graves* orbitopathy (GO)).

Study objective

1. Explore the diagnostic value by comparing muscle volume, fatty infiltration and oedema/inflammation using qMRI in MG patients, healthy controls and MG mimics (other neuromuscular diseases and Graves* ophthalmopathy (GO) patients).
2. Explore the pathophysiology by comparing these qMRI parameters in recently diagnosed and chronic MG patients
3. Explore whether these qMRI parameters can predict response to treatment by comparing these qMRI parameters in time to measures of severity of disease.
4. Explore the relationship to the symptoms by comparing these qMRI parameters to functional measures of each individual extraocular muscle.

Study design

The study is an observational case-control study. All participants will undergo an MRI scan In addition, functional measures will be obtained to quantify symptoms, fatigability and function of the extraocular muscles for comparison to the qMRI parameters. One group with recently diagnosed MG patients will undergo one follow-up measurement after six months.

Study burden and risks

This study has no invasive procedures. Subjects with contraindications for MRI will be excluded. There are no known risks known associated with the use of MRI and the ophthalmologic measures performed. Participants have no personal benefit from participating in this study. However, the results study may contribute to the diagnosis and predictability of therapeutic response in all MG patients.

Contacts

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Eligibility criteria

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

Inclusion criteria

Recently diagnosed MG patients
- Definitive diagnosis of MG defined as the presence of serum autoantibodies (anti-acetylcholine receptor [AChR], anti-muscle specific tyrosine kinase [MuSK])
- Start of symptoms was less than a year ago
- No corticosteroid treatment received in the past year
- No TSH-receptor auto-antibodies, no laboratory signs of thyroid dysfunction (T4, TSH), Chronic MG patients
- Definitive diagnosis of MG, defined as described above
- Persisting symptoms of diplopia
- Start of symptoms was more than a year ago
- No TSH-receptor auto-antibodies, no laboratory signs of thyroid dysfunction (T4, TSH), Seronegative MG patients
- Clinical diagnosis of MG with asymmetric, fluctuating and fatigable muscle weakness and at least one abnormal neurophysiological test, indicative of neuromuscular dysfunction (repetitive nerve stimulation or single fiber EMG)
- No serum autoantibodies (anti-acetylcholine receptor [AChR], anti-muscle specific tyrosine kinase [MuSK])
- No TSH-receptor auto-antibodies, no laboratory signs of thyroid dysfunction (T4, TSH)

Healthy controls
- No symptoms of diplopia
- No ophthalmopathy
- No prior systemic treatment with corticosteroids, Patient controls: Graves* orbitopathy
- Definitive diagnosis of Graves* orbitopathy, Patient controls: Other neuromuscular disease
- Definitive diagnosis of a neuromuscular disease other than Myasthenia gravis

Exclusion criteria

- Subjects who are not legally capable
- Subjects under the age of 18
- Contraindications to MRI scanning, including:
o Claustrophobia
o Pregnancy
o Pacemakers and defibrillators
o Nerve stimulators
o Intracranial clips
o Metallic fragments
o Cochlear implants
o Ferromagnetic implants
o Hydrocephalus pump
o Permanent make-up
o Tattoos above the shoulders
o Piercings (unless they can be removed)
o Subjects who cannot keep their head still (eg. Tremor, Parkinson*s disease)
o Severe physical restriction (completely wheelchair dependent)
* In the case of uncertainty about the MRI-contraindications, the MR-safety commission of the radiology department will decide whether this subject can be included in the study or not.

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-09-2019
Enrollment:	130
Type:	Actual

Ethics review

Approved WMO Date:	25-06-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23441
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL68612.058.18
OMON	NL-OMON23441

Study results

Date completed: 04-10-2022

Actual enrolment: 89

Summary results
Trial is onging in other countries