Similar but not the same - Why are specific muscles less susceptible to disease than others in muscular dystrophies?

Published: 28-02-2019
Last updated: 11-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON48735

Source
ToetsingOnline

Brief title
Muscle pathophysiology in MD

Condition

- Muscle disorders

Synonym
Duchenne muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: NWO

Intervention

Keyword: Exercise, Magnetic Resonance Imaging, Muscular Dystrophy, Skeletal muscle

Outcome measures

Primary outcome

Muscle characteristics, in terms of MRI and/or EMG outcome measures, of the

lower extremity which correlate with the order in which muscles degenerate in

DMD and BMD .

Secondary outcome

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Study description

Background summary

Duchenne and Becker muscular dystrophy (DMD and BMD, respectively) are X-linked diseases, characterized by progressive muscle degeneration and muscle weakness resulting in functional disabilities. The cause of muscle degeneration is the absence, in DMD, or dysfunction, in BMD, of the dystrophin protein. Both diseases currently lack full market approved therapy and treatment mainly consists of symptomatic care.
Histologically, muscles in DMD and BMD show fibrosis, inflammation and fat replacement. These processes start in only a few muscles, whereas nearly all muscles become involved with progression of the disease. Differences in fat infiltration are also observed within muscles. Given the fact that the mutant gene is expressed in all muscles, the specific order between and within muscles is puzzling. Elucidation of this phenomenon could hold the key for the development of therapies aiming to preserve the muscles as long as possible.
Dystrophin plays an important role in the mechanical functioning of a muscle and is believed to protect the muscle against damage due to contractions. As such, one would expect that the extent to which different muscles are challenged mechanically plays a role and that muscles which are heavily and/or constantly used are more prone to degeneration. It is difficult to directly quantify the mechanical use of an individual muscle during a dynamic movement. A common, but indirect method is the recording of the instantaneous activation

pattern of muscles using surface electromyography (EMG). An alternative method is to quantify the use of a muscle by assessing the metabolic results of exercise using magnetic resonance imaging (MRI). MRI is non-invasive and can give temporal and spatial information on metabolism and perfusion, and on structure, displacement and size of specific muscles.
Recent technological advances in image acquisition speed and interleaving of sequences now enable the acquisition of more characteristics in one imaging session. To enable such acquisitions, we recently purchased an MRI compatible ergometer, *the Cardiostep* (Ergospect GmbH, Innsbruck, Austria). With this ergometer, participants can perform an exercise task mimicking climbing stairs. The CE marking of the ergometer is in progress for cardiac diagnostics under stress, but not for our intended use. The construction of the ergometer is compatible with 3 Tesla (T) and 7T systems.

Study objective

The primary objectives are to:
1) Adapt and optimize sequences and protocols to enable acquisitions during exercise with MRI and/or surface EMG.
2) Perform a study in healthy volunteers using the sequences and protocols developed in 1) to correlate MR and/or surface EMG findings with a database of muscle MD degeneration patterns.

Study design

This experimental study will be conducted at the Leiden University Medical Center (LUMC). The design of the experiments will depend on the objective studied. For objective 1, protocol optimization, healthy volunteers will undergo an MRI measurement lasting one hour at maximum. During this scan, the participant will be asked to perform an exercise task using an MR-compatible ergometer mimicking stair walking.
For objective 2, the volunteers will undergo two measurements, both lasting no more than one hour. The first measurement will be an MRI measurement of muscle use while performing an exercise task in the scanner using the MR-compatible ergometer. The second measurement is an surface EMG measurement of muscle activation while performing an exercise task outside of the scanner. To guide the EMG electrode placement ultrasound will be used. Depending on the intensity of the exercise, these two experiments can take place on the same day with 2-4 hours rest in-between.

Intervention

the participant will be asked to perform an exercise task using an MR-compatible ergometer mimicking stair walking.

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, EMG and ultrasound. Participants have no personal benefit from participating in this study. The data will support approaches aiming to preserve the muscles as long as possible.

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

Objective 1 and 2:
- Between 18-65 years old;Objective 3:
- Between 18-35 years old

Exclusion criteria

- Mentally disabled persons
- Diagnosed with a musculoskeletal or neurological disorder
- Pregnancy and a chance of being pregnant (as reported by the volunteer)
- Not having a general practitioner
- MRI contraindication (see appendix III): e.g. cardiac pacemaker, implants not approved for MRI (see www.mrsafety.com), claustrophobia, metal objects attached to the body that cannot be removed (fillings and most of other dental works are allowed). Decision on the MRI contraindication is made according to the guidelines outlined in the MR safety document of the Department of Radiology (http://iprova.lumc.nl/iDocument/Viewers/Frameworks/ViewDocument.aspx?DocumentID=2a2abd19-03e0-49d8-8681-916c2bc154e7&NavigationHistoryID=8178328&PortalID=181&Query=MR+safety)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-02-2020
Enrollment:	200
Type:	Actual

Medical products/devices used

Generic name:	MR compatible ergometer
Registration:	No

Ethics review

Approved WMO Date:	28-02-2019
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
CCMO	NL66392.058.18