The background of the reduced cerebral blood flow in Duchenne muscular dystrophy

Published: 28-09-2016
Last updated: 15-04-2024

The primary aim is to study if systemic or cerebral reactivity in DMD patients differs from healthy age-matched controls, to determine whether 1) cerebral autoregulation or 2) systemic blood pressure underlies the reduced cerebral perfusion in DMD....

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

Summary

ID

NL-OMON50456

Source
ToetsingOnline

Brief title
DMDPF - Duchenne muscular dystrophy cerebral perfusion study

Condition

- Muscle disorders

Synonym
duchenne muscular dystrophy, Duchenne's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Grant van het Duchenne Parent Project - NL

Intervention

Keyword: Brain, Cerebral blood flow, Duchenne muscular dystrophy, Vasculature

Outcome measures

Primary outcome

The primary end-points of this study are differences in systemic blood

pressure, global cerebral blood flow velocity and local cerebral perfusion

between healthy controls and patients with DMD.

Secondary outcome

- Systolic / diastolic blood pressure

- Heart rate

- Total peripheral resistance

- End-tidal CO¬2 content (PetCO¬2)

- Blood volume shift

- Sustained attention to response task score and regional brain blood flow

response

- General intellectual function based on PPVT

- Response time and pressing endurance measured with FePsy

- Cardiac function: stroke volume and shortening fraction of left ventricle

Study description

Background summary

Duchenne muscular dystrophy (DMD) is characterized by severe and progressive muscle weakness due to mutations in the DMD gene which lead to the absence of the dystrophin protein. A significant proportion of the affected children suffer from specific learning and behavioral disabilities which are more common

with distal mutations in the DMD gene that lead to absence of multiple dystrophin isoforms. Recently we reported a reduction in the amount of grey matter volume, altered white matter microstructure and reduced cerebral blood flow, assessed with magnetic resonance imaging (MRI) in DMD. Cerebral blood flow plays an important role in cognitive functioning and is potentially amenable to treatment. Therefore, we aim to explore the mechanism underlying the reduced perfusion in DMD.

Study objective

The primary aim is to study if systemic or cerebral reactivity in DMD patients differs from healthy age-matched controls, to determine whether 1) cerebral autoregulation or 2) systemic blood pressure underlies the reduced cerebral perfusion in DMD. The secondary aim is to study if changes in cerebral autoregulation are regional or global in nature.

Study design

We postulate that either cerebral autoregulation is disturbed or systemic blood pressure is reduced. We will use a two-step approach in an observational study design: (1) we will assess the response to orthostatic change using continuous transcranial Doppler (TCD) and finger plethysmography to monitor systemic and global cerebral blood flow velocity during head-up tilt (HUT). (2) We will quantify local cerebral blood flow using MRI during resting conditions and during two different tasks, one motor independent test that only targets the visual cortex, and one cognitive sustained attention task that involves multiple brain regions to study regional changes in cerebral autoregulation.

Study burden and risks

There is a risk of syncope during the HUT procedure. The participant will be tilted back to supine position should any pre-syncope symptoms occur. The MRI scans of the brain will be reviews by a radiologist for unexpected findings, which could be a burden. The participants have no personal benefits to taking part, but the data will aid our understanding of the brain involvement in DMD and help improve clinical care.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA

NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

* Age over 10 years (DMD) or 12 years (healthy)
* Male
* Ambulant
For patients only:
- a mutation in the DMD gene that affects both Dp427 and Dp140

Exclusion criteria

* No informed consent
* Medical history of CV disease, diabetes mellitus, neurological disease (other than DMD)
* History of recurrent syncope
* Joint contractures preventing the use of the HUT
* Contraindication to MRI exposure (*vragenlijst MRI onderzoek*)
* Inability to lie supine for at least 45 minutes

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-01-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	28-09-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	10-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Not approved

Date:	14-06-2017
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	09-03-2020
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

No registrations found.

In other registers

Register	ID
CCMO	NL58182.058.16

Study results

Date completed:	30-12-2020
Actual enrolment:	27