Brain INvolvement in Dystrophinopathies: BIND: Deep functional phenotyping of Duchenne Muscular Dystrophy and Becker Muscular Dystrophy patients (WP5) Part 2

Published: 13-05-2022
Last updated: 04-04-2025

The primary objective of the second part of the study, which is the focus of this application, is to perform a comparative analysis of the cognitive profile and MRI outcomes of DMD/BMD patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON51699

Source
ToetsingOnline

Brief title
BIND

Condition

- Musculoskeletal and connective tissue disorders congenital
- Neuromuscular disorders

Synonym
Becker muscular dystrophy, Duchenne muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: University college London
Source(s) of monetary or material Support: EU H2020 en Duchenne Parent projecten

Intervention

Keyword: Brain, Dystrophinopathies, MRI, Neuropsychology

Outcome measures

Primary outcome

The primary outcome measure for this study is the measure of intelligence as estimated by the Wechsler Intelligence test. As the sample includes participants from a range of age groups the most appropriate version will be used accordingly*

Secondary outcome

- Intelligence assessment:

o Raven 2 nonverbal concept formation

- Cognitive function assessments:

o Rey auditory learning task

o NEPSY-II comprehension of instruction

o NEPSY-II speeded naming

o NEPSY-II phonological processing

o NEPSY-II theory of mind (social cognition)

- Attention assessment:

o Fepsy simple reaction times

- Executive function assessment:

o BADS-C key search

- Academic attainment assessments:

o Speeded reading (WIAT-III, word reading subtest)

o Speeded arithmetic (WIAT-III, maths fluency subtest)

- MRI

o brain (sub-)volumes, cortical thickness, a voxel wise comparison of the local distributions of grey and white matter. Possible changes in volume of specific structures like the hippocampus or the amygdale should also follow from this analysis.

o anatomical connectivity(mean diffusivity (MD) and fractional anisotropy (FA).

o Resting state and task-based analysis of functional connectivity (ICA and Seed based)

o cerebral perfusion by ASL

o Analyses of MR spectroscopy with editing for GABA

Study description

Background summary

Intellectual disability and neurobehavioural comorbidities affect at least 50% of the individuals with Duchenne muscular dystrophy (DMD), which, although a rare genetic disease, is the most common form of muscular dystrophy in childhood. Approximately 800 new cases are diagnosed annually in Europe (~80 in the UK), with a worldwide prevalence of ~ 250,000 individuals. Several studies have documented that 25% of the DMD population has intellectual disability with recent studies suggesting that autism and clinically relevant hyperactivity affects 20% and 25% of DMD boys respectively [1-2]. A milder allelic variant, named Becker muscular dystrophy (BMD), has similar prevalence in the population and is also associated with variable degrees of central nervous system (CNS)

comorbidities [3], which however have been less well defined.

Whilst improvement in the standards of care of DMD have resulted in improved survival of these patients into adult life, the CNS comorbidities still have an impact on the quality and participation in life for DMD and BMD patients.

Currently there is a lack of phenotypically rich information to assist in the prognostication of CNS comorbidities, as existing databases and registries (e.g. UK NorthStar registry) typically focus on the motor milestones and associated physical disability of these patients. There is therefore, an urgent need to delineate the course and outcomes in DMD and BMD patients with a wide range of DMD mutations to provide information at the point of diagnosis and onwards for families, clinicians and service providers, as well as to pave the way to greater biological understanding and the personalization of interventions.

The study is divided into 2 parts, and this application refers to the second part of the study (the first part is ongoing).

Study objective

The primary objective of the second part of the study, which is the focus of this application, is to perform a comparative analysis of the cognitive profile and MRI outcomes of DMD/BMD patients.

Study design

Observational case-control and cohort study

Study burden and risks

There are no invasive procedures involved in this study. There is also no personal gain to taking part. Participants will need to come to the investigating site in person for half a day; if they opt for MRI this may require an additional 1.5 hour session. Travel expenses will be reimbursed and a gift certificate of 20 euros will be given.

Contacts

Public
University college London

Gower street 0
London WC1E6BT

GB
Scientific
University college London

Gower street 0
London WC1E6BT
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

For DMD patients:
- Male
- age 5-17 years
- genetically-proven diagnosis of DMD
- genetic mutation that abrogates expression of Dp427 alone (assigned in DMD Group 1: Dp427-/Dp140+) or both Dp427 and Dp140 (assigned to DMD Group 2: Dp427-/Dp140-); or all isoforms (assigned to DMD group 3)
- corticosteroid use either 10 days on/10 days off prednisolone or Vamorolone

For BMD patients:
- Male
- age 18-50 years
- genetically-proven diagnosis of BMD
- genetic mutation that decreases expression of Dp427 alone (assigned to BMD Group 1), of both Dp427 and Dp140 (assigned to BMD Group 2), or that eliminates expression of Dp140 while preserving expression of Dp427 albeit at reduced levels (assigned to BMD Group 3) or of all the isoforms (assigned to BMD Group 4).

For MRI healthy controls:
- Male
- age 5-50 years

Exclusion criteria

For DMD and BMD patients:
- Lack of a molecular diagnosis of DMD or BMD
- Mutation falls outside the regions of interest
- Any other severe co-morbidity or planned surgical intervention within 6 months from the study
- Inability to consent (for parents/guardians and adults) or assent. This will exclude the rare individuals with extremely severe learning disability, as the assent in these patients is impossible (or the consent in the adults); in addition it will not be feasible to perform MRI in this group of patients as we will not administer general anaesthetic. We anticipate this group will be enriched in the genotype lacking all dystrophin isoforms, and it is because of this that we have not indicated what is the precise number of individuals with this genotype to be recruited.
- Non-Dutch speakers.

For MRI healthy controls:
- any muscle disease
- a brain disorder (such as severe brain concussion in past history, congenital brain anomalies, epilepsy)
- Non-Dutch speakers

General exclusion criteria for MRI:
- Claustrophobia
- Pacemakers and defibrillators
- Nerve stimulators
- Intracranial clips
- Intraorbital or intraocular metallic fragments
- Cochlear implants
- Ferromagnetic implants (e.g. thoracic implant for scoliosis)
- Inability to lie supine for 45 minutes
- not having a general practitioner
- severe learning disability which will require a general anaesthetic

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:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-08-2022
Enrollment:	120
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	13-05-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	11-12-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	25-03-2025

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	NL79997.058.21