MR imaging of the spinal cord in patients with spinal muscular atrophy (SMA) and healthy controls

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To investigate the potential value of magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) on a 3 Tesla MRI system to visualize the spinal cord in SMA patients and to investigate motor connectivity in vivo in patients with SMA.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON42601

Source
ToetsingOnline

Brief title
MuSIC study

Condition

- Neurological disorders congenital
- Neuromuscular disorders

Synonym
progressive muscle disease, spinal muscular atrophy

Research involving
Human

Sponsors and support

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

Intervention

Keyword: diffusion tensor imaging, magnetic resonance imaging, spinal cord, Spinal muscular atrophy

Outcome measures

Primary outcome

The main study parameters will be both qualitative in terms of anatomy based on the anatomical MR images, and quantitative in terms of diffusion parameters including the fractional anisotropy, mean diffusivity, axial diffusivity and radial diffusivity. Structural changes will be regarded in relation to clinical characteristics (e.g. duration of illness, disease progression), genetic factors and clinical scores.

Secondary outcome

N/A.

Study description

Background summary

Spinal muscular atrophy (SMA) is a disorder characterized clinically by axial and proximal muscle weakness and pathologically by degeneration of α-motor neurons, and is caused by the homozygous deletion of the survival motor neuron (SMN) 1 gene. It is the most common genetic cause of infant mortality and causes significant disability and morbidity in survivors. The highly homologous SMN2 gene produces low amounts of functional SMN mRNA in patients with SMA, resulting in varying levels of SMN protein deficiency. SMN is important for RNA splicing and axonal transport, but the mechanisms that cause SMA are largely unknown. Recent findings in SMA animal models suggest that SMN deficiency causes abnormal connectivity of α-motor neurons with muscle at the neuromuscular junction (NMJ) and with sensory afferents in the spinal cord. Reduced connectivity of motor neurons may therefore be an important cause for muscle weakness in SMA. We have recently found that dysfunction of the neuromuscular junction is common in patients with SMA, which suggests that reduced pre- and postsynaptic connectivity of motor neurons is indeed an

important characteristic of SMA. Robust biomarkers for SMA severity and disease progression are needed because the relatively slow rate of progression has complicated the selection of clinical outcome measures for clinical trials. We hypothesise that reduced connectivity can be visualised in the spinal cord by using magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI). DTI could be helpful as a biomarker to evaluate efficacy of experimental treatment strategies. We believe that the results of this study may help to gain more insight in both pathogenic mechanisms and the applicability of DTI as a biomarker for disease severity in SMA patients.

Study objective

To investigate the potential value of magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) on a 3 Tesla MRI system to visualize the spinal cord in SMA patients and to investigate motor connectivity in vivo in patients with SMA.

Study design

Observational cross-sectional pilot study (time frame: 12 months)

Study burden and risks

Participants will undergo a clinical assessment and MRI at the University Medical Center (UMC) Utrecht. There are no known risks associated with MRI, besides temporary dizziness and claustrophobia. No contrast is needed. There are no direct benefits for the individual participant. We expect that the information acquired by this research project will provide new insights in the pathogenesis of SMA.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age 12 years or older
- Capable of thoroughly understanding the study information given
- Given written informed consent;Additional inclusion criteria for SMA patients:
- A diagnosis of SMA type 2 or 3, diagnosed on clinical grounds and confirmed by homozygous deletion of the SMN1 gene;;Additional inclusion criteria for healthy volunteers:
- Controls are healthy and do not have any history of SMA or other neuropathy related diseases;

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Tracheostomy, tracheostomal ventilation of any type, (non)-invasive ventilation
- Presence of pronounced swallowing disorders or orthopnoea (which make it dangerous to lie supine in the MRI scanner)
- Forced Vital Capacity >15% postural change between sitting and supine or symptoms of nocturnal hypoventilation (recurrent morning headaches, nightsweats, orthopneu).
- Contra-indications for MRI (e.g. a pacemaker, claustrophobia, pregnancy)
- Previous trauma or surgery of the (cervical) spine

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-08-2015
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	13-05-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL52615.041.15