SMA Motor Map - an extensive neurophysiologic protocol to assess (dys)function of the peripheral motor circuits in SMA

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

Summary

ID

NL-OMON49834

Source
ToetsingOnline

Brief title
SMA Motor Map

Condition

- Neurological disorders congenital

Synonym
Spinal Atrophy, Spinal Muscular Atrophy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Prinses beatrix spierfonds

Intervention

Keyword: Electromygram, EMG, SMA, Spinal Muscular Atrophy

Outcome measures

Primary outcome

Part 1

CMAP (APB (median nerve))

CMAP scan (APB (median nerve))

Excitability testing (APB (median nerve))

H-reflex (FCR (median nerve))

RNS (3Hz at APB (median nerve) and trapezoid (n accesorius); 50Hz at APB

(median nerve))

SNAP (median/radial/ulnar nerve, sural nerve)

Part 2

CMAP scan (APB (median nerve))

SNAP (median nerve, sural nerve)

Excitability testing (APB (median nerve))

Secondary outcome

n.a.

Study description

Background summary

Spinal muscular atrophy (SMA) is a monogenetic neuromuscular disorder in children and adults with a wide range in severity but a high degree of morbidity and impairment across the spectrum. SMA is a motor neuron disorder, with evidence for additional abnormal function of the axon and the neuromuscular junction (NMJ). The relative contributions of dysfunction of the different parts of the motor circuit to the clinical phenotype are unknown. The variability of dysfunction of the different parts of the motor unit might explain (parts of) the clinical variability between SMA types and individual patients.
The introduction of the intrathecally injected and high-cost drug *nusinersen* (Spinraza) that showed efficacy in survival and motor function in patients with SMA types 1 and 2 younger than 13 years, represents a major breakthrough. Followed by introduction of Risdiplam, which showed effacacy in survival and motor function as well. Important remaining questions are whether this treatment is efficacious in older patients and how to identify patients non-responsive to treatment. The relatively slow disease progression and insensitivity of clinical scales to detect subtle functional changes underlines the urgent need for new biomarkers.

Study objective

The goal of this research project comprises two important components that are intricately related:
1) To define the pathophysiological state of the peripheral motor pathway in patients with SMA and to determine the contribution of the constituting parts to disease severity and variability by means of the SMA Motor Map (SMM) (Part I)
2) To establish the usefulness of the targeted SMA Motor Map (tSMM) as a therapeutic biomarker in patients treated with SMN modulators (e.g. nusinersen or risdiplam) (Part II)

Study design

We will perform 2 parallel, observational studies:
Part One: Cross-sectional study
• Analyse the different parts of the motor circuit by use of the SMA Motor Map
Part Two: Longitudinal study
• Analyse the motor neuron status and its changes to treatment
• Analyse the biomarker function of the targeted SMA Motor Map for the efficacy on motor neuron function of the SMN modulating drug longitudinally (baseline, two and 14 months) in 100 patients treated with nusinersen. Children and adults who recently have started (<1 month) or will start nusinersen treatment will be enrolled in the sec-ond arm of the study.
SMA Motor Map and clinical scores will be performed and correlated with SMA type, disease duration, age and SMN2 copy number. Objective and patient-reported outcomes will be cor-related to the SMA Motor Map in order detect neurophysiologic biomarkers for (non-) re-sponse on therapy.

Study burden and risks

This research will be done in children and adults with SMA. The burden of participation con-sists of undergoing the (targeted) SMA Motor Map.
Overall, the burden and risk associated with participation in the study will be minor using the correct equipment and protocols. All study personal will be trained to perform the investigations safely.
The criteria of the Nederlandse Vereniging voor Kindergeneeskunde (Dutch association of Paediatrics) concerning research involving children will be strictly applied.

Contacts

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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

Part One:
• SMA type 1, 2, 3 and 4, confirmed with a homozygous or heterozygous deletion of SMN1
• *12 years and older
• Treatment-naïve concerning SMN- modulators or NMJ-modulators (including pyri-dostigmine and oral salbutamol)
o In case of the use of pyridostigmine by indication of SMA, patients are asked to stop treatment 1 day prior to the examination

Part Two:
• SMA type 1, 2, 3 and 4, confirmed with a homozygous or heterozygous deletion of SMN1
• *12 years and older
• Treatment with SMN- modulator

Exclusion criteria

Strong apprehension against the performance of EMG of any kind

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-05-2020

Enrollment:	177
Type:	Actual

Ethics review

Approved WMO Date:	15-04-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC NedMec

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	NL72562.041.20