Natural history and biomarker identification in Spinocerebellar Ataxia type 7

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Primary objective:- To identify (a combined set of) clinical and non-clinical markers most sensitive to disease progression in Dtuch SCA7 mutation carriers.Secondary objectives:- To quantify the annual change in disease-relevant clinical scales and...

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

Summary

ID

NL-OMON51803

Source
ToetsingOnline

Brief title
SCA7

Condition

- Neurological disorders congenital
- Movement disorders (incl parkinsonism)

Synonym
Ataxia, disorder of coordination

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Hersenstichting

Intervention

Keyword: Ataxia, Biomarker discovery, Natural history study, SCA7

Outcome measures

Primary outcome

- To identify (a combined set of) clinical and non-clinical markers most sensitive to disease progression in Dtuch SCA7 mutation carriers.

Secondary outcome

- To quantify the annual change in disease-relevant clinical scales and patient-reported outcome measures in SCA7 patients.

- To establish the utility of ophthalmologic assessment analysis as a surrogate biomarker in SCA7.

- To establish the utility of MR measures as surrogate disease progression markers in SCA7.

- To develop and establish the utility of biochemical disease and progression markers.

- To establish the utility of automated gait analysis as surrogate biomarker in SCA7.

- To generate a natural history data set of clinical parameters, MRI, ophthalmologic, and biochemical biomarker measurements in SCA7 that can be exploited for further collaborative research in SCA7.

Study description

Background summary

SCA7 is a rare, genetic, currently untreatable neurological disorder that leads to immobility and blindness. The chance the gene is passed on to children is 50%. The brain abnormality in SCA7 is mostly found in the cerebellum, but other areas are also affected, as is the eye. The cause of these abnormalities is an error in the ataxin-7 protein.

Currently patients are treated symptomatically, which often is ineffective against progressive loss of mobility and independence, eventually leading to an early death. There are high expectations for the development of a genetic therapy that could halt the disease progression. The low number of SCA7 patients makes it essential to have sensitive surrogate markers for disease progression. Validated clinical parameters are present for ataxia, but their interaction and sensitivity in SCA7 are unknown. There is a lack of biomarkers for SCA7, but the availability of these is essential for trials in rare diseases. This study will therfore develop and validate biomarkers for SCA7 as well as map the disease progression of this disorder.

Study objective

Primary objective:
- To identify (a combined set of) clinical and non-clinical markers most sensitive to disease progression in Dtuch SCA7 mutation carriers.

Secondary objectives:
- To quantify the annual change in disease-relevant clinical scales and patient-reported outcome measures in SCA7 patients.
- To establish the utility of ophthalmologic assessment analysis as a surrogate biomarker in SCA7.
- To establish the utility of MR measures as surrogate disease progression markers in SCA7.
- To develop and establish the utility of biochemical disease and progression markers.
- To establish the utility of automated gait analysis as surrogate biomarker in SCA7.
- To generate a natural history data set of clinical parameters, MRI, ophthalmologic, and biochemical biomarker measurements in SCA7 that can be exploited for further collaborative research in SCA7.

To reach trial-readiness

Study design

A prospective cohort study will capture the natural history of Dutch SCA7 patients over the course of one year. We will include 20 SCA7 patients and 20 matched controls. All study participants will undergo detailed annual

assessments at baseline and 1 year after baseline.

The age matched controls will be recruited from an already existing cohort of controls for SCA1, they will be asked formal consent for the use of their data for the SCA7 study. If needed the existing cohort will be enriched with new controls recruited for the SCA7 study.

Study burden and risks

Deelnemers bezoeken het studiecentrul eenmaal per jaar, gedurende 1 jaar (2 bezoeken in totaal). Deze bezoeken omvatten voor alle deelnemers een klinisch onderzoek, MRI scan (45 minuten), looptesten, oogheelkundig onderzoek, bloedmonsters, en vragenlijsten. Patiënten kunnen tevens kiezen om mee te doen aan het optionele onderdeel om tweemaal een lumbaalpunctie te ondergaan.

Participants will visit the study centre once a year for one year. These two visits include a clinical assessment battery, including validated ataxia-scales and tests to assess cognitive function, mood, activities of daily living. Ophthalmologic assessment, MRI-scans (45 minutes) and blood samples will be acquired at each visit. Patients will be asked to optionally undergo a lumbar puncture twice (baseline and after 1 year), to obtain a cerebrospinal fluid sample. Controls will receive a similar assessment protocol, without the lumbar puncture.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Participants have to be 16 years or older;
- Particpants need to have a proven mutation in the SCA7 gene (patient cohort only);
- Participants is able and willing to sign the informed consent.

Exclusion criteria

- Participant has prior history of any neurological disorder, or another disease that significantly influences gait;
- Participant has any general contraindications for MRI

For participants who consider to consent for a lumbar puncture extra exclusion criteria apply:
- Allergy to local anesthetic agents;
- Medical history of compression of spinal cord, spinal surgery, skin infection, developmental abnormalities in lower spine;
- Use of blood coagulopathy and/or anticoagulant medication;
- Clinical (or previous MRI) evidence of structural (space occupying) cerebral abnormalities that are not compatible with the performance of an LP including malignancies, abscess or obstructive hydrocephalus;
- Another brain disorder, besides SCA7

The following exclusion criteria are used to exclude research participants from undergoing an ophthalmological assessment:
Being diagnosed with (or with a combination of):
- Clinical manifest glaucoma
- Diabetic maculopathy
- Moderate non-proliferative diabetic retinopathy or worse
- Age-related macular degeneration
- Retinal degeneration besides SCA-7 related

Having a history of:
- Retinal detachment surgery
- Ocular trauma involving the posterior segment

Study design

Design

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

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2022
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	12-07-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-09-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL81226.091.22