Looking beyond the central nervous system in SCA3: nerve and muscle ultrasound as potential imaging markers to quantify and monitor peripheral nervous system degeneration

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To investigate whether peripheral nerve and muscle ultrasound can be used as reliable diagnostic and monitoring biomarkers of PNS involvement in SCA3. Specifically, we will examine: 1) Whether peripheral nerve and muscle ultrasound are able to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON53256

Source
ToetsingOnline

Brief title
Nerve and muscle ultrasound in SCA3

Condition

- Movement disorders (incl parkinsonism)

Synonym
Spinocerebellar ataxia type 3

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: National Ataxia Foundation en Ataxia UK

Intervention

Keyword: Muscle, Nerve, Spinocerebellar ataxia type 3, Ultrasound

Outcome measures

Primary outcome

Nerve ultrasound:

- Cross-sectional areas of the median, ulnar, superficial radial, tibial, and sural nerves.

Muscle ultrasound:

- Muscle volume, fasciculations, and echo intensity of the geniohyoid, digastric, masseter, sternocleidomastoid, trapezius, biceps brachii, flexor carpi radialis, first dorsal interosseus, rectus abdominis, rectus femoris, tibialis anterior, and medial gastrocnemius muscles.

Secondary outcome

Nerve conduction studies:

- Sensory nerve action potential (SNAP) amplitudes and conduction velocities of the median, ulnar, superficial radial, and sural nerves.
- Compound muscle action potential (CMAP) ampliitudes, motor nerve conduction velocities, and distal motor latencies of the median, ulnar, and tibial nerves.

Plasma neurofilament light chain concentration.

Clinical measures / questionnaires:

Scale for the Assessment and Rating of Ataxia (SARA), SCA Functional Index (SCAFI), Total Neuropathy Score clinical version, muscle cramp scale (MCS), Cramps Disability Scale (CDS), Friedreich Ataxia Rating Scale Activities of Daily Living (FARS ADL), cerebellar cognitive affective syndrome (CCAS) scale, EQ-5D-5L, Patient Health Questionnaire-9 (PHQ-9), Fatigue Severity Scale (FSS), International Restless Legs Scale (IRLS), Pittsburgh Sleep Quality Index (PSQI), Patient-Reported Outcome Measure of Ataxia (PROM-Ataxia), Personal Questionnaire (PQ), Goal Attainment Scale (GAS), Utrecht Coping List (UCL-P), Utrecht Proactive Coping Competention List (UPCC) and Neuropathic Pain Scale (NPS).

Study description

Background summary

Spinocerebellar ataxia type 3 (SCA3) is a progressive multisystemic disorder that severely impacts quality of life. Besides degeneration of the cerebellum, brainstem, spinal cord, and basal ganglia, the disease is characterized by widespread involvement of peripheral nervous system (PNS) components, including the dorsal root ganglia, peripheral nerves, and anterior horn cells. Degeneration of these structures not only leads to bothersome complaints that impair patients* daily functioning and quality of life (e.g., muscle cramps, pain, tingling, numbness, and muscle atrophy), but may also importantly add to sensory ataxia severity and therefore accelerate overall ataxia progression. Nonetheless, the vast majority of studies looking for potential biomarkers focused on the central nervous system, most notably cerebellar and pontine MRI volumes and cerebrospinal fluid proteins. Driven by this lack of PNS markers and the extensive application of peripheral nerve and muscle ultrasound for patients with neuromuscular disorders in our center, we aim to investigate whether both imaging techniques can yield reliable diagnostic and monitoring biomarkers of PNS involvement in SCA3.

An additional subcomponent of this study is aimed to examine the feasibility of

implementing the 'Goal Attainment Scale' (GAS), an alternative clinical outcome measure, within this specific patient population. We will explore its correlation with other clinical outcome measures obtained in this study, and also evaluate associations between patient-reported outcome measures obtained in this study and passive and proactive coping capacities.

Study objective

To investigate whether peripheral nerve and muscle ultrasound can be used as reliable diagnostic and monitoring biomarkers of PNS involvement in SCA3. Specifically, we will examine:

1) Whether peripheral nerve and muscle ultrasound are able to adequately differentiate SCA3 mutation carriers from healthy controls without a neuropathy or myopathy (i.e., if these techniques could serve as diagnostic biomarkers of PNS degeneration).
2) Whether peripheral nerve and muscle ultrasound are able to detect abnormalities already in pre-ataxic SCA3 mutation carriers.
3) Whether peripheral nerve ultrasound is able to already detect abnormalities in individuals without electrophysiological evidence of nerve dysfunction.
4) Whether peripheral nerve and muscle imaging abnormalities correlate with ataxia severity, disease duration, activities of daily living, patient-reported cramp and neuropathy severity score, cerebellar cognitive affective syndrome scale score, health-related quality of life, fatigue, mood, restless legs severity, sleep quality, and PROM-Ataxia score.
5) Whether nerve and muscle imaging abnormalities correlate with serum neurofilament light chain concentrations, which is a marker of damage to large-caliber myelinated axons.
6) Whether nerve and muscle ultrasound are able to detect changes at a follow-up measurement after 1 year (i.e., if they could serve as monitoring biomarkers of PNS degeneration).
7) Whether the Goal Attainment Scale is applicable to SCA3 patients and what factors should be considered for its future use in a trial setting.
8) Whether there is a relationship between a patient's coping strategy and the outcomes of patient-reported outcome measures (such as EQ-5D-5L, PHQ-9, and PROM-ataxia)

Study design

Prospective longitudinal study.

Study burden and risks

The burden for participants consists of two study visits. All measurements are without significant side effects ("negligible risk").

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

SCA3:
(1) Adults with a (2) genetically confirmed SCA3 mutation spanning the disease spectrum (i.e., from preclinical mutation carriers to moderate/severe ataxia), and (3) able and willing to sign the informed consent.

Healthy controls:
Age- and sex-matched healthy controls (without a medical history of neurological disorders), able and willing to sign the informed consent.

Exclusion criteria

Other diseases or conditions associated with neuropathy (e.g., diabetes mellitus, previous exposure to cytostatic drugs, alcohol abuse, inflammatory neuropathy, hereditary neuropathy, etc.) and myopathy (e.g., inflammatory/immune-mediated myopathy, metabolic myopathy, toxic myopathy, muscular dystrophy, myotonia, etc.).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-10-2023
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	11-07-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2024
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	NL84104.091.23