PROSPAX: An integrated multimodal progression chart in spastic ataxias

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Primary Objective: • To chart longitudinal disease progression rates for SPG7 and ARSACS by a multisite, prospective natural history study. Secondary Objective(s): • Development of a new clinical SPAX composite scale.• To identify (a combined set of...

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

Summary

ID

NL-OMON55341

Source
ToetsingOnline

Brief title
PROSPAX

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: ZonMW

Intervention

Keyword: Biomarker discovery, Natural history study, Spastic ataxia

Outcome measures

Primary outcome

- Annual rate of change measured by SARA and SPRS.

Secondary outcome

- Annual rate of change measured by newly designed SPAX composite scale.

- Longitudinal change in patient-reported, MRI, clinical assessments and blood

biomarker outcome measures in patients versus controls.

- Disease progression measured by alternative patient-centered, digital

sensor-based smartwatch biomarkers via the SPAX.app (mobile SPAX disease score).

In addition to the endpoints, demographical characteristics (age, gender,

disease duration) and mutation type, will be collected at baseline.

Study description

Background summary

Spastic ataxias (SPAX) represent a rapidly growing group of >100 rare neurodegenerative genetic diseases (prevalence 10-15/100.000) with joined affection of the cerebellum and corticospinal tract (CST), They often manifest early in life, with devastating chronically progressive consequences on daily life while treatment options are limited to symptom relief. The two most common SPAX disease are Autosomal-recessive Spastic Ataxia Charlevoix Saguenay (ARSACS) and SPG7, accounting for about 10-60% of all SPAX patients. Recent genetic advances facilitate the development of targeted molecular therapies and pave the way towards a precision medicine approach of SPAX.

However, effective trial-planning in SPAX diseases is hampered by several challenges. First of all, SPAX patients and clinical data or biomarker

collections are fragmented. There are limited numbers of patients per center and per disease, often scattered over large geographic areas. Besides, clinical assessments are non-standardized and biomaterial or brain imaging collections are small, decentralized and unconnected. Second, there is lack of SPAX-specific, longitudinally validated outcome measures and a complete lack of digital and patient-reported outcomes. Although PROSPAX partners have developed and validated the two main clinical rating scales capturing ataxia and spasticity (Scale for the Assessment and Rating of Ataxia (SARA) and Spastic Paraplegia Rating Scale (SPRS), respectively, the sensitivity of these measures to track and understand overlapping dysfunction of the cerebellum and CST can be further increased. Besides, models of disease progression in SPAX, capturing the relative dynamics of outcome measure changes over the course of the disease, are lacking.

Therefore the aim of this study is to longitudinally validate existing disease markers and develop novel clinical, digital, imaging and molecular outcome measures specifically tailored to cerebellar and CST dysfunction, in a cohort of ARSACS and SPG7 patients.

Study objective

Primary Objective:
• To chart longitudinal disease progression rates for SPG7 and ARSACS by a multisite, prospective natural history study.

Secondary Objective(s):
• Development of a new clinical SPAX composite scale.
• To identify (a combined set of) clinical and non-clinical markers (PROMs, MRI, clinical assessments, biochemical markers) most sensitive to change over time in SPAX patients in comparison with controls.
• To map the effects of disease progression during daily living with SPAX by creating and validating a mobile toolbox (SPAX.app) of digital, smartphone and wristband sensor-based performance measures of daily living that will capture patient-centered outcomes (PCOM) of daily living with SPAX.

Study design

This prospective cohort study will capture the natural history of Dutch spastic ataxia patients over the course of 4 years. We will include 15 SPAX patients and 5 matched healthy controls. All study participants will undergo detailed annual assessments at baseline, 1 year after baseline and 2 years after baseline. After three and four years, the participants will have a telephone consultation to administer a set of questionnaires. Besides, participant will participate in the development of the SPAX.app. They will undergo an extra assessment in the gait and balance lab of the Rehabilitation department and will participate in self-assessment of the SPAX.app in their homesetting (6

weeks for healthy controls, +-30 weeks for SPAX patients)

Study burden and risks

Participants will visit the study centre once a year for two consecutive years. These three visits include a clinical and motor assessment (validated ataxia and spasticity-scales and sensor-based quantitive assessment of motor deficits) MRI (60min) scans. Blood samples will be acquired at each visit. Besides patients will complete questionnaires from PROMIS®, which stands for Patient Reported Outcomes Measurement Information System. Measuring patient-reported health status for physical, mental, and social well-being. After three and four years, the participants will have a telephone consultation to administer a set of questionnaires (FARS-ADL and PGI-C).

For development of SPAX.app, patients will visit the gait and balance lab of the Rehabilitation department once, and will participate in self-assessment of the SPAX.app in their homesetting (6 weeks for healthy controls, +-30 weeks for SPAX patients)

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

• Participant is 16 years or older;
• Participant has a proven mutation in the SACS (ARSACS) or SPG7 gene (patient cohort only).
• Participant is able and willing to sign the informed consent.

Exclusion criteria

• Prior history of any neurological disorder, or another disease that significantly influences motor function;
• General contraindications for MRI (only for MRI study).

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):	25-01-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	23-09-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-04-2024
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	NL73094.091.20