Network Patterns in SCA3 and SCA6 Imaged by DWI, fMRI, MRI-T1 and FDG-PET

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

Summary

ID

NL-OMON41274

Source
ToetsingOnline

Brief title
Imaging of SCA3 and SCA6

Condition

- Movement disorders (incl parkinsonism)

Synonym
spinocerebellar ataxia | inherited disorder in which an inability to coordinate movement occurs

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Ataxia, Diffusion Imaging, SCA, Spherical Deconvolution

Outcome measures

Primary outcome

- the distribution of regional decreased directionality of diffusion (based on diffusion weighted images);

- decreased functional coherence between GM areas (based on Blood Oxygen Level Dependent (BOLD) RS-fMRI images);

- GM atrophy (based on T1 images);

- decreased GM FDG uptake (based on FDG-PET images);

- clinical assessment scores on the Scale for the Assessment and Rating of Ataxia (SARA), language tests (the Aachen Aphasia Test, the Boston naming test, the Semantic Verbal Association Test, and the Semantic Visual Association Test) and executive functioning tests (Letter and Category fluency, the Rule Shift Test from the Behavioural Assessment of the Dysexecutive Syndrome, charts 1 and 2 from the Stroop Test and the Hayling Sentence Completion Test).

Secondary outcome

(not applicable)

Study description

Background summary

The Spinocerebellar Ataxias (SCA) constitute a group of hereditary neurodegenerative disorders that share the clinical feature of ataxia as their most prominent characteristic. Neuropathologically, the various genetic subtypes are all associated with cerebellar atrophy, but apart from this,

specific subtypes display specific clinical features and patterns of neurodegeneration that affect other parts of the central and peripheral nervous system. E.g., while the SCA6 genotype manifests clinically as a *pure cerebellar syndrome*, SCA3 is characterized by multiple extracerebellar features. But due to the rarity of these diseases and their protracted disease courses that span many years to decades, the amount of information on the extent of neuropathological alterations, particularly in early disease stages, is scarce.
Although the cerebellum is traditionally considered to be involved in motor coordination, its role in cognitive and emotional processing has received increasing attention in the past two decades. In line with this notion, people with spinocerebellar ataxia often complain not only about motor impairment and coordination problems, but also about cognitive and emotional changes and fatigue. In a recent study, we demonstrated language impairment in SCA6 patients, not only in expression but also in perception, which was related to the severity of ataxia (paper submitted). An important issue here is whether these symptoms are caused by the cerebellar degeneration itself, or by associated neuropathological changes outside the cerebellum, e.g. in the basal ganglia or the cortex.
To gain more insight in the extent of cerebellar vs. extracerebellar pathology this study aims to employ multimodal brain imaging in patients with two genetically distinct forms of spinocerebellar ataxia, SCA6 and SCA3, as well as in controls. To that end, various Magnetic Resonance Imaging (MRI) modalities will be combined with Positron Emission Tomography (PET) imaging. Diffusion Weighted Imaging (DWI) will be used to study white matter (WM) tracts whose structural integrity may be particularly sensitive to degeneration. Structural MRI, Resting State Functional MRI (RS-fMRI) and FluoroDeoxyGlucose PET (FDG PET) will help to assess grey matter (GM) integrity. In addition, a number of tests that assess language and cognitive executive functioning will be applied to subjects, in order to confirm our previous findings of language impairment in SCA6 patients.

Study objective

The main objective of this study is to characterize the features and the extent of extracerebellar structural pathology in SCA3 and SCA6 patients.
Secondary objectives are:
- To explore the sensitivity of DWI and other imaging modalities in detecting neuropathological features in SCA3 and SCA6.
- To establish correlations between findings of the various imaging modalities employed (DWI, VBM, RS-fMRI and FDG PET, i.e. to examine the WM/GM correlation).
- To establish correlations between abnormalities found by the various imaging modalities and the clinical, neuropsychological and genetic characteristics of the included patients.

Study design

A cross-sectional study of patients with SCA3 and SCA6 as well as healthy control subjects who will undergo neurological and neuropsychological examination, a MRI scan (acquiring T1, T2, DWI, RS-fMRI and Fluid Attenuated Inversion Recovery (FLAIR)) and a FDG-PET scan.

Study burden and risks

The risks associated with participation are considered negligible and the burden can be considered minimal as there is ample experience with these PET and MRI investigations. Subjects will undergo 1 MRI scan (+/- 1 hour), 1 FDG-PET scan (+/- 45 minutes), 1 neurological examination (+/- 10 minutes) and 1 cognitive examination (+/- 1.5 hour). Taken into account the switches between the diverse locations where the various examinations will be performed, as well as rest moments in between, the total examination time will come down to one visit to the UMCG lasting a maximum of 8 hours (or, under exceptional circumstances when planning will not permit, to two visits to the UMCG lasting a maximum of 4 hours each).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

patients: genetically confirmed SCA3 or SCA6 in an early stage (that is, not wheelchair-bound) and aged 18-65
healthy controls: aged 18-65

Exclusion criteria

history or presence of neurological disorders (in case of patients: other than SCA) for which referral to a neurologist/neurosurgeon was necessary and for healthy controls also a family history of SCA, if genetic information on the absence of the particular SCA mutation is not available;
presence of ferromagnetic material in the body, (suspicion of) pregnancy (which implies that in case of doubt subjects will be denied to enroll in the study), claustrophobia, age below 18 or above 65 and having received radiation in the context of medical research in the past 5 years constitute exclusion criteria for all subjects.

Study design

Design

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

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	12-02-2015
Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	20-03-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL45036.042.13