Determination of presymptomatic disease features in Spinocerebellar Ataxia type 6 (SCA6) patients

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

Summary

ID

NL-OMON35909

Source
ToetsingOnline

Brief title
PRESCA

Condition

- Movement disorders (incl parkinsonism)

Synonym
ADCA, SCA6

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cerebellum, Motor behavior and learning, Presymptomatic, SCA6

Outcome measures

Primary outcome

In order to determine pre-symptomatic features in SCA6 we will study use of a broad range of behavioral and motor tests: delay eyeblink conditioning, prepulse inhibition, prism adaptation test and motor performance (nose point). We will follow alterations of the brain with magnetic resonance imaging technique (MRI) without use of contrast agents. Specific attention will be paid on the atrophy in the brainstem, pons and cerebellum. Furthermore, neurological and clinical genetically investigations will be performed (SARA, INAS, SCAFI). Daily functioning and other relevant factors (like medication use) will be reviewed through questionnaires. Correlations between MRI-scores and data from behavioral-en motortests will be investigated.
Scores on classical delay eyeblink conditioning, PPI, PRISMA adaptation test and finger nose point of patients will be compared to controls

Secondary outcome

CAG repeat in relation to the found scores on classical delay eyeblink conditioning, PPI, PRISMA adaptation test and finger nose point.

Study description

Background summary

Spinocerebellar Ataxia type 6 (SCA6) is one of the dominant hereditary ataxias.
In this disease onset is defined as the moment permanent ataxia manifests

itself. However, early features in this disease, named the pre-symptomatic features, are often present prior to the onset of permanent ataxia and question whether the criteria used for onset of the disease are correct.
SCA6 is a hereditary disease that manifests during aging, averaging at 50 years of age. The genetical defect however, is already present at birth. The cause of this delay in onset is still unclear. SCA6 is caused by a polyglutamine repeat in a subunit of a voltage gated calciumchannel that is located in the Purkinjecells. This faulty subunit causes the channels to disfunction and this eventually leads to cell loss in the cerebellum. In later stages of the disease there is marked atrophy of the cerebellum on MRI.
During motor performance, motor learning and motor control the cerebellum is heavily involved in adjusting movements. In cerebellar ataxia patients these performances are disturbed and we use behavioral tests to detect cerebellar dysfunction.

SCA6 patients, who carry the disease mutation, but do not express any permanent symptoms yet, are called presymptomatic patients. These individuals offer an opportunity to study presymptomatic manifestations of cerebellar disease that might not be clinically apparent, but could be measurable before permanent symptoms of ataxia appear.
We already examine the motor performance and motor learning behaviors in symptomatic SCA6 patients. In this study we will yearly examine pre-symptomatic patients to detect the transition from the pre-symptomatic stage towards SCA6.
It is important to detect early signs if disease modulating compounds become available. Treatment may be most efficient when introduced in the earliest stage of disease but is not recommended before disease onset considering the side effects. Therefore, recognition of pre-symptomatic features is valuable and can be a promising approach.

Study objective

We aim to determine onset of SCA6 disease more accurate then with the clinical scores and questionnaires that are currently used.
We will study motor performance, motor learning behavior, PPI and MRI scans in pre-symptomatic SCA6 patients and compare these results to controls. The main objective is to find early pre-symptomatic disease features that can predict onset of disease more accurately than clinical assessment.
By following the presymptomatic patients in their transition towards symptomatic disease we also hope to elucidate SCA6 performance.
Last, we will examine correlations between CAG repeat length and early symptoms, impaired delay eyeblink conditioning and PPI. This will be done by making a comparison between results in presymptomatic patients and in healthy controls.

Study design

All patients and control subjects will be examined yearly during a ten years follow-up case-control study.

Study burden and risks

There are no risks associated with participation.
Subjects will not have a direct benefit of joining this study. This is why we strive to make the burden as low as possible. They will only be asked to come in for testing once a year and will undergo an MRI once every 3 years. If necessary we can visit people at their homes with our mobile testing unit (the NeurasBus) to ensure proper follow-up.

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: Subjects from 18 years and up with genetically diagnosed SCA6 without clinical symptoms of ataxia
Controls: Healthy subjects from 18 years and up.

Exclusion criteria

Patients and controls:
Other neurodegenerative conditions than SCA6
Other conditions than SCA6 that influence gait
History of psychiatric or neurological disease
Deafness or hearing difficulties
Pregnant women and people with other contra-indications for MRI will be included but in the study, but will not undergo MRI. In the case of pregnancy MRI will be planned around it.

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):	29-09-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	15-07-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL35484.078.11