# Understanding and manipulating neural compensatory mechanisms in SCA3 patients

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We expect to isolate system-level neural mechanisms that support compensation for gait and balance in patients with SCA3 following an intensive five-week training programme on a virtual reality treadmill. The goal of the project is to understand...

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

## Summary

### ID

NL-OMON38791

**Source**
ToetsingOnline

**Brief title**
Compensatory mechanisms in SCA3

### Condition

- Movement disorders (incl parkinsonism)

**Synonym**
Cerebellar ataxia, coordination difficulties

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radboud Universiteit Nijmegen
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Cerebellar ataxia, Compensation, MRI, Training

## Outcome measures

### Primary outcome

- Changes in grey matter volume (cerebellum or other brain areas)

-Changes in functional connectivity between the cerebellum and the rest of the

brain

-Changes in the neural circuitry that supports gait and balance

We will focus on changes between patients and controls, as well as between

patients before and after training

### Secondary outcome

Not applicable

# Study description

### Background summary

Dominantly inherited spinocerebellar ataxias (SCAs) are a clinically, genetically, and pathologically heterogeneous group of neurodegenerative disorders mainly affecting the cerebellum and its connections. SCA3 is the most common genotype. This disorder gives rise to progressive difficulties of gait, dexterity, speech and eye movements, and leads to immobility and loss of independence. There is currently no treatment.
Own pilot data suggest that specific forms of training are able to induce improvements in gait and balance. We think that this is due to cerebral compensation. We wish to capture these compensatory mechanisms by means of sophisticated MRI scans before and after this training. The future goal is to find ways to further stimulate such compensatory mechanisms as a form of treatment.

### Study objective

We expect to isolate system-level neural mechanisms that support compensation for gait and balance in patients with SCA3 following an intensive five-week training programme on a virtual reality treadmill. The goal of the project is to understand whether the behavioral improvements observed in SCA3 patients after the training programme are supported by cerebral circuits directly targeted by the neurodegenerative process, or by system-level reorganization across vicarious cerebral circuits that support the same function. We will consider three types of changes that have proven sensitive to capture physiological and pathological variations in the human brain, namely changes in the grey matter structure of the cerebellum, changes in the functional connectivity of the cerebellum, and changes in the cerebral circuits supporting gait and balance. The results of this project will be important for structuring future training interventions.

## Study design

Explorative study.

Before the training:
Fysical examination
Kinematic analysis of gait and balance
Baseline MRI scan session including: structural MRI, DWI, funtional restingstate MRI en functional task MRI.

Training:
5 weeks of C-mill training, twice a week, one hour per session

After training:
Kinematic analysis of gait and balance
MRI session including: structural MRI, DWI, funtional restingstate MRI en functional task MRI

To control if the cerebral changes are due to the training, rather than to spontaneous fluctuations, 5 patients and 5 healthy subjects will undergo an extra MRI measurement 5 weeks before the start of the C-mill training. This MRI protocol is similar to those above.

## Study burden and risks

There are no clear risks for the participants.

The burden consists of undergoing MRI scans, kinematic analysis of gait and balance, and 10 training sessions.
This will take about 15 hours in total (excluding time for travel)

# 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

Proven mutation of the SCA3 gene
Age > 18 years
Symtomatic ataxia
SARA score of gait is maximally 3 (they need to be ambulant)

## Exclusion criteria

Contraindications for MRI scanning (e.g. pacemaker, claustrofobic)
Epilepsy
Other neurological disorders

Other gait disorders

# Study design

## Design

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

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 24-01-2014 |
| Enrollment: | 40 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 25-07-2013 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 09-07-2014 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 11-08-2015 |
| 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 | NL44688.091.13 |