# Freezing of gait in Parkinson's disease: in search of the underlying mechanism and the application of a new treatment option

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To investigate whether impairments of shifting between response sets underlie motor freezing in PD and to investigate the efficacy and the neural mechanism by which MPH improves gait and cognition in PD patients with FOG.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Movement disorders (incl parkinsonism) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON33147

**Source**
ToetsingOnline

**Brief title**
Freezing of gait in Parkinson's disease

### Condition

- Movement disorders (incl parkinsonism)
- Cognitive and attention disorders and disturbances

**Synonym**
Hyperkinetic rigid syndrome

**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:** Freezing of Gait, Methylphenidate, Parkinson□s disease, Set shifting

## Outcome measures

### Primary outcome

First primary outcome: performance of PD patients with FOG on behavioral tasks compared to PD patients without FOG and healthy controls.

Second primary outcome: cerebral activation patterns during shifting between response sets in PD patients with FOG, relative to PD patients without FOG and healthy controls.

Third primary outcome: change of performance on response shifting task and gait trajectory after administration of MPH in PD patients with FOG, relative to placebo.

Fourth primary outcome: cerebral activation change after administration of MPH in PD patients with FOG, relative to placebo.

### Secondary outcome

First secondary outcome is the performance on the motor tasks of all groups, compared to the performance on the cognitive task and dual task.

Second secondary outcome is the cerebral activation patterns during shifting between motor tasks in all groups compared to the cerebral activation patterns during shifting between cognitive tasks and during dual tasks.

# Study description

### Background summary

Freezing of gait (FOG) is common in Parkinson*s disease (PD). The underlying mechanism of FOG is however unknown. It was hypothesized that PD patients with FOG are unable to keep different tasks (motor or cognitive) on-line and can not flexibly shift between response sets. Whether shifting impairments underlie the mechanism of motor freezing has never been investigated.
Impairments in set-shifting have been associated with a reduced activation in the fronto-striatal circuits in PD. Thus, if impairments in shifting between response sets underlie motor freezing there may be a close inter-relationship between the fronto-striatal circuitry disturbances underlying both shifting impairments and motor freezing.
Treatment options are insufficient to relieve FOG in PD. Recently, Methylphenidate (MPH) has been introduced as a treatment option. No randomized, clinical controlled trial has been performed to investigate the efficacy of MPH for FOG in PD.
Furthermore, there is no understanding of the neural mechanism by which MPH ameliorates cognition and gait in PD. Studies suggest that the neural effects of MPH vary according to task requirements. In healthy controls MPH modulated the striatal activity when response shifting was required.

### Study objective

To investigate whether impairments of shifting between response sets underlie motor freezing in PD and to investigate the efficacy and the neural mechanism by which MPH improves gait and cognition in PD patients with FOG.

### Study design

This study can be described as a randomized, double-blind, controlled trial, which will consist of the following parts:
a. Pilot study. This part of the study is focused on the applicability of the behavioral task and the efficacy of Methylphenidate. The set-shifting may be adjusted based on the results of the pilot.
b. Selected participants will be invited for two visits to the UMCG. The first visit will consist of a short neuro(psycho)logical exam and performing the set-shifting task. In all patients it will in addition be determined whether they are freezers. PD patients with FOG will also receive a physical exam. During the second visit all participants will be assessed with the shifting task during fMRI-EMG.
c. PD patients with FOG will be treated with MPH for three months.
d. After three months the behavioral assessment and fMRI-EMG will be repeated

in PD patients with FOG.

### Intervention

Methylphenidate or a placebo shall be administered to all Parkinson's disease patients with Freezing of Gait.

### Study burden and risks

No direct risks are associated with performing the set-shifting task during fMRI-EMG or outside the scanner. Also the burden of this part of the study is minimal, since it only requires a certain amount of concentration from which one normally can recover during a short break.
PD patients with FOG may suffer from adverse events after the administration of MPH or placebo. In the case of severe or untolerable adverse events the use of MPH or placebo will be terminated immediately. However, PD patients with FOG may have a benefit after the administration of MPH, given studies that show a improvement of gait and cognition in PD from MPH. The risk and burden of this part of the study may thus be different between patients, depending on the experienced benefits and adverse events.

## 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

Parkinson's disease according to the criteria of the UK brain bank criteria.

## Exclusion criteria

- Presence of neurological central nervous system disorders other that idiopathic PD.
- Surgical treatment for idiopathic PD, such as deep brain stimulation
- Dementia (i.e. a score below the cut-off of the Mattis Dementia Rating Scale)
- Other significant co-morbidity
- Contraindications to MRI scanning (see protocol for a specification)
- Contraindications to the adminstration of Methylphenidate (see protocol for a specification)

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Basic science |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-09-2010 |
| Enrollment: | 75 |
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Ritalin |
| Generic name: | Methylphenidatehydrochloride |
| Registration: | Yes - NL outside intended use |

## Ethics review

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| Approved WMO Date: | 30-11-2009 |
| Application type: | First submission |
| 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

ID: 23006
Source: Nationaal Trial Register
Title:

### In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2009-012643-42-NL |
| CCMO | NL28119.042.09 |
| OMON | NL-OMON23006 |