Postural instability and gait disability: related but separable manifestations of Parkinson’s disease

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25618

Source
Nationaal Trial Register

Brief title
Postural instability versus Gait disability in PD

Health condition

Parkinson's disease

Sponsors and support

Primary sponsor: Donders Institute for Brain, Cognition and Behavior
Centre for Cognitive Neuroimaging

Radboud University Medical Centre, Nijmegen, The Netherlands
Source(s) of monetary or material Support: NWO
Prinses Beatrix Fonds
SOFPEL

Intervention

Outcome measures

Primary outcome

The primary objective of this study is to compare the brain activity of PD patients with prominent balance or gait impairments while they mentally imagine swaying or walking respectively.

Secondary outcome

A secondary objective of this study is to compare the brain activity of PD patients with balance impairments and a group of healthy subjects while they mentally imagine swaying. We will also analyse the covariation of the BOLD signal with behavioural variables in PD patients. Namely, baseline GBI severity (measured quantitatively) will be used as covariate.

Study description

Background summary

Background of the study: Postural instability and gait disturbances are among the most incapacitating features of Parkinson’s disease (PD), both for patients and their caregivers. Better pathophysiological insights are needed to provide a rational basis for improved treatment strategies. It is widely assumed that the neural substrate is identical for gait and balance problems. We propose a new pathophysiological scenario, suggesting that although gait impairment and postural instability may temporally coincide in PD, they have distinct neural substrates.
Objective of the study: The primary objective of this study is to compare the brain activity of PD patients with prominent balance or gait impairments while they mentally imagine swaying or walking respectively. A secondary objective of this study is to compare the brain activity of PD patients with balance impairments and a group of healthy subjects while they mentally imagine swaying.
Study design: We will test the hypothesis according to which gait and balance have distinct neural substrates using functional magnetic resonance imaging (fMRI) to document brain activity during task performance.
Study population: We will include 30 PD patients and 20 matched healthy volunteers. We only include patients with dopa-resistant gait and balance problems, because this represents the greatest treatment challenge in clinical practice, and because the pathophysiology underlying dopa-resistant symptoms remains unknown.

Study objective

This research aims at better understanding the pathophysiology of gait and balance disorders in Parkinson's disease. Specifically, we propose a radically new and contrasting viewpoint,

namely that even though gait impairment and postural instability may temporally coincide in Parkinson's disease, they actually have distinct neural substrates. Proving this concept and identifying the respective neural substrates could
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potentially have great clinical and therapeutic implications. If proven to be correct, this would imply that gait and balance difficulties would require different therapeutic approaches. Having a better understanding of the underlying cerebral substrates will also help to better understand why certain therapies have adverse effects on just gait or balance, and better inform clinicians how to avoid this.

Study design

N/A

Intervention

We will test the hypothesis according to which gait and balance have distinct neural substrates using functional magnetic resonance imaging (fMRI) to document brain activity during task performance.
To avoid confounding influences of actual movements, subjects are instructed to mentally simulate the act of swaying and walking, but without actually performing it (‘motor imagery’). To characterize the neural circuit underlying gait control in PD, we use a validated motor imagery protocol. To characterize the neural circuit underlying postural control, we extend this approach and apply a newly developed protocol for motor imagery of balance that closely matches the protocol used for gait. Specifically, we will use a dynamic balance task (imagining to sway on a balance board), because this is clinically more relevant than static balance. By asking subjects to alternately imagine walking or sway, we can directly contrast and isolate the neural substrates of gait and postural control. Finding differences in neural substrate between gait and balance would have great fundamental and clinical implications. First, this would imply that gait impairment and postural instability result from different pathologies in the brain. Second, this would help to create a model for designing specific therapeutic approaches that are required to combat each of these symptoms.

Contacts

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Eligibility criteria

Inclusion criteria

Parkinson's disease patients
• right-handed men/women of age > 18 years.
• written informed consent
• idiopathic PD, according to the UK Brain Bank Criteria.
• disease severity 2.5, 3 or 4 on the Hoehn & Yahr scale (gait and/or balance disorders but still able to walk/stand independently.
• gait and/or balance impairments that remain present during an optimal ON state, i.e. after a challenge with a supramaximal levodopa dosage. For this purpose, we will use criteria used previously in neurosurgery studies by our collaborators in Grenoble, and define ‘gait impairment’ as a UPDRS part III score ≥2 for the Gait item. Similarly, postural instability will be defined as a UPDRS III score ≥2 for the Pull test item, or a score ≥2 for the item ‘Falls unrelated to freezing’ of the UPDRS part II.

Controls
• right-handed men/women of age > 18 years
• written informed consent

Exclusion criteria

Parkinson disease patients
• patients with levodopa-induced gait or balance disorders (e.g., levodopa-induced freezing of gait). We will therefore exclude patients who score greater on levodopa than off levodopa on the gait, balance or freezing items of the UPDRS. • failure to lay still for 90 minutes in the scanner (for example due to head tremor or medication-induced excessive movement)
• failure to stand/walk independently
• other causes of clinically relevant gait difficulties (eg, orthopedic or vestibular disorders)
• contra-indications for MR scanning (eg, clautrophobia)
• other neurological disorders such as stroke in history or a psychiatric disease
• depression
• cognitive impairment (MMSE <26).

• severe comorbidity (eg cancer)
• pregnancy
• poor eyesight

Controls
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Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2012
Enrollment:	50
Type:	Anticipated

Ethics review

Positive opinion

Date:	21-01-2014

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40055
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4271
NTR-old	NTR4407
CCMO	NL41481.091.12
OMON	NL-OMON40055

Study results