Freezing of gait and the levodopa paradox

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To compare the presence of freezing of gait in levodopa-naïve patients with Parkinson*s disease from Tanzania/Brazil with the presence of freezing of gait in Dutch Parkinson patients (matched for disease duration) who have received chronic pulsatile...

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

Summary

ID

NL-OMON50066

Source
ToetsingOnline

Brief title
Freezing of gait and the levodopa paradox

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW Off Road grant

Intervention

Keyword: freezing of gait, levodopa, Parkinson

Outcome measures

Primary outcome

The presence and severity of freezing of gait will be assessed subjectively using the New-Freezing of gait Questionnaire. Moreover, the presence of freezing of gait will be objectified using the timed-up-and-go test, and four rapid 360-degrees turns in both directions.

Secondary outcome

Phenotype of freezing of gait.

Study description

Background summary

Freezing of gait is among the most mysterious and dramatic symptoms in patients with Parkinson*s disease. Although freezing is both common and disabling, its pathophysiological substrate remains to be unravelled. Levodopa is the current *gold-standard* symptomatic treatment for Parkinson*s disease. An increase in the dosage of levodopa is also the *gold-standard* treatment for freezing of gait in Parkinson*s disease. Shortly after the introduction of levodopa in the sixties of the previous century, two publications suggested that levodopa resulted in a clear increase in freezing of gait. However, these early observations did not receive any further attention in the decades that followed. In 2018 and 2019, I have published historical studies on untreated Parkinson patients with severe disease, suggesting that chronic levodopa might be the very culprit in causing freezing of gait. My work also suggested that the phenotype of freezing changes after the introduction levodopa treatment, with freezing with attempted stepping occurring significantly more often. This hypothesis is provocative and in need of further evidence. To obtain this, out-of-the-box methods are needed, as it is unethical to purposely withhold levodopa from patients with Parkinson*s disease for several years. I therefore aim to perform an observational study in sub-Saharan Africa/South-America, where levodopa is generally unavailable and unaffordable. I will compare the presence and phenotype of freezing of gait in the African/South-American cohort

with the presence of freezing of gait in a matched cohort in the Netherlands.

Study objective

To compare the presence of freezing of gait in levodopa-naïve patients with Parkinson*s disease from Tanzania/Brazil with the presence of freezing of gait in Dutch Parkinson patients (matched for disease duration) who have received chronic pulsatile levodopa treatment.

Study design

Observational cohort study in Tanzania/Brazil and the Netherlands.

Study burden and risks

Patient recruited from the Netherlands will be assessed OFF-dopaminergic medication, which is expected to cause an increase in Parkinsonian symptoms, during the measurement day. However, this is an internationally accepted and applied procedure, without risks.

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

In Tanzania/Brazil, I will include 75 patients with idiopathic Parkinson*s disease who have not been treated with any form of dopaminergic medication (including Mucuna pruriens, which is a tropical legume native to Africa, rich of levodopa). In the Netherlands, I will include 75 patients who have received levodopa-treatment (patients will be matched for disease duration, age and gender).
In both cohorts, patients should have a disease duration of at least 5 years, because freezing is rare for patients with a shorter disease duration.

Exclusion criteria

Exclusion criteria include significant co-morbidity limiting the interpretation of ambulation and inability to walk unaided.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-09-2020
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO Date:	03-06-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-06-2020
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	NL72917.091.20