

# Structural and functional MRI in Parkinson\*s disease and healthy carriers with GBA mutation, an exploratory study

Published: 08-10-2020

Last updated: 21-12-2024

Identifying the genotype-phenotype-imaging correlates in GBA mutation carriers with and without Parkinson\*s disease using functional and structural magnetic resonance imaging (MRI).

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Completed
<b>Health condition type</b>	Neurological disorders congenital
<b>Study type</b>	Observational non invasive

## Summary

### ID

NL-OMON49472

### Source

ToetsingOnline

### Brief title

Cerebral correlates of GBA mutations.

### Condition

- Neurological disorders congenital
- Movement disorders (incl parkinsonism)

### Synonym

Parkinson's disease

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Radboud Universiteit Nijmegen

**Source(s) of monetary or material Support:** Luxemburg Parkinson studie;gesubsidieerd

door Fonds National de la Recherche (FNR);Luxemburg

## Intervention

**Keyword:** GBA, Neuroimaging, Parkinson's disease

## Outcome measures

### Primary outcome

Motor task-related brain activity as a function of genotype (with or without GBA mutations) and disease (with or without PD).

### Secondary outcome

Reward task-related brain activity as a function of genotype (with or without GBA mutations) and disease (with or without PD).

Motor and reward task-related cerebral activity as a function of medication status in PD patients (ON vs. OFF medication).

Structural MRI measures as a function of genotype (with or without GBA mutations) and disease (with or without PD).

## Study description

### Background summary

Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide. Clinically, PD is characterized by motor slowing (bradykinesia), stiffness (rigidity) and resting tremor. A mutation in the glucocerebrosidase (GBA) gene represents the most common strong risk for developing (PD), although only a relatively small proportion of patients carry this mutation in Western Europe (5-10%). PD patients with a GBA mutation likely manifest worse disease evolution and high progression rates of motor and cognitive symptoms. However, clinical characterization of different PD phenotypes remains challenging given

the lack of studies combining extensive genetic and (longitudinal) clinical data. In the prospective open-end Luxembourg Parkinson's study (NCER-PD program: National Centre for Excellence in Research in Parkinson's Disease), both these datatypes are combined for extensive phenotyping with stratified treatment as end-goal. In the study proposed here, we add neuroimaging measures to the Luxembourg Parkinson's study. This allows insight into pathophysiological mechanisms underlying different PD phenotypes (with and without GBA gene mutations). This knowledge will help to understand why GBA variants carriers follow a different clinical course compared to non-GBA variants carriers. This may form the basis for new future treatments, and personalised medicine.

## **Study objective**

Identifying the genotype-phenotype-imaging correlates in GBA mutation carriers with and without Parkinson's disease using functional and structural magnetic resonance imaging (MRI).

## **Study design**

Cross-sectional observational study, which will be combined with the prospective longitudinal Luxembourg Parkinson's study.

## **Study burden and risks**

The load on the patients consist of travelling, time spent on this project, and potentially a temporary worsening of symptoms caused by withholding medication. Participants will be asked to travel to the Donders Centre for Cognitive Neuroimaging from Luxembourg, since MRI facilities are lacking in Luxembourg. The Luxembourg study team will arrange all transport and hotel stays. A qualified medical team member (neurologist or specialized PD nurse) will join all participants during their travel. Travel and hotel costs are covered. Healthy controls will be measured once (one hotel night) and PD patients will be measured on two consecutive days (ON and OFF dopaminergic medication, two hotel nights). For the OFF-medication measurement, the antiparkinsonian medication will be temporarily stopped once overnight to reach at least 12 hours OFF medication state. Immediately after the measurements, participants will resume their normal medication regime. For ON-medication measurements, patients will take their own regular dopaminergic medication. All measurements are non-invasive, painless, and without nuclear radiation. Individual participants do not directly benefit from participation. However, we expect that this study will improve our knowledge about the cerebral mechanisms underlying symptoms in PD patients with GBA mutations. This may lead to new biomarkers for disease progression and new ways of treating this relatively malignant form of Parkinsonism.

## Contacts

### Public

Radboud Universiteit Nijmegen

Kapittelweg 29  
Nijmegen 6525 EN  
NL

### Scientific

Radboud Universiteit Nijmegen

Kapittelweg 29  
Nijmegen 6525 EN  
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

- Subjects participating and consented in the Luxembourg Parkinson\*s Study.
- Subjects of both genders with a full capacity of consent for MRI data collection and analysis.
- The participants fall within one of the four targeted groups (Parkinson patients and healthy controls with and without GBA gene mutation)
- Use of anti-parkinsonian medication (for PD patients)
  - Age 18 years or older

### Exclusion criteria

- Subjects who are not consented participants in Luxembourg Parkinson\*s Study.

- Refusal to sign the informed consent for MRI data collection and analysis.
- Contraindication for MRI data collection (metal implants, pacemakers, etc...)

## Study design

### Design

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	
Recruitment status:	Completed
Start date (anticipated):	25-10-2022
Enrollment:	80
Type:	Actual

## Ethics review

Approved WMO	
Date:	08-10-2020
Application type:	First submission
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	NL73032.091.20