

# Predictors of progression to freezing of gait in Parkinsons disease

<https://www.neurodegenerationresearch.eu/survey/predictors-of-progression-to-freezing-of-gait-in-parkinsons-disease/>

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## Contact information of lead PI Country

USA

## Title of project or programme

Predictors of progression to freezing of gait in Parkinsons disease

## Source of funding information

NIH (NINDS)

## Total sum awarded (Euro)

€ 1,511,185.32

## Start date of award

01/09/2015

## Total duration of award in years

3

## The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

## Keywords

Gait, REM Sleep, Gait abnormality, Freezing, Levodopa

## Research Abstract

? DESCRIPTION (provided by applicant): Postural instability and gait disturbances, including freezing of gait are common, disabling and poorly understood symptoms that afflict

approximately half of all patients with Parkinson's disease. With disease progression these symptoms become resistant to treatment and are major causes of falls, immobility and increased morbidity. Currently there are no effective treatments. Degeneration of the pedunculopontine nucleus, a region in the brainstem that controls locomotor pattern generation and postural tone, has been hypothesized to mediate the pathogenesis of postural instability and gait dysfunction. The pedunculopontine nucleus also plays a role in suppressing muscle activity during rapid eye movement (REM) sleep. Thus, the loss of the pedunculopontine nucleus should manifest as disturbances in both sleep and gait. This project will conduct a series of experiments to establish that neurodegenerative processes that disrupt the control muscle activity during REM sleep are closely linked to the development and progression of treatment-resistant postural instability and gait dysfunction. Quantitative assessments of sleep and motor function (gait, gait initiation, postural stability), in conjunction with magnetic resonance imaging measures of structural (from diffusion-weighted imaging) and functional connectivity (from resting-state functional imaging) of the region of the pedunculopontine nucleus, will be obtained in a cohort of patients with early stage Parkinson's disease. These patients will be followed for three years to map the progression of changes in sleep, motor function and organization of brainstem locomotor pathways. We hypothesize that the loss of suppression of muscle activity during REM sleep will be predictive of the rate of progression of treatment-resistant motor features of disease and changes in structural and functional connectivity of the PPN region. Establishment of a link between REM sleep disorder and the development of treatment-resistant motor features of disease will help to identify individuals at risk of developing these symptoms. Since REM sleep disturbances can often be recognized years or decades before the emergence of parkinsonian motor symptoms, this may provide a critical period for early intervention to slow or prevent disease progression. Overall the study section was very enthusiastic about the focus of this application which addresses an area of high significance, but specific concerns reduced the overall level of enthusiasm.

### **Lay Summary**

**PUBLIC HEALTH RELEVANCE:** Treatment resistant motor features, such as postural instability and freezing of gait are common in people with Parkinson's disease and major contributors to morbidity and mortality. This project will use sleep studies, quantitative motor assessments and magnetic resonance imaging to examine the hypothesis that abnormally increased muscle activity during rapid eye movement sleep is closely linked to the development and progression of treatment-resistant postural instability and gait disturbances. Since sleep disorders can emerge years before a diagnosis of Parkinson's disease, establishment of a link between sleep and treatment-resistant posture and gait disorders will help identify individuals at risk of developing these disabling motor features of disease.

### **Further information available at:**

#### **Types:**

Investments > €500k

#### **Member States:**

United States of America

#### **Diseases:**

Parkinson's disease & PD-related disorders

#### **Years:**

2016

**Database Categories:**

N/A

**Database Tags:**

N/A