Controllability estimation in Parkinson's disease: role of dopamine

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON56646

Source
ToetsingOnline

Brief title
Controllability estimation in Parkinson

Condition

- Other condition

Synonym
Parkinson's disease

Health condition

Neurological disorder

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Controllability, Dopamine, fMRI, Parkinson's disease

Outcome measures

Primary outcome

Behavioral estimation of controllability between study sessions and BOLD

response differences related to behavioral manipulations of the task between

study sessions.

Secondary outcome

NA

Study description

Background summary

Parkinson's disease (PD) is the second most common neurodegenerative disorder and is marked by motor, cognitive, and affective dysfunction related to pathology of the dopaminergic system. It is estimated that up to 50% of PD patients suffer from depression at some point during the disease. The depressive symptoms have been suggested to stem from maladaptive learning about the consequences ones decisions have on the immediate environment. Indeed, learned helplessness has been proposed as a model of depression which has been shown to involve estimations of how much control one have over the environment. Dopamine might act as an arbiter between modes of decision-making where stimulus-response associations are formed from either passively (spectator) observing or by actively exploring the environment (actor). A lack of endogenous dopamine might thus bias patients into the passive mode of decision-making causing them to erroneously perceive their environment as uncontrollable. In this study we investigate the impact LDOPA has on how PD patients estimate decision controllability.

Study objective

This study aims to elucidate the relationship between subjective controllability and dopamine in PD patients. We hypothesize that lower levels of dopamine will be related to lower estimations of controllability. Using fMRI, we will investigate the neural correlates of differences in controllability. We hypothesize a difference in subcortical BOLD responses when encountering prediction errors during the actor decision-making mode as a function of dopaminergic innervation. Dopaminergic innervation will be manipulated through measuring patients off and on L-DOPA.

Study design

A within-subjects repeated measure design will be used in this study. PD patients will be tested twice, (1) on their regular L-DOPA medication, (2) off their regular L-DOPA medication.

Study burden and risks

Participants will attend two identical study sessions on and off medication. Participants will complete a series of questionnaires, structural and functional MRI where the main task will be completed, out of scanner tasks to independently measure associative learning and working memory capacity. Tremor response will be measured during the functional MRI. There is no risk to the patients concerning L-DOPA administration since it will be their normal dose. Potential discomfort might be associated with the off medication session, similar L-DOPA withdrawal designs in PD patients have been approved and performed safely. Participating in this study is associated with minimal burden and risk. The study can only be performed using this patient group due to the unique disease profile of decreased dopaminergic innervation.

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

• Age >= 18 years
• Disease duration <= 10 years
• Use L-DOPA to treat their symptoms

Exclusion criteria

o Taking any other dopaminergic medication to treat their symptoms (except decarboxylase inhibitor)
o Have other neurological diagnosis (such as stroke, epilepsy and dementia)
o Taking anti-depressants such as SSRI's.
o Negative indications for MRI
o Incompatible medical devices (e.g. pacemaker)
o Incompatible metal implants
o Claustrophobia
o If you are pregnant or suspect that you are pregnant

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-02-2025
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	21-03-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-01-2025
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	NL82892.091.22