Ultra-high field imaging of the cortico-striato-subthalamic functional and structural connectivity to improve deep brain stimulation surgery in Parkinson's disease patients

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

Summary

ID

NL-OMON41696

Source
ToetsingOnline

Brief title
STN connectivity in PD with MRI

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's, Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Deep brain stimulation, MRI, Parkinson's disease, Subthalamic nucleus

Outcome measures

Primary outcome

The main study endpoint will be the structural and functional partition of the

STN into its motor and non-motor regions in PD patients and healthy controls.

Secondary outcome

The secondary study parameters are:

1. The strength of the functional and structural connectivity between the STN

and the motor and non-motor cortical areas in PD patients and controls.

2. The brain areas that show a significantly stronger or weaker functional or

structural connectivity from the STN to the motor or limbic cortical areas or

vice versa in PD patients than in controls.

3. The brain areas structurally and functionally connected to the stimulation

zone of the optimal electrode (only in patients).

4. Brain areas that show an activation related to the fMRI task.

5. The brain areas that show significantly more or significantly less

activation during the task fMRI in PD patients than in healthy subjects.

6. The deviation between the computed STN motor area (with 7T MRI) and the

surgically determined optimal electrode location.

7. The deviation between the pre-surgically determined target location with 3T

MRI (current clinical practice) and the surgically determined optimal electrode

location.

Study description

Background summary

Parkinson disease (PD) is a common neurodegenerative disorder characterized by motor symptoms and also non-motor symptoms. Patients are initially treated successfully with drugs, but prolonged drug use is limited due to dyskinesias, motor fluctuations and debilitating side effects. In these advanced stages of PD, deep brain stimulation (DBS) of the subthalamic nucleus (STN) (which involves the placement of an electrode in the deeply situated STN) is the next therapeutic option. Multiple long-term follow-up studies have demonstrated long lasting beneficial effects on the motor function of PD patients due to STN DBS. However, there are two major drawbacks. One is the induction of psychiatric side-effects, which are expected to be caused by stimulation of the non-motor territories of the STN. And the other is the long duration of the surgery; because the STN and its subregions cannot be detected precisely on conventional images, the patients need to be tested extensively intra-operatively to find the right spot.

So in order to decrease side-effects and shorten the duration of the surgery, accurate imaging of the STN and its subregions is required. It is expected that at 7T MRI, the contrast and anatomic delineation of the STN improve greatly compared to convectional imaging (1.5T or 3T MRI). Furthermore, with the use of functional and diffusion MRI sequences, connections between cortical regions and deep brain structures, which are expected to reveal information on the segregation of the STN, can be investigated.

Therefore, we propose a set of experiments to test the hypothesis that with ultra high field structural, functional and diffusion MRI we will be able to identify the STN and its functional subterritories in PD patients and age- and sex-matched control subjects. In the end this might serve to improve targeting of the motor-part of the STN and decrease surgery time.

Study objective

The primary objective is to assess the structural and functional segregation of the STN into its motor and non-motor regions in PD patients and healthy controls.

The secondary objectives are:

1. To compare the strength of the functional and structural connectivity between the STN and the motor and non-motor cortical areas between PD patients and controls.
2. To compare the brain areas structurally and functionally connected to the STN with the brain areas structurally and functionally connected to the stimulation electrode in implanted PD patients.
3. To assess the difference between the brain activation pattern during the task fMRI between PD patients and healthy controls.
4. To compare the final optimal electrode location as established during surgery, to the STN motor area as determined with our methods (based on 7T MRI) and to the pre-operatively defined target (based on 1.5T or 3T MRI) according to current clinical protocol.
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Study design

The study will be an observational study that investigates and compares the structural and functional connectivity of the subthalamic nucleus in 35 PD patients who are eligible for DBS surgery, 10 PD patients who are not eligible for DBS surgery, and 10 healthy controls. The experiment consists of a one hour 7T MRI scan that subjects will undergo.

Study burden and risks

The burden consists of an investment of 90 minutes of time and a slight risk of discomfort during scanning, mainly during entry or exit of the bore.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P.Debeylaan 25
Maastricht 6202AZ
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P.Debeylaan 25
Maastricht 6202AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For all groups:
1. Subjects must be mentally competent;For group 1 (PD patients scheduled for DBS surgery):
1. Patients suffering from Parkinson's disease who are eligible for deep brain stimulation surgery.;For group 2 (PD patients not scheduled for DBS surgery):
1. Diagnosis of idiopathic PD according to the UK Brain Bank Criteria
2. Excellent levodopa response
3. Disease course of > 3 years;For the healthy controls only:
1. Healthy volunteers with the same age and gender distribution as both patient populations.

Exclusion criteria

For all groups:
1. Metallic prostheses or pacemaker in the subject's body or other contra indications for MRI.
2. Any neurological disease (other than PD).;For group 1 (PD patients scheduled for DBS surgery):
1. Any neurological or psychiatric disease other than PD.;For group 2 (PD patients not scheduled for DBS surgery)
1. Any neurological or psychiatric disease other than PD.;For healthy volunteers:
1. Any neurological or psychiatric disease.
2. The use of medication affecting the central nervous system.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-04-2014
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	02-09-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-12-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-06-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL42613.068.13