Deep Brain Stimulation for MOtor symptoms in patients with Parkinson*s disease DEmentia (DBS- MODE)

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Ethical review	Approved WMO
Status	Recruitment started
Health condition type	Nervous system, skull and spine therapeutic procedures
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON54196

Source
ToetsingOnline

Brief title
DBS-MODE

Condition

- Nervous system, skull and spine therapeutic procedures
- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease, shaking palsy

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Collectebussenfonds

Intervention

- Surigical procedure

Keyword: Deep brain stimulation, Dementia, Motor symptoms, Parkinson's disease

Explanation

N.a.

Outcome measures

Primary outcome

Patients will be assessed at baseline, 15 weeks, 30 weeks and 52 weeks after
 randomization. The primary outcome measure is the change from baseline to 30
 weeks follow-up of motor symptoms in off-drug phase measured with the Movement
 Disorder Society - Unified Parkinson*s Disease Rating Scale (MDS-UPDRS) part
 III.

Secondary outcome

The secondary outcome measures include neuropsychological evaluation,
 psychiatric assessment, additional motor evaluations during on-drug phase,
 functional health status, falls, usage of medication, (S)AEs, treatment
 satisfaction, caregiver burden, medical care consumption and recruitment and
 retention rate.

The outcome measures of the exploratory part of the study include low-fidelity
 LFP data, high-fidelity LFP data, triggered LFP recordings, and paper patient
 diaries.

Study description

Background summary

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an established treatment for disabling motor symptoms of Parkinson*s disease (PD) that persist despite optimal pharmacological treatment. Currently, apparent cognitive impairment (e.g., dementia) is considered a contra-indication for DBS. However, the scientific underpinning to withhold these patients DBS is weak. In addition, DBS-surgical procedures have developed considerably in recent years. If the proposed research demonstrates that DBS is efficacious in patients with PD and dementia (PDD), a large group of patients may benefit from the treatment.

The explorative part of the study will investigate the correlation between cognitive and neuropsychiatric symptoms and neuronal activity in PDD. The objectives hereof are to determine if specific local field potential (LFP) patterns in the STN are linked to cognitive fluctuations and neuropsychiatric symptoms (such as psychotic symptoms and anxiety) in patients with PDD.

Study objective

The primary objective of the proposed research is to investigate in patients with PDD the efficacy of STN-DBS with best oral medical treatment (DBS-group) for disabling motor symptoms during off-drug phase compared to best oral medical treatment alone (BMT-group). The secondary objective is to compare development of cognitive and psychiatric problems, on-drug phase motor symptoms, functional health status, falls, usage of medication, (serious) adverse events ((S)AEs), treatment satisfaction, medical care consumption and caregiver burden between the DBS-group and BMT-group in addition to determining the recruitment and retention rate.

Study design

The study is a single center prospective, randomized, open-label, blinded end-point clinical trial (PROBE design).

Intervention

During the DBS surgery high frequency stimulation electrodes will be placed bilaterally in the STN. Next a pulse generator will be implanted subcutaneously under the clavicula, which can adjust current, pulse width and frequency. All patients will receive BMT, consisting of PD-treatment according to current guidelines and can be adjusted accordingly.

Study burden and risks

Currently, dementia is considered a contra-indication for DBS in PD, because a thought of concern is that patients with dementia have a greater risk of cognitive deterioration and complications such as delirium and psychosis. However, there is no evidence suggesting that this risk is much higher for patients with dementia compared to patients without dementia. DBS appears to be safe in case series including patients with PDD as well as in clinical studies with patients undergoing experimental DBS for dementia. An important possible benefit is the improvement in motor symptoms.
It is hypothesized that the risks for (S)AEs is acceptable for patients with PDD undergoing DBS, however, the study could show that this is actually not the case. The operation will take place under general anesthesia instead of local anesthesia. The surplus in burden related to treatment for patients randomized to DBS-group consists of the screening of motor symptoms during on-drug and

off-drug phase with the MDS-UPDRS 30 weeks after randomization (a two-days hospital stay), and four days of hospitalization for the DBS surgery. The surplus in burden for evaluating the outcome measures and travel time accounts for approximately 5 to 8 hours. Patients allocated to BMT-group experience no additional burden related to treatment, as they will receive care in line with standard practice. The burden associated with the extra assessments is approximately 6 to 9 hours.

If patients randomized to DBS agree to collect additional observational data for the explorative part investigating the correlation between cognitive and neuropsychiatric symptoms and neuronal activity in PDD, one additional hospital visit of 15 minutes and an at-home observation period of seven days will be added to the burden. The in-hospital visit encompasses extensive LFP recordings while sitting still and performing cognitive tasks. During the at-home observations, participants and caregiver will be instructed to trigger a broad-band (0-125 Hz) LFP recording (i.e., an *event*) via their patient programmer upon the occurrence of psychotic symptoms (hallucinations), anxiety symptoms (nervousness, restless or tense), at a moment of bad cognition, and at a moment of relatively good cognition. Additionally, participants and caregivers will fill out paper patient diaries on the aforementioned symptoms.

Contacts

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Trial sites

Trial sites in the Netherlands

Amsterdam UMC
Target size: 90

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- age 18 years and older;
- diagnosis of PD according to the clinical diagnostic criteria of the Movement Disorder Society (MDS);
- despite optimal pharmacological treatment, at least one of the following symptoms, that are severe enough to impair functioning in daily life independent of dementia:
  - motor response fluctuations;
  - dyskinesia;
  - painful dystonia;
  - levodopa-responsive bradykinesia;
- diagnosis of probable or possible PDD based on the MDS clinical diagnostic criteria (amongst others this encompasses the development of dementia áfter established diagnosis of PD). This will be based on a standardized neuropsychological examination:

1. 1 impaired cognitive domain consisting of 2 abnormal tests (i.e., ≤ 2 standard deviations);
2. 1 impaired cognitive domain consisting of 2 MCI tests (i.e., ≤ 1.5 standard deviations);

3. Cognitive deficits severe enough to impair daily life (social, occupational, or personal care), independent of the impairment ascribable to motor of autonomic symptoms.

   If a test cannot be executed due to severe cognitive difficulties the test is regarded to be abnormal. In case of doubt regarding the presence of PDD, the case will be discussed in a multidisciplinary meeting with neurologists and neuropsychologists;

- a life expectancy of at least two years;
- subject has decision capacity to give informed consent, judgement of which is at the discretion of an experienced neurologist from the study team (see 7.3);
- subject provides written informed consent;

- regular contact with a caregiver, who has at least approximately twice a week contact with the subject and also provides written informed consent for their own participation.

Exclusion criteria

• any neurodegenerative disorder other than PD;
• previous neurosurgery for PD (e.g., DBS, pallidotomy, thalamotomy). Nota bene: intrajejunal levodopa infusion or subcutaneous apomorphine infusion are not considered an exclusion criterion;
• contraindications for DBS-surgery, such as a physical disorder making surgery hazardous;
• Hoehn and Yahr stage 4 or 5 at the best moment during the day;
• co*existence of another abnormality or disorder:
o that causes cognitive impairment that may improve with specific treatment; OR
o that besides PDD is judged to contribute significantly to the cognitive impairment by the treating physician;
• current major depressive episode according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5);
• current psychosis (treatment with antipsychotics is allowed);
• other severely disabling condition;
• immobility during the greater part of the day not related to off-drug phase (e.g., due to apathy);
• pregnancy, breastfeeding, and women of childbearing age not using a reliable method of contraception.

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	No intervention
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment started
Start date (anticipated):	02-11-2021
Enrollment:	90
Duration:	12 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	21-06-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO
Date: 29-01-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 05-11-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 19-11-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO Date:	28-03-2025
Application type:	Amendment
Review commission:	METC Amsterdam

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24650
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
OMON	NL-OMON54196
CCMO	NL76772.018.21
CCMO	NL76772.018.21
Research portal	NL-007778