# A multicenter double blind randomized crossover study comparing the impact of dorsal versus ventral subthalamic nucleus deep brain stimulation on apathy in Parkinson*s disease

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In this study, we will test whether STN-DBS related apathy can be reversed by switching stimulation to a more dorsal contact on the electrode.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Movement disorders (incl parkinsonism) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50175

**Source**
ToetsingOnline

**Brief title**
Apathy and DBS in Parkinson*s disease

### Condition

- Movement disorders (incl parkinsonism)
- Psychiatric and behavioural symptoms NEC

**Synonym**
a behavioral and motivational disorder, Apathy

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Parkinson Vereniging in Nederland

## Intervention

**Keyword:** Apathy, Deep brain stimulation, Parkinson's Disease, Subthalamic nucleus

## Outcome measures

### Primary outcome

The primary outcome is the difference in SAS score change from one month of dorsal stimulation versus ventral stimulation

### Secondary outcome

Secondary outcomes are MOCA: Montreal Cognitive Assessment. MDS-UPDRS-III: Movement Disorder Society*s Unified Parkinson*s Disease Rating Scale, motor part III. MADRS: Montgomery- Åsberg Depression Rating Scale (MADRS). PDQ-39: 39-item Parkinson*s disease Questionnaire. QUIP: Parkinson's Disease Impulsive-Compulsive Disorders Questionnaire. LEDD: levodopa-equivalent daily dosage. AES-I: Apathy Evaluation Scale, a second apathy scale rated by the informal caregiver if the patient has one. SF-36: Short-Form Health Survey. Suspected Arm: Patients will be asked to choose which arm they think they were randomized for. Preferred Settings: Patients will be asked to choose which of the settings they will continue with. *Although the timing for these questionnaires is the same as the visits for the patients, these questionnaires will be send by regular mail to the informed caregiver.

# Study description

**Background summary**

Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is part of the standard care for advanced Parkinson*s Disease (PD) in developed countries. Multiple studies have shown that STN DBS is able to reduce motor symptoms by on average 50 percent (6,7). After implantation of the DBS-system, the stimulation parameters are optimized for the best improvement of motor symptoms using the Unified Parkinson*s Disease Rating Scale (UPDRS). This questionnaire is primarily focused on motor symptoms and has only one item evaluating behavioural changes, the effect of STN DBS on non-motor symptoms is therefore less recognized. STN DBS is likely to have no negative effect on most mental abilities (8,9), except for an increase in symptoms of apathy (1). Apathy is best described as a loss of motivation with decreased initiative, interest and energy and an emotional indifference with flat affect (10).

We found 16 studies that measured symptoms of apathy after STN DBS, of which 13 reported an increase of apathy despite motor improvement (1,2,11). Based on nine studies using the proposed cut-off for apathy on scales, the point prevalence of apathy was approximately 46%, ranging between 21% and 71%. These studies suggest that apathy may be a common adverse effect of STN DBS and an important trade-off for patients suffering from advanced PD and relying on this treatment. Apathy in PD is associated with the lowest quality of life compared to all other PD symptoms (12). A recent study showed that patients suffering from apathy after STN DBS did not experience improved quality of life despite improvement of motor symptoms (11).
One explanation for the occurrence of apathy after STN-DBS is the reduction of dopaminergic medication after motor improvement by STN-DBS. However, longitudinal studies show no correlation to the decreased LEDD and the occurrence of apathy (11,13). Two recent neuroimaging studies suggest an association between apathy after STN DBS and stimulation of the ventral part of the STN, associated with non-motor limbic circuits involved in emotion regulation and motivation. (2,14)
The STN is a relatively small brain structure with three regions that separately connect to motor, limbic and cognitive circuits. As these neuronal tracks are closely situated to each other and their projections partly overlap, stimulating the motor region with STN DBS may also influence limbic and cognitive circuits. The effect of STN DBS on motor symptoms is directly visible during parameter optimization, while cognitive, affective and behavioural effects may become apparent only after several months and may not be detected during the optimization process. In the Academic Medical Center (AMC) in Amsterdam, we have described at least three cases of post-operative apathy after DBS, which improved after switching the parameters to activate a more dorsal contact on the STN electrode (Zoon et al., in preparation).

### Study objective

In this study, we will test whether STN-DBS related apathy can be reversed by switching stimulation to a more dorsal contact on the electrode.

### Study design

This is a multicenter double blind randomized crossover placebo controlled study. We will include 26 PD patients with apathy after six months of STN DBS, i.e. a minimum score of 14 points on the Starkstein Apathy Scale (SAS). We will compare a phase receiving dorsal stimulation versus a phase receiving original stimulation in a double-blinded fashion

### Intervention

We will randomize patients into two arms, one receiving one month of dorsal STN DBS first and then one month of regular DBS, the other arm will follow the reversed order.

### Study burden and risks

The burden of adjusting the DBS settings can include cognitive, affective, behavioural and motor adverse effects. Severe adverse effects are unlikely and all patients will be installed with the previously optimized settings intact and professional care will be available 24 hours a day to instruct patients to reverse the intervention settings when needed.
The experimental settings are closely situated to the original settings and patients have already been stimulated at all contacts during the optimization process of the DBS. The expected burden of the questionnaires is minor. Patients included in this study will be offered the opportunity to receive DBS with these settings. The outcome of this study could improve the quality of life of a large group of patients relying on DBS for PD.

## 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

Patients suffering from Parkinson's Disease and relying on deep brain stimulation for the treatment of this disease who develop apathy within 6 months after deep brain stimulation implantation

## Exclusion criteria

Patients with peri-operative intracerebral complications related to SNT-DBS placement (e.g. bleeding or infection) inflicting permanent changes will be excluded.
Dementie

# Study design

## Design

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| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Crossover |

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| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 11-02-2020 |
| Enrollment: | 26 |
| Type: | Actual |

### Medical products/devices used

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| Generic name: | Deep Brain Stimulation |
| Registration: | Yes - CE intended use |

## Ethics review

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| Approved WMO Date: | 23-09-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 30-09-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-12-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

## 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 | NL64385.018.19 |