Deep Brain Stimulation of the Nucleus Basalis of Meynert in patients with Parkinson's Disease

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON45897

Source
ToetsingOnline

Brief title
NBM-DBS in PD

Condition

- Movement disorders (incl parkinsonism)
- Dementia and amnestic conditions

Synonym
Parkinson's, Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: deep brain stimulation, nucleus basalis of Meynert, Parkinson's disease

Outcome measures

Primary outcome

The primary measure of this study is the cognitive performance of the subjects, assessed by the symbol digit modality test (SDMT), the Vienna test system (VTS) - Attention, and the verbal fluency test.

Secondary outcome

(1) The measure of resting cortical activity performed by electroencephalography (EEG) at baseline and weekly at the end of each period of crossover trial

(2) Assessment of motor function. The Unified Parkinson*s Disease Rating Scale (UPDRS) part III (motor examination) and part IV (motor complication) will be performed at the beginning of the screening trial before adjusting the DBS setting, and at the end of the three-day screening trial of the NBM-DBS.

(3) Safety and tolerability of the low-frequency stimulation of the NBM in this study is defined as any adverse effects associated with the adjustment of the DBS setting during the screening phase as well as in the crossover phase.

Study description

Background summary

Cognitive impairment leading to dementia is prevalent in Parkinson*s disease (PD), and mainly exhibits deficits in attention, memory, visuospatial function and executive function. It is pathologically characterized by a profound degeneration of cortically projecting cholinergic neurons of the basal

forebrain, mainly in the region named the nucleus basalis of Meynert (NBM). Low-frequency deep brain stimulation (DBS) of the NBM has emerged as an alternative therapy for Parkinson*s disease dementia since acetylcholinesterase inhibitor, as current pharmacotherapy, cannot halt disease progression, and therefore, causing suboptimal efficacy. The technique to implant DBS quadripolar electrodes, targeting to the globus pallidus interna (GPi) for PD motor symptom treatment, gives a high possibility of placing the most distal electrode at the NBM. Therefore, stimulation of the NBM in these patients is feasible by switching the stimulation program which is initially targeting to the GPi. It is hypothesized that low-frequency stimulation of the NBM will increase cholinergic neurotransmission from the NBM to its cortical projection and thereby improving patients* cognition.

Study objective

The primary objective is to investigate the cognitive effect of low-frequency stimulation of the nucleus basalis of Meynert (NBM) in advanced Parkinson*s disease (PD) patients, who were previously treated with deep brain stimulation (DBS) of the globus pallidus interna (GPi). The secondary objectives are to investigate the effect of low frequency stimulation of the NBM on cortical activity; to investigate the safety and tolerability of low frequency stimulation of the NBM in patients who were previously treated with GPi-DBS; to investigate the effect of temporarily switching off DBS of GPi on motor function.

Study design

this is a pilot study to perform DBS of the NBM, which consists of two phases: three days of a screening trial followed by two weeks of a randomized, single-blind, crossover trial.

Intervention

Using an external programming device provided by Medtronic, the existing DBS program which initially aims to stimulate the GPi will be temporarily reconfigured to stimulate the NBM. In the screening phase, the pulse width and the frequency of the stimulation parameters will be locked at 90 µsec and 20 Hz, while while the voltage will be set according to the predictive value of the minimal voltage which is able to reach the NBM, up to 4 Volt, or the highest voltage that is well-tolerated by the subject. These parameters are further used in the crossover phase.

Study burden and risks

The first phase of the study requires subjects to be hospitalized for three days in order to evaluate the safety and tolerability of the NBM DBS as well as

to determine an optimal voltage of NBM stimulation to be used in the crossover trial. The former DBS setting, aiming to stimulate the GPi at high frequency, will be altered temporarily to stimulate the NBM at low frequency. Evaluations on subjects* motor and cognitive function, taking about 60 minutes, will be performed at the beginning and at the end of the screening phase. During this phase, the dose of dopaminergic medications will be adjusted and if necessary subcutaneous apomorphine will be used, to compensate the change of DBS setting. Only if there is no significant deterioration of motor function (an increase of UPDRS part III more than 30%), subjects are eligible to continue to the second phase of the study which is the crossover trial phase. Subjects will undergo a week of stimulation of the NBM and another week without DBS stimulation. Three visits are planned during this two-week study. EEG and NPE will be performed at each visit, which takes about 1.5 hours. With regard to the safety of stimulating the NBM, based on previous studies (Freund et al., 2009; Kuhn et al., 2009), low-frequency stimulation of the NBM was well tolerated and several improvements of cognitive performance were shown. No further adverse event was found except one complaint about inner restlessness due to stimulation intensity more than 5V. Of note, the NBM will be stimulated by the most distal electrode of the same lead used for GPi-DBS. No additional surgery or any other invasive intervention will be performed.

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

1. Patient with GPi stimulation, with the NBM in reach of the electric field at least one DBS electrode
2. Patients should be able to give informed consent
3. patients should be on a stable medication regimen for at least 4 weeks

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study if any unstable internal disease is found.
Additional exclusion criteria is made to determine whether or not a subject can continue to the crossover trial. Subject with significant worsening of motor function during the screening trial, which is indicated by an increase of the UPDRS part III score more than 30%, will not continue to the crossover trial.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Will not start

Enrollment: 11

Type:	Anticipated

Medical products/devices used

Generic name:	Deep brain stimulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	23-05-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-02-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
ClinicalTrials.gov	NCT02763397
CCMO	NL57011.042.16