

# Deep brain stimulation of the pedunculopontine nucleus for Parkinson's Disease

**Submission date**  
28/05/2010

**Recruitment status**  
No longer recruiting

☐ Prospectively registered

☐ Protocol

**Registration date**  
28/05/2010

**Overall study status**  
Completed

☐ Statistical analysis plan

☐ Results

**Last Edited**  
10/08/2016

**Condition category**  
Nervous System Diseases

☐ Individual participant data

☐ Record updated in last year

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

4455

# Study information

## Scientific Title

Deep brain stimulation of the pedunclopontine nucleus for Parkinson's Disease: a single centre randomised interventional treatment trial

## Study objectives

In patients with Parkinson's disease problems with balance, walking and speech are considered to be some of the most disabling symptoms. The symptoms are collectively known as axial symptoms. At present the available medical therapy and surgery, in the form of deep brain stimulation result in a limited improvement in axial symptoms especially in the later stages of this disease. Research work over the past 20 years has indicated that degeneration of an area in the brainstem, the pedunclopontine nucleus (PPN) may be involved in producing axial symptoms in Parkinson's disease. Work by Professor Aziz in Oxford has shown an improvement in axial symptoms in primate models of Parkinson's disease following stimulation of the PPN.

Following on from this work, our research group was one of the first to publish on deep brain stimulation of this area in patients with Parkinson's Disease. Our initial results have shown a significant improvement of not only axial symptoms but patients also reported improvement in other symptoms including appetite and concentration. Following the success of our early pilot cases we now intend to perform a formalised trial in order to:

1. Determine the safety and efficacy of deep brain stimulation of the pedunclopontine nucleus (PPN) in conjunction with stimulation of the caudal zona incerta (cZi) (conventional site of stimulation in Parkinson's Disease) in patients with medically refractory Parkinson's Disease who have predominant symptoms of postural instability and gait dysfunction both in the on and off medication states)
2. Obtain greater understanding of the mechanism by which deep brain stimulation of the PPN and cZi region results in clinical improvement by studying the changes in regional cerebral blood flow using positron emission tomography (PET) scanning and electrical activity at these two sites using temporary externalised cables and electroencephalogram (EEG) readings from the scalp in the post-operative period whilst stimulating these two regions separately and in combination

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

South West 5 REC, 28/04/2006, ref: 06/Q2007/20

## Study design

Single centre randomised interventional treatment trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

**Study type(s)**

Treatment

**Participant information sheet****Health condition(s) or problem(s) studied**

Topic: Dementias and Neurodegenerative Diseases Research Network; Subtopic: Parkinsons Disease; Disease: Parkinson's disease

**Interventions**

Following fully informed consent and surgical implantation of DBS electrodes to both the PPN and subthalamic region bilaterally, patients will enter into an initial 6 week period over which the Subthalamic region and PPN electrodes will be programmed individually and in combination in order to define the optimal settings for symptom control. At the end of the first 6 week period patients will be randomised into receiving deep brain stimulation at the predetermined optimal setting at either the Subthalamic region or the both the PPN and Subthalamic region simultaneously. This will occur for a further 6 - 12 week period at the end of which the primary and secondary outcome measures will be assessed. Following assessment of the outcome measures, patients will crossover to the other stimulator setting for a further 6 - 12 weeks. With two possible combinations of stimulator settings and an initial period used to define optimal stimulator settings the total duration of the trial will be 18 - 30 weeks.

**Intervention Type**

Other

**Phase**

Phase II

**Primary outcome measure**

Change in frequency of gait freezing, measured for 3 days in each condition and averaged.

**Secondary outcome measures**

1. Quality of life questionnaires (39-item Parkinson's Disease Questionnaire [PDQ-39] and 36-item Short Form Health Survey [SF-36])
2. The Unified Parkinson's Disease Rating Scale (UPDRS)
3. Change in concomitant antiparkinsonian medications
4. Neuropsychological assessment
5. Parkinson's Disease Non-Motor Symptoms Questionnaire
6. Timed walk, upper and lower limb movements and Purdue Pegboard
7. Tinetti balance and gait assessment tool

Measured pre-operatively and after each of the two randomisation settings (which could be at 12 - 18 weeks, or 18 - 30 weeks depending on how long the patient needs to be on each stimulation setting in order to reach a stable clinical state on each of the stimulation settings.

**Overall study start date**

22/10/2007

**Completion date**

28/02/2011

# Eligibility

## Key inclusion criteria

1. Diagnosis of advanced idiopathic Parkinson's disease poorly controlled on optimum medication with significant functional disability and predominant symptoms of postural instability and gait dysfunction in both the on and off medication states
2. They will have a Unified Parkinson's Disease Rating Scale (UPDRS) motor score of 30 or greater in their practically defined off condition at an initial evaluation. They will each show at least a 30% improvement in the UPDRS motor score from that of the practically defined off condition following a morning levodopa challenge.
3. At two preoperative evaluations the practically defined off UPDRS motor score should differ no more than  $\pm 15\%$
4. Subjects will be under the age of 70 years, either sex
5. Appropriate surgical candidate with no medical conditions that would interfere with long-term implantation of device and follow up
6. Patient must give signed informed consent

## Participant type(s)

Patient

## Age group

Adult

## Sex

Both

## Target number of participants

Planned sample size: 8; UK sample size: 8

## Key exclusion criteria

1. Known current or past diabetes
2. Evidence of dementia, head trauma or medical conditions that may alter cerebral functioning
3. Past or present history of alcohol or substance abuse
4. Mini-mental state examination (MMSE) scores below 27 or above 30
5. Evidence of past or current serious psychopathology likely to affect the patients ability to benefit from surgery

## Date of first enrolment

22/10/2007

## Date of final enrolment

28/02/2011

# Locations

## Countries of recruitment

England

United Kingdom

**Study participating centre**  
**Frenchay Hospital**  
Bristol  
United Kingdom  
BS16 1LE

## **Sponsor information**

**Organisation**  
North Bristol NHS Trust (UK)

**Sponsor details**  
Trust Headquarters  
Beckspool Road  
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**Sponsor type**  
Hospital/treatment centre

**Website**  
<http://www.nbt.nhs.uk/>

**ROR**  
<https://ror.org/036x6gt55>

## **Funder(s)**

**Funder type**  
Industry

**Funder Name**  
Medtronic PLC

## **Results and Publications**

**Publication and dissemination plan**  
Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration