

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

Submission date 28/05/2010	Recruitment status No longer recruiting	☐ Prospectively registered
Registration date 28/05/2010	Overall study status Completed	☐ Protocol
Last Edited 10/08/2016	Condition category Nervous System Diseases	☐ Statistical analysis plan
		☐ Results
		☐ Individual participant data
		☐ Record updated in last year

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

Protocol serial number

4455

Study information

Scientific Title

Deep brain stimulation of the pedunculo pontine 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 pedunculo pontine 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 pedunculo pontine 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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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.

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 +/- 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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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**

United Kingdom

England

Study participating centre

Frenchay Hospital

Bristol

United Kingdom

BS16 1LE

Sponsor information

Organisation

North Bristol NHS Trust (UK)

ROR

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

Funder(s)**Funder type**

Industry

Funder Name

Medtronic PLC

Results and Publications**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration