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

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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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 pedunculopontine 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 pedunculopontine 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 pedunculopontine 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 +/- 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
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Sponsor information

Organisation
North Bristol NHS Trust (UK)

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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