NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of deep brain stimulation for Parkinson's disease

Introduction

This overview has been prepared to assist members of IPAC advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by specialist advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Procedure name

Deep brain stimulation for Parkinson's disease
Subthalamic nucleus deep brain stimulation

Specialty society

British Society of Neurological Surgeons

Indication(s)

Parkinson's disease.

Parkinson's disease is a chronic disease of the brain characterised by gradually worsening tremor, muscle rigidity and difficulties with starting and stopping movements. The condition is usually treated with drugs. Surgery may be considered in people who have responded poorly to drugs, who have severe side-effects from medication, or who have severe fluctuations in response to drugs (on-off syndrome).

Parkinson's disease is common, affecting about 0.5% of people aged 65 to 74 and 1-2% of people aged 75 and over. Experts believe that 1 to 10% of people with Parkinson's disease might be suitable for brain surgery.[1]

Summary of procedure

Surgery for Parkinson's disease is carried out on structures within the brain that are responsible for the modification of movements, such as the thalamus, the globus pallidus and the subthalamic nucleus. Each of these structures consists of two parts; one on the left hand side of the brain and one on the right. Surgery may be carried out on one or both sides.

Surgical treatment aims to correct the imbalance created by diminished function of the substantia nigra, the underlying abnormality in Parkinson's Disease. Surgery alters, through either destruction or electrical stimulation, the function of brain nuclei, such as the thalamus, globus pallidus or subthalamus that interact functionally with the substantia negra (nigra). All these procedures carry the risk of stroke, confusion and speech and visual problems.

Surgery involves inserting very fine needles into the brain through small holes made in the skull to determine the exact position of the nucleus, which may be different in each patient. This part of the procedure is usually carried out under local anaesthetic. A permanent electrode is then placed into this nucleus. Under general anaesthetic this wire is then connected to a pulse generator subcutaneously on the anterior chest wall.

Literature review

Appraisal criteria

We included studies on stimulation of the subthalamic nucleus in Parkinson's disease.

List of studies found

We found two systematic reviews.[1,2] The conclusions of the second[2] were based mainly on the findings of the first,[1] so the second is not described further.

We found one randomised controlled trial.[3]

We found six non randomised controlled studies; the table gives details of the three largest.[4-6]

We found eight case series including 50 or more people.

The table give details of the largest case series.[7]

References to smaller studies are given in the Annex.

Summary of key efficacy and safety findings (1)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Nicholson T[1] Study design: systematic review Search date: September 1999	• identified no controlled studies • identified four studies comparing function with stimulaton on and stimulation off, and one case series Insufficient evidence of efficacy of subthalamic stimulation	Insufficient evidence of safety of subthalamic stimulation	Search date and primary sources described Selection criteria for studies described Quality of included studies assessed: All papers had methodological limitations including poorly defined patient selection criteria; mixed interventions; short follow up; incomplete follow-up; blinding of assessment unclear and pre-specified outcome measures not always reported
Burchiel KJ[3] Randomised controlled trial Portland Oregon, USA 1996 to 1997 n=10 • 5 subthalamic nucleus stimulation (STN), average age 63 • 5 stimulation of the globus pallidus internus (GPS), average age 47 Inclusion criteria: • prominent rigidity and bradykinesia • minor tremor • stable dose of medication for at least 1 month Exclusion criteria: • major psychiatric illness • low intelligence • abnormal radiological findings • history of fits • previous surgery for Parkinson's • other substantial medical problems Follow up: 12 months	Mean improvement in motor score before medication: • STN: 44% • GPS: 39% p=0.71 Mean improvement in Activities of Daily Living Score before medication: • STN: 78% • GPS: 63% P=0.41 Reduction in Dyskinesia Rating Scale after medication: • STN: 67% • GPS: 47% p=0.45	Perioperative complications: Severe dyskinesia • STN: 1 person • GPS: none Haematoma • STN: 1 person • GPS: none Anxiety attack • STN: 3 people • GPS: none Transient confusion • STN: 2 people • GPS: none	Randomisation method not described STN patients older with less disability before surgery than GPS patients Power very low Patients and physicians blinded to stimulation site Outcomes appropriate Losses to follow up: • STN: none • GPS: 1

Summary of key efficacy and safety findings (2)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Obeso JA[4] Cohort study Multicentre: Australia, Canada, France, Germany, Italy, Spain, Sweden and USA 1995 to 1999 140 people • n=102 subthalamic nucleus stimulation (STN), average age 59 • n=38 stimulation of globus pallidus (GPS), average age 56 Inclusion criteria: • good response to levodopa • minimum of 30 points on functional score before medication • symptoms not controlled Exclusion criteria: • major psychiatric illness • cognitive impairment • other substantial medical problems • cardiac pacemaker • previous intracranial surgery Follow up: 6 months	Change in motor score before medication: • STN: 51% • GPS: 33% Change in motor score after medication: • STN: 26% • GPS: 27% Home diary assessments of increase in time with good mobility during day: • STN: 27% to 74% • GPS: 28% to 64% Physician global assessment of presence of severe disability: • STN: 74% to 15% • GPS: 76% to 11% Patient global assessment of presence of severe disability: • STN: 77% to 23% • GPS: 82% to 14%	Stroke: • STN: 3 people • GPS: 4 people Fits: • STN: 3 people • GPS: 1 person Infection: • STN: 4 people • GPS: none Brachial plexus injury: • STN: 1 people • GPS: none Pulmonary embolism: • STN: 1 person • GPS: none Device migration: • STN: 3 people • GPS: 2 people Broken lead: • STN: 1 person • GPS: person	Reasons for allocating people to STN or GPS not described GPS group was younger and included more men Losses to follow up: • STN: 5 • GPS: 2 Funded by manufacturer

Summary of key efficacy and safety findings (3)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Volkmann J[5] Cohort study Cologne, Germany 1996 to 2000 n=27 • 16 subthalamic nucleus stimulation (STN), average age 60 • 11 stimulation of the globus pallidus (GPS), average age 57 Inclusion/exclusion criteria not described Follow up: 12 months	Change in mean motor score before levodopa: • STN: 56/108 to 22/108 • GPS: 53/108 to 17/108 Change in mean motor score after levodopa: • STN: 15/108 to 16/108 • GPS: 30/108 to 17/108 Change in mean Activities of Daily Living score before levodopa: • STN: 29/52 to 13/52 • GPS: 21/52 to 12/52 Change in mean Activities of Daily Living score after levodopa: • STN: 14 /52 to 11/52 • GPS: 12/52 to 6/52	Deaths: none Infection: • STN: 1 people • GPS: 2 people Skin erosion: • STN: none • GPS: 2 people Weight gain>10kg: • STN: 6 people • GPS: 3 people Speech difficulties: • STN: 9 people • GPS: none Depression requiring inpatient treatment: • STN: 2 people • GPS: none Sleepiness: • STN: 3 people • GPS: none	Reasons for allocating people to STN or GPS not described STN group older with longer duration of disease Power limited Non-blinded assessment of outcomes Outcomes appropriate Losses to follow up: • STN: none • GPS: 1

Summary of key efficacy and safety findings (4)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Krause M[6] Non randomised controlled study Heidelberg, Germany 1995 onwards (published 2001) n=18 • 12 subthalamic nucleus stimulation (STN), average age 59 (range 45-69) • 6 stimulation of globus pallidus internus (GPS), average age 57 (range 46-65) Inclusion criteria • advanced Parkinson's (defined) Follow up: 12 months	Change in mean Activities of Daily Living Score: • STN: 24/52 to 17/52 • GPS: 17/52 to 17/52	Deaths: none Stroke: • STN: 1 person • GPS: none Strong increase in libido: • STN: 1 person • GPS: 2 people Speech difficulties: • STN: 2 people • GPS: 2 people Hyperkinesias: • STN: 2 people • GPS: none	Reasons for allocating people to STN or GPS not described Groups of similar age and duration of disease Power limited Assessor of outcomes blinded to procedure Outcomes appropriate
Vesper J[7] Case series Multicentre: 18 centres in Australia and Canada and 16 in Europe 1998 to 1999 n=111 people, average age 59 Inclusion criteria: • severe disease with motor fluctuations or dyskinesia or tremor • medical therapy ineffective Exclusion criteria: • dementia or other psychiatric conditions • pregnancy Follow up: 6 months	• mean operation time 5 hours (range 3 hours to 8 hours) • activity of daily living score 'significantly improved' ($p<0.0001$) • motor scores 'significantly improved' ($p<0.0001$) • duration and severity of levodopa-induced dyskinesia 'significantly reduced' ($p<0.0001$) (Data presented graphically – no absolute figures provided)	Complications: • death: 1 person • subcutaneous haematoma: 6 people • stroke: 3 people • dislodged lead: 2 people • fit: 1 person • infection: 9 people • seromas: 2 people • pain at neurostimulator site: 1 person • gait disorders: 10 people • psychiatric disturbances: 10 people • speech difficulty: 3 people • difficulty swallowing: 3 people • pins and needles: 3 people • difficulty with shutting eye: 3 people	Uncontrolled case series Data available for 44/111 patients at 6 months Short follow up

Validity and generalisability of the studies
All the studies were carried out in settings applicable to the UK.

We found one very small randomised controlled trial which lacked power to demonstrate statistically significant differences in efficacy and safety outcomes between subthalamic and globus pallidus stimulation.[3]

We found three non-randomised studies comparing subthalamic and globus pallidus stimulation.[4-6] These studies are susceptible to confounding. One was fairly large so provides useful information on risk of complications.[4]

We found no studies comparing subthalamic stimulation with non-surgical treatment.

Bazian comments
None.

Specialist advisor's opinion / advisors' opinions
Specialist advice was sought from the British Society of Neurological Surgeons

- Now established practice
- Randomised controlled trial currently in progress comparing subthalamic stimulation versus medical treatment
- Long term efficacy unknown
- Specialised training essential

Issues for consideration by IPAC
None other than those discussed above.

References

1. Nicholson T, Milne R. Pallidotomy, thalamotomy and deep brain stimulation for severe Parkinson's disease. Southampton: Wessex Institute for Health Research and Development; 1999 December. Development and Evaluation Committee Report No. 105

2. MSAC Assessment Report Application 1031. Deep brain stimulation for the symptoms of Parkinson's disease. Canberra 2002. http://www.msac.gov.au

3. Burchiel KJ, Anderson VC, Favre J, Hammerstad JP. Comparison of pallidal and subthalamic nucleus deep brain stimulation for advanced Parkinson's disease: results of a randomized, blinded pilot study. Neurosurgery 1999; 45:1375-1382

4. The Deep-Brain Stimulation for Parkinson's Disease Study Group. Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. New England Journal of Medicine 2001; 345: 956-963

5. Volkmann J, Allert N, Voges J, Weiss PH, Freund HJ, Sturm V. Safety and efficacy of pallidal or subthalamic nucleus stimulation in advanced PD. Neurology 2001; 56: 548-551

6. Krause M, Fogel W, Heck A, Hacke W, Bonsanto M, Trenkwalder C et al. Deep brain stimulation for the treatment of Parkinson's disease: subthalamic nucleus versus globus pallidus internus. Journal of Neurology, Neurosurgery & Psychiatry 2001; 70: 464-470

7. Vesper J, Chabardes S, Fraix V, Sunde N, Ostergaard K, The Kinetra Study Group. Dual channel deep brain stimulation system (Kinetra) for Parkinson's disease and essential tremor: a prospective multicentre open label clinical study. Journal of Neurology, Neurosurgery & Psychiatry 2002; 73: 275-280

Annex: References to studies not described in the table

Reference	Number of study participants
Comparison studies	
Scotto di Luzio AE, Ammannati F, Marini P, Sorbi S, Mennonna P. Which target for DBS in Parkinson's disease? Subthalamic nucleus versus globus pallidus internus. Neurological Sciences 2001; 22: 87-88	14
Krack P, Pollak P, Limousin P, Hoffmann D, Xie J, Benazzouz A et al. Subthalamic nucleus or internal pallidal stimulation in young onset Parkinson's disease. Brain 1998; 121: 451-457	13
Linazasoro G, Gorospe A, Guridi J, Ramos E, Figueiras R, os C et al. Pallidal and subthalamic stimulation in Parkinson's disease: Lessons from the unsatisfactory results. Neurologia 2001; 16: 298-302	211 but number who had subthalamic stimulation not clear
Charles PD, Van Blercom N, Krack P, Lee SL, Xie J, Besson G et al. Predictors of effective bilateral subthalamic nucleus stimulation for PD. Neurology 2002; 59: 932-934	54
Benabid AL, Benazzouz A, Hoffmann D, Limousin P, Krack P, Pollak P. Long-term electrical inhibition of deep brain targets in movement disorders. Movement Disorders 1998; 13 (Suppl 3): 119-125	51
Ardouin C, Pillon B, Peiffer E, Bejjani P, Limousin P, Damier P et al. Bilateral subthalamic or pallidal stimulation for Parkinson's disease affects neither memory nor executive functions: a consecutive series of 62 patients. Annals of Neurology 1999; 46(2):217-223	49
Pillon B, Ardouin C, Damier P, Krack P, Houeto JL, Klinger H et al. Neuropsychological changes between "off" and "on" STN or GPi stimulation in Parkinson's disease. Neurology 2000; 55(3):411-418	48
Welter ML, Houeto JL, Tezenas du MS, Mesnage V, Bonnet AM, Pillon B et al. Clinical predictive factors of subthalamic stimulation in Parkinson's disease. Brain 2002; 125: 575-583	40
Mogilner AY, Sterio D, Rezai AR, Zonenshayn M, Kelly PJ, Beric A. Subthalamic nucleus stimulation in patients with a prior pallidotomy. Journal of Neurosurgery 2002; 96:660-665	32

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