Deep Brain Stimulation For Parkinson’s Disease

What’s new in brain “circuit training”

Associate Professor Robert Wilcox

Flinders University & University of South Australia
Neurology Department, Flinders Medical Centre,
Adelaide, Australia

Disclaimer Statement

Dr Robert Wilcox holds the following positions:

- Senior Consultant Neurologist at Flinders Medical Centre & Alice Springs Hospital & privately at Neurology South Australia & Wakefield Hospital.
- Associate Professor academic appointments at both the Flinders University & the University of South Australia.
- The views, data and opinions expressed in today’s presentation those of Dr Wilcox & are not necessarily endorsed or shared by the above institutions.
- Dr Wilcox has no conflicts of interest related to this presentation.

Deep Brain Stimulation for Parkinson’s Disease

What is DBS?

DBS Team based in SALHN FMC & Wakefield Street Hospital

- Dr Matt McDonald – Neurosurgeon
- Dr Randall Long – Psychiatrist
- Dr Tony Kneebone – Neuropsychiatrist
- Sue Sharrad – Parkinson’s & Movement disorder Nurse
- Dr Shav Parasivam – Neurologist
- A.Prof Rob Wilcox - Neurologist

Deep Brain Stimulation for Parkinson’s Disease

What is Deep Brain Stimulation?

• Many important functions of the brain and brainstem are organised into nuclei, discrete collections of grey matter often with specific brain functions.
• Nerve fibre pathways converge at brain nuclei, these are those that are most easily electrically stimulated.
• In Parkinson’s disease, several bilateral nuclei in the basal ganglia & the deeper brainstem have been implicated in disease onset & progression.

Deep Brain Stimulation for Parkinson’s Disease

What is DBS?

• Deep brain stimulation involve stereotactically guiding stimulating electrodes into brain nuclei targets & their converging nerve fibres.
• Then providing constant electrical stimulation to stimulate them or hijack their tract connections.
• In fact because the nerve fibre pathways care the most readily electrically stimulated DBS probably primarily works by stimulating these fibres.
Parkinson’s Disease DBS
What are the common brain targets?

The most popular targets are the:

- Globus Pallidus internus (GPi)
- Subthalamic Nucleus (STN)

Subthalamic Nucleus DBS

- STN-DBS is more challenging, but addresses bradykinesia, rigidity & tremor & has the major advantage of allowing reduction or even cessation of dopaminergic Rx.

Finding the Target in STN
Deep Brain Stimulation

The STN is easier to see in 3T MRI slices than in unstained brain slices.

Good Reasons To Consider DBS-STN
Selecting Good Candidates for DBS

- Significant fluctuating motor symptoms or wearing off not responsive to medications.
- Significant asymmetry of PD motor signs.
- Severe medication refractory tremor or dystonia.
- Psychological/Psychiatric problems that only occur when attempts are made to increase or maintain the dopaminergic medication dose to treat motor symptoms.
- Severe GI side effects or fainting caused by all oral dopaminergic medications.
- Previous bowel shortening surgery.

Recognizing Poor Candidates for DBS

- Currently excellent medication response – no need for early DBS (risk/benefit)
- “PD with no L-dopa response” – usually poor result predominantly because the patient probably does not have PD !
- PD dementia (PDD) or another dementia syndrome; because there is lots of to & fro collaboration to get DBS working well & DBS can cause further cognitive compromise.
- Florid hallucinations, these often precede PDD.
- Predominantly axial motor symptoms.
- History of poor medical compliance/co-operation.
- Psychogenic symptoms.
- Technically impossible to target the STN. e.g. old stroke lesion, AVM, aneurysm or tumour in target path.
- Likely ongoing IV drug abuse.

Early Stimulus DBS patient Selection Tool

All 5 questions must be answered YES to score ≥ 5.

<table>
<thead>
<tr>
<th>ABSOLUTE CRITERIA FOR PD DBS SELECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Parkinson’s disease* for at least 4 years</td>
</tr>
<tr>
<td>2. Presence of bothersome disease-related symptoms and/or side-effects*</td>
</tr>
<tr>
<td>3. Motor improvement with dopaminergic medication or presence of medically refractory tremor</td>
</tr>
<tr>
<td>4. Absence of medical conditions preventing surgery (e.g. terminal cancer, severe cardio-respiratory insufficiency)</td>
</tr>
<tr>
<td>5. Absence of ongoing severe, medically-resistant neuropsychiatric disease (e.g. severe depression/severe anxiety/severe agitation)</td>
</tr>
</tbody>
</table>

AGE RESTRICTION: DBS results are generally better in patients under the age of 75. But patients >75 years old will be considered if in exceptionally good health & have no major surgical risk factors.
Early Stimulus DBS patient Selection Tool

**Part 1: Absolute Criteria for considering PD patient referral for DBS**

The expert panel considered the below criteria as minimum requirements for the consideration of DBS therapy. All 5 questions must be answered YES to score ≥ 5.

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Parkinson’s disease for at least 4 years</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2. Presence of bothersome disease-related symptoms and/or side-effects</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>- Motor fluctuations, dyskinesia, persisting tremor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hyperdopaminergic or cholinergic non-motor side effects of medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Motor improvement with dopaminergic medication or presence of medically refractory tremor</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. Absence of medical conditions preventing surgery (e.g. terminal cancer, severe cardiorespiratory insufficiency)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. Absence of ongoing severe, medically-resistant neuropsychiatric diseases (e.g. severe depression, severe cognitive impairment)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**AGE RESTRICTION:** DBS will be considered in patients >75 years old in excellent health - if biological age appears younger than chronological age.

---

DBS: Targeting

Fusing MRI & CT with the 9 frame rod fiducial markers

Microelectrode recording (MER) in STN, Thalamus & GPi

DBS surgery

Microelectrode recording (MER) to target
**DBS surgery**

**Intraoperative Micro- & Macro Stimulation**

- Stimulation with MER tip, then later the permanent electrode.
- Test for reduced tremor, tone & improved motor function - patterning & motor decay assessed.
- Test speech & eye movements.
- Ask about sensory symptoms

---

**Intraoperative testing in STN-DBS**

- The STN is deliberately over-stimulated to map nearby structures.
- This activates surrounding structures in the enlarged electrical field.

---

**O-arm CT Imaging to confirm lead placement while still in the operating theatre**

Brain leads with 4 electrodes in situ

---

**Deep Brain Stimulation:**

Post-op imaging to confirm lead placement

---

**Deep Brain Stimulation:**

Post-op imaging to confirm lead placement
**DBS Surgery**
Brief operation to place connector leads from brain to the stimulators in the chest wall.

**Fibre Tractography to map Functioning Brain Circuits**
A constrained spherical deconvolution fiber tractography map (Dr Marc Agzarian & Dr Donald McRobbie) showing the orientation and pathways of functional brain nerve fibers. This allowed targeting of the still living areas of the brain to suppress the tremor.

**Fibre Tractography Guided DBS**
- PD where a stroke has caused damage to normal target area.
- Dystonia caused by stroke or brain trauma.
- Multiple sclerosis where “plaques” have produced tremors & dystonia.

**Directional-Steerable DBS**
- Standard DBS leads deliver a spherical or teardrop electrical field around the DBS lead & electrode.
- But DBS targets are often small & the electrical field can spread to nearby areas and cause side-effects.
- Therefore the ability to steer or direct the DBS electrical field may produce better stimulation & reduce side-effects.

**Directional-Steerable DBS**
- Special DBS leads & electrodes are used to direct constrain the electric field.
- Simplest approach uses 120 degree 3-way leads.
**Directional or Steerable DBS**

- Complex approach uses multiple “spot” electrodes around a DBS lead that can direct electrical fields in multiple directions.

**Tyrx Antibacterial Sleeve for the Implantable Pulse Generator**

- The commonest site of post-operative infection is the IPG pocket.
- Most infections are early but some infections can occur many years after surgery.

**Brain Radio & Closed Circuit DBS**

- Current DBS systems require external programming to modify brain stimulation as Parkinson's disease symptoms progress & fluctuate.
- Several research groups are working on “brain radios” that not only stimulate, but also transmit information from neurons deep in the brain.

**Closed Circuit Adaptive DBS**

- Brain radios allow researchers to study the living brain, but better still for the first time offer the chance of “close circuit” DBS control.

**Adaptive DBS**

- Brain radios allow researchers to study the living brain, but better still for the first time offer the chance of “close circuit” DBS control.
THE END of THE BEGINNING

Now this is not the end.
It is not even the beginning of the end.
But it is, perhaps, the end of the beginning

Winston Churchill
The Bright Gleam of Victory Speech,
Nov 10, 1942, Mansion House, London

THE HUMAN DESIRE FOR RENEWAL
“THE FOUNTAIN OF YOUTH”

THE END