Deep Brain Stimulation for Psychiatric and Movement Disorders: Technology and Applications

Hugh McDermott
Deputy Director (Research)
Bionics Institute
FDA approval for DBS treatments

• Essential Tremor – 1997
• Parkinson Disease – 2002
• Dystonia – 2003 (HDE)
• Obsessive-Compulsive Disorder – 2009 (HDE)
  – persistent obsessive thoughts and repetitive ritualistic behaviours
  – ~2% of population, of whom ~10% may be suitable for DBS

Many other neurological and psychiatric conditions may respond well to DBS, including depression, chronic pain, Tourette syndrome, addictions, etc.
Why Deep Brain Stimulation?

- Can be very effective where other treatments have failed
- Few permanent, serious adverse effects have been reported
- Is relatively non-destructive and reversible
- Utilises proven technologies
Worldwide market projections

Growth ~ 20% p.a.

Mostly cochlear implants
### DBS for Obsessive-Compulsive Disorder

<table>
<thead>
<tr>
<th>Reference(s)</th>
<th>Patients</th>
<th>Stimulation site</th>
<th>Effect*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuttin et al., 2003 (1)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
<td>Observation for up to 20 months: Reduction in Y-BOCS score: 3 full response 1 partial response 2 no response</td>
</tr>
<tr>
<td>Gabriels et al., 2003 (4)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
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<tr>
<td>Nuttin et al., 1999 (5)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
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<td>Nuttin et al., 2003 (6)</td>
<td>6</td>
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<tr>
<td>van Laere et al., 2006 (7)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
<td></td>
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<tr>
<td>Cosyns et al., 2003 (8)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
<td></td>
</tr>
<tr>
<td>Nuttin et al., 2003 (9)</td>
<td>6</td>
<td>Anterior limb of internal capsule, bilateral</td>
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<tr>
<td>Abelson et al., 2005 (2)</td>
<td>4</td>
<td>Anterior limb of internal capsule, bilateral</td>
<td>Observation 4 to 23 months: Reduction in Y-BOCS score: 2 full response 2 no response</td>
</tr>
<tr>
<td>Greenberg et al., (2006) (10)</td>
<td>10</td>
<td>Anterior limb of internal capsule (7/10), caudal part of nucleus accumbens (3/10), bilateral (8/10)</td>
<td>Observation for 38 months (data for 8 patients were evaluated): Significant reduction in Y-BOCS score: 4 full response 2 partial response 2 no response</td>
</tr>
<tr>
<td>Mallet et al., (2008) (3)</td>
<td>16</td>
<td>Subthalamic nucleus, bilateral</td>
<td>Observation in 13 months: Randomized, controlled comparison of on-off (off-on) condition: Significant reduction in Y-BOCS score after on-stimulation; high rate of adverse effects</td>
</tr>
<tr>
<td>Huff et al., (in press) (11)</td>
<td>10</td>
<td>Nucleus accumbens, right</td>
<td>Observation for 12 months: Significant reduction in Y-BOCS score: 1 full response 1 partial response 8 no response</td>
</tr>
</tbody>
</table>

*Full response: >35% reduction in Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score; partial response: <35% >25% reduction in Y-BOCS score; no response: <25% reduction in Y-BOCS score (from e13)

Kuhn, 2010
DBS of the nucleus accumbens for OCD

Clapp, 2009
Medtronic DBS implant system

4 discrete stimulation sites

Diameter $\phi = 1.27$ mm

Each ring:
- length 1.5 mm
- spacing 1.5 mm

3387 electrode array
Medtronic DBS implantable pulse generators (IPGs)

77 mm

Thickness: 10-15 mm

Current & voltage modes

Rechargeable; Current & voltage modes

Over 80,000 implants in use to treat movement and psychiatric conditions
Ensuring a successful outcome

- Select appropriate patients
- Optimise any concurrent therapies
- Deliver the stimulation to the most effective site(s)
- Optimise settings of the stimulation parameters
Optimising electrode placement

Neuromate surgical robot

Robocast
Improving electrode arrays

4 DBS electrodes in ventral capsule / ventral striatum

3 mm long, spaced 4 mm
1.5 mm long, spaced 1.5 mm

Mian, 2010
Typical programming procedure

- Select electrode
- Increase current/voltage
- Increase rate
- Increase pulse width

- Therapeutic benefit?
- Unacceptable side-effects?
Variable parameters of biphasic pulses

- Current (or voltage) amplitude
- Pulse (phase) duration
- Inter-phase gap
- Charge = Current $\times$ Phase duration
- Pulse rate (or period)
Constant-current or constant-voltage?

• Earlier stimulators used constant voltage pulses
• Usually constant current is preferred, because:
  – electrode impedance may vary
  – currents in tissue are not affected by impedance variations
  – effects of stimulation are generally charge- or current-dependent
  – charge balance is easy to maintain (with biphasic pulses)
Safe chronic stimulation

• Charge must be balanced between phases
  – minimal net direct current (< 0.1 µA average)
• Charge per phase below specified limit
• Charge density below specified limit
The ratio \( V_p / \text{Current} \) is conventionally called the electrode impedance, but other measurements may be used.
Stimulator compliance

• If $V_p$ exceeds the stimulator's *compliance voltage*, the current will not be maintained at the intended level
• This may happen if:
  – the electrode impedance is too high
  – the stimulation current is too high
• Exceeding the compliance voltage may result in unsafe stimulation (e.g., through charge imbalance)
Safe stimulation parameters

- Charge = current × phase duration
- Charge density = charge / electrode area

Kuncel & Grill, 2004
Stimulator programming

• Generally, the effects of stimulation increase with:
  – increasing current (or voltage)
  – increasing phase duration
  – increasing pulse rate
  – increasing separation between active electrodes
  – increasing gap between pulse phases

\[ increasing\ charge \]
Effect of pulse parameters

• Generally, stimulation effects are related to charge per pulse; however:
  – varying the current (or voltage) and the phase duration may activate different neurons
  – varying the pulse rate may also affect outcomes

Kringelbach, 2007
Maximising battery lifetime

• Non-rechargeable Medtronic stimulators may require battery replacement every 6 months to 2 years

• To minimise the power consumption:
  – use the shortest effective phase duration (pulse width)
    • for the same charge, shorter phases are more effective
    • increasing the inter-phase gap may also increase effect
  – use the lowest effective rate
Medtronic DBS implant system

4 discrete stimulation sites

Diameter $\phi = 1.27$ mm

Each ring:
- length 1.5 mm
- spacing 1.5 mm

3387 electrode array
Cochlear implant system

Over 180,000 implants in use by hearing-impaired children and adults
# Medtronic IPGs compared with Cochlear stimulators

<table>
<thead>
<tr>
<th></th>
<th>Medtronic IPG</th>
<th>Cochlear stimulator</th>
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</thead>
<tbody>
<tr>
<td>Stimulation voltage range</td>
<td>0-10.5 V</td>
<td>N/A</td>
</tr>
<tr>
<td>Stimulation current range</td>
<td>0-25.5 mA (some models)</td>
<td>0-2 mA</td>
</tr>
<tr>
<td>Typical stimulus current</td>
<td>2-8 mA</td>
<td>0.5-2 mA</td>
</tr>
<tr>
<td>Typical electrode impedance</td>
<td>0.5-2 kΩ</td>
<td>2-12 kΩ</td>
</tr>
<tr>
<td>Pulse width</td>
<td>60-450 µs</td>
<td>&lt; 25-800+ µs</td>
</tr>
<tr>
<td>Pulse rate (maximum)</td>
<td>250 Hz</td>
<td>31.5 kHz</td>
</tr>
<tr>
<td>Number of electrodes</td>
<td>8 (two leads × 4 electrodes)</td>
<td>22 + 2 monopolar grounds</td>
</tr>
<tr>
<td>Electrode configurations</td>
<td>MP, BP</td>
<td>MP, BP (var), CG</td>
</tr>
<tr>
<td>Outward telemetry</td>
<td>Electrode impedances?</td>
<td>Electrode voltages, NRT</td>
</tr>
</tbody>
</table>
Multipolar focused stimulation

Neural targets

Desired voltage distribution

Applied electrode currents

15 mm

van den Honert & Kelsall, 2007
Future developments

• Adaptive/responsive stimulation techniques
• Simpler, faster, more precise surgical procedures
• Optimised, systematic fitting based on reliable (objective) outcome measures
• Improved understanding of the mechanisms of action; better (functional) imaging
• Improved device reliability with no repeat surgeries
• Demonstration of cost-effectiveness
Acknowledgments

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• Cochlear Ltd

• The Bionics Institute has new funding to expand research in this area. If you are interested in participating as a student, engineer, clinician, or scientist, please contact Hugh McDermott: HMcDermott@bionicsinstitute.org