Deep Brain Stimulation: A Physician and Patient Perspective

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Summary

- Deep brain stimulation of the globus pallidus can be effective at reducing **motor dysfunction** in patients with dystonia, including those with Cerebral Palsy.
- There is corresponding reduction in disability.
- Patient selection still needs further assessment.
- Managing outcome expectations is important.
“an elegant interplay of neuronal discharges, with changes in pattern, frequency, and synchronization, as well as feedback from other brain regions.”

Abnormal movements result from an imbalance between positive and negative actions.

Comella & Shannon, Continuum, June 2004
Tone

- Resting muscle tension - Not strength
Spasticity vs. Dystonia

- Hypertonia Assessment Tool (HAT) (0 or 1)
- Distinguish between the types of hypertonia in children
  - Spasticity (2)
  - Dystonia (2)
  - Rigidity (3)

Jetwa, Mink et al DMCN 2010,52:e83-87
Spasticity

- Velocity-dependent increase in resistance to passive movement
- Rapid increase in movement leads to a “catch” with a subsequent “release.”

- Modified Ashworth
- Tardieu
Treatments for spasticity

- Therapy
- Oral pharmacocology
  - Baclofen, tizanidine, benzodiazepines
- Targeted therapies
  - Botulinum toxins
- Neurosurgical
  - Selective Dorsal Rhizotomy
  - IntraThecal Baclofen
Dystonia

• Syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures\(^1\)

• Primary dystonia is defined by the existence of dystonia alone without any underlying disorder.\(^2\)

• Childhood-onset and adolescent-onset (<28) begins in early childhood after a period of normal physical development.\(^2\)

• Adult-onset dystonia (>28) typically starts between ages 30 to 50 following decades of normal physical function. The symptoms tend to remain focal, affecting one particular part of the body.\(^2\)


Dystonia

Functionally may include co-contraction of agonist/antagonist muscle groups.

- Burke-Fahn Marsden
- Barry Albright

Gale et al. Neurosci and Beh reviews 2008;32:378-387
### Burke-Fahn Marsden - Motor

<table>
<thead>
<tr>
<th>Region</th>
<th>Provoking Factor</th>
<th>Severity Factor</th>
<th>Weight Factor</th>
<th>Product</th>
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<td>0.5</td>
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<tr>
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<td>Walking</td>
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<td><strong>TOTAL</strong></td>
<td><strong>N/30</strong></td>
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</table>
Pediatric Onset Dystonias

**Genetic/Metabolic**
- **Genetic**
  - Dyt 1
  - Dyt 6
  - Dopa-responsive
  - Paroxysmal
- **Metabolic**
  - NBIA/Wilsons
  - Carbon Monoxide
  - Glutaric Acidemias
  - Lesch Nyhan
  - Juvenile Parkinson’s

**Acquired**
- Cerebral palsy (2.8/1000)
- Brain injuries
  - TBI (accidental and inflicted)
  - HIE (near drowning)
  - Infections (meningitis, septic shock)
  - Tumors (most common solid tumors in pediatrics)
  - Others (electrocution, ?)
Cerebral Palsy

- Incidence 2.8/1000 children
- Most common disabling movement disorder in children
- Most common cause of dystonia
- Long-term survival likely
  - Personal
  - Social
  - Economic
Individualized Goals of Tone Management

- Improve/preserve function
- Improve ease of care/comfort
- Decrease pain/discomfort
- Decrease orthopedic deformities
- Promote general health and well-being
- Promote integration in school and community life
- Consider secondary morbidities
- Plan for long-term outcome
Treatment Considerations

Is the movement or tone abnormality regional or widespread?

What is the etiology?
- Static vs Progressive
  - May impact treatment responsiveness
  - Patient size and age (ITB > 25#; DBS ≥ 7 years)

Will treatment have generalized or local effects?

Is the treatment permanent or reversible?

Will side effects result in a loss of function?

Is there an developmentally optimal time for a particular treatment modality?
Treatment Strategy

- **Reversible**
  - Intrathecal Baclofen
  - Selective Dorsal Rhizotomy

- **Permanent**
  - Pallidotomy
  - Deep Brain Stimulation

- **Focal**
  - Physical Therapy
  - Oral Medications

- **Spasticity**
  - Botulinum Toxin
  - Orthopedic Surgery

- **Dystonia**
  - ITB

Modified from Graham et al (2000)
Pharmacologic options for dystonia

- Acetylcholine antagonist
- α Adrenergic agonist
- Dopamine supplementation
- Dopamine agonist
- Dopamine antagonist
- Dopamine depletion
- Gaba-B agonist
- Gaba-A agonist
- Chemodenervation
- Trihexyphenidil
- Clonidine
- Levodopa/carbidopa
- Requip/Mirapex
- Risperidone
- Tetrabenazine
- Baclofen, Benzodiazepines
- Zolpidem
- Botulinum toxins A,B
Background

- DBS approved for dystonia 2003, HDE
- Scattered reports of patients with CP
- 2 large series (> 10 patients)
  - Vidhaillet 2009: Adults, athetoid-dystonic CP
  - Marks, 2011: Children and young adults, mixed CP
- Meta-analysis (61 patients)
  - Koy et al 2013: Children and adults
Field of Influence
Clearpoint: Asleep DBS

- Exciting option for our patients
- Seems to be very accurate
- Time is no different than awake surgery
- Difficulty with pins
  - 1 EDH / 1 CSF leak from pins
- Flexible coils are key for pediatric cases
Primary implants

- All
- < 16 years
- > 17 years


Values on the y-axis range from 0 to 20.
DBS: Opportunities for failure

Pre/Peri-operative
- Patient selection
- Implant site
- Surgical issues
  - Technical
  - Patient centered anesthesia
- Generator selection

Postoperative
- Programming
- Hardware malfunction
- Compliance

N=100

[Graph showing complication types with numbers: Stroke 6, Infection 8, Hemorrhage 1, Hardware Malfunction 11, None 75]
Patients

All: $n=100$
- Mean 14.33 years
- Median 13.80 years
- Min 7.06 years
- Max 29.57 years

Pediatric ($\leq 16$ years): $n=70$
- Mean 11.56 years
- Median 11.81 years
- Min 7.06 years
- Max 16.38 years
Opportunities for success:
Dystonia Implants (9/2007 – 12/13)

<table>
<thead>
<tr>
<th>Primary dystonias</th>
<th>N=17</th>
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<tr>
<td>Dyt-1 (14)</td>
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<td>Other (3)</td>
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<table>
<thead>
<tr>
<th>Secondary dystonias</th>
<th>N=61</th>
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<tr>
<td>CP (37)</td>
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<tr>
<td>NBIA (5)</td>
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<td>CVA (3)</td>
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<td>TBI (3)</td>
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<td>HIE (4)</td>
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<td>Other (9)</td>
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GA1 (2); AT (1); DDON (1); PDH (2); TD (1); PNKD (2)
Bilateral pallidal DBS for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study

- 13 adults; choreoathetoid-dystonic CP
- Mean BFMDRS improvement 21.1% at 1 year
  - 34.7 (baseline) – 24.4 (1 year)
- Stimulation rate 130

- Functional disability, pain, mental health related QOL all improved

Vidhaillet: Lancet Neurology 2010
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Baseline Mean ± SD</th>
<th>6-Month Follow-up Mean ± SD</th>
<th>% Improvement Mean ± SD</th>
<th>Significance p&lt;0.05</th>
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<tr>
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<tr>
<td><strong>Burke-Fahn-Marsden-Motor</strong></td>
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<tr>
<td>Group 1</td>
<td>61.13 ± 27.21</td>
<td>35.00 ± 12.32</td>
<td>37.84% ± 22.56</td>
<td>.012</td>
</tr>
<tr>
<td>Group 2</td>
<td>91.5 ± 9.75</td>
<td>82.83 ± 12.63</td>
<td>8.96% ± 14.48</td>
<td>.172</td>
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<tr>
<td>Total</td>
<td>74.14 ± 26.05</td>
<td>55.50 ± 27.32</td>
<td>25.46% ± 23.97</td>
<td>.004</td>
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<td><strong>Burke-Fahn-Marsden-Disability</strong></td>
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<tr>
<td>Group 1</td>
<td>18.63 ± 7.74</td>
<td>16.00 ± 6.65</td>
<td>14.44% ± 11.07</td>
<td>.020</td>
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<tr>
<td>Group 2</td>
<td>24.83 ± 4.02</td>
<td>24.00 ± 1.55</td>
<td>1.63% ± 13.60</td>
<td>.453</td>
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<tr>
<td>Total</td>
<td>21.29 ± 6.98</td>
<td>19.43 ± 6.45</td>
<td>8.95% ± 13.42</td>
<td>.027</td>
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<td><strong>Barry-Albright-Scores</strong></td>
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<tr>
<td>Group 1</td>
<td>21.13 ± 7.38</td>
<td>16.88 ± 6.33</td>
<td>19.48% ± 15.27</td>
<td>.024</td>
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<tr>
<td>Group 2</td>
<td>25.50 ± 3.73</td>
<td>24.83 ± 4.02</td>
<td>1.39% ± 20.40</td>
<td>.586</td>
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<tr>
<td>Total</td>
<td>23.00 ± 6.30</td>
<td>20.21 ± 6.41</td>
<td>11.73% ± 19.29</td>
<td>.029</td>
</tr>
</tbody>
</table>

1 Group 1 - Less than 16 years of age (n=8); Group 2 - Greater than or equal to 16 years of age (n=6).

2 Wilcoxon Sign Rank

Marks, et al; Movement Disorders 2011;
Baseline

**DCP**
- 11.02 +/- 3.09 years
- M:F 6:3
- BFM-M: 75.7 (120)
- BFM-D: 22.1 (30)
- BAS: 24.4 (32)
- 34.78 +/- 12.17 months
  - Range: 19-55 months
- 16.5 (+/- 4.04) mm lateral
- 75 Hz

**Dyt-1**
- 10.15 +/- 2.93 years
- M:F 3:5
- BFM-M 36.2 \(p=0.004\)
- BFM-D: 10.5 \(p=0.002\)
- BAS: 12.3 \(p<0.001\)
- 29.63 +/- 9.32 months
  - Range 20-40 months
- 15.66 (+/- 1.46) mm lateral
- 75 Hz
Mean BFM-M Scores

Individual Raw BFM-M Scores

BFM-Motor (120)

DCP

DYT-1
BFM-D: % Change over time

BFM-D: % Change over time
Motor outcomes: Patients (≤ 16 years)

Percentage improvement:

- n=18; 68%
- n=36; 44.4%

P = 0.03
Disability outcomes: Patients (≤ 16 years)

Percent improvement

CP (n=18) 29.2%
Other (n=36) 28.2%

BFM-D

BAS

P=0.006

26.5%
22.6%
Summary

- Deep brain stimulation of the globus pallidus is effective at reducing motor dysfunction in patients with dystonia due to Dyt-1 and CP
- There is corresponding reduction in disability
- Patients with Dyt-1 have ongoing gradual improvement and may take months to stabilize
- CP patients seem to respond more quickly, but less completely than patients with Dyt-1

Marks, et al. J Child Neurol
On line 5/10/2013
Summary

• Effectiveness shown in improving motor rating scales
• Small gains in function can be important in improving quality of life
  – Reducing contracture load
  – Reducing caretaker burden
  – Hand and finger function
  – Pain
• Quality of life and neuropsychological impacts needs to be formally addressed
Summary

• Even though the complication rate is high, we believe pediatric DBS affords another viable treatment option that movement disorder teams can offer to these challenging patients.

• This information about complications enables families to learn about risks associated with pediatric DBS placement.
More work needs to be done

- Long-term follow-up
- Patient selection, target optimization, stimulation parameters
- Regional body differences
- Quality of life
- Economic impact

International registry

Why do we persist?