Outcomes of Deep Brain Stimulation for Pediatric Dystonia: A Meta-Analysis with Individual Participant Data

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Disclosure

• There are no actual or potential conflicts of interest in relation to this presentation
Introduction

Dystonia is the most common disease among pediatric movement disorders\(^1\). Presenting as a combination of repetitive involuntary muscular contractions resulting in twisting and abnormal postures, it can have a profound impact on patient and caretaker quality of life.

The mainstay of treatment for pediatric dystonia is conservative treatment with medication. However, medical treatment is often refractory, with high rates of adverse drug reactions\(^2\).

Recently, there has been increased emphasis on deep brain stimulation (DBS) as a treatment strategy for dystonia. However, its use in children remains limited. We performed a systematic review of literature and meta-analysis of DBS for childhood dystonia to establish DBS safety and efficacy. These data may inform clinical decision-making and surgical candidacy for pediatric DBS.

Methods

- A systematic review of literature was performed by searching three electronic databases, Pubmed, Web of Science, and EMBASE from inception-August 2017.
- Individual participant data (IPD) were collected from dystonic, pediatric (≤21) patients treated with DBS.
- The primary outcome of interest was the percentage change in BFMDRS$^3$ or BAD$^4$ score post-operatively compared to pre-operatively.
- Secondary objectives were to identify patient phenotypes associated with treatment response.
- Extracted IPD was analyzed using a hierarchical mixed-effects model.

Demographics

- 72 articles reporting on n=321 patients were included
- Mean age at surgery was 13.0, (SD 4.3)
- Mean Follow up was 24.6 months (SD 27.4)
- 44% of patients were male. 56% were female.
- The GPI was the main target in 95.3% of patients

Fig 1 (left). Distribution of pediatric patients treated with DBS, by etiology
Fig 2. Mean BFM motor score percent improvement after deep brain stimulation in pediatric patients with primary, secondary, and myoclonus dystonia.
## Predictors of Outcome: Multivariable Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>t-value</th>
<th>Model Coefficients (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset</td>
<td>2.4*</td>
<td>2.8 (0.6 - 4.9)</td>
</tr>
<tr>
<td>Life with dystonia (years)</td>
<td>1.3</td>
<td>1.6 (-0.9 - 4.0)</td>
</tr>
<tr>
<td>Secondary Dystonia (contrast: primary)</td>
<td>-3.3*</td>
<td>-34.7 (-57.5 - -12.2)</td>
</tr>
<tr>
<td>Myoclonus Dystonia (Contrast: primary)</td>
<td>-0.02</td>
<td>-0.4 (-39.4 – 37.8)</td>
</tr>
<tr>
<td>Trunk affected</td>
<td>3.7*</td>
<td>36.0 (16.3 - 54.5)</td>
</tr>
</tbody>
</table>

Table 1. Multivariable hierarchical mixed effects analysis of independent participant data. Age at onset and truncal involvement were associated with better outcome. Secondary dystonia (compared with primary) portended poor outcome.
Safety

• The overall risk of infection, reported in 305 patients, was 3.5%

• Death (peri-operative heart failure) occurred in 1 patient

• Patients in status dystonicus were at significantly higher risk of infection and other complications. However, resolution of dystonic storm after DBS was observed in 15/16 patients
Discussion

The present study presents the most comprehensive account of the published literature on childhood dystonia treated with DBS using individual participant data meta-analysis methodology. Several findings are reported. First, the most consistent positive responses to DBS are among patients with primary generalized dystonia and myoclonus-dystonia. Poor treatment response is associated with secondary dystonia, younger ages at dystonia onset and lack of truncal involvement. Although less effective in secondary dystonia, DBS may be considered due to the high number of medically refractory patients.
Conclusion

• Patients with primary dystonia tend to have better outcomes.
• DBS seems to be effective in treating myoclonus-dystonia.
• DBS should be considered as an emergency treatment for status dystonicus, although it may be associated with greater incidence of complication.
• Taken together, DBS for childhood dystonia is an effective and safe procedure in carefully selected pediatric cohorts.

Thank You!

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