Pediatric Deep Brain Stimulation for Dystonia: Current State and Ethical Considerations

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BRAIN INITIATIVE

BACKGROUND

Dystonia is a movement disorder that can have a debilitating impact on motor functions and quality of life. There are 250,000 cases in the US, most with childhood onset. There are two major types of dystonia. Inherited dystonia, commonly known as primary dystonia, is caused by mutations in single genes (e.g. *TOR1A*), which may or may not accompany degeneration or structural lesions. Acquired dystonia, commonly known as secondary dystonia, generally develops out of neurological disease or injury (e.g., cerebral palsy). Dystonia may also be idiopathic and have no known cause.

Available Treatments

- Botox injections, medications (e.g., benztropine), intrathecal baclofen (ITB)
- Treatments are limited in effectiveness and accompany side effects (e.g., drowsiness, memory difficulties, sedation) (8).

Refractory Dystonia:

- Uncontrolled muscular contractions can interfere with everyday purposeful movements and cause difficulty in feeding, swallowing, breathing, and communicating.
- Musculoskeletal deformity and fractures can develop over time, which profoundly affect movement, speech, vision and functionality (8).
- Refractory symptoms can also have a significant and persistent impact on patients' lives (e.g., social isolation, low self-esteem, compounded psychopathology).

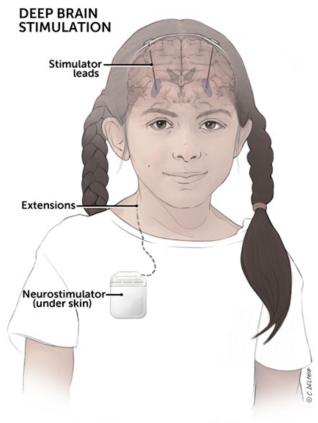
Pediatric Deep Brain Stimulation (pDBS) for Dystonia:

- The globus pallidus interna (GPi) or the subthalamic nucleus (STN) is targeted.
- Currently, pDBS is offered under an FDA Humanitarian Device Exemption (HDE) for children (≥ 7 years old) with refractory dystonia.

THE PROBLEM

An FDA Humanitarian Device Exemption does not mean the device has been found to be safe and effective, only that the device has a *probable benefit* and will not expose patients to *unreasonable risk*. Further, there is little systematic research (e.g., clinical trials) regarding its safety and effectiveness in minors, and limited examination of the ethical challenges and implications of this practice.

➢ Our research sought to answer the question: **Is it currently ethically justifiable to offer DBS to children with refractory dystonia?**



http://www.childrenshospital.org/conditions-and-treatments/treatments/deep-brain-stimulation

CLINICAL RISK-BENEFIT ANALYSIS

Benefits	Risks
Clinical Benefits: A recent meta-analysis by Elkaim et al. in 2019 analyzed the impact of pDBS for different kinds of dystonia based on the *Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS),* which includes motor and disability score. **Clear Improvement in Symptoms** = • Inherited dystonia (*without* degeneration or structural lesions) • Idiopathic dystonia (5) **Less Clear Improvement in Symptoms** = • Inherited dystonia (*with* degeneration or structural lesions) • Acquired dystonia (5) Non-Clinical Benefits: pDBS for dystonia has been shown to positively impact other meaningful aspects of patients' lives (e.g., quality of life and perceived functional performance).	The most common risks: **infection** and **hardware complications** • The infection rate for pediatric dystonia patients is about twice as high as adult populations (10.3%) (7). • Hardware malfunctions include electrode migration (2.3%),electrode/extension fracture (4.6%), electrode/extension malfunction (7.7%) (7). • Different strategies can be used to manage hardware issues (e.g., changing stimulation parameters, prolonged lead activation, and surgical revision). • Infections and hardware malfunction can lead to additional surgical risks, but generally can be managed without significant harm to patient health.

Given the favorable risk-benefit profile, we argue that it is ethically justified to offer pDBS for certain etiologies of dystonia (including inherited dystonia without degeneration or structural lesions), but it is less clear for others (such as acquired dystonia). It remains unclear as to whether small clinical improvements in symptoms can translate to meaningful changes in quality of life.

ADDITIONAL FACTORS

Other ethical and policy issues must also be addressed to optimize the practice of offering pDBS for dystonia

Determinations of Candidacy and Elimination of Bias: Institutions may use clinical and social support criteria when determining candidates, which should be evaluated to avoid inappropriate or unfair patient selection (2).

Managing Expectations: Families may overemphasize potential benefits while downplaying risks of pDBS, leading to unrealistic expectations. The inaccuracy of beliefs underlying unrealistic optimism can hinder informed decision-making, but in some cases, could "provide sustaining power in times of trial and tribulation" similarly to hope (3).

Access and Cost Barriers: Other burdens must be considered, such as the high cost of pDBS and uncertainties in health insurance coverage, which can generate access to care concerns for most families (4).

Identity Formation: Ethical considerations related to identity could be exacerbated in the pDBS setting given that childhood and particularly adolescence is considered a key period for identity formation (1). Different types of changes related to identity could in principle be beneficial or harmful. Further empirical and theoretical investigation is needed.

pDBS Unknowns: There are important unknowns of pDBS for dystonia, including its long-term benefits and harms and its effectiveness particularly for acquired dystonias. Unlike adult DBS, pDBS is performed in young individuals whose brains are still growing and developing, which could result in outcomes that researchers and clinicians have not yet uncovered.

Exacerbated in the pediatric setting?

PRACTICAL RESPONSES

➢ *Need for Active Data Registries:* To better evaluate risks and benefits, it is important for clinicians to share clinical and quality of life outcomes in data registries.

➢ *Need for a pDBS Decision Aid:* As part of this research, we are interviewing different stakeholders, including clinicians, patients, and caregivers, to better understand their perspectives on pDBS for dystonia. With this data, we will develop a decision aid tool to help caregivers and patients decide whether pDBS is good option for them.

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