ORIGINAL ARTICLE

Deep brain stimulation in childhood: an effective treatment for early onset idiopathic generalised dystonia

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Video footage is available at http://adc.bmj.com/supplemental

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Background: Early onset idiopathic generalised dystonia is a progressive and profoundly disabling condition. Medical treatment may ameliorate symptoms. However, many children have profound, intractable disability including the loss of ambulation and speech, and difficulties with feeding. Following the failure of medical management, deep brain stimulation (DBS) of the globus pallidus internus (GPi) has emerged as an alternative treatment for the disorder.
Methods: We describe four children who presented with dystonia.
Results: Following the failure of a range of medical therapies, DBS systems were implanted in the GPi in an attempt to ameliorate the children's disabilities. All children found dystonic movements to be less disabling following surgery. Compared with preoperative Burke, Fahn and Marsden Dystonia Rating Scale scores, postoperative scores at 6 months were improved.
Conclusions: DBS is effective in improving symptoms and function in children with idiopathic dystonia refractory to medical treatment. Whilst surgery is complex and can be associated with intraoperative and postoperative complications, this intervention should be considered following the failure of medical therapy.

Early onset idiopathic generalised dystonia (IGD), previously known as primary idiopathic generalised dystonia, is a progressive neurological clinical syndrome characterised by sustained muscle contractions and abnormal posture associated with twisting and repetitive movements.[1] Onset is usually before age 10 years[2 3] and although misdiagnosis is common,[4 5] at least 1:10 000 individuals are thought to be affected.[6] Clinical features are dependent on the affected territory, and may be focal, segmental, multifocal or generalised. Initial presentation is almost invariably with focal difficulties in one lower limb, resulting in foot inversion and plantar flexion, leading to a disturbance of gait; the affected limb subsequently becomes fixed in posture, and contractures follow.[2 3 7] The majority of children presenting with focal dystonia subsequently develop the more generalised form.[7 8] Oromotor musculature may be affected late in the disease, particularly in association with cervical dystonia,[9] and spasmodic dysphonia is described.[10] In the majority of individuals with onset before age 15, the condition stabilises after 5–10 years[2 4] and most individuals are left with severe disability. An important and potentially serious clinical manifestation is the uncommon status dystonicus.[11] IGD causes very significant functional disability and impaired quality of life, including loss of ambulation and independence, and difficulties with speech, feeding and self-care.[12 13]

IGD is genetically heterogeneous. However, 20% of children have the most common trinucleotide deletion in the DYT-1 gene (localised to 9q34), leading to a defective gene protein "Torsin A".[14 15] Whilst X-linked forms are described,[16] autosomal dominant inheritance occurs in most cases with approximately 30% gene penetrance.[4 5 17]

The neuropathological aetiology of IGD is unknown. Neurometabolic investigations and cranial imaging with MRI are unhelpful, other than excluding treatable secondary causes of dystonia (such as Wilson disease). Motor analysis and neuropsychological and neurophysiological evaluation enable clinicians to identify individuals with psychogenic dystonia, who may be harmed by unnecessary medication and interventions.[3 18] IGD is therefore differentiated from secondary and neurodegenerative dystonia by the typical clinical features and the lack of an alternative diagnosis.

Medical therapy is of limited efficacy in the treatment of IGD.[17] All individuals with dystonia should receive a levodopa trial for 1–3 months (L-dopa, 1–10 mg/kg/day in four to six divided doses)[19] as a diagnostic test for treatable dopa responsive dystonia (DRD); individuals without DRD may benefit.[17 20 21] Following the limited effect of medication, surgical treatments have been used to ameliorate dystonia. However, these techniques are associated with variable responses and significant morbidity.[17]

Recently, bilateral deep brain stimulation (DBS) of the globus pallidus internus (GPi) has proved efficacious in movement disorders,[17] although the mechanism of action is unknown.[22] Electrodes are implanted stereotactically under general anaesthetic[23] and connected to an implantable battery-powered pulse generator (IPG) positioned in the chest or abdominal wall. Previously, repeated IPG battery changes led to multiple scars and an increased risk of wound infections, but the introduction of smaller rechargeable IPGs has lessened local side effects. Treatment parameters are altered using a remote device and optimal clinical benefit may take up to 2 years to achieve.[24] Postoperatively individuals may continue to use medication.[25]

Abbreviations: BFMDRS, Burke, Fahn and Marsden Dystonia Rating Scale; DBS, deep brain stimulation; DRD, dopa responsive dystonia; IGD, idiopathic generalised dystonia; GPi, globus pallidus internus; IPG, implantable pulse generator

Table 1 Clinical data

Case number	Initial clinical presentation	DYT-1 status	Evolution of dystonia (functional impairment prior to DBS insertion)	Age at GPi DBS insertion	Preoperative BFMDRS Severity/ Disability	Postoperative BFMDRS (6 months) severity/disability	% Improvement in severity/disability (functional ability)
Case 1	F, aged 10 years. Handwriting deterioration	Negative	Bilateral upper limb and truncal dystonia; unable to walk, feed or wash unaided. Schooling affected	14 years	77/21	30/20 (34/20 at 18 months)	61/5. Walked unaided; easier wheelchair use; self-care skills modestly improved
Case 2	M, aged 8 years. Dystonia right foot	Positive	Limbs, trunk and laryngeal muscles affected; severe difficulties with walking, feeding and washing. Schooling affected	15 years	66/10	10/5 (8/3 at 13 months)	85/50. Almost normal gait (in-toe, right foot); independent care skills
Case 3	F, aged 18 months. Dystonia left foot	Negative	Limbs, trunk, laryngeal and oromotor muscles affected; unable to use wheelchair due to posture. Crawled to move; unable to stand or walk. Schooling affected	8 years; revision aged 9 years due to lead displacement and infection	103/28	36/10 (41/17 at 36 months, after battery change)	65/64. Walked and used wheelchair; independent care skills
Case 4	M, aged 14 months. Paroxysmal dystonic episodes	Negative	Increased frequency of 1–2 min episodes. Wheelchair bound, unable to walk, feed or wash unaided. Schooling affected	10 years	85/17	62/9 (53/11 at 12 months)	27/47. Paroxysmal dystonic episodes eradicated, walked unaided; self-care skills improved

BFMDRS, Burke, Fahn and Marsden Dystonia Rating Scale; DBS, deep brain stimulation; GPi, globus pallidus internus.

Results of DBS for IGD have led to this approach being adopted as the treatment of choice, with a postoperative reduction in Burke, Fahn and Marsden Dystonia Rating Scale (BFMDRS)[i] scores.[27–33] Of 34 children reported in these series, 32 children showed functional improvement and had lower BFMDRS scores postoperatively. Recently, the first prospective, double-blind controlled multicentre study of DBS in 22 patients (mostly adults) was undertaken.[25] In the majority of individuals, dystonia severity and disability scores were significantly improved at 12 months. However, the majority of individuals using medication continued to do so postoperatively. Whilst treatment with DBS has shown excellent results in IGD, DBS may be less efficacious in the treatment of secondary dystonia.[17 34]

Whilst DBS seems to benefit individuals with IGD, intraoperative and postoperative side effects may occur. Intracranial haemorrhage, infection of implanted hardware, deterioration in skin viability, and electrode and lead displacement are all serious potential sequelae.[34] Furthermore, malfunction of the DBS unit or connections causes loss of stimulation, resulting in ''rebound dystonia'' and status dystonicus.[30]

METHODS

We describe four children with IGD who had DBS units implanted into the GPi following the failure of standard medical management. Preoperatively, children were assessed using the BFMDRS (severity and disability)[26] and examples of dystonic movements were recorded on videotape. Known secondary causes of dystonia had been excluded by paediatric neurologists on the basis of clinical history and examination and by performing relevant investigations.

[i]BFMDRS scores[26] comprise a severity score (range 0–120) and a functional disability score (range 0–30). Whilst BFMDRS validation studies have not been completed in children, the scale is the most frequently used measure of the efficacy of DBS in childhood.[27–33] The severity score is calculated by combining the degree of provocation required to cause dystonia (ranging from no dystonia at rest, to dystonia present at rest) and the severity in various muscle groups (eyes, mouth, speech and swallowing, neck, arm, trunk and leg). The functional disability score represents the degree of disability caused to speech, eating/swallowing, feeding, walking, handwriting, hygiene and dressing.

Neuropsychological assessments were completed to aid diagnosis, assess patients' and families' suitability for surgery, and to obtain a preoperative cognitive, behavioural and social-emotional profile. As a result of dystonia, two children had been compelled to shift hand preference and three children had significant speech-motor difficulties. Assessment of cognitive skills and attainments took account of the confounding influence of medication and behavioural difficulties. All four children had mild learning disability (IQ range 60–80) and received some special educational provision. By contrast, individual cognitive domain scores ranged from low average to average; relative preservation of cognition was most likely secondary to the lesser effect of physical disability on cognitive task performance.

The clinical presentation, DYT-1 status and 6-month postoperative progress (including percentage improvements in BFMDRS severity and disability scores) of all children are shown in table 1. Mean differences between pre- and postoperative BFMDRS scores (severity and disability) for the group were computed using paired sample *t* tests. Where further follow-up BFMDRS scores were available, these are shown.

RESULTS

All children responded to bilateral GPi stimulation and voltage and pulse width were increased at 3-monthly clinic visits until maximum clinical effect was achieved. Comparison of pre- and 6-month postoperative BFMDRS scores revealed improvement in all four individuals (table 1). Comparing preoperative and 6-month postoperative data, the group mean severity score was significantly improved postoperatively (83 vs 35 (56% improvement); paired samples *t* test, $p = 0.014$). Compared with preoperative data, the postoperative group mean disability score was non-significantly improved (19 vs 11 (42% improvement); paired samples *t* test, $p = 0.12$). At 6 months, functional ability was improved in all four individuals.

Videotape footage of the individual identified as case 2 shows the disabling effect of dystonia preoperatively, and the striking postoperative improvement (parental/guardian informed consent was obtained for showing this video; see http://www.archdischild.com/supplemental).

What is already known on this topic

- Early onset idiopathic generalised dystonia is a progressive and profoundly disabling condition.
- Despite medical treatment many children have significant functional disability and impaired quality of life.

What this study adds

- Deep brain stimulation is an effective treatment for early onset idiopathic generalised dystonia.

DISCUSSION

Idiopathic torsion dystonia is a clinically heterogeneous condition causing significant functional neurodisability. Our experience of the failure of medical management is in keeping with previous reports[3] and all individuals were subsequently treated with DBS of the GPi, resulting in marked clinical and functional improvement in ambulation and self-care skills; all individuals were able to attend school postoperatively. Similar findings have been described in a number of recent series[27–33] and a prospective double-blind controlled study (individuals randomised to stimulation switched on or off for 3 months following insertion) has shown benefit in a predominantly adult sample.[25] All four individuals in our series responded gradually to increasing stimulation. However, in keeping with previous studies, some children improved more than others and rates of progress differed.[32] Individuals who are unresponsive to ''standard'' stimulator programming settings (10–20% in our experience) may suffer a marked delay in improvement and may notice no improvement at all.[25] Overall, clinicians, patients and parents should recognise that dystonia may be ameliorated rather than completely abolished.

Regular postoperative review is necessary to monitor both technical aspects relating to the DBS unit and BFMDRS scores. Subsequently, IPG battery life is checked 6 monthly, and batteries recharged or replaced prior to reaching their ''end of life'', thus reducing the possibility of a rebound dystonic crisis. In our series, case 3 suffered a clinical deterioration 2 years postoperatively secondary to an expired battery. BFMDRS severity and disability scores increased to 80 and 25, respectively; when retested following emergency battery replacement, scores were immediately improved (severity 41, disability 17).

Postoperative neuropsychological follow-up is also required to monitor children's and families' psychosocial adjustment to surgical outcomes, and to mediate necessary changes in educational provision. When stimulator levels are judged optimally titrated and stable, detailed neuropsychological follow-up should include neuropsychometric tests and the comparison of pre- and postoperative cognitive profiles. Regular neuropsychometric review should continue as the cognitive and neurodevelopmental implications of long-term GPi stimulation are unknown.[35 36]

Whilst the individuals we describe suffered no intraoperative complications, case 3 has undergone operations for battery changes and lead displacement (caused by sliding downstairs); subsequently, the unit required revision due to infection, and treatment with intravenous antibiotics was necessary. As demonstrated, the recommencement of usual childhood activities can result in difficulties; climbing and contact sports may result in lead displacement and should be avoided. A balance between allowing a better quality of life and the likely risk to equipment should be sought; of the four individuals described, one now skis (whilst sitting down), another plays football and one child has recently started riding a quad bike.

CONCLUSIONS

Whilst not free of potential side effects, DBS of the GPi is clinically indicated to treat IGD and improves daily functioning. Longitudinal studies of the effectiveness of DBS are necessary to assess possible negative effects and long-term clinical outcome.

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The effect of environmental pollutants on foetal and child development: a global issue

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