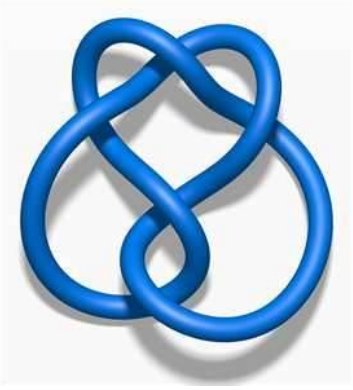


Dystonia

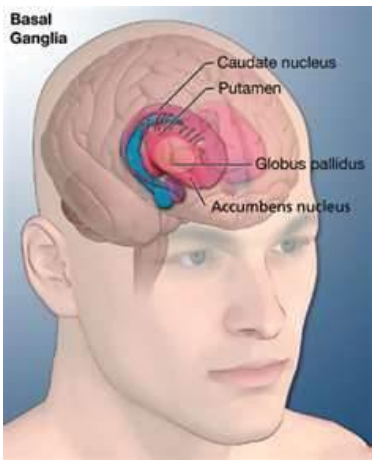
A New Twist on an Old Problem

Dr. Kathryn A. Chung
Associate Director of Clinical Care
Northwest PADRECC

Facts and Definitions

- A disorder of sustained muscle contractions that cause abnormal body positions (sometimes painful).
- Thought to arise in the basal ganglia and an inherent or acquired neurotransmitter processing abnormalities.

Basal Ganglia



What goes wrong in dystonia?

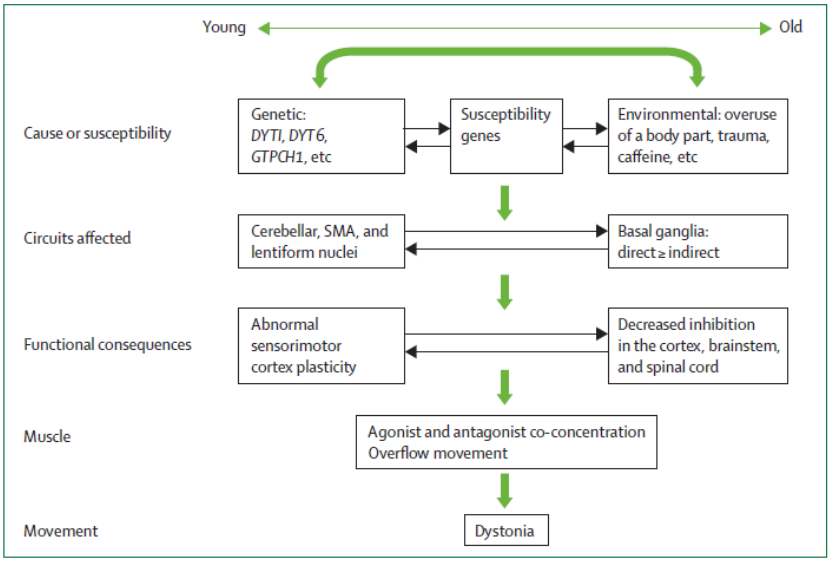


Figure: **Pathogenetic mechanisms in primary dystonia**
GTPCH1=GTP cyclohydrolase 1. SMA=supplementary motor area.

From Phukan et al Lancet Neurology 2011

- Nutt et al suggested 250,000 people in the US are affected by dystonia, but this number may be much higher due to missed diagnoses.
- European study: prevalence of primary dystonia in the general population >50yo was estimated at 732/100,000.

Classification of Dystonia

- 1. Etiology
  - Primary—not caused by any other identifiable condition, no other neurologic abnormalities on exam
    - Often "genetic" or inherited ie DYT-1 gene abnormalities
  - Secondary
    - Due to another disease : stroke, perinatal injury, cerebral palsy, head injury, multiple sclerosis, parkinson disease, parkinson plus syndromes, Wilson's disease, exposure to offending drugs like neuroleptics, probably methamphetamine too, or toxins like heavy metal, Carbon monoxide poisoning, or psychiatric illness .
- 2. Bodily Distribution of symptoms
  - Generalized
  - Segmental
  - Focal
    - Multifocal, hemidystonia
- 3. Age of onset
  - Early onset (childhood, young adult) vs late onset (> 27 yo)

Primary Dystonias

Dystonia Type	Genetic Designation	Inheritance	Chromosomal Location	Gene Product	OMIM Identifiers
Primary Dystonia					
Early-onset generalized torsion dystonia	DYT1	AD	9q34	Torsin 1A	605204, 128100
Adolescent-onset torsion dystonia of mixed type	DYT6	AD	8p21–8p22	Unknown	602629
Adult-onset focal torsion dystonia	DYT7	AD	18p	Unknown	602124
Mixed onset cranial/cervical/brachial	DY13	AD	1p36.13–36.32	Unknown	
Primary Plus Dystonia					
Dystonia-Parkinsonism					
Dopa-responsive dystonia/Segawa's	DYT5	AD/AR	14q22.1–q22.2	GTP cyclohydrolase	600225, 128230
		AR	11p15.5	Tyrosine hydroxylase	605407, 191290
6-pyruvoyl-tetrahydropterin synthase (6-PTPS) deficiency		AR	11q22.3–q23.3	6-pyruvoyl–tetrahydropterin synthase	261640
Sepiapterin reductase deficiency		AR	2p14–p12	Sepiapterin reductase	182125
Dihyropteridine reductase (DHPR) deficiency		AR	4p15.31	Dihyropteridine reductase	261630
Aromatic L-amino acid decarboxylase (ALAAD) deficiency		AR	7p11	Aromatic L-amino acid decarboxylase	107930
Myoclonus Dystonia					
Myoclonus-dystonia	DYT11	AD	11q23	D2 dopamine receptor	159900
			7q21–31	Unknown	605408
Paroxysmal Dystonia					
Paroxysmal dystonic choreoathetosis	DYT8	AD	2q33–q35	Unknown	118800
Paroxysmal choreaoathetosis w/episodic ataxia/spasticity	DYT9	AD	1p21–p13.3	Unknown	601042
Paroxysmal kinesigenic choreoathetosis	DYT10	AD	16p11.2–q12.1	Unknown	128200

Hereditary forms of primary and primary-plus dystonias. Listed are the names of the disorders, genetic designation ("DYT number," if any), the pattern of inheritance (AD—autosomal dominant, AR—autosomal recessive), chromosomal location of the gene, the product of the gene, and the identifiers listed in Online Mendelian Inheritance in Man (OMIM; http://www.ncbi.nlm.nih.gov/Omim/).

Secondary Dystonias

Table 3. SECONDARY DYSTONIAS

Perinatal Cerebral Injury (onset of dystonia may be delayed)
- Perinatal anoxia
- Kernicterus

Congential Malformations
- Arteriovenous malformation
- Cerebellar ectopia and syringomyelia
- Pachygyria

Central and Peripheral Nervous System Insults or Injuries
- Hypoxia
- Brain tumor
- Stroke
- Head trauma
- Intracranial hemorrhage
- Multiple sclerosis
- Central pontine myelinolysis
- Spinal cord injury
- Peripheral nerve injury

Infectious, Postinfectious, Inflammatory, and Paraneoplastic
- Viral encephalitis (including HIV)
- Reye's syndrome
- Subacute sclerosing panencephalopathy
- Creutzfeldt–Jakob disease
- Tuberculosis
- Syphilis
- Paraneoplastic brain stem encephalitis
- Lupus
- Antiphospholipid antibody syndrome

Drug–Induced (may produce acute dystonic reactions or tardive dystonia)
- Dopamine stimulating agents (L-dopa, dopamine agonists)
- Dopamine D2 receptor blockers (antipsychotics, metaclopramide)
- Anticonvulsants
- Serotonin reuptake inhibitors (SSRIs)
- Buspirone
- Cocaine
- MAO inhibitors
- Flecainide
- Ergots

Neurotoxins
- Manganese
- Carbon monoxide
- Carbon disulfide
- Cyanide
- Methanol
- Disulfiram
- 3-nitroproprionic acid
- Wasp sting

Metabolic Disorders
- Hypoparathyroidism

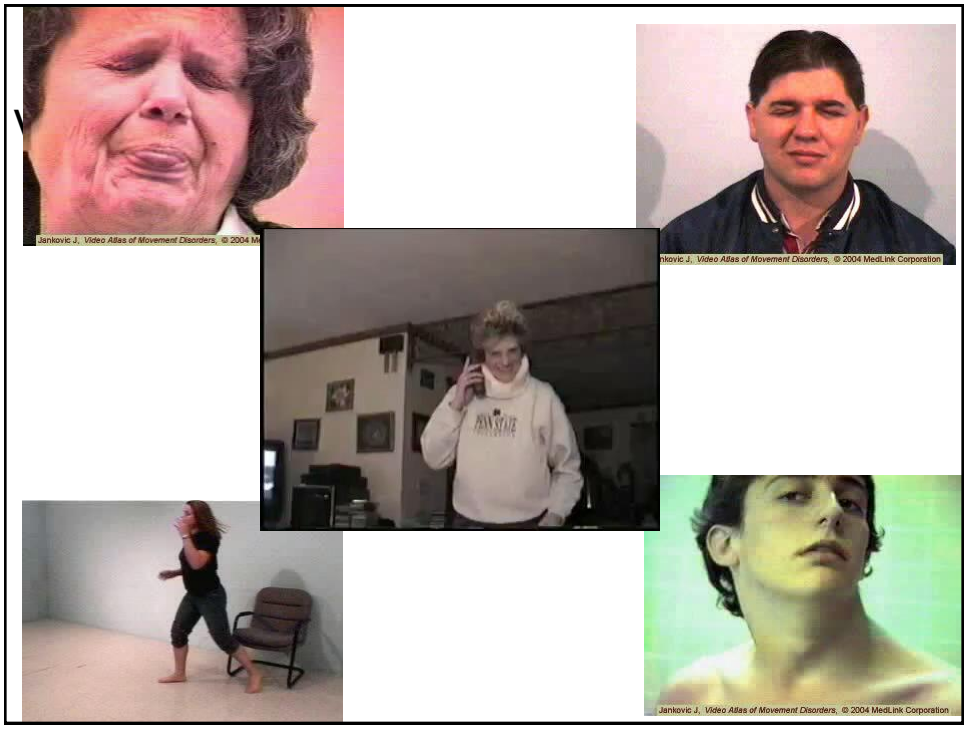
More Secondary Dystonias

Table 4. HEREDODEGENERATIVE DYSTONIAS

Disorder	Inheritance	Diagnostic Testing
Trinucleotide Repeat Disorders		
Huntington's Disease	AD	DNA Mutation Analysis
Machado–Joseph Disease	AD	DNA Mutation Analysis
Dentatorubropallidoluysian atrophy	AD	DNA Mutation Analysis
Parkinsonian Disorders		
Parkinson's Disease	SP, AR, AD	Clinical/Pathologic
Progressive Supranuclear Palsy	SP, AD	Clinical/Pathologic
Corticobasalganglionic Degeneration	SP	Clinical/Pathologic
Multiple System Atrophy	SP	Clinical/Pathologic
X-linked dystonia parkinsonism (DYT3)	X	Clinical/Pathologic/DNA Linkage in affected families
Rapid-onset Dystonia Parkinsonism	AD	Clinical/DNA Linkage in affected families
Lysosomal Storage Disorders		
Metachromatic Leukodystrophy	AR	WBC or fibroblast arylsulfatase A, urinary sulfatides
GM1 Gangliosidosis	AR	WBC or fibroblast beta-galactosidase activity
GM2 gangliosidosis	AR	Plasma, WBC, or fibroblast hexosaminidase A and B levels
Nieman Pick C	AR	Fibroblast cholesterol esterification and filipin staining
Krabbe Disease	AR	WBC or fibroblast galactocerebrosidase activity
Neuronal Ceroid Lipofuscinosis	AR	Clinical/Pathologic, Skin biopsy, DNA enzyme analysis in selected subgroups
Amino and Organic Acidurias		
Glutaric Acidemia type 1	AR	Quantitative urine organic acids, fibroblast glutary-CoA dehydrogenase
Homocysteinuria	AR	Quantitative plasma and urine amino acids
Hartnup Disease	AR	Quantitative plasma and urine amino acids
Methylmalonic Aciduria	AR	Quantitative urine organic acids, fibroblast methylmalonic CoA mutase activity
Fumarase Deficiency	AR	Quantitative urinary organic acids, WBC or fibroblast fumarase activity
Mitochondrial Disorders		
Leigh's Disease	AR, M	
Leber's Hereditary Optic Neuropathy	M	Clinical, MRI, serum lactate, pyruvate, alanine, urine organic acids, muscle OXPHOS enzymes, mitochondrial DNA mutation analysis fibroblast pryuvate dehydrogenase activity (Leigh's)
Dystonia Deafness/Mohr Tranenberg	X	

Table 4. HEREDODEGENERATIVE DYSTONIAS *Continued*

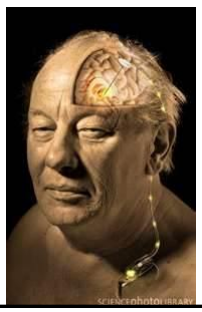
Disorders of Metal and Mineral Metabolism		
Wilson's Disease	AR	Ceruloplasmin, 24 hr urine copper, Kayser-Fleisher rings, DNA linkage analysis (95%), mutational analysis (70%)
Hallevorden–Spatz Syndrome	AR	Clinical/Imaging/Pathologic
Fahr's Syndrome	AD, AR, SP	Clinical/Imaging/Pathologic
Miscellaneous Metabolic Disorders		
Lesch-Nyhan Syndrome	X	RBC or fibroblast hypoxanthine guanine phosphoribosyl transferase
Molybdenum cofactor (Sulfite Oxidase) deficiency	AR	Urinary sulfite, thiosulfite, taurine and S-sulfocysteine measurement, fibroblast or liver sulfite oxidase activity
Cockayne's Disease	AR	Clinical, fibroblast UV survival curve assay, RNA synthesis inhibition by UV irradiation
Triosephosphate Isomerase Deficiency	AR	RBC triosephosphate isomerase activity
Ataxia Telangectasia	AR	Immunoglobulins, alphafetoprotein, colony survival assay in X-irradiated cultured fibroblasts, chromosomal studies
Guanidinoacetate methyltransferase deficiency	AR	Fibroblast or liver guanadinomethyltransferase activity, MR-SPECT, CSF creatine and creatinine
Glucose Transport Defects	AD	CSF glucose, RBC glucose uptake
Other Disorders		
Rett Syndrome	X	Clinical, DNA Mutational Analysis (70%)
Pelizaeus-Merzbacher Disease	X	Clinical, Imaging, DNA Mutational Analysis (80%)
Vitamin E deficiency	AR, SP	Vitamin E levels
Intraneuronal Inclusion Disease	SP	Clinical/Pathologic, Rectal biopsy
Xeroderma Pigmentosa	AR	Fibroblast UV survival curve assay, unscheduled DNA synthesis assay
Neuroacanthocytosis	UN	Blood smear to evaluate for acanthocytes
Familial Striatal Necrosis	UN, M, AR	Clinical/Imaging/Pathologic
Infantile Bilateral Striatal Necrosis	UN	Clinical/Imaging/Pathologic
Progressive Pallidal Degeneration	UN	Clinical/Imaging/Pathologic



- Oral medications

- Chemo denervation

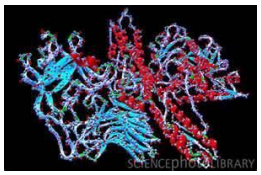
- Deep Brain Stimulation



- Blepharospasm: With the exception of baclofen, oral medications are disappointing
- Limb dystonia: drug toxicity and adverse effects often outweigh benefit, but medications that can be tried include
  - anticholinergics
  - dopamine agonists (esp sinemet)
  - dopamine antagonists
  - baclofen
  - clonazepam, other benzodiazepines
  - muscle relaxants (ie tizanidine, cyclobenzaprine)

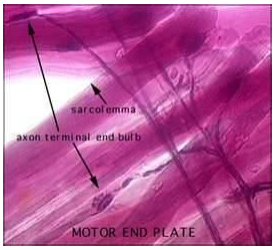
Chemodenervation

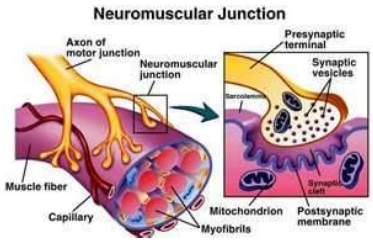
- Injection directly into abnormally contracting muscles or nerves
- Nerve injections agents include phenol, ethyl alcohol (not often used anymore)
- Muscles are injected by a toxin
  - *Clostridium botulinum* makes 7 potent paralysing neurotoxins



- Botulinum Toxins Type A and B are used
  - A: onabotulinum, incobotulinum, abobobotulinum
  - B: rimabotulinum

- Muscles contract when a neurotransmitter called acetylcholine crosses the synapse (distance) between the nerve ending and onto the muscle.





Chemodenervation (cont)

- Injection of botulinum toxin into dystonic muscles was recommended by the NIH in 1990 "FDA approved" indications vary depending on which toxin is considered.
- Used for treatment of torticollis, blepharospasm, hemifacial spasm, writer's cramp, oromandibular dystonia, spasmodic dysphonia and other focal dystonias.

Treatment indications

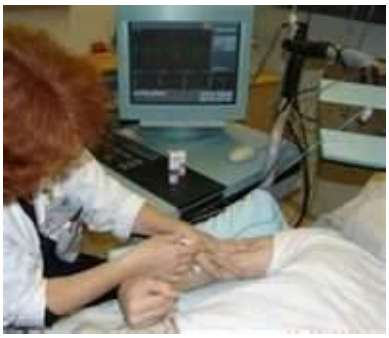
1. The dystonia should be significant enough to cause functional problems, discomfort or interference with personal care (affects daily living).
2. Focal muscle weakening by toxin should not cause functional impairment.
3. The patient understands that this treatment may not complete alleviate dystonia

Contraindications

- Pregnancy, lactation, comorbid neuromuscular disease like myasthenic gravis or amyotrophic lateral sclerosis (Lou Gehrig's disease)
- Concomitant use of an aminoglycoside (ie gentamicin, tobramycin) .

Other

- Need for botox needs to be evaluated before each injection session. In general this is at least every 3 mos.
- Clinician may use an EMG machine to help locate dystonic muscles



Goals and Outcomes

- To Palliate pain/discomfort, improve neck (or other body parts) position, and to decrease disability/improve function.
- Injections takes 2-12 days to "kick in" and may seem best in efficacy for another 2-6 weeks. Relief usually lasts a total of 12-16 weeks.
- Occasionally, some patients develop antibodies to botox A, and will usually be switched to try serotype B.
- Unfortunately, some patients have trouble lasting 12 weeks, which is considered the minimal time to wait between treatments.

Clinical Trials

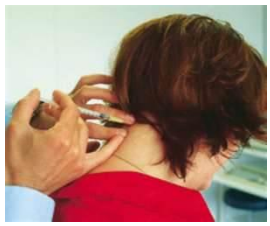
Open-Label Non-Inferiority Study Evaluating the Efficacy and Safety of Xeomin® in Subjects With Cervical Dystonia Flex

- Purpose: This study will compare Xeomin®, a botulinum toxin medication, in shorter treatment intervals (Short Flex dosing) to the standard interval dosing (Long Flex dosing) to determine if the response to treatment is comparable in both how it works and any side effects.

VA Research Opportunity

- The current practice for botulinum toxin injection treatment is to inject patients every 3 months. However, not all patients receive continuing benefit from botulinum toxin injections for an entire 3 months.
- In a recent survey, approximately 45% of patients report that they would prefer a treatment cycle of less than 10 weeks.
- This study will compare XeominÂ®, a botulinum toxin treatment, in shorter treatment intervals (Short Flex dosing) to the standard interval dosing (Long Flex dosing) to determine if the response to treatment is comparable in both how it works and any side effects.

Sponsored by: Merz Pharmaceuticals, LLC



Official(s) and/or principal investigator(s):
Eric J. Pappert, MD, Study Director,
Affiliation: Merz Pharmaceuticals, LLC

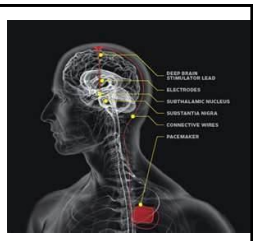
- **Eligibility** Minimum age: 18 Years. Maximum age: 81 Years. Gender(s): Both.
- **Criteria:**
  - Inclusion Criteria:

    - Documented clinical diagnosis of idiopathic or genetic Cervical Dystonia

  - Exclusion Criteria:

    - Current treatment with botulinum toxin of any type for any other indication (including aesthetic indications) and for any body region during the study.

Surgical Treatment of Dystonia



- 2003: FDA approval under a humanitarian exemption of Deep brain stimulation (DBS) of the subthalamic nucleus (STN) or Globus Pallidus interna (GPi)
  - In primary generalized dystonia patients 7yo or older.

What is the evidence?

Isaias et al

- 30 PGD patients with DBS followed for 3 years
- Clinical rating scales improved by 82% by 2 years, disablity decreased by 75%
- In a subgroup of 5 subjects followed 7 years, improvements still topped 80%
- Some adverse problems included speech difficulties and transient blepharospasm were reported in one.

Vidailhet et al

- 22 PGD patients followed for 3y
- Motor function improved by 58% after 3y on average
- Health related Quality of Life improved significantly
- In 3 subjects, serious adverse events were reported including one infection and 2 broken leads

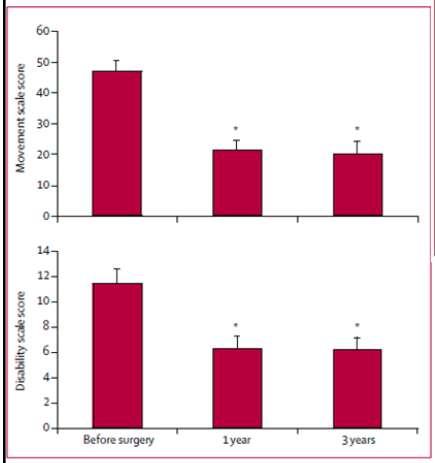


Figure 2: **Burke-Fahn-Marsden dystonia scale before and 1 and 3 years after surgery**
Data are means. Vertical bars represent SEM. *p<0·001 for the comparison with the preoperative score.

	Before surgery	1 year after surgery	3 years after surgery	p (3 years *vs* baseline)	p (3 years *vs* 1 year)
Movement scale (range)					
Axis: neck and trunk (0–24)	12·5 (7·9)	3·9 (4·1)	4·4 (5·09)	<0·0001	0·43
Limbs: lower, upper (0–64)	28·5 (16·3)	13·6 (12·2)	11·8 (13·5)	<0·0001	0·04
Face: eyes and mouth (0–16)	2·1 (2·5)	1·3 (2·1)	1·3 (2·0)	0·03	0·64
Speech and swallowing (0–16)	2·8 (3·9)	2·2 (2·8)	2·1 (3·1)	0·17	0·89
Total	46·3 (21·3)	21·0 (14·1)	19·8 (17·4)	<0·0001	0·03
Disability scale (range)					
Speech (0–4)	1·3 (1·3)	1·3 (1·3)	1·4 (1·3)	0·62	0·40
Writing (0–4)	2·0 (1·1)	1·2 (0·9)	1·2 (0·7)	0·004	1·00
Feeding (0–4)	1·6 (0·9)	0·5 (0·7)	0·5 (0·7)	0·0004	1·00
Eating and swallowing (0–4)	1·1 (1·0)	0·5 (0·7)	0·3 (0·6)	0·004	0·51
Hygiene (0–4)	1·4 (0·8)	0·5 (0·7)	0·6 (0·9)	0·002	0·50
Dressing (0–4)	1·3 (0·9)	0·5 (0·8)	0·5 (0·8)	0·002	0·78
Walking (0–6)	3·0 (1·6)	2·0 (1·5)	1·9 (1·5)	0·002	0·62
Total	11·6 (5·5)	6·7 (5·2)	6·3 (4·9)	0·0001	0·84

Data are mean (SD). A reduction in scores indicates an improvement in dystonia.

Table 2: **Effect of bilateral pallidal stimulation on Burke-Fahn-Marsden subscores at 1 and 3 years after surgery**

Quality of Life Measures

	Before surgery	1 year after surgery	3 years after surgery	p (3 years *vs* baseline)	p (3 years *vs* 1 year)
General health	47 (24)	63 (27)	64 (21)	0·02	0·50
Physical functioning	41 (28)	62 (29)	68 (32)	0·008	0·48
Role physical	53 (43)	58 (39)	69 (37)	0·34	0·26
Role emotional	59 (48)	77 (37)	71 (39)	0·72	0·51
Social functioning	57 (36)	58 (29)	63 (30)	0·59	0·51
Body pain	39 (32)	56 (36)	61 (25)	0·01	0·40
Vitality	40 (24)	50 (24)	47 (21)	0·98	0·53
Mental health	54 (20)	64 (23)	58 (21)	0·45	0·38

Data are mean (SD). The possible score range is 0–100. An increase in scores indicates an improvement in function.

Table 3: **Health-related quality-of-life subscores (SF-36) before and 1 and 3 years after surgery**

Double-blinded Trial

- DBS vs sham DBS in 40 patients with PGD or segmental dystonia.
- At 3 mos, dystonia severity improved by 16% in DBS, 1% in sham.
- When the sham patients received real DBS for 3 mos, they improved as well.
- Patient ratings of disability and quality of life improved in DBS.
- Dysarthria occurred in 5 subjects, serious infection in 4, and lead displacement in 1.
- Dyt-1 did not confer any better or worse outcomes in adults, but in children, those with Dyt mutations did better.

DBS reduced the abnormal scores in the stimulation group

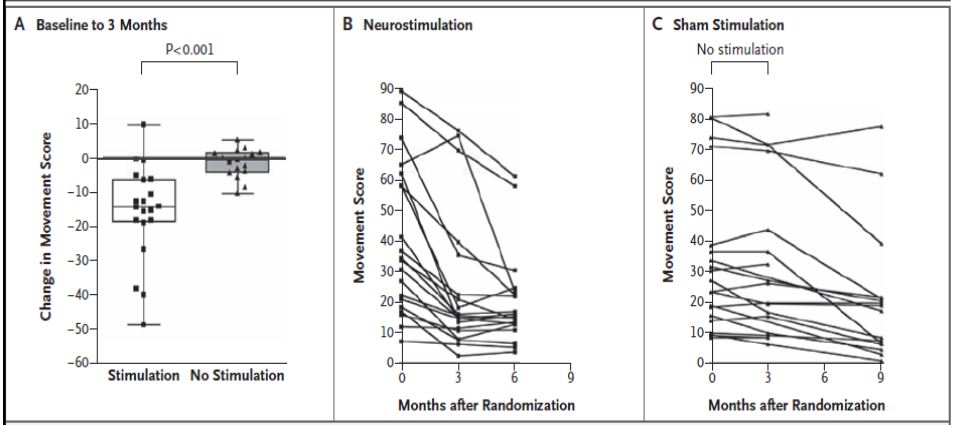


Figure 2. Changes in Movement Scores from Baseline to 3 Months and the Effects of 6 Months of Neurostimulation, as Compared with Sham Stimulation.

From Kupsch et al, NEJM 2006

Quality of life improves with DBS

TABLE 1. *Results of the 3-mo study phase*

	Baseline				3 Mo				Change from baseline to 3 mo				
	Stimulation		Sham stimulation		Stimulation		Sham stimulation		Stimulation		Sham stimulation		
Variable	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	*P* value
BFMDRS movement score[a]	20	40.2 ± 24.9	20	32.6 ± 24.3	20	24.5 ± 22.8	18	31.7 ± 25.2	20	−15.8 ± 14.1	18	−1.6 ± 4.0	<0.001
BFMDRS disability score	20	10.4 ± 6.2	20	9.6 ± 7.1	20	6.5 ± 5.5	19	8.5 ± 7.0	20	−3.9 ± 2.9	19	−0.8 ± 1.2	<0.001
SF-36 domain scores[b]													
Physical function (PF)	18	39.9 ± 25.0	19	38.7 ± 19.7	18	67.2 ± 29.8	18	42.5 ± 20.1	18	27.3 ± 24.8	18	3.0 ± 22.1	0.001
Role physical (RP)	18	29.2 ± 40.4	19	32.9 ± 35.4	19	56.6 ± 35.2	17	48.5 ± 39.0	18	25.0 ± 44.6	17	13.2 ± 34.4	0.20
Bodily pain (BP)	19	49.8 ± 31.1	19	38.6 ± 27.2	19	72.5 ± 23.4	18	46.9 ± 32.3	19	22.7 ± 23.9	18	9.7 ± 25.4	0.04
General health (GH)	19	41.3 ± 16.4	19	44.5 ± 16.0	19	58.9 ± 18.3	18	46.8 ± 15.5	19	17.6 ± 20.7	18	2.1 ± 17.2	0.02
Vitality (VT)	19	46.8 ± 23.3	19	43.9 ± 18.3	19	61.6 ± 13.5	18	46.4 ± 17.7	19	14.7 ± 21.7	18	2.0 ± 13.8	0.047
Social function (SF)	19	47.4 ± 39.4	19	71.1 ± 28.6	19	68.4 ± 29.6	18	72.9 ± 27.2	19	21.1 ± 40.8	18	0.7 ± 19.9	0.07
Role emotional (RE)	19	61.4 ± 42.0	19	63.2 ± 44.3	19	86.0 ± 30.1	17	72.5 ± 41.2	19	24.6 ± 33.0	17	13.7 ± 50.1	0.43
Mental health (MH)	19	61.3 ± 22.0	19	58.7 ± 17.9	19	72.0 ± 16.1	18	61.6 ± 17.3	19	10.7 ± 25.5	18	2.0 ± 11.9	0.54
Physical component score (PCS)	17	33.9 ± 9.0	17	33.5 ± 6.6	18	44.1 ± 9.0	18	37.7 ± 10.3	17	10.1 ± 7.4	16	3.8 ± 8.4	0.02
Mental component score (MCS)	19	45.1 ± 15.1	19	47.1 ± 11.7	16	50.7 ± 11.3	16	48.7 ± 11.6	17	5.2 ± 15.0	16	0.2 ± 8.7	0.39
Beck depression inventory[c]	16	10.5 ± 7.3	18	9.7 ± 5.8	14	6.4 ± 8.9	16	10.6 ± 10.1	14	−5.1 ± 8.4	16	−0.5 ± 10.2	0.42
Beck anxiety inventory[c]	18	13.7 ± 11.0	19	12.1 ± 10.5	16	8.0 ± 6.5	17	10.5 ± 7.4	16	−6.9 ± 10.2	19	−2.4 ± 11.4	0.10
Brief psychiatric rating scale[c]	19	27.0 ± 7.3	19	27.8 ± 8.0	18	21.4 ± 4.6	19	24.8 ± 5.5	18	−5.9 ± 6.3	19	-3.0 ± 8.4	0.09

[a]The total movement score of the Burke–Fahn–Marsden Dystonia Rating Scale (BFMDRS) is the sum of individual scores for each body region and represents the severity of symptoms of dystonia.
[b]A higher score on this scale indicates a higher level of function.
[c]A higher score on this scale indicates a greater severity of symptoms.

Selection of Patients for surgery

- Patients must be diagnosed with dystonia and be significantly disabled
- Secondary dystonia generally doesn't respond as well as primary
  - Tardive dystonia may be an exception.
    - In these cases, the dystonia should have been going on long enough that spontaneous remission seems unlikely (because it can happen).
  - Limb and axial dystonia may respond better than for dystonic speech and swallowing.
  - Dynamic or phasic dystonia (ie jerky) dystonia likely responds better than a more fixed dystonia.
  - If it's not muscle, it probably won't respond ie rule out bony spine deformities, tendon shortening or joint disease.

DBS for cervical dystonia: results of a multi-Center single-blinded trial of Gpi stimulation Kiss et al Brain 2007

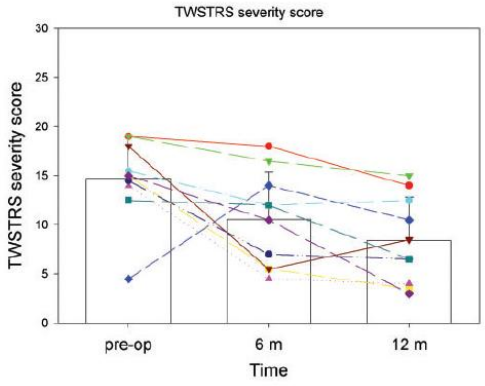
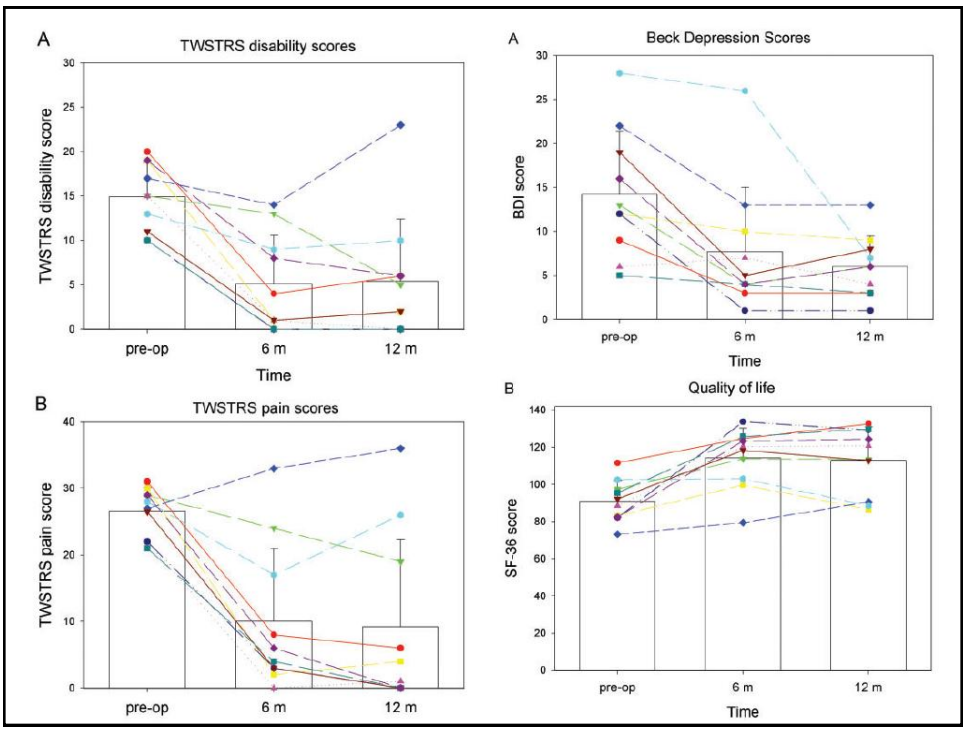
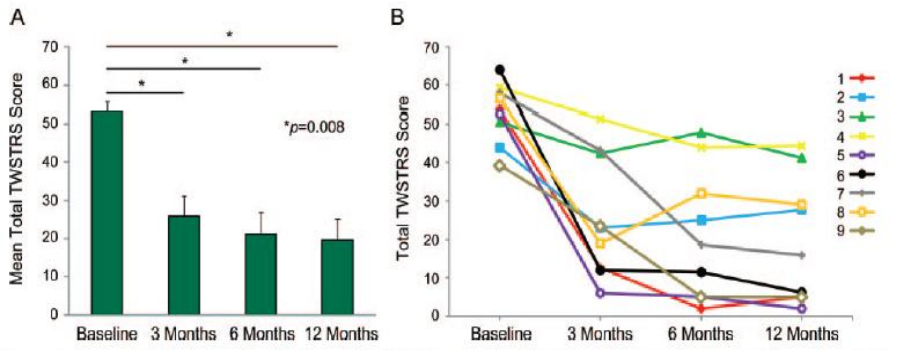


Fig. 1 Primary outcome measure, the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) change over time. Each patient is illustrated as an individual symbol and line indicating their outcomes. The mean (SD) scores for the whole group are shown as bar graphs. Severity is significantly better at both 6 and 12 months post-operatively in comparison to baseline scores ($P = 0.003$, RM-ANOVA).



DBS of the subthalamic nucleus looks promising too Ostem et al Neurology 2011

Figure Effects of deep brain stimulation on Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) scores



(A) Bar graph of the mean (+SEM) scores of the blinded rater TWSTRS total scores at baseline, 3, 6, and 12 months after surgery. p Values determined by post hoc testing using the Wilcoxon signed-rank test. All post hoc comparisons had a $p = 0.008$. (B) Line graph showing individual scores of the blinded rater TWSTRS total scores at baseline, 3, 6, and 12 months

Table 3 Adverse events

Adverse events	No.	Comment
Dyskinesia	8	See text
Depression, transient worsening	5	See text, preexisting in all patients
Weight gain	4	See text
Anxiety, worsened	2	Preexisting in all patients
Dysarthria	2	Transient after DBS programming
Dysphasia	2	Transient after DBS programming
Confusion	1	Postoperative
Transient erythema around parietal incision site	1	Resolved with antibiotics
Subgaleal cerebral fluid collection around burr-hole cap	1	Resolved without treatment
Persistent pain at IPG site	1	Resolved without treatment
Shock-like sensations	1	Transient in cold weather
Migraine headaches, worsened	1	Preexisting
Sensory deficit in hand, worsened	1	Secondary to carpal tunnel syndrome
Lower extremity paresthesias	1	Associated with high dose of intrathecal baclofen
Blood pressure instability	1	Associated with changes in intrathecal baclofen dose
Fall	1	Not related to dyskinesia, no resulting injury
Knee dislocation	1	Worsening of old injury
Knee injury (torn ligament)	1	Occurred after motorcycle accident
Hip pain, worsened	1	Longstanding from arthritis
Fourth cranial nerve palsy, preexisting	1	Corrective surgery improved this longstanding condition
Handwriting difficulties	1	Patient would not allow reprogramming of device to improve this symptom for fear of worsening the dystonia control
Humming sound in ear, worsened	1	Longstanding before surgery

Abbreviations: DBS = deep brain stimulation; IPG = implantable pulse generator.

Summary

- **Dystonia may affect up to 1/100**
- **Dystonia is classified variously, sometimes by body part(s) involved, age of onset or etiology**
- **Oral drug treatments tend to be less effective because of side effects**
- **Injections with botulinum toxin have significantly improved treatment options**
- **DBS is an evolving option**
- **New clinical trials may help us improve treatment options for patients.**