DBS for Tremors & Dystonia

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Outline

- Approach to Diagnosis
- Diagnostic Criteria
- Treatment Strategies
- Neurosurgical interventions
- Long term outcomes

Disclosures

- Consultant for Supernus Pharmaceuticals and Abbott Technologies
- Will discuss off label uses of therapies

What is a Tremor?

- *An involuntary, rhythmic, oscillatory movement of a body part.*
  - Physiological tremor
    - May be present when limbs or head are unsupported
    - Generally not visible unless enhanced by fatigue or anxiety
  - Pathological tremor
    - Tremor is usually visible and present
    - Causes some degree of disability with activities of daily living

Bhatia KP, Bain P, Bajaj N et al. Consensus Statement on the Classification of Tremors. From the task Force on Tremor of the International Parkinson and Movement Disorders Society. Mov Dis. 2018 22(1):75-87

Tremor

- Amongst the most common movement disorder

- Characterized by involuntary rhythmic oscillations of a part of the body
  - Rest: body part is supported against gravity
  - Activity:
    - Postural: maintenance of body part in antigravity posture
    - Kinetic: during active movement
    - Task specific: specific for goal directed movement

- Common Diagnoses:
  - Essential Tremor
  - Parkinson's disease
  - Other

Hess C, Pullman S. Tremor: Clinical phenomenology and Assessment Techniques. Tremor and other Hyperkinetic Movements. 2012; 2.

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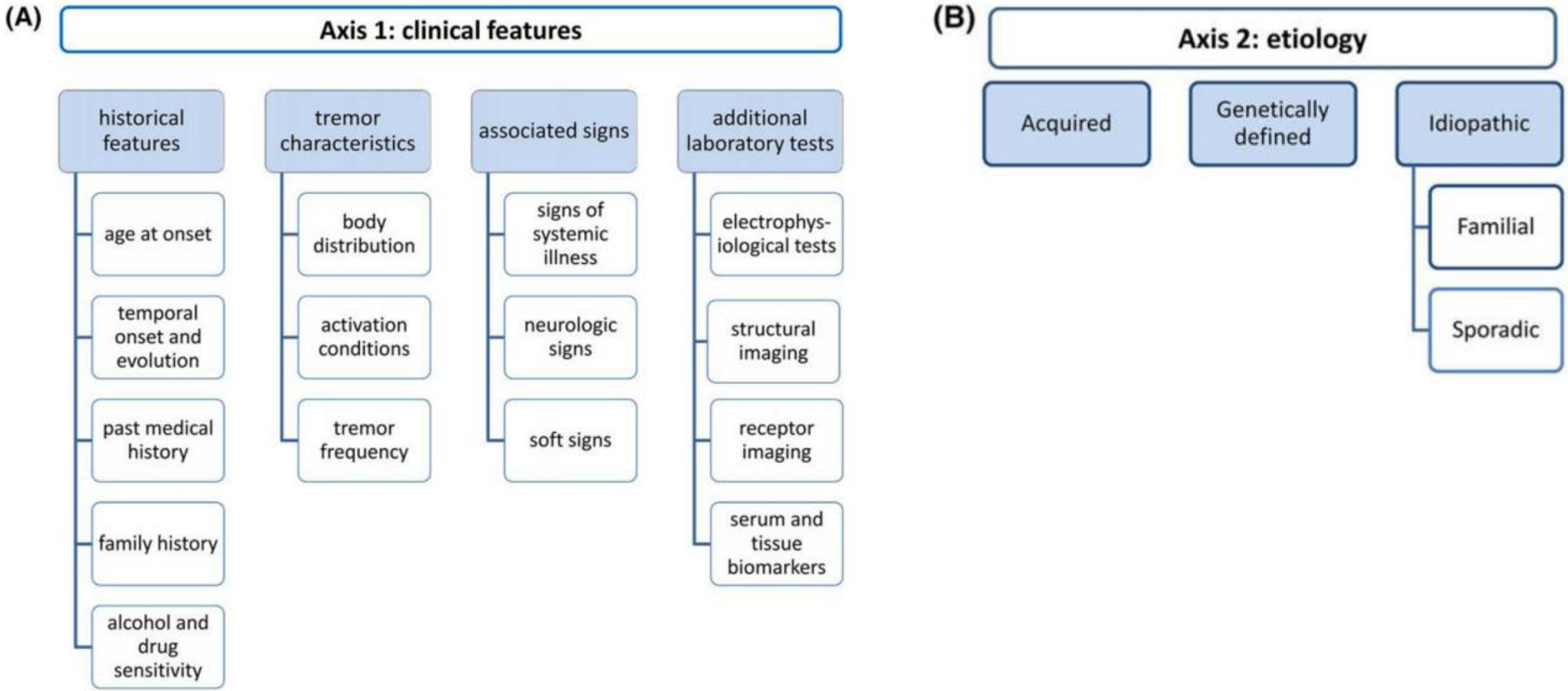
Tremor Phenomenology

Etiology	Rest tremor	Action Tremor		Notable Characteristics
		Postural	Kinetic	
Physiologic		++	++	Non-pathological 6-12Hz associated with stress, anxiety etc
Essential	+	+++	+++	4-12Hz can be associated with in longstanding disease can be associated with ataxia
Parkinsonism	+++	+	+	3-6Hz (re-emergent tremor)
Drug induced		++	++	Non-progressive, symmetric, dose-responsive
Midbrain	++	+	+	Irregular large amplitude, proximal +/- distal
Thalamic	++	++	++	Rare, can be associated with pain or sensory symptoms
Cerebellar		+	++	<5Hz, predominately intention tremor associated with other cerebellar symptoms
Orthostatic		+++		>13Hz occurs with weight bearing or isometric muscle contraction
Dystonic	+	++	++	Ususally <7hz jerky and rhythmic irregular accompanied by abnormal posturing, often having null point
Neuropathic	+	+	++	3-6Hz predominantly affecting more distal muscles, often irregular accompanied by neuropathy
Task-specific		+	+++	4-8Hz occurring predominantly with a specific task or posture (primary writing tremor)

Hess C, Pullman S. Tremor: Clinical phenomenology and Assessment Techniques. Tremor and other Hyperkinetic Movements. 2012; 2.

Approach to Diagnosis



Bhatia K, Bain P, Bajaj N et al. Consensus Statement on the classification of tremors from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018; 33(1):7r-87.

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Differential Diagnosis

TABLE 2. Etiological causes of tremor (selection)

Neurodegenerative disease
- PD
- Multiple system atrophy
- Corticobasal degeneration
- PSP
- Genetic disorders: genes causing predominantly parkinsonism
- Genes causing frontotemporal dementia with parkinsonism
- Genes causing predominantly dystonia
- Neuroferritinopathy
- Spinocerebellar ataxias
- Genes causing Fahr's disease
- Genes causing peripheral neuropathies that produce tremor
- Wilson's disease
- X-linked dystonia parkinsonism/Lubag
- Lesch-Nyhan's syndrome
- Fragile X–associated tremor/ataxia syndrome
- Spinal muscular atrophy

Chromosomal aneuploidy
- XYY, XXY (Klinefelter's syndrome), and XXYY syndromes

Mitochondrial genetic disorders
- Leigh's syndrome
- Mitochondrial polymerase gamma mutations

Infectious and other inflammatory diseases
- Demyelinating diseases such as multiple sclerosis
- Encephalitis lethargica, subacute sclerosing panencephalitis,
- HIV
- Tuberculosis, syphilis, measles, typhus, neuroborreliosis
- Bacterial or viral encephalitis
- Antineuronal antibody disease

Endocrine and metabolic disorders
- Nephrotic or liver failure
- Hyperthyroidism

Neuropathies and spinal muscular atrophies
- Kennedy's syndrome
- Guillain-Barre's syndrome
- Gammopathy-induced neuropathies

Toxins
- Mercury
- Lead
- Manganese
- Arsenic
- Cyanide, DDT, CO
- Naphthalene
- Toluene
- Lindane

Drugs
- Anticonvulsants: valproate, carbamazepine, phenytoin
- Tetrabenazine, antidepressants, sympathomimetics, bronchodilators, beta-2 agonists
- Lithium
- Neuroleptics, metoclopramide
- Amiodarone
- Thyroid hormone replacement
- Anticancer drugs: vincristine, cisplatin, paclitaxel, doxorubicin, cytosine arabinoside, ifosfamide, tacrolimus, 5-fluorouracil, methotrexate
- Drug and alcohol withdrawal

Others
- Brain neoplasms
- Brain injury: head trauma, brain surgery, and electrical injury
- Vascular: ischemia, hemorrhage, and arteriovenous malformations
- Anxiety and stress
- Fatigue
- Cooling
- Trauma of peripheral tissues
- HIV, human immunodeficiency virus.

Bhatia KP, Bain P, Bajaj N et al. Consensus Statement on the Classification of Tremors. From the task Force on Tremor of the International Parkinson and Movement Disorders Society. Mov Dis. 2018 22(1):75-87

Essential Tremor (ET)

- Most prevalent movement disorder (~0.4-5.5%)
  - 14% prevalence in ≥65yrs
- Characterized by upper extremity postural or kinetic tremor (4-12Hz)
  - head, voice, tongue, chin or other body regions may be affected
- Heritable
  - Strong family history suggesting AD
  - No causative gene has been identified

Jimenez-Jimenez FJ, Alonso-Navarro H, et al. Update on genetics of essential tremor. Acta Neurol Scand. 2013

Essential Tremor (ET)

2000 Diagnostic Criteria ET

Core Criteria	Secondary Criteria
Bilateral action tremor of hand & forearm (not rest tremor)	Long duration (≥3years)
Absence of other neurological signs (except cogwheel phenomenon)	~~Positive family history~~
May have isolated head tremor with no signs of dystonia	~~Beneficial response to alcohol~~

Bain P, Brin M, Deuschl G et al. Criteria for the diagnosis of essential tremor. Neurology. 2000;54(11 Suppl 4):S7

2018 Updated Diagnostic Criteria for ET

Onset of **rest** or action tremor in upper limbs

May have "Neurological soft signs" (classified as ET plus)

- Mild memory impairment
- Impaired tandem gait
- Subtle body posturing
- Interpretation of soft signs is subjective and left to investigator

3-year history of tremor

Excludes isolated head and isolated voice tremors

Bhatia KP, Bain P, Bajaj N et al. Consensus Statement on the classification of tremors from the task force of the International Parkinson and Movement Disorder Society. 2018(1):75-87

ET is a diagnosis of exclusion
Minimum work-up:
Review medication list
Check TSH
Additional testing as indicated by neurological exam

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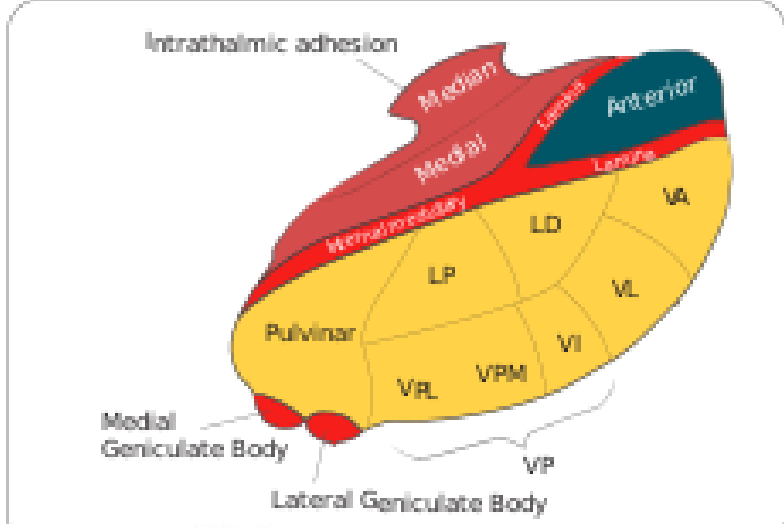
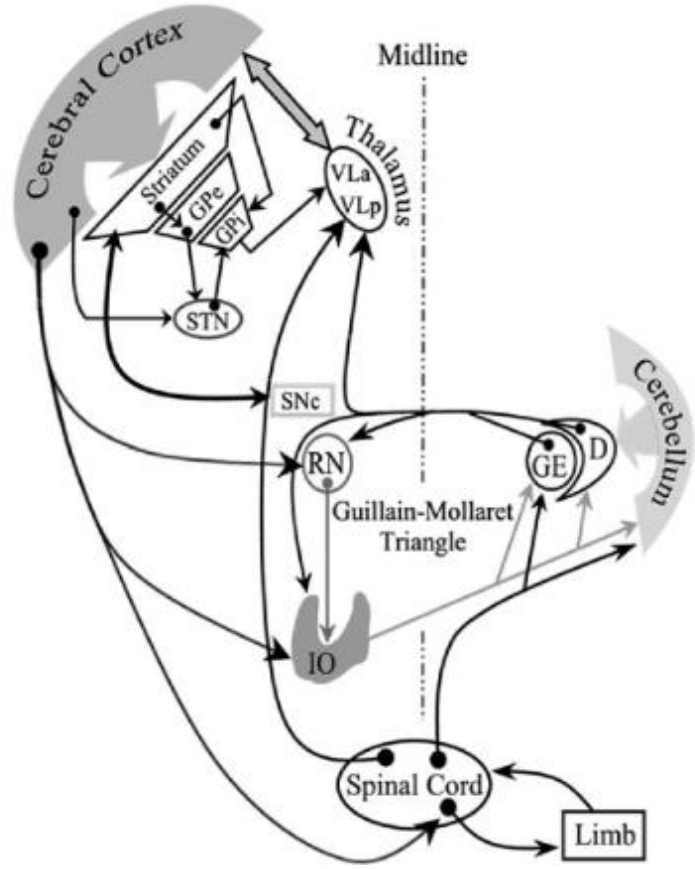
Tremor Pathophysiology

- Peripheral oscillation due to impaired synchronization of peripheral sensory feedback loops

- CNS generator
  - Unstable loop circuit within CNS
  - Normal rhythmicity of nucleus which drives the otherwise normal circuit
  - Ventral intermediate nucleus (ViM) is hypothesized to be the tremor pacemaker





Hallett M. Tremor: Pathophysiology. Parkinsonism Relat Disord. 2014; 20 Suppl 1: S118-22.

Treatment Strategies for ET/Tremor

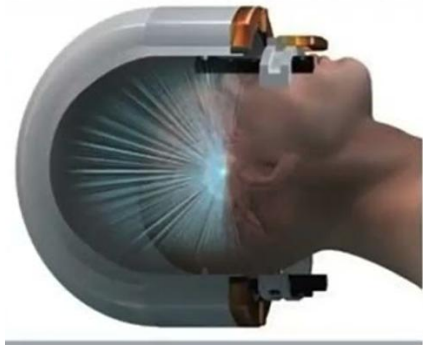
Treatment/ Level of Evidence	Medication Class/ Mechanism of Action	Common side effects
Pharmacological/Biological Therapies		
Propranolol (Level A)	**Non-selective β-adrenoreceptor antagonist**	**Bradycardia, fatigue, exercise intolerance bronchospasms, dizziness**
Primidone (Level A)	**Anticonvulsant**	**Sedation, drowsiness, imbalance**
Topiramate (Level B)	Anticonvulsant	Paresthesia, weight loss, loss of appetite, nausea, memory changes
Gabapentin (Level B)	Anticonvulsant	Sedation, weight gain, dizziness
Alprazolam (Level B)	Benzodiazepine	Sedation, habit-forming
Clonazepam (Level C)	Benzodiazepine	Sedation
Botulinum neurotoxin (BoNT) (Level C)*	Neuromuscular blocking agent	Muscle weakness in region treated
Peripheral Non-invasive Stimulation		
CALA kIQ	Structured stimulation to wrist via band	Paresthesias, spasms
Felix Neuro AI	AI generated stimulation to wrist via band	Paresthesias, spasms
Neurosurgical Intervention		
Ventral Intermediate nucleus(ViM) Deep Brain Stimulation (DBS)	High frequency stimulation delivered to ViM	Surgical: infection, hemorrhage, stroke Stimulation: paresthesia, dysarthria, imbalance, ataxia, spasms
MRI-Guided High Frequency Focused Ultrasound (HiFU) to ViM	High frequency ultrasound induced tissue ablation	Paresthesia, dysarthria, ataxia, imbalance & gait changes, weakness

* Injection to affected muscles

Neurosurgical Interventions

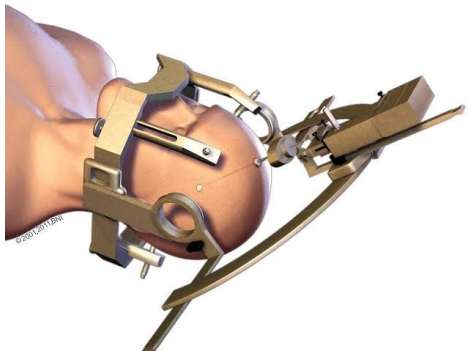
HiFU

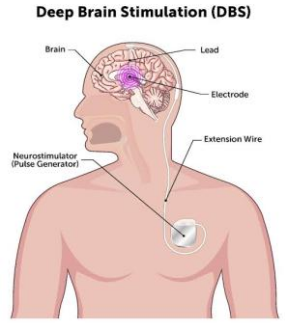
- Minimally invasive ablative surgery
- One time permeant treatment
- Unilateral or Staged bilateral



DBS

- Implantation of hardware
- Continued expert care
  - Programming of device
  - Hardware maintenance
- Adjustable & Reversible





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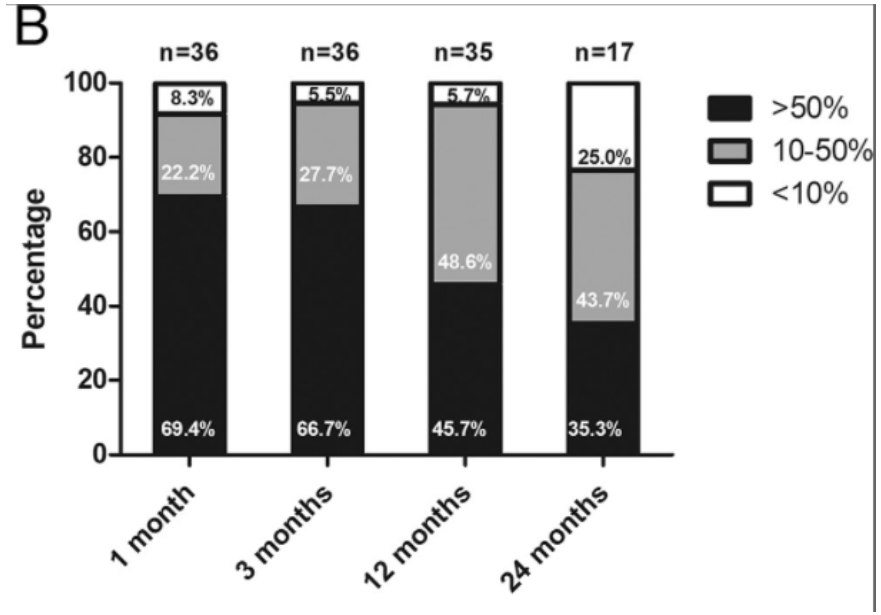
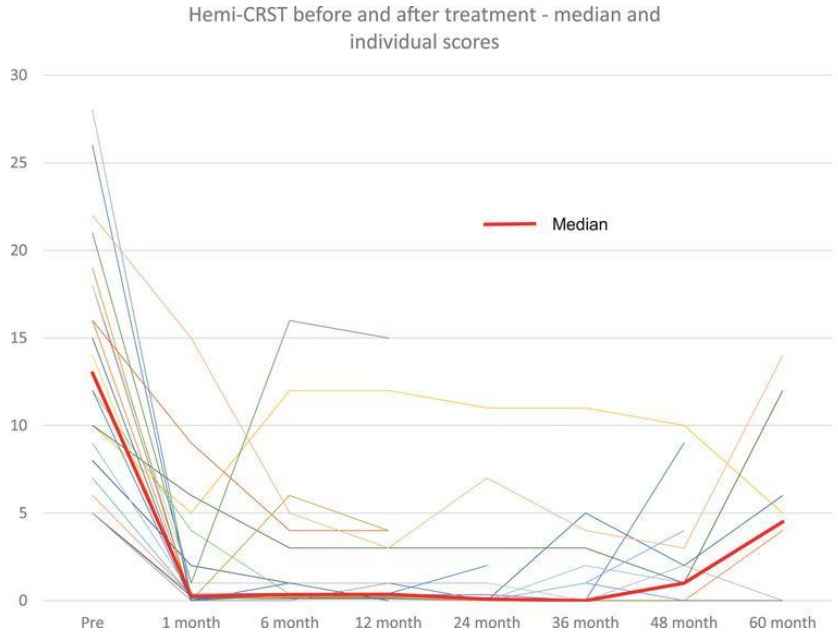
Long Term HiFU Outcomes

Essential Tremor



Meng Y, Solomon B, Boutet A et al. Magnetic resonance-guided focused ultrasound thalamotomy for treatment of essential tremor: 2-year outcome study. 2018; 33(10):1647-1650.

Parkinsonian Tremor



Sinai A, Nassar M, Sprecher E, et al. Focused Ultrasound Thalamotomy in Tremor Dominant Parkinson's Disease: Long-term Results. J Parkinons Dis. 2021. doi:10.3233

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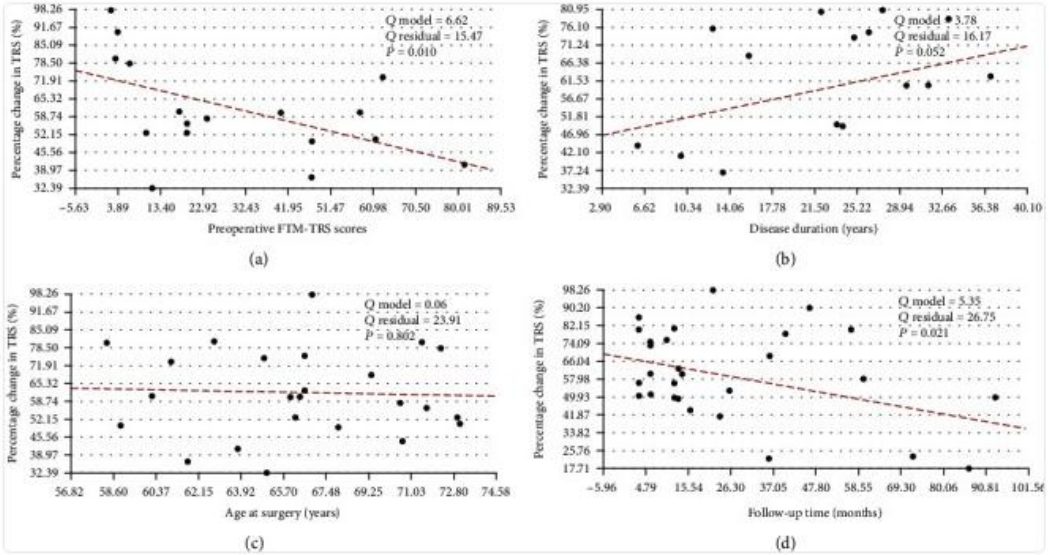
Long term DBS Outcomes

Positive Predictive Factors

- Longer duration of tremor
- Location of tremor



Loss of Long- Term Tremor Control

- Natural disease progression
- Tolerance to stimulation
- Suboptimal electrode placement
- Stimulation induced side effects
- Changes in brain impedances

Lu G, Luo L, Liu M, et al. Outcomes and adverse effects of deep brain stimulation on the ventral intermediate nucleus in patients with essential tremor. Neural Plast. 2020;2020:1-13

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Patient Selection Considerations

- Medication Refractory Tremors causing functional disability

ViM HiFU

- Skull density ratio (SDR)
- Unilateral hand tremor
- High surgical risk

Cautious consideration:

- Bilateral hand tremor
- Tremor in other regions
- Gait Disorder

ViM DBS

- Bilateral hand tremor
- Severe disability
- Gait & balance Disorder*

Cautious consideration:

- Cognitive Disorders
- Gait Disorder*

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Dystonia

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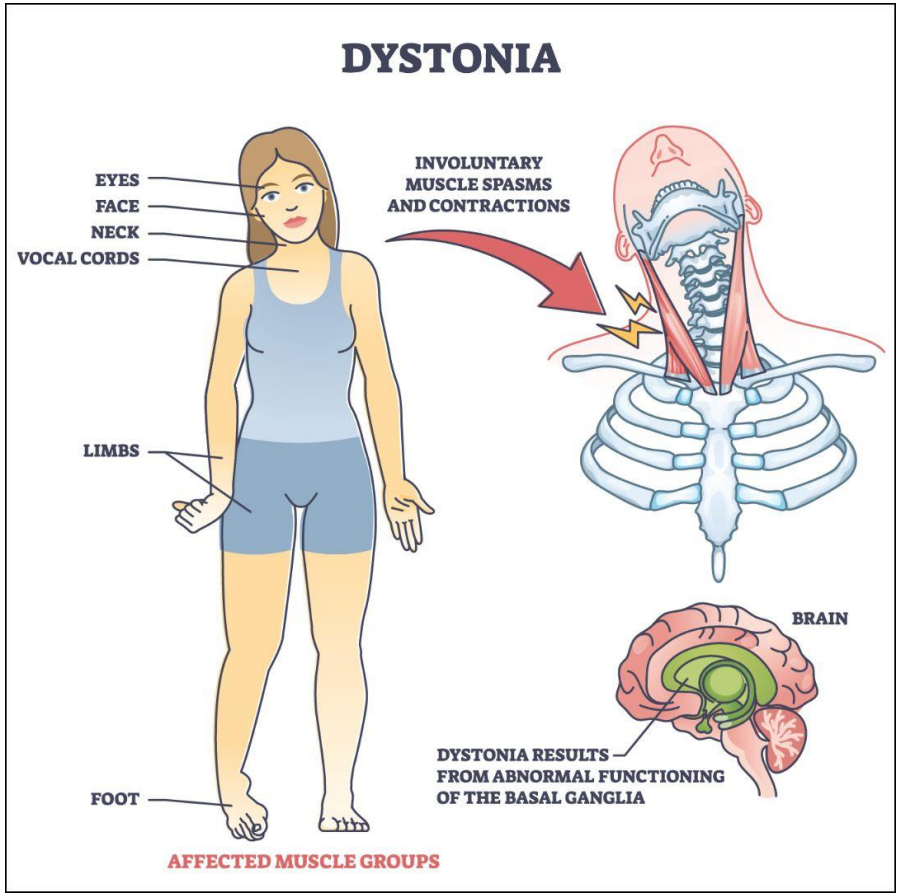
What is Dystonia?

"Dystonia is a [hyperkinetic] *movement disorder characterized by* ***sustained*** *or* ***intermittent*** *muscle contractions causing abnormal, often* ***repetitive, movements, postures*** *or both. Dystonic movements are typically* ***patterned***, ***twisting***, *and may be* ***tremulous***. *Dystonia often initiated or worsened by voluntary action and associated with overflow muscle activation".*



Albanese A, Bhatia K, Fung V, et al. Definition and Classification of Dystonia. Mov Disord. 2025; 40(7):1248-1259.
Klein C, Fahn S. Translation of Oppenheim's 1911 Paper on Dystonia. Mov Disord. 2013; 28(7):851-62.

Classification of Dystonia

I. Clinical characteristics		
Category	**Subcategory**	**Description**
Age at onset	Infancy	Birth to 2 years
	Childhood	3–12 years
	Adolescence	13–20 years
	Early adulthood	21–40 years
	Late adulthood	>40 years
Body distribution	Focal	Only one affected body region
	Segmental	Two or more contiguous body regions
	Multifocal	Two or more noncontiguous body regions
	Hemidystonia	More body regions restricted to one body site
	Generalized (with or without leg involvement)	Involvement of the trunk and at least two other body regions with or without leg involvement
Temporal pattern: disease course	Static	No progression over the course of the disease
	Progressive	Progression over the course of the disease
Temporal pattern: variability	Persistent	Persistent to approximately the same extent throughout the day
	Action-specific	Occurring only during a particular activity or task
	Diurnal	Fluctuations during the day with recognizable variations in occurrence, severity, and phenomenology
	Paroxysmal	Sudden self-limited episodes usually induced by a trigger with return to preexisting state
Associated features	Isolated dystonia	Dystonia as the only motor feature, except for a possible tremor
	Combined dystonia	Dystonia combined with another movement disorder (e.g., myoclonus, parkinsonism, etc.)
	Complex dystonia (10)	Occurrence of other neurological or systemic manifestations; dystonia may be less prominent
II. Etiology		
Nervous system pathology		Evidence of degeneration Evidence of structural (often static) lesions No evidence of degeneration or structural lesions
Inherited, acquired, or idiopathic		Inherited: autosomal dominant, autosomal recessive, X-linked, mitochondrial Acquired: perinatal brain injury, infection, drug, toxic, vascular, neoplastic, brain injury, psychogenic Idiopathic: dystonia without identifiable cause, sporadic or familial

Thomsen M, Lange L, Zech M et al. Genetics and Pathogenesis of Dystonia. Annu Rev Pathol. 2024. 24;19:99-131.
Albanese A, Bhatia K, Fung V, et al. Definition and Classification of Dystonia. Mov Disord. 2025; 40(7):1248-1259

Motor Phenomenology

- Relationship to Voluntary action
  - Action induced
  - Task specific
  - At rest and during action
  - Fixed
- Dystonic movements
  - Sustained posture(s): maintained at rest for prolonged periods overcome by passive movements
  - Fixed dystonia: Persistent or prolonged postures that cannot be changed by passive movements
  - Jerky dystonia: When movements resemble myoclonic jerks
  - *Dystonia tremor: rhymical although inconsistent patterned movement (term no longer recommended)*
- Overflow
  - Unintentional muscle contraction which accompanies, but is anatomically distinct from the primary dystonic movement
- Mirror dystonia
  - Same or similar character of dystonic movement that can be elicited when moving the contralateral side
- Alleviating maneuvers (ie sensory trick, *geste antagoniste*)
  - Voluntary actions that specifically correct the abnormal posture to alleviate the dystonic movement

Albanese A, Bhatia K, Fung V, et al. Definition and Classification of Dystonia. Mov Disord. 2025; 40(7):1248-1259.
Patel N, Jankovic J, Hallett M. Sensory Aspects of Movement Disorders. Lancet Neurol. 2014; 13(1):100-12.

Common Features/ Terms

Age of onset

- Infancy (≤ 2 years)
- Childhood (>2-12 years)
- Adolescence (>12-20 years)
- Early Adulthood (20-40 years)
- Late Adulthood (>40 years)

Body Distribution

- Focal: single area of the body
- Segmental: ≥2 contiguous areas
- Multifocal: 2 or more non-contiguous
- Hemidystonia: ½ of body affected
- Generalized: combination segmental crural (legs ± trunk) + another region

Albanese A, Bhatia K, Fung V, et al. Definition and Classification of Dystonia. Mov Disord. 2025; 40(7):1248-1259.

Adult onset Focal Dystonias

- Primarily idiopathic
  - Possible atypical presentation of genetic dystonia
- Can affect any area of the body
- Most commonly affected sites
  - Cervical dystonia
  - Blepharospasm
  - Hand dystonia
- Overlapping features
  - Can spread to contiguous body parts

FIG. 2 *Blepharospasm and spasm of jaw closure and mouth-pursing in a 61 year old lady with symptoms for three years.*

FIG. 3 *Spasm of jaw opening and mouth retraction in a 65 year old lady with symptoms for four years.*

Table 12.11 -- Comparisons of the focal dystonias

Feature	Blepharospasm	Dysphonia	Cervical dystonia	Hand dystonia
Prevalence per million	17–133	11–59	23–130	3.8–80
Predominant gender	Female	Female	Female	Male
Age at onset, mean	55.7	43	40.7	38
% spread by 5 years	58%	9–19%	12–35%	13%
Sensory trick	Yes	No	Yes	Yes
Task specificity	No	Yes	No	Yes
Possible risk factors	Dry eyes, irritation	Sore throat	Neck-trunk trauma	Repetitive task

Adapted from Defazio G, Berardelli A, Hallett M. Do primary adult-onset focal dystonias share aetiological factors? Brain 2007;130(Pt 5):1183–1193.

Fahn S, Hallett M, Jankovic J. Principles and Practice of Movement Disorders. 2011 (271-2)

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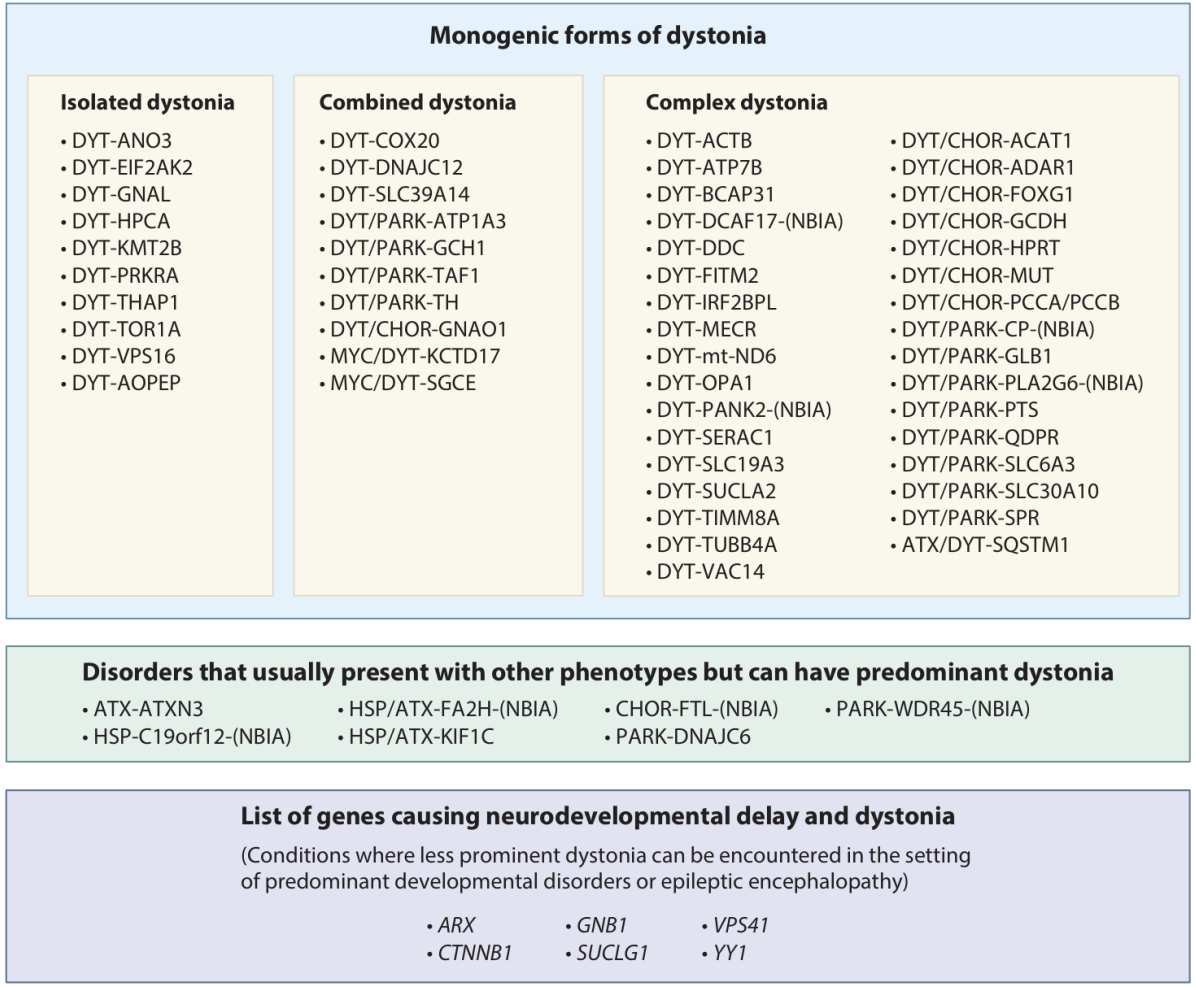
Genetic Causes of Dystonia



Thomsen M, Lange L, Zech M et al. Genetics and Pathogenesis of Dystonia. Annu Rev Pathol. 2024. 24;19:99-131.

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Dystonic Storm/Status Dystonicus

Triggers

- Infections
- Medication Adjustment
- Hyperthermia
- Trauma
- Dehydration
- Respiratory Compromise

Complications

- Hyperpyrexia
- Dehydration
- Respiratory failure
- Rhabdomyolysis
  - ± renal failure

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Dystonia Pathophysiology

Genetic contributors

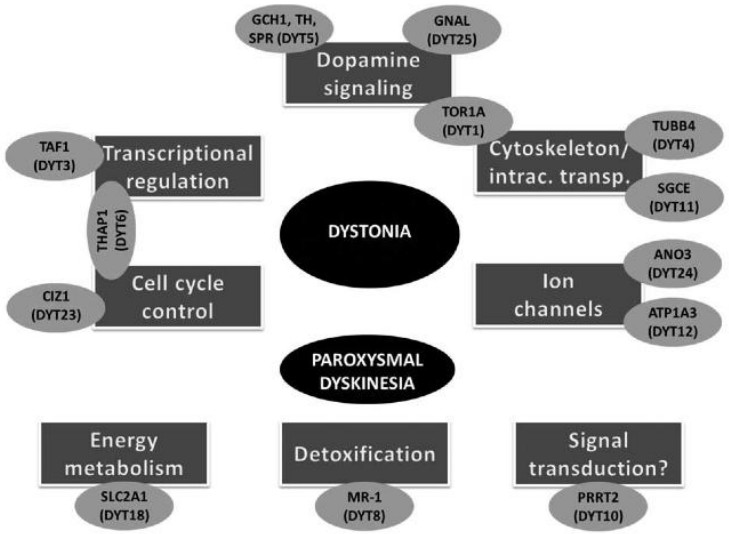
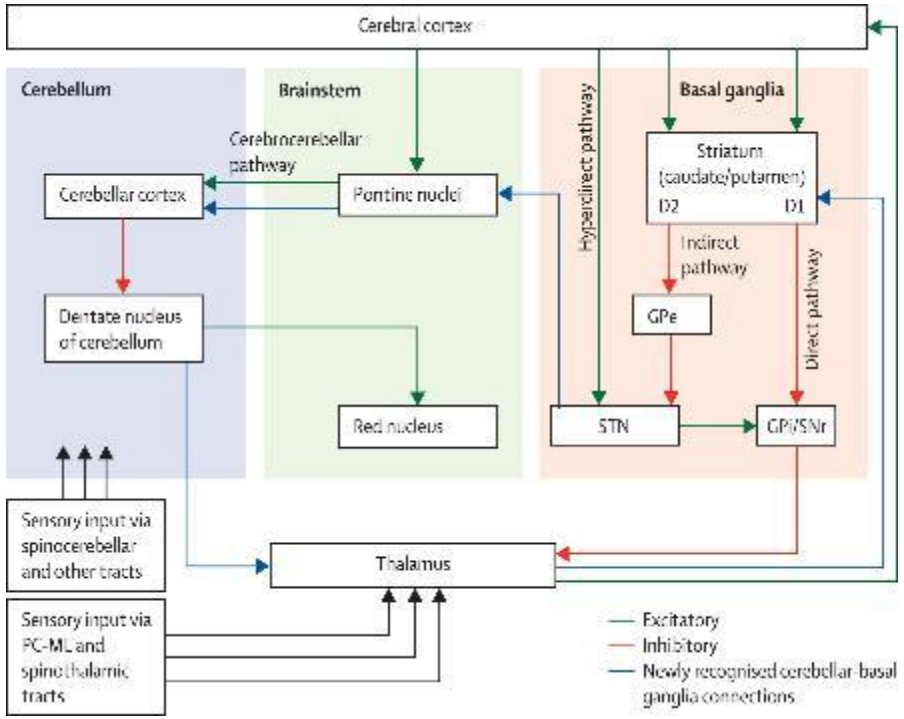


FIG. 3. Overview of the diverse pathways currently linked to dystonia. The known dystonia genes are thought to be involved in different cellular pathways as indicated and thus contribute to the pathogenesis of dystonia and paroxysmal dyskinesia. For some of the gene products, such as for TOR1A, a variety of cellular functions have been reported. The role of PRRT2, a transmembrane protein, is currently largely unknown (symbolized by a question mark).

Lohmann, K et al. Genetics of Dystonia: What's known? What's new? What's next?. Mov Disord 2013; 28 (7): 899-905.

Network Model



Patel N, Jankovic J, Hallett M. Sensory Aspects of Movement Disorders. Lancet Neurol. 2014; 13(1):100-112.

Bruggemann N. J Neural Transm. 2021; 218(4): 499-508.

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Treatment Strategies for Dystonia

Treatment	Dystonia Features	Medication Class/ Mechanism of Action	Common side effects
Pharmacological/Biological Therapies			
Botulinum Neurotoxin (BoNT) (level A) *	**Focal/segmental dystonias** Regional treatment for other dystonias	**Neuromuscular blocking agent**	**Muscle weakness in region(s) treated**
Trihexyphenidyl (level B)	Generalized/multifocal/hemidystonia Children with dystonia	Acetylcholine receptor antagonist	Dry eye, dry mouth, constipation, hallucinations/cognitive changes (in adults)
Carbidopa/Levodopa	Dopa responsive dystonia subtypes, Diurnal fluctuations ± generalized dystonia, children with dystonia	Precursor to Dopamine Replenishes brain dopamine stores	Nausea, vomiting, motor fluctuations
Benzodiazepines (clonazepam, diazepam)	All dystonia subtypes	Brain $GABA_A$ allosteric modulator	
Baclofen (oral/intrathecal)	All dystonia subtypes	Spinal $GABA_B$ receptor agonist	Sedation, generalized fatigue and weakness
Tizanidine	All dystonia subtypes	Spinal α2- adrenergic receptor agonist	
Neurosurgical Intervention			
Bilateral globus pallidus interna (GPi) Deep Brain Stimulation (DBS)	Generalized/multifocal/hemidystonia Cervical dystonia	High frequency stimulation delivered to GPi	Surgical: infection, hemorrhage, stroke Stimulation: phosphenes, paresthesia, dysarthria, imbalance, ataxia, spasms, suboptimal response

* Injection to affected muscles

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DBS for Dystonia

- FDA approved in 2025

- Toxin/medication refractory primary isolated dystonias
  - Cervical dystonia
  - Generalized dystonia

- DBS specific considerations
  - Globus pallidus interna (GPi) is preferred target
  - Subthalamic nucleus (STN) being explored
  - ViM tremor/myoclonic predominant symptoms (DYT-SGCE)
  - Optimal effect may take months-years to achieve

- Variability in treatment outcomes
  - Primary non-responders <25% change in symptoms at 12months
  - Secondary non-responders lose benefit years after receiving good effects
  - Optimal effect may take months-years to achieve

Tisch S. Deep brain Stimulation in dystonia: factors contributing to variability in outcome in short and long term follow-up. Curr Opin Neurol. 2022;35(4):510-517.
Ostrem JL, Markun LC, Glass GA et al. Effect of frequency on subthalamic nucleus deep brain stimulation in primary dystonia. Parkinsonism Relat Disord. 2014

DBS Outcomes: Dystonia Specific Considerations

Worse outcome	Factors	Better outcome
Acquired combined (secondary)	Dystonia Classification	Idiopathic isolated (primary)
Structural brain insult (trauma, cerebral palsy, stroke, multiple sclerosis)	Dystonia Etiology	Idiopathic, Tardive
Structural brain lesions, atrophy	MRI brain appearance	Normal
Rare genetic isolated (THAP1), some genetic combined (ATP1A3)	Dystonia Gene	DYT-TOR1A, DYT-SGCE, DYT-KM2B, DYT-PANK2
Bulbar, laryngeal	Dystonia body region	Limb, trunk, neck
Longer	Dystonia duration	Shorter
Tonic dystonic posturing	Dystonia Phenomenology	Phasic, jerking, tremulous
Fixed postures/contractures	Orthopedic deformity	Full range of movements in joints

Tisch S. Deep brain Stimulation in dystonia: factors contributing to variability in outcome in short and long term follow-up. Curr Opin Neurol. 2022;35(4):510-517.

DBS Outcomes: DBS related factors

Contact(s) outside of optimal target region	Factors Target selection/Accuracy of lead placement	Stimulated contacts are within optimal region
Inadequate parameters Incorrect contact(s) selected Interrupted stimulation	Stimulation Parameters & Continuity of Care	Adequate stimulation parameters Optimal contact(s) stimulated Uninterrupted stimulation
Insufficient follow-up	Time allowed for response	Sufficient follow-up (≥12months)
Possible older technology (constant voltage, non-directional stimulation)	DBS technology	Constant current, directional leads, image/ brain signal guided
Parkinsonism (GPi) Dyskinesia (STN)	Stimulation induced side effects	None experienced

Tisch S. Deep brain Stimulation in dystonia: factors contributing to variability in outcome in short and long term follow-up. Curr Opin Neurol. 2022;35(4):510-517.

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Long term care recommendations

- Patience!
  - Remind patients (and yourself) results may take 6-12months to achieve
  - Confirm lead position with imaging post-operatively
  - Slow gentle titration of stimulation
    - Delayed onset of side effects
- Continue BoNT and medications if partial benefit
  - Gradual reduction of therapies as symptoms begin to improve
  - May need to continue therapies long term to optimize symptom control

Martinez-Nunez AE, Sidiropoulous C, Wall J et al. Adjuvant medical therapy in cervical dystonia after deep brain stimulation: A retrospective analysis. Front Neurol. 2022; 13:927573.

Thank you!

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