

# Deep Brain Stimulation for Dystonia

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- No relevant disclosure

# Outline

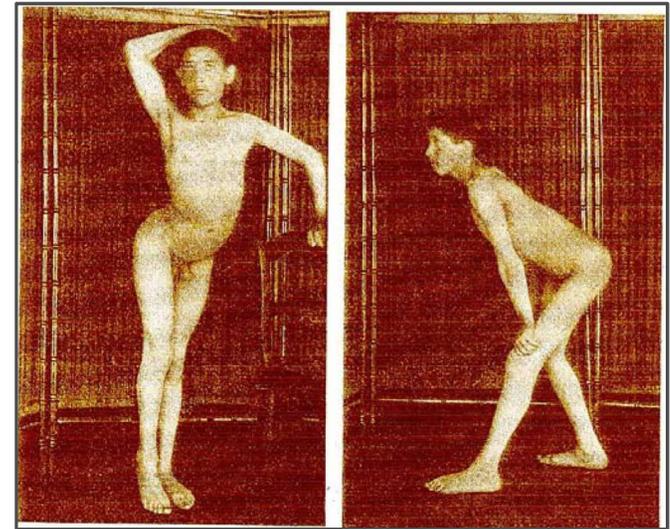
- Overview of Dystonia
  - Phenomenology & classification
  - Pathophysiology of dystonia
  - Management
- Deep Brain Stimulation for Dystonia
  - DBS overview
  - Outcomes of DBS in different forms of dystonia
  - Surgical procedure and programming
  - Patient selection and predictors of outcomes

# Dystonia

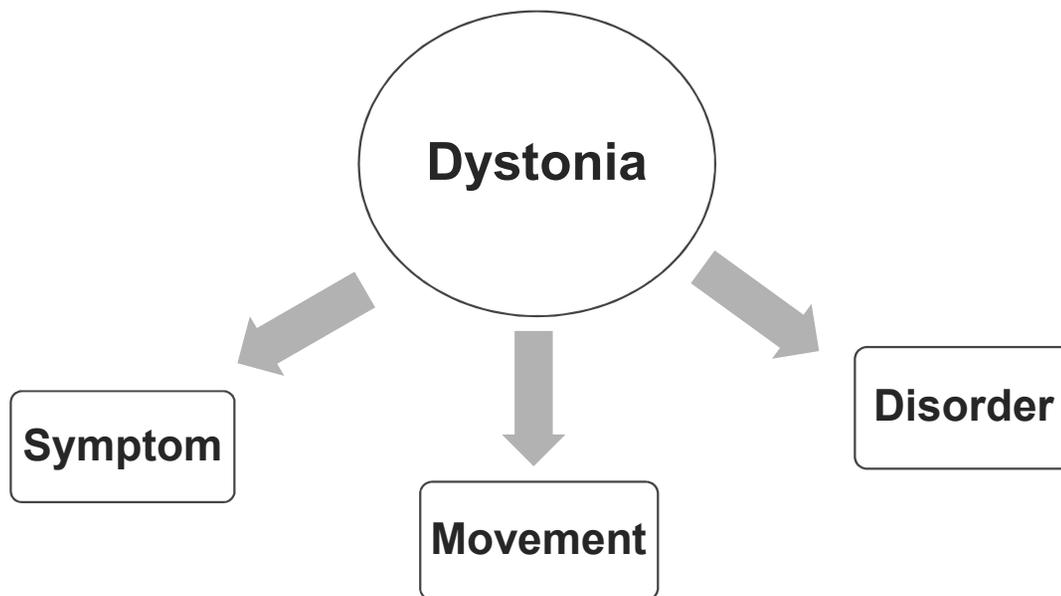
First modern description by Oppenheim — 1911

- 4 children with muscles spasms involving limbs, trunk
- Twisted postures, lordosis and scoliosis
- Movements worsened with walking

*Dystonia musculorum deformans* —muscle tone fluctuates between hypotonia and hypertonia



Translation of Oppenheim's 1911 paper on dystonia



# Dystonia

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Characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive movements, postures, or both.

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Dystonic movements are typically patterned, twisting, and may be tremulous.

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Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.

Albanese et al. Movement disorders 2013

## How to recognize Dystonia?

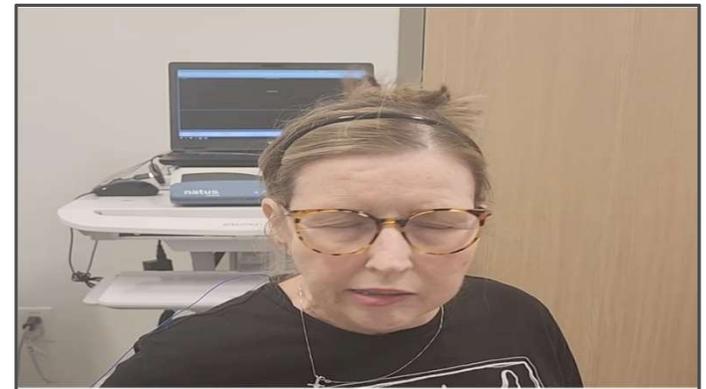


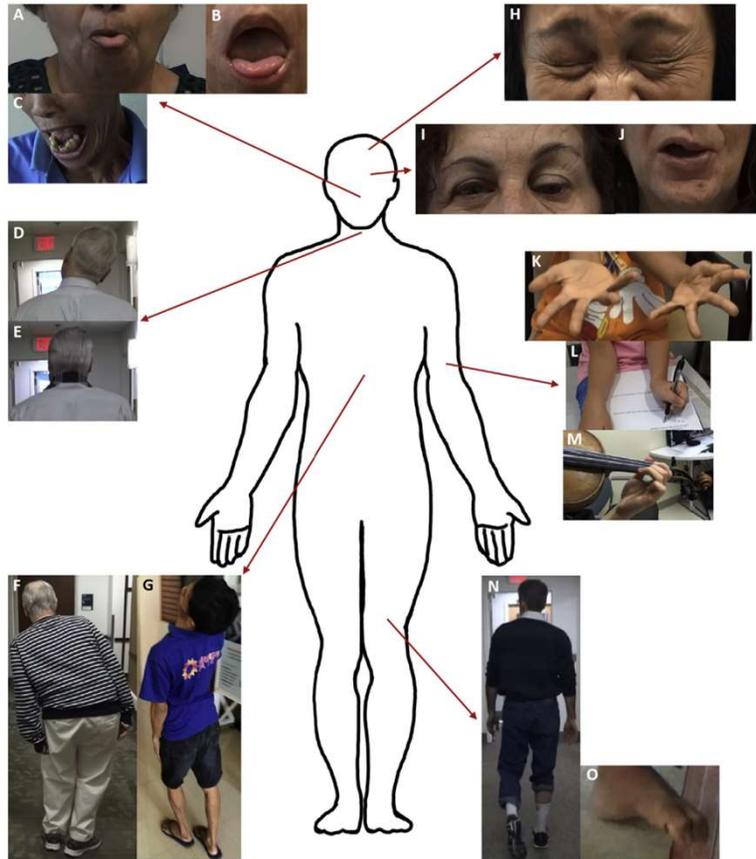
- Abnormal sustained posturing
- Sensory tricks

- Task specificity
- Mirror dystonia

- Null point in tremor, jerky tremor, directionality in one direction

- Recognize Pseudodystonia





Pic from Stephen et al. Neurobiology of Brain disorders

## Classification of Dystonia

### Axis I: Clinical characteristics

- Age at onset
- **Body distribution**  
Focal, Segmental, Generalized, Hemi-dystonia
- Temporal pattern
- **Associated features** — isolated or combined

### Axis II: Etiology

- Nervous system pathology : degenerative, static lesions
- Inherited
- Acquired: brain injury, vascular, psychogenic
- Idiopathic (unknown cause)

Albanese et al. Movement disorders 2013

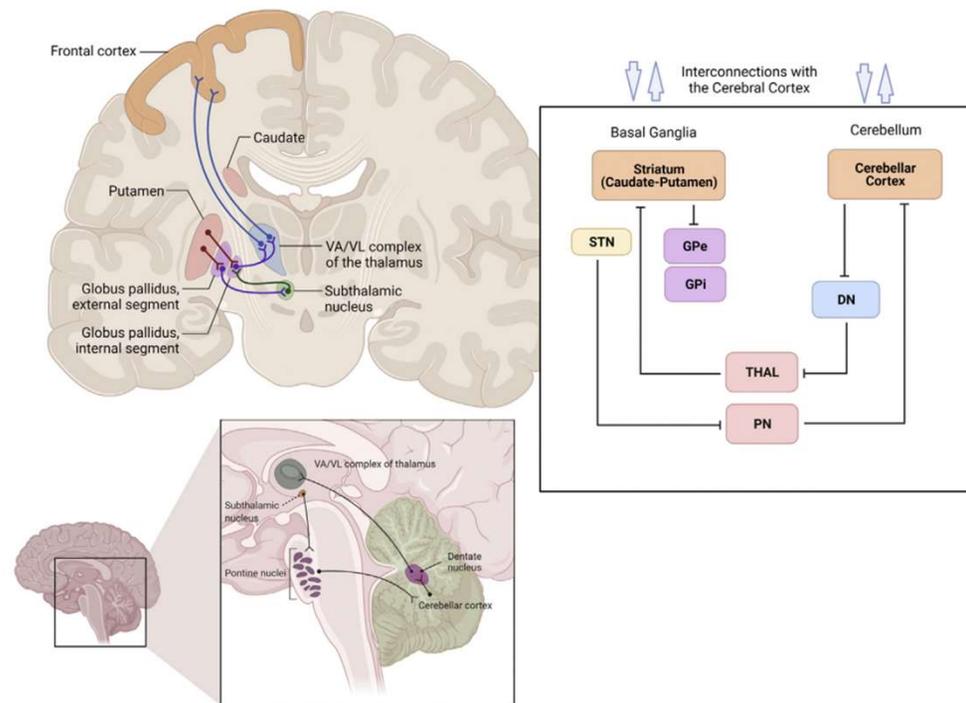
# Pathophysiology of Dystonia

Circuit disorder – abnormality in neural networks

Loss of inhibition

Impaired Sensorimotor integration

Maladaptive plasticity and reorganization of cortical regions



Quartrone & Hallett, 2013  
Stephen et al. Neurobiology of Brain disorders

## Management of Dystonia



Goal is to provide symptomatic treatment

Anticholinergics: Trihexyphenidyl

Gaba agonist: Baclofen



Benzodiazepines: Clonazepam, diazepam

Dopamine precursor: Levodopa for dopamine responsive dystonia

Antidopaminergic therapy: Tetrabenazine

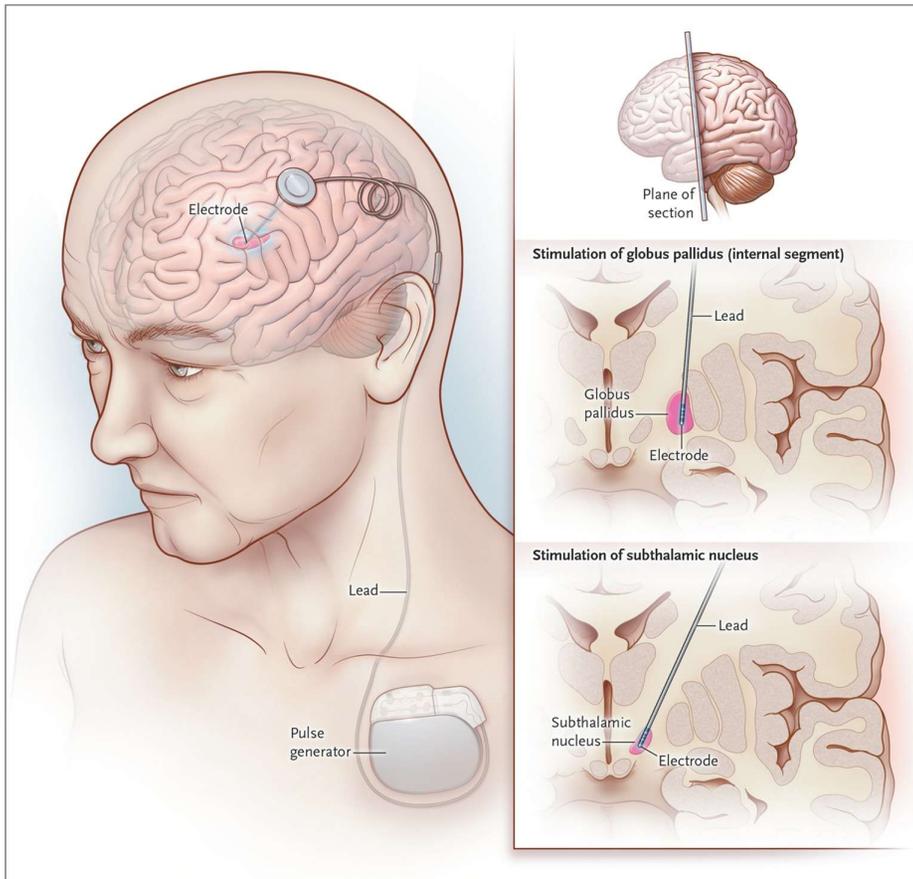


Botulinum toxin — first line therapy for focal/segmental dystonia



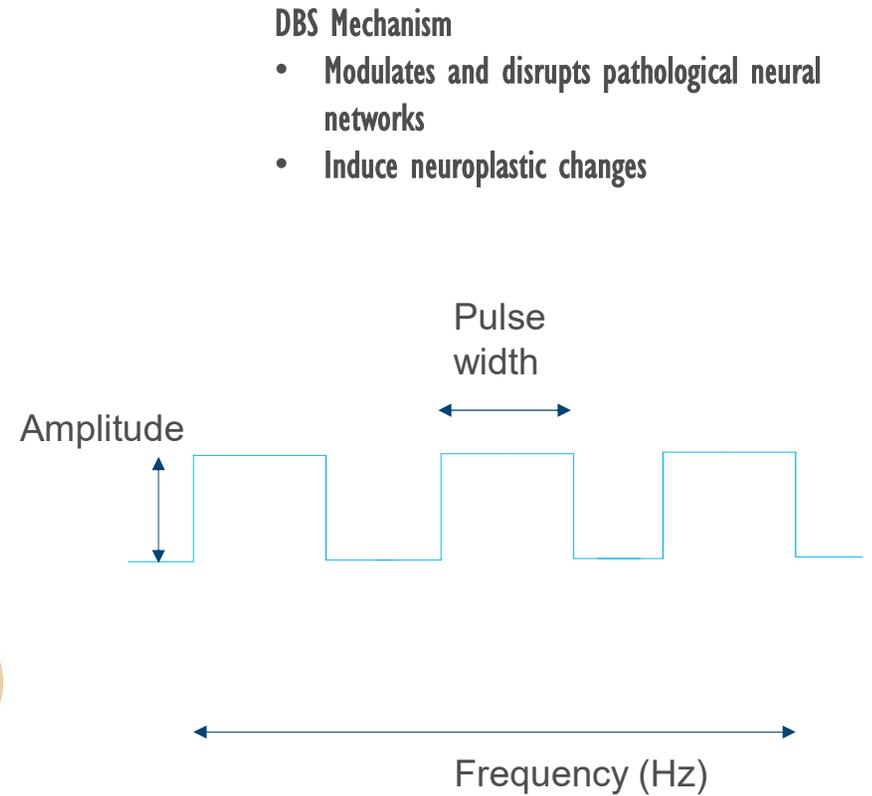
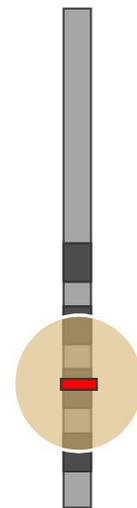
Surgical treatment — Deep brain stimulation or Lesioning surgeries

# Deep Brain Stimulation



Okun MS. New England Journal of Medicine 2012

+ IPG



## DBS for Dystonia: Timeline

Pallidotomy  
Thalamotomy

Munding- Thalamic  
DBS in dystonia

Thalamic DBS  
Pallidal DBS

Coubes et al.  
Krauss et al.  
Kumar et al.

DBS - FDA approval  
(HDE)

First randomized,  
double-blind, sham  
controlled study

1950s

1977

1980s-90s

1999

2003

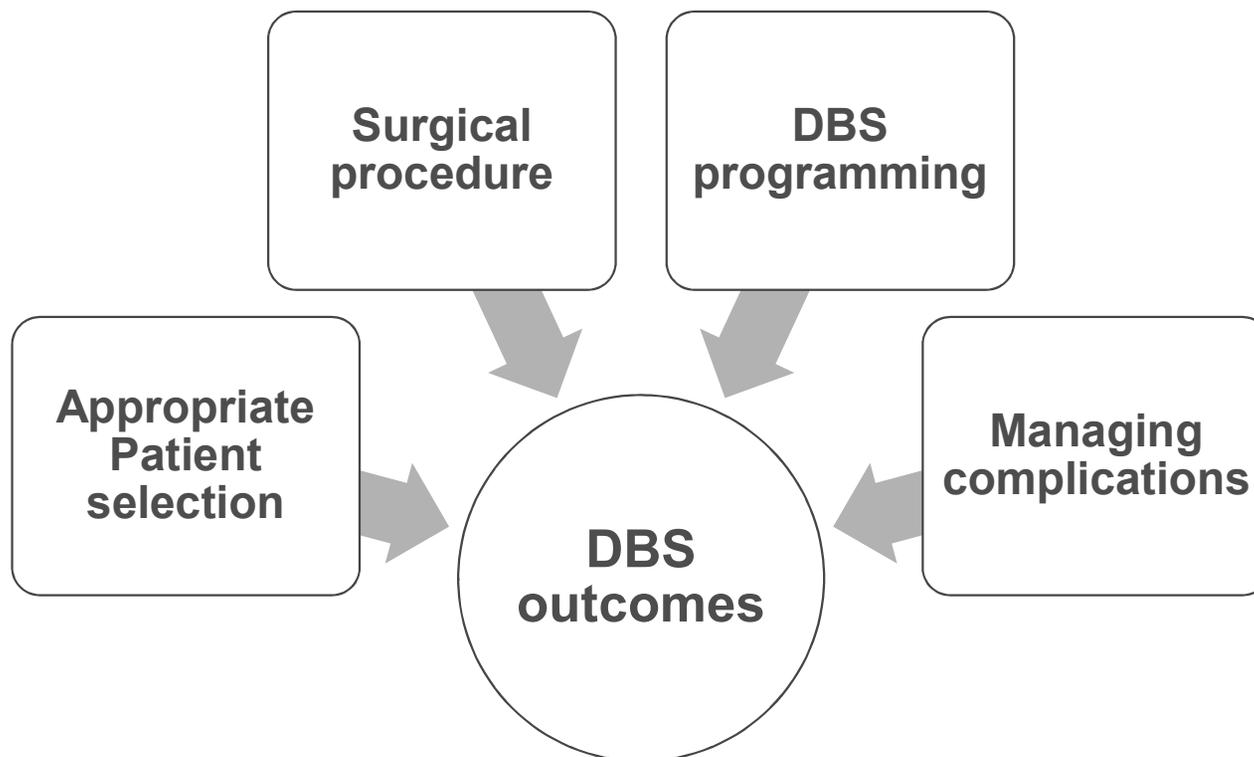
2006

Krack & Vercueil, 2001

Vidailhet et al. 2013

Miocionvic et al. 2013

## DBS for Dystonia



## Patient selection

- Multidisciplinary team evaluation is recommended
- Adequate trial of medications for generalized and botulinum toxin injections for focal/segmental dystonia
- Symptoms should be disabling enough to justify the surgical risk
- MRI brain
- Neuropsychiatric assessments (for selected patients)
- Psychiatry assessment (for selected patients)

- Outcomes depends on etiology and type of dystonia

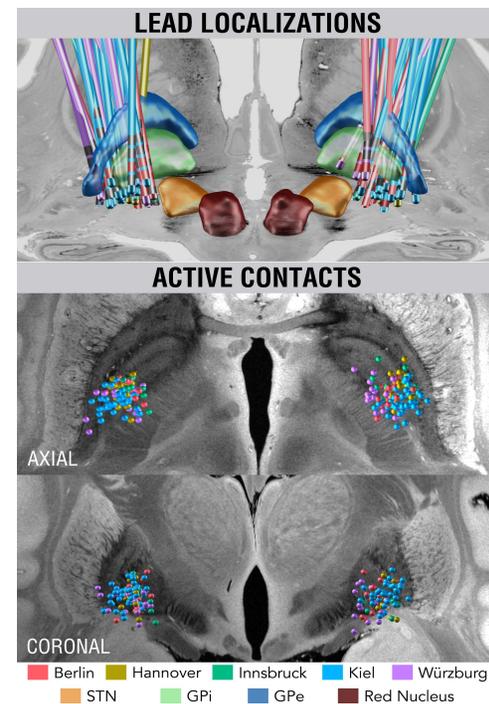
Good: Isolated generalized and segmental

Poor: Combined dystonia

Acquired combined dystonia (Post-stroke, brain injury, CP)

- Target: Posteroventrolateral GPi, STN also similar outcomes
- Response is often delayed (days to months)

### Optimal deep brain stimulation sites



Horn et al. PNAS 2022

# DBS in isolated Generalized Dystonia

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

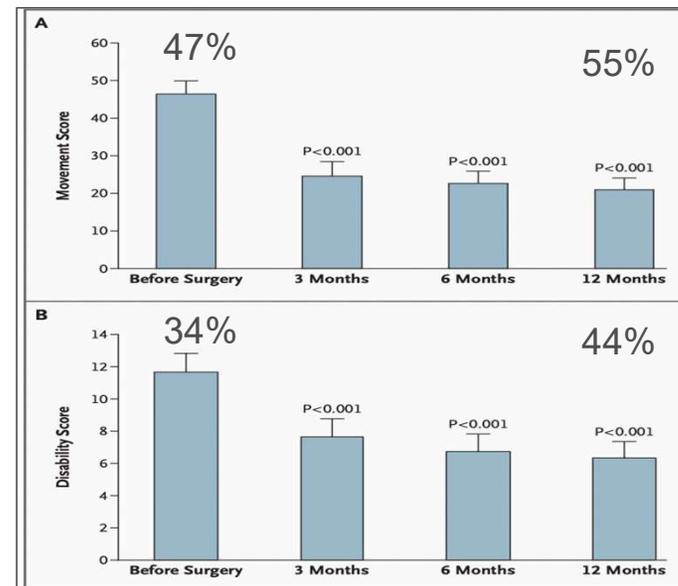
## Bilateral Deep-Brain Stimulation of the Globus Pallidus in Primary Generalized Dystonia

Vidailhet et al. 2005

Improvement occurred in most segments of the body (neck, trunk, and limbs)

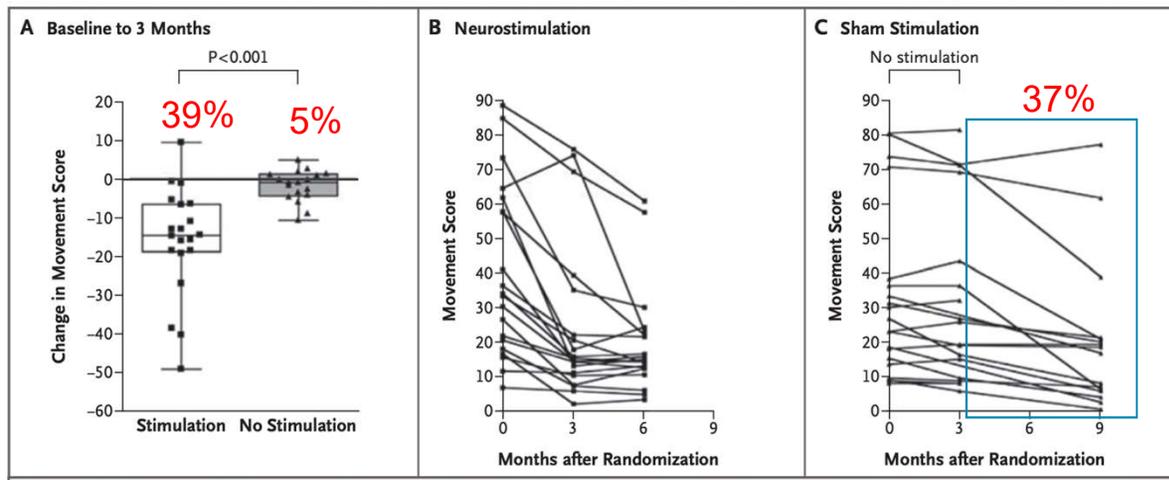
Facial movement and speech – limited response

N = 22, Mean age = 30 yrs



## DBS in isolated Segmental or Generalized Dystonia

N = 40



Disability scores: 38%  
QOL: 30%

Overall group: 46% improvement at 6 months

Poor response < 25%: 17%

Pallidal Deep-Brain Stimulation in Primary Generalized or Segmental Dystonia  
Kupsch et al. NEJM 2006

## DBS in Segmental Dystonia

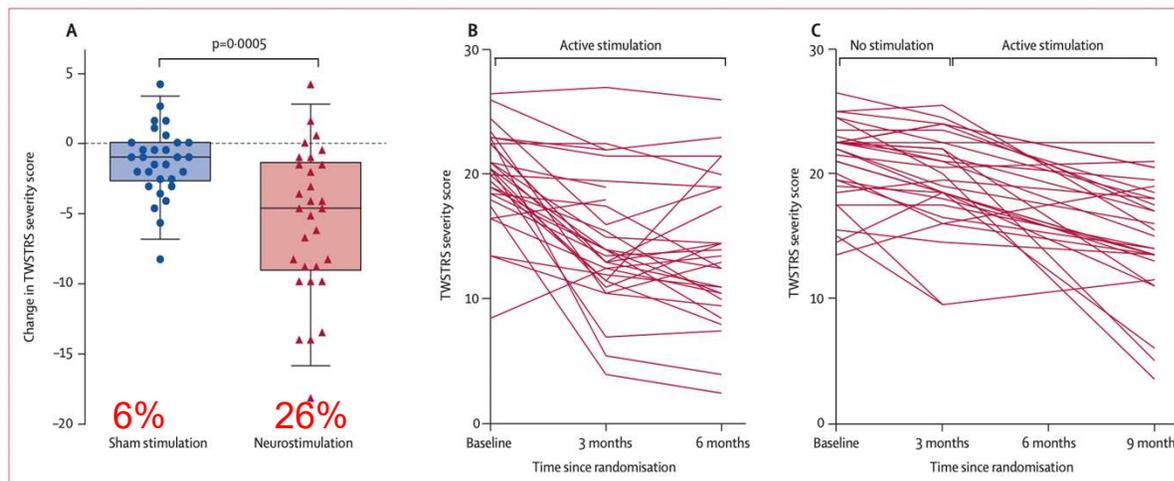
Patient 21  
Randomized to sham stimulation



Kupsch et al. NEJM 2006

# DBS in isolated Focal Dystonia

N = 60, Mean age = 57.1 yrs



TWSTRS and Disability score improved significantly

Pallidal neurostimulation in patients with medication-refractory cervical dystonia: a randomized, sham-controlled trial  
Volkman et al. Lancet Neurology 2014

5 years improvement of 48% in  
TWSTRS severity score

Walsh et al. Brain 2013

## DBS for Cervical Dystonia

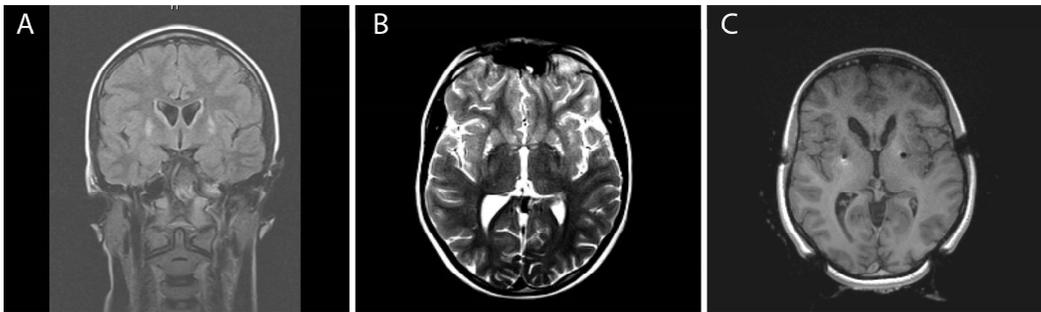


## Outcomes in other Dystonias

Dystonia	DBS target	Outcomes
Isolated, Idiopathic Focal/Segmental		
Cranial dystonia	GPi	Eyes 47%, Mouth 56% Speech/swallowing 40-60%
Isolated camptocormia	GPi	BFMDRS 82%
Acquired		
Medication induced (Tardive dystonia )	GPi	AIMS 62%, BFMDRS 76%
Cerebral Palsy	GPi	24% (-7.5 – 55%)
Combined, Inherited		
Myoclonus Dystonia	GPi, VIM	GPi –60-90% both myoclonus and dystonia VIM – improves myoclonus
Mitochondriopathies	GPi	No improvement to good improvement

Vidailhet et al. 2013; Reese & Volkmann 2017

## DBS for combined dystonia secondary to mitochondriopathy



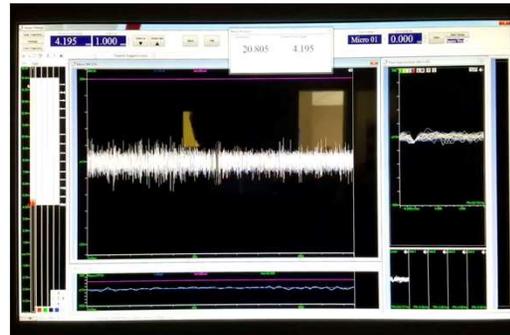
Novel mutation in SERAC 1 gene associated with MEGDEL syndrome

Sharma et al. MDCP, 2021

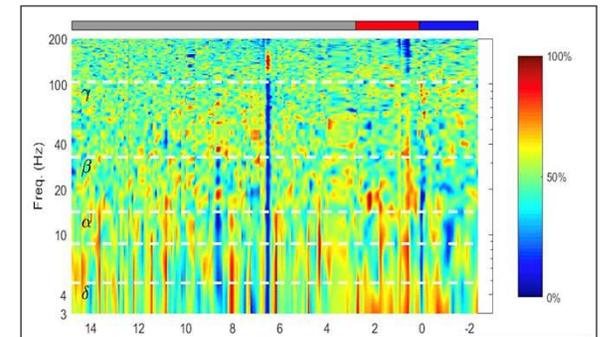
Pre-Op  
2014-2015

## DBS surgery

Awake



MER guidance



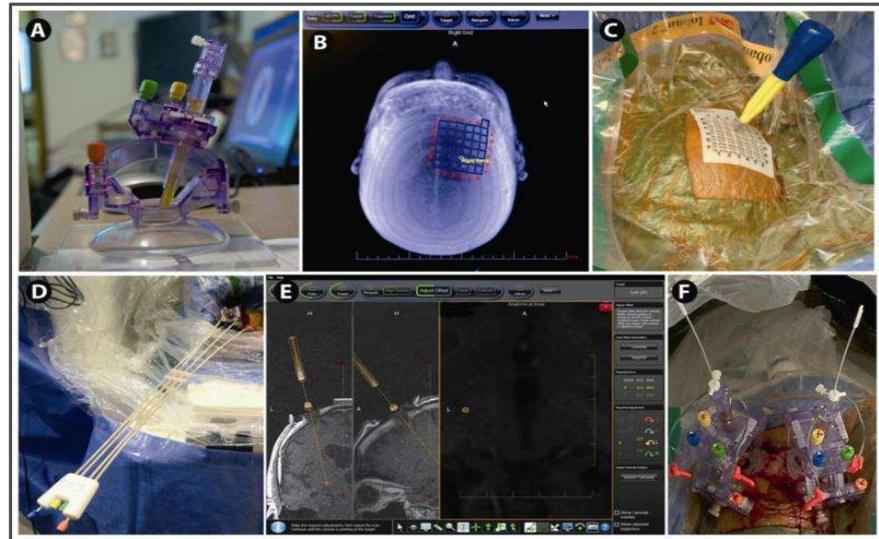
LFP guidance

Gross et al. Movement Disorders 2006  
Lozano et al. Journal of Neurosurgery 2018

# Asleep

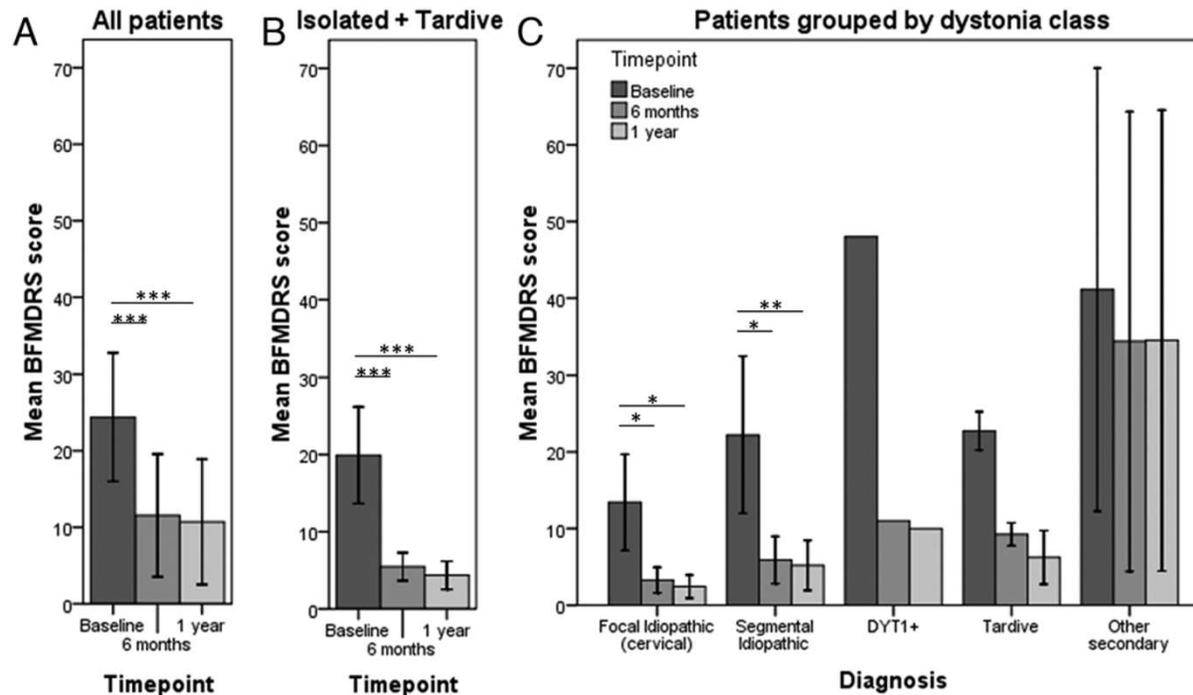


Intraoperative CT



Intraoperative MRI

# Intraoperative- MRI guided DBS placement for Dystonia



BFMDRS score

6 mo: 51.9%

12 mo: 63.4%

TWSTRS scores (CD)

6 mo: 53.3%

12 mo: 67.6%

Lead accuracy:  $0.93 \pm 0.12$  mm

Sharma et al. Journal of Neurosurgery, 2021

## Timing of surgery & DBS Programming

- No clear guidelines
  - Can be considered when medications and other treatment fails
- DBS Programming after 3-4 weeks of lead placement or early
  - Start with high stimulation and may reduce parameters after improvement is achieved
- Improvement with stimulation may take several days to months
  - ( full benefit may occur in 1 year or more)
- Stimulation induced Parkinsonism, freezing of gait can occur in some patients

## Status Dystonicus



Ruiz-Lopez & Fasano, *Movement Disorders*, 2017

- Worsening dystonic spasms requiring hospitalization
- Medical emergency, can lead to rhabdomyolysis, respiratory distress, bulbar dysfunction, metabolic derangements and pain.
- Cessation of DBS therapy: battery depletion, mechanical failure or removal of the implanted system due to infection, rarely with DBS placement.
- Urgent DBS surgery can be considered for management

## Predictors of good outcomes

- Younger age
- Shorter disease duration
- Phasic dystonia > tonic dystonia
- Isolated (idiopathic or genetic) dystonia responds >> combined (inherited or acquired dystonia)  
(exception tardive dystonia and myoclonus dystonia)
- Fixed skeletal deformities or myelopathy associated with poor outcomes
- Genetic status
  - DYT1: favorable outcomes
  - DYT1:I favorable outcomes
  - DYT6: respond less predictably
  - X-linked dystonia parkinsonism: favorable outcomes

## Key Takeaways

- DBS has emerged as an effective therapy for selected patients with dystonia refractory to medical therapy.
- The outcomes of DBS therapy depends on the clinical presentation and underlying etiology of dystonia.
- GPi DBS is the preferred target, STN-DBS has shown similar efficacy, but further studies are needed.
- Isolated generalized and segmental/focal dystonia responds best. Effectiveness is limited for acquired or inherited combined dystonia.
- Further understanding of predictors of outcomes will help in appropriate selection of patients.

THANK YOU