The Approach to Patients with Dystonia

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- Grant funding (active)

  NIH: U54 NS116025, R01 NS109242
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  Industry: Retrophin, Revance

- Professional societies

  International Parkinson and Movement Disorders

- Consulting

  Allergan, Bridge Bio, Cavion, CoA Rx, Ipsen, Retrophin, Revance

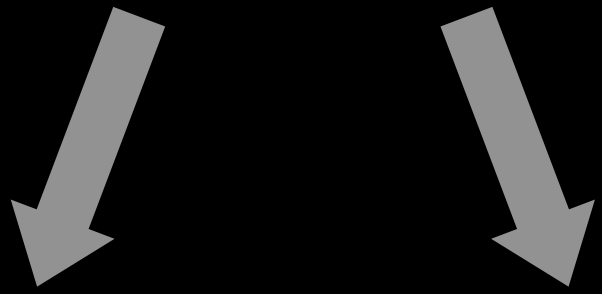
Learning Objectives

- Describe what is dystonia
- Describe how the many different types of dystonia are grouped and classified
- Summarize basic treatment strategies for the dystonias

Oppenheim's Historical Concept

The basic defect is a problem with muscle tone

"Dys - Tonia"



abnormal muscle tone

Modern Concept for Dystonia

Mov Disord 2013

REVIEW

Phenomenology and Classification of Dystonia: A Consensus Update

Alberto Albanese, MD,[1,2*] Kailash Bhatia, MD, FRCP,[3] Susan B. Bressman, MD,[4] Mahlon R. DeLong, MD,[5] Stanley Fahn, MD,[6] Victor S.C. Fung, PhD, FRACP,[7] Mark Hallett, MD,[8] Joseph Jankovic, MD,[9] Hyder A. Jinnah, PhD,[10] Christine Klein, MD,[11] Anthony E. Lang, MD,[12] Jonathan W. Mink, MD, PhD,[13] Jan K. Teller, PhD[14]

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

Dystonia: Key Clinical Features

- Characteristics of muscle contractions
  slow and sustained
  rapid and intermittent
  patterned

- Other helpful features
  overflow to nearby muscles
  triggered or worsened by voluntary action
  geste antagoniste (sensory trick)

Distinguishing Dystonia from related movement disorders

Clinical feature	Dystonia	Chorea	Athetosis
Sustained muscle contractions	often	no	no
Movements worse with action	yes	no	no
Movements are patterned	yes	no	no
Movement speed	slow or fast	medium to fast	slow to medium
Movements appear flowing	no	yes	yes
Overflow to extraneous muscles	yes	sometimes	no
Geste antagoniste	often	no	no

Distinguishing Dystonia from related hyper-tonias

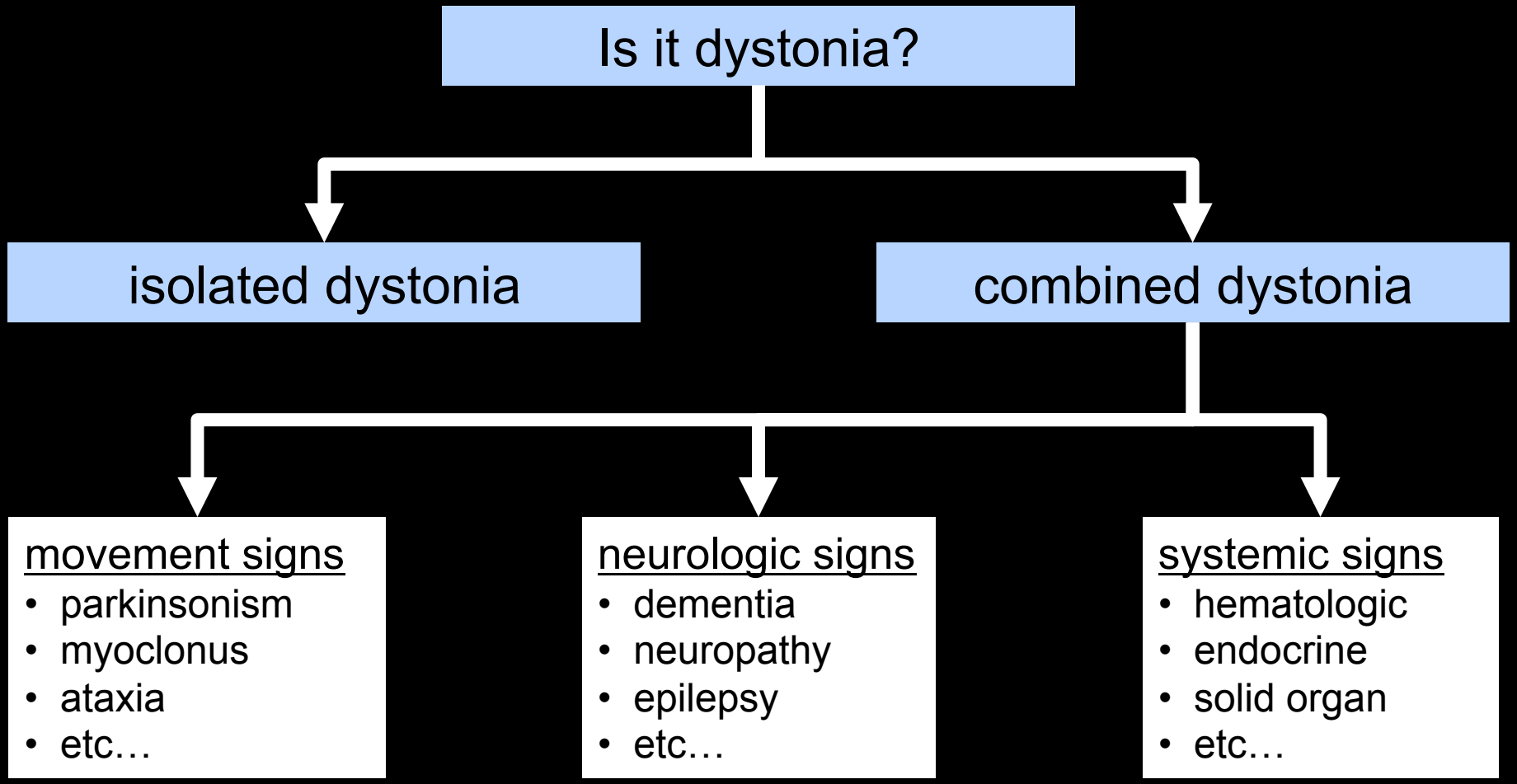
Clinical feature	Dystonia	Spasticity	Rigidity
Muscle tone increases with voluntary action	yes	no	no
Muscle tone decreases at rest	yes	no	no
Rate-dependent increase in muscle tone with passive movement	no	yes	no
Muscle tone is greater in extensors than flexors	no	yes	no
Other helpful features	geste antagoniste	corticospinal signs	cogwheeling

Classification of the Dystonias

- Axis I: Clinical features
  body distribution: focal, segmental, multifocal, generalized
  age at onset: infancy, childhood, adolescence, adult
  temporal aspects: progression and/or variability over time
  associated features: isolated (pure), combined

- Axis II: Etiology
  inheritance: inherited, acquired, idiopathic
  neuropathology: static lesion, degenerative, none

Using the Classification System for Clinical Diagnosis



Using the Classification System for Etiological Diagnosis

Mov Disord 2013

REVIEW

Assessment of Patients With Isolated or Combined Dystonia: An Update on Dystonia Syndromes

Victor S. C. Fung, PhD, FRACP,[1]* H. A. Jinnah, MD, PhD,[2] Kailash Bhatia, MD, FRCP,[3] and Marie Vidailhet, MD, PhD[4]

~200 different dystonic disorders
18 tables according to associated features

Treatment of the Dystonias

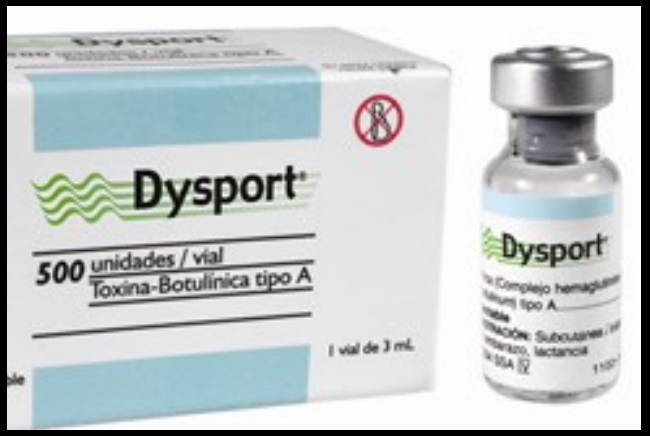
- All dystonias are “treatable”
  counseling
  physical and occupational therapy
  oral medications
  botulinum toxins

- Some dystonias have special treatments
  mechanism-specific treatments
  empirically discovered useful treatments

Dystonia Treatment: Oral Medications

Treatment class	Examples
Anticholinergics	benztropine, biperiden, ethopropazine, ophenadrine, procyclidine, trihexyphenidyl
Dopaminergics	levodopa, deutetrabenazine, tetrabenazine, valbenazine
GABAergics	alprazolam, baclofen, chlordiazepoxide, clonazepam, diazepam
Muscle relaxers	carisoprodol, chlorzoxazone, cyclobenzaprine, metaxolone, methocarbamol, orphenadrine
Miscellaneous	carbamazepine, cannabidiol, cyproheptadine, gabapentin, lithium, mexiletine, nabilone, riluzole, tizanidine, zolpidem

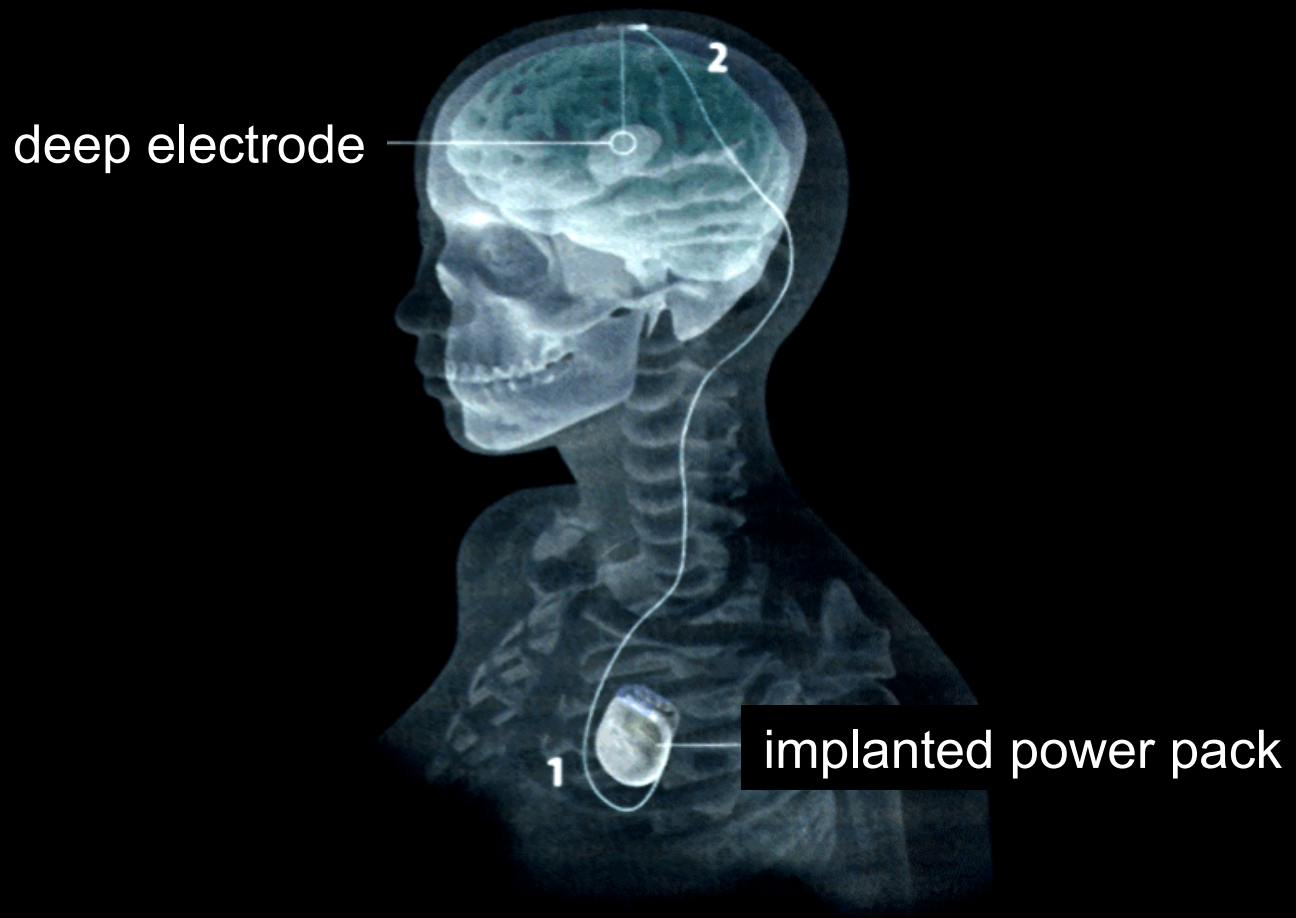
Dystonia Treatment: Botulinum toxins



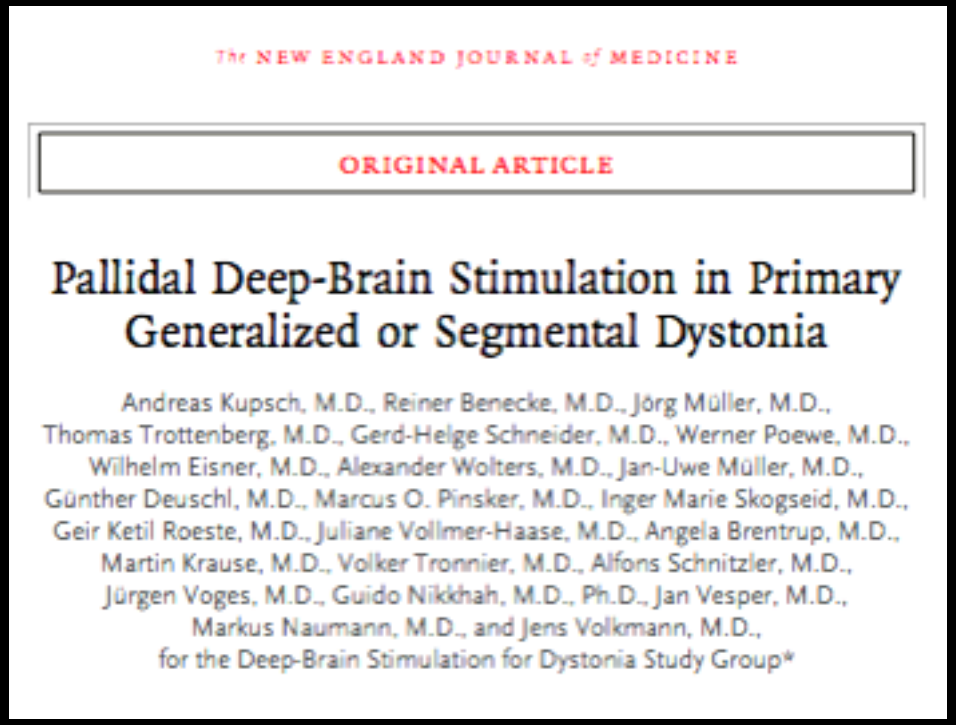
Dystonia Treatment: Botulinum toxins

Characteristic	Abo botulinum toxinA	Inco botulinum toxinA	Ona botulinum toxinA	Rima botulinum toxinB
Preparation supplied	freeze dried	powder	vacuum dried	liquid
Dose sizes	300, 500	50, 100	100, 200	2500, 5000, 10000
Storage	refrigerate	room temp	refrigerate	refrigerate
Approximate dose equivalents	2.5 - 3.0	1.0	1.0	40

Dystonia Treatment: Surgery



Dystonia Treatment: Surgery



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pallidal Deep-Brain Stimulation in Primary Generalized or Segmental Dystonia

Andreas Kupsch, M.D., Reiner Benecke, M.D., Jörg Müller, M.D., Thomas Trottenberg, M.D., Gerd-Helge Schneider, M.D., Werner Poewe, M.D., Wilhelm Eisner, M.D., Alexander Wolters, M.D., Jan-Uwe Müller, M.D., Günther Deuschl, M.D., Marcus O. Pinsker, M.D., Inger Marie Skogseid, M.D., Geir Ketil Roeste, M.D., Juliane Vollmer-Haase, M.D., Angela Brentrup, M.D., Martin Krause, M.D., Volker Tronnier, M.D., Alfons Schnitzler, M.D., Jürgen Voges, M.D., Guido Nikkhah, M.D., Ph.D., Jan Vesper, M.D., Markus Naumann, M.D., and Jens Volkmann, M.D., for the Deep-Brain Stimulation for Dystonia Study Group*

- Design
  multi-center
  DBS of GPi
  stimulation vs sham (3 months)
  additional un-blinded phase
- Patient Population
  N = 40
  generalized or segmental
  20 men, 20 women
  average age: 39 ± 13 yrs

Dystonia Treatment: Surgery

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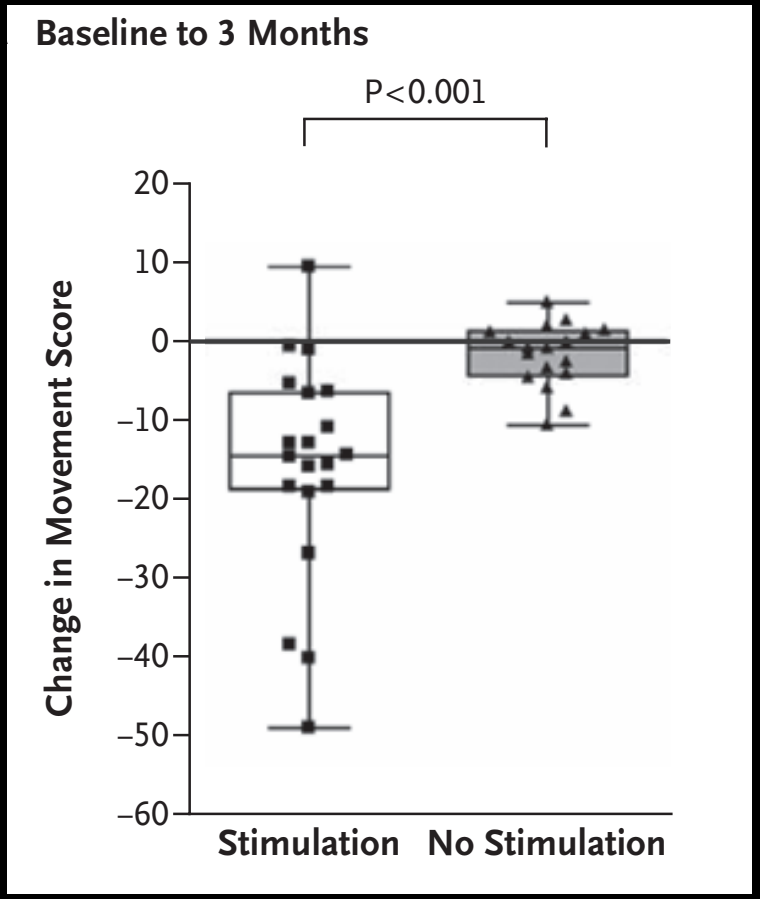
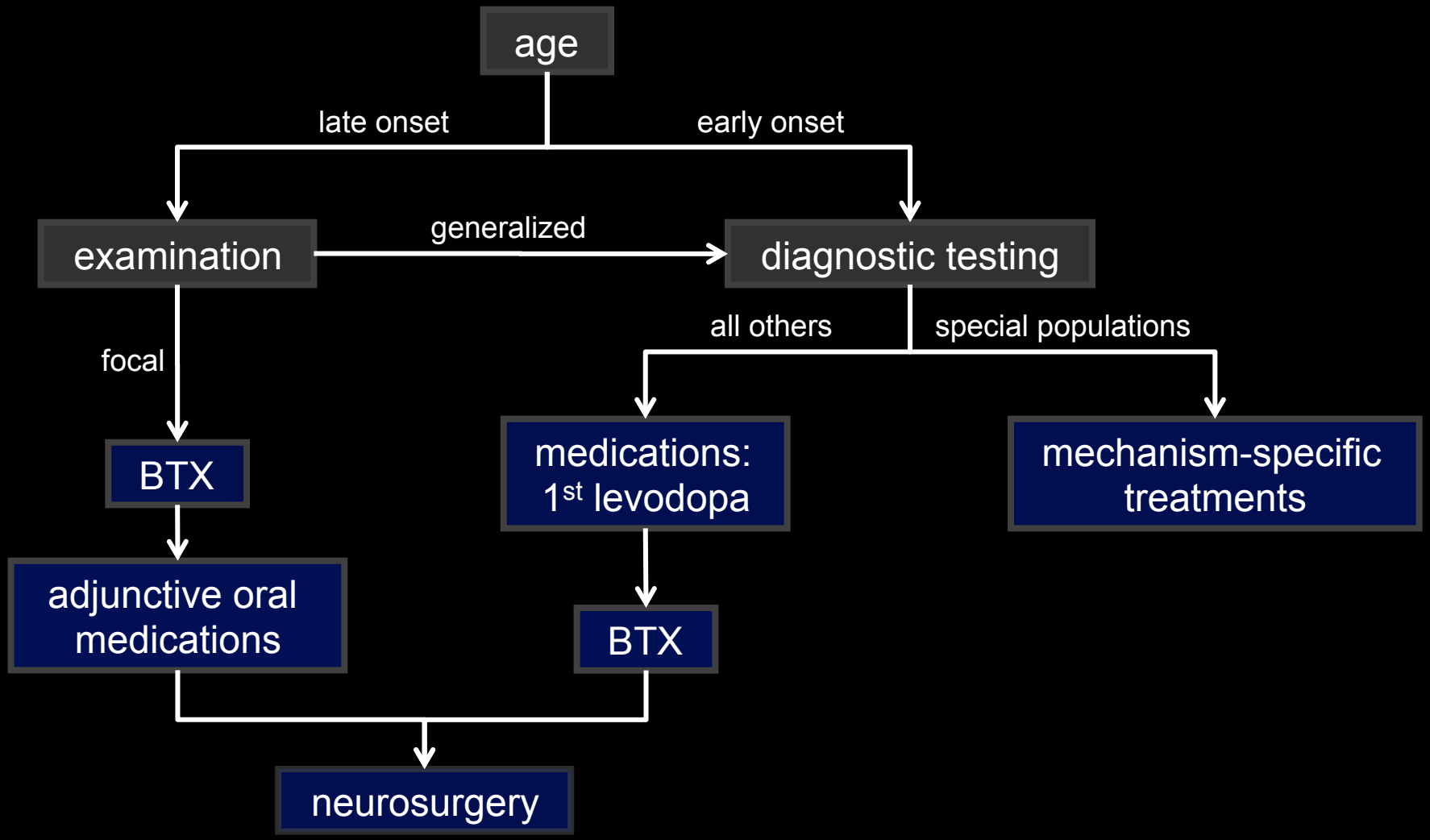


Algorithm for Diagnosis & Treatment



Dystonias with Special Treatments

Mov Disord 2018

REVIEW

CME

Treatable Inherited Rare Movement Disorders

H. A. Jinnah, MD, PhD,[1*] Alberto Albanese, MD,[2,3] Kailash P. Bhatia, MD,[4] Francisco Cardoso, MD,[5] Gustavo Da Prat, MD,[6,7] Tom J. de Koning, MD, PhD,[8] Alberto J. Espay, MD,[9] Victor Fung, PhD, FRACP,[10] Pedro J. Garcia-Ruiz, MD,[11] Oscar Gershanik, MD, PhD,[12] Joseph Jankovic, MD,[13] Ryuji Kaji, MD, PhD,[14] Katya Kotschet, MD,[15] Connie Marras, MD, PhD,[16] Janis M. Miyasaki, MD, MEd,[17] Francesca Morgante, MD,[18] Alexander Munchau, MD,[19] Pramod Kumar Pal, MBBS, MD, DM,[20] Maria C. Rodriguez Oroz, MD,[21,22,23,24] Mayela Rodríguez-Violante, MD,[25] Ludger Schöls, MD,[26,27] Maria Stamelou, MD,[28,29] Marina Tijssen, MD, PhD,[30] Claudia Uribe Roca, MD,[31] Andres de la Cerda, MD,[32] Emilia M. Gatto, MD,[33]
for the International Parkinson's Disease Movement Disorders Society Task Force on Rare Movement Disorders

- 30 inherited movement disorders; half with dystonia

Target reduction therapy

Vitamin/cofactor therapy

Avoid triggers

Dietary modifications

Specific drugs

For More Information On Dystonia

Continuum, 25: 976-1000, 2019

REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

The Dystonias

By H. A. Jinnah, MD, PhD

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