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Teaching Course 6

EAN/MDS-ES: Movement disorders for general neurolgists (Level 2)

Diagnosis and therapy of common dystonias

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Diagnosis and treatment of common dystonia (s)

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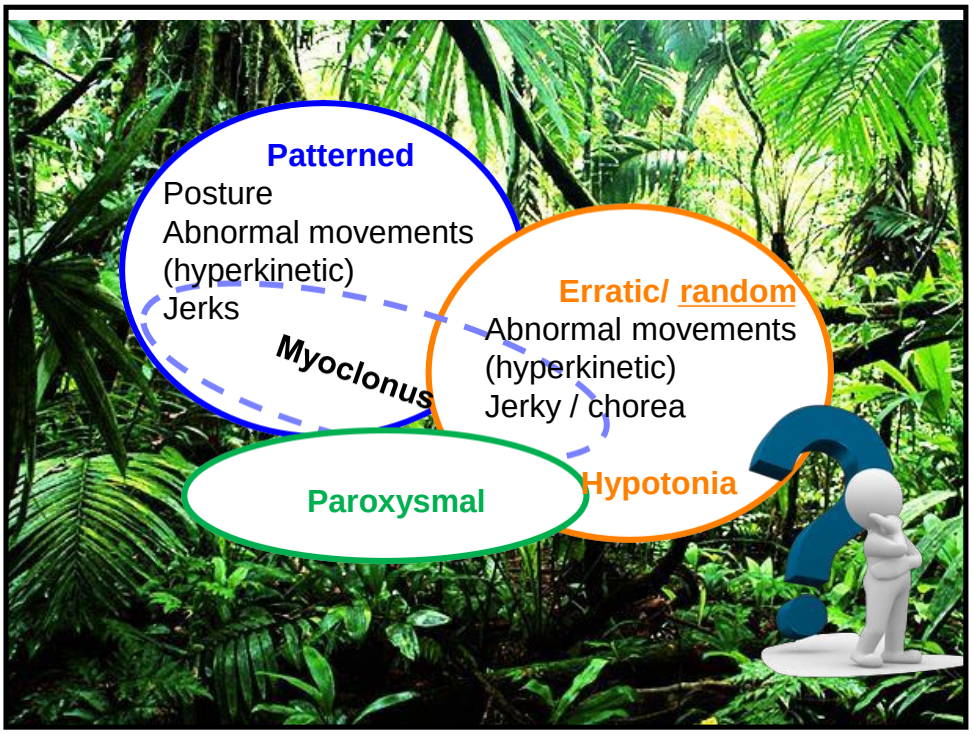
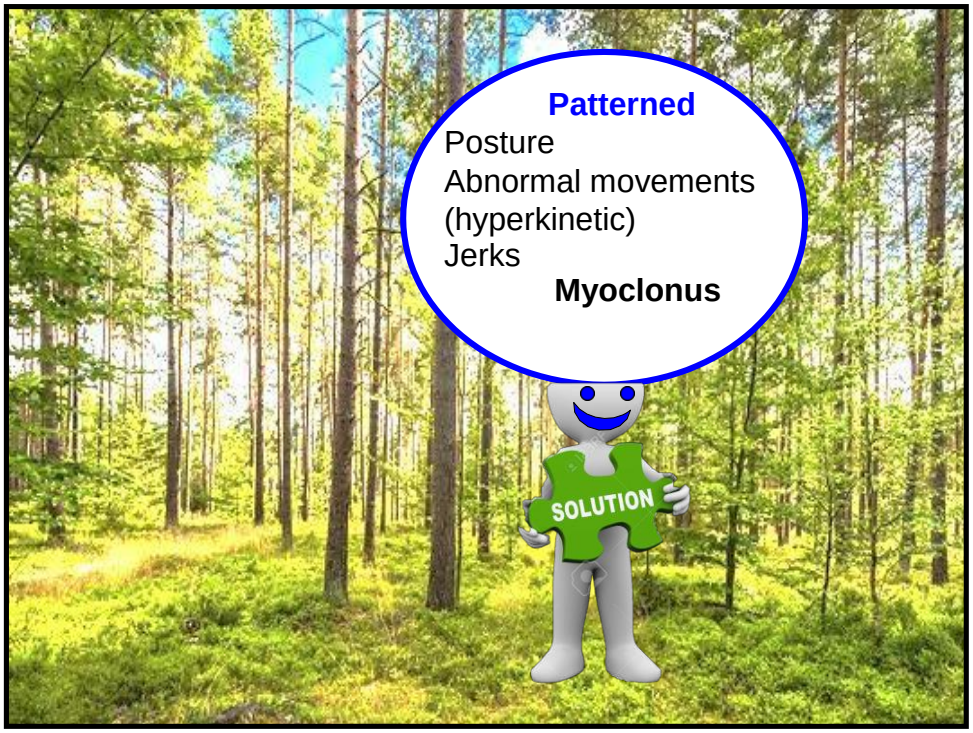
Conflict of Interest

In relation to this presentation and manuscript:

❑ the Author has no conflict of interest in relation to this manuscript.


Patterned
Posture
Abnormal movements
(hyperkinetic)
Jerks
Myoclonus
Erratic/ random
Abnormal movements
(hyperkinetic)
Jerky / chorea
Hypotonia
Paroxysmal


Patterned
Posture
Abnormal movements
(hyperkinetic)
Jerks
Myoclonus
SOLUTION

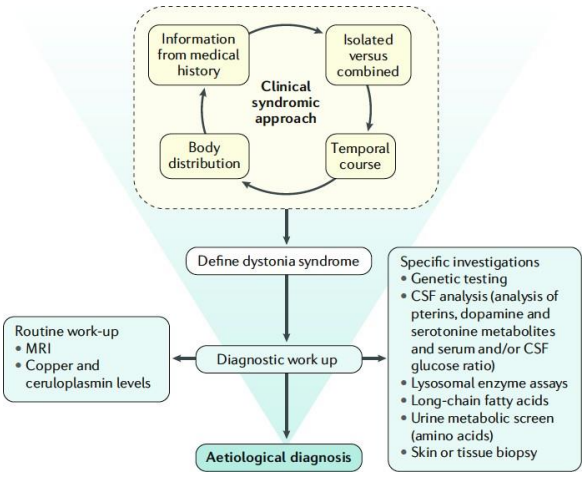
Définition of dystonia

- sustained or intermittent muscle contractions
- causing **abnormal movements, abnormal postures**, or both.
- Dystonic movements are typically **patterned**,
- **Twisting movements**, **may be tremulous** (e.g. myoclonic dystonia / dystonic tremor).

- Dystonia often initiated or worsened by voluntary action
- associated with **overflow muscle activation**.

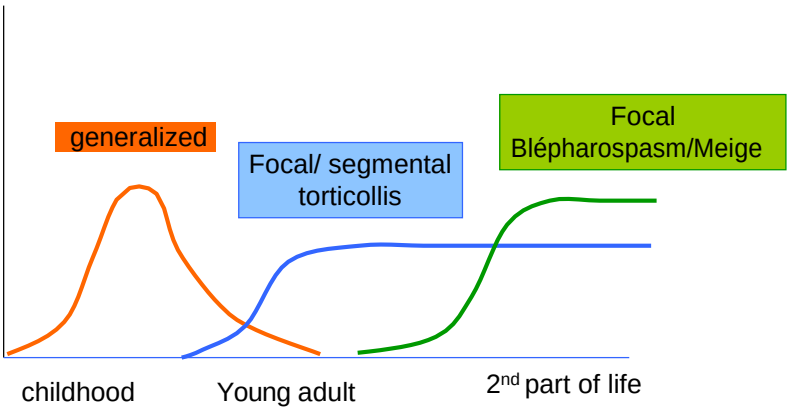
Consensus Update Albanese et al Mov Disord 2013

Algorithm for diagnosis



Balint B et al Nature Reviews primer 2018

Age and body distribution are inter-related



Step by step: Semiology and etiology

Axis I. Clinical Characteristics

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 body region
- ***Segmental***: ≥ 2 contiguous body regions
- ***Multifocal:*** ≥ 2 noncontiguous
- ***Generalized***: Trunk + at least 2 other sites.

Hemidystonia: e.g. acquired brain lesions

•**Isolated** dystonia. Dystonia is the only motor feature
•**Combined** dystonia = **plus other movements disorders** (myoclonus, parkinsonism)

Axis 2. Etiologies

Unknown causes

Idiopathic (unknown cause)
- focal or segmental (onset in adulthood)
- **Segmental or generalized** (variable age at onset (young onset)

Sporadic or familial

Secondary

Inherited
-Genetic , metabolic disorders

Acquired
birth injury, vascular, drugs: (e.g. post-neuroleptics), toxic: (e.g; Manganese), post-infectious, post-traumatic.

Epidemiology : frequency of dystonia

Dystonia represents 20% of patients in a movement disorders clinic

Prevalence depends on methodology countries, studies :

- 16 /100 000 for adult-onset focal dystonia
- prevalence increase with age

Adult onset focal dystonia is the most frequent form

- cervical dystonia twice most common in women than men (4th decade)
- blepharospasm / facial dystonia) more common in women ((6th decade)
- limb dystonia (4th decade) balanced men/ women ratio

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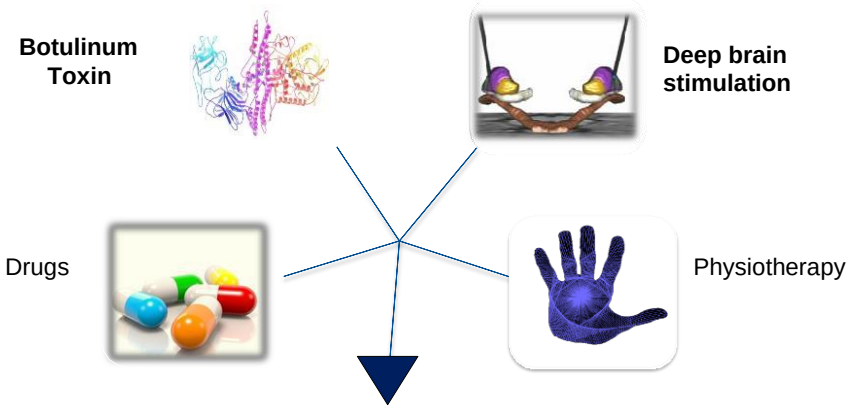
Diagnosis and treatment of common dystonia

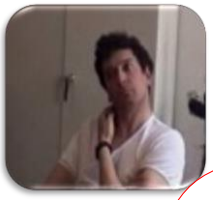


Symptomatic treatment

- Multimodal, multi-disciplinary approach
- Adapt strategy to the dystonia localisation / severity

Diagnosis and treatment of Focal dystonia(s)

Cervical dystonia

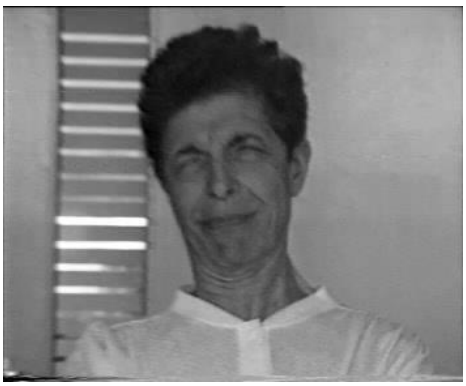


Task specific dystonia

?

Face dytonia

Facial dystonia



Blepharospasm / Meige Syndrome

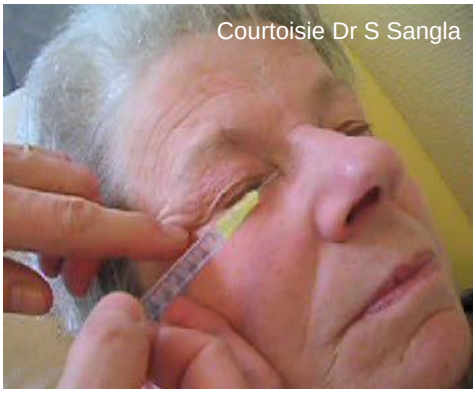
2nd part of life (5th decade)
bilateral
(diff. diag. hemi-ifacial spasm)

Oromandibular dystonia
- Jaw opening
- jaw closing

Laryngeal dystonia
- Adduction: harsh voice
- Abduction: whispering

Botulinum toxin injections

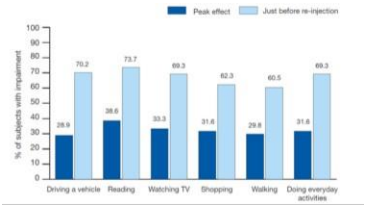
BoNT is now considered the initial treatment fo choice for most patients



Beneficial effect in ~ 90% of blepharospasm
Maintained throughout the disease course (follow up > 19 yrs

Blepharospasm : a patient centric approach

Disability : for all activities of daily life



Patient's needs and expectations

interview before the next injection

- 56.1% were at least somewhat satisfie

interview at peak of BTX effect

- 97.3% of subjects recalled being at least somewhat satisfied

Peak effect within 4 weeks began to wear off within 10 wks (70%)

- most subjects (52 %) prefer intervals <12 weeks, including 30% who would prefer intervals <10 weeks.
- 20% would prefer intervals ≥ 12 weeks.

Flexible doses

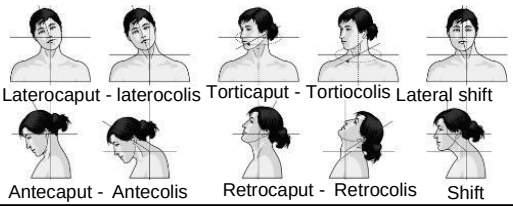
Survey 114 patients blepharospasm
Fezza J et al. J Neuol Sci 2016

Cervical dystonia

Simple rotation: torticolis

Geste antagoniste

Complex : lateral deviation/ rotation, anterior/posterior alteration of posture



Treatments

Depends on tolerance and severity

Botulinum Toxin

Abobotulinum toxin A
Onabotulinum toxin A
Incobotulinum toxin A

Deep brain stimulation

Physiotherapy

Drugs

- benzodiazepines
- anricholinergics (trihexyphenidyl, tropatepine)

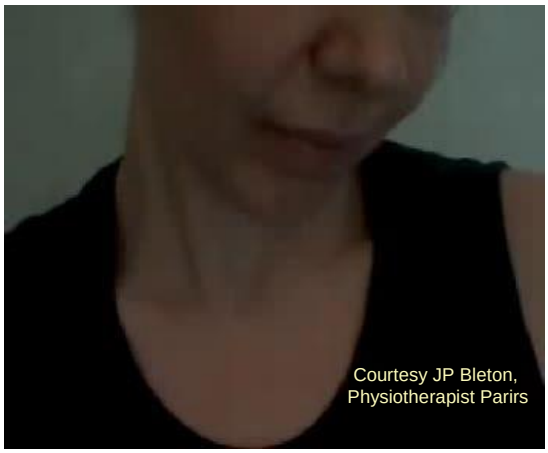
one of a few oral drugs tested in dystonia by a double blind placebo control study.

Burke RE, Fahn S, Marsden CD. Torsion dystonia: a double-blind, prospective trial of high-dosage trihexyphenidyl. Neurology 1986;36:160–164.

Anticholinergic medications might increase the risk of dementia

with a 10-year cumulative dose-response relationship. Gray SL et al JAMA Intern Med. 2015

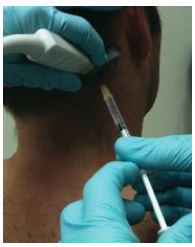
Physiotherapy

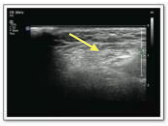


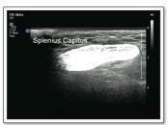
Botulinum toxin A injections

Courtoisie Dr C Vial (Lyon, France)

Clinical evaluation
EMG guidance +/- Ultrasounds







Patient's expectation:
- **Free from pain**
- **Free from spasms**
- **Back to normal**

A short visit to the clinic

Patients report the "wearing off" of the treatment effect and how it affects their quality of life

- "It is really efficient for a while but I still feel permanently ill / disabled because of early "wearing off""
- "It make me anxious and depressed" and "It affects my self-esteem"
- "It prevents me to resume my job because I have trouble driving my car when the effect decreases before the next injection"
- "It prevents me to have regular activities with others because sooner or later either they will see me during the bad period or I have to skip several sessions"

Flexible intervals and flexible doses according to the patient's needs and expectations to feel a sustained benefit

Current recommended intervals: 10-12 weeks but many (46 %) patients would prefer injection schedule <12 weeks

Albanese A et al J Neuro 2015

Bilateral pallidal stimulation :

10 years long term follow-up

Pre – operative

10 years follow-up stimulation ON (GPI bilateral)

Courtesy Pr Elena Moro/ Toronto, Grenoble

Writer's cramp

Risk of writer's cramp increases with the time spent writing each day

Associated with an abrupt increase in the writing time during the year before onset

- not significantly associated with peripheral trauma, left-handedness, constrained writing, writing in stressful situations or the choice of writing tool.

- Roze E et al Brain 2009

« Mirror abnormal posture» when writing with the non dominant hand

Treatment : retraining / physiotherapy and botulinum toxin injections

Over time , dystonia may evolve to disruption of other tasks / tremor

Generalized dystonia

- Idiopathic generalized dystonia
- Most frequent genetic forms : DYT1 (torsin), DTY11 (epsilon-sarcoglycan), KMT2B,
- Tardive dystonia

Similar strategy

- medical treatment : often disappointing with poor tolerance (anticholinergics)
- local injections of botulinum toxin (pain, servere posture..)
- Deep brain stimulation (Gpi, less frequent STN): > 50 % imorovement

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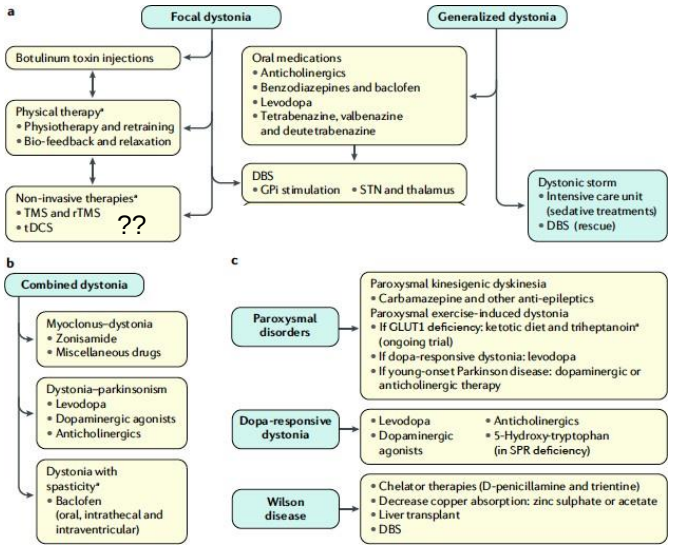
Algorithm for treatment



Balint B et al Nature Reviews primer 2018

Dopa-responsive dystonia

GCH1 mutations

due to enzymatic defect
decreases dopamine biosynthesis

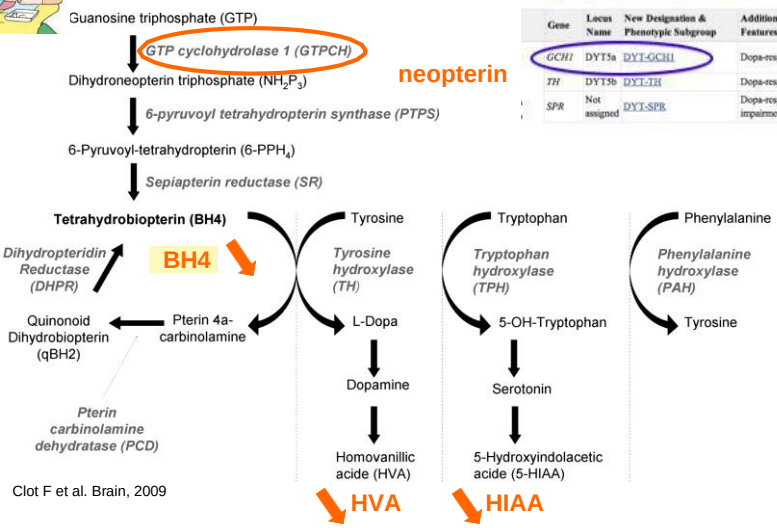
7 years-old , diurnal variations

L-Dopa, dramatic improvement

After treatment: L-Dopa 100 mg two times a day -> improved and stable over time

Always try L-Dopa treatment in dystonia or parkinsonism in children or adolescents

In the CSF



Clot F et al. Brain, 2009

Dystonia plus parkinsonism

Dopa responsive dystonia DRD

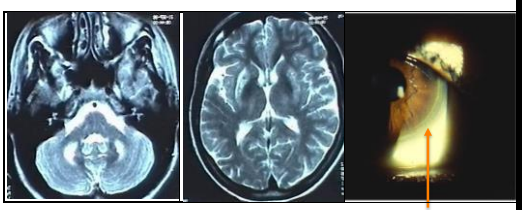
Gene	Locus Name	New Designation & Phenotypic Subgroup	Additional Distinguishing Features	MOI
GCH1	DYT5a	DYT-GCH1	Dopa-responsive	AD, AR
TH	DYT5b	DYT-TH	Dopa-responsive	AR
SPR	Not assigned	DYT-SPR	Dopa-responsive, cognitive impairment	AR

Metabolic pathway of BH4, dopamine, and serotonin

Wilson's disease

mutation of the **ATP7B gene**
inherited in an autosomal recessive manner

Low ceruloplasmin
Low « free copper »: exchangeable copper
High urinary copper



Kayser Fleischer's ring

- D-penicillamine , trientine, Zinc, (lifelong)
- liver transplant

Asymptomatic carriers:
-> detection,treatment

Summary

Diagnostic clues :

- Depending on the **age at onset** (infancy/childhood or adolescence adulthood) past *medical history* and *familial history*
- **Isolated** or **Combined** Dystonia (myoclonus dystonia, dystonia + parkinsonism)

- MRI
- Biological tests: Wilson's disease
- Therapeutic tests: L-Dopa

-> **Idiopathic, inherited, acquired**

Symptomatic treatment in most of the cases or specific treatments (DRD, Wilson)

Thank you for your attention