Approach to movement disorders

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Abnormal movement

Insufficient movement

Parkinsonism

Ataxia

Excessive movement

- Tics
- Tremor
- Chorea
- Dystonia
- Myoclonus
- Stereotypy, RLS, PLMT, ect

Hyperkinetic movement

Rhythmic

- Oscillatory → Tremor
- Repetitive
- Coordinated
- Patterned
- Motor/vocal
- Urge - → Stereotypy

Non-Rhythmic

Suppressible

- Repetitive
- Patterned
- Motor/vocal
- Urge + → Tics

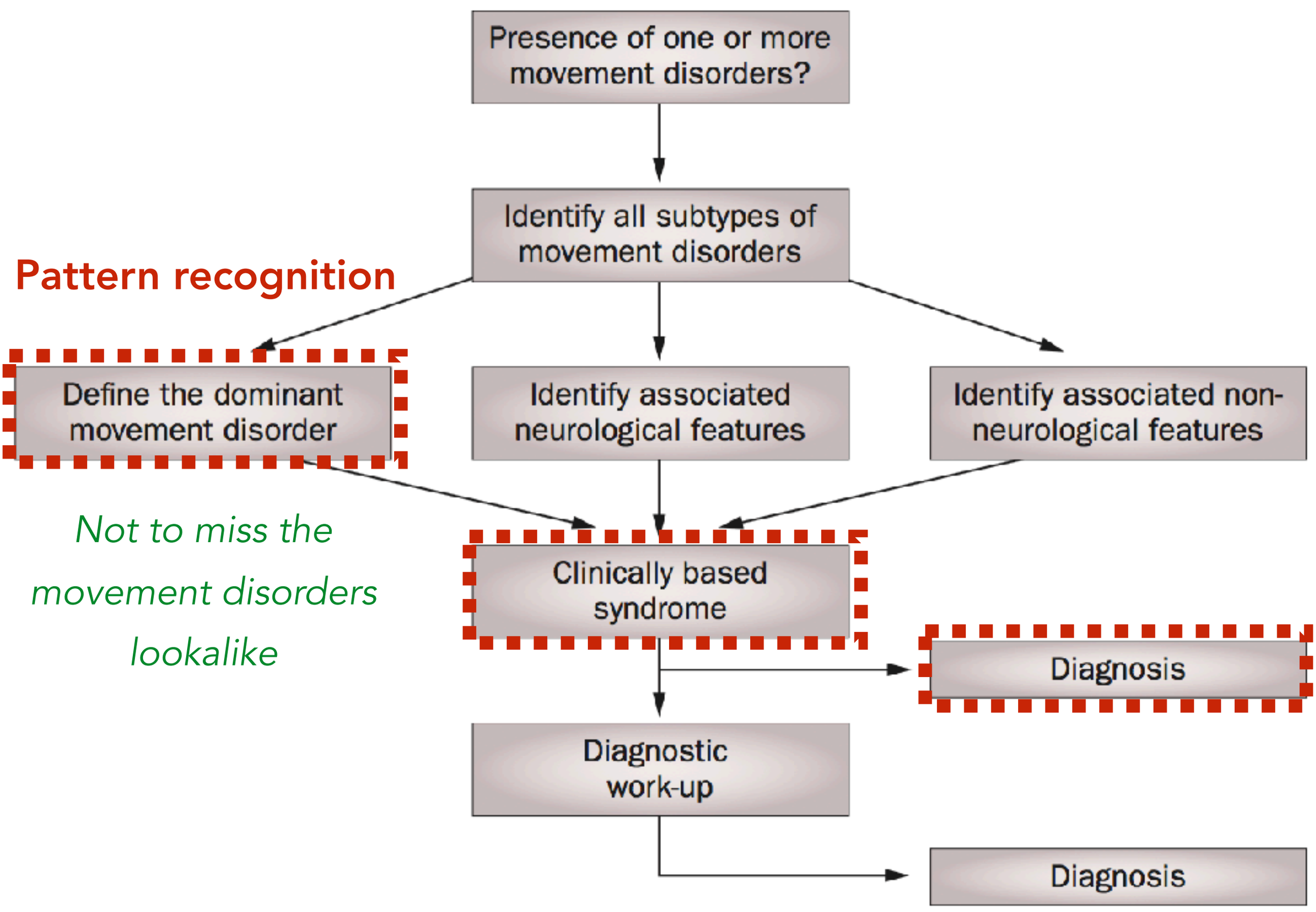
Non-suppressible

- Flow
- Random
- Unpredictable
- Unsustained → Distal :Chorea, Proximal : Ballism
- Sudden
- Brief
- Jerk → Myoclonus
- M. contraction
- AB posture
- Sustained
- Overflow → Dystonia

Classification of movement disorders 2016
Principle and Practice of Movement Disorders 2011

Pattern recognition

Not to miss the movement disorders lookalike



Abdo WF, et al. Nat Rev Neurol 2010;6:29-37

Parkinsonism

Definite
Probable
Possible

Parkinsonism

Bradykinesia

Resting tremor

Rigidity

Postural instability

Flexed posture

Freezing

Fahn. et al. Principles and practice of movement disorders 2011

Parkinsonism

- **Parkinson's disease**
  - **Idiopathic PD**
  - **Familial PD (PARK)**
- **Parkinsonism-plus (atypical parkinsonism syndromes)**
  - **Synuclein**
    - **MSA**
    - **DLB**
  - **Tau**
    - **PSP**
    - **CBD**
- Hereditary
  - Wilson
  - HD (Westphal)
  - Lubag
  - SCA
  - NBIA
  - OPCA
  - etc.
- Secondary
  - Vascular
  - Hydrocephalus
  - Tumor/ malignancy
  - Metabolic disorders
  - Endocrine disorders
  - Infectious and post infectious
  - Immune mediated
  - Drugs or Toxins
  - Other secondary causes

Have a look on atypical features!!

Principle and Practice of Movement Disorders 2011

	Parkinson's disease	Drug-induced parkinsonism
Bradykinesia	Essential feature in upper body	Dominating symptomatology
Rigidity	Marked and progressive, usually evident without reinforcement	Usually 'mild'–'moderate' severity only, often requires reinforcement, does not correlate with bradykinesia
Tremor	Evident in majority at presentation, virtually universal with progression	Resting: infrequent, late feature Postural: common, early feature
Posture (trunk)	Predominantly flexion	Extension/hyperextension common
Gait	All features characteristic and progressive	Uncommon: late or severe manifestation
Glabellar tap	Frequently positive	Equivocal/infrequently positive (? part of psychiatric disorder)
Distribution	Unilateral emphasis from diagnosis	Unilaterality may be evident but tends to generalised distribution, especially in younger patients

Asymmetry

Symmetry

Table 1. Common offending drugs of drug-induced parkinsonism

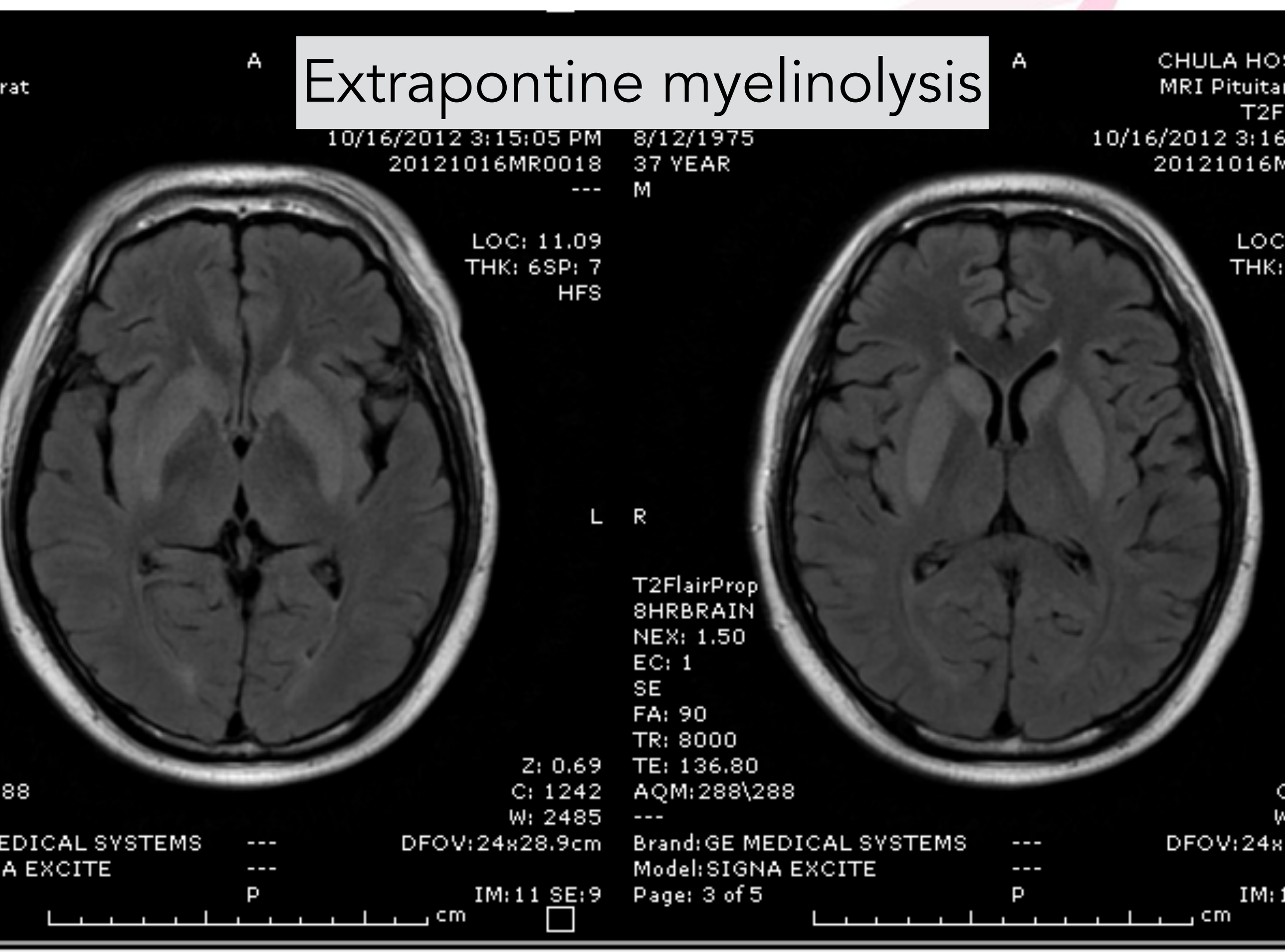
Drug frequently causing parkinsonism	
Typical antipsychotics	Phenothiazine: chlorpromazine, prochlorperazine, perphenazine, fluphenazine, promethazine
	Butyrophenones: haloperidol
	Diphenylbutylpiperidine: pimozide
	Benzamide substitutes: sulpiride
Atypical antipsychotics	Risperidone, olanzapine, ziprasidone, aripiprazole
Dopamine depleters	Reserpine, tetrabenazine
Antiemetics	Metoclopramide, levosulpiride, clebopride
Calcium-channel blocker	Flunarizine, cinnarizine

SSRI: selective serotonin reuptake inhibitor.

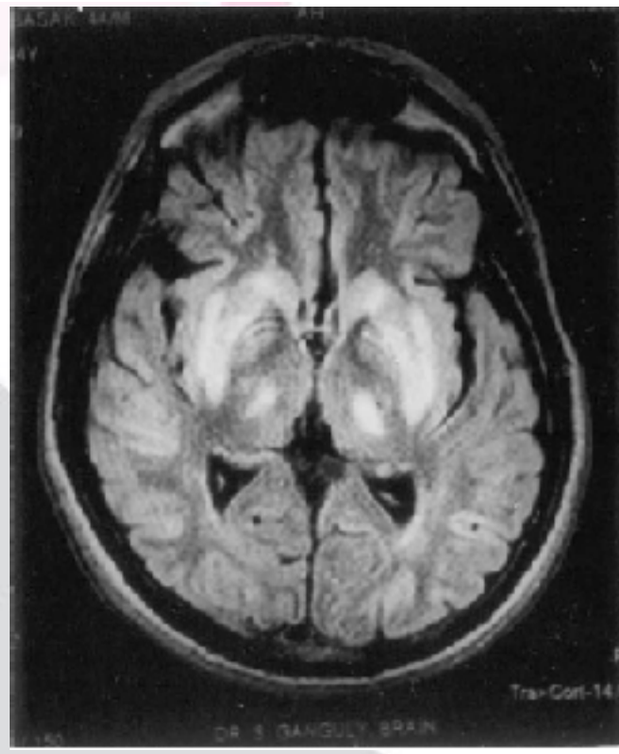
Flunarizine

A guided to the extrapyramidal side-effects of Antipsychotic drugs. Cambridge University Press 2014.
J Clin Neurol 2012;8:15-21

Extrapontine myelinolysis

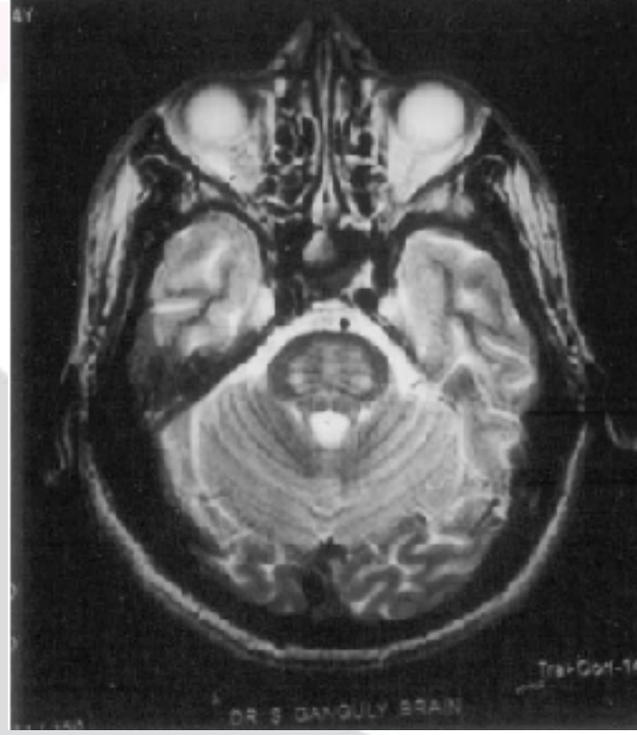


Extrapontine myelinolysis (EPM)



- The lesions are mostly predominated in basal ganglia (usually spare globus pallidus), thalamus, internal capsule, cerebellum, and subcortical white matter.
- Psychiatric and behavioral changes
- Variety of abnormal movement disorders : parkinsonism, chorea, dystonia, myoclonus, and ataxia

Central pontine myelinolysis (CPM)



- The lesions are mostly predominated in basis pontis (sparing the tegmentum) and may extend up to midbrain, but rarely down to the medulla.
- Corticobulbar fiber: dysarthria & dysphagia pseudobulbar Palsy
- Corticospinal tract: flaccid then Spastic Quadriparesis “Locked-in syndrome”

Tremor

Tremor classifications

Phenomenological classification

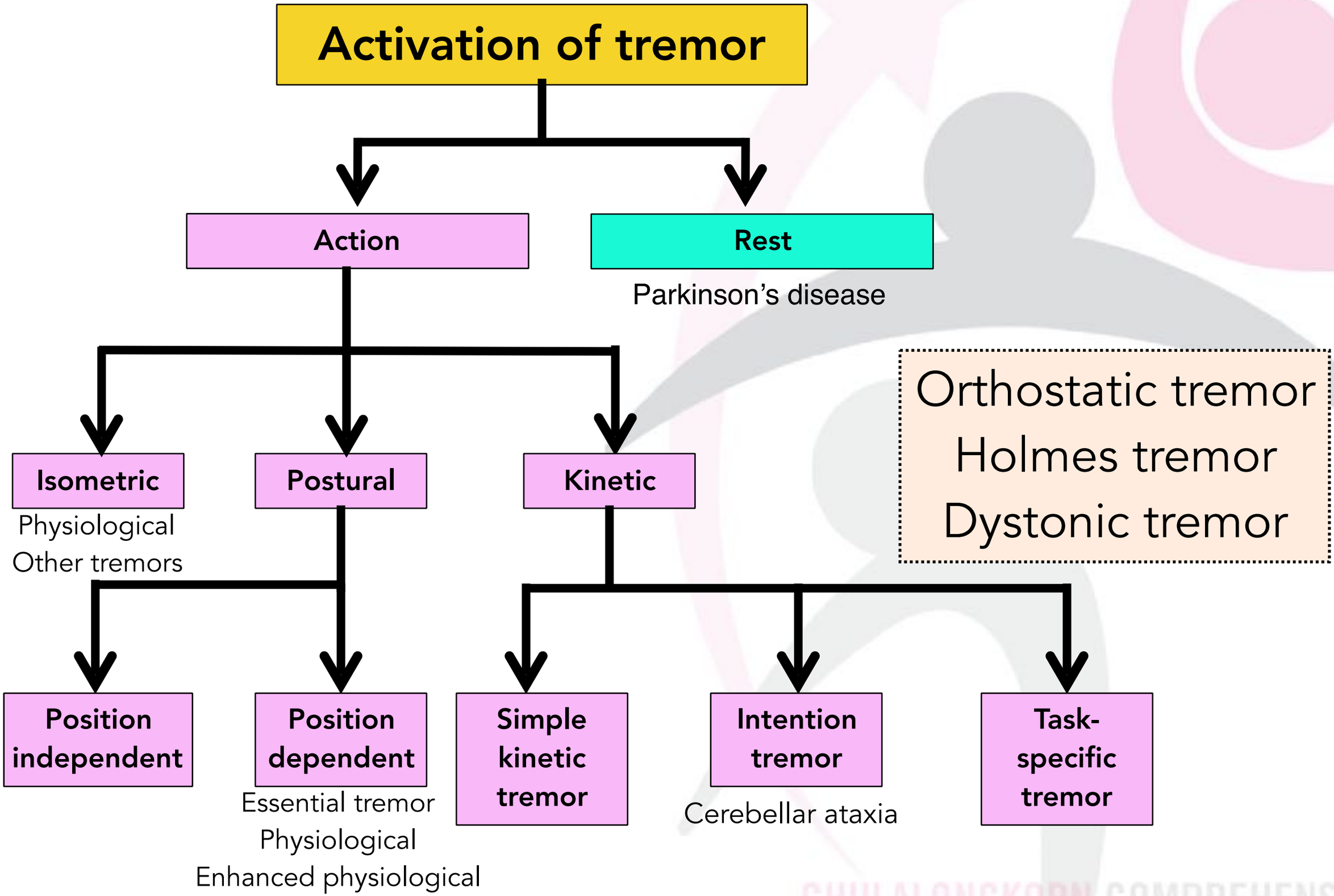
- **Rest tremor**
- **Action tremor**
  - Postural
  - kinetic
  - Task-specific
  - Isometric
- **Combined= Holmes**

Look for position, distribution, frequency, amplitude, regularity

Etiological classification

- Physiologic tremor
- Pathologic tremor

Deuschl G, et al. Mov Disord 1998

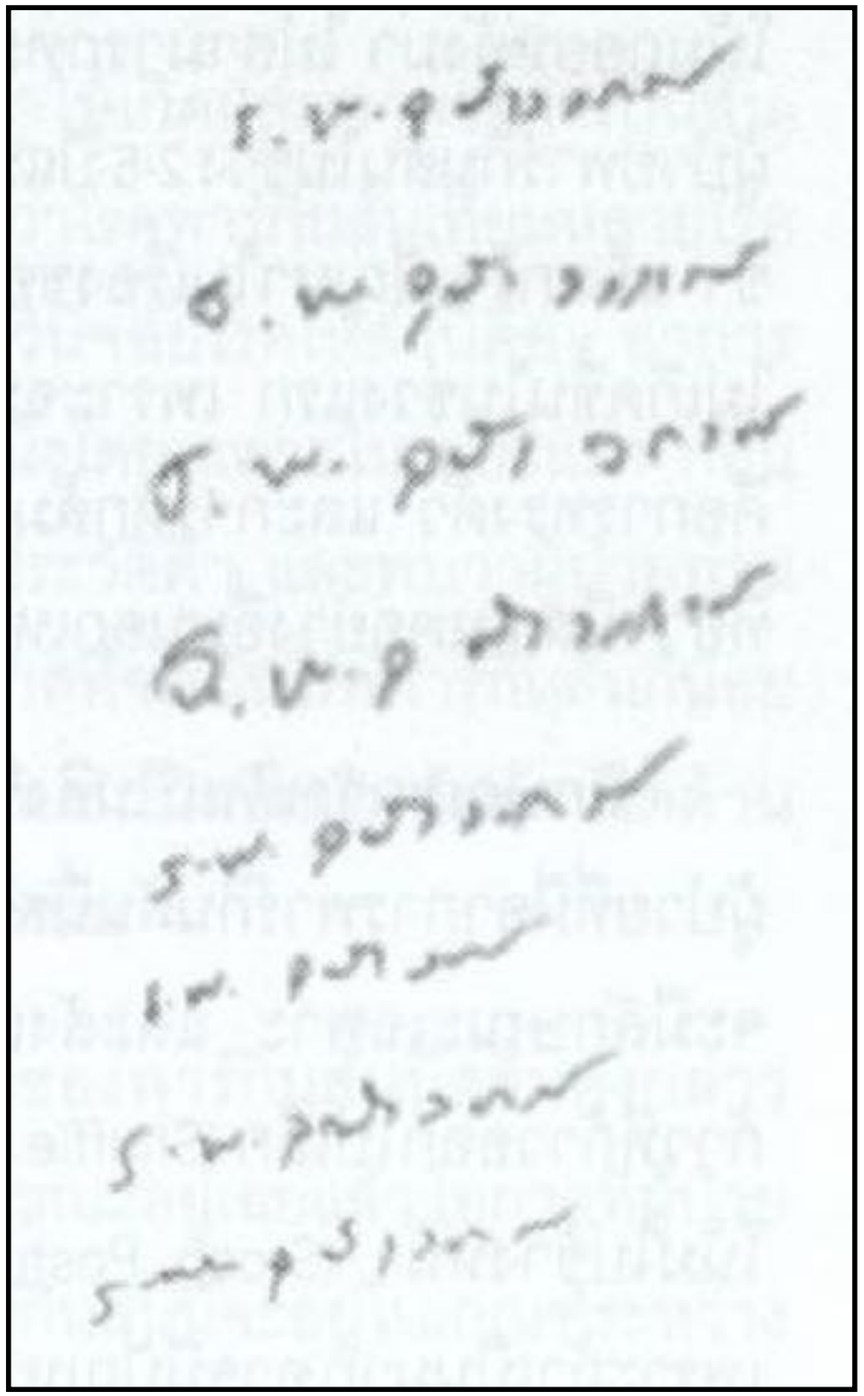


Bhatia KP, et al. Mov Disord 2018; 33: 75-87.

	Parkinson tremor	Essential tremor
Onset	Asymmetry	Symmetry, asymmetry but not unilateral ,
Activation	Rest > postural > kinetic, re-emerging tremor	Kinetic >= postural > rest (20%, severe case)
Distribution	Upper limb : pill rolling (abd/adduct thumb), finger F/E, wrist rotate, walking tremor Head : rarely Orolingual : jaw and tongue Lower limb (abduct/adduct)	Upper limb : wrist F/E Head : NO-NO, Yes-Yes, not isolated Vocal : not isolated Orolingual (20%) : lip (during action), severe limb Leg : rarely
Frequency	4-6 Hz	5-12 Hz
Association	Bradykinesia, rigidity, postural instability, FH +/- Levodopa responsiveness	Mild CB dysfunction, no parkinsonism FH +ve alcohol responsiveness (50%)

Ddx Hand writing

Parkinson's disease



Essential tremor

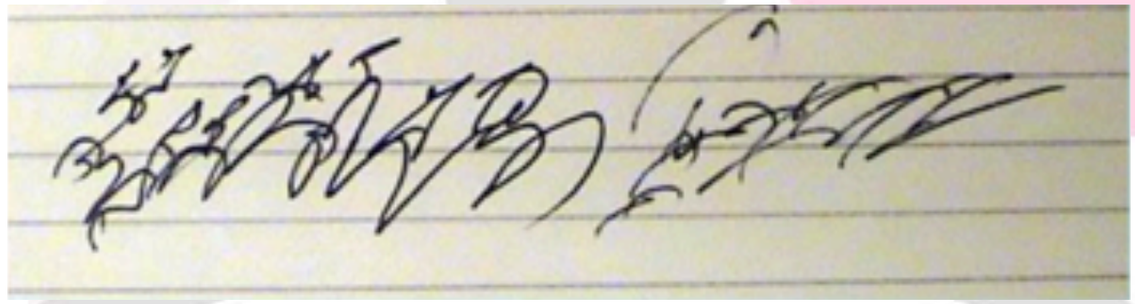


TABLE 1. Pharmacological management of ET (from Schneider and Deuschl[74])

Recommendation for Use	*Drug*	*Total Daily Dosage (mg/d)*	Daily Intakes
Recommended	Propranolol	40–320	2–3 standard 1–2 long-acting
	Primidone	62.5–750	1 (bedtime)-3
	Topiramate	50–300	2–3
Probable or weak efficacy	Atenolol	50–100	1
	Sotalol	80–240	1–2
	Gabapentin	1200–2400	3
	Alprazolam	0.75–3	Intermittent
Level C possibly effective	Clonazepam	0.5–6.0	2–3
	Clozapine	6.25–75	1–2
	Flunarizine	10	1
	Nadolol	120–240	1
	Nimodipine	120	3–6
	Botulinum toxin	OnabotulinumA* doses: vocal muscle: 1.25–3.75 U; cervical muscles: 40–400 U; forearm muscles: 50–100 U; tensor veli palatine: 4–10 U	NA
Recommendations against use	3,4-Diaminopyridine, acetazolamide/methazolamide, amantadine, carisbamate, isoniazid, levetiracetam, pindolol, trazodone, mirtazapine, nifedipine, verapamil		
Inadequate evidence to confirm or exclude efficacy	Olanzapine, pregabalin, tiagabine, sodium oxybate, zonisamide		

Abbreviations: *Conversion ratio OnabotulinumA: incobotulinumtoxinA = 1:1; conversion ratio OnabotulinumA: abobotulinumtoxinA = 1:3–5; NA, not available.

Before Dx ET : should exclude enhanced physiologic tremor (hyperthyroidism) and drug induced tremor

Table 3 Common Causes of Medication- or Toxin-Induced Tremors

Class of Medication or Toxin	Examples
Beta-adrenergic agonists	Terbutaline, metaproterenol, isoetharine, epinephrine (adrenaline)
Antidepressants	Bupropion, lithium, tricyclic antidepressants
Neuroleptics	Haloperidol
Anticonvulsants	Valproate sodium
Dopamine agonists	Amphetamine
Heavy metals	Mercury, lead, arsenic, bismuth
Xanthines or derivatives	coffee, tea, theophylline, cyclosporine

Chorea

Chorea

Genetic

AD

- HD
- HD-like 1,2,4
- DRPLA
- SCA 2,3,17
- NFT
- BHC

AR

- ChAc
- HD-like 3
- NBIA
- Wilson
- AR-ataxia

XR

- McLeod
- Lesch-Nyhan

Mitochon

- POLG

Secondary

- Vascular
- Metabolic disorders
- Endocrine disorders
- Infectious and post infectious
- Immune mediated
- Drugs or Toxins
- Other secondary causes

* HD; Huntington's disease

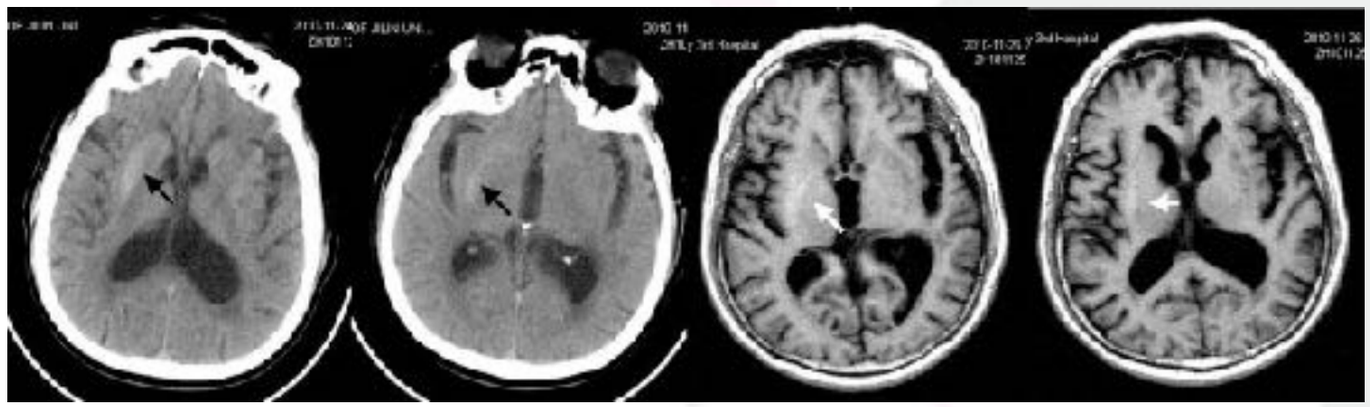
* ChAc ; Choreo-acanthocytosis

* POLG ; mitochondrial DNA polymerase gamma

Principles and Practice of Movement Disorders 2011

Hyperglycemia induced chorea

- Non ketotic hyperglycemia
- Elderly, female > male, longstanding poor controlled DM type 2
- Hemichorea-ballism or generalized
- Pathogenesis : vascular insufficiency and/or metabolic failure.



CT : hyperdensity lesion at right putamen

MRI : hyperSI lesion at right putamen

Movement Disorders Vol. 21, No. 11, 2006 pp. 2023-2025.

Dystonia

Definition of Dystonia "Sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures"

Classifications of dystonia

- Axis.1 Clinical characteristics
  - Characteristics
    - Age at onset
    - Body distribution
    - Temporal pattern
  - Assoc. features
- Axis.2 Etiology
  - Nervous system pathology
  - Inherited or acquired
    - Idiopathic
    - Inherited
    - Acquired

Albanese A, et al. Mov Disord 2013; 28: 863-73.

Dystonia

Primary

Young (generalized)
DYT 1
Adult (focal)
DYT 6,7,13

Dystonia-plus

Dopa-responsive dystonia **(DYT5)**
Myoclonus-dystonia **(DYT11)**
Rapid-onset dystonia-parkinsonism **(DYT12)**
Early-onset dystonia with parkinsonism **(DYT16)**

Hereditary

AD : HD, SCA3, DRPLA, NFT, Fahr
AR : Wilson, NBIA, FRDA/AT, neuroacanthocytosis
X-linked : Lubag(DYT3), Mohr-Tranejaerg syndrome
Mitochondrial : Leigh disease

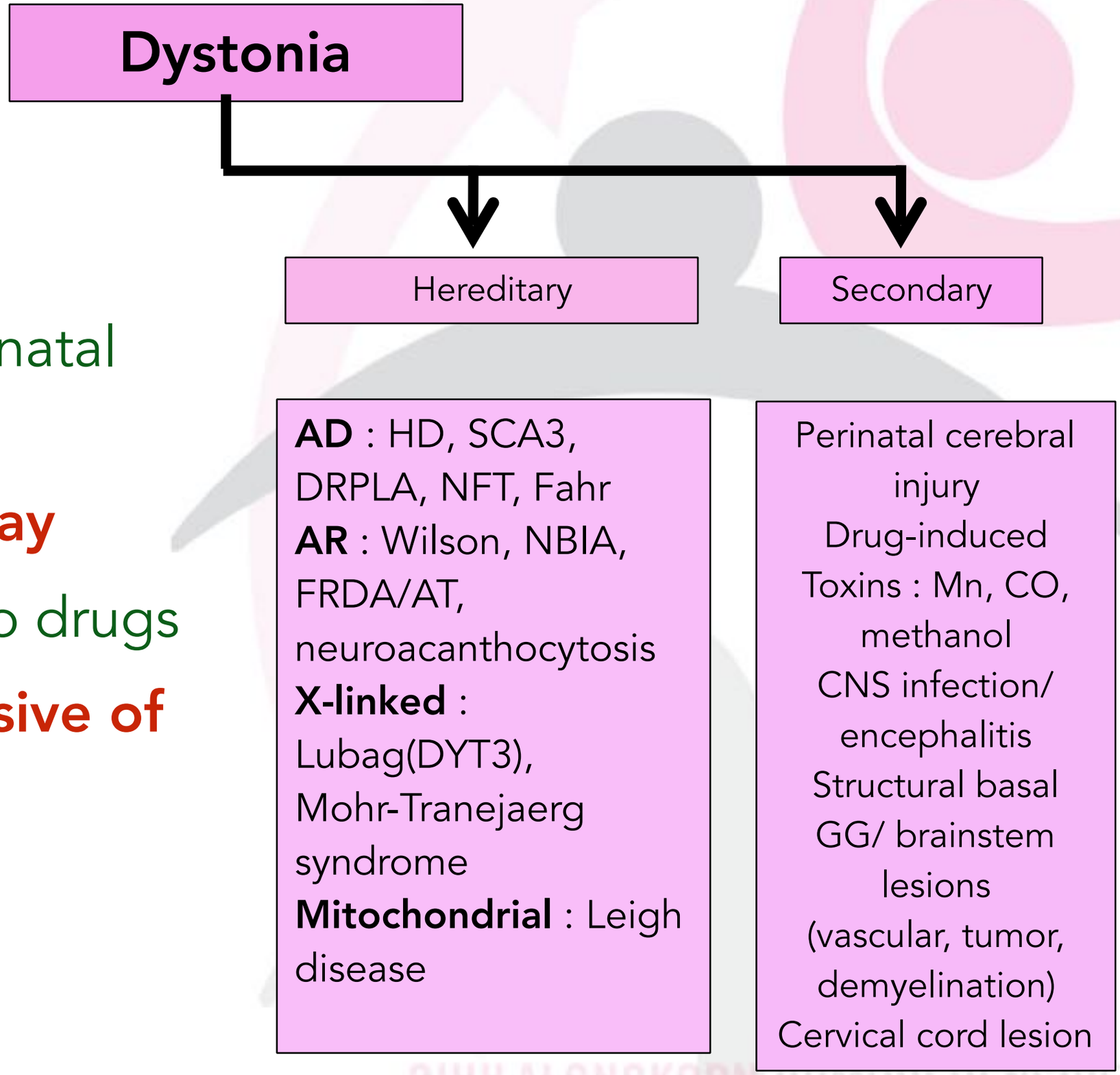
Secondary

Perinatal cerebral injury
Drug-induced
Toxins : Mn, CO, methanol
CNS infection/ encephalitis
Structural basal GG/ brainstem lesions (vascular, tumor, demyelination)
Cervical cord lesion

Fahn, 1995; Edward, 2008

Red flags

- Abnormal birth/perinatal history
- **Developmental delay**
- Previous exposure to drugs
- **Continued progressive of symptoms**
- Bulbar involvement
- **Dystonia at rest**
- Hemidystonia



Fahn, 1995; Edward, 2008

Wilson's disease

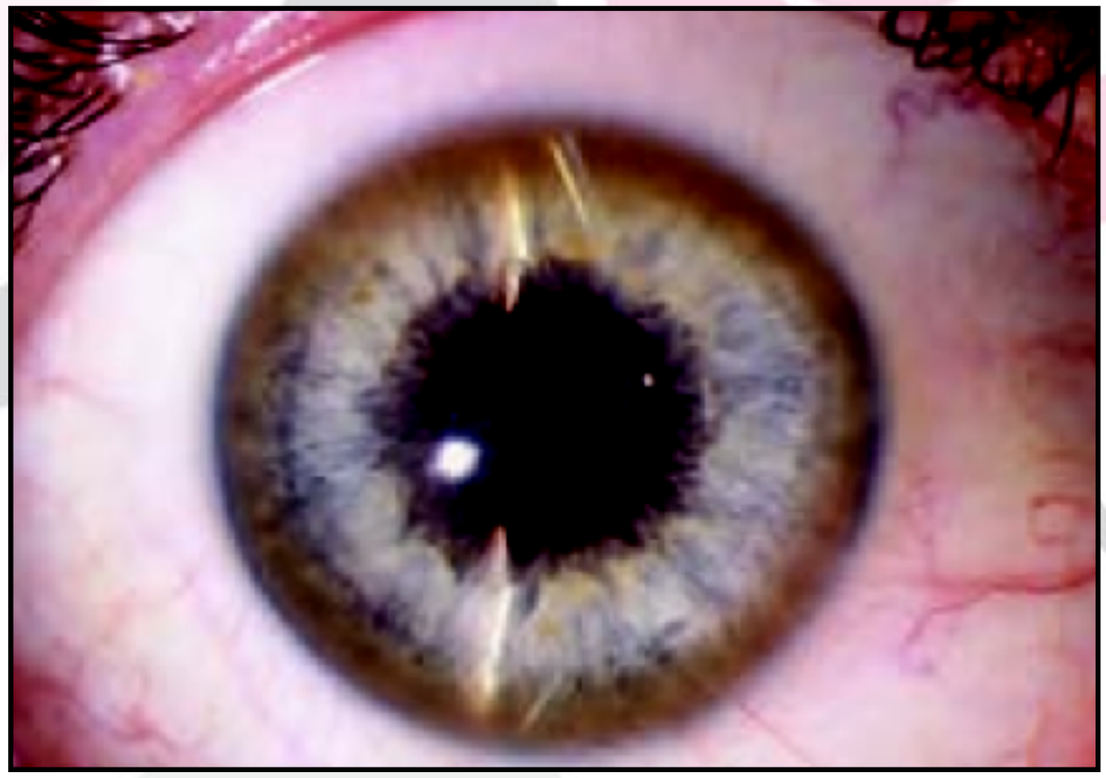
- Autosomal recessive disease, mutation of the ATP7B gene (encoding a copper transporter : bind copper to ceruloplasmin and secret into bile)
- Excessive copper accumulation in organs
  - liver : liver cirrhosis, fulminant hepatits
  - brain : mixed movement disorder (dystonia, tremor-wing beating, parkinsonism, chorea, ataxia, neuropsychiatric symptom, dysarthria)
  - eyes : **KF ring**, sunflower cataract
  - other organ : RTA, calculi, intravascular hemolysis

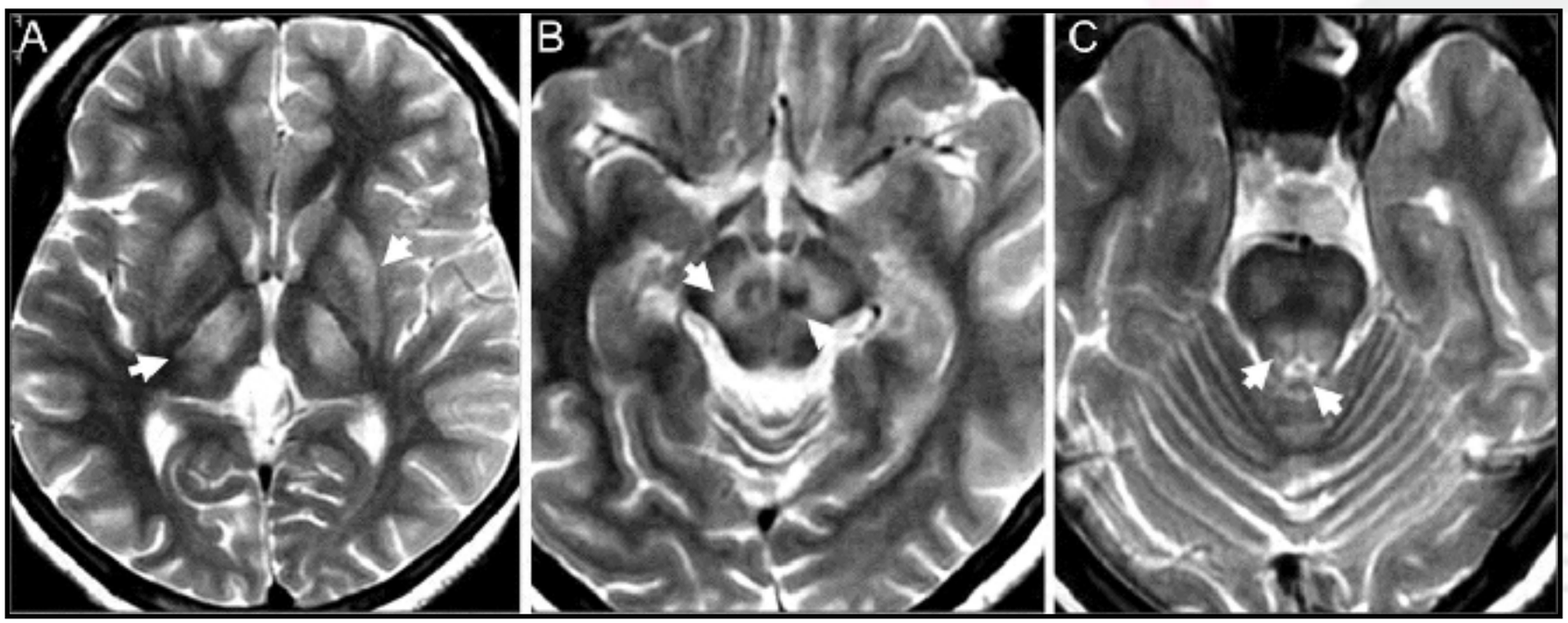
Fahn S,et al. Principles and Practice of Movement Disorders.

Wilson's disease

(hepatolenticular degeneration)

- ATP7B mutation
- Low serum cereloplasmin and serum copper
- MRI : Hyperintensity in lentiform nuclei and mesencephalic regions, face of giant panda and her cub.





Shivakumar et al. Neurology 2009.

Acute Dystonic Reaction

- Acute dystonic reaction is most commonly seen after exposure to dopamine receptor blockers, both neuroleptics and antiemetics.
- Dystonia begins within 24 hours of exposure, and 90% of reactions occur within 5 days.
- Clinical manifestations are diverse, usually affecting the head and neck. Laryngeal dystonia, blepharospasm, cervical dystonia, oculogyric crisis, and focal limb dystonia have all been reported.

Robottom R. Arch Neurol 2011: 68; 719-724.

Clinical manifestations	Descriptions
Oculogyric crisis	Spasm of the extraorbital muscles, causing upwards and outwards deviation of the eyes Blephorospasm
Torticollis	Head held turned to one side
Opisthotonus	Painful forced extension of the neck. When severe the back is involved and the patient arches off the bed.
Macroglossia	The tongue does not swell, but it protrudes and feels swollen
Buccolingual crisis	May be accompanied by trismus, risus sardonicus, dysarthria and grimacing
Laryngospasm	Uncommon but frightening
Spasticity	Trunk muscles and less commonly limbs can be affected

Keystep in treatment of ADR

- ABCD
- Treatment with an intravenous anticholinergic agent, such as benztropine mesylate (1-2 mg) or diphenhydramine (25-50 mg), is very effective.
- Because of the possibility of a reoccurrence, a short oral course of an anticholinergic (4-7 days) may be necessary.
- After an acute dystonic reaction, patients are at higher risk for future dystonic reactions when exposed to other dopamine receptor blockers.

Robottom R. Arch Neurol 2011: 68; 719-724.

Myoclonus

Classifications of myoclonus

- Anatomy/Physiology
  - Cortical
  - Cortical-subcortical
  - Subcortical-supraspinal
  - Spinal
  - Peripheral
- Etiology
  - Physiologic
  - Essential
  - Epileptic
  - Secondary

Drug
Metabolic

Hemifacial spasm

Caviness J. Lancet neurol 2004;3:598-607

Myoclonus classifications

Physiological Classification	Clinical Features	Electrophysiological findings	Etiology
Cortical	• Focal or multifocal myoclonus • Stimulus-sensitive (tactile, vision) • Rhythmic in case of EPC	• Brief EMG bursts (<75 ms) • Enlarged cortical SEP (common) • Timed locked cortical event (focal sharp wave 10-40 ms) preceding the jerks • May be presented C reflex at rest	• Post hypoxic action myoclonus (Lance-Adams syndrome) • Toxic-metabolic induced myoclonus • PME/PMA • Myoclonus in neurodegenerative disease
Cortical-subcortical	• Multifocal or bilaterally synchronized or generalized	• Brief EMG bursts (<100 ms) • Enlarged cortical SEP (possible) • Time-locked association • May be presented C reflex at rest	• Absence seizures • Primary generalized myoclonic epilepsy
Subcortical-supraspinal (brainstem)	• Generalized jerks with axial or proximal muscles involvement • Stimulus-sensitive (Auditory)	• Brief EMG bursts (10-30 ms) • Normal SEPs • No EEG correlates • Reflex response to sound (sometime)	• Essential myoclonus • Startle/Hyperekplexia • Reticular reflex myoclonus • Opsoclonus-myoclonus syndrome • Palatal myoclonus (tremor): essential and symptomatic
Spinal	• A specific dermatomal or segmental axial location (spinal segmental myoclonus) • Usually rhythmic and symmetrical • May be elicited by taps to the trunk and limbs	• EMG bursts > 100 ms, spreading rostrally or caudally from generator • Normal SEPs • Normal EEG	• Segmental spinal myoclonus • Propriospinal myoclonus
Peripheral	• Jerks in the distribution of peripheral nerve/lesion	• EMG with marked duration variability • Normal SEPs • Normal EEG	• Hemifacial spasm

SEP; Somatosensory evoked potential, EEG; electroencephalogram, EMG; electromyography
PME; progressive myoclonic epilepsy, PMA; progressive myoclonic ataxia
AD; Alzheimer's disease, CBD; Corticobasal degeneration, DLB; Dementia with Lewy bodies
CJD; Creutzfeldt-Jakob disease

Bhidayasiri R, Jitkritsadakul O. Movement Disorders curricular 2017

Negative myoclonus

- Negative myoclonus refers to an abrupt involuntary movement caused by sudden, brief interruptions of muscle activity.

- Negative myoclonus is classified into four types: asterixis, postural lapses, epileptic negative myoclonus, and physiologic negative myoclonus.

- Asterixis, which usually occurs in metabolic or toxic encephalopathies, is considered to be subcortical in origin but the cerebral cortex may be involved in some cases.

Bhidayasiri R. Negative Myoclonus. Movement Disorders: A Video Atlas 2012

Drug-induced myoclonus

- Psychotropic medication : TCAs, SSRIs, MAOI, Lithium, Buspirone
- Antibiotics : Penicillins, Cephalosporins, Quinolones, Imipenems, Acycxlovir, Isoniazid
- Narcotics : MO, fentanyl, Meperidine
- Anticonvulsants : Phenytoin, CBZ, Vigabatrin
- Contrast media

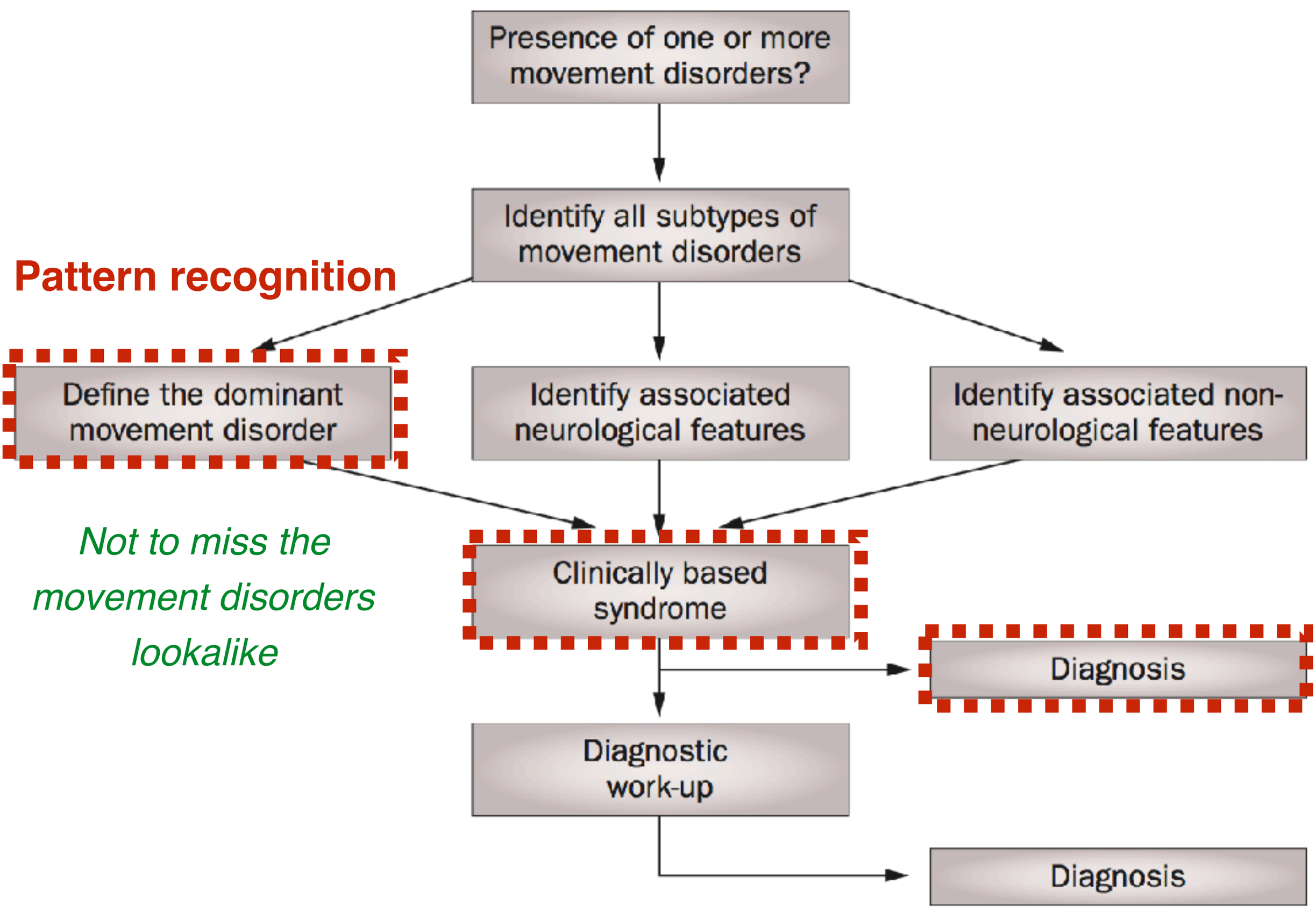
Post-hypoxic myoclonus

	Acute PHM	Chronic PHM
Onset	Within 24 hours	> 24 hours (> 3 days)
Distribution	Proximal, Axial, Distal Multifocal	Proximal, Axial, Distal Multifocal
Type of myoclonus	Cortical Subcortical (reticular reflex)	Cortical Subcortical (reticular reflex) Exaggerated startle Negative myoclonus (bouncing)
Association	Coma Periodic eye opening Swallowing movements Upward eye deviation	Mild cognitive impairment Cerebellar ataxia Gait disturbance, Seizure
Prognosis	Poor if status myoclonus	Good
Treatment	VPA, clonazepam, LVT	VPA, clonazepam, LVT, L-5-HTP

Gupta H and Caviness M. Tremor Other Hyperkinet Mov. 2016

Pattern recognition

Not to miss the movement disorders lookalike



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