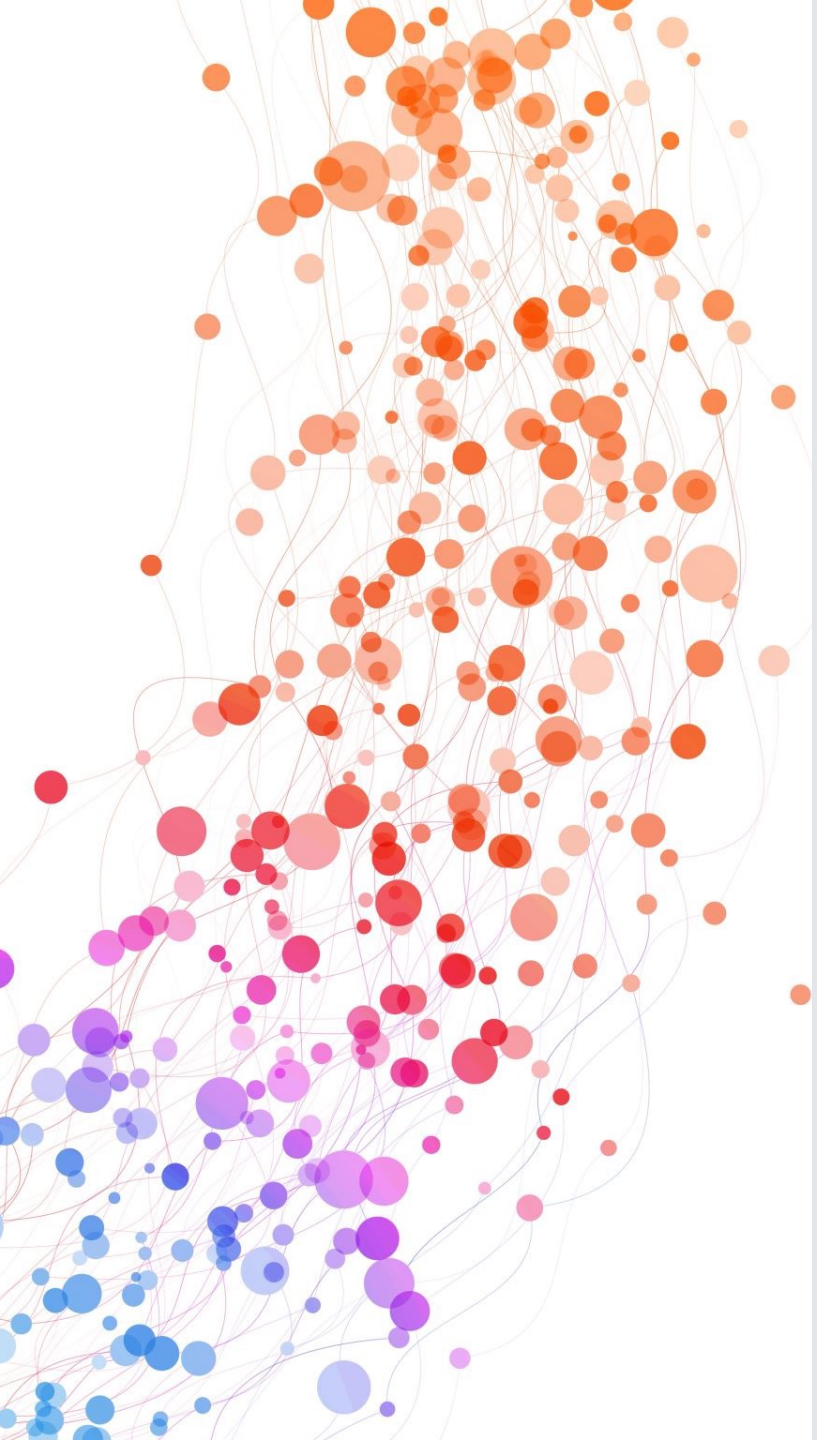

Parkinson Disease & Hyperkinetic Movement Disorders

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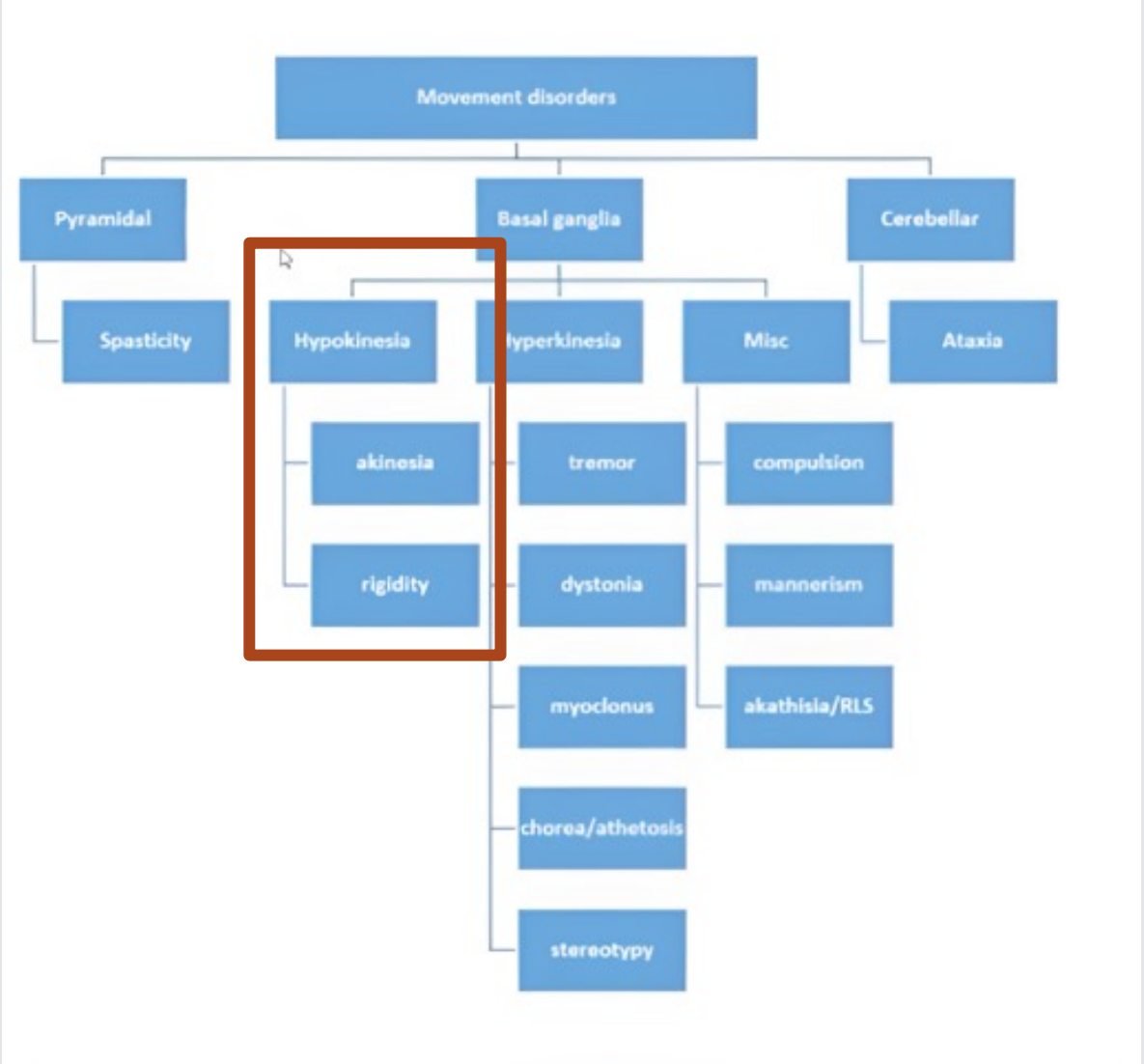
King Saud University

Outline:

1. Review etiologies for Parkinsonism
2. Review motor and non-motor manifestations of PD
3. Discuss treatment options for management of PD
4. Review features of Atypical Parkinsonian Syndromes
5. Overview of hyperkinetic movement disorders

Movement Disorders Classifications



Courtesy of Prof. J. Jankovich

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PARKINSONISM DOES NOT MEAN PARKINSON'S DISEASE

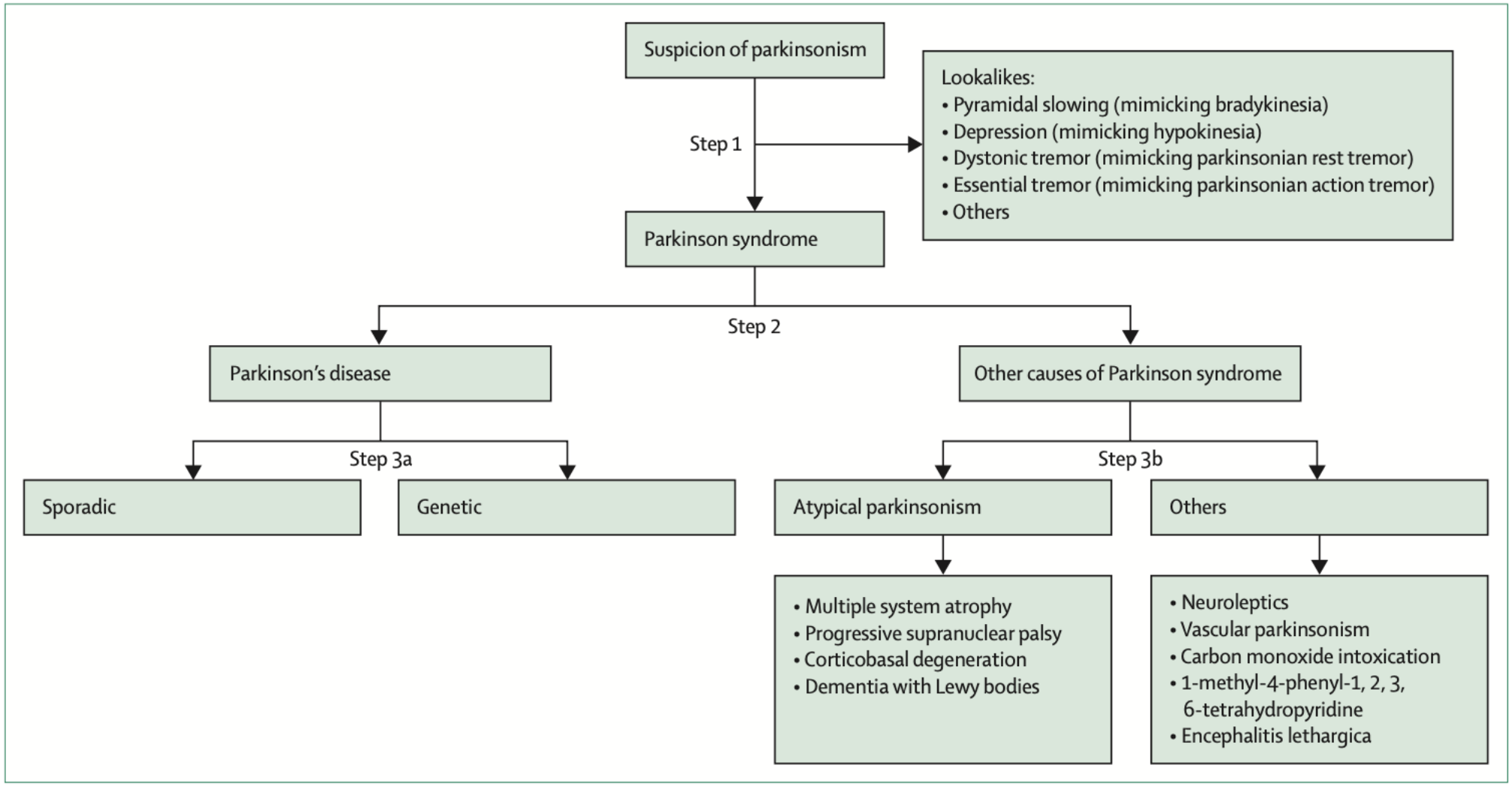
Parkinsonism

Parkinsonism is a **clinical motor syndrome, characterized by the presence of:**

- Tremor
- Rigidity
- Akinesia
- Postural instability

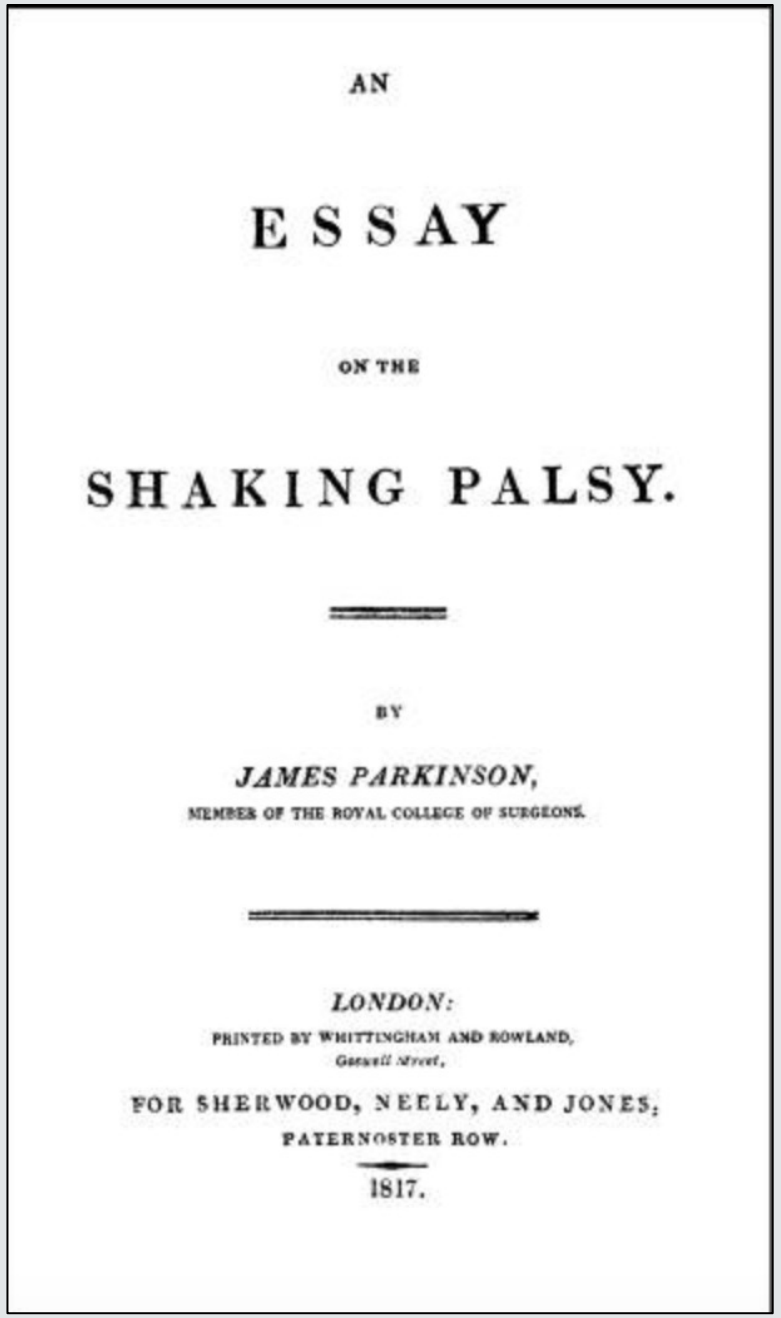
Differential Diagnosis of Parkinsonism

1. **Idiopathic Parkinson Disease**
2. **Atypical Parkinsonism**
   - Multiple System Atrophy (MSA)
   - Progressive Supranuclear Palsy (PSP)
   - Cortical Basal Syndrome (CBD)
3. **Secondary Parkinsonism**
   - Drug induced, vascular, structural, infectious, immunologic, traumatic, metabolic
4. **Heterodegenerative Parkinsonism**
   - Aceruloplasminemia, spinocerebellar ataxia, X-linked dystonia-parkinsonism


Suspicion of parkinsonism
Step 1
Lookalikes:
• Pyramidal slowing (mimicking bradykinesia)
• Depression (mimicking hypokinesia)
• Dystonic tremor (mimicking parkinsonian rest tremor)
• Essential tremor (mimicking parkinsonian action tremor)
• Others
Parkinson syndrome
Step 2
Parkinson's disease
Other causes of Parkinson syndrome
Step 3a
Step 3b
Sporadic
Genetic
Atypical parkinsonism
Others
• Multiple system atrophy
• Progressive supranuclear palsy
• Corticobasal degeneration
• Dementia with Lewy bodies
• Neuroleptics
• Vascular parkinsonism
• Carbon monoxide intoxication
• 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine
• Encephalitis lethargica

PARKINSON DISEASE

- Second most common neurodegenerative disease
- 1% of people over the age of 60
- First described in 1817 by James Parkinson
- A clinical diagnosis. No clinically available biomarkers to indicate presence or to track disease progression.



AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,

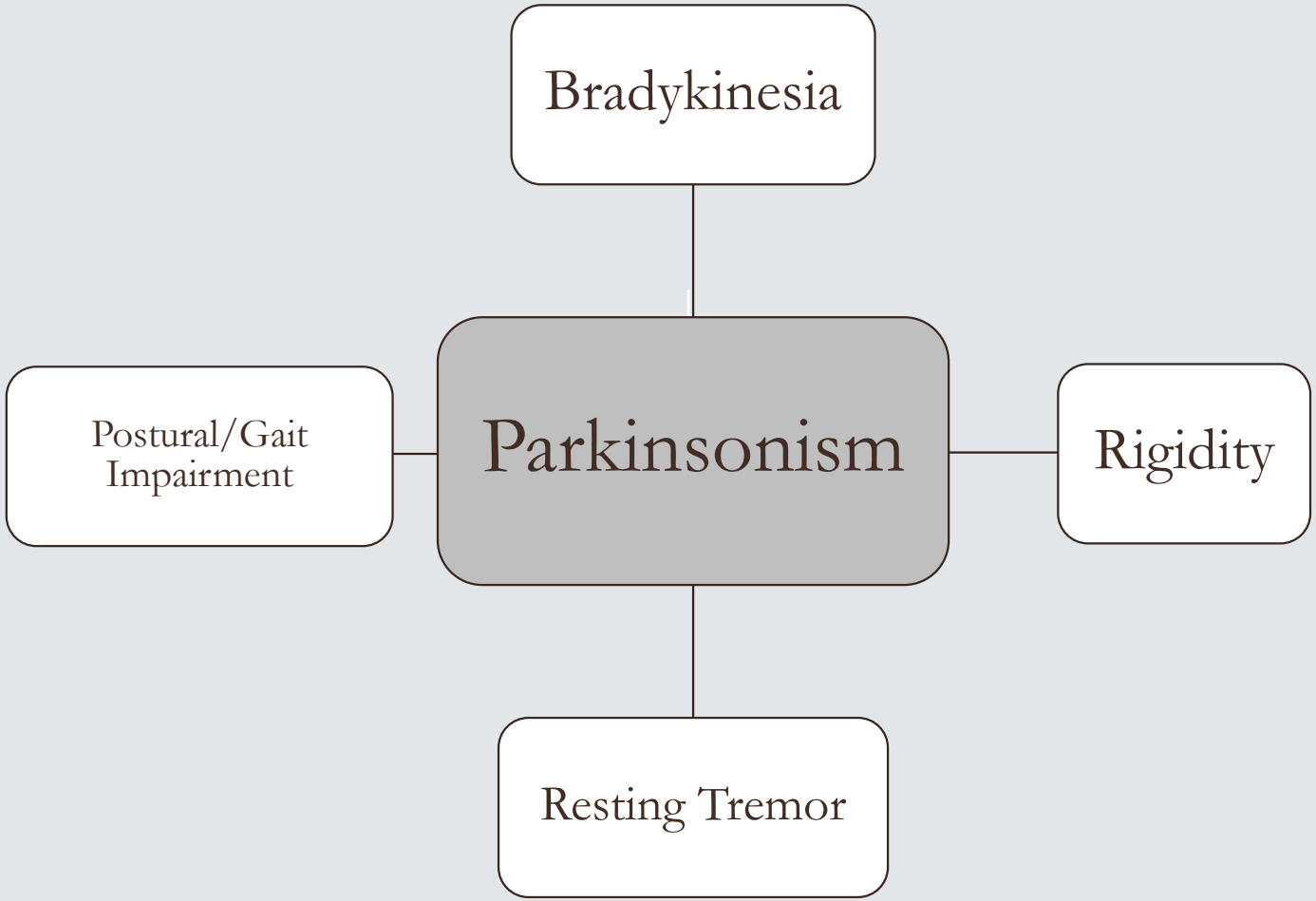
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,

PATERNOSTER ROW.

1817.

PD MOTOR SYMPTOMS



Tremor

- Resting tremor
- **4-6Hz** oscillations around the wrist and finger
  - ➢ *Pill-rolling*
  - ➢ *Pronation/supination at the wrist*
- Unilateral and distal
  - ➢ *Over time, becomes more proximal and over to the contralateral side*
- Intermittent, re-emergent, worse with distraction
- Not always levodopa responsive

Rigidity

- **Definition:** resistance of muscle to passive movement around a joint
  - *Use contralateral limb activation maneuvers*
  - *Watch out for paratonia*
- Cogwheeling and reduced arm swing
- Patient complaints:
  - *Stiffness*
  - *Shoulder pain*
  - *Difficulty turning over in bed*
- Early axial rigidity- think PSP

Bradykinesia/Akinesia

- **Bradykinesia:** slowness of movement
- **Decrement:** movements become progressively smaller
- **Hypomimia:** decreased facial expression
- **Hypophonia:** soft speech
- **Micrographia:** small handwriting

Postural instability

- Impairment in the ability to recover one's balance
  - *Very subtle early on*
  - *Uneven surfaces*
  - *Mild tripping*
- **Falls early** in the disease should trigger concern for **Atypical Parkinsonism (PSP, MSA) → NOT TYPICAL FOR PARKINSON'S DISEASE.**
- Pull test is used to test for Postural Instability

Other Motor Abnormalities

- Impaired finger dexterity
- Flexed/stooped posture
- Freezing phenomenon
- Gait initiation difficulties
- Dyskinesias: "Involuntary, erratic, writhing movements of the face, arms, legs or trunk"
- Motor fluctuations
- Swallowing difficulties (later)

PD NON-MOTOR SYMPTOMS

- Hyposmia (46%)
- Hypophonia
- Constipation (39%)
- Erectile Dysfunction (28%)
- Urinary Dysfunction (30%)
- REM Sleep Behaviour Disorder (28%)
- Insomnia (36%)
- Depression (43%)
- Anxiety (30%)
- Memory impairment (30%)
  - *MCI (15%)*
  - *Lewy body dementia*
- Fatigue (36%)
- Orthostatic hypotension (21%)

DDX FOR PARKINSON DISEASE

- Atypical Parkinsonism: MSA, PSP, CBD
- Dementia with Lewy Bodies (DLB)
- Dystonic Tremor
- Essential Tremor
- Frontotemporal Dementia (FTD)
- NPH
- Functional Movement Disorder

PD Treatment

Medications:

- *Levodopa Carbidopa (First line) (SE: Dyskinesias, hypotension, drowsiness etc)*
- *Dopamine agonists: Pramipexole, Ropinirole, Rotigotine (SE: Impulse control disorders and sleep attacks)*
- *COMT Inhibitors: Entacapone and Opicapone (SE: orange discoloration of urine, dyskinesias)*
- *MAO-B Inhibitors: Selegiline and Rasagaline (SE: Insomnia and risk of serotonin syndrome)*
- *Amantadine: (SE: leg edema, livedo reticularis, and confusion in elderly)*

Procedural treatments:

- *Deep Brain Stimulation (DBS):* Subthalamic nucleus or Globus Pallidus Interna
- Levodopa/carbidopa intestinal gel (LCIG) = (Duodopa®)

THINK ATYPICAL IF:

- *Early Falls*
- *Autonomic Failure*
- *Absence of Tremor*
- *Poor Levodopa Response*
- *Rapid Progression*

PROGRESSIVE SUPRANUCLEAR PALSY

- The most common form of atypical Parkinsonism → 5% - 6%.
- Age of onset → sixties (63-66 Years).

Hallmarks of the disease:

- **Gait:**
  - *Stiff, broad based, with knees extended and arms abducted → "drunken sailor" or "dancing bear,"*
  - *lateral deviations and step asymmetry, When turning, tend to pivot.*
  - *Prominent, early postural instability.*
  - *Axial rigidity and unexplained falls → First 2 years*

PROGRESSIVE SUPRANUCLEAR PALSY

- **Eyes signs:**
  - ➢ *Vertical* ***and lateral supranuclear palsy.***
  - ➢ *Slowed saccades and reduced OKN (V>H).*
  - ➢ *Square-wave jerks*
- **Progressive dementia and personality changes.**
- **Bulbar features: dysarthria, dysphagia, etc**
- **Mona Lisa stare or stone face:**

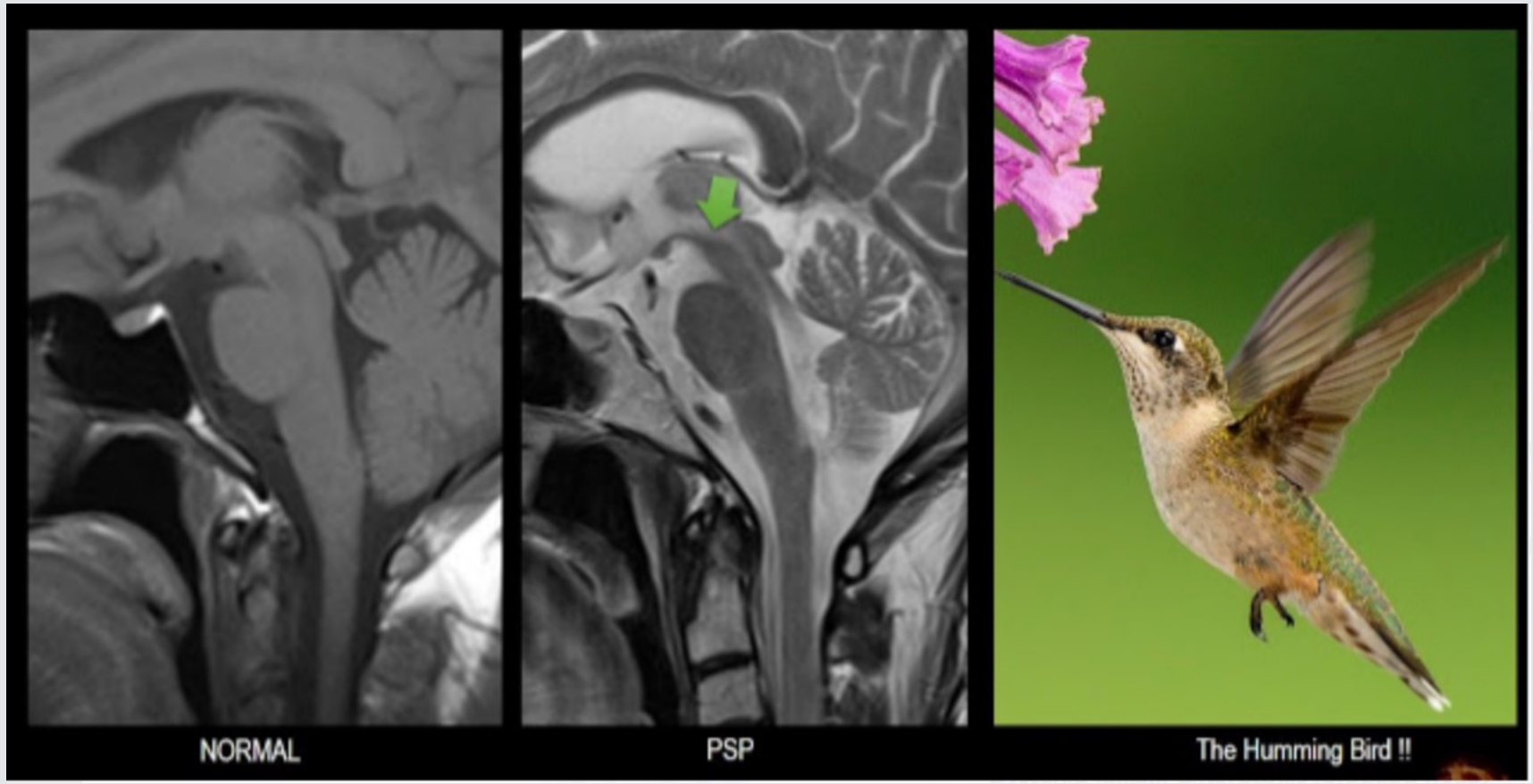
PSP Vs. IPD

Table 1 : Comparison between idiopathic Parkinson disease and PSP[1,2]

Features	Idiopathic Parkinsonism	Progressive Supranuclear Palsy
Rigidity	Present	Present
Bradykinesia	Present	Present
Tremors	Universal	Rare
Asymmetric findings	Common	Rare
Ocular problems	Uncontrolled blinking Excessive watering of eyes Diplopia	Vertical gaze palsy (Supranuclear) Eyelid apraxia, Blepharospasm (Lid freezing)
Posture	Tend to fall forwards as if chasing centre of gravity	Tend to fall backwards due to head tilt backwards.
Pseudobulbar features	Absent	Common
Cognitive deficits	Common in advanced disease.	Noted in virtually all patients
Dysautonomia	Infrequent	Infrequent
Pathology	α- Synucleinopathy	Tauopathy
MRI brain	Not required with typical presentations. Useful to rule out other disorders like normal pressure hydrocephalus, mass lesions and vascular disease	Midbrain atrophy
Response to dopaminergic agents	Good	Poor

HUMMINGBIRD SIGN

- Disproportionate atrophy of the midbrain and superior cerebellar peduncle



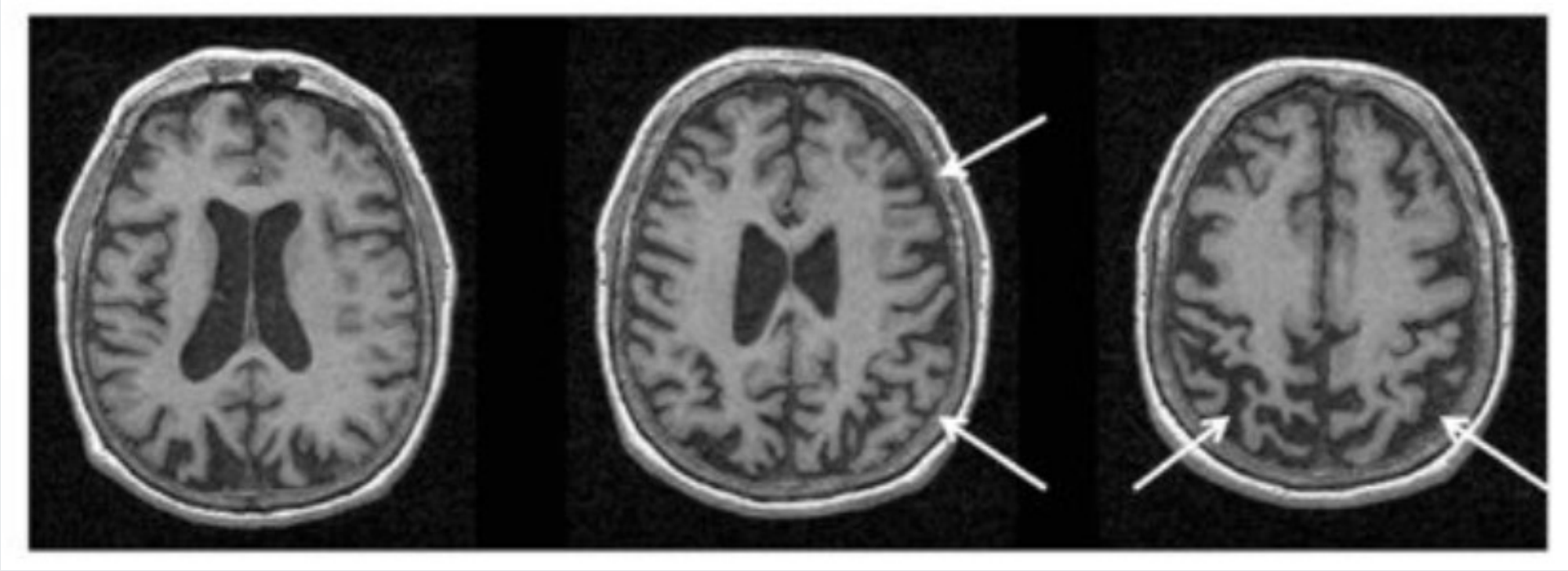
PSP

- *Early falls*
- *Gaze Palsy*
- *Bulbar Dysfunction*

CORTICOBASAL DEGENERATION/SYNDROME

- Predominant involvement of cortex and basal ganglia
- Average onset 60s, average survival of 7 years
- **Clinical features:**
  - **Apraxia/Cortical sensory loss**
  - *Marked limb asymmetry/Alien limb phenomenon*
  - *Limb dystonia/Myoclonus*
  - *Early dementia*
  - *Bulbar symptoms*

IMAGING



CBS

- *Alien Limb*
- *Apraxia*
- *Significant Asymmetry*

MULTIPLE SYSTEM ATROPHY

- Two variants- **MSA-P (Parkinsonism)** and **MSA-C (Cerebellar)**
- Onset late 50s, survival 6-9 years
- Symmetric bradykinesia, tremor, rigidity
- Pyramidal tract/cerebellar signs
- **Early dysautonomia**
  - Urinary/erectile dysfunction
  - Orthostatic hypotension
  - Constipation
- Severe spastic dysarthria, dysphonia, or strider
- Respiratory dysfunction
- Pisa syndrome

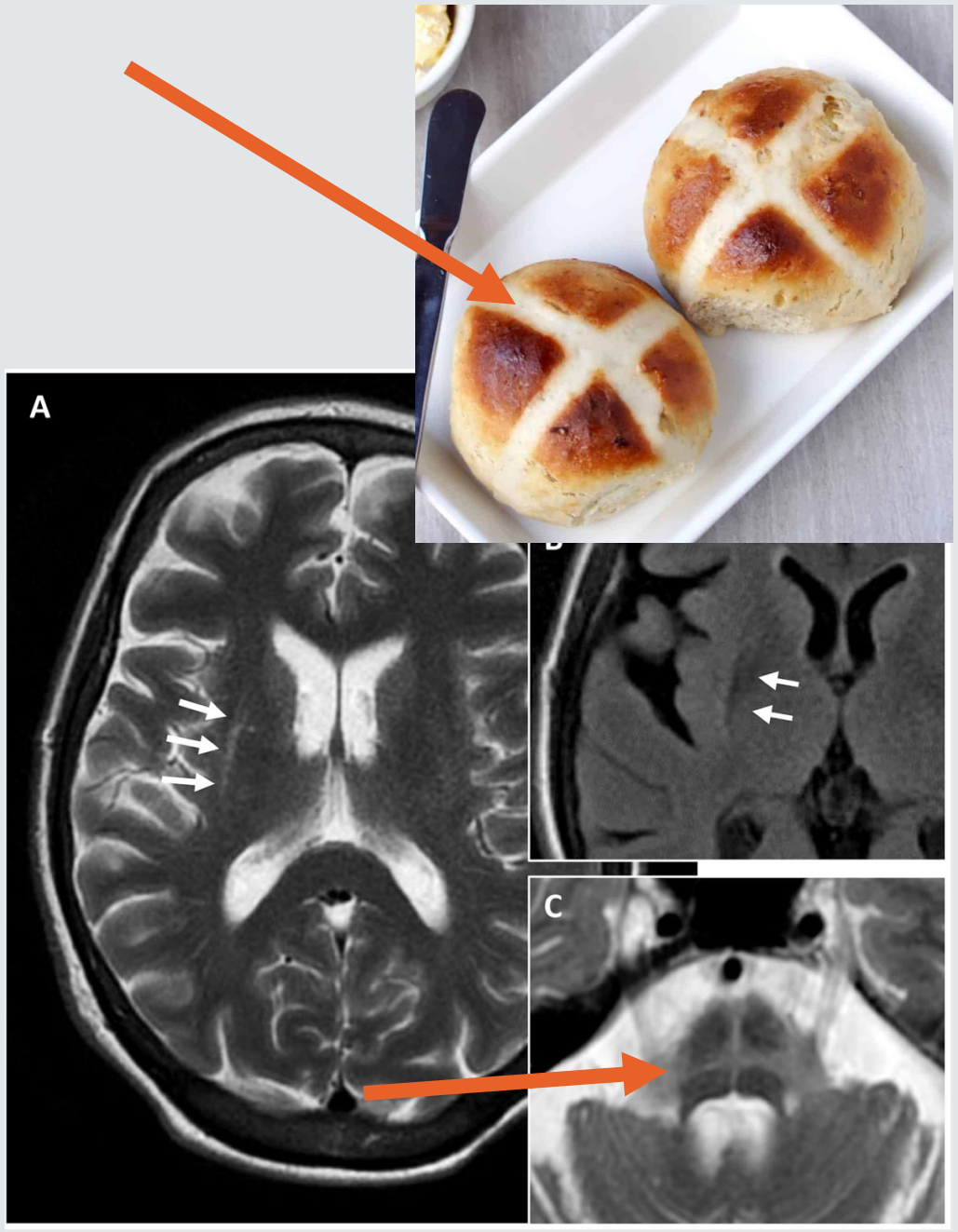
TABLE 5-7 Multiple System Atrophy Phenotypes

Clinical Presentation	Features[a]
Multiple system atrophy–parkinsonian type (MSA-P) (previously referred to as Shy-Drager syndrome or striatonigral degeneration)	Onset >40 years, duration <10 years, progressive parkinsonism poorly responsive to levodopa, with autonomic failure (induding orthostatic hypotension, impotence, bladder dysfunction)
Multiple system atrophy–cerebellar type (MSA-C) (previously referred to as olivopontocerebellar atrophy)	Ataxia; degeneration of ventral pons, olives, cerebellum; mild parkinsonism and cognitive decline

[a] Autonomic dysfunction, respiratory symptoms, and sleep disturbance can precede motor signs by months to years.

IMAGING

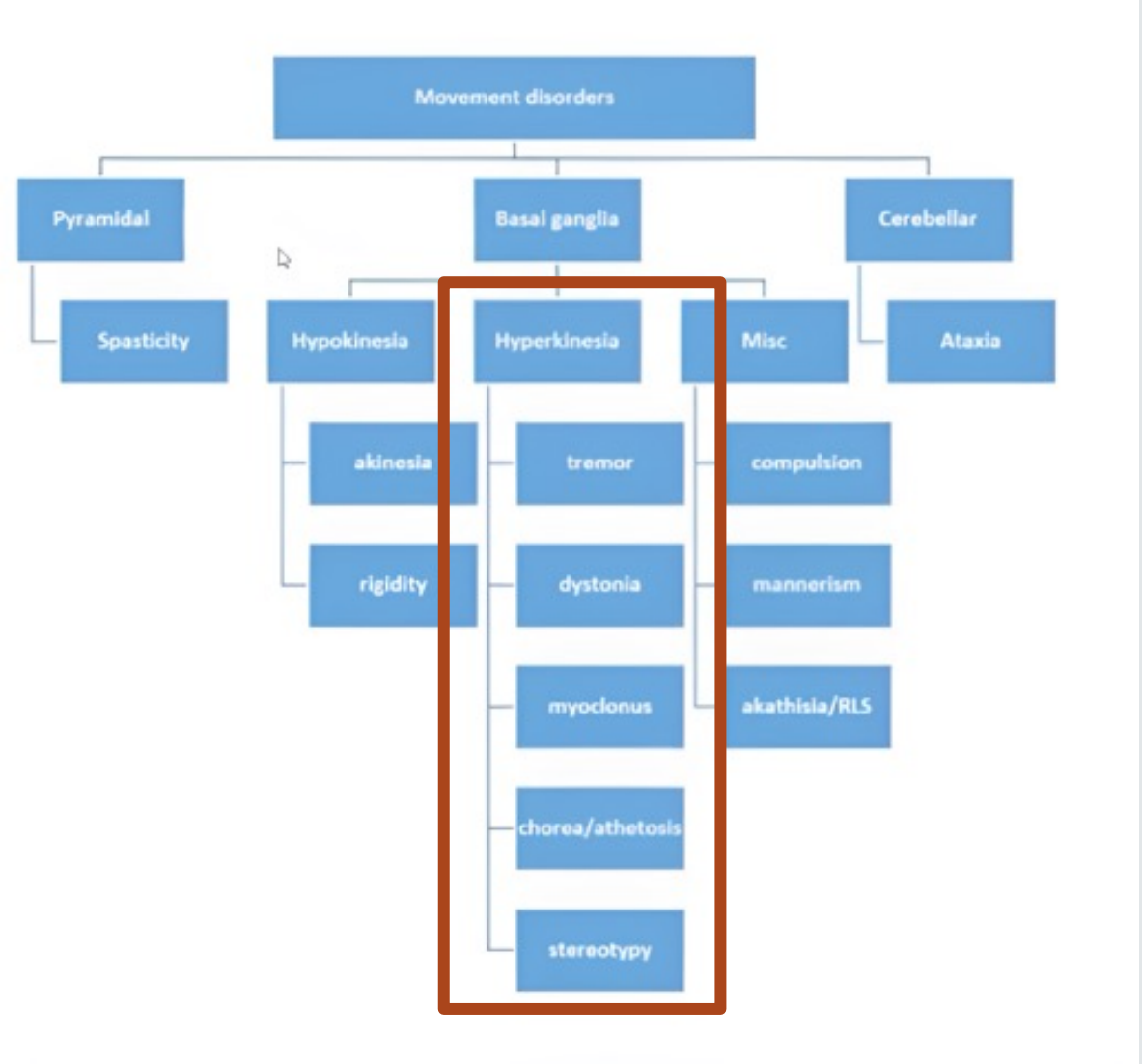
- "Hot Cross Bun Sign":
  - ➢ *Disproportionate atrophy and gliosis of the pons*
- Slit like hyperintensity of the putamen



MSA

- *Dysarthria*
- *Atypical Tremor*
- *Dysautonomia*

Movement Disorders Classifications



Courtesy of Prof. J. Jankovich

Tremor

- An involuntary, **rhythmic oscillatory movement** of a of body part(s).
- Classified based on activation:
- **Rest tremor**
- **Action tremor:**
  - *Postural tremor - on maintained posture-position specific*
  - *Kinetic tremor*

Tremor

- **Rest Tremor**
  - Parkinson disease
  - Drug-induced parkinsonism
  - Vascular parkinsonism
  - Multiple system atrophy and other degenerative causes of parkinsonism (eg, spinocerebellar ataxia types 2 and 3)—rare
- **Postural Tremor**
  - Enhanced physiologic tremor
  - Essential tremor
  - Dystonic tremor
  - Toxins (eg, mercury)
  - Drugs (of abuse, coffee, many medications—see **Table 2-2**)
  - Metabolic disturbance (eg, hyperthyroidism)
  - Neuropathy
  - Parkinson disease
  - Fragile X premutation (fragile X tremor-ataxia syndrome)
- **Kinetic Tremor**
  - Cerebellar disease (eg, demyelination, degenerative or secondary to toxins, stroke)
  - Holmes tremor
  - Wilson disease
  - Psychogenic (functional) tremor (commonly also present on rest and posture)

Dystonia

- 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**.
- **Sensory trick (Gestes Antagoniste):** Common action that improve dystonia.

Dystonia

Inherited or acquired	Inherited (dystonia forms of proven genetic origin):
	Autosomal dominant
	Autosomal recessive
	X-linked recessive
	Mitochondrial
	Acquired (dystonia due to a known specific cause):
	Cerebrovascular (infarction or hemorrhage)
	Perinatal brain injury
	Traumatic brain injury
	Infection
	Drug
	Toxic
	Neoplastic
	Psychogenic
Idiopathic (unknown cause)	Sporadic
	Familial

Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: a consensus update. Mov Disord 2013; 28:863.

UpToDate®

Chorea

- Is a hyperkinetic movement disorder, characterized by involuntary continuous, **abrupt, rapid, brief, unsustained, jerky, irregular movements** that flow randomly from one body part to another.
- **Associated Features:**
  - *Parakinesia (semipurposeful camouflage)*
  - *Motor persistence ("darting tongue", "milkmaid's grip")*
  - *Pendular reflexes*
  - *Irregular ("dance-like") gait*

Chorea

- **Causes:**

  • **Genetic:** Huntington's Disease and others

  • **Drugs:** Anti emetics, Anti epileptics etc.

  • **Autoimmune:** Sydenham's Chorea, APLAS, SLE, Behcet etc

  • **Infections:** Encephalitis, HIV, TB etc

  • **Vascular**: Polycythemia vera, ischemic stroke etc.

  • **Endocrine:** Hypo/hyperglycemia, hyperthyroidism etc.

Myoclonus

- A **quick, involuntary muscle jerk**, can be either irregular or rhythmic.
- **Can be either:**
  - *Spontaneous*
  - *Action myoclonus: activated or accentuated by **voluntary movement***
  - *Reflex myoclonus: activated or accentuated by **sensory stimulation***

Myoclonus

- **Causes:**
  - *Genetic: eg. Progressive Myoclonic Epilepsies*
  - *Hypoxic*
  - *Autoimmune*
  - *Infections: Measles*
  - *Metabolic: Liver failure (Asterixis), uremic encephalopathy*
  - *Drug induced*

Tics

- Sudden, brief, intermittent, repetitive, non-rhythmic, **involuntary or semi-voluntary movements or muscle contractions** (motor tics) or sounds (phonic tics) which abruptly interrupt otherwise normal motor activity or speech.
- Can be preceded by a **premonitory urge:**
- Regional or generalized sensory or mental phenomena or an urge that precede tics and are temporarily reduced by performance of tics

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WHAT
WHERE
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