

TREMORS

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Contents

Definition
Pathophysiology

Classification & Types
Diagnostic work-up

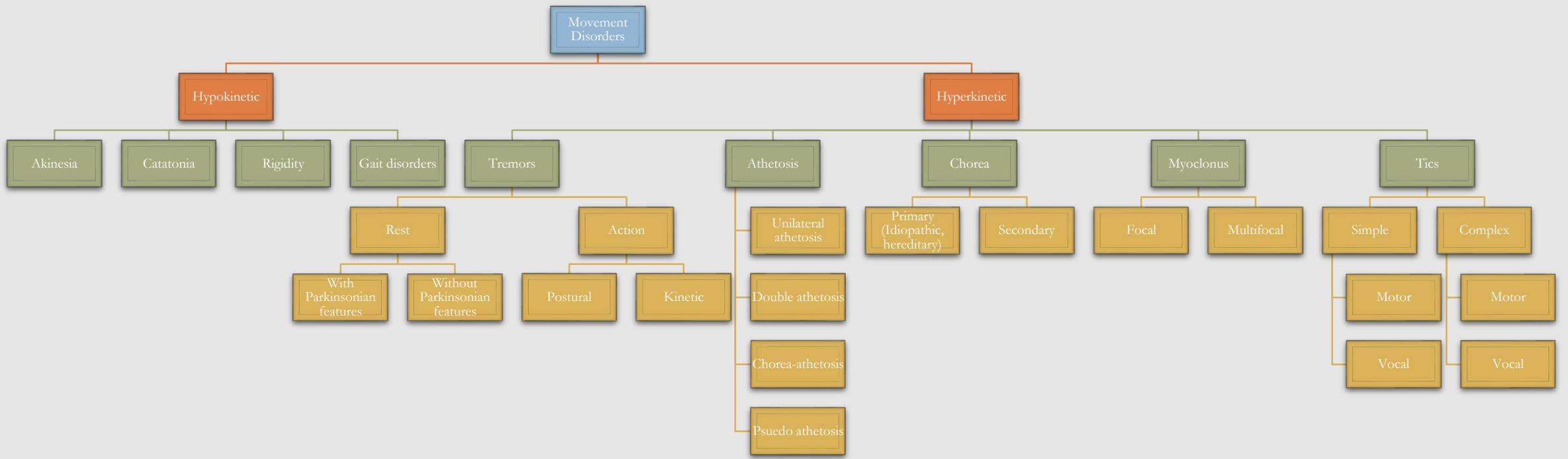
Treatment protocols

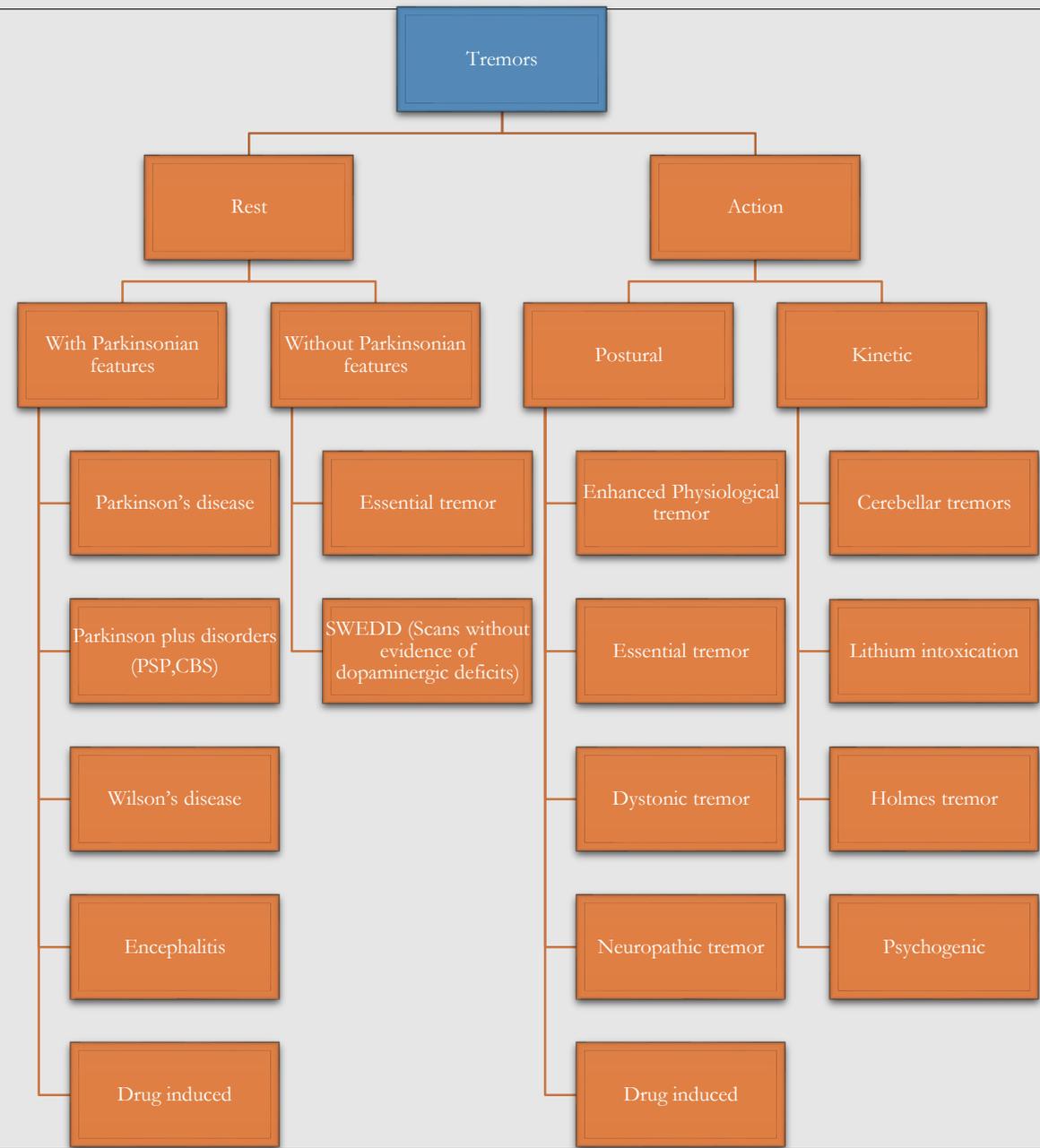
What is a tremor?

- Tremor is a **rhythmic**, **involuntary** and **oscillatory** movements around a joint.
- Though present physiologically, an exaggerated response is usually associated with a pathology.
- James Parkinson, identified the tremor as "involuntary tremulous motion in parts not in action," in his essay on the shaking palsy, in 1817

Physiology of tremor - Theories

- **Central oscillation** - firing is followed by a prolonged action potential and a subsequent prolonged hyperpolarization, which is terminated by a rebound spike leading to the next spike. Present in cells of inferior olive.
- **Mechanical tremor theory** – activation of a muscle fiber at the rate of resonance frequency of that body part [fingers – 25Hz, Hand – 6-8Hz, Elbow – 3-4Hz]
- **Reflex of CNS** – Any movement in one direction will cause an afferent volley exciting a reflex in antagonistic muscle.
- **Malfunction of feedforward loop** – Present in cerebellum. Agonist – antagonist – agonist activation.





Resting tremor – Parkinson disease

- Most common cause of resting tremor.
- Classically called ‘pill rolling tremor’ involving thumbs and forefingers.
- Typical tremor has a frequency of 4-6Hz.
- Males>Females. Mean onset 55-70yrs.
- Starts unilaterally in upper distal extremity and can progress bilaterally.
- There are three tremor syndromes associated with PD:
 - Classical resting tremor or one associated with postural/kinetic tremor of same frequency.
 - Rest plus postural/kinetic tremor with different frequency with latter being higher.
 - Isolated postural and kinetic tremor with 5-9Hz

Resting tremor – Other causes

- Monosymptomatic resting tremor.
- Scans without the evidence of dopaminergic deficit (SWEDD).
- Amplitude can be used to differentiate the cause.
- PD plus syndromes – MSA, PSP, CBD
- Drugs:
 - Affecting dopaminergic pathway – Antipsychotics, Metoclopramide, Prochlorperazine.
 - Non-dopaminergic drugs – Valproate, CCBs, Lithium

Enhanced physiological tremor

- Due to increased sympathetic activity by diseases or drugs.
- Most commonly a postural tremor of fingers or hands.
- Low amplitude and high frequency (7-12Hz)
- H/O pertaining to situations like stress, excessive caffeine intake, anxiety and medication use.
- No further investigation. Removal of offending agent.

Drugs and Toxins

- Beta agonists
- Antipsychotics
- Lithium
- Corticosteroids
- Acute alcohol withdrawal
- Amphetamines

Diseases

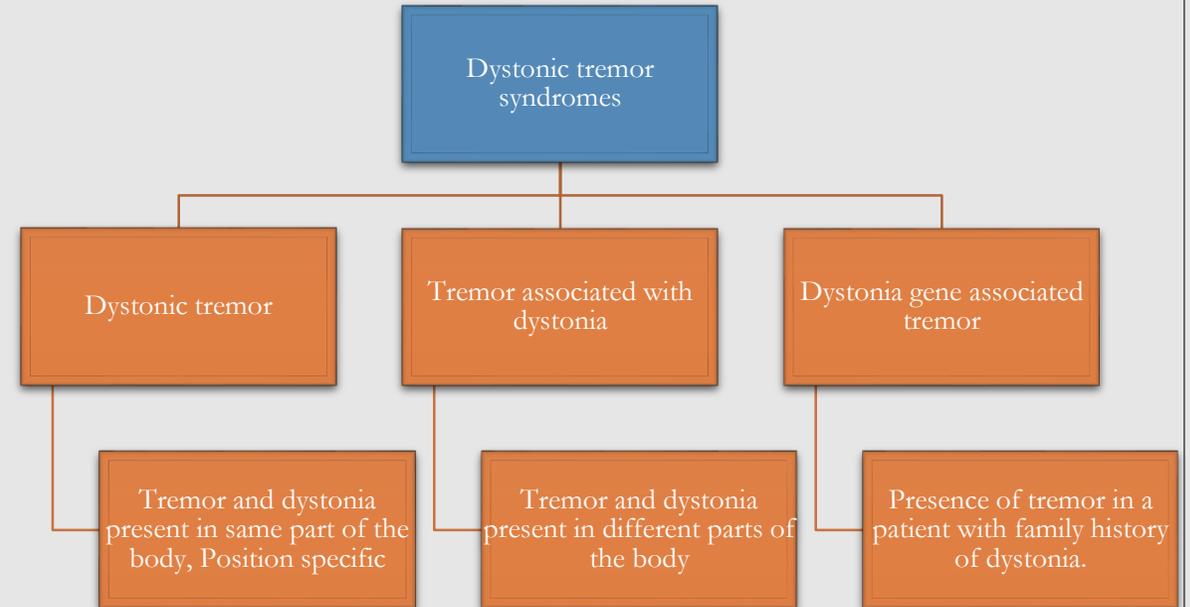
- Hyperthyroidism
- Pheochromocytoma
- Hypoglycemia
- Electrolyte abnormalities (Na, Ca, Mg²⁺)
- Hepatic encephalopathy

Essential tremor

- Bilateral, largely symmetric postural or kinetic tremor involving hands and forearms that is visible and persistent.
- Additional association with head (yes-yes or no-no).
- Duration > 5years, with normal neurological examination.
- Lately it has been associated with
 - Motor components: Gait ataxia, eye abnormalities, postural instability.
 - Non motor components: cognitive, sensory (olfactory and hearing loss) and psychiatric (anxiety, depression)
- Bimodal distribution (15-20 yrs / 55-70yrs) with equal incidence in both genders.
- Hereditary ET- LINGO1 gene.
- Response to alcohol in 50% of cases. No response to levodopa.

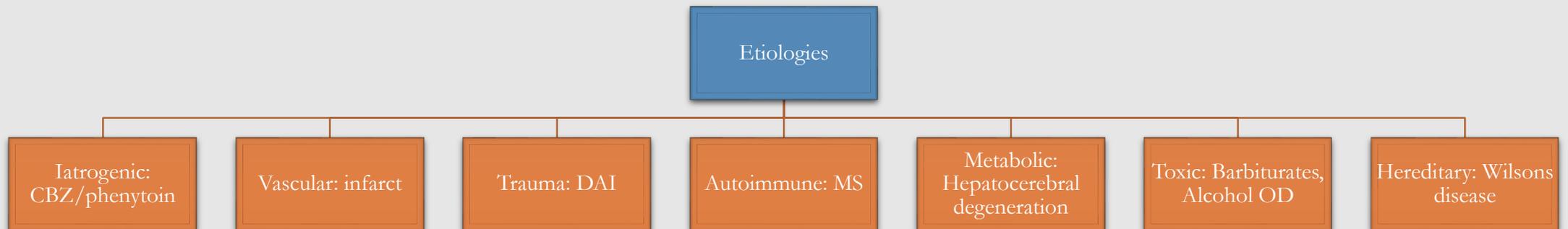
Dystonic tremor

- Coexistence of dystonia and tremors in a same patient.
- Occurs at any age with female preponderance.
- Asymmetrical . Frequency around 1-6Hz.
- DD:
 - ET: DT is jerky and pronounced. Head tremor raised upon head turn and persistent when lying down.
Null point phenomenon is seen in DT.
 - PD: DT is position/task specific. Absence of PD features.
 - Voice ET: DT has ‘geste maneuvers’



Cerebellar tremor/Intention tremor

- First described by Jean- Martin Charcot in 1868.
- Loss of feedback inhibition due to cerebellar injury leads to kinetic errors, mostly in fine motor skills.
- 50% in arms, 27% legs. Strong correlation with ET (38.5%).
- Difficulties with drinking from a cup, grabbing utensils to eat, problems with coordination eye to an object.
- Associated cerebellar signs may include nystagmus, dysmetria, dysdiadochokinesia, hypotonia, proprioception deficits, and gait ataxia.



Psychogenic tremor

- Tremor is the most common psychogenic movement disorder (50%)
- Can be rest, postural or kinetic but mostly unison is seen.
- Diagnostic criteria:
 - Abrupt onset
 - Changing characteristics
 - H/O psychiatric illness
 - No underlying organic cause
- Suggestibility, Entrainment, Coherence, Coactivation sign, Abnormal gait are present
- EMG showing all three entrainment, coherence and coactivation helps confirm the diagnosis

Neuropathic tremor

- Tremor due to peripheral demyelination of nerve
- 58% of CIDP develop neuropathic tremor
- 3-6Hz frequency with low amplitude
- No clear pathogenesis
- No causality has been established between amount of demyelination and tremors
- IVIg-refractory CIDP patients have Anti-Neurofascin-155. Oral prednisolone, plasmapheresis, and rituximab are effective.
- Good response to IVIG (CIDP patients) and Deep brain stimulation.

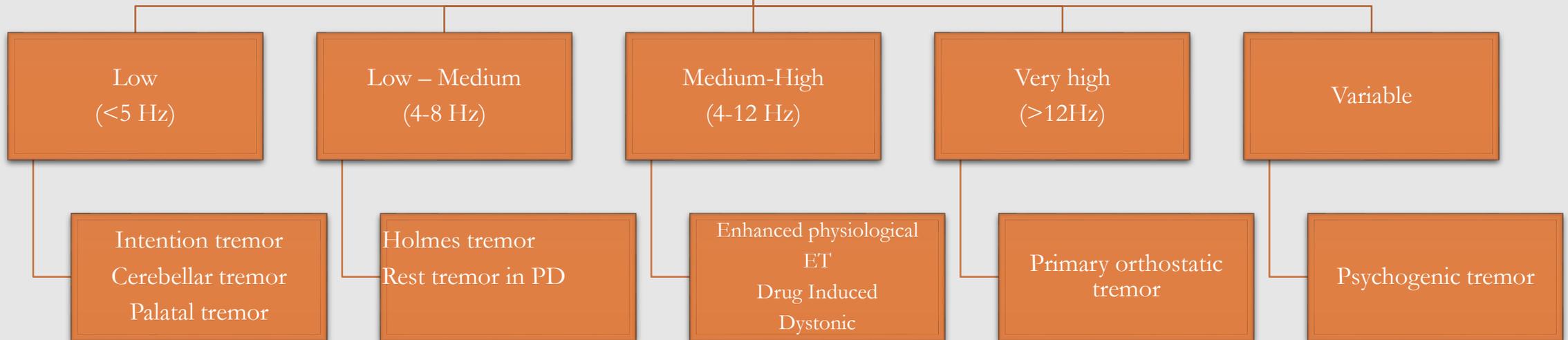
Holmes tremor (rubal tremor)

- Symptomatic, irregular tremor of low frequency (2-5Hz) with high amplitude in proximal muscles.
- Present at rest, worsened by movement.
- Dual lesion in the dopaminergic nigrostriatal system, cerebello-thalamo-cortical or dentate-rubro-olivary pathways is suspected.
- DD:
 - PD – resting tremor 4-6Hz pill rolling type in distal muscles
 - Thalamic tremor - present with dystonia
 - Myorhythmia – involves cranial muscles

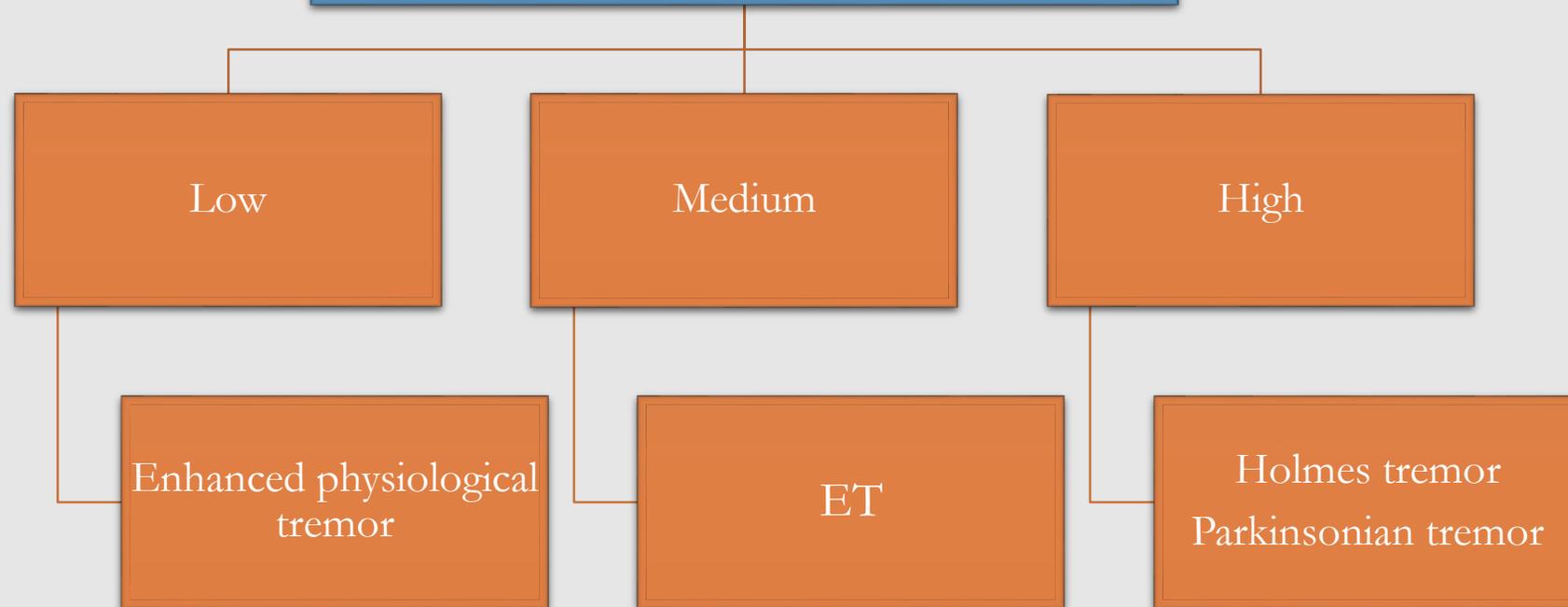
Orthostatic tremor | Tardive tremor

- OT- High frequency (13-16Hz) tremor of legs and trunk. Seen in 60-70yrs females.
 - Increases on standing, decreasing on walking, stops on sitting
 - Poor balance
 - Placing stethoscope on thigh produces helicopter like sounds – audible tremor.
- TT- postural tremor and can rarely be present at rest.
 - Frequency of 3–5 Hz with high amplitude.
 - Exposure to neuroleptic (dopamine receptor-blocking agents) drugs.
 - Resemble a Parkinsonian rest tremor (TT more symmetrical).
 - TT is nonprogressive and responds to drug withdrawal or reduction in dose.

Classification based on Frequency



Classification based on Amplitude



Classification based on Body part involved

Head

ET
Cervical dystonia
Cerebellar degenerative disorders

Jaw

PD
ET
Hereditary geniospasm
Orthostatic

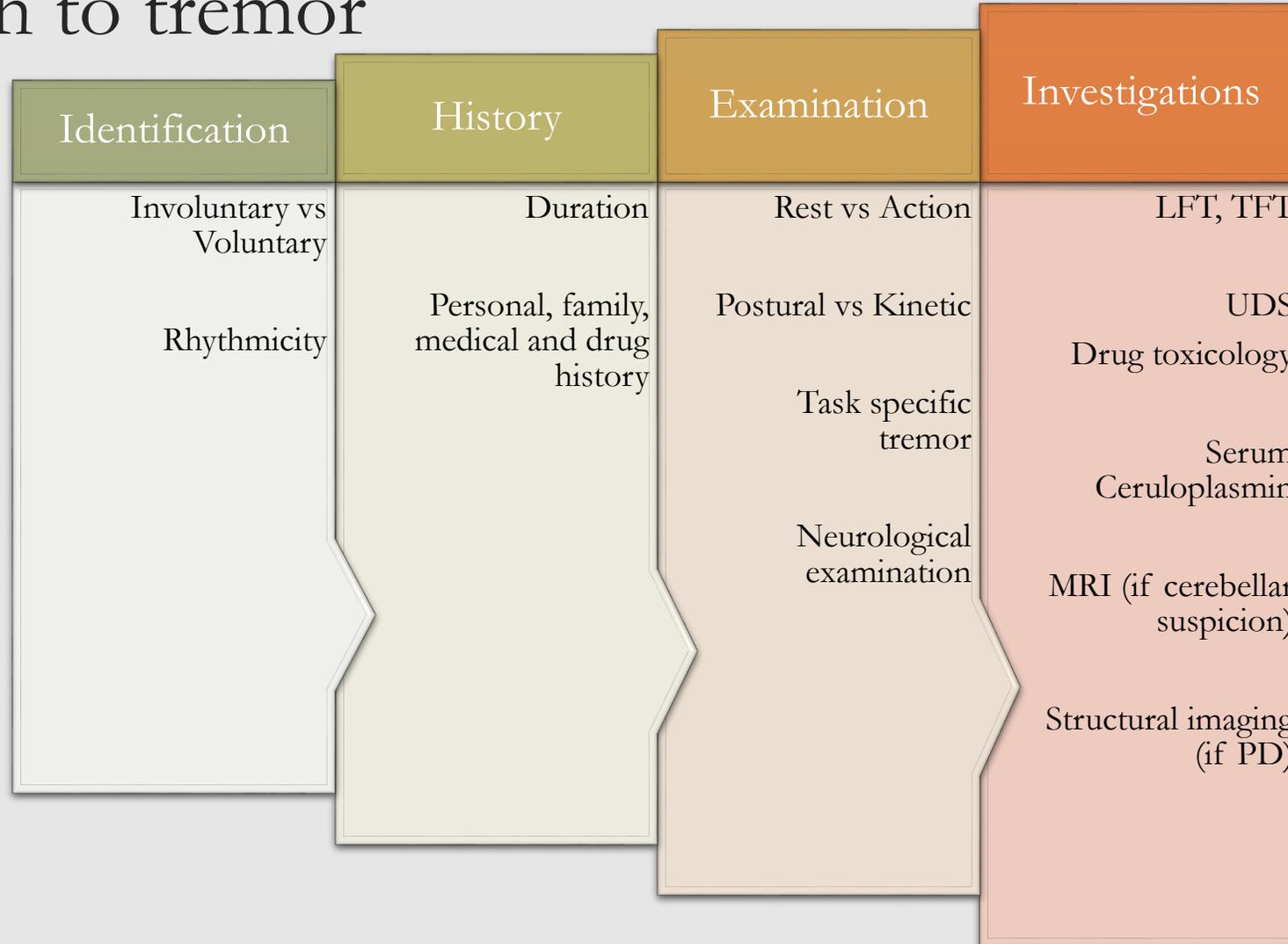
Voice

ET

Leg

PD
Orthostatic tremor

Approach to tremor



Examination

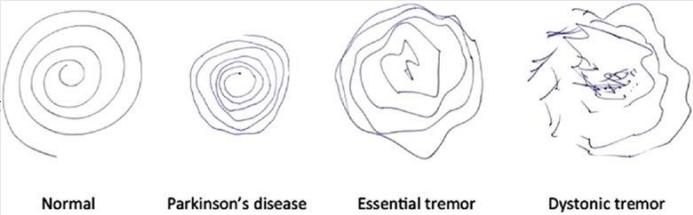
Ask the patient to extend his arms against the gravity, then to wing-beat position.
[POSTURAL COMPONENT]

- Rhythmicity, joints involved, synchronicity, reemergent quality. Association with abnormal postures and features of psychogenic tremors.



ask the patient to perform the finger-nose-finger maneuver, pour water between cups, draw spirals, or write a sentence.
[KINETIC COMPONENT]

- Intentional component. Dystonic component. Severity.



Tremor at rest in the arms can be assessed while the patient is seated, standing, walking, and lying down.
[REST COMPONENT]

- Associated PD symptoms.



Check for orthostatic component, tremor in the head, jaw, facial muscles, chin, tongue, and voice.

Assessment

CLINICAL RATING SCALES

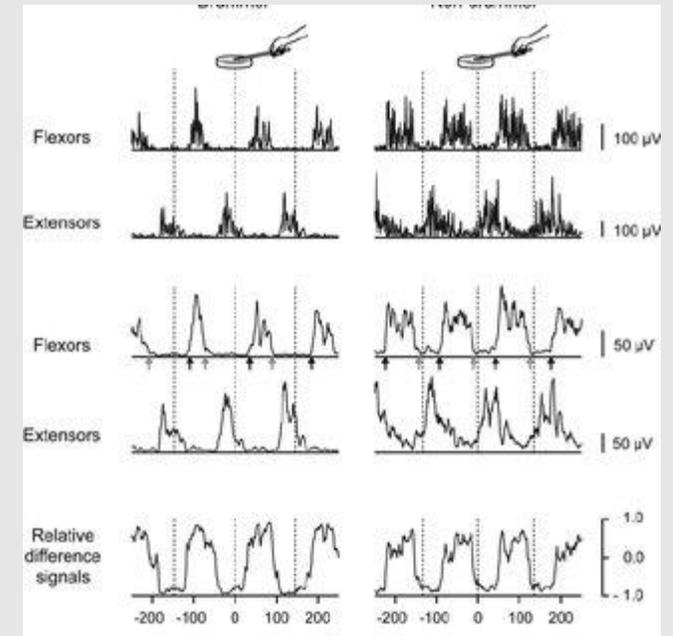
Scale	Parts	Score	Comments
Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS)	12 item ADL scale 9 item performance scale rating the action tremor that involves face, head, voice, limbs and trunk	Score 0-4 Score 0-4 (0.5 increments for upper limb tremor rating)	Easily done Was designed to specifically assess ET Very reliable scale in the assessment of ET The correlation of the severity of upper limb assessed by this scale are comparable to those measured by transducers Does not assess head tremors Can detect change in tremor severity on therapeutic intervention
The Fahn-Tolosa-Marin Tremor Rating Scale	Part A: assesses tremor at rest, postural and action in various body parts Part B: assesses tremor while writing, drawing and pouring Part C: assesses ADL	Each item rated on a scale of 0-4 0=none 1=slight 2=moderate 3=marked 4=severe	It's a widely used scale The correlation of the severity Assessment done by this scale is comparable to that assessed by a transducer
Bain and Findley Clinical Tremor Rating Scale and spirometry scale	The severity of the tremor in head, voice, limbs are scored separately and at each site the presence of rest, postural and kinetic tremor are scored separately Head: rest-head on pillow, postural-sitting unsupported Arm: rest-arm in the lap, postural-arms extended and pronated with spread fingers, kinetic- finger nose test, intention by observing the finger as it gets closer to an object Leg: rest-sitting with foot placed on floor, postural- sitting with leg extended Vocal: say name, address, birthday; hold the note 'aaah' Spiral drawing and handwriting specimen rated	Scale of 0-10 0=none 1-3=mild 4-6=moderate 7-9=severe 10=extremely severe Score of 0-10	Well known and widely used Can be done bedside Useful especially in assessing postural arm tremor and head tremor Correlates well with patient's self reported disability
Washington Heights-Inwood Genetic Study of Essential Tremor Tremor Rating Scale (WHIGET version 2)	Upper limb tremor: postural Upper limb tremor: kinetic	Score 0-3 Score 0-4	It is specifically designed for assessment of ET

Fahn-Tolosa-Marin Tremor rating scale

1. Face tremor	REST_____
2. Tongue tremor	REST_____
	POST_____
3. Voice tremor	ACT/INT_____
4. Head tremor	REST_____
	POST_____
5. Right upper extremity tremor	REST_____
	POST_____
	ACT/INT_____
6. Left upper extremity tremor	REST_____
	POST_____
	ACT/INT_____
7. Trunk tremor	REST_____
	POST_____
8. Right lower extremity tremor	REST_____
	POST_____
	ACT/INT_____
9. Left lower extremity tremor	REST_____
	POST_____
	ACT/INT_____
10. Handwriting	_____

TRANSDUCER BASED ASSESSMENT

- Can quantify the tremor based on frequency and amplitude
- Surface electromyography (surface EMG)
 - Quantification of pathological tremors
 - Can record entrainment, coherence
- ACCELEROMETER
 - Gold standard for identifying ET. Can identify subclinical cases of ET.
- GYROSCOPIC TRANSDUCERS



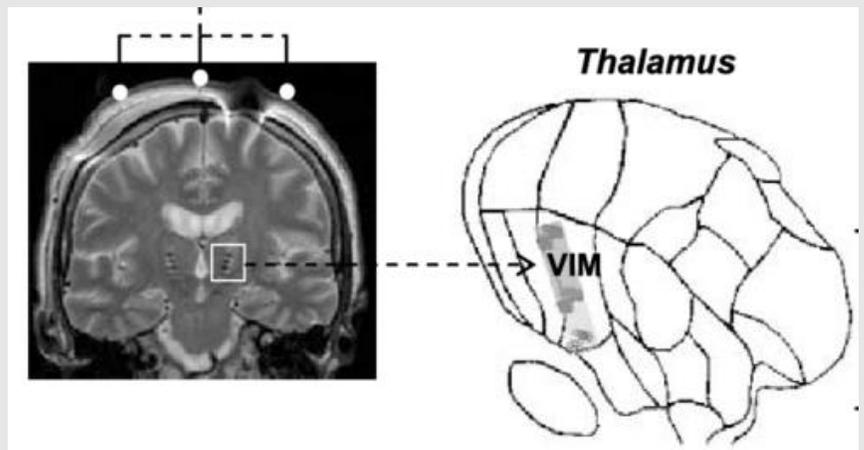
Treatment

Pharmacology:

- **Rest tremor of PD:** anticholinergic agents (trihexyphenidyl), amantadine, carbidopa/levodopa, dopamine agonists, and rasagiline.
- **Essential tremor:** Propranolol, primidone, long chain alcohol (octanol-1).
- **Dystonic tremor:** Botulinum toxin.
- **Cerebellar tremor:** Propranolol, Clonazepam.
- **Holmes tremor:** Carbidopa/levodopa (25/100mg to 100/250mg).
- **Orthostatic tremor:** Clonazepam, Clonazepam + primidone.

Deep brain stimulation and focused ultrasound

- Disabling ET:
 - Nearly 50% of ET doesn't respond to medical therapy.
 - DBS of the thalamic nucleus ventrointermedius (VIM) decreases tremor by 90%.
 - Transcranial MRI-guided focused ultrasound stimulation in VIM for drug resistant ET.
- Dystonic tremor:
 - Most of DT doesn't respond to medical therapy.
 - DBS is a good option in these patients with improvement seen in nearly 50–80% cases.
 - Sites could be VIM, globus pallidus internus, as well as caudal zona incerta



a Current DBS systems

- Electrode**
- Single or bilateral electrodes
 - Continuous stimulation

Extension cables

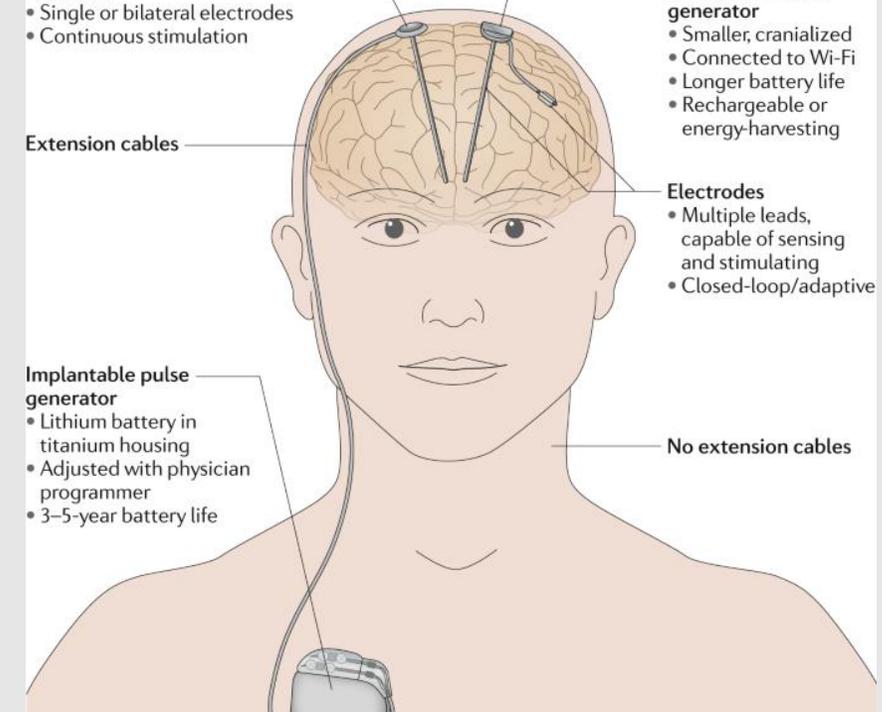
- Implantable pulse generator**
- Lithium battery in titanium housing
 - Adjusted with physician programmer
 - 3–5-year battery life

b Future DBS systems

- Implantable pulse generator**
- Smaller, cranialized
 - Connected to Wi-Fi
 - Longer battery life
 - Rechargeable or energy-harvesting

- Electrodes**
- Multiple leads, capable of sensing and stimulating
 - Closed-loop/adaptive

No extension cables



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