Tremor syndromes: Approach to diagnosis and management

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Plan

- Set some basic principles for tremor recognition and classification
- Identify some pitfalls
- Review the differential diagnosis of tremor
- Review management of essential tremor and Parkinson’s disease
What is tremor?

Tremor is an involuntary rhythmic oscillatory movement of a body part.
How should we describe it?

Its description may include:

- Which body part it affects
- Its frequency (low, mid, and high)
- Its amplitude
  - Small amplitude: Fine tremors
  - Large amplitudes: Coarse tremors
- Its context:
  - Rest tremor
  - Postural tremor
  - Kinetic tremor
Tremor present mainly at rest

Most common cause: Parkinson’s disease

- Typically starts on one side
- Often involves the thumb and forefinger (pill-rolling), but can be wrist flexion/extension or forearm pronation/supination tremor
- Frequency is typically 4 to 6 Hz.
- Some pts with PD have a postural tremor with same frequency as resting tremor or higher
- Tremor outside the arms: leg and jaw.
Pitfalls

Do not assume that all patients with resting tremor have PD.

30% to 40% of pts with PD will not have a tremor

Other causes of resting tremor:

- Medication induced tremor: Dopamine receptor blocking agents and some non-dopamine receptor blocking agents (lithium,…)
- Other parkinsonian syndromes (MSA, vascular parkinsonism…)
- Other neurodegenerative diseases (SCAs 2 and 3)
Tremor present mainly on posture

Most common cause: Essential tremor

- ET is defined as a bilateral, usually symmetrical, postural and kinetic tremor involving both hands and arms
- Tremor can involve the jaw or head
- There is family history in 50% of cases
- There are usually no other neurologic signs
- Progression is very slow
Tremor present mainly on posture

**Dystonic tremor:**

- Dystonia is a movement disorder that causes an abnormality of posture
- Many pts will have a tremor in the body part affected by dystonia
- Is typically jerky and may be position specific or task specific
Other causes of postural tremor

- Enhanced physiologic tremor: Fine symmetrical postural tremor of 7 to 12 Hz
- Drugs: Beta agonists, anticonvulsants, thyroxine, lithium, tricyclic antidepressants, caffeine, marijuana, amphetamines, nicotine, cocaine
- Drug withdrawal and alcoholism
- Hyperthyroidism
- Peripheral neuropathies: paraproteinemic
- Fragile X tremor-ataxia syndrome
Tremor present mainly during movement

- Intention tremor
  - Cerebellar dysfunction:
  - Structural lesions (MS….)
  - Degenerative diseases
  - Toxicity: Alcohol, phenytoin..

- Can be associated with a resting and postural tremor = Rubral or Holmes tremor
Pitfalls
Psychogenic tremor

- Can occur at rest, on posture, or during movement
- Oftentimes, in all 3 positions
- Distractible
- Variable
- Entrainable
- Suggestible
Body part-specific tremor

Head tremor
- Common feature of cerebellar disease
- Cervical dystonia
- Essential tremor
- Very uncommon in PD
Body part-specific tremor

- **Tremor of the chin and jaw**
  - Typically seen in PD
  - Dystonia
  - Hereditary geniospasm

- **Leg tremor**
  - Commonly occurs in PD
  - Orthostatic tremor: Very high frequency tremor that occurs exclusively on standing
A QUICK AIDE-MEMOIRE TO TREMOR HISTORY TAKING AND EXAMINATION
The most useful historical details

- Age at onset
- Body parts affected
- Nature of onset: Sudden vs slowly progressive
- Drug exposure
- Exacerbating factors
- Family history
- Associated neurologic and systemic symptoms
Examination of tremor

Examine the patient with her arms relaxed, half pronated. Ask the patient to close her eyes and count backward from 100.

Examine the arms on posture, stretched out with the fingers open.

Ask the patient to flex the arms at the elbows, then pronate and supinate them.

Finger to nose test looking for a kinetic or intention tremor.

Ask the patient to write and copy a spiral.
Treatment of tremor

Treatment of tremor due to drug use:
withdrawal of the offending drug

Treatment of the metabolic disturbance:
Primarily symptomatic for most other causes
Treatment of tremor

Certain causes of tremor have specific treatments

Parkinson’s disease tremor:
- Medical treatment
- Surgical treatment
Treatment of PD’s tremor

Medical treatment:
- Amantadine, Selegiline, Rasagiline
- Dopamine agonists: Ropinirole, Pramipexole, Rotigotine patch, and Apomorphine
- Carbidopa/levodopa:
  - Most effective symptomatic drug
  - Supplements missing dopamine
  - Improves patients’ quality of life
  - Long-term use often associated with motor complications
**Treatment of PD’s tremor**

- **Surgical treatment:**
  - Thalamotomy/Pallidotomy
  - Deep Brain Stimulation:
    - Uses high frequency electrical stimulation from an implanted electrode to modify activity in the target area
    - The electrode is connected to a pulse generator which is implanted in the chest wall.
Treatment of PD’s tremor

=DBS=

- Still L-dopa responsive
- Motor fluctuations
- Intolerable dyskinesias
- Wearing off, short duration of benefit
- ADL and QOL affected
- Cognitively intact
- Realistic risk/benefit expectations
- Minimal co-morbid conditions
Treatment of essential tremor

Beta blockers, particularly Propanolol, have class A evidence of efficacy (Atenolol and Sotalol)

- Propanolol (Inderal) is a first line agent for ET
- Dose: 60 mg to 320 mg daily
- Response rate: 50% to 70%
- Tremor improvement: 50%
- Dropout rate: 20%
- Side effects: Hypotension, bradycardia, fatigue, erectile dysfunction, drowsiness, dyspnea seen in 60%
Treatment of essential tremor

🌟 Primidone:

- Primidone (Mysoline) is a first line agent
- Dose: 250 mg to 750 mg daily
- Response rate: 30% to 50%
- Tremor improvement: 50% to 70%
- Dropout rate: 20% to 30%
- Side effects: Sedation, fatigue, dizziness, confusion, nausea, flu-like symptoms seen in 22% to 72%
Treatment of essential tremor

Topiramate (NOT FDA approved):
- A second line agent
- Dose: 150 mg to 300 mg daily
- Response rate: 30% to 40%
- Tremor improvement: 20% to 37%
- Dropout rate: 30%
- Side effects: Paresthesias, sedation, fatigue, weight loss, dizziness, confusion, nausea, seen in 50%
Treatment of essential tremor

- Gabapentin (Not FDA approved)
  - A second line agent
  - Dose: 1200 mg to 3600 mg daily
  - Response rate: 30%
  - Tremor improvement: 30% to 40%
  - Dropout rate: 10%
  - Side effects: Sedation, weight gain, dizziness, nausea seen in 30% to 40%
Treatment of essential tremor

- Pregabalin (not FDA approved)
- A second line agent for ET
- Dose: 150 mg to 600 mg daily
- Response rate: 30% to 50%
- Tremor improvement: 30% to 40%
- Dropout rate: 10%
- Side effects: Sedation, weight gain, dizziness, nausea seen in 30% to 40%
Treatment of essential tremor

- Clonazepam (Not FDA approved)
- A second line agent for ET
- Dose: 0.5 mg to 4 mg daily
- Response rate: 50% to 70%
- Tremor improvement: 30% to 50%
- Dropout rate: 10%
- Side effects: Sedation, cognitive impairment, Tolerance, dependence, abuse seen in 50%
Treatment of essential tremor

ABOUT 30 % TO 50 % OF ESSENTIAL TREMOR PATIENTS WILL NOT RESPOND TO MEDICAL THERAPY
Surgical treatment of ET

Thalamotomy is a stereotactic procedure that creates a lesion in the ventral intermediate nucleus (VIM) of the thalamus.

Studies have typically reported an 80–90% improvement in tremor symptoms compared to baseline.

Disadvantage:
Surgical treatment of ET: DBS

Indications:

- Certainty of diagnosis
- Severe symptoms with related disability
- Proper trial of pharmacological treatment

DBS anatomical Target:

- Ventral Intermediate nucleus of the thalamus
In summary

- Tremor is a common complaint
- A detailed history including medications is very important
- The most useful tremor description and classification is based on context