

TREMOR IN ESSENTIAL TREMOR (ET)

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- I. Essential tremor is one of the most common neurological disorders. A meta-analysis of 28 population based studies found a pooled prevalence of 0.9%. In the meta-analysis, prevalence \geq 65 years old was 4.6% (1). There may be a slightly higher prevalence among men. Essential tremor has a bimodal age of onset. Up to 20%-30% of adults with ET report a childhood onset (2, 3). A family history is very common in children, reported in up to 91% of cases. (4, 5) Adult onset is much more common and the second peak of onset is in the fifties. Approximately 50% of adult ET patients report a family history. Many patients with ET report improvement of symptoms after alcohol consumption. Alcohol-responsive patients may experience a “rebound” period, often 3-4 hours after consumption, during which time there is worsening of the tremor. Alcohol responsiveness is more common in the younger age of onset (6). Patients with older age of onset may have faster disease progression and an increased risk of dementia (7). Tremor is also ameliorated with rest. Exacerbation of tremor may occur with increased stress or fatigue, as well as with the addition of CNS stimulants.

A 1988 consensus statement on tremor defines ET as a “bilateral, largely symmetric postural or kinetic tremor involving hands and forearms that is visible and persistent” (8). Features of ET tremor include the following:

- A. ET upper extremity tremor is bilateral. There is small-to-moderate asymmetry in tremor severity between arms (9). Isolated limb tremor is uncommon and an alternate diagnosis should be considered (10).
- B. ET tremor is prominently a kinetic tremor. Patients may have absent or mild postural tremor, but kinetic tremor is almost always greater in amplitude (11). The postural tremor is out of phase and thus holding an object with two hands often dampens instead of enhances tremor (12). Isolated postural tremor is unusual. The kinetic tremor may have an intention component. Intention tremor is seen in approximately 1 of every 3 cases of ET and correlates with disease duration (13). It can also be present in the neck when patients demonstrate flexing the neck to drink (14). Rest tremor is present in a small portion of ET patients. These patients usually have advanced disease with a history of ET for many years (15, 16).
 - 1. PD vs ET: Action tremor in PD is less likely to have an intention component.
 - 2. PD vs ET: Rest tremor in PD is more often suppressible than in ET (17). When present, rest tremor in ET is seen in the arms and is not seen in the legs in ET.
 - 3. PD vs ET: In the presence of a rest tremor, a postural tremor can “re-emerge” in PD while there will be continuous tremor from rest to posture in ET. Postural tremor frequently involves several joints (shoulder, elbow, wrist) and the wrist movement is extension/flexion; Movement of the metacarpal joint movement is uncommon (12).
- C. ET tremor frequency is 4-10 Hz. As tremor progresses, there may be an increase in amplitude and a slowing of frequency (18). Presentation is insidious in onset.
- D. ET tremor can involve head and vocal cords.
 - 1. Head tremor is described as “yes-yes” or “no-no” to characterize direction. Upon initial presentation, the tremor may occur in one direction and may be infrequent. Overtime, the tremor may acquire additional directionality and occur more frequently (19). Head tremor may be observed in up to 50% of patients with ET and is more often present in patients with long disease duration (20). Head tremor is less common in children (21) and is more common in women (22). Patients may be unaware of its presence (23). Neck tremor typically disappears when the person lies down (24). If the patient ONLY has head tremor, the diagnosis of ET is in question.
 - 2. Studies have reported vocal tremor in as many as 62% of ET patients (20). Again, it is typically more common in the presence of long standing disease and is unusual as an isolated presentation (25). Women are more likely to have a vocal tremor (26).

- II. Although classically considered a benign motor condition, there is increasing evidence that essential tremor is a degenerative condition also associated with neuropsychiatric and cognitive impairment.
 - A. A population study of non-demented older adults followed over a three year period, found a greater rate of cognitive decline (using the MMSE) in patients with ET than in a control population (27). Adult onset ET is associated with an increased risk of dementia (28, 29). In most reports, the patients that became demented developed Alzheimer's disease.
 - B. Depressive symptoms are common in ET. A recent study of depressed ET patients found they were more likely to have difficulty concentrating and were more likely to complain of energy loss when compared to depressed individuals without ET (30).
- III. Neurological assessment:
 - A. Voice: Regular vocal oscillation may be heard with extended "ahhs" or "eees"
 - B. Neck: Regular oscillation with symmetrical rotation around a central axis. Approximately half of patients with head tremor may have agnosia to the tremor when it occurs (31). A reported bedside pearl describes the presence of a "head snap" that may be detected on examination (32). Testing for the head snap occurs as follows: When the patient is performing the finger-to-nose maneuver, the examiner may note a unidirectional jerking of the head as the patient's finger reaches his or her own nose.
 - C. Arm: Look for a regular, non-directional oscillation with finger-to-nose, water pouring, spiral (free and constrained) and loop drawing. Spiral wave forms appear to align along a single predominant axis in ET (33).

In 2005, the AAN published guidelines for ET therapy. The recommendations state that propranolol or primidone may be used as first line agents for patients with ET (34). Other medications such as gabapentin and topiramate may be useful. Side effects may limit topiramate use (35). Recommendations from the Italian Movement Disorder Association include zonisamide, alprazolam, olanzapine, and clozapine as second line agents. Medication adherence should be closely monitored as it is common for patients to miss medication doses which may lead to worse outcomes (36). Botulinum toxin in the neck or limbs can be effective in patients refractory to medication (37). Deep brain stimulation, targeted at the thalamus, is helpful in severe cases. MRI-guided focused ultrasound thalamotomy has been shown to be beneficial for the treatment of ET. Patients with moderate to severe tremor, who report impaired activities of daily living, and have failed at least two oral medications, can be considered. In the 2016 NEJM study by Elias et al., patients received unilateral lesions. Sensory alterations and gait imbalance were the most common side effects. Side effects persisted in a small portion of patients. This treatment is now FDA approved. There is no long term data on this procedure (38-40).

Comparison of Limb Tremor in PD, ET, and Dystonia

	Tremor in PD	Tremor in Dystonia	Tremor in ET
Activation of tremor	Rest>posture >> kinetic	Kinetic > posture >> rest	Kinetic > posture
Tremor frequency	4-6 Hz	< 7 Hz	4- 10 Hz
Tremor symmetry	Asymmetric	Asymmetric	Symmetric (or mild asymmetry)
Rhythmicity	Regular	Irregular/Jerky	Regular
Other common neurological findings in limb	<ul style="list-style-type: none"> • Cogwheel rigidity • Bradykinesia 	<ul style="list-style-type: none"> • Posturing of limb • Cramping with writing 	<ul style="list-style-type: none"> • None
Handwriting appearance	<ul style="list-style-type: none"> • Micrographic - may worsen with continuous writing • Spirals are small 	<ul style="list-style-type: none"> • Jerky tremor may be apparent on writing sample • Presses into paper • May have to stop writing (breaks can be seen) 	<ul style="list-style-type: none"> • Rhythmic tremor may be seen on writing sample • Spirals are large
Other common locations of tremor	<ul style="list-style-type: none"> • Jaw: rhythmic • Lips: rhythmic • Tongue: rhythmic 	<ul style="list-style-type: none"> • Neck: irregular, jerky, directional 	<ul style="list-style-type: none"> • Neck: Rhythmic "yes-yes", "no-no" • Voice

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