DIAGNOSING COMMON TYPES OF TREMOR in TWO SHAKES

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Tremor is defined as an involuntary, oscillatory, rhythmic movement of a body part produced by the alternating contractions of antagonistic pairs or muscles. It is the most common movement abnormality encountered and investigated in both primary care and neurology practice. Tremor is not a diagnosis in itself; rather it is symptomatic of an underlying disorder that should be identified and when possible treated. The diagnostic process ought to include a detailed medical history, a careful assessment of the characteristics of the tremor and a search for other neurological or physical signs. This process may present challenges, particularly in describing tremor phenomenology and linking it to the likely diagnosis. This article outlines briefly the main points to explore when evaluating a patient's tremor history, the key characteristics of tremor that should be examined for and the correct nomenclature for their description, followed by an overview of the common types of tremor encountered in clinical settings and pointers to their diagnosis.

EVALUATION OF THE PATIENT WITH TREMOR

MEDICAL HISTORY

- *Age at onset and progression since.*
- *Timing of the tremor* – does it mainly emerge at rest or on activity?
- *Past medical issues* – Up to 60% of patients with multiple sclerosis manifest tremor at some point in their disease, which may emerge and subside over time and have differing characteristics. Stroke survivors may also develop tremor, albeit far more acutely. Tremor-like movements may be seen in cases of kidney (action myoclonus) and liver (flapping asterixis) failure, but these movements are phenomenologically different. Anxiety is commonly associated with postural tremor, so if suspected one should enquire about relevant symptoms such as palpitations, chest pain and feelings of suffocation that have been already investigated unsuccessfully.
- *Family history of tremor* – essential tremor (ET) is considered genetic and hereditary though not all patients will report affected family members. Rarely, Wilson's disease will present initially with tremor.
- *Medication list and relation to onset of tremor* – drug-induced tremor is common, either as an iatrogenic adverse effect or due to toxicity from specific supra-therapeutic drug levels in serum.
- *Dietary habits* – regular excessive intake of strong coffee or energy drinks, as well as episodes of hypoglycaemia following skipped meals, may all cause tremor.
- *Alcohol intake and effect on tremor* – in people suffering from alcoholism, acute withdrawal can induce tremor, while chronic excessive alcohol intake causes tremor due to cerebellar degeneration. Conversely, small doses of alcohol will temporarily suppress ET.

CHARACTERISATION OF THE TREMOR

The assessment of a patient with tremor is based on two equally important actions - a careful observation of the characteristics of the tremor and the proper denotation of these observations. The former narrows down the list of differential causes and often may lead to establishing a diagnosis. The latter requires that physicians become familiar with and adopt the use of standardised nomenclature to avoid confusion and assist in the recording and conveying of information over time in patients' records.

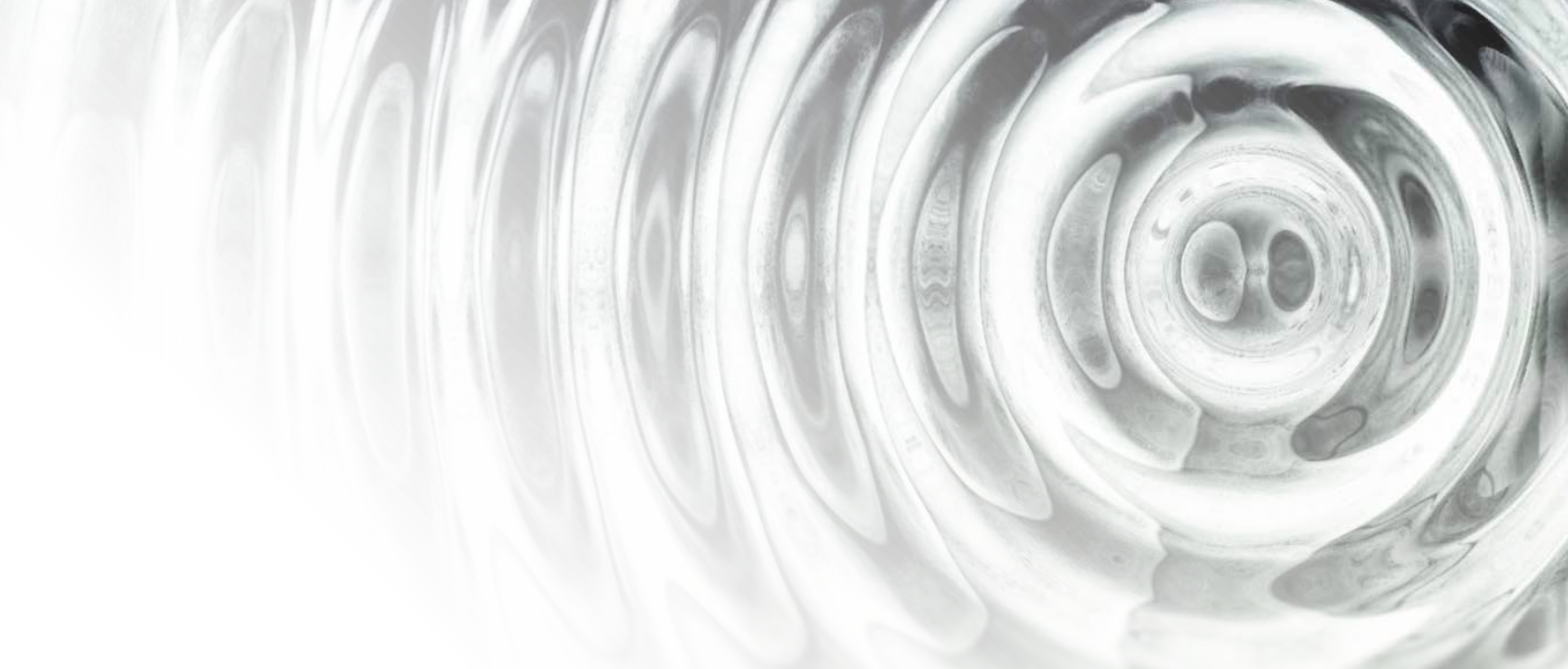
There are six primary characteristics of tremor that should be examined and recorded:

1. Anatomic distribution

- Note the affected body parts, which may include the head, tongue or palate, the upper or lower extremities, or the trunk. If the head is involved, note if the tremor is vertical (nodding / yes-yes tremor) or horizontal (shaking / no-no tremor).
- Look for vocal tremor while conversing with the patient and ask them to hum a note.

2. Frequency

The frequency of a tremor may not be measurable with the naked eye, but one may at least classify it as fast (>6Hz) or slow (<6Hz). Although there are differences in average tremor frequency among different types of tremors, the range of frequencies overlap considerably between disorders, so tremor



frequency is less helpful than other characteristics in reaching a diagnosis. However particularly slow tremors (≤4Hz) are only seen in Parkinson's disease (PD), cerebellar disorders, midbrain lesions or secondary to medication.

3. Position

The position of the affected body part when the tremor emerges or is most pronounced is the most important aspect of its evaluation. *Resting* tremor occurs when the body part is not voluntarily activated and is completely supported against gravity. *Action* tremor emerges during activity requiring voluntary muscle contraction and may be further specified into:

- *Postural tremor* which occurs when maintaining a voluntary posture against gravity as when holding the upper extremities in an outstretched position.
- *Isometric tremor* which occurs when muscles are contracted without appreciable movement (such as squeezing the examiner's fingers).
- *Non-target directed tremor* observed during non-goal oriented movements (such as flexion / extension of elbow or pronation / supination of the forearm).
- *Intention tremor* which occurs during target-directed movements, as in the finger-to-nose or heel-to-shin tests.
- *Task-specific tremor* appears or is exacerbated by performing specific tasks, such as writing, holding tools or playing a musical instrument.

4. Amplitude

Tremor is defined as either fine or coarse depending on the range of oscillatory movement in the affected body part(s). A general rule is to name the predominant tremor after the position in which the largest amplitude occurs (at rest / on posturing / during active movement).

5. Exacerbating or relieving factors

- Note if the amplitude is regular or variable and if it becomes more pronounced or lessens with distraction (ask the patient to say aloud the months of the year backwards with their eyes closed, or to flex and extend one elbow while examining the other hand).
- Ask if there is a temporary but significant reduction of tremor amplitude in response to alcohol, typical of ET (see below).

6. Associated symptoms and signs

- Eye movement abnormalities may suggest cerebellar disease or multiple sclerosis. Proptosis points to thyrotoxicosis (may also manifest tachycardia, a visible goitre and abnormal sweating).
- Kayser-Fleischer rings are specific for Wilson's disease.
- Torticollis, blepharospasm, orofacial twitching or spasmodic dysphonia (with effortful strained speech or a whispery voice) indicate dystonia.
- Extrapyramidal signs such as lack of facial expressivity, reduced blink rate, a monotonous voice, muscular rigidity or bradykinesia indicate idiopathic PD or parkinsonism.
- Gait may be parkinsonian (reduced length of stride, reduced or absent armswing, forward stoop, slow turning using several steps), cerebellar (broad based and ataxic) or spastic (suggesting multiple sclerosis).
- An otherwise completely normal neurological examination is both reassuring and usually suggestive of ET.

COMMON TYPES OF TREMOR PRESENTING TO GP CLINIC OR HOSPITAL OUTPATIENT SETTINGS

Exaggerated physiological tremor

Physiological tremor, a high frequency postural tremor of very small amplitude in the hands, is a normal phenomenon not associated with disease. This may not be visible to the naked eye but may be elicited more easily by placing a sheet of paper over an outstretched hand. The tremor may be magnified by anxiety, hypoglycaemia, exercise, caffeine or other stimulants. It may also become more pronounced in patients who withdraw from alcohol, use regular beta agonists, have thyrotoxicosis or Cushing syndrome. Reassurance, modification of health behaviours, or treatment of causative medical issues form the mainstay of its management, although tremor-suppressive agents or anxiolytics may sometimes have a role to play.

Essential tremor

Essential tremor (ET is the most common adult onset movement disorder. It is bilateral, usually but not invariably symmetrical, postural or kinetic, and involves the hands and forearms. It may also involve the neck (causing head titubation) and / or voice but rarely affects the legs. It tends to emerge gradually as a high frequency (>5Hz) slight tremor that increases slowly in amplitude over time, impacting progressively on activities of daily living such as eating with cutlery, holding beverages or bringing them to the lips without spilling, and activities requiring finger dexterity such as fastening buttons, threading a needle or writing. ET appears in people within the age bracket where idiopathic PD starts increasing in prevalence. An important distinguishing feature is that PD tremor may occur on posturing but appears after sustaining a fixed posture for several seconds, while ET does not manifest a delay its onset on posturing. A further distinguishing feature is a noticeable albeit temporary, reduction of tremor amplitude in response to alcohol. A positive family history is reported in about 50% of patients affected by ET.

Parkinsonian tremor

The typical PD tremor is a pure resting tremor with low frequency (4–6 Hz). Tremor amplitude varies both across and within patients, tending to become less notable over time as bradykinesia concomitantly becomes more pronounced. The correct diagnosis may be made very easily if the patient also manifests other cardinal signs of PD, namely bradykinesia or extrapyramidal rigidity. However tremor may be the sole presenting feature of PD, in which case telling it apart from ET may be challenging. In these cases, the following pointers may prove helpful:

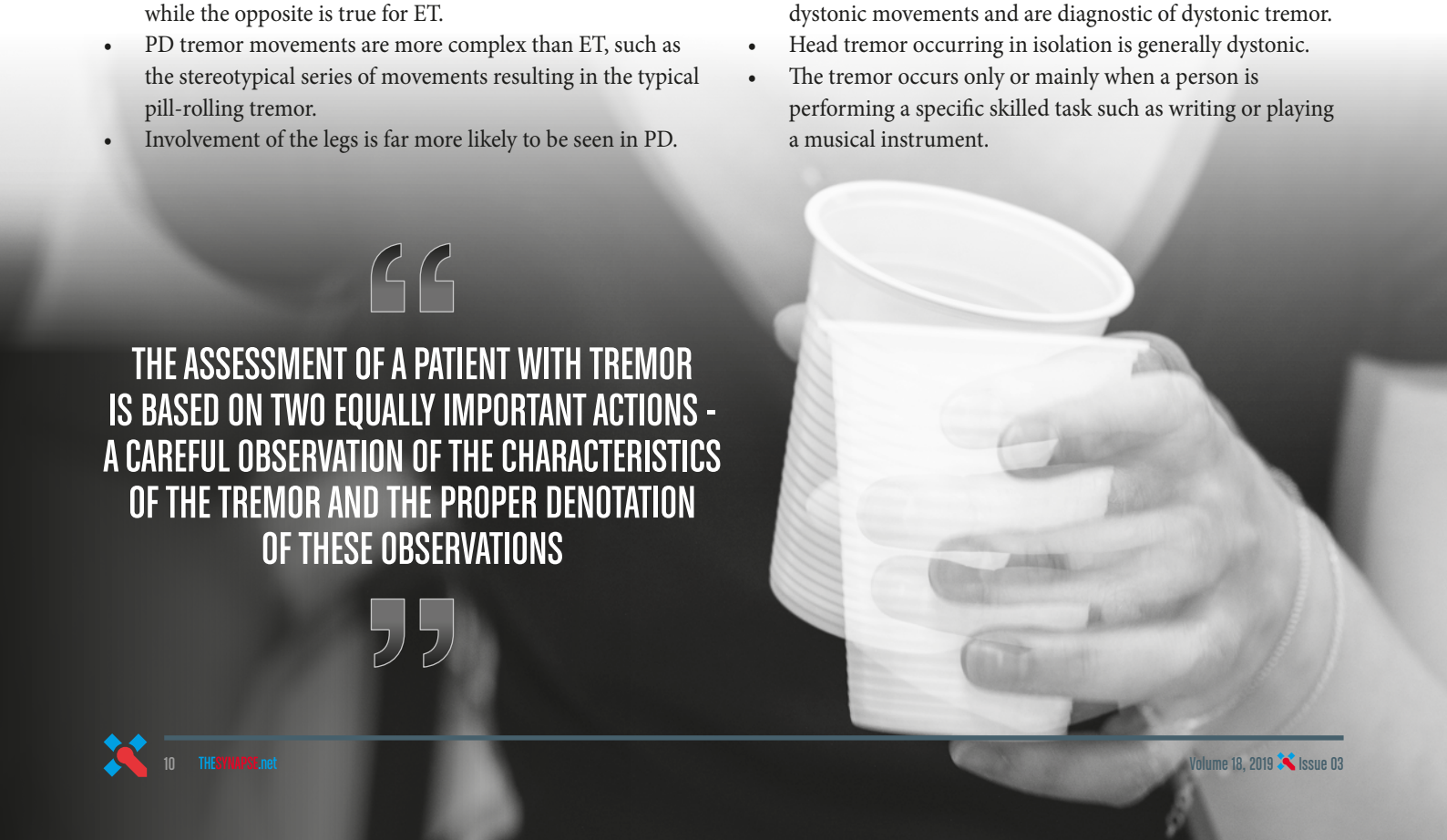
- PD tremor is much more likely to be unilateral or asymmetrical than ET.
- PD tremor at rest is more pronounced than on activity, while the opposite is true for ET.
- PD tremor movements are more complex than ET, such as the stereotypical series of movements resulting in the typical pill-rolling tremor.
- Involvement of the legs is far more likely to be seen in PD.
- When present, postural tremor in patients with PD will appear after a latent period of several seconds. This is referred to as a re-emergent tremor.
- Observing gait may confirm the presence of PD tremor as the arms are relaxed by the patient's sides, often with reduction in armswing, while patients with ET do not generally have tremor while walking.

When the diagnosis remains unclear, a trial of antiparkinsonian medications may help, as ET should not respond. Do keep in mind that tremor in PD is often more difficult to alleviate than bradykinesia and rigidity, and tends to respond less well to dopaminergic therapy or may not improve with medication at all. Some patients need to be followed up over time until emergent hypokinetic symptoms and signs confirm the diagnosis of PD.

Dystonic tremor

Dystonic tremor (DT) is a focal tremor in an individual with dystonia. The tremor is mainly postural or kinetic, and may occur in the body part affected by dystonia, or in different areas. The diagnosis of DT is straightforward when accompanied by overt focal or segmental dystonia, but may be misdiagnosed when tremor is the predominant complaint, and accompanying symptoms such as mild blepharospasm or torticollis are missed or their significance overlooked. However DT should be distinguishable in that:

- Careful observation will reveal tremor of irregular and variable frequency and amplitude.
- The affected body part tends to move more in a particular direction.
- The patient may report having a sensory trick to control the tremor. These '*gestes antagonistes*' are voluntary maneuvers (such as simply touching or putting light pressure on the affected area) that temporarily reduce the severity of dystonic movements and are diagnostic of dystonic tremor.
- Head tremor occurring in isolation is generally dystonic.
- The tremor occurs only or mainly when a person is performing a specific skilled task such as writing or playing a musical instrument.



> THE ASSESSMENT OF A PATIENT WITH TREMOR IS BASED ON TWO EQUALLY IMPORTANT ACTIONS - A CAREFUL OBSERVATION OF THE CHARACTERISTICS OF THE TREMOR AND THE PROPER DENOTATION OF THESE OBSERVATIONS

Cerebellar tremor

This is primarily an intention tremor that may also manifest on posture. It is of slow frequency (<5Hz) and its amplitude typically increases as the body part undergoing movement approaches the target, as in the finger-to-nose test. Tremor distribution primarily depends on aetiology. Focal structural pathologies due to neoplastic growths, and vascular or inflammatory insults to the cerebellum may present with unilateral tremor, while genetic or toxic disorders resulting in cerebellar degeneration, such as chronic alcoholism, long-term exposure to certain medications or spinocerebellar ataxias are likely to cause bilateral tremor. Other relevant clinical signs such as dysarthria, nystagmus and ataxia of gait, trunk or limbs, usually accompany the tremor and point to the correct diagnosis, with investigations mainly helping to identify the underpinning cause.

Drug-induced tremor

Medication should always be considered as a potential cause for a patient's tremor, although iatrogenic causes of tremor probably remain under-recognised. Identifying drugs that may cause or exacerbate tremor can expedite diagnosis, avoid unnecessary tests and ensure the right approach to management (discontinuing the tremor-inducing drugs rather than prescribing tremor-suppressive agents). There may be a significant time-lapse (months to several years) between starting the offending drug and onset of tremor. Likewise, once the drug is identified and removed, it can often take time for the tremor to improve. An exhaustive list of drugs causing tremor is beyond the scope of this article, but a comprehensive review of the subject has been authored by Morgan and Sethi (See Further Reading).

Diagnosis of a drug-induced tremor may be challenging for three reasons. Firstly, a large number of different medications are recognised as tremorogenic, and it would not be unusual to encounter elderly patients with tremor on a long list of medications that includes two or more of these. Secondly, stopping suspected drugs may be impossible or potentially unsafe if no equally effective alternative is available. Thirdly, drug-induced tremor may demonstrate the entire spectrum of clinical features of tremor, depending on the offending agent. Thus stimulants will cause an exaggerated physiological postural tremor, dopamine blocking agents will result in a Parkinsonian resting tremor, and chronic alcoholism or long-term valproate therapy will cause a cerebellar intention tremor.

Psychogenic tremor

Psychogenic tremor should be considered in the differential diagnosis of any patient with tremor.

Differentiating psychogenic tremor from an organic tremor can be very challenging, and misdiagnosis is not uncommon. There are however several clues that may point to a psychogenic cause:

- The tremor is often difficult to fit into a recognisable pattern, generally starts suddenly rather than gradually, and often varies in amplitude and frequency.
- Tremor may transiently disappear or change in its frequency with distraction maneuvers, such as asking the patient to perform voluntary movements in the contralateral limb such as alternate finger tapping or foot tapping. Suggestion is another method whereby a vibrating tuning fork is applied to the patient's forehead after giving the impression that this may stop the tremor – which typically stops or diminishes temporarily.
- A past history of somatisation (unexplained chest pain, breathlessness, fatigue, gastrointestinal symptoms or sensory disturbances despite multiple investigations) is often encountered when enquired about. Some patients may develop tremor during a grieving period.
- The diagnosis of psychogenic tremor, when suspected, should be confirmed by a neurologist, both due to the difficulty in reaching the diagnosis as well as the resistance by some patients to accept a non-organic reason for their symptoms.

Neuropathic tremor

Tremor may occur in patients suffering from peripheral neuropathies, in particular demyelinating neuropathies. An association should be considered in patients previously diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP), hereditary neuropathies including Charcot-Marie-Tooth disease or monoclonal gammopathy. The tremor is generally postural and kinetic in nature, predominantly distal in location with atypical jerky-like and pseudoathetotic or abduction-adduction pattern of movements in the fingers. It usually affects the upper limbs in a symmetric or asymmetric fashion and has a slow to moderate frequency (3-6Hz). When it is the first presenting symptom of neuropathy, examination will yield hallmarks of a generalised peripheral neuropathy including absent or subdued reflexes, weakness, impaired sensation, ataxia and gait disturbance.

Treatment of the underlying neuropathy (when possible) may suppress or resolve the tremor.

Orthostatic tremor

Orthostatic tremor is a tremor disorder of the lower extremities which is uncommon but worth highlighting due to its specific clinical presentation. Sufferers do not report tremor but rather a feeling of unsteadiness when attempting to stand still for longer than a few seconds. This feeling disappears on walking or on sitting down. Diagnosis is confirmed using surface electromyography which demonstrates a very high frequency (12–18 Hz) tremor in affected muscles. The muscle contractions can be auscultated through a stethoscope applied to the thigh or calf, as these generate a rapid staccato sound has been compared with that of a helicopter rotor ('helicopter sign').

FURTHER READING

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2. Elble RJ. Tremor. In: Tousi B, Cummings J, (eds) Neuro-Geriatrics. A Clinical Manual. Springer International Publishing; 2017. p. 311-326.
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