Approach to a tremor patient

Soumya Sharma, Sanjay Pandey

Department of Neurology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi, India

Abstract

Tremors are commonly encountered in clinical practice and are the most common movement disorders seen. It is defined as a rhythmic, involuntary oscillatory movement of a body part around one or more joints. In the majority of the population, tremor tends to be mild. They have varying etiology; hence, classifying them appropriately helps in identifying the underlying cause. Clinically, tremor is classified as occurring at rest or action. They can also be classified based on their frequency, amplitude, and body part involved. Parkinsonian tremor is the most common cause of rest tremor. Essential tremor (ET) and enhanced physiological tremor are the most common causes of action tremor. Isolated head tremor is more likely to be dystonic rather than ET. Isolated voice tremor could be considered to be a spectrum of ET. Psychogenic tremor is not a diagnosis of exclusion; rather, demonstration of various clinical signs is needed to establish the diagnosis. Severity of tremor and response to treatment can be assessed using clinical rating scales as well as using electrophysiological measurements. The treatment of tremor is symptomatic. Medications are effective in half the cases of essential hand tremor and in refractory patients; deep brain stimulation is an alternative therapy. Midline tremors benefit from botulinum toxin injections. It is also the treatment of choice in dystonic tremor and primary writing tremor.

Key Words

Botulinum toxin, deep brain stimulation, essential tremor, head tremor, Parkinson disease, tremor, tremor rating scales

For correspondence:
Dr. Sanjay Pandey, Academic Block, Room No 507, Department of Neurology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi - 110 002, India.
E-mail: sanjaysgpgi2002@yahoo.co.in

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Introduction

Tremor is the most common movement disorder encountered in clinical practice.[1] It is produced when there are alternating and synchronous contractions of reciprocally innervated agonistic and antagonistic muscles that cause a symmetrical displacement about the midpoint of the movement in both the directions.[1] Tremor is seen in nearly 5% of the population over the age of 40 years.[2] The most common tremors in clinical practice are enhanced physiological tremor, essential tremor (ET), and Parkinsonian rest tremor.[1,3] These tremors tend to occur more commonly in the older population. Despite its high prevalence, symptoms tend to be mild in the majority of patients and a very small proportion actually seeks medical attention. In patients who present to a clinician, the tremor could be disabling. Hence, a systematic approach is needed to classify the tremor and identify the underlying etiology. Once the cause of the tremor is established, appropriate treatment can be started.

Classification

Although tremors can be classified in several ways, the most important parameter used is the occurrence of tremor in relation to movement or position of a body part. Based on this, they are classified as rest or action tremor [Figure 1].[1,4] Action tremor is further classified into postural or kinetic tremor. When the tremor worsens on approaching a target, it is classified as intention tremor, which is considered to be a type of kinetic tremor. This distinction helps in identifying underlying pathophysiology

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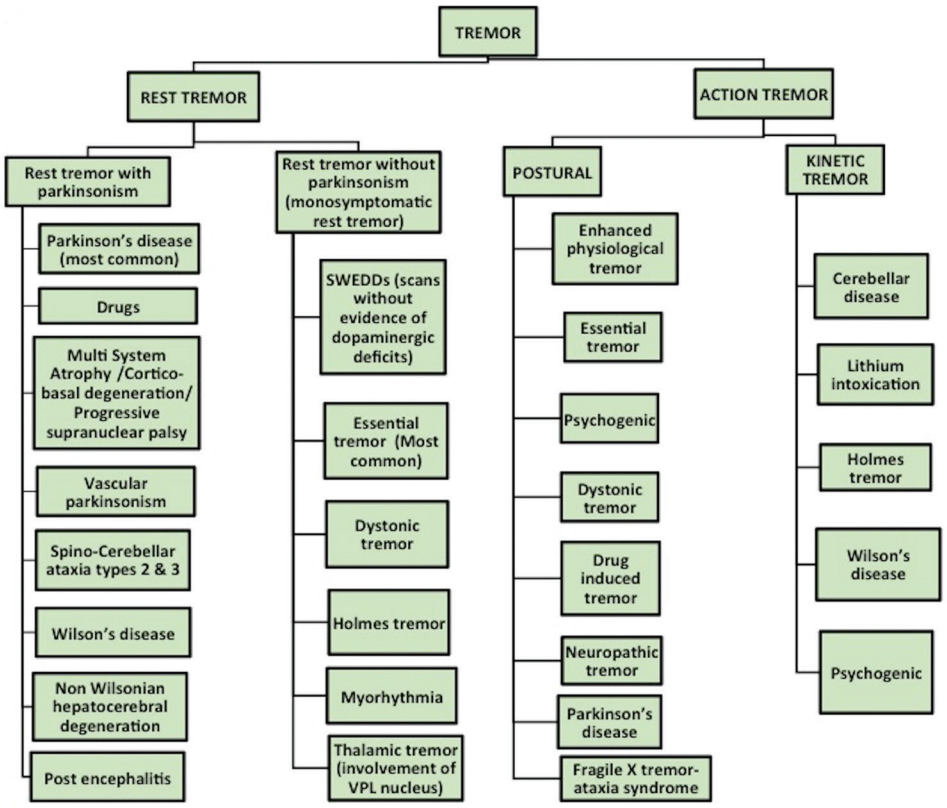

Figure 1: Classification and causes of different types of tremor

and etiology, which in turn aids in the management. Tremor can also be classified based on its frequency, amplitude, anatomical distribution, exacerbating or alleviating factors, and associated neurological signs [Table 1].[5-9]

Tremor Syndromes

Rest tremor

Rest tremor is characteristically present when the involved extremity is completely supported against gravity. They subside when the involved limb is put into action.

Parkinson's disease

The most common cause of rest tremor is Parkinson's disease (PD).[9] There are three tremor syndromes associated with PD.[1,9] These are the classical rest tremor or rest plus postural/kinetic tremor of same frequency (re-emergent tremor), second is the rest plus postural/kinetic tremor of differing frequencies with the latter having a higher frequency (5–8 Hz), and third isolated postural and kinetic tremor with a frequency of 4–9 Hz.

The typical tremor of PD is a 4–6 Hz rest tremor. It is characteristically unilateral at onset and involves the distal upper extremity initially. The classical "pill rolling" tremor consists of movement at the thumb and forefinger, giving the appearance as though the patient is trying to roll something in between these fingers. Rest tremor could also be in the form of flexion - extension of the wrist, pronation - supination at the forearm, and abduction - adduction of leg.[10,11] Rest tremor in PD not only involves hands but also involves lips, chin, jaw, and legs and rarely the neck, head, or voice which are seen more commonly with ET.[12]

Table 1: Classification of tremor according to frequency, amplitude, and body part involvement characteristics

Classification based on frequency
Low (<5 Hz): Intention tremor
Low to medium (3-6 Hz): Holmes tremor, PD rest tremor
Medium to high (4-12 Hz): Enhanced physiological tremor, ET
Very high (>12 Hz): Primary orthostatic tremor
Variable: Psychogenic tremor
Classification based on amplitude
Low: Enhanced physiological tremor
Moderate: ET
Large: Parkinsonian tremor, Holmes tremor
Classification based on body part involved
Head tremors: ET, cervical dystonia, cerebellar degenerative disorders, rarely in PD
Jaw tremor: PD, ET, orthostatic tremor, hereditary geniospasm
Voice tremors: ET
Leg tremor: PD, orthostatic tremor

ET = Essential tremor, PD = Parkinson disease

The "re-emergent" tremor appears after an interval of few seconds (range 1–47 s vs. a latency of 0 s in ET) of maintaining the arm in front and it has a similar frequency as that of a rest tremor.[13] Some patients with PD may have an associated or an isolated action tremor. This action tremor is responsible

for the motor disability in PD rather than the more common rest tremor.[13]

Other causes of rest tremor

When a patient presents with rest tremor, it is natural to assume that the patient has PD, even more so if the tremor is asymmetrical. However, it is important to remember that there are a few other causes of rest tremor, which have been highlighted in Figure 1.[3,14,15] Certain patients develop only a rest tremor, which persists beyond 2 years without development of other cardinal signs of PD [Figure 1].[1,16] The term "monosymptomatic rest tremor (mRT)" has been used to describe these patients. Majority of these patients are diagnosed as PD by functional imaging. In the minority, however, there is no presynaptic dopaminergic deficit and these cases are diagnosed as scans without evidence of dopaminergic deficits (SWEDDs).[17] A higher score on the motor examination of Unified Parkinson Disease Rating Scale and difficulty with gait, posture, and stance favor a diagnosis of PD, whereas the presence of bilateral tremor is more often a feature of SWEDDs. Furthermore, the amplitude of tremor may help determine the cause of the mRT with highest amplitude of rest tremor seen with PD while patients with SWEDDs, dystonic tremor, and ET have the highest amplitude during action.[18]

Parkinsonian syndromes other than PD such as multisystem atrophy, progressive supranuclear palsy, and corticobasal degeneration are important causes of rest tremor [Figure 1]. Certain drugs, which have dopamine receptor-blocking property, can also produce rest tremor. These drugs include antipsychotics, antiemetics (metoclopramide), and antivertigo medications (prochlorperazine).[1,3,14] Certain nondopamine receptor-blocking drugs can also produce rest tremor. These are valproate, calcium channel blockers (cinnarizine, flunarizine), selective serotonin reuptake inhibitors, lithium, tetrabenazine, and amiodarone [Figure 1].[1,3,14]

Action tremor

Action tremor occurs when a limb is voluntarily contracting. It is subdivided into postural, kinetic, and isometric tremor. Action tremors make up the largest group of tremors. ET is the most common neurological cause of action tremor.[3] Three important tremor syndromes included under this category are enhanced physiological tremor, ET, and cerebellar and psychogenic tremor (PT). Certain uncommon tremor syndromes such as orthostatic tremor, task-specific tremor, Holmes tremor (HT) also present with action tremor.

Enhanced physiological tremor

As the name suggests, physiological tremor occurs in all normal people when muscles are actively used. Physiological tremor is not usually visible to the naked eye because its amplitude is very low. When this tremor becomes visible due to increased sympathetic activity, it is termed as enhanced physiological tremor. Enhanced physiological tremor is the most common cause of a postural tremor. This increased sympathetic activity can be brought about by certain diseases or drugs [Table 2].[1,3,4,7,8,14] The tremor is typically a fine postural or kinetic tremor in the hands and fingers. It is symmetrical and has low amplitude and high frequency (7–12 Hz).[5,9] Patients typically give a history of the tremor surfaces only under certain conditions such as stress, fatigue, anxiety, medication use, or caffeine intake. Moreover, such patients do not require to be investigated any further. They improve by removal of the offending agent.

Table 2: Causes of enhanced physiological tremors

Drugs and toxins
Beta adrenergic agonists (P)
Amphetamines (P)
Methylphenidate (P)
Xanthines, theophylline (P)
Pseudoephedrine (P)
Nicotine (P)
SSRIs, TCAs (P)
Antipsychotics such as haloperidol
Levodopa
Caffeine (P)
Antiepileptic drugs such as carbamazepine and valproate (P)
Benzodiazepines
Opioids
Lithium - acute intoxication (I), chronic use (P)
Cardiac drugs such as amiodarone, verapamil (P)
Thyroid hormones (P)
Corticosteroids (P)
Cyclosporine (P)
Antiemetics such as metoclopramide (P)
Cocaine (P)
Calcium channel blockers (cinnarizine, flunarizine) (R)
Toxins - mercury (P)
Alcohol - acute withdrawal (P), chronic intake (I)
Diseases
Hyperthyroidism (P)
Pheochromocytoma
Hypoglycemia
Hyperparathyroidism
Hepatic encephalopathy
Electrolyte imbalances (hyponatremia, hypocalcemia, hypomagnesemia)
Hypoglycemia
Situations
Fatigue
Excitement
Anxiety
After a strenuous activity/exercise
Fever
Alcohol withdrawal

P = Postural tremor, I = Intention tremor, TCAs = Tricyclic antidepressants, SSRI = Selective serotonin reuptake inhibitor

Drug-induced tremor

Drug-induced tremor can present as rest or action tremor. The most common form is the enhanced physiological tremor due to drugs [Table 2]. Advancing age and consumption of multiple drugs is a strong risk factor.[19] Drug-induced postural tremor is symmetrical and has a frequency of 6–8 Hz.[9,20] Tardive tremor most commonly presents as postural tremor and can rarely be present at rest. It has a frequency of 3–5 Hz and is of high amplitude. It typically occurs on exposure to neuroleptic (dopamine receptor-blocking agents) drugs and can resemble a Parkinsonian rest tremor.[1,3,14] However, it tends to

be more symmetrical than Parkinsonian rest tremor.[3] Usually, this tremor is nonprogressive and responds to drug withdrawal or reduction in dose.

Essential tremor

ET is the most common tremor disorder as well as the most common movement disorder described.[5,21] It is defined as a symmetrical postural tremor with or without kinetic component that involves hands and forearms lasting for more than 5 years and having a gradual onset and should not be explained by any other underlying disorder.[1] ET has both components of postural and kinetic tremor, with predominance of one or the other. The amplitude of the kinetic tremor is more than that of the postural component and the kinetic tremor typically increases in amplitude as the target is approached (intention tremor). Age is a risk factor for the development of ET, with the prevalence estimated to be 0.9% in people older than 65 years and increasing to 21.7% in the oldest old.[22,23] ET predominantly involves the hands with involvement of upper limbs seen in 95% of the patients.[3] The typical frequency of the tremor is 5–10 Hz and it tends to be largely symmetrical.[5] However, it can be asymmetrical and more prominent in the dominant limb.[24] With the passage of time, typically, the tremor frequency decreases and the amplitude increases.

The tremor in ET may involve other body parts such as voice, head, neck, and legs but not in isolation without the involvement of hands.[25] Head, voice, and jaw tremors tend to become more prevalent with longer duration of the disease. Important to remember is that if head tremor occurs, then it is a late manifestation of ET; hence, if there is an isolated head tremor in a young patient, then it is likely that he/she has cervical dystonia.[26] Isolated voice tremor was thought not to be seen in ET, but recent studies have shown that isolated voice tremor may be a spectrum of ET.[27] One-fourth of patients with ET have a voice tremor. Voice tremor as well as head tremor tends to occur in women and in the older population, suggesting that older age and female sex are defining features of the midline ET symptoms.[27,28]

In severe advanced cases, 20–30% of patients with ET may demonstrate rest tremor.[29] However, one important clue to differentiate the rest tremor of PD from that of ET is that in the former the rest tremor persists while walking and in the latter it disappears. Presence of isolated rest tremor in the upper limb in the absence of an action tremor is rarely seen in ET, also presence of rest tremor in the legs is extremely rare in patients with ET.[15] Red flags for the diagnosis of ET are presence of a unilateral tremor, tremor predominantly in the legs, tremor in a hemidistribution, isolated head tremor with posturing, isolated voice tremor, lip tremor, and predominant rest tremor. ET has been considered to be a monosymptomatic disorder, with tremor as its sole feature. However, recent studies have shown that it may not be the case. ET is associated with several other neurological findings, which include cerebellar signs, psychiatric and cognitive disturbances, olfactory and hearing impairments, as well as abnormal sleep patterns.[30]

Cerebellar tremor

Cerebellar tremor is classically defined as an intention tremor, i.e., the tremor that worsens/occurs only on approaching a target.[1,3,9] This tremor is of low frequency and variable amplitude. The tremor frequency in the arms is about 3–8 Hz but lower in the legs (1–3 Hz) and trunk (2–4 Hz).[8] Cerebellar lesions can also produce a postural tremor.[1,3] A postural tremor of the head as well as that of the trunk may also be seen.[8]

Dystonic tremor syndromes

Tremor and dystonia, being one of the common neurological disorders, can coexist in the same patient. Dystonic tremor syndromes can be mistaken for ET or PD and the differentiation from them is given in Table 3. Dystonic tremor syndromes are divided into dystonic tremor, tremor associated with dystonia (TAWD), and dystonia-gene associated tremor.[1] Tremor in dystonia involves most commonly the head or arm, followed by the jaw, facial, or voice tremor and least the legs.[31]

In dystonic tremor, dystonia as well as tremor (postural/kinetic) is simultaneously present in the same body part, for example, dystonic head tremor.[32] This tremor is position specific. Dystonic head tremor differs from essential head tremor by being jerky, more pronounced when the head is turned to one side and by its persistence while lying down. It also shows the null point phenomenon, i.e., tremor decreases when placed in the direction of pull. Sensory tricks, neck pain, and hypertrophy of neck muscles are all seen in dystonic head tremor.

Features that favor a dystonic rather than Parkinsonian tremor are task- or position-specific tremor, presence of head tremor, dystonic voice, no evidence of other Parkinsonian features as well as the tremor being thumb extension, rather than the characteristic pill rolling tremor of PD.

Dystonic voice tremor can be differentiated from essential voice tremor by the presence of "geste maneuvers" such as cessation of tremor on changing pitch or singing.

TAWD is characterized by the presence of tremor in one body part and dystonia in another, for example, postural tremor in hands with cervical dystonia. The third type, i.e., dystonia-gene associated tremor is the presence of tremor in a patient who has family history of dystonia. Currently, dystonic tremor and TAWD are clubbed together since they tend to share demographic as well as clinical features.[22]

Uncommon tremor syndromes

Task-specific tremor occurs predominantly when executing a specific and a skilled task that is not associated with an abnormal posturing.[1,14] Primary writing tremor is considered to be the most common of these.[8] It can be associated with postural and intention tremor. The tremor is a pronation/supination that occurs at the wrist joint.[33] The frequency of this writing tremor is between 4 and 8 Hz.[8] It has been classified into two types depending upon whether the tremor occurs during the actual task of writing (type A, task-induced) or when the hand adopts a writing posture (type B, position-specific).[34] Other examples of task-specific tremor are voice tremor, golfers tremor, laughing tremor, tremor in musicians, and other trained professionals.[1,8]

Orthostatic tremor is a rare, high-frequency symmetrical tremor of 13–16 Hz involving the legs and trunk. It occurs more

Table 3: Differences between essential tremor, Parkinson disease tremor and dystonic tremor

Characteristics	Essential tremor	Parkinson disease	Dystonic tremor
Age of onset	Bimodal (15-20 years or between 50-70 years)	55-75 years	Any age
Sex distribution	Equal	Males >females	Females >Males
Laterality	Bilateral; very rarely unilateral	Unilateral at onset	Asymmetrical
Tremor frequency	5-10 Hz	4-6 Hz	1-6 Hz, increases on active movements
Tremor at rest	Rare, can be seen in advanced cases	Yes, characteristic	Less common, may resemble parkinsonian rest tremor
Re-emergent tremor	No	Yes	May be present
Tremor on action	Prominent	Lessens	Prominent
Head tremor	Common (late manifestation; yes-yes or no-no type)	Less common	Isolated head tremor without hand involvement suggests DT
Voice tremor	More common, may be present in isolation	Less common	Less common
Lip tremor	Rare	Yes	Rare
Jaw tremor	Yes	Yes	Rare
Rigidity, bradyki- nesia, and impaired postural reflexes	No	Yes	Dystonic slowness can resemble bradykinesia
Decreased arm swing	No	Yes	Maybe present in the dystonic limb
Handwriting	Large angulated loops and tremulous	Micrographia with mild tremors	Macrographia
Abnormal posturing of head/limb	No	No	Yes
Task or position specificity	No	No	Yes
Sensory tricks	No	No	Yes
Null point phenomenon	No	No	Yes
May be associated with myoclonus	Never	No	Yes
Dopaminergic deficits on functional imaging	No	Yes	No
Response to alcohol	Yes (in 50%)	May be seen (anxiolytic effect)	May be seen
Response to Levodopa	No	Yes	Dystonic posture improves in dopa responsive dystonia

commonly in women and is typically seen in the sixth to seventh decade.[8,20] It presents exclusively on standing, decreases on walking, and altogether disappears on sitting or lying down.[1,9] Patients may only complain of having poor balance while standing and assuming a wide base, which gets relieved on walking. Although classically described in the legs and trunk, it may also be seen in the arms, especially on weight bearing and also in the jaw.[35] This tremor may be visible as a fine ripple or palpable or could be heard via a stethoscope placed over the thigh or calf muscles, which produces a thumping sound resembling the sound of a helicopter.[14,20] HT is a rare tremor affecting the proximal parts of the limbs. It has been called by various names, which include rubral and mid-brain tremor. This tremor is typically present at rest and worsens on posture and movement. It has a low frequency (2–5 Hz) and high amplitude. A lesion in the thalamus, upper brainstem, or cerebellum can cause HT.[3,14] It is important to differentiate the rest tremor of HT from that of PD. In HT, the rest tremor has a frequency of <4 Hz and involves proximal part of the limbs whereas PD causes the classic pill-rolling tremor of 4–6 Hz involving the limbs distally.[14] Thalamic tremor occurs due to involvement of dorsolateral part of the thalamus and resembles HT. The differentiating feature is the presence of associated dystonia. HT should also be differentiated from myorhythmia, which is a slow (1–4 Hz) rhythmic movement mainly affecting the cranial or limb muscles. Typically, HT does not involve cranial muscles and has higher amplitude. Myorhythmia presents mainly at rest, whereas HT occurs as rest and kinetic tremor.

Wilson disease is an important treatable cause of action tremor before the age of 40.[3,8] All types of tremor are seen, but rest and/or postural tremor are the most common.[5] A very characteristic form of tremor in Wilson disease is the proximal "wing beating" pattern, which is brought out by placing the arms abducted with elbows flexed. Neuropathic tremor develops in patients with demyelinating peripheral neuropathy.[36] These tremors are usually postural or kinetic and occur in hands/arms which may be symmetrical or asymmetrical. Their frequency ranges from 3 to 6 Hz.[3,20]

Psychogenic tremor

Among all the psychogenic movement disorders (PMDs), tremor is the most common. It makes up 50% of all PMDs.[37] PT is characterized by the presence of rest, postural, or kinetic tremor, but most often all three types are seen in unison.[9] The tremor characteristically starts in both arms spreading to involve the head and legs.[3] Diagnosis of PT relies on history

and clinical examination. Tremor that is of abrupt onset, with changing characteristics, is suggestive of PT. Excluding other organic tremors to reach a diagnosis of PT is not sufficient enough, demonstrating certain signs which are compatible with PT is essential [Table 4]. These signs, especially entrainment, coherence, and coactivation, can also be objectively recorded using surface electromyography (EMG) and accelerometer.

Clinical Approach to Tremor

What do you see?

The first step in managing a patient with any movement disorder is to correctly identify the type of abnormal movement, which may be involuntary or voluntary (psychogenic). Involuntary movements are often nonsuppressible (tremor and myoclonus), but some can be partially suppressed (tics and stereotypy). Key feature that sets tremor apart from other movements is the rhythmicity, i.e., the oscillations occur at a regular frequency. Chorea, ballismus, and tics have a jerky component not seen in tremor. Rhythmic myoclonus, which includes epilepsia partialis continua and cortical tremor, can mimic tremor.[9] Clonus which occurs on passive stretching of joints could also be confused for tremor.

Clues in history

Once the movement has been recognized as tremor, the most important step is to establish the etiology. To do so, a stepwise systematic approach has to be adopted, and taking a good history is the first step. Age at onset could provide vital information. ET has a bimodal peak, whereas orthostatic tremor and PD occur in older age group. An acute onset would suggest a vascular event, tumor, cerebellitis, demyelinating lesion, toxin, or psychogenic origin. A slowly progressive tremor is more likely to be ET or PD. A symmetrical tremor is more likely to be due to ET or physiological tremor. Asymmetry is the hallmark of PD as well as an acute vascular event or tumors. As outlined, above drugs are capable of causing all forms of tremor; however, they tend to be symmetrical most often. Tremor exclusively brought about by fatigue, exercise, or caffeine could be enhanced physiological tremor, and just reassurance should be sufficient.

Examination of rest and action tremor

Observing the patient as he walks into a room and is seated could be very helpful. The patient may even be anxious enough in the beginning of the examination, which would bring out his rest tremor. Most tremors of clinical significance have a frequency range of 4–12 Hz.[1] The frequency range of rest tremor is 3–6 Hz and that of postural tremor is 4–12 Hz, and for kinetic tremor, it is 2–7 Hz in most instances [Table 1].[38] Subjecting the patient to stressful maneuvers could help in bringing out the subtle rest tremor [Table 5]. Action tremor is present during voluntary activity and when the limb in

Table 4: Diagnostic clues in psychogenic tremors

Historical clues
Abrupt onset
Changing tremor characteristics
Episodic with spontaneous remissions
Spontaneous recovery in one limb only to occur in another limb
Comorbid psychiatric illness
Associated somatic complaints
History of psychological stressors/stressful precipitating event
History of other functional disorders
Examination clues
Distractibility - Change in tremor amplitude/direction or complete cessation of tremor on distracting the patient with another task, for example, counting the months backward, serial sevens, or finger tapping with the other limb
Variability - A constant change in the amplitude, frequency, or the direction of the tremor
Presence of whole body tremor
Absence of finger tremors
Ballistic movement test/pointing test
Tremor in the “involved” limb stops while a sudden ballistic movement is performed by the unaffected limb
Entrainment - The tremor in the affected limb “takes on” the rhythm of the movement of the opposite, unaffected limb, i.e., it gets “entrained.” For example, ask patient to tap with “unaffected hand” at a lower frequency than “manifest tremor”
Coherence entrainment test - Demonstrating that two limbs are tapping at the same frequency helps identify psychogenic tremors as two hands cannot tap at different frequencies simultaneously
Suggestibility - Variation in the tremor with certain suggested stimuli, for example, tuning fork application to the affected limb and suggesting that patient will have tremors at the frequency that the fork is vibrating
Coactivation sign - Simultaneous activation of extensors and flexors in a limb before the alternating pattern of contraction of muscles develops clinically manifesting as increased tone. Once this increased tone disappears, so does the tremor
Tremor moves from one limb to another especially when the “tremulous” limb is held
When the examiner places his hands firmly on the tremulous limb, it gets exaggerated
Loading of the limb with weights enhances the amplitude of the tremor unlike a decrease seen in physiological and pathological tremor
“Give way” weakness on examination
Spiral drawing - Draws a spiral with several pauses, with parts of the drawing showing differing amplitude and directions
Gait - Has an irregular frequency, direction, deliberate pauses
Pull test - Exaggerated, but no fall

question is put into action [Table 5]. Spiral drawing could help differentiate between ET, DT, and PD [Figure 2]. Task-specific tremor is obvious during particular tasks such as primary writing tremor and voice tremor, which can be brought out by asking the patient to hold a long note.

Table 5: Examination of rest and action tremors

Type of tremor	Examination findings
Rest tremors	• Observe when taking history • Hold the arm so as to eliminate gravity (placing it on one's lap in semi-prone position of the arm or placing it on the armrest, letting the arms hang loosely by the side and if supine then place it on the abdomen) • Maneuvers to elicit subtle rest tremors (cognitive/motor co-activation)- count backwards from 100, recite months backwards, serial seven subtractions, name words starting with a particular letter, open/close opposite hand • Hold limb against gravity- re-emergent tremor seen in PD • Analyze the pattern of movement- pill rolling in PD, rarely in MSA, DLB and PSP; in dystonic tremor it is thumb extension tremor • Check for cog wheel rigidity- ask patient to draw imaginary circles in air with the non involved hand, tremor and rigidity becomes more pronounced in the involved limb
Postural tremors	• Hold the arms out in front of the chest with fingers open, forearm pronated for 10-15 seconds. • Subsequently supinate his arms to elicit the position specific dystonic tremor. • To better visualize the tremor place a slip of paper on top of the hands • Load the arm with weight (glass of water) to make the tremor obvious • Wing position: abduct shoulders, flex elbow, place index fingers an inch apart in front of chest; sensitive to proximal and dystonic tremors
Kinetic tremors	• Nose-finger-nose and finger chase test in the upper limbs • Knee-heel-shin and toe-to-finger test in the lower limbs • Simple maneuvers like pouring water from one glass to another or drinking a glass of water • Spiral drawing and handwriting are excellent ways of documenting kinetic tremors • Look for increase in tremor amplitude as the body part reaches its target (intention tremor)

PD = Parkinson's disease, MSA = Multiple system atrophy, DLB = Diffuse lewy body disease, PSP = Progressive supranuclear palsy

General physical and neurological examination

Before going to the neurological examination, it is important to look for some clues in the general physical examination. Tachycardia, neck swelling, and eye signs could suggest hyperthyroidism. Signs of liver dysfunction and chronic alcoholism should be noted.

A thorough neurological examination starting from the cranial nerves to gait is necessary.

Eye movement abnormalities are seen in cerebellar disorders and Parkinsonian syndromes. Any patient presenting with action tremor before 40 years should be examined for Kayser–Fleischer ring in the cornea to rule out Wilson's disease. Rigidity, especially cogwheeling and bradykinesia, should be looked for in all patients who present with a rest tremor. Eliciting intentional component of the tremor localizes the pathology to the cerebellum.

Examining the gait could also help in diagnosing the cause of the tremor with normal gait seen in ET and characteristic gait observed in cerebellar disorders or PD.

Investigations

Tests for chronic liver disease, thyroid function tests, serum ceruloplasmin, and 24-h urine copper and toxin screen should be done.[10] Magnetic resonance imaging (MRI) of the brain is indicated when a patient presents with acute onset intention tremor. It is, however, not indicated routinely in all patients.

Since structural neuroimaging would be normal in the early stages of PD, [^{18}F]-labeled L-3,4-dihydroxiphenylalanine positron emission tomography imaging is considered to be the best diagnostic modality and it also helps differentiate it from other Parkinsonian syndromes as well as ET.[20,39,40] Dopamine transporter single-photon emission computerized tomography could also be used for this purpose. The dopamine striatal neurotransmission in patients with ET, PT, and drug-induced tremor is normal.[30]

Assessment of tremor

Clinical rating scales

There are different ways to measure tremor, which includes either using a clinical rating scale or transducers-based measurement. The former is still popular, but the major

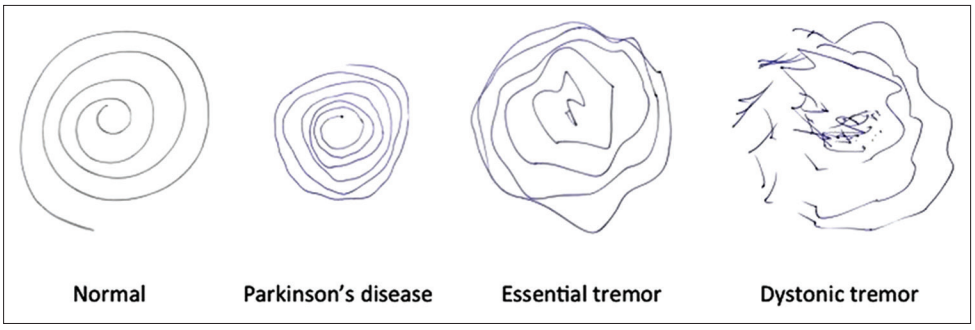

Figure 2: Archimedes spirals drawn by a normal volunteer and patients with Parkinson's disease, essential tremor, and dystonic tremor. A small spiral (micrographia) occurs in Parkinson's disease; whereas, in essential tremor, moderate amplitude of oscillations is present throughout the task. The spiral drawing in a dystonic tremor patient is showing a directional preponderance, which suggests the same muscle groups are constantly involved

drawback when compared to the electrophysiological analysis is that these cannot quantify the tremor in terms of frequency and amplitude. The current approved scales by MDS for tremor severity assessment are given in Table 6.[41]

Electrophysiology/biomechanical evaluation

Transducer-based measurements to quantify and characterize tremor include surface EMG, accelerometer, digitizing tablet-based measures, and several others. These transducers are especially useful in monitoring the disease progression as well as in noting the response to treatment.[42] Accelerometer, gyroscope, and surface EMG are equally good in assessing the tremor frequency; however, for measuring amplitude, only the former two transducers are good.[42]

Surface electromyography

Surface EMG is done using skin electrodes that are placed over muscle bellies. Surface EMG helps in identifying pathological tremor as well as in quantifying them [Table 5]. The majority of the healthy people with physiological tremor show no rhythmic EMG activity, which differentiates it from organic tremor.[43]

Accelerometer

It is the most common method used to electronically evaluate a tremor.[44] It is considered the gold standard in quantifying tremor amplitude.[45] A change in tremor frequency noted on accelerometer rather than amplitude is more suggestive of PT as organic tremors may also show change in amplitude [Table 7].[45-53]

Other transducers

Gyroscopic transducers are similar to accelerometers, but they measure angular acceleration compared to the linear acceleration measured by latter.[44] They are also useful in quantifying pathological tremor in terms of amplitude and frequency.[46] Actigraphs can be worn on the wrist and is the size of a watch. It can measure the tremor amplitude and frequency over prolonged periods and during various activities.[46] It can also be used to detect the presence of pathological tremor as well as to monitor the change in amplitude with treatment.[46]

Although accelerometer quantifies the postural tremor, the main disability in is the task-related kinetic tremor in ET. Spiral drawing and handwriting are useful tasks that can be performed and graded visually. Digitizing tablets are one-way

Table 6: Different scales for assessment of tremor severity

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 spirography 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

Table 7: Electrophysiology and biomechanical evaluation of tremors

Surface Electromyography (EMG)	Physiological tremors don't show any rhythmic activity on EMG
	Quantifies pathological tremors in terms of frequency
	Gives mean amplitude of oscillations and not the absolute amplitude
	Burst duration can be useful in identifying the type of pathological tremor
	Can identify if tremor contractions are synchronous or alternating
	Useful in studying upper limb pathological tremors
	Can record entrainment, coherence, distractibility, ballistic movement in psychogenic tremors
Accelerometry	Most common method used to electronically evaluate a tremor
	Measures tremor amplitude and frequency
	Can detect sub-clinical cases of essential tremor (ET)
	Study the effect of treatment
	Helps differentiate from other movements
	Wide variations in frequency and amplitude in psychogenic tremors can be measured
	The tremor frequency is the same when recording is made from several body parts in psychogenic tremor whereas it differs in the 2 arms in ET
	Arm loading increases amplitude in psychogenic tremors which is recordable
	Co-activation sign: tonic contraction of wrist extensor and flexor can be demonstrated before the alternating reciprocal tremor bursts develop
	Used intra-operatively to decide the best position for the placement of electrodes during DBS

to quantify the writing and drawing of a patient with tremor.[54] These devices, however, are unable to detect physiological tremor and mild organic tremor. These devices can quantify tremor severity but cannot differentiate between the various types of pathological tremors.[54]

Force sensors estimate the amount of joint movement, which is especially useful in the hands as it can give valuable information regarding the muscles involved. This in turn can be utilized in planning botulinum toxin injections.[42]

Treatment

The treatment of tremor is symptomatic. It can be treated with medications, botulinum toxin, or surgery.

Medical treatment

The medical treatment of tremor not only depends on the underlying disorder but also depends on how disabled the patient is due to the tremor.[55] The current treatment recommendation for postural limb tremor in ET is with propranolol or primidone as both these drugs reduce tremor amplitude by 50%.[56,57] Both these drugs are known to be efficacious for a year at least after starting treatment.[58] However, their long-term effects are unknown.[55] In nearly one-third to one-half of patients, these drugs fail to produce a response.[57] Drugs that are emerging as alternative therapy and could be effective for postural limb tremor in ET are topiramate, gabapentin, and clonazepam.[56] A trial of other beta blockers such as metoprolol, atenolol, sotalol, and nadolol can also be given, but none have them have been found to be superior to propranolol.[55] Insufficient evidence exists for diazepam, lorazepam, levetiracetam, pregabalin, zonisamide, tiagabine, sodium oxybate, phenobarbitone, flunarizine, and amantadine in the management of essential limb tremor.[55]

Recently, it was shown that long-chain alcohol, 1-octanol, could be effective in treating limb tremor in ET.[59] Parkinsonian rest tremor is treated with dopamine agonists and anticholinergics. Propranolol and clonazepam may benefit patients with neuropathic tremor, cerebellar tremor, and tremor seen in MS.[36] Gabapentin and clonazepam are useful in managing orthostatic tremor.[60] HT is difficult to treat, but a trial of clonazepam, trihexyphenidyl, or levodopa can be given.[55,61]

Botulinum toxin

Botulinum toxin benefits those patients who have tremor involving head, jaw, voice, and chin.[62] Its benefits in arm tremor are limited, and efficacy is modest, the side effect of wrist/finger weakness being the limiting factor.[55] However, botulinum toxin improves the clinical rating scale in patients with essential hand tremor. Therefore, it is recommended in patients with essential hand tremor that are of large amplitude, disabling, and refractory to medical treatment. Primary writing tremor shows good response to botulinum toxin.[63] Botulinum toxin is considered treatment of choice in dystonic head tremor also.[58]

Deep brain stimulation and focused ultrasound

Deep brain stimulation (DBS) could be effective in Parkinsonian rest tremor, HT, dystonic tremor, and cerebellar tremor but is most commonly used to treat ET.[5,64]

As already mentioned, nearly half of the patients with ET do not respond to medical management. DBS of the thalamic nucleus ventrointermedius (VIM) decreases tremor by 90% and should be considered in patients who do not respond to medical therapy and are severely disabled.[65] The treatment of ET with DBS produces significant response in the upper limbs, voice, and head tremor.[64] The long-term efficacy of DBS in ET has recently been shown, but the possibility of tolerance to DBS has to be kept in mind in patients with long-term stimulation.[65] Thus, DBS is a safe and effective treatment for patients with disabling ET.[64]

Dystonic tremor (axial/appendicular) tends to be medically refractory, and DBS is a good option in these patients with

improvement seen in nearly 50–80% cases.[66] The target for DBS in DT is uncertain with reports suggesting the sites could be VIM, globus pallidus internus, as well as caudal zona incerta.[66] DBS can produce side effects; however, in patients in whom all other treatments have failed, this could be a good option.

Recently, the use of transcranial MRI-guided focused ultrasound has been popularized for ET. The target site is the ventral intermediate nucleus of the thalamus. The procedure improves the hand tremor scores. It is a safe and a noninvasive procedure and can be especially considered in the treatment of disabling drug-resistant ET.[67]

Conclusion

Tremor is a common neurological condition encountered in clinical practice. Although the symptoms are minor in the majority of the patients, they can be disabling as well as resistant to treatment in some. An approach based on the phenomenological classification of tremor divides them broadly into rest and action tremor. This classification is useful since it helps in narrowing down the differential diagnosis. Although ET is the most common neurological cause of tremor, enhanced physiological tremor should always be kept in mind especially if the symptoms are brought about under certain circumstances. Parkinsonian tremor is the most common cause of rest tremor, but other causes especially long-term exposure to dopamine receptor-blocking drugs should always be ruled out.

Treatment of tremor is usually symptomatic. Propranolol, primidone, and topiramate are most commonly used for treatment in ET patients. New and upcoming therapies such as DBS and focused ultrasound could help manage patients with severe debilitating and drug-resistant ET. Botulinum toxin is the treatment of choice in primary writing tremor and dystonic tremor.

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Conflicts of interest
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