



정은 주

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Tremor

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Tremor is a rhythmic oscillation of a body part. It is the most common involuntary movement disorder in clinical medicine. Tremors are divided into those occurring mainly at rest, mainly on posture, and mainly during action. Rest tremors occur in a body part that is relaxed and completely supported against gravity. Action tremors occur with voluntary contraction of a muscle and can be further subdivided into postural, isometric, and kinetic tremors. Because tremor is usually diagnosed on the basis of their typical clinical presentation, description of tremor is very important for differential diagnosis of tremor. Therefore, the aim of this review is to describe a definition and classification of tremor in detail.

Key Words: Neurotology, Dizziness, Vertigo, Benign paroxysmal positional vertigo, Stroke

Introduction

Tremor is the most commonly encountered movement disorder symptom, and is frequently evaluated and treated in clinical practice,¹⁻⁴ and is frequently evaluated and treated in clinical practice because it may appear to be one of the simplest movement disorders.⁵

The most common tremor in patients presenting to primary care physicians is enhanced physiologic tremor, followed by essential tremor (ET) and parkinsonian tremor.^{3,6-8} Physiologic tremor is able to be enhanced by fear, excitement, or just too much coffee.⁵ All tremors are more common in older age.⁹

Because there is no diagnostic standard to distinguish among common types of tremor, which can make a difficulty in clinical separating different types of tremor.^{2,5} A

specific tremor syndrome can be diagnosed on the basis of the clinical presentation.¹⁰ For assessment of a patient with tremor, it is important in efforts to understand the pathophysiology and establish the underlying causes.^{2,5} The patient's history, the neurologic examination and the possible modifying influence of medications or alcohol can provide great clues to diagnose the cause assign of the tremor.^{2,11} In addition, the important step in diagnosis is the assignment of the patient's tremor to one of the main clinical types like rest tremor, position tremor, action tremor, and intention tremor.¹⁰

Herein, this article reviews the definition and classification of tremor in detail.

Definition and observation

Tremor is defined as a rhythmic oscillation of a body part with a relatively constant frequency and variable amplitude.^{2,5,12} The affected part in tremor must be oscillated by flexion/extension at the wrist, pronation/supination of the forearm, or continual nodding movements

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of the head.¹² For a detailed description, the clinical perspective such as its location, the circumstances in which it occurs or is maximal activation, its frequency and its amplitude are needed.¹²

First, clinician must observe the location, which is shaking.¹² The hands and arms are usually affected, but tremor is able to involve on the head, chin, leg or trunk.¹² Symmetry can give a vital clue to define; typical ET is usually affected on both hands equally, but Parkinson's disease (PD) tremor or dystonic tremor predominates on one side.¹² Second, the situation in which it occur and its aggravating factors are also important.¹² Clinician must observe whether tremor occurs at rest, or appears with posture.¹² Its situation related to movement in tremor corresponds with frequency and amplitude.^{5, 12} Third, frequency of oscillation in tremor is usually indicated as Hertz (1Hz = 1 tremor oscillation or cycle per second).⁵ The frequency of tremors can be separated into different categories: low frequency, <4 Hz; mid-frequency, 4 Hz to 7 Hz; high frequency, >7 Hz).⁵

Classification

According to its activation condition and frequency, tremor is usually divided as either resting or action.^{2, 5} A rest tremor occurs when the limbs are relaxed and completely supported against gravity.^{2, 5, 13, 14} It is typically enhanced by mental stress (e.g., counting backward) or movement of another body part (e.g., walking), and diminished by voluntary movement of the affected body part.^{1, 15, 16} Action tremors can be further subdivided into postural, isometric, and kinetic tremors.^{2, 13, 15} A postural tremor is present while maintaining a position against gravity.^{2, 5} An isometric tremor occurs with muscle contraction against a rigid stationary object (e.g., when making a fist).² A kinetic tremor presents during voluntary movement, may be significantly worsen with target-directed movement as in finger-nose testing, and includes intention tremor, which is produced with target-directed movement.^{4, 5}

1. Common or famous causes of tremor

1) Physiological tremor

A physiologic tremor is present in all persons.² Many people have a subtle, intermittent postural upper limb tremor, which may be appeared or can be enhanced by factors such as emotion, anxiety, stress, fatigue, caffeine, and certain medications and metabolic conditions.^{2, 3, 12, 13}

2) Essential tremor

The most common pathologic tremor is essential tremor.² One-half of cases show an autosomal dominant trait,¹⁷⁻¹⁹ and they affect 0.4 to 6 percent of the population.² ET is usually shown in the early adulthood but most patients do not notice until 70 years of age because of its slowly progressive nature.² Average age of onset is about 45 years and the incidence increases with advancing age.^{20, 21} Although most patients with ET have a long tremor history with little serious interference with daily living, some patients develop disability like difficult or impossible to eat with fork or to drink from a cup.^{10, 12} ET is an action tremor, usually postural, but kinetic and even sporadic rest tremors have also been described.^{1, 22} ET can affect the head, voice, and lower extremities as well as wrists and hands.^{2, 17, 23-25} It is generally bilateral, distal symmetrical tremor, and is present with a variety of tasks.^{3, 7} Low amplitude with a rapid frequency of 8 to 10 Hz is characteristic of ET.¹² Because ET is often improved with a small amount of alcohol, it is associated with increased risk of dependence in those people with a strong alcohol benefit.^{21, 26} ET can worsen with excitement.¹⁰

3) Parkinson's disease (PD) and parkinsonism

Tremor at rest suggests PD,¹⁰ although drug-induced parkinsonism and psychogenic tremors is also considered.¹² When patients show unilateral rest tremor, clinician should arouse suspicion of PD and immediately examine other manifestations such as bradykinesia, rigidity and postural instability.^{10, 27} The frequency of PD tremor is noticed at 3 to 4 Hz and it is usually lower than

that of ET.¹² It often has a pill-rolling vector, moderate amplitude and a tendency to increase with cognitive tasks or walking.¹² Tremor with slow frequency of 3 to 4 Hz does not present immediately after both arms are outstretched.¹² A re-emergent tremor, which presents with change of posture, may appear at rest after a few seconds later.¹² Despite less common, other types of rest tremor such as pronation-supination of the forearm, adduction-abduction of the leg and jaw tremor may also be seen in PD.^{12, 28} Other Parkinson plus disorders such as progressive supranuclear palsy and multiple system atrophy are usually less tremulous than PD, but may sometimes produce a rest tremor.^{29, 30}

4) Cerebellar tremor or intention tremor

This is a major one of various tremor types,¹⁰ and can be occurred on voluntary movement.¹² There is no tremor at rest, although a postural component (eg, head titubation) can occasionally be present.¹² Because it is associated with other cerebellar signs such as nystagmus, dysarthria and gait ataxia,¹² neurological examination is essential to diagnose. Various pathologies including demyelination, hereditary degeneration, tumor and stroke affecting the cerebellum may result in an intention tremor.¹² A goal-directed task looks wobbly and clumsy, when the hand approaches to a target.¹⁰ Although the classic cerebellar tremor presents a low frequency,² its amplitude and frequency increase towards the end point of the movement.³¹

5) Dystonic tremor

The term dystonia applies to abnormal co-contraction of agonist antagonist muscle pairs producing sustained abnormal postures, which tend to have a twisting character.¹² By definition, superimposed dynamic involuntary movements can also occur, and these can take the form of rhythmic oscillations.⁴ Therefore, diagnosis is difficult when the dystonia is subtle but the tremor is definitely evident. This is a rare tremor found in 0.03 percent of the population.³² It typically occurs in patients younger than 50 years.² The tremor is usually irregular

and jerky, and certain hand or arm positions will extinguish the tremor.² Other signs of dystonia (e.g., abnormal flexion of the wrists) are usually present.^{13, 32} Dystonic tremor is typically an asymmetric postural/kinetic tremor affecting one upper limb or the neck muscles, and it has a greater tendency to vary with different postures or voluntary motor tasks than other tremors.³³ Although dystonic tremor may mimic ET, it often looks more jerky than ET.³⁴ The severity of a dystonic tremor may be reduced by gently touching the affected part a phenomenon known as a sensory trick or 'geste antagoniste'.³⁵

6) Psychogenic tremor

Differentiation of organic from psychogenic tremor can be difficult.² Non-organic movement

disorders are not rare, and all of the common organic movement disorders can be mimicked by non-organic presentations.¹² Features consistent with psychogenic tremor are abrupt onset, spontaneous remission, changing tremor characteristics, and extinction with distraction.^{13, 36, 37} A psychogenic tremor may occur at rest, with posture, or on active motion and will often occur in all three situations.¹² The variability in direction, amplitude and frequency is a key sign to differentiate from other organic tremors.¹² The tremor is often enhanced when the limb is examined and reduced with distraction.¹² There is often associated with a stressful life event.¹ It may also entrain with movement of other limbs.^{4, 38-40} Patients with psychogenic tremor often show other 'non-organic' neurological signs, which include deliberate slowness of voluntary movement or sensory signs not explained by neuroanatomical principles.¹²

7) Drug- and metabolic-induced tremor

Drug-related tremors are usually postural type, and polypharmacy in elderly people is an important risk factor.⁴¹ Common tremor inducing drugs include β -receptor agonists, theophylline, antidepressants, lithium, thyroxine, amiodarone, caffeine, alcohol, marijuana, cocaine, terbutaline, pseudoephedrine, and amphetamines.⁴² Sodium val-

proate often causes a tremor that resembles ET, but can also produce a resting tremor.^{42, 43} Antipsychotics (haloperidol, flupenthixol, quetiapine, risperidone, olanzapine),^{44, 45} antiemetics (metoclopramide, prochlorperazine),⁴⁶ the dopamine-depleting drug, tetrabenazine,⁴⁷ and the calcium channel blockers, cinnarazine and flunarizine, which also have dopamine receptor antagonist properties.⁴⁸

Metabolic conditions of tremor should be considered, in particular, factors that increase plasma drug levels such as renal or liver impairment. Hepatic encephalopathy, hypocalcemia, hypoglycemia, hyponatremia, hypomagnesemia, hyperthyroidism, hyperparathyroidism, and vitamin B12 deficiency are also common metabolic causes of tremor.¹³ Hyperthyroidism, which is the most common metabolic cause of tremor,¹² produces a high frequency, fine amplitude postural tremor of the upper limbs that looks like enhanced physiological tremor (as seen with anxiety), usually with other systemic signs such as proptosis, sweating and weight loss.^{49, 50}

2. Rarer types of tremor

1) Holmes tremor

Despite of uncommon type of tremor, this is caused by damage to the cerebellar connections with the upper brainstem and thalamus.⁵¹ Multiple sclerosis and major head trauma are the most common causes.¹² Previously, Holmes tremor has been called various other nomenclature like midbrain tremor, rubral tremor, peduncular tremor) in the consensus classification.⁴ The tremor shows oscillations large amplitude and a low frequency.^{10, 12} Proximal parts, sometimes affecting the head and trunk as well as the limbs are generally affected.¹² It can be present at rest and is further activated by posture.^{10, 12}

2) Orthostatic tremor

This consists of a fine, very high frequency (13-18 Hz) tremor of both legs when standing but not sitting or lying down.^{10, 52} The tremor is symmetrical and is usually non-progressive.⁵³ The main manifestation of orthostatic

tremor is an unsteady stance.¹⁰ The patients report a feeling of uneasiness while standing,¹⁰ and complain a worsening of their problem when they have to stand in line.¹² In contrast, unsteadiness is alleviated by leaning against a wall.¹²

Patients generally unaware the tremor in the lower limb muscles,¹⁰ and do not also feel easily because of its high frequency.¹²

3) Neuropathic tremor

Tremor is associated with peripheral neuropathy and it may cause postural/action tremor.^{5, 12} A chronic acquired demyelinating neuropathy can produce distal upper limb tremor that is associated with obvious proprioceptive impairment and sensory ataxia.^{50, 54} An inherited demyelinating neuropathy such as Roussye-Lévy syndrome or Charcot-Marie-Tooth disease, causes postural tremor without major sensory loss.^{5, 55} All neuropathic tremors will be accompanied by some other signs including muscle weakness, absent reflexes, and glove and stocking sensory deficits as clues.¹²

4) Wilson's disease

Wilson disease (WD) is a rare, autosomal recessive disorder that manifests a "wing-beating" tremor or bats-wing tremor.^{2, 12} Tremor of WD in advanced stage may involve on proximal upper limb that has some similarities to a Holmes tremor.^{12, 56} Because it is a treatable but devastating disorder, serum ceruloplasmin and 24 hour urinary copper excretion should be considered when clinician see the tremor in young patients.^{2, 57}

5) Fragile X-associated tremor/ataxia syndrome

Fragile X syndrome is caused by triplet repeat expansion in the fragile X mental retardation 1 gene and is a common genetic cause of mental retardation.^{5, 12} About half of the males with premutations can present in adult life with a postural and kinetic tremor, progressive ataxia and cognitive decline.^{12, 58} Affected females commonly have ovarian failure.⁵ The tremor resembles ET, but it is often accompanied by some cerebellar disturbance and

by early cognitive or neuropsychiatric deficits.¹² One typical feature is the MRI finding of bilateral T2 hyperintense areas within the middle cerebellar peduncles.¹²

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