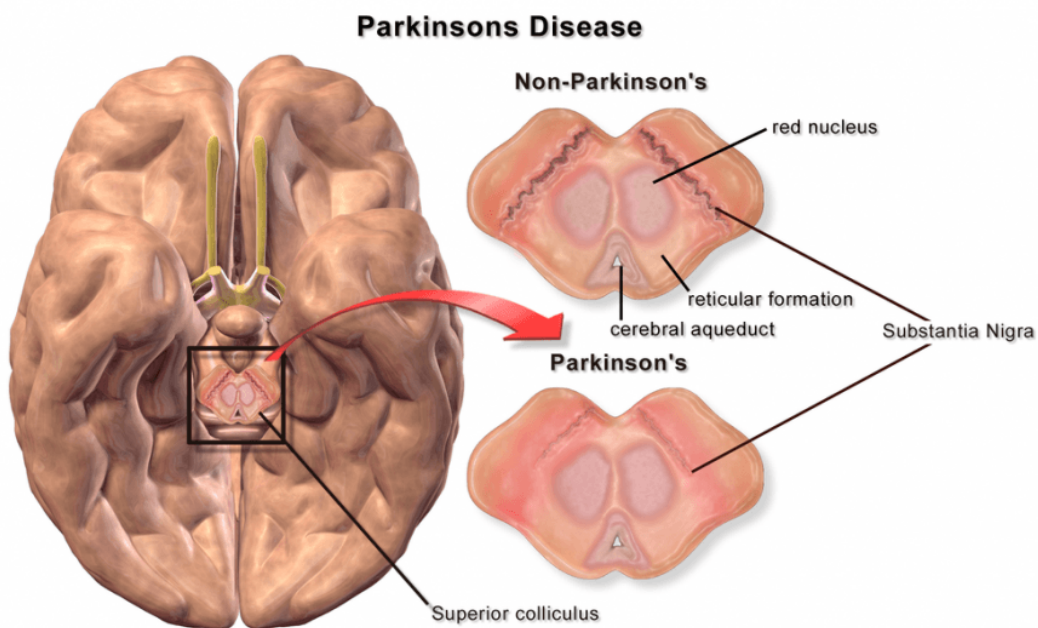


Neurology: Differential Diagnosis of Tremor

[See online here](#)

Rigor, tremor, akinesia: The classic triad of symptoms of Parkinson's disease, which you can probably recite in your sleep. However, a tremor is also a symptom of several other disorders that are relevant in clinical practice. In the following article we discuss the most important differential diagnosis of tremor. By studying the many examples and tips in this article you will be perfectly prepared for clinical exams.



Tremor: At a Glance

This article discusses the following forms of tremor, with the highlighted forms being particularly relevant for exams.

- Physiologic tremor
- **Rest tremor**
- **Essential tremor**
- Dystonic tremor
- **Intention tremor/cerebellar tremor**
- **Orthostatic tremor**
- Rubral tremor/Holmes tremor
- Neuropathic tremor
- Psychogenic tremor
- Wilson disease

Definition of tremor

Tremor: lat. tremere = shaking, trembling

Tremors are defined as involuntary, oscillatory, and rhythmic muscle contractions of a body part at a relatively constant rate. Alternate contractions in agonist and antagonist muscles lead to tremor. The tremor is the most common form of all movement disorders.

Diverse causes of tremor

TREMOR					
Essential	Neurological diseases	Internal diseases	Toxic	Drug-induced	Mental disorders
	Multiple sclerosis, Parkinson's disease, cerebellar disorders	Hyperthyreosis, diabetes mellitus, liver and kidney disease	Alcohol, lead, mercury, arsenic trioxide	Neuroleptics, lithium, bromocriptine, lidocaine, beta-sympathomimetic drugs	Anxiety disorders, affective disorders

Based on its pathophysiology, tremor is classified as an **extrapyramidal** disease and abnormal movement disorder, typically involving not only the hands but also, for example, the head, trunk, and voice, either individually or in different combinations.

The most common tremor seen in primary care is an enhanced physiologic tremor, followed by essential tremor and the tremor of Parkinsonism. All tremors present more commonly in old age.

Tremor assessment criteria

The 2 tremor assessment criteria are:

- Tremor frequency
- Situation of occurrence

Classification and characteristics of the 3 most important forms of tremor

Type of tremor	Description	Frequency	Example
Resting tremor	Occurs in a body part that is relaxed and completely supported against gravity.	4-6 Hz	Parkinson's disease
Postural tremor	Occurs when holding a position against gravity, such as holding your arm or leg outstretched.	4-8 Hz	Essential tremor
Action tremor	Only occurs when voluntary movements are attempted. This type of tremor also includes the intention tremor , which occurs specifically during voluntary movement towards a target.	2-4 Hz	Cerebellar damage, essential tremor, primary writing tremor

Source: A. Bender et al.: Mediscript Kurzlehrbuch Neurology. Elsevier Publishers, 2013. p. 293, tab. 12.3

Study tip: Read case studies well; the questions in exams on the various forms of tremor are frequently linked to the typical clinical symptoms mentioned in a case study given below.

Physiological Tremor

Physiological tremor is an action tremor and is present in every healthy person when the muscles are activated. Physiological tremor is characterized by a high frequency and a low amplitude of typically **8-13 Hz**. This type of tremor occurs in all people, in particular in the presence of stressors, for example, psychomotor agitation stressful situations, during exams, and when it is cold. The **enhanced physiological tremor** (drug-induced and toxic tremor) occurs as a side effect or sign of withdrawal from certain drugs.

Long list of medications can exacerbate tremors. Medicines most commonly implicated are sympathomimetics, (amphetamines, terbutaline, and pseudoephedrine), psychoactive medications (e.g., tricyclic antidepressants, haloperidol, and fluoxetine, lithium, valproic acid). Similarly, a large number of metabolic disorders can cause tremors. The most common ones are hepatic encephalopathy, hypocalcemia, hypoglycemia, hyponatremia, hypomagnesemia, hyperthyroidism, hyperparathyroidism, and vitamin B12 deficiency.

Alcohol withdrawal can also cause enhanced physiologic tremor.

Rest Tremor



Image: Sir William Richard Gowers, neurologist, researcher and artist, drew this illustration in 1886 as part of his documentation of Parkinson's Disease. The image appeared in his book, *A Manual of Diseases of the Nervous System*, still used today by medical professionals as a primary reference for this disease.

By: Beao. License: [Public domain](#)

Case study: For some time, a 65-year-old man has noticed a progressive slowing of his movements. When walking, his steps have become smaller and he has developed a forward-flexed posture. He has difficulty getting up from deep armchairs and turning over in bed at night. His writing has become smaller. Additionally, the patient presents with a slight resting tremor, which is more pronounced in the right hand than it is in the left. Furthermore, the patient suffers from significant back pain. [...] via [M. Wehling: Clinical Pharmacology. Thieme Publishers 2011](#)

Diagnosis of resting tremor

If a patient, as in this case, presents with resting tremor affecting one side, you have to primarily consider Parkinson's disease as the cause. To confirm this tentative diagnosis, look for the 2 other cardinal symptoms characteristic of Parkinson's disease—**rigor** and **hypokinesia**. An altered posture and decreased facial expressions usually occur early in Parkinson's disease and relatives are typically the first to notice these changes. Additional symptoms that may indicate an atypical Parkinson's disease must be excluded. Parkinson's tremor may be continuous or intermittent with fluctuating frequency and amplitude and increases with mental stress.

The characteristic **cogwheel rigidity** of Parkinson's disease may be the result of tremor and increased muscle tone (rigor). In Parkinson's disease, the frequency of rest tremor is at **4-6 Hz**, so it is also called the '**pill-turning tremor**'. More than 70% of patients with Parkinson's disease report tremors.

The tremor can become bilateral after several years, but the limbs do not tremble in synchrony.

Treatment of the parkinsonian resting tremor

The treatment of Parkinson's disease is discussed in this [link](#).

Essential Tremor

Case study: A 66-year-old woman is a carer for her considerably older husband. For some time she has observed a tremor in her hands. Her father also suffered from this in old age. However, she feels safe when climbing stairs or walking, and does not experience dizziness. The hand tremor occurs especially when she, for example, wants to pour tea into a cup or wants to carry out other focused activities. In emotionally stressful situations, the tremor also enhances.

Essential tremor is, as described in this case, action and postural tremor and occurs at the frequency of **4-8 Hz**, slightly below the frequency of physiological tremor. Essential tremor occurs with no apparent neurological underlying disease. The psychological strain is high in patients with essential tremor as people with trembling or shaking hands are often wrongly judged or labeled as alcoholics.

Epidemiology of essential tremor

Essential tremor is the most common form of tremor (5% of the population are affected).

Essential tremor may occur at any age, but most often in early adulthood. However, many patients seek help for it only after old age sets in because of its progressive nature. Men and women are equally affected.

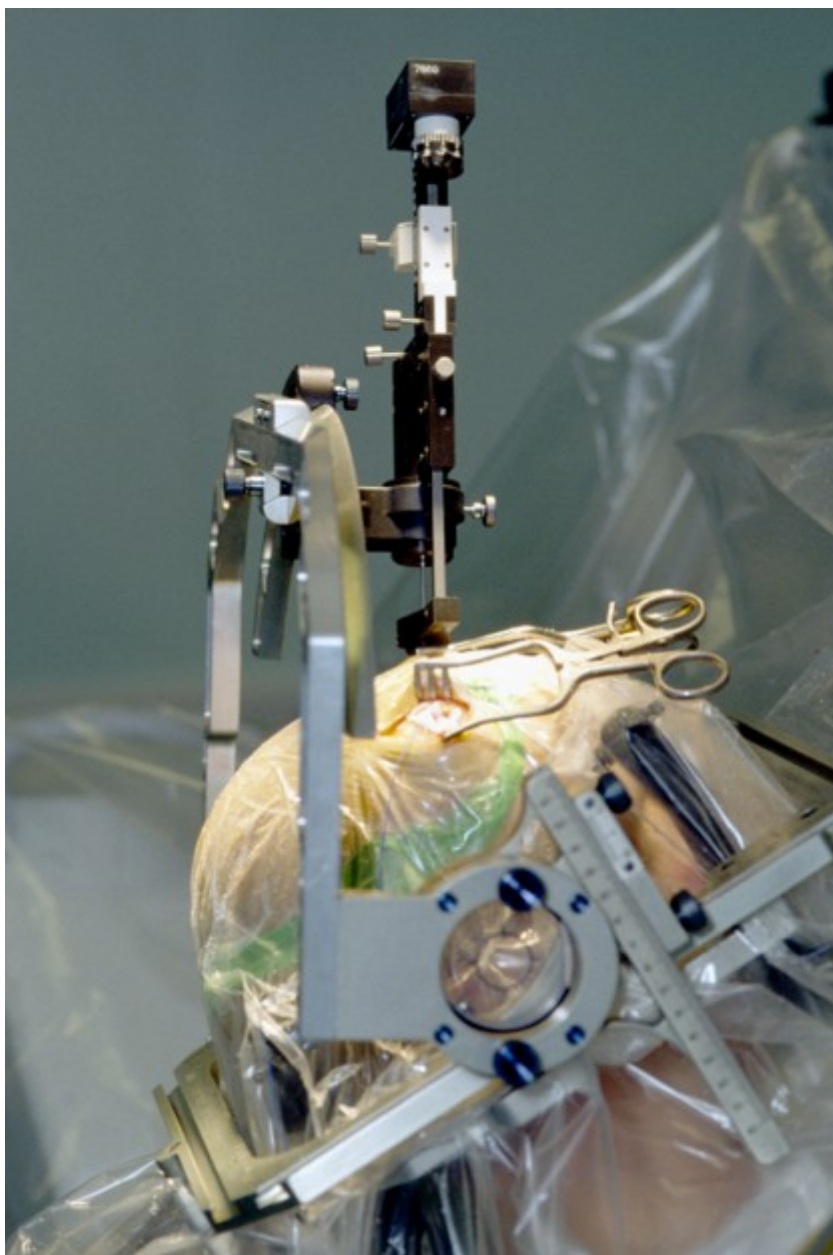
Clinical features and diagnostics for essential tremor

In patients with a positive family history, essential tremor is called **familial tremor**. The mode of inheritance is mostly [autosomal dominant](#). Unlike resting tremor, essential tremor usually begins symmetrically in both arms and can affect the head and larynx area. Depending on which muscles are affected, this can result in a **no-no tremor** (shaking of the head) or a **yes-yes tremor** (nodding of the head). If the vocal

cords are affected, patients suffer from shaking or quivering sound to the voice. Tremor involves multiple body parts in majority of cases (~50%), followed by the head in ~30% of cases, voice in ~20%, tongue in ~20%, face/jaw in ~10%, and lower limbs in ~10% of the cases. The tremor improves on consuming alcohol and worsens in times of stress.

Essential tremor treatment

Pharmacological treatment includes cardioselective beta-blockers such as propranolol, antiepileptic drugs such as primidone, gabapentin, and topiramate, or botulinum toxin type A. Patients with medication-resistant tremor may benefit from [deep brain stimulation](#) of the **ventral intermediate thalamic nucleus** instead.



[Image](#): Parkinson Surgery. By: Thomasbg. [License](#): CC BY-SA 3.0

Intention Tremor in Cerebellar Diseases

Case study: A 21-year-old previously healthy woman consults her physician. For a few days, she has experienced a slight tremor in her right hand, which increases when she carries out a deliberate target-directed movement. As she does not present with any other symptoms and has a busy professional and personal life, her GP, for the time being, suggests further observation of her symptoms [...] via [J. Priewe et al.: Das Erste. Springer Publishing 2007.](#)

Definition of intention tremor

Intention tremor (also ataxic tremor/cerebellar tremor) is a subtype of action tremor. This tremor is characterized by the trembling of the limbs during a voluntary targeted-directed movement. Intention tremor is caused by **lesions in or damage to the cerebellum**. Intention tremor does not occur during periods of rest. It affects the trunk and the extremities and can occur either unilaterally or bilaterally.

Etiology of intention tremor

Intention tremor is **symptomatic** and a clinical sign of cerebellar disease. Cerebellar lesions will result in a lack of coordination of ongoing movements (ataxia).

Causes of cerebellar tremor may be:

- Tumors
- [Hemorrhage](#)
- Ischemic strokes
- Inflammatory lesions, characteristic in multiple sclerosis (in the case study, the patient's intention tremor is the first clinical manifestation of [multiple sclerosis](#)). One of the commonest causes of intention tremor is multiple sclerosis.

Diagnosis and treatment of intention tremor

Intention tremor has the lowest frequency (**2-4 Hz**). Pathologic **finger-nose test** is indicative of an intention tremor. Frequently, difficulty executing fine motor movements can be observed for example if the affected person is asked to grasp an object with both hands. Dysmetria i.e. overshoot on finger-to-nose testing, dyssynergia i.e. abnormal heel-to-shin testing, ataxia, and hypotonia are suggestive of a cerebellar lesion.

Drugs such as topiramate, clonazepam, or propranolol are used to treat intention tremors in off-label use. In the case of unsatisfactory results, a deep brain stimulation of the **ventral intermediate thalamic nucleus** may be considered.

Dystonic Tremor

Definition of dystonic tremor

Dystonic tremor is predominantly a postural and kinetic tremor in muscles affected by dystonia. The frequency of dystonic tremor is **3-7 Hz**. Typical examples are the **dystonic head tremor**, **dystonic writing tremor**, or **dystonic vocal tremor**. The exact cause of dystonia is unknown. Some forms of dystonia are genetic, while others are secondary

(acquired). It is typically seen in patients younger than 50 years. Its frequency and amplitude are often irregular.

Clinical manifestation and treatment of dystonic tremor



Image: The muscles involved with torticollis. By: Henry Gray.
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Patients with dystonic head tremor often present with an abnormal head posture (**torticollis**). Dystonic tremors affecting the hands are frequently confused with resting tremors characteristic of Parkinson's disease. In many patients with dystonic tremors, **gestes antagoniste** (sensory trick, i.e. moving an arm to the face or head) leads to a reduction in tremor amplitude (and improvement of the dystonia). Treatment of the tremor is followed by the treatment of dystonia. The most common treatment involves drugs such as botulinum toxin, anticholinergics, and tiapride. In case of resistance to treatment, deep brain stimulation may be considered.

Orthostatic Tremor

Orthostatic tremor is a **high-frequency** tremor that is usually not visible on the outside. The **cardinal symptom** of orthostatic tremor is a sense of unsteadiness on standing. The primary causes of orthostatic tremor are unknown. Orthostatic tremor also occurs secondary to some disorders like Parkinson's disease.

Clinical features, diagnostics, and therapy for orthostatic tremor

Orthostatic tremor is characterized by a particularly high frequency of **16 Hz**, predominantly affecting the legs. Patients complain about a **feeling of swaying** and a **sense of unsteadiness on standing**. These symptoms often improve as the patient starts to walk. Patients often describe a typical unsteady feeling in the legs that may even lead to falls.

Note: In patients with orthostatic tremor, the symptoms resolve when the affected person is walking, sitting, or lying down.

Diagnosis is usually obtained based on clinical evaluation combined with surface electromyography (EMG). Confirmation of the diagnosis can be obtained by EMG showing

such high-frequency patterns.

For the treatment of orthostatic tremor, drugs like gabapentin or clonazepam are used. In very severe cases, deep brain stimulation of the **ventral intermediate thalamic nucleus** may be considered.

Holmes Tremor: Rubral Tremor in Brainstem Lesions

Definition of Holmes tremor

Clinically, Holmes tremor is defined as a **combination of symptomatic rest, action, and postural tremors**. Holmes tremor is caused by lesions affecting the brainstem, cerebellum, and thalamus. Brainstem stroke, trauma, vascular malformations, and inflammatory lesions, which are characteristic of multiple sclerosis, are the most common causes for Holmes' tremor.

Clinical manifestation and treatment of Holmes tremor

Holmes tremor tends to have a slightly lower frequency than Parkinson's tremor: **3-5 Hz**. The majority of cases of Holmes tremor do not respond to pharmacological treatment. Similar to the treatment of cerebellar tremor, Holmes tremor can also be treated using medications like L-dopa and dopamine agonists, anticholinergics, clonazepam, or clozapine in [off-label](#) use. Again, thalamic deep brain stimulation of the **ventral intermediate thalamic nucleus** may be considered.

Neuropathic Tremor

Definition of neuropathic tremor

Neuropathic tremor is a centrally generated tremor. This form of tremor often occurs in peripheral neuropathies, for example in **demyelinating neuropathy**. However, the severity of the tremor does not correlate with the severity of the neuropathy. Frequently, patients with demyelinating hereditary motor and sensory neuropathies (HMSN), or patients with inflammatory neuropathies (e.g. CIDP) are affected.

Clinical presentation and treatment of the neuropathic tremor

In addition to neuropathic pain, patients suffer from a high-amplitude tremor of a **4-8 Hz** frequency.

Treatment of the underlying inflammatory neuropathy usually improves the neuropathic tremor. In addition, medical treatment with propranolol, primidone, or pregabalin may be considered. According to case reports, deep brain stimulation of the **ventral intermediate thalamic nucleus** can provide remarkable therapeutic benefits.

Psychogenic Tremor

Psychogenic tremor can present with features like abrupt onset, spontaneous remission, changing tremor characteristics, extinction with distraction, and a history of an associated stressful life event.

Wilson disease

Wilson disease, an autosomal recessive disorder, can manifest in young persons with a 'wing-beating' tremor.

Overview: Treatment of the Most Common Forms of Tremor

	Medication	Surgical approach (if drug treatment is insufficient)
Parkinson's tremor	Dopamine agonist drugs	Deep brain stimulation (mainly nucleus subthalamus, exception VIM)
Essential tremor	Propranolol, primidone	Deep brain stimulation (VIM)
Cerebellar tremor (intention tremor)	Limited success with ondansetron, carbamazepine	Treatment success in select patients: Deep brain stimulation (VIM)
Dystonic tremor	Local botulinum toxin injections, anticholinergic drugs	Deep brain stimulation (VIM) may be considered in patients not responding to drug therapy
Enhanced physiological tremor	Treatment depends on the accurate diagnostic evaluation of the cause	
Orthostatic tremor	Gabapentin, clonazepam	In severe cases: Deep brain stimulation surgery (VIM)

Note: VIM = ventral intermediate thalamic nucleus (Source via [Ärzteblatt 13/2014](#))

Approach to Diagnosis of Tremor:

The following questions should be asked when evaluating a patient with tremor :

1. Is it an enhanced physiologic tremor?
2. History of using medications that can induce tremors?
3. Is tremor relieved with distraction?
4. Age group: young or old?
5. Young: Copper levels? Multiple anatomic/genetic/metabolic issues?
6. Old: Rest, Postural or action? History of Alcoholism?
7. Head imaging (MRI)?
8. Propranolol trial?

References

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