

Tremor

Tremor is a common condition that can occur in isolation or be part of an evolving neurological condition. It is amenable to treatment in most cases, but if first line therapies fail then often the management is complex and consideration for deep brain stimulation is considered. In this short review we outline a pragmatic approach to the patient with tremor.

Definition and Classification

Tremor is defined as a rhythmic sinusoidal movement of a body part, due to regular rhythmic muscle contractions. The most useful classification of tremors is clinical and based on the circumstances in which they are seen (see Table 1). Static tremor occurs when a relaxed limb is fully supported at rest. Postural tremor appears when a part of the body is maintained in a fixed position and may also persist during movement. Kinetic or action tremor occurs specifically during active voluntary movement of a body part. If the amplitude of such an action tremor increases as goal-directed move-

ment approaches its target, it is termed an intention tremor. This latter tremor suggests damage in the cerebellum and its efferent connections to the brainstem and is of a frequency of 2-3Hz. Psychogenic tremors are generally rare and typically are of sudden onset with a variable but rarely remitting clinical course and typically affect the trunk or limb with standing and/or using the limb respectively.

Physiologic tremor has a frequency in the 7-11 Hz band and is typically symptomatic in states of increased sympathetic nervous activity whilst symptomatic postural tremors occur in association with a wide range of neurologic



Roger Barker is co-editor in chief of ACNR, and is Honorary Consultant in Neurology at The Cambridge Centre for Brain Repair. He trained in neurology at Cambridge and at the National Hospital in London. His main area of research is into neurodegenerative and movement disorders, in particular Parkinson's and Huntington's disease. He is also the university lecturer in Neurology at Cambridge where he continues to develop his clinical research into these diseases along with his basic research into brain repair using neural transplants.



David J Burn is the editor of our conference news section and Consultant and Reader in Neurology at the Regional Neurosciences Centre, Newcastle upon Tyne. He qualified from Oxford University and Newcastle upon Tyne Medical School in 1985. His MD was in the functional imaging of parkinsonism. He runs Movement Disorders clinics in Newcastle upon Tyne and Sunderland. Research interests include progressive supranuclear palsy and dementia with Lewy bodies. He is also involved in several drugs studies for Parkinson's Disease.

Table 1: Classification of tremor

Type	Definition	Causes
STATIC or REST	Present with hands or head held relaxed at rest	<ul style="list-style-type: none"> • Parkinson's disease • Parkinsonism (inc. drug-induced, postencephalitic) • Other extrapyramidal diseases • Multiple sclerosis
POSTURAL	When limb or body is held in certain position	<ul style="list-style-type: none"> • Physiological tremor • Exaggerated physiological tremor, as in: Thyrotoxicosis anxiety states and stress alcohol drugs (e.g. sympathomimetics, anti depressants, sodium valproate, lithium) heavy metal poisoning (i.e. mercury—the 'hatter's shakes') • Structural neurological disease, as in: severe cerebellar lesions ('red nucleus or midbrain tremor')¹ Wilson's disease Neurosyphilis peripheral neuropathies • Essential (familial) tremor • Task specific tremors (e.g. primary writing tremor)²
KINETIC or ACTION (inc intention)	When performing an action of some sort, such as picking up cup of tea	<ul style="list-style-type: none"> • Brain-stem or cerebellar disease, as in: Multiple sclerosis Spinocerebellar degenerations Vascular disease Tumour
PSYCHOGENIC		

¹ Midbrain tremors results from damage in the region of the red nucleus, typically in the context of either MS, head trauma or a vascular insult. It is characterised by a combination of rest, postural and action tremor which is often severely disabling and very hard to treat, and this includes using stereotactic surgical thalamic lesions.
² Dystonic tremors can be kinetic, postural or task specific and are irregular asynchronous and usually affect the arm and neck. Primary writing tremor is such an example.

disorders. These tremors can be distinguished neurophysiologically as they have a different frequency, although there is significant overlap in tremor frequency in several common conditions associated with tremor (for example, essential tremor and Parkinson's disease).

Clinical approach to the patient with tremor

The most useful approach to a patient with tremor is a clinical one.

History and examination:

- **When did it first appear?**

Long standing implies essential tremor (ET)

- **Where is the exaggerated physiological tremor?**

Hands: Unilateral versus bilateral with bilateral tremor implying exaggerated physiological or ET. Unilateral tremor is more suggestive of either Parkinson's disease or dystonic tremor

Voice involvement implies dystonic or ET

Head involvement with head titubation suggests either cerebellar/brainstem pathology, dystonic head tremor or ET

Legs/body involvement especially when at rest with a feeling that standing still produces an intense sense of imbalance that passes off with walking is highly suggestive of orthostatic tremor

- **What, if anything, makes it better?**

Alcohol helping the tremor suggests ET

- **What brings out the tremor?**

Certain actions or movements implying it is either an action tremor, postural tremor, intention tremor or dystonic (e.g. with writing) (see Table 1).

All tremors worsen with stress and anxiety, so this is non-discriminatory

- **Is there any family history of a tremor?**

Helpful for ET and other inherited conditions where tremor is a feature (beware of the patient diagnosed as "tremor dominant Parkinson's disease" where ET was actually more likely). Are there any other neurological symptoms – bradykinesia, myoclonus and so on suggestive of Parkinson's disease or other neurodegenerative condition

- **Are there any medical problems and what drugs is the patient taking?**

Especially important to look for thyrotoxicosis or paraproteinaemic neuropathies. For example, consider cimetidine, valproate, amiodarone,

Table 2: Investigation of tremor

Routine haematology and biochemistry to exclude major metabolic problem including renal failure, liver disease +/- alcoholism
Thyroid function tests
Immunoglobulins and electrophoretic strip
Copper/Caeruloplasmin in young patients
Consider genetic tests such as SCA screening

Consider imaging, EMG-NCS, and CSF but only if tremor is late onset or evolving with other neurological signs and symptoms

Table 3: Treatment of tremor*

Stop any drug that may be causing tremor
Inc. Lithium, SSRIs, neuroleptics, sodium valproate, beta agonists, thyroxine, aminophylline etc

Drugs which are worth trying:

Beta blockers
Primidone
Benzodiazepines
Gabapentin
Topiramate

Botulinum toxin injections for some dystonic tremors

Deep brain stimulation/Thalamotomy of VIM thalamic nucleus

Other drugs and manipulations which have been tried in the treatment of tremor (ET unless otherwise indicated) with possible benefit in some cases:

Phenobarbitone
Carbonic anhydrase inhibitor (Methazolamide)
Clonidine
Amantadine
Clonidine (probably not effective in ET)
Isoniazid (probably not effective for intention tremor)
Clozapine/Olazepine/Quetiapine
Mirtazapine
Vagal nerve stimulation

* the treatment of the tremor in PD lies outside the scope of this article but clearly revolves around the use of L-dopa and dopamine agonists. It is controversial whether anti-cholinergic agents and the newer dopaminergic agonists have more anti-PD tremor effects than L-dopa based therapies.

Correspondence to:
Roger Barker, E-Mail:
rab46@cus.cam.ac.uk or
David Burn, E-Mail:
David.Burn@nuth.nhs.uk