The clinical approach to movement disorders

Wilson F. Abdo, Bart P. C. van de Warrenburg, David J. Burn, Niall P. Quinn and Bastiaan R. Bloem

Abstract | Movement disorders are commonly encountered in the clinic. In this Review, aimed at trainees and general neurologists, we provide a practical step-by-step approach to help clinicians in their 'pattern recognition' of movement disorders, as part of a process that ultimately leads to the diagnosis. The key to success is establishing the phenomenology of the clinical syndrome, which is determined from the specific combination of the dominant movement disorder, other abnormal movements in patients presenting with a mixed movement disorder, and a set of associated neurological and non-neurological abnormalities. Definition of the clinical syndrome in this manner should, in turn, result in a differential diagnosis. Sometimes, simple pattern recognition will suffice and lead directly to the diagnosis, but often ancillary investigations, guided by the dominant movement disorder, are required. We illustrate this diagnostic process for the most common types of movement disorder, namely, akinetic–rigid syndromes and the various types of hyperkinetic disorders (myoclonus, chorea, tics, dystonia and tremor).

Abdo, W. F. *et al. Nat. Rev. Neurol.* **6**, 29–37 (2010); doi:10.1038/nrneurol.2009.196

Introduction

Movement disorders, such as Parkinson disease (PD), tremor, tics and dystonia, are common conditions. The overall prevalence of PD, for example, is 1% in people aged 65–85 years, increasing to 4.3% above the age of 85 years.[1] The prevalence of essential tremor—the most common form of tremor—is 4% in people aged over 40 years, increasing to 14% in people over 65 years of age.[2,3] The prevalence of tics in school-age children and adolescents can be as high as 21%.[4]

The clinical presentation of movement disorders is complex, often variable, and sometimes even bizarre. Establishing the correct diagnosis can, therefore, be difficult, even in the hands of experienced movement disorder specialists. However, accurate recognition based on clinical acumen is important for several reasons.

First, correct classification of the type of movement disorder forms the basis for the subsequent diagnostic process. For most disorders, no specific biological marker is available that can unambiguously diagnose the underlying disease. Many diagnostic tests are available,[5,6] but these are often expensive and time-consuming, and sometimes invasive. Moreover, the diagnostic value of these tests (over and above clinical judgment) is often limited, especially in early stages of the disease. Hiding clinical uncertainty behind a broad battery of ancillary studies (the 'scattergun' approach) is generally unrewarding because of the large range of potential diagnoses. The investigational work-up can be greatly simplified once the type of movement disorder has been defined properly, because the approach to each type of movement disorder then becomes more focused. The work-up for dystonia, for example, is very different from that for chorea. Second, adequate classification—as a means to establish the correct diagnosis—often has prognostic implications. For example, essential tremor is sometimes mistaken for early PD, but the prognosis is clearly different. Furthermore, since several movement disorders are genetically determined (for example, Huntington disease [HD]), accurate classification leading to the

Competing interests
The authors, the Journal Editor H. Wood and the CME questions author D. Lie declare no competing interests.

Parkinson Centre Nijmegen (ParC), Department of Neurology, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands (**W. F. Abdo**, **B. P. C. van de Warrenburg**, **B. R. Bloem**). Institute for Ageing and Health, Newcastle University, Campus for Ageing and Vitality, Newcastle upon Tyne NE4 5PL, UK (**D. J. Burn**). UCL Institute of Neurology, Queen Square, London WC1N 3BG, UK (**N. P. Quinn**).

Correspondence to: B. R. Bloem b.bloem@neuro.umcn.nl

Key points

- The key to diagnosing movement disorders is establishing the phenomenology of the clinical syndrome
- The phenomenology is determined from the specific combination of the dominant movement disorder, the presence of any additional abnormal movements, and any further neurological or non-neurological abnormalities
- A range of conditions, both neurological and non-neurological, can mimic various movement disorders, and it is vital not to miss these lookalikes
- A systematic approach is recommended when clinicians see patients who present with one or more types of movement disorder

Box 1 | Main categories of movement disorders

Insufficient movement

Akinetic, hypokinetic or bradykinetic syndromes

Too much movement (hyperkinesias or dyskinesias)

Jerky movements

- Myoclonus (including excessive startle)
- Chorea (including ballism)
- Tic disorders

Non-jerky movements

- Dystonia (including athetosis)
- Tremor

proper diagnosis could also have implications for the patient's family. Last, differentiating between the different types of movement disorder can have important consequences for treatment.

Unfortunately, the diagnostic process is commonly perceived as being difficult, is frequently protracted, and commonly leads to misdiagnosis. Owing to their often unusual presentations, patients with movement disorders can be diagnosed as having a psychogenic disease (and vice versa).

In this Review, we present a practical approach to help clinicians in the 'pattern recognition' of movement disorders, and in the process of translating a particular movement disorder syndrome—once it has been classified clinically—into an etiological diagnosis. Our aim is not to provide an exhaustive review of the literature, and we will only touch briefly on ancillary investigations, which are beyond the scope of this article. Instead, we concentrate on the most important step in the diagnostic process; that is, the clinical approach. An unambiguous diagnostic process begins with the crucial step of recognizing the type of movement disorder that is present in the patient. We first highlight the salient features of the different types of movement disorder, attaching to each of them one or more specific keywords for ease of recognition. We then propose a practical approach, using the identified movement disorder (or disorders) as the starting point for a stepwise diagnostic work-up.

General classification principles

Generally speaking, two main categories of movement disorder phenomena can be distinguished, with several specific subdivisions (Box 1). The first category corresponds broadly to akinetic–rigid disorders, the second to hyperkinetic disorders. The hyperkinetic disorders are usually perceived as being more difficult to diagnose correctly. A helpful approach is to separate this group into two main subdivisions, one in which the movements have a jerky character, and a second in which this jerky character is absent. Few disorders feature a combination of both categories.

Akinetic–rigid syndromes

The literature uses the terms akinesia, bradykinesia and hypokinesia inconsistently. We define akinesia as an umbrella term for a symptom complex that can include bradykinesia (slowness of movement) and hypokinesia (poverty of movement, and movements that are smaller than intended), but also—crucially and fundamentally—the progressive fatiguing and decrement of repetitive alternating movements seen during finger or foot tapping. We ask the patient to make large, regular, repetitive alternating movements of each extremity in turn: opposition of the thumb to the crease between the terminal phalanges of the index and third fingers, and repeatedly tapping the forefoot on the floor, keeping the heel on the ground. It is easy to see—or, at the ankle, to hear—early progressive reduction in amplitude or speed of the movements. Sometimes, however, the clinical question is not whether akinesia or bradykinesia is present, but whether they are absent. Demonstrating absence of these features is more time-consuming, and in order to be certain we recommend asking the patient to perform up to 64 repetitions in each extremity, if necessary. Sometimes severe tremor can intervene to 'hijack' the movements, thereby making this assessment difficult or even impossible.

In the widely used Queen Square Brain Bank Criteria[7] for the diagnosis of parkinsonism, bradykinesia is defined as including fatiguing and decrement of repetitive alternating movements, which we would consider under the broader rubric of akinesia. The variability in terminology is not in itself important, provided that, whatever name one gives, fatiguing and decrement are defining features for untreated parkinsonism (note that signs of akinesia can be masked in treated patients). One must also recognize that slowness of movement, without fatiguing and decrement, is seen in pyramidal and cerebellar dysfunction (often with additional clumsiness or irregularity). This observation could explain why patients with an upper motor neuron presentation of amyotrophic lateral sclerosis (with pyramidal slowing, and increased tone due to spasticity) can, in rare cases, be misdiagnosed as having parkinsonism.[8]

An additional component of akinesia is absence or poverty of automatic movements (we refer to this as hypokinesia), manifested by, for example, hypomimia with reduced blinking, or a reduced arm swing during walking. Care should be taken not to mistake depression for a masked face, and to recognize other possible causes for reduced arm swing, since this feature can be seen in individuals who are unsteady for any reason, in patients with dystonia, and in patients with musculoskeletal

problems such as frozen shoulder (although the latter not uncommonly precedes the diagnosis of PD).

Increased muscle tone across a joint due to rigidity or spasticity can be differentiated while examining the full range of motion of a joint at varying speeds. In rigidity, the resistance is more or less stable, and equal between flexion and extension movements, during the whole trajectory. In spasticity, the tone is preferentially increased in arm flexors and leg extensors, and sudden decreases of muscle resistance (the 'clasp-knife phenomenon') can be felt.

Jerky hyperkinetic syndromes

The jerky hyperkinetic syndromes include myoclonus (together with excessive startle), chorea and tics. Jerky movements might be seen in isolation or in combination with non-jerky movements.

Myoclonus

Myoclonic movements are sudden, brief, shock-like involuntary movements, which are usually positive (caused by muscle contraction), but can sometimes be negative (due to brief loss or inhibition of muscular tonus, as in asterixis—for example, when caused by hepatic enkephalopathy ['liver flap']—or in uremic enkephalopathy). Negative myoclonus can also be seen while walking, producing a typical veering gait pattern, or the sudden postural lapses ('bouncy gait') seen in post-anoxic myoclonus. Myoclonic muscle contractions are mostly accompanied by some movement of the affected body segment, in contrast to, for example, fasciculations or myokymia, where the twitches remain within the affected body segment. Myoclonus is best likened to the effect seen after stimulating the nerve supplying the muscle with a single electric shock (or with a train of shocks, because the myoclonic jerks can occur repetitively within the same muscle). Therefore, the keywords in identifying myoclonus are 'shock-like movements'.

When myoclonus occurs in series, the timing of the jerks can be either rhythmic or irregular. Sometimes rhythmic myoclonus can be mistaken for tremor (examples include spinal segmental myoclonus, and hereditary cortical myoclonus, which has also been erroneously labeled 'cortical tremor'). If myoclonus is repetitive but more arrhythmic (as in 'polyminimyoclonus', which consists of fine myoclonic individual finger jerks seen in the outstretched hands in, for example, patients with multiple system atrophy), the movements can be mistaken for irregular tremor. However, isolated tremor lacks the defining abrupt and shock-like character of myoclonus. The condition that was originally called palatal myoclonus is now termed palatal tremor because of its rhythmic nature and lack of abrupt jerky movements.

Myoclonus can be described and classified in several ways. The distribution of myoclonus can be focal, multifocal, segmental or generalized. Etiologically, myoclonus can be subdivided into physiological myoclonus (for example, hypnic jerks), essential myoclonus (idiopathic or hereditary), epileptic myoclonus, or symptomatic myoclonus in cases where the myoclonus is secondary to an underlying disorder. Physiologically, myoclonus is subdivided into cortical, subcortical, spinal and peripheral types.[9] In addition, careful assessment of the specific moments of occurrence for myoclonus is important. Myoclonus can occur spontaneously (at rest), but is also often present—and usually worsened—during movement (action myoclonus), or can be provoked by external tactile or acoustic stimuli (reflex myoclonus). Cortical myoclonus is usually action sensitive or stimulus sensitive, mostly occurring in response to distal touch or stretch, and occasionally to visual stimuli. Brainstem myoclonus, by contrast, is more commonly provoked by auditory stimuli, or by tactile stimuli around the face or snout. It is important, therefore, to look for stimulus sensitivity when assessing suspected myoclonus. Cortical myoclonus tends to be focal, whereas subcortical myoclonus is more often generalized. The various types of myoclonus have differing neurophysiological characteristics.[10]

Propriospinal myoclonus; that is, myoclonus generated within the spinal cord with subsequent upward and downward spread, is a clinically difficult category, as these movements are perceived as being too slow and insufficiently jerky in character to be classed as myoclonus.[11] Often, polymyographic recordings are needed to prove the myoclonic nature of these axial movements. Spinal pathology can be demonstrated in some cases, but this is a rare occurrence. A notable proportion of cases of propriospinal myoclonus are psychogenic, but the semiology and physiology can mimic organic cases, so determining the pathogenesis is difficult.

Startle reactions, which are part of the spectrum of myoclonus, are also provoked by external stimuli—most often by auditory triggers, but also by surprise, alarm or acute pain. The startle reaction is characterized by a bilaterally synchronous shock-like set of movements.[12]

Chorea

Chorea may not be immediately appreciated as being a jerky movement disorder, perhaps because the word chorea (Greek for 'dance') suggests a certain grace rather than abrupt, jerky movements. If one carefully observes a patient with chorea, however, it immediately becomes evident that the 'choreography' includes a constellation of randomly flowing movements, which are, individually, jerky in nature. Thus, chorea can be defined as involuntary movements that are abrupt, unpredictable and nonrhythmic, resulting from a continuous random flow of muscle contractions. A key difference from myoclonus is that the pattern of movements randomly changes from one body part to another, conveying the impression of 'fidgeting' to the observer. So, if we were to attach a key description to chorea, it would be 'randomly flowing jerks'. Other typical signs of chorea are motor impersistence, as seen in the fluctuating strength of the grip (so-called 'milkmaid's grip'), or hung-up reflexes (sustained contractions and choreatic movements of the leg after the knee-jerk reflex).[13] Some patients with chorea—in HD, for example—can exhibit additional brief (<100 msec) muscle jerks that are myoclonic, and/or longer (>50 msec) co-contracting muscle spasms that are dystonic.

Mild chorea may be subtle, but can usually be detected if the clinician carefully observes the patient with this possibility in mind. Finger chorea is best brought out by the individual counting backwards with their eyes closed and arms outstretched, or when walking with or without counting. Identification of chorea is sometimes hampered by the fact that patients frequently try to mask their chorea by incorporating the jerks into voluntary movements. Another pitfall is that choreatic patients themselves often have relatively few subjective complaints, especially in early stages, when it is usually their partner who complains about the movements. This is not an uncommon situation in HD, for example.

Ballism is typically considered under the rubric of chorea because it shares the same pathophysiology and treatment. Ballistic movements are uncontrollable, severe, mainly proximal, large-amplitude choreatic movements. They are usually unilateral (hemiballism), and are classically described after an acute lesion in the region of the contralateral subthalamic nucleus.[14] The term 'hemichorea' can be used if the amplitude of the movement is small. Sometimes, the movements involve only one limb (monoballism). Bilateral ballistic movements are rare, and are mostly due to metabolic abnormalities.

Tics

Tics are the third category of sudden and jerky movements, but in this case the keyword for recognition is the 'stereotyped' character of the recurrent movements. Another fundamental difference from myoclonus and chorea is that patients report that their tics are preceded by rising discomfort or urge ('sensory tic') that is relieved by the actual movement ('itch and scratch' analogy). Another important feature is that tics can usually be largely suppressed for short periods by an effort of will. However, suppression of tics typically comes at the expense of mounting inner tension, leading to a 'rebound' of tics afterwards. Owing to their stereotyped character, tics can usually be mimicked easily.

Tics usually predominate in the face, upper arms and neck. They can be divided into simple tics (for example, eye blinking, nose wrinkling, shoulder shrugging or throat clearing) or complex tics (for example, touching things, smelling objects, echopraxia or jumping). Another subdivision is into motor tics (such as stereotyped head jerks) or phonic tics (repetitive sniffs or sounds, words or even sentences). A notorious diagnostic pitfall is that tics are often less prominent or even absent in the clinical examination room, apparently because the anxiety associated with being examined suppresses the phenomenon. Videotaping the patient without an examiner present can, therefore, be very helpful. Occasionally, a motor tic can have an abrupt onset, but the subsequent movement or posture might be slow or prolonged rather than jerky. This phenomenon is referred to as a dystonic tic, but the suppressibility and stereotyped nature are the clinical clues to classifying such movements as a tic. Dystonic tics can occur in conjunction with other, nondystonic tics.

Stereotypic movements resemble tics, but the actions consist of a complex set of movements that are longer lasting, patterned, repetitive, purposeless and/or ritualistic. These stereotypies are less paroxysmal than tics, but occur repeatedly in a more continuous fashion. The movements can be simple (composed of a few maneuvers; for example, rocking or head banging) or more complex (composed of multiple simple maneuvers performed together or in sequence). Stereotypies are typically seen in patients with autism, mental retardation, Rett syndrome, psychosis, or congenital blindness and deafness.[15,16]

Non-jerky hyperkinetic syndromes

The non-jerky hyperkinetic syndromes include tremor and dystonia. Although dystonia can have a jerky nature, its core feature is prolonged muscle spasms, which is why we have placed it here in the non-jerky category.

Tremor

By definition, tremor is characterized by involuntary, rhythmic and sinusoidal alternating movements of one or more body parts. The movement does not necessarily involve a limb, as tremor can affect almost any body part, including the head, chin and soft palate. The keyword in identifying tremor is 'rhythmicity'; that is, the oscillations occur at a regular frequency. Identifying rhythmicity with the naked eye is not always easy, however, because despite having a fixed frequency, tremors often have a variable amplitude. Such changes in amplitude with time can occur spontaneously, but might also result from movements or changes in posture assumed by the patient, or from emotion and fatigue. Despite the amplitude change, tremor frequency remains unchanged. In patients who show changes in tremor amplitude, objective and quantitative tremor registration, by use of electromyography and accelerometry, can confirm rhythmicity.

Tremors can be classified in various ways. One important classification system is based on the characteristic moment or situation of occurrence (Table 1).[17] A resting tremor can only be definitively identified when the affected body part is not actively moving, and when the effect of gravity is removed completely. Resting tremor usually disappears during voluntary actions. Sometimes, eye closure or distraction is needed to provoke the resting tremor (for example, asking the patient to count backwards while they are sitting with their arms resting on the arms of a chair). Occasionally, the tremor is only seen in the arm when the individual is walking ('dependent tremor'). The resting tremor can be highly focal; for example, tremor in PD might begin in a single digit. A common diagnostic pitfall is failure to recognize that resting tremors can occur in any position assumed by the affected body part, even when this involves a posture that is actively maintained against gravity (thereby mimicking a 'postural tremor'). For example, the typical resting tremor in the hands of patients with PD can also be observed when the arms are stretched out in front of the individual. In this case, distinction between postural tremor (as in essential tremor) and true resting tremor can be accomplished by carefully examining how rapidly the tremor becomes manifest after the new posture has been assumed—immediately in case

Table 1 | Classification of tremors according to moment of occurrence

Moment of occurrence	Features	Example of underlying disorder
A. At rest	Best judged in a body part that is fully supported against gravity	Parkinson disease
B. With action		
Postural	Occurs in body part that assumes a posture against gravity	Physiological; enhanced physiological (stress, endocrine disorders or intoxications); essential tremor
Kinetic		
Simple	Occurs during entire movement trajectory	Essential tremor
Intention	Progressively increases towards intended target	Cerebellar ataxia
Task specific	Occurs only during specific activities	Dystonic writing tremor
Isometric	Occurs during voluntary muscle contractions against a stationary resistance	Physiological; associated with other types of tremor
C. Combinations	Various	Severe essential tremor; atypical parkinsonism; dystonic tremor; rubral (Holmes) tremor

The above classification was proposed by a Consensus Statement of the Movement Disorder Society.[17]

of postural tremor, but after a delay of several seconds in the case of resting tremor (a phenomenon termed 'resetting' or 're-emergent tremor'). The frequency of a resetting tremor is the same as that observed in the rest position.[18]

Kinetic tremors occur during volitional movements. A distinction is made between simple or action tremor (evident during a target-directed movement), terminal tremor (evident at the end of a target-directed movement) and intention tremor (which increases progressively in amplitude throughout the movement until the intended target is reached). Isometric tremor occurs when muscles forcefully contract without shortening; for example, while pushing against a wall. Finally, psychogenic tremor is characterized by a variable frequency, direction and amplitude, as well as by distractibility.[19]

Attempts have been made to classify tremor according to its frequency. However, establishing a diagnosis purely on the basis of this parameter is rarely possible, for two reasons. First, accurate assessment of tremor frequency is difficult to accomplish in the clinic without neurophysiological equipment. Second, the frequency spectrum between different tremor types overlaps considerably. One exception is primary orthostatic tremor, a leg tremor that is present during standing, and which is characterized by an unusually high and pathognomonic tremor frequency of 14–18 Hz.[20] This particular tremor is barely visible to the naked eye, although patients can manifest a discernable leg or trunk tremor with a lower frequency. Although commonly said to be mainly present during standing, electromyographic studies have shown that the high-frequency orthostatic tremor persists in the trunk and weight-bearing leg during walking, and that this tremor can also arise in the upper extremities when patients support their weight with the arms.[21]

Many disorders are characterized by the presence of 'mixed' tremors. Patients with PD, for example, not only have resting tremor, but commonly also show a postural tremor with a higher frequency. Another example is Holmes tremor (also known as midbrain or rubral tremor), which typically has resting, postural and intention components, often at an unusually low frequency of around 2–3 Hz.

When tremor involves a body part already affected by dystonia (see below), it is classified, according to the Movement Disorder Society Consensus Statement, as 'dystonic tremor'.[17] Many patients with spasmodic torticollis also have a postural tremor of one or both arms.[22] The Consensus Statement uses the somewhat unwieldy term 'tremor associated with dystonia' but, since most experts believe that the tremor is in fact part of the patient's dystonia, we prefer to use the term 'dystonic tremor', provided that no other cause is identified. Dystonic tremor can mimic the tremor of PD, especially when it precedes overt dystonia or when the dystonia is subtle, thereby leading to a misdiagnosis of PD. To confuse matters further, arm swing is often reduced in patients with dystonia, even in torticollis patients with no other arm involvement. People with dystonic tremor do not have true akinesia, however, and they also show normal dopamine transporter imaging, in contrast to patients with PD.[23] Many dystonic tremors are also misclassified as essential tremor.[24] To further complicate matters, postural tremors similar to essential tremor are frequently present in patients with dystonia. The presence of (often subtle) dystonic postures should distinguish between these two diagnoses; for example, 'dinner-fork' posture of the outstretched hand, or a tendency for the ulnar fingers or thumb to point downwards with the arms held out, are characteristics of dystonia.

Some tremors are easier to feel than to observe. Superficial palpation of involved muscles can suffice—sometimes at rest, but in particular during passive movements of the affected muscles. 'Cogwheeling' is a phenomenon that is felt by the observer, during testing for muscle tone, as jerky, brief contractions throughout the entire range of passive movement. Cogwheeling in some respects resembles the sensation of pulling the handbrake of a car. When noticing this cogwheeling phenomenon, the observer actually feels the underlying tremor, irrespective of its cause. Cogwheeling can be felt in patients with essential or dystonic tremor, and in patients with PD. In the first two examples, however, there is no additional rigidity (in which case one speaks of 'cogwheel rigidity') or akinesia, whereas these features are present in PD. Orthostatic tremor can also be palpated as

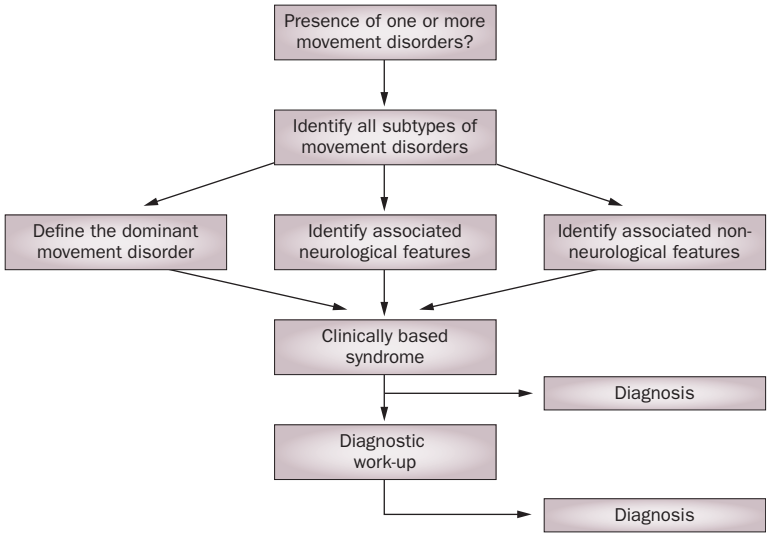

Figure 1 | A systematic approach to diagnosis in patients presenting with movement disorders.

a kind of 'rhythmic shivering' of the legs, or can be heard through a stethoscope (thumping sound like a helicopter) in cases where it is not obviously visible.[25]

Dystonia

One definition of dystonia is "an involuntary abnormal co-contraction of antagonistic muscles, which may cause sustained abnormal postures or twisting and repetitive movements." Another definition is "abnormal characteristic postures and movements, produced by slow sustained muscle contraction, which distort limbs, trunk, neck, face or mouth." Both definitions emphasize that the important keywords in identifying dystonia are 'abnormal posture'. As such, dystonia is the only movement disorder that can be visualized in a static image, even though additional rhythmic, irregular or paroxysmal jerky involuntary movements can frequently accompany the abnormal postures. An example of such an involuntary associated movement is athetosis, which is defined as 'distal mobile dystonia': slow, writhing and irregular movements of the distal extremities, with abnormal posturing.[26] In the past, the term 'choreoathetosis' was used to describe a mixture of chorea and dystonia (as seen in levodopa-induced dyskinesias in some patients with PD), but we now prefer the term 'mobile choreodystonic movements'.

Dystonias can be classified in several ways, on the basis of their distribution (focal, segmental, multifocal, generalized, or hemidystonia), age at onset (early, ≤26 years; or late, ≥26 years), or cause (primary, dystonia-plus, degenerative or secondary).[27]

Clinical features are helpful in distinguishing primary from secondary dystonia.[28] Primary dystonia is characterized by the presence of dystonia only (although tremor is seen in some cases). Dystonia-plus syndromes present with a second and relevant neurological feature, such as parkinsonism (as in dopa-responsive dystonia), or sometimes, as has recently become apparent, ataxia.[29] The term 'myoclonus–dystonia' crept into usage in relation to the very brisk, brusque, lightning-like tic–tac jerks that are typical of patients with hereditary alcohol-responsive myoclonus with dystonia (DYT11); this syndrome is often caused by mutations in the gene encoding ε-sarcoglycan. In secondary dystonias, clinical features other than dystonia are usually present, and an identifiable cause can often be found.

Several characteristics support the presence of dystonia, and the features described below are especially applicable for primary dystonias. The abnormal posturing typically has a consistent directionality (a torticollis with rightward head rotation will not usually change suddenly to a leftward torticollis, for example). The abnormal movements are patterned and repeatedly involve the same muscle groups. In early stages, the dystonia is typically 'mobile' (that is, the patient can still actively or passively move the affected body part), but the dystonia might become more fixed with further disease progression. Note that fixed dystonia may be a relatively early feature in patients with corticobasal degeneration, while fixed posturing that is present immediately at disease onset is often felt to reflect a psychogenic cause.[30] A further typical feature of dystonia is the presence of a sensory trick, or 'geste antagoniste', which is a mechanism (usually identified and used by the patient) to reduce dystonia; for example, gently touching the cheek to correct torticollis, or chewing gum to reduce oromandibular dystonia. Dystonia is commonly brought out by action or activity (note that this is not the same thing as paroxysmal dystonia). Often, this can take the form of an element of task specificity; that is, the movements or postures are predominantly or even exclusively present under specific circumstances. Examples of this phenomenon include writer's cramp or the various forms of musician's dystonia. The task specificity can lead to diagnostic confusion, such as in patients with leg dystonia who have severe difficulty walking forwards, but can walk backwards or run normally. If no problem is apparent and the complaint is highly task specific, a helpful approach can be to ask the person to bring along the relevant equipment—for example, a musical instrument or golf club—to demonstrate the problem. Failing this, asking the patient to bring in a home video segment to highlight the symptom can be revealing.

Diagnostic levels

A systematic approach is recommended when clinicians see patients who present with one or more types of movement disorder (Figure 1). The work-up that we use in every patient consists of four key questions that need to be addressed consecutively in order to establish the correct diagnosis. Of course, not every question can always be answered unambiguously in each patient.

A range of conditions, both neurological and non-neurological, can mimic various movement disorders, and it is vital not to miss these lookalikes. Several common examples are shown in Box 2.

Which types of movement disorder are present?

Some movement disorders can occur almost in pure isolation. One example is essential tremor, in which affected patients typically present with a symmetrical action and

postural tremor in the arms but, by definition, without other neurological abnormalities,[31] except perhaps for a mildly unsteady gait that might only become apparent during the tandem walk test.[32] However, many clinical syndromes are characterized by the presence of several different types of movement disorder that occur in the same patient—the 'mixed movement disorder' (Table 2). A patient with multiple system atrophy, for example, can present with a combination of akinesia, rigidity, tremor, ataxia, and fine polyminimyoclonus in the outstretched hands.[33,34] If one looks carefully, such overlap is more often the rule than the exception in patients with movement disorders. The nature of this overlap varies between different disorders, between individual patients with the same disorder, and even within a given patient depending on their disease stage.

To differentiate between clinical syndromes—a process that relies heavily on pattern recognition; that is, specific combinations of symptoms and signs—precise classification of the type of movement disorder that occurs in individual patients is important. Some combinations immediately raise a specific diagnostic suspicion, such as the combination of dystonia and 'lightning' myoclonic jerks, which are characteristic of myoclonus dystonia (DYT11).

Importantly, whenever patients present with a mixed movement disorder, one should always consider the possibility of adverse effects of medication (most commonly dopamine D_2 receptor-blocking agents such as neuroleptics). Drug-induced movement disorders are frequently encountered in patients with a known movement disorder, but can also be seen in patients without a history of movement disorders. For example, the presence of chorea in a patient with a previous diagnosis of primary dystonia could be due to the use of anticholinergics, and should not necessarily lead to an extensive work-up for secondary dystonia. Patients without a known history of movement disorders who use antipsychotics can develop tremor, a hypokinetic rigid syndrome, or orofacial dyskinesias. The risk increases with prolonged medication use, but even single doses can be responsible. Requesting a comprehensive list of previous medications from the general practitioner might be necessary, as the effects of an offending agent can persist for months following discontinuation.

What is the dominant movement disorder type?

Even when the clinical syndrome is characterized by the simultaneous presence of different types of movement disorder, one type will typically predominate. For example, most adult patients with HD not only have the characteristic chorea, but also display bradykinesia when this condition is carefully sought. In the typical early-to-middle-stage case, however, the clinician will usually have little difficulty in identifying chorea as the dominant type of movement disorder. This distinction is important, because the specific diagnostic work-up for chorea is different from that for bradykinesia. Thus, determining the dominant movement disorder syndrome is an essential step, as it steers the differential diagnosis and determines the subsequent diagnostic trajectory.

Box 2 | Commonly seen movement disorder mimics

Mimics of parkinsonism
- Depression
- Obsessive slowness
- Hypothyroidism
- Spasticity
- Dystonic tremor
- Frozen shoulder
- Slowing due to normal aging
- Catatonia

Mimics of craniocervical dystonia (torticollis)
- Retropharyngeal abscess
- Atlanto-axial subluxation
- Congenital muscular torticollis
- Correcting head tilt in cranial nerve palsy ('ocular torticollis')
- Space-occupying lesion in posterior fossa
- Sandifer syndrome with head tilt
- Dropped head syndrome in neuromuscular disease

Mimics of limb dystonia
- Contracture
- Spasticity
- Abnormal posture due to paresis or atrophy
- Myotonia or neuromyotonia
- Sensory ataxia and/or pseudoathetosis
- Stiff-person syndrome
- Tonic spasms
- Seizures or epilepsia partialis continua

Mimics of facial dystonia
- Ptosis or pseudoptosis
- Trismus
- Hemimasticatory spasm
- Hemifacial spasm (tonic component)
- Myotonia
- Tetanic spasms
- Apraxia of eyelid opening (levator inhibition)

Mimics of myoclonus
- Tics
- Tremor
- Fasciculations (spontaneous contractions of muscle fibers supplied by a single motor unit that are too small to cause movement across a joint)
- Myokymia (involuntary, subtle, continuous, rippling quivering of muscles, which does not produce movement across a joint)[40]
- Chorea

Recognizing the dominant type of movement disorder is often easiest in the early stages of the disease. In patients with more-advanced disease, the originally dominant signs might become masked by secondary disease complications or newly emerging movement disorders. In advanced stages of HD, for example, chorea is often no longer prominent, and akinesia, rigidity and dystonia may

Table 2 | Commonly seen 'mixed' movement disorders

Combinations	Possible etiology
Tremor and akinesia	Parkinson disease or atypical parkinsonism
Parkinsonism, ataxia, autonomic dysfunction, spasticity, myoclonus	Multiple system atrophy
Vertical supranuclear gaze palsy and falls, symmetrical parkinsonism	Progressive supranuclear palsy
Akinesia, rigidity, myoclonus, dystonia and apraxia, asymmetrical clinical phenotype	Corticobasal degeneration
Chorea, dystonia and bradykinesia	Huntington disease
Dystonia plus tremor	Primary dystonia
Tremor (rest and postural), dystonia, akinetic–rigid syndrome	Wilson disease
Ataxia and myoclonus (Ramsay Hunt syndrome, 'progressive myoclonic ataxia')	Mitochondrial disease; celiac disease; Unverricht–Lundborg disease

predominate. Another example is levodopa-induced dyskinesia in patients with PD. Sometimes, patients with PD can simultaneously have tremor in one part of the body and levodopa-induced dyskinesia–dystonia in other body parts. Indeed, levodopa-induced dyskinesias can dominate the clinical picture and overshadow tremor, clinically resembling choreoathethosis (best defined as mobile choreodystonic movements). The solution in such cases lies in obtaining a detailed medical history, as well as being familiar with all stages of the disease.

What are the associated features?

The complexity of the clinical picture increases when patients exhibit additional neurological or non-neurological symptoms or signs. Clinicians can, however, take advantage of this situation, as these associated features can provide important clues about the underlying etiology. For example, examining the eyes for oculomotor apraxia and telangiectasia in patients with chorea and ataxia may lead to a diagnosis of autosomal recessive ataxia telangiectasia. Similarly, finding Kayser–Fleischer rings in the cornea in a patient with dystonia would indicate a diagnosis of Wilson disease, and early and prominent autonomic dysfunction in a patient with parkinsonism should raise the possibility of multiple system atrophy.[33,34]

Sometimes, elements of the history provide important clues, such as specific factors that exacerbate or relieve the abnormal movements. For example, involuntary movements that present in frequent, brief attacks that are induced by sudden movements (such as rising from a chair) suggest a diagnosis of paroxysmal kinesigenic dyskinesias.[35,36] If patients with torticollis report that their head jerks improve dramatically with alcohol, a diagnosis of myoclonus dystonia (DYT11) should be suspected.[37] Associated non-neurological clues are also important; for example, chorea in a woman with migraine, recurrent venous thrombosis or multiple spontaneous abortions suggests antiphospholipid syndrome. The presence of associated neurological and non-neurological features can, therefore, help to narrow the differential diagnosis that was initially based on the dominant movement disorder syndrome.

Family history and ethnicity can also be critical for the diagnosis. Parental consanguinity, a positive family history and a specific ethnicity in otherwise classic idiopathic parkinsonism raises the possibility of a monogenic cause of PD. A dominant family history of tremor in patients with a postural tremor suggests essential tremor or dystonic tremor. In dystonia, many inherited forms are known. A positive family history of dystonia combined with Filipino ethnicity raises the possibility of the X-linked DYT3 dystonia ('Lubag').

What is the differential diagnosis?

Taken together, an overall clinical syndrome is determined from the specific combination of one (dominant) movement disorder with, perhaps, several concurrent types of movement disorder, plus a set of associated neurological and non-neurological abnormalities. This clinical syndrome should in turn lead to a differential diagnosis. Sometimes simple pattern recognition will suffice and lead directly to the diagnosis, but often ancillary investigations are required. In such cases, the diagnostic process will be guided by the dominant movement disorder.

Note that some specific types of movement disorder always influence clinical decision-making, even when present in a subtle form and not as the 'dominant' movement disorder. For example, when patients present with predominant dystonia but also with mild signs of ataxia, the work-up should include—and perhaps even primarily focus on—a search for causes of ataxia; in particular, a hereditary cause.[38]

Details of the diagnostic work-up largely depend on the dominant type of movement disorder and the residual clinical uncertainties with respect to the differential diagnosis. In patients with unexplained chorea that looks like HD, for example, the initial diagnostic step may often simply involve genetic testing for HD, after appropriate counselling. If the test is negative, the diagnostic work-up can then be expanded.[39] Each movement disorder and each clinical syndrome thus has its own specific diagnostic approach. A detailed discussion of these diagnostic trajectories is beyond the scope of this Review.

Conclusions

We have outlined a suggested clinical approach to the patient with a movement disorder. In the supplementary online material, we provide examples of how this method might work for patients presenting predominantly with myoclonus (Supplementary Table 1 online), chorea (Supplementary Table 2 online) or dystonia (Supplementary Table 3 online). We hope that application of the proposed serial diagnostic steps will help clinicians in the identification of overall clinical syndromes, which will, in turn, guide the diagnostic process.

Review criteria

This review represents the views of movement disorder specialists, based on their personal opinion and extensive clinical experience in approaching patients with movement disorders.

1. de Rijk, M. C. *et al.* Prevalence of parkinsonism and Parkinson's disease in Europe: the EUROPARKINSON Collaborative Study. European Community Concerted Action on the Epidemiology of Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* **62**, 10–15 (1997).
2. Dogu, O. *et al.* Prevalence of essential tremor: door-to-door neurologic exams in Mersin Province, Turkey. *Neurology* **61**, 1804–1806 (2003).
3. Moghal, S., Rajput, A. H., D'Arcy, C. & Rajput, R. Prevalence of movement disorders in elderly community residents. *Neuroepidemiology* **13**, 175–178 (1994).
4. Kurlan, R. *et al.* The behavioral spectrum of tic disorders: a community-based study. *Neurology* **59**, 414–420 (2002).
5. Piccini, P. & Whone, A. Functional brain imaging in the differential diagnosis of Parkinson's disease. *Lancet Neurol.* **3**, 284–290 (2004).
6. Seppi, K. & Schocke, M. F. An update on conventional and advanced magnetic resonance imaging techniques in the differential diagnosis of neurodegenerative parkinsonism. *Curr. Opin. Neurol.* **18**, 370–375 (2005).
7. Litvan, I. *et al.* Movement Disorders Society Scientific Issues Committee report: SIC Task Force appraisal of clinical diagnostic criteria for parkinsonian disorders. *Mov. Disord.* **18**, 467–486 (2003).
8. Norlinah, I. M. *et al.* Primary lateral sclerosis mimicking atypical parkinsonism. *Mov. Disord.* **22**, 2057–2062 (2007).
9. Caviness, J. N. & Brown, P. Myoclonus: current concepts and recent advances. *Lancet Neurol.* **3**, 598–607 (2004).
10. Shibasaki, H. & Hallett, M. Electrophysiological studies of myoclonus. *Muscle Nerve* **31**, 157–174 (2005).
11. Roze, E. *et al.* Propriospinal myoclonus revisited: clinical, neurophysiologic, and neuroradiologic findings. *Neurology* **72**, 1301–1309 (2009).
12. Bakker, M. J., van Dijk, J. G., van den Maagdenberg, A. M. & Tijssen, M. A. Startle syndromes. *Lancet Neurol.* **5**, 513–524 (2006).
13. Hallett, M. & Kaufman, C. Physiological observations in Sydenham's chorea. *J. Neurol. Neurosurg. Psychiatry* **44**, 829–832 (1981).
14. Postuma, R. B. & Lang, A. E. Hemiballism: revisiting a classic disorder. *Lancet Neurol.* **2**, 661–668 (2003).
15. Muthugovindan, D. & Singer, H. Motor stereotypy disorders. *Curr. Opin. Neurol.* **22**, 131–136 (2009).
16. Shprecher, D. & Kurlan, R. The management of tics. *Mov. Disord.* **24**, 15–24 (2009).
17. Deuschl, G., Bain, P. & Brin, M. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. *Mov. Disord.* **13** (Suppl. 3), 2–23 (1998).
18. Jankovic, J., Schwartz, K. S. & Ondo, W. Re-emergent tremor of Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* **67**, 646–650 (1999).
19. Bhatia, K. P. & Schneider, S. A. Psychogenic tremor and related disorders. *J. Neurol.* **254**, 569–574 (2007).
20. Gerschlager, W. *et al.* Natural history and syndromic associations of orthostatic tremor: a review of 41 patients. *Mov. Disord.* **19**, 788–795 (2004).
21. Britton, T. C. *et al.* Primary orthostatic tremor: further observations in six cases. *J. Neurol.* **239**, 209–217 (1992).
22. Munchau, A. *et al.* Arm tremor in cervical dystonia differs from essential tremor and can be classified by onset age and spread of symptoms. *Brain* **124**, 1765–1776 (2001).
23. Schneider, S. A. *et al.* Patients with adult-onset dystonic tremor resembling parkinsonian tremor have scans without evidence of dopaminergic deficit (SWEDDs). *Mov. Disord.* **22**, 2210–2215 (2007).
24. Jain, S., Lo, S. E. & Louis, E. D. Common misdiagnosis of a common neurological disorder: how are we misdiagnosing essential tremor? *Arch. Neurol.* **63**, 1100–1104 (2006).
25. Brown, P. New clinical sign for orthostatic tremor. *Lancet* **346**, 306–307 (1995).
26. Morris, J. G. *et al.* Athetosis II: the syndrome of mild athetoid cerebral palsy. *Mov. Disord.* **17**, 1281–1287 (2002).
27. Geyer, H. L. & Bressman, S. B. The diagnosis of dystonia. *Lancet Neurol.* **5**, 780–790 (2006).
28. Tanabe, L. M., Kim, C. E., Alagem, N. & Dauer, W. T. Primary dystonia: molecules and mechanisms. *Nat. Rev. Neurol.* **5**, 598–609 (2009).
29. van de Warrenburg, B. P. *et al.* The syndrome of (predominantly cervical) dystonia and cerebellar ataxia: new cases indicate a distinct but heterogeneous entity. *J. Neurol. Neurosurg. Psychiatry* **78**, 774–775 (2007).
30. Schrag, A., Trimble, M., Quinn, N. & Bhatia, K. The syndrome of fixed dystonia: an evaluation of 103 patients. *Brain* **127**, 2360–2372 (2004).
31. Nahab, F. B., Peckham, E. & Hallett, M. Essential tremor, deceptively simple. *Pract. Neurol.* **7**, 222–233 (2007).
32. Stolze, H., Petersen, G., Raethjen, J., Wenzelburger, R. & Deuschl, G. The gait disorder of advanced essential tremor. *Brain* **124**, 2278–2286 (2001).
33. Quinn, N. Multiple system atrophy—the nature of the beast. *J. Neurol. Neurosurg. Psychiatry* **Jun.** (Suppl.), 78–89 (1989).
34. Wenning, G. K., Colosimo, C., Geser, F. & Poewe, W. Multiple system atrophy. *Lancet Neurol.* **3**, 93–103 (2004).
35. van Rootselaar, A. F., van Westrum, S. S., Velis, D. N. & Tijssen, M. A. The paroxysmal dyskinesias. *Pract. Neurol.* **9**, 102–109 (2009).
36. Bhatia, K. P. Familial (idiopathic) paroxysmal dyskinesias: an update. *Semin. Neurol.* **21**, 69–74 (2001).
37. Gerrits, M. C. *et al.* Phenotype–genotype correlation in Dutch patients with myoclonus–dystonia. *Neurology* **66**, 759–761 (2006).
38. Schmitz-Hubsch, T. & Klockgether, T. An update on inherited ataxias. *Curr. Neurol. Neurosci. Rep.* **8**, 310–319 (2008).
39. Cardoso, F., Seppi, K., Mair, K. J., Wenning, G. K. & Poewe, W. Seminar on choreas. *Lancet Neurol.* **5**, 589–602 (2006).
40. Dimutru, D., Amato, A. A. & Zwarts, M. J. *Electrodiagnostic Medicine,* 2nd edn (Hanley & Belfus, Philadelphia, 2002).

Acknowledgments

This clinical approach was handed down to us by the late Professor David Marsden. This work was supported by The Netherlands Organization for Scientific Research (NWO) Vidi research grant #016.076.352 to B. R. Bloem. W. F. Abdo was supported by a research grant from the Stichting Internationaal Parkinson Fonds.

Désirée Lie, University of California, Orange, is the author of and is solely responsible for the content of the learning objectives, questions and answers of the MedscapeCME-accredited continuing medical education activity associated with this article.

Supplementary information

Supplementary information is linked to the online version of the paper at www.nature.com/nrneurol