

Chapter 17

Dyskinesias

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Chapter Plan

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Dyskinesia is a generic term encompassing all involuntary movements (e.g., tremor, tic, dystonia). This term is currently used more commonly than the synonym *hyperkinesia*, which has a longer historical tradition. Other motor abnormalities, such as akinesia, ataxia, or paralysis, are not considered dyskinesias.

As a neurologic sign, dyskinesias can be transient, permanent, or paroxysmal (which means that they have an abrupt onset, usually in relation to a voluntary movement). Based on topography, dyskinesias may be focal (just one body part), segmental (two contiguous body parts), multifocal (two non-contiguous body parts), or generalized. As a nosologic entity, dyskinesias are clinical syndromes characterized by a number of clinical signs and symptoms in which dyskinesias are a prominent

clinical feature. Usually, just the same dyskinesia term (e.g., chorea, dystonia) is used at times with reference to the occurrence of a clinical sign or, alternatively, to indicate a nosologic entity characterized by a prominent occurrence of the homonymous clinical sign.

The student or resident who tries to address the clinical issues related to dyskinesias will find this task quite difficult. At first sight, involuntary movements very much resemble each other; they may appear funny, bizarre, or frightening to the inexperienced. This explains why, historically, dyskinesias have been defined quite late in the neurologic literature. The chronology of the first official recognition of the main dyskinesias is reported in Table 17-1. It is remarkable to note that students and residents usually learn to recognize dyskinesias with a similar sequence. The chronology of clinical observations therefore parallels the common chronology of the learning curve of an inexperienced clinician.

In a synthetic chapter such as this, it is not possible to describe dyskinesias in full, nor is it possible to teach the inexperienced. Learning in this field requires a good degree of careful observation.

Tremor

Tremor consists of an involuntary, rhythmic, oscillatory movement around a joint. Resting tremor occurs when muscles are entirely relaxed; postural tremor is present on maintaining active postures

Table 17-1. Learning of Diagnostic Skills in the Field of Dyskinesia Reflects the Chronology of First Identification

Date	Dyskinesia	First Usage
Ancient Greece	Tremor	τρεμω (to tremble, to fear)
Fourteenth century	Chorea	Choreomania (ritual dance)
Seventeenth century	Tic	Horse breeders
1871	Athetosis	Hammond
1881	Myoclonus	Friedreich
1885	Ballism	Kussmaul
1911	Dystonia	Oppenheim

Table 17-3. Tremor Classification by Frequency

Frequency	Tremor Type
1–4 Hz	Cerebellar
1–5 Hz	Parkinsonian
5–8 Hz	Essential
7–8 Hz	Shivering, fear
8–12 Hz	Physiologic
8–16 Hz	Orthostatic
10–16 Hz	Thyrotoxic

(e.g., holding the arms against gravity); action tremor (i.e., kinetic tremor) occurs during voluntary motion. *Intention tremor* is a term encompassing postural and action tremor (Tables 17-2 and 17-3). The motion of a tremor can be graphically represented by a sine curve, the amplitude of which reflects the amplitude of the joint displacement produced by the tremor. Tremors of very low amplitude are difficult to detect, as in the case of physiologic tremor, which is usually not seen because of its very low amplitude. Rather, it becomes evident in some physiologic conditions (i.e., stress, fear, cold, hypoglycemia), after administration or deprivation of drugs, or after endocrinologic changes. The expression “enhanced physiologic tremor” is used to indicate such paraphysiologic conditions.

Tremor is thought to be produced by a closed feedback neural loop that comes into a state of oscillation after increased gain, reduced conduction along the loop, or both. Different motor loops (central or peripheral) are responsible for different forms of tremor.

Table 17-2. Tremor Classification by Relation with Voluntary Movement

Feature	Disorder
Rest*	Parkinson’s disease, “midbrain” tremor
Postural	Thyrotoxic, alcoholic, hepatic, essential, orthostatic, paleocerebellar syndrome, Parkinson’s disease, “midbrain” tremor, peripheral neuropathies
Action	Neocerebellar syndrome, “midbrain” tremor

*Also called *parkinsonian tremor*.

Physiologic tremor is a normal postural and action tremor with a frequency between 5 and 15 Hz (mean, 8–12 Hz, decreasing with age to about 6 Hz) resulting from peripheral mechanical properties of the musculoskeletal system. Parkinsonian tremor occurs at rest. It is usually asymmetric and has a frequency of 4–6 Hz. As a rule, parkinsonian tremor decreases in amplitude or disappears when an active movement is performed. Some parkinsonian patients also have a postural tremor that generally has a slightly higher frequency. Parkinsonian tremor classically affects the hands, with flexion-extension or abduction-adduction of the fingers (“pill-rolling”), but it can be observed in the legs, the chin, or the head in patients with tremor-dominant forms of Parkinson’s disease. A postural tremor similar to essential action tremor can also be observed. Antiparkinsonian medications have a moderate effect on parkinsonian tremor, which instead responds to lesions or to high-frequency stimulation of the ventrointermedio-median (Vim) thalamic nucleus or of the subthalamic nucleus.

Essential tremor is a sporadic or familial disorder characterized by the occurrence of postural tremor with a frequency of 5–8 Hz, which is similar to physiologic tremor but has a higher amplitude. A number of patients affected by essential tremor report benefit with consumption of alcohol, and in more than 60% of them there is a family history. Beta-blockers and primidone are the most effective drugs; benzodiazepines are also of some value. Approximately 30% of essential tremor patients do not have benefit from any drug therapy and can be effectively treated by implanting a high-frequency stimulator in the Vim thalamic nucleus.

Cerebellar tremor is an action tremor of low frequency (1–4 Hz) that appears during fine voluntary movements. It is well demonstrated by the finger-

to-nose or heel-to-knee maneuver. Cerebellar tremor is associated with other cerebellar features. Its treatment has been disappointing.

A combination of resting and postural tremors can be seen after lesions of the midbrain. Such tremors are capable of interrupting at one time the nigrostriatal pathway and the cerebellar pathway. This is the so-called rubral or mesencephalic tremor, which has, in fact, been shown not to be related to a lesion of the red nucleus.

Primary writing tremor is a rare condition that resembles essential tremor but occurs only during handwriting. Holding the arms outstretched does not produce tremor. This condition is considered to be a mild form of upper limb focal dystonia. Orthostatic tremor is also a rare form of high-frequency (14–18 Hz) tremor that occurs while standing.

Tics

Tics may be motor, vocal, or mixed. They may be simple or complex and are usually preceded by an uncomfortable sensation or by a compulsive thought (mental tic). Tics are repetitive, unpredictable, stereotyped, and generally brief. Examples of simple motor tics are blinking, tongue protrusion, eyebrow elevation, eye rotation, brisk motions of the neck, and shoulder shrugging. Examples of complex motor tics are rubbing, touching, jumping, hopping, stamping, and squatting. Patients with tics may also have peculiar features, such as copropraxia (obscene gestures) or echopraxia (imitating someone's gestures). Examples of simple vocal tics are barking, humming, sniffing, coughing, grunting, or the emission of high-pitched or loud sounds. Examples of complex tics are coprolalia (obscene expressions or sentences) and palilalia (repetition of the last syllables of a word). The pathophysiology of tics is still obscure; some degree of dysfunction of dopaminergic neurotransmission has been advocated.

Tics are often preceded by a sensory sensation ("sensory tics"); these recurrent, involuntary somatic perceptions in joints, muscles, throat, or other parts of the body often precede the motor tic of the same body part. A feeling of relief from the sensory perception is usually associated with the motor tic.

Obsessive-compulsive disorder is usually associated with tics. Obsessions are the fixation of the

mind on a word, a sentence, or an idea thought or heard. Compulsions consist of a repetition of a simple or complex movement or gesture.

Gilles de la Tourette's syndrome is a familial disease with incomplete autosomal dominant transmission that is characterized by the association of tics and obsessive-compulsive features. Attention deficit and hyperactivity disorder is often seen in children who carry the Gilles de la Tourette's gene. The *Diagnostic and Statistical Manual for Mental Disorders* (DSM) has set some artificial guidelines that have been repeatedly changed for the classification of tic disorders and Gilles de la Tourette's syndrome. Tics, which are not associated with the other features of Gilles de la Tourette's syndrome, are also usually familiar and occur more frequently in families carrying the Gilles de la Tourette's gene. The pathophysiology of this condition is still unknown. An abnormality in dopaminergic neurotransmission is generally believed to be a possible cause; abnormalities in the size of the basal ganglia have also been reported. The symptomatic treatment of tics is with neuroleptics (e.g., tiapride, haloperidol, lithium). Antidepressants are usually associated with other drugs in Gilles de la Tourette's syndrome.

Dystonia

Dystonia is characterized by sustained muscle contractions, which cause twisting or repetitive movements or gestures. Dystonia usually presents as a focal, segmental, or generalized disorder. Some forms of focal dystonias have specific names that are commonly used in clinical practice: Dystonia of the eyelids is called *blepharospasm*, dystonia of the vocal folds is called *spasmodic dysphonia*, cervical dystonia is called *torticollis*, and upper limb dystonia is often called *writer's cramp* (other names, such as "musician's cramp" or "professional cramp" are used for other task-specific dystonias of the upper limbs).

Dystonia is characterized by a typical combination of dystonic postures and dystonic movements. Dystonic postures are generally associated with a feeling of rigidity, traction, pain, or a cramp in relation to flexion, extension, or abnormal rotation of a body part along its major axis (torsion). Dystonic

movements may be fast or slow and are superimposed on dystonic postures; in some cases, the jerky movement is very similar to tremor (although irregular at times). Dystonia is typically associated with some peculiar voluntary movements that the patient performs in order to overcome abnormal postures; these are called "sensory tricks" or "gestes antagonistes." Their observation is very useful in confirming the diagnosis.

The severity of dystonia is variable. In milder forms, dystonia occurs when a specific voluntary movement is performed; in more severe forms, dystonia occurs in association with more than one kind of voluntary movement of the affected body part; in very severe forms, dystonia occurs when any body part is voluntarily moved or even at rest. These differences in relation to voluntary movement are seen either in focal or in generalized forms of dystonia with increasing severity.

The pathophysiology of dystonia is still unclear. Lesions at all levels of the basal ganglia, from the caudate nucleus to the thalamus, have been associated with dystonia, but peripheral nerve and spinal cord lesions have also been described in association with focal dystonia.

Focal dystonias generally appear in adults and are usually sporadic. In the majority of cases, focal dystonia is idiopathic, as no obvious cause or lesion is observed. A significant number of these cases occur with familial aggregation and are of genetic origin. Post-traumatic or symptomatic focal dystonia has also been described. In a number of cases, and particularly in familial cases, focal dystonia tends to spread to contiguous body parts, giving rise to segmental or generalized forms. Blepharospasm is a spasmodic contraction of the orbicularis oculi that is usually bilateral and is often triggered by exposure to light (hence, dark glasses worn by the patients). Talking often decreases the spasm. Patients can be functionally blind. A peculiar form of blepharospasm, called *pretarsal blepharospasm*, or apraxia of lid opening, causes an intermittent inability to open the eyelids. Spasmodic torticollis is the most common focal adult dystonia. An abnormal posture of the neck is generally observed at rest, producing a rotation (torticollis), inclination (laterocollis), anteflexion (antecollis), or retroflexion (retrocollis). In addition, mixed forms, in which different involuntary forms of movements and postures are superim-

posed, are quite frequent. A compensatory scoliosis, the elevation of the shoulder, as well as a postural tremor are frequently associated. Spasmodic dysphonia is caused by an abnormal contraction of the vocal muscles typically presenting with adduction ("strangled" or high-pitched voice) or abduction ("aphonic voice") of the vocal cords. Meige's syndrome is characterized by a variable combination of blepharospasm and oromandibular dystonia. Writer's cramp is a focal involuntary contraction of the forearm muscles that usually worsens with handwriting, while other motor tasks are well preserved. When a task-specific dystonia occurs during the use of a musical instrument or another professional tool, the professional or occupational dystonia bears a different name (e.g., pianist's cramp, typist's cramp).

Hemidystonia is generally symptomatic of a lesion in the contralateral hemisphere. Generalized dystonia occurs more commonly in childhood and generally is of familial origin.

Autosomal dominant, recessive, and X-linked forms of dystonia have been described. Clinical-genetic correlates of dystonia are currently one of the more lively areas of research in movement disorders. The gene *DYT-1* for generalized dystonia has been found in Ashkenazic Jews; other genes for focal dystonias have been localized or are being sought. The pathogenesis of dystonia is not understood. Dopa-responsive dystonia responds to low doses of levodopa. Other forms are treated with systemic medications or with local injections of botulinum toxin.

Chorea, Athetosis, and Ballism

Chorea is an irregular, unpredictable, involuntary movement with variable sequences, usually composed of very brisk and short-lasting jerks. Sometimes, choreic movements are slower and more complex, mimicking dystonia. Rapid flexion-extension, rotation, or crossing of the upper or lower limbs are frequent, together with some grimacing, tongue protrusion, vocalization, or respiratory noises. Two clinical features are specific for chorea and allow this dyskinesia to be distinguished from other movement disorders. First, choreic movements are fluent, meaning that they involve contiguous body parts in sequence and

almost invariably affect the face; second, chorea is associated with hypotonia and with motor impersistence, meaning that a patient is unable to hold a posture (e.g., sustained tongue protrusion, fist closure, or lateral rotation of the eyes) for 20 seconds or more. These features are so specific for chorea that they occur not only in Huntington's disease, but also in Sydenham's chorea and in other choreic disorders. Will can control chorea for only a few seconds. Choreic motor patterns are often combined with voluntary executed movements, which explains in part why many patients are often unaware of their chorea (Figure 17-1).

Athetosis is an old term that groups together two quite different dyskinesias. In some instances, athetosis is used to name a slower form of chorea, essentially distal and of low amplitude, irregular, and more stereotyped with snakelike motions. In other instances, the term refers to dystonia. Extension of the neck, flexion or torsion of the limbs or of the axial segments, or slow grimacing and dysphonic voice are characteristic features of dystonic "double athetosis," which is a common aftermath of cerebral palsy.

A proximal and axial form of chorea with large throwing movements of amplitude is called *ballism*. Ballism is increased by stress and emotions and can be confused with action myoclonus. Unilateral ballism (hemiballism) is by far the most frequent presentation. Ballism is characteristically associated with lesions of the subthalamic nucleus, but examples of different anatomic lesions have been reported.

Chorea, athetosis, and ballism can be symptomatic of a focal lesion in the basal ganglia or the thalamus. In such cases, the presentation is usually unilateral (hemichorea-hemiballism). In many instances, chorea is the result of hereditary causes (e.g., Huntington's disease, acanthocytosis, benign familial chorea, paroxysmal choreoathetosis, Hallervorden-Spatz disease, Wilson's disease). Inflammatory diseases (e.g., Sydenham's chorea, lupoid chorea, subacute sclerosing panencephalitis, Henoch-Schönlein purpura, vaccines), and drugs (e.g., levodopa, dopamine agonists, anticonvulsants, oral contraceptives, amphetamines, isoniazid, lithium) are also other important causes of chorea. Choreoathetosis and ballism can be treated symptomatically with neuroleptics.

Myoclonus

Myoclonus is a brisk and brief involuntary muscle contraction, that is usually intermittent and arrhythmic but occasionally rhythmic or repetitive. Myoclonus never produces abnormal postures or torsion of a limb. Positive myoclonus is a muscle contraction associated with a synchronous short EMG burst lasting 50–300 ms; negative myoclonus (asterixis) (Figure 17-2) is a sudden muscle decontraction associated with a brief loss of muscle activity that produces a sudden drop when maintaining postures. As with other dyskinesias, myoclonus can be focal, segmental, generalized, or multifocal. The amplitude may be variable with partial or global involvement of just a segment of a limb or the entire limb or the entire body.

Myoclonus is a reflex phenomenon that is usually triggered by a stimulus (a somatic sensation or an active or a passive movement) that may also occur without any apparent triggering phenomenon. Spontaneous myoclonus is thought to be a reflex response to common stimuli of low intensity that are not perceived as triggering factors. Reflex myoclonus is usually evoked by external stimuli (e.g., a noise, light, a sensory stimulus). Being a reflex phenomenon, myoclonus may be integrated at the level of the cerebral cortex (cortical myoclonus) or the brain stem (reticular myoclonus). Cortical reflex myoclonus is usually a focal or multifocal action myoclonus; reticular myoclonus is usually axial or proximal, whereas spinal myoclonus is usually focal.

Physiologic myoclonus occurs in the first stages of sleep or as a familial condition denominated essential benign myoclonus. In addition, myoclonus is a pathologic phenomenon that can be seen in many brain diseases (e.g., after anoxic injury) and in intoxications. Anticonvulsant medications are generally effective in the treatment of myoclonus.

Other Dyskinesias

Akathisia

Akathisia is the inability to stay put. Akathisia is associated with a state of physical and mental unease and the urge to move with an aimless, poorly organized motor hyperactivity. Akathisia has



Figure 17-1. Automatic photographic sequence (1.5 frames per second) of the involuntary movements observed in a patient with Huntington's disease. The time lapse between two consecutive images is approximately 600 ms. It can be observed that choreic movements are fast and fluent. Chorea is stereotyped (e.g., compare C and N). The high speed of choreic movements is demonstrated by the observation of a change in posture in two consecutive frames. (Reprinted with permission from A Albanese. *I Gangli Motori e i Disturbi del Movimento*. Padua: Piccin, 1991.)

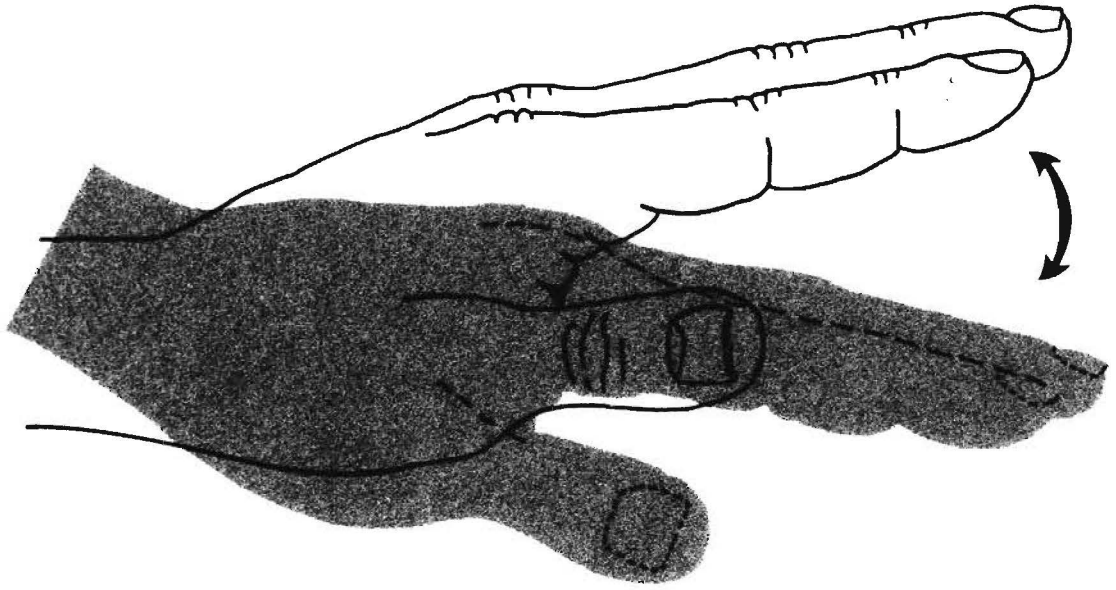


Figure 17-2. Asterixis is a negative myoclonus that can be elicited by asking the patient to outstretch the arms. Under this condition, the hand flexes abruptly and soon afterward regains the original position. (Reprinted with permission from A Albanese. *I Gangli Motori e i Disturbi del Movimento*. Padua: Piccin, 1991.)

no specific clinical features; it appears as an odd movement disorder that is described as an inner restlessness, a feeling of tension, an urge to move, or a distressing sensation in the limbs or trunk, usually associated with anxiety.

Akathisia is typically secondary to the use of neuroleptics and can occur within hours to years after the start of medication. Discontinuance of neuroleptics is the best treatment. In addition, akathisia is frequently seen in Parkinson's disease.

an irresistible urge to move the limbs followed by some relief in the symptoms. The patients may rub the skin, stretch, kick, swing the legs or walk, or press one foot against the other or against the calf. The pathophysiology is unknown. Familial restless legs syndrome can be associated with a polyneuropathy. Symptomatic forms can be associated with the use of various drugs, particularly with their withdrawal. The treatment mainly consists of dopaminergic drugs (levodopa or dopamine agonists).

Restless Legs Syndrome

Restless legs syndrome is characterized by sensory and motor features. The sensory syndrome is an uncomfortable sensation frequently reported in the legs, sometimes in the trunk, arms, or face, rarely asymmetric or alternating, which is usually ill-described by the patients. Adjectives such as creeping, stretching, itching, and burning are used. Characteristically, the symptoms occur only when the limbs are at rest, lying or sitting, especially in the evening and at night. Some mild discomfort can be described during the day. The motor features are

Syndrome of Painful Legs and Moving Toes

Painful legs and moving toes is a dysesthetic dyskinesia characterized by pain in the legs or feet (rarely the hands) that is described as aching, burning, a feeling of pressure, or pulling with variable degrees in intensity. It is often decreased by immersion in water and it is associated with movements of the toes (e.g., wiggling, fanning, clawing), the feet, or the legs. These movements are stereotyped, are continuous or intermittent, and can be suppressed for a few seconds voluntarily. The syndrome is generally bilateral; it starts usually after

40 years of age and may present in two forms: with or without polyneuropathy. The other main condition in the differential diagnosis is restless legs, which occur only at rest.

Abnormal Startle

Startle is a normal physiologic reaction of a newborn to unexpected stimuli. It is elicited as a reflex phenomenon by pediatricians (reflex of Moro) and disappears with normal development. In some people, based on their genetic makeup, startle is maintained into adult life. People with such features suffer from a disease called *hyperplexia*. The milder form is expressed as an increased startle reaction to unexpected stimuli, whereas in the severe form, startle is accompanied by a muscular rigidity of short duration with hyperextension of the arms. Families with hyperplexias have been described in the United States ("Jumping Frenchmen of Maine") and elsewhere. In these cases, everyday life becomes very much impaired because of a series of startle reactions and of violent jumping after normal stimuli. Automatic obedience, echolalia, and echopraxia are also features observed in these forms. The treatment of choice is benzodiazepines.

Tardive Dyskinesias

Tardive dyskinesias are the movement disorders produced by a chronic administration of neuroleptic drugs. They usually present the features of a focal or segmental dystonia, which is often combined with some facial chorea, akathisia, and parkinsonian features. Tardive dyskinesias are most commonly involved and often have the aspect of art movement disorders. A history of neuroleptic administration may be concealed or

may not be immediately recognized, particularly in those individuals who take neuroleptics for circulatory disorders (e.g., flunarizine, cinnarizine) or for gastrointestinal disturbances (e.g., tiapride).

Psychogenic Dyskinesias

Psychogenic dyskinesias are not a rare occurrence and can resemble any movement disorder (e.g., chorea, dystonia, tremor). Psychogenic dyskinesias are sometimes difficult to differentiate from organic dyskinesias, as the emotional impact of the doctor-patient relationship sometimes does not allow for an objective evaluation of the clinical features. These movement disorders must also be differentiated from tardive dyskinesia, which also occurs in patients who have psychopathologic traits and usually have complex or bizarre clinical presentations. According to DSM criteria, psychogenic dyskinesia should be classified as somatoform disorders or malingering.

Suggested Reading

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