

Chapter 11

Dystonic Tremor

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Abbreviations

CD	Cervical dystonia
DAT-SPECT	Dopamine transporter single photon emission computed tomography
DBS	Deep brain stimulation
ET	Essential tremor
PD	Parkinson's disease
PWT	Primary writing tremor
SWEDD	Scans without evidence of dopaminergic deficit.

Keywords Dystonia • Mirroring • Sensory tricks • Torticollis • Spasmodic dysphonia • Primary writing tremor

Tremor is the most common movement disorder, known since the time of Galen, and defined as a rhythmic involuntary movement of one or several regions of the body (Albanese and Jankovic 2012). Many attempts have been made in the last century to define and classify normal and pathological tremors, but a comprehensive summary did not exist until the Movement Disorder Society developed a first consensus statement (Deuschl et al. 1998). Among several types of tremor, essential tremor (ET) is the most common, although its epidemiology is still unclear (see also Chap. 10). The clinical signs and symptoms of ET are much

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broader than previously thought, ranging from a relatively benign postural tremor to a disabling kinetic or intention tremor that affects the hands and also the head (Leegwater-Kim et al. 2006). Even rest tremor has been observed in advanced ET. A tremor similar to ET may occur in dystonia and can be mistaken for non-dystonic tremor, particularly when it is isolated (Lalli and Albanese 2010). Various types of focal task-specific tremors (e.g., vocal tremor, primary writing tremor) have been described in the past 35 years and it is still a matter of debate whether these tremors are focal tremulous dystonias, focal essential tremors, or an independent condition.

The term “dystonic tremor” appeared in the 1980s in papers recognizing that dystonic patients sometime have rhythmic movements, particularly in the arms and neck, manifesting as tremor (Jankovic and Fahn 1980). This concept was not easy to accommodate and the current consensus statement from the Movement Disorder Society defines dystonic tremors by three features: an associated dystonic posture, irregular amplitudes and frequency (usually 7 Hz), and postural/intentional tremor rather than resting tremor (Deuschl et al. 1998). This consensus attempted to distinguish dystonic tremor from tremor associated with dystonia, a more generalized tremor type observed in limbs that are not affected by the dystonia. This is a relatively symmetrical type, often seen in the upper limbs in patients with spasmodic torticollis (Munchau et al. 2001). Isolated action tremor can be the initial symptom of dystonia, and dystonia may develop years after the onset of isolated tremor in the neck, trunk, or limbs (Deuschl 2003). Consequently, isolated focal and task-specific tremors should raise the suspicion of dystonia, and long-term follow-up may be confirmatory.

11.1 Epidemiology

Primary dystonia, the most common form of dystonia, includes early-onset dystonia with onset in a limb and a tendency to generalize, and late-onset dystonia, which most commonly presents with a focal or a segmental form. Focal dystonias are adult-onset forms that affect a specific area of the body: eyes, mouth, vocal cords, neck, hands, and feet. Types of focal dystonia include blepharospasm, cervical dystonia (spasmodic torticollis), oromandibular dystonia (cranial dystonia), laryngeal dystonia (spasmodic dysphonia), and hand dystonia (writer’s cramp) (Albanese 2003). Among focal dystonias, cervical dystonia (CD) is the most common form seen by neurologists with a prevalence ranging from 5.7 to 6.1 per 100,000 persons (Stacy 2008). Patients with CD may have coexisting signs of limb tremor (Velickovic et al. 2001) or head tremor and trunk (Rivest and Marsden 1990), which makes differential diagnosis between dystonic and essential tremor difficult.

ET is the most common adult movement disorder, although its epidemiology is still unclear. As a result of application of imprecise and variable diagnostic

criteria, prevalence estimates range from 0.4% to 3.9%, with an increase with age (Louis et al. 1998). More recently, three large population-based surveys with narrow diagnostic criteria found prevalence data of 4%, 4.8%, and 3.06% (Benito-Leon et al. 2003; Dogu et al. 2005; Wenning et al. 2005). In a retrospective 45-year study, the age-adjusted incidence was estimated to be 17.5/100,000 per year (Rajput et al. 1984); a large population-based study in Spain reported an incidence rate of 616/100,000 per year in a population older than 65 years (Benito-Leon et al. 2005).

The prevalence of dystonic tremor is not known. In one Brazilian cross-sectional study, the evaluation of the frequency of postural hand tremor in idiopathic and symptomatic dystonia patients showed that tremor might be seen in 22.5% of primary dystonia and in 21.5% of secondary dystonia (Ferraz et al. 1994). In a large survey of patients from a large Indian movement disorder center, dystonic tremor constituted about 20% of all patients presenting with non-parkinsonian and non-cerebellar tremors (essential tremor, 60%) (Shukla and Behari 2004).

11.2 Phenomenology

11.2.1 *Essential Tremor*

ET is a slowly progressive tremor disorder that sometimes causes severe disability, but is not life-threatening. Its phenomenology has been reviewed in Chap. 10 (Essential Tremor and Other Forms of Kinetic Tremor). The traditional view of ET as a monosymptomatic disorder has been revised when its complexity and heterogeneity have been recognized (Lou and Jankovic 1991). ET may begin in childhood, but its incidence increases after 40 years, with a mean onset of 35–45 years in different studies. The few data available on the progression of this condition have shown a decrease of tremor frequency in the elderly with a linear relationship between age and tremor frequency decrement and a tendency to develop larger amplitudes (Elble 2000a).

ET usually starts with a postural tremor that can still be suppressed during goal-directed movements. In advanced stages, an “intention” (kinetic) tremor can develop. This is accompanied by signs of cerebellar dysfunction of hand movements like movement overshoot and slowness of movements (Deuschl et al. 2000). In more advanced stages, a resting tremor can develop. Also, a mild gait disorder observed during tandem gait is frequently found (Stolze et al. 2001). Kinetic tremor develops at various intervals between 3 and 30 years after the onset of postural tremor (Deuschl et al. 2000). Disease-related disability varies greatly and is dependent on the severity of intention tremor. ET affects the hands in 94% of cases, the head in 33%, the voice in 16%, the legs in 12%, the jaw in 8%, the face in 3%, and the trunk in 3% (Elble 2006). In some body areas (e.g., head, voice, or chin), tremor may occur in isolation. About 50–90% of the patients improve with alcohol ingestion.

11.2.2 Dystonia

Dystonia is a neurological syndrome characterized by involuntary muscle contractions causing twisting, repetitive movements, or abnormal postures. Etiologically dystonia syndromes can be primary or secondary. In primary forms there is no identifiable exogenous cause or evidence of neurodegeneration, and dystonia is the only sign of the disease (with the only possible addition of tremor); the cause is either genetic or unknown. Non-primary forms encompass hereditodegenerative syndromes, where dystonia is a prominent sign of a hereditodegenerative condition and symptomatic syndromes, where dystonia is due to exogenous factors (e.g., perinatal injury, medications, brain tumor, infections, etc.). In 1984, an ad hoc committee of the Dystonia Medical Research Foundation documented the occurrence in all forms of dystonia “of sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures” (Fahn et al. 1987); later, it was recognized that the association of slow tonic posturing with faster (phasic) movements and tremor is the clinical hallmark of this movement disorder (Albanese 2003). The combination of tremor and dystonia is a feature of almost all dystonia syndromes and may be easily recognized. Isolated dystonic tremor, instead, is often misdiagnosed for ET (Lalli and Albanese 2010).

Similarly to ET, the prevalence values for primary dystonia vary greatly. It is reckoned that there are between 0.2 and 5 cases per 100,000 for early-onset cases, and between 3 and 732 cases per 100,000 for late-onset cases (Defazio et al. 2004). A possible explanation of such ample variability of incidence and prevalence values is the difficulty or the delay of the clinical diagnosis and lack of diagnostic markers. There is no dopaminergic denervation either in dystonia or in ET resulting in a normal dopamine transporter single photon emission computed tomography (DAT-SPECT) (Kagi et al. 2010). The most obvious reason for diagnostic errors is lack of appreciation of the specific clinical features of dystonia, which can be appreciated by using a structured diagnostic flow chart (Albanese and Lalli 2009). Table 11.1 proposes a recently systematized description of the cardinal physical signs observed in dystonia (Albanese 2007). Overflow is observed when dystonia extends to a contiguous body region where it is not observed as an independent phenomenon. An example is overflow to the upper limb in patients with cervical dystonia. Mirroring occurs when, during a voluntary task involving a limb, similar albeit involuntary movements (often with dystonic features) arise in the contralateral limb. Mirroring is not a specific feature of dystonia, although it may reveal a latent dystonia, particularly in subjects belonging to dystonia families. Mirroring can be considered as a minimal expression of focal dystonia observed in otherwise unaffected body regions. Dystonic movements and postures may be alleviated by some specific voluntary movements, also called *gestes antagonistes*, or by “sensory tricks.” Their presence strongly supports the diagnosis of dystonia. When the full-house phenomenology is observed, the clinical diagnosis is plainly achieved by direct physical examination. Otherwise, additional clinical signs are necessary. The observation of abnormalities at the electromyography (EMG) that are typical of dystonia is helpful when the clinical features are considered insufficient for the diagnosis (Pullman et al. 2000).

Table 11.1 Clinical criteria for the physical signs observed in patients with dystonia [from Albanese and Lalli (2009)]

Physical sign	Description
Dystonic postures	• A body part is flexed or twisted along its longitudinal axis (not available for blepharospasm or laryngeal dystonia) • A sensation of rigidity and traction is present in the affected part
Dystonic movements	These features have to be looked for in all movement disorders, either fast or slow, also when the immediate impression is that of a “tremor,” “tic,” “chorea,” or “myoclonus” • A twisting nature or a pull in a preferred direction is detected (also when the movement appears as tremor) • Movements are repetitive and patterned (i.e., consistent and predictable) • Movements are often sustained at their peak to lessen when a given posture (usually opposite to the preferred direction) is identified (“null point”)
Gestes antagonistes (“sensory tricks”)	• Alleviation of dystonia occurs during the geste movement, usually soon after its start • Alleviation may last for as long as the geste or slowly reverses spontaneously before its end • The geste movement is natural and “elegant,” never forceful • The geste movement does not push or pull the affected body part, but simply touches it (“sensory trick”) or accompanies it during alleviation of dystonia
Mirror dystonia	• At least three different types of repetitive tasks (e.g., finger sequence, normal writing, or piano-like movements) are performed at low and fast speed in the non-affected limb
Overflow dystonia	• Dystonic movement or dystonic postures extend beyond the commonly involved body region • It is observed at least once, ipsilaterally or contralaterally, either by inspection or EMG mapping, in coincidence with the peak of dystonic movements

11.2.3 Dystonic Tremor

This is a debated entity and different descriptions have been made without achieving consensus on a unitary definition (Table 11.2). Dystonic tremor is frequently observed in patients with dystonia who often show tremulous muscle activities. Virtually any dystonic syndrome may manifest with dystonic tremor. The EMG-pattern may be more variable than in other tremors such as essential tremor or parkinsonian tremors (Deuschl 2003). Burst-like activity may be synchronous or asynchronous (Cohen and Hallett 1988), without a detectable agonist–antagonist coupling. The Movement Disorder Society Consensus Statement on Tremor (Deuschl et al. 1998) considered a continuous gradient between tremor and dystonia with three possible transition spectra: dystonic tremor, tremor associated with dystonia, and dystonia gene-associated tremor.

Dystonic tremor is considered a tremor in a body part affected by dystonia. This involves: tremor in an extremity or body part that is affected by dystonia, focal

Table 11.2 Timeline for definitions of dystonic tremor

Year	Descriptions of dystonic tremor
1976	Dystonia and tremor in spasmodic torticollis patients (Couch 1976)
1976	Benign essential tremor in combination with idiopathic torsion dystonia (Marsden 1976)
1978	Clinical features of 12 patients with spasmodic dysphonia: the voice was strained, harsh, tight, and tremulous (Aminoff et al. 1978)
1988	Focal tremor and focal dystonia related to generalized essential tremor and generalized dystonia (Rosenbaum and Jankovic 1988)
1989	The “yips” is an involuntary motor disturbance affecting golfers described most frequently as jerks, tremors, and spasms affecting the preferred arm distally and primarily during putting (McDaniel et al. 1989)
1990	Patients presenting with isolated tremors of the trunk or neck are described. Their clinical features were similar to seven other patients who presented with head tremor, or arm and head tremor, but then eventually developed obvious torticollis, sometimes with arm dystonia (Rivest and Marsden 1990)
1990	Patients with reflex sympathetic dystrophy (RSD) who manifested abnormalities of movement. The patients had focal dystonia, weakness, spasms, tremor, difficulty initiating movement, and increased tone and reflexes (Schwartzman and Kerrigan 1990)
1991	Patients with early-onset ET were more likely to have hand involvement and associated dystonia than patients with late-onset ET. Dystonia was more frequently associated with mild ET than with severe ET (Lou and Jankovic 1991)
1991	Dystonic tremor in idiopathic dystonia described to be postural, localized, and irregular in amplitude and periodicity, absent during muscle relaxation, exacerbated by smooth muscle contraction. “Although it resembles essential tremor, dystonic tremor seems to be a distinct entity: it is more irregular with a broader range of frequencies; it is asymmetric and remains localized; myoclonus is sometimes associated. This type of tremor is most often seen in the presence of dystonia, but may be observed without evident dystonic symptoms” (Jedynak et al. 1991)
1996	Cases of focal tremors induced by different specific tasks. There was no overt dystonia in any of the cases, but these tremors may be forms of focal dystonia, rather than a manifestation of essential tremor (Soland et al. 1996)

tremors, usually with irregular amplitudes and variable frequency (mainly less than 7 Hz), and mainly postural/kinetic tremors usually not seen during complete rest. Tremor associated with dystonia is a tremor occurring in a body part not affected by dystonia, although the patient has dystonia elsewhere. In dystonia gene-associated tremor, tremor is an isolated finding in patients with a dystonic pedigree. These definitions are quite clear, albeit artificial and unpractical. Furthermore, patients who exhibit focal tremors without overt signs of dystonia have been retrospectively considered to have a dystonic tremor (Rivest and Marsden 1990) because later developed overt dystonia. There are neurophysiological evidences that such tremors preceding the onset of dystonic tremor are common among patients presenting otherwise with essential-like tremor (Munchau et al. 2001). It is not uncommon that patients with dystonic tremor may be considered to have parkinsonian or essential

tremor and—at a closer look—are found to match diagnostic criteria for dystonia. *Gestes* and mirroring are particularly helpful for orientation and should be looked for in all cases of primary tremor disorder. Hand mirror movements have also been described in ET (Louis et al. 2009), being more common in ET cases with rest tremor (18.8%) than in cases without rest tremor (14.3%). Differently from ET, dystonic tremor does not occur during rest and the incidence of a mirroring associated with postural or kinetic hand tremors should lead, at first, to a suspicion of dystonic tremor.

There are no descriptions of mirroring in sites different from the hands in patients with ET, whereas mirroring occurs in all districts of dystonic movements. Many patients with dystonic tremor use their own tricks (*geste antagoniste* or sensory tricks) to reduce the tremor amplitude. This is well known for dystonic head tremor in the setting of cervical dystonia with tremor reduction if patients touch the head or only lift the arm (Masuhr et al. 2000). The effect of these maneuvers can sometimes be difficult to observe clinically, and may be revealed by suppression of surface EMG from the affected muscles (Masuhr et al. 2000). Other important, albeit less specific, diagnostic clues are the focal nature and low frequency of dystonic tremor. In addition to these features, dystonic tremor may also be distinguished by some other possible features, including a “null point” (i.e., specific posture which when held by the patient alleviates the tremor), and features atypical for ET (e.g., lack of tremor when the finger touches the nose, but severe tremor when attempting an arm movement toward an extended target such as an examiner’s finger) (Jedynak et al. 1991).

The diagnosis of dystonia can be missed or delayed in a number of patients with task- and position-specific tremors, particularly primary writing tremor (PWT), occupational tremors, or isolated voice tremor, as typical features of dystonia may not develop until after many years from onset (Rivest and Marsden 1990). The differential diagnosis between ET and dystonia may be difficult and their phenomenological overlap is well accounted. A tremor similar to ET may occur in dystonia and can be mistaken for non-dystonic tremor, particularly when it is isolated (Lalli and Albanese 2010). For example, head or voice tremors observed in tremulous forms of cervical dystonia can be very hard to distinguish from ET (Elble 2000b). In some cases, family history may orientate in favor of the correct diagnosis, particularly if family members are ascertained to have dystonia. This differential diagnosis is not always straightforward and the variability of epidemiological data for ET unveils diagnostic uncertainties. There are also a number of ET cases where there is suspicion that dystonia features may have been overlooked. Commonly, in epidemiological studies on ET several aspects which might indeed have suggested a dystonia phenotype (head tremor, voice tremor, very asymmetric limb tremor, and a positive family history in absence of any known cause not considered in the inclusion criteria) are not included (Benito-Leon et al. 2009).

Patients with dystonic tremor may have a resting tremor mimicking a Parkinson’s disease (PD)-like tremor, especially in cases in which dystonic posturing is not well evident (sometimes only a dystonic thumb extension) (Lalli and Albanese 2010).

Table 11.3 Clues suggesting a diagnosis of dystonia in patients presenting with tremor syndromes [from Lalli and Albanese (2010)]

Clinical orientation	Clues suggesting dystonic tremor
Parkinson's disease	Diagnostic inconsistencies • There is no progression to develop features other than tremor and dystonia • There is no clear fatiguing or decrement while performing repetitive movements • DAT scan is normal (SWEDD) • Features do not improve with dopaminergic treatment (consider acute challenge) Features suggesting the dystonic nature of movements or postures • There is thumb extension tremor, and tremor does not have a pill-rolling aspect • Tremor is task- or position-specific • There is head tremor • Voice is dystonic • Variation of tremor following positional changes of the arms (positional dystonic tremor) • EMG mapping supports a diagnosis of dystonia
Essential tremor	Diagnostic inconsistencies • Head tremor is isolated • Patients with voice tremors cannot change pitch during vocalization • Tremor does not improve with ET therapy (i.e., propranolol, primidone) Features suggesting the dystonic nature of movements or postures • With head rotation there is clear asymmetry of tremor • Tremor disappears with geste maneuver • There is neck pain or hypertrophy of neck muscles (particularly if asymmetric) • EMG mapping or tremor analysis support a diagnosis of dystonia • Mirroring produces torsional movements • Family history is positive and dystonia has not been ruled out in other family members

Dystonic patients sometimes have jaw tremor, facial hypomimia, loss of arm swing on the affected side, increased limb tone, and clumsiness often misdiagnosed as bradykinesia. In this context, there is an intriguing condition in which patients who received a diagnosis of PD present a scans without evidence of dopaminergic deficit (SWEDD). The issue whether patients with PD-like phenomenology and normal DAT-SPECT may in fact be affected by dystonia has recently emerged (Lalli and Albanese 2010). Aside clinical features suggesting a diagnosis of dystonia, a normal DAT SPECT can rule out PD. This finding is not specific of primary dystonia and also occurs in dopa-responsive dystonia, ET, psychogenic tremor, or cases of vascular parkinsonism or of drug-induced parkinsonism (Albanese and Lalli 2010). In order to familiarize with features that orientate to a diagnosis of dystonia, we have listed a number of diagnostic clues for each condition in which misdiagnosis has been reported (Table 11.3).

11.3 Pathophysiology

The pathophysiology of dystonic tremor is largely unknown. Inhibitory circuits within the central nervous system may be abnormal in dystonic tremor. Especially reciprocal inhibition was found to be reduced in those conditions associated with dystonic tremors (Munchau et al. 2001; Berardelli et al. 1998). In addition, when assessing the reciprocal inhibition between forearm muscles, two different patterns have been described: patients with normal levels of presynaptic inhibition are affected by an ET-like tremor starting simultaneously with torticollis; in patients with reduced or absent presynaptic inhibition, arm tremor preceded onset of torticollis by a longer interval (Munchau et al. 2001). Recent research studies focus on reorganization of cortical motor maps for the hand (Byrnes et al. 1998) as well as the abnormal finger representation in the primary sensorimotor cortex in patients with focal hand dystonia (Bara-Jimenez et al. 1998, 2000). An abnormal finger representation in sensorimotor cortex occurs in dystonia (Elbert et al. 1998), and this abnormality, in the absence of congenital brain abnormalities, is thought to reflect the enlarged and overlapping receptive fields. Moreover, it has been hypothesized that a possible clinical correlate of this cortical remodeling is a dysfunction of spatial discrimination. This may cause difficulties to selectively innervate individual muscle groups and may thereby contribute to dystonic movements.

A specific secondary dystonia syndrome featuring tremor and associated with thalamic lesions has been called “thalamic tremor” (Miwa et al. 1996). The phenomenology here is part of a specific dystonia–athetosis–chorea–action tremor syndrome due to lateral–posterior thalamic strokes (Kim 2001). In the setting of a well-recovered severe hemiparesis, the combination of tremor with a kinetic component, dystonia, and a severe sensory loss are the important clues for the diagnosis. Proximal segments are often involved. The syndrome also may develop with a certain delay after the initial insult.

11.4 Dystonic Tremor Phenotypes

11.4.1 *Head and Upper Limb Tremor in Cervical Dystonia*

Tremor is a common feature in patients with cervical dystonia. Dystonic head tremor usually has a jerky attitude and side prevalence, being more pronounced and forceful when the head is rotated on one side. All forms of genetically determined dystonia may present with dystonic tremors of the head or hands (Albanese 2003; Bressman et al. 2000). Most dystonic movements are accompanied by tremulous movements. In some cases, tremor may occur in extremities which are not or not yet affected by dystonia. Furthermore, tremor may precede the onset of dystonia. Cervical dystonia patients presenting with head tremor often have

also hand tremor and a family history of tremor or other movement disorders (Pal et al. 2000). Head tremor can be the presenting sign of cervical dystonia and remain isolated for long periods and even for the whole disease course. In such cases, the differential diagnosis with ET may become a difficult task. The presence of a sensory trick can help recognize the dystonic nature of head tremor (Masuhr et al. 2000), for example when a light touch of the chin or of another head region improves tremor.

Hand and arm tremors have been described in patients with primary cervical dystonia (Couch 1976). This type of tremor usually has the same frequency and recruitment characteristics as physiological tremor and is considered a variant of physiological tremor (Deuschl et al. 1997). Some of these patients are considered to have ET in addition to dystonia (Elble 2000b). The study of reciprocal inhibition allowed to identify two groups of patients (Munchau et al. 2001): one with normal levels of presynaptic inhibition and another with reduced or absent presynaptic inhibition. In the first group, arm tremor started simultaneously with cervical dystonia whereas in the other group it preceded the onset of dystonia. These physiological data suggest that there may be two subgroups of cervical dystonia patients, one with “dystonic arm tremor,” another with ET-like phenomenology, called “tremor associated with dystonia” (Berardelli et al. 1998). The description of these cases, however, did not consider the occurrence of activation/deactivation features and other semeiologic maneuvers aimed at detecting the occurrence of mild limb dystonia. The implementation of current diagnostic criteria (Albanese and Lalli 2009) may provide different views in future observations.

11.4.2 Voice Tremor in Spasmodic Dysphonia

Voice tremor has been described as a feature of a number of neurological conditions, including PD (Midi et al. 2008), ET (Sulica and Louis 2010), ataxic dysarthria (Boutsen et al. 2011), and spasmodic dysphonia (SD) (Gillivan-Murphy and Miller 2011; Kendall and Leonard 2011). SD affects the laryngeal muscles causing involuntary and sustained muscle contraction. Patients with SD have an approximate 7% risk that dystonia may spread to another body part (Svetel et al. 2007).

The clinical picture may be that of an adductor-type or an abduction-type speech impairment (Barkmeier et al. 2001). The adduction-type dysphonia is a voice disorder characterized by a strained strangled voice quality and intermittent voice stoppages, or breaks associated with over-adduction of the vocal folds. These voice breaks typically occur during speech associated with voiced speech sounds and during sustained phonation in moderate to severe cases of the disorder. Stressful speaking situations may exacerbate speech symptoms while they appear absent, or reduced in severity, during activities such as laughing, throat clearing, coughing, whisper, humming, and falsetto speech productions (Ludlow and Connor 1987). Abductor spasmodic dysphonia is characterized by intermittent breathy breaks

associated with prolonged abduction of the vocal folds during voiceless consonants in speech. These voice breaks typically occur during speech associated with voiceless speech sounds (Ludlow et al. 1991). Vocal tremor often co-occurs in dysphonia (Aminoff et al. 1978). A recent study (White et al. 2011) showed that patients with spasmodic dysphonia were 2.8 times more likely to have co-prevalent tremor than the control group (other voice disorders). This study suggests the need to properly evaluate patients with voice tremor looking for body tremor and other dystonias.

11.4.3 Primary Writing Upper Limb Tremor

PWT is a condition in which tremor, usually characterized by prominent pronation/supination wrist movements, occurs predominantly or exclusively during writing (Rothwell et al. 1979). No other neurological signs are evident except for slight postural and terminal kinetic tremor. PWT can be task-induced or position-sensitive. The epidemiology and the natural course of PWT have not been fully elucidated. Age at onset varies and cases manifesting during childhood have been reported. The disorder begins slowly, progresses for years, and becomes stabilized. Family history is generally unremarkable (Klawans et al. 1982).

This focal task-specific tremor has been variably classified as an independent entity, an ET variant, a focal dystonia, or a bridging entity (Soland et al. 1996). In the first reported cases, the writing disorder and tremor were both temporarily abolished by a partial motor point anesthesia of the pronator teres, suggesting that tremor was caused by an abnormal central response to muscle spindle discharges originating in the pronator teres (Rothwell et al. 1979). Although it resembles ET (where tremor is present on action, and on maintenance of a posture, and may affect hand-writing), the task-specific nature, lack of response to propranolol, and the documented effect of central cholinergic drugs (Klawans et al. 1982) suggest that PWT is more closely related to primary dystonia than ET (Elble 2000b; Elble et al. 1990). The observation of an abnormal co-activation of antagonist muscles also supports this view (Elble et al. 1990). However, PWT can be differentiated from focal task-specific dystonia (such as writer's cramp) by the lack of excessive overflow of EMG activity into the proximal musculature, and the absence of reciprocal inhibition of the median nerve H-reflex upon radial nerve stimulation (Bain et al. 1995; Modugno et al. 2002).

11.5 Treatment

There is a paucity of information about the treatment of dystonic tremor. There are no specific therapeutic trials evaluating treatment efficacy on dystonic tremor. The efficacy of botulinum toxin for dystonic head tremor (Jankovic and Schwartz 1991)

and tremulous spasmodic dysphonia (Watts et al. 2006) is well documented. A double-blind study has also documented the efficacy of botulinum toxin for hand tremor (Brin et al. 2001), but its use for this indication is limited due to the risk of secondary muscle weakness. Clonazepam was observed to be beneficial in cervical dystonia with a predominant head tremor (Davis et al. 1995; Hughes et al. 1991). The usual starting dose is 0.5 mg in the evening. Doses up to 8 mg can be used. Propranolol (up to 320 mg per day) and primidone (up to 250 mg three times daily) are the mainstay treatments for ET, but are also useful for patients with dystonic tremor syndromes (Bain 2002).

Severe tremor cases in the setting of the context of a generalized dystonia have been successfully treated with deep brain stimulation (DBS) of the internal globus pallidus (Coubes et al. 2004). Bilateral subthalamic nucleus DBS has also been reported to improve cervical dystonia, dystonic head tremor, and ET-like hand tremor in one patient (Chou et al. 2005). DBS of the subthalamic region, including the zona incerta, remarkably improved proximal dystonic tremor refractory to Vim thalamotomy (Plaha et al. 2008). The subthalamic region contains pallidal outflow pathways and may be considered a target equivalent to the internal globus pallidus.

There are no controlled studies on PWT. Propranolol, primidone, levodopa, and neuroleptics have proven ineffective. Anticholinergics, when tolerated, may help (Klawans et al. 1982). Botulinum toxin has been reported to be helpful in PWT (Papapetropoulos and Singer 2006). Notwithstanding this evidence, treatment of PWT is often ineffective. The disability caused by this condition can vary from mild to considerable, depending on the patient's profession and needs. The resulting functional impairment may be not considered sufficient to warrant DBS treatment, particularly in the Western culture. In Eastern Asia, instead, where calligraphy is an important occupation, thalamotomy has been considered an indication for PWT when it threatens a patient's professional career (Ohye et al. 1982). Successful Vim DBS procedures have also been reported (Racette et al. 2001).

Improvement of PWT with a simple hand orthotic device has also been observed (Espay et al. 2005). Similar results have been reported using a thermoplastic hand orthosis for writer's cramp patients, who showed improvement in their writing ability (Tas et al. 2001). Other non-pharmacological approaches considered in upper limb dystonia may apply to PWT. Immobilization by a plastic splint has led to intriguing hypotheses (Priori et al. 2001) which have not received confirmation. It has been affirmed that limb immobilization might be useful particularly in patients with a short history of dystonia (<18 months) (Pesenti et al. 2004), whereas patients with longer disease duration may fail to obtain consistent benefit. Immobilization could be useful as a preparatory phase for other rehabilitative approaches, such as sensory retraining (Zeuner et al. 2008). Studies on focal hand dystonia in musicians suggest that a combination of constraint-induced therapy and specific motor control retraining may provide a successful strategy for the treatment of focal dystonias (Altenmüller and Jabusch 2010; Berque et al. 2010).

References

- Albanese A. The clinical expression of primary dystonia. *J Neurol*. 2003;250(10):1145–51.
- Albanese A. Dystonia: clinical approach. *Parkinsonism Relat Disord*. 2007;13 Suppl 3:S356–61.
- Albanese A, Jankovic J. Distinguishing clinical features of hyperkinetic disorders. In: Albanese A, Jankovic J, editors. *Hyperkinetic movement disorders: differential diagnosis and treatment*. 1st ed. London: Blackwell; 2012. p. 3–14.
- Albanese A, Lalli S. Is this dystonia? *Mov Disord*. 2009;24(12):1725–31.
- Albanese A, Lalli S. Distinguishing scan without evidence of dopaminergic depletion patients with asymmetric resting tremor from Parkinson's disease: a clinical diagnosis of dystonia is required. *Mov Disord*. 2010;25(16):2899.
- Altenmüller E, Jabusch HC. Focal dystonia in musicians: phenomenology, pathophysiology, triggering factors, and treatment. *Med Probl Perform Art*. 2010;25(1):3–9.
- Aminoff MJ, Dedo HH, Izdebski K. Clinical aspects of spasmodic dysphonia. *J Neurol Neurosurg Psychiatry*. 1978;41(4):361–5.
- Bain PG. The management of tremor. *J Neurol Neurosurg Psychiatry*. 2002;72 Suppl 1:I3–9.
- Bain PG, Findley LJ, Britton TC, Rothwell JC, Gresty MA, Thompson PD, et al. Primary writing tremor. *Brain*. 1995;118(Pt 6):1461–72.
- Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C. Abnormal somatosensory homunculus in dystonia of the hand. *Ann Neurol*. 1998;44(5):828–31.
- Bara-Jimenez W, Shelton P, Hallett M. Spatial discrimination is abnormal in focal hand dystonia. *Neurology*. 2000;55(12):1869–73.
- Barkmeier JM, Case JL, Ludlow CL. Identification of symptoms for spasmodic dysphonia and vocal tremor: a comparison of expert and nonexpert judges. *J Commun Disord*. 2001;34(1–2):21–37.
- Benito-Leon J, Bermejo-Pareja F, Morales JM, Vega S, Molina JA. Prevalence of essential tremor in three elderly populations of central Spain. *Mov Disord*. 2003;18(4):389–94.
- Benito-Leon J, Bermejo-Pareja F, Louis ED. Incidence of essential tremor in three elderly populations of central Spain. *Neurology*. 2005;64(10):1721–5.
- Benito-Leon J, Louis ED, Bermejo-Pareja F. Risk of incident Parkinson's disease and parkinsonism in essential tremor: a population based study. *J Neurol Neurosurg Psychiatry*. 2009;80(4):423–5.
- Berardelli A, Rothwell JC, Hallett M, Thompson PD, Manfredi M, Marsden CD. The pathophysiology of primary dystonia. *Brain*. 1998;121(Pt 7):1195–212.
- Berque P, Gray H, Harkness C, McFadyen A. A combination of constraint-induced therapy and motor control retraining in the treatment of focal hand dystonia in musicians. *Med Probl Perform Art*. 2010;25(4):149–61.
- Boutsen F, Duffy JR, Dimassi H, Christman SS. Long-term phonatory instability in ataxic dysarthria. *Folia Phoniatr Logop*. 2011;63(4):216–20.
- Bressman SB, Sabatti C, Raymond D, De LD, Klein C, Kramer PL, et al. The DYT1 phenotype and guidelines for diagnostic testing. *Neurology*. 2000;54(9):1746–52.
- Brin MF, Lyons KE, Doucette J, Adler CH, Caviness JN, Comella CL, et al. A randomized, double masked, controlled trial of botulinum toxin type A in essential hand tremor. *Neurology*. 2001;56(11):1523–8.
- Byrnes ML, Thickbroom GW, Wilson SA, Sacco P, Shipman JM, Stell R, et al. The corticomotor representation of upper limb muscles in writer's cramp and changes following botulinum toxin injection. *Brain*. 1998;121(Pt 5):977–88.
- Chou KL, Hurtig HI, Jaggi JL, Baltuch GH. Bilateral subthalamic nucleus deep brain stimulation in a patient with cervical dystonia and essential tremor. *Mov Disord*. 2005;20(3):377–80.
- Cohen LG, Hallett M. Hand cramps: clinical features and electromyographic patterns in a focal dystonia. *Neurology*. 1988;38(7):1005–12.
- Coubes P, Cif L, El FH, Hemm S, Vayssiere N, Serrat S, et al. Electrical stimulation of the globus pallidus internus in patients with primary generalized dystonia: long-term results. *J Neurosurg*. 2004;101(2):189–94.

- Couch JR. Dystonia and tremor in spasmodic torticollis. *Adv Neurol*. 1976;14:245–58.
- Davis TL, Charles PD, Burns RS. Clonazepam-sensitive intermittent dystonic tremor. *South Med J*. 1995;88(10):1069–71.
- Defazio G, Abbruzzese G, Livrea P, Berardelli A. Epidemiology of primary dystonia. *Lancet Neurol*. 2004;3(11):673–8.
- Deuschl G. Dystonic tremor. *Rev Neurol (Paris)*. 2003;159(10 Pt 1):900–5.
- Deuschl G, Heinen F, Guschlbauer B, Schneider S, Glocker FX, Lucking CH. Hand tremor in patients with spasmodic torticollis. *Mov Disord*. 1997;12(4):547–52.
- Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. *Mov Disord*. 1998;13 Suppl 3:2–23.
- Deuschl G, Wenzelburger R, Löffler K, Raethjen J, Stolze H. Essential tremor and cerebellar dysfunction clinical and kinematic analysis of intention tremor. *Brain*. 2000;123(Pt 8):1568–80.
- Dogu O, Louis ED, Sevim S, Kaleagasi H, Aral M. Clinical characteristics of essential tremor in Mersin, Turkey—a population-based door-to-door study. *J Neurol*. 2005;252(5):570–4.
- Elbert T, Candia V, Altenmüller E, Rau H, Sterr A, Rockstroh B, et al. Alteration of digital representations in somatosensory cortex in focal hand dystonia. *Neuroreport*. 1998;9(16):3571–5.
- Elble RJ. Essential tremor frequency decreases with time. *Neurology*. 2000a;55(10):1547–51.
- Elble RJ. Diagnostic criteria for essential tremor and differential diagnosis. *Neurology*. 2000b;54 Suppl 4:S2–6.
- Elble RJ. Report from a U.S. conference on essential tremor. *Mov Disord*. 2006;21(12):2052–61.
- Elble RJ, Moody C, Higgins C. Primary writing tremor. A form of focal dystonia? *Mov Disord*. 1990;5(2):118–26.
- Espay AJ, Hung SW, Sanger TD, Moro E, Fox SH, Lang AE. A writing device improves writing in primary writing tremor. *Neurology*. 2005;64(9):1648–50.
- Fahn S, Marsden CD, Calne DB. Classification and investigation of dystonia. In: Marsden CD, Fahn S, editors. *Movement disorders 2*. London: Butterworths; 1987. p. 332–58.
- Ferraz HB, de Andrade LA, Silva SM, Borges V, Rocha MS. Postural tremor and dystonia. Clinical aspects and pathophysiological considerations. *Arq Neuropsiquiatr*. 1994;52(4):466–70.
- Gillivan-Murphy P, Miller N. Voice tremor: what we know and what we do not know. *Curr Opin Otolaryngol Head Neck Surg*. 2011;19(3):155–9.
- Hughes AJ, Lees AJ, Marsden CD. Paroxysmal dystonic head tremor. *Mov Disord*. 1991;6(1): 85–6.
- Jankovic J, Fahn S. Physiologic and pathologic tremors. Diagnosis, mechanism, and management. *Ann Intern Med*. 1980;93(3):460–5.
- Jankovic J, Schwartz K. Botulinum toxin treatment of tremors. *Neurology*. 1991;41(8):1185–8.
- Jedynak CP, Bonnet AM, Agid Y. Tremor and idiopathic dystonia. *Mov Disord*. 1991;6(3): 230–6.
- Kagi G, Bhatia KP, Tolosa E. The role of DAT-SPECT in movement disorders. *J Neurol Neurosurg Psychiatry*. 2010;81(1):5–12.
- Kendall KA, Leonard RJ. Interarytenoid muscle botox injection for treatment of adductor spasmodic dysphonia with vocal tremor. *J Voice*. 2011;25(1):114–9.
- Kim JS. Delayed onset mixed involuntary movements after thalamic stroke: clinical, radiological and pathophysiological findings. *Brain*. 2001;124(Pt 2):299–309.
- Klawans HL, Glantz R, Tanner CM, Goetz CG. Primary writing tremor: a selective action tremor. *Neurology*. 1982;32(2):203–6.
- Lalli S, Albanese A. The diagnostic challenge of primary dystonia: evidence from misdiagnosis. *Mov Disord*. 2010;25(11):1619–26.
- Leegwater-Kim J, Louis ED, Pullman SL, Floyd AG, Borden S, Moskowitz CB, et al. Intention tremor of the head in patients with essential tremor. *Mov Disord*. 2006;21(11):2001–5.
- Lou JS, Jankovic J. Essential tremor: clinical correlates in 350 patients. *Neurology*. 1991;41(2 Pt 1): 234–8.
- Louis ED, Ottman R, Hauser WA. How common is the most common adult movement disorder? Estimates of the prevalence of essential tremor throughout the world. *Mov Disord*. 1998;13(1):5–10.

- Louis ED, Rios E, Henschcliffe C. Mirror movements in patients with essential tremor. *Mov Disord.* 2009;24:2211–7.
- Ludlow CL, Connor NP. Dynamic aspects of phonatory control in spasmodic dysphonia. *J Speech Hear Res.* 1987;30(2):197–206.
- Ludlow CL, Naunton RF, Terada S, Anderson BJ. Successful treatment of selected cases of abductor spasmodic dysphonia using botulinum toxin injection. *Otolaryngol Head Neck Surg.* 1991;104(6):849–55.
- Marsden CD. Dystonia: the spectrum of the disease. In: Yahr MD, editor. *The basal ganglia.* New York: Raven; 1976. p. 351–67.
- Masuhr F, Wissel J, Muller J, Scholz U, Poewe W. Quantification of sensory trick impact on tremor amplitude and frequency in 60 patients with head tremor. *Mov Disord.* 2000;15(5):960–4.
- McDaniel KD, Cummings JL, Shain S. The “yips”: a focal dystonia of golfers. *Neurology.* 1989;39(2 Pt 1):192–5.
- Midi I, Dogan M, Koseoglu M, Can G, Sehitoglu MA, Gunal DI. Voice abnormalities and their relation with motor dysfunction in Parkinson’s disease. *Acta Neurol Scand.* 2008;117(1):26–34.
- Miwa H, Hatori K, Kondo T, Imai H, Mizuno Y. Thalamic tremor: case reports and implications of the tremor-generating mechanism. *Neurology.* 1996;46(1):75–9.
- Modugno N, Nakamura Y, Bestmann S, Curra A, Berardelli A, Rothwell J. Neurophysiological investigations in patients with primary writing tremor. *Mov Disord.* 2002;17(6):1336–40.
- Munchau A, Schrag A, Chuang C, MacKinnon CD, Bhatia KP, Quinn NP, et al. Arm tremor in cervical dystonia differs from essential tremor and can be classified by onset age and spread of symptoms. *Brain.* 2001;124:1765–76.
- Ohye C, Miyazaki M, Hirai T, Shibasaki T, Nakajima H, Nagaseki Y. Primary writing tremor treated by stereotactic selective thalamotomy. *J Neurol Neurosurg Psychiatry.* 1982;45(11):988–97.
- Pal PK, Samii A, Schulzer M, Mak E, Tsui JK. Head tremor in cervical dystonia. *Can J Neurol Sci.* 2000;27(2):137–42.
- Papapetropoulos S, Singer C. Treatment of primary writing tremor with botulinum toxin type A injections: report of a case series. *Clin Neuropharmacol.* 2006;29(6):364–7.
- Pesenti A, Barbieri S, Priori A. Limb immobilization for occupational dystonia: a possible alternative treatment for selected patients. *Adv Neurol.* 2004;94:247–54.
- Plaha P, Khan S, Gill SS. Bilateral stimulation of the caudal zona incerta nucleus for tremor control. *J Neurol Neurosurg Psychiatry.* 2008;79(5):504–13.
- Priori A, Pesenti A, Cappellari A, Scarlato G, Barbieri S. Limb immobilization for the treatment of focal occupational dystonia. *Neurology.* 2001;57(3):405–9.
- Pullman SL, Goodin DS, Marquez AI, Tabbal S, Rubin M. Clinical utility of surface EMG: report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. *Neurology.* 2000;55(2):171–7.
- Racette BA, Dowling J, Randle J, Mink JW. Thalamic stimulation for primary writing tremor. *J Neurol.* 2001;248(5):380–2.
- Rajput AH, Offord KP, Beard CM, Kurland LT. Essential tremor in Rochester, Minnesota: a 45-year study. *J Neurol Neurosurg Psychiatry.* 1984;47(5):466–70.
- Rivet J, Marsden CD. Trunk and head tremor as isolated manifestations of dystonia. *Mov Disord.* 1990;5(1):60–5.
- Rosenbaum F, Jankovic J. Focal task-specific tremor and dystonia: categorization of occupational movement disorders. *Neurology.* 1988;38(4):522–7.
- Rothwell JC, Traub MM, Marsden CD. Primary writing tremor. *J Neurol Neurosurg Psychiatry.* 1979;42(12):1106–14.
- Schwartzman RJ, Kerrigan J. The movement disorder of reflex sympathetic dystrophy. *Neurology.* 1990;40(1):57–61.
- Shukla G, Behari M. A clinical study of non-parkinsonian and non-cerebellar tremor at a specialty movement disorders clinic. *Neurol India.* 2004;52(2):200–2.

- Soland VL, Bhatia KP, Volonte MA, Marsden CD. Focal task-specific tremors. *Mov Disord.* 1996;11(6):665–70.
- Stacy M. Epidemiology, clinical presentation, and diagnosis of cervical dystonia. *Neurol Clin.* 2008;26 Suppl 1:23–42.
- Stolze H, Petersen G, Raethjen J, Wenzelburger R, Deuschl G. The gait disorder of advanced essential tremor. *Brain.* 2001;124(Pt 11):2278–86.
- Sulica L, Louis ED. Clinical characteristics of essential voice tremor: a study of 34 cases. *Laryngoscope.* 2010;120(3):516–28.
- Svetel M, Pekmezovic T, Jovic J, Ivanovic N, Dragasevic N, Maric J, et al. Spread of primary dystonia in relation to initially affected region. *J Neurol.* 2007;254(7):879–83.
- Tas N, Karatas GK, Sepici V. Hand orthosis as a writing aid in writer's cramp. *Mov Disord.* 2001;16(6):1185–9.
- Velickovic M, Benabou R, Brin MF. Cervical dystonia pathophysiology and treatment options. *Drugs.* 2001;61(13):1921–43.
- Watts C, Nye C, Whurr R. Botulinum toxin for treating spasmodic dysphonia (laryngeal dystonia): a systematic Cochrane review. *Clin Rehabil.* 2006;20(2):112–22.
- Wenning GK, Kiechl S, Seppi K, Muller J, Hög B, Saletu M, et al. Prevalence of movement disorders in men and women aged 50–89 years (Bruneck Study cohort): a population-based study. *Lancet Neurol.* 2005;4(12):815–20.
- White LJ, Klein AM, Hapner ER, Delgado JM, Hanfelt JJ, Jinnah HA, et al. Coprevalence of tremor with spasmodic dysphonia: a case-control study. *Laryngoscope.* 2011;121(8):1752–5.
- Zeuner KE, Peller M, Knutzen A, Hallett M, Deuschl G, Siebner HR. Motor re-training does not need to be task specific to improve writer's cramp. *Mov Disord.* 2008;23(16):2319–27.