Dystonia

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ABSTRACT

Introduction: Dystonia is a clinically heterogeneous group of hyperkinetic movement disorders. Recent advances have provided a better understanding of these conditions which significant clinical impact.

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Areas of agreement: a recent consensus classification, including the assessment of phenomenology and identification of the dystonia syndromes, has provided a helpful tool for the clinical assessment. New forms of monogenic dystonia have been recently identified.

Areas of controversy: despite recent advances in the understanding of dystonia, treatment remains symptomatic in most patients.

Growing points: recent advances in genetics have provided a better understanding of the potential pathogenic mechanisms involved in dystonia. Deep brain stimulation has shown to improve focal and combined forms of dystonia and its indications are constantly expanding.

Areas timely for developing research: growing understanding of the disease mechanisms involved will allow the development of targeted and disease-modifying therapies in the future.

INTRODUCTION

Since Oppenheim coined the term *"dystonia musculorum deformans"* in 1911, the definition of dystonia has been a subject of debate and controversy.[1] It refers to a group of conditions defined by the nature of the hyperkinetic movement disorder but with highly heterogeneous clinical presentations and underlying aetiologies.[2] The diagnosis of dystonia is purely based on the clinical phenomenology and it is considered to be one of the most poorly recognized movement disorders even among neurologists. Recent advances in its clinical classification, genetics and underlying pathophysiology have provided a better understanding of this condition and important tools for the clinician to guide diagnosis and management.

DEFINITION, PHENOMENOLOGY AND CLINICAL ASSESSMENT

A revised definition of dystonia has recently been proposed after a consensus agreement by international experts.[1] *Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous. Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.*

The underlying hallmark of dystonia is involuntary sustained muscle contractions producing abnormal postures or movements. However, there is a great phenotypic variability which might contribute to its under recognition in mild or atypical cases. Given the absence of specific diagnostic tests, the diagnosis remains clinical and recognition of the multiple clinical manifestations of this hyperkinetic movement disorder is crucial for a correct diagnosis. Key clinical features and additional clinical signs that can be useful diagnostic clues in cases with atypical phenomenology are summarised in table 1. In most cases dystonia combines sustained postures, as well as discontinuous and irregular contractions leading to dynamic postures and intermittent movements. Sometimes these movements can have tremor-like

characteristics (oscillatory and seemingly rhythmical though often inconstant) referred to as dystonic tremor. Postures and movements in dystonia are patterned: they are usually repetitive, stereotyped and predictable, involving the same body part and directionality. Dystonia is often triggered or worsened by voluntary actions including movements and sustained postures against gravity. Severity of the symptoms can be also modified by sustaining the affected body part in different positions: symptoms may worsen when the body part is held against the direction of the dystonic movement (eg, turning the head to the left in right laterocollis) and may temporarily resolve when the body part is positioned in the maximum direction of the movement (eg, turning the head to the right in right laterocollis; this position is called null point). Sensory tricks (or g*estes antagonistes)* are voluntary simple manoeuvres not consisting in a forceful resistance of the dystonic movements (typically described in cervical dystonia as a light touch to the face or the chin), that can alleviate temporarily the symptoms. Sometimes dystonia is only present when performing a specific motor skill (task-specific dystonia) such as writing in writers' cramp/dystonia or musicians' dystonia. Dystonic contractions in the affected limb can also be triggered by contralateral motor tasks (eg, finger tapping in the non-affected hand can cause dystonic contractions in the contralateral arm) called mirror dystonia. Overflow refers to the spread of involuntary muscle contractions to an unaffected (usually contiguous but also contralateral) body part distinct from the primary site of dystonia.

Although in most cases recognition of dystonia is easily achieved by clinical examination, in some cases multisurface (mapping) electromyography (EMG) may be a useful complementary diagnostic tool in differentiating dystonia from other movement disorders (mainly tremor and myoclonus) by detection of the pattern of muscle activation (agonist-antagonist muscle coactivation, phasic and tonic activation, mirror dystonia and sensory tricks).[3] It may also be useful in identification of dystonic muscles to guide the treatment as discussed later. [4, 5] Patients with dystonia can present with asymmetric rest tremor, sometimes with pill-rolling characteristics, hypomimia, increased limb tone without rigidity,

reduced arm swing and even slow repetitive movements but without true bradykinesia.[6] The nigrostriatal system is spared in patients with dystonia and a normal dopaminergic transporter imaging may also be useful diagnostic tool in certain cases to differentiate dystonia from patients with degenerative parkinsonism.[7]

Isolated dystonia has classically been considered a purely motor condition but, as in other movement disorders, the presence of multiple other associated non-motor symptoms has been recently recognised with important clinical implications in disability and quality of life. These include sensory symptoms such as discomfort in that body part prior to development of dystonia, sensory tricks, pain or photosensitivity in blepharospasm, neuropsychiatric abnormalities such as depression, and sleep disturbances.[8, 9]

CLASSIFICATION

To incorporate recent advances in dystonia and address some of the limitations of previous classifications, an international consensus committee proposed a new classification system in order to facilitate diagnosis and treatment, but also a basis for development of research and pathogenesis.[1] The new classification scheme has two distinct axes: clinical characteristics (axis I) and aetiology (axis II) (Table 2).

- Axis I: clinical characteristics. They include age at onset, body distribution, temporal pattern and associated features with different subgroups. The aim of this axis is the recognition of the phenotypic characteristics of the different dystonic syndromes.
- Axis II: etiology. It contains two non-mutually exclusive subgroups: presence of identifiable nervous system pathology and pattern of acquisition. The aim of this axis is to classify dystonia according to common biological and pathophysiological mechanisms. This is a constant evolving area which will require regular update as advances improve the understanding of the underlying mechanisms.

DIAGNOSTIC APPROACH

Owing to the clinical heterogeneity and the growing number of causes, an accurate diagnosis of dystonia can be sometimes challenging. Classically movement disorder specialists have used a syndromic approach to diagnose dystonia, targeting diagnostic tests after matching the clinical features of the patient to known diseases. This approach relies in the clinician's expertise and the use of growing exhaustive lists of the causes of dystonia which might not be practical in clinical settings for the non-experts. Therefore more dynamic algorithms have been suggested [1, 10, 11] where classification and characterization of the main clinical features (using clinical characteristics from axis I of the classification) should guide the clinicians in the diagnostic decision making process, tailor the diagnostic tests and avoid unnecessary investigations. A suggested diagnostic pathway is proposed in Figure 1. Ideally an etiological diagnosis of the dystonic syndrome (axis II of the classification) should be reached after taking together the definition of the clinical characteristics and the results of the ancillary investigations. Following the current classification, we present the most common forms of dystonia based on their etiology and describe their most frequently associated clinical presentations.

IDIOPATHIC DYSTONIA WITHOUT EVIDENCE OF NERVOUS SYSTEM PATHOLOGY

Cervical dystonia

Cervical dystonia is the most common form of focal dystonia with a prevalence of 5 cases per 100000, symptom onset in the fifth decade and 2:1 female predominance.[12] It presents most frequently with abnormal postures including lateral tilting (laterocollis) and turning (torticollis) of the head, head tremor or a combination of both. Sensory tricks are reported in up to 80% of patients involving usually light touch to the lower face or neck.[13] Palpation

usually reveals increased muscle tone and hypertrophy of the muscles involved. Cervical dystonia commonly progresses within the initial few years before the symptoms stabilise.

Blepharospasm

Blepharospasm is characterised by bilateral synchronous spasms of the orbicularis oculi muscle resulting in repeated blinking and forceful closure of the eyelids with various degrees of functional blindness in most severe cases. Onset is usually insidious in the sixth decade with female predominance and associated with sensory symptoms including dry eyes, photosensitivity and sensory tricks. [14] Blepharospasm has the highest risk of spread among focal dystonias (around a third of patients) usually happening within the first few years of onset and involving lower face and jaw muscles (Meige syndrome).[15]

Oromandibular dystonia

Oromandibular dystonia affects the jaw muscles more common manifesting as closing-jaw dystonia with additional involvement of tongue and pharyngeal muscles. Typically dystonic spasms worsen during talking, chewing or eating and may result in impairment of speech and feeding in severe cases.[16]

Laryngeal dystonia (spasmodic dysphonia)

Laryngeal dystonia is a rare task-specific speech dystonia characterised more commonly by involuntary closure of the vocal cords (adductor spasmodic dysphonia) causing effortful, strained, strangulated voice interrupted by phonatory breaks. Voice is typically worse when speaking but it may improve with singing, whispering, shouting or changing the pitch. It usually presents in the fifth decade with a slight female predominance. Other less common

manifestations include abductor spasmodic dysphonia (resulting in a whispery voice interrupted by breathy breaks especially with consonants), voice tremor, stridor, dyscoordinate breathing, paroxysmal cough, hiccups, and sneezing.[17]

Task-specific dystonia

Task-specific dystonia is a form of isolated focal dystonia that occurs only during the performance of highly skilled, overlearned motor tasks. The most common forms are writers' dystonia and musicians' dystonia but it can involve any body part and tasks, including facial muscles in wind instrument players, golfers' yips in the upper limbs or foot dystonia in dancers.[18] Symptoms usually start insidiously during the fourth decade perceived initially as loss of fine motor control associated to a feeling of tightness that subsequently progresses to evident dystonic posturing. Dystonic contractions can remain highly task-specific but in a significant proportion of patients symptoms may develop during performance of other fine movements different from the initial motor tasks and may spread to the contralateral hand.[19] Examination should look for any dystonic contractions while performing specific triggering motor tasks but also body parts involved should be observed while at rest, holding different positions and performing other unrelated common motor tasks looking for mirror dystonia, overflow and null points.[18] Some patients may show additional increased tone, reduced arm swing and effortful repetitive movements in the involved limb but without decrement of the amplitude of the movement (bradykinesia).

INHERITED DYSTONIA WITHOUT EVIDENCE OF NERVOUS SYSTEM PATHOLOGY

Recent advances in the genetic of dystonia have led to the identification of a growing number of new forms of monogenic dystonia and expansion of the associated phenotype in both, isolated and combined dystonia syndromes.[20, 21] They have also provided better

understanding of the potential pathogenic molecular pathways including dysfunction in the endoplasmic reticulum-associated protein degradation and nuclear envelope systems, vesicle/protein trafficking in synaptic transmission and involvement of cell cycle control and transcriptional regulation.[22]

Isolated dystonia

DYT1 and DYT6 are the most common genetic causes of isolated dystonia. Both forms are autosomal dominant with reduced penetrance due to mutations in *TOR1A* (DYT1) and *THAP1* (DYT6) genes.[23, 24] DYT1 is classically associated with early-onset limb dystonia that gradually spreads to generalised dystonia while DYT6 typically remains segmental involving upper limbs and craniocervical regions with prominent laryngeal involvement.

Since the use of next-generation sequencing techniques, additional genes have been associated to adult-onset dominant forms of isolated dystonia: mutations in *CIZ1* gene (DYT23) have been associated with cervical dystonia,[25] mutations in *ANO3* gene (DYT24) with cervical dystonia with prominent tremor,[26] and *GNAL* gene mutations (DYT25) with craniocervical dystonia.[27] All three conditions are thought to be very rare and genetic testing is not commercially available or clinically recommended but mutations of these genes have also been described in cases without family history and may be responsible for a proportion of sporadic cases. Recently, heterozygous variants in the *KMT2B* (MLL4) gene have been identified in individuals with familial dystonia with prominent cervical, cranial and laryngeal dystonia.[28]

Combined dystonia syndromes

Dopa-responsive dystonia

The term dopa-responsive dystonia (DRD) encompasses a clinically and genetically heterogeneous group of conditions with a classic phenotype of early-onset lower limb dystonia with diurnal fluctuation and excellent and sustained response to levodopa. The most common and best characterised DRD is an autosomal dominant form due to mutations in the *GTP cyclohydrolase 1* gene (DYT5a also known as Segawa disease). It typically presents as childhood dystonia involving the lower limbs with diurnal fluctuations (worsening in the evenings and improvement with sleep) causing gait disturbances that gradually progresses to segmental or generalised dystonia. Other atypical features include brisk reflexes and extensor plantar response which may lead to the misdiagnosis of cerebral palsy, parkinsonism in adult-onset presentations, oculogyric crisis, myoclonus and neuropsychiatric symptoms such as anxiety, depression, sleep disturbances and obsessive-compulsive disorders.[29] Once the response of the symptoms is established after a levodopa trial, the diagnosis can be confirmed using genetic testing for most common *GTP cyclohydrolase 1* gene mutations. However commercially available genetic testing is not comprehensive and in cases with negative results but suggestive phenotype, additional analysis of cerebrospinal fluid levels of neurotransmitters and phenylalanine loading test may be useful to reach a diagnosis.[30] Dopamine transporter imaging shows normal results in DRD and may be useful in differentiating it from idiopathic Parkinson's disease (PD). However, adult-onset cases of degenerative parkinsonism with nigrostriatal degeneration (and abnormal dopamine transporter imaging) have been described in families with DRD secondary to rare *GTP cyclohydrolase 1* variants and the authors suggested that some mutations should be considered as risk factors for PD.[31] Symptoms of DRD have a dramatic and sustained response to small doses of levodopa (50-200 mg/day) even if the treatment is delayed for many years, and patients do not develop motor complications usually seen in patients with PD.

Other rare forms of DRD can be caused by recessive mutations in other genes encoding enzymes involved in the biosynthesis of dopamine such as tyrosine hydroxylase, sepiapterin

reductase and PTP synthase. These rare recessive forms usually present at an earlier age with a more severe phenotype and other associated neurological features (including cognitive impairment, hypotonia, seizures) but show similar good response to low doses of levodopa.[30]

Myoclonus dystonia syndrome

Myoclonus dystonia syndrome (MDS) is a rare condition with onset in the first two decades of life with a typical clinical pattern of alcohol-responsive upper body myoclonus with associated dystonia in two thirds of patients. Myoclonus is usually the main and most disabling symptom while dystonia is mild and manifests as cervical dystonia or writer's cramp. Psychiatric disorders including depression, anxiety, panic attacks and obsessive-compulsive behaviour are commonly reported.[32] MDS is inherited in an autosomal dominant manner and mutations in the epsilon-sarcoglycan gene (*SGCE*; DYT11) are responsible in less than half of the cases with reduced penetrance and maternal imprinting.[33] Recently, mutations in the *KCTD17* gene have been associated with MDS[34] and some cases may be secondary to mutations in genes classically related to other dystonic syndromes (*TOR1A, ANO3* and DRD associated genes) but also related to other genes yet to be identified.

Rapid-onset dystonia parkinsonism

Rapid-onset dystonia parkinsonism (DYT12) is a rare disorder that typically presents after triggering factors and progresses rapidly over hours to days with involuntary movements characterised by dystonia, bradykinesia and postural instability without tremor. Potential triggers include physical exertion, overheating, infections, alcohol binging, mild head trauma or emotional stress. Sometimes mild limb dystonia can precede the abrupt onset of the symptoms. Symptom onset is in childhood or early adulthood, they usually have a

rostrocaudal gradient with prominent bulbar involvement and they stabilise after the initial progression with little improvement.[35] Psychiatric disorders including anxiety, depression, obsessive-compulsive behaviour and psychosis have also been reported.[36] Rapid-onset dystonia parkinsonism is inherited in an autosomal dominant manner but commonly presents de novo caused by mutations in the ATP1A3 gene, which is also associated with alternating hemiplegia of childhood and more recently to paroxysmal dyskinesias and CAPOS syndrome (Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy and Sensori-neural hearing loss).[37]

Paroxysmal dyskinesias

Paroxysmal dyskinesias are a heterogeneous group of conditions characterised by recurrent episodes of hyperkinetic movements including dystonia. Three different forms are recognised although there is some clinical and genetic heterogeneity.[38, 39]

The most common subtype is paroxysmal kinesigenic dyskinesia (PKD) where attacks start in childhood and are triggered by sudden movements (such as standing from a sitting position or running from walking). Attacks can be preceded by an abnormal sensation, duration is short (usually < 1 min) but can happen multiple times per day with a peak in puberty. Symptoms usually respond to antiepileptics and carbamazepine is the drug of choice.[38] Mutations in the *PRRT2* gene account for the majority PKD cases and can also be associated to epilepsy, ataxia, hemiplegia and migraine.[39] In paroxysmal non-kinesigenic dyskinesia (PNKD) attacks last longer (usually several minutes), are triggered by coffee, alcohol or strong emotions but they are more infrequent. PNKD has been associated with mutations in the *MR-1* gene, also known as *PNKD* gene. Paroxysmal exercise-induced dyskinesia (PED) is thought to be the rarest form, where attacks are triggered by prolonged exercise usually lasting for several minutes. Mutations in the SLC2A1 gene, which encodes

the glucose transporter 1 (GLUT 1), are responsible for PED and it can be associated to migraine, hemiplegia, ataxia and epilepsy.[39]

ACQUIRED DYSTONIA

Acquired dystonia is a large and heterogeneous group of disorders.

Cases of dystonia secondary to structural lesions such as perinatal brain injury, central nervous system infections, brain tumours or vascular events commonly show abnormal findings on neuroimaging. They usually present as either hemidystonia or focal limb dystonia.

Drug-induced is a common form of dystonia and can present as an acute reaction to medications such as levodopa, dopamine agonists, dopamine-receptor blocking drugs, anticonvulsants and serotonin reuptake inhibitors, or as a persistent tardive syndrome after prolonged exposure to antipsychotics. Dystonia can also be caused by the toxic effect of manganese, cobalt, carbon monoxide, carbon disulphide, cobalt, methanol and other chemicals.

Dystonia can be part of the presentation of acquired neurodegenerative disorders although in these cases other neurological signs predominate on the examination. Examples include foot dystonia in PD, anterocollis in multiple system atrophy, blepharospasm in progressive supranuclear palsy or dystonic arm in corticobasal degeneration.

TREATMENT

Management of dystonia is typically symptomatic and oral medications, chemodenervation with botulinum toxin (BT) and surgical interventions are the three mainstays. Usually, symptomatic treatment is only partially effective and should not only focus on the management of the movement disorder but also other aspects of the condition. A

multidisciplinary approach including physical and psychological therapies should be considered in order to improve quality of life and specific tools to assess the impact of the treatment have been developed.[40] The choice of treatment will depend mainly on age, severity and distribution of the symptoms. [41] For patients with multifocal or generalised dystonia oral drugs are commonly the initial treatment although efficacy may only be partial and side effects may limit their use particularly in adult patients. On the other hand, focal or segmental dystonia are usually initially managed with botulinum toxin injections. Surgical procedures are generally considered in severe medication-refractory dystonia, particularly those with a genetically proven condition with generalised distribution, although its indications are constantly expanding.

The list of combined dystonia syndromes with available specific disease treatment is constantly expanding. It is essential not to miss them as a timely treatment might slow disease progression or even revert the symptoms. Wilson's disease and DRD are the most common examples but the list also includes other metabolic disorders such as GLUT1 deficiency, organic acidurias, lysosomal storage disorders or brain manganese accumulation.[42]

Oral medications

Pharmacological treatment is largely guided by empirical trials and personal experience as well-designed studies are scarce.[43]

Dopaminergic therapy, and particularly levodopa, is the specific treatment for DRD and patients have a dramatic and sustained response to small doses (50-200 mg/day) even if the treatment is delayed for many years.[30] An empirical trial with levodopa for 1 month is recommended in any dystonia with onset in childhood and young adulthood to rule out DRD even when the presentation lacks some classical features. Patients with other forms of

dystonia may also benefit of treatment with levodopa though the response is often only minimal.

Anticholinergics are considered the first line drug in patients with generalised dystonia and owing to the evidence from a double-blinded placebo-controlled trial, trihexyphenidyl is the preferred agent.[44] It should be started at 1mg/d and the dose slowly titrated to avoid side effects which may limit its benefit and include drowsiness, confusion, memory impairment and dry mouth. Therapeutic dose ranges from 6-40mg/d and children usually tolerate much higher doses having a better chance of benefit. Baclofen is usually better tolerated (side effects include sedation, dizziness and cognitive impairment) and high doses (therapeutic dose 40-120mg/d divided in 3 doses) may be beneficial especially in children with spasticity associated to dystonia. Dopamine depleting drugs such as tetrabenazine (starting dose 12.5mg/d; therapeutic dose 50-150mg/d divided in 3 daily doses) has also shown some improvement particularly in those with tardive dystonia. Potential side effects include drowsiness, depression and parkinsonism. Benzodiazepines (clonazepam: starting dose 0.5mg/d, therapeutic dose 1-6mg/d) may also be beneficial particularly as an adjunctive therapy.

Botulinum toxin

BT is the treatment of choice in most patients with focal or segmental dystonia including cervical dystonia, blepharospasm, oromandibular dystonia, laryngeal dystonia and writer's cramp.[45, 46] BT causes a chemodenervation of the muscle by interfering with the release of acetylcholine from the nerve terminals into the neuromuscular junction. As a consequence of changes in the peripheral sensory input, BT could also have a therapeutic effect on the central nervous system by modifying the excitability and plasticity of central pathways.[47] There are two different serotypes with several available formulations without marked differences in efficacy or side effects:[48] serotype A (onabotulinumtoxinA,

abobotulinumtoxinA, incobotulinumtoxinA) and serotype B (incobotulinumtoxinB). Improvement usually starts a few days after the injections with a peak in 4-6 weeks. The effect gradually wears off but the benefit usually persists for 12-16 weeks, so the injections are repeated 3-4 times per year. The dose, selection of muscles and number of injection sites should be highly individualised based on severity, distribution of the symptoms, response to previous injections and bulk of the muscles. Identification of dystonic muscles is usually through careful clinical examination, but in complex cases use of ultrasound or electromyography can improve target muscle selection.[4, 5] Adverse effects are local and temporary generally due to diffusion of BT to adjacent structures: ptosis, dry eyes and diplopia in blepharospasm, dry mouth, neck weakness and dysphagia in cervical dystonia, and excessive weakness in limb dystonia. Most cases of reduced response to BT treatment are due to suboptimal injection schemes (inappropriate BT dose or muscle target selection) although in a proportion of secondary non-responders development of neutralising antibodies may block BT action.[49]

Deep brain stimulation

Deep brain stimulation (DBS) of the globus pallidus internus (GPi) has become the preferred surgical procedure and ablative and denervation techniques have been largely abandoned. GPi DBS has been shown to be effective in the treatment of isolated generalised, segmental and medication-refractory cervical dystonia [50, 51] with better response in those with DYT1 mutations. Patients with dystonia have a delayed clinical response with the phasic component of dystonia usually improving within weeks while dystonic postures may take several months or even longer. Risks are due to the surgical procedure (but lower than for other patients undergoing DBS as dystonia patients are younger), complications of the device (infections, lead breakage) and stimulation-related which can be resolved with modification of the settings (dysarthria, parkinsonism). Other focal isolated dystonias

(writer's cramp), combined dystonias (myoclonus dystonia syndrome), dystonia associated to PD and tardive dystonia may also benefit from GPi DBS. There is a less favourable response in those with dystonia secondary to structural brain lesions (eg; cerebral palsy).[52]

Other therapies

Physical therapies are aimed at maintaining a full range of motion and prevent contractures. Several interventions including rehabilitation, physical devices, sensori-motor training and behavioural therapy have shown to improve dystonia, mainly as adjunctive therapies, although the supporting evidence to recommend them is limited.[53]

Recent advances in the understanding of the pathophysiological mechanisms of dystonia have prompted the assessment of transcranial magnetic stimulation as a potential treatment for dystonia. Results have been conflicting and heterogeneity of the protocols makes difficult to draw any conclusions although this is an area of active research.[54]

CONCLUSIONS

Recognition of the dystonia phenomenology and identification of the dystonia syndrome using the consensus classification is essential for an accurate clinical diagnosis which then guides potential therapy. Symptomatic treatment with oral medication and BT should be highly individualised based on severity and distribution of the symptoms and GPi DBS is a successful option for an increasing number of patients. Recent advances in genetics, neurophysiology and imaging studies have provided a better understanding of the underlying pathophysiology of dystonia. Further research on these areas will allow developing disease-modifying therapies in the future.

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TABLES

Table 1. Motor phenomenology in dystonia.

Clinical feature	Description
Dystonic posture / movement	A body part is flexed, extended or twisted along its longitudinal axis with associated sensation of rigidity and traction. Postures can be sustained or dynamic. Movements can be fast or slow, continuous or intermittent.
Dystonic tremor	Oscillatory and seemingly rhythmical though often inconsistent and irregular dystonic movements. Dystonic tremor is often exacerbated by positioning the affected area against the maximum direction of the pull.
Patterning	Postures and movements are stereotyped, involving the same body part and with a characteristic directionality.
Voluntary action	Dystonia is typically influenced by voluntary actions and sometimes it is only activated by performing a specific motor task (task-specific dystonia)
Overflow	Unintentional muscle contraction that accompanies the primary site of dystonia but is anatomically distinct (usually contiguous but also contralateral)
Mirror dystonia	Dystonic symptoms triggered in the affected limb when the unaffected limb performs a motor task
Null point	Resolution of dystonic symptoms when the body part affected is placed in the maximum direction of the pull
Alleviating manoeuvres (*geste antagoniste,* sensory trick)	Simple voluntary manoeuvres not consisting in a forceful opposition of the movement that can temporarily minimize dystonic symptoms
Pseudodystonia	Abnormal movements and/or postures that do not share the clinical phenomenology of dystonia and are caused by a known or presumed cause with a different pathophysiological basis.

Table 2. New consensus classification of dystonia according to clinical and etiological features.

Axis I: clinical characteristics	
Age at onset	- Infancy (0-2 years) - Childhood (3-12 years) - Adolescence (13-20 years) - Early adulthood (21-40 years) - Late adulthood (>40 years)
Body distribution	- Focal: one body region (blepharospasm, cervical dystonia) - Segmental: >2 contiguous body regions (blepharospasm + oromandibular dystonia) - Multifocal: >2 non-contiguous body regions - Hemidystonia: one body side - Generalised: trunk and 2 other sites
Temporal pattern	- Disease course: static vs progressive - Variability: persistent, action-specific, diurnal fluctuations, paroxysmal
Associated features	- Isolated (may include tremor) - Combined with other movement disorder - Co-occurring neurological or systemic manifestations
Axis II: etiology	
Nervous system pathology	- Degenerative - Structural (static) lesions - No evidence of degenerative or structural lesions
Mode of acquisition	- Inherited: autosomal dominant, autosomal recessive, X-linked recessive, mitochondrial - Acquired (known cause): perinatal brain injury, infection, drugs, toxins, vascular, neoplastic, brain injury, psychogenic - Idiopathic (unknown cause): sporadic, familial

FIGURE CAPTION

Figure 1. Diagnostic algorithm of dystonia