

The New Classification System for the Dystonias: Why Was It Needed and How Was It Developed?

H.A. Jinnah, MD, PhD,^{1,*} Alberto Albanese, MD^{2,3}

Evolving the Definition of Dystonia

The term dystonia originated in 1911 with Oppenheim's description of 4 individuals who were floppy at rest, yet developed stiffness when they tried to move.¹ He believed the core problem was a defect in muscle tone, so he coined the term *dys-tonia*, which literally means abnormal muscle tone. Over the next decades, additional clinical manifestations of dystonia were recognized, and various authorities began to alter Oppenheim's definition according to their own views. It was not until 1984 that the Dystonia Medical Research Foundation (DMRF) created a committee to develop a more unified definition: "Dystonia is a syndrome of sustained involuntary muscle contractions, frequently causing twisting or repetitive movements, or abnormal postures."

In the decades that followed this definition, more was learned about the manifestations of dystonia, and expert opinions again led to varying adjustments to the definition. As a result, a new consensus committee revised the definition.² This committee was again supported by the DMRF, but also by Dystonia Europe, the International Parkinson and Movement Disorder Society (formerly the Movement Disorders Society), and an international panel with broad expertise in the clinical and biological basis of the dystonias: "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 essential change was the addition of the word intermittent and two other sentences. The word intermittent was added to address the frequent misconception that dystonic movements are always sustained, slow, or twisting.^{3,4} Examples of rapid, intermittent dystonic movements include blinking in blepharospasm, voice breaks in spasmodic dysphonia, tremor-dominant dystonias, and myoclonic dystonia. One sentence was added to

emphasize that the varied clinical manifestations may be tremulous or twisting, but they tend to be patterned. The second sentence was added to emphasize characteristic worsening with voluntary action, a feature noted in Oppenheim's original concept.

Evolving the Classification of the Dystonias

An increasing appreciation of the varied clinical manifestations and causes for dystonia over the years also led to varying proposals for how to classify them (Table 1). The committee that recently revised the definition agreed that a more widely acceptable system would be useful, and it began by delineating the problems that were motivating many of the recently proposed changes for classification (Table 2).

The changes recommended by the committee are summarized in Table 3. The most significant change involved dividing the classification system into two separate axes, one for clinical features and the other for etiologies. The reason was that the design of any classification system depends, in large part, on its goals, and for the dystonias, there are two main goals. A major goal for the clinician is to organize the many dystonias into clinically meaningful groups to facilitate diagnosis, treatment, and clinical research. On the other hand, an etiology-based classification is directly related to treatment algorithms and for organizing biological knowledge to guide the development of novel concepts regarding pathogenesis and the design of new therapies.^{5,6}

These two goals are only partly overlapping, so the importance of both was addressed by dividing the classification of the dystonias into two main axes.² The first axis focuses on clinical manifestations with four dimensions that address the character of dystonia, including body region affected, age at onset, temporal aspects, and any associated clinical manifestations. The second axis focuses on etiology with two dimensions for inheritance or underlying neuropathology. The two different axes

¹Departments of Neurology, Human Genetics and Pediatrics, Emory University, Atlanta, Georgia 30322, USA; ²Department of Neurology, Catholic University, Milan, Italy; ³Department of Neurology, Carlo Besta Institute of Neurology, Milan, Italy

*Correspondence to: Dr. H.A. Jinnah, Departments of Neurology, Human Genetics and Pediatrics, Emory University, Suite 6300, Woodruff Memorial Building, 101 Woodruff Circle, Atlanta, GA 30322, USA; E-mail: hjinnah@emory.edu

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TABLE 1 Evolving classifications for the dystonias

Fahn and Eldridge (1976)	Fahn (1988)	Fahn (1998)	Bressman (2004)	Albanese (2011)
Primary Hereditary Sporadic	Idiopathic	Primary Hereditary Sporadic	Primary Hereditary Sporadic	Primary Pure Dystonia plus Paroxysmal
Secondary Heredodegenerative Environmental	Symptomatic	Dystonia Plus	Secondary Dystonia plus Degenerative Complex Acquired	Heredodegenerative
Psychological		Heredodegenerative Acquired		Secondary

This table shows a representative sample of some of the most commonly used classifications for dystonia.

TABLE 2 Weaknesses of historical terminology

Basis for Classification	Weaknesses Identified
Primary vs. secondary	Inconsistent use of terms across proposals Inappropriate cultural connotations following translation
Dystonia-plus	Concept not logically based on etiology Inconsistent inclusion of different dystonias across proposals Arbitrary meaning of "plus"
Heredodegenerative	Concept not logically based on etiology Some disorders are hereditary, but not degenerative. Some disorders are degenerative, but not hereditary. Waste-basket category with little value for organizing knowledge

were not envisioned as being independent. Instead, the goal of delineating the clinical phenomenology (Axis I) is to build a comprehensive picture of a syndromic pattern (Fig. 1). This pattern can then be used to narrow down potential causes for diagnostic testing.⁷ The rationale for revising the original dimensions for classification are outlined below.

Revising Classification According to Body Region Affected (Axis I)

The classification of the dystonias by the body region affected has enormous practical value in guiding treatment decisions. Patients with focal or segmental dystonias are more likely to be treated with botulinum toxins, and those with broader distributions are more likely to require oral medications or surgery. This approach for classification was retained, with the only recommendation being more-specific guidelines regarding the diagnosis of *generalized* dystonia. Previous classifications relied on involvement of one or both legs, but the new classification requires involvement of the trunk and at least two other sites.

Revising Classification According to Age at Onset (Axis I)

Classification by age at onset also has practical clinical value for counseling regarding prognosis and guiding diagnostic testing.

TABLE 3 Classification of the dystonias

Axis	Dimension for Classification	Subgroups
Axis I: clinical features	Age at onset	Infancy (birth to 2 years) Childhood (3–12 years) Adolescence (13–20 years) Early adulthood (21–40 years) Late adulthood (40 years and older)
	Body distribution	Focal (one isolated body region) Segmental (two or more contiguous regions) Multifocal (two or more noncontiguous regions) Hemidystonia (half the body) Generalized (trunk plus two other sites)
	Temporal pattern	Disease course (static vs. progressive) Short-term variation (e.g., persistent, action specific, diurnal, or paroxysmal)
	Associated features	Isolated (with or without tremor) Combined (with other neurological or systemic features)
Axis II: etiology	Nervous system pathology	Degenerative Structural (e.g., focal static lesions) No degenerative or structural pathology
	Heritability	Inherited (e.g., sex linked or autosomal, dominant or recessive, or mitochondrial) Acquired (e.g., brain injury, drugs/toxins, vascular, or neoplastic)
	Idiopathic	Sporadic Familial

Childhood-onset dystonias are much more likely to become generalized and much more likely to have a discoverable cause. Whereas earlier classifications recognized two groups (early and late onset) with an age cutoff of 26 years, the new classification system has five age groups recognizing a spectrum of onset from pediatric to adult.

The reason for this change was that the previous concept of two groups divided at 26 years of age was based on a single study that focused on discriminating patients with DYT1 dystonia from those who did not.⁸ This age discriminator is not suitable for application to all dystonias. For example, metabolic disorders with dystonia generally begin before 3 years of age,

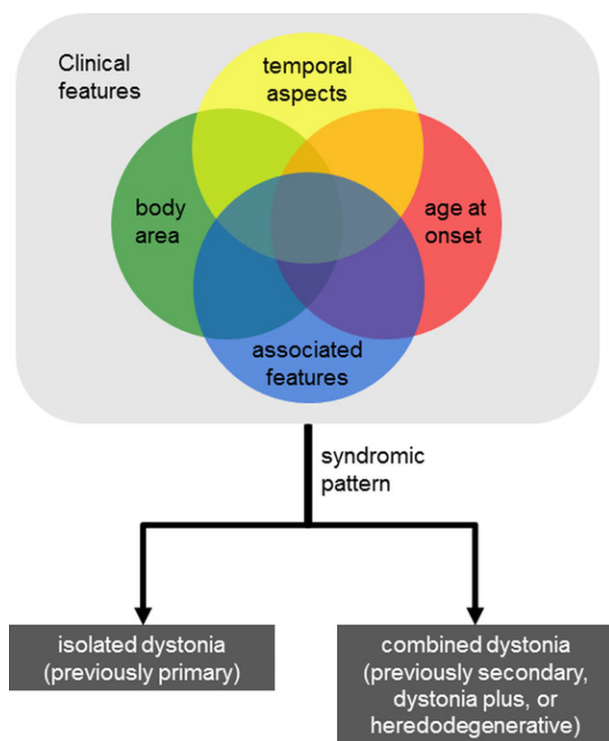


Figure 1 Axis I guides on the recognition of the phenomenology of dystonia and of the prevalent syndromic pattern.

and the median age for development of DYT6 dystonia is 28 years.⁹ Patients with dopa-responsive dystonia and Wilson's disease usually develop symptoms before 20 years of age, but most investigators encourage testing for these diagnoses at least through the age of 40, because they are treatable.

Rather than have different age discriminators for each type of dystonia, the new classification system is based on five standard age groups that are used for other neurological disorders. In this classification system, metabolic disorders will fall mostly in the first two age groups, generalized dystonias will fall mostly in the middle age groups, and the adult-onset focal dystonias will fall in last two groups. This is more complicated than the original two-group classification system, but it also is much more broadly applicable.

Adding Classification According to Temporal Aspects (Axis I)

Temporal aspects include manner of onset (acute or insidious), short-term variations in symptoms (diurnal, intermittent, or action induced), and longer-term variations in overall severity (static or progressive). These features had not been considered by any previous classification, but have important implications for diagnostic testing, counseling, and treatment options. Acute-onset dystonia is relatively uncommon and often signifies a conversion disorder or less-common conditions, such as rapid-onset dystonia parkinsonism or glutaric aciduria. Diurnal patterns are suggestive of dopa-responsive dystonia, and intermittent patterns suggest one of the paroxysmal dyskinesias. Relentlessly progres-

sive dystonia often signifies a degenerative process. The importance of these aspects is now formally recognized by a distinct dimension relating to temporal aspects.

Resolving Ambiguities in the Classification According to Etiology Into Associated Clinical Features (Axis I) Versus Causes (Axis II)

The classification of the dystonias according to etiology has seen the most changes over the years, in part because of enormous progress in understanding their many potential causes. The earliest etiological classification was based on two groups (Table 1). One group was idiopathic, and the other was secondary to a known cause. As more was learned about the many causes of dystonia over the years, additional subgroups were introduced. However, these additions often were defined by clinical phenomenology, not etiology, creating a hybrid classification system that mixed etiology with phenomenology. Because this hybrid system lacked a logical organizational plan according to etiology (Table 2), it was not ideal for organizing our growing knowledge of biological causes.

For example, the commonly used terms primary and secondary have led to confusion because they have been used by different investigators to mean different things over the years (Table 2). In early classifications, the term primary was used to refer to idiopathic dystonia, but more recently to phenotypically isolated dystonia, regardless of etiology. The term dystonia-plus was introduced to highlight disorders where dystonia was a prominent feature, but combined with other neurological abnormalities, again regardless of etiology. Exactly how dominant the dystonia had to be was arbitrary, leading different investigators to include different disorders in this group. The term heredodegenerative was the only category that was based strictly on etiology. Unfortunately, this group became a waste-basket list for an enormous number of unrelated disorders. As a result, it did not provide a plan that organized etiologies in a meaningful way.

The problem of a hybrid dimension for classification was addressed by creating a clinical axis to address associated clinical features and creating a distinct etiological axis for biological causes. The associated neurological and non-neurological features provide critical information for diagnosis and treatment, but previously they were divided across categories such as "dystonia-plus" or "heredodegenerative." Because these aspects relate to clinical phenomenology and not etiology, it was necessary to introduce a new dimension of the clinical axis to emphasize the importance of these associated features (Table 3).

Associated features may include a related movement disorder, such as parkinsonism or myoclonus. They may also include other neurological abnormalities, such as dementia, seizures, or neuropathy. Finally, they may include non-neurological abnormalities, such as liver disease or hematological abnormalities. A complete assessment of all of the clinical features is essential for delineating syndromic patterns that can aid in diagnosis.⁷

A separate axis for etiology was established to accommodate any evidence for inheritance or acquired causes, as well as idiopathic (genetically unclassified) sporadic or familial cases. In addition, the etiologic classification includes information regarding any associated neuropathology. This last aspect is compatible with earlier classifications, where the terms primary and dystonia-plus were sometimes used to highlight forms of dystonia without evidence of structural pathology.

Our understanding of the biological bases for dystonia has grown rapidly in the past few years, with an increasing number of shared biological principles being recognized that could be used to subgroup them.^{10,11} Included are shared genetic mechanisms,^{12,13} shared molecular mechanisms,¹⁴ shared anatomical pathways,^{15–17} and shared physiological substrates.^{18,19} However, there is currently insufficient information regarding how these biological mechanisms should be organized in the classification of the dystonias. Other dimensions may be added in the etiological axis as more is learned in the future.

Past, Present, and Future

Medicine is a living science. In order to thrive and grow, it must adapt as new information is obtained from both clinical and basic research. Sometimes our fundamental medical concepts need only minor revisions, but other times they must be thrown out and replaced by ones that are more in step with modern knowledge and more adaptable to future needs.

Concepts regarding the definition and classification of the dystonias are no exception. The recently proposed changes are some of the most significant ones proposed in recent years. As a result, they are likely to meet resistance from the inertia of traditional habits and beliefs. However, these changes address numerous weaknesses in existing proposals for classification in a more clinically useful and biologically logical manner. It seems likely that these concepts will evolve again in the future as we continue to learn more about this unique group of disorders.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the First Draft, B. Review and Critique.

H.A.J.: 1A, 1B, 1C, 3A

A.A.: 1A, 1B, 1C, 3B

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