

“Complex” Dystonia Is Not a Category in the New 2013 Consensus Classification

The Task Force for Nomenclature of Genetic Movement Disorders recently proposed a new system of naming genetically determined movement disorders.¹ These recommendations apply to a wide spectrum of movement disorders, including parkinsonisms, dystonias, choreas, paroxysmal movement disorders, cerebellar ataxias, and spastic paraplegias. We agree that current genetic classifications are cumbersome and “unsuitable” for accurate and comprehensive categorization of genetic movement disorders.

We appreciate that the task force addressed the discordance between phenotype and list designation by assigning more appropriate phenotype-prefix relationships. They propose 29 DYT symbols for inherited dystonias that occur in isolation or combined with other movement disorders, designated by an additional symbol: PARK, CHOR, or NBIA. The task force focuses on “prominent features” of diseases linked to mutations in a specific gene. It remains unclear, however, whether prominent features are the “most common” or rather the “most severe” reported phenotype. The terms “prominent” and “common” are subjective, therefore matter to dispute, and were not used in the 2013 consensus classification for the dystonias.

Concerning dystonia, the task force review mentions implementing the recently published new classification but mistakenly refers to 3 dystonia subgroups of isolated, combined, and complex and incorrectly suggests that these categories correspond to the previous terms of primary, dystonia-plus and secondary dystonia.

The 2013 consensus classification of dystonia has 2 separate axes: clinical and etiological. Axis I provides a guide to patient evaluation based on clinical characteristics, allowing construction of a syndromic (phenotypic) diagnosis that then guides etiological differential diagnosis, including genetic etiologies. In considering whether there are any associated movement disorders, there are only 2 subgroups: isolated and combined dystonia (disorders in which dystonia frequently coexists with other movement disorders).² The task force review added a third category of “complex” dystonias (in which dystonia dominates the clinical picture, but this occurs in the context of a complex phenotype including symptoms other than movement disorders). In the consensus classification of dystonia, other neurological or systemic features are a separate item of axis I, in recognition that these can be present both in patients with simpler, isolated

dystonia phenotypes and those with more complex combined phenotypes. The tripartite definition proposed by the task force review does not accommodate for genetic conditions with isolated dystonia phenotypes that occur in combination with extraneurological manifestations (eg, liver involvement in Wilson disease presenting with isolated dystonia).

To clarify the distinction between associated movement disorder features and coexisting neurological or systemic manifestations in the 2013 classification of dystonia, here we provide an explanatory figure to prevent further misinterpretations of the new classification scheme of dystonia.

The main innovation of the 2013 dystonia classification is the distinction between clinical features and etiology, which is separated into 2 separate axes. A similar distinction is being adopted for new classifications of other movement disorders. This also fits well with the proposed new genetic nomenclature, in which the “prefix” denotes a broad clinical syndrome (phenotype) and the “suffix” the gene. However “complex” dystonia is not a category in axis I of the dystonia classification, and genotype falls under the etiological axis II of inherited dystonia. ■

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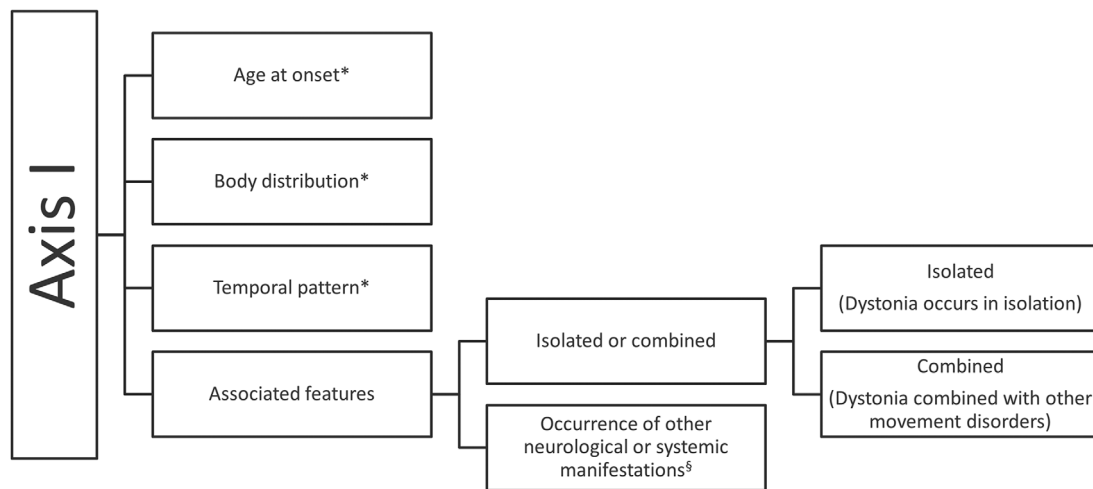


FIG. 1. Clinical characteristics listed under axis I. The distinction of isolated and combined dystonias is reported under “Associated features.” *Further subdivisions of this axis I category are not shown here and can be found in the published classification²; §Other neurological or systemic manifestations may coexist with either isolated or combined dystonia.

Locus Pocus

The International Parkinson Disease and Movement Disorders Task Force for Nomenclature of Genetic Movement Disorders recently proposed a new approach for nomenclature.¹ The traditional approach has numerous problems, and the task force should be congratulated for trying to fix them. The new approach is markedly different from the existing one. Like a good magician, the task force has put a bunch of ugly rats into a hat and pulled out a beautiful bird. The task force pointed out some of the weaknesses of the new plan, but its logic reveals some further problems.

In the proposed plan, assigning a prefix (DYT, PARK, SCA, etc.) requires that the phenotype be a *prominent* feature in the *majority* of cases. What is *prominent* or a *majority* is subject to debate. For example, Lesch-Nyhan disease was conferred DYT/CHOR-HPRT1, to emphasize the prominence of dystonia and chorea. However, chorea is not usually prominent and does not occur in the majority.^{2,3} Spasticity is nearly as prominent as chorea, so why not add HSP to make DYT/CHOR/HSP-HPRT1? Another example is myoclonus-dystonia, designated DYT-SCGE to emphasize the dystonia. Dystonia is often minor or absent, yet myoclonus is universal.^{4,5} So why not MYOC-SCGE or MYOC/DYT-SCGE? Also, there currently is no prefix for tremor.

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Once tremor genes are delineated and a TREM prefix is created, will we need to add TREM to many existing disorders including PARK, DYT, and SCA?

The proposed plan also permits a prefix only after confirmation by 2 *independent groups*. For rare disorders, most reports are initially based on very small cohorts. The discovery of a genetic defect almost invariably leads to appreciation of a broader phenotype or alternative phenotypes that are quite distinct. What if 2 groups do not agree? This means the prefix will be subject to frequent change — and frequent dispute.

The proposed plan also assigns a prefix based exclusively on the movement disorder, overlooking other phenotypic features, which are sometimes more important. For example, all patients with Lesch-Nyhan disease have severe self-injurious behavior, cognitive disability, and overproduction of uric acid. For myoclonus-dystonia, psychiatric features are prominent and frequent. So why not add prefixes for these problems? Will others outside of movement disorders use a system that focuses only on movement?

Historically, the traditional *locus* nomenclature aimed at designating a gene's approximate *location* in the genome. It was not designed for classification of phenotypes. The new plan attempts to link phenotypes and genotypes. However, there are already better tools for linking phenotypes and genotypes. The new plan will create confusion because nomenclature will be unstable because of subjective and arbitrary phenotype assignments, constant evolution with expanding knowledge, and almost certain disagreement among experts. Also unclear is who will have authority to adjudicate disagreements and render decisions. Before adopting the new plan, we must ask whether it is merely replacing old problems with new ones (Table 1). Instead of fixing the broken locus nomenclature system, perhaps we should put it into our magician's hat and make it disappear. ■

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