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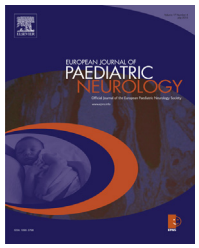

Gene table

Primary dystonias and genetic disorders with dystonia as clinical feature of the disease

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ABSTRACT

Dystonia is probably the most common form of movement disorder encountered in the clinical practice. It is characterized by sustained muscle contractions, usually producing twisting and repetitive movements or abnormal postures or positions. Dystonias can be classified in several ways, including primarily by the clinical phenomenology or by the underlining etiology, in particular to understand if the presentation is genetically determined. By advances of genetics, including contemporary genomic technologies, there is a growing understanding of the molecular underpinnings of genetically determined dystonias. The intricacy of information requires a user friendly, novel database that may efficiently serve clinicians to inform of advances of the field and to diagnose and manage these often complex cases.

Here we present an up to date, comprehensive review – in tabulated formats – of genetically determined primary dystonias and complex Mendelian disorders with dystonia as central feature. The detailed search up to December 24, 2012, identified 24 hereditary primary dystonias (DYT1 to DYT 25) that are mostly monogenic disorders, and a larger group (>70) of genetic syndromes in which dystonia is one of the characteristic clinical features. We organized the findings not only by individual information (name of the conditions, pattern of inheritance, chromosome and gene abnormality, clinical features, relevant ancillary tests and key references), but also provide symptom-oriented organization of the clinical entities for efficient inquiries.

1. Introduction

Dystonia is probably the most common form of movement disorder encountered in the clinical practice. It is characterized by sustained muscle contractions, usually producing twisting and repetitive movements or abnormal postures or positions.[1] Dystonias can be classified in several ways, including primarily by the clinical phenomenology or

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Table 1A – Hereditary primary dystonias.

Disease symbol OMIM#	Disease name	Inheritance	Age of onset	Chromosome	Gene symbol OMIM#	Protein	Clinical manifestation	Key references and PubMed ID
DYT1 128100	Early-onset generalized primary torsion dystonia (PTD)	AD, reduced penetrance	Childhood-adolescence	9q34.11	*TOR1A* 605204	TorsinA AAA + superfamily ATP-binding protein	☐ Early-onset, usually starts as action dystonia one limb then spreads to other body parts, most spares facial, cervical and laryngeal muscles -Molecular genetic testing	Johnson et al. (1962)[9] 14029356 Kostic et al. (2006)[10] 17027035
DYT2 224500	Primary torsion dystonia (PTD)	AR	Childhood-adolescence	Unknown	Unknown	Unknown	☐ Early limb onset followed by rapid, generalized dystonia	Gimenez-Roldan, S et al.(1976)[11] 941766 Zlotogora, J.et al. (2004)[12] 15477576
DYT3 314250	X-linked dystonia parkinsonism; "Lubag"	XR	Adult	Xq13.1	*TAF1* 313650	Transcription initiation factor TFIID subunit 1	☐ Segmental or generalized dystonia with parkinsonism in about 50% of cases -Molecular genetic testing	Lee LV et al. (1976)[13] 21047175 Evidente, V. G. H (2004)[14] 15596620
DYT4 128101	"Non-DYT1" PTD with whispering dysphonia	AD	Adolescence-adult	19p13.3	TUBB4A 602662	Tubulin, beta-4A	☐ Whispering dysphonia- one large Australian family with extrusional tongue dystonia and a unique "hobby horse" gait	Ahmad, F et al. (1993)[15] 8432555 Hersheson, J et al. (2013)[179] 23424103
DYT5 128230	Dopa-responsive dystonia with or without hyperphenyl-alaninemia (Segawa Syndrome autosomal dominant) Note : - rare,early-onset cases with AR inheritance - AR BH4-dependent hyperphenylalaninemia (233910) is allelic disorder	AD	Childhood	14q22.1-22.2	*GCH1* 600225	GTP cyclohydrolase I	☐ Initial limb dystonia-parkinsonism, brisk tendon reflexes Diurnal worsening of symptoms, dramatic and sustained response to levodopa Female predominance -Clinical response to oral levodopa -Low cerebrospinal fluid (CSF) biopterin and neopterin -Molecular genetic testing	Segawa M (1976)[16] 945938 Segawa (2011)[17] 21496606
DYT6 602629	Adolescent-onset "mixed" type PTD	AD reduced penetrance	Adolescence	8p11.21	*THAP1* 609520	THAP domain-containing protein 1	☐ Craniocervical and limb dystonia rarely affecting the leg, speech involvement is very common -Molecular genetic testing	Almasy, L et al. (1997)[18] 9382482 Clot, F et al. (2011)[19] 21110056
DYT7 602124	Adult-onset focal PTD	AD	Adult	18p11.32	Unknown	Unknown	☐ Adult onset focal dystonia (cervical dystonia, writer's cramp, dysphonia, or blepharospasm)	Waddy, H. M et al. (1991)[20] 2042948 Leube et al. (1997)[21] 9342206
DYT8 118800	Familial paroxysmal nonkinesigenic dyskinesia (PNKD)	AD	Childhood – adolescence	2q35	*PNKD* (*MR1*) 609023	PNKD (Myofibrillogenesis regulator 1)	☐ Attacks of dystonia with choreic and ballistic movements, may be accompanied by a preceding aura, precipitated by stress, fatigue, alcohol, coffee or tea but NOT by movements -Molecular genetic testing	Richards, R. N et al. (1968)[22] 5691173 Bruno et al. (2007)[23] 17515540