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The proposed new list of isolated, combined and complex hereditary dystonia

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| **New designation** | **Less common movement phenotype** | **Clinical clues** | **Inheritance pattern** | **Locus symbol** |
| **Isolated dystonias** | | | | |
| DYT-*TOR1A*[*1*](#_ENREF_1) |  | Early-onset generalized dystonia  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1492/  OMIM 128100 | AD | *DYT1* |
| DYT-*THAP1*[*2*](#_ENREF_2) |  | Adolescent-onset dystonia of mixed type  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1155/  OMIM 602629 | AD | *DYT6* |
| DYT-*GNAL*[*3*](#_ENREF_3) |  | Adult onset cranial-cervical dystonia  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1155/  OMIM 615073 | AD | *DYT25* |
| DYT-ANO3[4](#_ENREF_4) | tremor | Cranial-cervical dystonia  GeneReviews <https://www.ncbi.nlm.nih.gov/books/NBK1155/>  OMIM 615034 | AD | *DYT24* |
| DYT-KMT2B[5](#_ENREF_5), [6](#_ENREF_6) |  | Childhood-onset, generalized dystonia  Additional clinical manifestations may include intellectual disability, microcephaly  GeneReviews: n/a  OMIM 617284 | AD | *DYT28* |
| **Combined dystonias (disorders where dystonia frequently coexists with other movement disorders)** | | | | |
| DYT-*PRKRA*[*7*](#_ENREF_7) |  | Rare form of usually generalized  dystonia, parkinsonism inconsistent  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1155/  OMIM 612067 | AR | *DYT16* |
| DYT/PARK-*GCH1*[*8*](#_ENREF_8) |  | GTP cyclohydrolase I deficiency (mild form)[9](#_ENREF_9): Childhood-onset dopa-responsive dystonia, adult-onset dystonia-parkinsonism  Additional clinical manifestations: diurnal fluctuation, pyramidal signs  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1508/  OMIM 128230 | AD | *DYT5a* |
|  | GTP cyclohydrolase I deficiency (severe form)[10](#_ENREF_10): Dystonia, parkinsonism  Additional clinical manifestations: Developmental delay, truncal hypotonia, spasticity, oculogyric crises, seizures, with or without hyperphenylalaninemia  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1508/  OMIM 128230 | AR | none |
| DYT/PARK-*TH*[*11*](#_ENREF_11) |  | Tyrosine hydroxylase deficiency  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1155/  OMIM 605407 | | |
|  | Mild form: dopa-responsive infantile to early childhood onset dystonia | AR | *DYT5b* |
|  | Severe form: infantile-onset dystonia and parkinsonism, truncal hypotonia, global developmental delay | AR | None |
|  | Very severe form: infantile-onset dystonia and parkinsonism, oculogyric crises, severe global developmental delay, truncal hypotonia, limb spasticity, autonomic dysfunction | AR | None |
| DYT/PARK-*ATP1A3*[*12*](#_ENREF_12) |  | Rapid-onset dystonia-parkinsonism, chorea in later life\*\*  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1115/  OMIM 128235 | AD | *DYT12* |
| DYT/PARK-*TAF1*[*13*](#_ENREF_13)*\** |  | Dystonia-parkinsonism  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1155/  OMIM 314250 | X-linked | *DYT3* |
| DYT-*SGCE*[*14*](#_ENREF_14) |  | Myoclonus-dystonia  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1414/  OMIM 159900 | AD | *DYT11* |
| **Complex dystonias** **(where dystonia dominates the clinical picture but this occurs in the context of a complex phenotype including symptoms other than movement disorders)** | | | | |
| CHOR/DYT-*ADCY5*[*15*](#_ENREF_15) |  | Facial dyskinesias, occasional myoclonus. May have paroxysmal worsening.  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK263441/  OMIM 600293 | AD | None |
| DYT/CHOR-*HPRT*[*16*](#_ENREF_16) |  | Lesch-Nyhan syndrome: Dystonia, chorea, occasionally ballism  Additional clinical features: Hyperuricemia, crystalluria, developmental delay/intellectual disability, eye movement abnormalities, spasticity, compulsive self-injurious behavior, gouty arthritis, nephrolithiasis, renal failurebehavior  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1149/  OMIM 300322 | X-linked | None |
| DYT/CHOR-*ACAT1*[*17*](#_ENREF_17) |  | Mitochondrial acetoacetyl-CoA thiolase deficiency: metabolic decompensation and basal ganglia injury during acute stress resulting in dystonia and chorea  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1134/  OMIM 203750 | AR | none |
| DYT/CHOR-*GCDH*[*18*](#_ENREF_18) |  | Glutaric aciduria type I[19](#_ENREF_19): Dystonia, chorea (usually following acute metabolic crises), parkinsonism (later)  Additional clinical features: Acute metabolic crises with basal ganglia injury (predominantly putamen and caudate nucleus), severe truncal hypotonia, macrocephaly, orofacial dyskinesias, spasticity, cognitive impairment (variable), enlarged subdural space, subdural hygroma/hemorrhages, headaches, seizures  http://www.ncbi.nlm.nih.gov/books/NBK1134/  OMIM 231670 | AR | None |
| DYT/CHOR-*MUT*[*20*](#_ENREF_20) |  | Methylmalonic aciduria: Dystonia, chorea, occasionally ataxia  Additional clinical features: Neonatal-onset vomiting, seizures, lethargy and hypotonia, ketoacidosis, hyperammonemia, developmental delay, spasticity, pancreatitis, nephritis, growth failure, acute metabolic crises with confusion / encephalopathy, basal ganglia injury (predominantly globus pallidus)  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1134/  OMIM | AR | None |
| DYT/CHOR-*PCCA/PCCB*[*21*](#_ENREF_21) |  | Propionic aciduria[22](#_ENREF_22): Dystonia, occasionally chorea  Additional clinical features: Neonatal-onset vomiting, seizures, lethargy and hypotonia, ketoacidosis, hyperammonemia, developmental delay, spasticity, cardiomyopathy, acute metabolic crises with confusion / encephalopathy, basal ganglia injury (predominantly putamen and caudate nucleus)  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1134/  OMIM | AR | None |
| NBIA/DYT- *DCAF17*[*23*](#_ENREF_23) | chorea[24](#_ENREF_24) | Woodhouse-Sakati syndrome[25](#_ENREF_25):  Iron accumulation: GP, SN, other BG (variable)  Additional clinical features: Dysarthria, deafness, seizures, cognitive impairment, hypogonadism, alopecia, diabetes mellitus, thyroid dysfunction, acanthosis nigrans, keratoconus, camptodactyly  GeneReviews: n/a  OMIM 241080 | AR | None |
| DYT-*DDC*[*26*](#_ENREF_26) |  | Aromatic l-amino acid decarboxylase deficiency[27](#_ENREF_27): Dystonia, occasionally chorea, hypokinesia  Additional clinical features: Developmental delay, truncal hypotonia, oculogyric crises, ptosis, autonomic symptoms, sleep disorder, diurnal fluctuations with sleep benefit  GeneReviews: n/a  OMIM 608643 | AR | None |
| DYT/PARK-*SLC30A10*[*28*](#_ENREF_28)*,* [*29*](#_ENREF_29) |  | Hypermanganesemia with dystonia, polycythemia, and liver cirrhosis:  Dystonia, parkinsonism  Additional clinical features: Hypermanganesemia, polycythemia, chronic liver disease, dysarthria  GeneReviews:  http://www.ncbi.nlm.nih.gov/books/NBK100241/  OMIM 611146 | AR | None |
| DYT/PARK-*SPR*[*30*](#_ENREF_30) |  | Sepiapterin reductase deficiency: Dystonia, parkinsonism  Additional clinical features: Motor and speech delay, truncal hypotonia, limb hypertonia and hyperreflexia, oculogyric crises, psychiatric symptoms, autonomic dysfunction, diurnal fluctuation and sleep benefit, no hyperphenylalaninemia[31](#_ENREF_31" \o "Friedman, 2012 #1503)  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK304122/  OMIM 612716 | AR | None |
| DYT/PARK-*QDPR*[*32*](#_ENREF_32) |  | Dihydropteridine reductase deficiency[33](#_ENREF_33): Dystonia, parkinsonism  Additional clinical features: Developmental delay, truncal hypotonia, seizures, autonomic dysfunction, hyperphenylalaninemia  GeneReviews: n/a  OMIM 612676 | AR | None |
| DYT/PARK-*PTS*[*34*](#_ENREF_34) |  | 6-pyruvoyl-tetrahydropterin synthase deficiency[35](#_ENREF_35): Dystonia, parkinsonism  Additional clinical features: Neonatal irritability, truncal hypotonia, developmental delay, seizures, oculogyric crises, autonomic dysfunction, hyperphenylalaninemia  GeneReviews: n/a  OMIM 612719 | AR | None |
| DYT/PARK-*SLC6A3*[*36*](#_ENREF_36) |  | Dopamine transporter deficiency syndrome[37](#_ENREF_37): Dystonia and parkinsonism (typically infantile-onset, atypical cases with juvenile-onset exist), occasionally chorea in infancy  Additional clinical features: Mild developmental delay, truncal hypotonia, ocular flutter / oculogyric crises, saccade initiation failure, bulbar dysfunction34  GeneReviews: n/a  OMIM 126455 | AR | None |
| NBIA/DYT-*PANK2*[*38*](#_ENREF_38) | parkinsonism, chorea | Pantothenate kinase-associated neurodegeneration (PKAN):  Iron accumulation: GP – eye of the tiger sign  Additional clinical features: Spasticity, dysarthria, cognitive decline, gaze palsy, psychiatric symptoms, pigmentary retinopathy  GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK121988/  OMIM 234200 | AR |  |
| NBIA/DYT/PARKǂ -*PLA2G6*[*39*](#_ENREF_39) | ataxia[40](#_ENREF_40) | *PLA2G6*-associated neurodegeneration (PLAN):  Dystonia, parkinsonism, cognitive decline, pyramidal signs, psychiatric symptoms (adult phenotype), ataxia (childhood phenotype)  Iron accumulation: GP, SN in some; adults may have striatal involvement; about half of INAD and the majority of adult-onset cases lack brain iron accumulation on MRI  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1675/  OMIM 612953 | AR | NBIA2, PARK14 |
| DYT-*ATP7B*[*41*](#_ENREF_41)*,* [*42*](#_ENREF_42) |  | Wilson’s disease: Dystonia, occasionally parkinsonism and/or chorea  Additional clinical features: Flapping tremor, rest-, action- and intention tremor, orofacial dyskinesias, dysarthria, liver disease, Kayser-Fleischer rings, psychiatric symptoms  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1512/  OMIM 277900 | AR | None |
| DYT- *SLC19A3*[*43*](#_ENREF_43) |  | Biotin-responsive basal ganglia disease (within the thiamine transporter–2 (hTHTR2) deficiency spectrum)[44](#_ENREF_44): Dystonia, parkinsonism (mainly rigidity), occasionally ataxia, chorea  Additional clinical features: Subacute encephalopathy/coma (often triggered by febrile illness), cranial nerve palsy, pyramidal signs, cerebellar signs, dysphagia, intellectual disability, epilepsy, responsive to thiamine and/or biotin therapy  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK169615/  OMIM 606152 | AR | None |
| DYT-*TIMM8A*[*45*](#_ENREF_45) |  | Mohr-Tranebjaerg syndrome[46](#_ENREF_46): Dystonia  Additional clinical features: Sensorineural deafness, visual impairment, cognitive impairment, behavioral problems, pyramidal signs92  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1216/  OMIM 304700 | X-linked | None |
| DYT-*mt-ND6*[*47*](#_ENREF_47) |  | Leber’s hereditary optic neuropathy/dystonia (G14459A mutation)[48](#_ENREF_48): Dystonia  Additional clinical features: Juvenile-onset subacute vision loss (Leber hereditary optic neuropathy), encephalopathy, spasticity, bulbar dysfunction, cognitive impairment  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1174/  OMIM 516006 | Mitochondrial | None |
| DYT/PARK-*GLB1*[*49*](#_ENREF_49)*,* [*50*](#_ENREF_50) |  | GM1 gangliosidosis (type III, chronic/adult form)[51](#_ENREF_51): Dystonia, parkinsonism  Additional clinical features: Pyramidal signs, dysarthria, cognitive deficits (often mild initially), skeletal abnormalities and short statue, corneal clouding, vacuolated cells, cardiomyopathy, progressive disease  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK164500/  OMIM 230650 | AR | None |
| NBIA/DYT/PARK-*CP*[*52*](#_ENREF_52) | chorea | Aceruloplasminemia[53](#_ENREF_53" \o "Vroegindeweij, 2017 #1564): Dystonia, ataxia, chorea, parkinsonism, tremors  Iron accumulation: More homogeneous involvement of primarily, caudate, putamen, thalamus, dentate  Additional clinical features: Cognitive impairment, psychiatric symptoms, diabetes mellitus, retinal degeneration, anemia, liver iron storage  GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1493/  OMIM 604290 | AR |  |
| DYT-*SUCLA2*[*54*](#_ENREF_54)*,* [*55*](#_ENREF_55) |  | SUCLA2-related mitochondrial DNA (mtDNA) depletion syndrome[56](#_ENREF_56), [57](#_ENREF_57), encephalomyopathic form, with mild methylmalonic aciduria: Dystonia  Additional clinical features: Severe hypotonia, developmental delay, seizures, progressive spasticity, cerebral atrophy, sensorineural hearing loss, ophthalmoplegia, feeding problems and postnatal growth retardation, ptosis  GeneReviews:  http://www.ncbi.nlm.nih.gov/books/NBK6803/  OMIM 603921 | AR | None |
| DYT\*\*\*-*TUBB4A*[*58*](#_ENREF_58)*,* [*59*](#_ENREF_59) | HSP[60](#_ENREF_60), [61](#_ENREF_61) | Spasmodic dysphonia is most common dystonic presentation. Alternative, phenotype: Hypomyelinating leukodystrophy[62](#_ENREF_62" \o "Simons, 2013 #1613) (see footnote) | AD | DYT4 |
| DYT/CHOR-ADAR1[63](#_ENREF_63) | Spasticity | Aicardi-Goutières syndrome, includes dystonia and spatic paraparesis, MRI may reveal isolated bilateral striatal necrosis, adult-onset psychological difficulties[64](#_ENREF_64), linked to characteristic interferon signature (upregulation of interferon-stimulated genes)[63](#_ENREF_63)  GeneReviews: <https://www.ncbi.nlm.nih.gov/books/NBK1475/>  OMIM: 615010 | mostly AR, rarely AD | None |
| **Disorders that usually present with other phenotypes but can have predominant dystonia** | | | | |
| SCA-*ATXN3*[*65*](#_ENREF_65) | Spastic paraplegia[66](#_ENREF_66),  Dystonia[67](#_ENREF_67) | Marked non-ataxia features; can have predominant parkinsonism, dystonia, chorea, spasticity, neuropathy, lower motor neuron involvement  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1196/  OMIM 109150 | AD | SCA3 |
| NBIA/PARK- *WDR45*[*68*](#_ENREF_68) | dystonia | Beta-propeller protein-associated neurodegeneration (BPAN, previously SENDA syndrome)[69](#_ENREF_69):  Iron accumulation: SN>GP Halo of hyperintensity surrounding linear hypointensity in SN on T1 scans.  Additional clinical features: Developmental delay / intellectual disability, progressive cognitive decline, seizures, spasticity, Rett-like stereotypies, autistic-features, neuropsychiatric symptoms, sleep disorders, bowel/bladder incontinence, infantile epileptic encephalopathy  GeneReviews https://www.ncbi.nlm.nih.gov/books/NBK424403/  OMIM 300894 | X-linked | NBIA5 |
| NBIA/CHOR-*FTL*[*70*](#_ENREF_70) | Dystonia, parkinsonism | Neuroferritinopathy:  Dystonia, chorea, parkinsonism[71](#_ENREF_71)  Iron accumulation: GP, caudate, putamen, SN, red nucleus; cystic BG changes – pallidal necrosis  Additional clinical features: Oromandibular dyskinesia, dysphagia, cognitive impairment, behavioral symptoms, low serum ferritin  GeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1141/  OMIM 606159 | AD | NBIA3 |
| HSP/NBIA- *FA2H*[*72*](#_ENREF_72) | Dystonia, parkinsonism, ataxia[73](#_ENREF_73) | Fatty Acid Hydroxylase-associated Neurodegeneration (FAHN)[73](#_ENREF_73):  Iron accumulation: GP (more subtle than other NBIAs)  Additional clinical features: Spastic tetraparesis, cognitive decline, cerebellar and brainstem atrophy, dysarthria, dysphagia, optic nerve atrophy, seizuresGeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK1509/  OMIM 612319 | AR | SPG35 |
| HSP-*KIF1C*[*74*](#_ENREF_74)  Allelic with autosomal recessive spastic ataxia at the SAX2 locus. | Dystonia, ataxia | Pure and complicated, chorea, myoclonus, dysarthria, developmental delay, mild mental retardation, hypodontia, ptosis, short stature, sensorineural deafness, pes planus, white matter lesions.  GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK1509/  OMIM 611302 | AR | SPG58 |
| HSP/NBIA-*C19orf12*[*75*](#_ENREF_75) | Dystonia, parkinsonism | Mitochondrial membrane protein-associated neurodegeneration (MPAN)[76](#_ENREF_76):  Iron accumulation: GP - hyperintense streaking of medial medullary lamina between GPi and GPe; SN  Additional clinical features: Progressive spastic paresis, dysarthria, dysphagia, cognitive decline/dementia, motor axonal neuropathy, optic nerve atrophy, psychiatric symptoms, bowel/bladder incontinenceGeneReviews  http://www.ncbi.nlm.nih.gov/books/NBK185329/  OMIM 614298 | AR | NBIA4/SPG43 |
| GNB1[77](#_ENREF_77) | Chorea, ataxia[78](#_ENREF_78) | In combination with global development delay and seizures[79](#_ENREF_79)  GeneReviews: n/a  OMIM 616973 | AD | None |
| DYT/CHOR-FOXG1[80](#_ENREF_80) | Dyskinesia[81](#_ENREF_81), [82](#_ENREF_82) | Rett-like phenotype (with congenital encephalopathy), GeneReviews: <https://www.ncbi.nlm.nih.gov/books/NBK1497/>  OMIM 613454 | AD | None |

INAD: infantile NeuroAxonal Dystrophy

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