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Differential diagnosis of dystonia

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Dystonia is a movement disorder characterized by sustained muscle contractions causing twisting and repetitive movements and abnormal postures. Diagnosing dystonia may be difficult, because of variability of dystonia presentation, uncertain recognition of the specific clinical signs, wide etiological spectrum, and coexistence of other movement disorders. The major difficulties in the diagnostic assessment of primary and non-primary dystonia derive from its confusion with other movement disorders or with a psychogenic disorder. The clinical heterogeneity of dystonia and some examples of misdiagnosis are reviewed here. The movement disorders that can be most commonly taken for dystonia are tremor, Parkinson's disease, myoclonus, chorea, and tics. Given the occurrence of confounding factors, along with specific genetic and laboratory test, it is of great importance to apply a specific algorithm to recognize the clinical signs of dystonia.

Clinical and genetic heterogeneity of dystonia

Dystonia (Greek for 'altered muscle tone') refers to the occurrence 'of sustained muscle contractions frequently causing twisting and repetitive movements or abnormal postures' [1]. The association of slow tonic posturing with faster (phasic) movements, sometimes resembling tremor, is the clinical hallmark of this movement disorder [1–3]. The difficulties surrounding the clinical diagnosis of dystonia syndromes have been recently reviewed [4]. Non-primary cases represent a particular diagnostic challenge, because the picture may show less typical features of dystonia sometimes intermixed with other clinical signs [5]. Table 1 lists the clinical features observed in primary and non-primary dystonia syndromes.

Not considering the possible association of features pertaining to other movement disorders, the clinical spectrum of dystonia is remarkably variable. The features of dystonia are more homogeneous in primary torsion dystonias, where there are no identifiable exogenous causes or other inherited or degenerative diseases [5,6] and no coincident movement disorder. However, also in such cases, dystonia may have features resembling tremor or myoclonus that can mislead the examining neurologists.

The rich clinical appearance of primary dystonias encompasses symptoms that are stigmata of other conditions, such as tremor in essential tremor (ET) [3,7] or tremor in Parkinson's disease (PD) [8]; in such conditions, a correct diagnosis of dystonia could be missed or delayed. A correct recognition of the physical signs that constitute the hallmark of most dystonia syndromes provides the grounds to perform a structured diagnostic sequence and share a consistent methodology. Diagnosis and classification of dystonia are highly relevant for providing appropriate management, prognostic information, genetic counseling, and treatment.

The clinical features of dystonia encompass a combination of dystonic movements and postures to create a sustained postural twisting (torsion dystonia). Dystonia has some specific features that can be recognized by clinical examination [6]. Speed of contractions of dystonic movements may be slow or rapid, but at the peak of movement, it is sustained. Contractions almost always have a consistent directional or posture-assuming character. Dystonia is commonly aggravated during voluntary movement and may only be present with specific voluntary actions, or may be temporarily alleviated by specific voluntary tasks, called gestes antagonistes, also known as sensory tricks. Overflow to other body parts, while activating the affected region, is also a feature of dystonia [4].

Lack in the recognition of dystonia is responsible for a number of errors in clinical series and also in linkage studies of dystonia families. A recent striking case is the supposed identification of the DYT14 locus. A genome-wide analysis performed in a family with an undisclosed number of patients considered affected by DOPA-responsive dystonia (DRD) suggested linkage to a 30-cM region on chromosome 14q13 [9]. This locus was named DYT14 and its location was considered not to

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Table 1 Combinations of physical signs observed in different dystonia syndromes (from [4])

Dystonia syndromes	Physical signs observed
Primary (or idiopathic) dystonias	Dystonia
Dystonia plus syndromes	Dystonia, parkinsonism, myoclonus
Paroxysmal dystonias	Dystonia, chorea, myoclonus
Heredodegenerative dystonias	Dystonia, parkinsonism, chorea, myoclonus, spasticity, cerebellar features, dysautonomia, cognitive impairment, epilepsy
Symptomatic dystonias	Same as for heredodegenerative dystonias plus focal neurological signs, if present

overlap with the GCH-1 gene. The phenotype described in this family included foot dystonia with childhood onset, marked worsening toward the evening, progression to generalized dystonia, and parkinsonian features in the elder patients. Later, the same authors reconsidered this family and recognized that one family member, whom they initially considered affected, had a more complex phenotype, including mental retardation and seizures [10]. When this subject was excluded from linkage analysis, the remaining affected members all linked to a region encompassing the GCH1 gene, leading to reclassify this family as affected by DYT5 DRD.

The cause for the erroneous classification of the 'DYT14' family was largely based on lack of *a priori* diagnostic criteria for the assignment of patients to the status of affected by dystonia. This further emphasizes that the success of linkage analysis in positional cloning entirely depends on the precise characterization of the clinical phenotype of each subject in families affected by movement disorders [11].

At present, there are only two known primary dystonia genes and three mapped loci out of a total of seven coded forms (Table 3). In all these cases, the clinical status of patients has been established based on subjective clinical criteria. Particularly for genetic studies, three diagnostic levels have been identified [12–14]. In patients with 'definite' dystonia, overt twisting or directional movements and postures are consistently present; in 'probable' cases, postures or movements suggestive of dystonia are insufficient in intensity or consistency to merit classification as definite; in 'possible' cases, muscle contractions are not considered abnormal but remotely suggestive of dystonia. The criteria underlying these definitions of definite, probable or possible cases have never been validated, and the classification of patients greatly depends on the examiner's level of expertise. For this reason, a European

Table 2 Tasks required for the evaluation of a patient suspect to have dystonia. This set of tasks can be easily incorporated into a video recording to facilitate consultation among doctors

Subjects should only wear shorts and bra. Ask the patient to rest in a comfortable position such that overcompensation does not occur. Observe whole body at rest with eyes open and with eyes closed.	
Head and neck	Observe the patient in resting position, with eyes open and with eyes closed.
	Observe the patient while performing voluntary movements: open and close eyes tightly, open and close mouth, protrude tongue, count from 1 to 10, vocalize a sustained high-pitch 'e', read a standardized passage, hold a brief conversation.
	Ask the patient to describe the occurrence of swallowing difficulties.
Upper body (neck, shoulders, and arms)	Observe the patient in the resting position, both with eyes open and shut.
	Observe the patient while performing voluntary movements with the head: turn the head to the right and to the left, up and down, tilt ear to shoulder on either side.
	Observe the patient while performing voluntary movements with both arms, independently and together: hold arms outstretched straight in front, with fingers spread apart, bring prone arms to supine position, finger to nose, finger tapping, open and close fists, fingers extending toward each other but not touching. Repeat unilateral maneuvers with eyes shut to detect mirroring.
	Observe subject while writing 'today is a sunny day' 3 times, while tracing a continuous line of cursive lower case 'L's without lifting pen from paper and while drawing a spiral without the hand resting on paper. Perform maneuvers with either hand.
Lower body (trunk and legs)	Observe the patient in the resting position, with eyes open and with eyes shut.
	Observe the patient while performing voluntary leg movements: rapid heel stomping on the floor, toe tapping with heel on floor and heel to toe taps. Perform maneuvers on either side and alternating both legs.
Full body in standing position	Observe the patient in the resting position, with eyes open and with eyes closed in the frontal, lateral and back views.
	Observe the patient while performing voluntary movements: walking onward and backward, away from and toward the examiner.
Identify and document the *gestes antagonistes* and sensory tricks used by the patient; If necessary, perform EMG mapping to detect features of dystonia.	

consensus panel on the diagnosis of dystonia recognized the lack of specific diagnostic criteria and recommended referral to expert observation in all uncertain cases to achieve a correct diagnosis [6].

The diagnostic challenge of dystonia

Primary dystonia or essential tremor?

According to the Tremor Investigation Group criteria [15], ET refers to a phenomenological criterion of a tremor syndrome classically defined by a mostly hereditary and mainly postural tremor of the hands and sometimes of head. ET is usually bilateral, largely symmetric, postural, or kinetic involving hands and forearms, and it is visible and persistent. Additional or isolated tremor of the head may occur, but in the absence of abnormal posturing [15]. Patients with dystonia can be mistaken to have ET because dystonia manifesting as tremor may precede clear abnormal posturing. These definitions highlight that tremor, even if defined as ET, has to be always kept as a possible differential diagnosis of dystonia.

The consensus statement of the Movement Disorder Society on tremor classification reports how difficult is to separate tremor from dystonia [15]. Three types of tremors linked to dystonia are reported: dystonic tremor, tremor associated with dystonia, and dystonia gene-associated tremor.

'Dystonic tremor' is a tremor in a body part affected by dystonia. This is a focal tremor, usually with irregular amplitudes and variable frequency (mainly <7 Hz), mainly postural/kinetic tremor and usually not seen during complete rest. A typical example of dystonic tremor is tremulous spasmodic torticollis (or dystonic head tremor). In many patients with dystonic tremor, *gestes antagonistes* lead to a reduction in the tremor amplitude. This is to be considered part of the typical dystonia phenotype [3].

'Tremor associated with dystonia' occurs in a body part not affected by dystonia, but the patients have dystonia elsewhere. For example, patients with cervical dystonia often show upper limb postural tremor that is indistinguishable from enhanced physiologic tremor or ET. Dystonic tremor and tremor associated with dystonia are different because postural tremors resembling mild classic ET can occur at extremities not involved in dystonia (for example, hand tremor in patients with otherwise monosymptomatic blepharospasm).

In 'dystonia gene-associated tremor,' tremor is an isolated finding in patients with a dystonic pedigree. The prevalence of ET and dystonia has not yet been established with precision. In a review of more than 20 studies, estimates of the crude prevalence of ET range widely from 0.08 to 220 cases per 1000 persons, a 2750-fold difference [16]. The prevalence of dystonia is wide ranging as well. Prevalence estimates from available studies are between 0.002 and 0.05 cases per 1000 for early-onset dystonia and between 0.03 and 7.32 cases per 1000 for late-onset dystonia [17]. Among several explanations for such variability, there is the likely overlap between ET and dystonia, whereby ET might be overdiagnosed and dystonia underestimated.

There are proven cases of primary focal dystonia, who initially received a diagnosis of ET because of the occurrence of isolated tremor and insufficient recognition of dystonia features. A patient with DYT1 with atypical phenotype was mistaken for ET. This patient belonged to a DYT1 family and developed leg tremor at age 40 [18]. She was initially diagnosed with ET and treated accordingly; only upon re-examination at age 67 was finally diagnosed as having dystonia. Diagnostic hallmarks of dystonia were present in this patient and not recognized: task-specific leg tremor (present only while walking), inversion of the right foot while walking and compensatory gait to prevent foot-drag.

The diagnosis of dystonia can be mistaken or delayed in patients with task- and position-specific tremors, particularly primary writing tremor, occupational tremors, or isolated voice tremor. These disorders can be difficult to classify at onset, and dystonia may not develop until after many years of a typical ET-like presentation [19]. It is thus not surprising that an initial diagnosis of ET is changed to dystonia after years of observation. We have reviewed a published teaching videotape for the assessment of ET looking for features suggestive of primary dystonia [20]. In the published video clips, there are aspects that may indicate dystonic features (such as marked asymmetry of upper limb tremor or task-specificity of limb tremor). Unfortunately, the clips do not report all the information needed to assess the features of dystonia. This raises the issue of clearly defining the task to be shown on videotapes of patients who may have dystonia features. To allow external review and discussion of videotapes, it is highly important that patients with movement disorders are evaluated according to a standard set of tasks, including those required for the evaluation of dystonia (Table 2).

Primary dystonia, Parkinson's disease, or parkinsonian syndrome?

The clinical diagnosis of PD requires the presence of bradykinesia, rigidity, or resting tremor [21,22]. Dystonia unrelated to motor complications is a feature of PD that can occur at disease onset, especially in younger patients. Particularly, patients with mutations

in the parkin gene may present with gait disturbances caused by foot dystonia [23] and may be thought to have a primary dystonia syndrome.

DYT1 cases with atypical phenotype have been mistaken for PD. A patient with DYT1 with adult onset of task-specific tremor was diagnosed as having a benign tremulous PD. At 69 years of age, he presented evident rest tremor of both arms. The diagnosis of PD was retained until a DAT scan resulted normal [24]. The issue whether patients with diagnosis of PD and normal DAT scan (SWEDD: Scans Without Evidence of Dopaminergic Deficit) may in fact be affected by dystonia is an intriguing one. The possible occurrence of dystonic tremors in patients with SWEDD is a new hypothesis, which has been suggested only recently [25].

Clinical heterogeneity of DRD is also a cause of diagnostic uncertainty. The DRD phenotype can include adult-onset parkinsonism with tremor and levodopa-induced dyskinesias, introducing the additional diagnostic issue of confusion with patients carrying mutations in the parkin gene [23]. Generally, the presence of early prominent parkinsonism and severe dyskinesias favors parkin mutations. Patients with DRD have a normal DAT scan, at variance with parkin disease patients. DRD can also masquerade as a different disorder, such as spastic diplegic cerebral palsy or hereditary spastic paraplegia or progressive paraparesis. In one series, up to 24% of patients with DRD were misdiagnosed as cerebral palsy [26].

In addition to pure PD and pure dystonic syndromes, there are a group of disorders with overlapping features, some of which have broadly intermediate and more complex phenotypes. The differential diagnosis of these dystonia–parkinsonism syndromes can be complex including primary and secondary forms. Various dominant, recessive, or X-linked genes expressing a dystonia–parkinsonism phenotype have been identified [27]. Most of these cases have a recessive transmission and may appear as sporadic cases; hence, clinicians must consider an increasing range of differential diagnoses when they encounter a dystonia–parkinsonism syndrome, particularly with early onset.

Primary dystonia or myoclonus?

Myoclonus is characterized by sudden, brief, jerky, shock-like movements caused by abrupt muscle contraction (positive myoclonus) or sudden cessation of muscle contraction associated with a silent period in the electromyographic discharge (negative myoclonus). Positive myoclonus is commonly observed during sustained posture or action, interfering with purposeful action [28].

Brief reinforcement of dystonic posturing, often referred to as dystonic spasms, may occur in dystonia [3]. Such spasms are simple in nature, brief in duration, and yield a shock-like aspect to the dystonic movements. In such cases, the differentiation between myoclonus and dystonia is difficult. Only duration of muscle contraction on surface EMG (electromyography) recording can provide arguments in favor of one or the other hypothesis, because dystonic spasms often last more than 200 ms, longer than myoclonus [28].

Primary dystonia syndromes can present true myoclonus. DYT1 cases with atypical phenotype that was associated with myoclonus have been reported. Early-onset action myoclonus of the right hand during writing was the presentation of DYT1 dystonia in a patient [29] who later was recognized to have associated features of dystonia. Another patient with DYT1 developed jerky movements of the trunk leading to gait imbalance at 9 years of age and remained stable for 50 years to worsen thereafter [30]. Another patient affected by DYT1 dystonia was described as having early-onset myoclonus [31].

In myoclonus–dystonia (DYT11), the features of two different movement disorders are combined [32] and myoclonus can often be distinguished from dystonia based on clinical and electrophysiological features [33]. In these patients, because of the possible late occurrence of dystonia, isolated myoclonus can be the only presenting sign for long time. Essential myoclonus is the disorder where myoclonus classically occurs in isolation, whereas myoclonic dystonia refers to a combination of dystonia and fast movements resembling myoclonus [34].

Primary dystonia or chorea?

Chorea is defined as a syndrome characterized by abrupt involuntary movements resulting from a continuous flow of random muscle contractions. The pattern of movement can sometimes seem playful and convey a feeling of restlessness to the observer. The differential diagnosis of choreic syndromes relies not so much on differences in the phenomenology of the hyperkinesia but the presence of accompanying findings. The unpredictable nature of chorea is a feature that distinguishes it from dystonia [35]. In patients with a clinical diagnosis of benign hereditary chorea, a dystonic syndrome has been recognized as an alternative diagnosis after reviewing the phenotype [36]. Chorea is characterized by rhythmic and oscillatory movements of body parts, whereas the hallmark of dystonia is the presence of sustained muscular contractions resulting in abnormal postures or torsion

movements. Chorea and dystonia may be associated in disorders such as Huntington's disease or other genetic choreas [35].

Primary dystonia or psychogenic movement disorder?

Psychogenic movement disorders are a common diagnostic issue in clinical practice. They are estimated to comprise 2–25% of the patient population in a neurology clinic [37]. Fahn and Williams identified a list of criteria suggesting a psychogenic origin [38]. These included abrupt onset, inconsistency/incongruency, distractibility, false weakness, false sensory changes, pain, exhaustion, excessive startle, bizarre movements, and concomitant somatizations, among others. They proposed diagnostic criteria for psychogenic dystonia that were later expanded to apply to all movement disorders [38]. Recently, more strict criteria, which would probably increase diagnostic accuracy, were proposed [39,40].

Given the uncertainties of diagnostic criteria for psychogenic dystonia, it is not surprising that a number of patients diagnosed as having a psychogenic movement disorder were later considered to have dystonia. In a series of 84 patients affected by primary dystonia, 37 had originally been misdiagnosed as primarily psychogenic [41]. More recently, other examples of dystonia mistaken for psychogenic disorders have been described, such as a focal lower limb primary dystonia that was considered psychogenic based on lack of improvement after treatment [42]. The area of psychogenic dystonia will be substantially reshaped in the near future. Although psychiatric etiology is very likely relevant in most cases, it is difficult to prove and the pathophysiology is unknown. All varieties of movement disorders may be mimicked by a psychogenic disorder, dystonia being one of the most common, followed by tremor and parkinsonism.

Patients with a consistent diagnosis of psychogenic movement disorder may also be erroneously considered to be affected by dystonia, particularly if the affected individual belongs to a family with an inherited movement disorder. In an Italian family with four definitely affected members showing a typical DYT1 phenotype, one GAG mutation carrier (mother of the most severely affected individual), presented with a clinically established psychogenic movement disorder that resembled his son's dystonia and was initially diagnosed as generalized DYT1 dystonia based on the positive diagnostic test in this obligate gene carrier [43]. The low penetrance of DYT1 dystonia (30% approximately) does not allow to perform a diagnosis solely based on genetic test if the clinical picture is inconsistent.

Conclusions

The etiological classification of patients with dystonia syndromes is the diagnostic goal for the examining neurologist. The diagnosis can be made difficult, delayed, and often misled by several factors: variability of dystonia presentation, uncertain recognition of the specific physical signs, lack of diagnostic tests, wide etiological spectrum, and coexistence of other movement disorders. A correct recognition of the physical signs that constitute the hallmark of most dystonia syndromes provides the grounds to perform a diagnosis even in the presence of confounding factors. The phenotypic consistency of dystonia symptoms can be evaluated based on a recently proposed algorithm [4] before performing genetic testing.

Classification of dystonias is based on etiology, age at onset of symptoms, and distribution of body regions affected [6]. The etiological axis defines primary pure dystonia with no identifiable exogenous cause or evidence of neurodegeneration in which dystonia is the only clinical sign (apart from dystonic tremor). In primary dystonia plus, instead, usually there are additional movement disorders. Non-primary dystonia is because of heredodegenerative diseases or secondary (symptomatic) to known causes; these forms are characterized by the presence of additional symptoms or signs, apart from movement disorders [6].

The clinical presentation of dystonias is complex, often variable, and sometimes even bizarre. In addition, the clinical appearance of non-primary dystonias can widely overlap with primary forms, and establishing the correct diagnosis can be difficult. A large number of genes and gene loci have been identified for primary as well as for other forms of dystonia making the differential diagnosis quite articulated. Table 3 provides a list of the several dystonia syndromes that have been genetically characterized. Their phenotype can help orientating to the correct diagnosis, which is a prerequisite for providing appropriate management, prognostic information, genetic counseling, and treatment [6]. Correct classification of dystonias is the basis for the subsequent diagnostic process. The starting point for a stepwise diagnostic work-up is the recognition of dystonia and then the detection of associated features [44]. In atypical cases, other features (e.g. family history, age at onset, presenting symptoms, and clinical evolution) orientate toward further work-up.

Conflicts of interest

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Table 3 Genetic forms of dystonias. The gene name is indicated whenever possible; otherwise, the locus is reported

Disease (OMIM)[a]	Gene/locus[b]	Phenotype	Transmission[c]
Primary pure dystonias			
DYT1 (128100)	TOR1A	Generalized early-limb onset dystonia	AD
DYT2 (224500)	None	Early-onset generalized dystonia with prominent cranial-cervical involvement	AR
DYT4 (128101)	None	Whispering dysphonia	AD
DYT6 (602629)	THAP1	Mixed-type dystonia	AD
DYT7 (602124)	18p	Adult-onset cervical dystonia	AD
DYT13 (607671)	1p36.13–36.32	Mixed-type dystonia	AD
DYT17 (612406)	20p11.2-q13.12	Segmental or generalized dystonia with severe dysphonia	AR
Primary dystonia plus syndromes			
DYT5 (128230)	GCH1	Dopa-responsive dystonia	AD
THD (605407)	TH	Dopa-responsive dystonia	AR
DYT11 (159900)	SGCE	Myoclonus–dystonia	AD
DYT12 (128235)	ATP1A3	Rapid-onset dystonia parkinsonism	AD
DYT15 (607488)	18p11	Myoclonus–dystonia	AD
DYT16 (612067)	PRKRA	Early-onset dystonia parkinsonism	AR
Heredodegenerative syndromes with dystonia as a frequent clinical feature			
AT (208900)	ATM	Cerebellar ataxia, telangiectases	AR
CHAC (200150)	VPS13A	Parkinsonian features, orofacial dyskinesias	AR
CLF (204200)	CLN3	Cerebral atrophy, macular degeneration	AR
DDS (304700)	TIMM8A	Progressive deafness and dystonia	XR
DPRLA (125370)	ATN1	Ataxia, chorea, dementia	AD
DYT3 (314250)	TAF1	Dystonia–parkinsonism	XR
FC (230000)	FUCA1	Mental retardation, seizures, neuropathy	AR
GA (231670)	GCDH	Infantile encephalopathy with choreoatetosis e dystonia	AR
HD (143100)	IT-15	Chorea, dystonia, dementia	AD
HDL2(605268)	JPH3	Chorea, parkinsonism, dementia	AD
LHON (535000)	Several genes	Optic atrophy, tremor, dystonia	M
LNS (300322)	HPRT	Mental retardation, motor delay, spasticity	XR
LS (256000)	Several genes	Early onset, rapid progression, clinical heterogeneity	M or AR
MLD (250100)	ARSA	Mental retardation, spasticity, bulbar palsies	AR
NFP (606159)	FTL	Neurodegeneration with brain iron accumulation type 2	AD
NPC1 (257220)	NPC1	Mental retardation, motor delay, spasticity	AR
NPC2 (607625)	HE1	Mental retardation, motor delay, spasticity	AR
PARK14	PLA2G6	Neurodegeneration with brain iron accumulation type 2	AR
PARK2 (600116)	PRKN	Early-onset parkinsonism	AR
PARK7 (606324)	DJ1	Early-onset parkinsonism	AR
PKAN (234200)	PANK2	Neurodegeneration with brain iron accumulation type 1	AR
PMD (312080)	PLP1	Progressive pyramidal and cerebellar signs, ''rolling'' head tremor	XR
RTT (312750)	MECP2	Mental retardation, motor delay, autism, epilepsy	XD
SCA17 (607136)	TBP	Parkinsonism, chorea, dementia	AD
SCA3 (109150)	ATXN3	Ataxia, spasticity, ocular movement abnormalities	AD
SCA6 (183086)	CACNA1A	Chorea, spasticity, cervical dystonia, or blepharospasm	AD
TSD (272800)	HEXA	Infancy onset, paralysis, dementia and blindness fatal by age 2 or 3	AR
WD (277900)	ATP7B	Tremor, dystonia, parkinsonian features	AR

[a]Abbreviations: AT, ataxia-telangiectasia; CHAC, choreoacanthocytosis; CLF, ceroid-lipofuscinosis; DDS, dystonia-deafness syndrome; DPRLA, dentatorubral–pallidoluysian atrophy; FC, fucosidosis; GA, glutaricacidemia; HD, Huntington's disease; HDL2, Huntington like disease type 2; LHON, Leber hereditary optic neuropathy; LNS, Lesch–Nyhan syndrome; LS, Leigh syndrome; MLD, metachromatic leukodystrophy; NFP, neuroferritinopathy; NPC1, Niemann-Pick type C1; NPC2, Niemann-Pick type C2; PKAN, pantothenate kinase-associated neurodegeneration; PMD, Pelizaeus–Merzbacher disease; RTT, Rett syndrome; THD, tyrosine hydroxylase deficiency; TSD, Tay-Sachs disease; WD, Wilson disease;
[b]Abbreviations: ARSA, arylsulfatase A; ATM, ataxia-telangiectasia mutated gene; ATN1, atrophin 1; ATP1A3, ATPase, $Na+/K+$ transporting; ATP7B, ATPase, Cu^{++}-transporting beta polypeptide; ATXN3, ataxin-3; CACNA1A, calcium channel, voltage-dependent, p/q type, alpha-1a subunit; CLN3, CLN3 gene; DJ1, oncogene DJ1; FUCA1, alpha-L-fucosidase 1; FTL, ferritin light chain; GCH1, guanosine triphosphate cyclohydrolase 1; GCDH, glutaryl-CoA dehydrogenase; HE1, epididymal secretory protein; HEXA, hexosaminidase A alpha polypeptide; HPRT, hypoxanthine guanine phosphoribosyl-transferase 1; IT-15, important transcript 15 (huntingtin); JPH3, junctophilin 3; MECP2, methyl-CpG-binding protein 2; NPC1, Niemann-Pick type C1 gene; PANK2, pantothenate kinase 2; PRKN, parkin; PRKRA, double-stranded RNA-activated protein kinase; PLA2G6, phospholipase A2 group VI; PLP1, proteolipid protein 1; SGCE, ϵ-sarcoglycan; TAF1, TATA boxing-binding protein associated factor; TBP, TATA box-binding protein; TH, tyrosine hydroxylase; THAP1, Thanatos associated protein; TIMM8A, translocase of inner mitochondrial membrane 8; TOR1A, torsin A gene; VPS13A, vacuolar protein sorting 13; [c]Transmission: AD, autosomal dominant; AR, autosomal recessive; M, mitochondrial; XR, X-linked recessive.

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