Test Specific Guidelines

Spinocerebellar Ataxia Genetic Testing

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Introduction

Spinocerebellar ataxia genetic testing is addressed by this guideline.

Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures addressed by this guideline	Procedure codes
ATXN1 gene analysis, evaluation to detect abnormal (eg,expanded) allele	81178
ATXN2 gene analysis, evaluation to detect abnormal (eg,expanded) allele	81179
ATXN3 gene analysis, evaluation to detect abnormal (eg,expanded) allele	81180
ATXN7 gene analysis, evaluation to detect abnormal (eg,expanded) allele	81181
ATXN8 gene analysis, evaluation to detect abnormal (eg, expanded) alleles	81182
ATXN10 gene analysis, evaluation to detect abnormal (eg, expanded) alleles	81183
CACNA1A gene analysis; evaluation to detect abnormal (eg, expanded) alleles	81184
CACNA1A gene analysis; full gene sequence	81185
CACNA1A gene analysis; known familial variant	81186
Genomic Unity CACNA1A Analysis	0231U
PPP2R2B gene analysis, evaluation to detect abnormal (eg, expanded) alleles	81343
SCA multigene panel	81479

Procedures addressed by this guideline	Procedure codes
TBP gene analysis, evaluation to detect abnormal (eg, expanded) alleles	81344

What Is Spinocerebellar Ataxia?

Definition

Spinocerebellar ataxias (SCA) are a group of autosomal dominant ataxias that have a range of phenotypes. There are various subtypes of SCA, which are denoted by numbers (e.g. SCA1, SCA3, etc.)

Prevalence

The prevalence of autosomal dominant cerebellar ataxias, as a whole, is 1-5:100,000.[1] SCA3 is the most common autosomal dominant form of ataxia. This is followed by SCA1, SCA2, SCA6, and SCA7.[1] The prevalence of specific subtypes of SCA vary by region. SCA3 is most common is Portugal.[1]

Symptoms

Although the specific phenotype of each subtype varies, most individuals with SCA have "progressive adult-onset gait ataxia (often with hand dysmetria) and dysarthria associated with cerebellar atrophy on brain imaging."[1] The age of onset for the different subtypes also overlaps, which it makes it difficult to distinguish between subtypes based on clinical phenotype only.[1,2] See the table below for the various subtypes of SCA and the associated clinical features.

Cause

SCAs are caused by mutations in one of numerous genes. See the table below for the various subtypes of SCA and the associated genes.

Inheritance

SCAs are autosomal dominant disorders. Anticipation is observed in some of the SCAs. This means that as the disease passes through generations, the severity can increase and the age of onset can decrease.

Autosomal dominant inheritance

In autosomal dominant inheritance, individuals have 2 copies of the gene and only one mutation is required to cause disease. When a parent has a mutation, each offspring has a 50% risk of inheriting the mutation. Males and females are equally likely to be affected.

Diagnosis

Molecular genetic testing can be used to establish a specific diagnosis, which aids in understanding the prognosis and risk assessment for family members.[1]

Management

Treatment of ataxia is largely supportive, and includes the use of canes and walkers for ambulation, speech therapy, and other assistive devices.[1]

SCA subtype	Gene Associated	Clinical Features
SCA1	ATXN1	Progressive cerebellar ataxia, dysarthria, deterioration of bulbar functions, pyramidal signs, peripheral neuropathy[2,3]
SCA2	ATXN2	Progressive ataxia and dysarthria, nystagmus, slow saccadic eye movements, peripheral neuropathy, decreased DTRs, dementia[2,4]
SCA3	ATXN3	Gait problems, speech difficulties, clumsiness, visual blurring, diplopia, hyperreflexia, progressive ataxia, nystagmus, dysarthria, pyramidal and extrapyramidal signs; lid retraction, nystagmus, decreased saccade velocity; amyotrophy fasciculations, sensory loss[2,5]
SCA4	16q22.1	Sensory axonal neuropathy, deafness; may be allelic with 16q22-linked SCA[2]
SCA5	SPTBN2	Early onset, slow course[2]
SCA6	CACNA1A	Progressive cerebellar ataxia, dysarthria, nystagmus, sometimes episodic ataxia, very slow progression[2,6]

SCA subtype	Gene Associated	Clinical Features
SCA7	ATXN7	Progressive cerebellar ataxia, dysarthria, dysphagia, cone-rod and retinal dystrophy with progressive central visual loss resulting in blindness[2,7]
SCA8	ATXN8	Principally cerebellar ataxia, slowly progressing ataxia, scanning dysarthria, truncal instability, hyperactive tendon reflexes, decreased vibration sense; rarely, cognitive impairment[2,8]
SCA10	ATXN10	Progressive cerebellar ataxia, scanning dysarthria, dysphagia, upper-limb ataxia, generalized motor seizures and/or complex partial seizures, most families are of Native American background[2,9]
SCA11	TTBK2	Progressive cerebellar ataxia, abnormal eye signs (jerky pursuit, horizontal and vertical nystagmus), mild, remain ambulatory[2,10]
SCA12	PPP2R2B	Slowly progressive ataxia; action tremor in the 30s; hyperreflexia; subtle Parkinsonism possible; cognitive/psychiatric disorders including dementia[2]

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SCA subtype	Gene Associated	Clinical Features
SCA13	KCNC3	Ranges from progressive childhood-onset cerebellar ataxia, cerebellar dysarthria, occasional seizures to adult-onset progressive ataxia, mild intellectual disability, short stature[2,11]
SCA14	PRKCG	Progressive cerebellar ataxia, dysarthria, nystagmus, axial myoclonus, cognitive impairment, tremor, sensory loss, Parkinsonian features including rigidity and tremor[2,12]
SCA15	ITPR1	Progressive gait and limb ataxia, ataxic dysarthria, titubation, upper limb postural tremor, mild hyperreflexia, gaze-evoked nystagmus, and impaired vestibuloocular reflex gain[2,13]
SCA16	SCA16	Head tremor; reported in one Japanese family[2]
SCA17	TBP	Ataxia, dementia, mental deterioration; occasional chorea, dystonia, myoclonus, epilepsy; Purkinje cell loss, intranuclear inclusions with expanded polyglutamine[2,14]

SCA subtype	Gene Associated	Clinical Features
SCA18	7q22-q32	Ataxia with early sensory/motor neuropathy, nystagmus, dysarthria, decreased tendon reflexes, muscle weakness, atrophy, fasciculations, Babinski responses[2]
SCA19/22	KCND3	Slowly progressive, rare cognitive impairment, myoclonus, hyperreflexia[2]
SCA20	11q12.2-11q12.3	Progressive ataxia, dysarthria, palatal tremor (myoclonus), and/or abnormal phonation clinically resembling spasmodic adductor dysphonia, hyperreflexia, bradykinesia; calcification of the dentate nucleus.[2,15]
SCA21	TMEM240	Mild cognitive impairment[2]
SCA23	PDYN	Dysarthria, abnormal eye movements, reduced vibration and position sense; reported in one Dutch family; neuropathology[2]
SCA25	SCA25	Sensory neuropathy; reported in one French family[2]
SCA26	EEF2	Dysarthria, irregular visual pursuits; reported in one Norwegian-American family; MRI: cerebellar atrophy[2]
SCA27	FGF14	Early-onset tremor; dyskinesia, cognitive deficits; reported in one Dutch family[2]

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SCA subtype	Gene Associated	Clinical Features
SCA28	AFG3L2	Young-adult onset, progressive gait and limb ataxia resulting in coordination and balance problems, dysarthria, ptosis, nystagmus, and ophthalmoparesis, increased tendon reflexes; reported in two Italian families[2,16]
SCA29	ITPR1	Learning deficits, infant-onset hypotonia, motor delays[2,17]
SCA30	4q34.3-q35.1	Hyperreflexia[2]
SCA31	BEAN1	Normal sensation[2]
SCA35	TGM6	Hyperreflexia, Babinski responses; spasmodic torticollis[2]
SCA36	NOP56	Late-onset, slowly progressive cerebellar syndrome typically associated with sensorineural hearing loss, muscle atrophy and denervation, especially of the tongue, as well as pyramidal signs, muscle fasciculations, hyperreflexia[2]
SCA37	DAB1	Adult onset, abnormal vertical eye movements, dysarthria, dysmetria, dysphagia[1,18]
SCA38	ELOVL5	Adult onset, axonal neuropathy[1]
SCA40	CCDC88C	Adult onset, brisk reflexes, spasticity[1]
SCA41	TRPC3	Adult onset, uncomplicated ataxia[1]

SCA subtype	Gene Associated	Clinical Features
SCA42	CACNA1G	Mild pyramidal signs, saccadic pursuit[1]

Survival

The SCAs are a group of progressive disorders with a range of phenotypes. Specific symptoms and a genetically determined diagnosis can assist with determining predicted survival and prognosis.

Test Information

Introduction

Testing for SCA may include known familial mutation analysis, repeat expansion analysis, next generation sequencing, deletion/duplication analysis, and/or multigene panel testing. Test methods vary by gene of interest.

Known Familial Mutation Analysis

Analysis for known familial mutations is typically performed by nucleotide repeat expansion analysis. Some mutations may require Sanger sequencing or deletion/duplication analysis.

Known familial mutation analysis is performed when a causative mutation has been identified in a close relative of the individual requesting testing.

Repeat Expansion Analysis

Several of the SCAs are caused by repeat expansions. Testing for these conditions is performed by expansion analysis to identify the number of repeats. Expansion analysis can be performed for diagnostic testing, presymptomatic testing, as well as prenatal testing.

Next Generation Sequencing Assay

Next generation sequencing (NGS), which is also sometimes called massively parallel sequencing, was developed in 2005 to allow larger scale and more efficient gene sequencing. NGS relies on sequencing many copies of small pieces of DNA simultaneously and using bioinformatics to assemble the sequence. Sequence analysis detects single nucleotide substitutions and small (several nucleotide) deletions and insertions. Regions analyzed typically include the coding sequence and intron/exon boundaries. Promoter regions and intronic sequences may also be sequenced if disease-causing mutations are known to occur in these regions of a gene.

Deletion and Duplication Analysis

Analysis for deletions and duplications can be performed using a variety of technical platforms including exon array, Multiplex ligation-dependent probe amplification (MLPA), and NGS data analysis. These assays detect gains and

losses too large to be identified through standard sequence analysis, often single or multiple exons or whole genes.

Multi-Gene Testing Panels

The efficiency of NGS has led to an increasing number of large, multi-gene testing panels. NGS panels that test several genes at once are particularly well-suited to conditions caused by more than one gene or where there is considerable clinical overlap between conditions making it difficult to reliably narrow down likely causes. Additionally, tests should be chosen to maximize the likelihood of identifying mutations in the genes of interest, contribute to alterations in patient management, and/or minimize the chance of finding variants of uncertain clinical significance.

Guidelines and Evidence

Introduction

This section includes relevant guidelines and evidence pertaining to SCA testing.

European Federation of Neurological Sciences

The European Federation of Neurological Sciences (EFNS, 2014) stated the following with regard to testing for autosomal dominant cerebellar ataxia:[19]

"In the case of a family history that is compatible with an autosomal dominant cerebellar ataxia, screening for SCA1, SCA2, SCA3, SCA6, SCA7, and SCA17 is recommended (Level B). In Asian patients, DRPLA should also be tested for."

"If mutation analysis is negative, we recommend contact with or referral to a specialized clinic for reviewing the phenotype and further genetic testing (good practice point)"

"In the case of sporadic ataxia and independent from onset age, we recommend routine testing for SCA1, SCA2, SCA3, SCA6, and DRPLA (in Asian patients) (level B), the step one panel of the recessive ataxia workup, i.e. mutation analysis of the FRDA gene (level B), and biochemical testing that includes cholestanol, vitamin E, cholesterol, albumin, CK, and alpha-fetoprotein."

Selected Relevant Publications

de Silva R, Greenfield J, Cook A, et al. (2019) stated that as part of the diagnostic evaluation for progressive ataxias, genetic tests should include: [20]

"Genetic tests for FRDA, SCA 1, 2, 3, 6, 7 (12,17) and FXTAS"

Hadjivassiliou M, Martindale J, Shanmugarajah P, et al (2017) stated the following with regard to testing for hereditary ataxias:[21]

“We have shown that patients with early onset idiopathic ataxia (irrespective of family history) are much more likely to have a genetic aetiology (81%) than those with late onset idiopathic ataxia (55%). One possible selection criterion for genetic testing is early onset ataxia. Additional selection criteria may include the presence of other clinical features, for example, 91% of patients with histologically suspected/genetically confirmed mitochondrial disease had ataxia with other clinical features (eg, deafness, diabetes, myoclonus, etc) and only 9% pure ataxia.”

“Furthermore, the presence of severe cerebellar atrophy without any clinical correlation and with well-preserved spectroscopy of the cerebellum often suggests that the ataxia is long standing (maybe even early onset) and slowly progressive. Such patients should therefore be offered genetic testing. The pattern of cerebellar involvement on MR spectroscopy may also direct to a particular diagnosis. Most genetic ataxias involve both the hemispheres and the vermis while the majority of immune-mediated acquired ataxias (eg, gluten ataxia, anti-GAD ataxia and primary autoimmune cerebellar ataxia) have a predilection for the vermis.”

Jayadev S and Bird T (2013) stated the following:[2]

The "differential diagnosis of hereditary ataxia includes acquired, nongenetic causes of ataxia, such as alcoholism, vitamin deficiencies, multiple sclerosis, vascular disease, primary or metastatic tumors, and paraneoplastic diseases associated with occult carcinoma of the ovary, breast, or lung, and the idiopathic degenerative disease multiple system atrophy (spinal muscular atrophy). The possibility of an acquired cause of ataxia needs to be considered in each individual with ataxia because a specific treatment may be available."

Regarding establishing the diagnosis of hereditary ataxias:

"Detection on neurological examination of typical clinical signs including poorly coordinated gait and finger/hand movements, dysarthria (incoordination of speech), and eye movement abnormalities such as nystagmus, abnormal saccade movements, and ophthalmoplegia."

"Exclusion of nongenetic causes of ataxia."

"Documentation of the hereditary nature of the disease by finding a positive family history of ataxia, identifying an ataxia-causing mutation, or recognizing a clinical phenotype characteristic of a genetic form of ataxia."

Regarding testing when the family history suggests autosomal dominant inheritance:

"An estimated 50–60% of the dominant hereditary ataxias can be identified with highly accurate and specific molecular genetic testing for SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA10, SCA12, SCA17, and DRPLA; all have nucleotide repeat expansions in the pertinent genes."

"Because of broad clinical overlap, most laboratories that test for the hereditary ataxias have a battery of tests including testing for SCA1, SCA2, SCA3, SCA6,

SCA7, SCA10, SCA12, SCA14, and SCA17. Many laboratories offer them as two groups in stepwise fashion based on population frequency, testing first for the more common ataxias, SCA1, SCA2, SCA3, SCA6, and SCA7. Although pursuing multiple genes simultaneously may seem less optimal than serial genetic testing, it is important to recognize that the cost of the battery of ataxia tests often is equivalent to that of an MRI. Positive results from the molecular genetic testing are more specific than MRI findings in the hereditary ataxias. Guidelines for genetic testing of hereditary ataxia have been published."

"Testing for the less common hereditary ataxias should be individualized and may depend on factors such as ethnic background (SCA3 in the Portuguese, SCA10 in the Native American population with some exceptions [Fujigasaki et al., 2002]); seizures (SCA10); presence of tremor (SCA12, fragile X-associated tremor/ataxia syndrome); presence of psychiatric disease or chorea (SCA17); or uncomplicated ataxia with long duration (SCA6, SCA8, and SCA14). Dysphonia and palatal myoclonus are associated with calcification of the dentate nucleus of cerebellum (SCA20)."

"If a strong clinical indication of a specific diagnosis exists based on the affected individual's examination (e.g., the presence of retinopathy, which suggests SCA7) or if family history is positive for a known type, testing can be performed for a single disease."

Regarding testing for a simplex case:

"If no acquired cause of the ataxia is identified, the probability is ~13% that the affected individual has SCA1, SCA2, SCA3, SCA6, SCA8, SCA17, or FRDA, and mutations in rare ataxia genes are even less common."

"Other possibilities to consider are a de novo mutation in a different autosomal dominant ataxia, decreased penetrance, alternative paternity, or a single occurrence of an autosomal recessive or X-linked disorder in a family such as fragile X-associated tremor/ataxia syndrome."

"Although the probability of a positive result from molecular genetic testing is low in an individual with ataxia who has no family history of ataxia, such testing is usually justified to establish a specific diagnosis for the individual's medical evaluation and for genetic counseling."

"Always consider a possible nongenetic cause such as multiple system atrophy, cerebellar type in simplex cases."

Criteria

Introduction

Requests for SCA testing are reviewed using these criteria.

Known Familial Mutation Analysis

Genetic Counseling:

Pre- and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND

Previous Genetic Testing:

No previous genetic testing that would detect the familial mutation, AND

Presymptomatic Testing for Asymptomatic Individuals:

Member is 18 years of age or older, and

Known disease-causing mutation in SCA gene identified in 1st or 2nd degree relative(s), OR

Diagnostic Testing for Symptomatic Individuals:

Known disease-causing mutation in SCA gene identified in 1st or 2nd degree relative(s), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy

Single Gene Testing

Genetic Counseling:

Pre- and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND

Previous Genetic Testing:

No previous testing of requested gene(s), and

No mutation identified by previous analysis, if performed, and

No known familial mutation in a gene known to cause ataxia, AND

Diagnostic Testing for Symptomatic Individuals:

Individual has been diagnosed with cerebellar ataxia, and

Medical history points to the specific subtype of SCA requested (e.g. age of onset, distinguishing features present, etc), AND

Documentation from ordering provider indicating how test results will be used to directly impact medical care for the individual (e.g. change in surveillance or treatment plan), AND

The member does not have a known underlying cause for their ataxia (e.g. alcoholism, vitamin deficiencies, multiple sclerosis, vascular disease, tumors, known mutation, etc), AND

Family history is consistent with an autosomal dominant inheritance pattern (including simplex cases), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy

Multigene Panel Testing

Genetic counseling:

Pre- and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND

Previous Genetic Testing:

No previous testing of requested genes, and

No mutation identified by previous analysis, if performed, and

No known familial mutation in a gene known to cause ataxia, AND

Diagnostic Testing for Symptomatic Individuals:

Individual has been diagnosed with cerebellar ataxia, regardless of age of onset, AND

Documentation from ordering provider indicating how test results will be used to directly impact medical care for the individual (e.g. change in surveillance or treatment plan), AND

The member does not have a known underlying cause for their ataxia (e.g. alcoholism, vitamin deficiencies, multiple sclerosis, vascular disease, tumors, known mutation, etc), AND

Family history is consistent with an autosomal dominant inheritance pattern (including simplex cases), AND

Medical history does not point to a specific genetic diagnosis for which a more focused test or panel would be appropriate, AND

Rendering laboratory is a qualified provider of service per the Health Plan policy

Billing and Reimbursement Considerations

For information on broader hereditary ataxia panel testing, please refer to the guideline *Hereditary Ataxia Multigene Panel Genetic Testing*, as this testing is not addressed here.

Gene panels that are specific to SCA will be eligible for reimbursement according to the criteria outlined in this guideline. Test methodology should be appropriate to the disease-causing mutations that are commonly reported for the disorder in question (e.g., sequencing only panels will not detect triplet repeat or large deletion/duplication mutations).

When multiple CPT codes are billed for components of a panel and there is a more appropriate CPT code representing the panel, eviCore will redirect to the panel code(s).

If the laboratory will not accept redirection to a panel code, the medical necessity of each billed component procedure will be assessed independently.

In general, only a limited number of panel components that are most likely to explain the member's presentation will be reimbursable. The remaining panel components will not be reimbursable.

When the test is billed with multiple stacked procedure codes, only the following genes may be considered for reimbursement:

ATXN1 (SCA1)

ATXN2 (SCA2)

ATXN3 (SCA3)

CACNA1A (SCA6)

ATXN7 (SCA7)

TBP (SCA17)

References

Introduction

These references are cited in this guideline.

Bird, TD. Hereditary Ataxia Overview. 1998 Oct 28 [Updated 2019 Jul 25]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1138/

Jayadev S, Bird T. Hereditary ataxias: overview. *Genet Med*. 2013;15(9):673-683.

Opal P, Ashizawa T. Spinocerebellar Ataxia Type 1. 1998 Oct 1 [Updated 2017 Jun 22]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1184/

Pulst SM. Spinocerebellar Ataxia Type 2. 1998 Oct 23 [Updated 2019 Feb 14]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1275/

Paulson H, Shakkottai V. Spinocerebellar Ataxia Type 3. 1998 Oct 10 [Updated 2020 Jun 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1196/

Casey HL, Gomez CM. Spinocerebellar Ataxia Type 6. 1998 Oct 23 [Updated 2019 Nov 21]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1140/

LaSpada, AR. Spinocerebellar Ataxia Type 7. 1998 Aug 27 [Updated 2020 Jul 23]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1256/

Cleary JD, Subramony SH, Ranum LPW. Spinocerebellar Ataxia Type 8. 2001 Nov 27 [Updated 2021 Apr 22]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1268/

Matsuura T, Ashizawa T. Spinocerebellar Ataxia Type 10. 2002 Apr 23 [Updated 2019 Sep 19]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1175/

Chen Z, Puzriakova A, Houlden H. Spinocerebellar Ataxia Type 11. 2008 Jul 22 [Updated 2019 Oct 31]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1757/

Waters MF. Spinocerebellar Ataxia Type 13. 2006 Nov 9 [Updated 2020 Jun 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1225/

Chen DH, Bird TD, Raskind WH. Spinocerebellar Ataxia Type 14. 2005 Jan 28 [Updated 2020 Feb 20]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1399/

Storey E. Spinocerebellar Ataxia Type 15. 2006 May 30 [Updated 2014 June 12]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1362/

Toyoshima Y, Onodera O, Yamada M, et al. Spinocerebellar Ataxia Type 17. 2005 Mar 29 [Updated 2019 Sep 12]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1438/

Storey E, Gardner RJM. Spinocerebellar Ataxia Type 20. 2007 Feb 27 [Updated 2019 Apr 18]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1471/

Brussino A, Brusco A, Durr A, et al. Spinocerebellar Ataxia Type 28. 2011 May 17 [Updated 2018 Mar 22]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK54582/

Zambonin JL, Bellomo A, Ben-Pazi H et al. Spinocerebellar ataxia type 29 due to mutations in ITPR1: a case series and review of this emerging congenital ataxia. *Orphanet J Rare Dis*. 2017;12(1):121.

Matilla-Dueñas A, Volpini V. Spinocerebellar Ataxia Type 37. 2019 May 30. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK541729

van de Warrenburg BPC, van Gaalen J, Boesch S, et al. EFNS/ENS Consensus on the diagnosis and management of chronic ataxias in adulthood. *Eur J Neurol*. 2014;21:552-562.

de silva R, Greenfield J, Cook A, et al. Guidelines on the diagnosis and management of the progressive ataxias. *Orphanet J Rare Dis*. 2019;14(1):51. doi: 10.1186/s13023-019-1013-9

Hadjivassiliou M, Martindale J, Shanmugarajah P, et al. Causes of progressive cerebellar ataxia: prospective evaluation of 1500 patients. *J Neurosurg Psychiatry*. 2017;88:301-309.

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