### Supplementary Table 1

**Neuroimaging demographics in pediatric chronic ataxia based on disease etiology**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Disease (in order of frequency of known etiologies)** | **No. of patients** | **No. of patients with imaging** | | | | **No. of patients with imaging reviewed** | **Age at first imaging (years)** | | |
|  |  | **Total** | **CT only** | **MRI only** | **CT and MRI** |  | **Median** | **Range** | **Age if No. of patients =1 or 2** |
| Angelman synd | 16 | 15 | 8 | 4 | 3 | 8 | 1.66 | 0.99-10.21 |  |
| AT | 13 | 11 | 1 | 6 | 4 | 7 | 5.59 | 1.92-19.43 |  |
| ? AT variant | 1 | 1 | 1 | 0 | 0 | 0 |  |  | 12.36 |
| **†Stroke:** |  |  |  |  |  |  |  |  |  |
| 1) Ischemic: |  |  |  |  |  |  |  |  |  |
| Pre- and postnatal arterial thrombo-embolic ischemic stroke | 6 | 6 | 0 | 2 | 4 | 3 | 5.90 | 1.32-16.36 |  |
| Vasculitis | 2 | 2 | 0 | 2 | 0 | 2 |  |  | 8.49, 11.75 |
| Aneurysm | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 1.17 |
| **All ischemic strokes** | 9 | 9 | 0 | 5 | 4 | 6 | 6.41 | 1.17-16.36 |  |
| 2) Hemorrhagic: |  |  |  |  |  |  |  |  |  |
| Cavernoma | 2 | 2 | 0 | 0 | 2 | 2 |  |  | 3.75, 13.05 |
| AVM | 1 | 1 | 0 | 0 | 1 | 1 |  |  | 2.38 |
| **All strokes** | 12 | 12 | 0 | 5 | 7 | 9 | 5.90 | 1.17-16.36 |  |
| Mitochondrial | 9 | 9 | 0 | 6 | 3 | 6 | 2.55 | 0.17-12.21 |  |
| FA | 7 | 6 | 2 | 4 | 0 | 3 | 12.35 | 7.64-16.21 |  |
| Episodic ataxia: |  |  |  |  |  |  |  |  |  |
| 1) Genetically confirmed | 3 | 3 | 0 | 1 | 2 | 0 | 13.56 | 7.87-15.09 |  |
| 2) Familial but not proven genetically | 4 | 3 | 1 | 2 | 0 | 1 | 15.68 | 13.98-16.39 |  |
| NCL types 1 & 2 | 5 | 5 | 1 | 1 | 3 | 4 | 2.94 | 1.65-3.81 |  |
| NCL type 3 | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 6.09 |
| Intractable epilepsy | 5 | 5 | 0 | 4 | 1 | 5 | 2.02 | 1.09-7.16 |  |
| HIE | 5 | 5 | 1 | 2 | 2 | 3 | 0.01 | 0.003-6.29 |  |
| NMD | 5 | 5 | 1 | 3 | 1 | 4 | 4.64 | 2.5-16.22 |  |
| JSRD | 5 | 5 | 0 | 4 | 1 | 5 | 2.78 | 0.41-14.35 |  |
| Rett synd | 4 | 4 | 1 | 3 | 0 | 2 | 5.25 | 1.49-6.35 |  |
| Salla disease | 4 | 4 | 0 | 3 | 1 | 4 | 1.59 | 0.75-3.25 |  |
| Other leukodystrophies | 2 | 2 | 0 | 2 | 0 | 2 |  |  | 5, 8.58 |
| Trauma | 2 | 2 | 1 | 1 | 0 | 2 |  |  | 11.75, 16.85 |
| DWM | 2 | 2 | 0 | 1 | 1 | 2 |  |  | 10.57, 17.4 |
| DES-Hutterites | 2 | 2 | 0 | 1 | 1 | 0 |  |  | 1.13, 1.77 |
| Mar-Sjög synd | 2 | 2 | 0 | 1 | 1 | 1 |  |  | 0.78, 5.55 |
| Multiple sclerosis | 2 | 2 | 0 | 0 | 2 | 2 |  |  | 12.55, 15.09 |
| Prematurity | 2 | 1 | 0 | 1 | 0 | 1 |  |  | 8.41 |
| Rit-Schin synd | 2 | 2 | 0 | 1 | 1 | 2 |  |  | 0.01, 2.35 |
| Homocystinuria | 1 | 1 | 0 | 0 | 1 | 1 |  |  | 2.15 |
| CPS deficiency | 1 | 1 | 0 | 0 | 1 | 0 |  |  | 4.56 |
| ADEM | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 7.81 |
| ‡Gaucher type 3 | 1 | 1 | 0 | 0 | 1 | 1 |  |  | 2.67 |
| Glut 1 deficiency | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 9.26 |
| Chiari I malformation | 1 | 1 | 0 | 0 | 1 | 1 |  |  | 4 |
| L1CAM mutation | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 2.97 |
| ? PCH 3 | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 3.67 |
| Post-radiation | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 12.19 |
| Post-infectious | 1 | 1 | 0 | 0 | 1 | 0 |  |  | 8.2 |
| Smith-Mag synd | 1 | 1 | 0 | 1 | 0 | 1 |  |  | 11.65 |
| Sotos synd | 1 | 1 | 0 | 0 | 1 | 0 |  |  | 3.21 |
| Wernicke enceph | 1 | 1 | 0 | 1 | 0 | 0 |  |  | 11.21 |
| **Ataxia NYD:** |  |  |  |  |  |  |  |  |  |
| 1) Non-progressive ataxia with: |  |  |  |  |  |  |  |  |  |
| DD and ≥2 UMN | 13 | 13 | 0 | 8 | 5 | 11 | 3.29 | 0.59-21.52 |  |
| DD and 1 UMN | 9 | 9 | 1 | 7 | 1 | 7 | 5.98 | 0.45-17.08 |  |
| DD, ≥1 UMN, and epilepsy | 7 | 6 | 0 | 6 | 0 | 6 | 6.95 | 0.61-15.18 |  |
| DD and epilepsy | 5 | 5 | 0 | 3 | 2 | 3 | 7.96 | 0.75-16.03 |  |
| DD | 5 | 5 | 0 | 5 | 0 | 5 | 6.12 | 2.92-13.53 |  |
| Pure ataxia | 2 | 2 | 0 | 2 | 0 | 2 |  |  | 5.85, 12.07 |
| 2) Intermittent ataxia | 6 | 6 | 0 | 2 | 4 | 6 | 1.61 | 1.44-9.94 |  |
| 3) Ataxia/ dev reg | 3 | 3 | 0 | 1 | 2 | 2 | 1.71 | 0.87-4.26 |  |
| 4) Progressive: |  |  |  |  |  |  |  |  |  |
| Familial prog ataxia | 2 | 2 | 0 | 2 | 0 | 2 |  |  | 2.66, 15.85 |
| Prog ataxia | 2 | 2 | 0 | 1 | 1 | 1 |  |  | 1.08, 8.8 |
| 5) Self-limiting ataxia | 2 | 2 | 0 | 2 | 0 | 2 |  |  | 9.86, 11.24 |
| **Total** | **184** | **177** | **19** | **103** | **55** | **130** |  |  |  |

No.: number, synd: syndrome, AT: ataxia telangiectasia, FA: Friedreich ataxia, † two other strokes occurred. The first was in a patient with Friedreich’s ataxia and the second was in a patient with developmental delay and non-progressive spastic ataxia, who had a stroke secondary to embolic pneumococcal meningitis, AVM: arterio-venous malformation, NCL: neuronal ceroid lipofuscinosis, HIE: hypoxic-ischemic encephalopathy, NMD: neuronal migration disorder, JSRD: Joubert syndrome related disorder, DWM: Dandy-Walker malformation, DES-Hutterites: dysequilibrium syndrome (also known as autosomal recessive cerebellar hypoplasia in the Hutterite population), Mar-Sjög: Marinesco-Sjögren syndrome, Rit-Schin synd: Ritscher–Schinzel syndrome, CPS: carbomyl phosphate synthetase, ADEM: acute disseminated encephalomyelitis, ‡ this patient also had a very small cavernoma, L1CAM: L1 cell adhesion molecule, PCH 3: pontocerebellar hypoplasia type 3, Smith-Mag synd: Smith-Magenis syndrome, enceph: encephalopathy, NYD: not yet diagnosed, DD: developmental delay, UMN: upper motor neuron sign, dev reg: developmental regression, Prog: progressive.

**Supplementary Table 2**

**Neuroimaging findings in pediatric chronic ataxia based on etiological categories**

|  |  |
| --- | --- |
| **Disorder** | **Neuroimaging findings (the numbers in the brackets refer to the number of patients with the imaging finding)** |
| **Metabolic:** |  |
| Mitochondrial | Normal (1); abnormal T2-weighted signal intensity in the cerebral hemispheres grey or white matter (7), thalami (3), basal ganglia (3), brainstem (3), cerebellum (2), cervical spinal cord (2), hypothalamus (1); pancerebellar hypoplasia (1); hypomyelination (1); increased extra-axial CSF/ ventricular spaces (3), MCM (1) |
| NCL types 1 & 2 | Hyperintense signal abnormality on FLAIR MRI in the periventricular white matter (3), hypointense signal abnormality on T2-weighted MRI in the thalami (4) and globi pallidi (2), pancerebellar atrophy (5), diffuse cerebral atrophy (4), basal ganglia atrophy (2), brainstem atrophy (1), increased extra-axial CSF/ ventricular spaces (3), MCM (2) |
| NCL type 3 | Hyperintense signal abnormality on FLAIR MRI in the periventricular white matter, hypointense signal abnormality on T2-weighted MRI in the thalami and globi pallidi, pancerebellar atrophy, diffuse cerebral atrophy |
| Salla disease | Diffuse hyperintense signal abnormality on T2-weighted MRI in the white matter of the cerebrum, specifically involving the centrum semiovale and U-fibres at the depth of the sulci (4) and deep cerebellar white matter (1) consistent with hypomyelination. Myelination of the corticospinal tracts and fornix was normal in all four patients. Other features included thin corpus callosum (3), progressive vermis atrophy (1), increased extra-axial CSF/ ventricular spaces (1), MCM (2) |
| Other leukodystrophies | Abnormal diffuse T2-weighted signal intensity in the white matter (2) consistent with hypomyelination (1) and demyelination (1), pancerebellar atrophy (2), thin corpus callosum (2), increased extra-axial CSF/ ventricular spaces (1), MCM (1), cerebral atrophy (1), prominent superior colliculi (1) |
| CPS deficiency | Generalized brain edema, enlarged lateral ventricles, MCM (1) |
| Homocystinuria | Normal (1) |
| Glut 1 deficiency | Normal (1) |
| Wernicke enceph | Cerebellar hemisphere atrophy, enlarged lateral ventricles, patient has an unconfirmed ‘parietal lobe pachygyria’ on an old MRI report (1) |
| Gaucher type 3 | Left caudate head cavernoma with hemorrhage, hyperintense T2-weighted signal abnormality in left periventricular white matter next to trigone region, MCM (1) |
| **DNA repair defects:** |  |
| AT | Normal (5), cerebral mass lesion (3, 2 of 3 showed post-tumor treatment calcification), cerebellar hemispheres only or diffuse atrophy (3), MCM (3), Chiari I malformation (1) |
| ? AT variant | Cerebellar atrophy (1) |
| **Genetic:** |  |
| *1) Normal MRI* |  |
| Angelman synd | Normal (8: 5 on CT, 3 on MRI), delayed myelination (3), progressive cerebellar hemisphere atrophy due to phenytoin (1), increased extra-axial CSF/ ventricular spaces (3), subarachnoid cyst (1) |
| Episodic ataxia: | Normal (6) |
| Rett synd | Normal (4) |
| Sotos synd | Incidental pineal cyst otherwise normal (1) |
| *2) Developed an abnormality later* |  |
| FA | Spinal cord atrophy (3, with cerebellar tonsils atrophy in 1 and medulla atrophy in 1), normal (2), asymmetric lateral ventricles (1), increased extra-axial CSF space (1), right middle cerebral artery territory infarct with thrombus and thin optic nerves/ chiasm (1) |
| Smith-Mag synd | Pancerebellar atrophy with progressive vermis atrophy and then cerebellar and cerebral atrophy, left parasagittal frontal lesion that is hypointense on FLAIR with enhancing meninges (stable over several years), MCM (1) |
| *3) Malformations* |  |
| NMD | Pachygyria of the parietal-occipital lobes (1); pachygyria of the frontal lobes, polymicrogyria of the occipital lobes, thin posterior body and splenium of the corpus callosum, enlarged sylvian fissure, supratentorial subarachnoid cyst (1); diffuse polymicrogyria (1); diffuse pachygyria, flat pons, pancerebellar hypoplasia, microcephaly (1); occipital and temporal periventricular heterotopic grey matter, gliosis in left putamen, bilateral cysts in thalami (1) |
| JSRD | Thickened superior cerebellar peduncles (5), bat-shaped wing of the 4th ventricle (4), hypoplastic and/or dysplastic vermis (5), dysplastic cerebellar hemispheres (1), midbrain anterior-posterior diameter is small (5), lipoma in right superior cerebellar peduncles (1) |
| Mar-Sjög synd | Stable pancerebellar atrophy, MCM, medulla small anterior-posterior diameter, delayed myelination (1); small pons and inferior vermis, cerebellar hemispheres atrophy (1) |
| DWM | Large posterior fossa cyst communicating with 4th ventricle, enlarged lateral, 3rd and 4th ventricles, vermis hypoplasia, torcula elevation, right CSF shunt, right frontal lobe porencephalic cyst (1); large posterior fossa cyst communicating with 4th ventricle, enlarged lateral and 3rd ventricles, porencephalic cyst, torcula elevation, dysplastic vermis and tectum, atrophic right cerebellar hemisphere, thin corpus callosum with hypoplastic splenium, elongated brainstem in anterior-posterior diameter (1) |
| DES-Hutterites | Reduced gyral pattern especially in the frontal and temporal lobes, hypoplastic posterior vermis and cerebellar hemispheres, enlarged 4th ventricle, MCM, delayed myelination (1); reduced cerebral gyral pattern, hyperintense T2-weighted signal abnormality in the periventricular white matter, agenesis of the inferior vermis and cerebellar hemispheres bilaterally (1) |
| Rit-Schin synd | All vermis atrophy, diffuse cerebral atrophy, MCM (1); pancerebellar hypoplasia with left > right cerebellar hemisphere hypoplasia, hypoplastic pons and medulla, large posterior fossa cyst communicating with 4th ventricle (stable) (1) |
| L1CAM mutation | Partial agenesis of the corpus callosum, MCM, diffuse white matter atrophy especially centrum semiovale (1) |
| ? PCH 3 | Severe vermis hypoplasia but the floccular nodular lobes are present, hypoplastic pons and cerebellar hemispheres, small midbrain in anterior-posterior diameter, large posterior fossa cyst communicating with 4th ventricle, small optic nerves and chiasm (stable) (1) |
| Chiari 1 malformation | Tonsillar herniation with cervico-medullary kink, decompressed then stabilized (1) |
| **Epilepsy:** |  |
| Intractable epilepsy | Cerebellar, brainstem, spinal cord, and cerebral shrinkage following ACTH treatment (improved on repeat imaging), thin optic nerves and chiasm, hyperintense T2-weighted signal abnormalities in the periventricular white matter (improved), basal ganglia (resolved) and thalami (persisted), increased extra-axial CSF/ ventricular spaces (improved) (1); restricted diffusion and hyperintense T2-weighted signal abnormalities over left basal ganglia, hippocampus, temporal lobe cortex, and thalamus, increased diffusion followed by restricted diffusion in the genu of left internal capsule, then atrophy of left cerebral hemisphere white matter and increased lateral ventricular size followed by right cerebral hemisphere atrophy (1); small optic nerves, medulla, and spinal cord (stable), MCM (1); hyperintense T2-weighted signal abnormality over the frontal lobes subcortical to periventricular white matter (stable) (1); vermis atrophy (stable) (1) |
| **Strokes:** |  |
| 1) Ischemic: |  |
| Postnatal arterial ischemic stroke (5) | Left > right thalami, left medial and inferior cerebellar hemisphere, and tonsil infarcts following the distribution of the basilar artery and left posterior inferior cerebellar artery territories (1); cerebellar hemispheres, right occipital and anterior pons infarct, MRA: absent right vertebral artery, tortuous left vertebral artery, MCM (1); right > left cerebellar/ inferior vermis, right parietal/ thalamus/ parietal-occipital, pons, left cerebellar peduncle infarcts from vertebral-basilar artery stenosis or occlusion, subarachnoid cysts in the posterior fossa (1); right cerebellar hemisphere infarct (1); left > right pons infarct from basilar artery thrombosis (1). [Summary of regions involved: cerebellar (4), pons (3), parietal-occipital lobes (2), thalamus (2), midbrain (1)] |
| Vasculitis (2) | Hyperintense T2-weighted signal abnormalities in the thalamus and bilateral white and grey matter with left side enhancement (improved and then normalized), abnormal angiogram consistent with vasculitis (1); abnormal signal intensity in different parts of the brainstem > thalami suggestive of infarct followed by recovery or gliosis, frontal lobe hemorrhage (1) |
| Prenatal stroke (1) | Left parietal-occipital lobes cleft with gliosis from prenatal stroke (1) |
| Aneurysm (1) | Aneurysm at top of basilar artery with embolic ischemic infarcts involving left pons, superior vermis, left > right cerebellar hemispheres causing edema and mild Chiari I malformation. Subsequent infarcts following the distribution of the left posterior cerebral artery territory occurred over the left hippocampus gyri and left occipital lobe, (atrophied on follow up scan) (1) |
| †FA and stroke (1) | Right middle cerebral artery thrombus with infarct involving the right insular cortex, precentral gyrus, posterior putamen, hippocampal uncus, and temporal lobe (1) |
| †Non-progressive spastic ataxia NYD and stroke (1) | Right cerebral peduncle and pons atrophy, white matter loss in the periventricular region of the right occipital lobe from pneumococcal sepsis and multiple emboli (1) |
| *2) Hemorrhagic:* |  |
| Cavernoma (2) | Left tectal plate cavernoma with calcification. It worsened with hemorrhage twice then stabilized (1); midbrain edema and hemorrhage from venous cavernoma (1) |
| Gauchers type 3 and cavernoma (1) | Left caudate head cavernoma with hemorrhage, hyperintense T2-weighted signal abnormality in the left periventricular white matter next to trigone region, MCM (1) |
| AVM (1) | Large AVM in the right middle cerebellar peduncle extending into the right cerebellar hemisphere white matter, 4th ventricle, medulla, and inferior pons causing right cerebellar hemisphere and medulla infarct. It worsened with further cerebellar hemisphere infarct followed by atrophy. Subsequent hemorrhage occurred with pancerebellar and cerebrum edema (1) |
| **Inflammatory:** |  |
| Multiple sclerosis | Hyperintense T2-weighted signal abnormalities in the cerebral and cerebellar white matter including middle cerebellar peduncles and two lesions in the cervical spine (improved or atrophy later), new lesions with hyperintense T2-weighted signal abnormalities in the cerebrum and corpus callosum, left optic nerve and chiasm (1); multifocal lesions with hyperintense T2-weighted signal abnormalities in the cerebellum, brainstem, corpus callosum, cervical and lumbar spinal cord, left optic nerve, new lesions with or without enhancement in the cerebrum, middle cerebellar peduncles, midbrain (improved in the brainstem and cerebellar regions) (1) |
| ADEM | Hyperintense T2-weighted signal abnormalities in the basal ganglia, left splenium of the corpus callosum, dorsal brainstem, right superior cerebellar peduncle, thalami, left occipital white matter. There was improvement followed by worsening with hyperintense T2-weighted signal abnormalities in the middle cerebellar peduncles, bilateral cerebellar white matter and bilateral basal ganglia, left pons and posterior limb of internal capsule left > right (improved then normalized) (1) |
| Post-infectious | Cerebellar hemispheres atrophy then vermis atrophy (1) |
| **Acquired:** |  |
| HIE | Periventricular white matter loss (especially parietal-occipital regions) with enlarged lateral ventricles (2), atrophy of corpus callosum, optic nerves, and chiasm (1); hyperintense T2-weighted signal abnormality in the posterior aspect of basal ganglia and subgaleal hematoma (1); normal on two CTs (1); relatively hypoplastic right inferior cerebellar hemisphere with subarachnoid cyst in posterior fossa, and MCM (1) |
| Prematurity | Hyperintense T2-weighted signal abnormalities over the periventricular occipital lobe white matter and posterior limb of the internal capsule (stable), mild atrophy of the thalami |
| Trauma | Cysts with hemosiderin in the left putamen, right genu of internal capsule, bilateral hypothalamic, subdural hemorrhage over right occipital lobe, brainstem, cerebral hemispheres left temporal and frontal, and right parietal lobes (1); punctate hemorrhages in the cerebral hemispheres, diffuse edema, blood in occipital horn of right lateral ventricle, obstructive hydrocephalus, depressed left posterior fossa skull fracture, left cerebellar contusion with mass effect followed by left cerebellar hemisphere gliosis (1) |
| Post-radiation | Hyperintense T2-weighted signal abnormalities in the periventricular and cerebellar white matter and basal ganglia, hypointense T2-weighted signal abnormalities in the thalami, cerebral and pancerebellar atrophy (1) |
| **Ataxia NYD:** |  |
| 1) Non-progressive ataxia with: |  |
| DD and ≥2 UMN | Small left cerebellar hemisphere and adjacent cysts (1); progressive pancerebellar atrophy (1); hyperintense T2-weighted signal abnormality in the cerebellar white matter bilaterally, then a stroke occurred (see † above), superior vermis/ cerebellar hemispheres folia prominence with right cerebral peduncle and pons atrophy, white matter loss in periventricular region of right occipital lobe (1); possible macrocerebellum (1); gliosis and atrophy of subcortical grey and white matter with atrophy of the cerebellar hemispheres (1); normal (5) with 3 remaining normal; pancerebellar/ midbrain/medulla atrophy (1); pancerebellar and brainstem hypoplasia with superior vermis dysplasia (stable) (1); MCM (4, 3 in the patients already described and in 1 patient as the only finding) |
| DD and 1 UMN | Normal (2); MCM (1); absent septum pallucidum and progressive diffuse cerebellar atrophy (1); vermis > cerebellar hemisphere hypoplasia (1); mild ventriculomegaly, periventricular edema with tonsils in foramen magna, possible features of raised intracranial pressure (1); absent posterior part of the corpus callosum (1); dysplastic posterior vermis, right cerebellar ectopia (1); pancerebellar hypoplasia, prominent inferior colliculi (stable) (1) |
| DD, ≥1 UMN, and epilepsy | MCM and small midbrain in anterior-posterior diameter (1); normal (2); loss of white matter bulk, asymmetrical cerebellar hemispheres with unusual shape of the cerebellum, microcephaly (1); vermis > cerebellar hemisphere atrophy affecting grey > white matter, thin tectum (1); cyst in periventricular white matter near the occipital horn of the left lateral ventricle (1) |
| DD and epilepsy | Pancerebellar atrophy (1); normal (1); ventricular enlargement and increased extra-axial space (1); small brainstem, small right brachium pontis, corpus callosum splenium cyst, right > left hypoplastic cerebellar hemispheres and hypoplastic medulla on CT, on MRI posterior vermis and cerebellar hemispheres and pons atrophy possibly secondary to hemorrhage (1); diffuse white matter loss, hyperintense T1-weighted signal abnormality in the centrum semiovale (likely gliosis), cerebellar hemisphere atrophy, thin corpus callosum, increased extra-axial CSF space in all ventricles (1) |
| DD | Normal (3); hypoplastic vermis (1); non-specific hyperintense T2-weighted signal abnormality in the subcortical white matter of the frontal lobes (stable) (1) |
| Pure ataxia | Pancerebellar atrophy (1); normal (1) |
| 2) Intermittent ataxia | MCM (1); small posterior fossa with crowding and low torcula (1); progressive hyperintense T2-weighted signal abnormality in the dentate nucleus (1); macrocerebellum (stable) (1); normal (1); hyperintense T2-weighted signal abnormality in the periventricular white matter of the frontal lobes, which progressed with dentate nucleus involvement and syrinx T10-T12 (1) |
| 3) Ataxia/ dev reg | Pancerebellar, cerebral, brainstem diffuse atrophy, patchy hyperintense T2-weighted signal abnormalities in the cerebrum and cerebellum white matter (1); normal (1); delayed myelination in temporal lobes (1) |
| 4) Progressive ataxia: |  |
| Familial prog ataxia | MCM (1); atrophy of the superior vermis (stable) (1) |
| Prog ataxia | Normal (1); venous angioma in the right middle cerebellar peduncles (stable) (1) |
| 5) Self-limiting ataxia | Normal (1); increased extra-axial CSF space in the parietal-occipital regions (1) |

Pancerebellar: cerebellar vermis and hemispheres, MCM: mega cisterna magna, FLAIR: fluid-attenuated inversion recovery, NCL: neuronal ceroid lipofuscinosis, CPS: carbomyl phosphate synthetase, enceph: encephalopathy, AT: ataxia telangiectasia, synd: syndrome, FA: Friedreich ataxia, Smith-Mag synd: Smith-Magenis syndrome, Mar-Sjög: Marinesco-Sjögren syndrome, L1CAM: L1 cell adhesion molecule, PCH 3: pontocerebellar hypoplasia type 3, NMD: neuronal migration disorder, JSRD: Joubert syndrome related disorder, DWM: Dandy-Walker malformation, DES-Hutterites: dysequilibrium syndrome (also known as autosomal recessive cerebellar hypoplasia in the Hutterite population), Rit-Schin synd: Ritscher–Schinzel syndrome, † two other strokes occurred. The first was in a patient with Friedreich’s ataxia and the second was in a patient with developmental delay and non-progressive spastic ataxia NYD, who had a stroke secondary to embolic pneumococcal meningitis, AVM: arterio-venous malformation, ADEM: acute disseminated encephalomyelitis, HIE: hypoxic-ischemic encephalopathy, NYD: not yet diagnosed, DD: developmental delay, UMN: upper motor neuron sign, dev reg: developmental regression, Prog: progressive.

**Supplementary Table 3**

**Number of patients with relevant and other neuroimaging findings and the diagnostic utility of neuroimaging in pediatric chronic ataxia based on etiological categories**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Disorder** | **No. of patients** | **No. of patients with images** | **No. of patients with relevant findings** | **Diagnostic utility of imaging** | **No. of patients with other abnormalities** | **No. of patients with normal neuroimaging** |
| **Metabolic:** |  |  |  |  |  |  |
| Mitochondrial | 9 | 9 | 7 | B | 1 | 1 |
| NCL types 1-3 | 6 | 6 | 5 | B | 1 | 0 |
| Salla disease | 4 | 4 | 4 | B | 0 | 0 |
| Other leukodystrophies | 2 | 2 | 2 | B | 0 | 0 |
| CPS deficiency | 1 | 1 | 0 | D | 1 | 0 |
| Homocystinuria | 1 | 1 | 0 | D | 0 | 1 |
| Glut 1 deficiency | 1 | 1 | 0 | D | 0 | 1 |
| Wernicke enceph | 1 | 1 | 0 | D/(B)\* | 1 | 0 |
| ‡ Gaucher type 3 | 1 | 1 | 0 | D | 1 | 0 |
| **DNA repair defects:** |  |  |  |  |  |  |
| AT | 13 | 11 | 6 | C | 0 | 5 |
| ? AT variant | 1 | 1 | 1 | C | 0 | 0 |
| **Genetic:** |  |  |  |  |  |  |
| *1) Normal MRI:* |  |  |  |  |  |  |
| Angelman synd | 16 | 15 | 0 | D | 7 | 8 |
| Episodic ataxia | 7 | 6 | 0 | D | 0 | 6 |
| Rett synd | 4 | 4 | 0 | D | 0 | 4 |
| Sotos synd | 1 | 1 | 0 | D | 1 | 0 |
| *2) Developed an abnormality later:* |  |  |  |  |  |  |
| FA | 7 | 6 | 3 | B | 1 | 2 |
| Smith-Mag synd | 1 | 1 | 1 | C | 0 | 0 |
| *3) Malformation:* |  |  |  |  |  |  |
| NMD | 5 | 5 | 5 | A | 0 | 0 |
| JSRD | 5 | 5 | 5 | A | 0 | 0 |
| Mar-Sjög synd | 2 | 2 | 2 | C | 0 | 0 |
| DWM | 2 | 2 | 2 | A | 0 | 0 |
| DES-Hutterites | 2 | 2 | 2 | B | 0 | 0 |
| Rit-Schin synd | 2 | 2 | 2 | C | 0 | 0 |
| L1CAM mutation | 1 | 1 | 1 | C | 0 | 0 |
| ? PCH 3 | 1 | 1 | 1 | B | 0 | 0 |
| Chiari 1 malformation | 1 | 1 | 1 | A | 0 | 0 |
| **Intractable epilepsy** | 5 | 5 | 0 | D | 5 | 0 |
| **Strokes:** |  |  |  |  |  |  |
| 1) Ischemic: |  |  |  |  |  |  |
| Postnatal stroke | 5 | 5 | 5 | A | 0 | 0 |
| Vasculitis | 2 | 2 | 2 | B | 0 | 0 |
| Prenatal | 1 | 1 | 1 | A | 0 | 0 |
| Aneurysm | 1 | 1 | 1 | A | 0 | 0 |
| 2) Hemorrhagic: |  |  |  |  |  |  |
| Cavernoma | 2 | 2 | 2 | A | 0 | 0 |
| AVM with ischemia | 1 | 1 | 1 | A | 0 | 0 |
| **Inflammatory:** |  |  |  |  |  |  |
| Multiple sclerosis | 2 | 2 | 2 | B | 0 | 0 |
| ADEM | 1 | 1 | 1 | B | 0 | 0 |
| Post-infectious | 1 | 1 | 1 | C | 0 | 0 |
| **Acquired:** |  |  |  |  |  |  |
| HIE | 5 | 5 | 3 | B | 1 | 1 |
| Prematurity | 2 | 1 | 1 | B | 0 | 0 |
| Trauma | 2 | 2 | 2 | B | 0 | 0 |
| Post-radiation | 1 | 1 | 1 | B | 0 | 0 |
| **Ataxia NYD:** |  |  |  |  |  |  |
| 1) Non-progressive ataxia with: |  |  |  |  |  |  |
| DD and ≥2 UMN | 13 | 13 | 0 | D | 7 | 6 |
| DD and 1 UMN | 9 | 9 | 0 | D | 6 | 3 |
| DD, ≥1 UMN, and epilepsy | 7 | 6 | 0 | D | 4 | 2 |
| DD and epilepsy | 5 | 5 | 0 | D | 4 | 1 |
| DD | 5 | 5 | 0 | D | 2 | 3 |
| Pure ataxia | 2 | 2 | 0 | D | 1 | 1 |
| 2) Intermittent ataxia | 6 | 6 | 0 | D | 4 | 2 |
| 3) Ataxia/ dev reg | 3 | 3 | 0 | D | 2 | 1 |
| 4) Progressive: |  |  |  |  |  |  |
| Familial prog ataxia | 2 | 2 | 0 | D | 1 | 1 |
| Prog ataxia | 2 | 2 | 0 | D | 0 | 2 |
| 5) Self-limiting ataxia | 2 | 2 | 0 | D | 1 | 1 |
| **Total** | 184 | 177 | 73 |  | 52 | 52 |

No.: number, A: imaging is diagnostic, B: imaging is very helpful but not diagnostic, C: imaging is of limited diagnostic usefulness, D: imaging is not helpful, NCL: neuronal ceroid lipofuscinosis, CPS: carbomyl phosphate synthetase, enceph: encephalopathy, \* the patient had an unconfirmed finding of pachygyria on an old MRI report, ‡ this patient also had a very small cavernoma, AT: ataxia telangiectasia, synd: syndrome, FA: Friedreich ataxia, Smith-Mag synd: Smith-Magenis syndrome, NMD: neuronal migration disorder, JSRD: Joubert syndrome related disorder, Mar-Sjög: Marinesco-Sjögren syndrome, DWM: Dandy-Walker malformation, DES-Hutterites: dysequilibrium syndrome (also known as autosomal recessive cerebellar hypoplasia in the Hutterite population), Rit-Schin synd: Ritscher–Schinzel syndrome, L1CAM: L1 cell adhesion molecule, PCH 3: pontocerebellar hypoplasia type 3, AVM: arterio-venous malformation, ADEM: acute disseminated encephalomyelitis, HIE: hypoxic-ischemic encephalopathy, NYD: not yet diagnosed, DD: developmental delay, UMN: upper motor neuron sign, dev reg: developmental regression, Prog: progressive.

**Supplementary Table 4**

**Number of patients with repeat neuroimaging and frequency of changes on repeat neuroimaging in pediatric chronic ataxia based on disease etiology**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Disease (in order of frequency of known etiologies)** | **No. of patients** | **No. of patients with imaging** | **No. of patients with repeat imaging** | **Frequency of changes on repeat imaging** | | | | |
|  |  |  |  | No change | Better | Worse | Fluctuating | U |
| Angelman synd | 16 | 15 | 6 | 1 | 1 | 1 | 0 | 3 |
| AT | 13 | 11 | 6 | 2 | 0 | 1 | 1 | 2 |
| ? AT variant | 1 | 1 | 0 |  |  |  |  |  |
| **†Strokes:** | 12 |  |  |  |  |  |  |  |
| 1) Ischemic: |  |  |  |  |  |  |  |  |
| Pre- and post natal arterial thrombo-embolic ischemic stroke | 6 | 6 | 6 | 3 | 2\* | 0 | 0 | 1 |
| Vasculitis | 2 | 2 | 2 | 0 | 1 | 0 | 1 | 0 |
| Aneurysm | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 |
| **All ischemic strokes** | **9** | **9** | **9** | **3** | **3** | **1** | **1** | **1** |
| 2) Hemorrhagic: |  |  |  |  |  |  |  |  |
| Cavernoma | 2 | 2 | 2 | 0 | 1 | 0 | 1 | 0 |
| AVM | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 |
| Mitochondrial | 9 | 9 | 8 | 3 | 2 | 2 | 0 | 1 |
| Friedreich ataxia | 7 | 6 | 1 | 0 | 0 | 1 | 0 | 0 |
| Episodic ataxia | 7 | 6 | 2 | 0 | 0 | 0 | 0 | 2 |
| NCL types 1 & 2 | 5 | 5 | 5 | 0 | 0 | 5 | 0 | 0 |
| NCL type 3 | 1 | 1 | 0 |  |  |  |  |  |
| Intractable epilepsy | 5 | 5 | 5 | 4 | 0 | 0 | 1 | 0 |
| HIE | 5 | 5 | 5 | 2 | 0 | 0 | 0 | 3 |
| NMD | 5 | 5 | 2 | 0 | 0 | 0 | 0 | 2 |
| JSRD | 5 | 5 | 2 | 1 | 0 | 0 | 0 | 1 |
| Rett synd | 4 | 4 | 2 | 1 | 0 | 0 | 0 | 1 |
| Salla disease | 4 | 4 | 3 | 2 | 0 | 1 | 0 | 0 |
| Other leukodystrophies | 2 | 2 | 2 | 1 | 0 | 1 | 0 | 0 |
| Trauma | 2 | 2 | 0 |  |  |  |  |  |
| DWM | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| DES-Hutterites | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| Mar-Sjög synd | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| Multiple sclerosis | 2 | 2 | 2 | 0 | 0 | 0 | 2 | 0 |
| Prematurity | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Rit-Schin synd | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| CPS deficiency | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| Homocystinuria | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| ADEM | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 |
| Gaucher type 3 | 1 | 1 | 1 | 0 | 1\*\* | 0 | 0 | 0 |
| Glut 1 deficiency | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Chiari I malformation | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| L1CAM mutation | 1 | 1 | 0 |  |  |  |  |  |
| ? PCH 3 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Post-radiation | 1 | 1 | 0 |  |  |  |  |  |
| Post-infectious | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Smith-Magenis synd | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 |
| Sotos synd | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Wernicke enceph | 1 | 1 | 0 |  |  |  |  |  |
| **Ataxia NYD:** |  |  |  |  |  |  |  |  |
| 1) Non-progressive ataxia with: |  |  |  |  |  |  |  |  |
| DD and ≥2 UMN | 13 | 13 | 8 | 2 | 0 | 2 | 0 | 4 |
| DD and 1 UMN | 9 | 9 | 4 | 2 | 0 | 1 | 0 | 1 |
| DD, ≥1 UMN, and epilepsy | 7 | 6 | 4 | 1 | 0 | 0 | 0 | 3 |
| DD and epilepsy | 5 | 5 | 3 | 1 | 0 | 2 | 0 | 0 |
| DD | 5 | 5 | 1 | 0 | 0 | 0 | 0 | 1 |
| Pure ataxia | 2 | 2 | 0 |  |  |  |  |  |
| 2) Ataxia/ dev reg | 3 | 3 | 2 | 1 | 0 | 0 | 0 | 1 |
| 3) Intermittent ataxia | 6 | 6 | 5 | 1 | 0 | 3 | 1 | 0 |
| 4) Progressive: |  |  |  |  |  |  |  |  |
| Familial prog ataxia | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| Prog ataxia | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 0 |
| 5) Self-limiting ataxia | 2 | 2 | 0 |  |  |  |  |  |
| **Total** | **184** | **177** | **108** | **41** | **9** | **23** | **8** | **27** |

No.: number, U: unknown, AT: Ataxia telangiectasia, synd: syndrome, † two other strokes occurred. The first was in a patient with Friedreich’s ataxia and the second was in a patient with developmental delay and non-progressive spastic ataxia, who had a stroke secondary to embolic pneumococcal meningitis, \*: one scan improved following epilepsy surgery, AVM: arterio-venous malformation, NCL: neuronal ceroid lipofuscinosis, HIE: hypoxic-ischemic encephalopathy, NMD: neuronal migration disorder, JSRD: Joubert syndrome related disorder, DWM: Dandy-Walker malformation, DES-Hutterites: dysequilibrium syndrome (also known as autosomal recessive cerebellar hypoplasia in the Hutterite population), Mar-Sjög: Marinesco-Sjögren syndrome, Rit-Schin synd: Ritscher–Schinzel syndrome, CPS: carbomyl phosphate synthetase, ADEM: acute disseminated encephalomyelitis, \*\*: incidental small asymptomatic cavernoma was present, L1CAM: L1 cell adhesion molecule, PCH 3: pontocerebellar hypoplasia type 3, enceph: encephalopathy, NYD: not yet diagnosed, DD: developmental delay, UMN: upper motor neuron sign, dev reg: developmental regression, Prog: progressive.

**Supplementary Table 5**

**Proportion of patients with repeat neuroimaging, imaging modalities, and timing of repeat neuroimaging in 108 pediatric patients with chronic ataxia based on disease etiology**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Disease (in order of frequency of known etiologies)** | **Proportion of patients with repeat imaging** | **No. of patients with repeat imaging per imaging modality** | | | **Timing between the first two scans (years)** | | |
|  |  | **CT only** | **MRI only** | **CT & MRI** | **Median** | **Range** | **Timing if No. of patients = 1 or 2** |
| **†Strokes:** |  |  |  |  |  |  |  |
| 1) All ischemic strokes | 9/9 | 1 | 6 | 2 | 0.40 | 0.003-4.18 |  |
| 2) Hemorrhagic: |  |  |  |  |  |  |  |
| Cavernoma | 2/2 | 0 | 1 | 1 |  |  | 0.003, 0.20 |
| AVM | 1/1 | 0 | 0 | 1 |  |  | 0.04 |
| Mitochondrial | 8/9 |  | 6 | 2 | 1.05 | 0.04-3.23 |  |
| Angelman synd | 6/15 | 3 | 2 | 1 | 1.36 | 0.71-6.80 |  |
| Ataxia telangiectasia | 6/11 | 0 | 4 | 2 | 2.32 | 0.39-21.36 |  |
| NCL types 1 & 2 | 5/5 | 1 | 3 | 1 | 0.85 | 0.04-2.88 |  |
| Intractable epilepsy | 5/5 | 0 | 4 | 1 | 1.69 | 0.29-2.97 |  |
| HIE | 5/5 | 1 | 3 | 1 | 4.64 | 0.01-8.98 |  |
| Salla disease | 3/4 | 0 | 3eskodystrophy | 0 | 1.84 | 0.08-3.12 |  |
| Episodic ataxia | 2/6 | 0 | 1 | 1 |  |  | 0.64, 5.01 |
| NMD | 2/5 | 0 | 2 | 0 |  |  | 0.03, 1.25 |
| JSRD | 2/5 | 0 | 2 | 0 |  |  | 1.78, 2.21 |
| Rett synd | 2/4 | 0 | 2 | 0 |  |  | 1.69, 1.75 |
| Other leukodystrophies | 2/2 | 0 | 2 | 0 |  |  | 2.00, 2.87 |
| Multiple sclerosis | 2/2 | 0 | 2 | 0 |  |  | 0.06, 0.44 |
| Friedreich ataxia | 1/6 | 0 | 1 | 0 |  |  | 7.05 |
| DWM | 1/2 | 0 | 0 | 1 |  |  | 3.56 |
| DES-Hutterites | 1/2 | 0 | 1 | 0 |  |  | 0.12 |
| Marinesco-Sjögren synd | 1/2 | 0 | 1 | 0 |  |  | 1.42 |
| Prematurity | 1/1 | 0 | 1 | 0 |  |  | 2.30 |
| Ritscher–Schinzel synd | 1/2 | 1 | 0 | 0 |  |  | 0.27 |
| CPS deficiency | 1/1 | 0 | 1 | 0 |  |  | 3.90 |
| Homocystinuria | 1/1 | 0 | 1 | 0 |  |  | 0.14 |
| ADEM | 1/1 | 0 | 1 | 0 |  |  | 0.01 |
| Gaucher type 3 | 1/1 | 0 | 0 | 1 |  |  | 0.08 |
| Glut 1 deficiency | 1/1 | 0 | 1 | 0 |  |  | 1.90 |
| Chiari I malformation | 1/1 | 0 | 1 | 0 |  |  | Same day |
| ? PCH 3 | 1/1 | 0 | 1 | 0 |  |  | 1.90 |
| Post-infectious | 1/1 | 0 | 0 | 1 |  |  | 0.08 |
| Smith-Magenis synd | 1/1 | 0 | 1 | 0 |  |  | 0.31 |
| Sotos synd | 1/1 | 0 | 1 | 0 |  |  | 4.10 |
| **Ataxia NYD:** |  |  |  |  |  |  |  |
| 1) Non-progressive ataxia with: |  |  |  |  |  |  |  |
| DD and ≥2 UMN | 8/13 | 1 | 7 | 0 | 2.25 | 0.88-7.60 |  |
| DD and 1 UMN | 4/9 | 0 | 4 | 0 | 3.02 | 0.81-6.66 |  |
| DD, ≥1 UMN, and epilepsy | 4/6 | 0 | 4 | 0 | 2.46 | 2.00-8.21 |  |
| DD and epilepsy | 3/5 | 0 | 3 | 0 | 1.73 | 0.27-3.61 |  |
| DD | 1/5 | 0 | 1 | 0 |  |  | 3.05 |
| 2) Intermittent ataxia | 5/6 | 0 | 5 | 0 | 0.64 | 0.11-0.89 |  |
| 3) Ataxia/ dev reg | 2/3 | 0 | 1 | 1 |  |  | 0.25, 0.83 |
| 4) Progressive: |  |  |  |  |  |  |  |
| Prog ataxia | 2/2 | 0 | 2 | 0 |  |  | 2.42, 2.66 |
| Familial prog ataxia | 1/2 | 0 | 1 | 0 |  |  | 0.50 |
| **Total per neuroimaging modality** |  | **8** | **83** | **17** |  |  |  |

No.: number, synd: syndrome, † two other strokes occurred. The first was in a patient with Friedreich’s ataxia and the second was in a patient with developmental delay and non-progressive spastic ataxia, who had a stroke secondary to embolic pneumococcal meningitis, AVM: arterio-venous malformation, NCL: neuronal ceroid lipofuscinosis, HIE: hypoxic-ischemic encephalopathy, NMD: neuronal migration disorder, JSRD: Joubert syndrome related disorder, DWM: Dandy-Walker malformation, DES-Hutterites: dysequilibrium syndrome (also known as autosomal recessive cerebellar hypoplasia in the Hutterite population), CPS: carbomyl phosphate synthetase, ADEM: acute disseminated encephalomyelitis, PCH 3: pontocerebellar hypoplasia type 3, enceph: encephalopathy, NYD: not yet diagnosed, DD: developmental delay, UMN: upper motor neuron sign, dev reg: developmental regression, Prog: progressive.

### Supplementary figures legends

### Supplementary figure 1

### Brain MRI of a 6-year old girl with neuronal ceroid lipofuscinosis. A) Axial FLAIR image (TR 8002, TE 129.4, slice thickness 6 mm) shows hyperintense signal abnormality in the periventricular white matter (arrow). B) Midsagittal T1WI (TR 450, TE 20, slice thickness 6 mm) shows enlarged vermis fissures (interfolial spaces) consistent with significant vermis atrophy. The fourth ventricle is enlarged and the corpus callosum is thin. C) Supratentorial axial T2WI (TR 2517, TE 113.3, slice thickness 6 mm) shows hypointense signal abnormality in the thalami (arrow). In addition, there is ventriculomegaly and prominent extra axial CSF spaces consistent with diffuse cerebral atrophy.

### Supplementary figure 2

### Brain MRI of a 10-year old boy with neuronal migration disorder. Coronal T1W images (TR 6.9, TE 1.536, slice thickness 3 mm) show: Abnormal thickening of the cerebral cortex within the temporal lobes (arrows) in (A) and multiple small gyri in the occipital lobes in (B). The findings are consistent with temporal lobes pachygyria (arrows) and occipital lobes polymicrogyria.

### Supplementary figure 3

### Brain MRI of a six-year old girl with Salla disease. Supratentorial axial T2WI (TR 3417, TE 113.6, slice thickness 6 mm) shows diffuse hyperintense signal abnormality in the white matter involving both cerebral hemispheres, especially the central white matter (arrow) consistent with hypomyelination. Normal myelination of the white matter in the posterior limbs of the internal capsule is evident. Several repeat MRI showed no improvement in myelination.

### Supplementary figure 4

### Brain MRI of a one-year old girl with Joubert syndrome related disorder. A) Midsagittal T1WI (TR 450, TE 20, slice thickness 6 mm) shows deep interpeduncular fossa and cerebellar vermis hypoplasia. The arrow shows the abnormally high position of the lower vermis border, which is normally at the same level as the obex. B) Axial T2WI (TR 2517, TE 113.3, slice thickness 6 mm) shows an abnormally thickened superior cerebellar peduncles (arrow) giving the appearance of the molar tooth sign. C) Coronal T2WI (TR 2717, TE 123, slice thickness 5 mm) shows more clearly the abnormally thickened superior cerebellar peduncles.