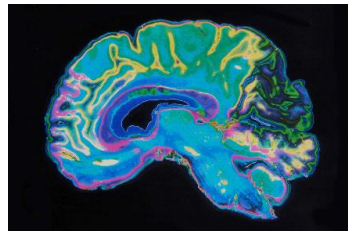
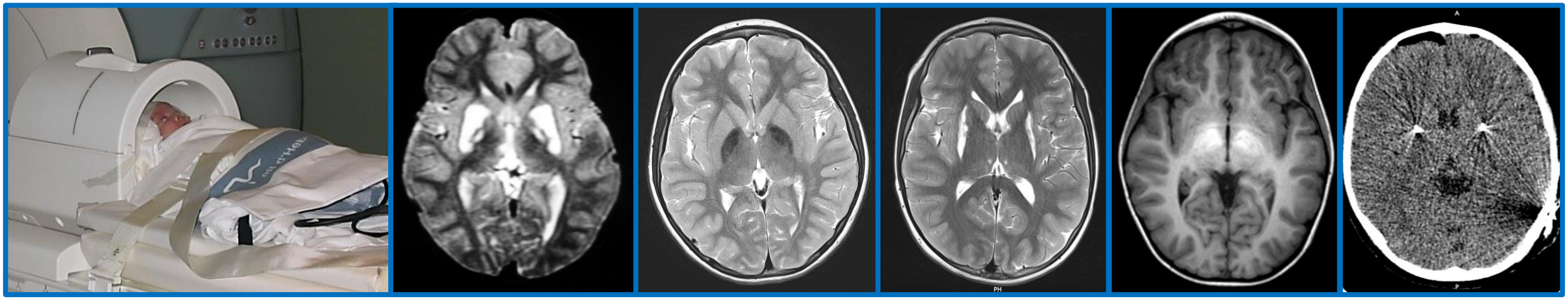
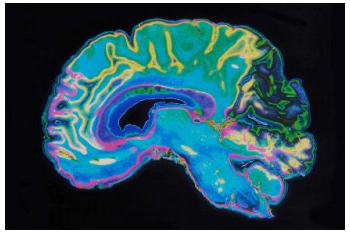


HYPERKINETIC DISORDERS

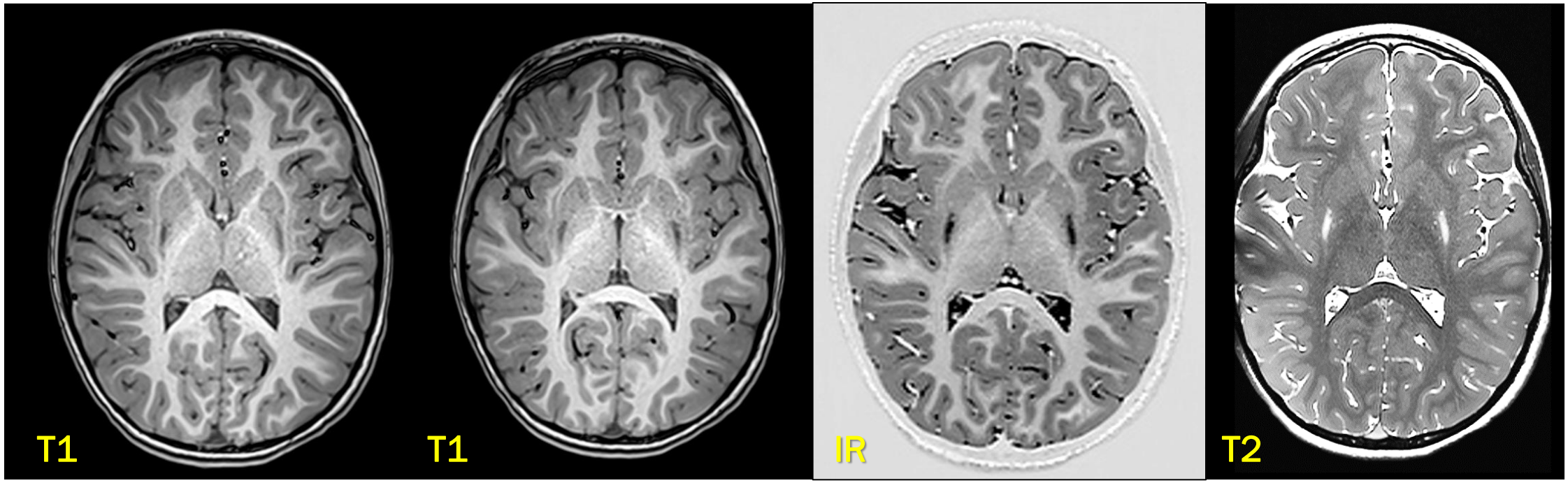
Élida Vázquez, MD, PhD
Ignacio Delgado, MD
Hospital Vall d'Hebron. Barcelona



ERN-RND Winter School Neuroimaging 2023



Case 1 >>> NICO



Nico, male, 7 years old. Spastic-dystonic tetraparesis, with a right predominance

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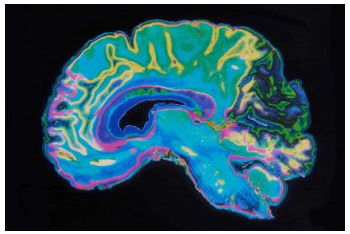

- **What are the main MR imaging findings in Nico's case? (one option)**

a. Bilateral thalamic lesion
b. Bilateral putaminal lesion
c. Bilateral globus pallidus lesion
d. Normal study
e. I don't know

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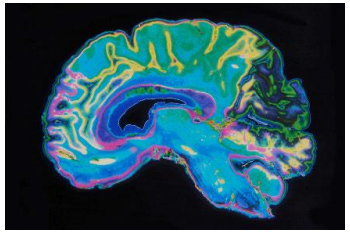

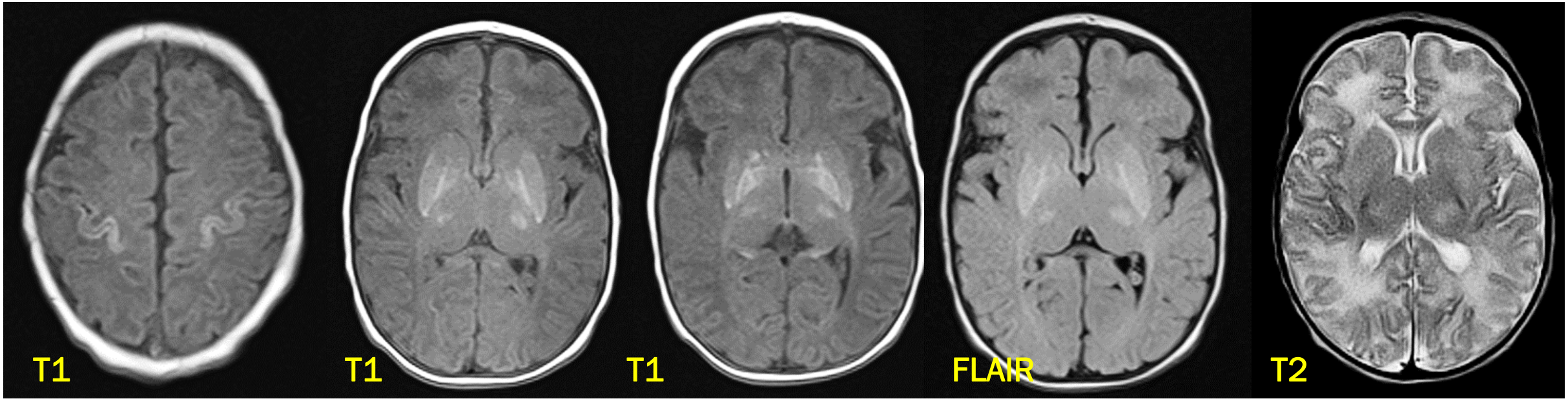

Nico, MRI performed at 10 days of age

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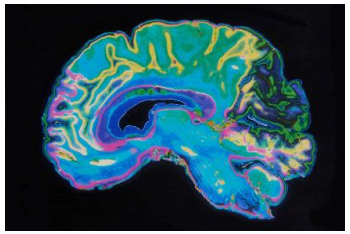
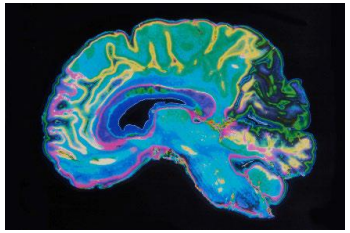
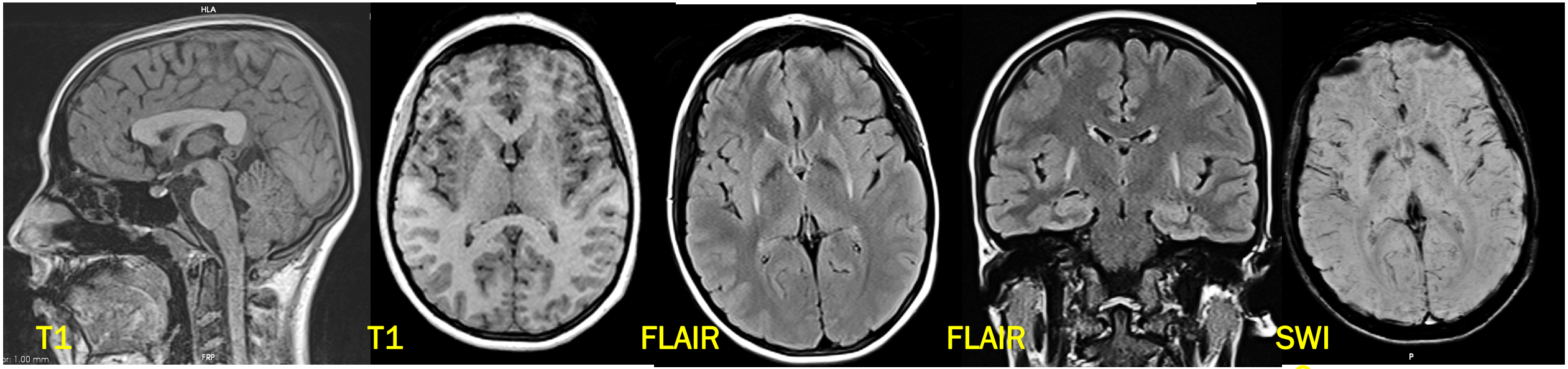


- **What is the most likely diagnosis in Nico's case?**

a. Leigh syndrome
b. Krabbe disease
c. Propionic acidemia
d. Hypoxic-ischemic injury
e. I don't know

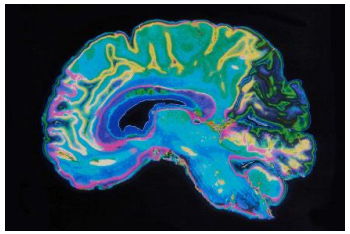


CASE 2 >>> ALBA



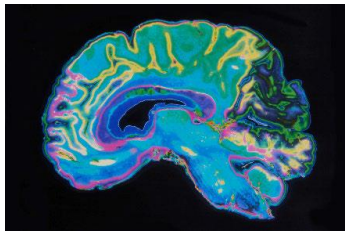
Alba, female, 19 years old. Generalized dystonia from 12 years of age

2



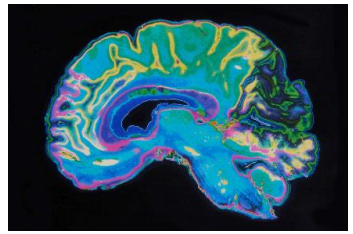
- What are the main MR imaging findings in Alba's case? (multiple answers)

a. Bilateral thalamic lesion
b. Bilateral putaminal lesion
c. Bilateral globus pallidus lesion
d. Excessive iron in both globus pallidus
e. I don't know



- What is the most likely diagnosis in Alba's case? (one option)

a. An NBIA disorder
b. Type III GM1 gangliosidosis
c. Urea cycle disorder
d. Krabbe disease
e. I don't know



HYPERKINETIC DISORDERS (DYSTONIA, CHOREA, MYOCLONUS)

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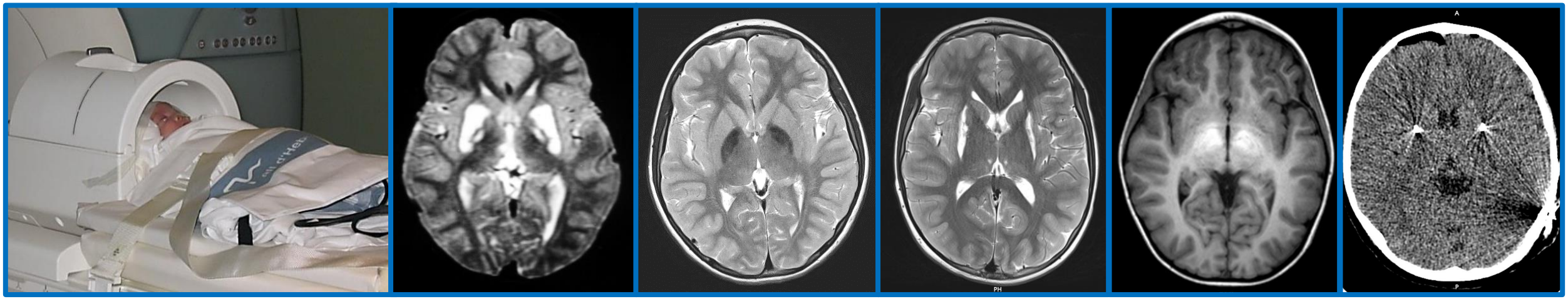
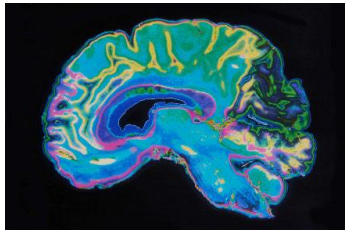
Ignacio Delgado, MD
Hospital Vall d'Hebron. Barcelona





ACKNOWLEDGMENTS

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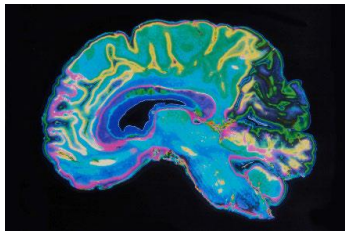
Pediatric Neuroradiology
Hospital Vall d'Hebron. Barcelona

Belen Pérez Dueñas

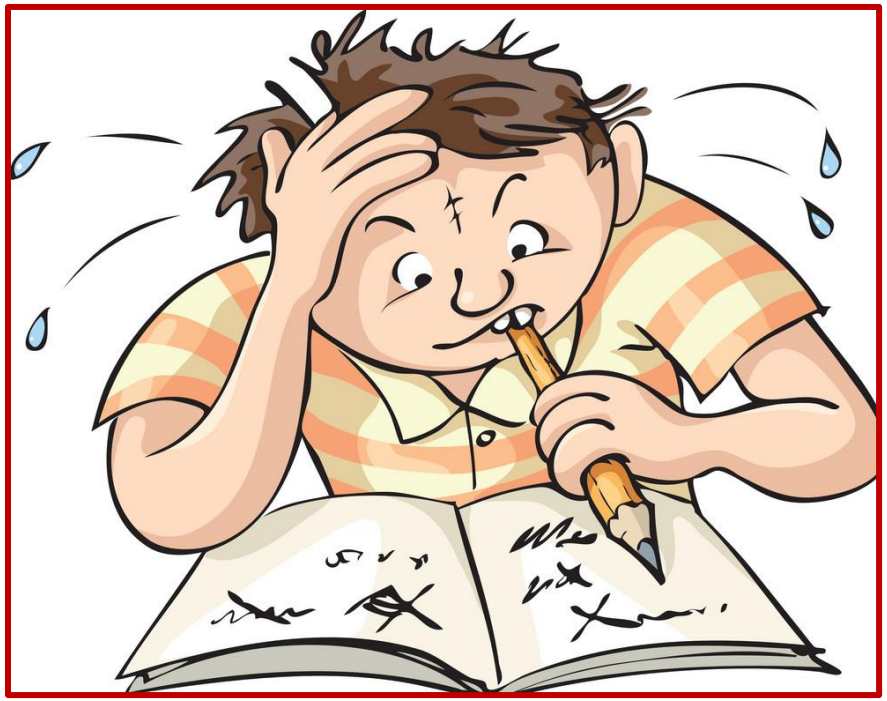
Pediatric Neurology
Hospital Vall d'Hebron. Barcelona

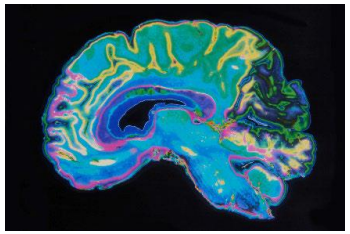


LEARNING OBJECTIVES

1. To go back to the imaging phenotype
2. To learn about imaging clues for the recognition of diverse conditions, either genetic or metabolic
3. More importantly, directed to treatable diseases

Difficult task !!





OVERVIEW

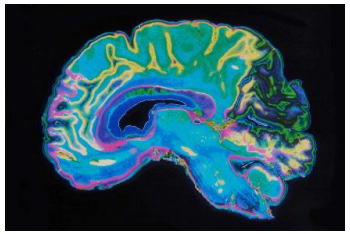
- **DEFINITION**
- Hyperkinetic movement disorders or dyskinesias, refer to a group of excessive, abnormal and involuntary movements

- **ETIOLOGY**
- *Genetic abnormalities*
- *Neurodegenerative diseases*
- Structural lesions
- Infection
- Drugs and toxins
- Psychogenic causes
- Idiopathic

Major Types of Hyperkinetic Movement Disorders

Tremors	Involuntary, alternating movements involving one or more joints occurring at a regular frequency resulting in "rhythmic oscillations"
Chorea	Involuntary, non-rhythmic, abrupt movements resulting from continuous flow of muscle contractions from one muscle group to another resulting in jerky or dance like movements
Dystonia	Involuntary, slow, sustained contractions of agonist and sometimes also antagonist muscles producing twisting movements and/or abnormal posturing
Myoclonus	Involuntary, sudden, brief muscle contractions (positive myoclonus) or inhibition of muscle contractions (negative myoclonus) leading to shock like movements
Tics	Simple or complex, repetitive, abnormal movements or sounds usually preceded by an uncomfortable feeling or sensory urge that is relieved by carrying out the behavior. Tics can often be easily mimicked and suppressed by short efforts of will.

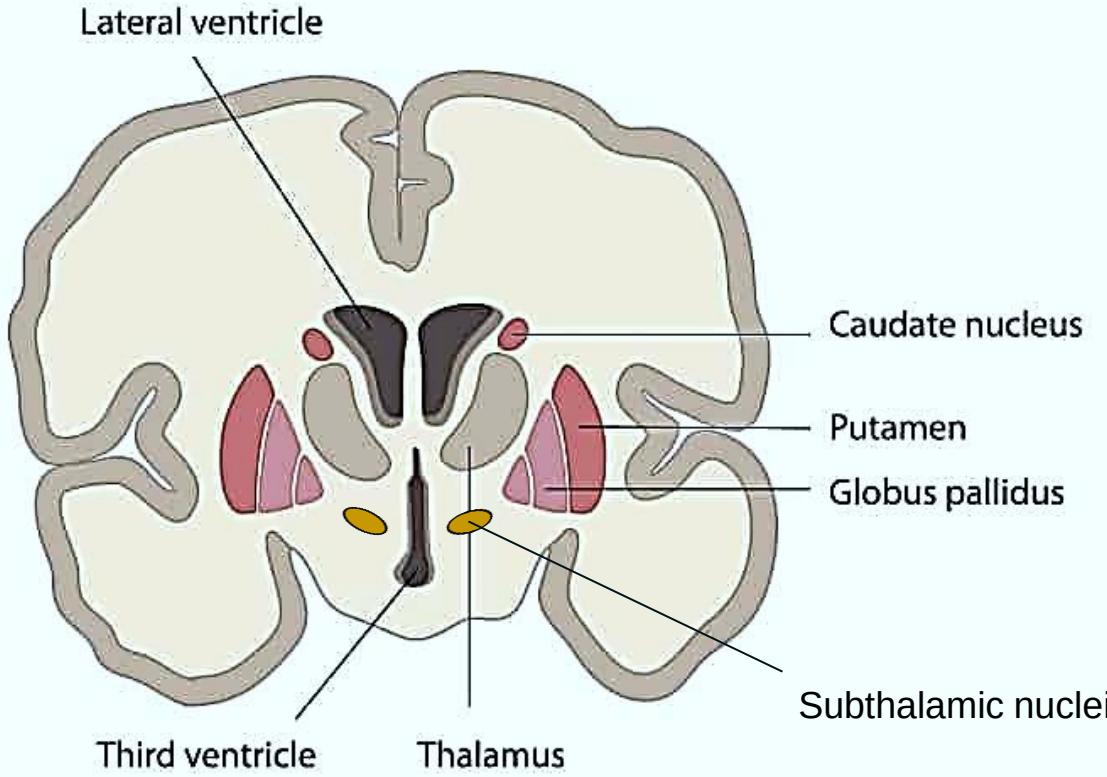
Hyperkinetic Movement Disorders. Moon D, Ferro N. 2014



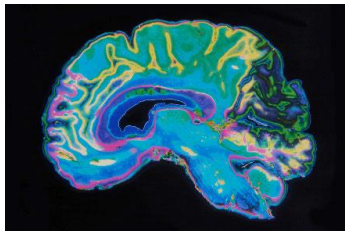
Anatomical correlation

What structures of the nervous system are affected?

- **Physiology**
- **Tremors** are associated with brainstem, cerebellum or *thalamic* lesions
- **Chorea and ballism** have been linked to lesions in the *subthalamic nucleus*
- **Dystonia** is primarily associated with dysfunction of the *putamen or globus pallidus*
- **Myoclonus** can be caused by irritation or destruction of *gray matter*
- **Tics** can involve inflammation or degeneration of the *basal ganglia* in rare cases



Paprocka J, et al. Brain Sci. 2020;10(11):849.



PRACTICAL IMAGING APPROACH

Imaging and genetic studies have been predominant in the investigation of many pediatric neurologic disorders, particularly

- Congenital malformations
- Inherited metabolic disorders

- **Systematic approach:**
  - Analysis
  - Interpretation
  - Notification

GOAL

Discriminating **specific** imaging findings

Recognize neuroimaging phenotype

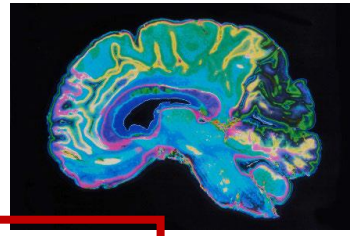
Pattern recognition MRI

+

Clinical clues

GUIDE GENETIC AND METABOLIC ANALYSIS

Pérez-Dueñas B, et al. The Genetic Landscape of Complex Childhood-Onset Hyperkinetic Movement Disorders. Mov Disord. 2022;37(11):2197.



MRI TECHNIQUES

- **Anatomical or structural imaging**
  - *Image contrast based on anatomy differences*
  - T1, T2, T2*/SWI, 3D MPGR
  - FLAIR of limited value in the neonate
  - Standard MR sequences must be adapted neonates
  - MR compatible incubators and neonatal coils

- **Functional imaging**
  - *Image contrast based on differences in function*
  - **MR Spectroscopy**
  - Perfusion-weighted imaging (ASL)
  - BOLD (fMRI)
  - **Diffusion-weighted/DTI**

SELECTED SEQUENCES

❑ < 2 years

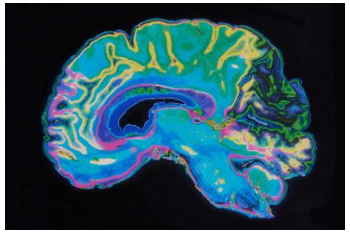
- Sag T1
- Ax IR T1
- Ax IR T2
- T2* GE
- Diffusion
- Spectroscopy

❑ > 2 years

- Sag & Cor T1
- Ax & Cor T2
- Cor Flair
- T2* GE
- Diffusion
- Spectroscopy

European Reference Network
for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

MR SPECTROSCOPY



- ***Assessing levels of metabolites in vivo***

➢ **N-acetylaspartate**
- Marker viable neurons, reduced with neuron injury, immaturity

➢ **Creatine/Phosphocreatine**
- Possibly energy supply

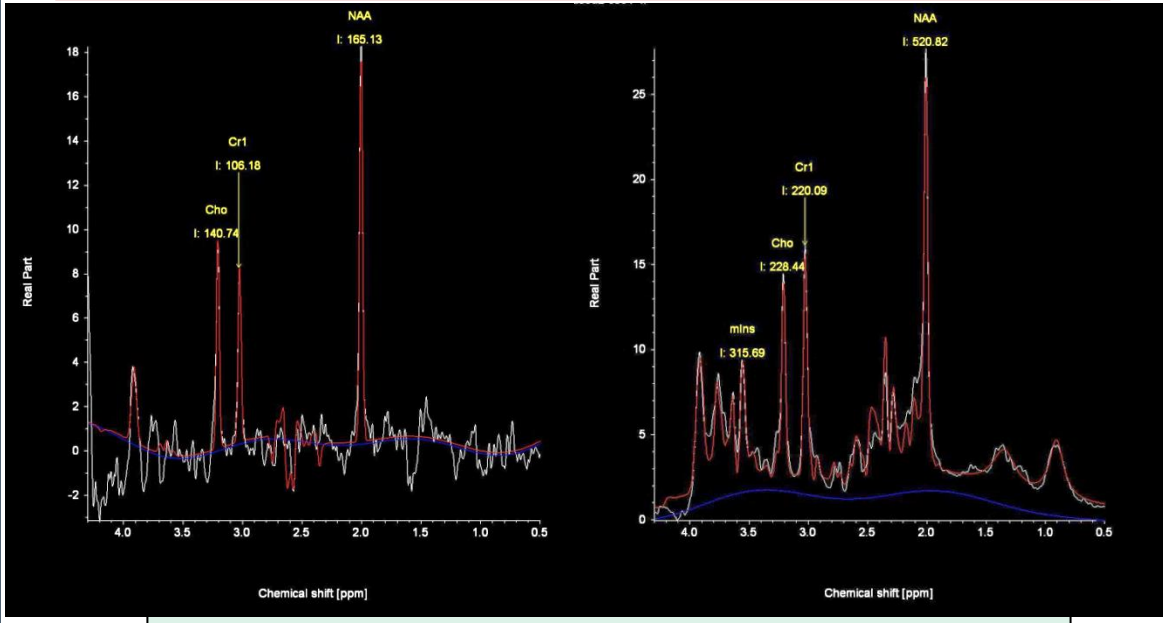
➢ **Choline**
- Membrane turnover, > infection, inflammation, neoplasm

➢ **Myo-Inositol**
- Marker of glia.

➢ **Lactate**
- Anaerobic

➢ **Glx - (sho**
- Glutamate

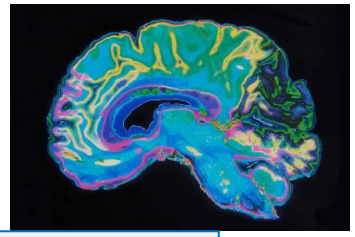
Long and Short TE Spectra



2-year-old boy. Normal WM MRS

❑ **TEACHING POINT**
- **Metabolite concentration varies with progressing development**

✓ Cho peak > NN due to unmyelinated WM



GRAY MATTER DISORDERS

❑ Basal Ganglia Involvement

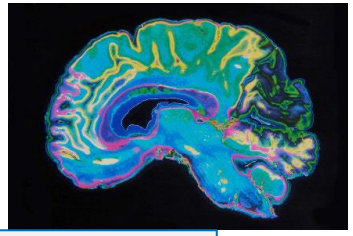
- Short T2 – PKAN
- Long T2 – Many disorders

- **STRIATUM**
- **Leigh syndrome**
- Juvenile Huntington disease
- **Wilson disease**
- **Glutaric aciduria type I**
- Molybdenum co-factor deficiency
- Propionic acidemia

- **GLOBI PALLIDI**
- **Methylmalonic acidemia**
- Succinic semialdehyde dehydrogenase
- Urea cycle disorders
- GAMT deficiency
- **Pyruvate dehydrogenase deficiency**
- Isovaleric acidemia

Barkovich AJ. An approach to MRI of metabolic disorders in children. J Neuroradiol. 2007.

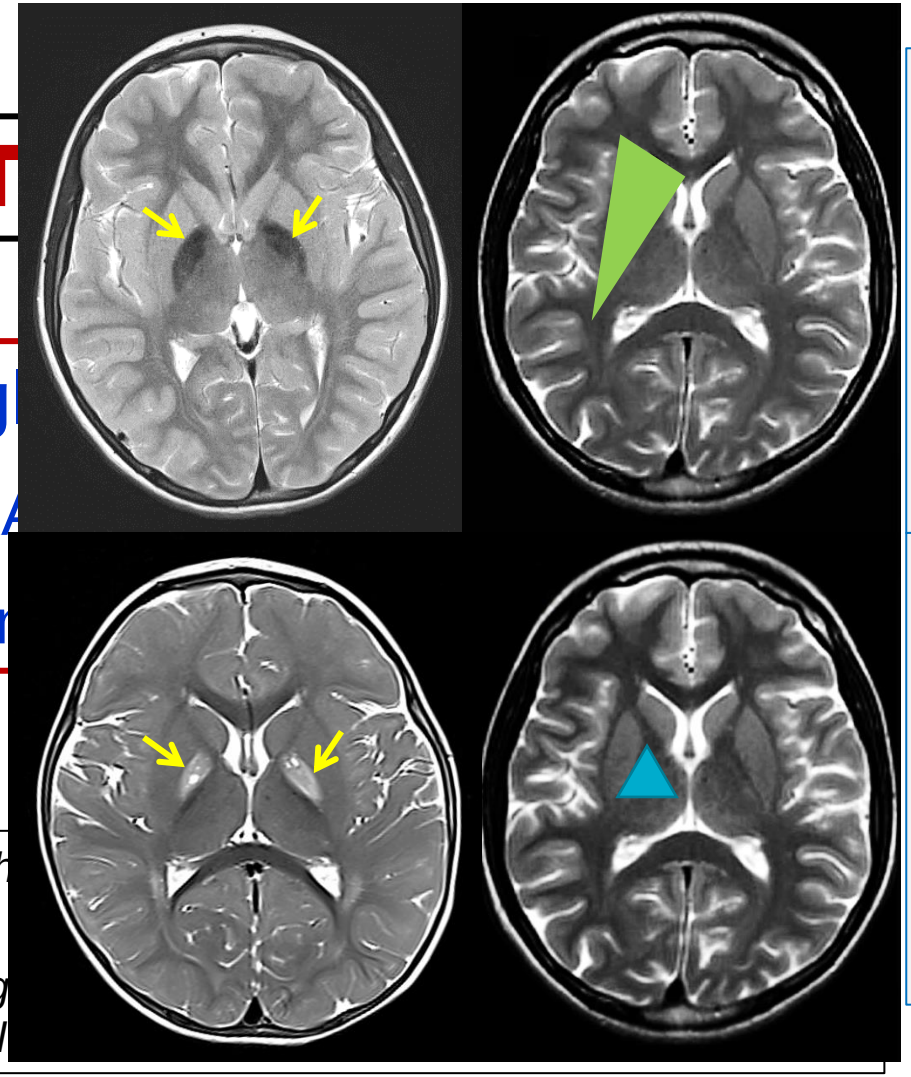
Mohammad SS, et al. Magnetic resonance imaging pattern recognition in childhood bilateral basal ganglia disorders. Brain Commun. 2020



GRAY MAT

❑ Basal Gangl

- Short T2 – PKA
- Long T2 – Mar



- **STRIATUM**
- **Leigh syndrome**
- Juvenile Huntington disease
- **Wilson disease**
- **Glutaric aciduria type I**
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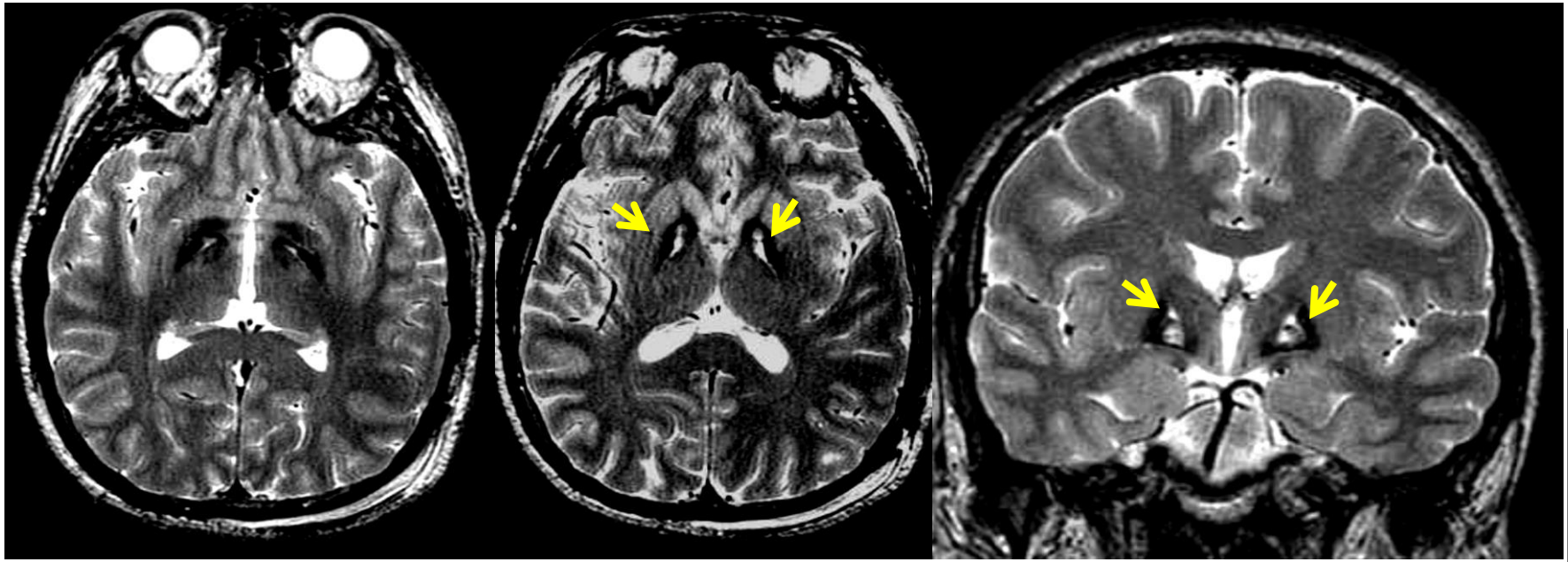
Barkovich AJ. An approach Neuroradiol. 2007.

Mohammad SS, et al. Mag in childhood bilateral basal

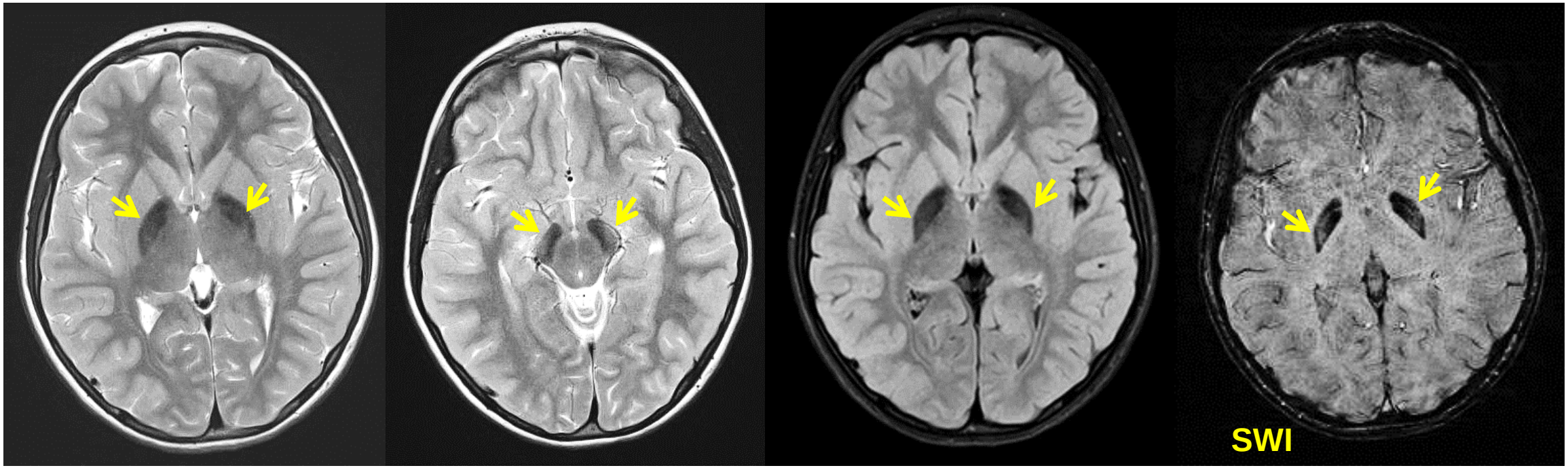
Neurodegeneration with brain iron accumulation disorder NBIA



14-year-old girl with progressive dystonia
Globi Pallidi (dark)
"eye of tiger"
Dx: PKAN

❑ Pantothenate Kinase Associated Neuropathy (PKAN)

- Formerly called Hallervorden Spatz disease. **Neurodegeneration with Brain Iron Accumulation 1**
- Progressive gait impairment, increasing rigidity, slow voluntary movements, choreoathetosis
- Mutations found on ***NBIA1*** 20p12.3-p13 and pantothenate kinase gene (***PANK2***)
- Imaging characterized by iron deposition in globi pallidi (**eye of tiger**)
- MRS shows **elevated Glx**

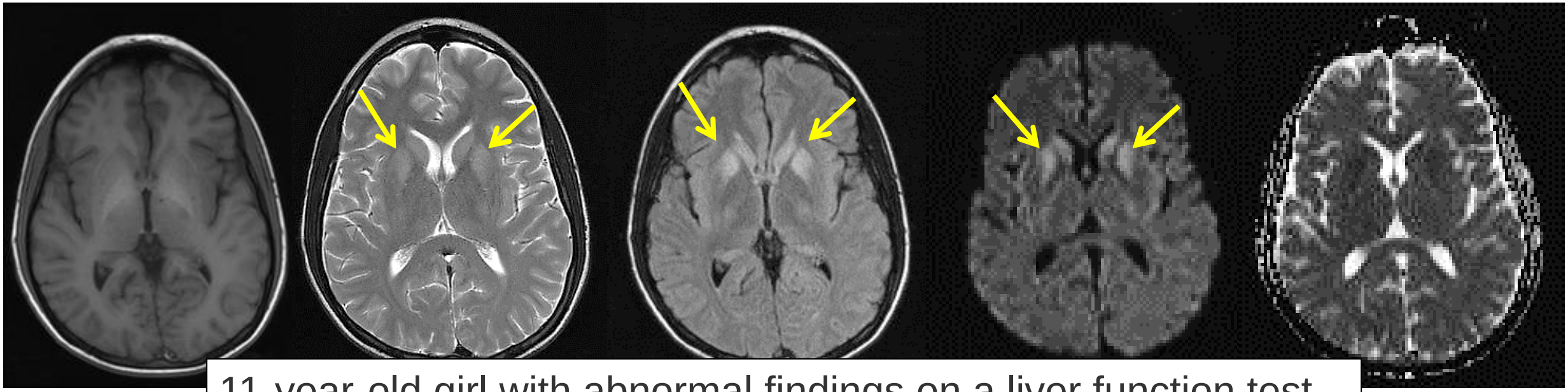


9-year-old boy with optic atrophy and spasticity
MPAN mutation in homocigosis gene C19orf12 c.245c>T, p.Pro74Leu.

❑ Mitochondrial Membrane Protein-Associated Neurodegeneration (MPAN)

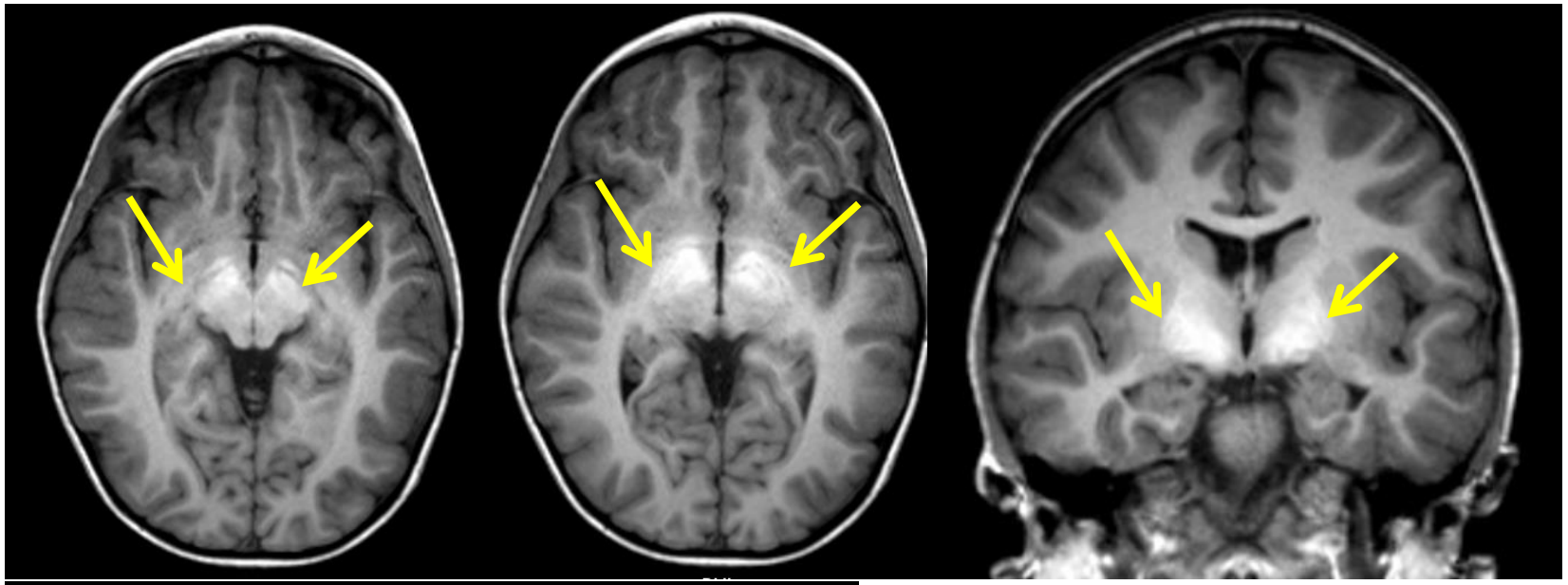
- Neurodegeneration with Brain Iron Accumulation 4 (NBIA4)
- Onset in childhood to early adulthood with slow progression, cognitive decline progressing to severe dementia, optic atrophy, motor neuron signs, dysarthria
- Imaging characterized by iron deposition in globi pallidi (No “eye of tiger”) and substantia nigra

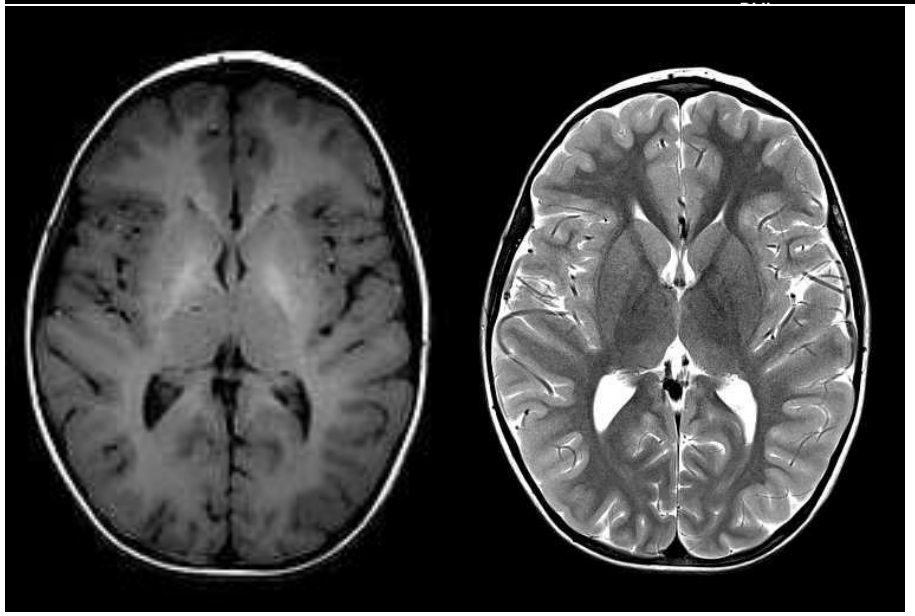
WILSON DISEASE
(Hepatolenticular degeneration)



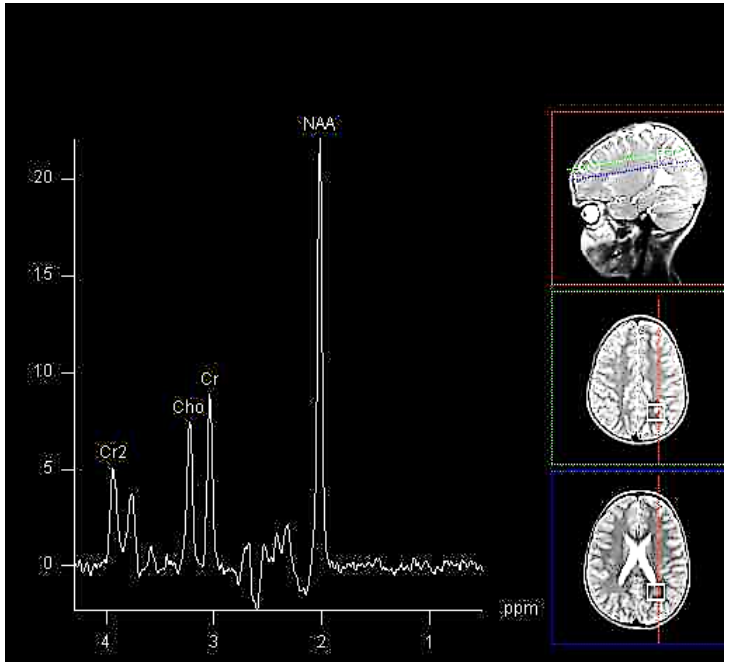
11-year-old girl with abnormal findings on a liver function test

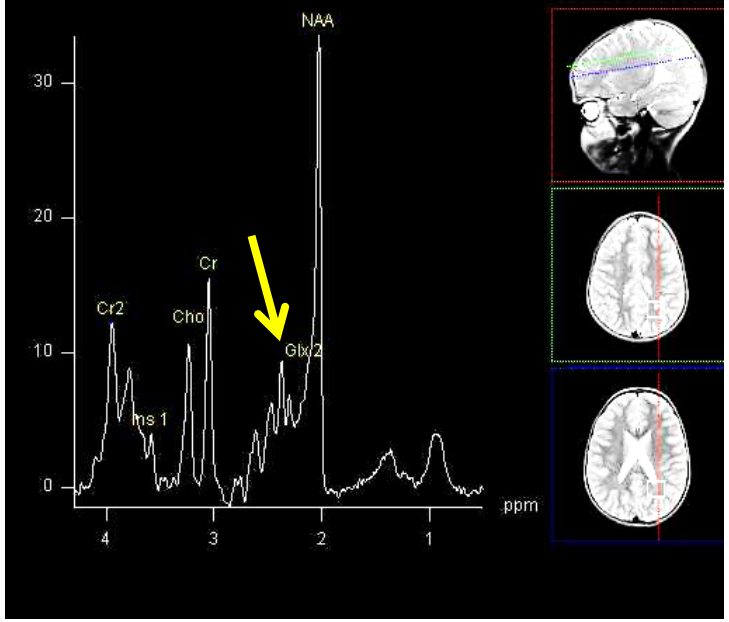
- Results from an inborn error of copper metabolism
- Usually presents in young adults with neurologic deterioration
- When presenting in childhood, onset is insidious
- When detected early, can be treated by chelating agent
- **Imaging: high SI on T1 and T2 in the BG**, less thalamus





T1 hyperintensity in the basal ganglia in patients with liver disease correlates with blood manganese levels





5-year-old boy with **Abernethy syndrome**

GRAY AND WHITE MATTER DISORDERS

- **Mitochondrial disorders**
- **Organic acidopathies**
- **Peroxisomal disorders**
  - Zellweger
  - Chondrodysplasia punctata
- **Lysosomal disorders**
  - Tay-Sachs, others

THALAMIC INVOLVEMENT
Krabbe disease
GM 1
GM 2

STRIATAL INVOLVEMENT
Leigh syndrome
MELAS
Propionic acidemia
Glutaric acidemia type I
Isolated sulfite oxidase deficiency

GLOBUS PALLIDUS INVOLVEMENT
Canavan disease
Methylmalonic acidemia
Kearns–Sayre syndrome
L-2-Hydroxyglutaric aciduria
Maple syrup urine disease

Barkovich AJ. An approach to MRI of metabolic disorders in children. J Neuroradiol. 2007;34(2):75.

Disorders involving energy metabolism

Clinical findings related to a deficiency in energy production or utilization

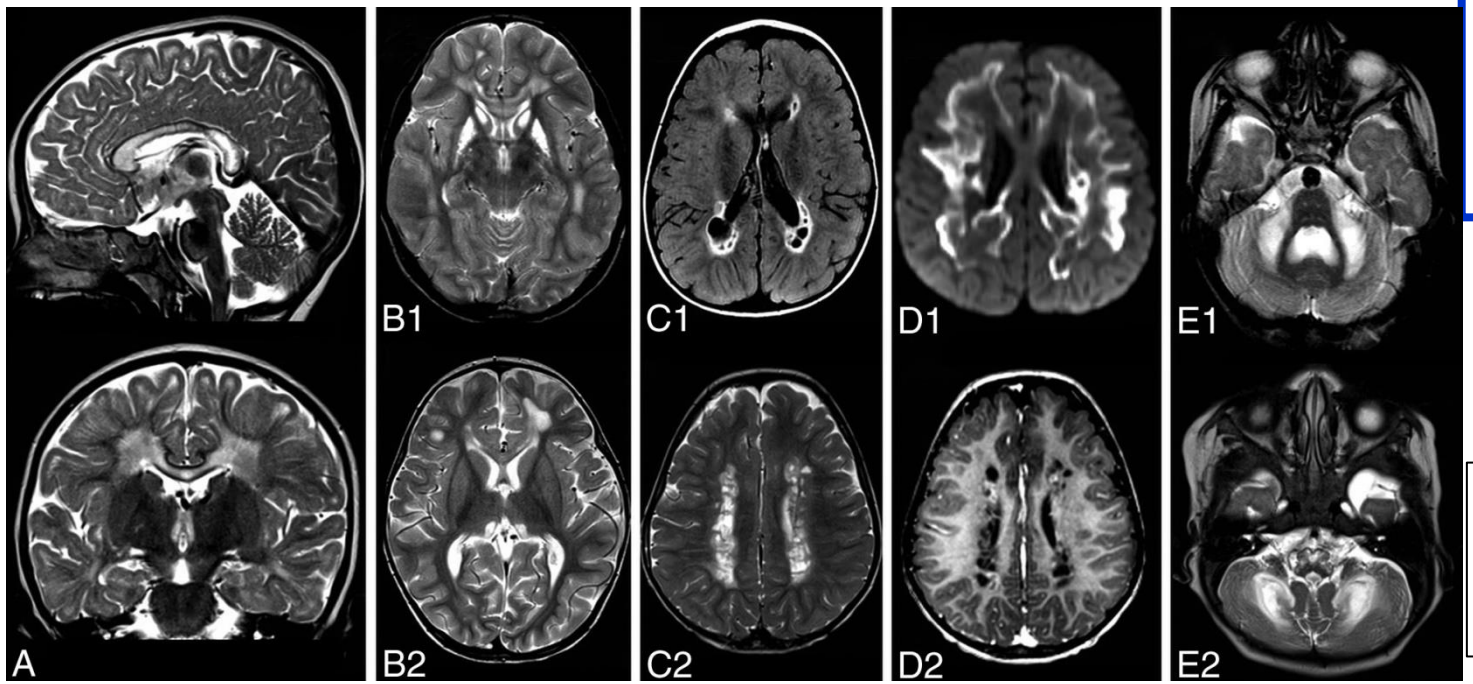
- **Mitochondrial defects**
- Disorders of glycolysis
- Glycogen metabolism
- Gluconeogenesis
- Creatine metabolism

Clinical manifestations

optic atrophy, seizures, strokelike episodes, ataxia, neuropathy

Neuroimaging findings

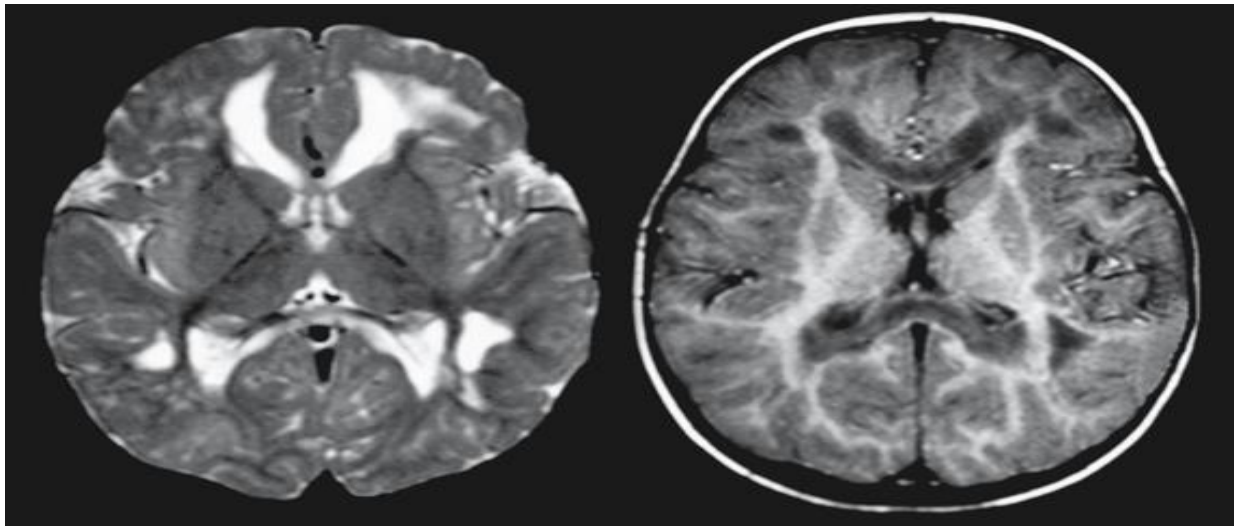
- focal or diffuse lesions in cerebral cortex, white matter, basal ganglia, and brainstem
- **restricted diffusion**
- lactate peak on MR spectroscopy

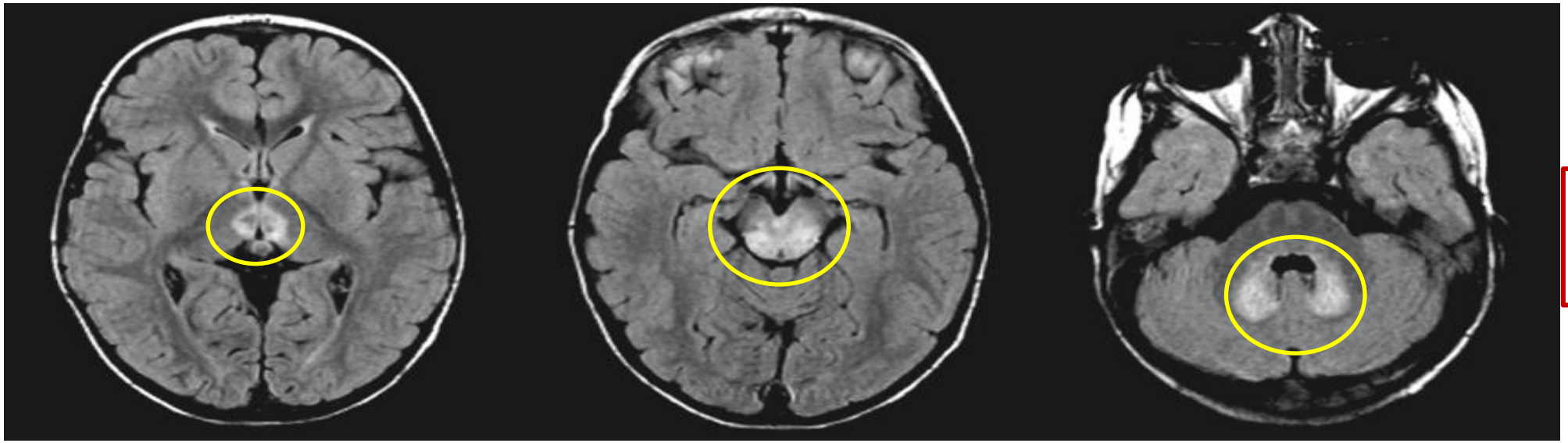


Roosendaal SD, et al. Imaging Patterns characterizing mitochondrial leukodystrophies. AJNR 2021;42:1334.

Complex respiratory chain deficits

- Leigh-like presentation
- Extensive leukoencephalopathy
- Initial edema
- Followed by macrocystic degeneration
- Corpus callosum involvement
- Possible lesions in GB, thalami

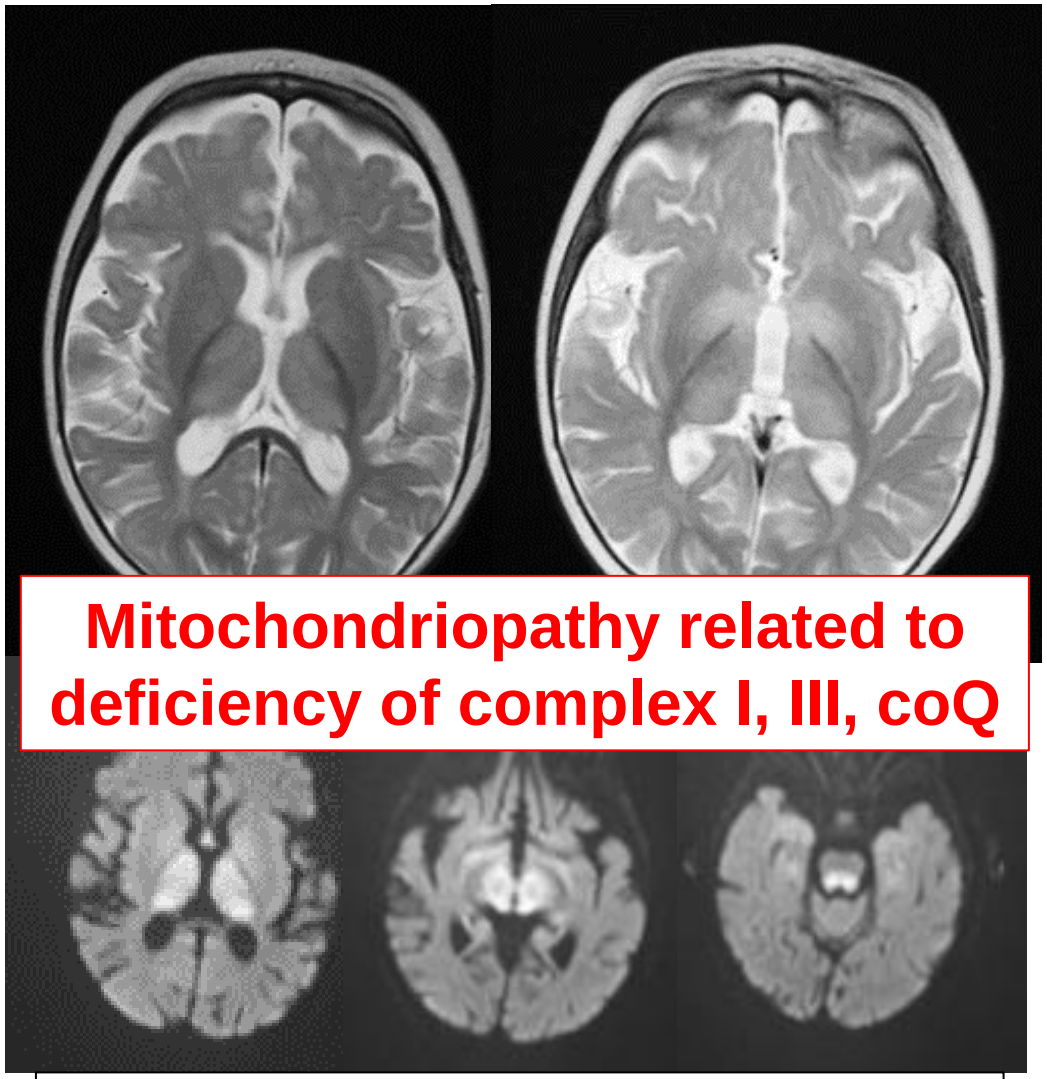




Complex 1 deficiency

Leigh Syndrome

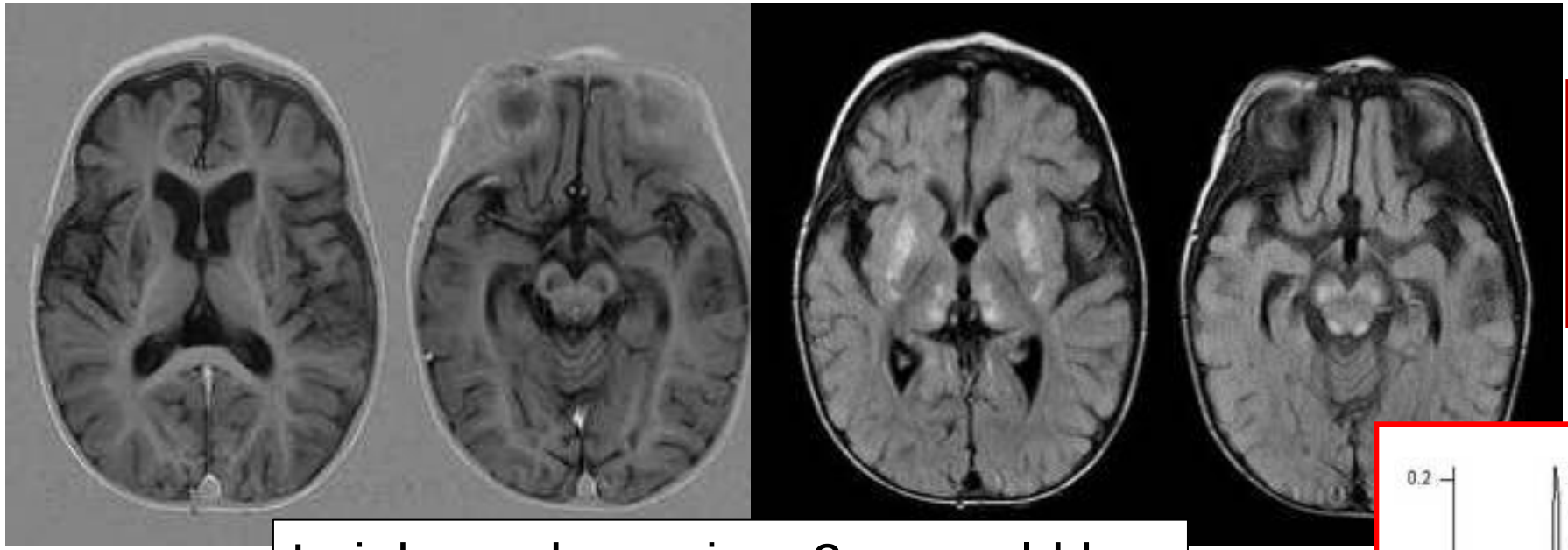
- Subacute necrotizing encephalomyelopathy
- Symptom complex, characterized by progressive neurodegeneration, with variable clinical and pathologic manifestations
- Microcystic cavitation, vascular proliferation, neuronal loss, and demyelination in the **midbrain**, **BG, cerebellar dentate nuclei**, and **cerebral WM**
- More than 80 mitochondrial and nuclear genes related to LS have been described; **next generation sequencing (NGS) is the technique of choice** for diagnosis of LS, achieving molecular confirmation in 38-50% of the cases.
- **SURF1 mutations** presents a peculiar MRI pattern of bilateral involvement of the subthalamic nuclei, with more spared basal ganglia



Mitochondriopathy related to deficiency of complex I, III, coQ

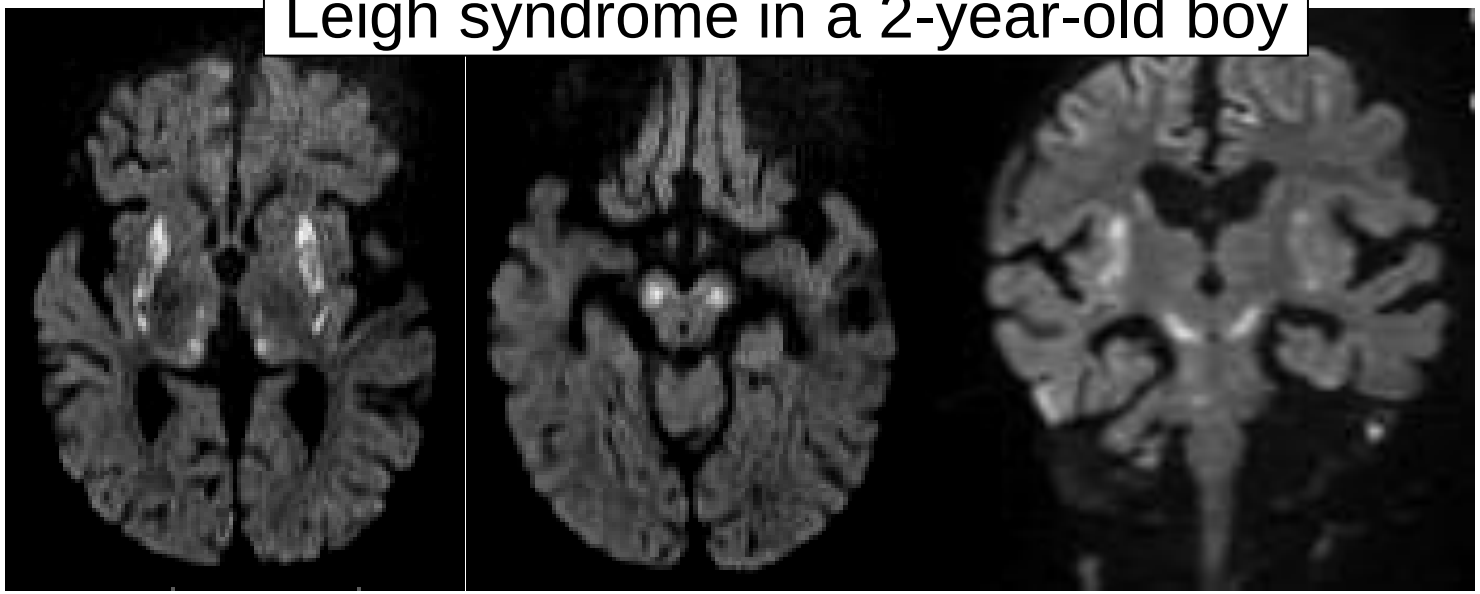
12 month-old girl, West syndrome and global developmental delay

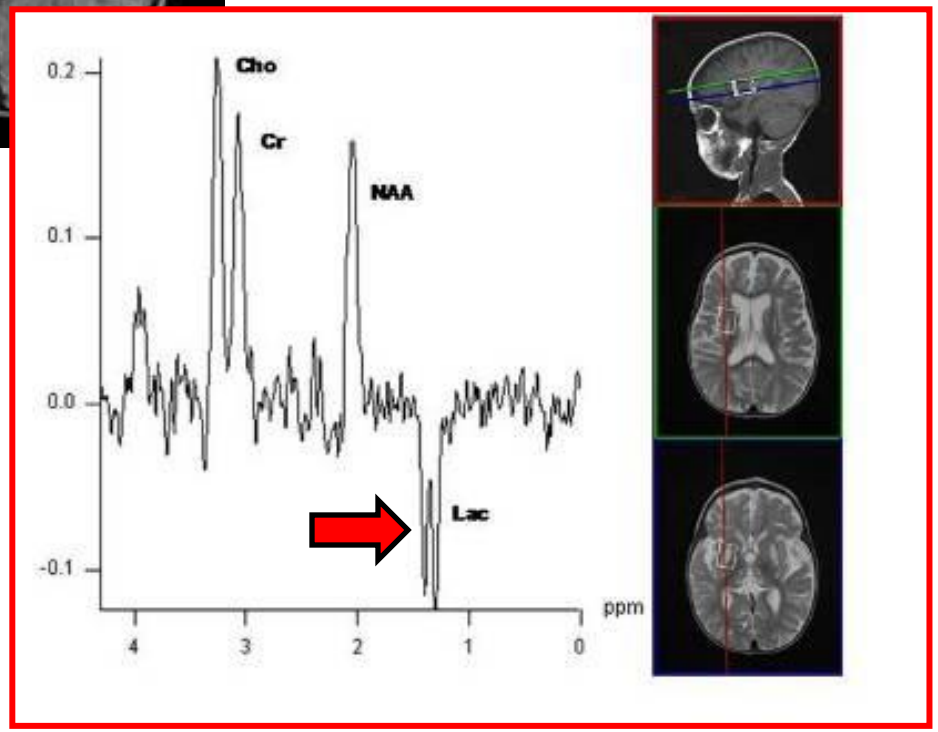
Leigh Syndrome Phenotype



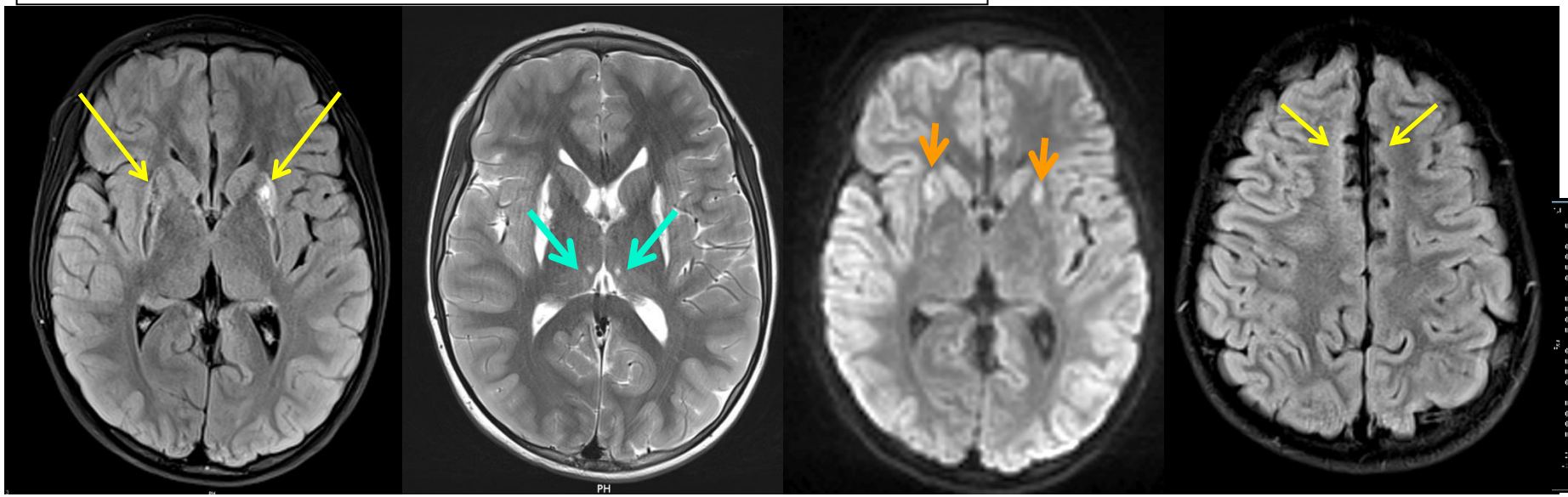
BG involvement (putamen)
Thalami and brainstem
Restricted diffusion
Typical lactate peak on MRS

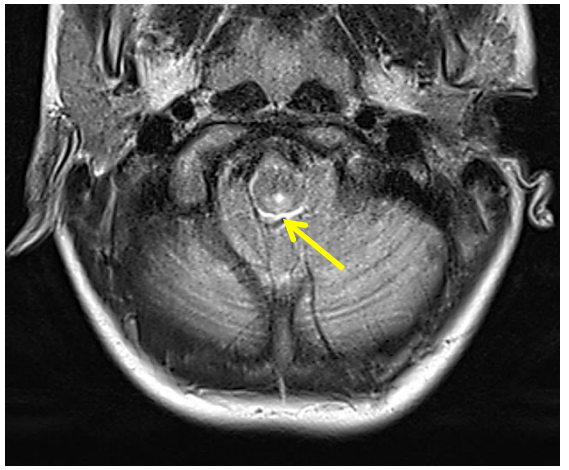
Leigh syndrome in a 2-year-old boy

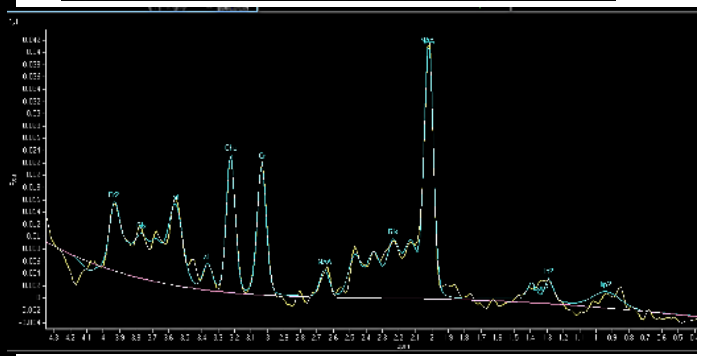




Leigh Syndrome Phenotype

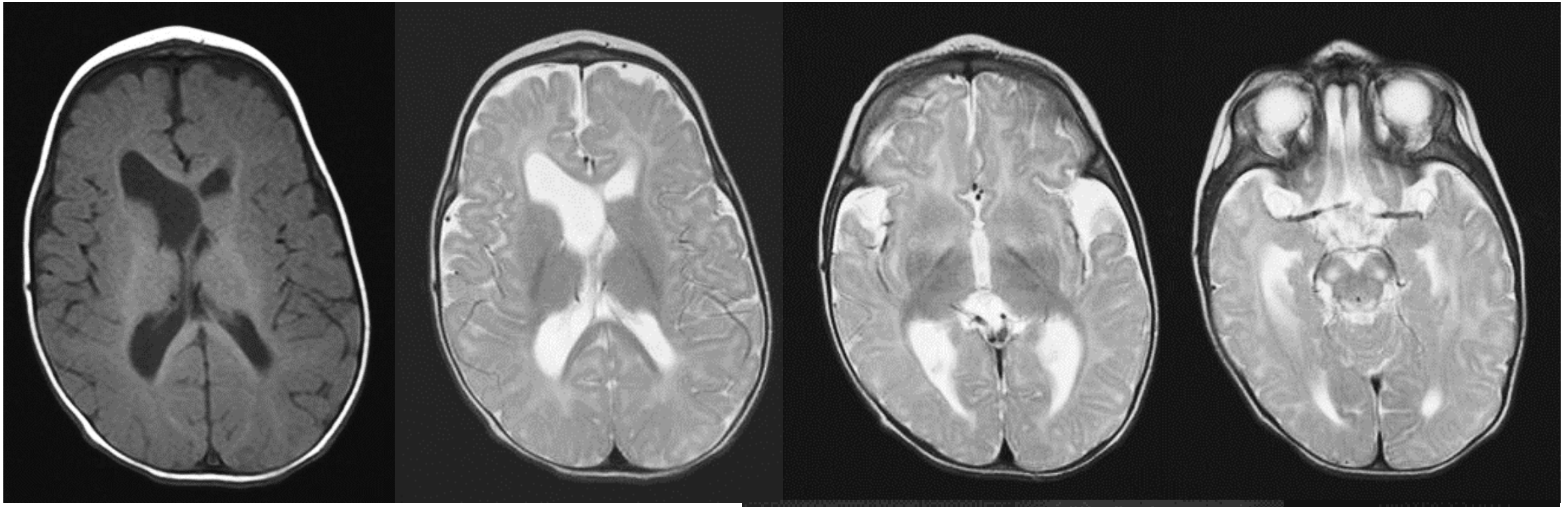




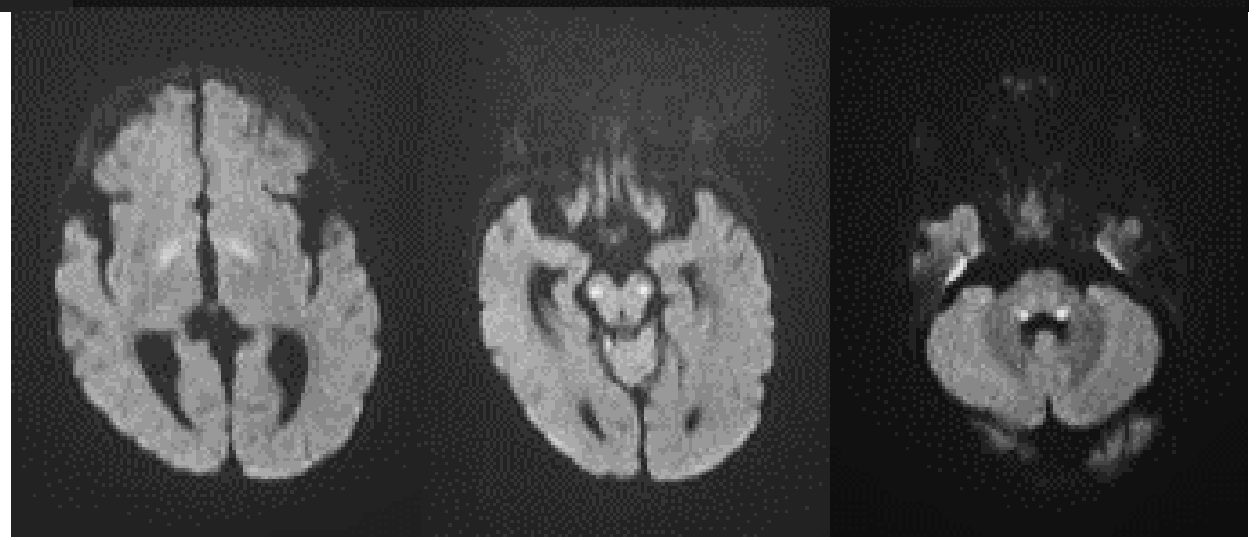


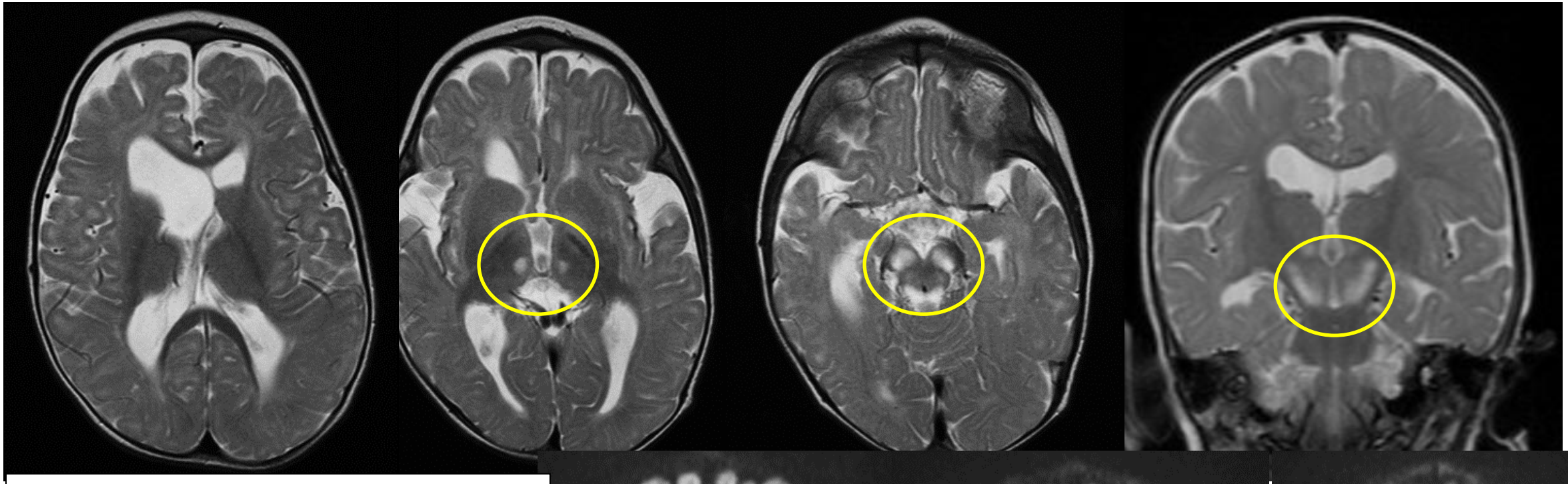
7-year old boy. Consanguineous parents originally from Morocco with mental retardation and progressive dystonic tetraparesis

Mitochondrial respiratory chain complex I deficiency due to mutation in the *NDUFAF5* gene

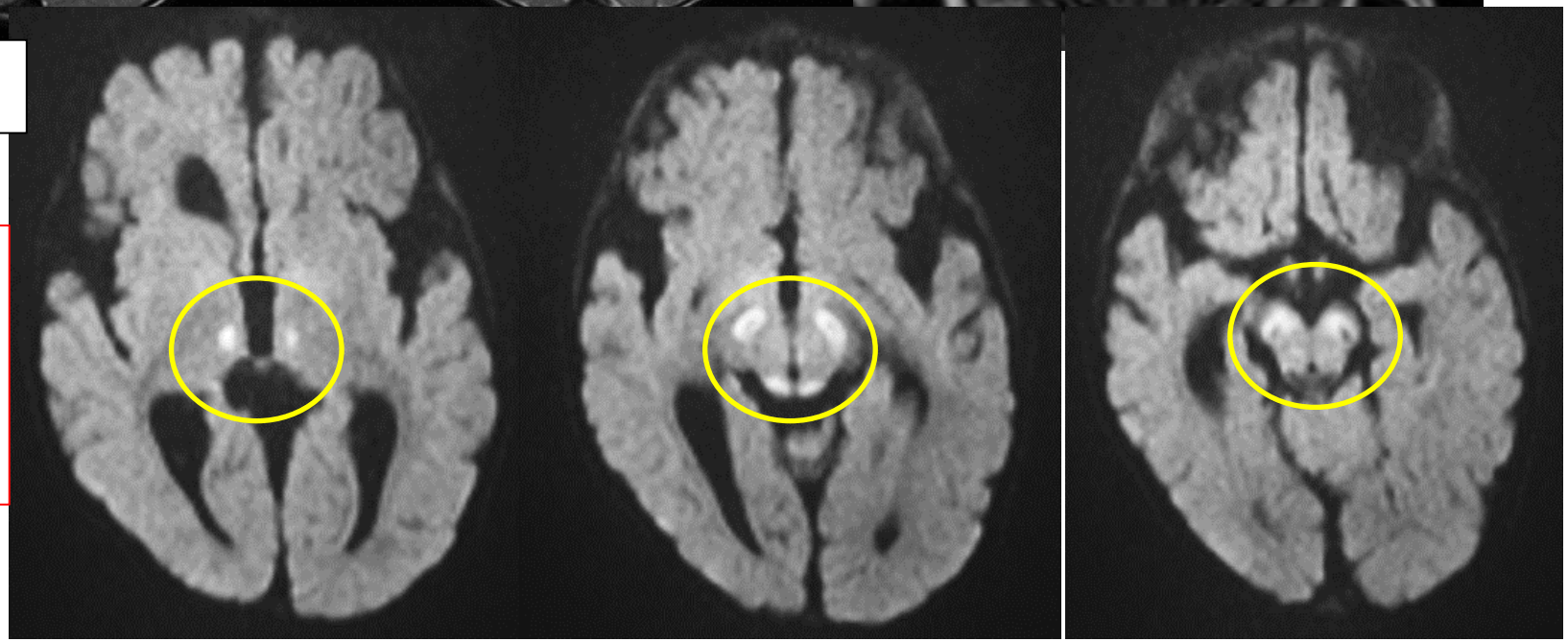


9-month-old boy with visual deficit, flexion spasms and hyperlactydemia



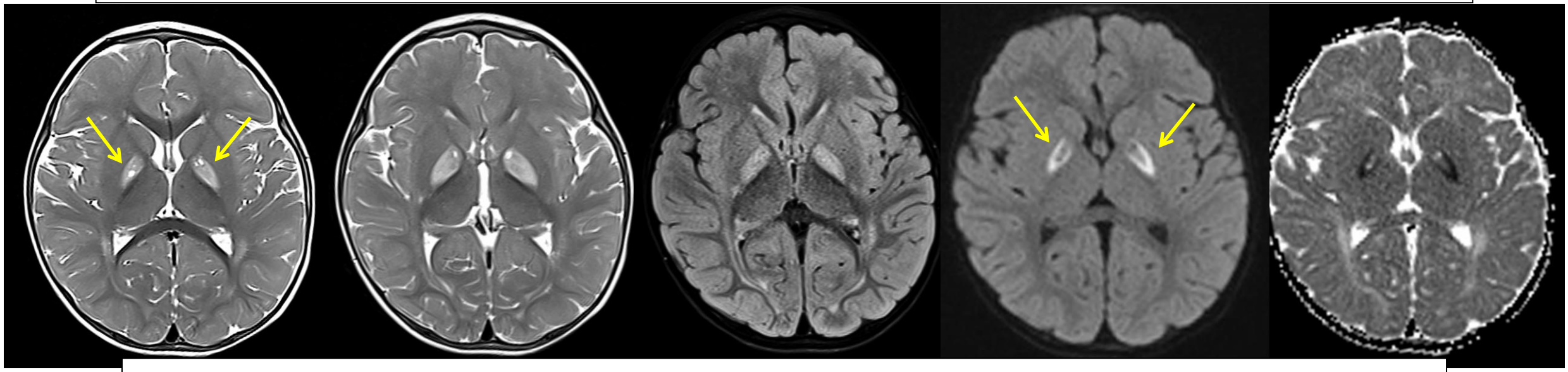


Follow-up 12-month-old



MT-ND5 gene mutation,
at position 13513
(G13513A)

Valine catabolism pathway defects

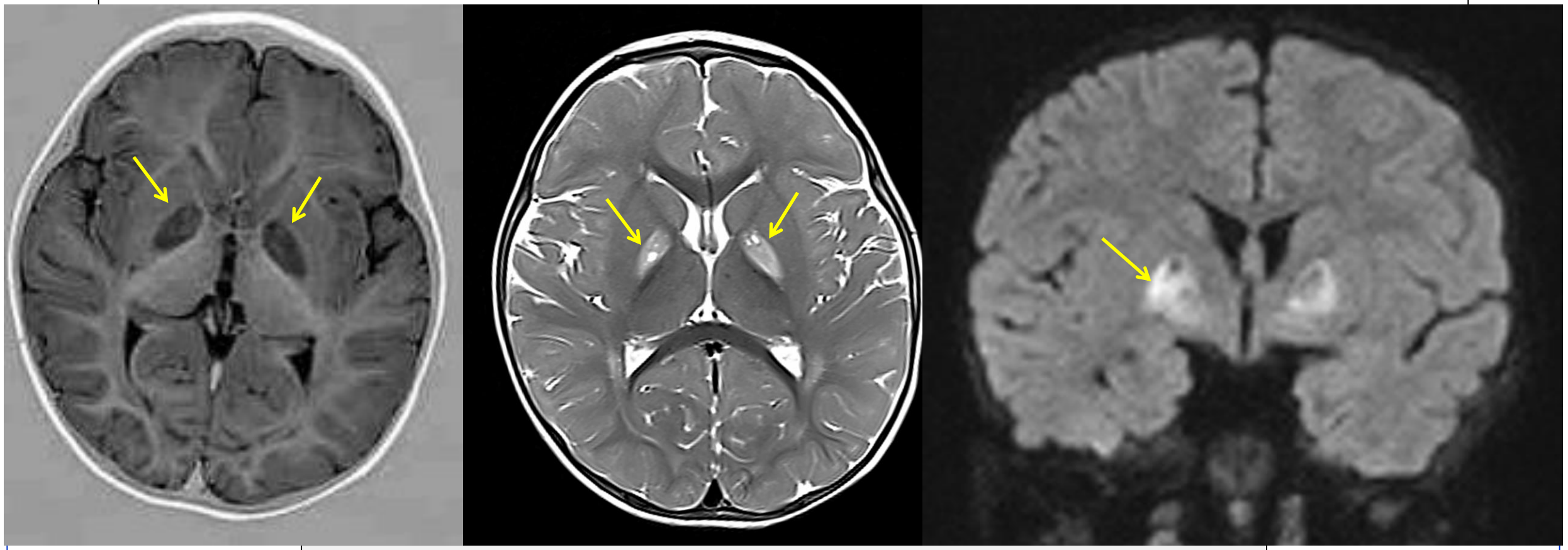


13-month-old male patient with irritability, gait disturbance and paroxysmal dystonia

- **Mutation ECHS1 (short-chain enoyl-CoA hydratase) gene**
- **SCEH and HIBCH defects in the catabolic valine** pathway frequent cause of **Leigh syndrome**
- Similar to defects in 3-hydroxyisobutyryl-CoA hydrolase (HIBCH)
- BG lesions with **small cysts** in putamen/pallidum, characteristic hallmark for diagnosis

Marti-Sanchez L, et al. Delineating the neurological phenotype in children with defects in ECHS1 or HIBCH gene. J Inherit Metab Dis. 2021;44(2):401.

Valine catabolism pathway defects

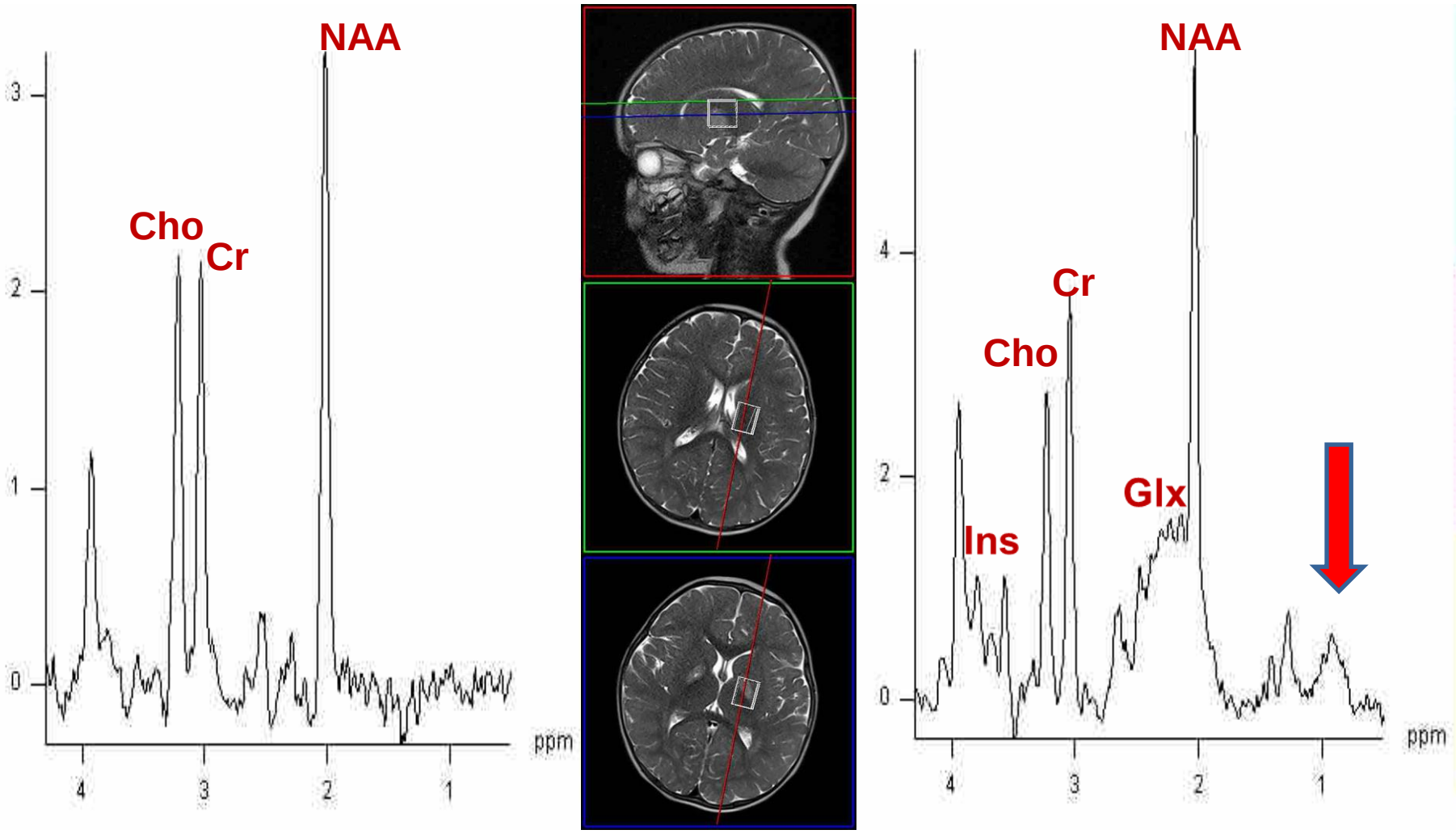


- Similar to defec
- BG lesions with

gnosis

Small cysts in putamen/pallidum, characteristic hallmark for diagnosis

Marti-Sanchez L, et al. Delineating the neurological phenotype in children with defects in ECHS1 or HIBCH gene. J Inherit Metab Dis. 2021;44(2):401.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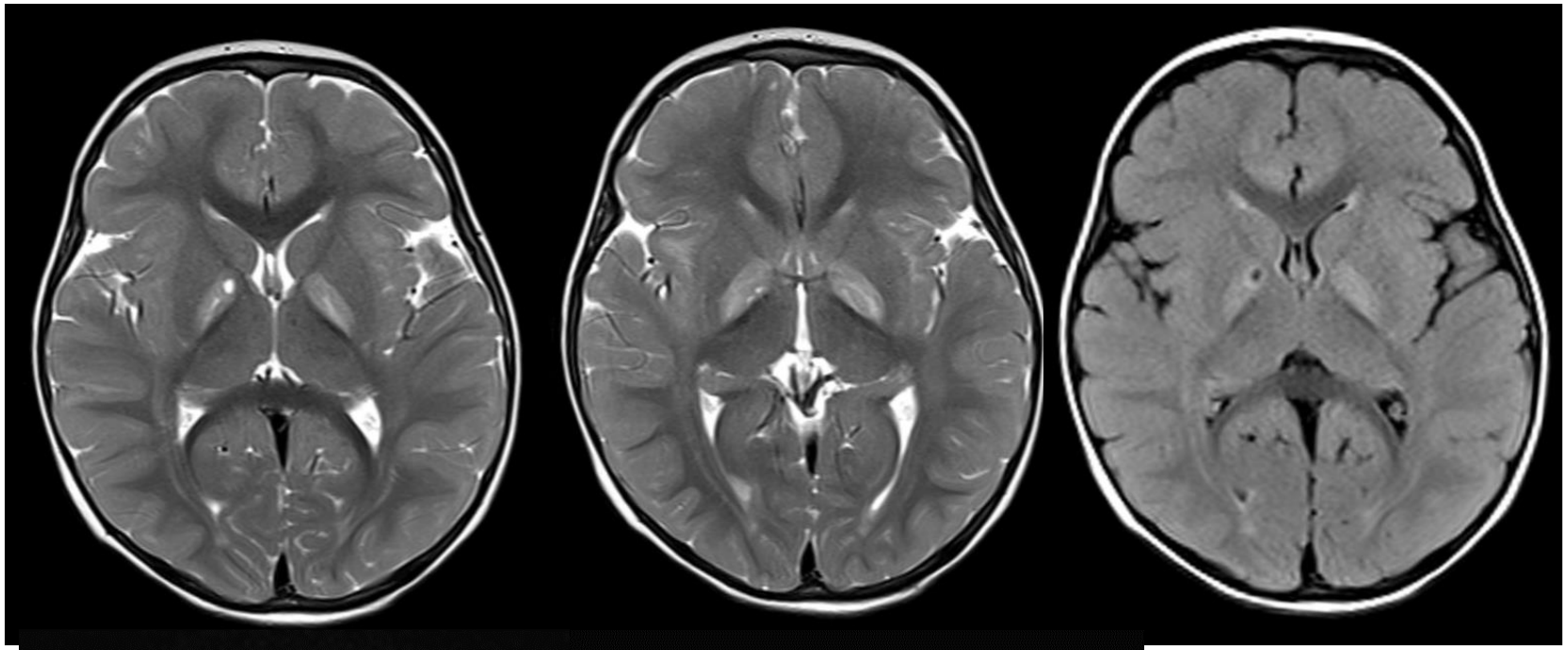
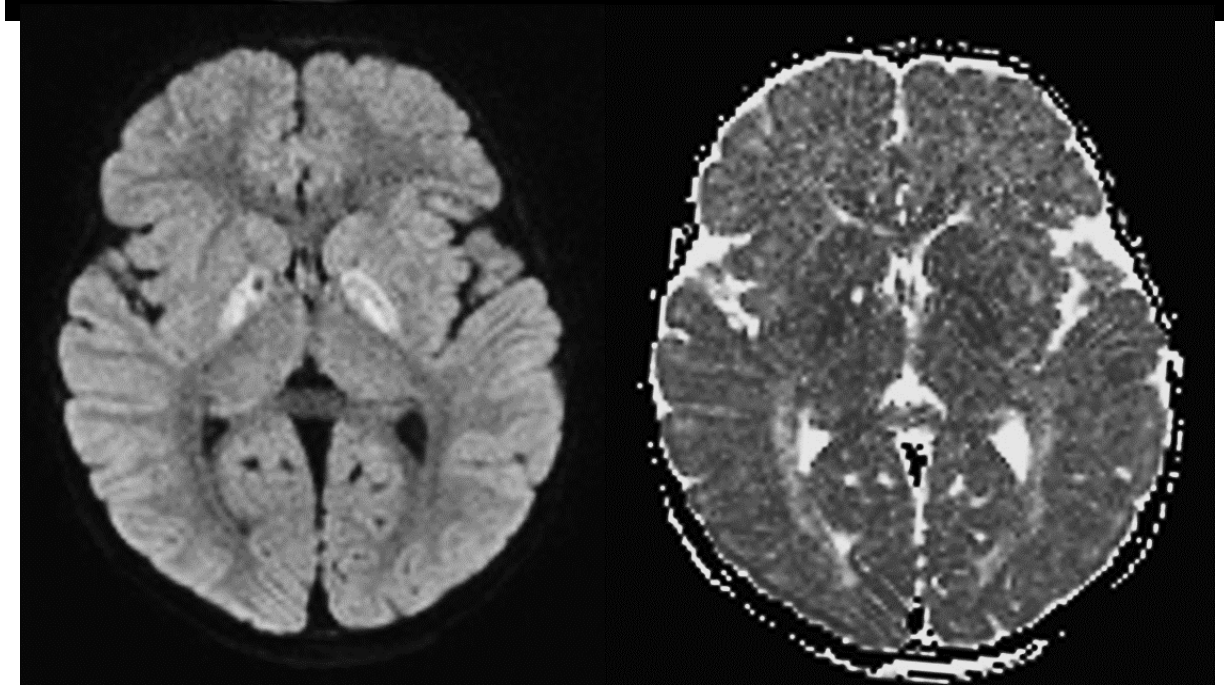
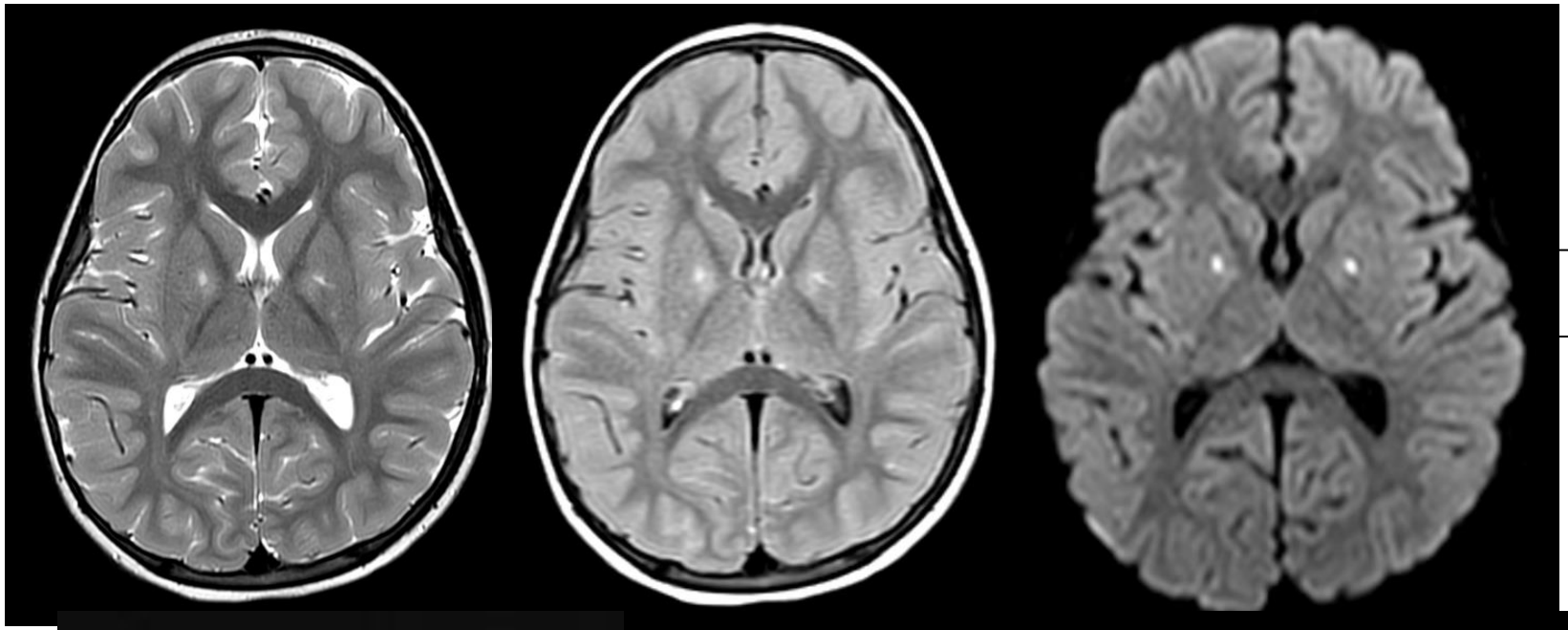




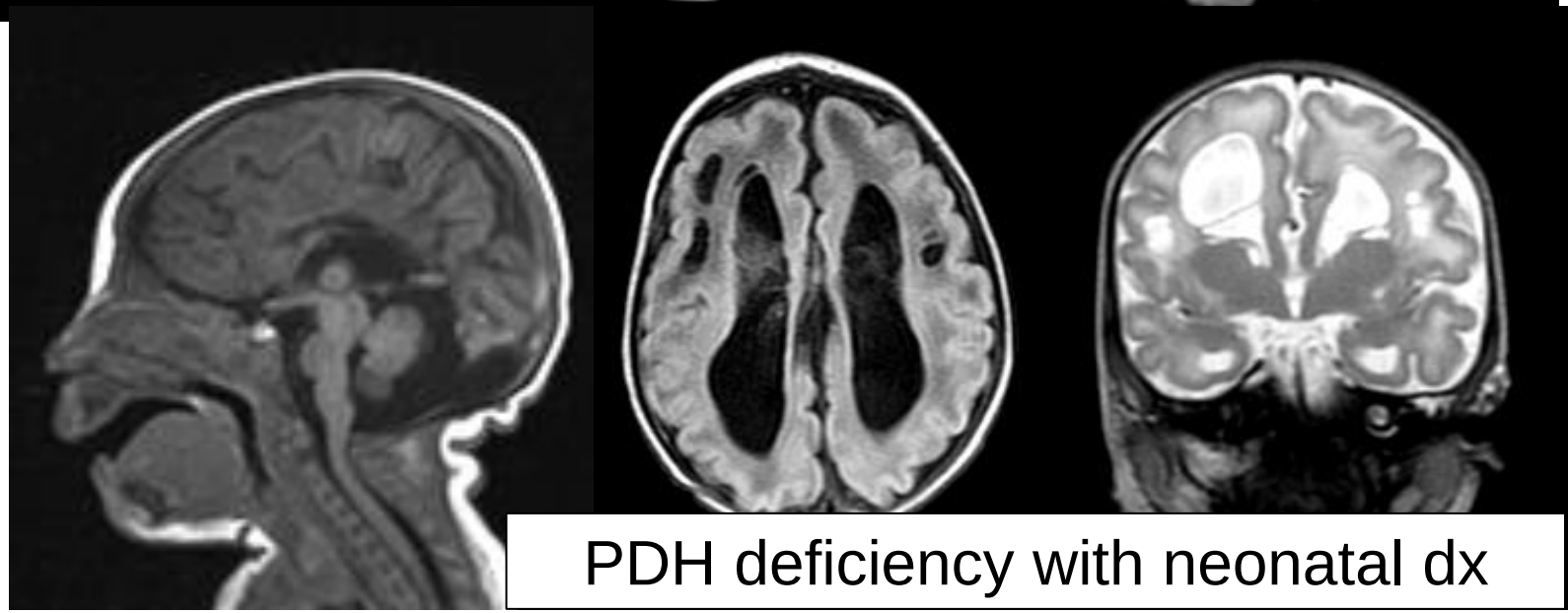
Brother male, 19-month-old
Intermittent episodes of EEII debilitation (episodic dystonia)

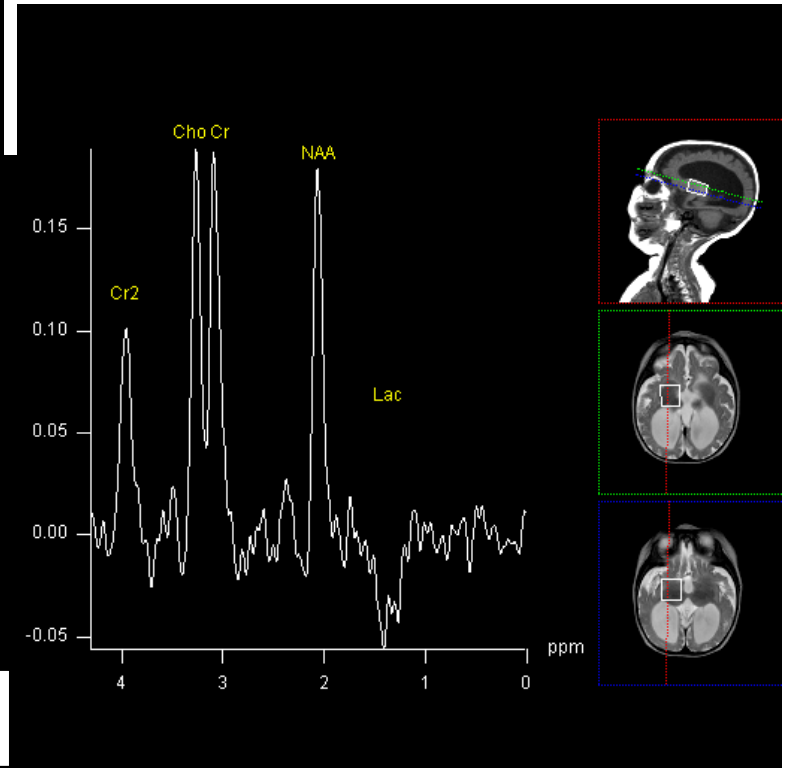
- Heterozygous carrier of changes c. 830C>T (p.T277I) and c.248G>A (p.G83E) in the **ECHS1 gene**
- These changes were identified in heterozygosity in the maternal (IMEGEN-97659) and paternal (IMEGEN-97660) samples

Leigh syndrome secondary to PDHA1 deficiency



7-year-old girl with spastic ataxia

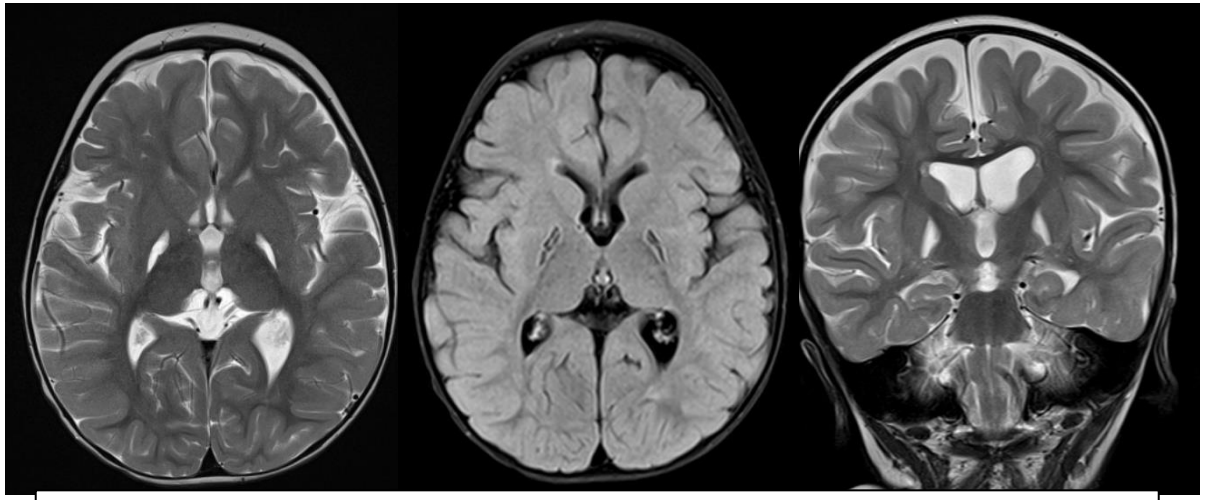




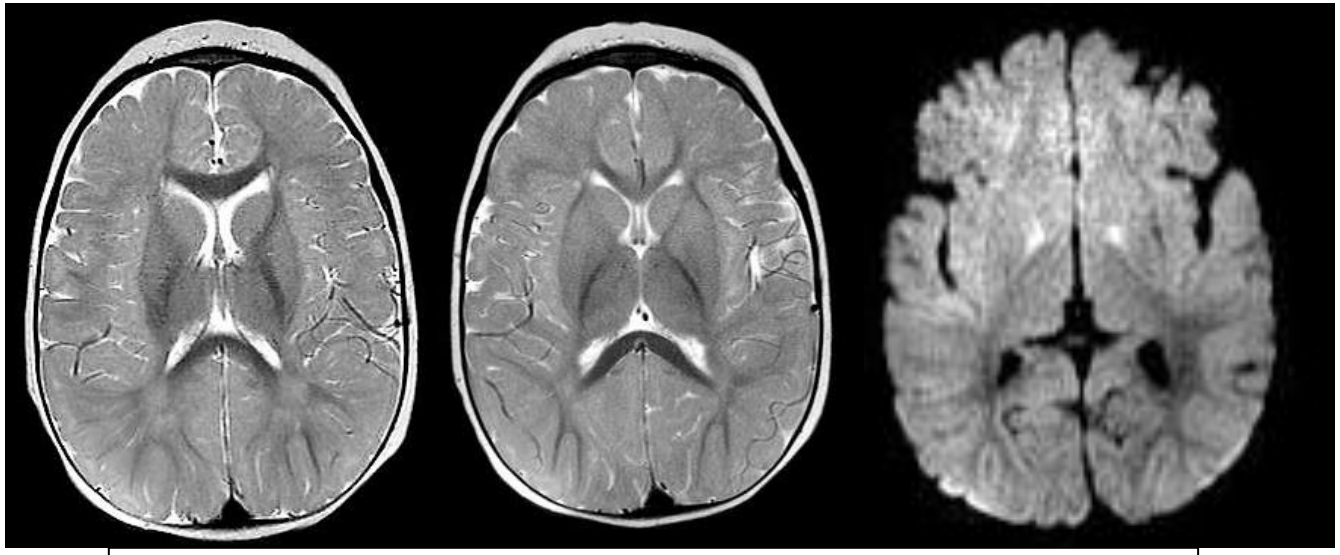
PDH deficiency with neonatal dx

Organic acid disorders

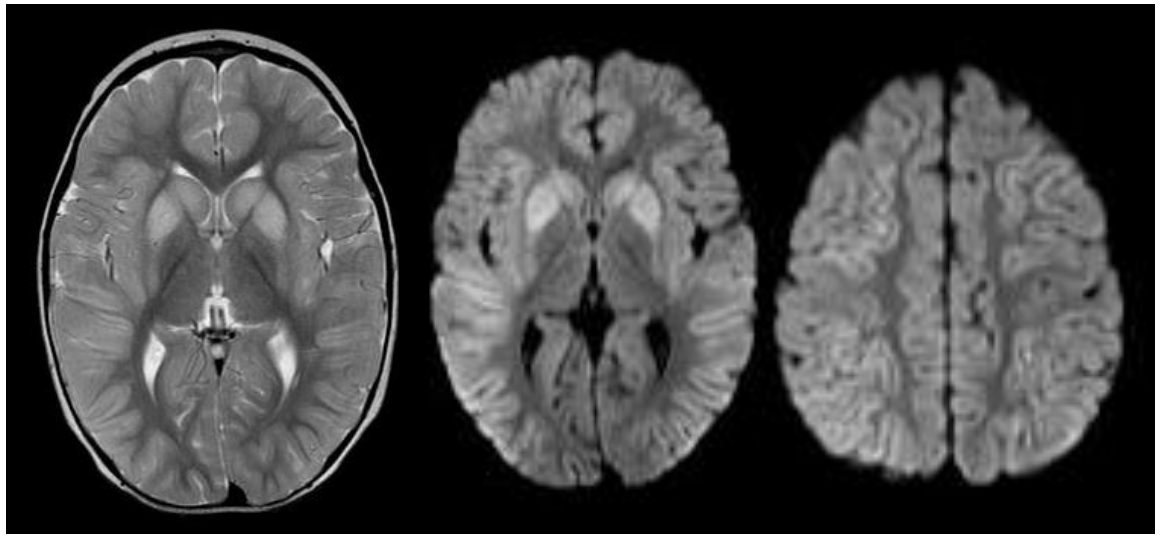
- Group of disorders characterized by the accumulation of organic acids (e.g., glutaric, propionic or methylmalonic acids) in the CSF, urine, or blood.
- Patients may present with developmental delay or in acute metabolic crisis, often triggered by infection
- Many organic acids are involved in mitochondrial function; therefore, may closely resemble mitochondrial disorders on imaging studies



2-year-old girl with **methylmalonic aciduria**

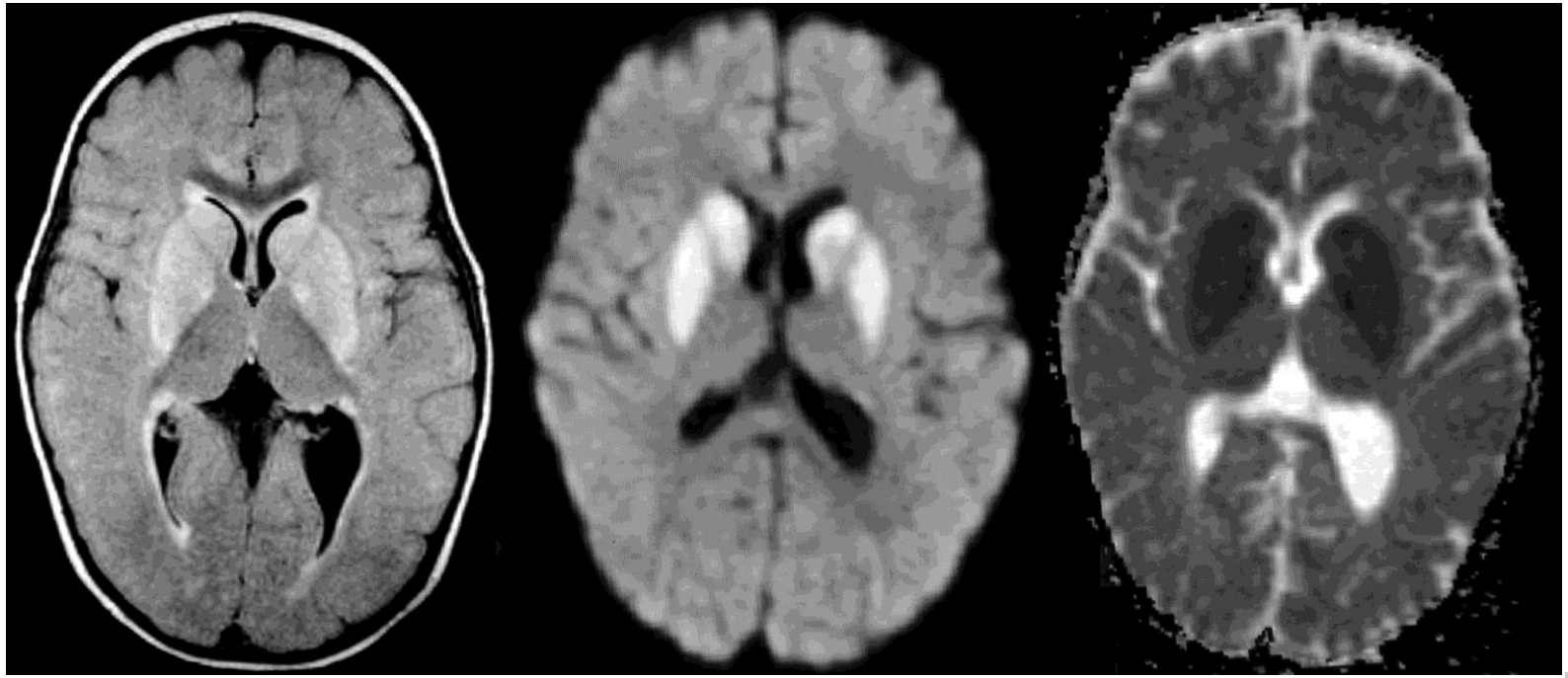


3-year-old boy with **propionic aciduria**

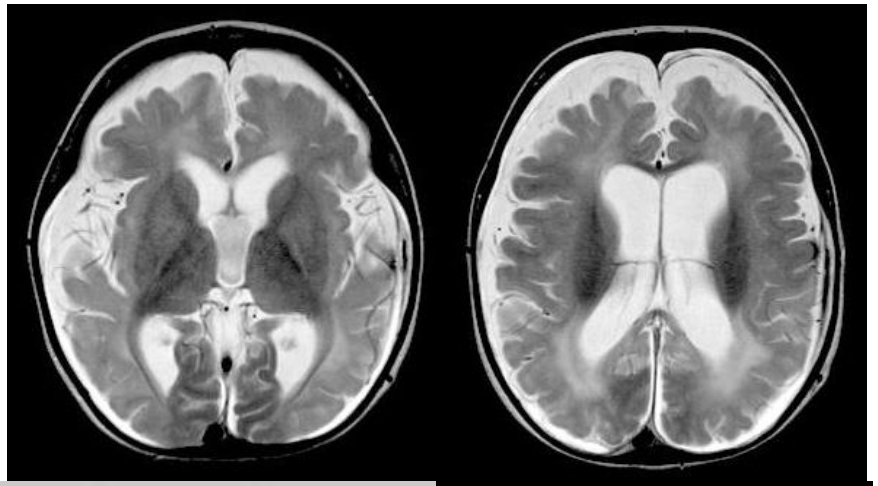


F/up 3 months, coinciding with metabolic crisis

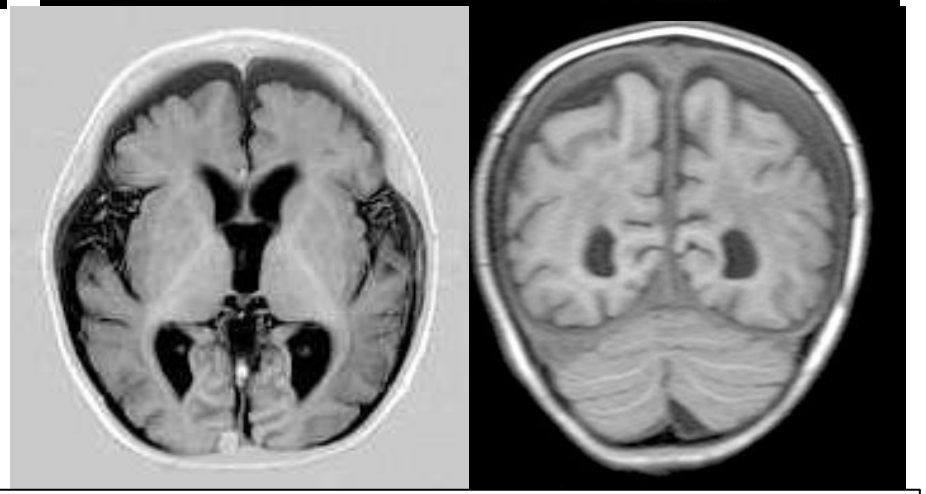
Glutaric Aciduria Type 1



Early treatment can improve outcome!!

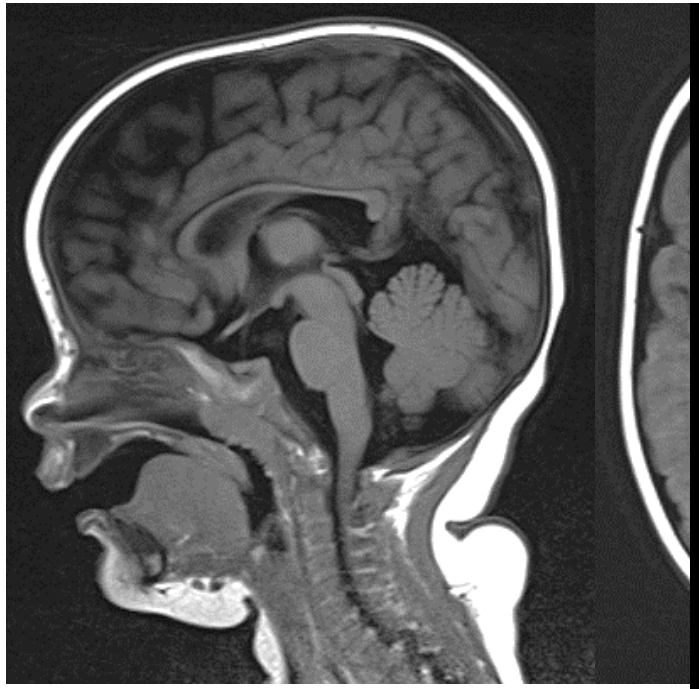


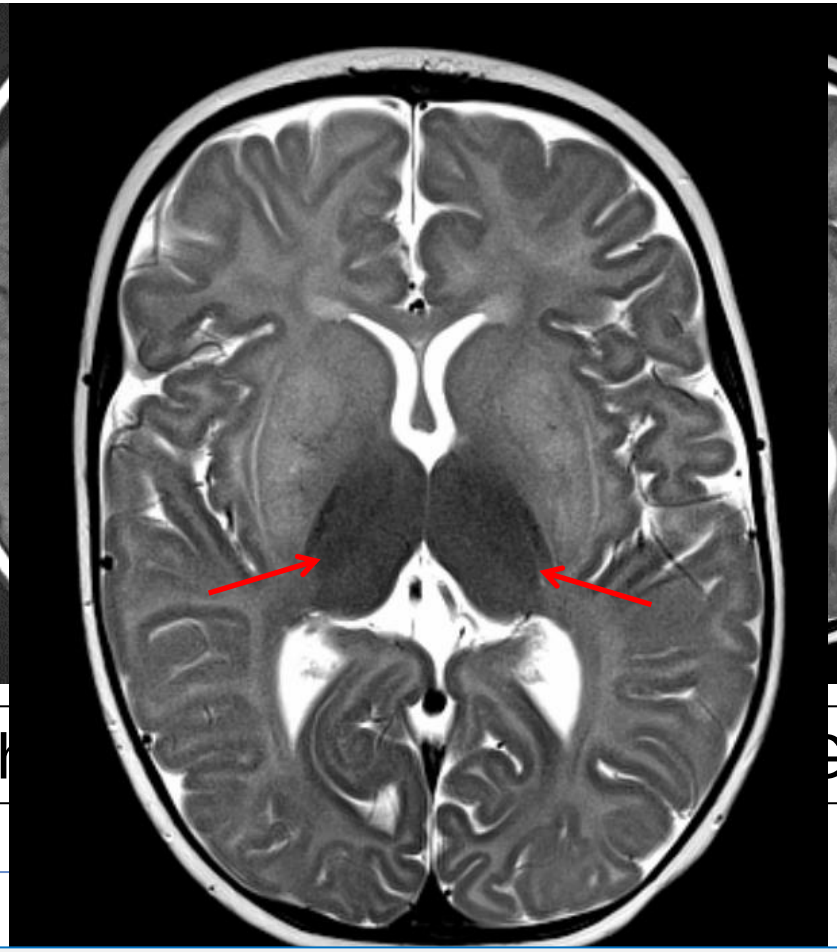
- AR, Glutaryl-CoA dehydrogenase deficiency
- **Macrocephaly**
- Acute neurological crises, typically related to infections
- **Imaging:**
- Widening of Sylvian fissures (operculization deficit)
- Mild ventriculomegaly
- Abnormal GB signal +/- periventricular WM
- Subdural collections

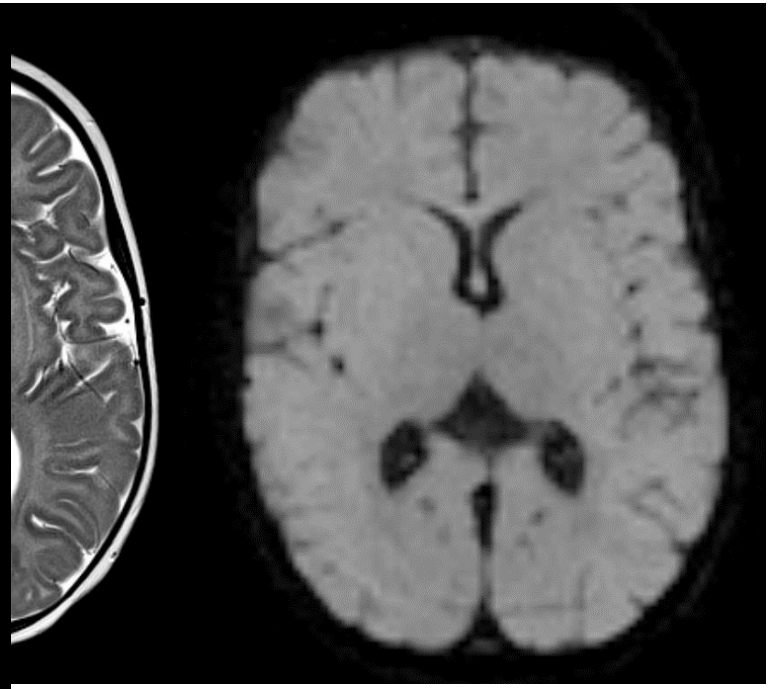


8-month-old boy. DD abusive head injury

Sphingolipidosis







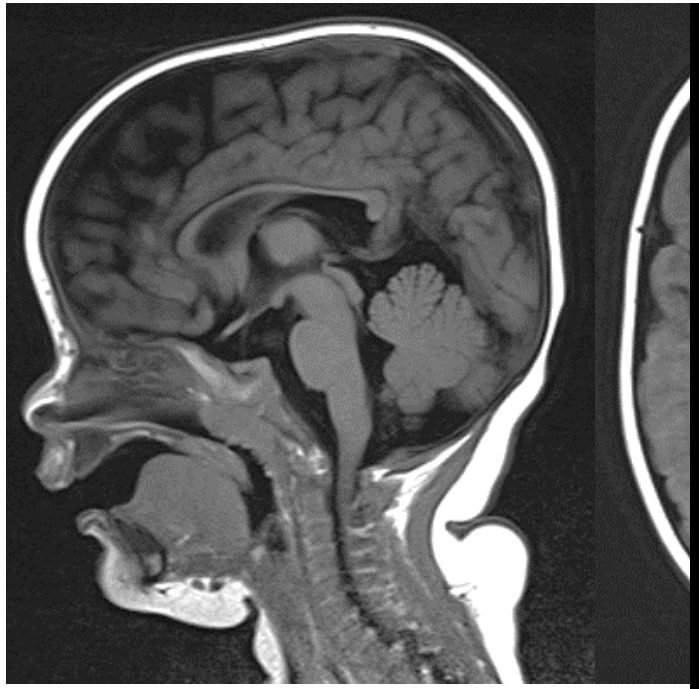
8-month-old boy with

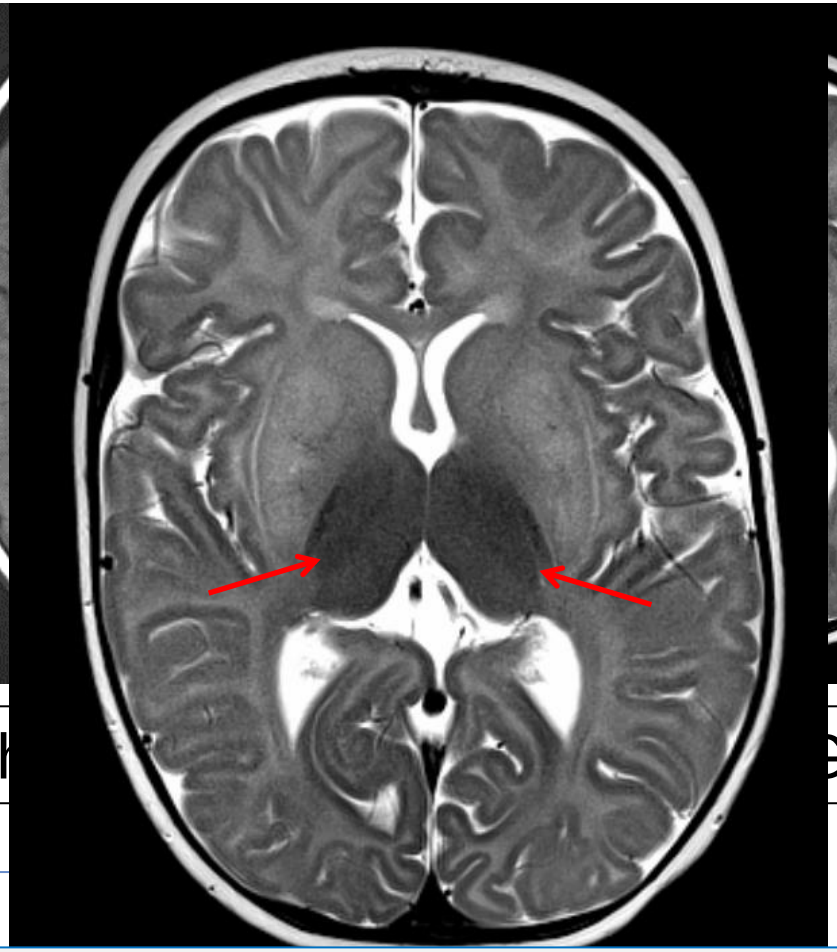
GM2 (Sanhof disease)

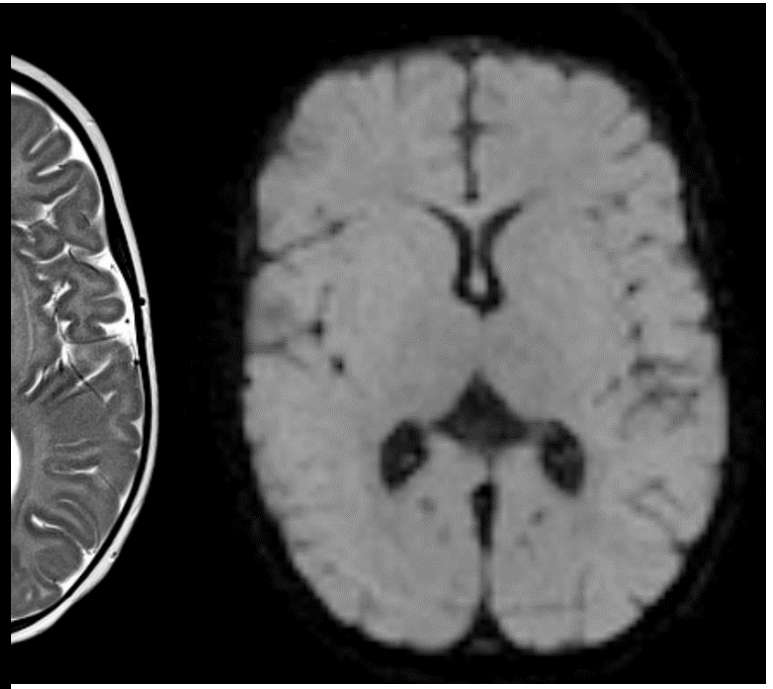
A cherry-red spot was identified in eye examinatio

Characteristic low SI in thalami on T2WI

Sphingolipidosis





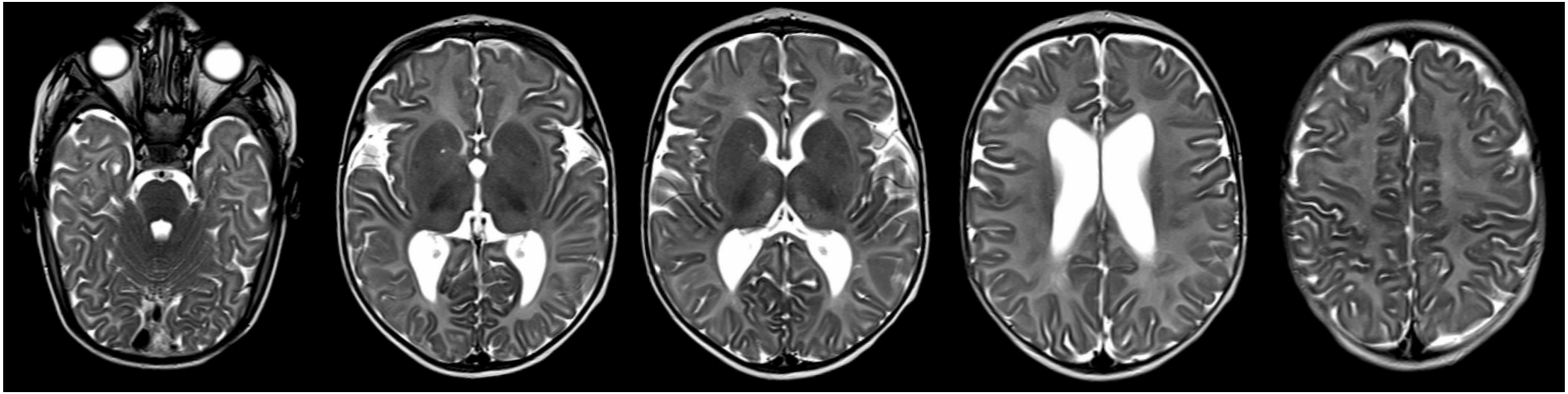


8-month-old boy with

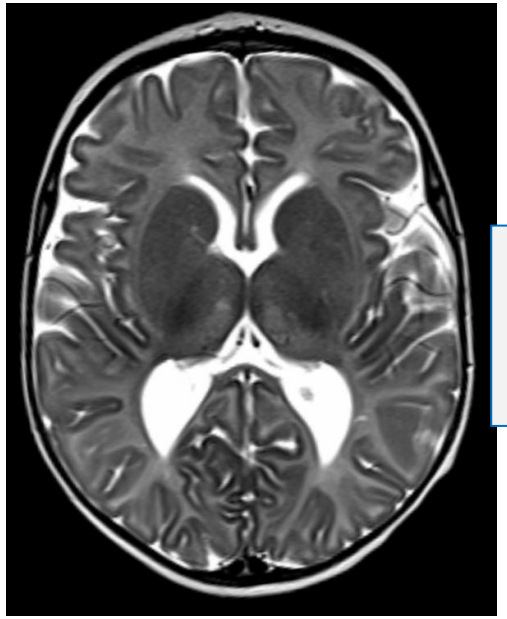
GM2 (Sanhof disease)

A cherry-red spot was identified in eye examinatio

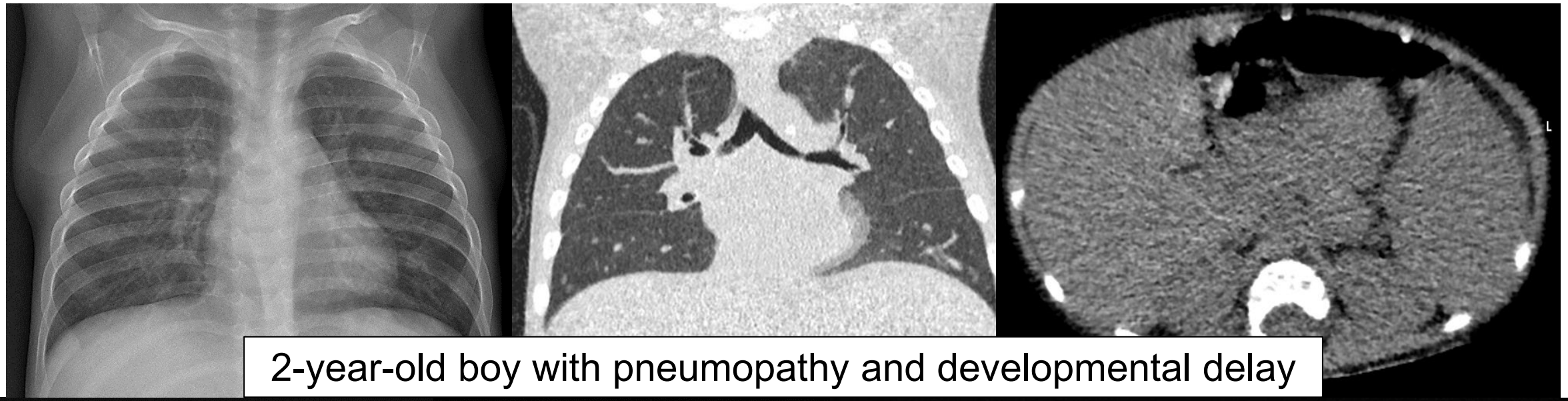
Characteristic low SI in thalami on T2WI



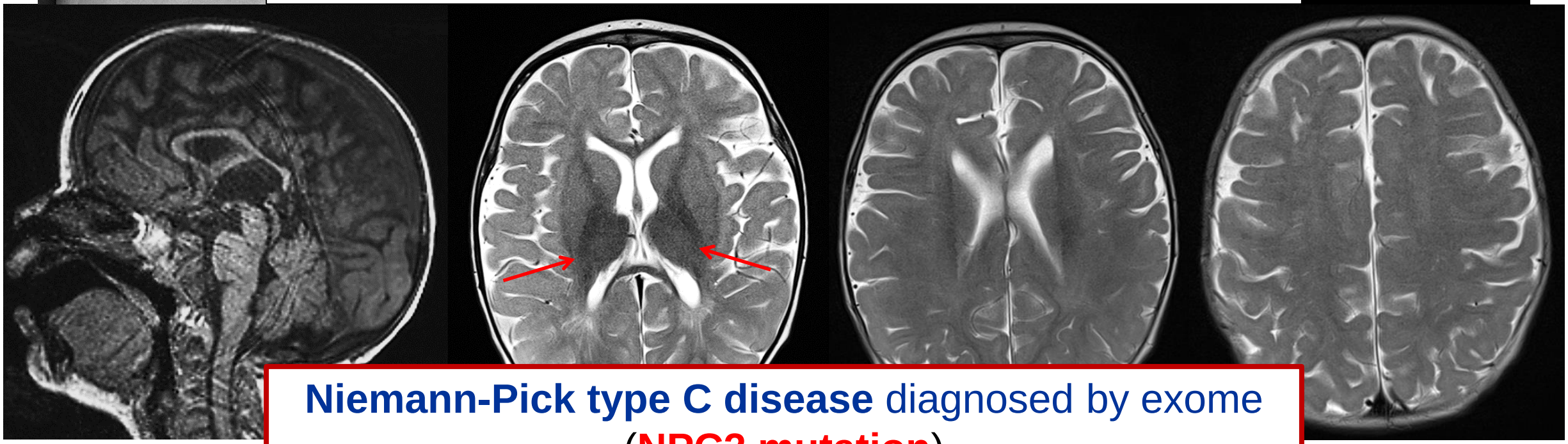
3-month-old boy with vomits, neutropenia and DD. **Gangliosidosis GM1**



Characteristic low SI in thalami on T2WI



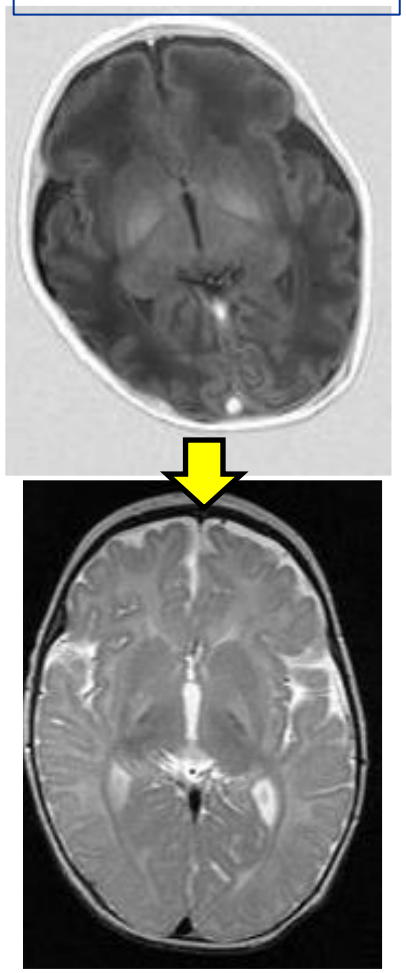
2-year-old boy with pneumopathy and developmental delay



Niemann-Pick type C disease diagnosed by exome
(**NPC2 mutation**)

DIFFERENTIAL DIAGNOSIS

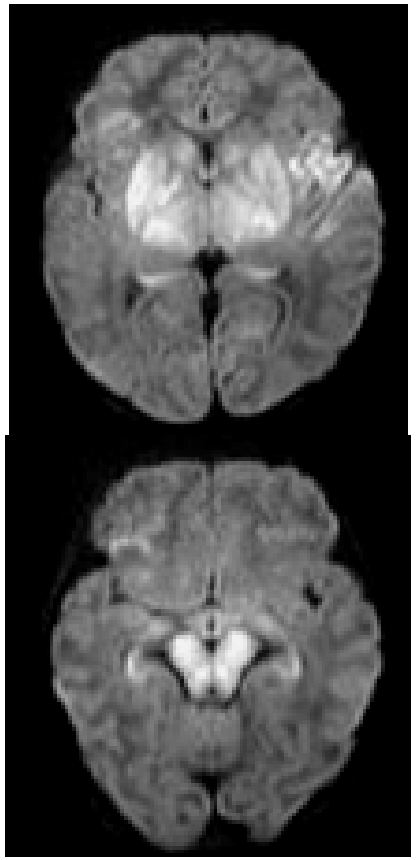
Kernicterus



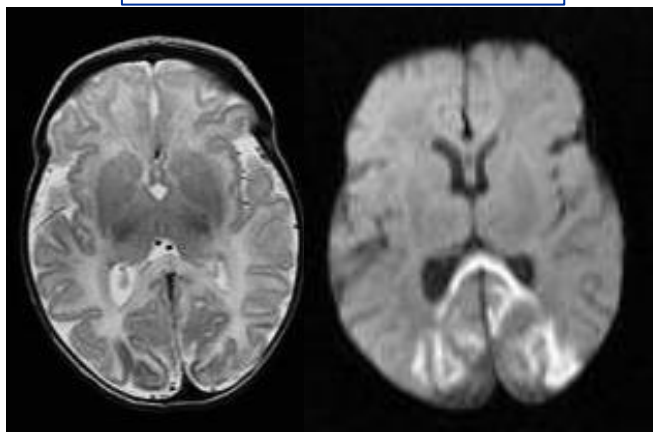
MIMICS

- Kernicterus/bilirubin encephalopathy
- Neonatal hypoglycemia
- Toxic encephalopathy
- Hypoxic ischemic encephalopathy

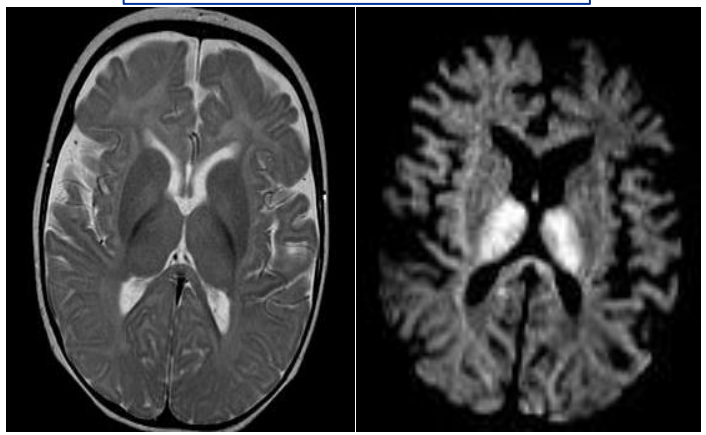
NN hypoxia

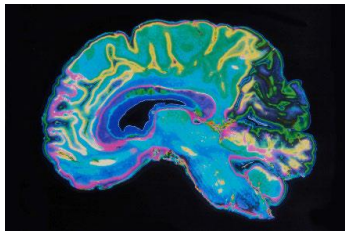


NN hypoglycemia



Vigabatrin toxicity

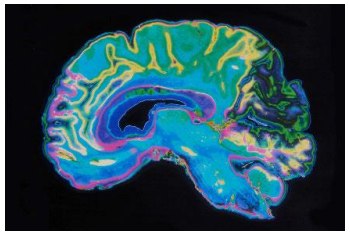




DYSTONIA

- **Third most prevalent movement disorder, most common after Parkinson**
- **PRIMARY DYSTONIA**
- Dystonia as the sole neurologic sign
- Classified into **early-onset** and adult-onset forms
- ***DYT 1*** and ***DYT 6***, the main two genes responsible for early onset of primary dystonia
- **SECONDARY DYSTONIA**
- Caused by environmental insults, such as head injury, drug side effects, or neurological disease
- **DYSTONIA PLUS SYNDROME**
- No acquired etiology, but with neurologic symptoms other than dystonia
- Includes dopa-responsive dystonia (DRD/DYT5), myoclonus dystonia (MD/DYT11), and rapid-onset dystonia-parkinsonism (RDP/DYT12)

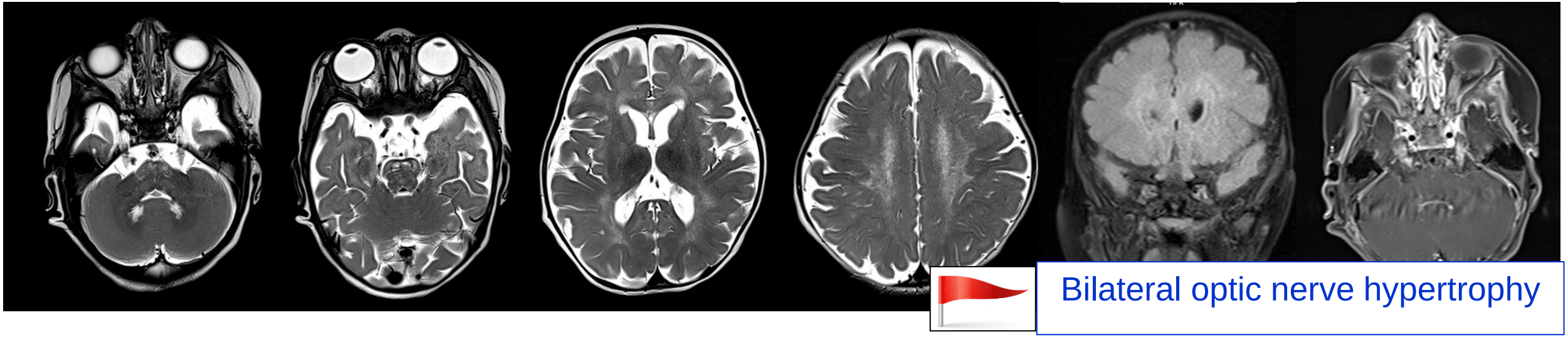
Pana A, Saggu BM. Dystonia. https://www.ncbi.nlm.nih.gov/books/NBK448144/



SECONDARY DYSTONIA

Hereditary disorders associated with neurodegeneration

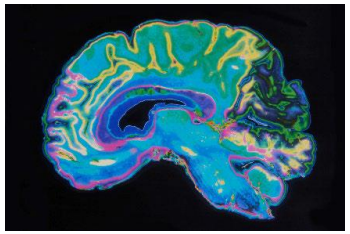
Krabbe disease



Bilateral optic nerve hypertrophy

A 6-month-old girl with neurological regression, dystonia, and hyperreflexia

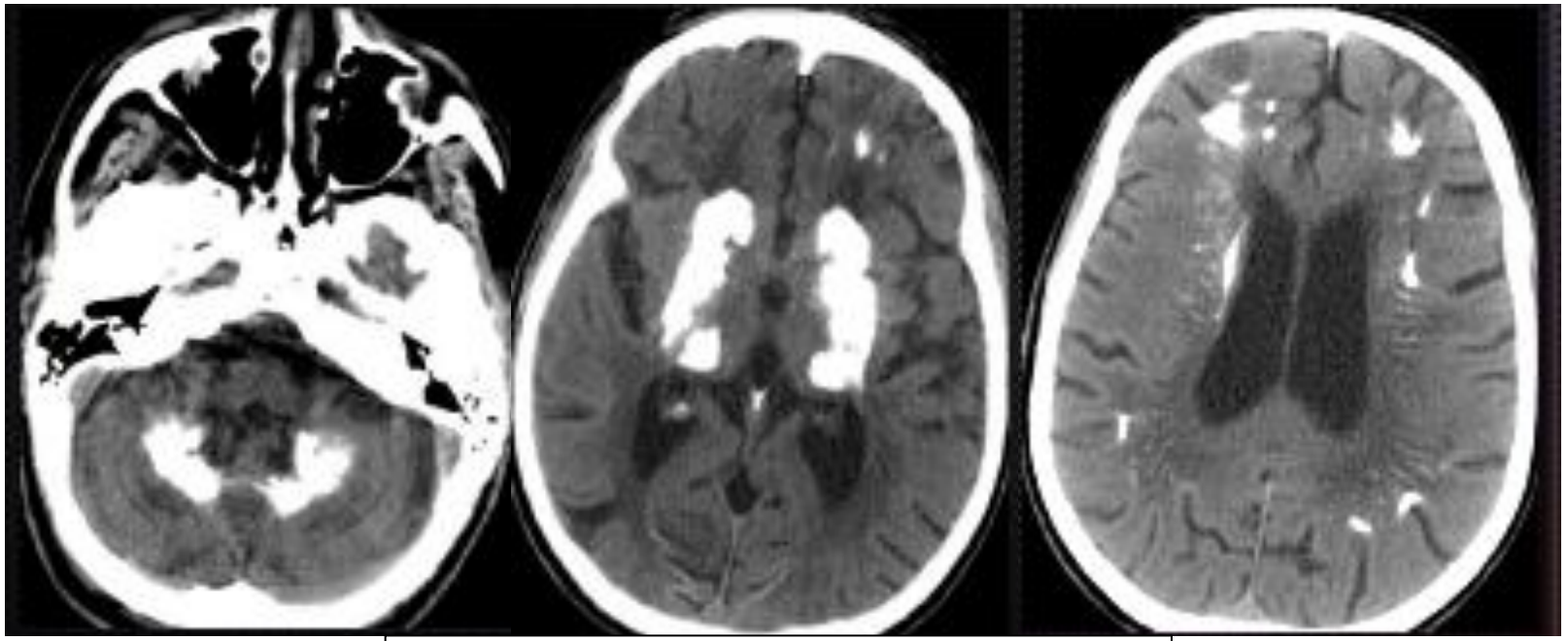
AR (*GALC*, 14q31)



SECONDARY DYSTONIA

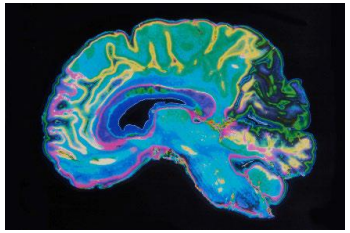
Hereditary disorders associated with neurodegeneration

Familial basal ganglia calcification (Fahr's disease)



Courtesy M. Jorquera
Hospital Clínico San Carlos. Madrid

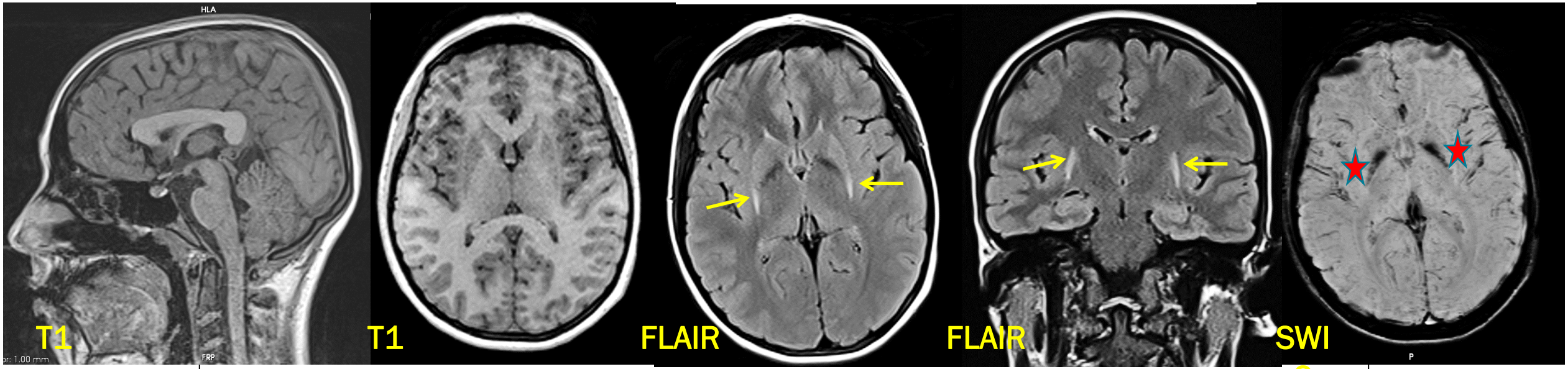
- AD disease
- **Calcifications** in BG, thalamus, cerebral WM, and cerebellar dentate nuclei
- Extrapyramidal symptoms 30-60 years, schizophrenia-like, and dementia



SECONDARY DYSTONIA

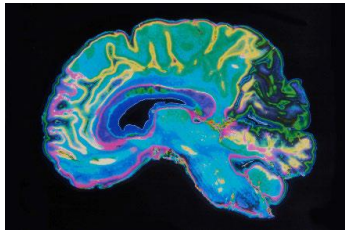
Hereditary disorders associated with neurodegeneration

GM1 gangliosidosis



Female, 19 years old. Generalized dystonia from 12 years of age
Bilateral putaminal lesion and excessive iron in globus pallidus

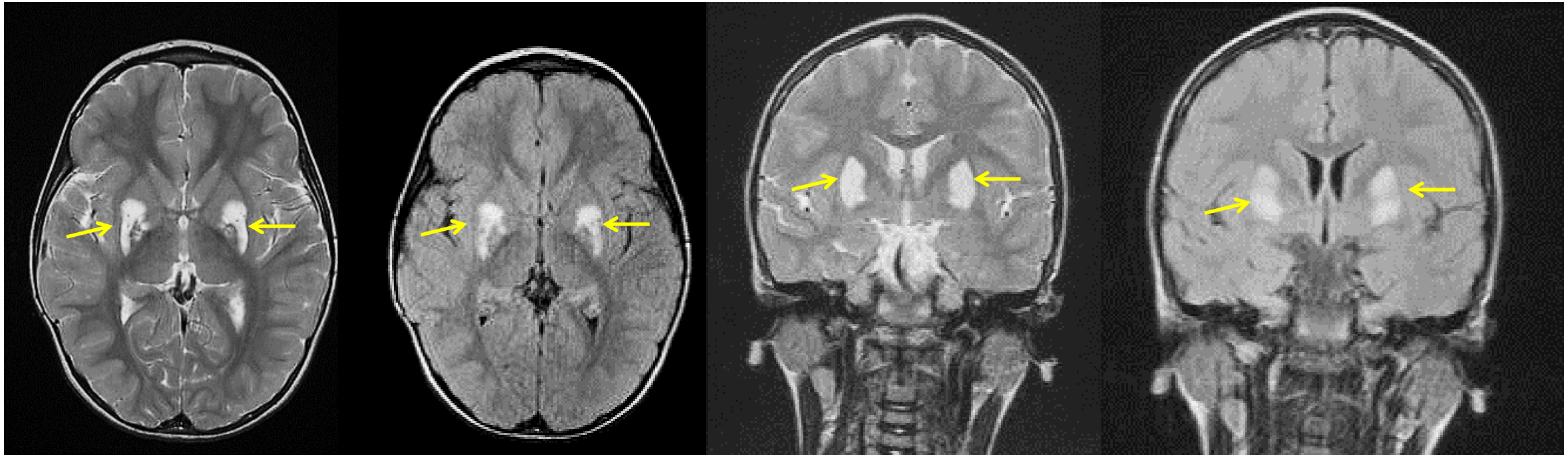
2

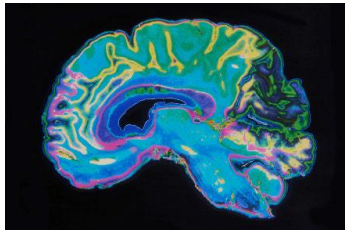


SECONDARY DYSTONIA

Hereditary disorders associated with neurodegeneration

Mitochondrial disease

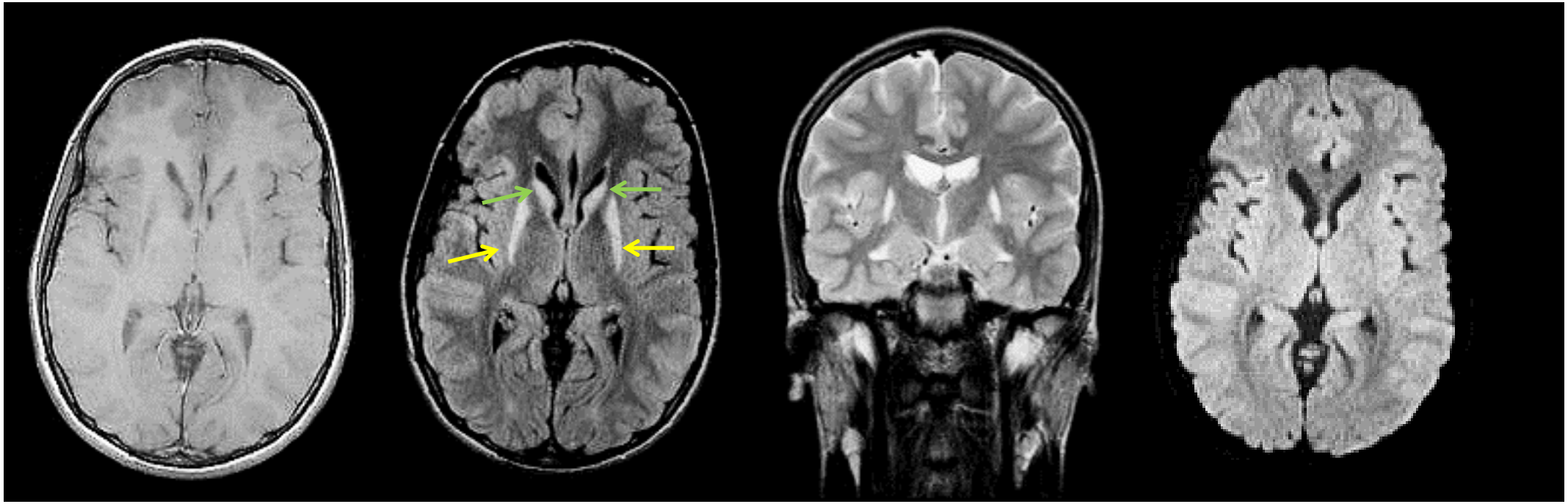




SECONDARY DYSTONIA

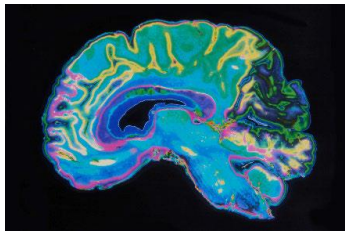
Hereditary disorders associated with neurodegeneration

Mitochondrial disease



Male 17 years. Chronic bilateral striatal lesion. Respiratory chain complex I.

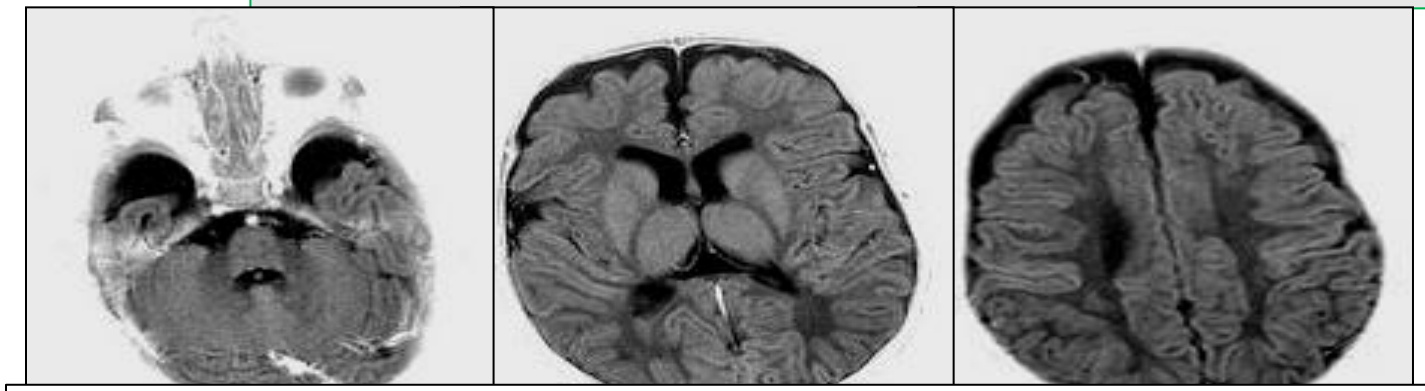
NDU6 mutation



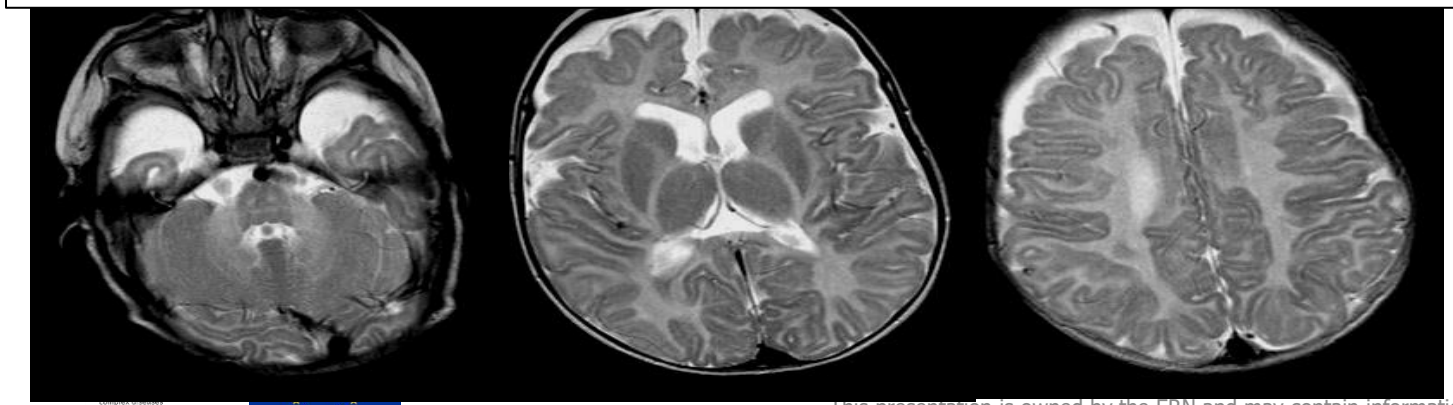
SECONDARY DYSTONIA

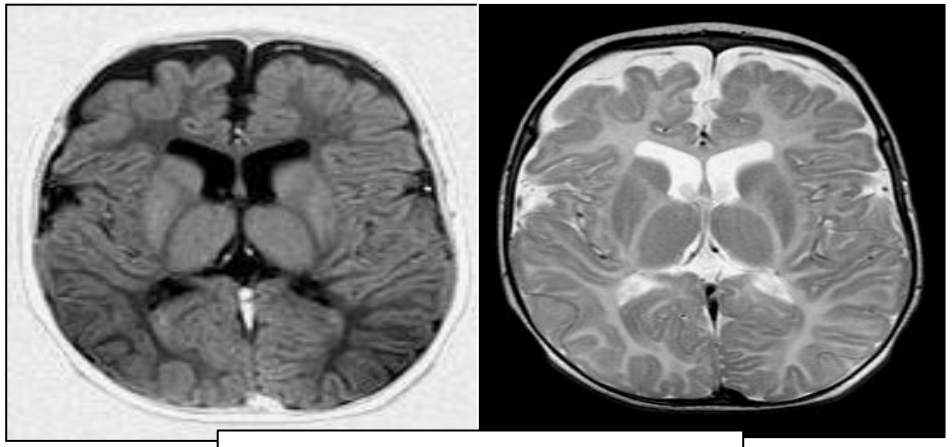
Hereditary disorders associated with neurodegeneration

Pelizaeus-Merzbacher disease



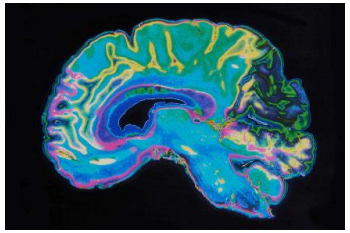
10-month-old boy, hypotony and global developmental delay





Follow 22 months

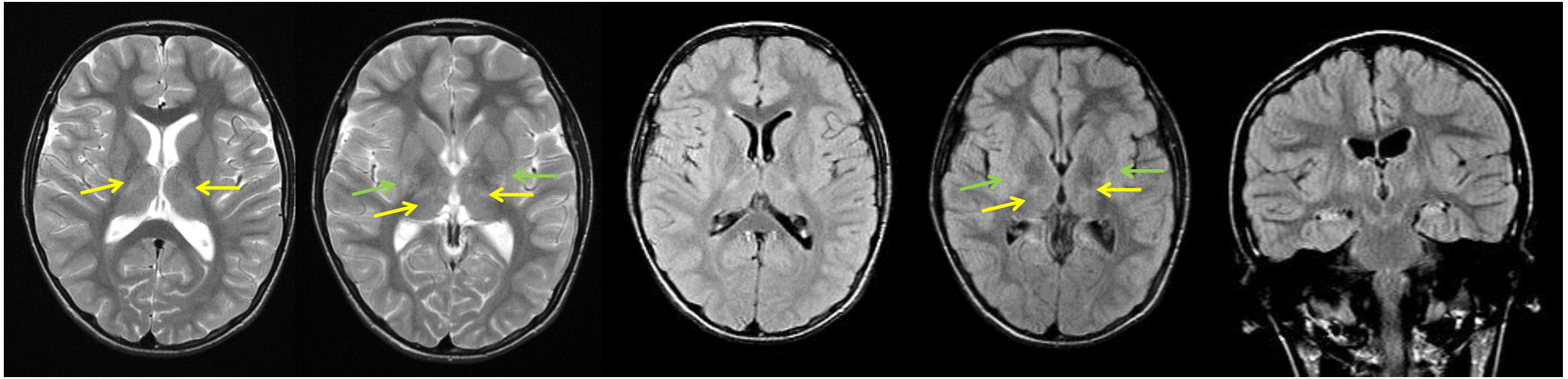
(*PLP1 Xq22*)
MALES



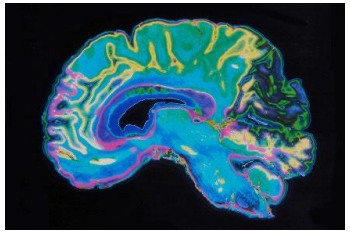
SECONDARY DYSTONIA

Acquired/exogenous causes

Perinatal cerebral injuries: Cerebral palsy



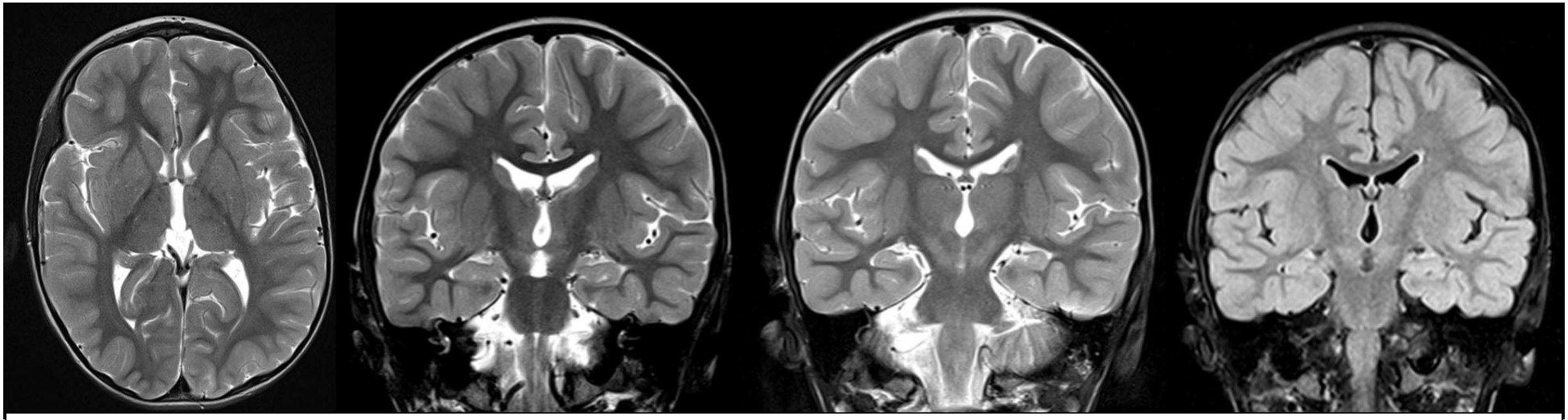
Male 7 years. Chronic bilateral thalamic and posterior putaminal lesion



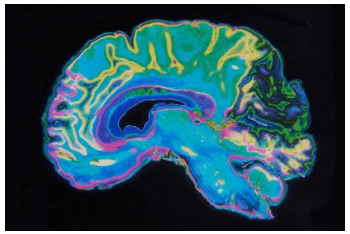
SECONDARY DYSTONIA

Acquired/exogenous causes

Perinatal cerebral injuries: Kernicterus



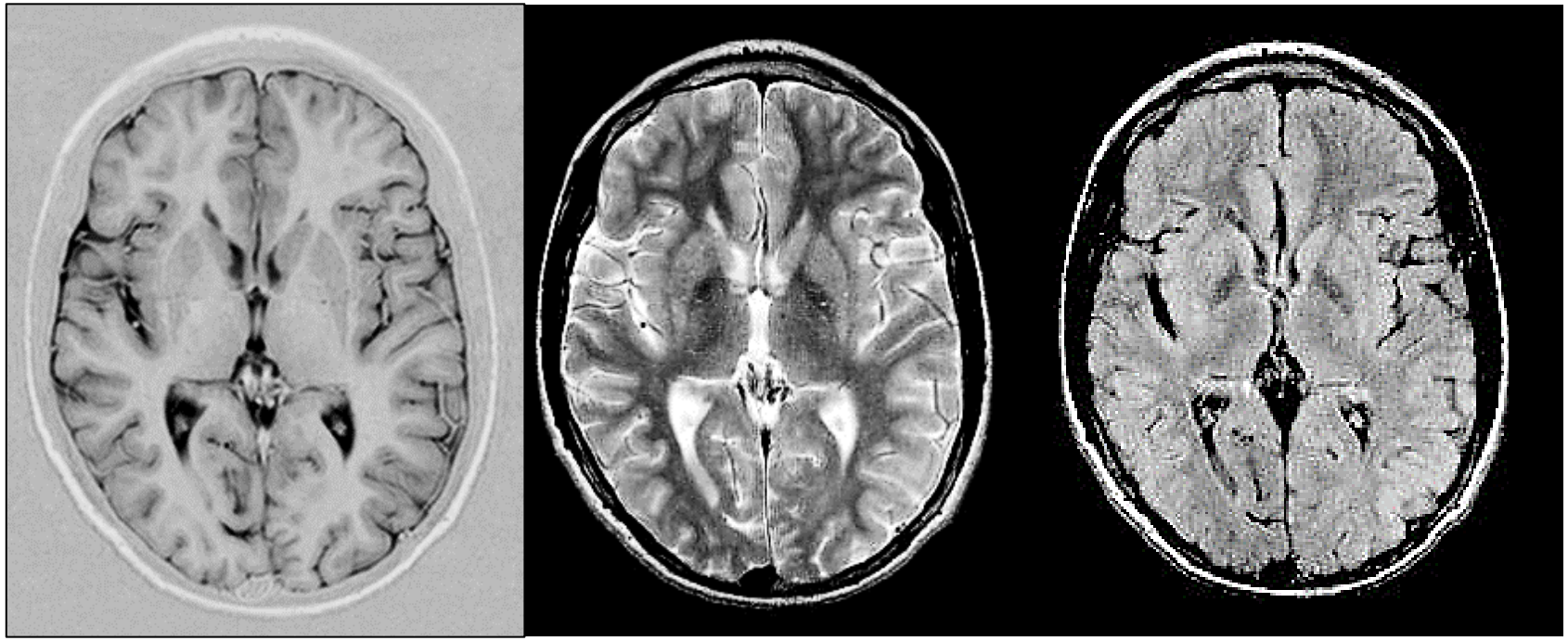
Male, 4 years, dystonic tetraparesis, sensorineural hearing loss, history of prematurity (26WG, 840g)
Subtle lesions involving bilateral globus pallidus and subthalamic nuclei

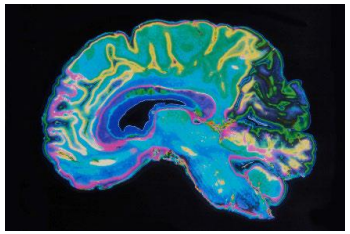


SECONDARY DYSTONIA

Acquired/exogenous causes

Vascular lesions: Stroke

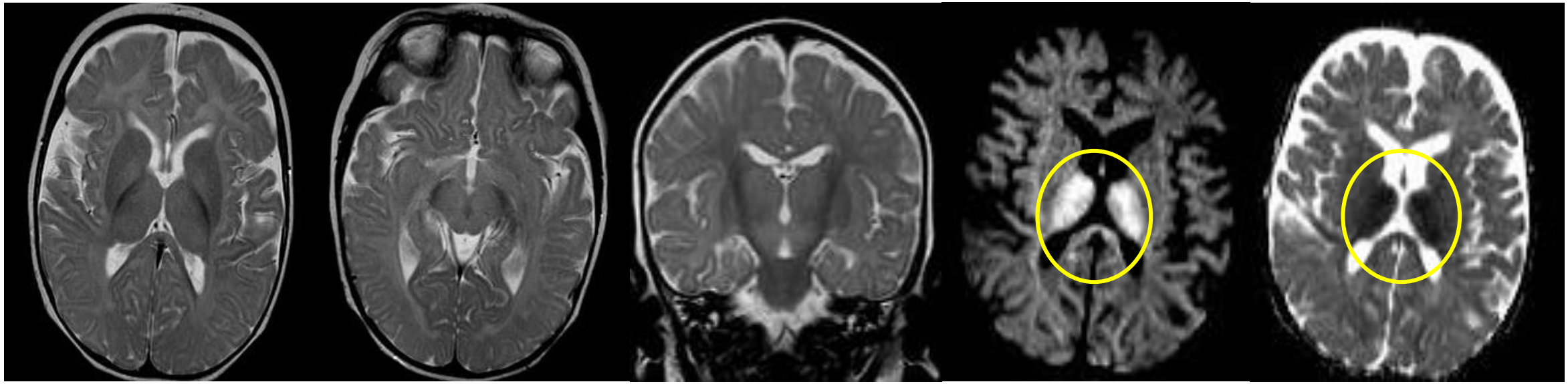




SECONDARY DYSTONIA

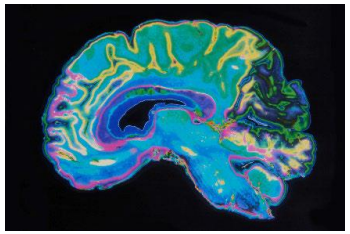
Acquired/exogenous causes

Toxics/Drugs



5-month girl with developmental delay and seizures.

Vigabatrin toxicity



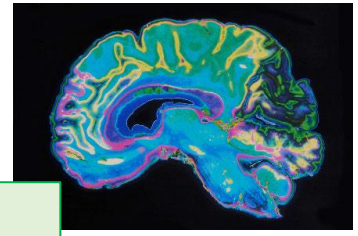
IMAGING ROLE IN DYSTONIA

- **DYSTONIA:**
- **Normal structural MRI**
- **Bilateral lesions in the basal ganglia**

• Wilson's disease
• Leigh's síndrome / mitochondrial disorders
• Post anoxic/ toxins/ acidosis
• Infantile striatal necrosis
• Hemolytic-uremic syndrome

- **HEMIDYSTONIA:**
- **Contralateral basal ganglia lesion**

- **DIAGNOSIS**
- **THERAPY DBS** (deep brain stimulation)
- **Preoperative MRI** for localization of the posteroventral globus pallidus
- Alternative diagnoses. anatomical variants
- **Preoperative CT** with stereotaxic frame and fiduciary markers
- Security. Dose reduction (ALARA)
- **Postoperative CT** with checking electrode placement
- Complications
- Follow-up



MRI protocol for stereotactic target assessment

3D MRI Navigation

Magnets

SIEMENS Avanto 1,5 T

SIEMENS Trio 3 T

- T1-weighted volumetric gradient echo sequence (3D-GRE). Axial **MPRAGE**
- 3D-FAST SPIN ECHO isotropic 3D T2-weighted. **T2 SPACE 3D** "Sampling Perfection with Application optimized Contrasts using different flip angle Evolution
- **Sagittal CISS** (Constructive Interference Steady State). High resolution T2 with greater anatomical detail and greater sensitivity in the differentiation between CSF and parenchymal structures
- T1-weighted volumetric gradient echo sequence (**3D-GRE) with IV contrast.** For vascular assessment
- Isotropic: The voxels generated by the 3D acquisition measure the same in each direction, 0.6mm x 0.6mm x 0.6mm, allowing images to be reformatted with equal resolution in either direction

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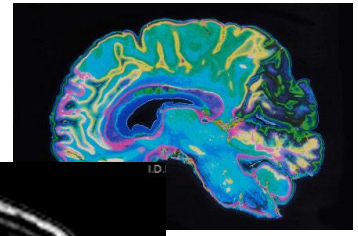
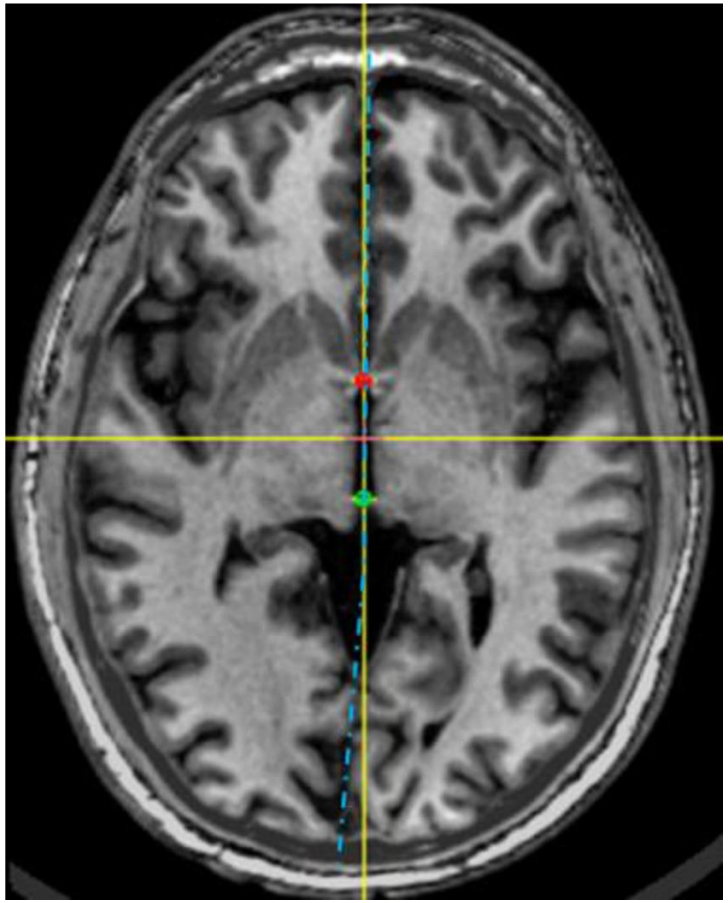
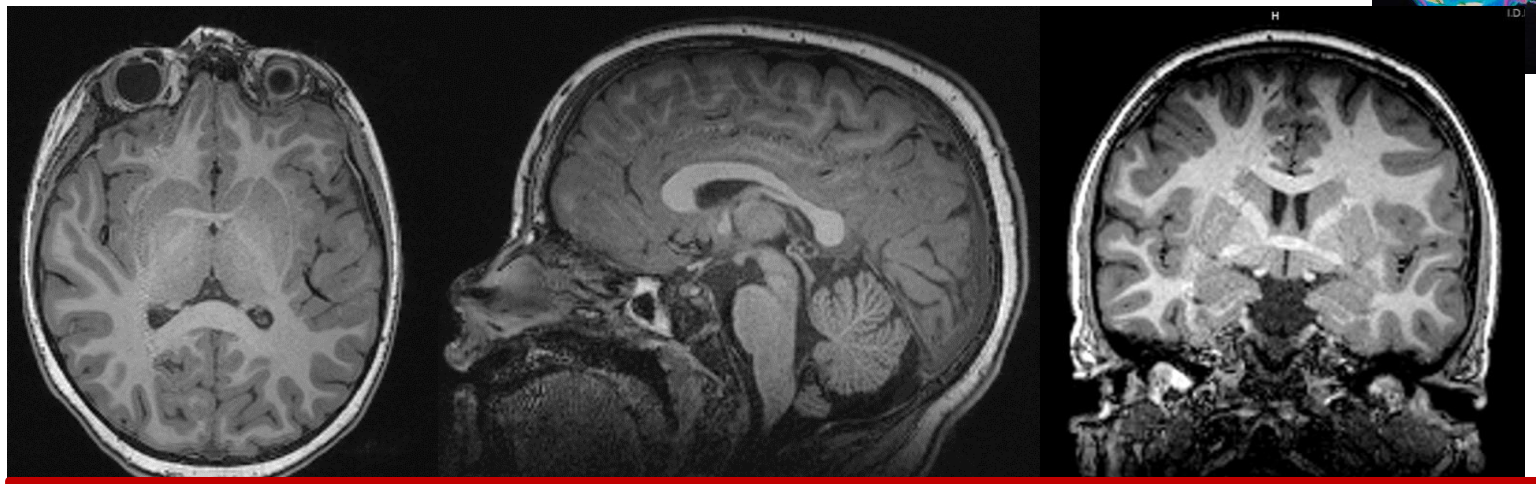
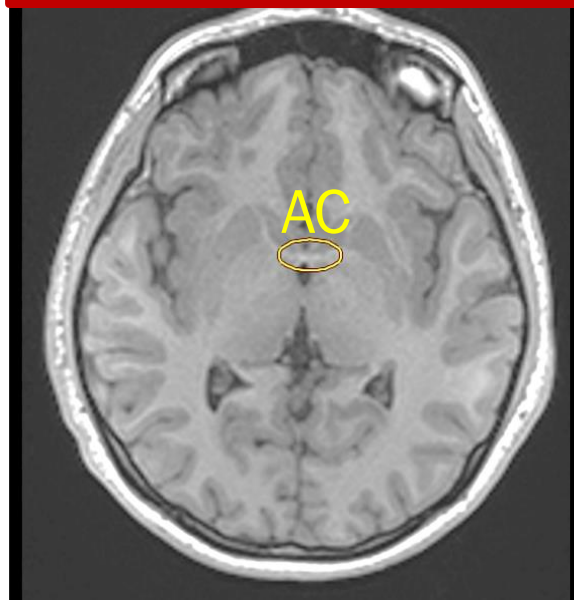
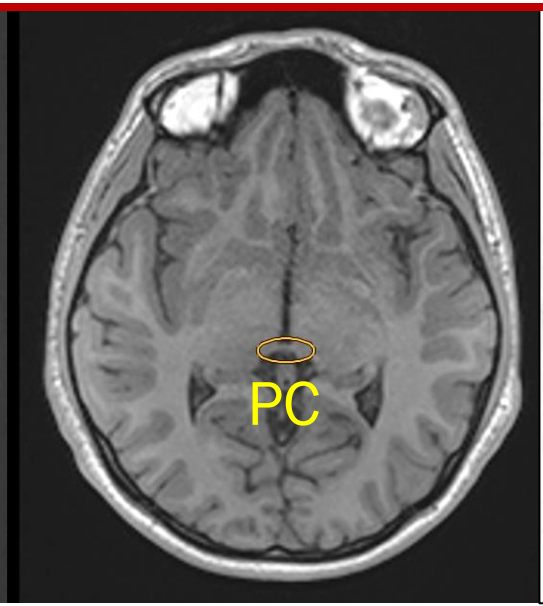


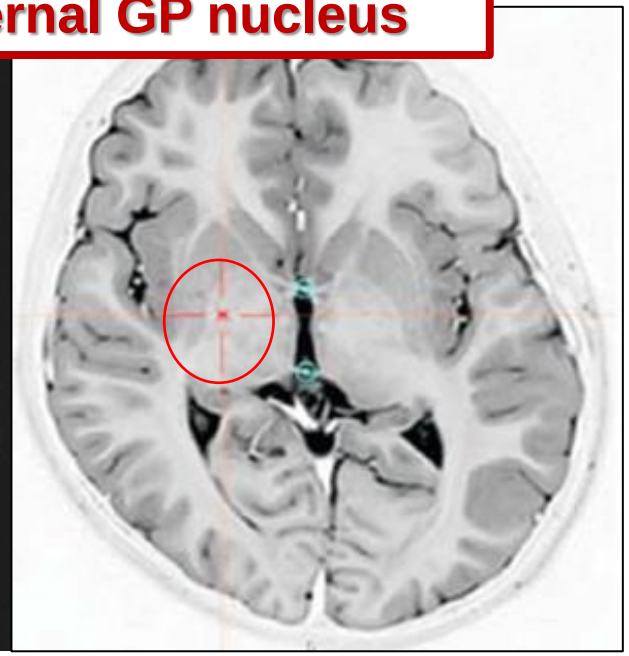




Target location: postero-ventral zone internal GP nucleus







European Reference Network for rare or low prevalence complex diseases
Network Neurological Diseases (ERN-RND)

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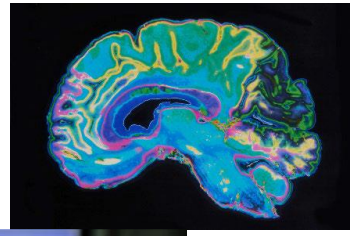
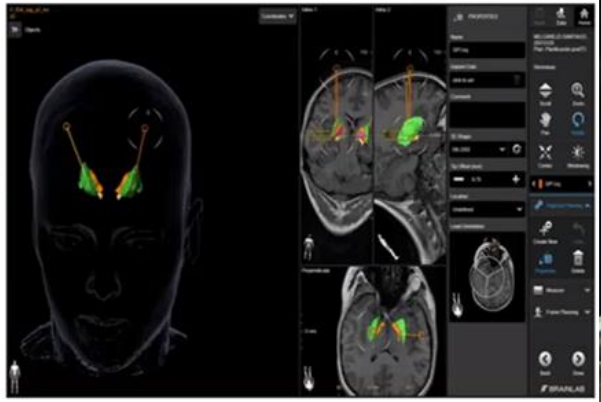
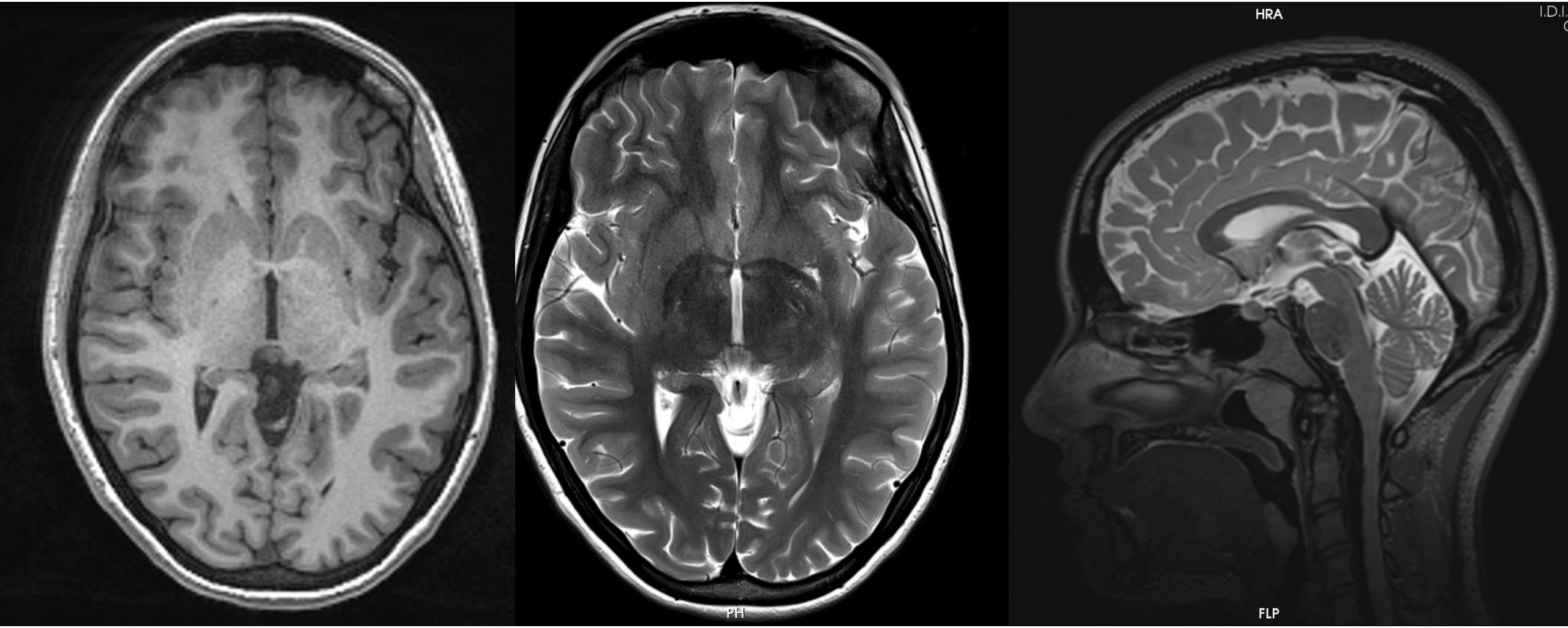


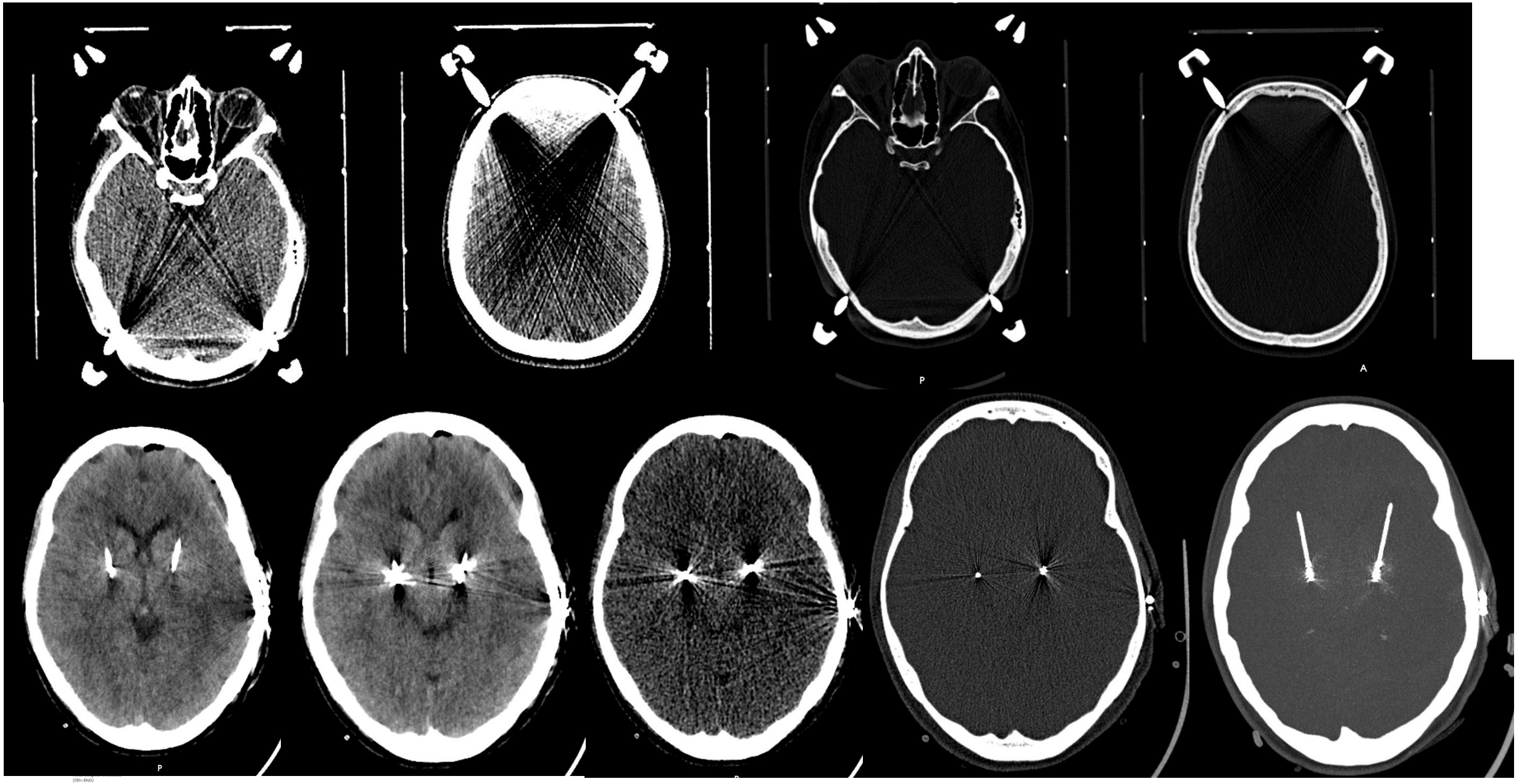
Stereotactic Software BrainLab. Elements



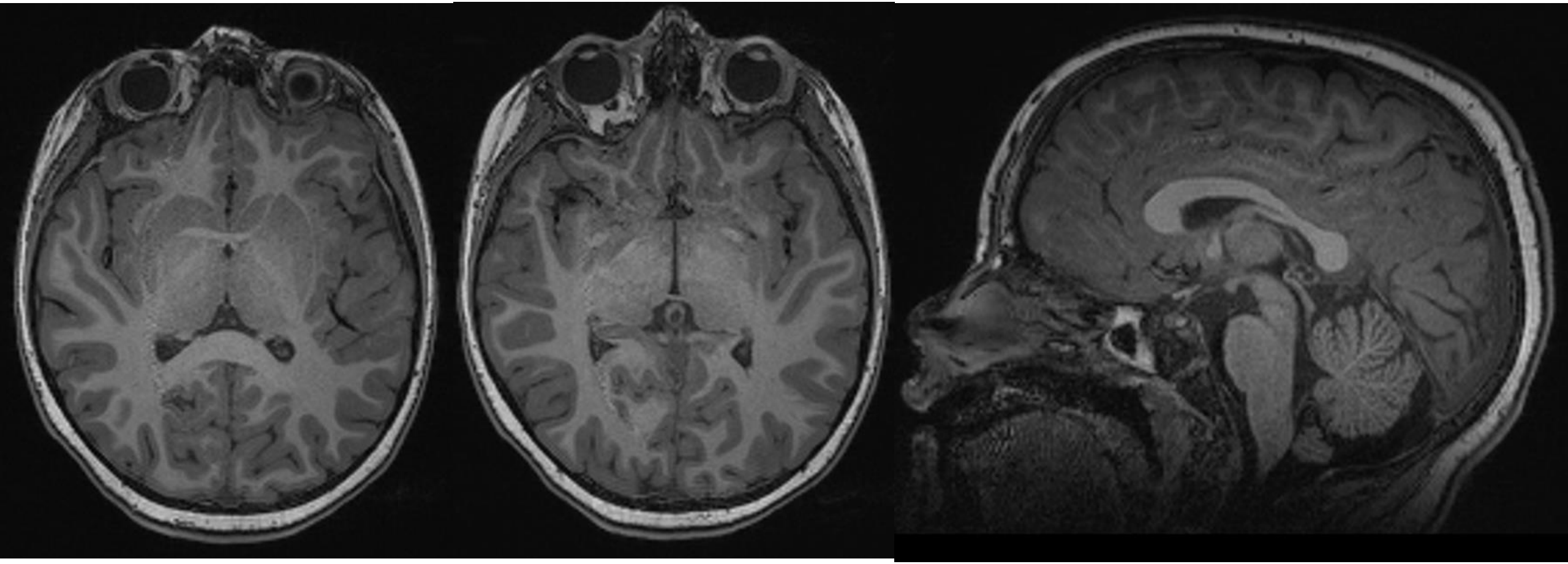
Marta G. 16 y.



Marta G. 16 y.



Darío L. 8 y.



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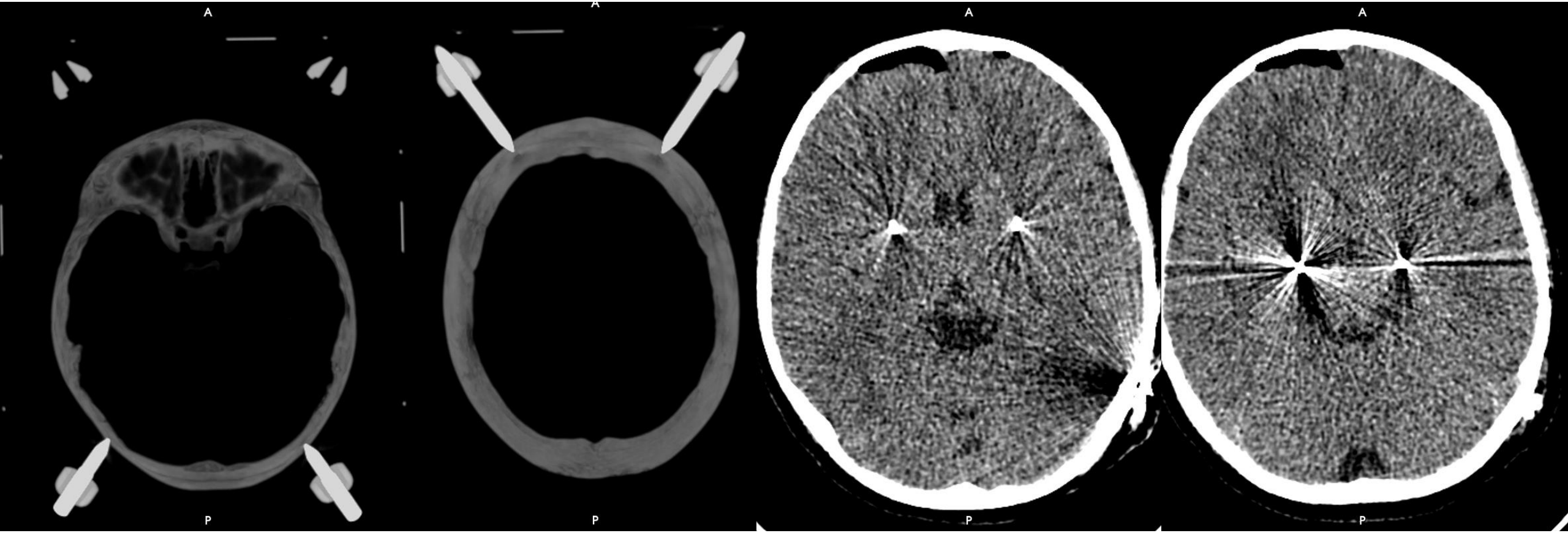

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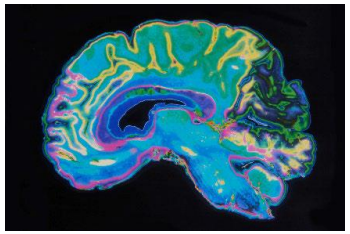
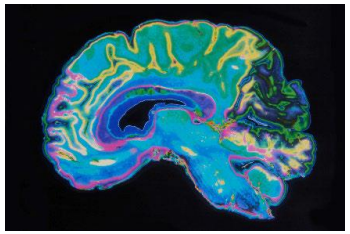


Pallidal Stimulation was safe and effective in children with genetic dystonia

- TOR1A, SGCE, GLB1 and GNAO1 (>40% improvement)
- SGCE gene (improvement >80%)

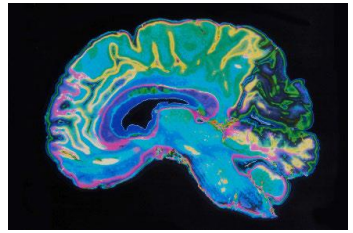
VHIR Pediatric Neurology Department
Vall d'Hebron hospital. Barcelona

Courtesy Dr. Ainara Salazar & Dr. Belen Pérez-Dueñas
Pediatric Neurology. Vall d'Hebron hospital. Barcelona



SUMMARY

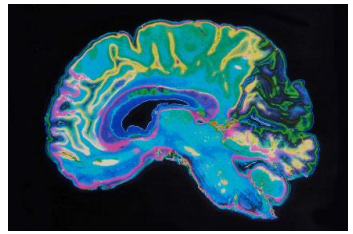
1. Nowadays, **MRI** is essential to detect and adequately characterize deep gray matter lesions in children
2. It is important to know **all the clinical data**, as well as the normal brain anatomy and myelination advances
3. DW imaging and MR spectroscopy provide functional information and improve the imaging diagnosis
4. Advisable to go deeper into **Neurogenetics** and into the knowledge of the **main MR phenotypes**
5. Required to integrate the MRI information with clinical and **genetic data**, working in **a multidisciplinary way** for adequate diagnosis and early treatment



Pediatric Radiology Department

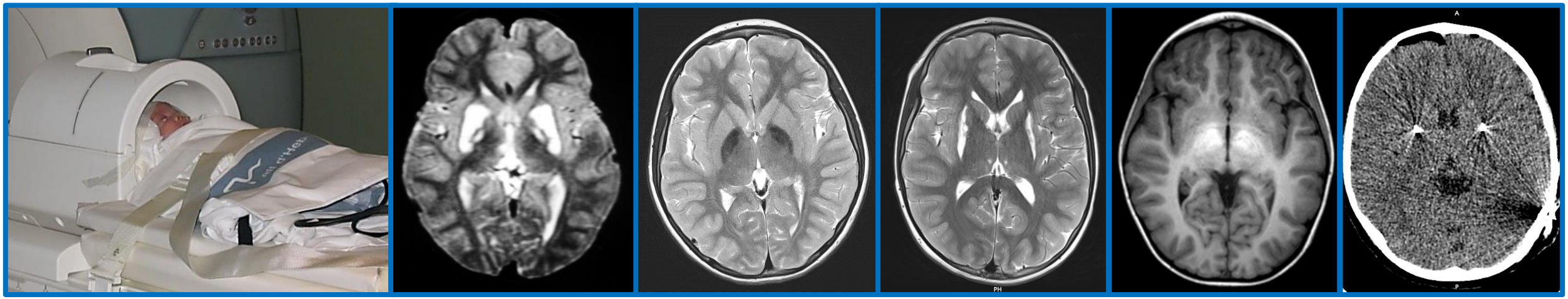
THANK YOU FOR YOUR ATTENTION

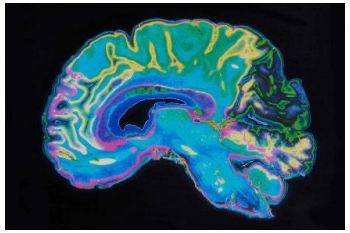
elidavazquez@vallhebron.cat



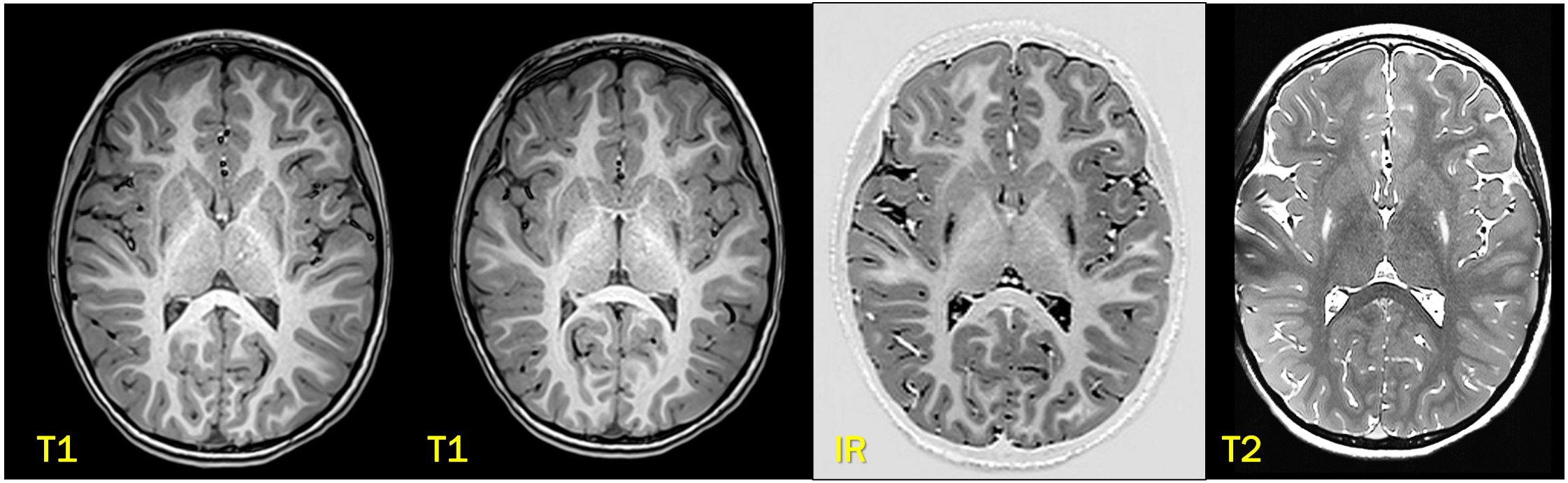
HYPERKINETIC DISORDERS QUESTIONS

Élida Vázquez, MD, PhD
Ignacio Delgado, MD
Hospital Vall d'Hebron. Barcelona

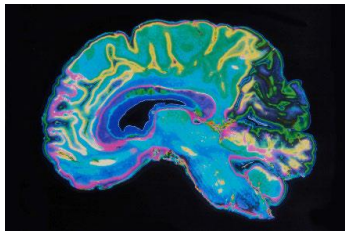




CASE 1 >>> NICO



Nico, male, 7 years old. Spastic-dystonic tetraparesis, with a right predominance



- What are the main MR imaging findings in Nico's case? (one option)

a. Bilateral thalamic lesion
b. Bilateral putaminal lesion
c. Bilateral globus pallidus lesion
d. Normal study
e. I don't know

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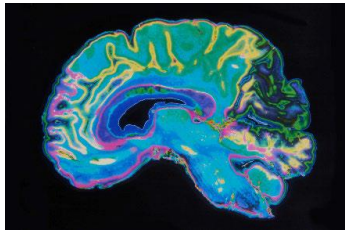
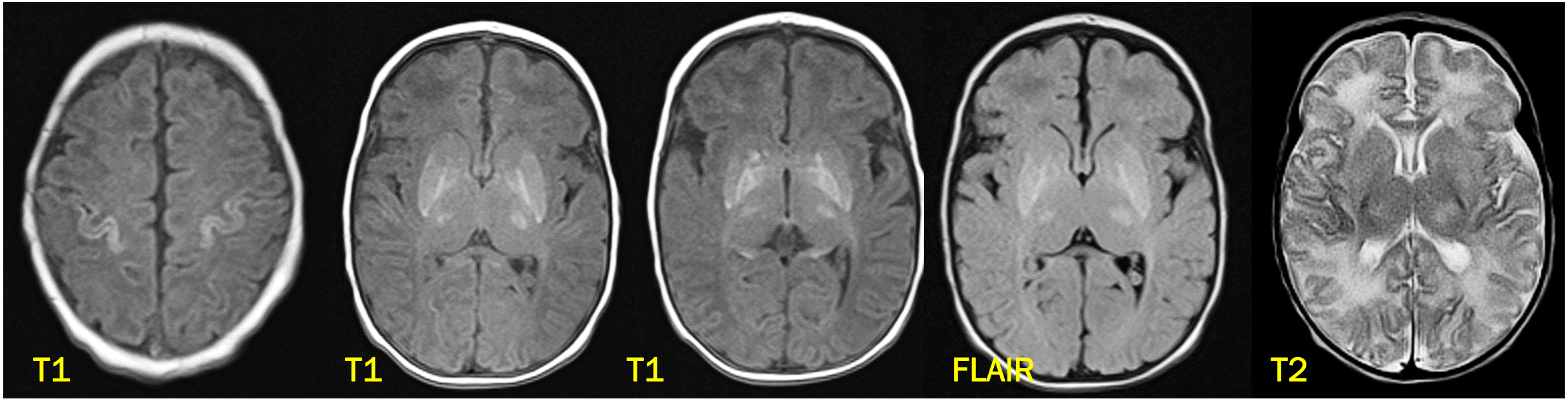
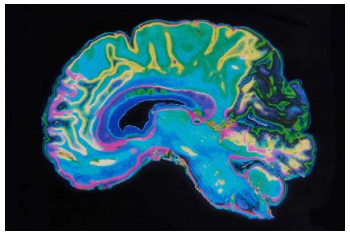


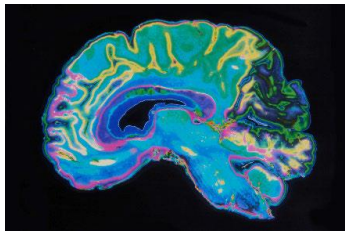


Nico, MRI performed at 10 days of age



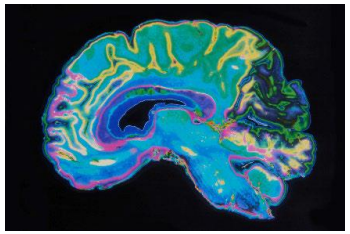
- What is the most likely diagnosis in Nico's case?

a. Leigh syndrome
b. Krabbe disease
c. Propionic acidemia
d. Hypoxic-ischemic injury
e. I don't know



Nico's clinical antecedents

- Term newborn 41+2 WG. 3300g
- Negative serology, low-risk ST, normal US
- Eutocic delivery in a home birth center. Apgar score 9/10
- **CR arrest** in 1st hour of life, being in the arms of his mother, and recovered after 10 minutes
- Normal metabolic study
- Normal echocardiography

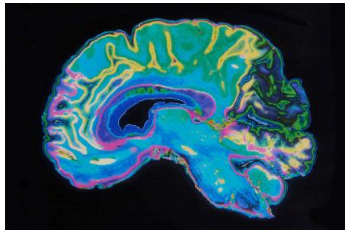


Nico's final diagnosis

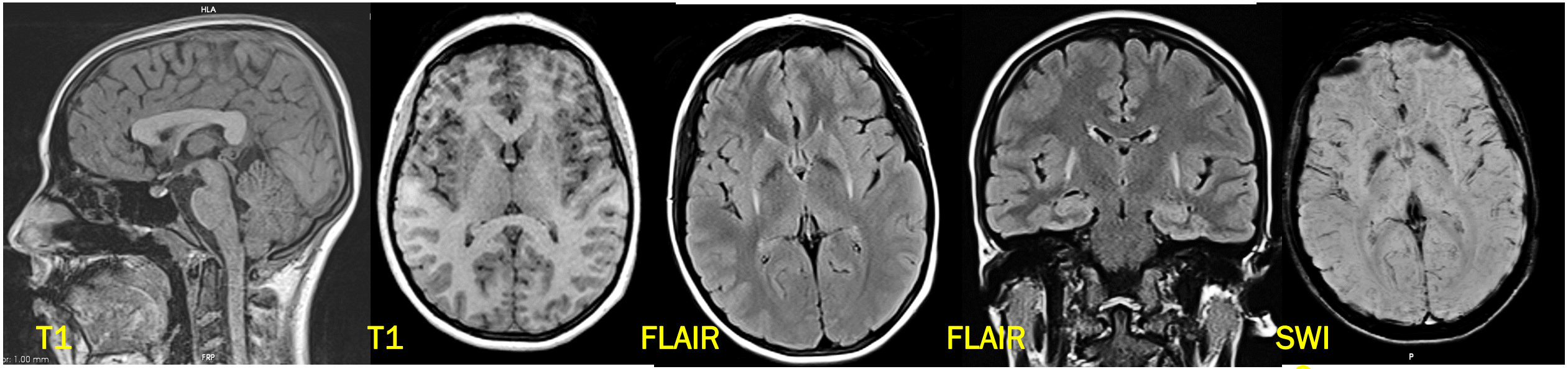
Neonatal hypoxic-ischemic injury, in the chronic stage

REFERENCE

Laporta-Hoyos O, Fiori S, Pannek K, Ballester-Plané J, Leiva D, Reid LB, Pagnozzi AM, Vázquez É, Delgado I, Macaya A, Pueyo R, Boyd RN. Brain lesion scores obtained using a simple semi-quantitative scale from MR imaging are associated with motor function, communication, and cognition in dyskinetic cerebral palsy. Neuroimage Clin. 2018;19:892-900.

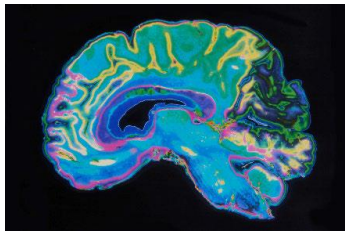


CASE 2 >>> ALBA



Alba, female, 19 years old. Generalized dystonia from 12 years of age

2



- What are the main MR imaging findings in Alba's case? (multiple answers)

a. Bilateral thalamic lesion
b. Bilateral putaminal lesion
c. Bilateral globus pallidus lesion
d. Excessive iron in both globus pallidus
e. I don't know

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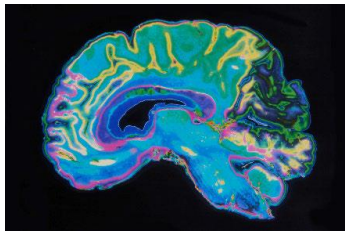
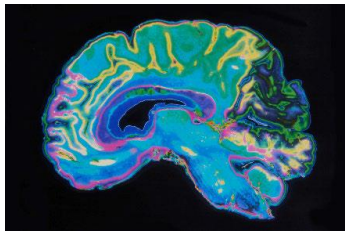


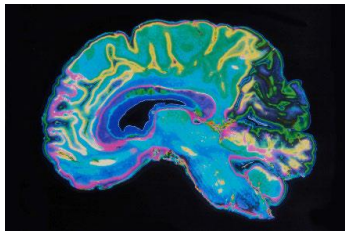
- What is the most likely diagnosis in Alba's case? (one option)

a. An NBIA disorder
b. Type III GM1 gangliosidosis
c. Urea cycle disorder
d. Krabbe disease
e. I don't know



Alba's clinical antecedents

- Normal pregnancy. Newborn at term, PN 2850g. No incidences in the perinatal period.
- She walked at 1 year of life. Normal language development in the first 3 years of life
- From the third year of life appears repetition of syllables and is diagnosed with dysphemia
- At 5 years of age, she was diagnosed with non-specific psychomotor immaturity
- Between 7-12 years of age, motor difficulties progressed with difficulty in jumping and running
- She was diagnosed with generalized dystonia at 12 years of age
- At 15 years of age, she was diagnosed with **gangliosidosis type 3,** with the presence in heterozygosis of the changes c.107 A>G and c.176G>A in the GLB1 gene; which was confirmed as pathological with significantly decreased enzyme activity (beta-galactosidase) activity



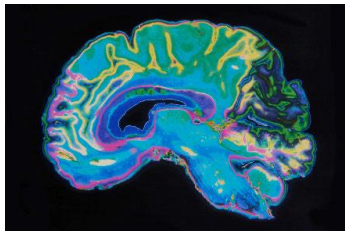
Alba's final diagnosis

Type III GM1 gangliosidosis

REFERENCE

Malik P, Muthusamy K, C M, Danda S, Sudhakar SV. Teaching NeuroImages: Wishbone pattern of iron accumulation: A characteristic imaging sign in GM1 gangliosidosis. Neurology. 2019;92(18):e2176-e2177.

ERN-RND Winter School Neuroimaging 2023



THANK YOU FOR YOUR ATTENTION

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