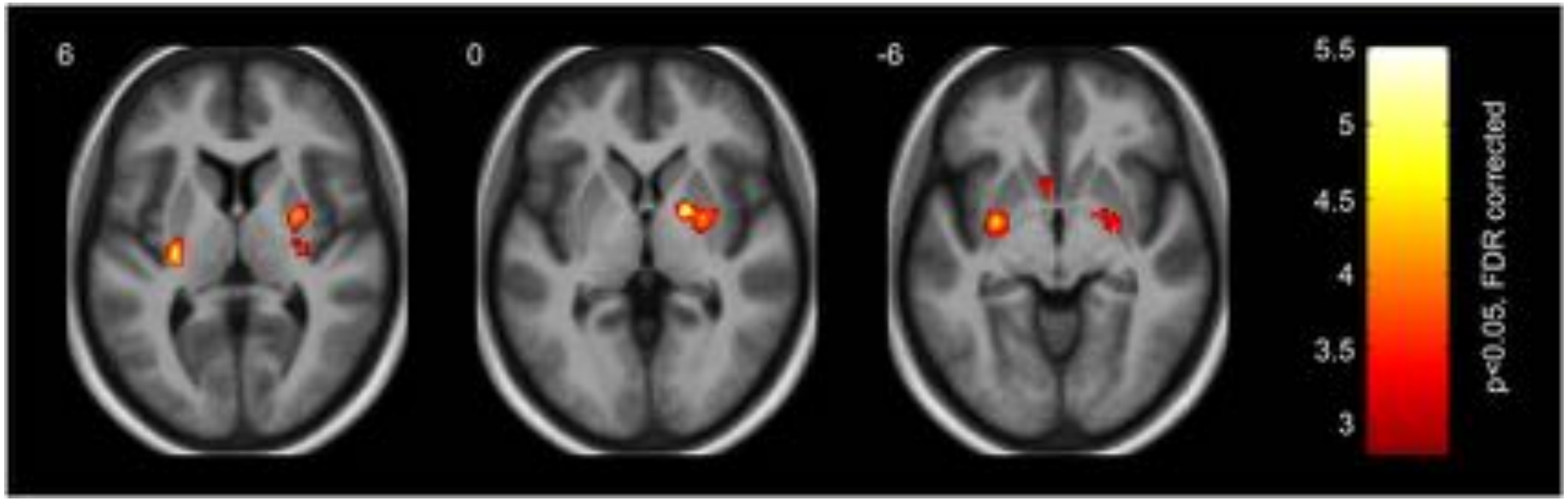

Bilateral Striatal Necrosis

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19 May 2021

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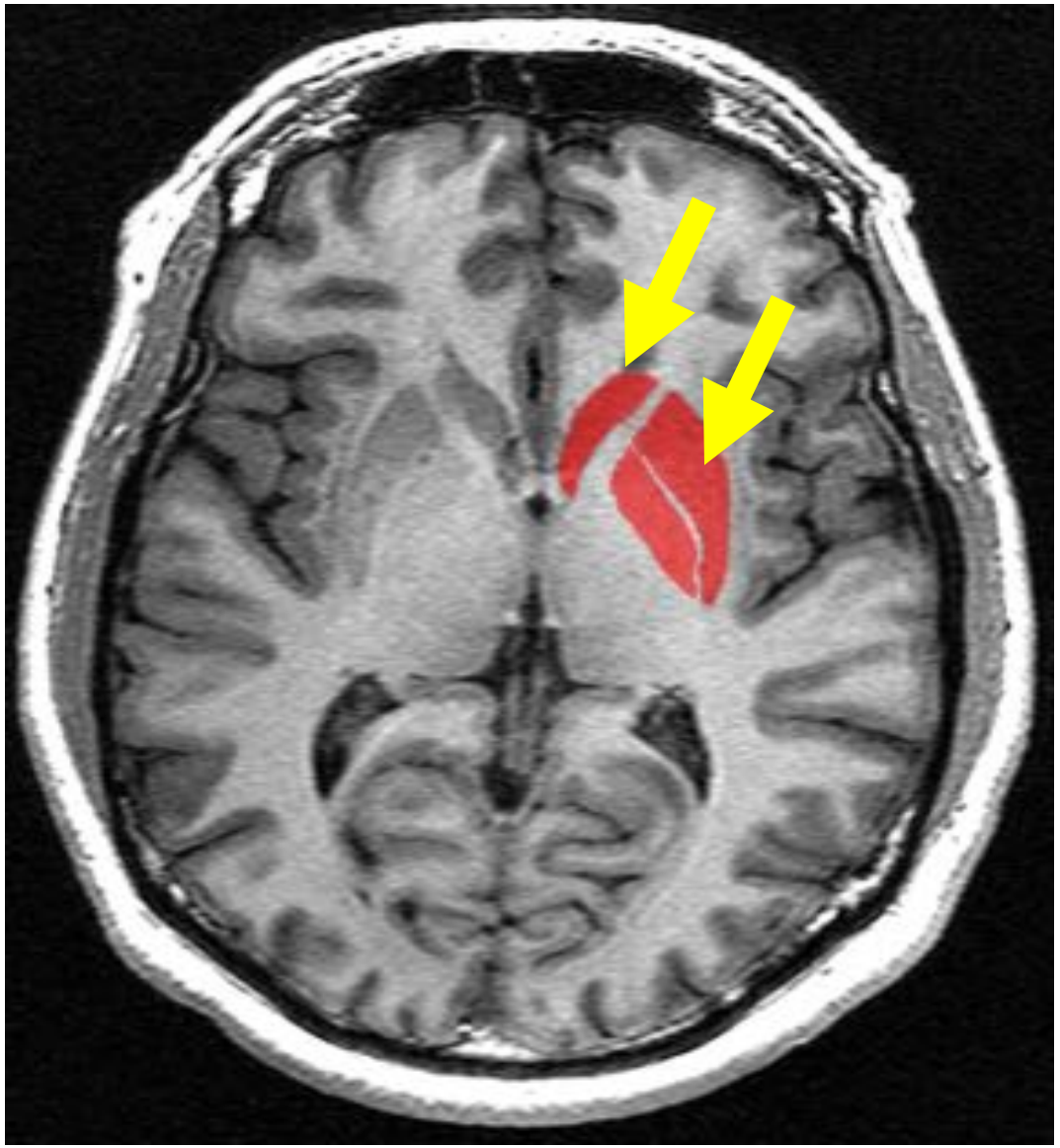
Introduction

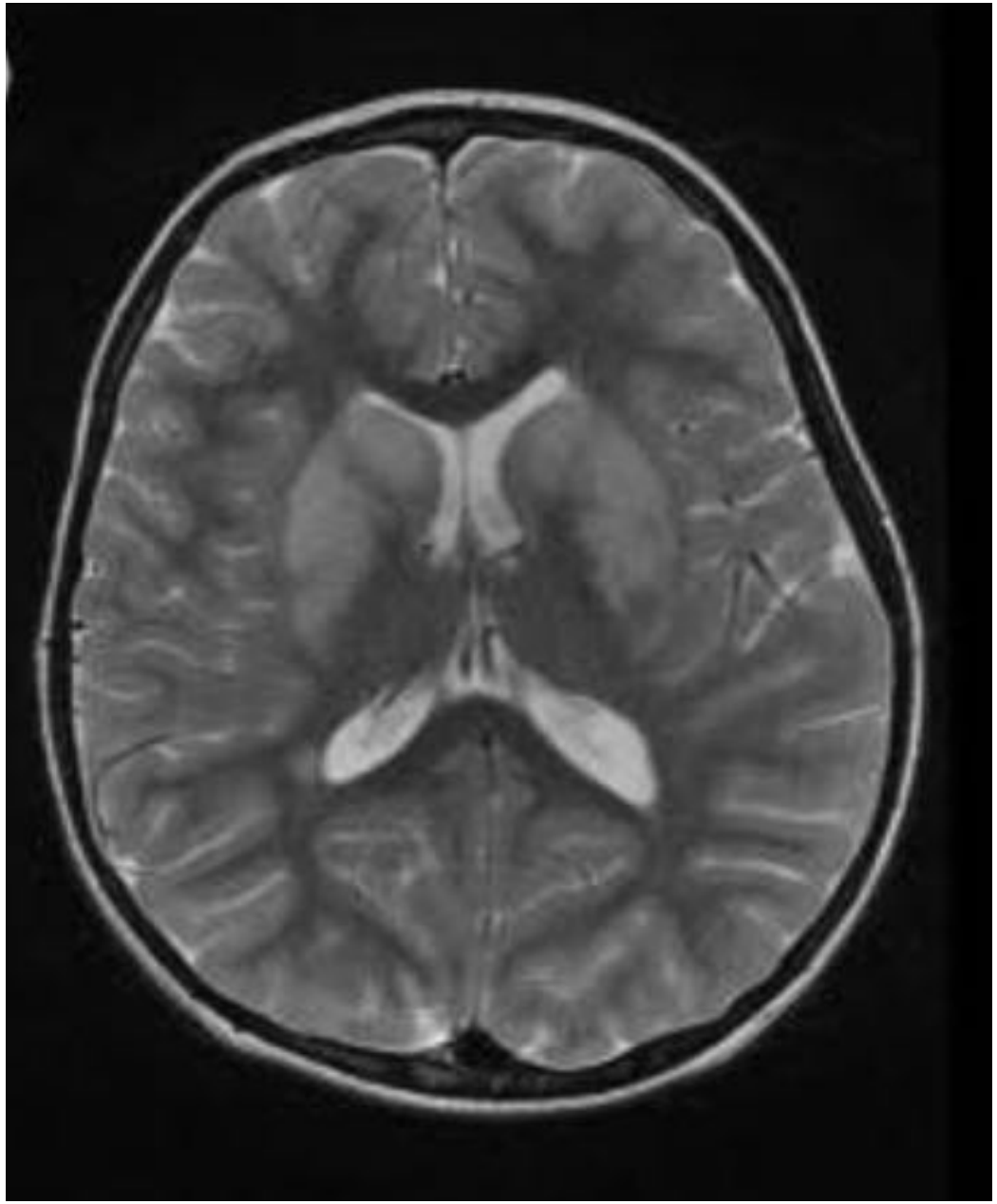
- Bilateral Striatal Necrosis is a **radiologica**l entity.
- Defined in 1975 to be involving the neostriata (putamen and caudate) with initial swelling and then degeneration and ultimately cellular necrosis.
- Striatal abnormalities can be observed in a large number of neurological conditions that are dominated by the presence of **movement disorders**.

ANATOMY

The striatum includes the caudate nucleus , and the lentiform nucleus (putamen and lower left the globus pallidus)



Bilateral Striatal Necrosis



Basal ganglia

Indirect pathway

Cortex

↓ Excitatory

Striatum
(putamen + caudate nucleus)

↓ Inhibitory

External globus pallidus

↓ Inhibitory

Subthalamic nuclei

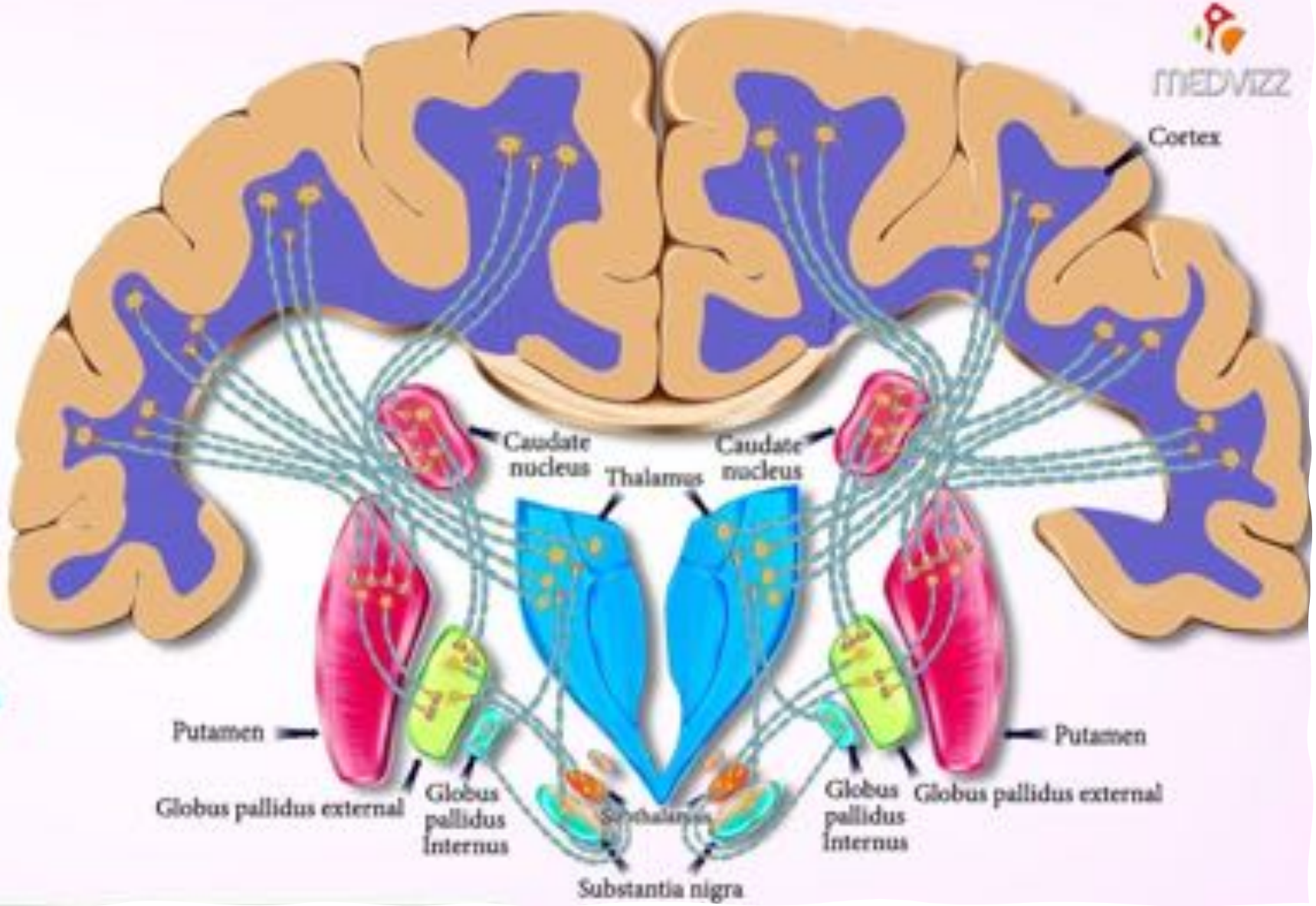
↓ Excitatory

Internal globus pallidus &
Substantia nigra pars reticulata

↓ Inhibitory

Thalamus

↓ Excitatory



When to think of Bilateral Striatal Necrosis (Clinical Presentation)

- Acute / Subacute onset of:
- Dystonia
- Extra-Pyramidal component
- Lethargy
- +/- other systemic involvement

Causes of Bilateral Striatal Lesions

- A: **Causes of Bilateral Striatal Necrosis**
  - Acquired
    - Infectious and Post-Infectious
  - Inherited
    - Mitochondrial
    - Organic Acidurias
    - Thiamine Transport Disorders SLC19A3, SLC 25A19,
    - NUP62 – Related Disorders
- B: **Striatal Lesions PLUS**
  - Acquired
  - Inherited

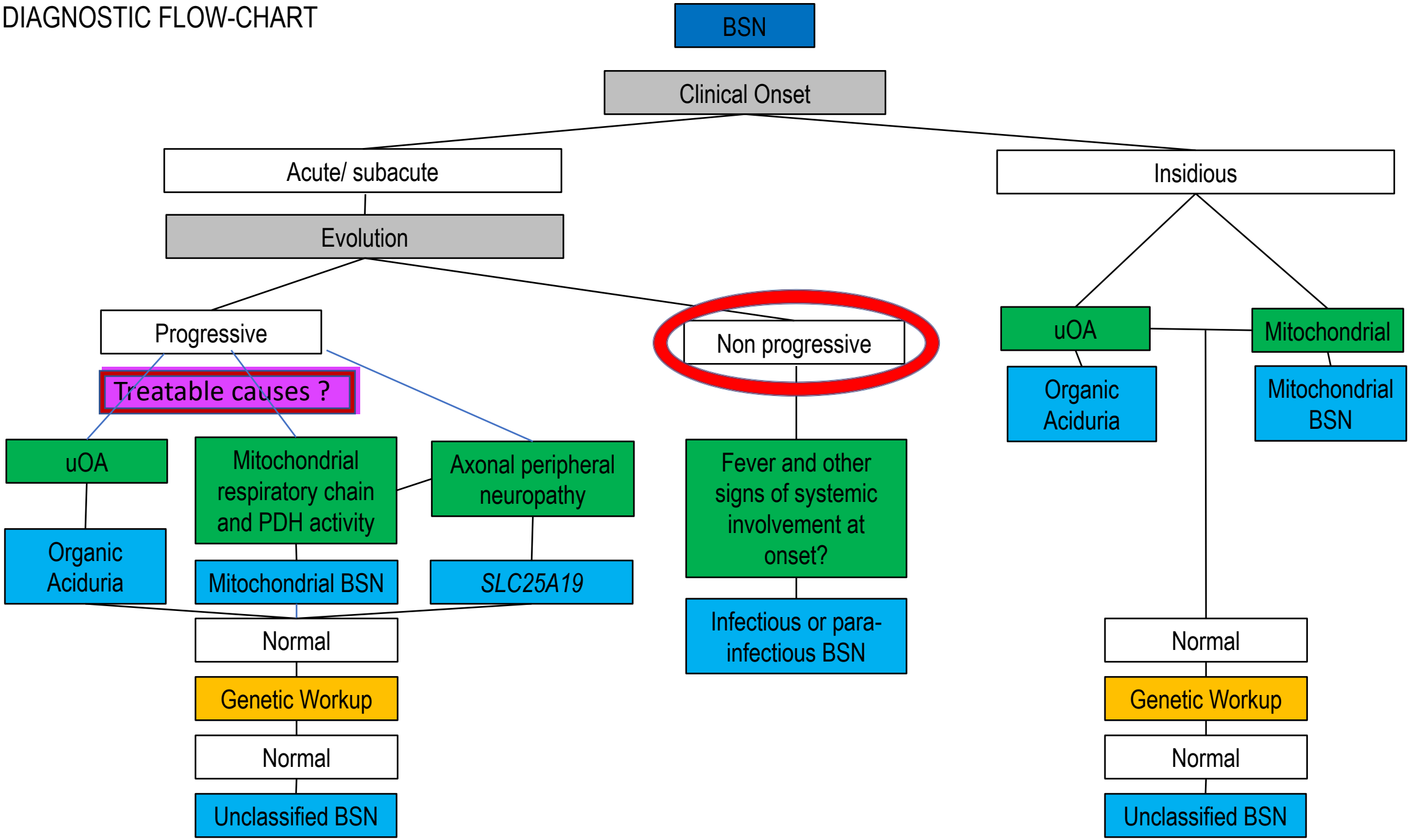
SL-plus
Acquired

- **Hypoxic- ischemic** brain injury in term newborns
- Symptomatic **hypoglycaemia**
- Organophosphate, methanol, **carbon monoxide poisoning**
- **Cardiac arrest and stroke**
- Brain **tumours**
- Creutzfeldt–Jakob's disease
- Systemic lupus erythematosus (**SLE**)
- **Autoimmune** encephalitis, particularly anti-D2R encephalitis and more rarely anti-NMDAR encephalitis
- Rasmussen's encephalitis

SL- plus
Inherited

- **ADAR1-**Related Disorders
- Sulfite Oxidase and Molybdenum Cofactor Deficiency
- **Alexander's** Disease
- GM2 Gangliosidosis
- Giant Axonal Neuropathy
- H-ABC (Hypomyelination with Atrophy of Basal Ganglia and Cerebellum)
- **Wilson's Disease**
- Huntington's Disease and Neuroacanthocytosis Syndromes
- COASY Deficiency (**NBIA)**
- Neuroferritinopathy

DIAGNOSTIC FLOW-CHART



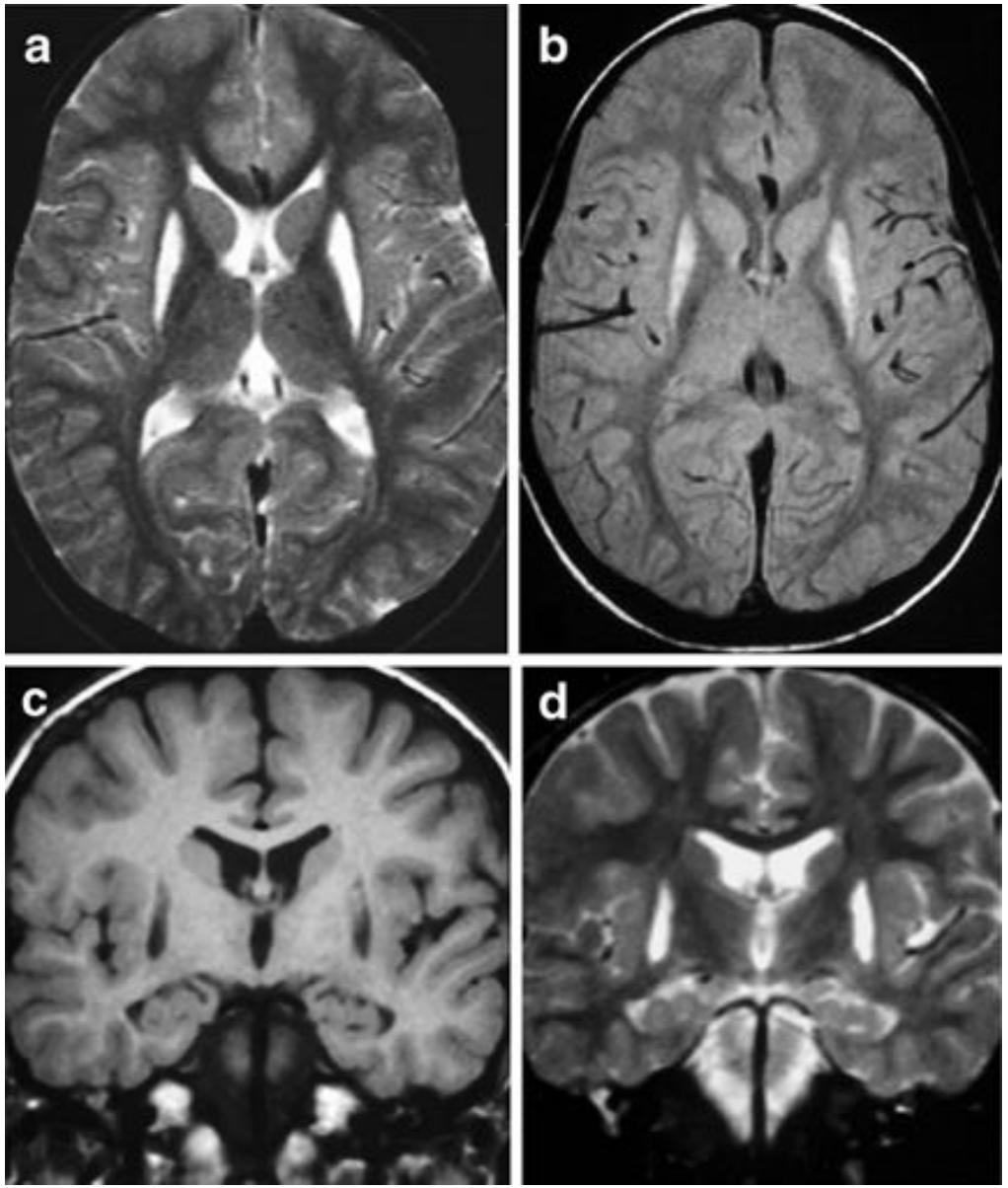
Acquired-
Infectious and Post-infectious

- **Multiple organisms:**
- Mycoplasma pneumoniae –reported as the most common organism
- Streptococcus
- Measles
- Herpes Human Virus 6
- Rotavirus
- Herpes Simplex 1

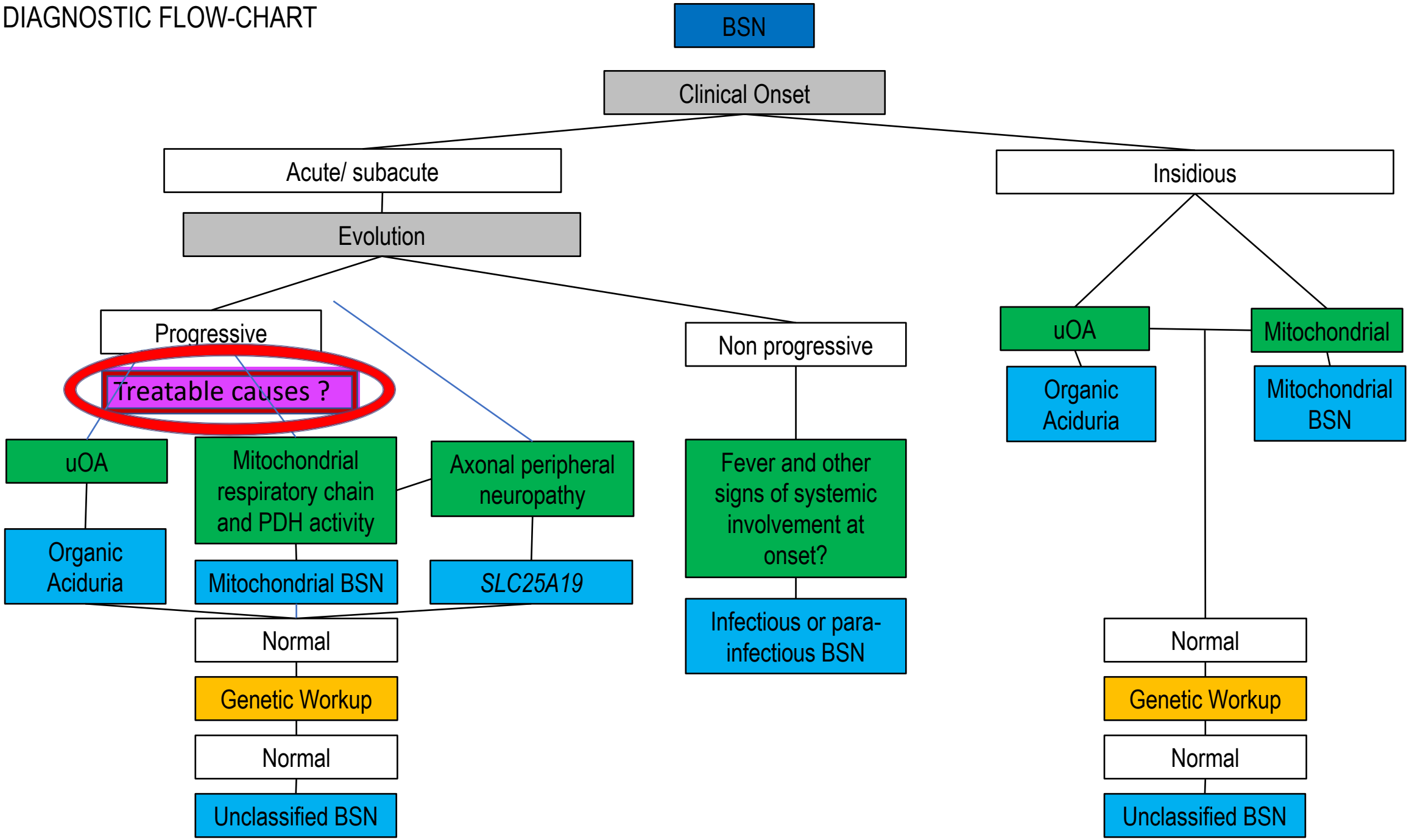
Acquired-
Infectious and Post-infectious

- **Acute onset**
- **Systemic illness** due to causative agent
- Dystonia and/or parkinsonism rarely associated with seizures, decreased consciousness, or ataxia- that appear rapidly or shortly after resolution of systemic illness
- Acute Phase resolves – **non-progressive**
- Some recovery but - not complete.
- MRI

Post-infectious infantile bilateral striatal necrosis.



DIAGNOSTIC FLOW-CHART

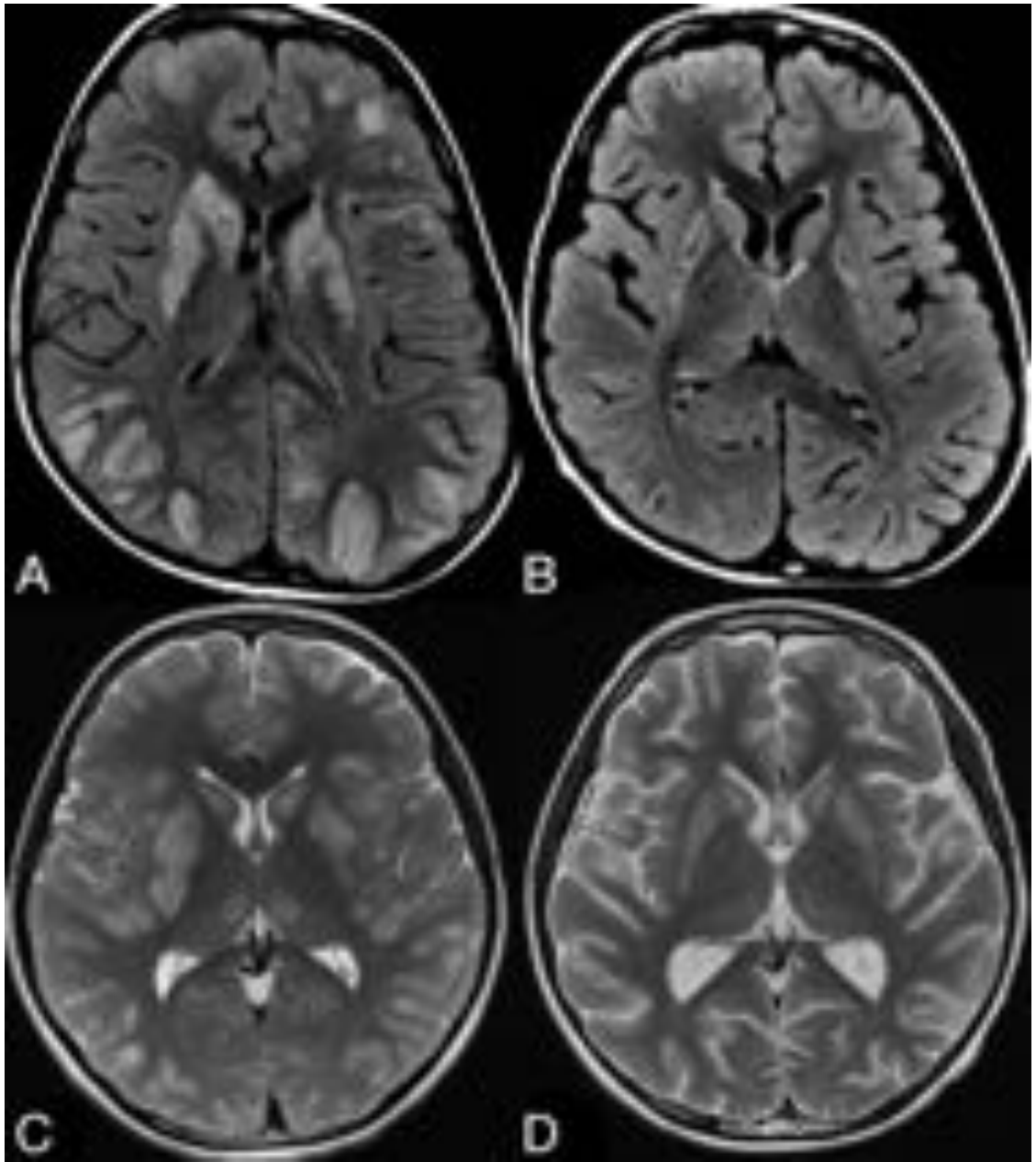


Inherited-
Thiamine Transport Disorder- SLC19A3

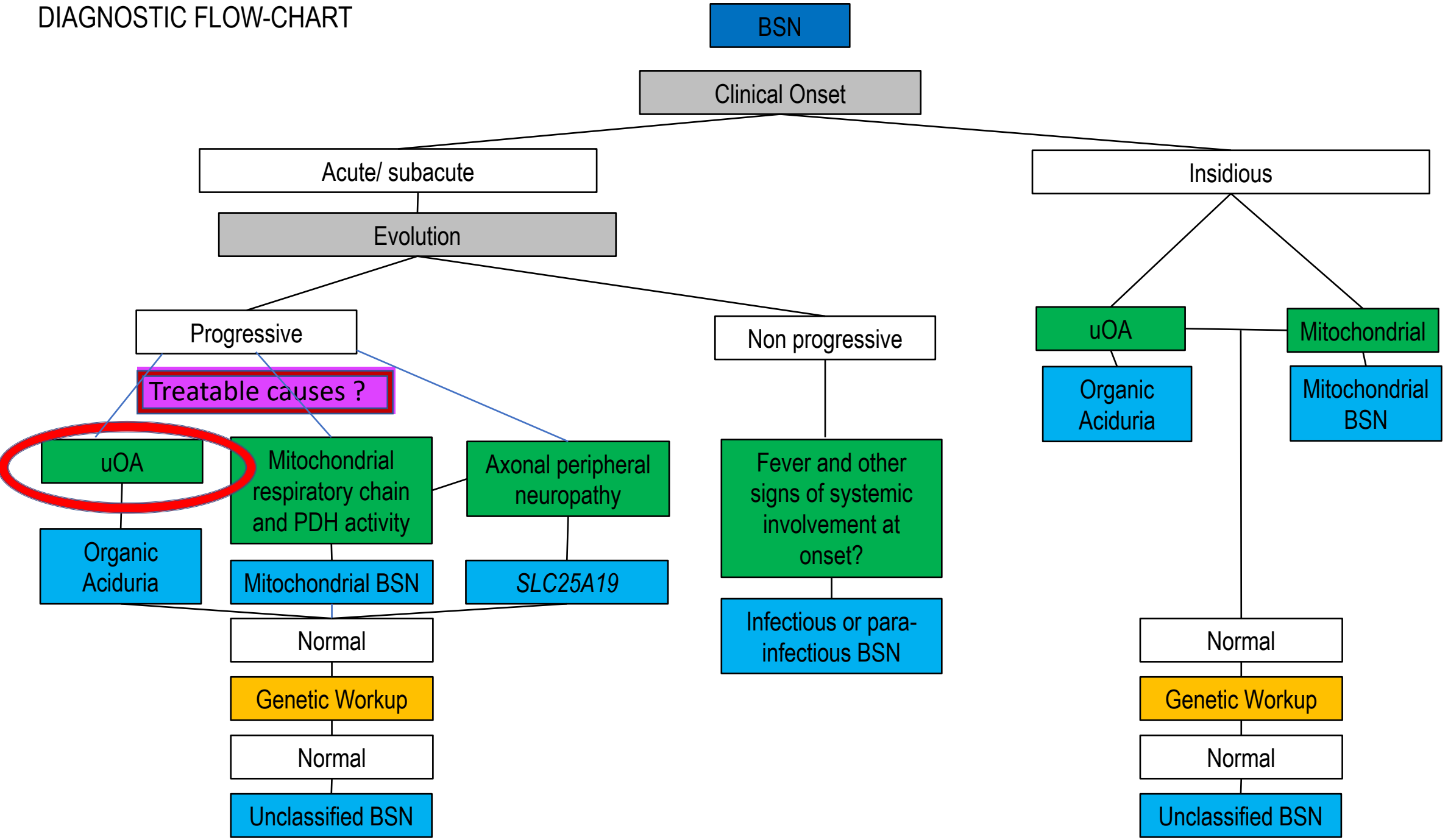
Thiamine Transport Disorders: SLC19A3, Biotin-Thiamine Responsive Basal Ganglia Disease

- **Recurrent episodes of encephalopathy**, often triggered by febrile illness or mild trauma - characterized by confusion, seizures, dysarthria, dysphagia, and external ophthalmoplegia, generalized dystonia
- MRI
- EARLY Biotin and Thiamine Therapy may lead to RESOLUTION of symptoms

Biotin-Thiamine Responsive Basal Ganglia Disease in two patients



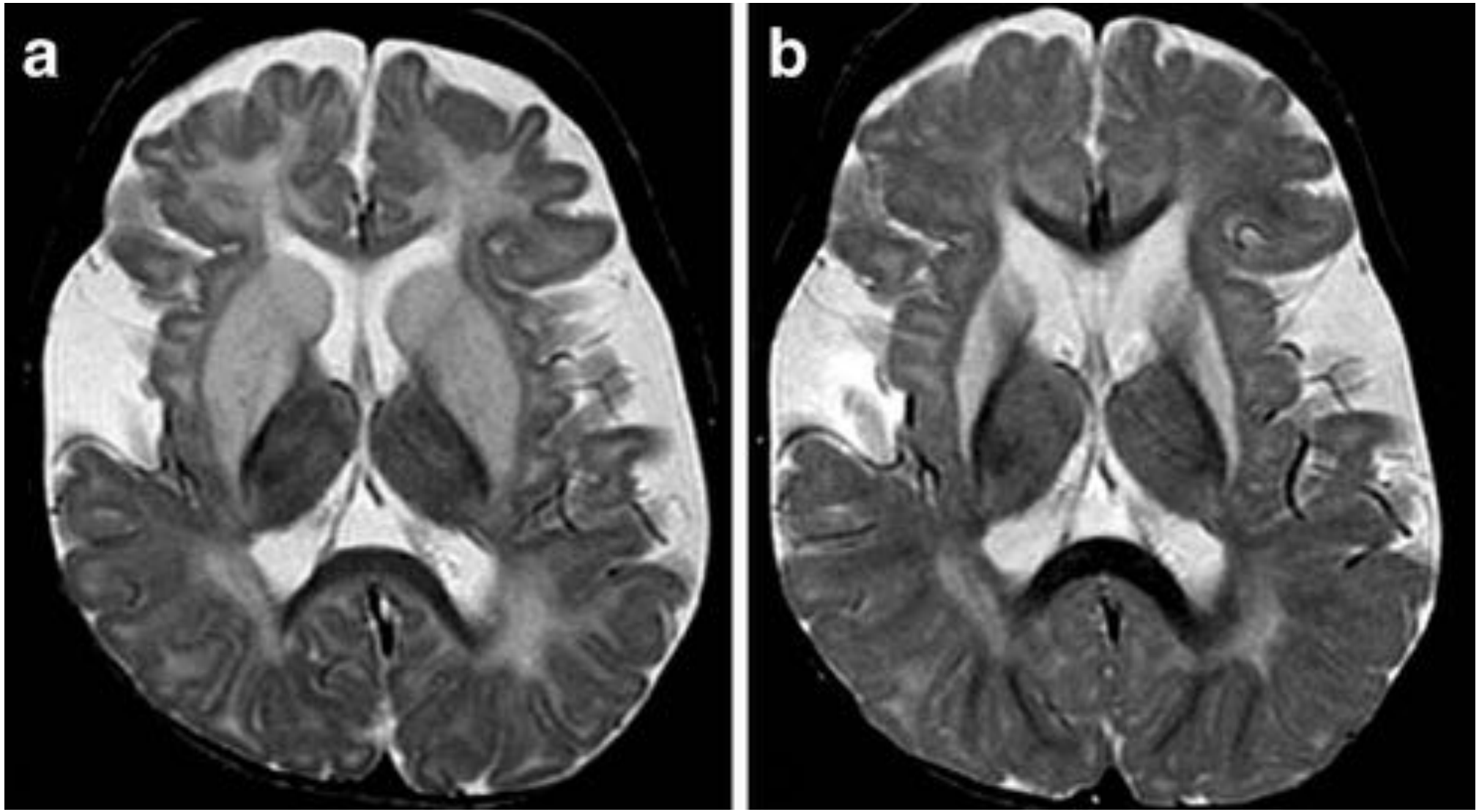
DIAGNOSTIC FLOW-CHART



Inherited-
Organic acidurias

- Bilateral Striatal Necrosis can be associated with **glutaric aciduria type I.**
- Presenting with progressive **Macrocephaly**
- Between 3 months - 3 years develop **encephalopathic crises** with generalised **dystonia** often during systemic illness.

7-mnd old with Glutaric aciduria Type 1



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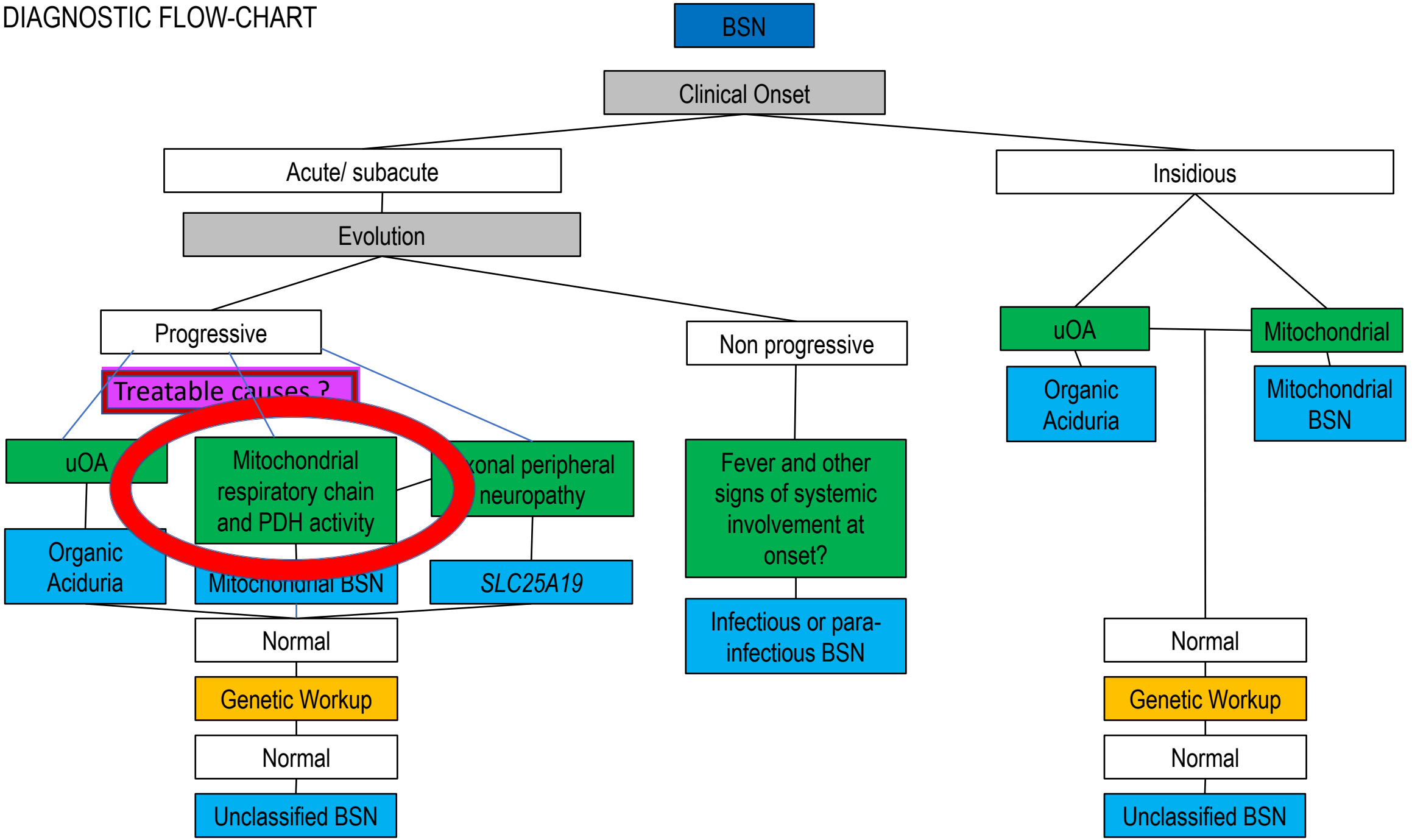
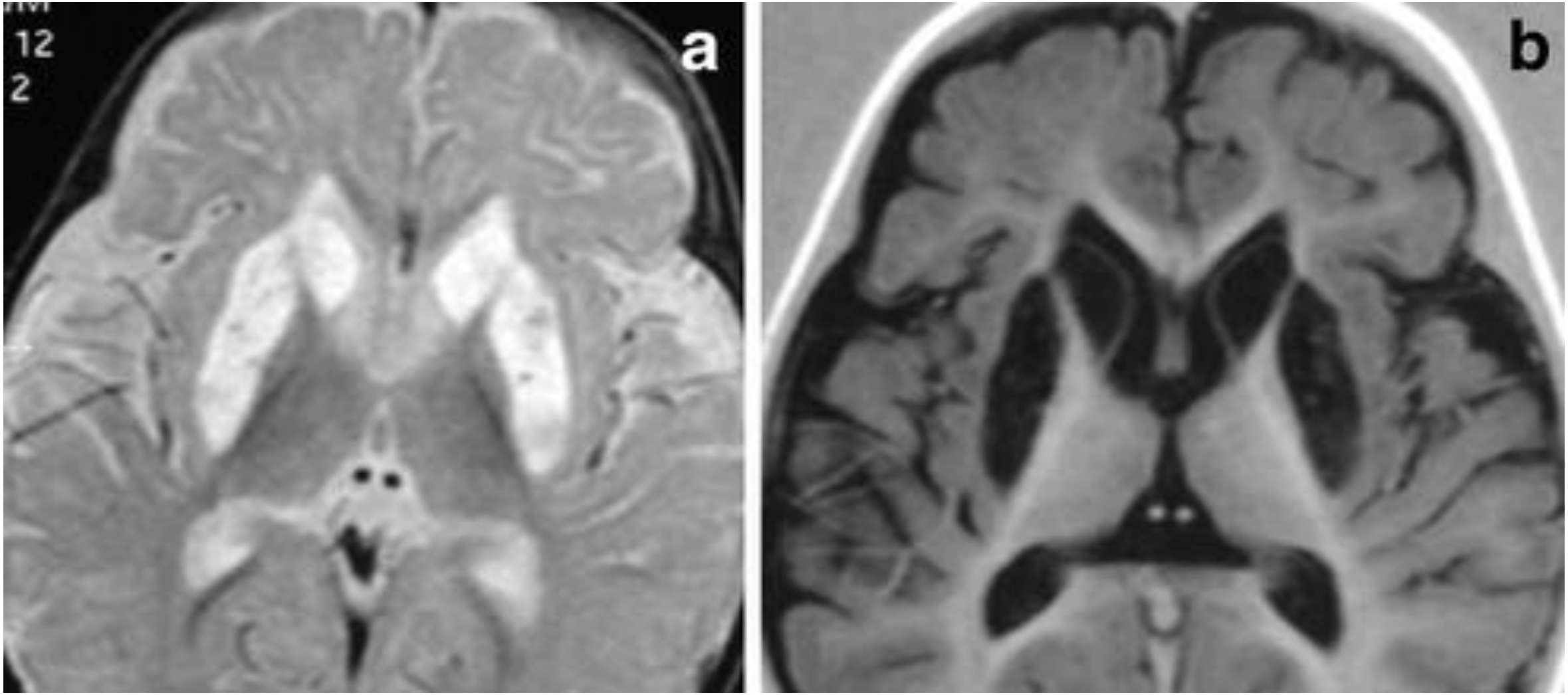


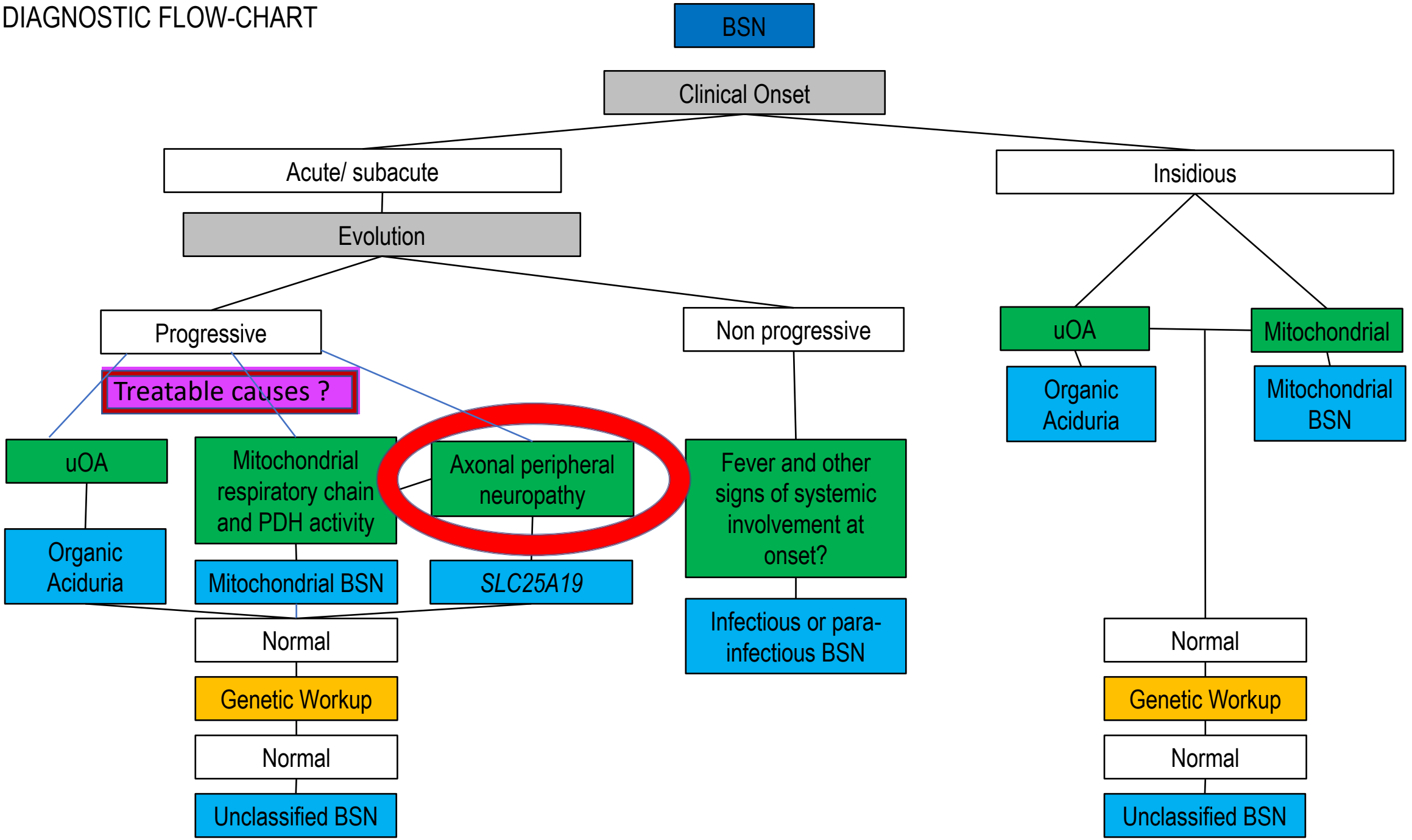
Inherited-
Mitochondrial

- Commonest is **Leigh's** disease:
- Hypotonia and Psychomotor regression.
- **Systemic symptoms**: failure to thrive, vomiting, proximal renal tubulopathy
- **Movement disorders-** dystonia, parkinsonism and cerebellar and pyramidal signs.
- MRI

Leigh’s disease in a 3 year old child.



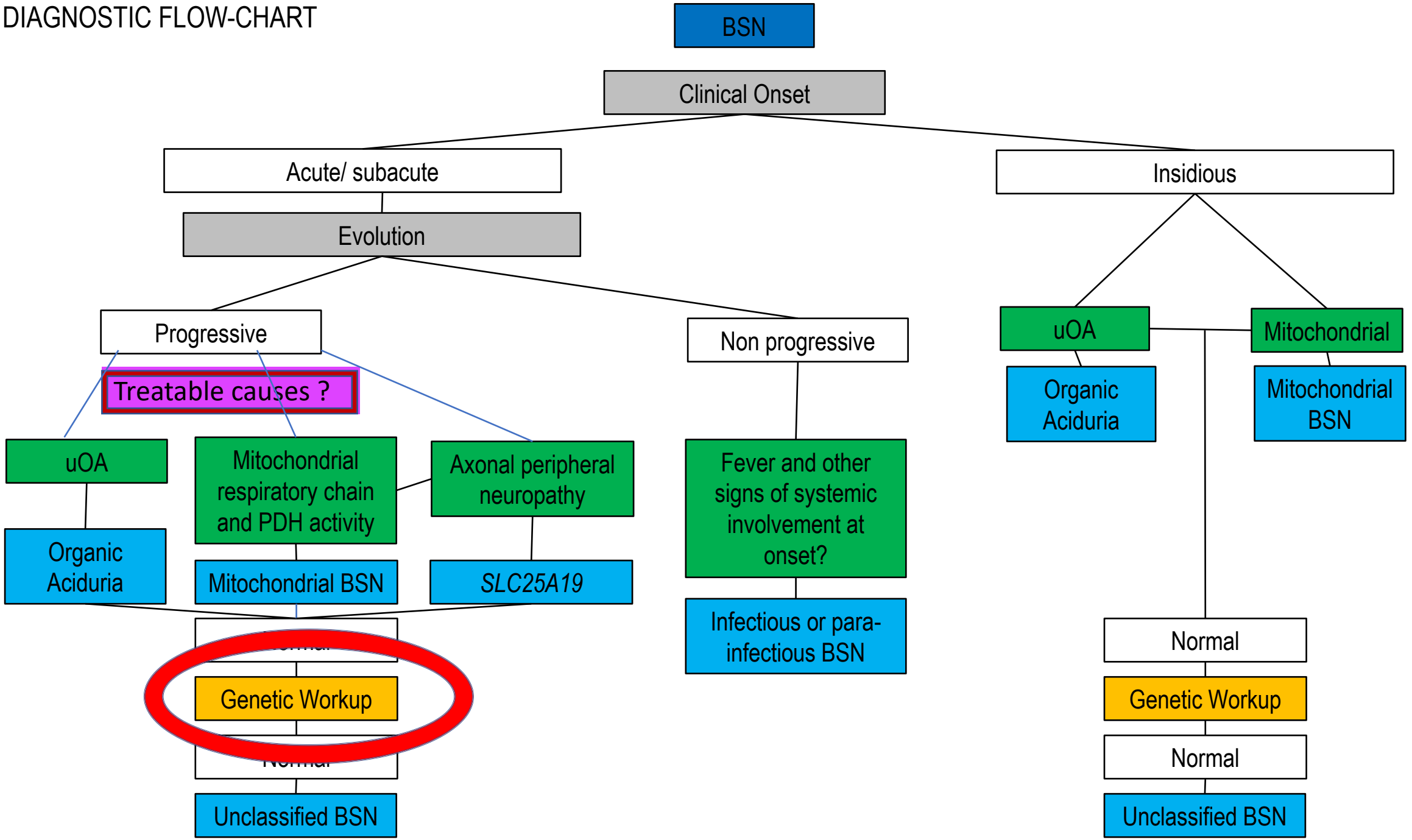
DIAGNOSTIC FLOW-CHART



Inherited-
Thiamine Transport Disorders

- Thiamine Transport Disorders: SLC25A19
  - Present in Infancy, episodes of **acute weakness progressing to flaccid paralysis** and encephalopathy.
  - Acute phase , then recovery but with chronic progressive axonal neuropathy.
    - Mutations of this gene is associated with encephalopathy and microcephaly in Amish population

DIAGNOSTIC FLOW-CHART



Inherited

NUP62-Related Disorder

- First 2 years of life
- Dysphagia, vomiting, cognitive regression
- Psychomotor delay
- **Extrapyramidal** involuntary movements.
- Benefit of Biotin is described

Inherited
ADAR1 related disorders

- Mutations in *ADAR1* - type 1 interferonopathy where stimulation/ unregulated control - leads to inappropriate or excessive interferon output.
- ADAR1 gene is associated with autosomal dominant dyschromatosis symmetrica hereditaria (DSH) and Aicardi Goutieres Syndrome (AGS)
  - **Infantile onset of severe generalized dystonia**.
- ADAR1 mutations can also be found in Infantile Bilateral Striatal Necrosis.

Diagnostic work-up

Approach to conditions associated with MRI evidence of bilateral striatal lesions

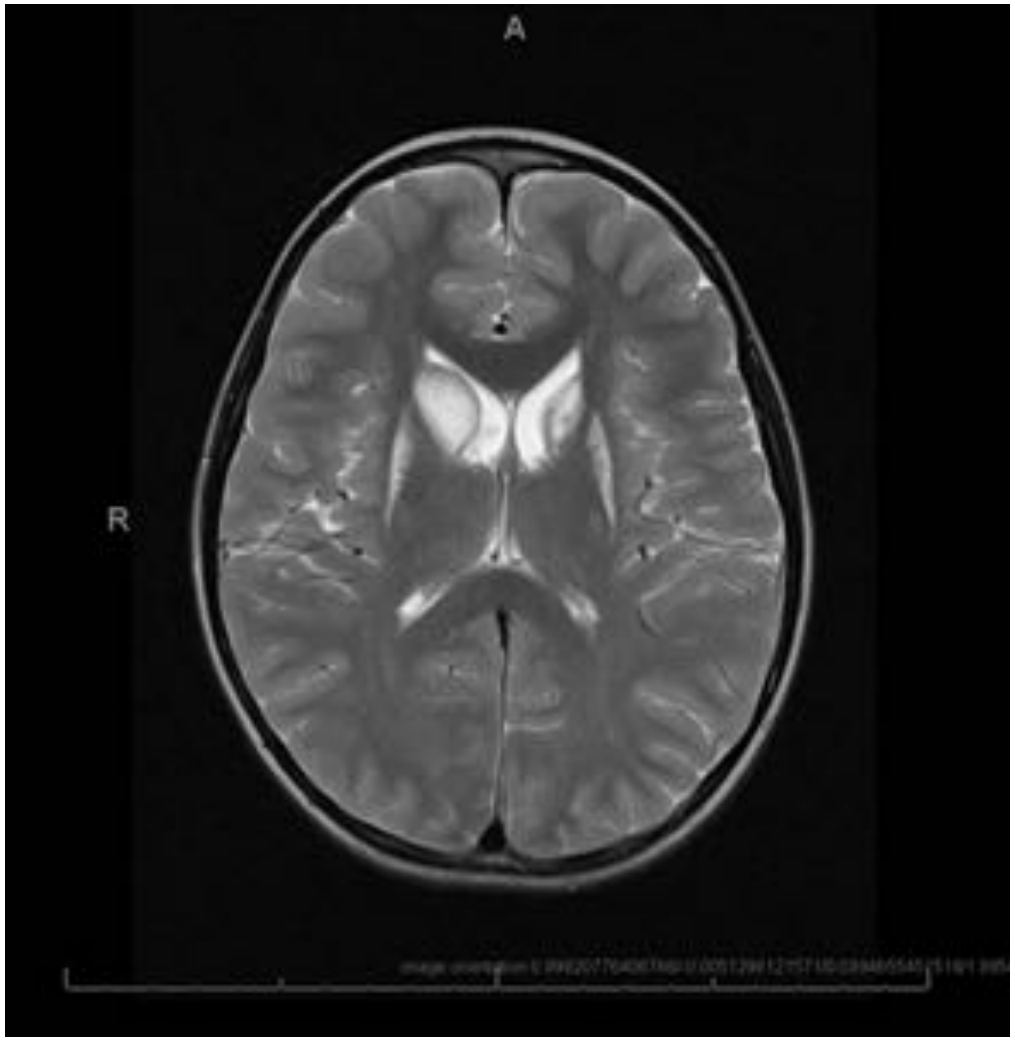
1. To be led by presenting **symptoms and progression**/evolution of disease.
2. Systemic inflammatory markers and CSF analysis
3. TRIAL: Biotin (2–10 mg/kg/day) and Thiamine (100–300 mg/day)
4. Metabolic and Mitochondrial workup: U-Organic Acids, plasma Amino Acids, uric acid, urinary sulfites, plasma and CSF lactate, pyruvate, ammonia level, CK
5. Genetic: CP Panel or Mitochondrial Panel

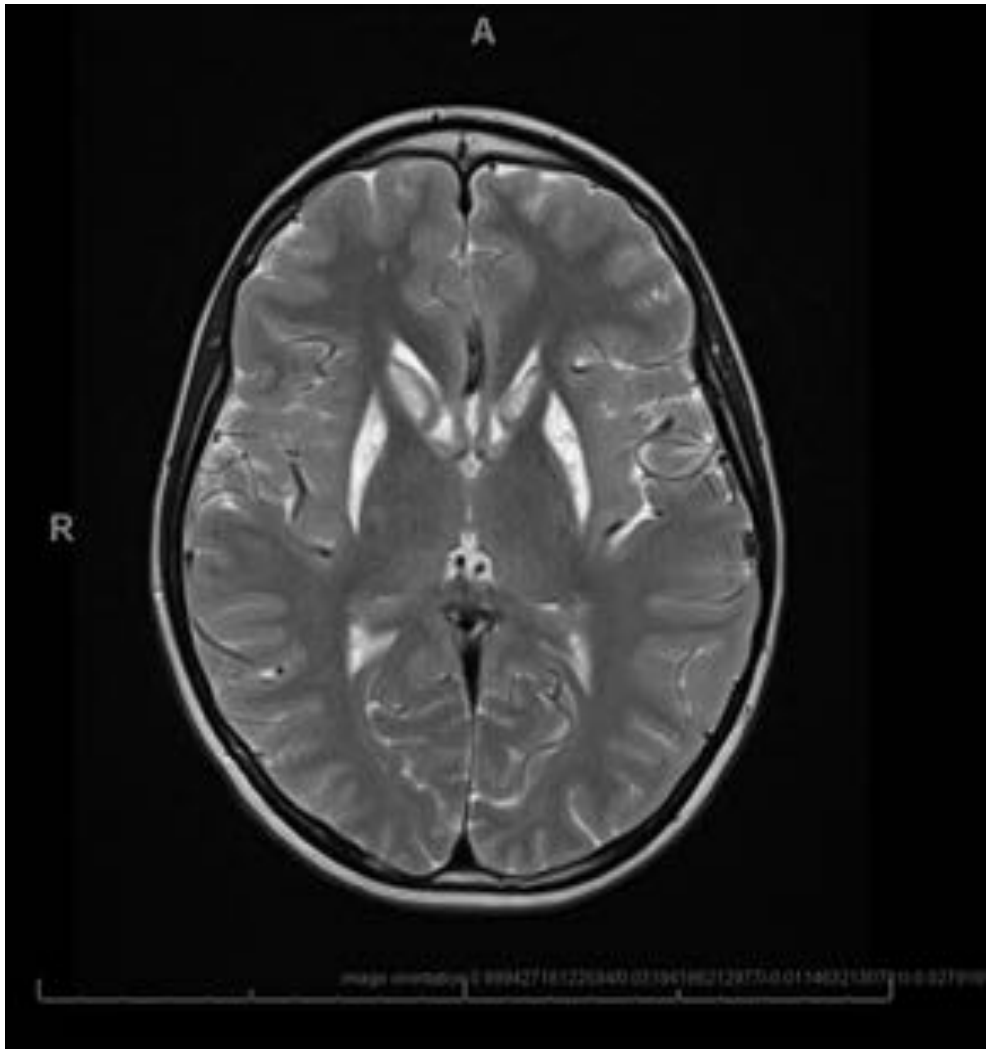
Tygerberg Hospital Case Studies

Case A - (Patient V)

18 year old man

- Presented at 4 years with a Dystonic gait and Bradykinesia, Intellect intact.
- MRI showed BSN
- No response or improvement with Biotin and Thiamine.
- Bilateral Striatal Necrosis workup was unremarkable.
- Serial MRI scans - 5 year intervals - **non-progressive.**
- Clinically not worsening.





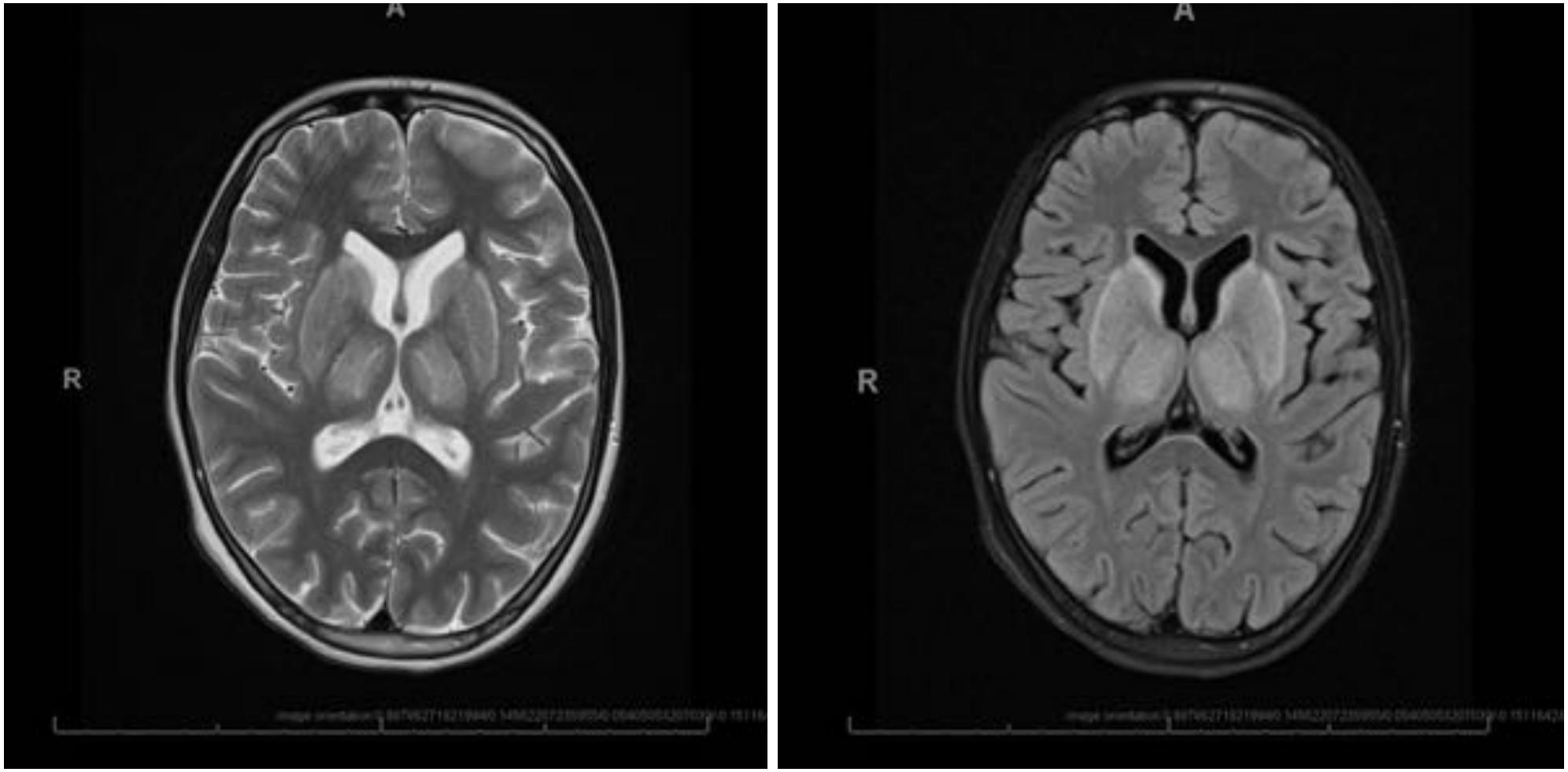
Case A. MRI T2 . Sept 2012 and Aug 2017
Bilateral Hyperintensities of Caudate and Putamen. Showing atrophy of the Caudates in 2017

Case B (patient M)

- 12y old female
- Presented in Nov 2018 with History of Aphasia and abnormal behaviour,
- Cognitive decline and emotional lability
- CT at referring Hospital showed Hyperdensities in bilateral Thalami.

Case B (patient M)

- Next step in investigations?



Case B. MRI T2 and Ts flair Nov 2018.
Bilateral Symmetrical Caudate Striatal and Thalamic Hyperintensities with volumetric gain.

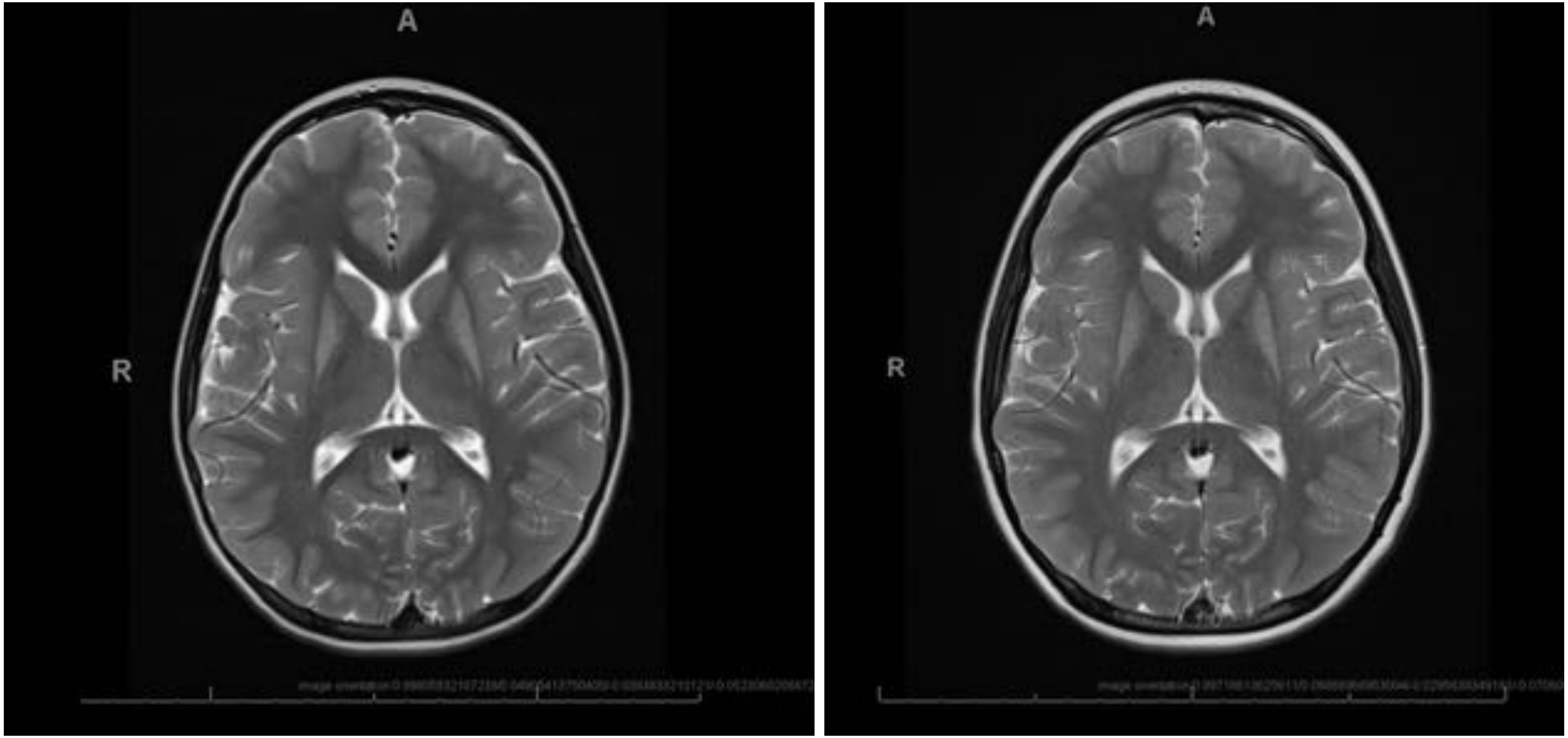

PANDA

Case B (patient M) – Wilson's Disease

- Urine and Serum Copper
- Serum Ceruloplasmin
- Placed on Trientine HCL and Zinc therapy

Case C (patient J)

- Now 9 year old male
- Presented with Bronchiolitis at 18mnd age
- Acute onset dystonia and extrapyramidal features.
  - History noted the possibility of carbon monoxide poisoning.
  - Diagnosis of Dystonic Cerebral Palsy was made.
- Seen at TBH at 7 years old with debilitating dystonia and recurrent transaminitis(raised LFT's, vomiting and lethargy)
- Intellect intact
- Ix- Organic aciduria and mitochondrial workup - normal
- Biotin and Thiamine Trial – no response.



Case C. MRI T2 June 2017 and March 2021
Hyperintensity of bilateral caudate and lentiform with atrophy of Putamen

Case C (patient J)

- Genetic workup:
- Cerebral Palsy Panel.

Case (patient J)
Genetics: INVITAE

Reason for testing

Diagnostic test for a personal history of disease

Test performed

Sequence analysis and deletion/duplication testing of the 265 genes listed in the Genes Analyzed section.

- Invitae Cerebral Palsy Spectrum Disorders Panel

RESULT: POSITIVE

One Pathogenic variant and one Variant of Uncertain Significance identified in ADAR. ADAR is associated with autosomal dominant dyschromatosis symmetrica hereditaria and autosomal recessive Aicardi Goutieres syndrome.

Additional Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
ADAR	c.2128_2131dup (p.Asn711Thrfs*34)	heterozygous	PATHOGENIC
ADAR	c.577C>G (p.Pro193Ala)	heterozygous	Uncertain Significance
DLAT	c.1406A>G (p.Glu469Gly)	heterozygous	Uncertain Significance
NBAS	c.336-3C>A (Intronic)	heterozygous	Uncertain Significance
ZFYVE26	c.605G>A (p.Arg202Gln)	heterozygous	Uncertain Significance
GALC	c.742G>A (p.Asp248Asn)	homozygous	Benign (Pseudodeficiency allele)

About this test

This diagnostic test evaluates 265 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Key message

BSN is group of diseases with a diverse clinical presentation.

1. Radiological identification is the first step.
2. Work-up to be guided by presenting symptoms and progression/evolution of disease.
3. Genetic testing forms an integral part of this entity
4. A Trial of Biotin and Thiamine, even while the work-up is in progress, is suggested as this is a potentially treatable condition.

Resources

- Aicardi's Diseases of Nervous System in Children
- Neurological Disorders associated with Striatal Lesions: Classification and Diagnostic Approach. https://link.springer.com/article/
- American Journal of Neurology. Biotin-Responsive Basal Ganglia Disease: Neuroimaging Features before and after Treatment. http://www.ajnr.org/content/35/10/1990