



Universitair Ziekenhuis Brussel



Cliniques universitaires
SAINT-LUC
UCL BRUXELLES

Démarche diagnostique devant une atteinte des noyaux gris centraux

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Les noyaux gris ?
Aucun secret pour
moi...



Un petit rappel anatomique

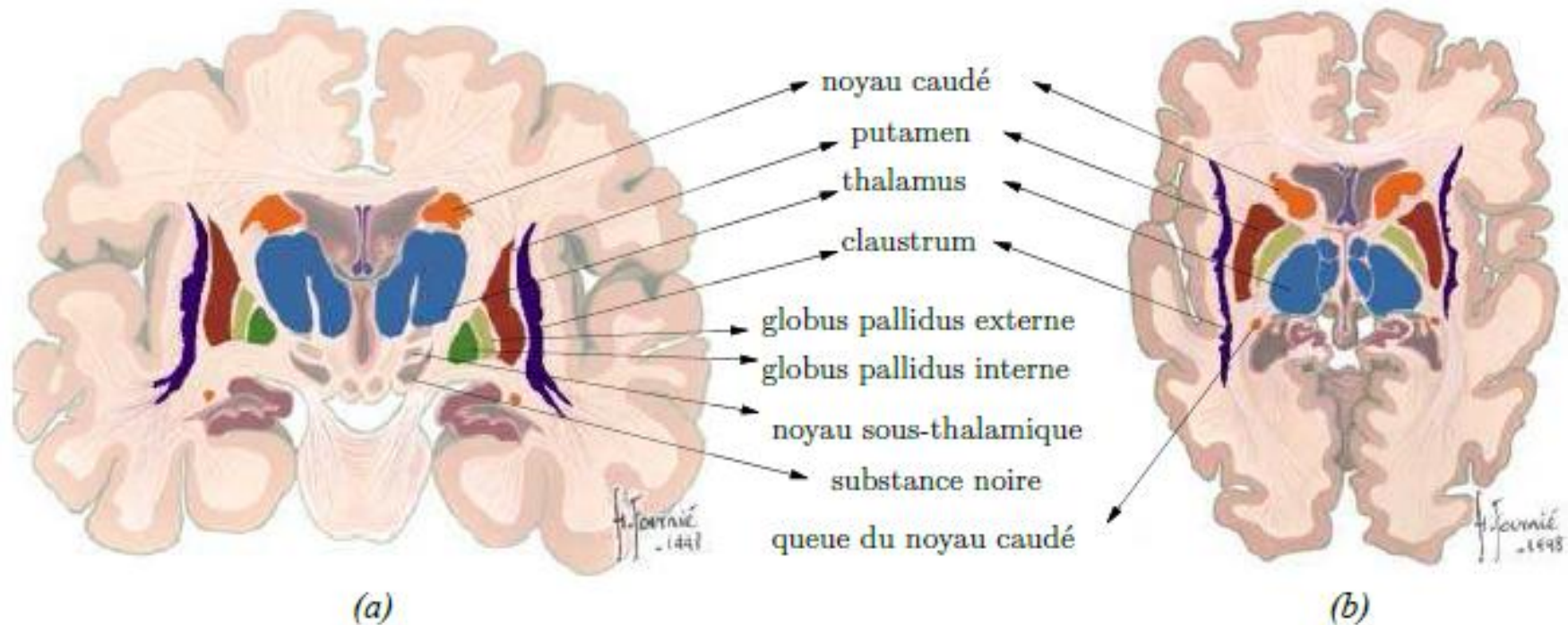


FIG. 3.6: Noyaux gris centraux en vue : (a) cornale, (b) axiale. Figure adaptée de (www.chups.jussieu.fr/ext/neuranat)



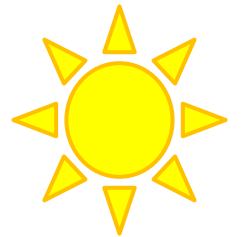
Atteinte des noyaux gris centraux

Unilatérale

Bilatérale

- Vasculaire
- Espaces de Virchow-Robin
- Encéphalite de Rasmussen
- Hyperglycémie
- Tumorale

- Hypoxie-ischémie
- Hypoglycémie-hyperbilirubinémie
- Infections
- Maladies métaboliques
- Iatrogènes
- Intoxications
- Maladies dégénératives



Atteinte anatomique ./maladie

Maladie	Pallidum	Thalamus	Putamen	Tronc cérébral	Noyau dentelé
Energy metabolism dis					
Respiratory chain dis.	+	+	+	+	+
BBGD			+	+	
PDH deficiency	+	+	+	+	+
CoQ10 deficiency			+	+	
Thiamine transporter (SLC25A19)			+		
Lipid storage					
CTX	+				+
AMACR deficiency		+		+	
GM1 gangliosidosis			+		
Fabry disease		+			

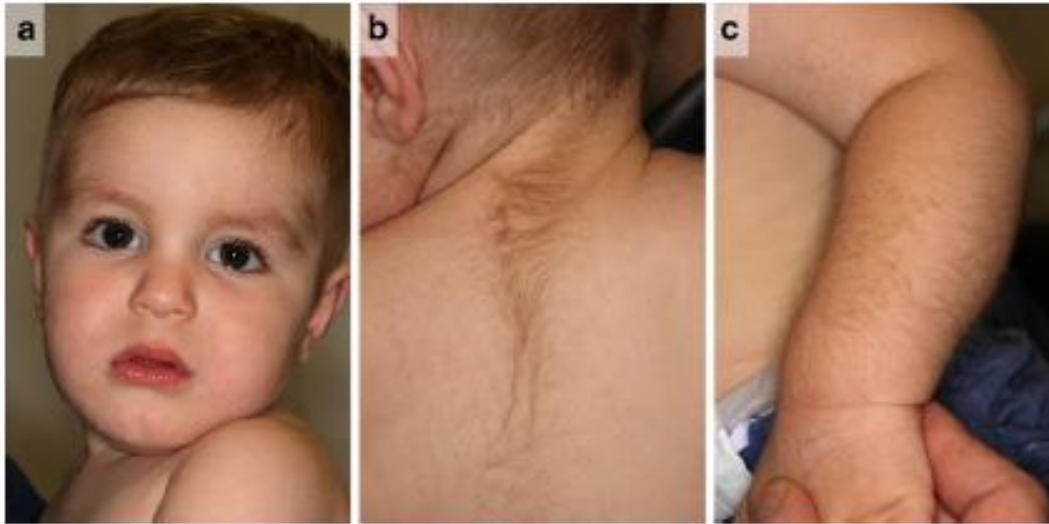
Atteinte anatomique ./maladie

Maladie	Pallidum	Thalamus	Putamen	Tronc cérébral	Noyau dentelé
Intoxications					
MMA	+				
SSADH deficiency	+				+
Urea cycle disorders	+				+
Glutaric aciduria type 1			+		
Metal storage disorders					
Wilson disease	+	+	+	+	+
Aceruloplasminemia	+	+	+	+	+
Neuroferritinopathy	+		+	+	+
PANK2	+				
PLA2G6	+			+	
Hypermanganesemia	+		+		+

Leigh's encephalopathy

- ▶ Specific progressive neurological disease
- ▶ Basal ganglia and brainstem involvement
 - ▶ Increased signals in basal ganglia and brainstem typically symmetric
 - ▶ Putamen, globus pallidus, caudate, thalamus, substantia nigra, inferior olivary nuclei, periaqueductal area, brainstem tegmentum
- ▶ Increase of lactate in CSF
- ▶ A differential diagnosis is necessary
- ▶ Clues
 - ▶ family history
 - ▶ increased hair growth
 - ▶ retinitis pigmentosa





Complex IV deficiency
SURF1; TACO1

mt DNA depletion
SUCLA2

ATPase 6

tRNA genes

ND5, ND6, ND3

mtDNA deletions

Nuclear gene mutations

LEIGH

mtDNA mutations

Complex I deficiency
NDUFS8; NUDFV1
NDUFS1 *ao.....*

Leigh-like

Other mitochondrial encephalomyopathies

Complex II deficiency
SDH

PDH deficiency
E1 α
PC

MUSCLE BIOPSY
DNA BLOOD
FIBROBLASTS



Leigh syndrome : investigations

- ▶ Lactate, lactate/pyruvate in blood, urines and CSF
- ▶ ? Glucose tolerance test
- ▶ Blood amino-acids
 - ▶ Alanine
 - ▶ Citrulline : low in mt DNA mutation T8993G
- ▶ Urines amino-acids : tubulopathy
- ▶ Urine organic acids
 - ▶ Citric acid cycle intermediates : succinate, fumarate, malate, 2-oxyglutarate
 - ▶ Ethylmalonic acid : cytochrome c oxidase deficiency
 - ▶ 3-methylglutaconic acid : MEGDEL association due to SERAC1 mutation deafness)
 - ▶ Methylmalonic aciduria : + deafness in SUCLA2 and SUGL1 mutations



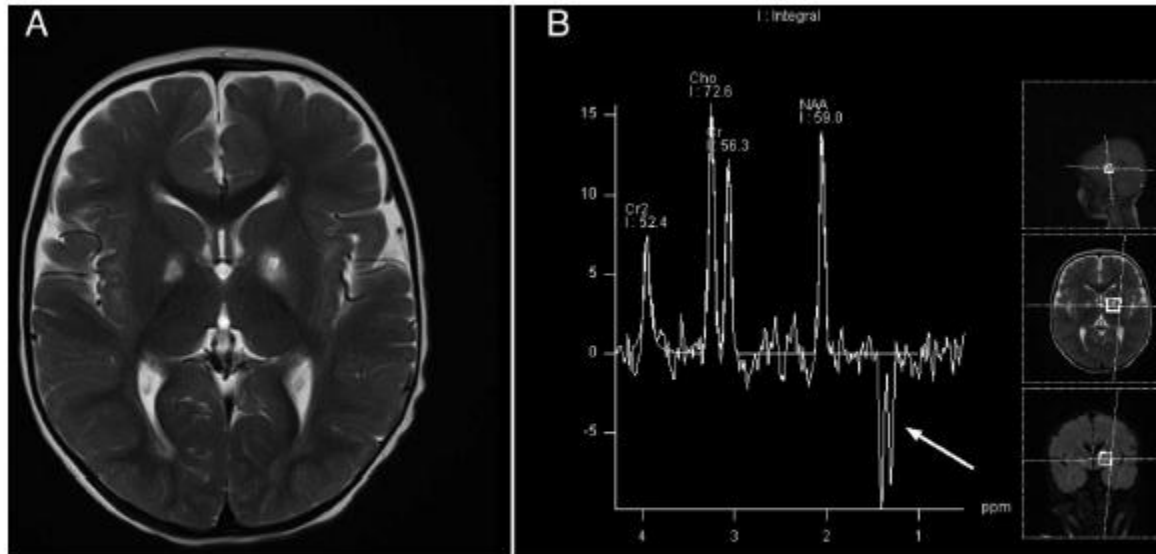
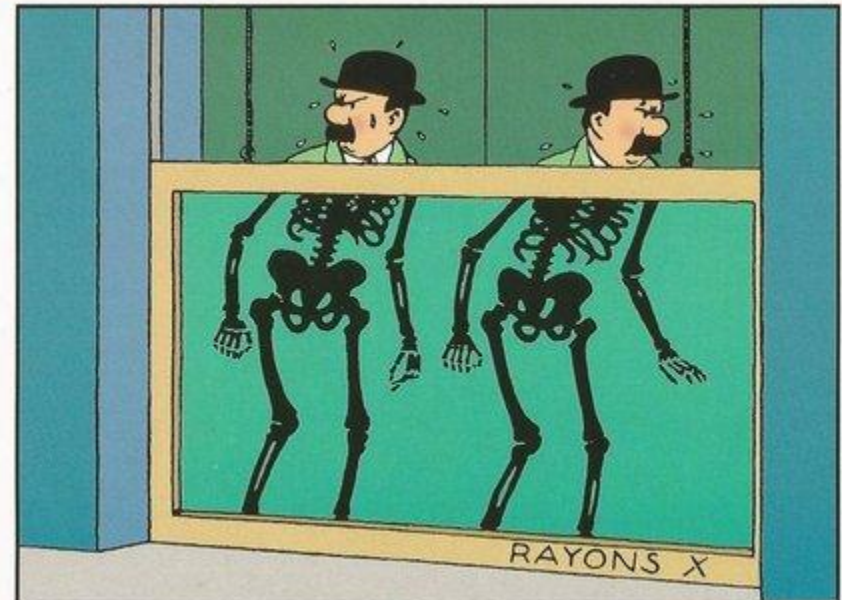


Figure 1 Typical imaging findings in a 14-month-old girl with Leigh syndrome caused by isolated complex III deficiency. (A) Axial T2-weighted brain MRI showing bilateral lesions in the globus pallidus with focal necrosis on the left side. (B) Single voxel spectroscopy, demonstrating an intense lactate peak at 1.35 ppm (white arrow) and a reduced N-acetyl-aspartate peak.

► Specific MRI patterns ?

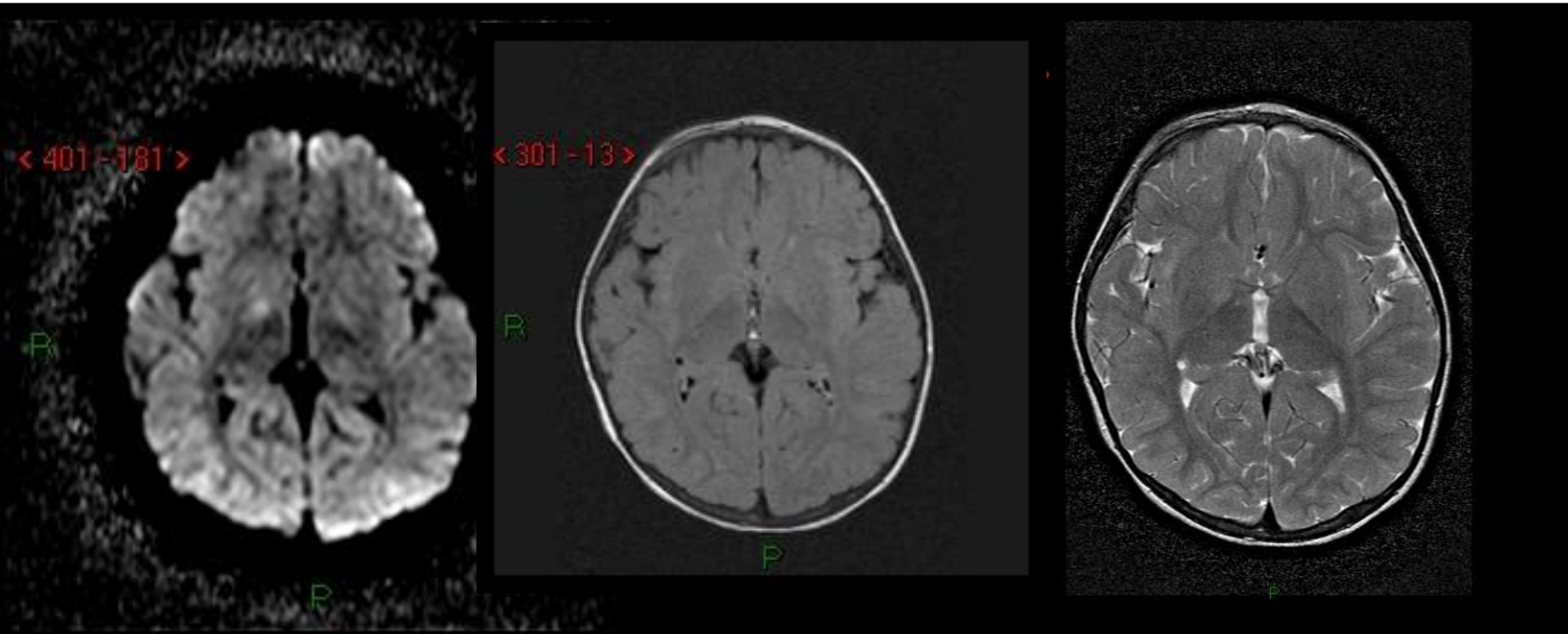


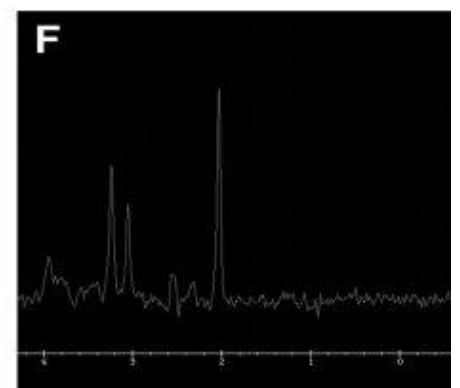
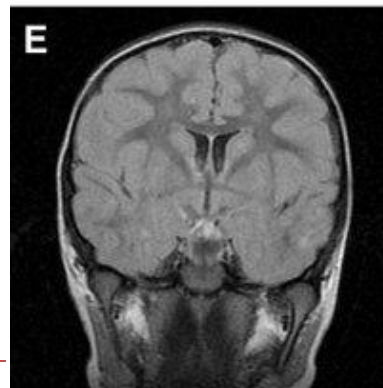
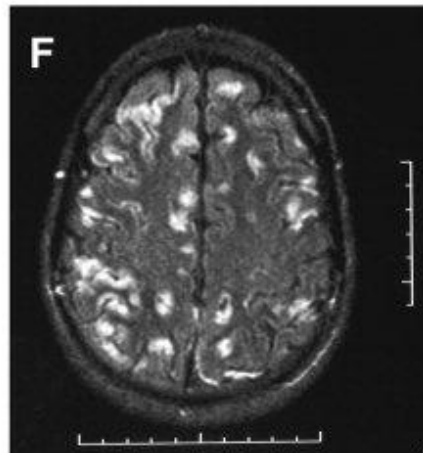
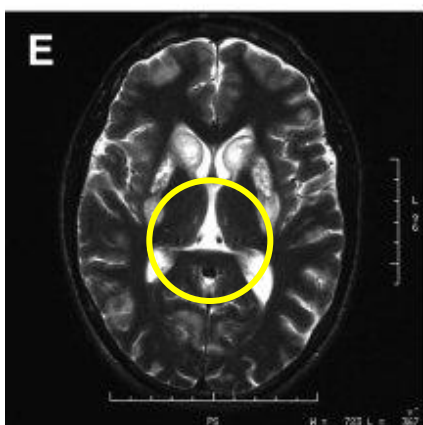
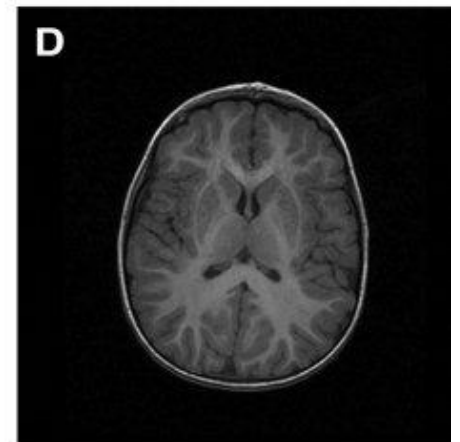
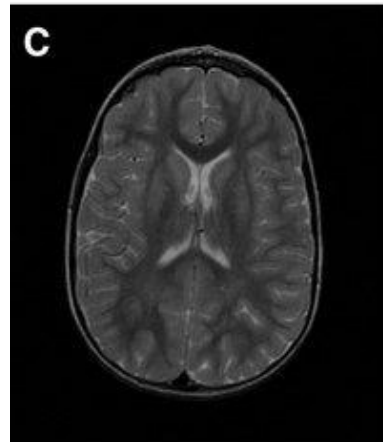
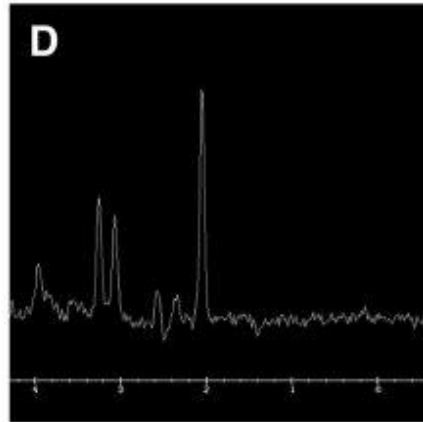
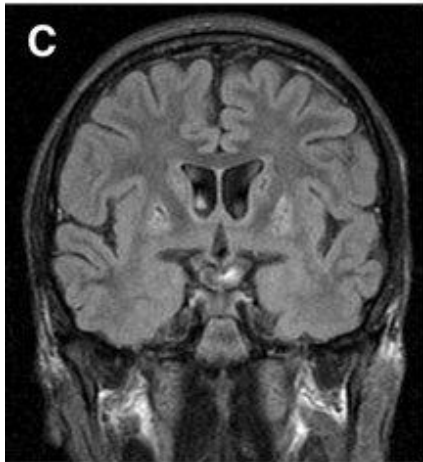
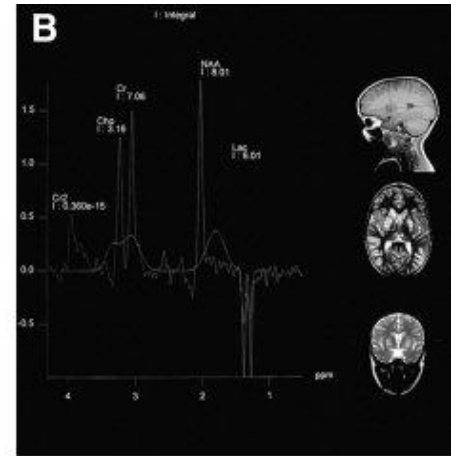
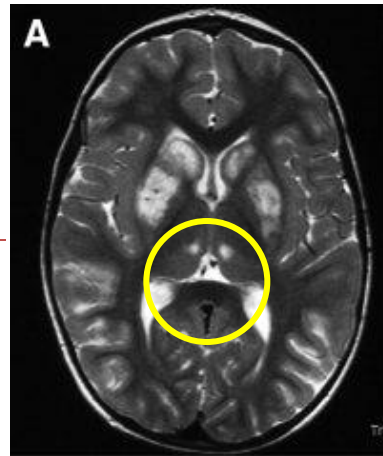
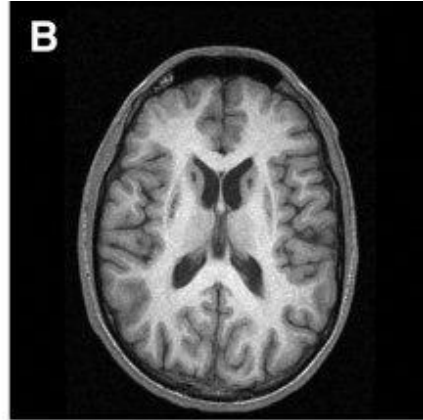
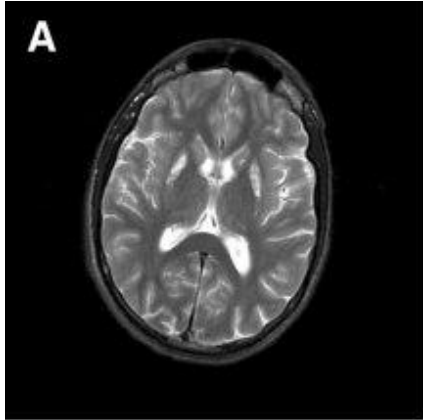
Strategy in Leigh syndrome

- ▶ Specific mt DNA mutations
- ▶ Full sequence analysis of mtDNA
- ▶ Muscular biopsy :
 - ▶ respiratory chain analysis
 - ▶ Mt DNA depletion
- ▶ Liver biopsy
- ▶ Molecular analysis



Gabriel : 22 mois





Atteinte des noyaux gris centraux

Contexte clinique
Antécédents familiaux

Biologie sanguine

- Hémogramme
- pH, ionogramme
- Bilan hépatique
- Cuivre, céruloplasmine
- Profil acide lactique/pyruvique
- Acides aminés

Urines

- Acide organiques
- Acides aminés

Etude du LCR

- **Acide lactique/pyruvique**
- Acides aminés plasmatiques
- Neurochimie

Imagerie

- IRM cérébrale
- **Spectro-IRM**

Merci à tous les
participants

