Amsterdam Neuroscience

Imaging as pathfinder in IEM

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Contents

- What is pattern recognition?
- Some basics
  - MR Imaging (including normal and abnormal myelination)
  - ^{1}H MR spectroscopy
- IEM: Malformations
- IEM: Grey matter disorders
- IEM: White matter disorders
- What to remember

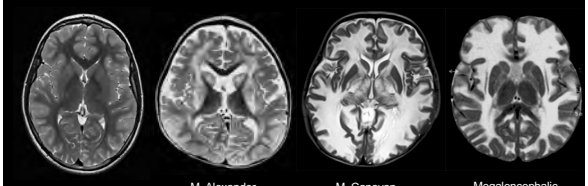
MRI pattern recognition

→ Very useful for white matter disorders

→ Not useful for "cortical grey matter disorders

→ Often useful for deep grey matter disorders

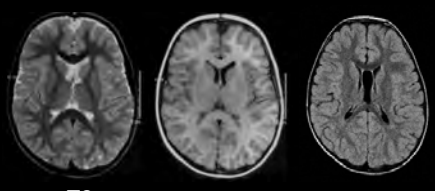
Pattern recognition



M. Alexander | M. Canavan | Megalencephalic leukoencephalopathy with subcortical cysts (MLC)

Macrocephaly

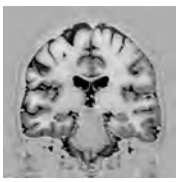
MRI: basic basics



T2 | T1 | FLAIR

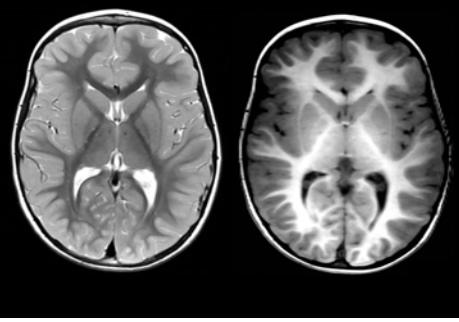
Sequences used: when what sequence?

- Anatomy: T1, IR (inversion recovery)
- Pathology: T2, FLAIR
- Blood, calcium deposits, iron storage: SWI (susceptibility-weighted imaging)
- Orbita / optic nerve imaging…: STIR (to suppress fat)
- Time matters, moving patient: HASTE or comparable sequences
- Oedema, cell density, myelin vacuolation: DWI (Diffusion-weighted imaging)

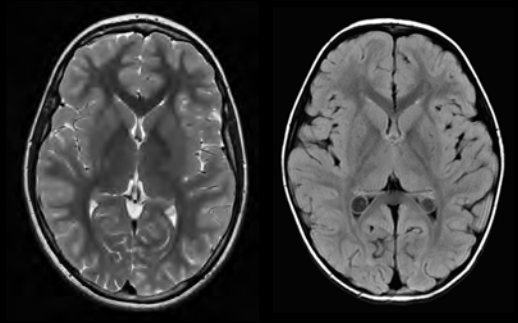


IR

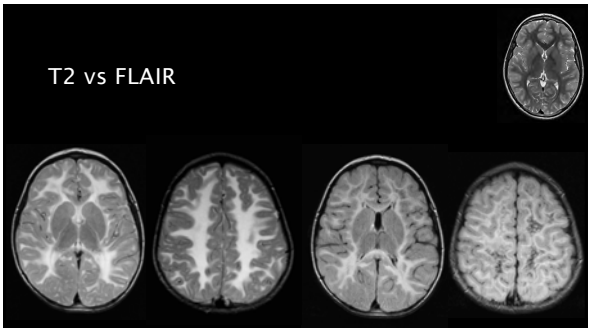
T2 vs T1



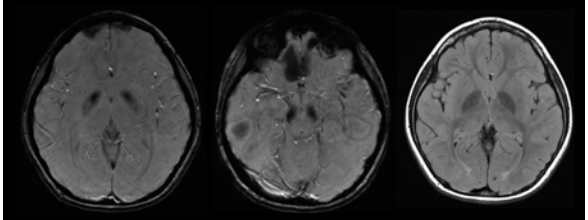
T2 vs FLAIR



T2 vs FLAIR



SWI (susceptibility-weighted imaging)

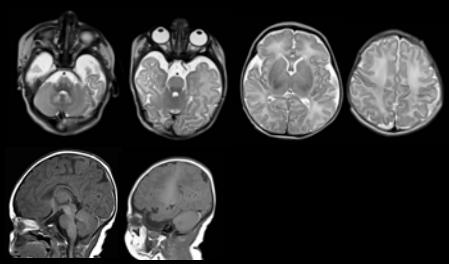


SWI: mineralisation (calcifications, iron)

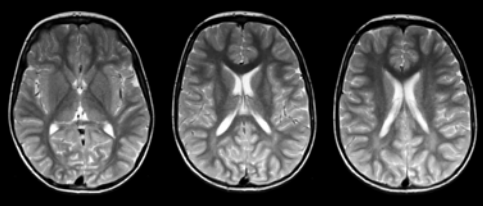
Myelination: Term neonate

T2w

T1w

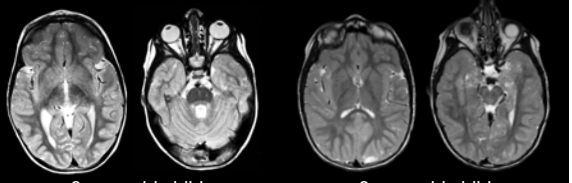


Normal: “Terminal zones” of myelination



3 year-old child

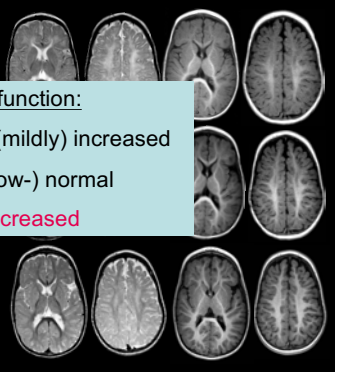
Non-specific: Incomplete myelination



3 year-old child

8 year-old child

Delayed myelination: MCT8



12 m

Thyroid function:

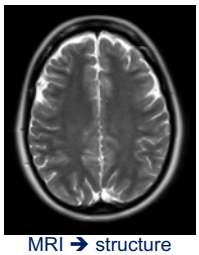
→ TSH (mildly) increased

→ fT4 (low-) normal

→ fT3 increased

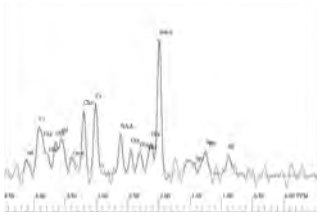
3.5 y

MRI vs MRS

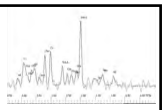


MRI ➔ structure

MRS ➔ metabolites

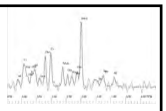


What is ^{1}H-MRS?



- MR method to analyse “brain biochemistry”
- Special MR sequences used
- Protons resonate slightly differently depending on their binding partners ➔ differentiation of certain molecules
- Water: must be suppressed
- Short and long echo times ➔ depending on what you look at
- Single voxel MRS: one small cube is measured
- Chemical shift imaging (CSI): acquisition of measurements in multiple voxels

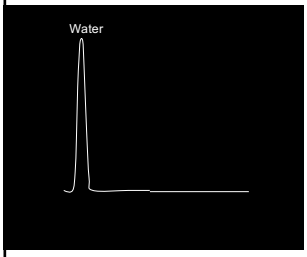
More on ^{1}H-MRS



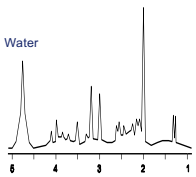
- Quantification of metabolites possible, but challenging: every MRI system needs its own set of controls
- Often used: metabolite ratios, usually to creatine
- Visual inspection of spectra sometimes enough for interpretation
- Abnormal peaks: can be tricky!

Making metabolites visible

Without water suppression



With water suppression

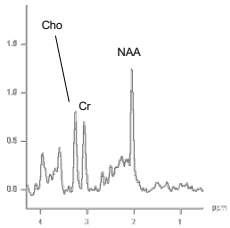


Sensitivity (water) / sensitivity (metabolites) > 10000

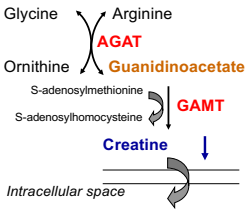
What can we see?

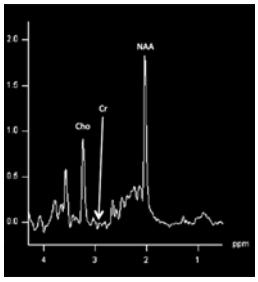
- Concentrations of molecules: in the millimolar range!
- No “complex” molecules
- No molecules with low concentrations (neurotransmitters…)
- Most important metabolite with the highest concentration: N-acetylaspartate (NAA)
- Abnormal findings can be:
  - too much of too little (or nothing) of a substance
  - presence of an otherwise undetectable substance

How does it look like?



Cerebral creatine deficiency





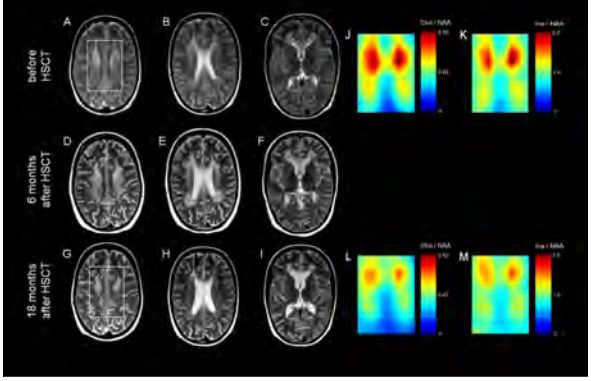
Other disorders with typical ^{1}H-MRS

- Absence of NAA in the brain (deficiency of one of the N-acetyltransferases, *NAT8L*)
- Elevated glycine (non-ketotic hyperglycinaemia)
- Lactate, alanine and pyruvate in pyruvate dehydrogenase deficiency

Less specific:

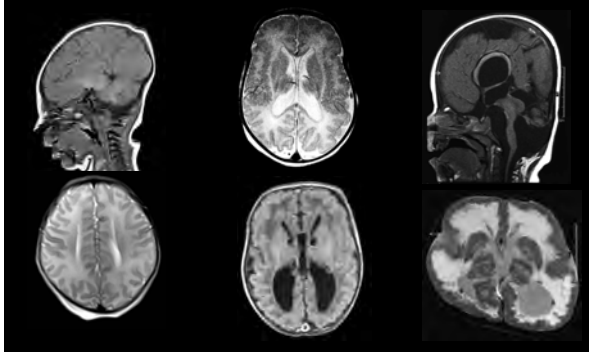
- Low NAA in neurodegenerative disorders
- Low choline in hypomyelination
- Lactate elevation

Chemical shift imaging



Malformations in IEM

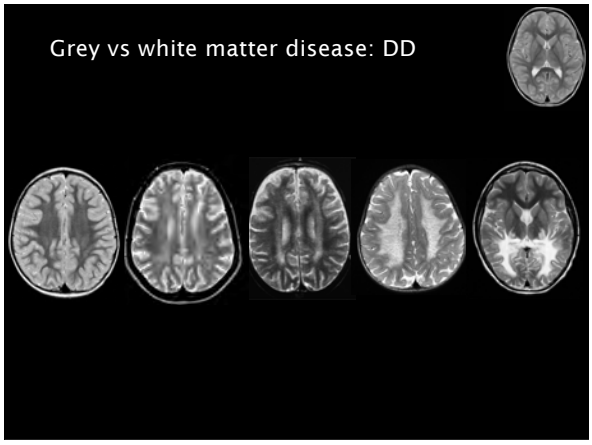
Malformations in IEM



(Cortical) Grey vs white matter disorders: MRI

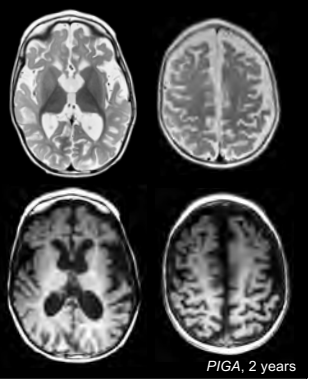
Grey matter disorders	*White matter disorders*
➢ often "mild" MRI abnormalities, contrasting to clinical picture	➢ often "severe" MRI abnormalities, contrasting to clinical picture
➢ "secondary" white matter involvement, first mild, later more severe	➢ Signal of abnormal white matter rather bright (T2)
➢ Often early atrophy	➢ "primary" white matter involvement
➢ Early grey matter disorders: interfere with myelination ("secondary hypomyelination")	➢ Usually late atrophy
➢ Clinical clues helpful	➢ Clinical clues helpful

Grey vs white matter disease: DD



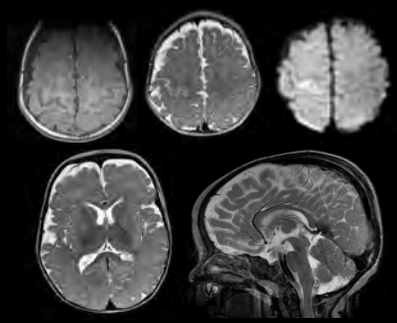
MRI in primary grey matter disorders

- ➢ Supratentorial atrophy
- ➢ Thin cortex
- ➢ Early onset: Clearly delayed myelination, often abnormal myelin signal
- ➢ Differential diagnosis huge
- ➢ Often also epilepsy / early epileptic encephalopathy



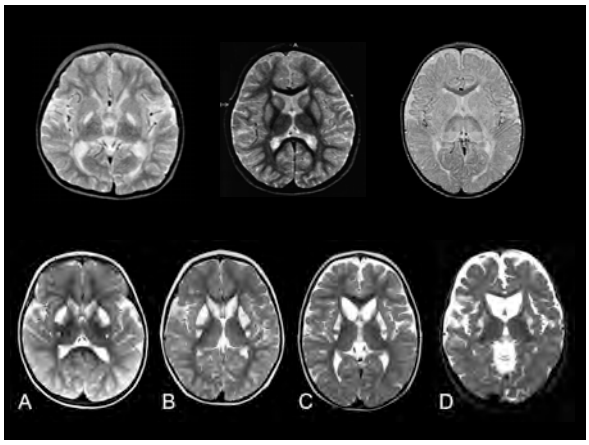
PIGA, 2 years

Focal status epilepticus in an infant

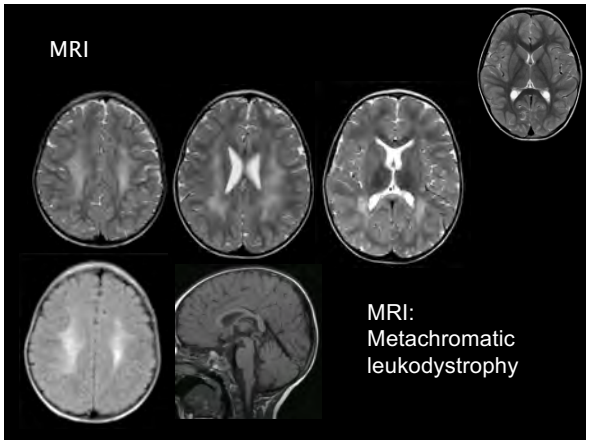


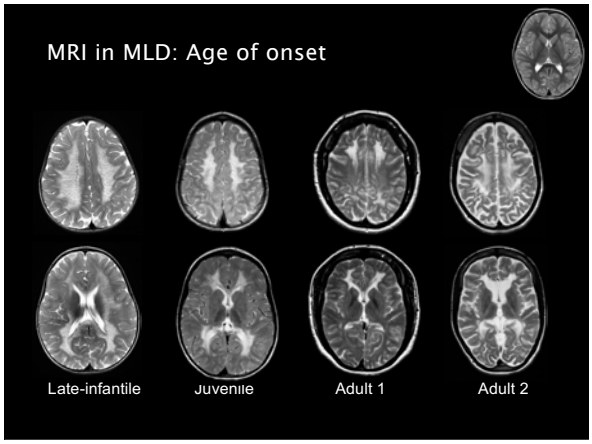
Alpers disease in an infant

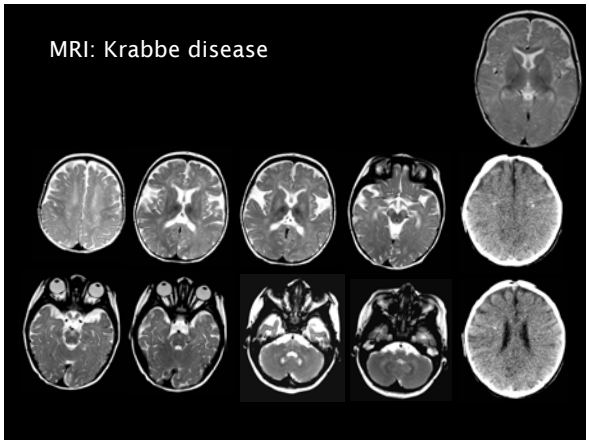
Grey matter disorders with deep grey matter involvement



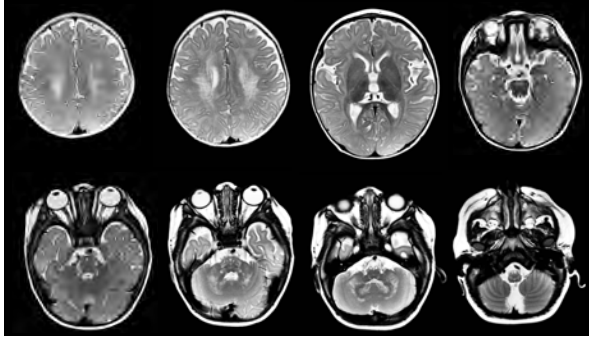
Metabolic Leukodystrophies with early onset



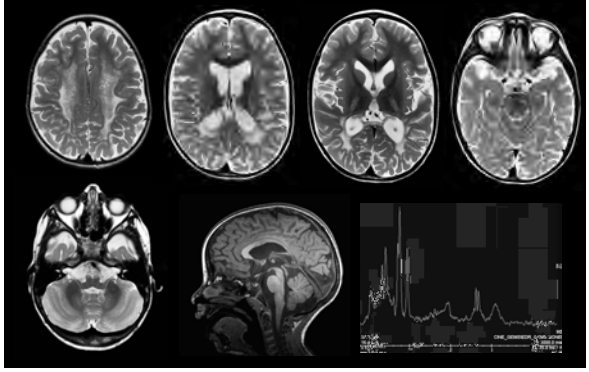




MRI: Krabbe disease with later onset



MRI: juvenile Krabbe disease



What to remember

- Look careful at the imaging.
- Axial T2-weighted images should be always performed.
- Proton spectroscopy may be very helpful, but you can make a diagnosis also without it.
- Look for clinical clues.