

Developmental neurology

Jeroen Vermeulen
Child neurologist
16-05-2022

1

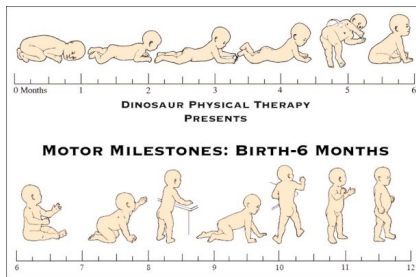
Early brain development

- Motor development
- Neural tube development
- Development of diencephalon, telencephalon
- Development of gyration
- Development of myelination



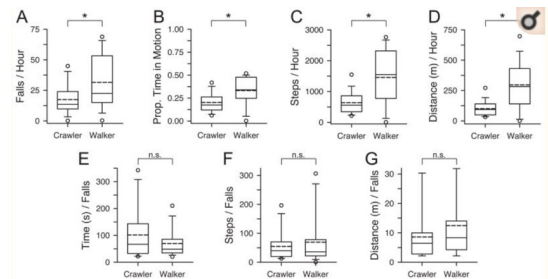
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Stages of motor development



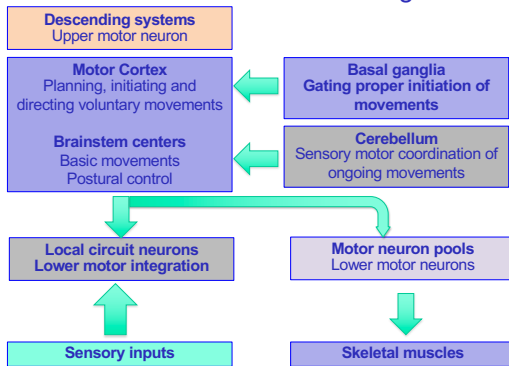
3

Learning how to walk



4

Central control of walking

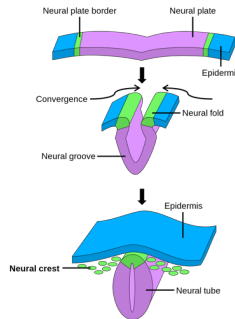


5

Brain development from a child neurology perspective

6

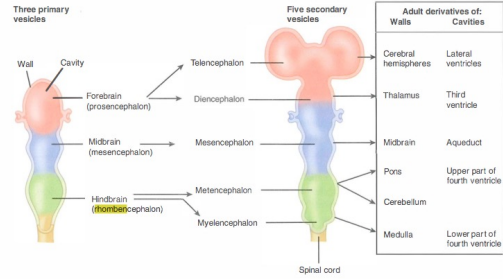
Neural tube development



SOURCE: https://en.wikipedia.org/wiki/Neural_tube

7

Regional specification of developing brain

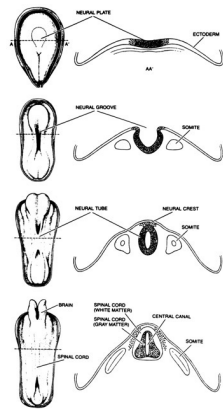


<https://www.studyblue.com/notes/note/n/path-2-study-guide-2012-13-evans/deck/9723277>

8

Spina bifida

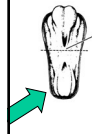
- Abnormal closure of the neural tube
- Timing:...



Cowan 1979

9

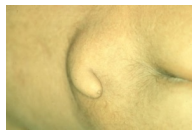
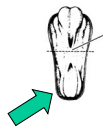
Meningomyelocele



10

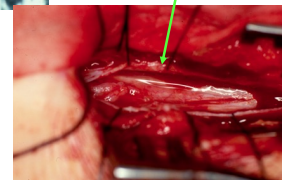
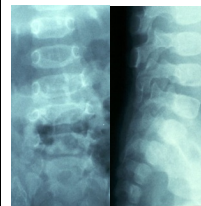
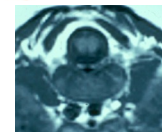
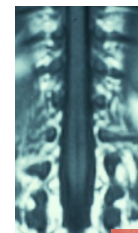


Spina bifida occulta

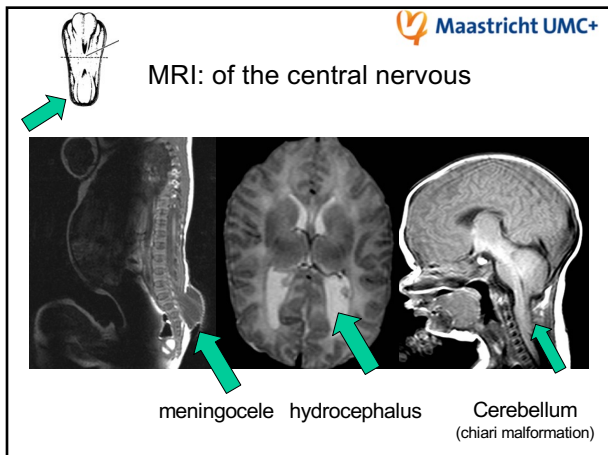


11

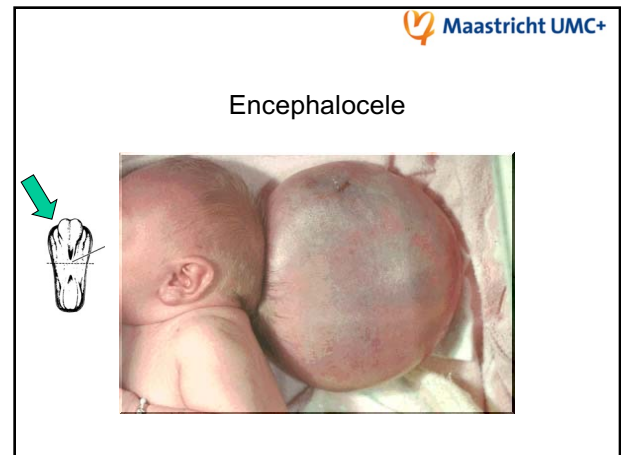
Split cord malformation: diastematomyelia



12



13



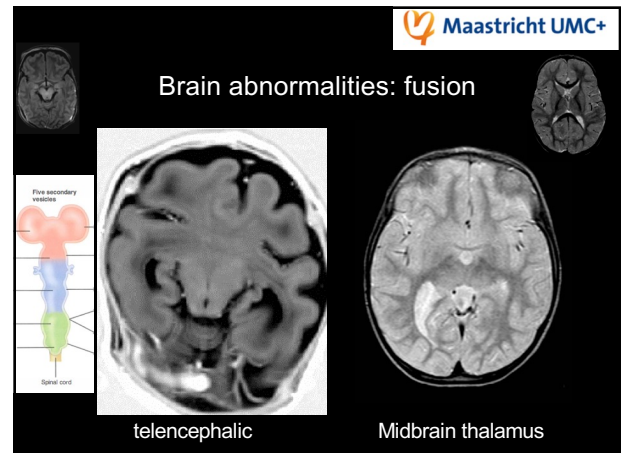
14

Maastricht UMC+

Clinical effect of neural tube defects

- Impairment of bladder and sphincter functions
- Impairment of movement of the lower limbs (level)
- Hydrocephalus
- Cognitive impairment (spectrum)

15



16

Maastricht UMC+

Clinical effect of brain maldevelopment

- Cognitive impairment (spectrum)
- Movement disorders (thalamus -> dystonia)
- Ataxia (cerebellum)

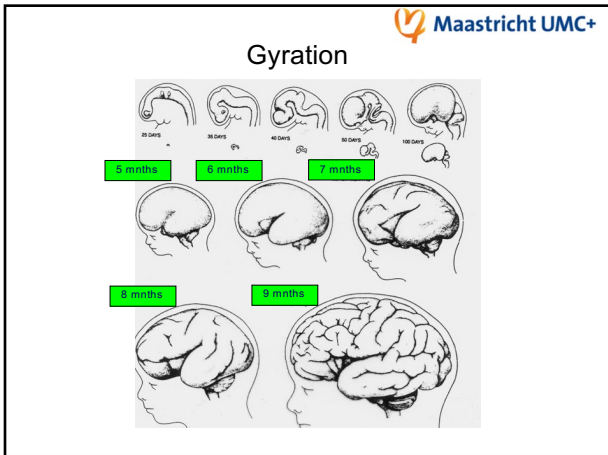
17

Maastricht UMC+

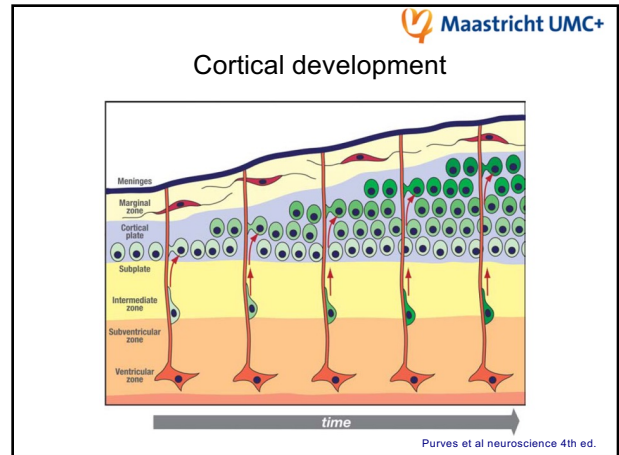
Early spinal cord and brain development take home messages

- Neural tube formation
- Forming of the CNS vesicles
 - Phase 1: 3 primitive vesicles
 - Phase 2: 5 secondary vesicles

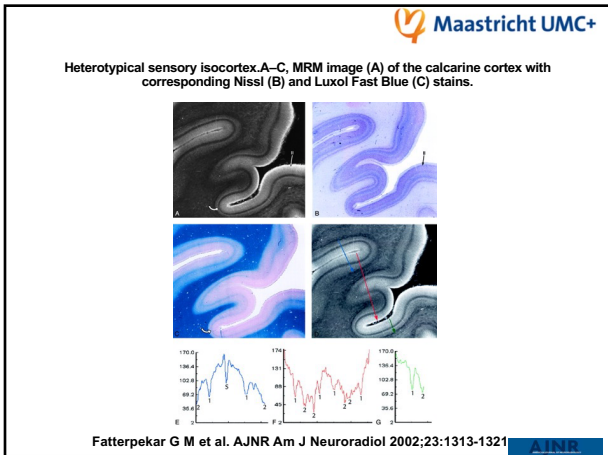
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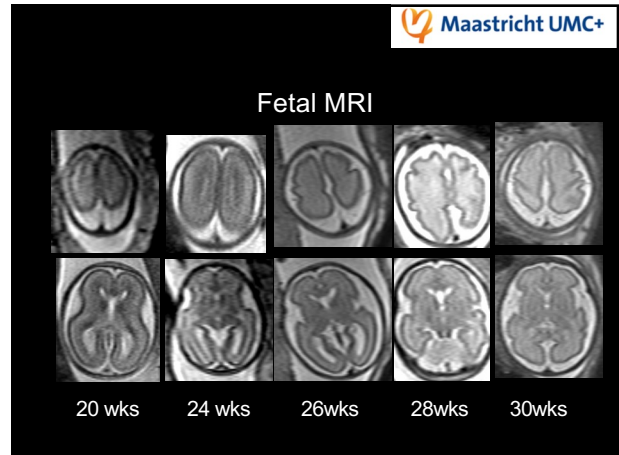
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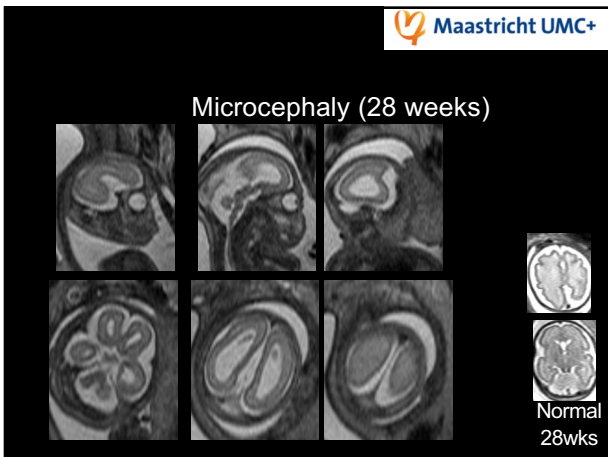
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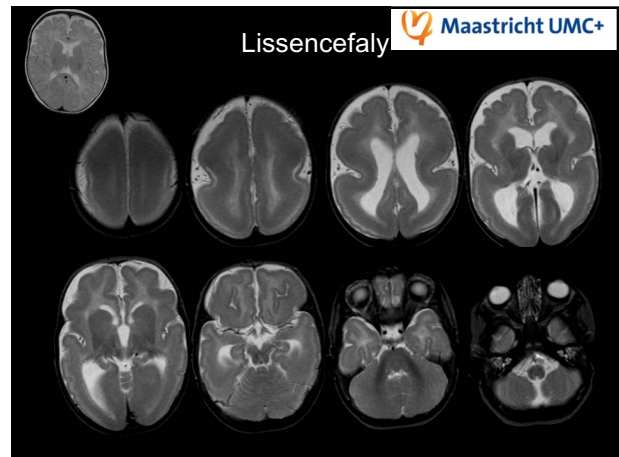
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22

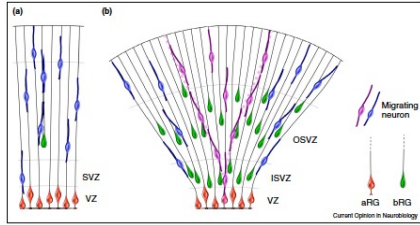


23



24

Neuronal migration



RG radial glia
VZ Ventricular zone
SVZ subventricular zone
IPC intermediate progenitor cells
OSVZ outer subventricular zone

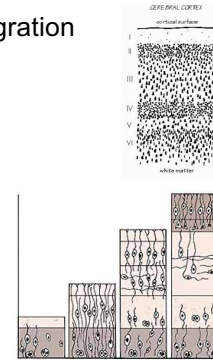
bRGs basic radial glial cells
aRGs apical radial glial cells

Current Opinion in Neurobiology 2014, 27:39-46

25

Timing migration

- 12-24th week
 - Start germinal matrix
 - Formation Subpial pre-plate (primitive plexiform zone)
 - dividing "neurons"
 - Formation cortical plate
 - Migration to the pre-plate
 - Formation cortical layers:
 - "Inside-out principle"



26

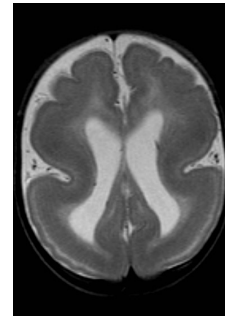
gyration abnormalities

- Type of movement
- Genes involved in neuronal migration (examples):
 - *FLN1* - actin-cross-linking binding protein
 - *PAFAH1B1 (LIS1)* - microtubule asso. protein
 - *DCX (XLIS)* - microtubule asso. Protein
 - *RELN* - extracellular matrix protein
 - *FUKUTIN* - extracellular protein
 - *POMGnT1* - glycosylation enzyme
 - *TUBA1A* - Tubulin-encoding genes

Whole exome sequencing

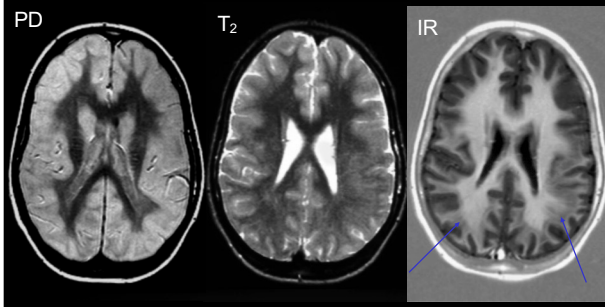
27

LIS1 mutations



28

Subcortical band heterotopia (SBH)



29

DCX mutations

Families with SBH/LIS
60-90% women with SBH
12% males with sporadic LIS

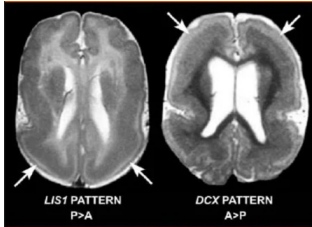
(somatic and germline mosaicism)

Phenotype: Non-random X-inactivation

30

DCX mutaties

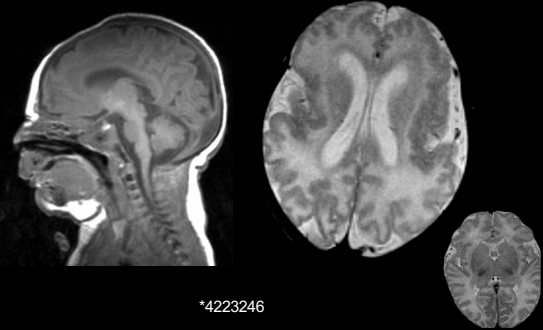
MRI gradient, Anterior>Posterior



https://www.medscape.com/viewarticle/507351_2

31

MRI Anterior > Posterior gradient

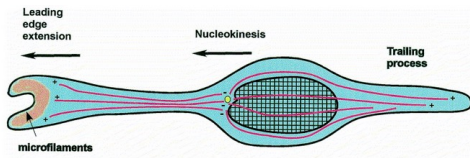


32

Periventricular heterotopia

Complete migration disturbance of a group of neurons

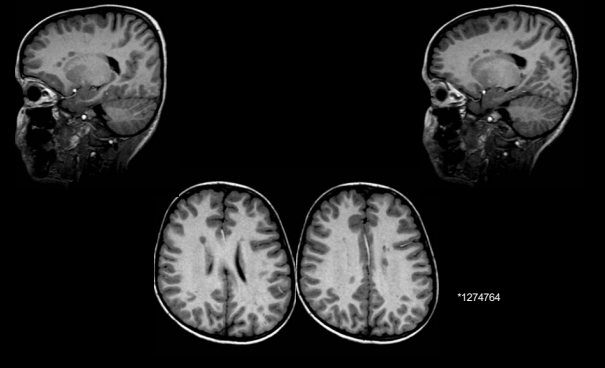
X-linked



Filamin involvement:
FLN1 on Xq28

33

5 years with focal epilepsy

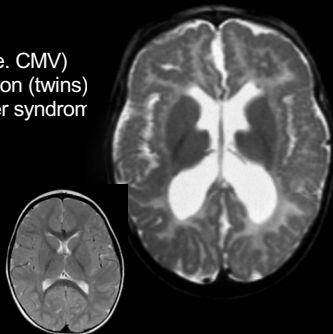


34

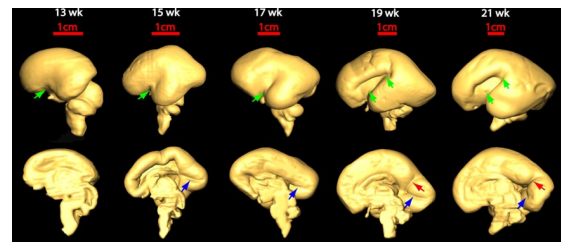
Polymicrogyria

Etiology

- intrauterine infection (i.e. CMV)
- intrauterine hypoperfusion (twins)
- metabolic (i.e. Zellweger syndrom peroxisomal disorders)



35

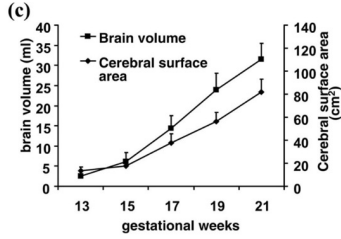


Sylvian fissure (green arrow),
Calcarine fissure (blue arrow)
Parieto-occipital sulcus (red arrow)

J Neurosci 2009 April 1; 29(13): 4263-4273

36

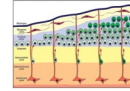
Consequences of growth



37

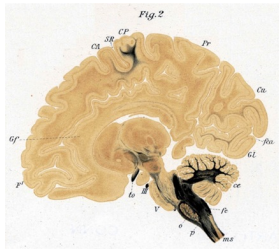
Take home message cortical development

- Germinal matrix
- Formation Subpial pre-plate (primitive plexiform zone)
 - dividing "neurons"
- Formation cortical plate
 - Migration to the pre-plate
- Formation cortical layers:
 - "Inside-out principle"



38

Myelination

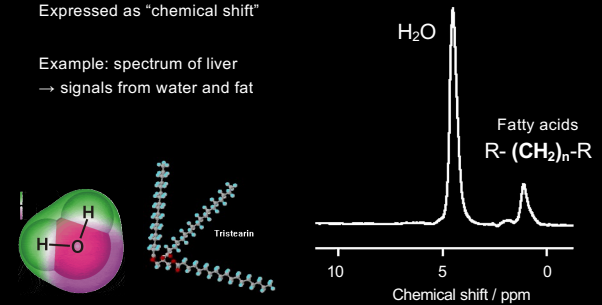


39

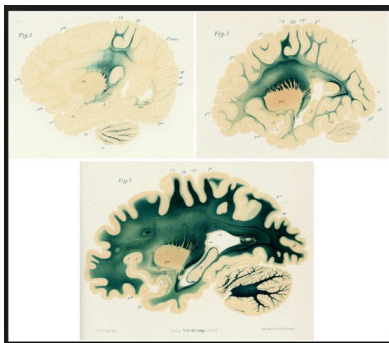
MR spectroscopy

Resonance frequency of ¹H nuclei depends on local magnetic field and thus on their position in a molecule. Expressed as "chemical shift"

Example: spectrum of liver
→ signals from water and fat

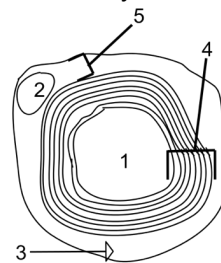


40



41

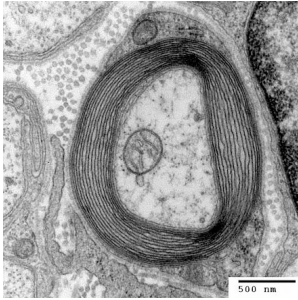
Myelination proces



1. Axon
2. Nucleus of Schwann Cell
3. Schwann Cell
4. Myelin Sheath
5. Neurilemma

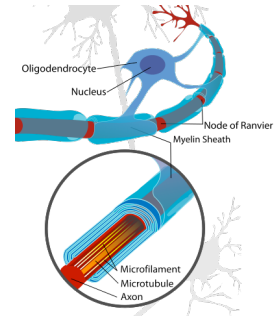
42

Electron microscopy



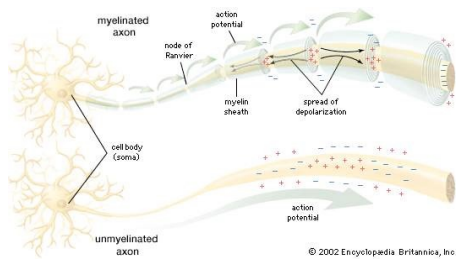
43

Effect of myelination



44

Saltatory current and nodes of Ranvier

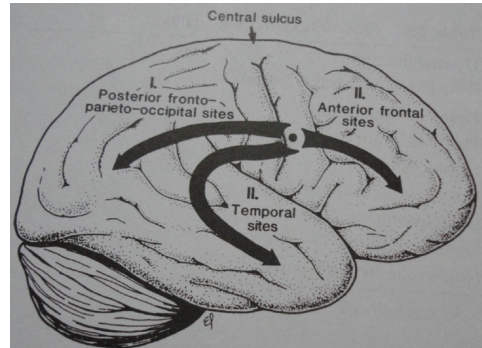


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<https://www.britannica.com/science/node-of-Ranvier>

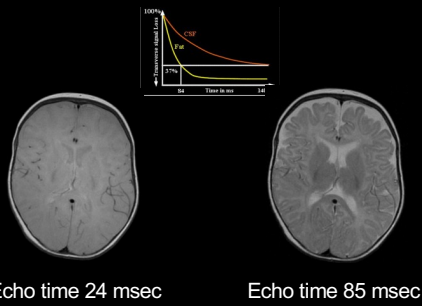
45

Direction of myelination



46

Young brain: Effect of T2 echo time

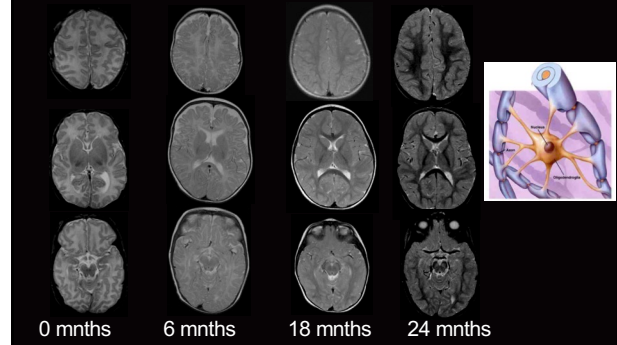


Echo time 24 msec

Echo time 85 msec

47

Myelination stages: T2



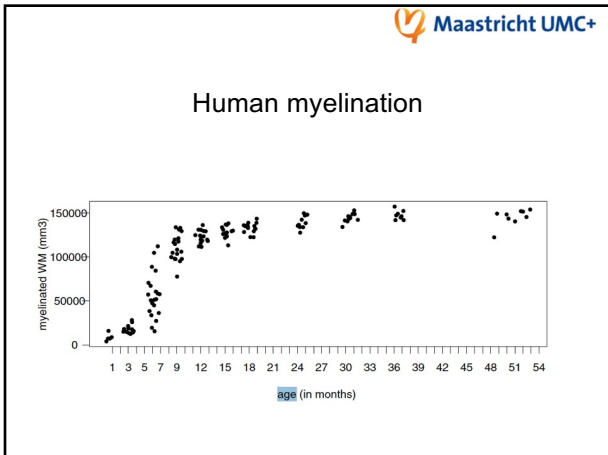
0 mnths

6 mnths

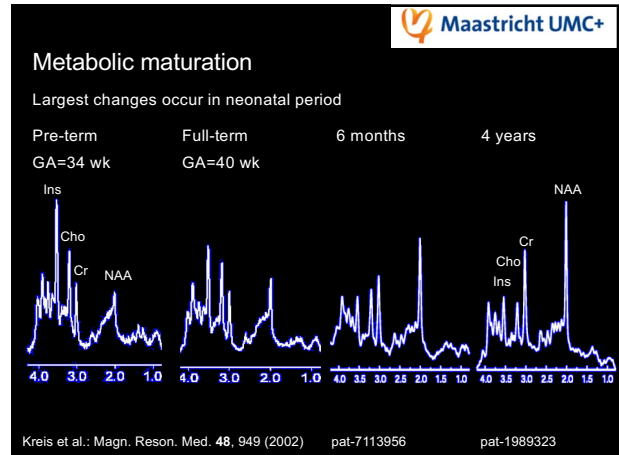
18 mnths

24 mnths

48



49



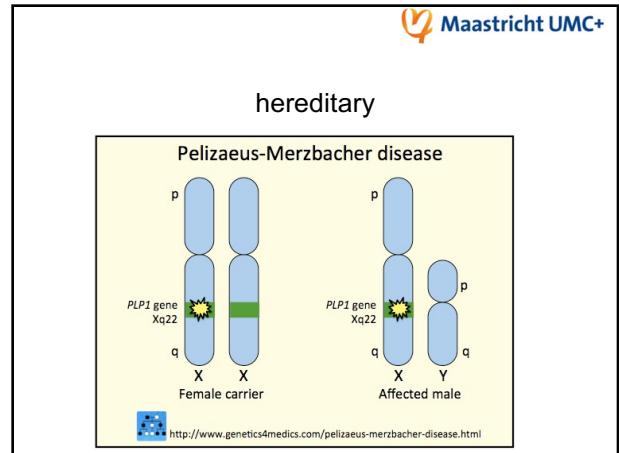
50

Maastricht UMC+

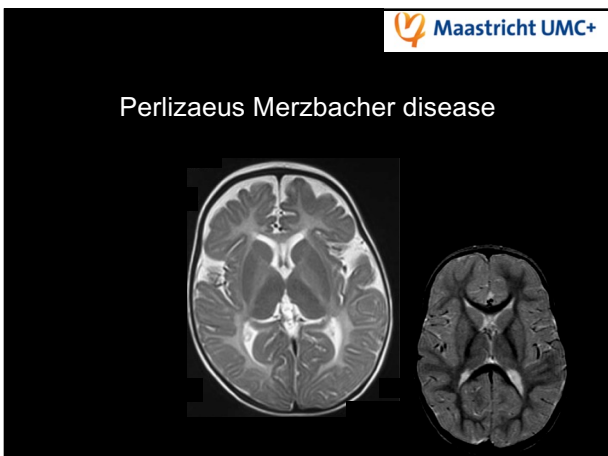
Causes of abnormal myelination

- Hereditary white matter disorders (hypomyelination)
 - Mitochondrial genes
- Acquired
 - Prematurity

51



52



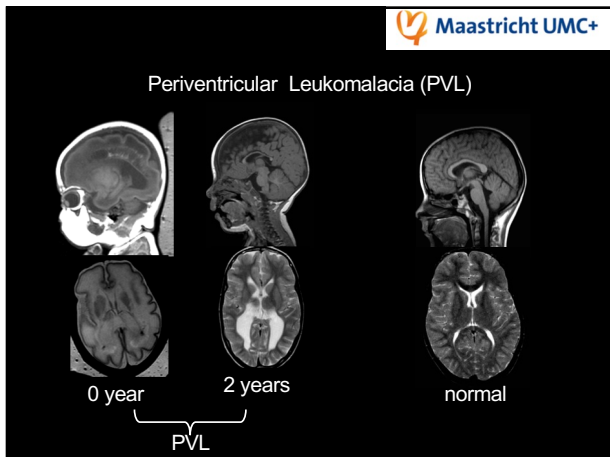
53

Maastricht UMC+

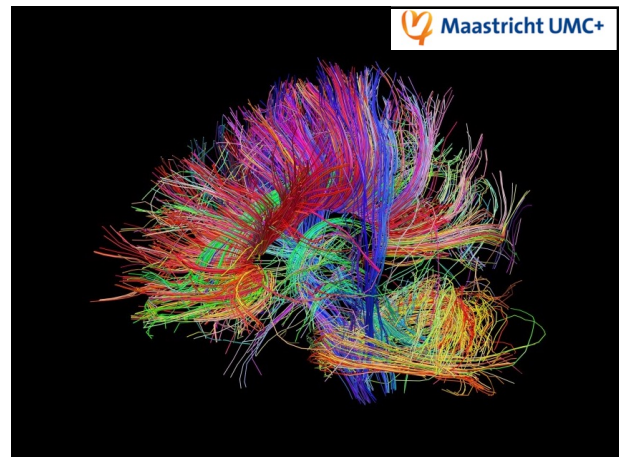
Preterm origin

- White matter damage
- Intra cerebral hemorrhages

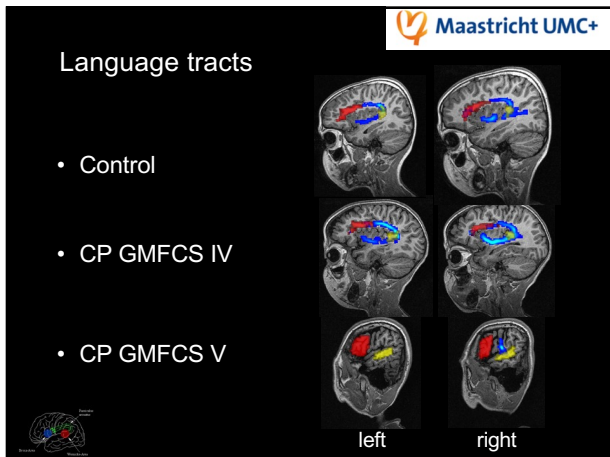
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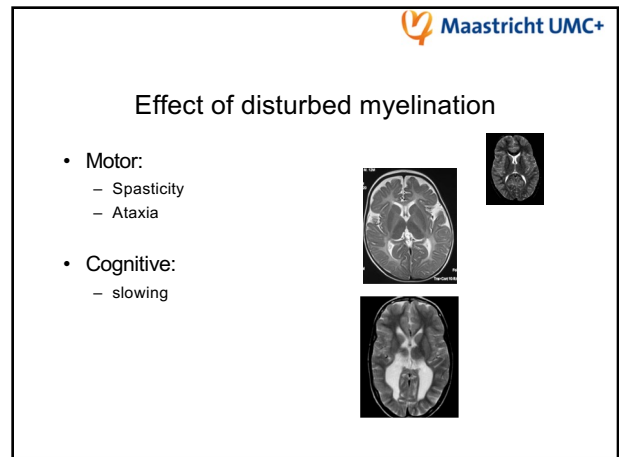
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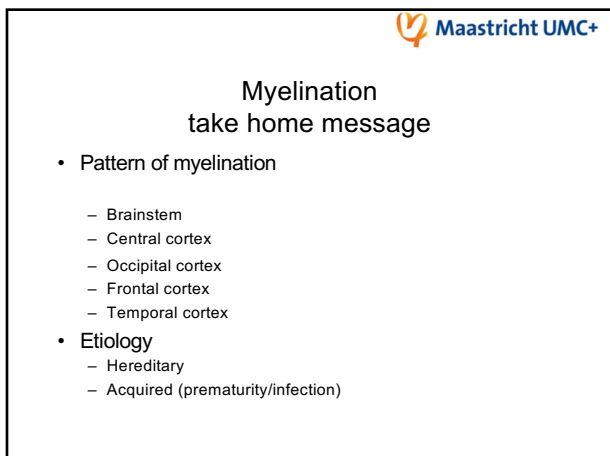
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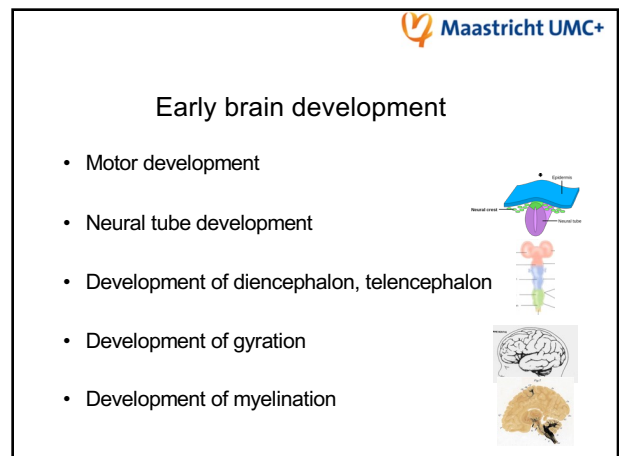
57



58



59



60