

Advanced magnetic resonance imaging for monitoring brain development and injury

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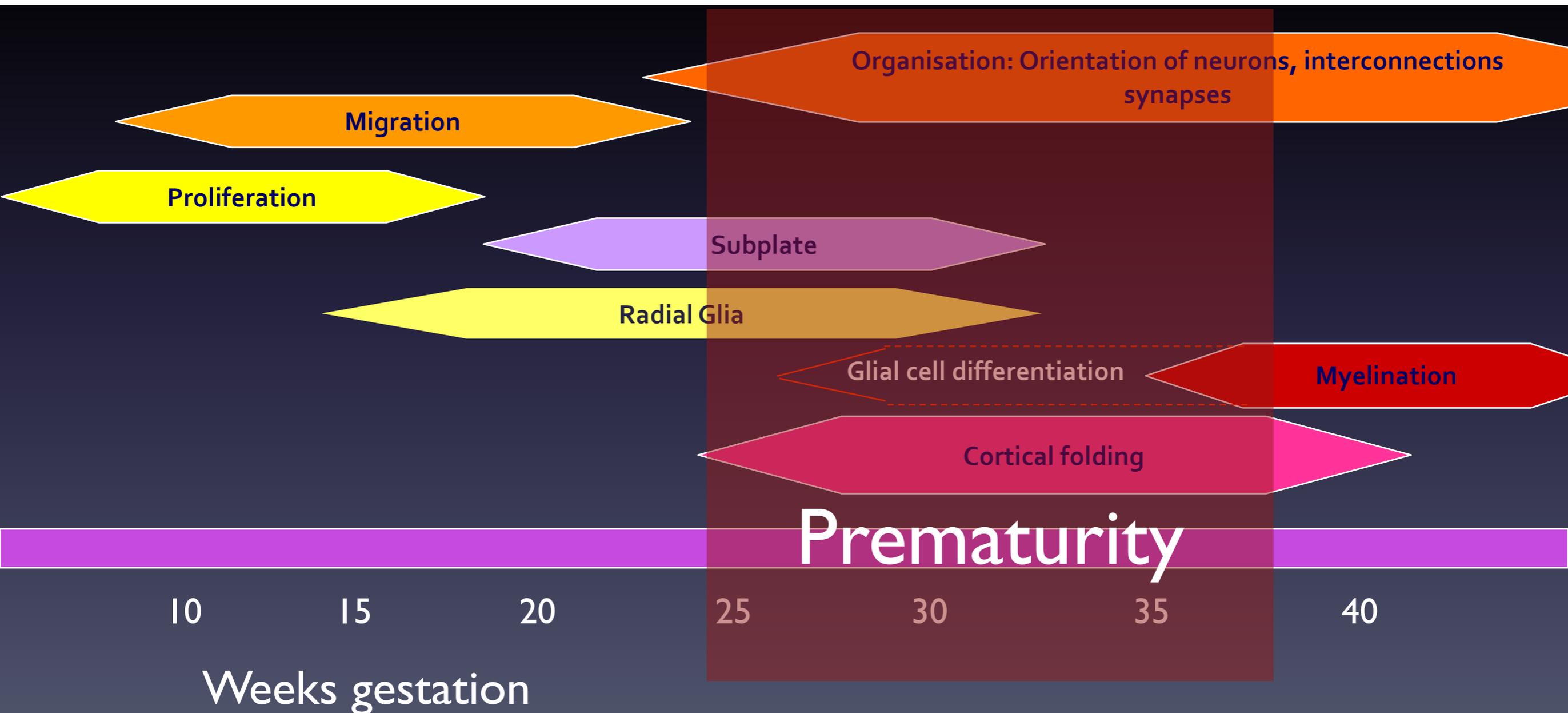
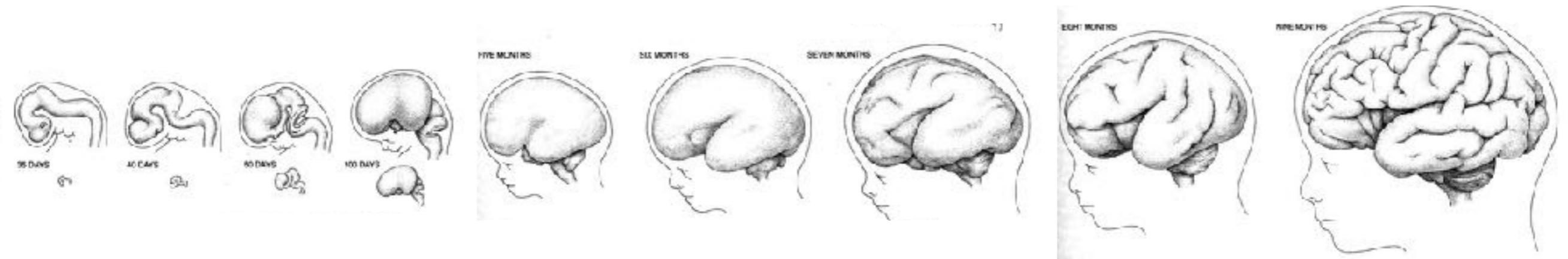


Vulnerability of the developing brain: prematurity-growth restriction

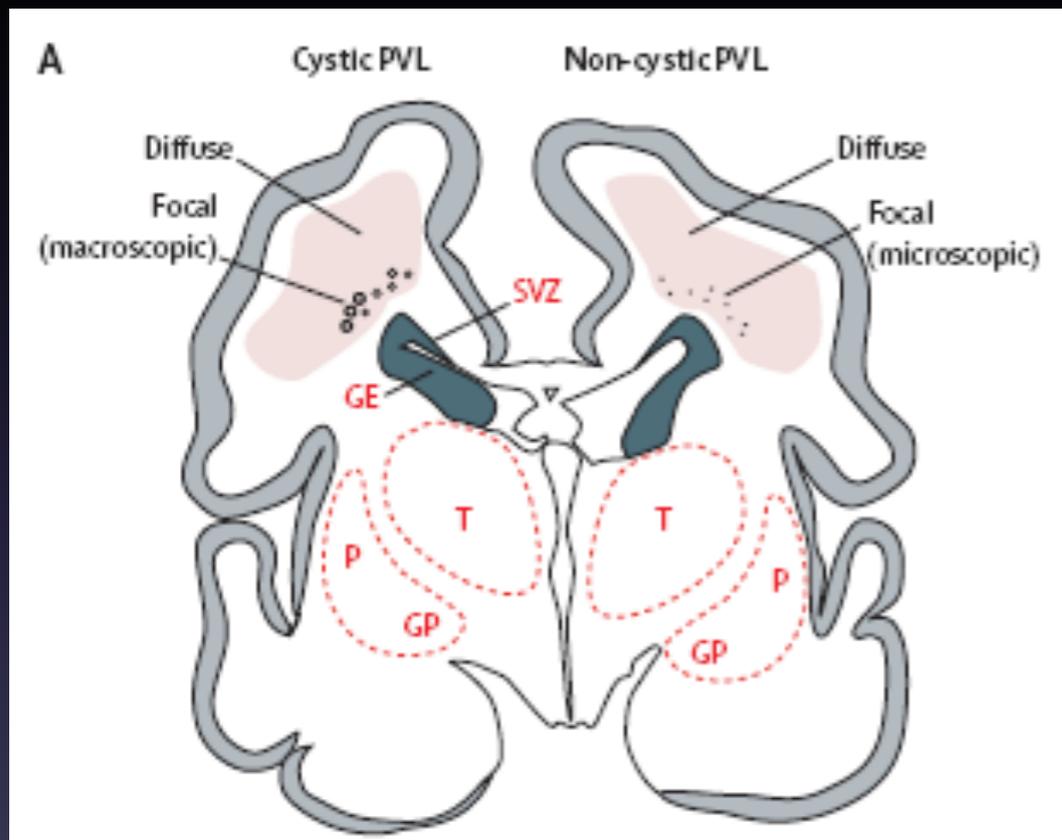
- Preterms <1500g and IUGR
- 5-15% major neurological deficits
 - Cerebral palsy, hemiplegia, diplegie, quadriplegia.
- 25-50% neurodevelopmental deficits
 - Cognitives deficits, attention, learning disabilities, behavioural difficulties
 - ADHD
- Risk factor for adult psychiatric diseases



The making of the brain



Encephalopathy of Prematurity



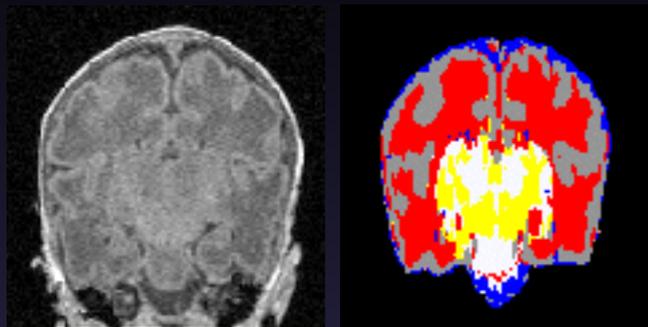
Volpe JJ Lancet Neurol 2009;8:110-24

- Vulnerability of the SVZ vs stimulation of stem cells of the SVZ
- Focal & diffuse lesion of the white matter
- Necrosis, apoptosis of OL progenitors
- Arrest of maturation of OL lineage
- Myelination deficit
- Astrogliosis / microglia activation
- Neuro-axonal damage
- Cortical and subcortical grey matter damage
- Cortical lamination alteration
- Subplate neuronal damage
- Connectivity alteration

Advanced MR imaging: Multimodal tool to study brain development and injury

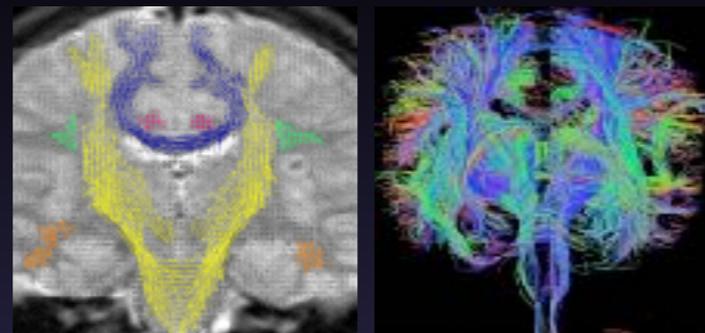
T1-T2, 3D MRI

MACROSTRUCTURE



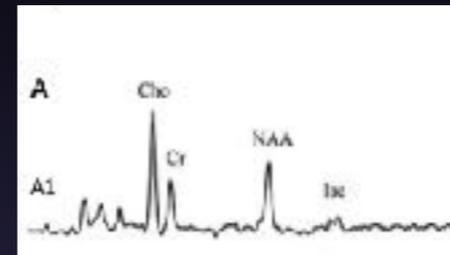
DWI-DTI

MICROSTRUCTURE



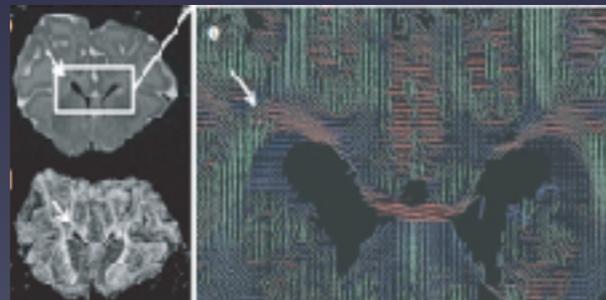
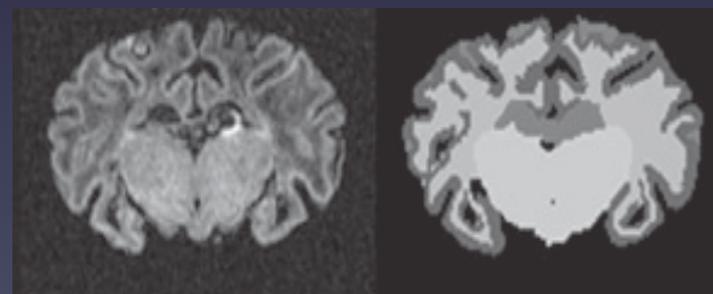
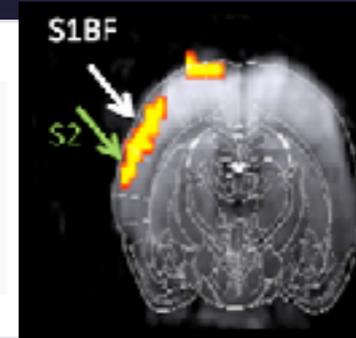
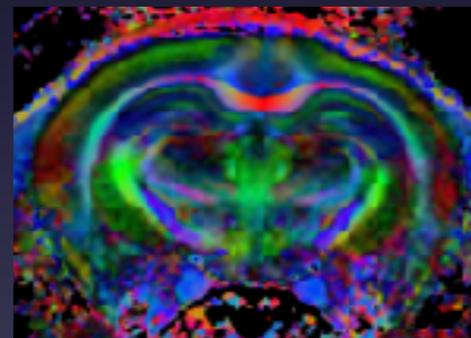
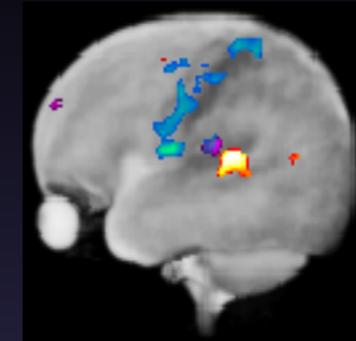
1H-MRS

METABOLISM



f-MRI

FUNCTION

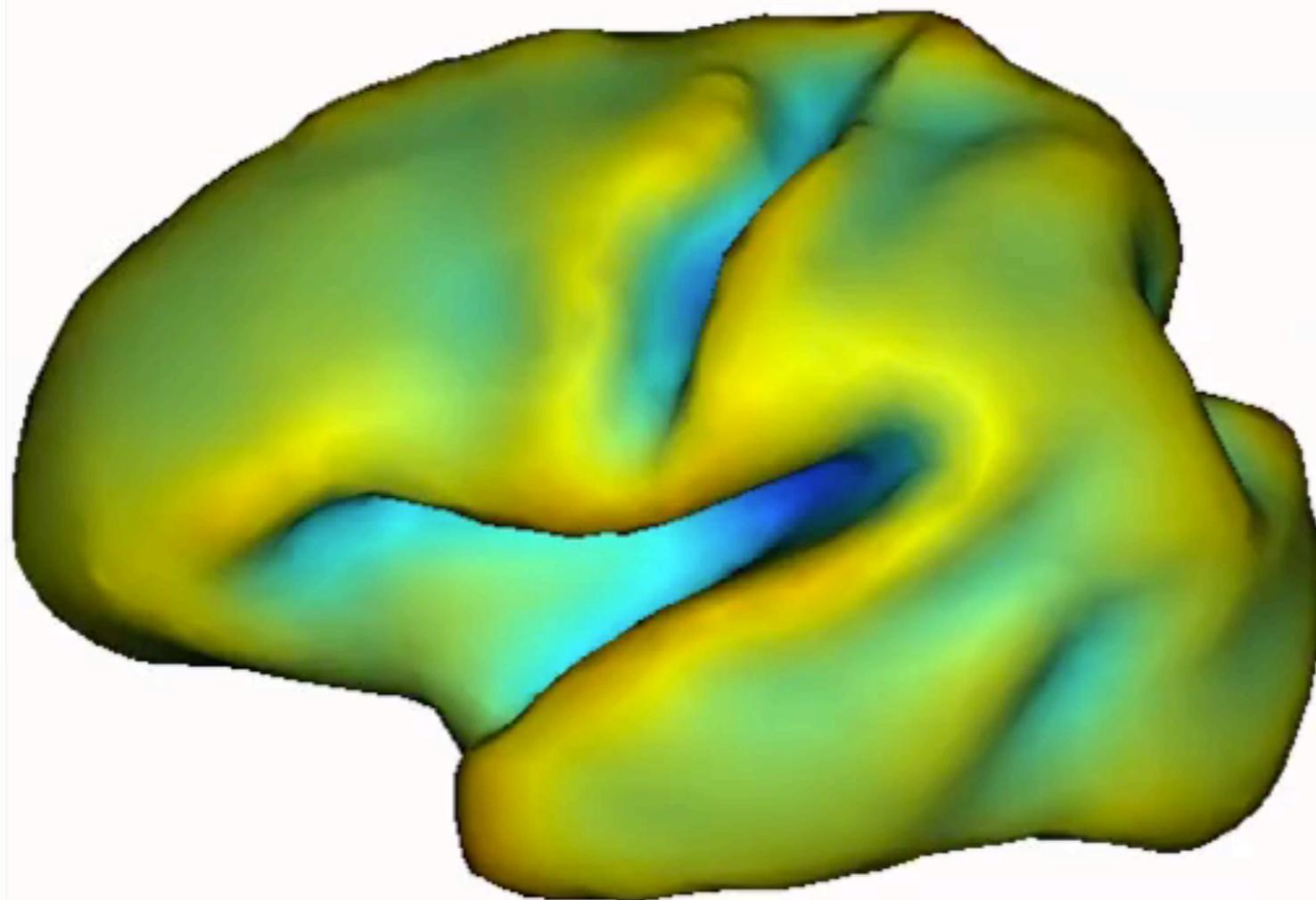


Human

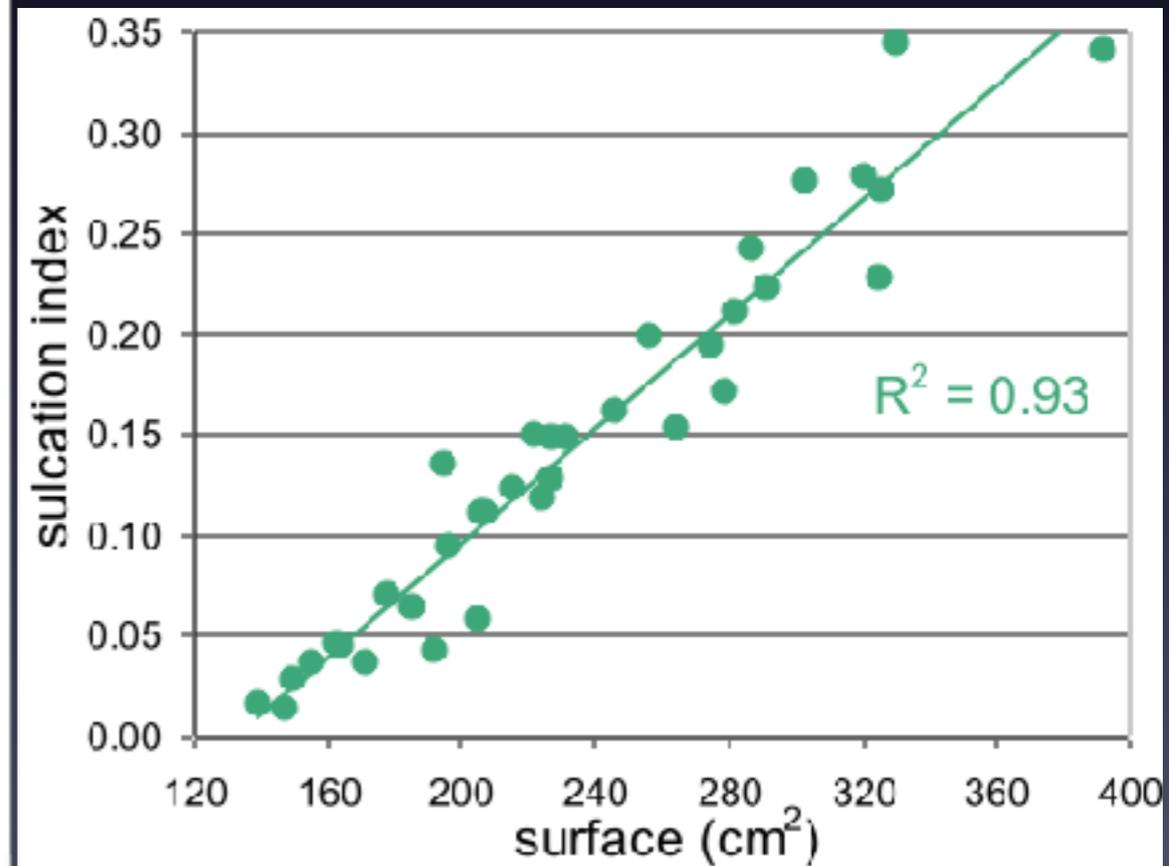
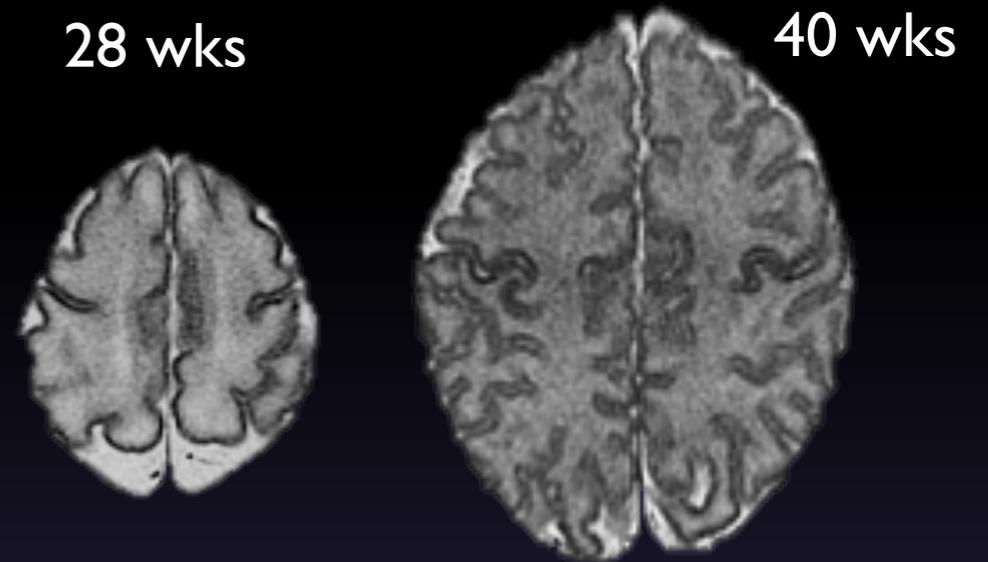
Rodent

Sheep

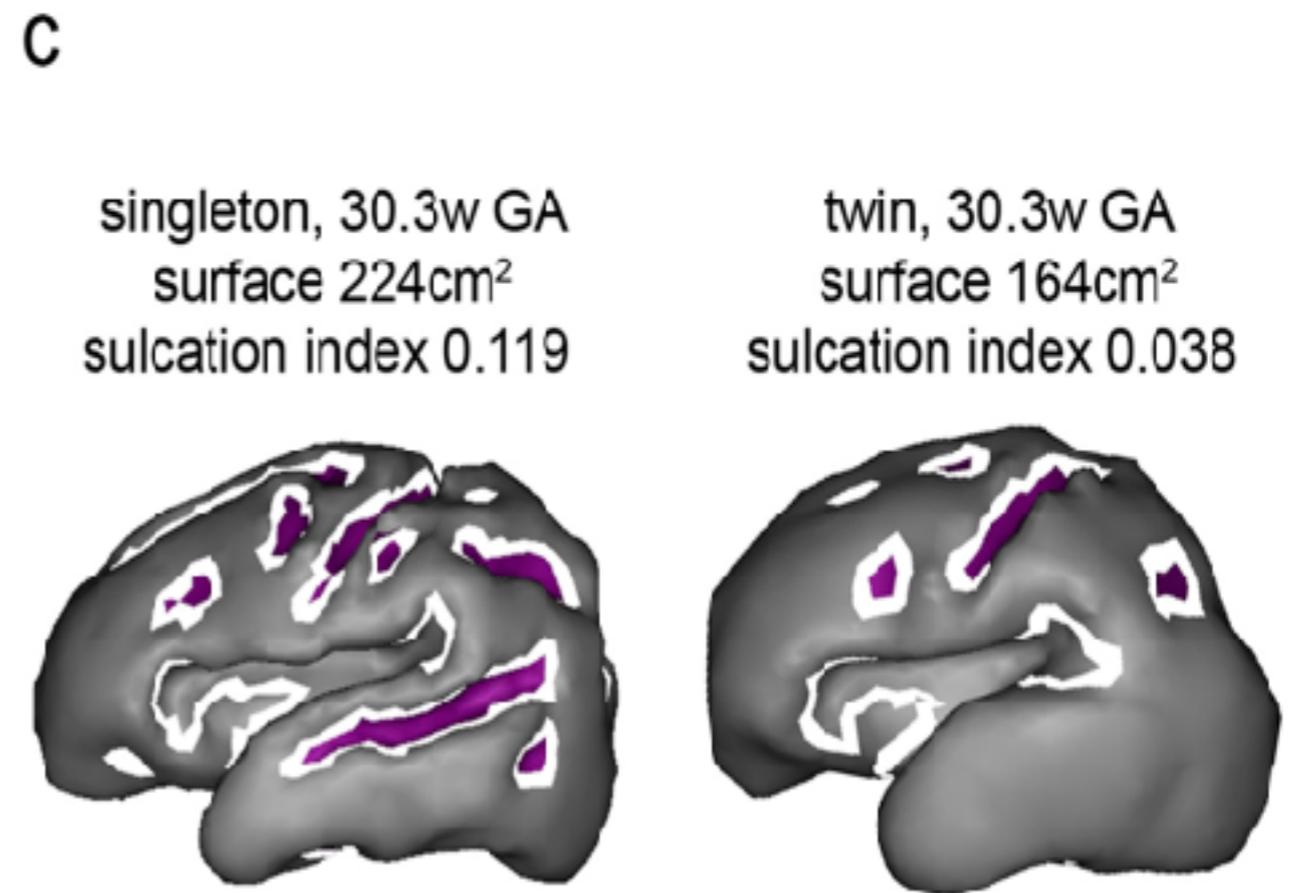
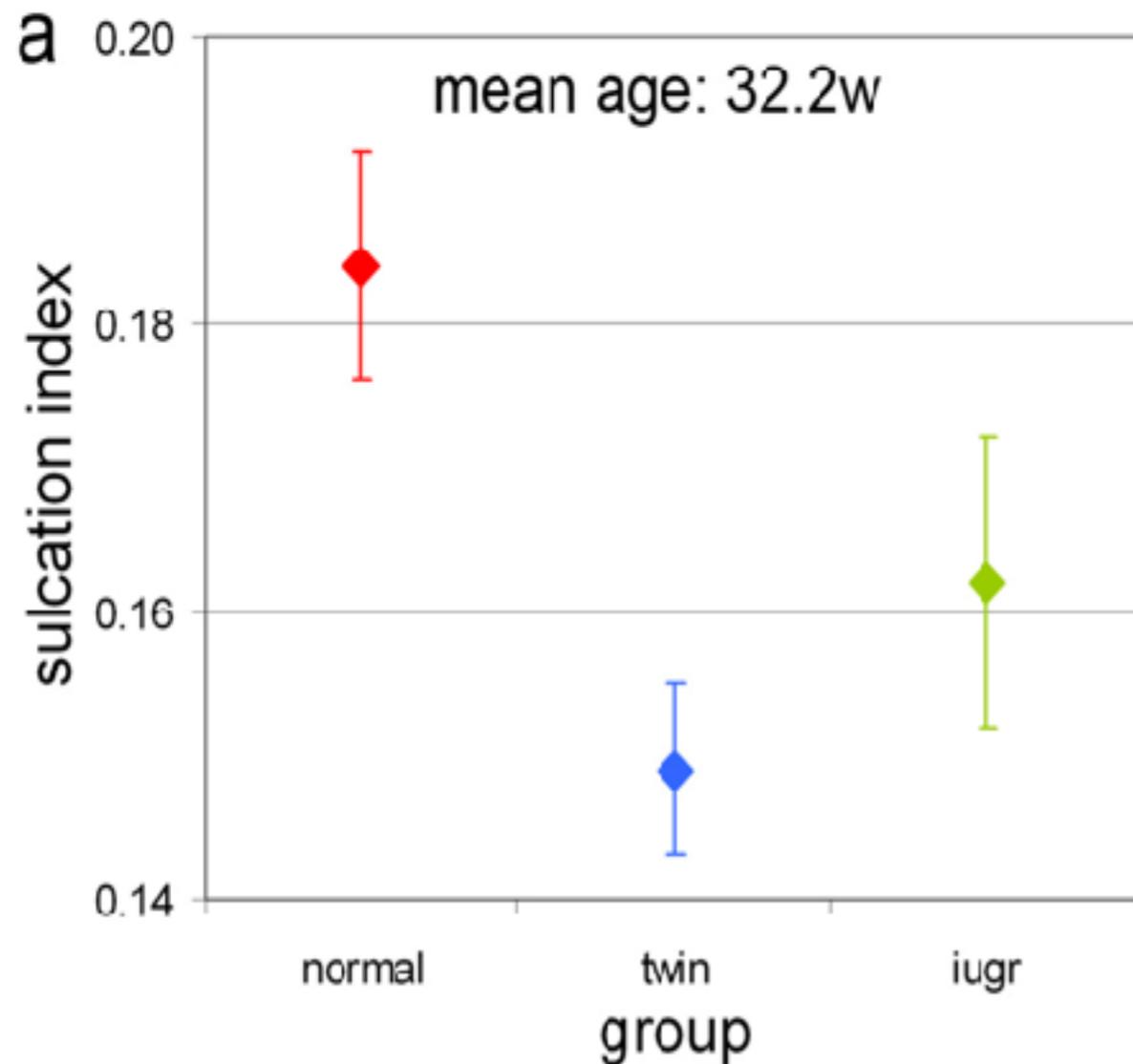
Gyrification index: internal cortical surface



26 weeks to 36 weeks

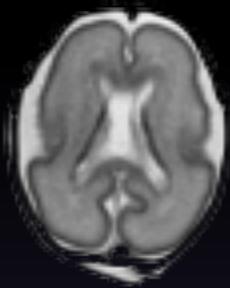


Cortical maturation: effect of twinning and IUGR in preterm

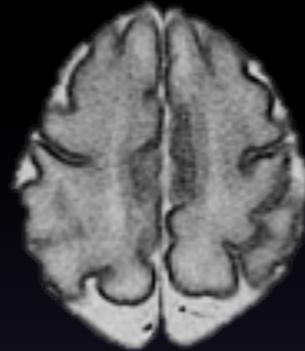


Cortical grey matter development

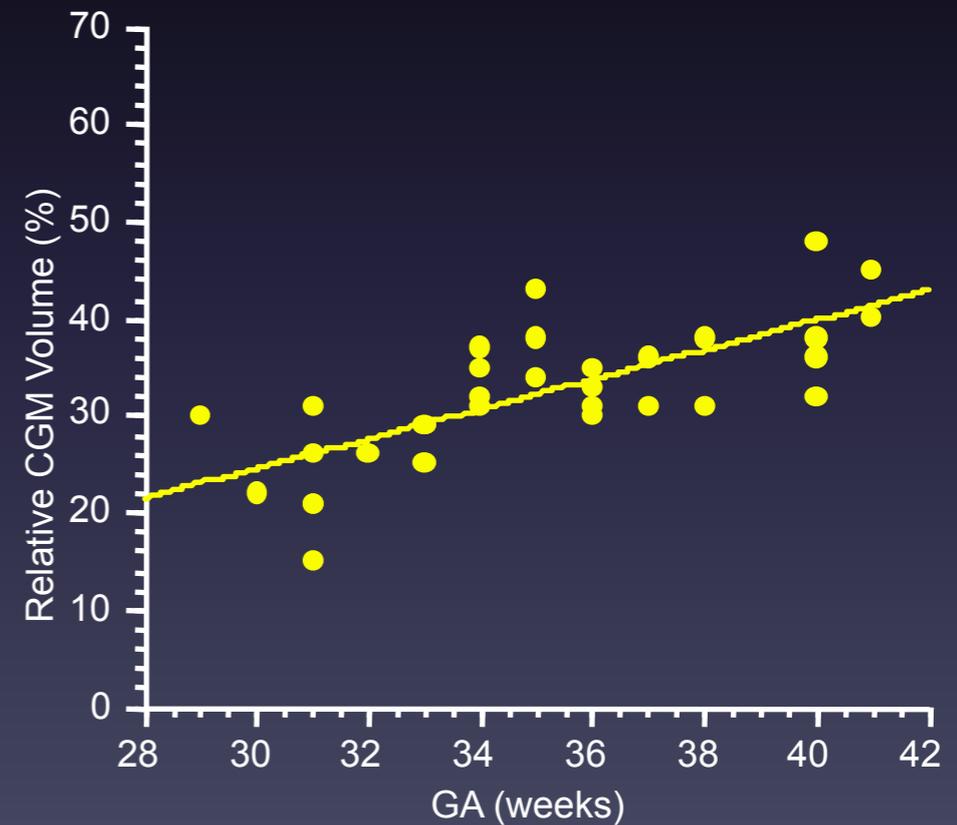
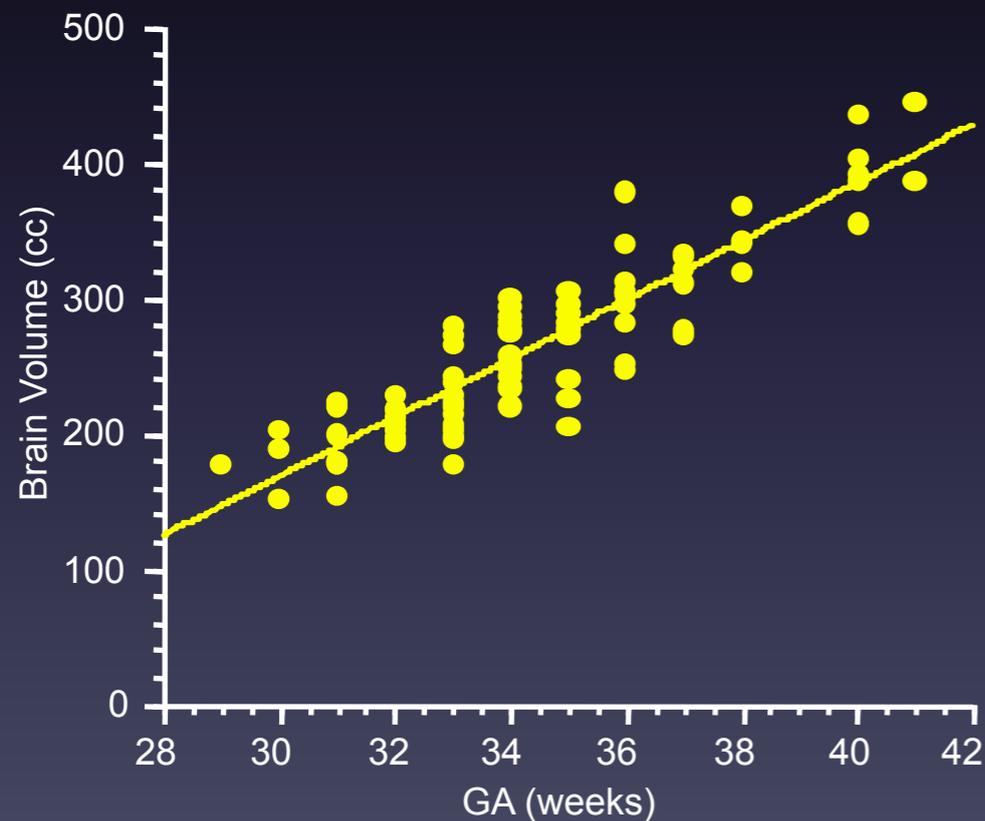
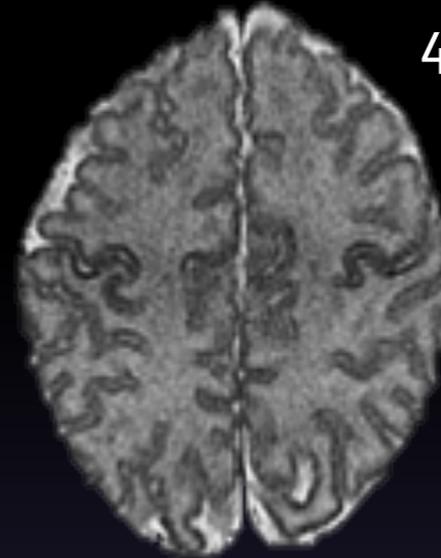
25 wks



28 wks



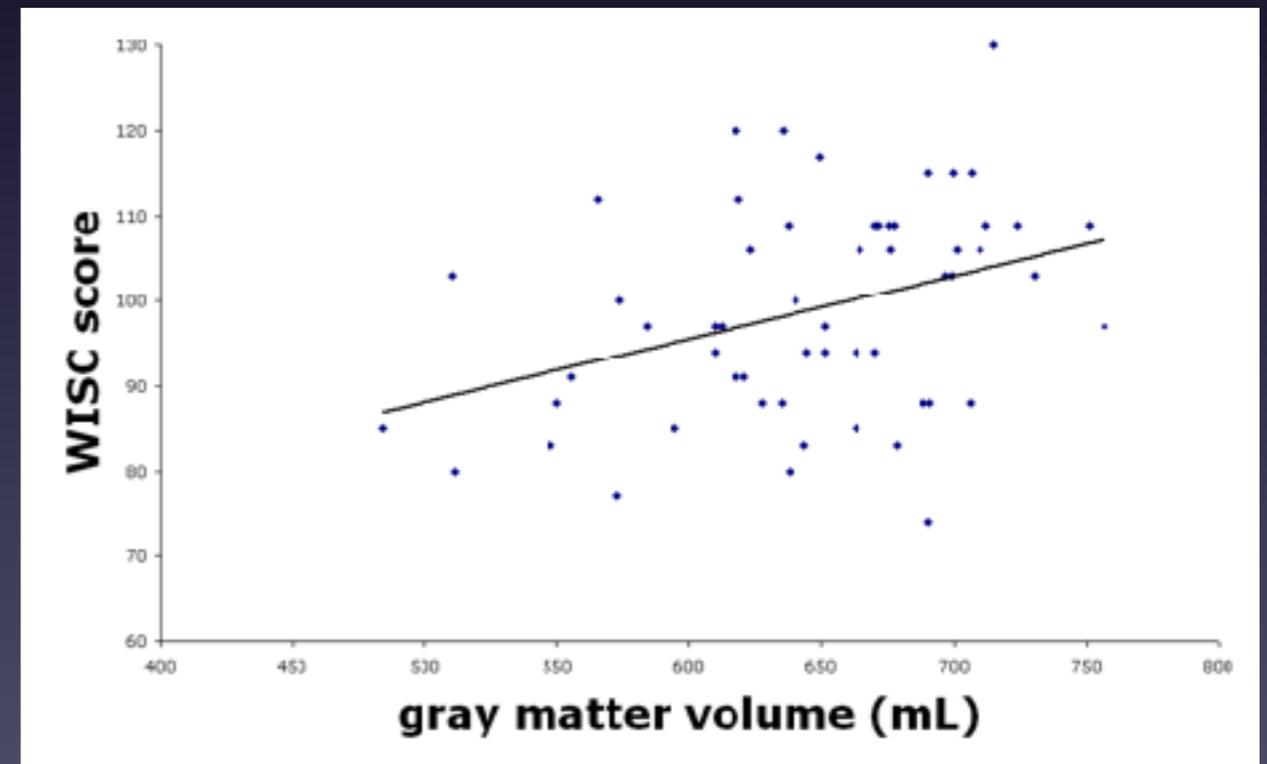
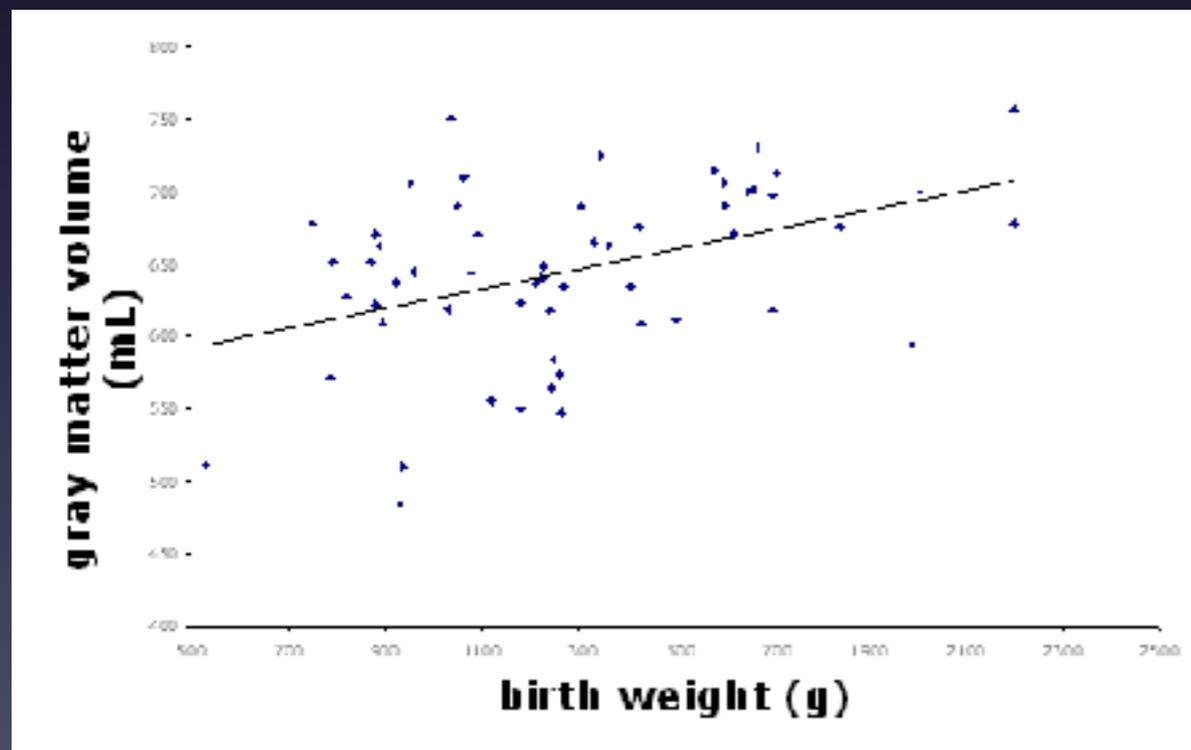
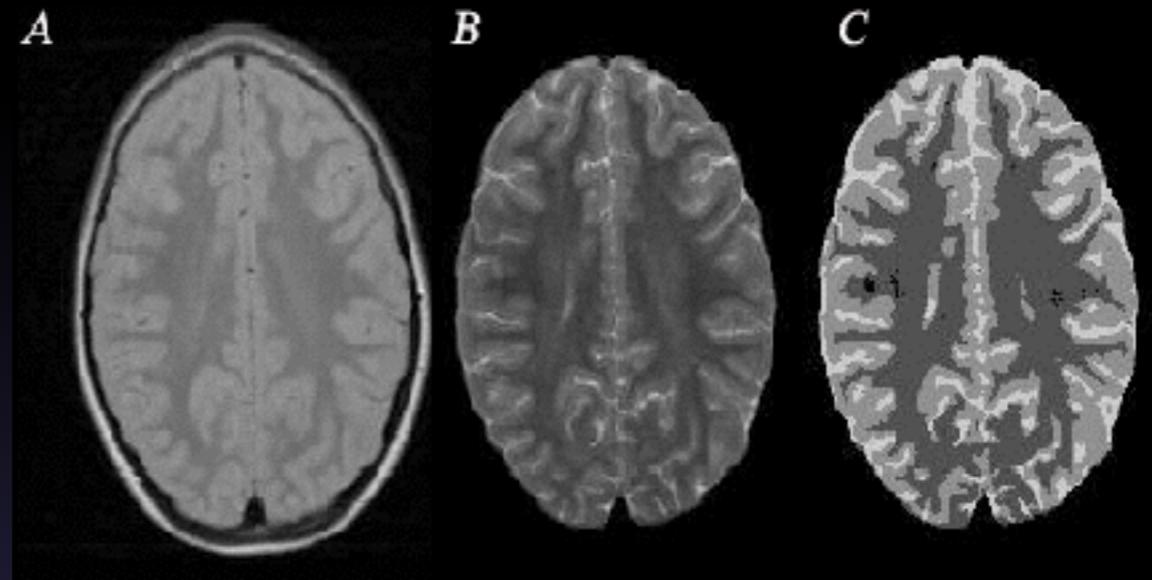
40 wks



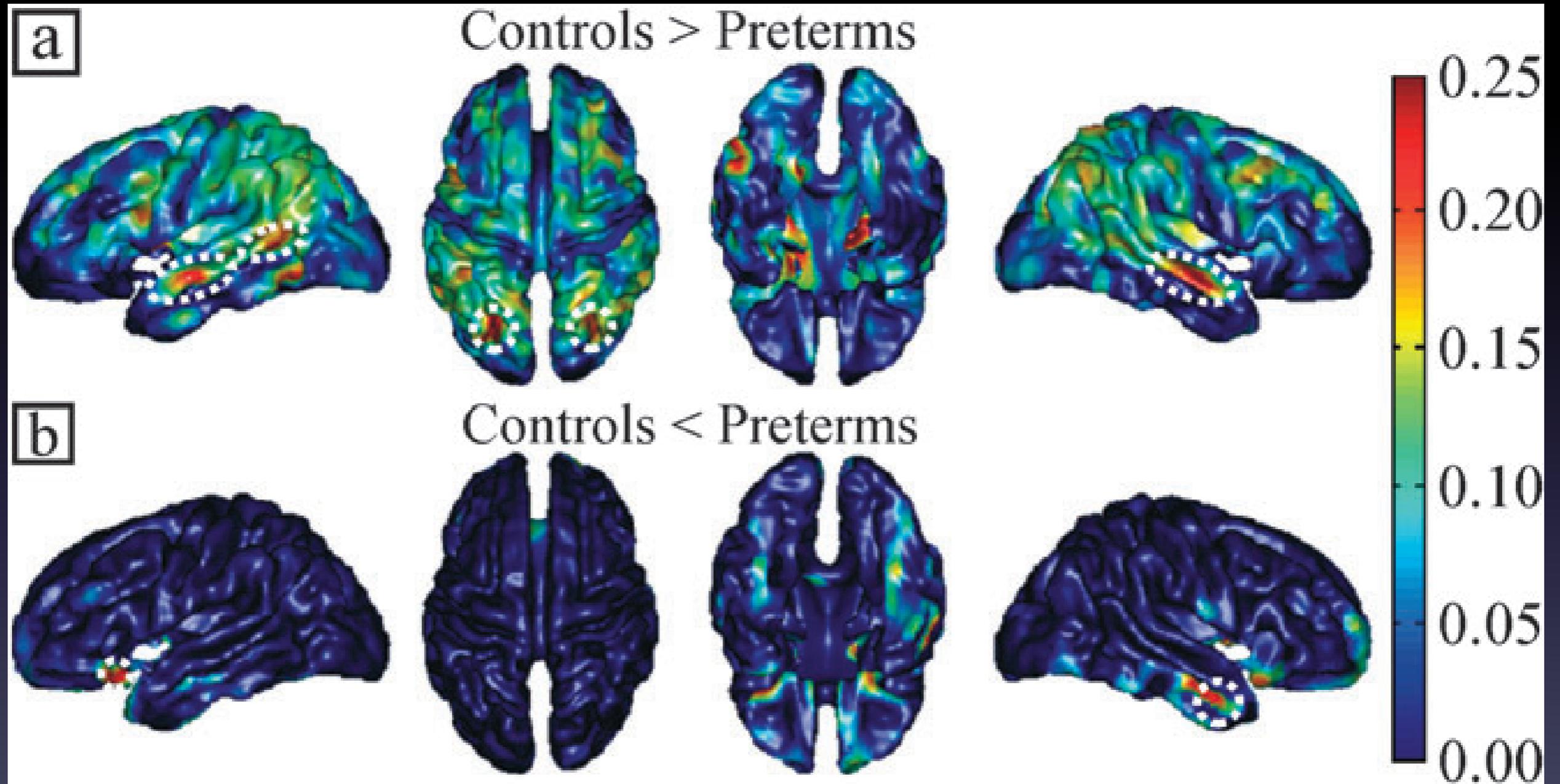
Hüppi, PS et al *Ann Neurol* 1998 43(2) 224-235
Ball, G., et al. (2012). *Cereb Cortex* 22(5): 1016-1024.

Long term alteration of grey matter development at 8 years in preterms

3D-MRI at 8 years
WISC score of development

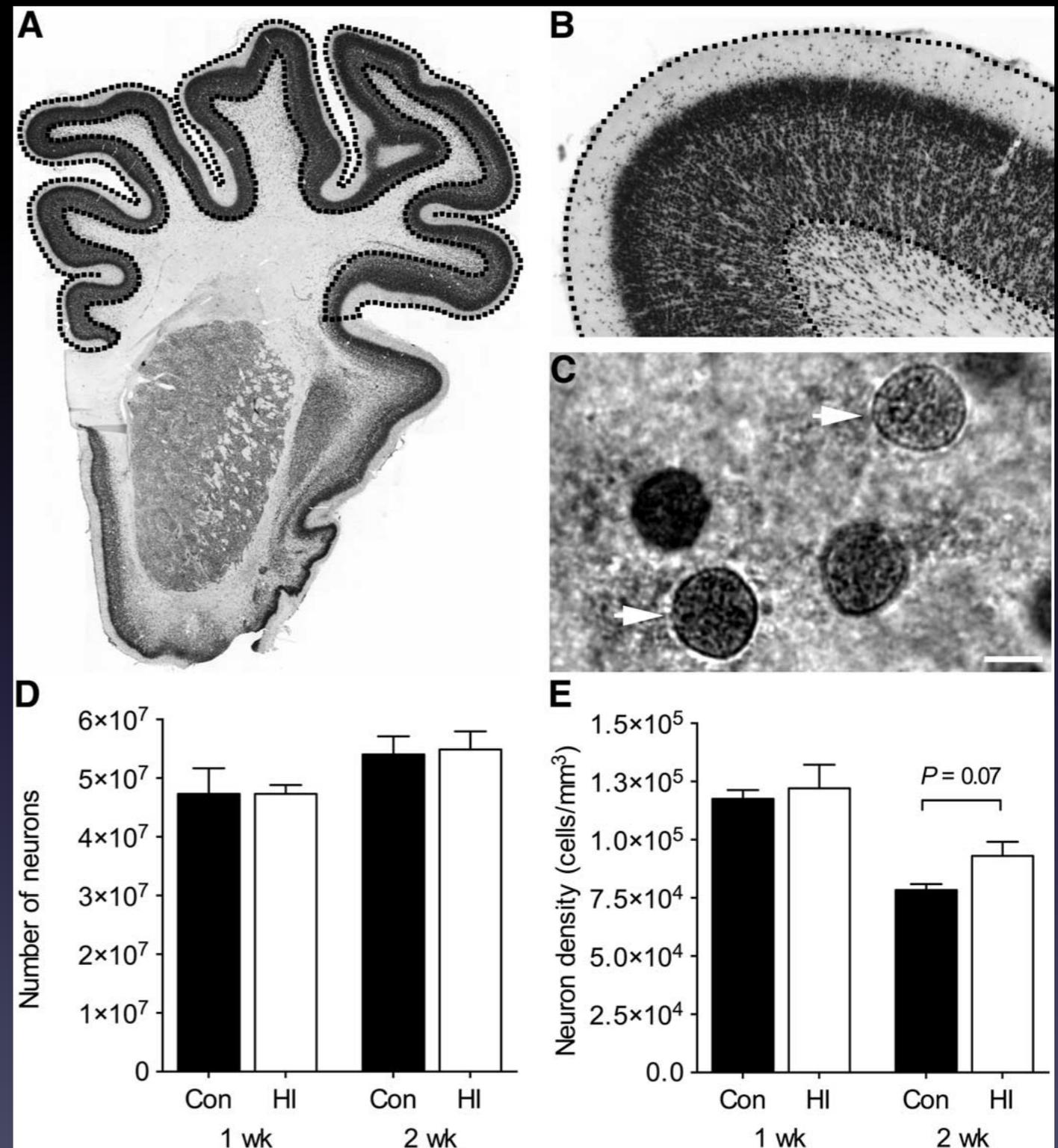
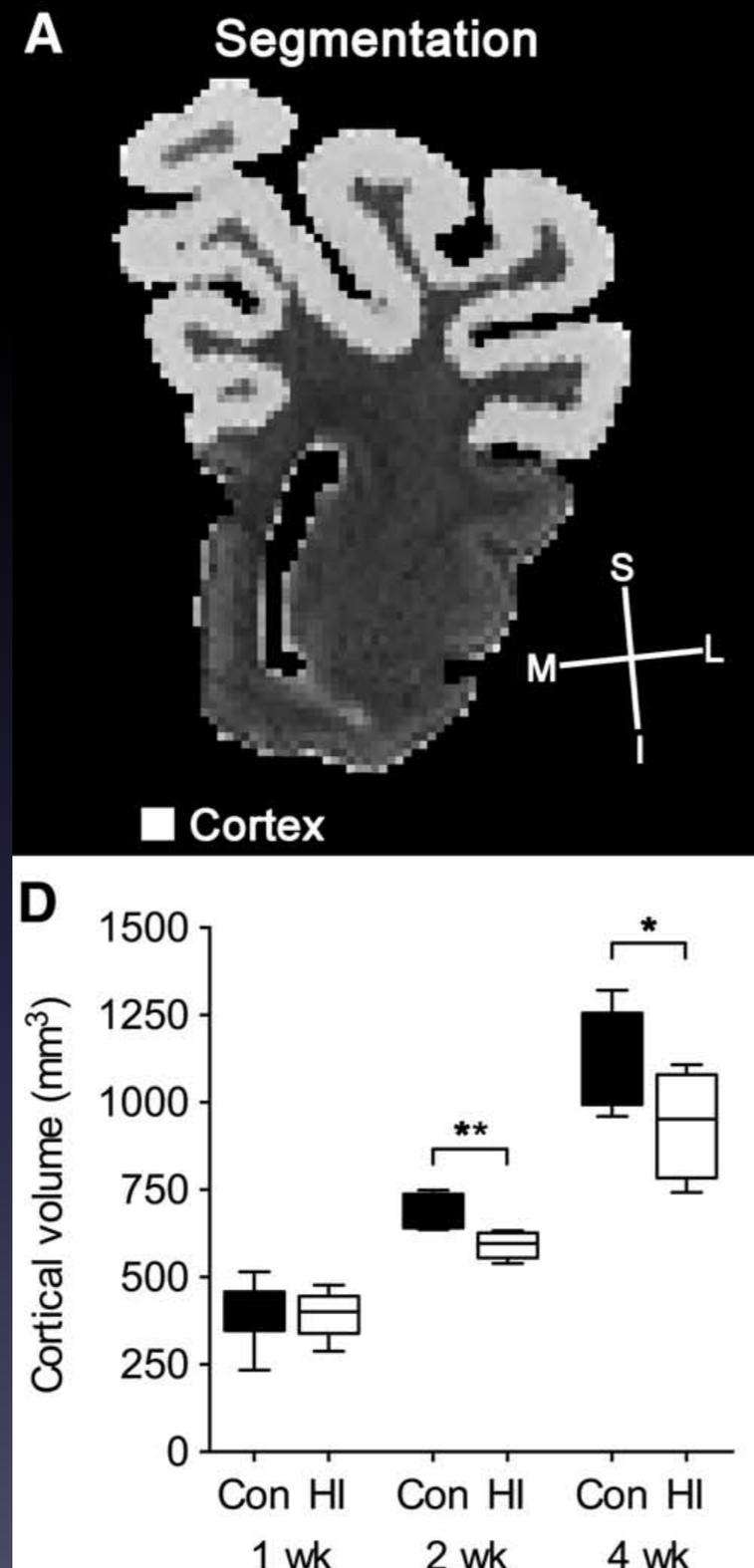


Cortical Thickness at adolescence



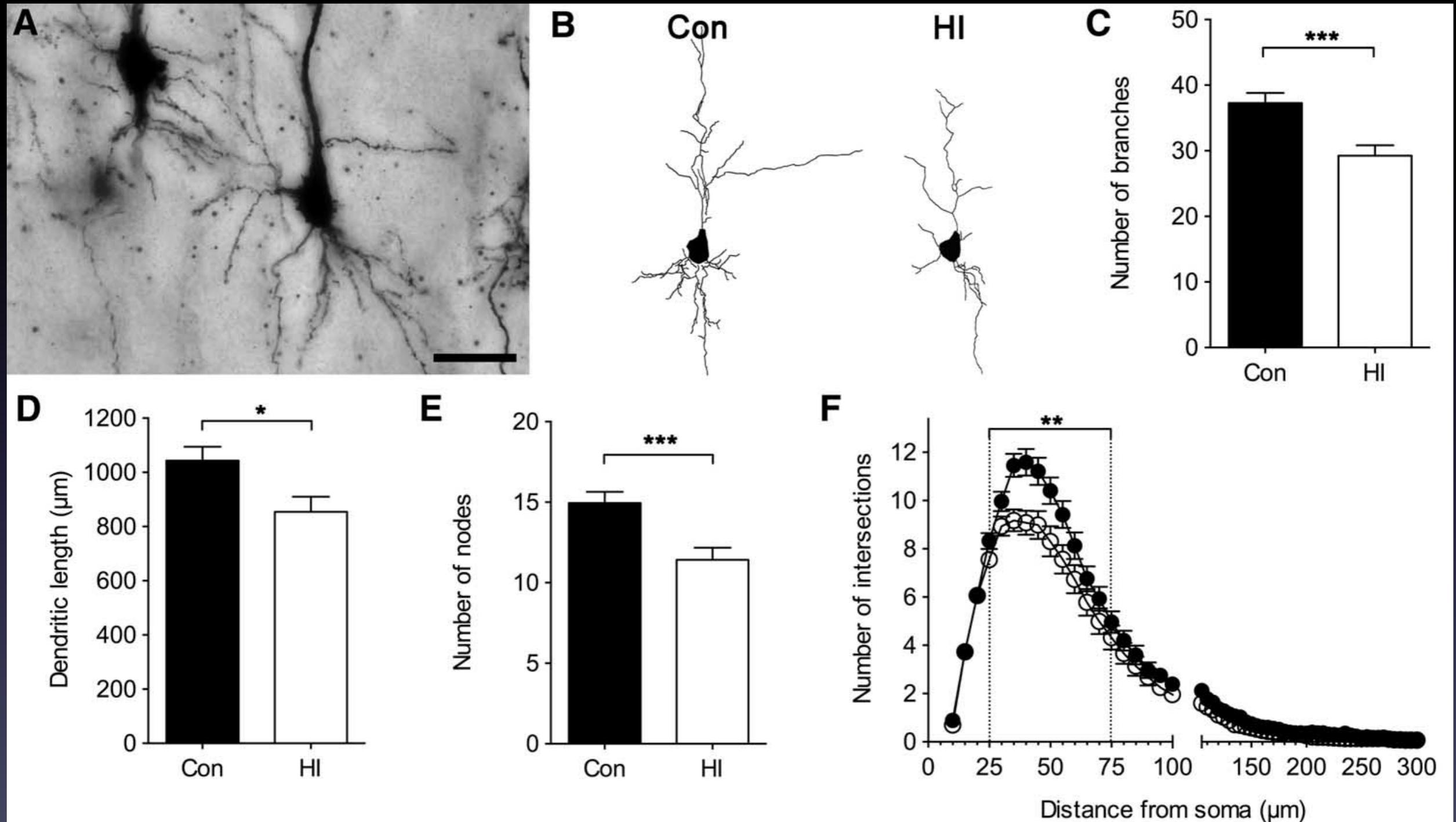
Nagy, Z., et al. (2011). *Cerebral Cortex* 21(2): 300-306.

Cortical alteration after HI injury



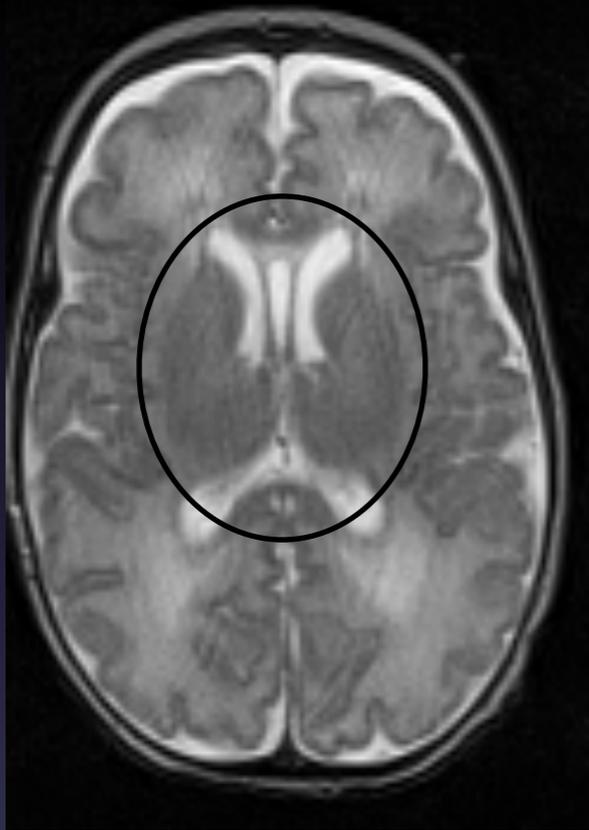
Dean, J. M., et al. (2013). *Science translational medicine* 5(168): 168ra167.

Cortical alteration after HI injury

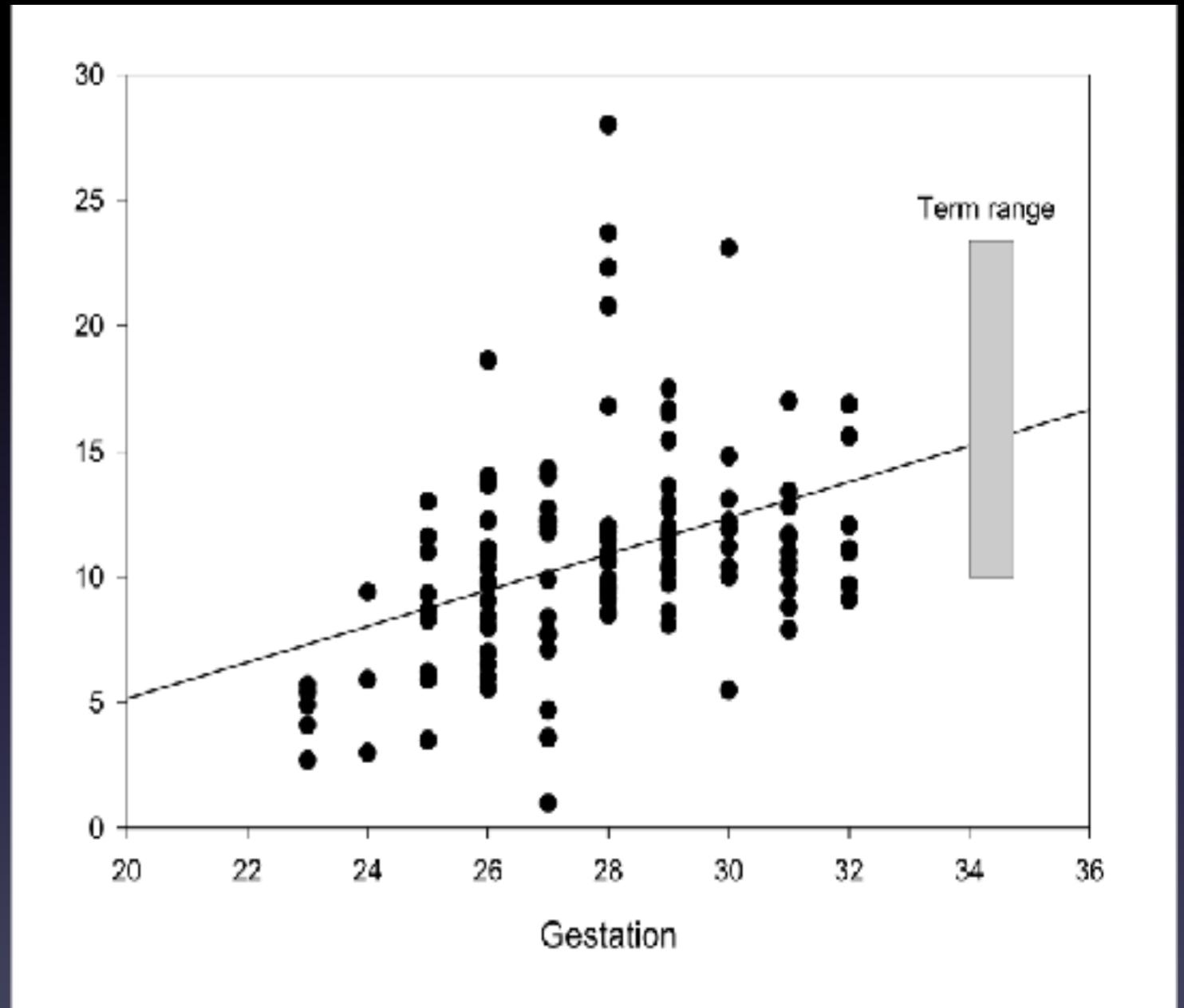


Dean, J. M., et al. (2013). *Science translational medicine* 5(168): 168ra167.

Prematurity and basal ganglia development

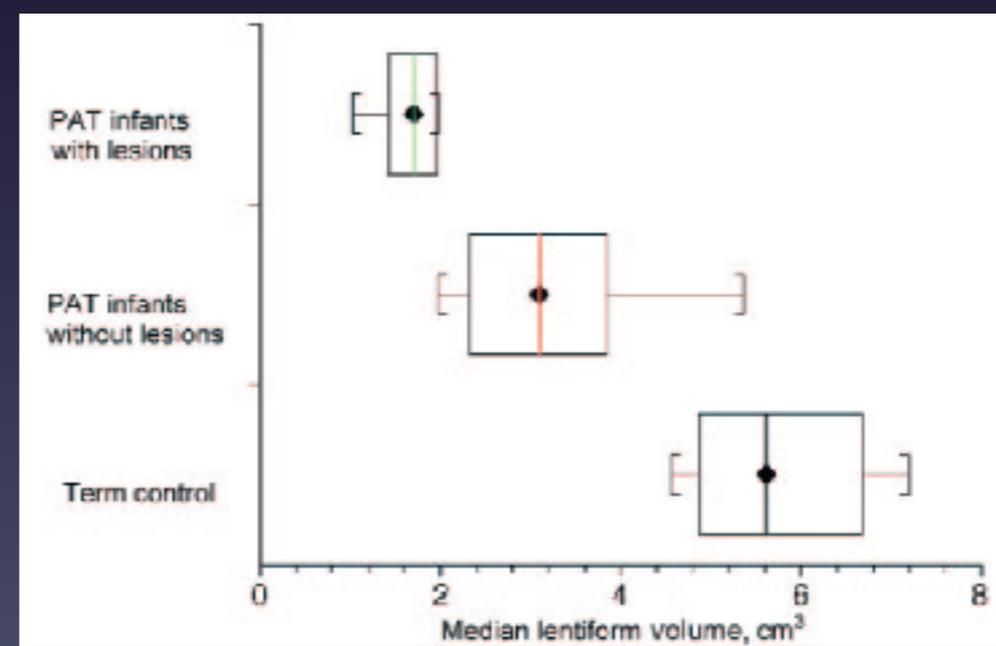
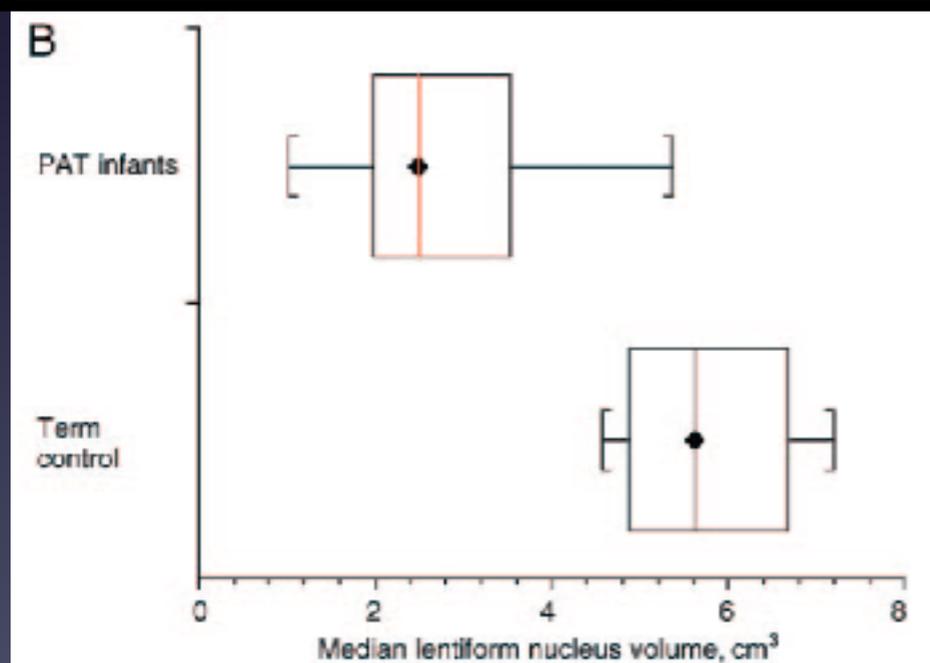
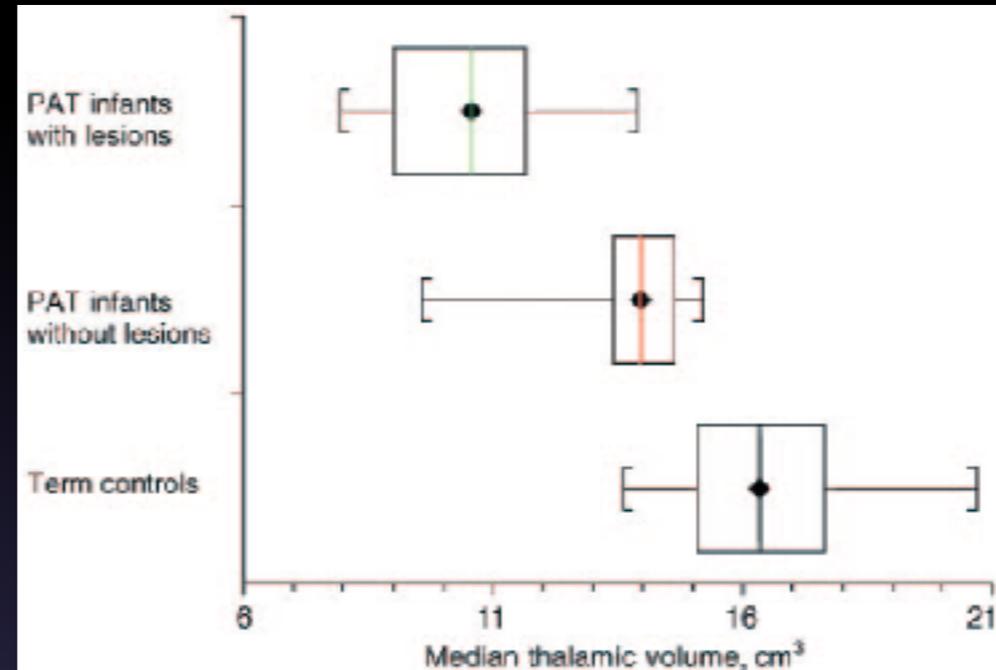
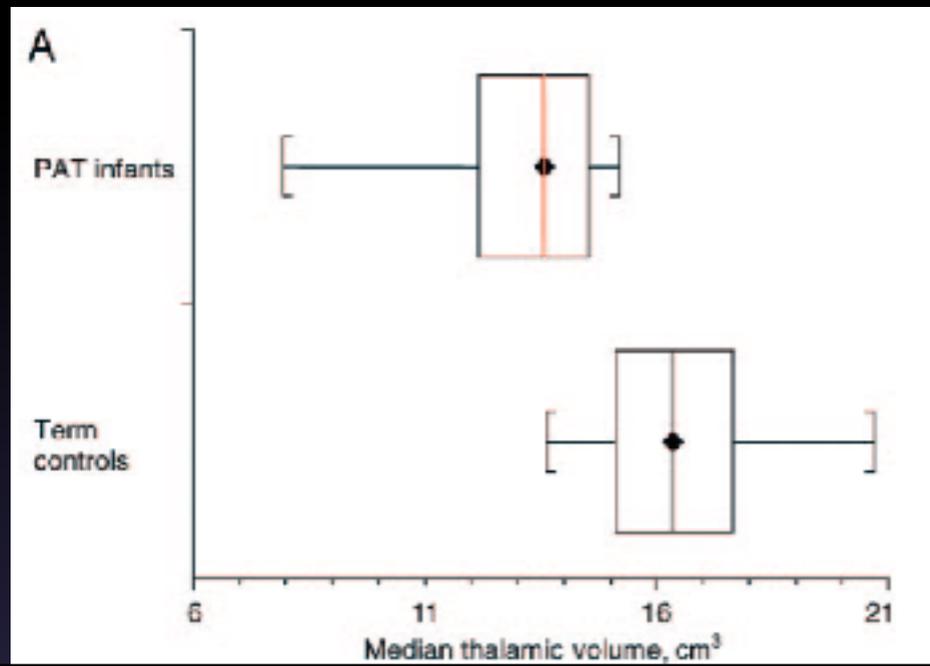


27 wks at term



Inder TE et al Pediatrics 2005;115:286-294
Ball, G., et al. (2012). Cereb Cortex 22(5): 1016-1024.

Basal ganglia volume and WWM injury

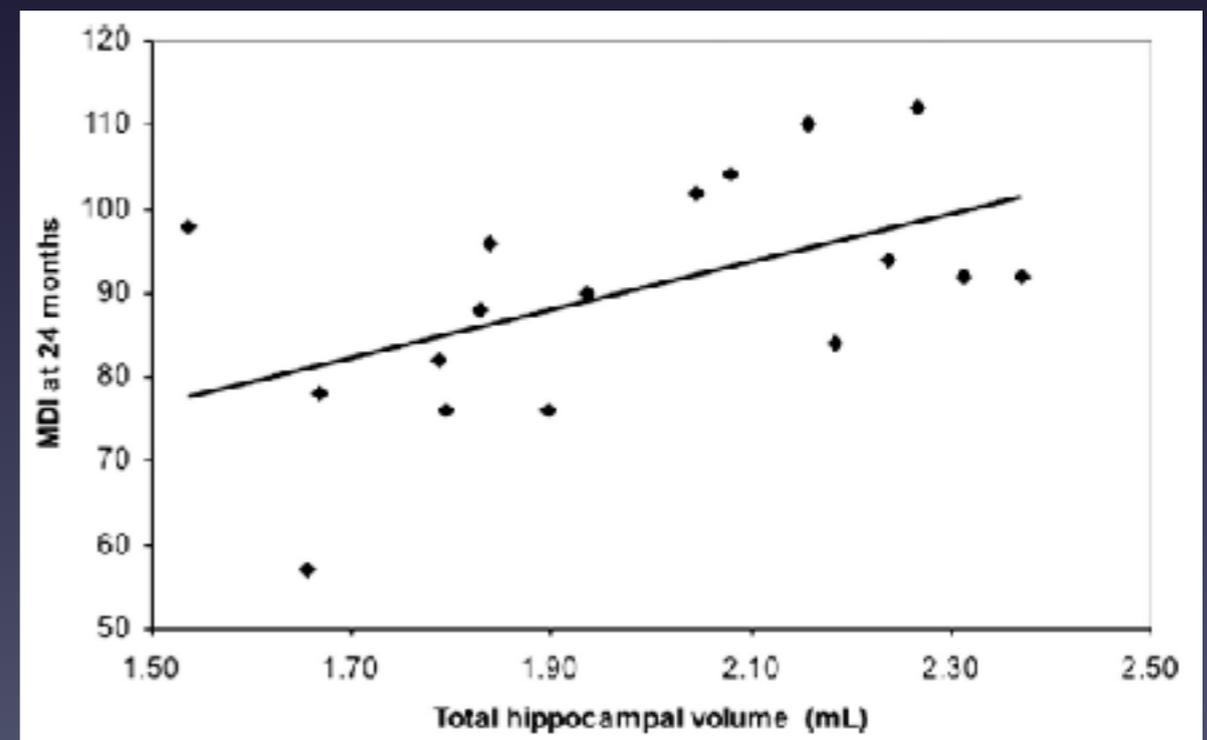
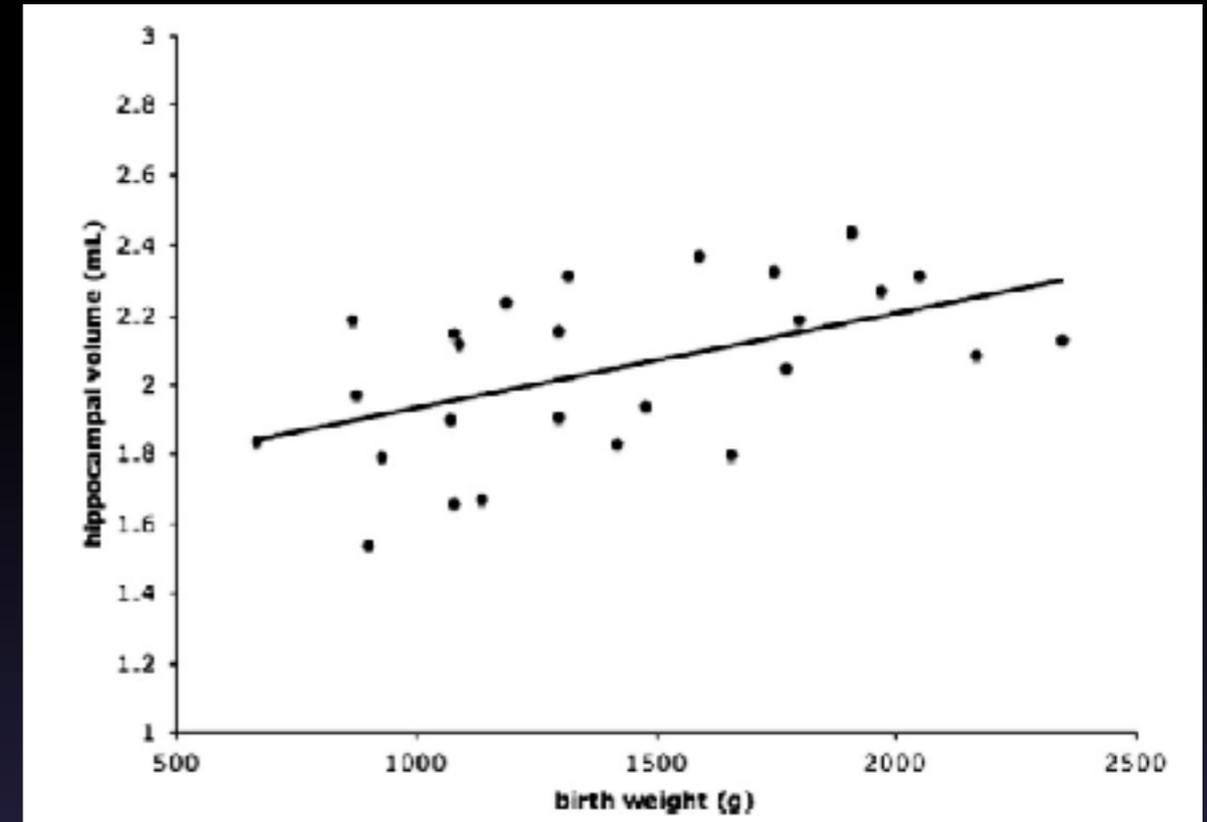
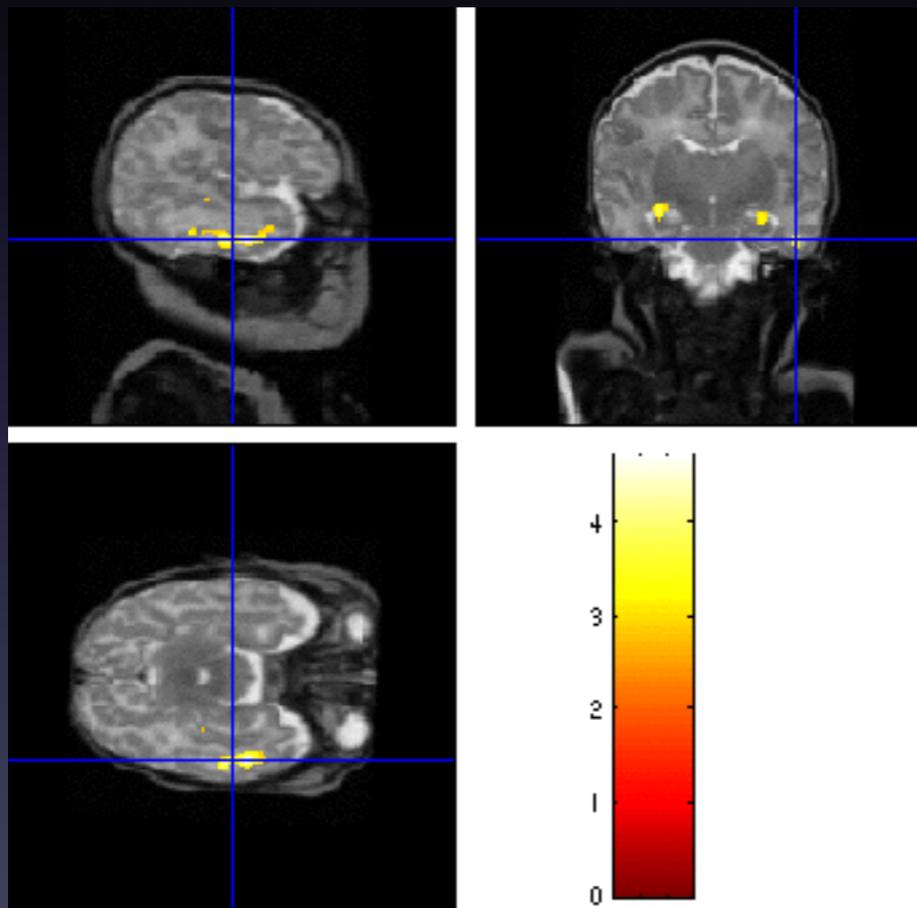


Srinivasan L et al, 2007, Pediatrics

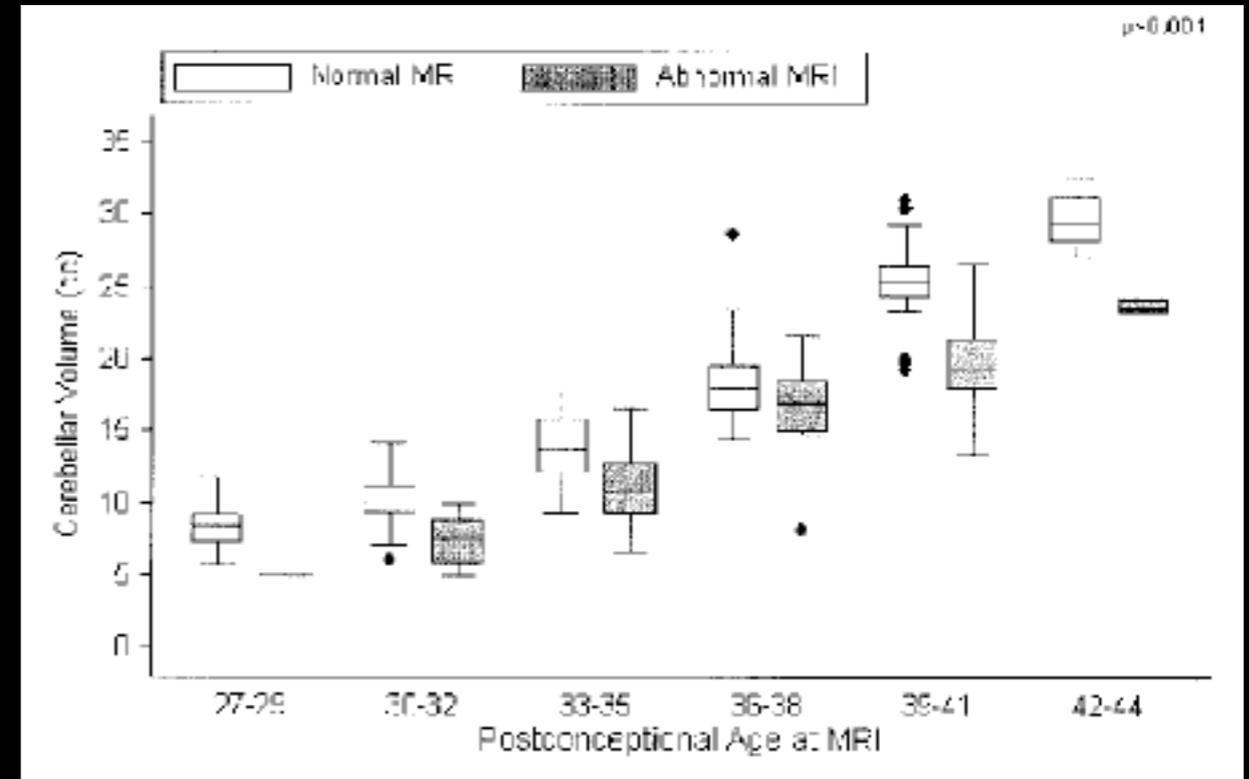
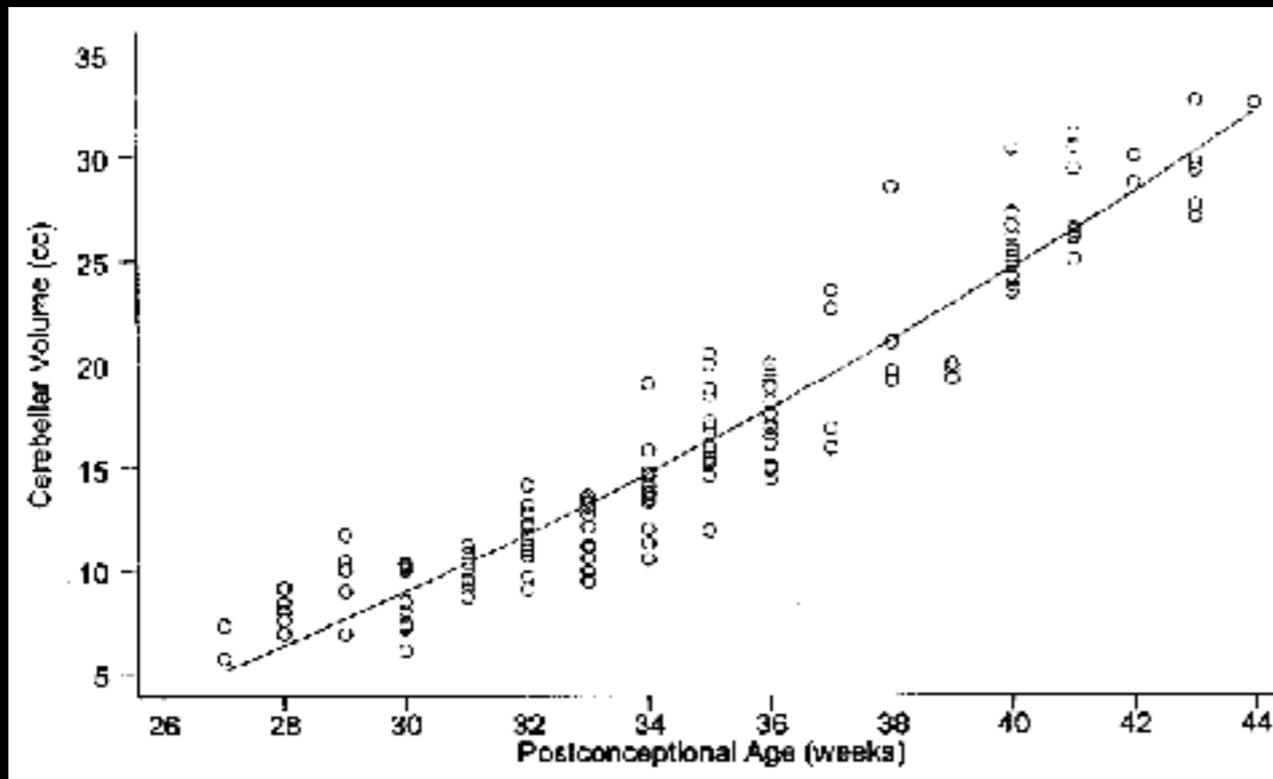
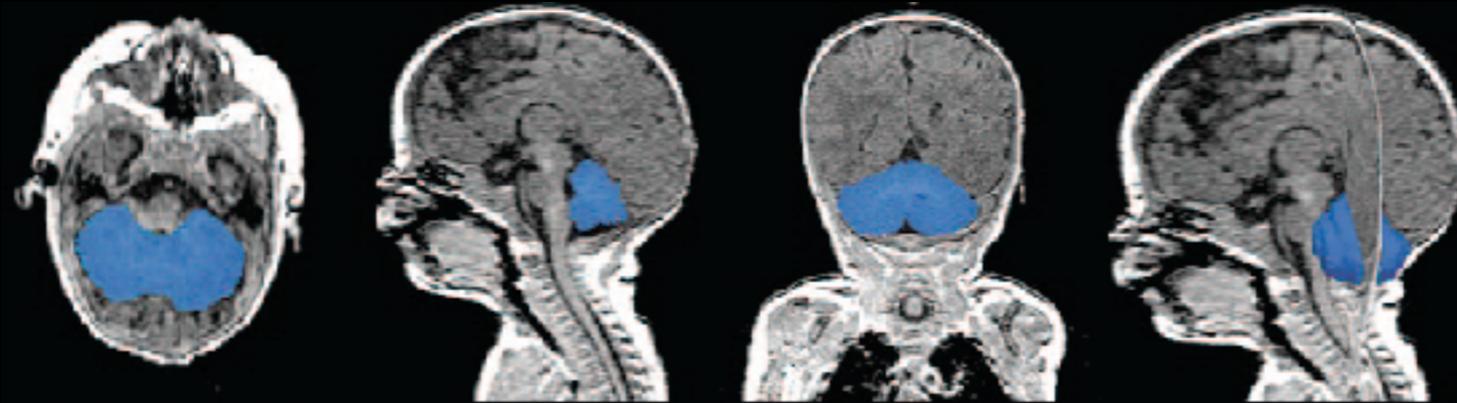
Nagasunder, A. C., et al. (2011). AJNR Am J Neuroradiol 32(1): 185-191.

Hippocampus

Image analysis by Group comparison, voxel-based-morphometry: Bilateral Hippocampus



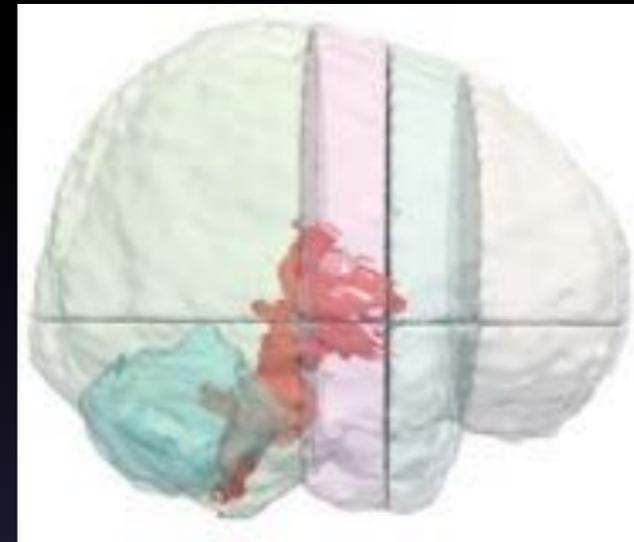
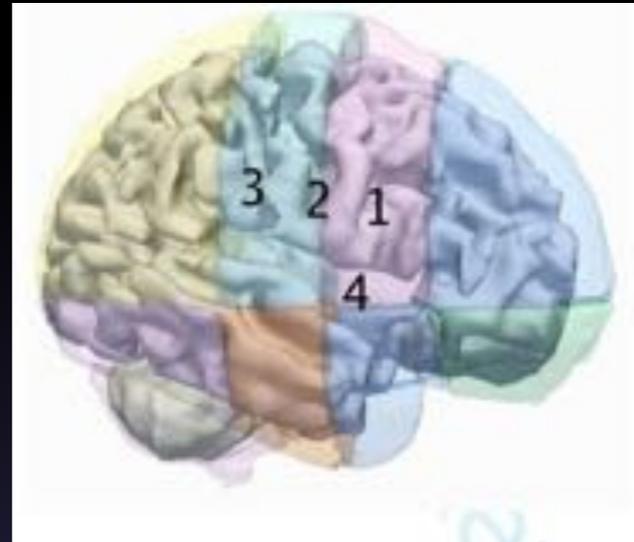
Cerebellum development and WMI



Limperopoulos et al Pediatrics 2005;115:688-695; Limperopoulos et al Pediatrics 2005;116:844-250

Regional volume quantification: Reduction of white matter in preterms

- 1 precentral Sulcus
- 2 central sulcus
- 3 postcentral sulcus
- 4 sylvian fissure

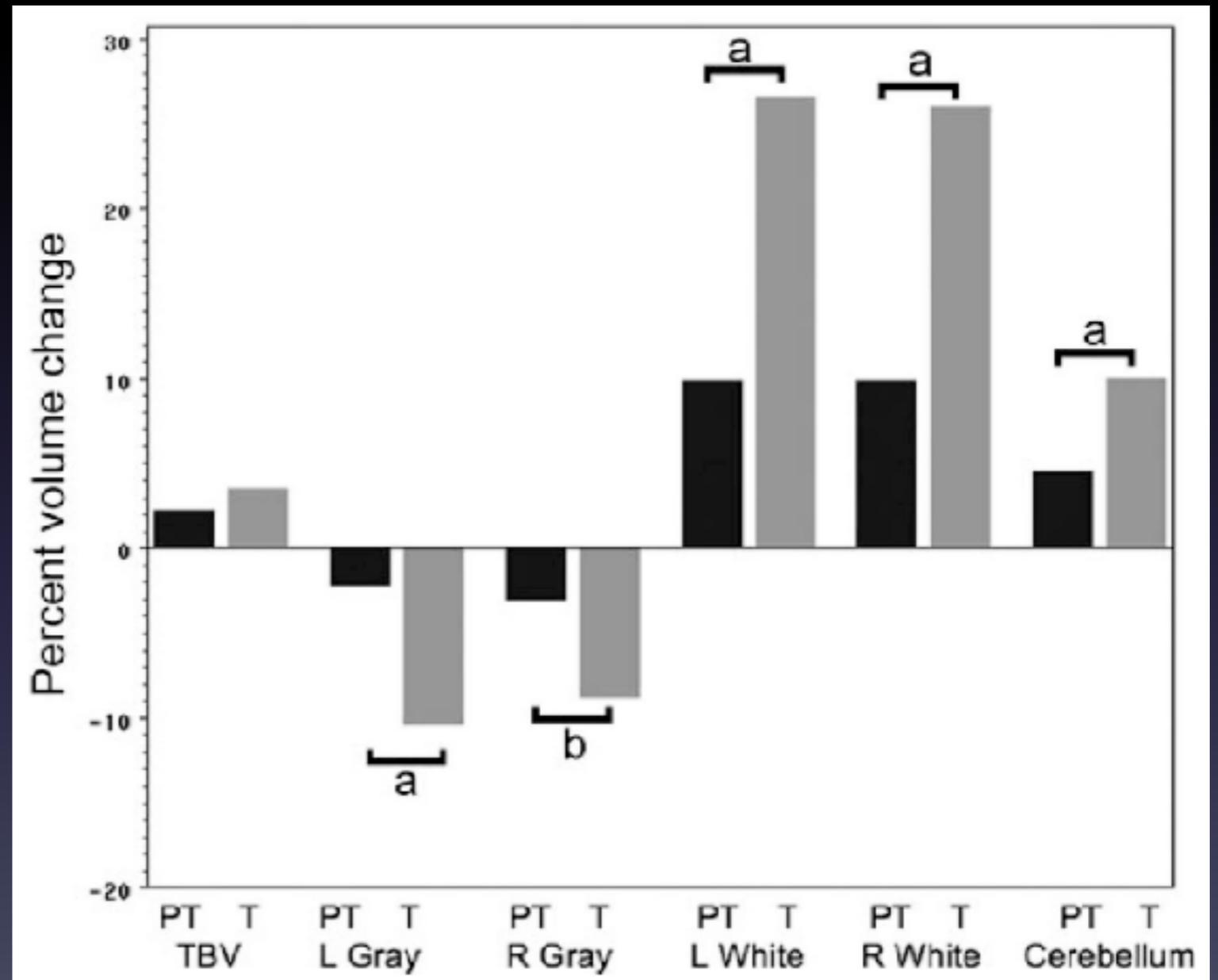


<i>Volume, ml, Mean±SD</i>	<i>Preterm</i>	<i>term</i>	<i>p</i>
<i>Central unmyelinated WM</i>	36.1±6.0	40.2±5.6	<0.01
<i>Right inferior central UMWM</i>	6.8±1.1	8.0±1.1	<0.0005
<i>Myelinated WM</i>	7.3±2.4	9.8±3.8	<0.02
<i>Central myelinated WM</i>	3.7±1.2	4.8±1.9	<0.05
<i>Occipital myelinated WM</i>	3.1±1.4	4.4±1.9	<0.02

Mewes A et al. Pediatrics 2006; 118:23-33.

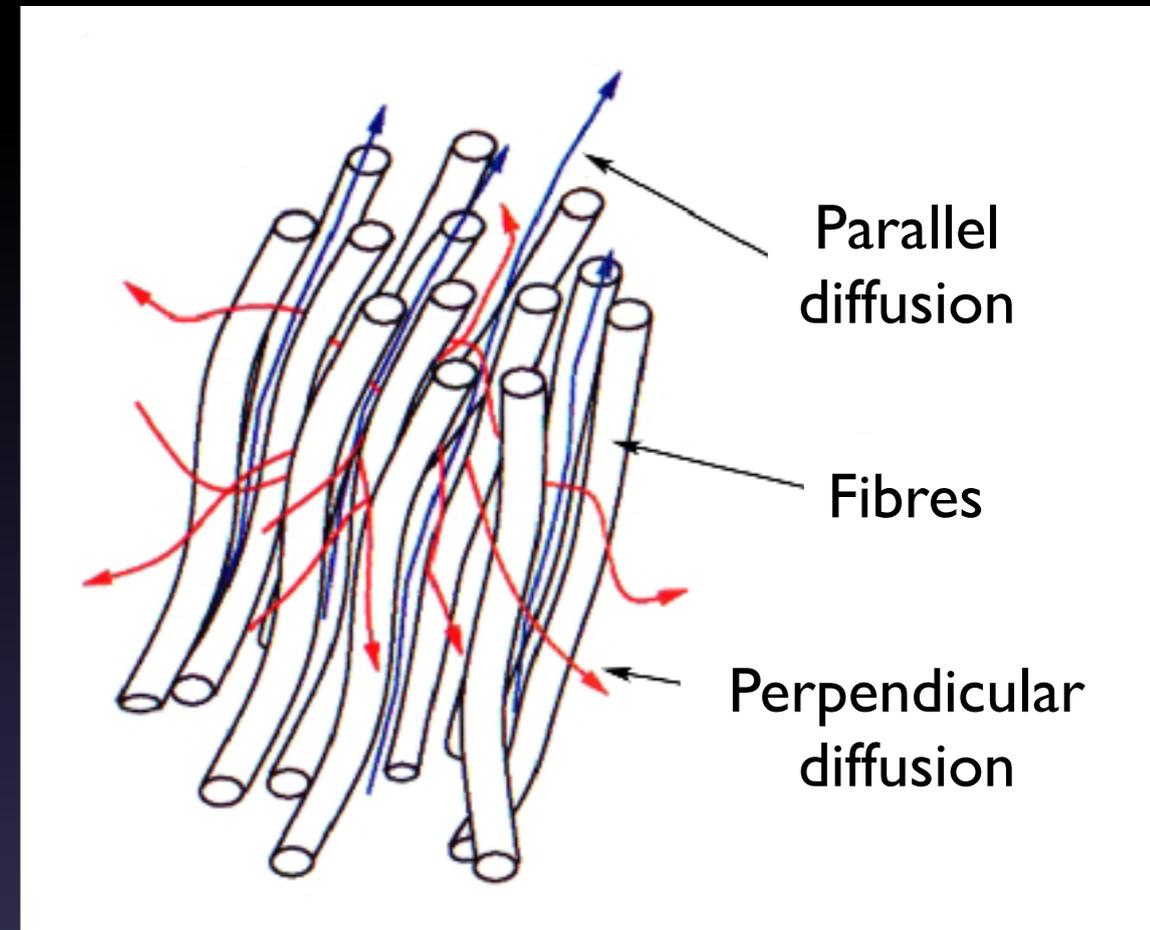
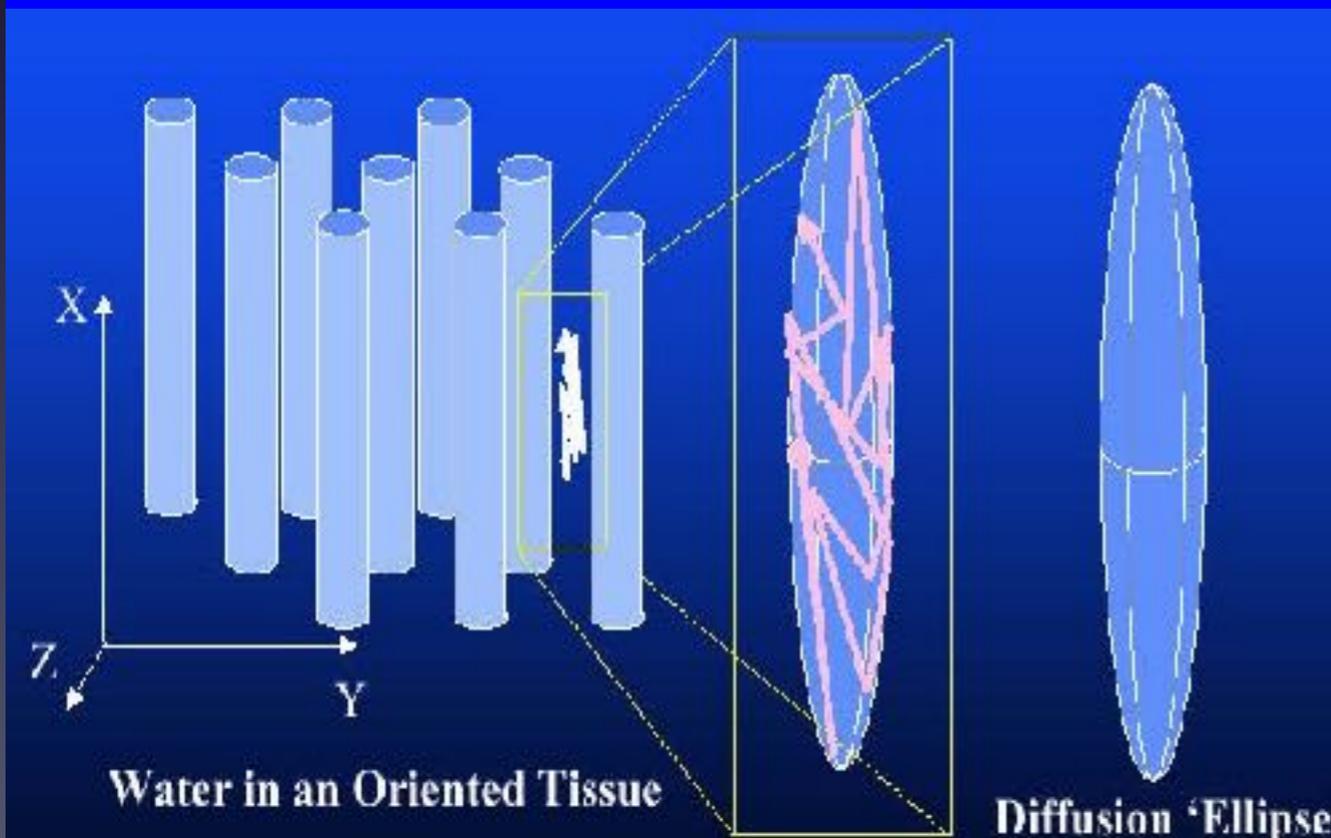
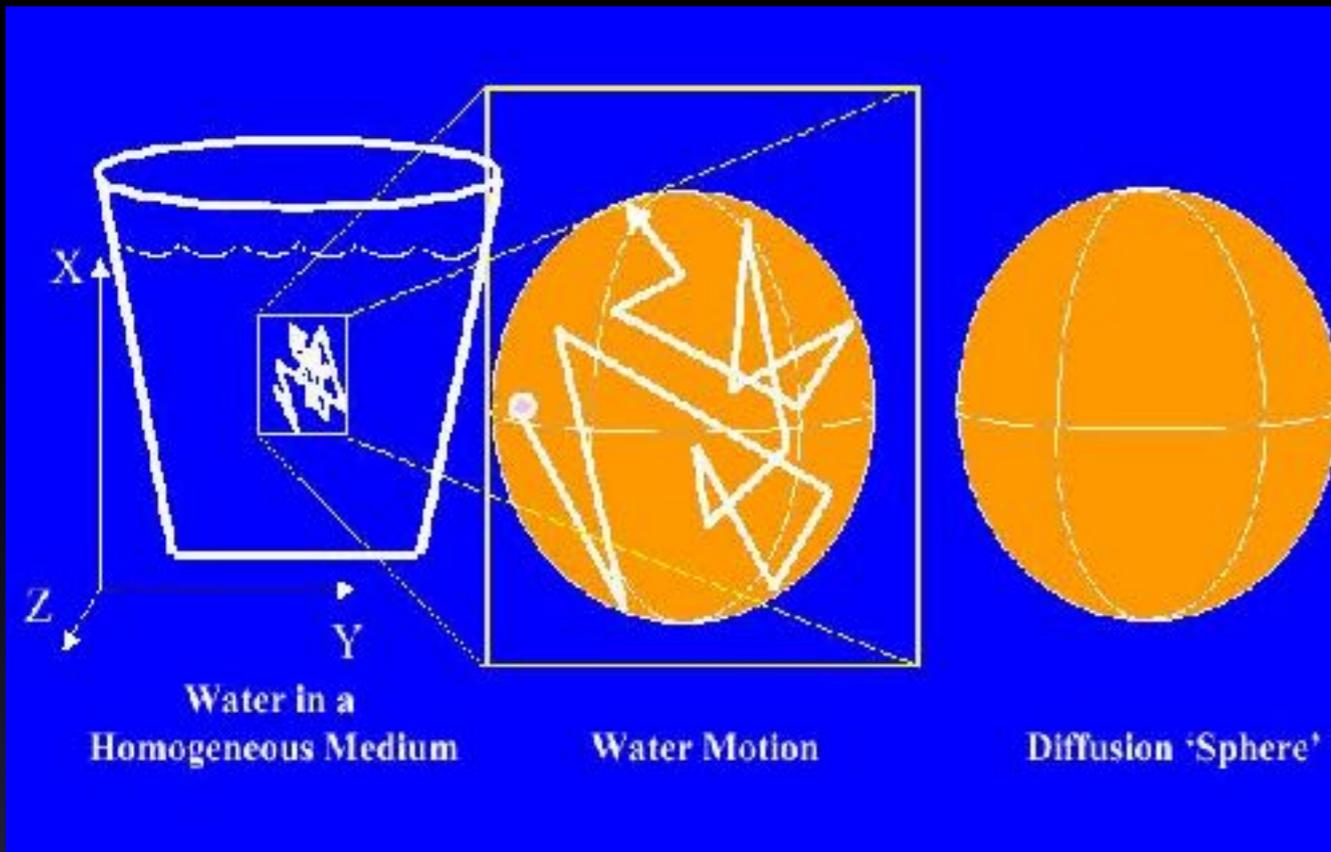
Change in cerebral growth during early adolescence in preterm

Percentage of total cerebral volume change, of grey matter and cerebellum between 8 and 12 in preterm (PT) and term (T)



Ment L et al, Pediatrics, 2009

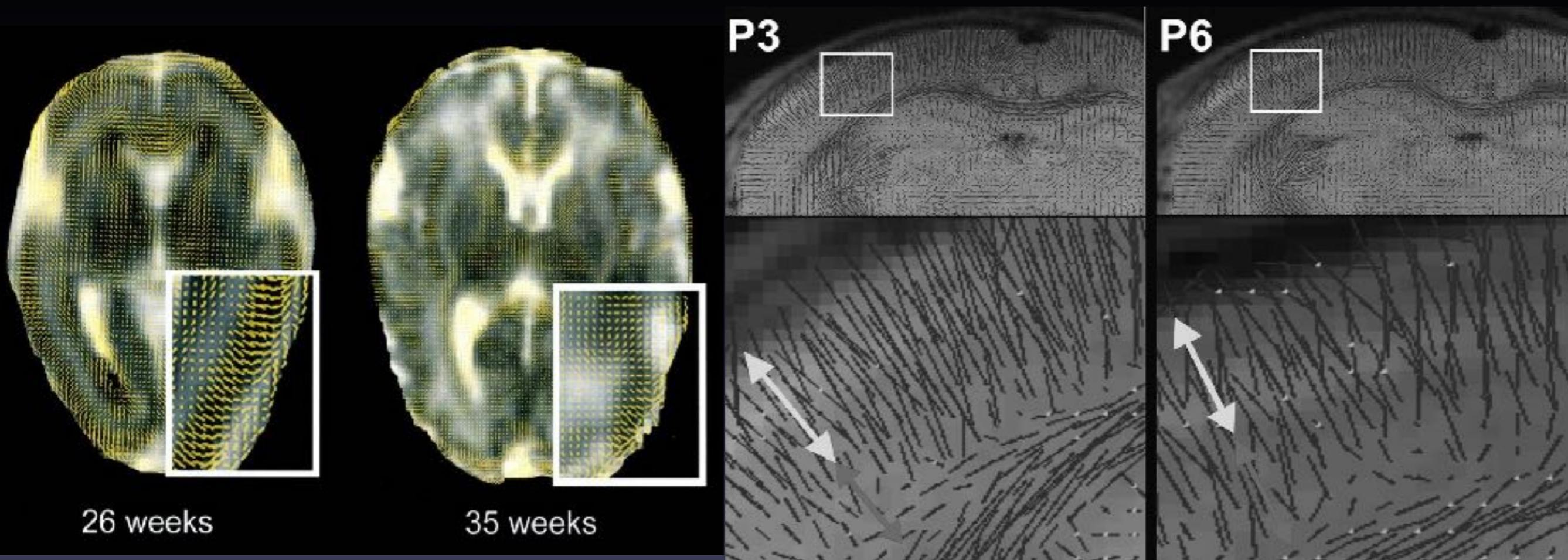
Diffusion imaging of microstructure



*Le Bihan D, Breton E. CR Acad Sci Paris
1985; 301: 1109-1112*

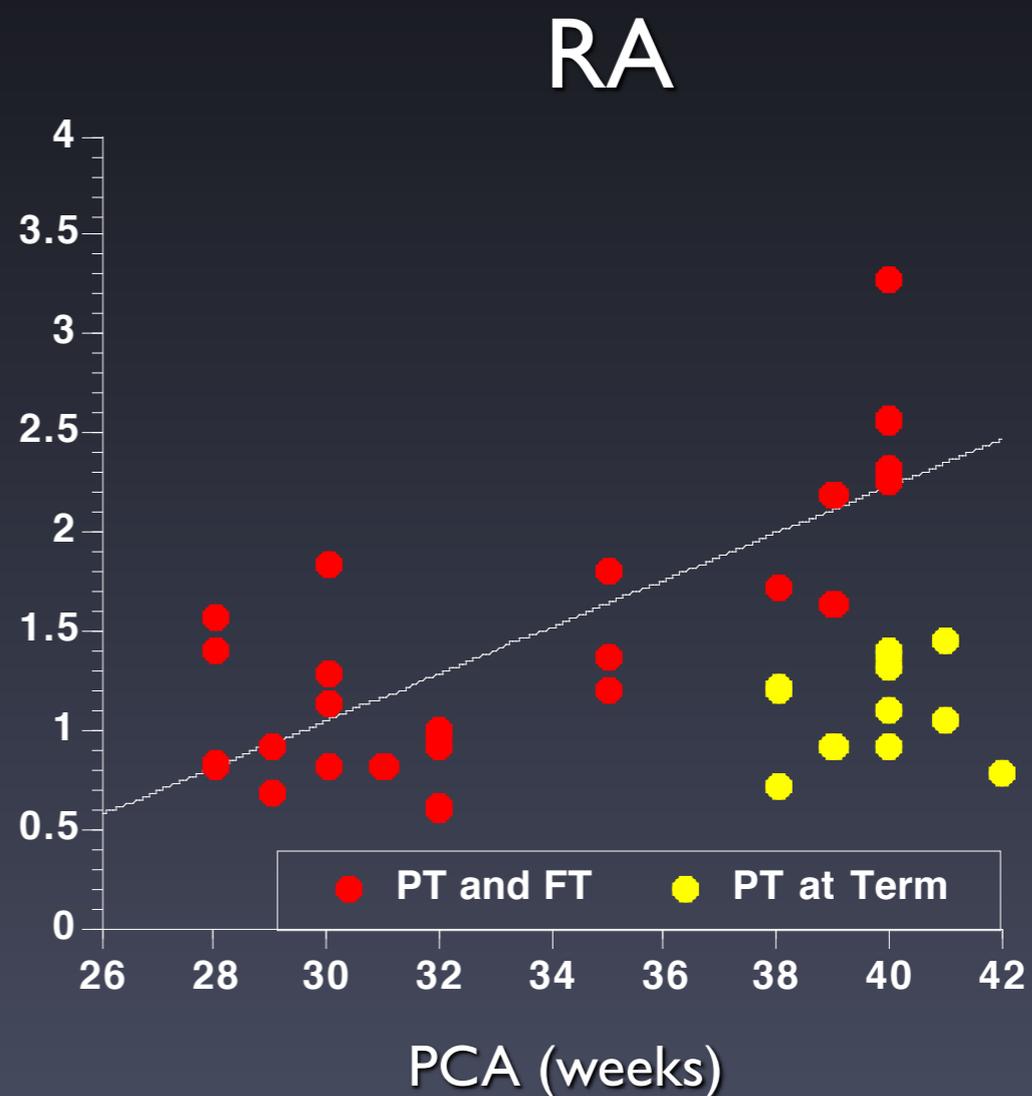
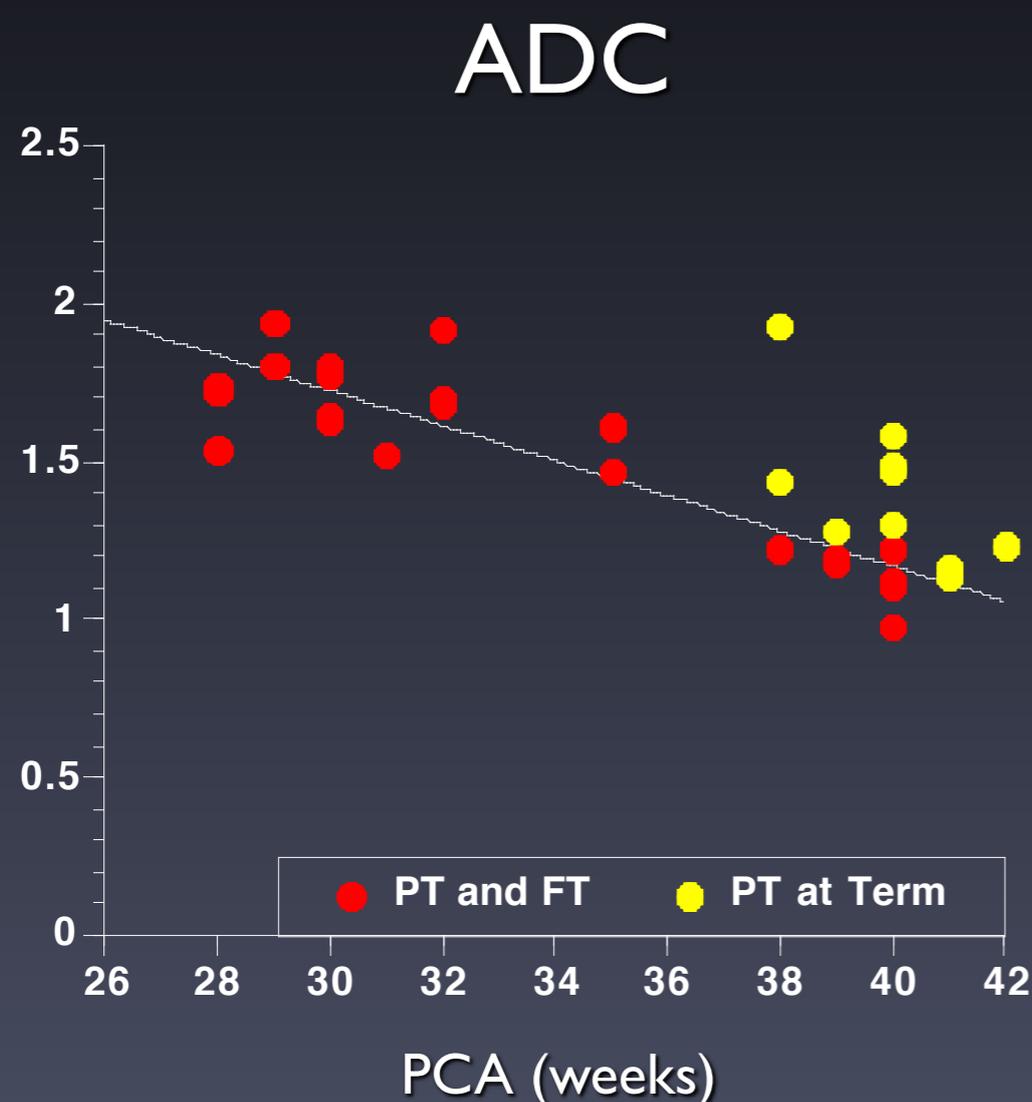
*Le Bihan D et al J Magn Reson Imaging
2001 13:534-546*

Tissue characteristics during early cortical development



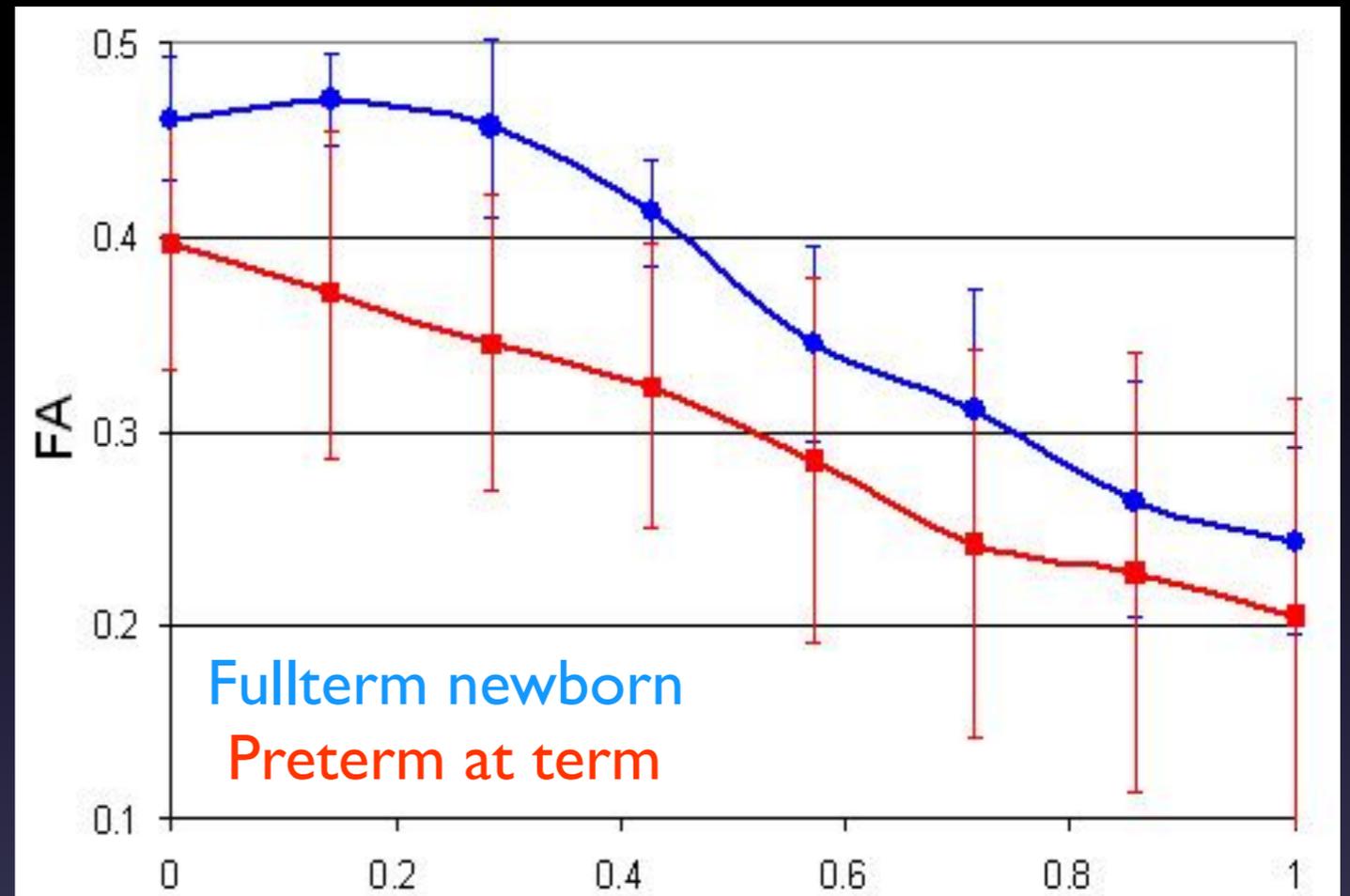
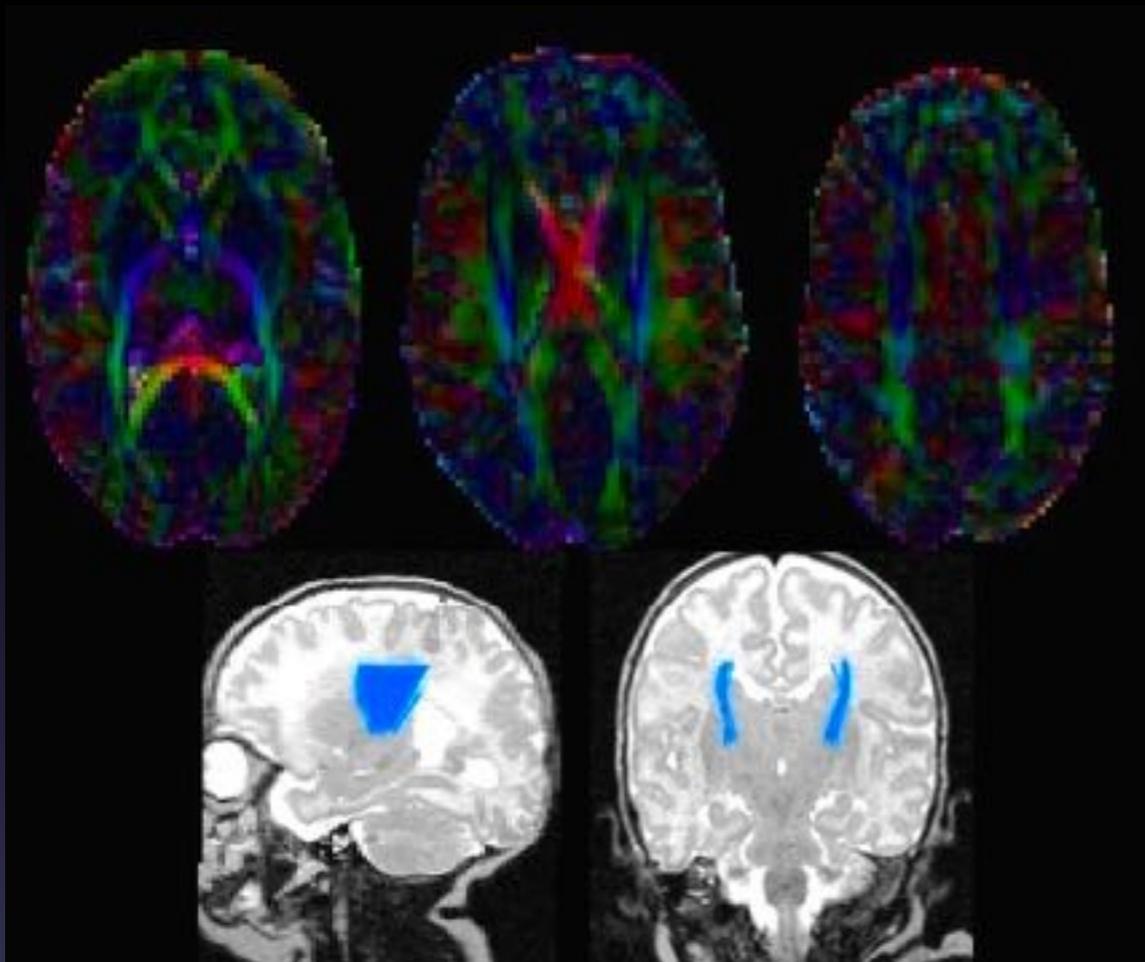
Neill JJ, Miller J, Hüppi PS *NMR in Biomedicine* 2002;15:543-552
Sizonenko et al, *Cerebral Cortex*, 2007; 17(11): 2609-2617

Apparent coefficient diffusion (ADC) and anisotropy (RA) in WM



Hüppi PS et al *Pediatr Res* 44:584-590 (1998)

Maturation along WM tract and effect of prematurity



Indices quantification along the cortico-spinal tract, between the internal capsule (abscissa=0) and the high centrum semiovale (abscissa=1)

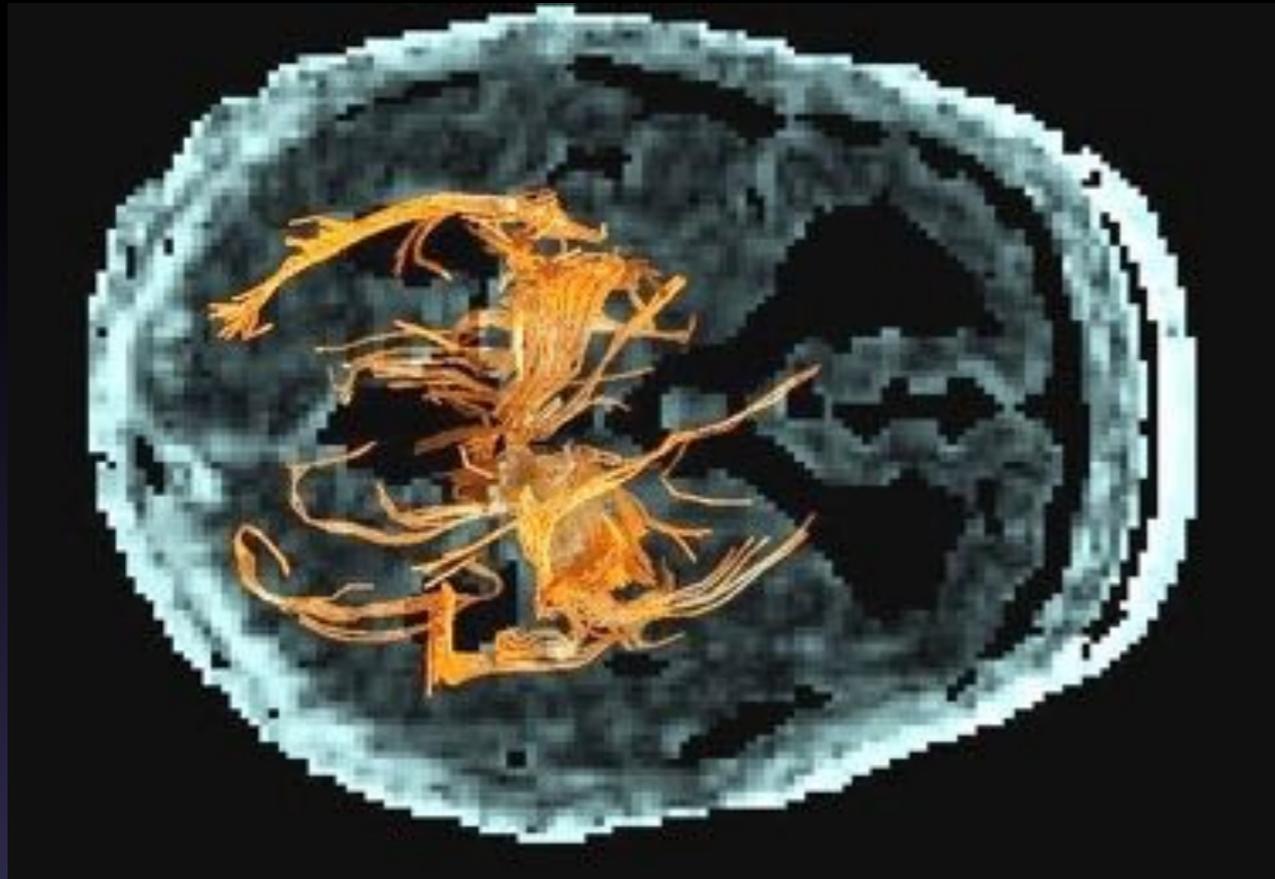
J. Dubois et al. 2007, Cerebral Cortex
J. Dubois, et al. 2014, Neuroscience

Alteration of white matter microstructure in preterm with injury

Diffusion MRI	PT with WMI mean±SD(n=10)	PT at T mean±SD (n=10)	p-value
FA(%): central WM	9.5±1.7	12.9±3.3	0.03
FA(%): Int. Capsule	17.2±3.9	22.8±4.7	0.02
ADC(μm ² /ms) Central WM	1.5±0.2	1.5±0.2	n.s.
ADC(μm ² /ms) Int. Capsule	1.1±0.1	1.0±0.1	n.s.
Myelinated WM(cc)	14.5±4.5	23.1±6.9	0.002

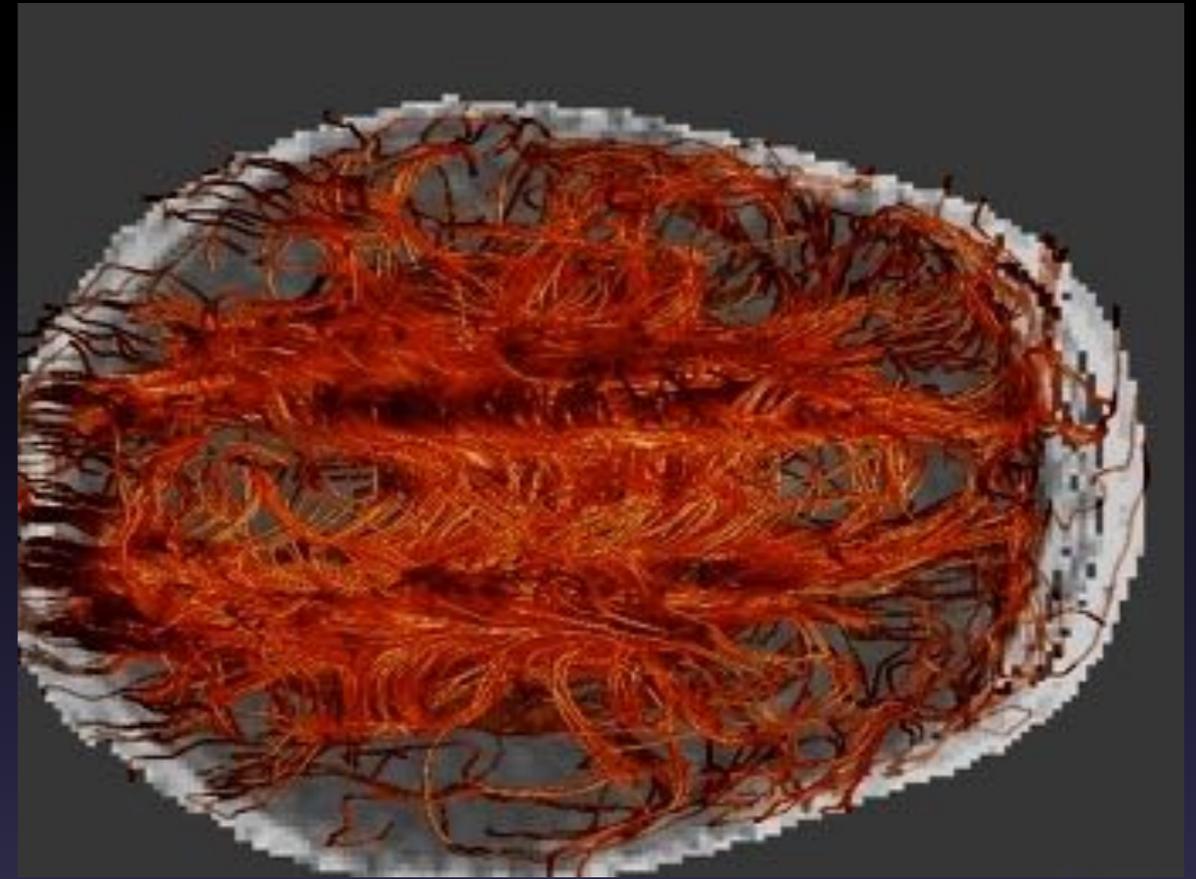
Huppi, P. S., et al. (2001). Pediatrics 107(3): 455-460.
Li, K., et al. (2015). Dev Med Child Neurol 57(4): 328-338.
Counsell, S. J., et al. (2003). Pediatrics 112(1 Pt 1): 1-7.

White matter tractography in injury



Twin 1

28 weeks



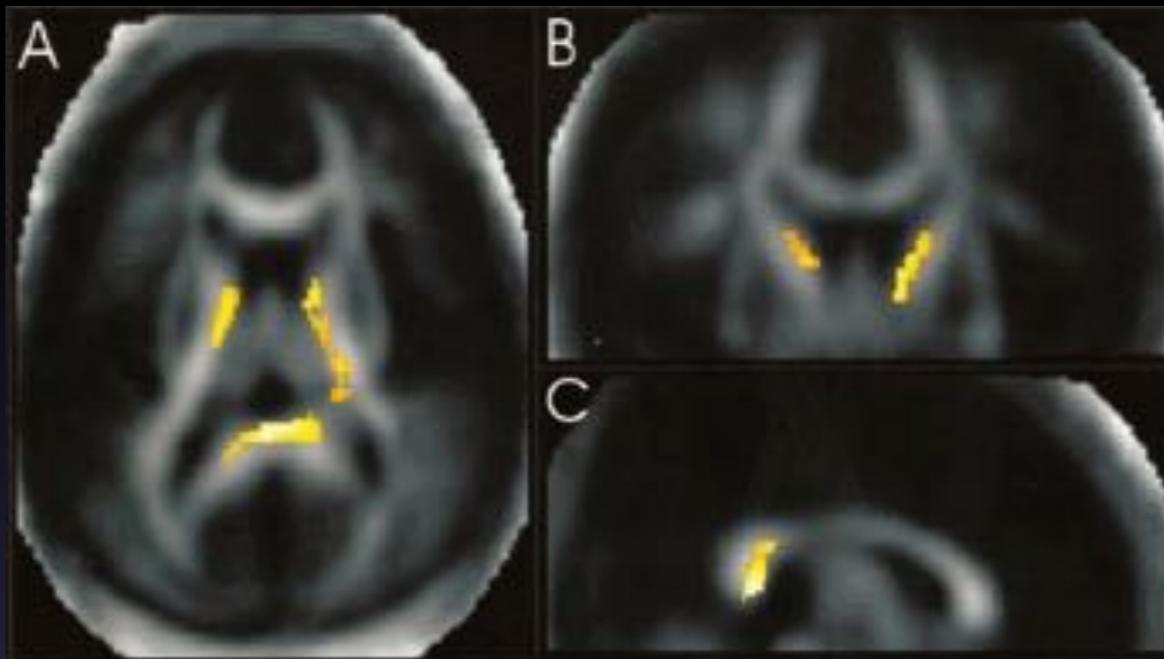
Twin 2

Twin 1: WM injury and severe neurodevelopmental delay

Twin 2 : no damage and normal neurodevelopment

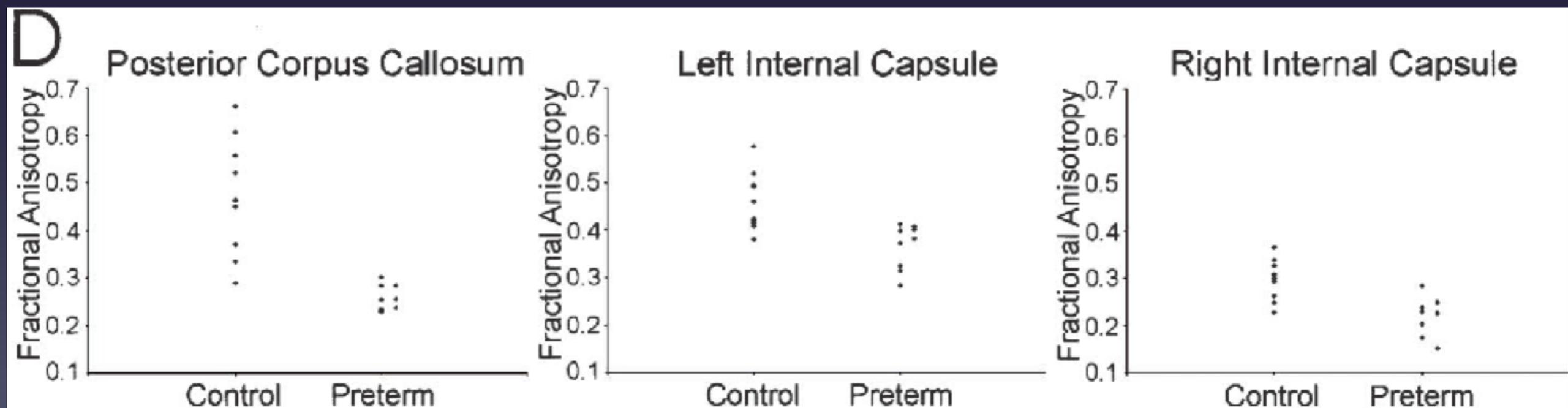
(courtesy of Simon Warfield and Terrie Inder, Boston)

Long-term alteration of white matter microstructure



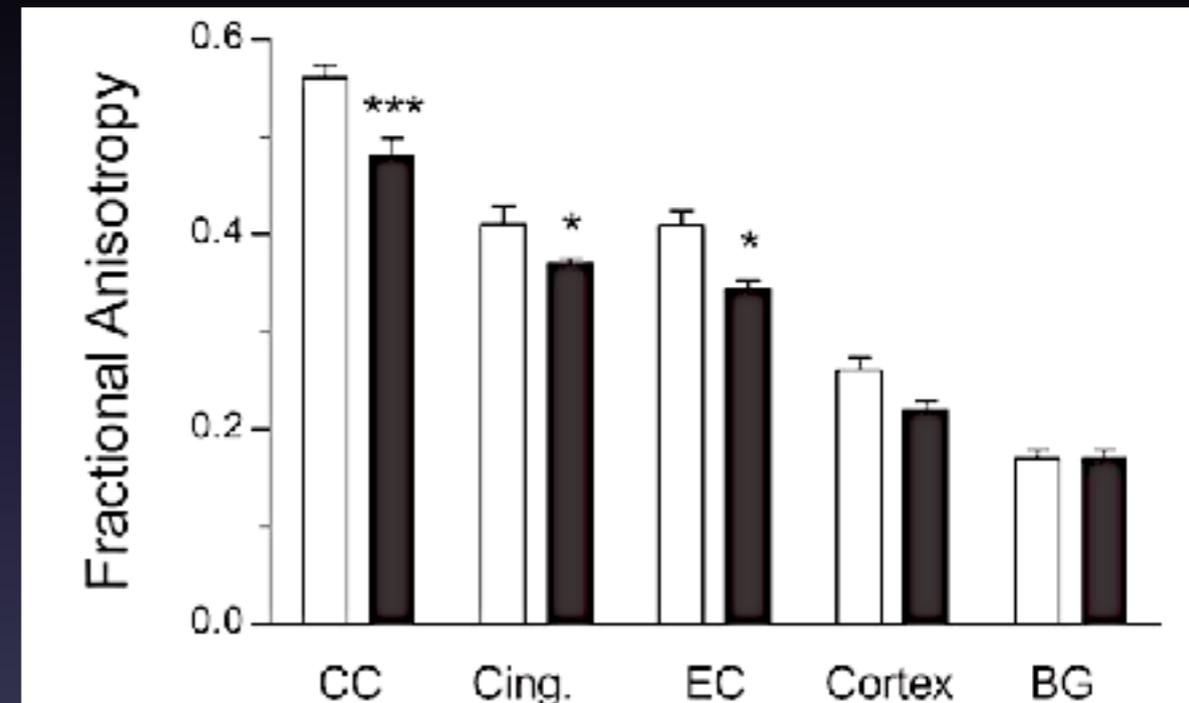
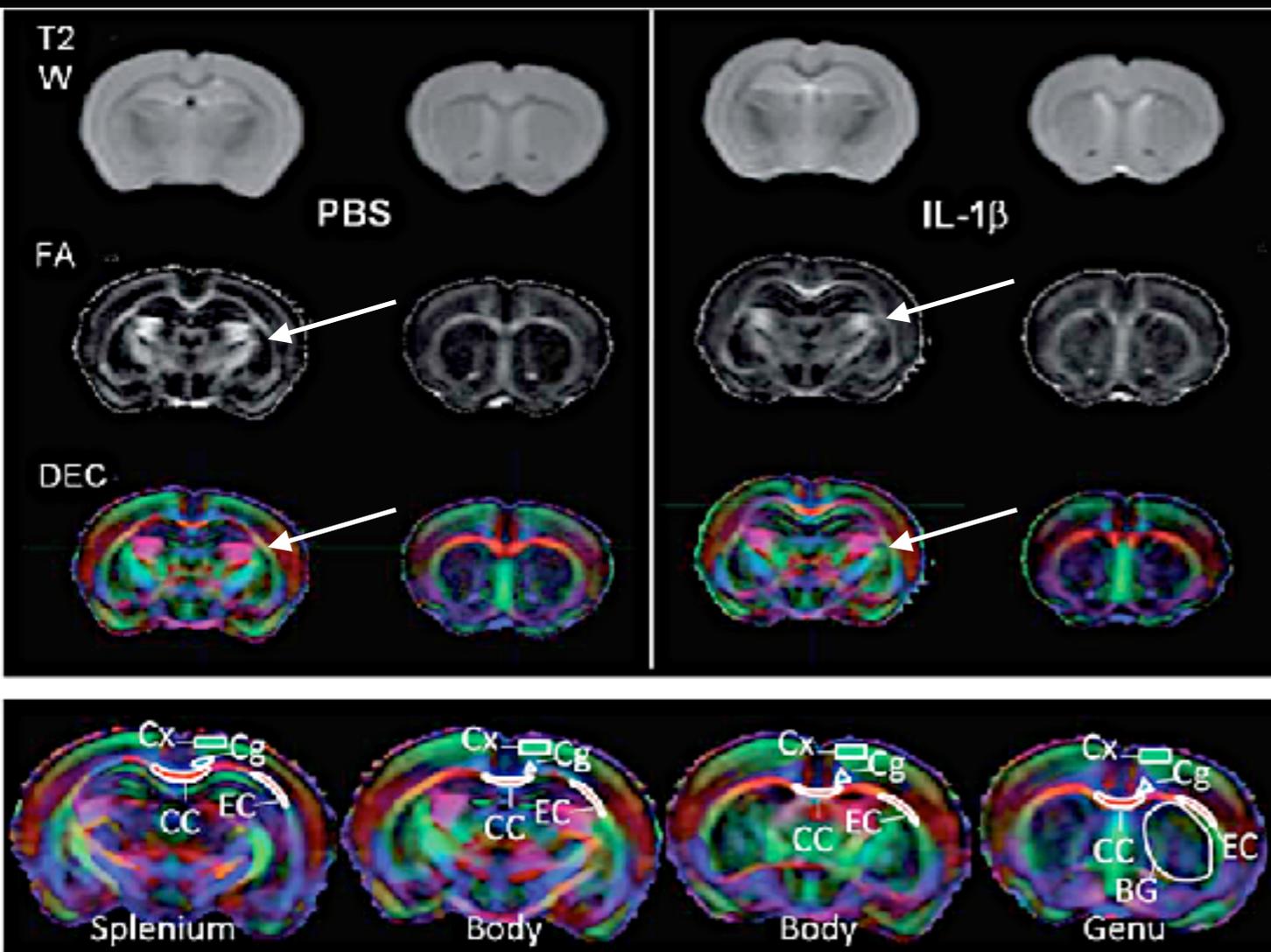
Reduction of FA at 11 years
in WM tracts

Nagy Z et al Pediatr Res 2003



Inflammation: white matter alteration

IL-1 β injection in newborn mice

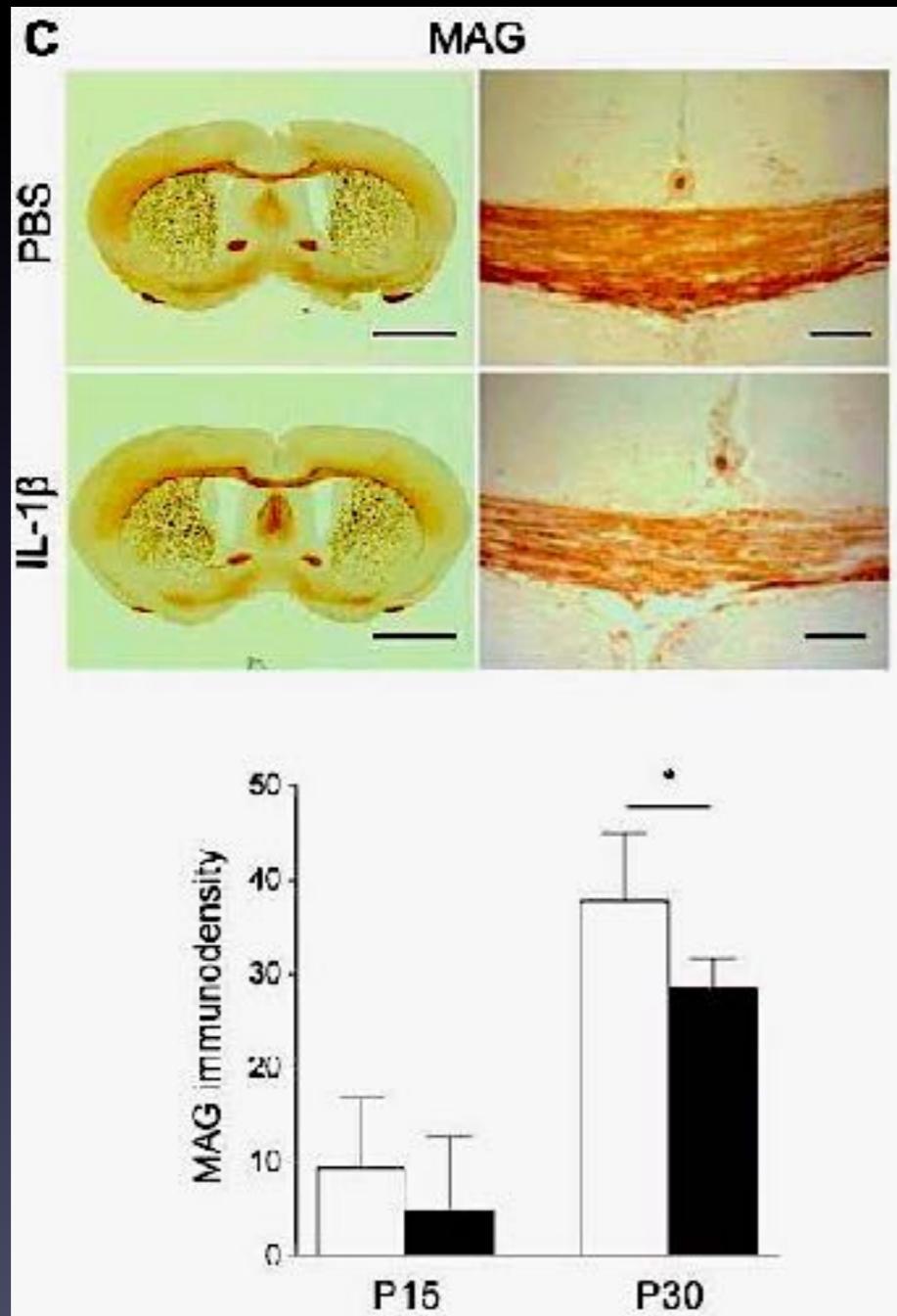


Favrais, G., et al. (2011) *Ann Neurol.*

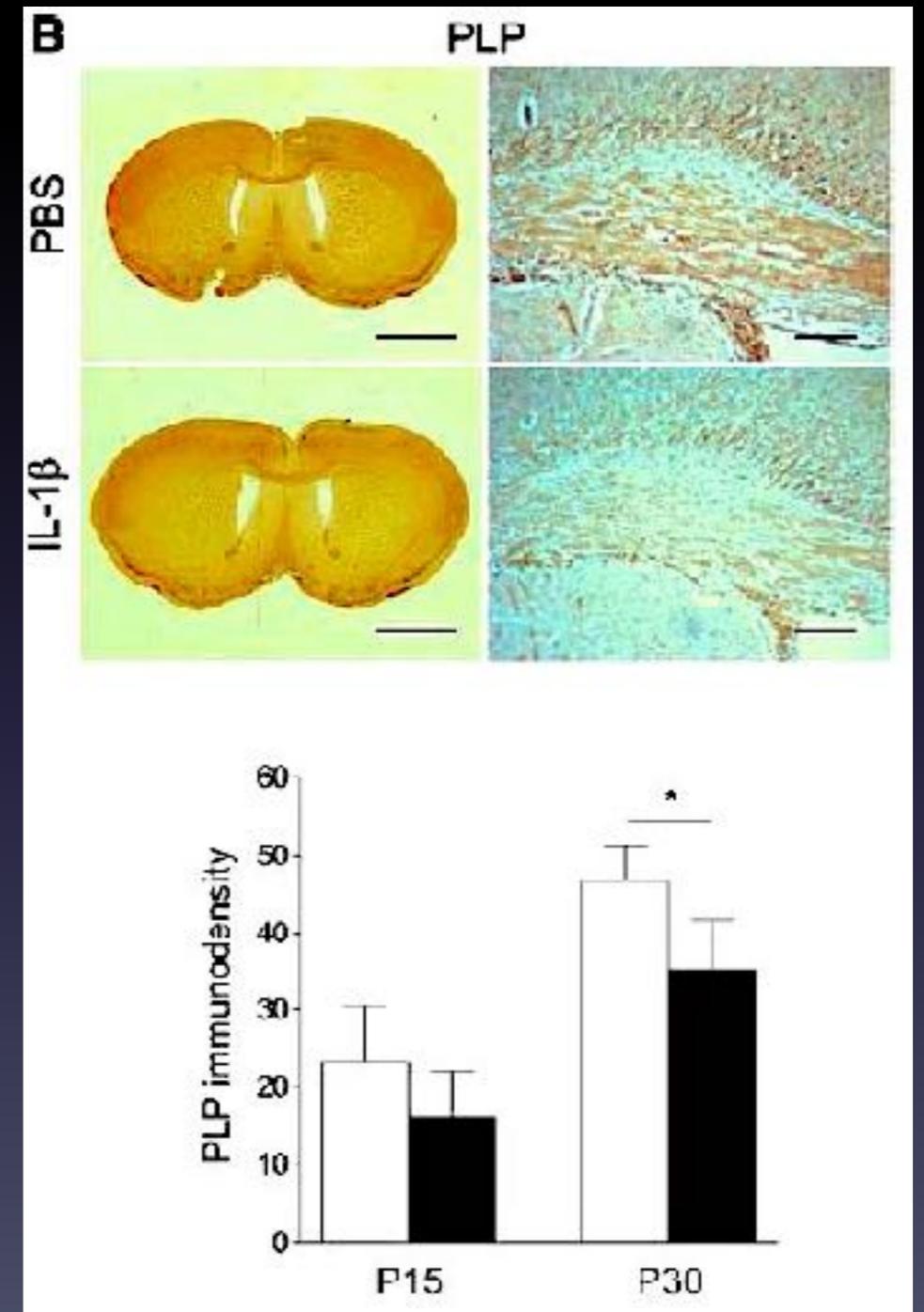
Inflammation: white matter alteration

IL-1 β injection in newborn mice

Myelin



Oligodendrocytes



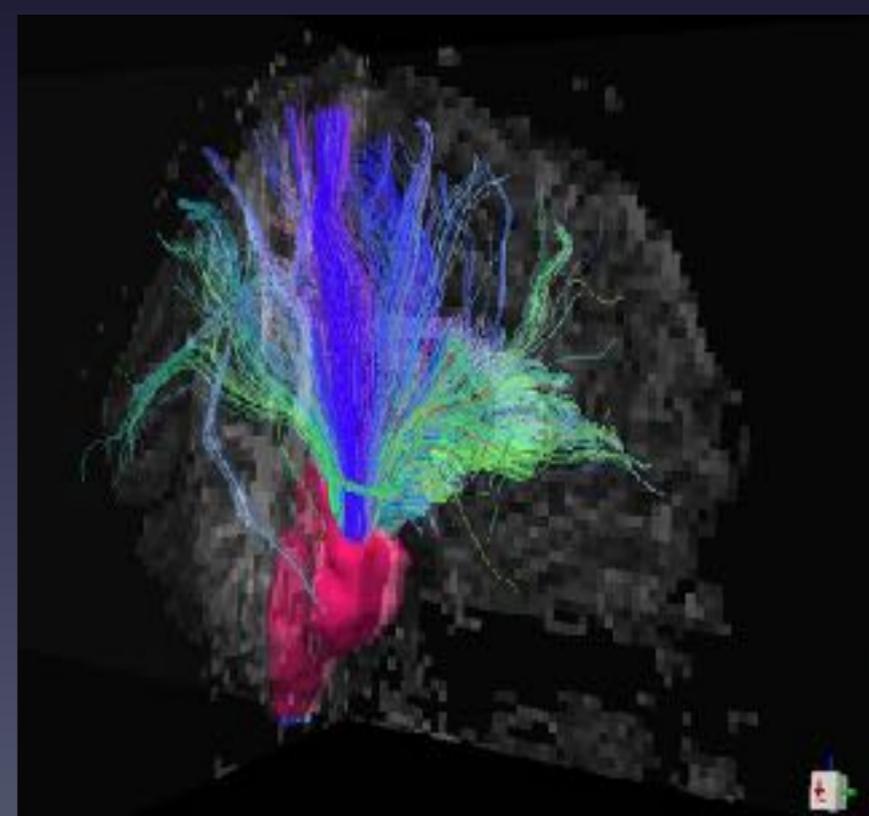
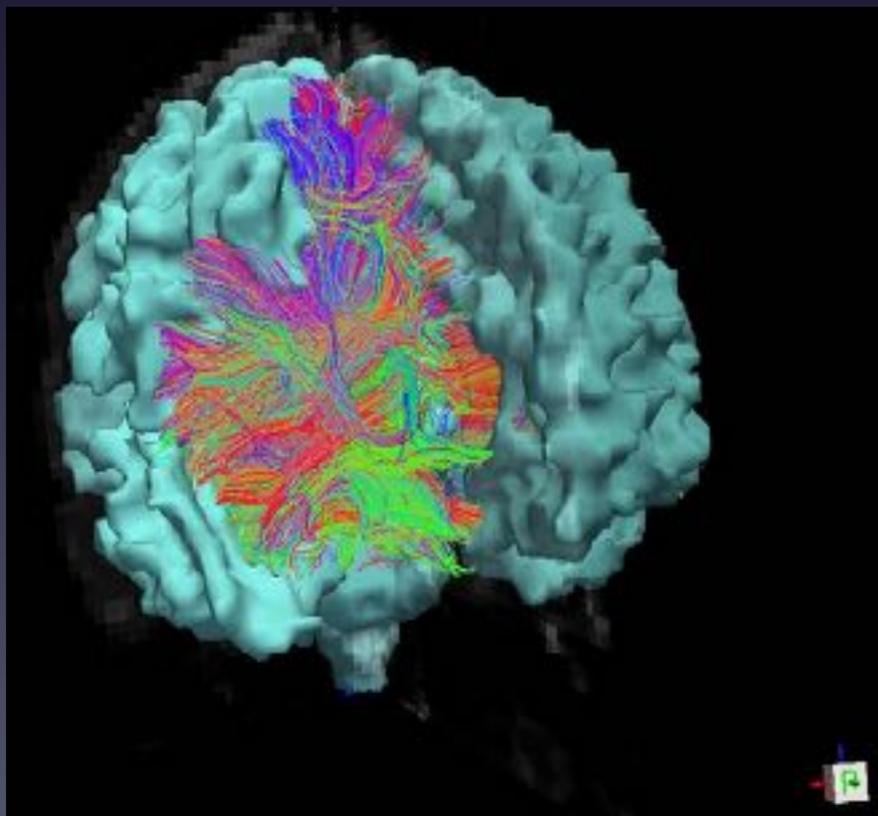
Connectivity assessment by MRI

With tractography and cortex parcellation, we can depict the fibers that link determined areas in the brain and compare them between different groups

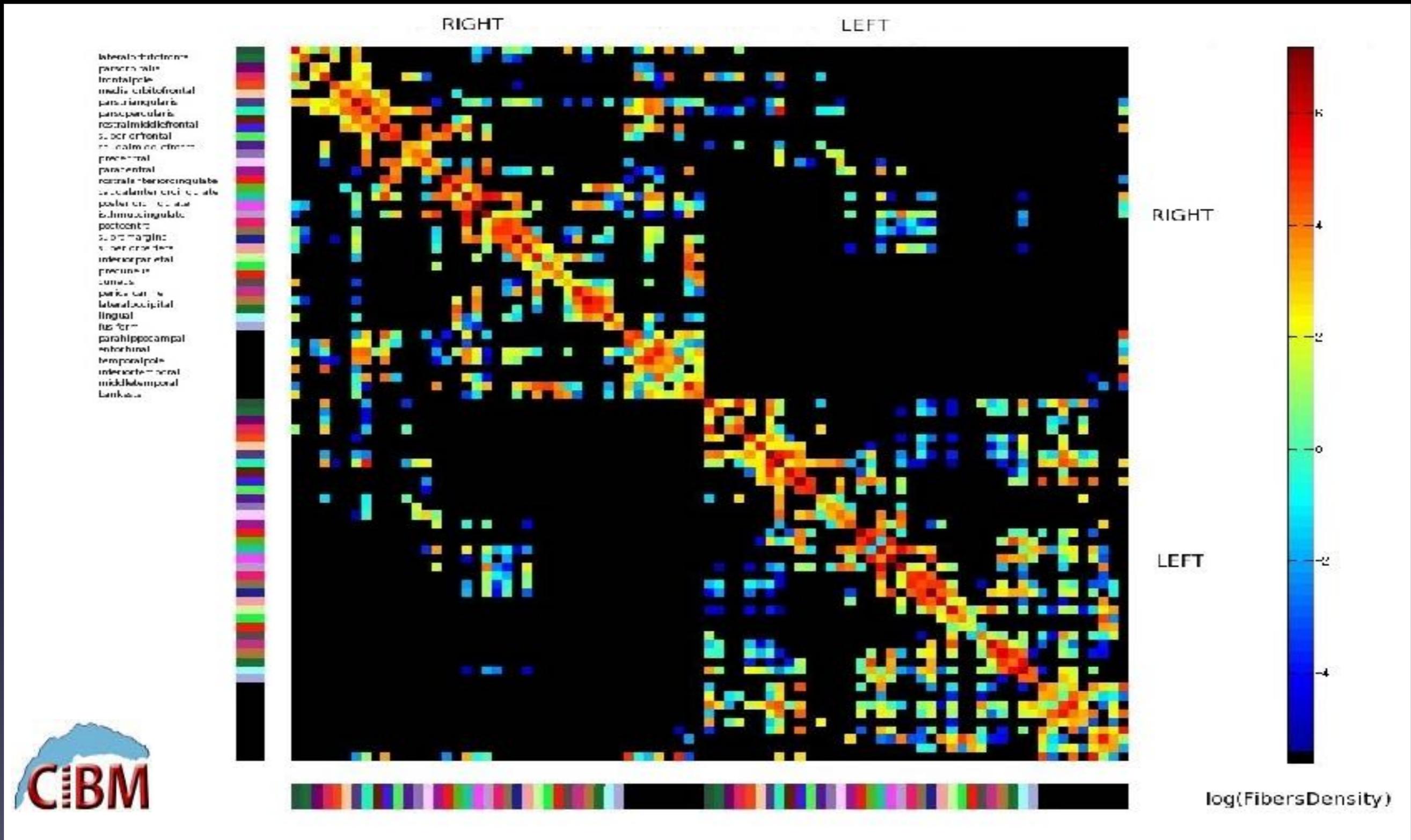
Tractography



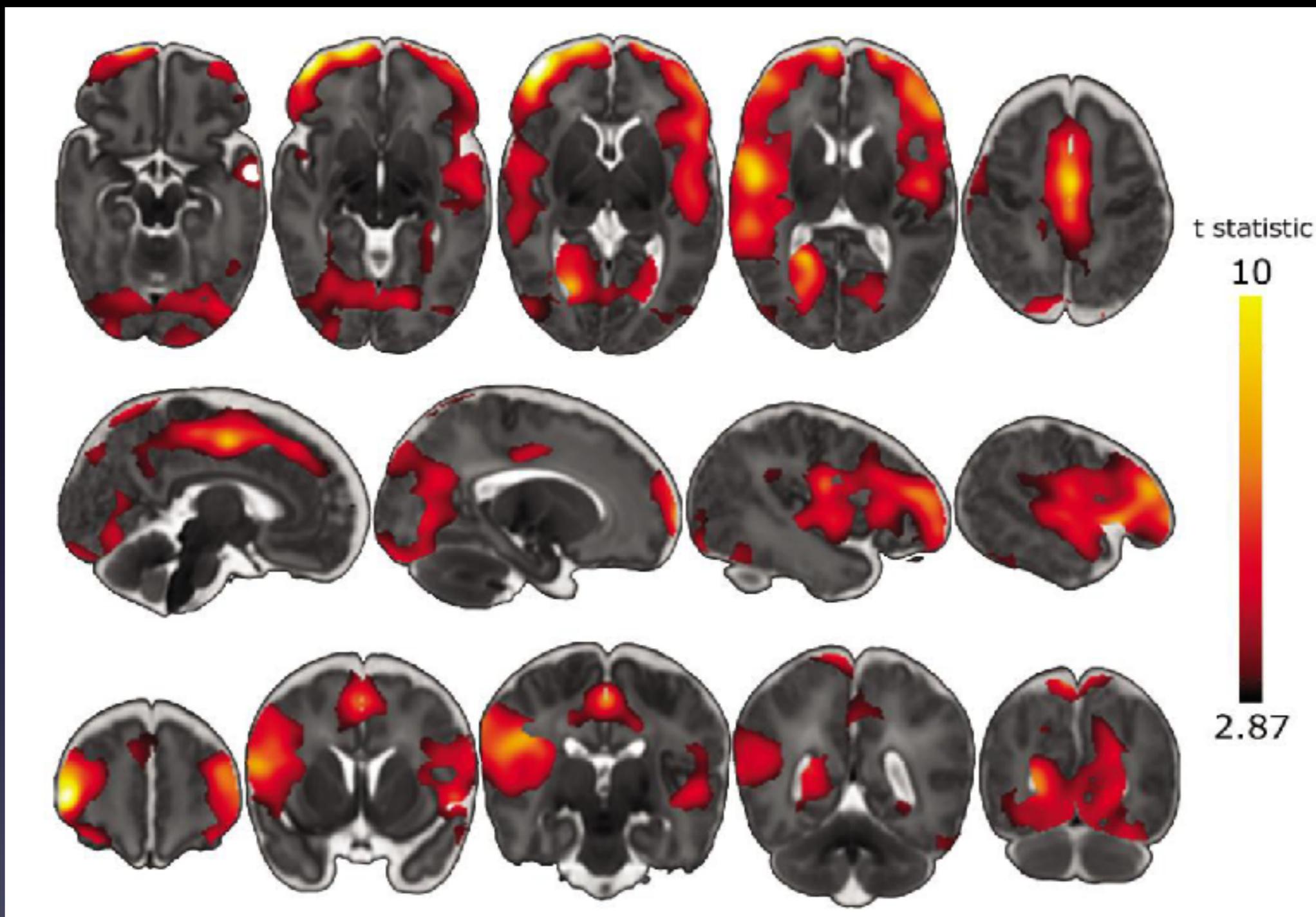
Parcelisation



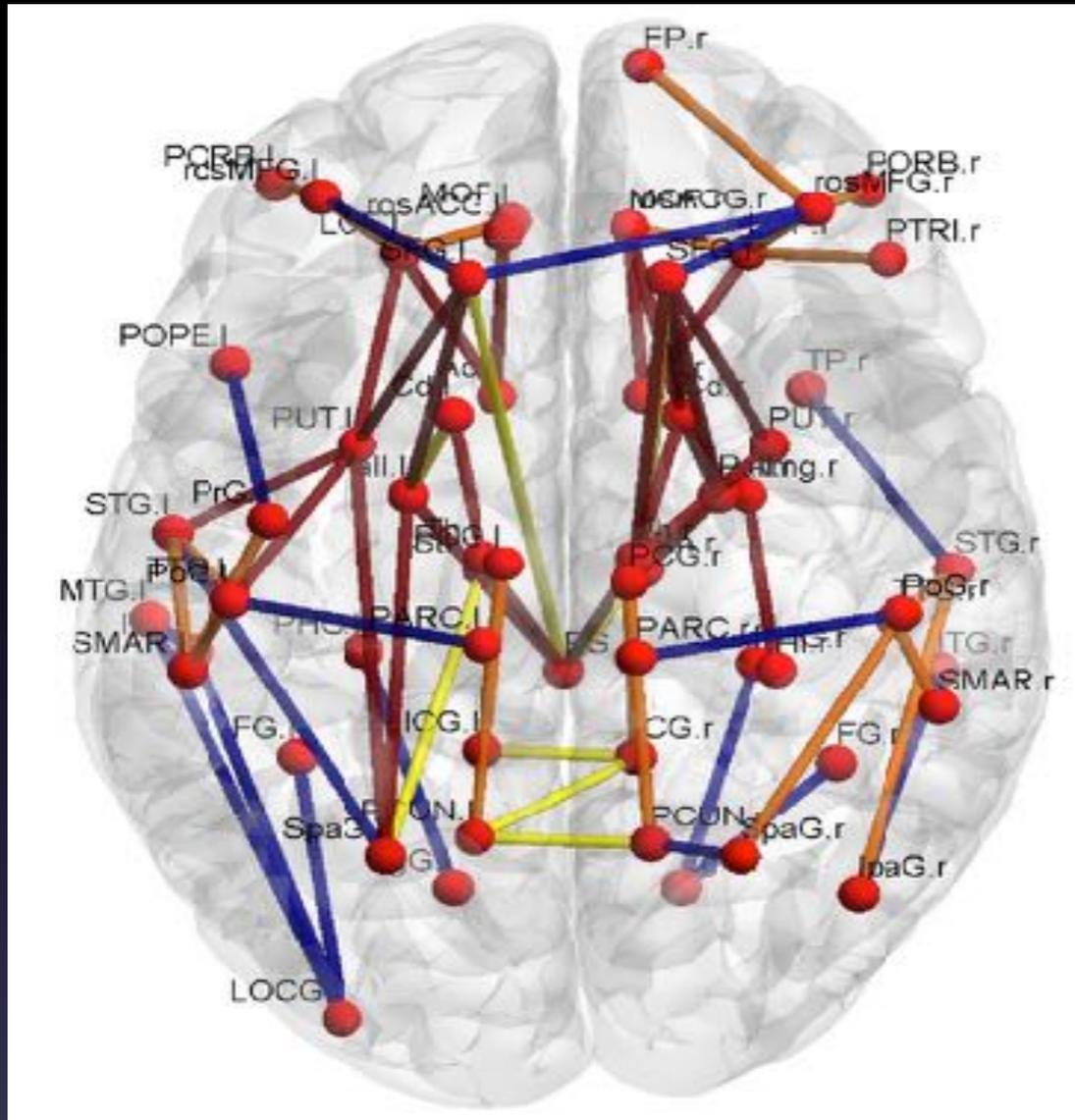
Connectivity matrix



Thalamocortical connectivity

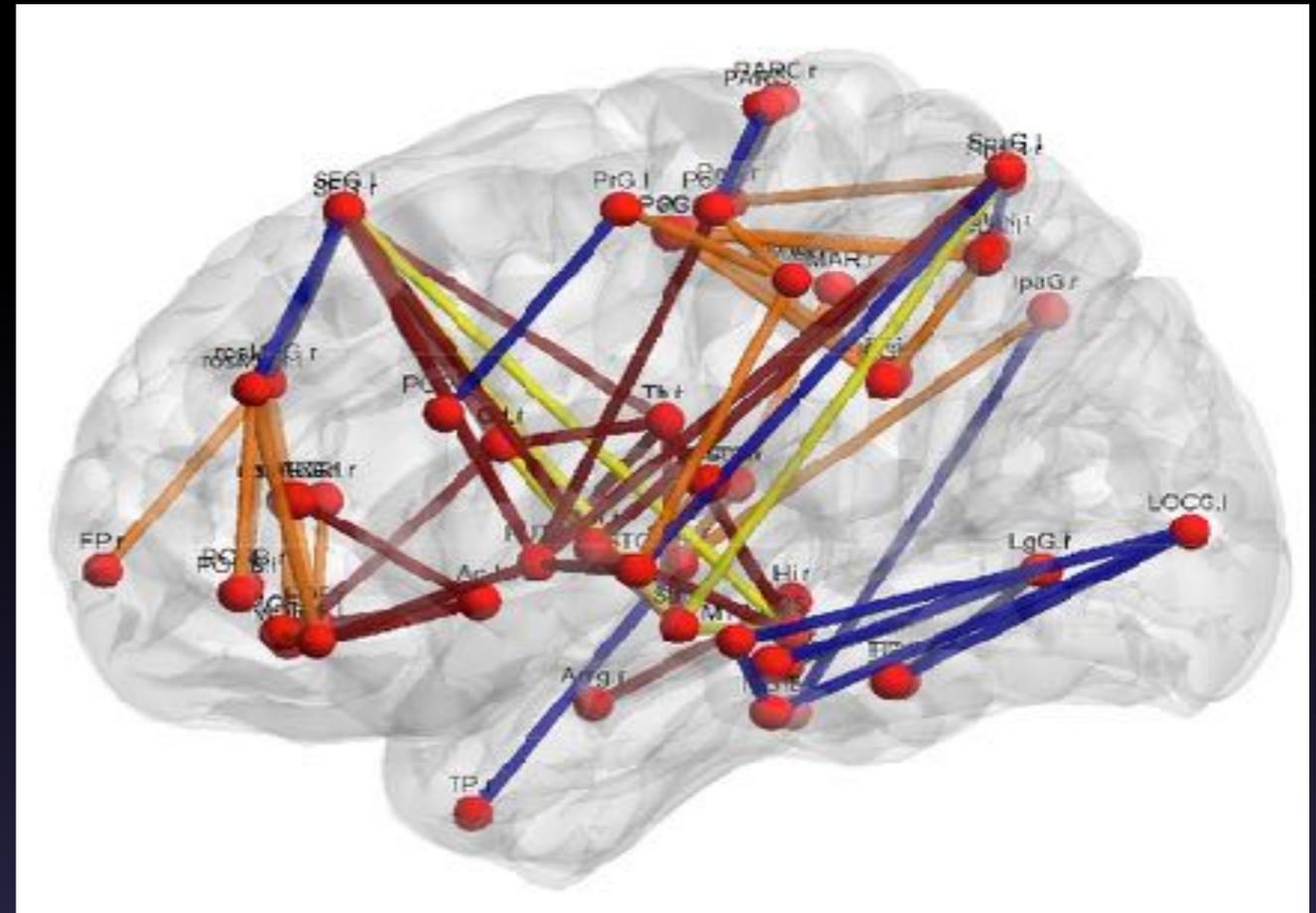


Connectivity at 6 years



Preterm > Controls

Short Cortico-cortical



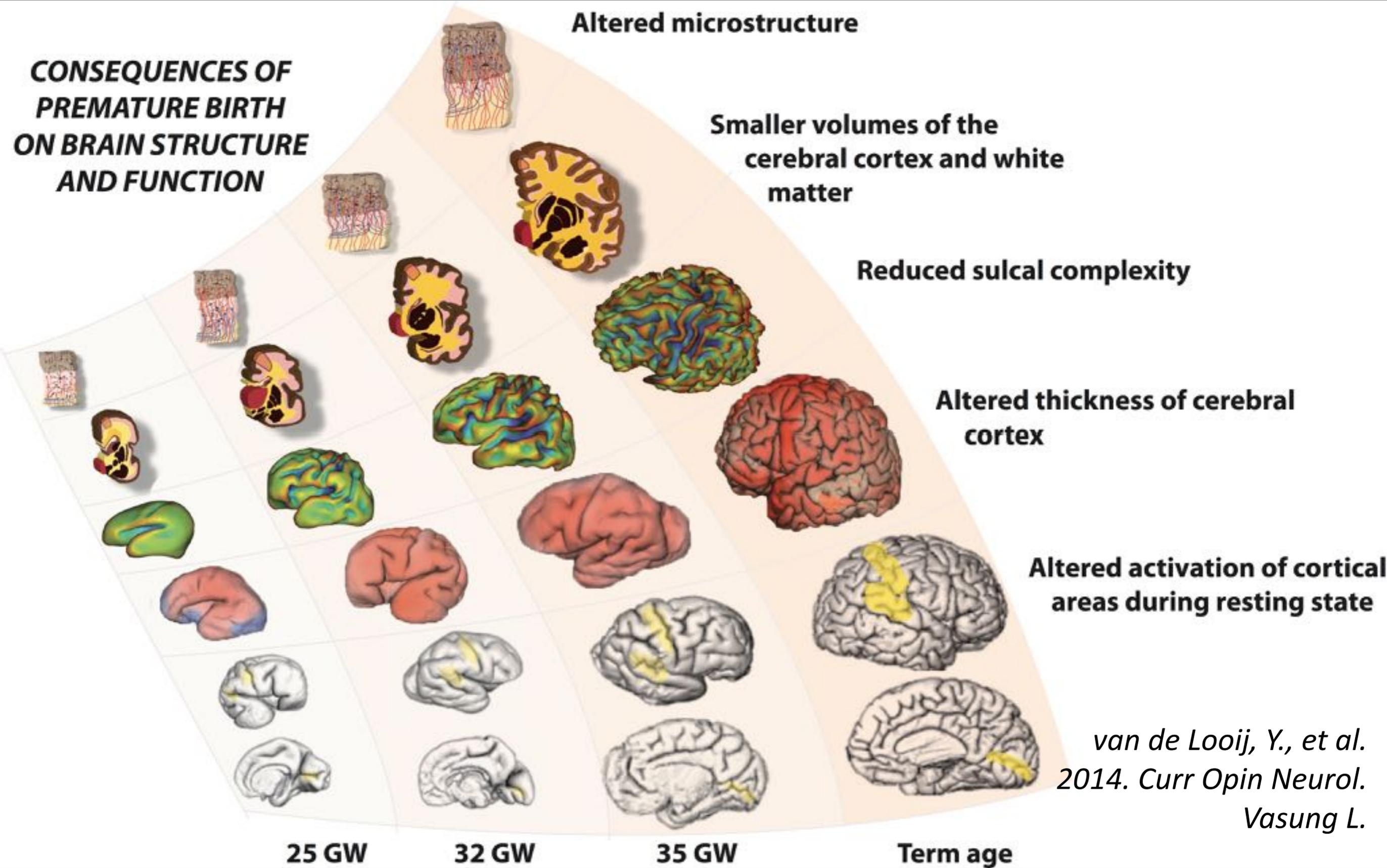
Preterm < Controls

Cortico Basal ganglia Thalamo Cortical Loop

Short Cortico-cortical Brain Stem

Subthalamic Commissural

Summary



*van de Looij, Y., et al.
2014. Curr Opin Neurol.
Vasung L.*

Thank you for
your attention

