Cortical development in the *ex utero* fetus

aka the preterm infant

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The Third International Symposium on the Fetal Brain
November 1-2, 2018
Disclosure

Jeff Neil has no relevant financial relationships to disclose or conflicts of interest to resolve.
• Diffusion imaging
• Cortical cartography
• Functional connectivity MRI
MR Imaging

• Detect signal from $^1$H of H$_2$O, which is present at a concentration of approximately 100 M.

• In conventional imaging, signal intensity (greyscale) is related to MR relaxation properties of $^1$H$_2$O such as T1 or T2 relaxation times.

• Water in grey matter has different T1 and T2 relaxation times than water in white matter or CSF.
Water motion in white matter

Perpendicular to axons

Parallel to axons
Hindered Diffusion

- Isotropic
- Anisotropic

without hindrance

with hindrance
Ellipsoid Image

Information available through DTI -- ADC

- Related to the overall size of the ellipsoid.
- Values for ADC change with brain maturation.
- Values of ADC change dynamically after injury (useful for early detection of injury).
Perinatal Injury

T2

DWI
Information available through DTI – $A_\sigma$

- Related to the shape of the ellipsoid
- Independent of ADC (normalized)
- Zero for a sphere, positive for other shapes
- Sensitive to myelination and cortical development

$$A_\sigma = \frac{1}{\sqrt{2}} \frac{\sigma(D)}{ADC}$$
Normal Adult Brain
Information available through DTI – Orientation of $\lambda_1$

- Useful for following white matter tracts
Diffusion Tracking of Geniculo-Calcarine Tracts

Whisker Plot:
26 Weeks GA
Whisker Plot: 35 Weeks GA
Human and Baboon Comparison

Average 125-day

Sidman and Rakic
Anisotropy Versus Distance from Insula

Anisotropy Versus Gestational Age

Kroenke et al. Neuroimage 25, 1205 (2005)
Human cortical anisotropy

27 weeks

33 weeks

Anisotropy

low

high
• Diffusion imaging
• Cortical cartography
• Functional connectivity MRI
Cortical Cartography

Preterm at Term

34 weeks

Term (38 weeks)

Adult (~20 years)

Jason Hill, Donna Dierker, David van Essen
The Brain at Term
Cortical Shape and Variability

Average Right Fiducial (n=12)

Neonate

-22 mm to 5 mm

Adult

-30 mm to 5 mm

Average Sulcal Depth

Sulcal Depth Variability

3D Positional Variability

0 mm to 3.7 mm

0 mm to 4.5 mm

0 mm to 6.5 mm

0 mm to 7.2 mm
The Brain at Term
Hemispheric Asymmetries

Postnatal Cortical Expansion

Right Hemisphere

Absolute Areal Expansion

2x 4x

-50% +50%

Relative Areal Expansion

Postnatal Cortical Expansion
Non-Uniformity at Term

Orange Regions
- Synaptic Density: Low
- % Peak Synaptic Density: Low
- % Peak Spine Density: Low
- FDG PET Signal: Low

Blue Regions
- Synaptic Density: High
- % Peak Synaptic Density: High
- % Peak Spine Density: High
- FDG PET Signal: High

High Expansion
Less Structurally Complex
Less Functionally Mature
More Complex Adult Structure

Differing developmental endpoints and greater impact of postnatal experience
Cortical Expansion Evolution

Speculation

Greatest Evolutionary Pressure to Expand → Relatively Immature at Term

Regions for Expansion Reserved to have Postnatal Influence on Development

Evolution

Development

Adult

-30 mm 5 mm

0 mm 6.5 mm

0 mm 7.2 mm
Speculation

Greatest Evolutionary Pressure to Expand → Relatively immature at term

Prioritize Regions for Early Survival

Mechanics of Birth
Preterm babies at term equivalent PMA
Cortical cartography

Preterm Birth
Depth and Variability

Average Sulcal Depth
Sulcal Depth Variability
3D Positional Variability
Hemispheric Depth Difference

Term
-22 mm
0 mm
0 mm
L > R

Preterm
At term
5 mm
3.7 mm
4.5 mm
R > L

Note temporal and frontal regions
Sulcal depth differences
Control vs. Preterm
Gyrification index

\[
\text{Cortical surface area} = \frac{\text{Hull surface area}}{} \quad \text{Gyrification index}
\]
Cortical cartography

Cortical cartography

- Lower birthweight
- Poor head growth
- Higher critical illness score during the first day of life
- Exposure to postnatal steroids
- Prolonged endotracheal intubation
Language outcome

\[ \beta = -8 \]
\[ \text{(}-14, -2) \]

*Linear regression; controlling CRIB, cerebral injury, social risk and family functioning
Sulcal Asymmetry

Open ward

Private room

left deeper

right deeper

-3 mm 0 +3 mm
• Diffusion imaging
• Cortical cartography
• Functional connectivity MRI
Functional MRI

fcMRI

From Tootell RBH et al. PNAS 95, 818-824 (1998)
Default mode network (DMN)

Emerging networks

Smyser et al. Cerebral Cortex 20, 2852 (2010)
Differential maturation rates

Smyser et al. Cerebral Cortex (2014)
Network correlations

Left and right motor cortex

\[ z(r) \]

Bayley-III motor score

\[ r = 0.705 \]
\[ p < 0.001 \]
Network correlations

Left motor and medial prefrontal cortex

\[ r = -0.735 \]
\[ p < 0.001 \]
Network correlations

Left motor and visual cortex

$z(r)$

Bayley-III motor score

$r = 0.133$

$p = 0.485$
Acknowledgements

WUNDER Lab
Chris Smyser
Cynthia Rogers
Josh Shimony
Chad Sylvester
Cindy Ortinau
Tara Smyser
Jim Alexopoulos
Jeanette Kenley
Sydney Kaplan
Karen Lukas
Rachel Lean
Muriah Wheelock
Jessie Perkins
Rebecca Brenner
Peppar Cyr
Teran Mickens

Funding Support
NIH/NIMH – R01 MH113570
NIH/NIMH – R01 MH113883
NIH/NINDS – K02 NS089852

Bill and Melinda Gates Foundation

Dana Foundation
Child Neurology Foundation
Children’s Discovery Institute
Cerebral Palsy International Research Foundation

https://neuro.wustl.edu/Fellowships/Neonatal-Neurology