Interhemispheric Connections Related to Reading Skill Measured with Diffusion Tensor Imaging

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SIRL Longitudinal Study of Reading Development

- Behavioral assessment
- Anatomical Imaging
- Diffusion Tensor Imaging
- Functional MRI
- 50 7-11 yr olds
- 3 years (4 measurements)
  - Completed 1st and 2nd measurement (1yr)
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What's the Matter?

- Gray matter: the connections (synapses)
  - Functional activity (EEG, MEG, PET, fMRI)
- White matter: the wiring (myelinated axons)
  - Looks white due to high lipid content (myelin)
  - Connections develop early and limit plasticity
  - Connections define cortical modularity
Why You See with the Back of Your Brain

Brain dissection image from: The Virtual Hospital (http://www.vh.org)
White Matter is Crucial for Understanding Brain Development

- Connections form early (genetic program)
- Myelin limits new long-range connections
  - Exuberant connectivity before myelination
  - Experience can:
    - Prune existing connections
    - Strengthen existing connections
- Long-range connections limit adult plasticity
  - Neighboring regions can densely connect
  - Distant regions can increase direct connections only if some connections already exist
Tracking Axons is Hard

- Lethal to the subject
  - Human
    - Freeze-fracture dissection
    - Dil- post-mortem tracer
    - Lesion patients die-> stain for degeneration
  - Non-human
    - Induce lesion-> stain for degeneration
    - Various (toxic) tracers

- Tedious, slow work
Diffusing Water Probes
Microscopic Tissue Structure

• Tissue structures affect water diffusion
• Diffusion through white matter probes:
  • Axon density & myelination, principal fiber
direction and directional coherence
• MR Diffusion weighting measures diffusion
• Fiber tracking using diffusion data
  • Hints at axonal connectivity
  • Your subjects get to live
Protons Precessing in Phase
Diffusion Weighting: First Pulse
Time to Diffuse
Diffusion Weighting: Second Pulse
Reduced Signal from Dephasing
Water Diffusion in the Brain

Unimpeded direction - higher diffusion rate

\[ \text{H}_2\text{O} \]

Impeded direction - lower diffusion rate

\[ \text{H}_2\text{O} \]
The Diffusion Tensor: 3x3 Covariance Matrix (Ellipsoid)

• Water molecules move in Brownian motion
• 3D Gaussian (3x3 covariance matrix) model
  • Eigenvalues & vectors define ellipsoidal isodiffusion surface

\[
D = \begin{pmatrix}
D_{xx} & D_{xy} & D_{xz} \\
D_{xy} & D_{yy} & D_{yz} \\
D_{xz} & D_{yz} & D_{zz}
\end{pmatrix} = 
\begin{pmatrix}
\vdots & \vdots & \vdots \\
\lambda_1 & 0 & 0 \\
\nu_1 & \lambda_2 & 0 \\
\vdots & \vdots & \lambda_3 \\
\vdots & \vdots & \vdots
\end{pmatrix}
\begin{pmatrix}
\cdots & \nu_1 & \cdots \\
\cdots & \nu_2 & \cdots \\
\cdots & \nu_3 & \cdots
\end{pmatrix}
\]
DTI Reveals White Matter Structure

T1

DTI (FA)

DTI (PDD)
Trace Paths Through Tensor Field

- Stream-tubes tracking algorithm
  - Assume principal diffusion direction is tangent to the local fiber tract
  - Runge-Kutta path integral estimate
  - Tri-linear interpolation of tensors
  - 1 mm step size
  - Stop at FA<0.15 or angle > 30°

- Data acquisition
  - 1.5T, DW-EPI, 2x2x2mm voxels, 12 directions, 10-14 repeats

From Watts et. al. (Cornell)
Occipital Fibers
Occipital Callosal Fibers
Occipital Callosal Fibers
Splenial Fiber Pathway in Average Tensor Map (53 Children)

Dougherty et. al. (2005) PNAS; Dougherty et. al. (2005) Annals of the NYAS
Neural Basis of Reading

- Behavior
- Gross Anatomy
  - Brain shape/size analysis
- White matter structure
  - Diffusion imaging
- Cortical activity
  - Functional MRI
Name the ink colors:

XXXXXX

XXXX

XXXXXX

XXX

XXXXXX
Name the ink colors:

red
green
blue
orange
purple
Why the Corpus Callosum?

- CC in developmental dyslexia
  - Morphological differences in shape and size of CC
  - Abnormal language lateralization
- CC in acquired dyslexia (alexia)

Mao-Draayer & Panitch (2004), Alexia without agraphia in multiple sclerosis...

The Virtual Hospital (http://www.vh.org)
Every Brain is Different...
FA is Negatively Correlated with Reading and PA in Splenium

\[ r = -0.44 \ (p=0.001) \]

\( N = 53 \)
Reduced FA in Good Readers Could Mean...

- Increased language lateralization
  - Requires fewer inter-hemispheric connections between language regions
- More efficient visual field integration
  - Requires fewer inter-hemispheric connections between visual regions
Previous WM Findings in Reading

- Decreased FA in low readers in temporal-parietal WM region (esp. on left)

Klingberg et. al. 2000
Deutsch et. al. 2005
Beaulieu et. al. 2005

Some overlap in extent; voxels of maximal difference <1cm apart
Why Previous Studies Did Not See FA Differences in CC

- Statistical power for FA varies greatly across brain regions when spatial normalization methods are used.
Unified Hypothesis

• More callosal connections in low readers:
  • Larger posterior CC (e.g. Rumsey et. al. 1996)
  • Higher FA in posterior CC pathway (this study)
  • Decreased FA in posterior corona radiata due to more crossing fibers
  • Increased functional symmetry (e.g. Simos et. al. 2000)

• Axonal guidance receptor gene ROBO1 is a candidate dyslexia gene (Hannula-Jouppi et. al. 2005)
Conclusions

• Splenium FA is *lower* in skilled readers
  • Consistent with previous studies of dyslexia
    • Less lateralized language
    • Enlarged posterior callosum
  • Visual system differences?

• Posterior callosum crucial for skilled reading
  • Lesions there result in alexia
  • But which lobe? Occipital? Parietal? Temporal?
    • Segment callosum by projection zone
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