Interhemispheric Connections Related to Reading Skill Measured with Diffusion Tensor Imaging

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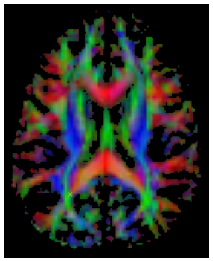
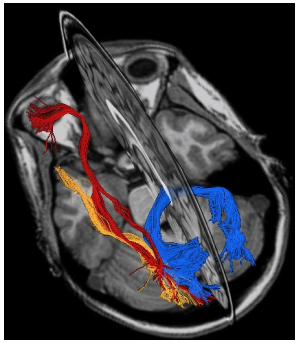
SIRL Longitudinal Study of Reading Development

- 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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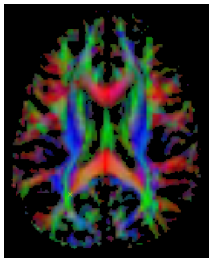
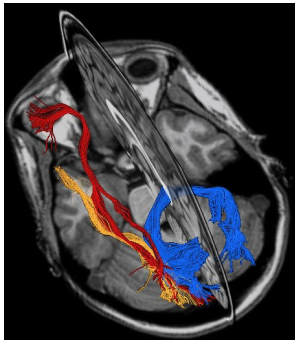
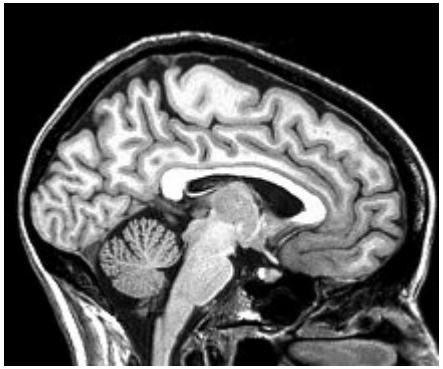
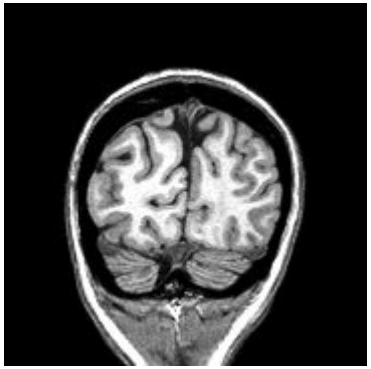




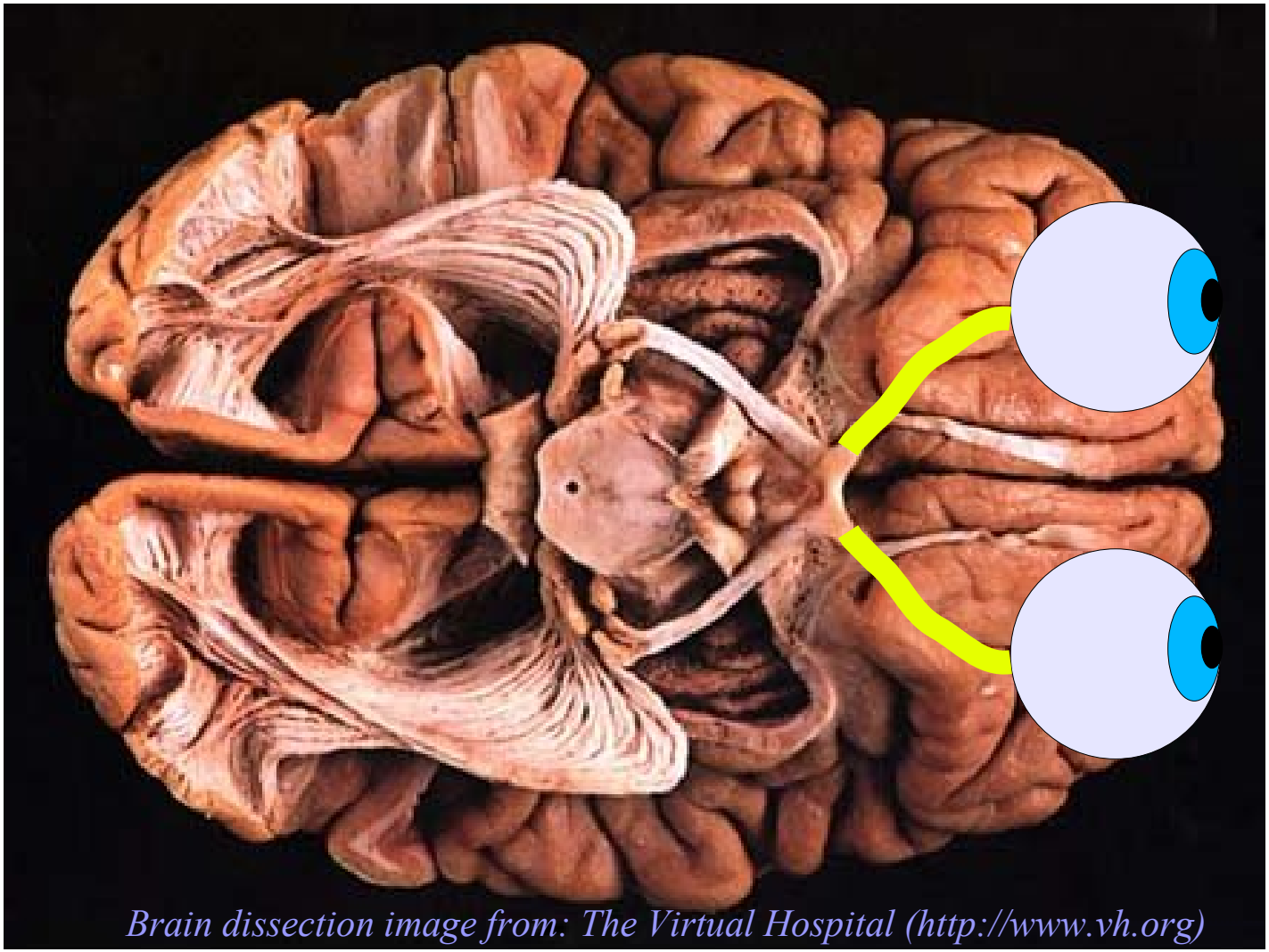
What's the Matter?

- 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

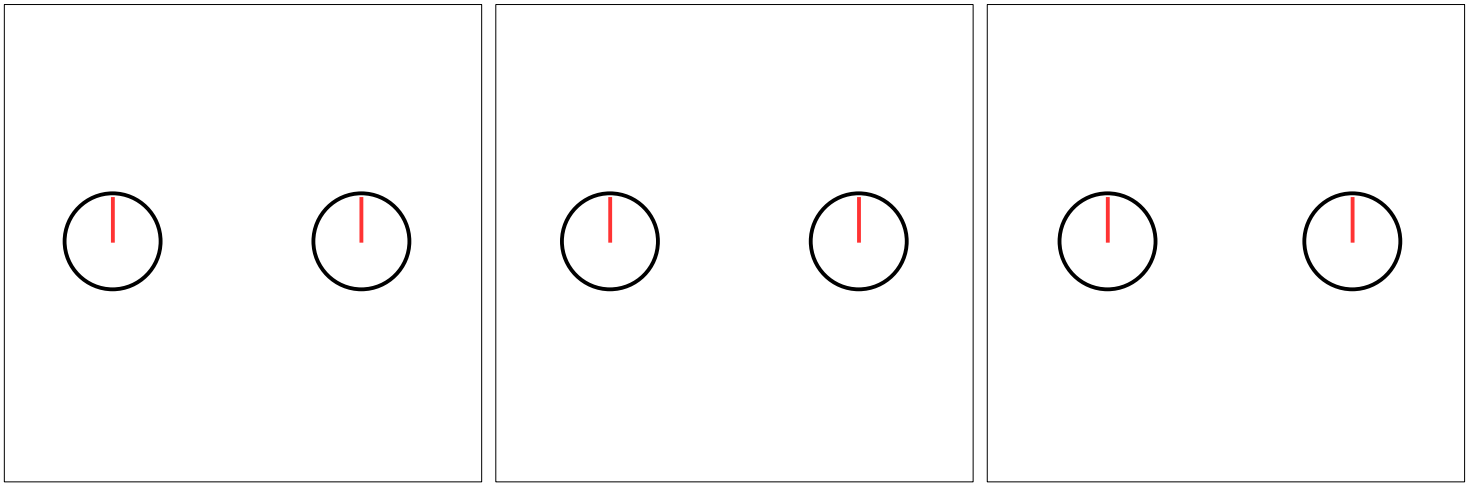
Tracking Axons is Hard

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

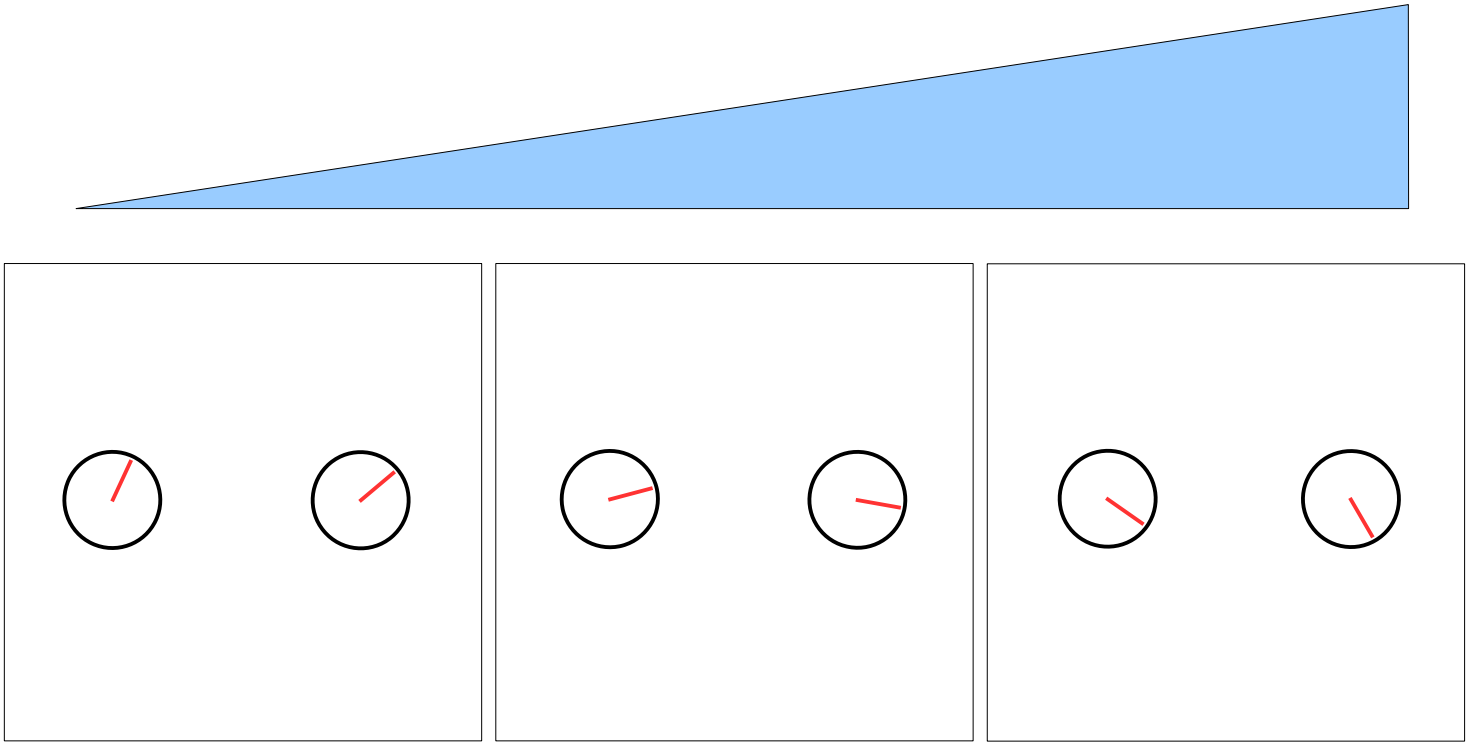
Diffusing Water Probes Microscopic Tissue Structure

- 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

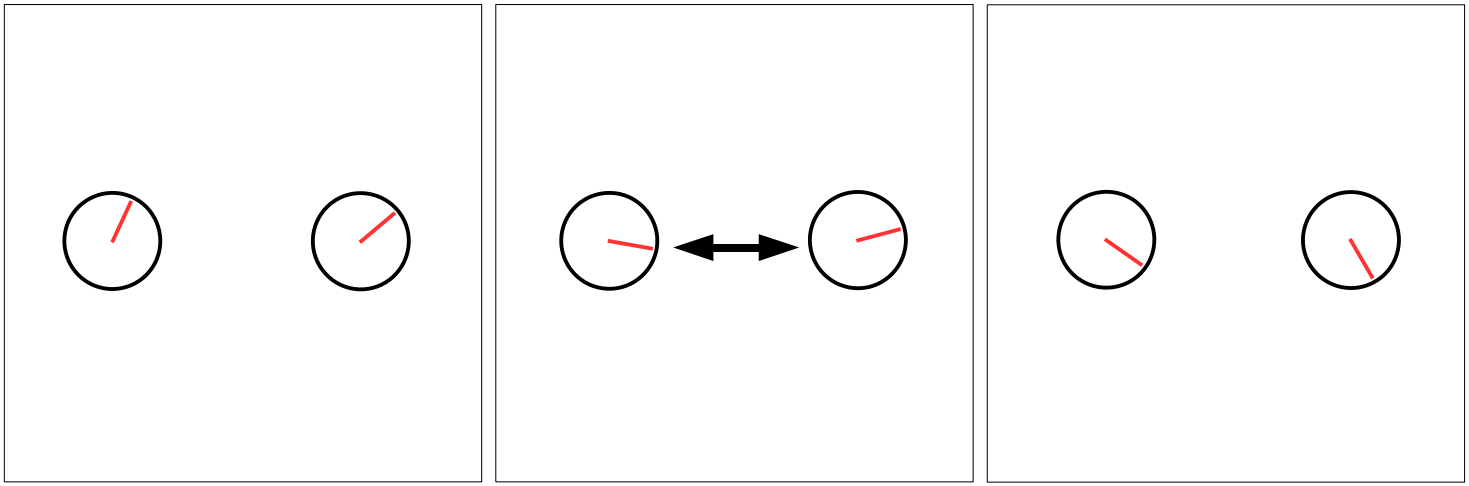
Protons Precessing in Phase



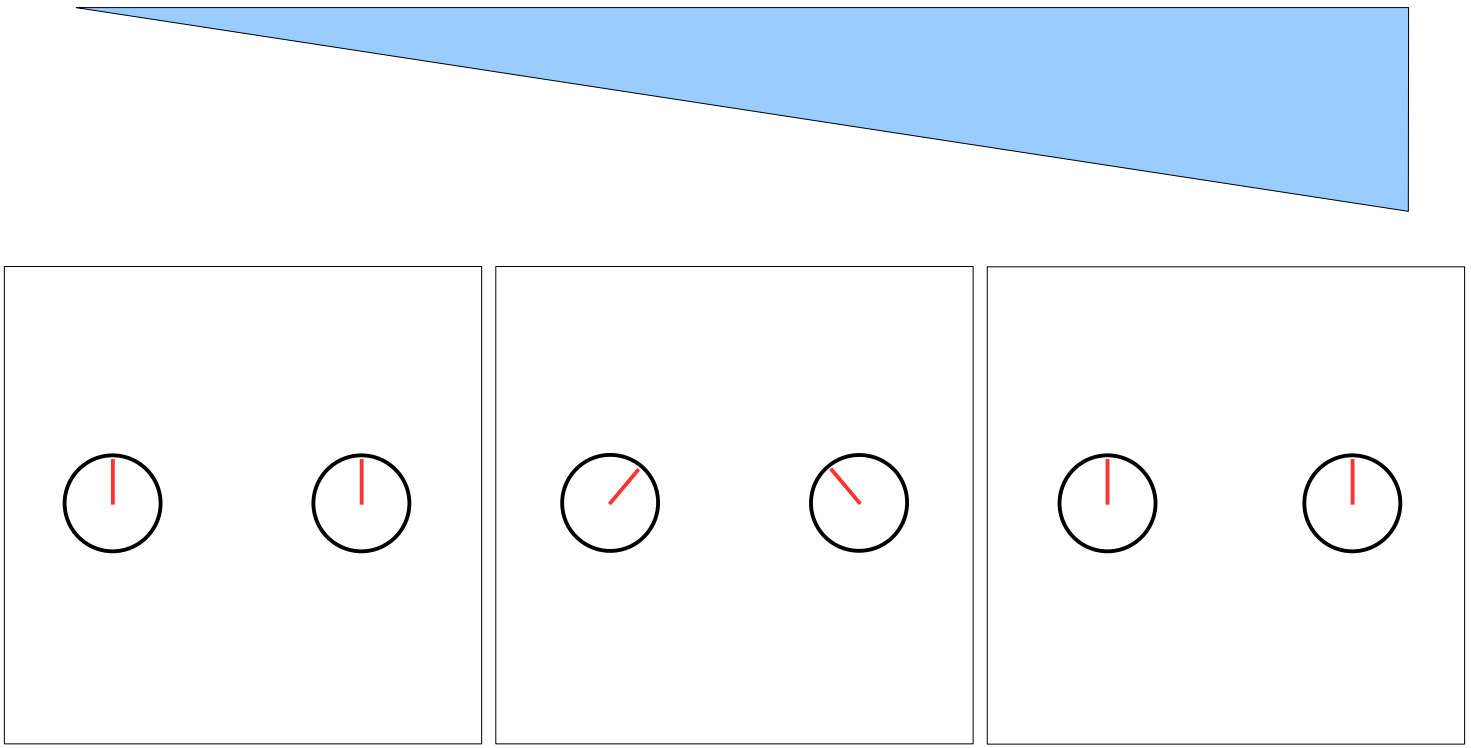
Diffusion Weighting: First Pulse



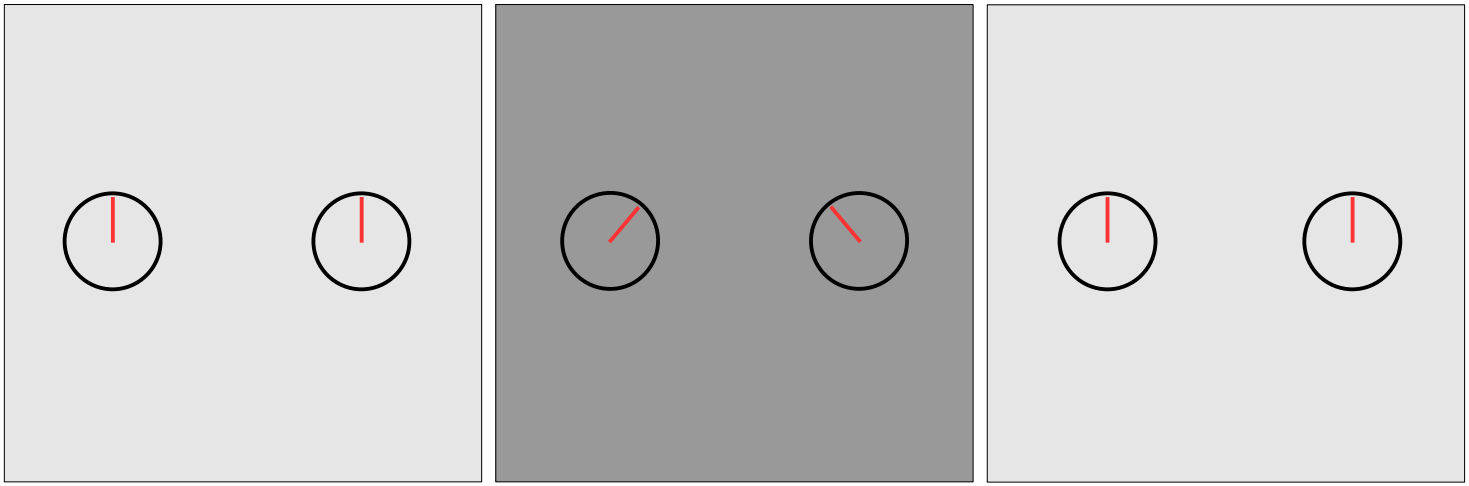
Time to Diffuse



Diffusion Weighting: Second Pulse

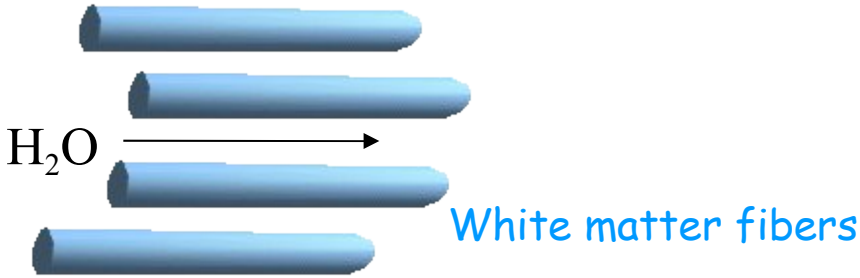


Reduced Signal from Dephasing

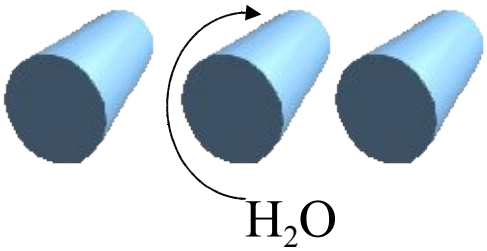


Water Diffusion in the Brain

Unimpeded direction- higher diffusion rate



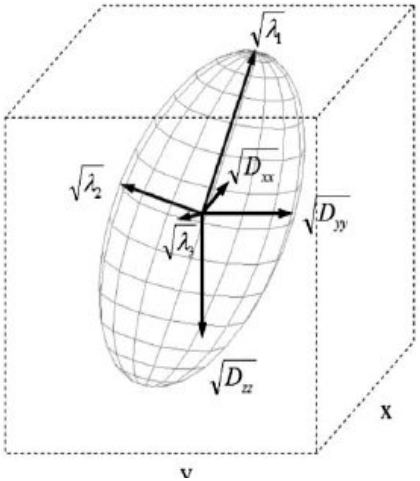
Impeded direction- lower diffusion rate



The Diffusion Tensor: 3x3 Covariance Matrix (Ellipsoid)

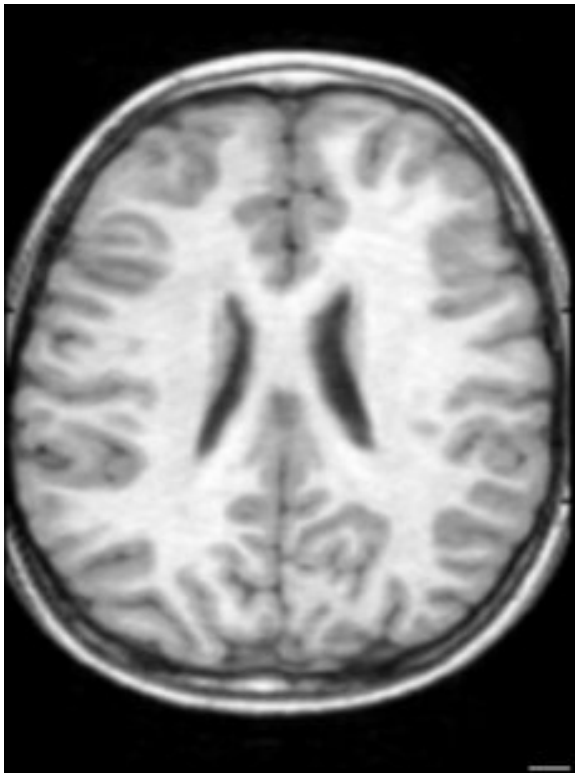
- Water molecules move in Brownian motion
- 3D Gaussian (3x3 covariance matrix) model
  - Eigenvalues & vectors define ellipsoidal isodiffusion surface

$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} = \begin{pmatrix} \vdots & \vdots & \vdots \\ v_1 & v_2 & v_3 \\ \vdots & \vdots & \vdots \end{pmatrix} \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \begin{pmatrix} \cdots & v_1 & \cdots \\ \cdots & v_2 & \cdots \\ \cdots & v_3 & \cdots \end{pmatrix}$$

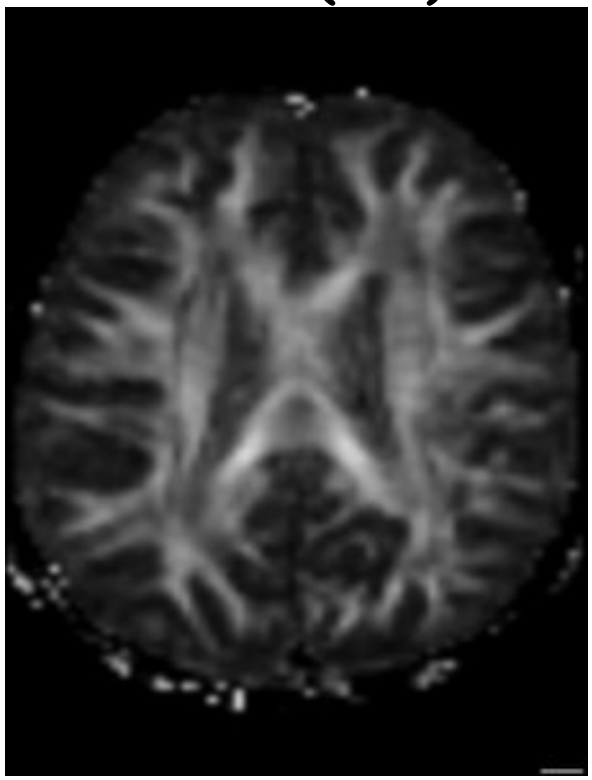


DTI Reveals White Matter Structure

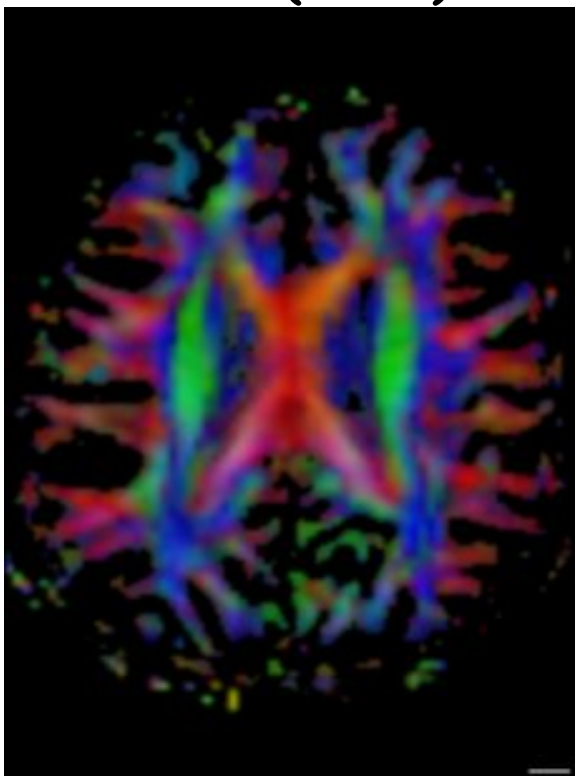
T1

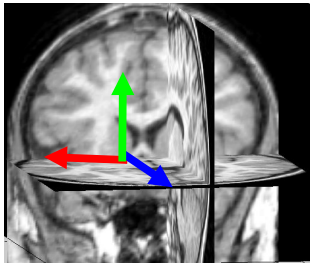


DTI (FA)



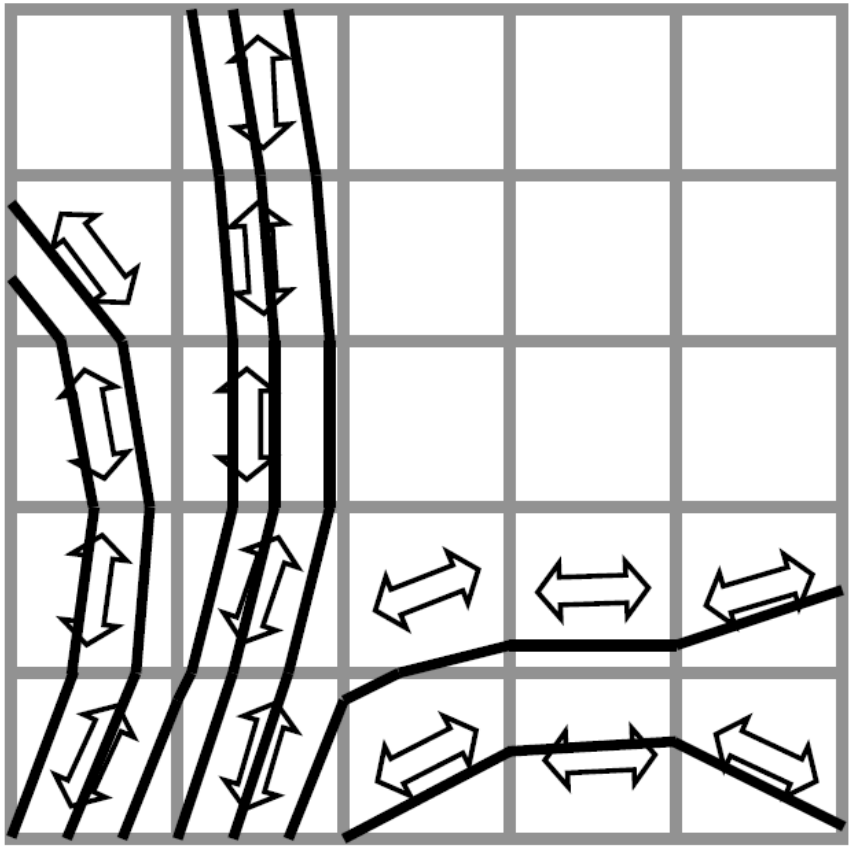
DTI (PDD)





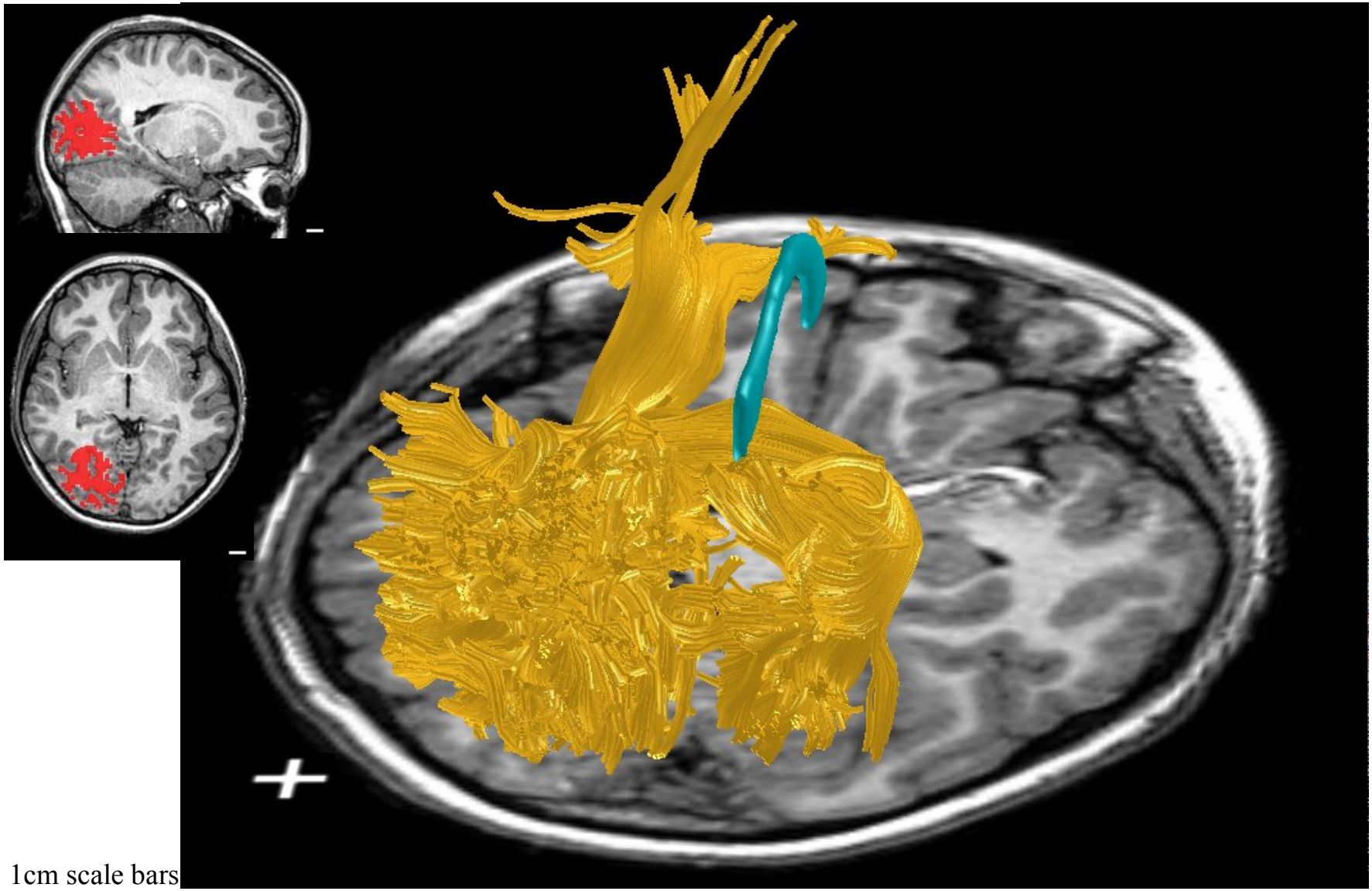
Trace Paths Through Tensor Field

- 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



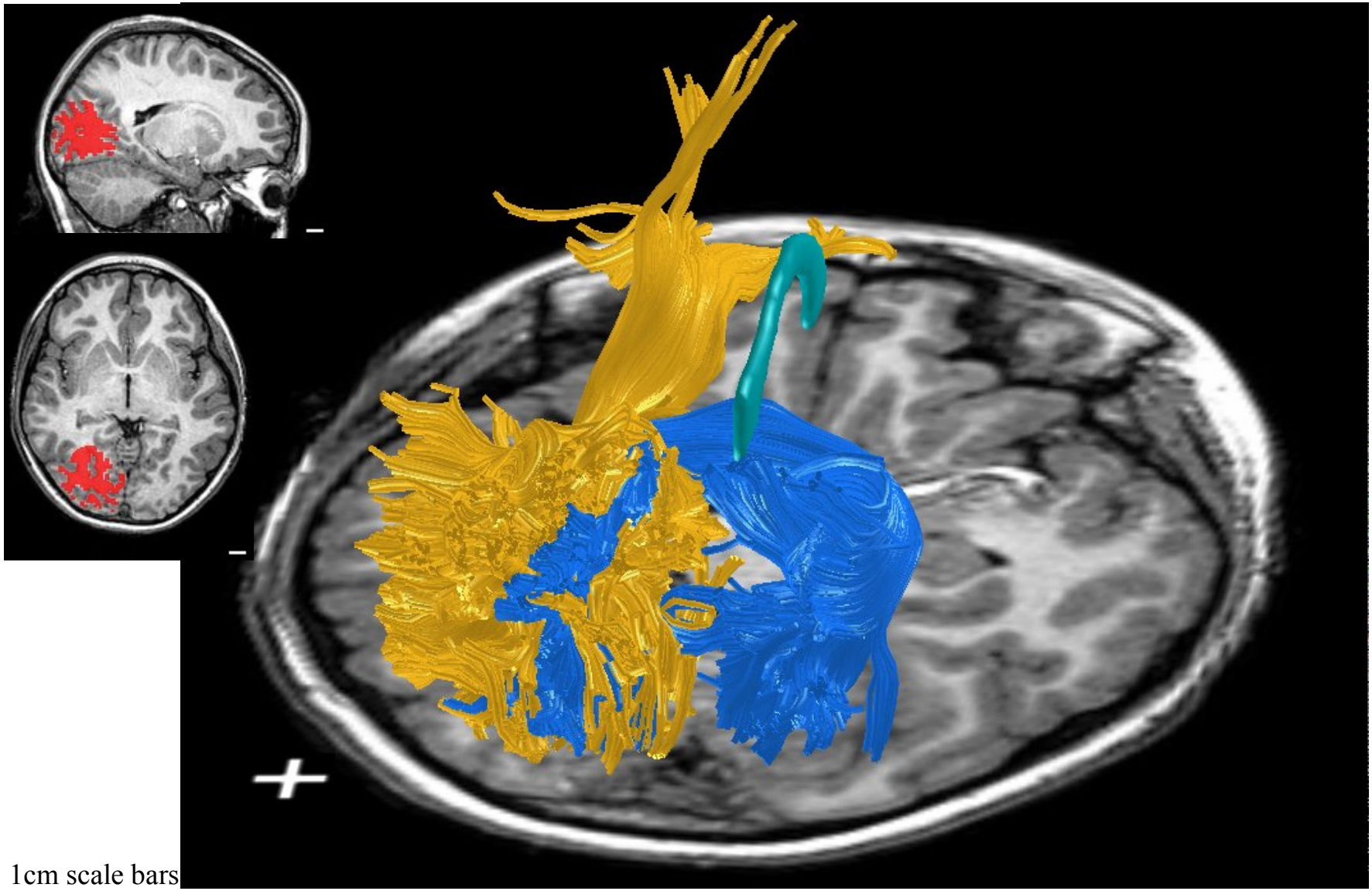
From Watts et. al. (Cornell)

Occipital Fibers



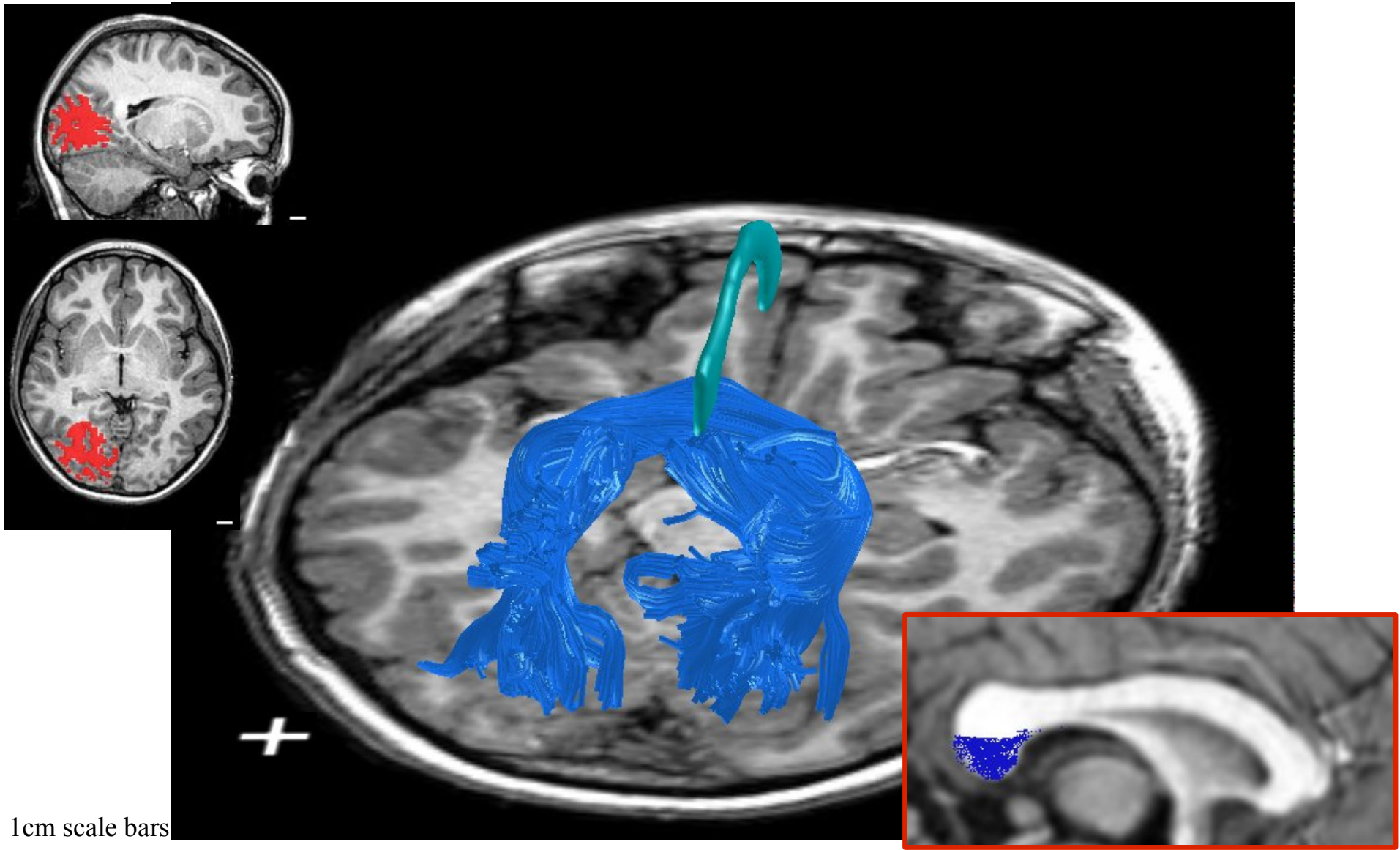
1cm scale bars

Occipital Callosal Fibers



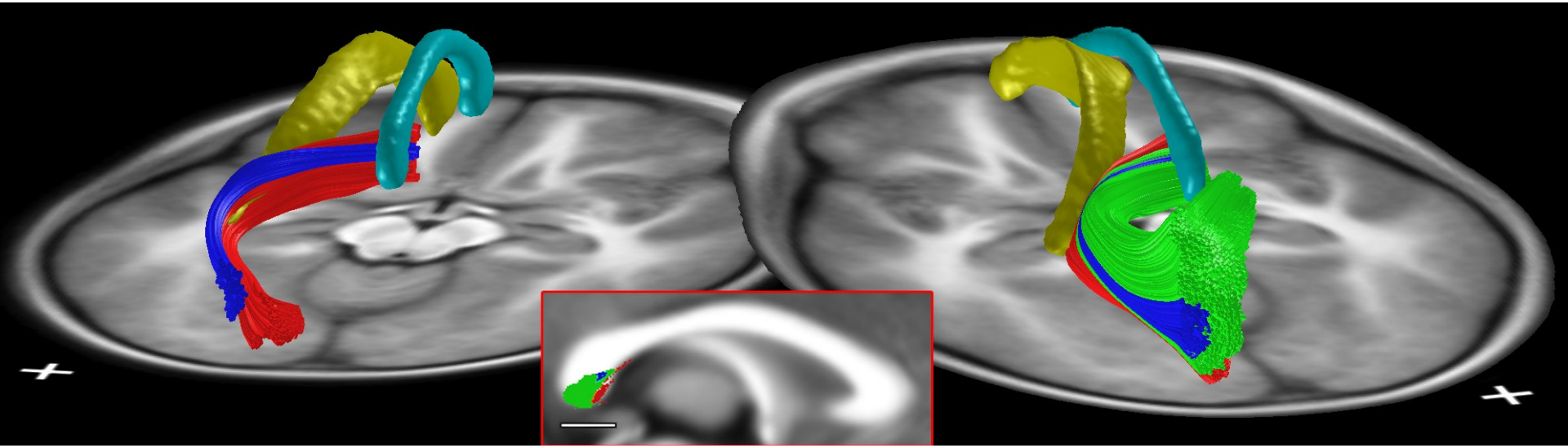
1cm scale bars

Occipital Callosal Fibers



1cm scale bars

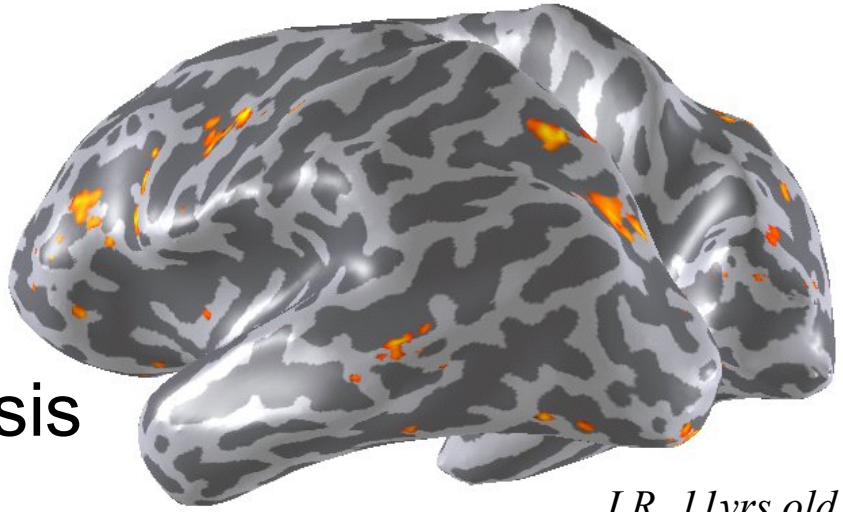
Splenial Fiber Pathway in Average Tensor Map (53 Children)



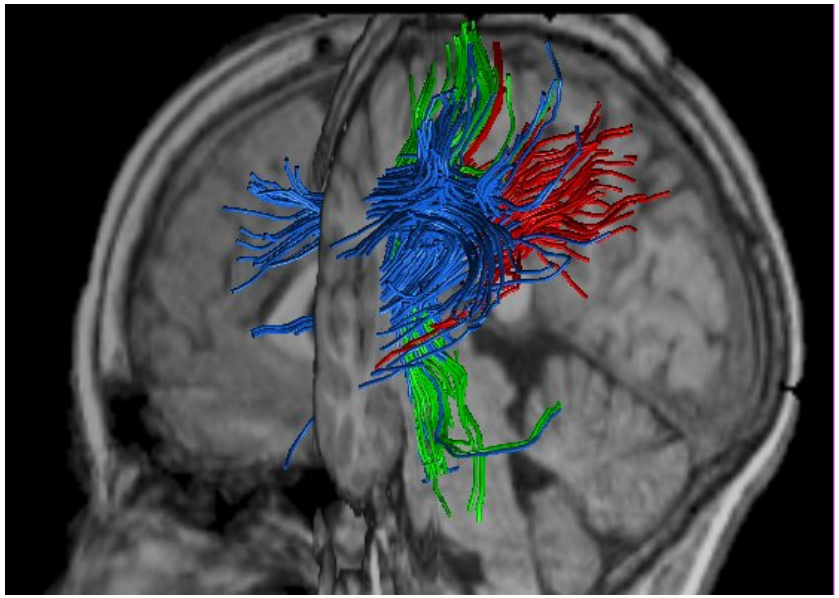
Dougherty et. al. (2005) PNAS; Dougherty et. al. (2005) Annals of the NYAS

Neural Basis of Reading

- Behavior
- Gross Anatomy
  - Brain shape/size analysis
- White matter structure
  - Diffusion imaging
- Cortical activity
  - Functional MRI



LR, 11yrs old



Name the ink colors:

xxxxxx

xxxx

xxxxx

xxx

xxxxxx

Name the ink colors:

red

green

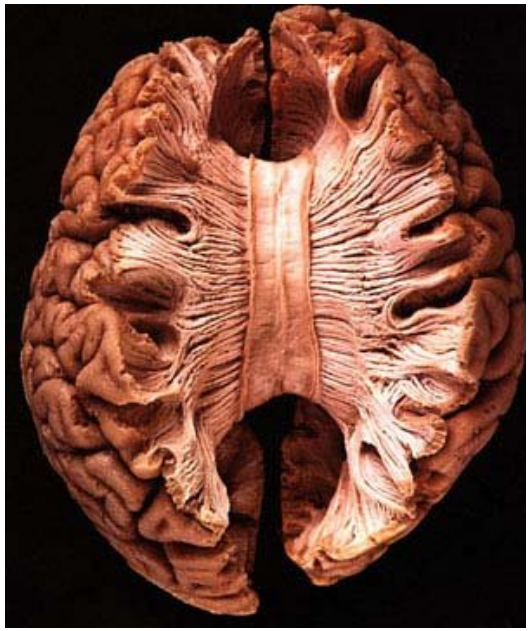
blue

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)



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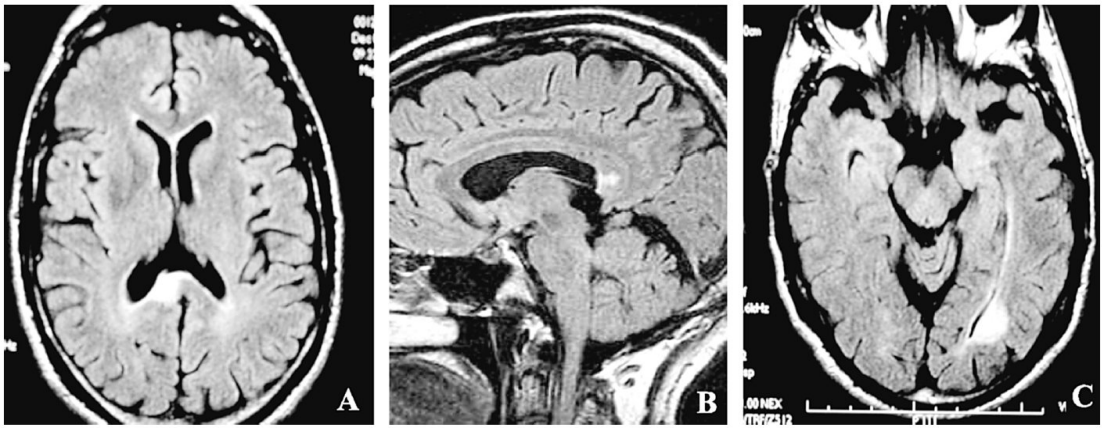
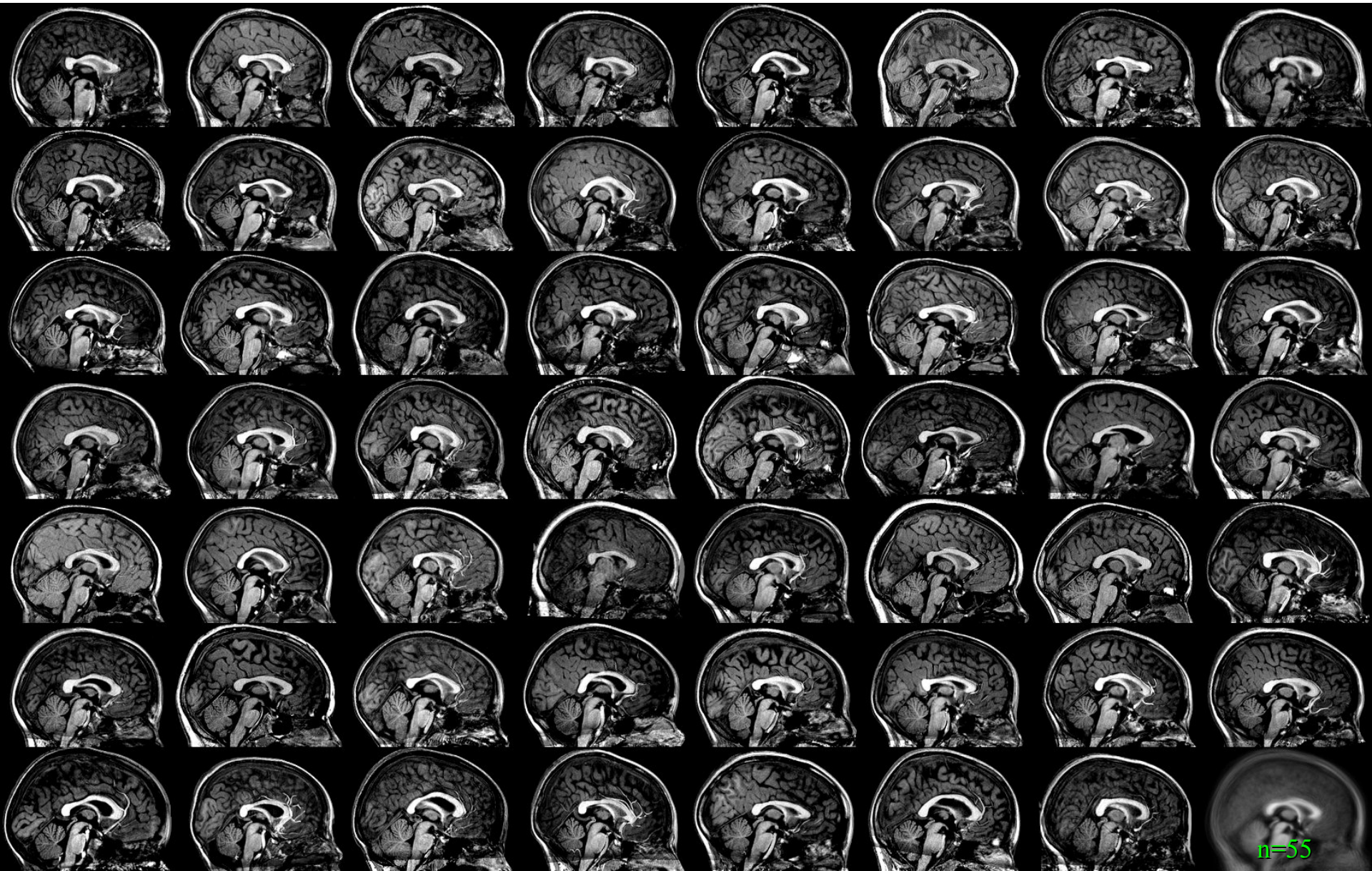
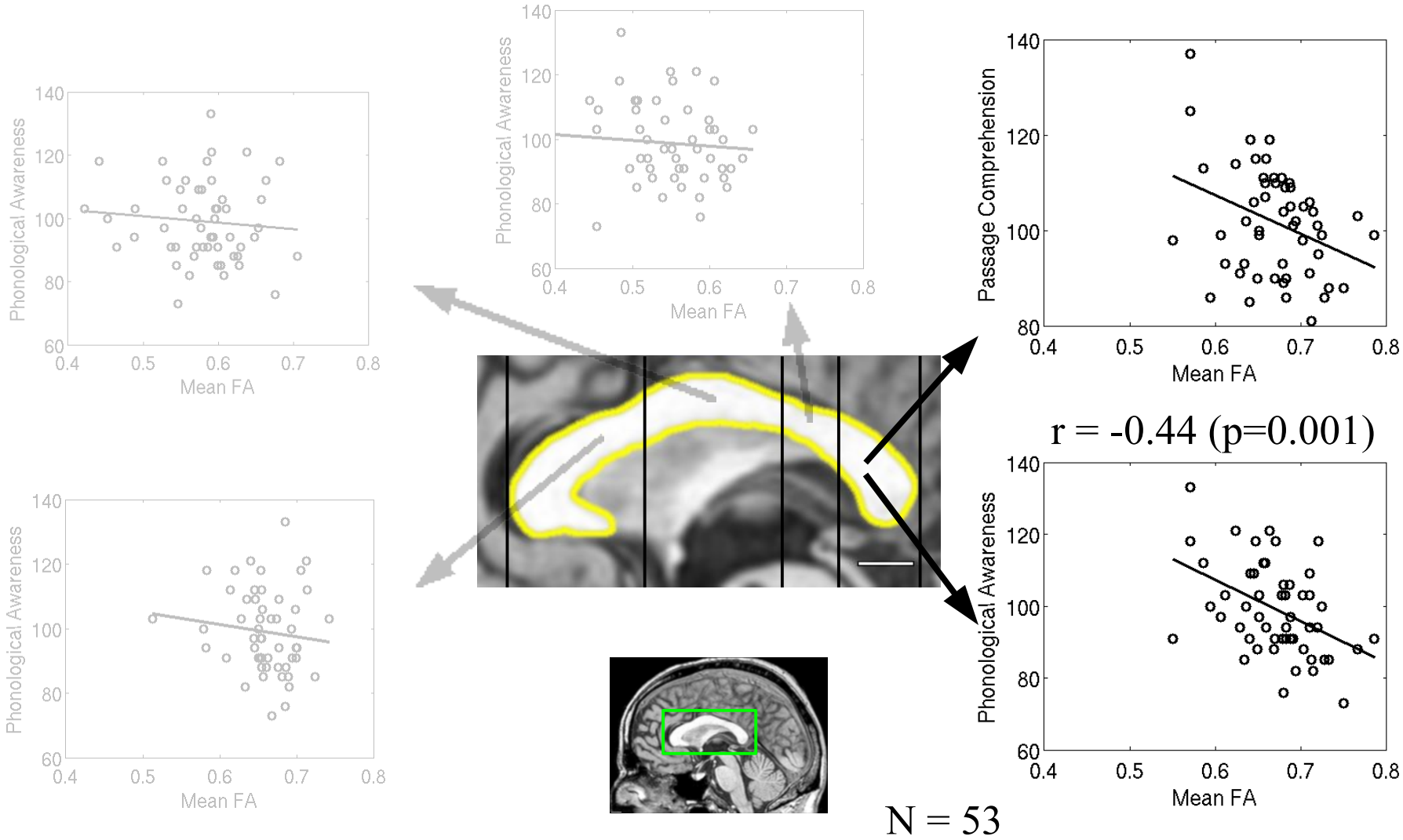


Mao-Draayer & Panitch (2004), Alexia without agraphia in multiple schlerosis...

Every Brain is Different…

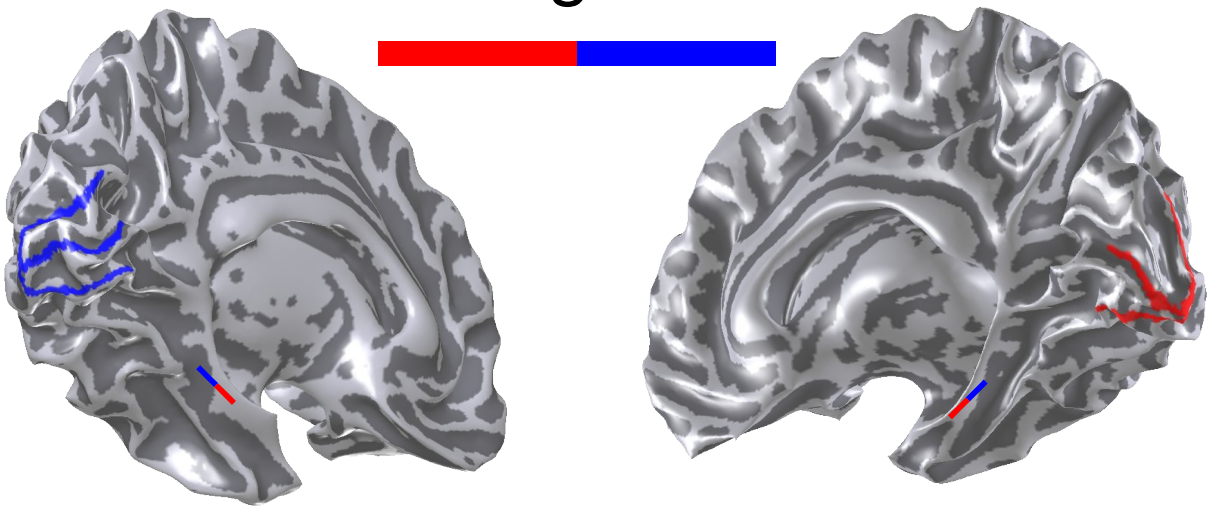


FA is Negatively Correlated with Reading and PA in Splenium



Reduced FA in Good Readers Could Mean…

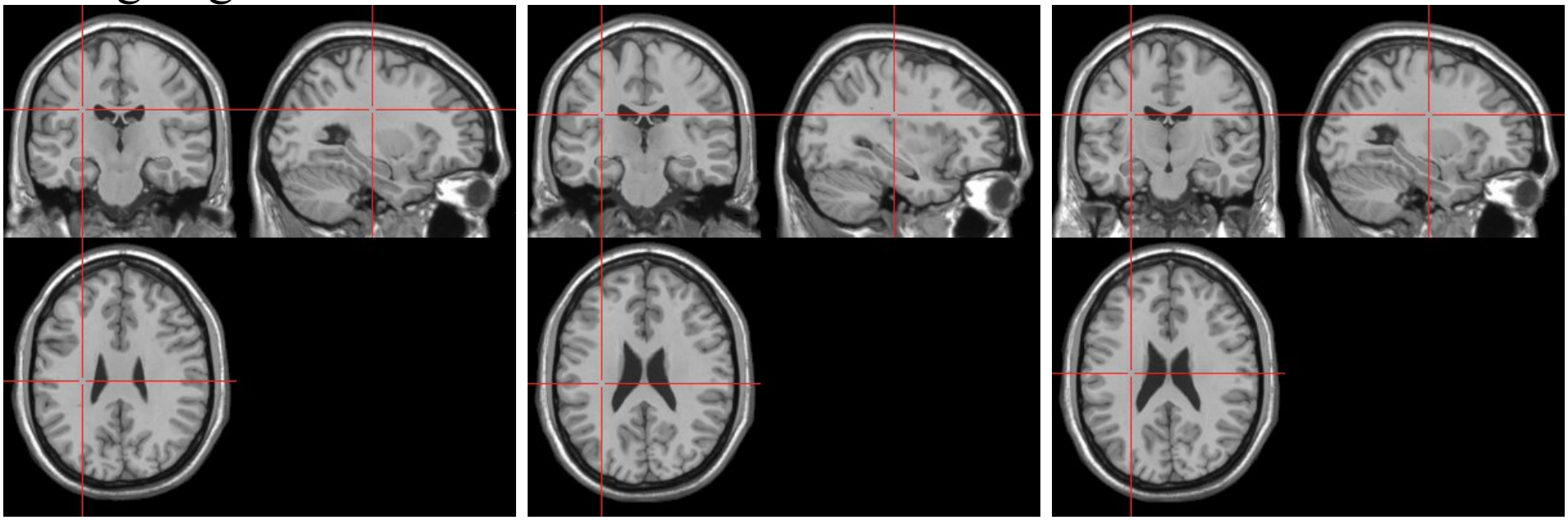
- Increased language lateralization
  - Requires fewer inter-hemisperic connections between language regions
- More efficient visual field integration
  - Requires fewer inter-hemisperic connections between visual regions



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

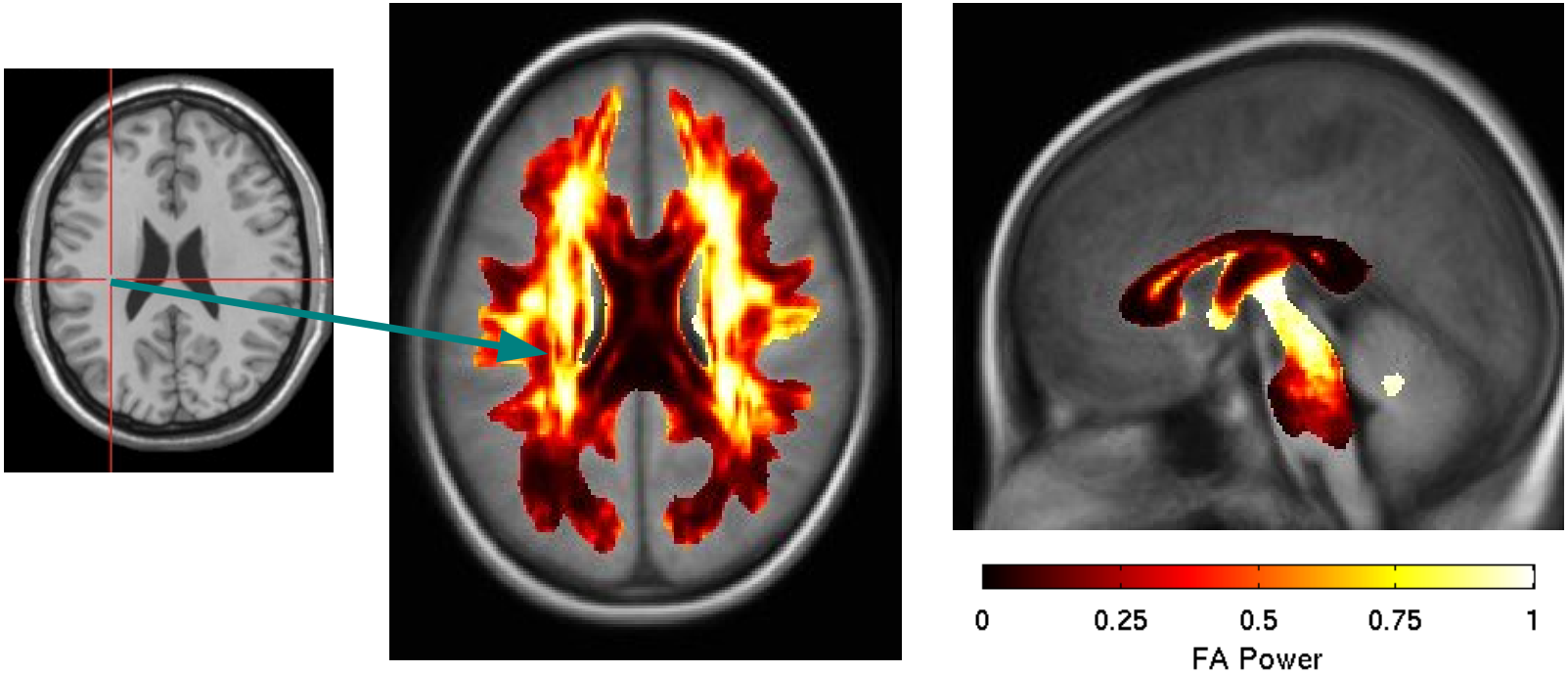


adults *children*

Some overlap in extent; voxels of maximal difference <1cm apart

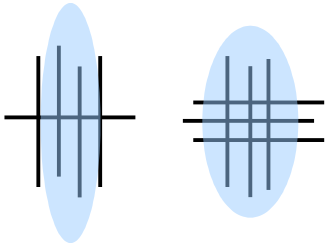
Why Previous Studies Did Not See FA Differences in CC

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



Unified Hypothesis

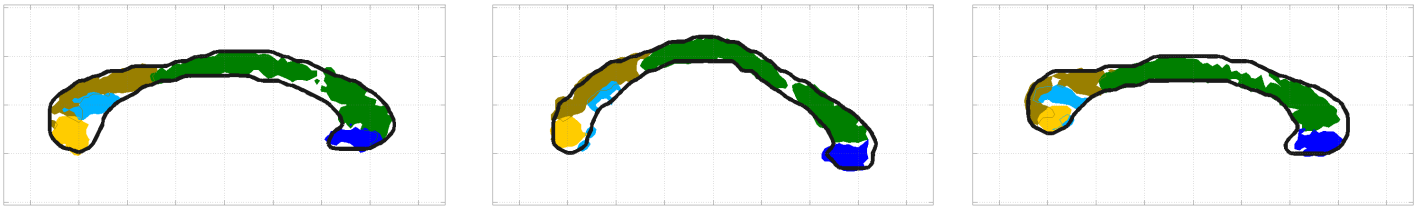
- More callosal connections in low readers:
  - Larger posterior CC (e.g. Rumsey et. al. 1996)
  - Higher FA in posterior CC pathway (this study)
  - Decreased FA in posterior corona radiata due to more crossing fibers
  - Increased functional symmetry (e.g. Simos et. al. 2000)



- 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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Thank you!