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# Microstructural Measures of the Developing Brain and it's Response to Learning: Evidence from Neuroimaging

Chris Clark
Imaging and Biophysics Unit
UCL Institute of Child Health

# Overview

Dyscalculia and the IPS

Some brief basics of diffusion MRI

Sexual dimorphisms: role of puberty

Tractography and advances in diffusion MRI

Graph theory and brain networks

Mapping the g ratio

Learning effects: what can be measured with qMRI?

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*Brain* (2001), **124,** 1701–1707

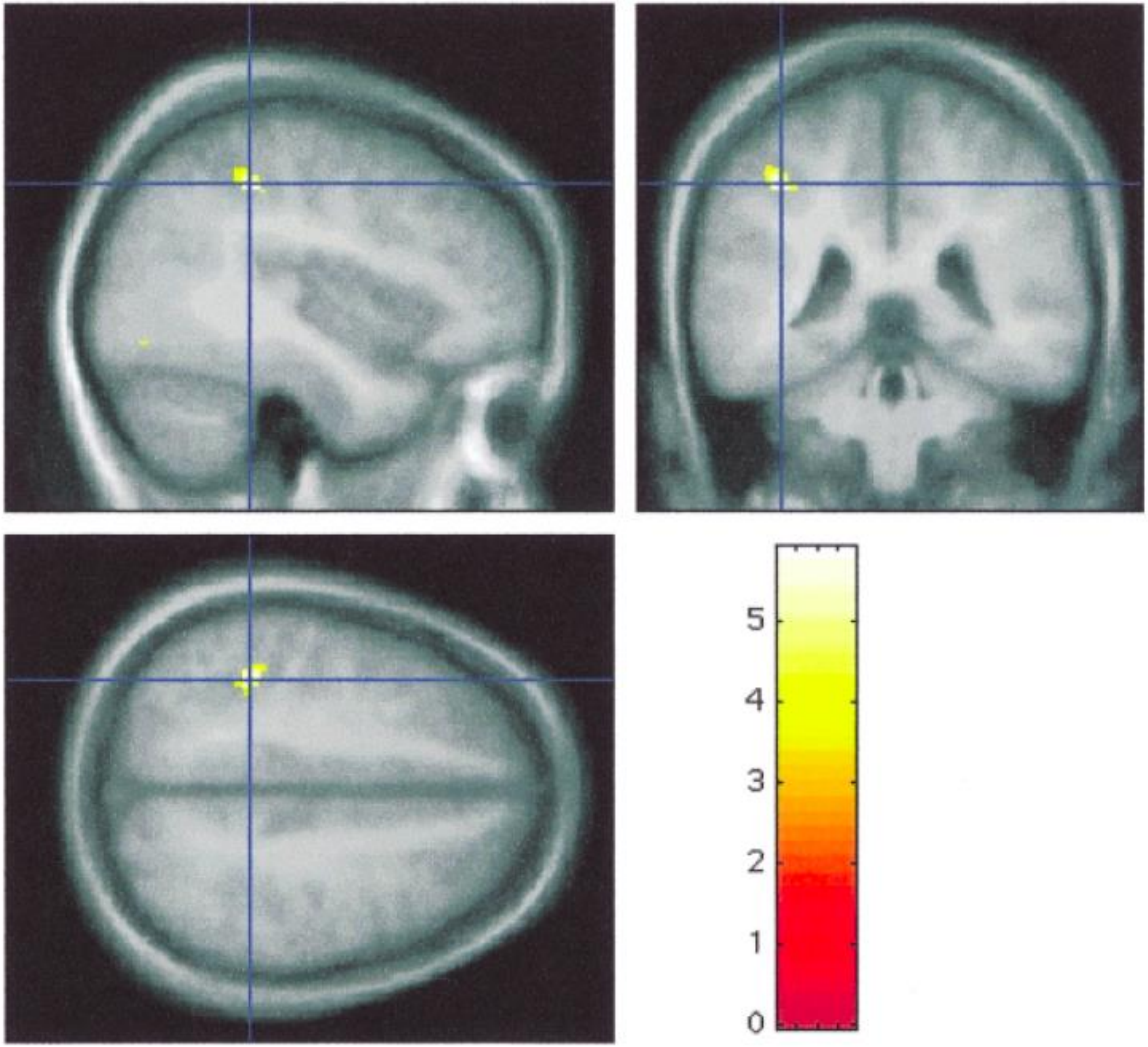
# Calculation difficulties in children of very low birthweight

## A neural correlate

E. B. Isaacs,[1] C. J. Edmonds,[1] A. Lucas[1] and D. G. Gadian[2]

[1]*MRC Childhood Nutrition Research Centre and*
[2]*Radiology and Physics Unit, Institute of Child Health, University College London, 30 Guilford Street, London WC1N 1EH, UK*

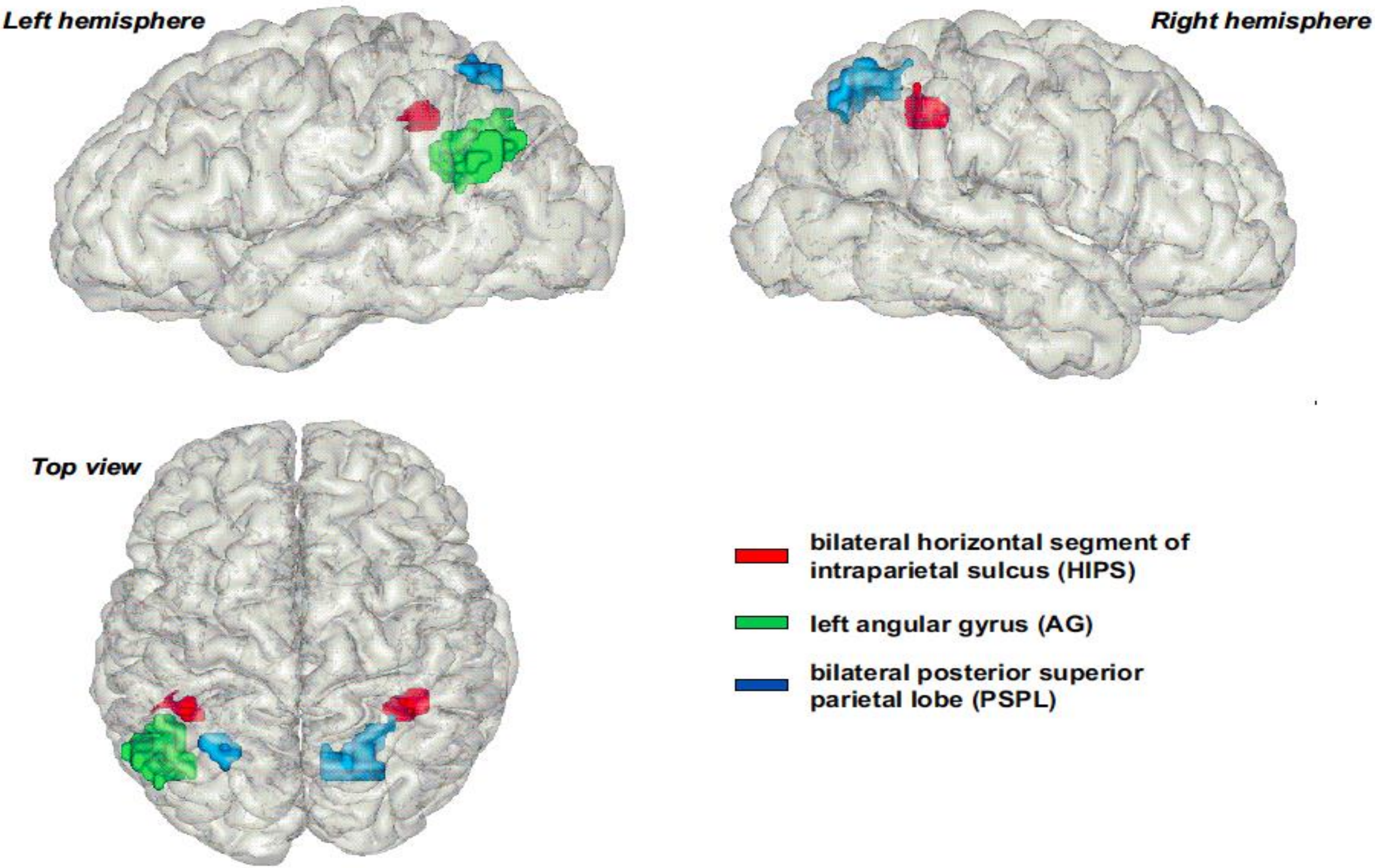
*Correspondence to: Dr E. B. Isaacs, MRC Childhood Nutrition Research Centre, Institute of Child Health, University College London, 30 Guilford Street, London WC1N 1EH, UK*
*E-mail: E.Isaacs@ich.ucl.ac.uk*


5
4
3
2
1
0

COGNITIVE NEUROPSYCHOLOGY, 2003, 20 (3/4/5/6), 487–506

# THREE PARIETAL CIRCUITS FOR NUMBER PROCESSING

Stanislas Dehaene, Manuela Piazza, Philippe Pinel, and Laurent Cohen
*INSERM-CEA, Service Hospitalier Frédéric Joliot, Orsay, France*


Left hemisphere
Right hemisphere
Top view
bilateral horizontal segment of intraparietal sulcus (HIPS)
left angular gyrus (AG)
bilateral posterior superior parietal lobe (PSPL)

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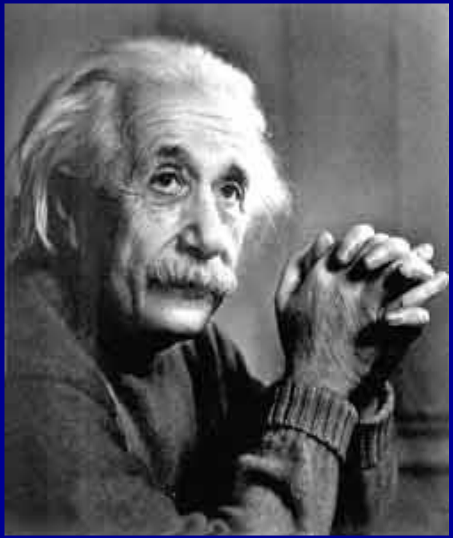
# Diffusion Coefficient

Diffusion is a time dependent process

Molecules diffuse further from their starting point as time increases

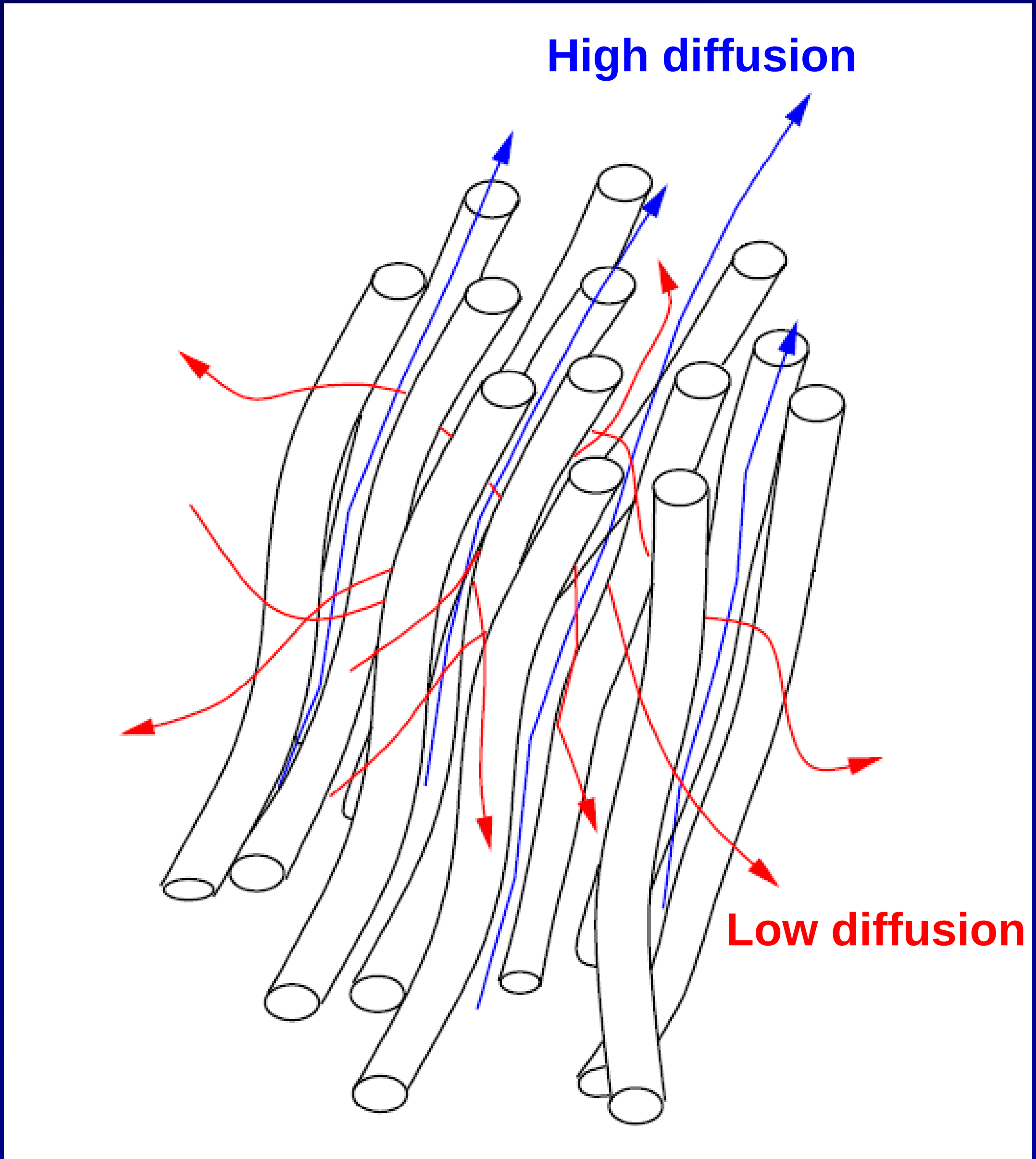
$$\langle r^2 \rangle = 6Dt$$

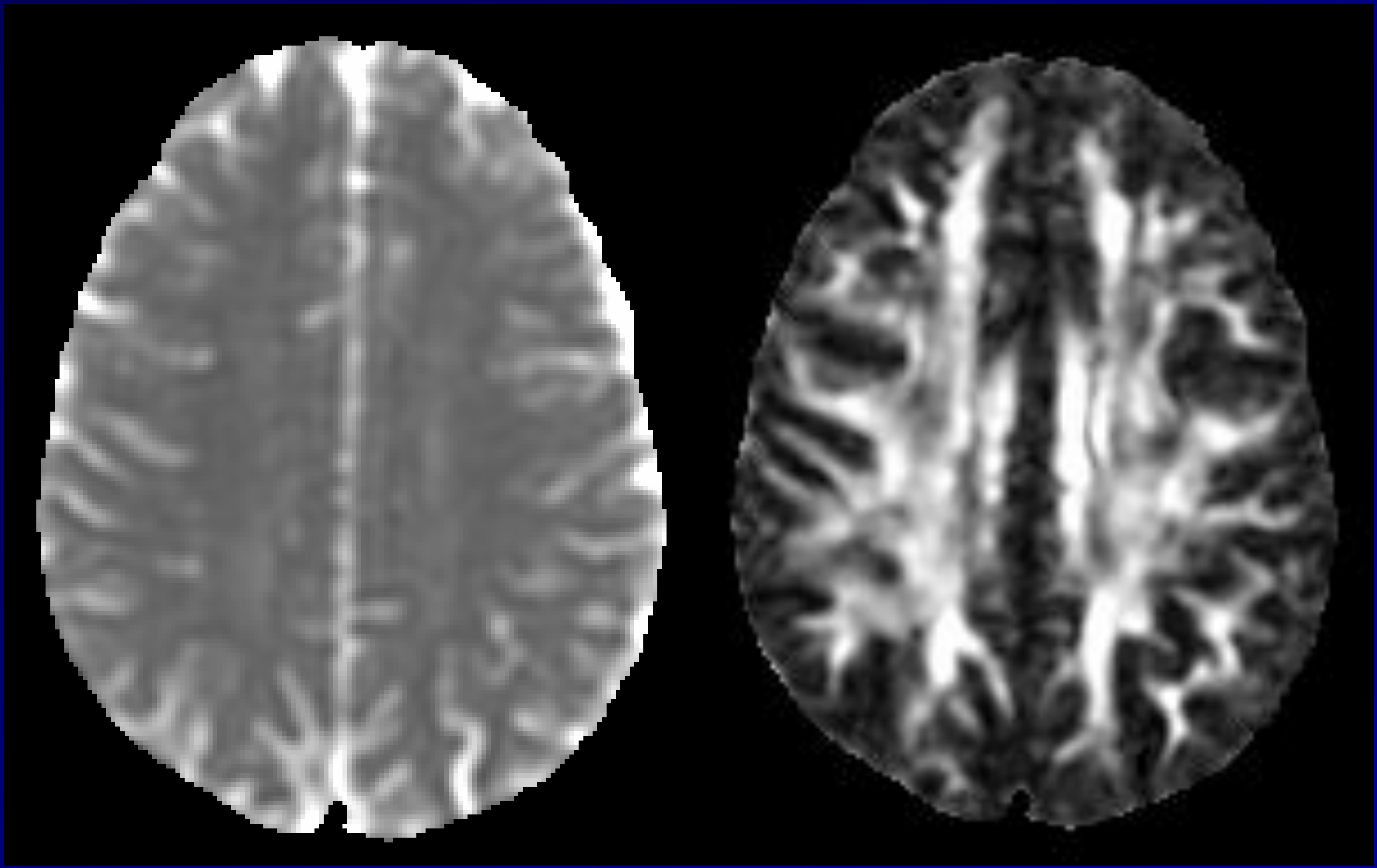


# Diffusion is sensitive to tissue structure

Diffusion is lower (slower) in tissue than free water

Due to presence of cell membranes and structures


High diffusion
Low diffusion



Mean diffusivity (MD)

Fractional anisotropy (FA)

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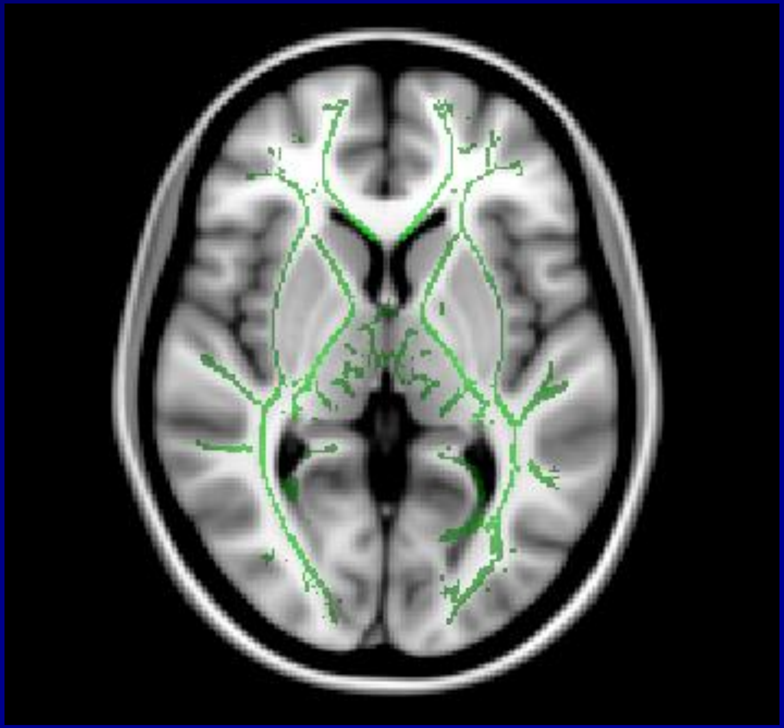
# Tract-Based Spatial Statistics (TBSS)

Pros:

- Voxel-based analysis (local differences)
- No need for smoothing
- Reduces multiple comparisons problem

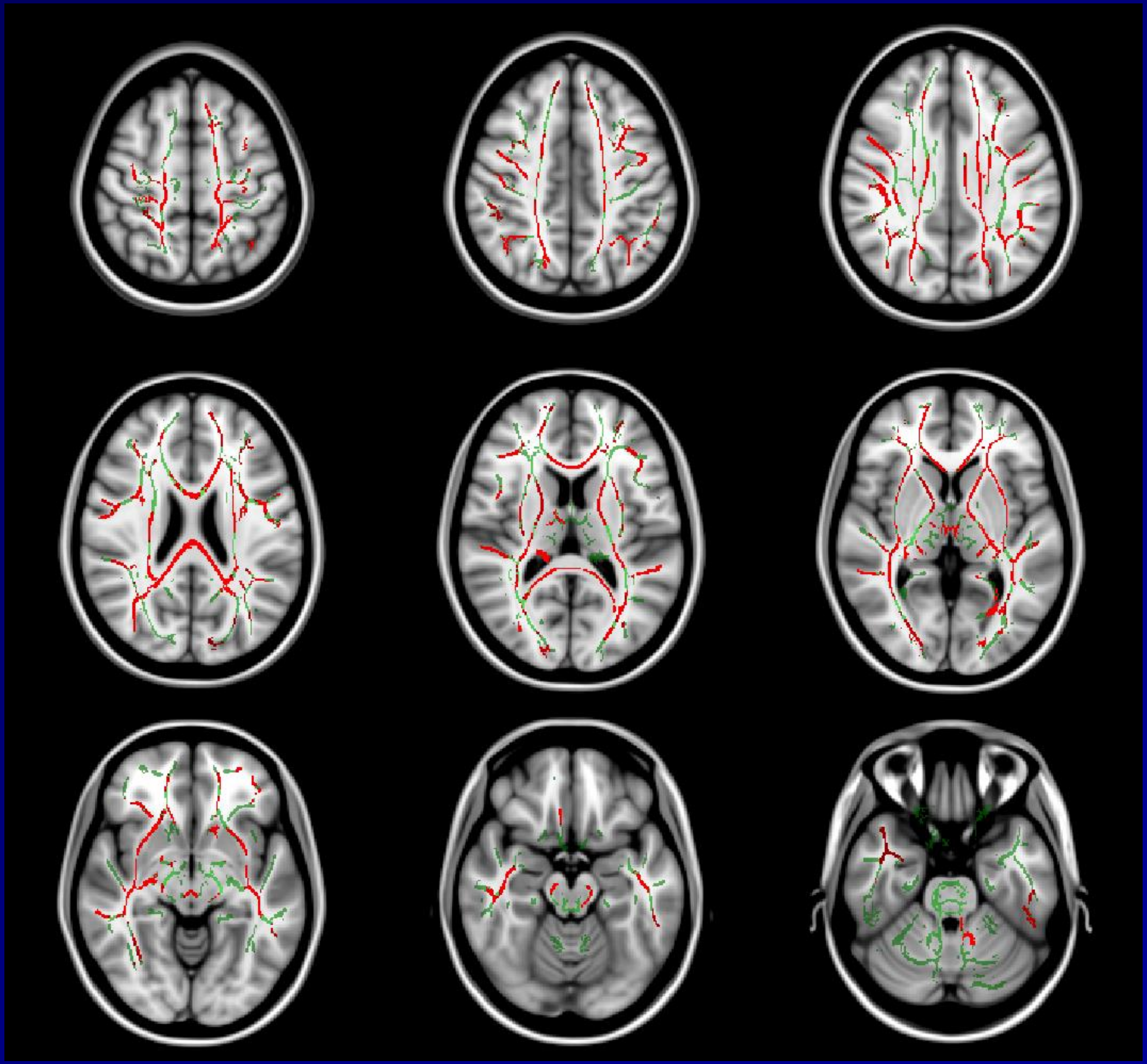
Cons:

- Only looks at centre of white-matter tracts (lots of voxels excluded)
- Not focussing on individual tracts



Smith et al, NeuroImage 31:1487-1505 (2006)

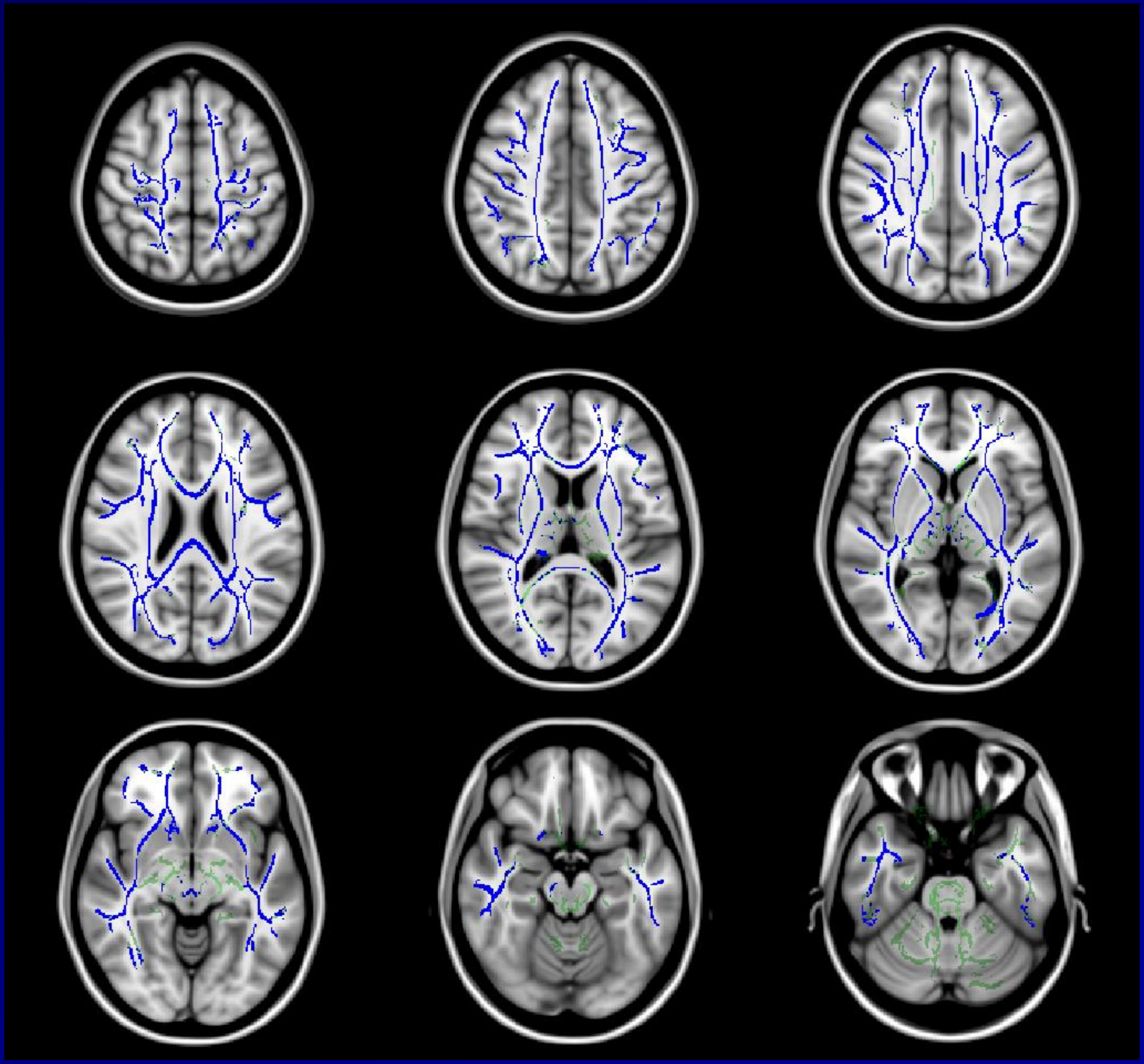
# TBSS results (FA – boys, positive correlation)



$p<0.05$

Kiran Seunarine et al

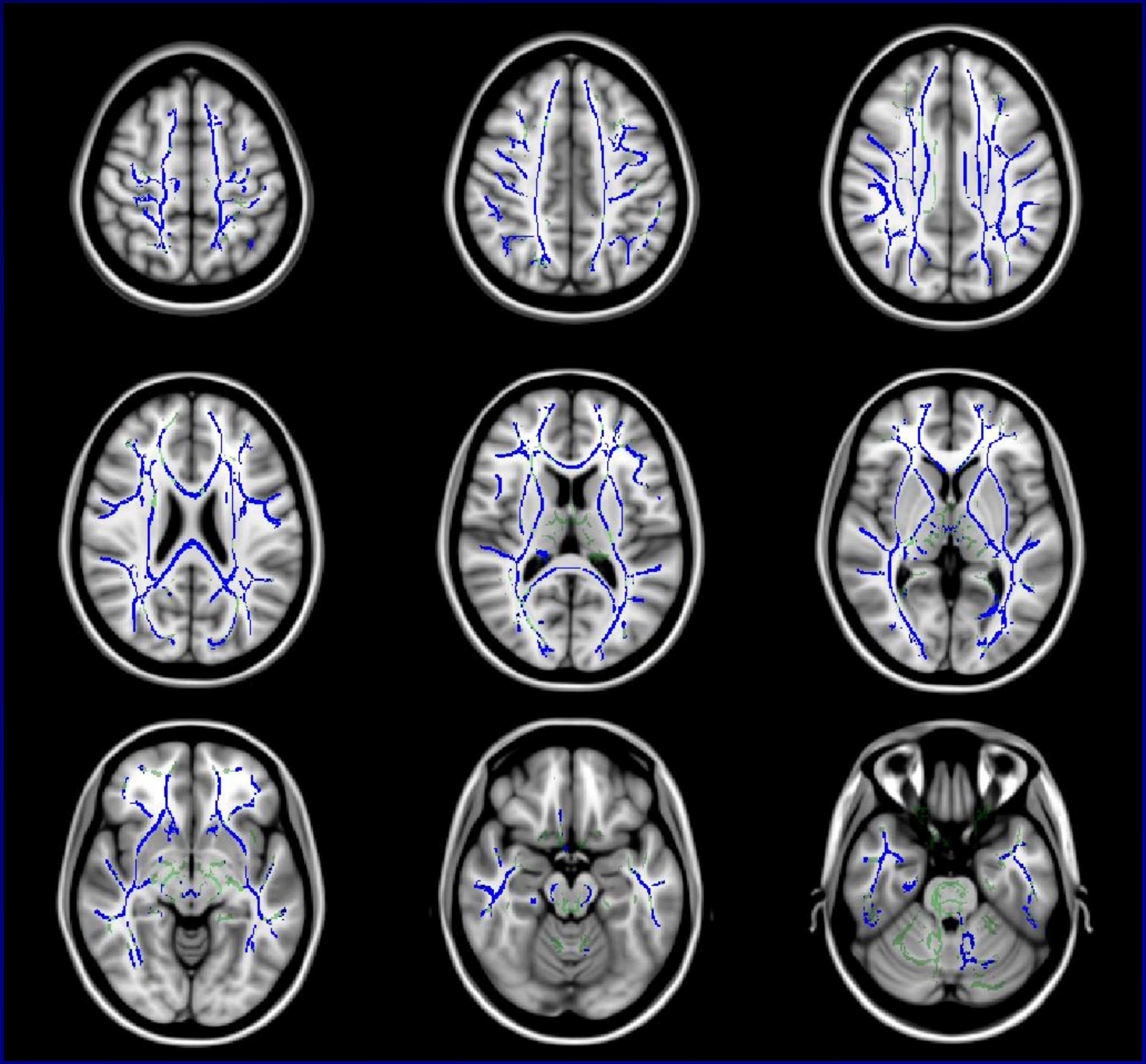
# TBSS results (MD – boys, negative correlation)



$p<0.05$

Kiran Seunarine et al

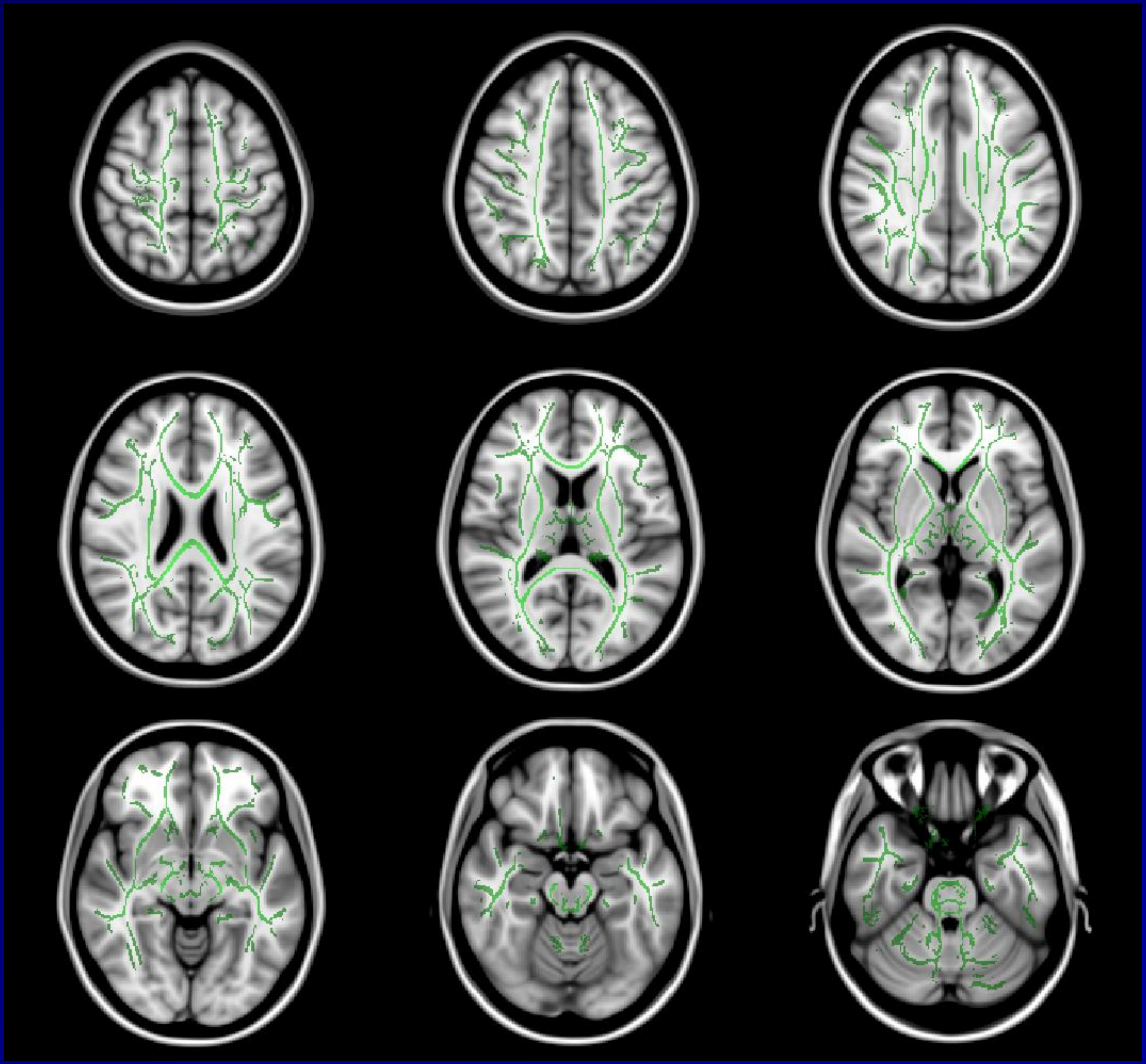
# TBSS results ($\lambda_{radial}$ – boys, negative correlation)



$p<0.05$

Kiran Seunarine et al

# TBSS results (girls FA, MD – no correlation)



p<0.05

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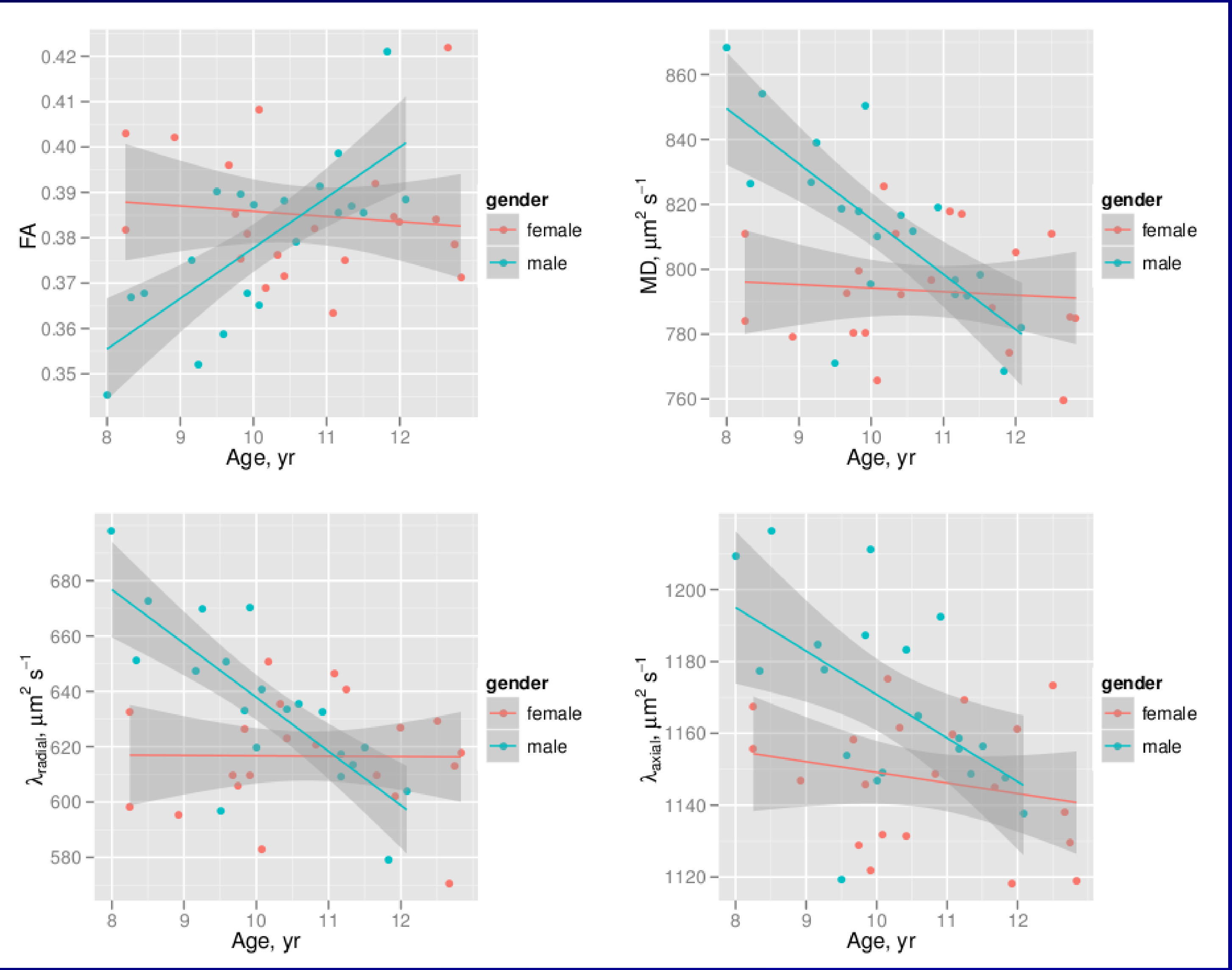
# Gender differences in white matter development



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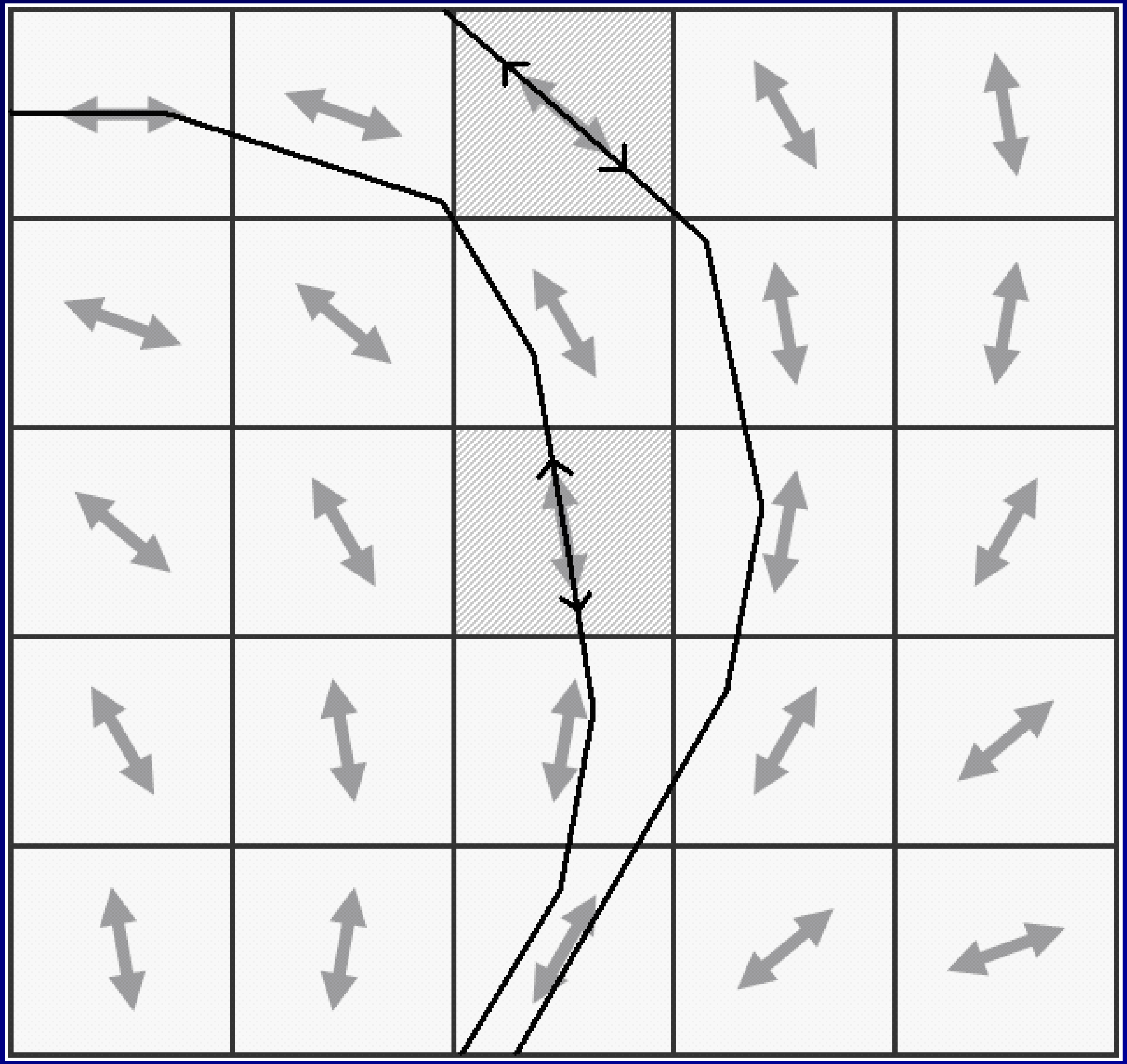
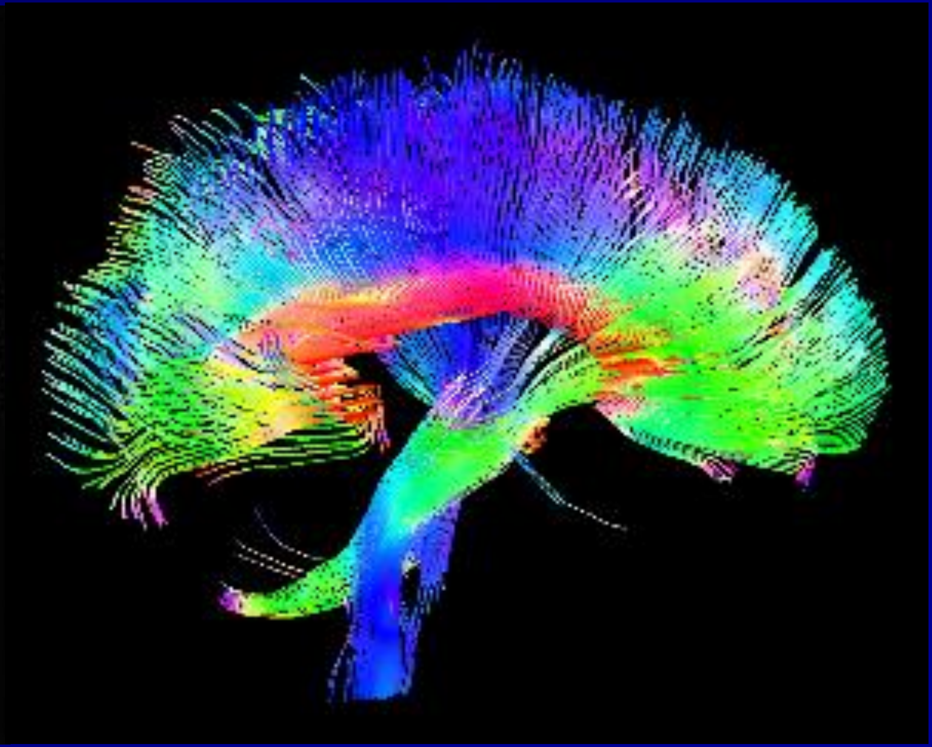
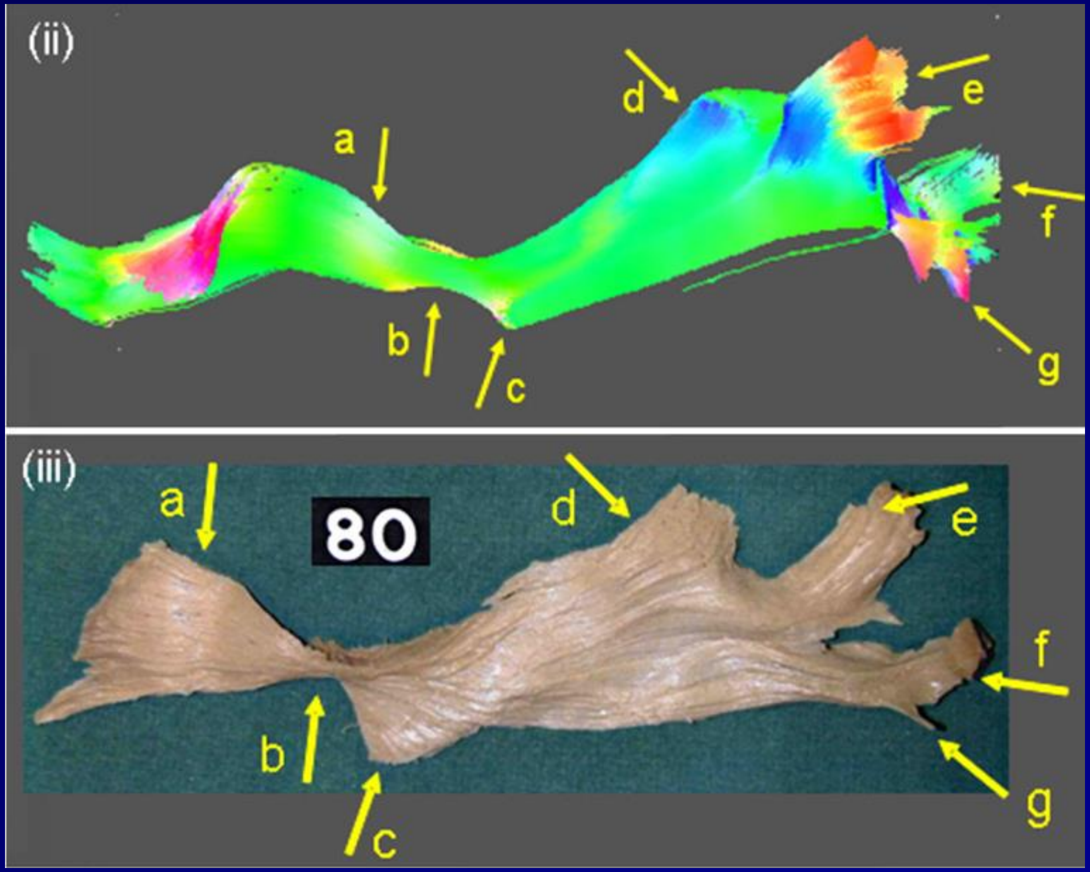
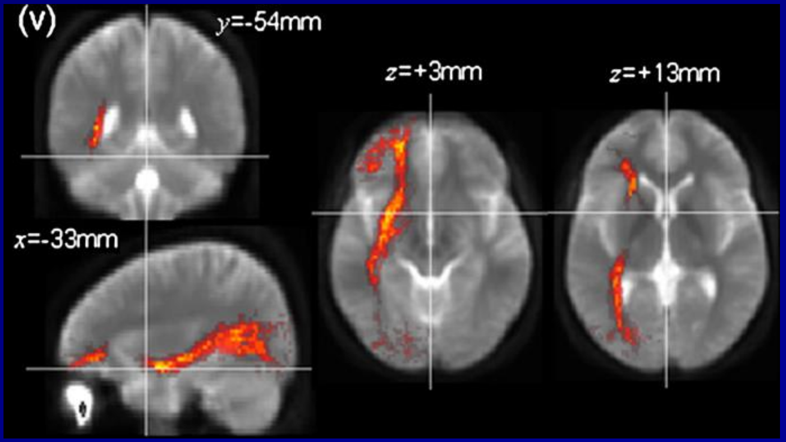
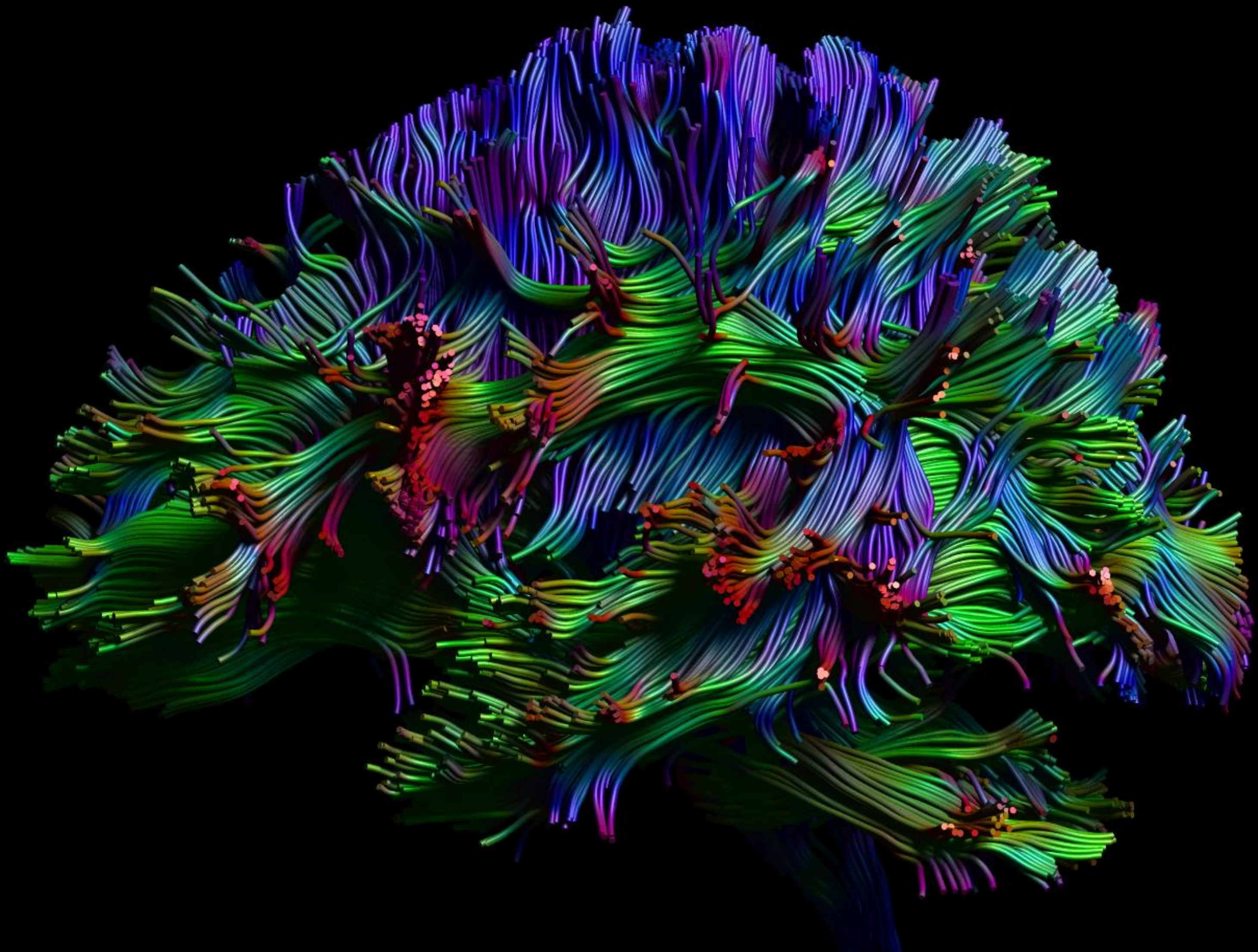


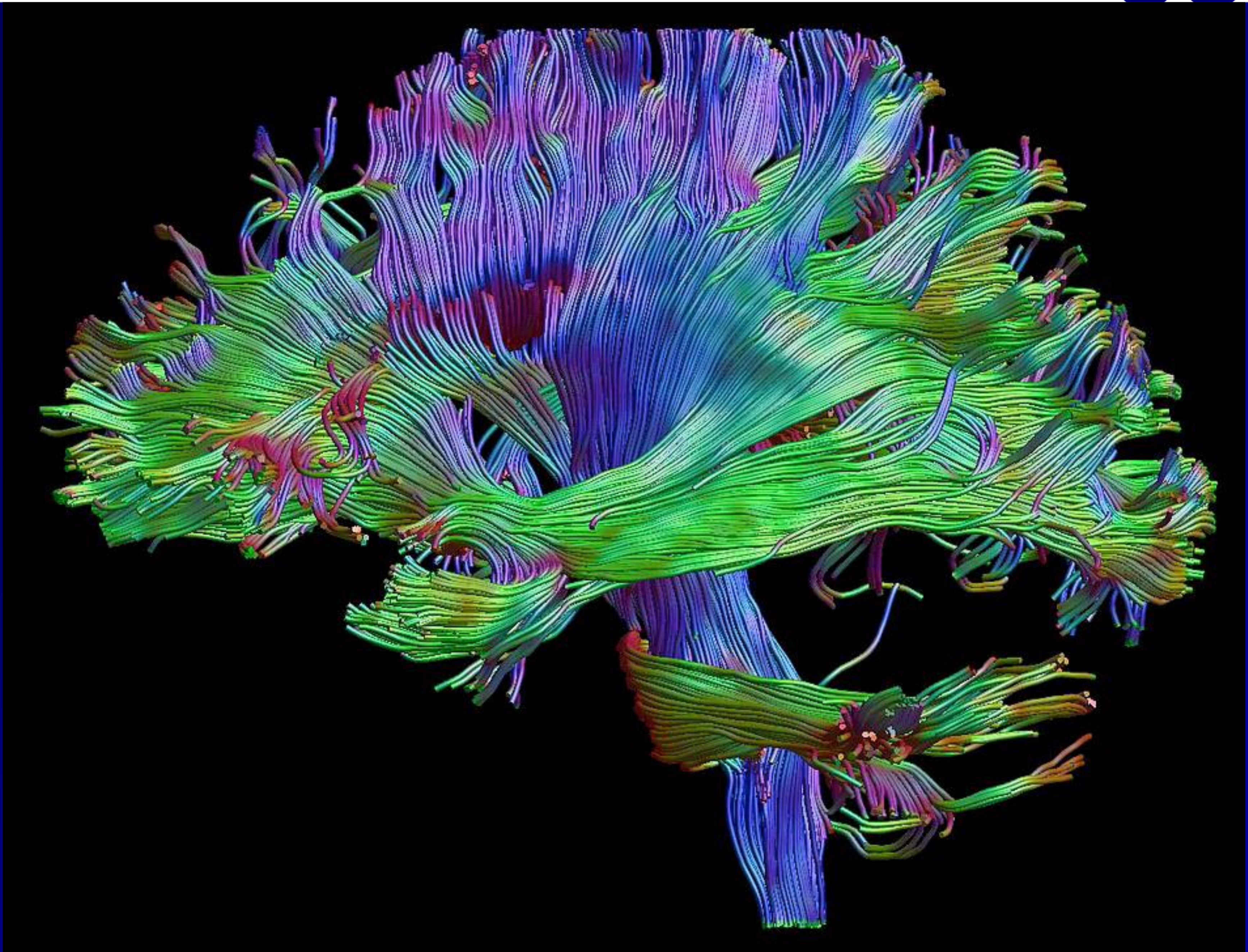


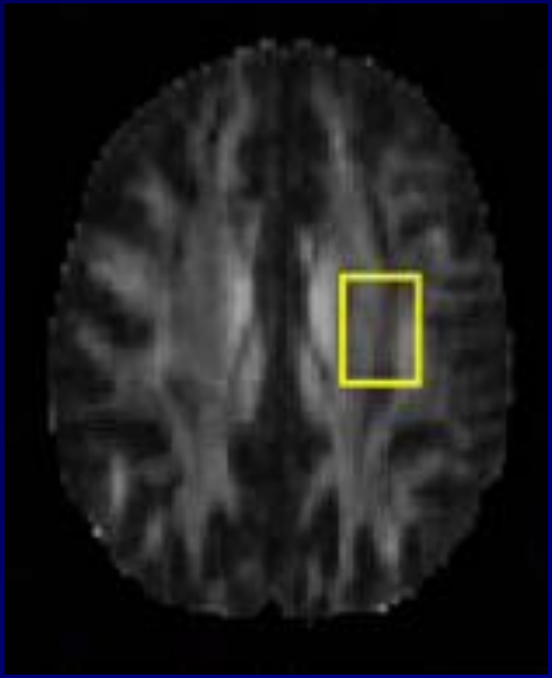


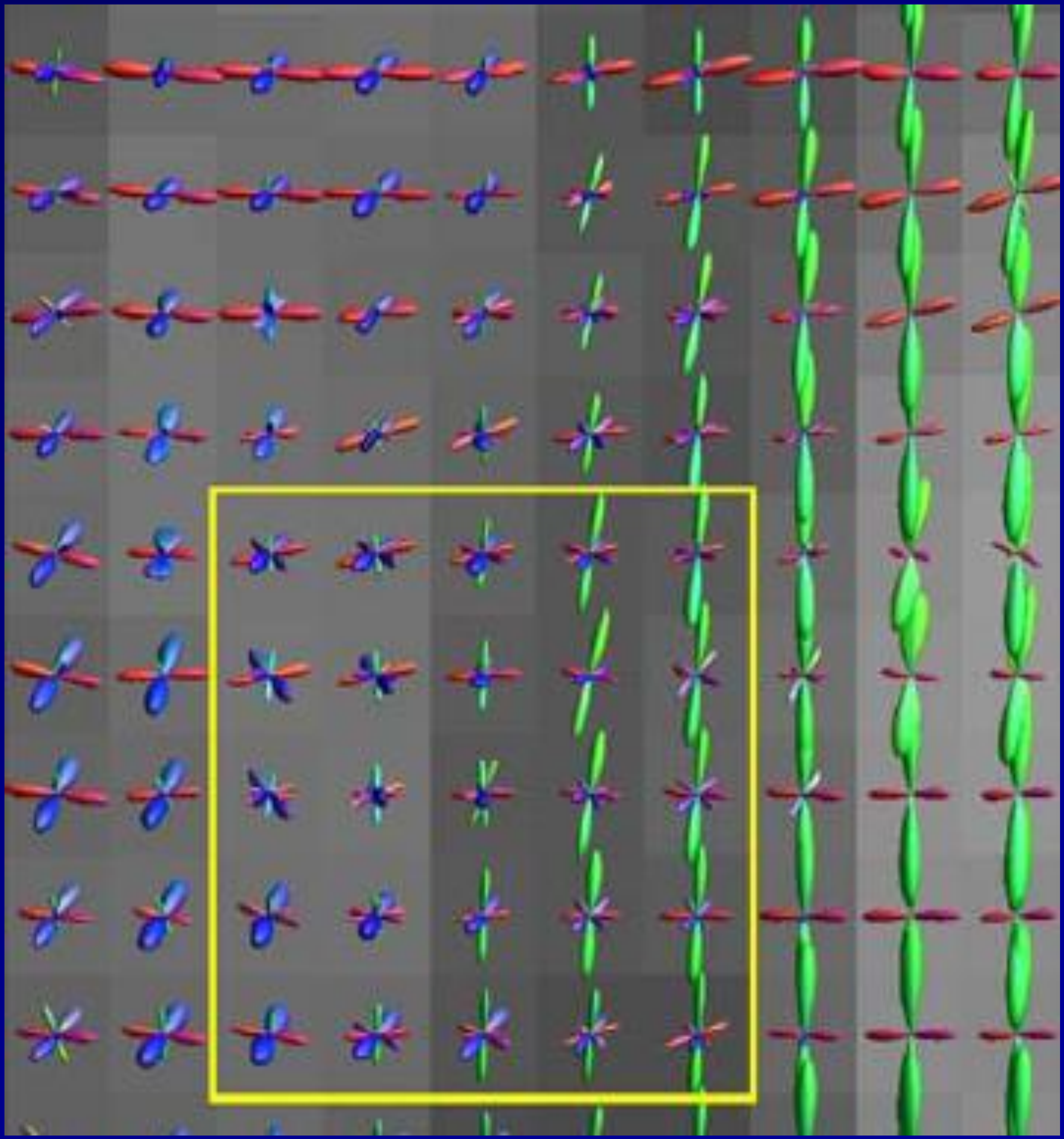




Lawes et al Neuroimage 2008

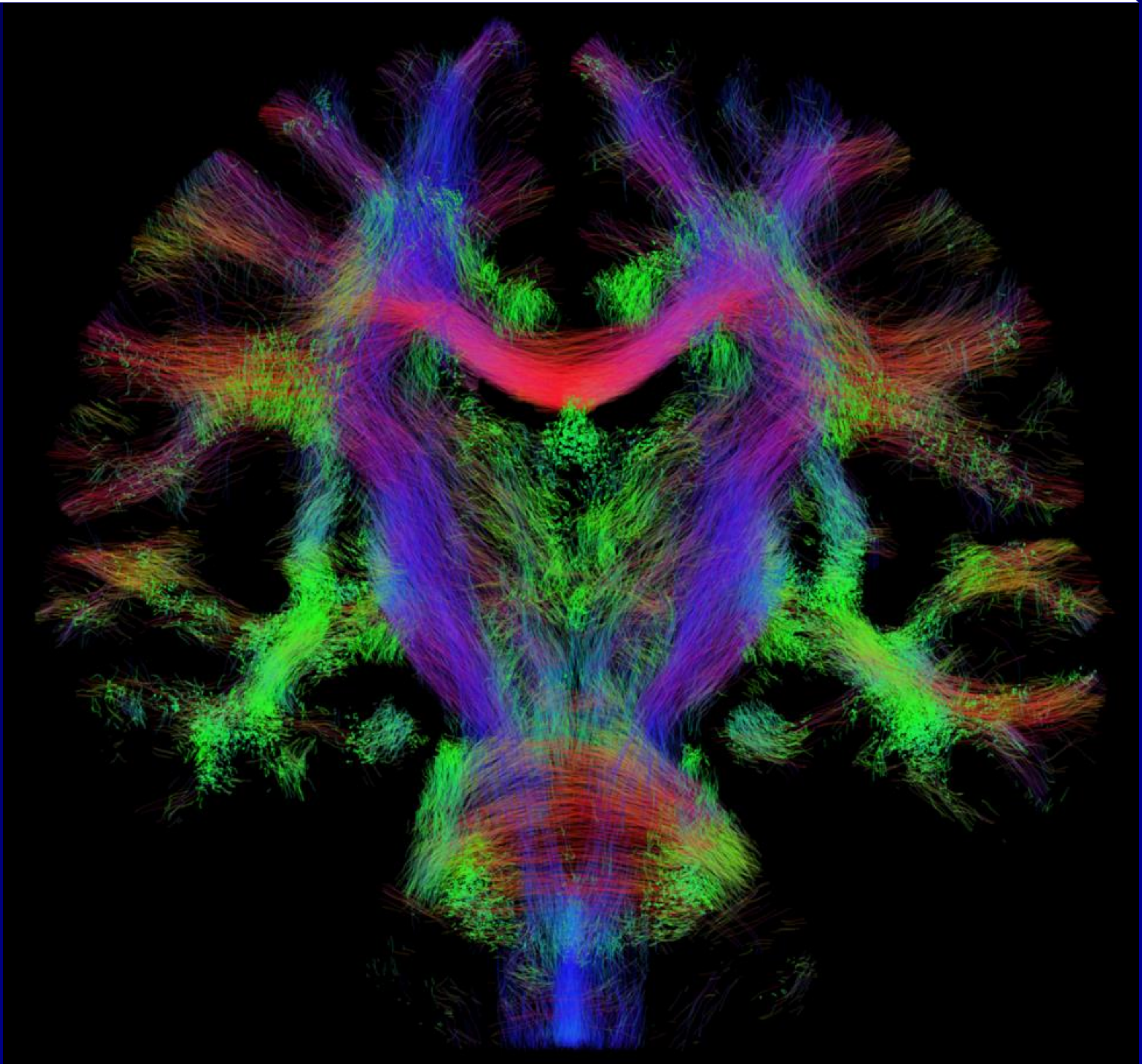


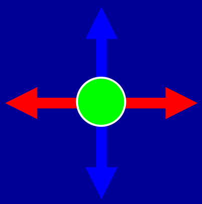


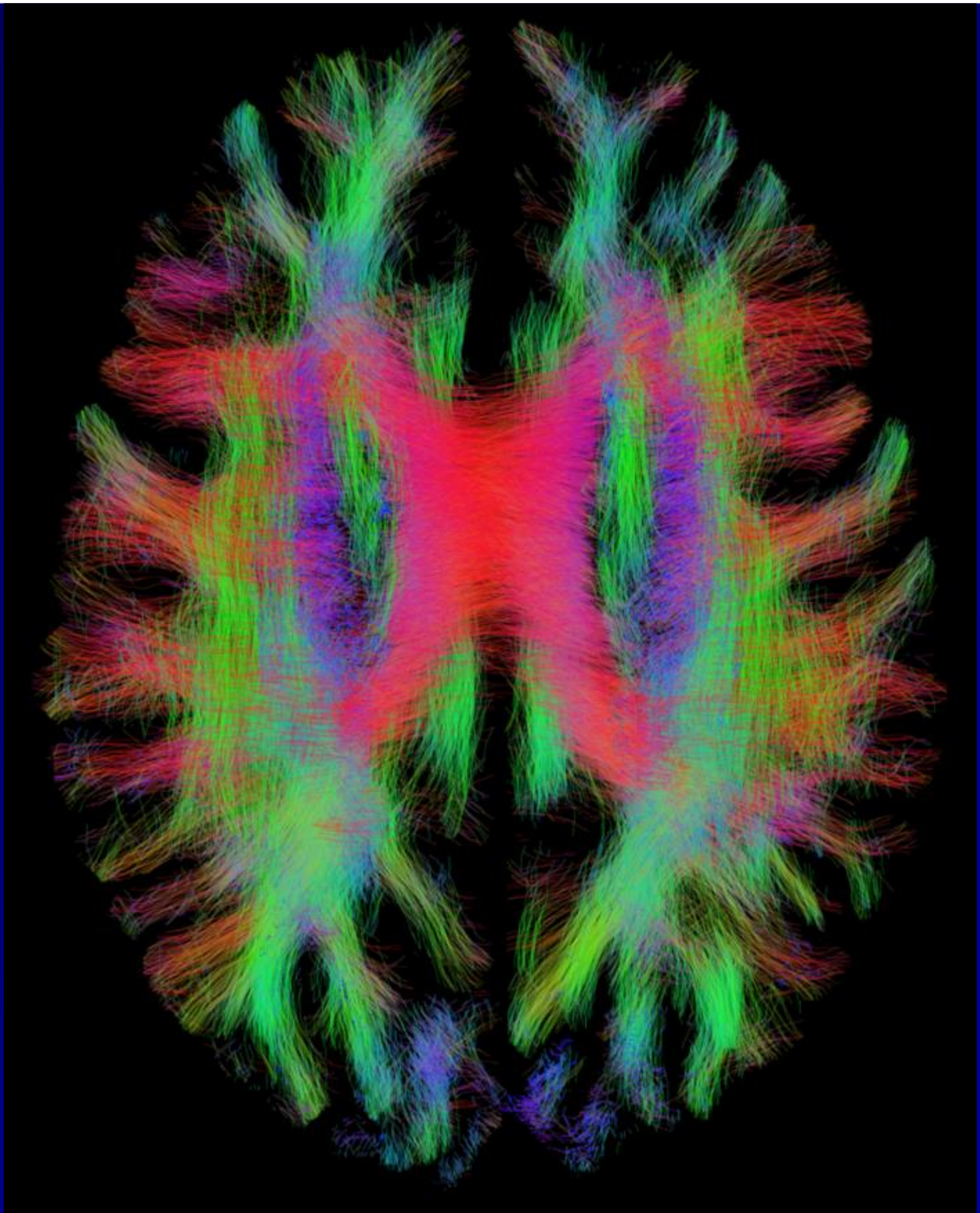


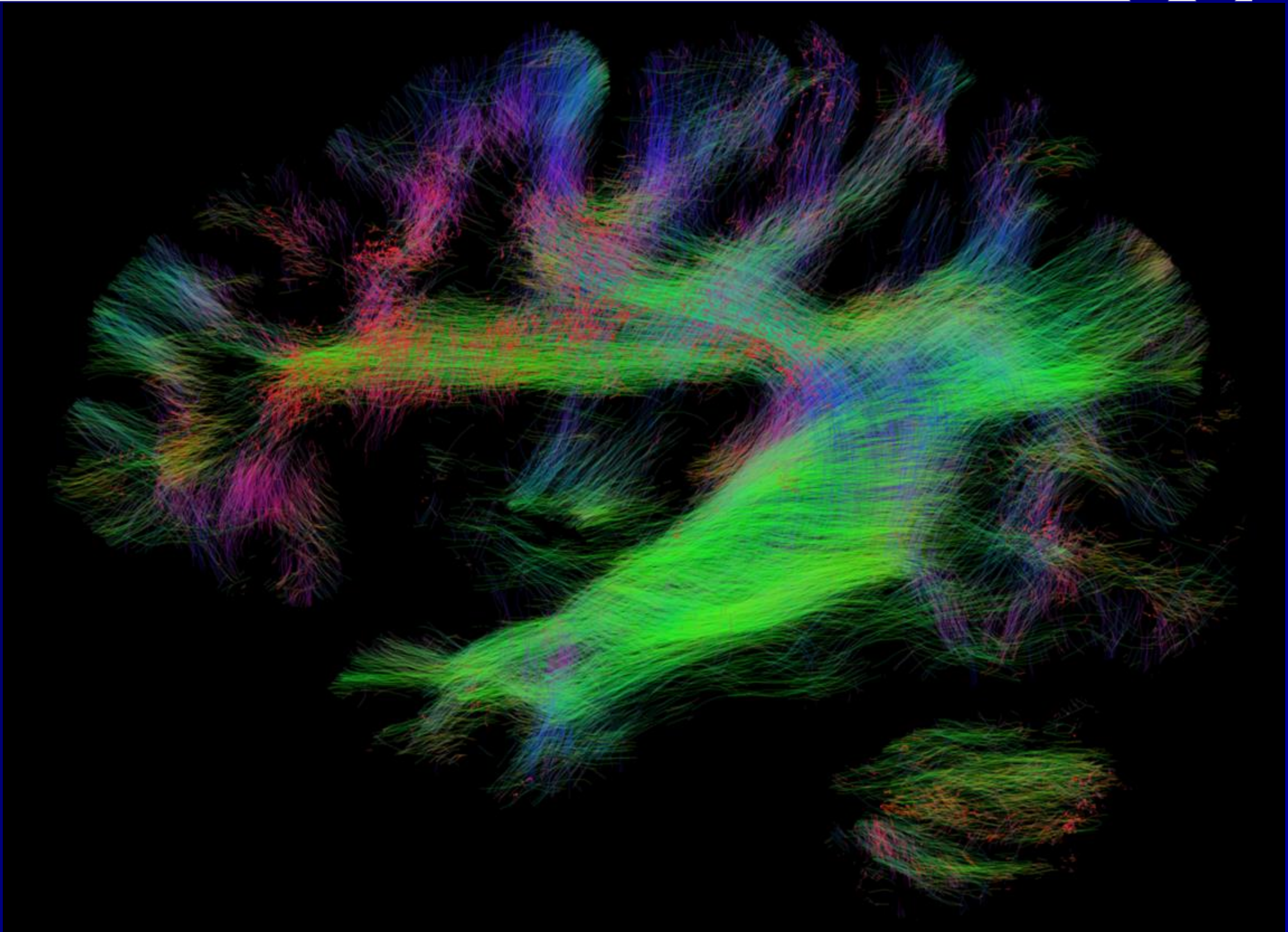


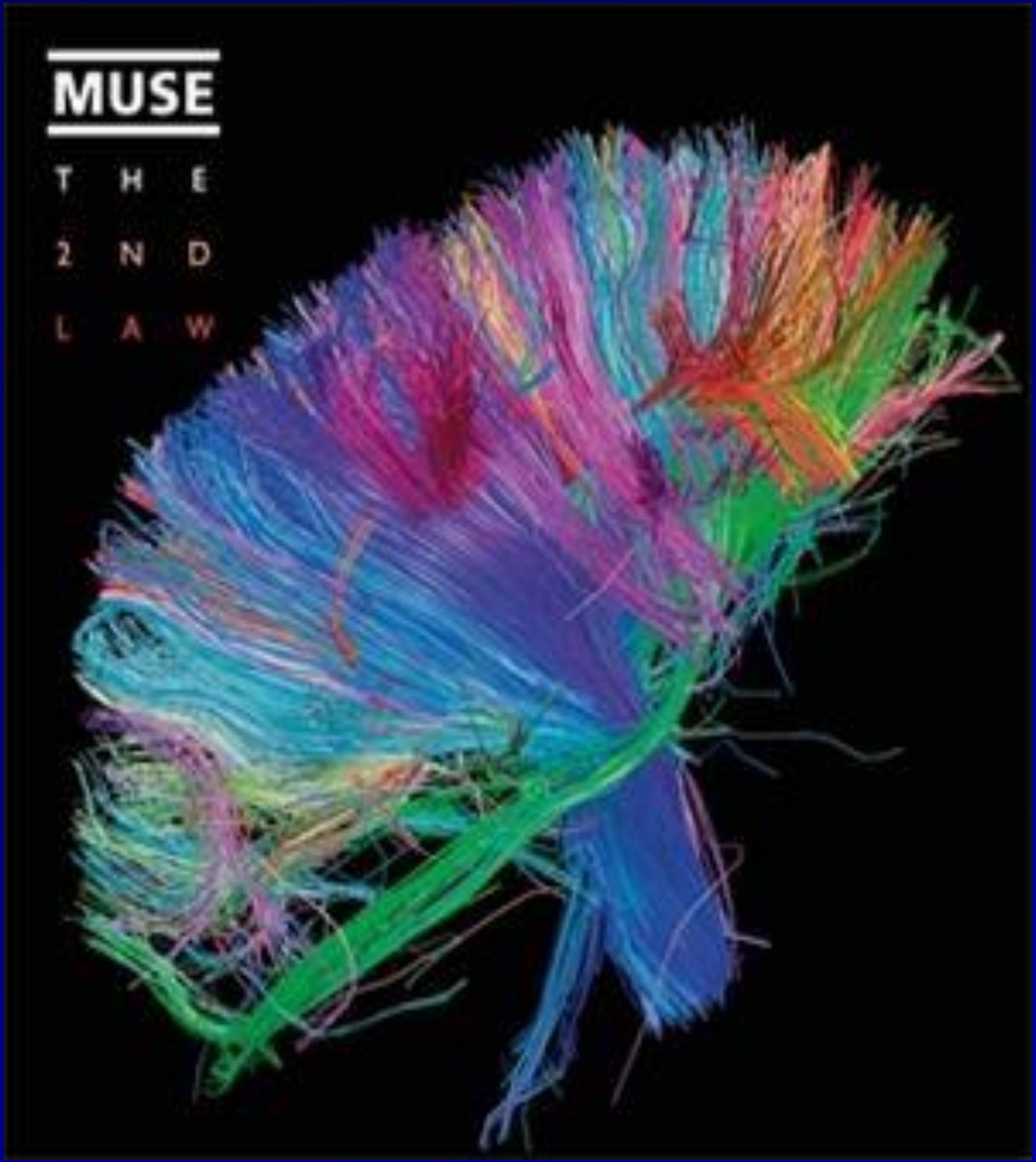
Tournier et al Neuroimage 2007







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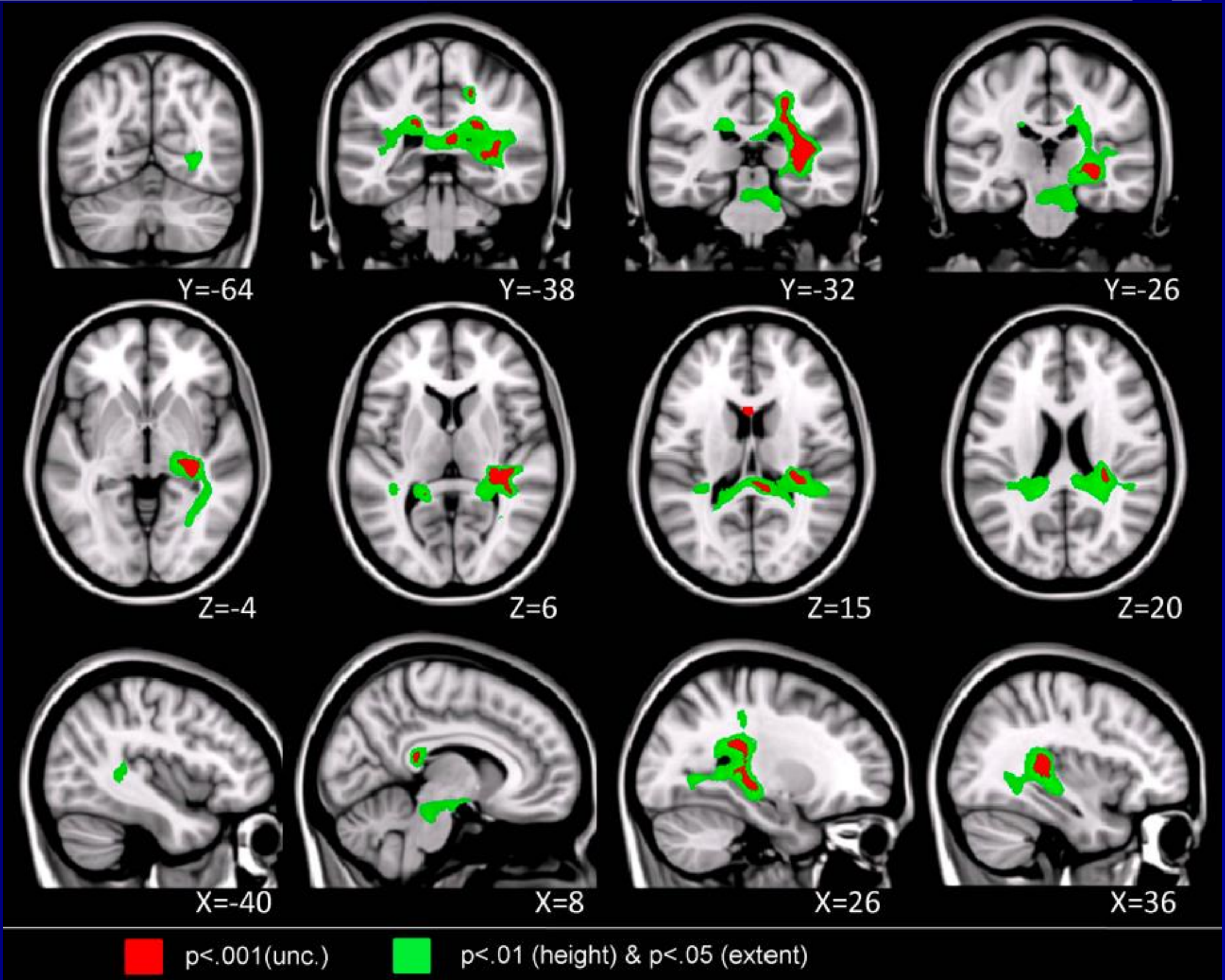
frontiers in
HUMAN NEUROSCIENCE

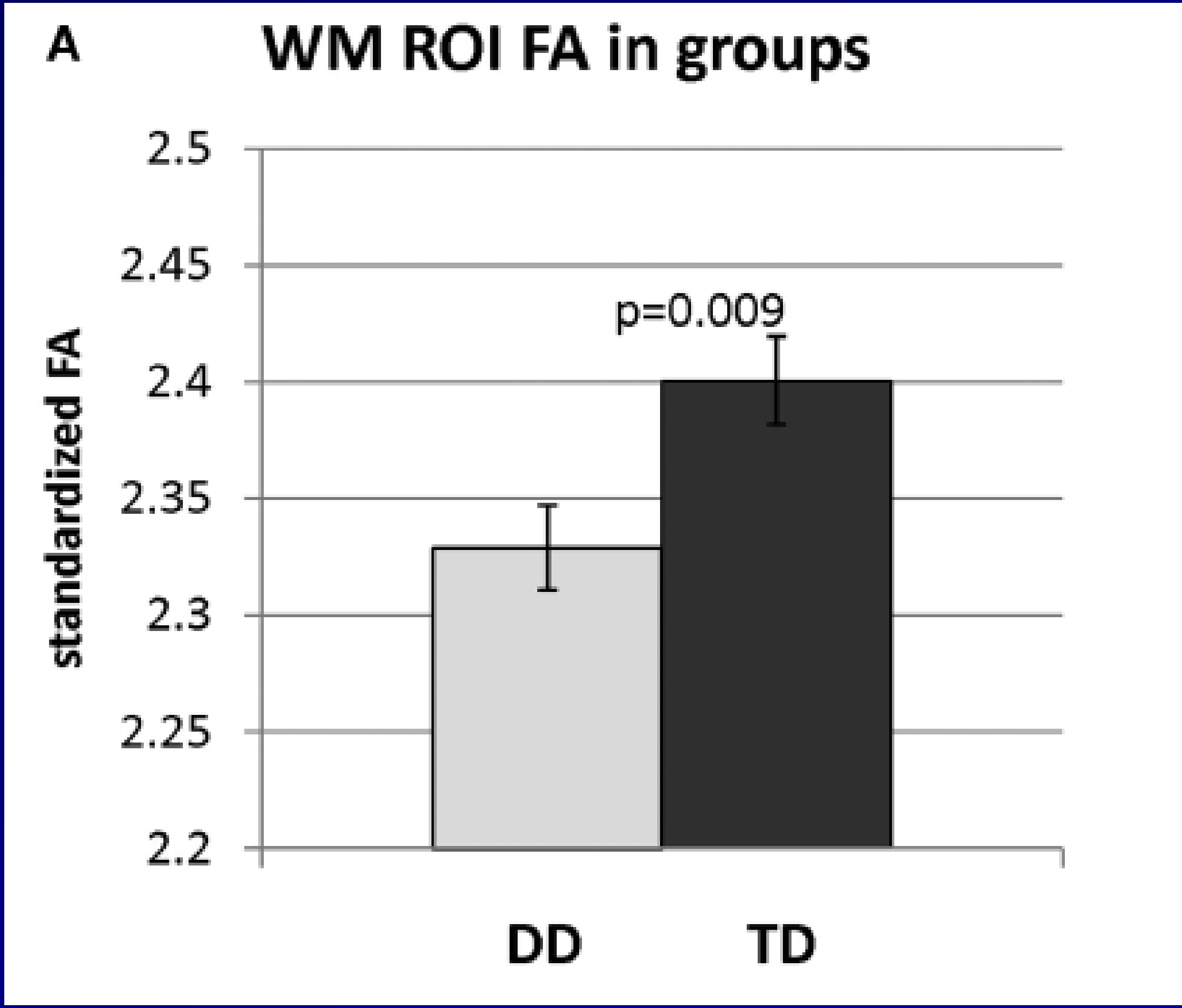
ORIGINAL RESEARCH ARTICLE
published: 24 November 2009
doi: 10.3389/neuro.09.051.2009

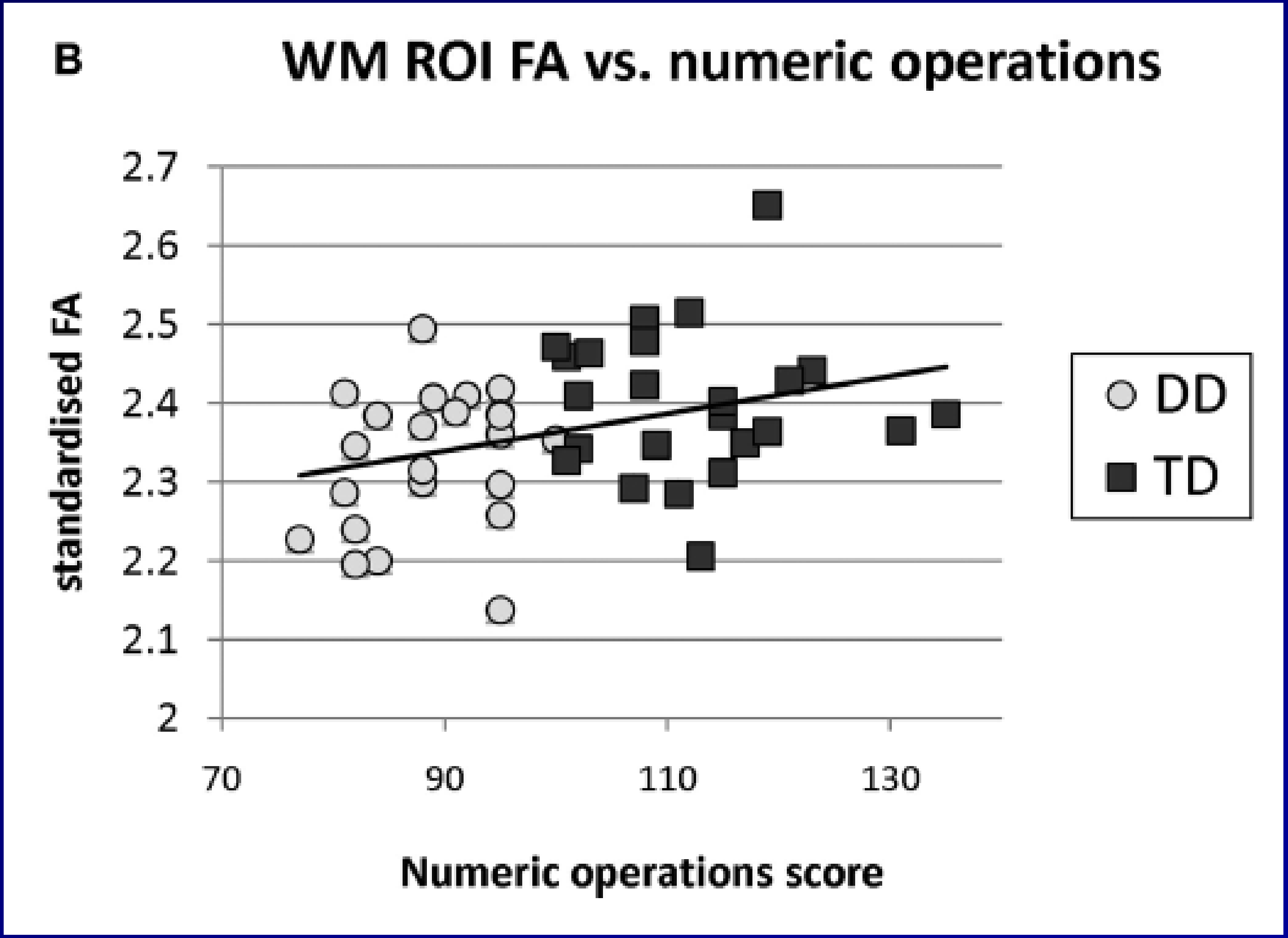
# Neuroanatomical correlates of developmental dyscalculia: combined evidence from morphometry and tractography

***Elena Rykhlevskaia[1,2], Lucina Q. Uddin[1], Leeza Kondos[1] and Vinod Menon[1,3,4]****

[1] *Department of Psychiatry and Behavioral Sciences, Stanford University, CA, USA*
[2] *Department of Psychology, Stanford University, CA, USA*
[3] *Program in Neuroscience, Stanford University, CA, USA*
[4] *Symbolic Systems Program, Stanford University, CA, USA*


Y=-64
Y=-38
Y=-32
Y=-26
Z=-4
Z=6
Z=15
Z=20
X=-40
X=8
X=26
X=36
p<.001(unc.)
p<.01 (height) & p<.05 (extent)


A
WM ROI FA in groups
standardized FA
2.5
2.45
2.4
2.35
2.3
2.25
2.2
p=0.009
DD
TD


B
WM ROI FA vs. numeric operations
standardised FA
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2
70
90
110
130
Numeric operations score
DD
TD

# Limitations of FA and some ways forward

Use more advanced models of diffusion for tractography

However, DTI parameters still the mainstay and reported in tracts

Suffer from lack of specificity

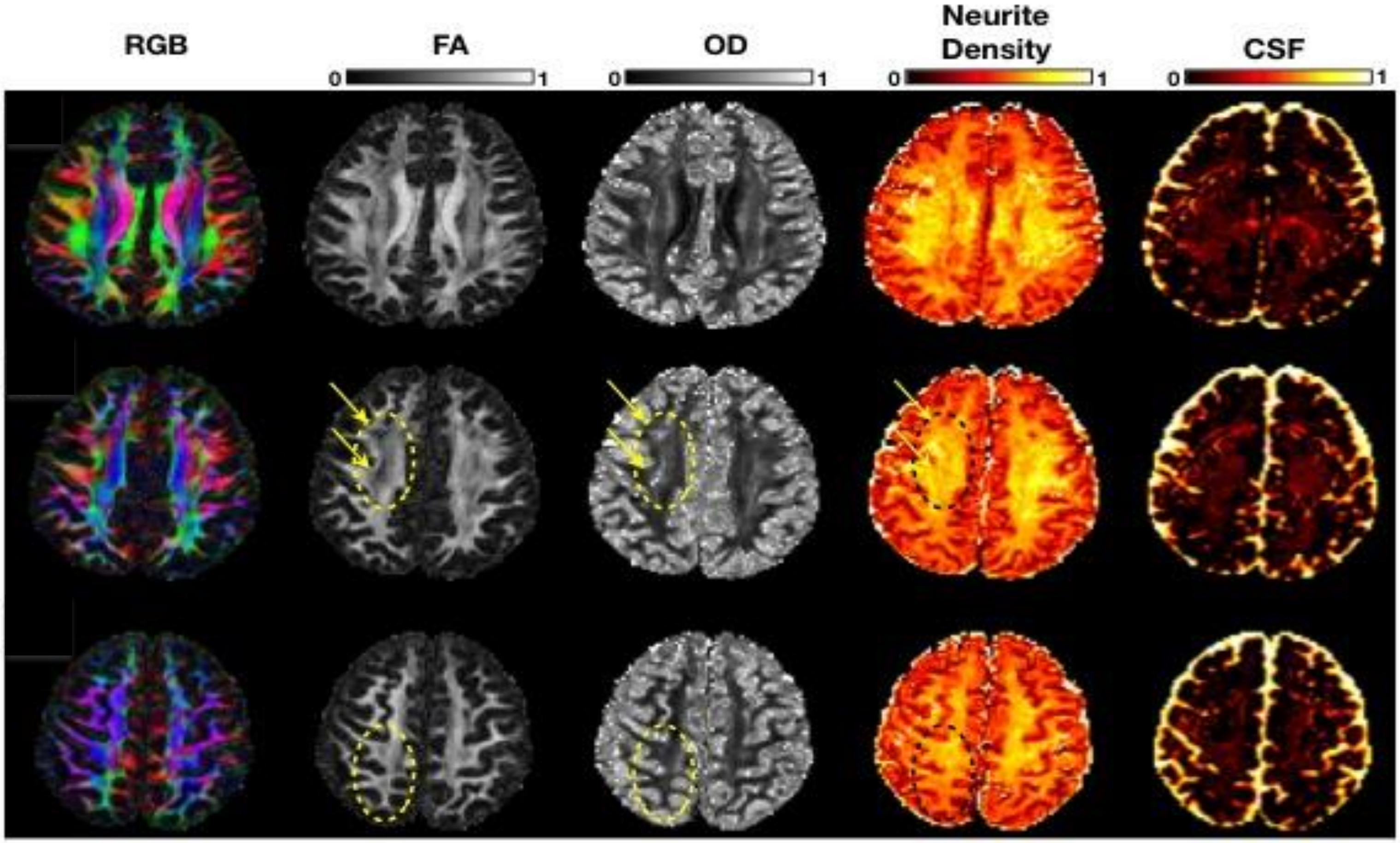
For example FA affected by both axon density/diameter and dispersion

More sophisticated models available

Based on multi-compartmentation

Note: more complex models require more data!

# Zhang et al Neuroimage 2012




Maps of FA and NODDI estimates: Orientation Dispersion (OD), Neurite Density, and CSF fraction. Arrows highlight areas where disentangling the two main factors contributing to FA provides more specific information about the underlying tissue.

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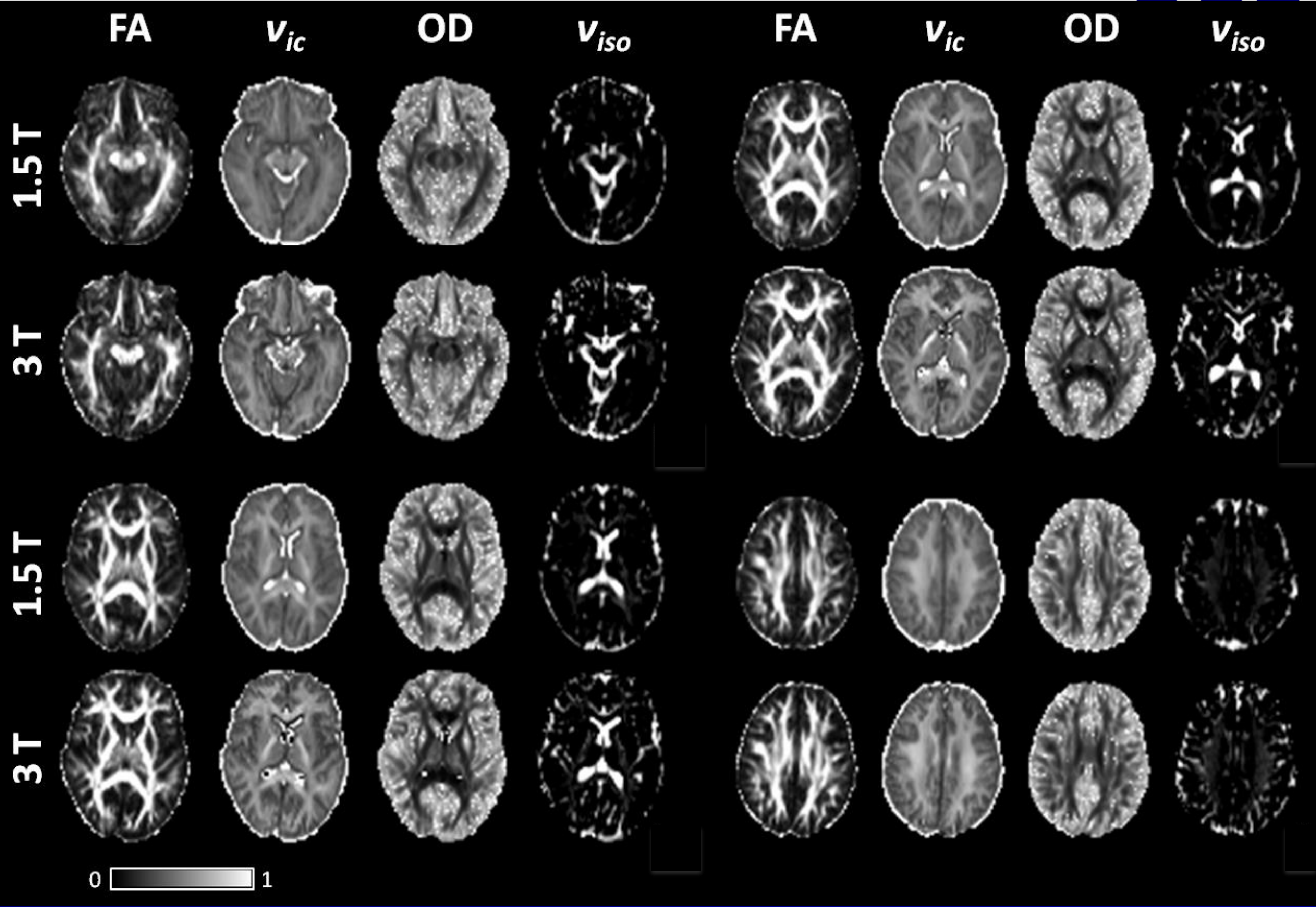

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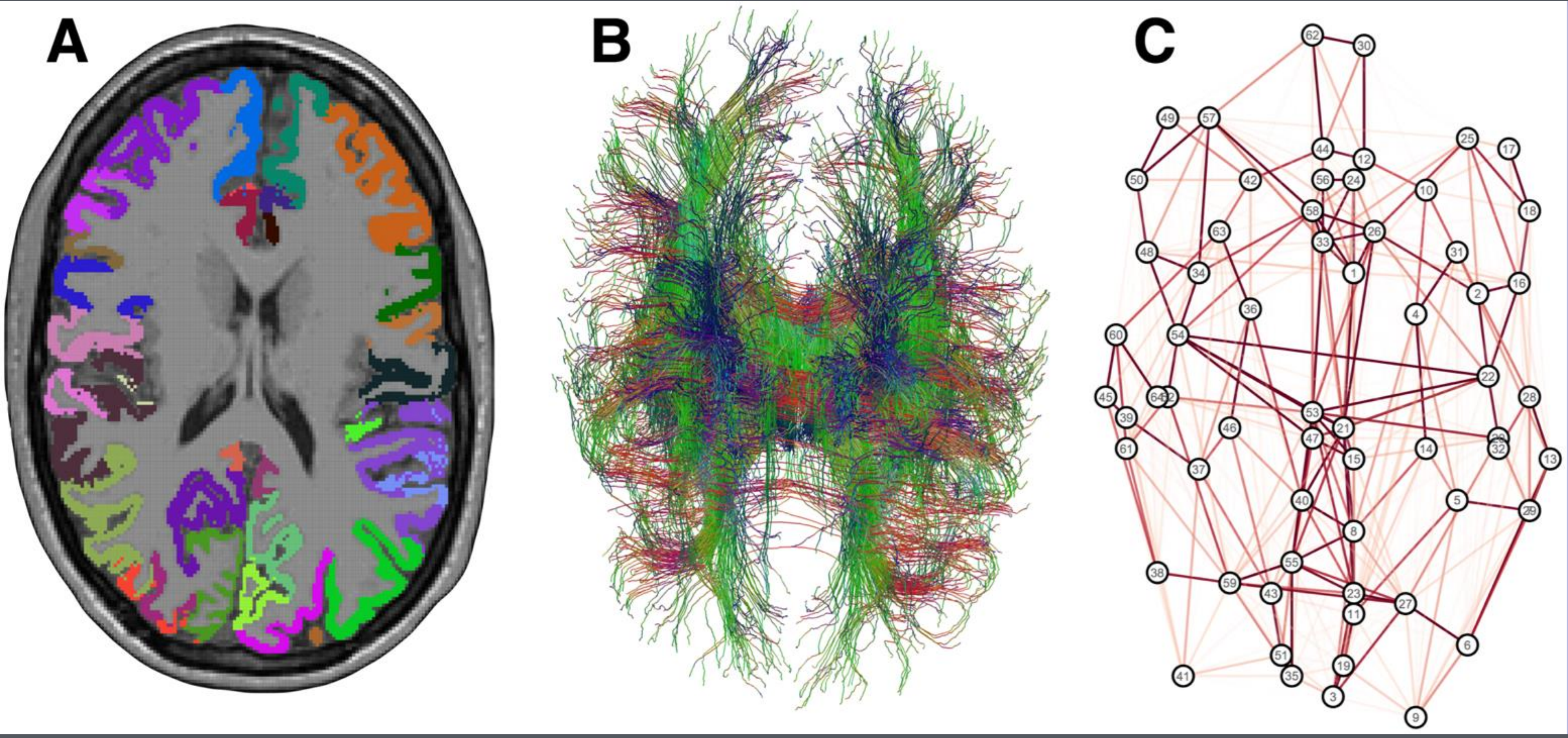
# Networks and the "connectome"




Bullmore & Sporns, *Nat Rev Neurosci*, 2009

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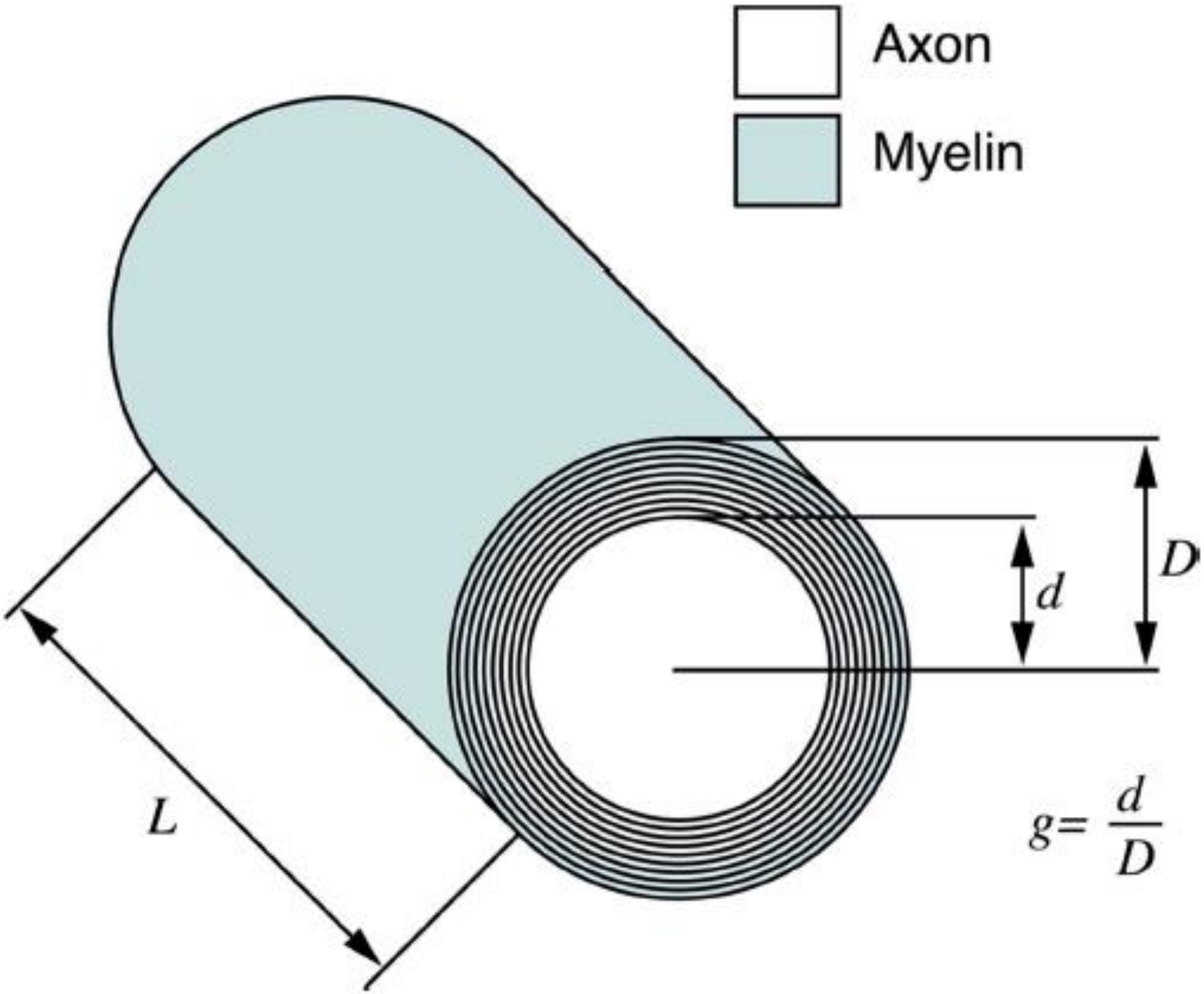
frontiers in
NEUROANATOMY

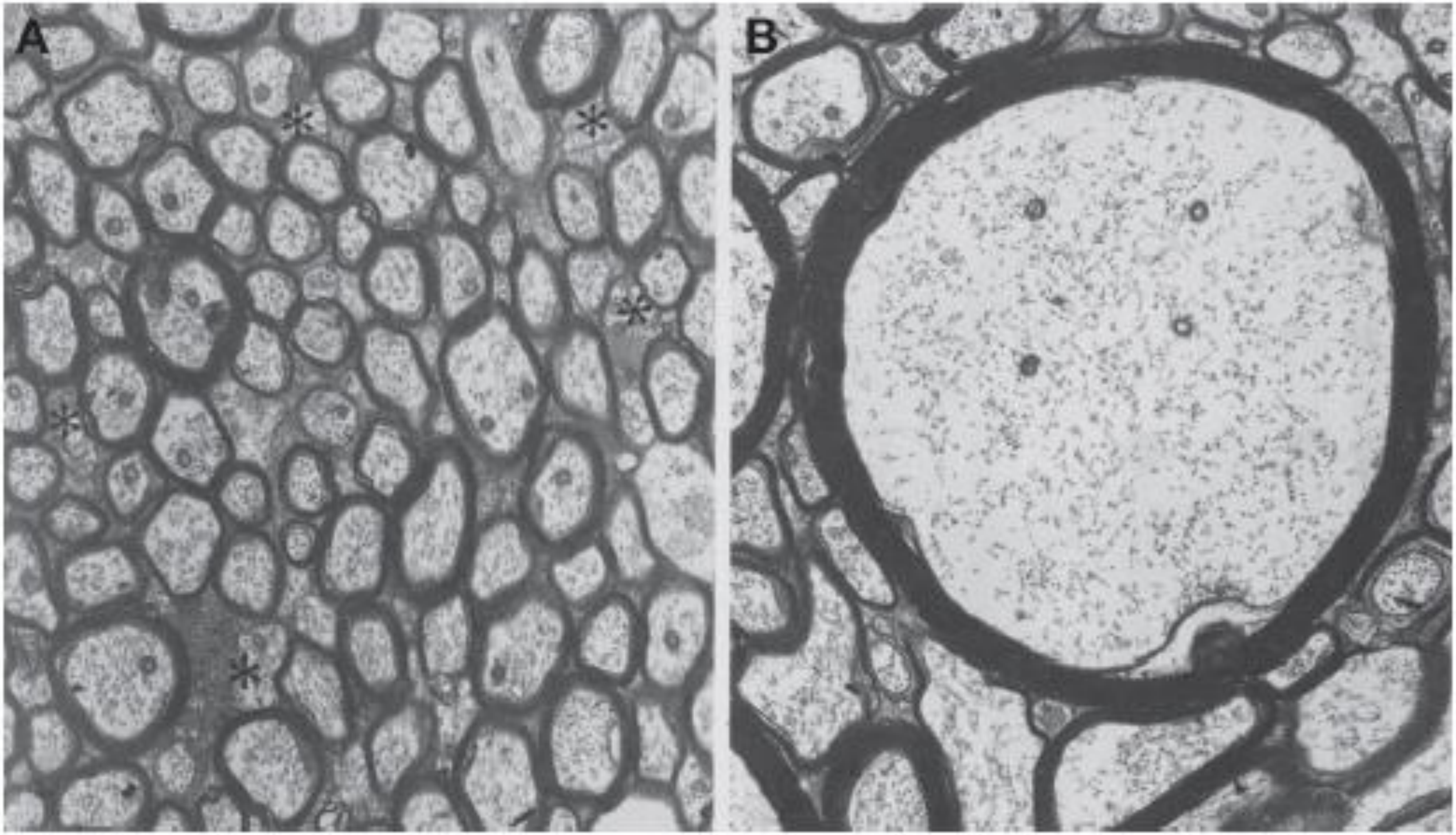
REVIEW ARTICLE
published: 04 September 2009
doi: 10.3389/neuro.05.014.2009

# Could sex differences in white matter be explained by *g* ratio?

***Tomáš Paus[1,2]* and Roberto Toro[3]***

[1] *Brain and Body Centre, University of Nottingham, Nottingham, UK*
[2] *Montreal Neurological Institute, Montreal, QC, Canada*
[3] *Institut Pasteur, Paris, France*


Axon
Myelin
D
d
L
g= d/D


A
B

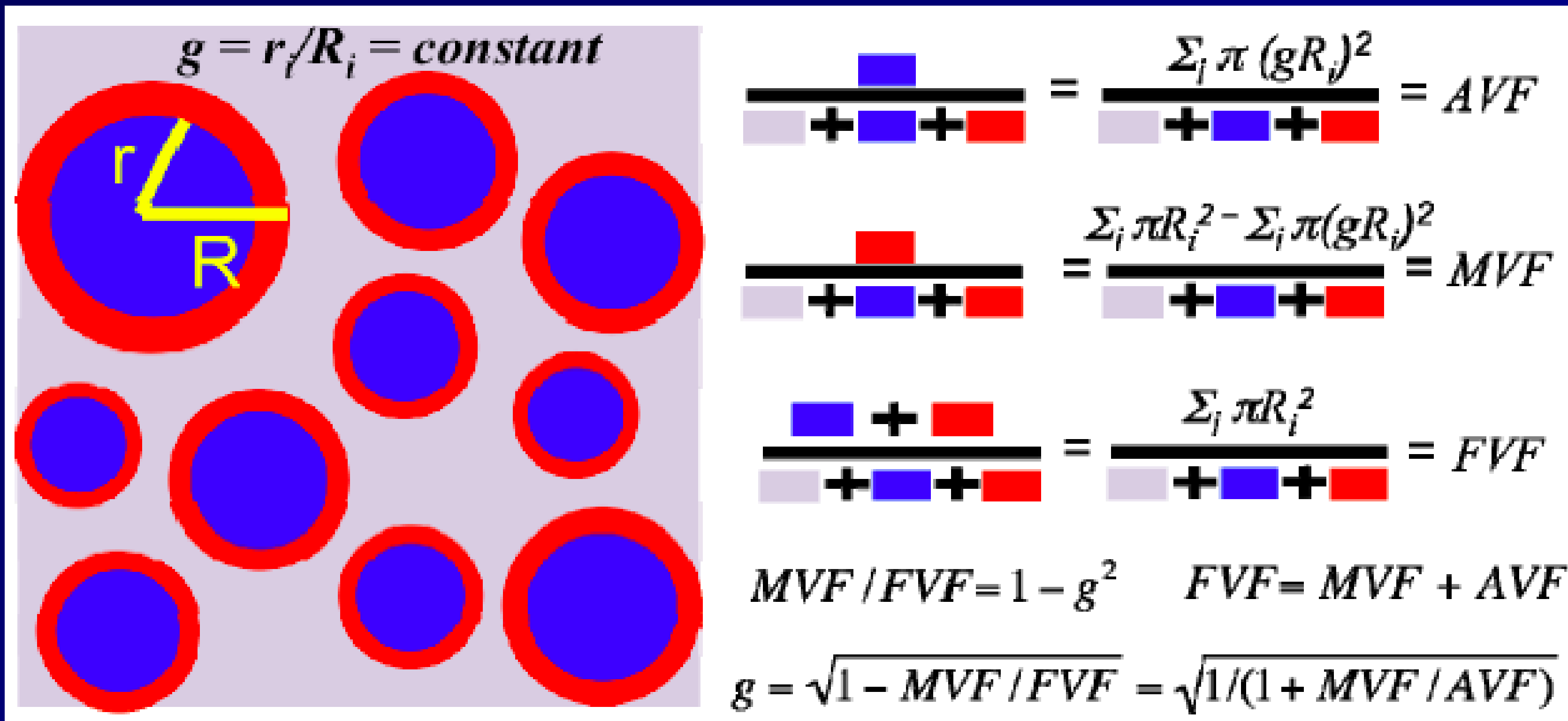
# Can the g ratio be measured using MRI *in vivo*?

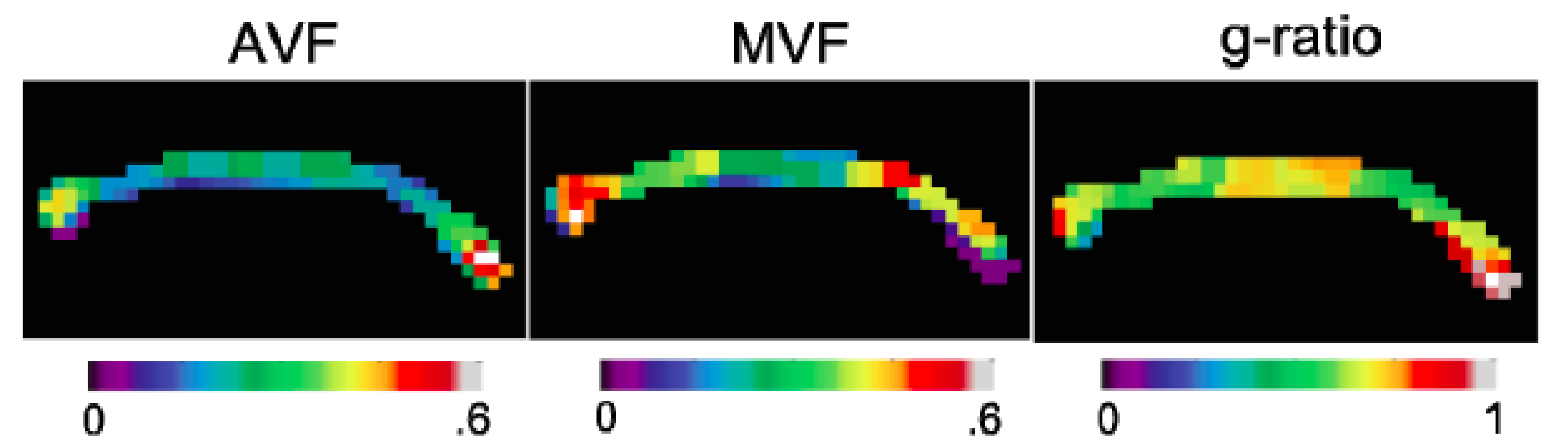
***In vivo* measurement of the myelin g-ratio with histological validation**

Nikola Stikov[1], Jennifer S.W. Campbell[1], Mariette Lavallée[1], Thomas Stroh[1], Stephen Frey[1], Jennifer Novek[1], Stephen Nuara[1], Ming-Kai Ho[1], Barry Bedell[1], and G. Bruce Pike[1,2]

[1]*Montreal Neurological Institute, McGill University, Montreal, QC, Canada,* [2]*Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada*

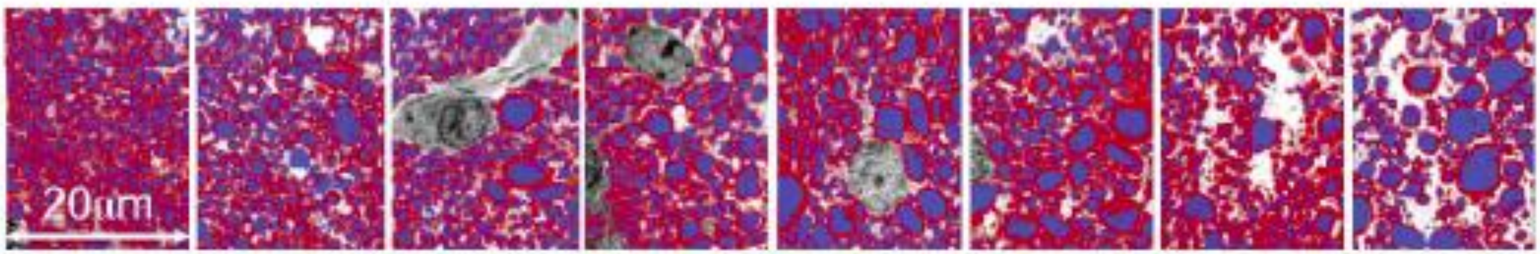
Proc. Intl. Soc. Mag. Reson. Med. 22 (2014) 0102.


g = r_i/R_i = constant
r
R
Σ_i π (gR_i)² = AVF
Σ_i πR_i² − Σ_i π(gR_i)² = MVF
Σ_i πR_i² = FVF
MVF / FVF = 1 − g²
FVF = MVF + AVF
g = √(1 − MVF / FVF) = √(1/(1 + MVF / AVF))


AVF
MVF
g-ratio
0
.6
0
.6
0
1

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| AVF | .42 | .36 | .38 | .35 | .30 | .38 | .27 | .71 |
| MVF | .40 | .40 | .47 | .29 | .34 | .35 | .58 | .28 |
| g-ratio | .72 | .69 | .67 | .74 | .69 | .72 | .57 | .85 |

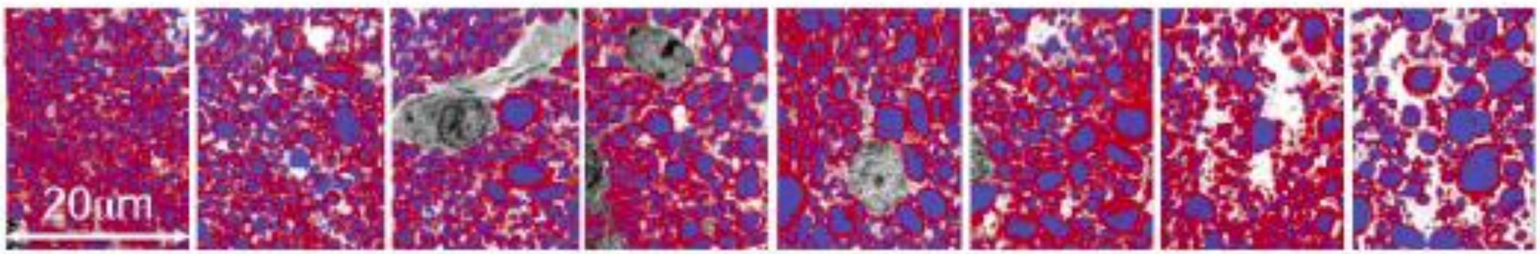
**Imaging**




| Histology | Genu (1) | (2) | (3) | (4) | (5) | (6) | (7) | Splenium (8) |
|---|---|---|---|---|---|---|---|---|
| AVF | .36 (.02) | .33 (.04) | .25 (.03) | .33 (.02) | .39 (.03) | .31 (.02) | .25 (.01) | .37 (.04) |
| MVF | .40 (.05) | .38 (.02) | .35 (.02) | .36 (.03) | .37 (.02) | .44 (.02) | .43 (.03) | .29 (.03) |
| g-ratio | .69 (.03) | .69 (.03) | .64 (.04) | .69 (.02) | .72 (.02) | .64 (.01) | .60 (.02) | .74 (.04) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| AVF | .42 | .36 | .38 | .35 | .30 | .38 | .27 | .71 |
| MVF | .40 | .40 | .47 | .29 | .34 | .35 | .58 | .28 |
| g-ratio | .72 | .69 | .67 | .74 | .69 | .72 | .57 | .85 |

Imaging




| Histology | Genu (1) | (2) | (3) | (4) | (5) | (6) | (7) | Splenium (8) |
|---|---|---|---|---|---|---|---|---|
| AVF | .36 (.02) | .33 (.04) | .25 (.03) | .33 (.02) | .39 (.03) | .31 (.02) | .25 (.01) | .37 (.04) |
| MVF | .40 (.05) | .38 (.02) | .35 (.02) | .36 (.03) | .37 (.02) | .44 (.02) | .43 (.03) | .29 (.03) |
| g-ratio | .69 (.03) | .69 (.03) | .64 (.04) | .69 (.02) | .72 (.02) | .64 (.01) | .60 (.02) | .74 (.04) |

$r = 0.88, p = 0.011$

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# Microstructural plasticity

Most plasticity studies have involved medium to long term learning (ie weeks or months of training)

Studies have mainly looked for gross changes to the shape or volume of grey matter areas, or signs of improved connectivity of the white matter tracts

Yaniv Assaf’s group in Tel Aviv has conducted a series of studies using DTI techniques to examine microstructural changes within the brain’s grey matter induced by training over a period of hours

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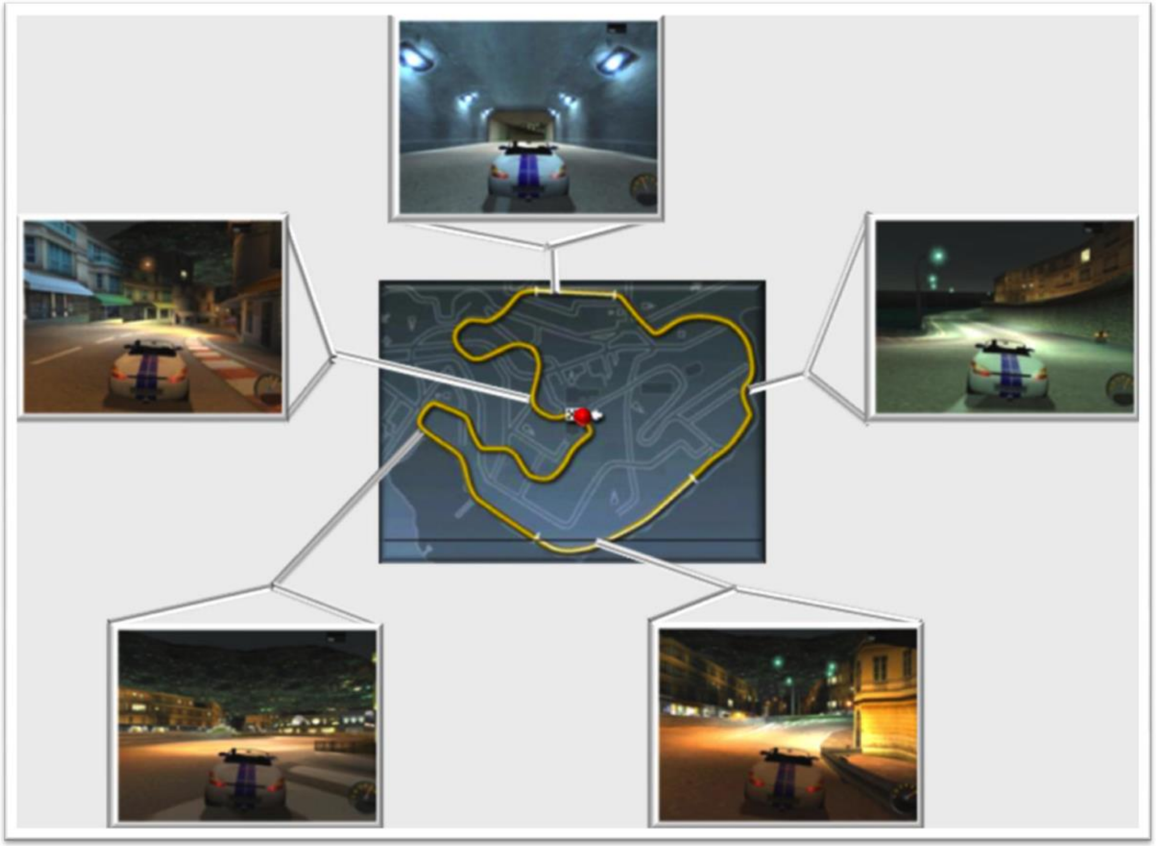
Neuron
Article

# Learning in the Fast Lane: New Insights into Neuroplasticity

Yaniv Sagi,[1,2] Ido Tavor,[1,2] Shir Hofstetter,[1] Shimrit Tzur-Moryosef,[1] Tamar Blumenfeld-Katzir,[1] and Yaniv Assaf[1,*]
[1]Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel
[2]These authors contributed equally to this work
*Correspondence: assafyan@post.tau.ac.il
DOI 10.1016/j.neuron.2012.01.025

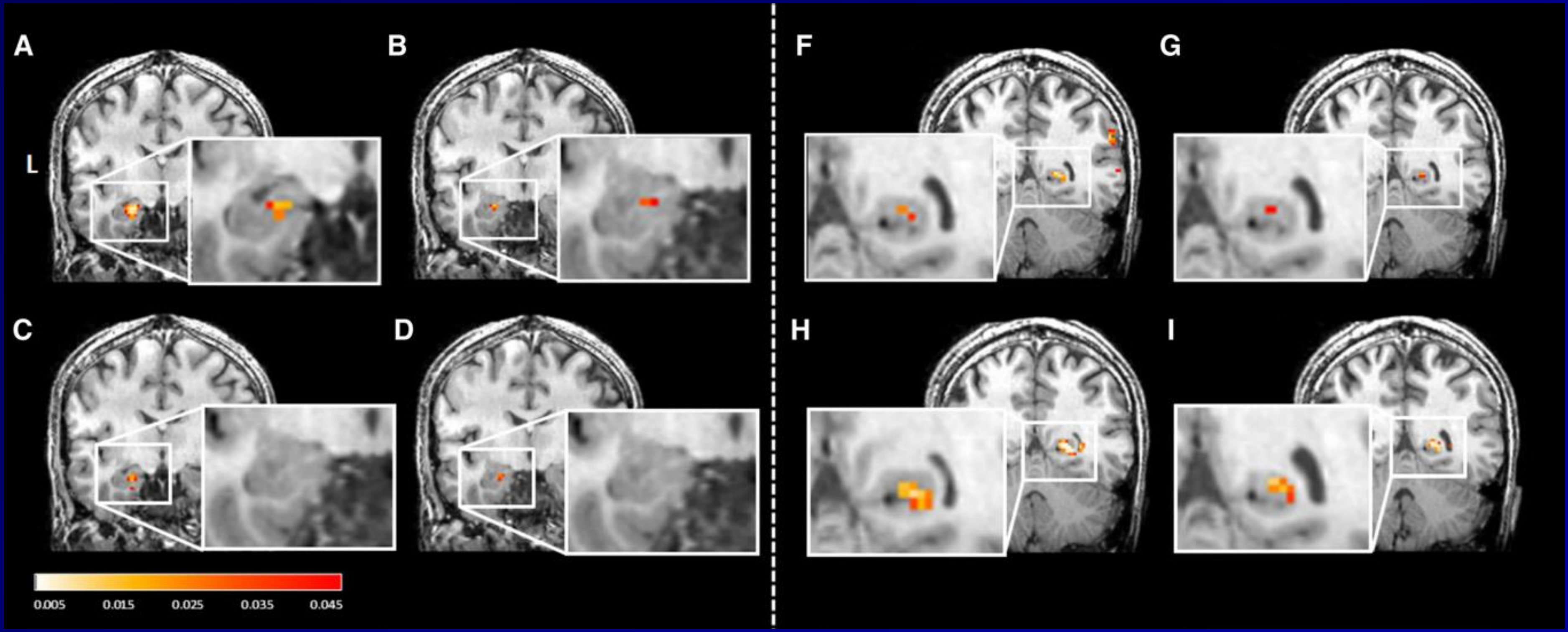


**The Learning Task:**

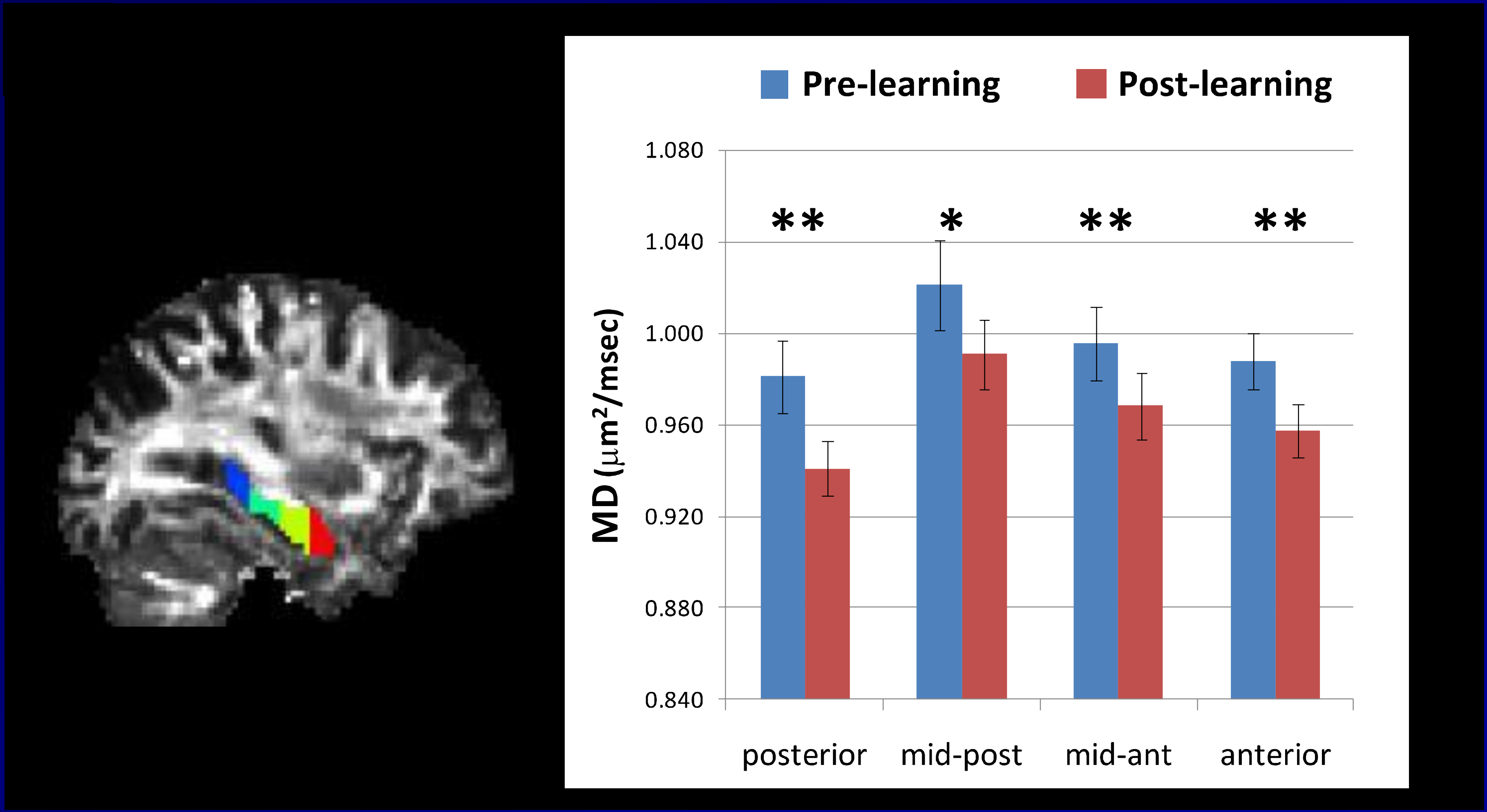
Subjects performed 16 laps of the same computer car game track, divided into 4 sessions. The objective was to learn the track and achieve better lap times.

While repeating the same track over and over again, subjects can memorize the track and its scenery and learn to perform better from trial to trial.

# Changes in Mean Diffusivity (MD)



# Region of Interest (RoI) analysis



# Overview : Conclusions

Dyscalculia: IPS and many other brain areas involved

Diffusion MRI used sparingly so far

Sexual dimorphisms: puberty may be important

More specific diffusion MRI methods such as NODDI have potential

Graph theory and networks can provide a whole brain approach

New methods can potentially map the g ratio

Learning effects can have short term effects on brain structure: implications for maths learning in normal learners and dyscalculics?

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Diffusion MRI used sparingly so far

Sexual dimorphisms: puberty may be important

More specific diffusion MRI methods such as NODDI have potential

Graph theory and networks can provide a whole brain approach

New methods can potentially map the g ratio

Learning effects can have short term effects on brain structure: implications for maths learning in normal learners and dyscalculics?

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# Acknowledgements

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# Thank you for listening