Diffusion Tensor MRI: What can it tell us about white matter in alcoholism?

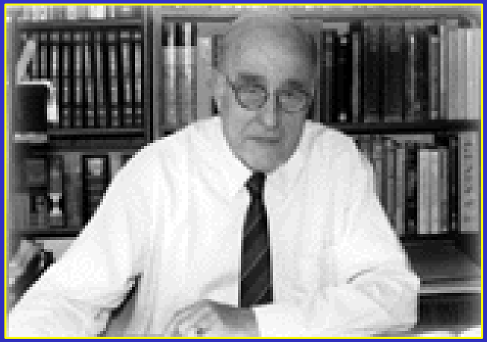
Derek K. Jones

STBB, LIMB, NICHD, National Institutes of Health, USA.

Post-Mortem Findings in Alcoholism

(e.g. Harper and Krill, 1989)

- Volume reduction
- Demyelination
- Loss of myelinated fibers
- Axonal deletion



Nieuwenhuys *et al.*, 1988

The Human Central Nervous System

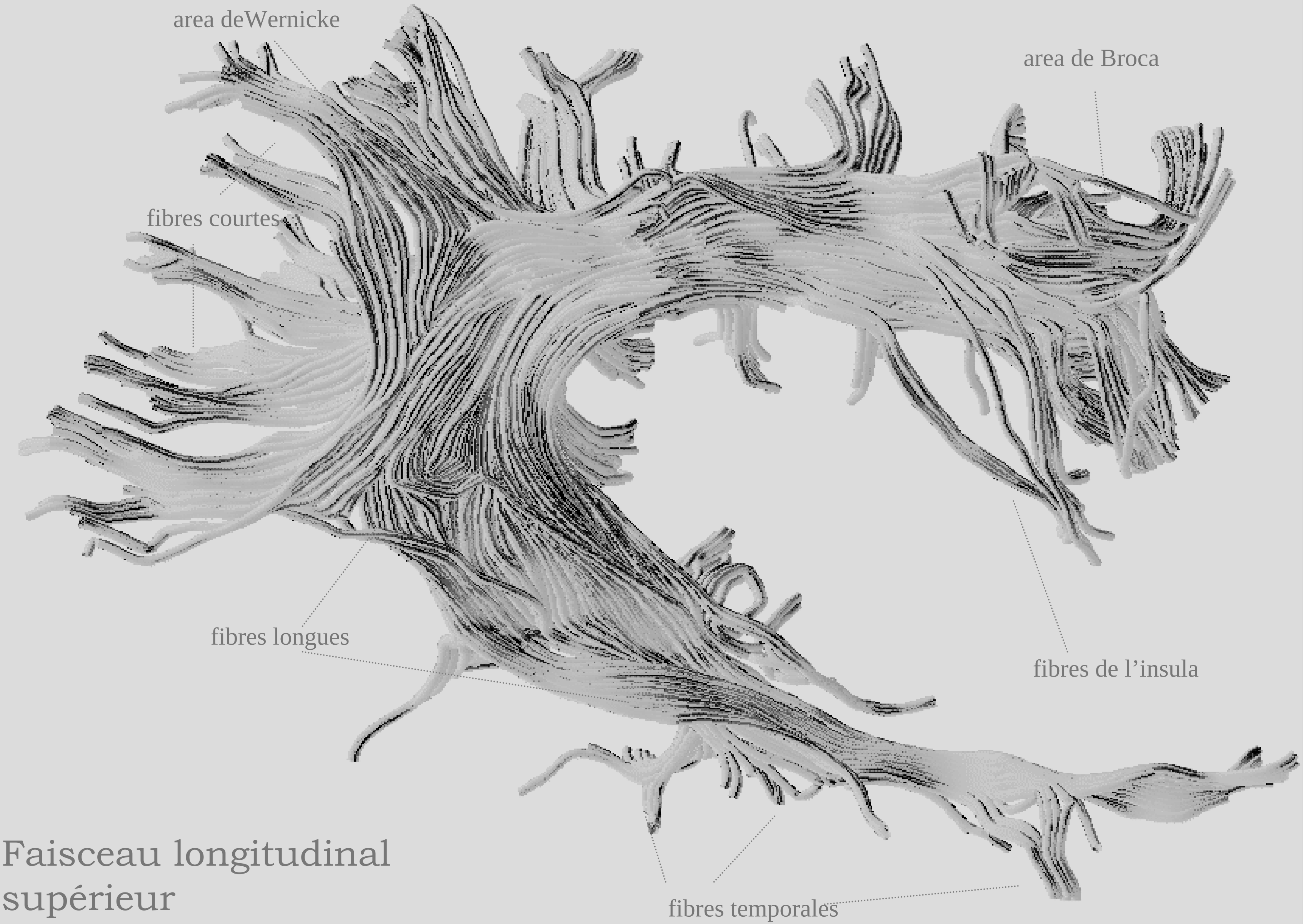
Crosby *et al.*, 1962

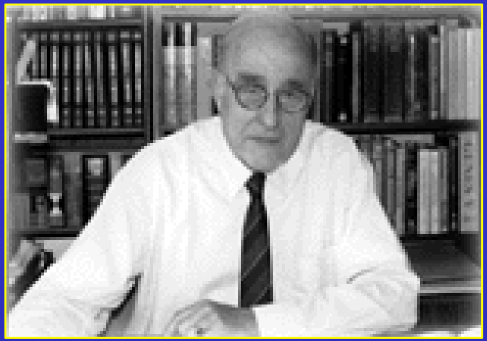
Correlative Anatomy of the Nervous System

Dejerine, 1895

Anatomie des Centres Nerveux

Faisceau longitudinal supérieur





Nieuwenhuys *et al.*, 1988

The Human Central Nervous System

Crosby *et al.*, 1962

Correlative Anatomy of the Nervous System

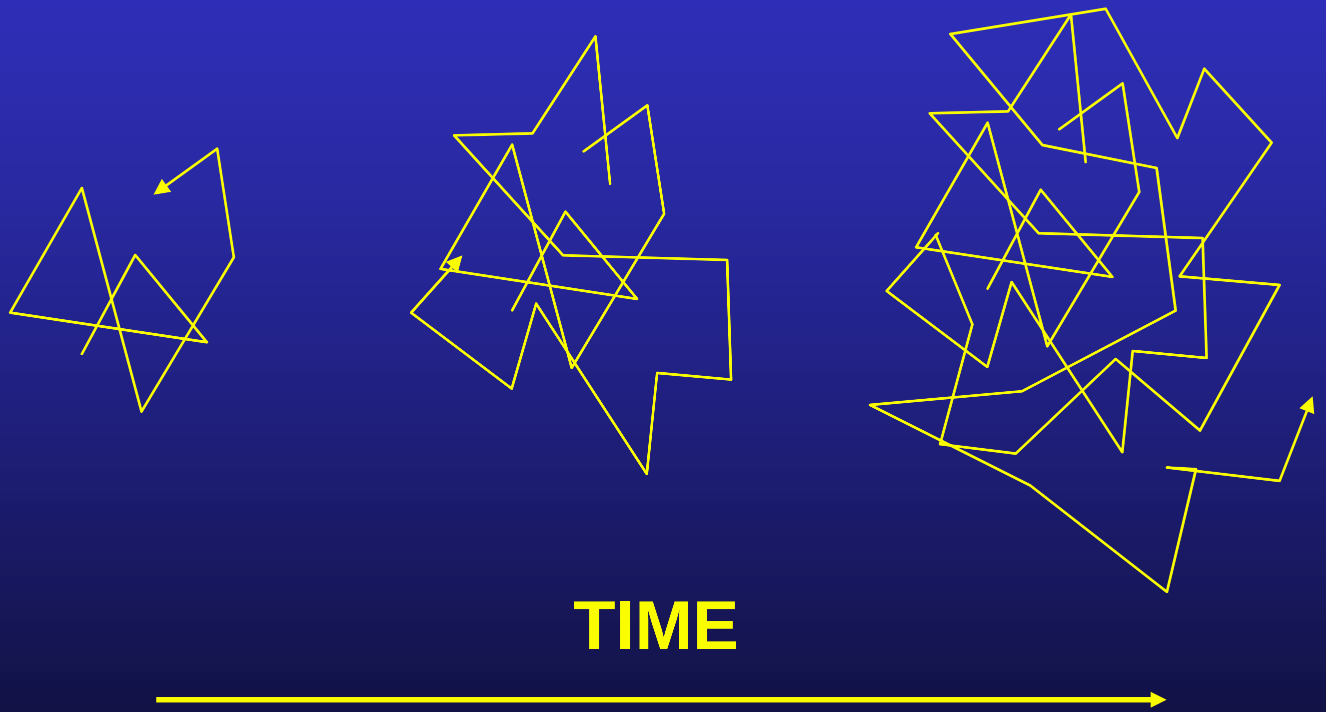
Dejerine, 1895

Anatomie des Centres Nerveux

ROBERT BROWN

1773 - 1858

Diffusion



Diffusion in Biological Systems

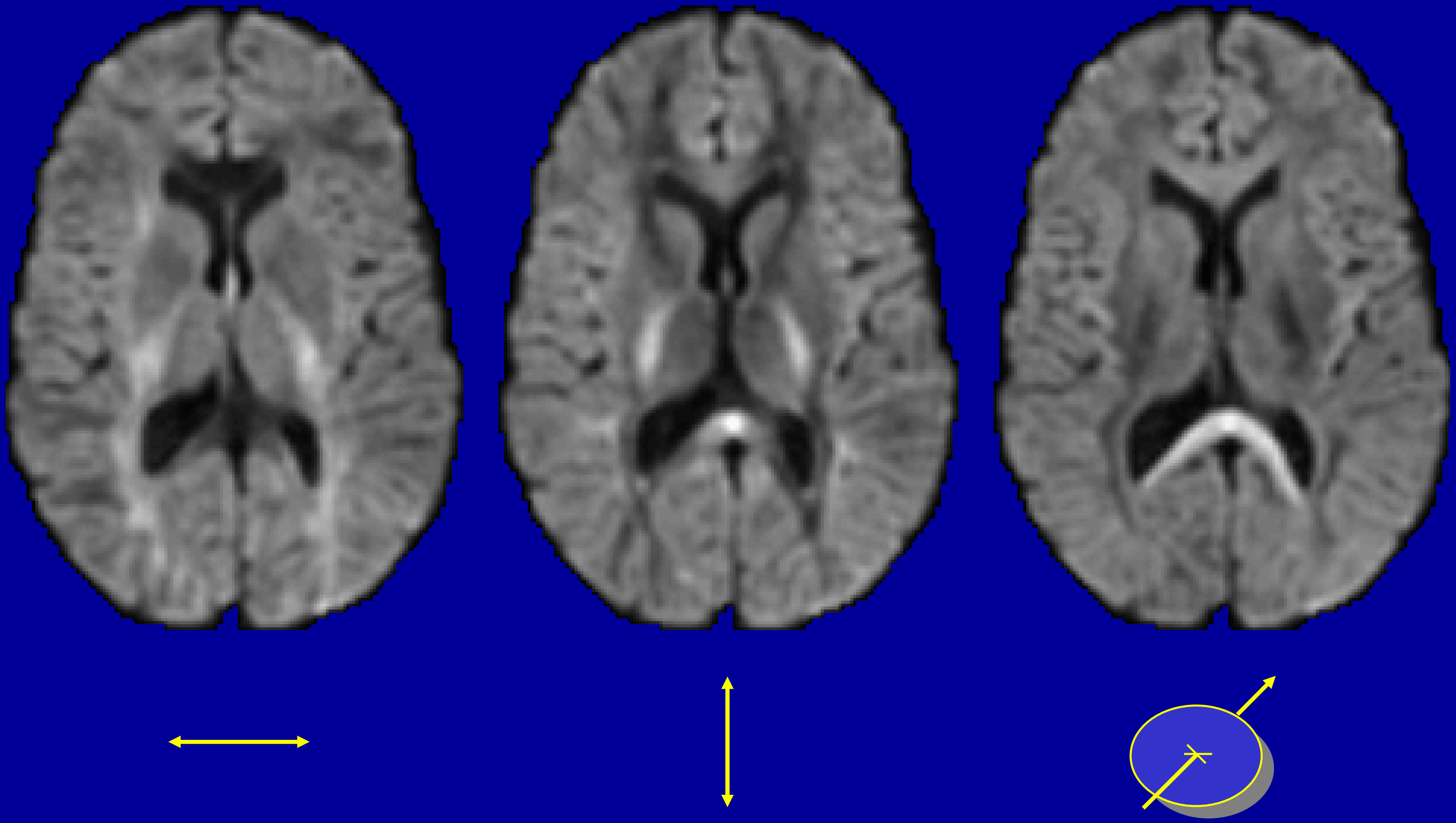
Pulsed NMR study of water mobility in muscle and brain tissue.
Hansen JR. *Biochim Biophys Acta* **230**:482-6 (1971)

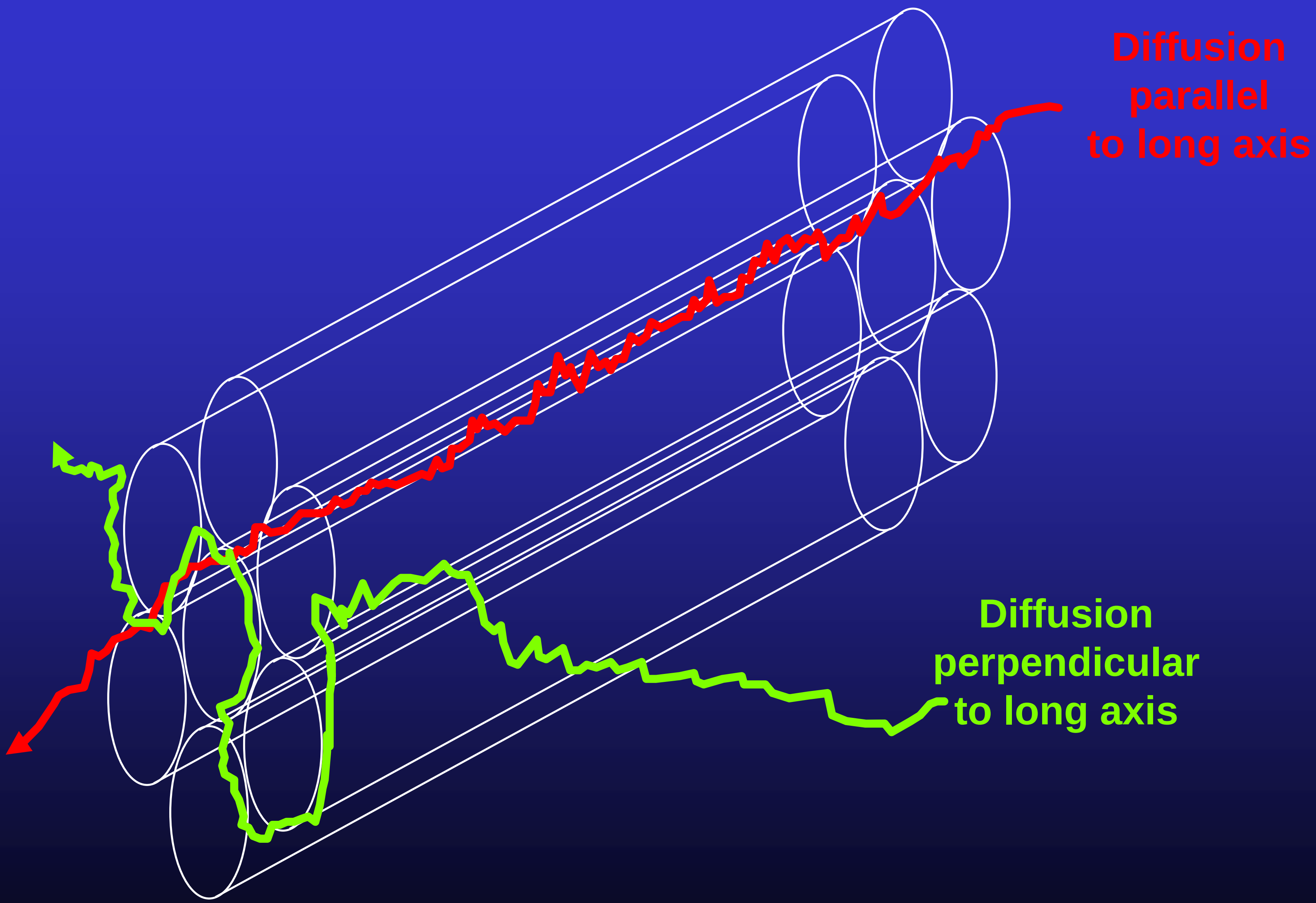
Nuclear magnetic resonance measurement of skeletal muscle: anisotropy of the diffusion coefficient of the intracellular water.
Cleveland GG *et al*. **16:** 1043-53 (1976)

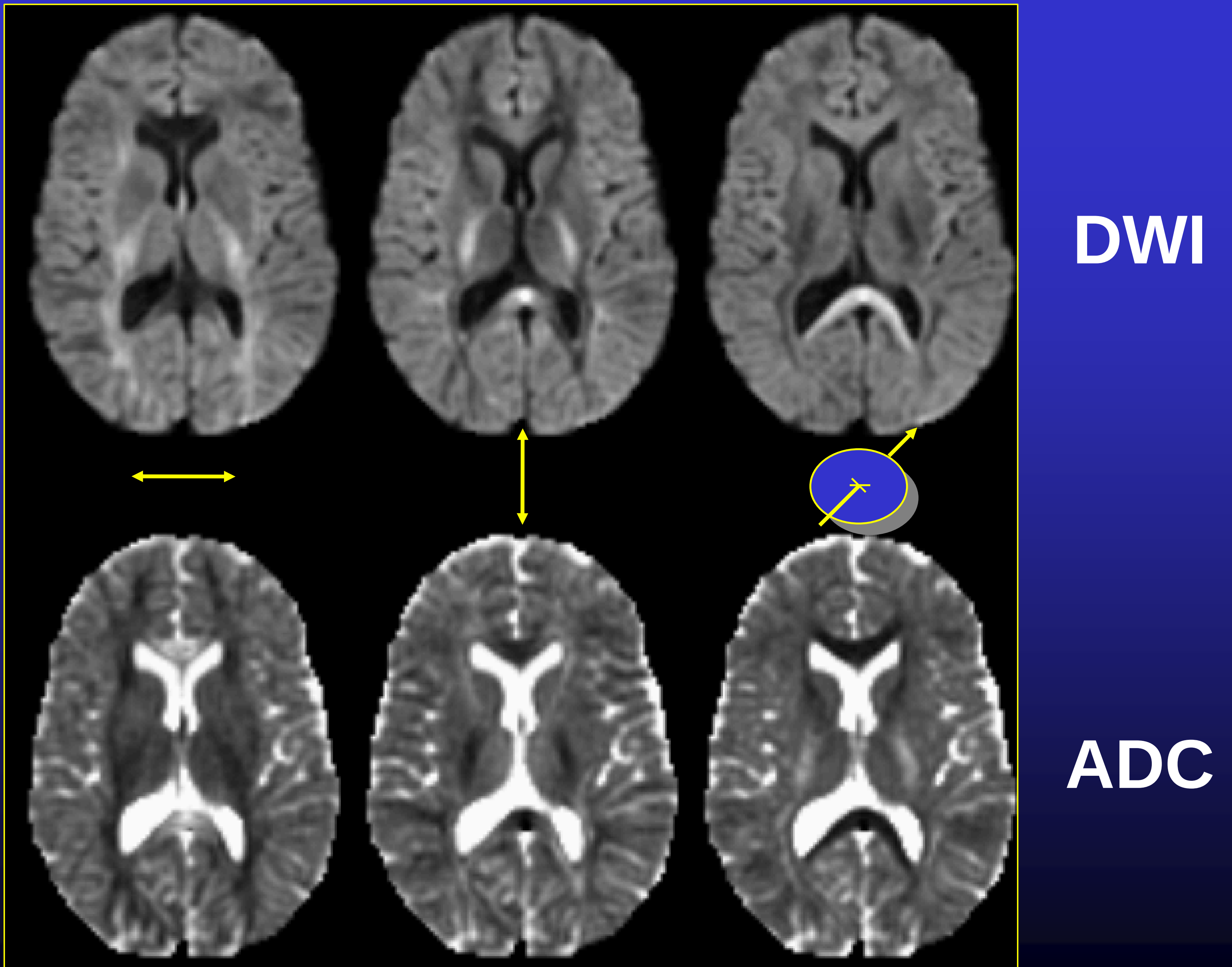
Self diffusion of water in frog muscle.
Tanner JE *Biophys J* 28: 107-16 (1979)

Diffusion weighted MR imaging of anisotropic water diffusion in cat central nervous system.
Moseley ME *et al*. *Radiology* **176:** 439-45 (1990)

DIFFUSION WEIGHTED IMAGES

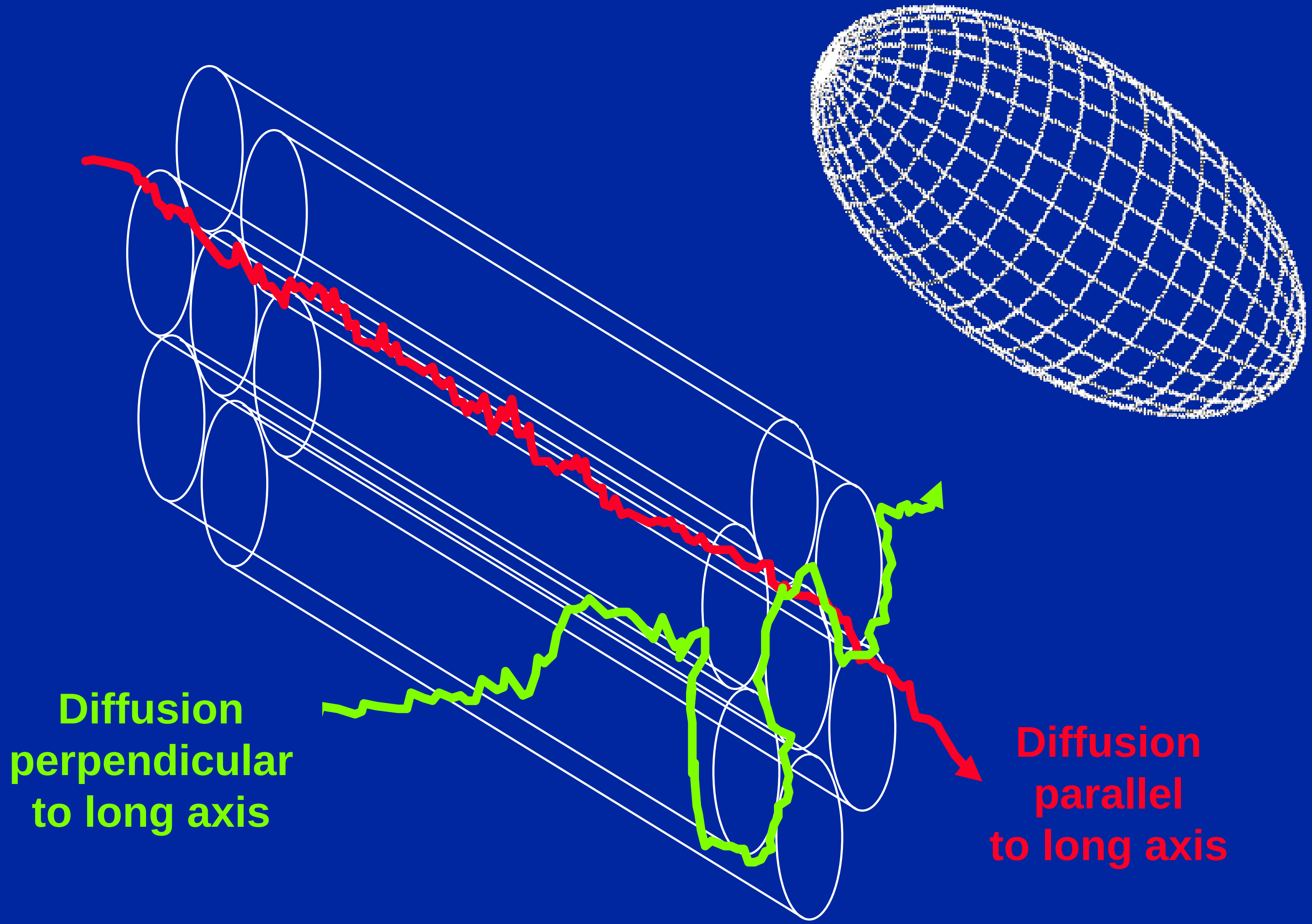


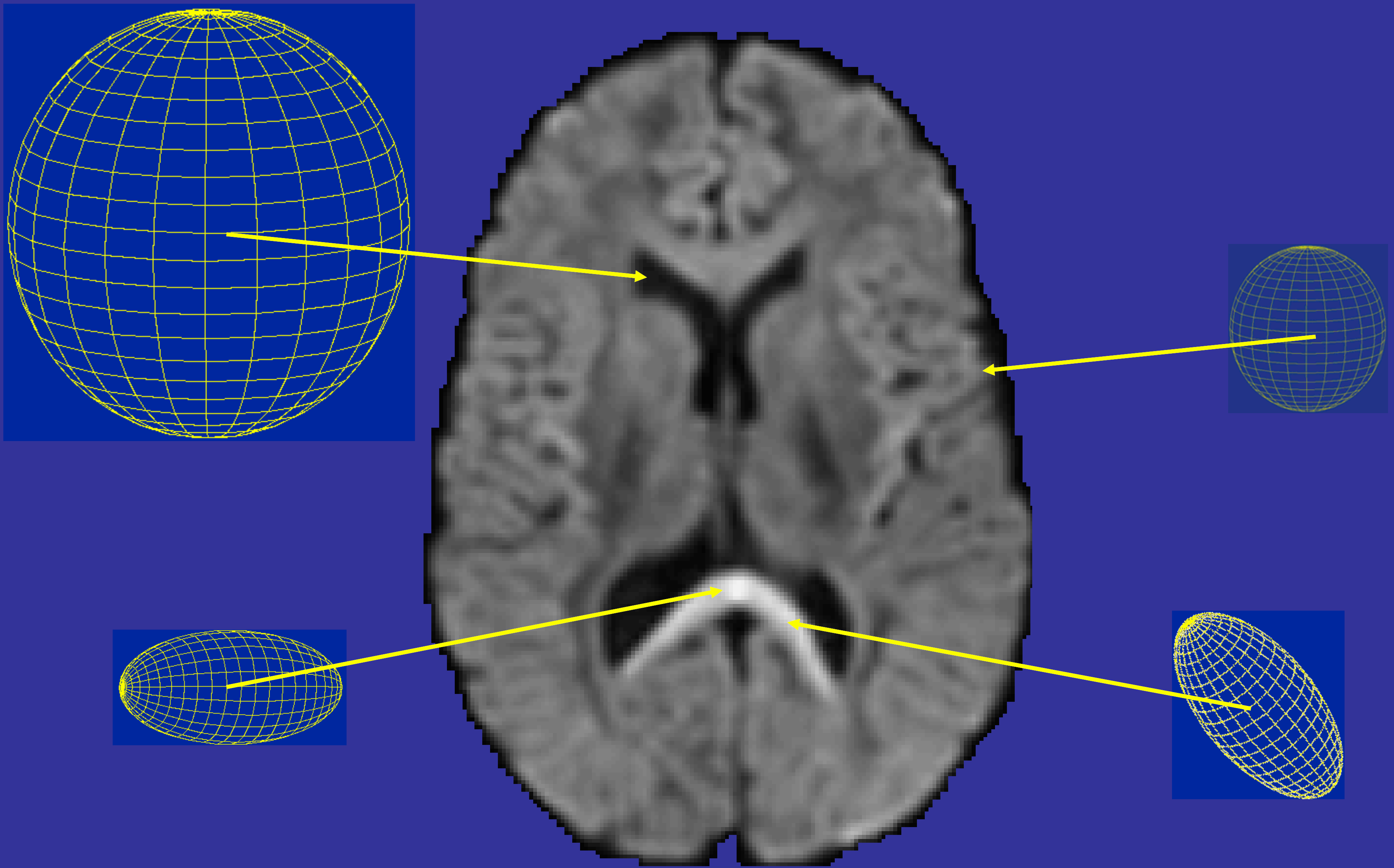

Diffusion
parallel
to long axis
Diffusion
perpendicular
to long axis


DWI
ADC

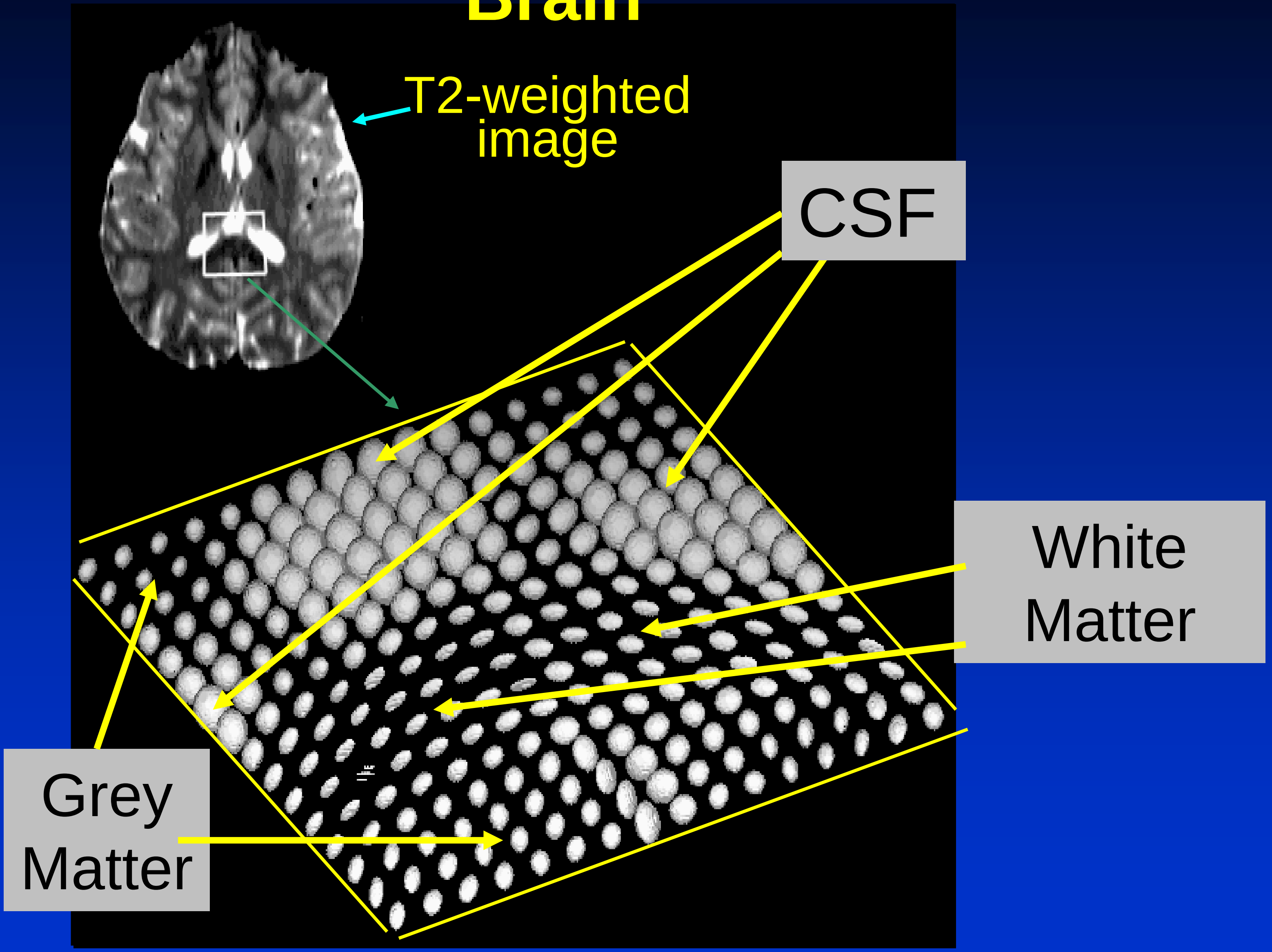
DIFFUSION TENSOR

$$\mathbf{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$


Diffusion perpendicular to long axis
Diffusion parallel to long axis

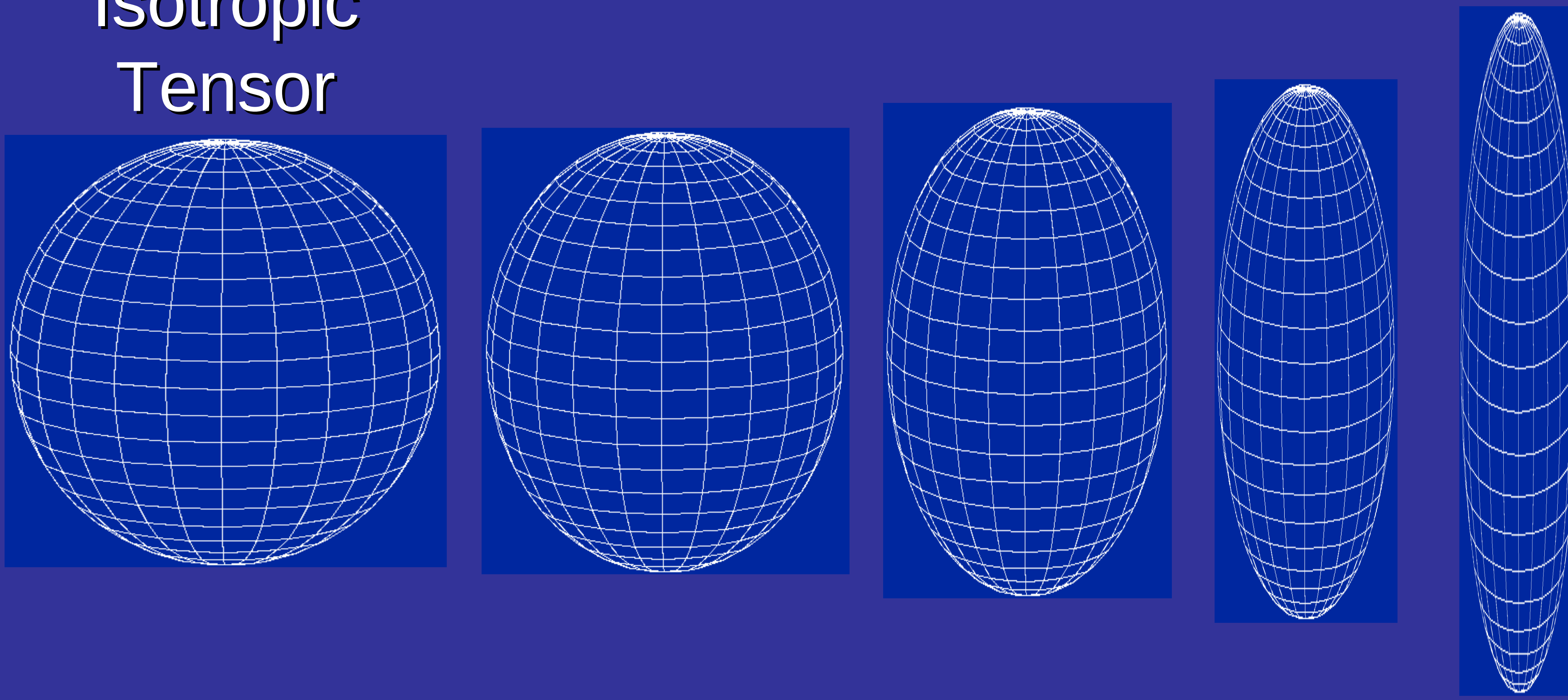


Measured Diffusion Ellipsoids in Human Brain

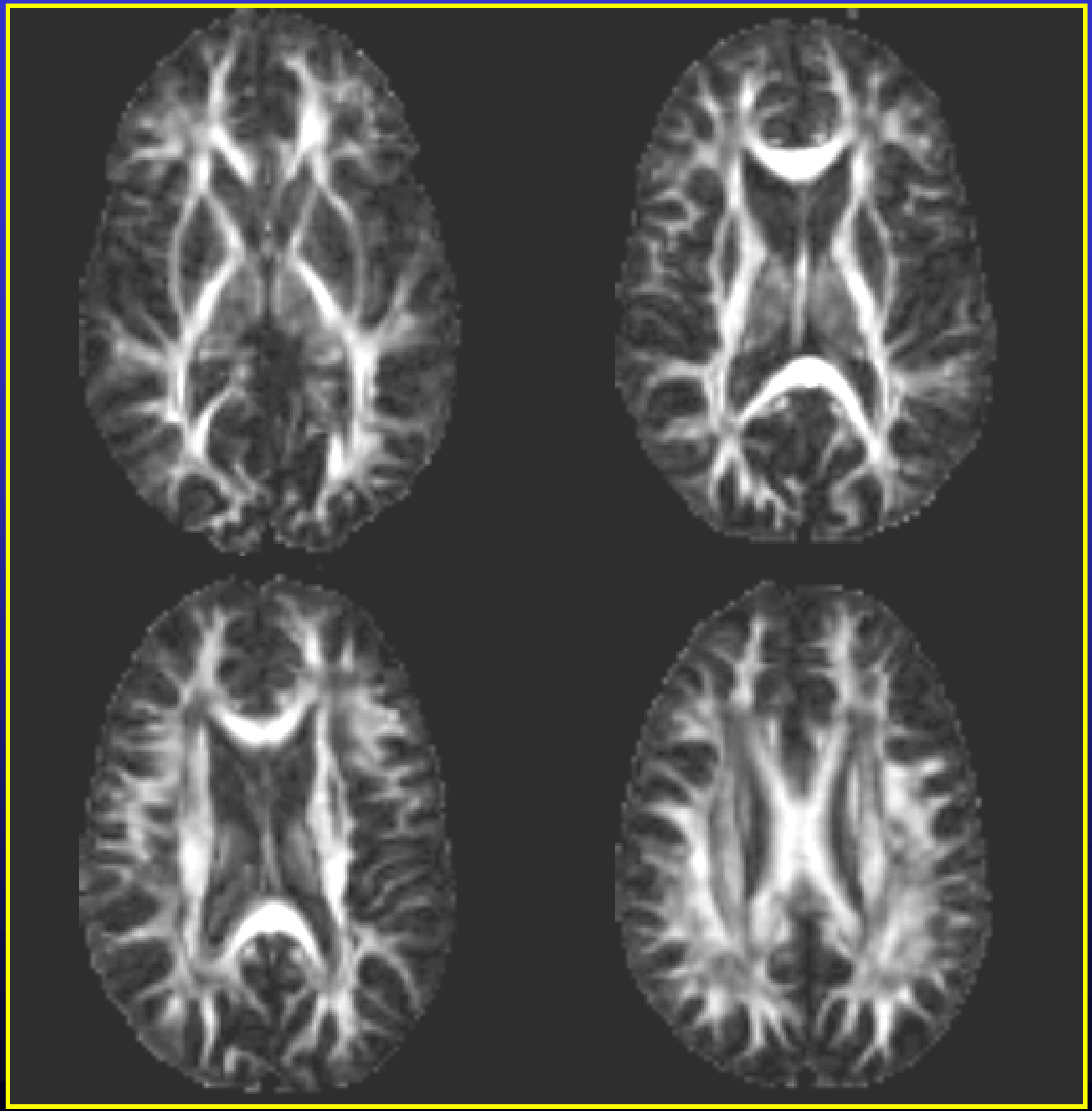


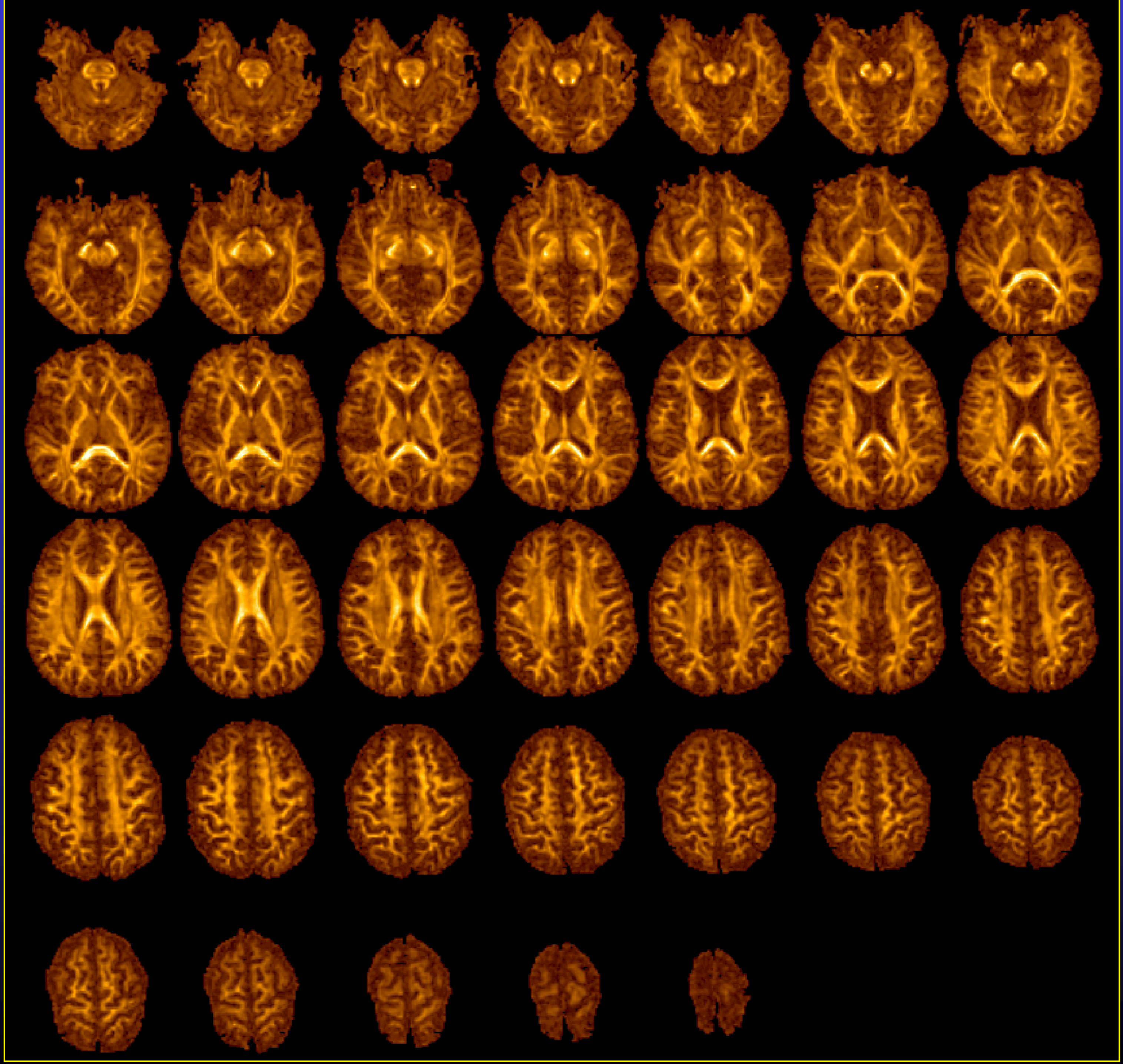
Pierpaoli C, Jezzard P, Basser PJ, Barnett A, Di Chiro G. *Diffusion tensor MR imaging of the human brain*. Radiology 1996; 201:637-48.

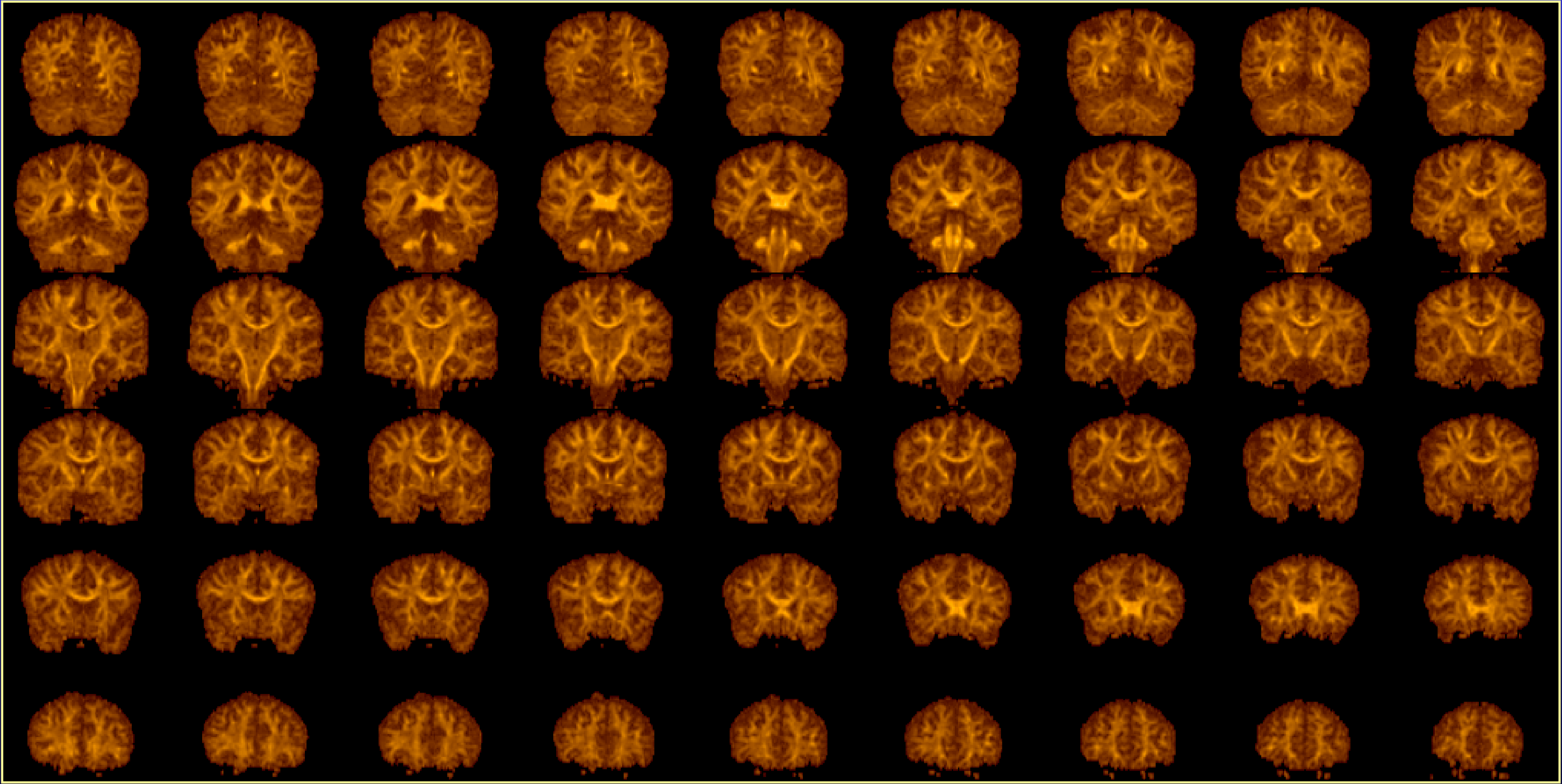
Isotropic
Tensor

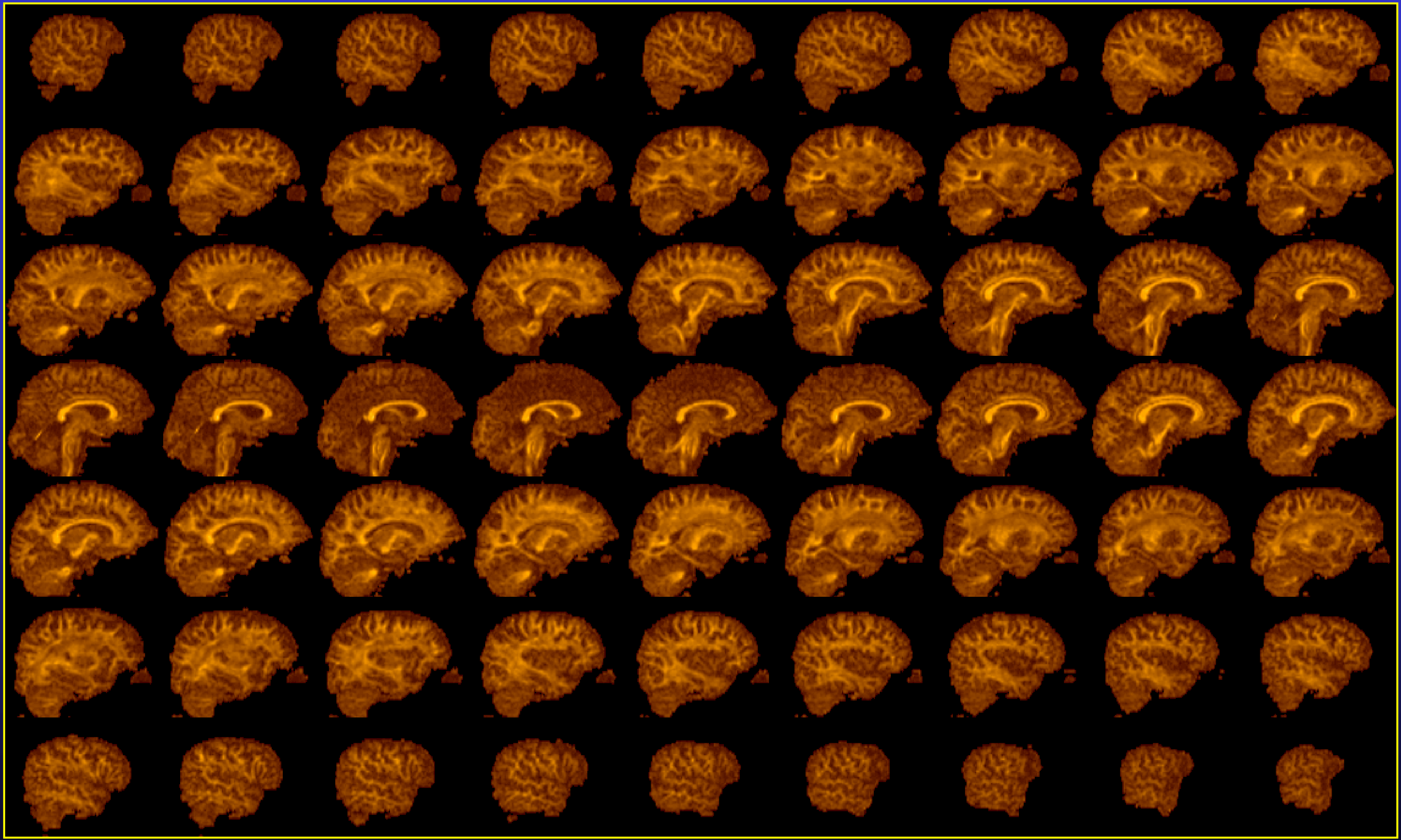


ANISOTROPY →

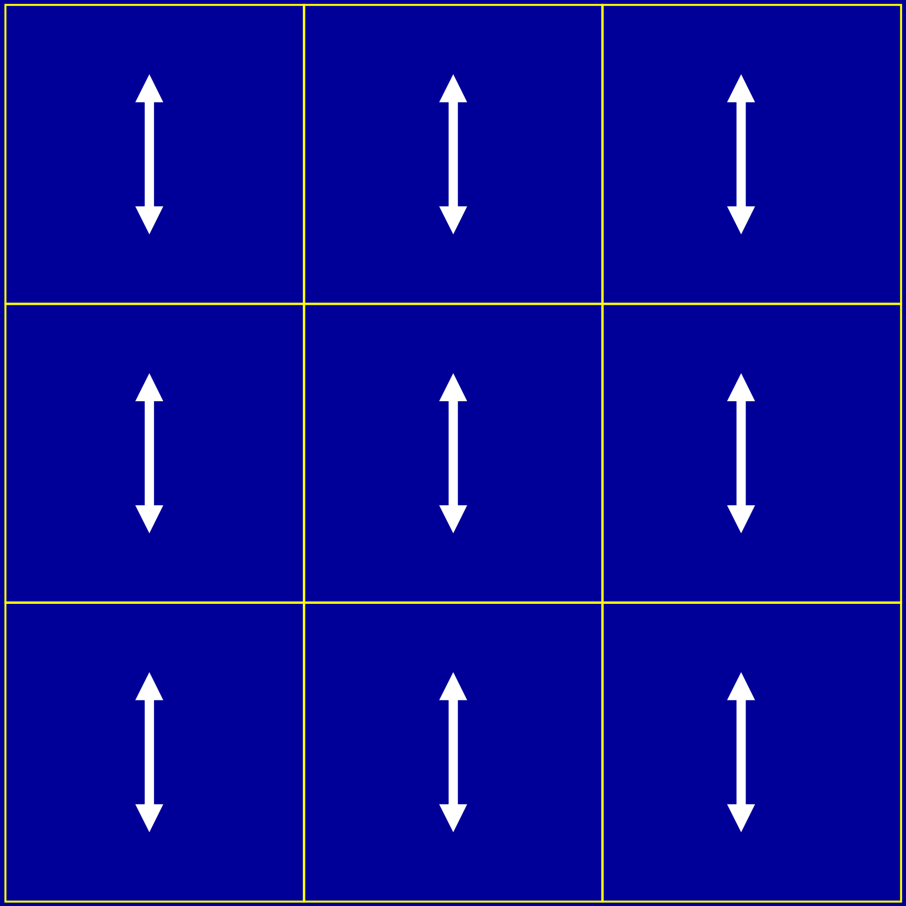




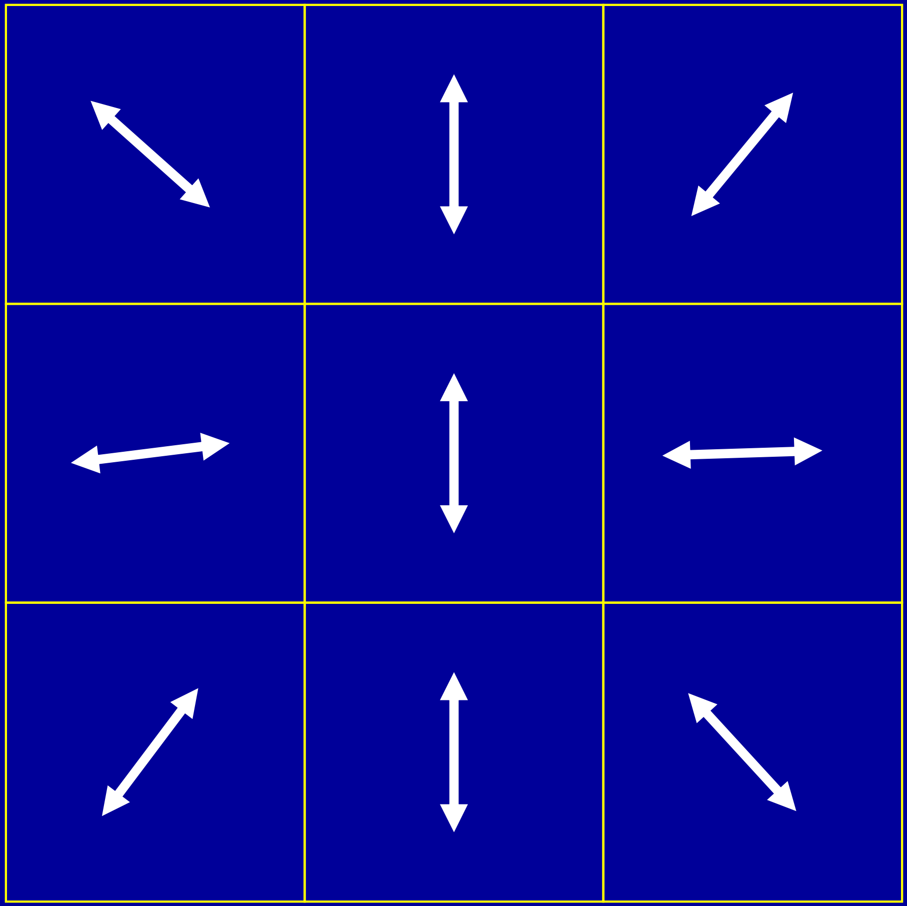




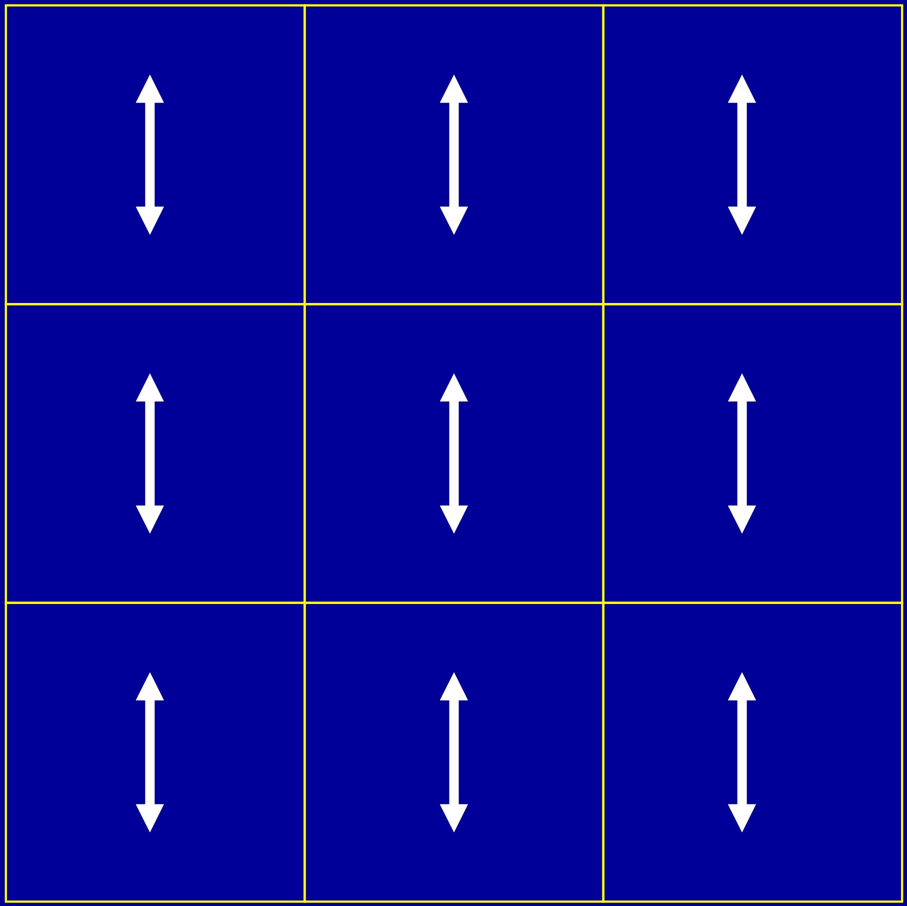
High Anisotropy, High Coherence



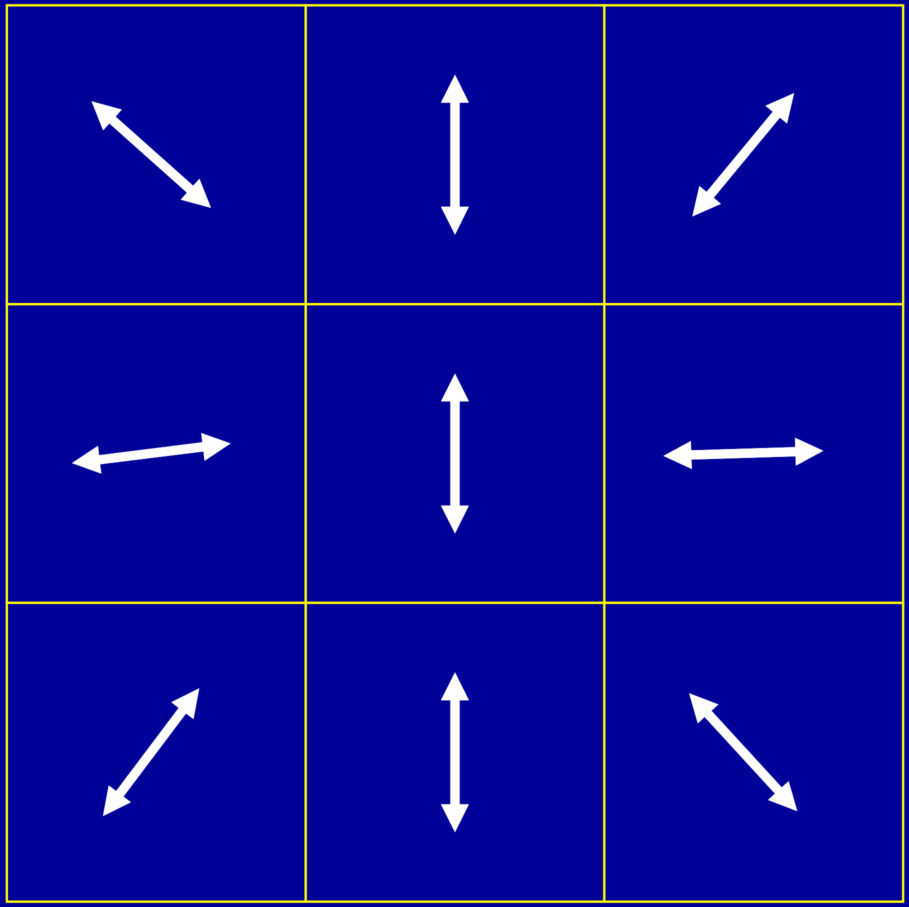
High Anisotropy, Low Coherence



High Anisotropy, High Coherence



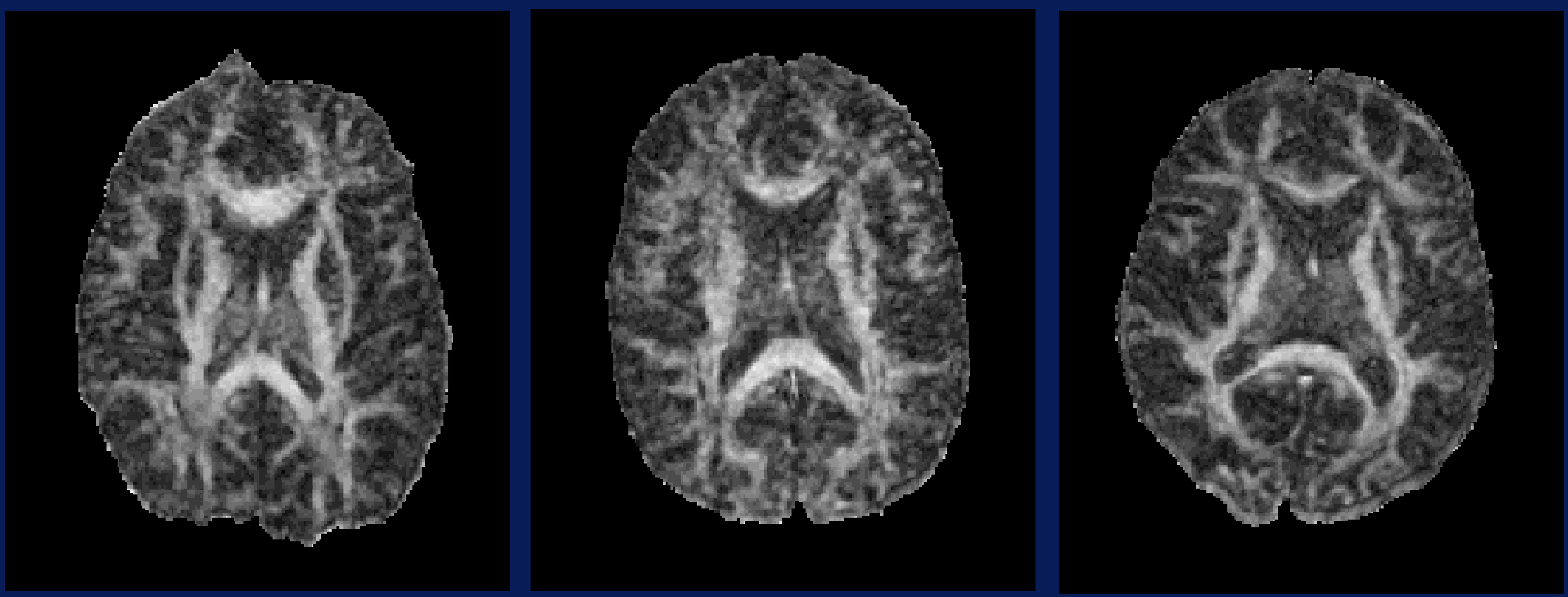
High Anisotropy, Low Coherence



Applications

- Ageing
- Alcoholism
- Alzheimer’s Disease
- ALS
- Development
- Dysexlia
- Epilepsy
- HIV
- Leukoaraiosis
- Multiple Sclerosis
- Schizophrenia
- Tumours
- Wallerian Degeneration

White Matter Anisotropy with Age



23 years old
genu FA = .633

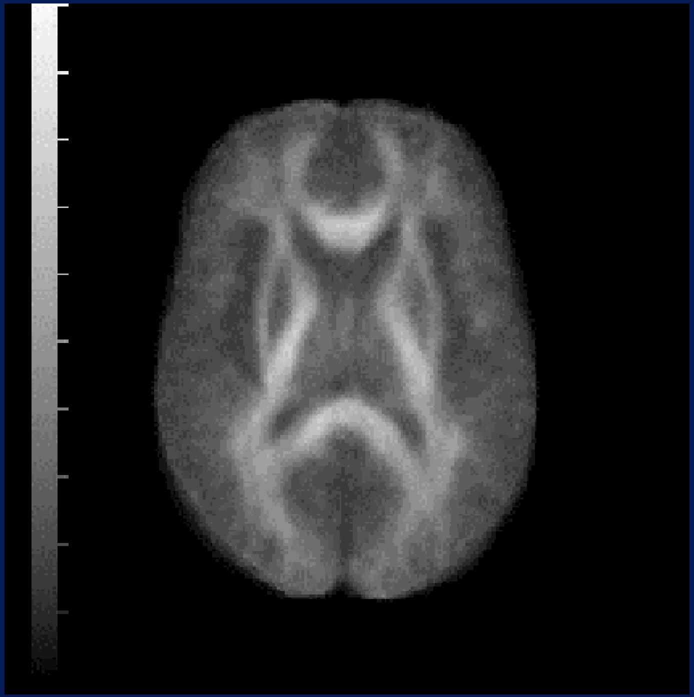
45 years old
genu FA = .521

79 years old
genu FA = .466

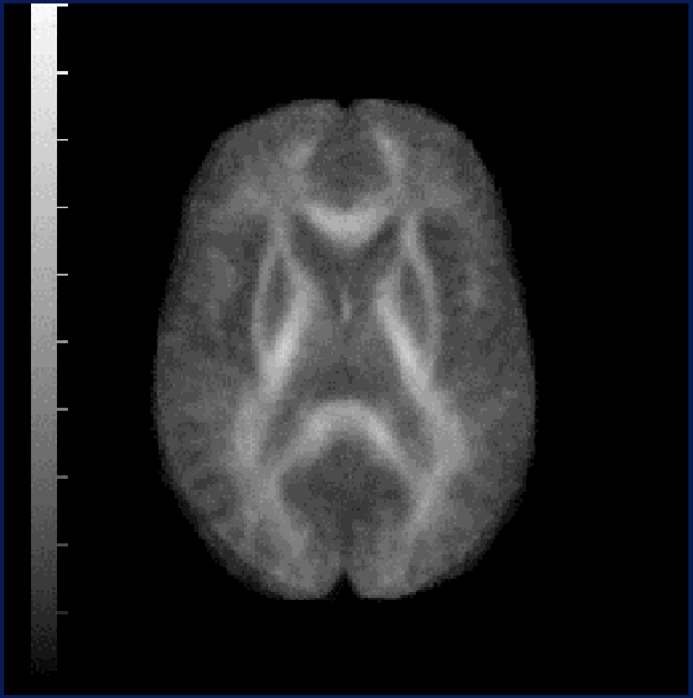
Sullivan & Pfefferbaum
EJR 2003

Fractional Anisotropy

Grand averages aligned at inferior genu



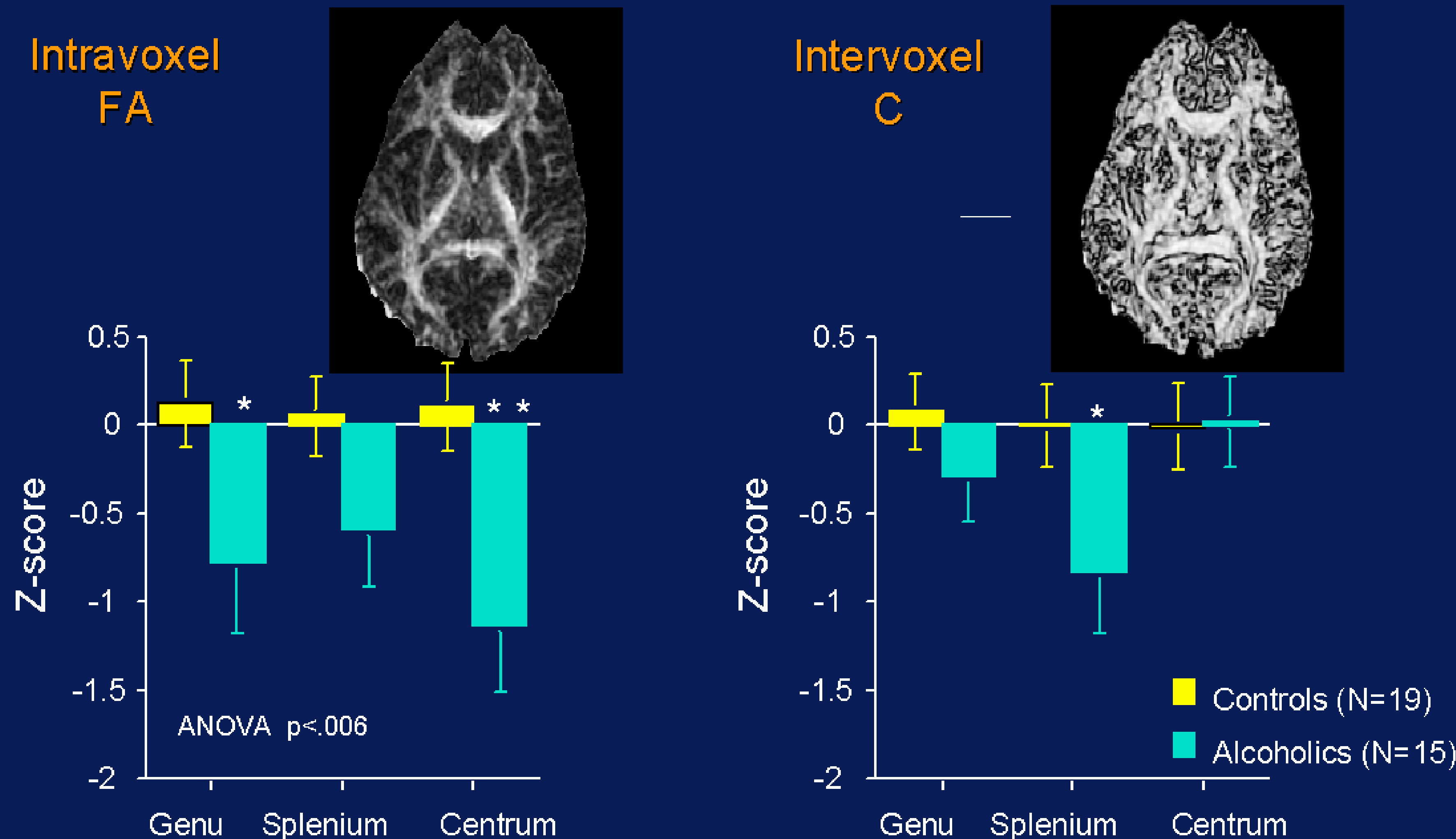
10 Controls



14 Alcoholics

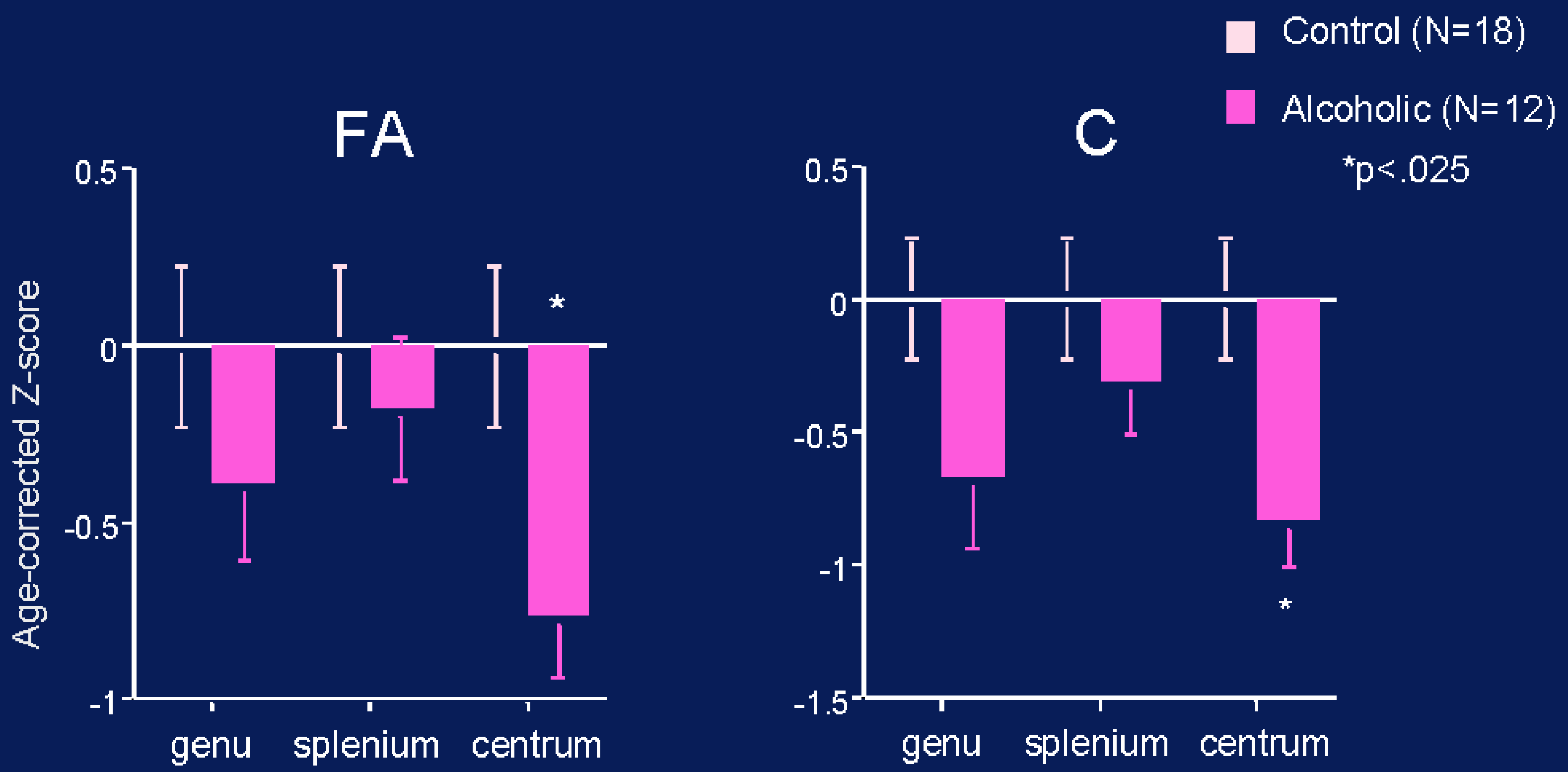
Pfefferbaum et al.
ACER 2000

DTI in Alcoholic Men



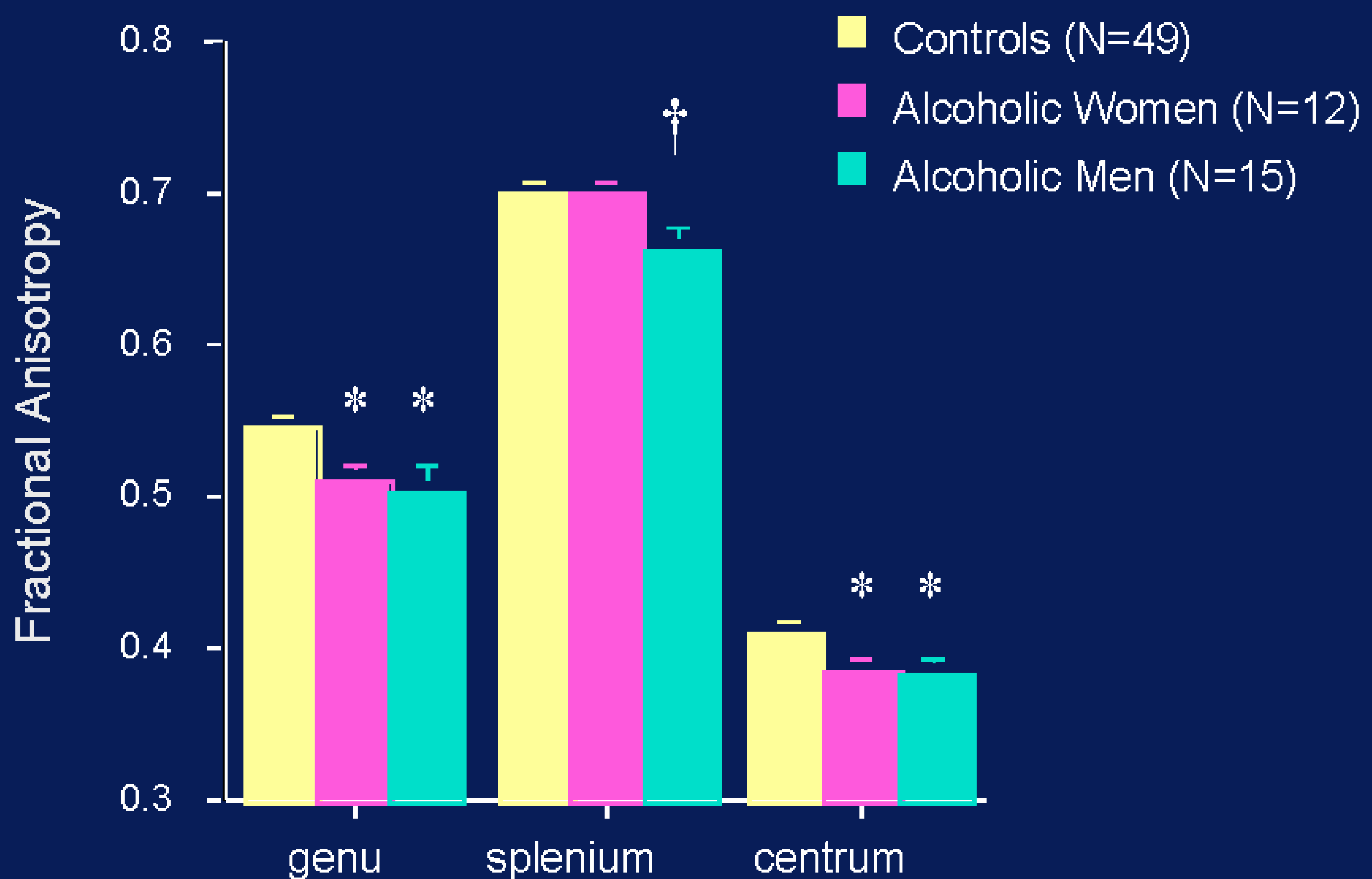
Pfefferbaum et al. *ACER* 2000

DTI in Alcoholic Women



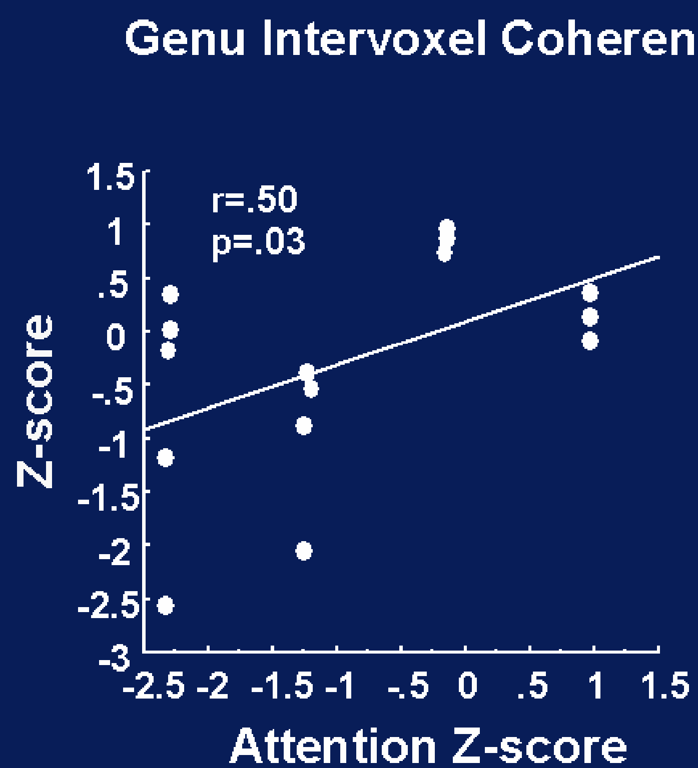
Pfefferbaum & Sullivan
NeuroImage 2002

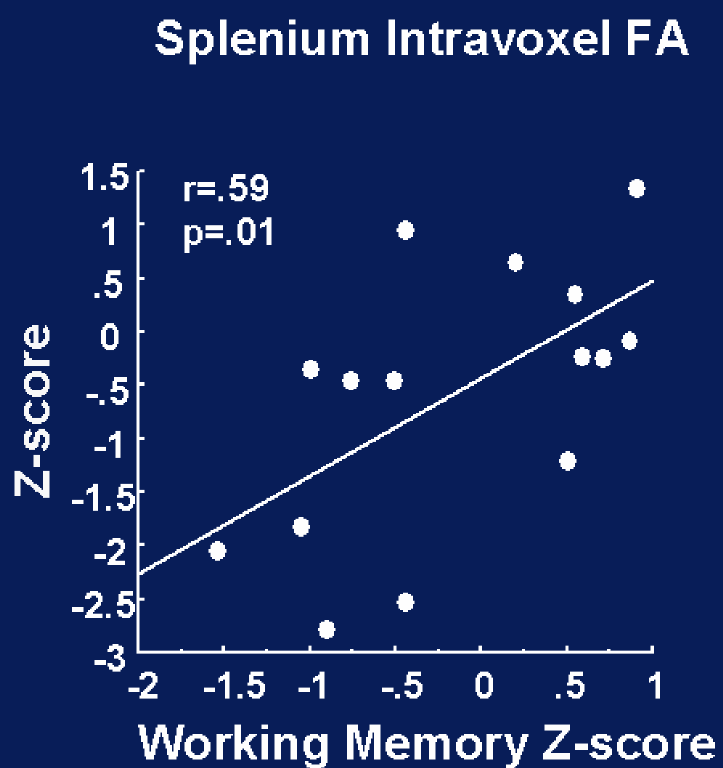
FA in Alcoholic Men and Women



Pfefferbaum & Sullivan
NeuroImage 2002

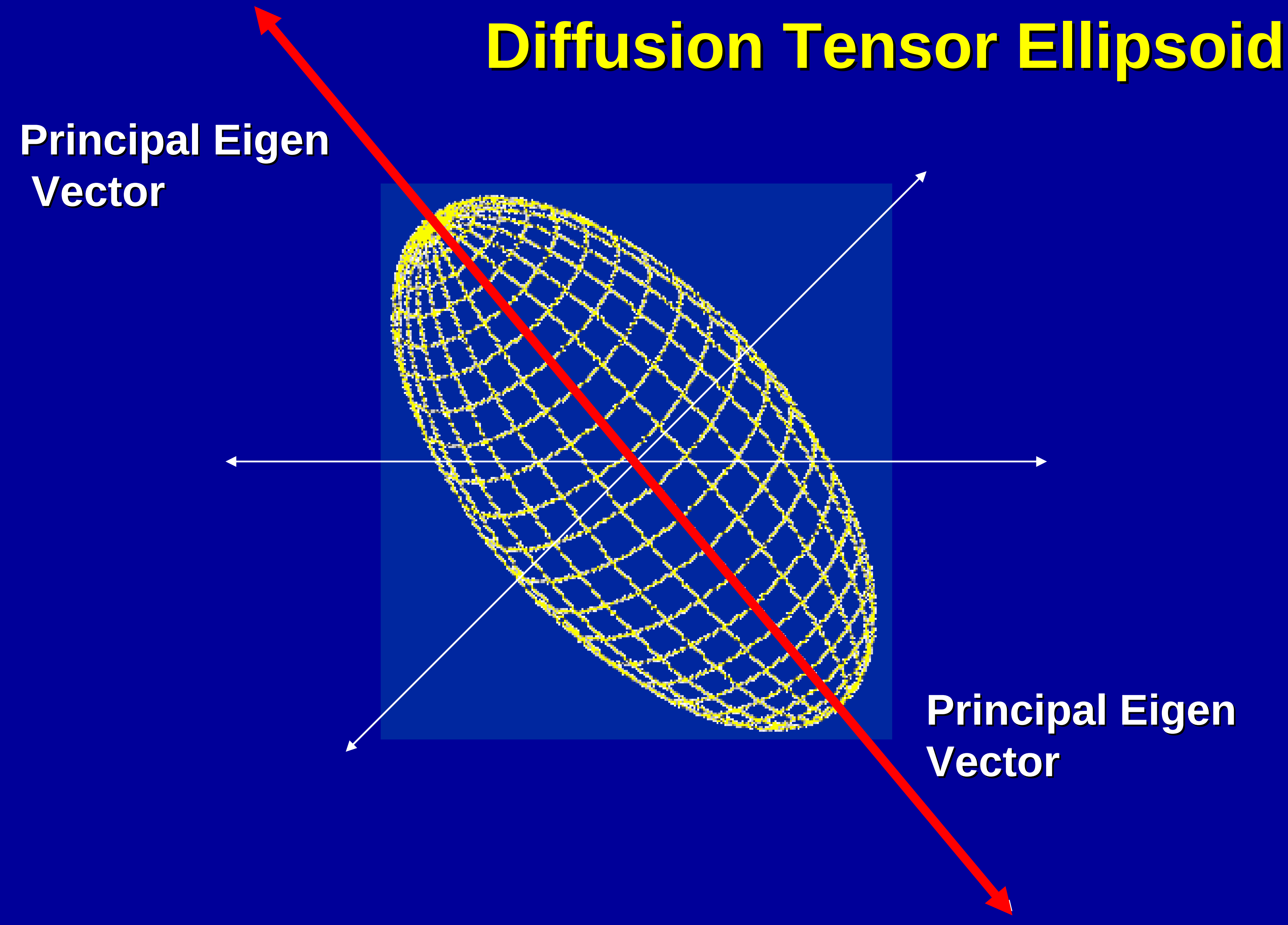
Selective DTI Coherence and Performance Relationships

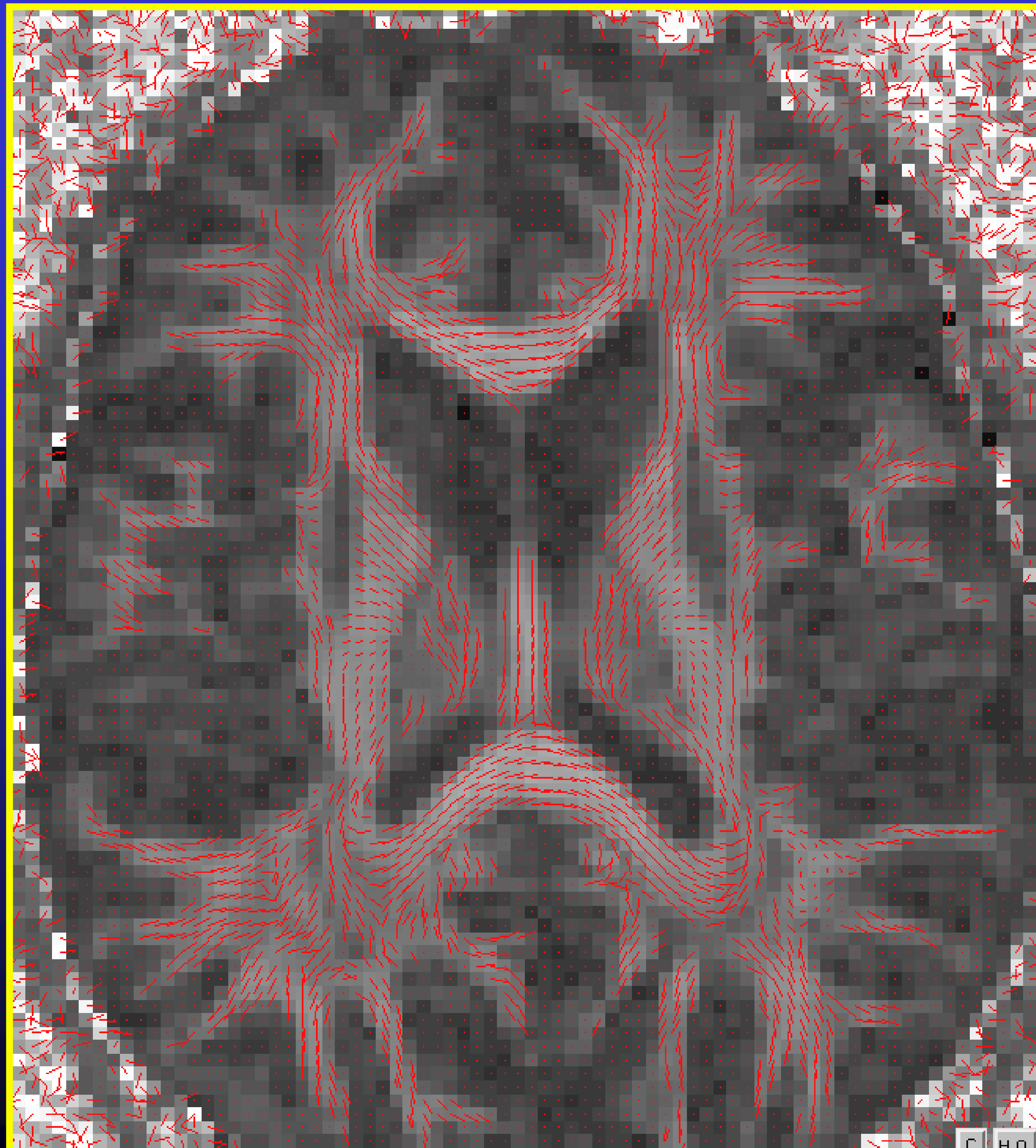


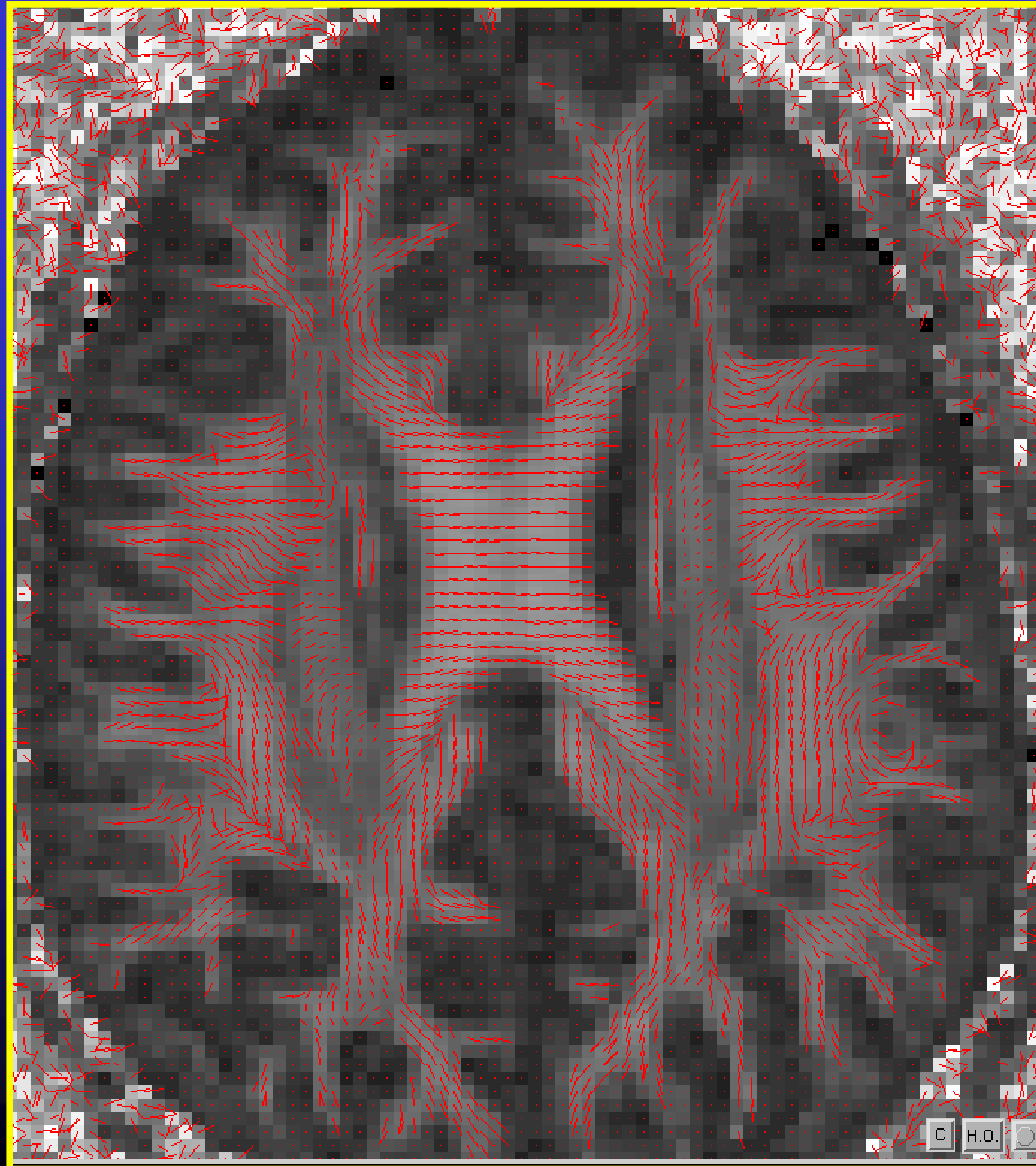


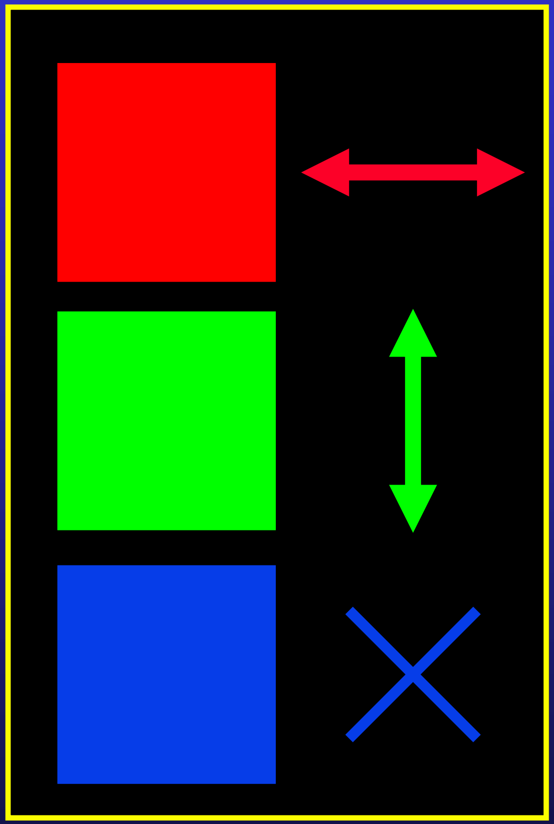
Pfefferbaum et al. *ACER* 2000

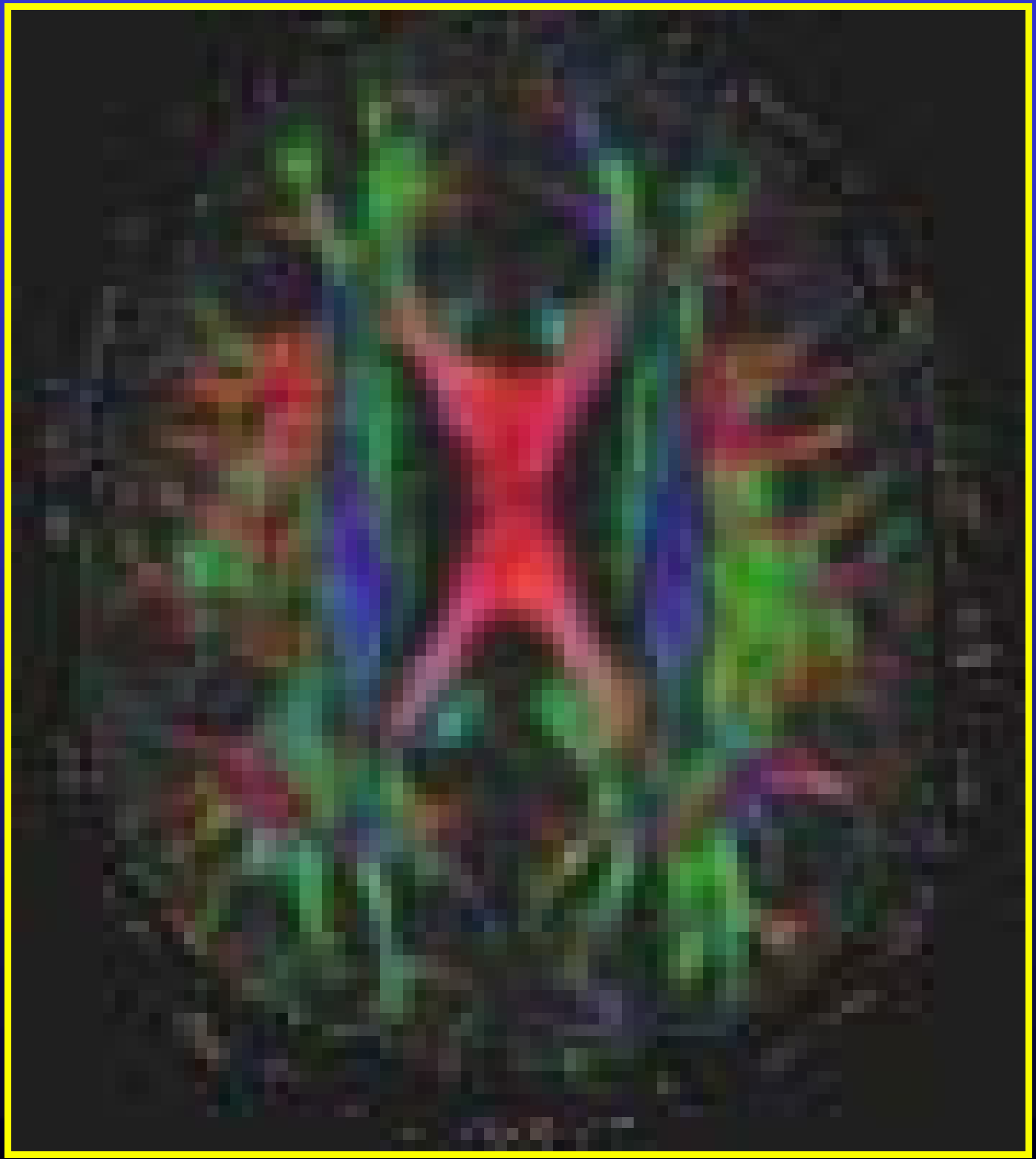
Diffusion Tensor Ellipsoid

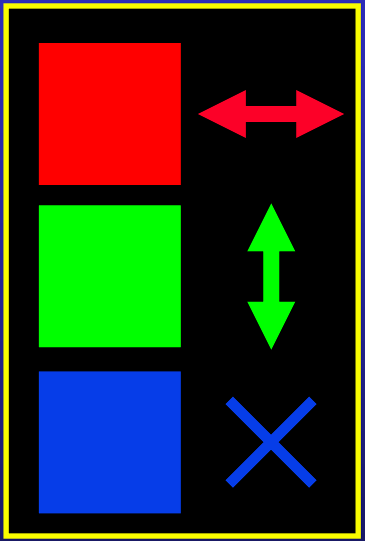
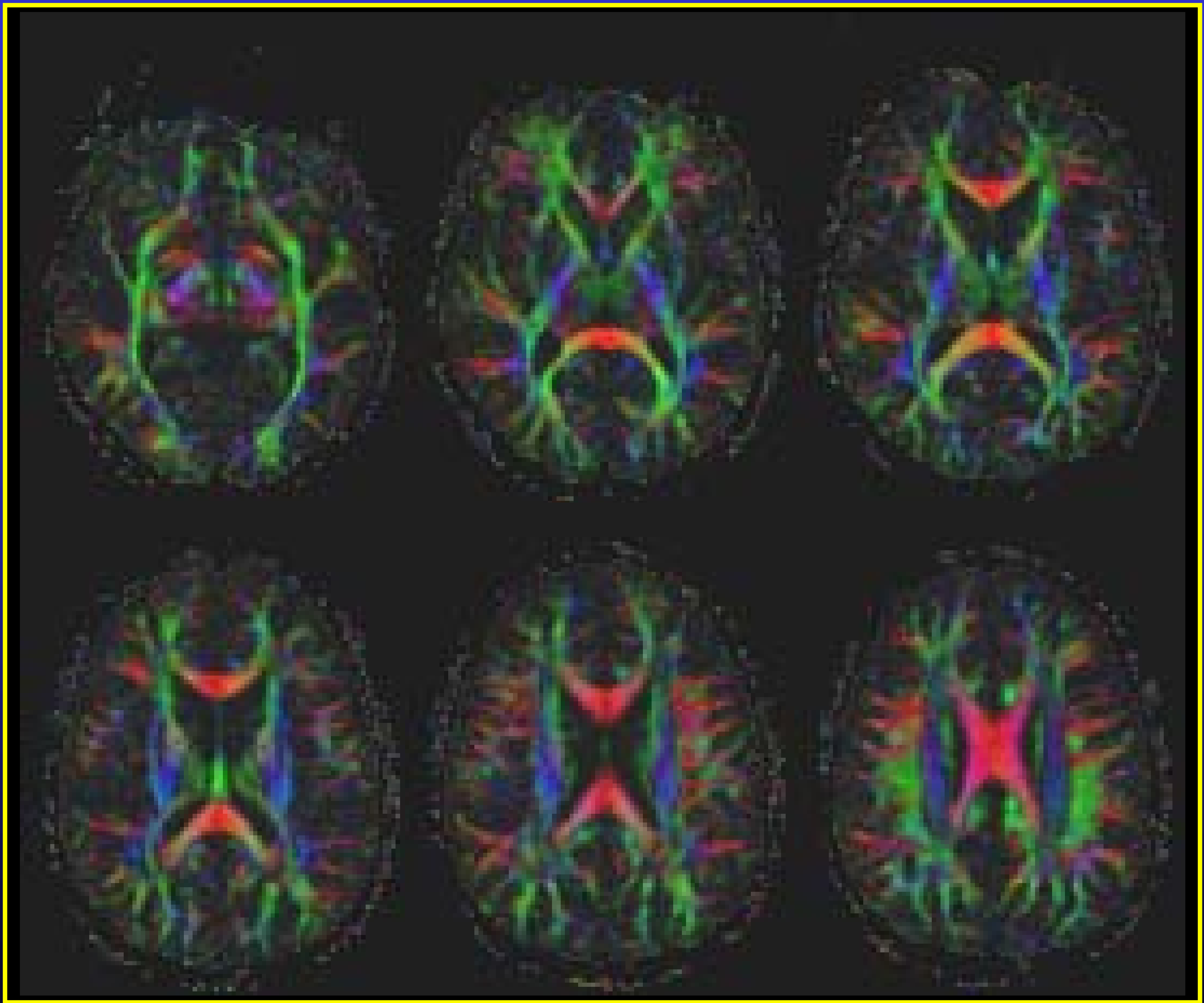


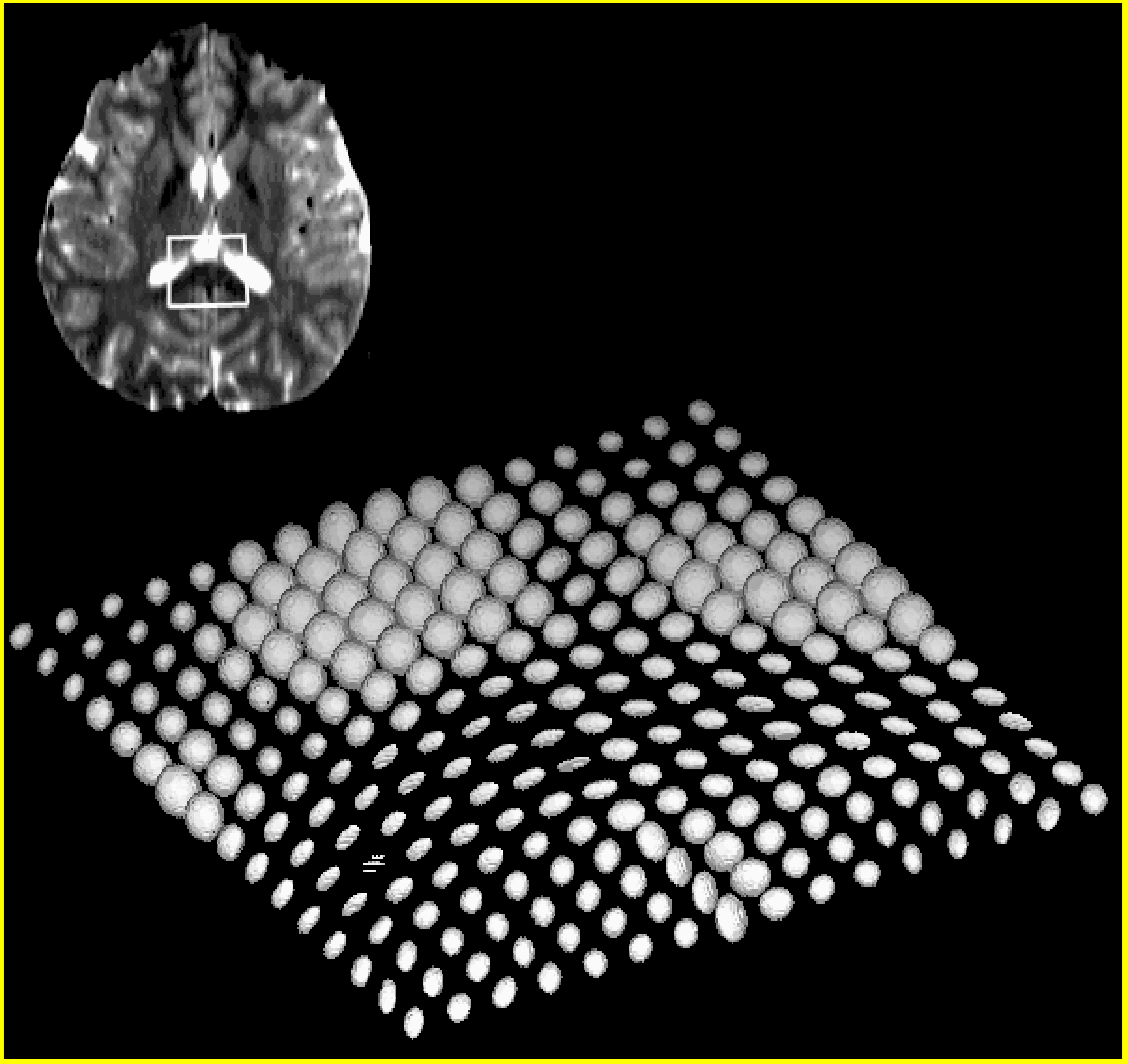

C
H.O.

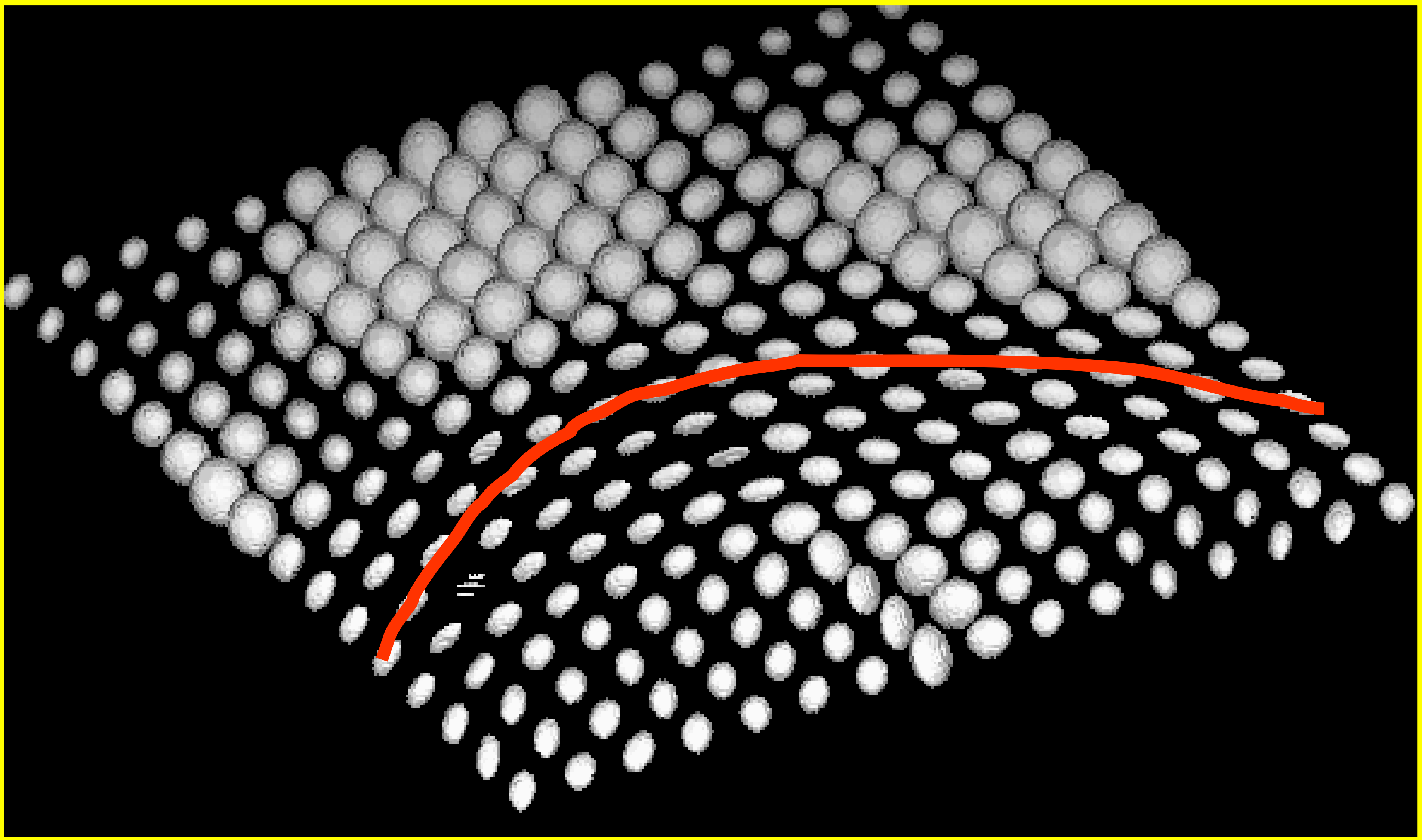

C
H.O.

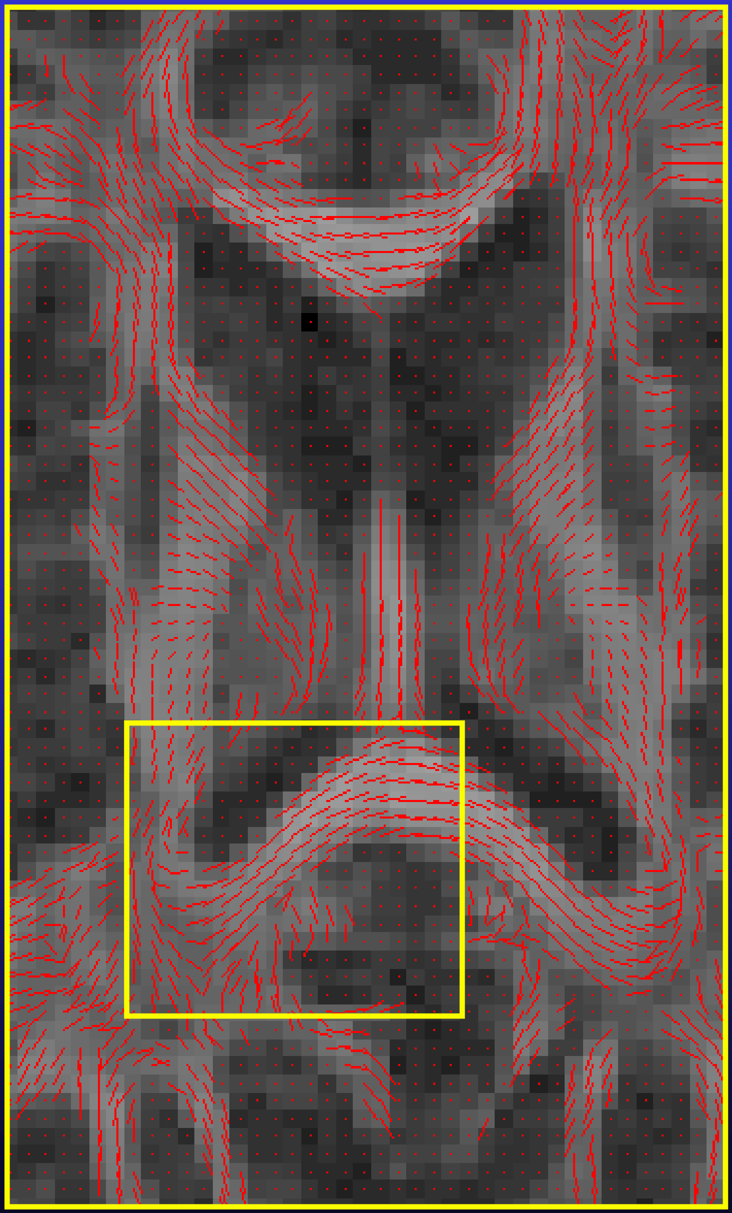
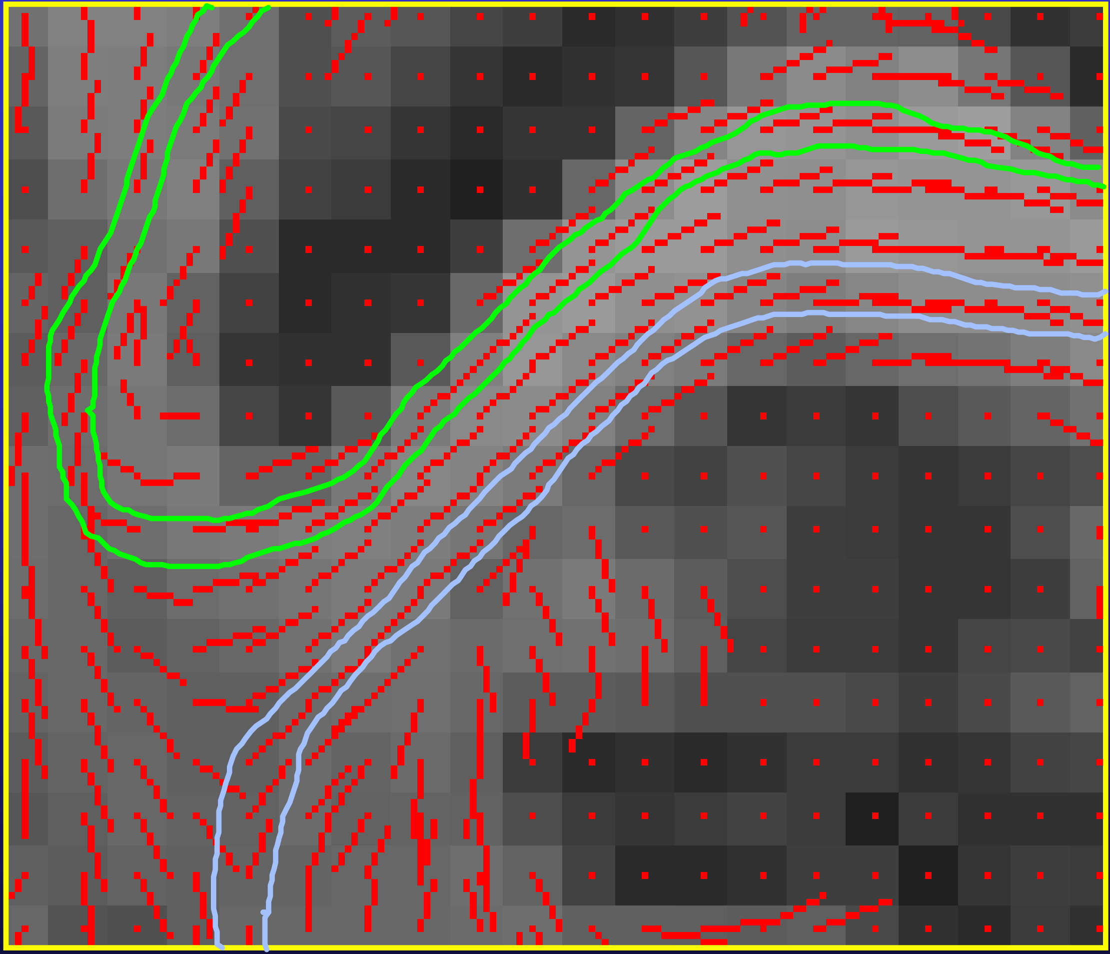


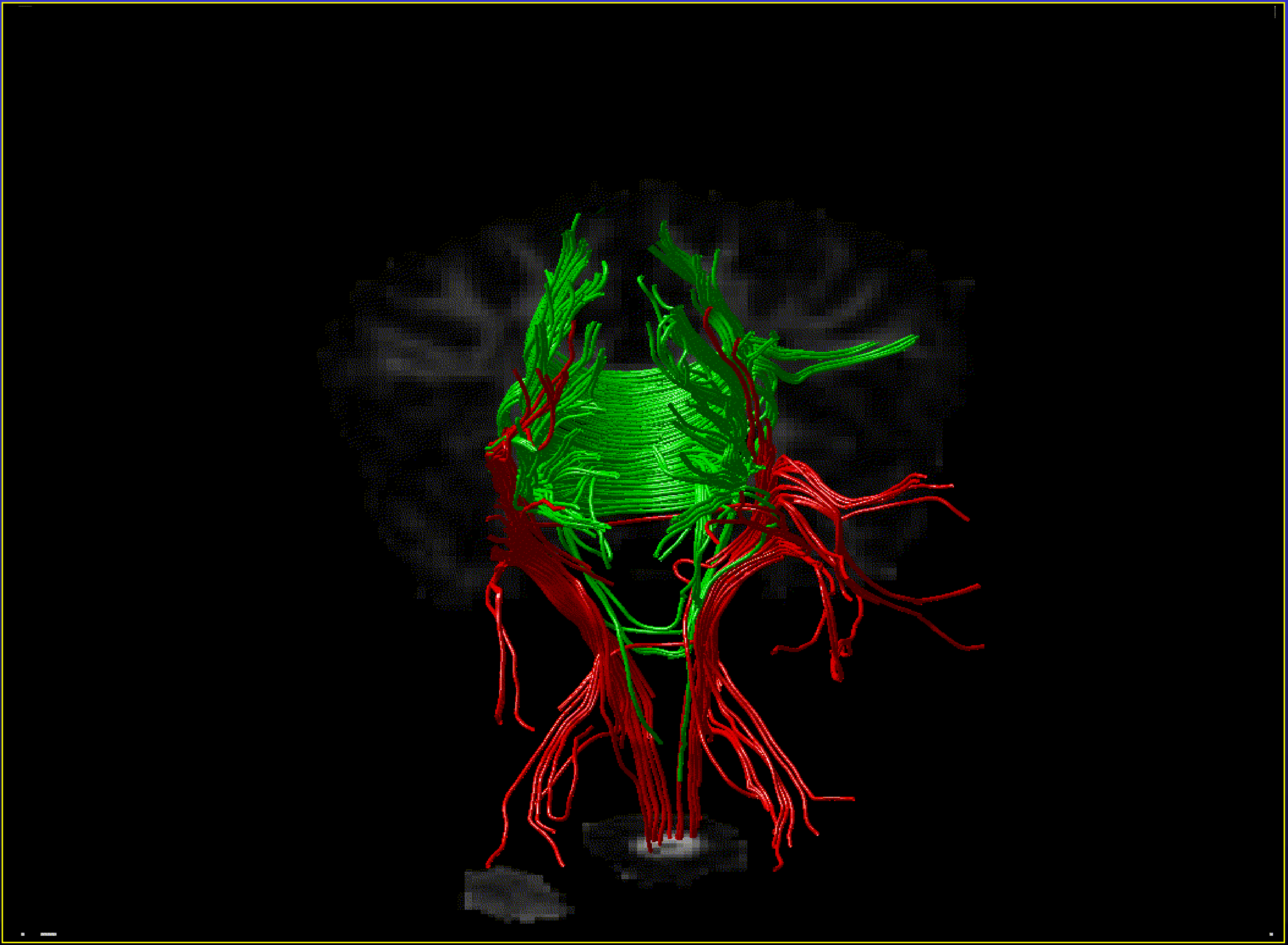




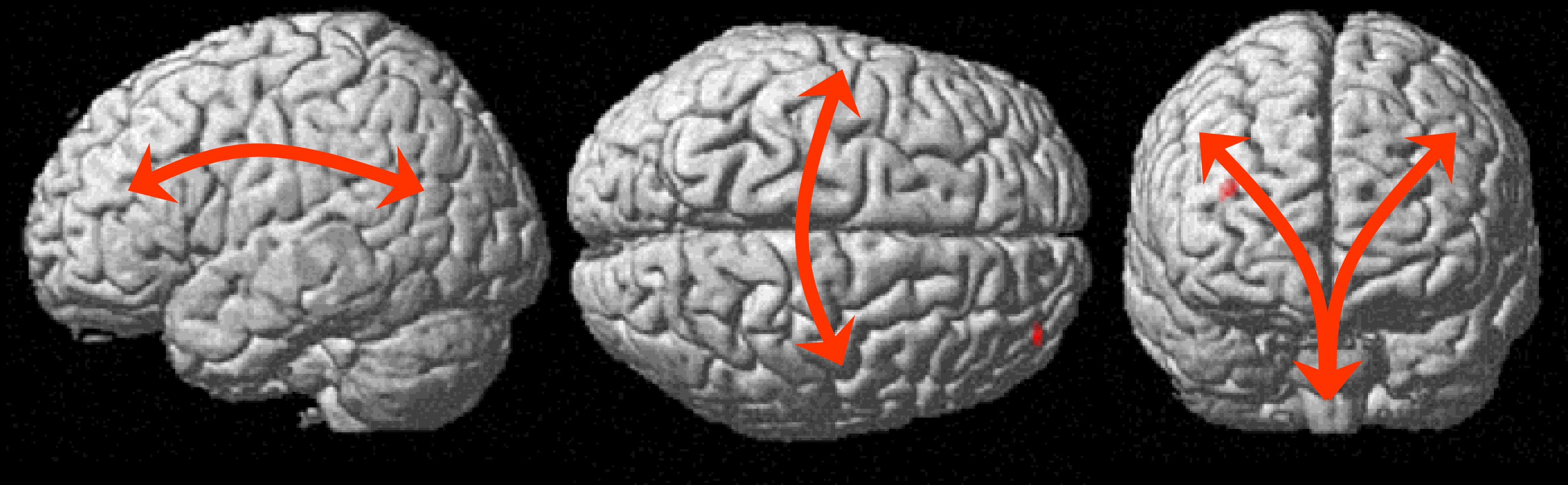


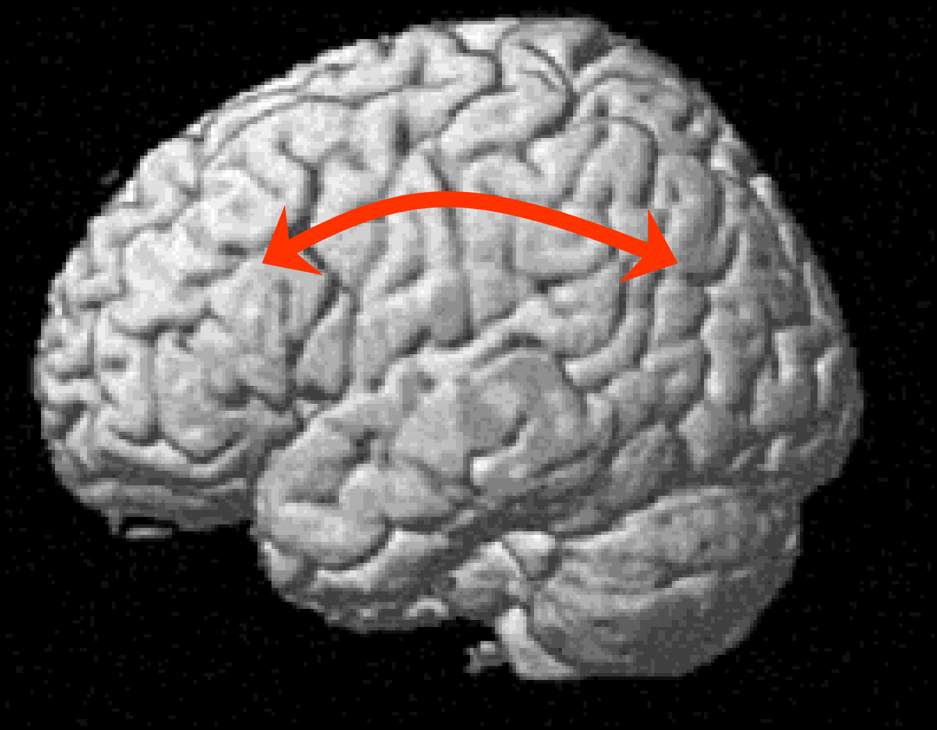


WHITE MATTER FASCICULI

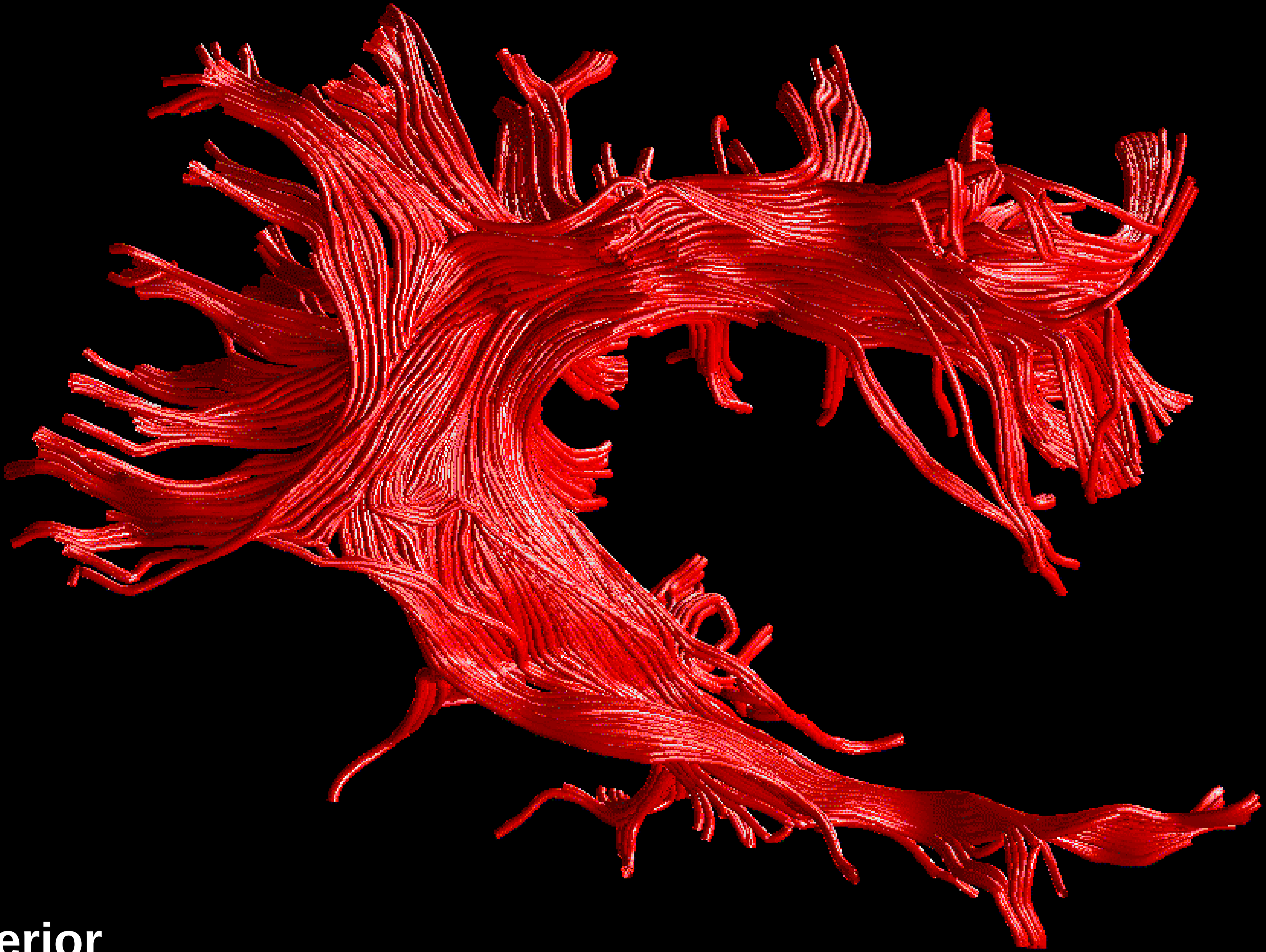
Association **Commissural** **Projection**



ASSOCIATION FASCICULI

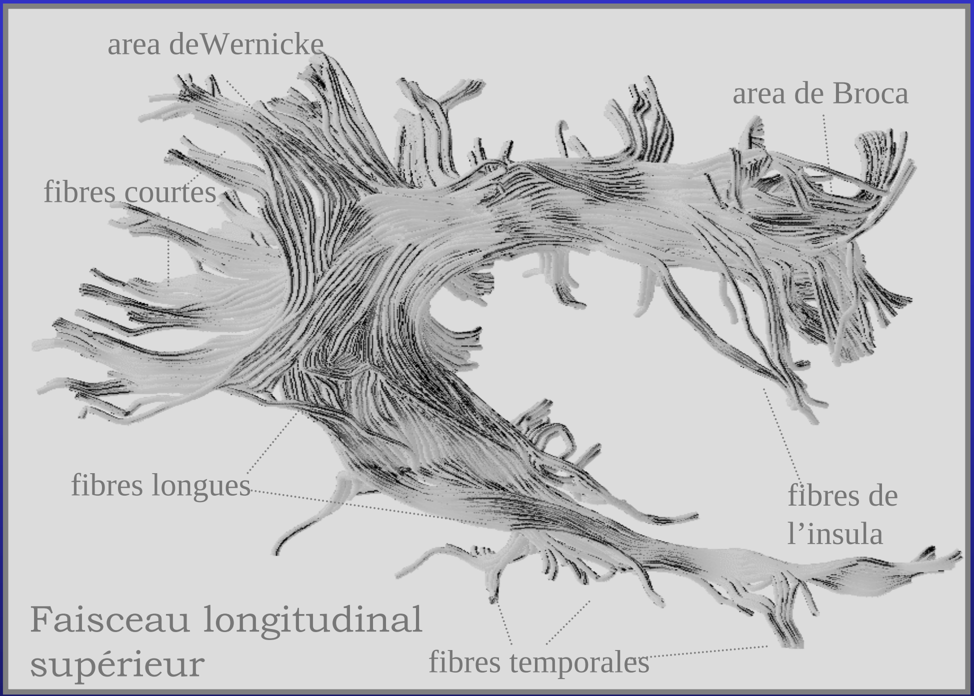


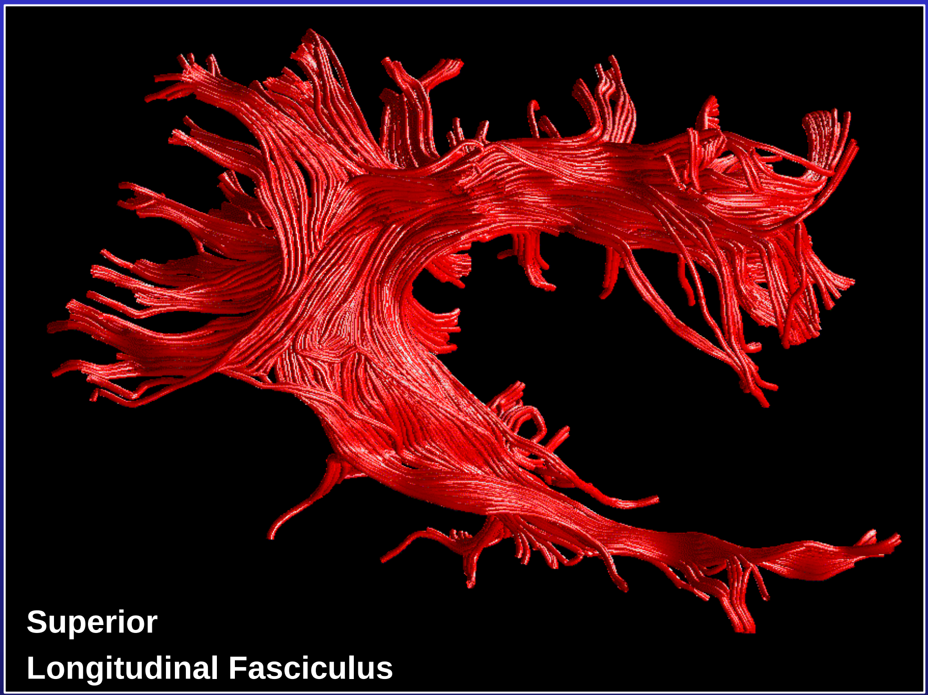
- Superior and inferior longitudinal fasciculi
- Superior and inferior fronto-occipital fasciculi
- Uncinate fasciculus
- Cingulum

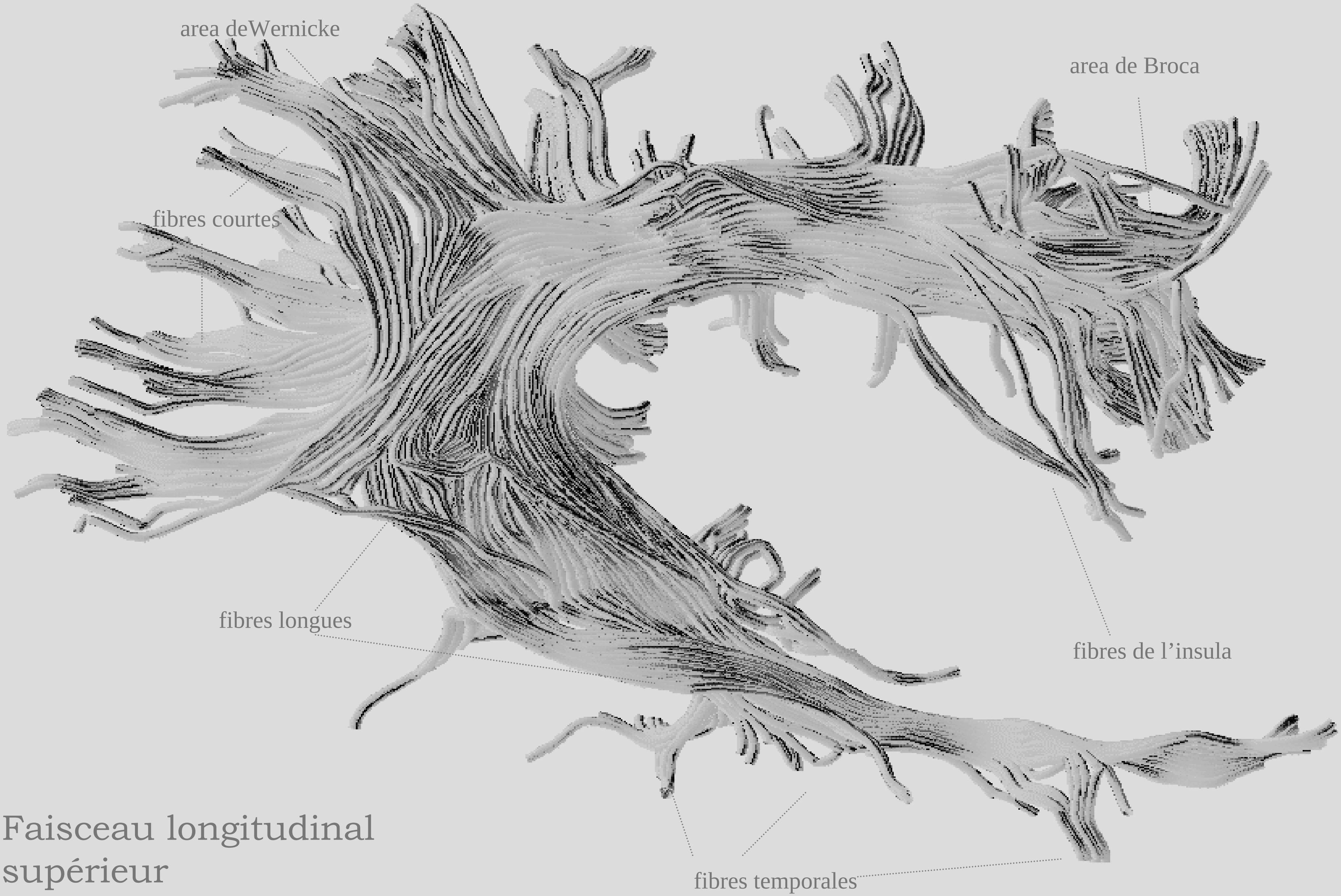


Superior

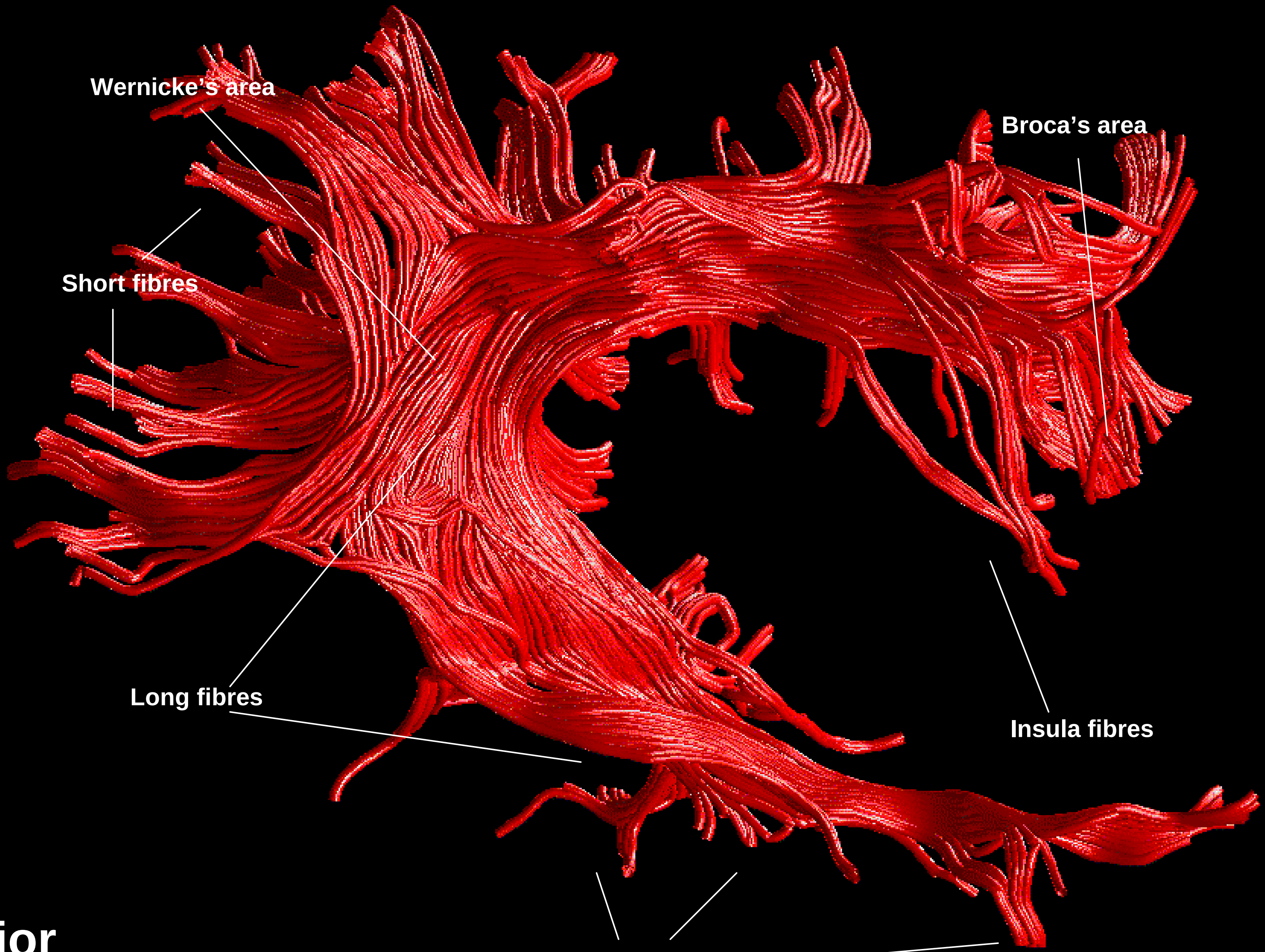
Longitudinal Fasciculus


area deWernicke
area de Broca
fibres courtes
fibres longues
fibres de
l'insula
Faisceau longitudinal
supérieur
fibres temporales


Superior
Longitudinal Fasciculus



Faisceau longitudinal supérieur



Superior Longitudinal Fasciculus

Virtual *In Vivo* Interactive Dissection

Virtual In Vivo Interactive Dissection of White Matter Fasciculi in the Human Brain

Marco Catani, Robert J Howard, Sinisa Pajevic, Derek K Jones

NeuroImage **17:** 77-94 (2002)

Superior Longitudinal Fasciculus

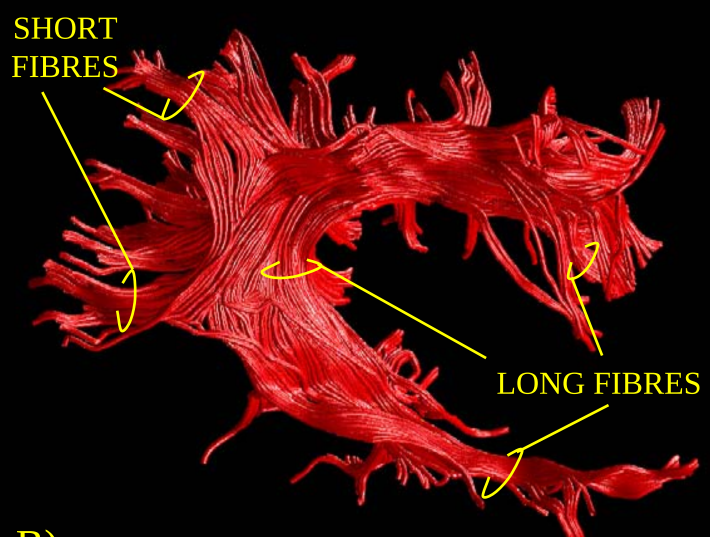
BROCA'S AREA

WERNICKE'S AREA

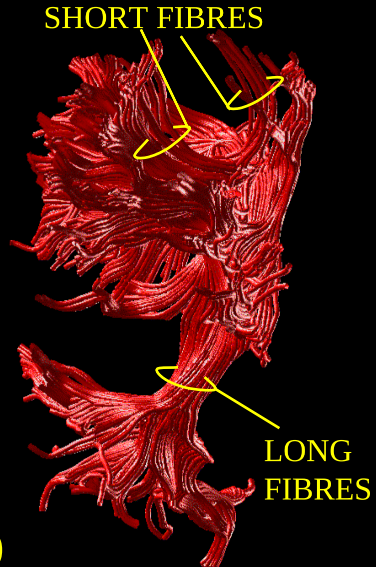
INSULAR FIBRES

TEMPORAL FIBRES

A)



B)



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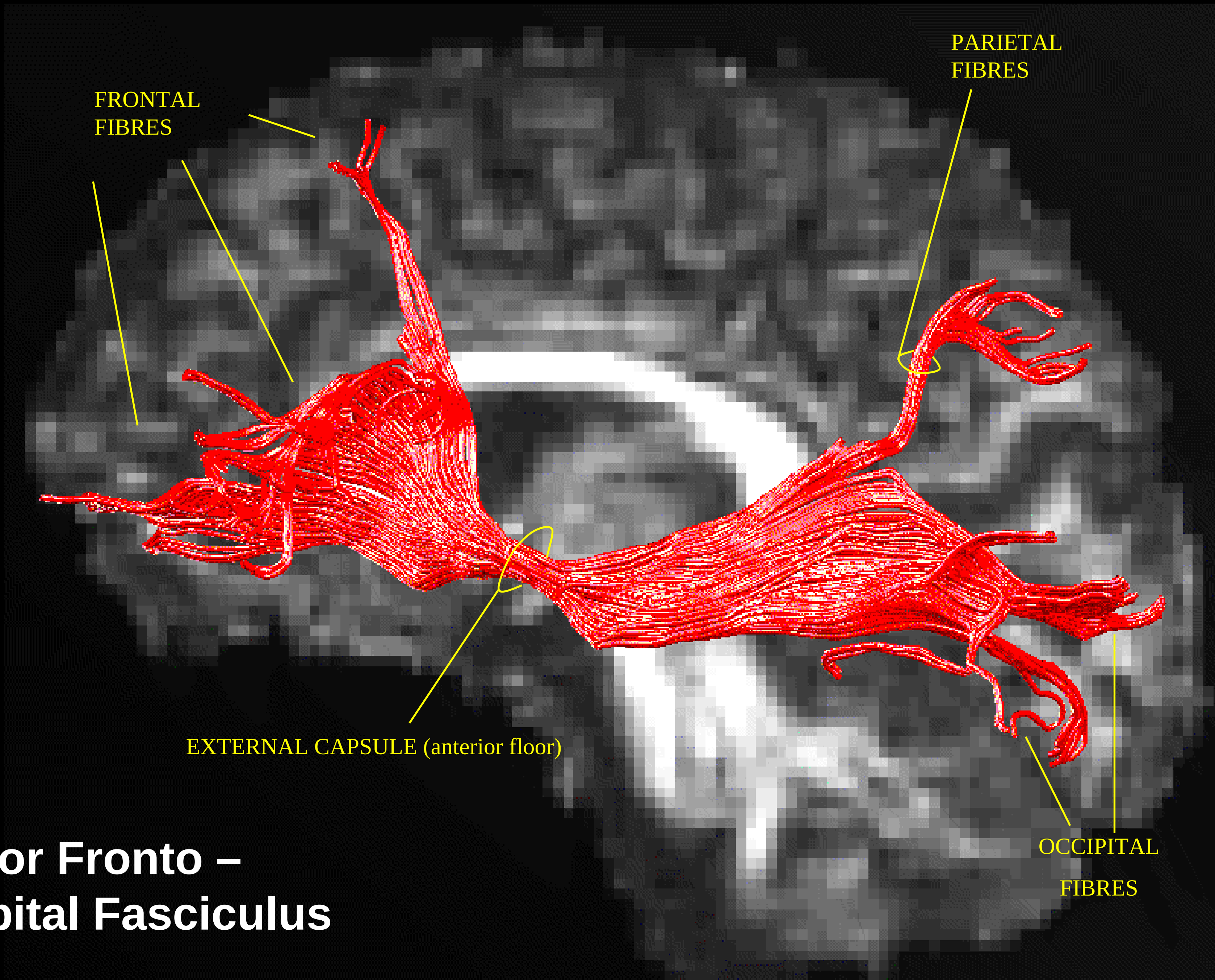
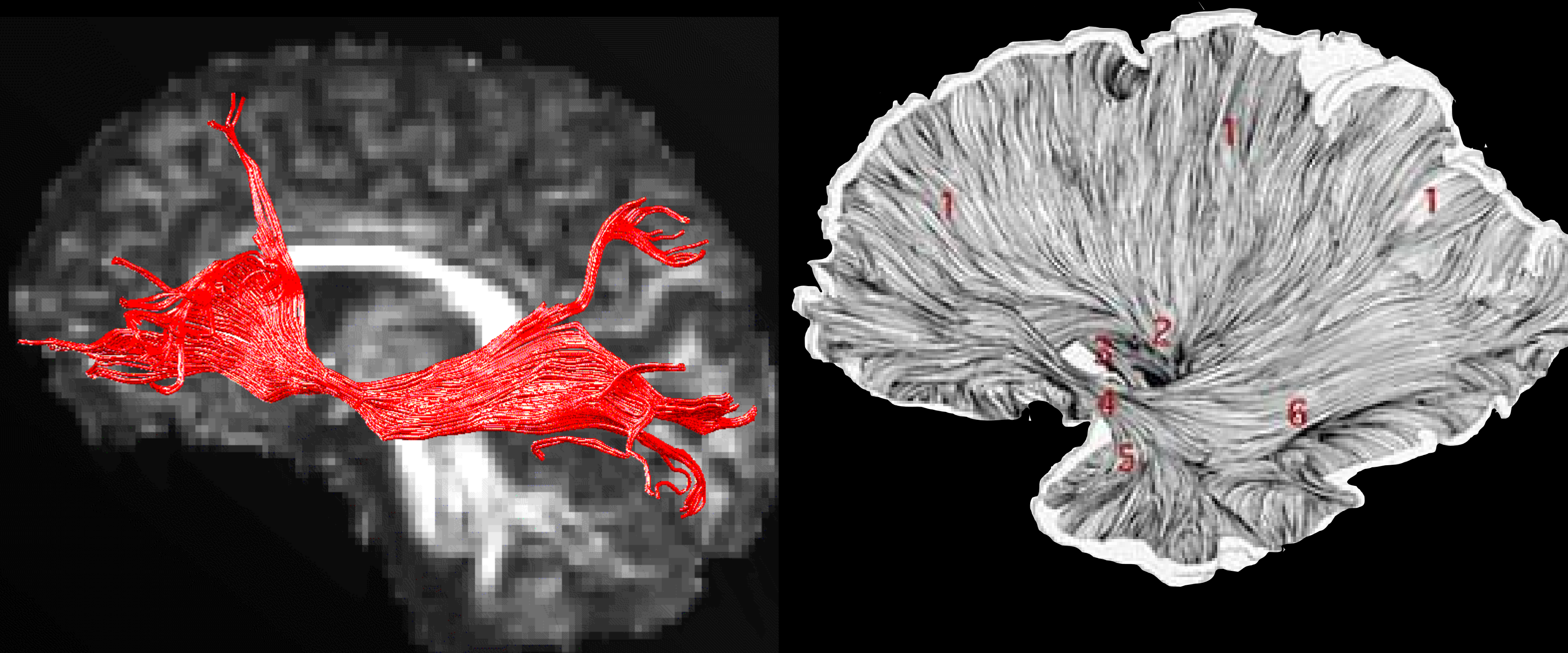
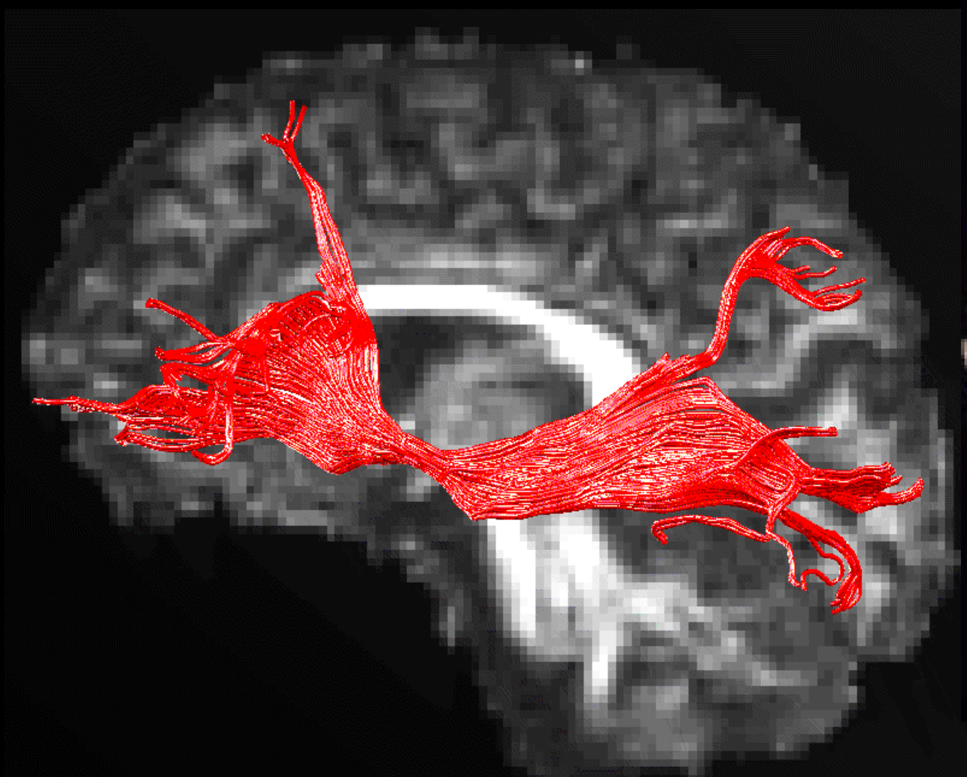
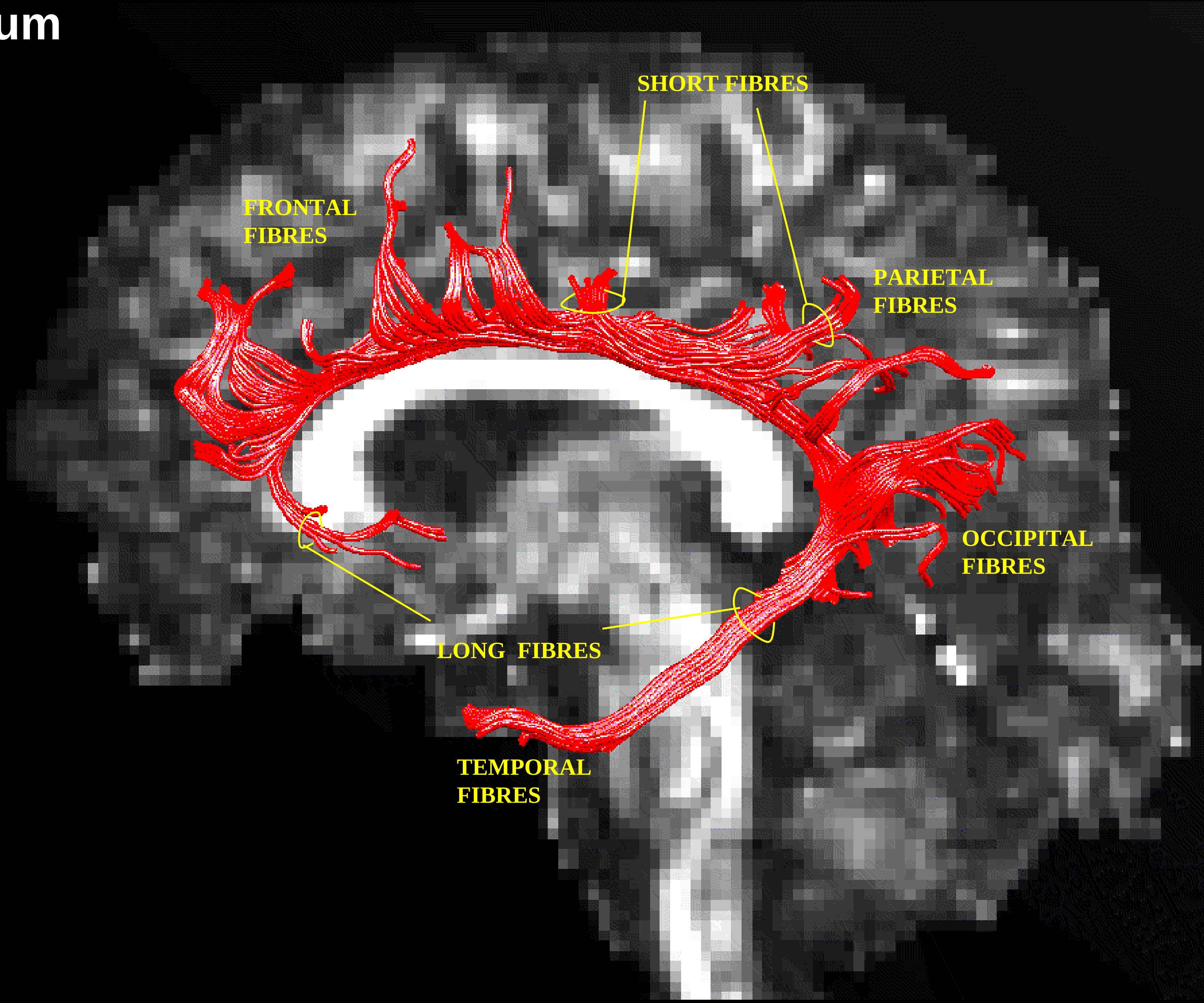


Inferior Fronto – Occipital Fasciculus

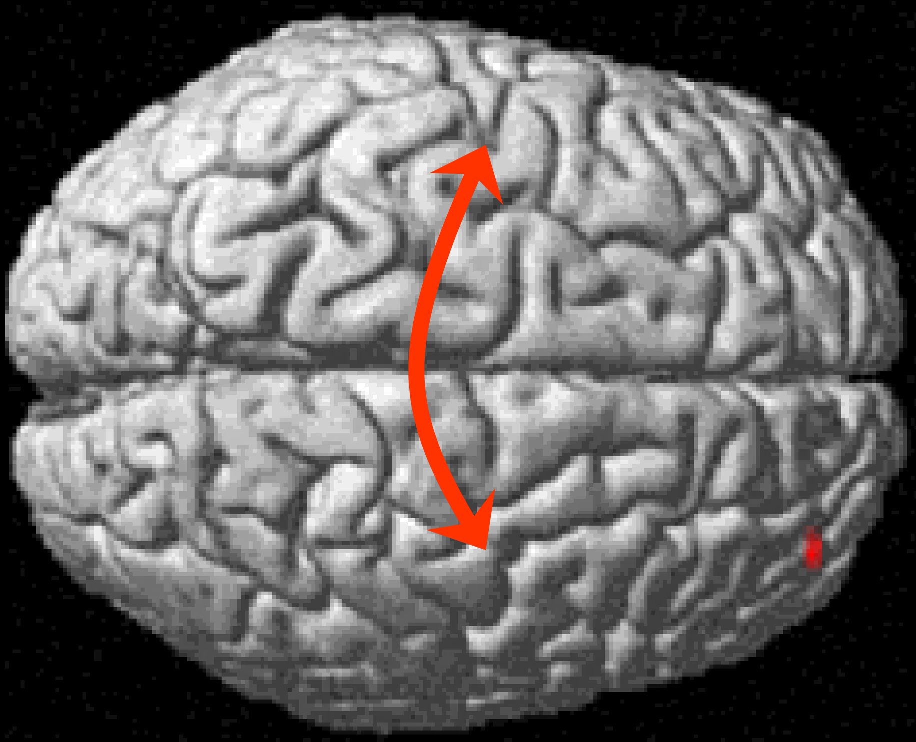

1
1
1
2
4
5
6



Cingulum

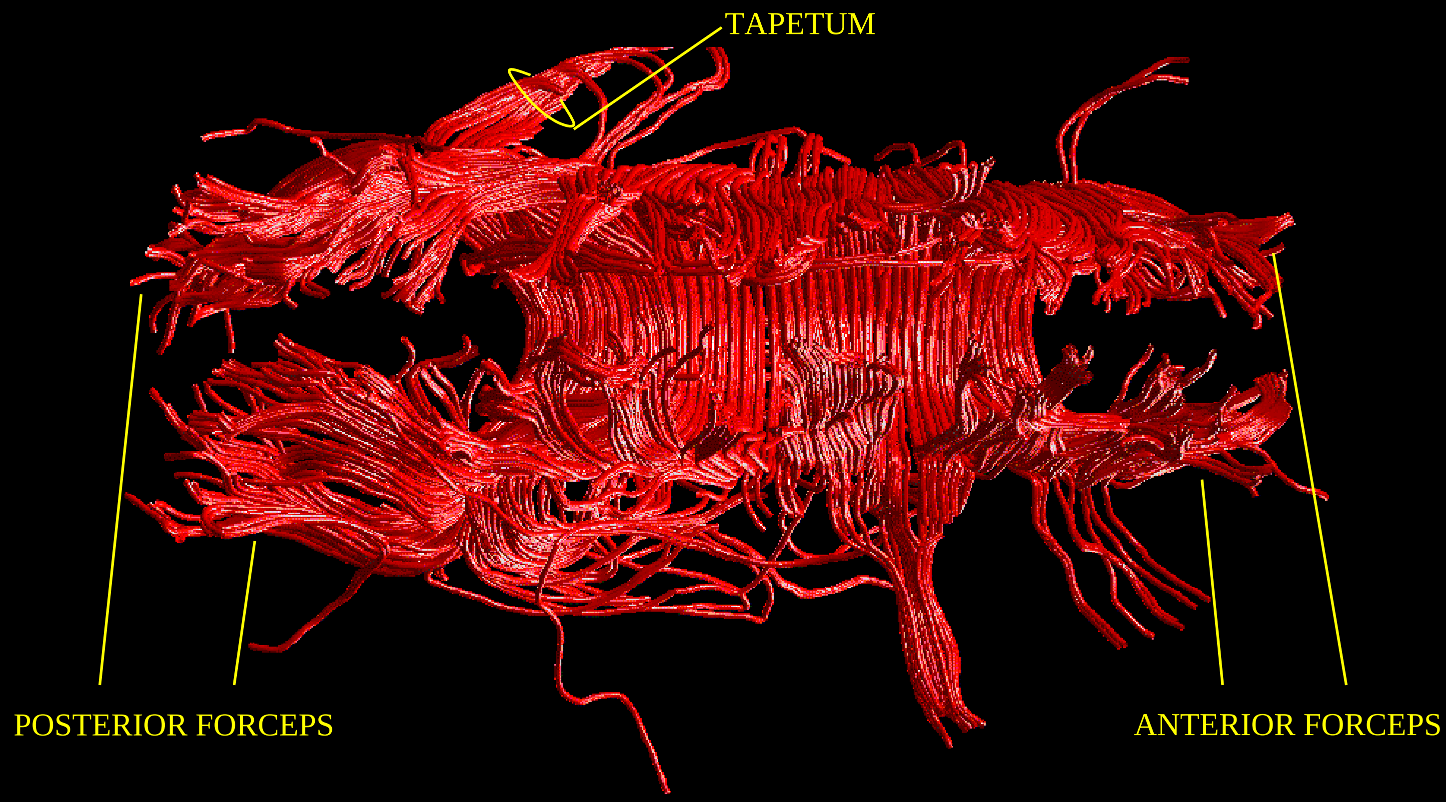

SHORT FIBRES
FRONTAL FIBRES
PARIETAL FIBRES
OCCIPITAL FIBRES
LONG FIBRES
TEMPORAL FIBRES

COMMISSURAL FASCICULI

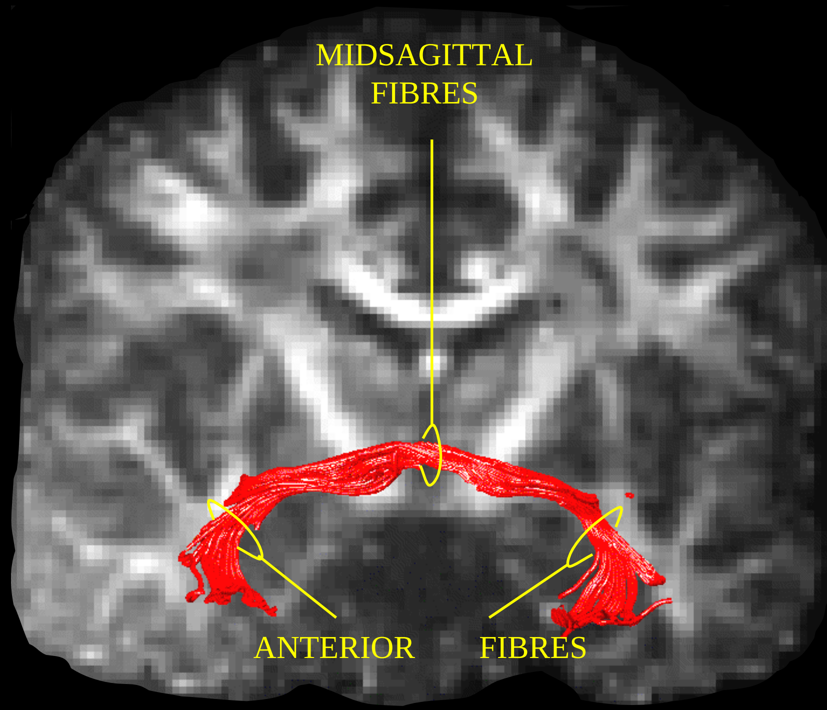


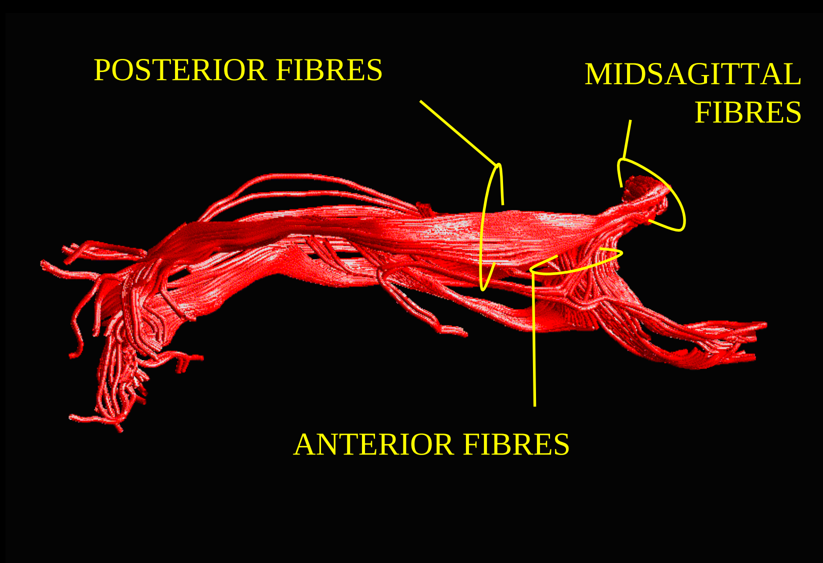
- Corpus callosum
- Anterior commissure

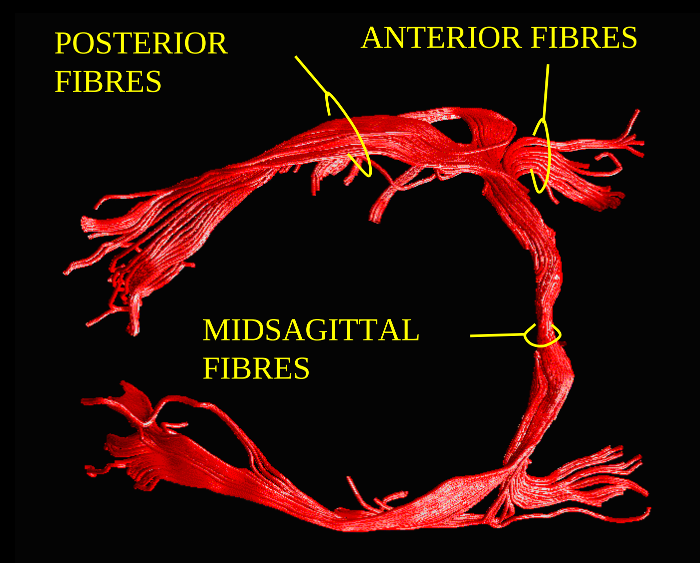
Corpus Callosum



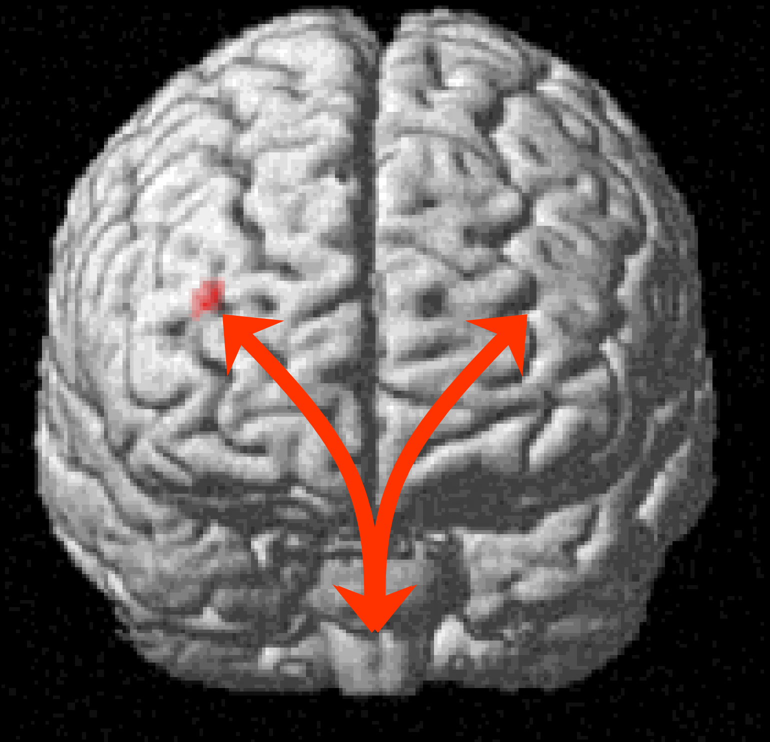
Anterior Commissure





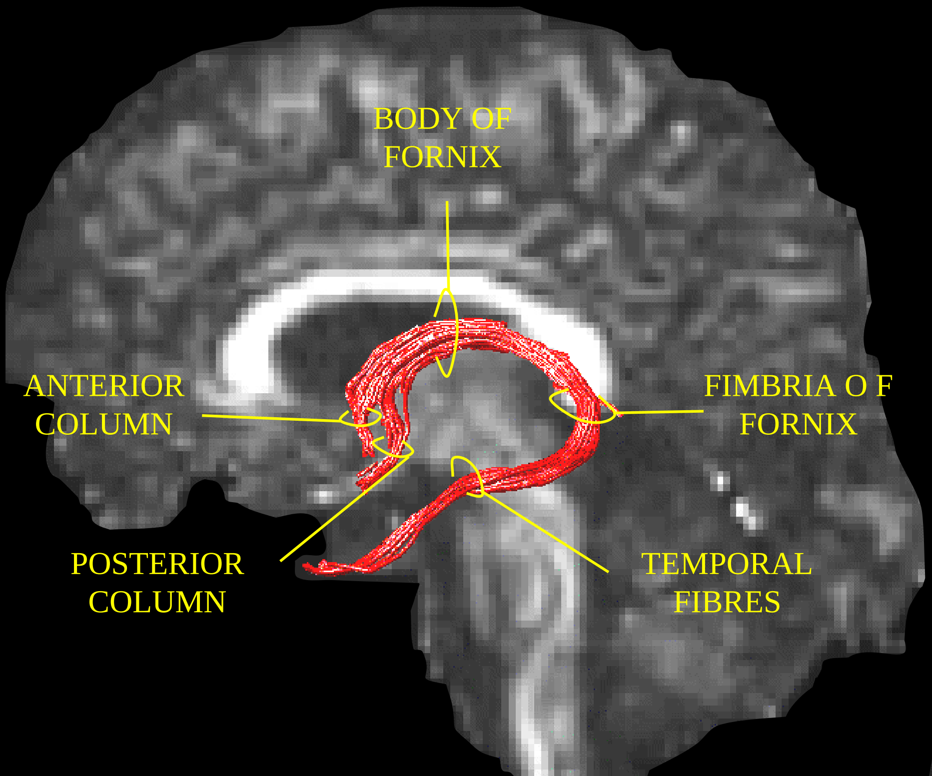


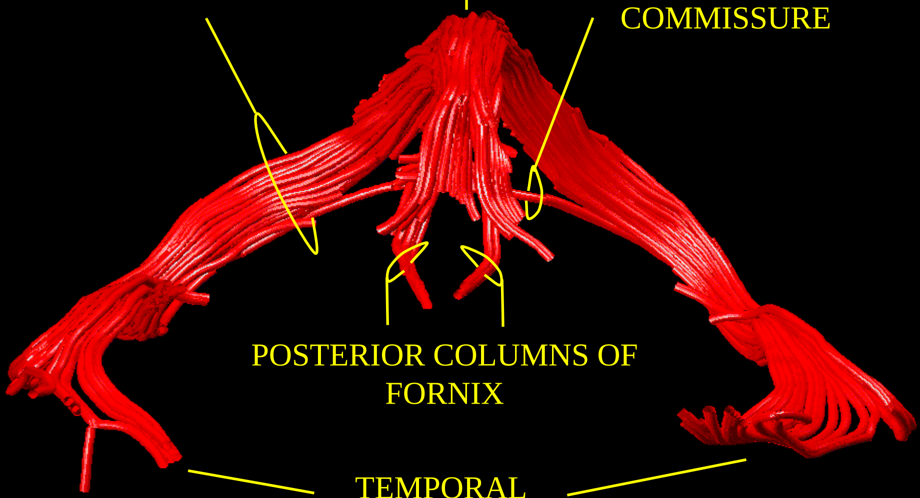
PROJECTION FASCICULI

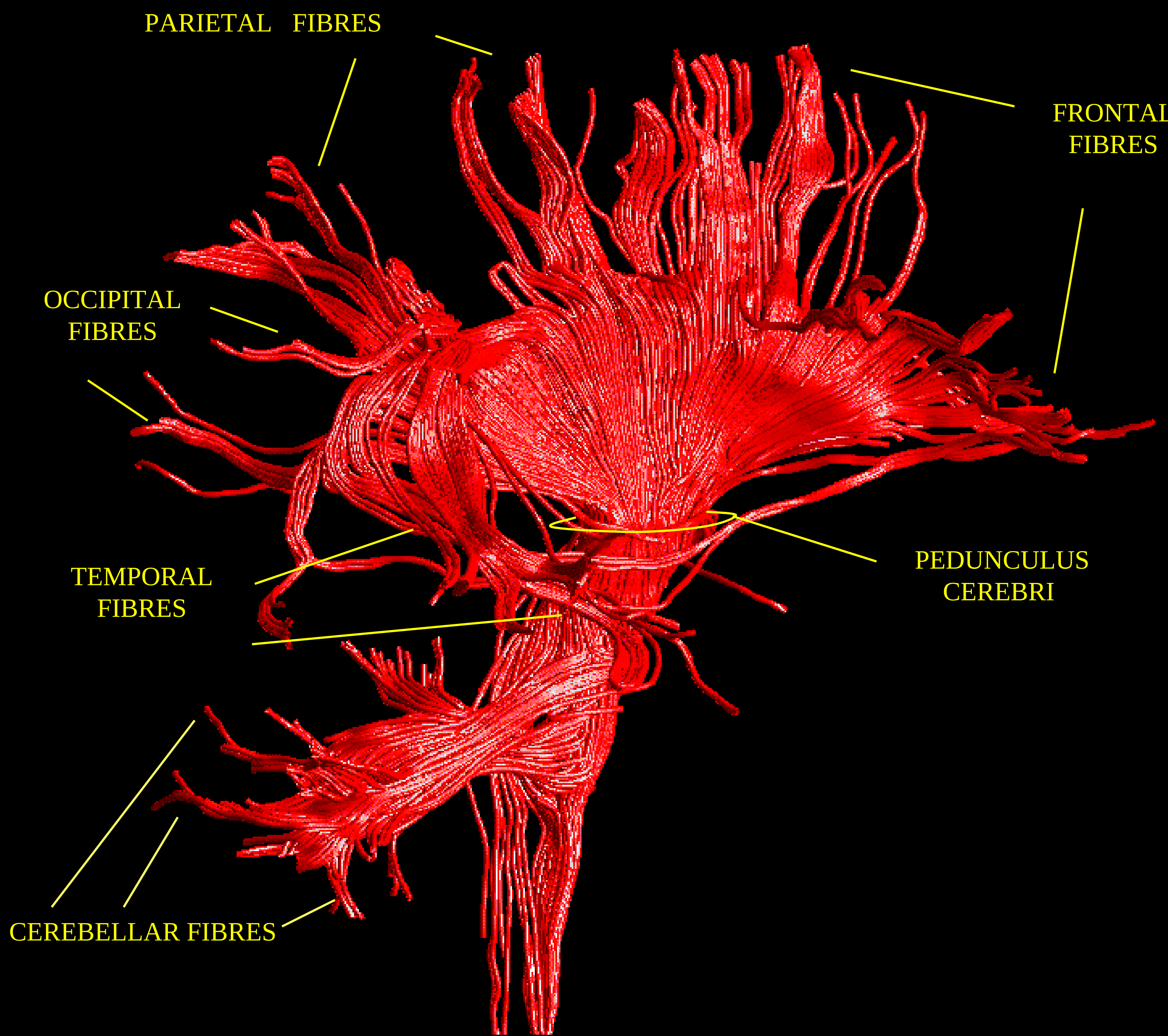


- Fornix
- Internal capsule

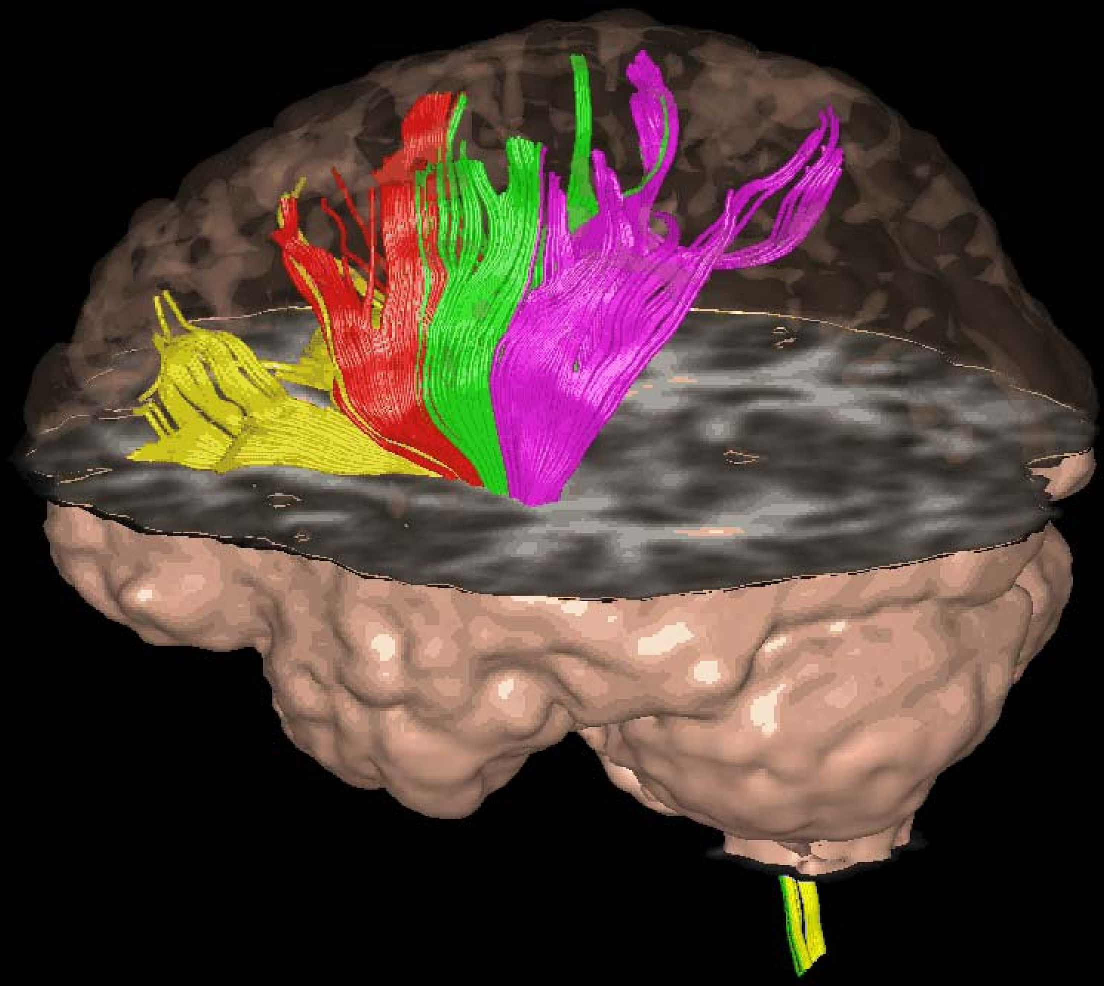
Fornix


BODY OF
FORNIX
ANTERIOR
COLUMN
FIMBRIA O F
FORNIX
POSTERIOR
COLUMN
TEMPORAL
FIBRES


BODY OF FORNIX
FIMBRIA OF FORNIX
POSTERIOR
COMMISSURE
POSTERIOR COLUMNS OF
FORNIX
TEMPORAL
FIBRES



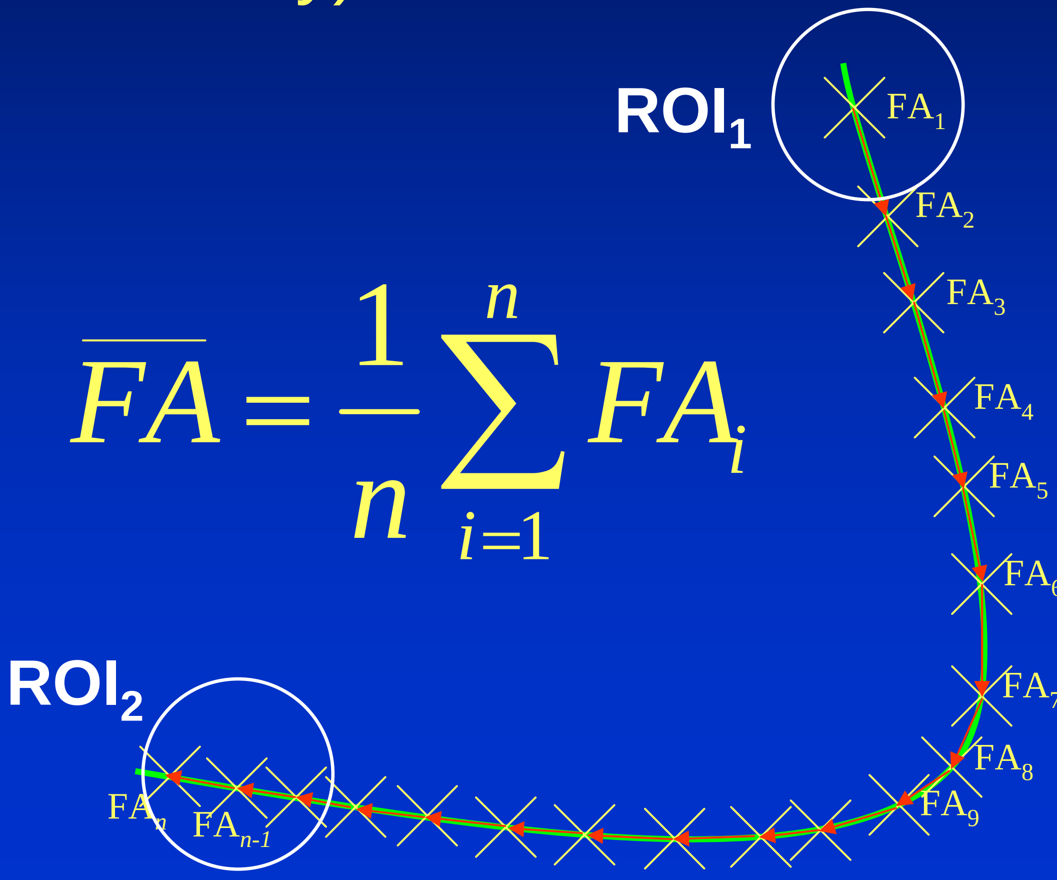
Internal Capsule



Tract Specific Measurements

- At end of every incremental step (0.5 mm), fractional anisotropy is determined
- Mean FA (or diffusivity) for entire bundle computed

$$\overline{FA} = \frac{1}{n}\sum_{i=1}^{n} FA_i$$



A Tractography Approach to Studying Fronto-Temporal Fasciculi in Schizophrenia and Late Onset Schizophrenia-Like Psychosis

Jones DK *et al.*

Proc ISMRM 11th Ann Meeting, p 244.

SUBJECTS

Young Patients

14 right-handed males	
Median age:	34 years (22-53 years)
Median duration of illness:	8 years (1 – 25 years)
Mean IQ:	110 (98 – 124)

Young Controls

14 right-handed males	
Median age:	34 years (22-53 years)
Median IQ:	109 (99 – 123)

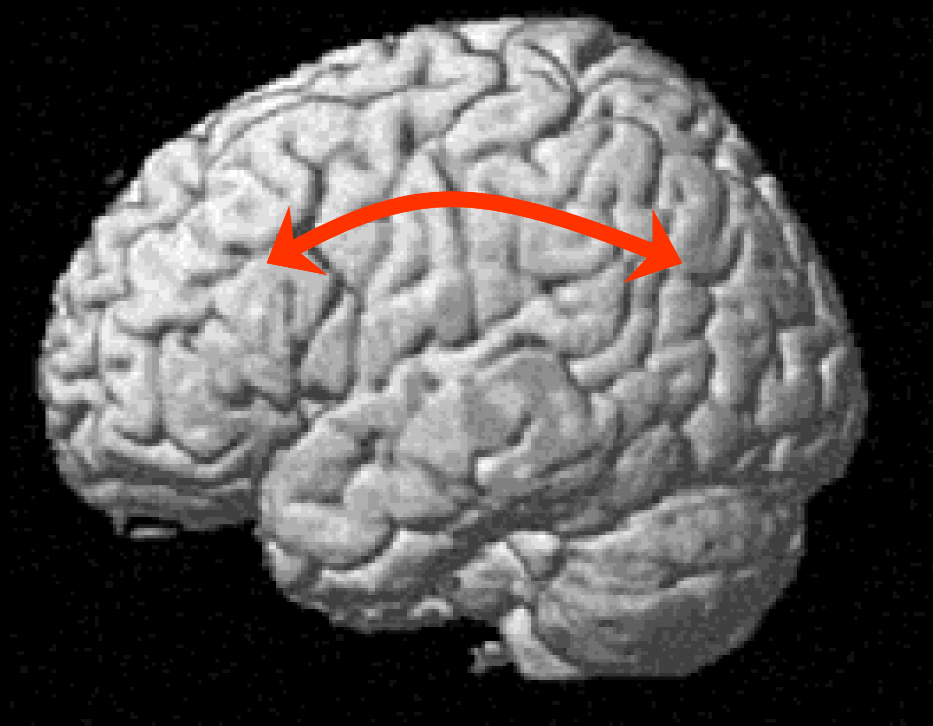
ACQUISITION PROTOCOL

1.5 T GE Signa LX (G_{max}= 40 mT m^{-1})

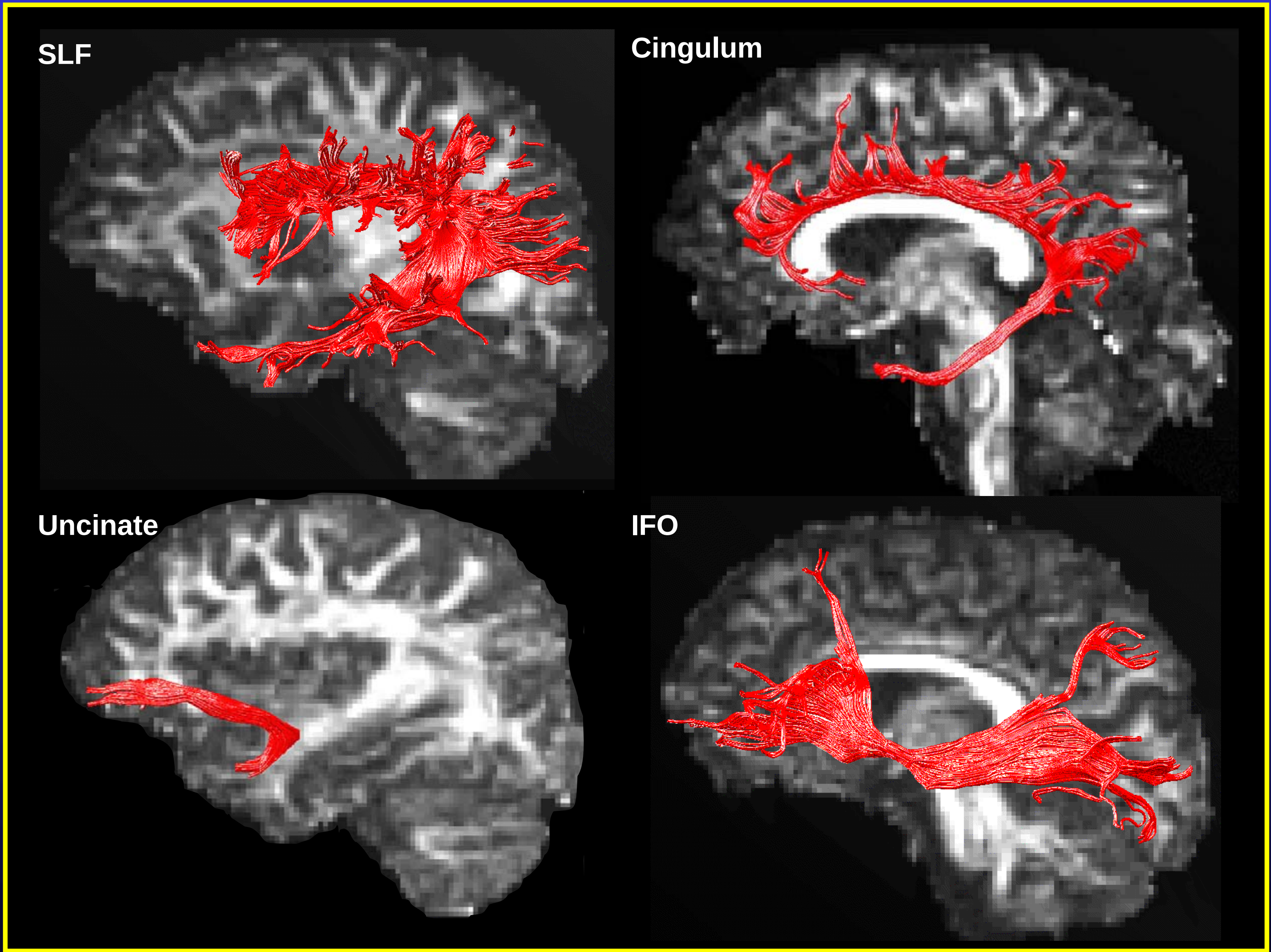
<u>Imaging Parameters</u>	
Acquisition Matrix	96 x 96
Field of View	240 mm
Slice Thickness / Gap	2.50 mm / 0.0 mm
# Slice Locations	60
Echo Time	102 ms
Repetition Time	15 R-R (delay = 200ms)
Duration of diffusion grads	17.3 ms
# *b*-matrices	71 (N_{low} = 7, N_{high}= 64)
Total scan time	14 minutes

Jones et al. Human Brain Mapping 15: 216-230 (2002)

ASSOCIATION FASCICULI



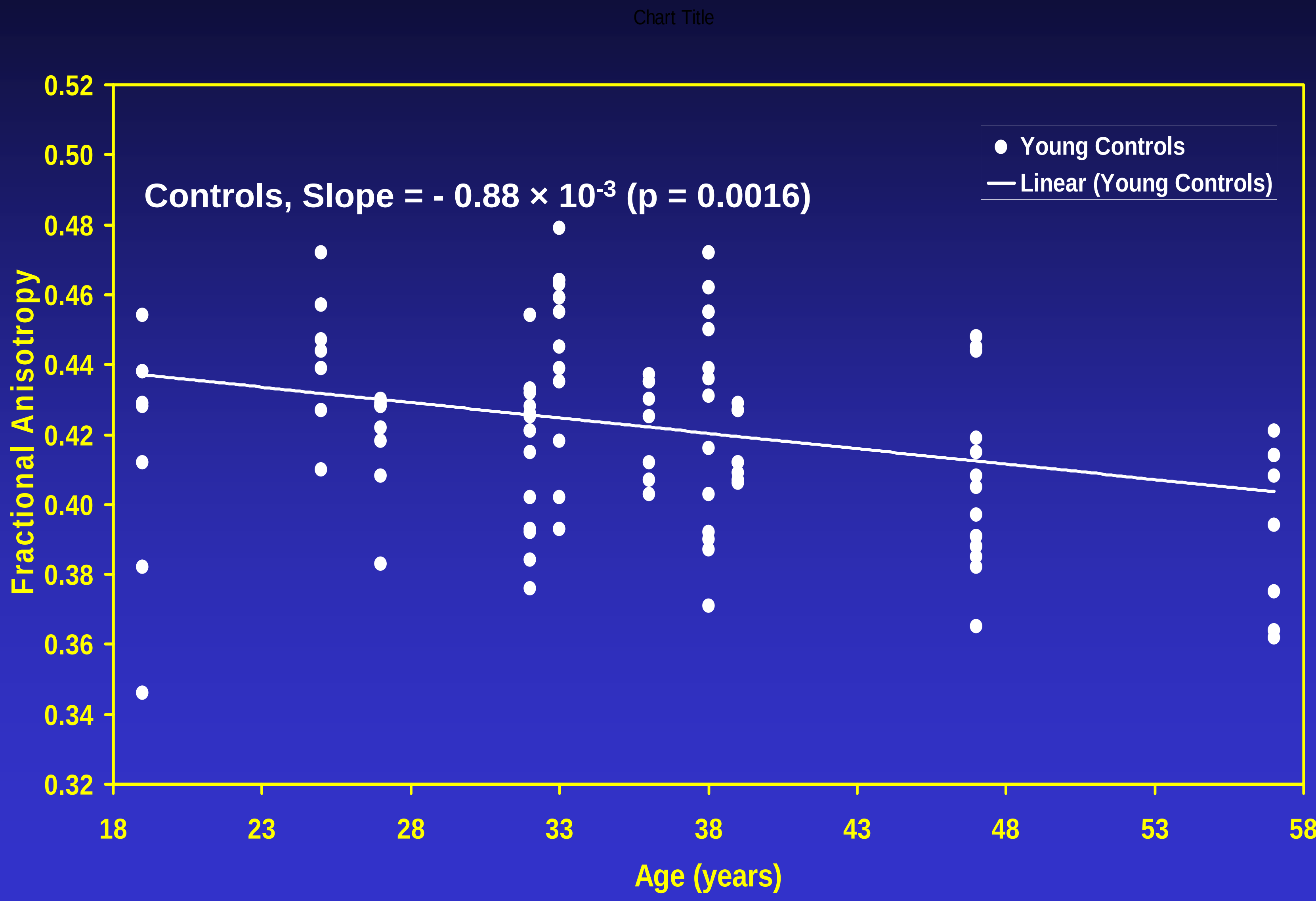
- Superior longitudinal fasciculus
- Inferior fronto-occipital fasciculus
- Uncinate fasciculus
- Cingulum

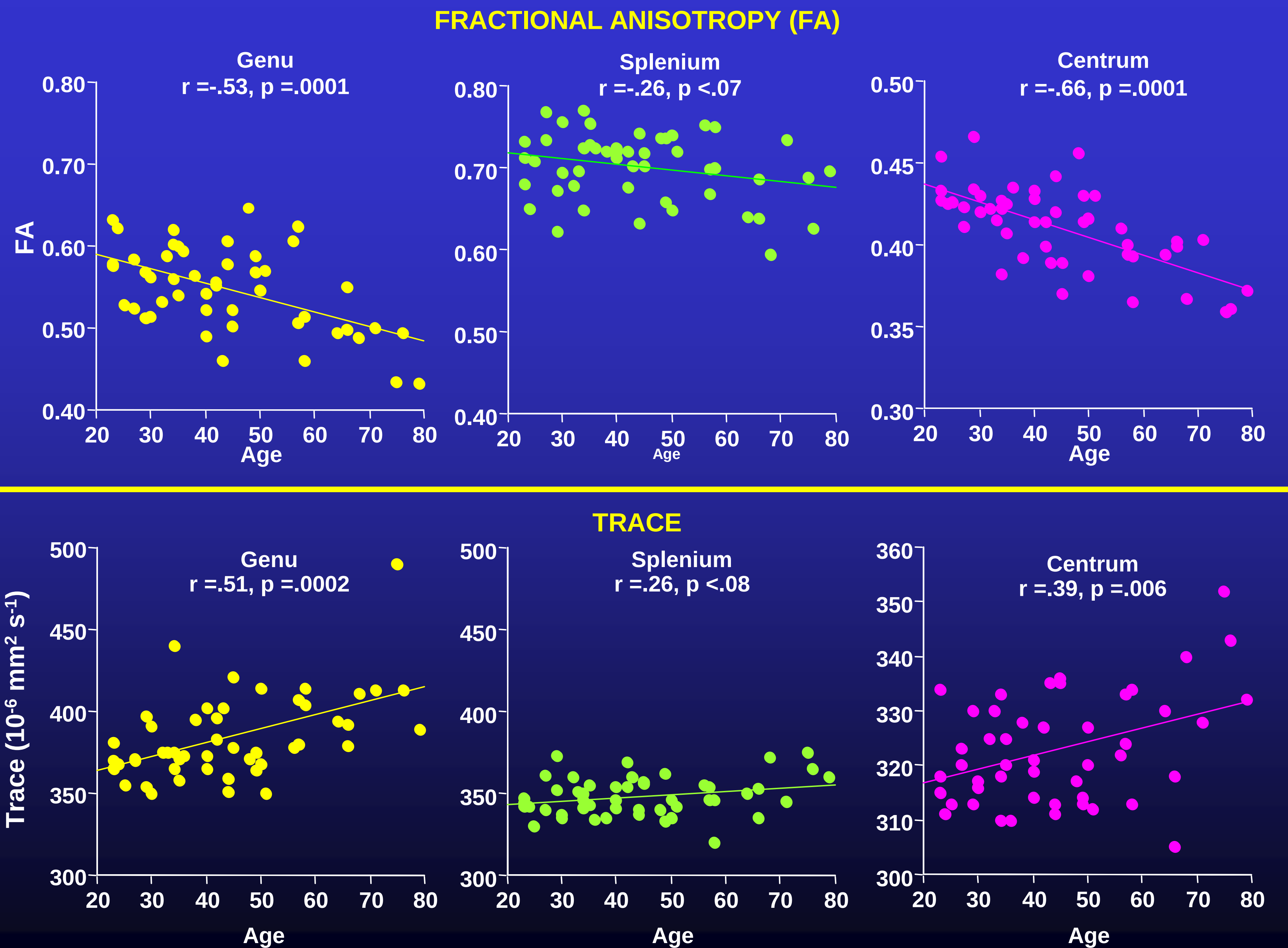

SLF
Cingulum
Uncinate
IFO

ANALYSIS

- Blind observer, tract-specific measurements of fractional anisotropy and mean diffusivity in (both hemispheres):
  - Uncinate Fasciculus (UF)
  - Superior Longitudinal Fasciculus (SLF)
  - Inferior Fronto-Occipital Fasciculus (IFO)
  - Cingulum
- ANCOVA (age as covariate) with effects:
  - Subject group (Patient / Control)
  - Hemisphere (Left / Right)
  - Fasciculus (UF / SLF / IFO / Cingulum)
- *Post-hoc* tests:
  - Tukey-Kramer for comparison of means
  - Holm procedure for comparisons of slopes

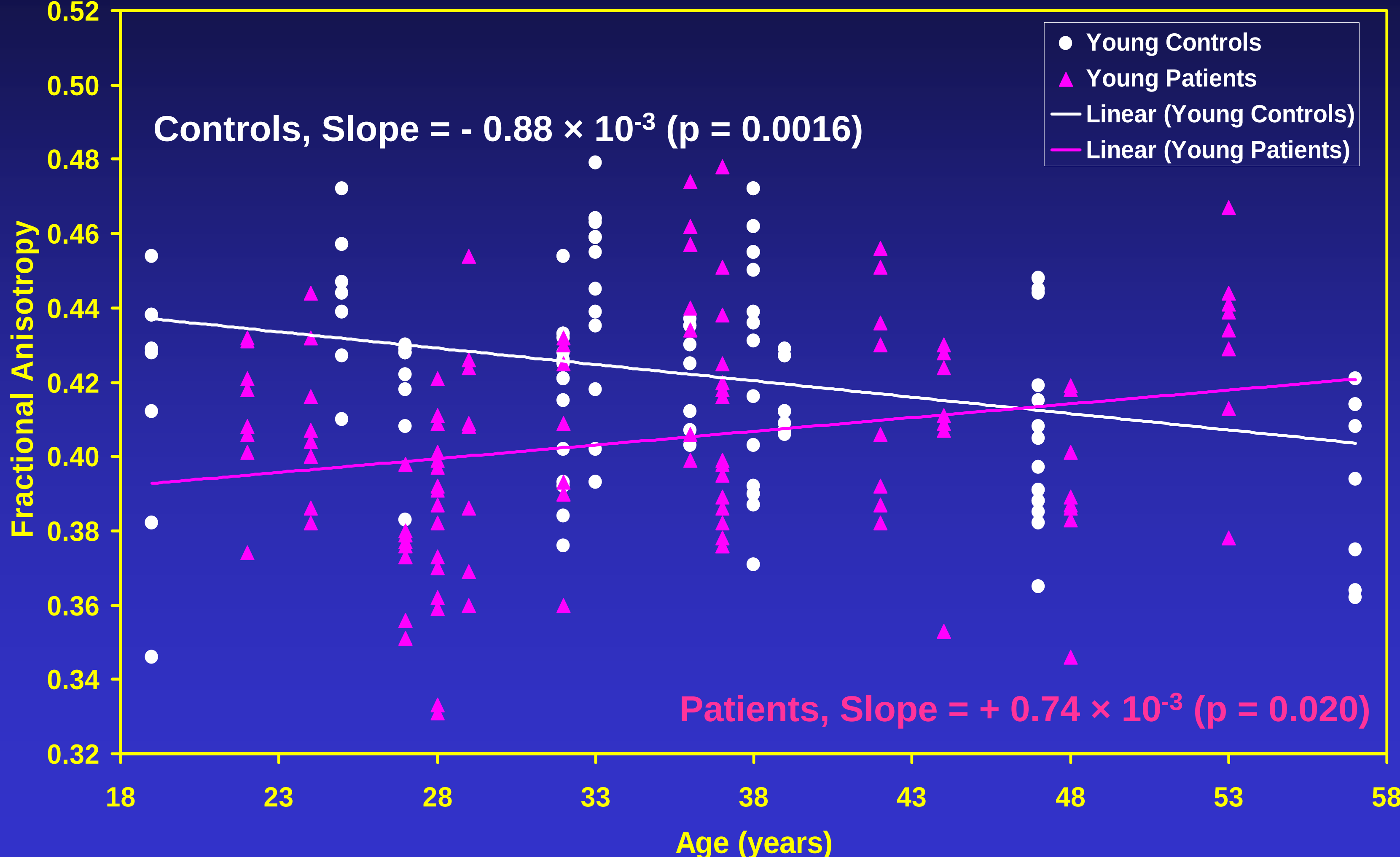
Fractional Anisotropy *vs* Age in Controls





Pfefferbaum & Sullivan *MRM* 49:953-961 (2003)

Fractional Anisotropy *vs* Age in Patients and Controls

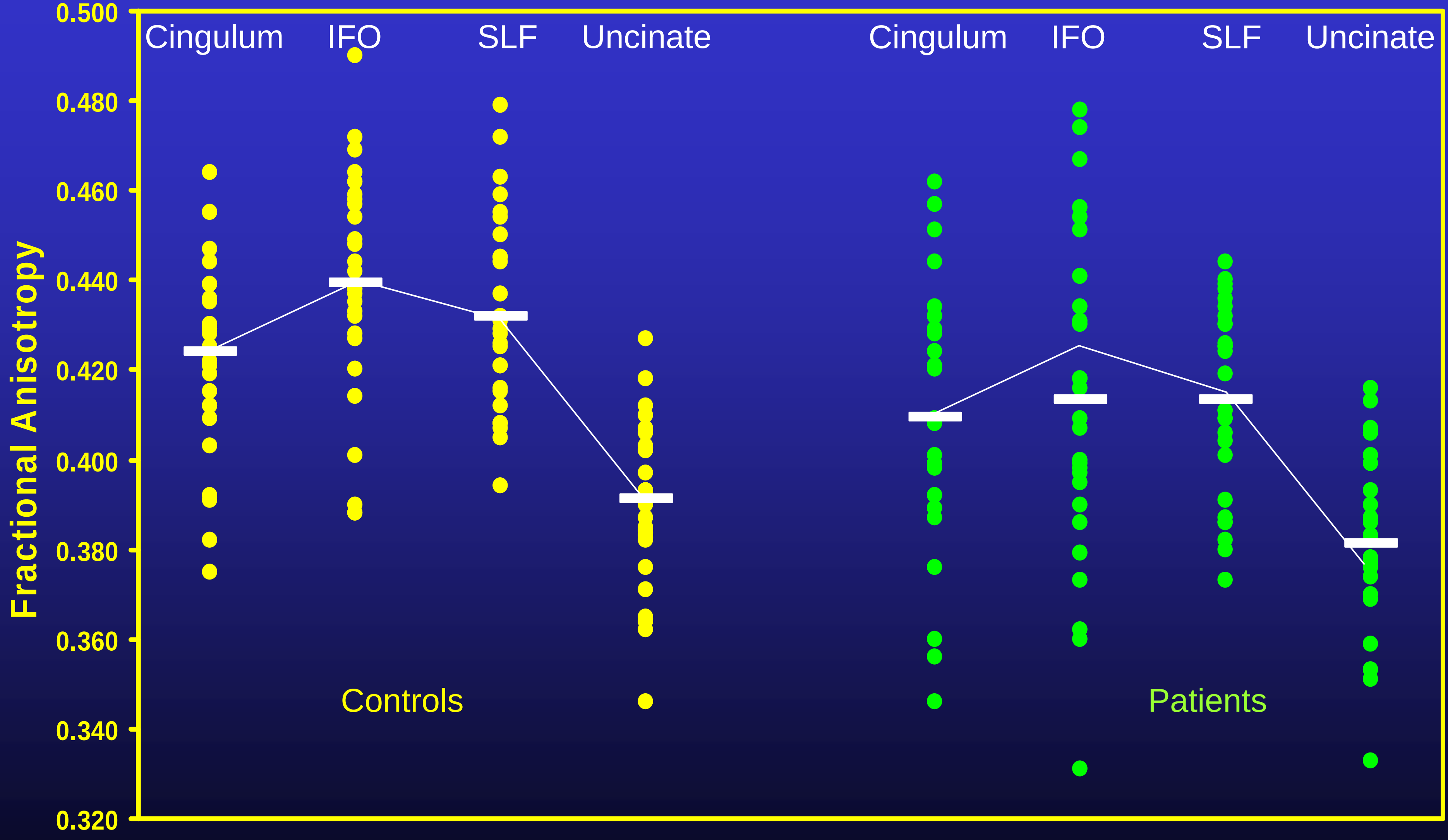


Slopes significantly different ($p = 0.0001$)

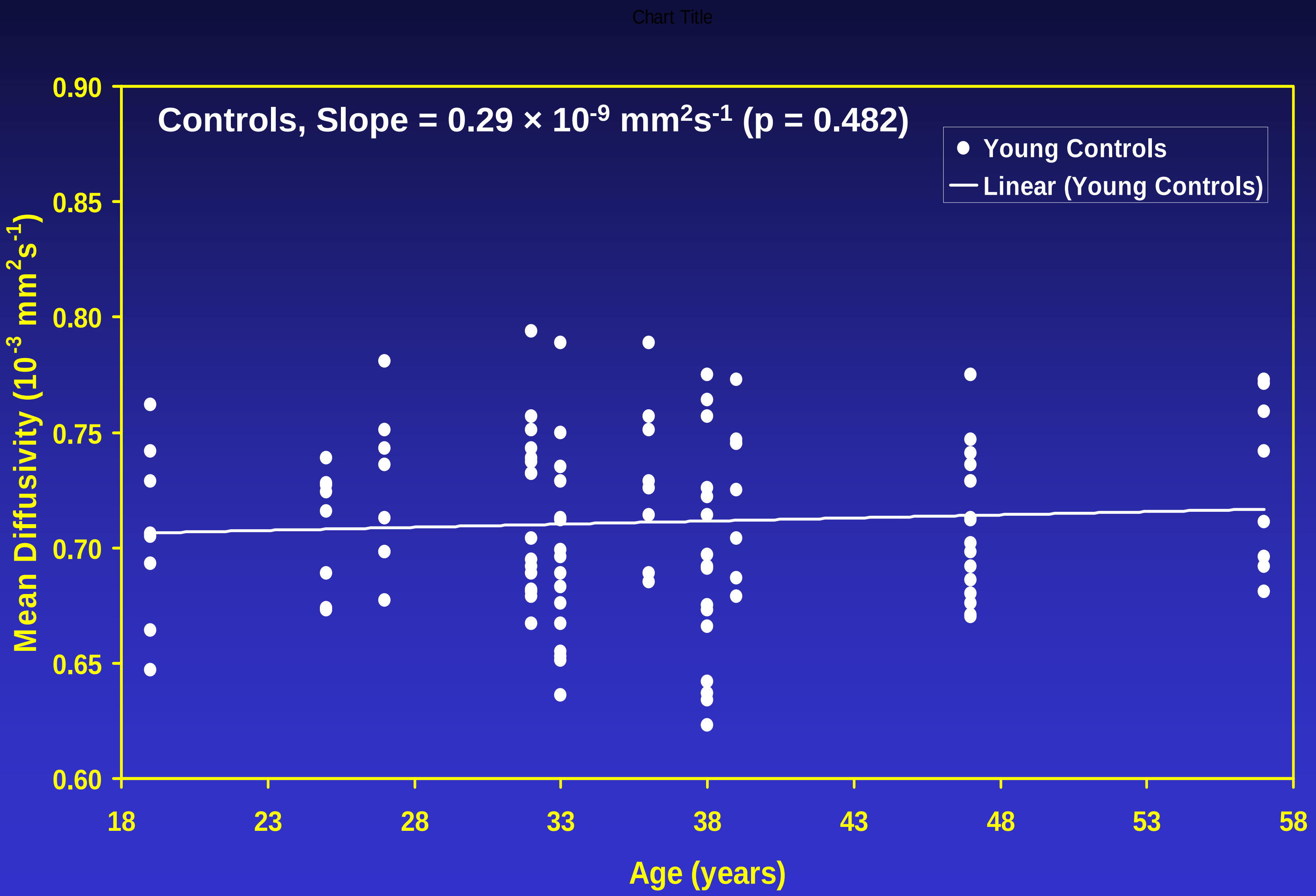
Fractional Anisotropy in Patients and Controls

Effect	Controls	Patients
Age	$p < 0.0001$	$p = 0.0106$
Hemisphere	$p = 0.1311$	$p = 0.8747$
Fasciculus	$p < 0.0001$	$p < 0.0001$

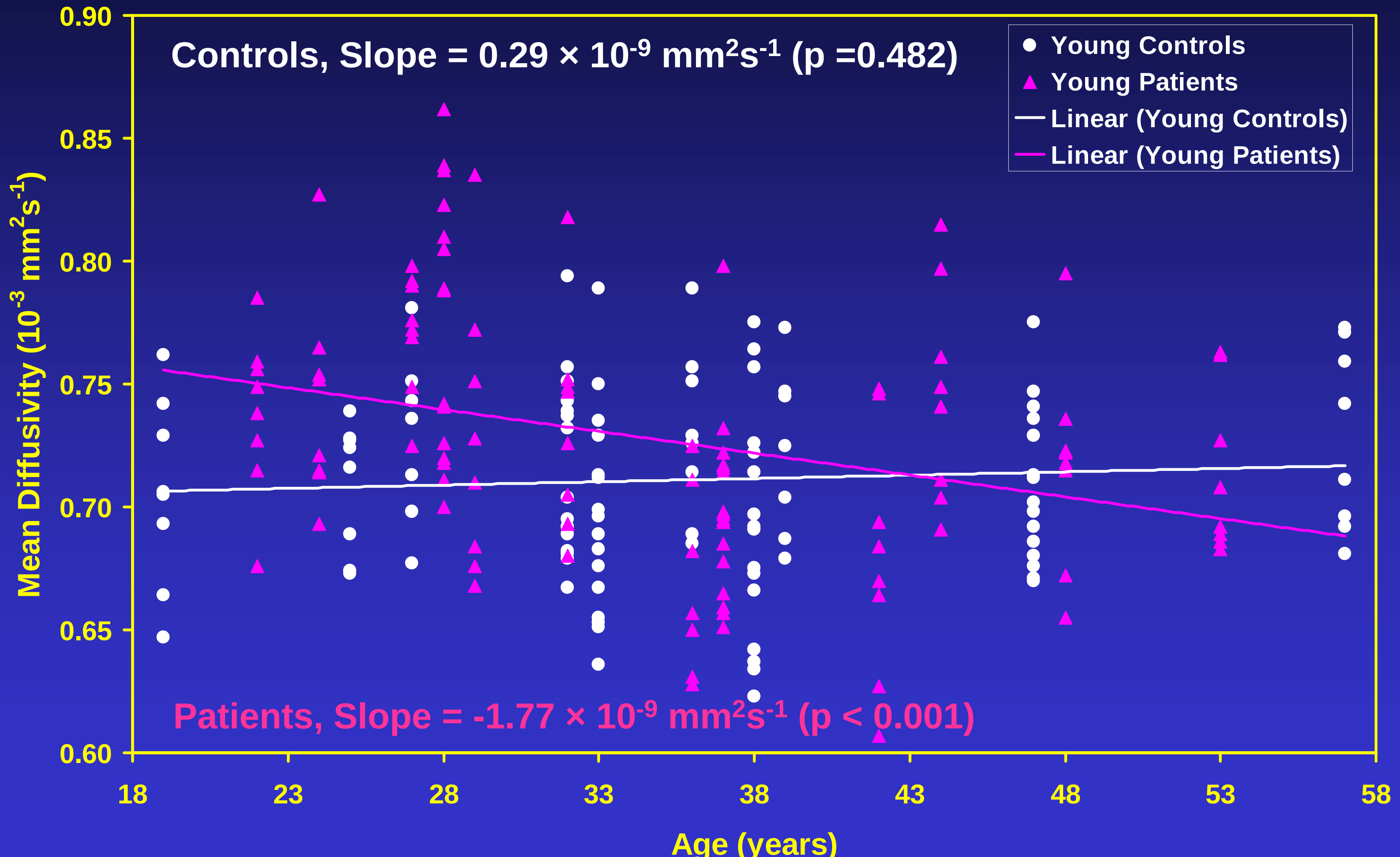
Tract-Specific FA Measurements In Patients and Controls



Mean Diffusivity *vs* Age in Controls



Mean Diffusivity *vs* Age in Patients and Controls



Slopes significantly different (p = 0.0041)

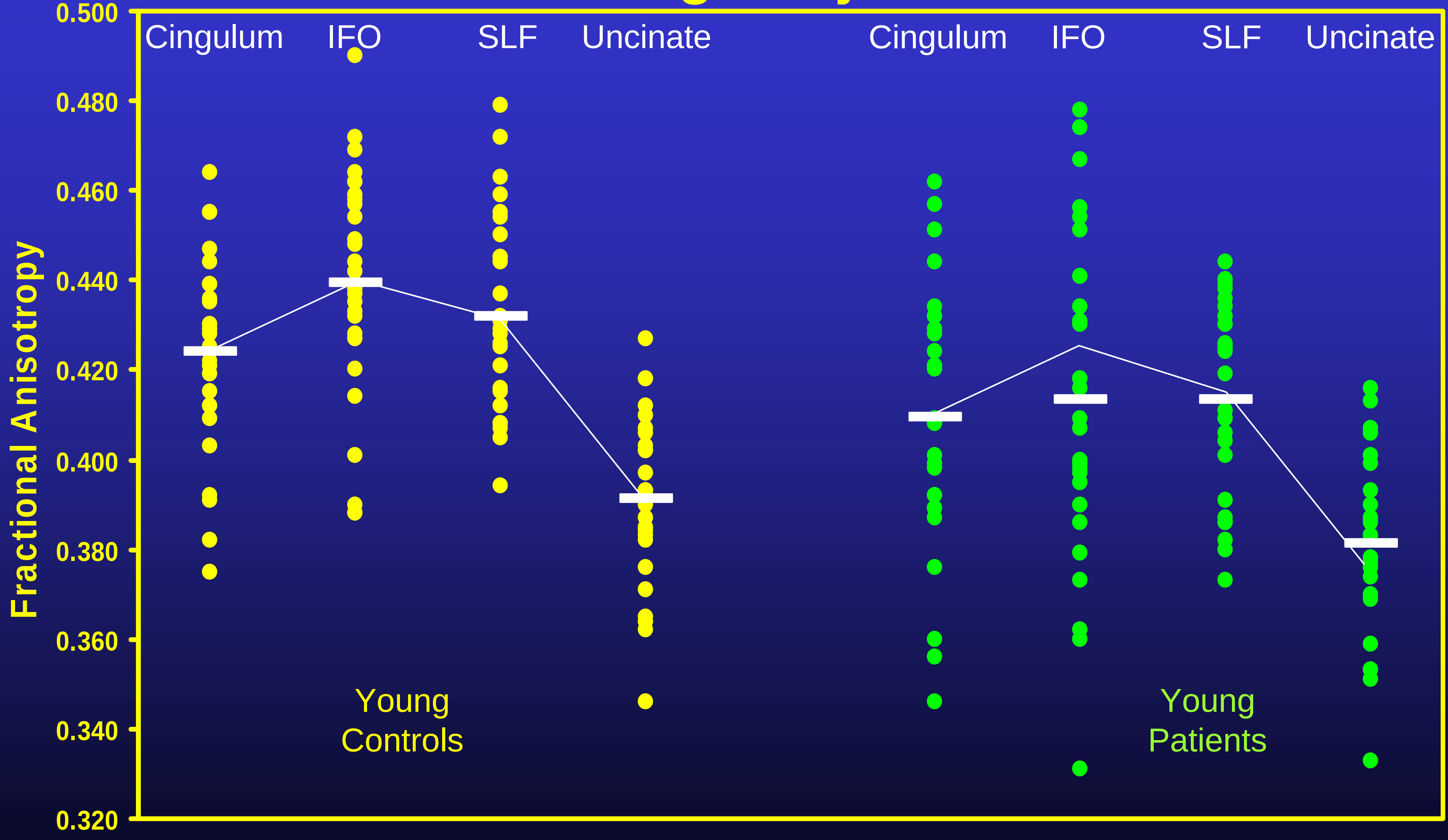
Mean Diffusivity in Patients and Controls

Effect	Controls	Patients
Age	$p = 0.2504$	$p < 0.0001$
Hemisphere	$p = 0.0978$	$p = 0.0032$
Fasciculus	$p < 0.0001$	$p < 0.0001$

Left hemisphere $D = 0.738 \pm 0.056 \times 10^{-3}\ mm^2 s^{-1}$

Right hemisphere $D = 0.717 \pm 0.044 \times 10^{-3}\ mm^2 s^{-1}$

Tract-Specific FA Measurements In Young Subjects



CONCLUSIONS

- DT-MRI provides unique non-invasive characterization of neural tissue *in vivo*.
- Anisotropy measurements provide evidence of *microstructural* changes in alcoholism (in absence of macrostructural changes)
- Possibility of studying effects on connections in different circuits – tract specific measurements.
- Correlate neurobehavioral patterns with DT-MRI characteristics.

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ICANA Organizing Committee