Advanced Imaging Techniques and Characterization of Residual Anatomy

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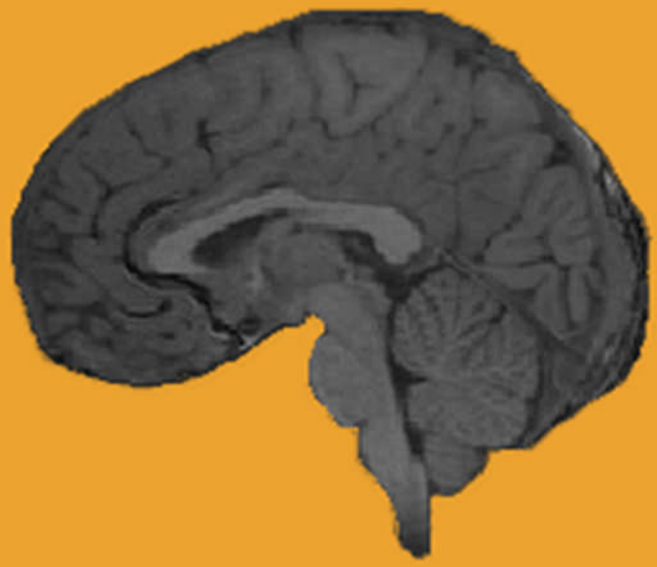


Imaging methods that are used, or being developed, for imaging the CNS span:

MRI, x-ray, CT, PET, SPECT, MEG, …

➔ **Focus on the most recent developments and those with the greatest potential for clinical use**

After an injury or disease, we need to see more than which regions have unchanged appearance - we need to know which tissues are still functioning

We need to be able to look at the whole CNS, not just localized regions

➔**Here I focus on three specific methods:**

Functional MRI
Resting-state fMRI
Diffusion-tensor imaging

The current workhorse – Anatomical Imaging

What is the effect of this damage?

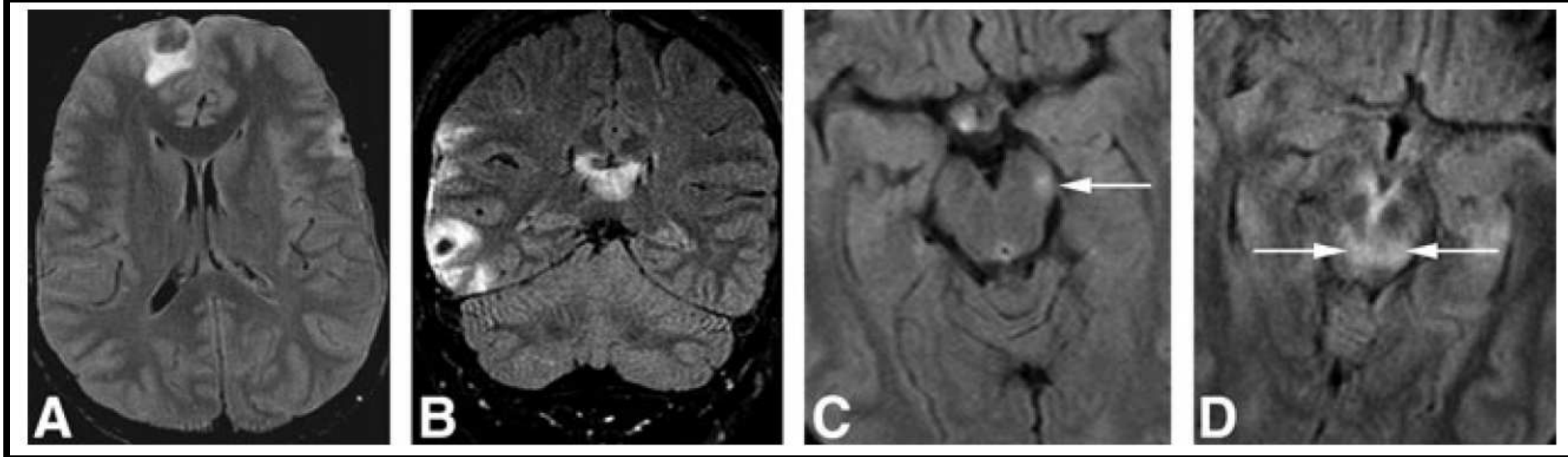


Figure 1 (reproduced with permission from Skandsen et al. J Neurotrauma 28:691-699, 2011

Functional MRI

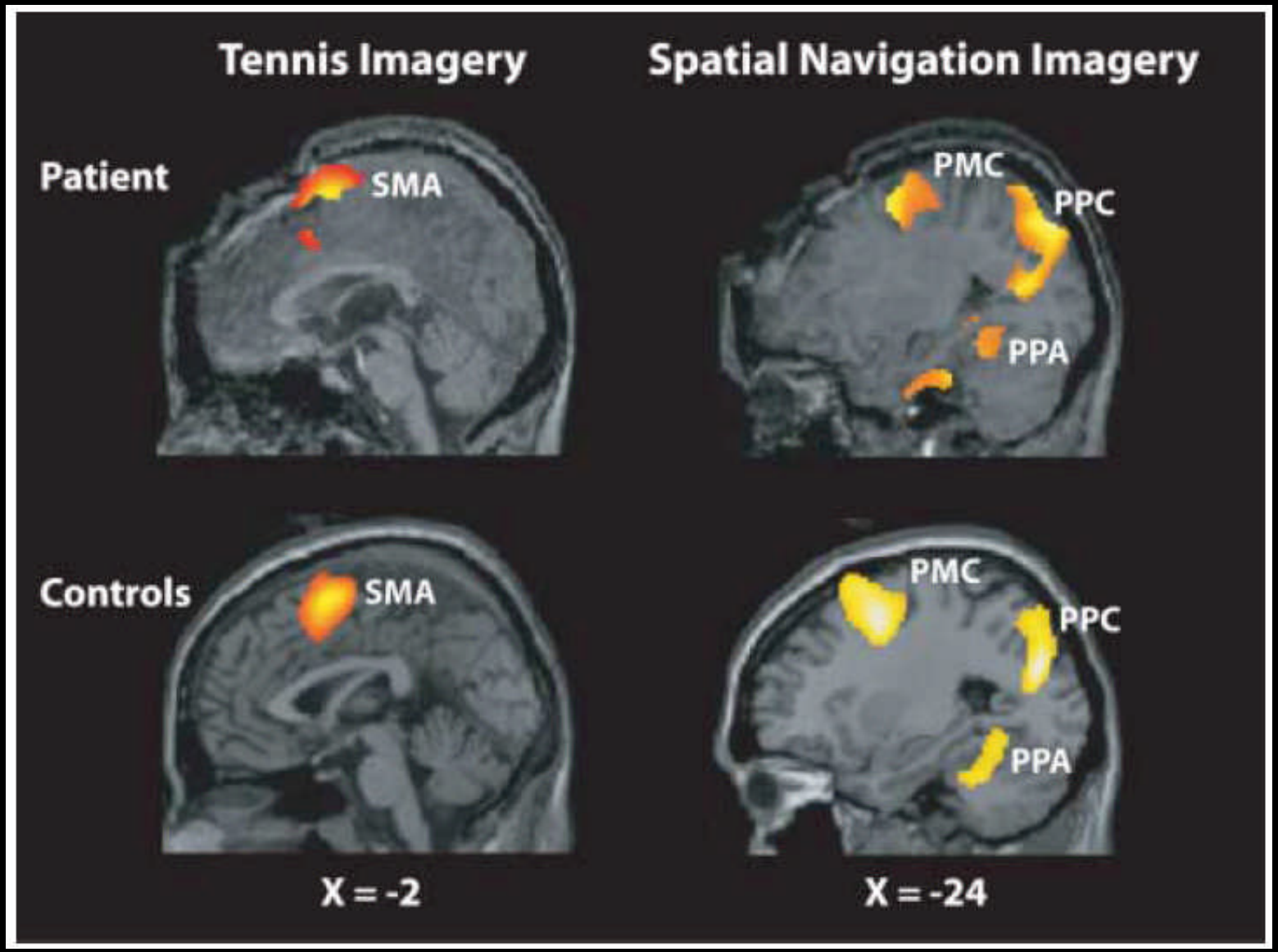
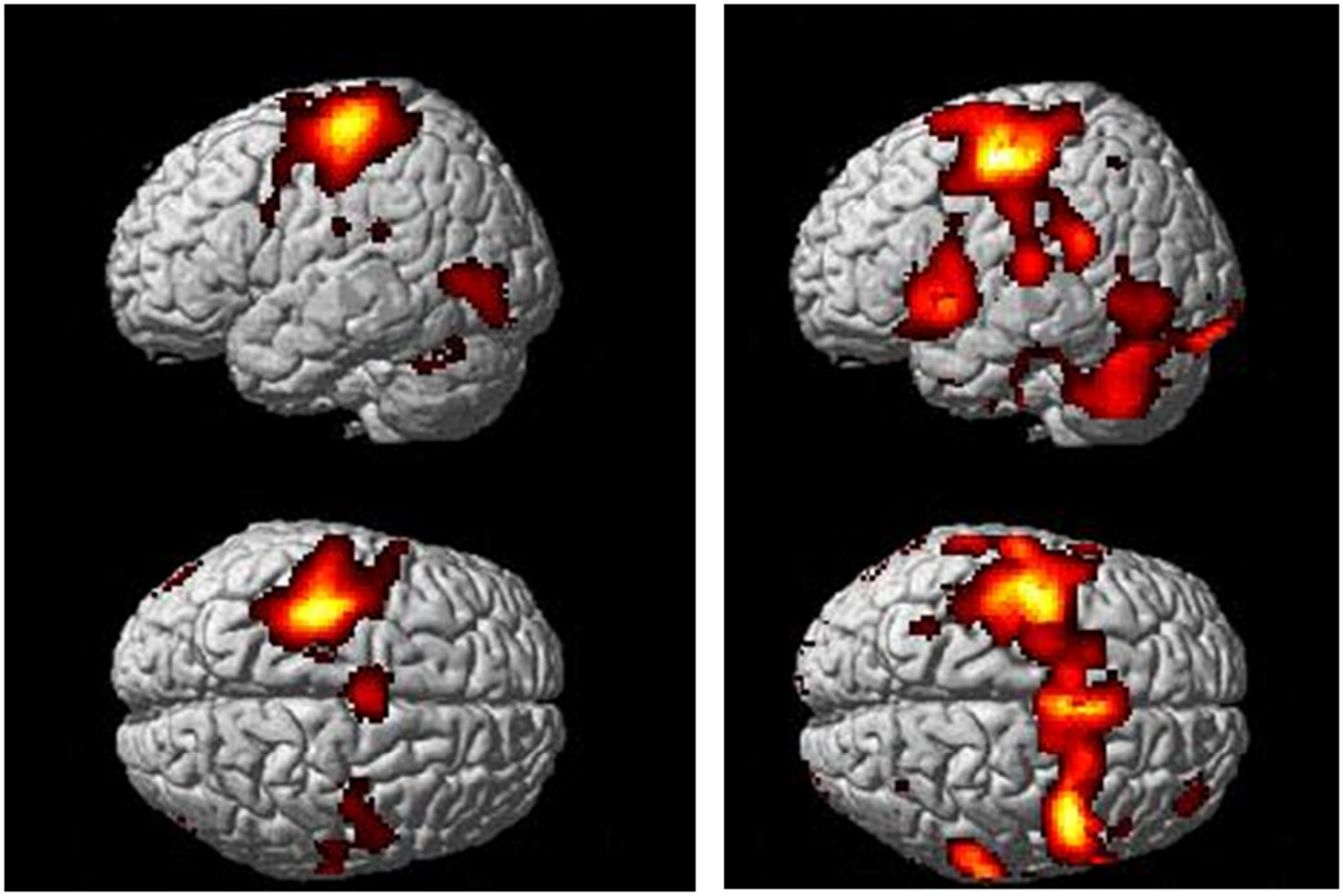


Figure 2 (reproduced with permission from Owen et al. Science 313:1402, 2006):

Example of Functional MRI - Multiple-Sclerosis

Motor task performed with the right hand (dominant hand)



Healthy Volunteer

Patient with Relapsing-Remitting Multiple Sclerosis (RRMS)

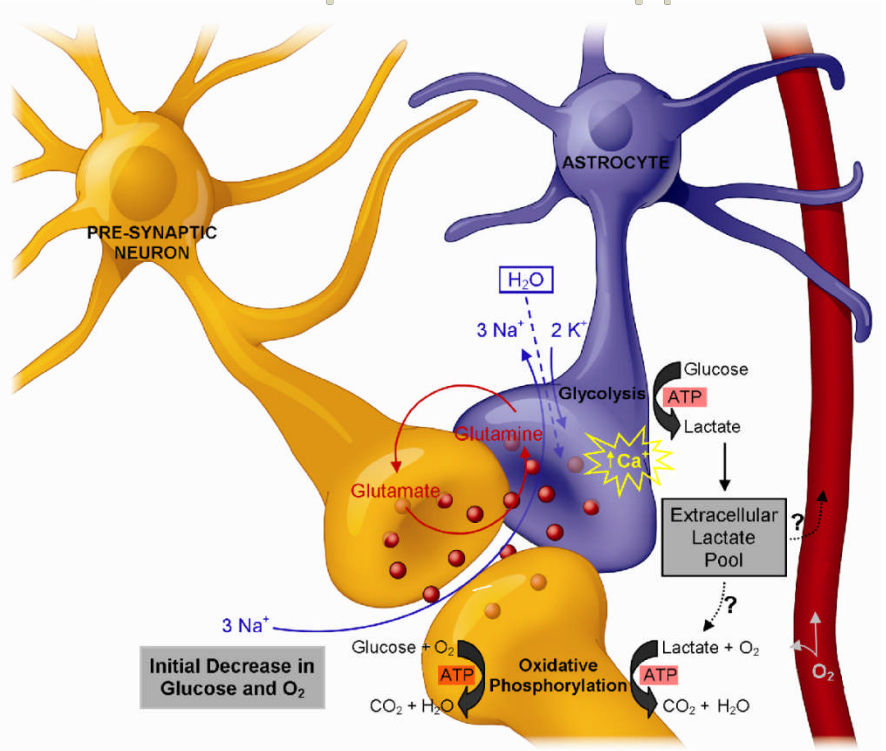
Figure courtesy of Dr Massimo Filippi, Neuroimaging Research Unit, Scientific Institute and University San Raffaele, Milan Italy.

How does fMRI demonstrate neural activity?

➔It doesn't, it shows changes in blood oxygenation,
related to changes in metabolic activity

- The areas of "activity" reflect pre-synaptic input, not necessarily output spiking rate

- Inhibitory and excitatory input cannot be distinguished, an increase in either one produces an apparent increase in "activity"



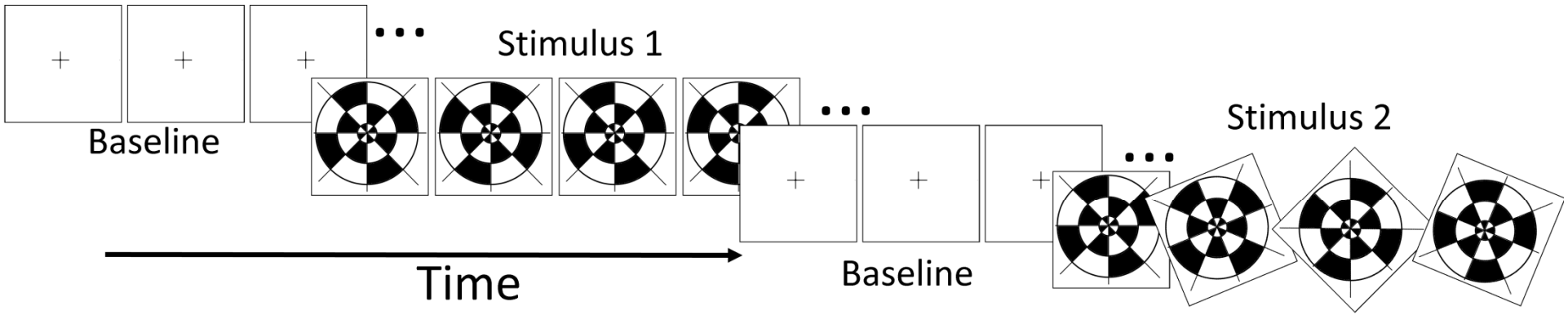
There are a number of ways of doing fMRI

blood oxygenation changes (BOLD)
blood volume changes (VASO)
perfusion changes (PWI)
diffusion changes (DWI)

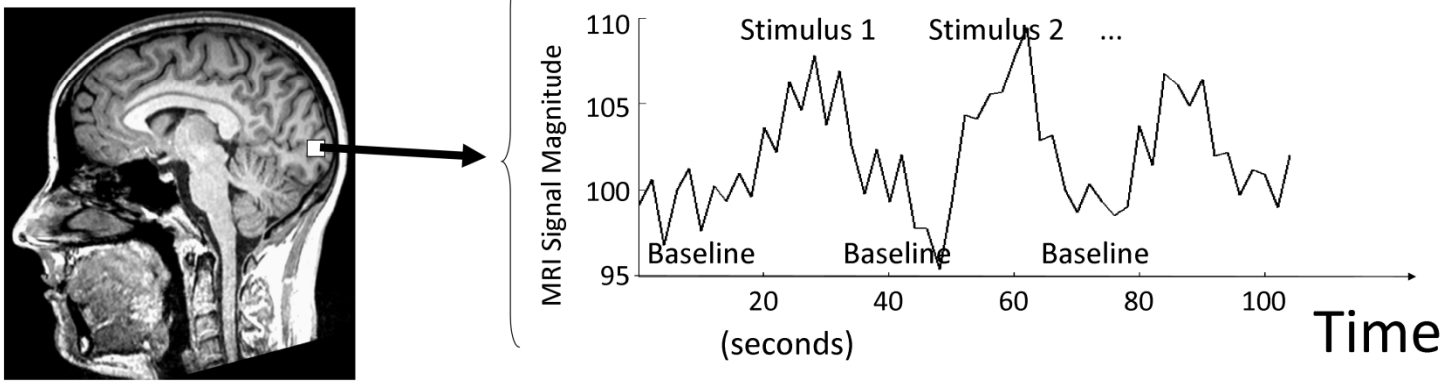
BOLD is by far the most commonly used

Figley and Stroman, European J. of Neurosci., Vol. 33, pp. 577–588, 2011

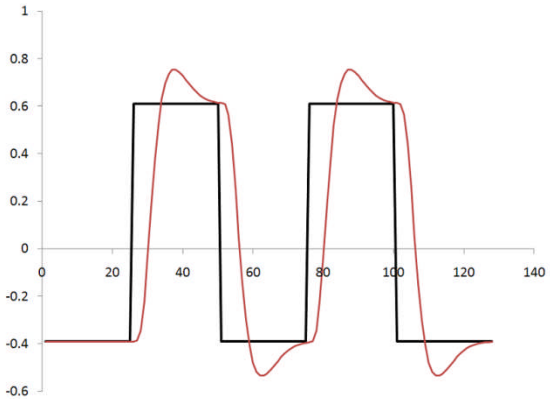
Visual Display



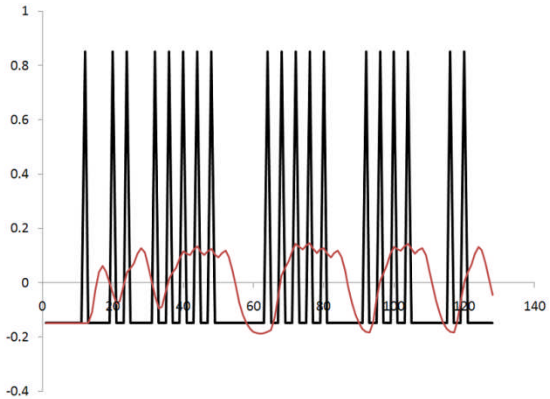
Repeated Imaging Over Time



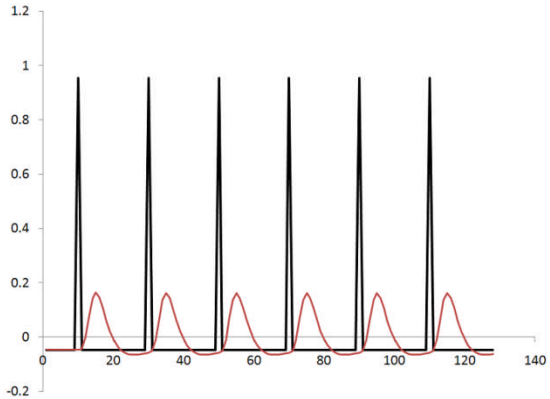
Design options for fMRI studies …



Block Design



Fast-Event-Related Design



Event-Related Design

Black lines: Timing of tasks Red lines: BOLD response

fMRI only shows changes in activity between tasks or cognitive states, it does not show the baseline metabolic level or baseline activity

➔ **Need to compare two or more states**

- **This allows for a huge number of options of how fMRI is done**

Advantages/disadvantages of functional MRI for assessing residual anatomy …

- **Results can reveal neurological function in the brain and spinal cord**
- **There are a huge number of options for how fMRI can be done**
- **Tasks/stimuli need to be selected to cause changes of activity in brain regions of interest**
- **There is so far no standardization – difficult to apply in a clinical setting**

Resting-state fMRI

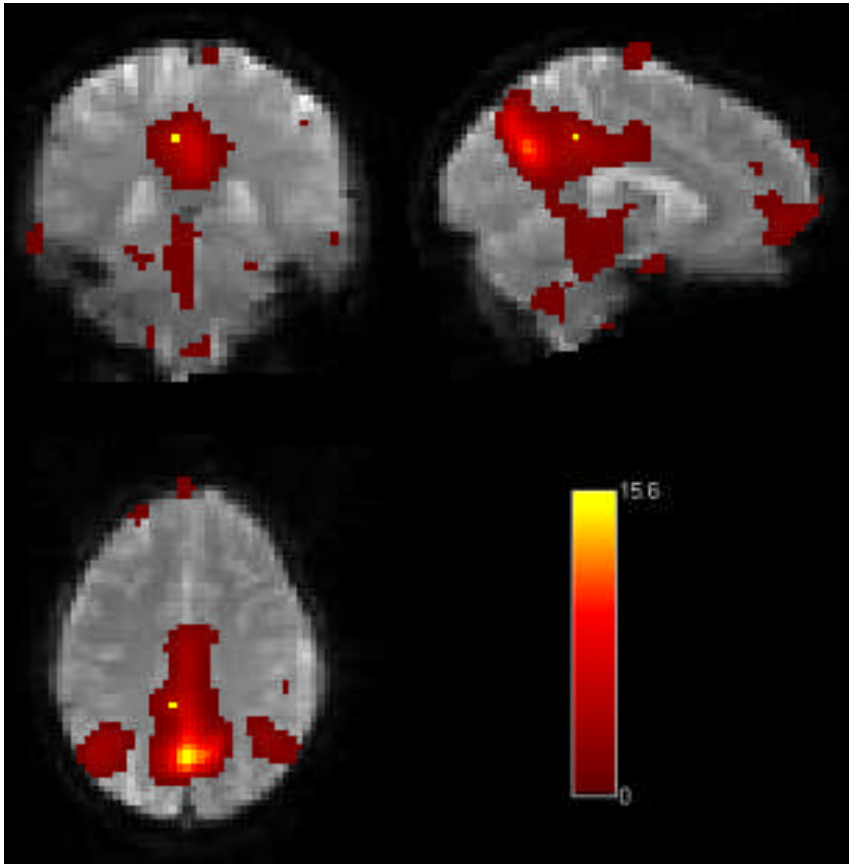
A special-case of fMRI

When a person is at rest, and focused attention is relaxed, specific areas of the brain have coordinated, low frequency, changes in activity

The areas involved produce a network that has been termed the "default mode" network (DMN)

This network can be detected with fMRI because there are corresponding BOLD fluctuations in the regions involved.

The degree of coordination across regions in the DMN has been seen to change with a wide variety of pathological states

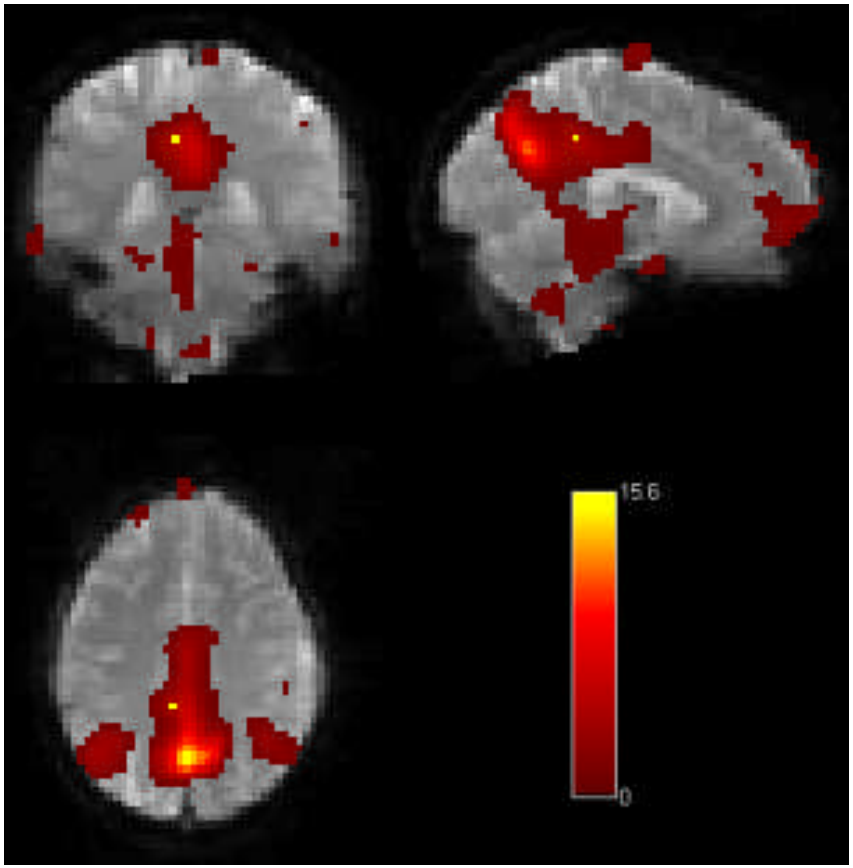


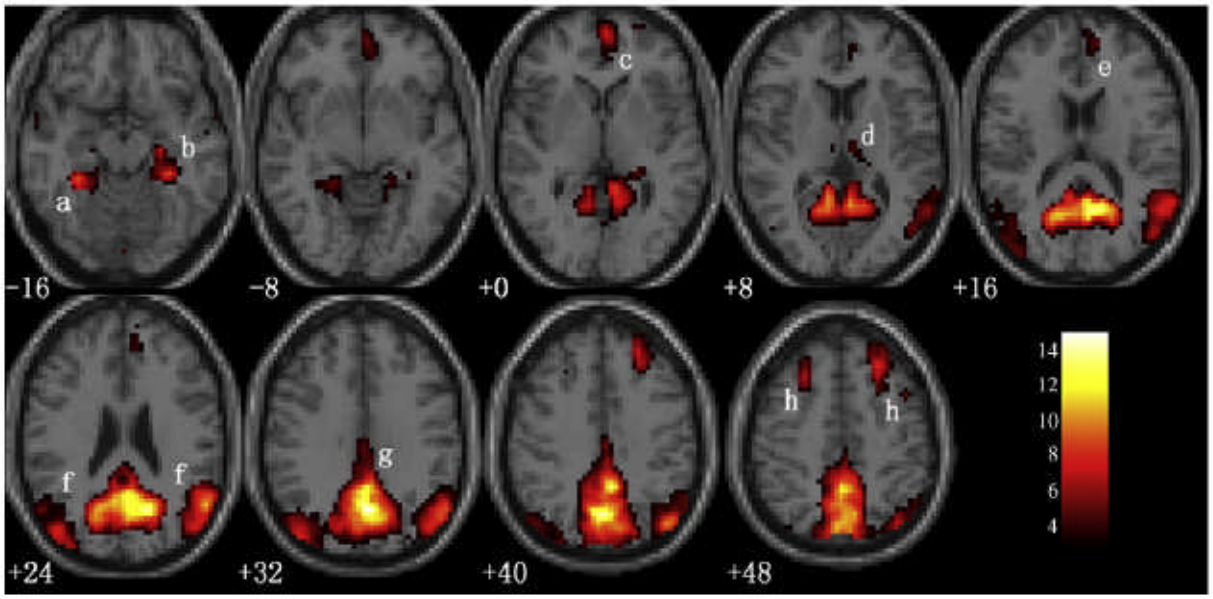
Example of resting-state fMRI in a healthy volunteer, showing typical pattern of DMN regions

Resting-state fMRI

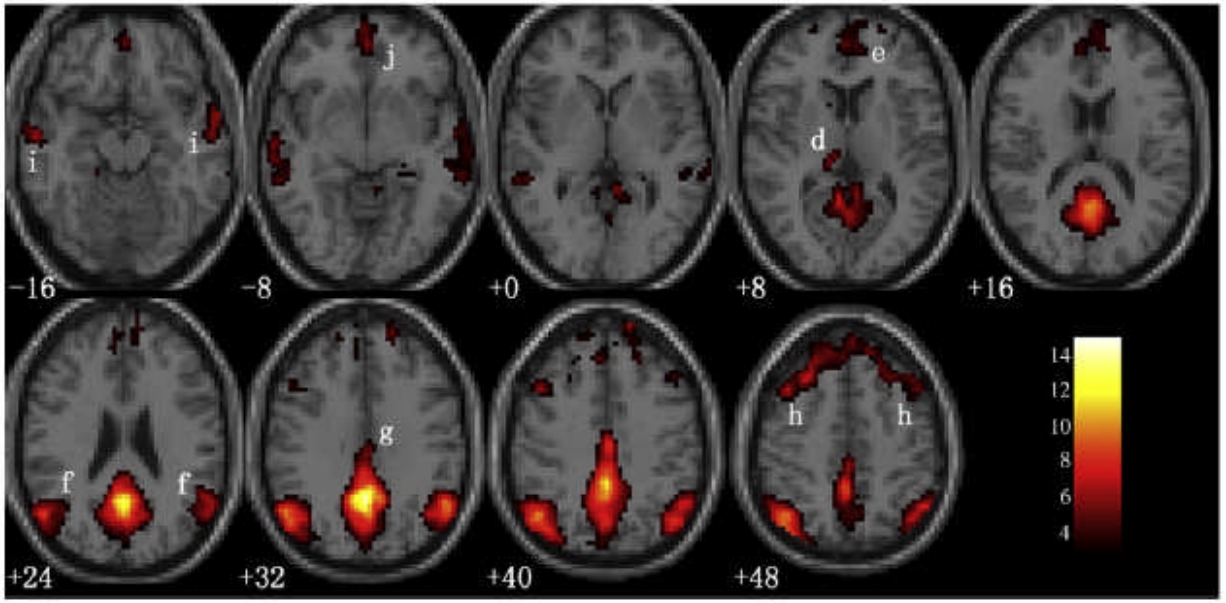
The network includes :

- **medial temporal lobe regions for memory,**
- **medial prefrontal cortex regions for mental simulations,**
- **posterior cingulate cortex for integration,**
- **also involves the precuneus, medial, lateral and inferior parietal cortex**





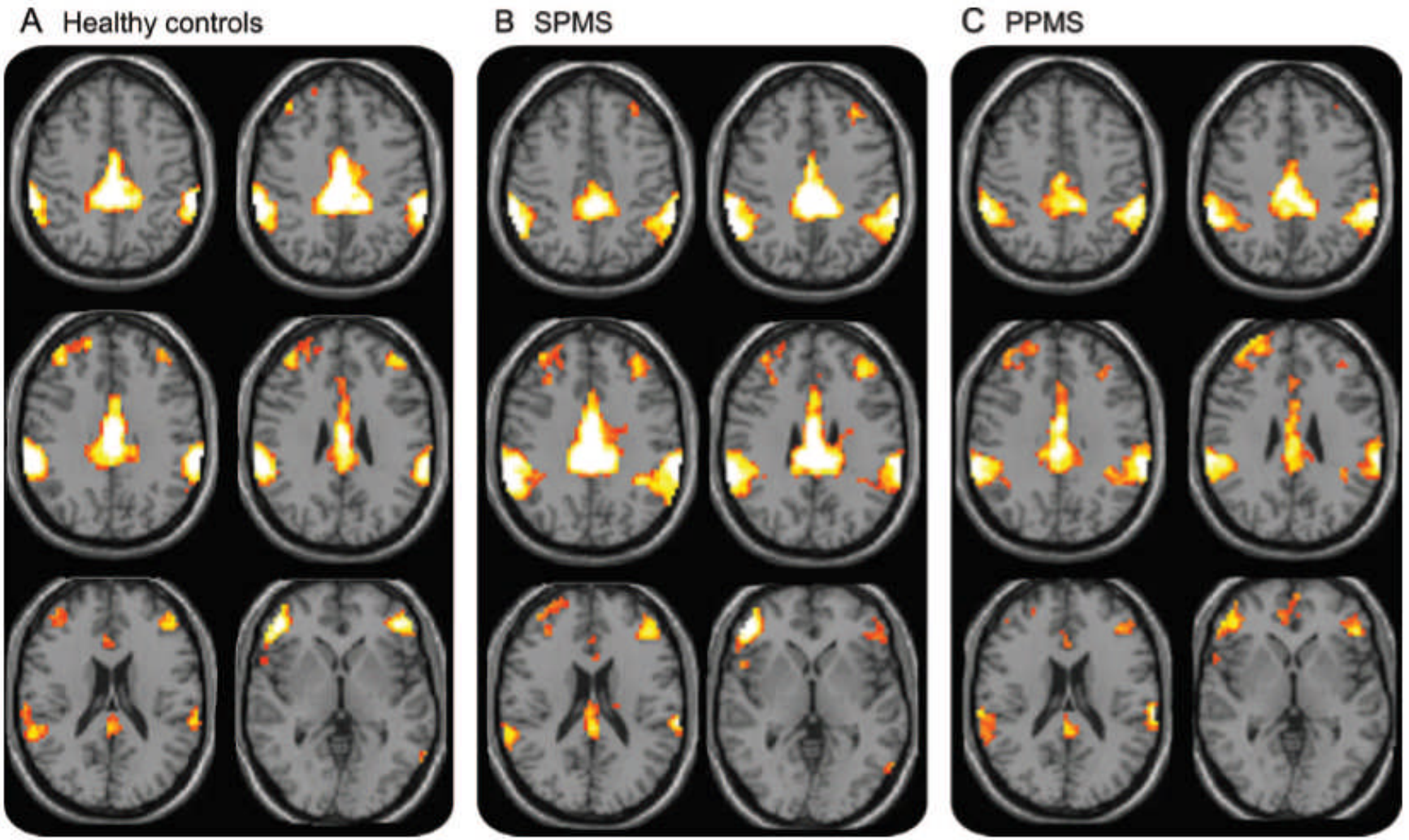
Healthy Elderly



aMCI Patients

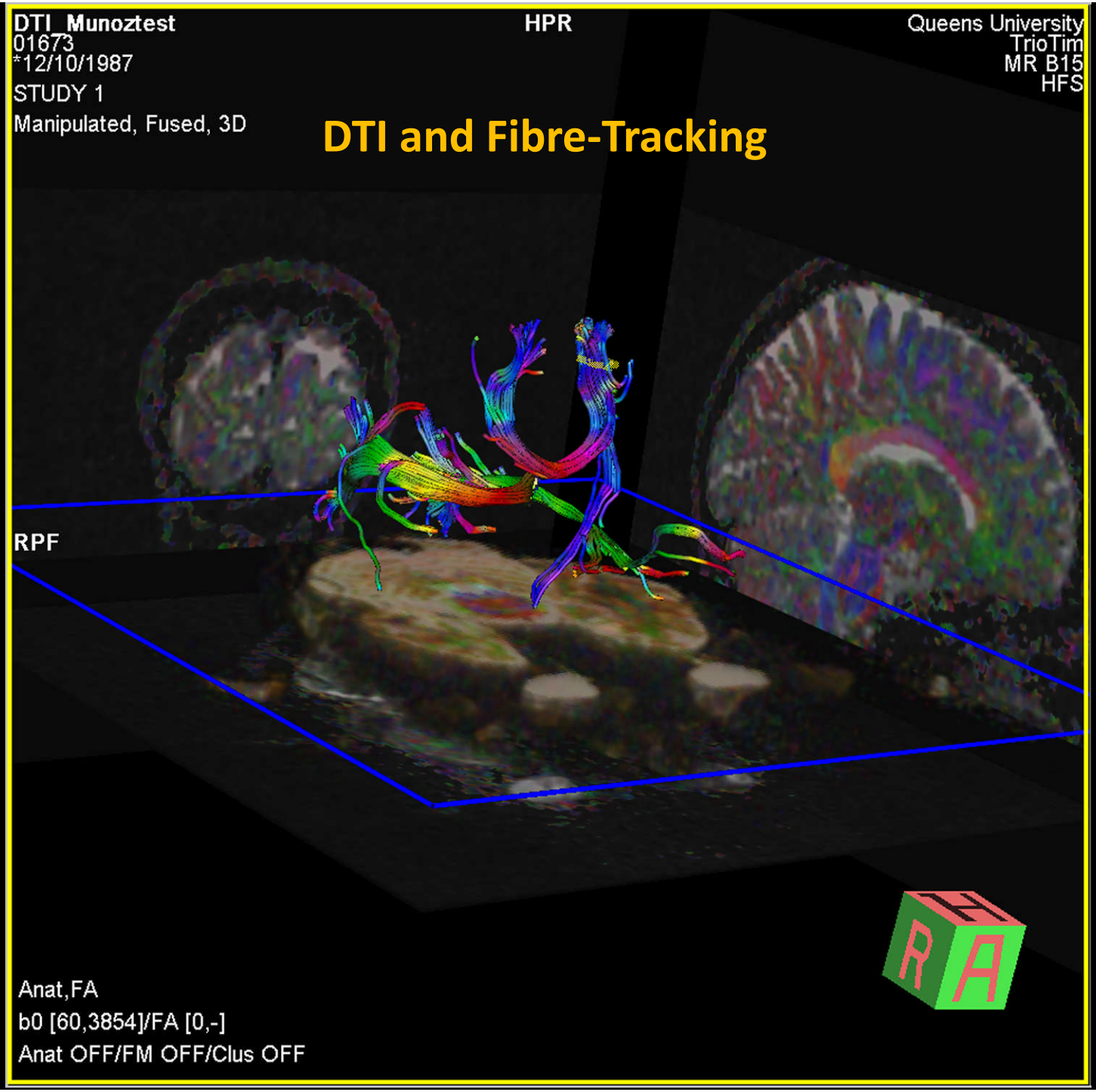
Rocca et al., Neurology April 20, 2010 74:1252-1259

Figure 1 Default-mode network in healthy controls and patients with multiple sclerosis



Advantages/disadvantages of resting-state fMRI for assessing residual anatomy …

- **A standardized method can be used for all applications**
- **Relatively easy to acquire in as little as 6 minutes**
- **No active tasks so any patient can be assessed, even if unconscious**
- **Data can be acquired on almost any up-to-date hospital MRI system**
- **Data need to be analyzed (could be automated) and interpreted afterward**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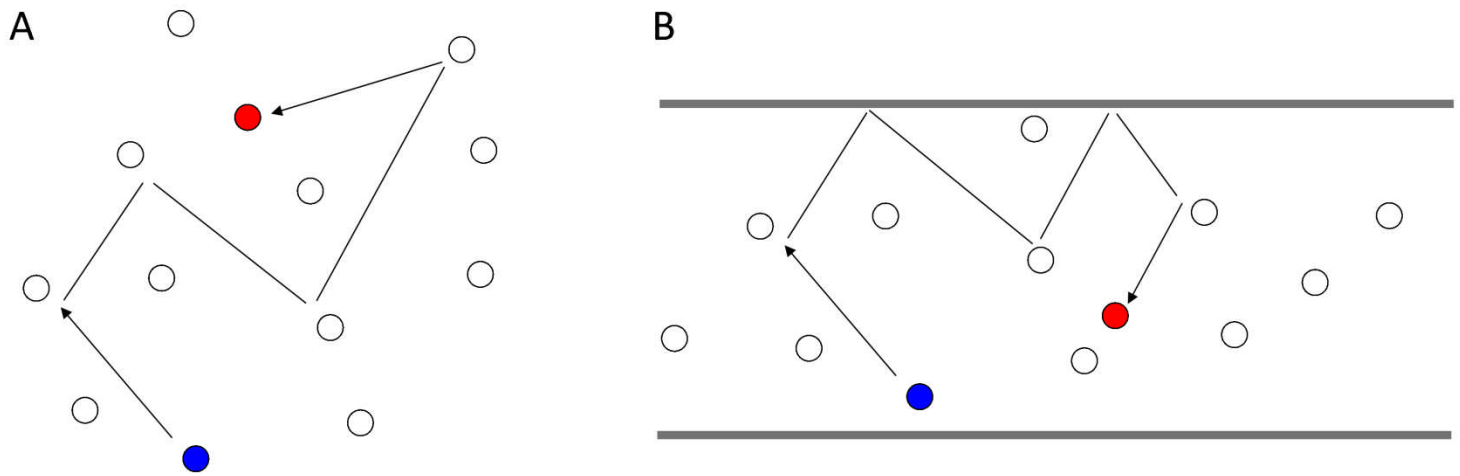


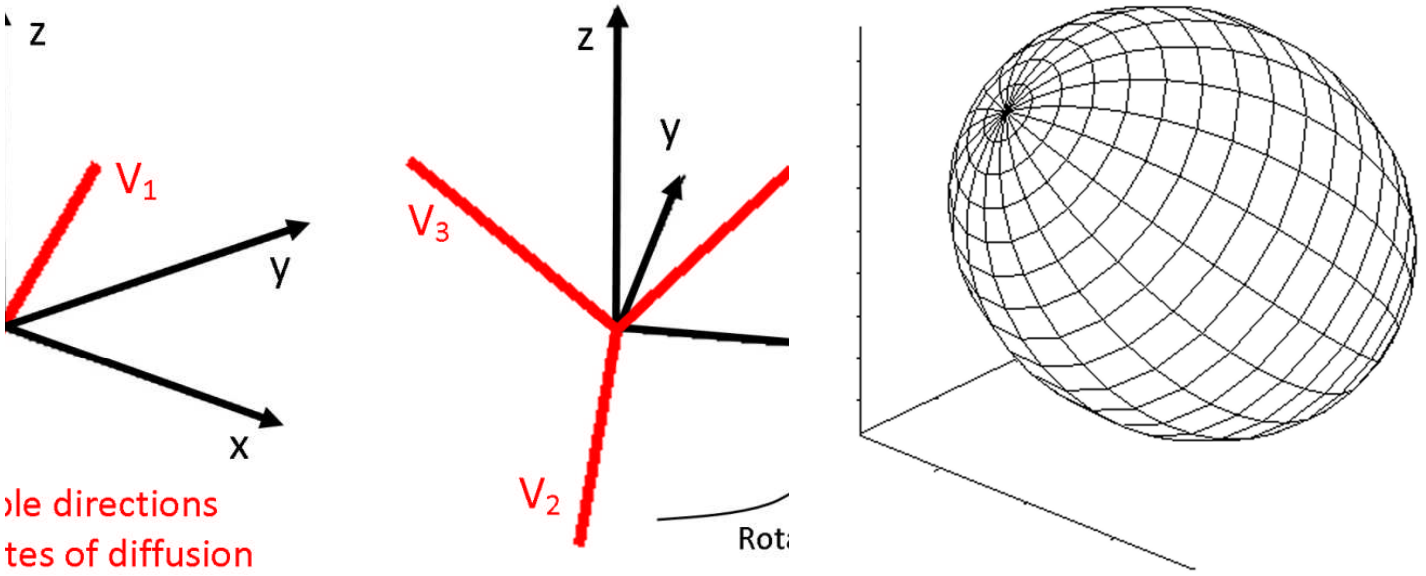
Unrestricted random diffusion **Restricted diffusion**

= Lower apparent diffusion coefficient

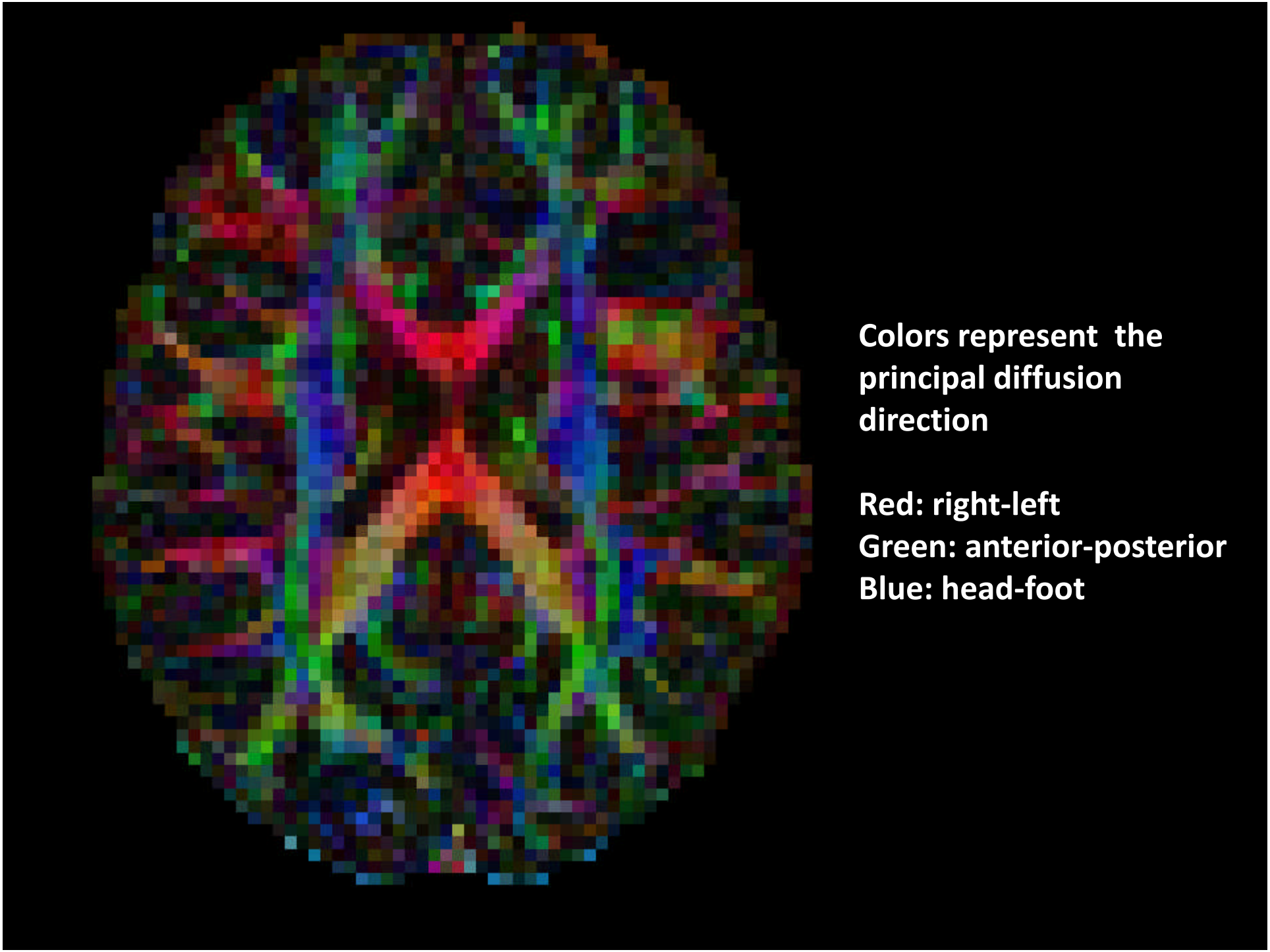
Water self-diffusion can be detected in a *specific direction* with "diffusion-weighted" MRI (DWI)

DWI with diffusion sensitivity in a number of different directions can be combined to characterize the direction dependence – create a tensor to describe it (DTI)

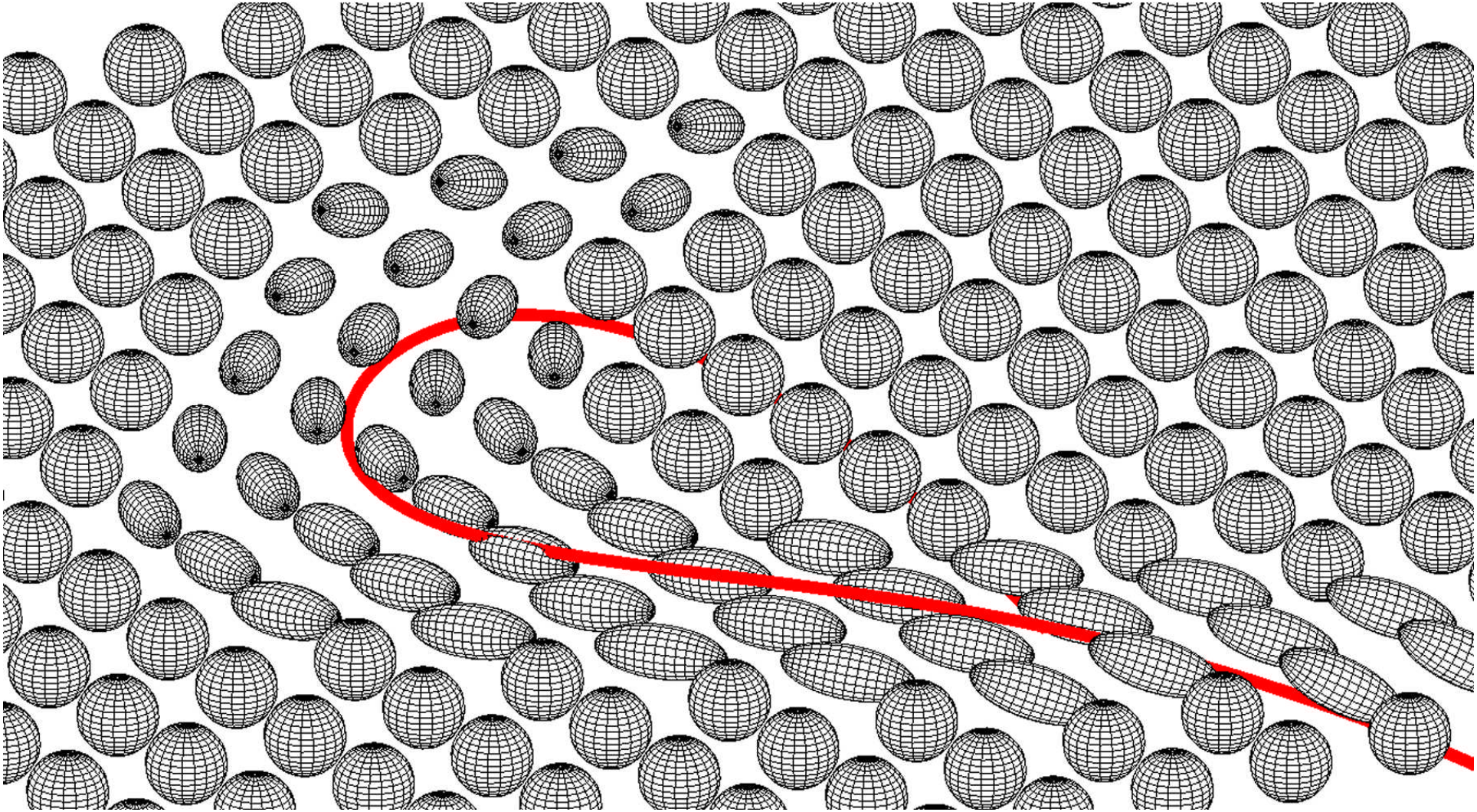
➔ The direction of least restriction, such as parallel to large white matter tracts, can be detected - connect lines along directions of diffusion at each voxel to *estimate fibre tracks*

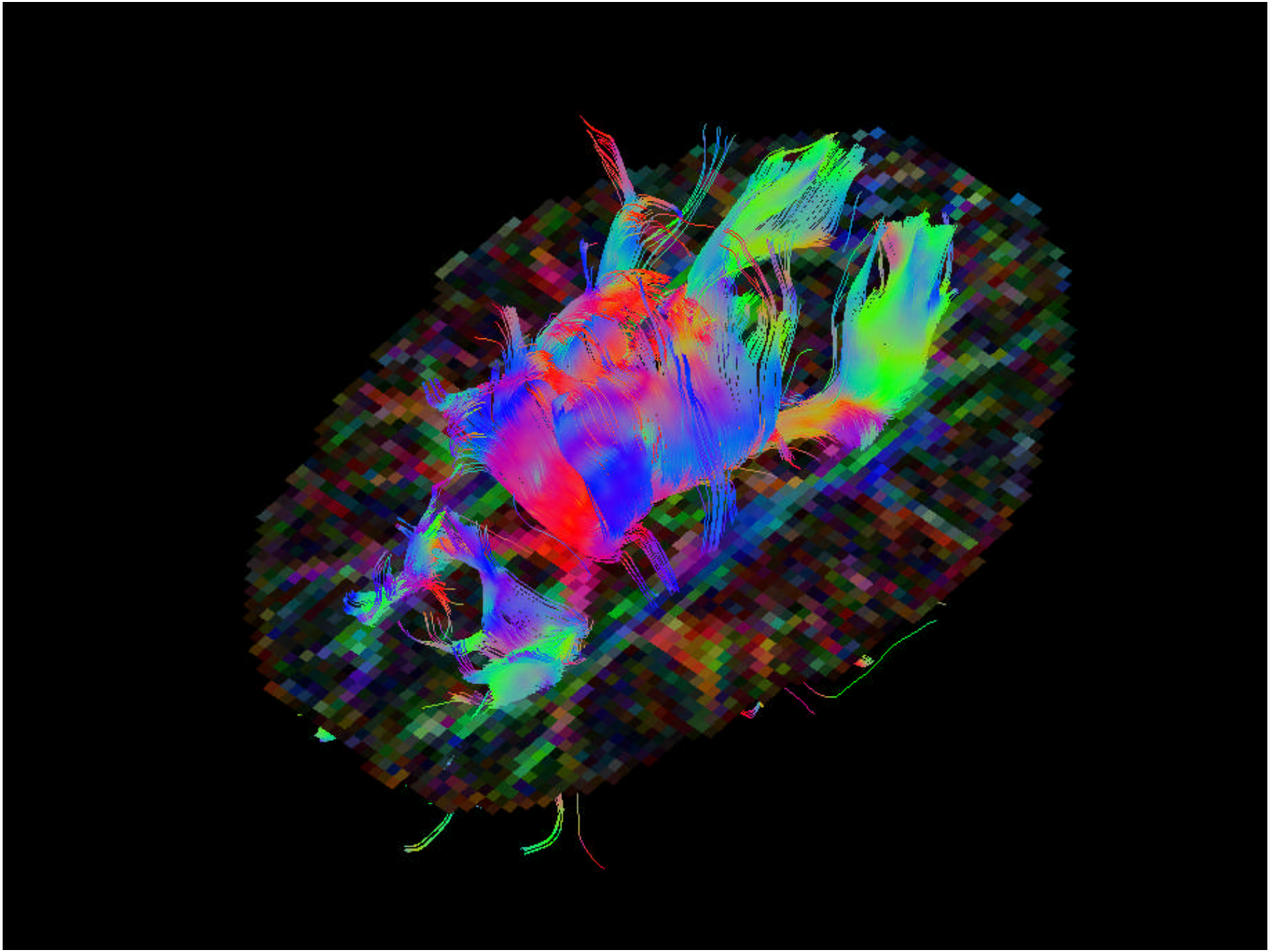


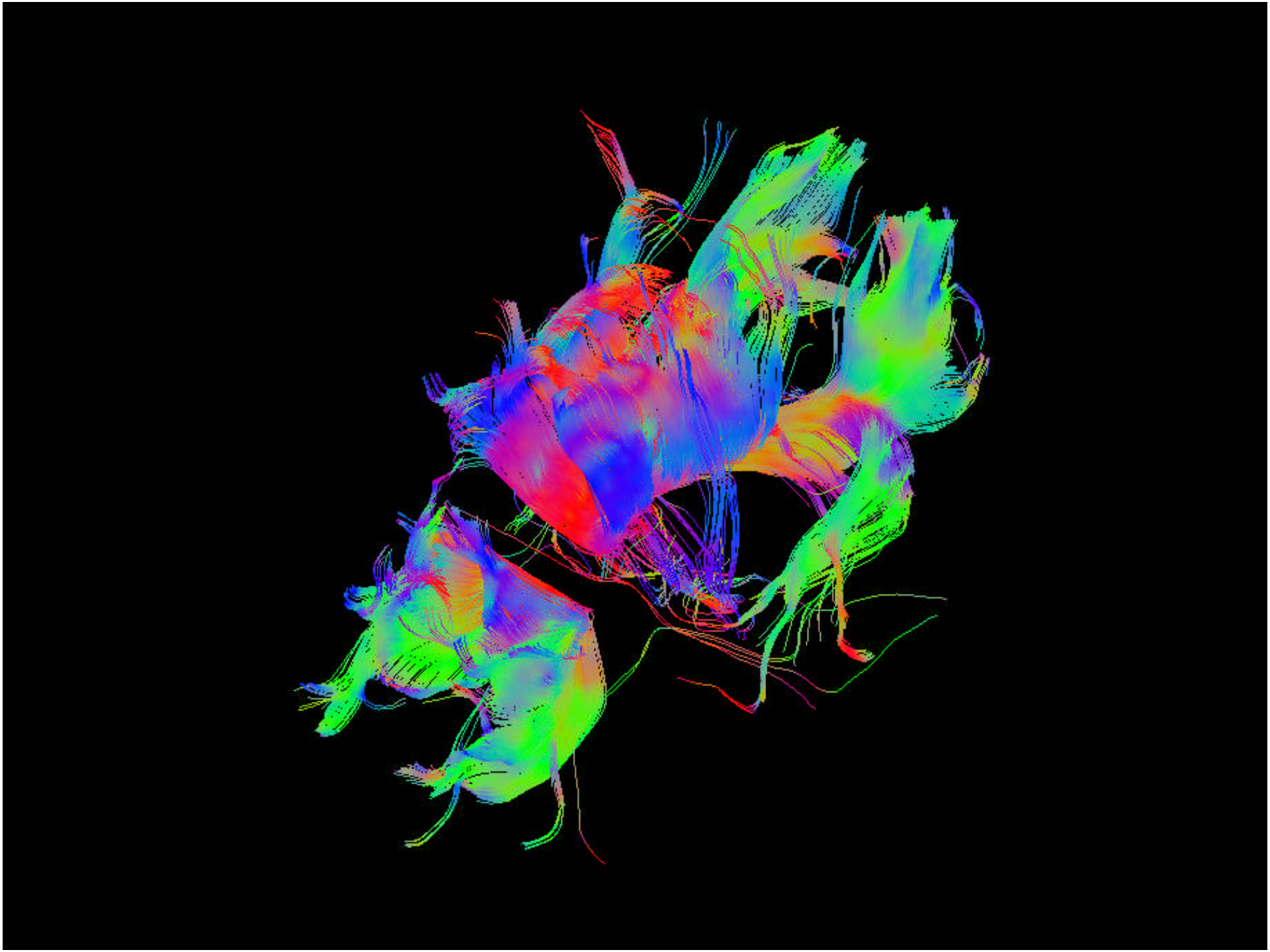
A spherical diffusion tensor represents isotropic diffusion – no preferred direction
Highly oriented structures tend to have a more elongated, ellipsoidal, tensor


Colors represent the principal diffusion direction
Red: right-left
Green: anterior-posterior
Blue: head-foot

Use the diffusion tensor at each voxel to estimate the paths of white matter tracts







Examples of using DTI and fibre-tracking for detecting “residual anatomy”

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journal homepage: www.elsevier.com/locate/ynimg

Multiple white matter tract abnormalities underlie cognitive impairment in RRMS

Hui Jing Yu [a,1], Christopher Christodoulou [b], Vikram Bhise [b,2], Daniel Greenblatt [b,3], Yashma Patel [b], Dana Serafin [b,4], Mirjana Maletic-Savatic [b,5], Lauren B. Krupp [b,*], Mark E. Wagshul [c,d,**]

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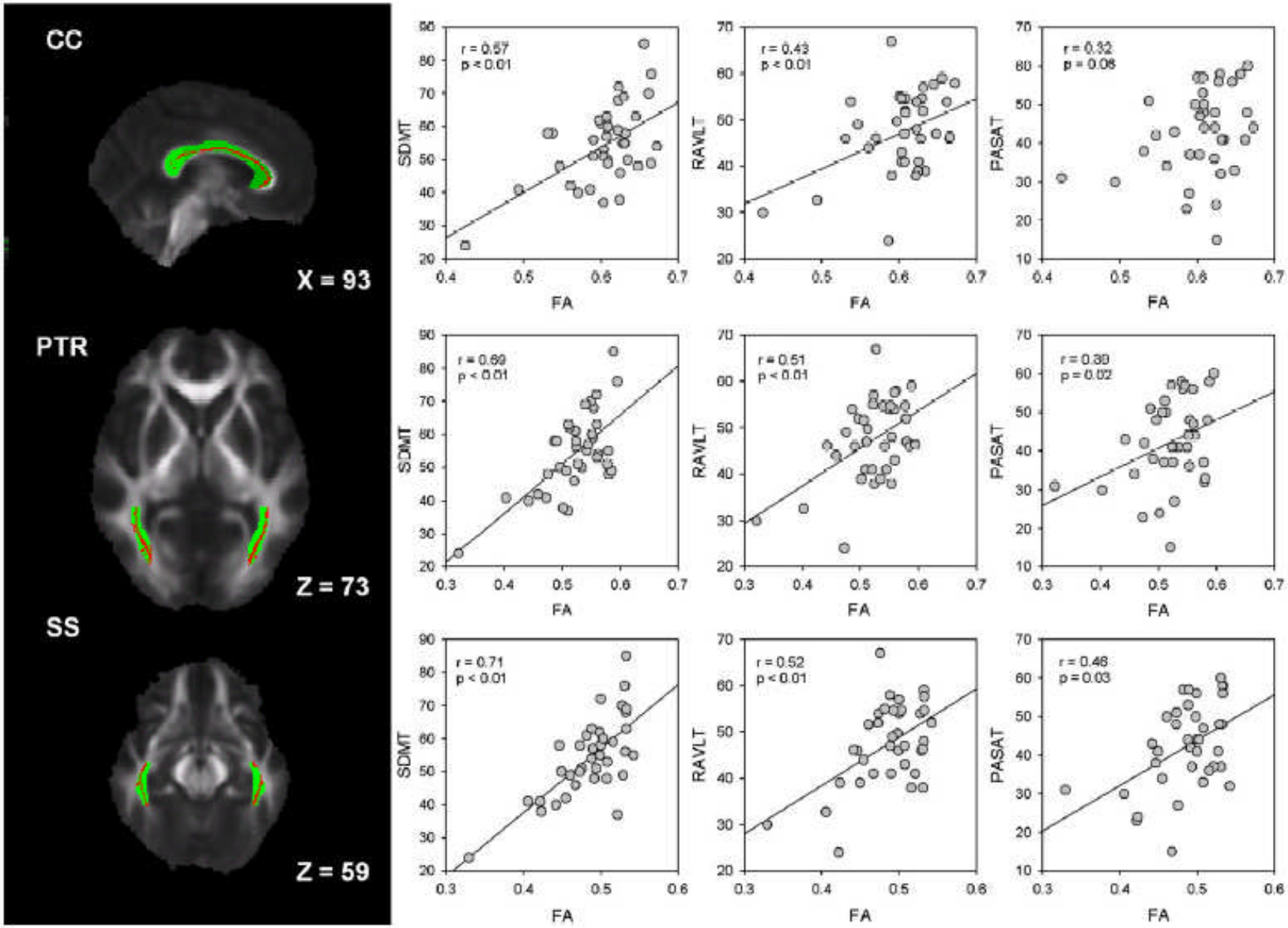
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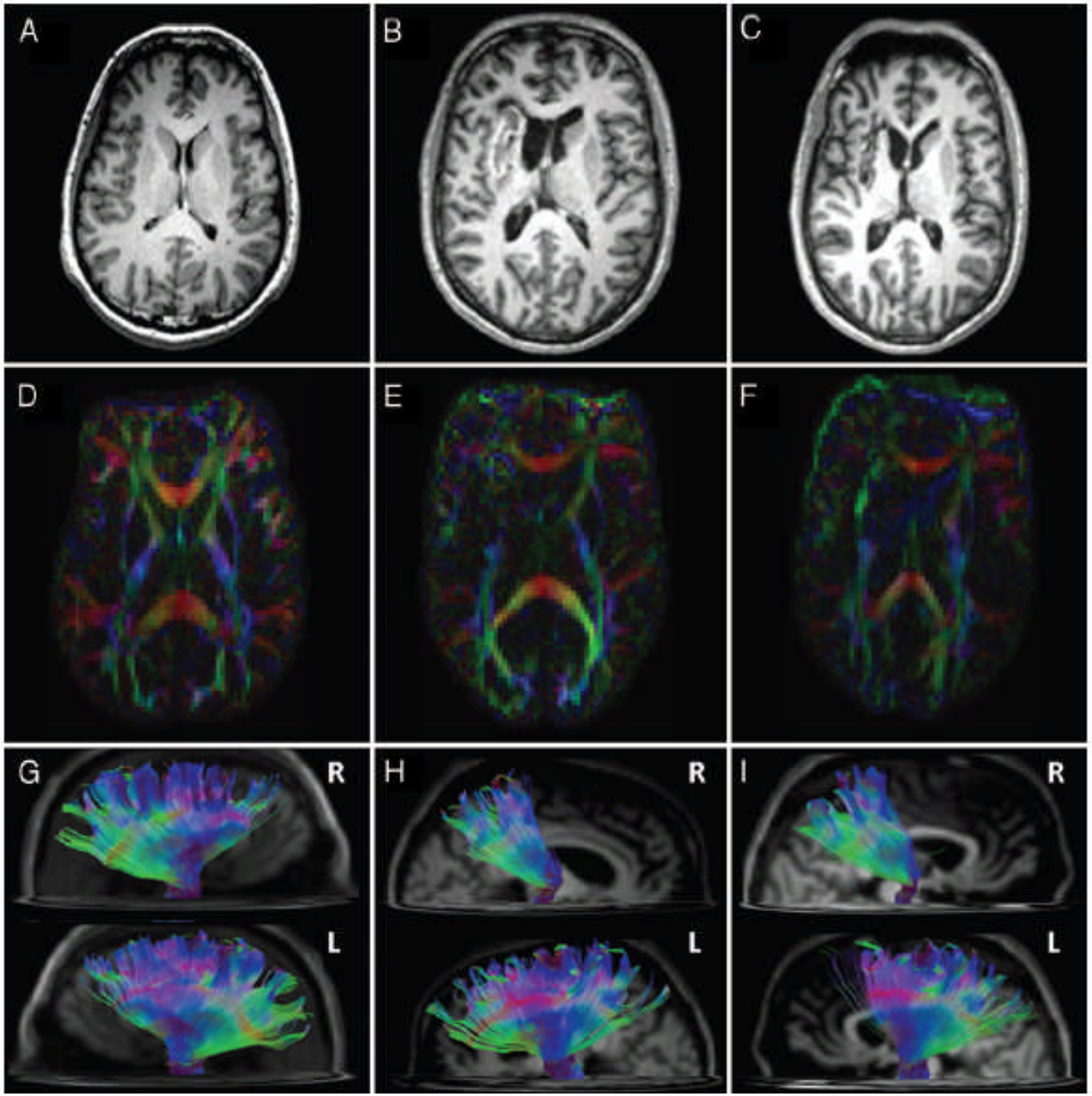
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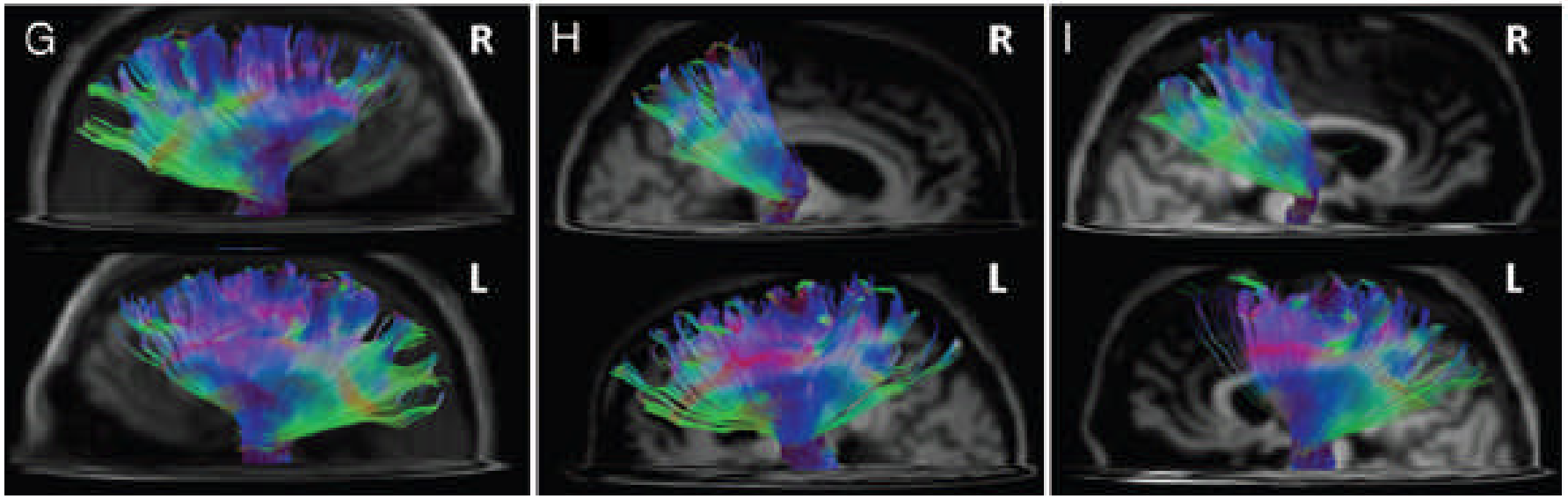
Shin et al., J Neurosurg, March 2, 2012, **DOI: 10.3171/2012.1.JNS111282**



Control **4 months post TB I** **10 months post TB I**

Advantages/disadvantages of DTI and fibre-tracking for assessing residual anatomy …

- **A standardized method can be used for all applications**
- **Relatively easy to acquire in as little as 7 minutes**
- **No active tasks so any patient can be assessed, even if unconscious**
- **Data can be acquired on almost any up-to-date hospital MRI system**
- **Data need to be analyzed (could be mostly automated), and seed-points selected (difficult to view all tracts at once)**
- **Results can be misleading/misinterpreted in areas of complex fibre paths, crossing paths, small tracts**

Summary and Concluding Points

Have shown three ways of visualizing changes in CNS structure and function as a result of injury or disease

Functional MRI may not be practical (yet) because there is no standardization of methods

Resting state fMRI can be done on any up-to-date MRI system
Results are typically robust

DTI and fibre-tracking can be done on most up-to-date MRI systems
Results are robust and sensitive in the large white matter tracts

These methods have been demonstrated to be powerful for research
They have potential to be powerful clinical assessment methods as well

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