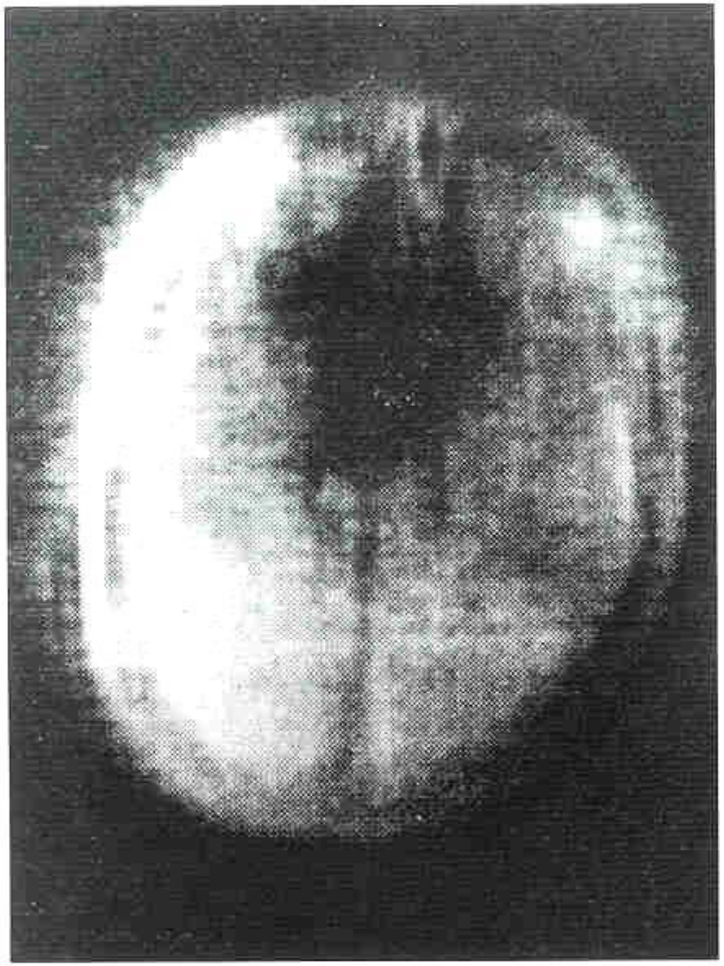


Fig. 4-46. The first published NMR reconstructed image of a head. (From Holland GN, Morre WS, Hawkes RC: J Comput Assist Tomog 69:262-277, 1980.)

First published NMR image of the head (Holland et al., 1980)

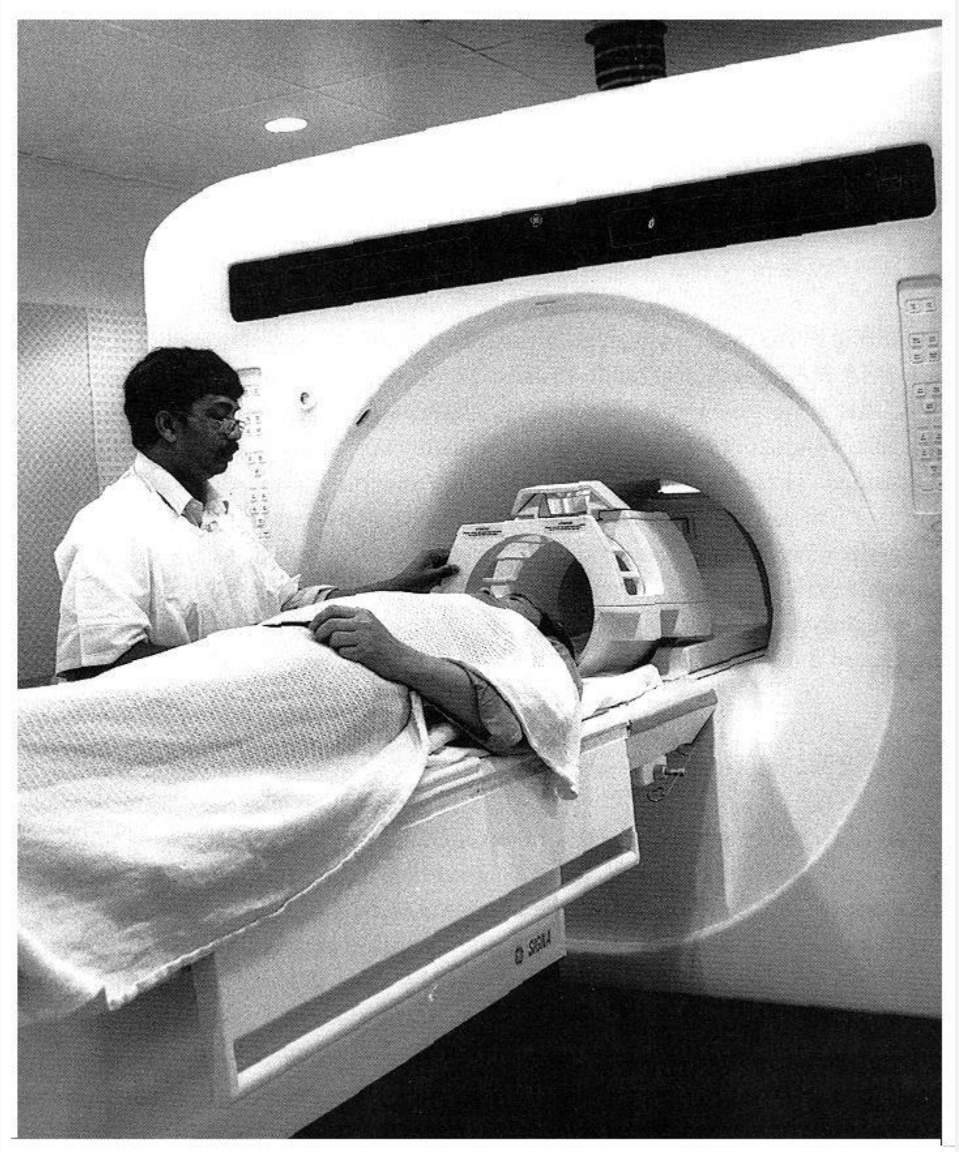
0.1 Tesla, 246 directions, backprojection reconstruction

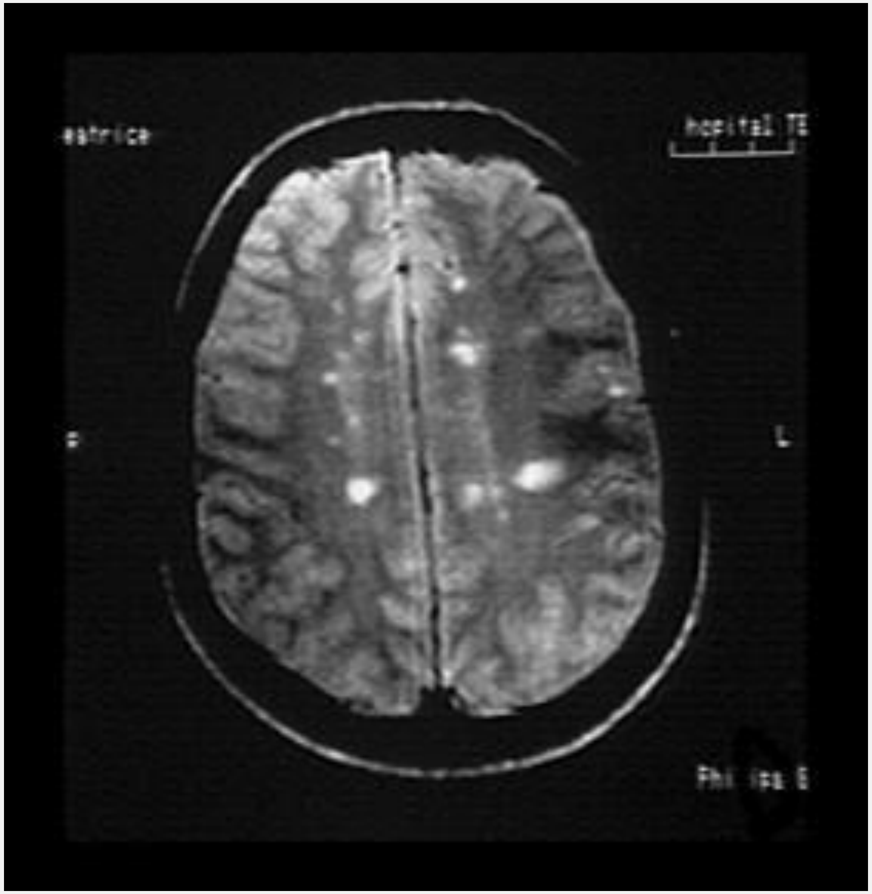
MRI: Tesla

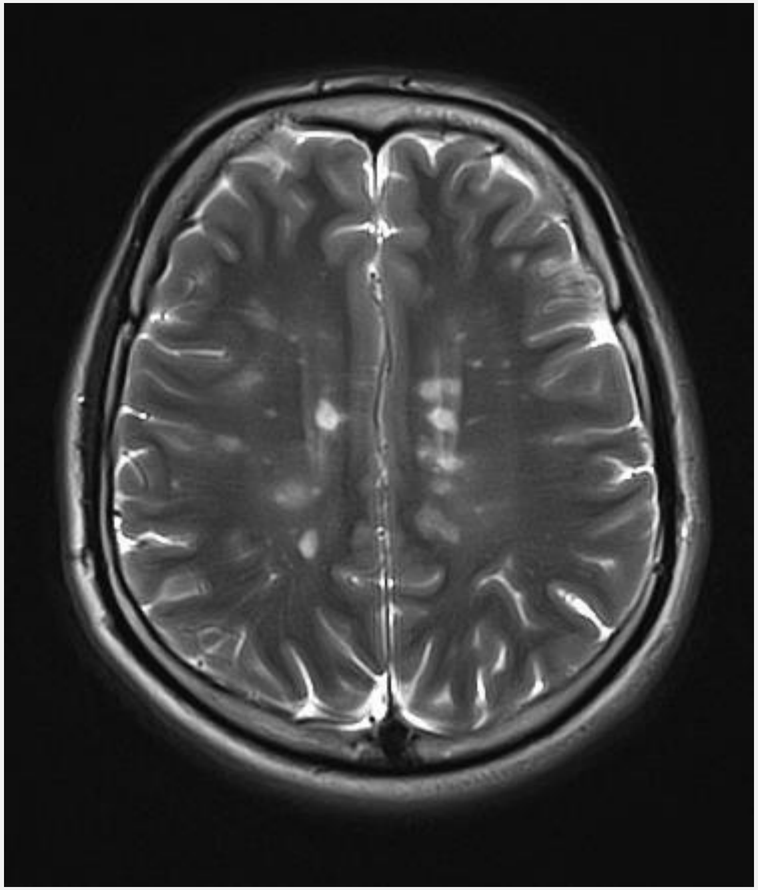
Earth's magnetic field = .5 gauss, or .00005 Tesla

1 Tesla = 10,000 gauss

3 Tesla = 60,000 times strength of earth's magnetic field



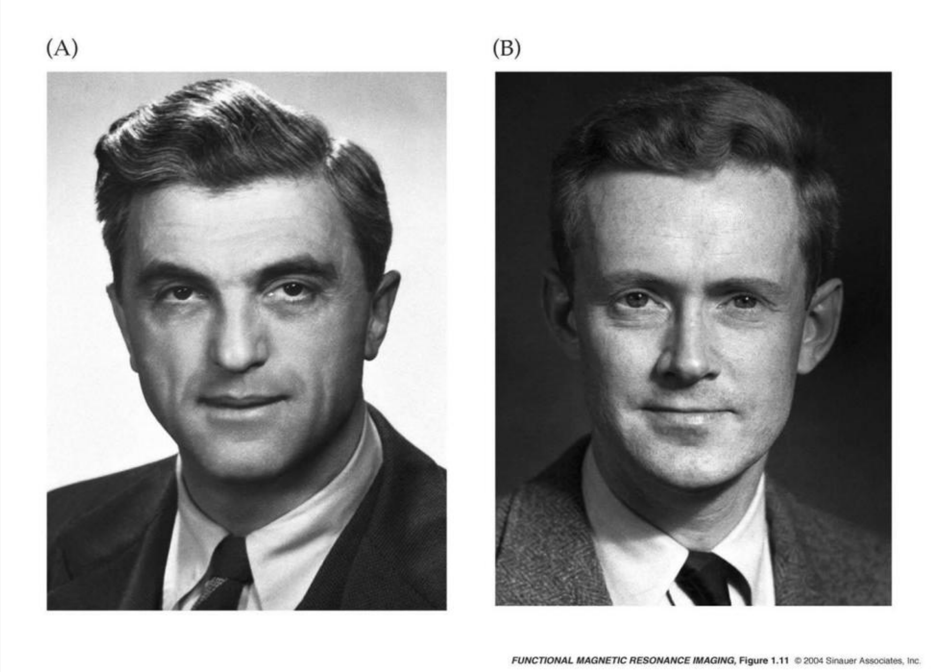




Multiple sclerosis (MS): Clinical trials for MRI began in 1983, FDA approved 1.5T two years later, in 1985.

Sensitivity of MRI to MS lesions compared to CT: 10 to 1.

3T was FDA approved in 2003.



Felix Bloch and Edward Purcell: Nobel Prize in Physics, 1952.

Bloch measured magnetic resonance in a block of material (paraffin wax) that was placed in a magnetic field.

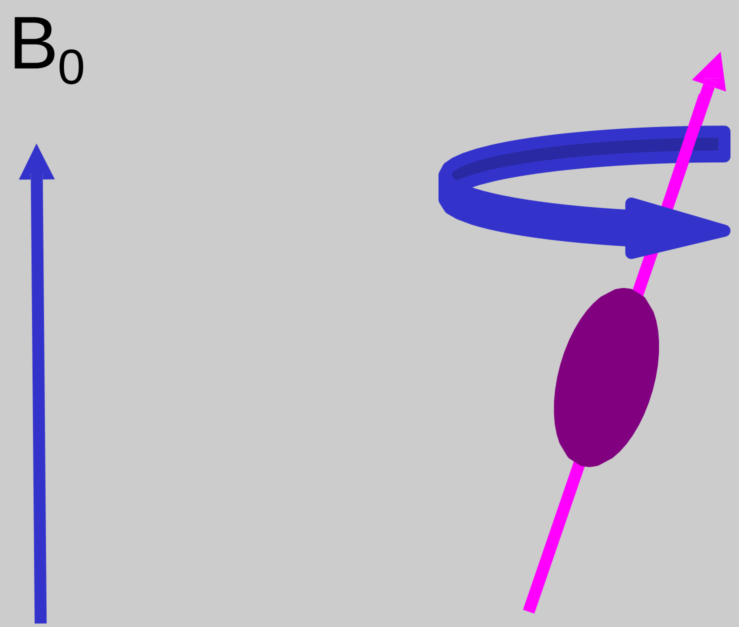
Purcell did the same with a container of water, devising a method that is identical to the basic MRI system: A static magnetic field, a transmit electromagnetic coil, and a coil for detecting emitted energy.

Magentic resonance:

- *Resonant frequency* – the frequency at which a particular molecule precesses or “spins” like a top around its axis. AKA “Larmor frequency”
- Energy at that frequency will be absorbed (“*excitation*”).
- Once the energy source is removed, the molecule will return back to its normal resting state, giving off energy (“*relaxation*”).
- *Magnetic resonance* – measureable energy emitted during relaxation.

MRI Signal:

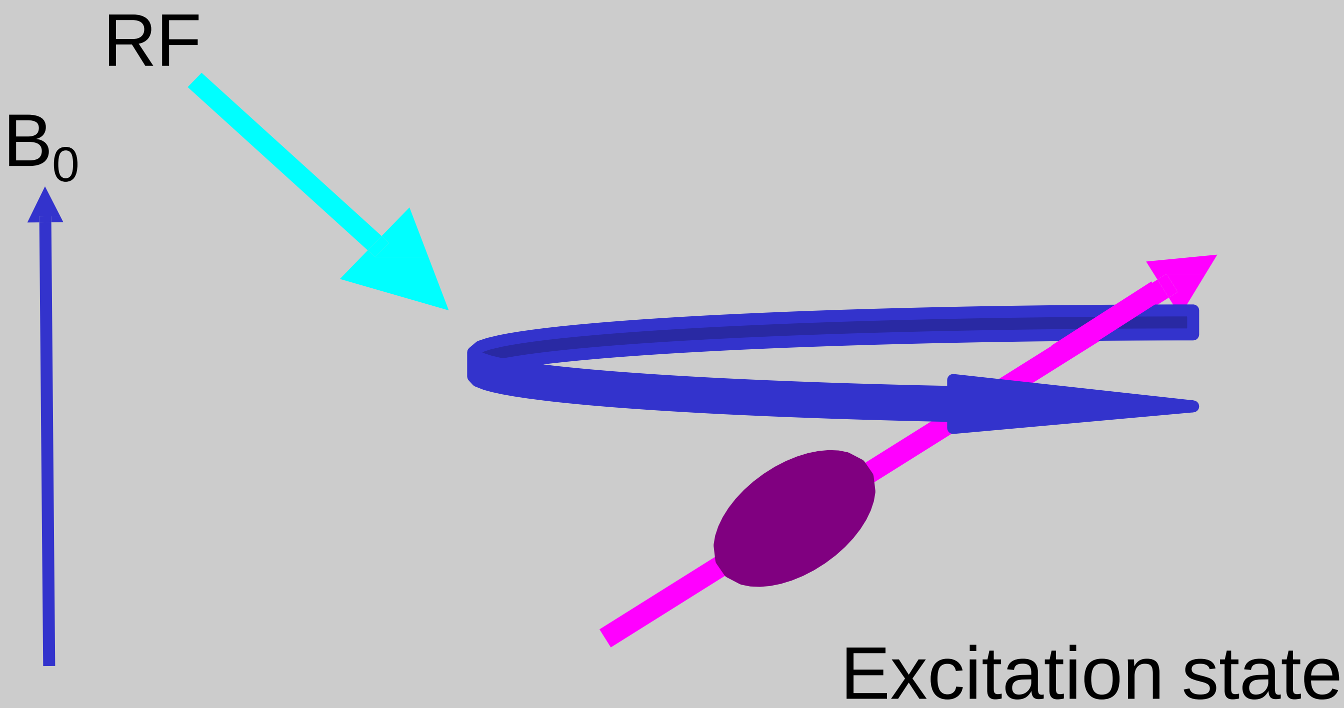
- *Step 1:* Atoms with an uneven number of protons act as dipoles – in a strong static magnetic field, they will align with the field and precess around that axis.



Resting state

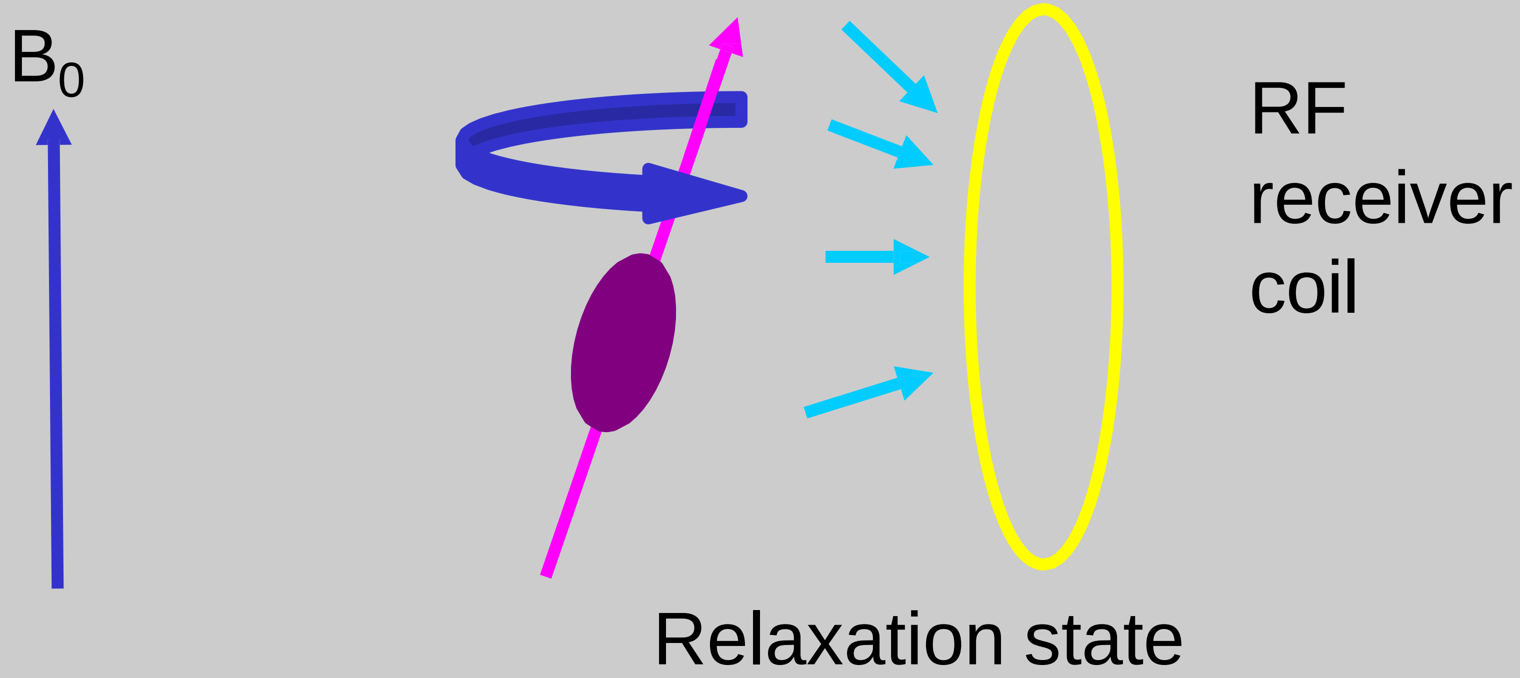
MRI Signal:

- *Step 2:* Apply energy pulse (normally in the radio frequency range) at the resonant frequency (aka Larmor frequency) of the molecule – the energy will be absorbed.



MRI Signal:

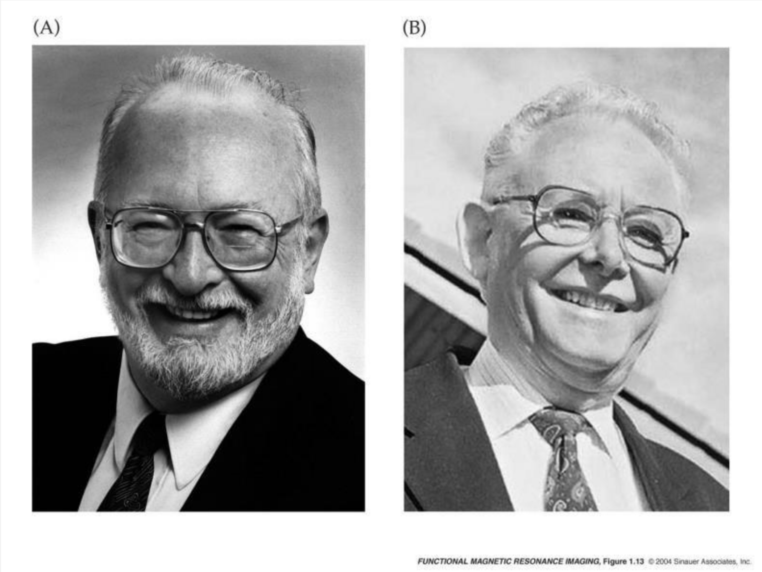
- *Step 3:* Turn off the RF pulse, and the molecule gives off the absorbed energy over time (relaxation rate), which can be measured with an RF receiver coil. This process is referred to as *magnetic resonance.*



MRI Signal:

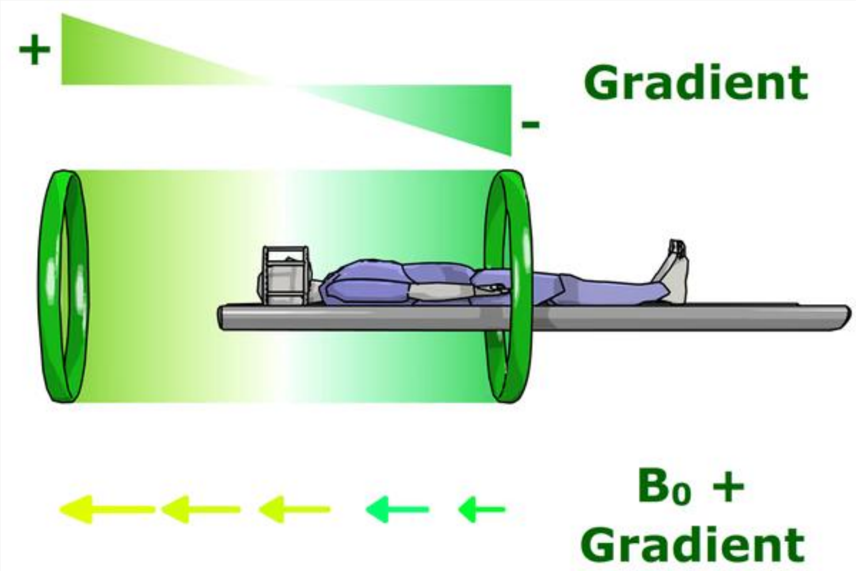
- *Molecule of measurement:* Hydrogen
- Why hydrogen? Lots of it in the brain (water)
- Differs in densities across tissue types (least in white matter, more in gray matter, most in CSF)
- Also differs in the strength of bonds (hydrogen in water is freely diffusing in CSF, but more tightly bound in fatty tissue such as myelin)
- Both these properties will affect the *relaxation rate* – how fast the hydrogen molecule returns to its low energy state

Paul Lauterbur and Peter Mansfield, Nobel Prize in Medicine, 2003



Lauterbur (1976) applied magnetic gradients to the static magetic field so that the field strength differed slightly depending on the spatial location.

The amount of energy emitted at a given frequency is determined by a) the number of nuclei and b) the strength of the magnetic field.



The strength of the magnetic field can be used to determine where the nuclei are located in 2D space.

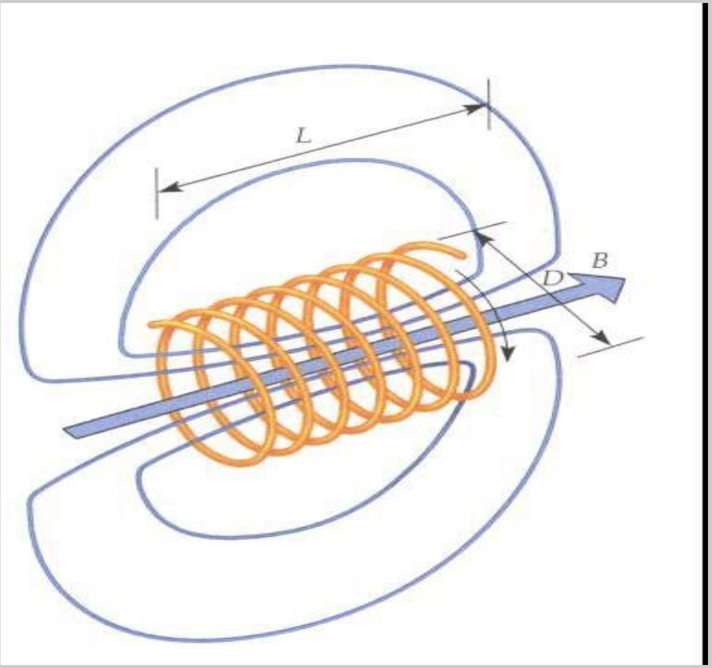
Mansfield (1977) found a way to speed up the data collection – echo planar imaging.

Components of MRI scanner:

- Static magnetic field
- Transmit radiofrequency coil
- Receiver radiofrequency coil
- Gradient coils (z, x, y)
- Shimming coils (1^{st}, 2^{nd}, 3^{rd} order)

Static magnetic field

- *Superconducting electromagnet* – a coil of wire, cooled with cryogens (helium, nitrogen) to near absolute zero, with a large current injected into wire.
- Resistance is near zero, can thus sustain high current without loss and with no power requirements.
- *Field strength* is proportional to the diameter of the coil and the strength of the current.



Radiofrequency coils

- Transmit coil: Electromagnetic coil used to generate oscillating energy (radiofrequency range) at the resonant frequency (Larmor frequency) of a sample being measured (*excitation*).
- Receive coil: EM coil used to measure energy emitted by a sample as it returns to its lower energy state (*relaxation*) once the excitation pulse is turned off.

Contrast mechanisms

1. Static contrasts: Proton density, T1, T2, T2*
2. Other types of contrast

    Endogenous

        Functional MRI (task based, at rest)

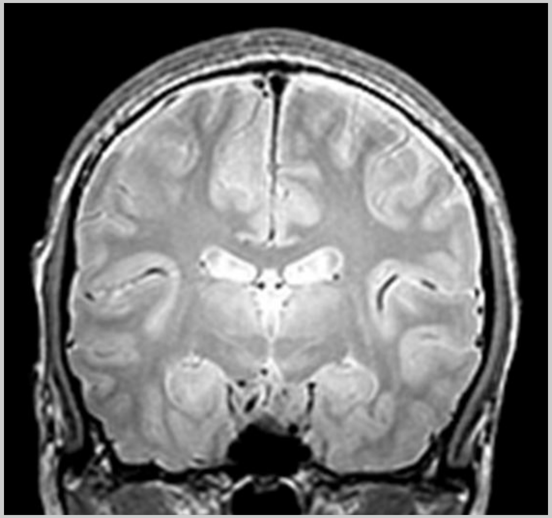
    Exogenous – Gadolinium

    Motion-weighted contrast

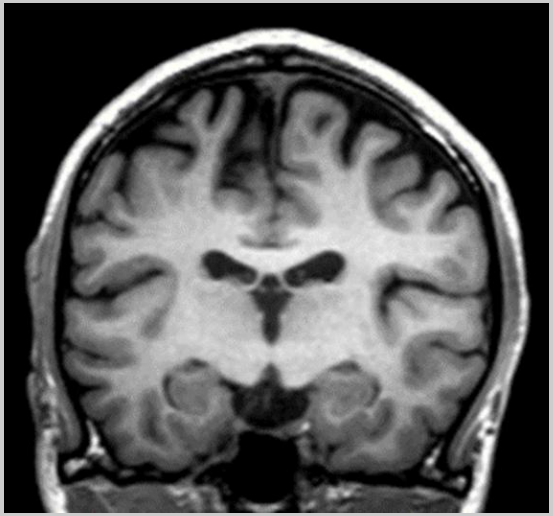
        Angiography

        Diffusion

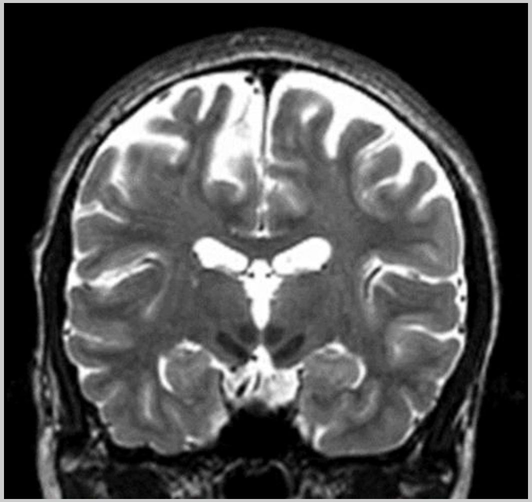
        Perfusion



Proton density gradient echo images:
Signal from CSF is high, gray is moderate, white matter is low (dark)

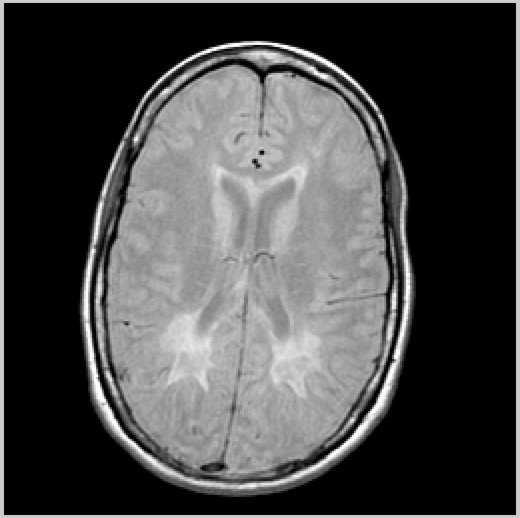


T1 weighted spin echo image:
White matter is brightest, moderate signal from gray matter, no signal from CSF

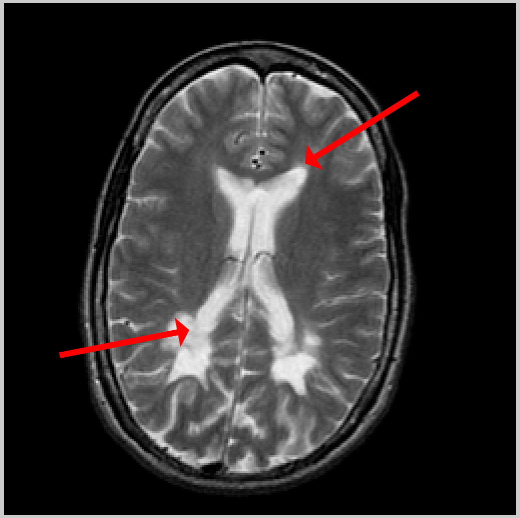


T2 weighted spin echo image:
CSF is bright, gray and white matter dark

26 yr old female with Multiple Sclerosis. Lesions are clearly evident on T2 weighted image (middle).



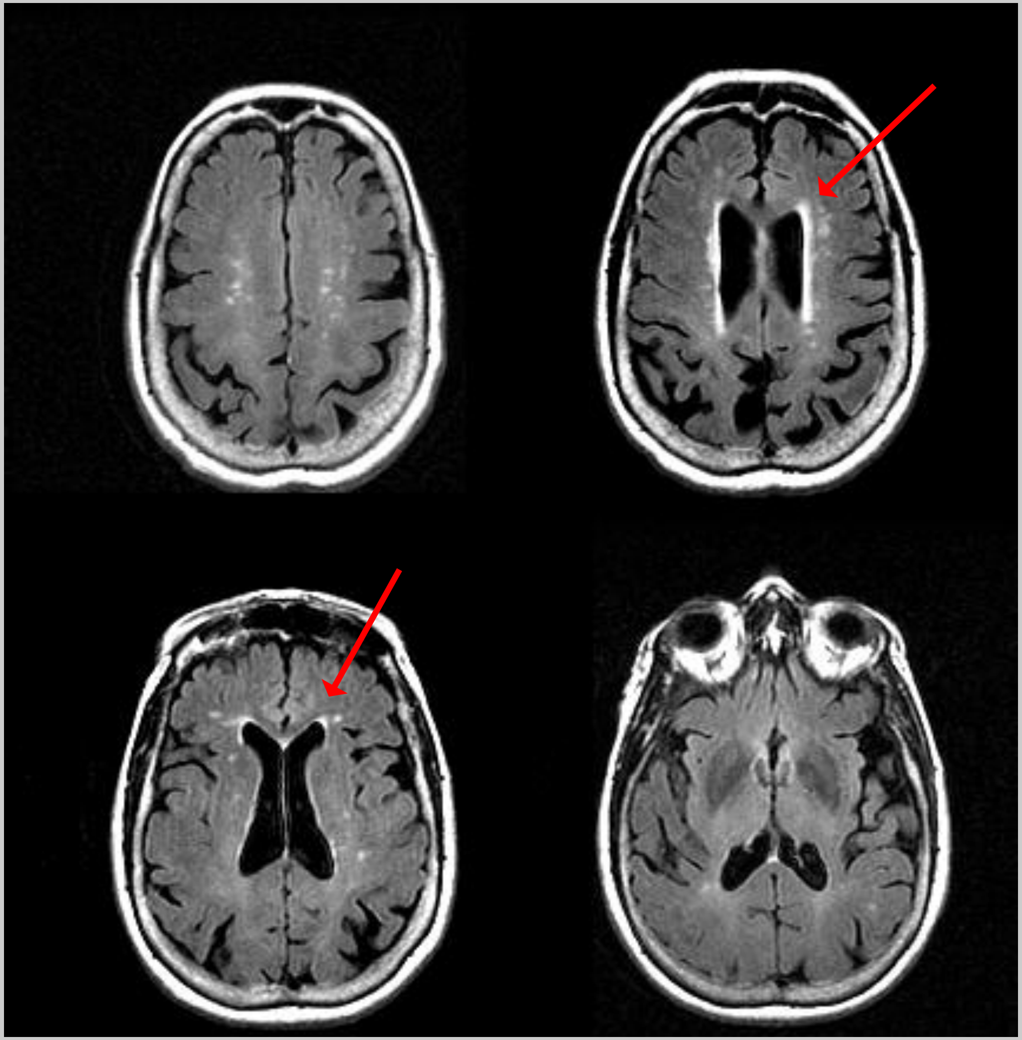
PD



T2

T1

Note how difficult it is to differentiate where ventricles end and abnormal white matter begins.

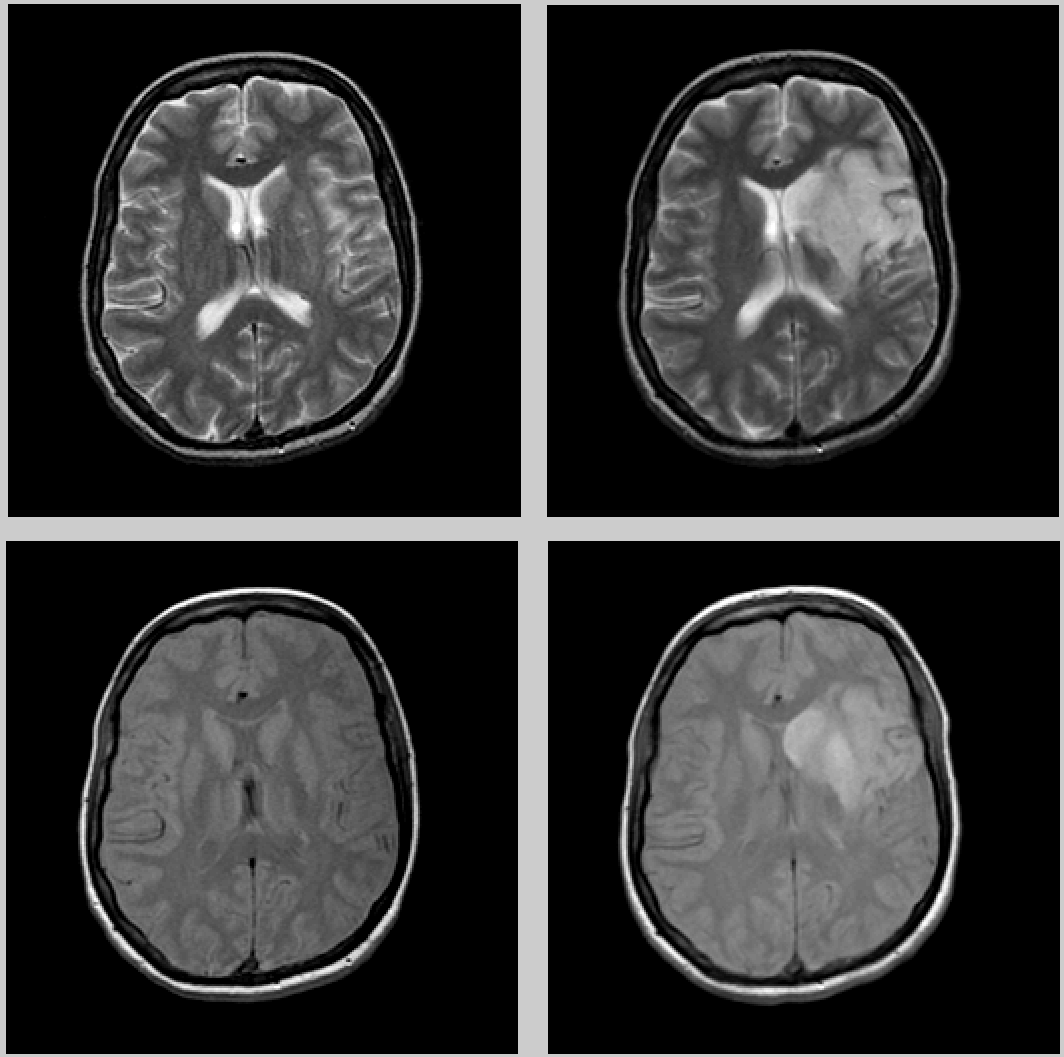


Multiple sclerosis:

T2 FLAIR (fluid attenuation inversion recovery)

Now CSF is dark, and abnormal white matter is easily differentiated from the ventricles.

40 yr old woman, T2 and PD MRI taken 8 hrs after presenting with aphasic symptoms vs 4 days later



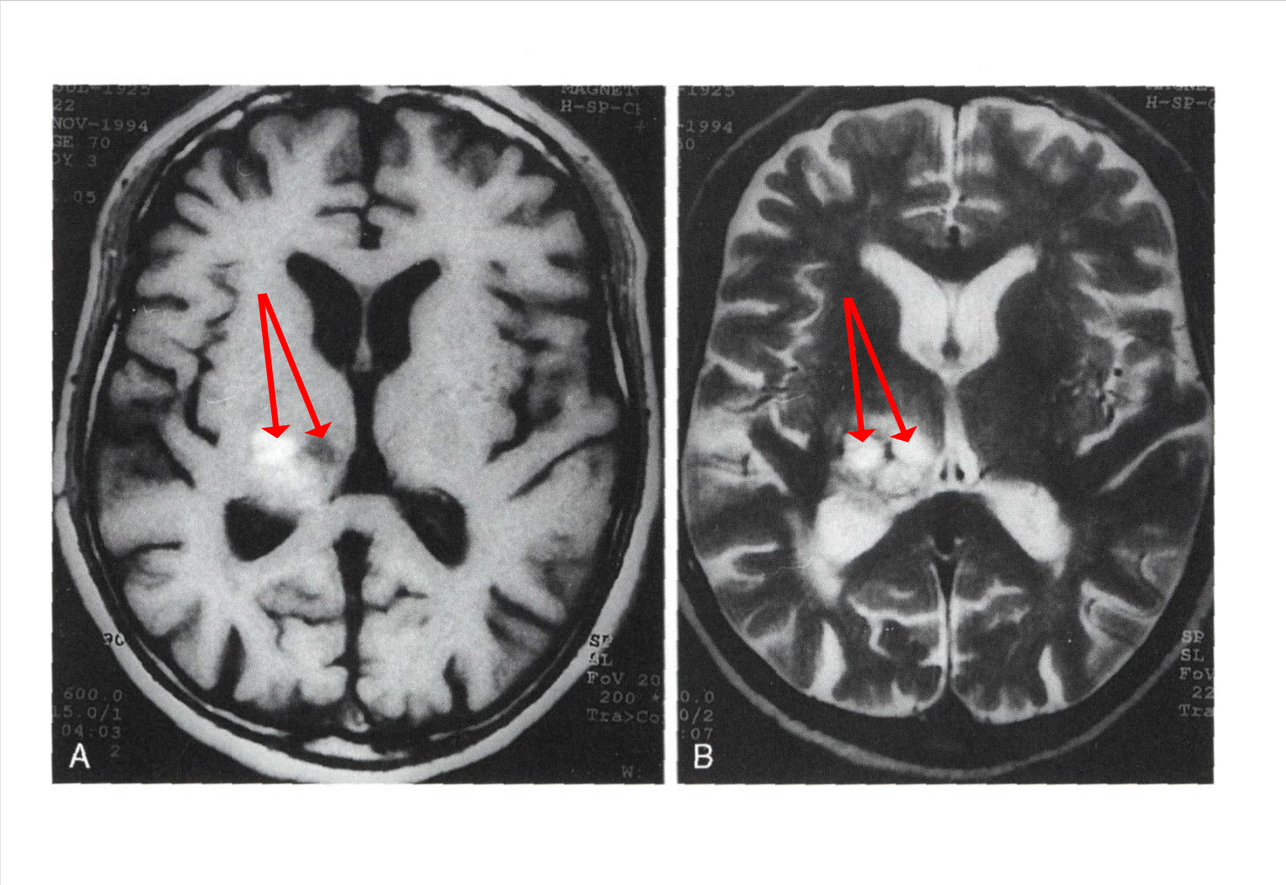
T2 weighted

Proton density

8 hrs post-stroke

4 days post-stroke

71-yr old man presenting with hemorrhage into a glioma.

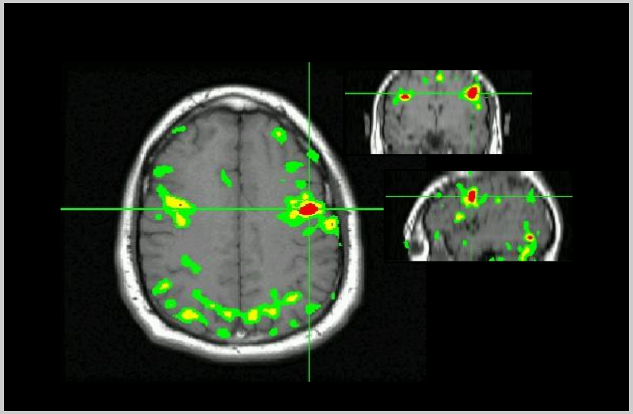


A. Axial T1 spin-echo (TR/TE = 600/15)

B. Axial T2 image (TR/TE = 3400/90)

Note how much more region of abnormality is evident on T2, but the hyperintense regions on T2 differentiate on T1.

Endogenous contrast:
Functional MRI



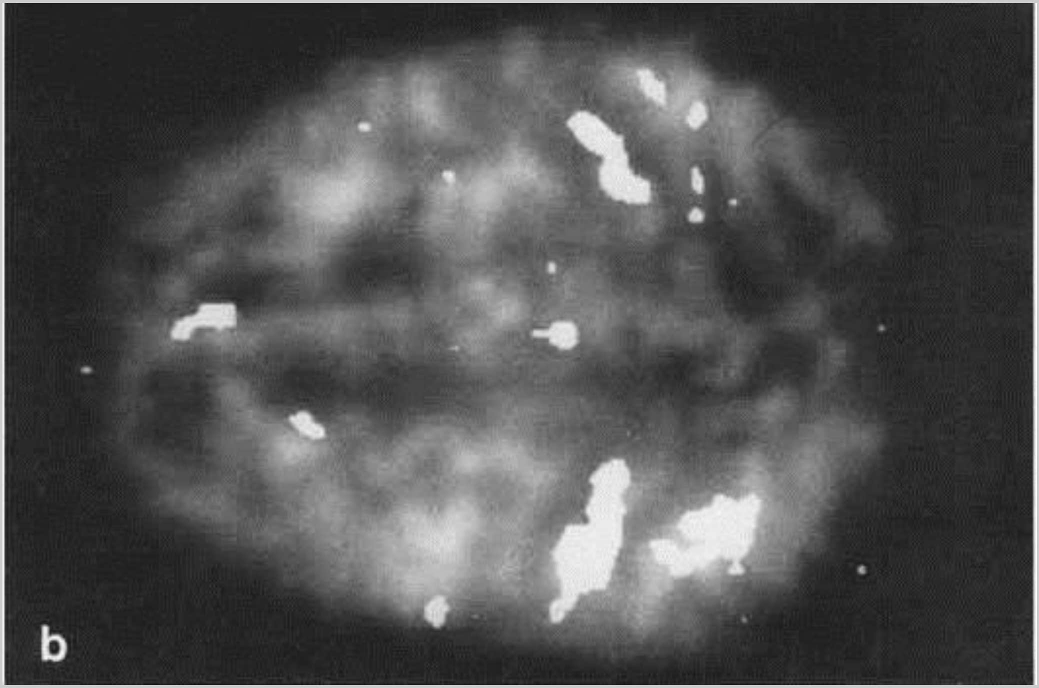
- Measures changes in signal intensity that arise from oxygenated blood in a region of brain tissue.

Good things:

- High resolution, fast scanning time, non-invasive

Not so good things:

- Very low signal to noise ratio, sensitive to motion, susceptibility artifacts



MAGNETIC RESONANCE IN MEDICINE 25,390-397 (1992)

Time Course EPI of Human Brain Function during Task Activation

PETER A . BANDETTINI , ERIC WONG, R. SCOTT HINKS, RONALD TIKOFSKY, JAMES S. HYDE

Department of Radiology, Medical College of Wisconsin

Using gradient-echo echo-planar MRI, a local signal increase of **0.3%** is observed in the human brain during task activation, suggesting a local decrease in blood deoxyhemoglobin concentration and an increase in blood oxygenation. Images highlighting areas of signal enhancement temporally correlated to the task are created.

Why functional neuroimaging?

1. **Brain architecture: Localization of function**

    Animal models

    Neuropsychology

    Task fMRI

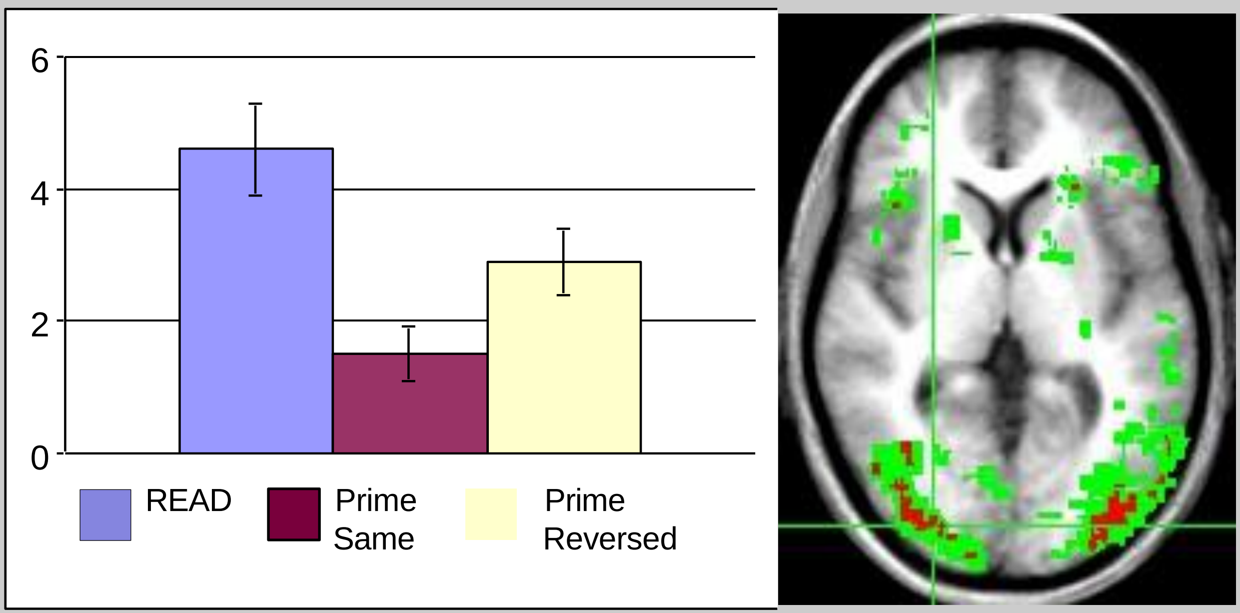
2. **Architecture of cognitive processes**

    Task and non-task fMRI

    Just like any other measure, behavioral or physiological, such as reaction times, skin conductance, etc.

    Requires understanding what is being measured, how it is measured, and the assumptions inherent in measurement.

- MRI signal is dependent on field strength of the magnet and the properties of the tissue.
- Also dependent upon changes in local environment.
- Paramagnetic substances (such as deoxyhemoglobin) will lead to loss of local signal on T2* weighted image.



Posterior cortical regions showed differential changes in neural activation resulting from format-specific priming. *Ryan, L., & Schnyer, D. (2006). Cerebral Cortex, 17, 982-92.*

Functional MRI signal

Local neuronal activity

→ Increased local metabolic rate

→ Increased blood flow

→ Increased oxygenated hemoglobin

→ Uptake of O_2 less than supply

→ Surplus oxygenated hemoglobin

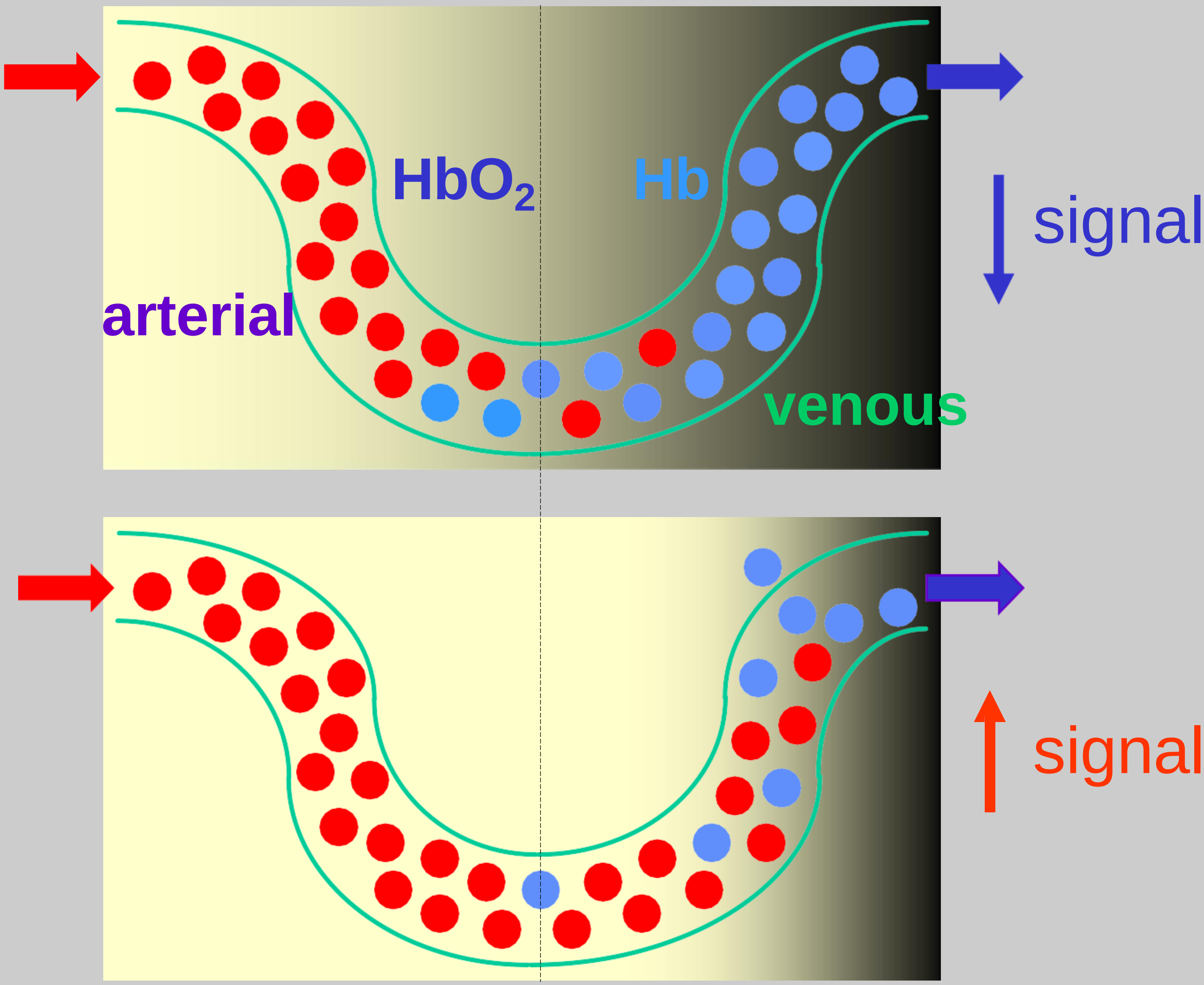
→ Decreased concentrations of deoxyhemoglobin

→ **Increased local fMRI T2* signal**

BOLD Contrast

Resting state

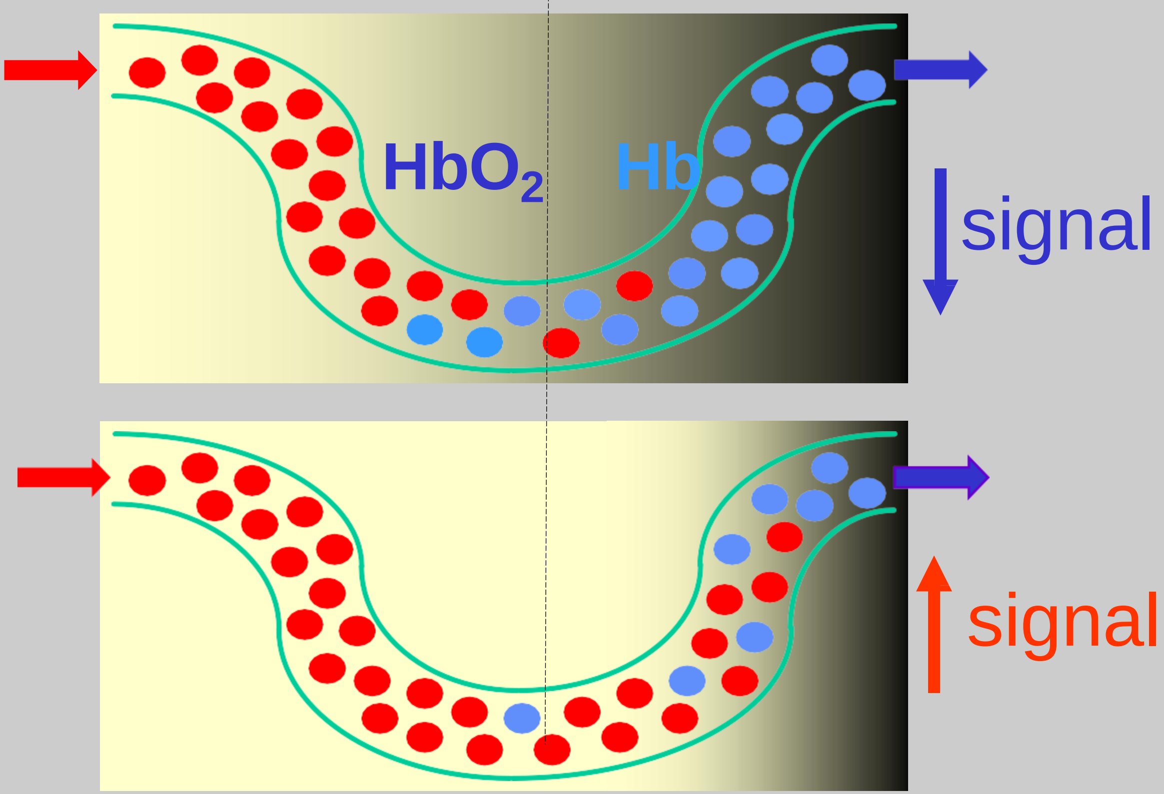
Stimulated state



Determining Activation:
A subtraction measure

Subject is
scanned at rest (R)

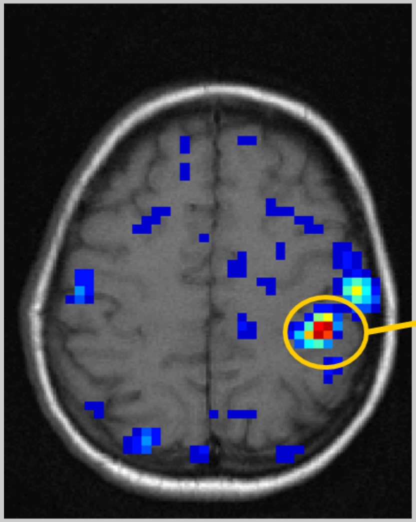
Subject is scanned
during cognitive
task (C)

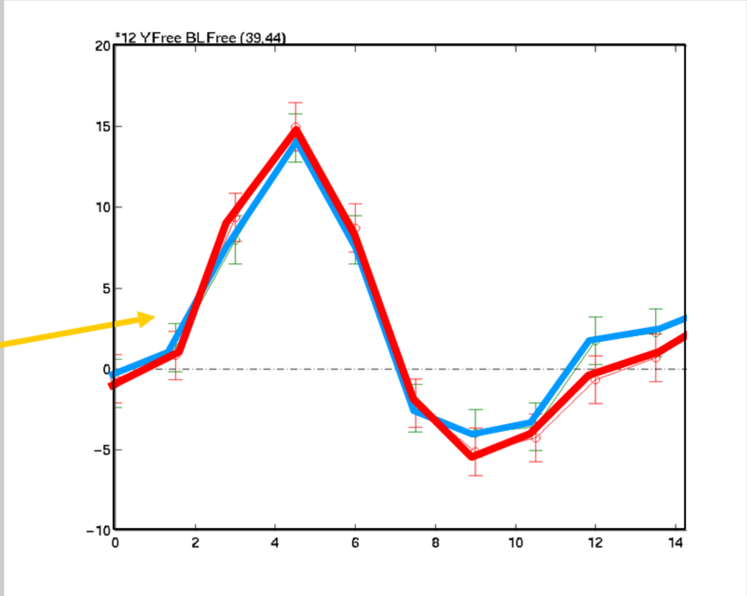


Regions of activity are determined the *differences* between scan R and scan C.

Caveats regarding fMRI:

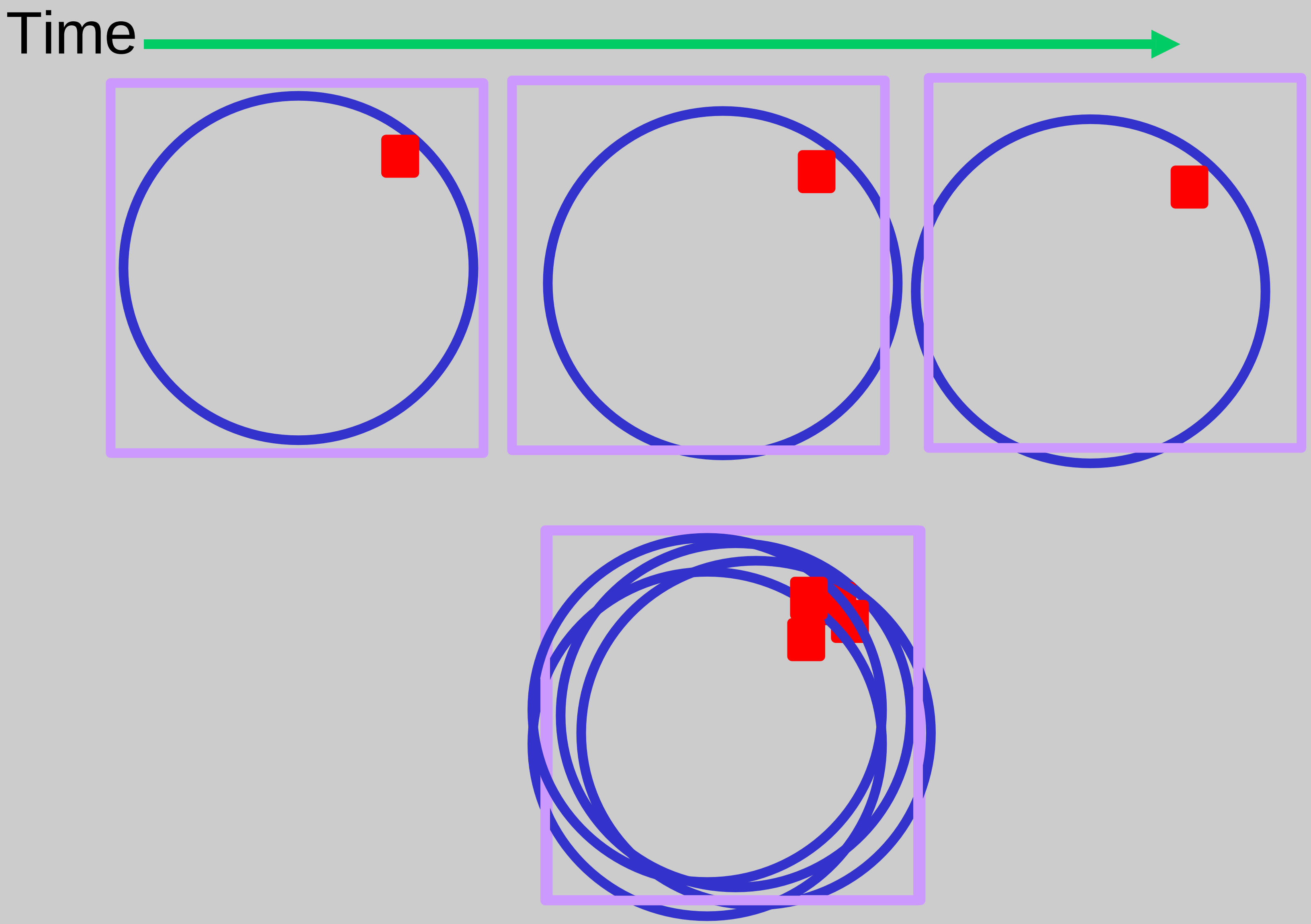
- Tertiary measure of neuronal activity.
- Very small signal changes, on order of 1 to 3%.
- Signal change predominates in region of large draining veins, not gray matter, and may vary in locality.
- Hemodynamic response is delayed – 30 msec scan, but 10-12 sec response.
- Extremely sensitive to motion.



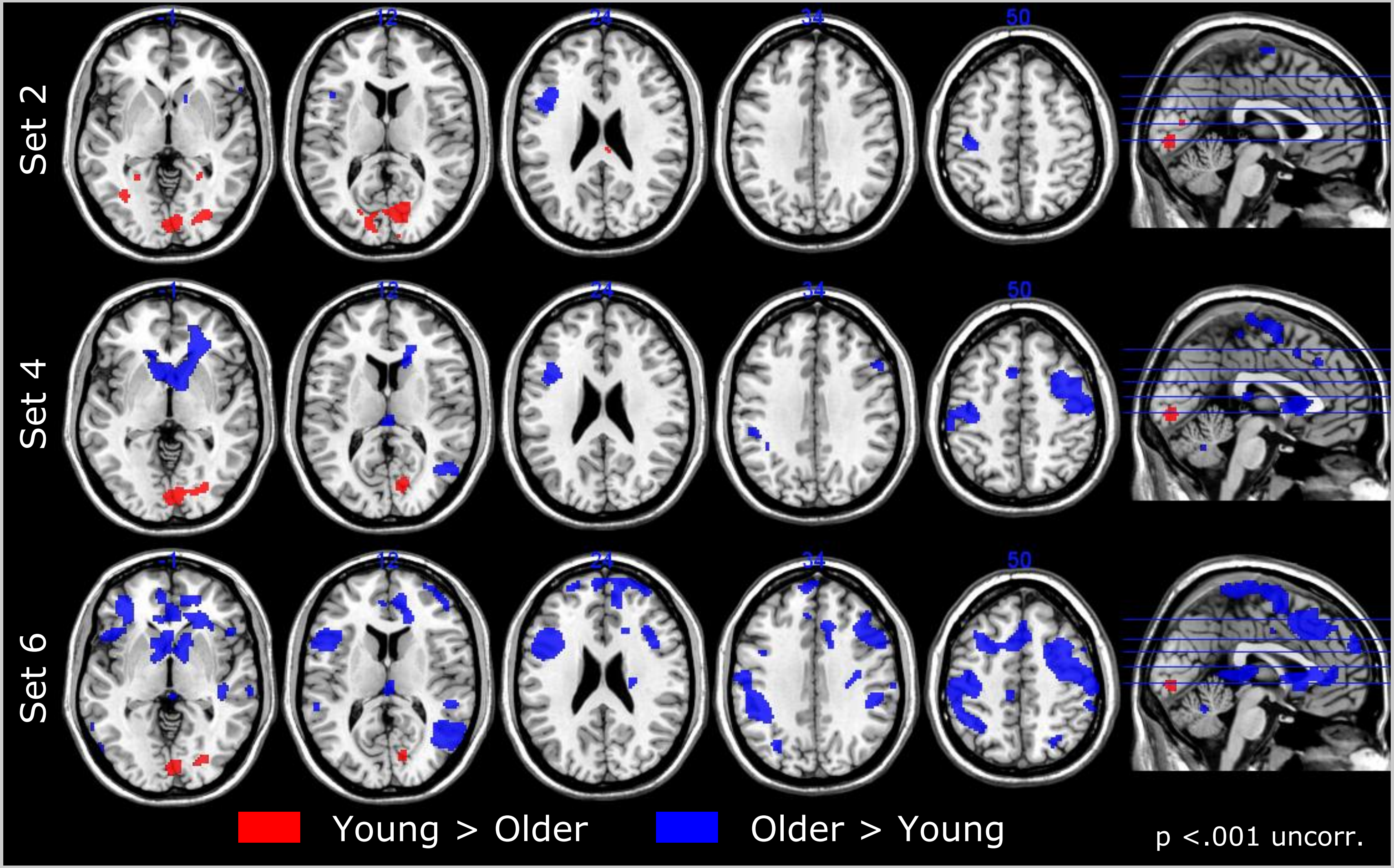


The hemodynamic response takes time, even for a single, fast behavioral response, like finger tapping.

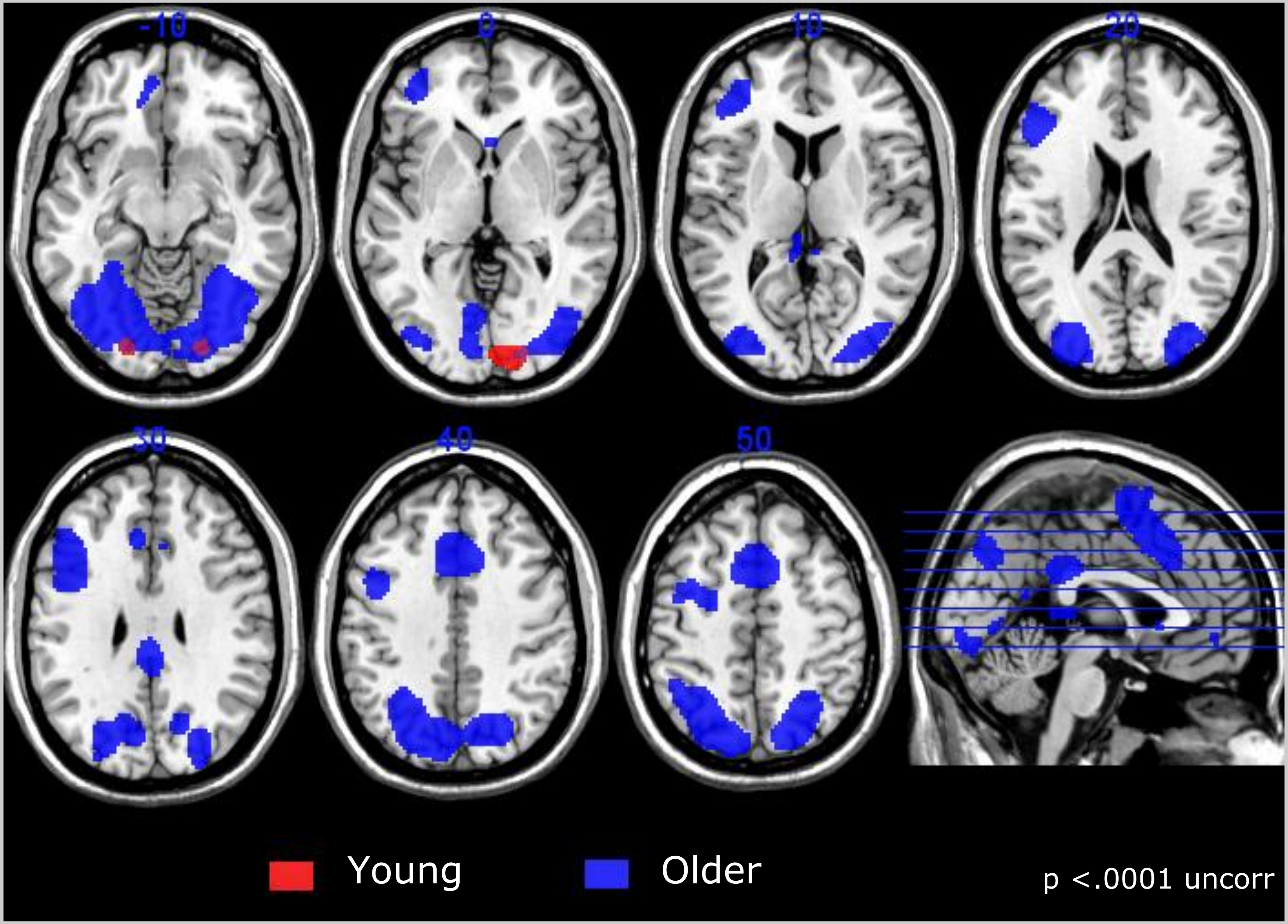
Motion:



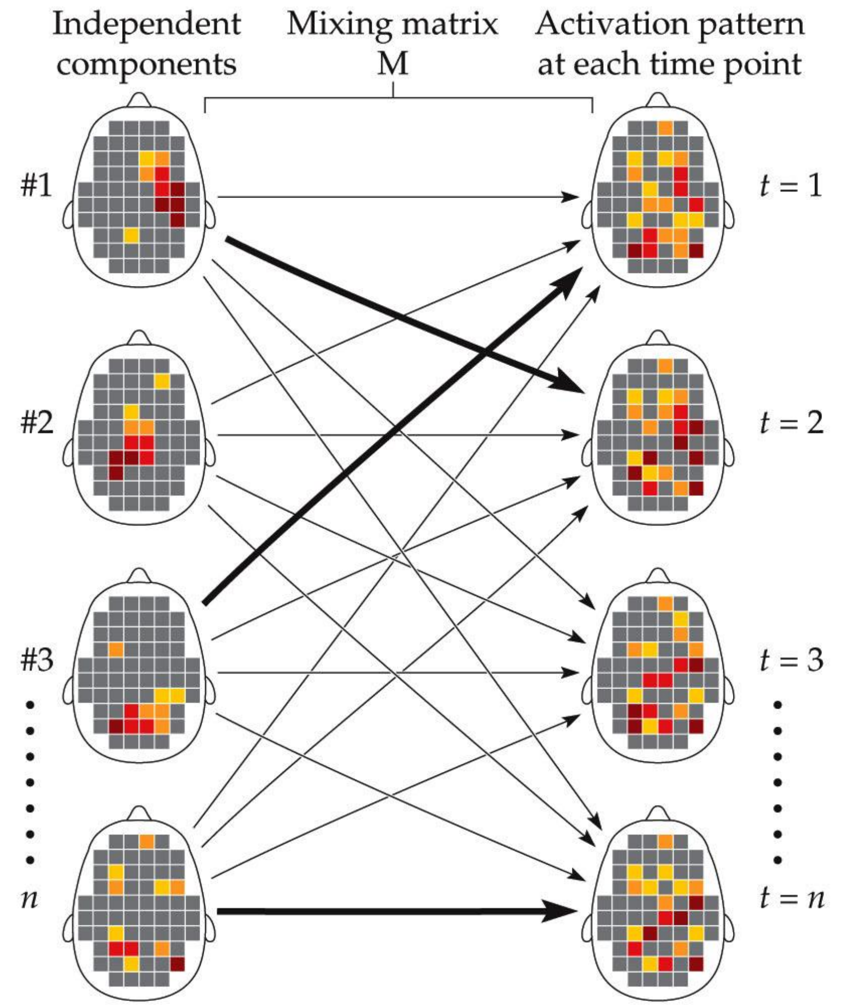
Group differences per study set



Linear increases with task difficulty

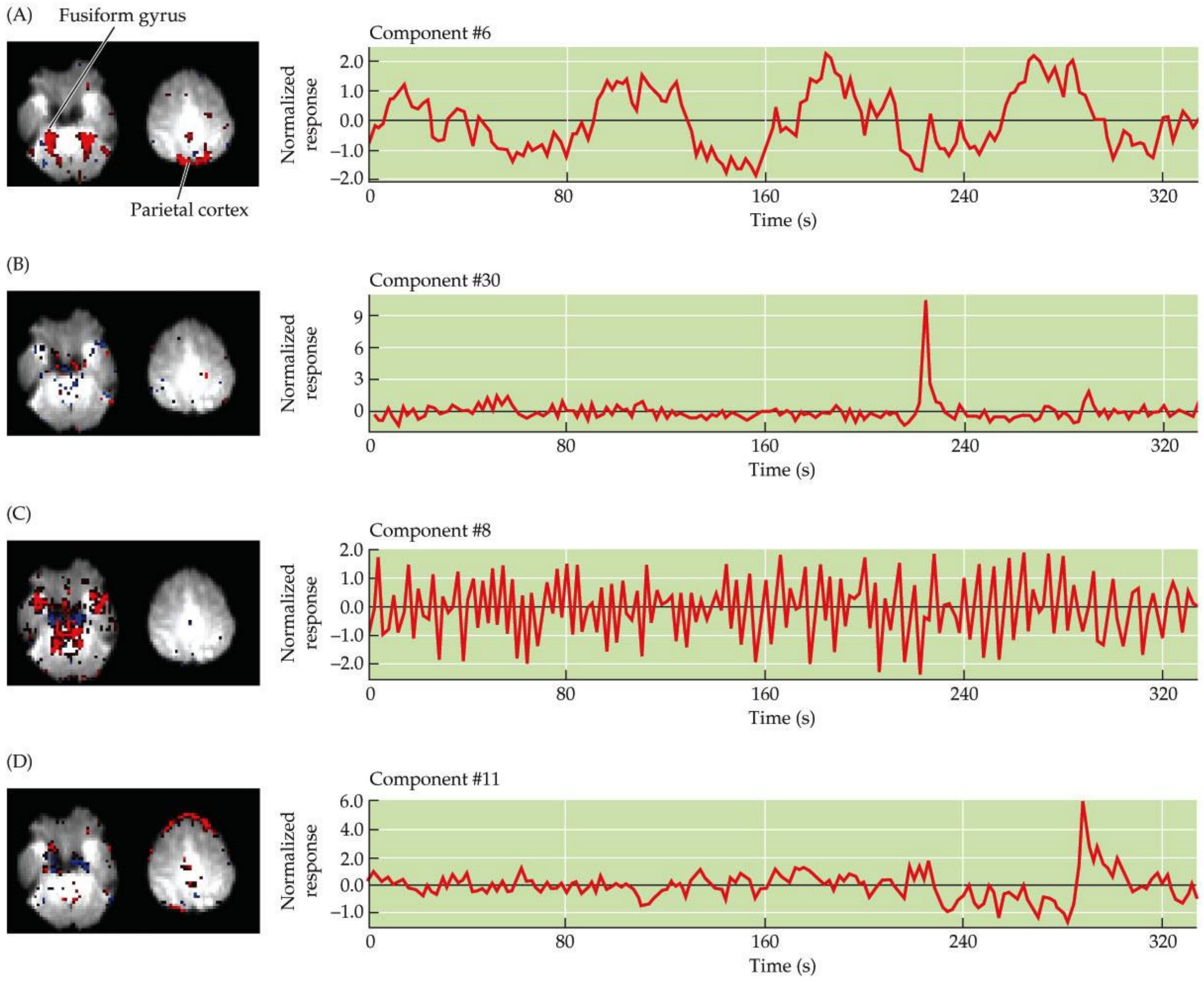


ICA: The goal of ICA is to identify stationary sets of voxels whose activity covaries across time and are maximally distinguishable from other sets of voxels.



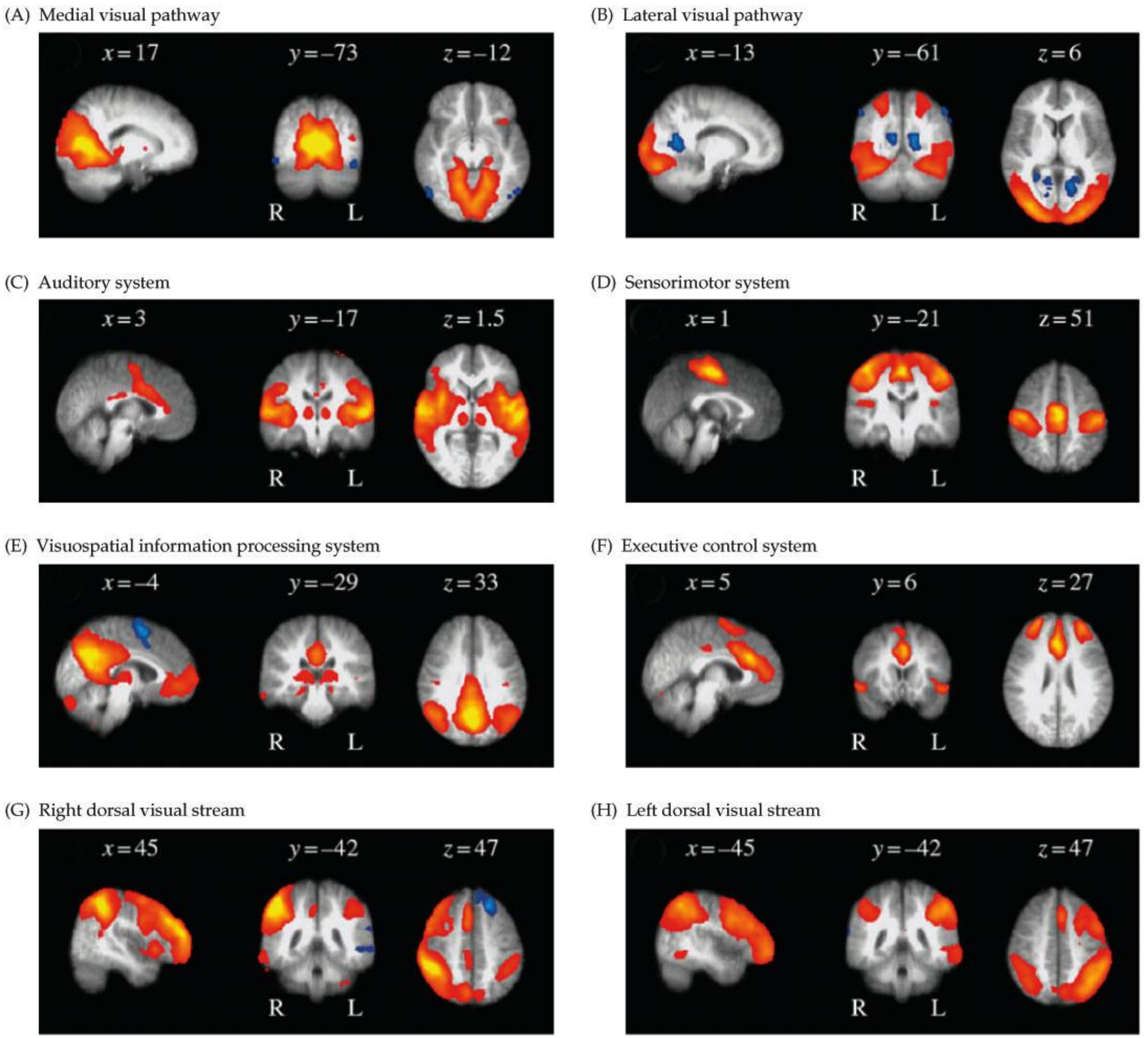
Functional Magnetic Resonance Imaging 2e, Figure 11.2

Extracting task-related and non-task-related components using ICA: Examples of signal, scanner artifact, large vessel fluctuations, and motion (edges)



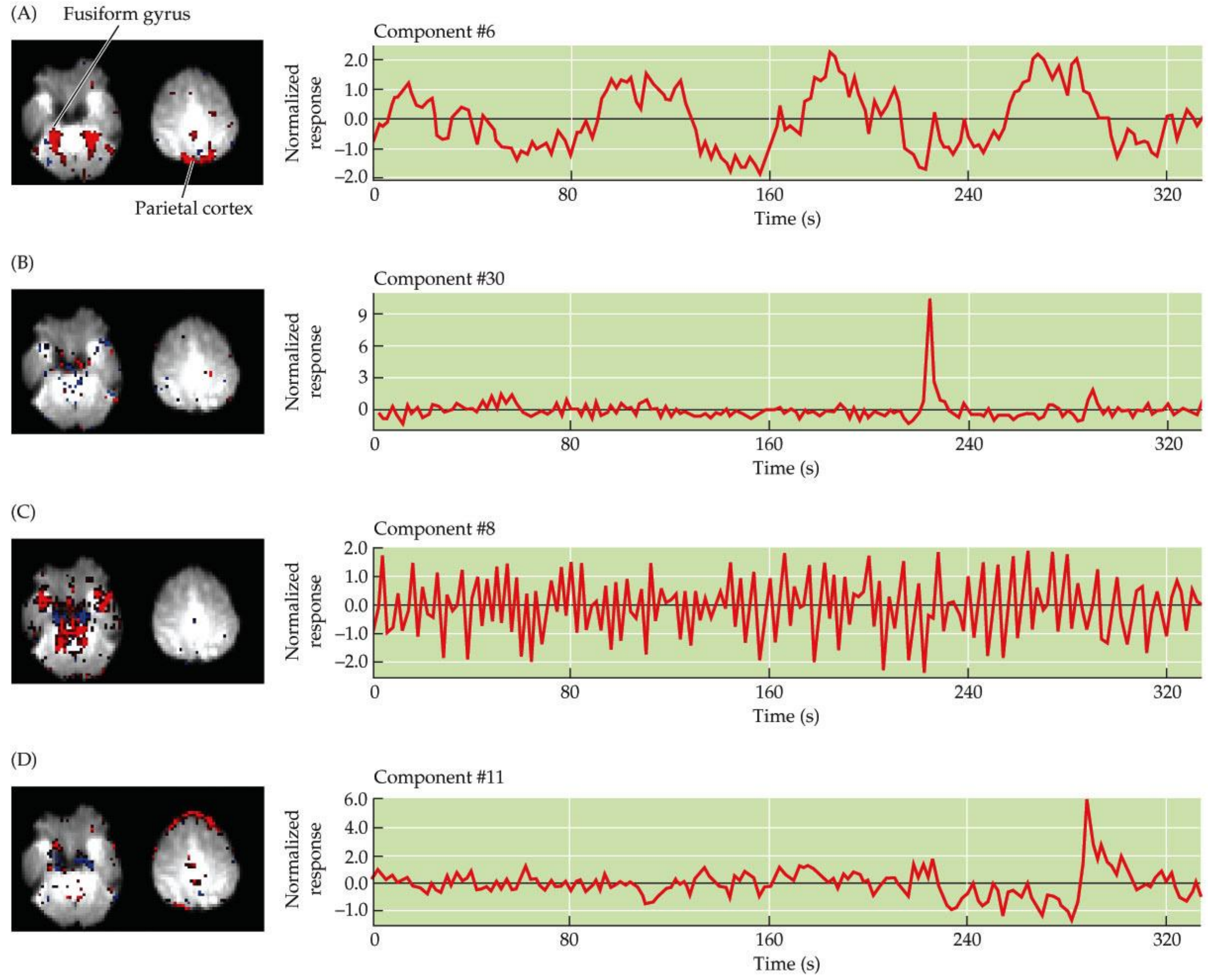
***Functional Magnetic Resonance Imaging 2e*, Figure 11.3**

Using ICA to identify brain networks showing high resting-state connectivity (Beckmann et al., 2005)



***Functional Magnetic Resonance Imaging 2e*, Figure 11.4**

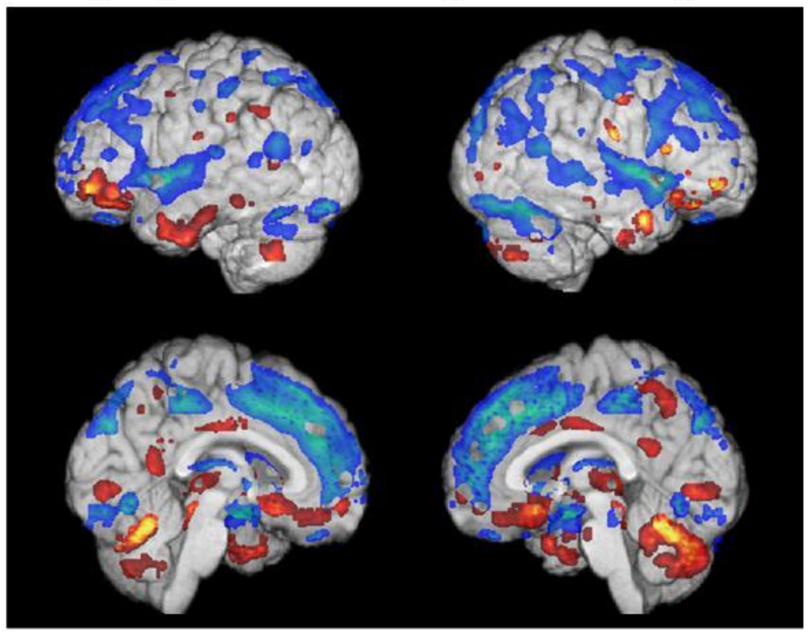
Problems with ICA: Too many components (usually hundreds), too little variability accounted for by each component – so how do you tell which ones are "of interest"?



***Functional Magnetic Resonance Imaging 2e,* Figure 11.3**

Structural equation modelling (Randy McIntosh) and scaled subprofile modelling (Jim Moeller, Gene Alexander): Identifying patterns of common covariance across the brain. Upside, like factor analysis can account for large amounts of variance in small numbers of patterns. Also provides a “pattern score” for each individual.

Network pattern of MRI gray matter associated with aging in 29 healthy adults, age 23-84



From: Bergfield KL, Hanson KD, Chen K, Teipel SJ, Hampel H, Rapoport SI, Moeller JR, Alexander GE. Age-related networks of regional covariance in MRI gray matter: Reproducible multivariate patterns in healthy aging. NeuroImage, in press.

Motion-weighted contrast

Angiography

Perfusion

Diffusion

3D time-of-flight image of the vasculature

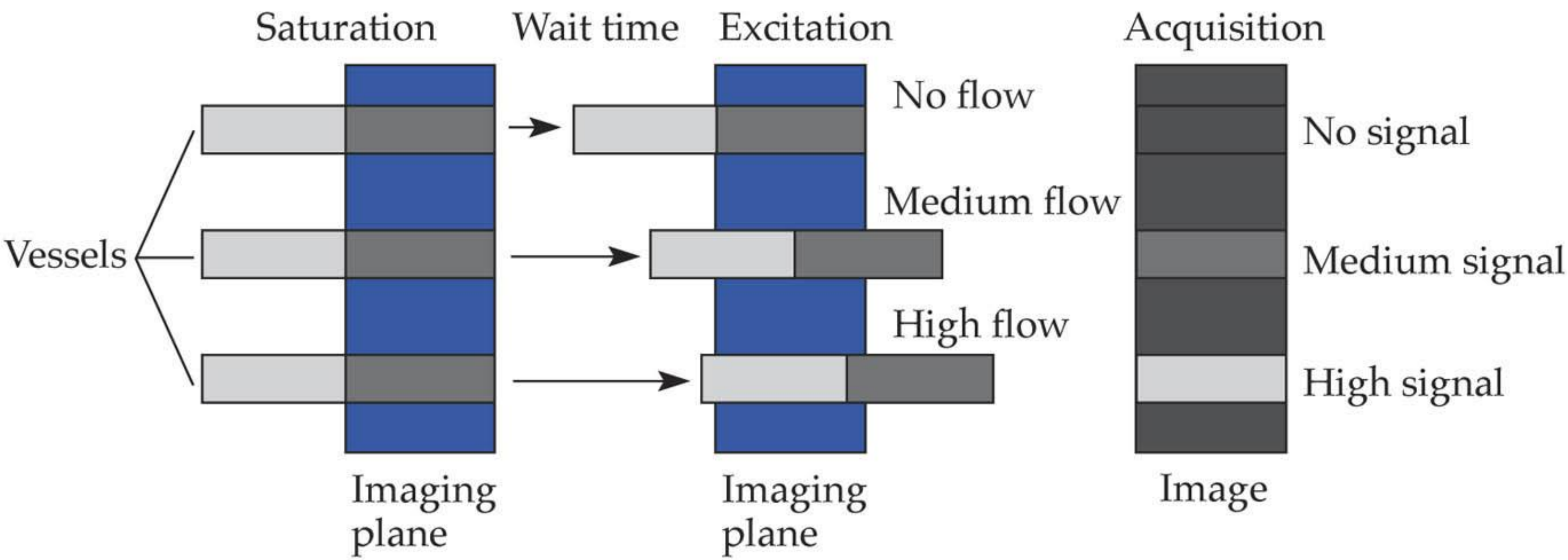
Classic angiography injected a contrast agent with Xray.

Time-of-flight angiography uses MRI to suppress signal from all tissue except blood flowing into the section.

Provides exquisite 3D images of vasculature.

Signal generation for TOF angiography

Spin saturation – apply excitation pulse and gradient pulses so that signal within a section will be virtually null

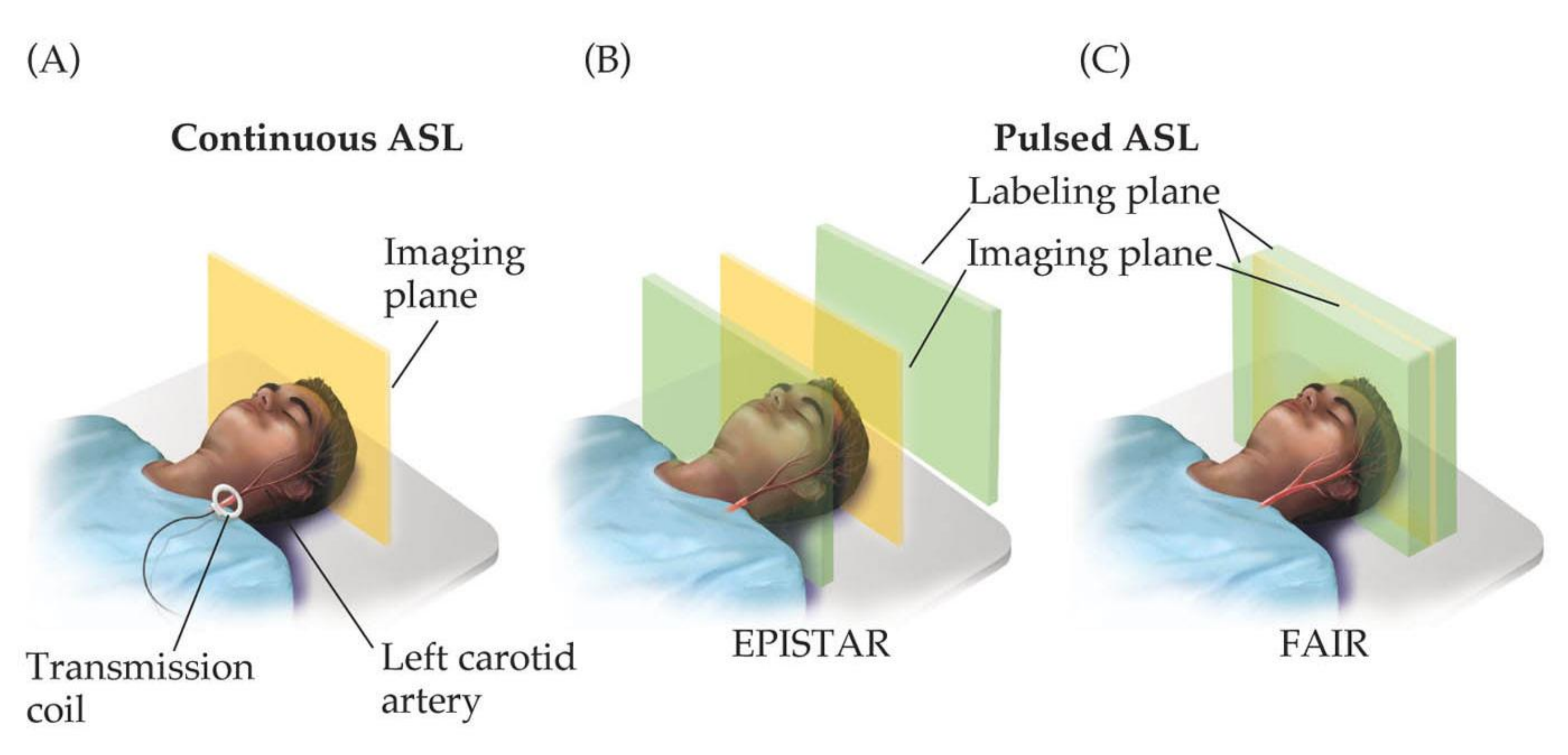


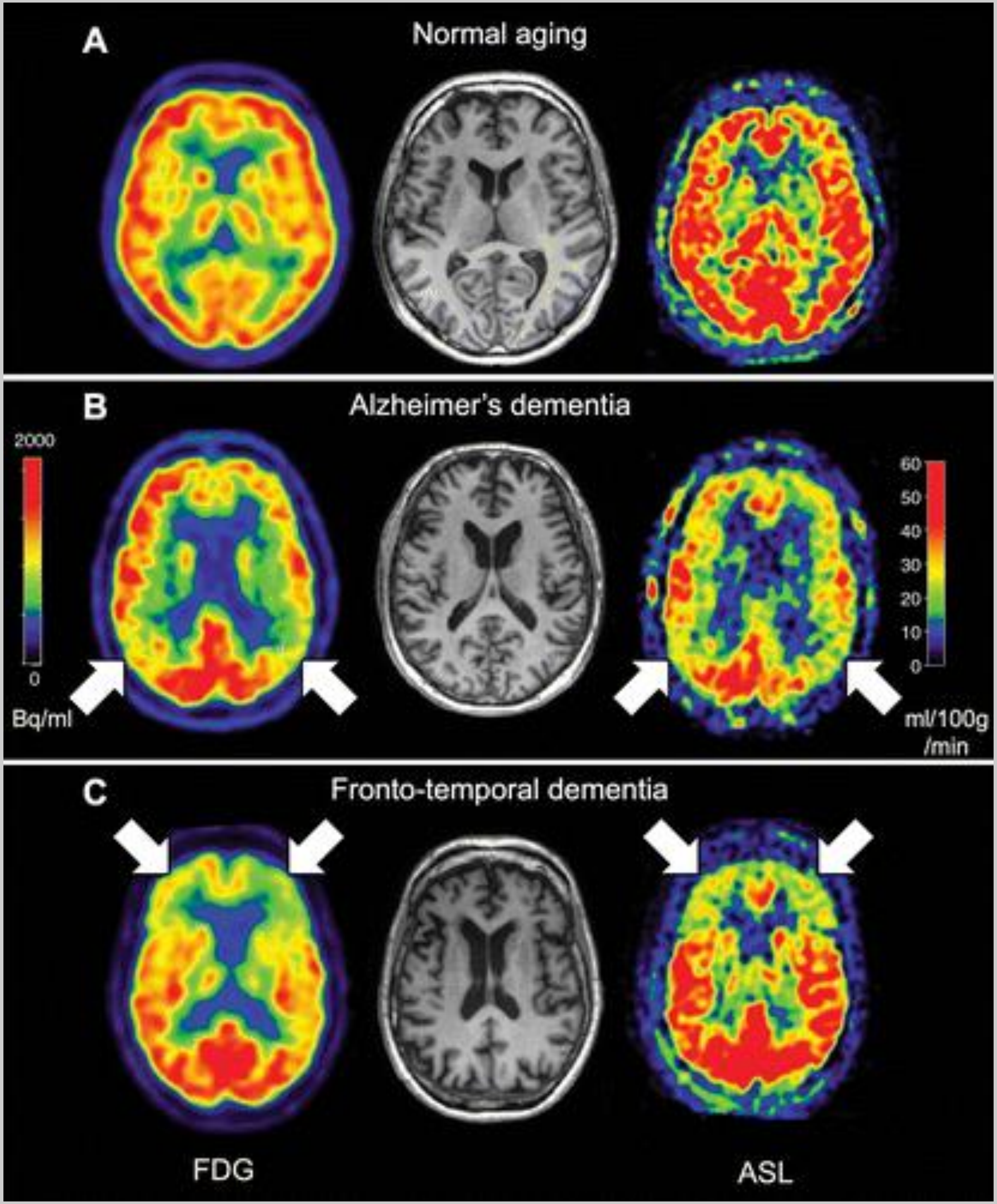
Blood vessels are replenished with new spins, thus they contribute MR signal to image. TOF contrast is proportional to the amount of flow into a section

FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 5.13**

Perfusion imaging

- Measuring blood flow through the capillary beds and small vessels.
- A subtraction method comparing images with and without tagging.
- Endogenous contrast – magnetic tagging of the blood outside the imaging plane, then wait (transit time) for blood to flow into imaging plane. Signal will be from the tagged (magnetized) blood in the image.





A comparison of FDG PET and ASL perfusion imaging.

Showing decreased perfusion in posterior regions (AD) and anterior regions (FTD).

Diffusion-Weighted MRI

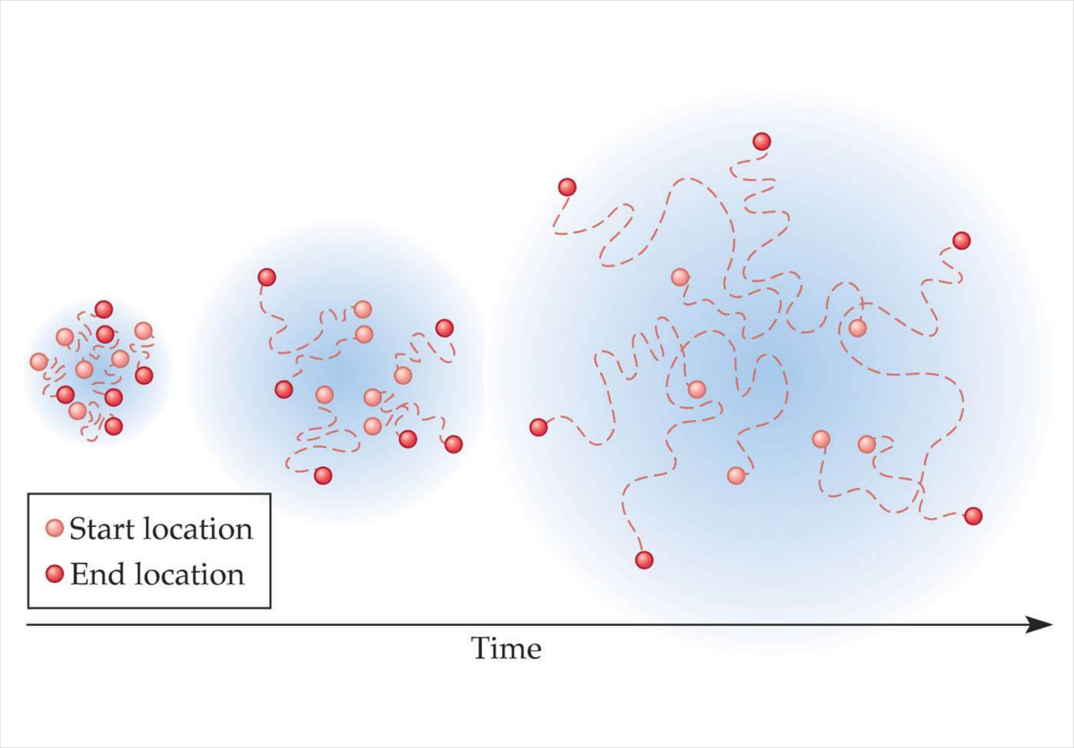
Measures motion of water molecules

Sensitive to microstructural changes in gray and white matter

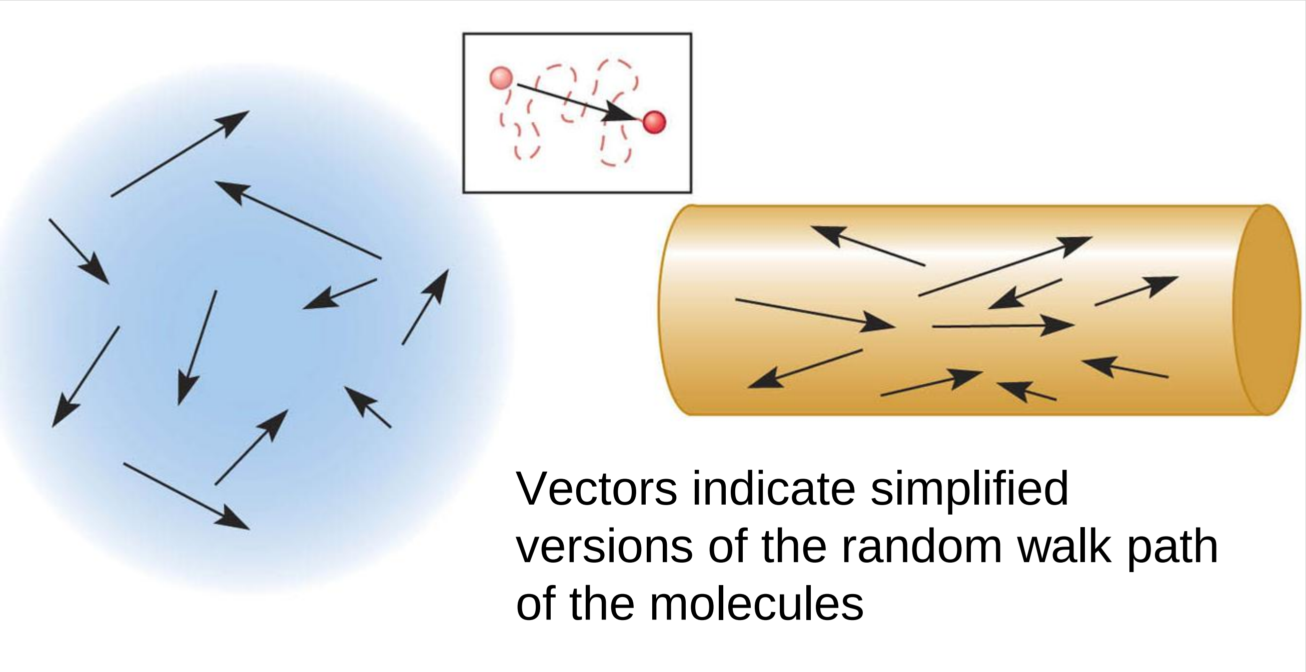
- Can be used to create maps of white matter tracts
- Sensitive to multiple changes to white matter integrity – demyelination, dysmelination, axonal damage, extracellular fluid, inclusion of pathologies
- Clinically, most often used for early detection of stroke, differentiating between ischemic (occlusive) and hemorrhagic stroke.

Diffusion

Over time, molecules within gases or liquids will move freely through the medium.



MRI diffusion-weighted gradient causes changes in the MR signal that are dependent upon the amplitude and direction of diffusion.



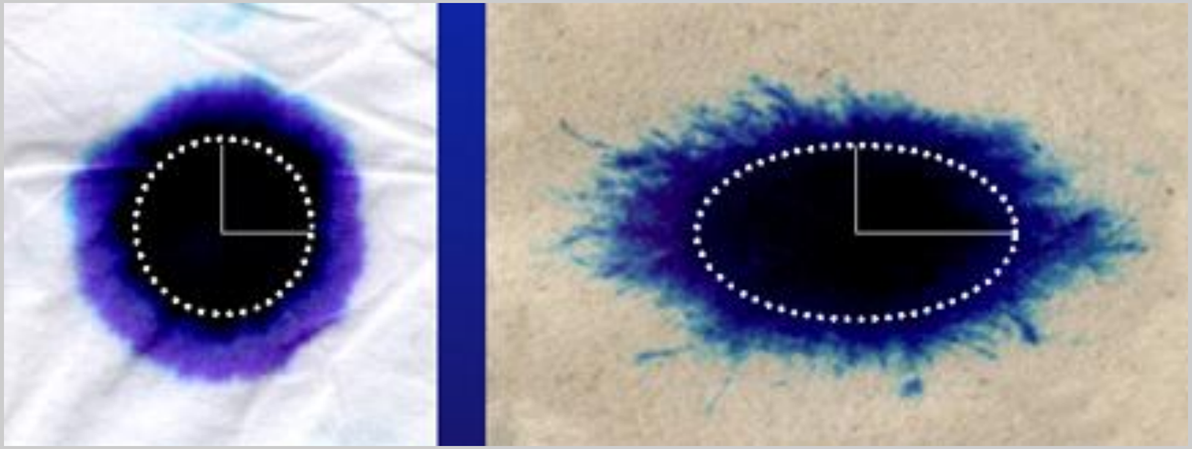
Isotropic diffusion – no restrictions in the direction of movement, measured as the apparent diffusion coefficient (ADC or MD).

Anistropic diffusion – movement is restricted in one or more directions, measured as fractional anisotropy (FA).

Where movement is relatively unrestricted, ADC will be high and FA will be low.

Where movement is relatively restricted (e.g., in a myelinated axon), ADC will be lower and FA will be high.

Isotropy to Anisotropy



Kleenex **Newspaper**

Isotropic **Anisotropic**

Anisotropy is sensitive to:

- Density of axons
- Degree of myelination
- Average fiber diameter
- Directionality of axons

Tensor model of diffusion

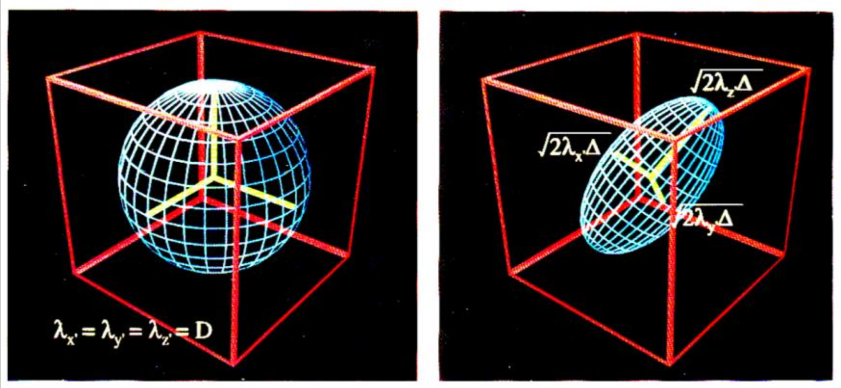
Tensor is a mathematical model of the directional anisotropy of diffusion.

Represented by a 3 x 3 symmetric matrix $\rightarrow$ 6 degrees of freedom.

Eigenvalues of the diffusion tensor are the diffusion coefficients (l_x, l_y, and l_z) in the three principal directions of diffusivity.

The eigenvector corresponding to the largest eigenvalue is the main diffusivity direction in the medium.

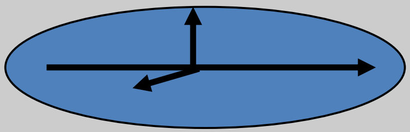
Maps are constructed from the main diffusivity direction, and for various anisotropy indices calculated from the eigenvalues.



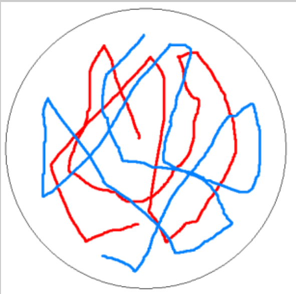
$$\overline{\overline{D}} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix}$$

Diffusion Measures

FA: Fractional Anisotropy, the degree to which the motion of molecules is directional relative to all motion.

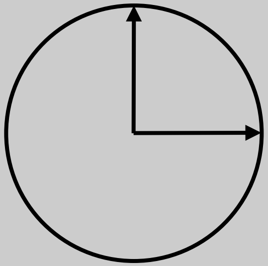


ADC (MD): Apparent Diffusion Coefficient, the average distance or magnitude of motion that a molecule will move in any direction due to random motion (Mean Diffusivity: ADC/3).

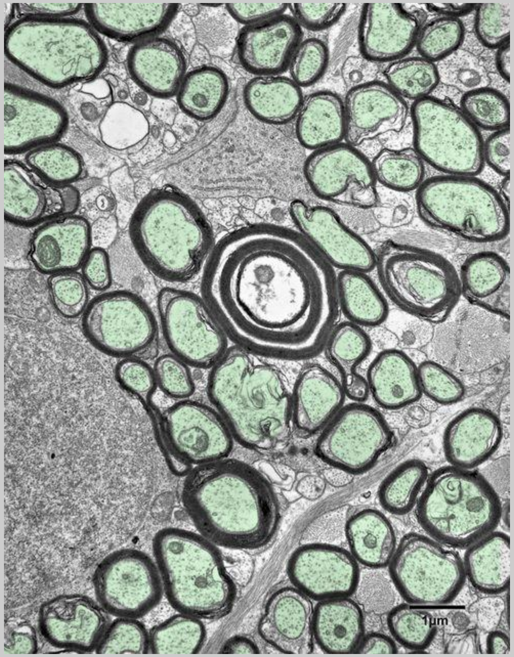


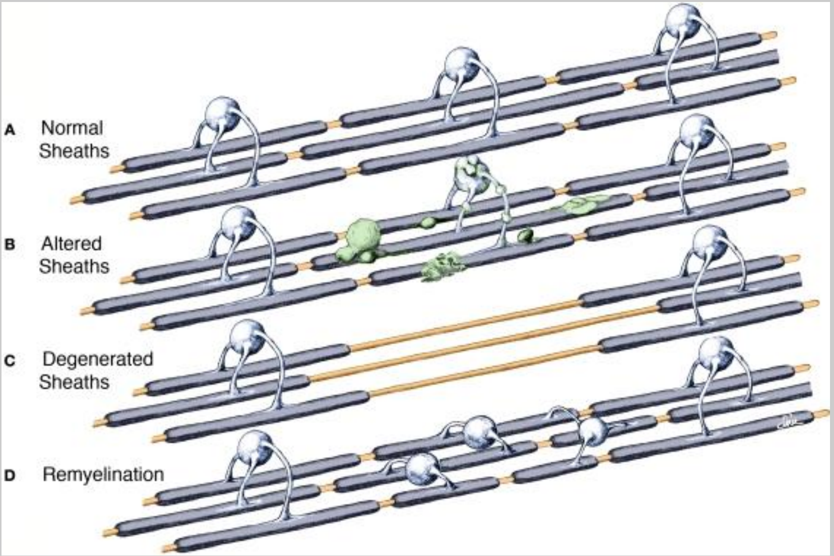
AD: Axial Diffusion, the magnitude of movement of molecules along the highest eigenvector.

RD: Radial Diffusion, the movement of molecules perpendicular to axonal fiber tracts (inferred by the highest eigenvector).



Cerebral white matter microstructure in aging





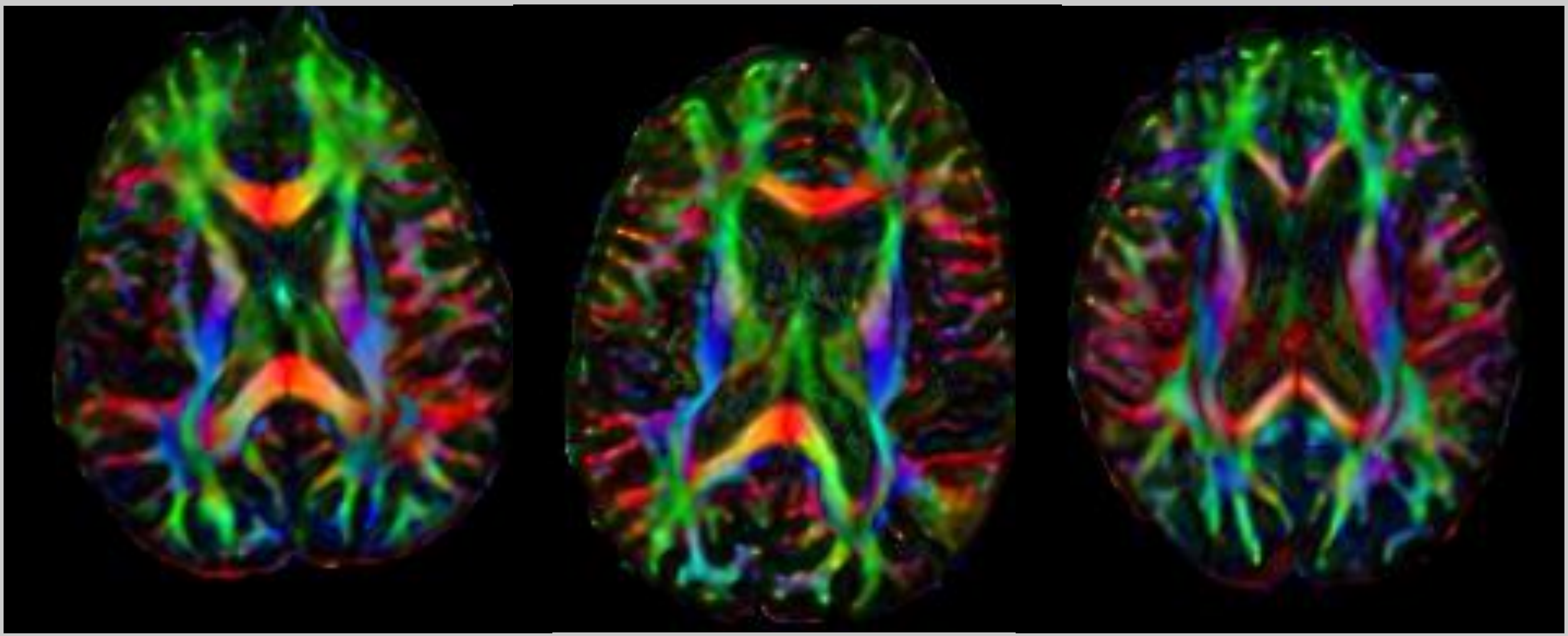
Peters (2009)

Precision Aging® Network

THE UNIVERSITY OF ARIZONA
COLLEGE OF SCIENCE
Psychology

Aging

3T, 25 directions, 2 B0, 2 averages



29 years | 75 years | 92 years

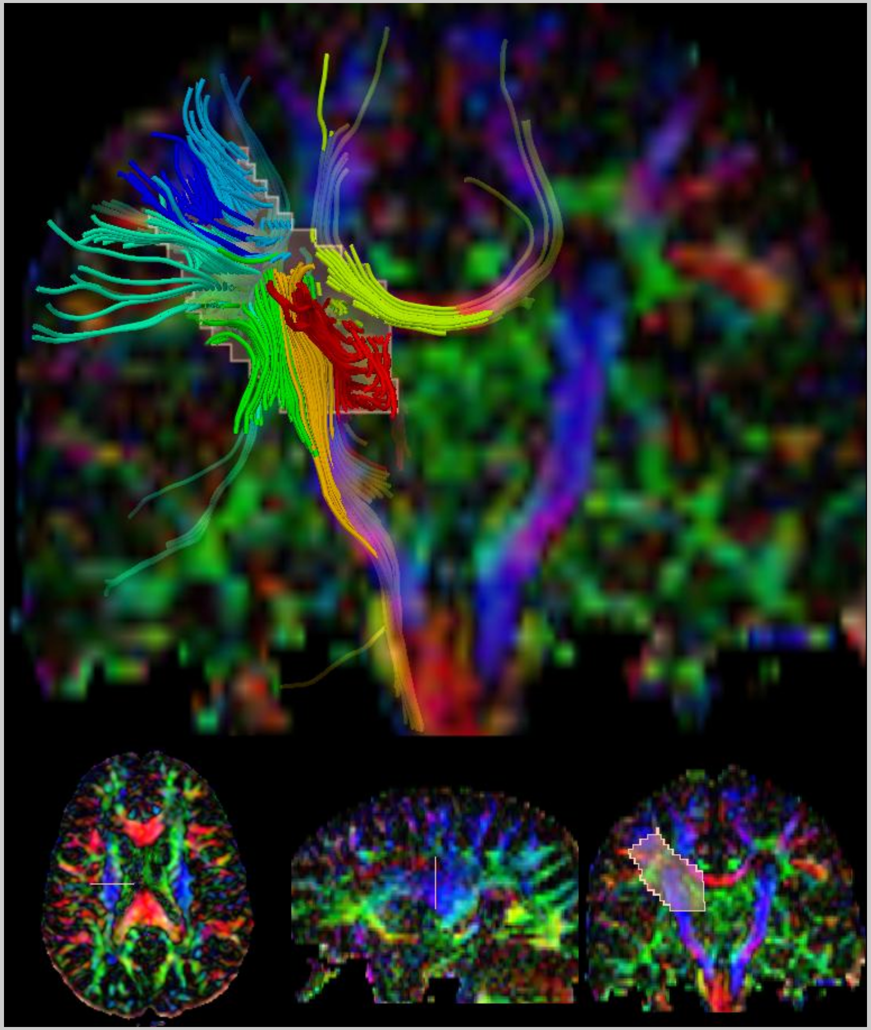
Tractography: Identifying the "Human Connectome"

Red – movement along the X axis (right to left)

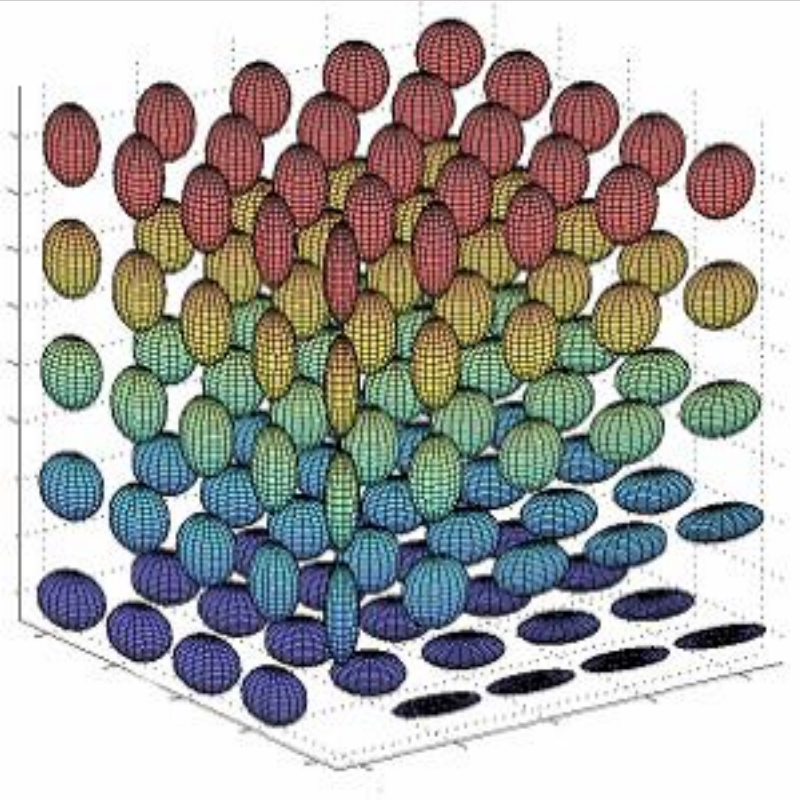
Green – movement along the Y axis (anterior to posterior)

Blue – movement along the Z axis (superior to inferior)

Requires higher numbers of directions (very minimum is 6 directions), smaller voxels (high resolution), and long imaging times

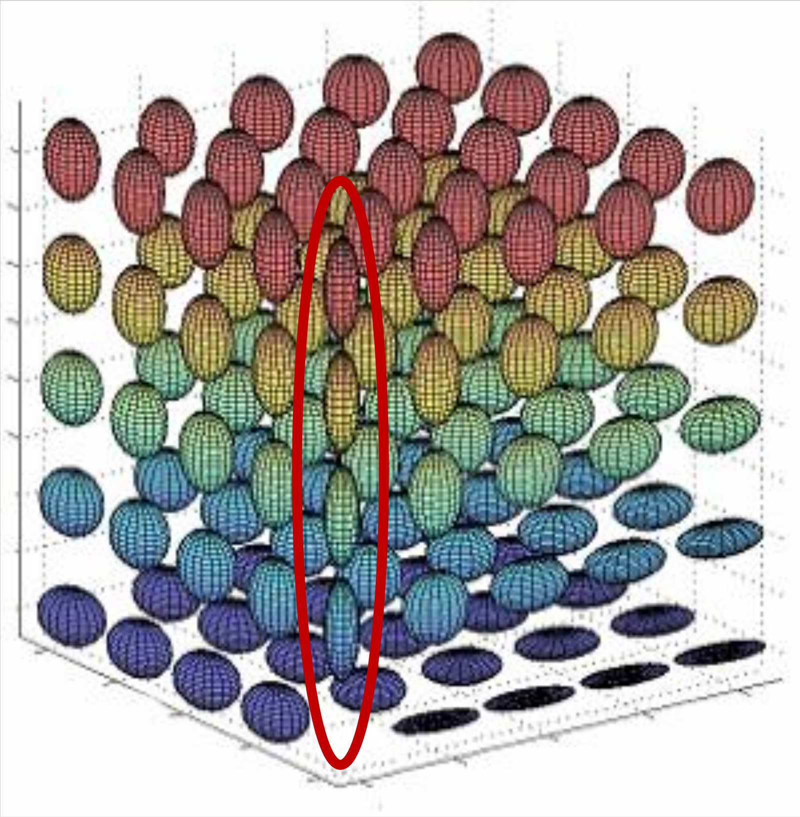


DTI datasets are volumes of diffusion surfaces



"The shape of the effective diffusion ellipsoid has a useful physical interpretation. … a diffusion tensor … defines a surface of constant mean translational displacement of spin-labelled particles."

Basser, Mattiello & LeBihan (1994) Biophysical Journal, pg. 261.



Deterministic Methods:

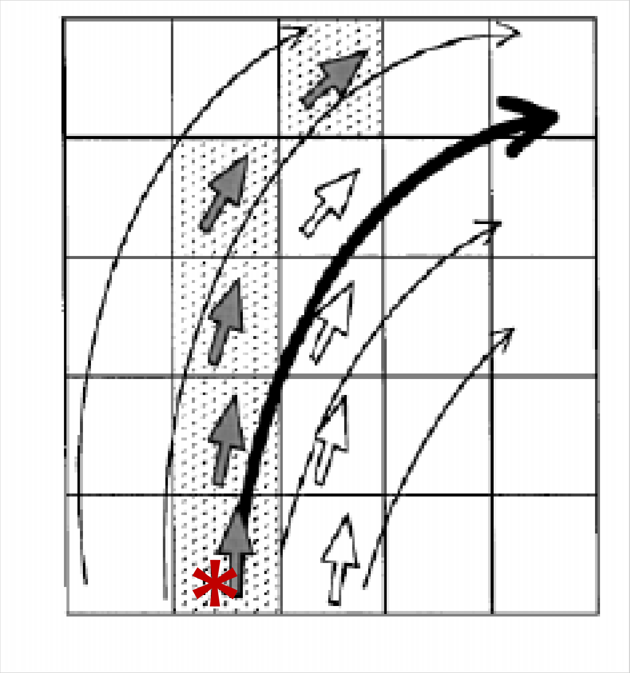
Assumes axon tracts are contiguous fibers across multiple voxels.

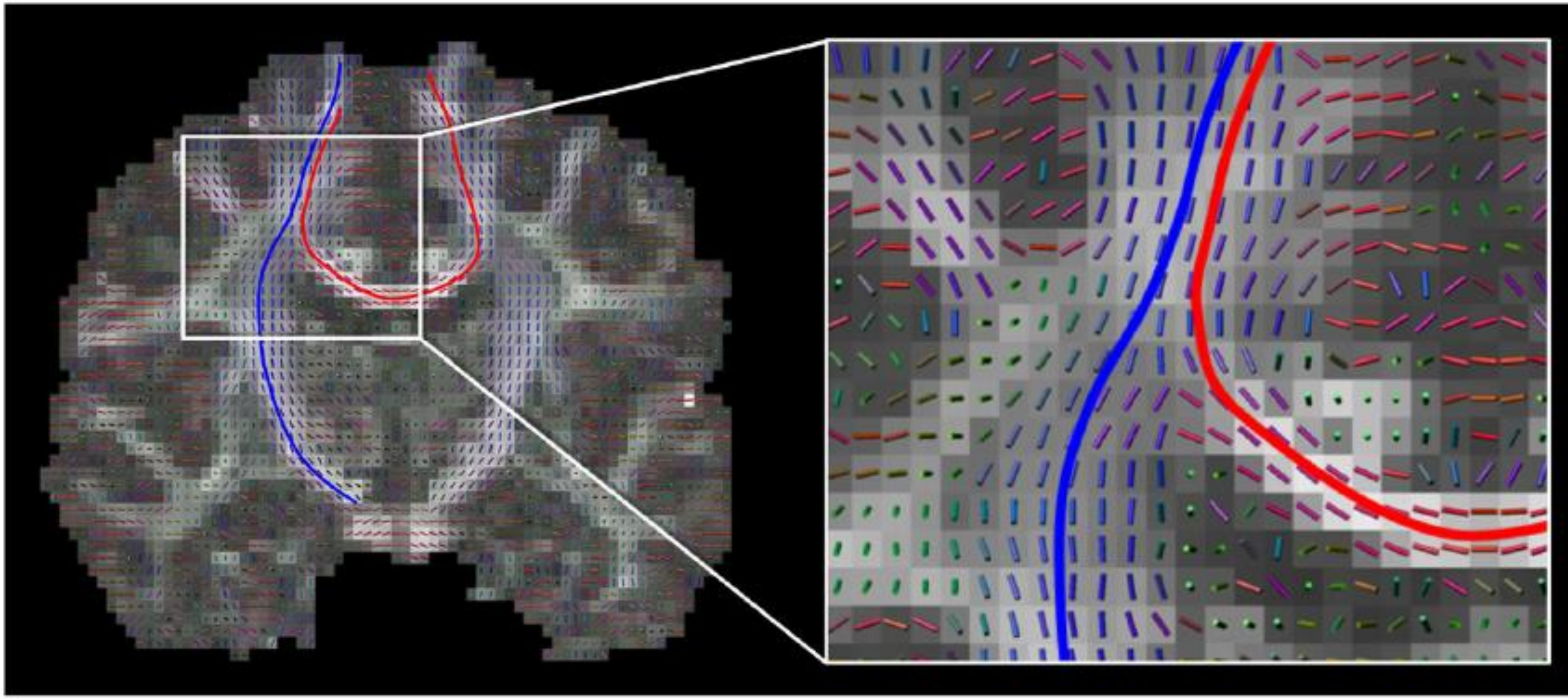
Basically, following the high FA values adjacent to one another – in a single line, or inferring a curved line through the vector field.

Fiber Assignment by Continuous Tracking FACT (Mori et al., 1999)

Identifying "streamlines" by assuming a single pathway from each seed point

- Starting in a seed voxel, move to voxel edge in highest direction
- Use tensor from next voxel
- Continue until the next edge (with variable step size)
- Paths fall between data samples: Separates tensor sampling resolution and path resolution

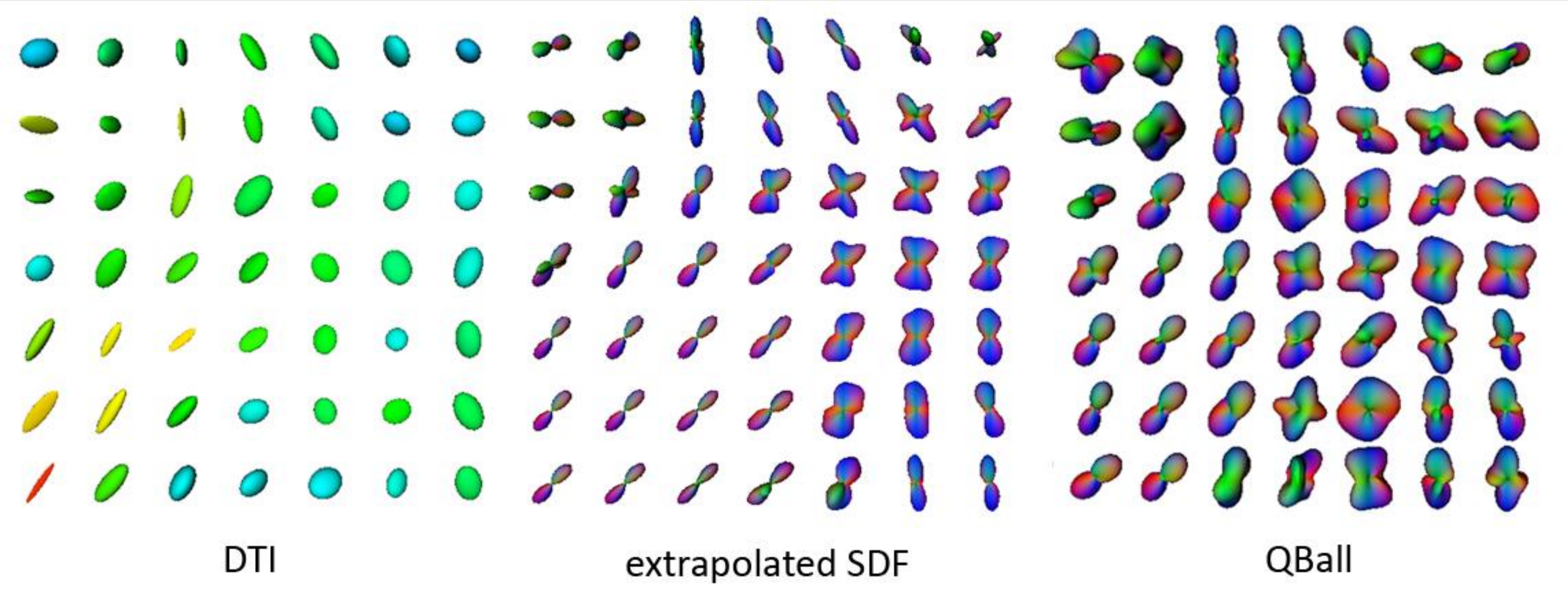




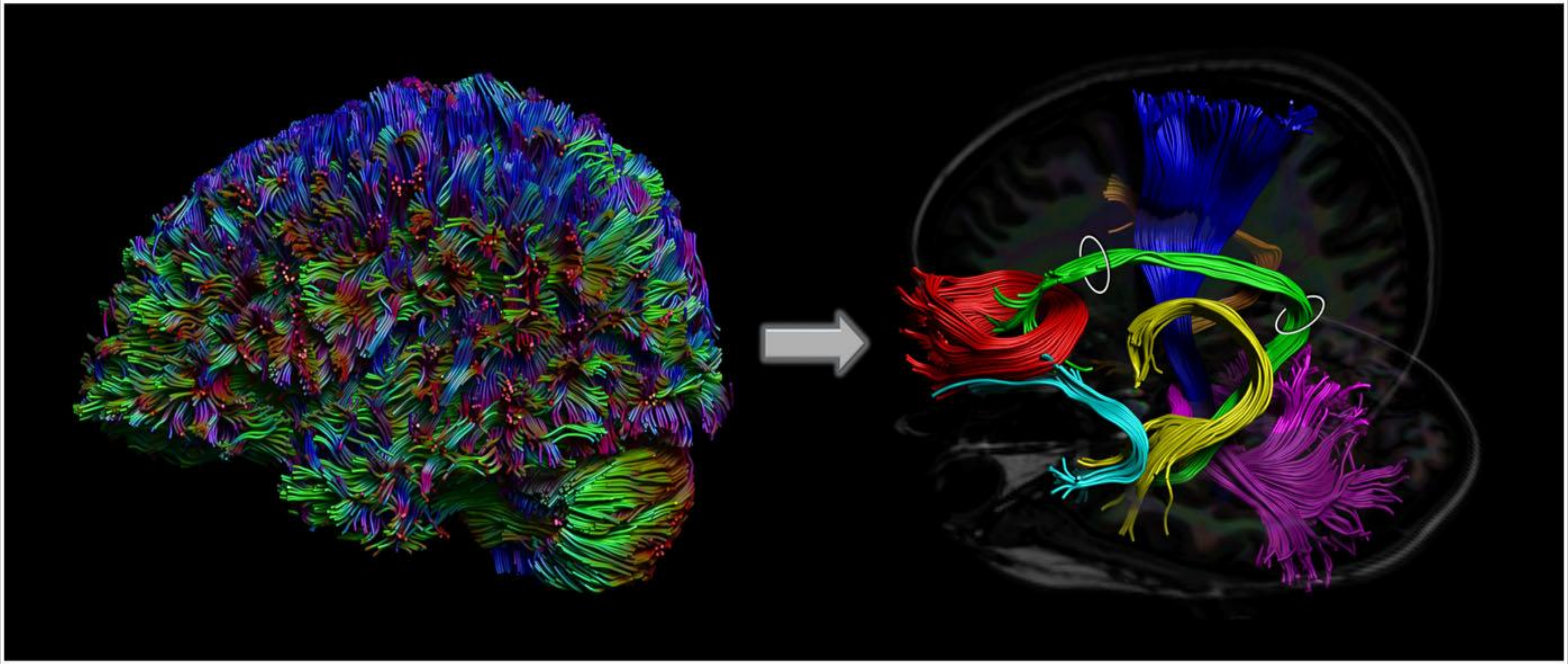
While white matter fibers in the brain are physical objects, “fiber tracks” or “streamlines” obtained with fiber tracking are virtual entities that encompass no physical volume and that are related only indirectly to the nerve fibers…. Even the most advanced tracking algorithms are bound to produce only very crude approximations to the actual connectome.   *Jeurissen et al., 2017*

Probabilistic Tracking:

High-angular-resolution diffusion imaging (HARDI) and Q-ball vector analysis (Tuch)



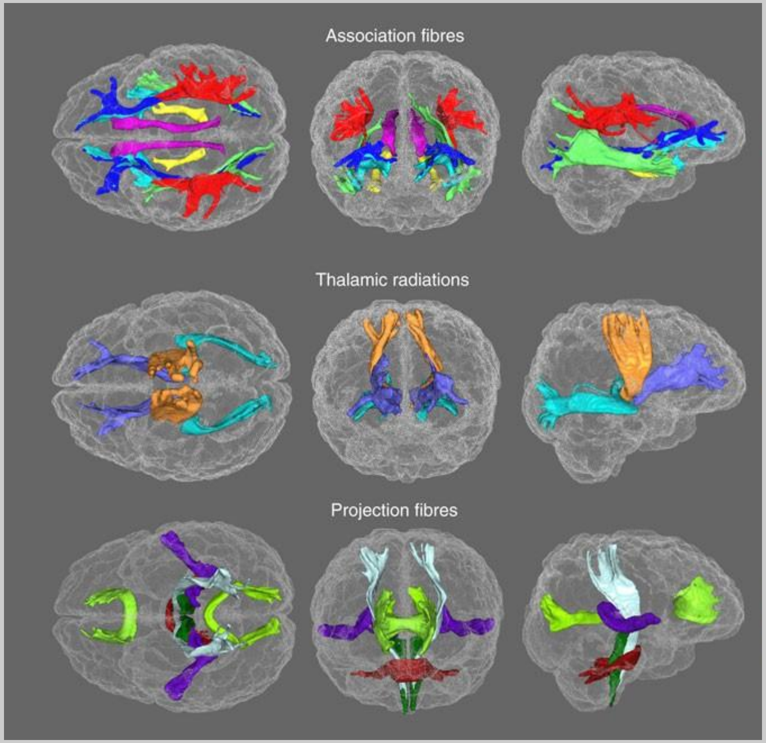
- HARDI is a MRI imaging technique that is able to better capture the intra-voxel diffusion patterns.
- Instead of assuming a single ellipsoid, it considers multiple potential directions of fibers within a voxel.
- Then applies probabilistic tracking through multiple adjacent voxels – determines the highest probability path.



Multiple fiber bundle trajectories can be virtually dissected from a whole-brain tractogram, using tract selection. For example, identifying the cingulum bundle in green (right) by tracking fibers connecting two regions (white circles).

Age differences in DTI measures of white matter integrity

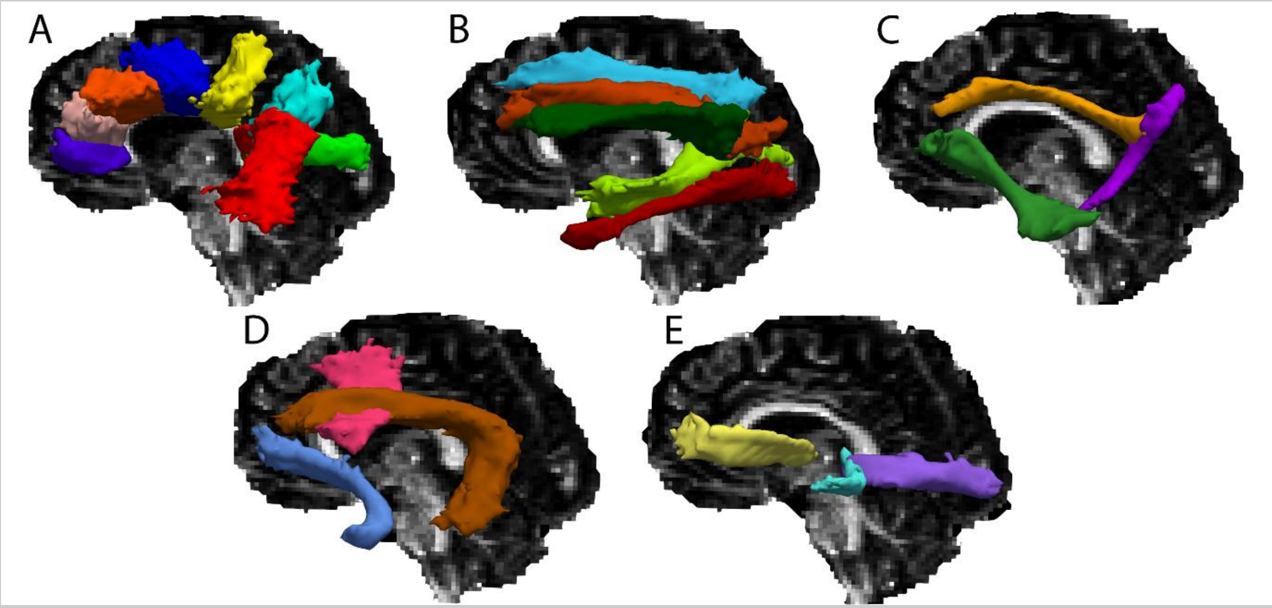
Are white matter alterations in aging best characterized as global or tract-specific?



Matijevic & Ryan (2021) *Front Aging Neurosci.*

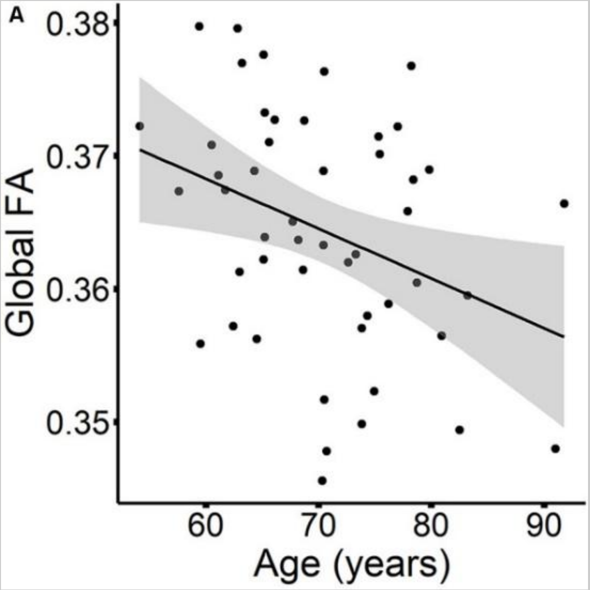
Age differences in DTI measures of white matter integrity

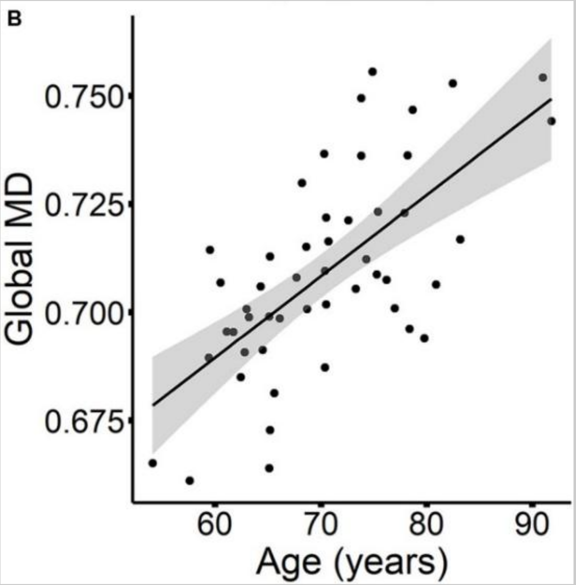
- Diffusion weighted images collected for 129 older adults (ages 52 – 82) and 71 younger adults (ages 18 – 37)
- FA, MD, RD, and AD analyzed from 36 tracts (callosal, association, and radiation)



Age differences in DTI measures of white matter integrity

Decreased fractional anisotropy and increased mean diffusivity values in whole-brain white matter

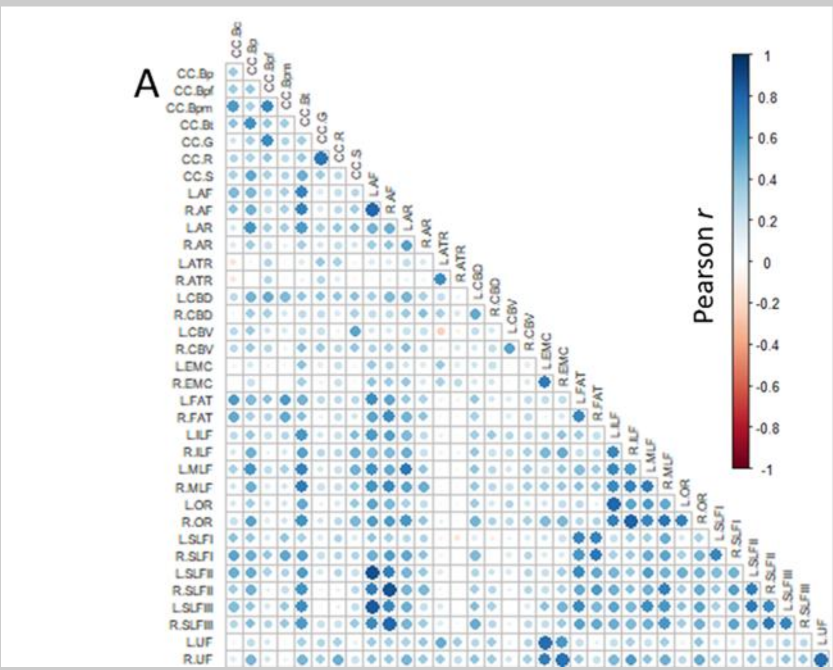




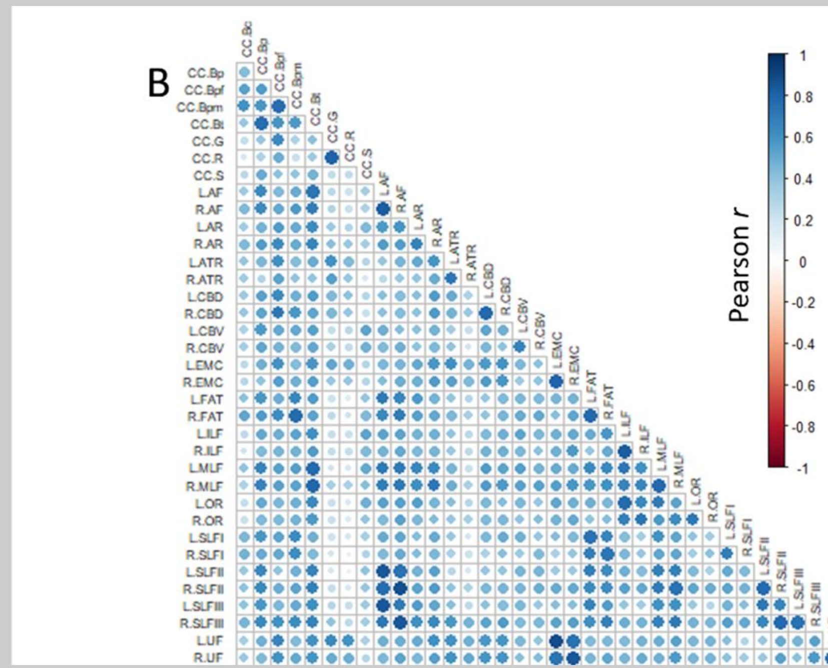
Age differences in DTI measures of white matter integrity

Stronger FA inter-tract correlations among older adults vs. younger adults

Younger adult FA inter-tract correlations



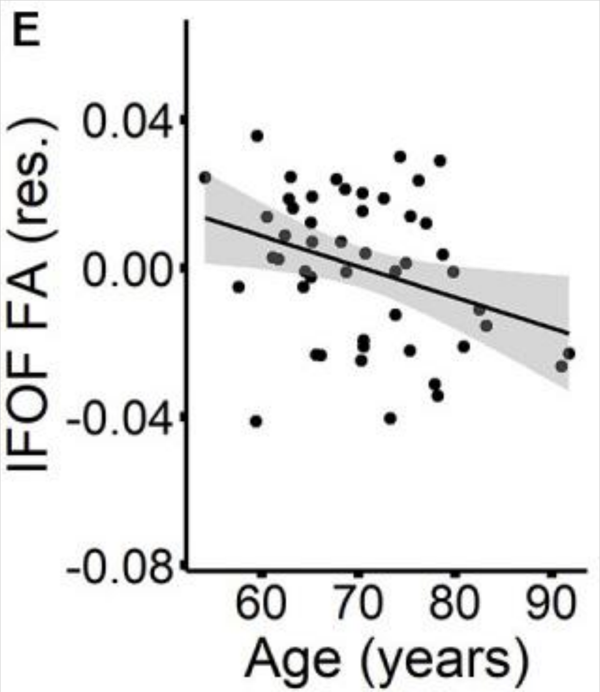
Older adult FA inter-tract correlations



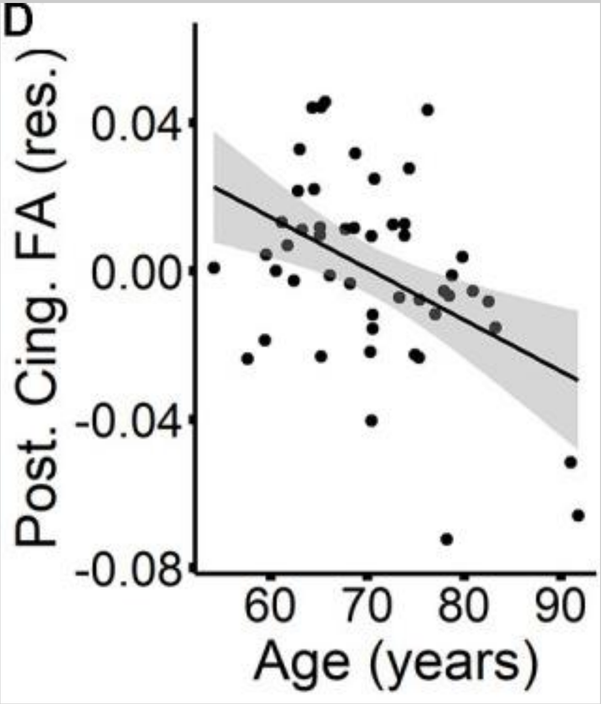
General factor derived through factor analysis accounts for a greater proportion of shared variance across tracts for older adults (48.5%) than younger adults (35.1%).

Age differences in DTI measures of white matter integrity

However, age accounted for additional variance in tract-specific FA measures beyond whole-brain FA, ranging from 6% - 20% across tracts.



Inferior frontal-occipital fasciculus

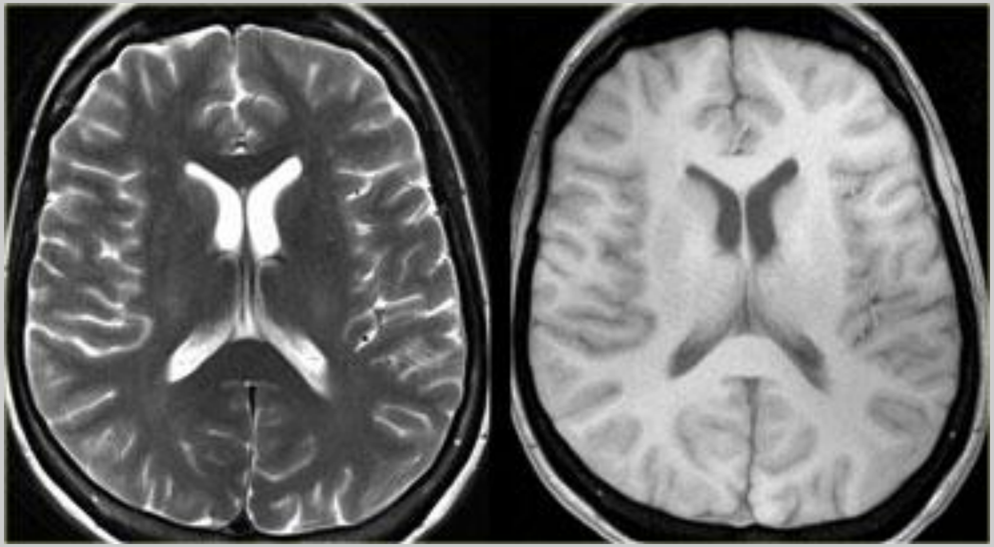


Posterior cingulate

Stroke Imaging:

Whether to treat with ‘clot-busting drugs’.

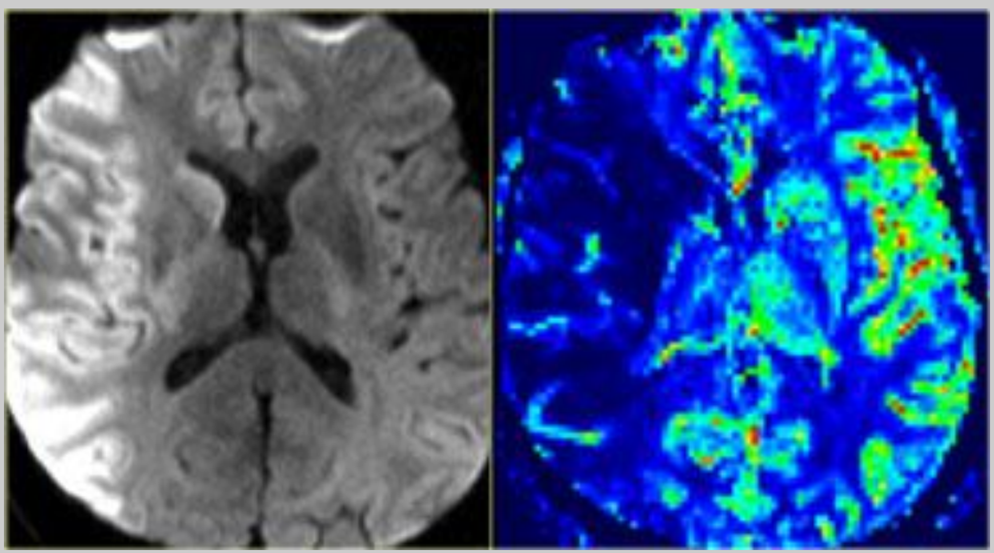
MR 1 hour after onset of sudden neurological symptoms.

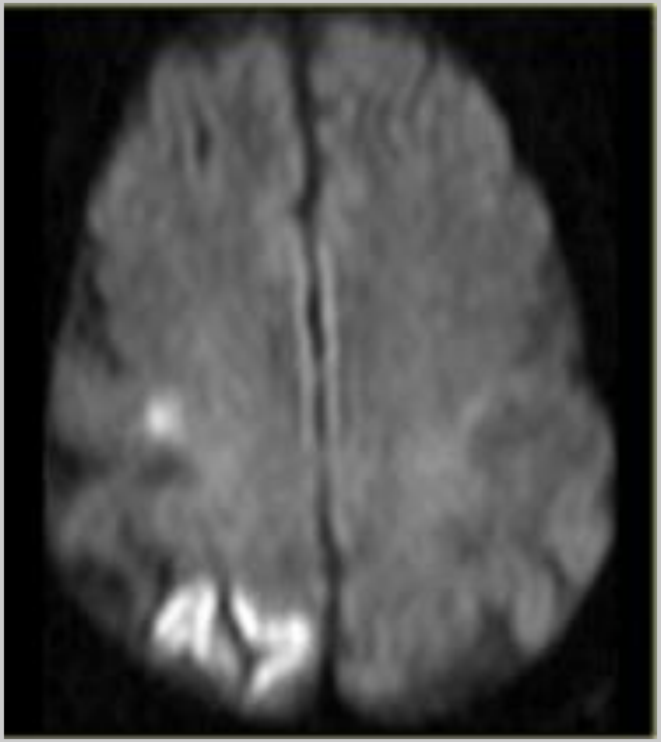


T2 T1

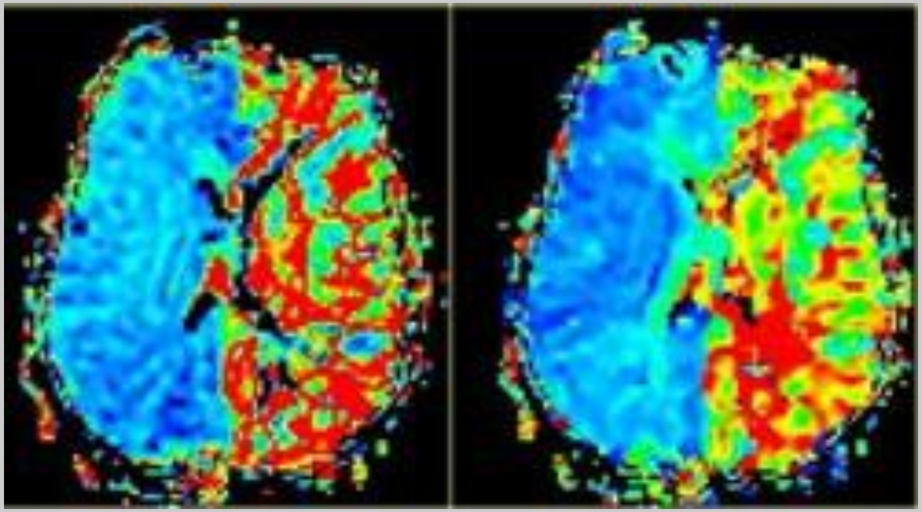
Left: DWI shows large area of restricted diffusion in right MCA territory.

Right: Perfusion map showing decreased perfusion perfectly matched with DWI image, suggesting hemorrhage. This patient should not undergo thrombolytic therapy.

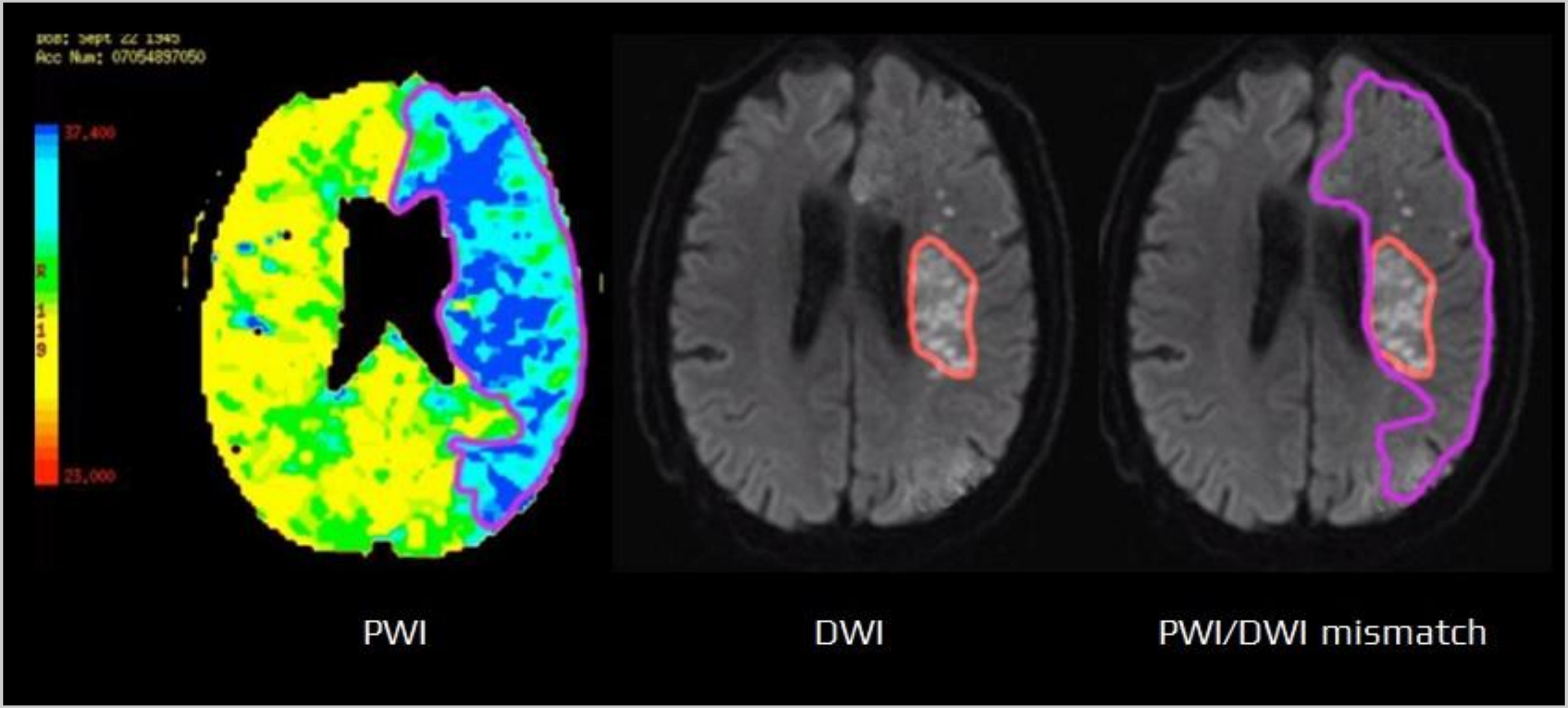




DWI showing restricted diffusion in posterior left occipital region.



However, on perfusion imaging, almost the whole left cerebral hemisphere is hypoperfused, suggesting occlusion causing ischemia. This patient is an ideal candidate for thrombolytic therapy.



Stroke penumbra: The mismatch between diffusion weighted MRI and perfusion weighted MRI soon after a stroke has occurred.