Imaging Brain Structure and Function

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CSE/EE 577
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Why image the brain?

- What's wrong? (Medical diagnosis)
- How does it work? (Neuroscience)
- To aid intervention (Medical treatment, Engineering)

Why is the brain hard to image?

- Different soft tissues (gray, white) give low contrast to xrays
- Cerebral anatomy is 3D complex and variable
- Neurophysiological processes must be imaged indirectly through their coupled vascular and metabolic effects
- Much of the organization of the brain is still poorly understood.
- Cerebral functional zones are defined by microscopic features that can’t be imaged directly

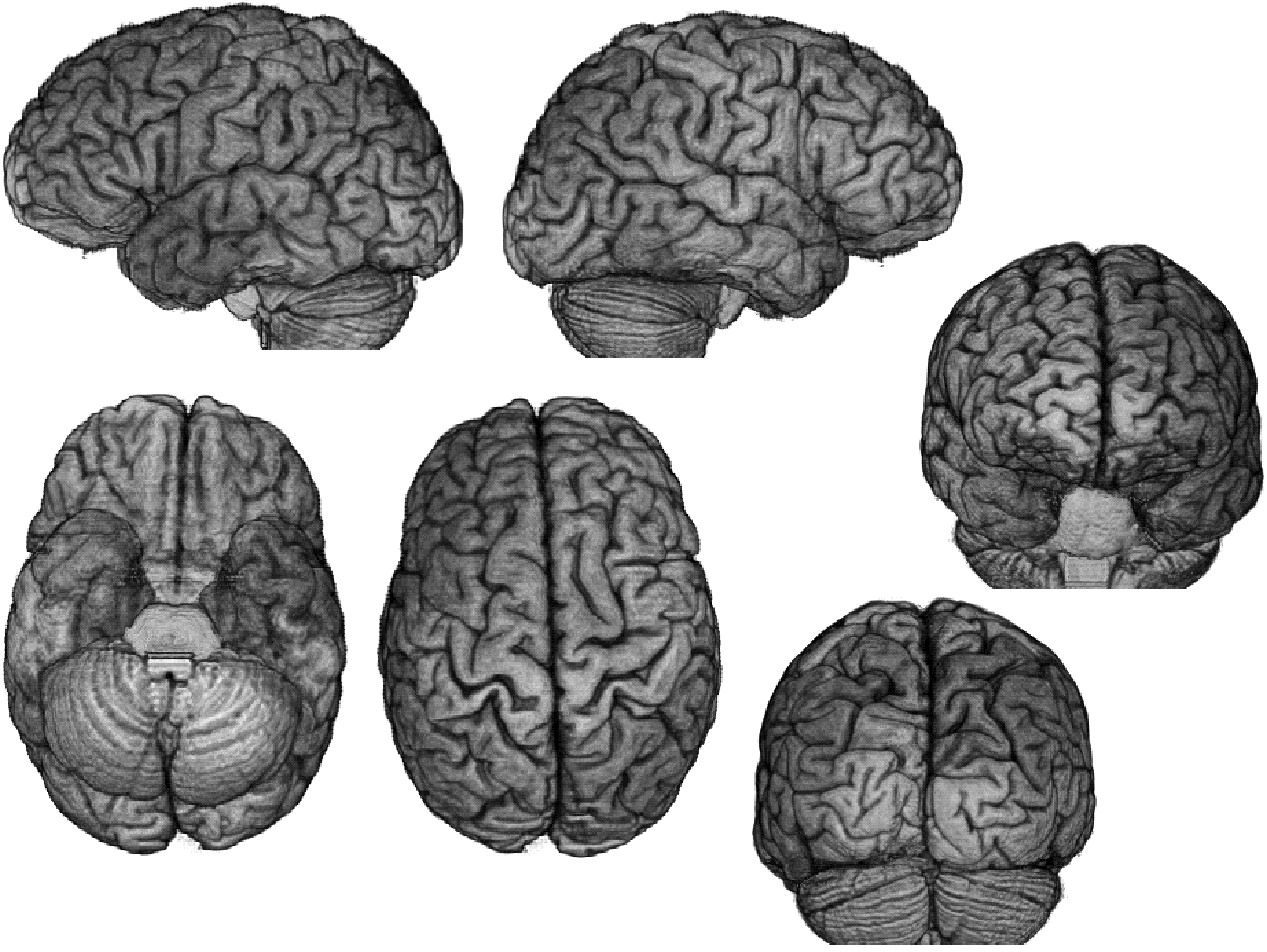
Digital image paradigm

- Images are matrices of values of a physical or physiological parameter, extended over an anatomic space.
- The parameter is not derived “directly” from hardware sensors, but by post-acquisition computation.
- Images may be inputs to further workflow.

Paradoxically, imaging is an abstract concept

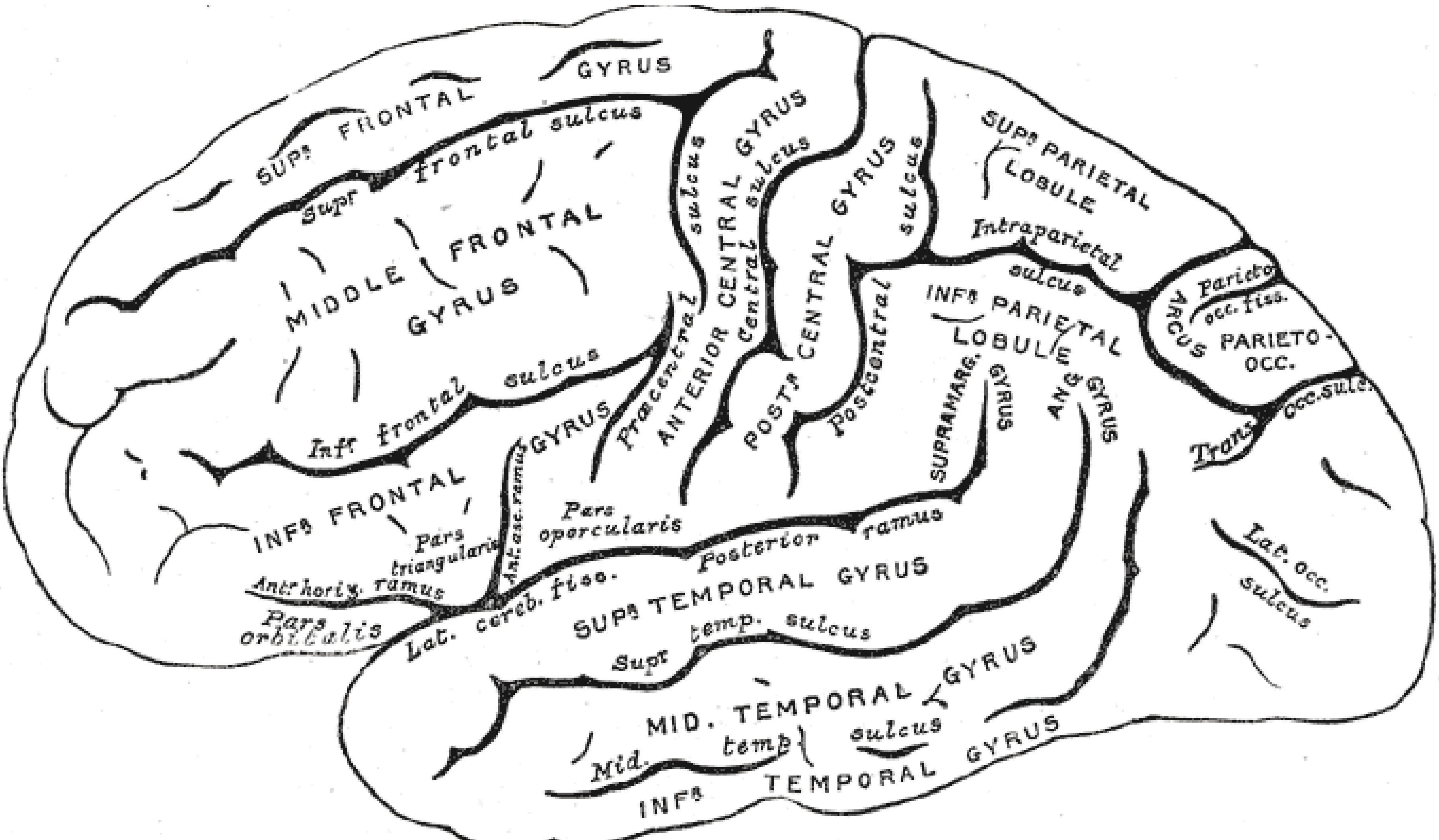
Outline

- The brain
- Brain imaging modalities
- Standard anatomical space
- Image processing

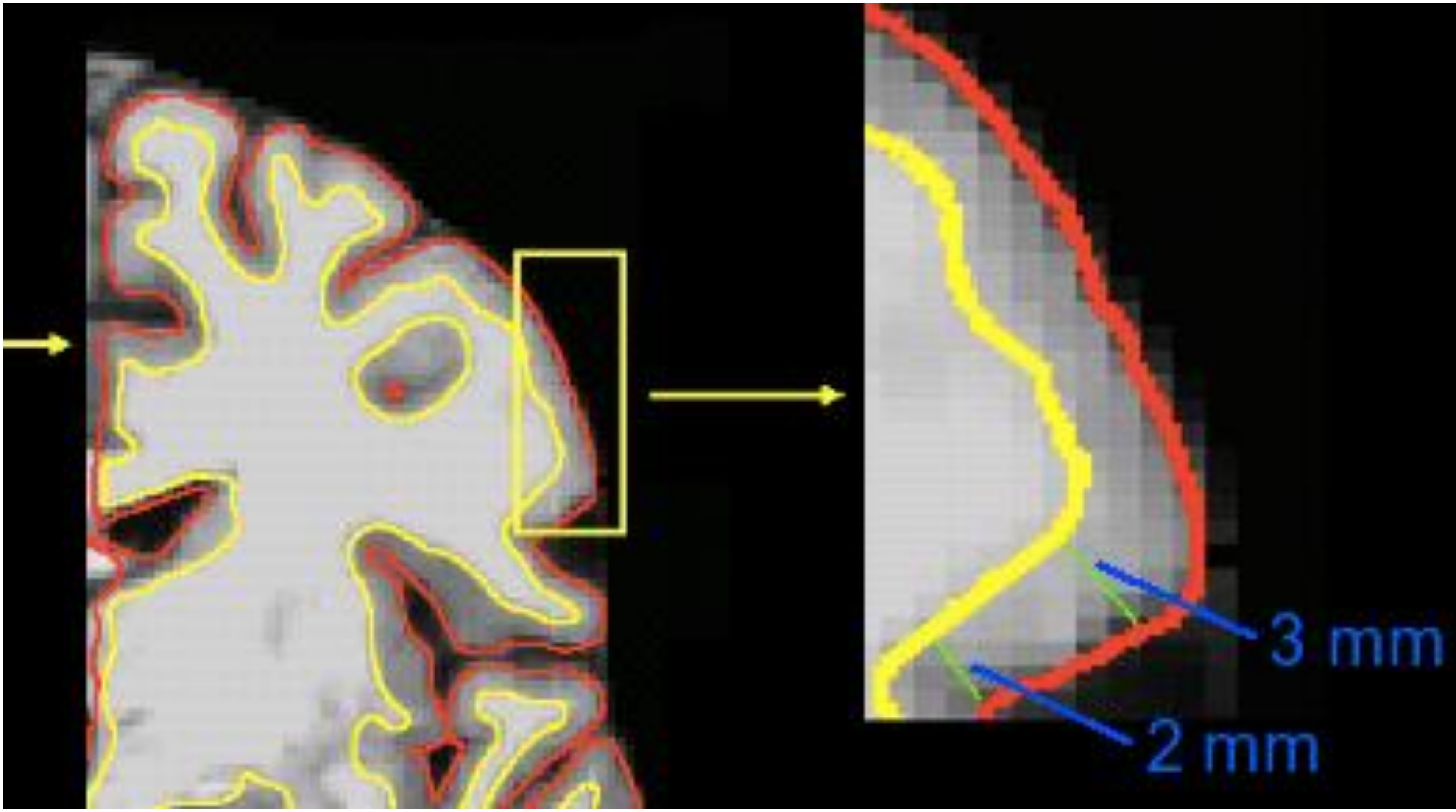


The brain is an organ

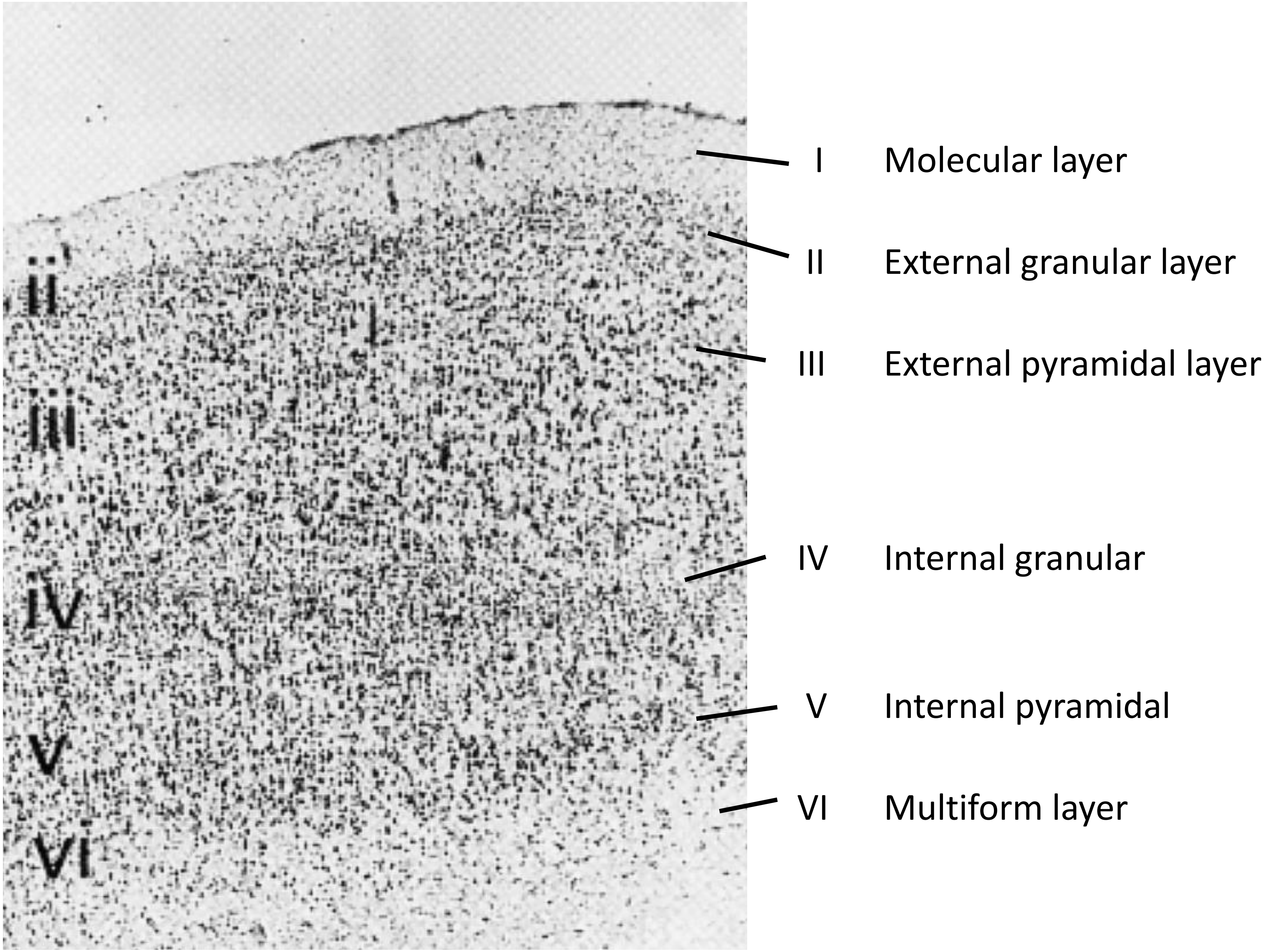
Sulci and Gyri of the Cerebral Cortex



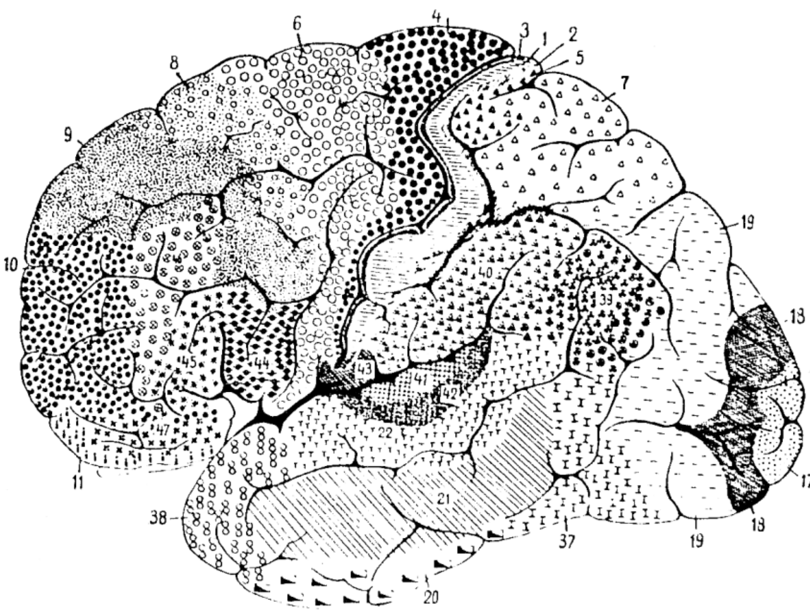
Cortical thickness

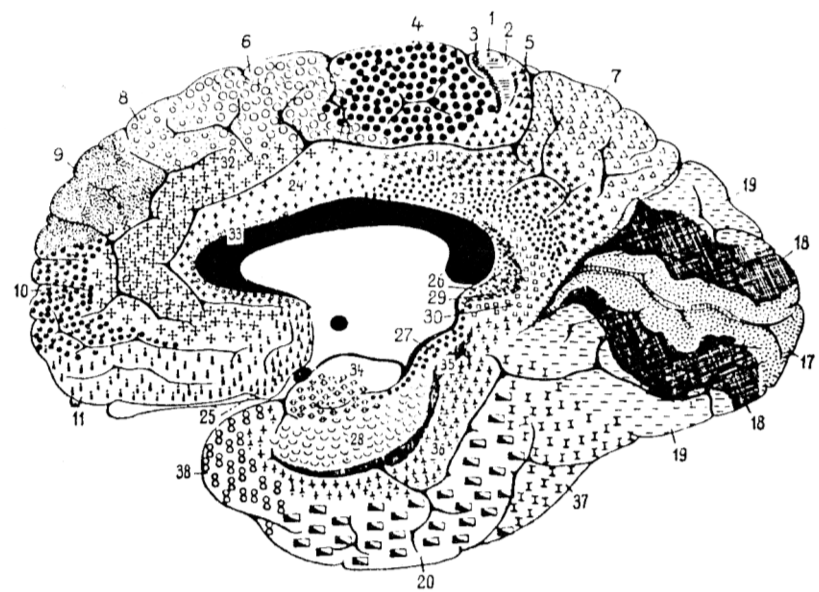


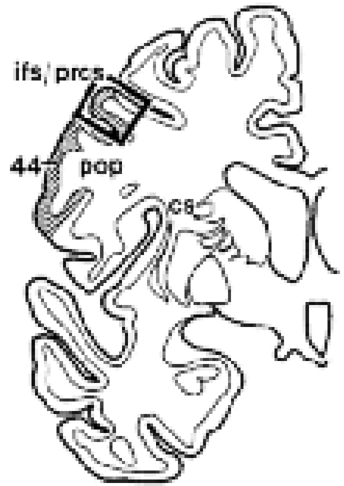
FreeSurfer, CARET

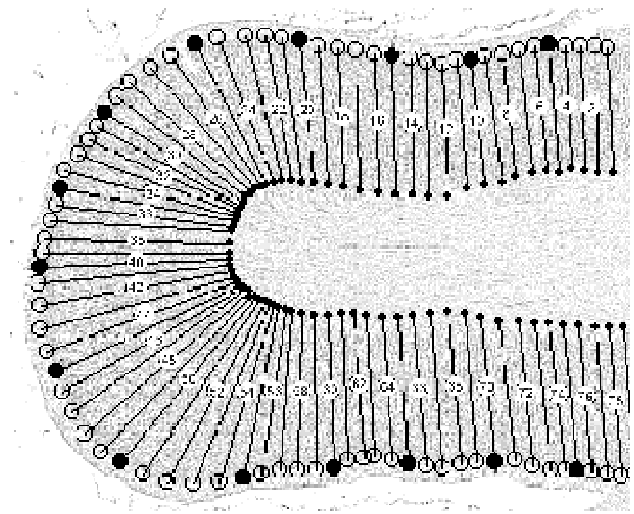

ii
iii
IV
V
VI
I Molecular layer
II External granular layer
III External pyramidal layer
IV Internal granular
V Internal pyramidal
VI Multiform layer

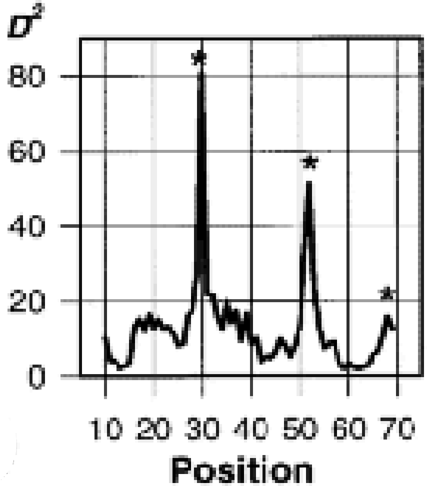
Brodmann’s cytoarchitectonic map (1909)

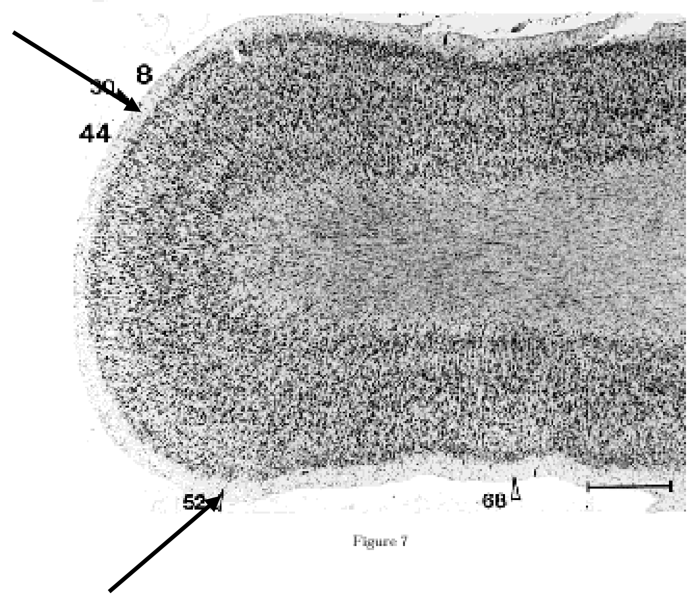






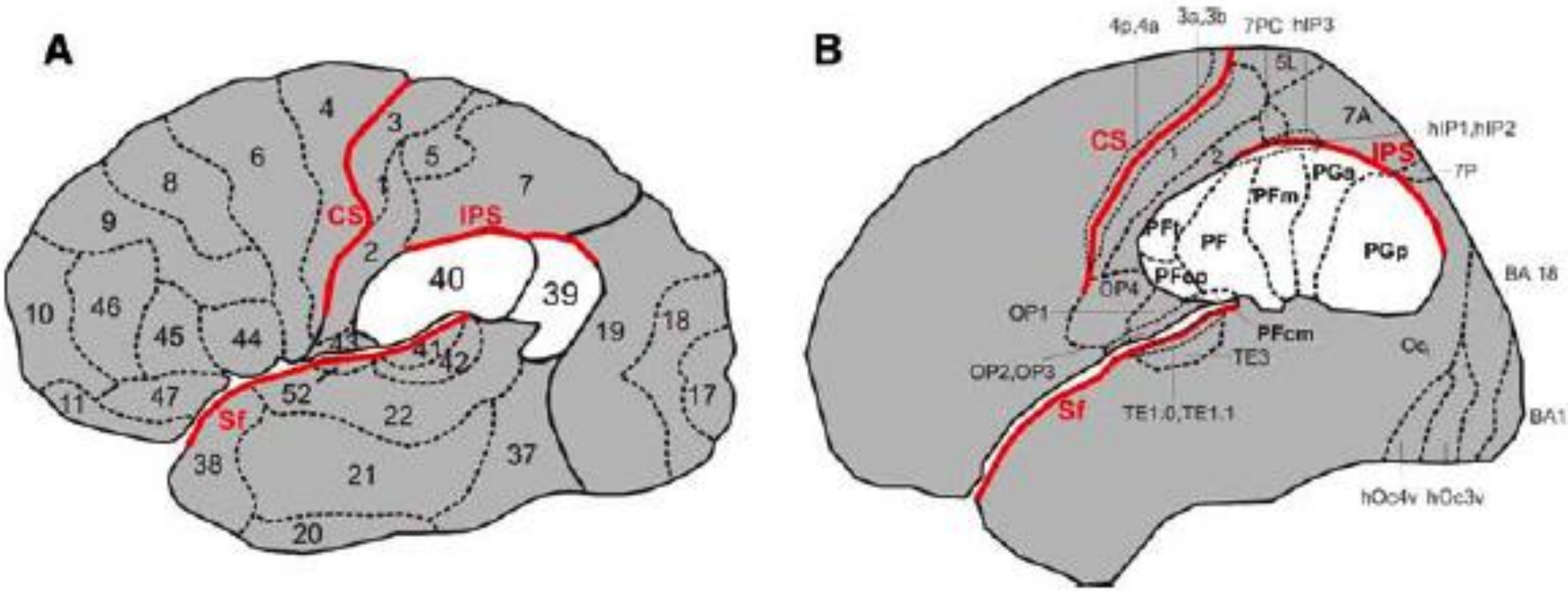




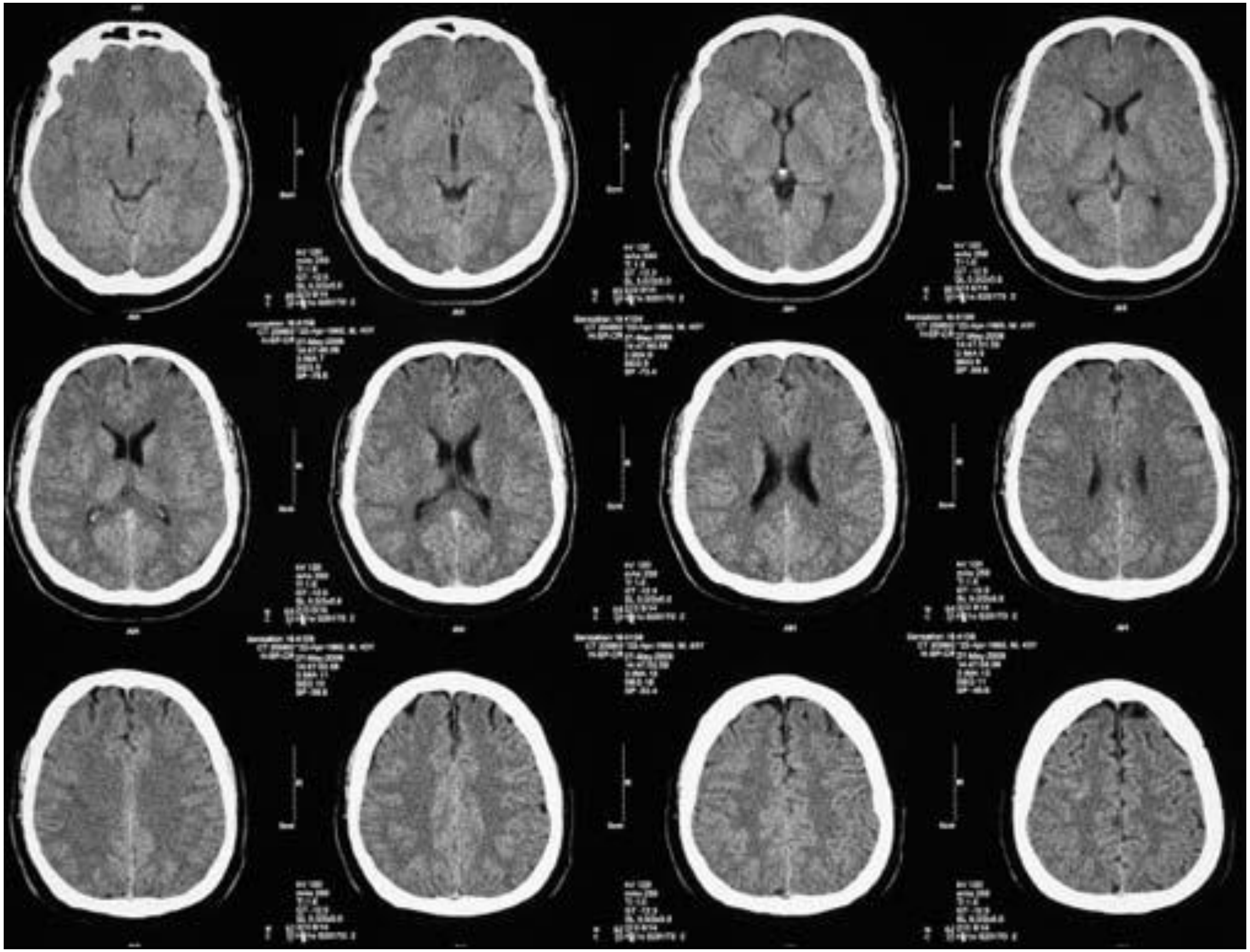


From Amunts et al

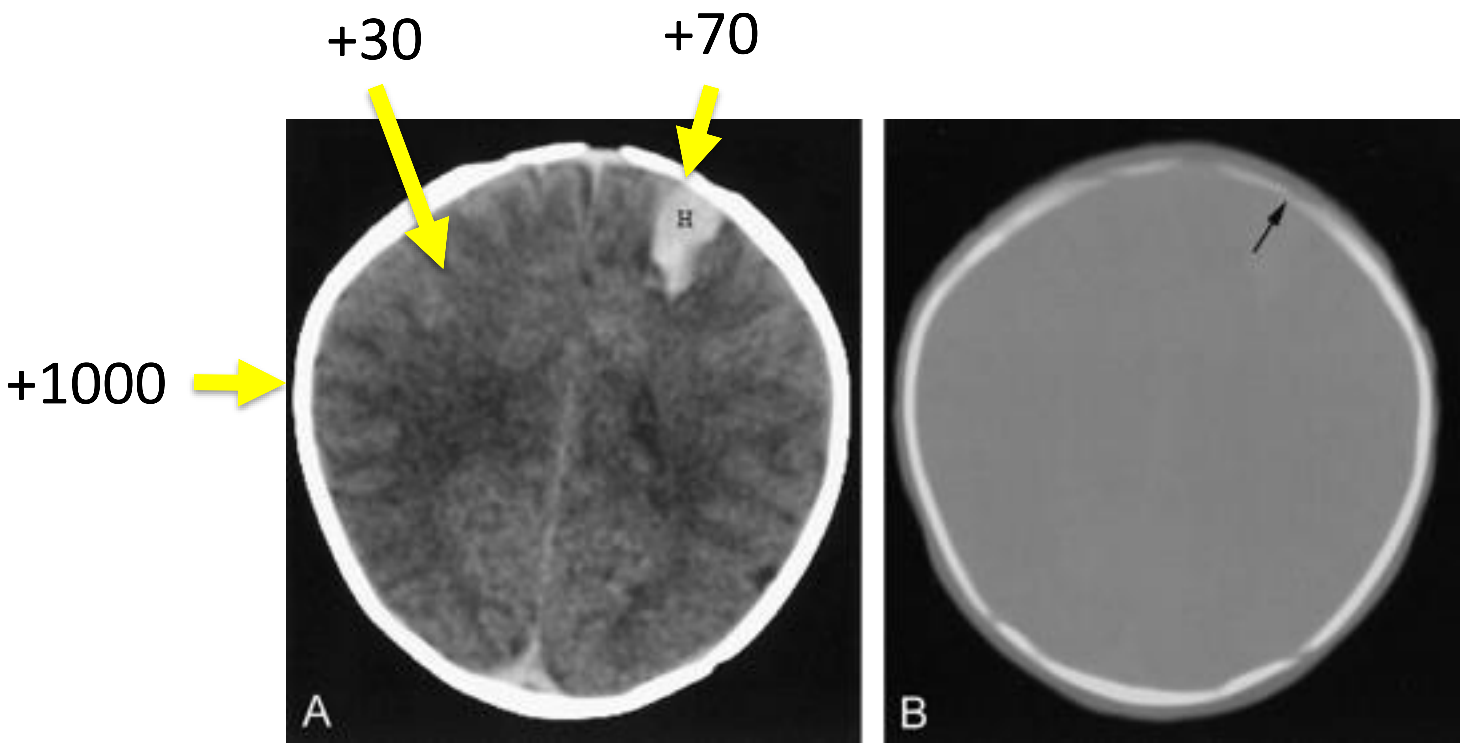
Julich cytoarchitectonic map (2009)



Xray Computed Tomography



Tissue vs. Bone Windows



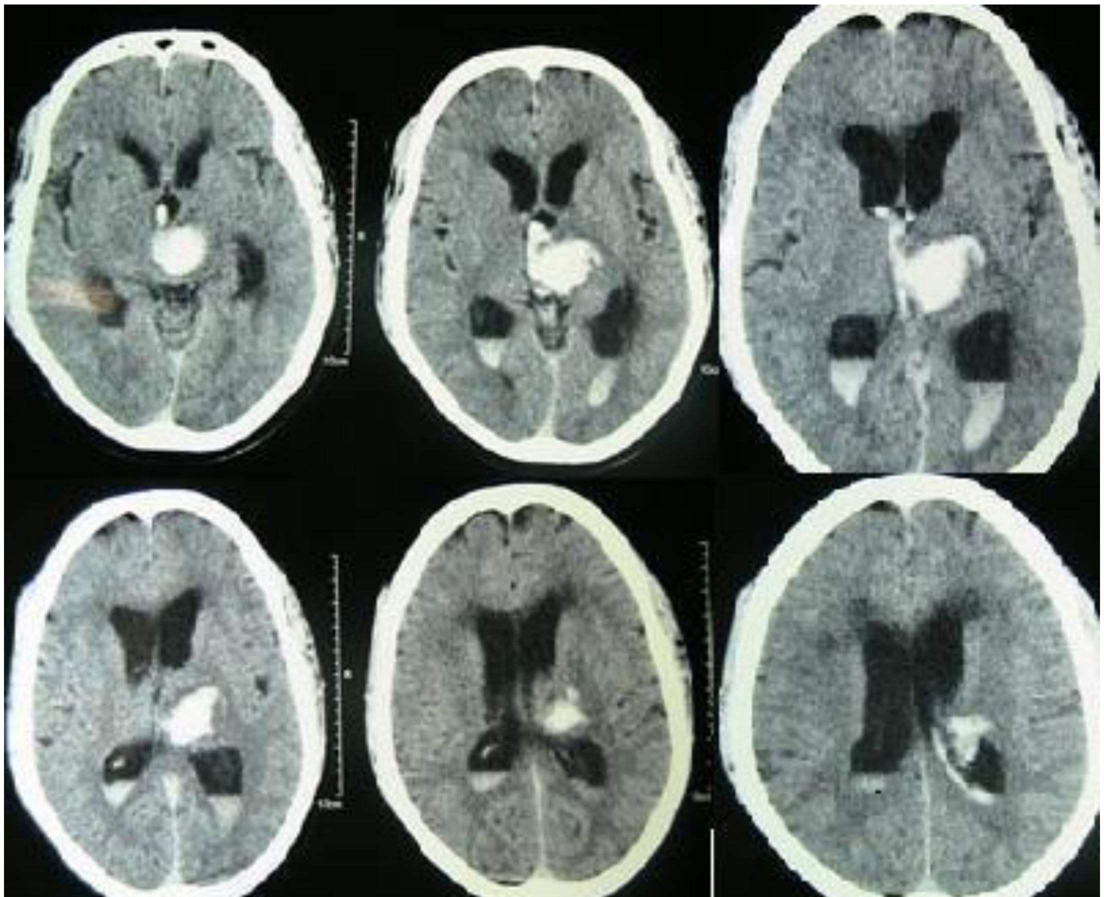
Hounsfield Number – radiodensity

Computed tomography

- First tomographic anatomic imaging technique
- Modest soft tissue contrast
- Contrast agent (iodinated) already existed
- Good sensitivity to pathology, esp. blood
- Good resolution of bony structures
- Rapid (good throughput, low sensitivity to motion)

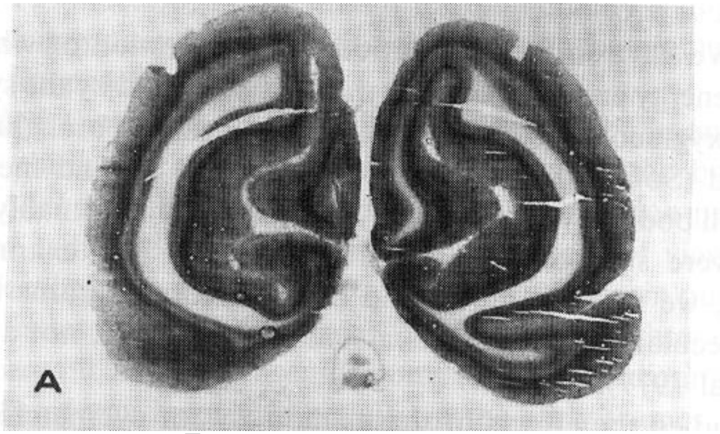
- Finds uses as a first-line emergency technique
- Integrated with PET for attentuation correction and anatomic image fusion
- Used very extensively in body imaging

Intracerebral hypertensive hemorrhage

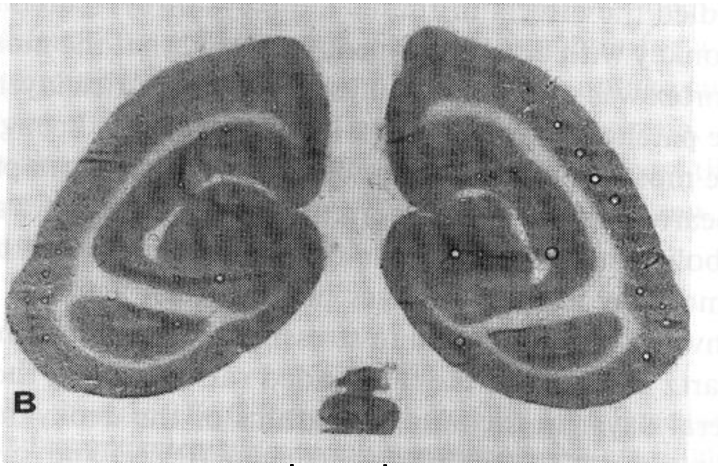


In theory, metabolic mapping techniques can resolve cortical processes at the level of cortical columns.

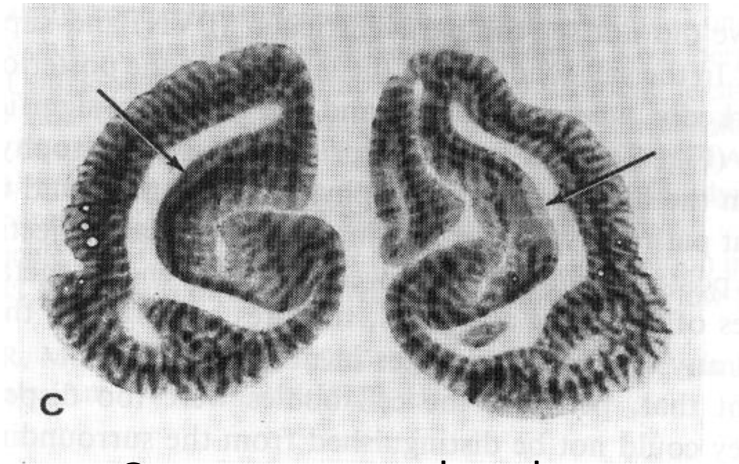
2-deoxyglucose: visual stim in cats



Eyes open



Eyes closed

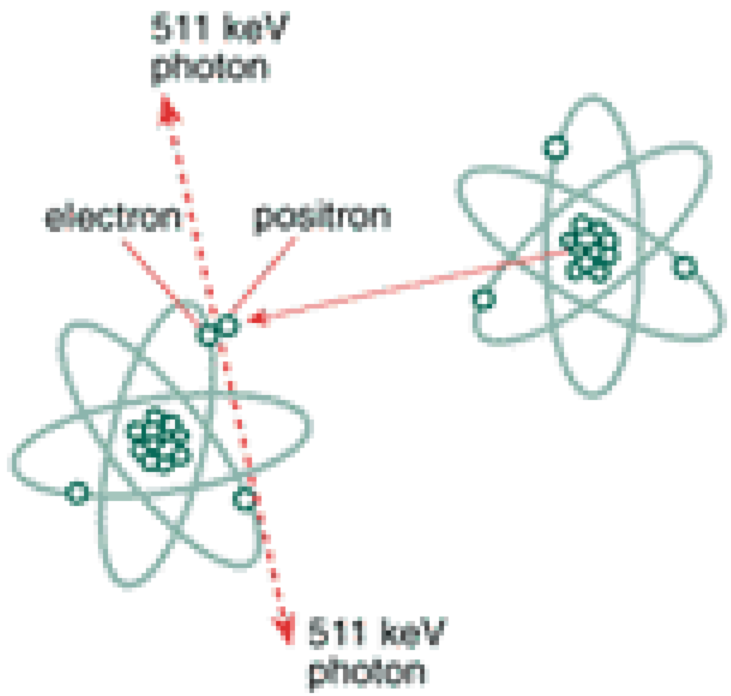


One open, one closed

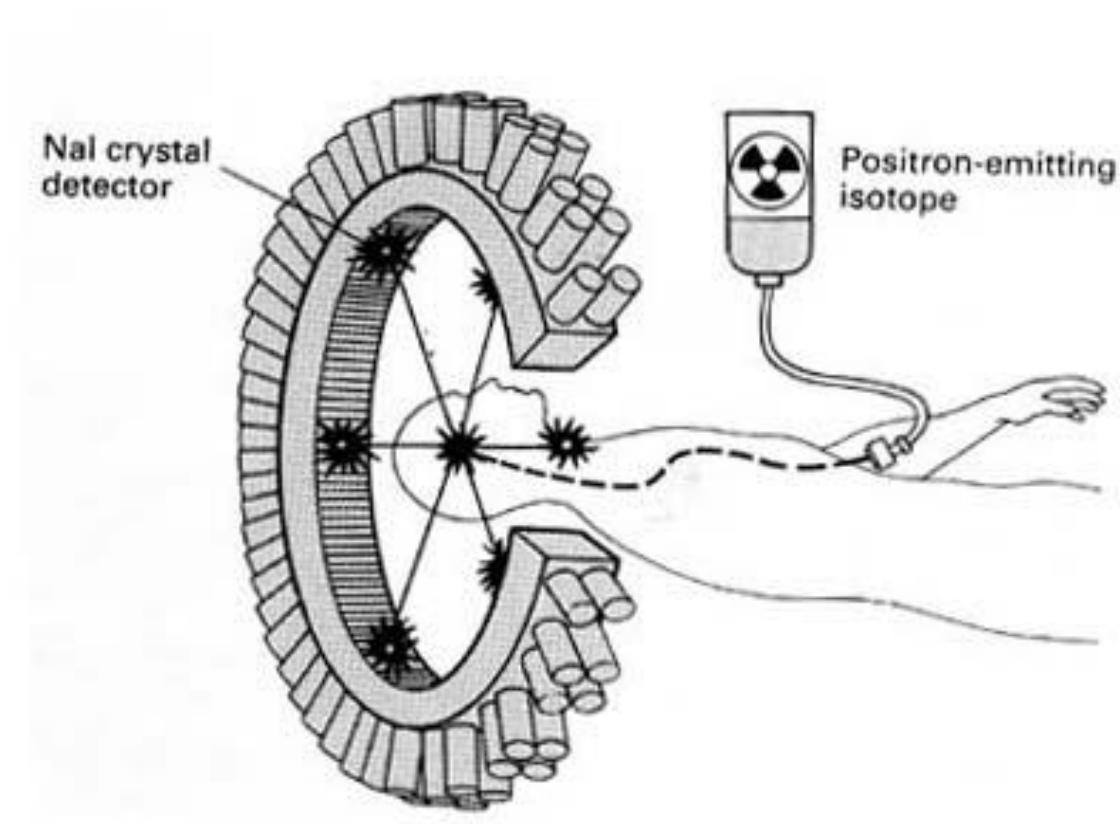
Positron Emission Tomography (PET)

Images of physiological parameters are inferred from the distribution of positron-emitting radiopharmaceuticals

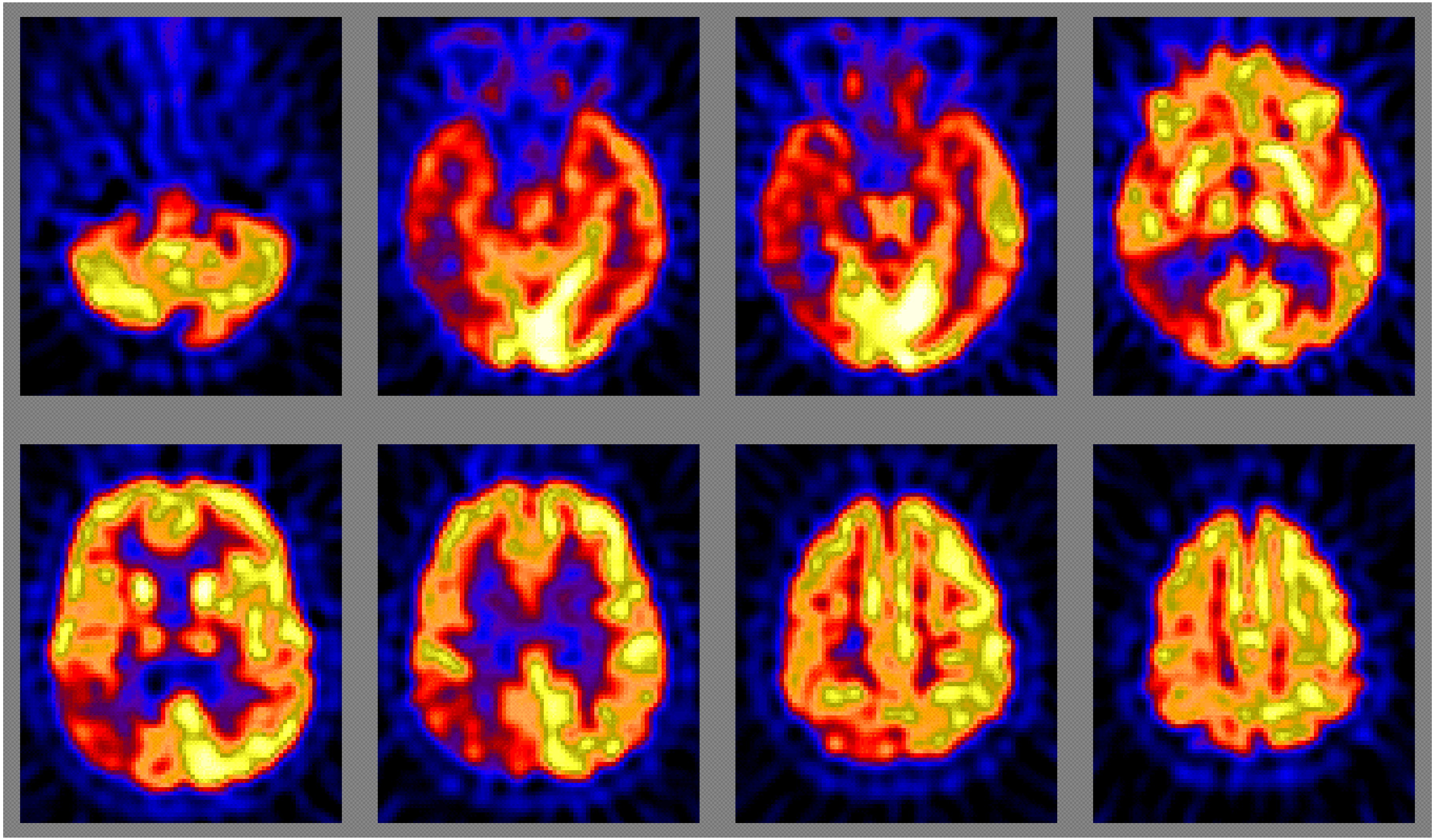
Positron emission



PET detectors



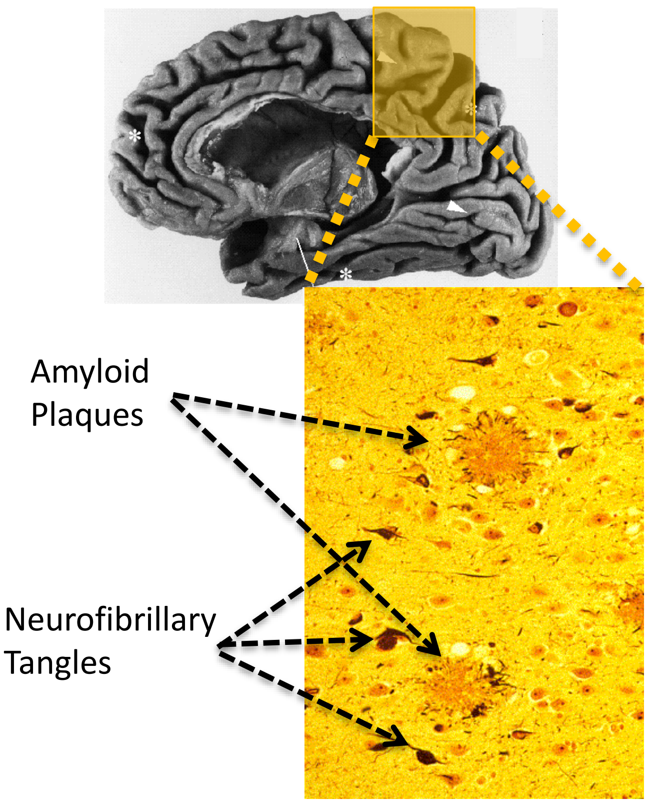
$[^{18}F]$Fluorodeoxyglucose PET

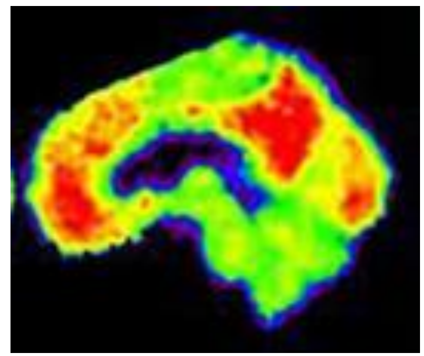


PET

- Physiologically distributed signal
- Unrivaled sensitivity
- A medical procedure with ionizing radiation
- Requires radionuclide source (cyclotron) and radiochemistry facilities
- Tracers exist for tissue metabolism (18F-FDG), blood flow (15O-water), DNA synthesis (18F-FLT), Alzheimer disease proteins, and more.

BRAIN IMAGING OF ALZHEIMER'S DISEASE

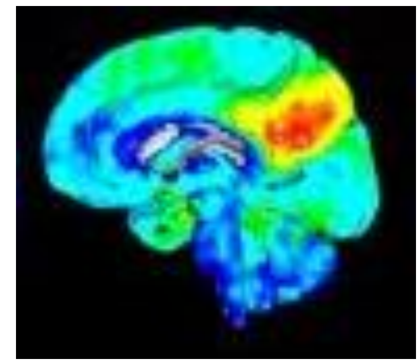




AMYLOID PET SCAN

Detects amyloid plaques
Stereotypical distribution
Leads symptoms by 15 years
Doesn't change over time

Use: to certify diagnosis
Spinal fluid is an alternative.



TAU PET SCAN

Detects tau tangles
Variable distribution
Correlates well with symptoms
Tracks advance of disease

Use: to delineate disease impact
To track treatment

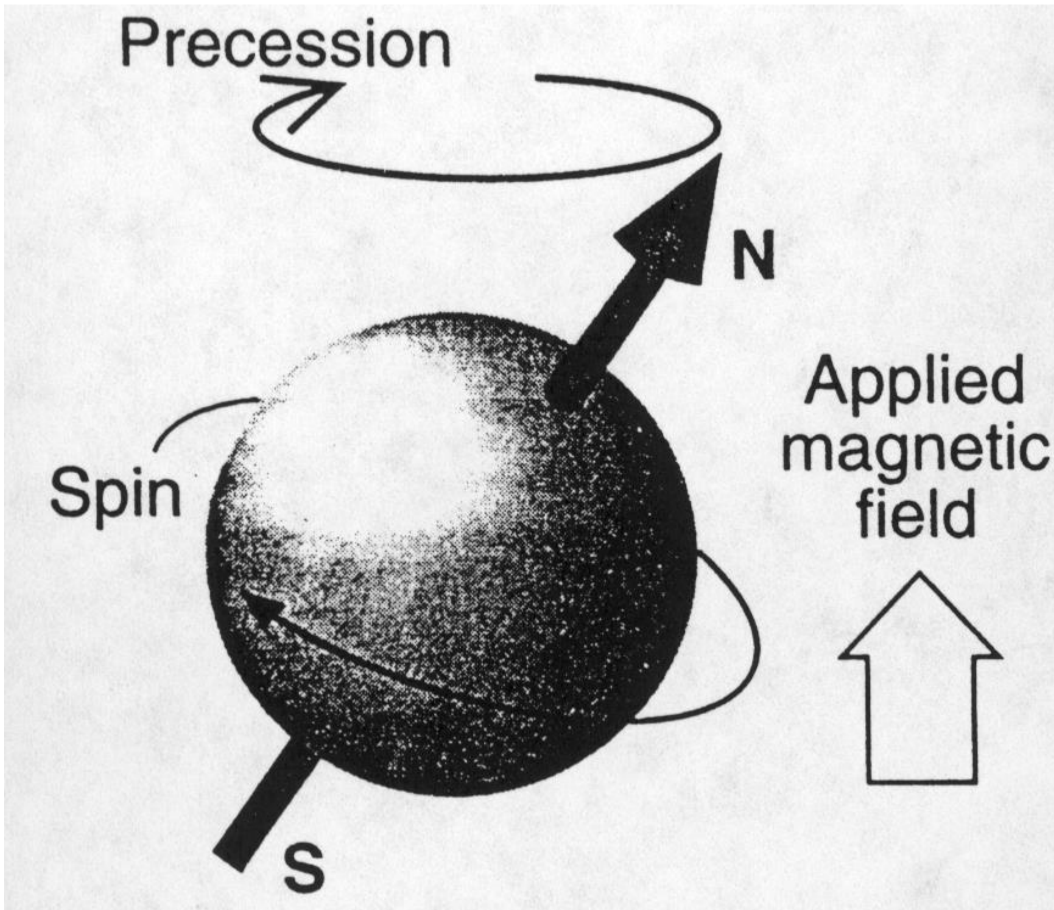
Magnetic Resonance Imaging (MRI)

Wassersteifel
Roman Signer
1986

MRI

- Water molecules have a natural frequency at which they can accept and radiate energy
- More precisely, the hydrogen nuclei have a quantum mechanical property called *spin angular momentum*
- The spin states of hydrogen nuclei diverge in energy level in the presence of a magnetic field
- Water protons absorb or give off energy to move between these energy levels, at the natural frequency, the Larmor frequency, which is a function of the magnetic field strength.

In a magnetic field, protons precess at a natural frequency.
Energy can go in or out of this system *only* at this frequency.



Excitation

- Radiofrequency energy at the Larmor frequency transfers to the water protons of the system.
- This does two things:
  - Introduces a transverse component to the magnetization
  - Synchronizes the precession of the protons
- When the pulse of RF input stops, the system (water in the magnet) will radiate radiofrequency energy for a little while

Relaxation: T1, T2, T2*

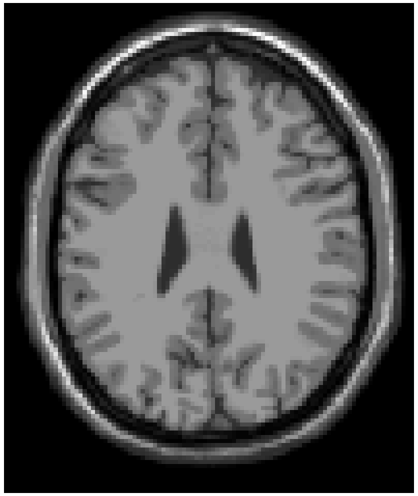
- With time (described by T1) the excited dipoles will relax back into alignment with the field.
- Before that happens, their precession will get out of phase (described by T2) and no more signal will be available.
- But even before that, local imperfections in the field will probably cause even faster dephasing (described by T2*).

T1 relaxation occurs at different rates in different tissues

- T1 relaxation is slowest in a homogeneous sample of water (e.g. in CSF)
- T1 relaxation is faster in lipid-rich white matter than in gray matter
- Differential relaxation is the key to tissue contrast in MRI

Together, the values of TR and TE emphasize different tissue parameters.

T1

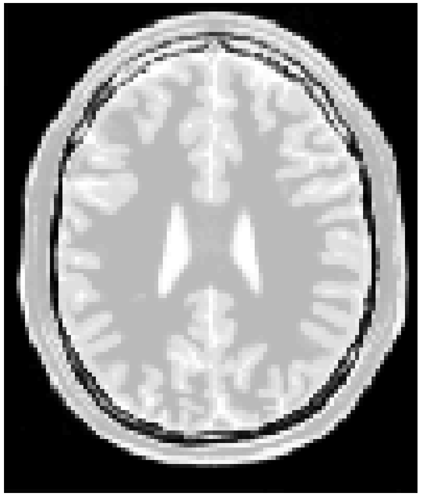


TR = 300 msec
TE = 20 msec

T2

TR = 3000 msec
TE = 120 msec

PD



TR = 3000 msec
TE = 20 msec

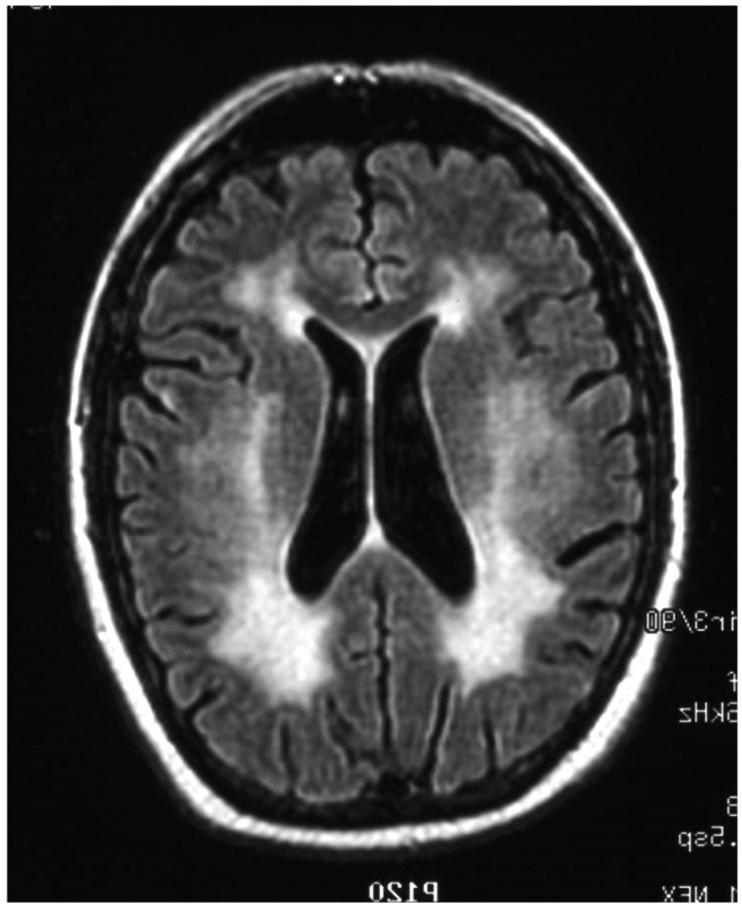
A **short** TR and **short** TE emphasizes T1 contrast.

A **long** TR and **long** TE emphasizes T2 contrast.

A **long** TR and **short** TE emphasizes proton density contrast.

FLAIR : FLuid-Attenuated Inversion Recovery

– T2 weighting with black spinal fluid



The MRI signal is rich

- Proton density
- Relaxation times (T1, T2)
- Magnetic field distortion (T2*)

- Flow
- Diffusion
- Chemical shift
- Magnetization transfer
- ……

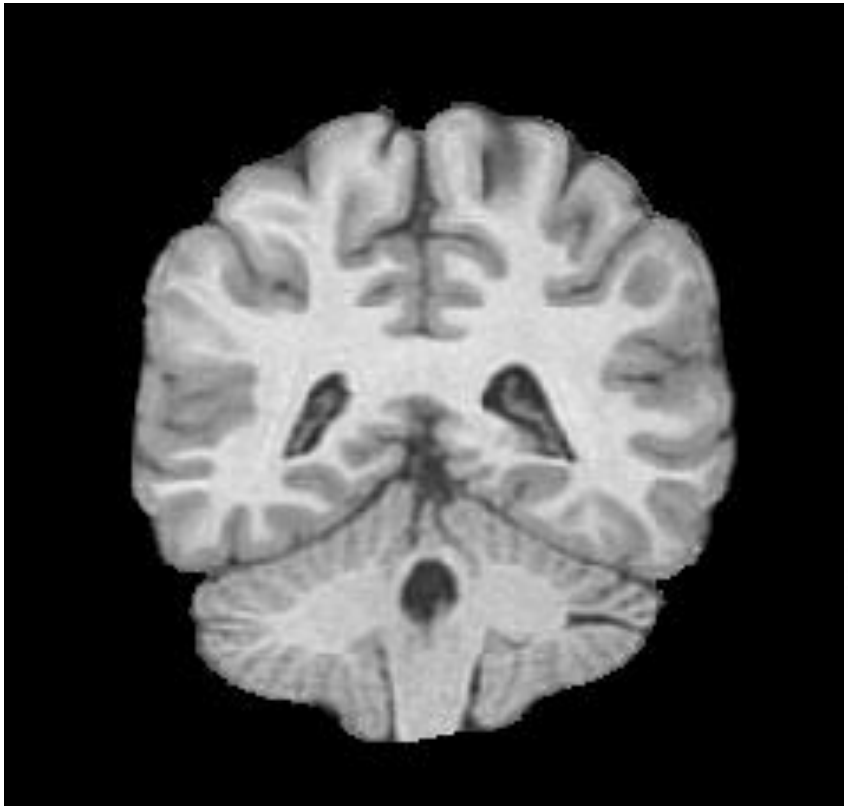
Magnetic resonance angiography “MRA”

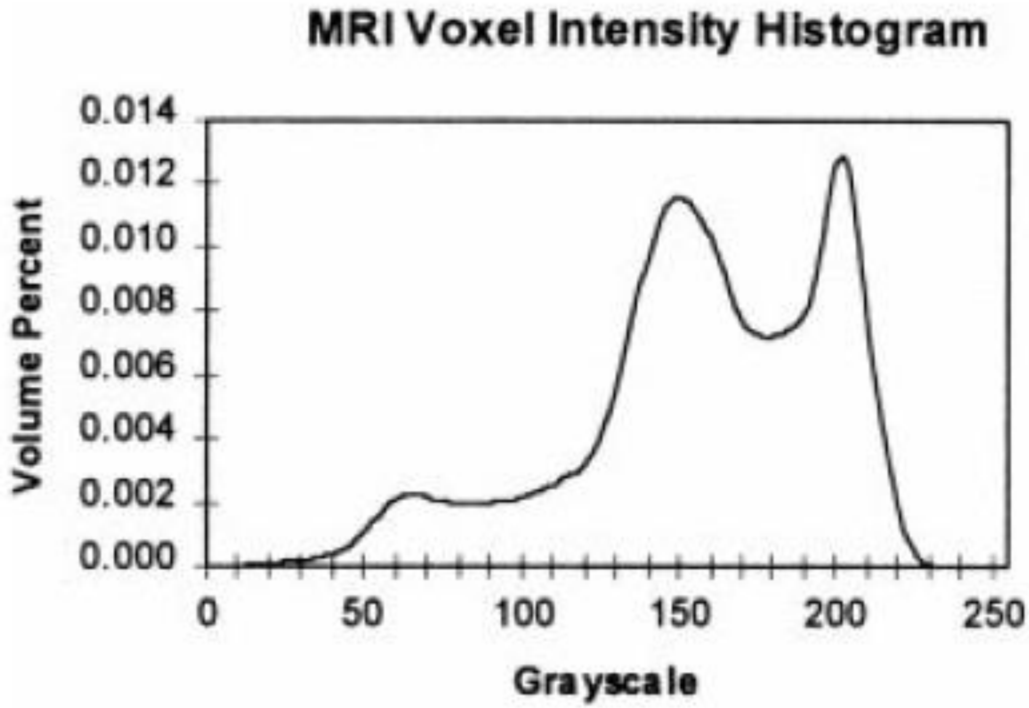
The “economy” of MRI

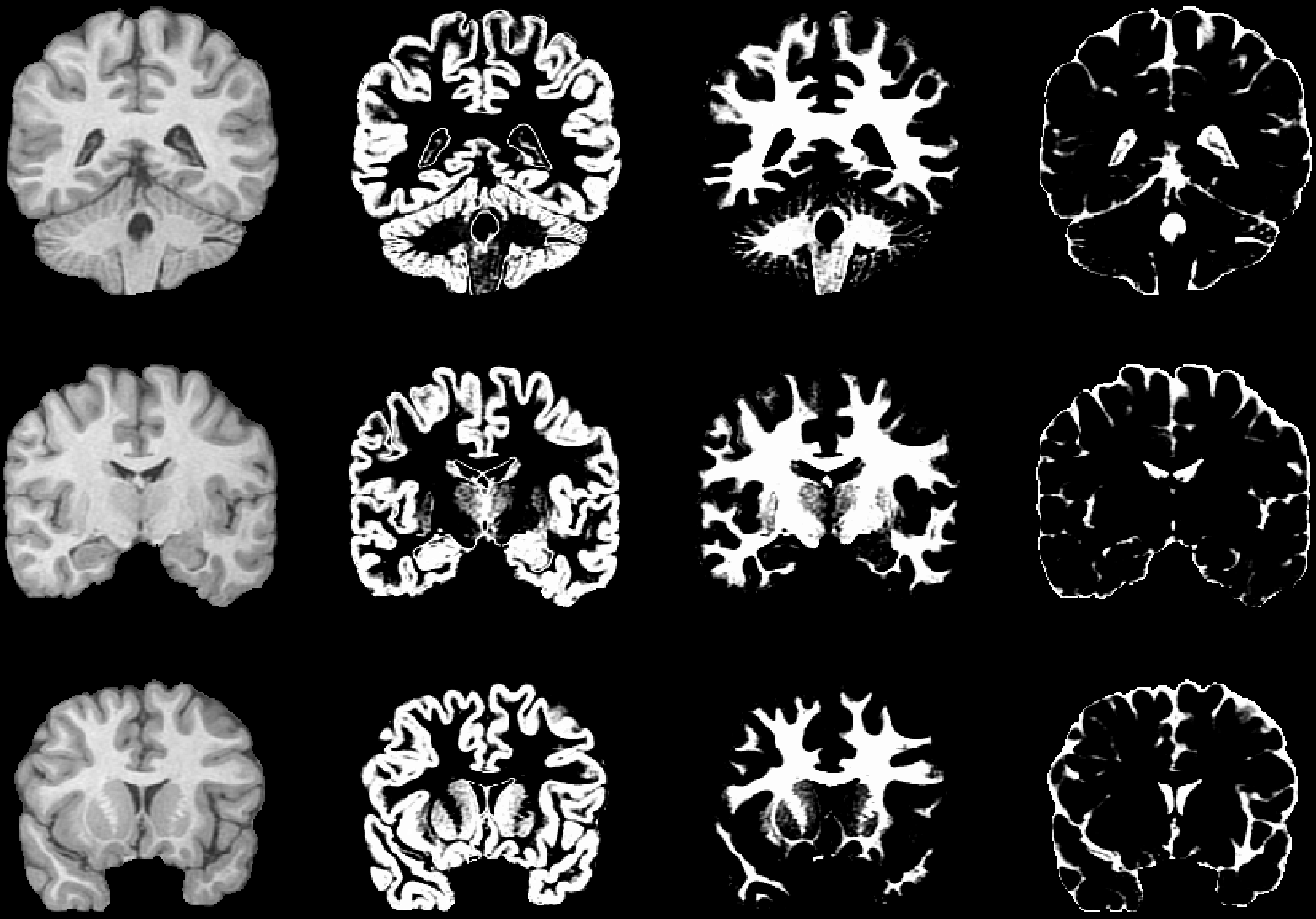
- In MRI signal is the sum of the longitudinal magnetization of the protons in the field of view
- This is a like fixed budget, that can be used more or less efficiently, and can be spent to obtain some combination of:
  - Better spatial resolution
  - Better signal to noise ratio (SNR)
  - Reduced imaging time
- There are always trade-offs!
- Advances in MRI are often in the form of a smarter pulse sequence.

Efficient pulse sequences

- Maximize the amount of time spent listening for the signal
- Maximize the number of protons in the sample that are being put to work at any one time
- Optimize the relationship between TR and TE to maximize signal
- We use two efficient sequences extensively: MP-RAGE and EPI GRE fMRI

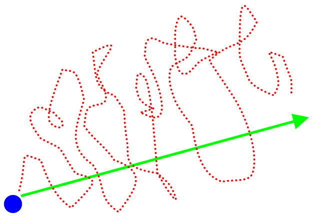



MRI Voxel Intensity Histogram
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
Volume Percent
0
50
100
150
200
250
Grayscale

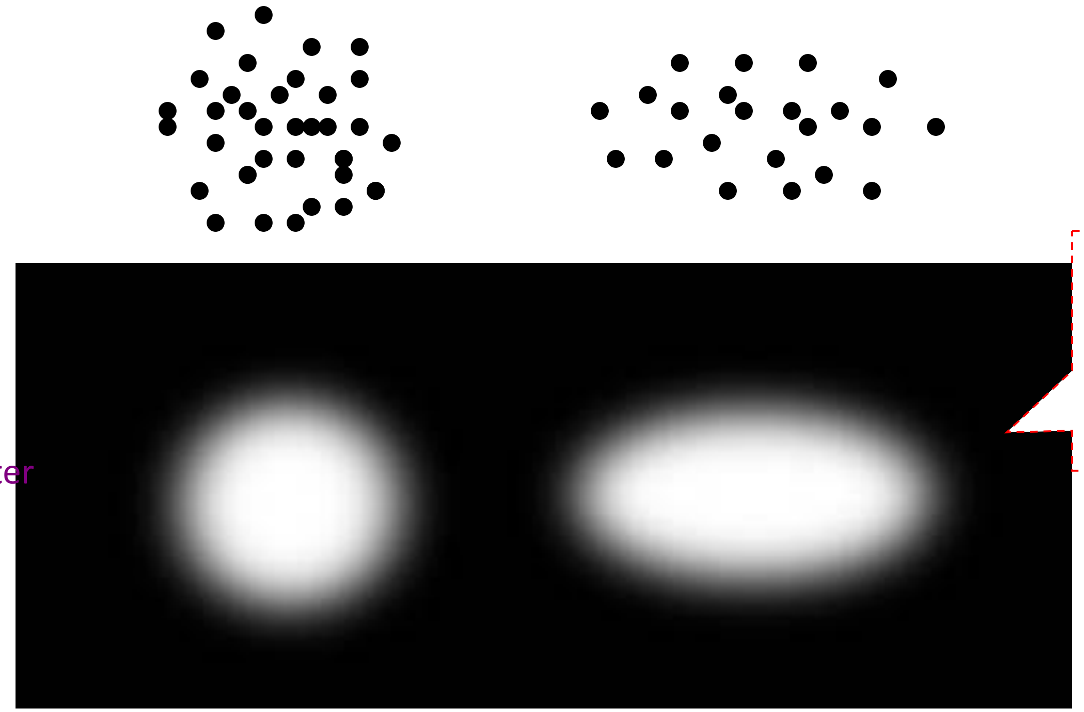


Diffusion Tensor Imaging

Diffusion



Random “walk” of the water molecular also known as “Brownian motion ”

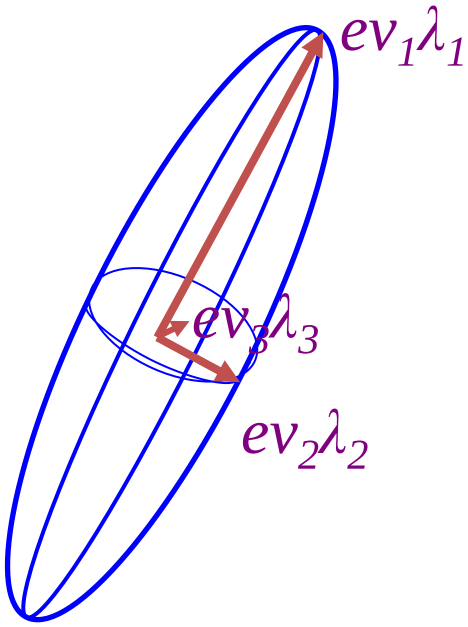


Ellipsoid = Probability of Diffusion Distribution

Isotropic Diffusion

Anisotropic Diffusion

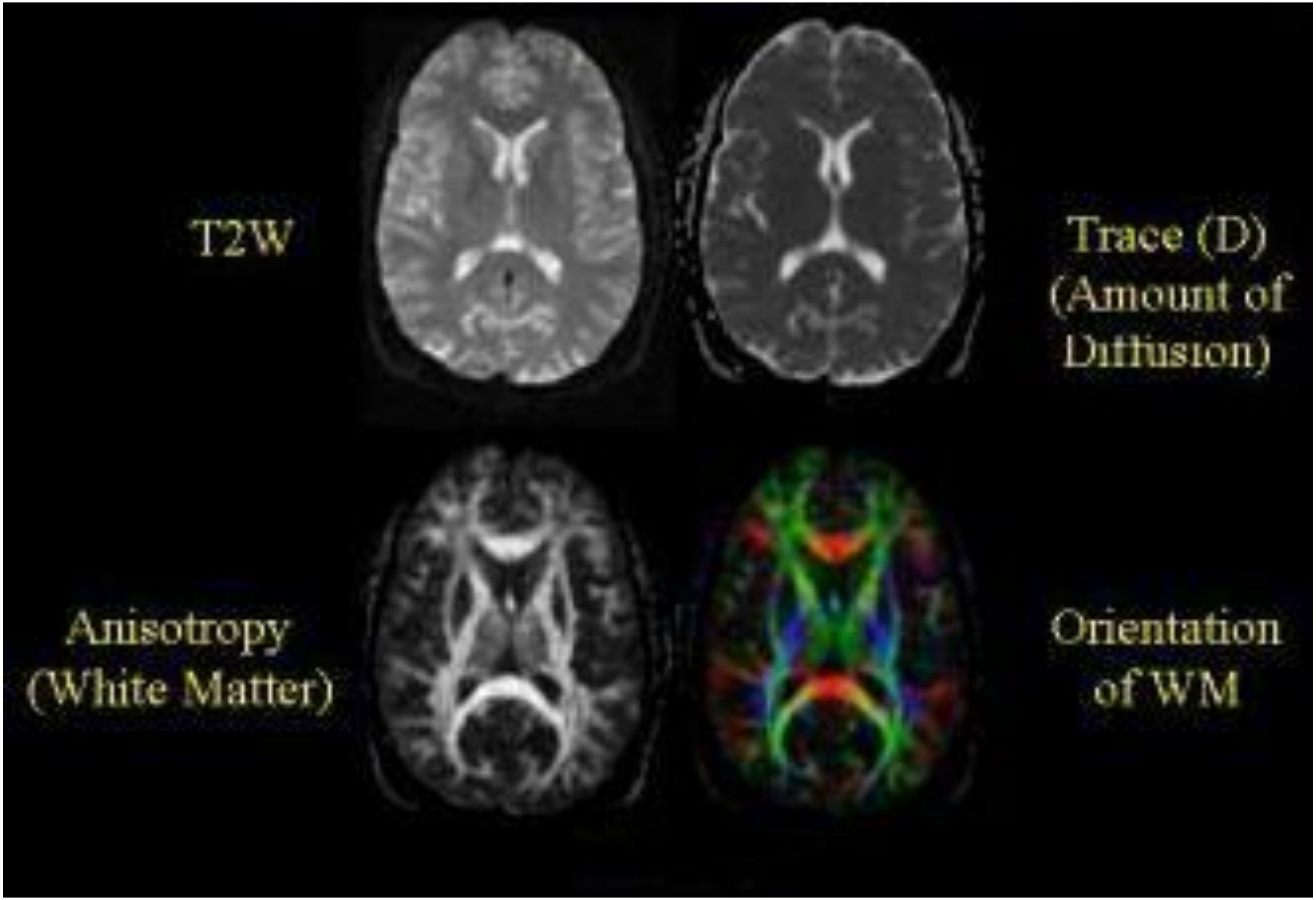
Diffusion eigenvectors



Diagonalization of this tensor provides three eigenvectors (*ev₁*, *ev₂* and *ev₃*) with three corresponding eigenvalues (*λ₁*, *λ₂* and *λ₃*)

$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} = E^T \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} E$$

Diffusion Tensor Images

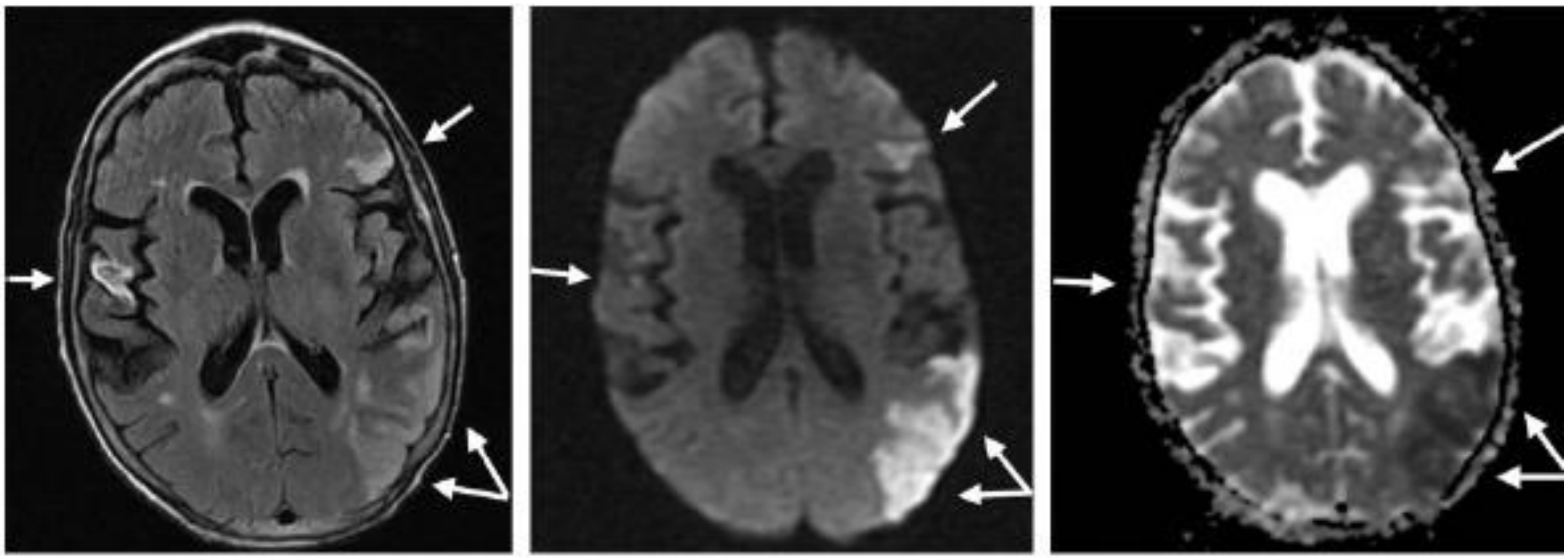


Diffusion imaging

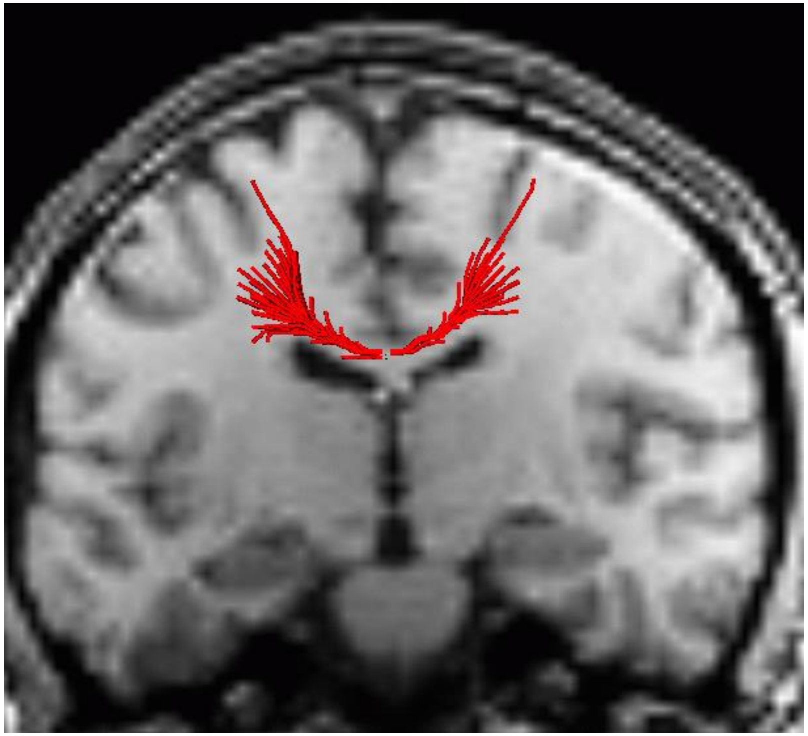
- Parameters neurologists are used to seeing
  - Diffusion-weighted image
  - Apparent diffusion coefficient - ADC
- Parameters neuroscientists are used to seeing
  - Diffusion fractional anisotropy – FA

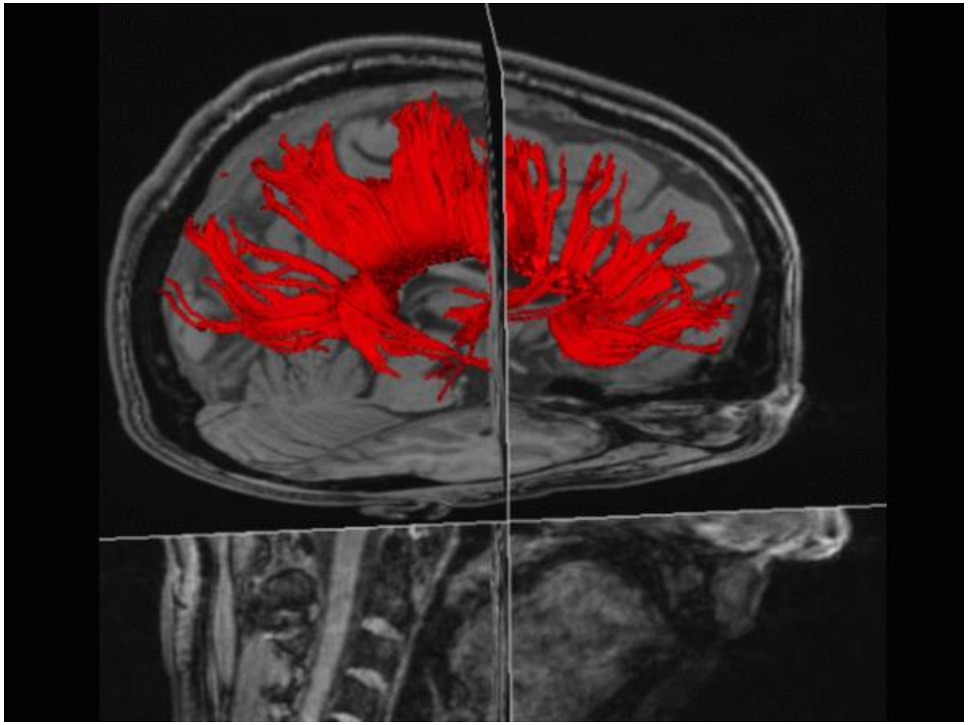
    A measure of how constrained water is to diffuse in only certain directions
  - Diffusion principal eigenvector

    The axis along which water diffuses most freely



DTI Tract Tracing



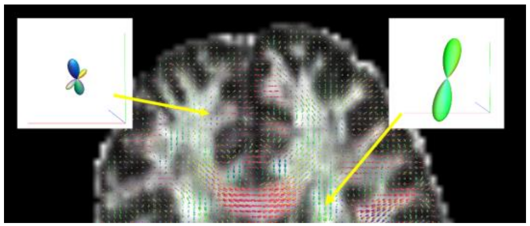


In vivo Connectivity-based Cortex Parcellation

Preprocess DWI

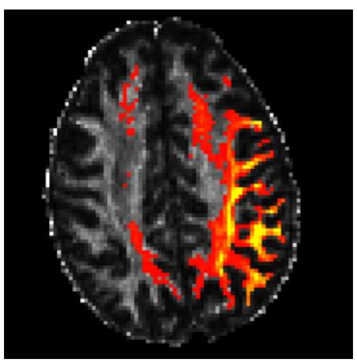
↓

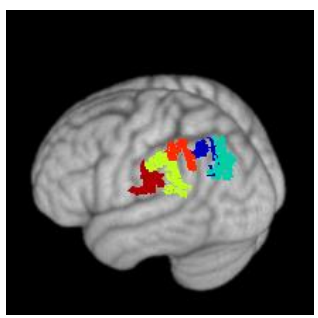
Model Diffusivity

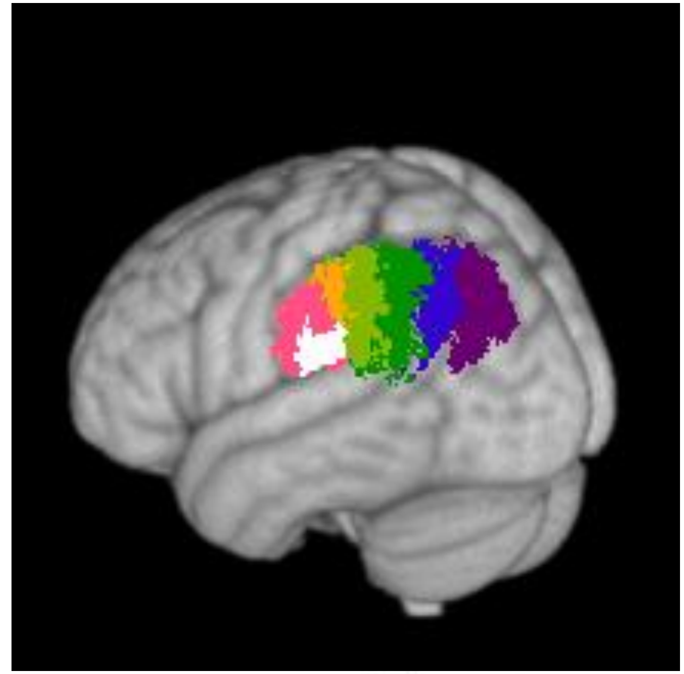


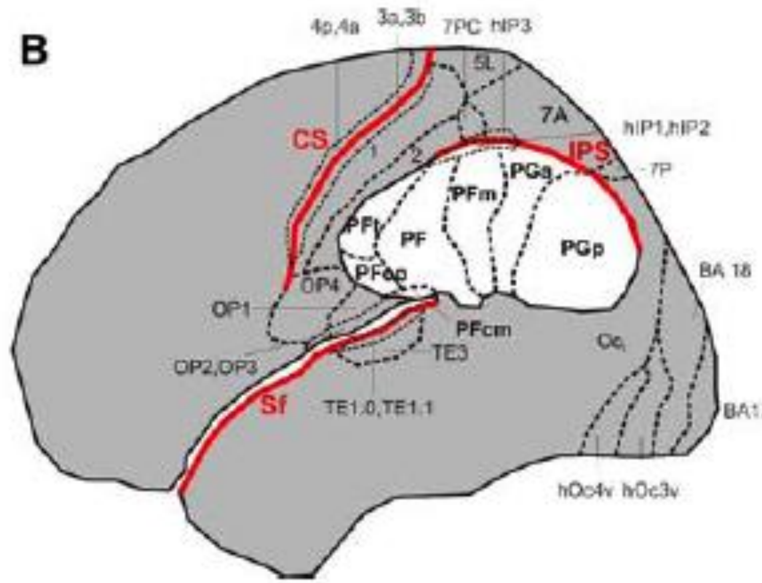
↓

Compute and cluster tractograms









Functional Magnetic Resonance Imaging (fMRI)

Physiological basis of fMRI

Brain activity is imaged *indirectly*, through parameters related to metabolic substrate delivery.

Neurovascular coupling

Synaptic electrochemical activity

DEPENDS ON

Maintenance of membrane potentials

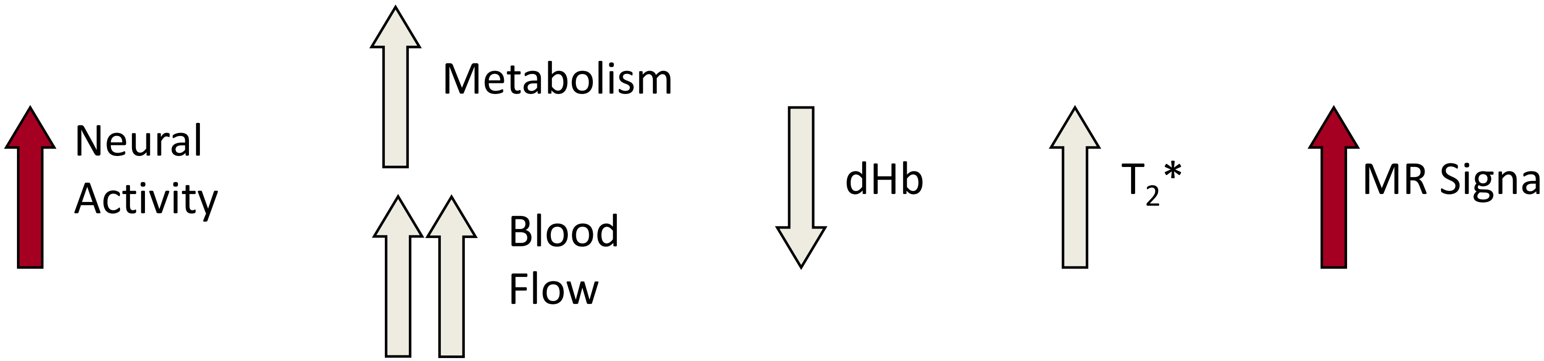
WHICH DEPENDS ON

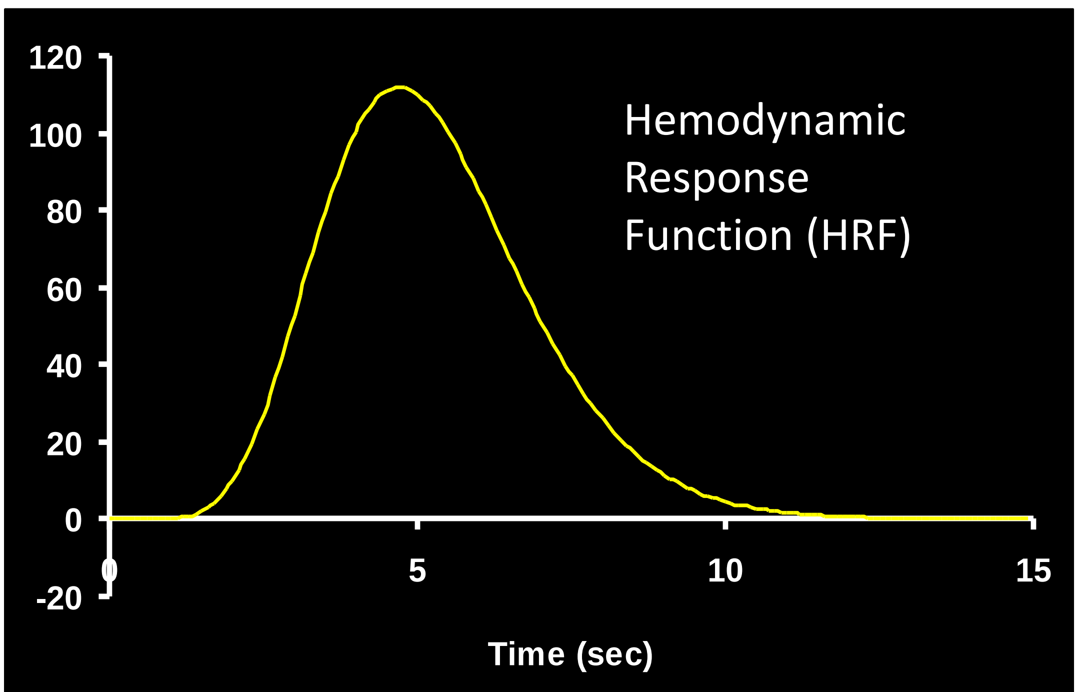
Metabolism of glucose

WHICH DEPENDS ON

Substrate delivery via blood flow

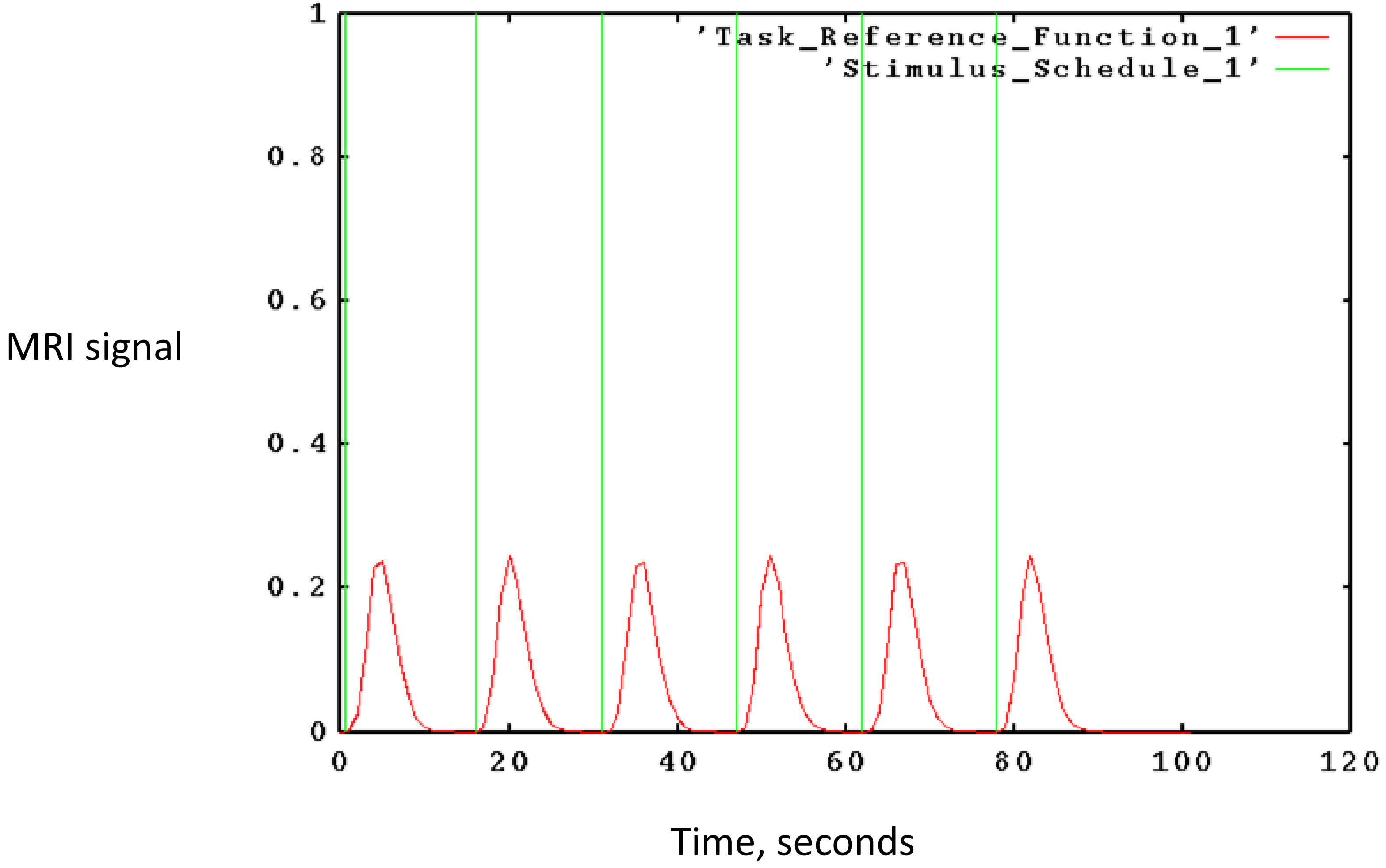
Basis of fMRI signal



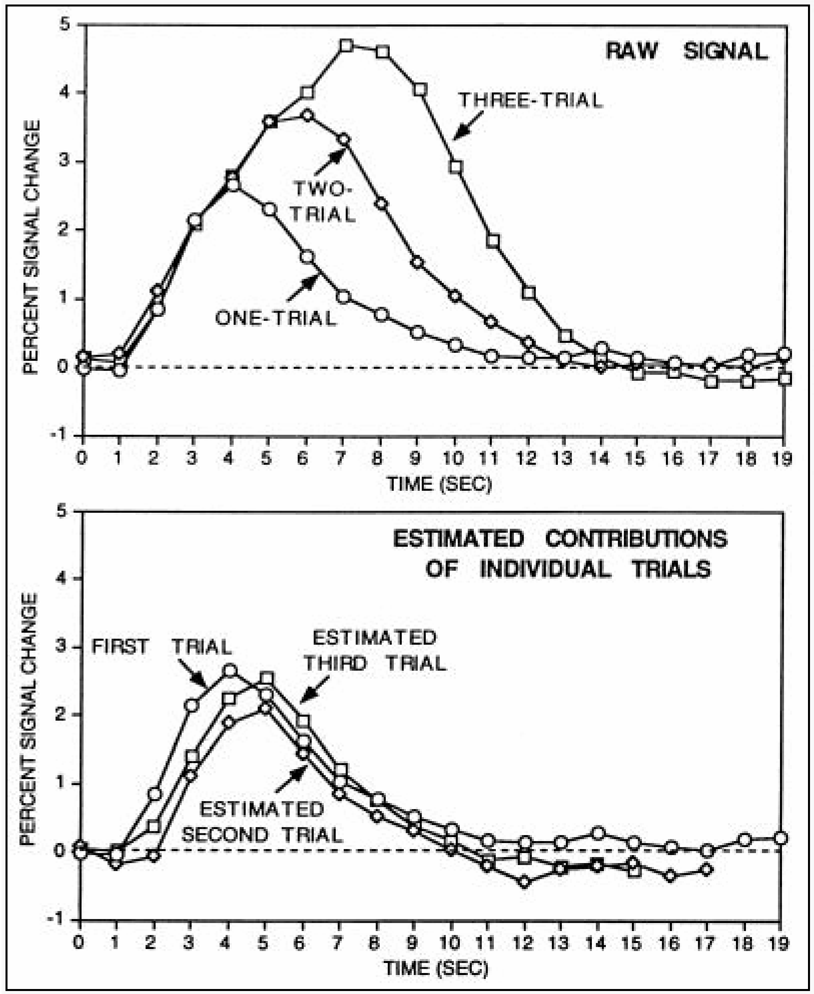


Blood
Oxygenation
Dependent
Signal

“BOLD”


'Task_Reference_Function_1'
'Stimulus_Schedule_1'
1
0.8
0.6
0.4
0.2
0
0
20
40
60
80
100
120
MRI signal
Time, seconds

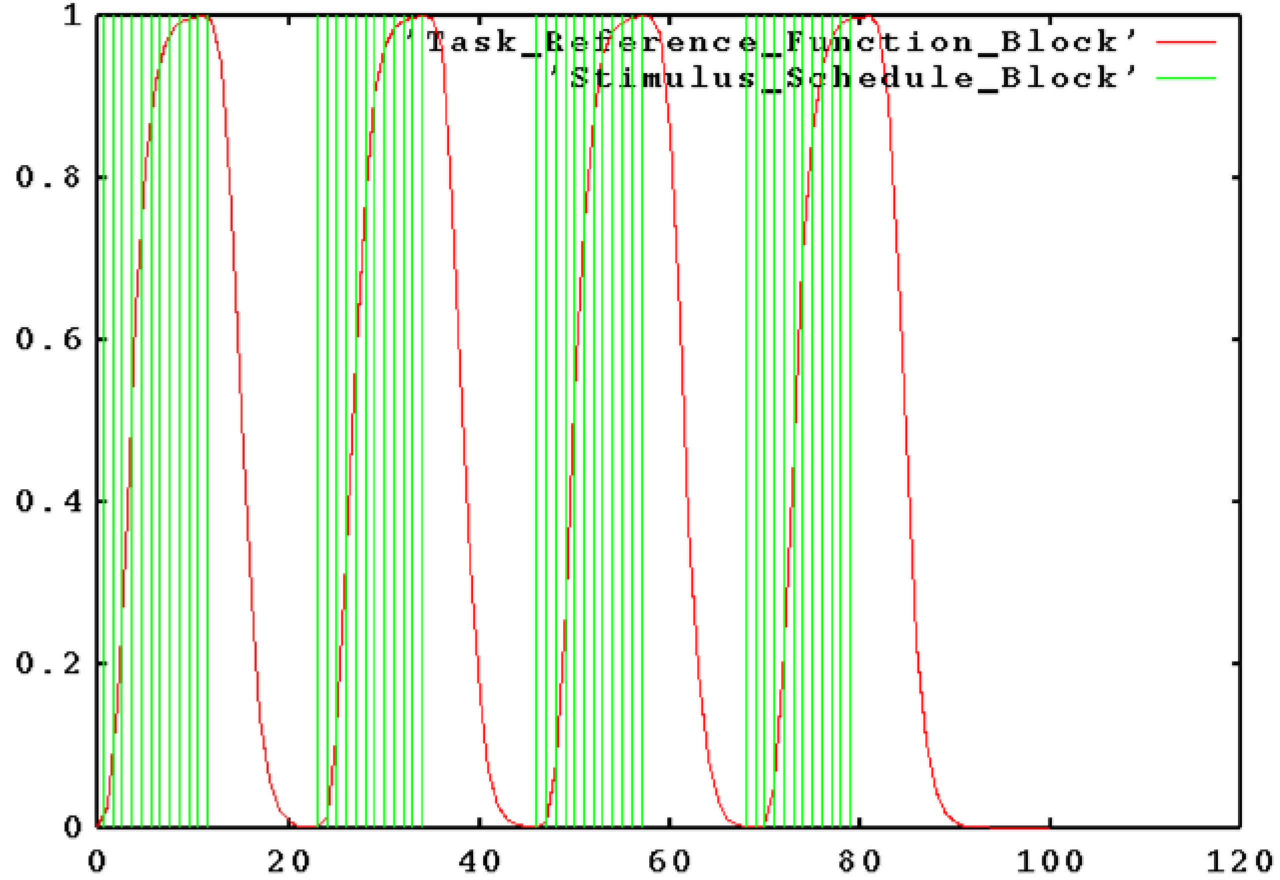
HRF sums linearly over trials



A. Dale and R. Buckner
Hum Brain Mapp 5:329
1997

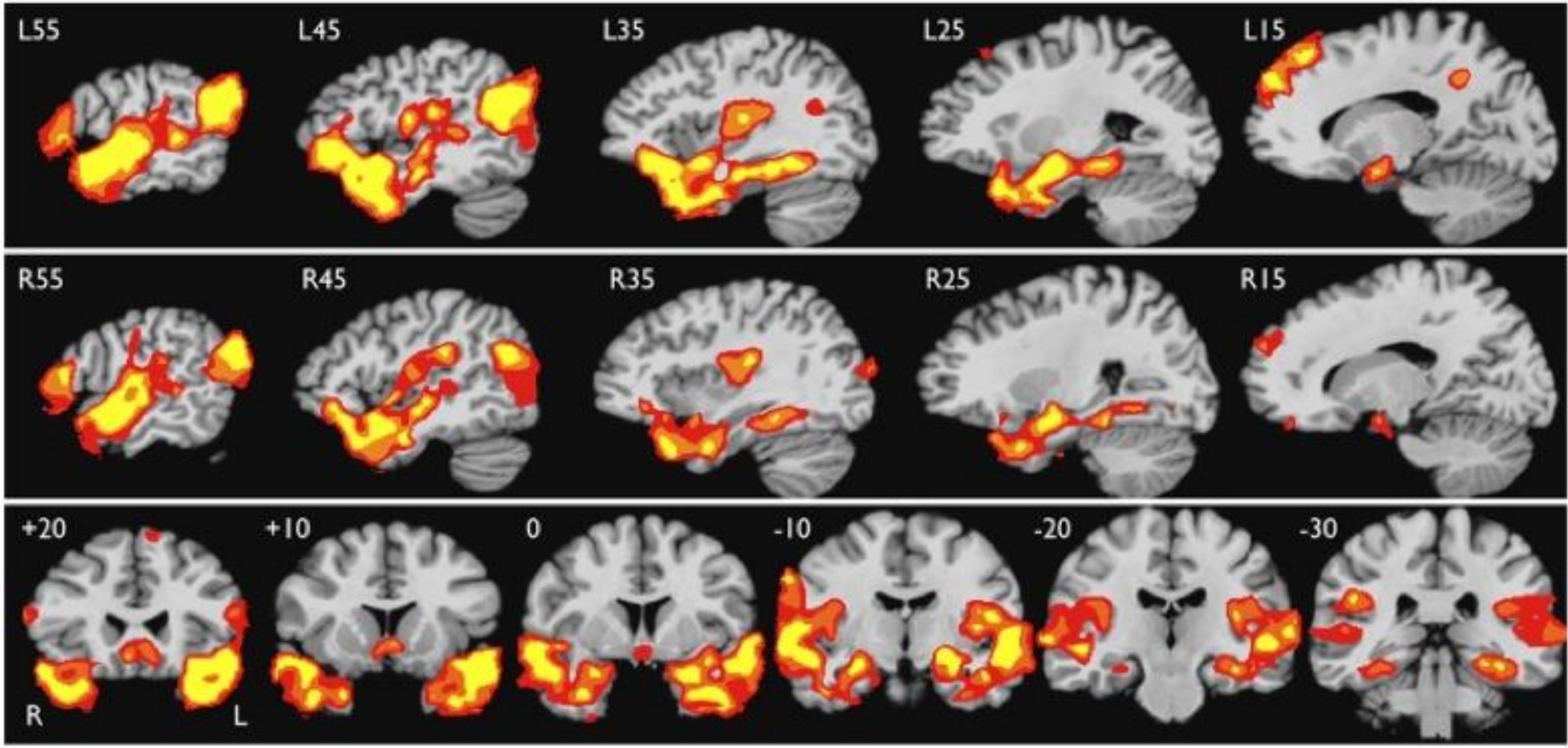
Block Design

MRI signal

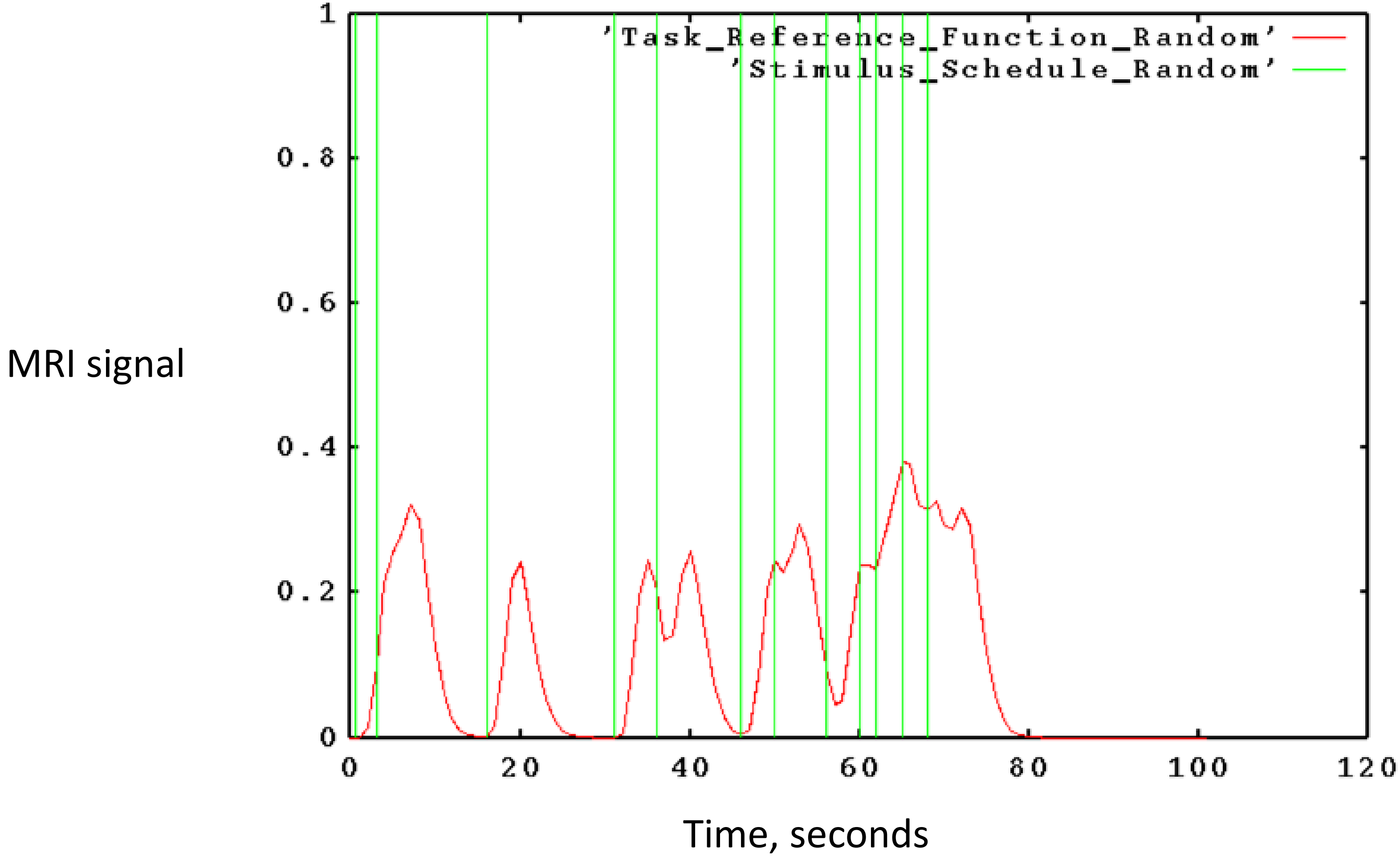


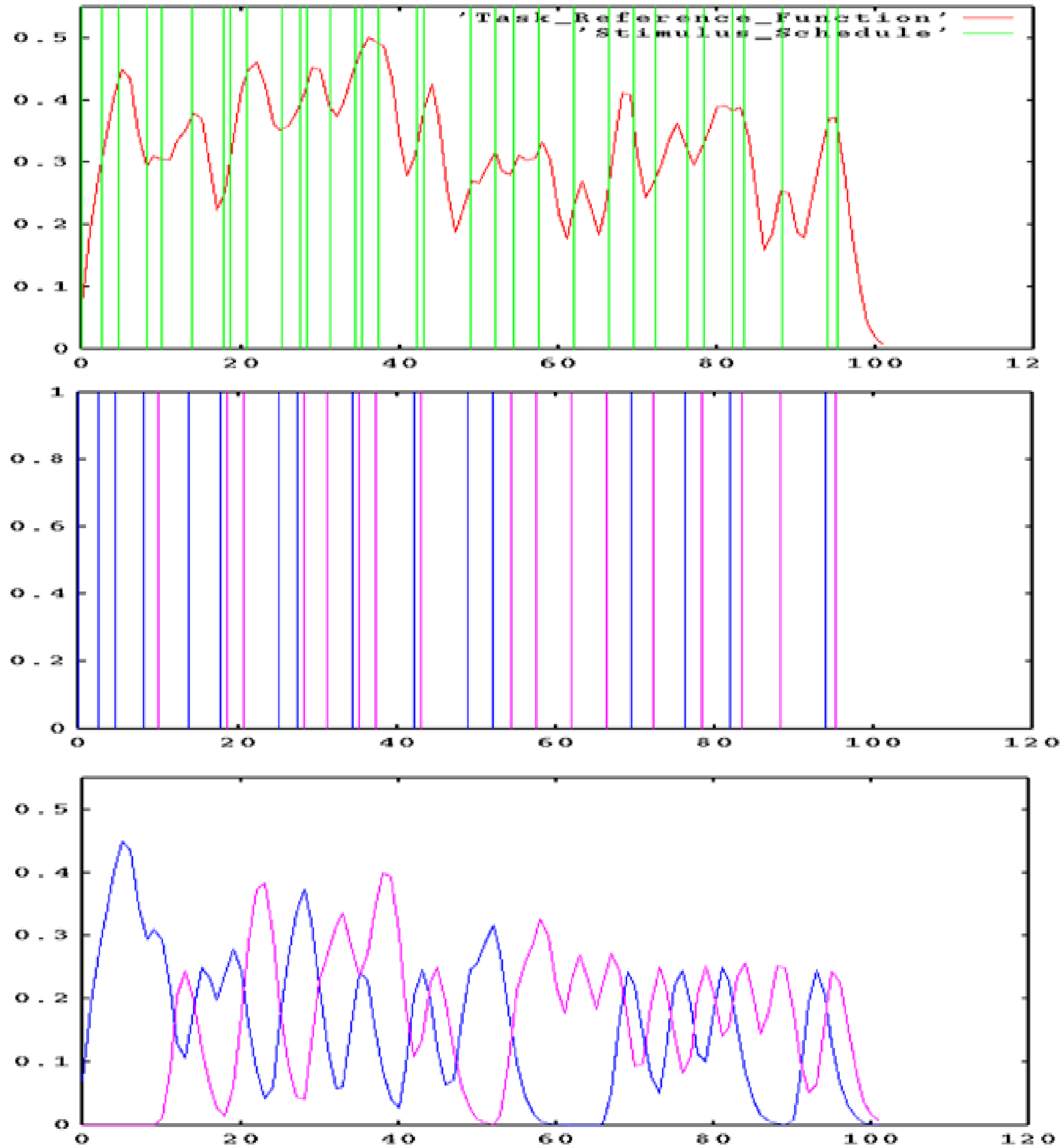
Time, seconds

Activation of the anterior temporal lobes during listening to discourse.



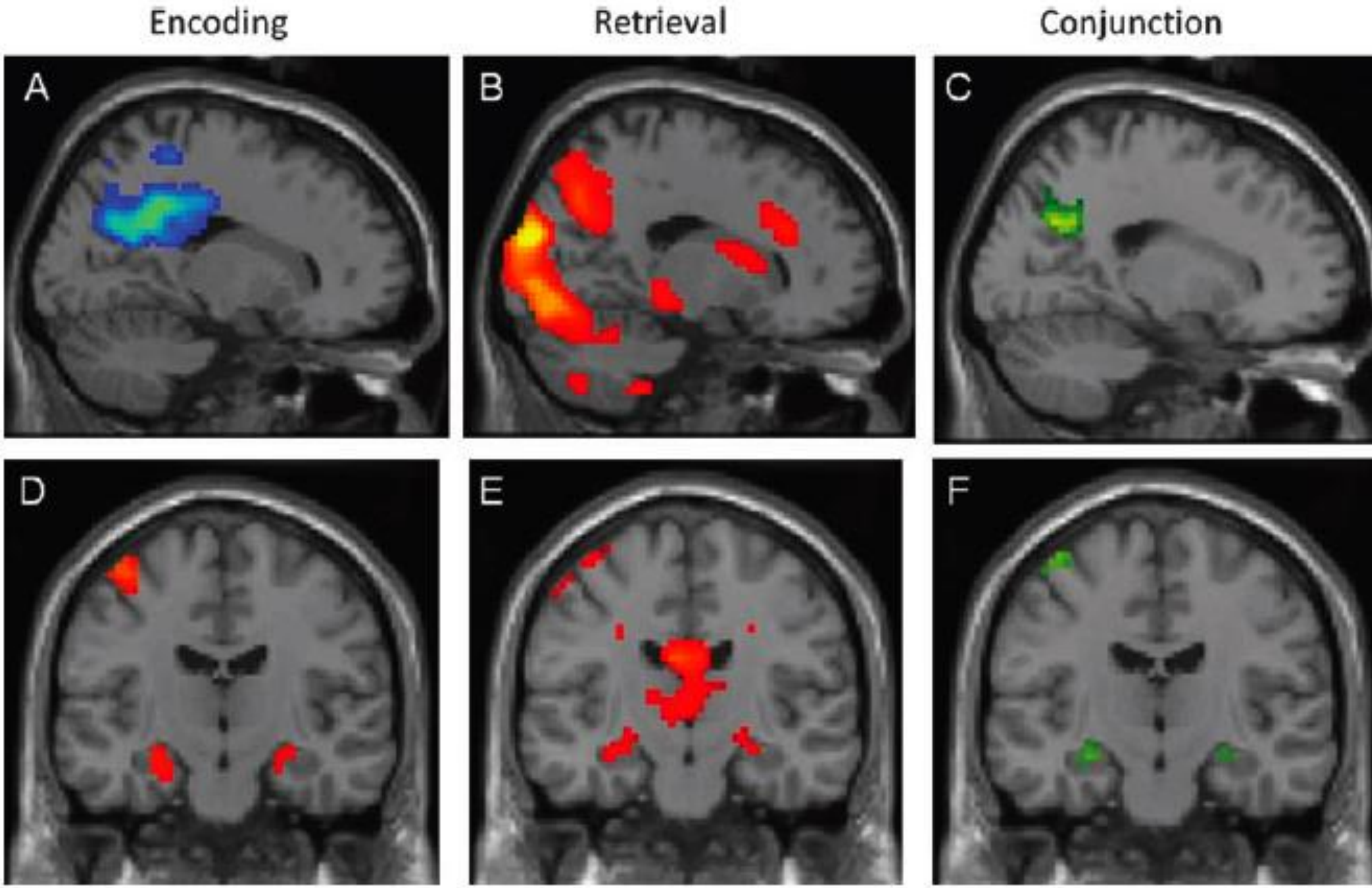
Event-Related Design





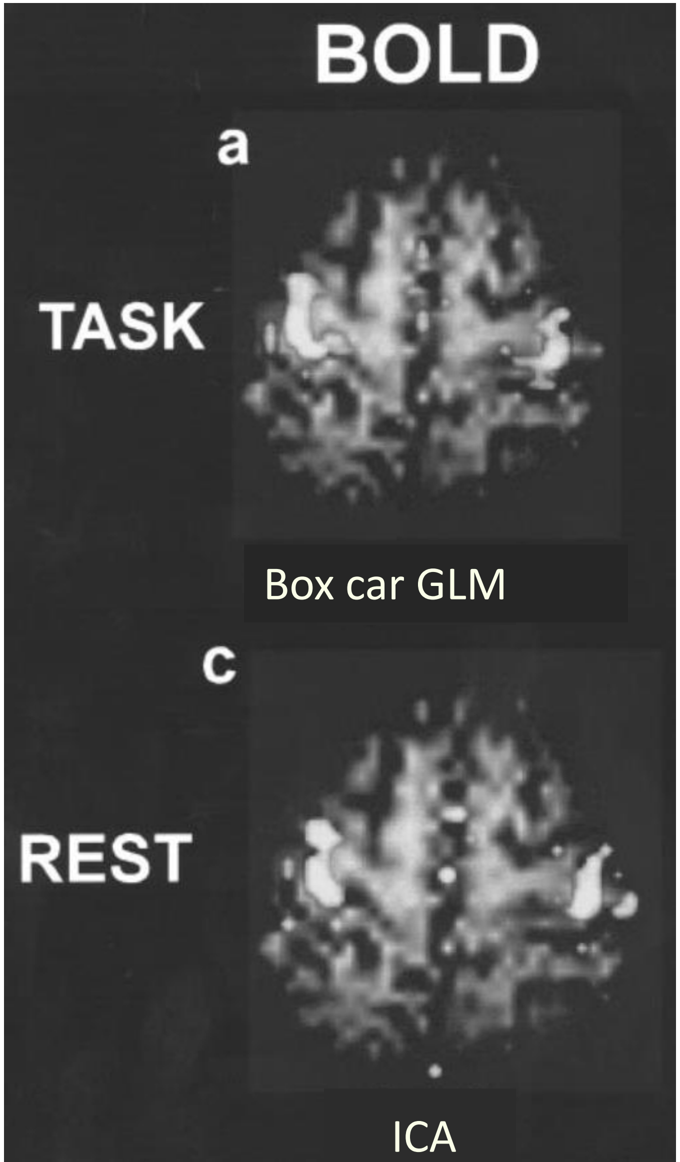
'Task_Reference_Function'
'Stimulus_Schedule'

Activation of hippocampus during successful memory encoding and retrieval



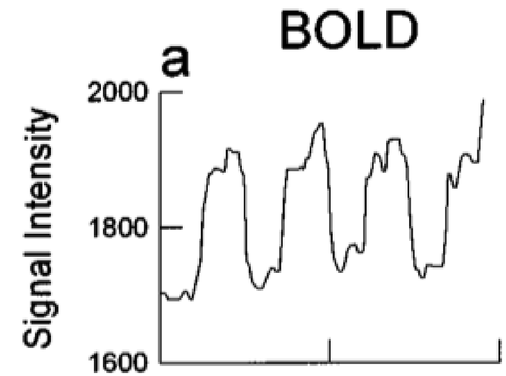
Two fMRI paradigms

- Activation paradigm
  - Signal model: predicted BOLD timecourse
- Functional connectivity paradigm
  - Signal model: correlated signal timecourses



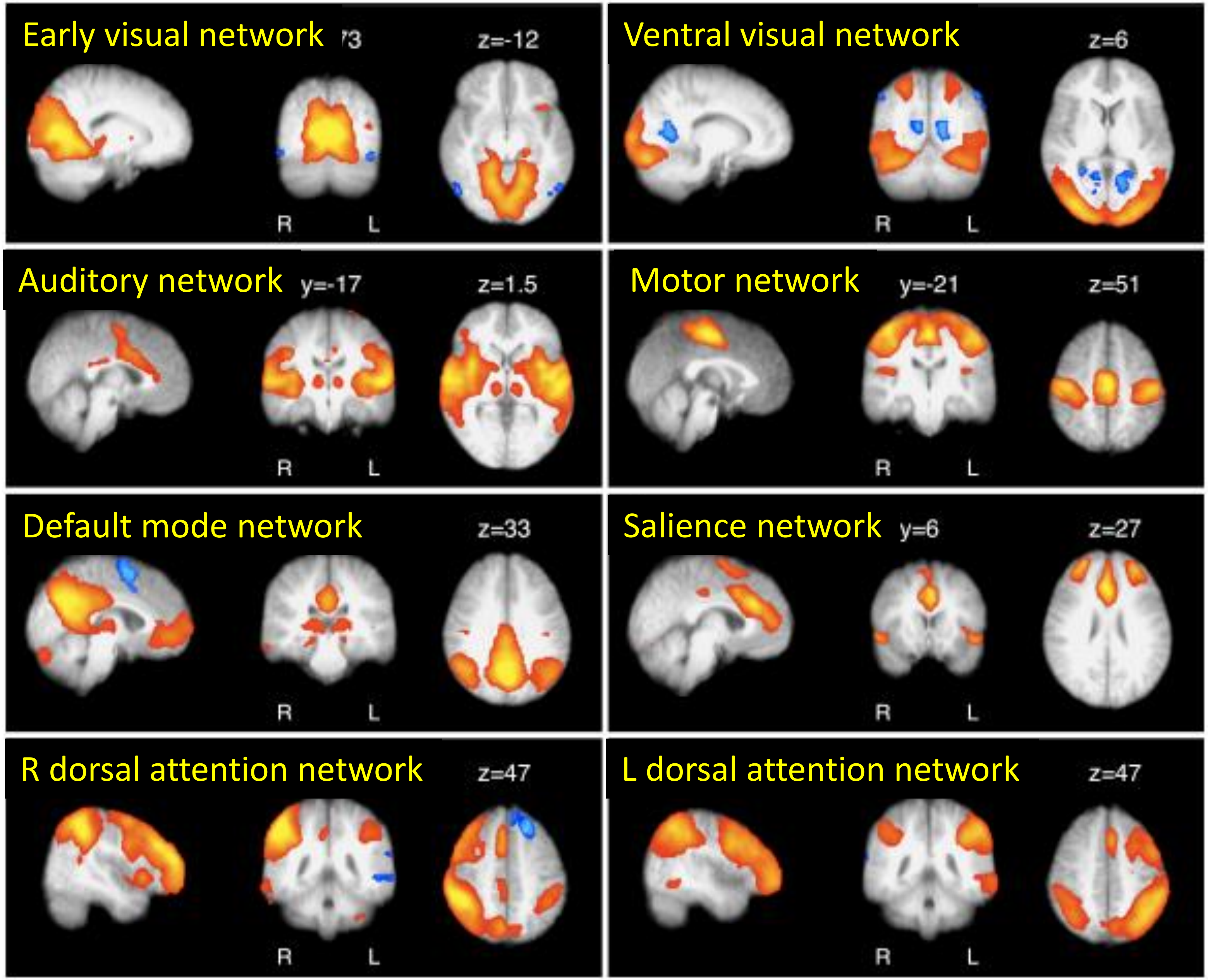
Biswal et al., 1997

Finger tapping



Resting

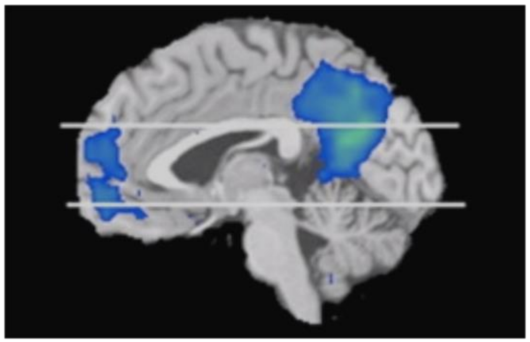
Fourier transform



Damoiseaux et al 2006

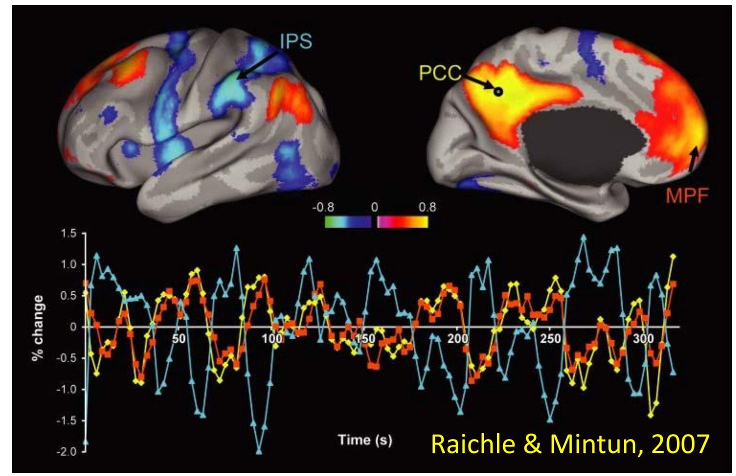
“Default” Mode Network

Relevance to adaptive behavior

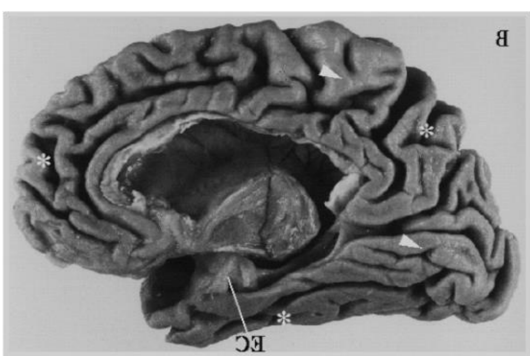


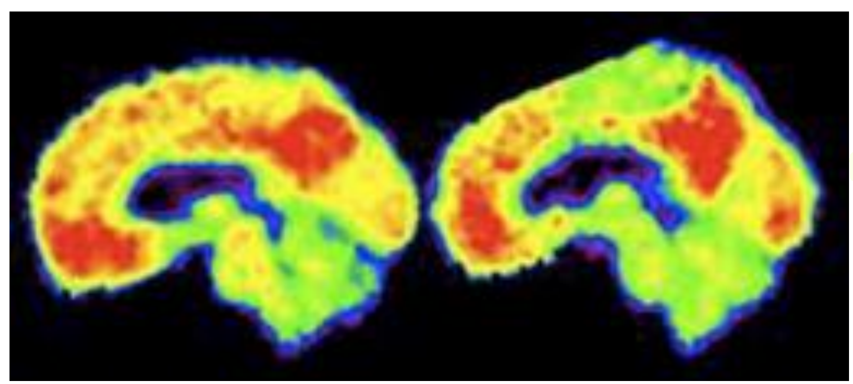
Deactivation DMN

Activation DAN



Relevance to disease

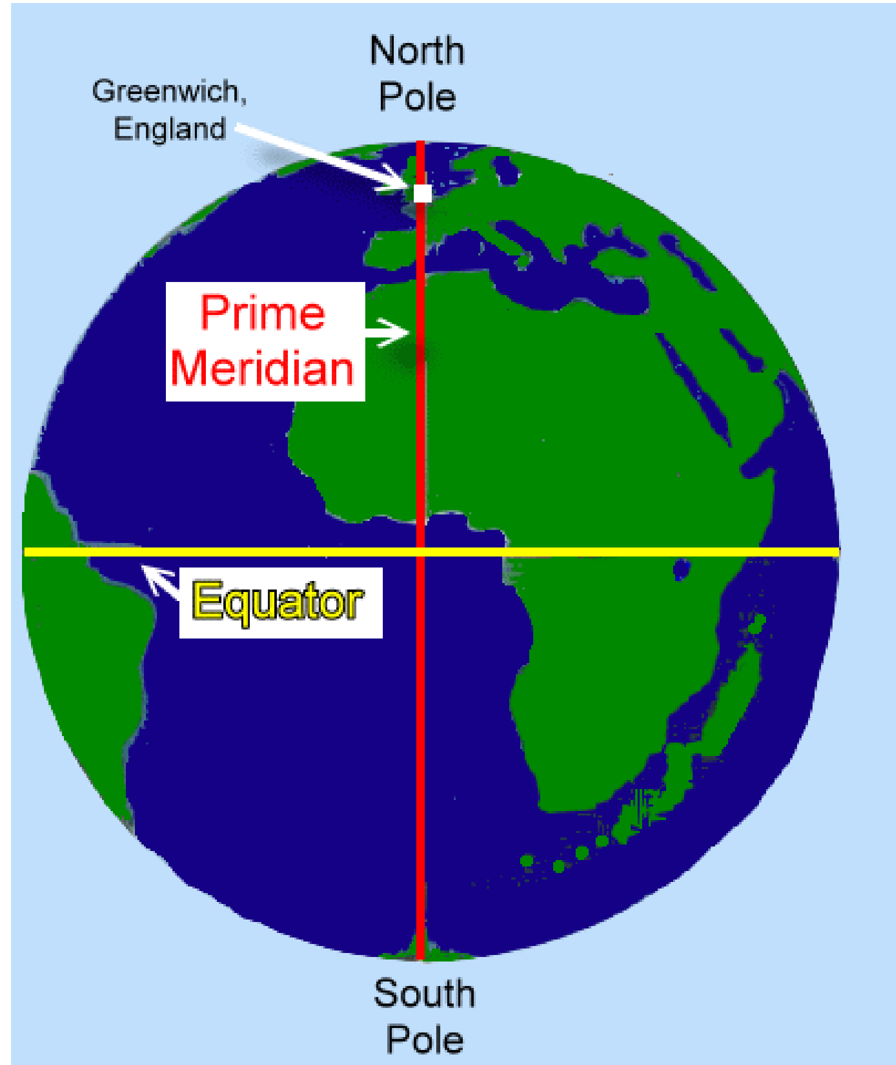




Summary: functional connectivity paradigm

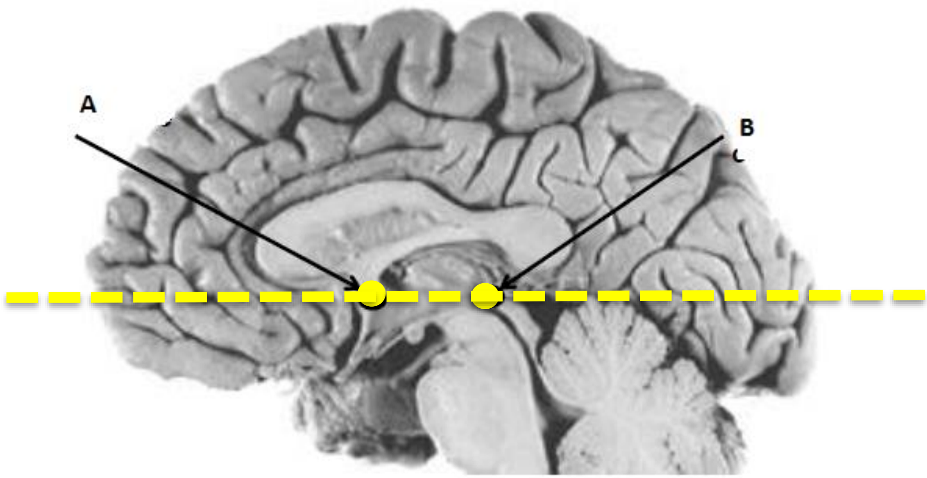
- BOLD fluctuations formerly thought to be "noise" are correlated across distant sites.
- Analysis of functional connectivity "at rest" identifies consistent "intrinsic networks"
- Functional connectivity is grounded in anatomic connectivity
- Intrinsic networks may reflect a fundamental level of large-scale physiologic organization

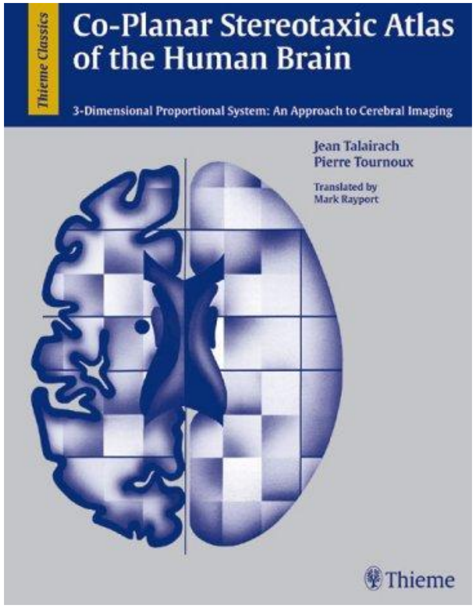
Anchoring standard space

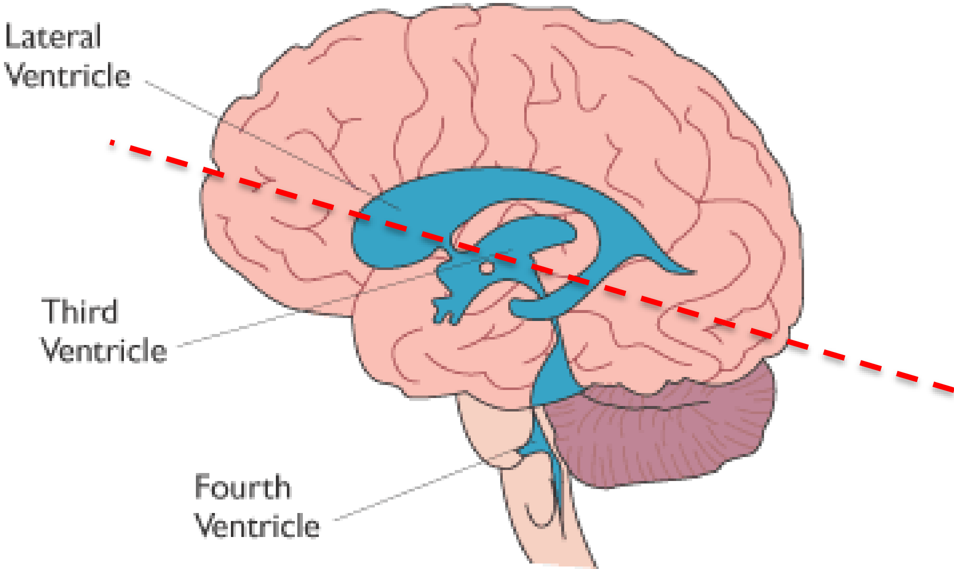


Anchoring standard space

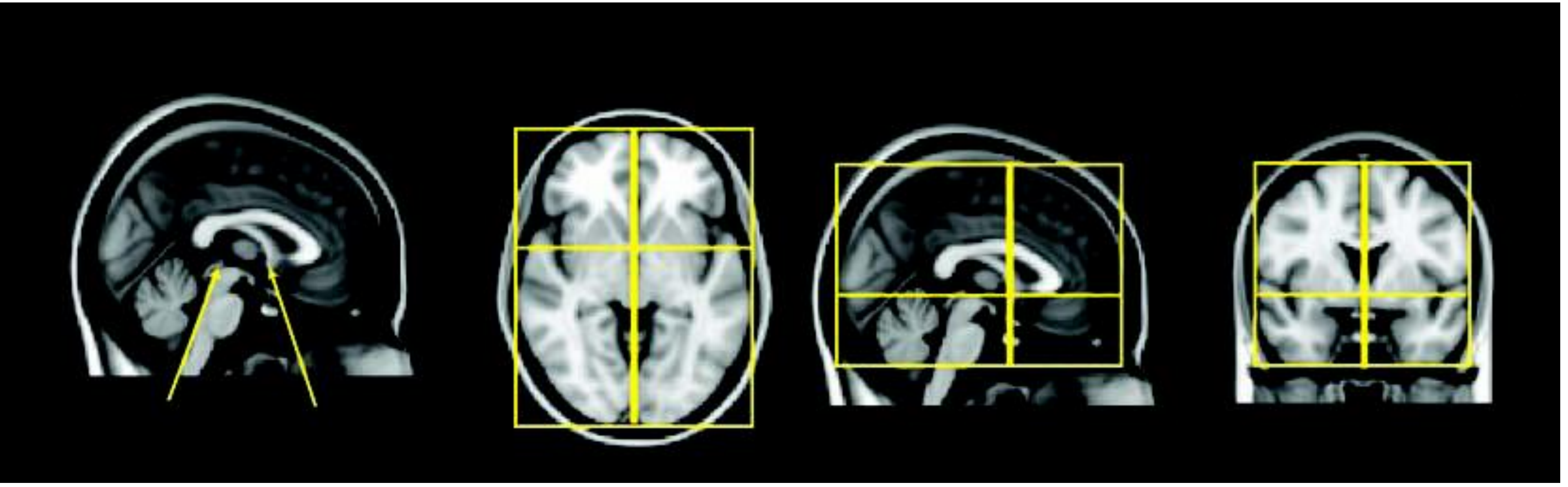
The brain “equator” is the intercommisural line



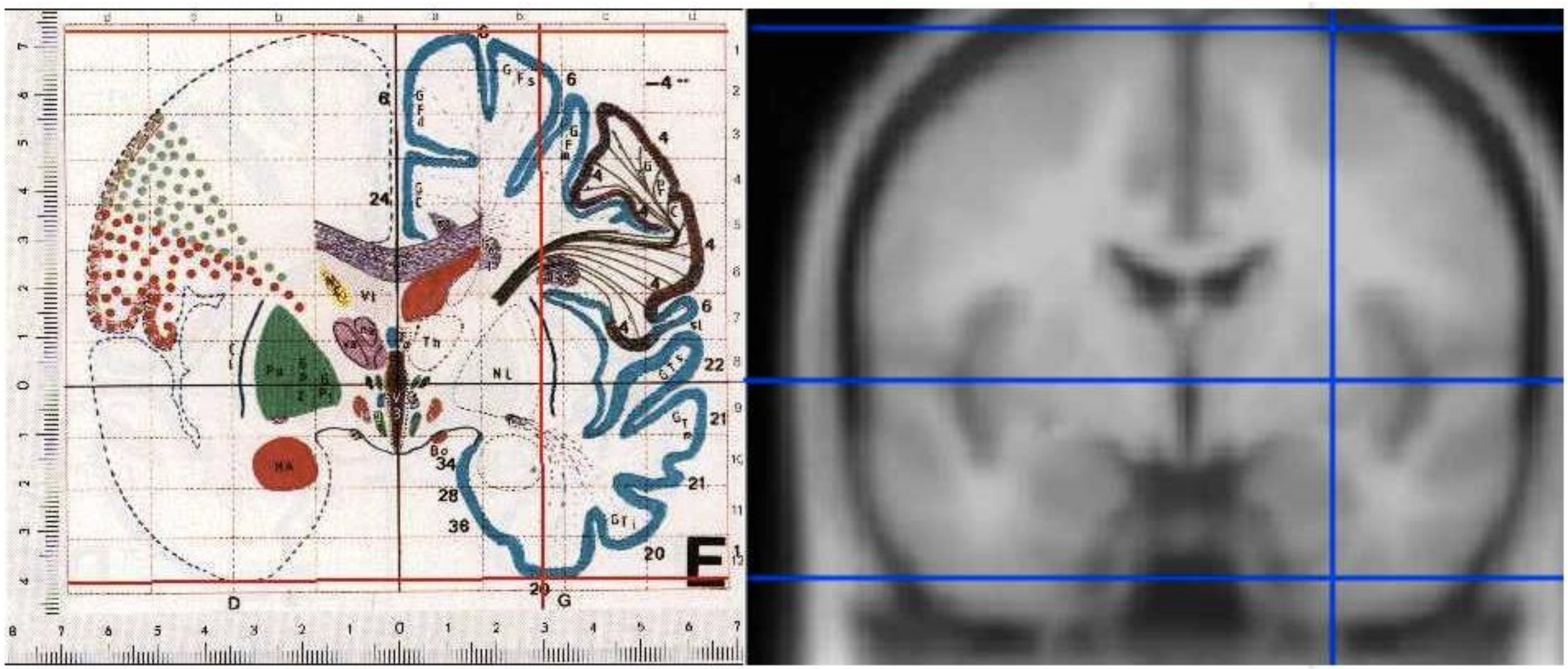


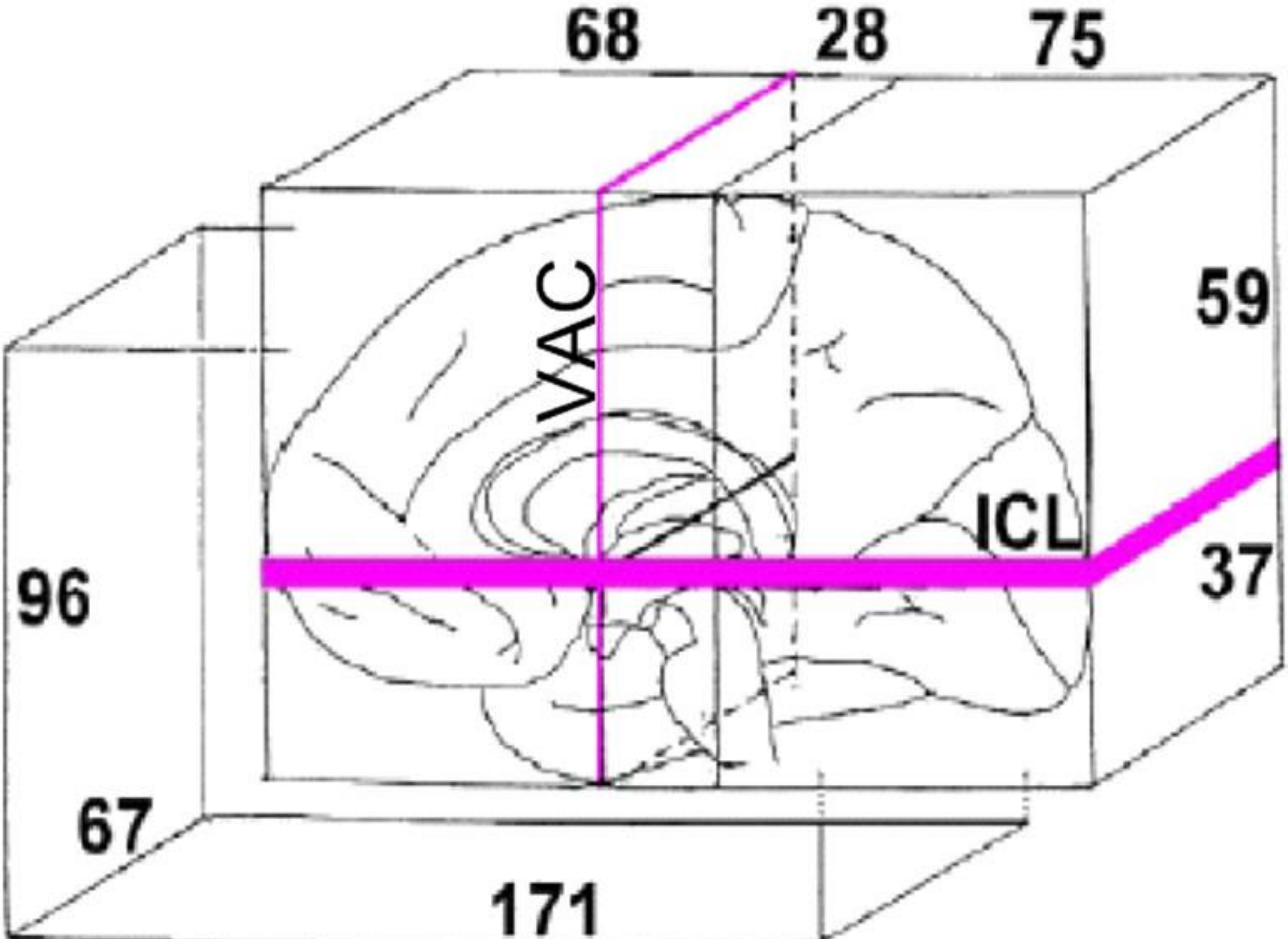


Talairach Space

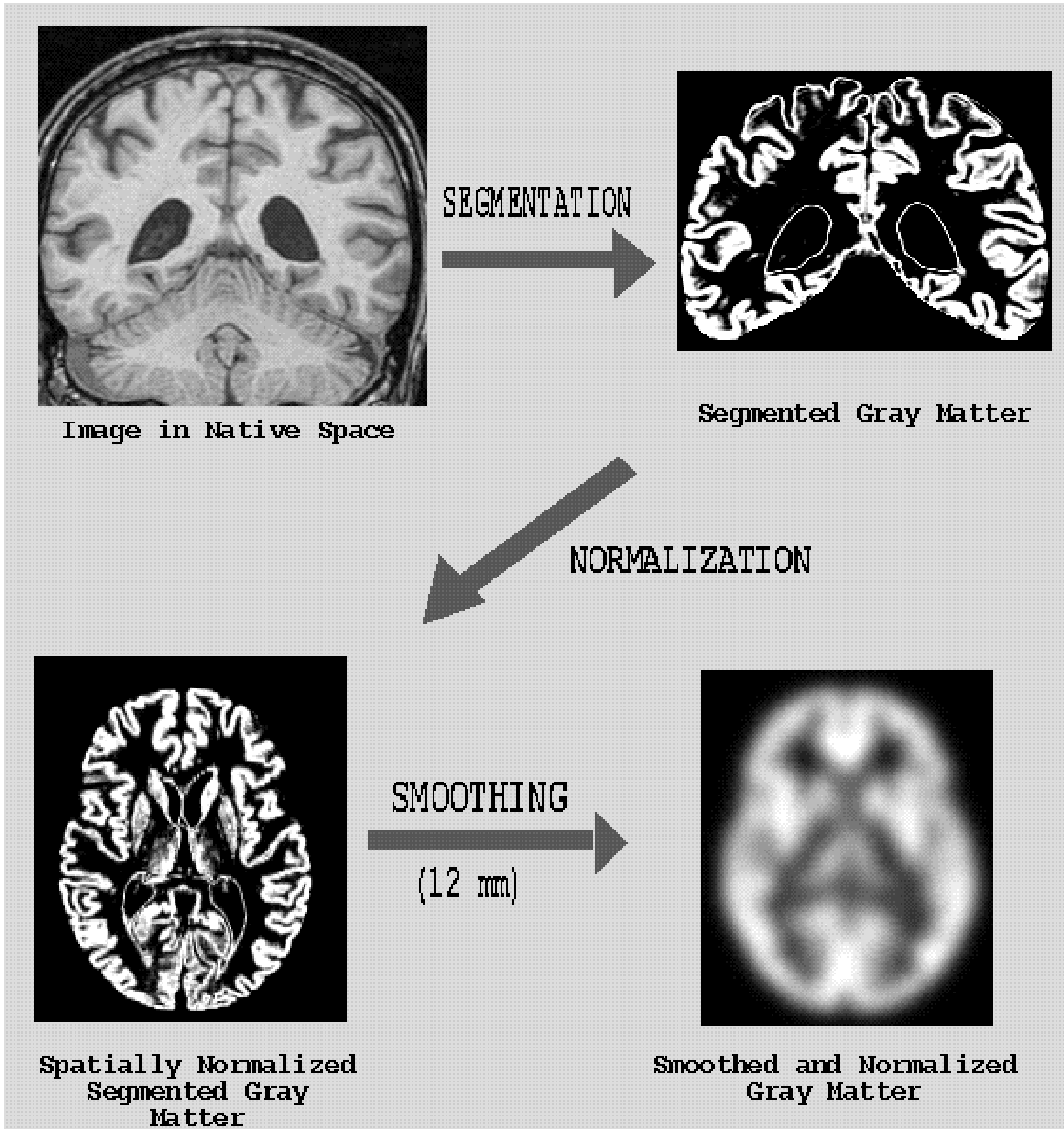


Talairach Space
Montreal Neurological Institute (MNI) space




68
28
75
VAC
59
ICL
37
96
67
171

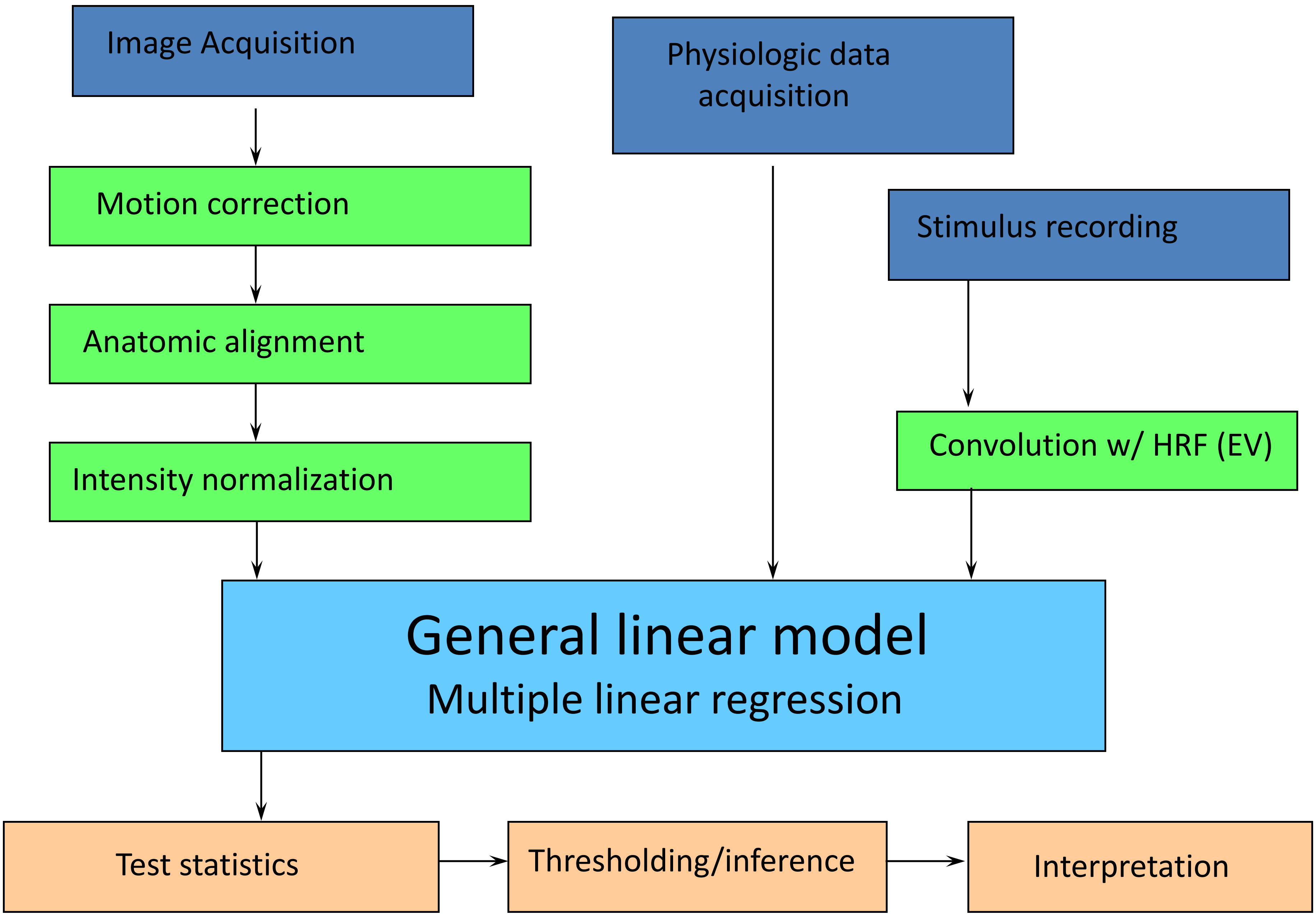
Voxel-based morphometry



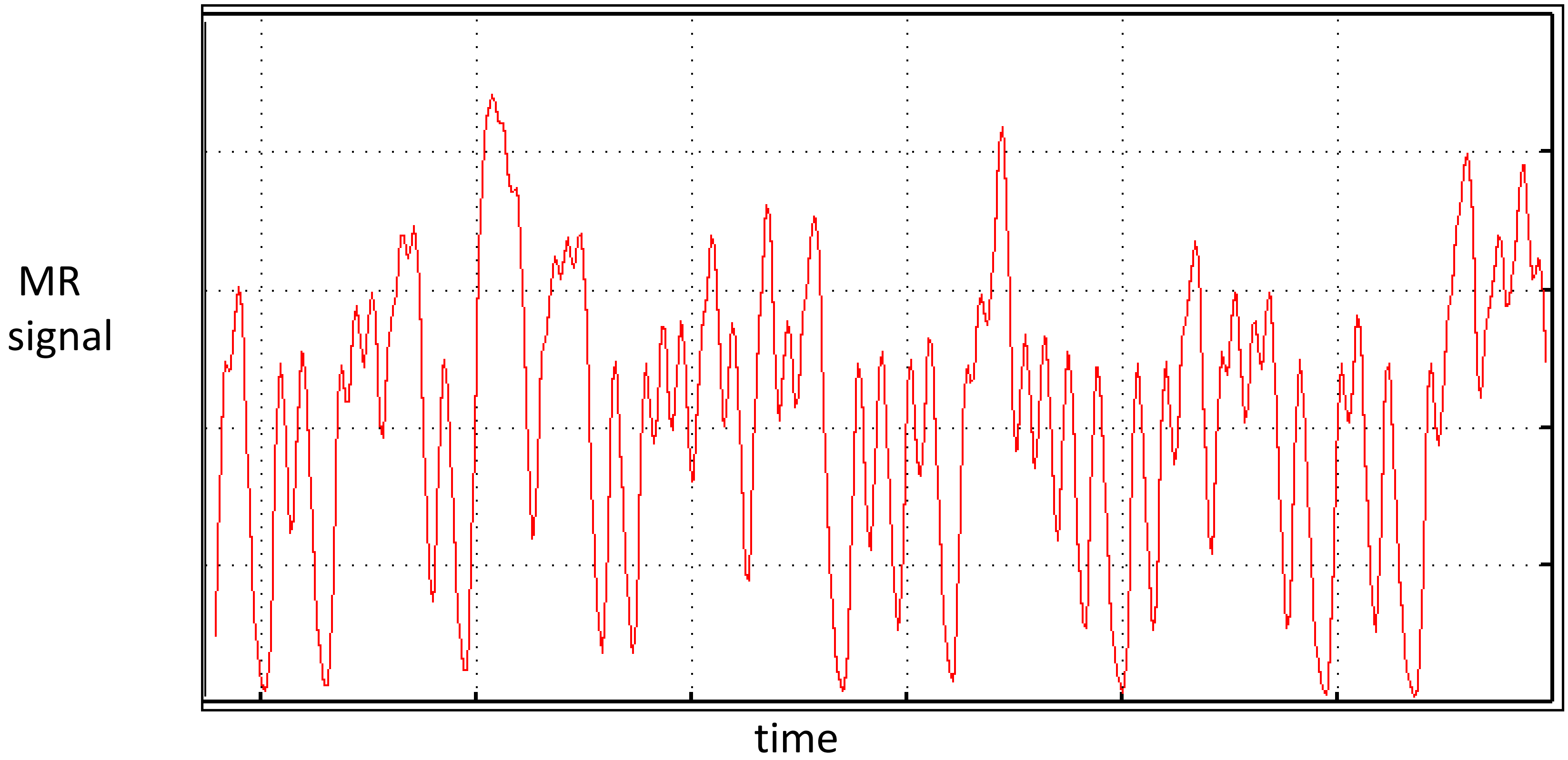
Limits on interpretation of spatial normalization

- Anatomic variability in Talairach space
  - 1.5 cm
- Irreducible cortical variability
  - This variability is itself variable
  - Cytoarchitecture adds another layer of variability
- Not always easy to assign results to one location
  - Local maximum of statistic field, vs center of mass
  - Extent-based statistics vs Magnitude-based statistics
- fMRI data are typically smoothed for SNR reasons

fMRI Data Post-Processing



fMRI time series



fMRI signal reflects multiple simultaneous effects

- Task
- Physiologic fluctuations
  - Cardiac pulsatility
  - Respiratory effects
  - CSF flow/pulsation
- Head motion/spin history
- Slow drifts
- Thermal noise

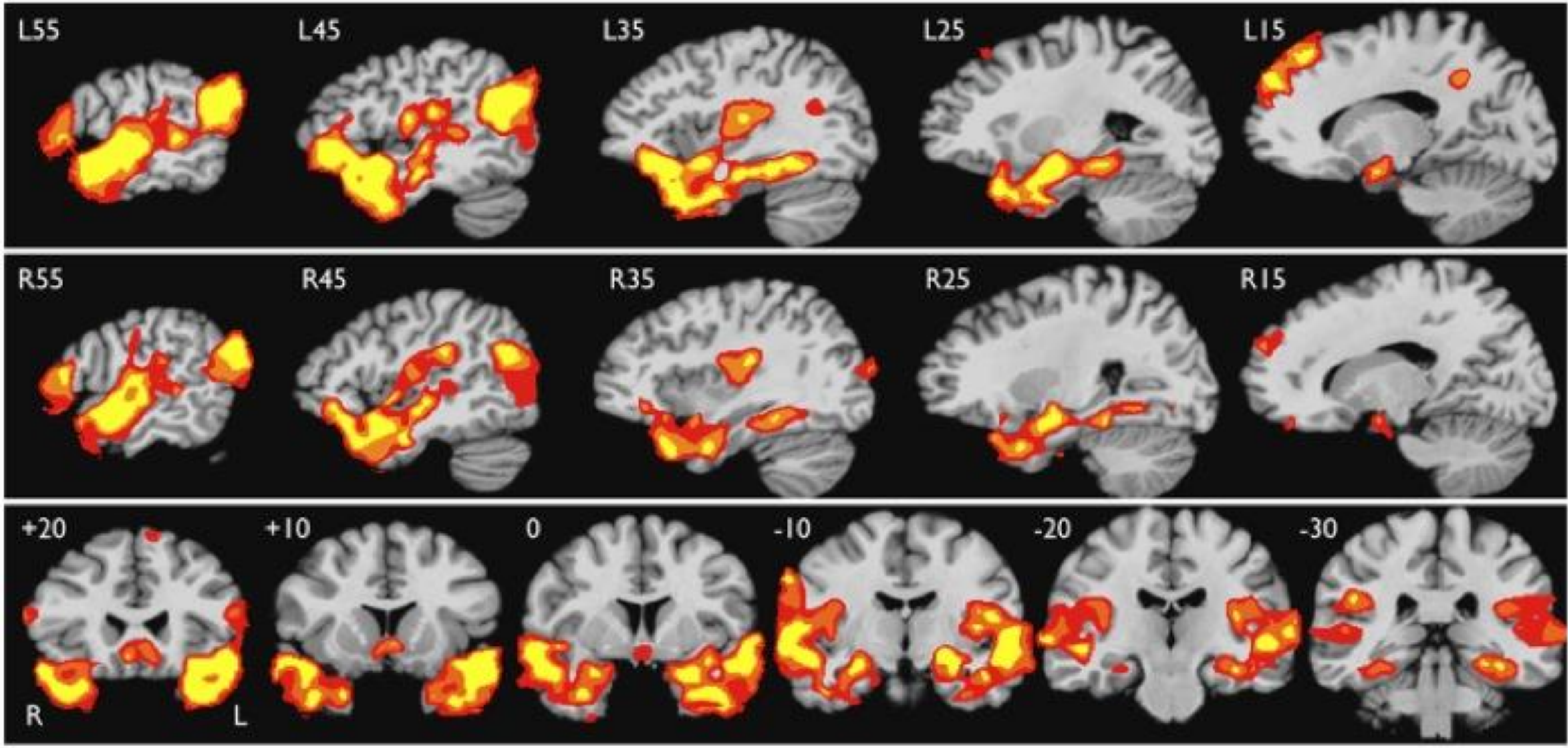
Statistical analysis

- Problem: at each voxel, estimate the task effect in the presence of other effects
- Technique: multiple linear regression supported by the general linear model:

$$Y = \boldsymbol{\beta}_1 X_1 + \boldsymbol{\beta}_2 X_2 + \ldots + \varepsilon$$

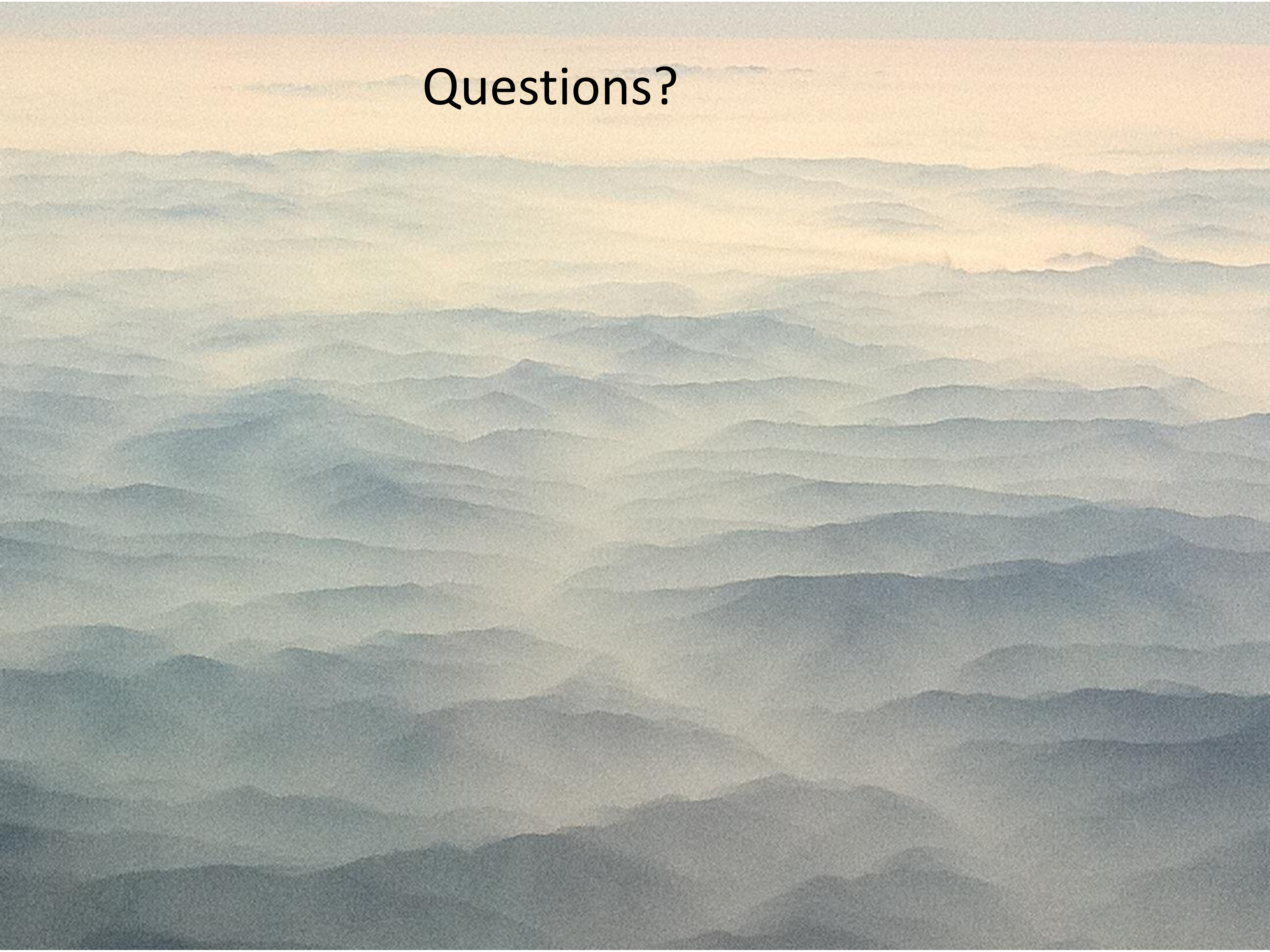
  - The task effect is estimated by regression coefficient (β) and tested with a *t* statistic

Activation of the anterior temporal lobes during listening to discourse.



Summing Up

- MRI approaches to brain structure and function continue to diversify and become more powerful, driven mostly by conceptual and software innovation.
- Multispectral/multimodal approaches are now common, clinically and in research.
- Imaging approaches are beginning to analyze brain activity in terms of natural systems structure (columns, fields, large scale systems)
- Most of the techniques have not (YET) found their way into clinical application


Questions?