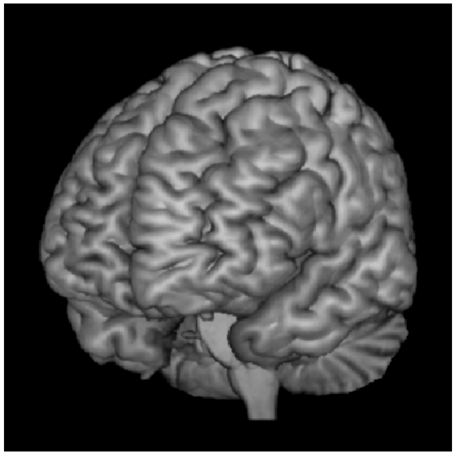
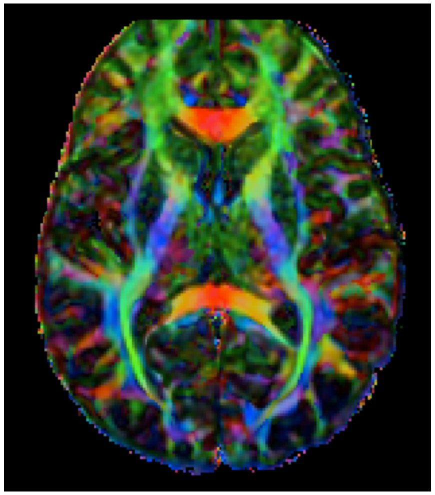


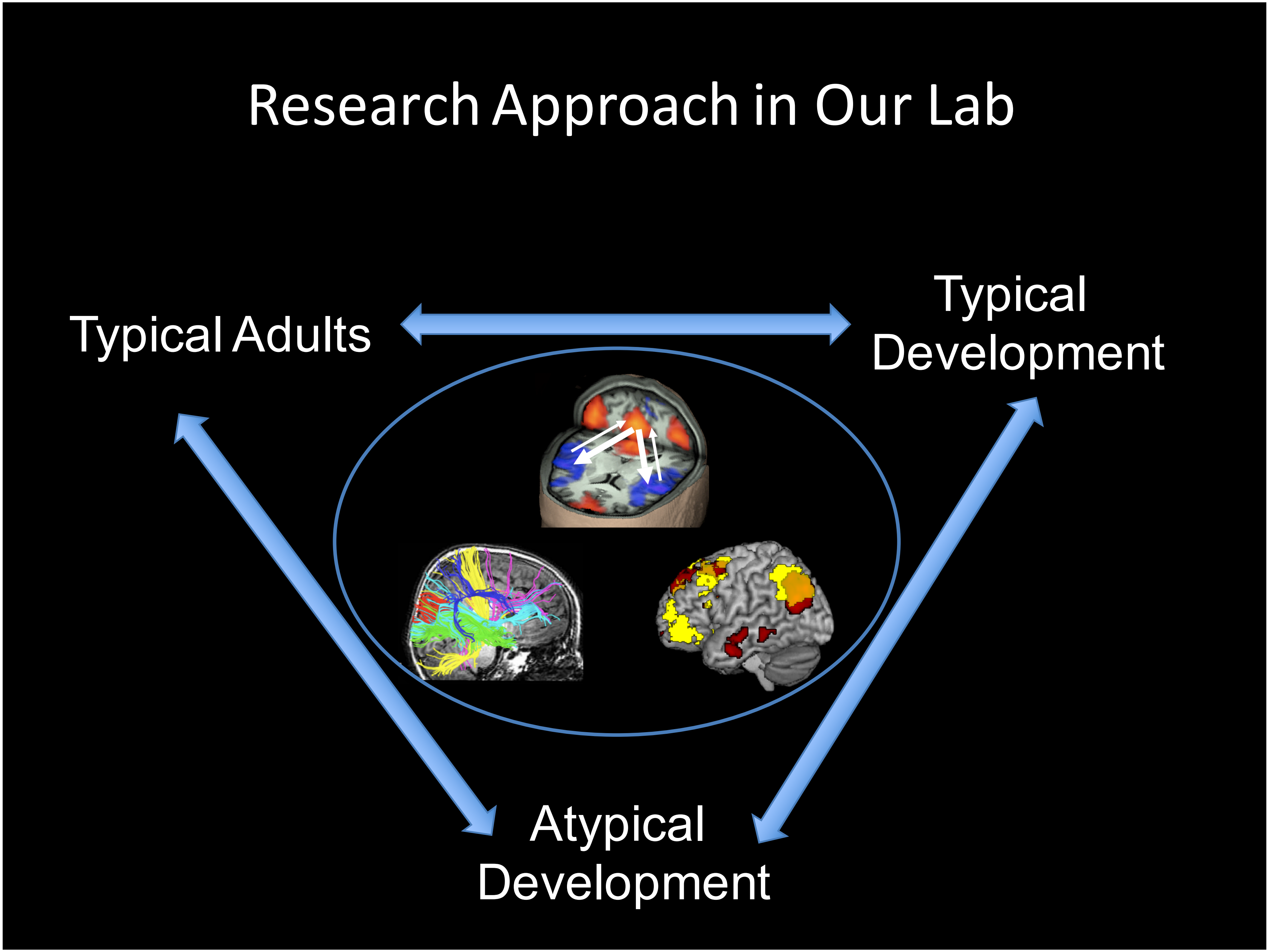
MRI Approaches for Investigating Brain Structure and Function

Jason S. Nomi, Ph.D. (jxn131@miami.edu)



Cognitive Neuroscience

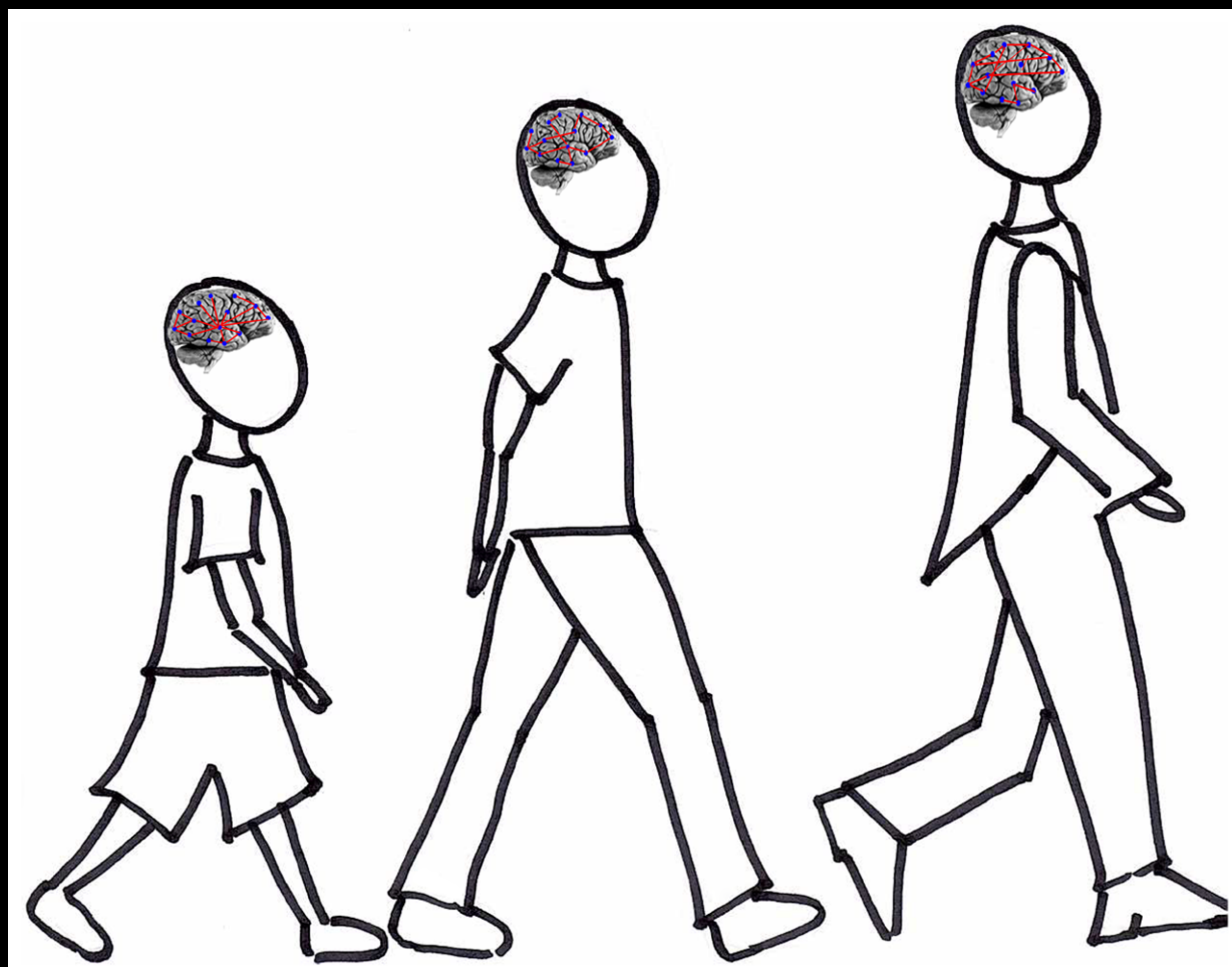
"the scientific study of biological substrates underlying cognition, with a specific focus on the neural substrates of mental processes…addresses the questions of how psychological functions are produced by the brain"


Research Approach in Our Lab
Typical Adults
Typical Development
Atypical Development

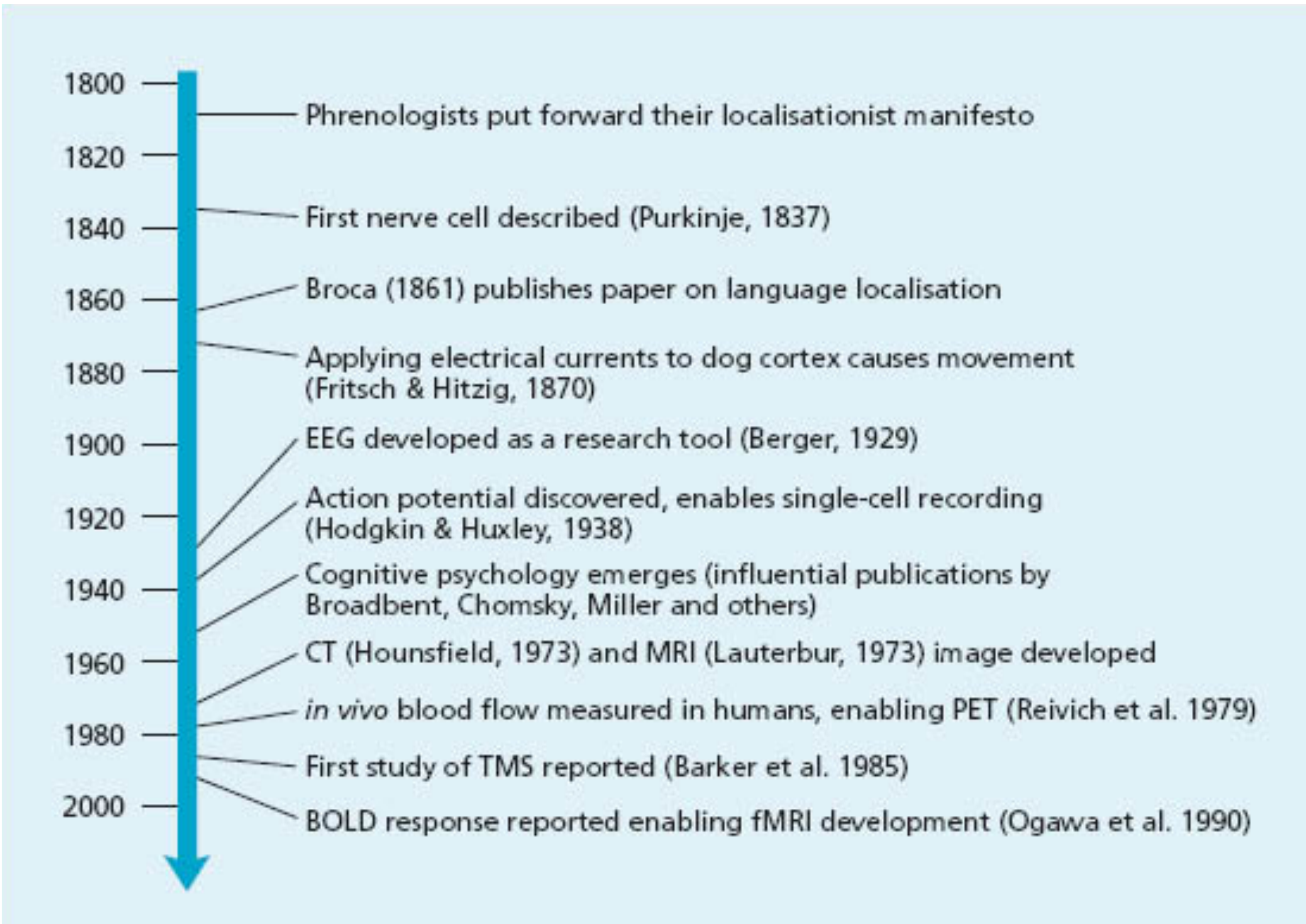
Critical Research Questions

Brain Network Development

Cognitive Maturation



Timeline for development of methods in cognitive neuroscience



Methods in Cognitive Neuroscience

Method	Method type	Invasiveness	Brain property used
EEG/ERP	Recording	Non-invasive	Electrical
Single-cell (and multi-unit) recordings	Recording	Invasive	Electrical
TMS	Stimulation	Non-invasive	Electromagnetic
MEG	Recording	Non-invasive	Magnetic
PET	Recording	Invasive	Haemodynamic
fMRI	Recording	Non-invasive	Haemodynamic

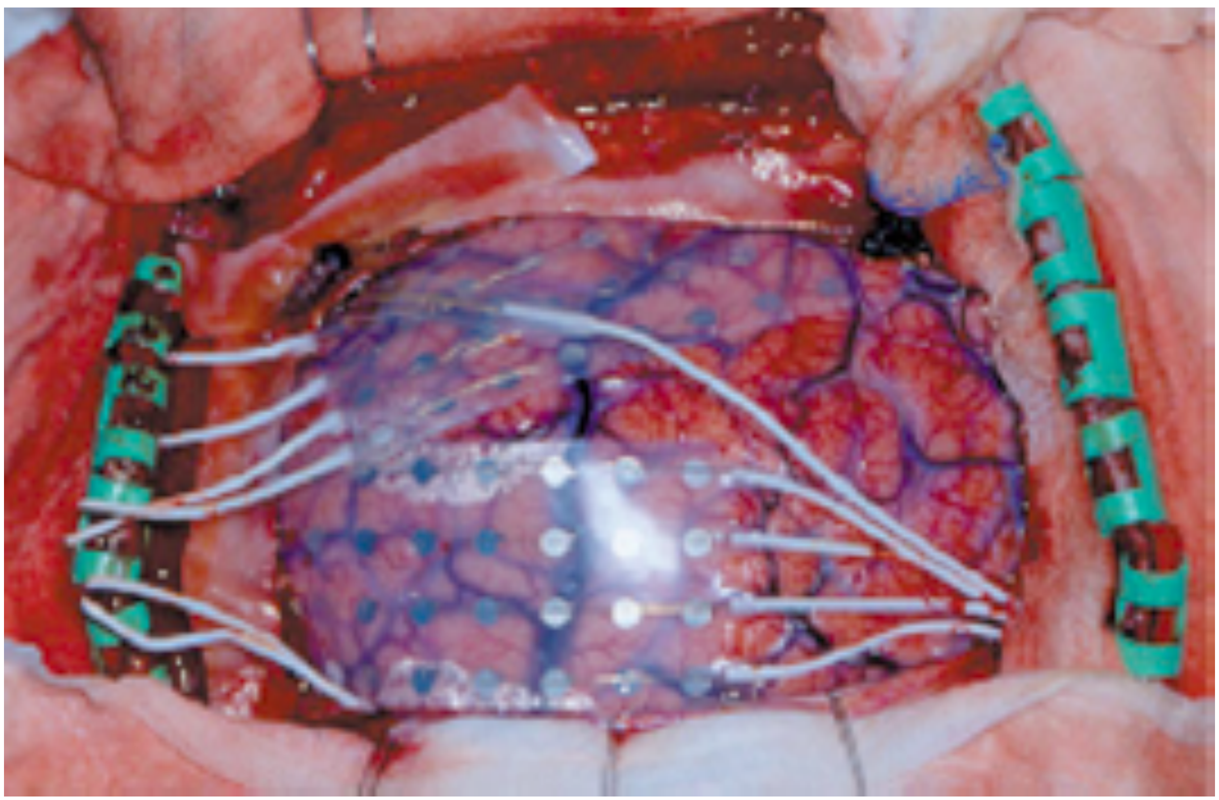
EEG = electroencephalogram, ERP = event-related potential, TMS = transcranial magnetic stimulation, MEG = magnetoencephalography, PET = positron emission tomography, fMRI = functional magnetic resonance imaging

Imaging methods can vary in several ways

- The **temporal resolution** refers to the accuracy with which one can measure *when* an event is occurring. The effects of brain damage are permanent and so this has no temporal resolution as such. Methods such as EEG, MEG, TMS and single-cell recording have millisecond resolution. PET and fMRI have temporal resolutions of minutes and seconds, respectively, that reflect the slower haemodynamic response.
- The **spatial resolution** refers to the accuracy with which one can measure *where* an event is occurring. Lesion and functional imaging methods have comparable resolution at the millimetre level, whereas single-cell recordings have spatial resolution at the level of the neuron.
- The *invasiveness* of a method refers to whether or not the equipment is located internally or externally. PET is invasive because it requires an injection of a radio-labelled isotope. Single-cell recordings are performed on the brain itself and are normally only carried out in non-human animals.

Electrical Recordings

- Direct measure of neural activity using implanted electrodes
- Sometimes called intracranial EEG (iEGG)



Advantages and disadvantages to electrical recordings

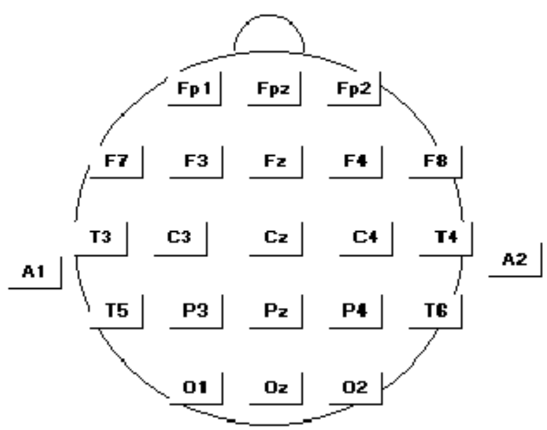
- Strengths: very high spatial and temporal resolution
- Weaknesses: invasive, can

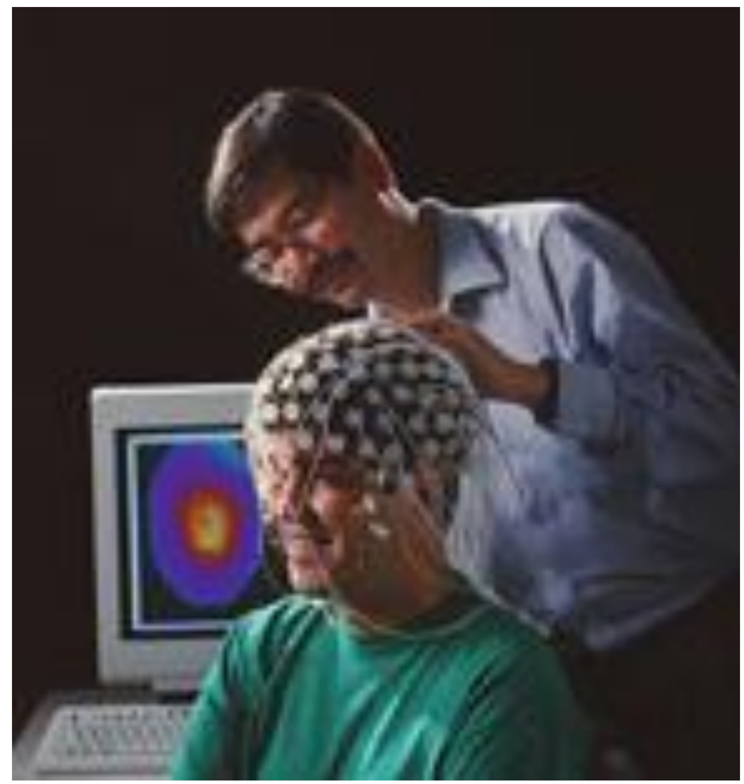
rarely be carried out in humans, most useful for researchers who use animal models

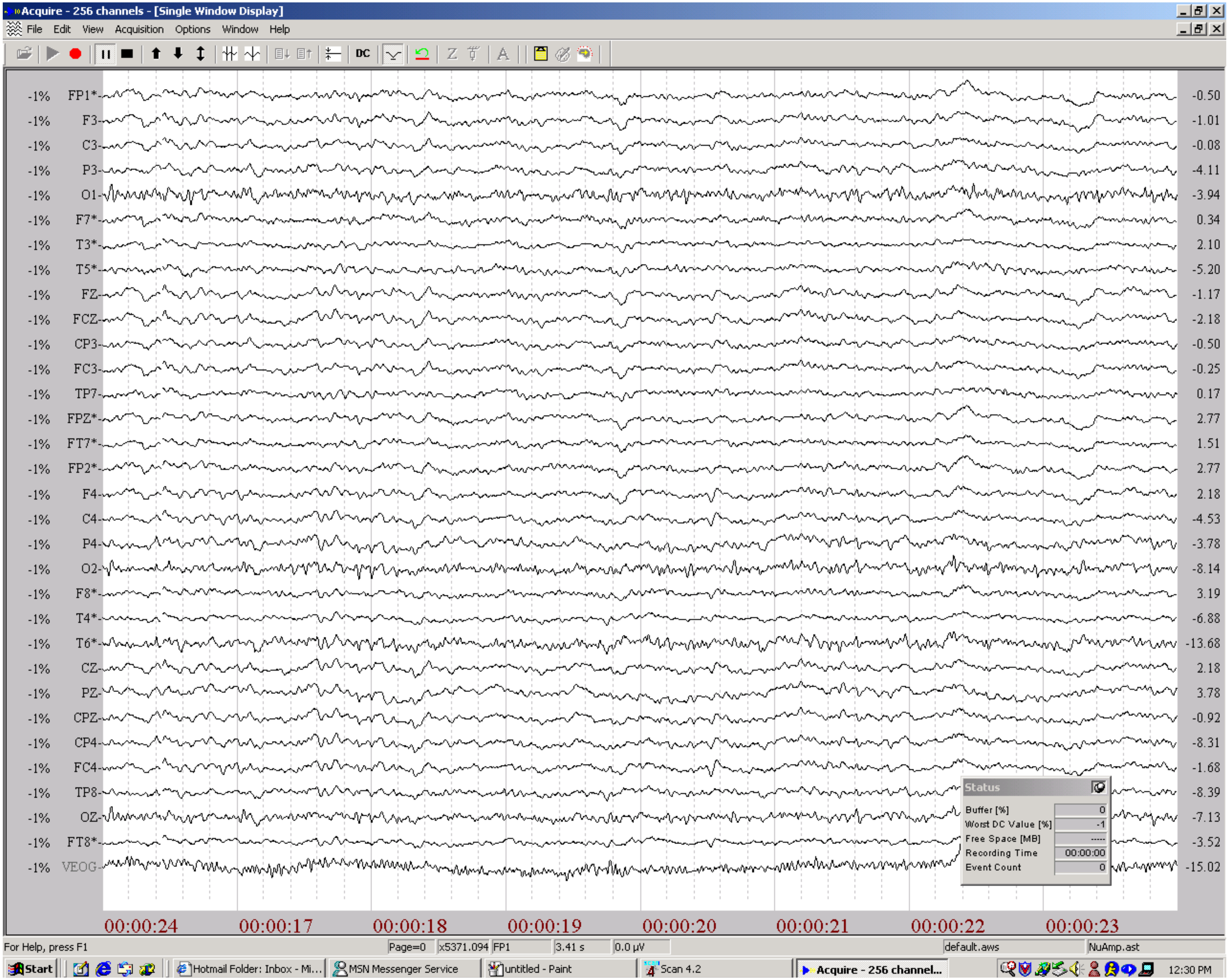
Electroencephalogram (EEG)

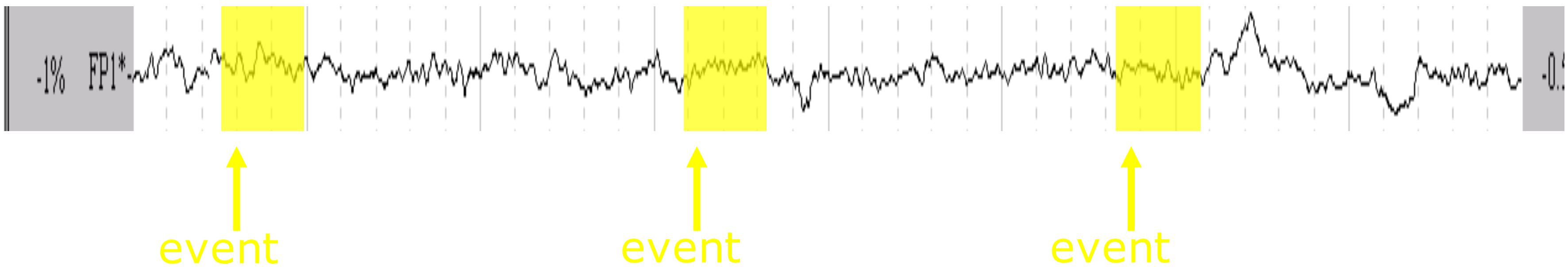
- Recording of electrical activity along the scalp produced by firing of neurons in the brain
- EEG activity reflects the sum

of activity across millions of neurons with similar orientations

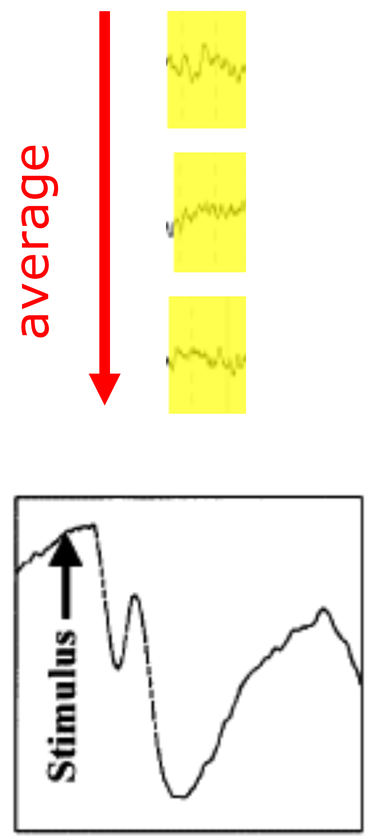




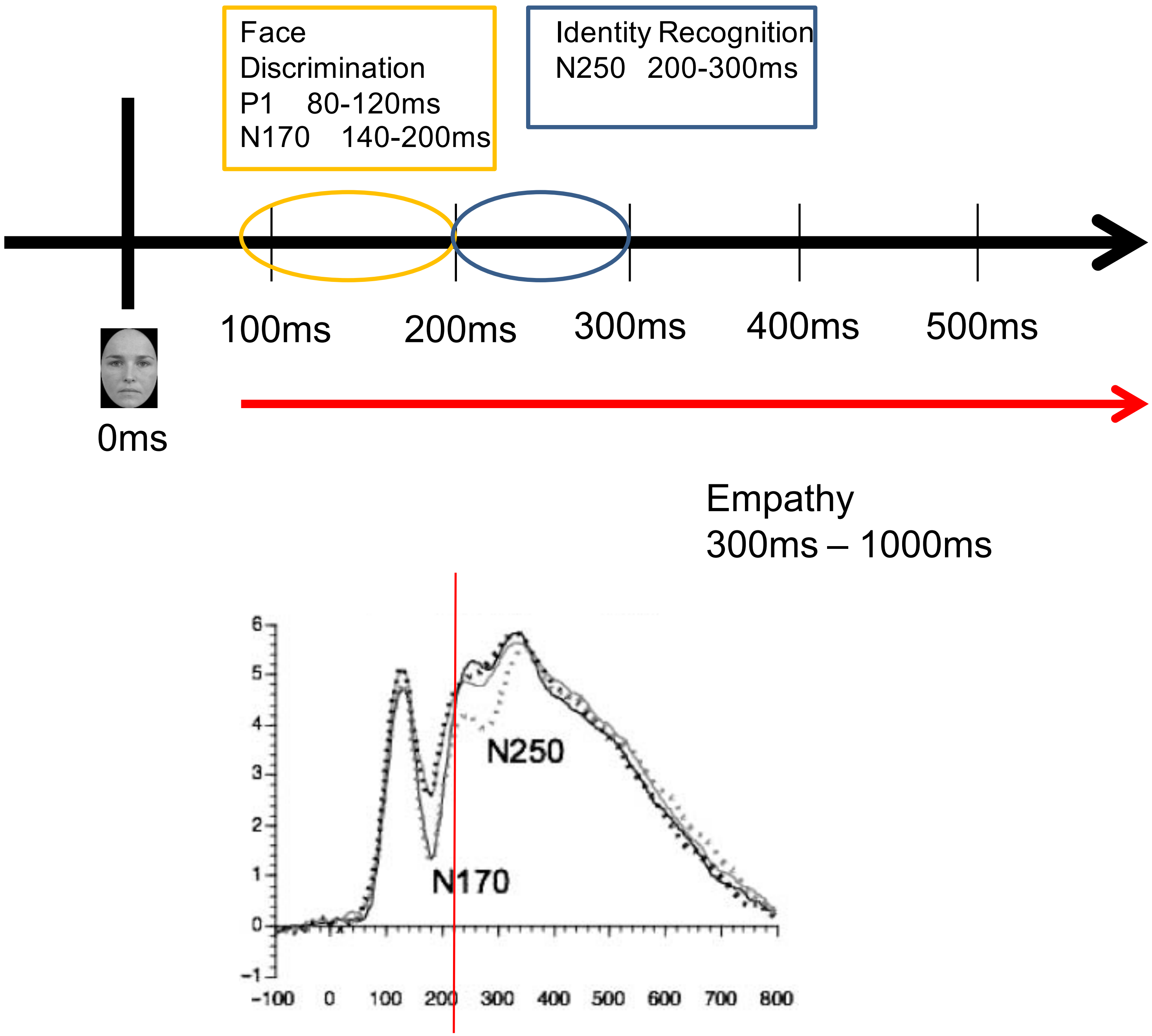

Acquire - 256 channels - [Single Window Display]
File Edit View Acquisition Options Window Help
DC
-1% FP1* -0.50
-1% F3 -1.01
-1% C3 -0.08
-1% P3 -4.11
-1% O1 -3.94
-1% F7* 0.34
-1% T3* 2.10
-1% T5* -5.20
-1% FZ -1.17
-1% FCZ -2.18
-1% CP3 -0.50
-1% FC3 -0.25
-1% TP7 0.17
-1% FPZ* 2.77
-1% FT7* 1.51
-1% FP2* 2.77
-1% F4 2.18
-1% C4 -4.53
-1% P4 -3.78
-1% O2 -8.14
-1% F8* 3.19
-1% T4* -6.88
-1% T6* -13.68
-1% CZ 2.18
-1% PZ 3.78
-1% CPZ -0.92
-1% CP4 -8.31
-1% FC4 -1.68
-1% TP8 -8.39
-1% OZ -7.13
-1% FT8* -3.52
-1% VEOG -15.02
Status
Buffer [%] 0
Worst DC Value [%] -1
Free Space [MB] ----
Recording Time 00:00:00
Event Count 0
00:00:24 00:00:17 00:00:18 00:00:19 00:00:20 00:00:21 00:00:22 00:00:23
For Help, press F1
Page=0 x5371.094 FP1 3.41 s 0.0 µV
default.aws NuAmp.ast
Start
Hotmail Folder: Inbox - Mi...
MSN Messenger Service
untitled - Paint
Scan 4.2
Acquire - 256 channel...
12:30 PM



Event-related potentials (ERPs)



- Measure continuous EEG while subject performs a psychological task
- Average the EEG waveform surrounding an event of interest (a stimulus or response)

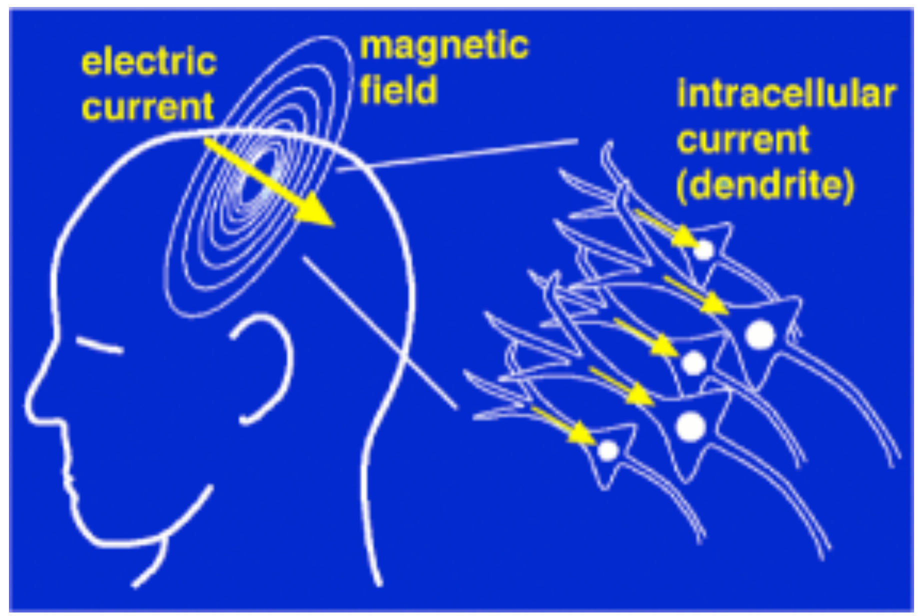

Face
Discrimination
P1 80-120ms
N170 140-200ms
Identity Recognition
N250 200-300ms
100ms
200ms
300ms
400ms
500ms
0ms
Empathy
300ms – 1000ms
N250
N170
6
5
4
3
2
1
0
-1
-100
0
100
200
300
400
500
600
700
800

Advantages and Disadvantages of ERPs

- Strengths: Very fine temporal resolution (milliseconds), can tolerate subject movement, machine is silent, equipment is relatively cheap compared to fMRI
- Weakness: Hard to localize source of electrical activity (low spatial resolution), messy

Magnetoencephalography (MEG)

- Mapping brain activity by recording magnetic fields produced by electrical currents in the brain



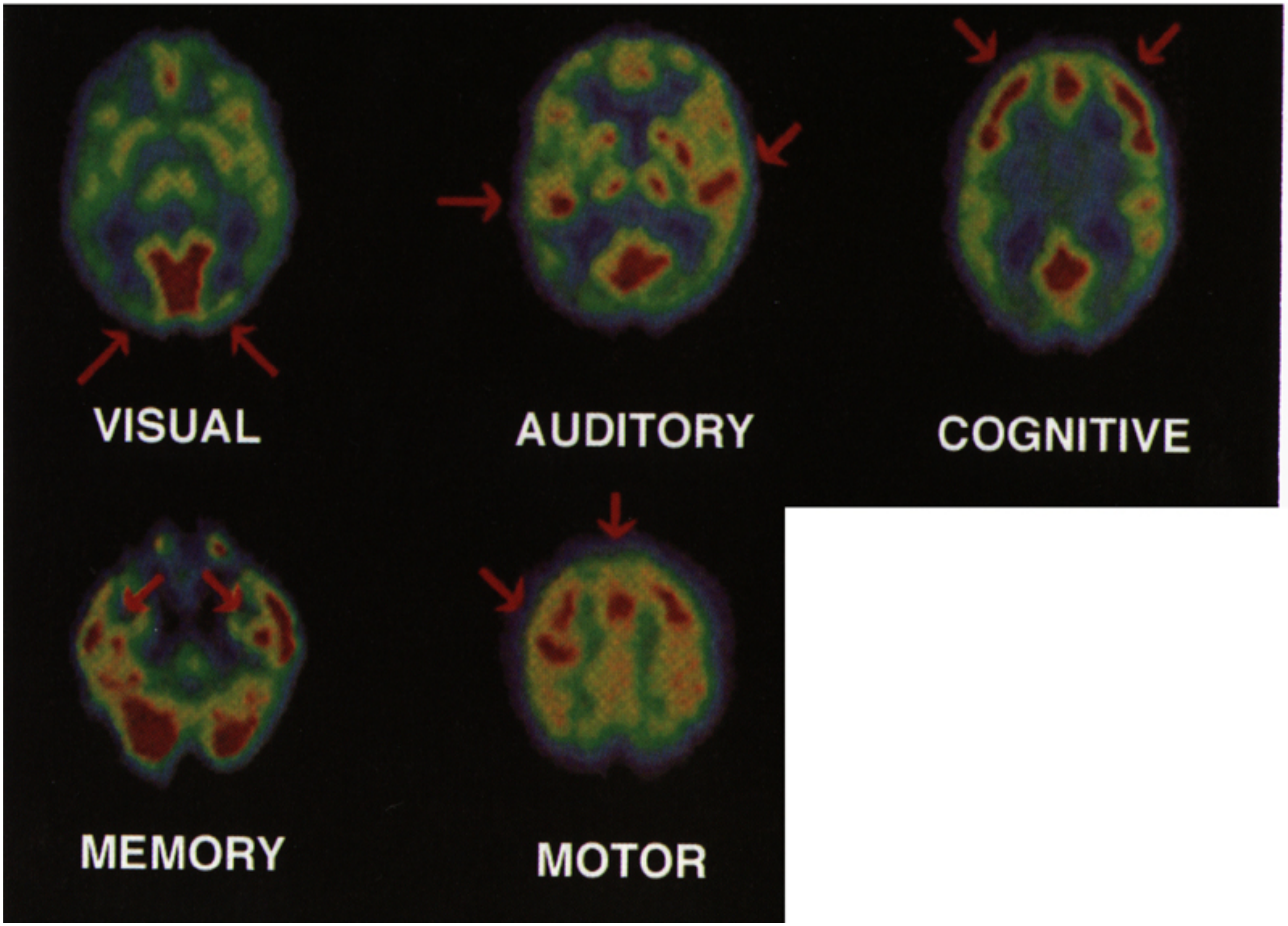
Advantages and disadvantages of MEG

- Strengths: non-invasive, very high temporal resolution (can detect events with precision of 10 milliseconds). High spatial resolution.
- Weaknesses: the magnetic field created by neural activity is very weak and difficult to detect, it is difficult to localize the source of the signal (but better than EEG). Cost: need both MRI and MEG.

Positron Emission Tomography (PET)

- Inject radioactively-labeled compound into the blood stream
- Detectors detect radioactive emissions and build an image of where in the brain the radioactive substance is concentrated

PET Images



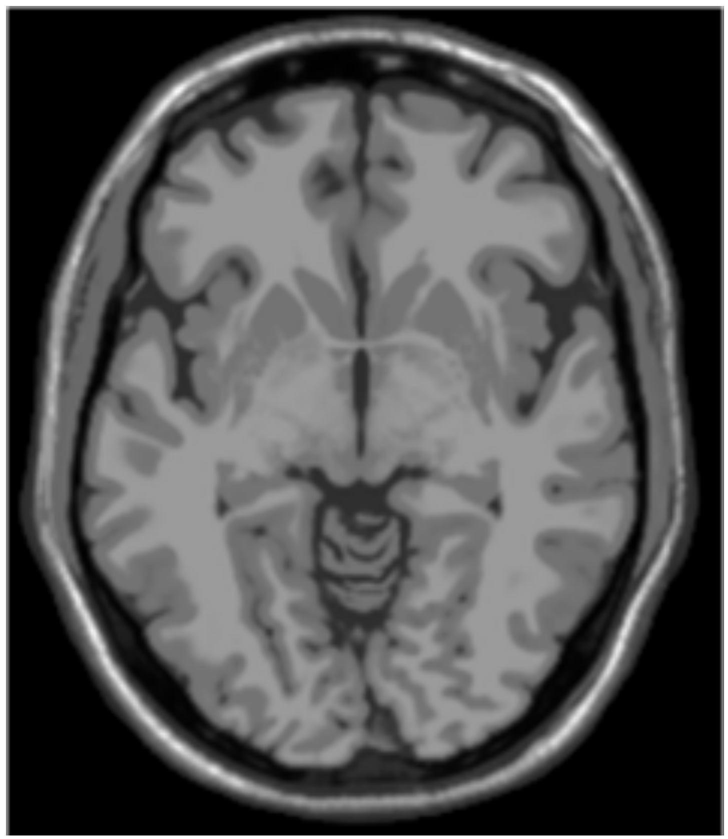
Advantages and Disadvantages to PET

- Strengths: useful in diagnosis of brain disease and assessing biochemical function in brain
- Weaknesses: invasive, radioactive tracers must be injected into the patients' bloodstream, high cost of producing radiotracers, cannot do repeated testing

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging

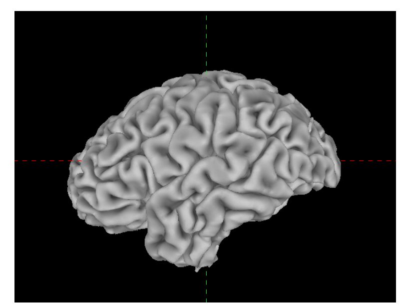
- Relatively new method, first used in humans in the 1970's



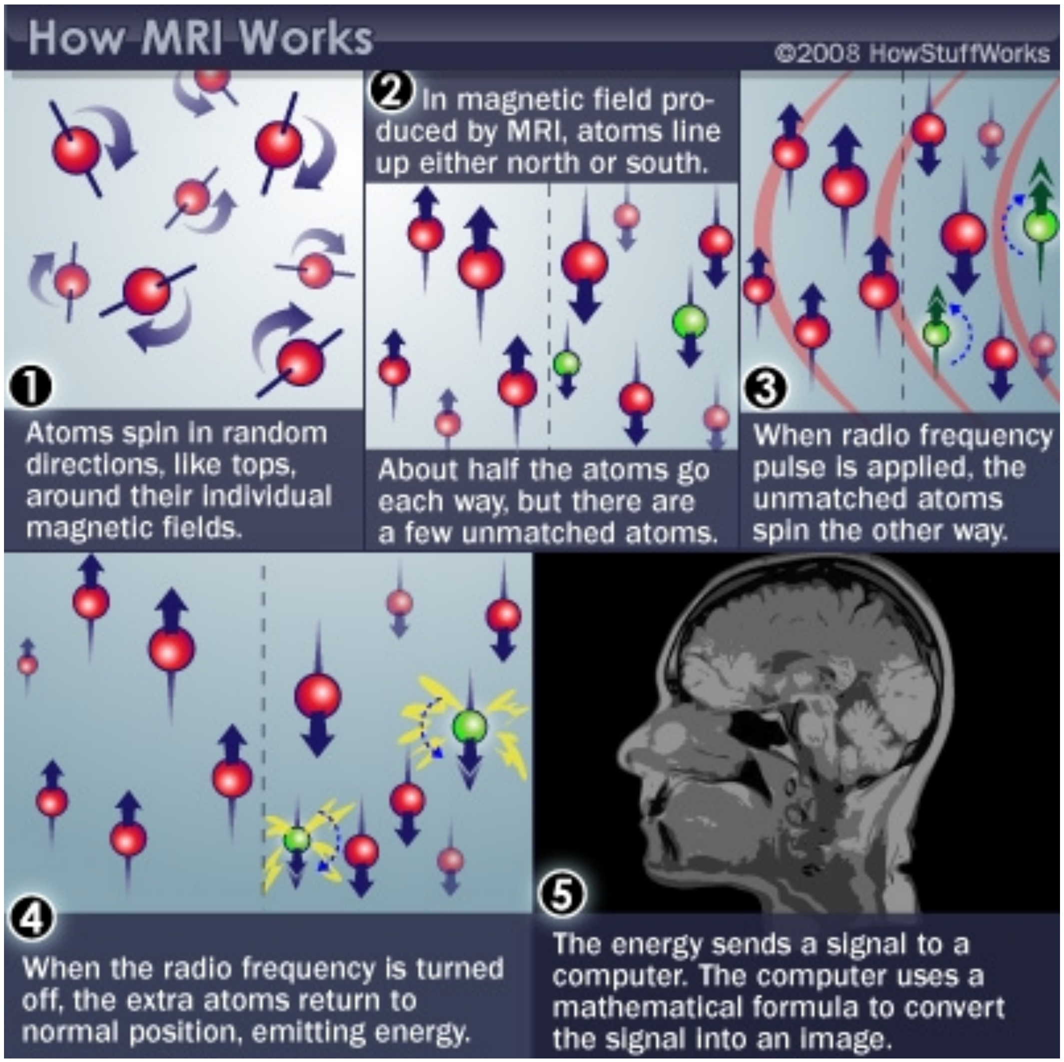
Advantages and Disadvantages to MRI

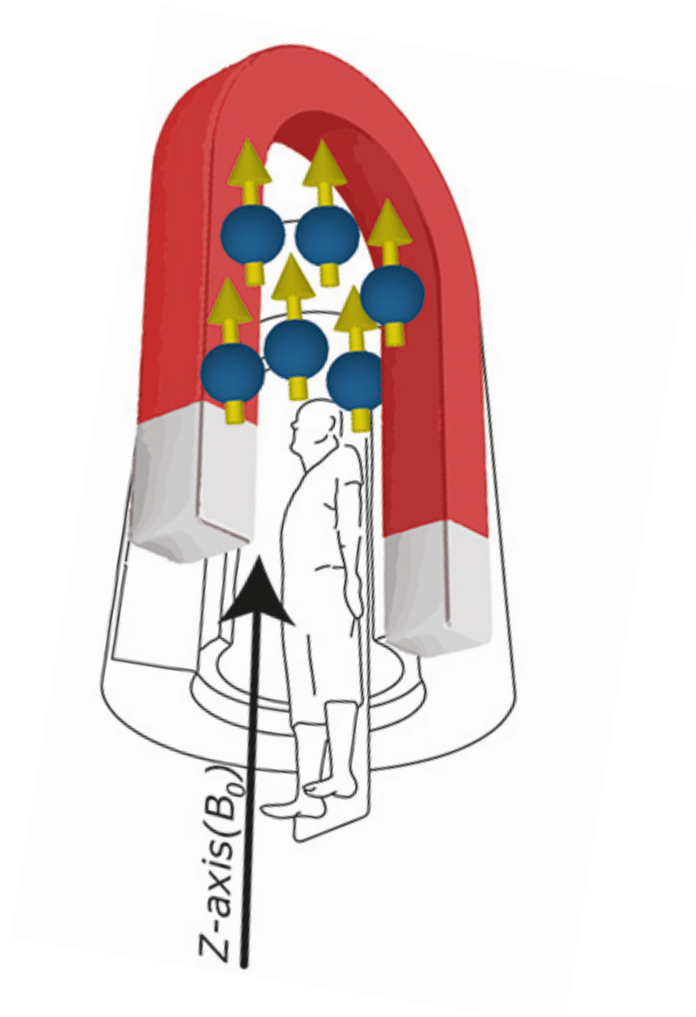
- <u>Strengths:</u> Excellent spatial resolution. Greater contrast between tissue types than CAT (high spatial resolution), does not expose subjects to radiation.

- <u>Weaknesses:</u> Poor temporal resolution. Expensive (compared to ERP), subjects have to remain very still for several minutes, the machine is very loud



Acquiring the MRI signal



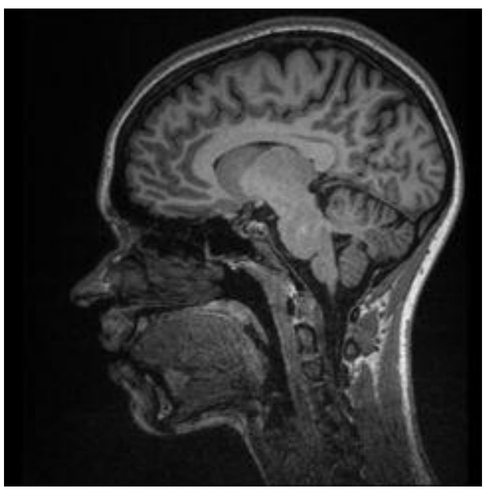


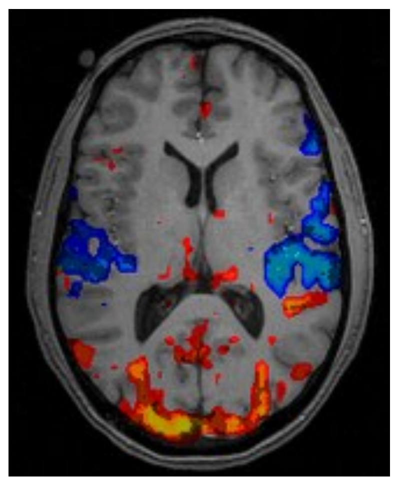
Structural vs. Functional MRI

- Structural Measures
  - Gray and white matter volume/density
  - Cortical thickness
  - Gyrification

- Functional Measures
  - BOLD signal (activation)

- Diffusion Measures
  - Water Movement
  - Axonal pathways





Functional MRI (fMRI)

- Uses MRI technique to map functional changes in brain activity
- fMRI measures changes in cerebral blood flow
- Blood flow (BOLD signal) is related to neural activity

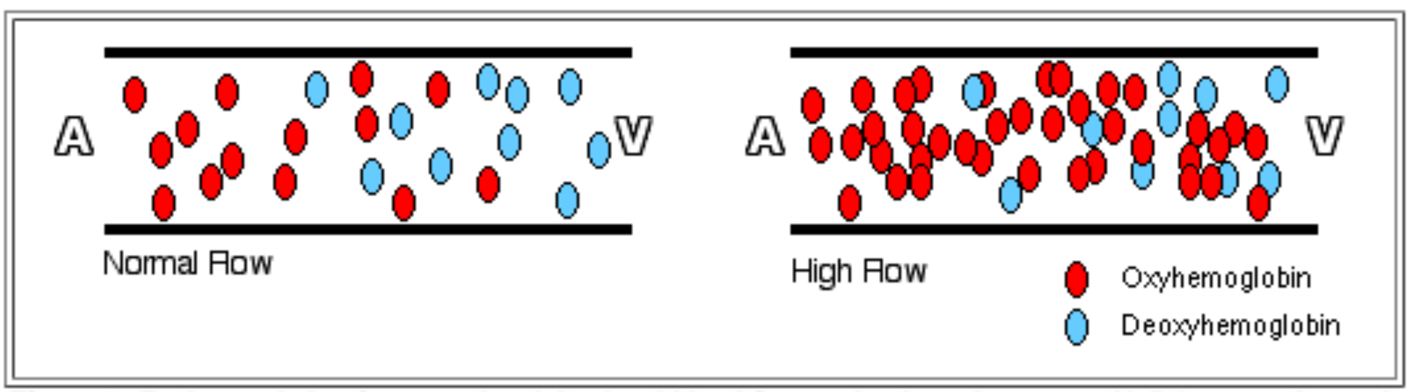
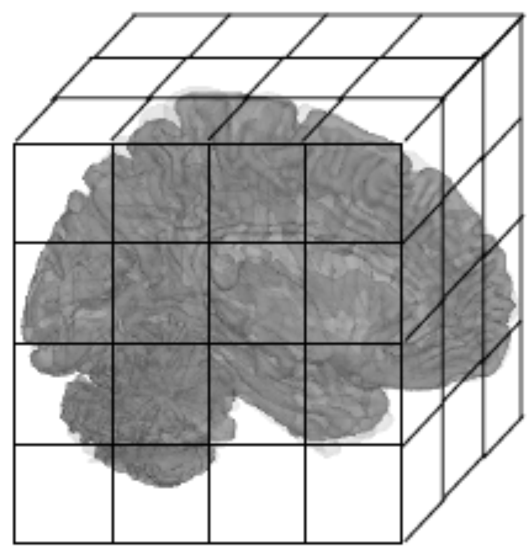


Figure 1. *During periods of neuronal activity, local blood flow and volume increase with little or no change in oxygen consumption. As a consequence, the oxygen content of the venous blood is elevated, resulting in an increase in the MR signal.*

Functional MRI

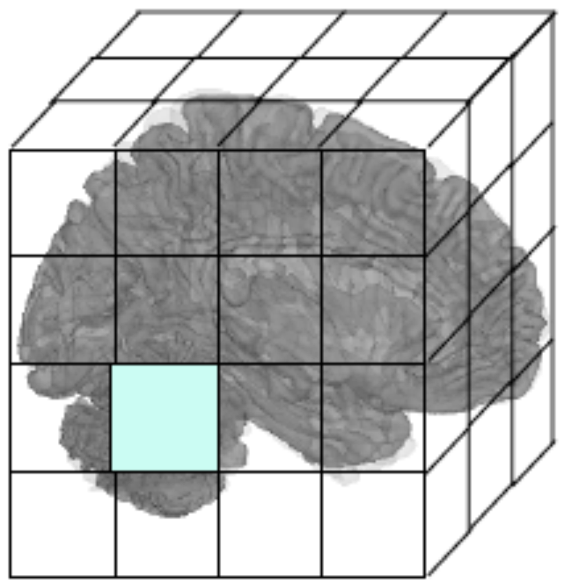
- Each image consists of ~100,000 voxels (3d pixels/cubic volumes) that span the entired space of the brain

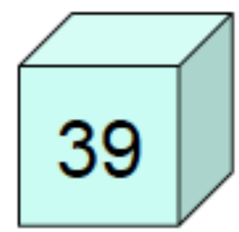


From Martin Lindquist: Coursera

Functional MRI

- Each voxel corresponds to a spatial location and has a number associated with it that represents its intensity

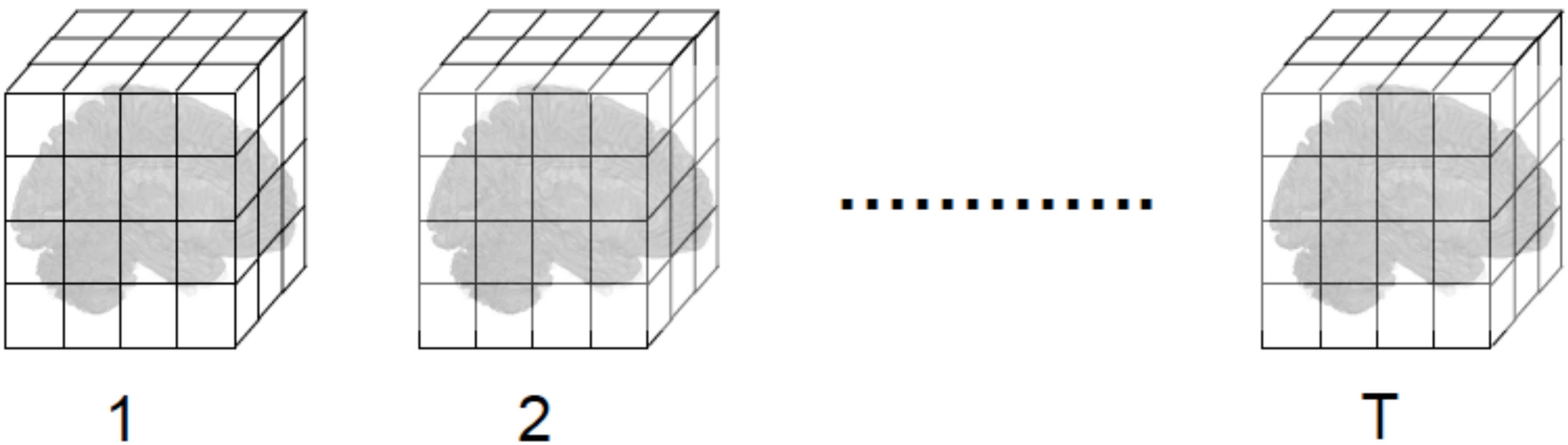




From Martin Lindquist: Coursera

Functional MRI

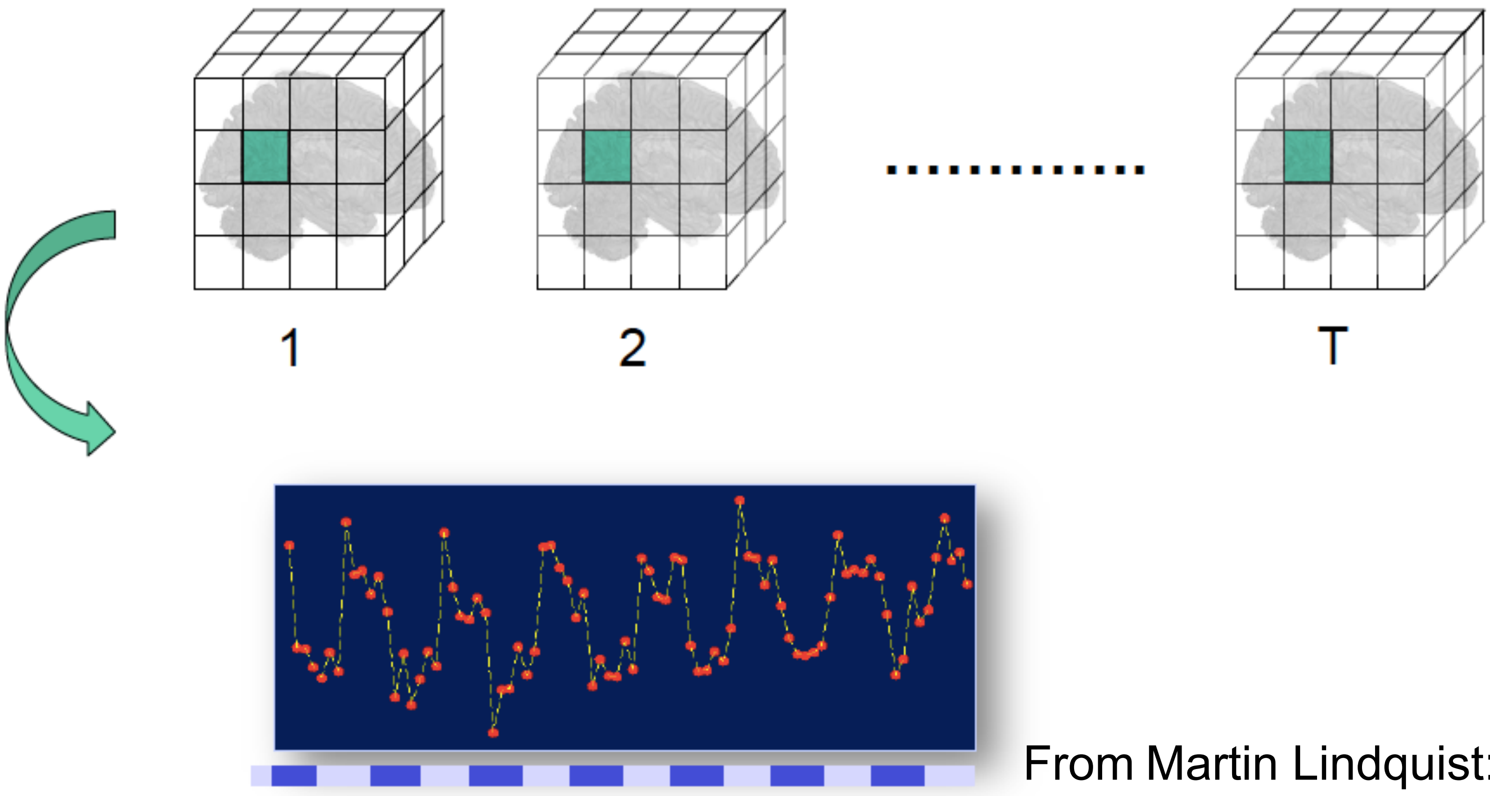
- During the course of an experiment, several hundred images may be acquired (if TR = 2, one acquisition every 2s)



From Martin Lindquist: Coursera

Functional MRI

- Tracking the intensity over time at each voxel gives us a "time series"



From Martin Lindquist: Coursera

Functional MRI

- Most commonly used approach in fMRI is Blood Oxygenation Level Depended (BOLD) contrast
- BOLD fMRI measures the ratio of oxygenated to deoxygenated hemoglobin in the blood
- So, fMRI measures oxygen consumption of active neurons (NOT neural activity directly)

From Martin Lindquist: Coursera

fMRI Data

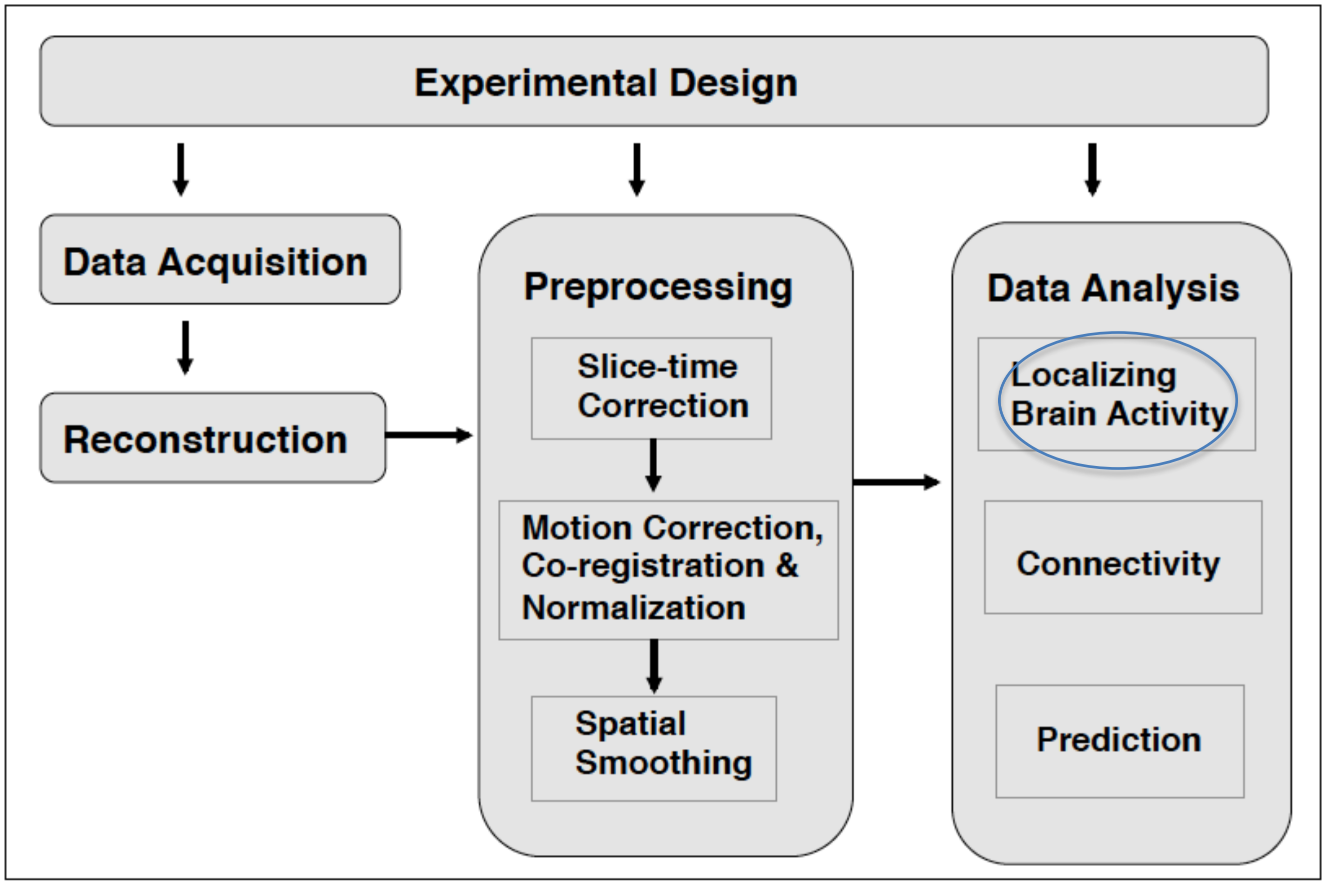
- fMRI data analysis is a massive data problem
  - Each brain volume consists of ~100,000 voxel measurements
  - Each experiment consists of hundreds of brain volumes
  - Each experiment may be repeated for multiple subjects to facilitate population inference
- This makes for a lot of data!

From Martin Lindquist: Coursera

Statistical analysis of fMRI data

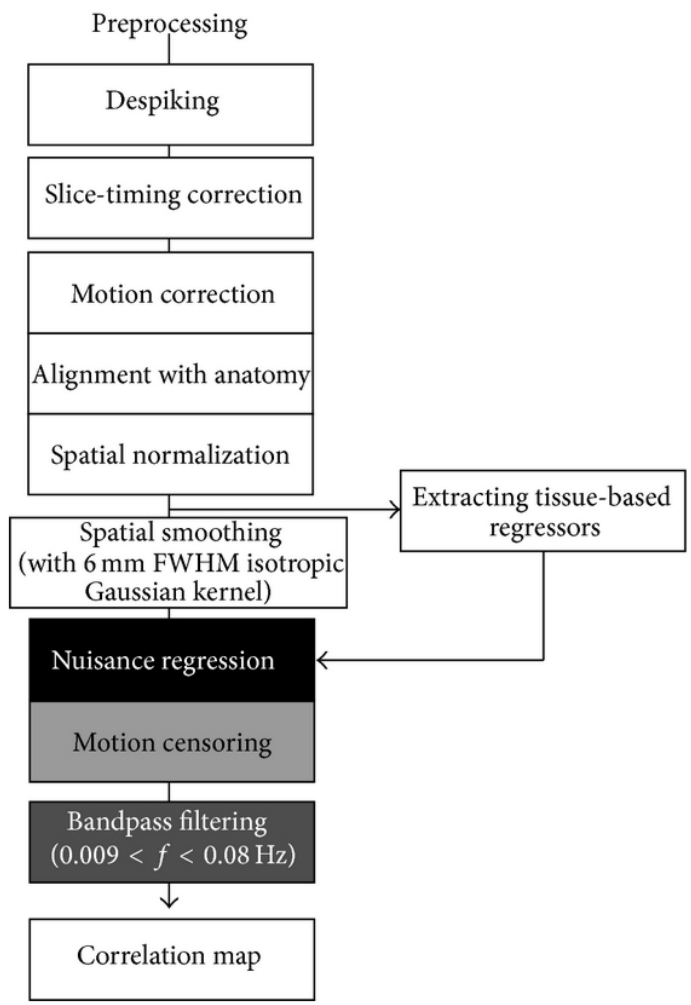
- Massive data problem
- Signal of interest is relatively weak
- The data exhibits a complicated temporal and spatial noise structure

Data processing pipeline



From Martin Lindquist: Coursera

Preprocessing Pipeline Example

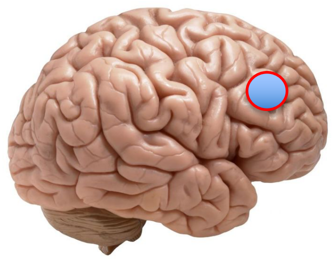


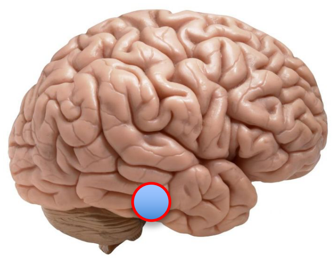
Order and specific steps can change depending on your analysis

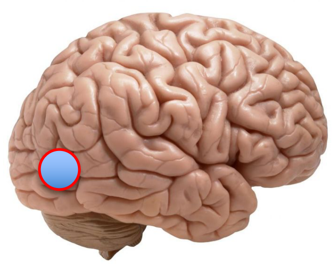
fMRI Experiments

- Participant performs a psychological task in the scanner
- Must be a baseline or control condition for comparison

Brain Localization

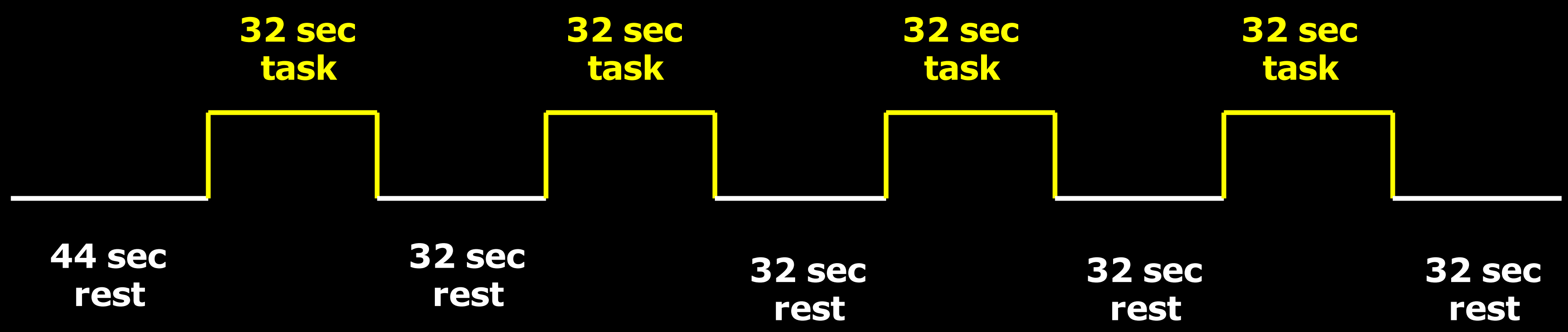


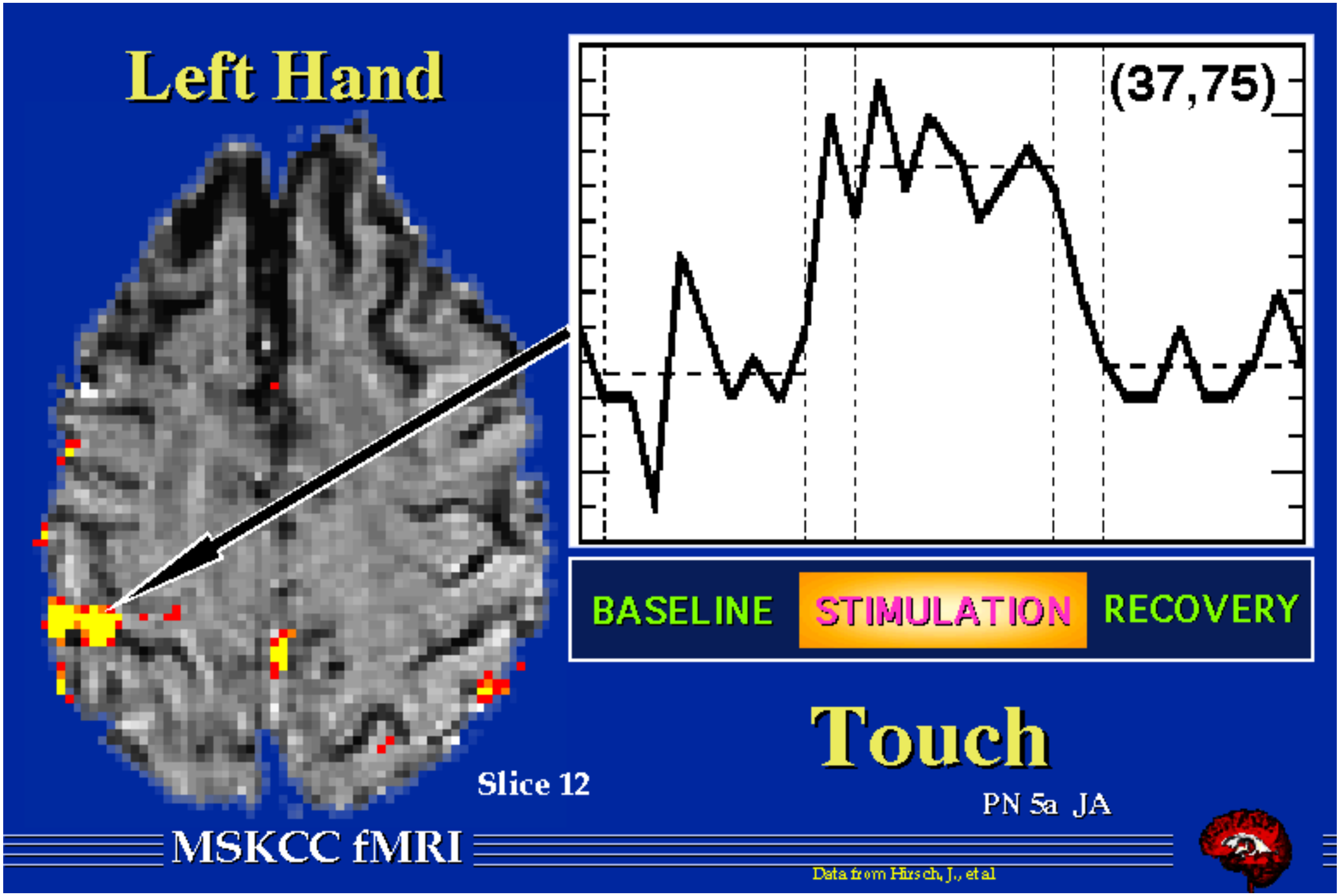


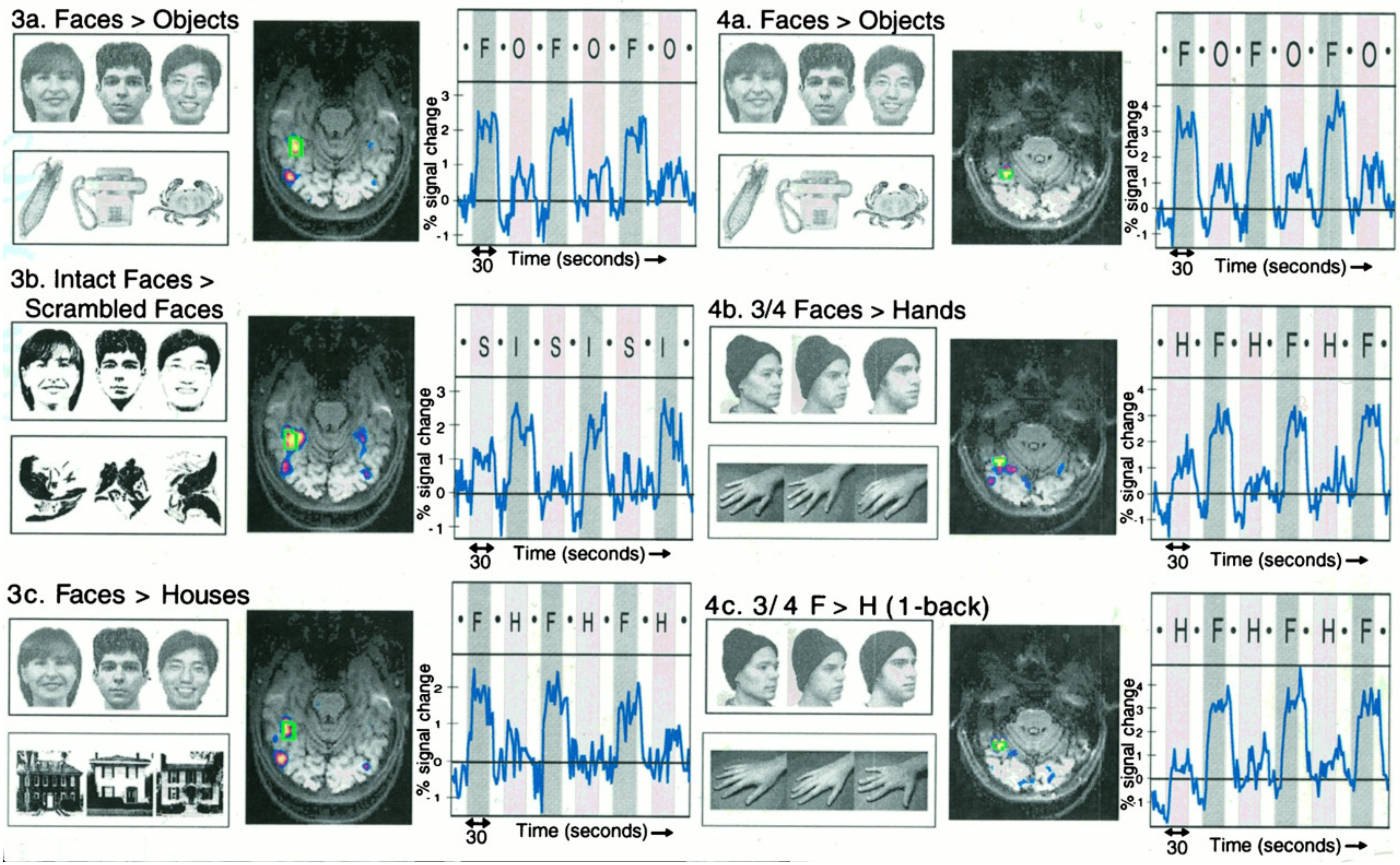


The quick fox jumped
over the lazy dogs

Block Design fMRI Experiment

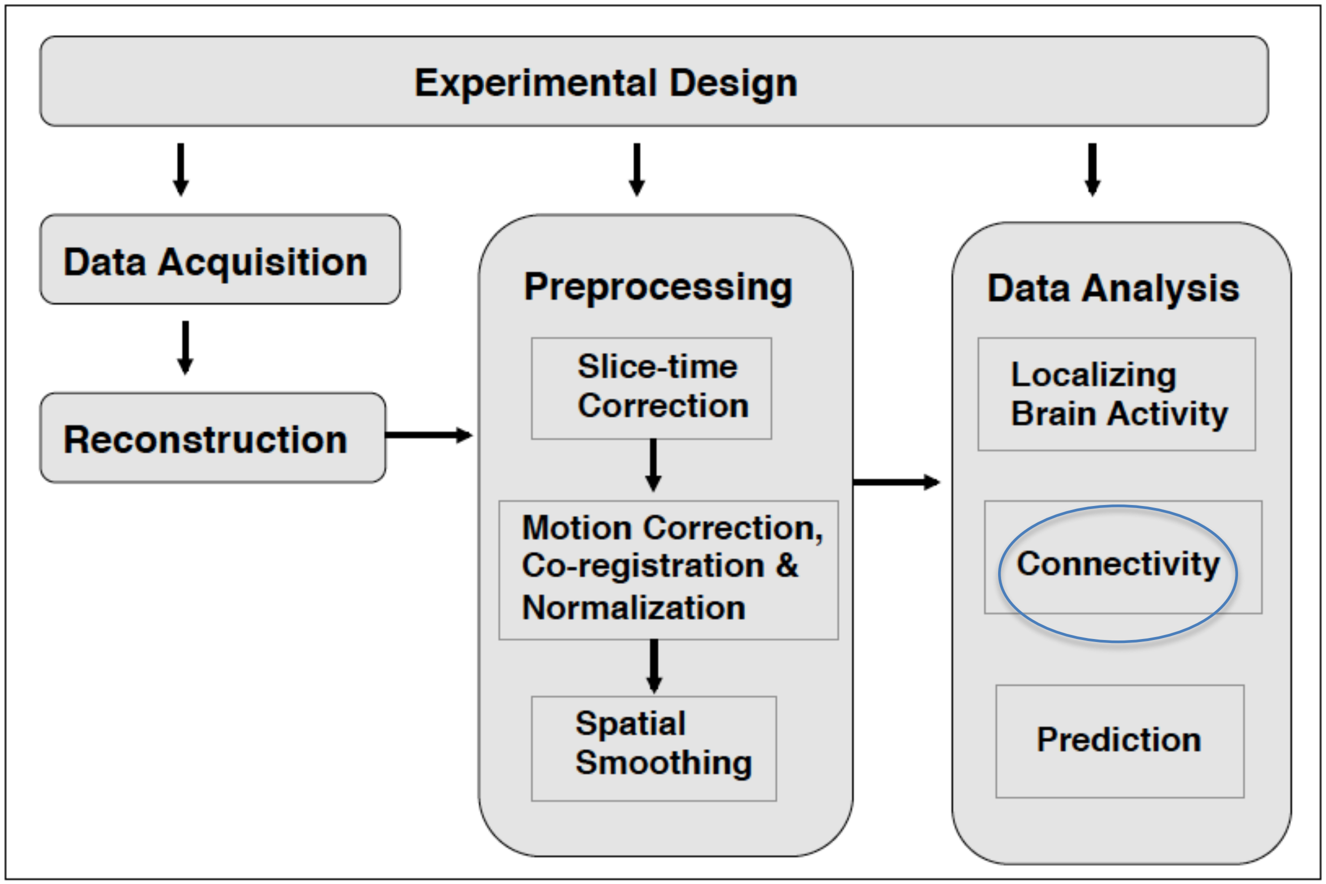



Left Hand
(37,75)
BASELINE
STIMULATION
RECOVERY
Touch
Slice 12
PN 5a JA
MSKCC fMRI
Data from Hirsch, J., et al



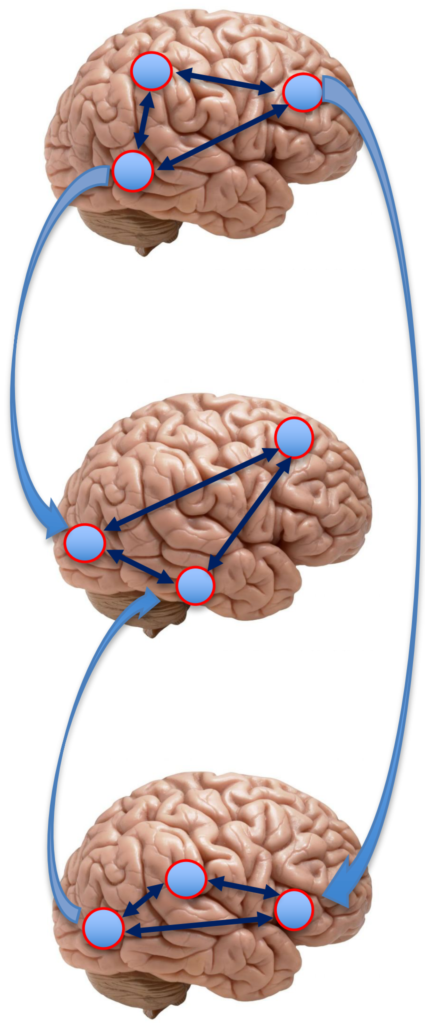
Kanwisher et al. 1997

Data processing pipeline



From Martin Lindquist: Coursera

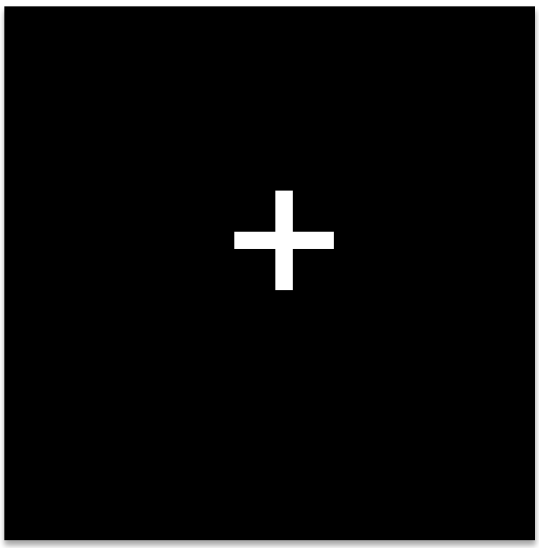
Network Neuroscience (Connectivity)



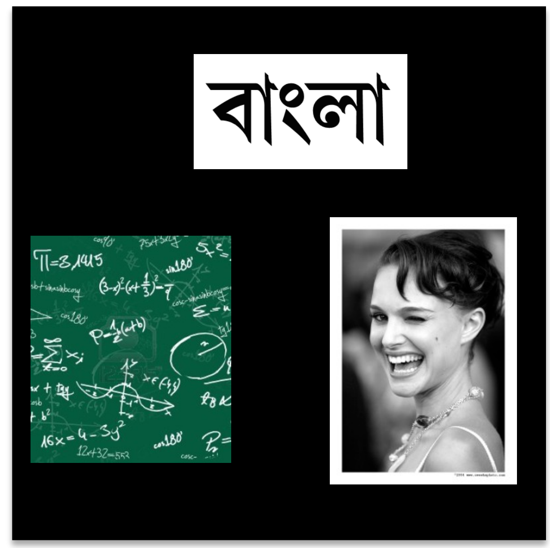
The quick fox jumped over the lazy dogs

Rest vs. Task

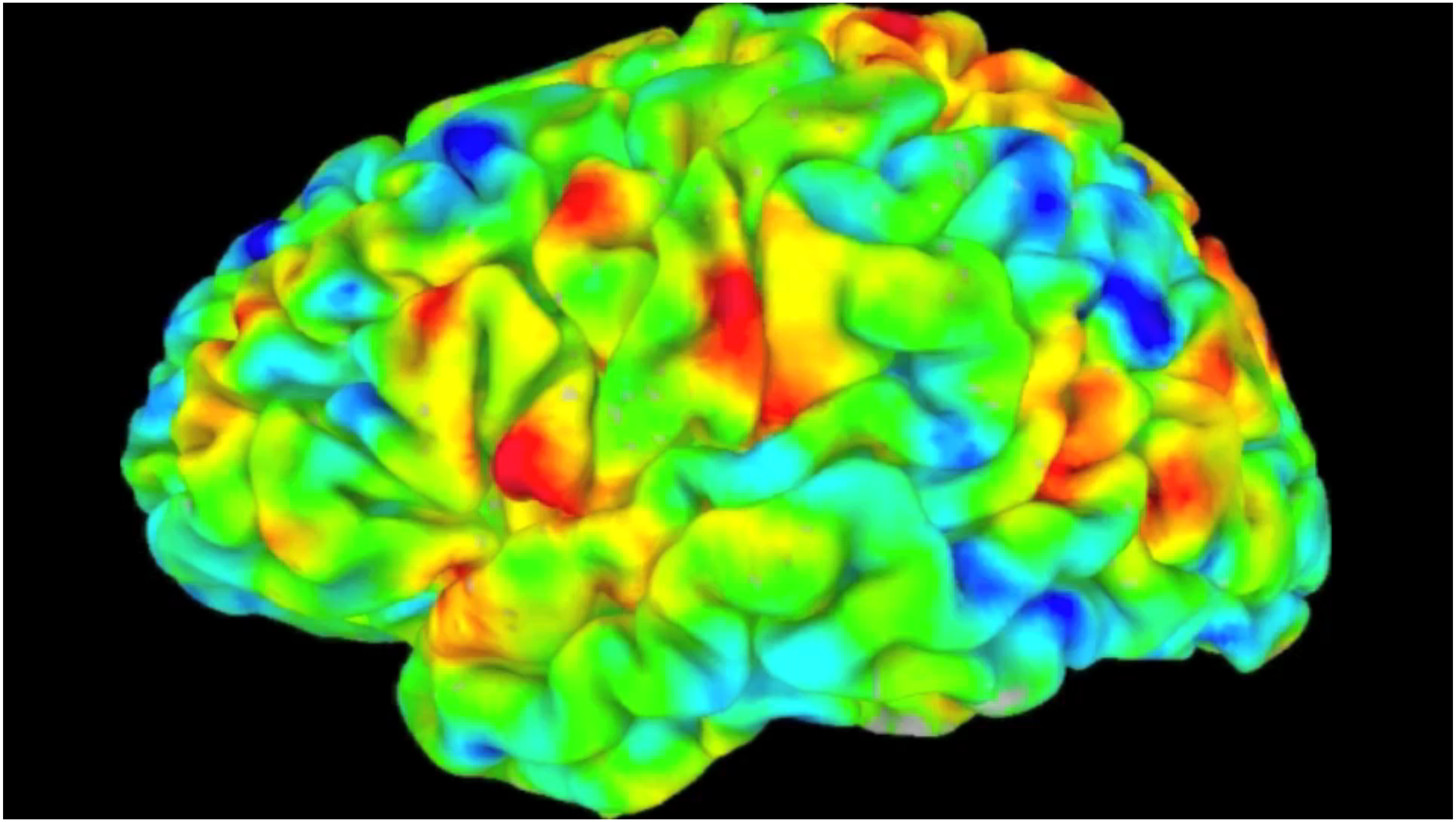
- What is your brain doing?



Vs.



- Early assumption in fMRI
  - The brain needed to be doing a task to identify coherent patterns of activity



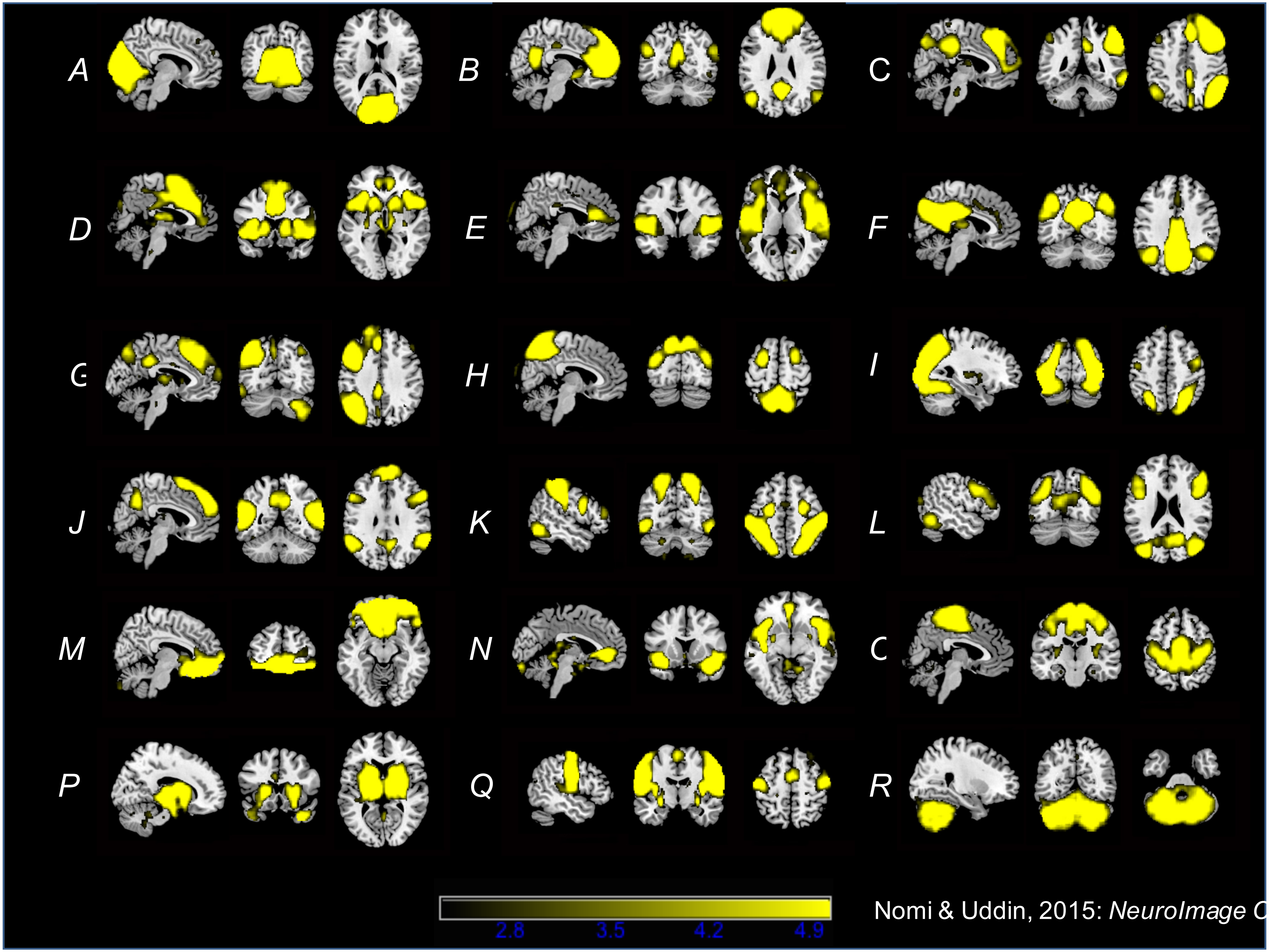
“Resting” State Networks

- Organized intrinsic structure
  - Newborns
  - Sleep
  - Monkeys
  - Rats
- Backbone of thought and cognition?
- “Resting state”
  - Misnomer
  - Brain is always active with coherent structure

Independent Component Analysis (ICA)

- "Cocktail Party" problem
  - Mix of voices
    - Different frequencies, different patterns of soundwaves

- Brain
  - Different patterns of blood flow
  - Identify voxels of the brain where blood flow is similar to each other, but different from other voxels


A
B
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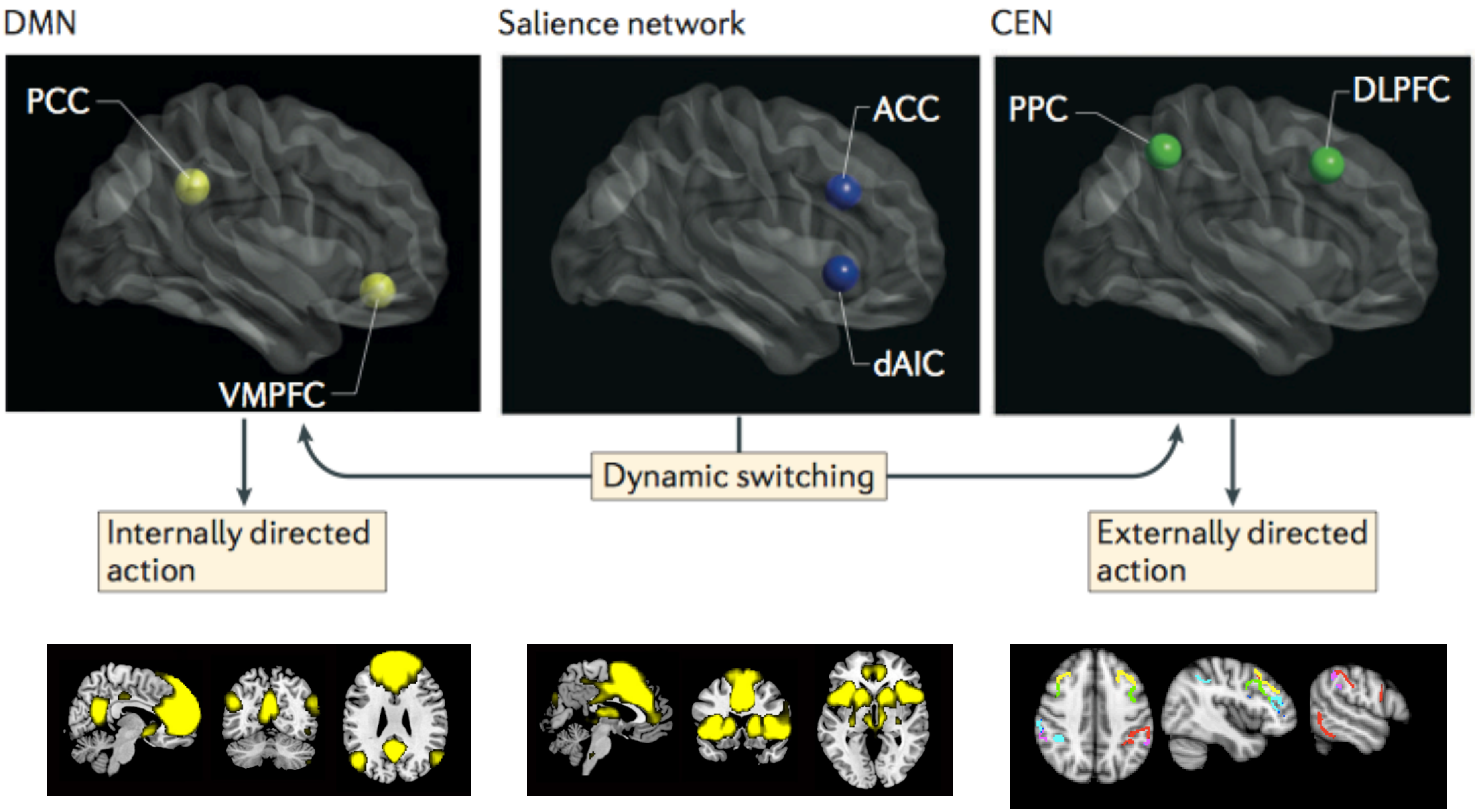
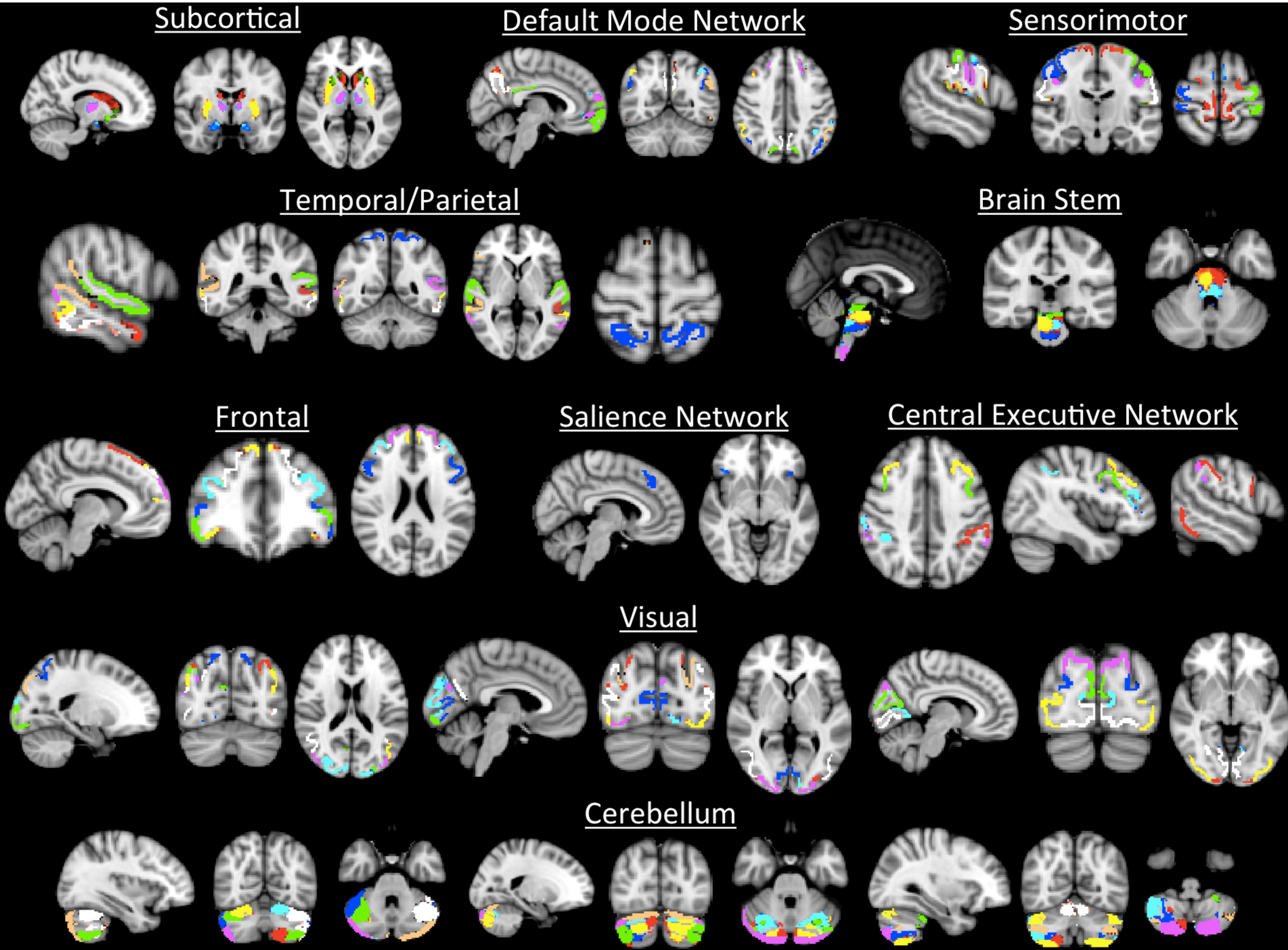
Q
R
2.8
3.5
4.2
4.9
Nomi & Uddin, 2015: *NeuroImage C*

Internal and External Cognition

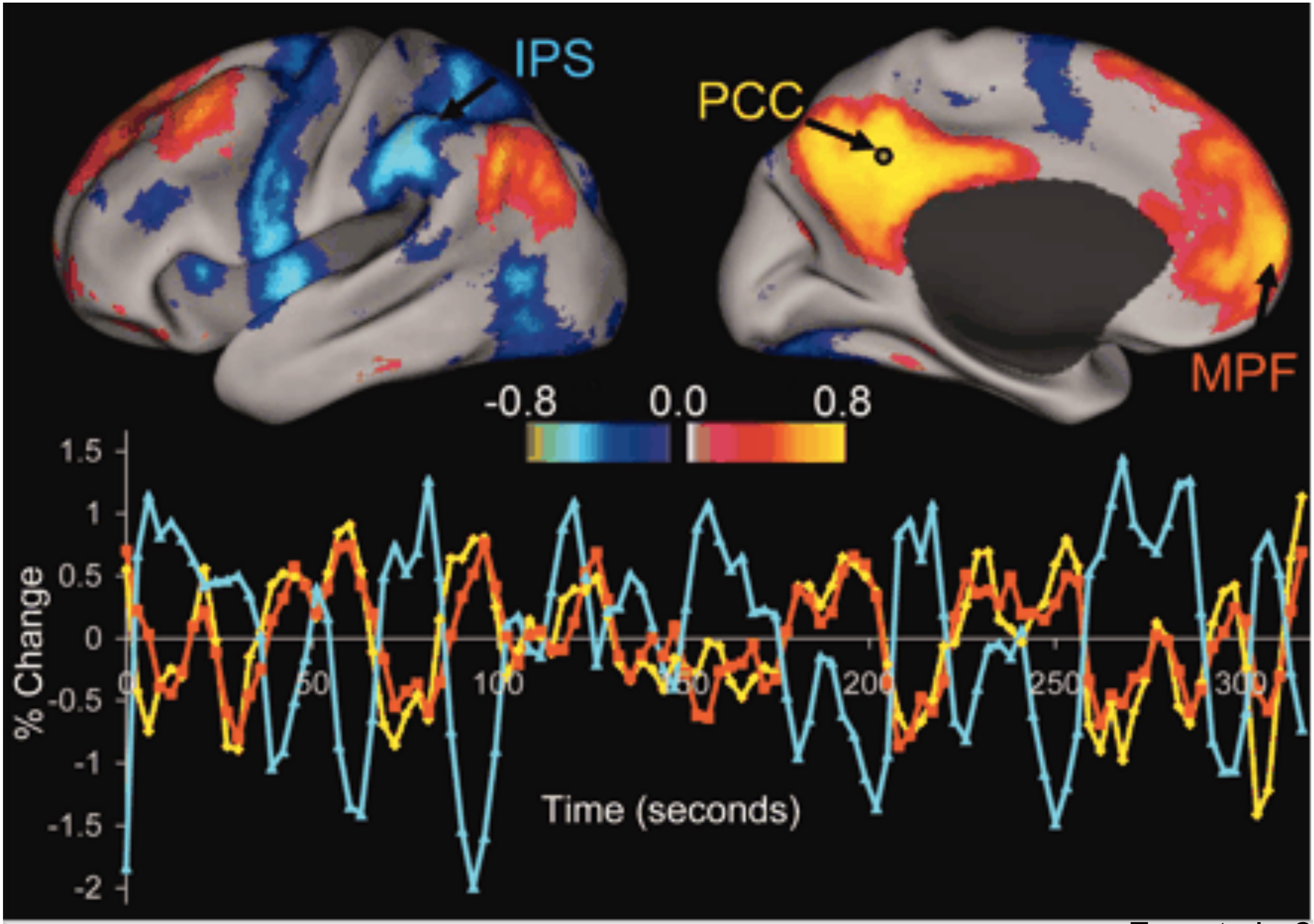


Menon & Uddin, 2010



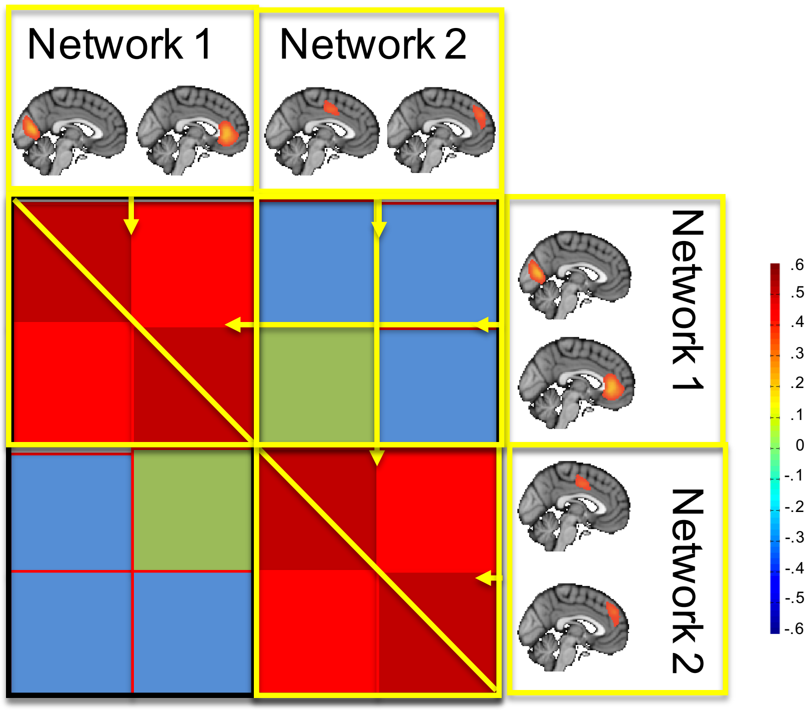
Nomi et al., 2017: NeuroImage

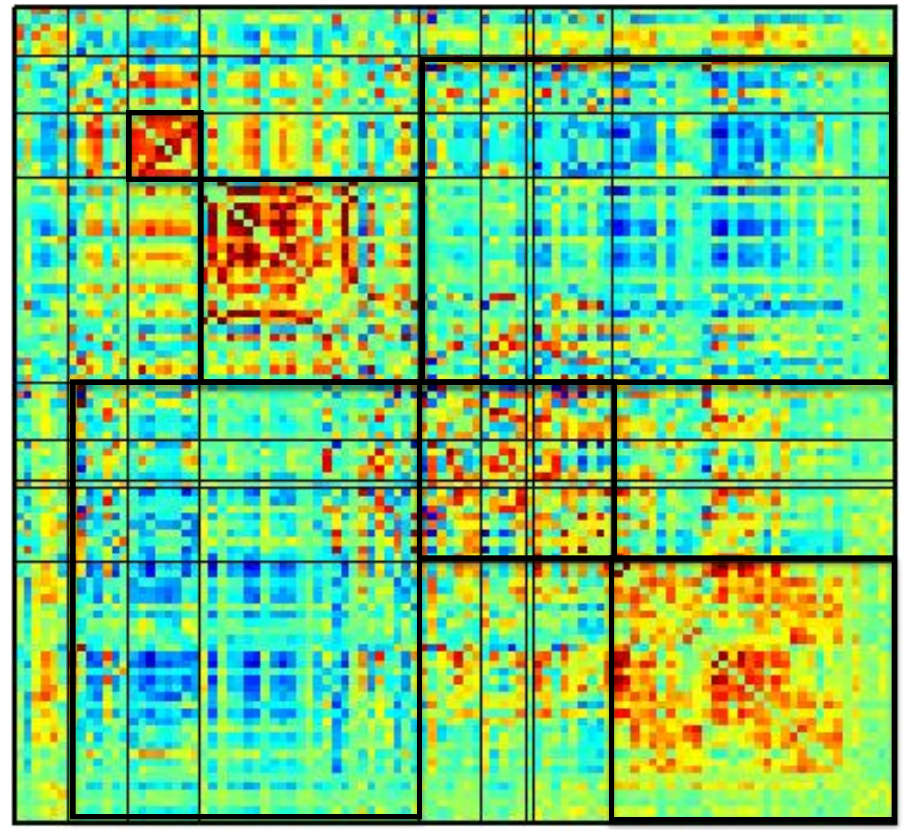
Functional Connectivity



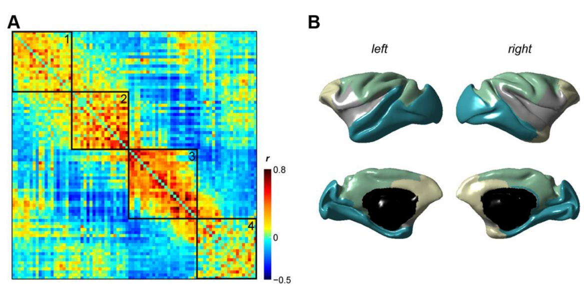
Fox et al., 2005

Correlation Matrix

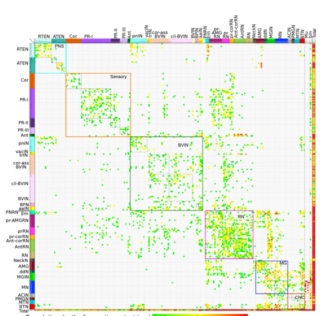




Nomi et al., 2017: *NeuroImage*



Macaque (Shen et al., 2012)

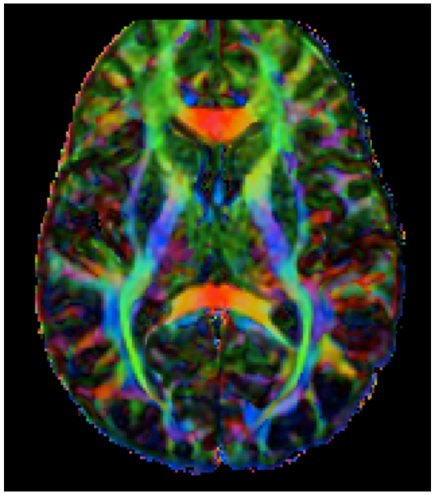


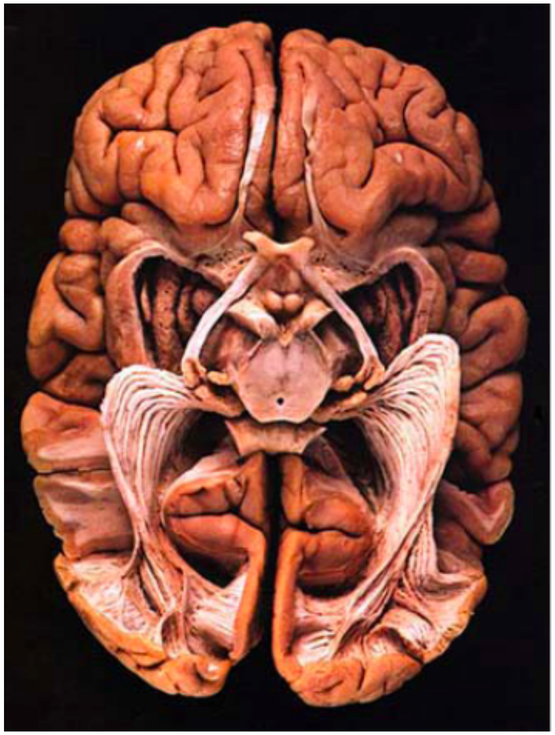
Tadpole (Ryan et al., 2016)

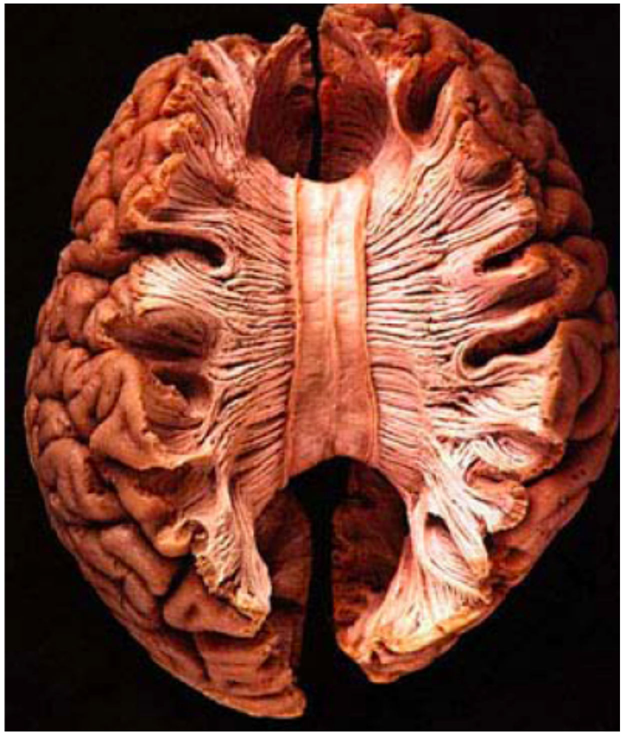
Diffusion MRI (dMRI)

- Diffusion Tensor Imaging is an MRI technique that provides quantitative information about the integrity and orientation of white matter tracts in the brain

(anatomical connectivity)

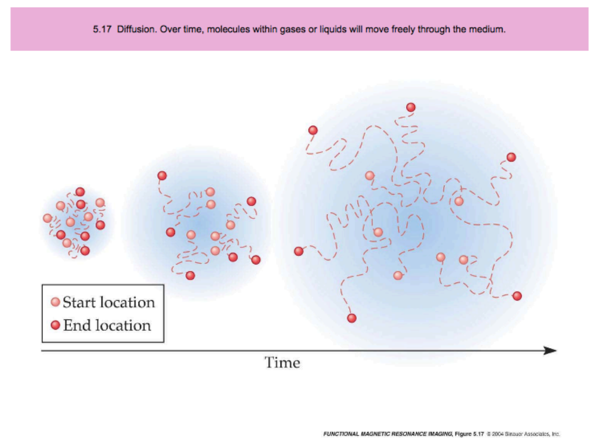




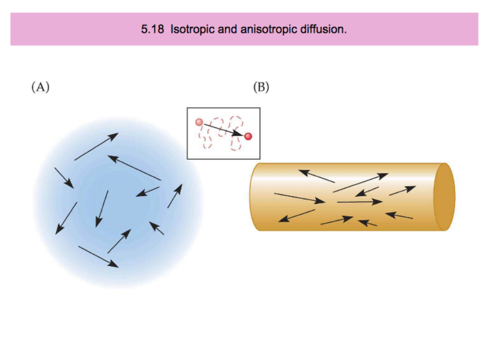


What is 'diffusion'?

- Random movement of (water) molecules

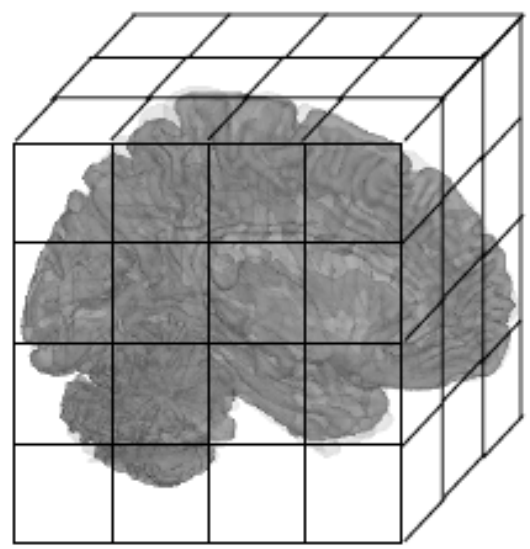


- Diffusion MRI
  - Mapping how water molecules move through the brain



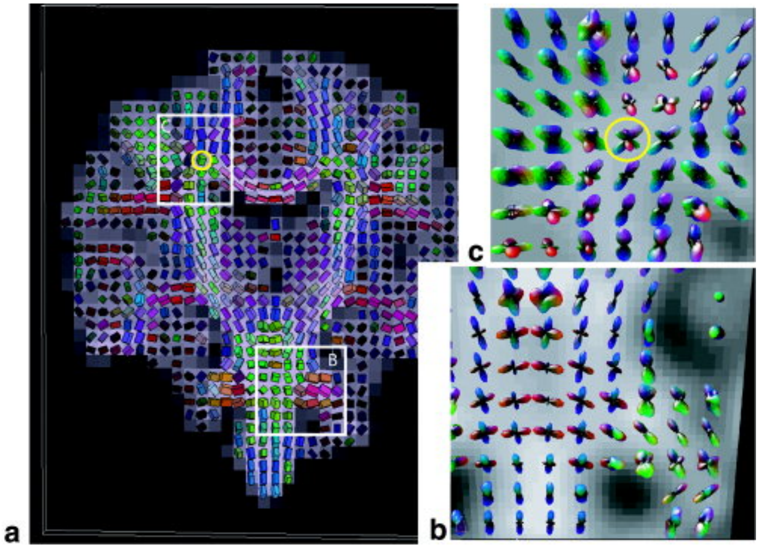
MRI

- Each image consists of ~100,000 voxels (3d pixels/cubic volumes) that span the entired space of the brain



From Martin Lindquist: Coursera

Tracking a Tract



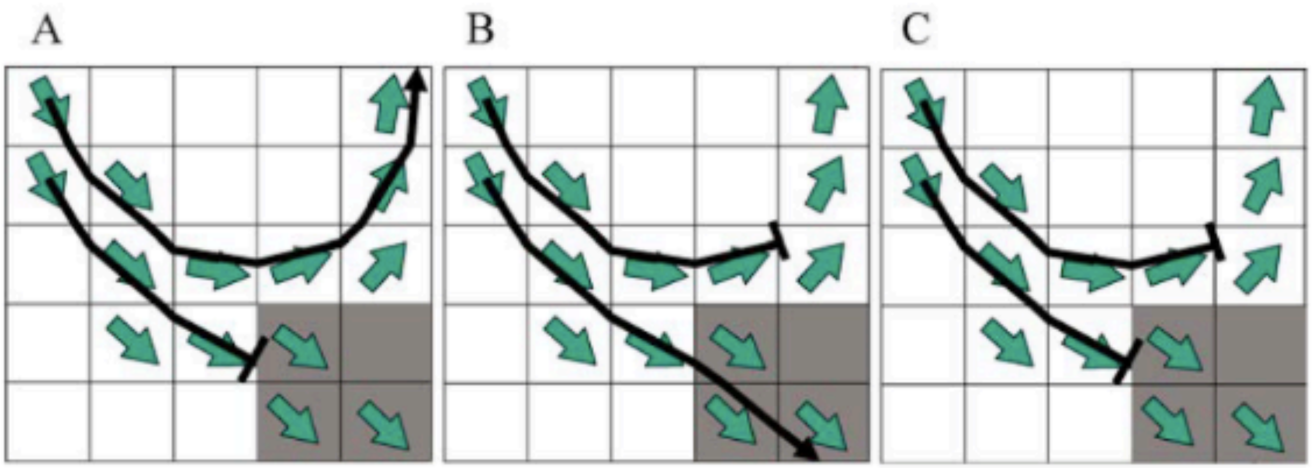


Fig. 1. Schematic diagram of FACT fiber tract reconstruction based on DTI data. Once the fiber orientation (v_1) is estimated at each pixel, putative projections are traced by propagating a line along the estimated fiber orientations. The propagation terminates either when it enters an area with anisotropy lower than a threshold (A: dark boxes) or when the trajectory has a turn judged as too sharp by an inner product between two connected pixels (B). In FACT, both criteria are applied (C).

Wedeen et al., 2005, Magnetic Resonance in Medicine

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