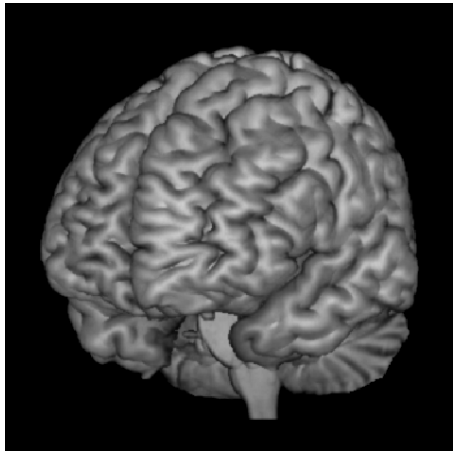
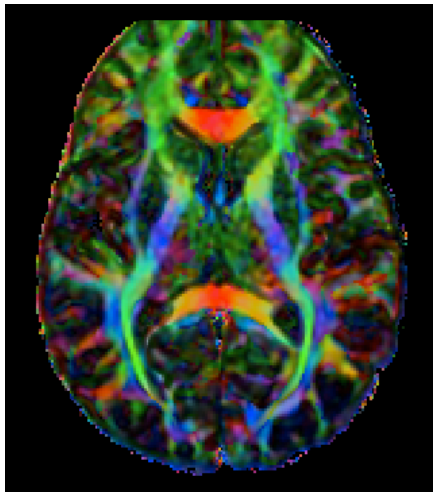


MRI Approaches for Investigating Brain Structure and Function

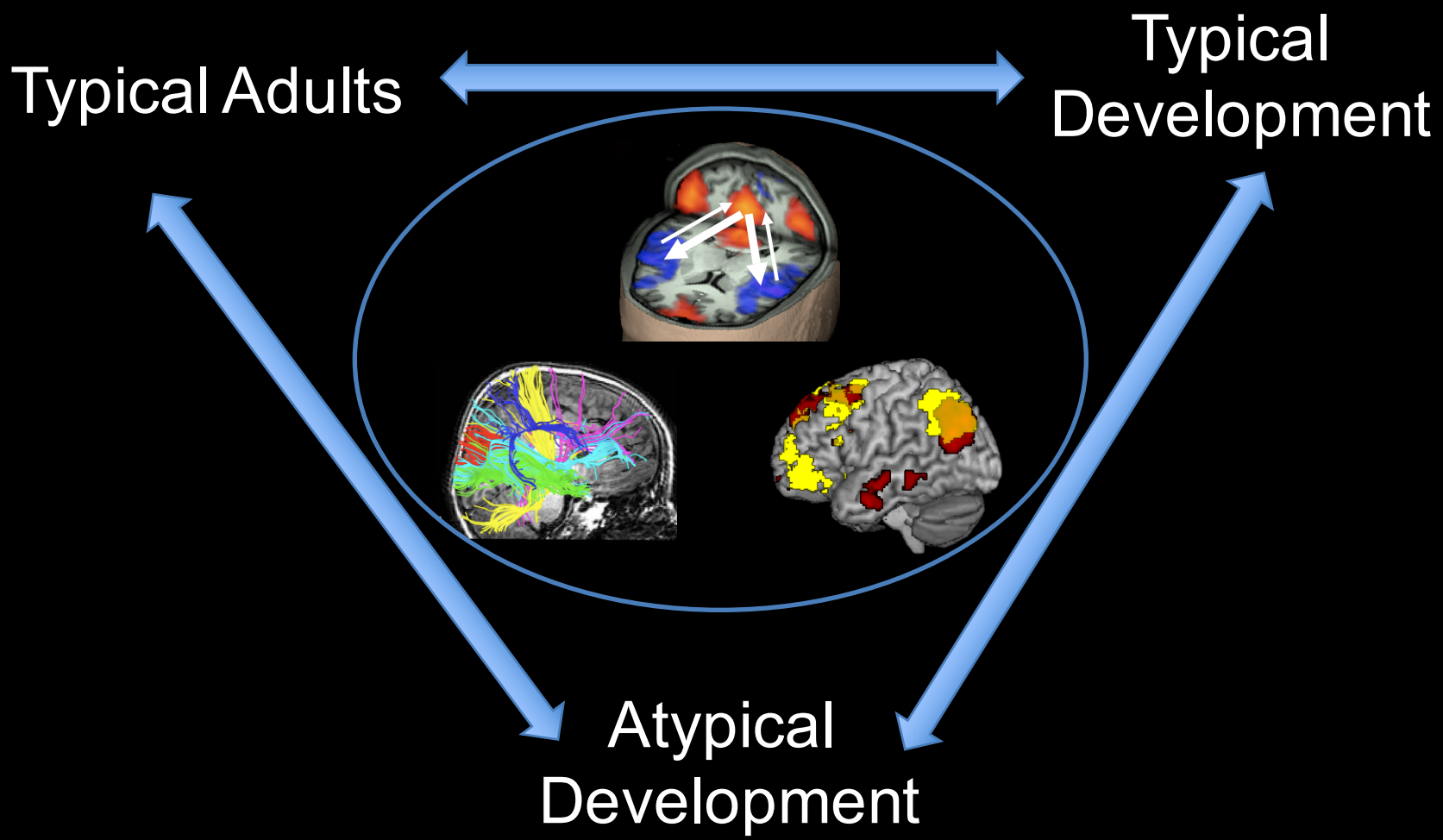
Jason S. Nomi, Ph.D. (jxn131@miami.edu)



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"

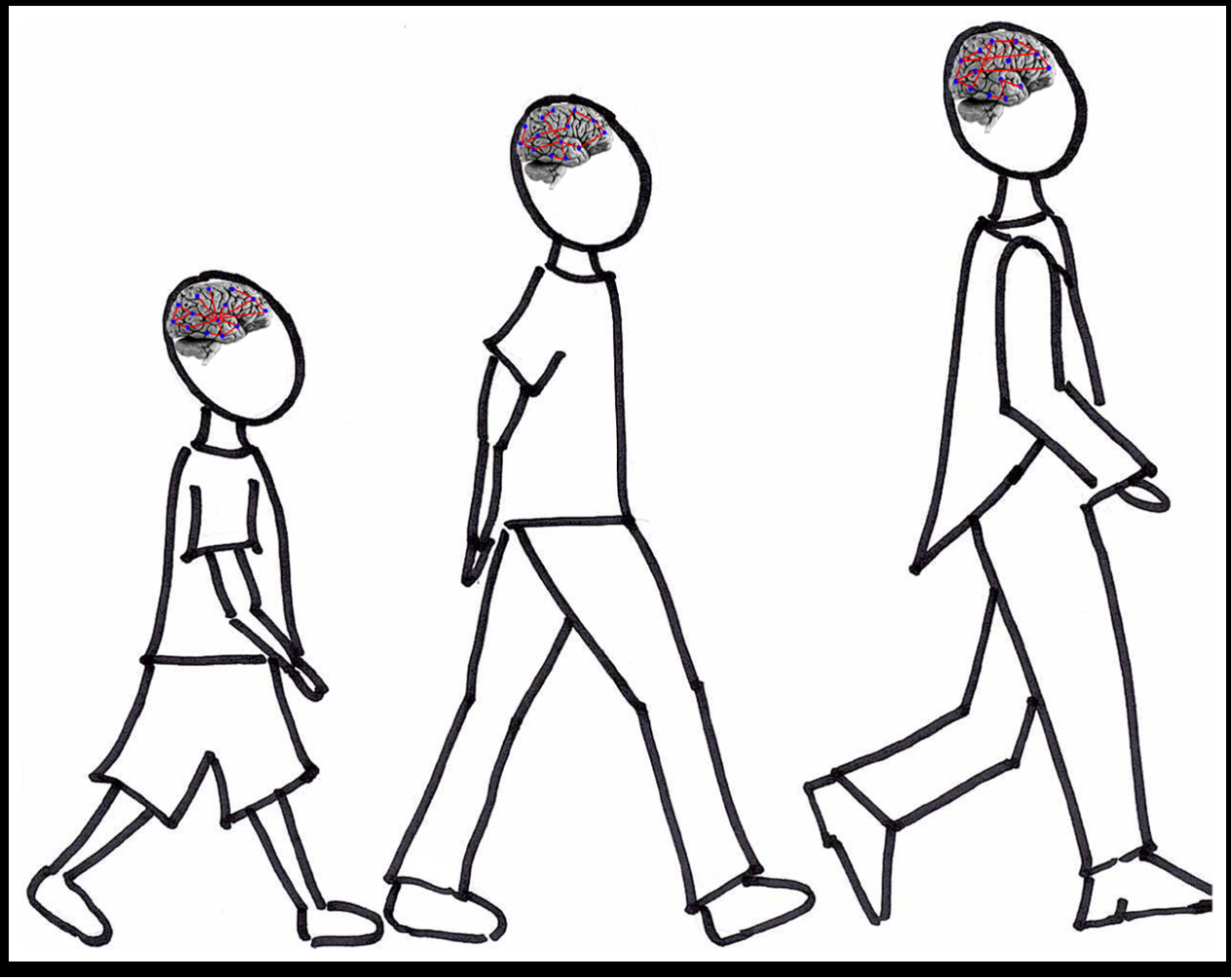
Research Approach in Our Lab



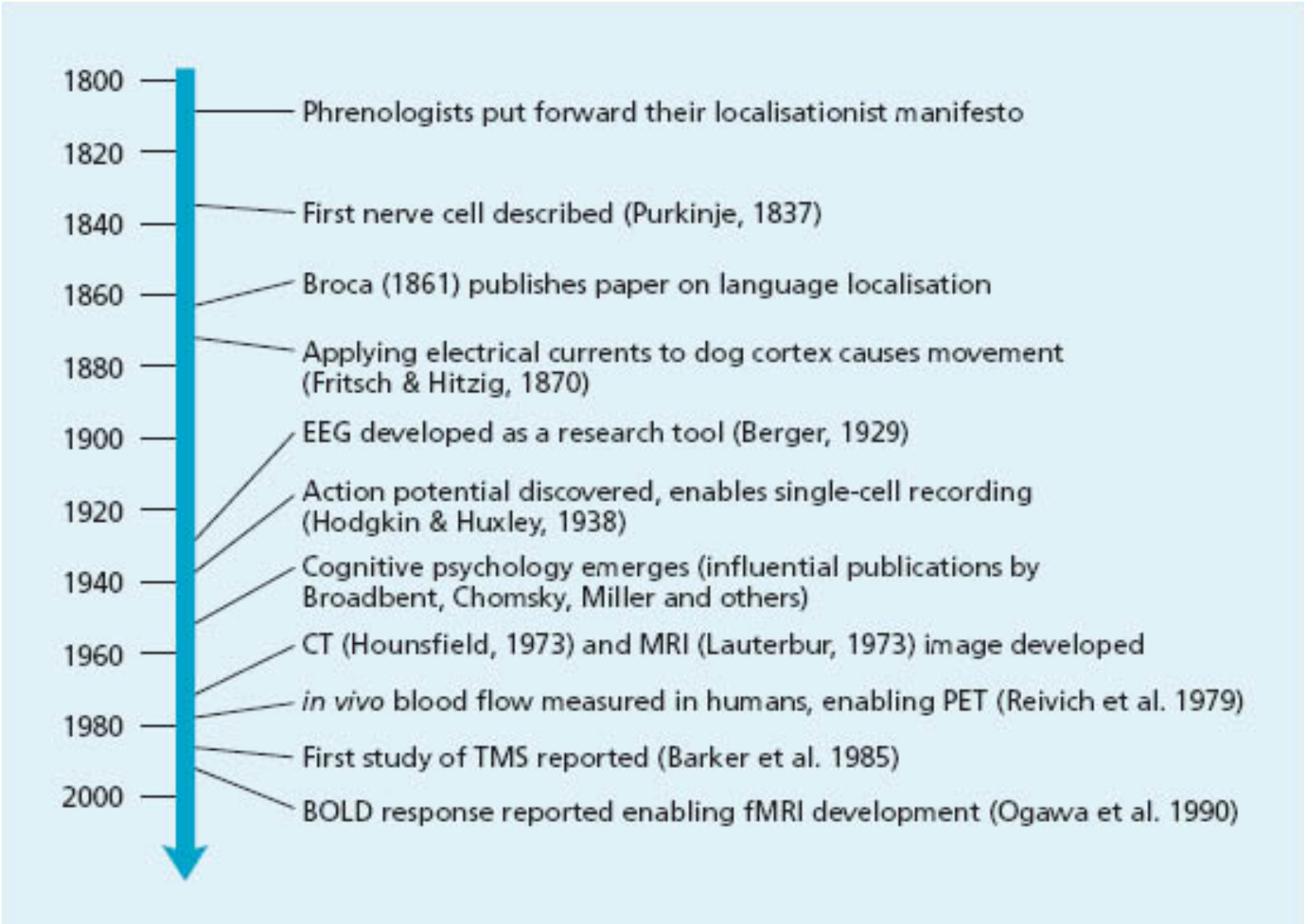
Critical Research Questions

Brain Network Development

Cognitive Maturation



Timeline for development of methods in cognitive neuroscience



Methods in Cognitive Neuroscience

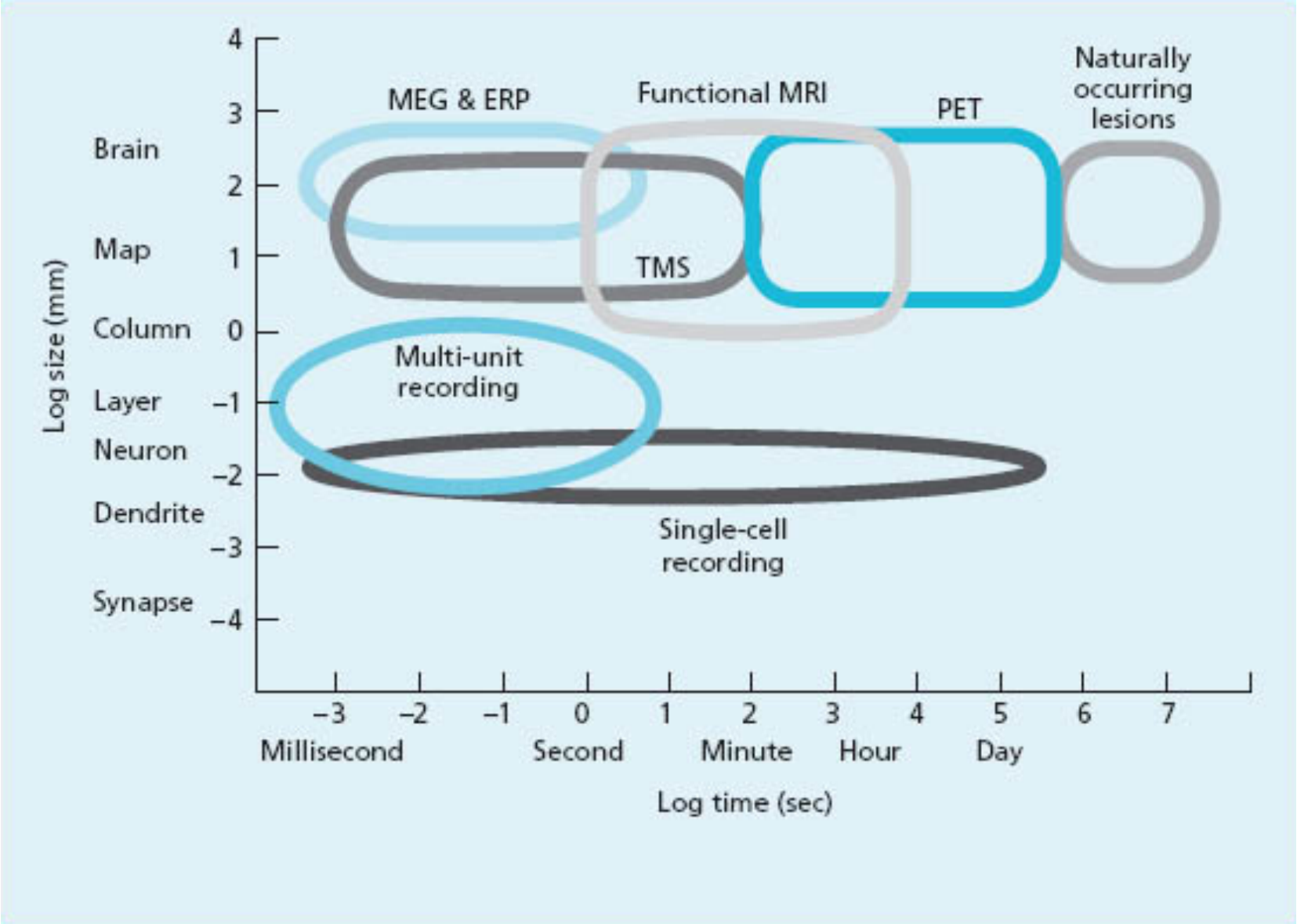
Method	Method type	Invasiveness	Brain property used
EEG/ERP	Recording	Non-invasive	Electrical
Single-cell (and multi-unit) recordings	Recording	Invasive	Electrical
TMS	Stimulation	Non-invasive	Electromagnetic
MEG	Recording	Non-invasive	Magnetic
PET	Recording	Invasive	Haemodynamic
fMRI	Recording	Non-invasive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

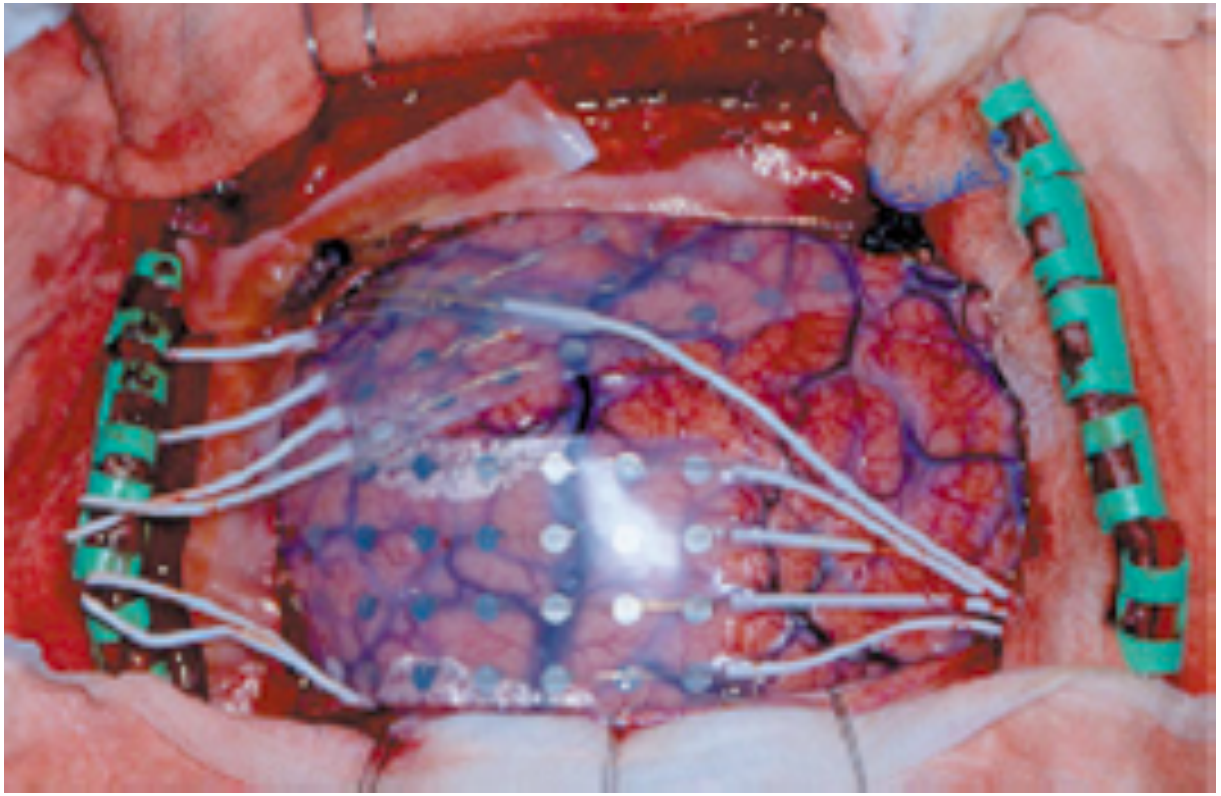
- The **temporal resolution** refers to the accuracy with which one can measure *when* an event is occurring. The effects of brain damage are permanent and so this has no temporal resolution as such. Methods such as EEG, MEG, TMS and single-cell recording have millisecond resolution. PET and fMRI have 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.

Methods Compared



Electrical Recordings

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



Advantages and disadvantages to electrical recordings

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

rarely be carried out in humans,

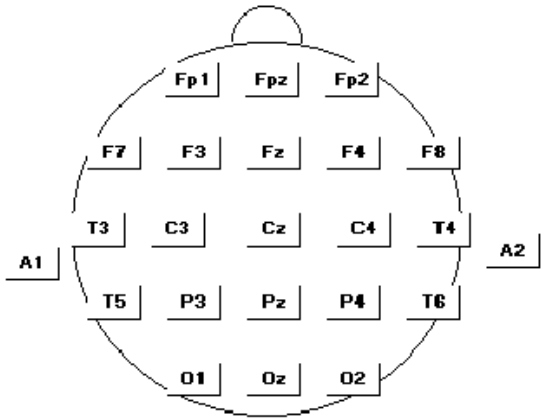
most useful for researchers

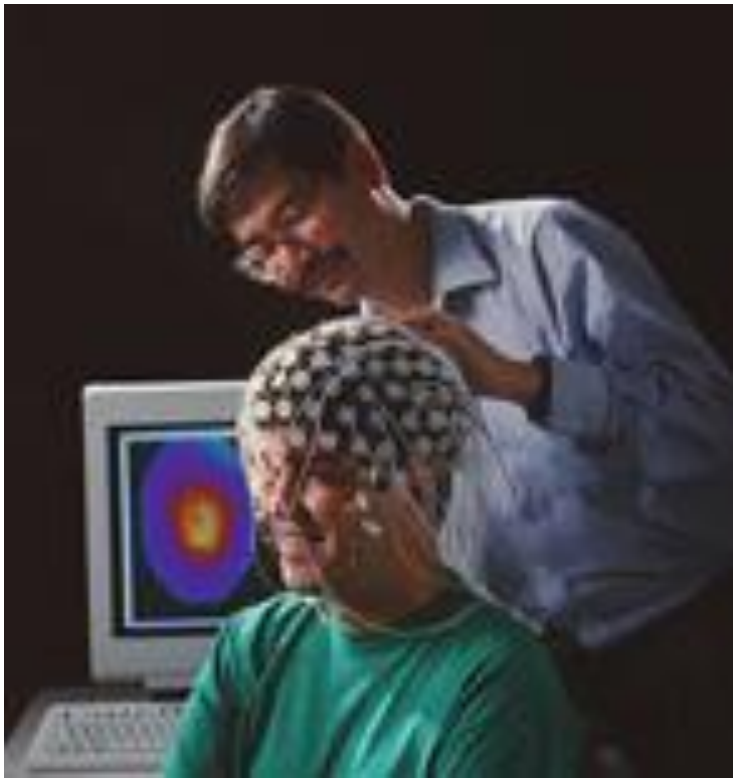
who use animal models

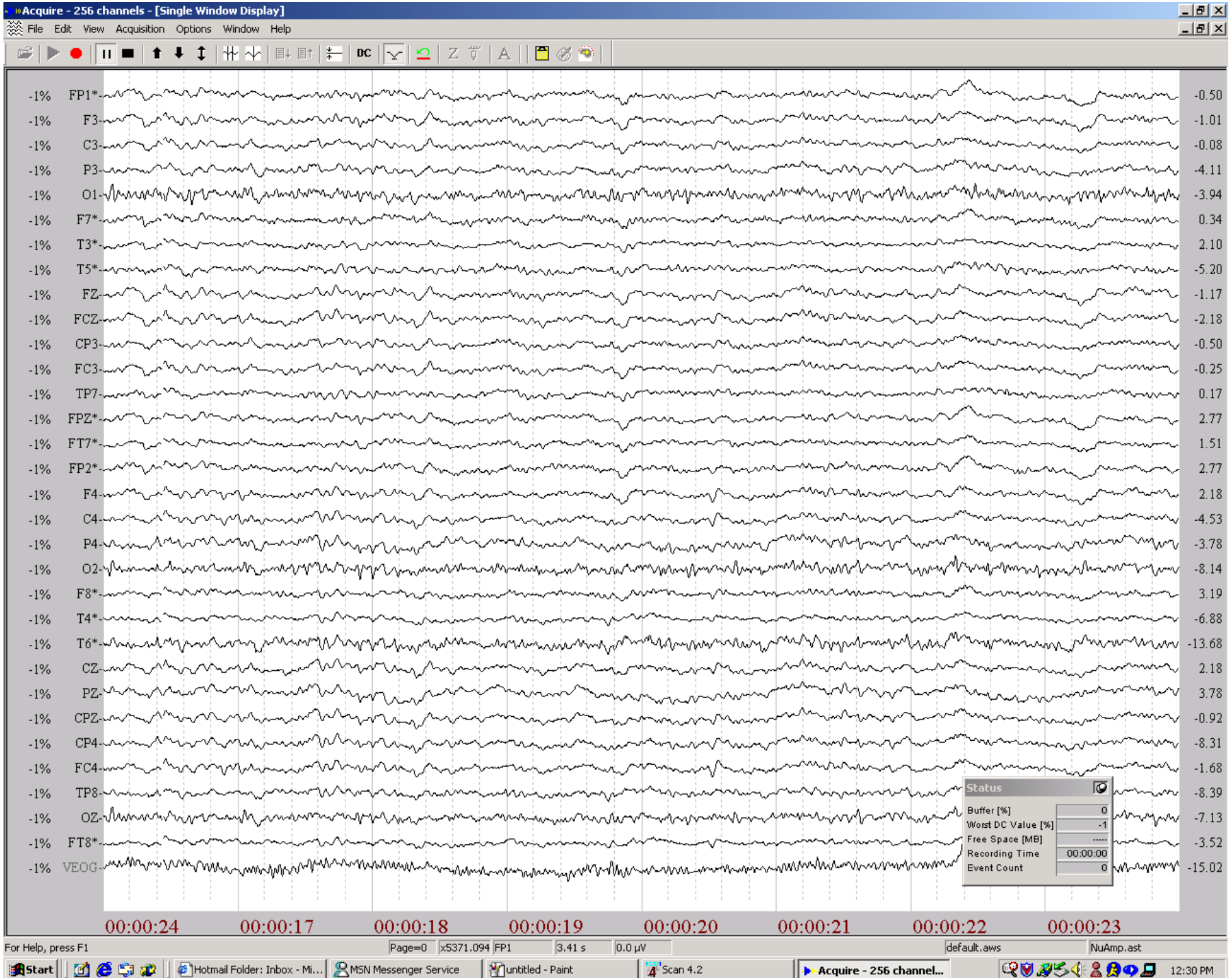
Electroencephalogram (EEG)

- 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



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-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
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-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
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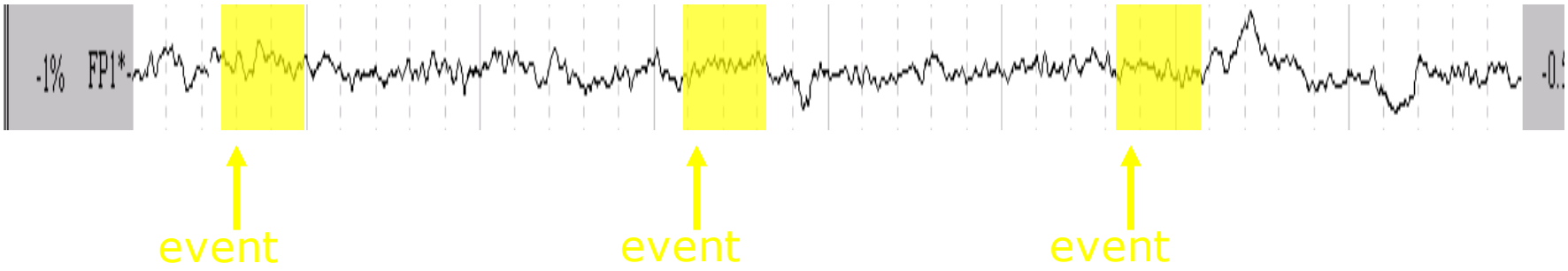
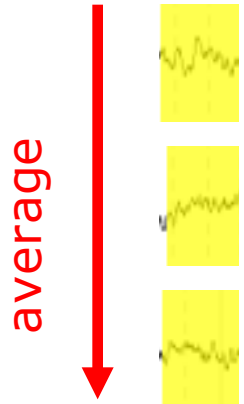
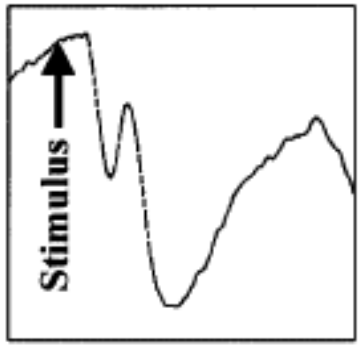
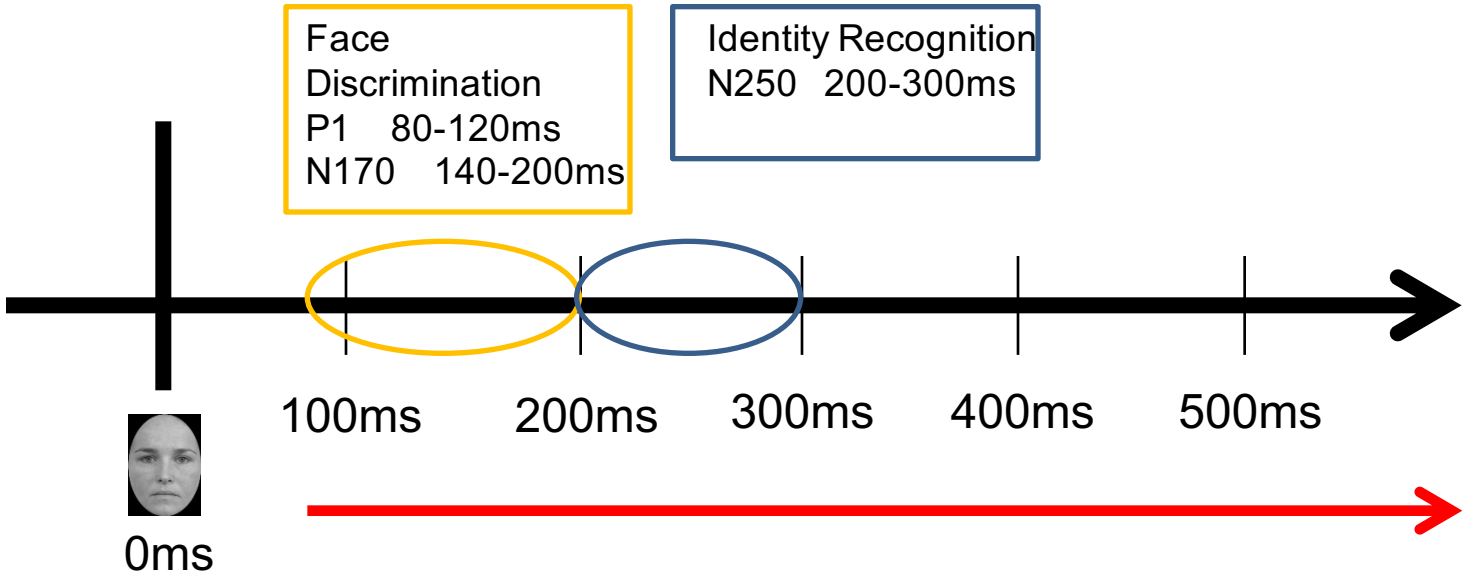


Event-related potentials (ERPs)

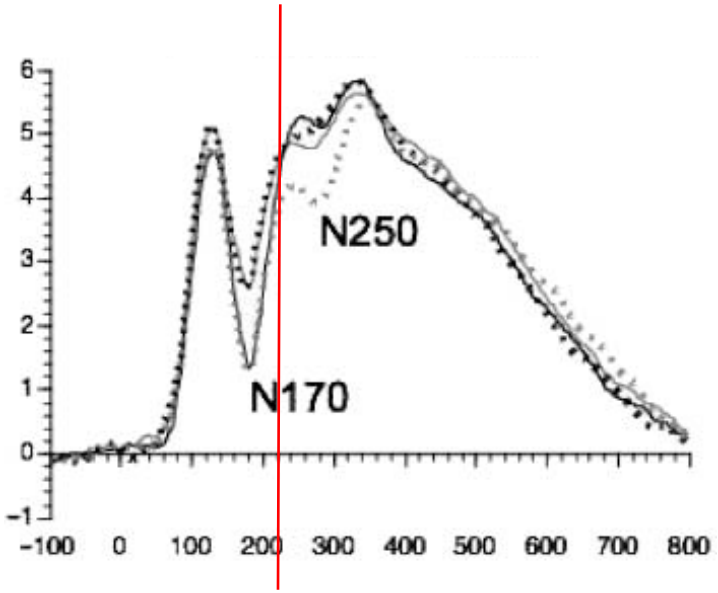




- Measure continuous EEG while subject performs a psychological task
- Average the EEG waveform surrounding an event of interest (a stimulus or response)



Empathy
300ms – 1000ms

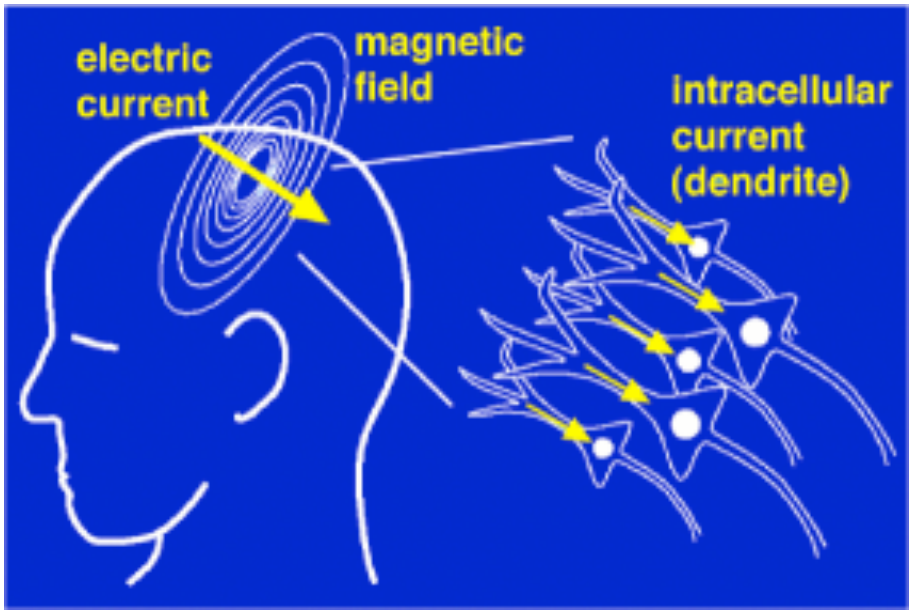


Advantages and Disadvantages of ERPs

- 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



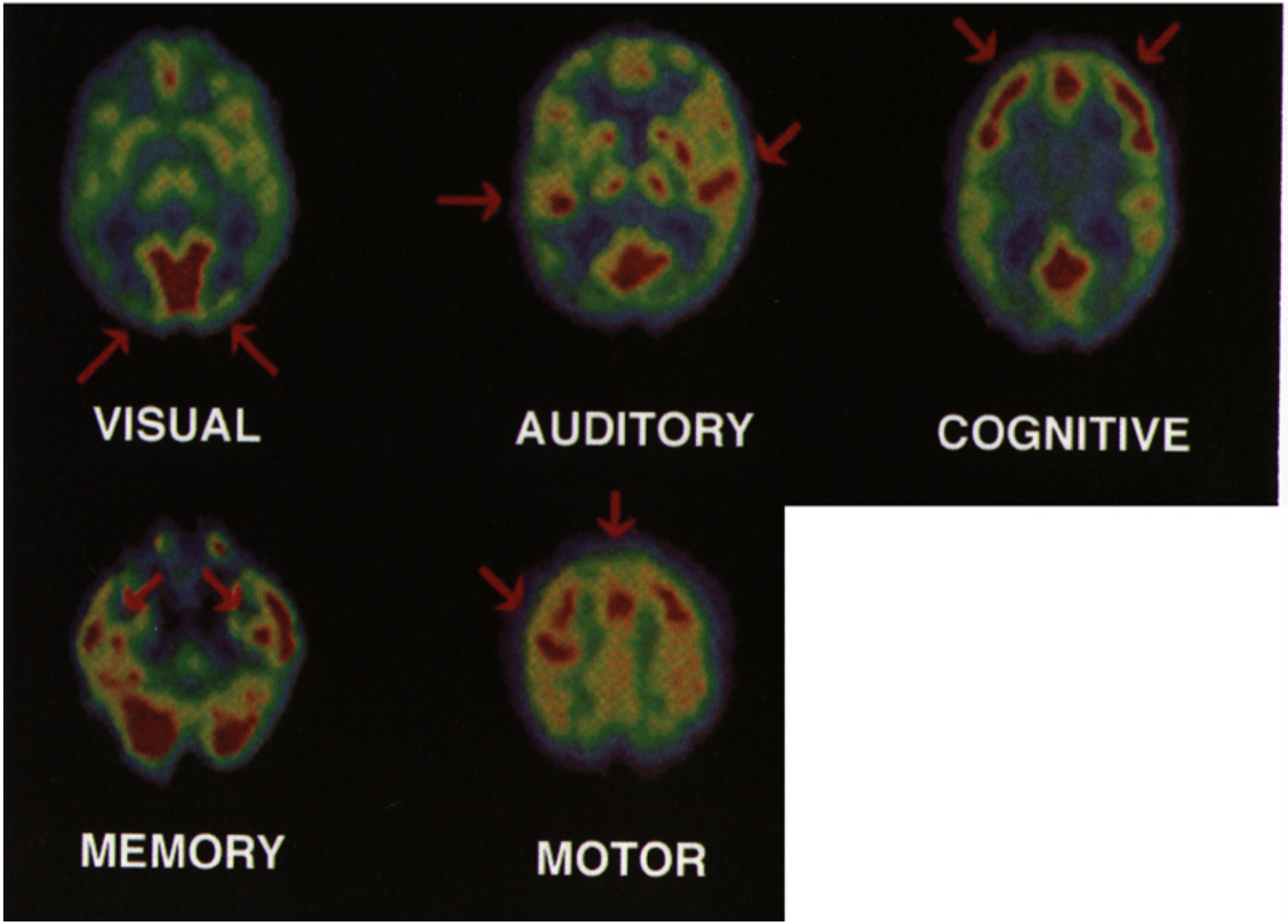
Advantages and disadvantages of MEG

- 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.

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



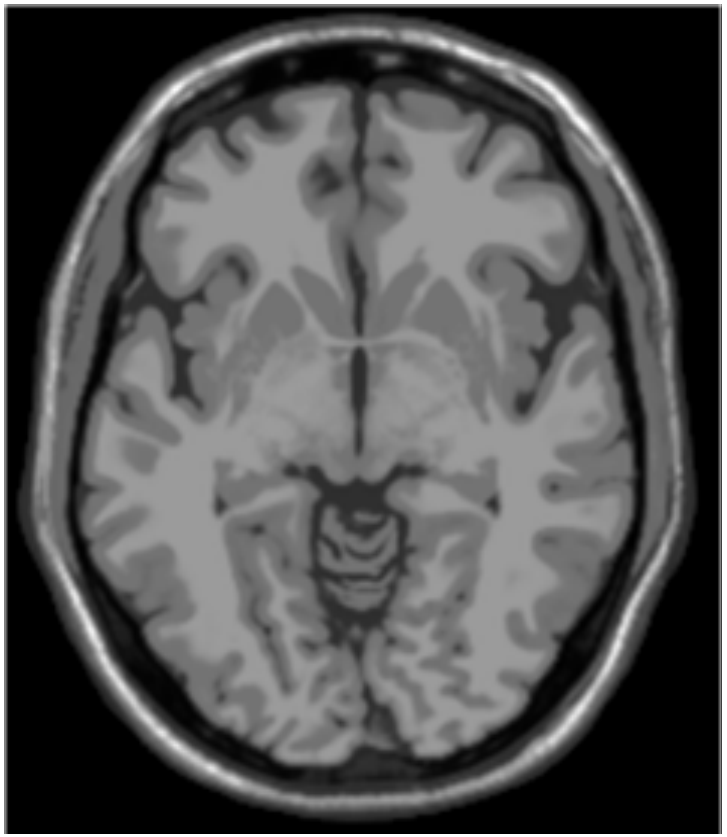
Advantages and Disadvantages to PET

- 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

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging

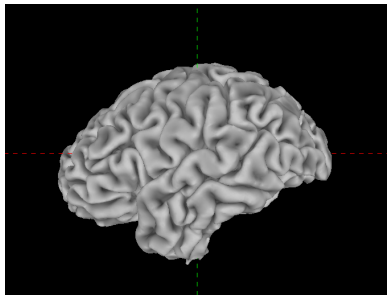
- Relatively new method, first used in humans in the 1970's



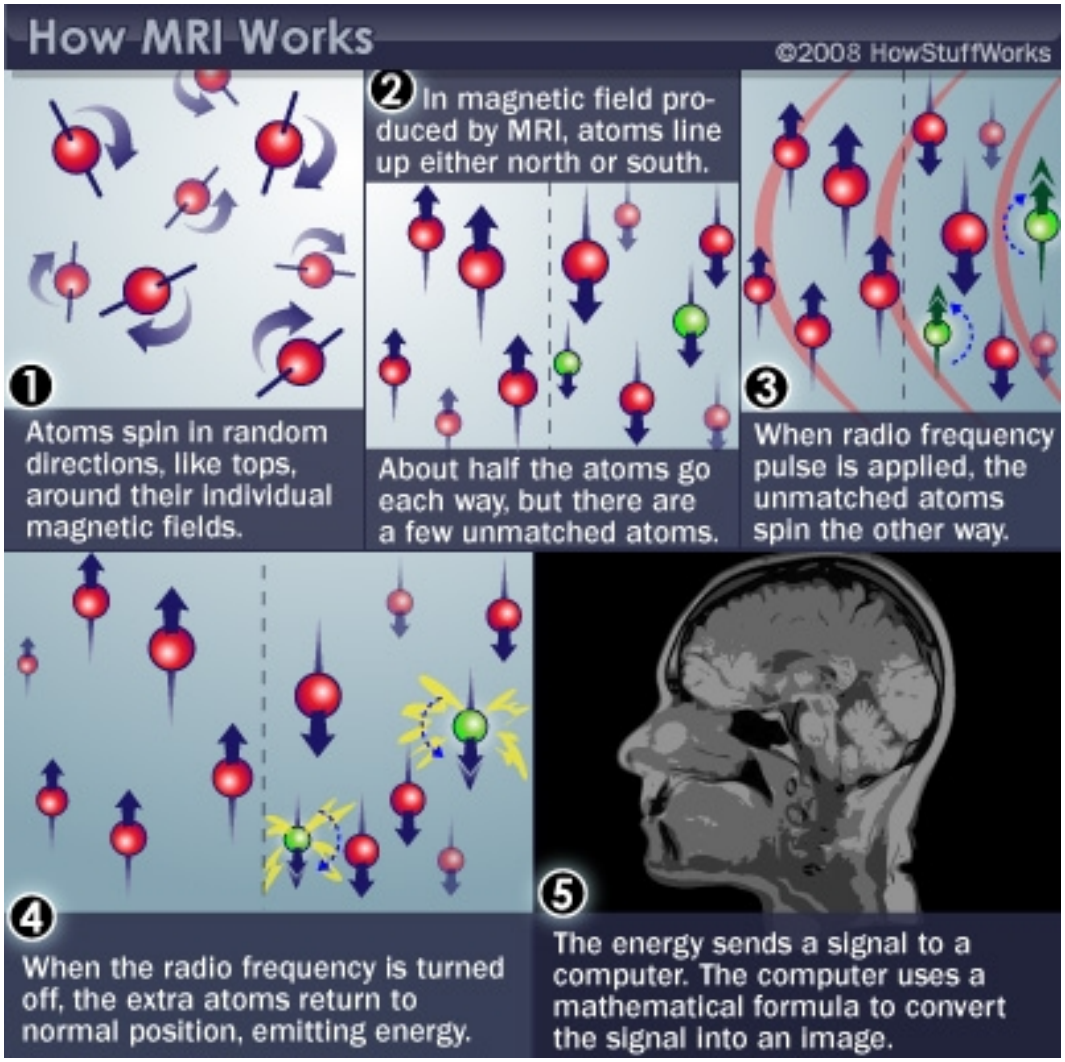
Advantages and Disadvantages to MRI

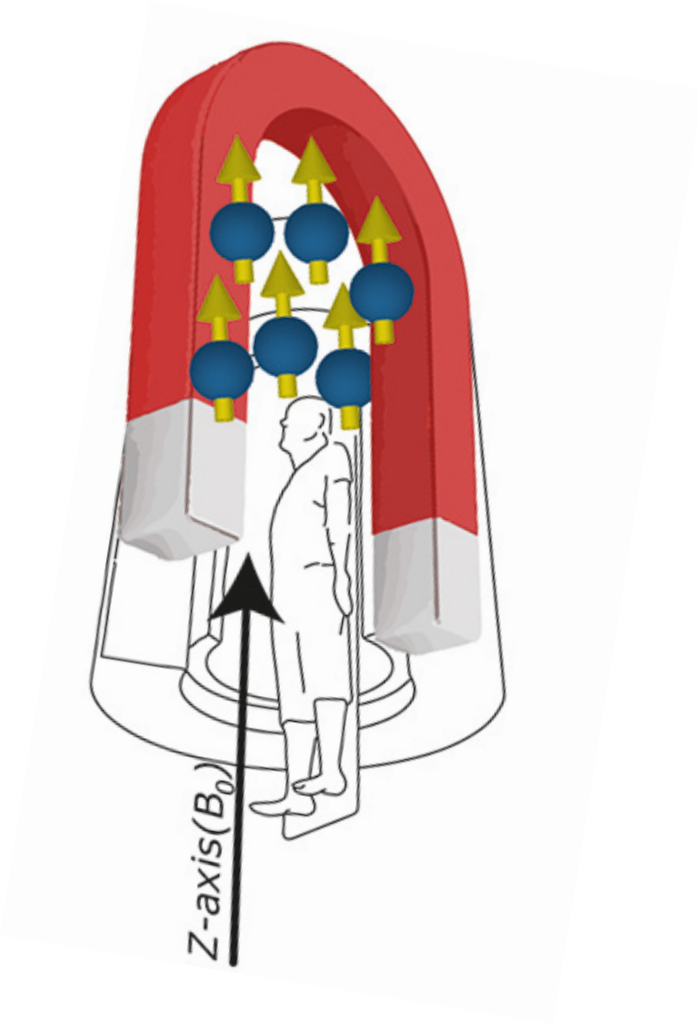
- Strengths: Excellent spatial resolution. Greater contrast between tissue types than CAT (high spatial resolution), does not expose subjects to radiation.

- Weaknesses: 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



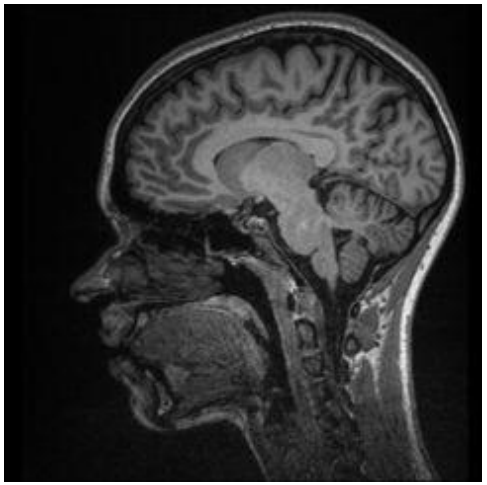


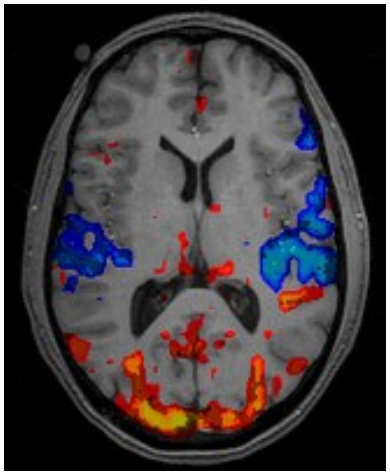
Structural vs. Functional MRI

- 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

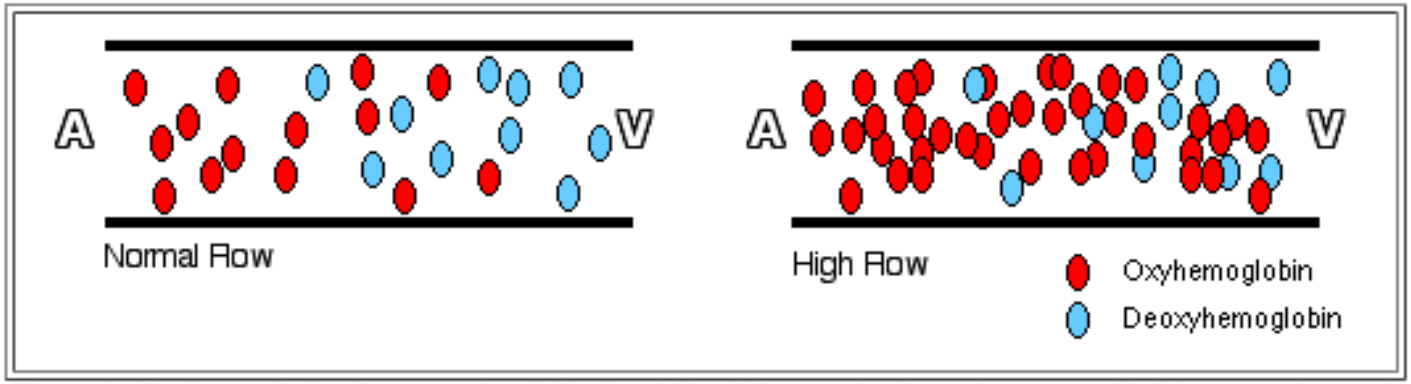
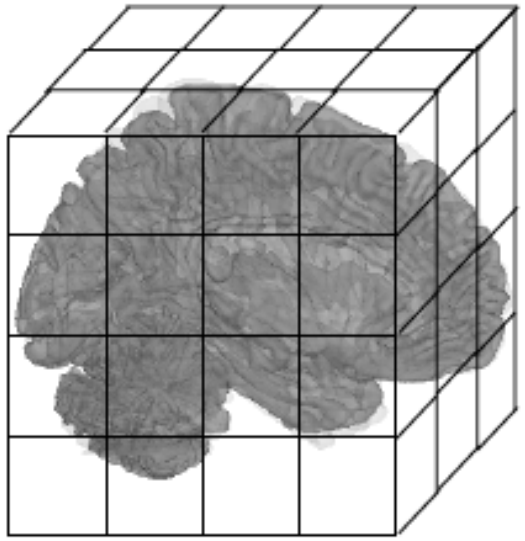


Figure 1. *During periods of neuronal activity, local blood flow and volume increase with little or no change in oxygen consumption. As a consequence, the oxygen content of the venous blood is elevated, resulting in an increase in the MR signal.*

Functional MRI

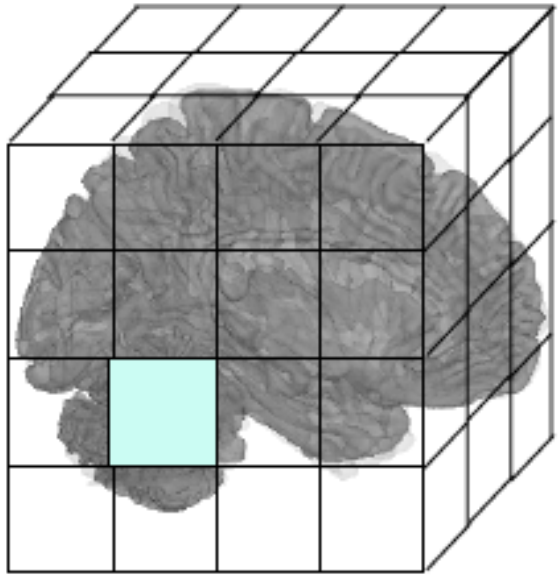
- Each image consists of ~100,000 voxels (3d pixels/cubic volumes) that span the entired space of the brain

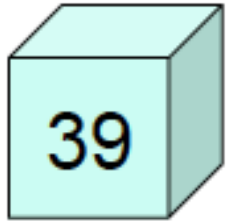


From Martin Lindquist: Coursera

Functional MRI

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

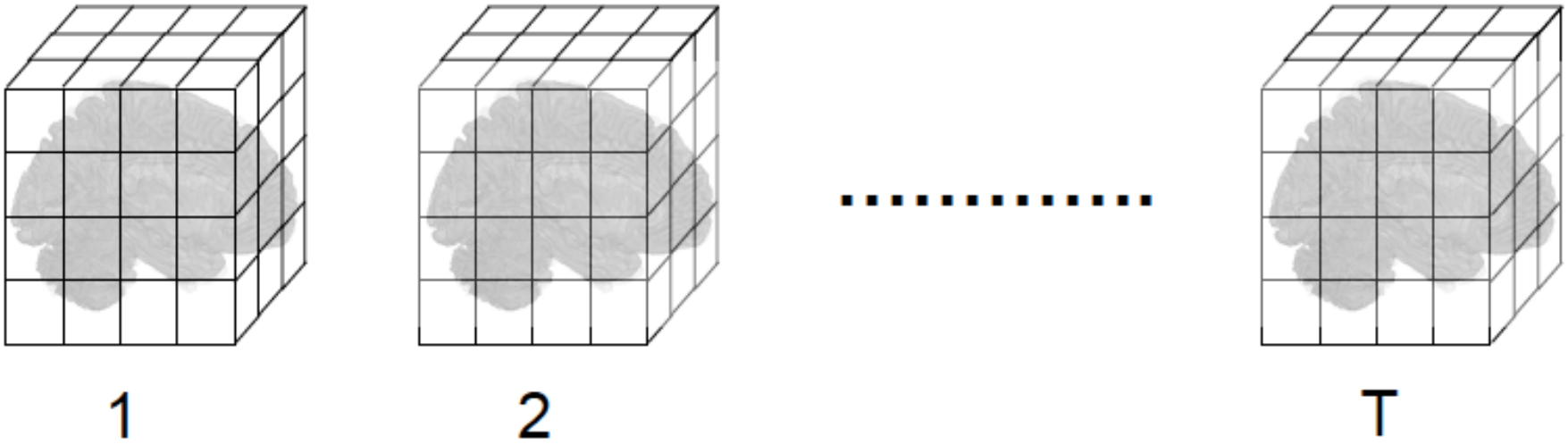




From Martin Lindquist: Coursera

Functional MRI

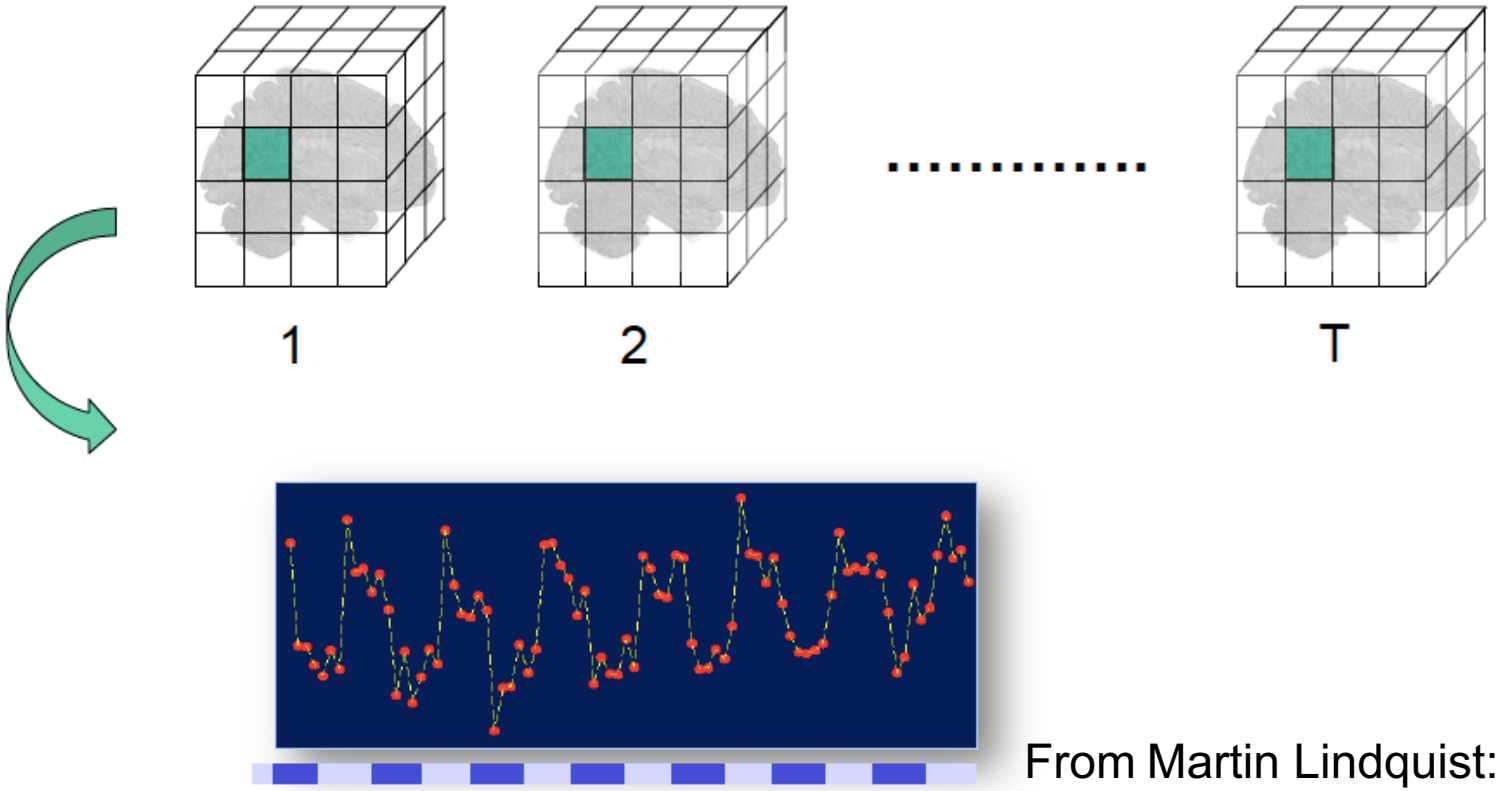
- During the course of an experiment, several hundred images may be acquired (if TR = 2, one acquisition every 2s)



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

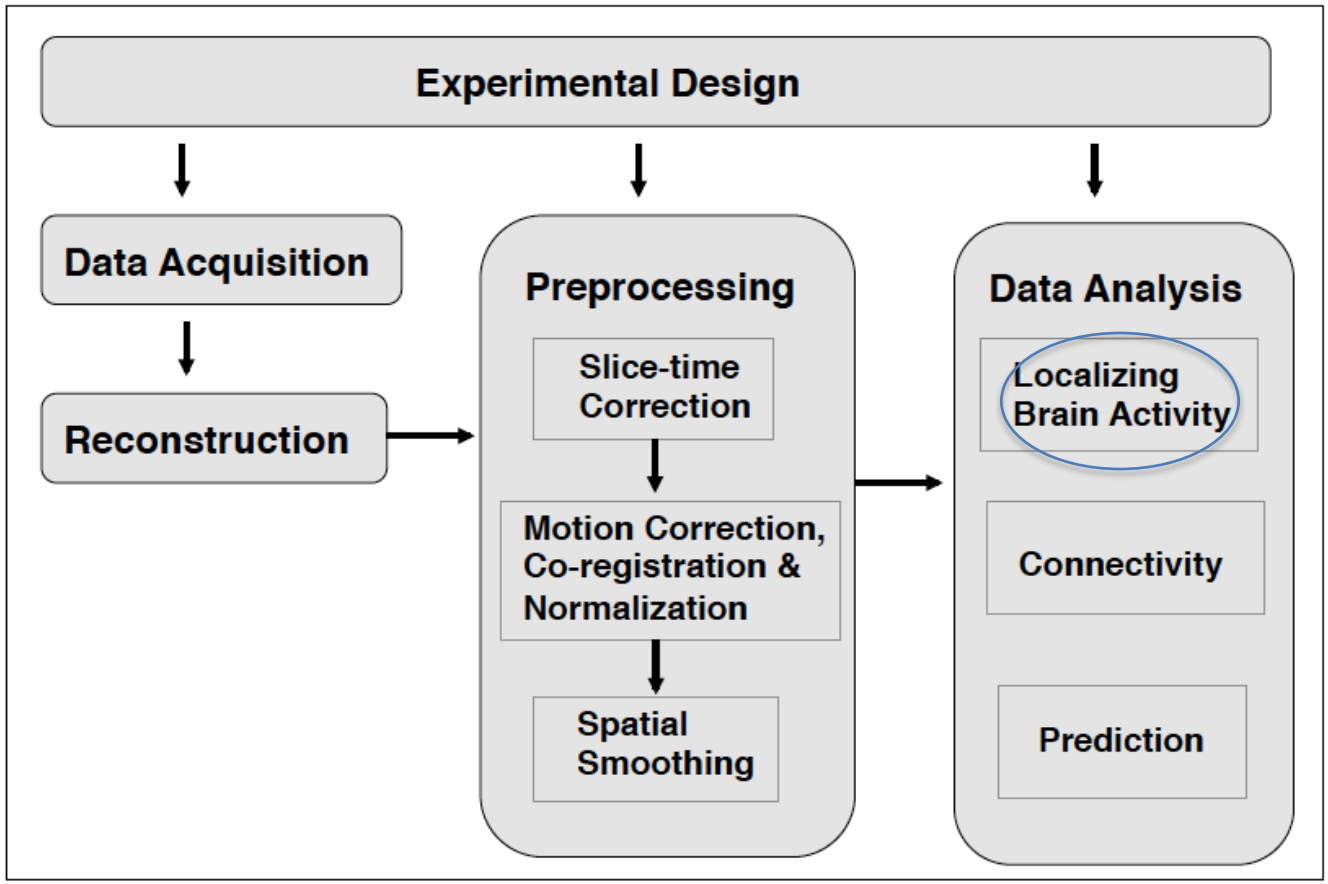
- fMRI data analysis is a massive data problem
  - Each brain volume consists of ~100,000 voxel measurements
  - Each experiment consists of hundreds of brain volumes
  - Each experiment may be repeated for multiple subjects to facilitate population inference
- This makes for a lot of data!

From Martin Lindquist: Coursera

Statistical analysis of fMRI data

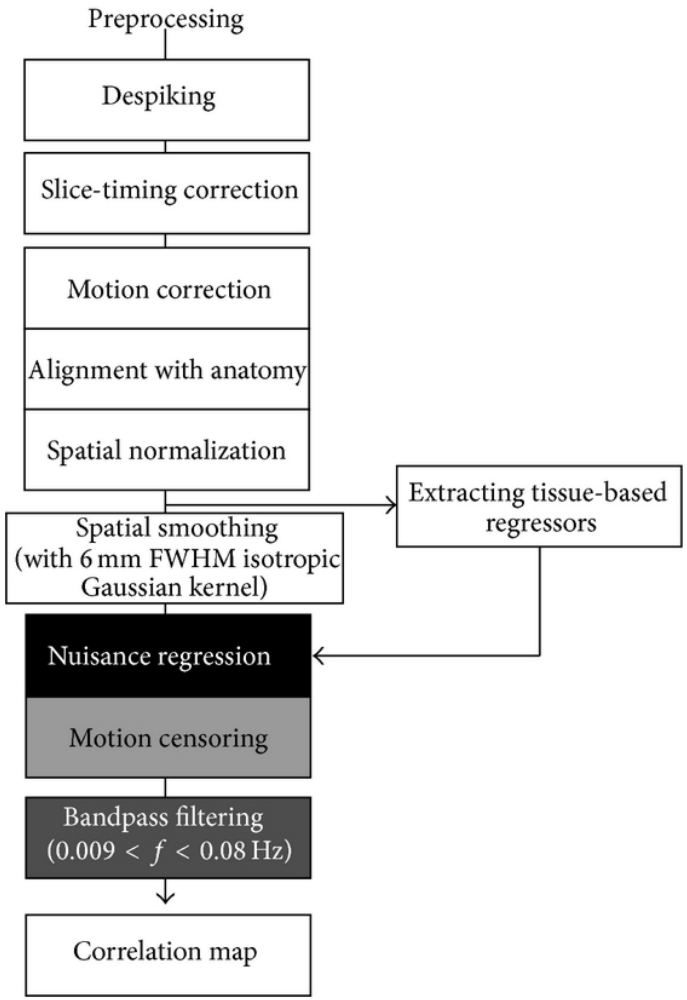
- Massive data problem
- Signal of interest is relatively weak
- The data exhibits a complicated temporal and spatial noise structure

Data processing pipeline



From Martin Lindquist: Coursera

Preprocessing Pipeline Example

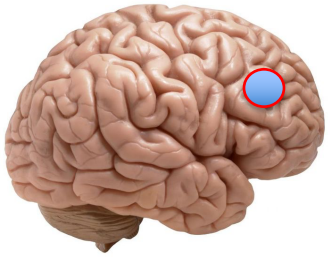


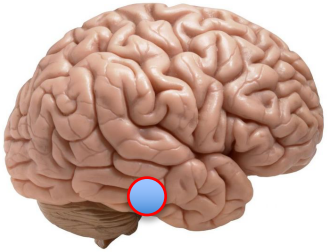
Order and specific steps can change depending on your analysis

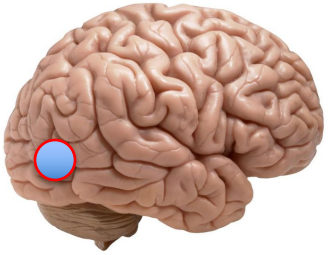
fMRI Experiments

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

Brain Localization

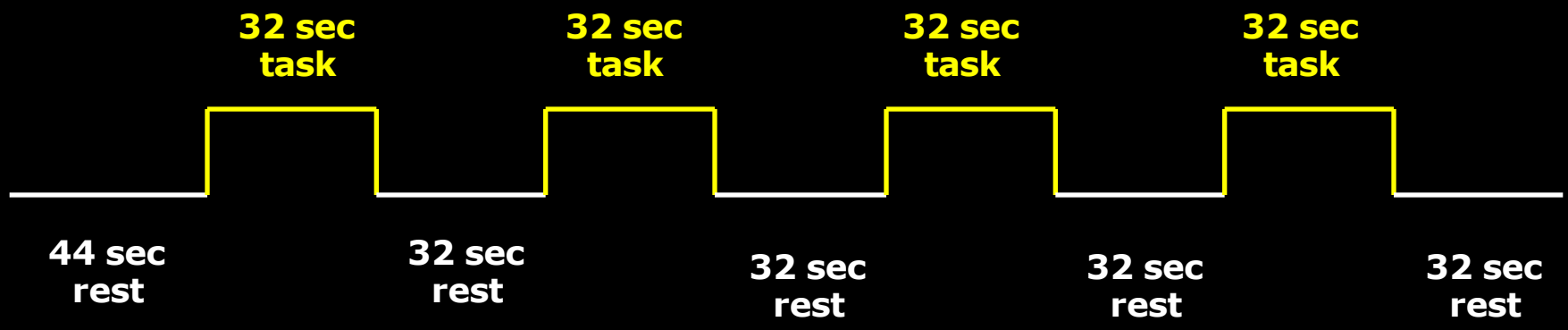




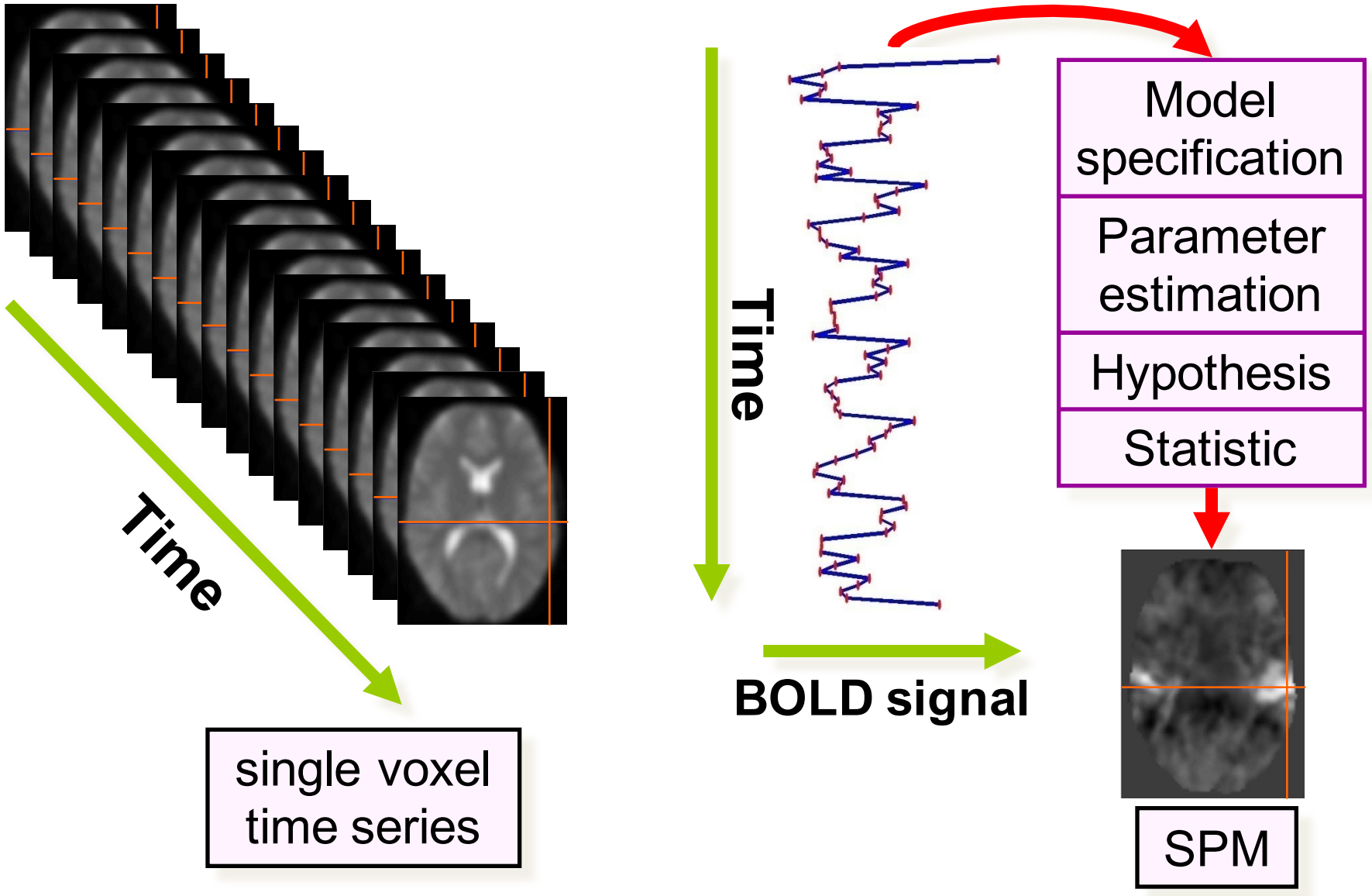


The quick fox jumped over the lazy dogs

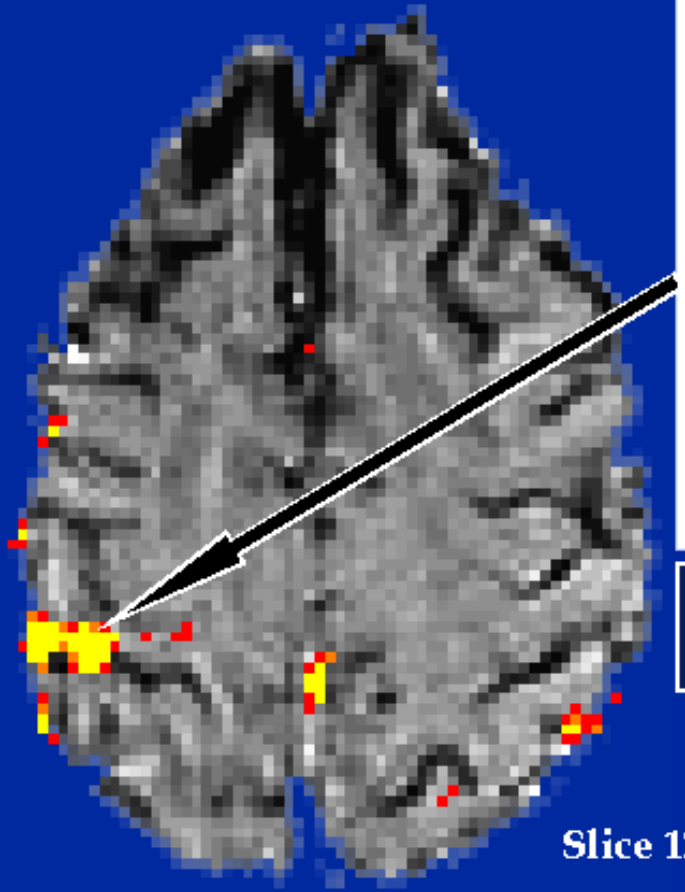
Block Design fMRI Experiment



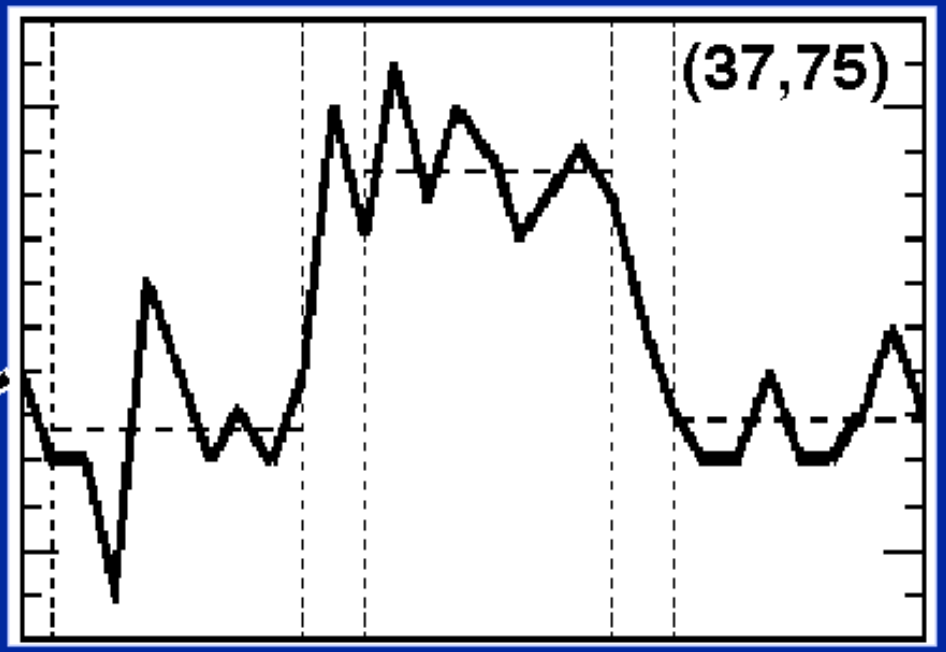
Voxel-wise time series analysis



Left Hand



Slice 12

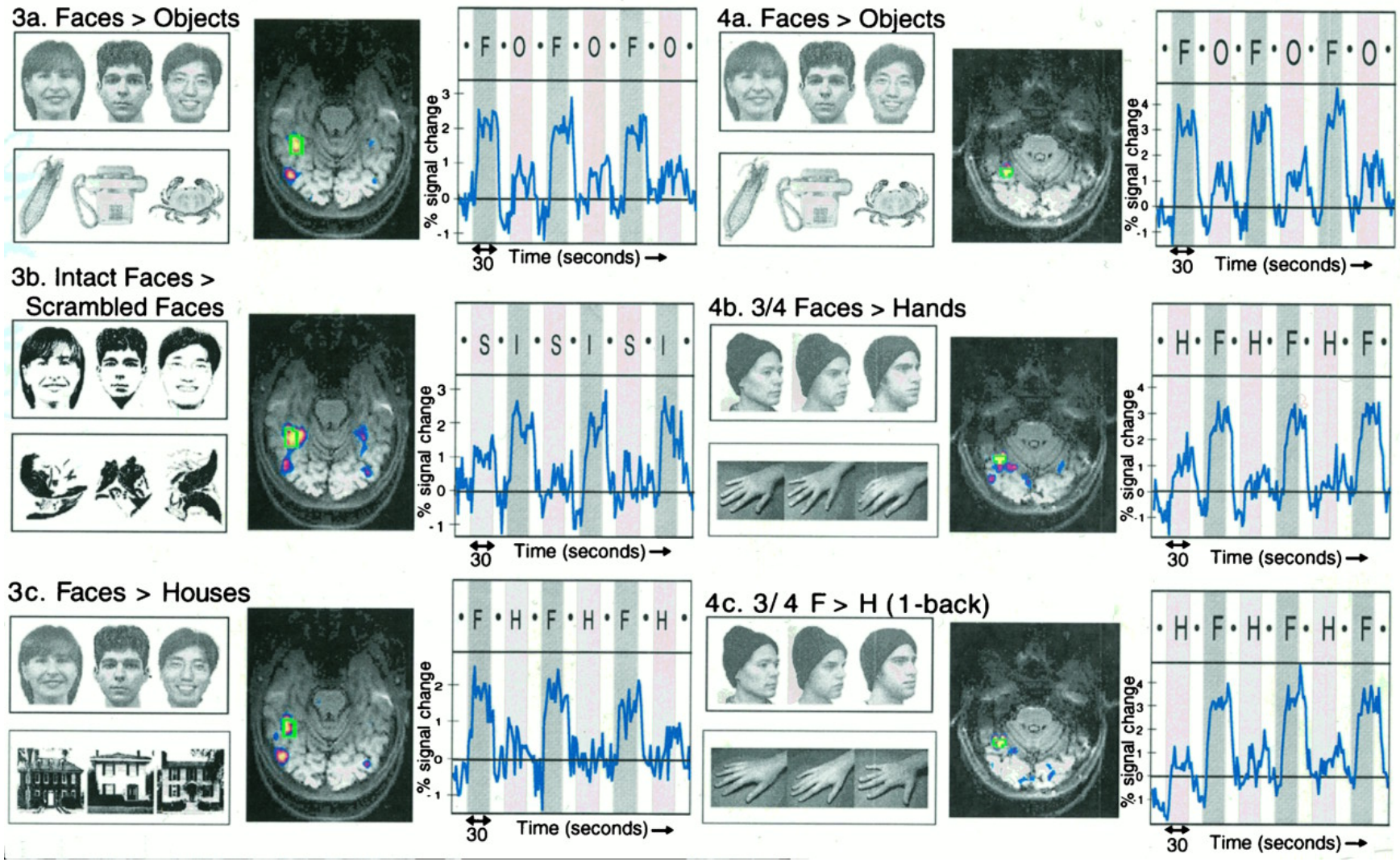


Touch

PN 5a JA

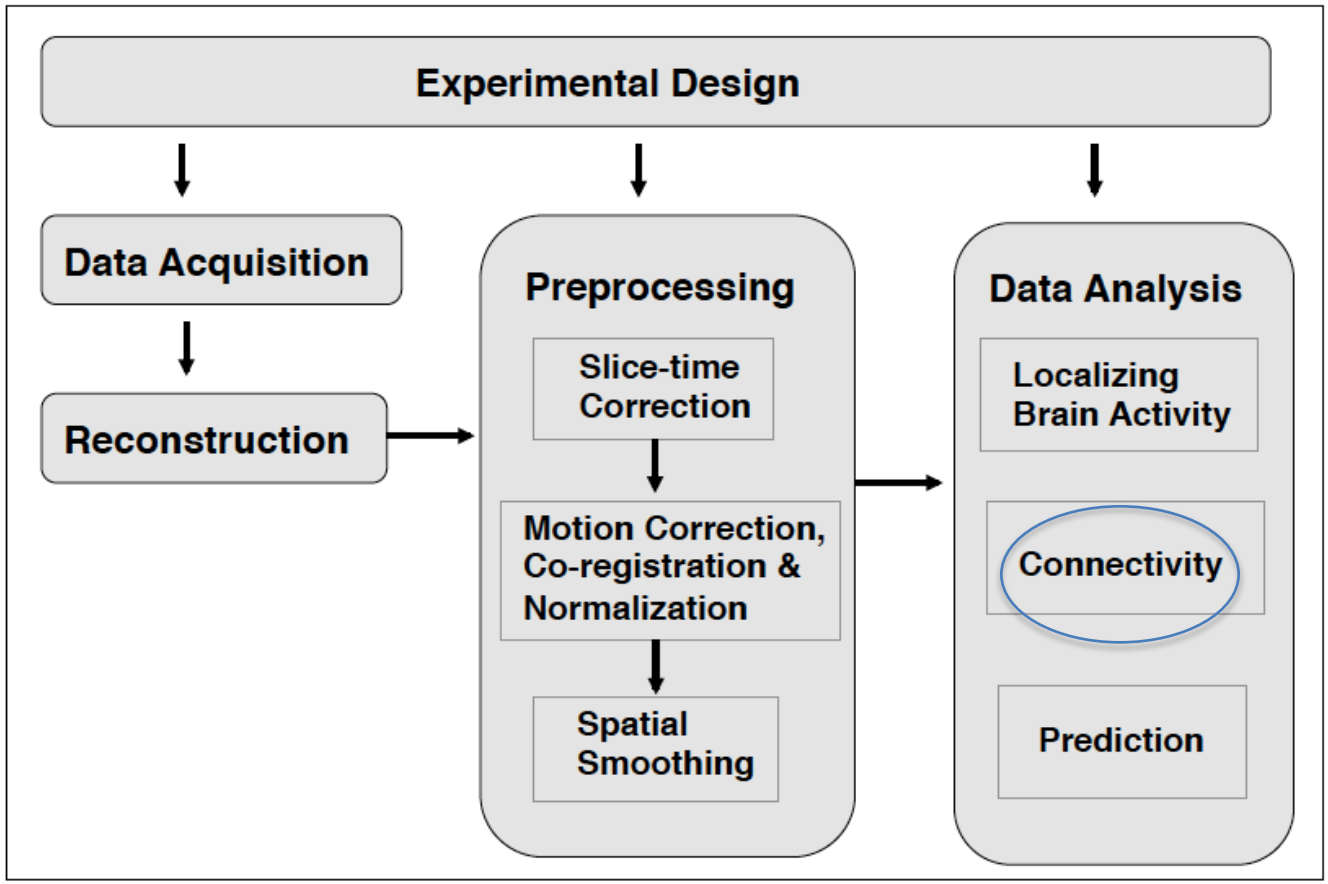
MSKCC fMRI

Data from Hirsch, J., et al



Kanwisher et al. 1997

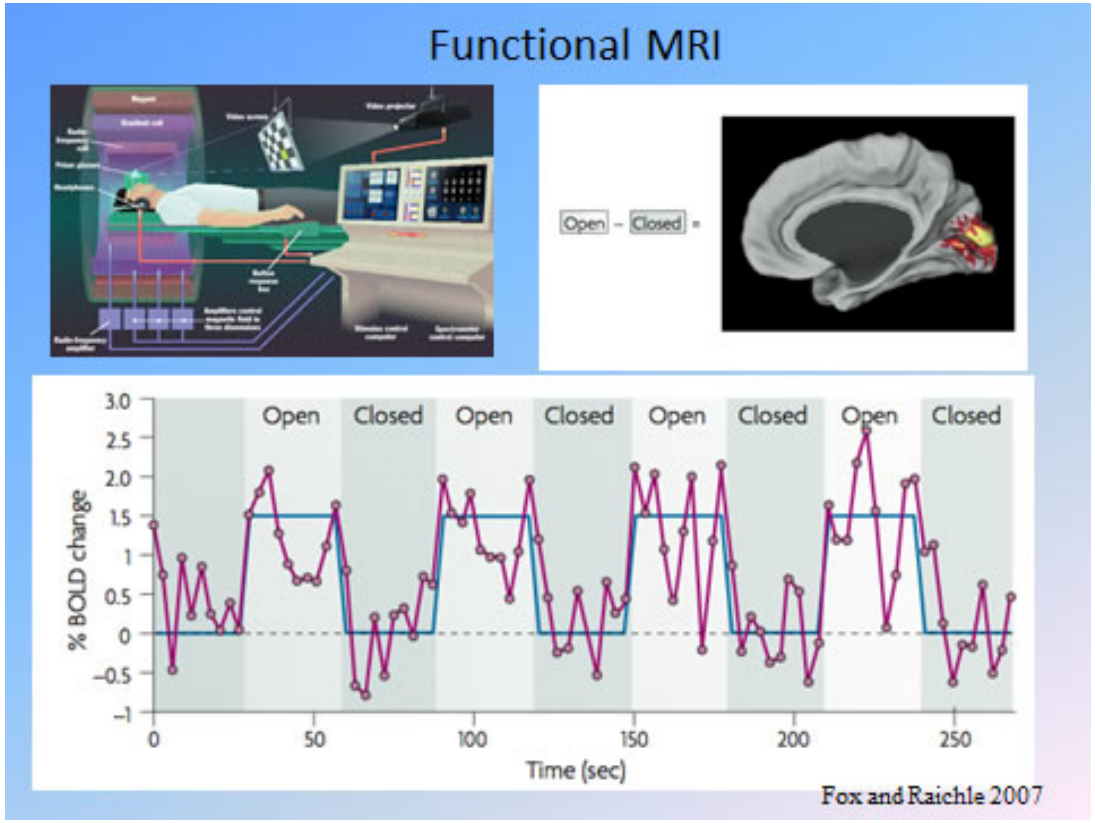
Data processing pipeline



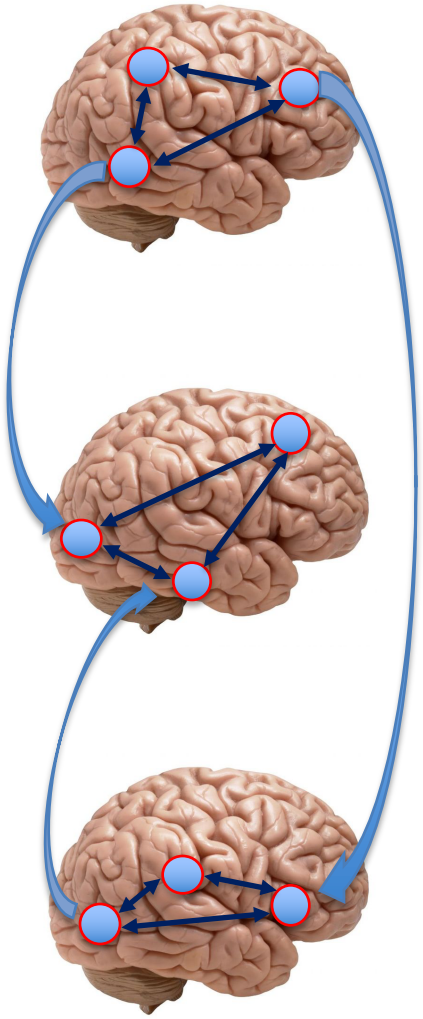
From Martin Lindquist: Coursera

Task based fMRI

- Correlation between BOLD signal and event of interest….



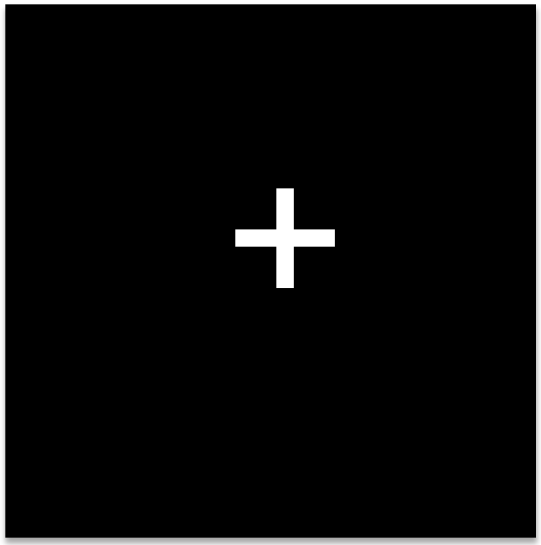
Network Neuroscience (Connectivity)



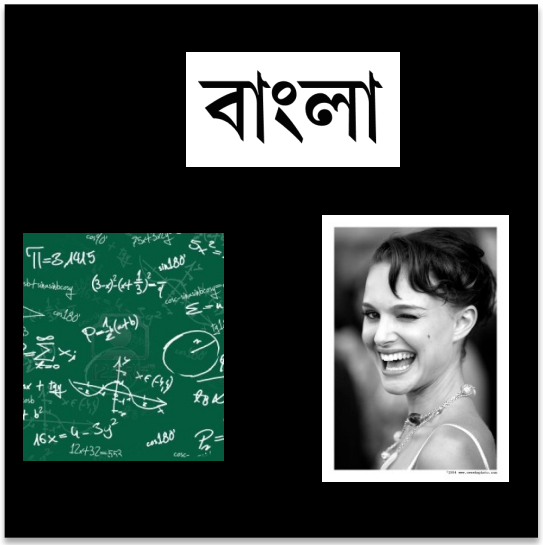
The quick fox jumped over the lazy dogs

Rest vs. Task

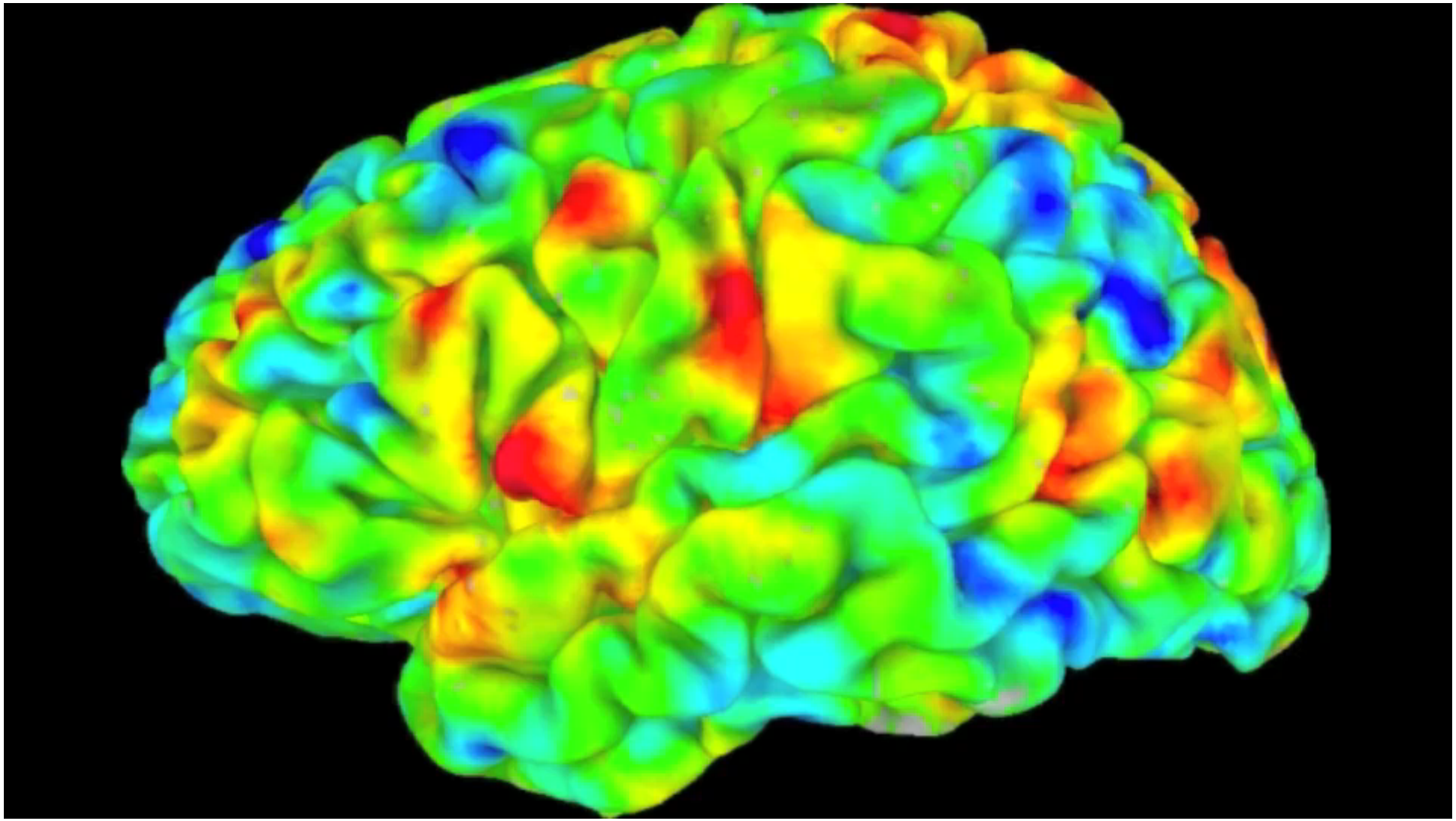
- What is your brain doing?



Vs.



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



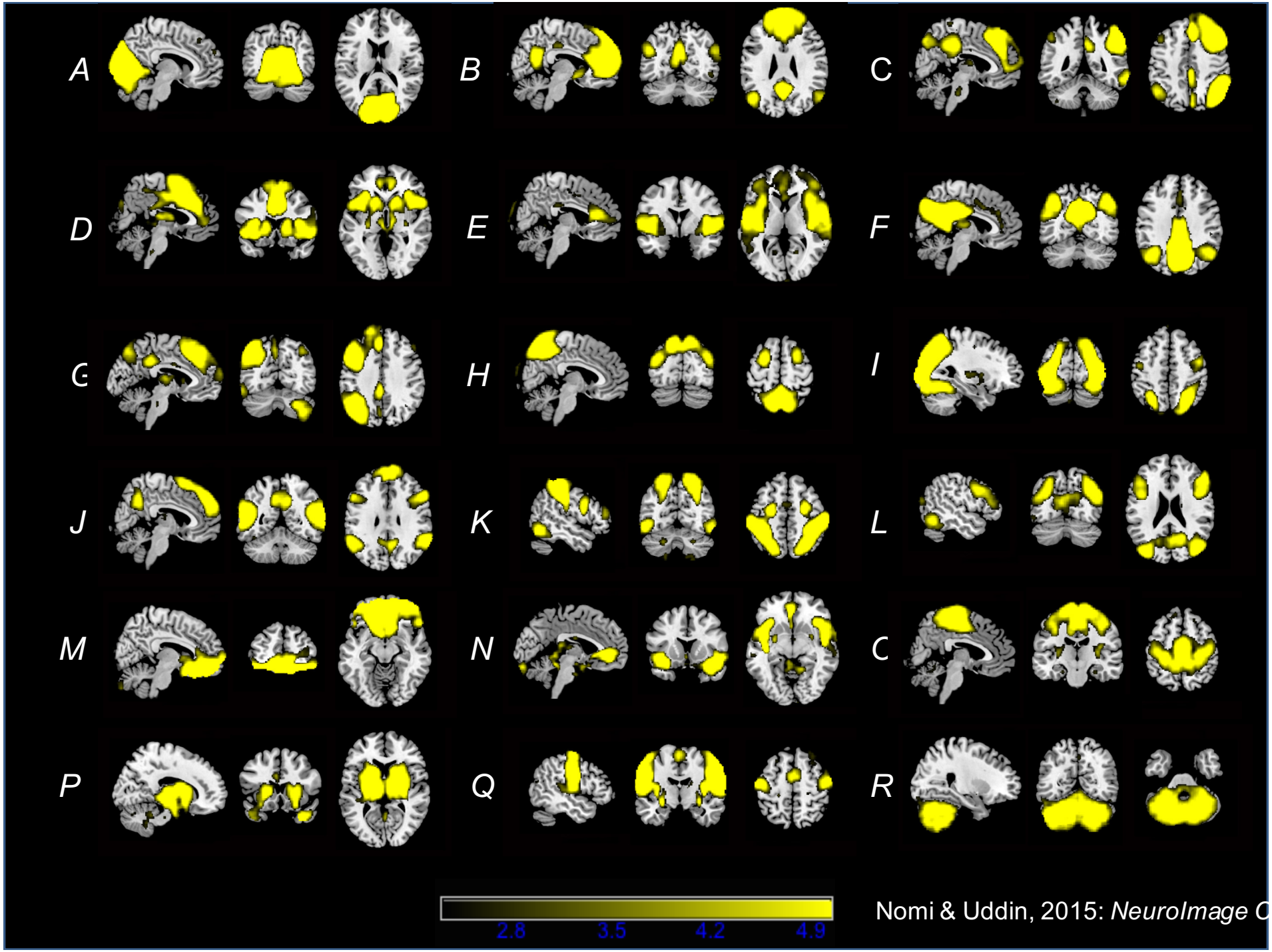
“Resting” State Networks

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

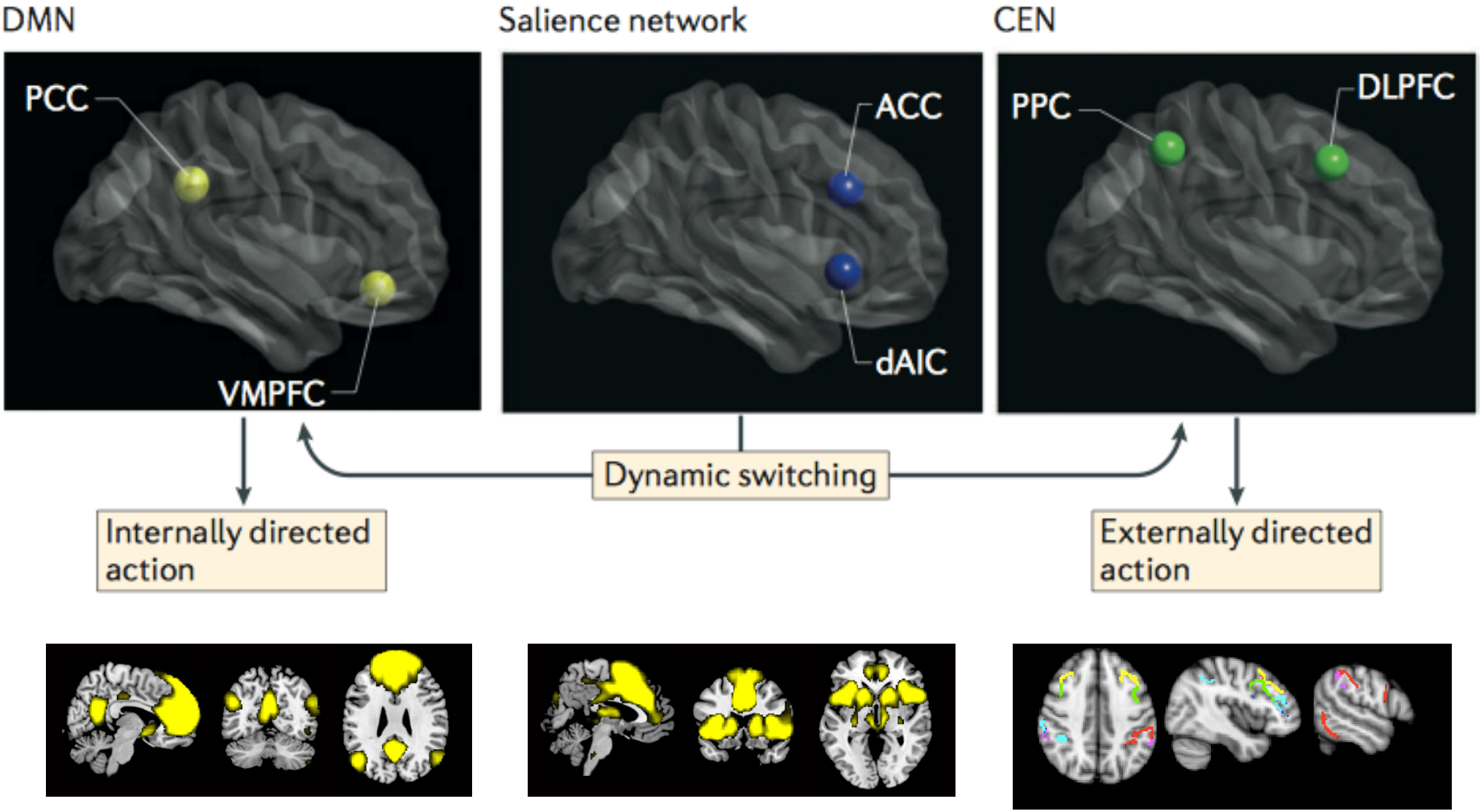
Independent Component Analysis (ICA)

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

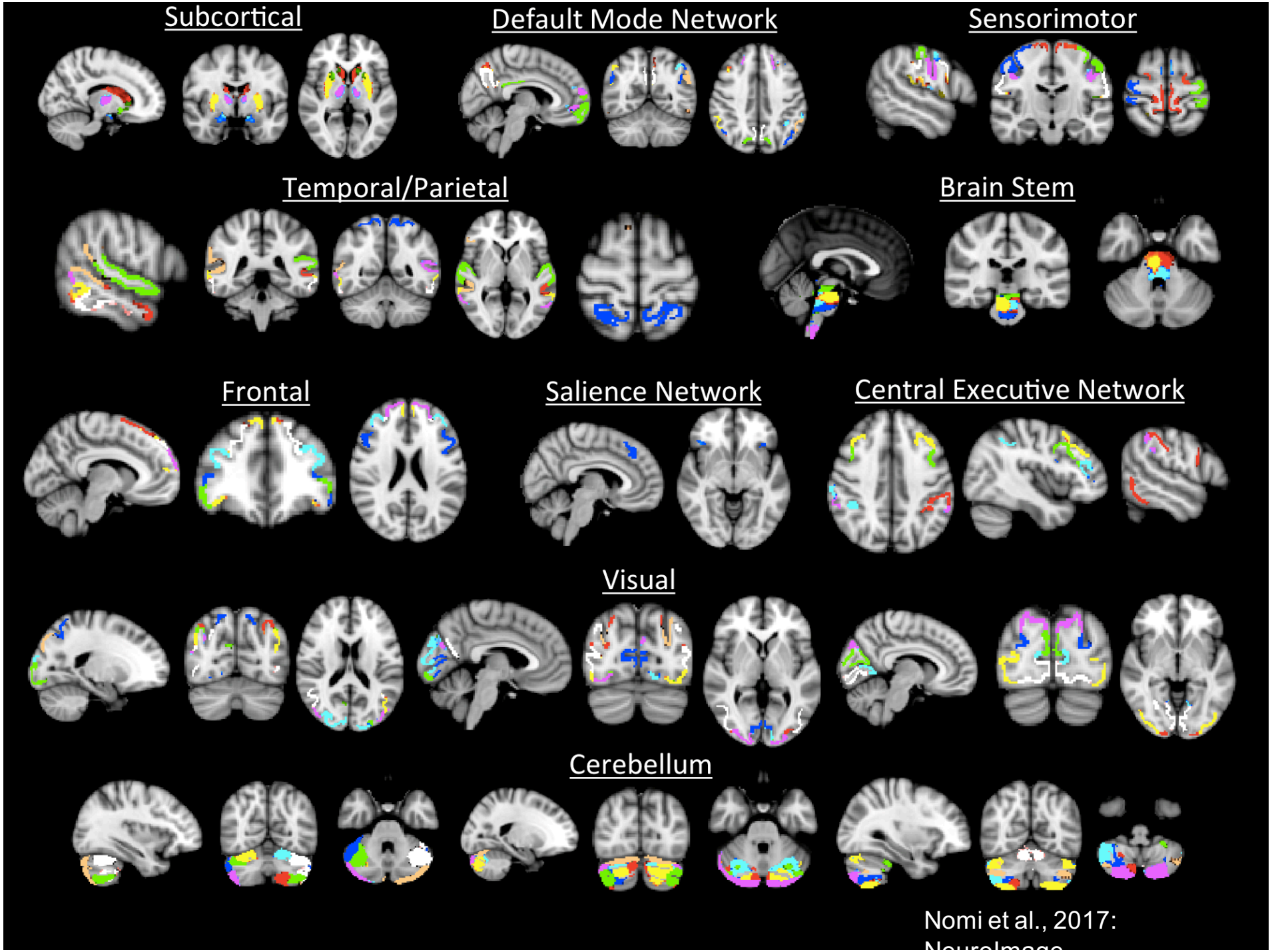
- Brain
  - Different patterns of blood flow
  - Identify voxels of the brain where blood flow is similar to each other, but different from other voxels


A
B
C
D
E
F
G
H
I
J
K
L
M
N
C
P
Q
R
2.8
3.5
4.2
4.9
Nomi & Uddin, 2015: *NeuroImage C*

Internal and External Cognition



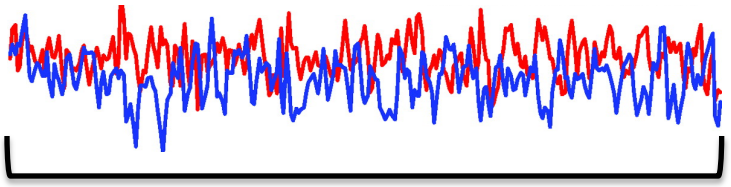
Menon & Uddin, 2010


Subcortical
Default Mode Network
Sensorimotor
Temporal/Parietal
Brain Stem
Frontal
Salience Network
Central Executive Network
Visual
Cerebellum
Nomi et al., 2017:

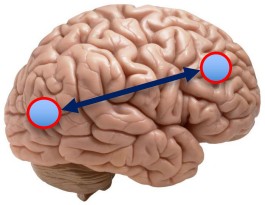
Brain Dynamics

Static Connectivity

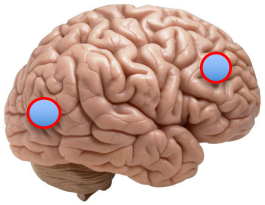
(Biswal et al., 1995)



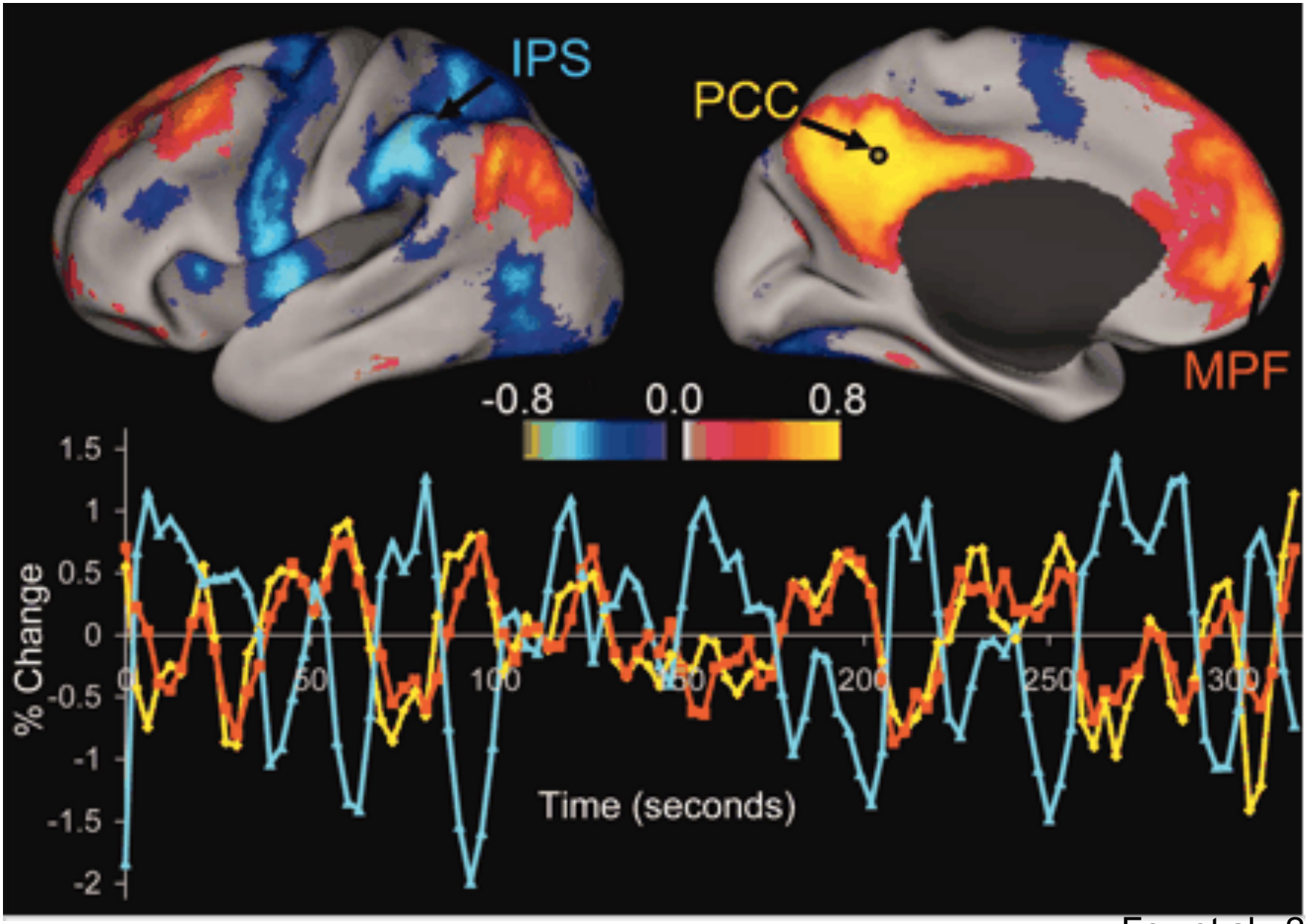
Strong



Weak

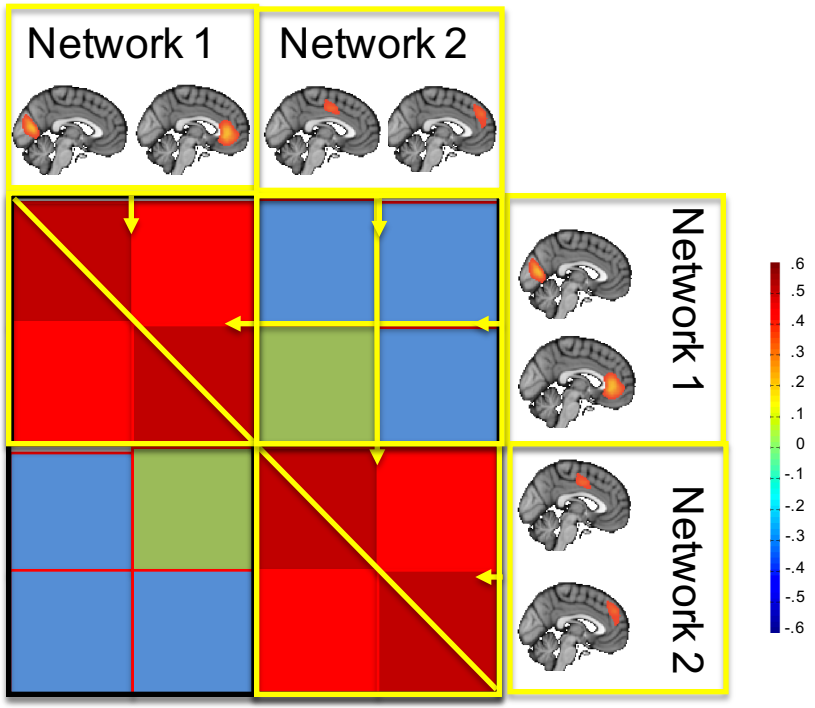


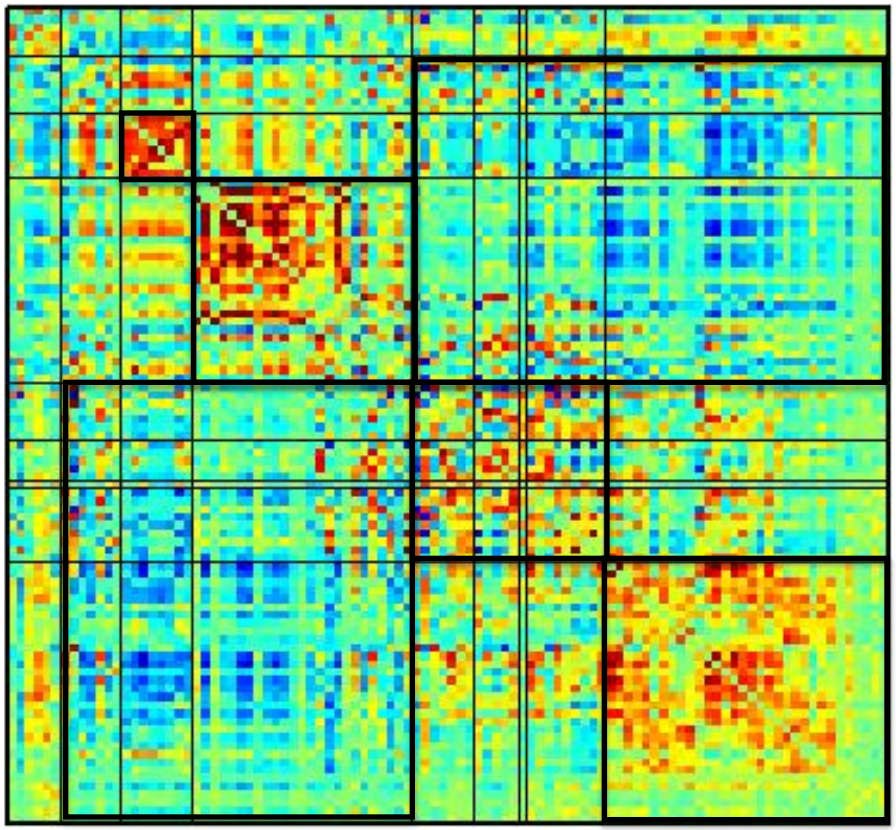
Functional Connectivity



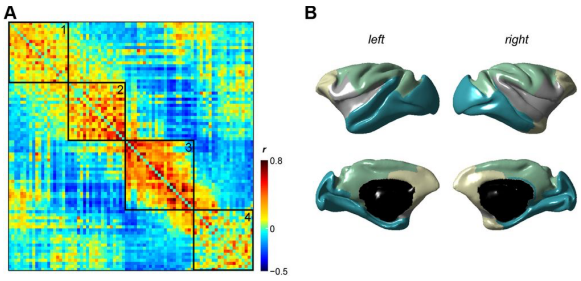
Fox et al., 200

Correlation Matrix

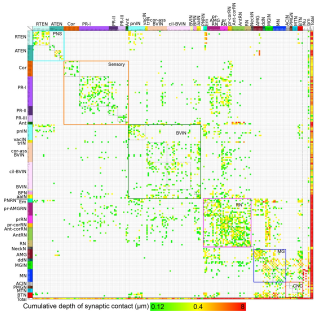




Nomi et al., 2017: *NeuroImage*



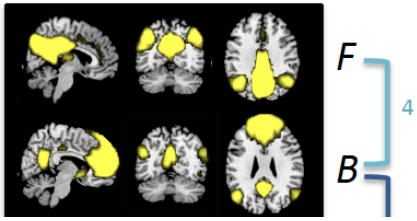
Macaque (Shen et al., 2012)

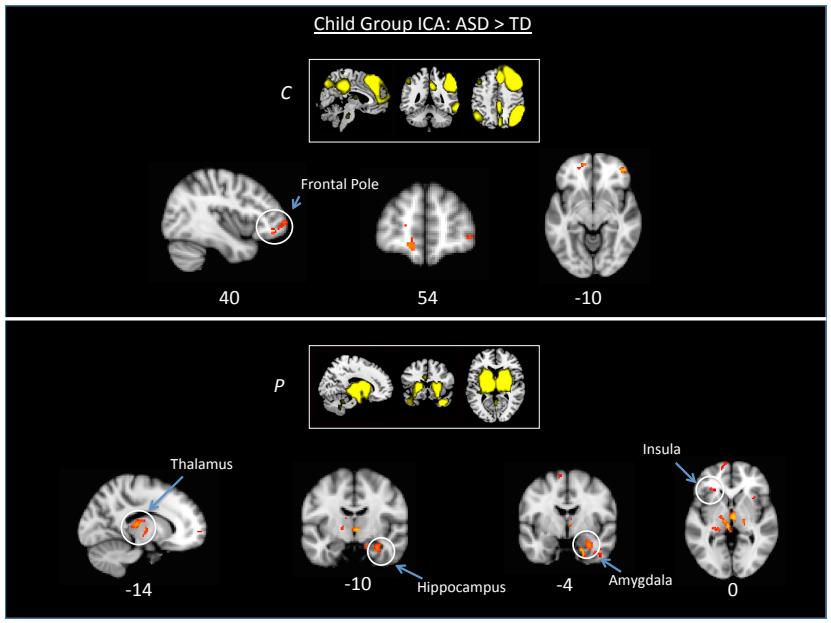


Tadpole (Ryan et al., 2016)

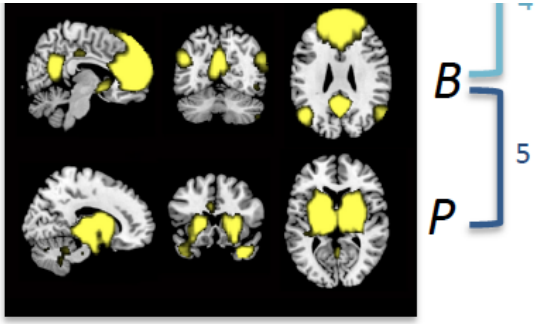
Static Network Connectivity in Autism across Development

- Children
  - Within Network
    - ASD > TD
  - Between Network
    - TD > ASD





- Adolescents
  - Between Network
    - TD > ASD



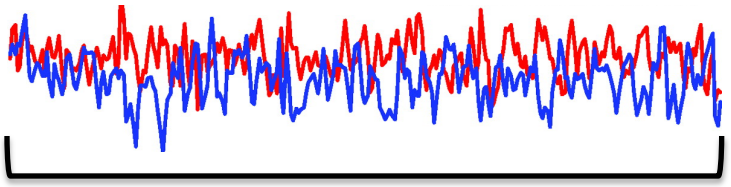
- Adults
  - No differences

Nomi & Uddin, 2015: *NeuroImage*

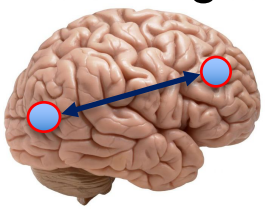
Brain Dynamics

Static Connectivity

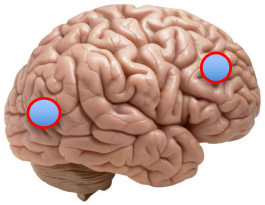
(Biswal et al., 1995)



Strong

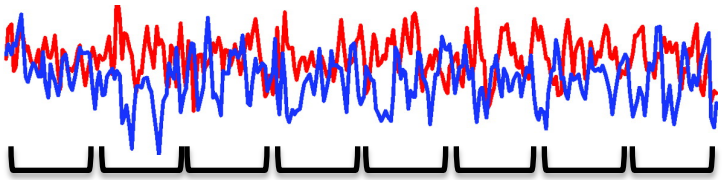


Weak

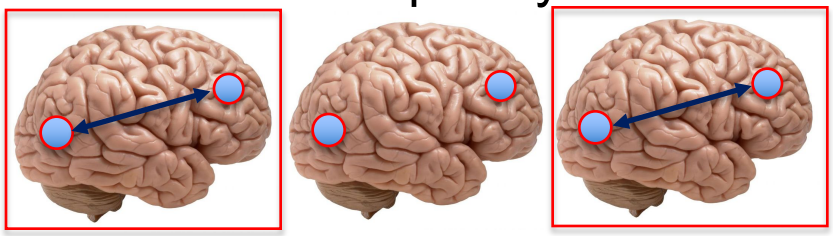


Dynamic Connectivity

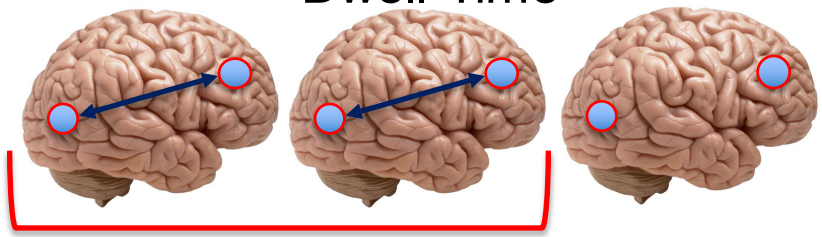
(Chang and Glover, 2010; Allen et al., 2012)



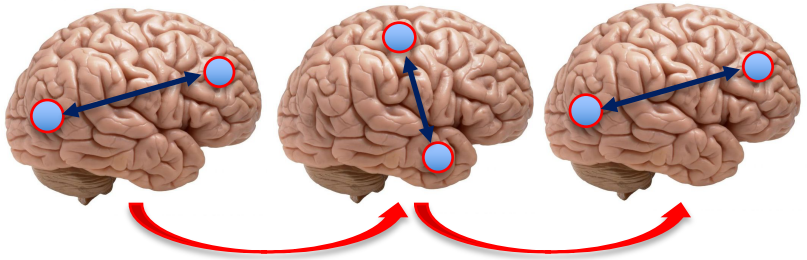
Frequency

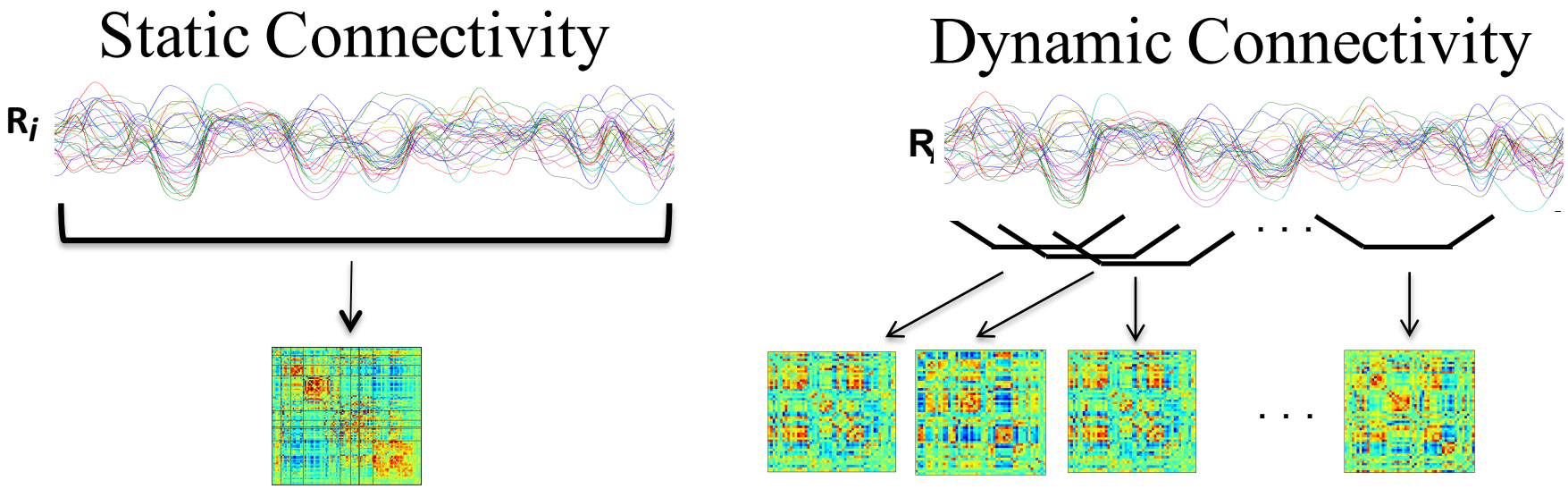


Dwell Time



Transitions





Nomi et al., 2016 *Human Brain Mapping*; **Nomi** et al., 2017 *NeuroImage*; Cheng, **Nomi** et al., 2017 *Human Brain Mapping*; Ciric, **Nomi** et al., 2017 *Scientific Reports;* Steimke, **Nomi** et al., *in press SCAN*

Flexible Cognition in Autism Spectrum Disorder (ASD)

- Flexible Cognition
  - Quickly adapt and respond to your environment
  - Facilitate learning and personal growth

- ASD
  - Affects nearly 1:68 children (CDC, 2016)
  - Family life, School life, Work life

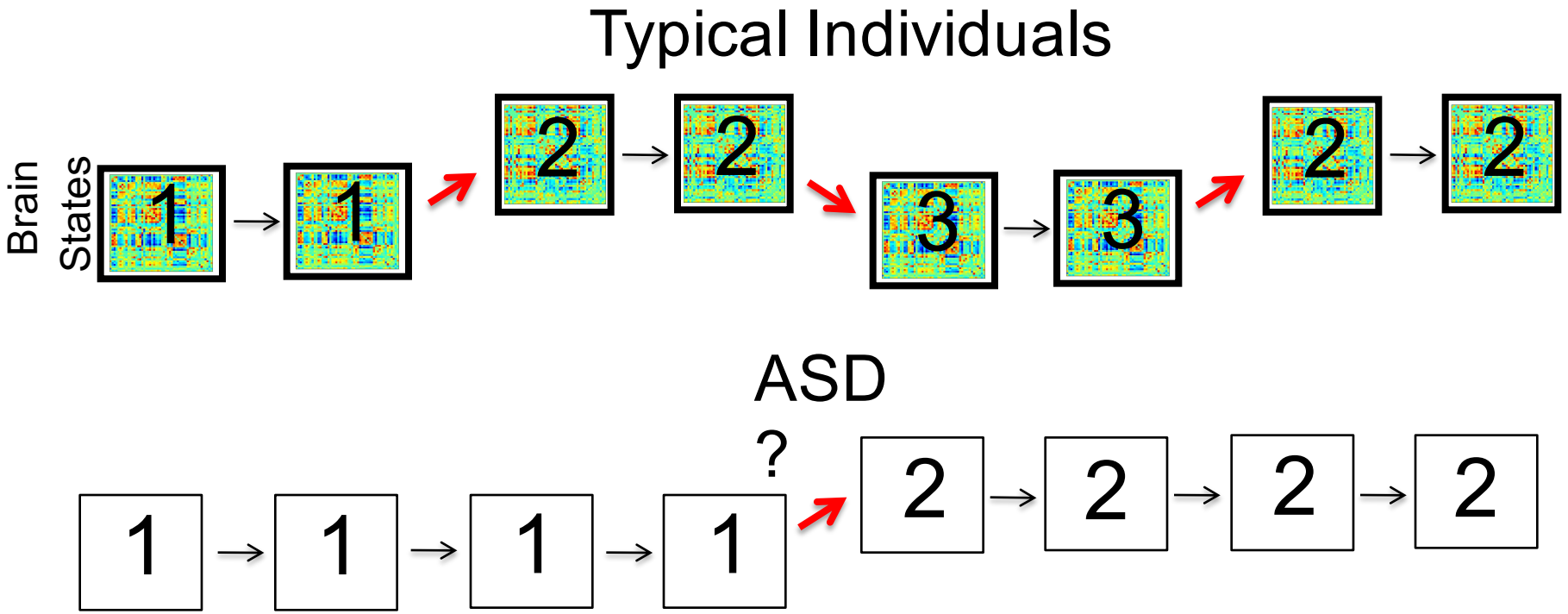
Restricted and Repetitive Behaviors in ASD

Behavioral Inflexibility ⟷ Cognitive/Neural Inflexibility (Geurrts et al., 2009)

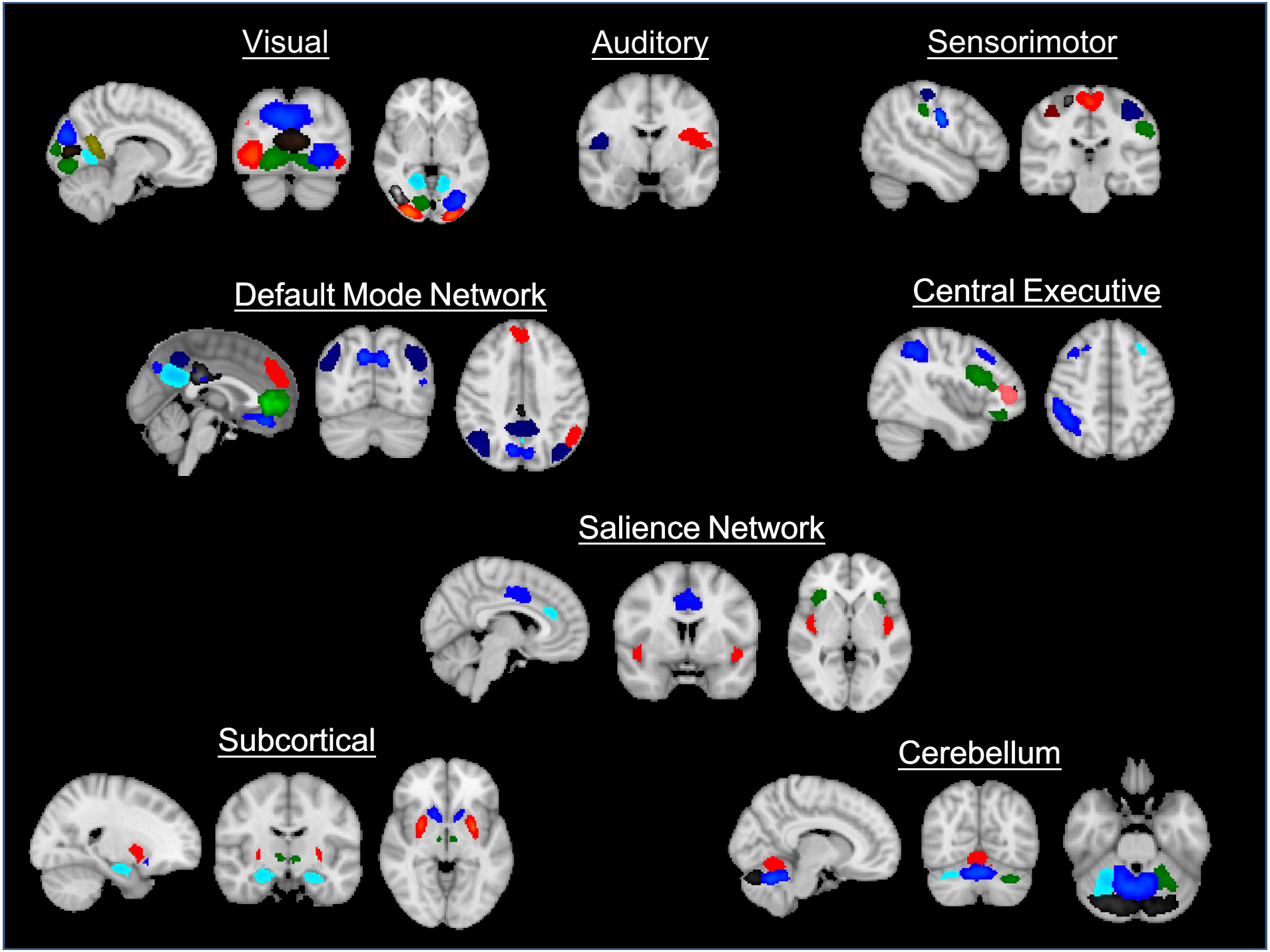
Restricted and Repetitive Network Switching

- 40 (Typical)
- 34 (ASD)
  - 18-39 years old

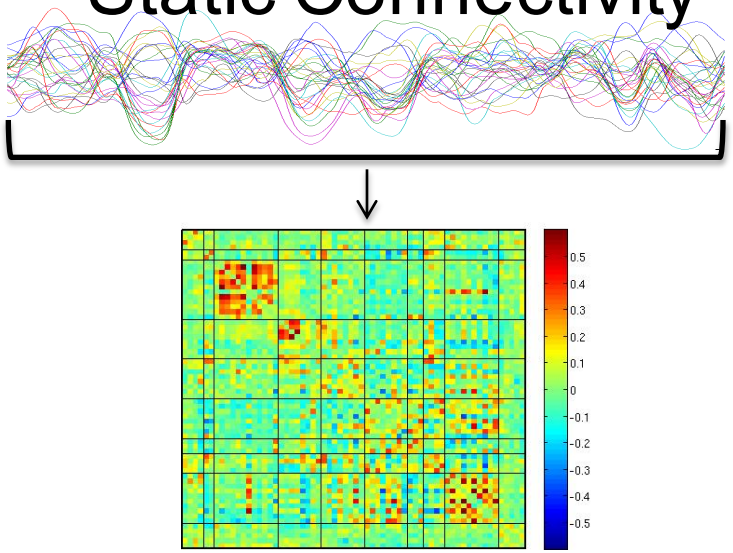
ABIDE
Autism Brain Imaging Data Exchange



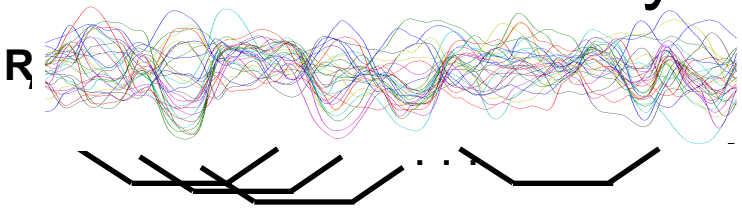
Preliminary Data


Visual
Auditory
Sensorimotor
Default Mode Network
Central Executive
Salience Network
Subcortical
Cerebellum

Static Connectivity

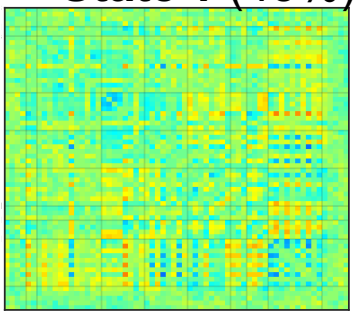


Dynamic Connectivity

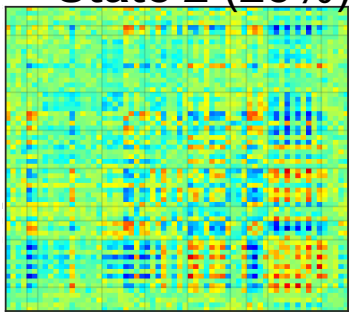


K-means Clustering

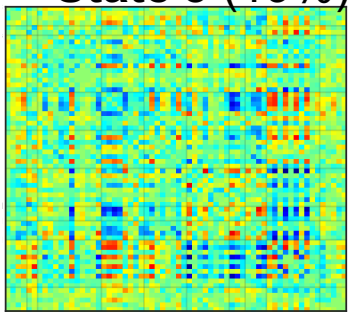
State 1 (45%)



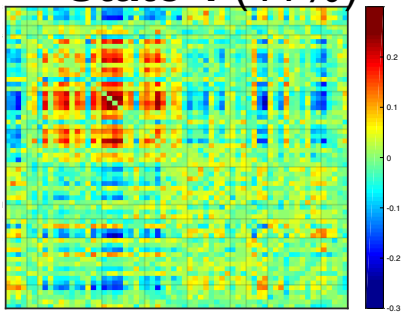
State 2 (25%)



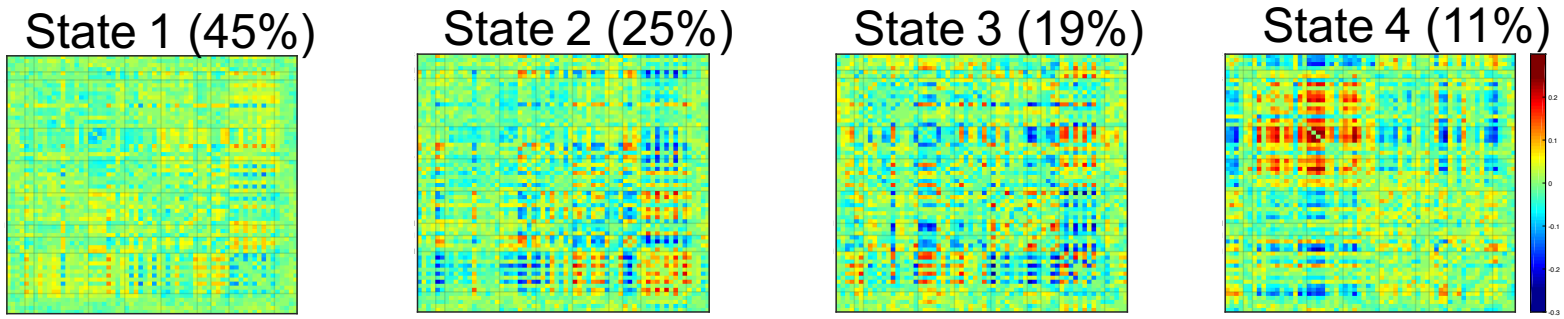
State 3 (19%)

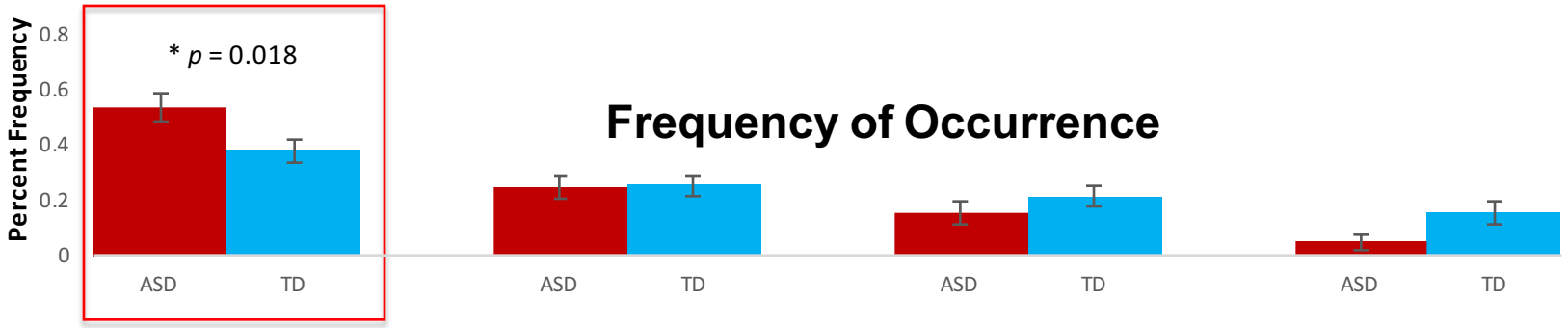


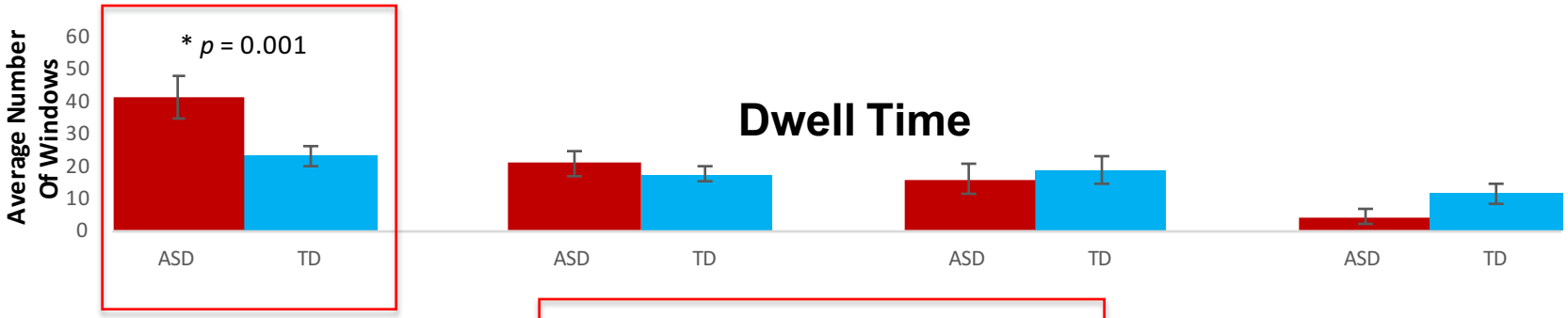
State 4 (11%)

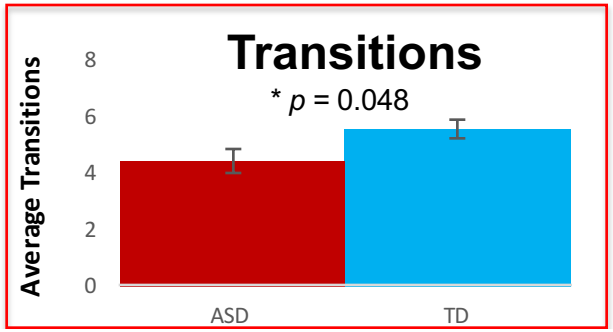


Preliminary Data







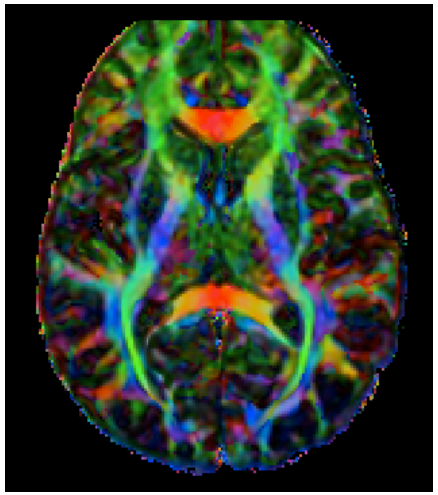


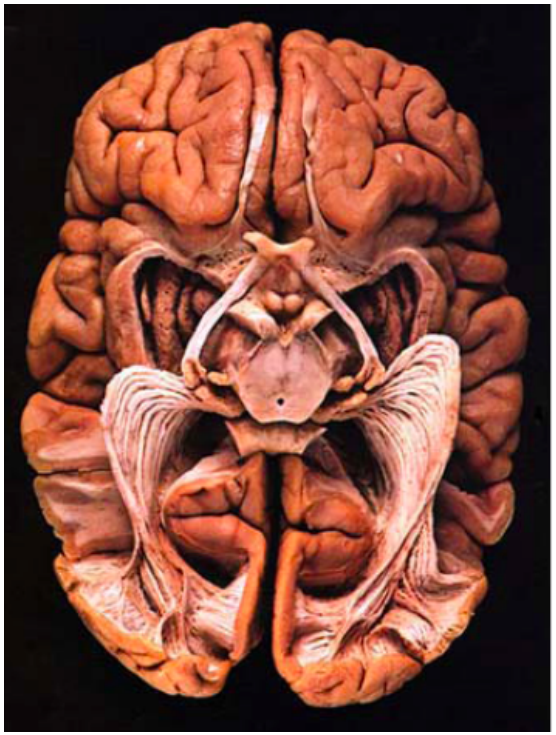
Preliminary Data

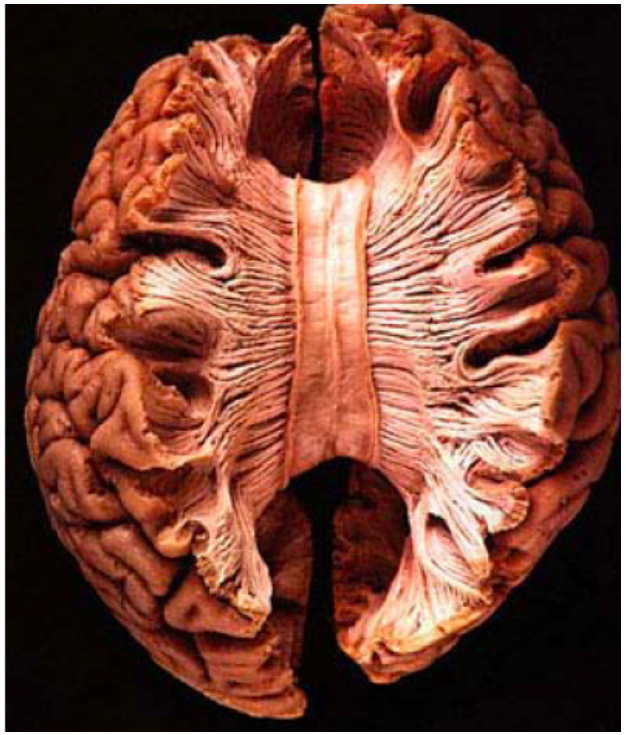
Diffusion Tensor Imaging (DTI)

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

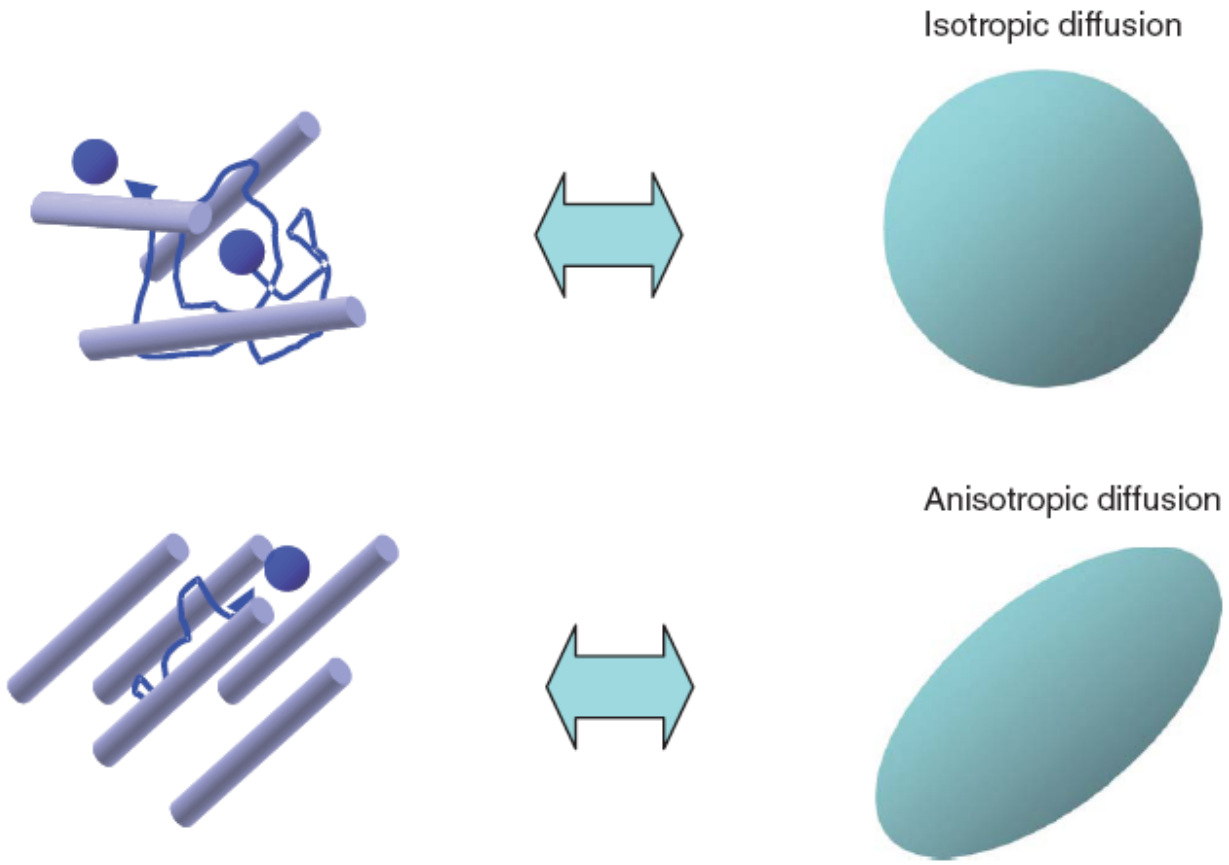
(anatomical connectivity)



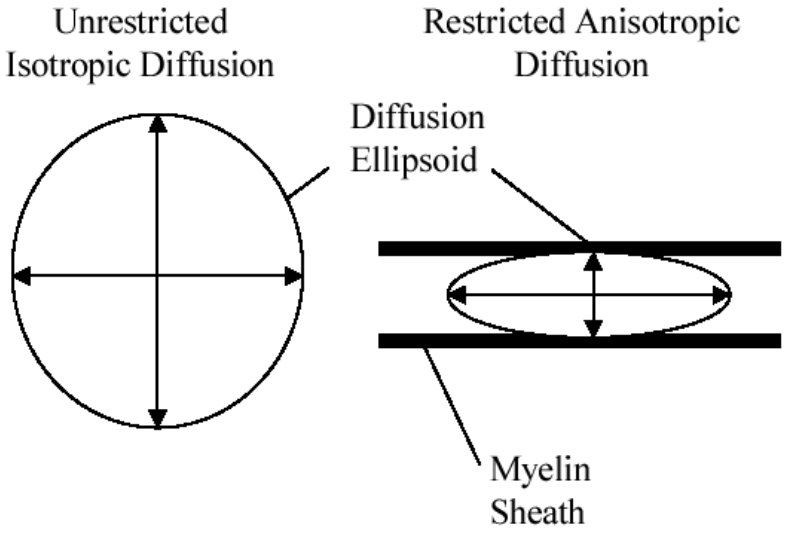


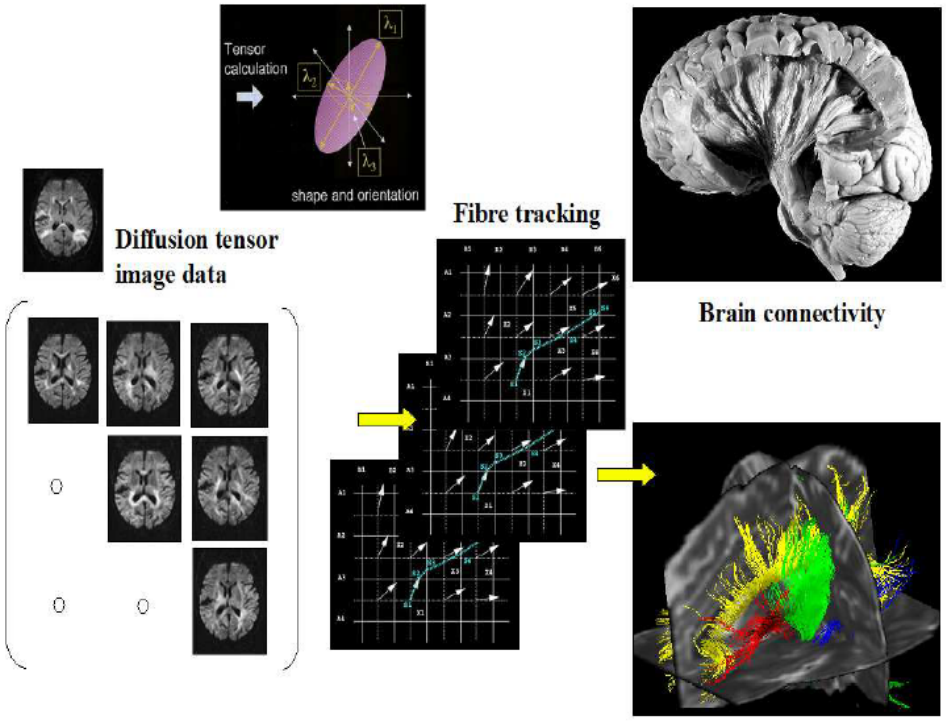


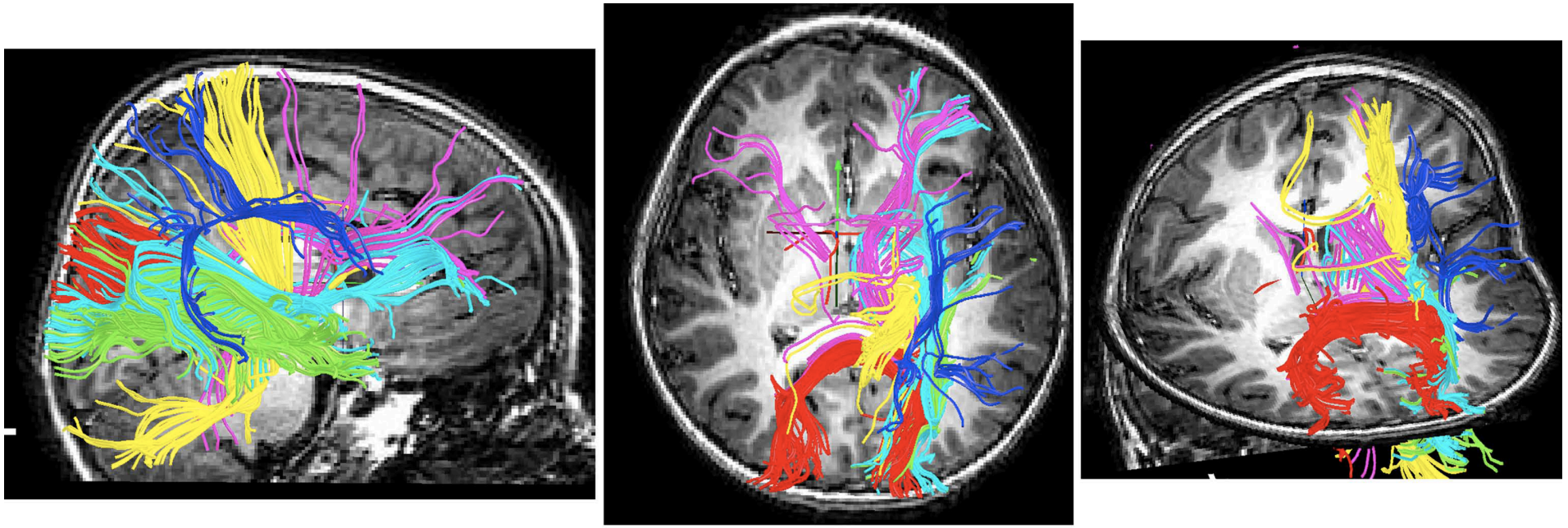
Water diffusion in structured tissue



DTI


Unrestricted
Isotropic Diffusion
Restricted Anisotropic
Diffusion
Diffusion
Ellipsoid
Myelin
Sheath


Tensor
calculation
shape and orientation
Diffusion tensor
image data
Fibre tracking
Brain connectivity



Inferior fronto-occipital

Forceps major

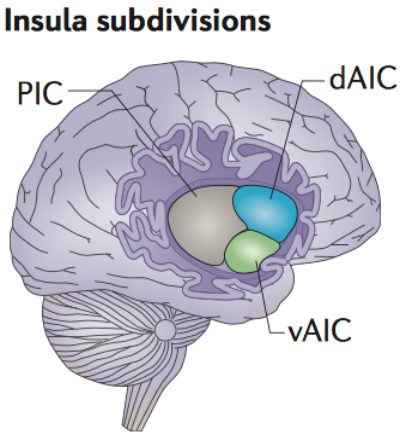
Corticospinal tract

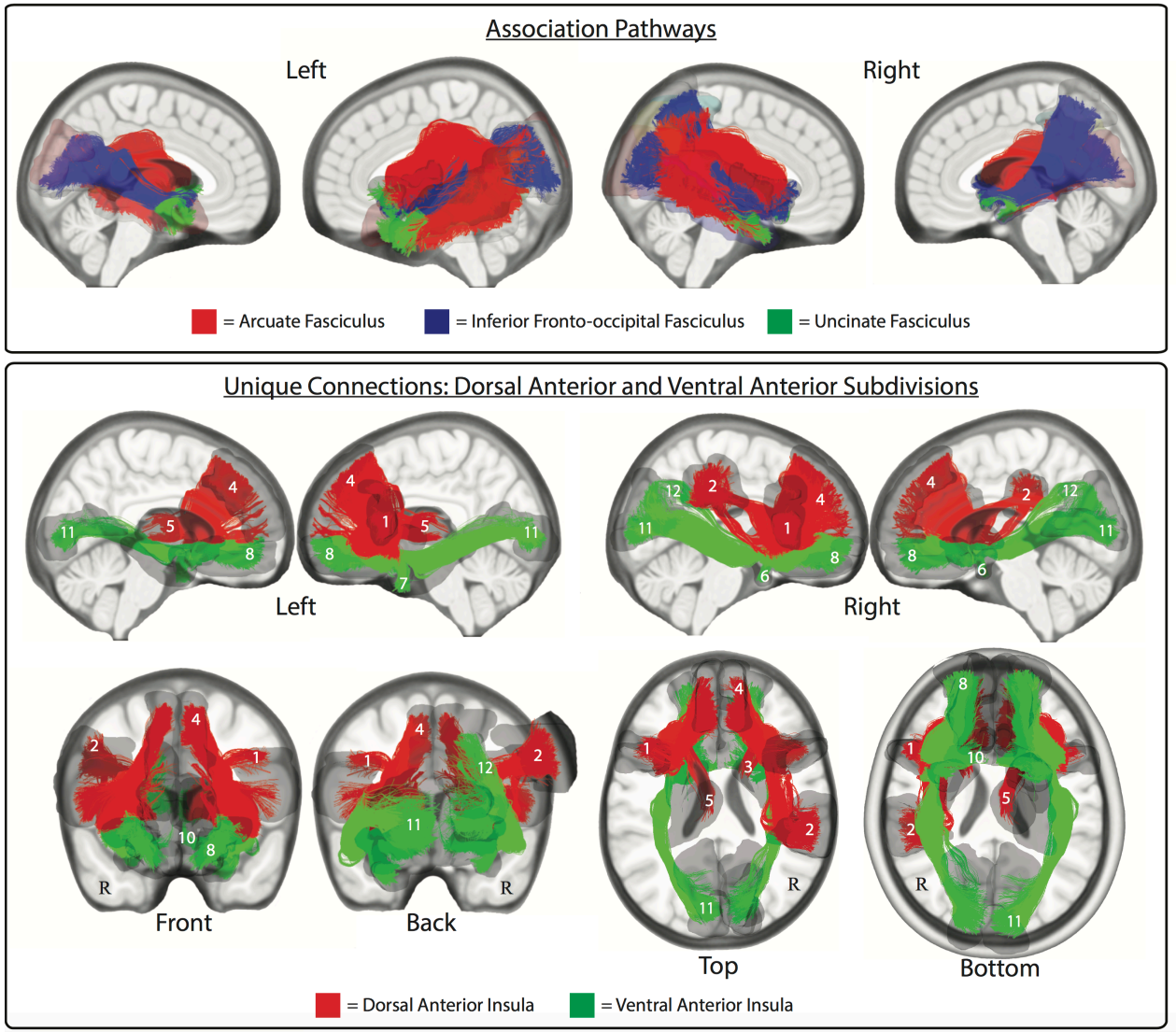
Anterior thalamic radiation

Inferior longitudinal fasciculus

Superior longitudinal fasciculus

Insula: Structural Connections





Nomi et al., In Press: *Cerebral Cortex*

Thanks!

UNIVERSITY OF MIAMI

BCCL Brain Connectivity and Cognition Laboratory

- Lucina Uddin
  - Taylor Bolt
  - Shruti Gopal-Vij
  - Dina Dajani

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  - Chiemeka Ezie

•New Mexico
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  - Eswar Damaraju
  - Srinivas Rachakonda

•FIU
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  - Kris Farrant
  - Iris Broce-Diaz

•Colorado State University/University of West Scotland
  - Lucy J. Troup

•Pamona College
  - Ajay Satpute
  - Rastko Ciric

•University of Electronic Science and Technology of China
  - Huafu Chen
  - Heng Chen

•Charité Universitätsmedizin Berlin
  - Walter Henrik
  - Rosa Steimke

•University of Pennsylvania
  - Rastko Ciric