Some Announcements

- For those taking lab: Meet in this lecture hall today at 2:00 for lab preview
- Lectures available each afternoon on the course website:
  - https://courses.lsa.umich.edu/fmri-training-course/

Other Resources

1. You can re-watch the lecture videos from this training course

2. The free online course site called Coursera has some great classes that you can take as a formal class or just watch the videos at your own pace such as
"Statistical Analysis of fMRI Data":
https://www.coursera.org/course/fmri

3. There is also a new course being offered that seems like it may be good: "Exploring Neural Data":
https://www.coursera.org/course/neuraldata

4. This is a useful course to learn about Matlab:
https://www.coursera.org/learn/matlab

5. There is a new course, Psychology 808 being offered fall and winter terms to cover analysis and to hear a selection of outside fMRI speakers

WEEK 1 LECTURE SCHEDULE

Date	Time	Topic	Instructor
Monday 8/1/2022	8:00 AM – 1:00 PM	Introduction to Neuroanatomy & Experimental Design	John Jonides University of Michigan
Tuesday 8/2/2022	8:30 AM – 12:30 PM	MRI Physics	Nicole Seiberlich University of Michigan
Wednesday 8/3/2022	8:30 AM – 12:30 PM	MRI & BOLD Physics	Doug Noll University of Michigan
	Recorded and can be viewed anytime on Wednesday.	Clinical Applications of fMRI (virtual lecture) Details to follow on how to access the recording.	Benjamin Hampstead University of Michigan
Thursday 8/4/2022	8:30 AM – 12:30 PM	fMRI Data Preprocessing	Luis Hernandez-Garcia University of Michigan
Friday 8/5/2022	8:30 AM – 12:30 PM	Level Analysis & Experimental Design	Andy Jahn University of Michigan
Sunday 8/7/2022	4:00 pm – 6:00 pm	Review of Basic Statistics and the GLM	Adriene Beltz University of Michigan

Week 2 Lecture Schedule

Monday 8/8/2022	8:30 AM – 12:30 PM	Contrasts, Group Analysis & Double Dissociations	Andy Jahn University of Michigan
	4:00 PM- 5:00 PM	Pattern Analysis & Classification via MVPA-virtual but live in 1360 East Hall. MUST be in 1360 for the virtual lecture.	Stephen LaConte Virginia Tech
Tuesday 8/9/2022	8:30 AM - 12:30 PM	Pitfalls in fMRI Research	Andy Jahn University of Michigan
Wednesday 8/10/2022	8:30 AM – 12:30 PM	Network Analysis & Tools	Scott Peltier University of Michigan Alex Iordan University of Michigan
Thursday 8/11/2022	8:30 AM – 12:30 PM	Part 1- Introduction to Open Science Part 2- BIDS, MRIQC & fMRI Prep	Andy Jahn University of Michigan Scott Peltier University of Michigan
Friday 8/12/2022	8:30 AM – 12:30 PM	Reproducibility	Andy Jahn University of Michigan

Week 1 – Lab Schedule

Monday 8/1/2022	2:00 – 5:00 PM	Matlab (Basic)	Krisanne Litinas University of Michigan
Tuesday 8/2/2022	1:30 – 5:00 PM	Matlab Programming for fMRI	Krisanne Litinas University of Michigan
Wednesday 8/3/2022	3:30 PM—5:00 PM	Virtual fMRI Lab Tour Meet in 1360 East Hall	fMRI LAB TOUR: John Jonides, Doug Noll & Scott Peltier
Thursday 8/4/2022	2:00 PM – 5:00 PM	SPM Introduction & Preprocessing: A hands-on demonstration & practice	Luis Hernandez-Garcia, Scott Peltier, Andy Jahn and Alex Iordan
Friday 8/5/2022	1:30 PM – 5:00 PM	Single-Subject Analysis	Luis Hernandez-Garcia, Scott Peltier, Andy Jahn and Alex Iordan

Week 2 – Lab Schedule

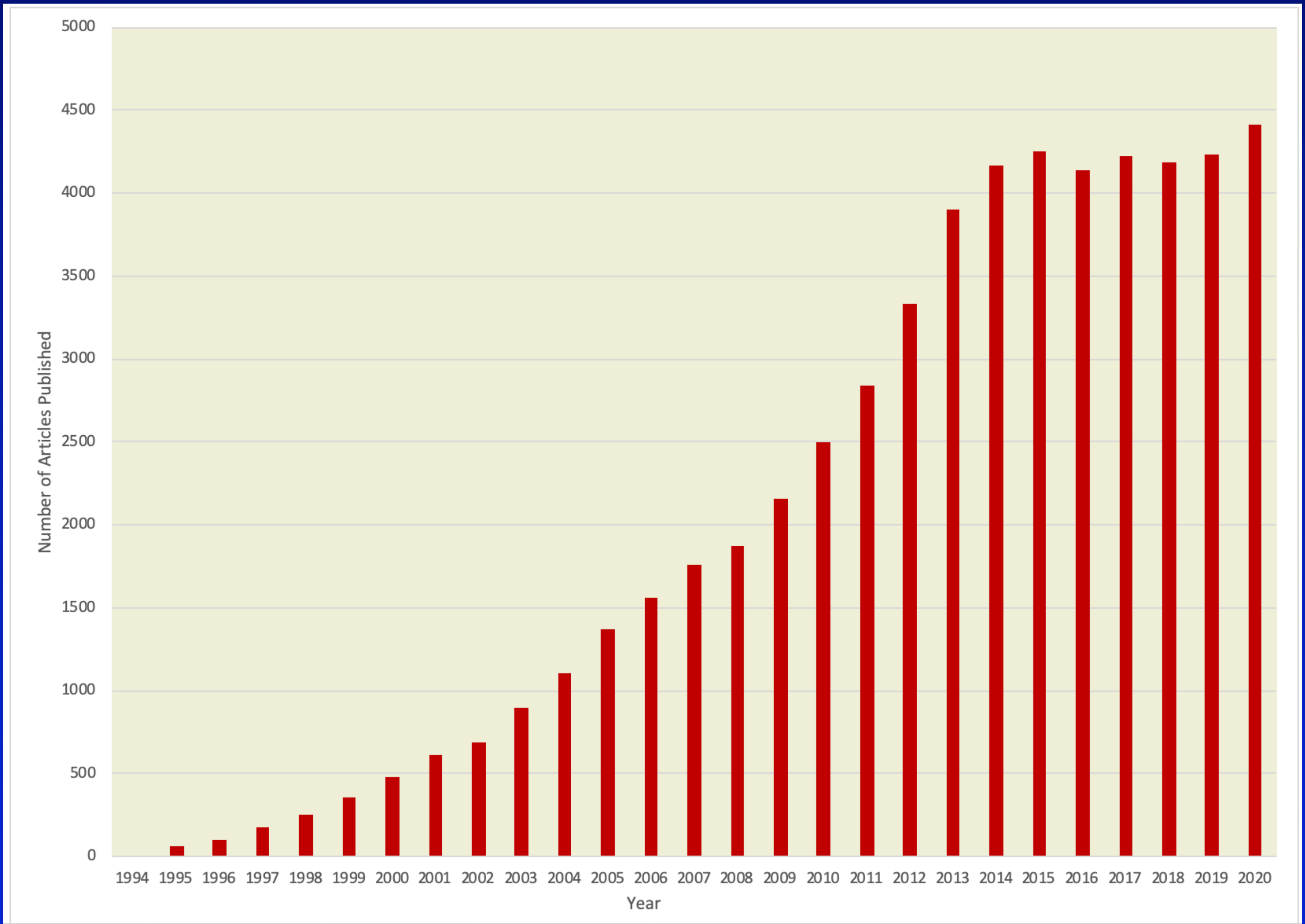
Monday 8/8/2022	1:30 PM – 3:55 PM	Design Optimization: Design Specification Basics	Luis Hernandez-Garcia, Scott Peltier, Andy Jahn and Alex Iordan
Tuesday 8/9/2022	1:30 PM – 5:00 PM	Group (2nd level) Analysis	Luis Hernandez-Garcia, Scott Peltier, Andy Jahn and Alex Iordan
	6:00 PM- 8:00 PM	Virtual Demonstration of Real-Time Data Collection & Analysis Using MVPA Meet in 1360 East Hall	Scott Peltier, Steve LaConte, Krisanne Litinas, and John Jonides
Wednesday 8/10/2022	1:30 PM – 5:00 PM	Students Choose Labs	Luis Hernandez-Garcia, Scott Peltier, Andy Jahn and Alex Iordan
Thursday 8/11/2022	1:30 PM – 5:00 PM	Open Science and BIDS	Andy Jahn
Friday 8/12/2022	NO LAB	NO LAB	NO LAB

1. What You Can Do With Neuroimaging Data

2. Very Basic Gross Human Neuroanatomy

3. Elements of Experimental Design for fMRI

Citations with fMRI in Title or Abstract



Agenda

- What neuroimaging data can tell us
  - Brain Mapping: Localization
  - Associations among psychological processes
    - Relationship to other association strategies
  - Dissociations among psychological processes
    - Relationship to other dissociation strategies
  - Individual differences
  - Testing psychological models

Brain Mapping: Localization

- Correlate structure with function
- Provide data to predict loss of function with brain injury
- Guide neurosurgical planning
- Map networks of regions that participate in complex tasks
  - Structural connectivity determined by DTI
  - Functional connectivity determined by techniques such as seed-based connectivity or multi-voxel pattern analysis

Caveats

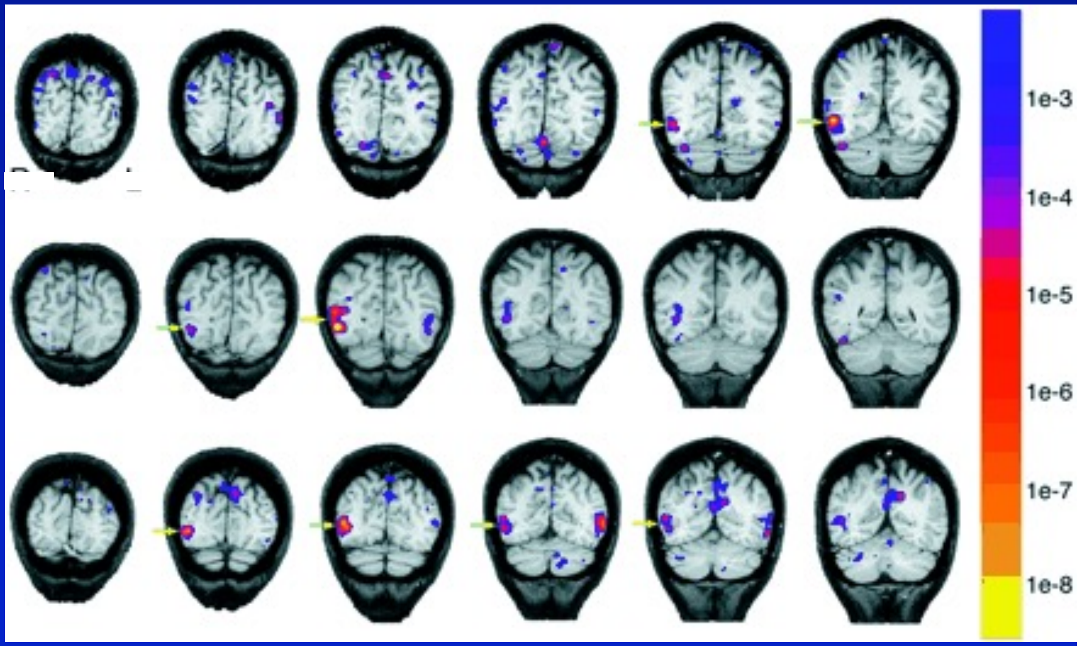
- Neuroimaging data do not establish necessity
  - Must accompany them with lesion data
- Are you localizing the process you want?
  - Control over subject's processing path
    - Alternative strategies

Localization of Object Recognition

- Downing et al. (2001)
  - Ss view pictures of human bodies or body parts
  - Compared to viewing of other objects (e.g., cars, birds, fish, trees, clothes, chairs, tools)
  - Right lateral occipitotemporal cortex selectively activated by body parts

P-values

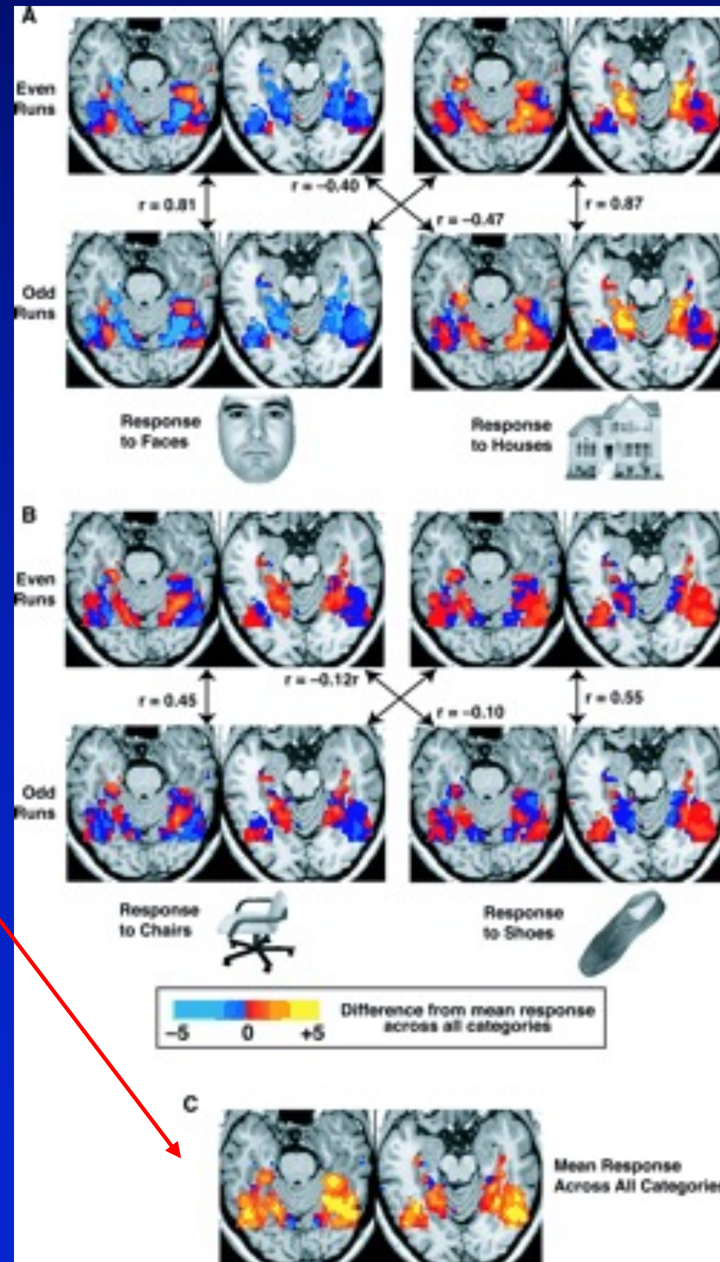
Individual Subjects



Activations in 3 participants

Localization is Distributed

- Haxby et al. (2001)
  - Ss viewed faces, cats, houses, chairs, scissors, shoes, nonsense objects
  - Find lots of inferior temporal activation



Localization is Distributed

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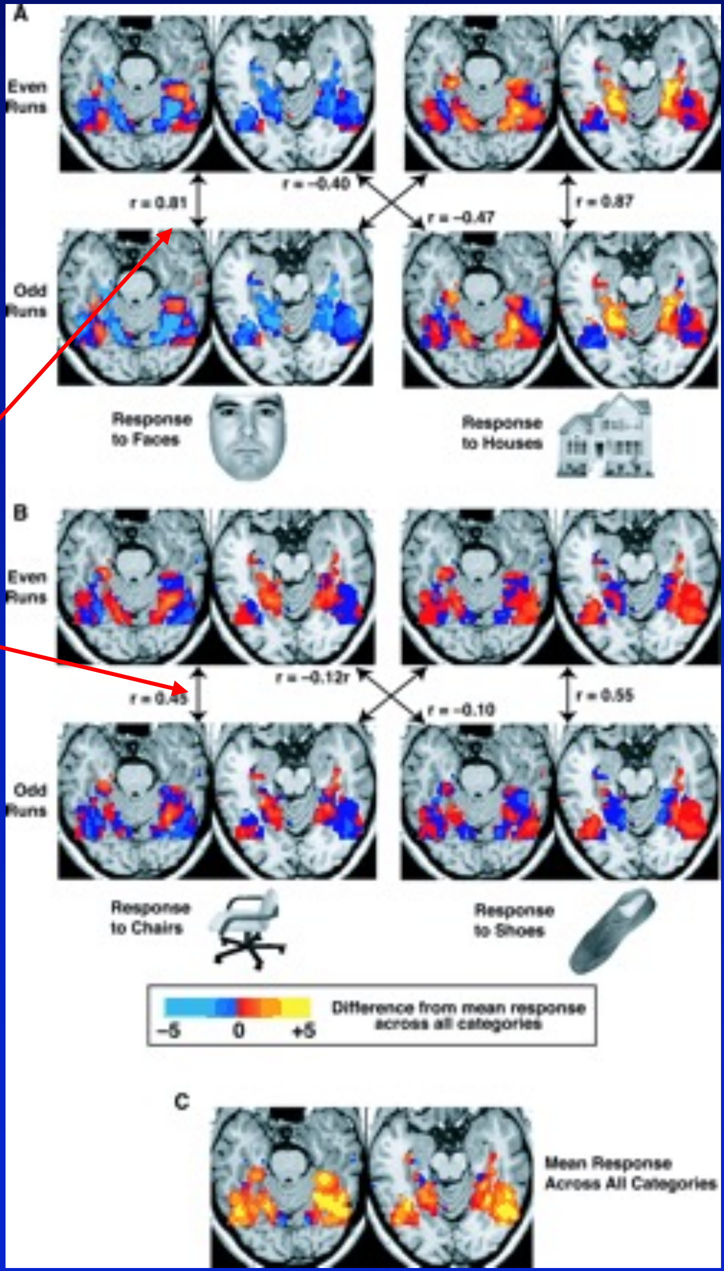
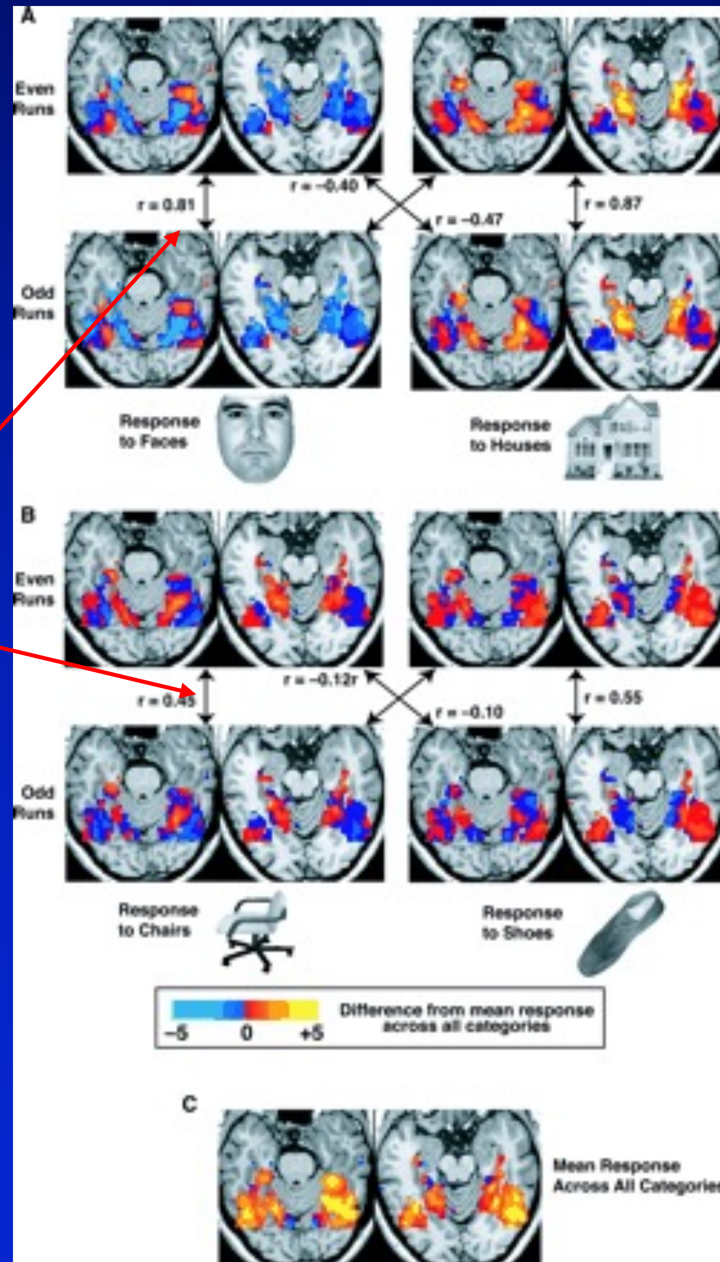
  - Within-category correlations higher than between-category

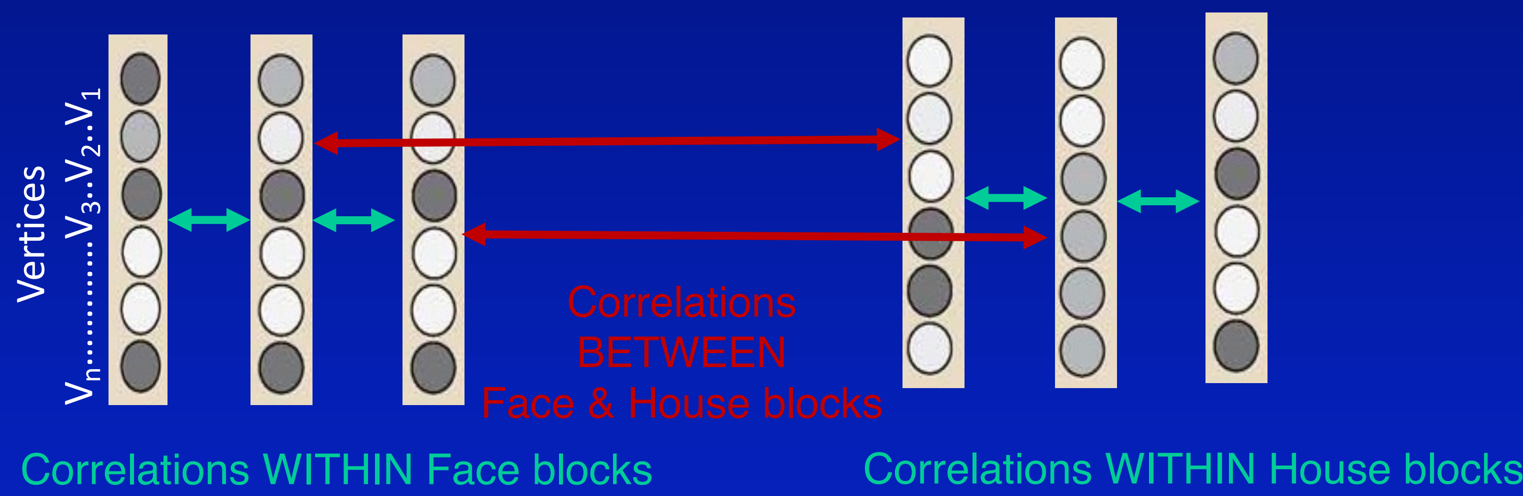


Localization is Distributed

- Haxby et al. (2001)
  - Ss viewed faces, cats, houses, chairs, scissors, shoes, nonsense objects
  - Find lots of inferior temporal activation
  - Within-category correlations higher than between-category
  - Taking out highest activation, remaining pattern still predicts the object class
    - Indicates need for pattern classification, not just univariate analysis



CORRELATIONAL APPROACH



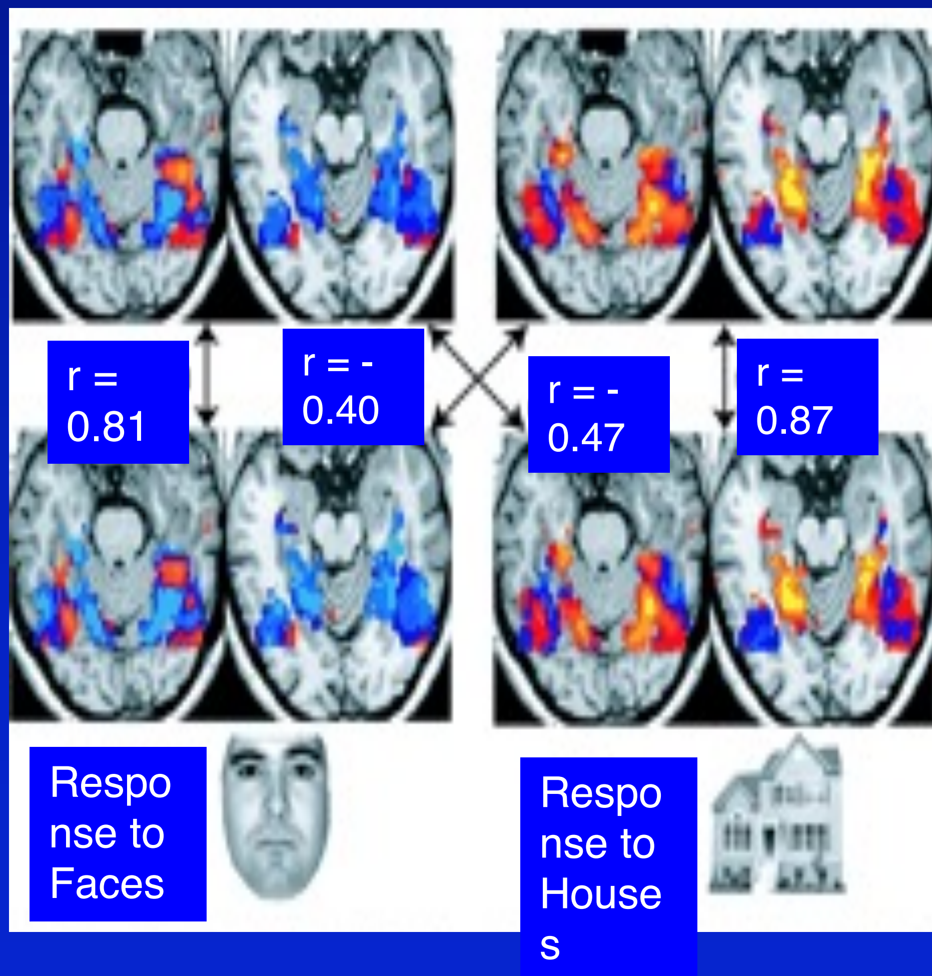
Distinctiveness = Avg. correlation WITHIN – Avg. correlation BETWEEN

Haxby et.al.,2001; Park

Back to Haxby

Even runs

Odd runs



MULTIVOXEL PATTERN ANALYSIS

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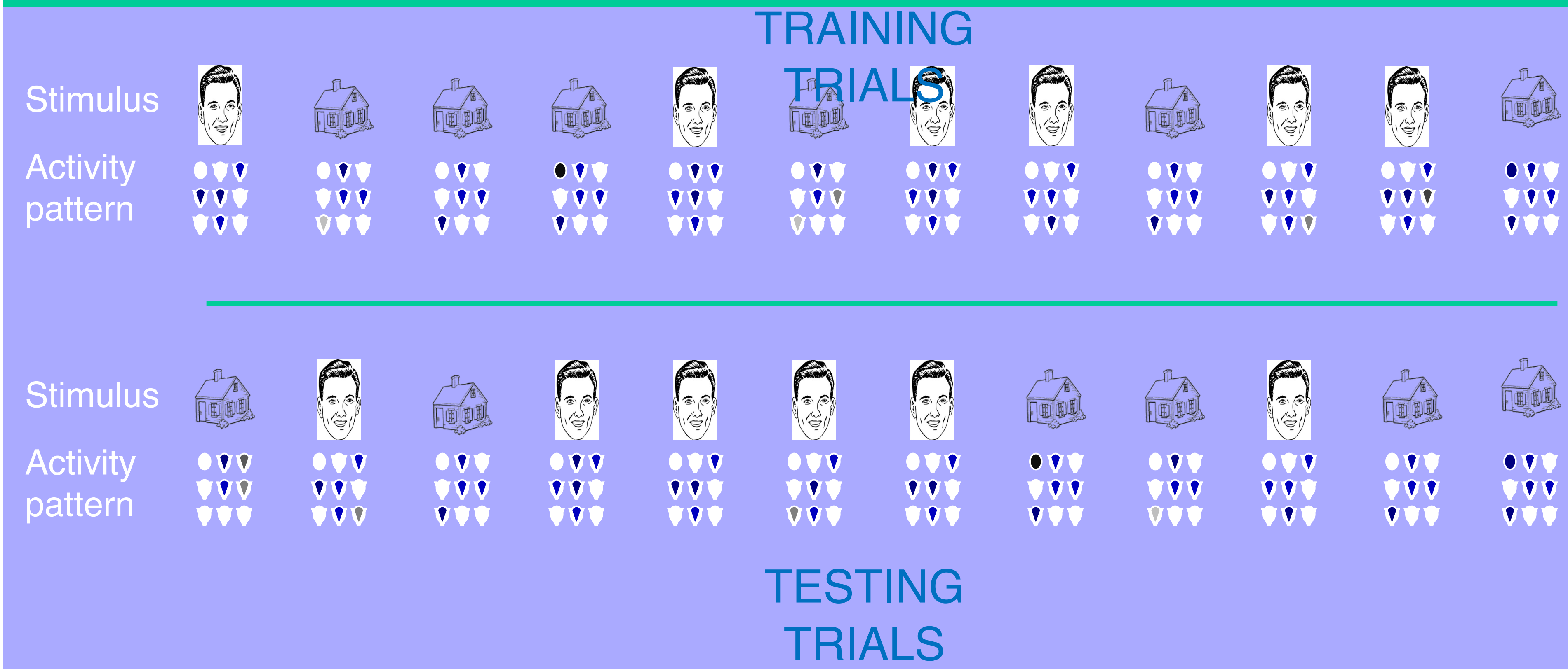

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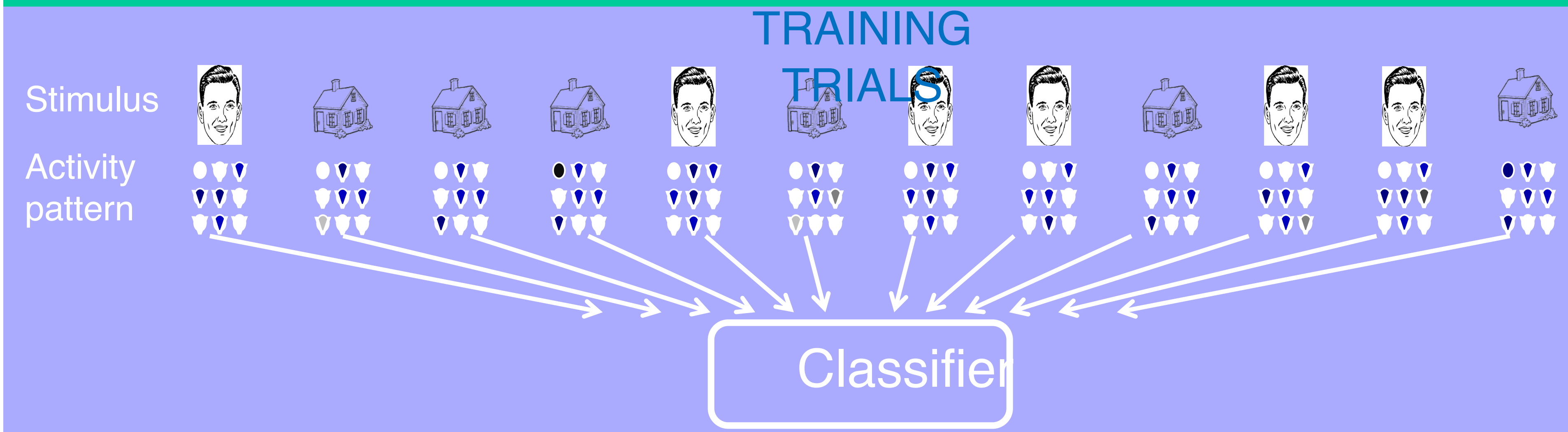

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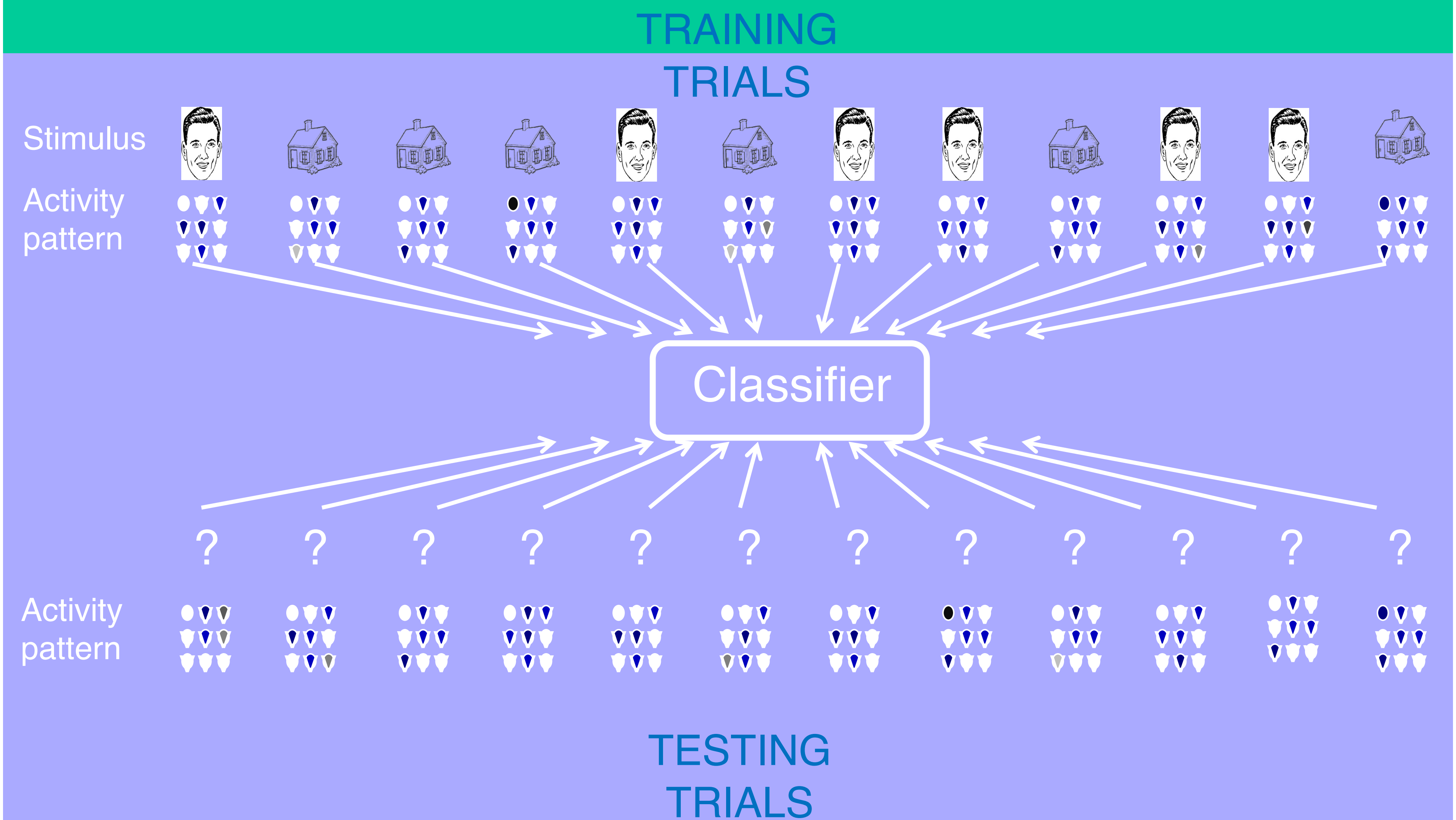

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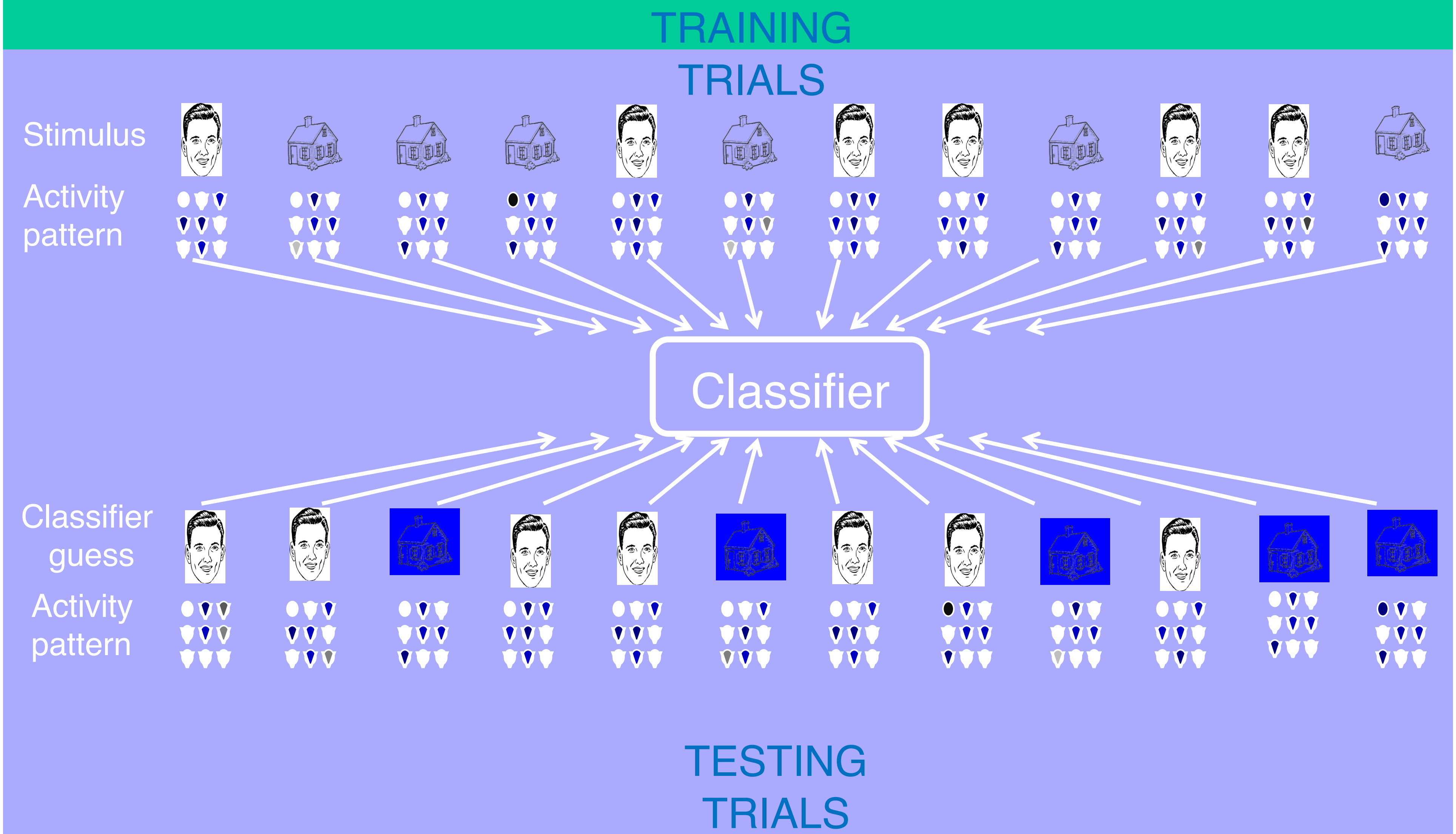

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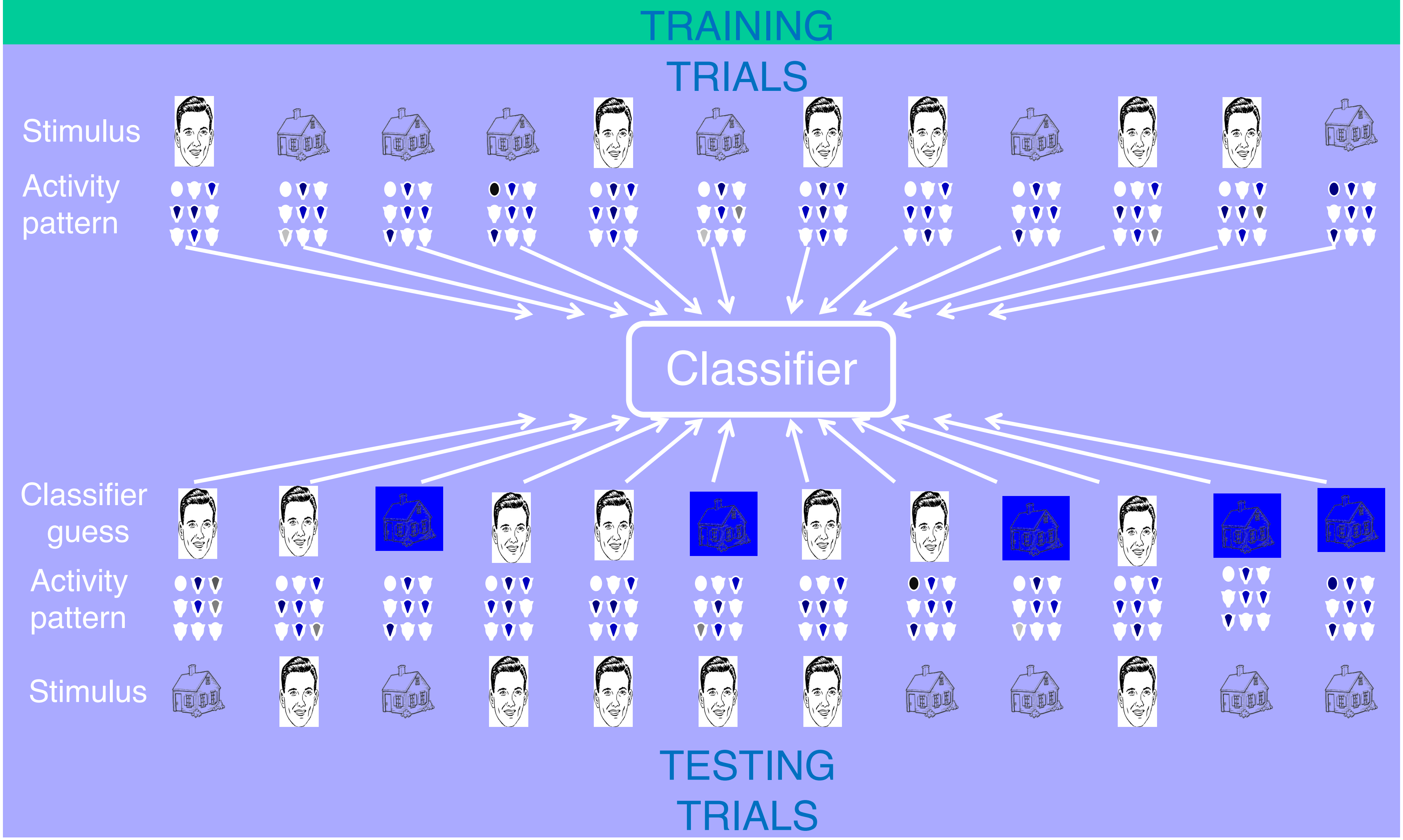

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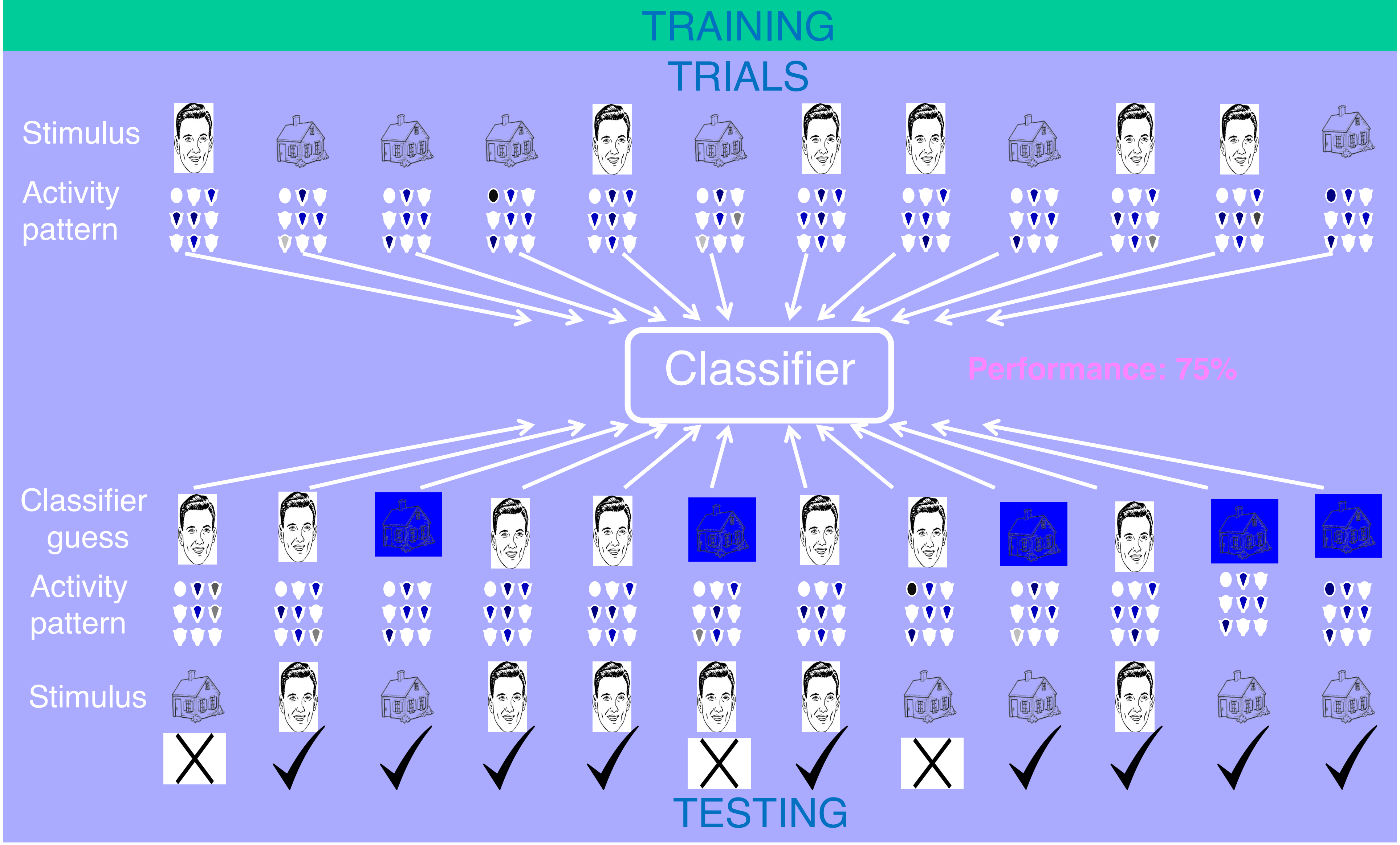

STEP 3. CLASSIFIER TRAINING

feed these patterns into multivariate pattern classification algorithm that maps between voxel patterns and experimental conditions

Linear classifiers

- Support vector machines
- Neural networks
- Linear discriminant analysis
- Gaussian Naïve Bayes
- Sparse Multinomial Linear Regression

Non-linear classifiers

- Nearest neighbor
- Non-linear support vector machines

STEP 3. CLASSIFIER TRAINING

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Linear classifiers

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Non-linear classifiers

- Nearest neighbor
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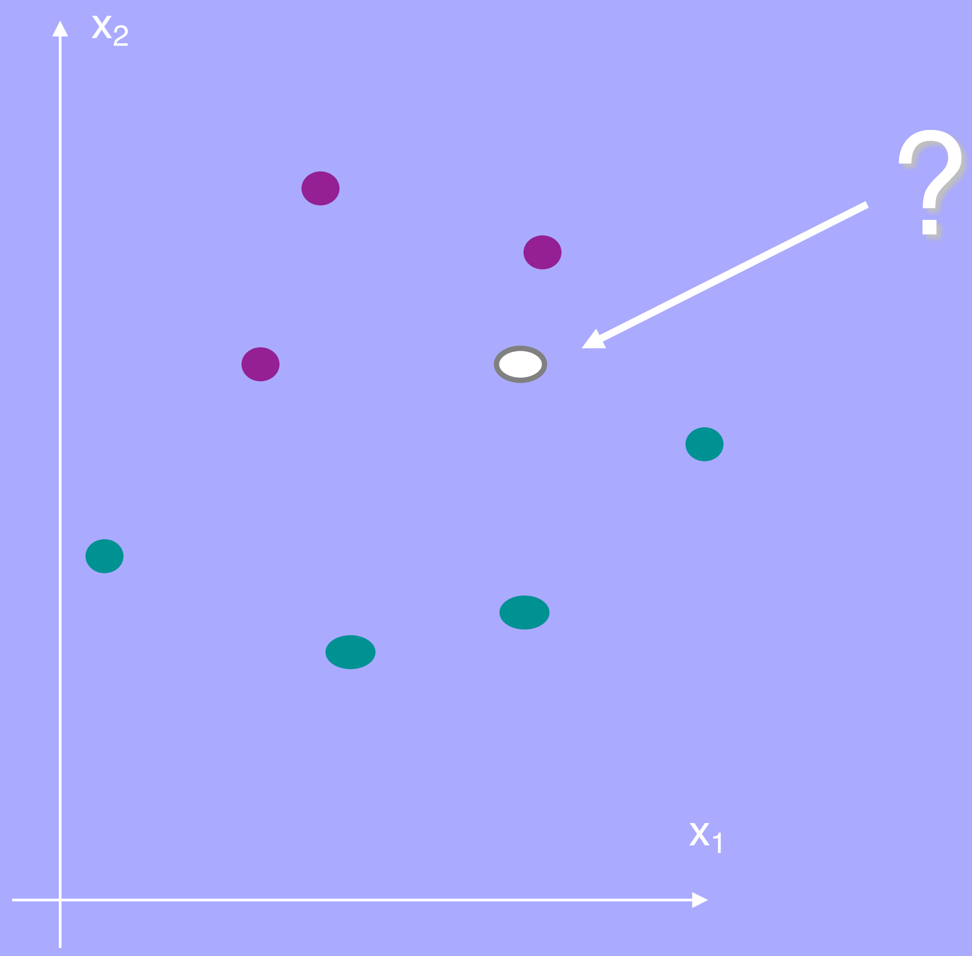
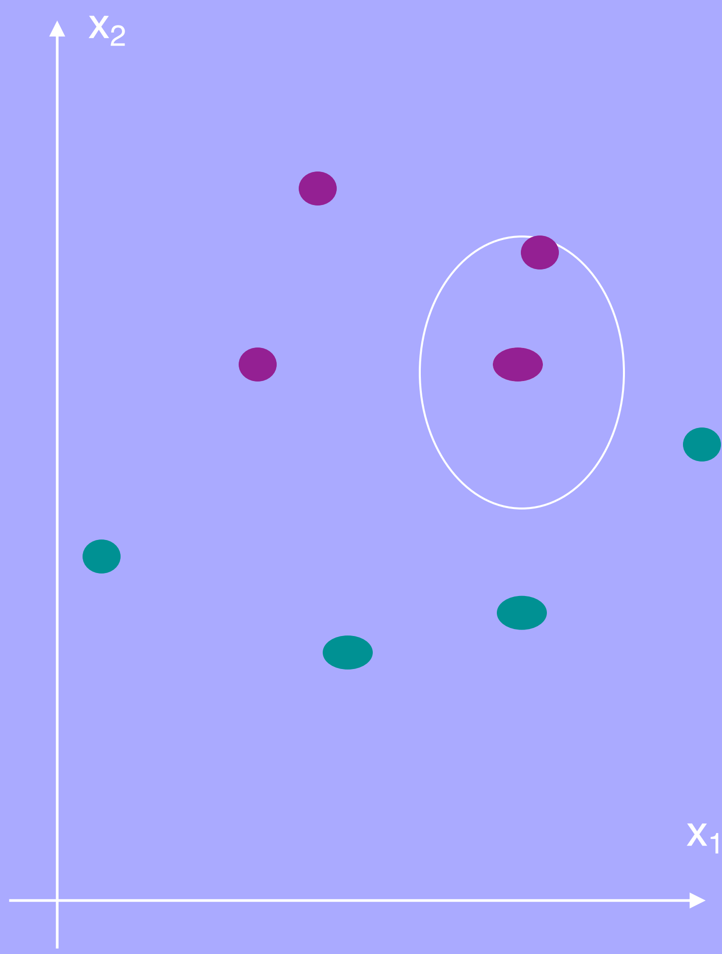
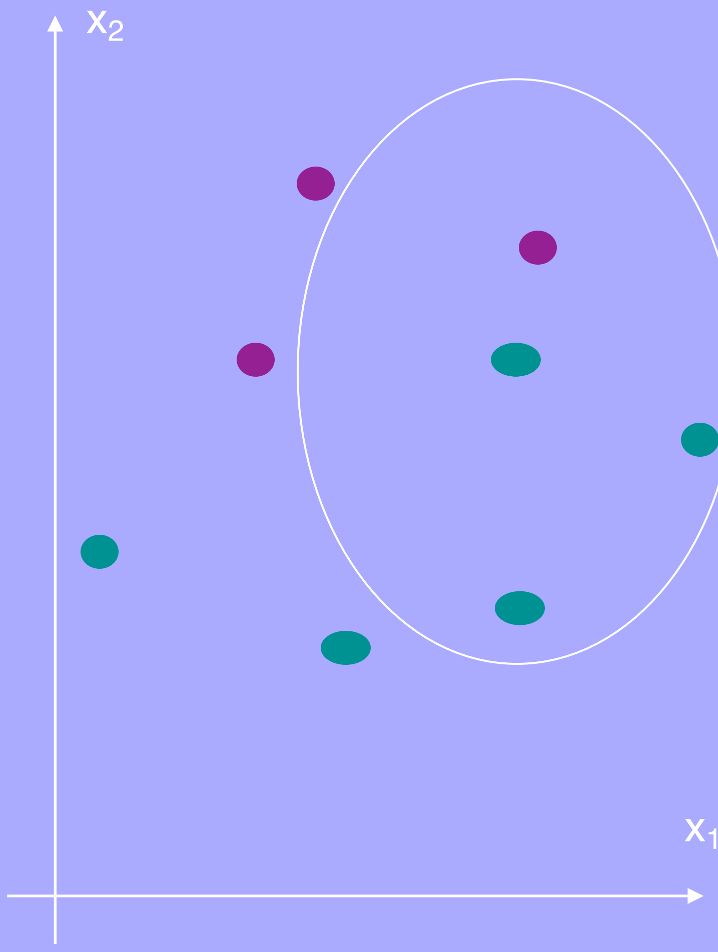
NEAREST NEIGHBOUR CLASSIFIERS



1-NEAREST NEIGHBOUR CLASSIFIERS



3-NEAREST NEIGHBOUR CLASSIFIERS



Using Neuroimaging to Associate Psychological Processes

General Logic

Assume:
System A underlies performance in Task 1
System A underlies performance in Task 2

Implementation

Task 1 → Recruitment of System A → Activation of Area a but not Area b

Task 2 → Recruitment of System A → Activation of Area a but not Area b

Associations

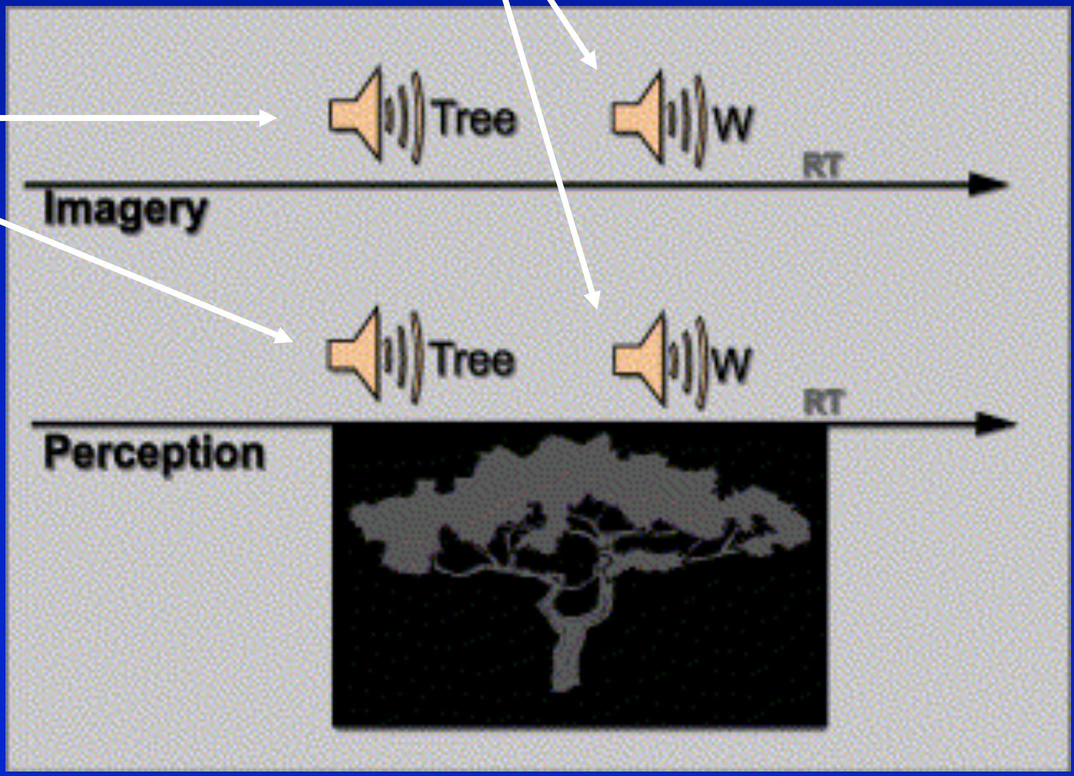
- Caution: reliance on null results
- Stronger inference with planned comparisons based on prior data
- Stronger inference when examining a network of regions
- Danger of reverse inference
  - Just because the same region is activated, one can't conclude that the same process is engaged
  - Regions may have multiple functions

Associating Perception and Imagination

Ganis et al., 2000

4.5 sec after instruction, given question about object

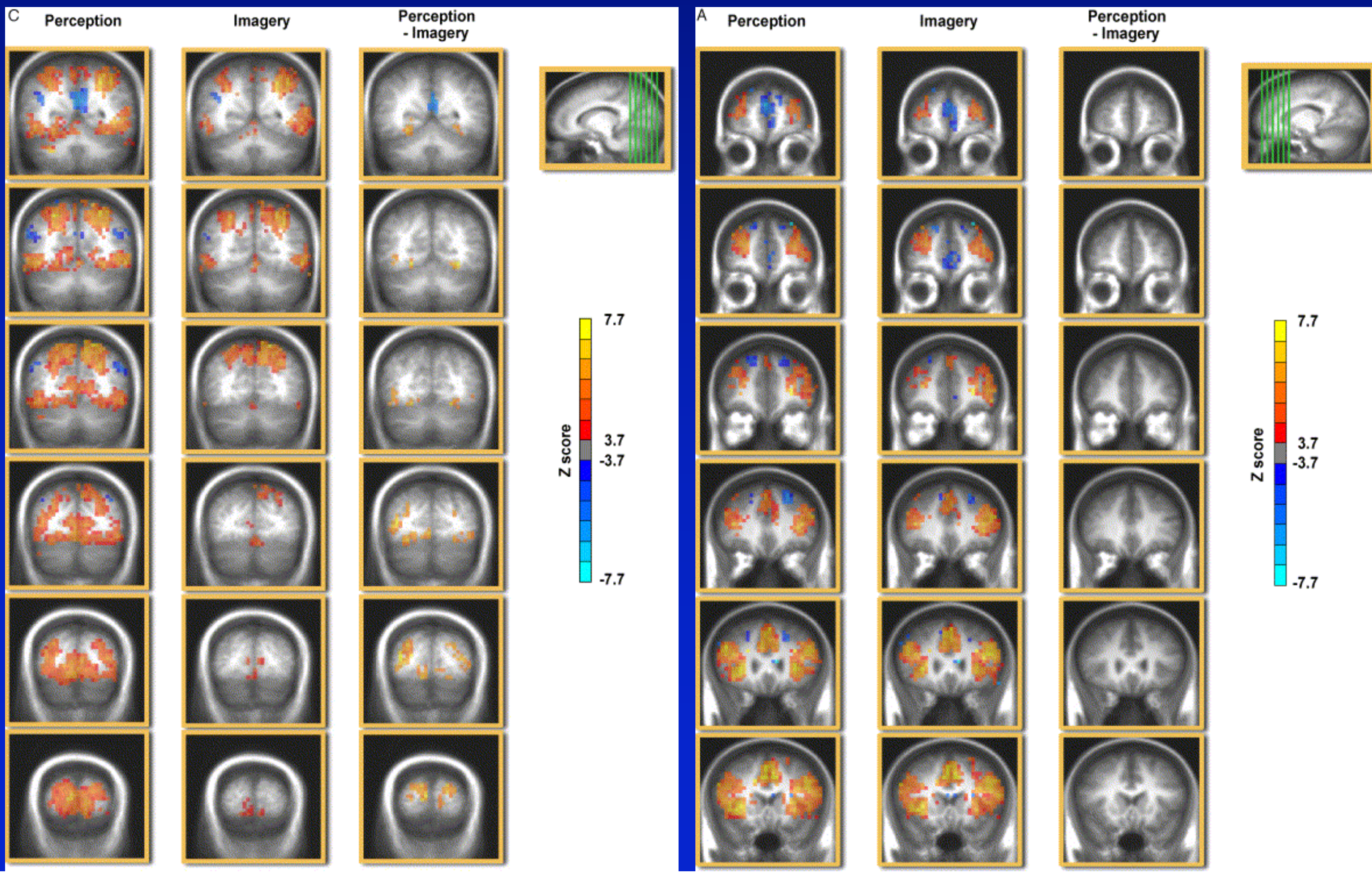
Auditory instruction to image or perceive



Compare activations to baseline

Perception and Imagery

Comparison of Imagery and Perception Conditions in
Anterior and Posterior Cortex: 92% Overlap



What Can Neuroimaging Tell Us?

Dissociating psychological processes

General Logic

Assume: System A underlies performance in Task 1
System B underlies performance in Task 2

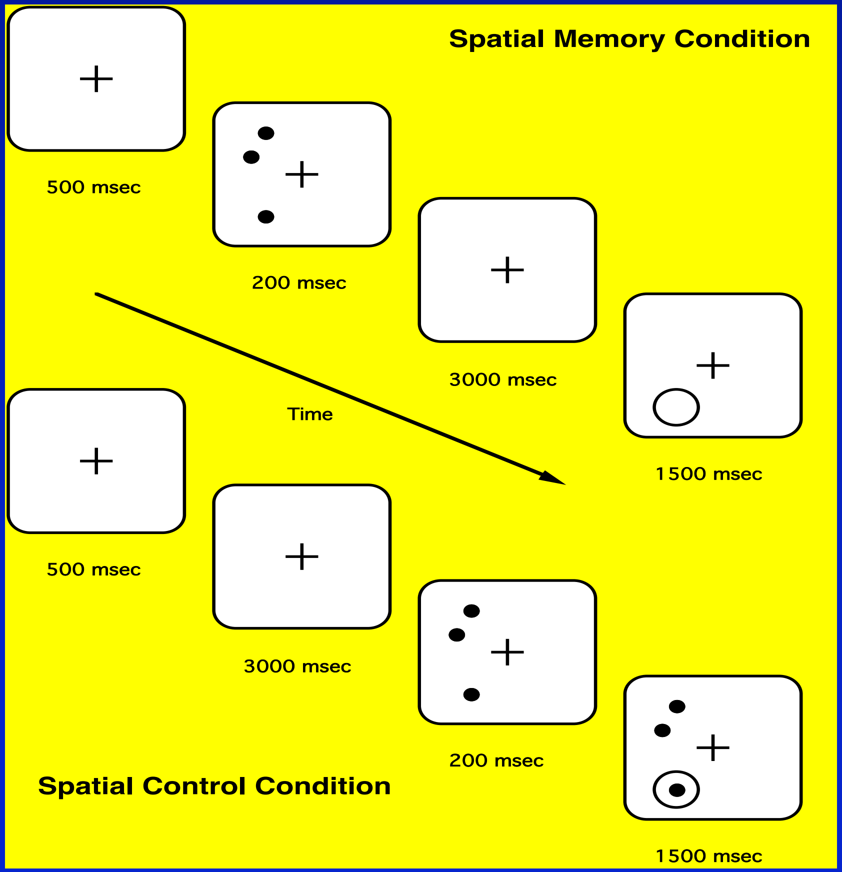
Implementation

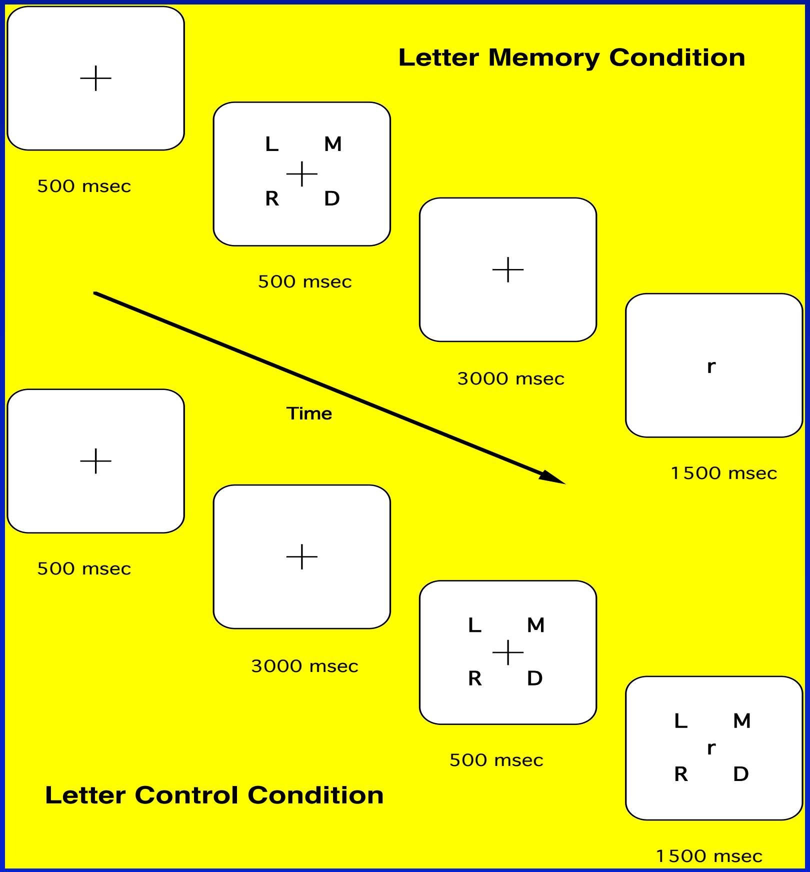
Task 1 → Recruitment of System A → Activation of Area a but not Area b

Task 2 → Recruitment of System B → Activation of Area b but not Area a

Spatial and Verbal Working Memory

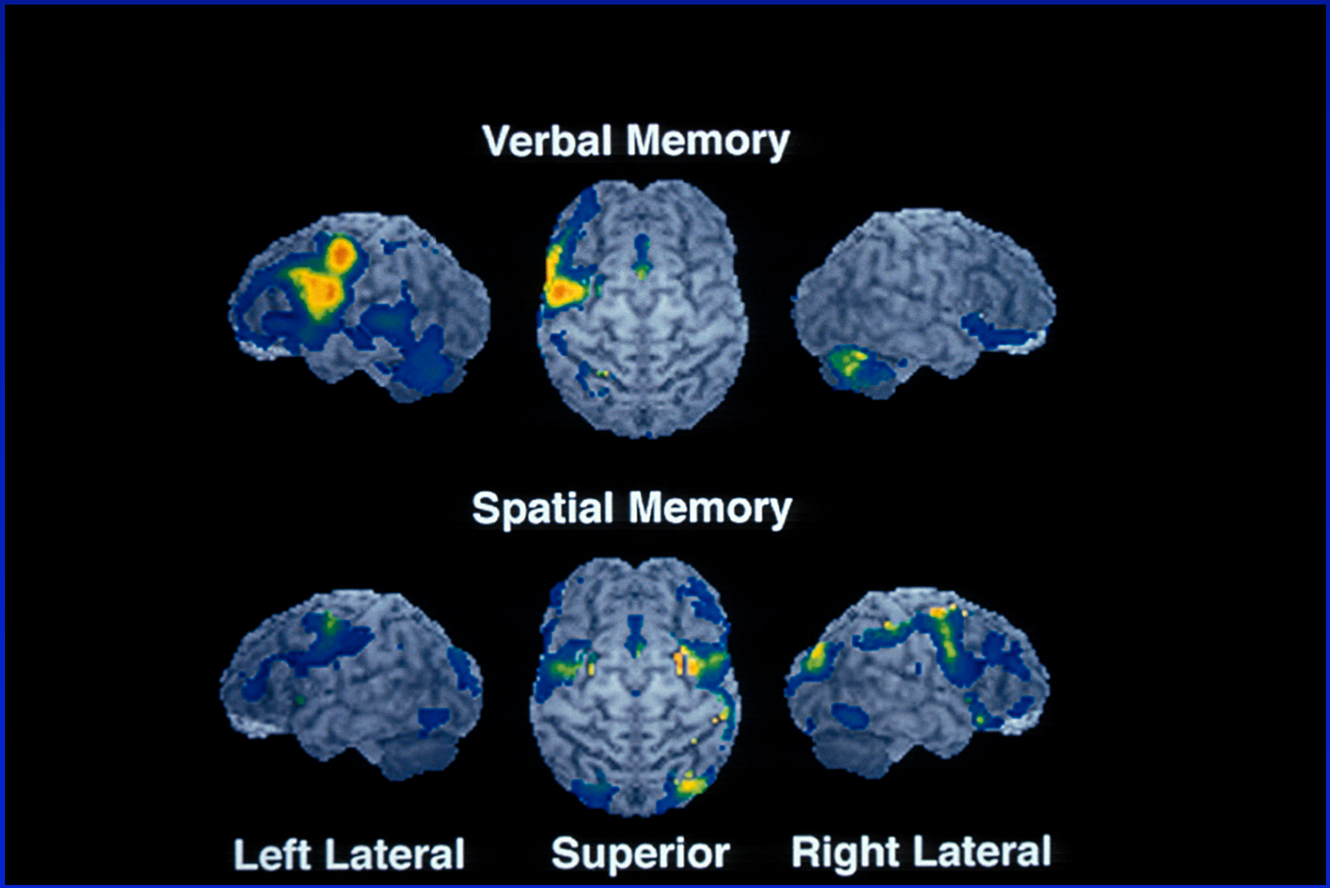
Similar tasks with different materials





Results from PET Measurements

Different regions of activation depending on type of material



Dissociations

Applied to data from patients

General Logic

Assume: System A underlies performance in Task 1
System B underlies performance in Task 2

Implementation

Task 1 → Pt with damage to System A → Deficit on Task 1 but not Task 2

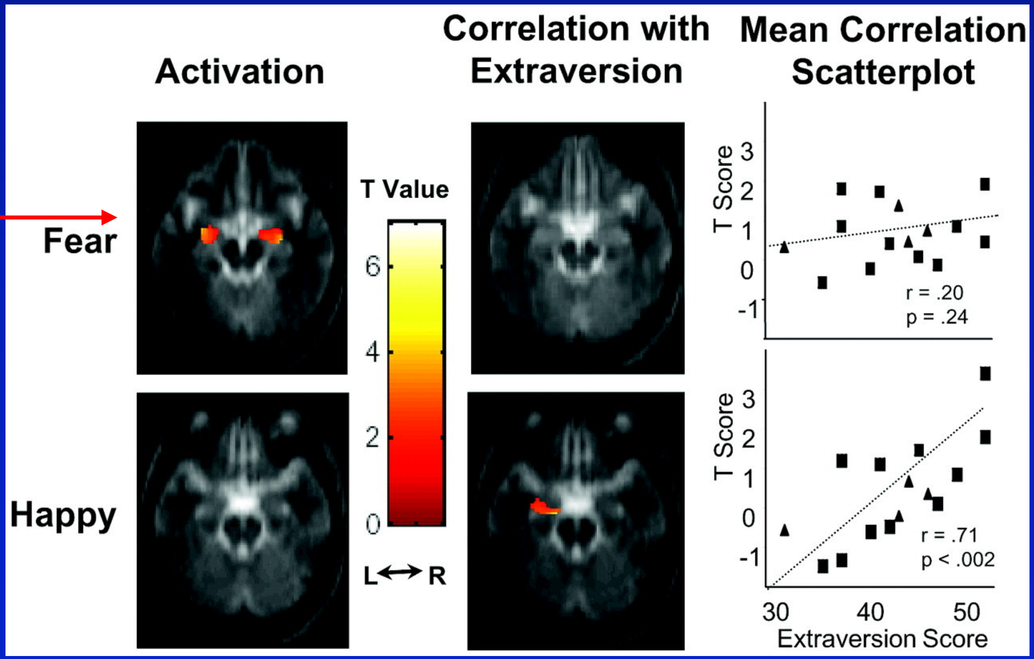
Task 2 → Pt with damage to System B → Deficit on Task 2 but not Task 1

Dissociations

- Applied to verbal vs. spatial working memory
  - Behavioral studies of patients
    - e.g., Basso et al. (1982) -- PV: left posterior lesion and deficit in verbal working memory
    - e.g., Hanley et al. (1991) -- ELD: right diffuse anterior and posterior lesion and deficit in spatial working memory

Studying Individual Differences

- Canli et al. (2002)
  - Ss classify emotional or neutral faces by gender
  - Fearful faces activated amygdala across subjects regardless of extraversion
  - Happy faces activated amygdala only to the extent that Ss scored high on a measure of extraversion



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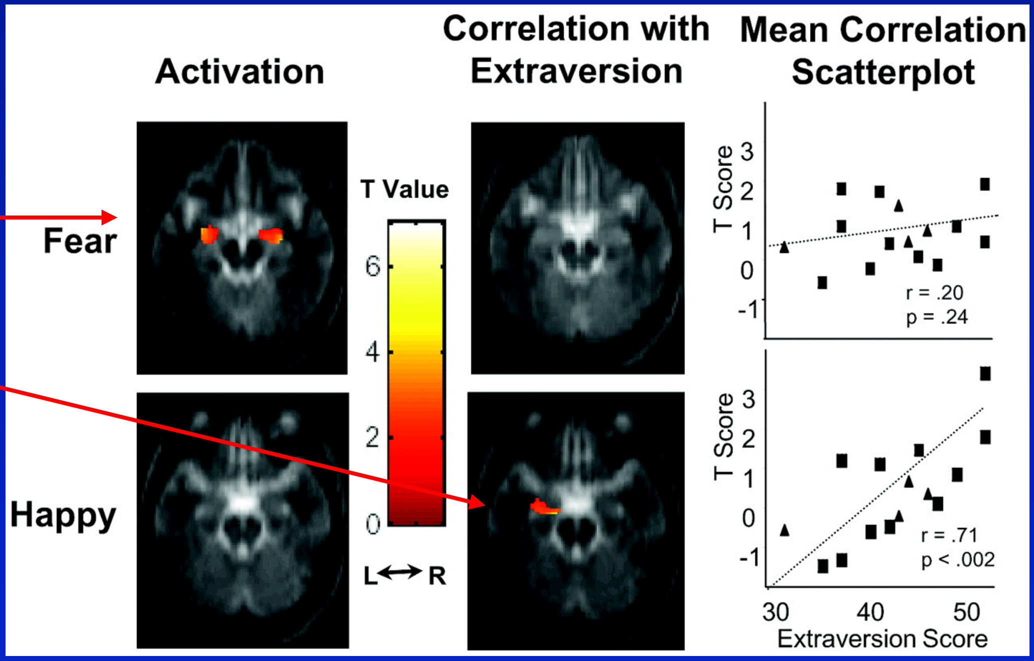


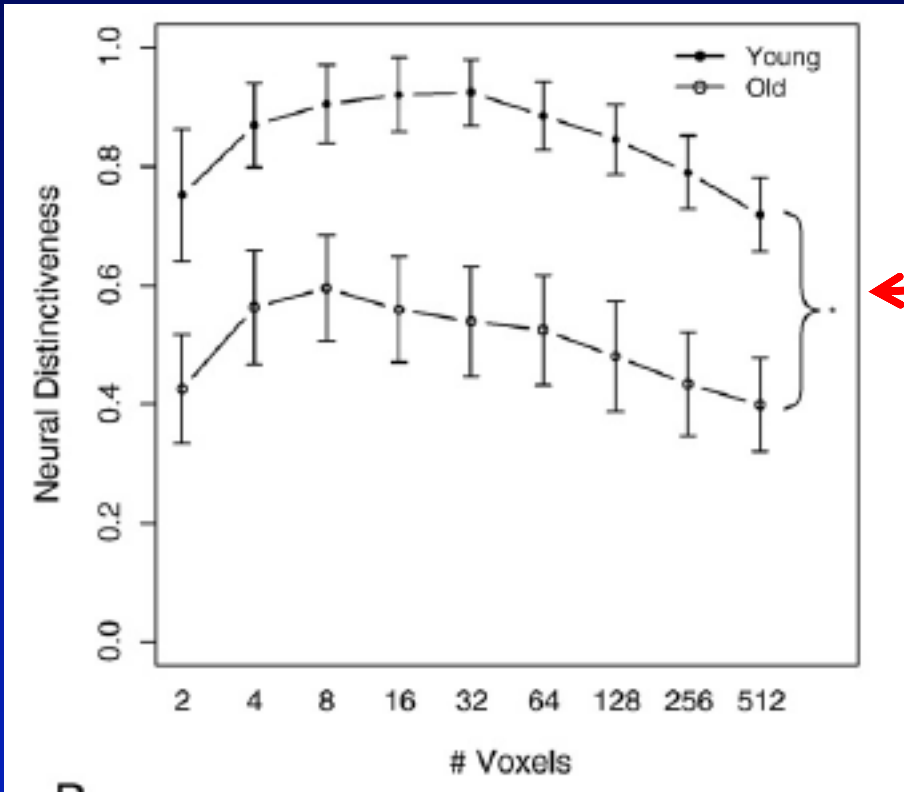
Modeling the Aging Brain

- Dedifferentiation
  - Increased intercorrelations among perceptual and cognitive processes
  - Thought to reflect a decline in integrity of the aging brain: reduced distinctiveness of neural representations
  - Frequently seen in more bilateral activation in older adults
    - Could reflect compensation
    - Could reflect impaired neural processing

Carp et al. (2011) on Dedifferentiation

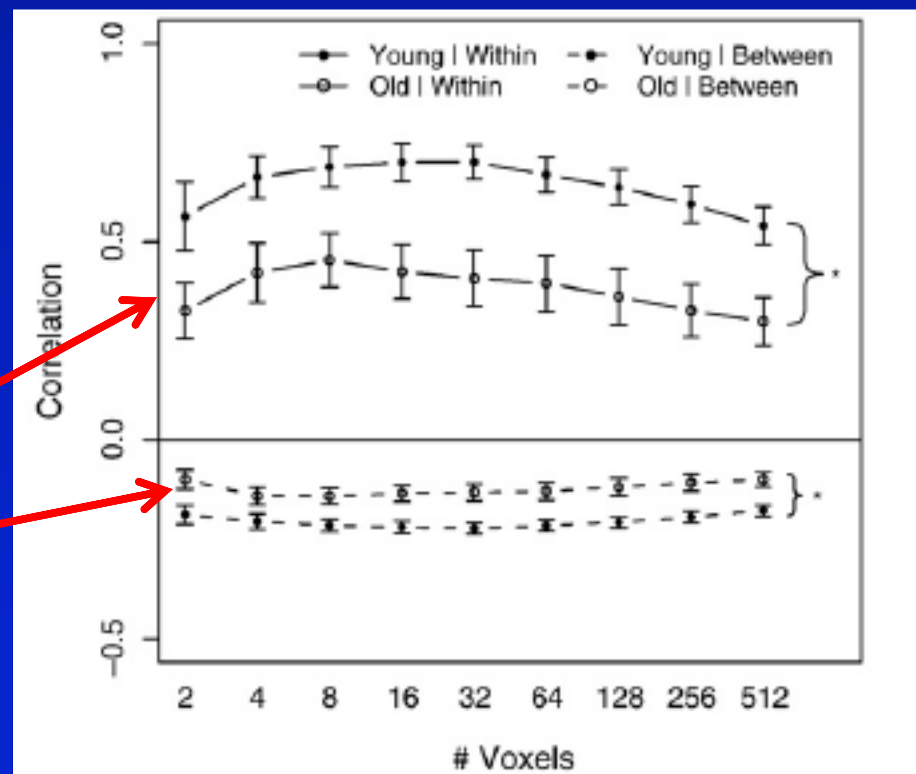
- Had older and younger adults view faces, houses, chairs, pseudowords, control images
- Used MVPA to test for distinctiveness in neural response

- Neural response to each category vs control images
- Compare within and between category correlations across all pairs of categories
- Neural distinctiveness = difference of within-between correlations
- Searchlight analysis:
  - For each voxel, assess how distinctive neural patterns for different categories are for a sphere surrounding that voxel

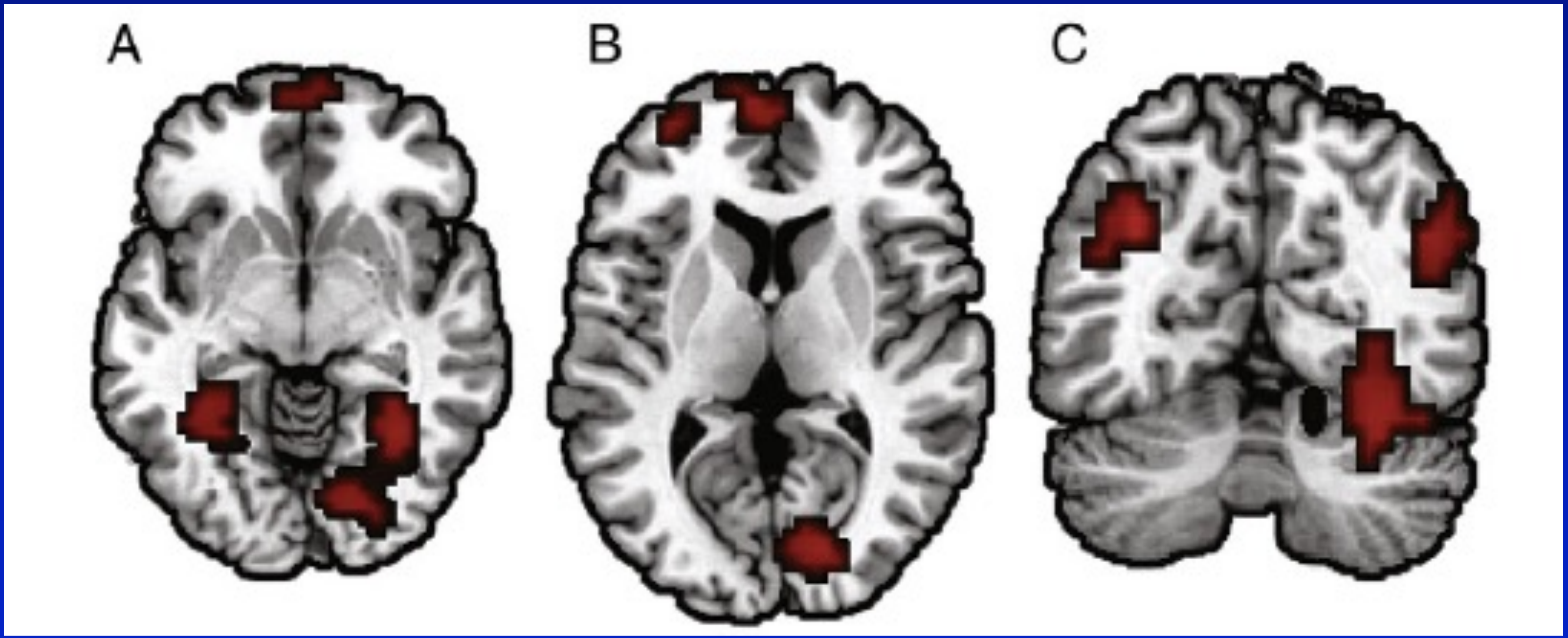


Older adults show less neural distinctiveness than young adults; activation patterns discriminate among categories less well in older adults

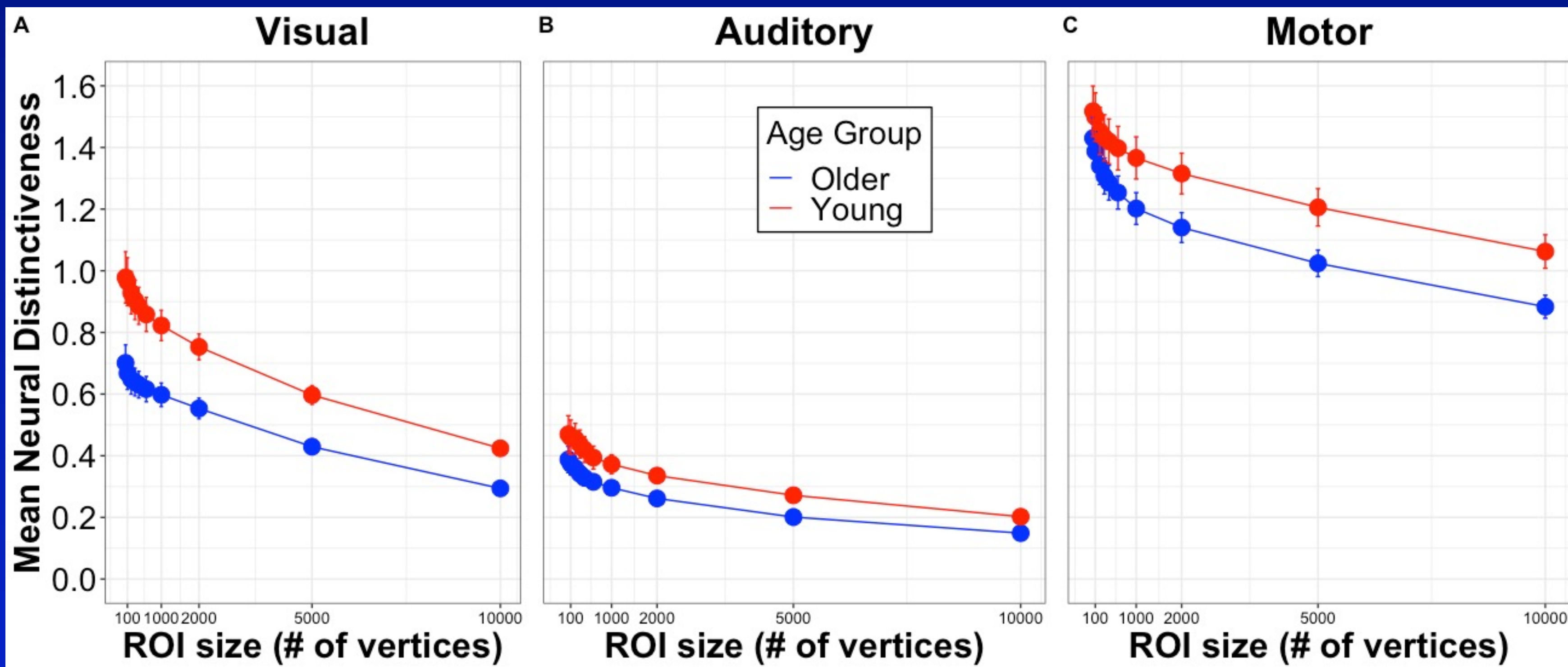
Older adults show lower within-category correlations and higher between-category correlations than younger adults



Searchlight Analysis

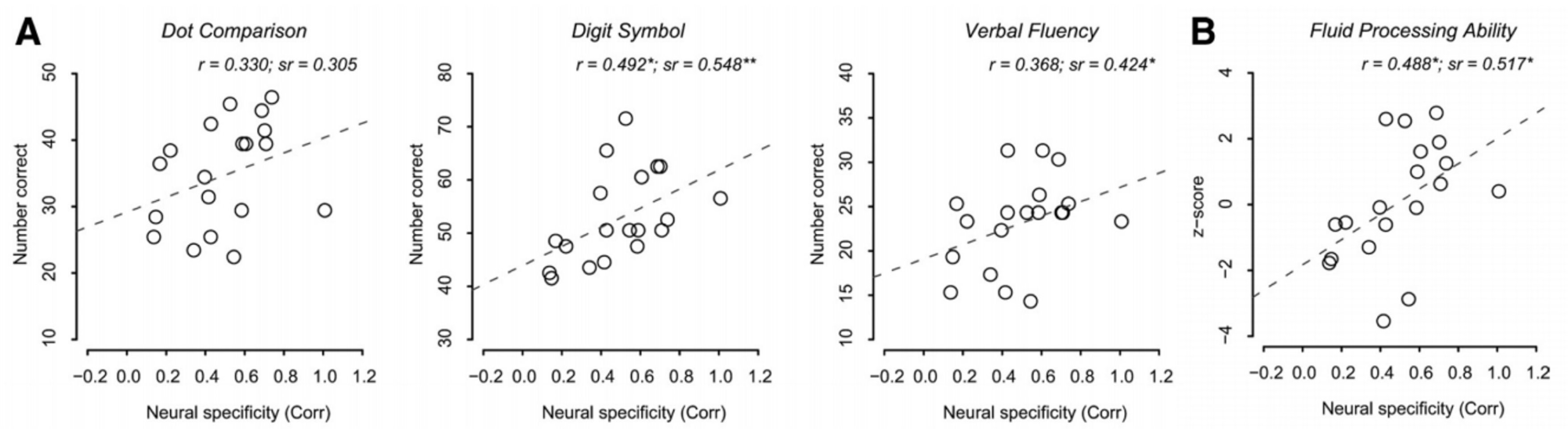


Higher neural distinctiveness regions for younger than older adults
No higher neural distinctiveness for older than younger adults


A
Visual
B
Auditory
C
Motor
Mean Neural Distinctiveness
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Age Group
Older
Young
100 1000 2000 5000 10000
ROI size (# of vertices)
ROI size (# of vertices)
ROI size (# of vertices)

Effects of Age on Neural Representations

- And older people with more distinctive representations perform better on a range of tasks:



(J Park et al., 2010, *J Neurosci*)

Effects of Age on Neural Representations

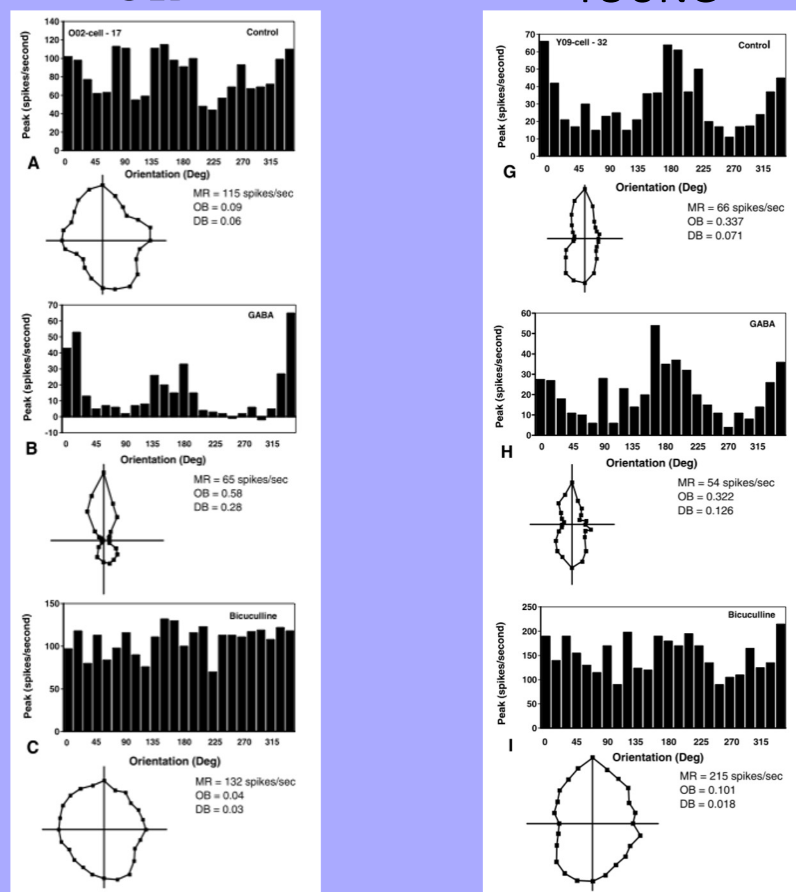
- Cause: Reductions in the inhibitory neurotransmitter GABA?

OLD

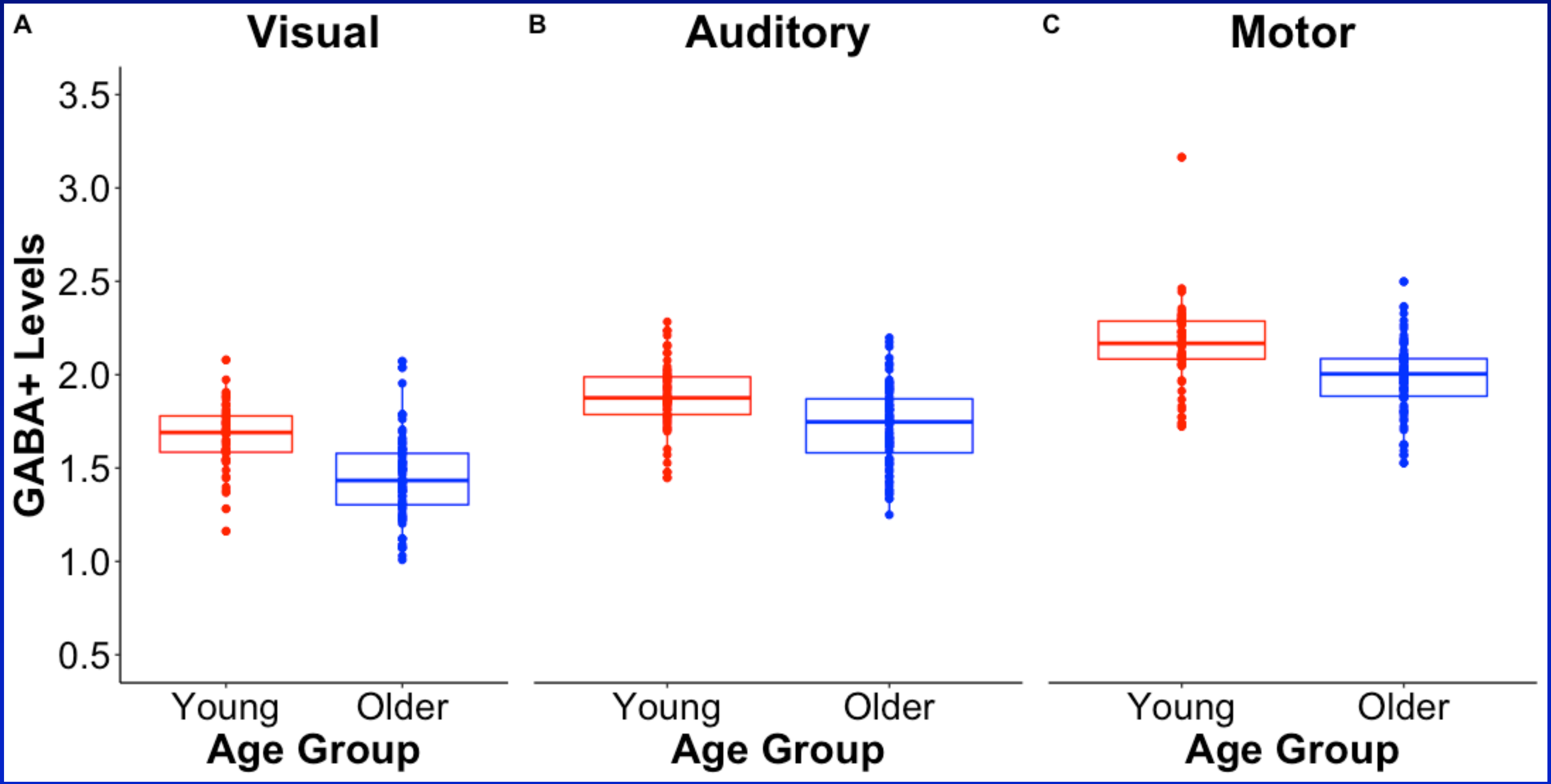
YOUNG

GABA

Blocking GABA



Leventhal et al., 2003, Science


A
Visual
B
Auditory
C
Motor
GABA+ Levels
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Young
Older
Age Group
Young
Older
Age Group
Young
Older
Age Group

The Place of Neuroimaging Data: No Time for Imperialism

- They provide information about brain-behavior correlations
- They provide a source of associations and dissociations to converge with other sources
- They permit an assessment of individual differences to complement other assessments
- They permit one to test models of processes
- In some cases (e.g., imagery, responding with interference), they are more probative
- In some cases (e.g., storage in memory), they may be redundant with other data
- In some cases (e.g., inductive reasoning), they have been less probative because of task complexity

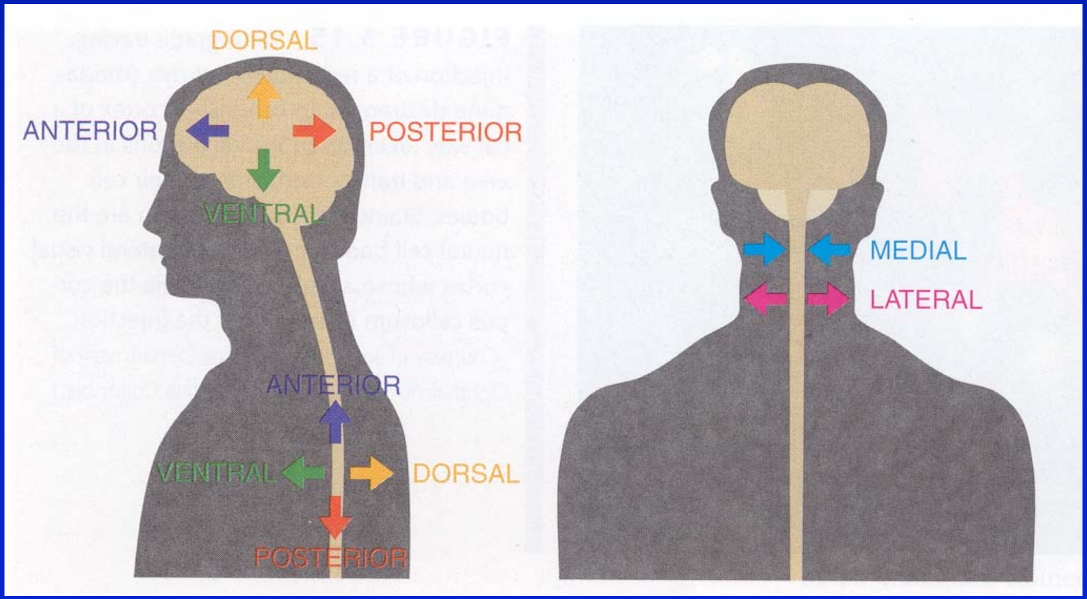
1. What You Can Do With Neuroimaging Data

2. Very Basic Gross Human Neuroanatomy

3. Elements of Experimental Design for fMRI

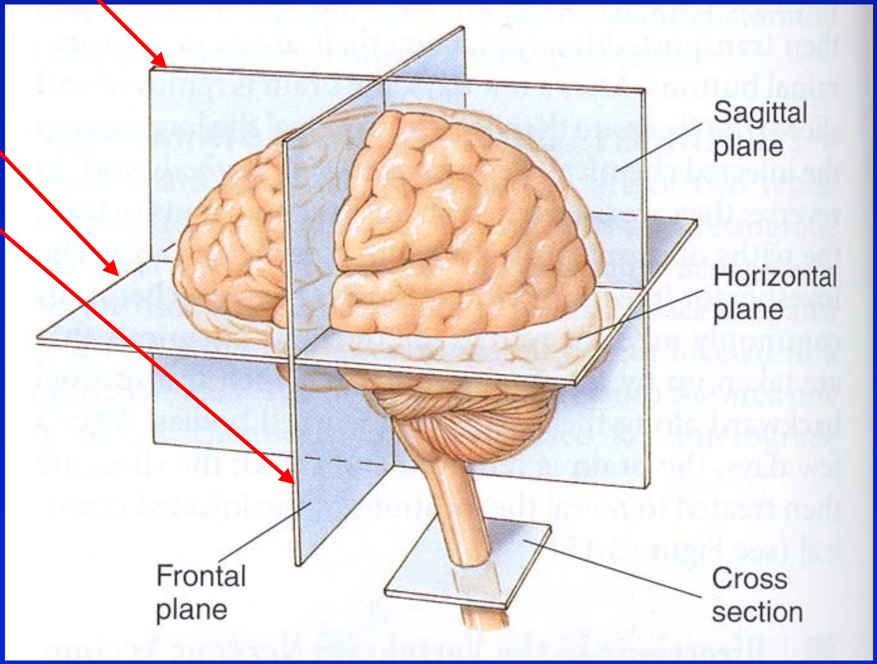
Directions in the Nervous System

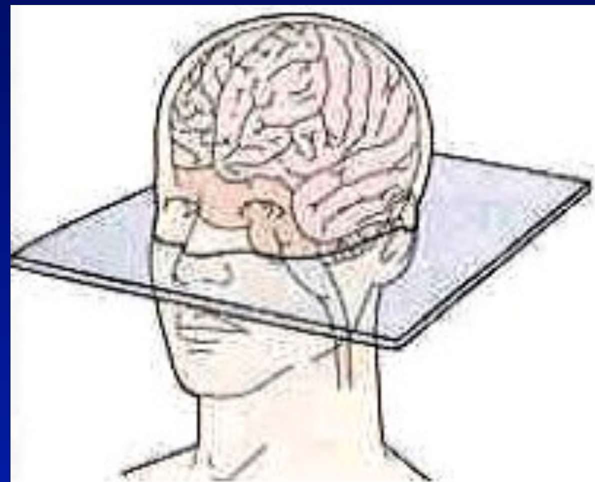
- For Human Brain:
  - Anterior/rostral: front
  - Posterior/caudal: back
  - Superior/dorsal: top
  - Inferior/ventral: bottom
  - Medial: toward middle
  - Lateral: toward outside

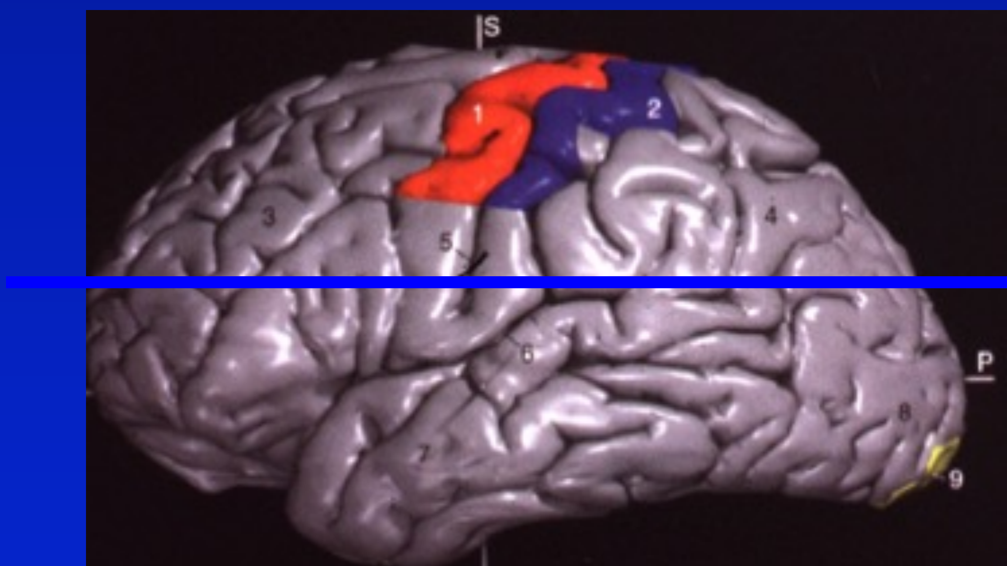


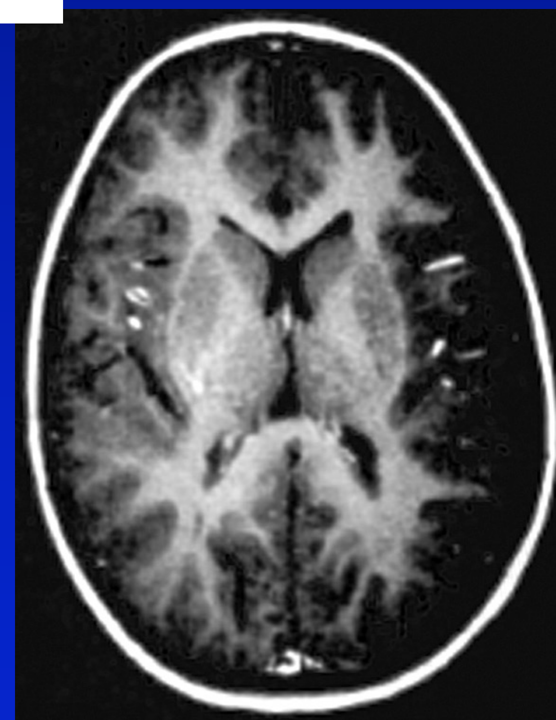
Planes of Section

- Sagittal
  - Mid-sagittal
  - Para-sagittal
- Horizontal/axial/transaxial
- Coronal/frontal

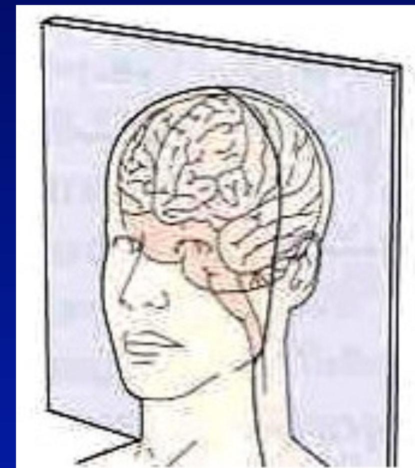


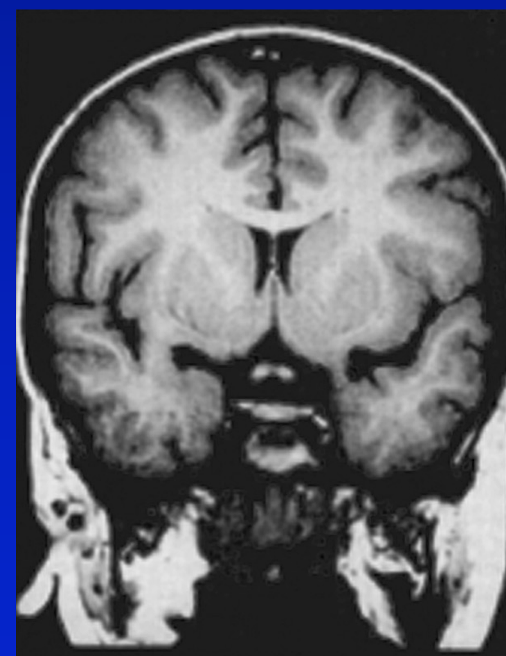




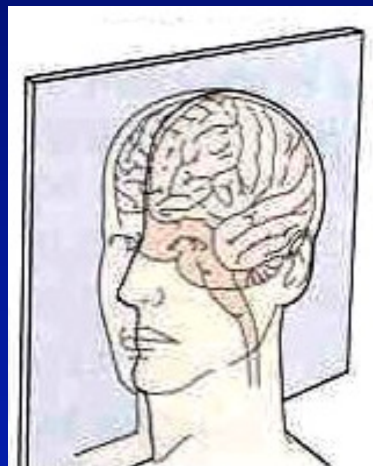


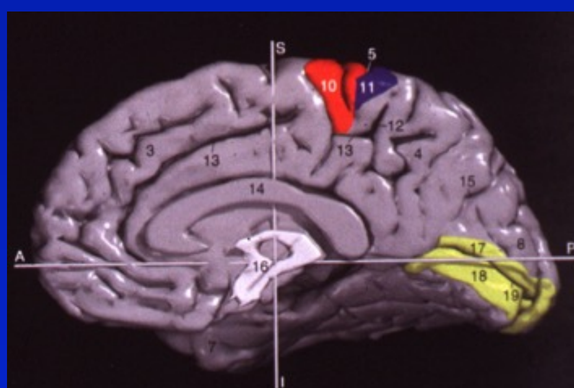
Axial

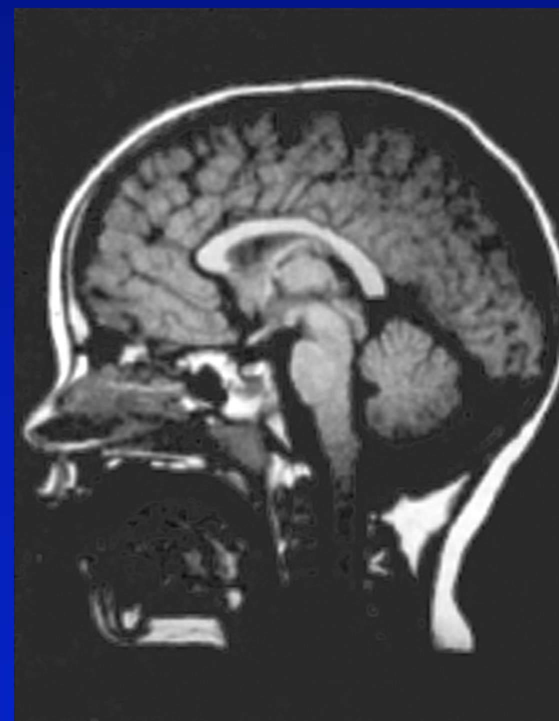




Coronal



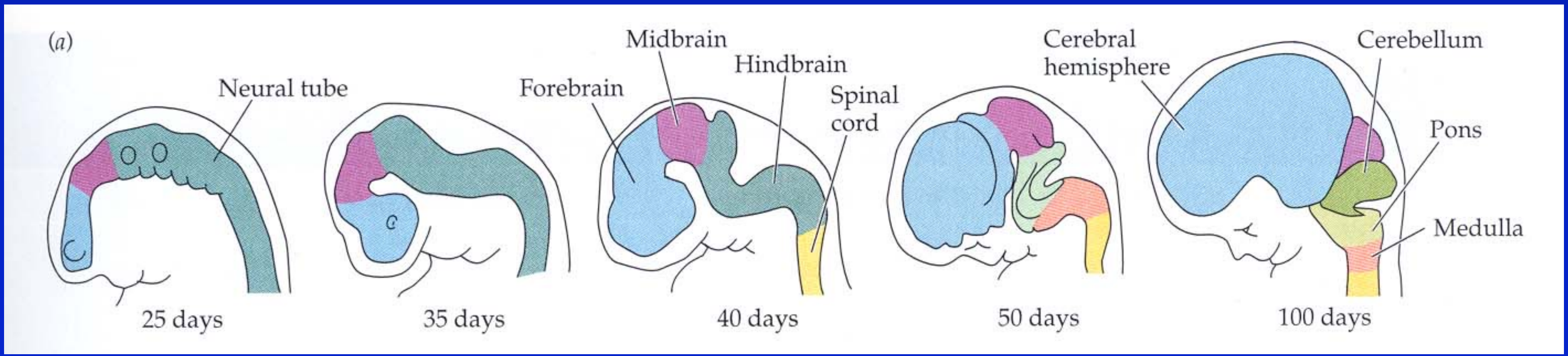




Sagittal

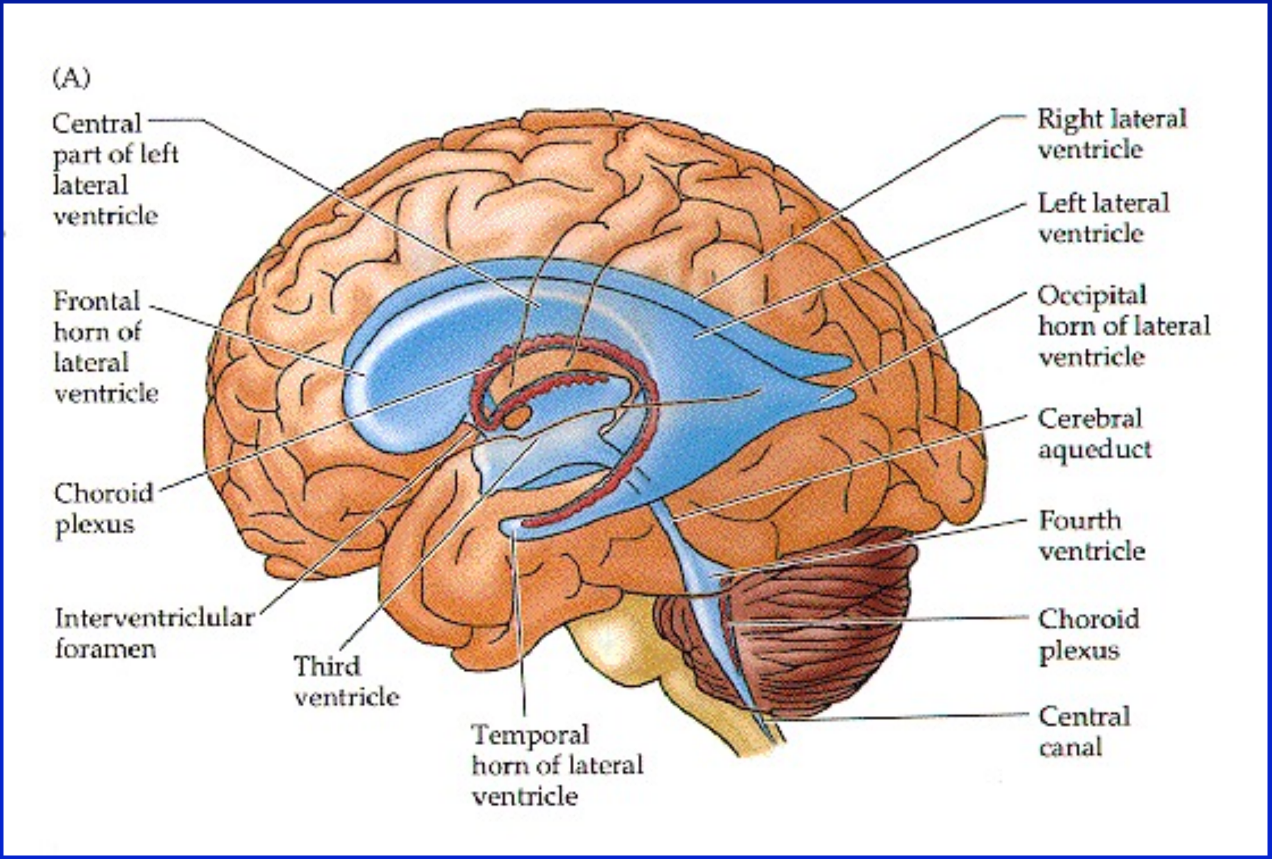
Early Brain Development

- Starts out as flat plate of ectodermal tissue that folds over to create a tube
- Parts of tube differentiate into different parts of nervous system



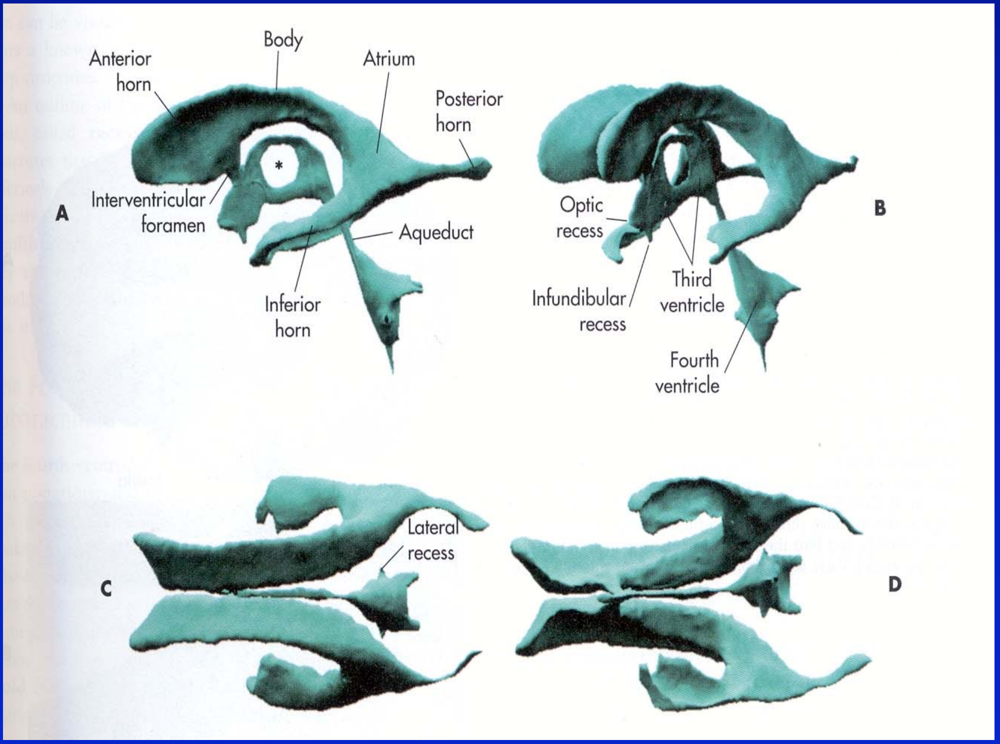
What Happens to the Lumen (hole) in the Tube

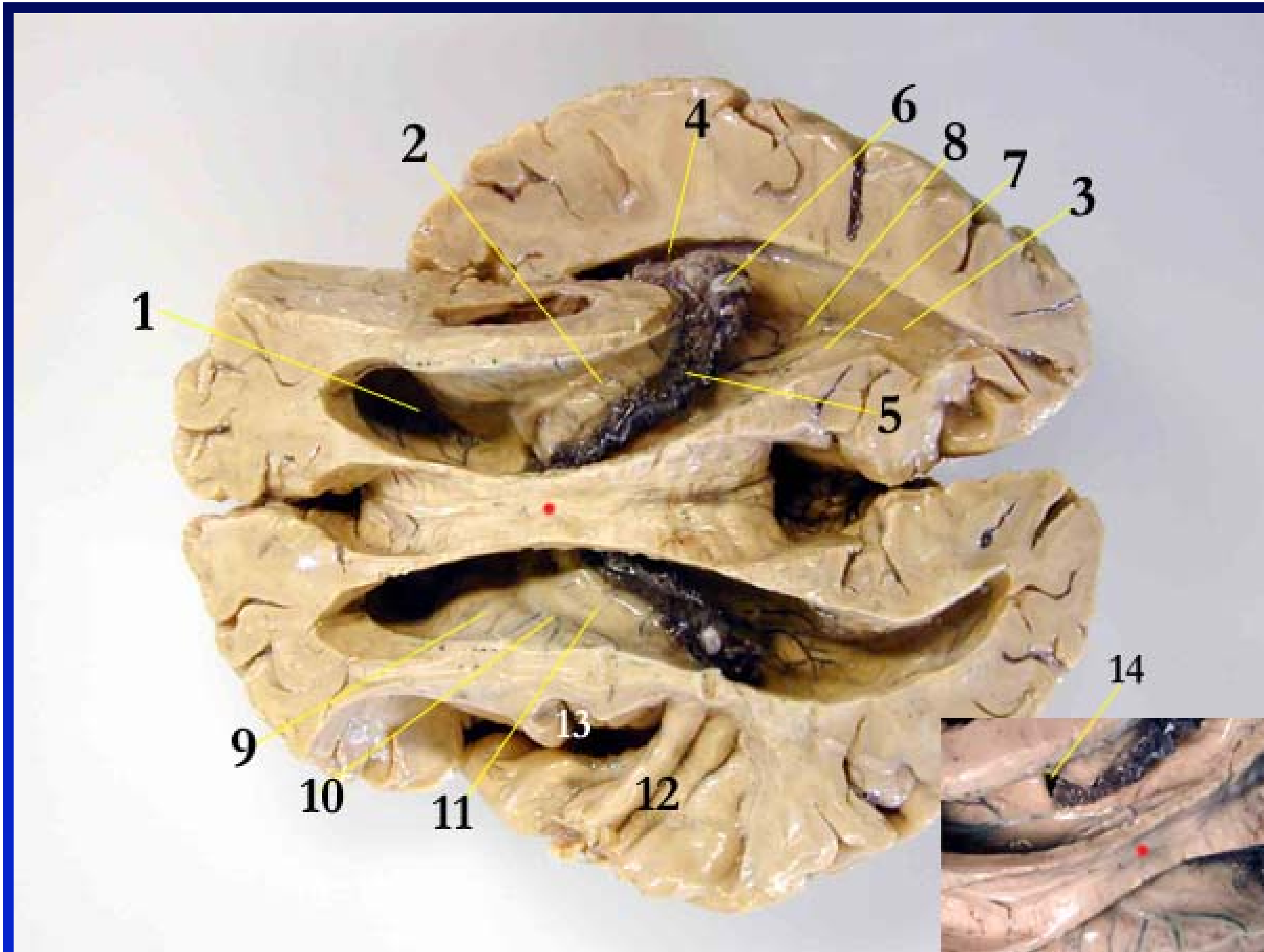
- Spinal cord channel
- Ventricles
  - Lateral
  - Third
  - Fourth



Layout of the Ventricles

- Lined with choroid plexus especially in lateral ventricles
  - Makes cerebrospinal fluid (CSF)





1
2
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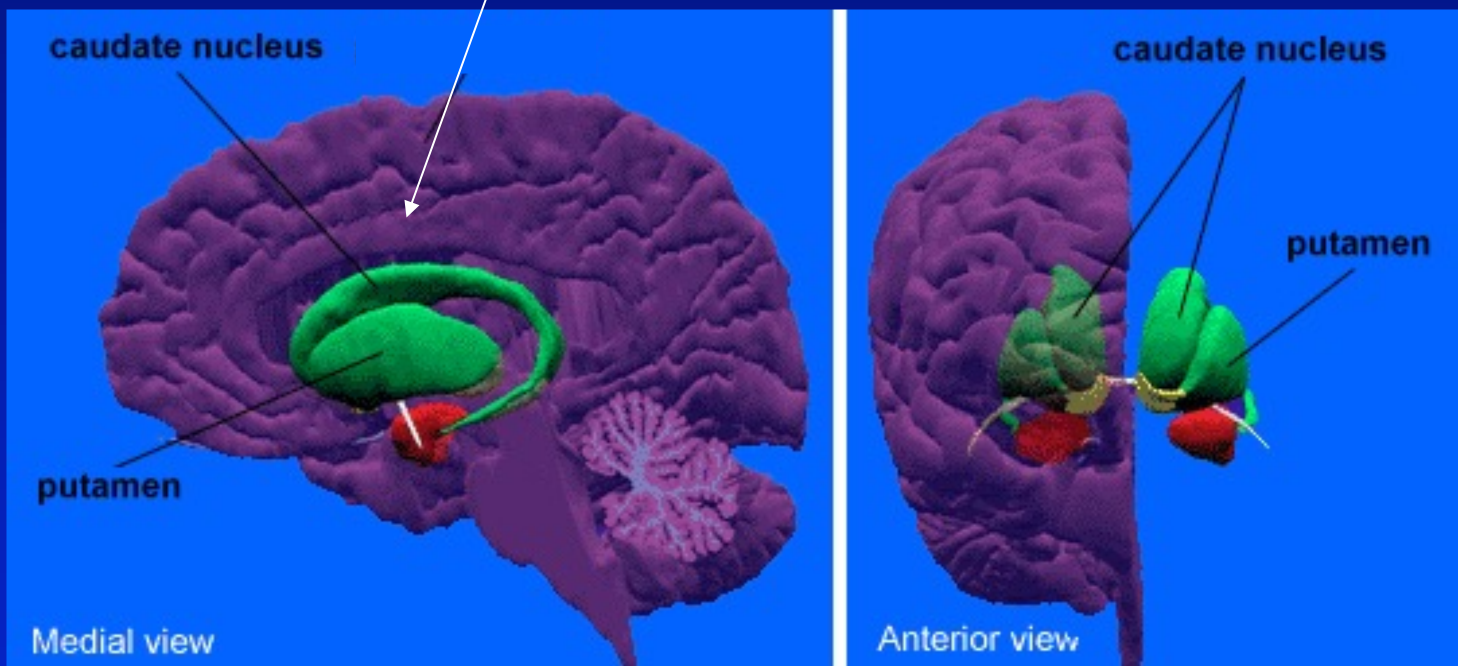
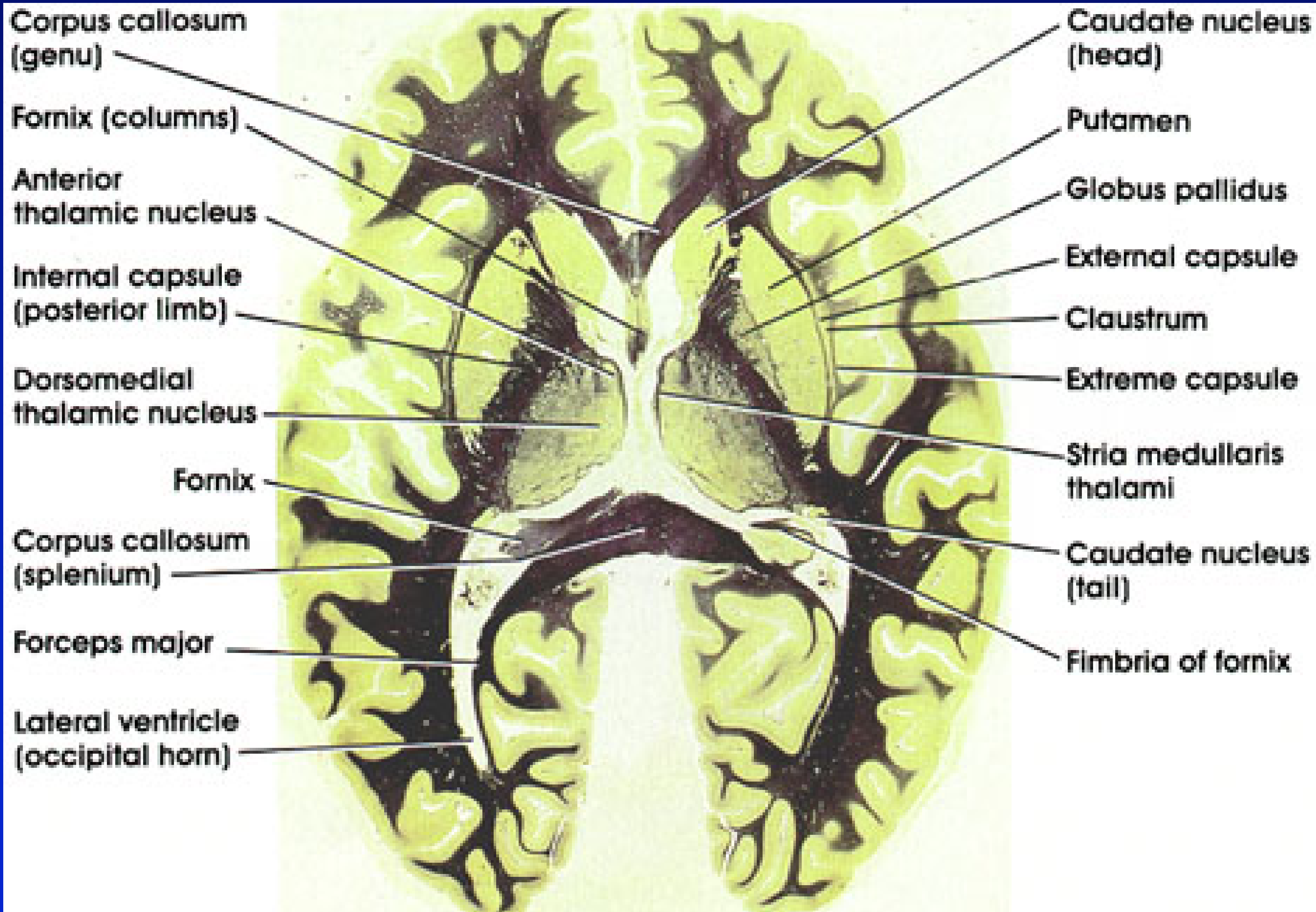
Basal Ganglia



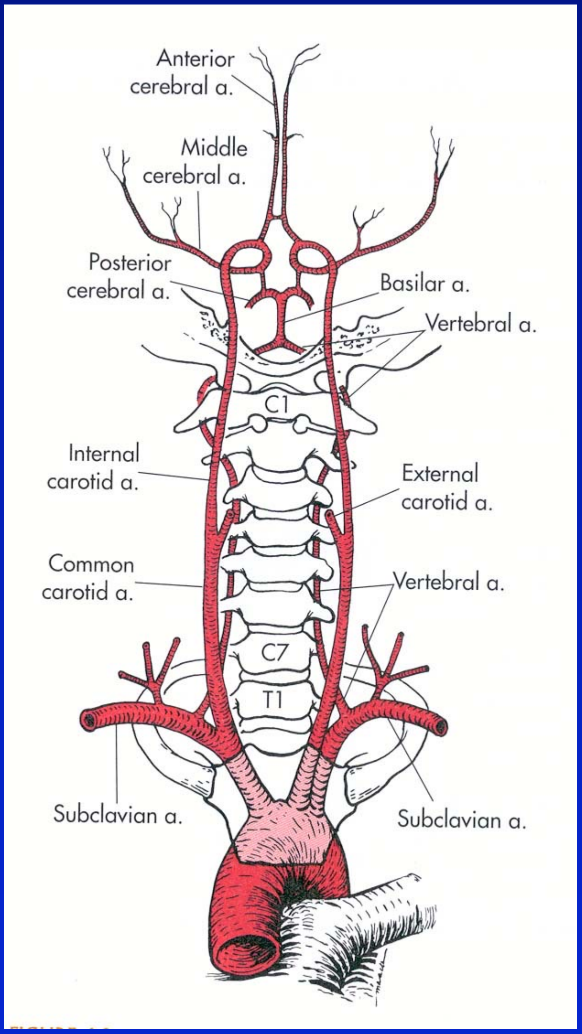
Horizontal Section

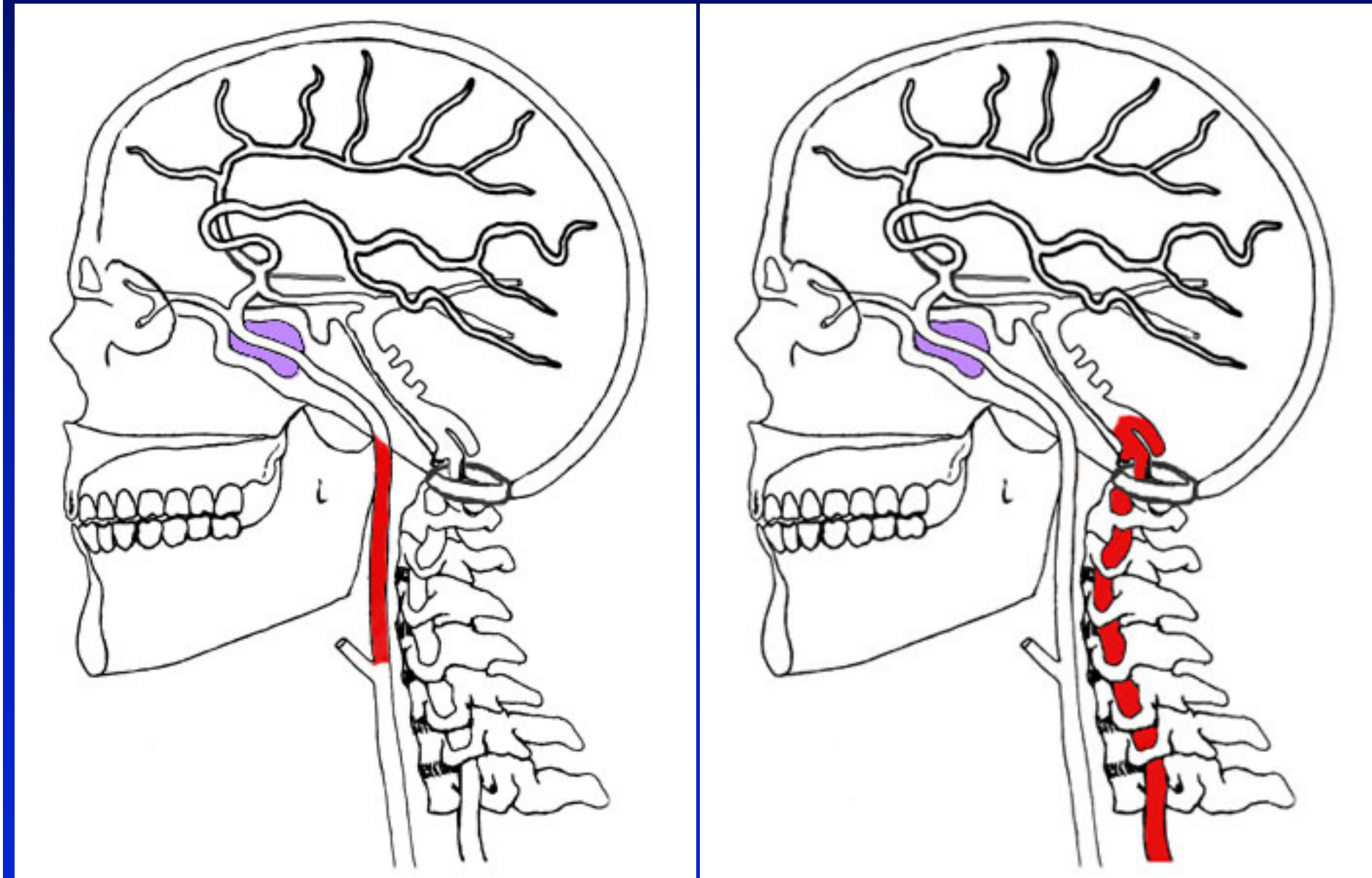


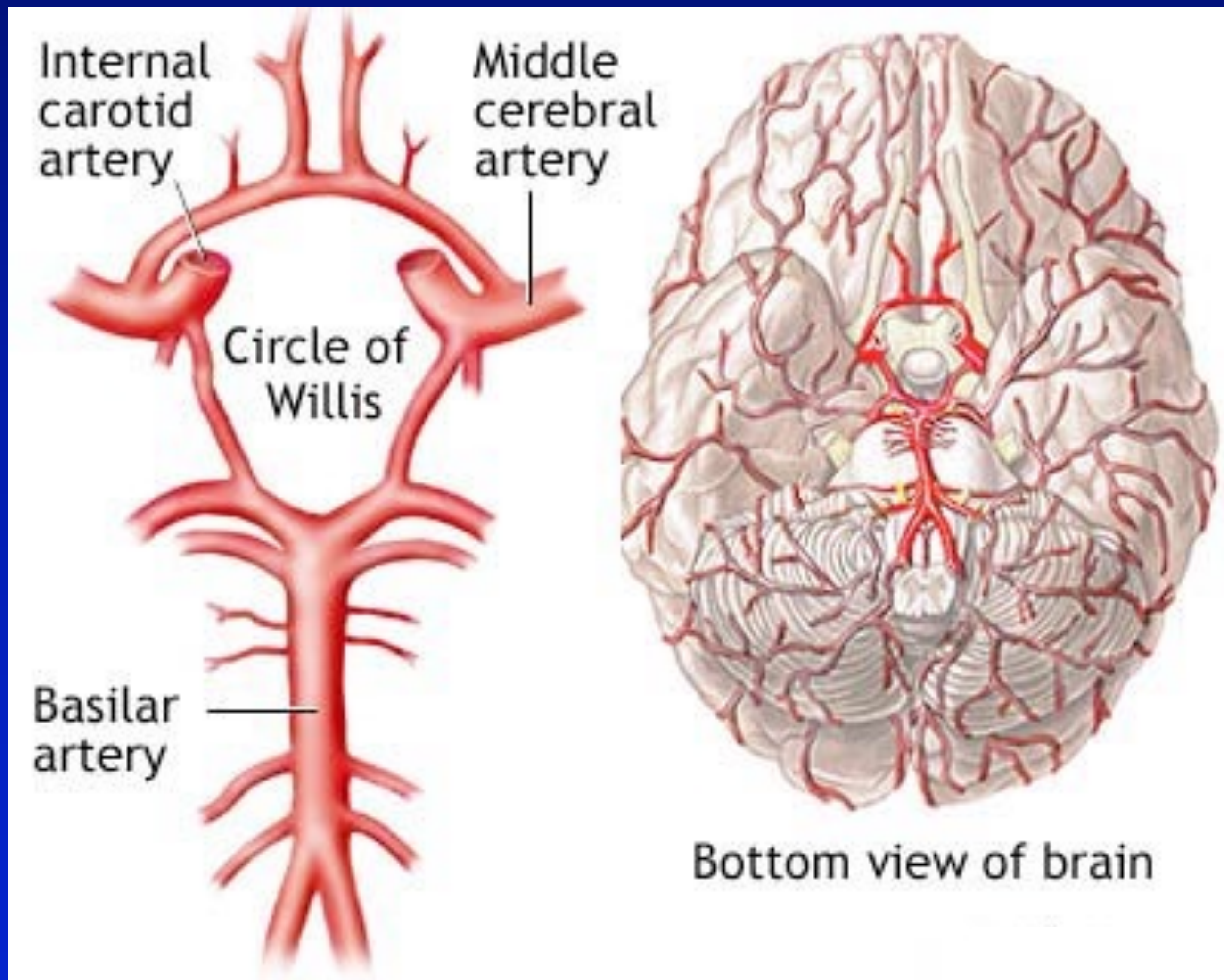
Coronal Section

Blood Supply to Brain

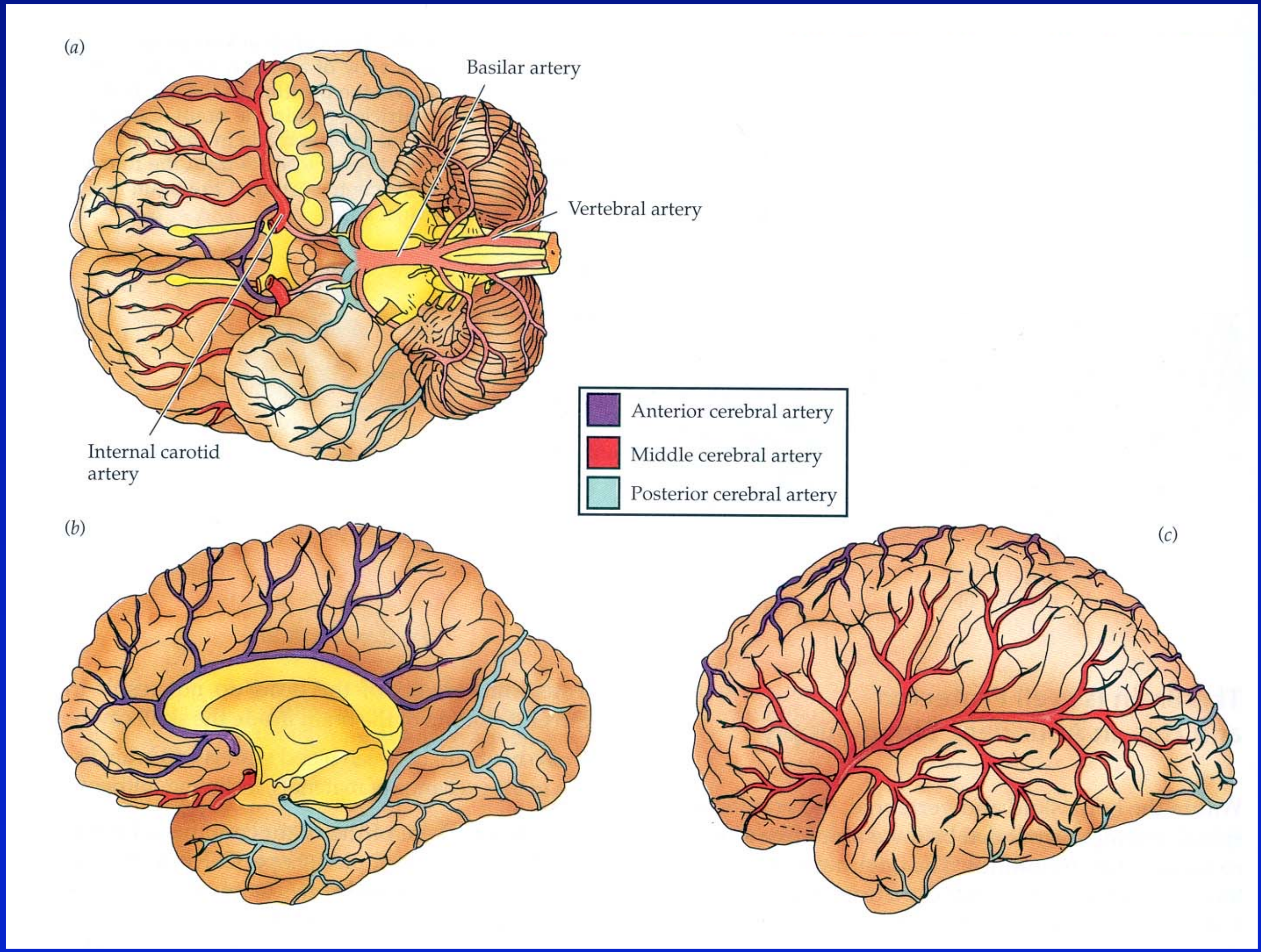
- Internal carotid artery feeds to anterior and middle cerebral arteries
- Vertebral arteries join to form basilar artery that feeds to posterior cerebral artery





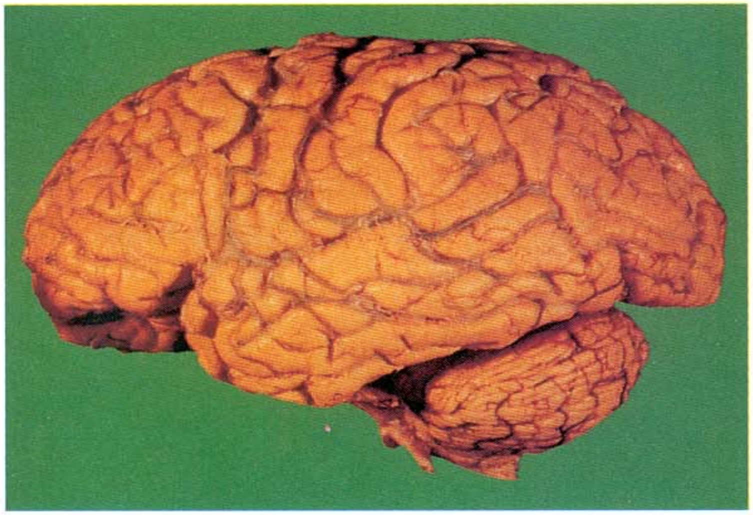

Internal carotid artery
Middle cerebral artery
Circle of Willis
Basilar artery
Bottom view of brain

Distribution of Main Arteries



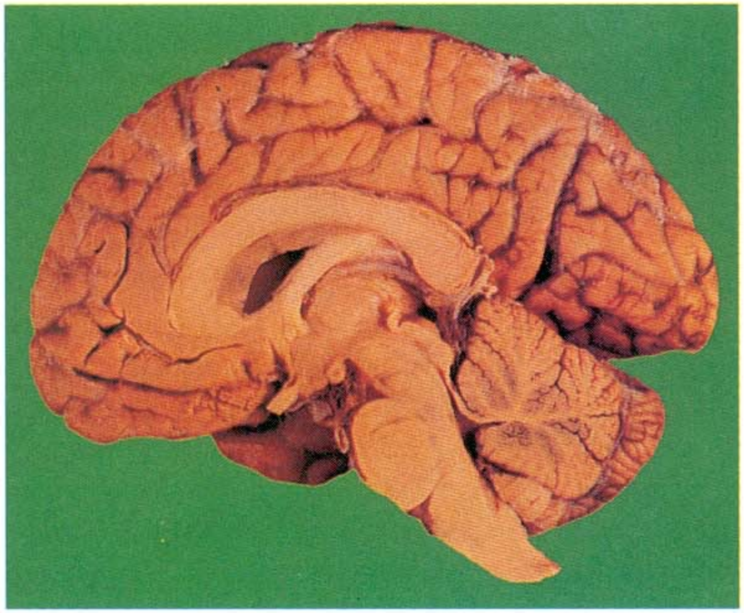
Coarse Structure of the Brain
Lateral View

- Cortical and subcortical structures
- Cortex divided into 4 lobes
  - Lobes have folded structure
    - Bumps are gyri (singular: gyrus)
    - Indentations are sulci (singular: sulcus)

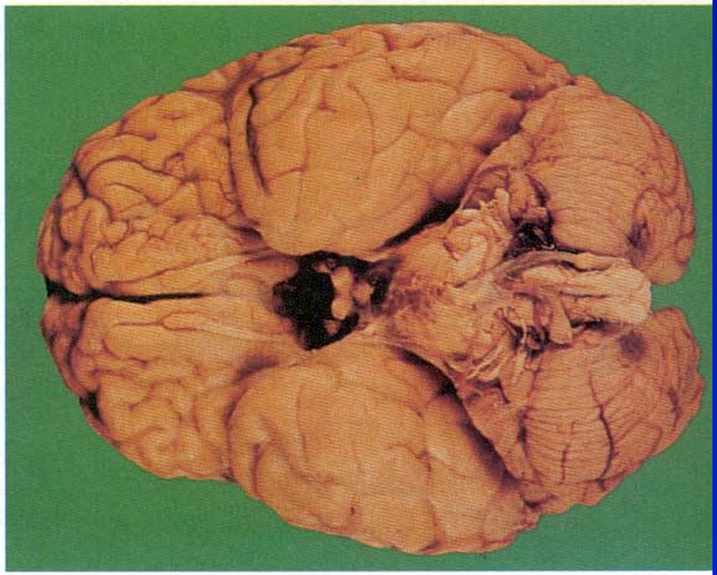


Coarse Structure of the Brain
Medial View

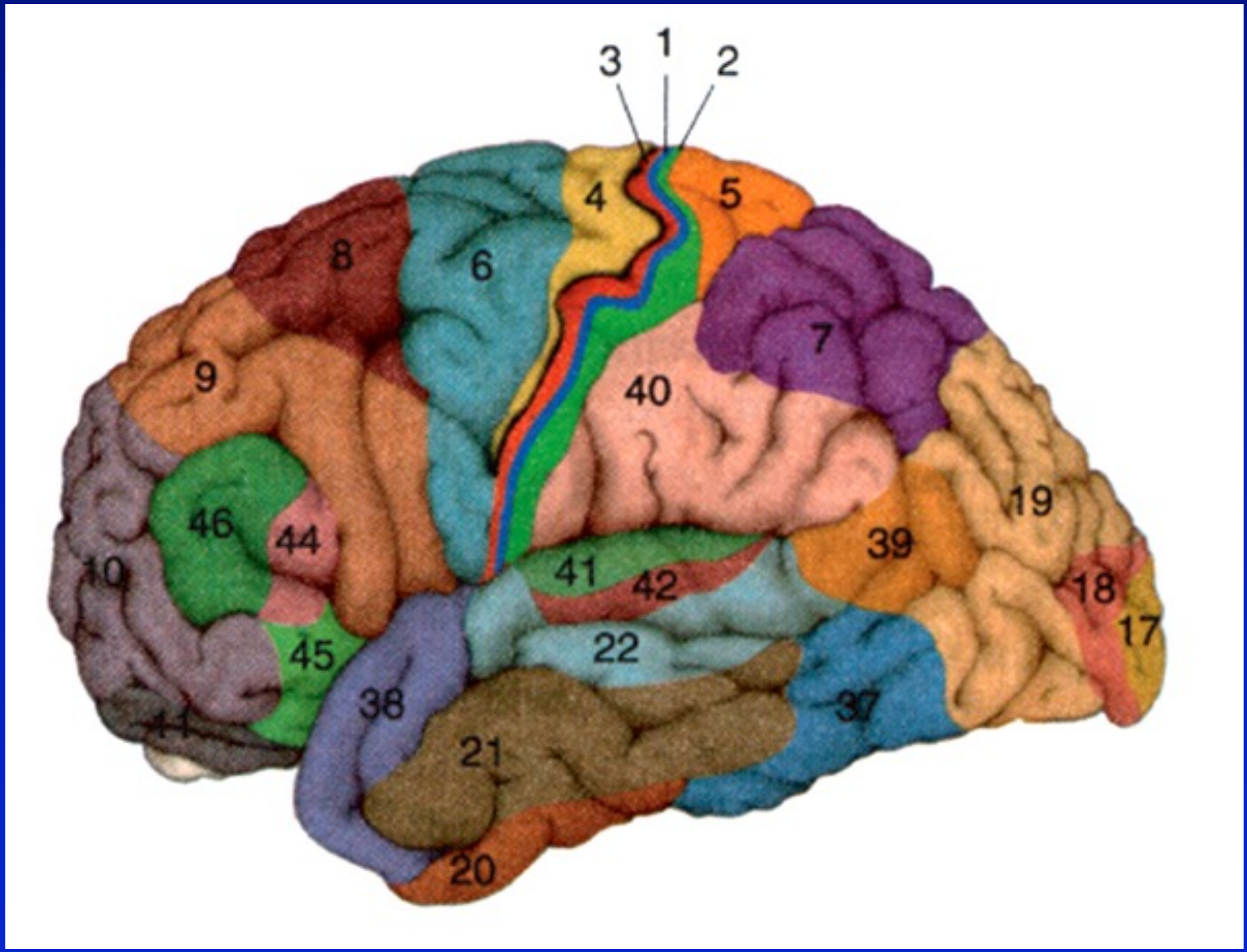
- Note connecting fibers between hemispheres



Coarse Structure of the Brain
Ventral View



Brodmann's Map



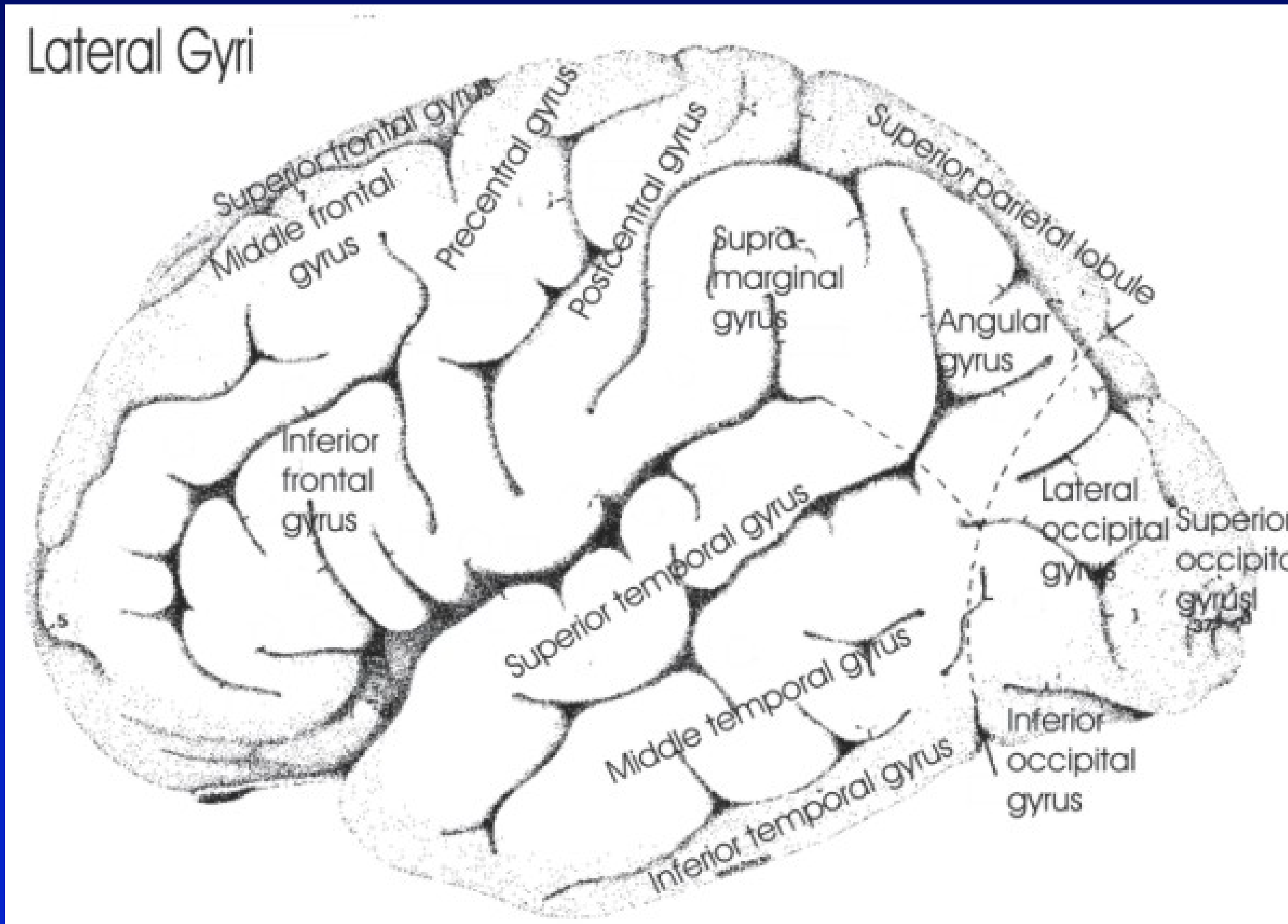
Words of Wisdom

- If you want to do fMRI, you must take neuroanatomy

- You need to always have a good atlas handy, such as:

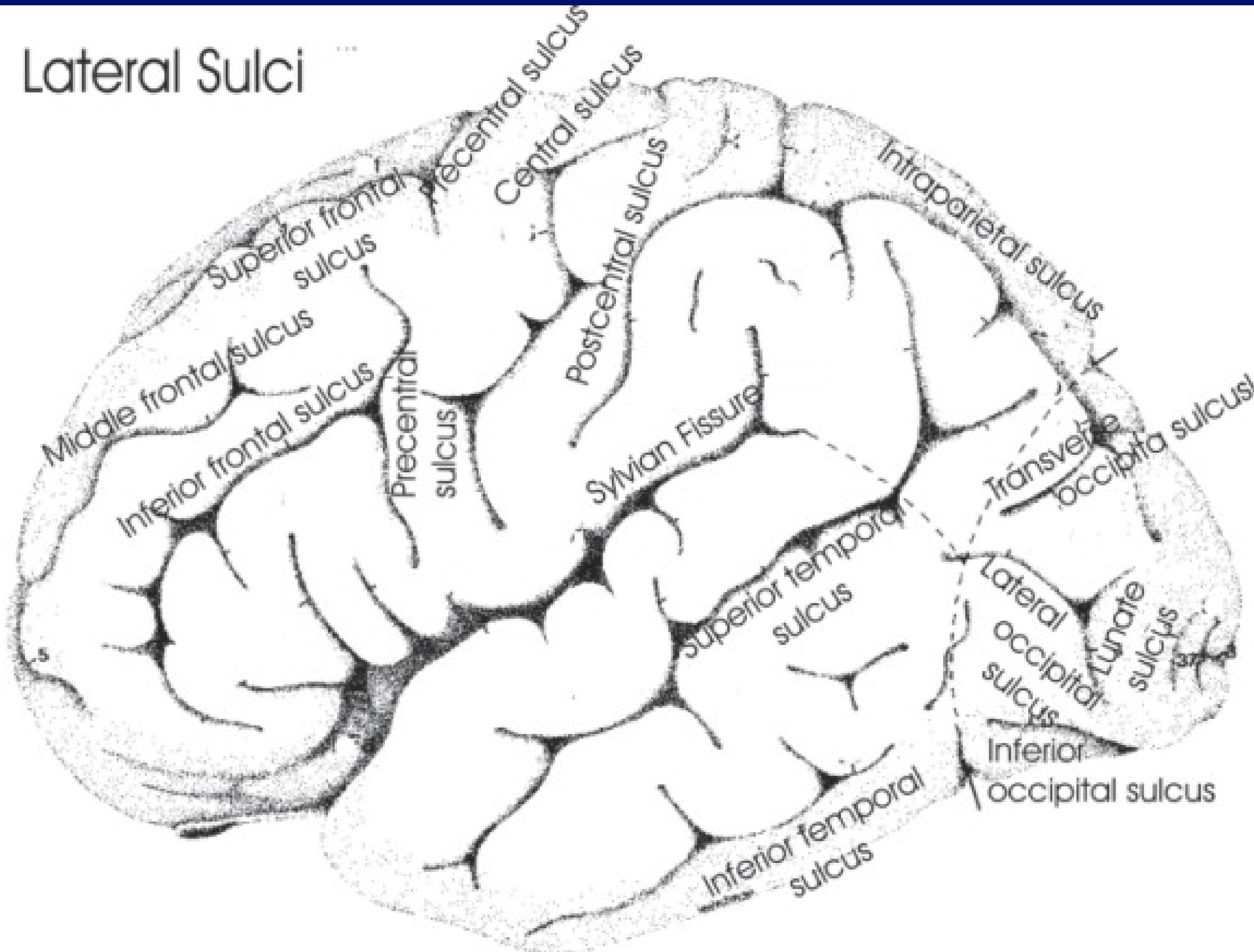
  Duvernoy, H. (1991) The Human Brain: Surface, Three-Dimensional Sectional Anatomy and MRI. Springer-Verlag, New York

- You should not describe areas of activation only in terms Brodmann's designations. Pay attention to gyri and sulci also

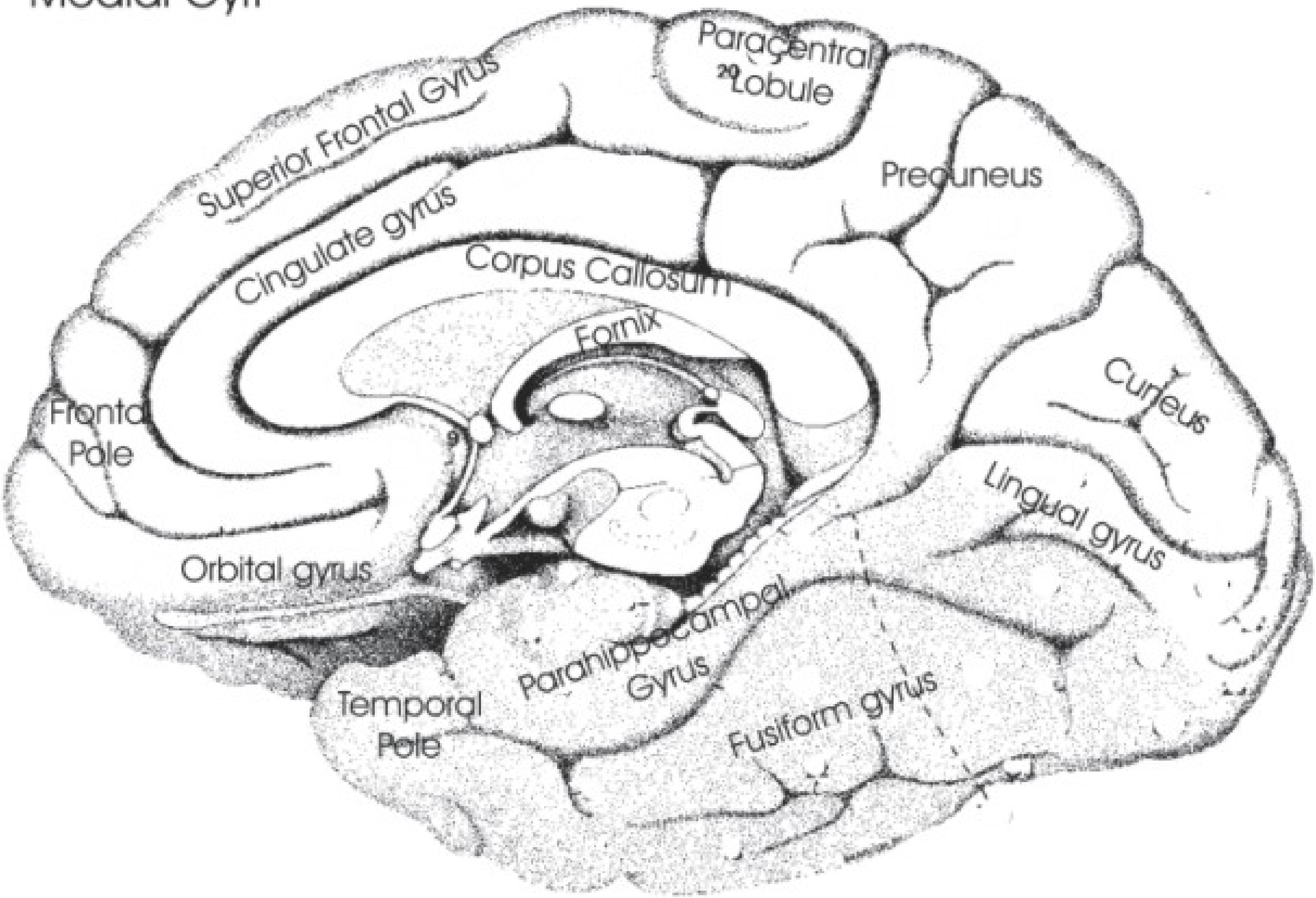


Lateral Gyri
Superior frontal gyrus
Middle frontal gyrus
Precentral gyrus
Postcentral gyrus
Supra-marginal gyrus
Superior parietal lobule
Angular gyrus
Inferior frontal gyrus
Lateral occipital gyrus
Superior occipital gyrus
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal gyrus
Inferior occipital gyrus

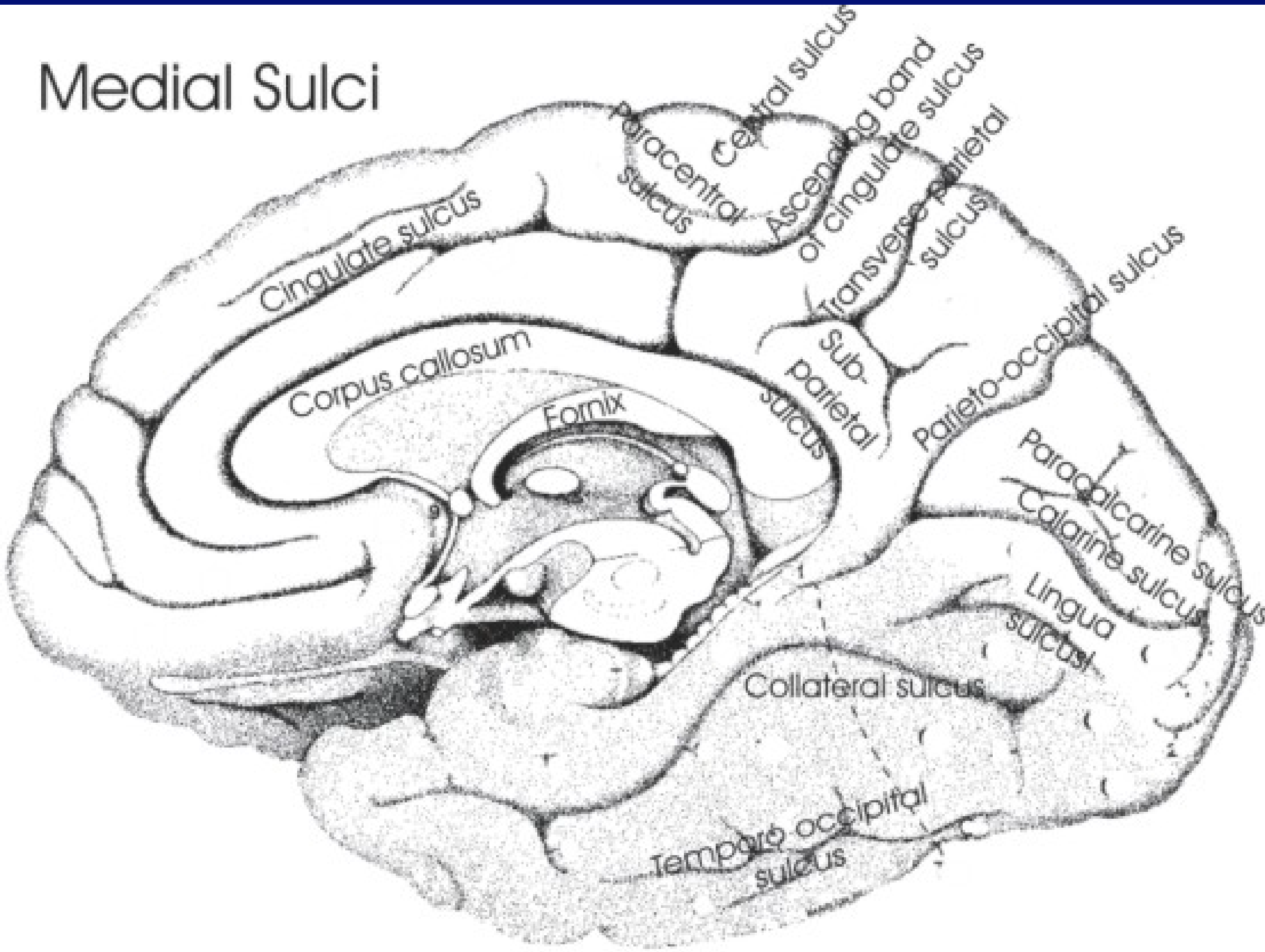
Lateral Sulci



Medial Gyri

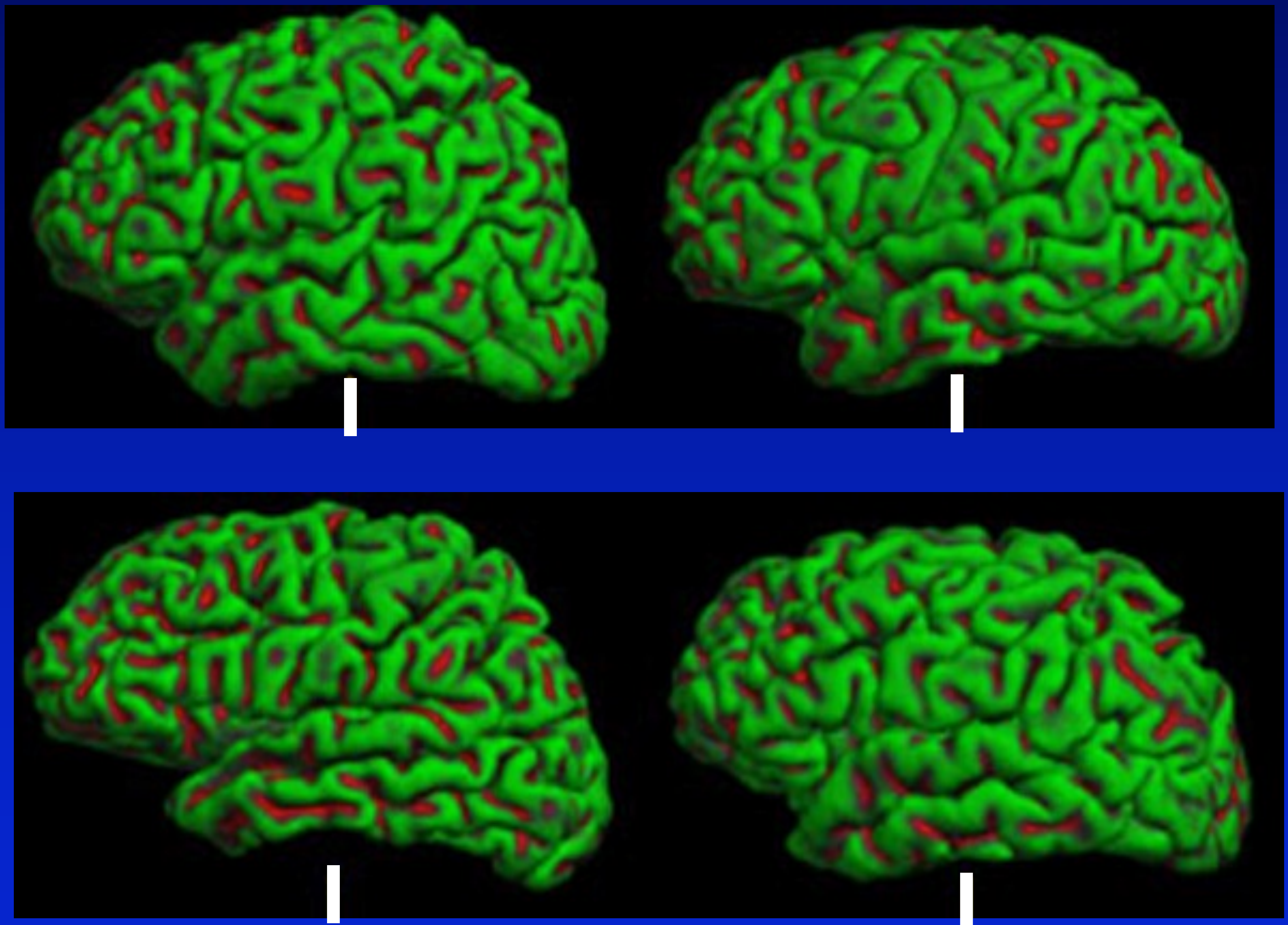

Superior Frontal Gyrus
Paracentral Lobule
Precuneus
Cingulate gyrus
Corpus Callosum
Fornix
Frontal Pole
Cuneus
Lingual gyrus
Orbital gyrus
Parahippocampal Gyrus
Temporal Pole
Fusiform gyrus

Medial Sulci

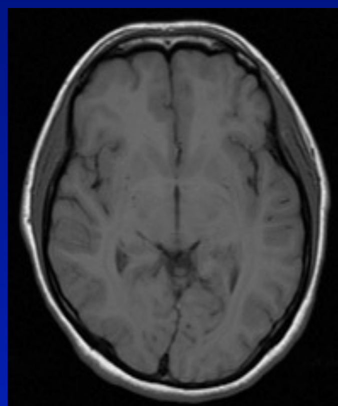


A Canonical Brain

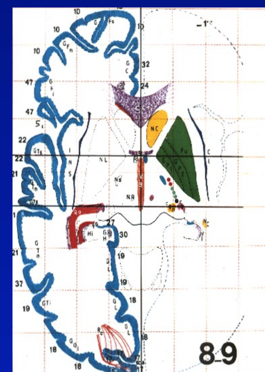
Variations in Brain Anatomy



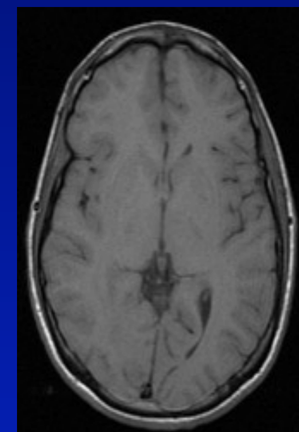
Dealing with different heads: spatial normalization



subject A



standard space



subject B

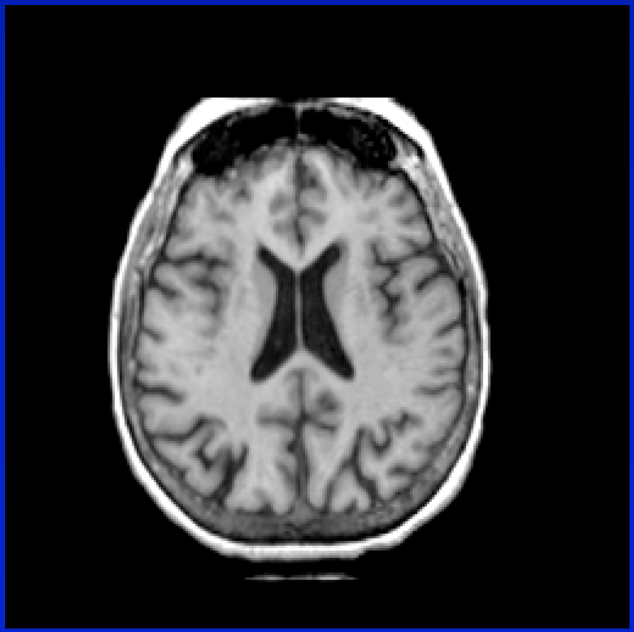
Caveat:

- variability in structure/function relationships

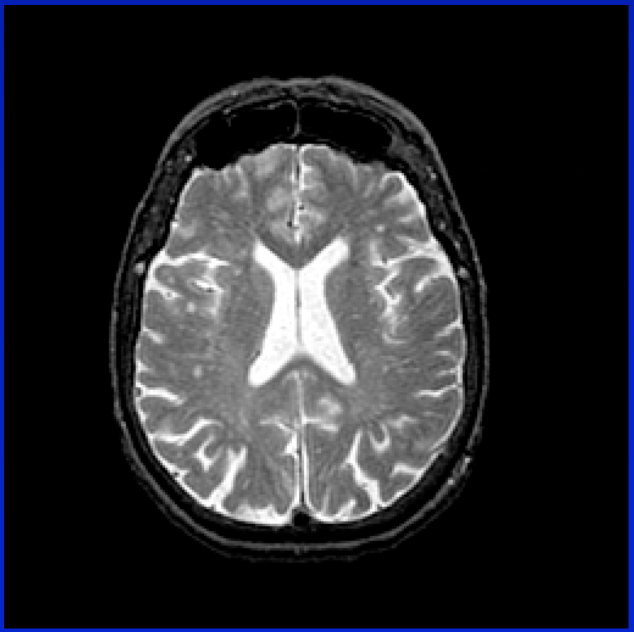
T1 and T2 Images

- Note gray-white matter distinction in T1
- Note reversed contrast of CSF in T1 and T2
- Note finer anatomical detail in T1

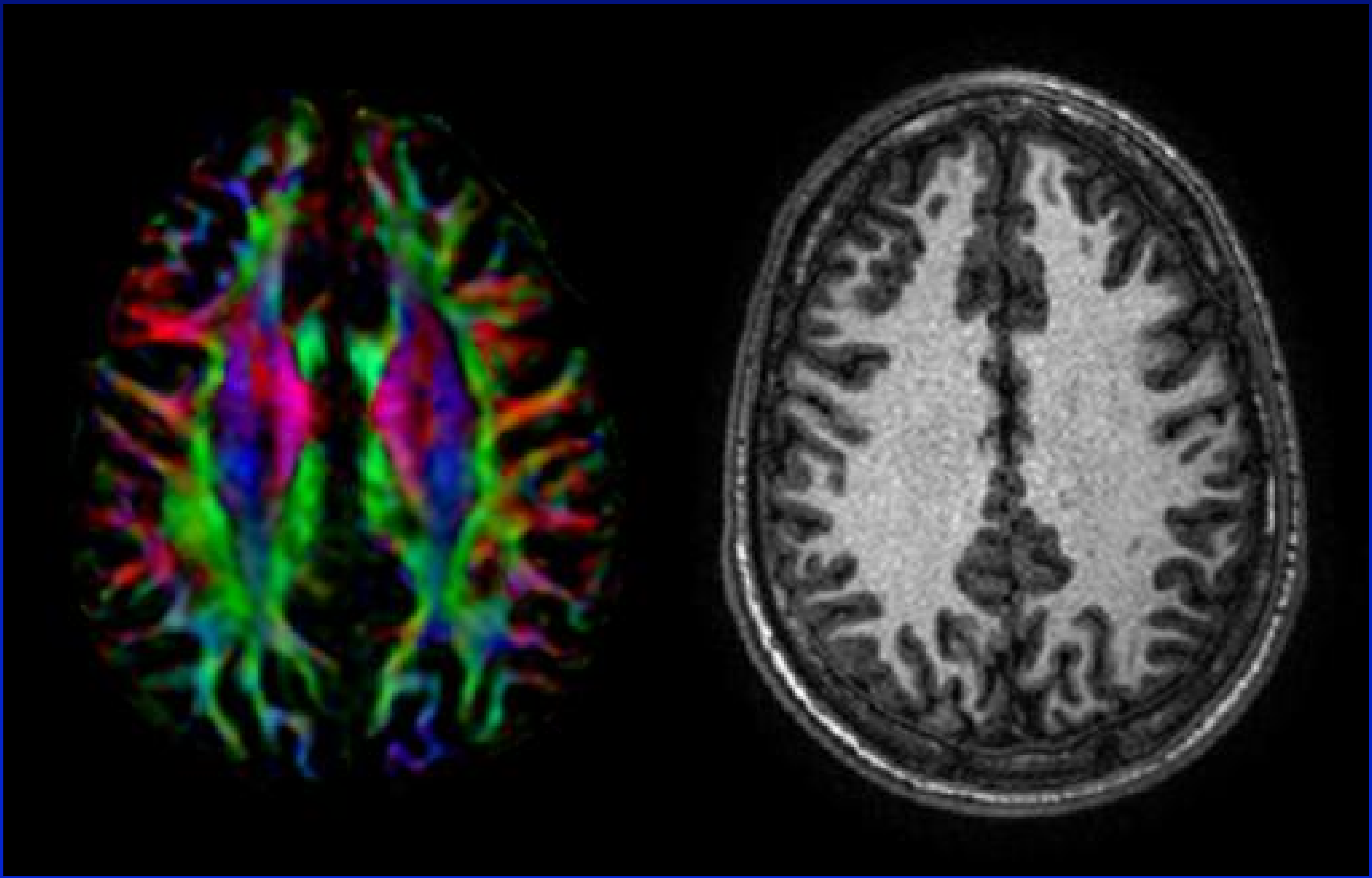
T1



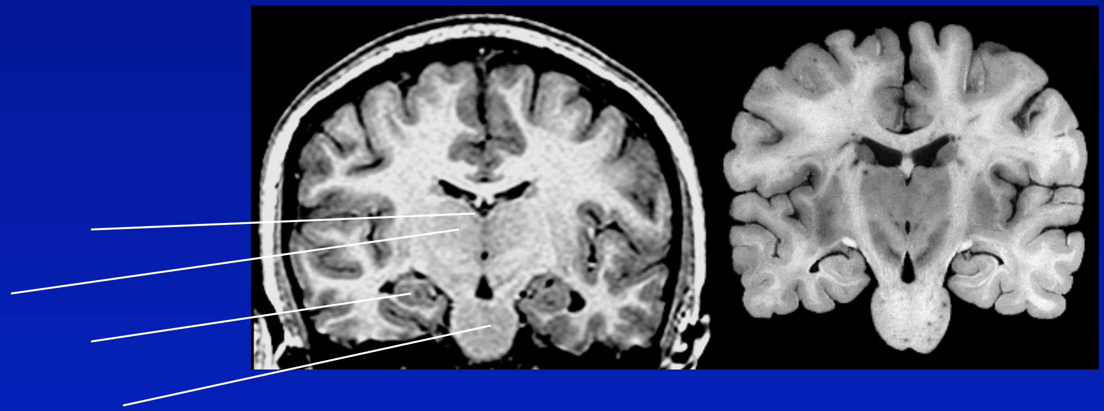
T2

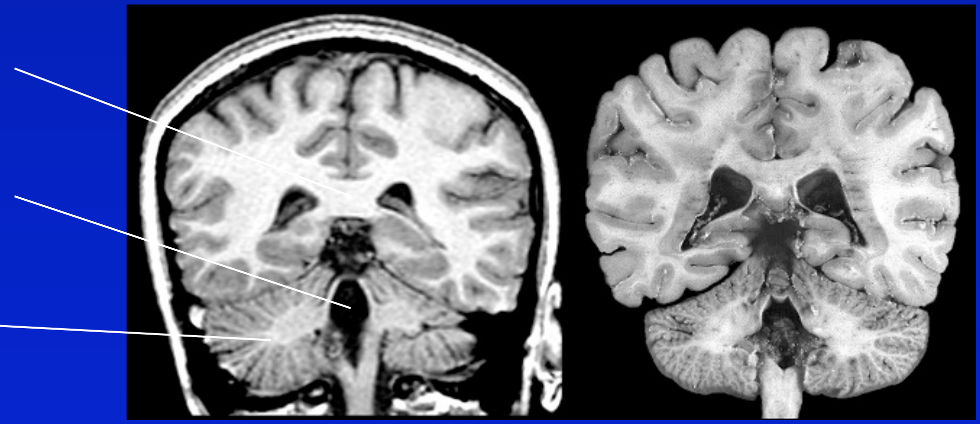


Diffusion Tensor Image

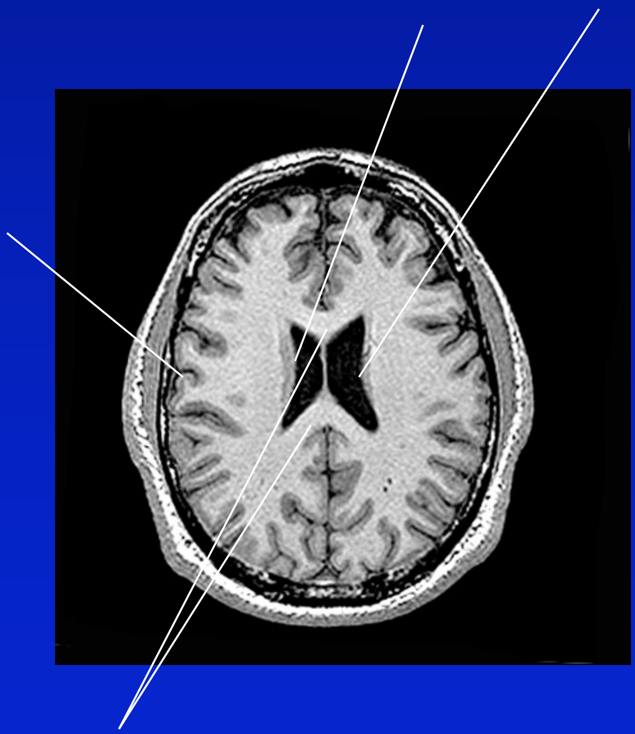


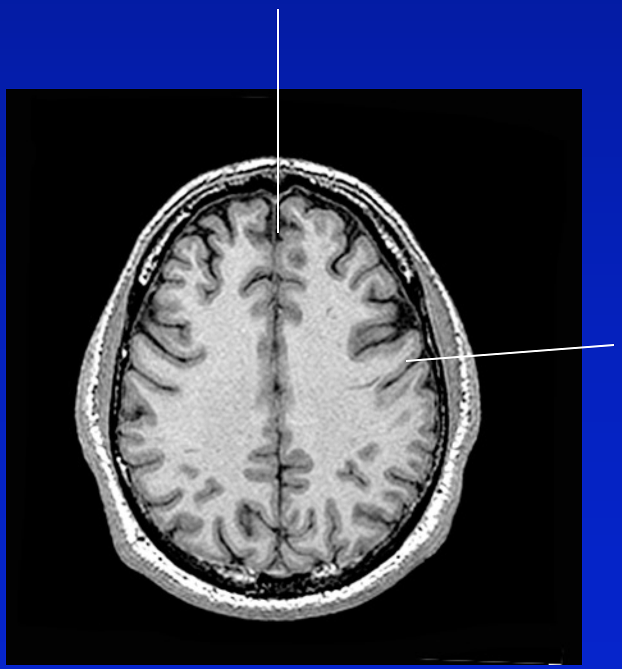
Which is More Caudal?



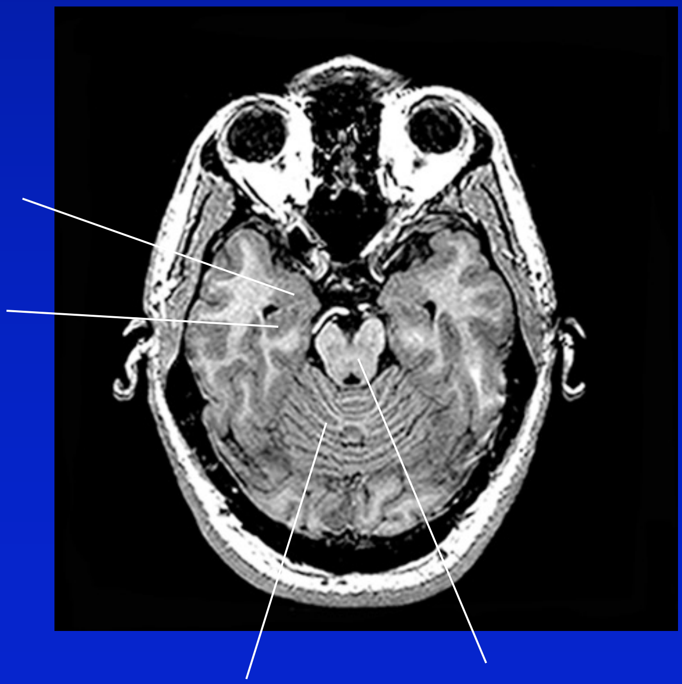


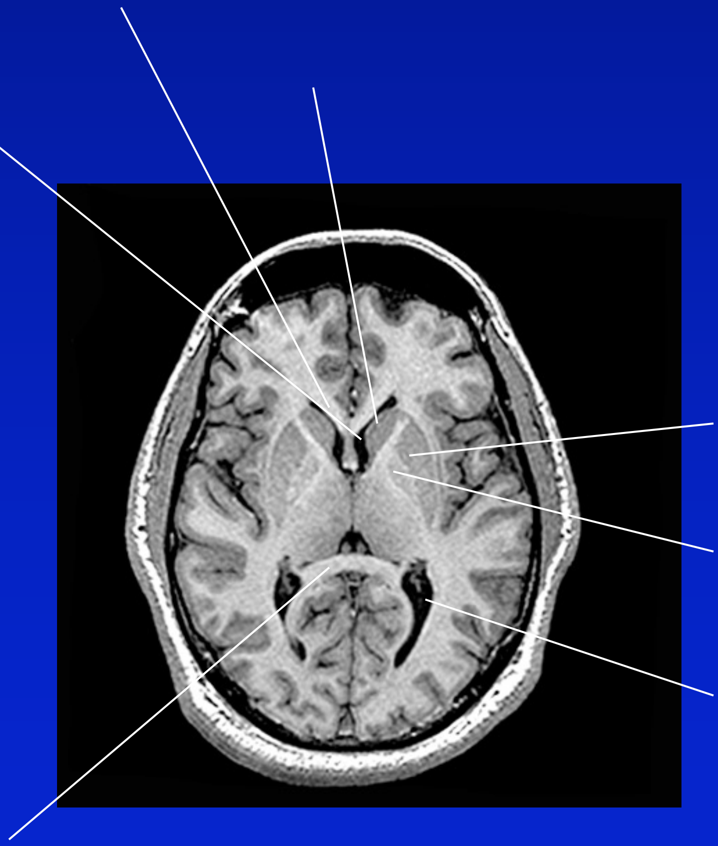
Which is more Dorsal?



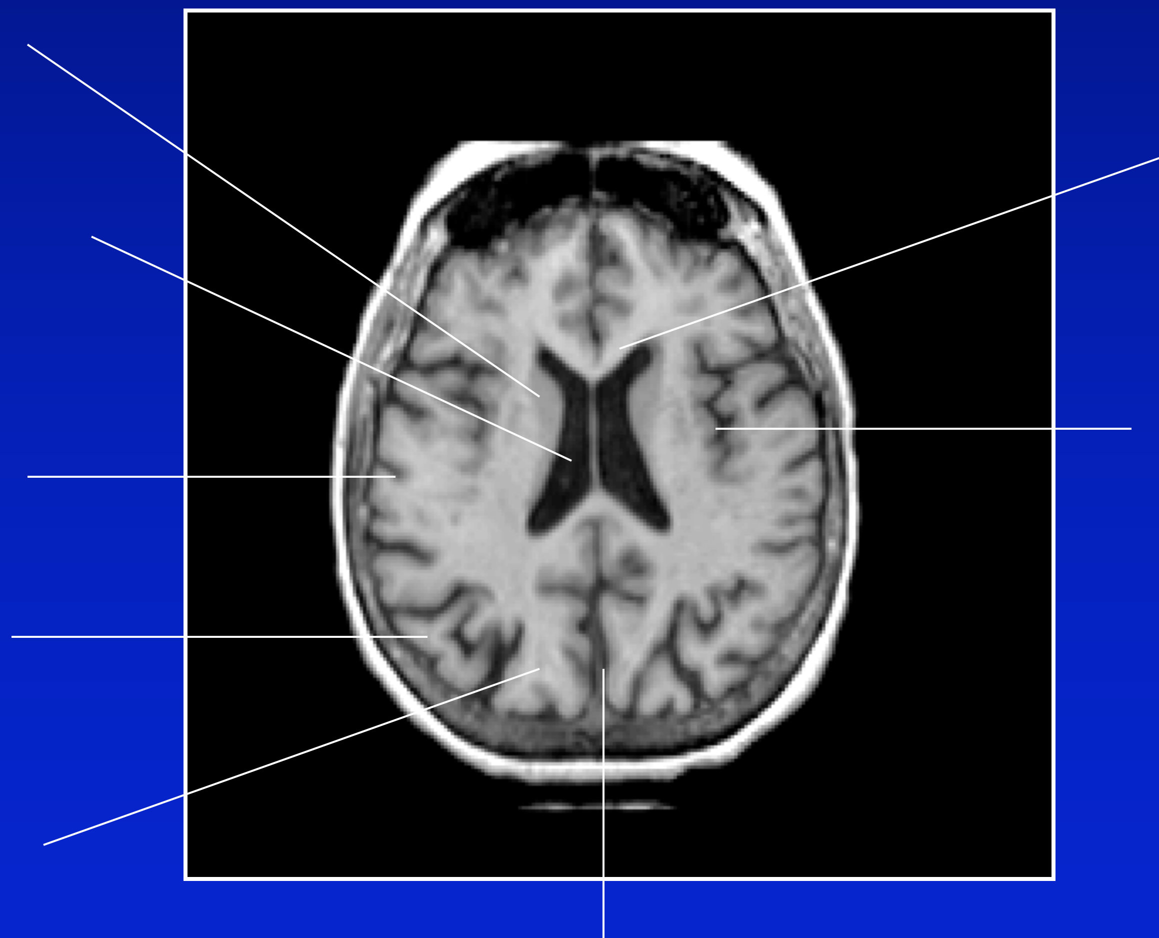


Which is more Dorsal?

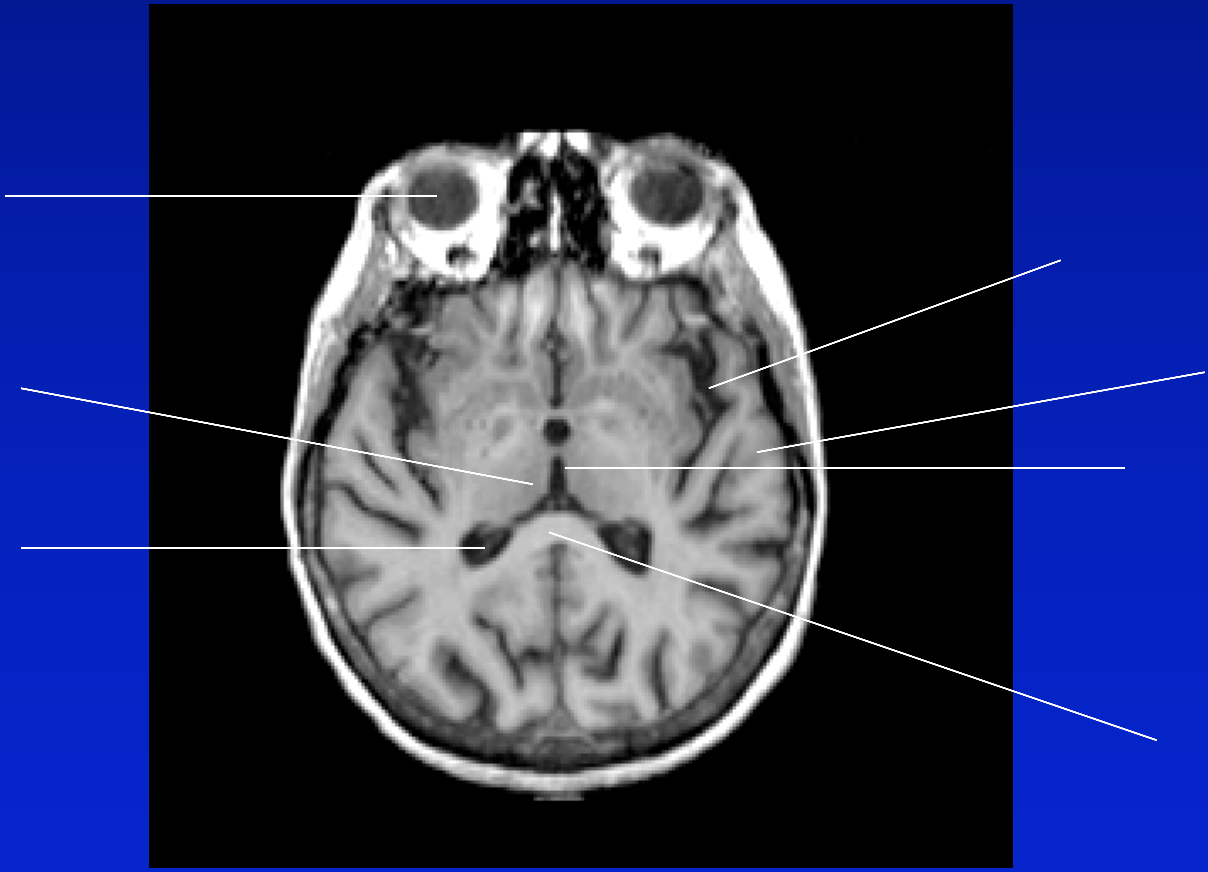




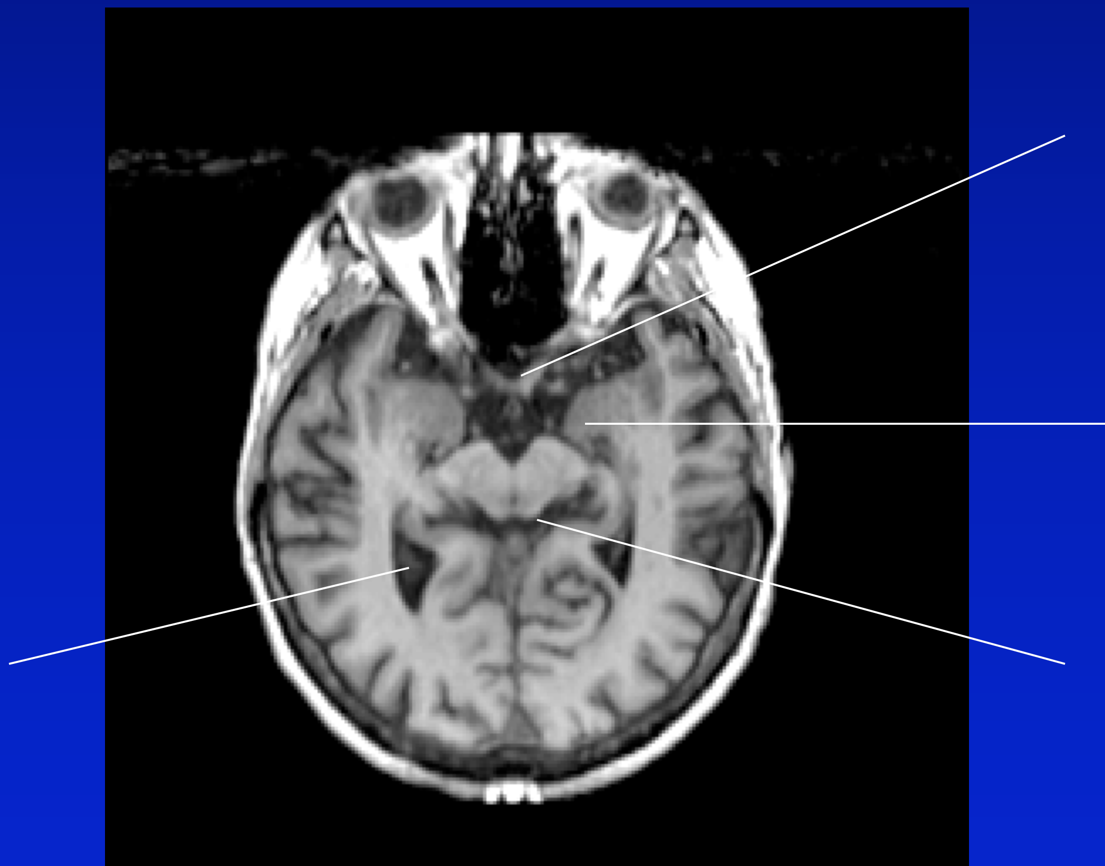
Identifying Structures



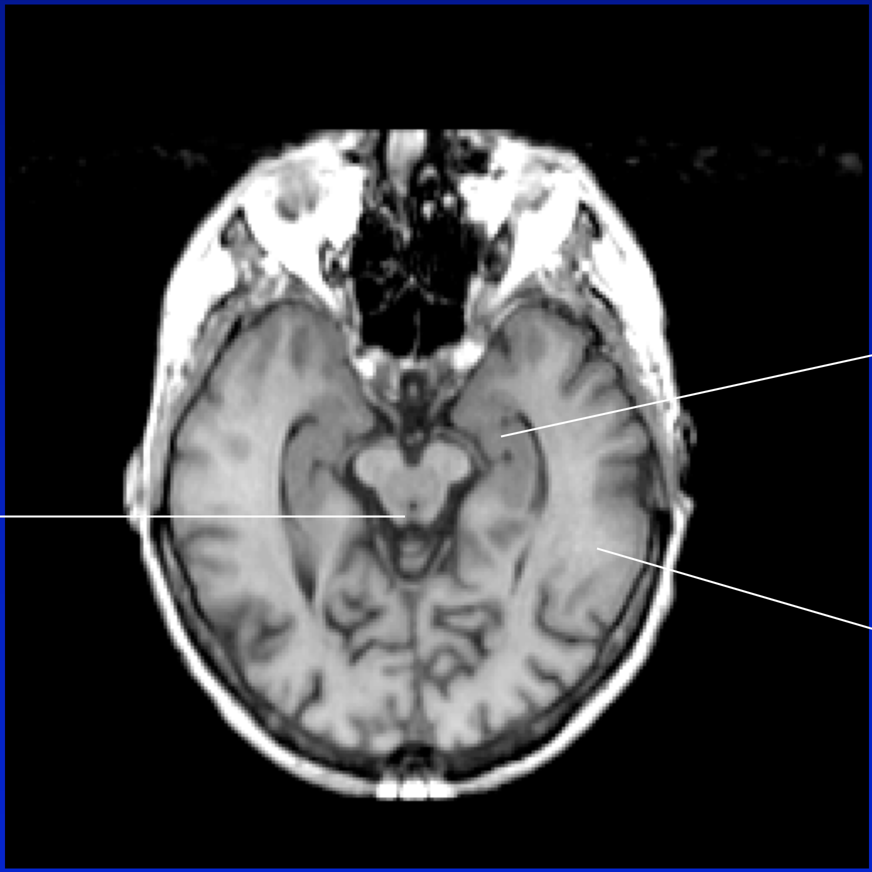
Low Axial Slice



Lower Still

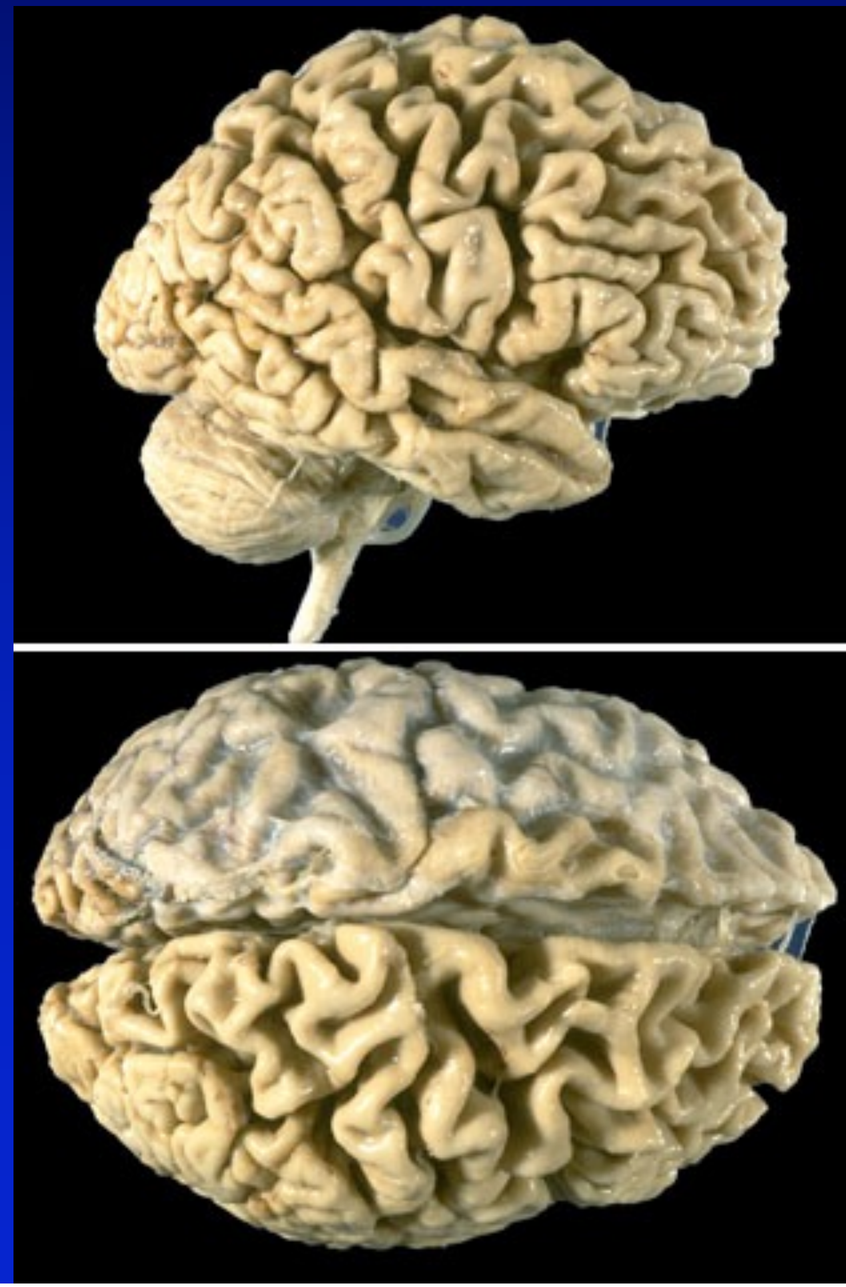


Lowest of All

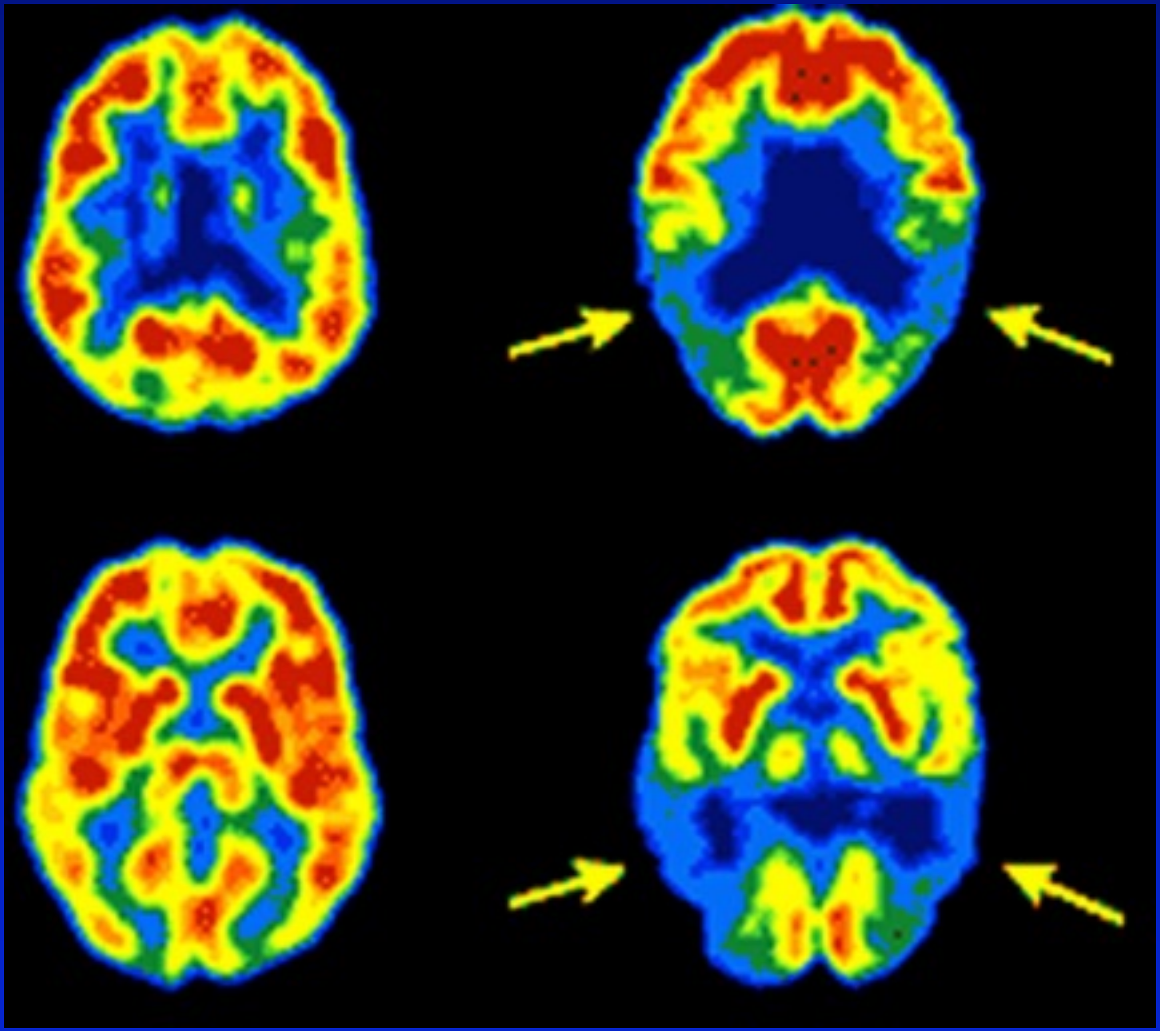


Normal brain

Cortical atrophy



Normal Alzheimer's



1. What You Can Do With Neuroimaging Data

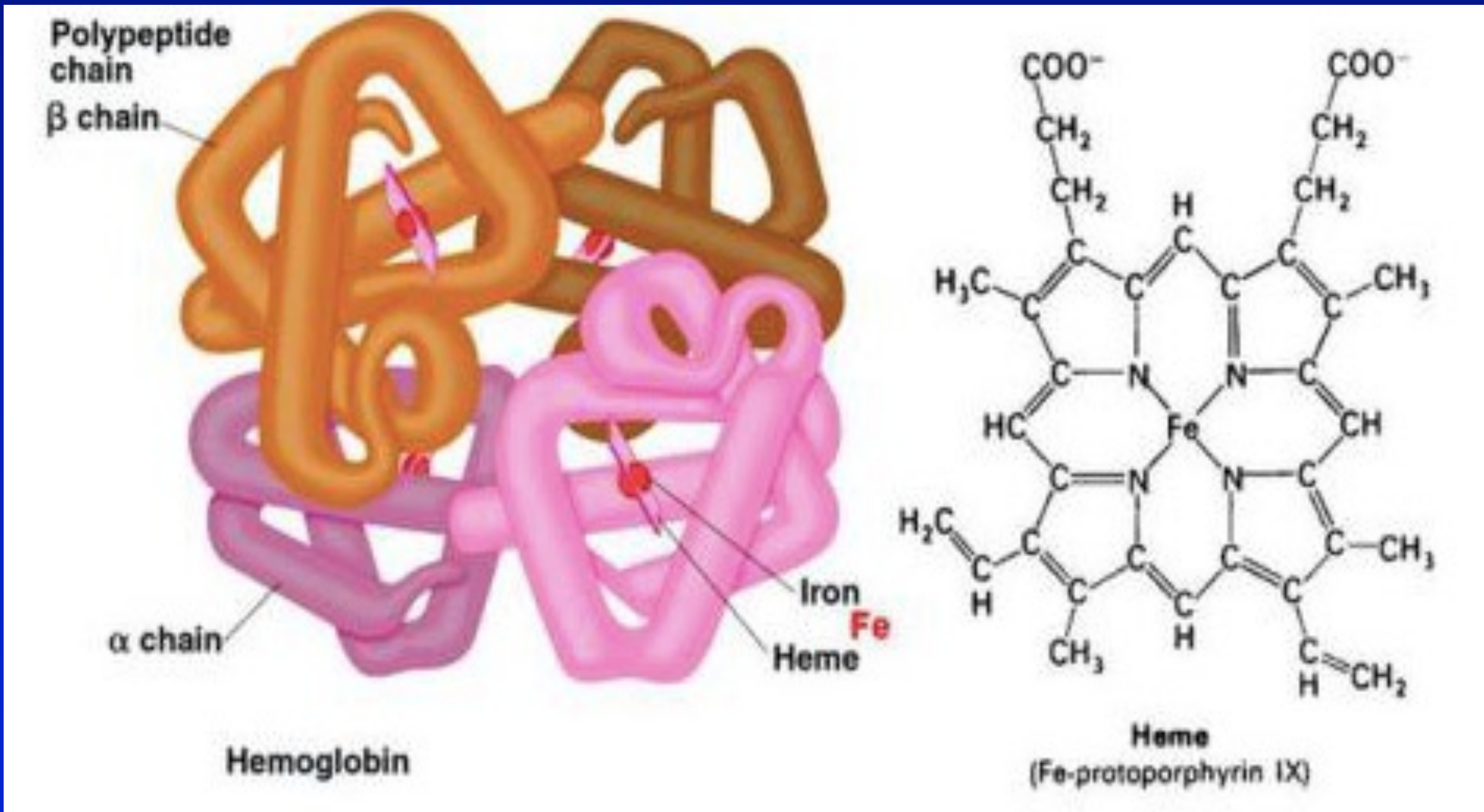
2. Very Basic Gross Human Neuroanatomy

3. Elements of Experimental Design for fMRI

A Bit of Background

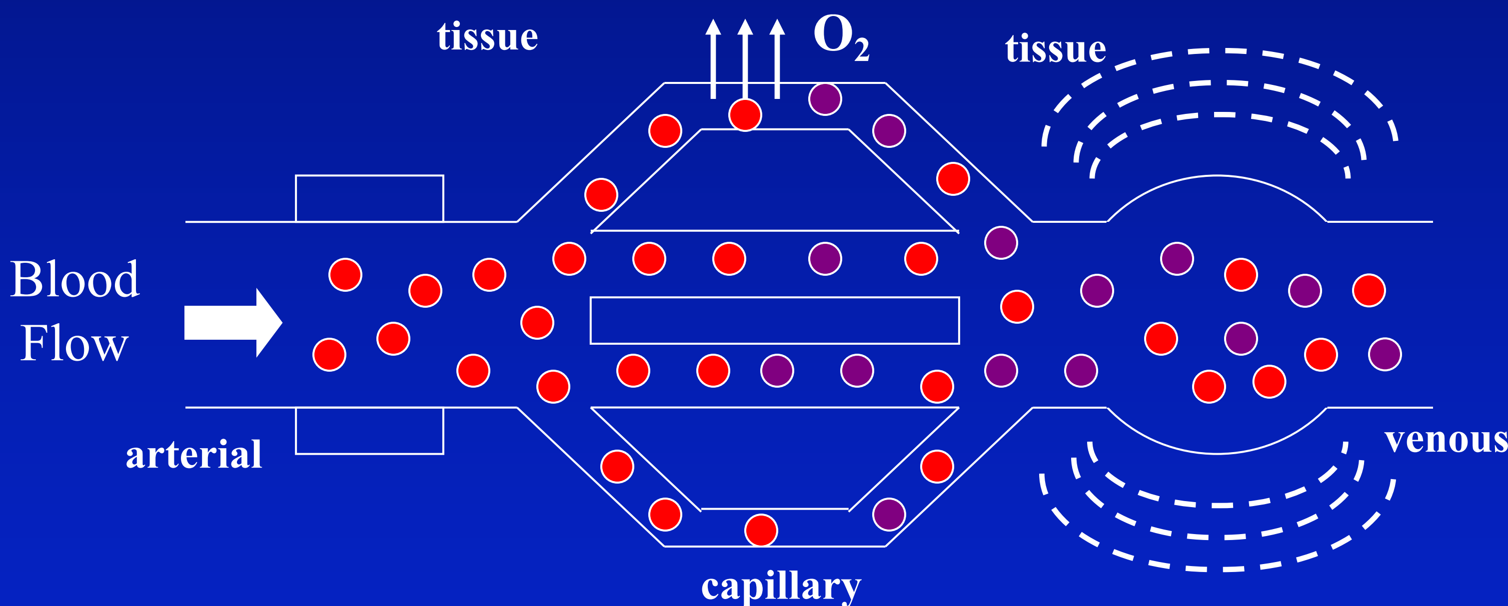
- What do you *want* to measure versus what *is* measured?
  - Interested in neural activity of single neurons or ensembles of neurons
  - No direct way of measuring neural activity in normal humans or most cases of pathology
  - Instead, need indirect measures that are correlated with neural activity
  - The BOLD (Blood Oxygenation Level Dependent) effect measures blood oxygenation in bulk neurons
    - (Actually, the name is a misnomer; it should be Blood Deoxygenation Level Dependent)
    - in a typical 3x3x3 mm voxel, there are 10 million neurons)

Hemoglobin



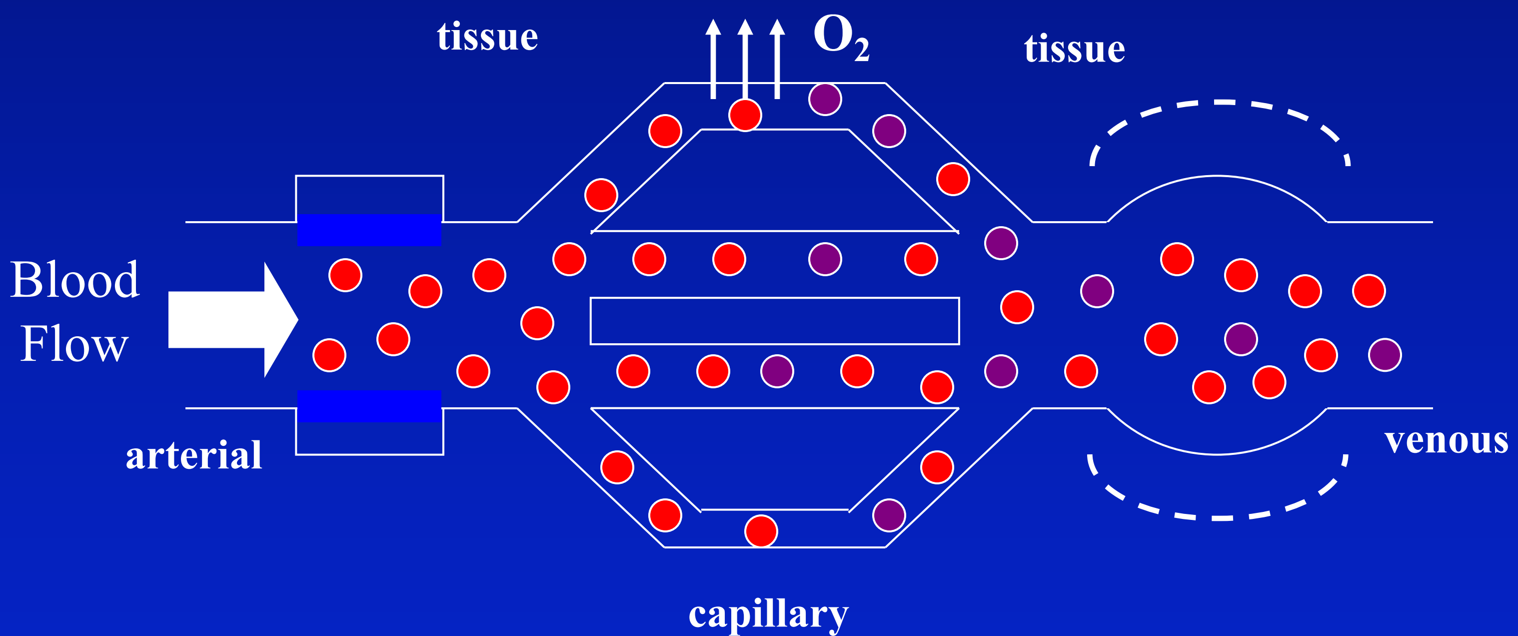
Polypeptide chain
β chain
α chain
Iron
Fe
Heme
Hemoglobin
COO⁻
CH₂
CH₂
H
C
H₃C
CH₃
N
Fe
HC
CH
H₂C
C—CH₃
CH₃
C=CH₂
Heme
(Fe-protoporphyrin IX)

Hemodynamics: Basal State



	O2 & Glu Metabolism	Blood Flow	Blood Volume	Blood O2
Baseline	—	—	—	—

Hemodynamics: Active State



	O2 & Glu Metabolism	Blood Flow	Blood Volume	Blood O2
Active	↑	↑↑↑	↑	↑↑

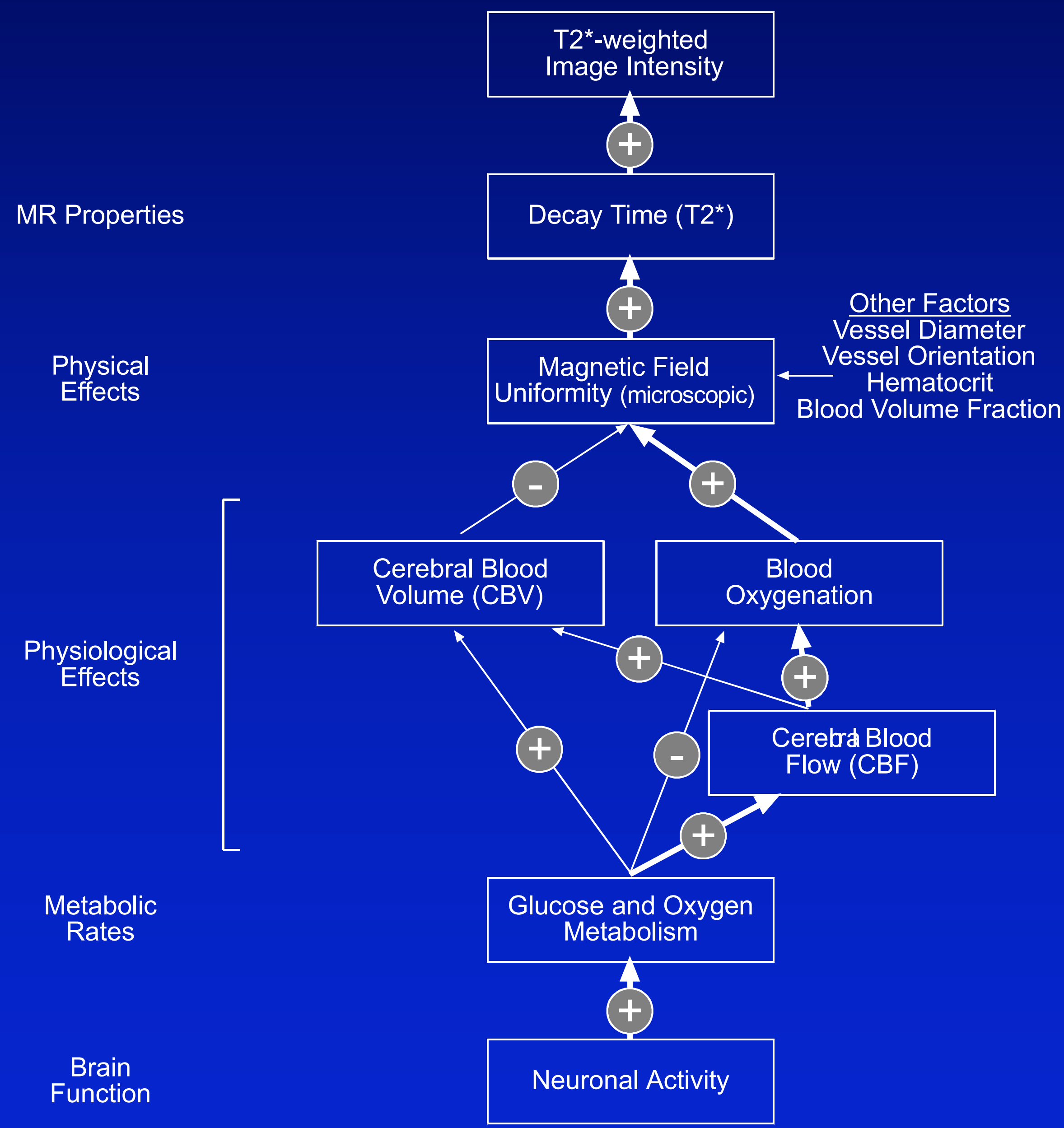
So, What Actually Causes the Signal?

- Increased flow of blood to an active region
- Increased delivery of oxygen that is magnetically inert
- Increased production of deoxygenated hemoglobin; this is magnetically susceptible
- But the increased production of deoxygenated hemoglobin is outstripped by the increased flow which removes the deoxy-hemoglobin
- Therefore, decreased perturbation of magnetic field in the active region
- So, signal due to reduction in level of deoxy-hemoglobin in draining veins

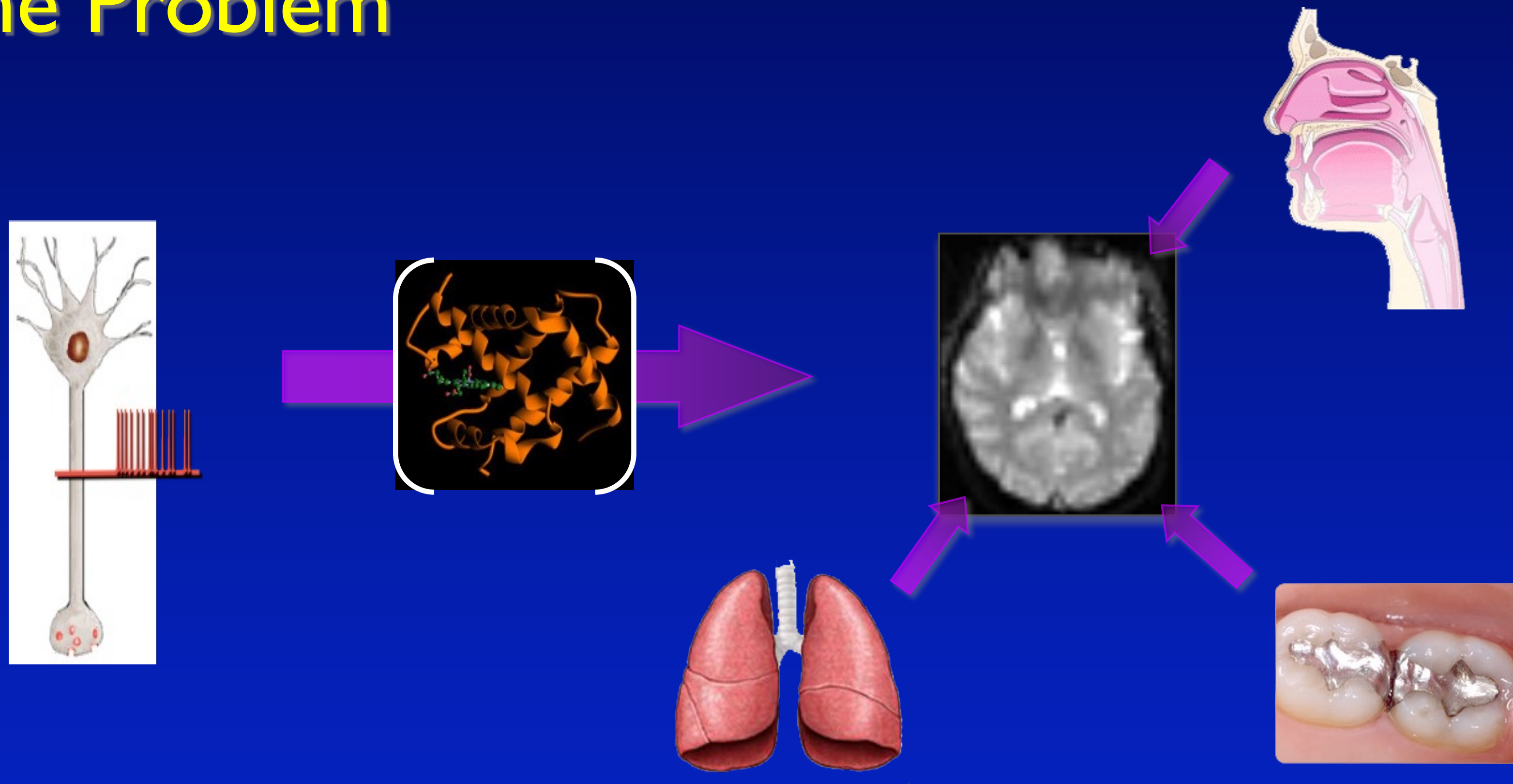
Digging Down

- BOLD signal coupled vascularly to neural activity
  - Neural activity causes increased flow of sodium, calcium, and potassium ions
  - Changes in extracellular potassium activates capillary endothelial cells
    - This causes upstream arteriolar constriction leading to increased blood flow

The BOLD Effect



One Problem

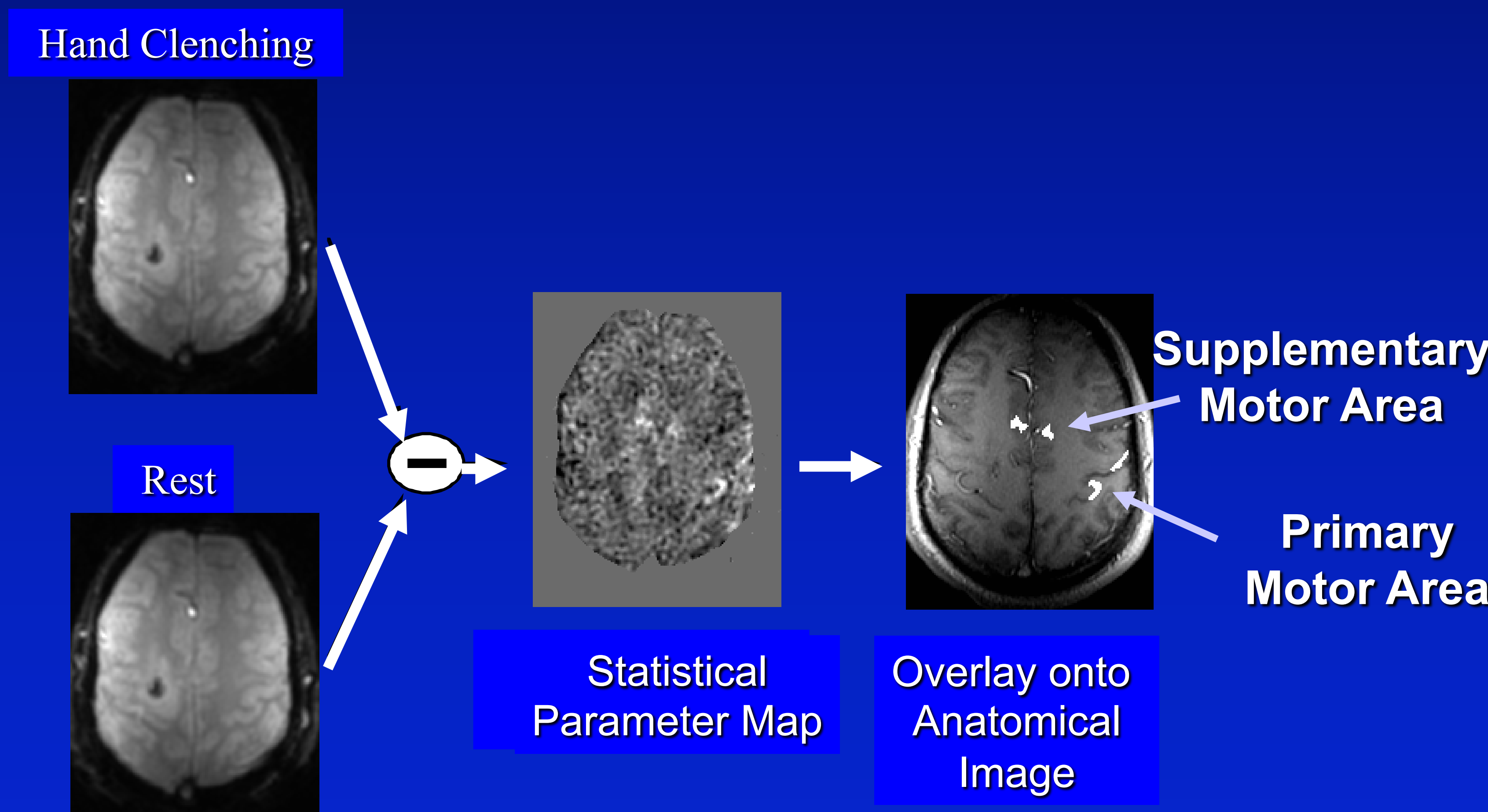


The BOLD fMRI signal has no direct, absolute interpretation. Must be compared between states studied close together in time.

A Solution: Cognitive Subtraction

- Identify the task that interests you
- Analyze the task into component processes
- Create another task that has all the same processes save the one of interest
  - Assumption of pure insertion
- Compare the two tasks

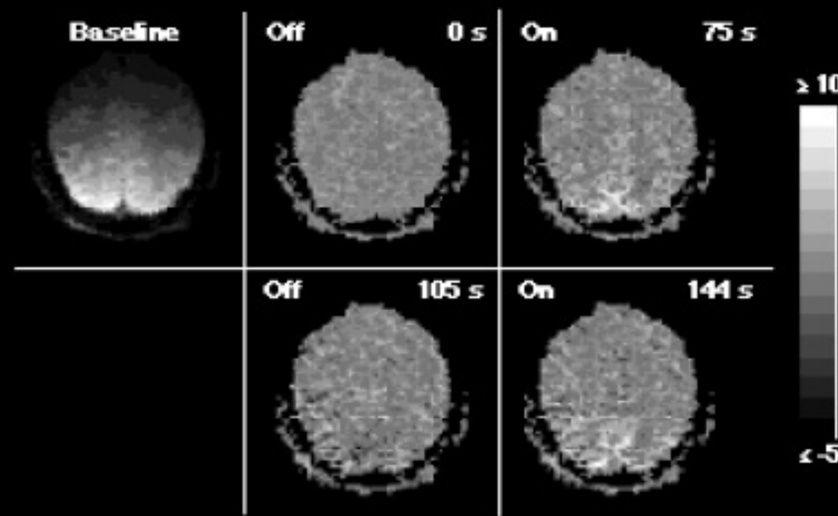
A Simple Case of Cognitive Subtraction



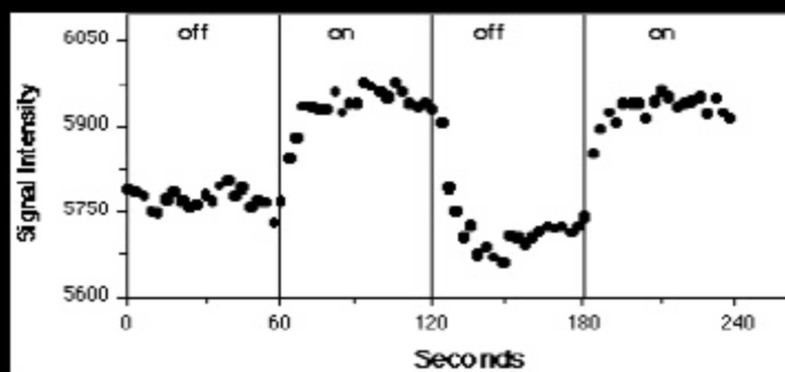
fMRI Activation

Flickering Checkerboard

OFF (60 s) ON (60 s) -OFF (60 s) - ON (60 s) - OFF (60 s)



Brain Activity



Time ⇨

Kwong et al., 1992

Courtesy of Jody Culham.
Used with permission.

Caveats

- You don't have direct access to the processes
  - Changing from one task to another may cause subjects to change strategies and component processes
- Adding a process may change the ones already in place

Functional Magnetic Resonance Imaging (fMRI) vs. Other Methods

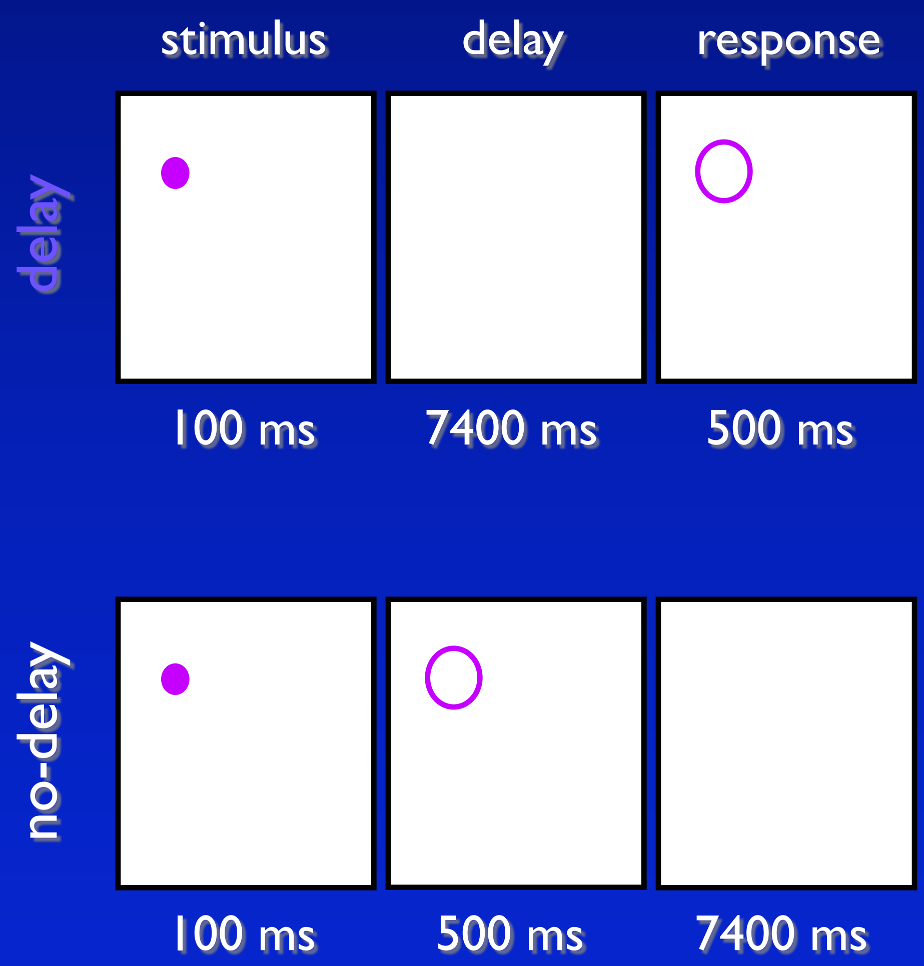
- Advantages:

The best spatial resolution available for studies on normal subjects.
Noninvasive.
Cheaper than PET (only $539/hour!).

- Disadvantages:

Temporal resolution not on a par with visual information processing.
Spatial resolution about one mm (hard/impossible to see cortical columns), can never get better than the vasculature.
"Susceptibility artifact" due to magnetic inhomogeneities near ear canals and sinuses.
Loud banging noise.
Uncertainty about the basis of the BOLD signal (spikes vs synaptic activity).

Separating Components of Memory

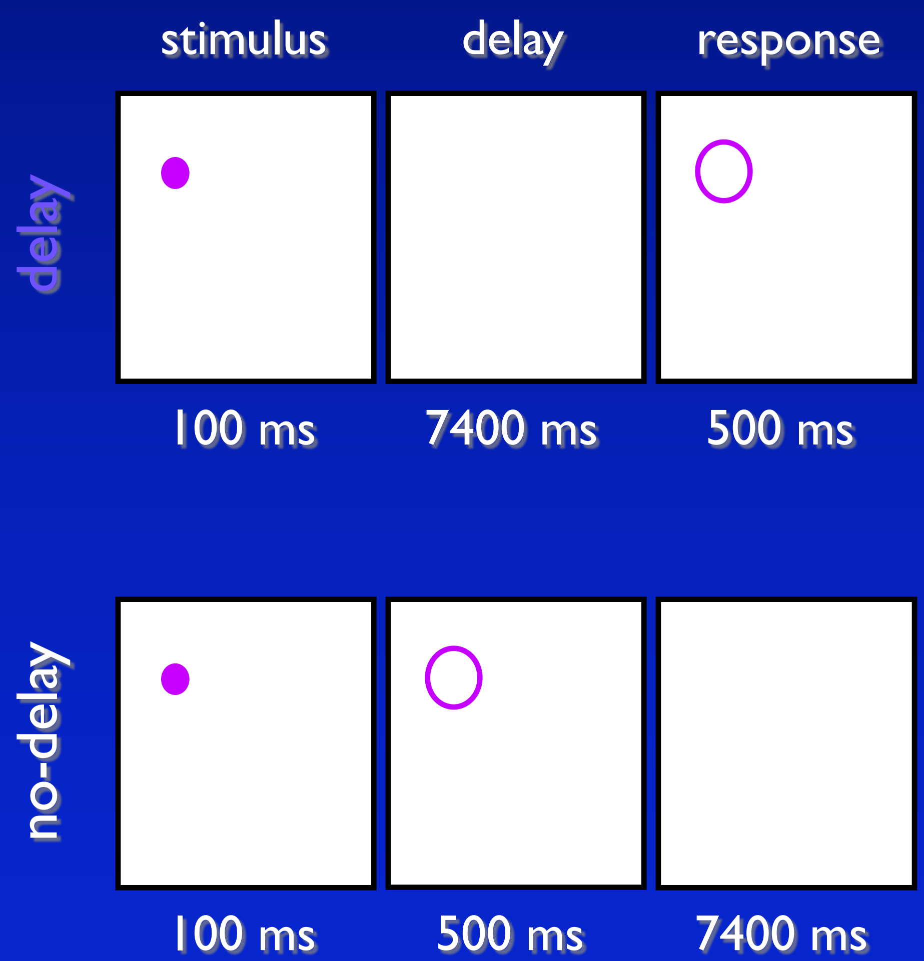


"task analysis"

stimulus encoding
working memory
response preparation
response execution

stimulus encoding
response preparation
response execution

Separating Components of Memory



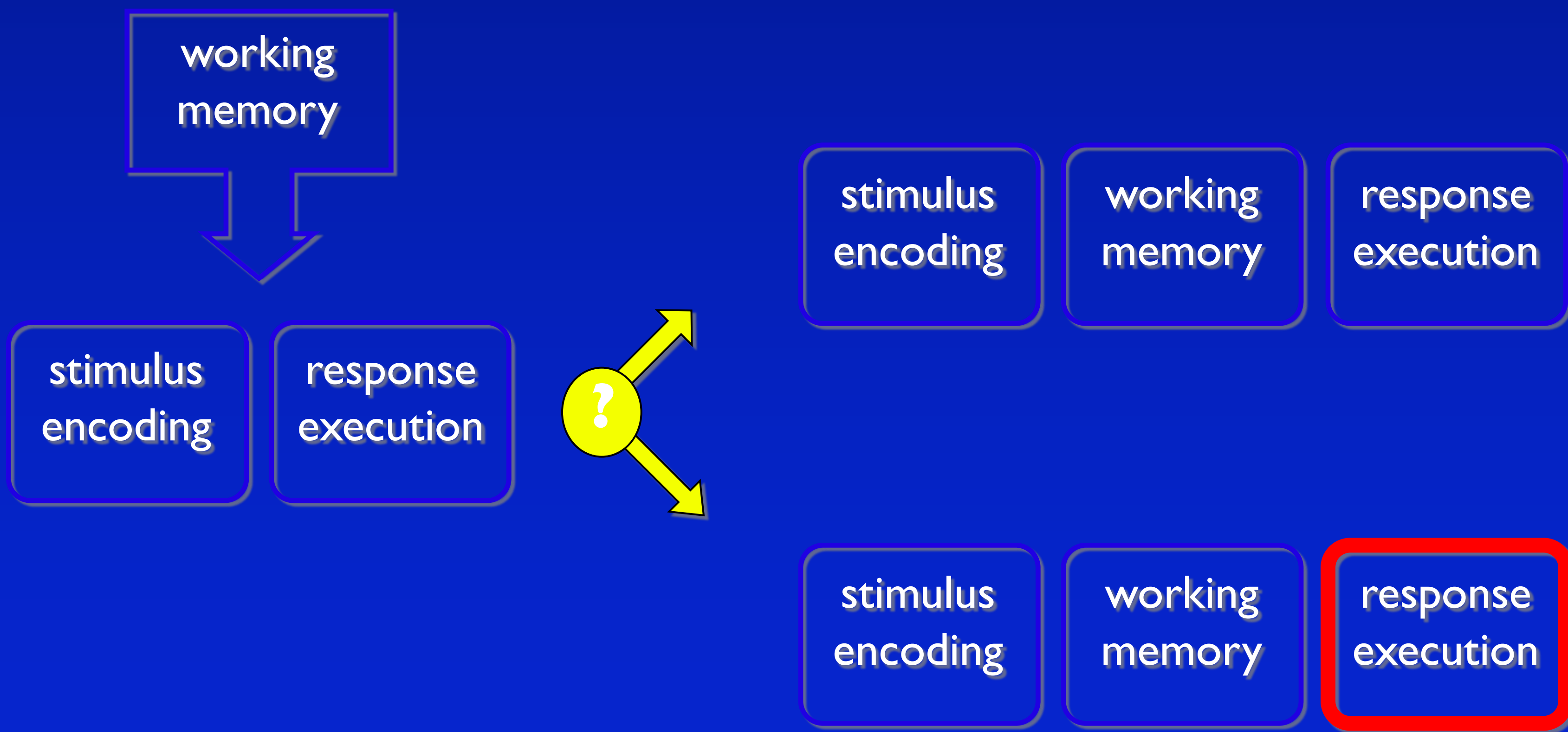
Note:
For this analysis to work, the assumption of linearity of the BOLD signal must hold true.

Suppose that in the no-delay condition, the signal saturates so that activation to the stimulus and the probe is not the sum of each separately

This will result in underestimation of no-delay activity and a conclusion that the difference between delay and no-delay is due to memory when it is, in fact, due to underestimation of the control

Pure Insertion

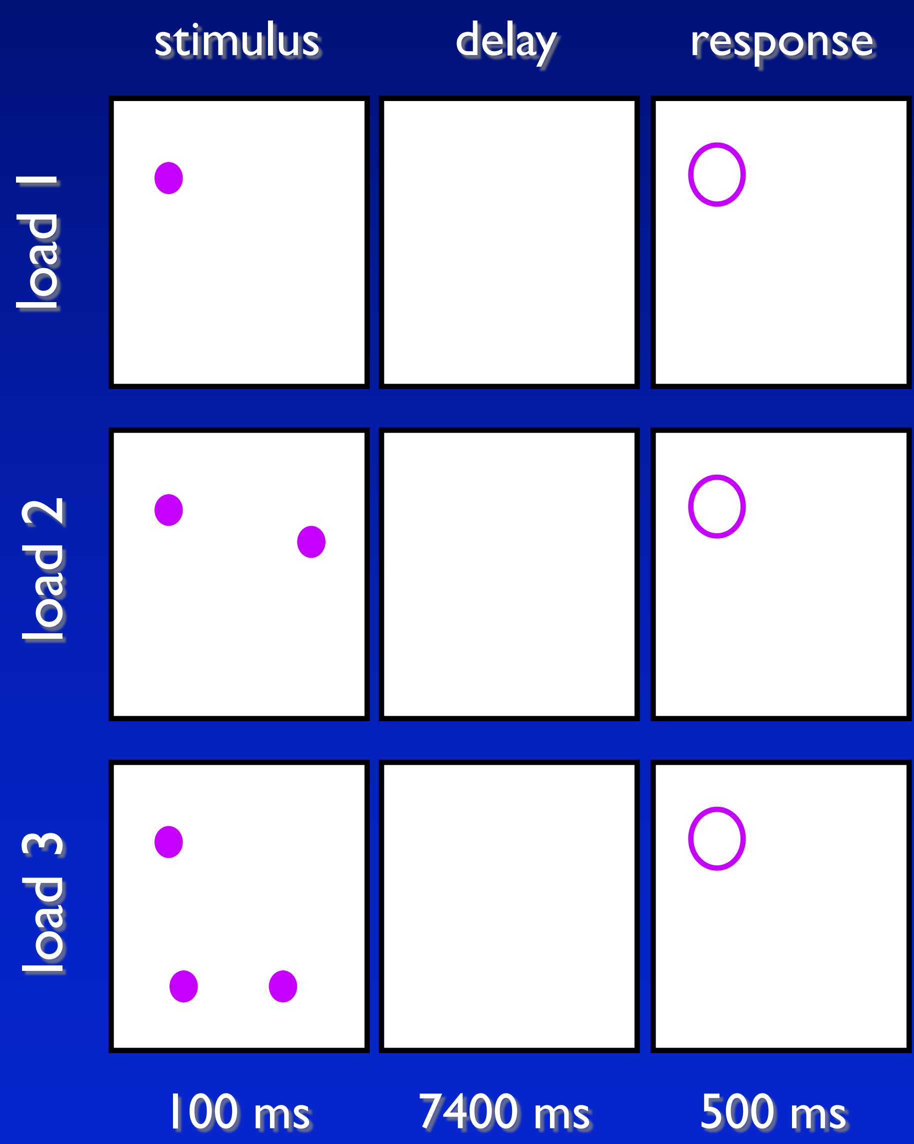
Can you add a cognitive process to a pre-existing set without interaction between processes?



Variations on Cognitive Subtraction

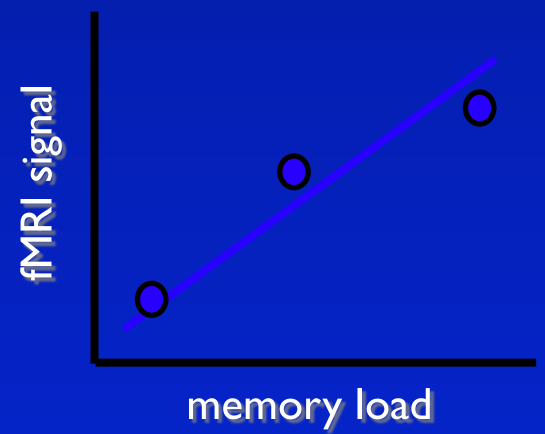
- Cognitive Conjunction Design
  - Create two situations each of which involves the same putative subtraction
  - See if the activations that result are the same
  - e.g., two different kinds of verbal working memory
- A Strong Case
  - Parametric design: Increase the level of a variable parametrically
  - Examine whether (Level 2-Level 1) yields activation similar to (Level 3-Level 2)
  - e.g., variations of working memory load

Parametric Design



This design manipulates the *amount* of the cognitive process present in each condition.

Test for systematic (linear or otherwise) relationships between the level of the cognitive process and neural activity.



Renders pure insertion more plausible

Another Alternative: Factorial Designs

- Examine more than one process to see whether there are interactions
- e.g., Do working memory load and response selection difficulty affect different brain systems?
  - e.g., if variation of memory load influences response selection regions, the two are not independent

The Lab Experiment

NeuroImage 99 (2014) 301–311

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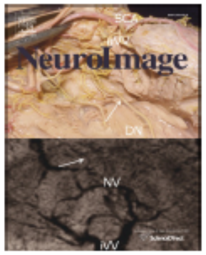


Validating the Why/How contrast for functional MRI studies of Theory of Mind

CrossMark

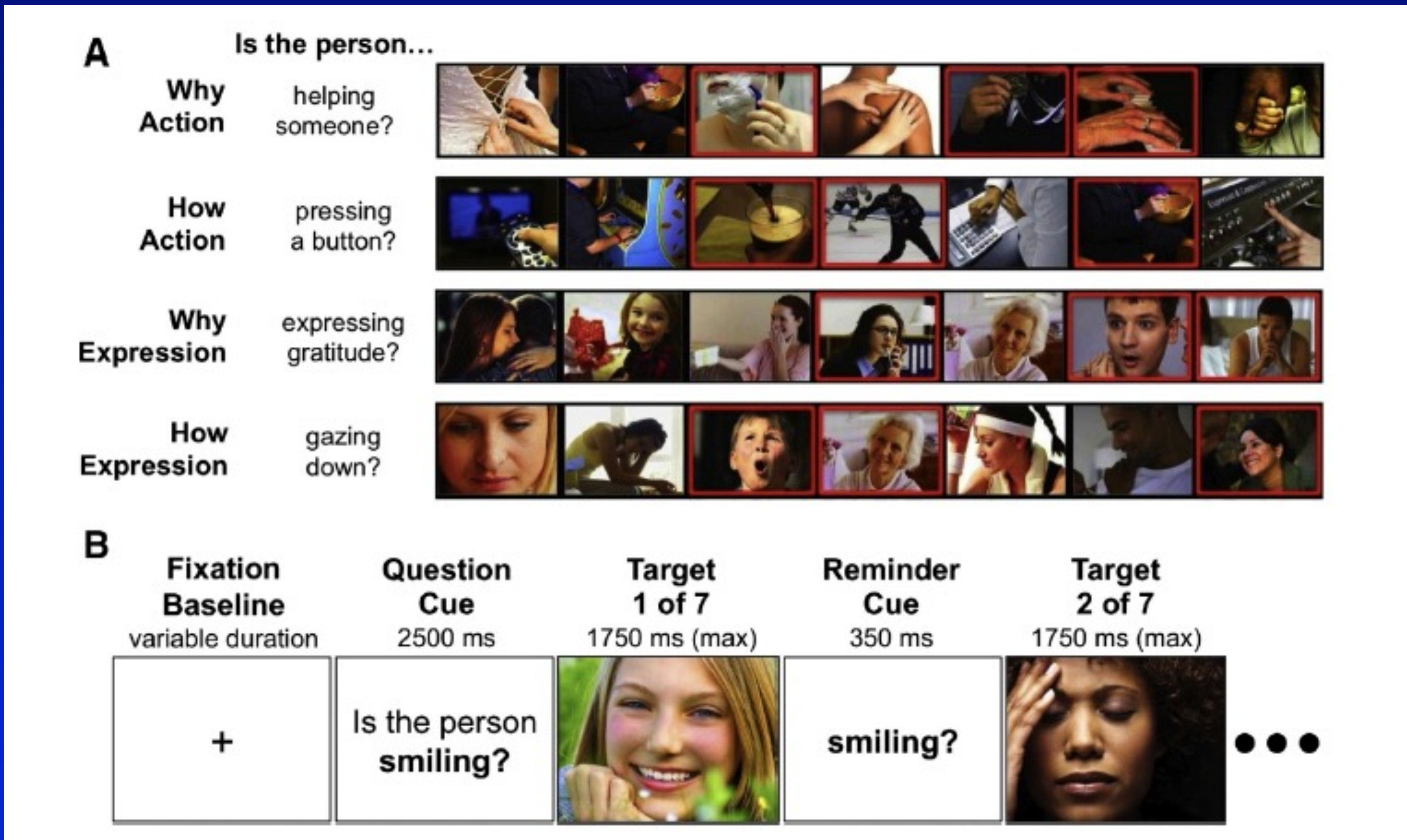
Robert P. Spunt *, Ralph Adolphs

California Institute of Technology, USA

Paradigm for Studying Theory of Mind

- Theory of Mind
  - Imputing mental states to others
  - e.g., What was Jill thinking after Jack made a comment?
  - e.g., What was the motive behind Jill slapping Jack?

Paradigm for Studying Theory of Mind

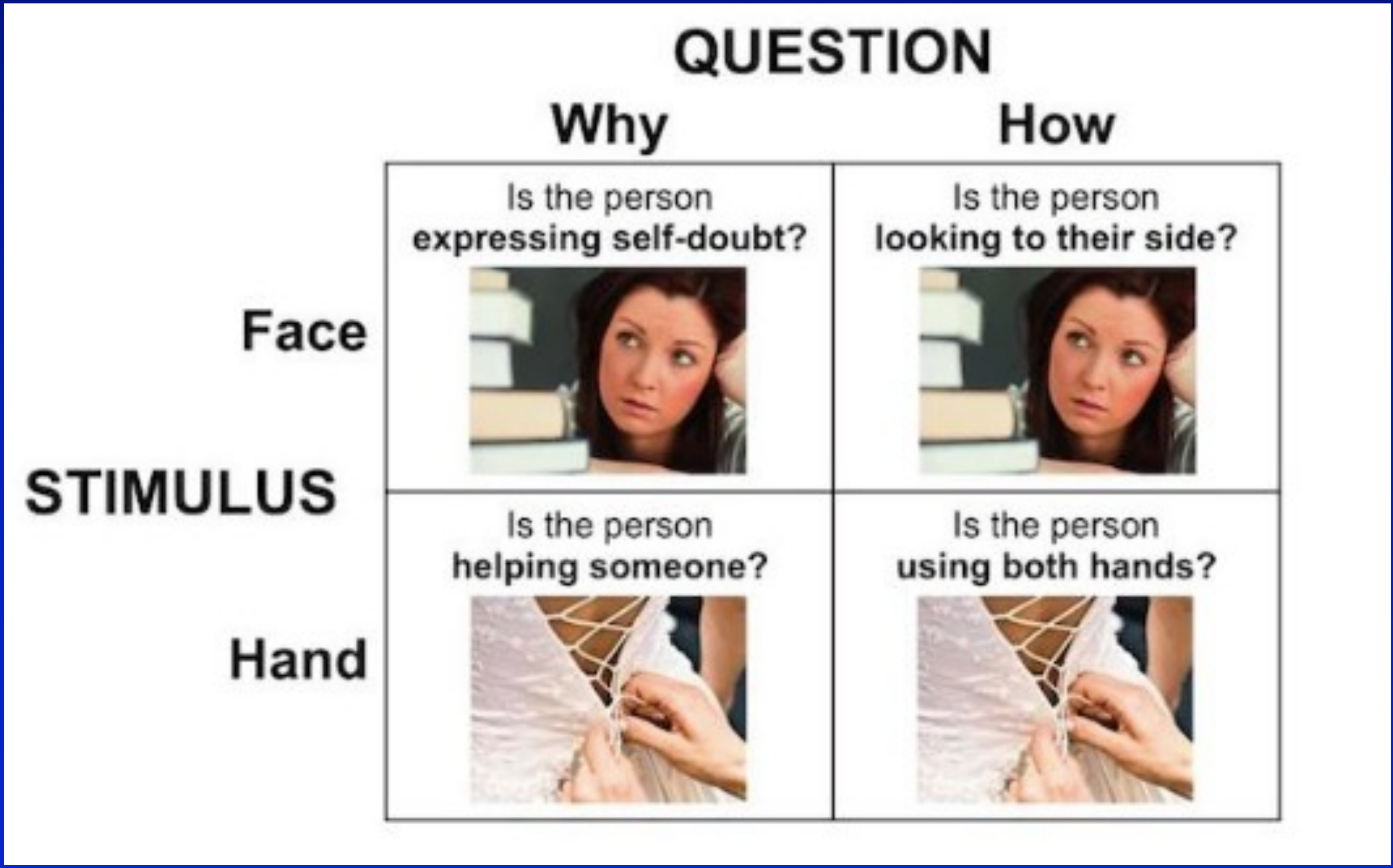


The Questions that Participants Answered

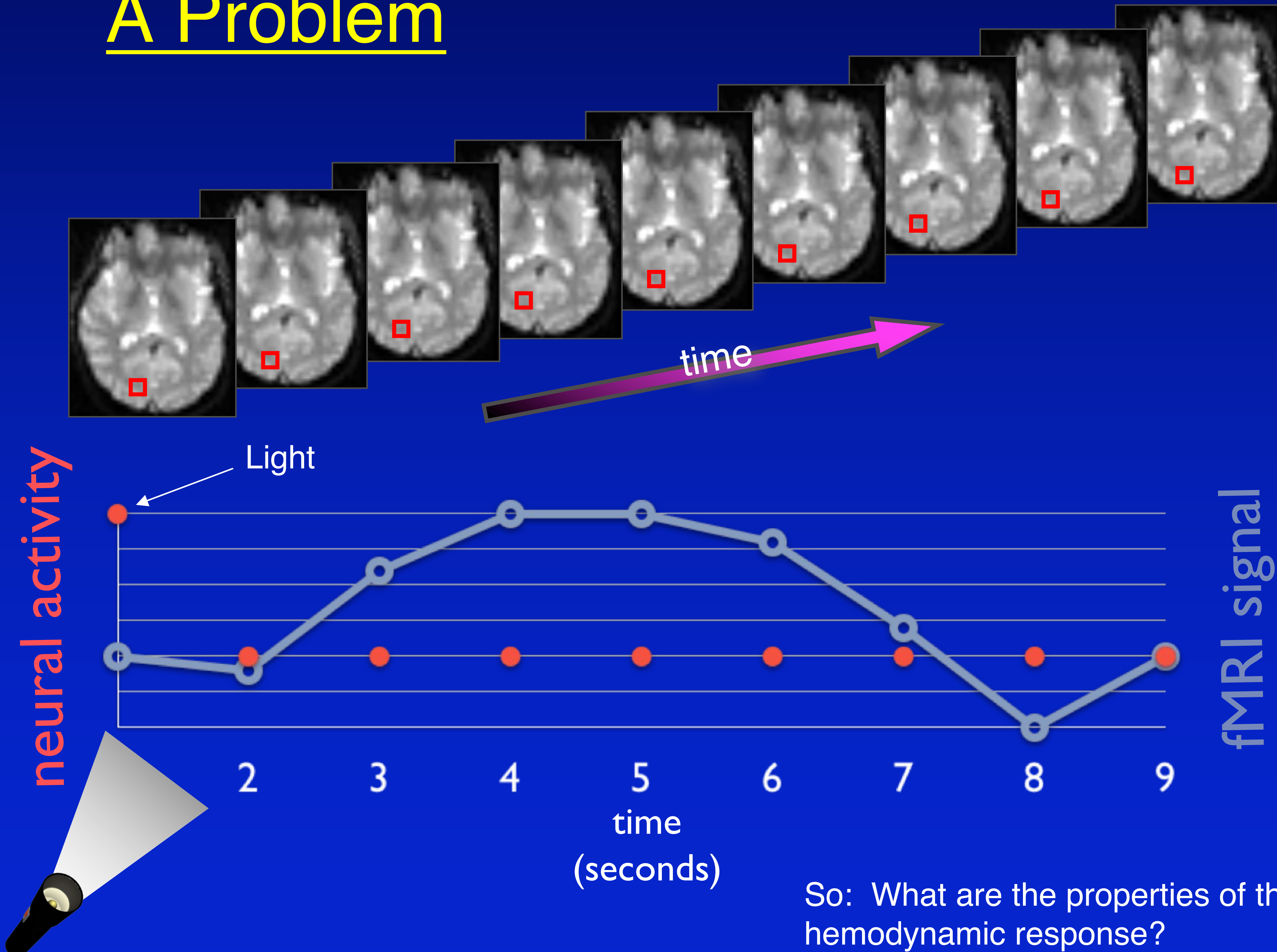
The questions used in the Yes/No Why/How Task to manipulate and measure attention to "why" versus "how" for actions and expressions. All questions began with the string "Is the person ". The questions used in Study 3 are marked with an asterisk.

Why		How	
Intentional actions	Emotional expressions	Intentional actions	Emotional expressions
Competing against others?*	Admiring someone?*	Holding a ball?	Gazing down?
Concerned with their health?*	Being affectionate?	Lifting something?*	Looking at the camera?*
Having fun?	Expressing gratitude?	Pressing a button?*	Looking to their side?*
Helping someone?*	Expressing self-doubt?*	Reaching for something?*	Opening their mouth?*
Protecting themselves?*	In an argument?*	Using a writing utensil?	Showing their teeth?
Sharing knowledge?	Proud of themselves?*	Using both hands?*	Smiling?*

Summary of ANOVA Design



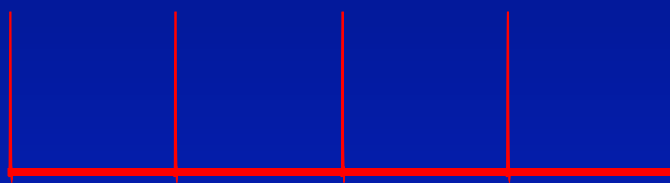
A Problem



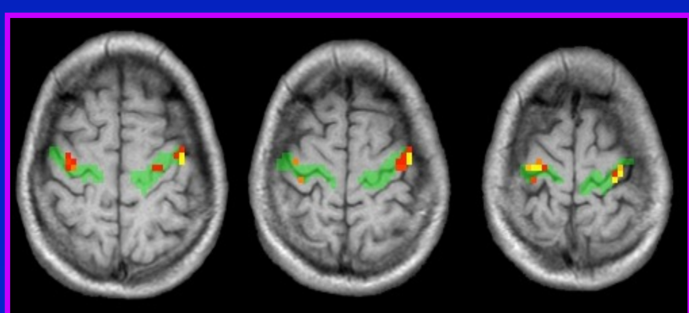
So: What are the properties of the hemodynamic response?

Defining the Hemodynamic Response Function

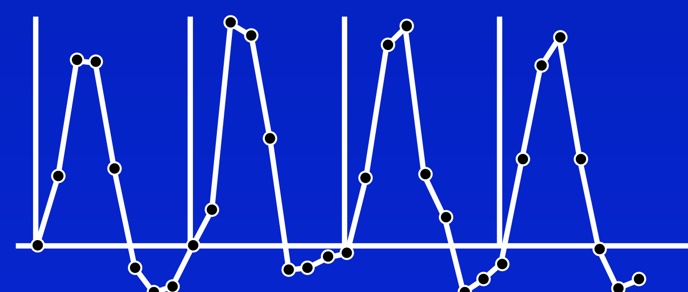
subject makes a bilateral button press in response to visual cue every 16 seconds



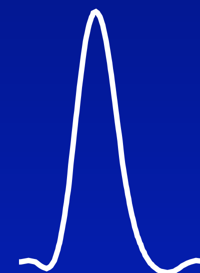
assumed pattern neural activity



voxels with significant signal within motor regions of interest

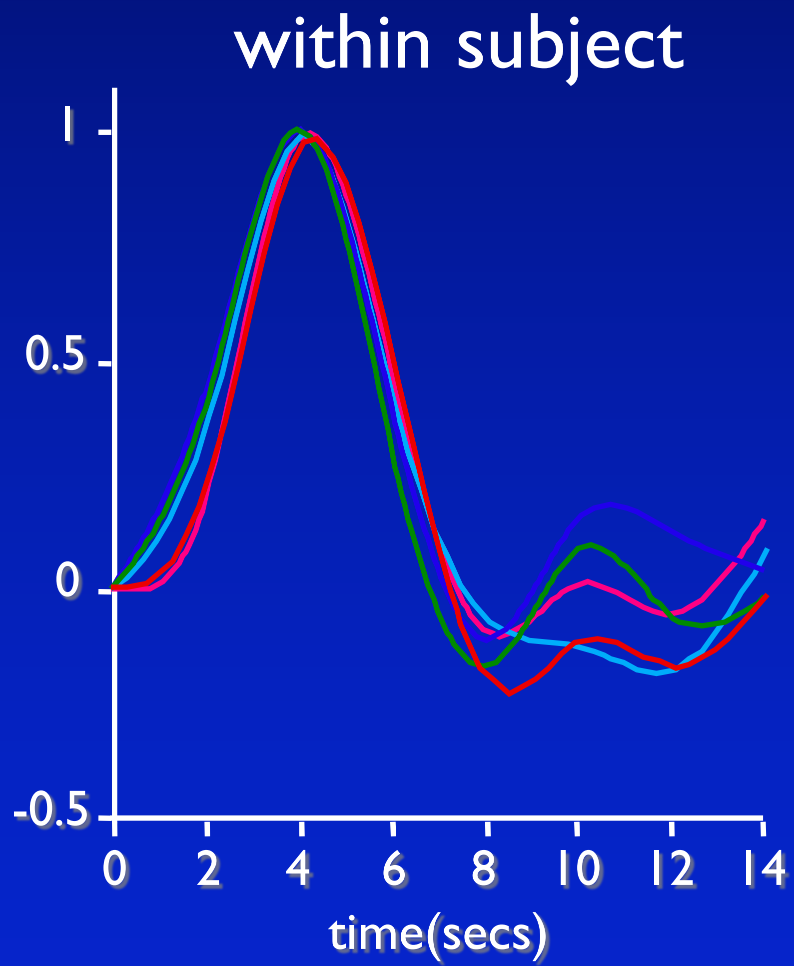


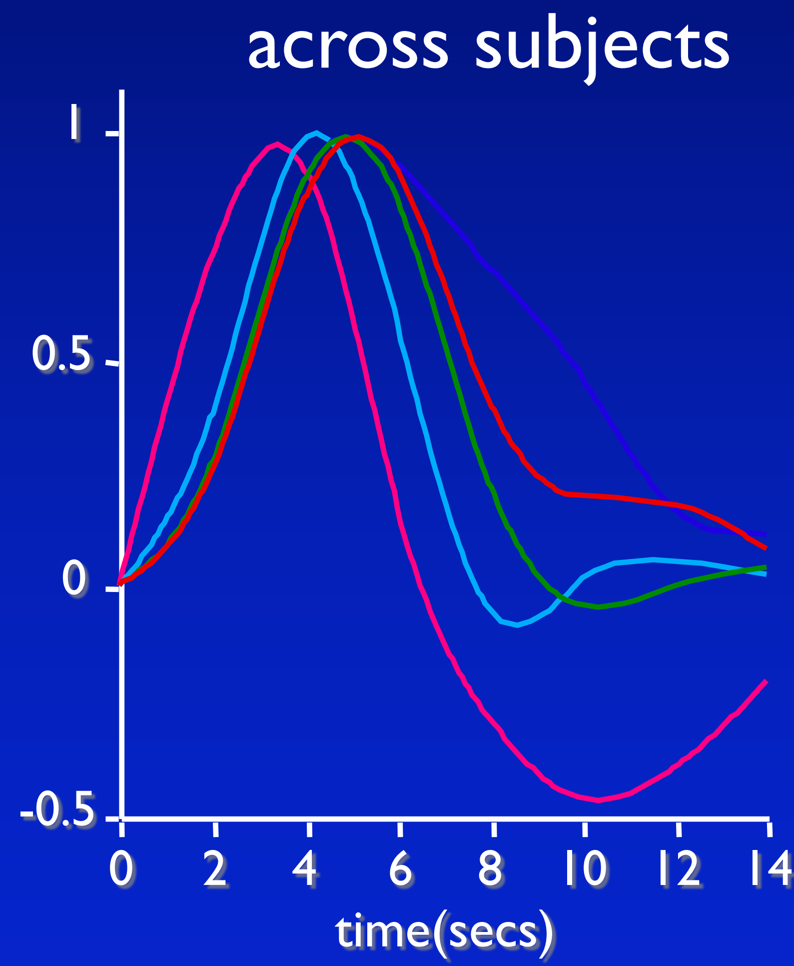
avg BOLD signal from active voxels



trial-averaged BOLD signal, an estimate of the HRF

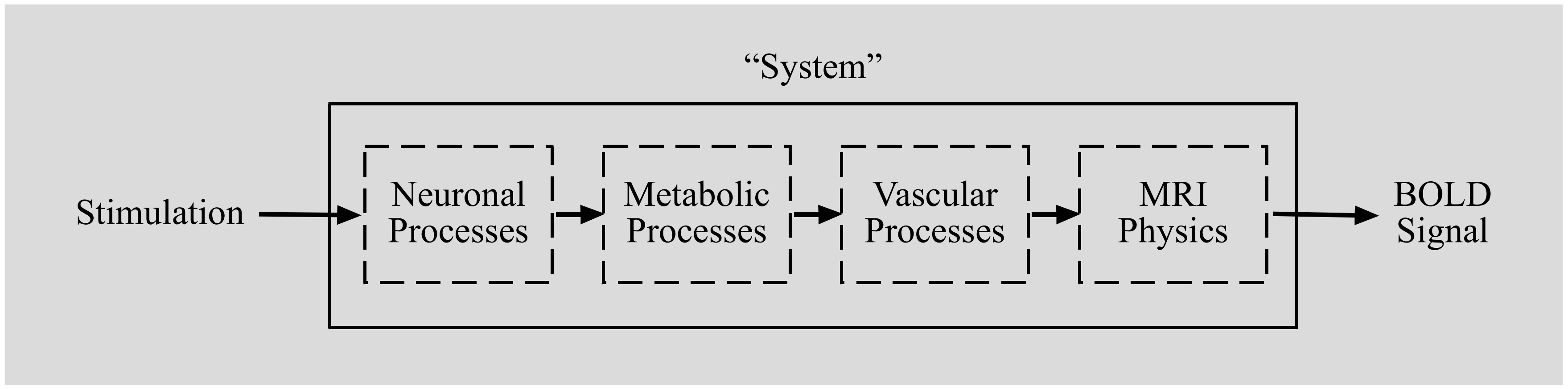
HRF Variability





Systems Analysis of the Signal

- Systems theory characterizes input/output relationships
- When examining the BOLD response we often look at a system composed of several subsystems

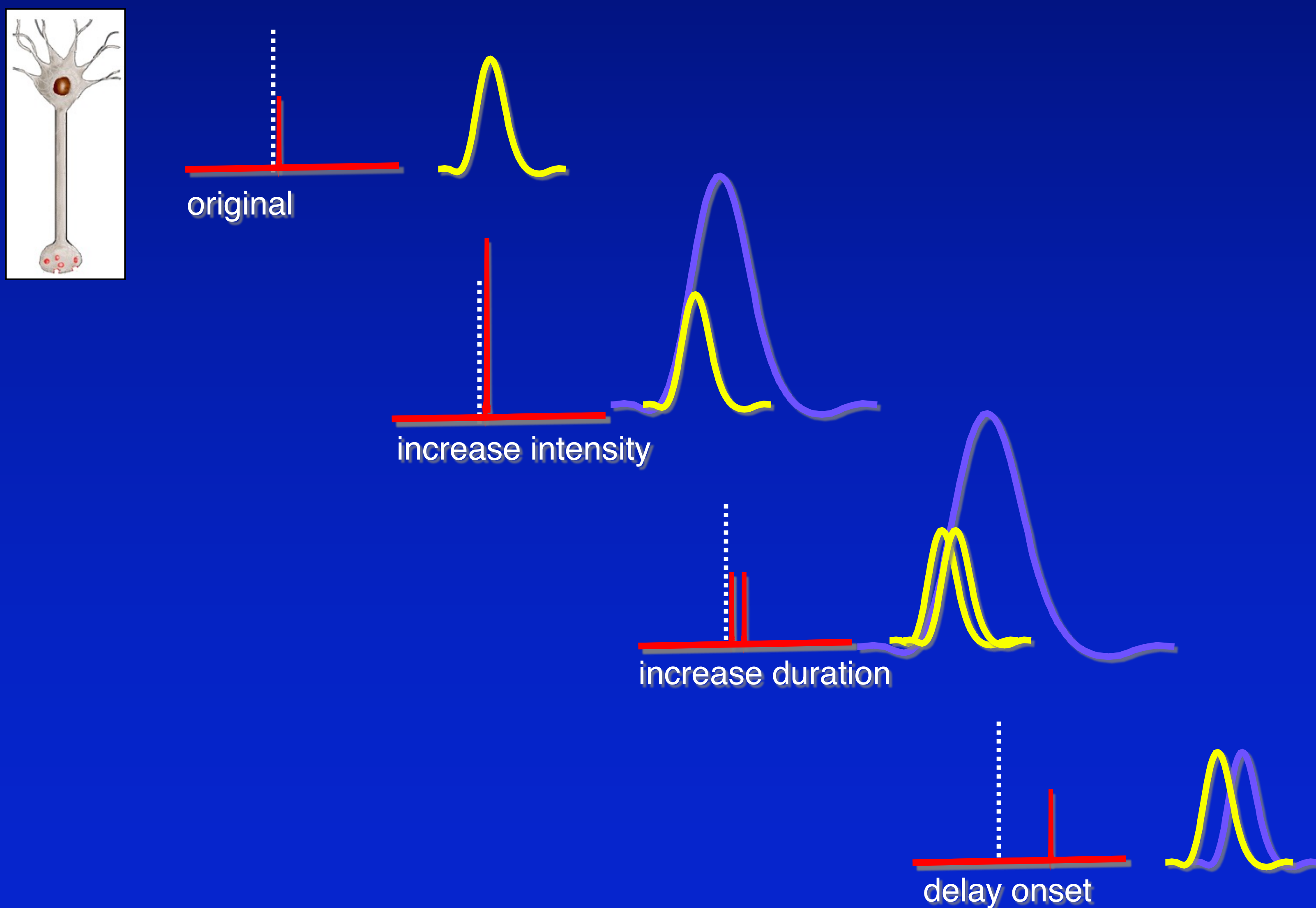


A Piece of Good News: The HRF is Roughly Linear

A linear system satisfies the following:

- Scaling
  - Increasing stimulation by some ratio will increase the output by the same ratio
- Superposition (additivity)
  - Combining (adding) any two stimuli will lead to an output that is the sum of the two responses
- Time-invariance
  - A response is the same irrespective of when it comes or what precedes or follows it

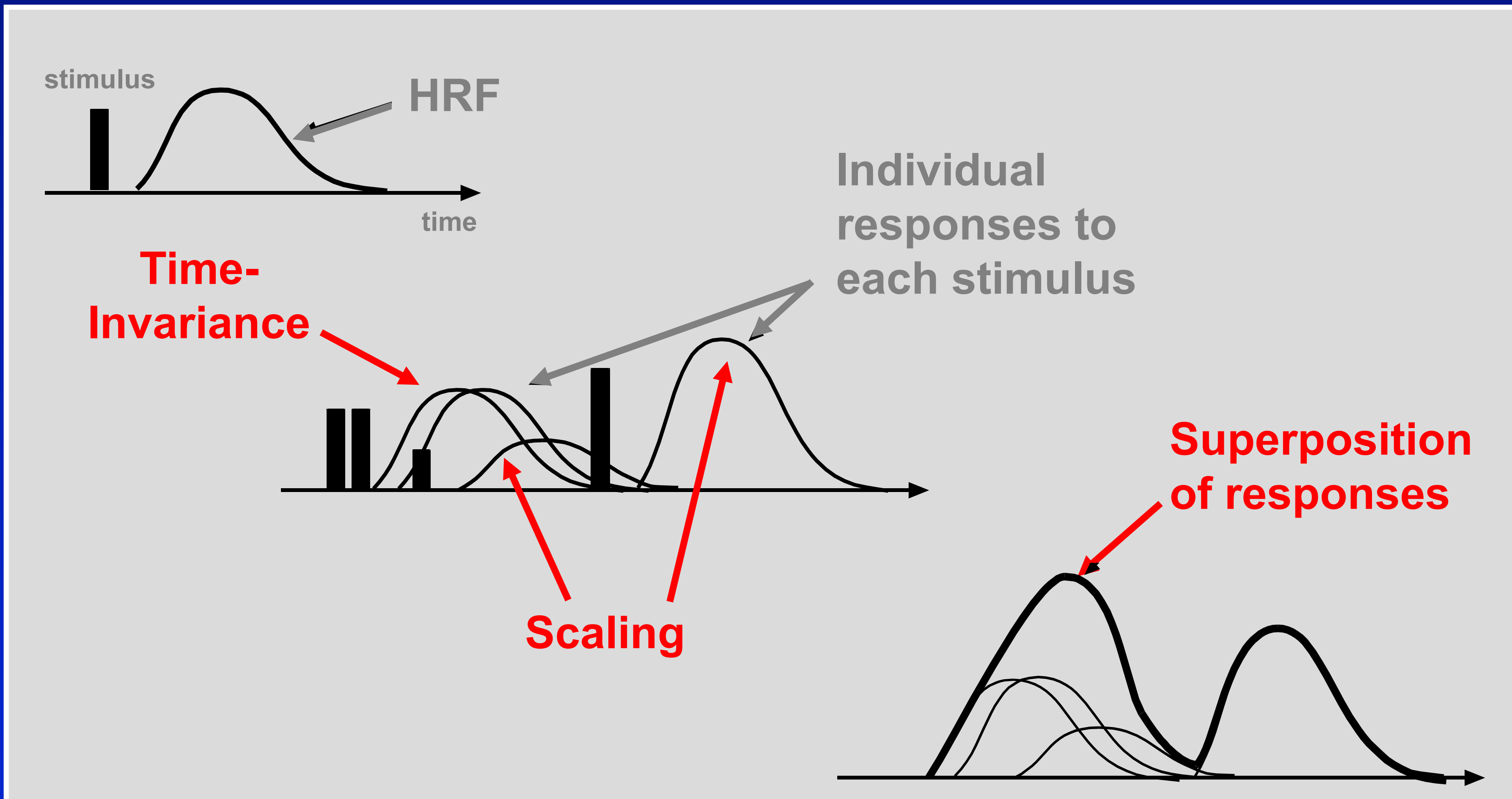
The BOLD fMRI System in Time



Why Is Linearity Good?

- Use theory of linear systems to predict responses
- Start with definition of an impulse response function
  - Hemodynamic response to a brief stimulus
  - Commonly known as the hemodynamic response function (HRF)
- Predicted responses are easily determined by mathematical operations performed on hemodynamic response functions
  - Can also allow "deconvolution" of response to get estimates of the system input

Predicted Responses



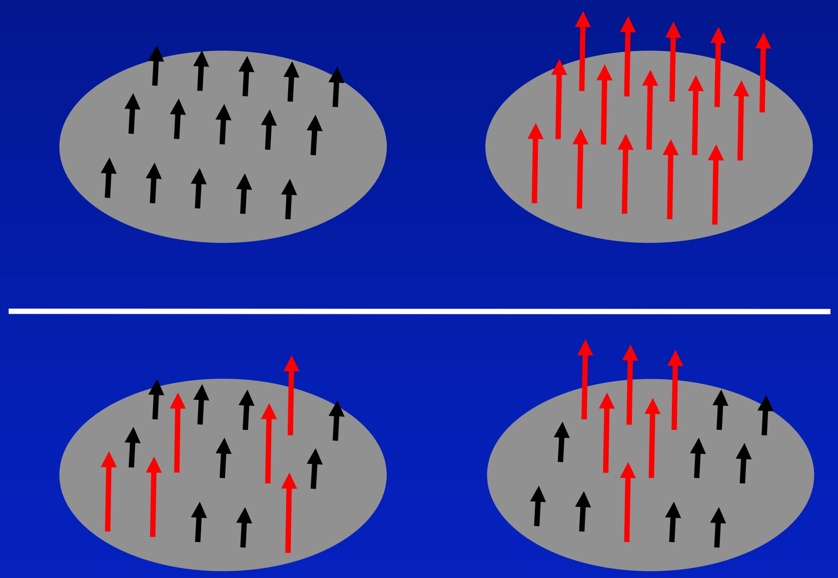
Keep This in Mind for Any Voxel

Detectable

- a bulk change in neural activity

Undetectable

- a change in population code



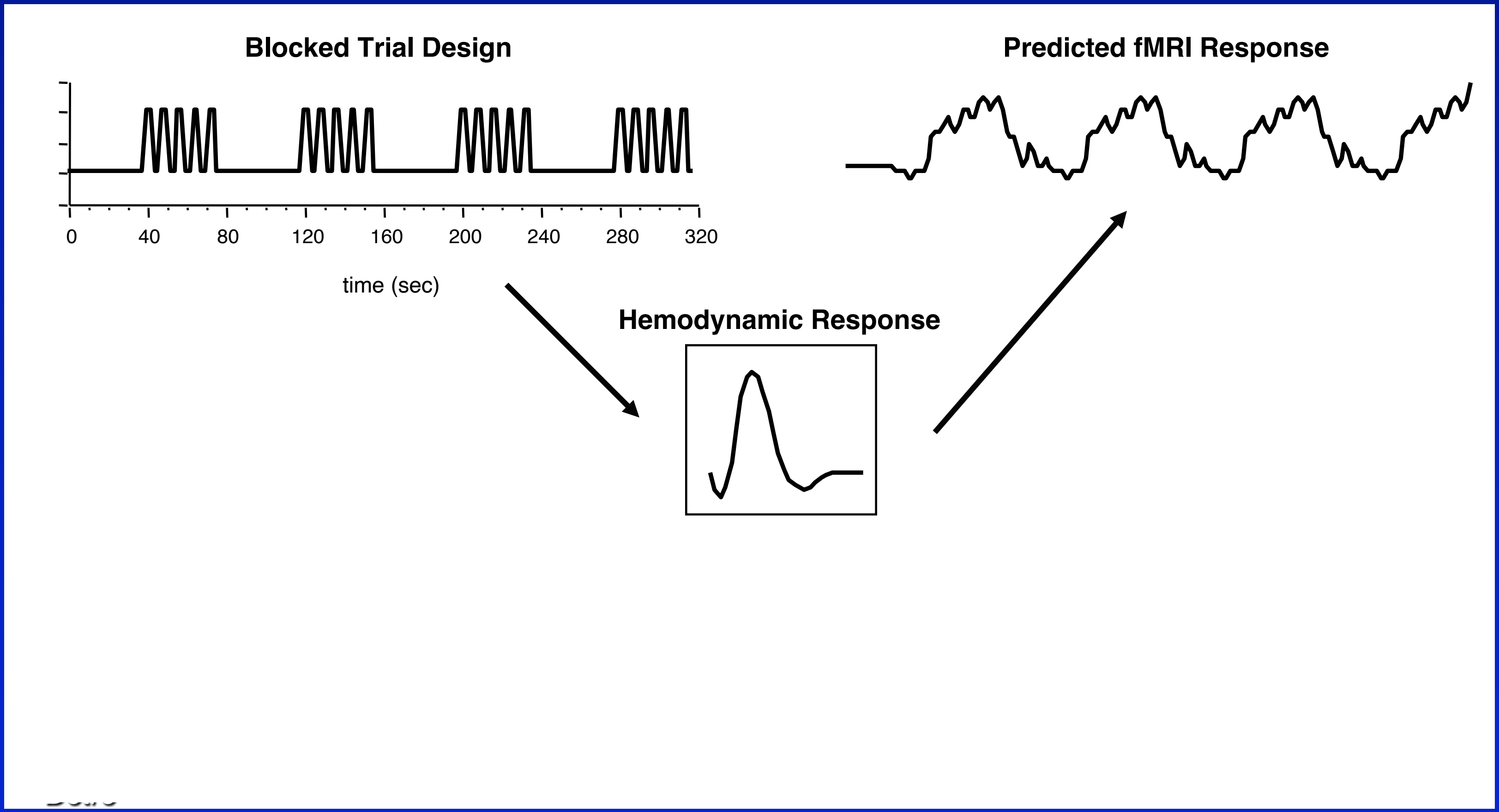
The BOLD fMRI signal integrates neural activity over seconds and millimeters.

Harnessing the Linear System

- Blocked Experimental Designs
  - Like tasks are clustered together in blocks of length 15-120 seconds
    - What's the optimal block length? More in a moment
  - Tasks are close together to allow the appearance of continuous activation during the block
  - Superior statistical power because you can construct a block to recognize low frequency noise and avoid it (more in a moment)

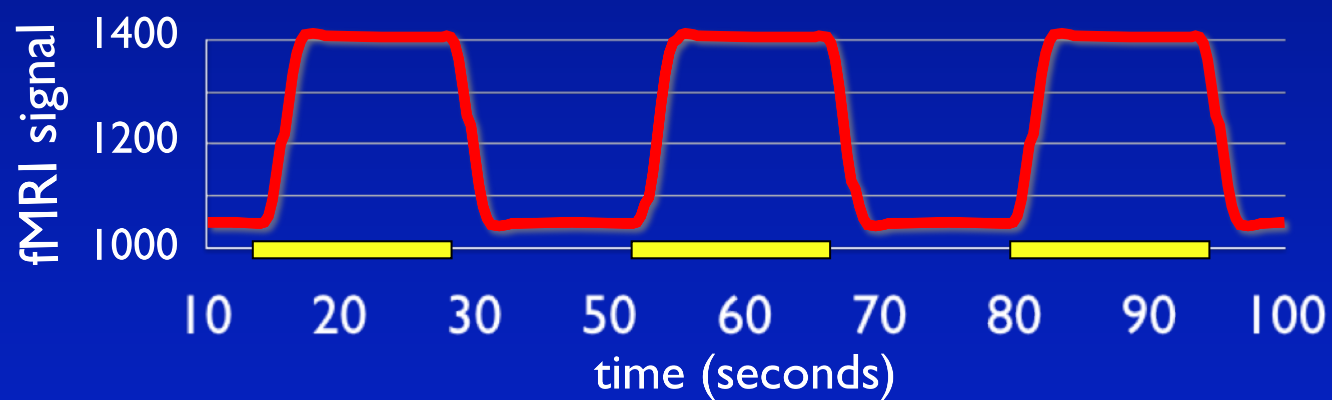
Task Design and Predicted Responses

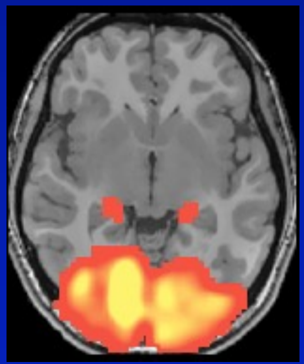
A blocked design and predicted fMRI response
based on linear system analysis



A Prototypical Experiment

Measure magnitude of neural response within primary visual cortex to a standardized patch of light in a group of subjects

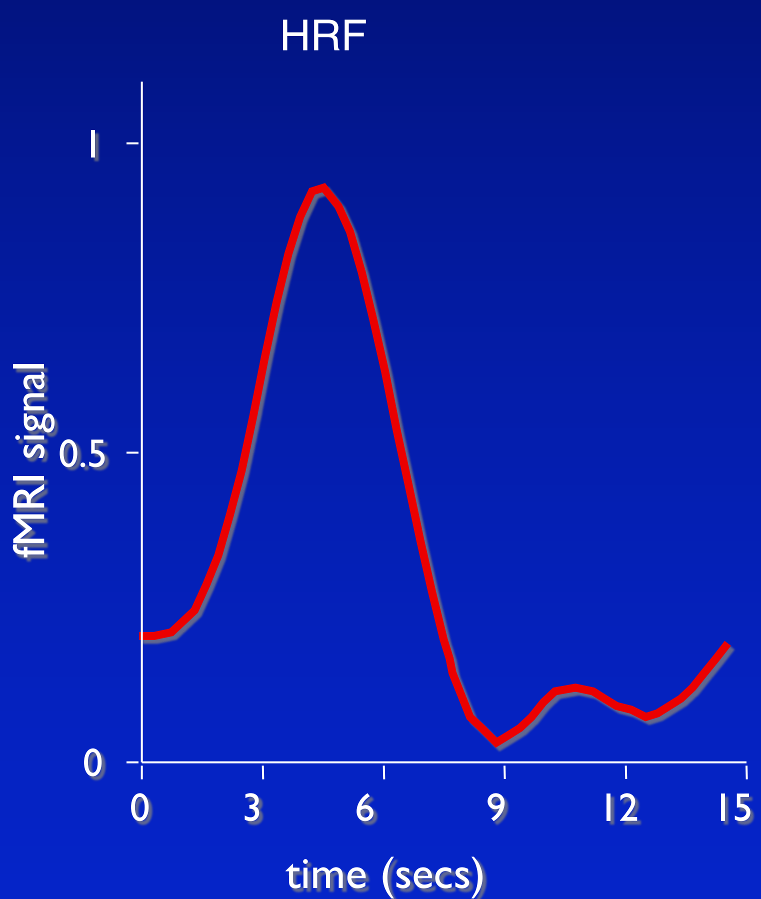




- relative signal
- indirect measure
- bulk activity change

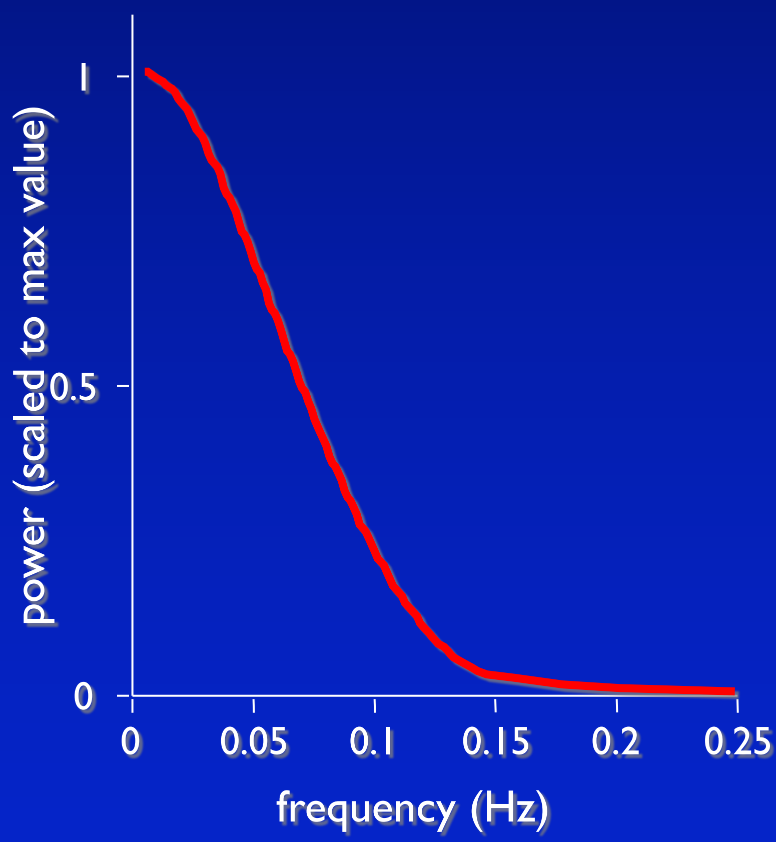
- subtraction design
- blocked order

Arranging Timing



The HRF favors designs with low temporal frequencies.
You could not, for example, have blocks of 1 sec each

Arranging Timing

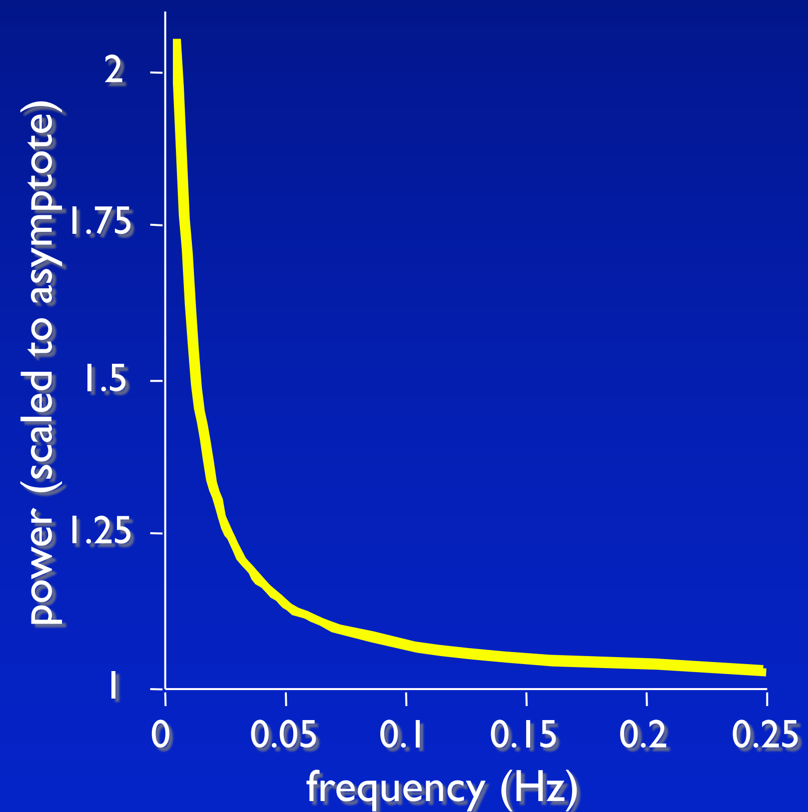


hemodynamic response

The HRF favors designs with power at low temporal freqs.

The Problem

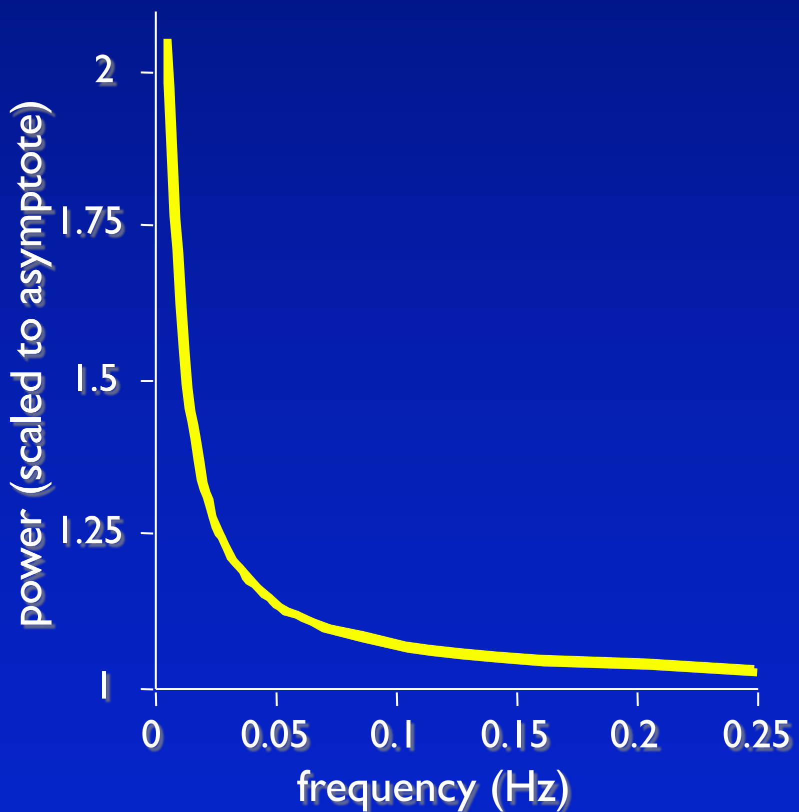
There is increasing power at low frequencies in the noise also (due to drift of the MRI signal) with power roughly equal to 1/f



intrinsic noise

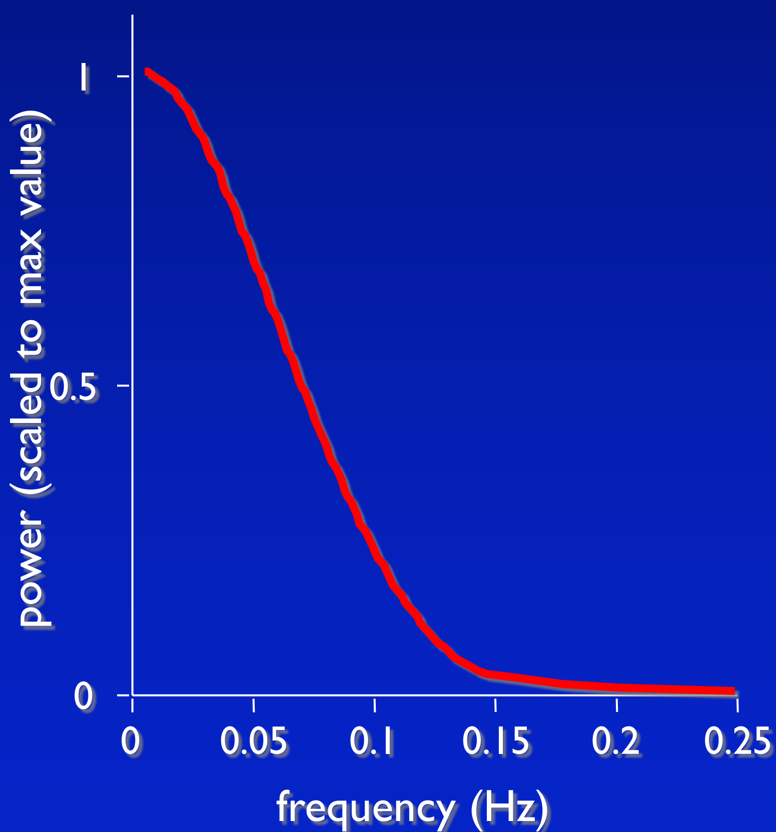
The Problem

The 1/f noise favors designs with power at high temporal frequencies, but the nature of the HRF does not allow this

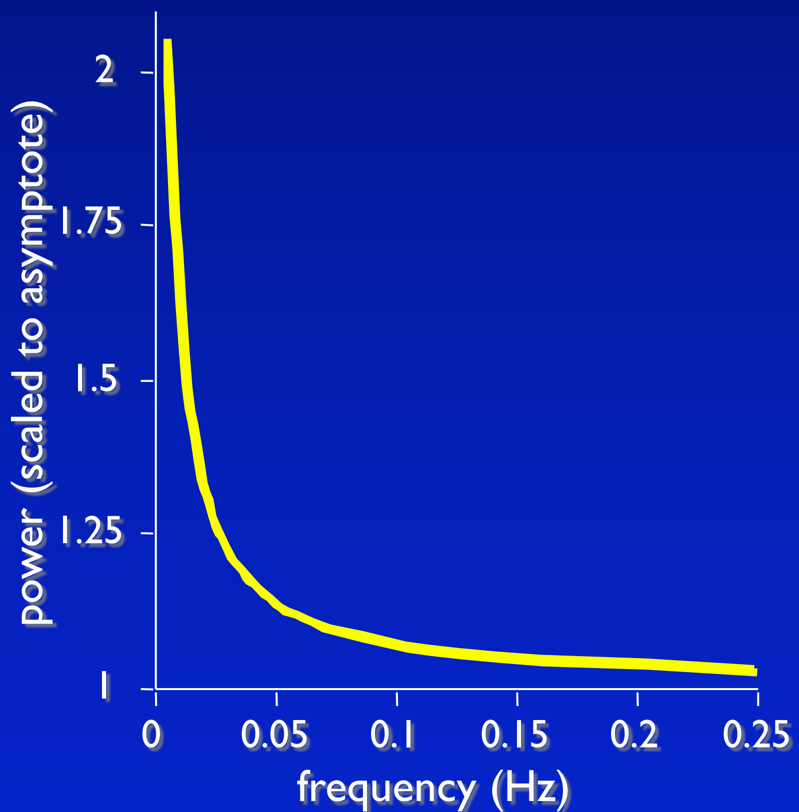


intrinsic noise

The Rock and the Hard Place

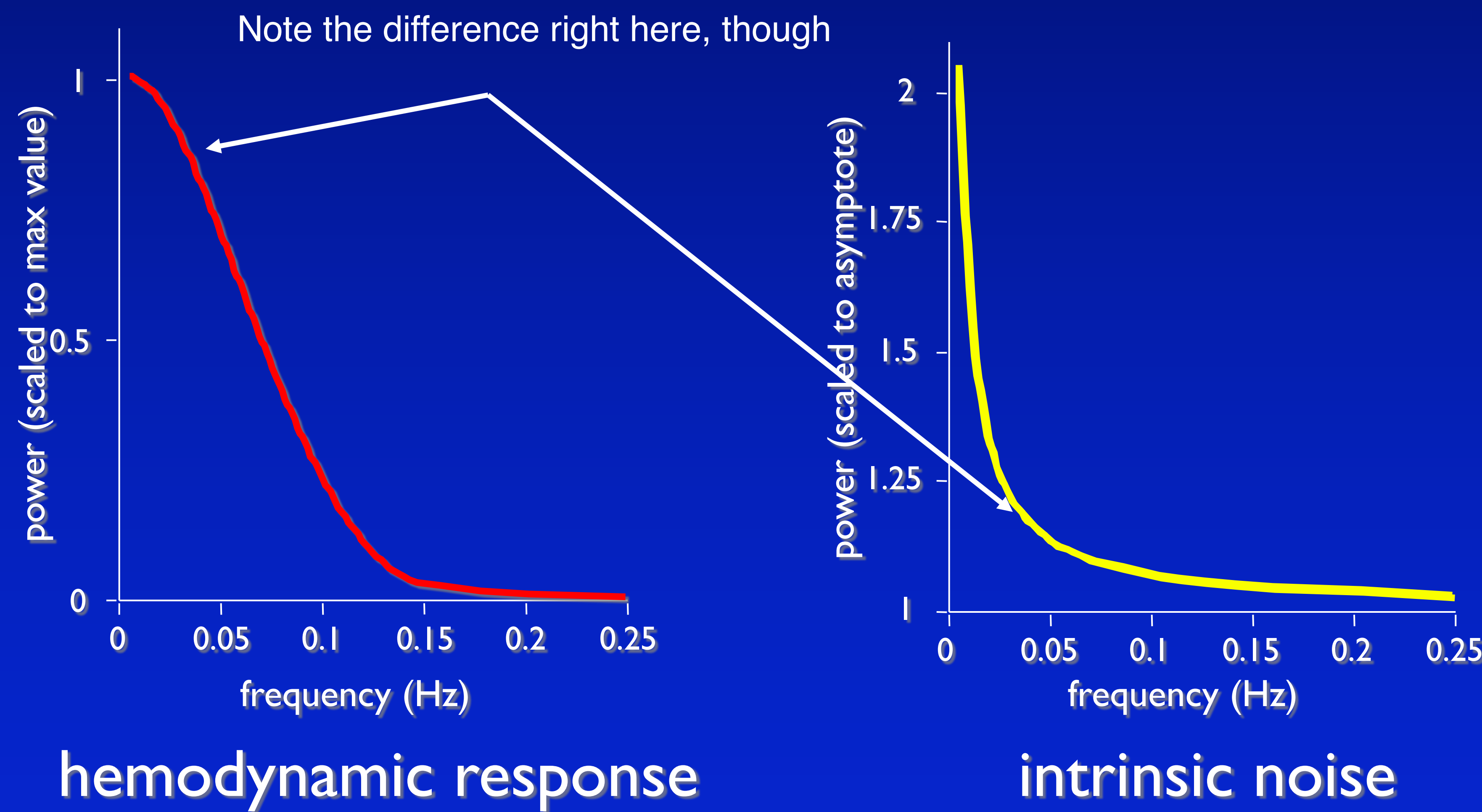


hemodynamic response

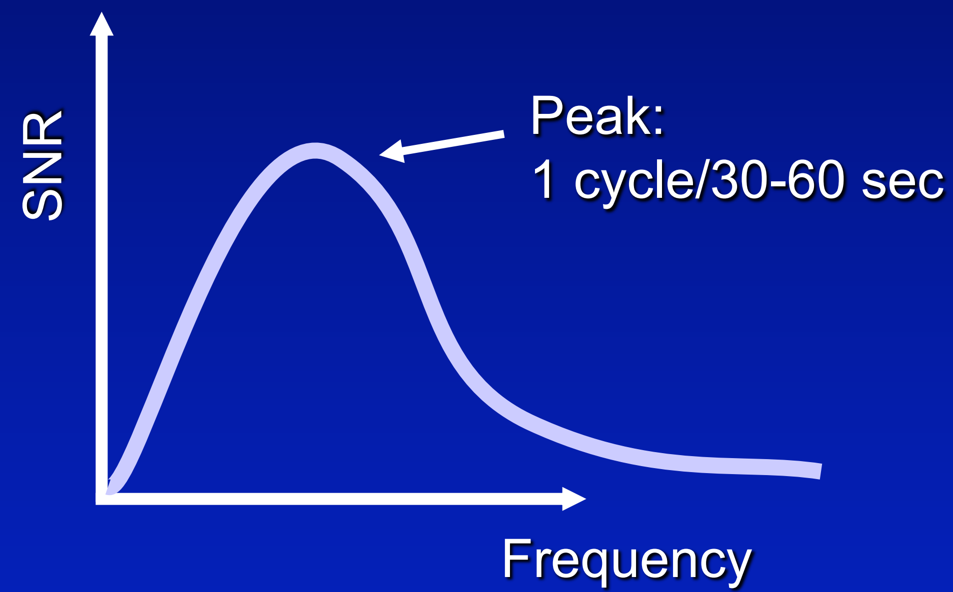


intrinsic noise

The Rock and the Hard Place



Signal-to-Noise Ratio



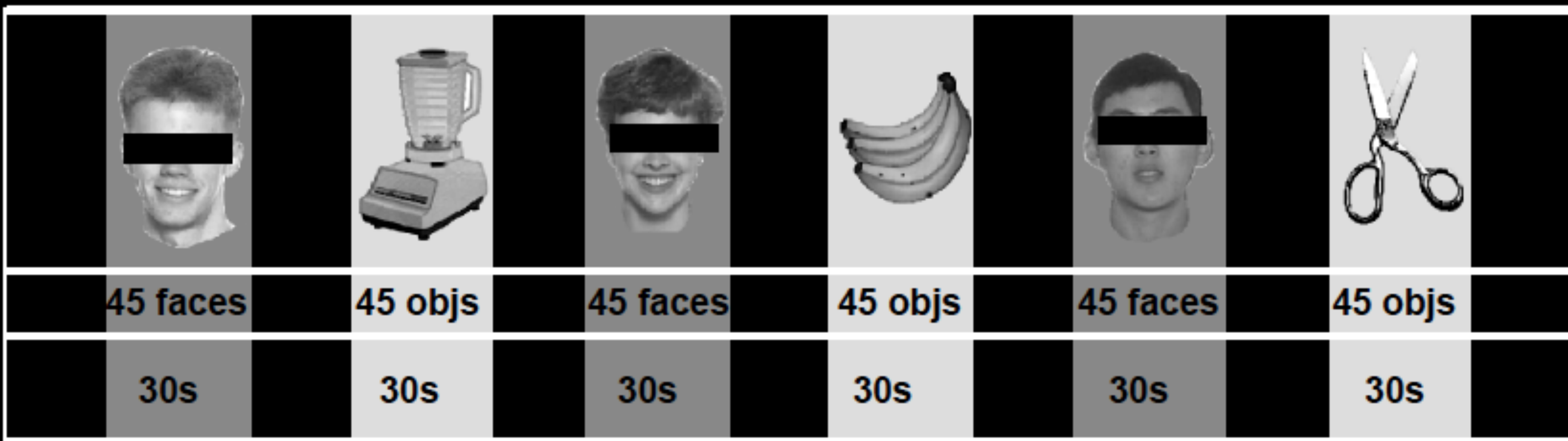
- Considering the two effects of noise and hemodynamic response, there is a sweet spot where the best blocked fMRI can be carried out
  – Full cycle every 30 to 60 seconds
  – Epochs of duration 15 to 30 seconds

Question:

Are there any parts of the brain that are specialized for perceptually processing faces, more than other kinds of visual stimuli?

Where are they?

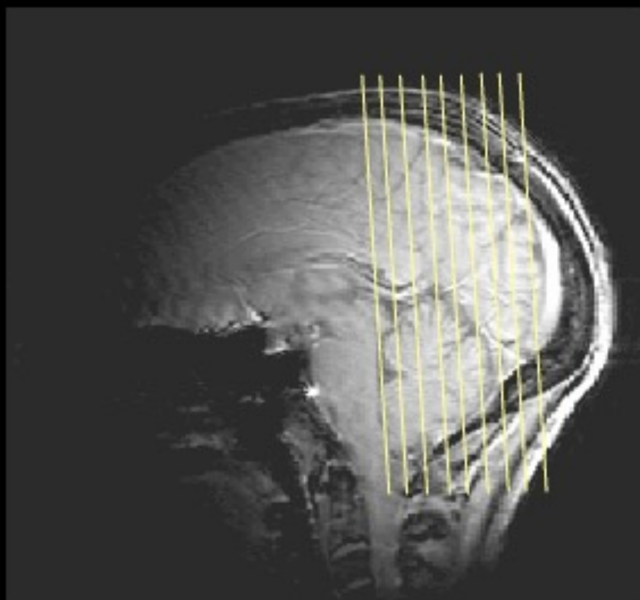
Stimulus Sequence
“blocked” design

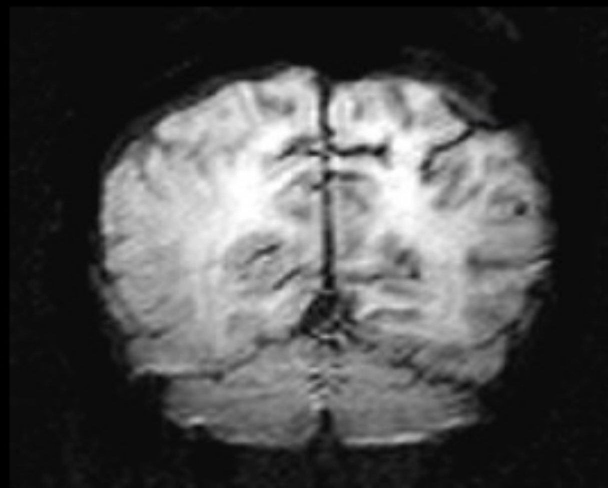


Face photos modified by OCW for privacy considerations.

- A single scan = 5.5 minutes long
- Presentation rate = 1.5 pictures/second

fMRI Data



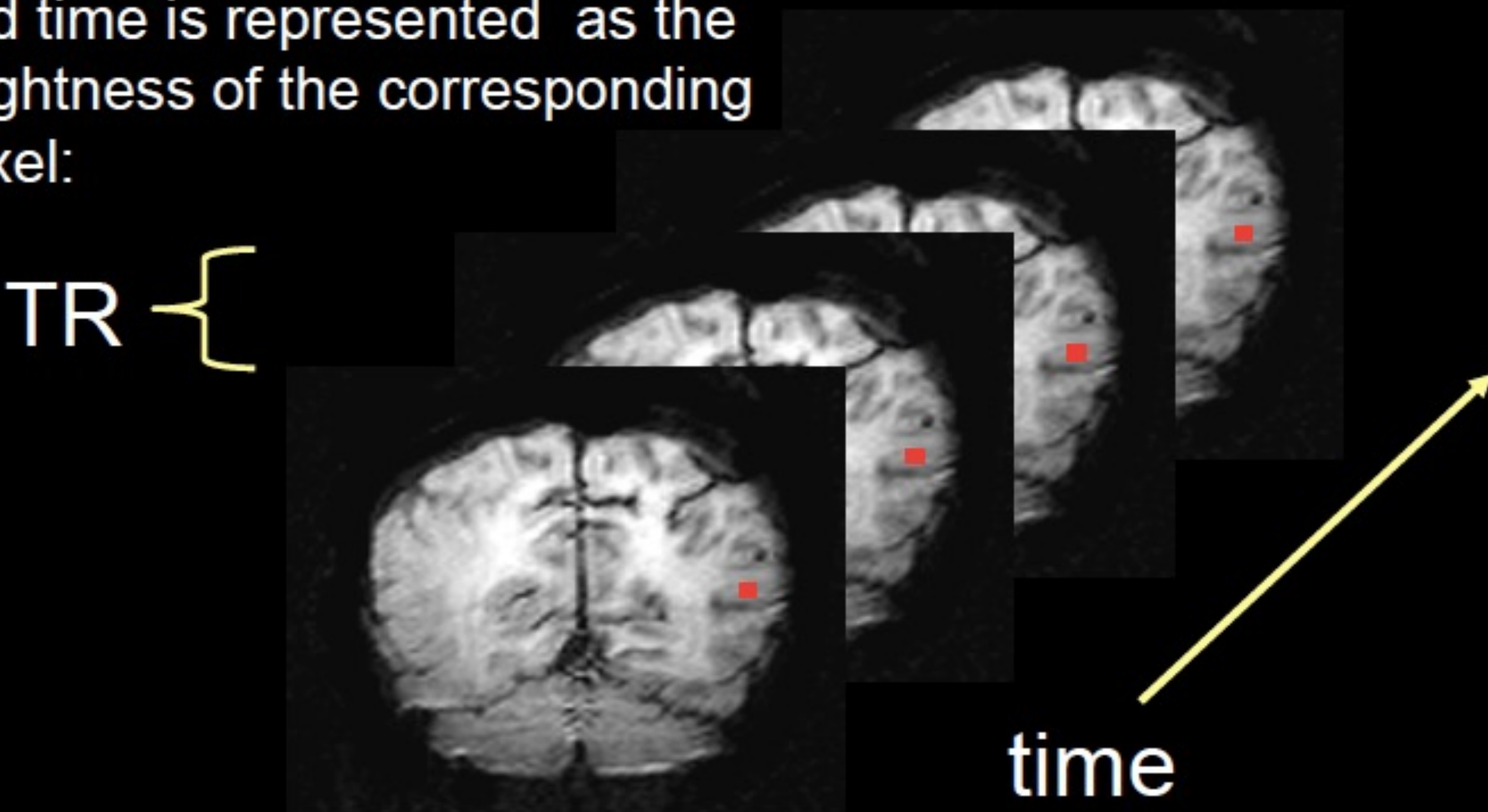


Chose slice number, position, thickness, and orientation

Each functional image of one slice is at least 64 x 64 voxels

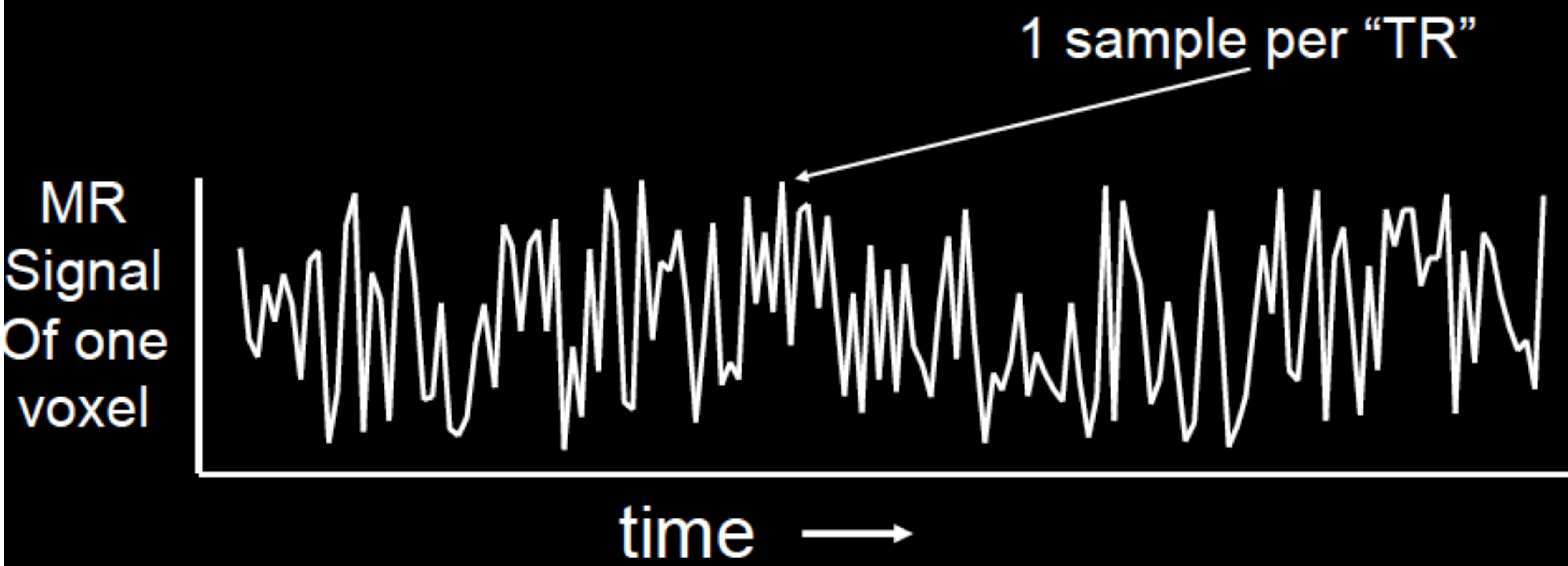
An image is made of each slice e.g. every 2 seconds (TR=2)

This makes a “movie” of each slice, in which the MRI signal intensity at each position and time is represented as the brightness of the corresponding voxel:

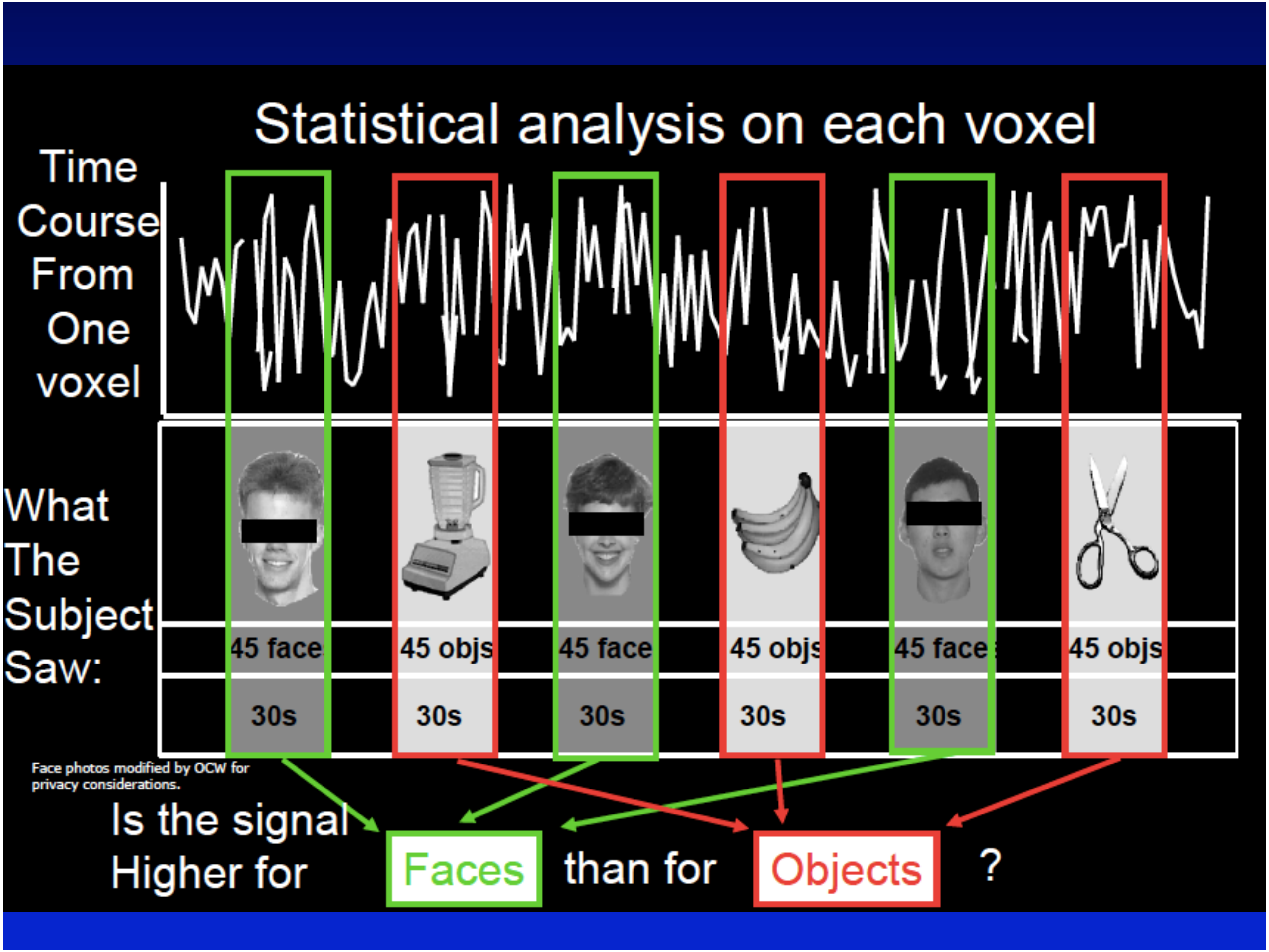


fMRI Data

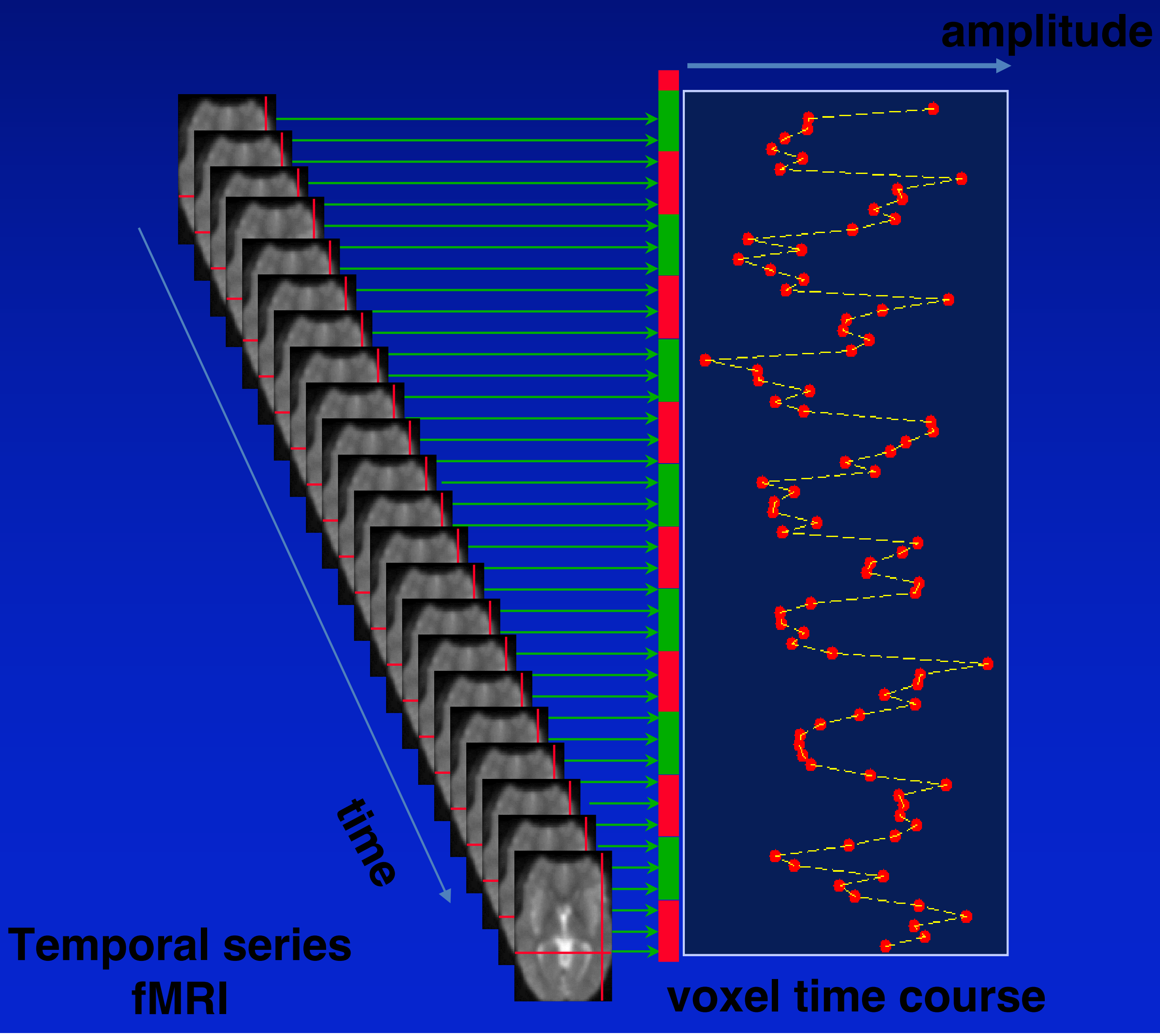
Each voxel has a "time course" like this:



We statistically test each voxel to see if it produced a stronger response, e.g. during the face epochs than during the object epochs…..

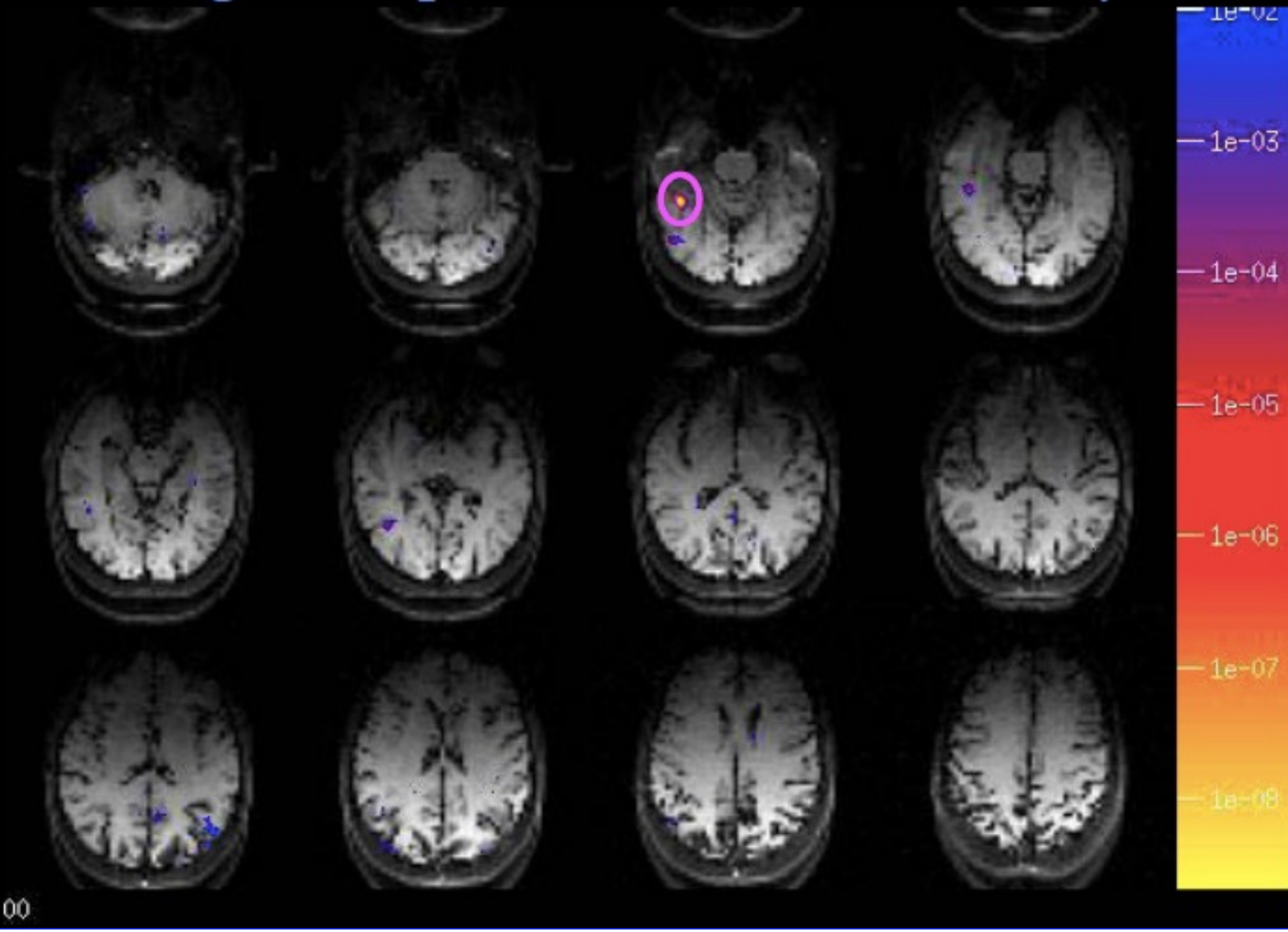

Statistical analysis on each voxel
Time Course From One voxel
What The Subject Saw:
45 face
45 objs
45 face
45 objs
45 face
45 objs
30s
30s
30s
30s
30s
30s
Face photos modified by OCW for privacy considerations.
Is the signal Higher for
Faces
than for
Objects
?

fMRI Example: One Voxel

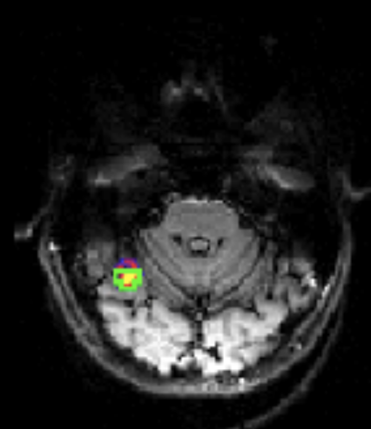


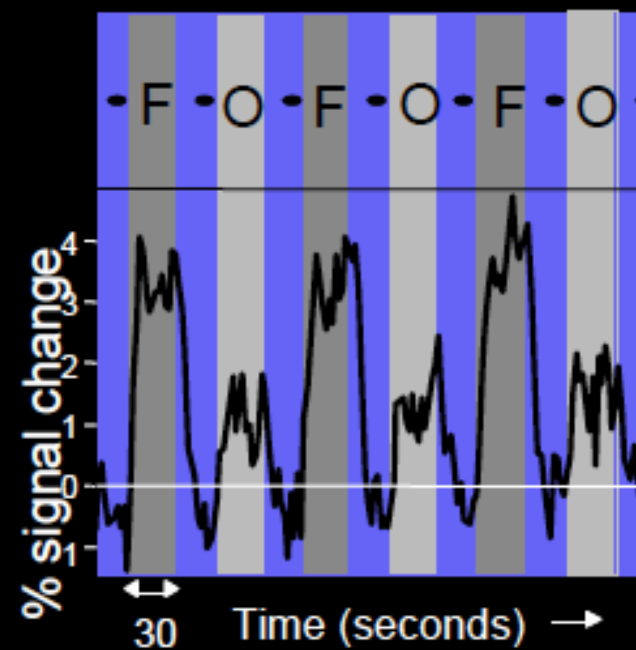
Source: J-B. Poline

Stronger Response to Faces Than Objects



Faces > Objects





Two-Condition Blocked Designs

- Cognitive subtraction assumption
- Design issues:
  - Two conditions differ by process of interest
  - Conditions should be as homogeneous as possible to minimize variation within block
  - Conditions should be densely populated by tasks to maximize actual performance time: high duty cycle
  - Trials within condition should be roughly equally spaced with SOA's of less than 3-5 second

Two-Condition Blocked Designs

- Challenges:
  - Might need instruction blocks
  - Task start-up time (e.g. N-back task requires N trials to fully load memory)
  - Habituation and anticipation effects due to similar sequential trials
  - In some tasks, blocks of similar trials aren’t psychologically appropriate
    - e.g., blocks of old and new items in recognition
  - Violations of pure insertion (e.g. difficult blocks may lead to changes in attention)
  - Rigid format – not suitable for all studies
- Advantages:
  - Simple analysis
  - Excellent statistical power
  - Very good for localizing regions to be tested in other designs
    - e.g., localizing face region for another task

Multiple-Condition Blocked Designs

- Typical:
  - Use a fixed order within a run (e.g., ABCABC…)
  - Counter-balance across runs (e.g., ABCABC vs. BCABCA vs. CABCAB)
  - Randomized blocks are also OK but be careful if only a small number of blocks are used
    - Randomized order may allow very low or high frequencies to creep into the design, neither of which is within the range that is optimal
      - e.g., AABCCB
  - Block should be long enough to reach signal plateau

Parametric Blocked Designs

- Uses blocks with a parametric task manipulation
  - e.g. graded visual stimuli, graded memory conditions (such as varying memory load)
  - Often easier to interpret and justify than the cognitive subtraction hypothesis – look for those areas that vary exactly as the parametric manipulation (by principle of scaling)
  - Analysis might use an ANOVA to find main effect of manipulation and then do a post-hoc analysis looking for increases that match manipulation
  - Pure insertion still assumed, but with the same process repeatedly (more plausible)

Event-Related fMRI

- Responses to brief events are almost always weaker than responses to blocks of events
- Event-related fMRI studies must consider the long duration of the BOLD hemodynamic response (delay = 2-3 sec; overall duration 8-16 sec)
  - How does one observe the course of a hemodynamic response to a neural event in this case?

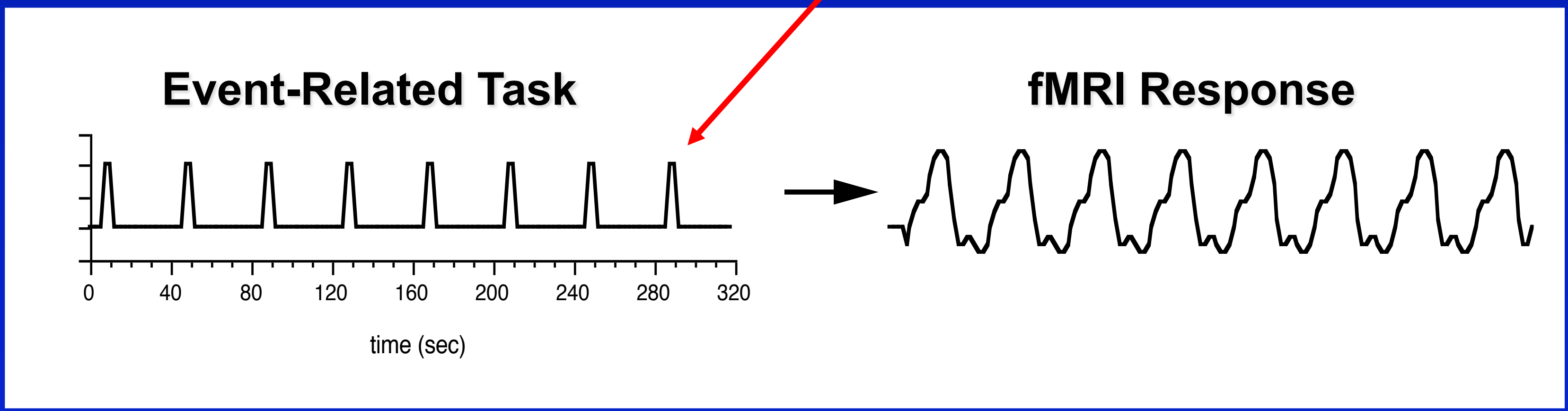
Event Related Designs

- Several different variants
  - Simple task, non-overlapping epochs, stretched out with fixed timing
  - Randomized ITI with faster presentation
  - Fixed ITI, randomized conditions with faster presentation
  - Mixed block/event-related designs

Event-Related fMRI - Extended Trials

- Behavioral trials have long gaps between them (long ITI)
  - Typically 10-20 sec ITI is used
- Example:

Individual events



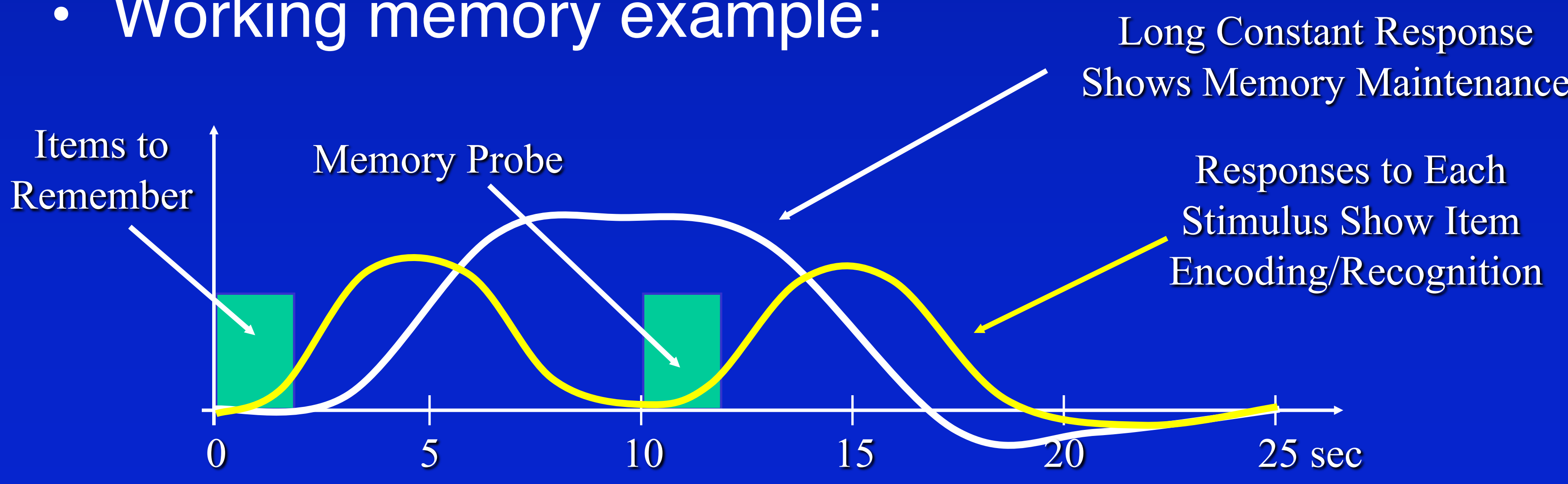
5. Mental Imagery Experiment (eyes closed)

O'Craven & Kanwisher (2000)

Subjects heard the name of a famous person or familiar place once every 12 seconds, in random order, and were instructed to image the face or place.

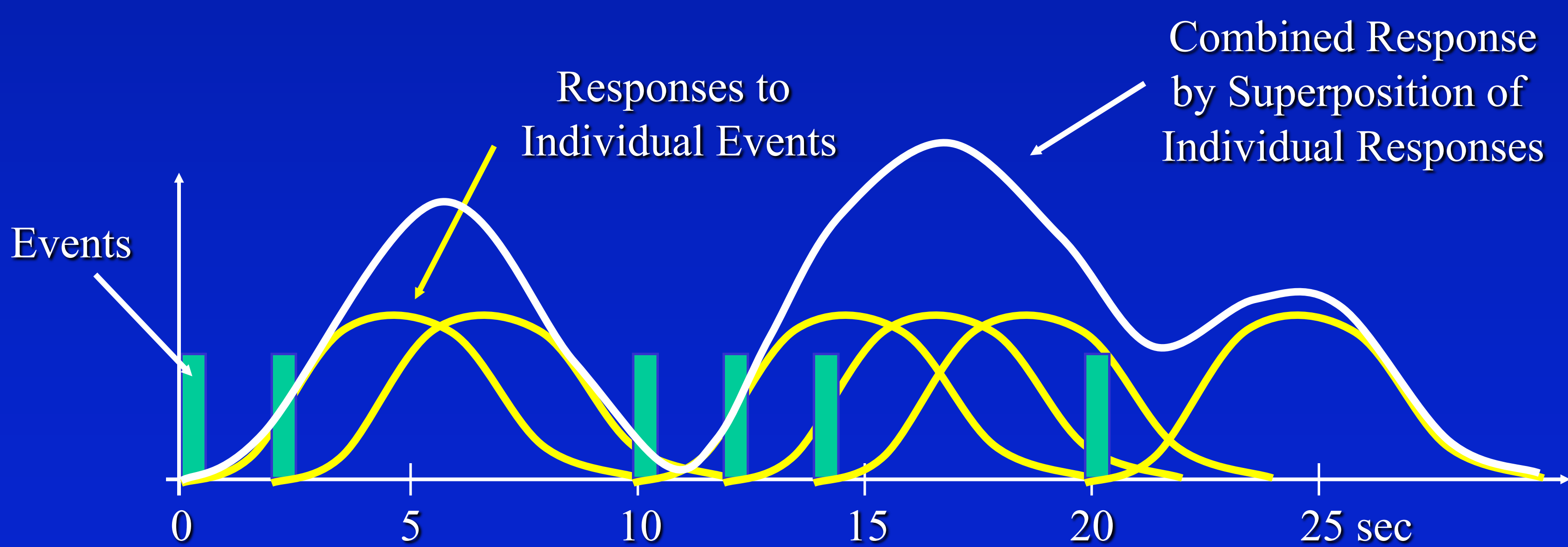
Event-Related fMRI - Extended Trials with Fixed Timing

- Behavioral trials are extended in duration to allow responses to the individual events to be seen
  - Often 10-15 sec is added at the end to get back to baseline state
  - Subtasks have unique temporal signature
- Working memory example:



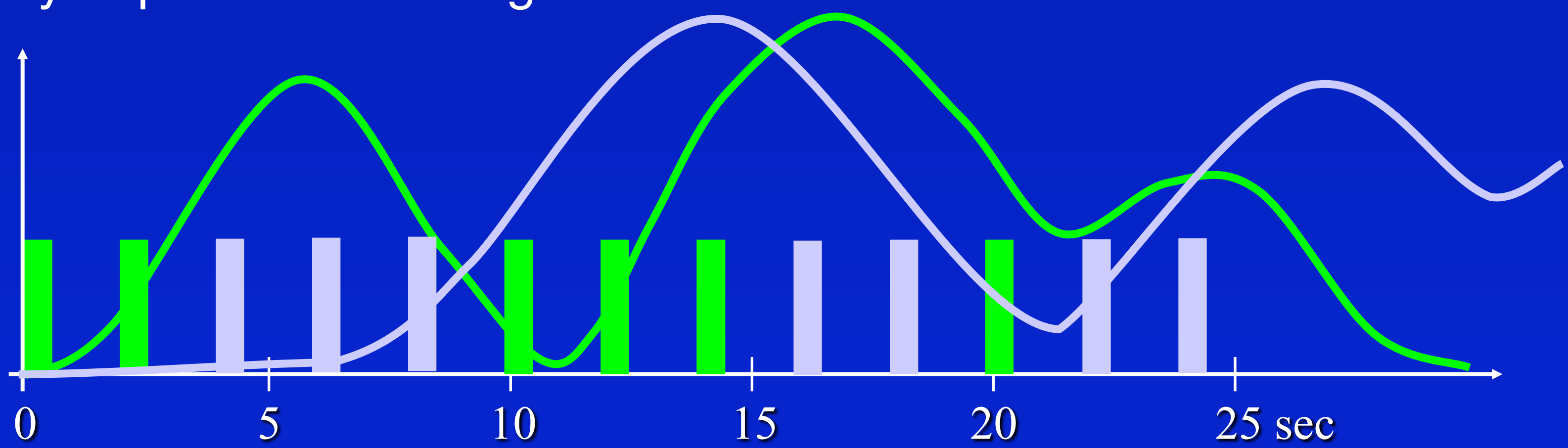
Event-Related fMRI with Randomized ITI, One Condition

- Behavior trials are presented rapidly, but with random timing
  - Overlapping responses are superimposed to yield a unique time-course (by principle of superposition)
  - Randomization causes the variation in the time-course

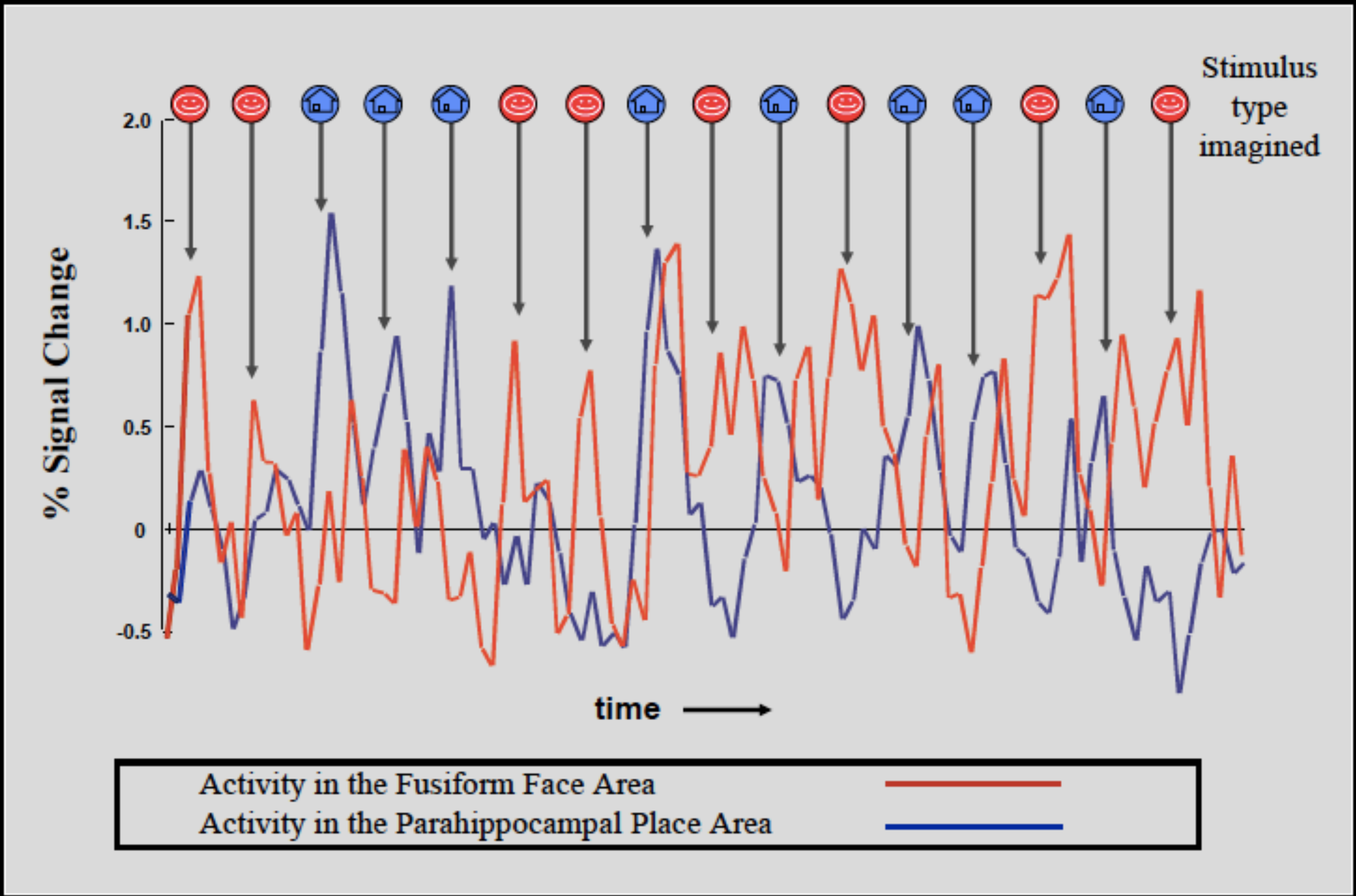


Event-Related fMRI with Randomized Trials, Two Conditions

- Behavioral trials are presented rapidly, but with random ordering
  - Overlapping responses are superimposed to yield a unique time-course (by principle of superposition)
  - E.g. AABBBAAABBABB…
  - Trial types A and B will have a unique temporal signature if the timing between them is right
  - In effect, you are detecting the low frequency envelopes caused by haphazard ordering

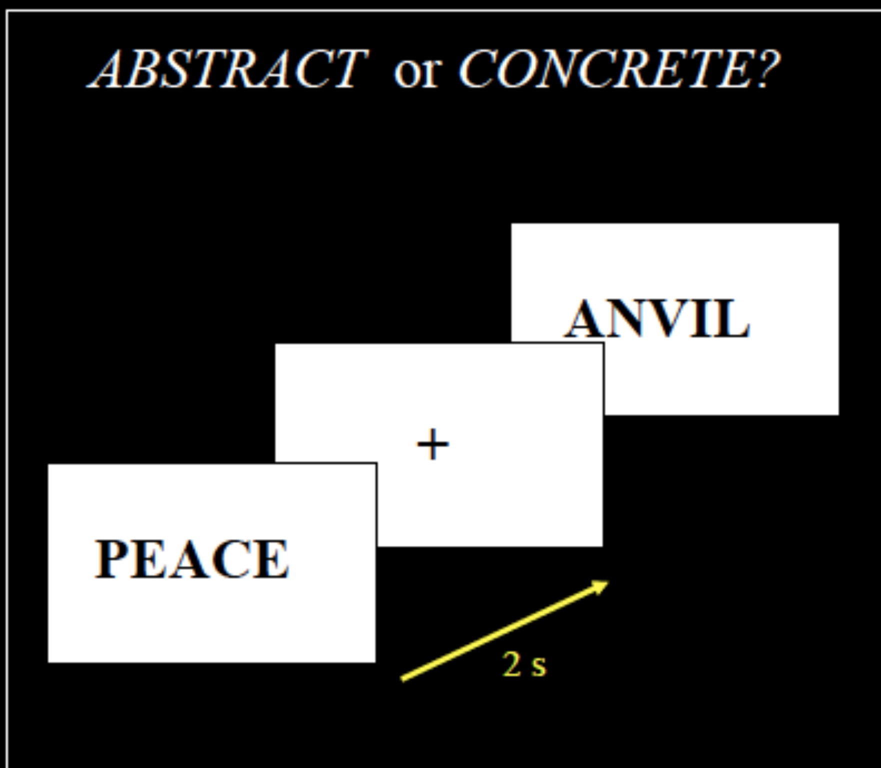


Imaging Single Mental Events

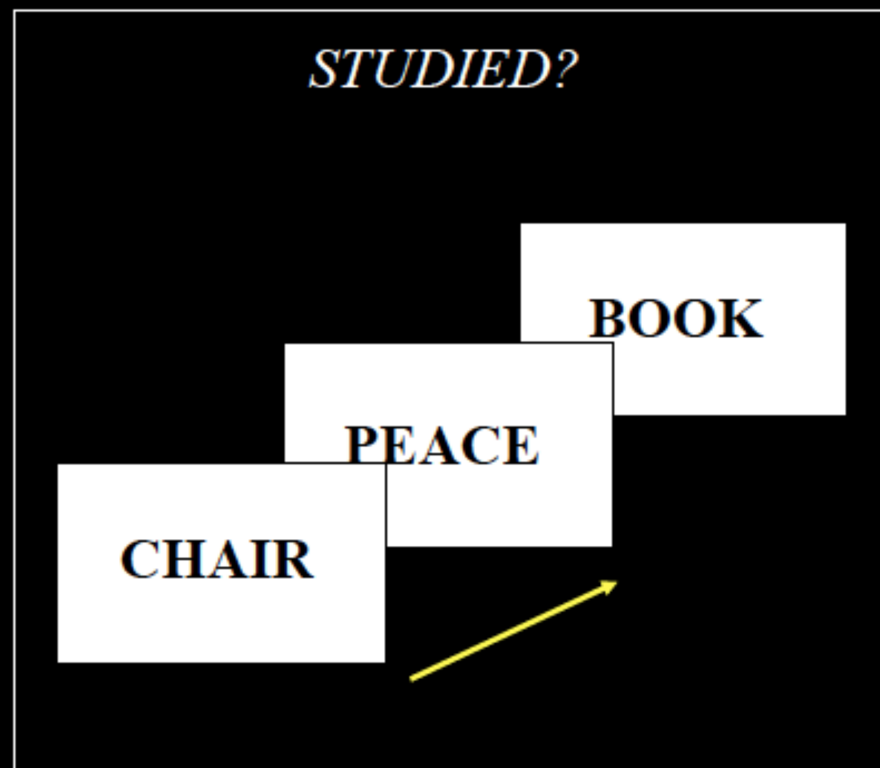


1. Predicting Verbal Explicit Memory

fMRI Scanning during Word Learning



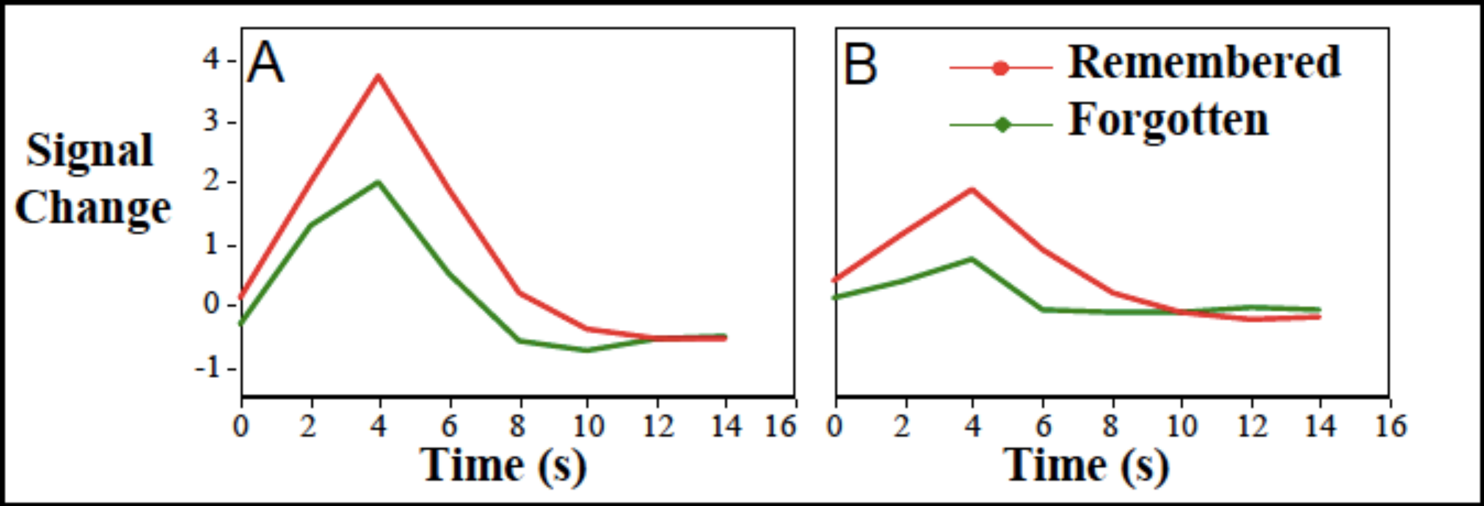
Post-Scan Memory Test



Predicting Verbal Explicit Memory: Left Ventrolateral PFC

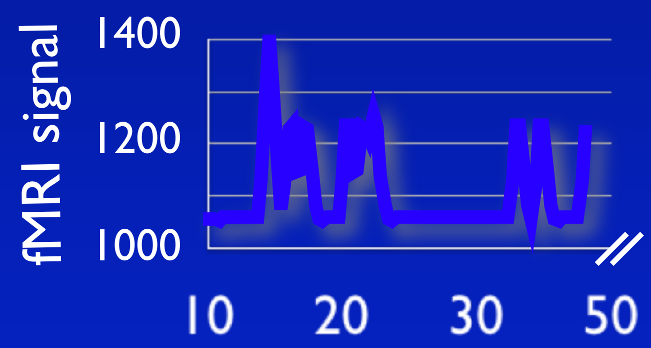
Wagner et al (1998)

Posterior LIPC Anterior LIPC



Arranging Timing in Event-Related Designs

Goals: 1) maximize statistical power
2) avoid the predictability of events



If the signal is linear (i.e., there is no saturation), events can be spaced as closely as 1-2 sec

Event-Related Design

- Advantages
  - Avoids habituation/behavioral issues
  - Very flexible
  - Allows self-paced tasks
  - Can model sub-epochs when they occur (e.g. a behavioral response, encoding, or memory storage)
  - Can separately analyze correct/incorrect responses
  - Can still do parametric manipulations

Event-Related Designs

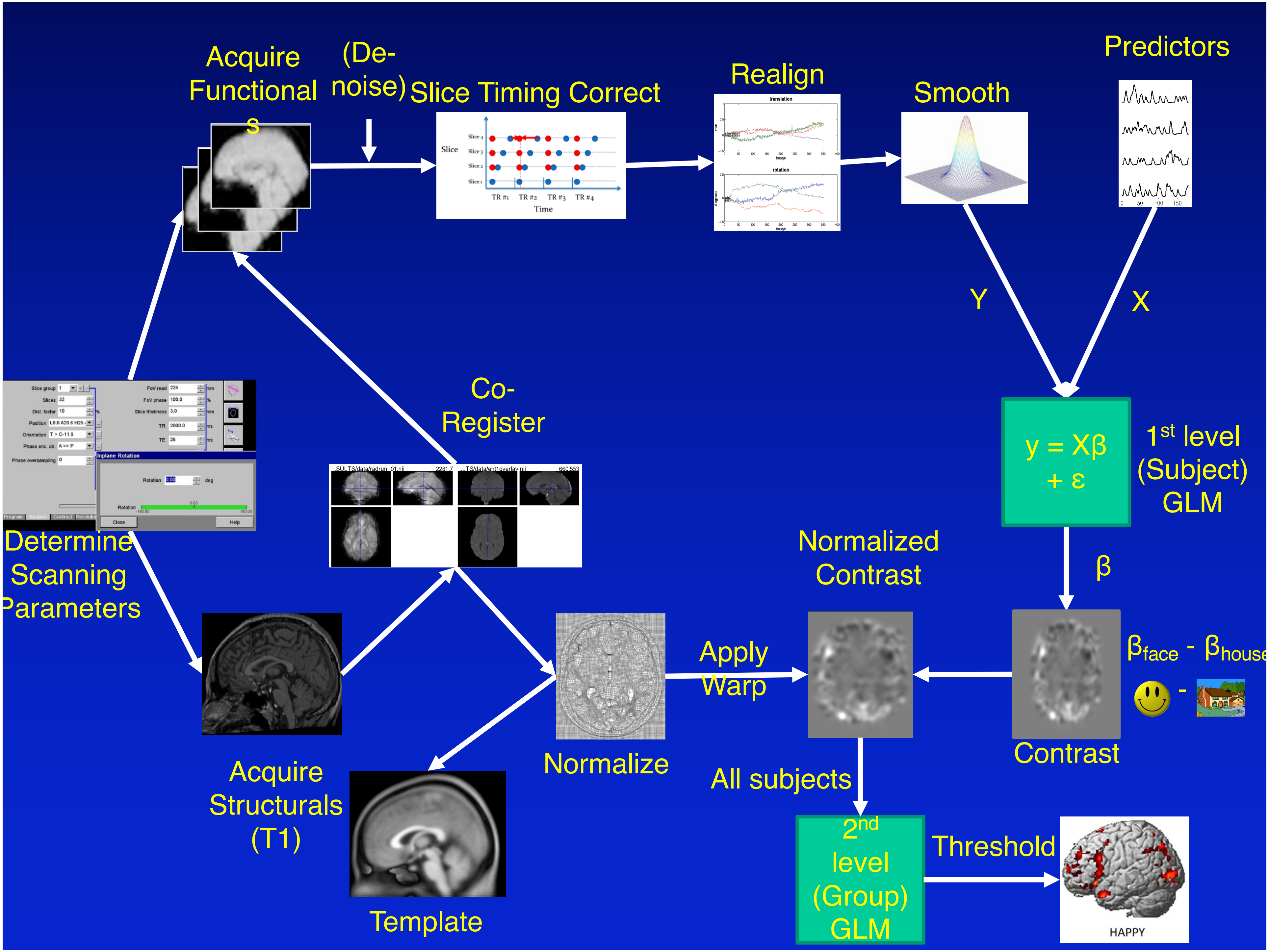
- Disadvantages
  - Sensitive to accuracy of shape of the BOLD response
  - Reduced sensitivity relative to blocked designs
    - The most sensitive ER designs have trials clustered into mini-blocks – that is, long runs of particular trial types (so they become blocked designs)
  - Difficult to include instruction blocks

Mixed ER/Blocked Designs

- Looks like a blocked design, but individual trials are analyzed within blocks
  - Often done so that behavioral errors can be analyzed
  - But they compromise on packing of trials within a block

Control/Baseline Conditions

- Raichle hypothesis (*Nature Reviews: Neuroscience* 2:685-692, 2001):
  - There are a set of "mental activities" associated with resting with eyes open (e.g. passive viewing of a blank screen)
  - During goal-directed behavior these resting-state activities are suppressed
  - May often see deactivations related to suppression of resting state activity
- Therefore, selection of control conditions must be carefully considered


Acquire Functionals
(De-noise)
Slice Timing Correct
Slice
Time
Realign
translation
rotation
Smooth
Predictors
Y
X
$y = X\beta + \varepsilon$
1st level (Subject) GLM
β
Contrast
β_{face} - β_{house}
Normalized Contrast
Apply Warp
Normalize
All subjects
2nd level (Group) GLM
Threshold
HAPPY
Co-Register
Determine Scanning Parameters
Inplane Rotation
Acquire Structurals (T1)
Template