# Functional Magnetic Resonance Imaging

Michele Diaz, Ph.D.
Brain Imaging and Analysis Center
Duke University

mtd3@duke.edu

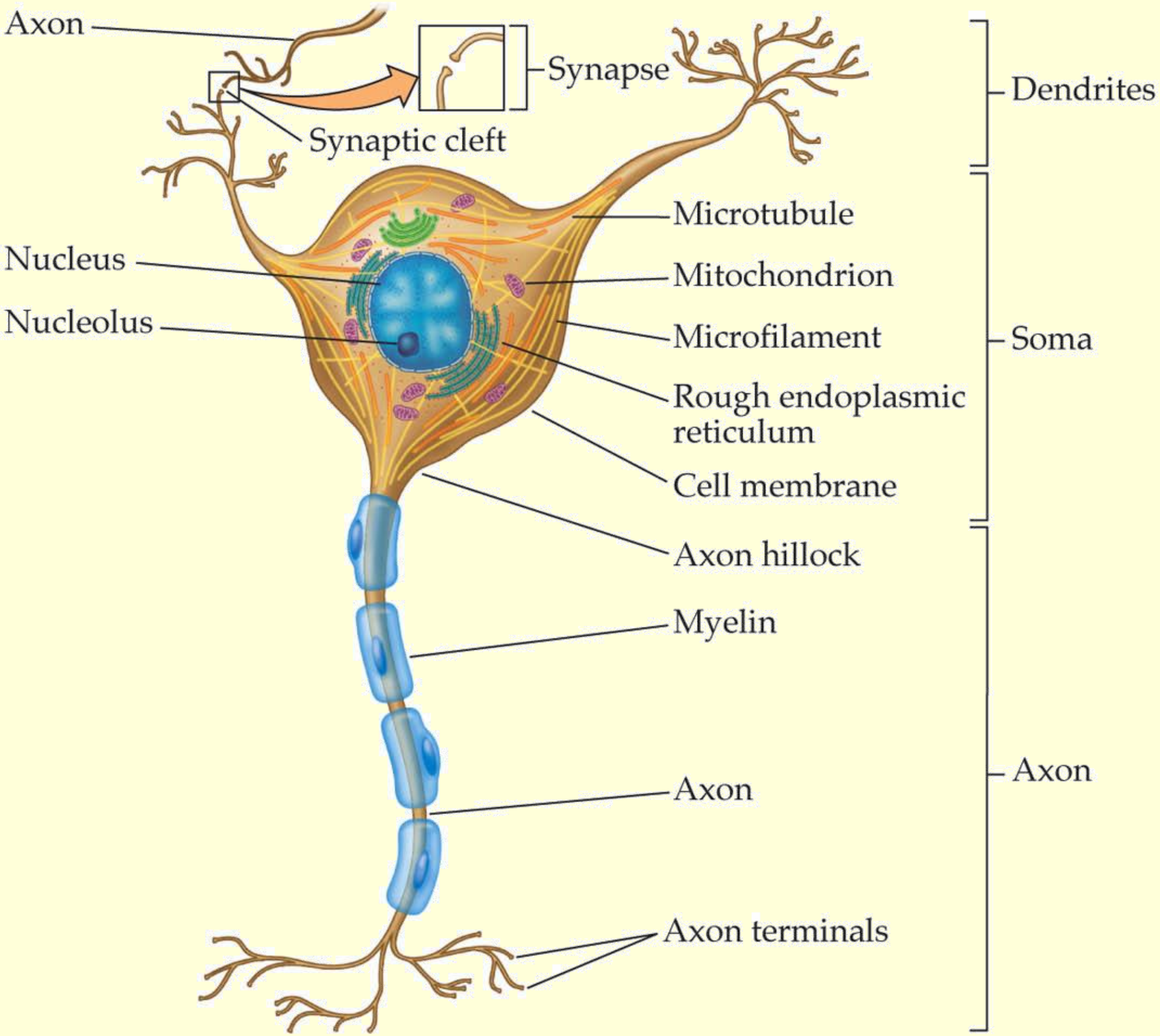
# Yesterday

- What is fMRI?
- Key Concepts
- MRI Scanners
- MRI in Detail

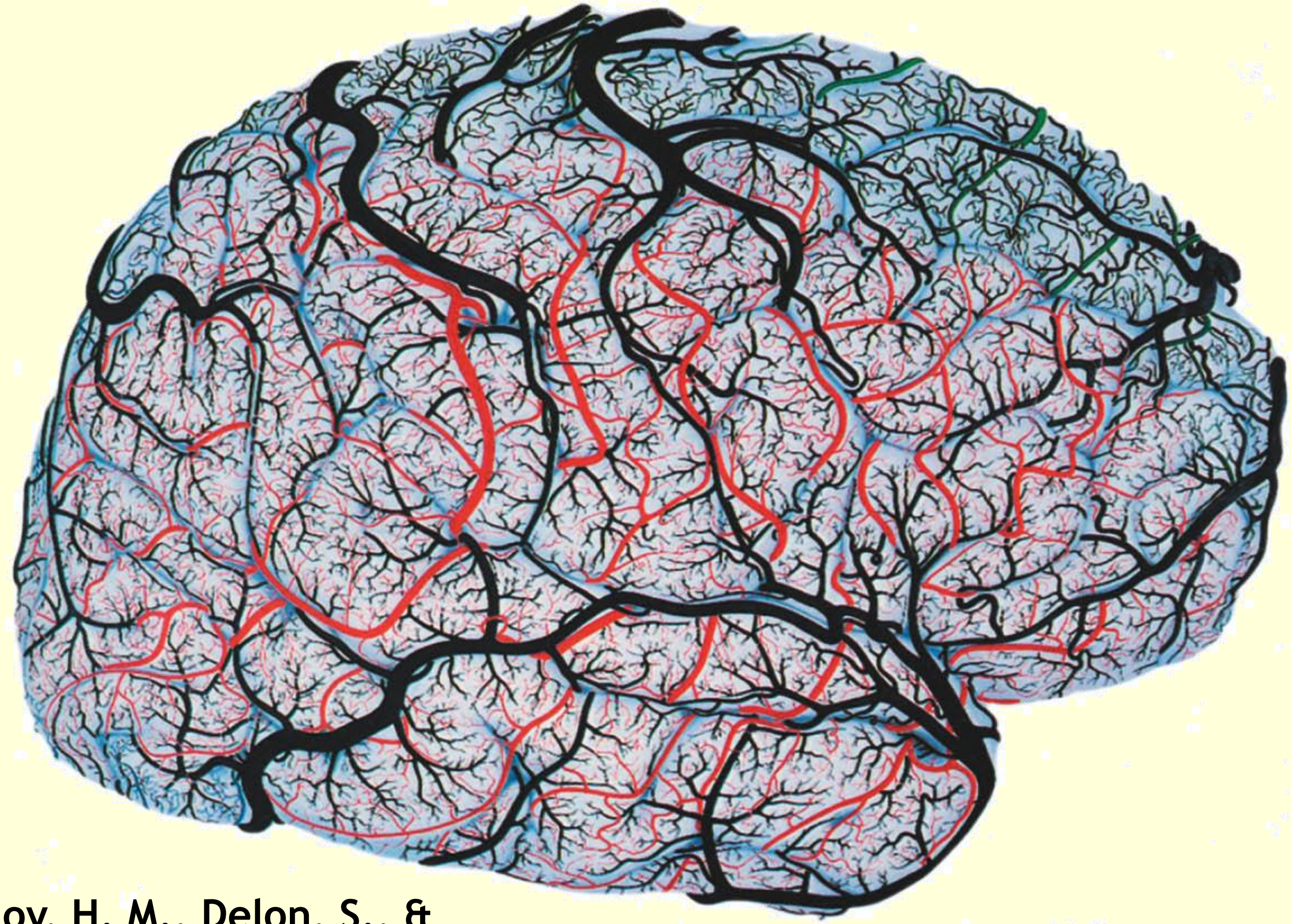
# Outline for Today

- Brain Physiology
- Neuroanatomy
- BOLD response
- Signal and Noise

# 1. Brain Physiology




FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 6.2 



**Duvernoy, H. M., Delon, S., & Vannson, J. L. (1981). Cortical blood vessels of the human brain. Brain Research Bulletin, 7(5), 519-579.**

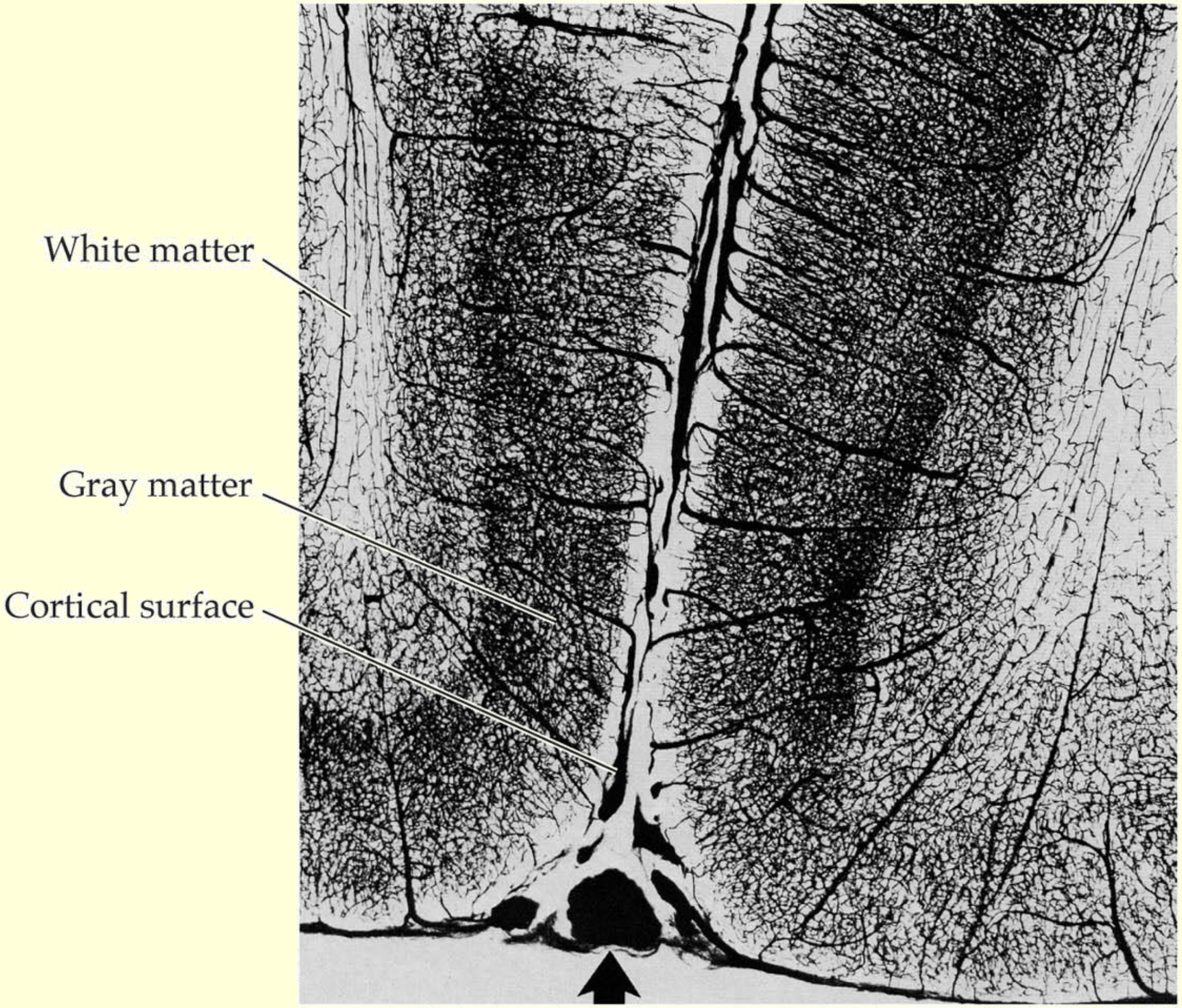
*FUNCTIONAL MAGNETIC RESONANCE IMAGING,* Figure 6.8 

**Because fMRI is dependent on blood flow and changes in levels of oxygen, it is important to understand the vascular system.**

# Key concepts in vascular system

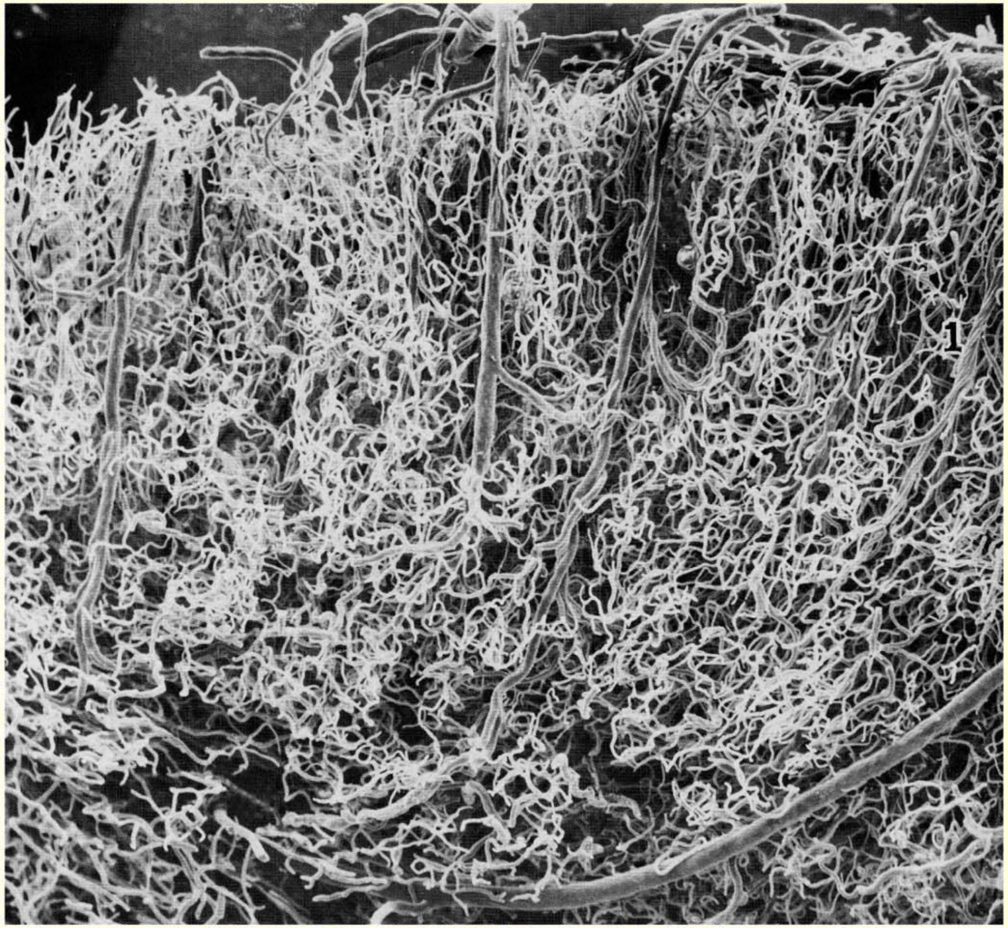
- Vast change in scale from largest arteries to capillaries
  - Small changes in diameter result in large changes in flow (2x diameter = 16x flow)
- Pulsatile flow in arteries smoothed out by resistance vessels (arterioles)
- Surface area of capillaries is essential for $O_2$ exchange
  - Neurons are usually within 20µm from a capillary
- Capillaries are not always fully perfused!
  - Blood can bypass capillaries
  - Saves weight, cost (in blood), etc.
  - Though never empty

# Distribution of vascularization across cortical layers




FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 6.13 

# Capillary structure

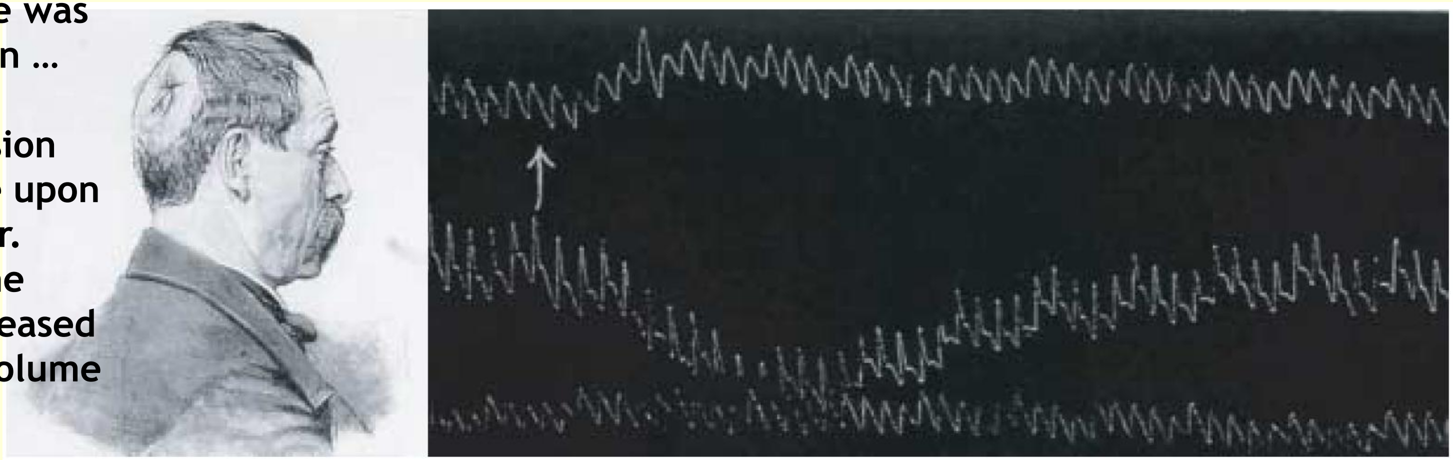



FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 6.9 

# How does function map onto blood flow?

Mosso, 1800’s

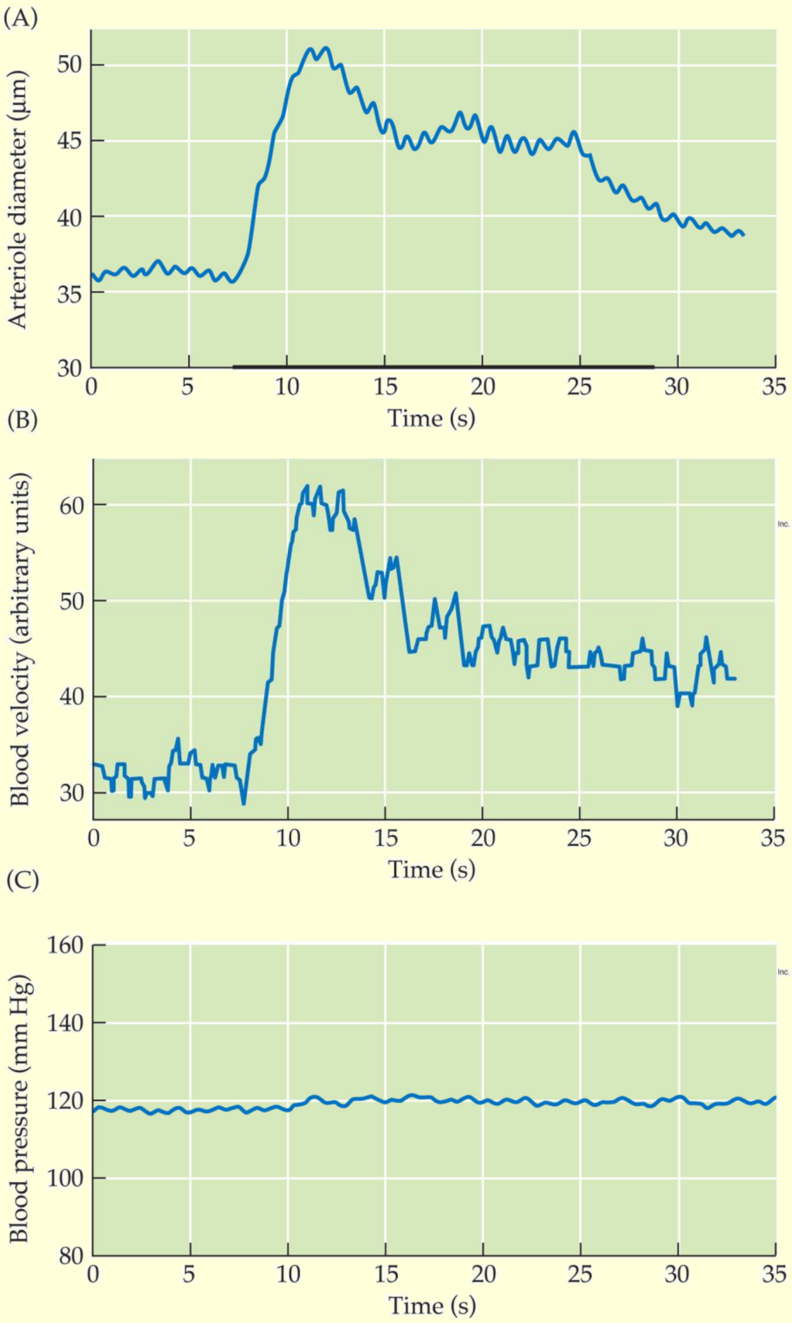
**Mosso writes: “Mr Cane was resting peacefully when … I said just a few words expressing the impression that his wife had made upon me when I first saw her. Cane did not speak. The blood to the brain increased immediately and the volume of the feet markedly diminished” (1894)**



Iadecola, *Nature Reviews Neuroscience*, 2004

"Blood very likely may rush to each region of the cortex according as it is most active, but of this we know nothing."

**[James, 1890]**




**Stimulation of the sciatic nerve (in a rat) results in arteriole dilation in somatosensory cortex.**

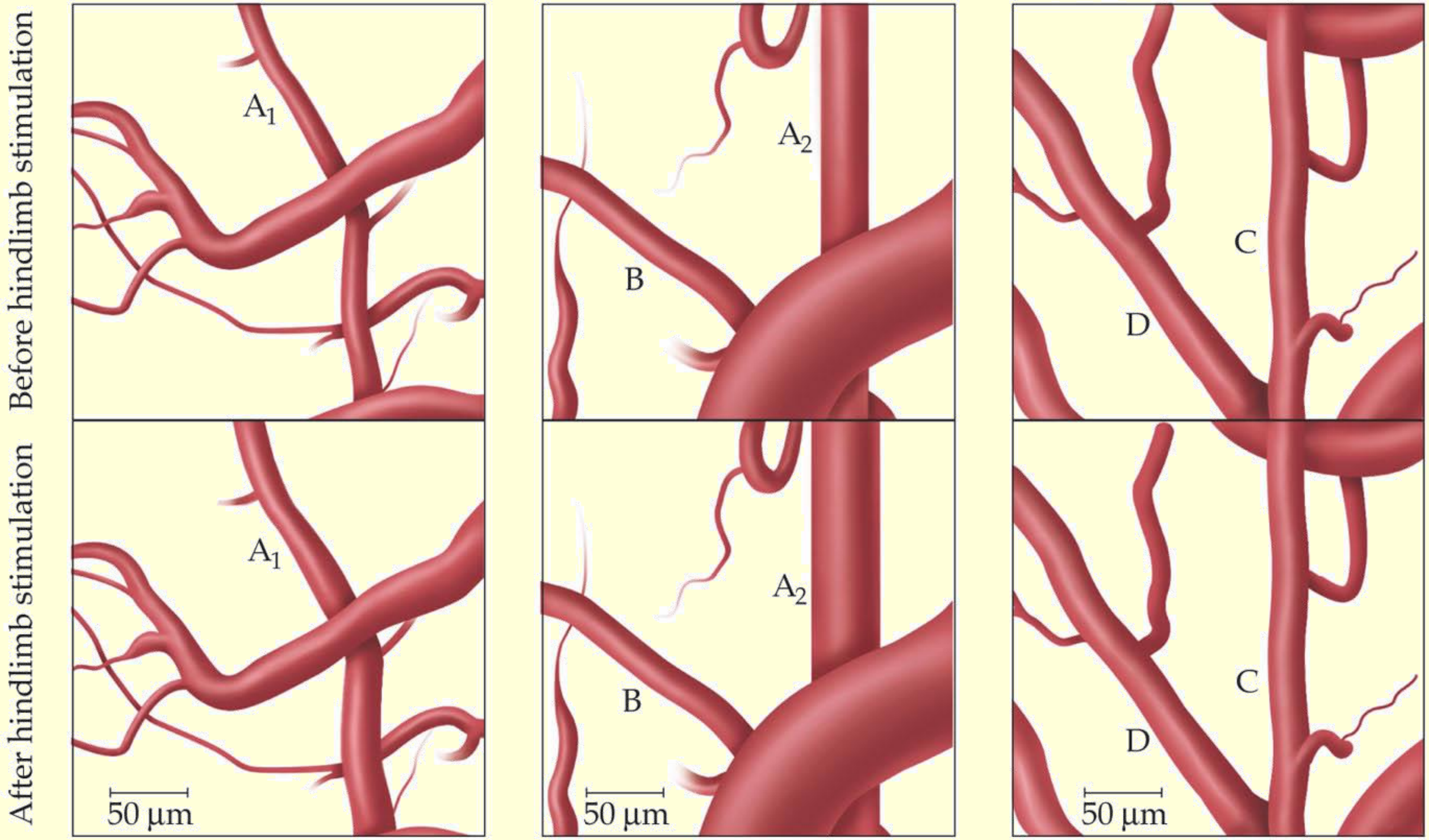
**There is a parallel change in blood velocity .**

**But, blood pressure remains relatively constant.**

**(This is a good thing.)**

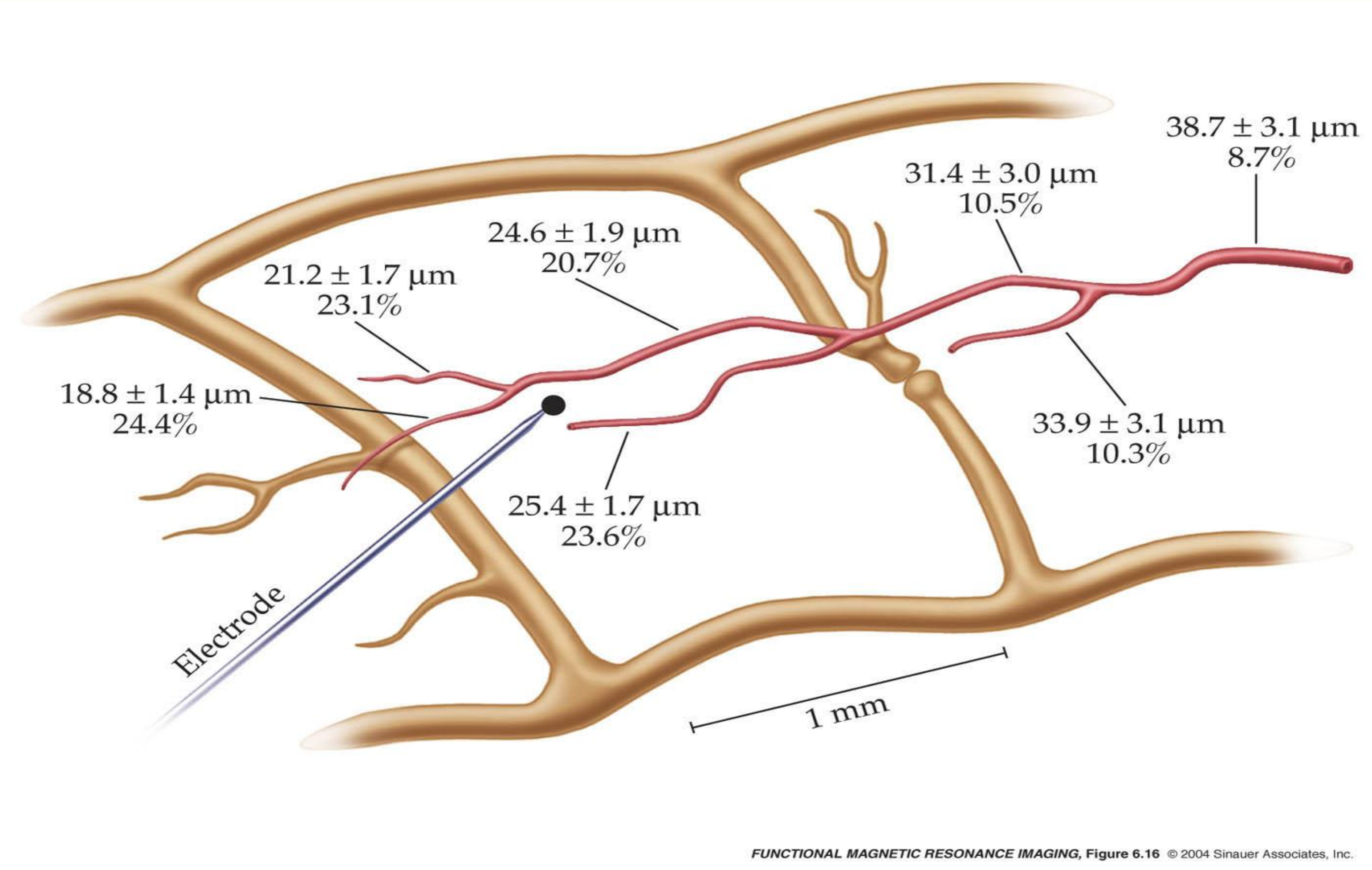
**Adapted from Ngai et al., 1988**

# Change in diameter of arterioles following sciatic (hindlimb) stimulation



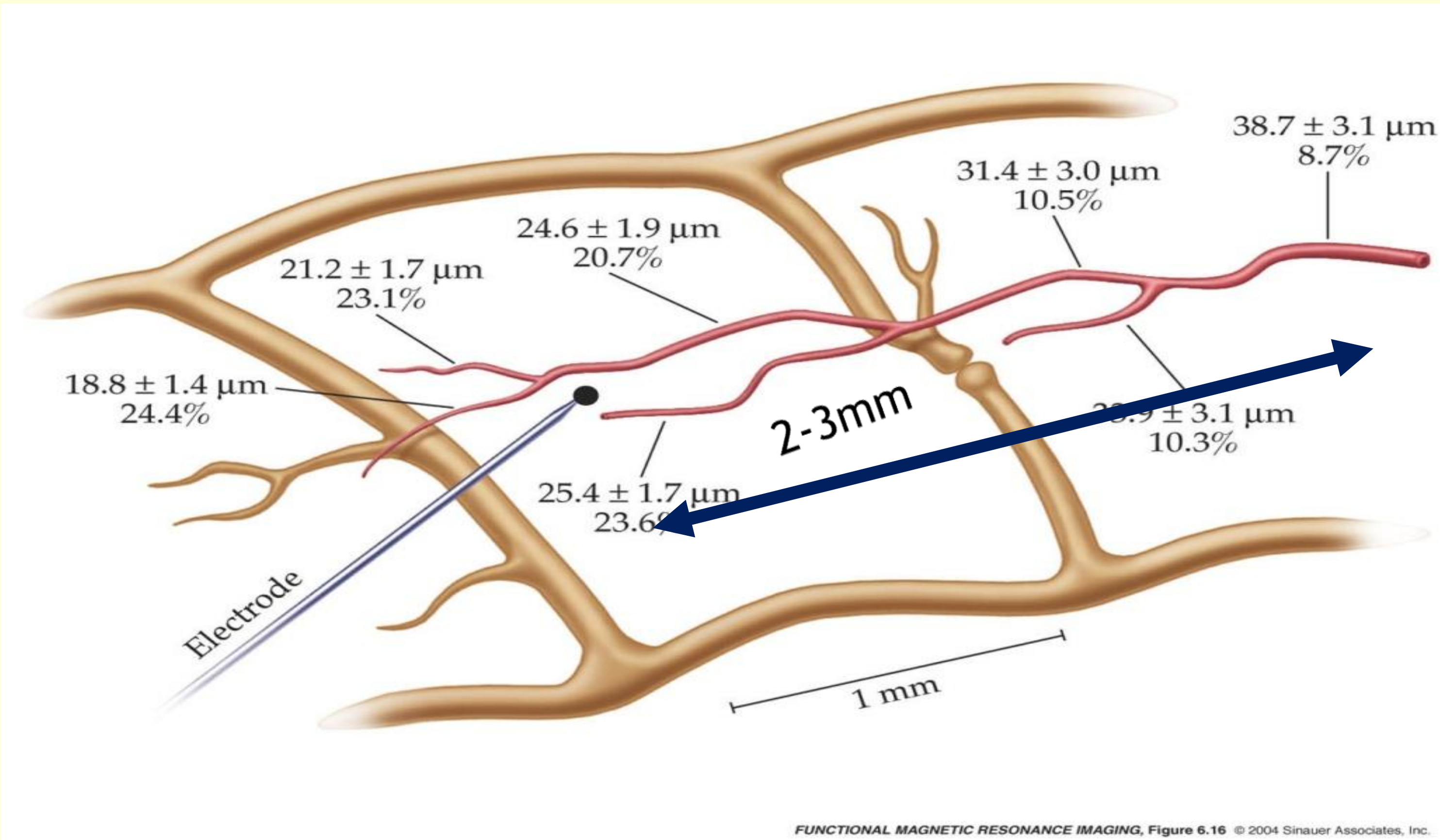

**Adapted from Ngai et al., 1988**

# Change in arteriole dilation as a function of distance from active neurons



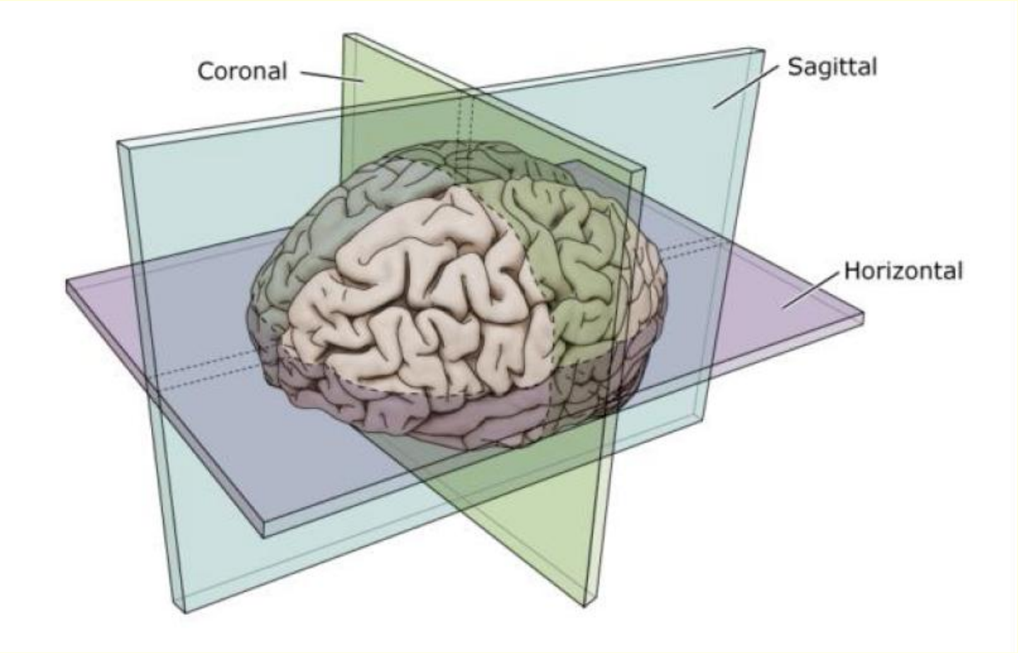

Rat Cerebellum, Adapted from Iadecola et al., 1997)

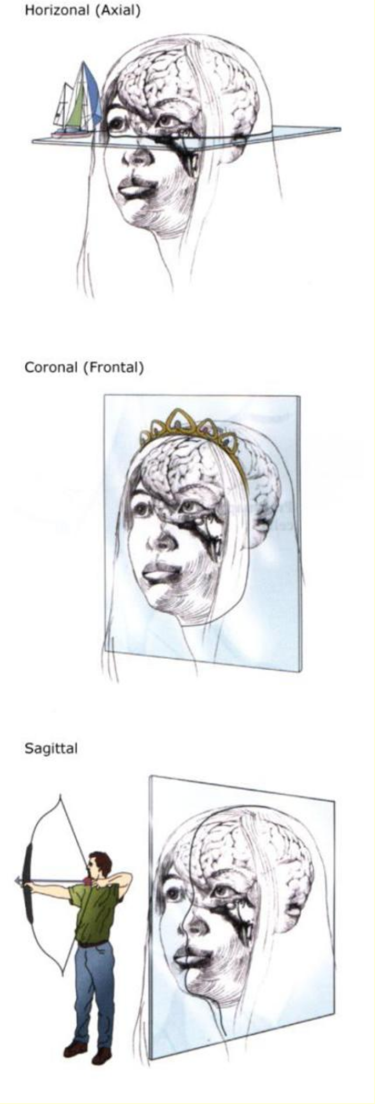
# What implications do these results have for the spatial resolution of MRI?



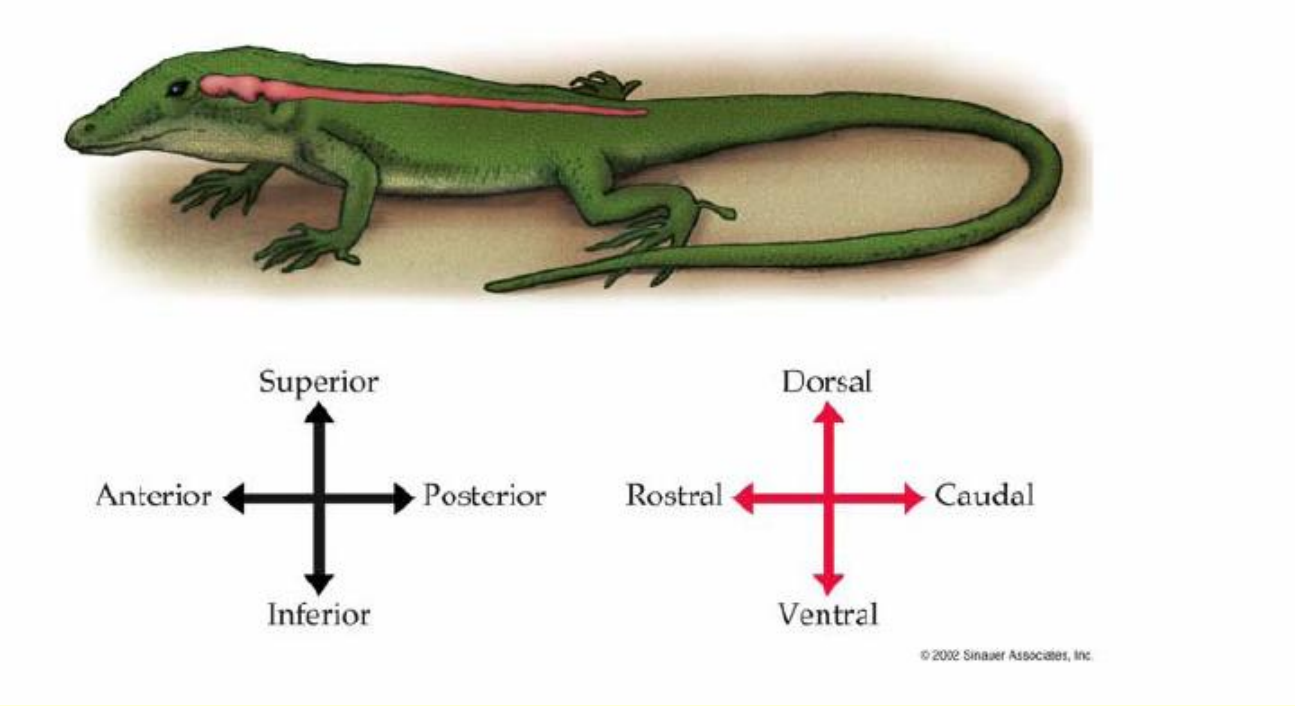
# 2. Neuroanatomy

# Terminology: Planes of Section



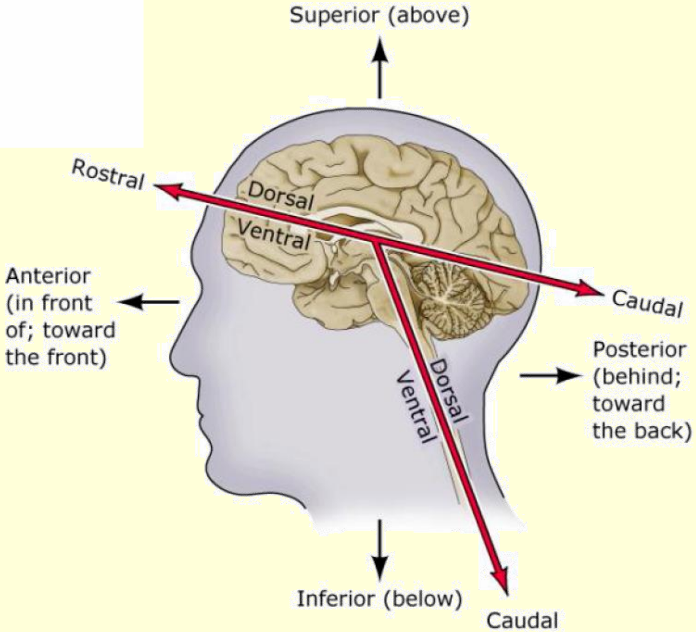
# Terminology: Labels



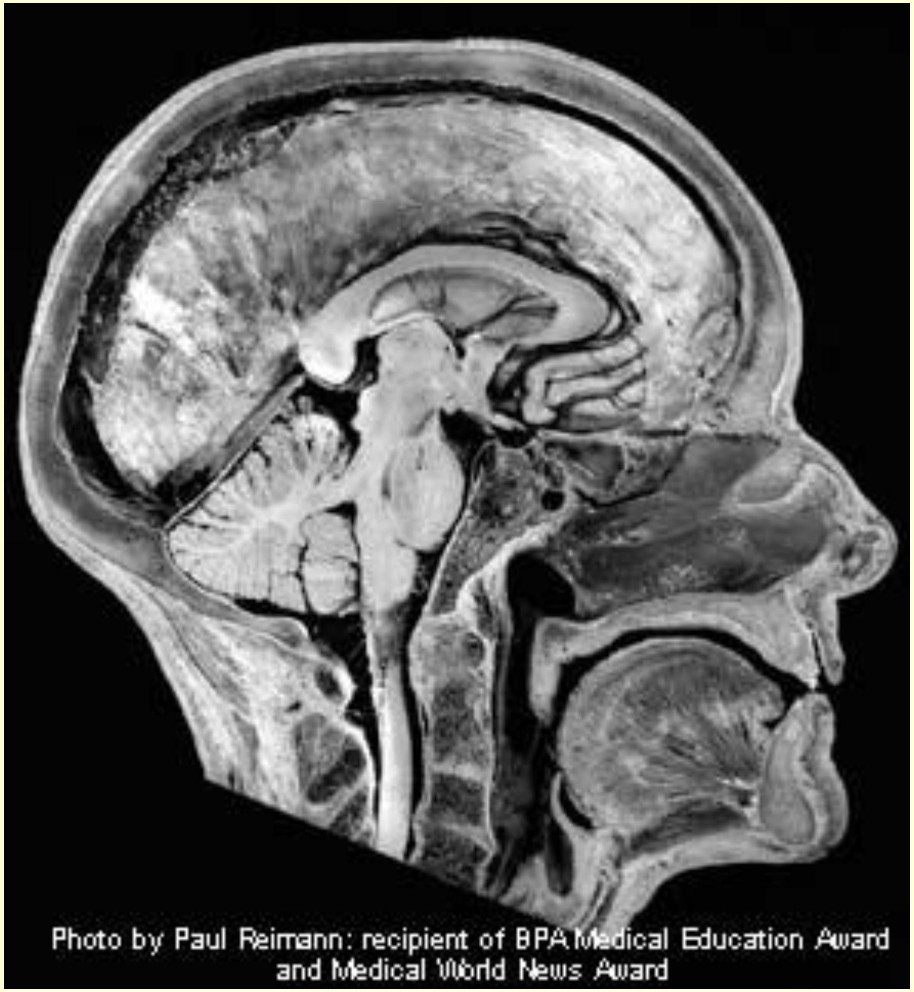

Other pairs of terms that are important to know are as follows:

Lateral - Toward the side; away from the midline
Medial - Toward the midline; away from the side

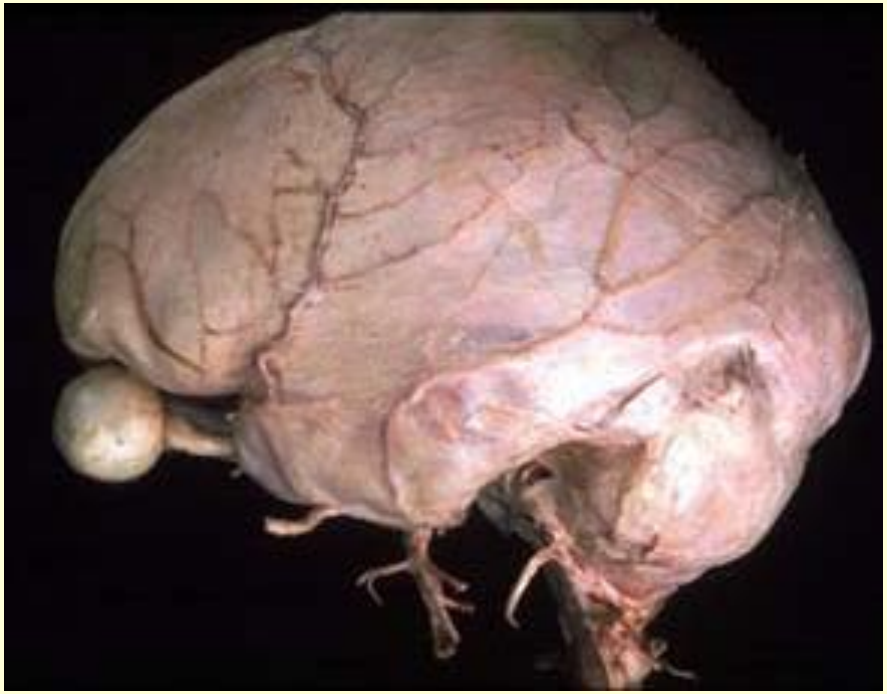
Ipsilateral - On the same side (as another structure)
Contralateral - On the opposite side

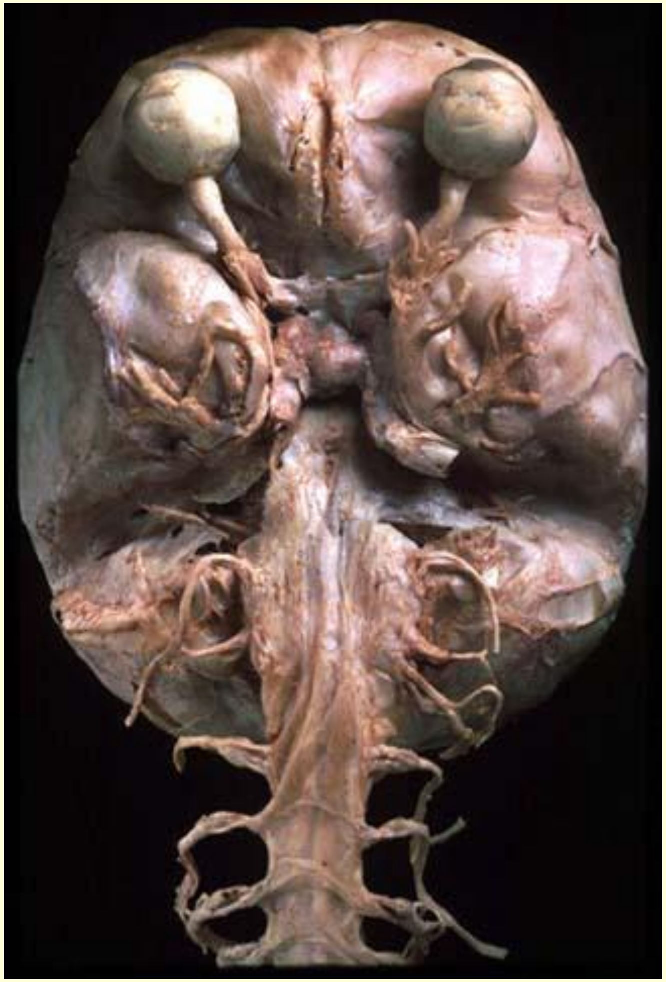


# Brain in skull

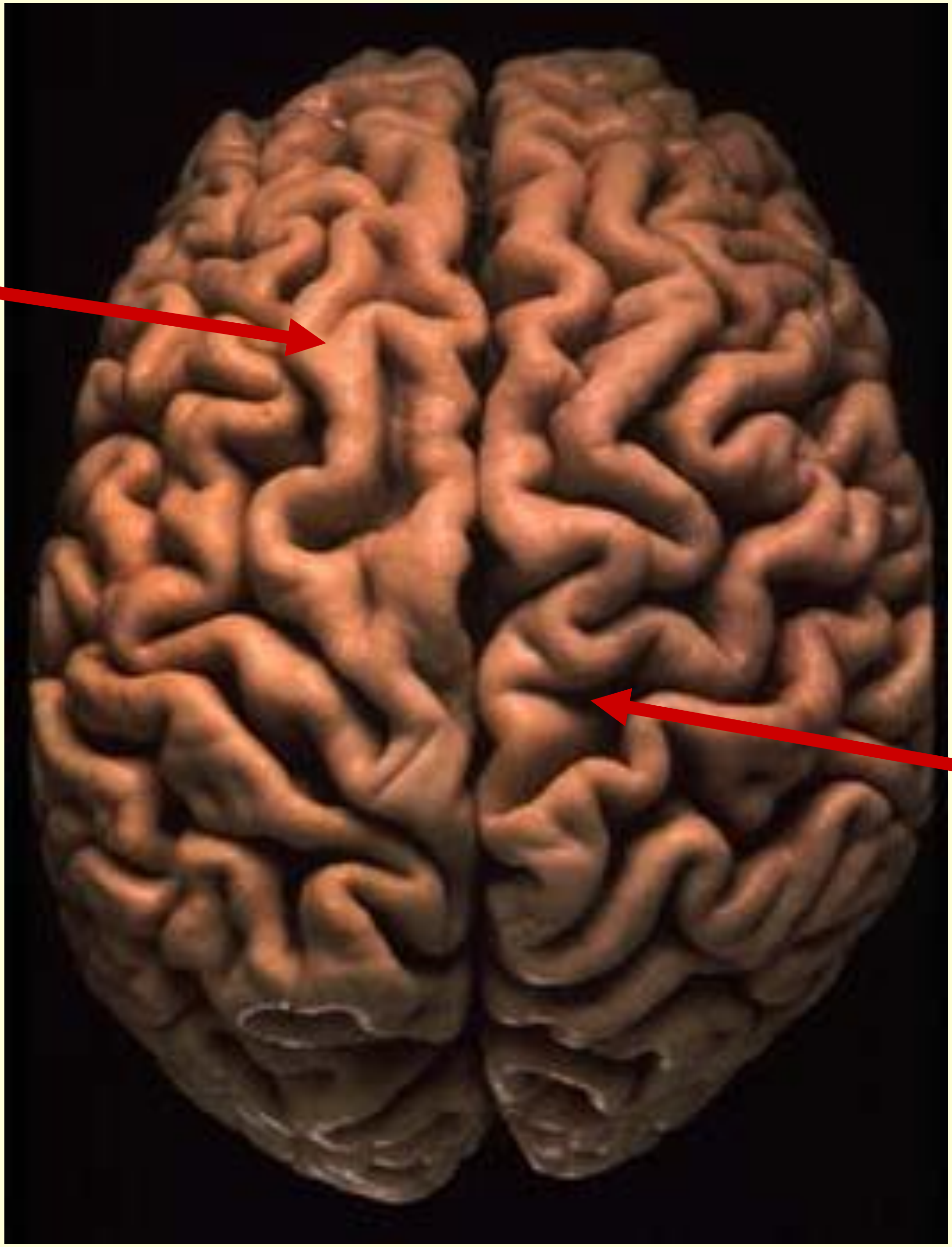


# Brain covered with dura mater



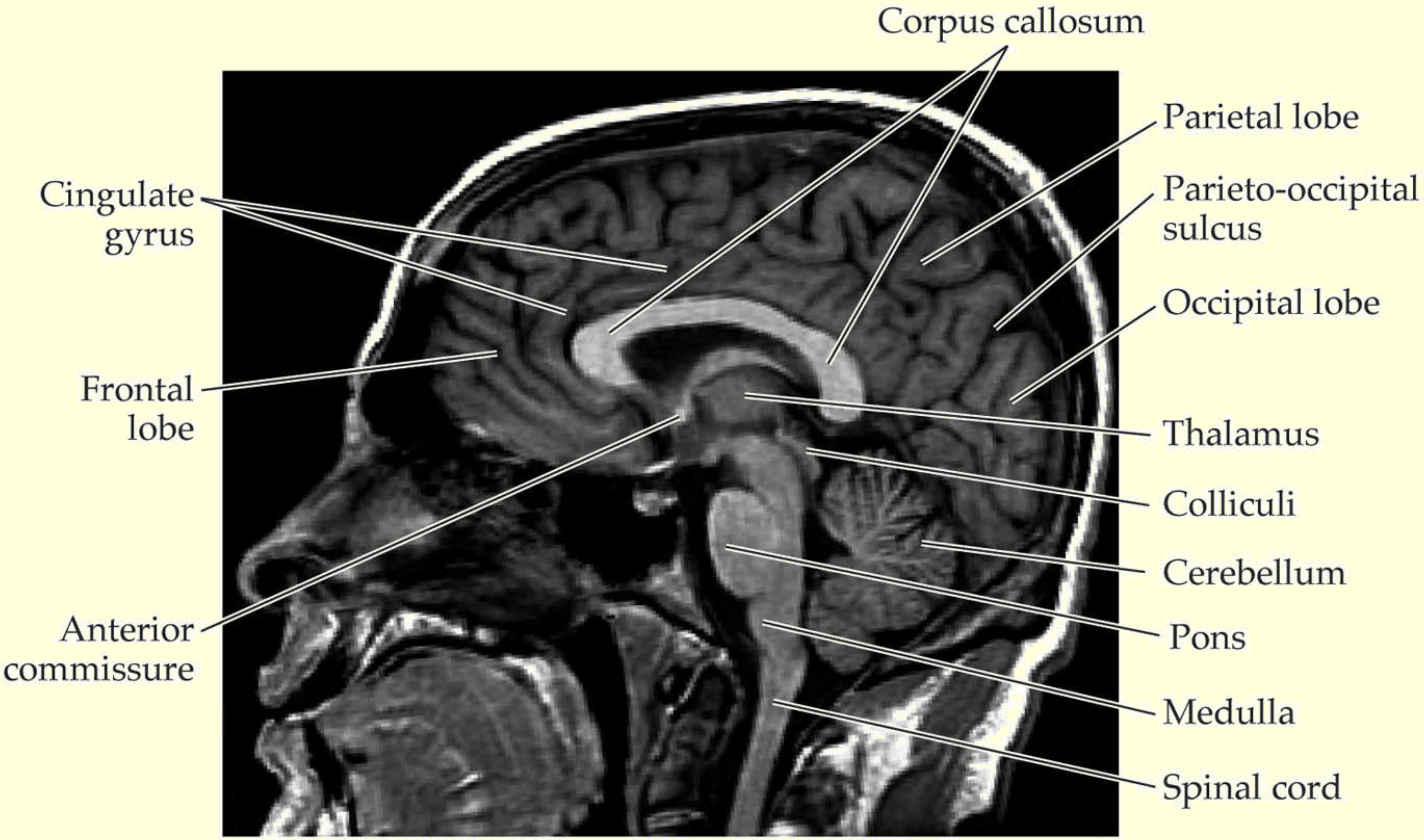


Gyri (bumps)

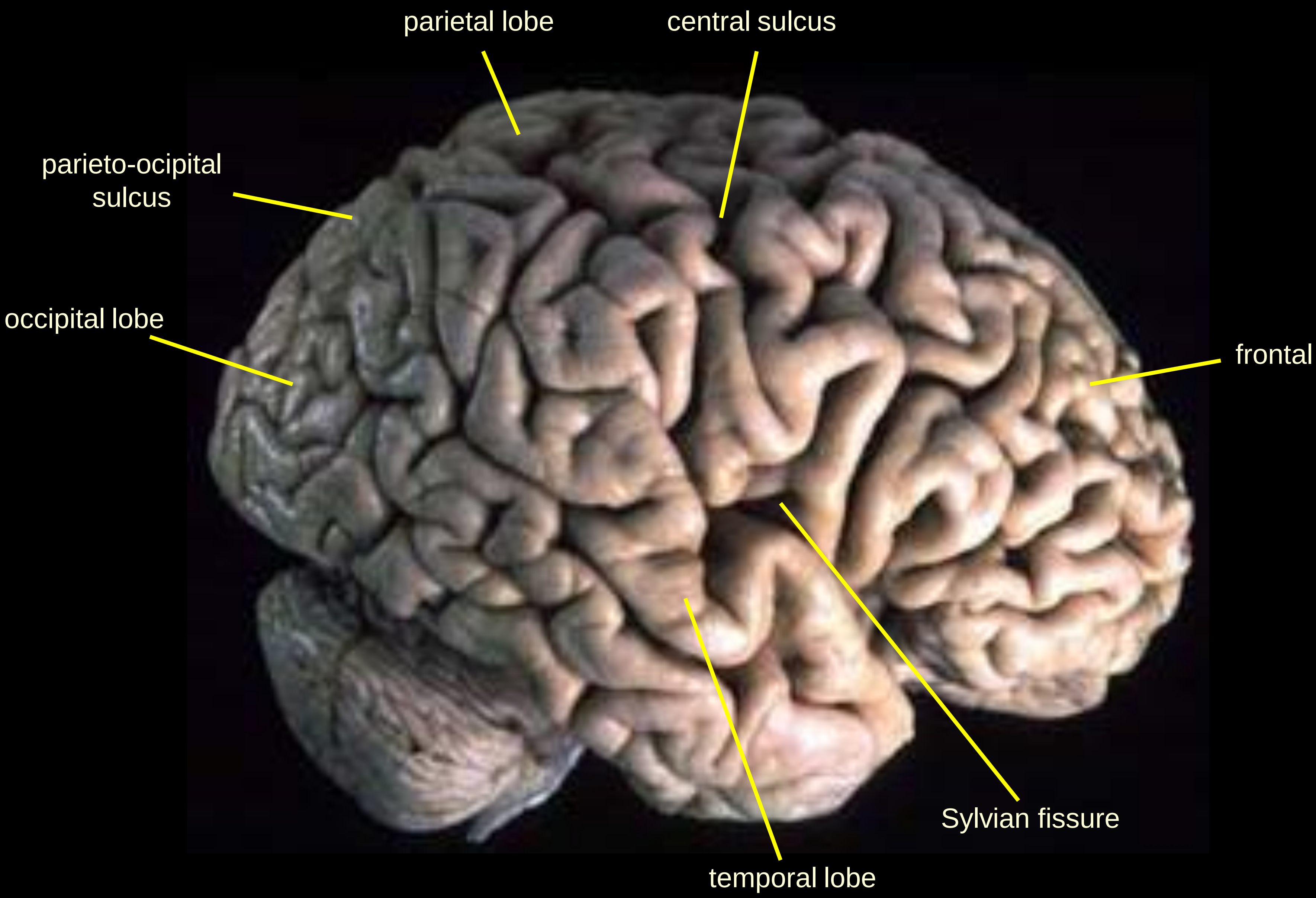


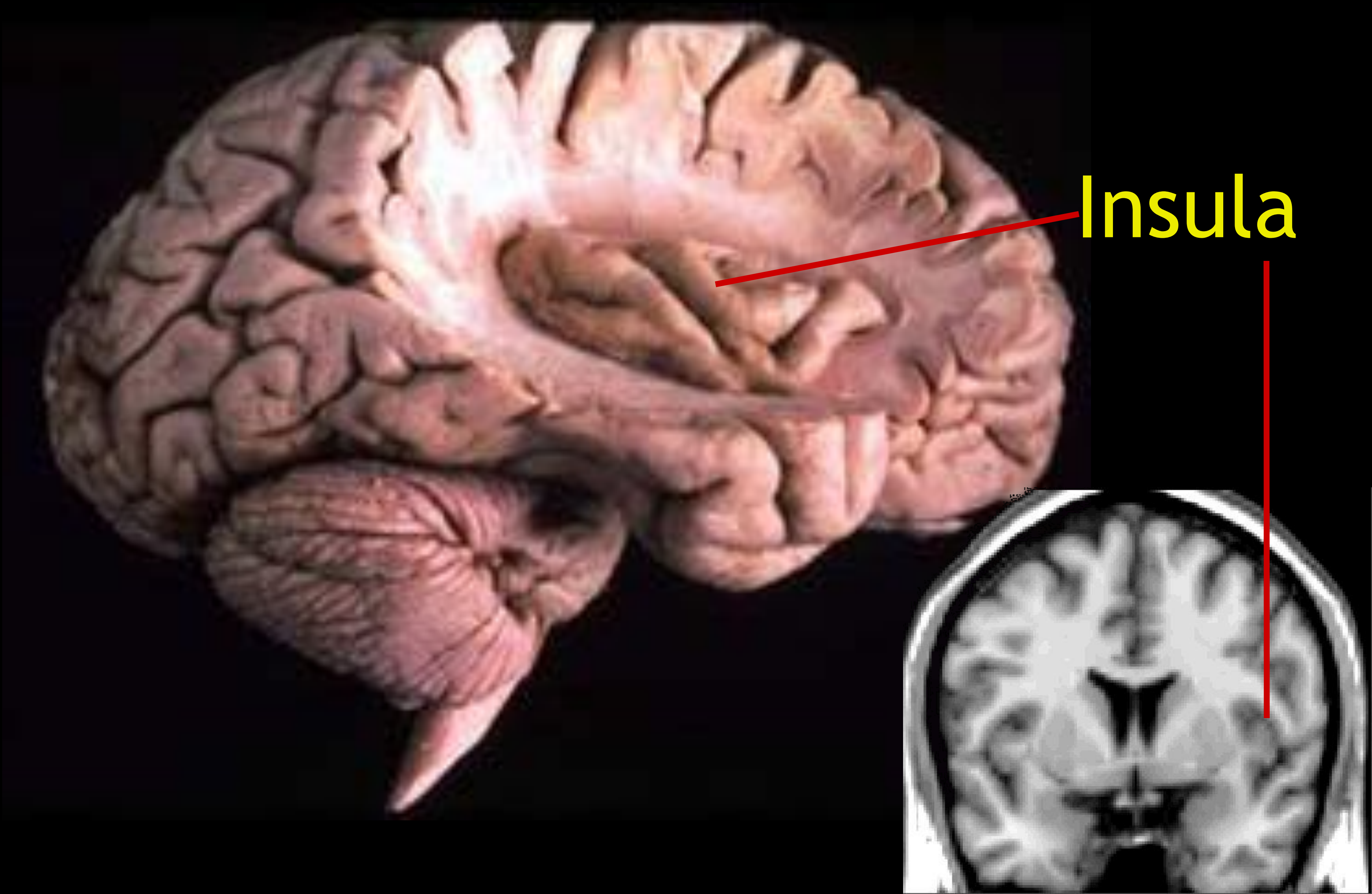
Sulci (valleys)

# A mid-sagittal MRI of the human head



# 5 lobes of the brain and demarcation point




Insula

# 3. BOLD contrast

# BOLD Endogenous Contrast

- Blood Oxyenation Level Dependent Contrast

- OxyHemoglobin is diamagnetic
  - no magnetic moment
- DeOxyHemoglobin is paramagnetic
  - Magnetic susceptibility of blood increases linearly with increasing deoxygenation

- Oxygen is extracted during passage through capillary bed
  - Brain arteries are fully oxygenated
  - Changes in levels of oxygenation are seen in capillary and venous blood.


Michele Diaz, Duke University

# So why do we see an increase in signal with neural activity?

- Blood Oxyenation Level Dependent Contrast
- Blood oxygenation depends on
  - Neural Activity
  - Metabolic Demands
  - Blood Flow
  - Blood Volume

# Signal and $O_2$ Concentration

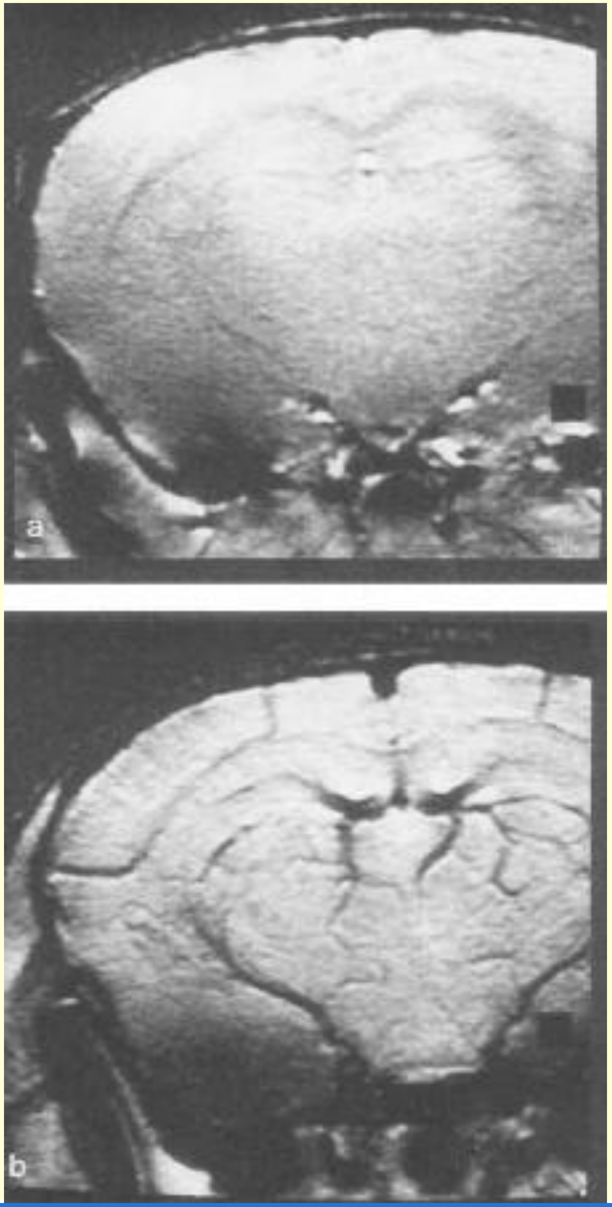
Breathing

100% $O_2$

Breathing

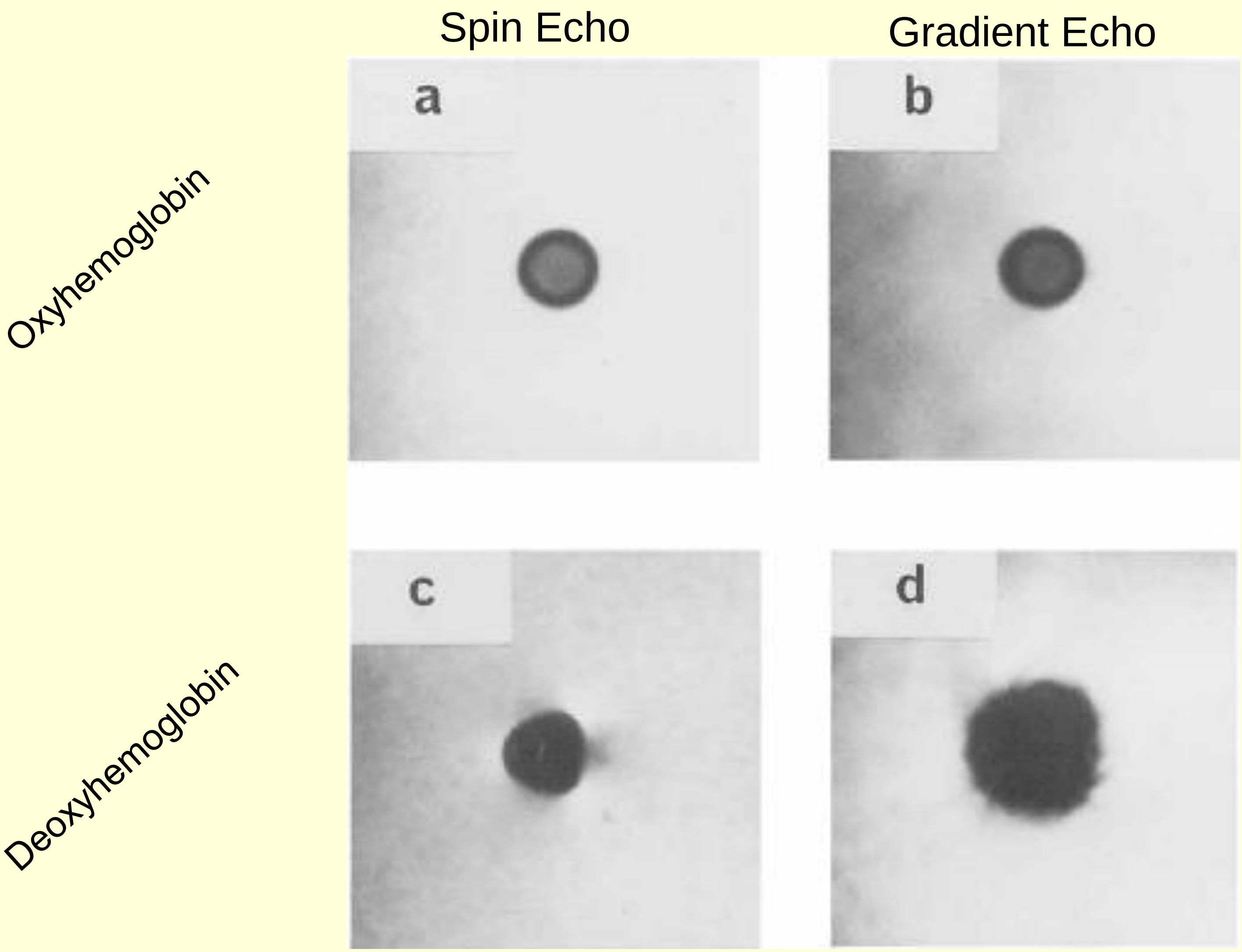
Air

~20% $O_2$



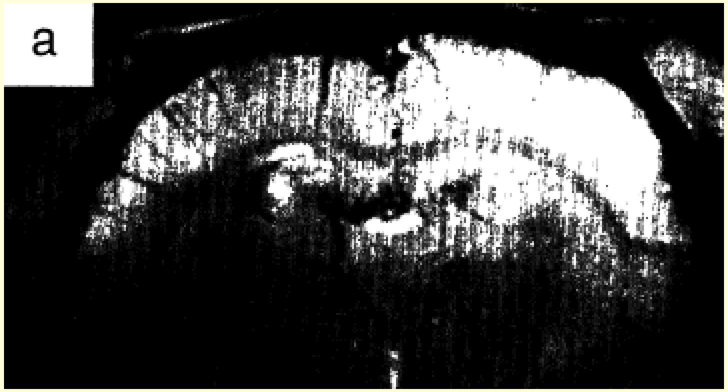

Ogawa et al., 1990a

# Pulse Sequences and $O_2$




Ogawa 1990a

# Signal and Blood Flow




100% $O_2$

Under anesthesia, rats breathing pure oxygen have some BOLD contrast (black lines).


90% $O_2$, 10% $CO_2$

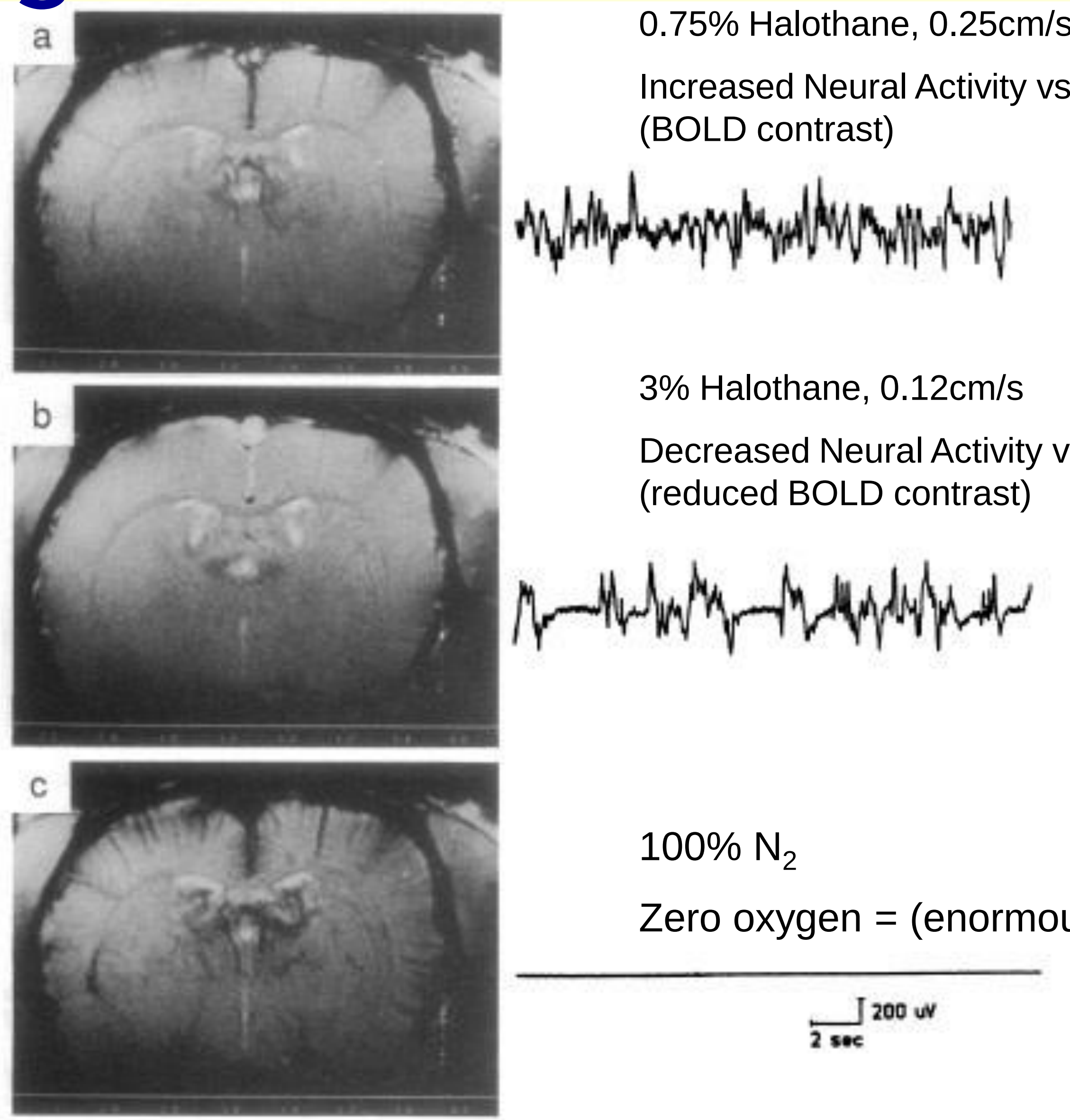
Breathing a mix including $CO_2$ results in increased blood flow, in turn increasing blood oxygenation.

Conditions have the same metabolic load (i.e., no task, under anesthesia)

Therefore, BOLD contrast is reduced.

Ogawa et al., 1990b

# Signal and Brain Activity




0.75% Halothane, 0.25cm/s

Increased Neural Activity vs. 3% Halothane = (BOLD contrast)

3% Halothane, 0.12cm/s

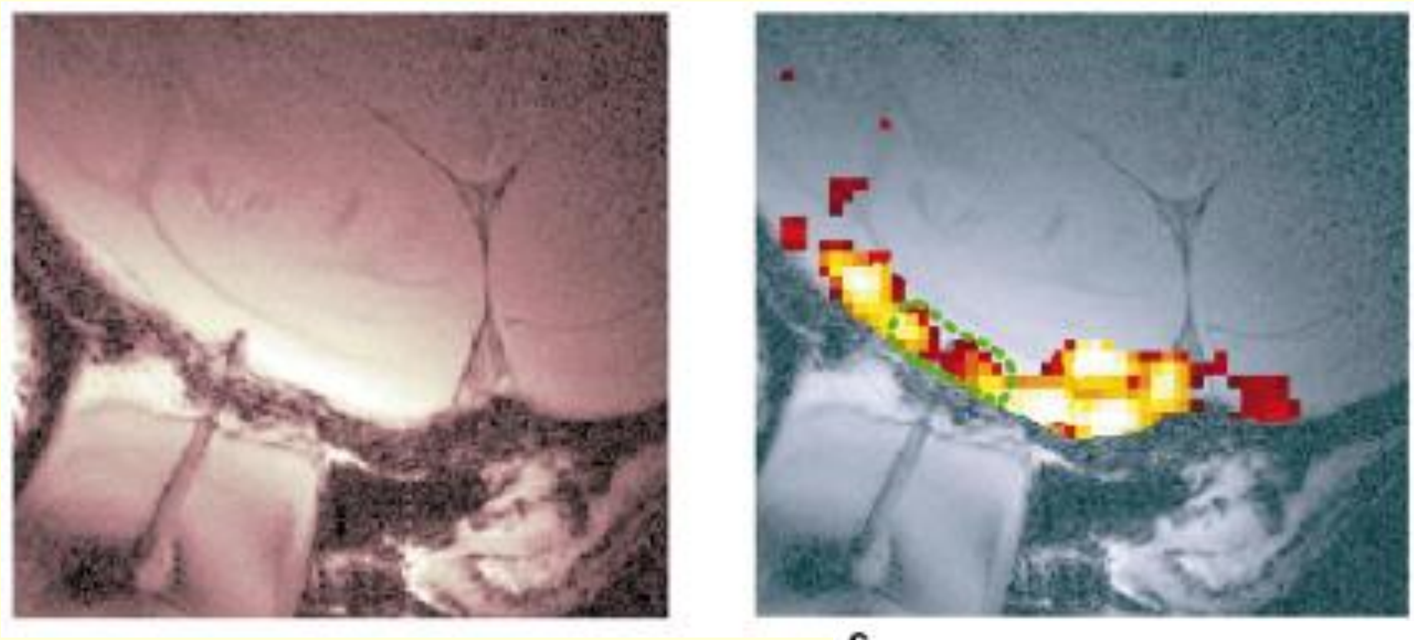
Decreased Neural Activity vs. 75% Halothane = (reduced BOLD contrast)

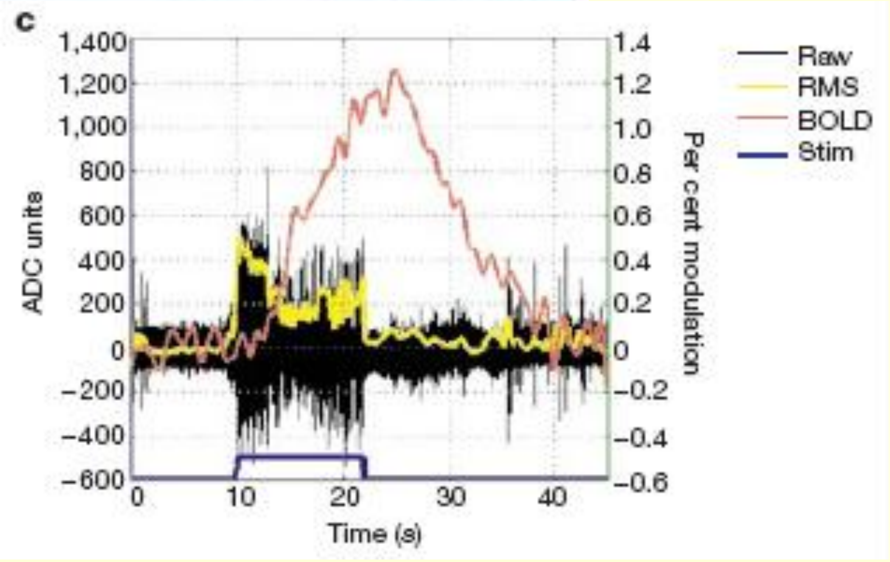
100% $N_2$

Zero oxygen = (enormous BOLD contrast)

Ogawa 1990c

# BOLD and Neuronal Activity

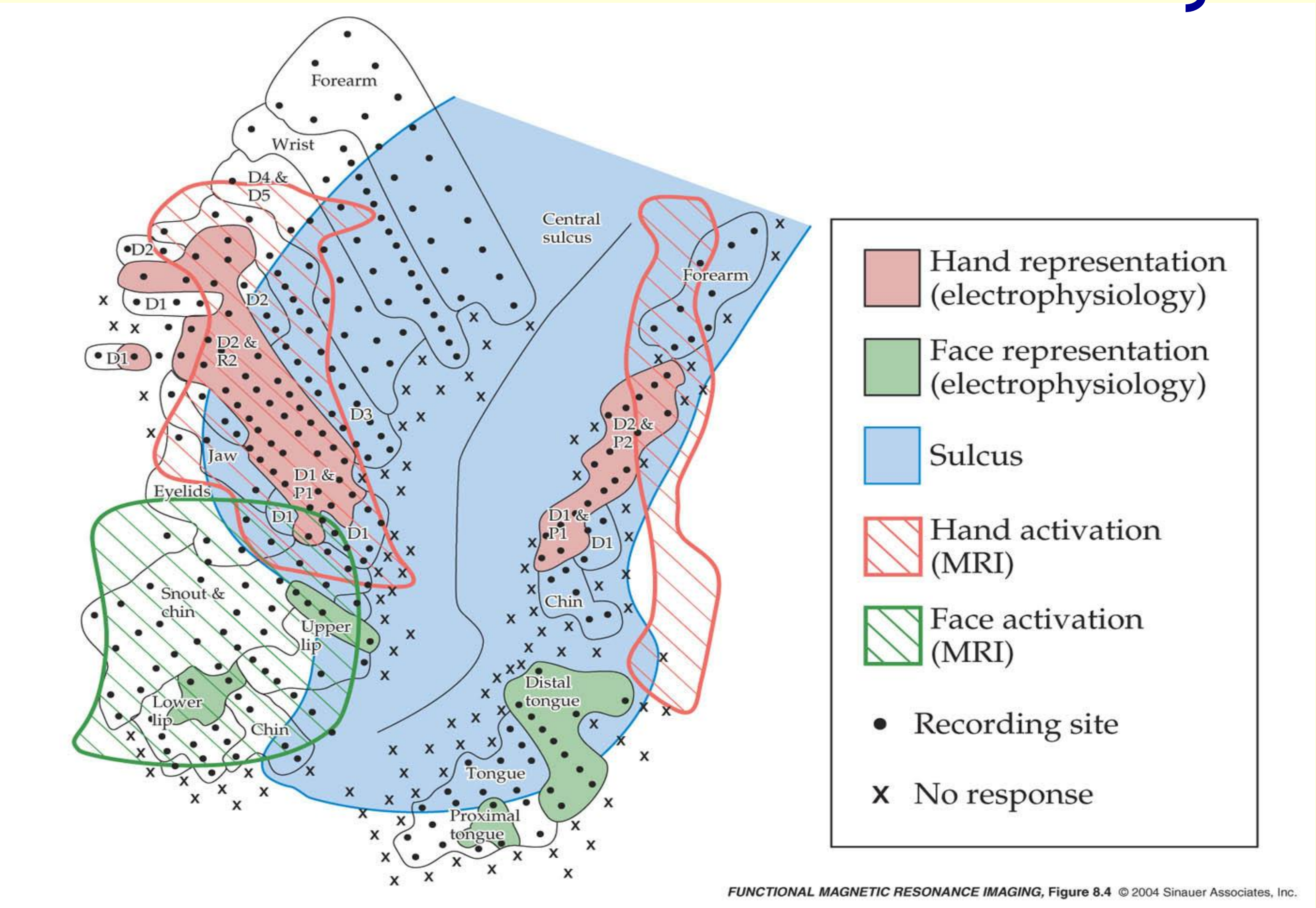





BOLD response reflects pooled local field potential activity

(Logothetis et al, 2001)

# BOLD and Neuronal Activity

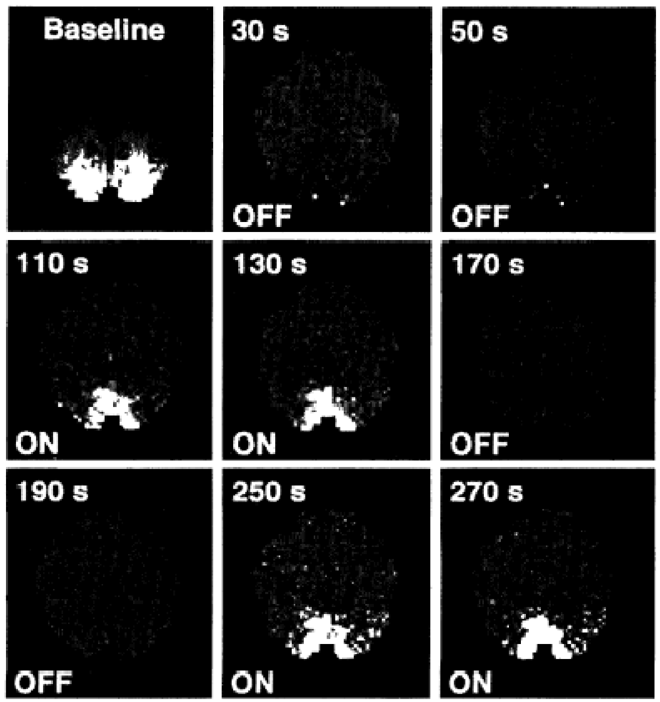



After Disbrow et al., 2000.)

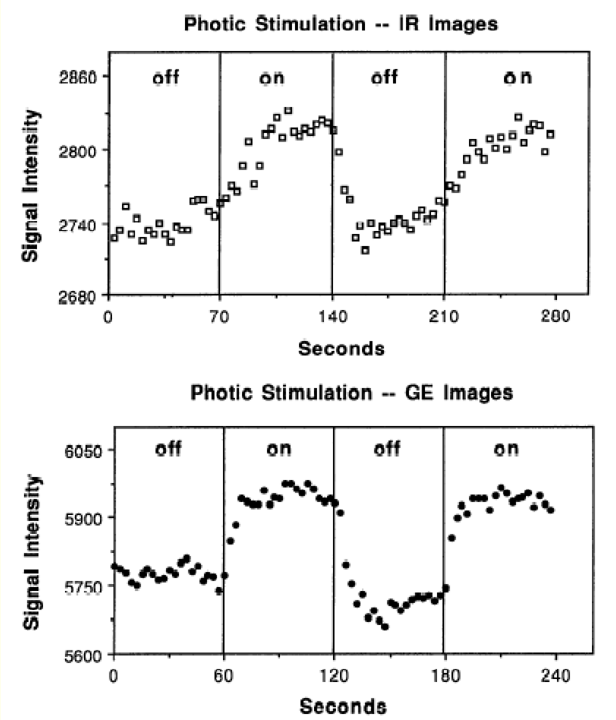
# BOLD Endogenous Contrast

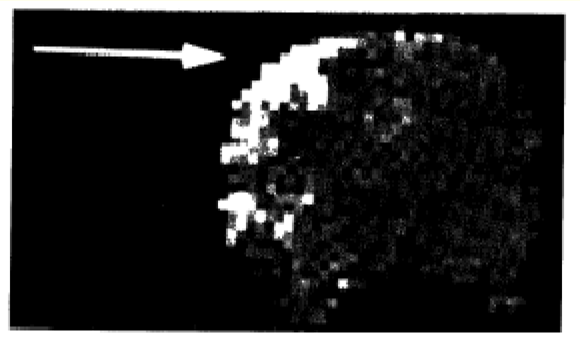
- Increasing oxygen (air vs $O_2$) increases signal (Ogawa 1990a)
- Deoxygenated Hgb distorts/reduces signal, especially on GRE images (Ogawa, 1990a)
- Increasing blood flow, increases signal (Ogawa 1990b).
- Increasing neuronal activity increases signal (Ogawa, 1990c).

# Kwong et al., 1992

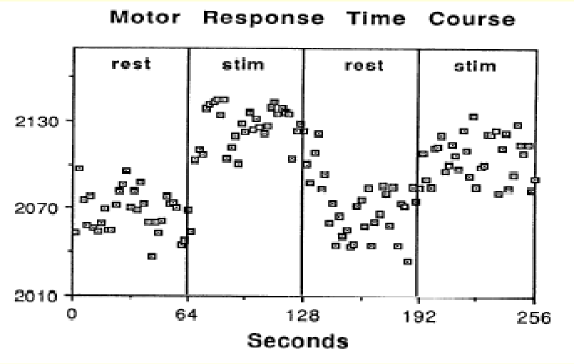



← VISUAL →

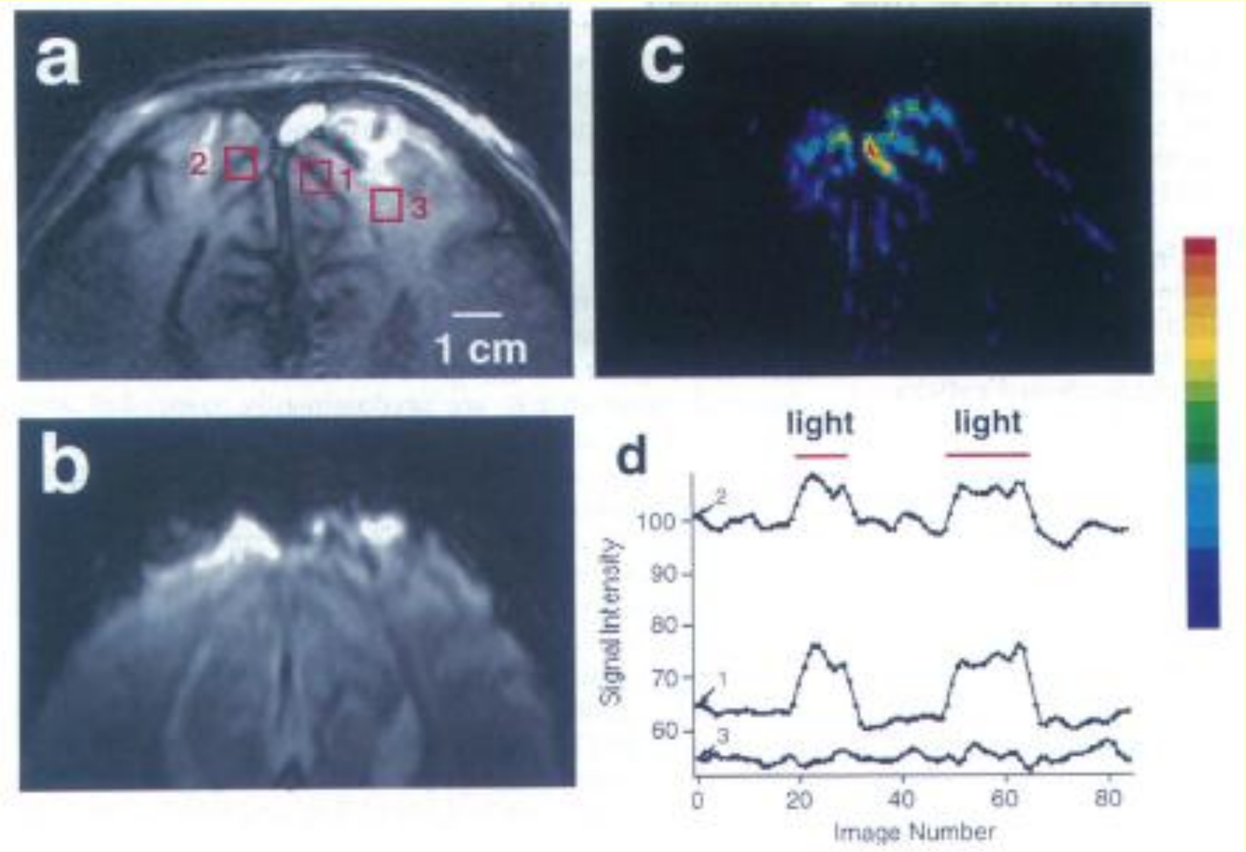


← MOTOR →



# Ogawa et al., 1992

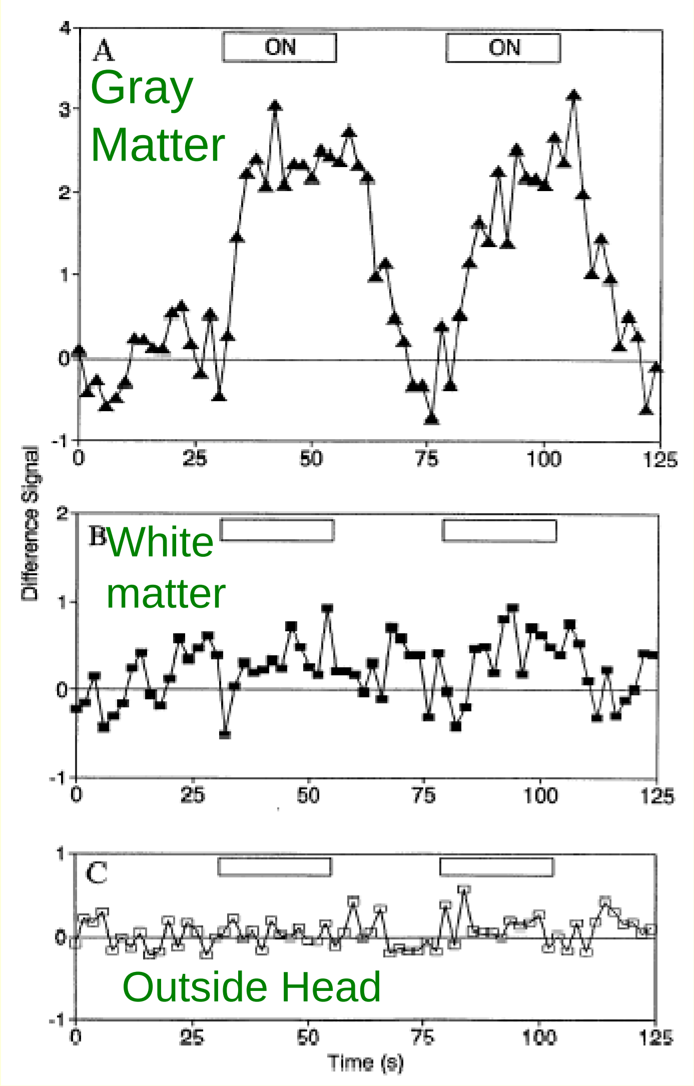



- High-field (4T) in humans
- Patterned visual stimulation at 10 Hz
- Significant image intensity changes in visual cortex

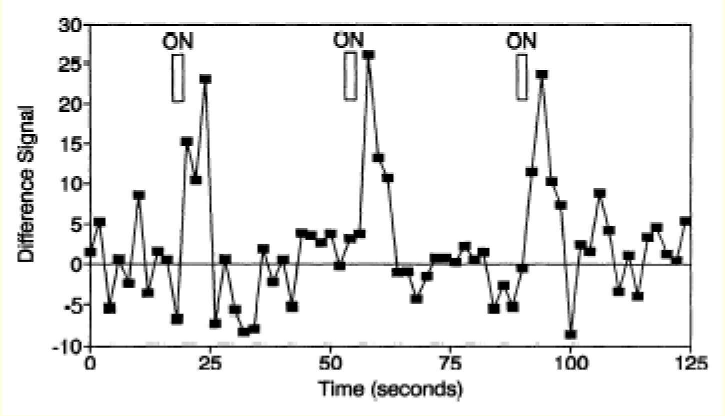
# Blamire et al., 1992

This was the first event-related fMRI study. It used both blocks and pulses of visual stimulation.

Hemodynamic response to long stimulus durations.

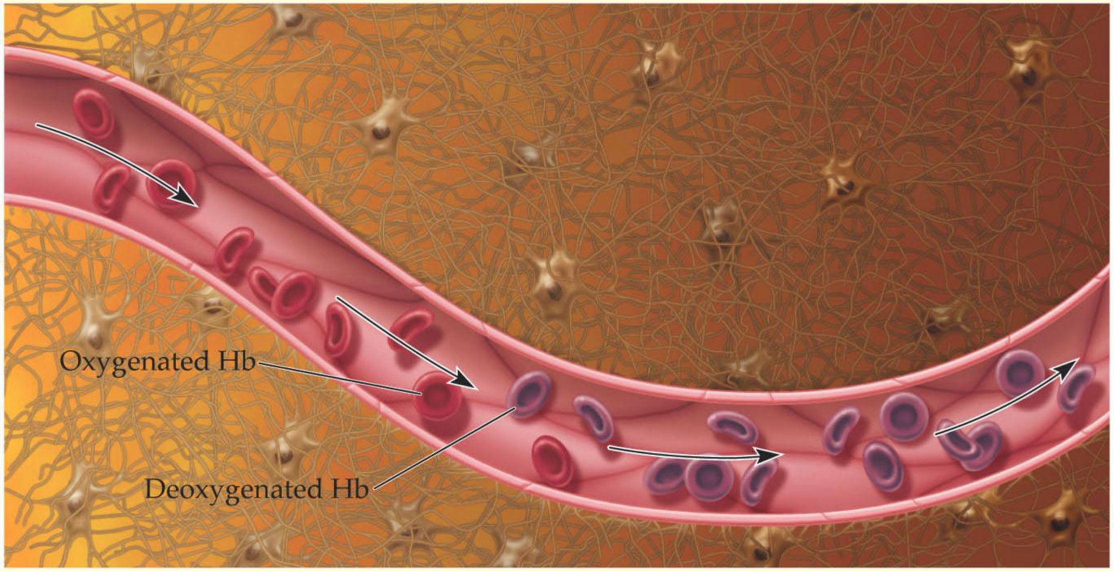



Hemodynamic response to short stimulus durations.



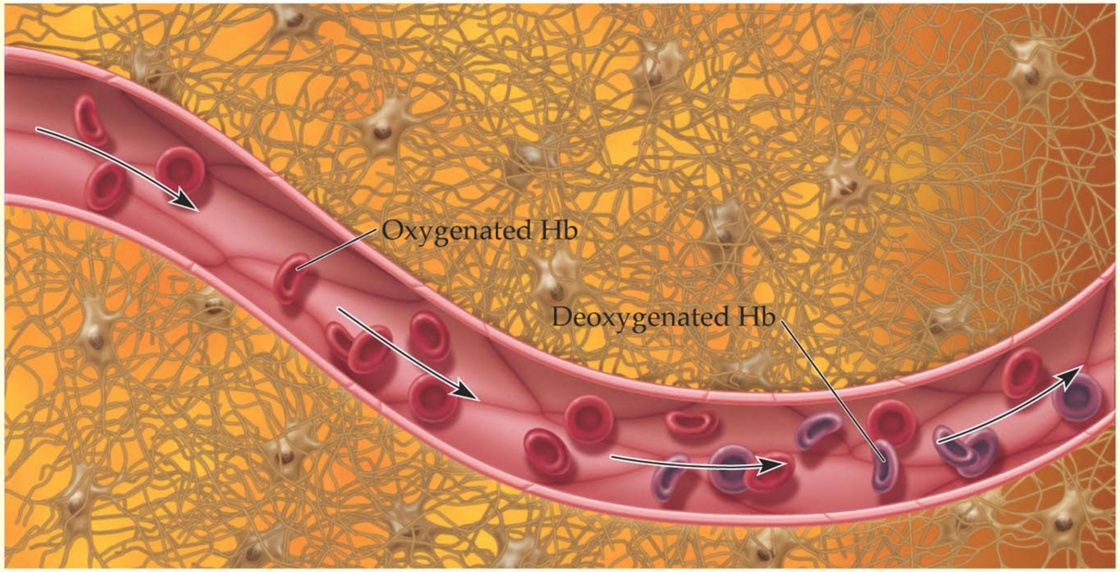
# A typical ~~The~~ Hemodynamic Response

Under normal conditions, oxygen is extracted from red blood cells within the capillaries.

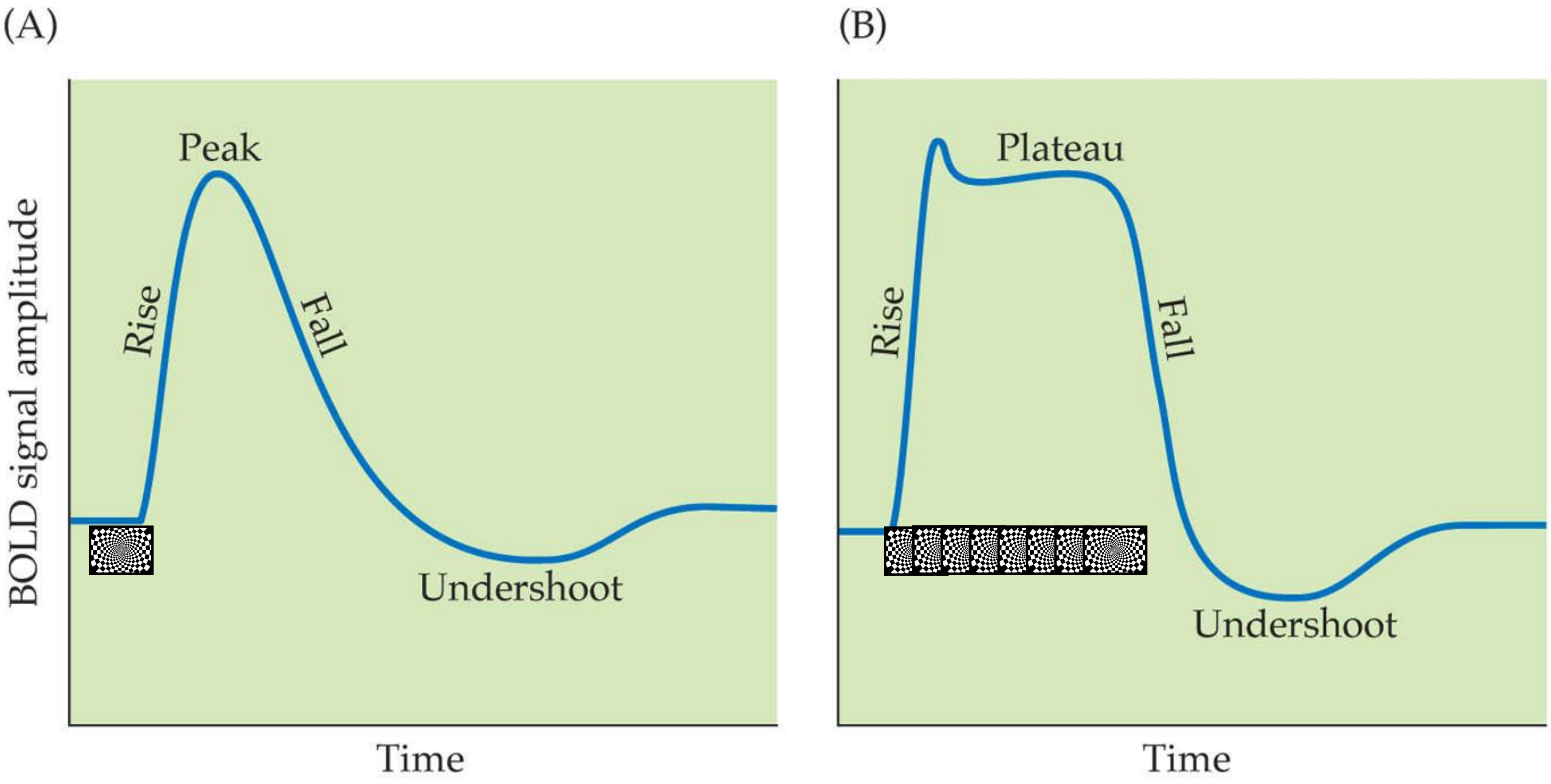



But when neurons are active, more oxygenated blood is supplied than needed.

This reduces the local quantity of deoxygenated hemoglobin.



# Basic Form of Hemodynamic Response




FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 7.15 © 2004 Sinauer Associates, Inc.

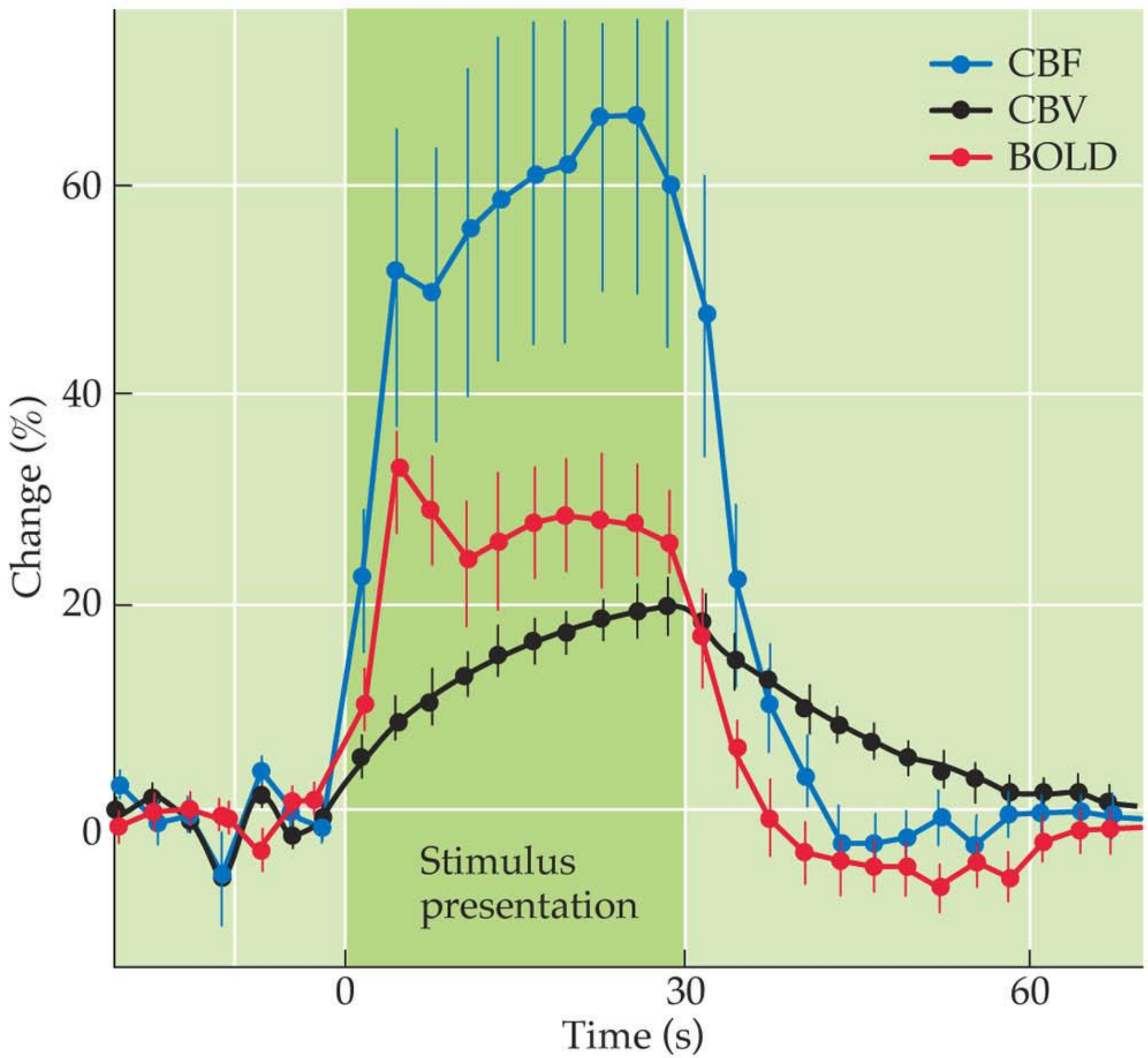
# Relationship between Deoxyhemoglobin & signal

- $T_2$* measurements are related to field inhomogeneity effects

- Deoxyhemoglobin causes field inhomogeneity and loss of signal

- The difference in $T_2$* signal is a function of the amount of deoxyhemoglobin.

- Highly oxygenated blood will have more $T_2$* signal compared to less oxygenated blood.

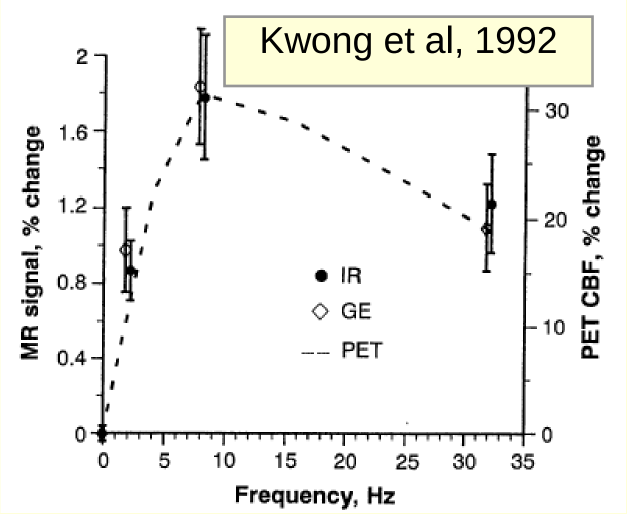

CBF
CBV
BOLD
60
40
20
0
Change (%)
Stimulus
presentation
0
30
60
Time (s)

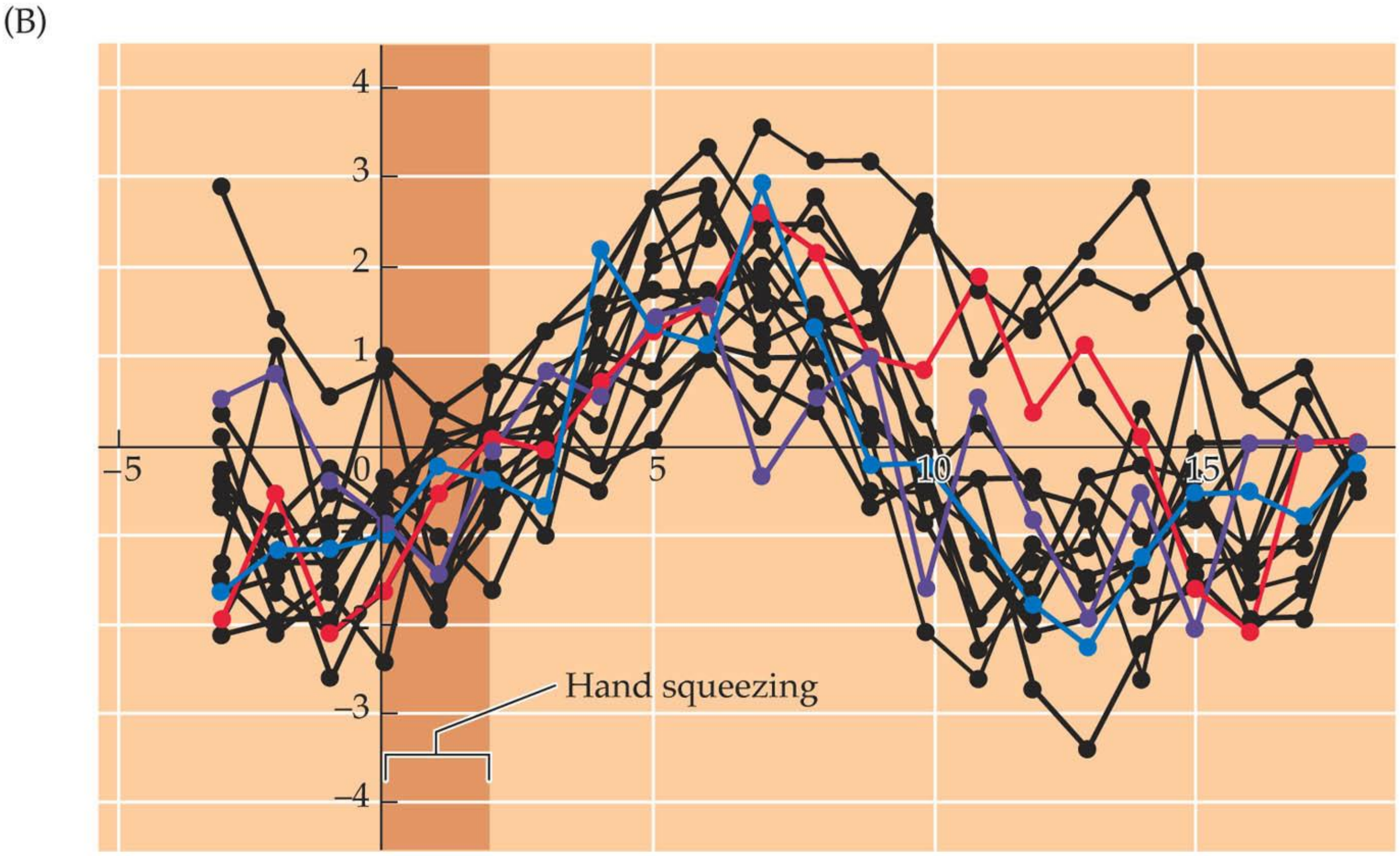
# Why does the hemodynamic response matter?

- Delay in the hemodynamic response (HDR)
  - Hemodynamic activity lags neuronal activity
- Amplitude of the HDR
- Variability in the HDR
- Linearity of the HDR
- HDR as a relative measure

# Amplitude of the HDR

- Peak signal change dependent on:
  - Brain region
  - Task parameters →
  - Voxel size
  - Field Strength



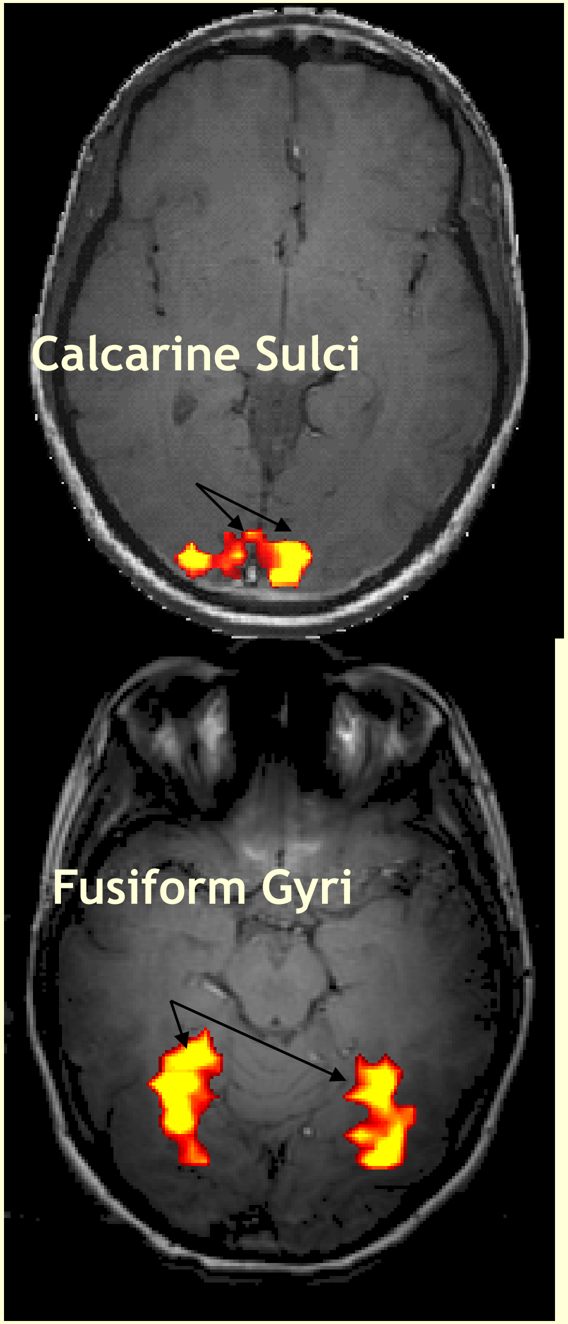


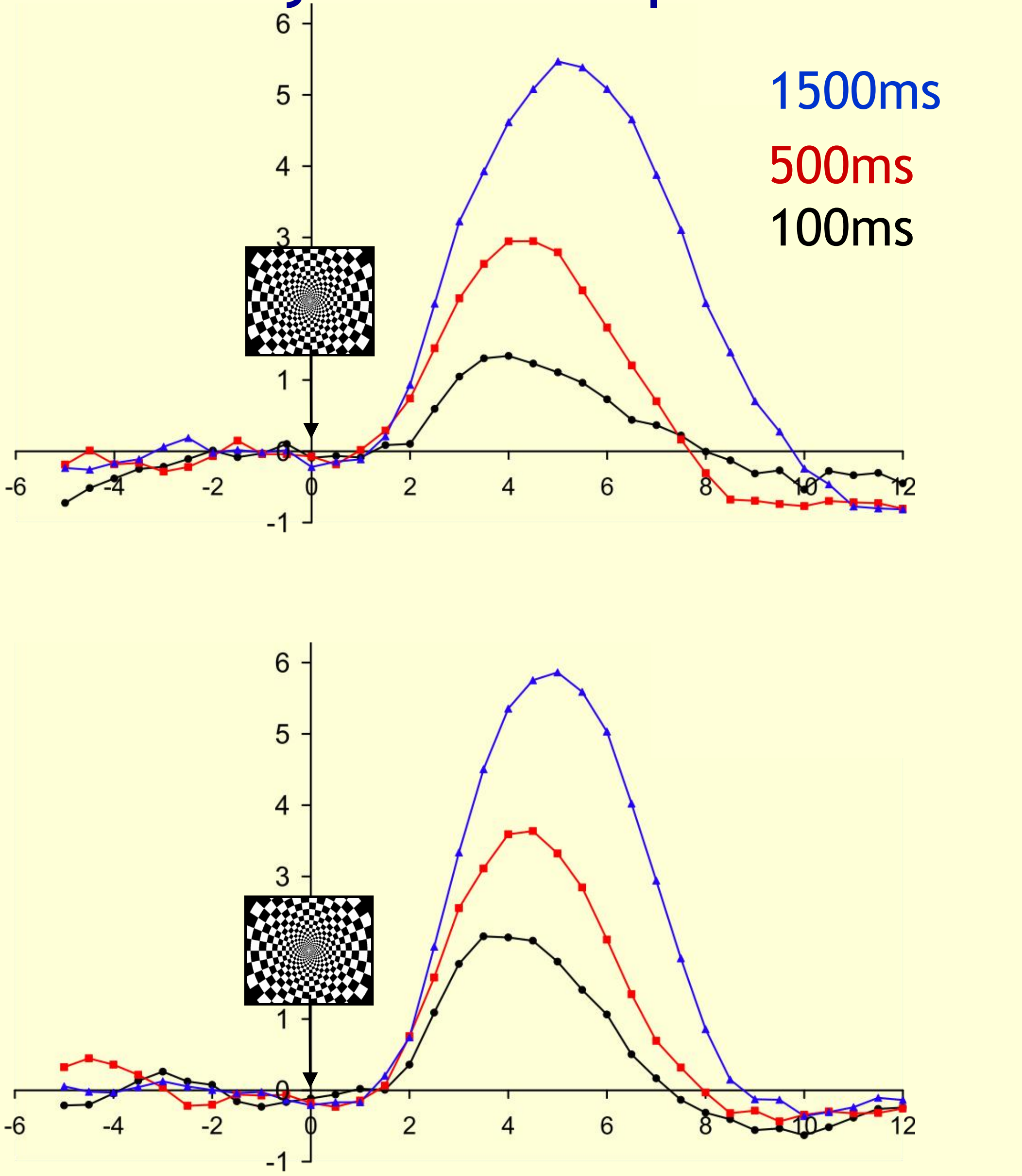

FUNCTIONAL MAGNETIC RESONANCE IMAGING, Figure 7.17 (Part 2) © 2004 Sinauer Associates, Inc.

# Relative vs. Absolute Measures

- fMRI provides <u>relative</u> change over time
  - Signal measured in “arbitrary MR units”
  - Percent signal change over baseline

# Example of Scaling of the Hemodynamic Response

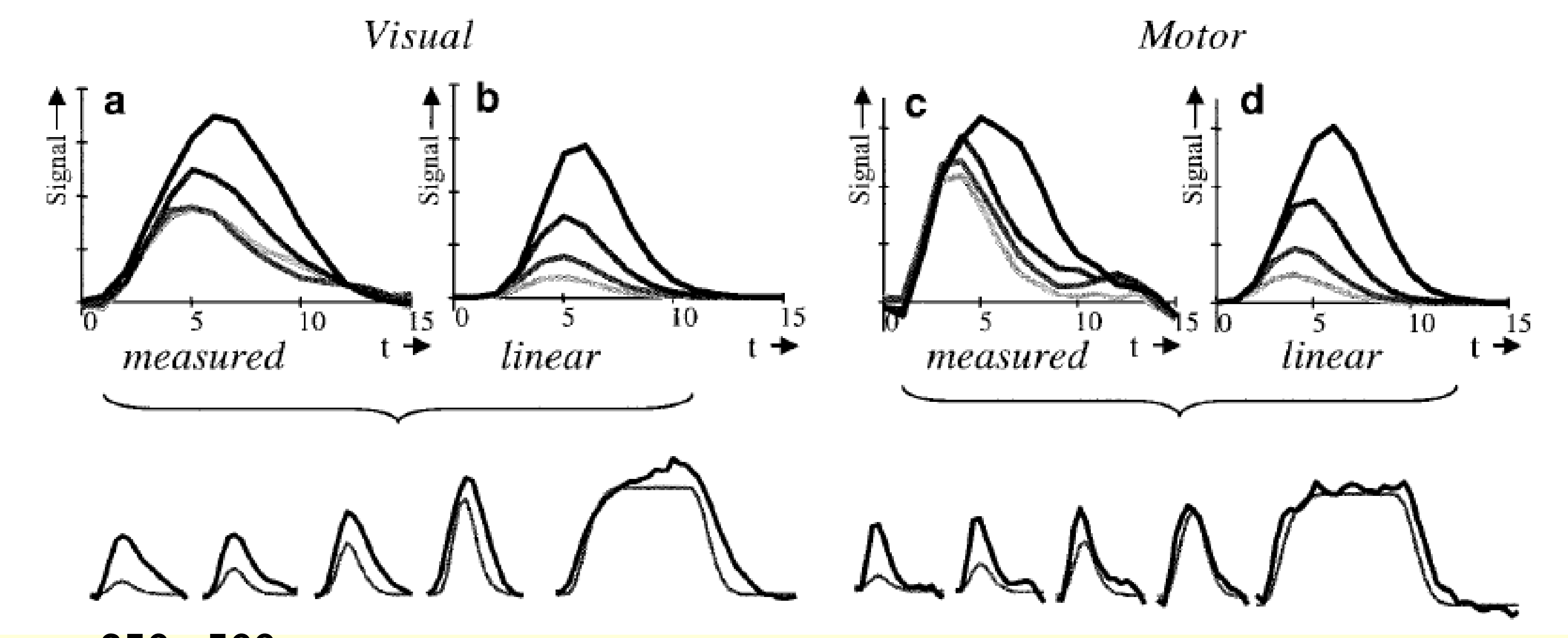


# Effects of Stimulus Duration

- Short stimulus durations evoke BOLD responses
  - Amplitude of BOLD response often depends on duration
  - Stimuli < 100ms evoke measurable BOLD responses
- Form of response changes with duration
  - Latency to peak increases with increasing duration
  - Onset of rise does not change with duration
  - Rate of rise increases with duration
- Key issue: deconfounding duration of stimulus with duration of neuronal activity

# Linearity (?) of the BOLD response



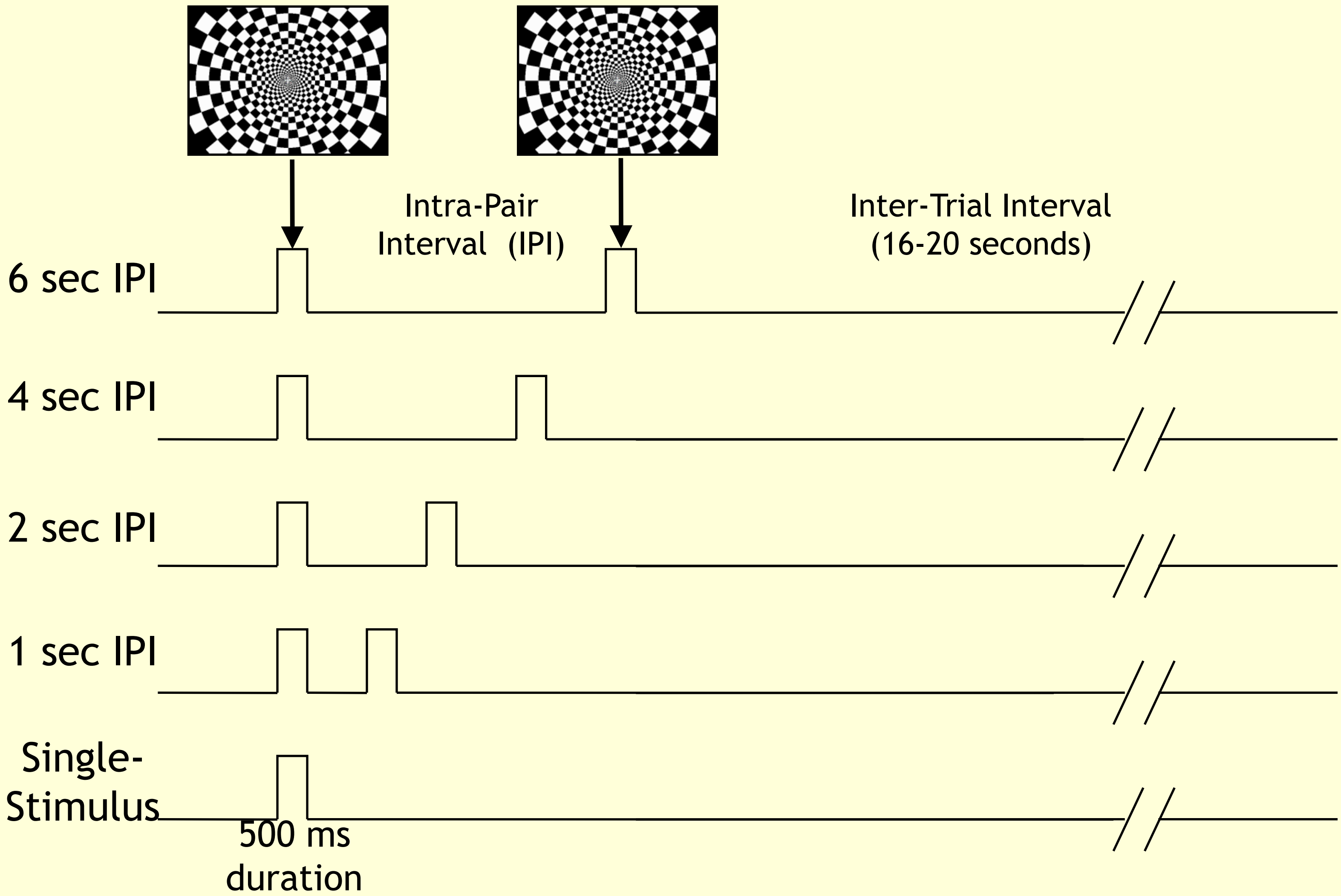

250 ms | 500 ms | 1s | 2s | 20s | 250 ms | 500 ms | 1s | 2s | 20s

Birn, et al, 2001

# Caveat: Stimulus Duration ≠ Neuronal Activity Duration

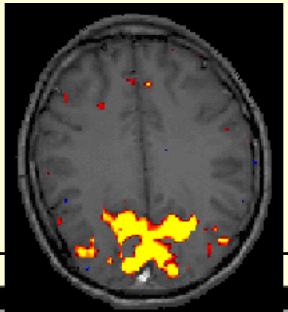
# Refractory Periods

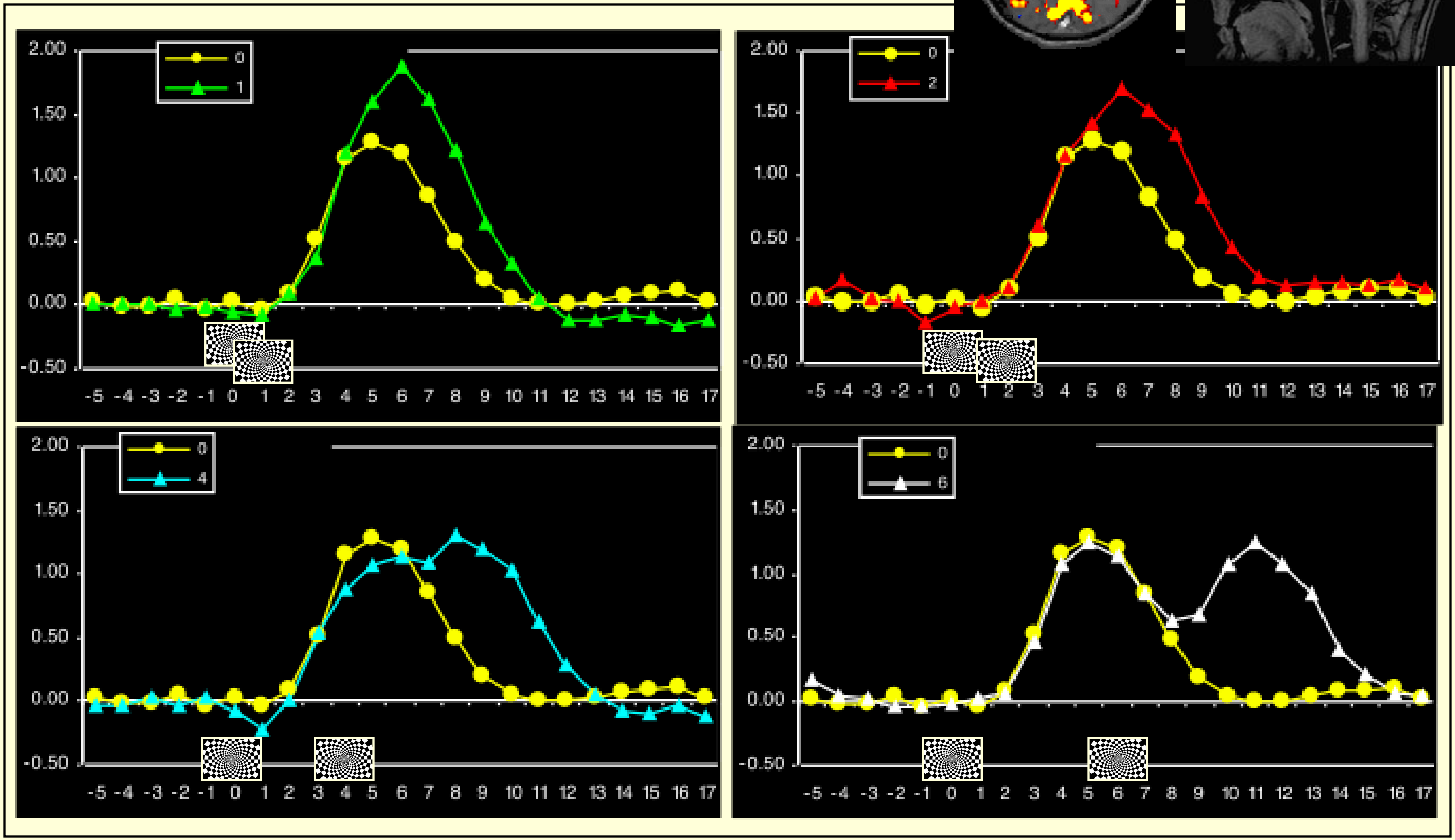
- Definition: a change in the responsiveness to an event based upon the presence or absence of a similar preceding event
  - Neuronal refractory period
  - Vascular refractory period



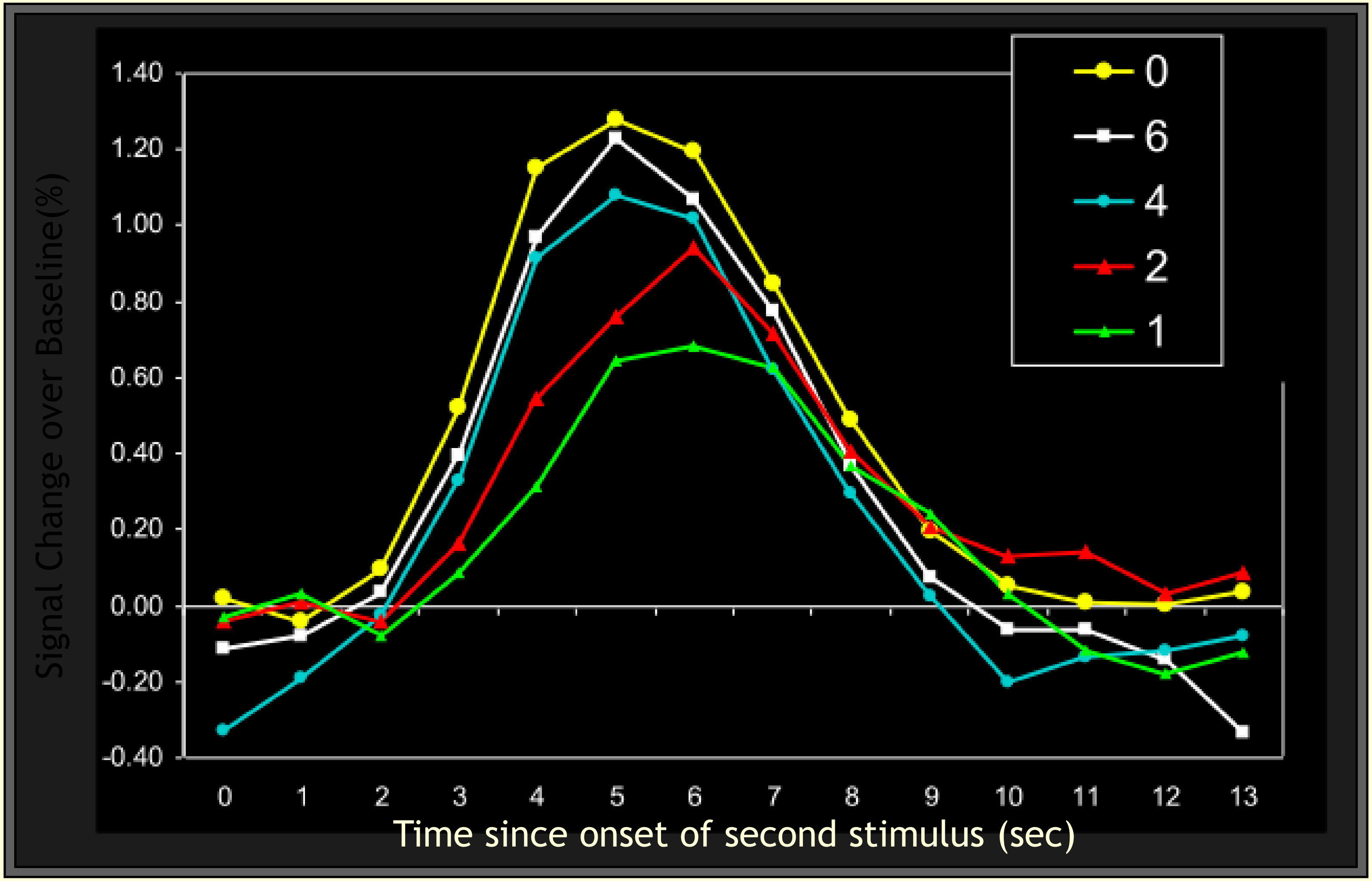

Huettel & McCarthy, 2000

# Hemodynamic Responses to Closely Spaced Stimuli





# “Rough Linearity”



# 4. Signal and Noise

# What is signal? What is noise?

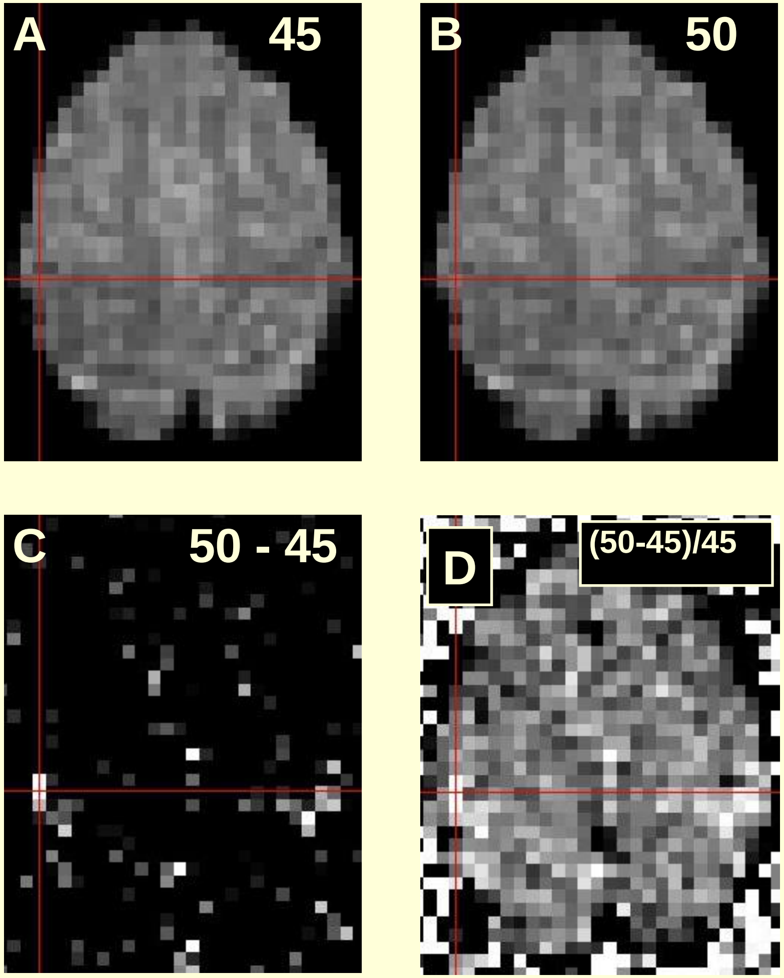
- Signal, literally: Amount of current in receiver coil
- Signal, practically: Task-related variability

- Noise, literally and practically: Non-task-related variability

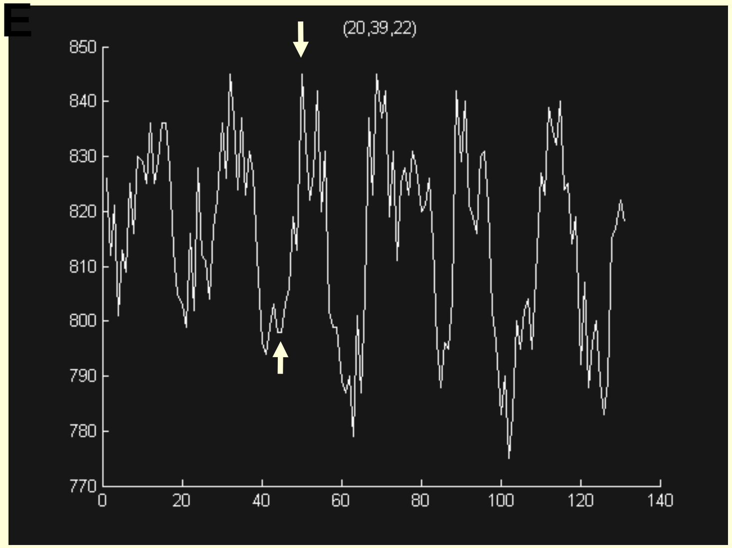
- How can we control the amount of signal?
  - Experimental task timing: efficient design
  - Scanner properties (e.g., field strength)
  - Subject compliance with task: through training

- How can we reduce the noise?
  - Choose good pulse sequences and have stable scanner
  - Minimize head motion, to some degree, with restrictors
  - Effectively *preprocess* our data

# Signal Size in fMRI




Let's look at two TRs (#s 45 and 50) of one dataset.



# Signal-Noise-Ratio (SNR)

**Task-Related Variability**

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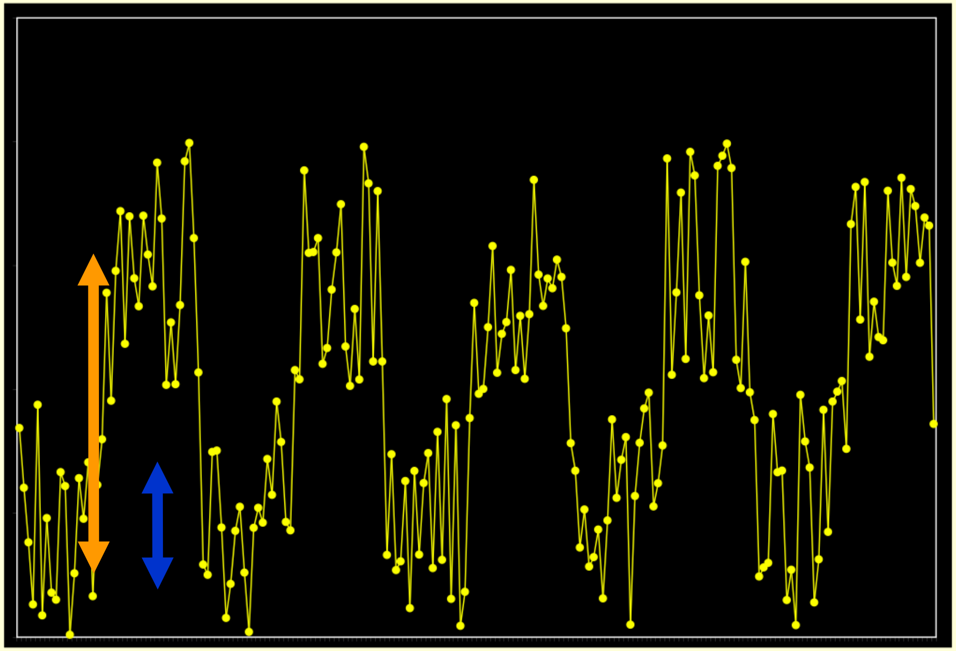
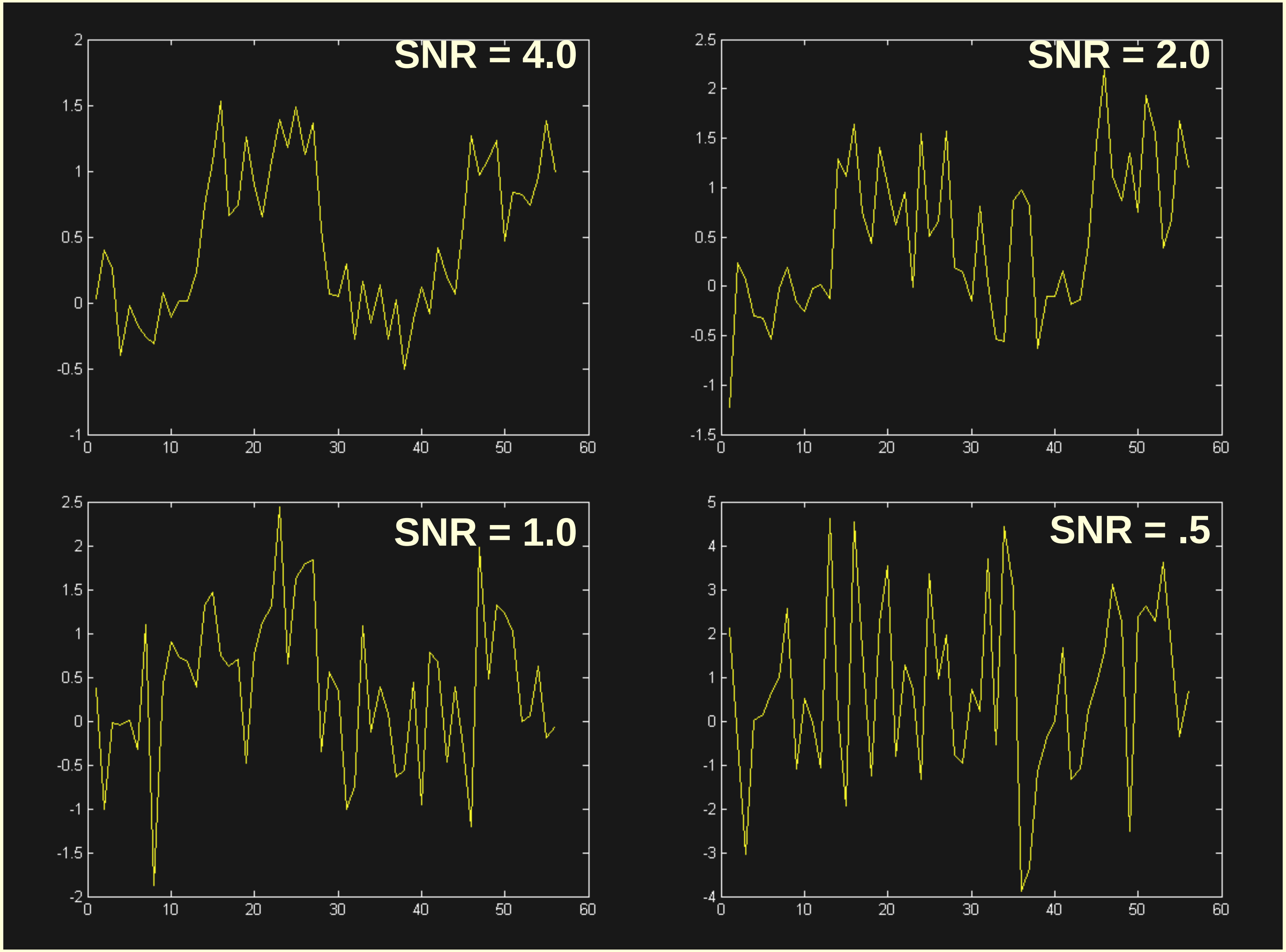
**Non-task-related Variability**

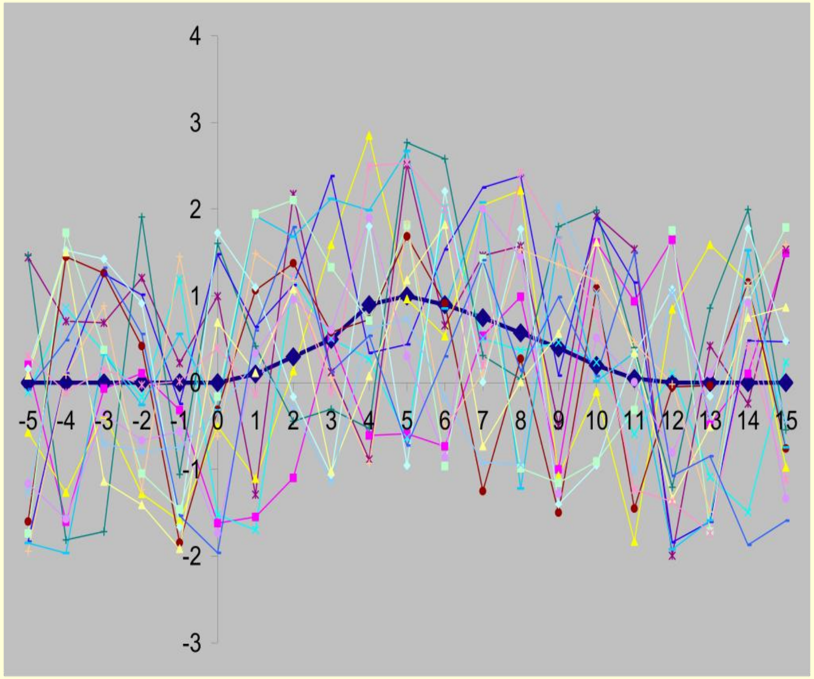


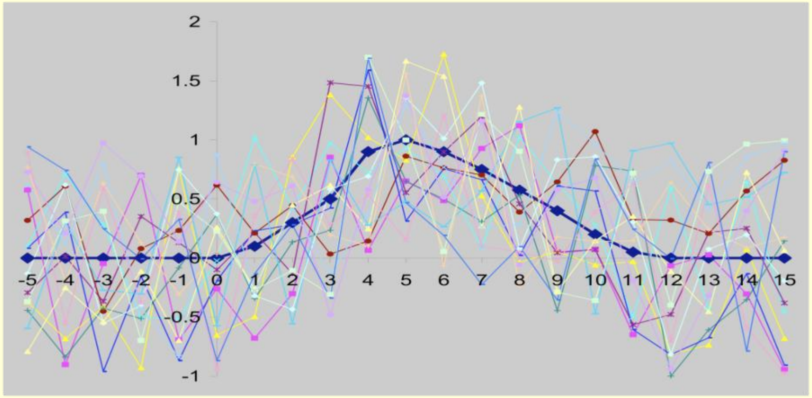

SNR = 4.0
SNR = 2.0
SNR = 1.0
SNR = .5
0
10
20
30
40
50
60

# What are typical SNRs for fMRI data?

- Signal amplitude
  - Percent signal change: 0.2-2%
- Noise amplitude
  - Percent signal change: 0.5-5%
- SNR range
  - Total range: <0.1 to 4.0
  - Typical: 0.2 – 0.5

# Typical SNRs for fMRI studies




SNR = 0.25

SNR = 0.5

# Types of Noise

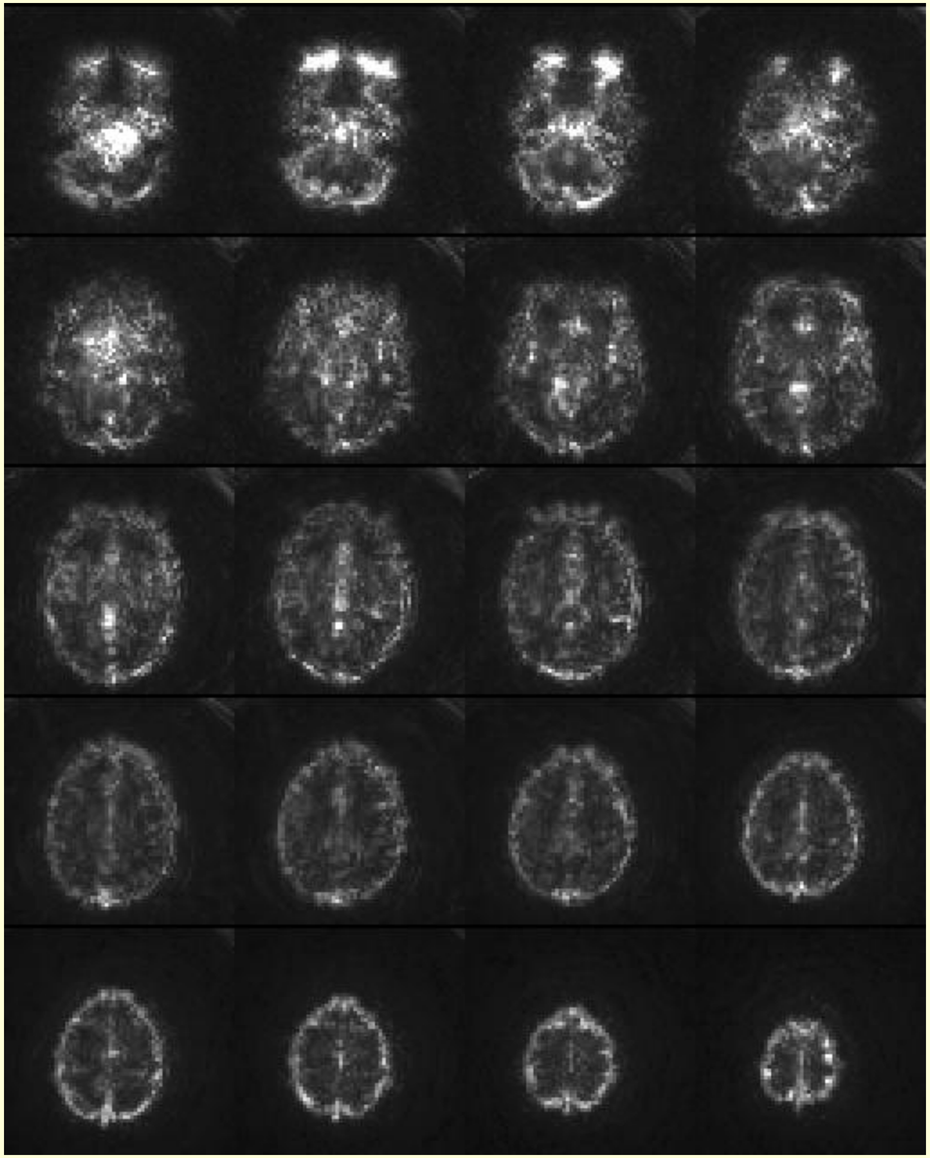
- Thermal noise
  - Responsible for variation in background of image
  - Eddy currents, scanner heating
- Power fluctuations
  - Typically caused by scanner problems
- Artifact-induced problems
- Variation in subject cognition
  - Timing of processes

- Head motion

- Physiological fluctuations
  - Respiration
  - Cardiac pulsation
- Differences across brain regions
  - Functional differences
  - Large vessel effects
  - Variability in gray and white matter

Is it a fair assumption that noise in fMRI is random?

# Standard Deviation Image



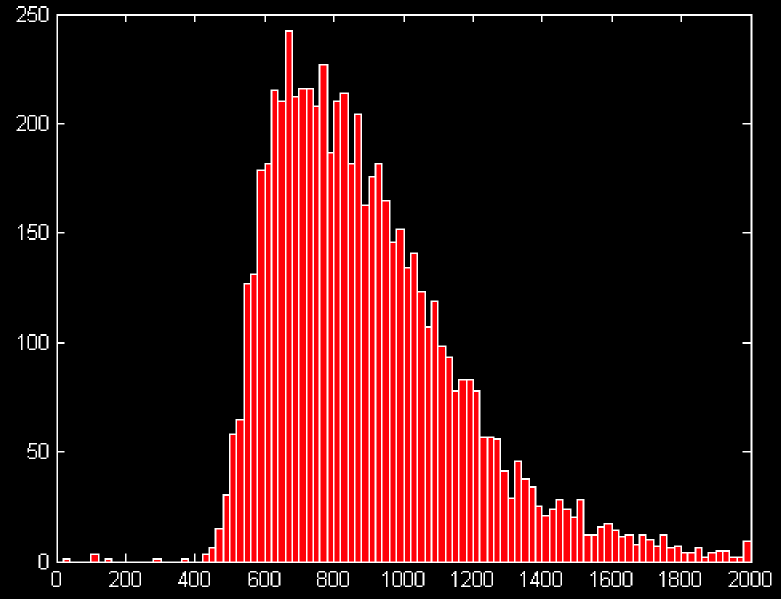
# Noise vs. *Variability*

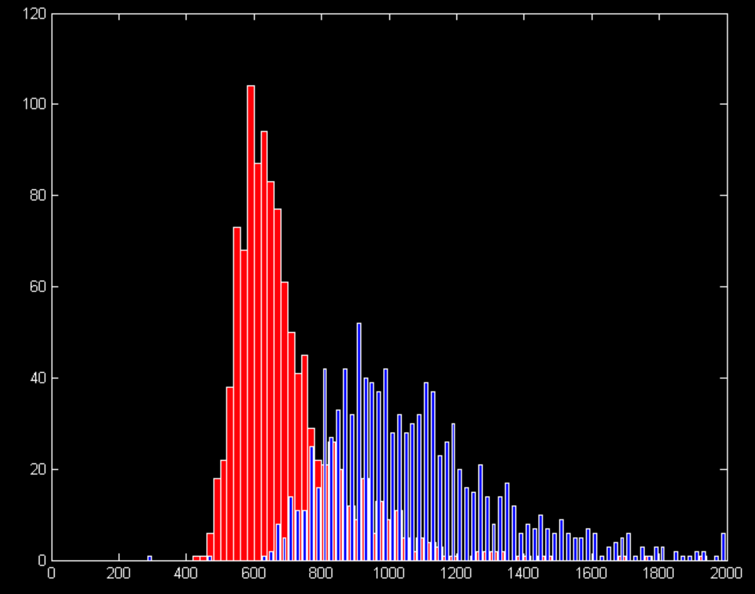
# Variability in Subject Behavior: Issues

- Cognitive processes are not static
  - May take time to engage
  - Often variable across trials
  - Subjects' attention/arousal wax and wane
- Subjects adopt different strategies
  - Feedback- or sequence-based
  - Problem-solving methods
- Subjects engage in non-task cognition
  - Non-task periods do not have the absence of thinking

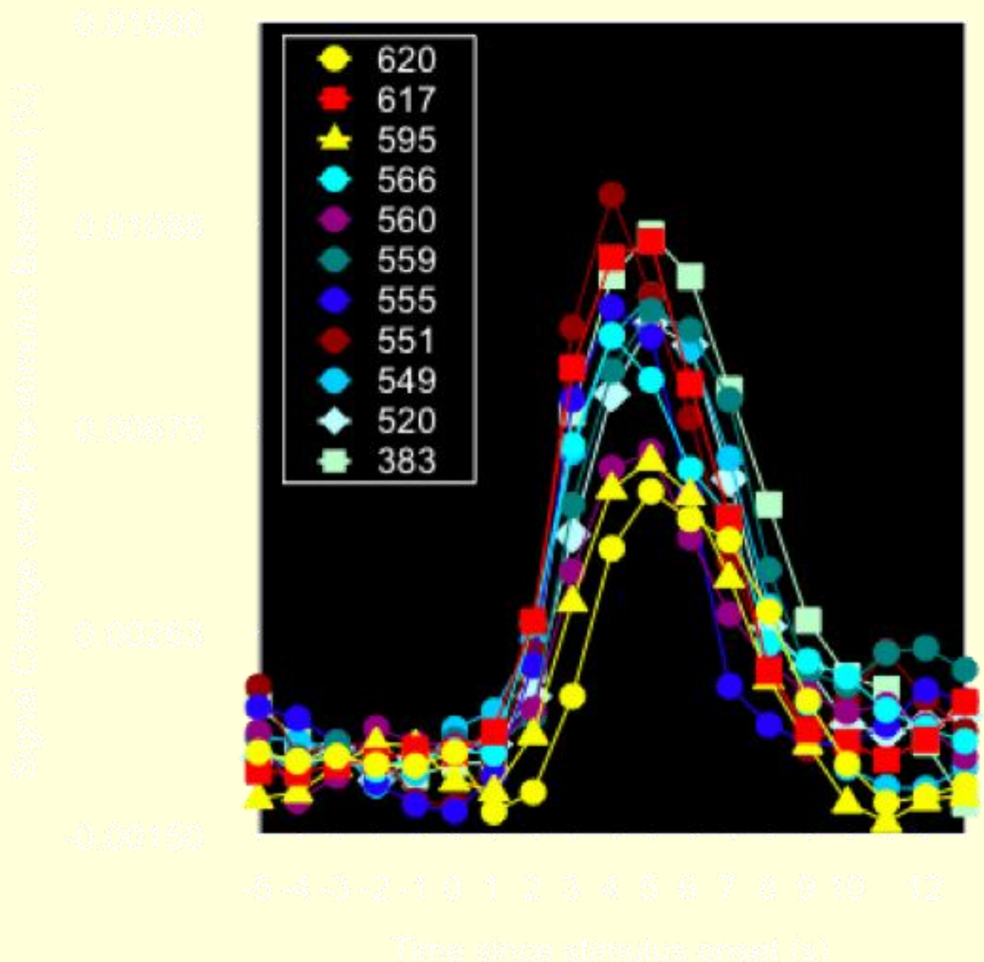
What can we do about these problems?

# Response Time Variability



# Consistency in the HDR



# Spatial Variability?

**Visual Paradigm**

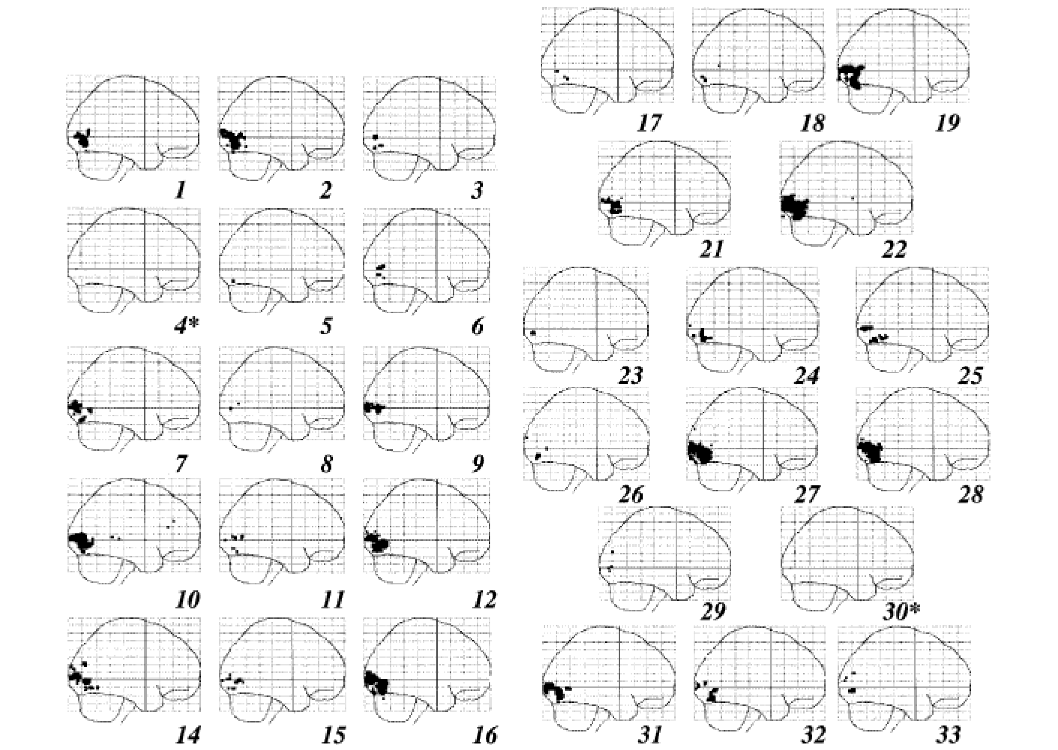
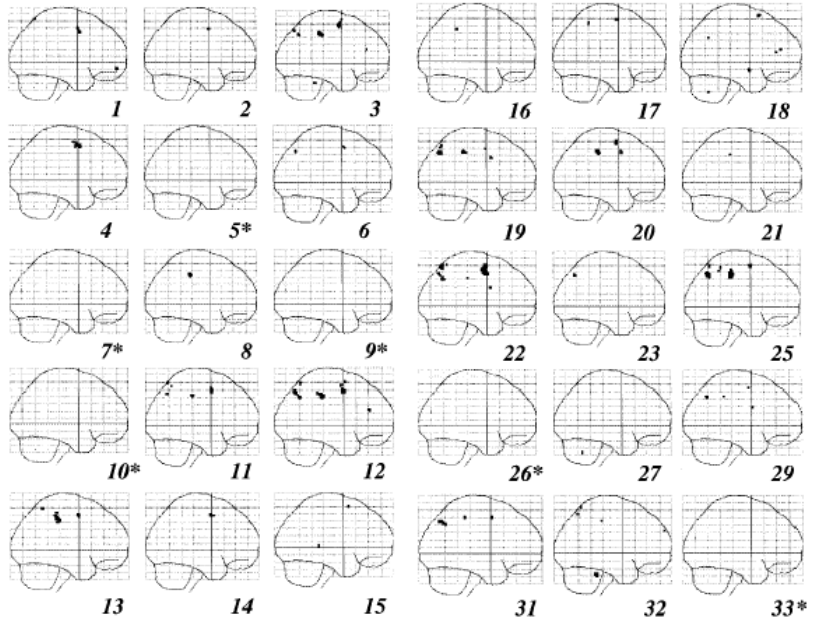



FIG. 4. Single-session sagittal MIPs for the visual paradigm. Similar to Figs. 2 and 3, only 31 sessions are displayed. Sessions marked with "*" contain no significant voxels.

**Cognitive Paradigm**

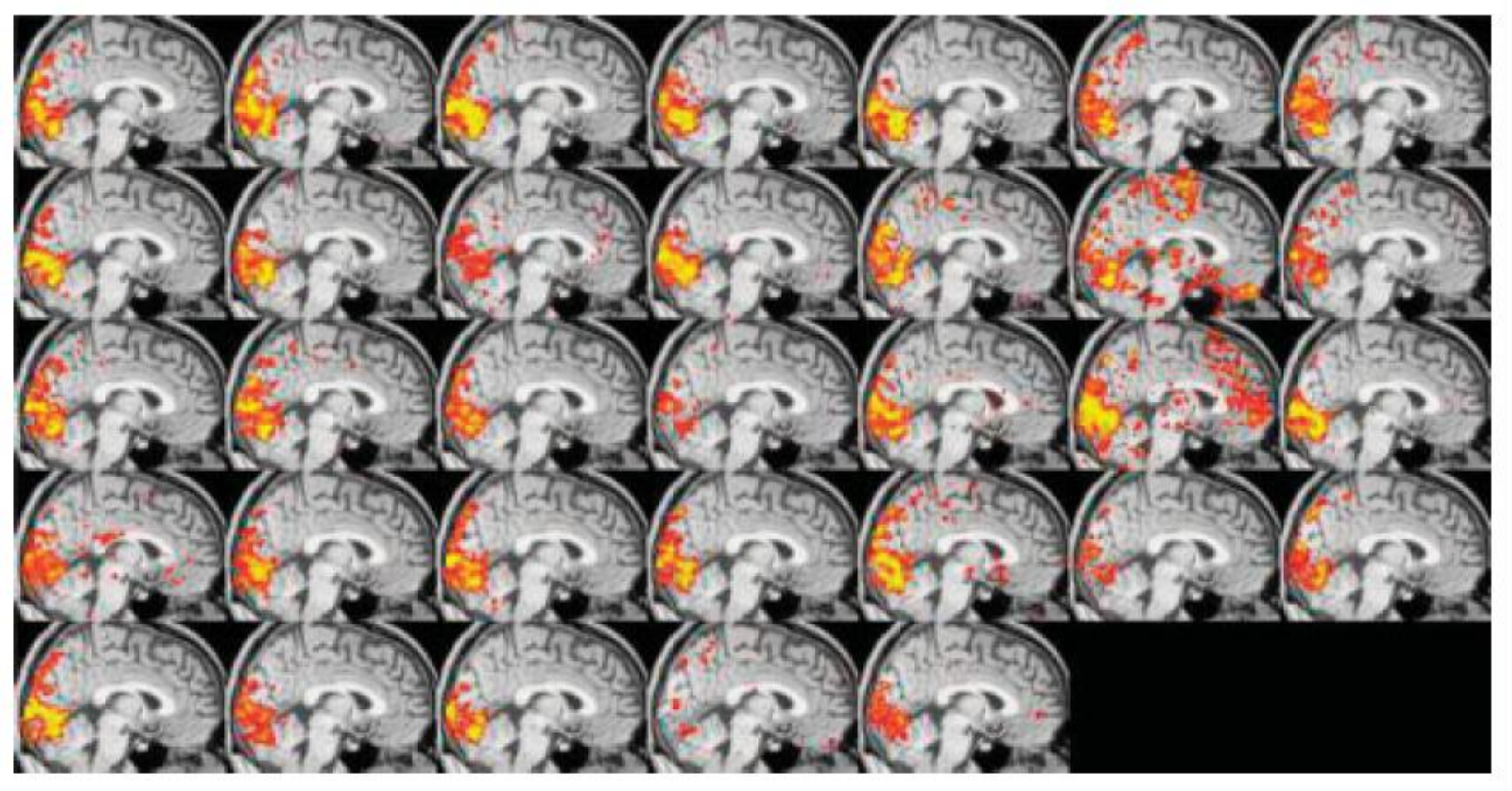



"The following precautions were taken: the same operators always controlled the scanner, ambient light and sound levels were similar between sessions, and spoken instructions to the subject were always exactly the same.

One obvious factor that we could not control was that our subject was always aware that he had performed the task before in the scanner, only under slightly different circumstances. We called this the "Groundhog Day" effect."

McGonigle et al., 2000

# “A reanalysis…”



Smith et al., 2005

**Reducing the threshold gives much less apparent variability.**

# Questions?