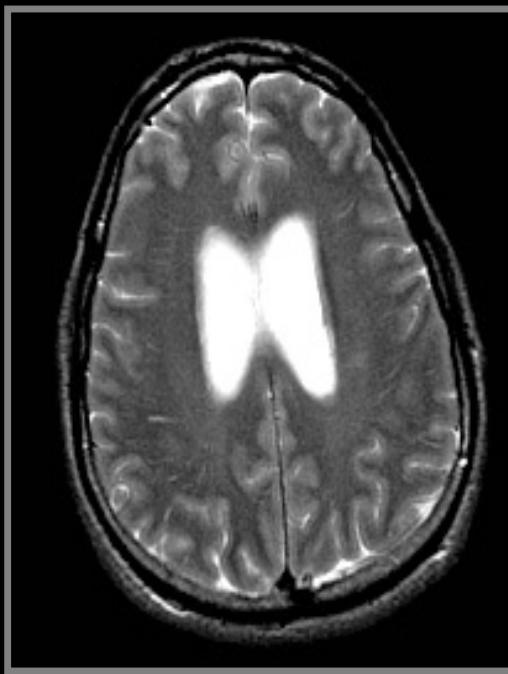


Spatial, Temporal, and Interpretive Limits of Functional MRI

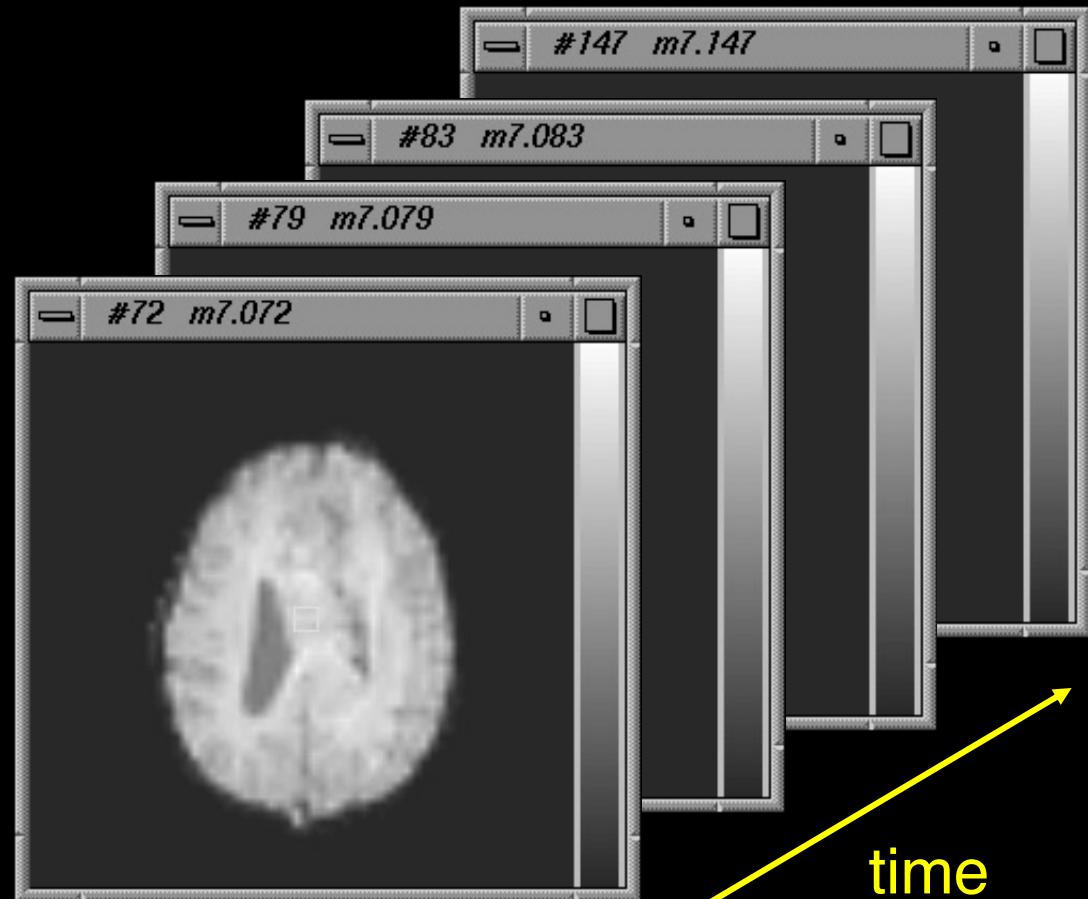
Peter A. Bandettini, Ph.D

Unit on Functional Imaging Methods
&
3T Neuroimaging Core Facility

Laboratory of Brain and Cognition
National Institute of Mental Health

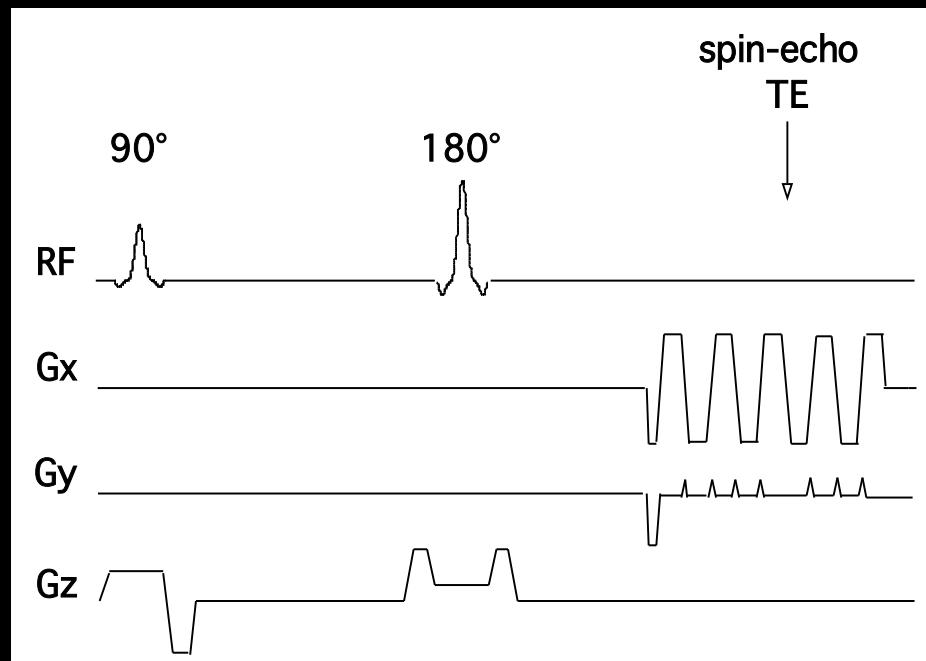
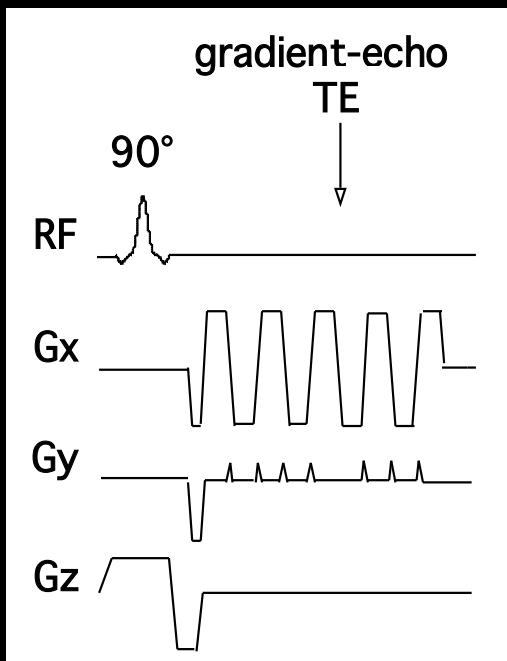


Anatomic



Functional

Echo-Planar Imaging

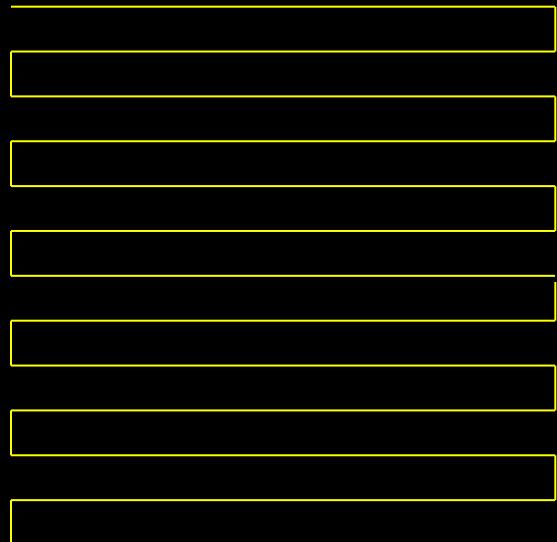


Single Shot Imaging

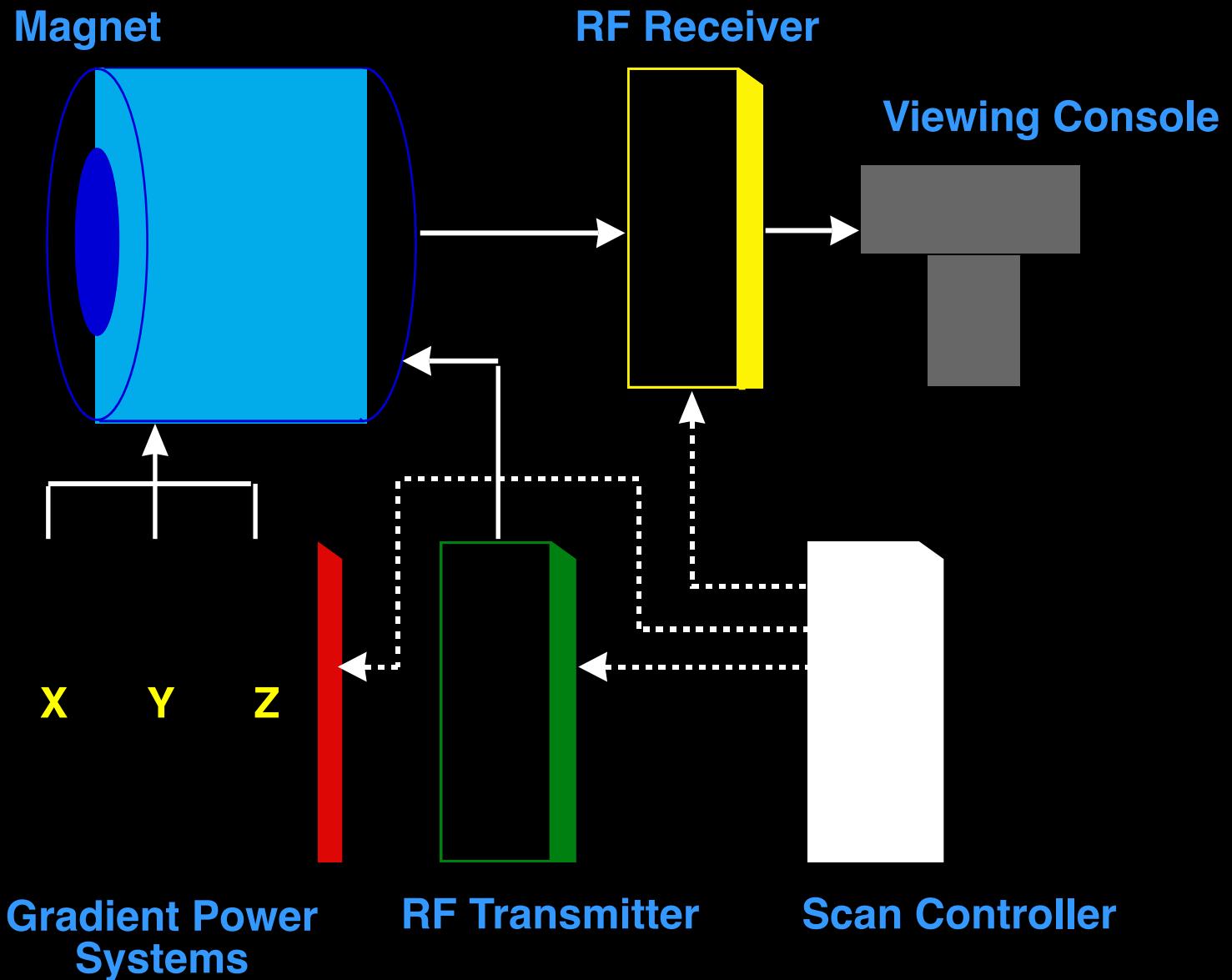


EPI Readout Window

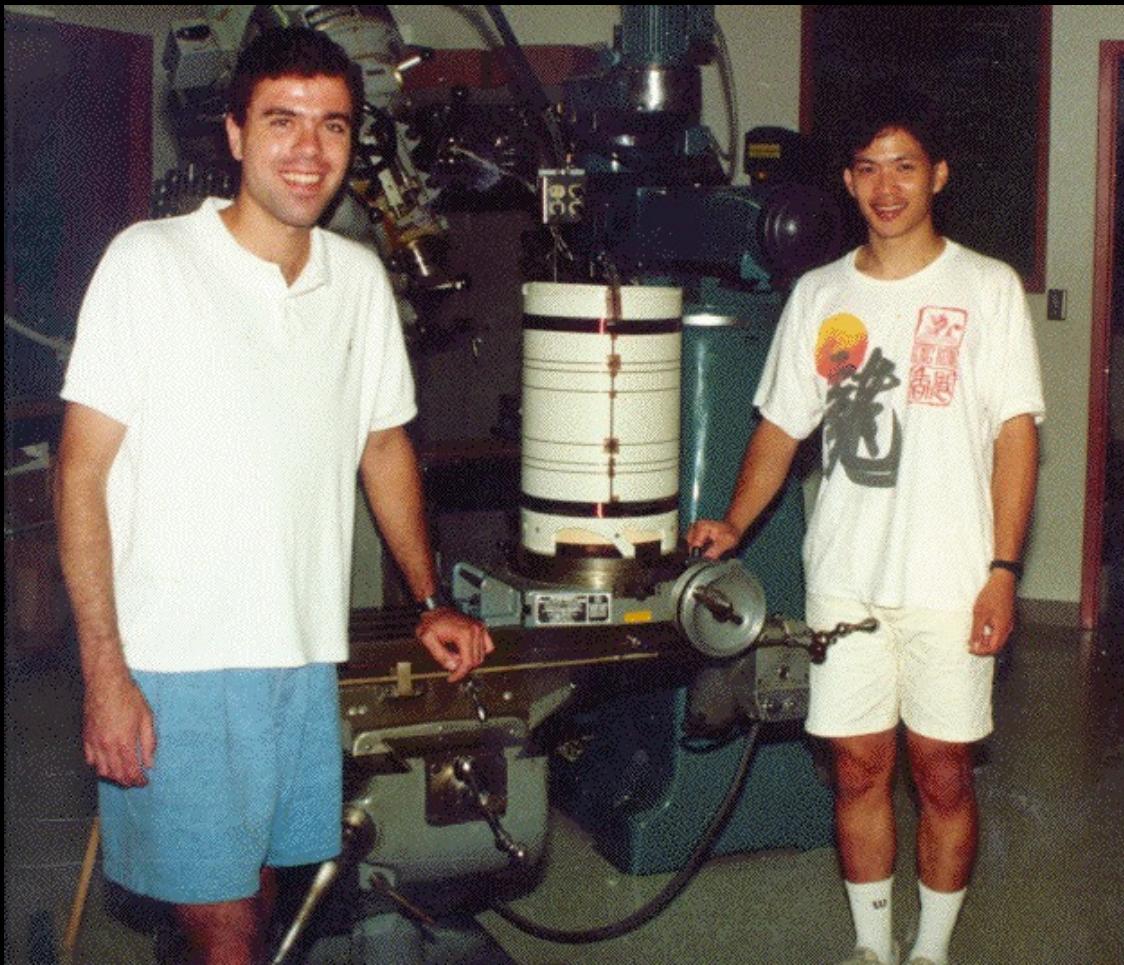
≈ 20 to 40 ms



Imaging System Components



Local gradients solved the problem



1991-1992



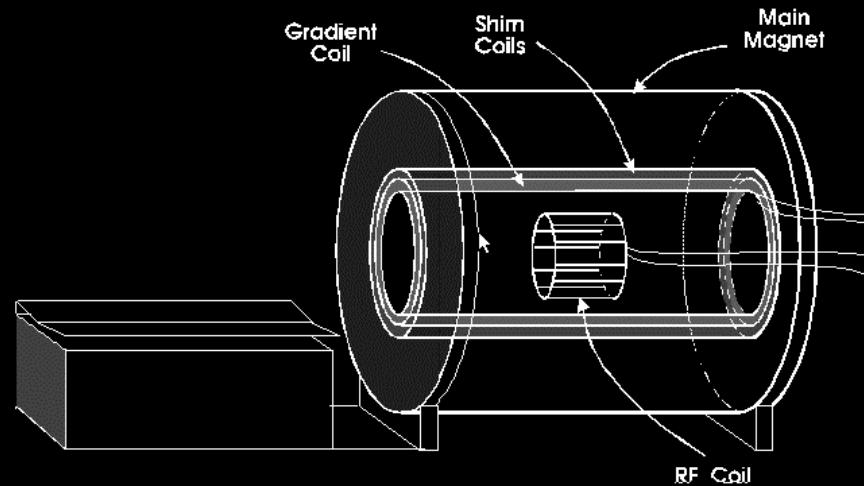
1992-1999



2 G/cm, 350 T/m/s



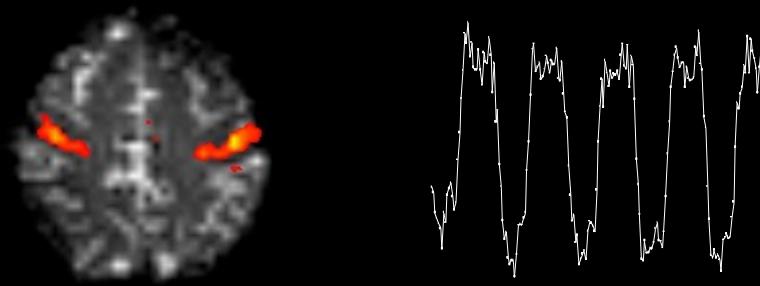
4 G/cm, 150 T/m/s



10 G/cm, 1000 T/m/s

The use of fMRI to Investigate Brain Function

Where?



When?

How much?

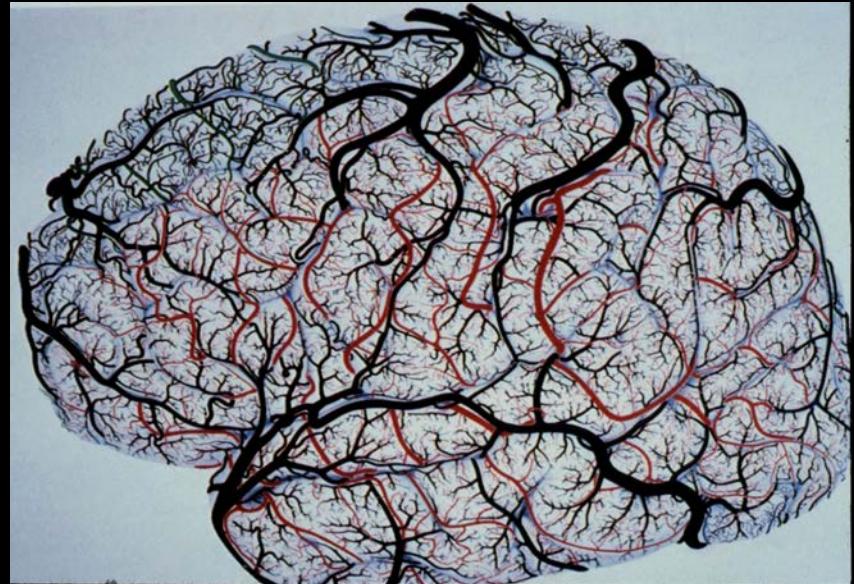
How to get the brain to do what we want it to do in the context of an fMRI experiment?

A Primary Challenge:

...to make progressively more precise inferences using fMRI without making too many assumptions about non-neuronal physiologic factors.



FIG. 43. Middle temporal gyrus. Female, 60 years. (1) Principal intracortical vein. The branches length regularly decreases from deep to superficial cortical regions, thus the vascular territory of the principal vein has a conical appearance (dotted line) ($\times 28$)



- Contrast in fMRI

Hemodynamic Specificity

- The Hemodynamic Transfer Function

Location, Latency, Magnitude

- Best Results So Far

Temporal Resolution, Spatial Resolution

- Neuronal Activation Input Strategies

Block Design

Phase and Frequency Encoding

Orthogonal Designs

Parametric Designs

Event-Related Designs

Free Behavior Designs

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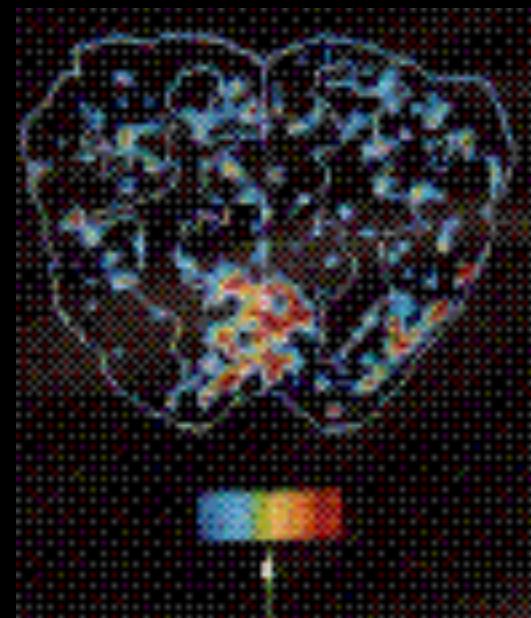
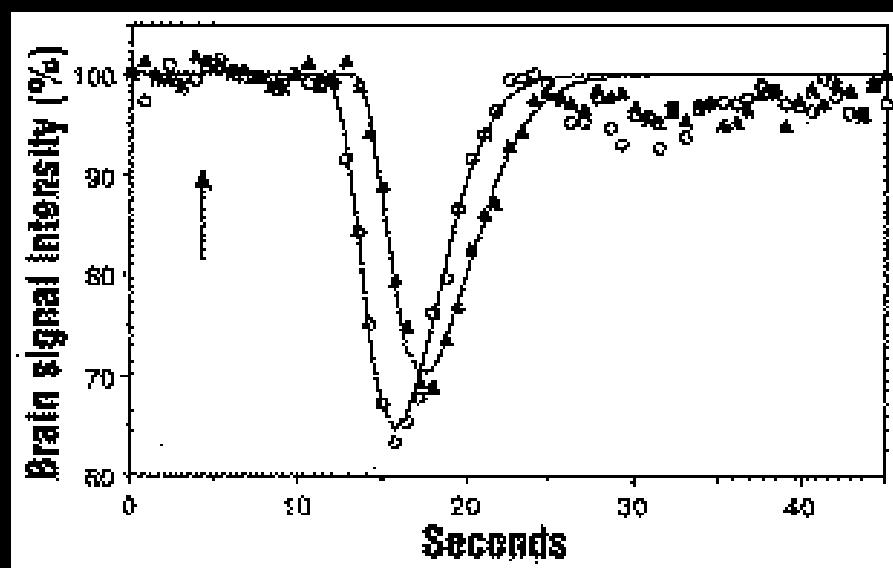
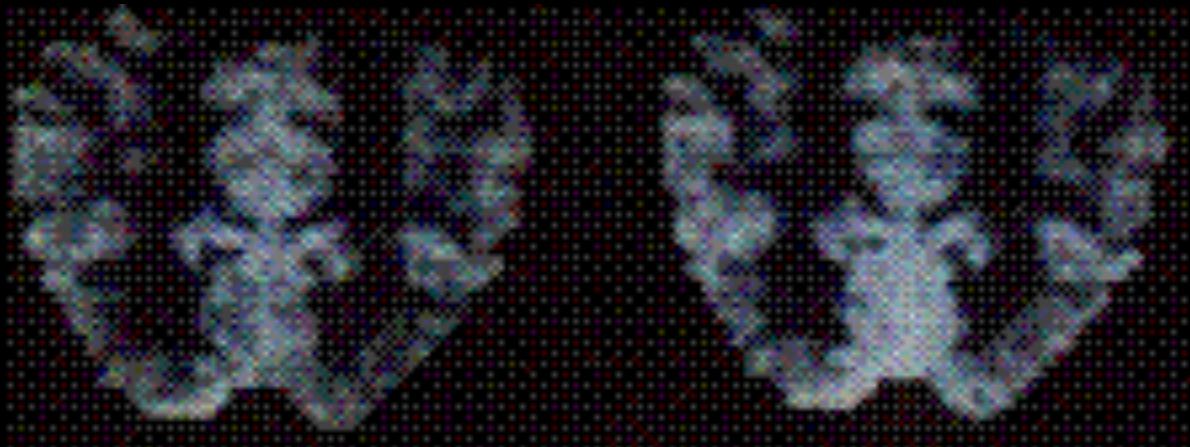
Free Behavior Designs

Contrast in Functional MRI

- **Blood Volume**
 - Contrast agent injection and time series collection of T2* or T2 - weighted images
- **BOLD**
 - Time series collection of T2* or T2 - weighted images
- **Perfusion**
 - T1 weighting
 - Arterial spin labeling
- **CMRO₂**
 - BOLD and Perfusion w/
Normalization to Global Perfusion Change

Resting

Active

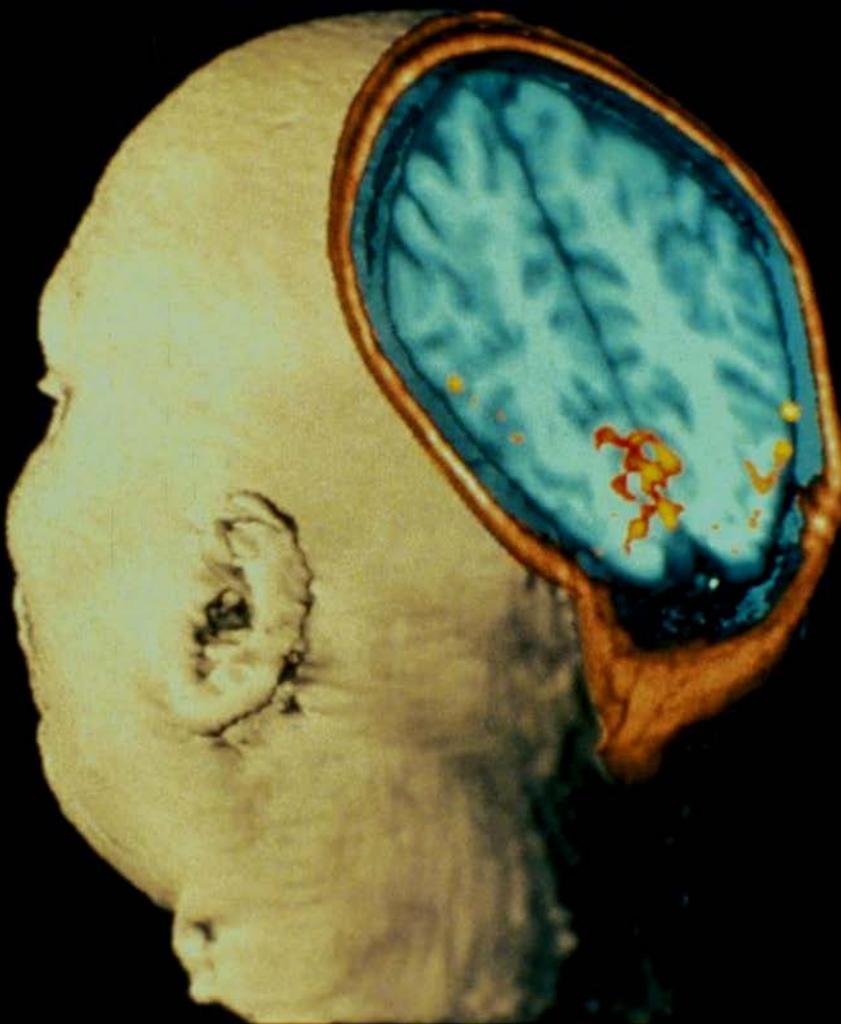


Photic Stimulation

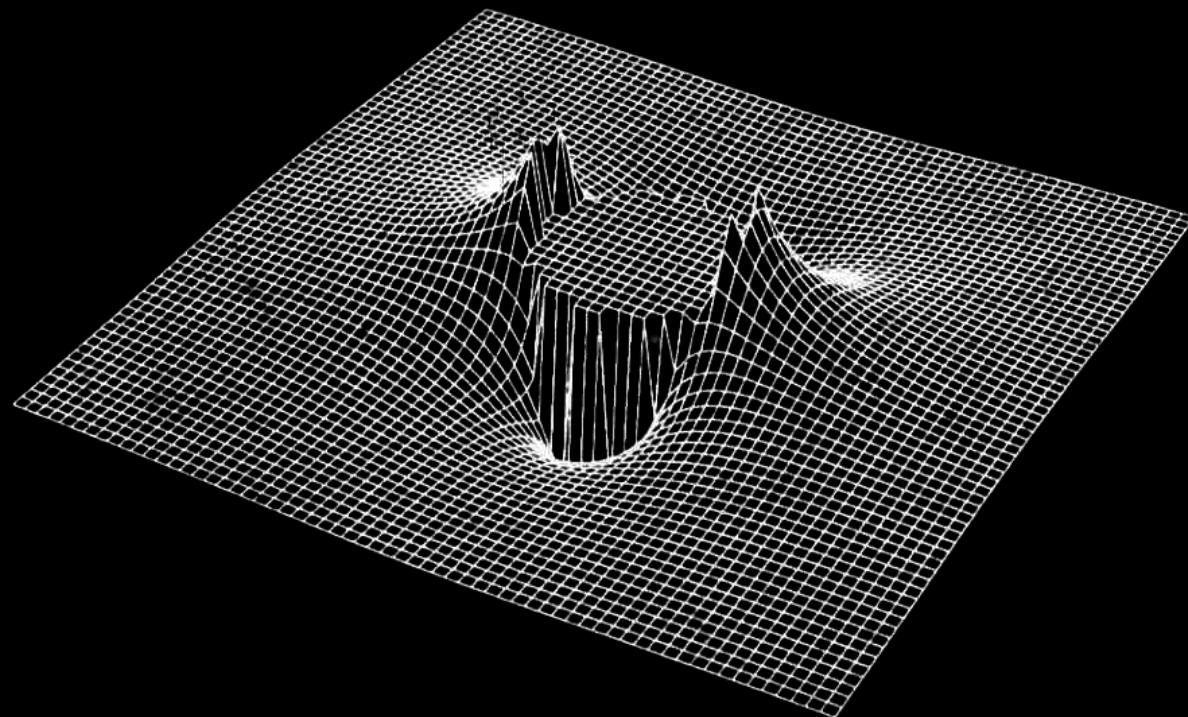
MRI Image showing
activation of the
Visual Cortex

From Belliveau, et al.
Science Nov 1991

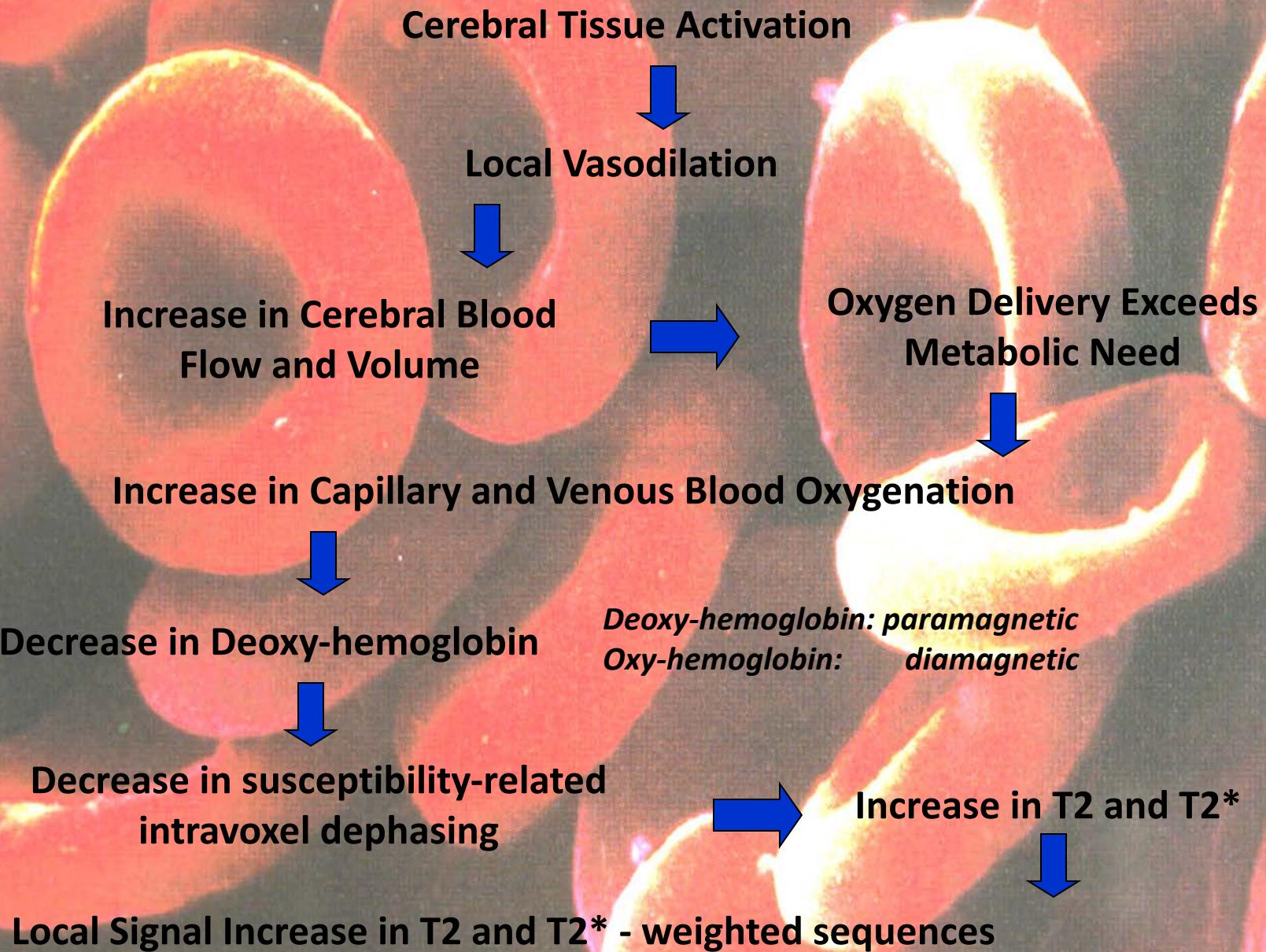
MSC - perfusion



Susceptibility-Induced Field Distortion in the
Vicinity of a Microvessel \perp to B_0 .

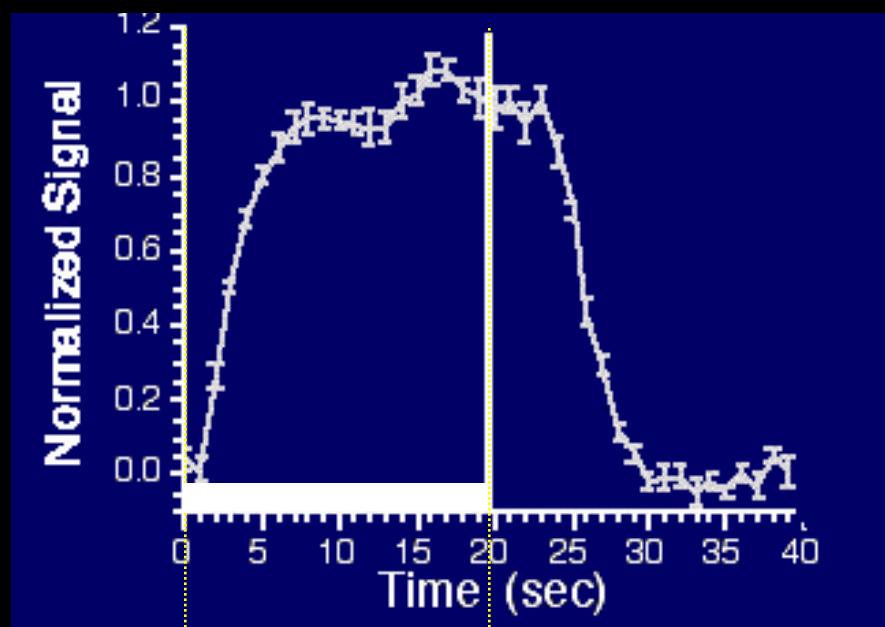


BOLD Contrast in the Detection of Neuronal Activity

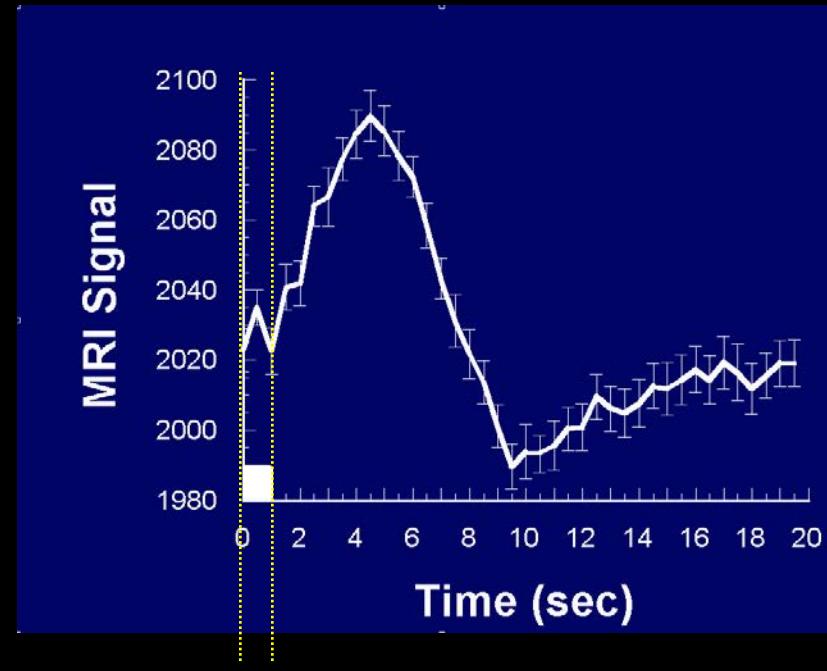


The BOLD Signal

Blood Oxxygenation Level Dependent (BOLD) signal changes



task



task

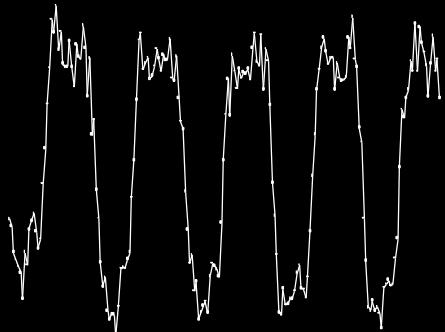
Alternating Left and Right Finger Tapping



~ 1992

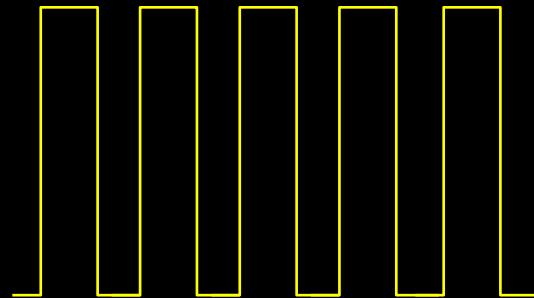
Creating a Functional Image

ON ON ON ON ON



Signal Time Course

X



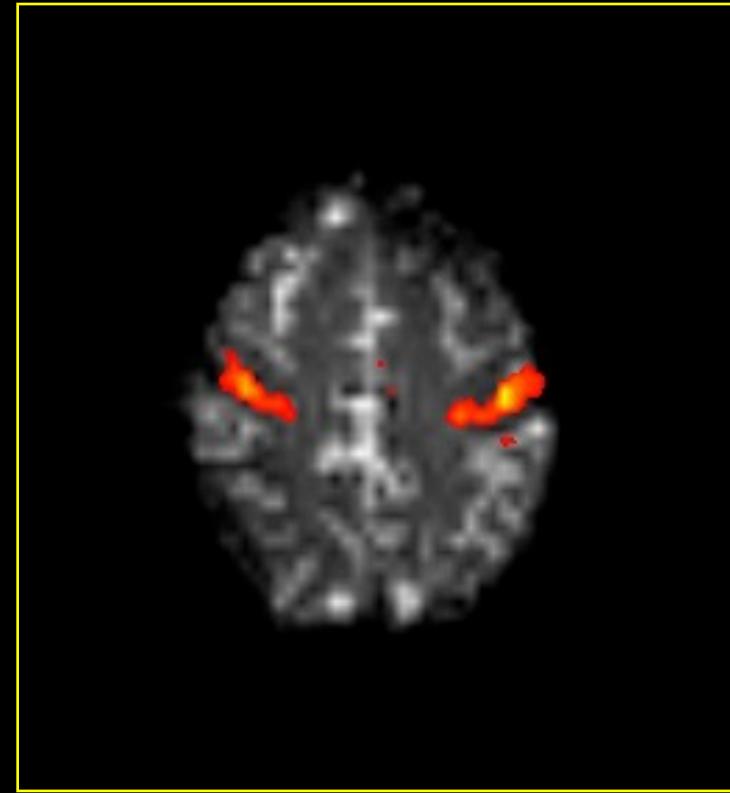
Reference Function

=



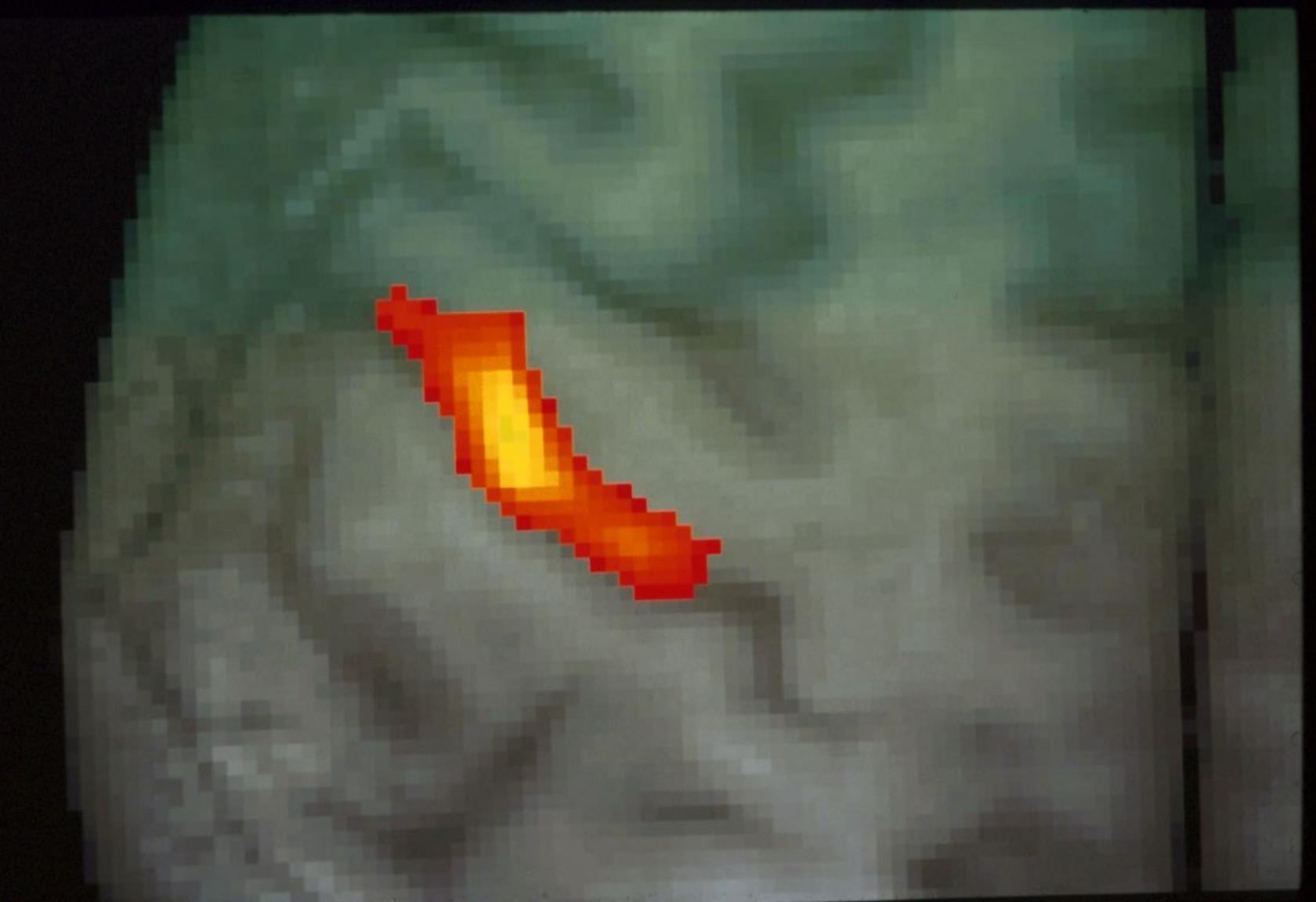


Cross Correlation Image



Cross Correlation Image

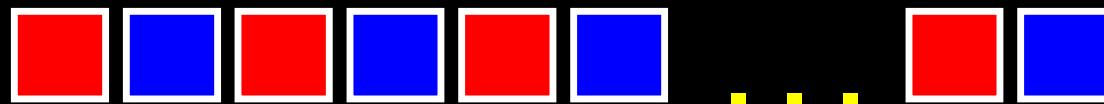
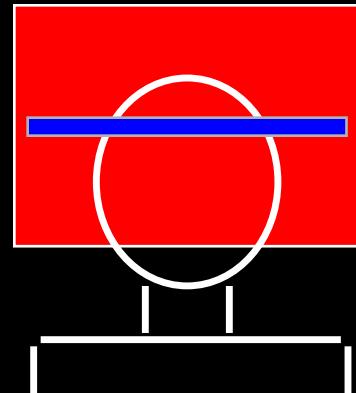
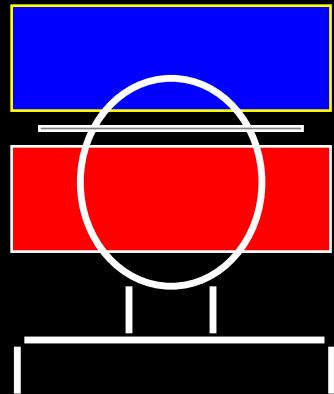
Anatomical Image



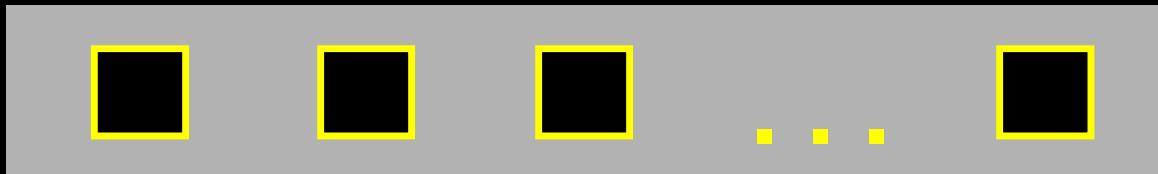
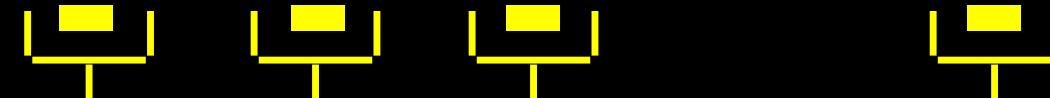
Perfusion / Flow Imaging

EPISTAR

FAIR

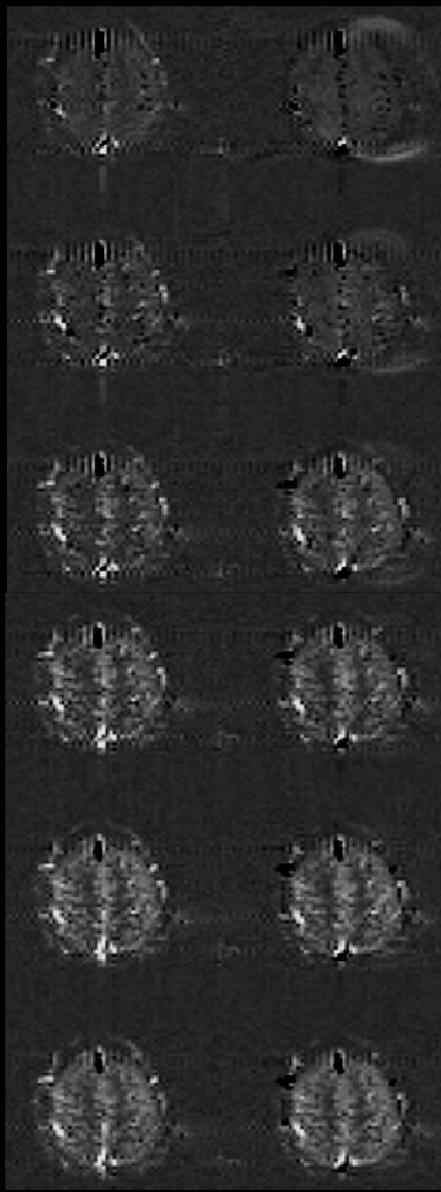


...



TI (ms) FAIR EPISTAR

200



400

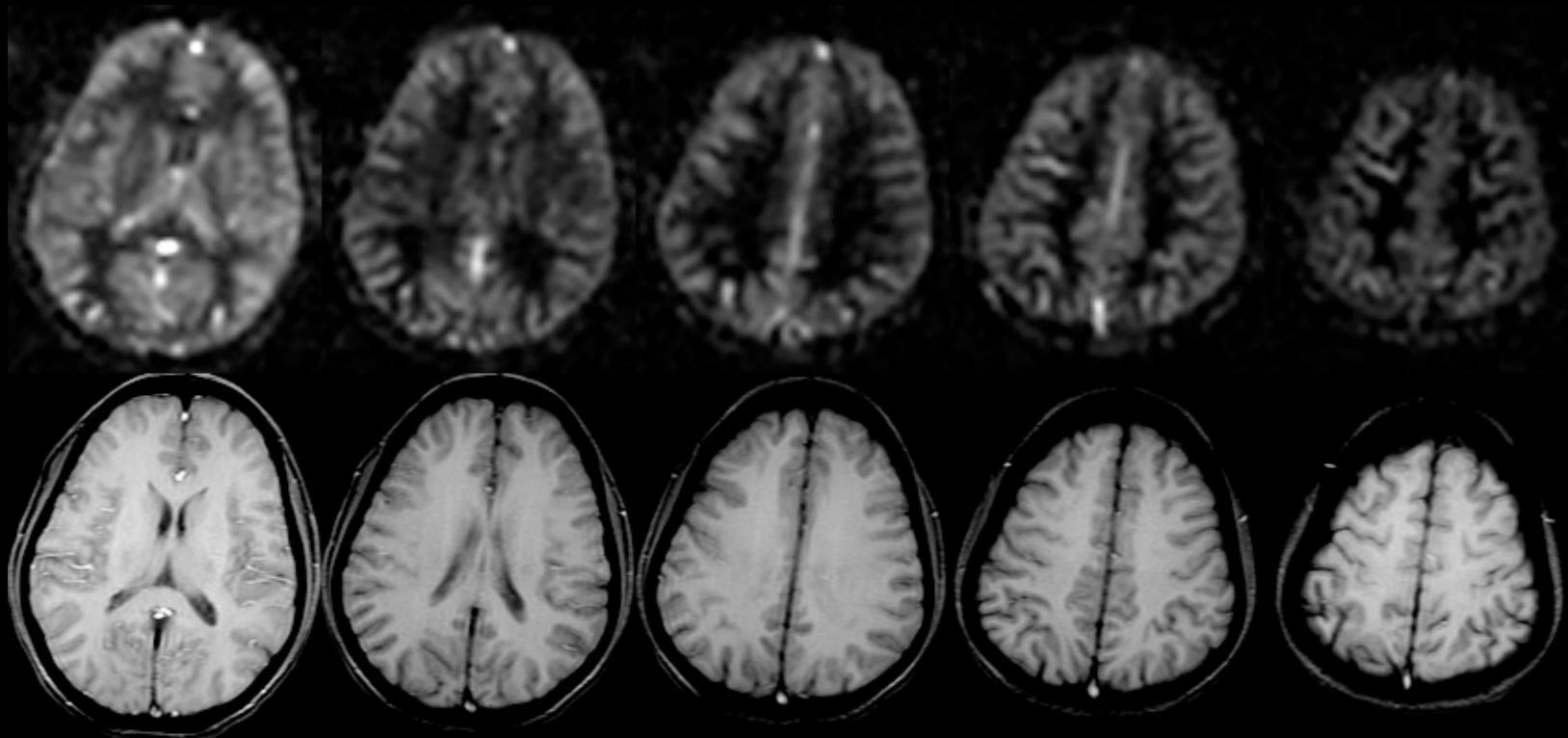
600

800

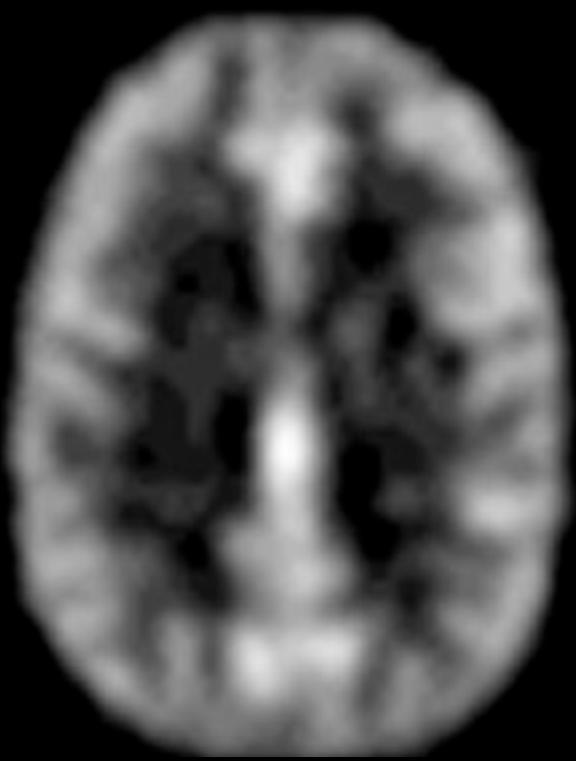
1000

1200

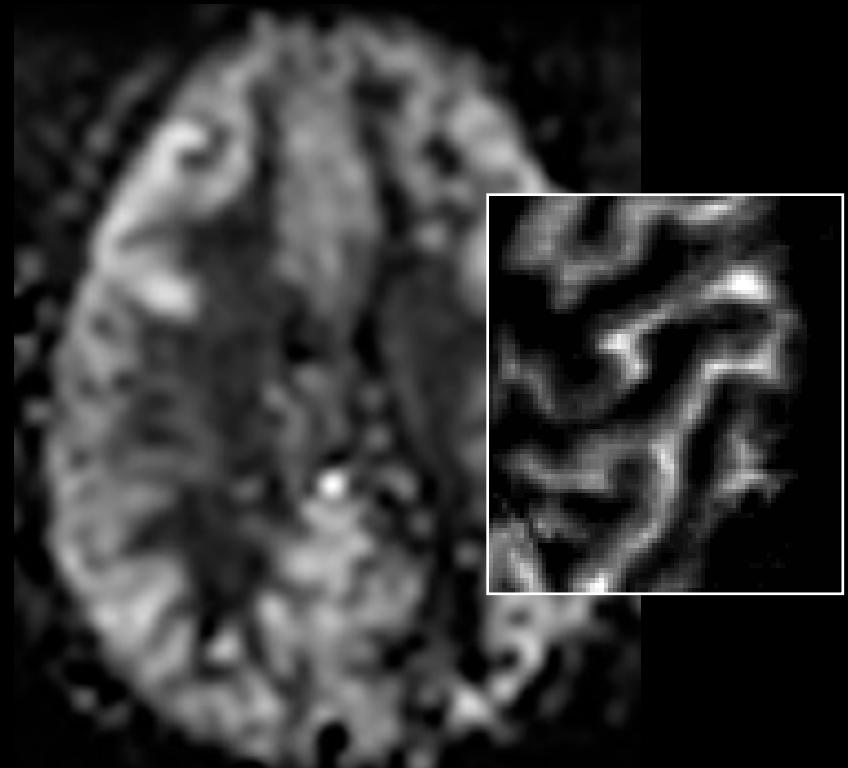
Resting ASL Signal



Comparison with Positron Emission Tomography



PET: H_2^{15}O



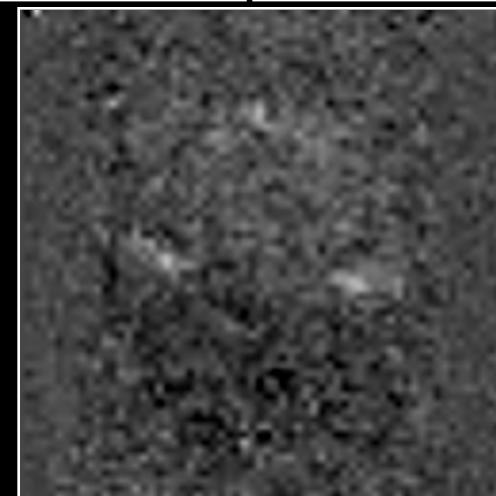
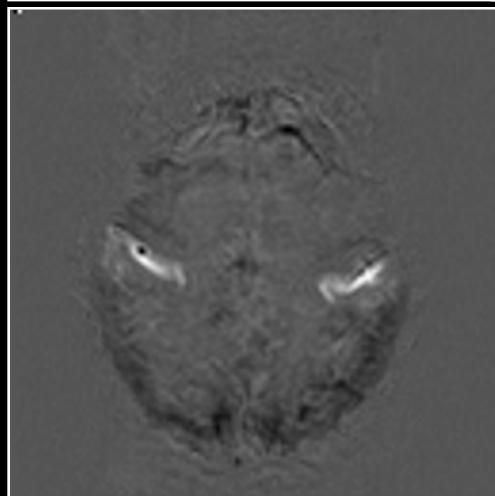
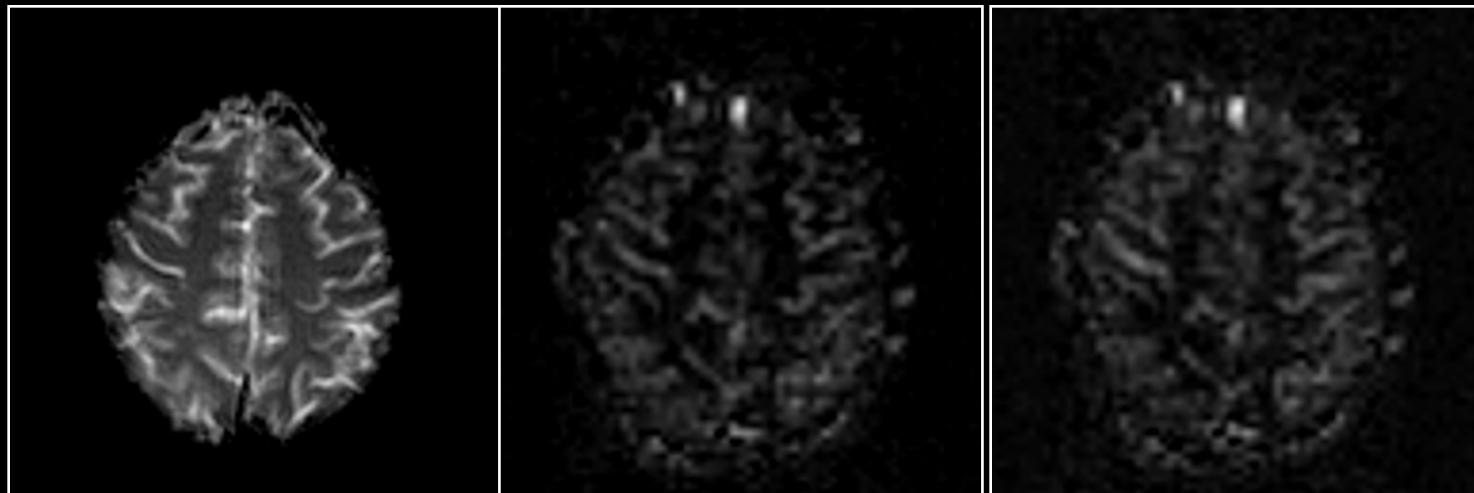
MRI: ASL

Perfusion

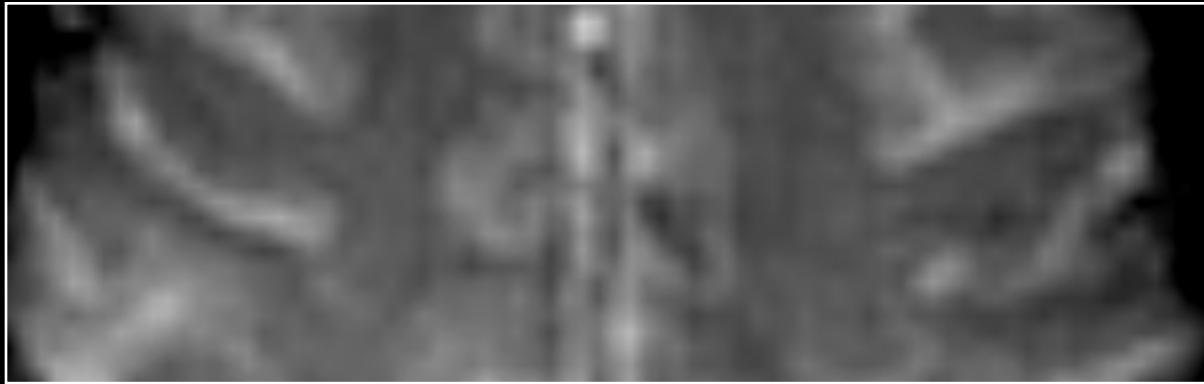
BOLD

Rest

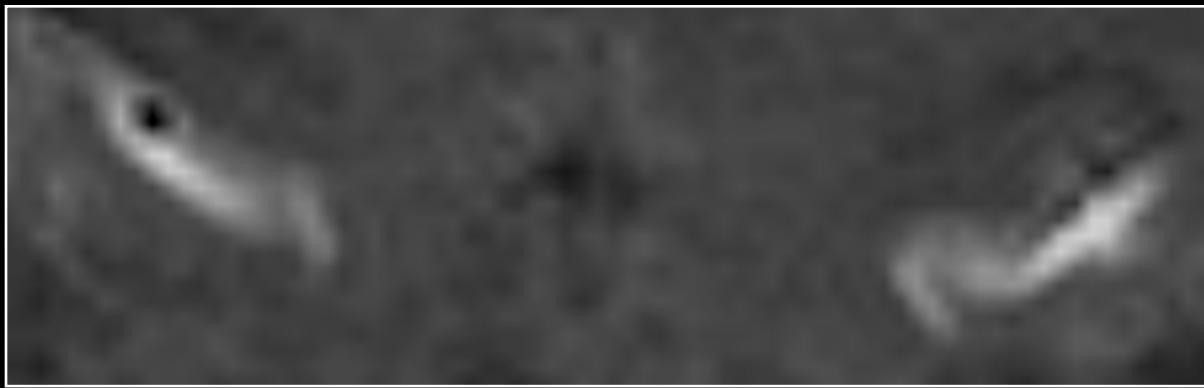
Activation



Anatomy

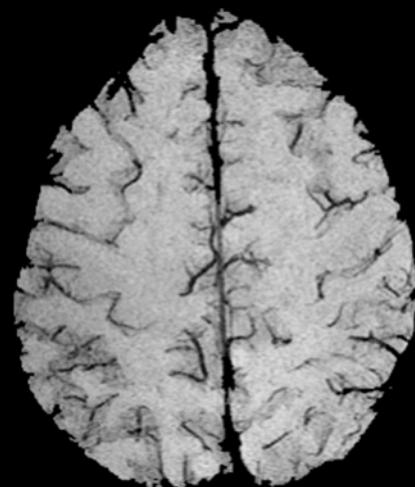
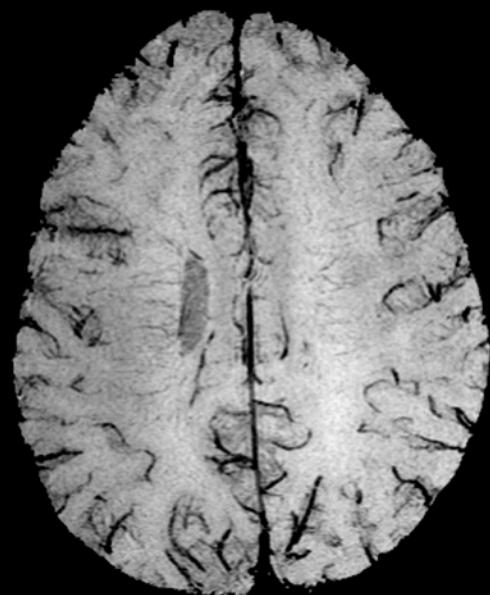


BOLD

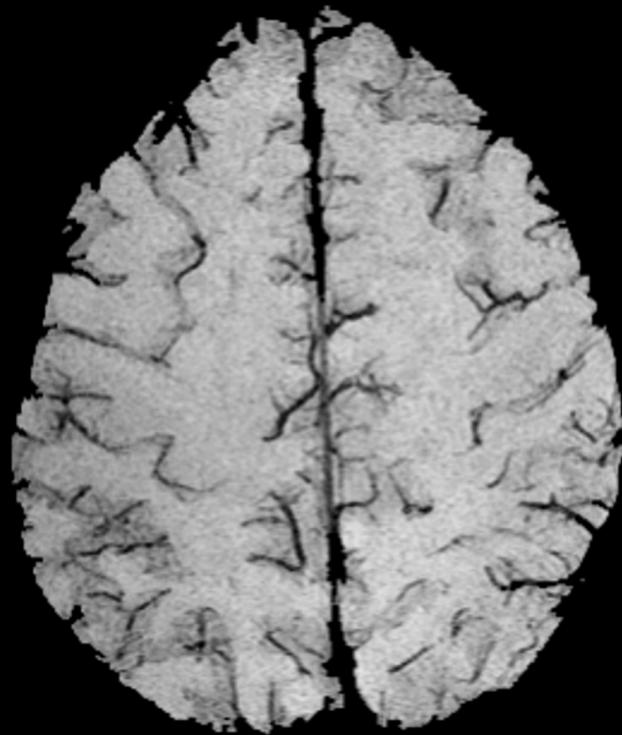


Perfusion



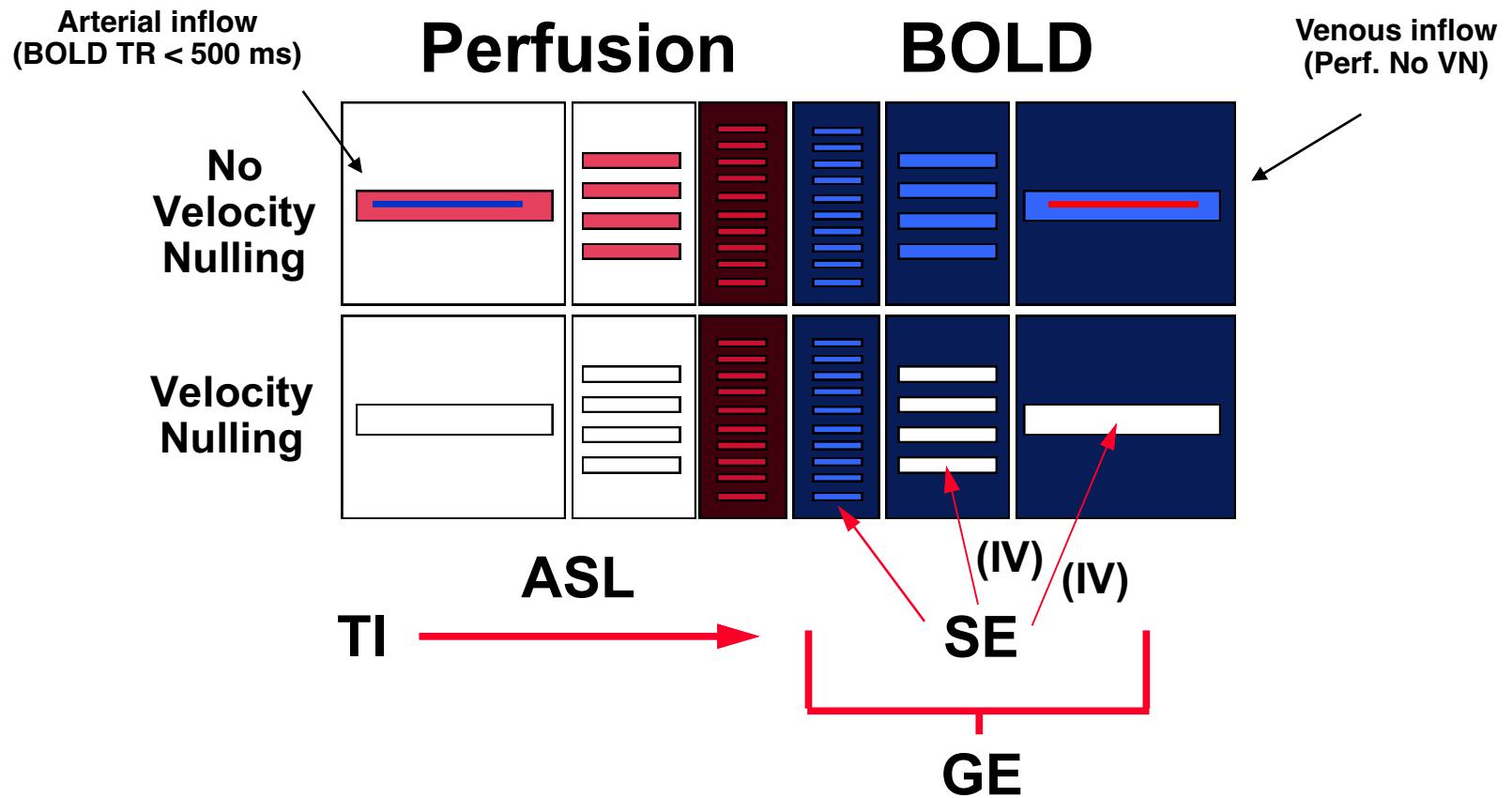




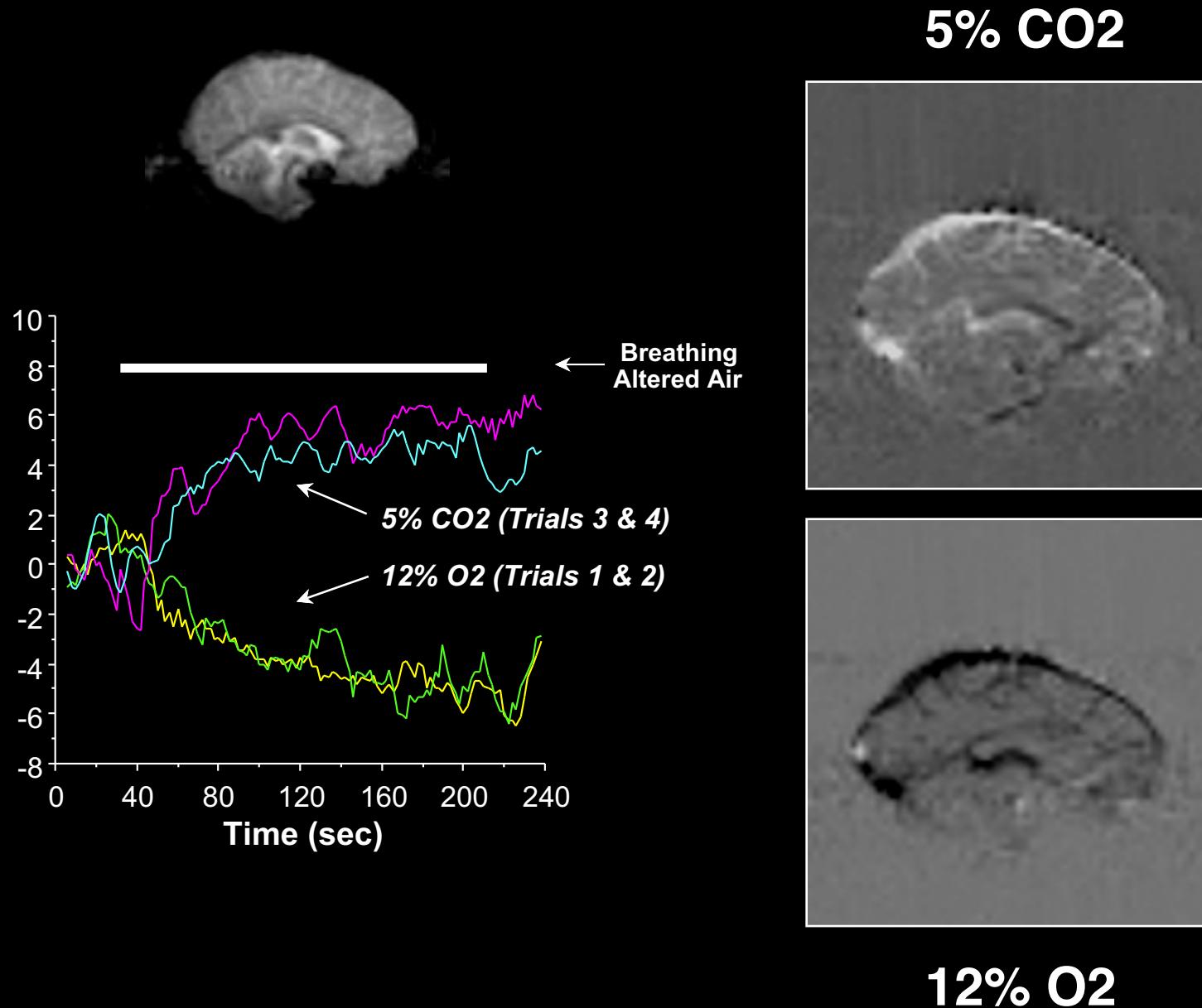




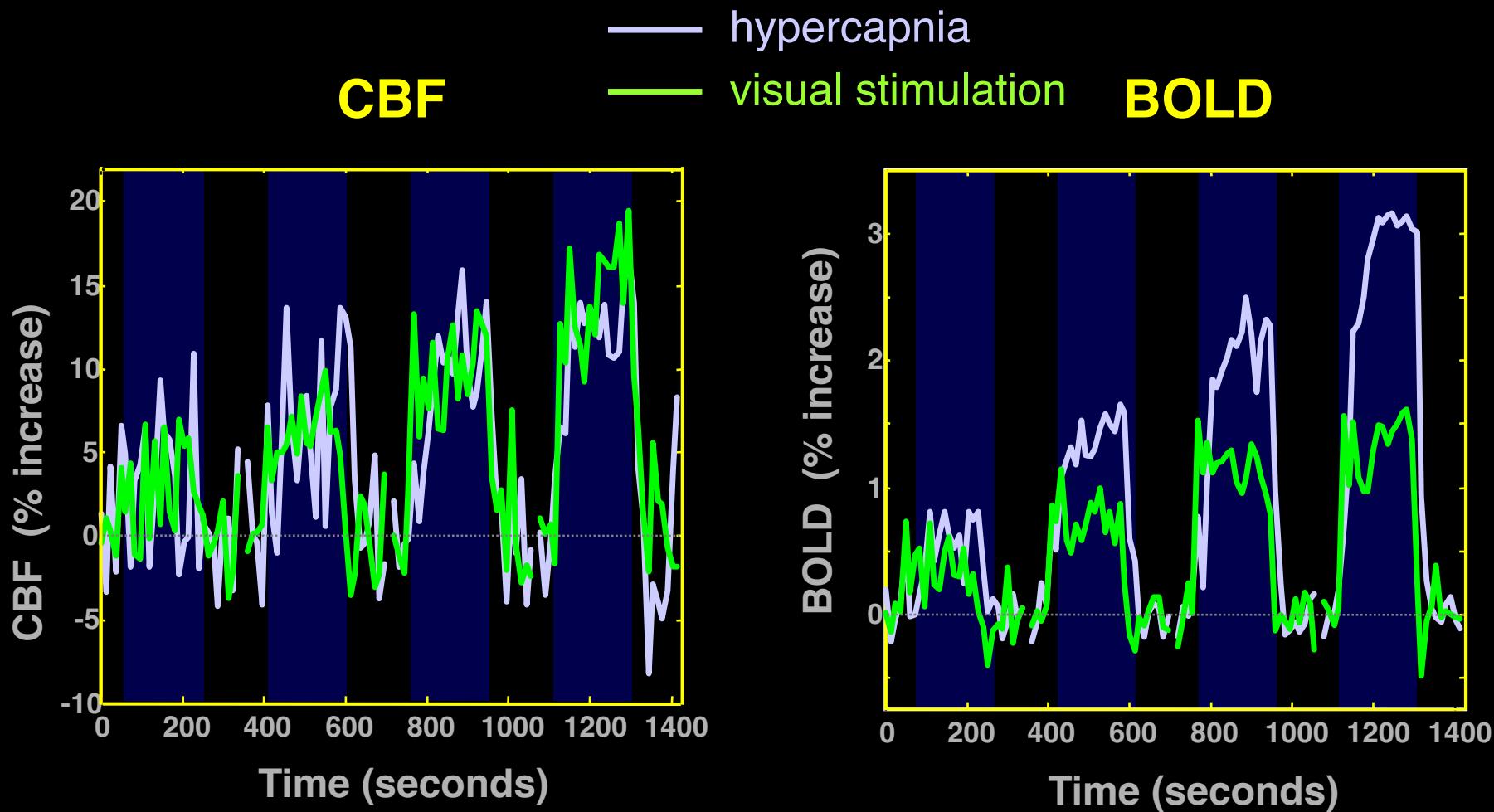
Hemodynamic Specificity



Hemodynamic Stress Calibration



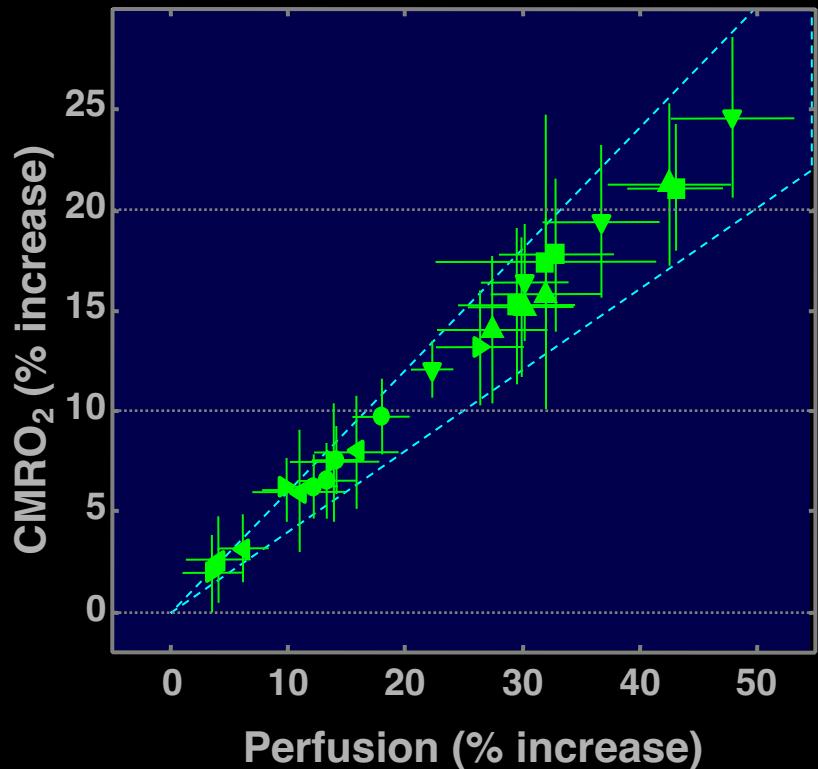
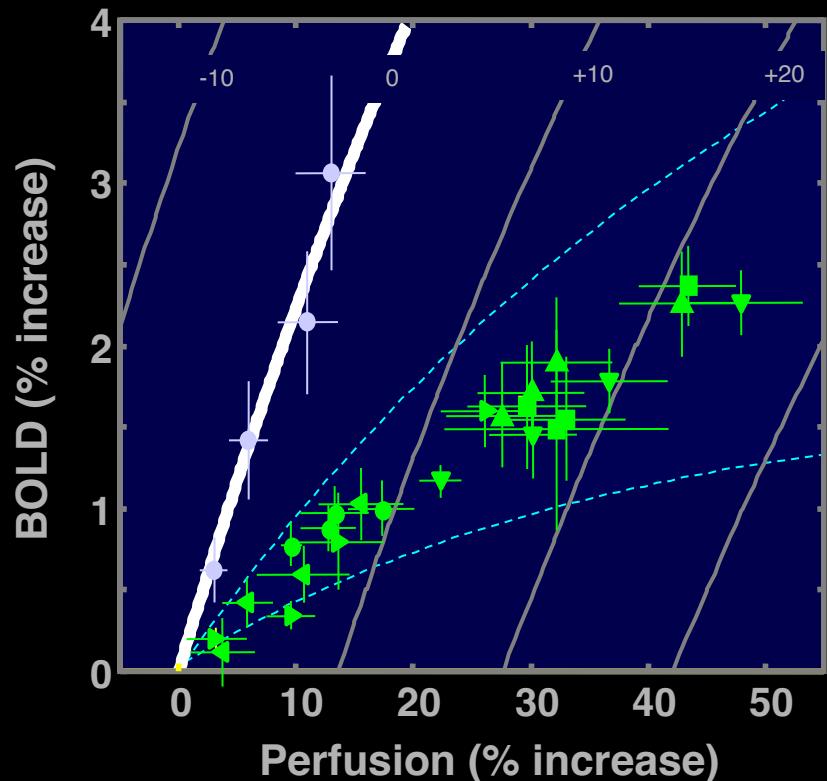
CMRO₂-related BOLD signal deficit:



Simultaneous Perfusion and BOLD imaging
during graded visual activation and hypercapnia

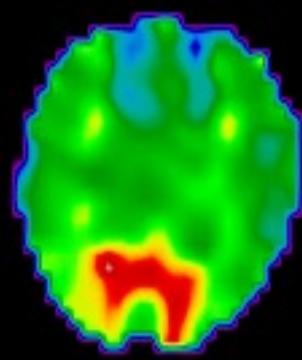
N=12

CBF-CMRO₂ coupling

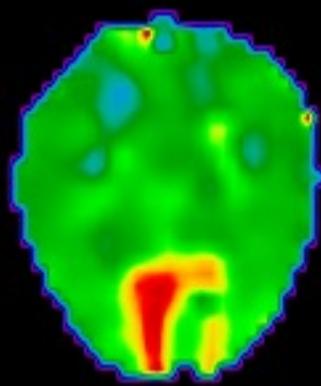


Characterizing Activation-induced CMRO₂ changes using calibration with hypercapnia

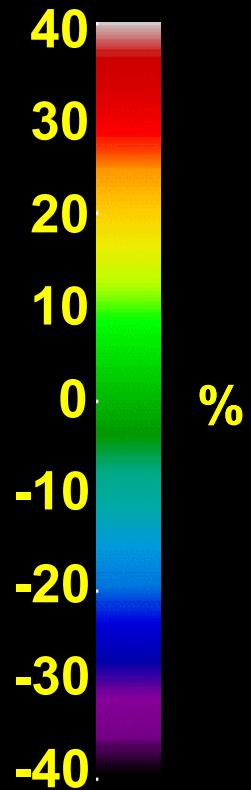
Computed CMRO₂ changes



Subject 1



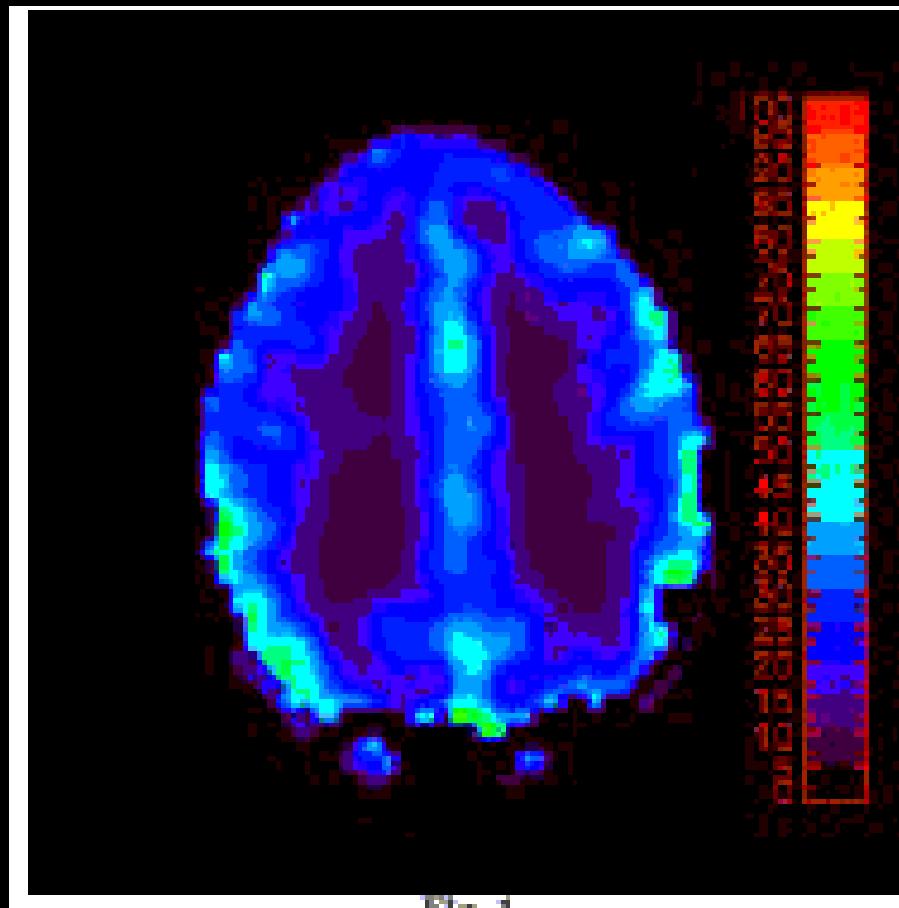
Subject 2



Quantitative Measurements of Cerebral Metabolic Rate of Oxygen (CMRO₂) Using MRI: A Volunteer Study

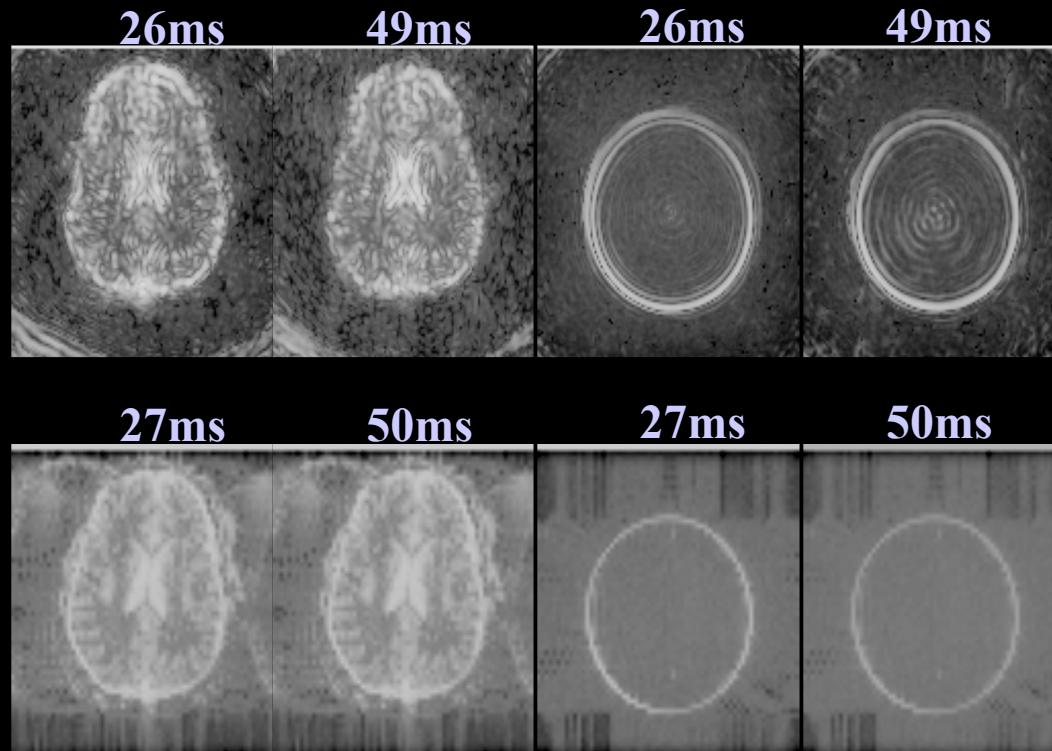
Honeyan AN¹, Weili LIN², Azim CELIK³, Yuesh Z. LEE⁴

¹Washington University, 600 Airport Road, Chapel Hill, NC USA; ²UNC-Chapel Hill, Department of Radiology, CB#7515, Chapel Hill, NC USA; ³GE Medical Systems; ⁴UNC-Chapel Hill, ;



Higher Signal to Noise **in a single image** does not necessarily translate to higher Signal to Noise **over time**.

Temporal vs. Spatial SNR- 3T



0.25 Hz Breathing at 3T

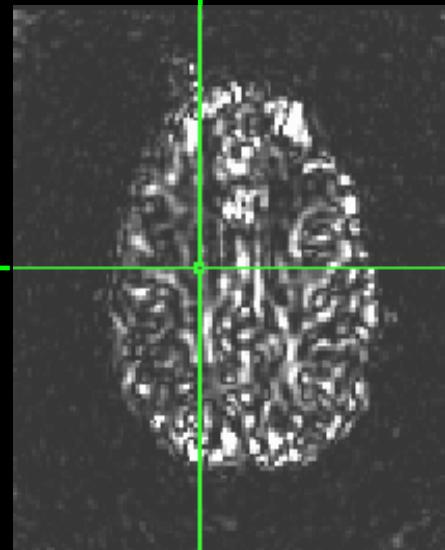
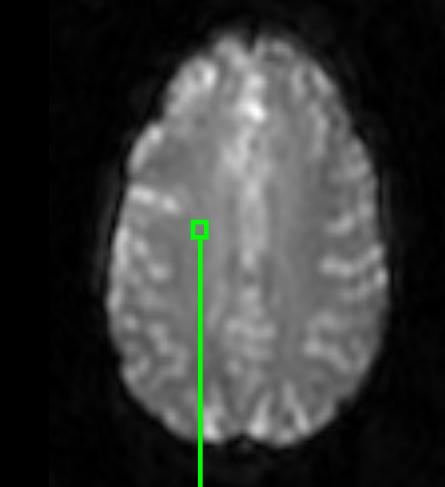
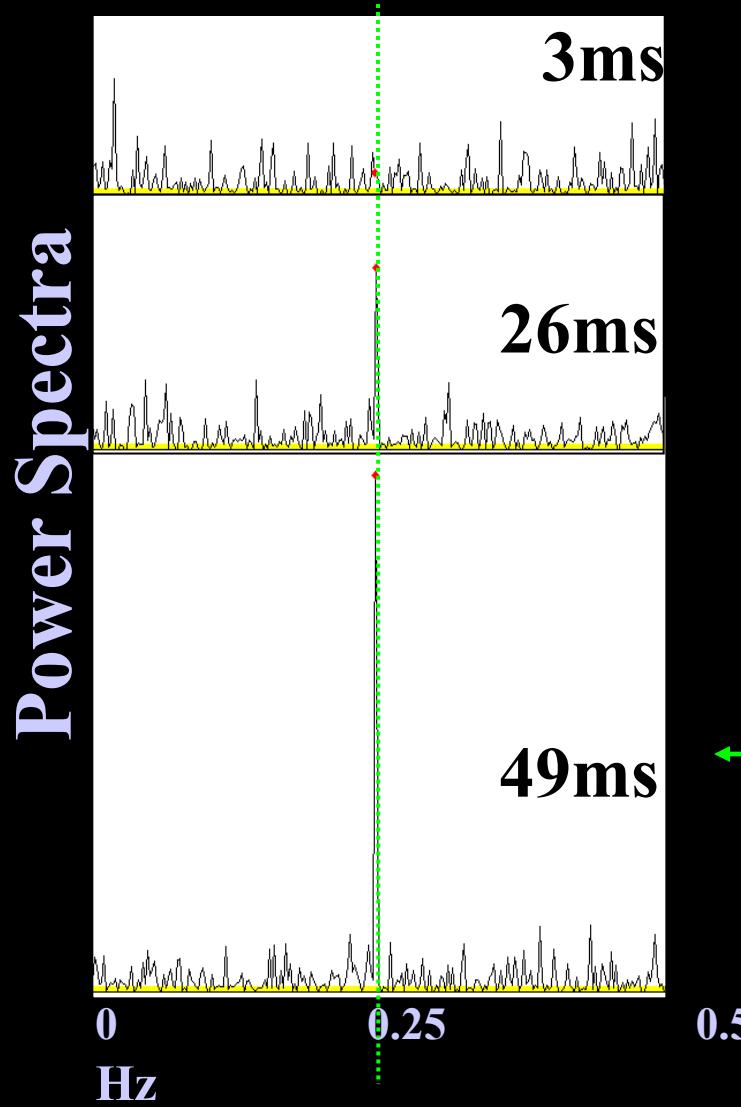


Image Respiration map

0.68 Hz Cardiac rate at 3T

Power Spectra

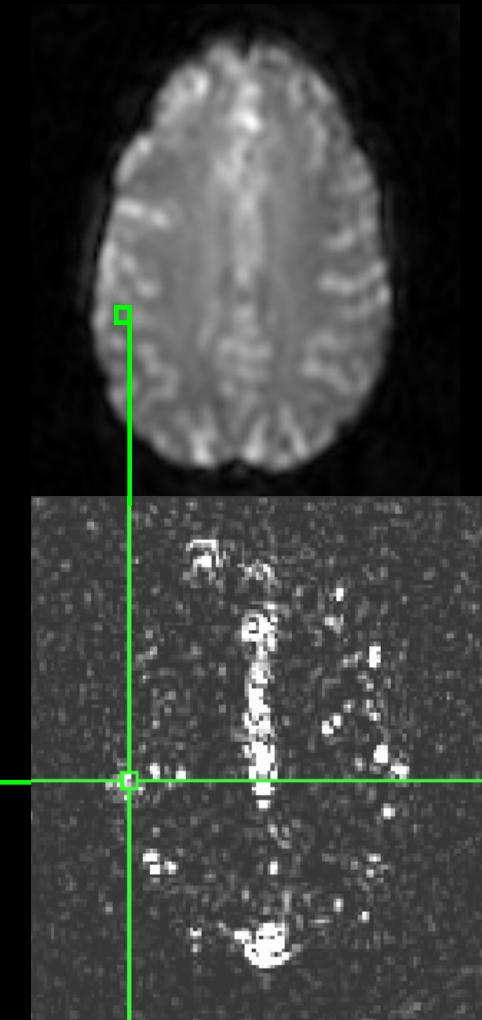
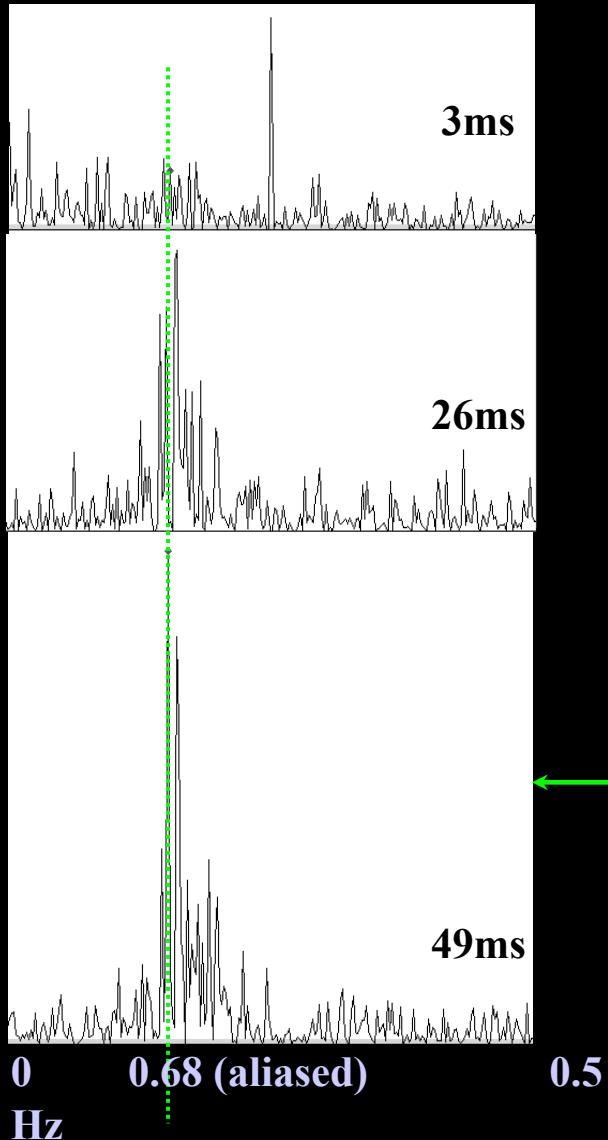
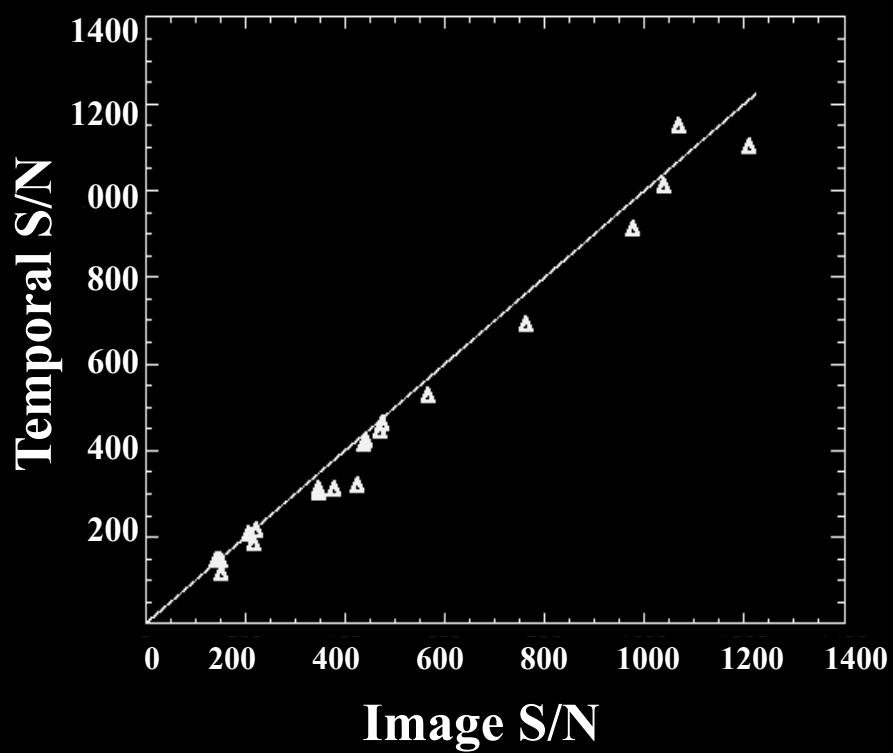


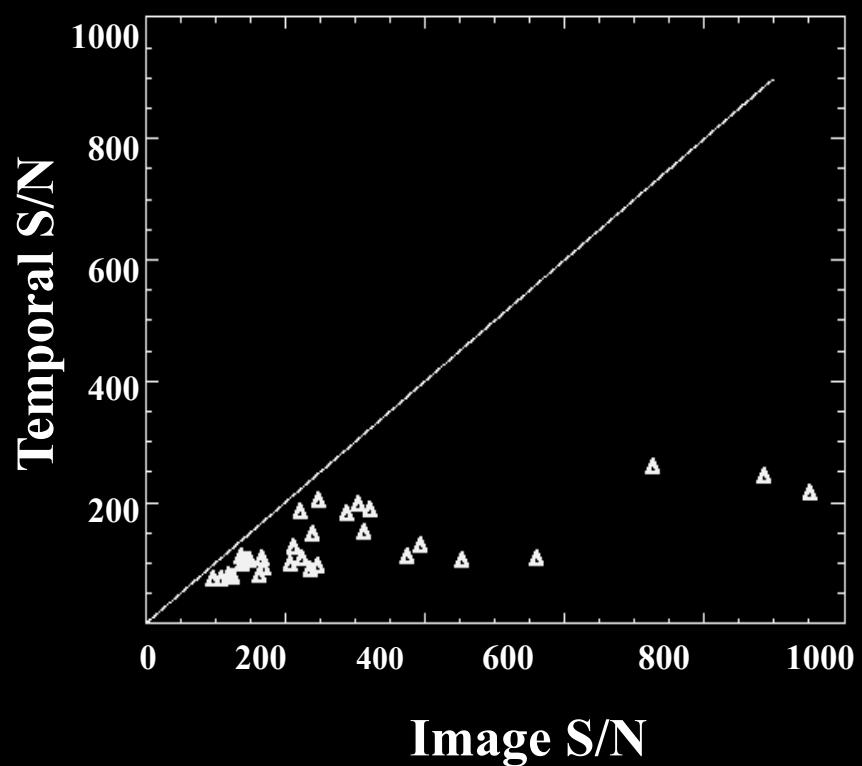
Image
Cardiac map

Temporal S/N vs. Image S/N

PHANTOMS

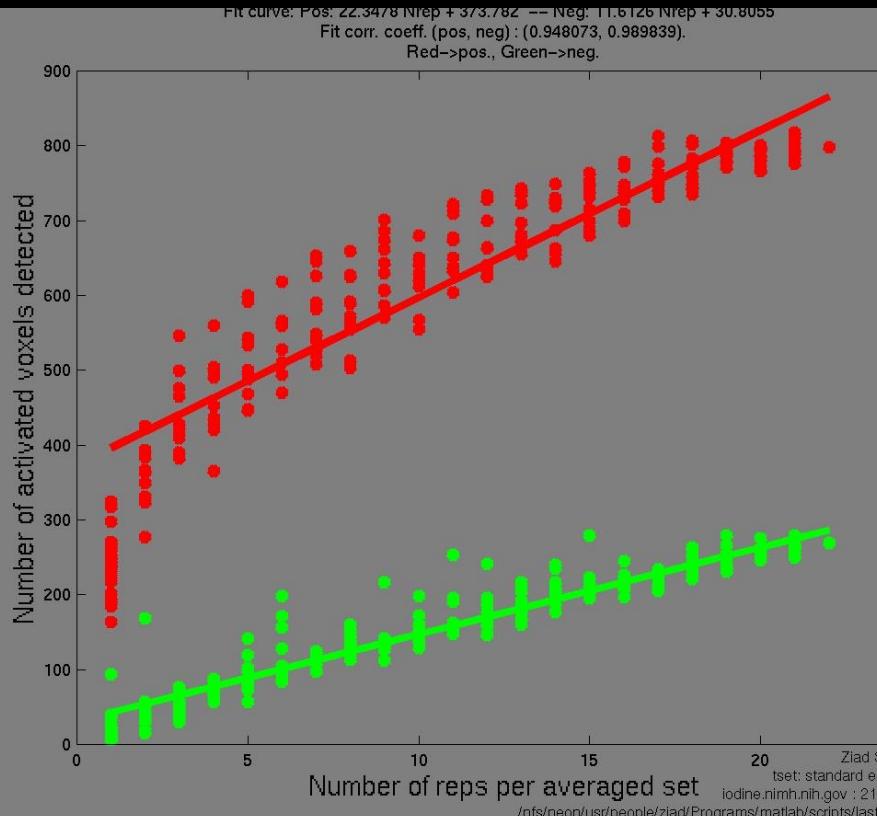


SUBJECTS

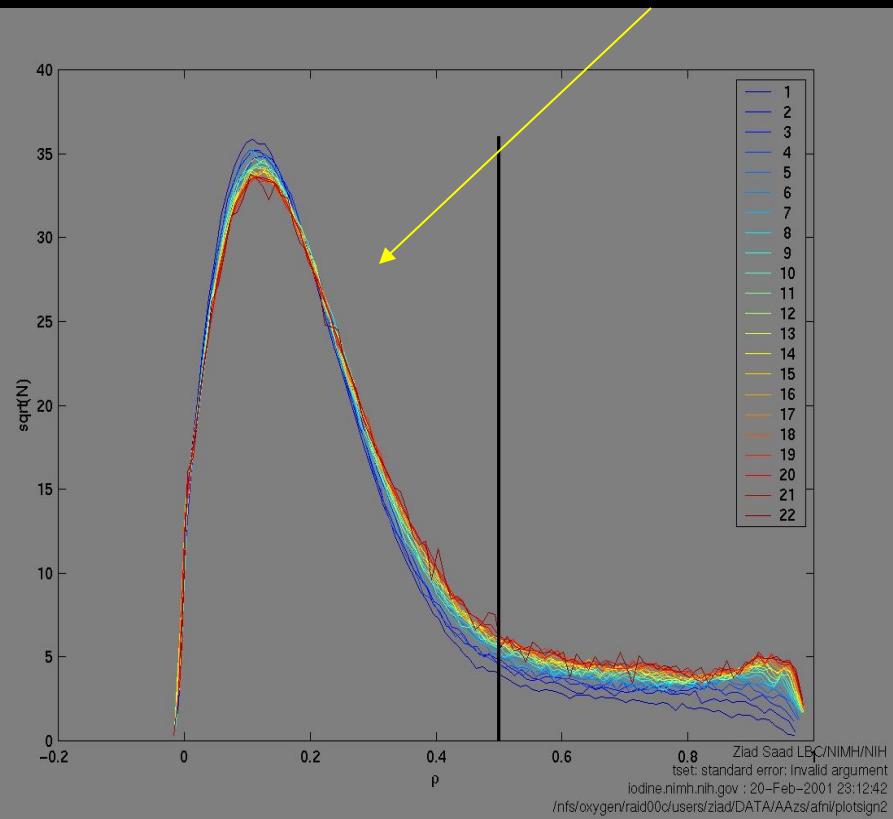


N. Petridou

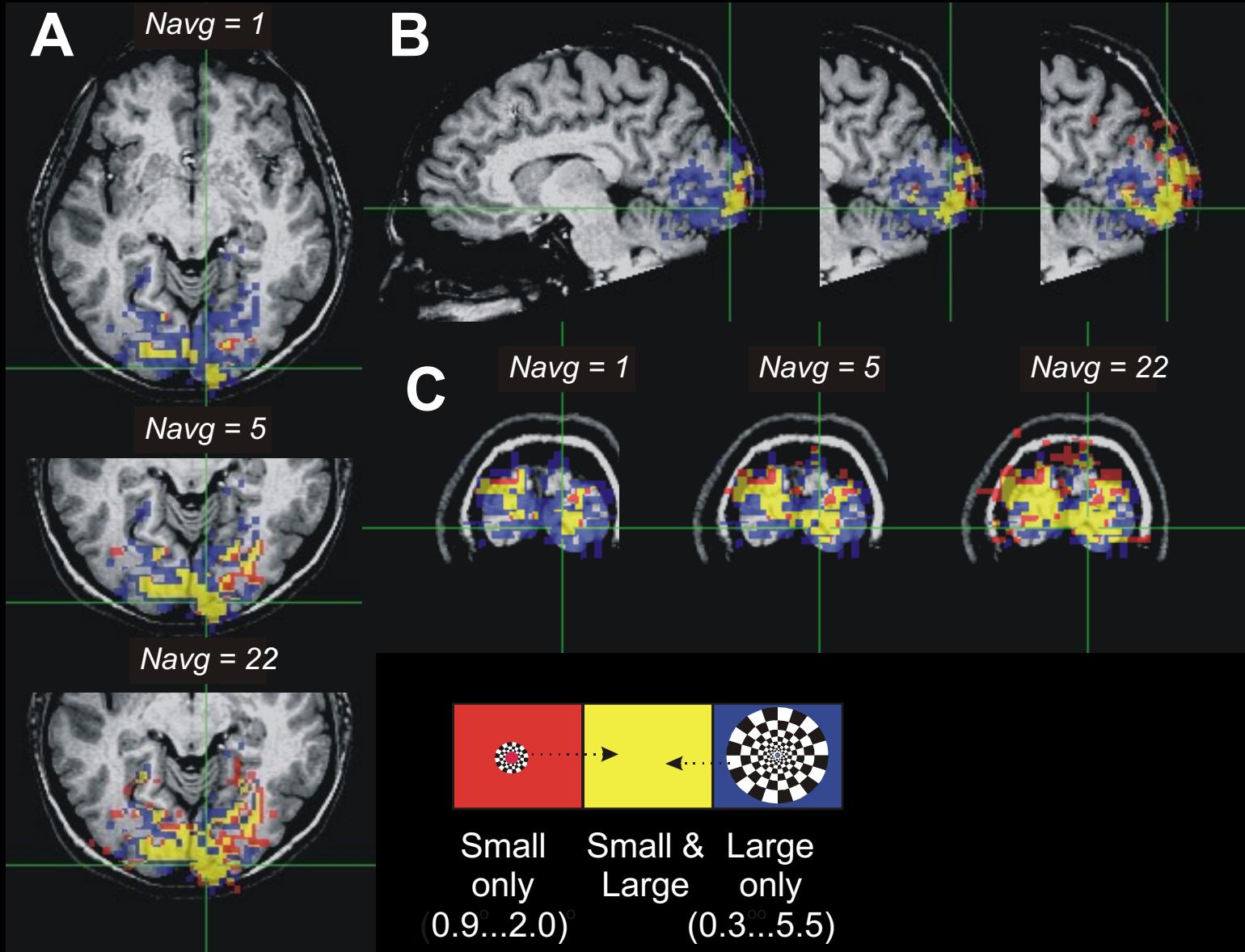
Continuously Growing Activation Area



CC Histogram Inflection Point



Ziad Saad, et al



- Contrast in fMRI

Hemodynamic Specificity

- The Hemodynamic Transfer Function

Location, Latency, Magnitude, Linearity

- Best Results So Far

Temporal Resolution, Spatial Resolution

- Neuronal Activation Input Strategies

Block Design

Phase and Frequency Encoding

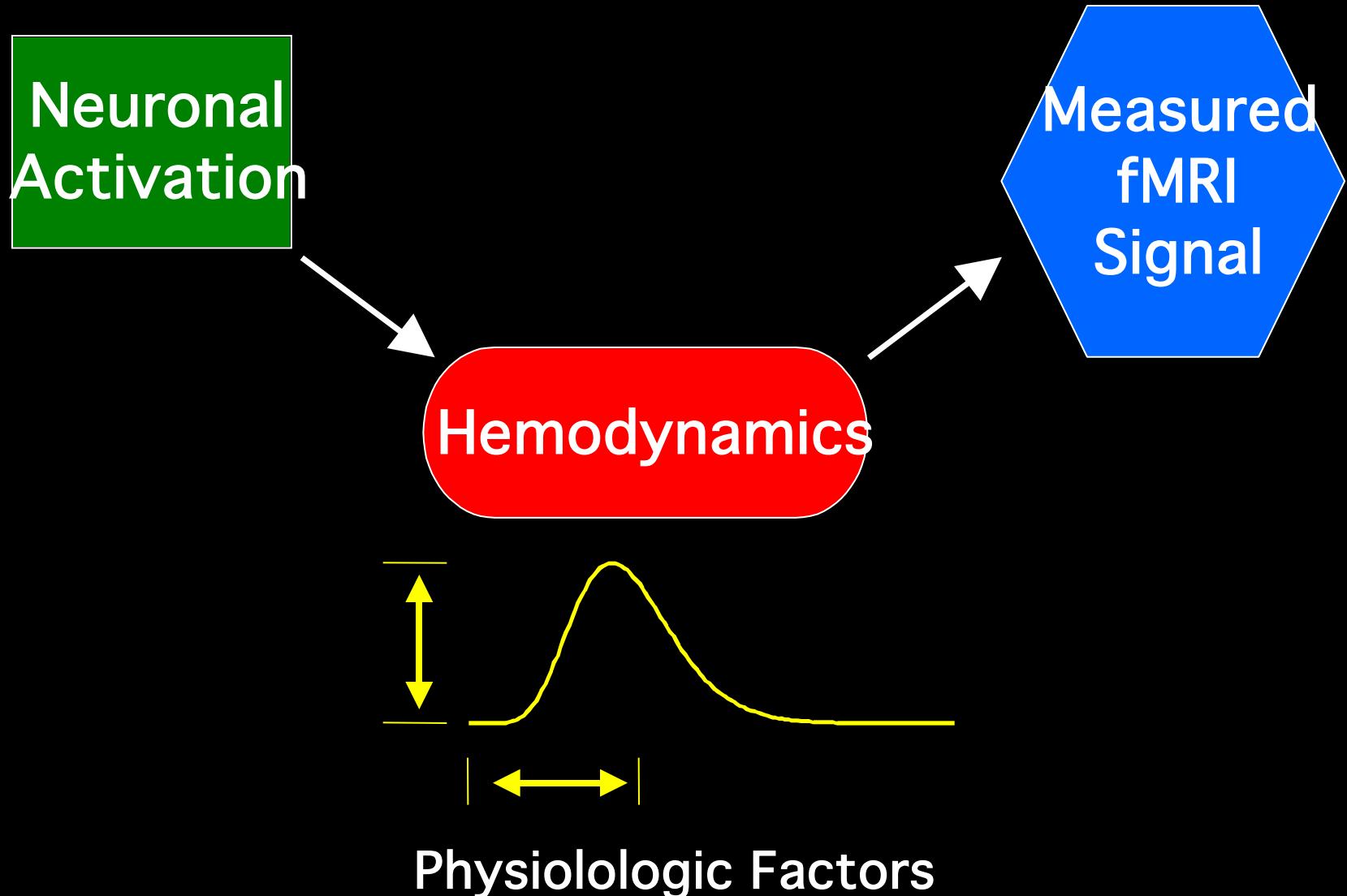
Orthogonal Designs

Parametric Designs

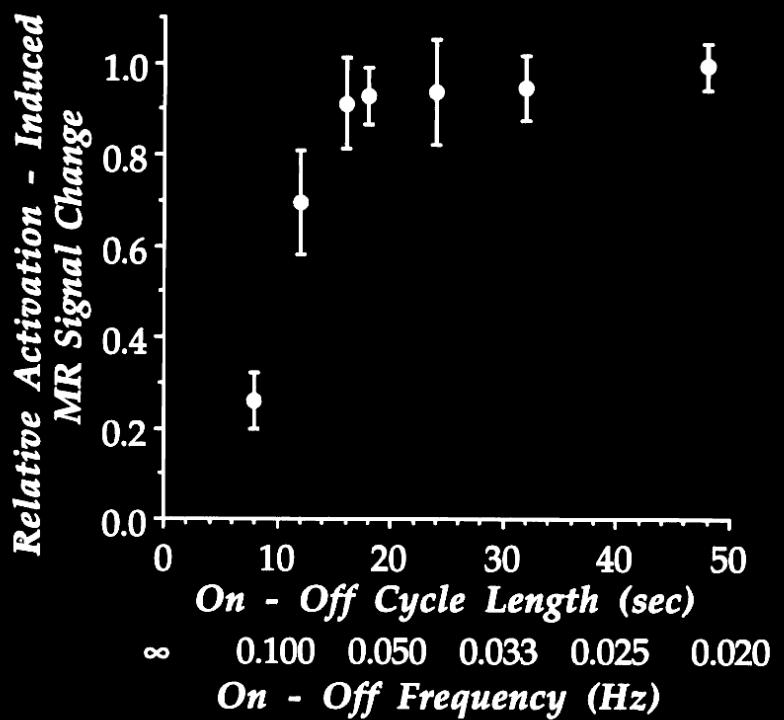
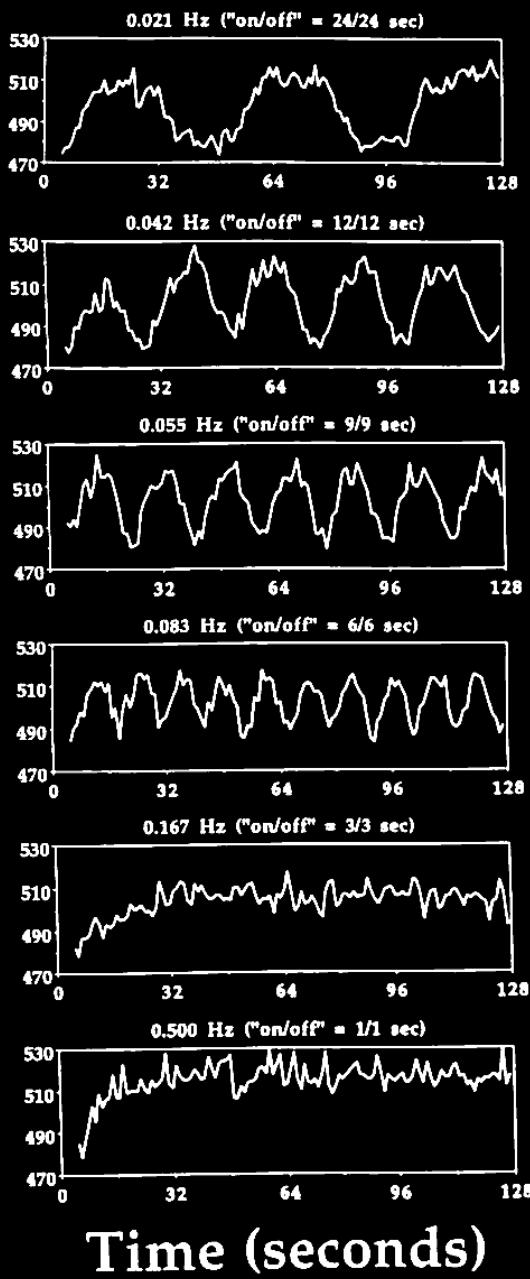
Event-Related Designs

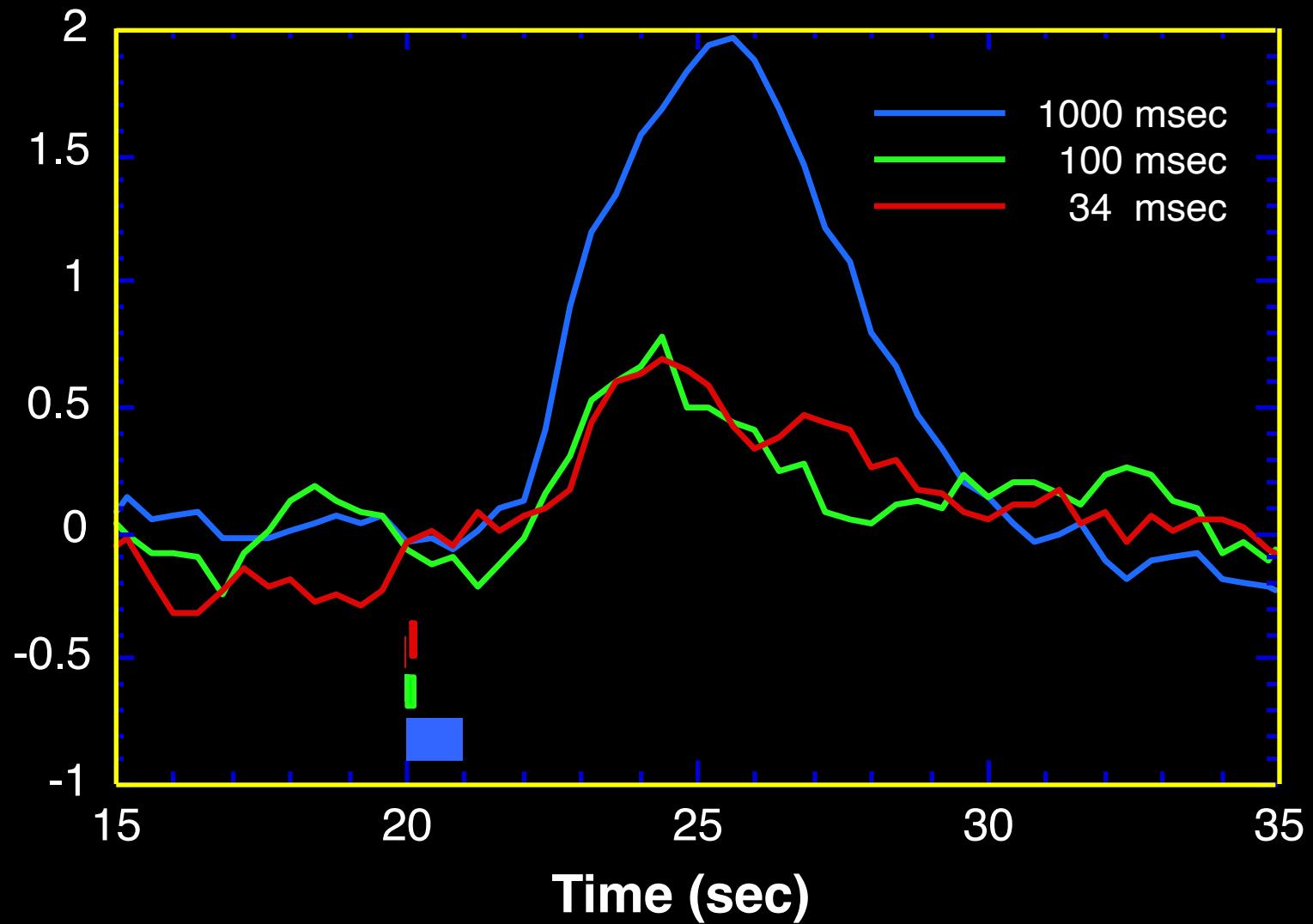
Free Behavior Designs

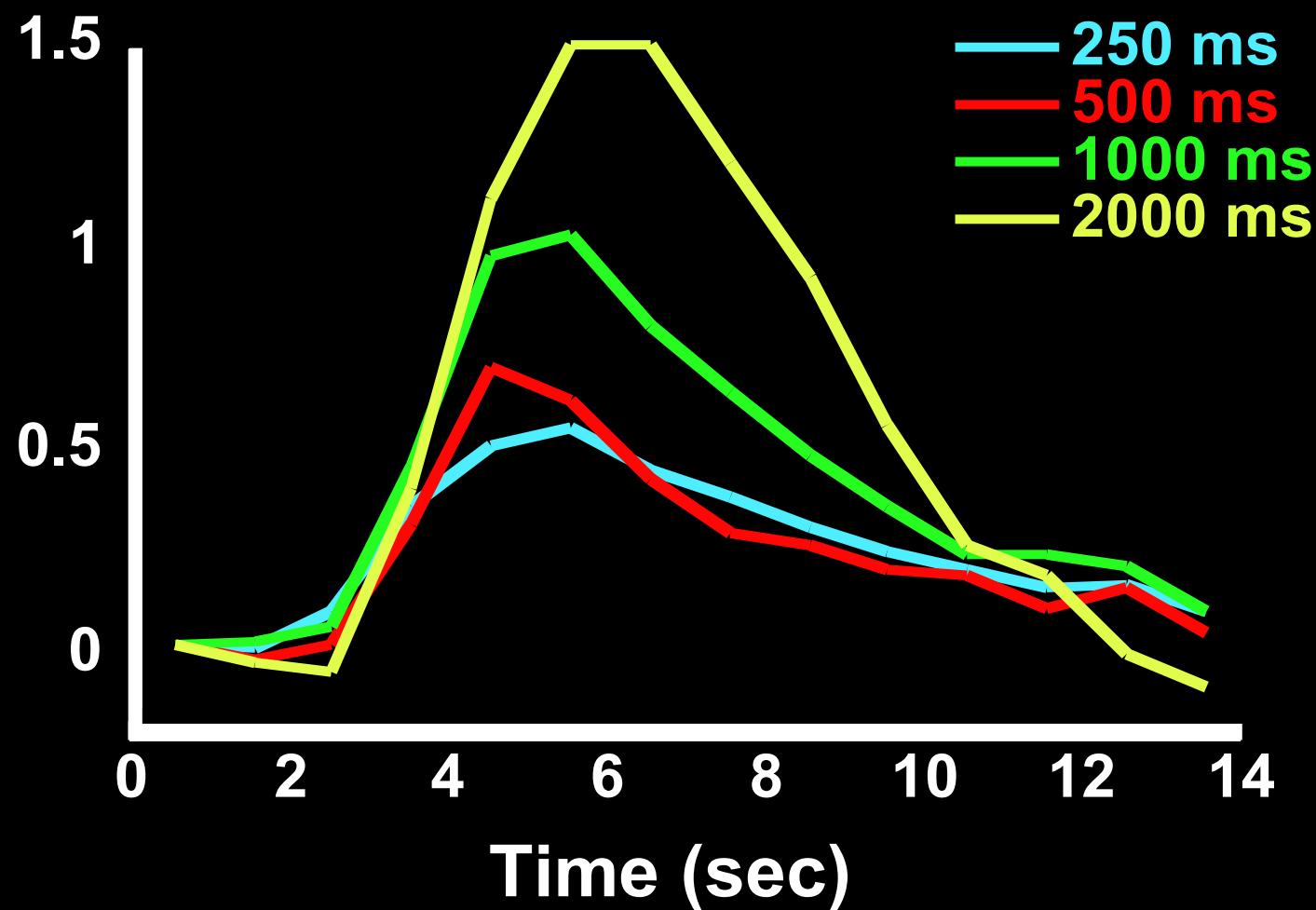
Hemodynamic Transfer Function



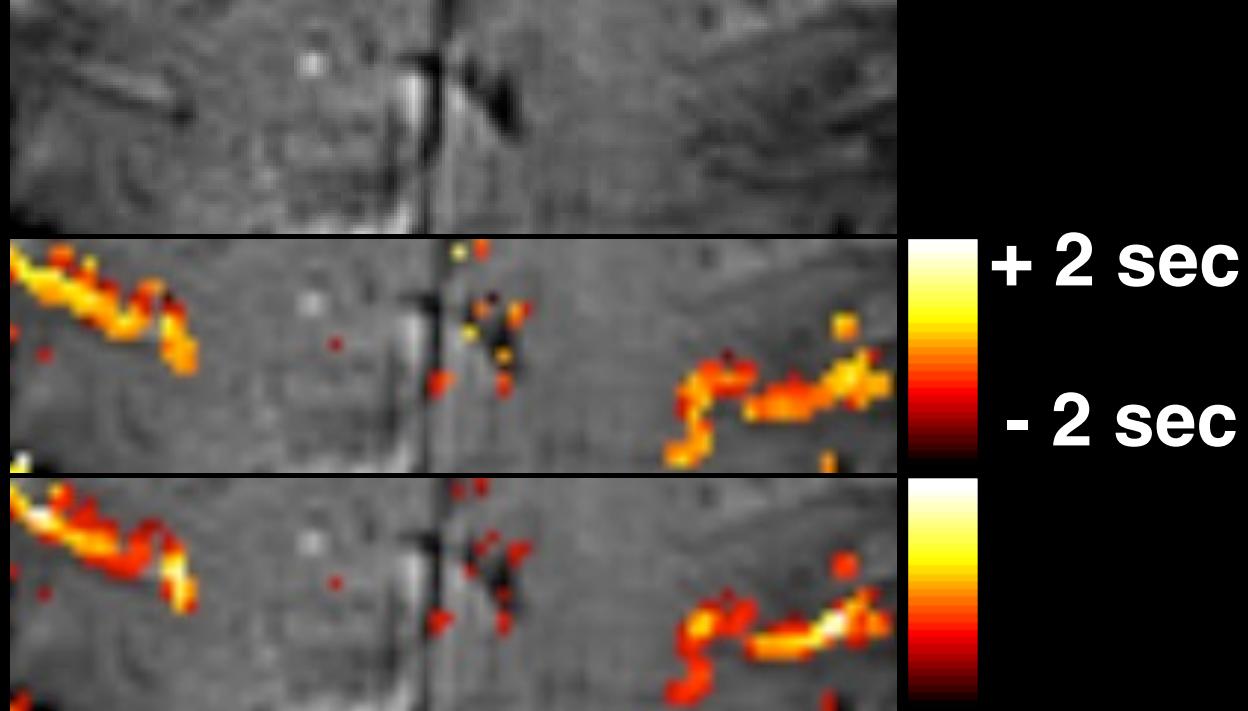
MRI Signal



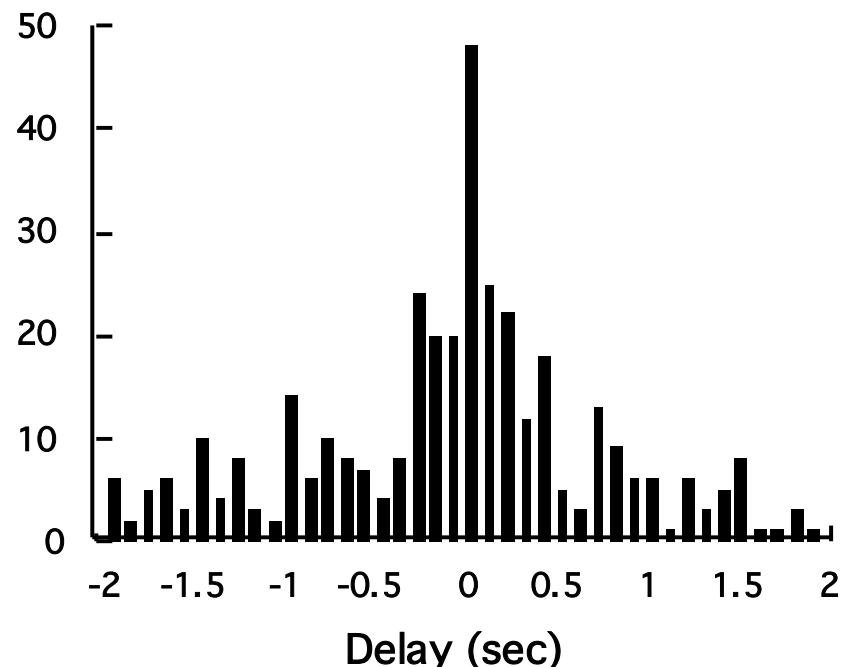
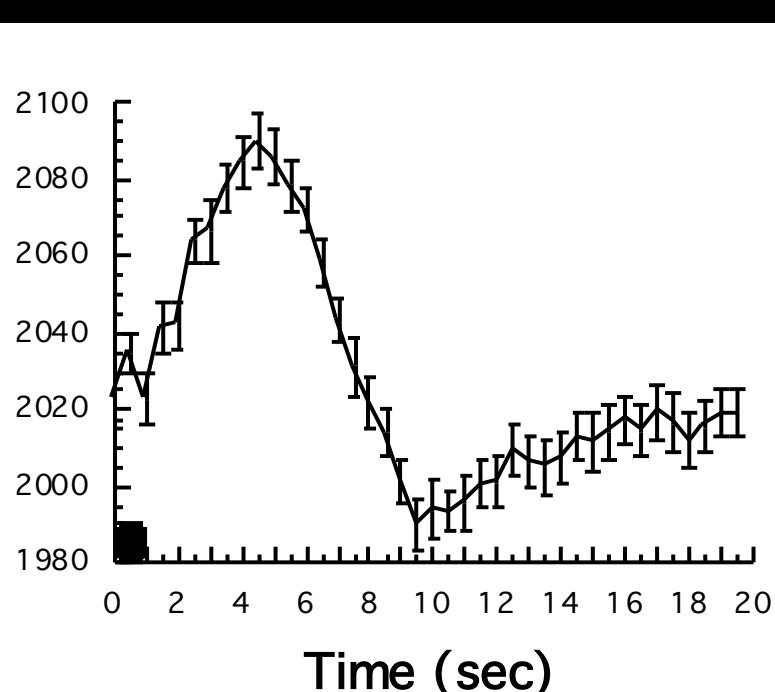


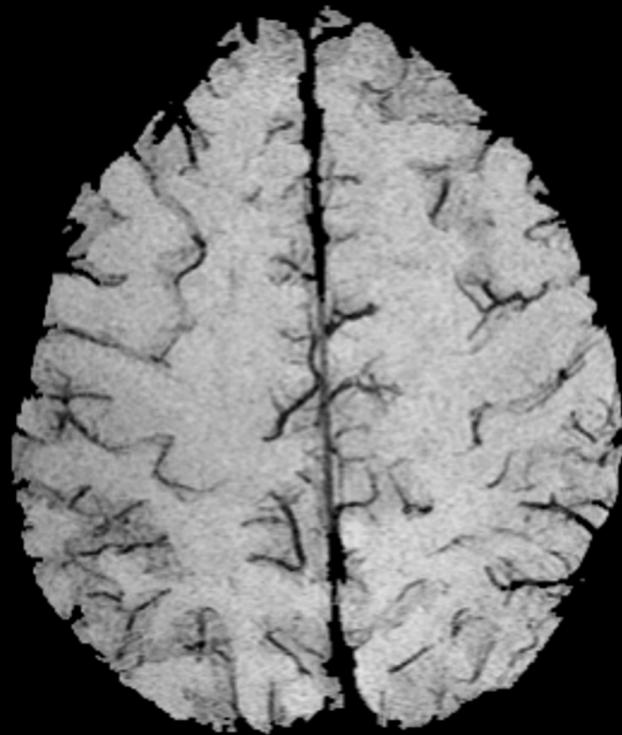


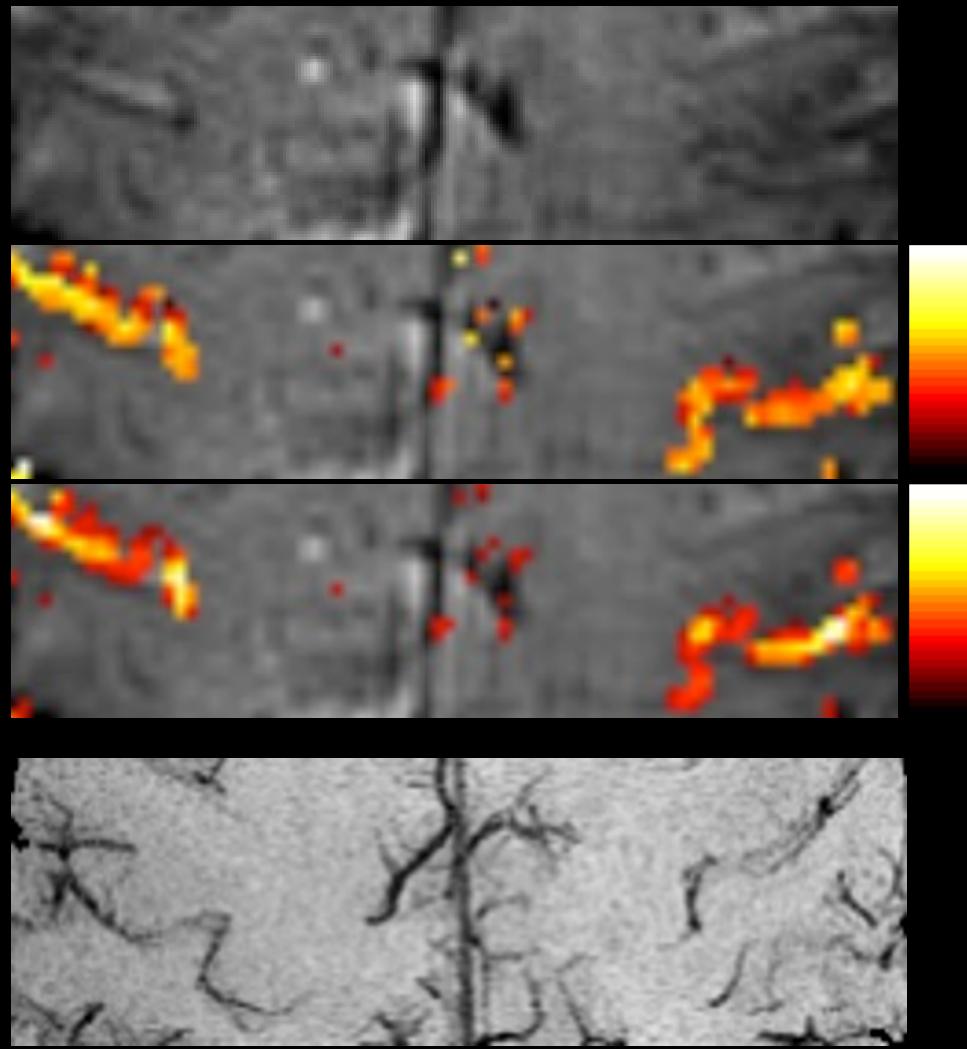
Latency



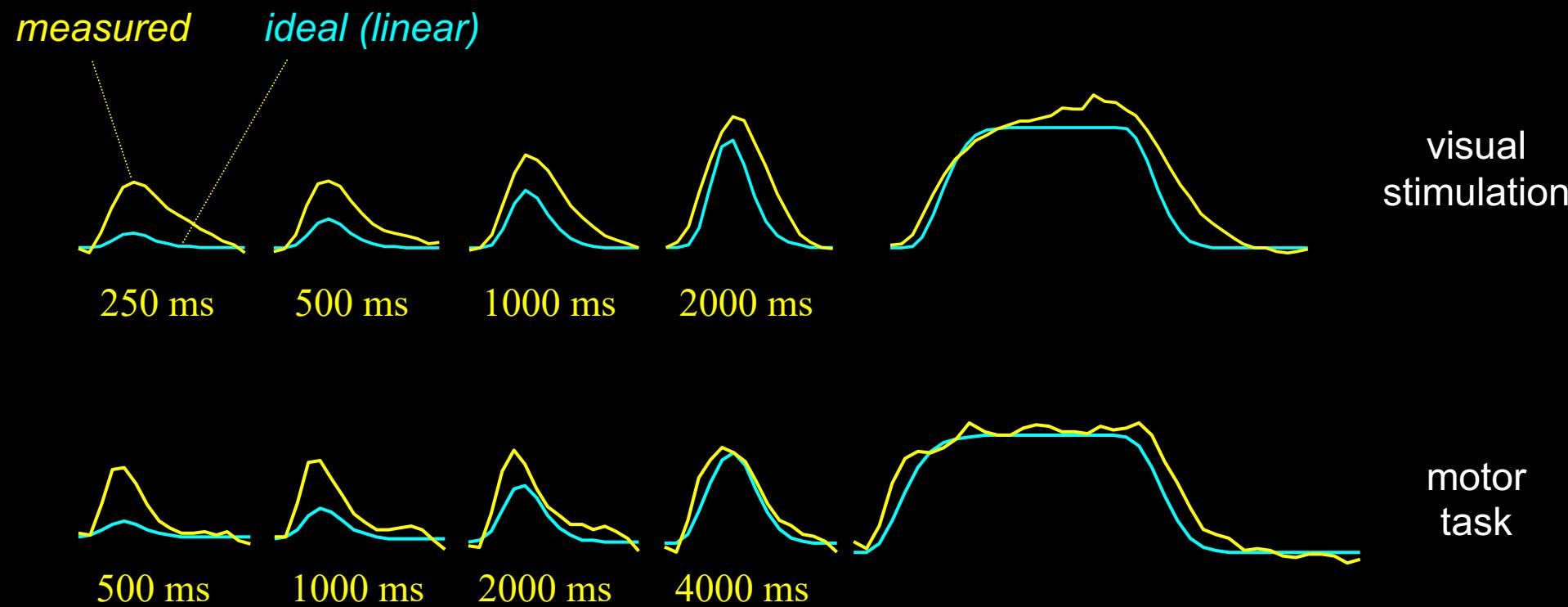
Magnitude



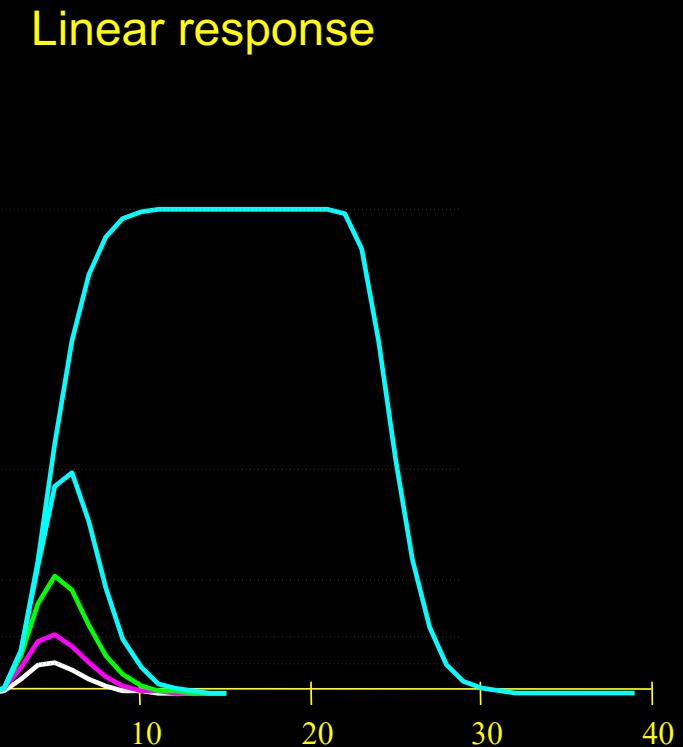
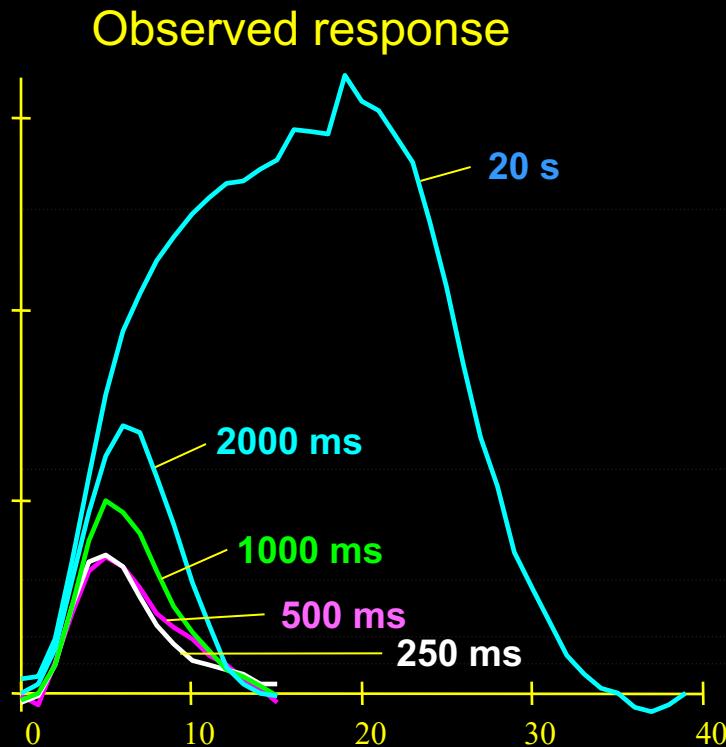




Observed Responses

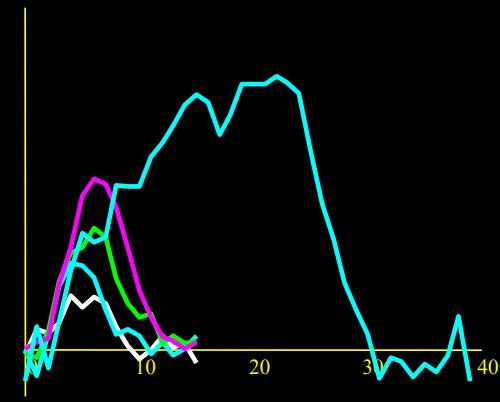
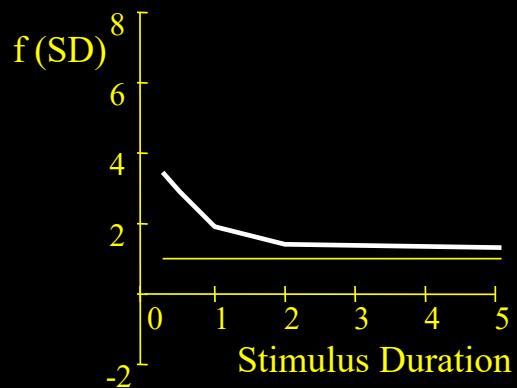
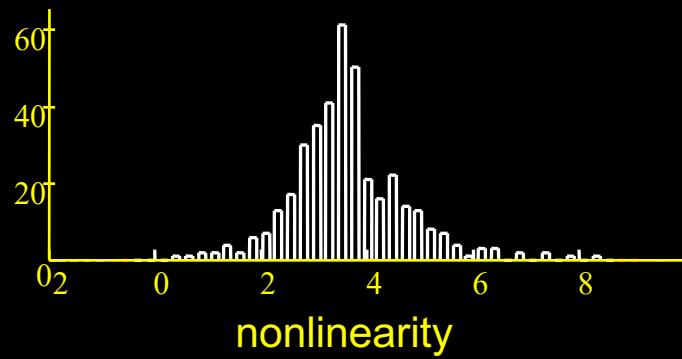
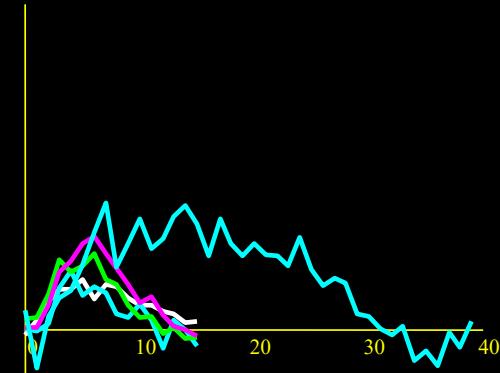
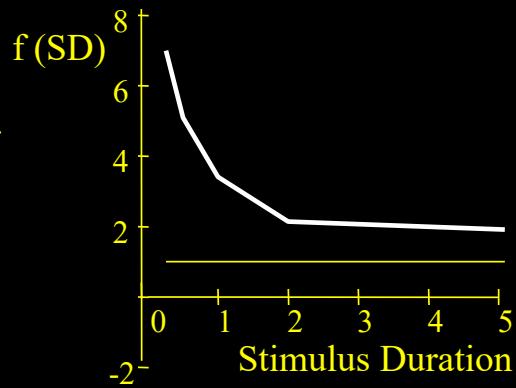
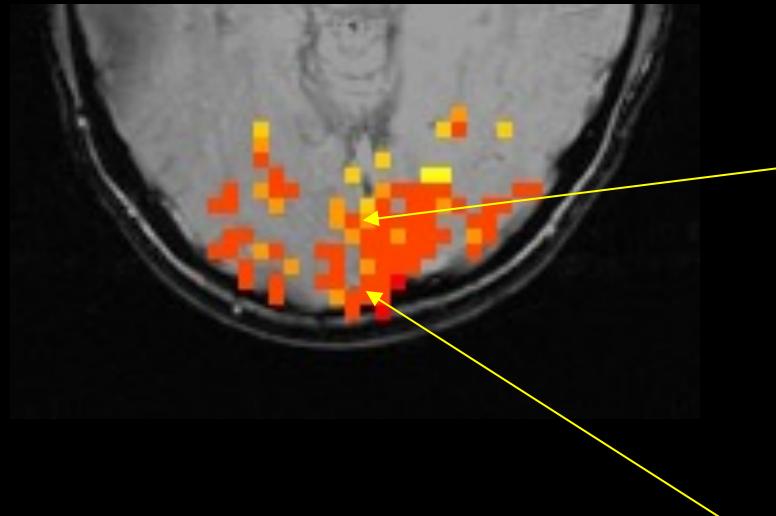


BOLD response is nonlinear



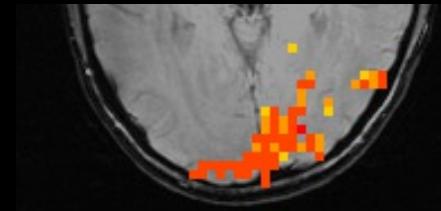
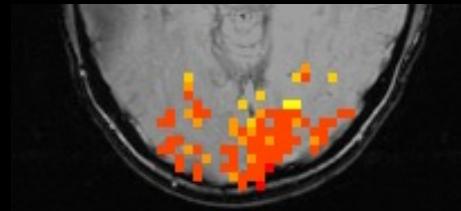
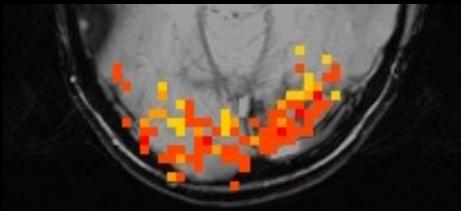
Short duration stimuli produce larger responses than expected

Results – visual task

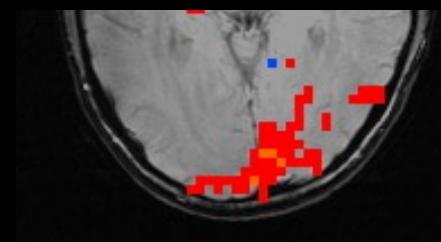
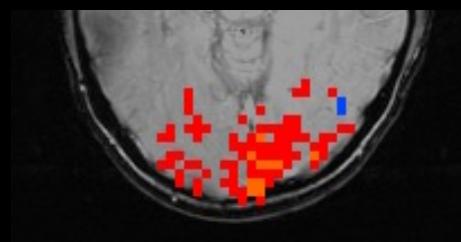
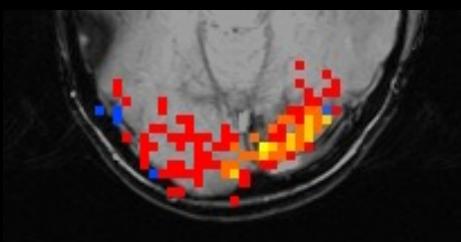


Results – visual task

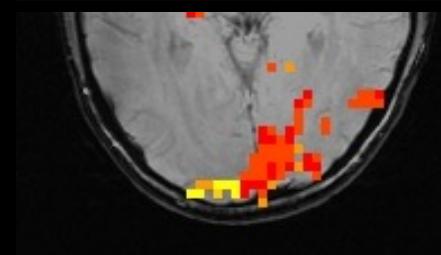
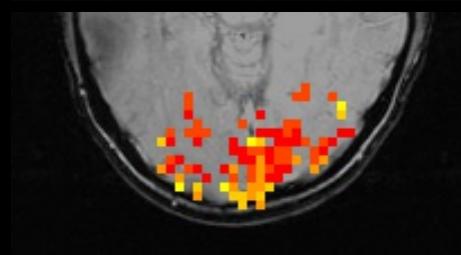
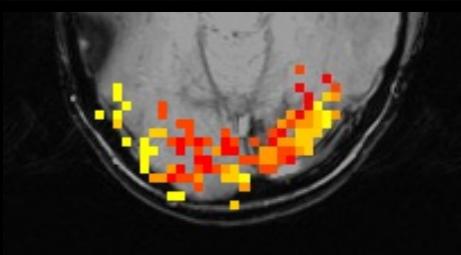
Nonlinearity



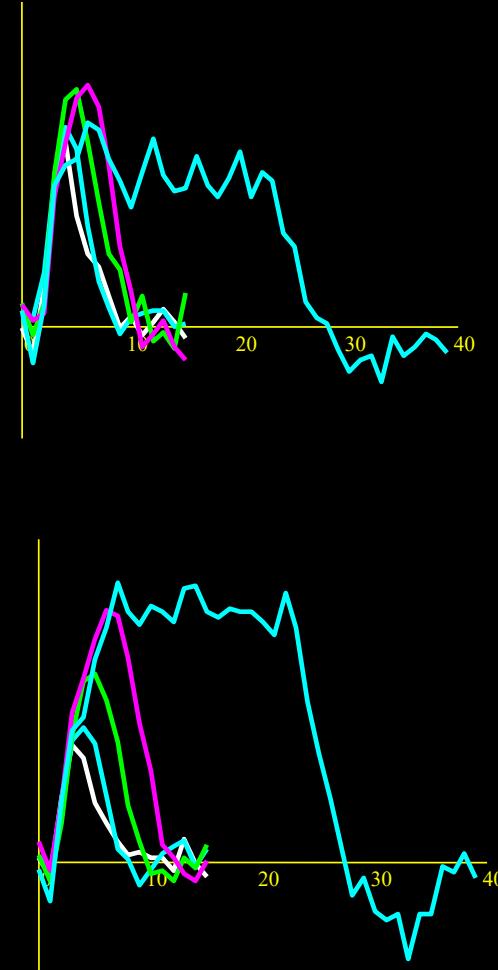
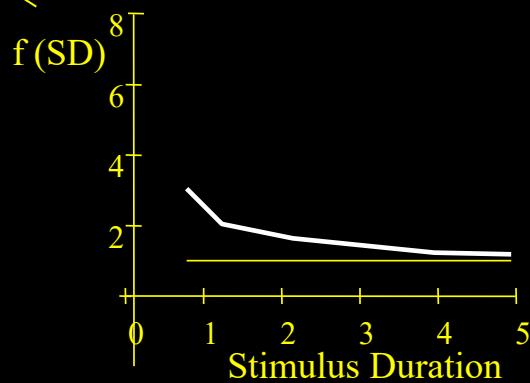
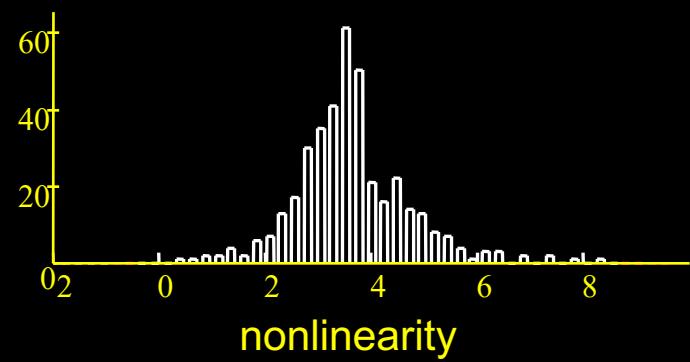
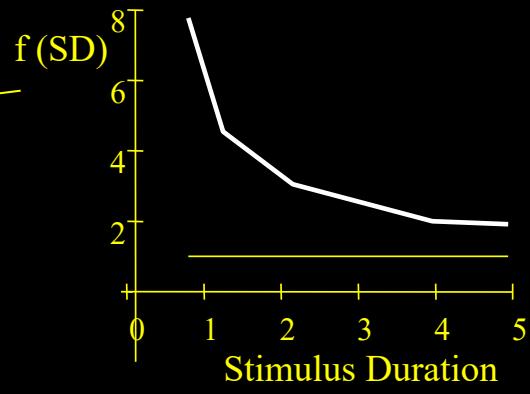
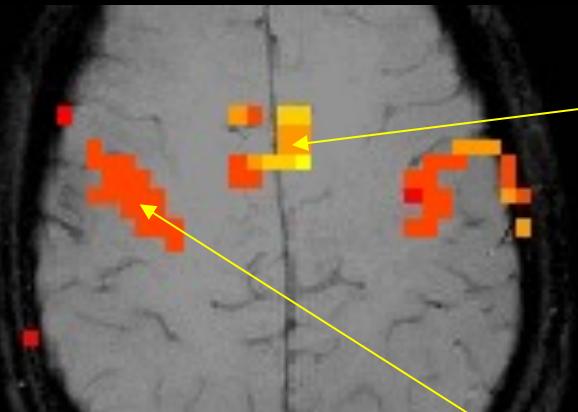
Magnitude



Latency

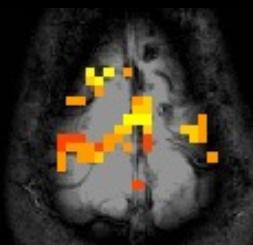
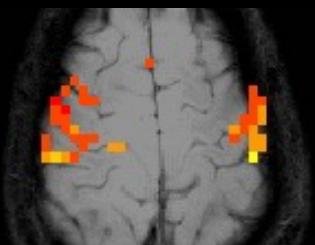
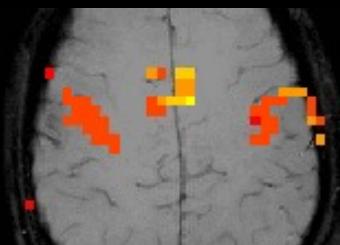


Results – motor task

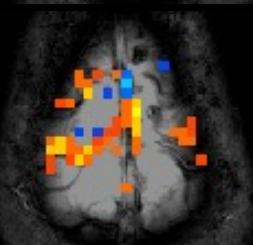
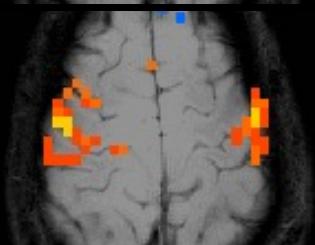
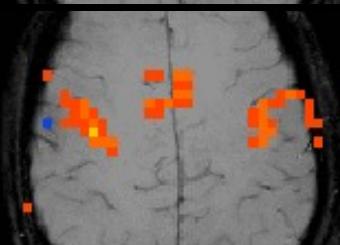


Results – motor task

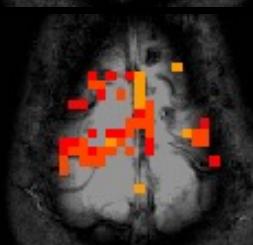
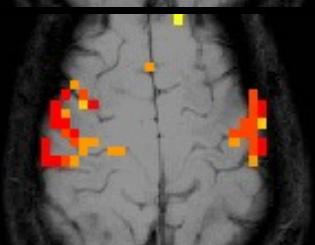
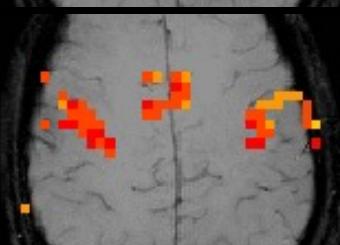
Nonlinearity



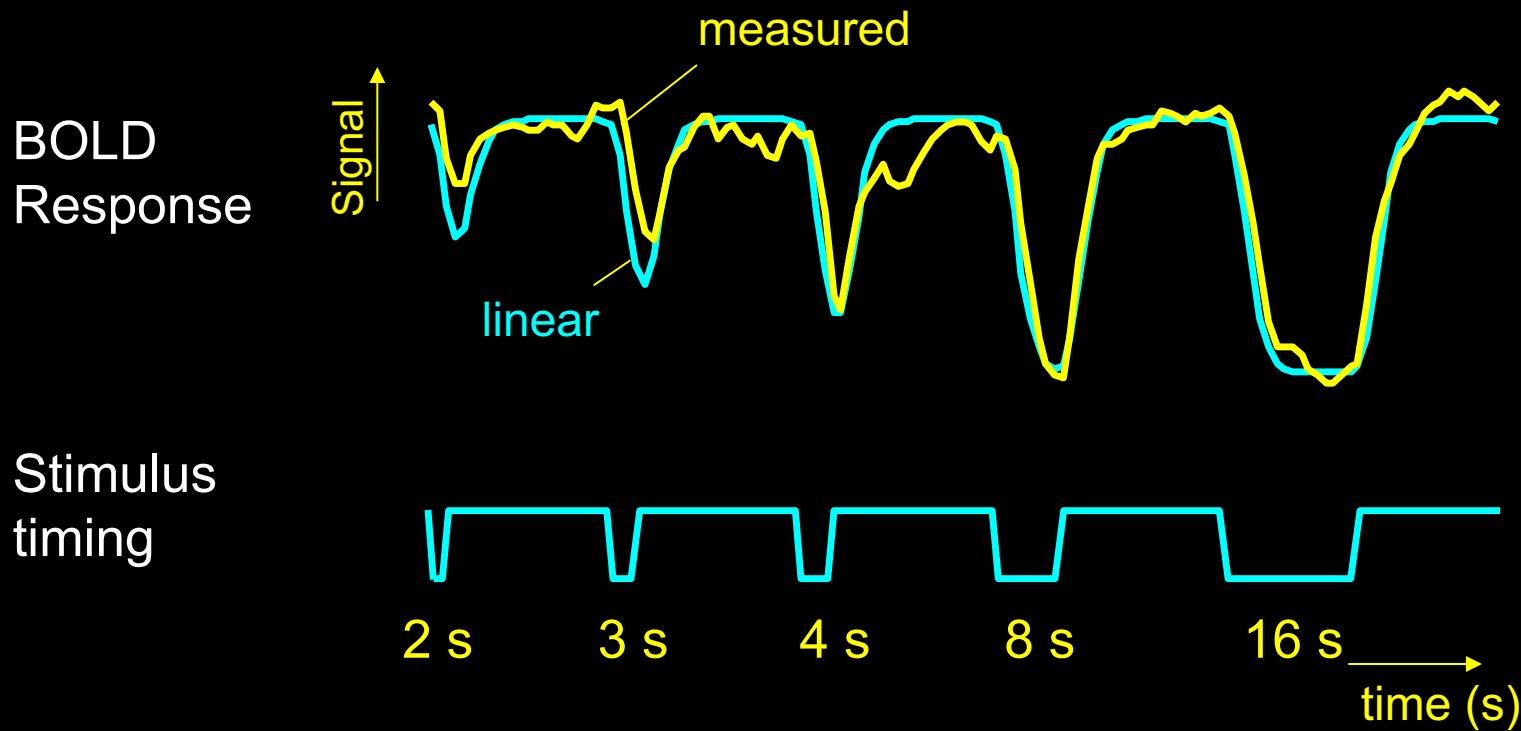
Magnitude



Latency



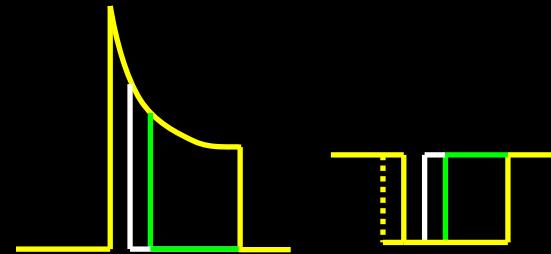
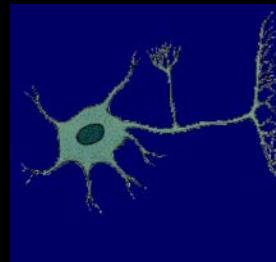
Different stimulus “ON” periods



Brief stimulus OFF periods produce smaller decreases than expected

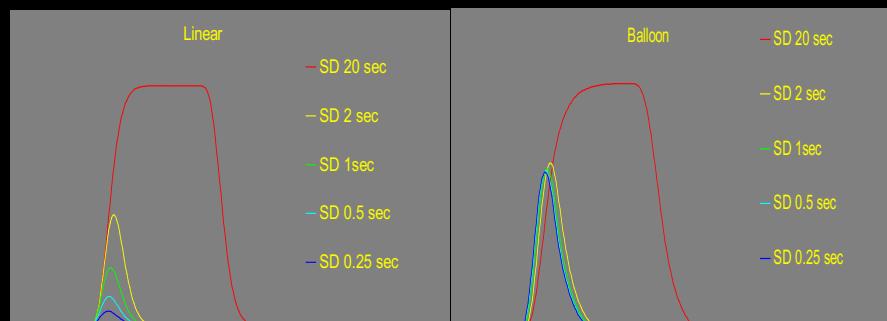
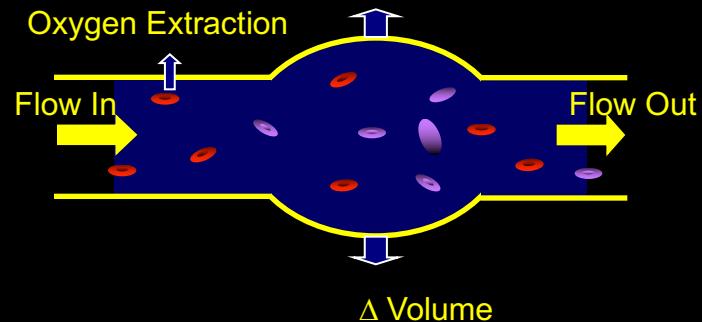
Sources of this Nonlinearity

- Neuronal



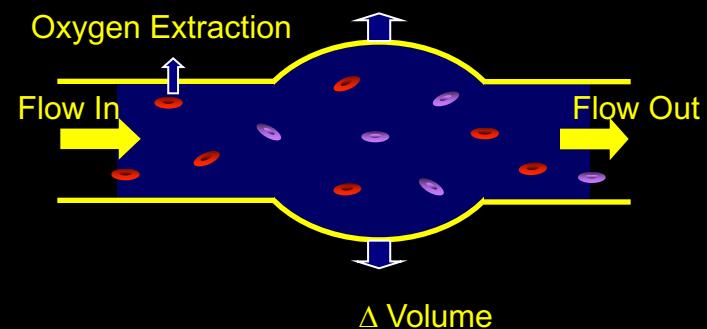
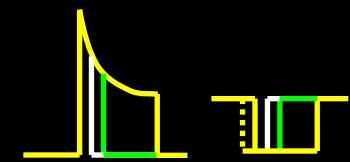
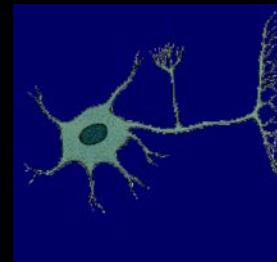
- Hemodynamic

- Oxygen extraction
- Blood volume dynamics

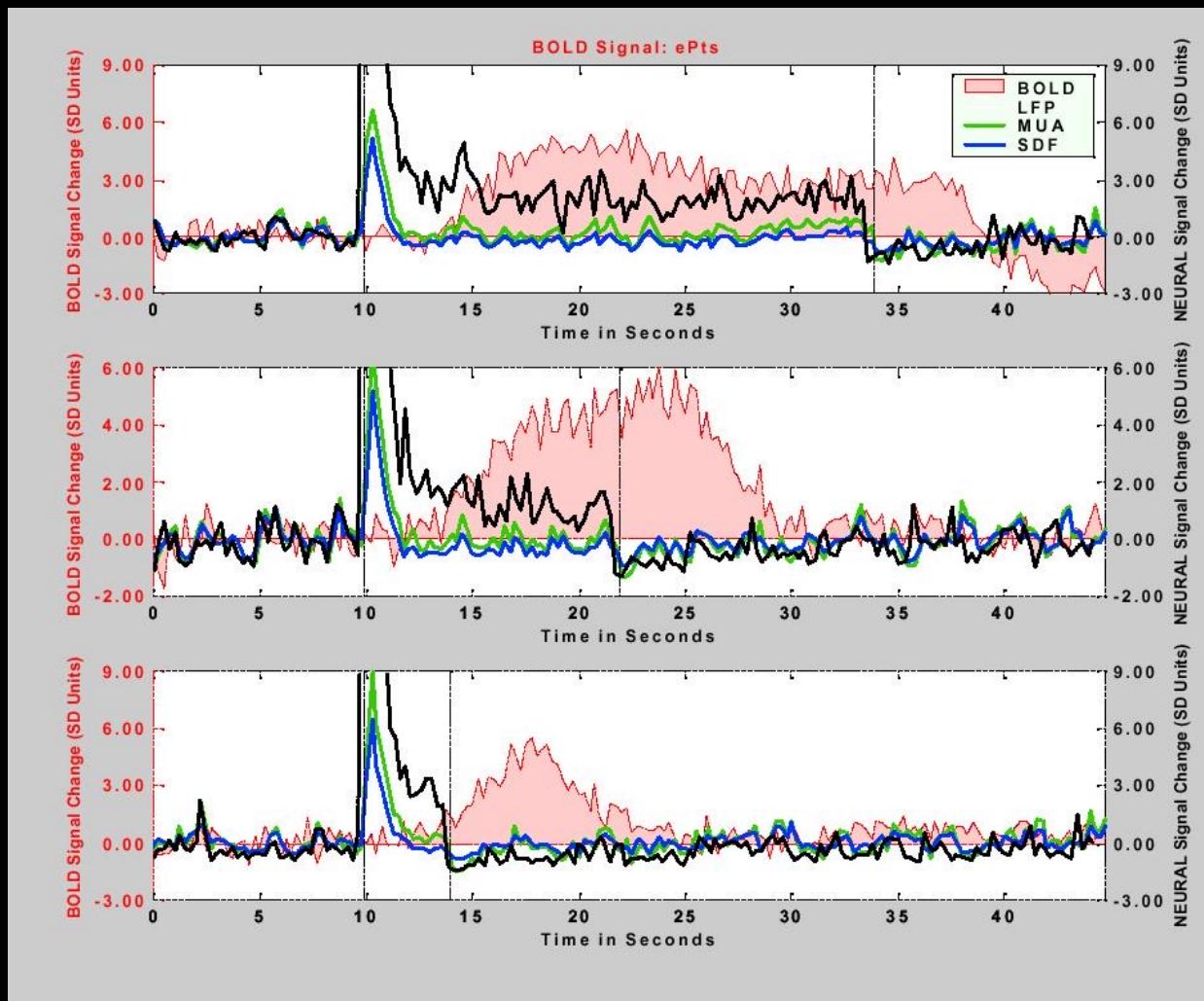


Sources of this Nonlinearity

- Neuronal
- Hemodynamic
 - Oxygen extraction
 - Blood volume dynamics

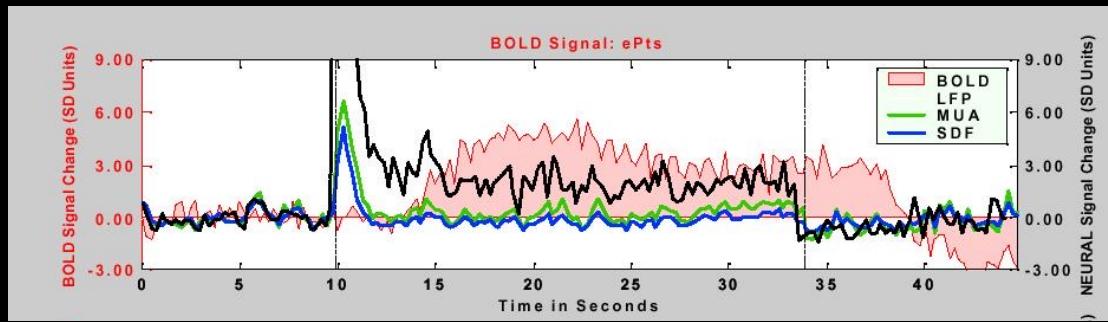


BOLD Correlation with Neuronal Activity

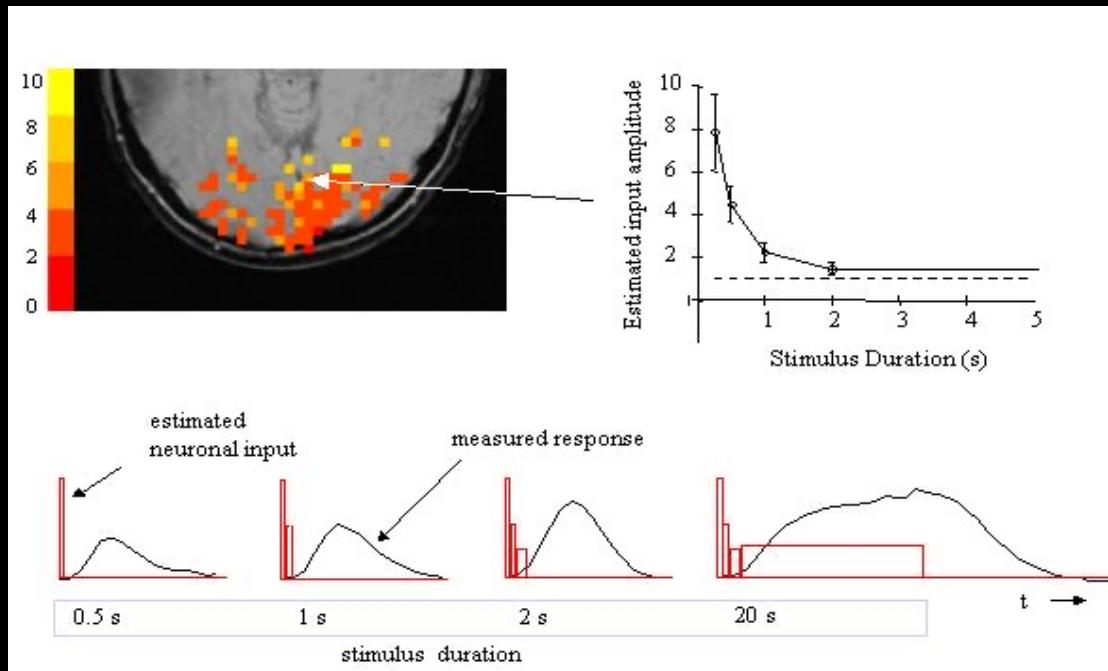


Logothetis et al. Nature, 412, 150-157

BOLD Correlation with Neuronal Activity



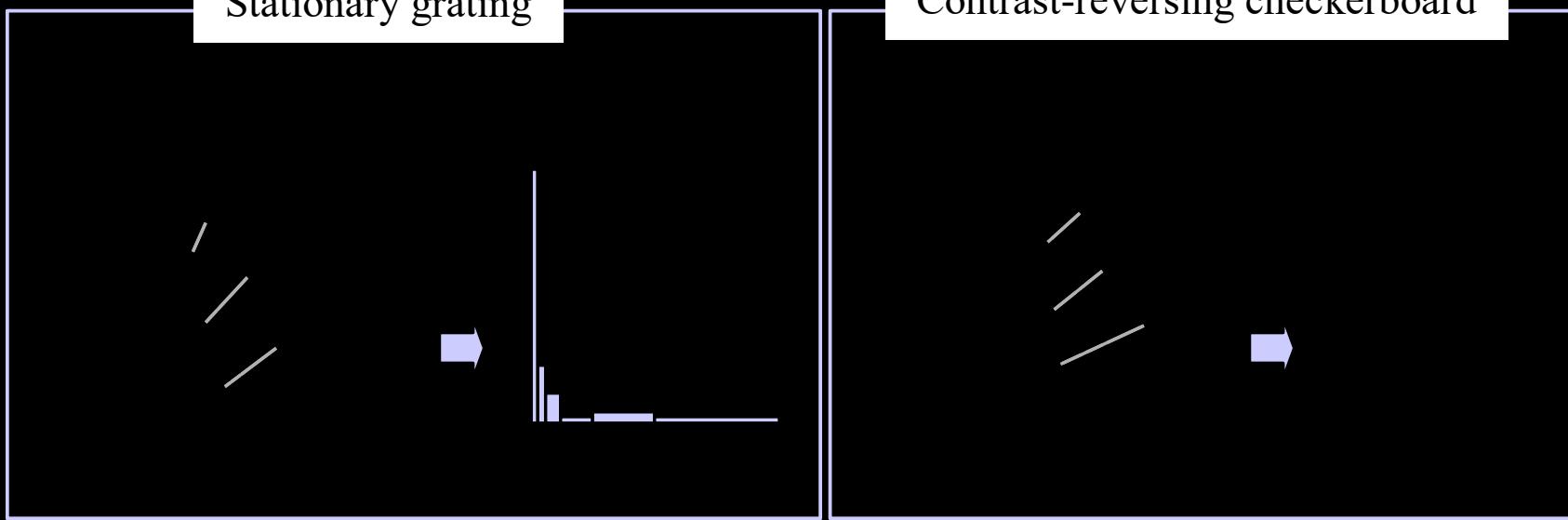
Logothetis et al. Nature, 412, 150-157



Bandettini and Ungerleider, Nature Neuroscience, 4, 864-866

Stationary grating

Contrast-reversing checkerboard



Varying “ON” and “OFF” periods

- *Rapid event-related design with varying ISI*



8% ON



25% ON

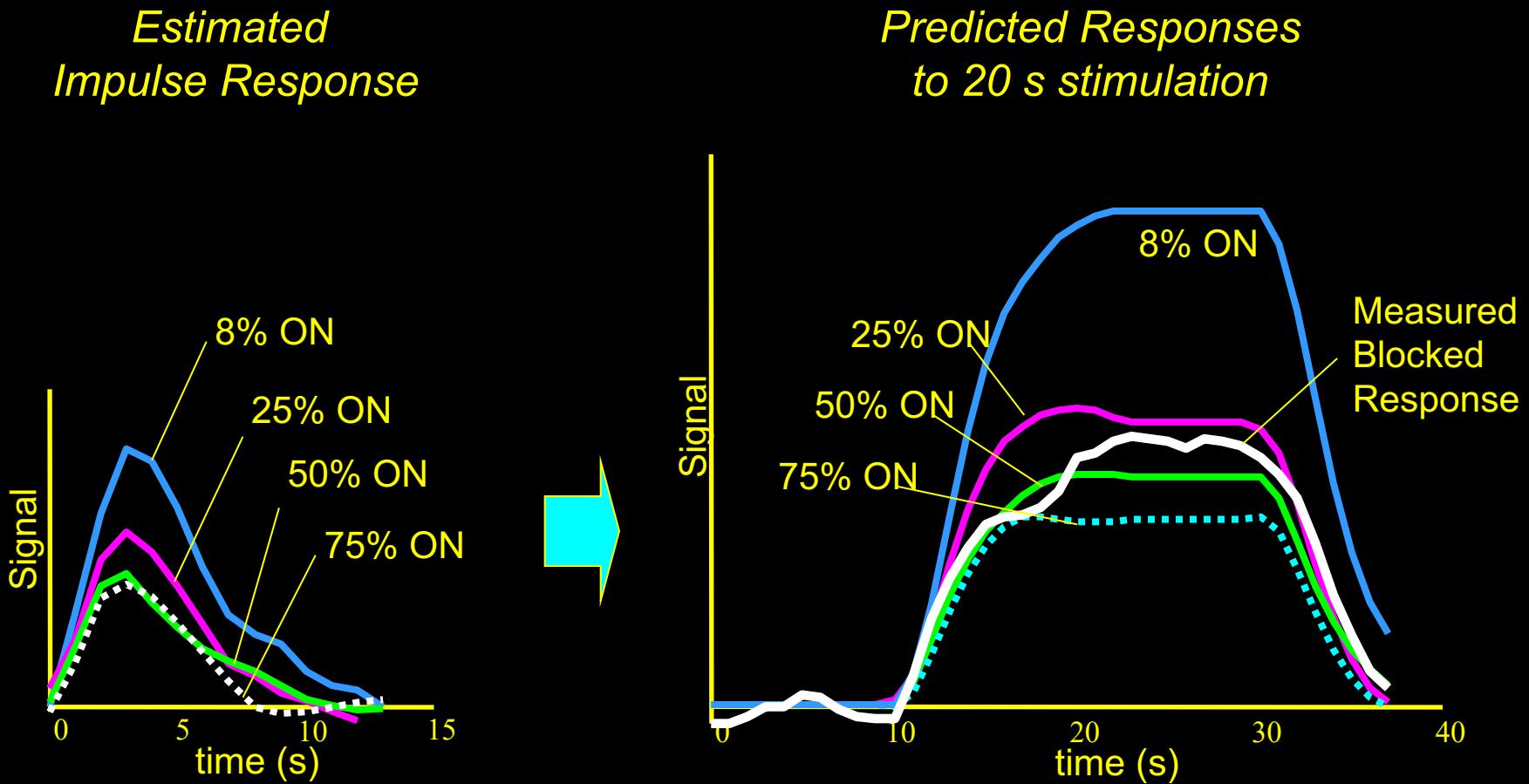


50% ON

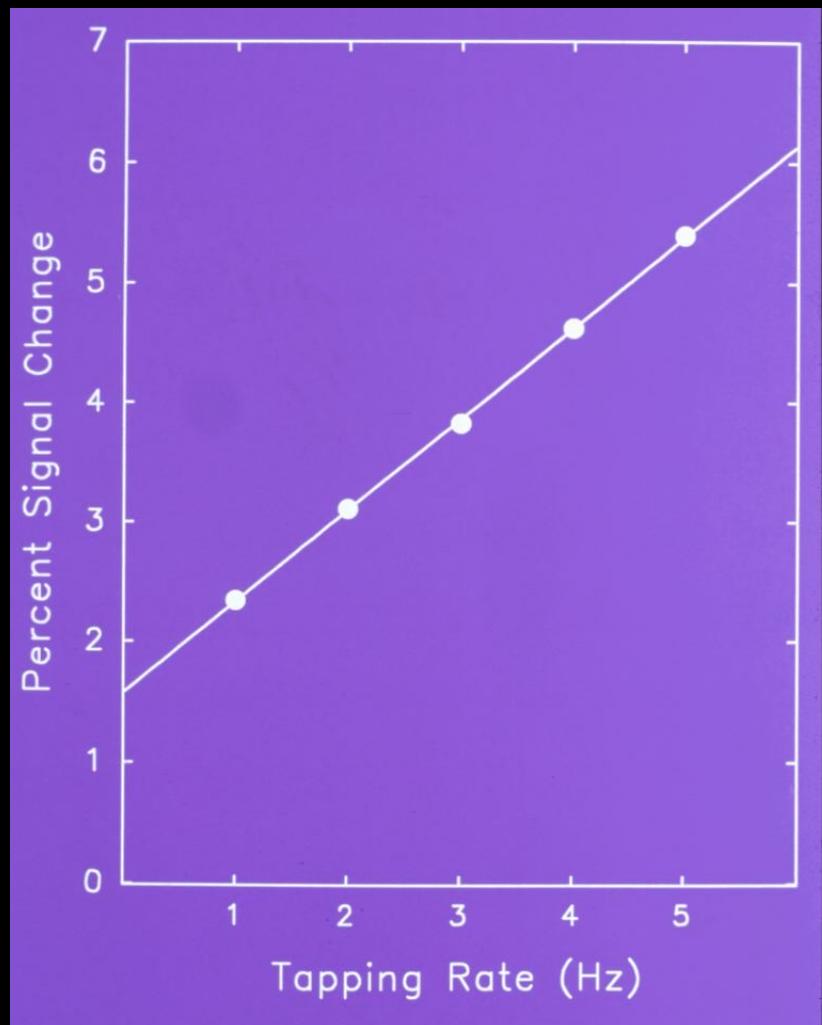


75% ON

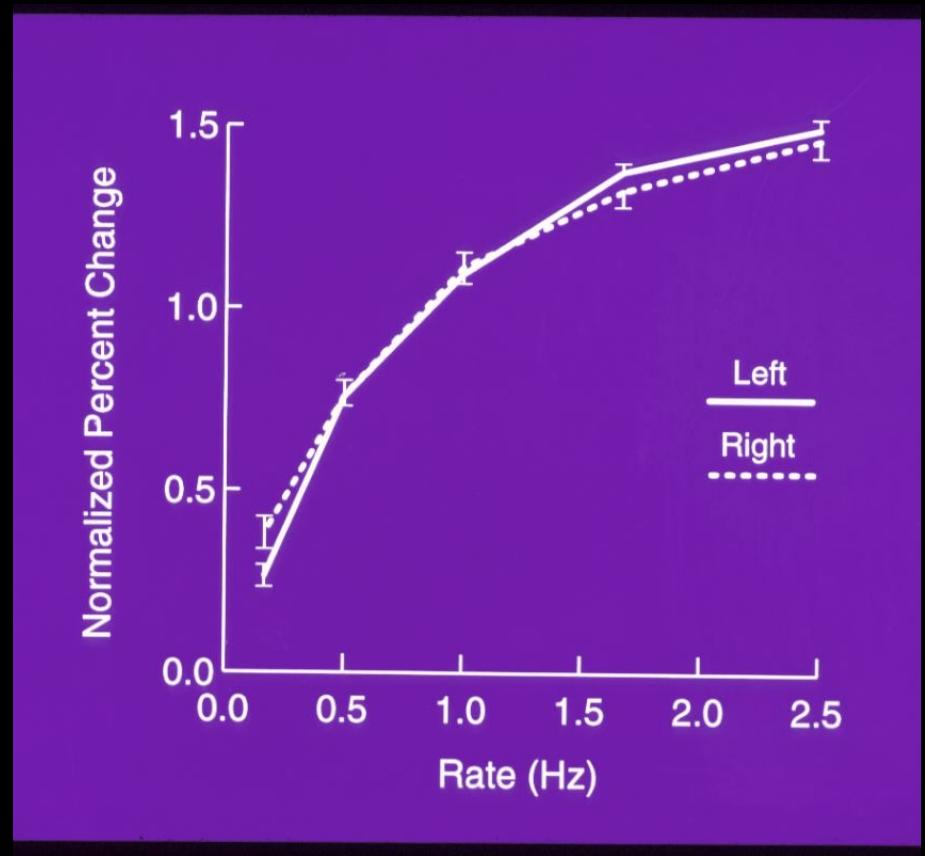
Varying “ON” and “OFF” periods

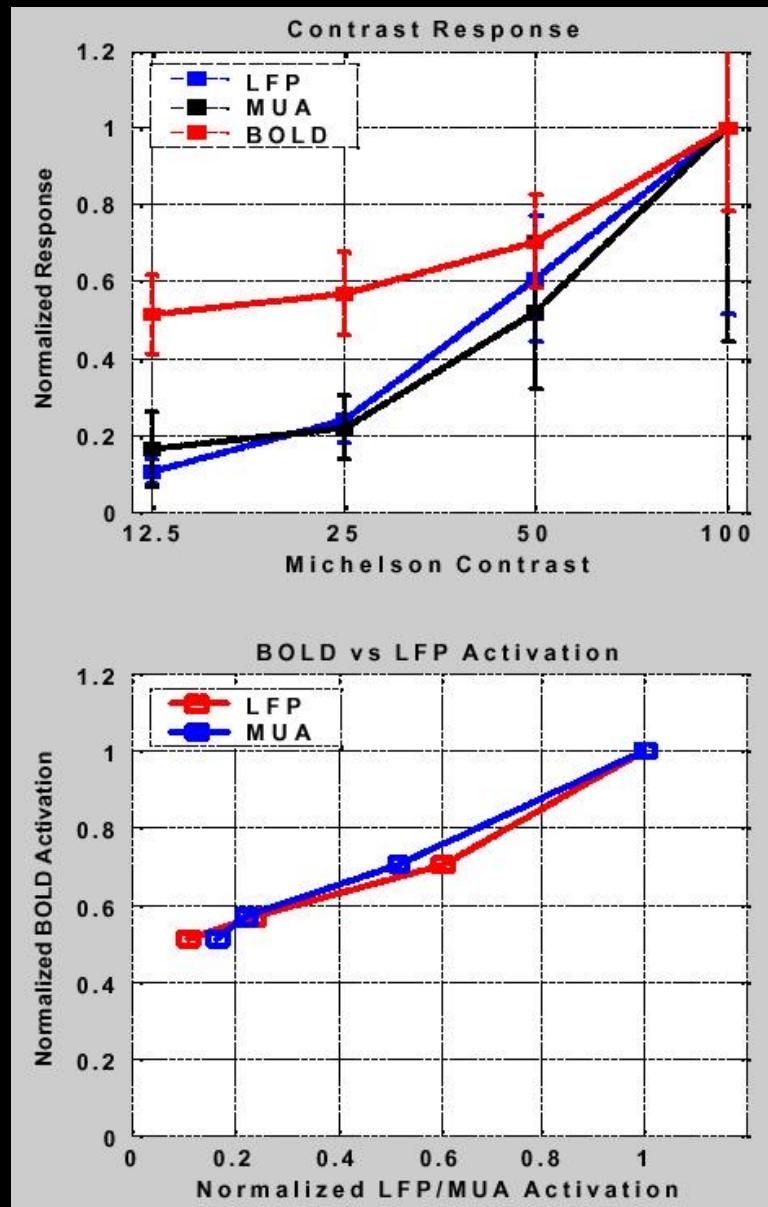


Motor Cortex



Auditory Cortex

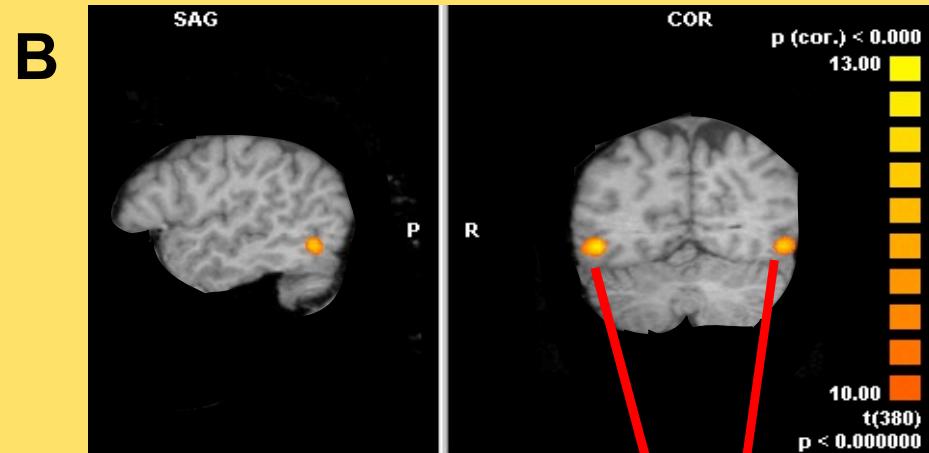
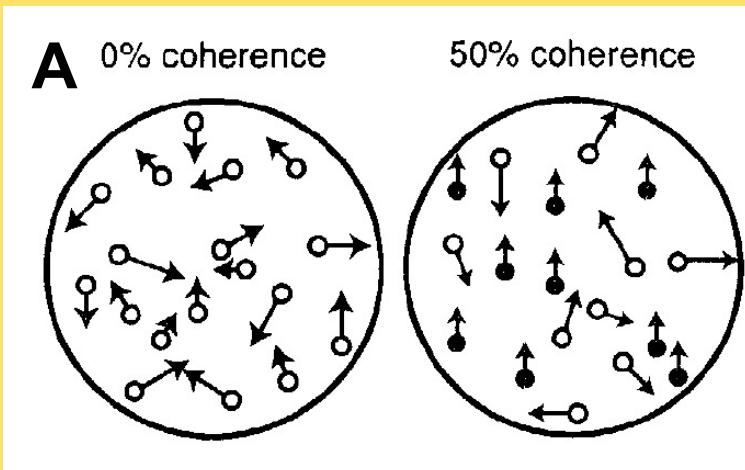




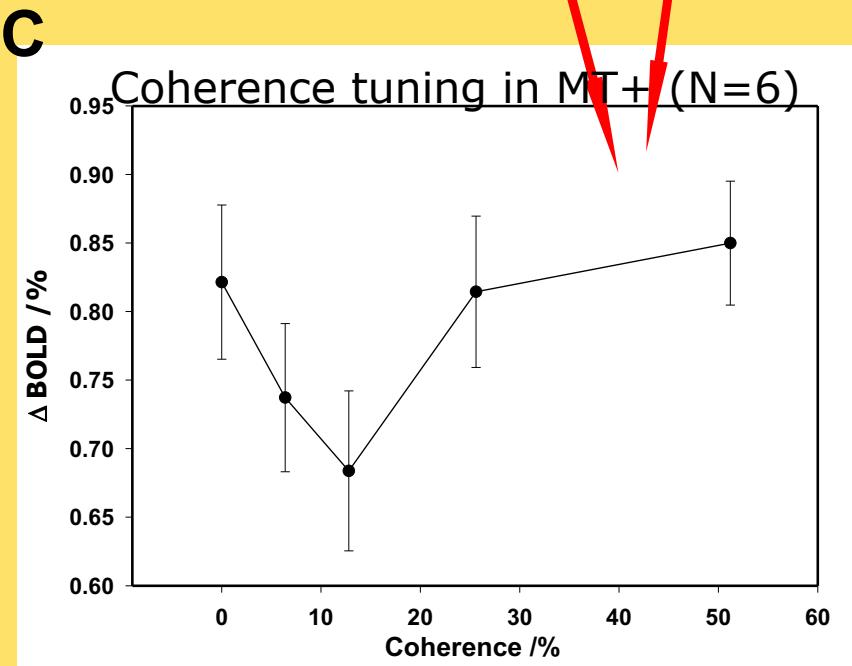
Logothetis et al. Nature, 412, 150-157

Coherence tuning in MT+

Heekeren et al.



- Subjects had to indicate whether dots presented with differing degrees of coherence were moving left or right (A, figure modified from Newsome, 1997).
- MT+ was functionally localized (low contrast moving stimulus, LCMS, [B]).
- MT+ showed a nonmonotonic coherence tuning curve, with a local minimum around threshold levels.



- Contrast in fMRI

Hemodynamic Specificity

- The Hemodynamic Transfer Function

Location, Latency, Magnitude

- Best Results So Far

Temporal Resolution, Spatial Resolution

- Neuronal Activation Input Strategies

Block Design

Phase and Frequency Encoding

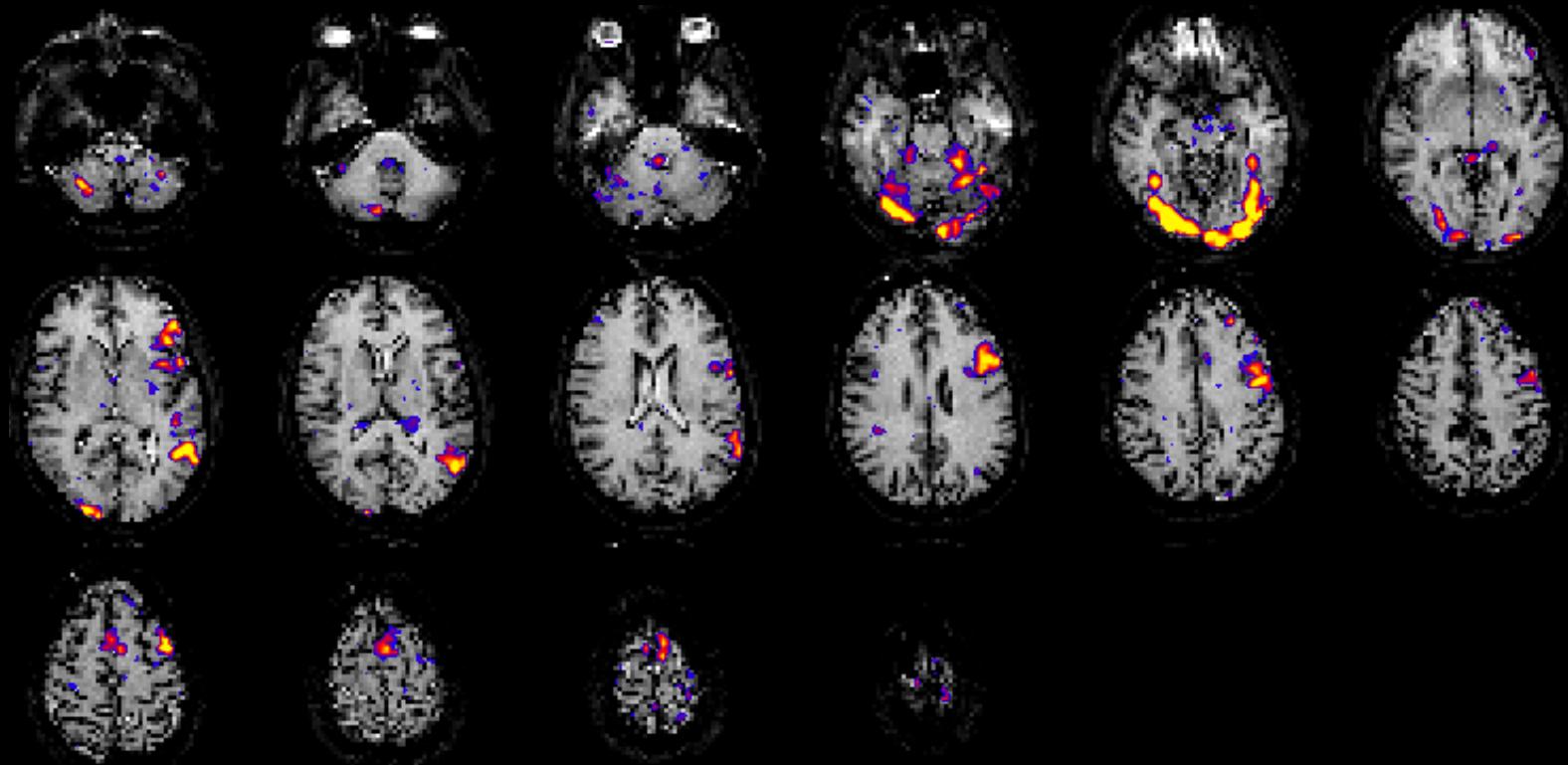
Orthogonal Designs

Parametric Designs

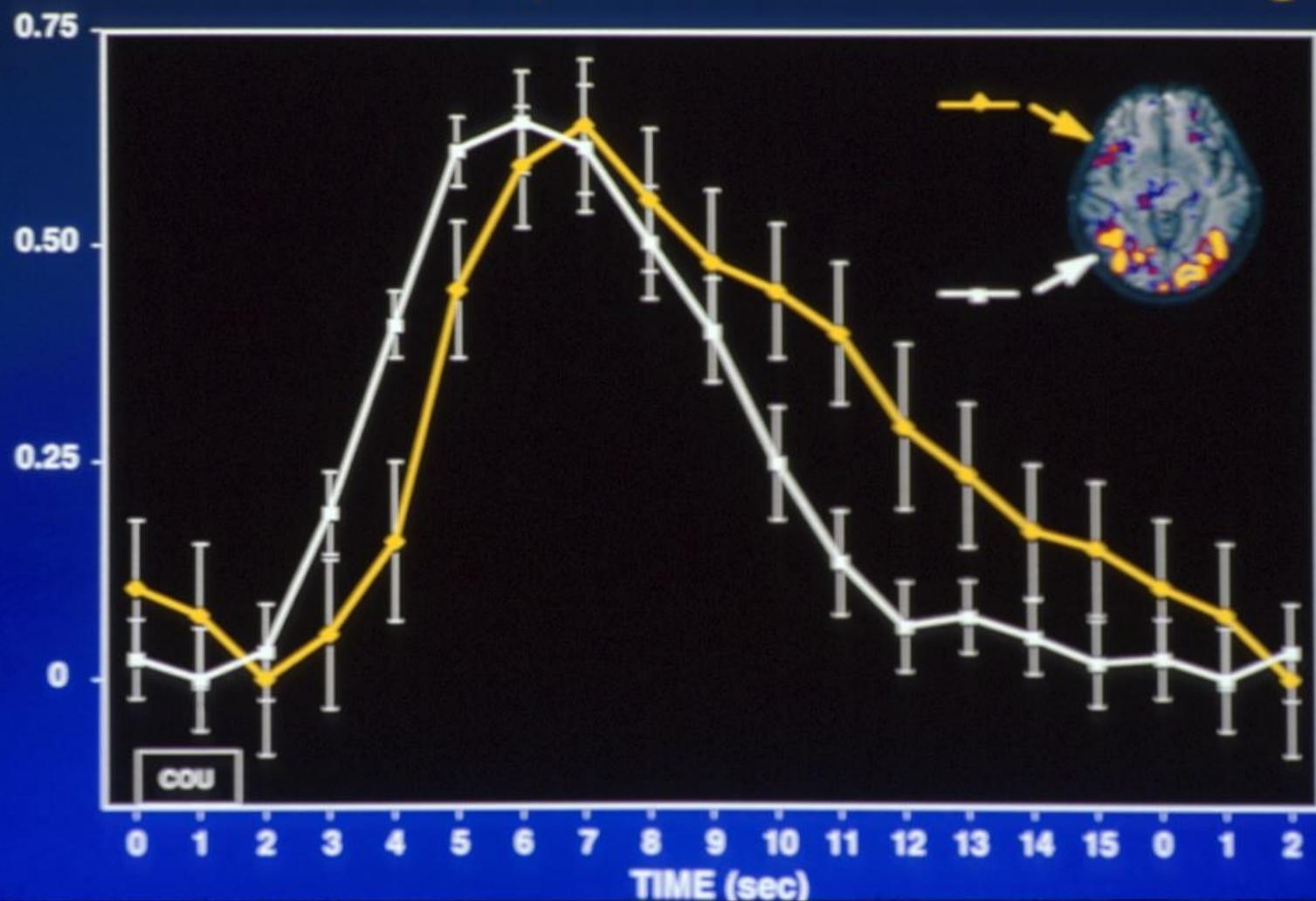
Event-Related Designs

Free Behavior Designs

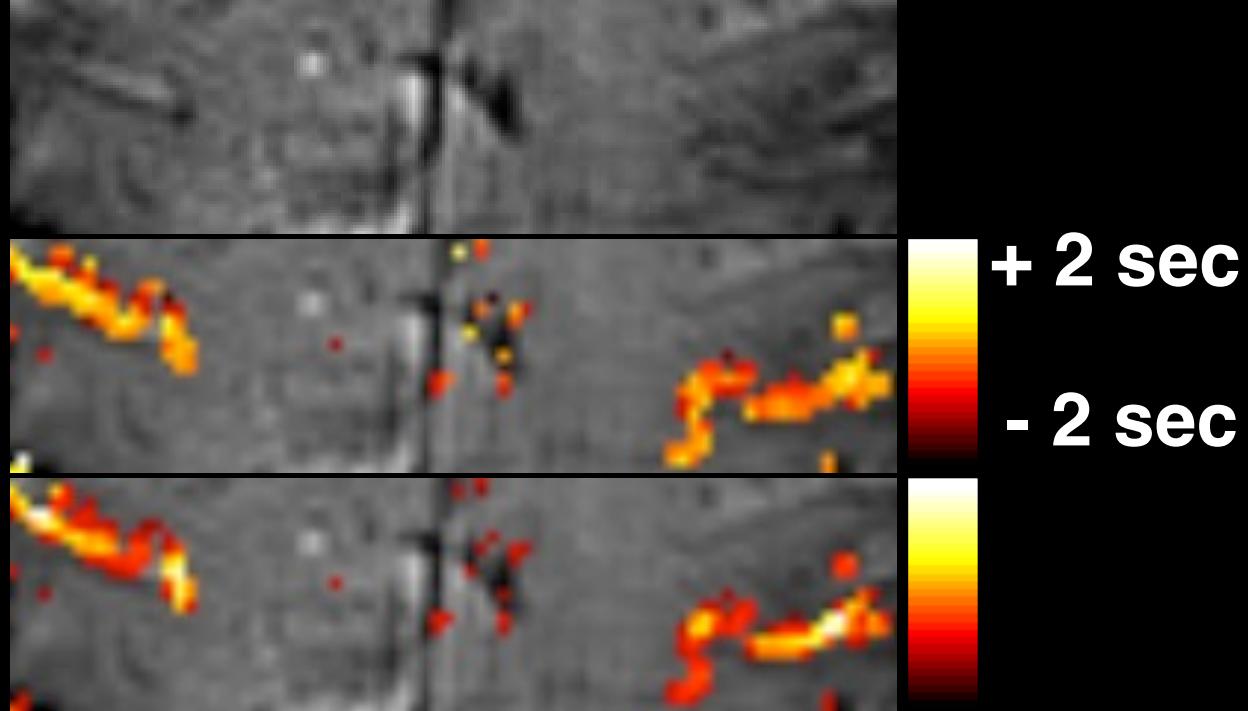
Word stem completion



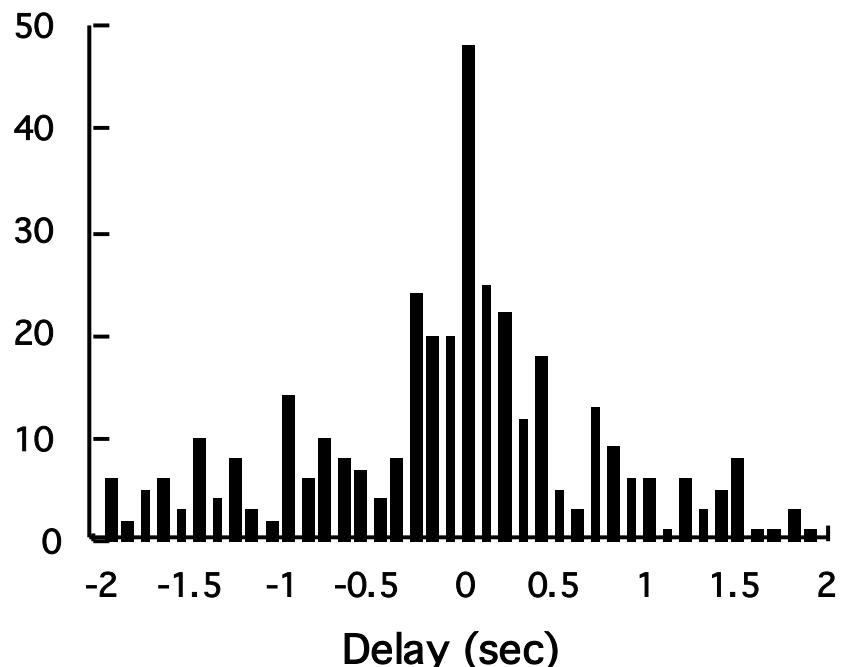
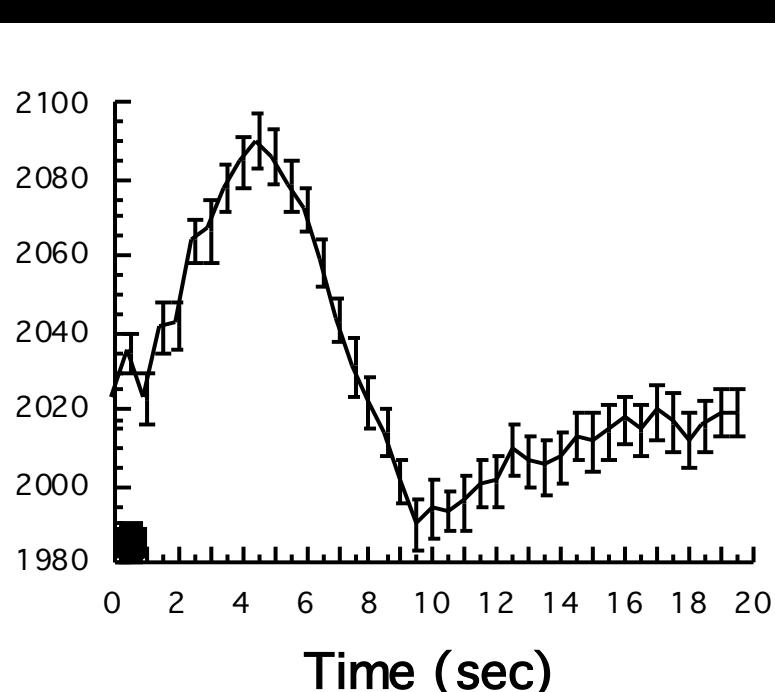
Time Course Comparison Across Brain Regions



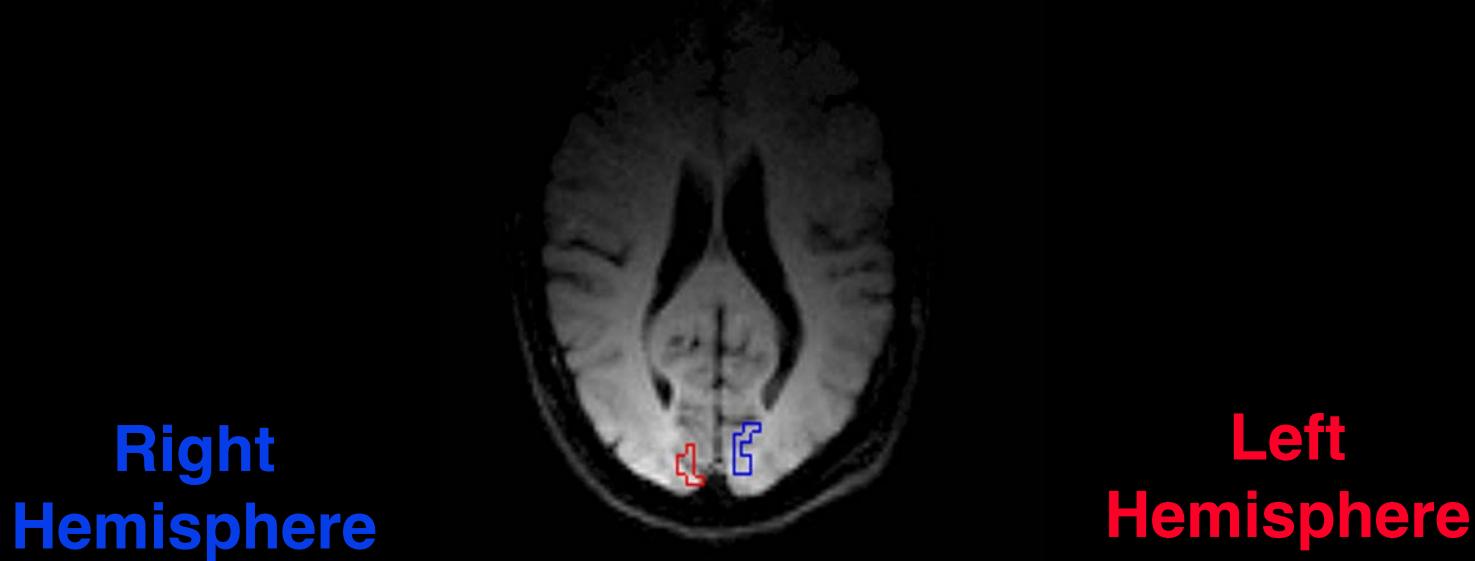
Latency

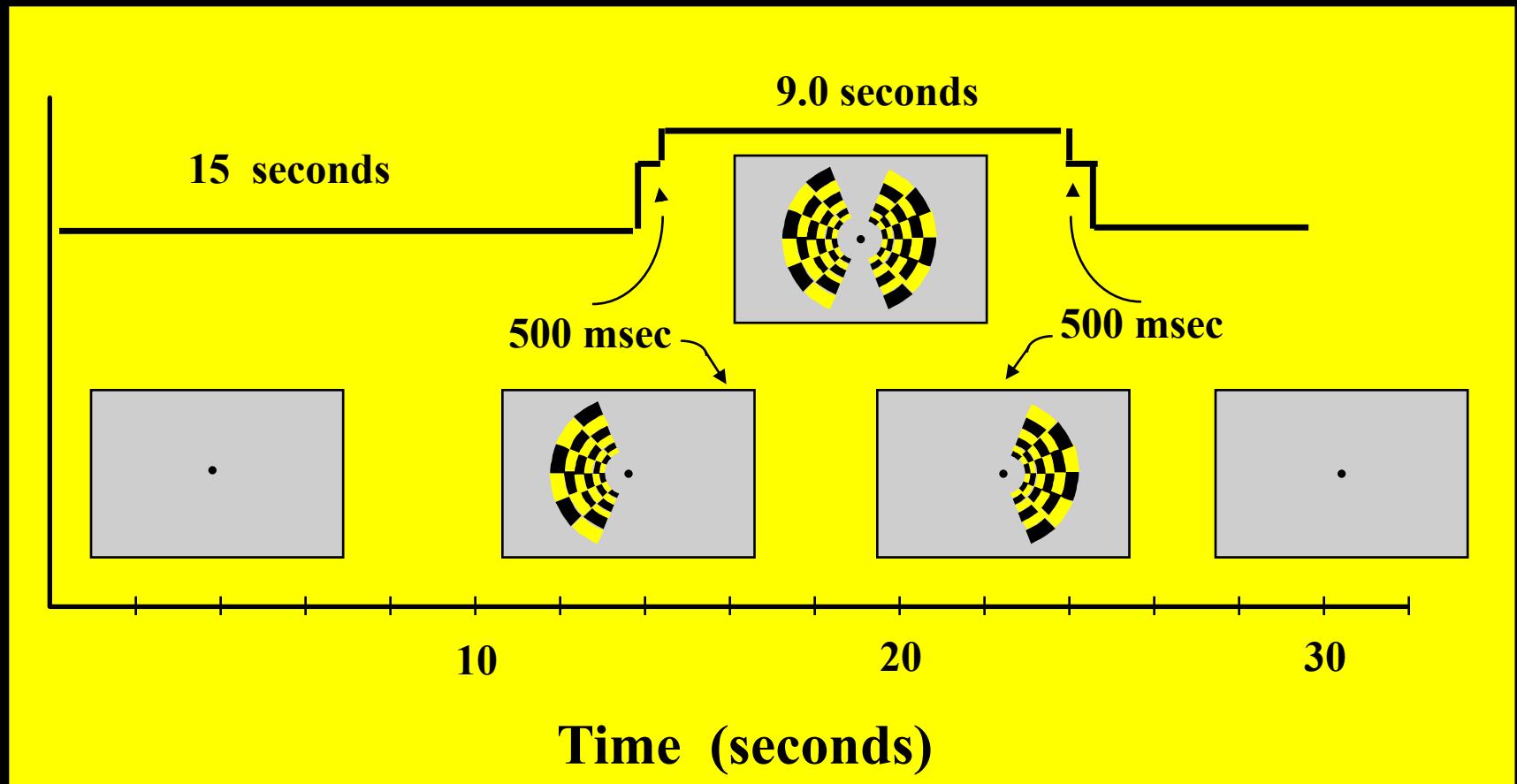


Magnitude



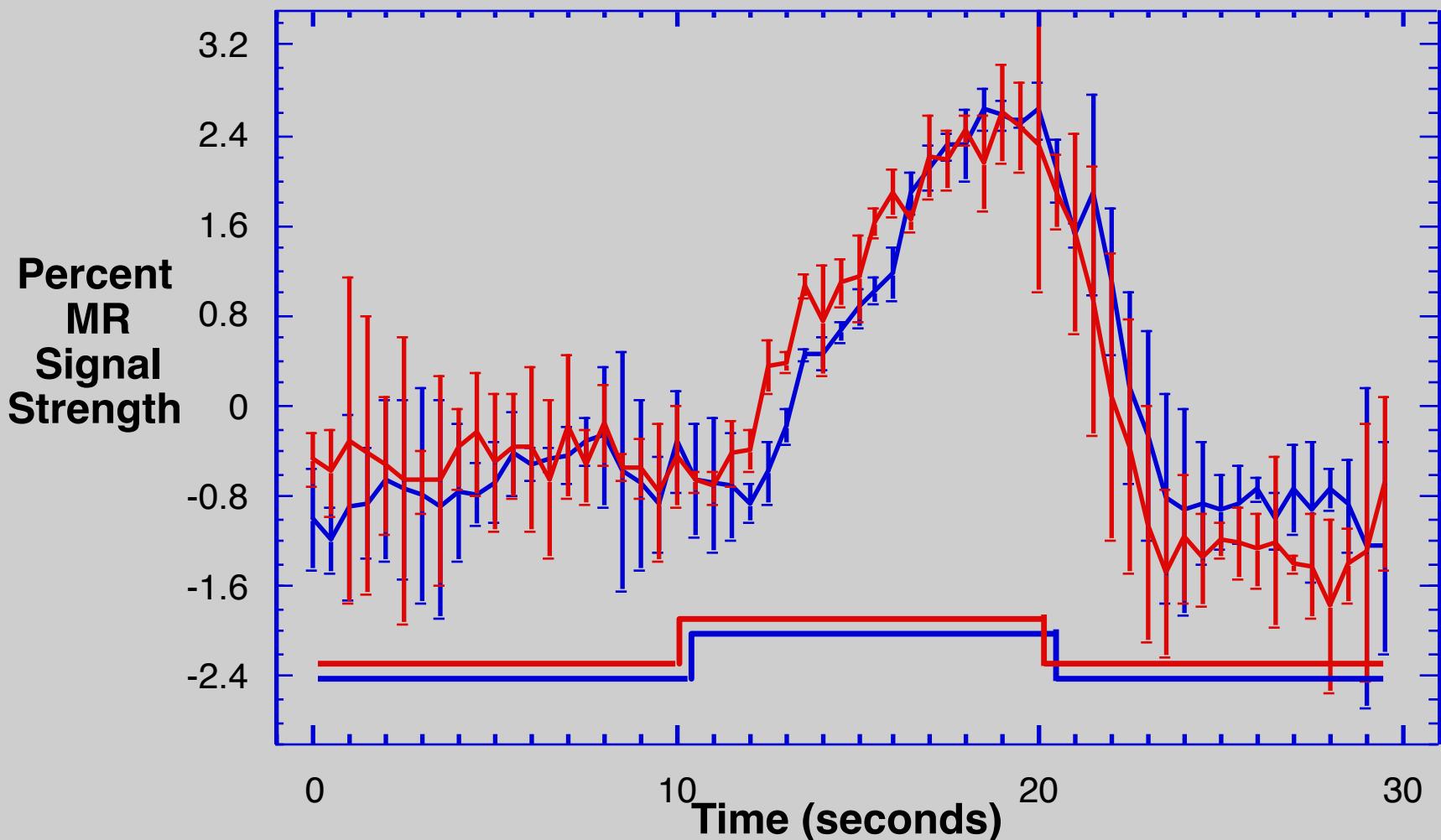
Regions of Interest Used for Hemi-Field Experiment

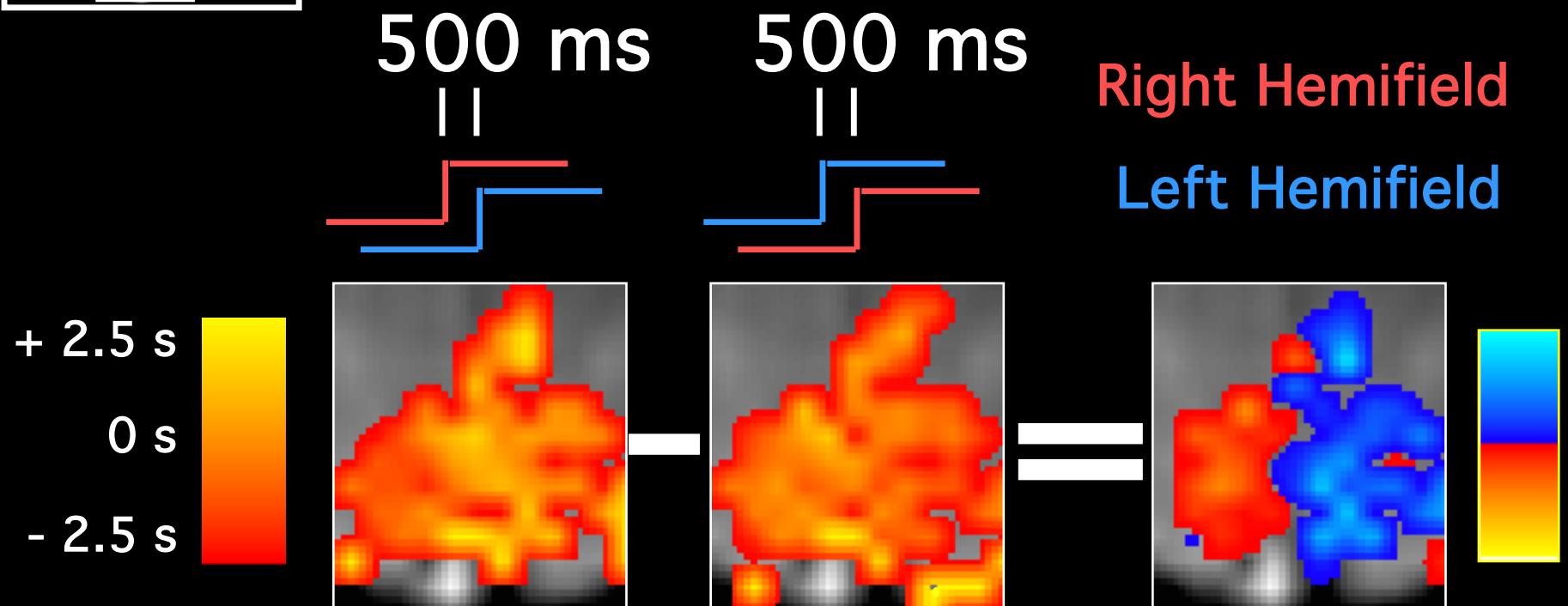
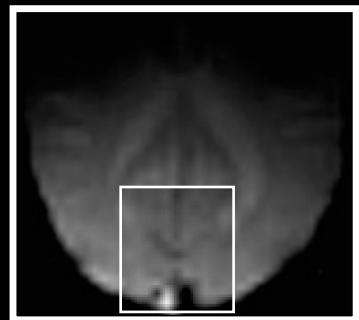


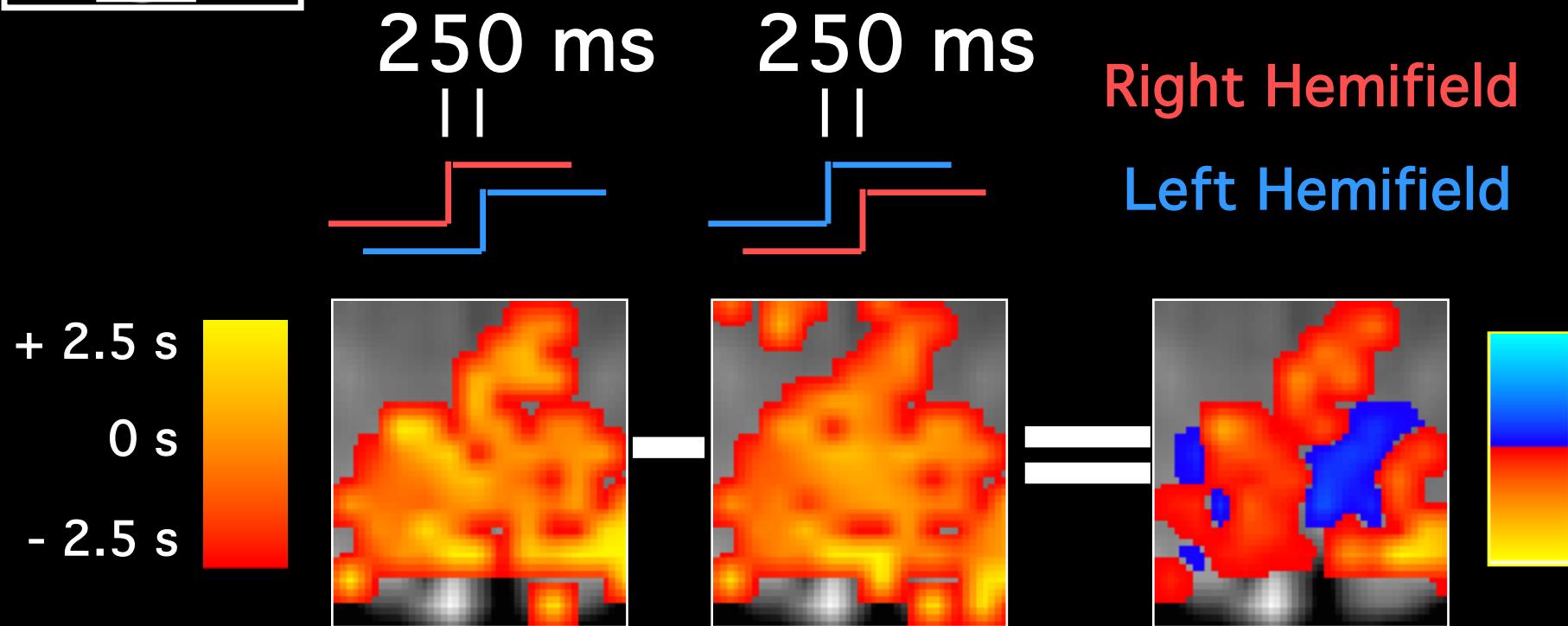
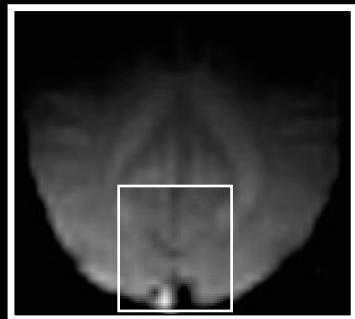


Hemi-field with 500 msec asynchrony

Average of 6 runs Standard Deviations Shown





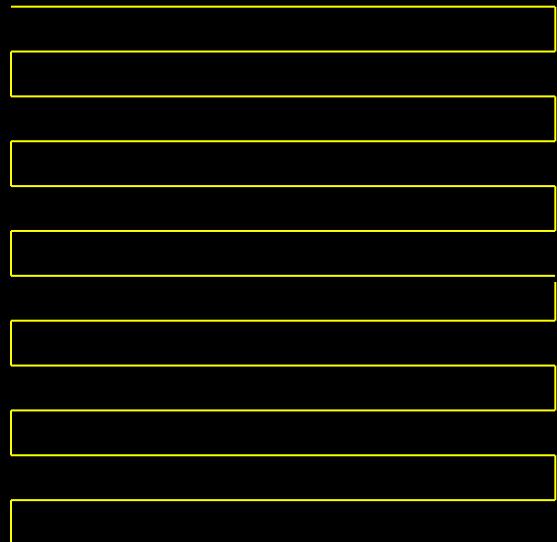


Single Shot Imaging

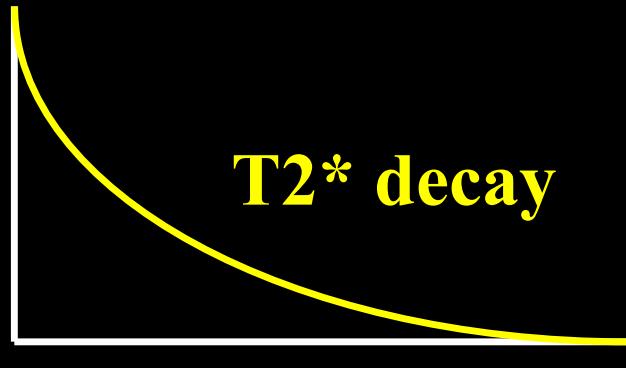


EPI Readout Window

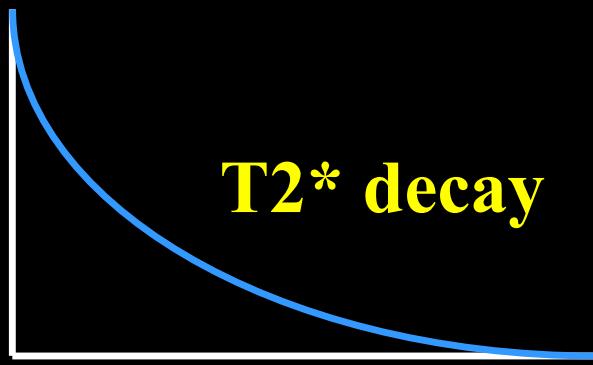
≈ 20 to 40 ms



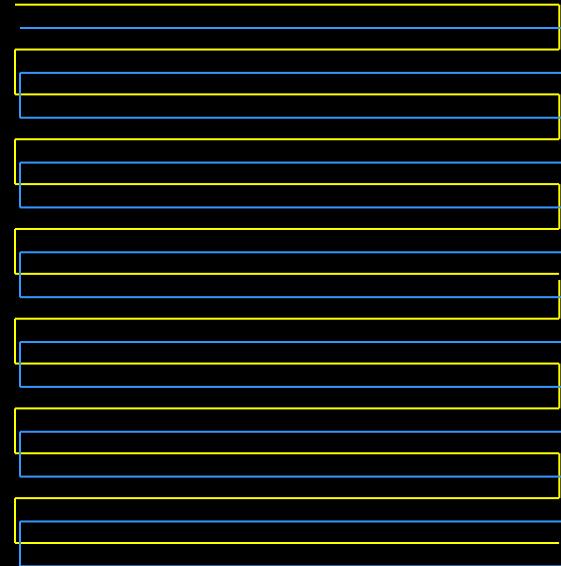
Multishot Imaging



$T2^*$ decay



$T2^*$ decay



Multi Shot EPI

Excitations

1

Matrix Size

64 x 64

2

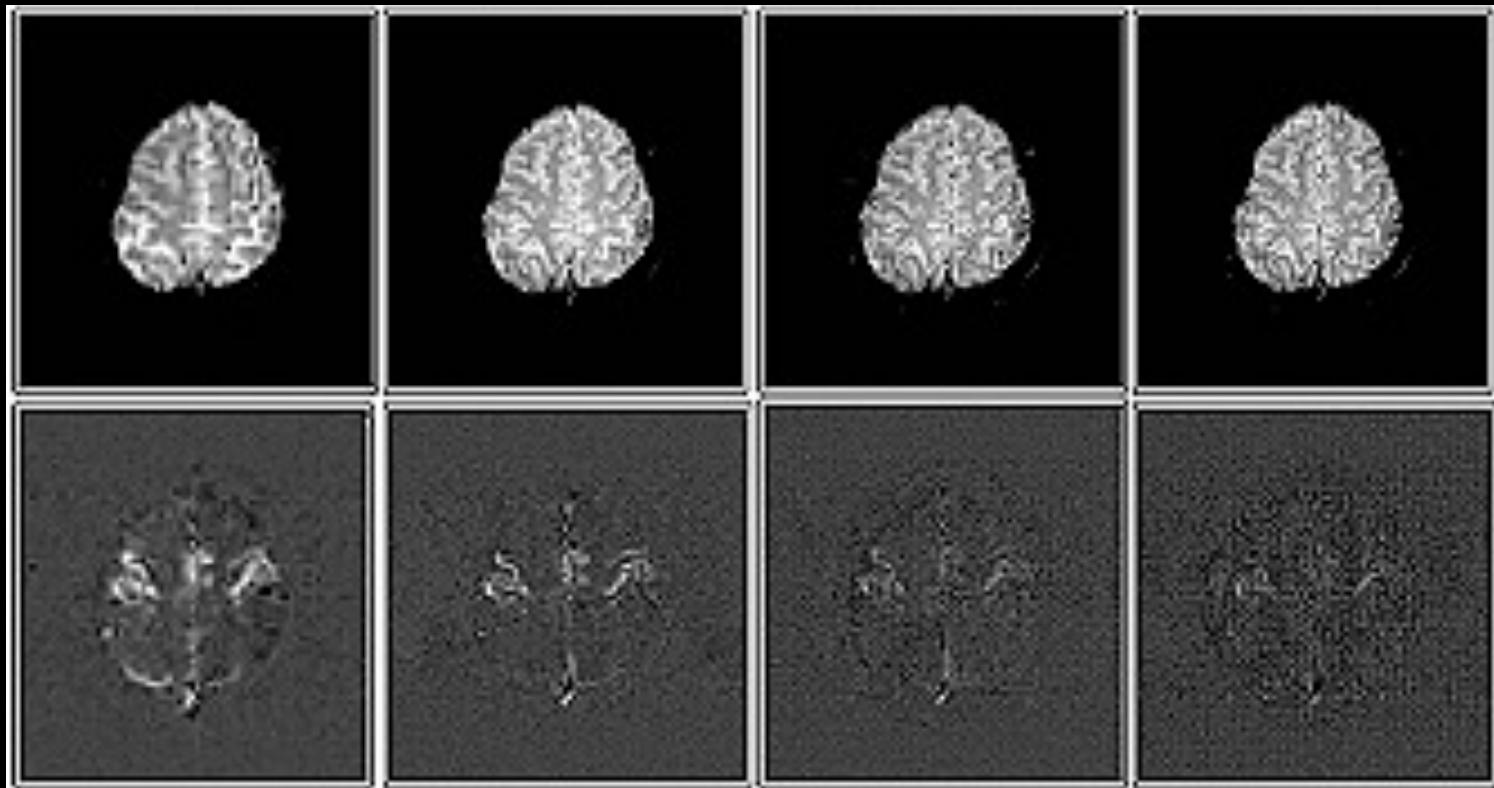
128 x 128

4

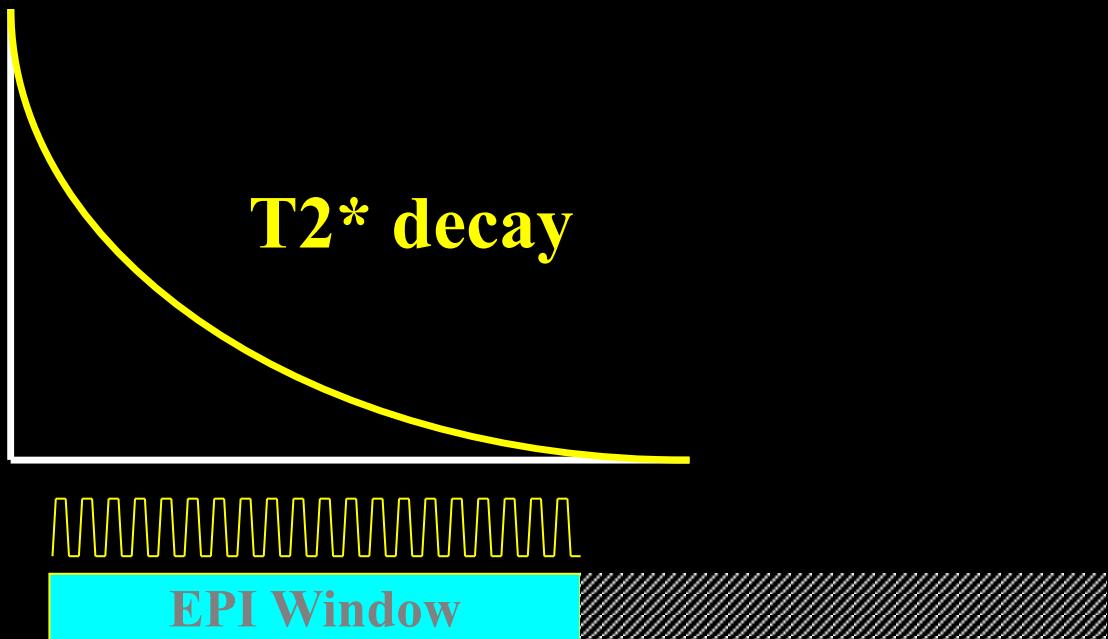
256 x 128

8

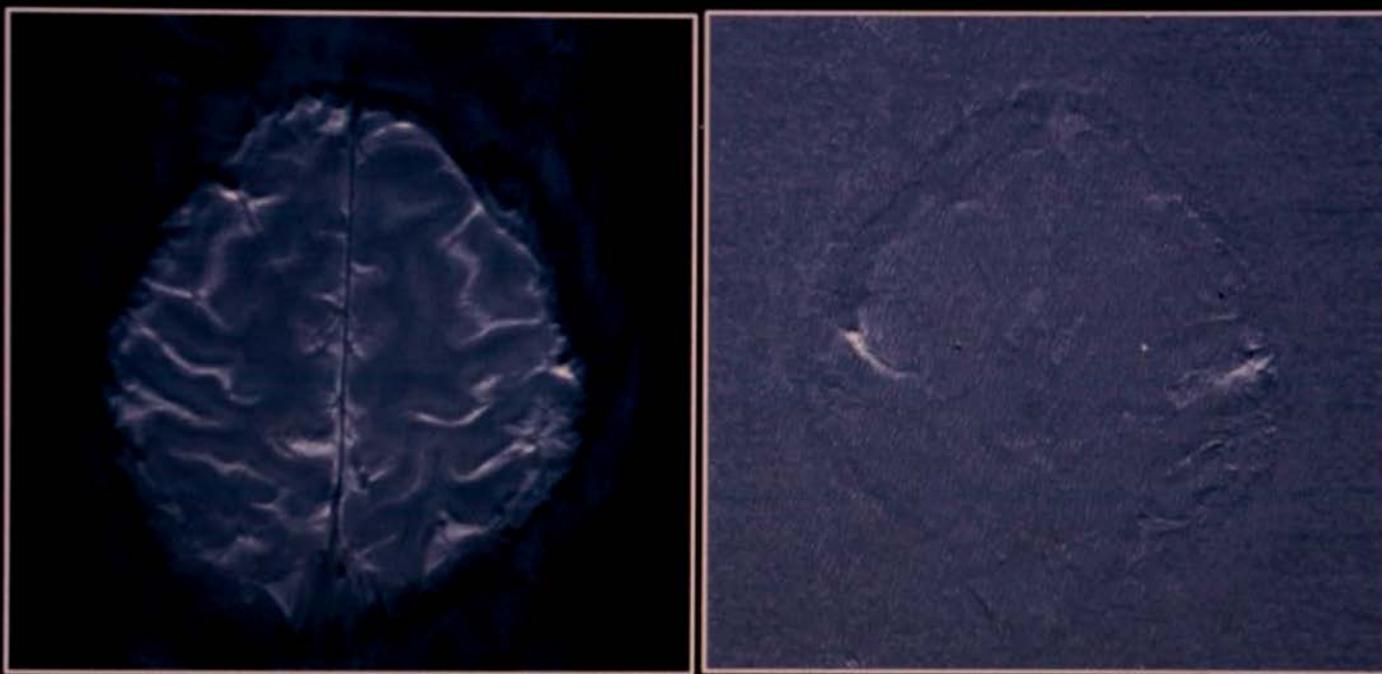
256



Partial k-space imaging

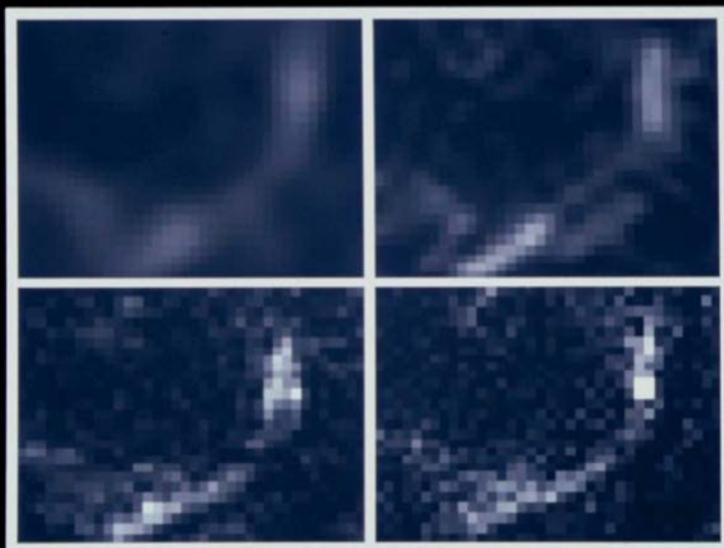


**Single - Shot EPI at 3T:
Half NEX, 256 x 256, 16 cm FOV**



Fractional Signal Change

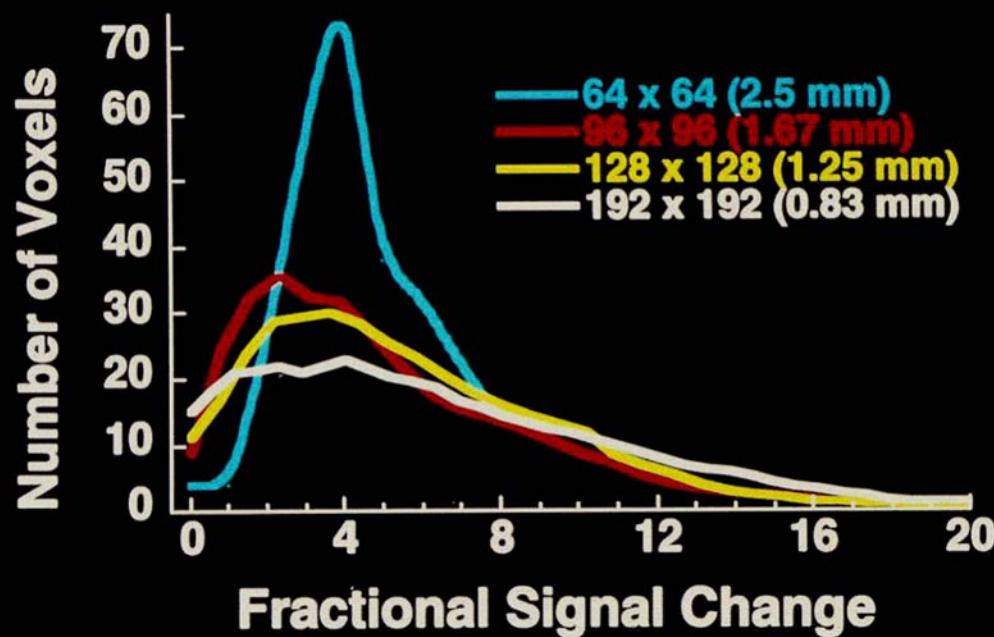
2.5 mm^2

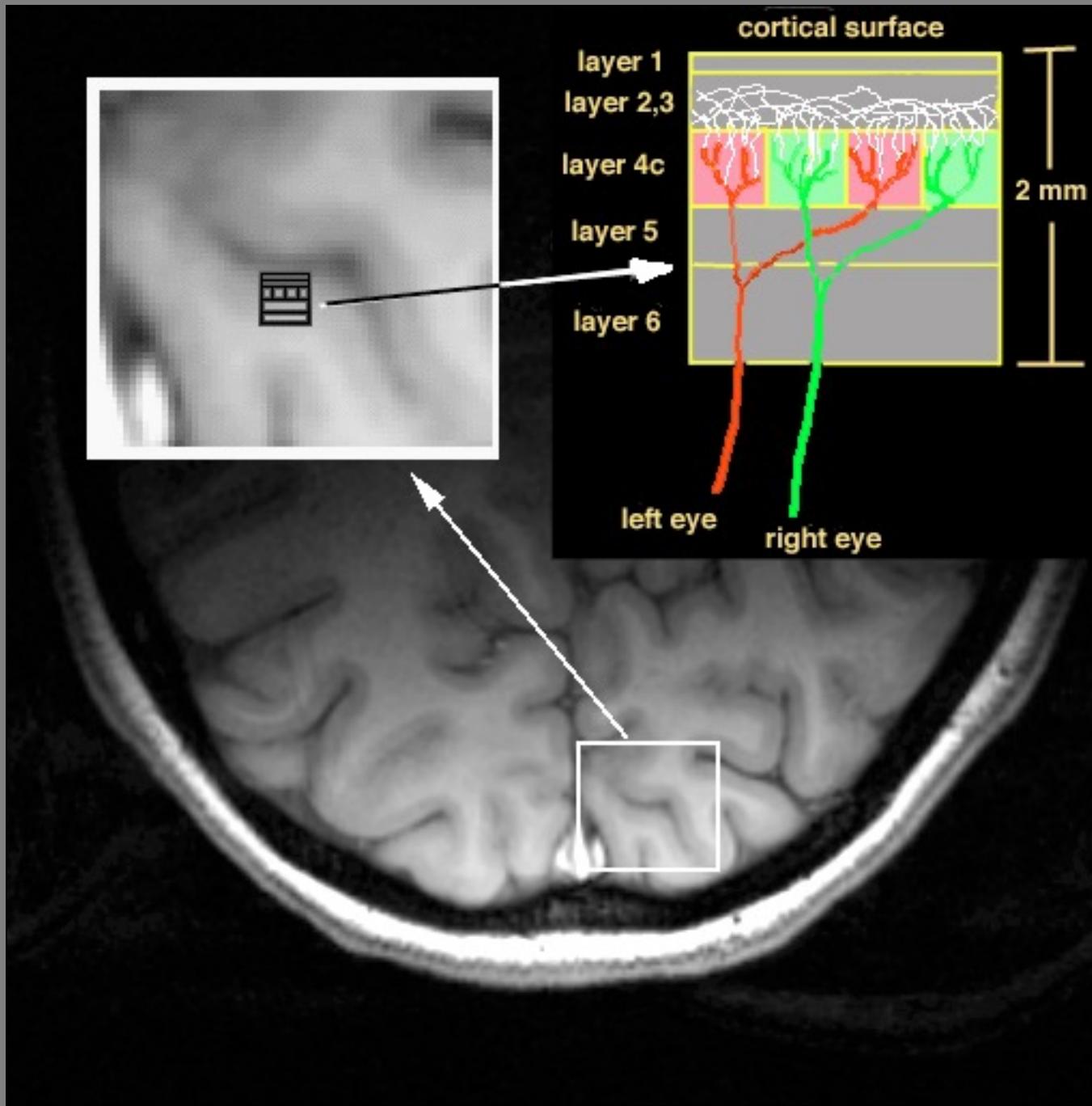


1.25 mm^2

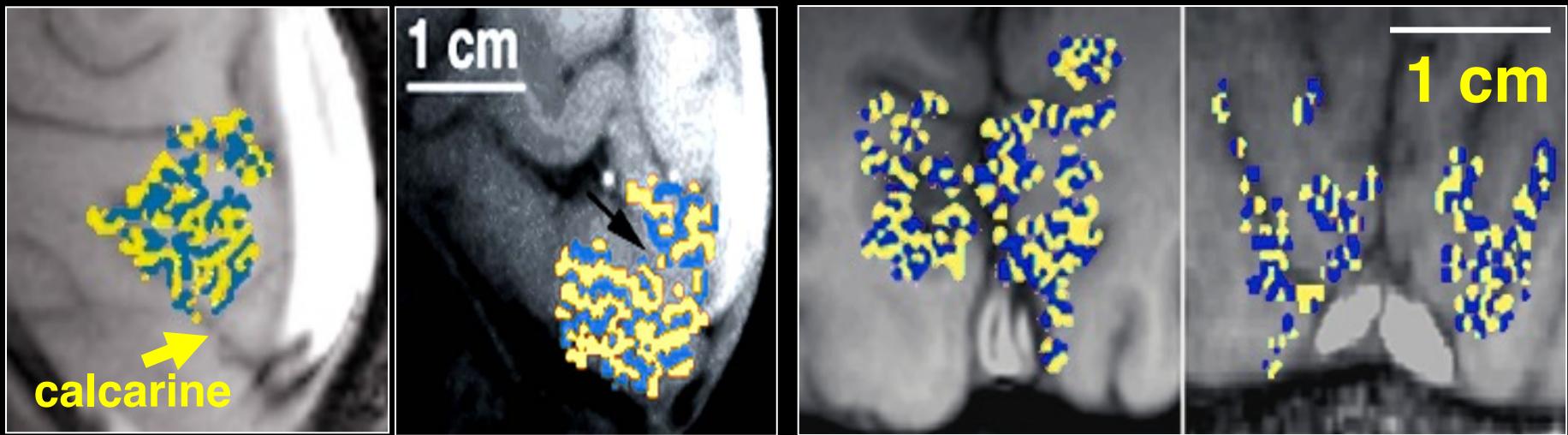
0.83 mm^2

0.62 mm^2





ODC Maps using fMRI



- Identical in size, orientation, and appearance to those obtained by optical imaging¹ and histology^{3,4}.

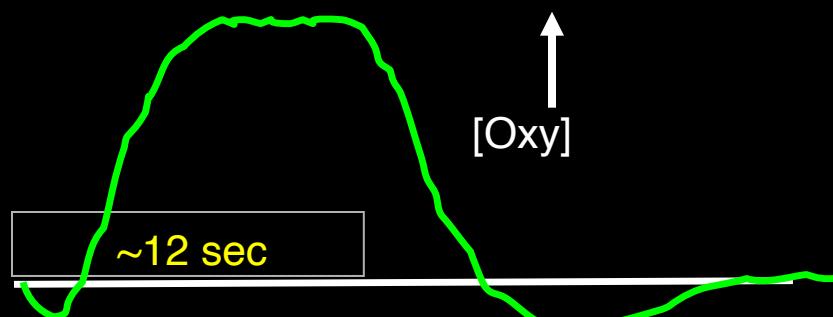
¹Malonek D, Grinvald A. *Science* 272, 551-4 (1996).

³Horton JC, Hocking DR. *J Neurosci* 16, 7228-39 (1996).

⁴Horton JC, et al. *Arch Ophthalmol* 108, 1025-31 (1990).

Why short is better than long

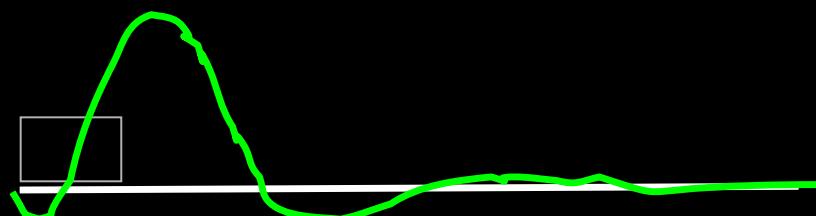
The vascular response to prolonged neural stimulation



It is argued that fMRI cannot achieve submillimeter functional resolution because a saturated hyperoxic vascular response to neural activity spreads over many millimeters^{1,2}.

However, optical imaging has demonstrated that the hyperoxic response can yield well-localized maps when using short duration stimuli (<5 sec)¹.

The vascular response to brief neural stimulation

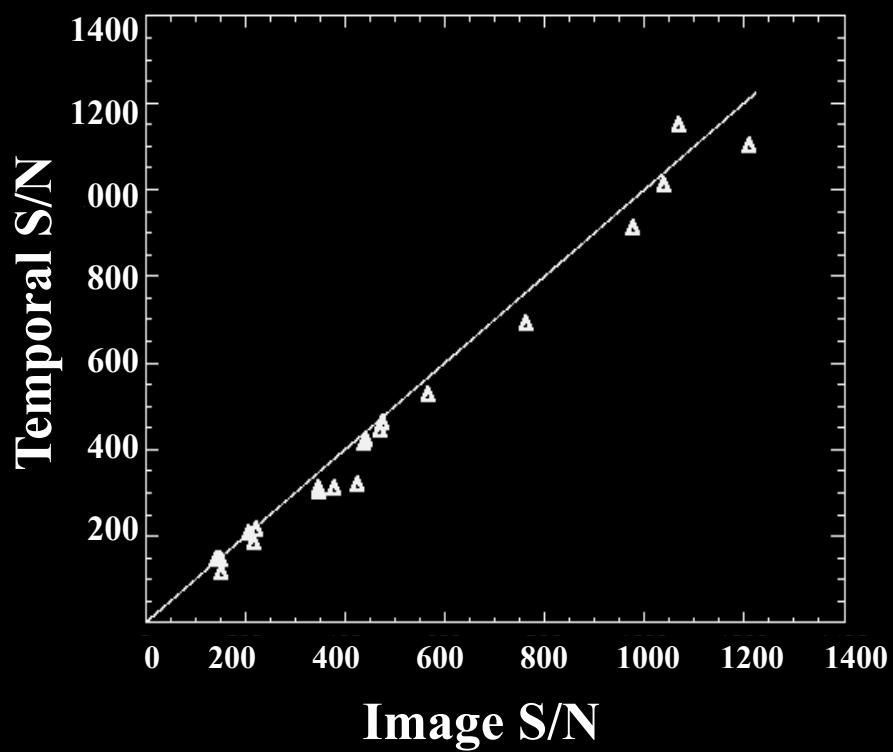


¹Malonek D, Grinvald A. Science 272, 551-4 (1996).

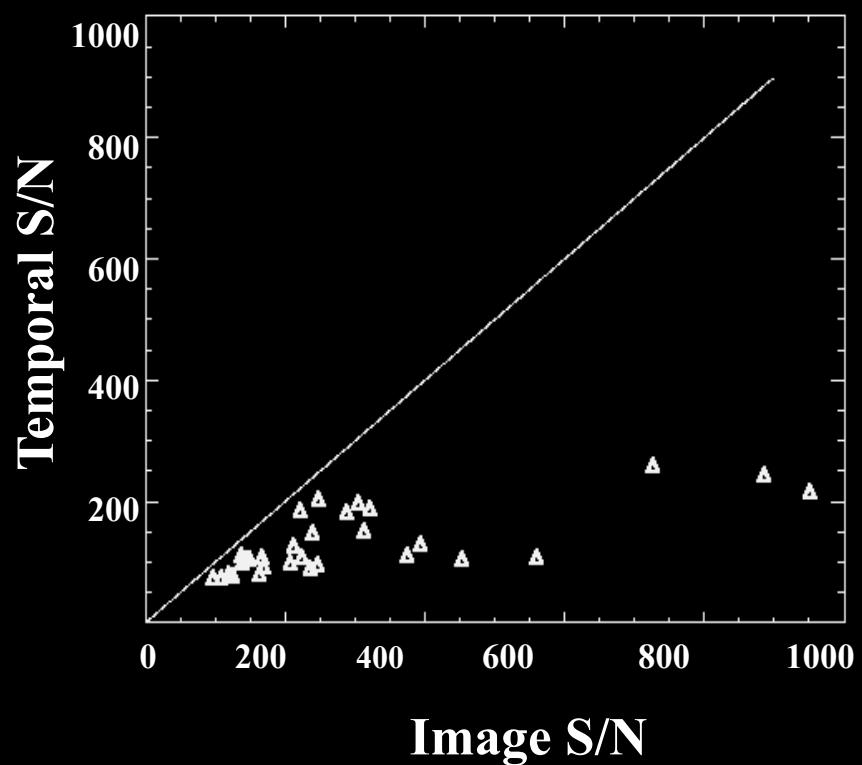
²Kim D-S, Duong T, Kim S-G. Nat Neurosci 3, 164-9 (2000).

Temporal S/N vs. Image S/N

PHANTOMS

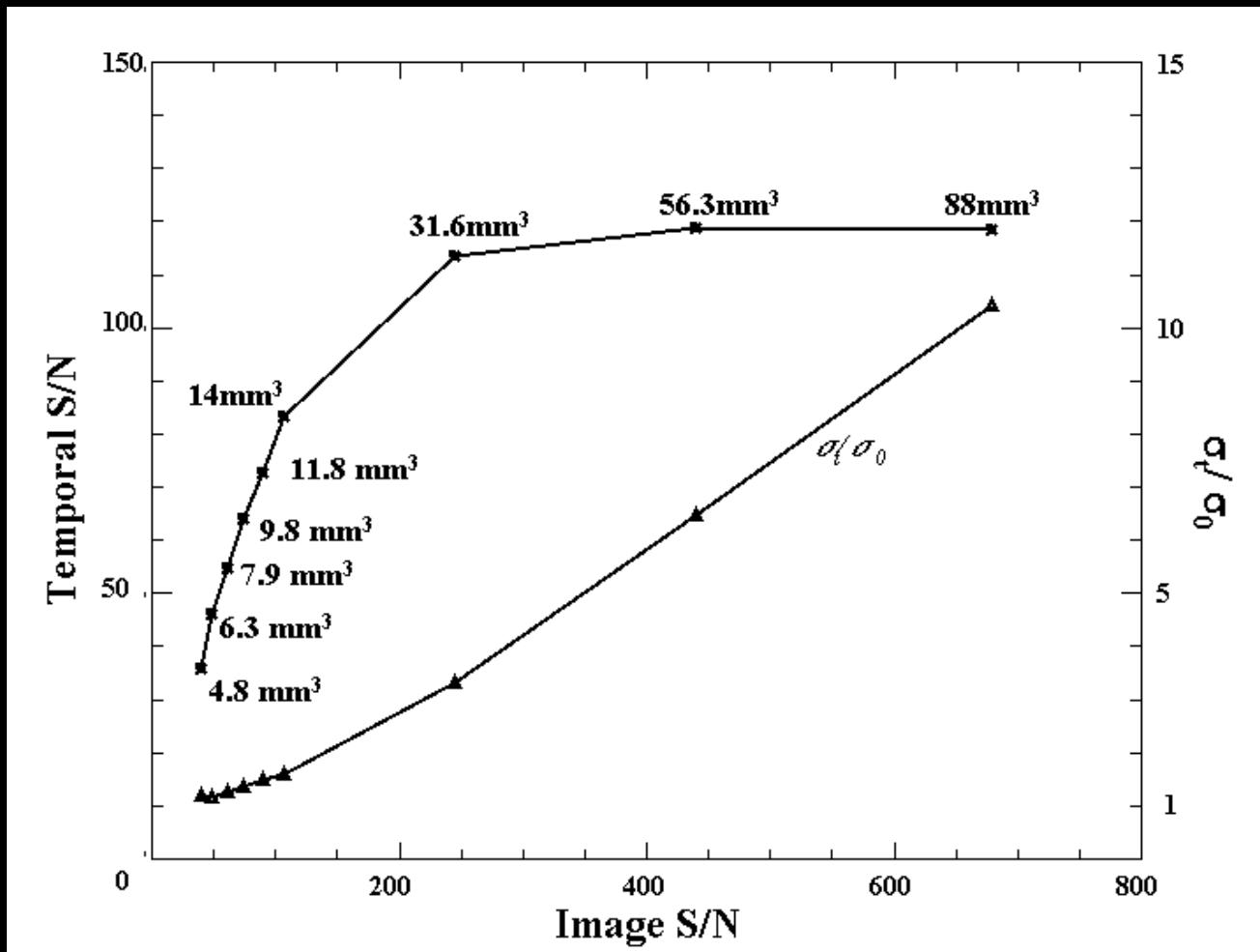


SUBJECTS



N. Petridou

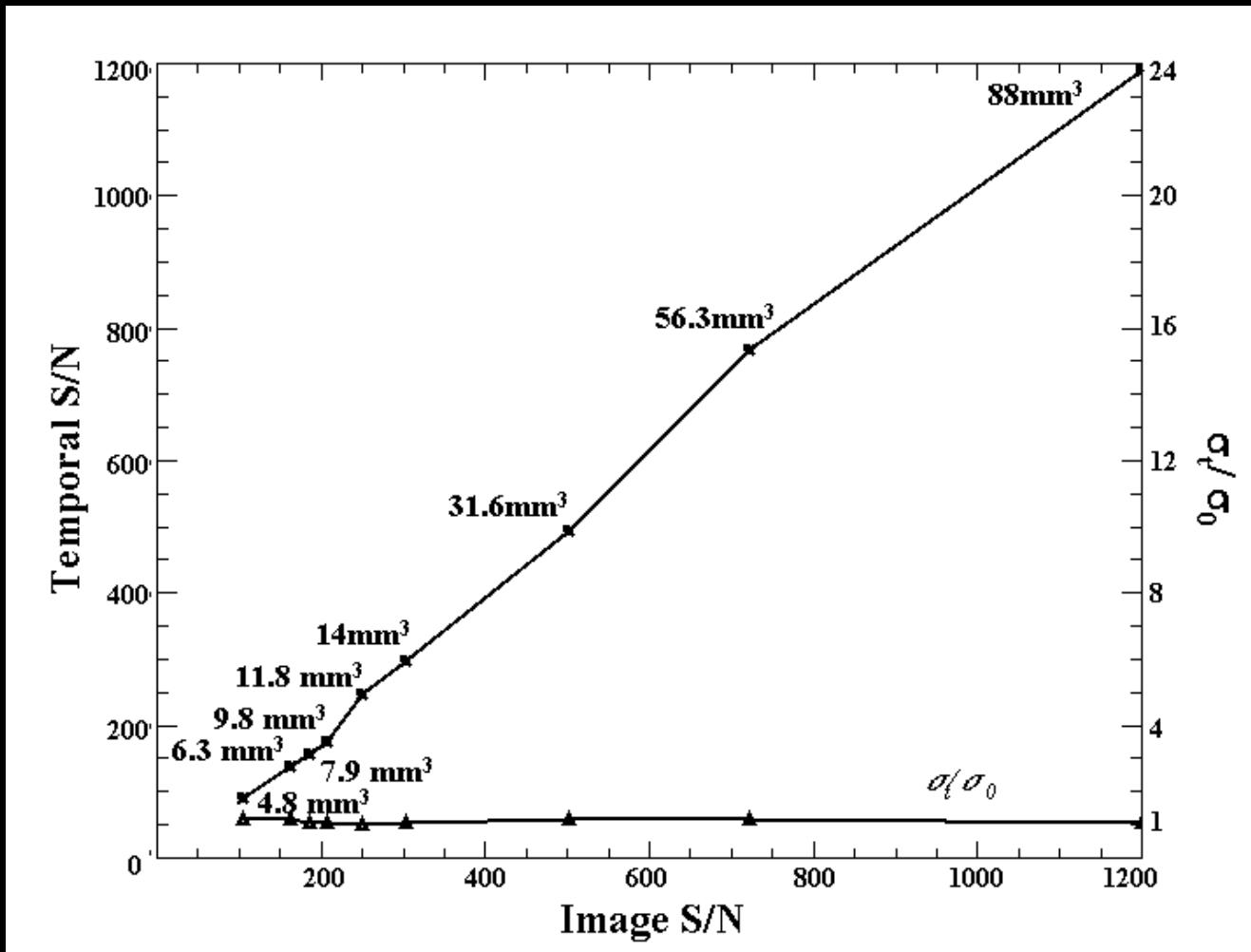
Temporal vs. Image S/N Optimal Resolution Study



Human data

Petridou et al

Temporal vs. Image S/N Optimal Resolution Study



Phantom data

Petridou et al

- Contrast in fMRI

Hemodynamic Specificity

- The Hemodynamic Transfer Function

Location, Latency, Magnitude

- Best Results So Far

Temporal Resolution, Spatial Resolution

- Neuronal Activation Input Strategies

Block Design

Phase and Frequency Encoding

Orthogonal Designs

Parametric Designs

Event-Related Designs

Free Behavior Designs

Neuronal Activation Input Strategies

1. Block Design

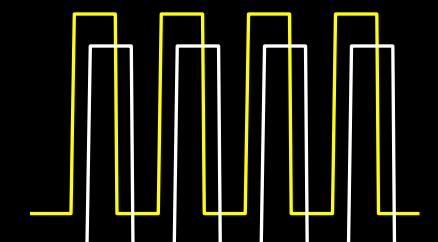
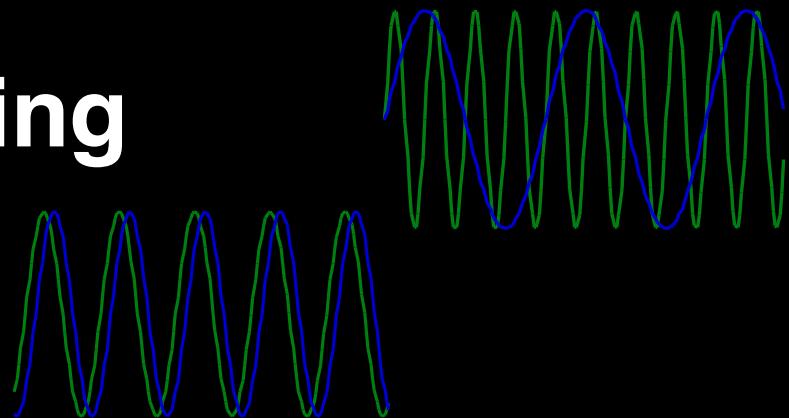
2. Frequency Encoding

3. Phase Encoding

4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.



Neuronal Activation Input Strategies

1. Block Design

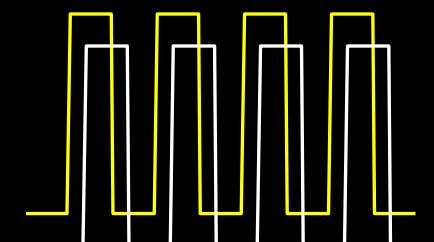
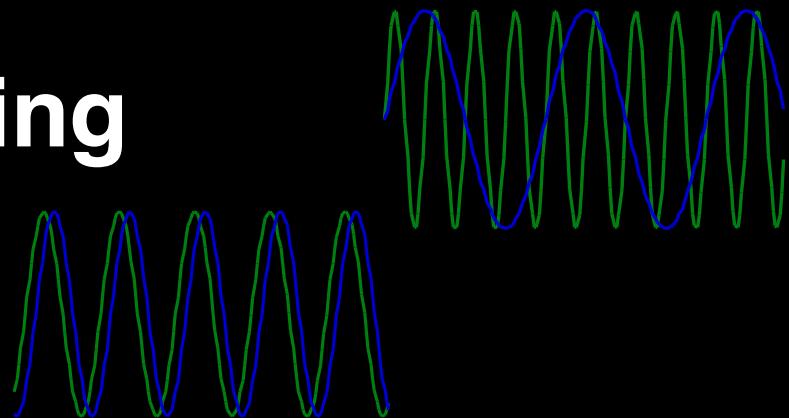
2. Frequency Encoding

3. Phase Encoding

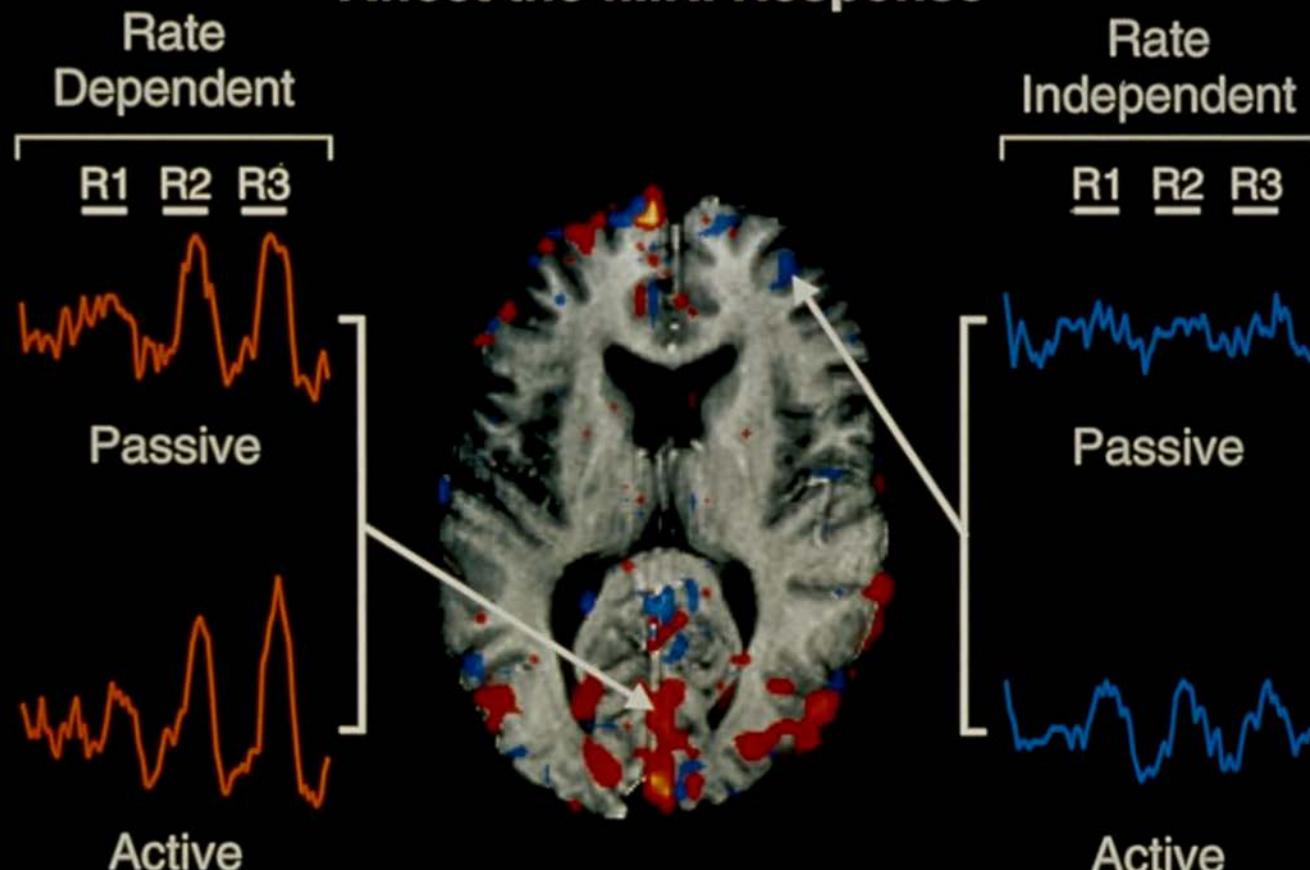
4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.



Both the Task and Presentation Rate Affect the fMRI Response



DeYoe et al.

Neuronal Activation Input Strategies

1. Block Design

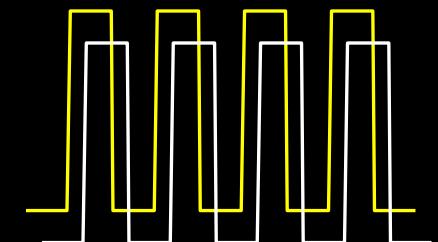
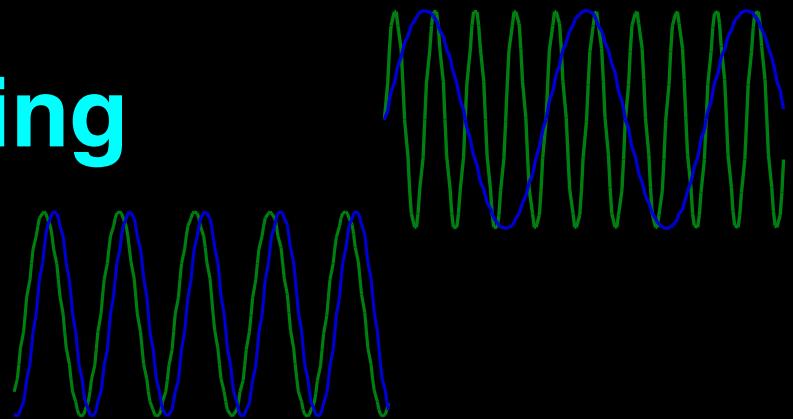
2. Frequency Encoding

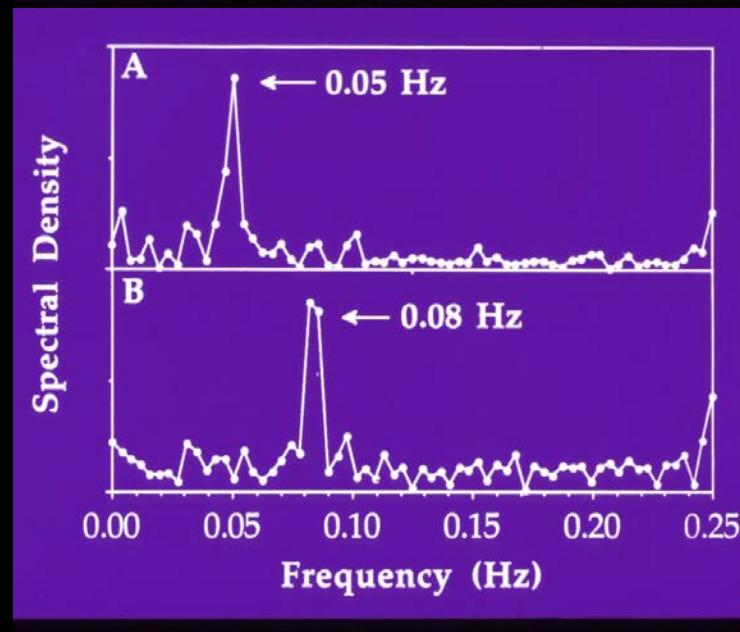
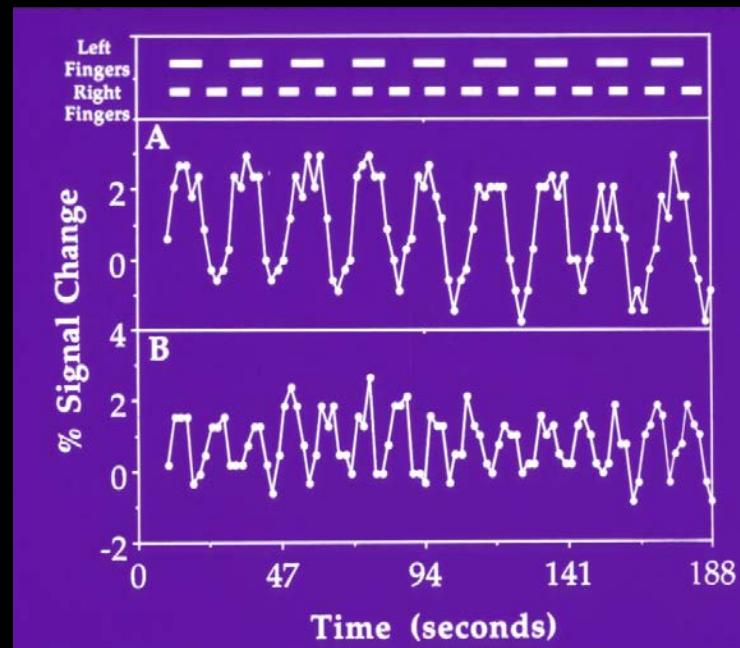
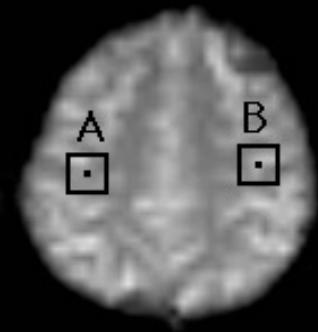
3. Phase Encoding

4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.

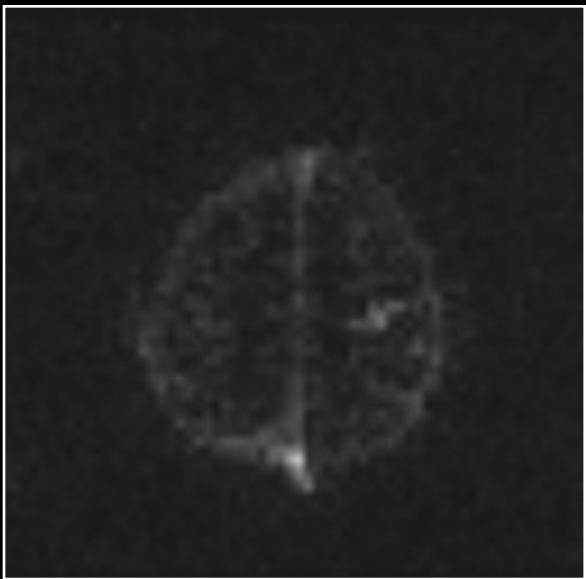




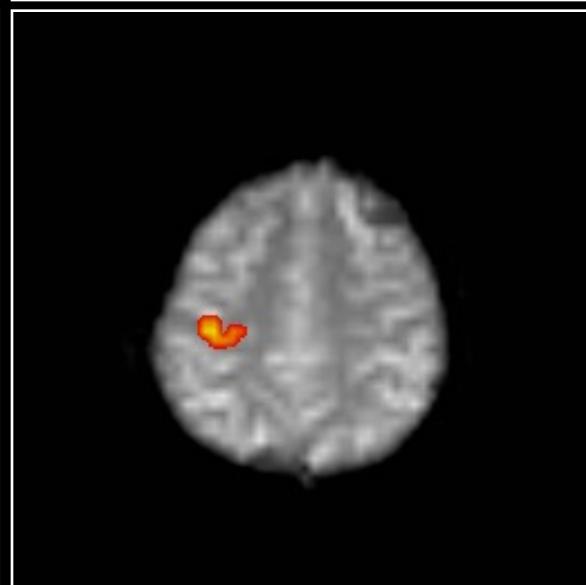
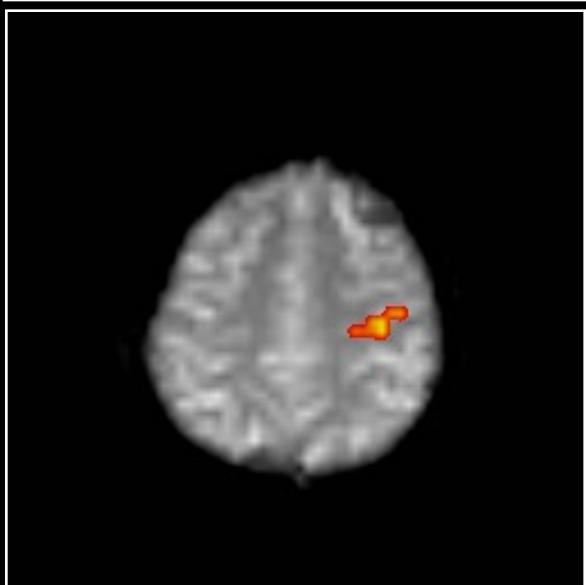
0.08 Hz

0.05 Hz

**spectral
density**



**c.c. > 0.5
with spectra**



Neuronal Activation Input Strategies

1. Block Design

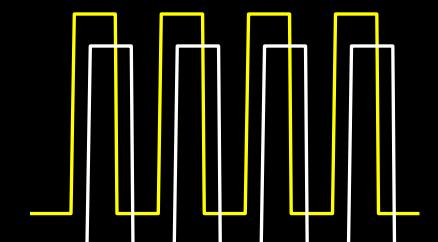
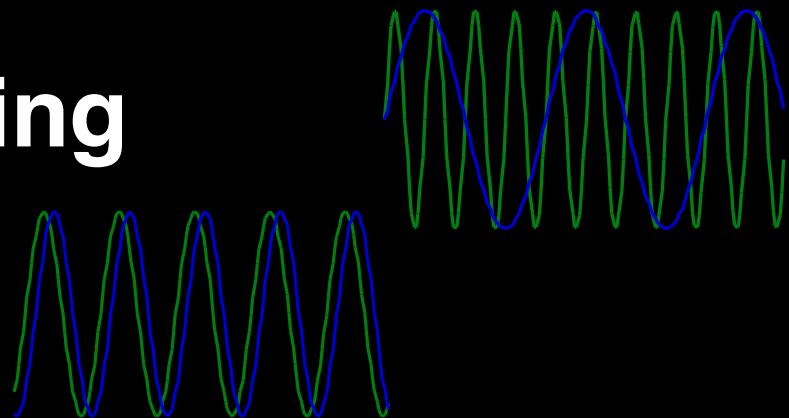
2. Frequency Encoding

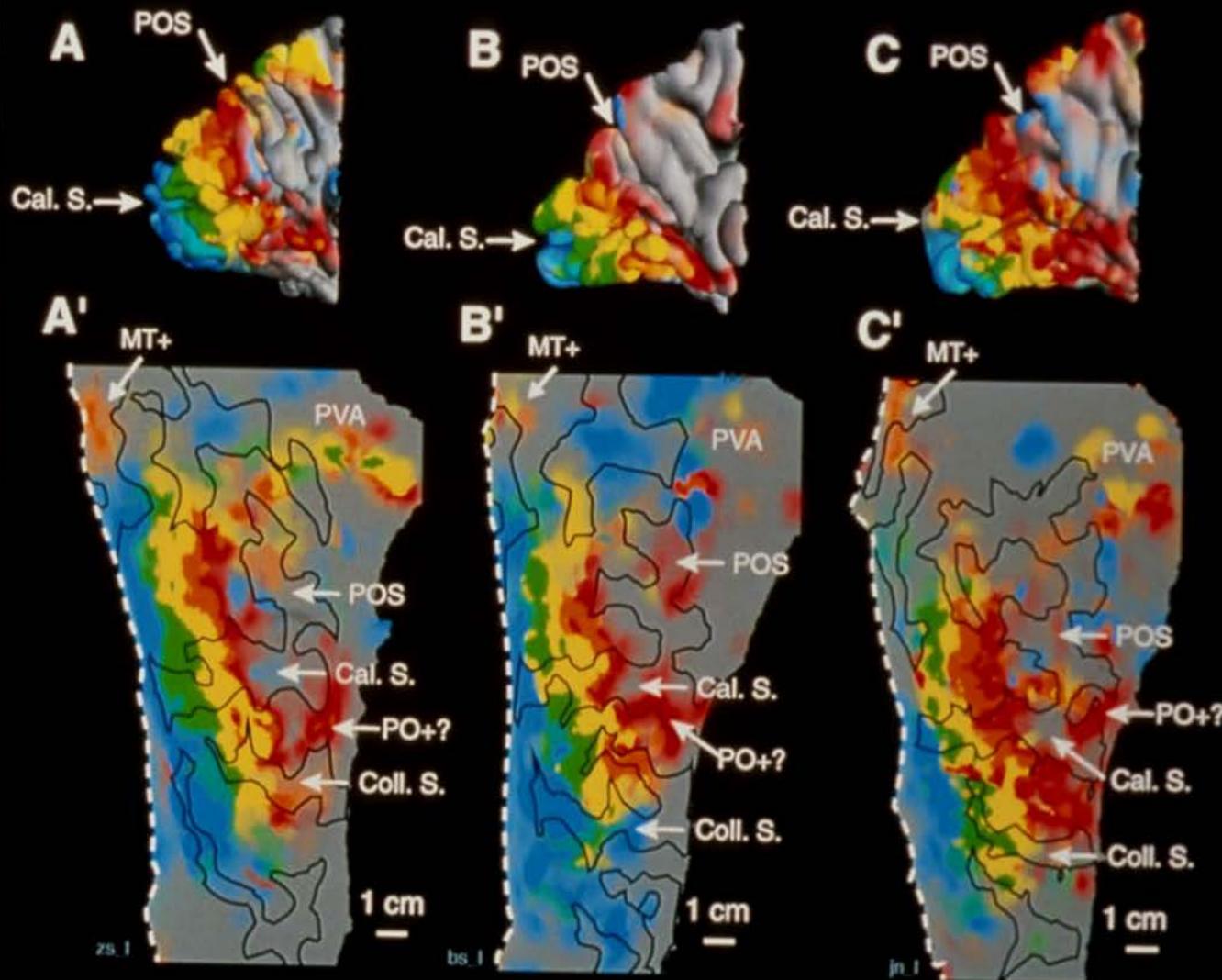
3. Phase Encoding

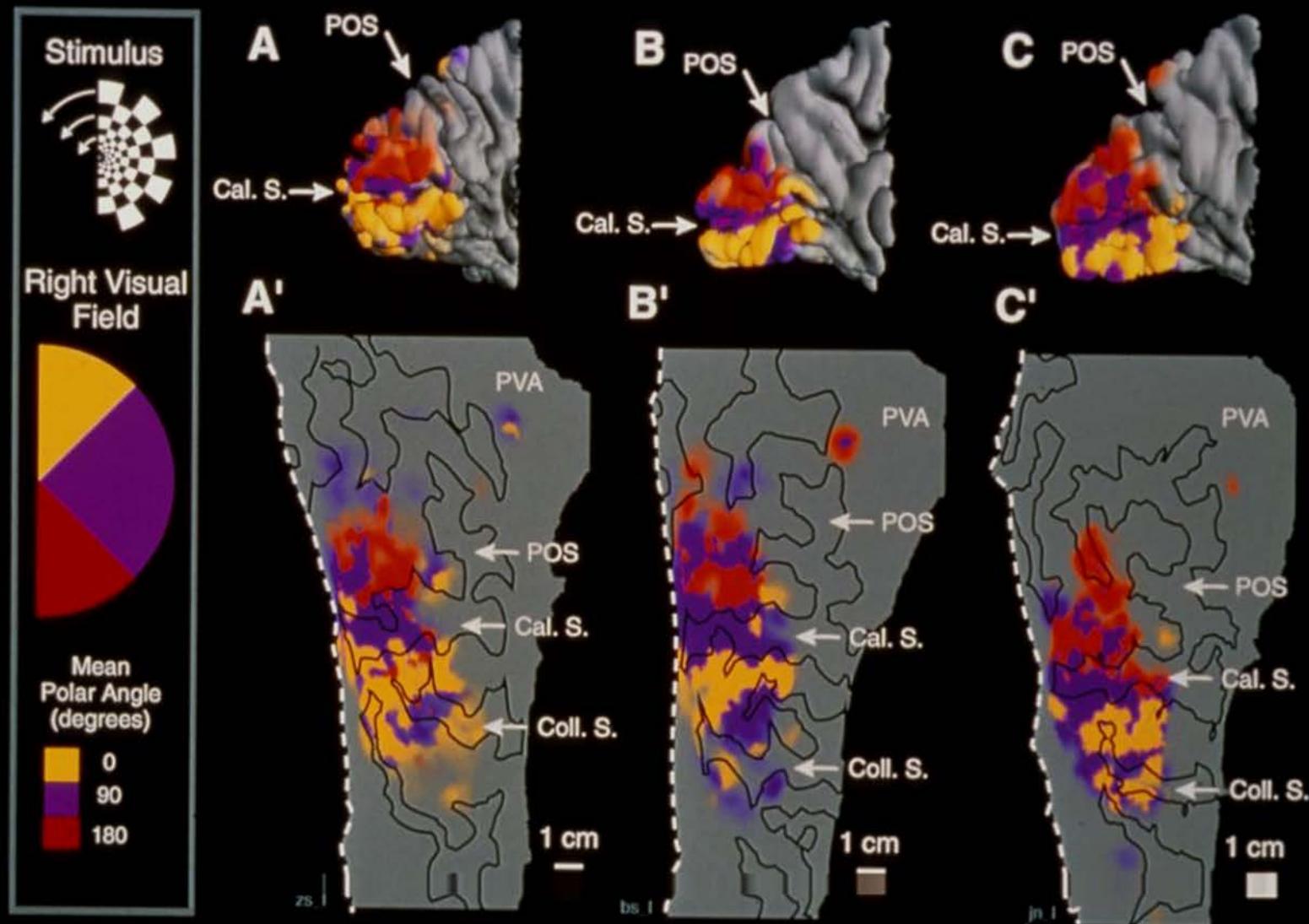
4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.







Neuronal Activation Input Strategies

1. Block Design

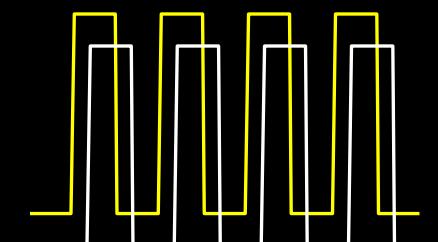
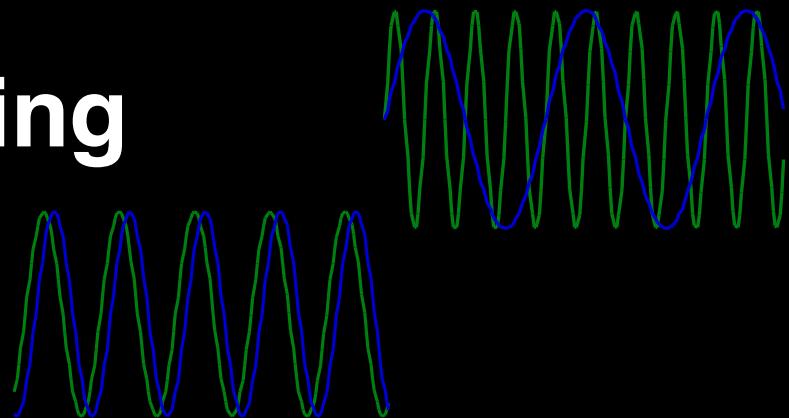
2. Frequency Encoding

3. Phase Encoding

4. Single Event

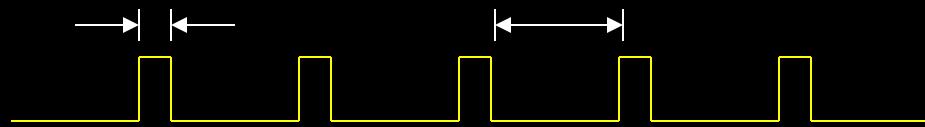
5. Orthogonal Block Design

6. Free Behavior Design.

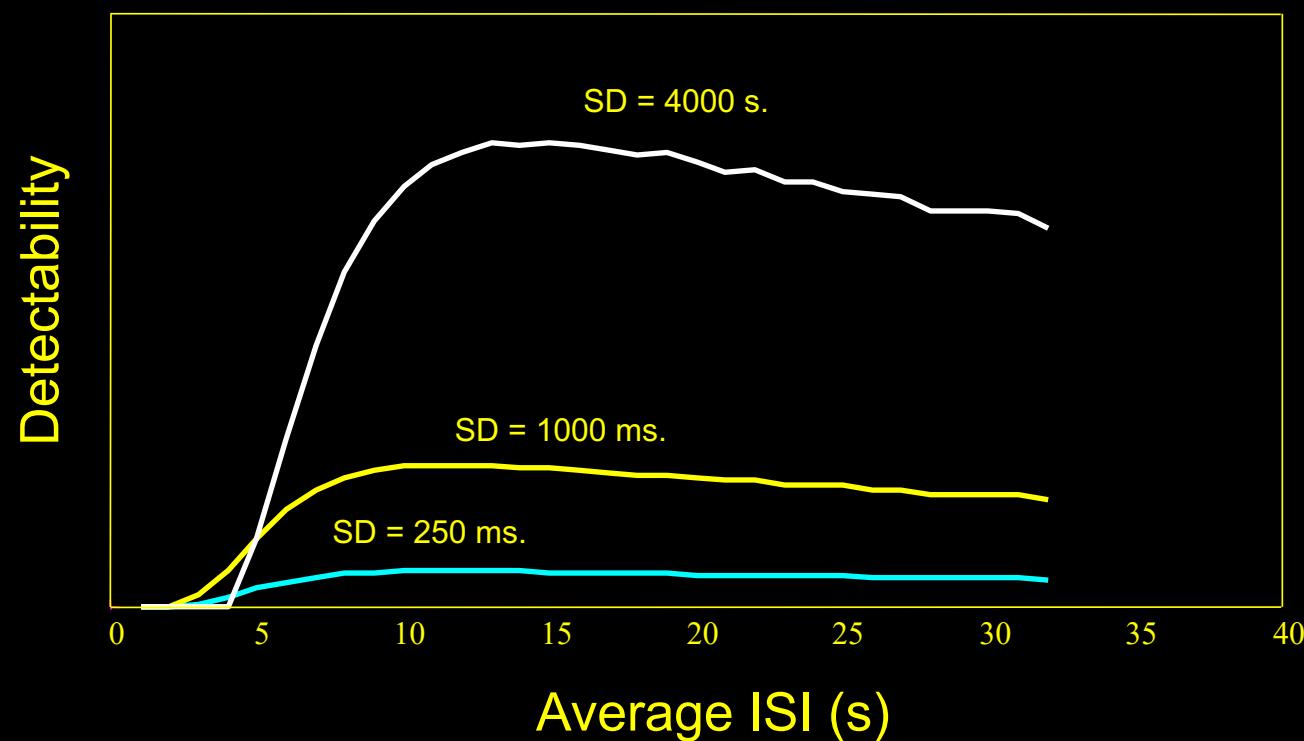


Detectability – constant ISI

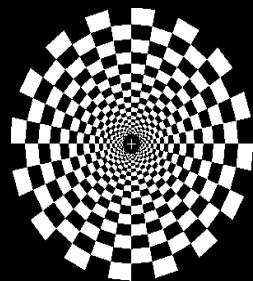
SD – stimulus duration



ISI – inter-stimulus interval

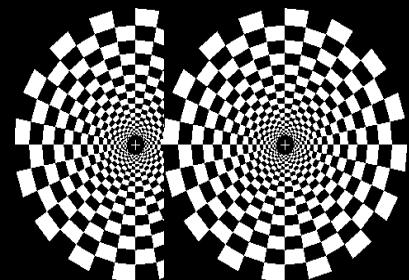


Visual Activation Paradigm: 1 , 2, & 3 Trials



0 sec

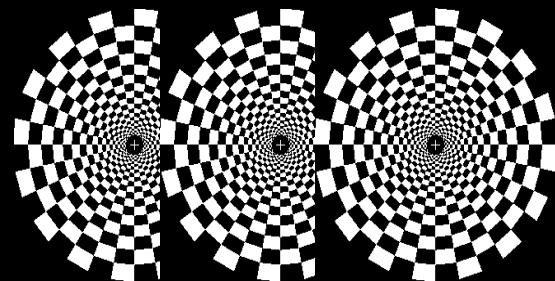
20 sec



0 sec

2 sec

20 sec



0 sec

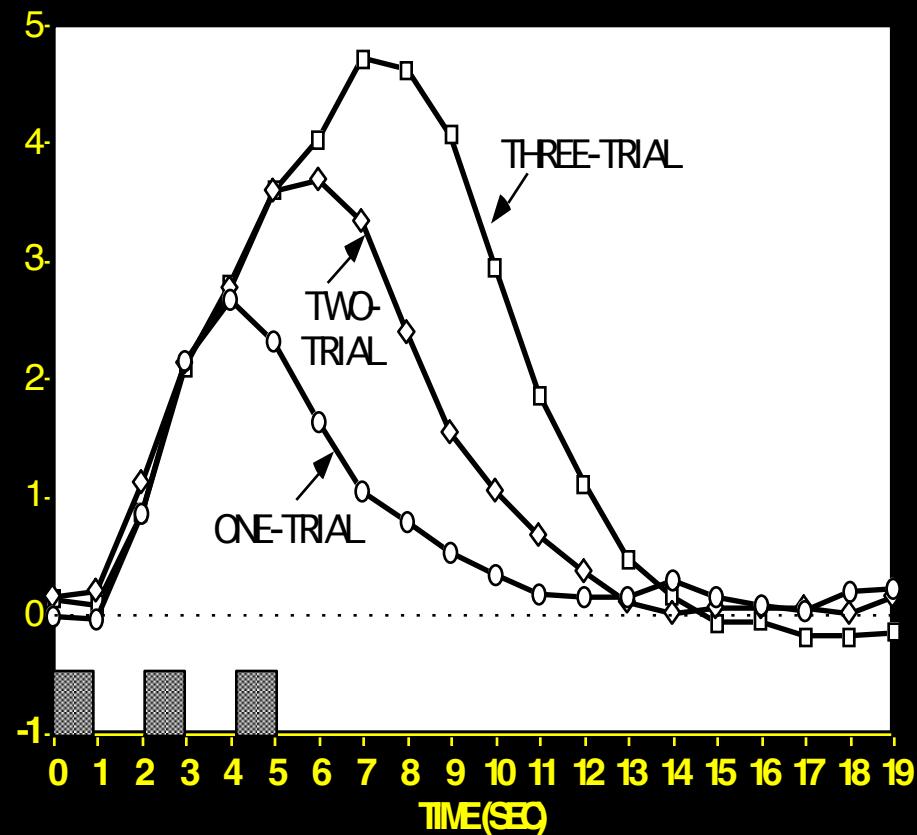
2 sec

4 sec

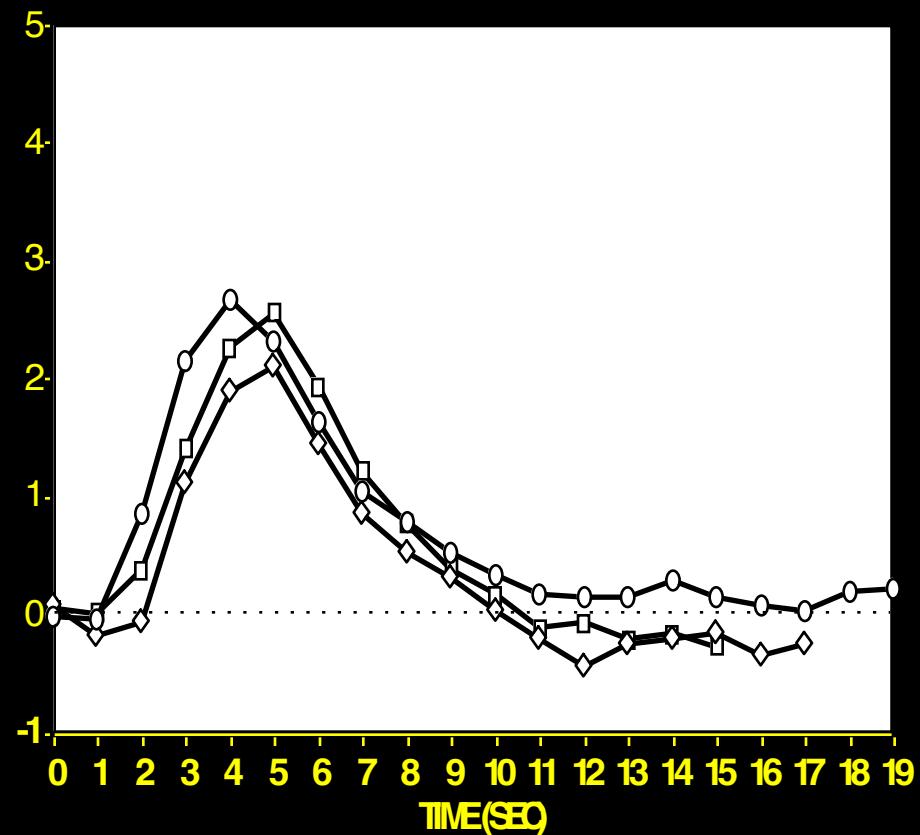
20 sec

Response to Multiple Trials: Subject RW

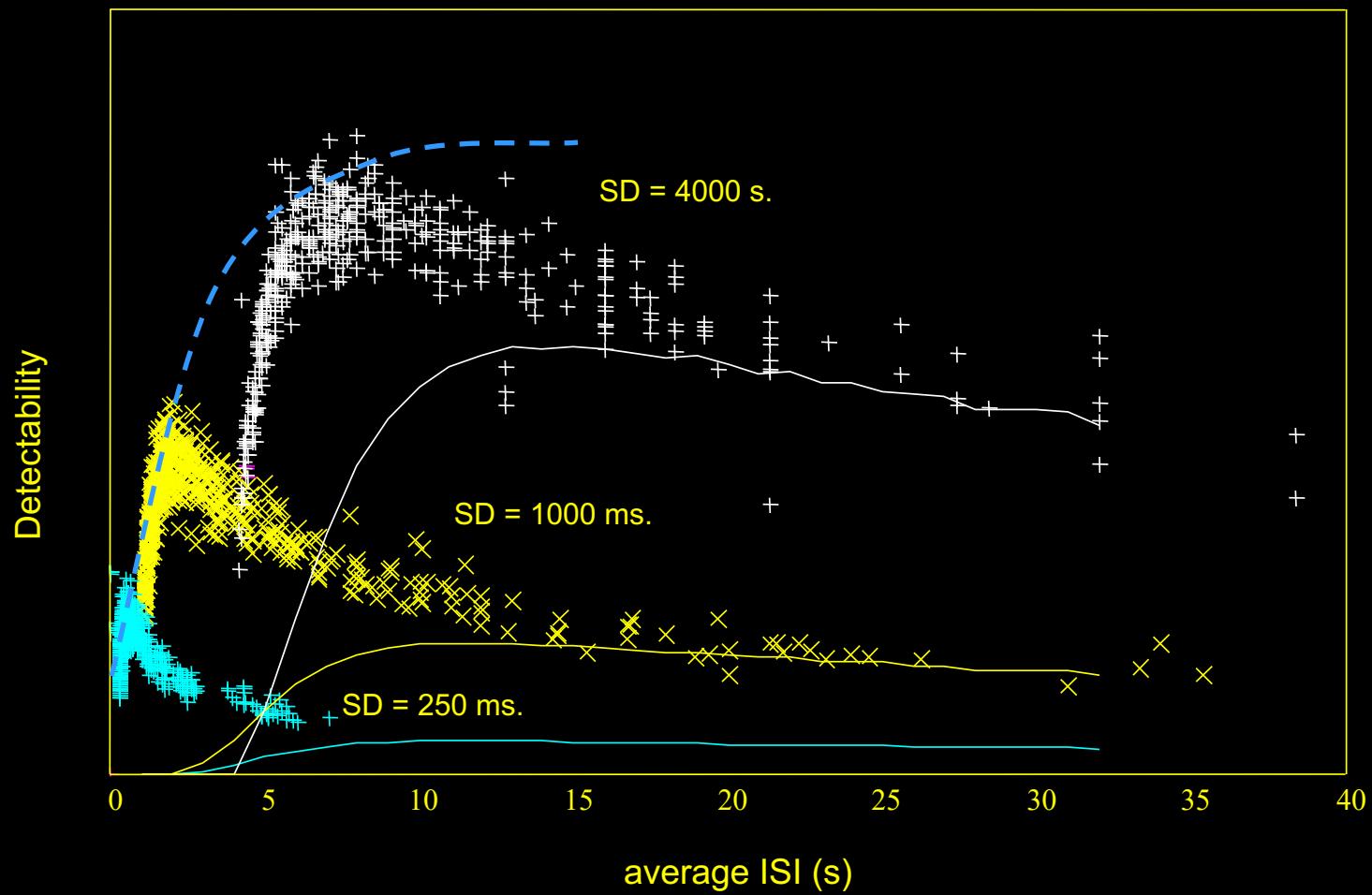
RAW DATA



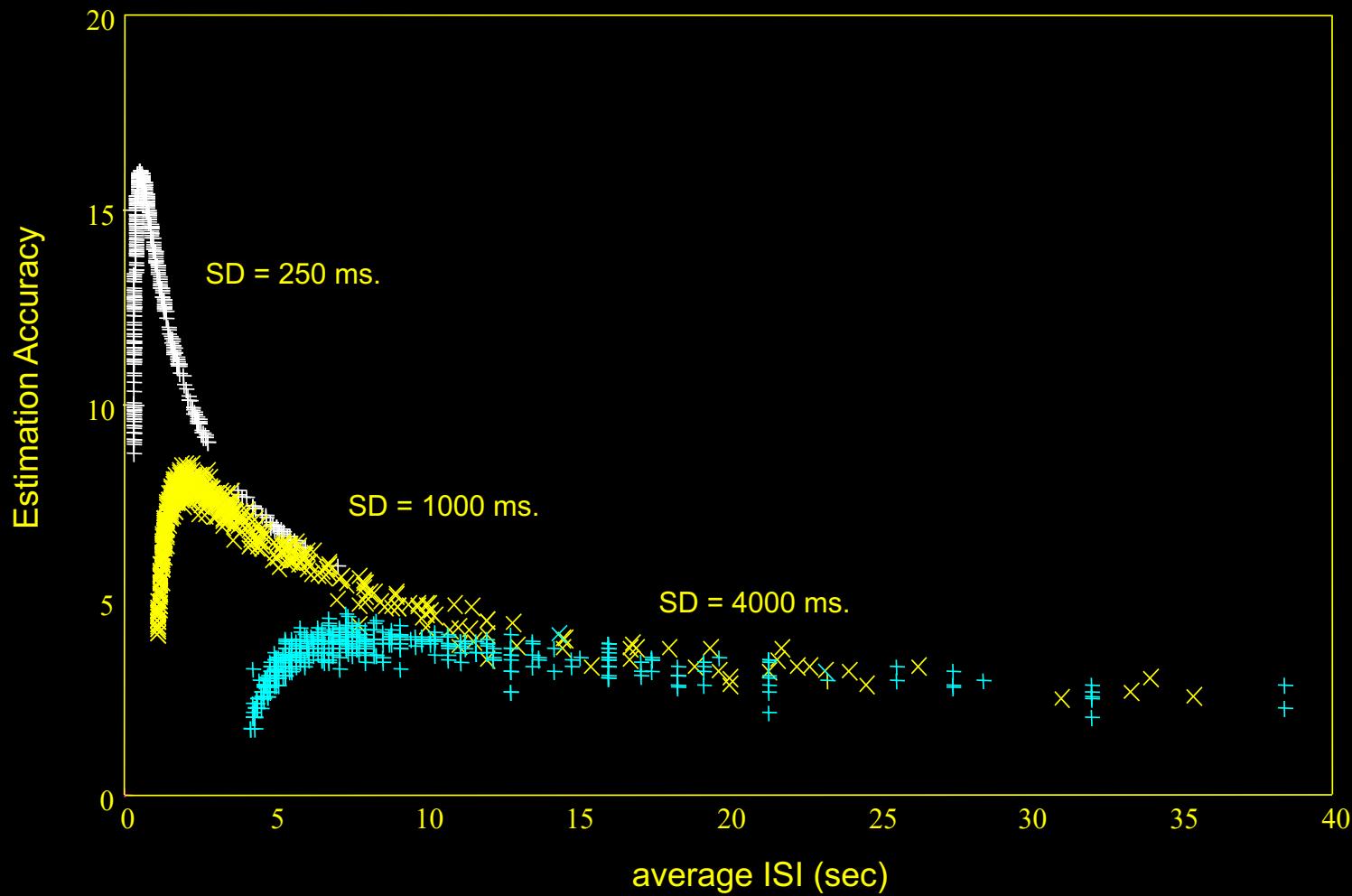
ESTIMATED RESPONSES



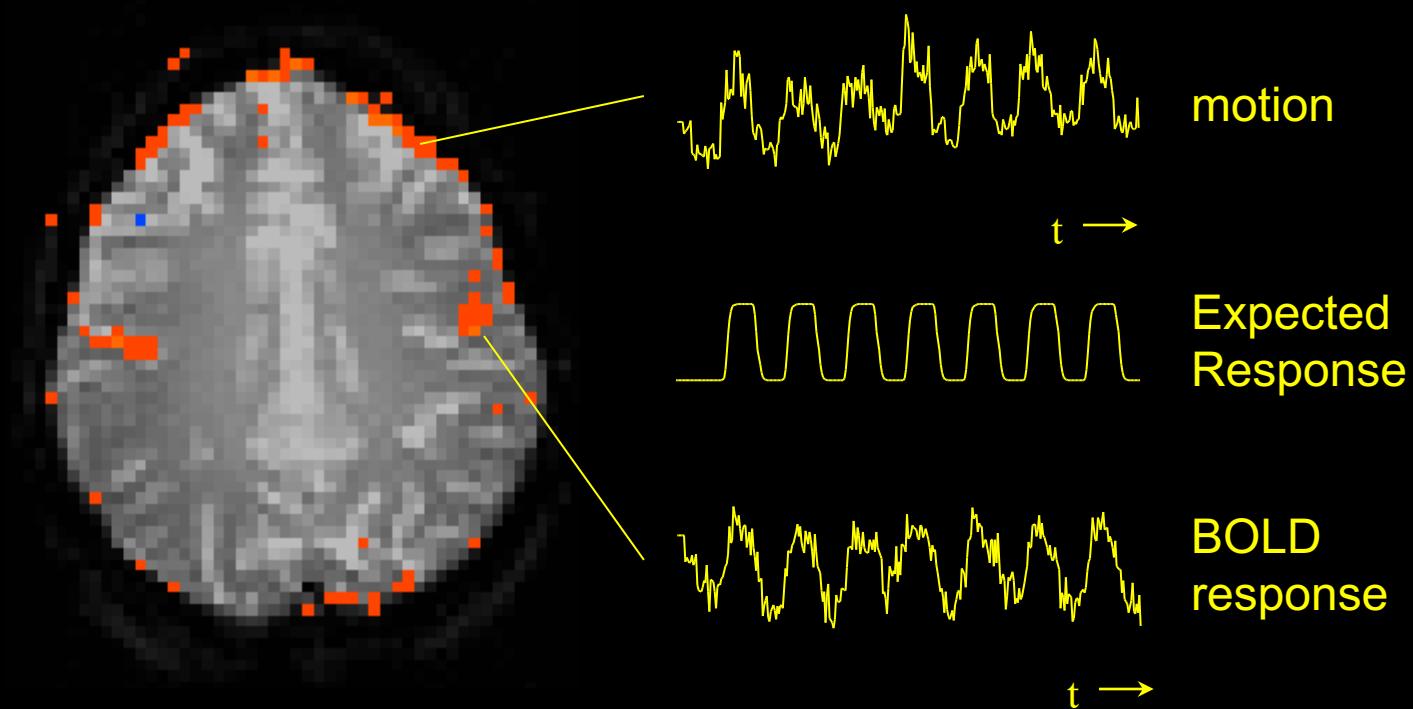
Detectability vs. Average ISI



Estimation accuracy vs. average ISI

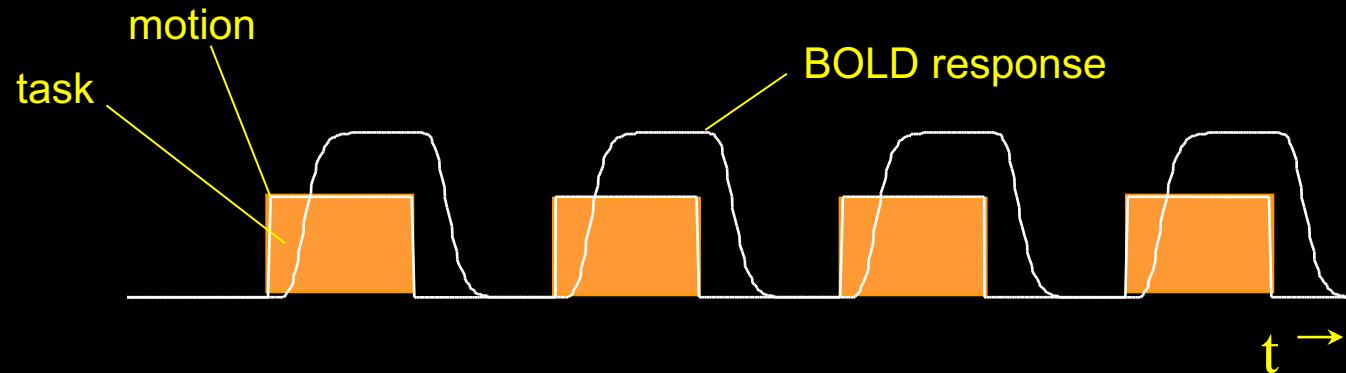


Speaking - Blocked Trial

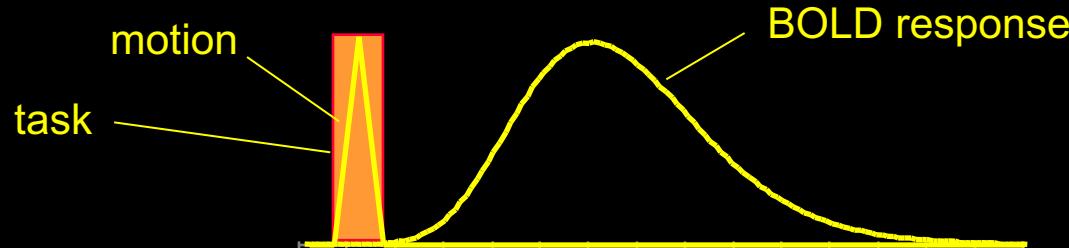


fMRI during tasks that involve brief motion

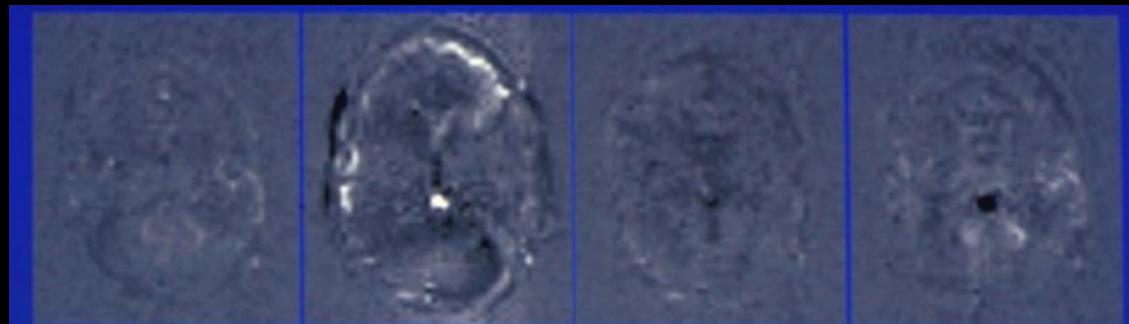
Blocked Design



Event-Related Design



Overt Word Production



2

3

4

5



6

7

8

9



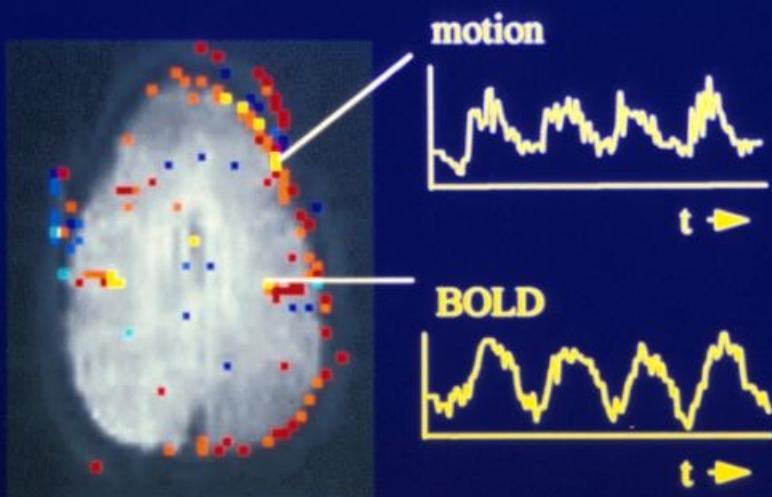
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11

12

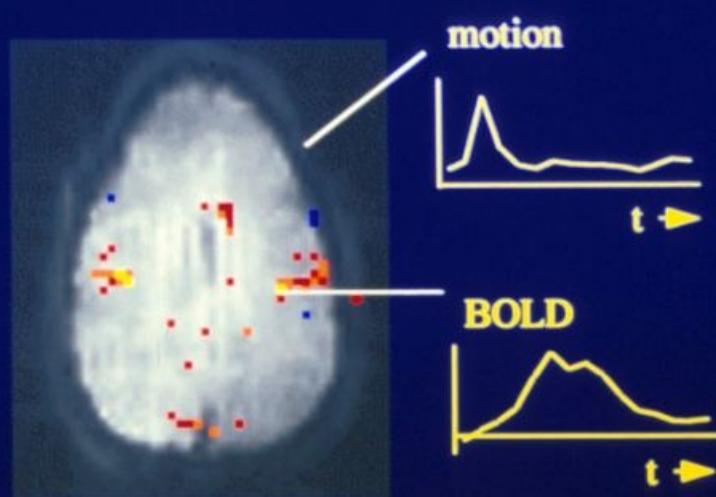
13

Motion-Decoupled fMRI: Functional MRI during overt word production



"block-trial" paradigm

Motion induced signal changes resemble functional (BOLD) signal changes

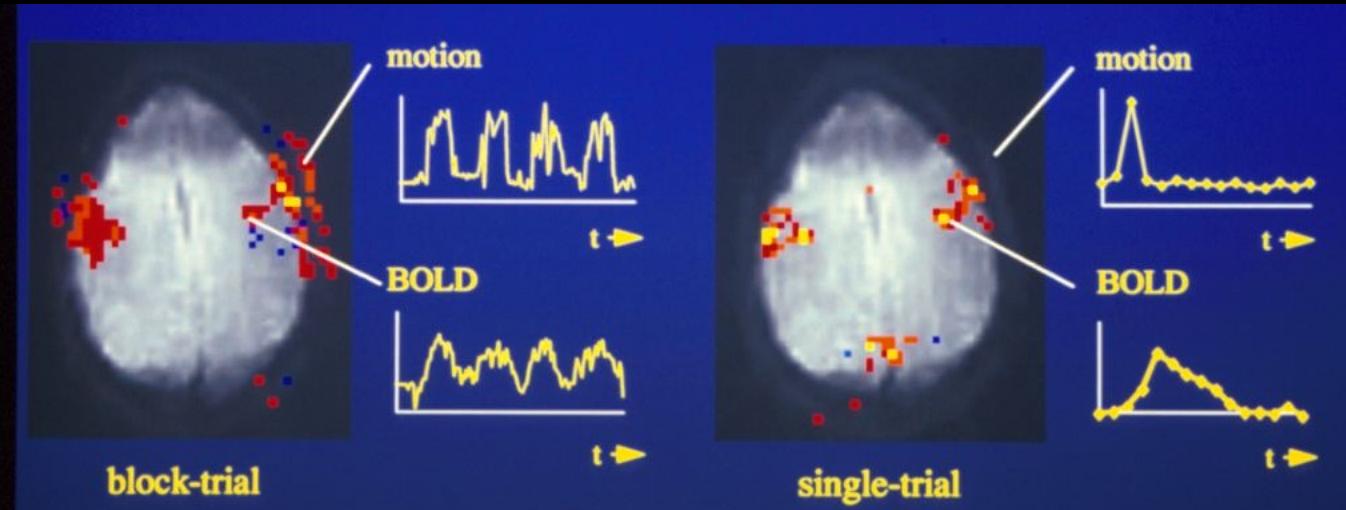


"single-trial" paradigm

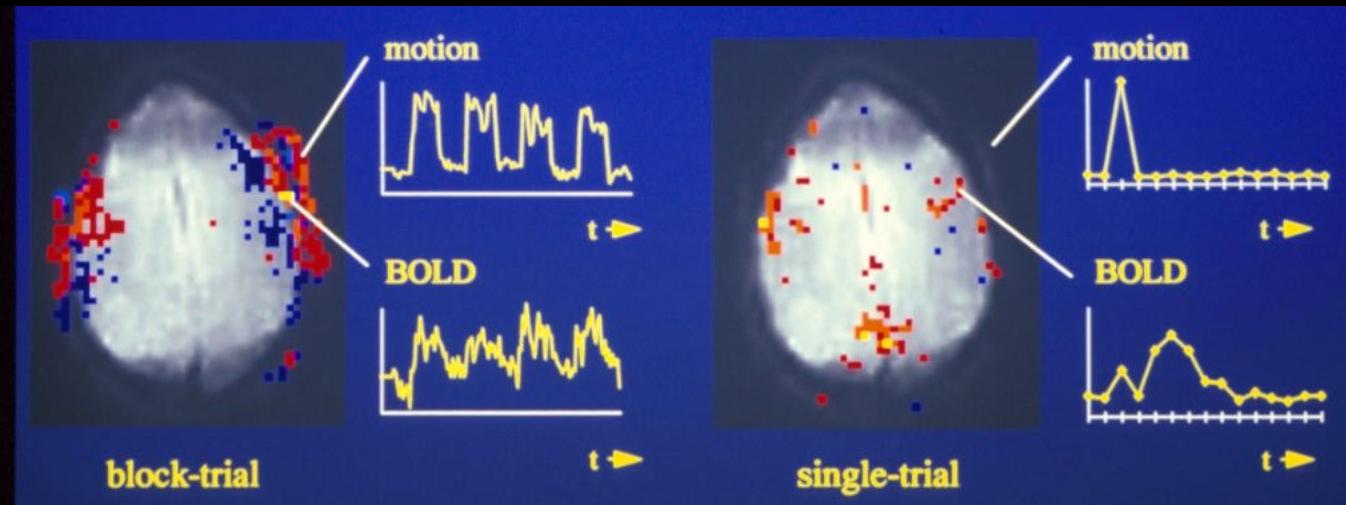
Motion induced and BOLD signal changes are separated in time

R.M. Birn, et al.

Tongue Movement

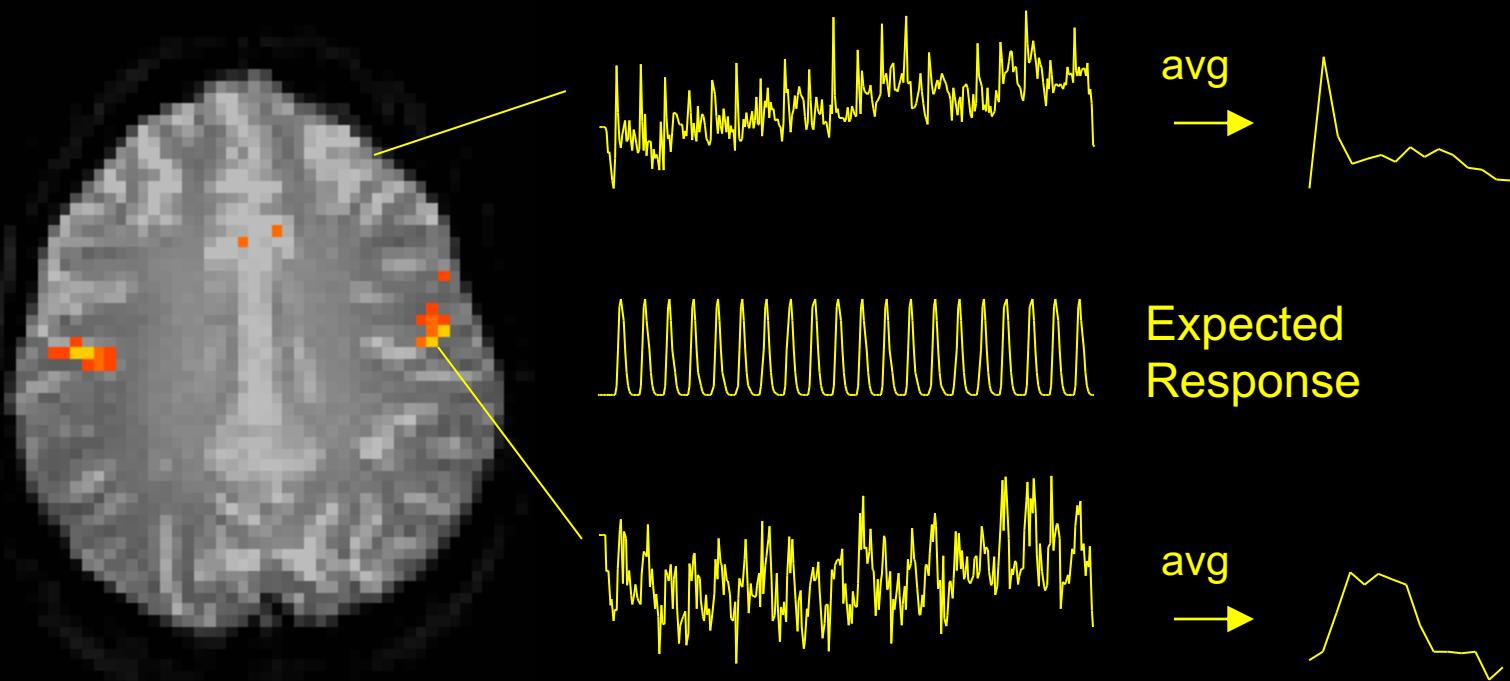


Jaw Clenching



Constant ISI

Speaking - ER-fMRI



Swallowing - Event-Related



Neuronal Activation Input Strategies

1. Block Design

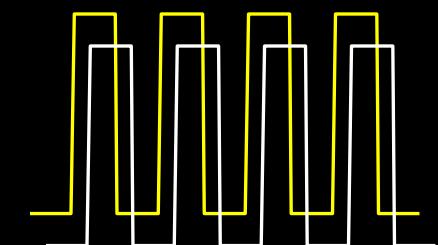
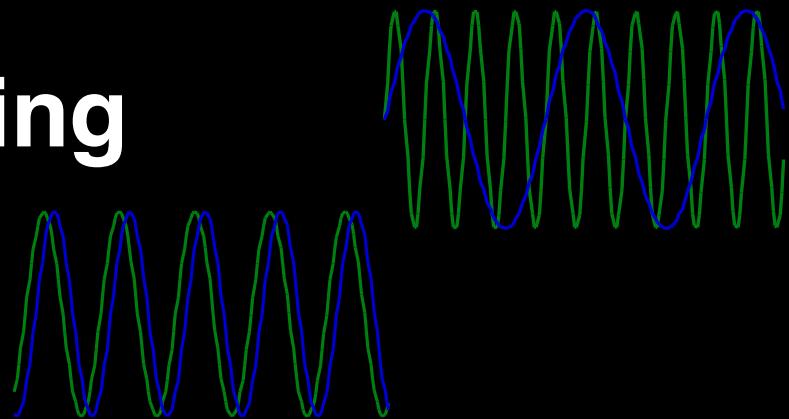
2. Frequency Encoding

3. Phase Encoding

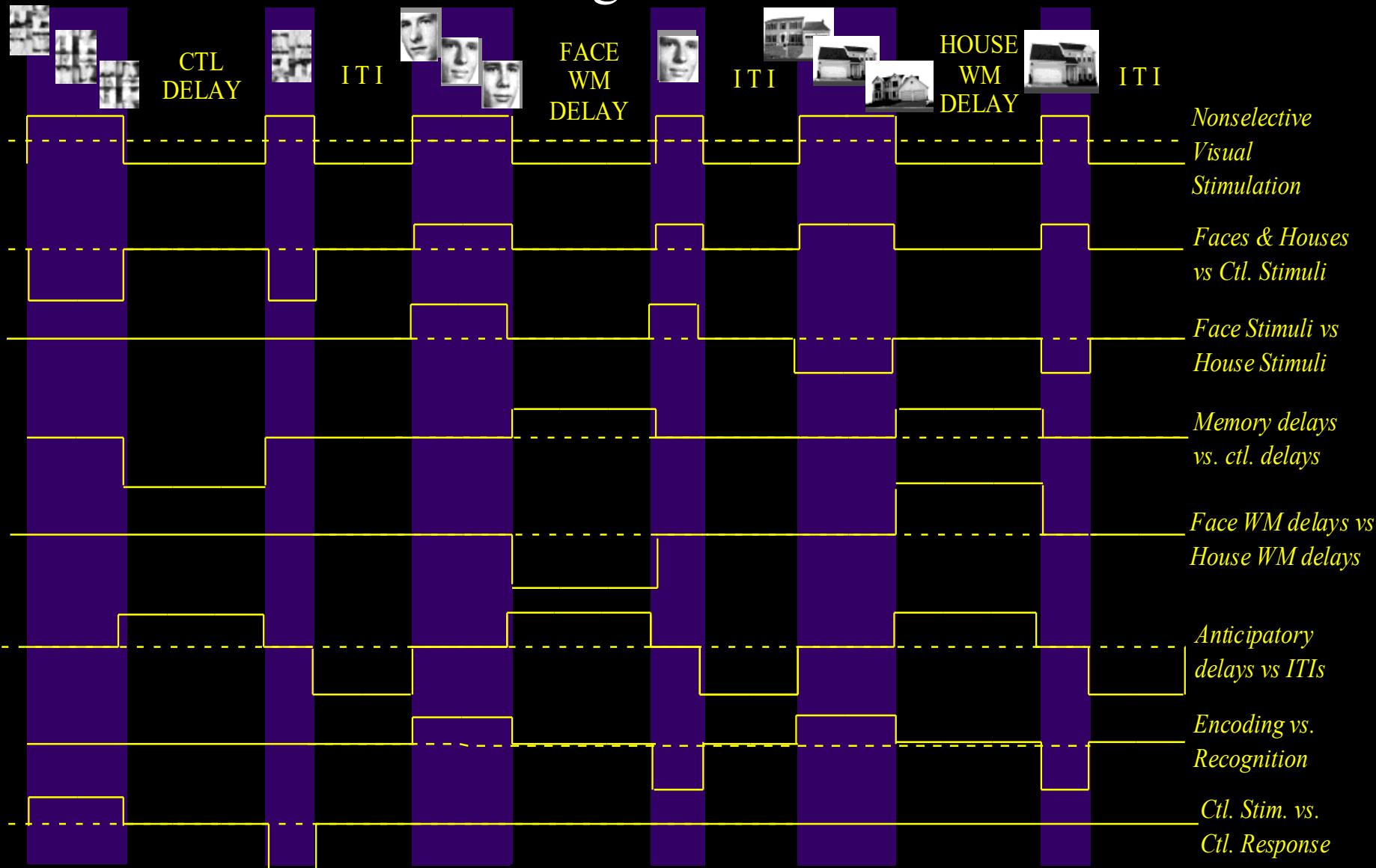
4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.



Example of a Set of Orthogonal Contrasts for Multiple Regression



Neuronal Activation Input Strategies

1. Block Design

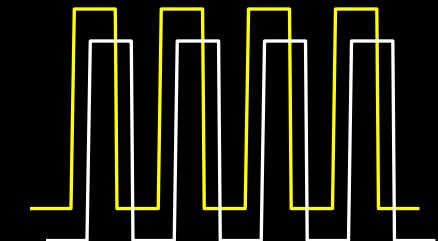
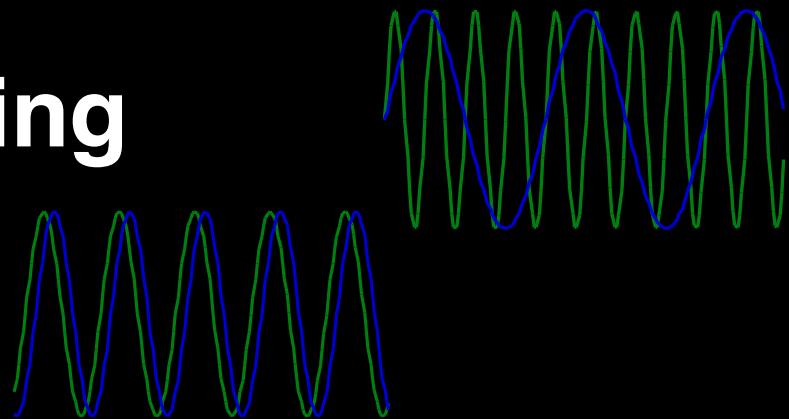
2. Frequency Encoding

3. Phase Encoding

4. Single Event

5. Orthogonal Block Design

6. Free Behavior Design.

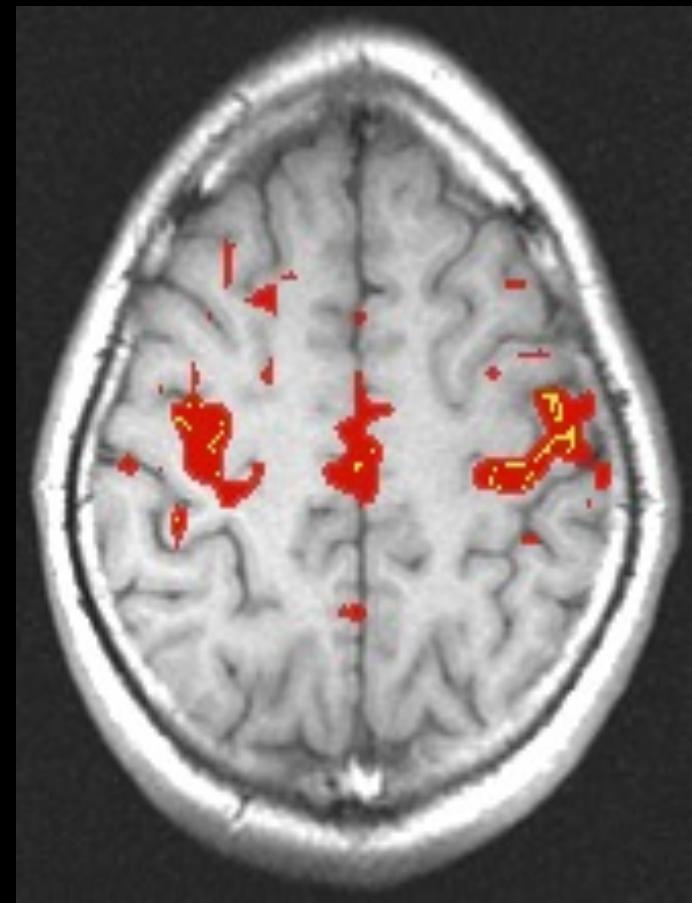
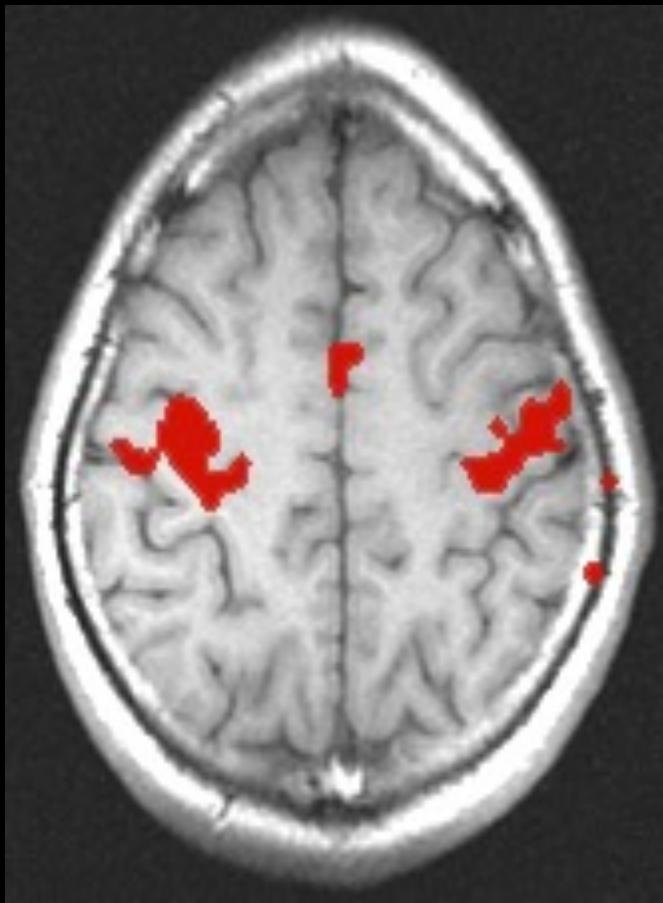


Free Behavior Design

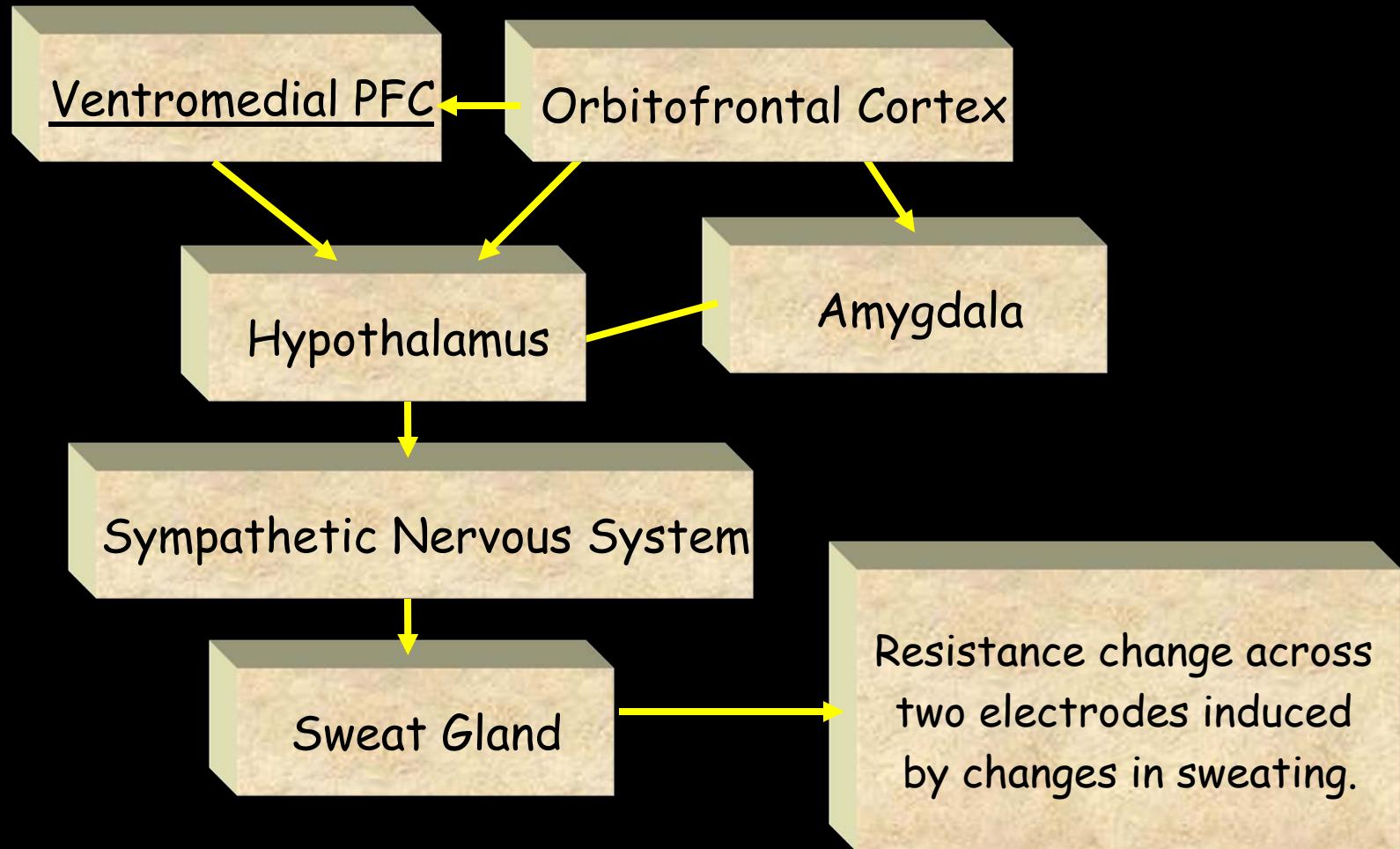
Use a continuous measure as a reference function:

- Task performance
- Skin Conductance
- Heart, respiration rate..
- Eye position
- EEG

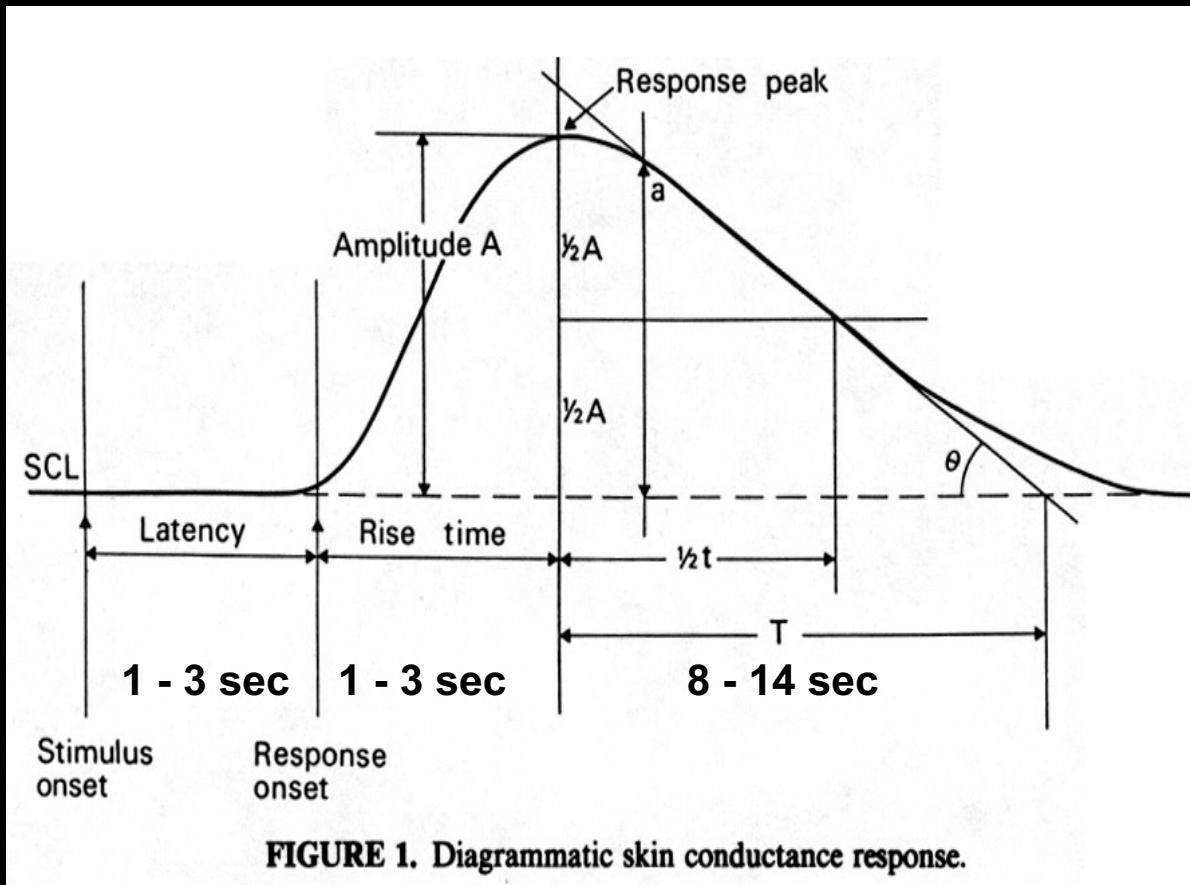
Resting Hemodynamic Autocorrelations



The Skin Conductance Response (SCR)

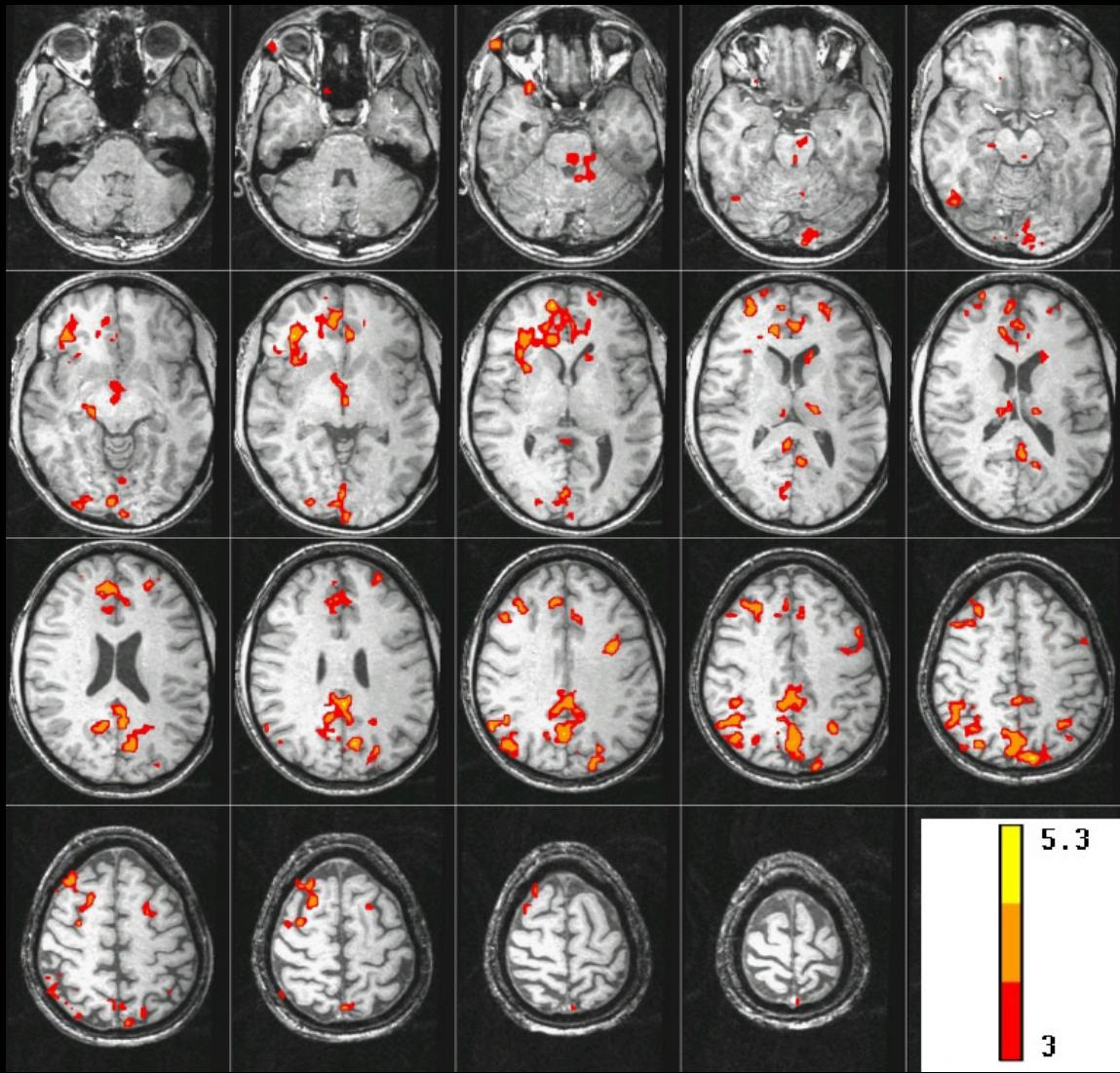


Skin Conductance Dynamics



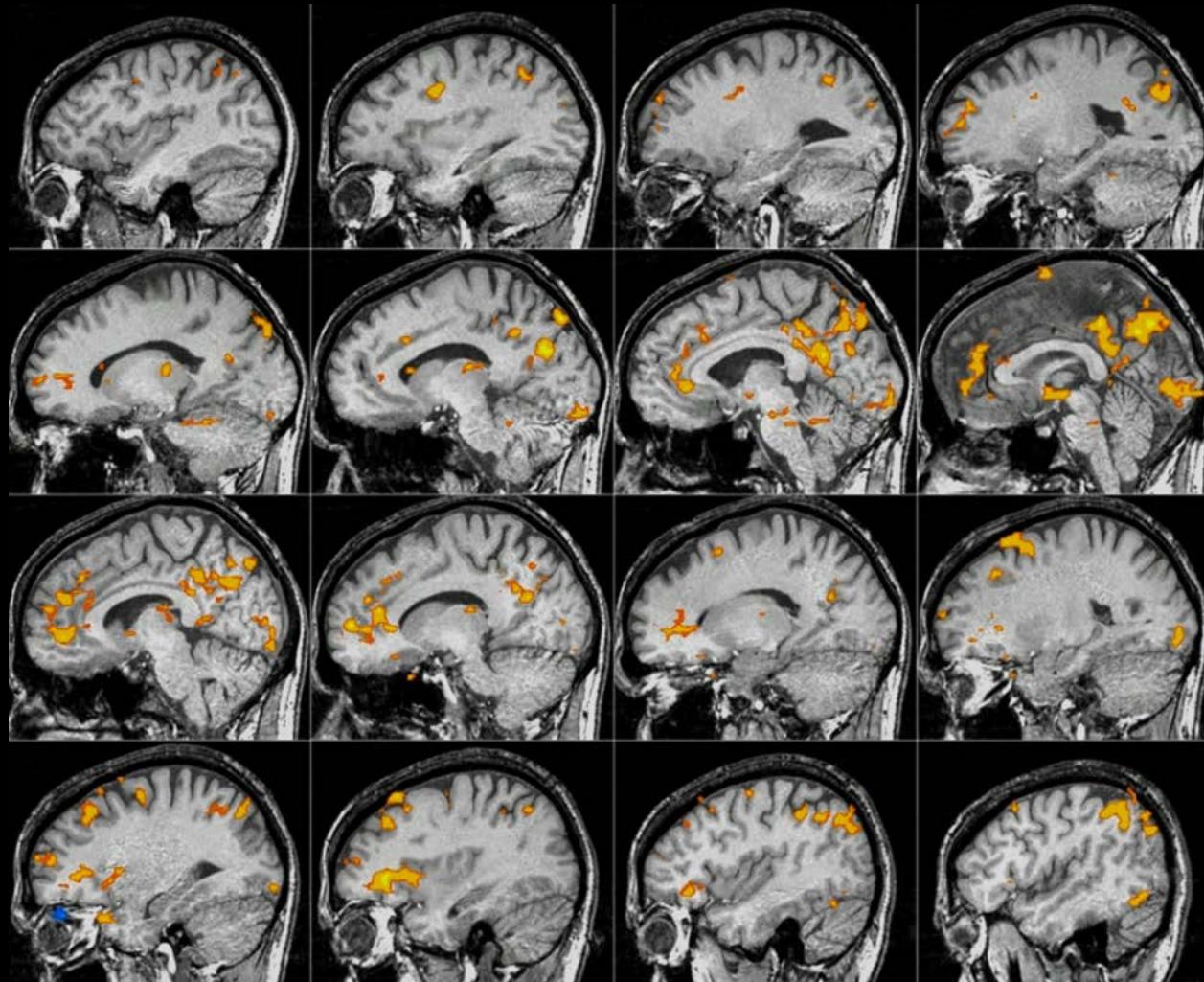
- Boucsein, Wolfram (1992). Electrodermal Activity. Plenum Press, NY
- Venables, Peter, (1991). Autonomic Activity ANYAS 620:191-207.

Correlation with Resting-State Skin Conductance



Patterson et al.

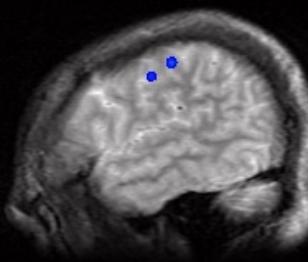
Brain activity correlated with SCR during “Rest”



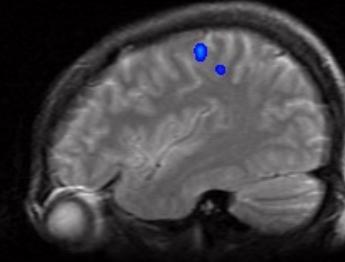
Left

Simple Finger Movement on the Left Hand

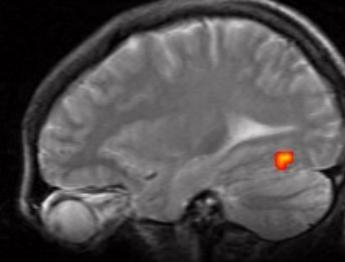
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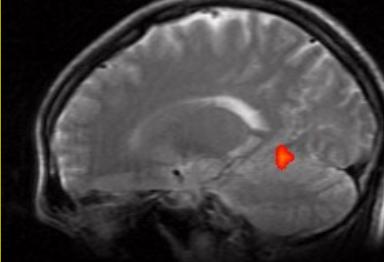
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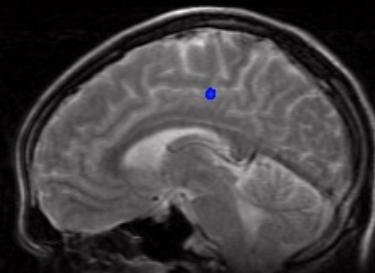
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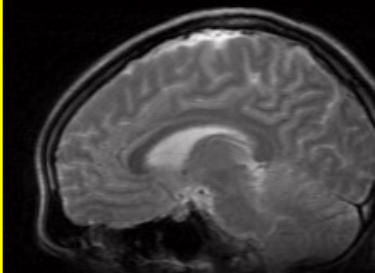
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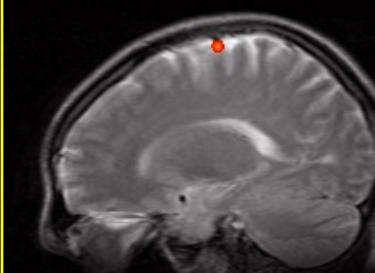
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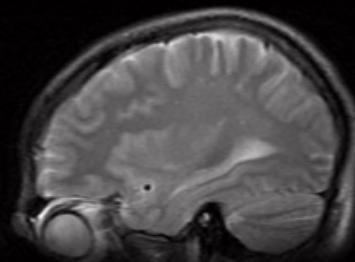
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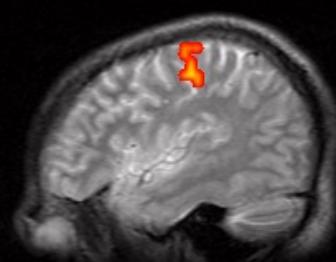
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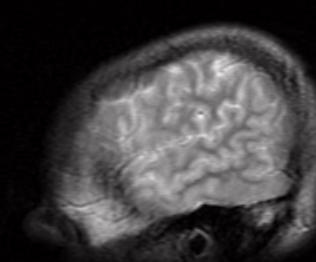
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9



10

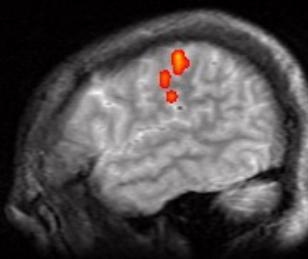


Right

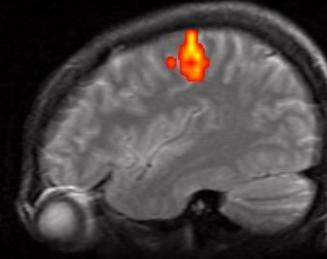
Left

Simple Finger Movement on the Right Hand

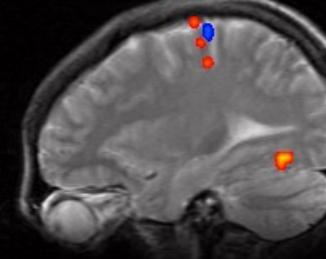
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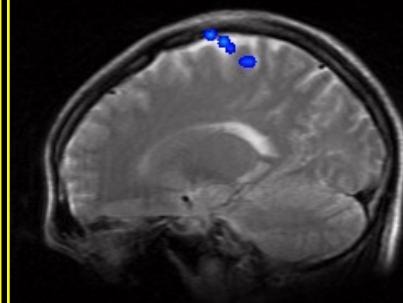
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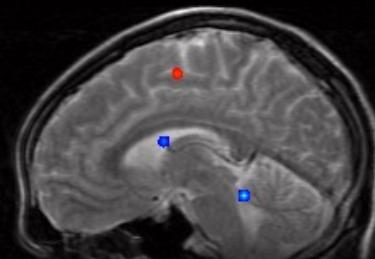
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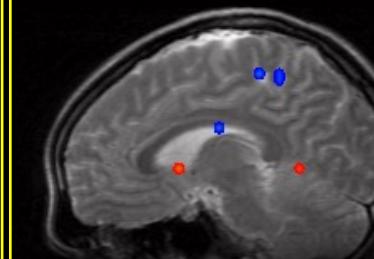
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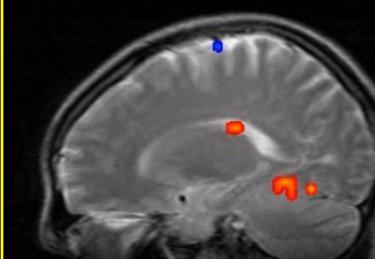
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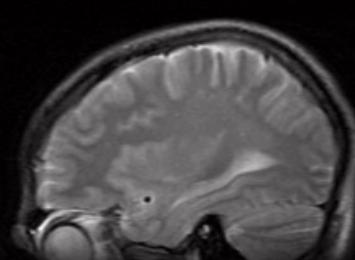
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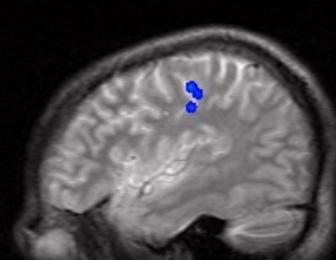
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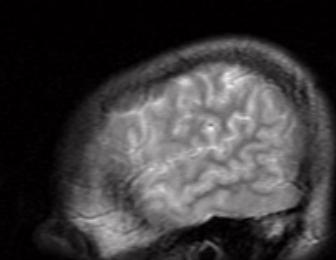
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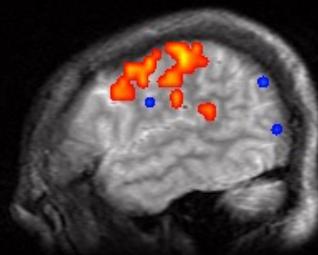


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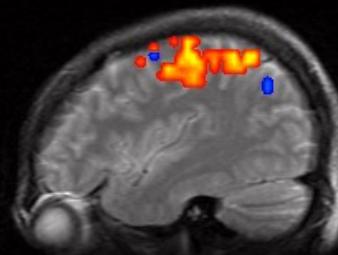
Left

Complex Finger Movement on the Right Hand

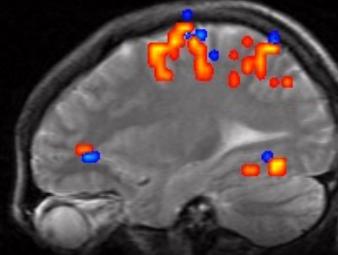
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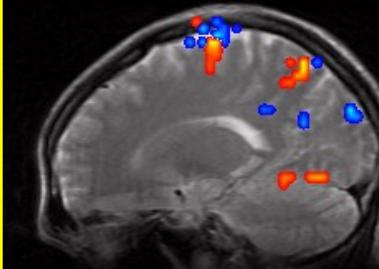
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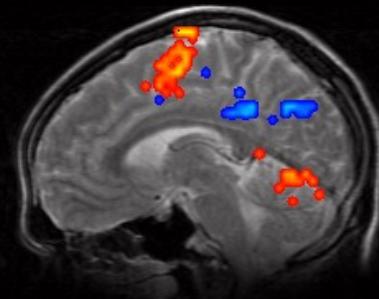
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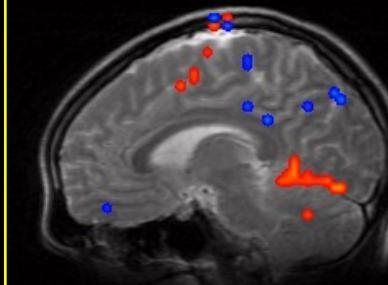
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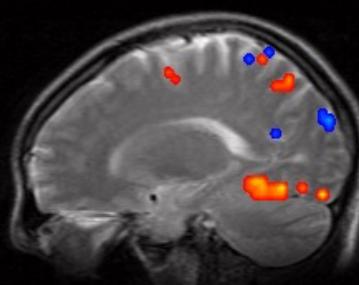
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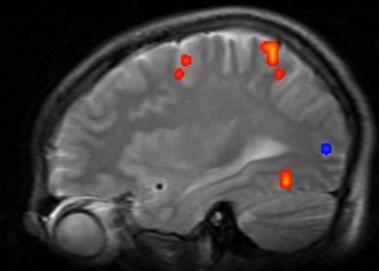
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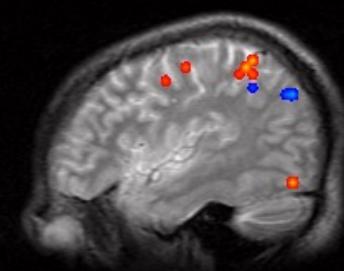
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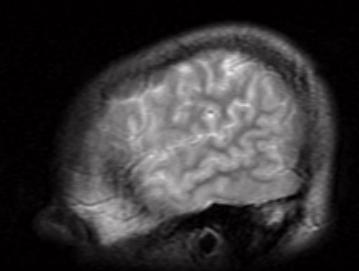
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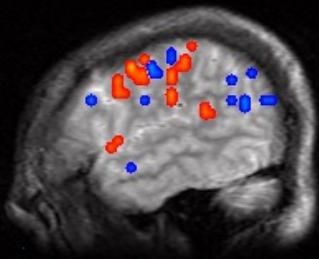


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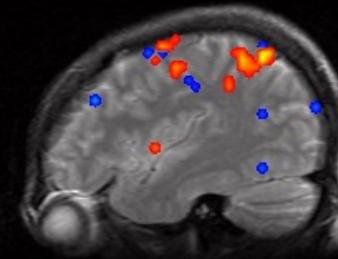
Left

Complex Finger Movement on the Left Hand

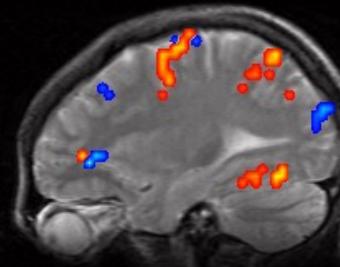
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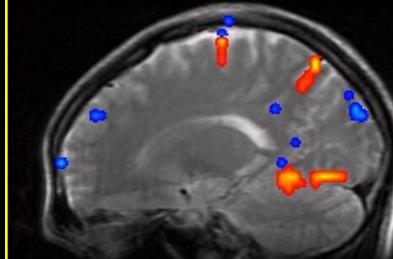
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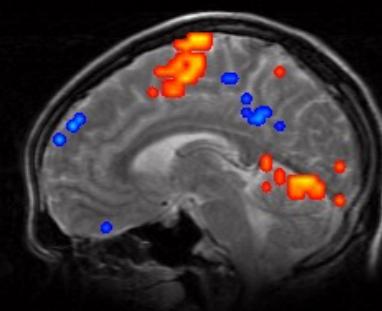
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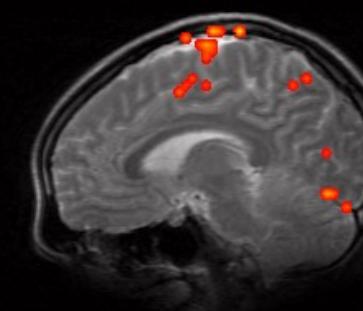
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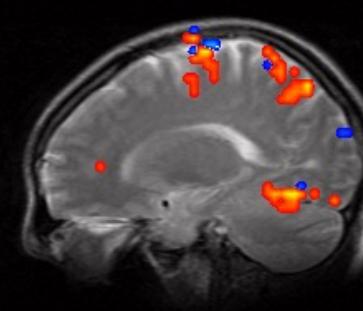
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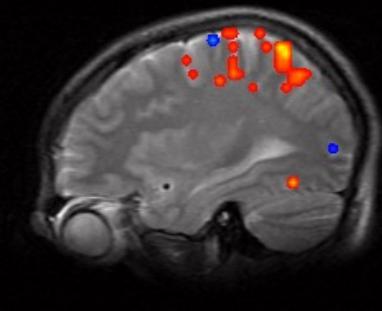
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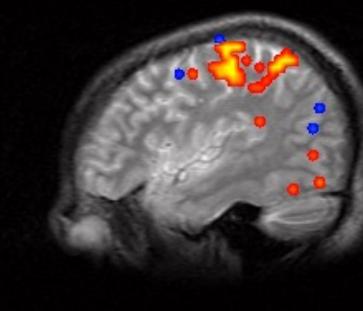
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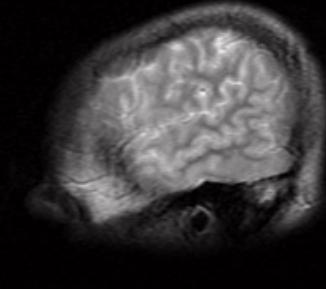
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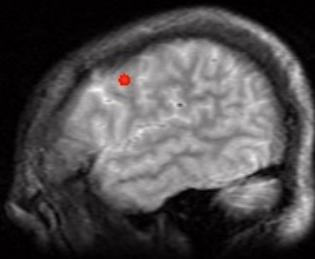


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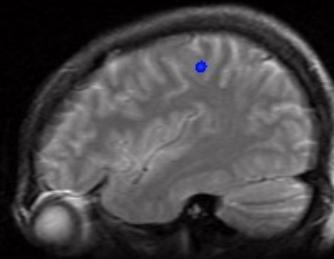
Left

Imagined Complex Finger Movement on the Left Hand

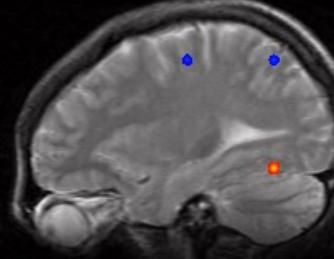
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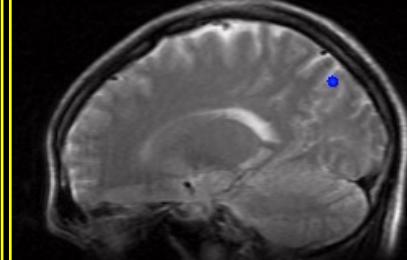
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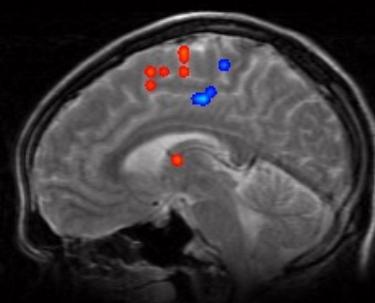
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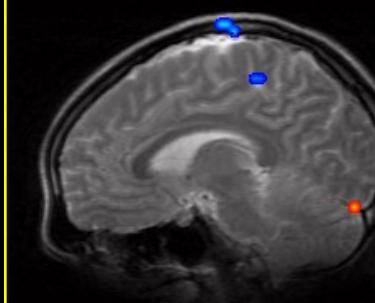
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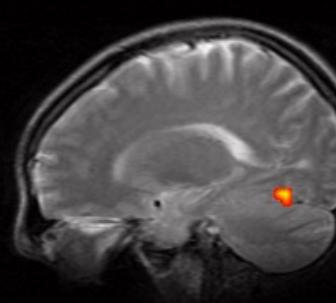
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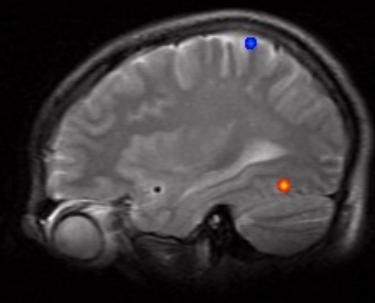
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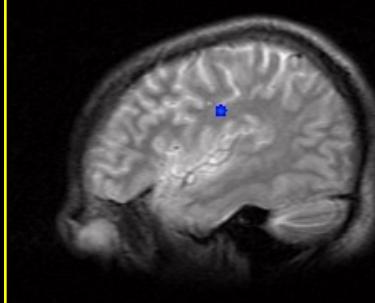
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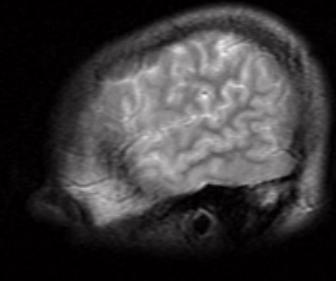
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9



10

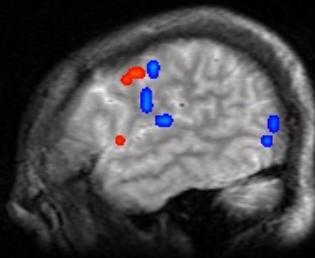


Right

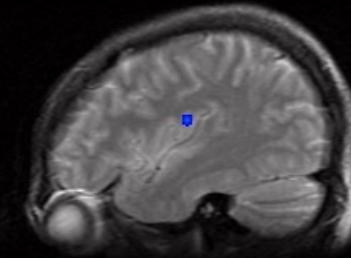
Left

Imagined Complex Finger Movement on the Right Hand

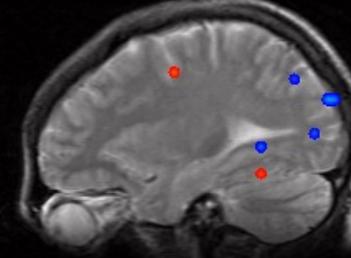
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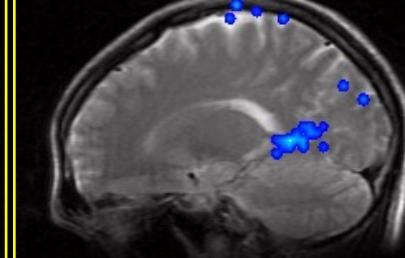
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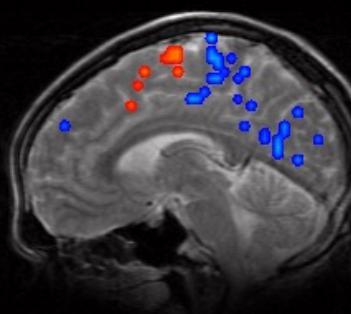
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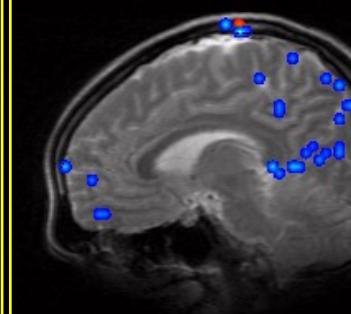
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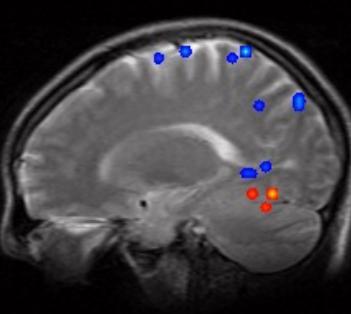
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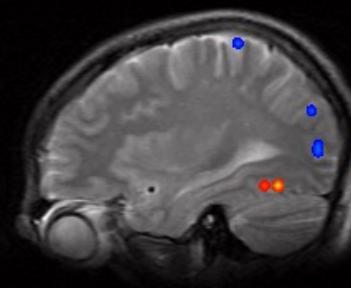
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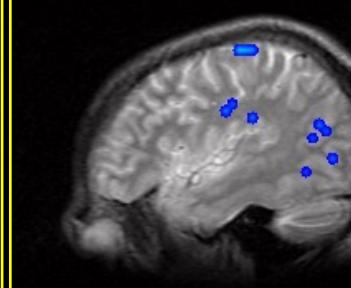
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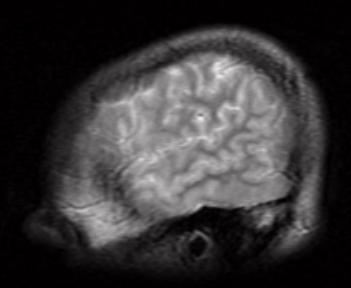
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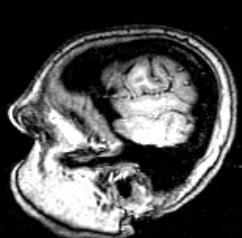
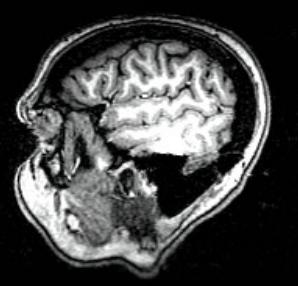
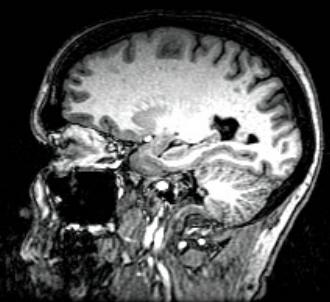
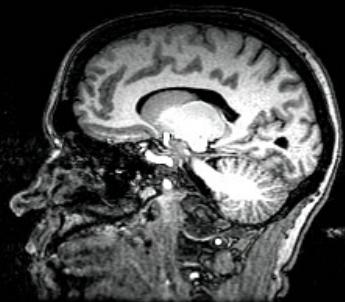
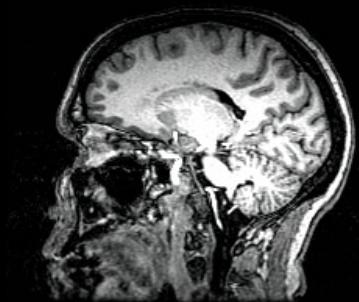
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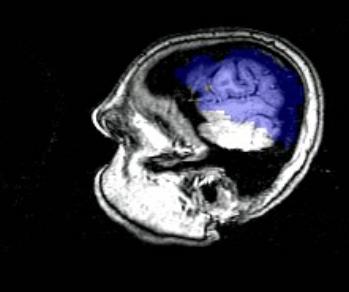
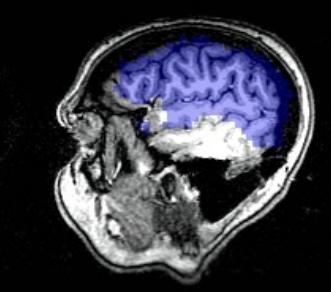
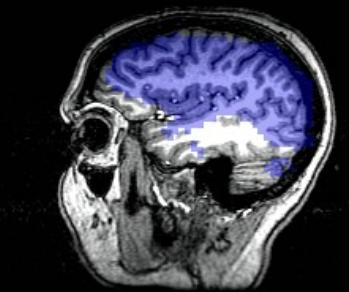
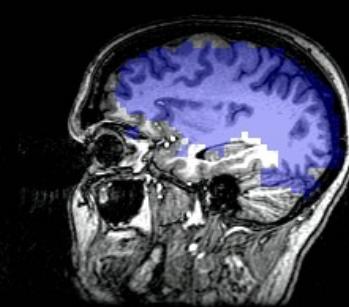
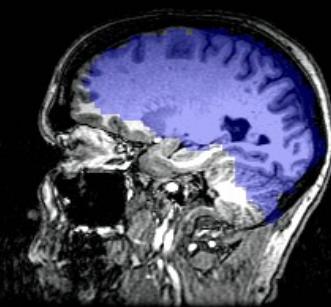
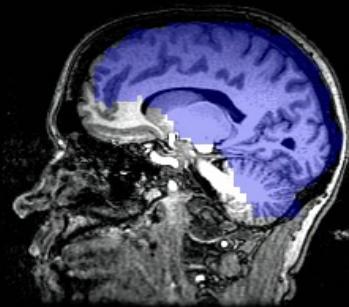
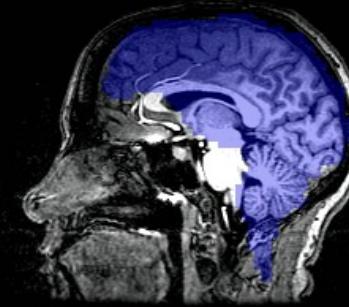
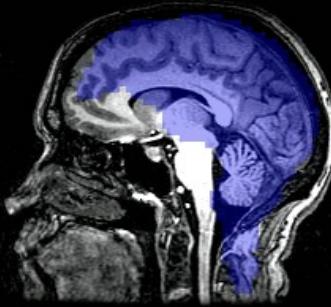
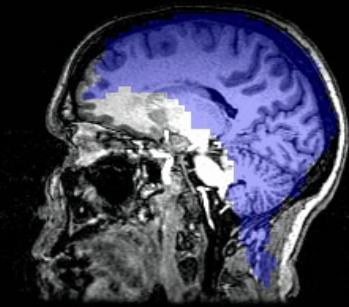
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Right

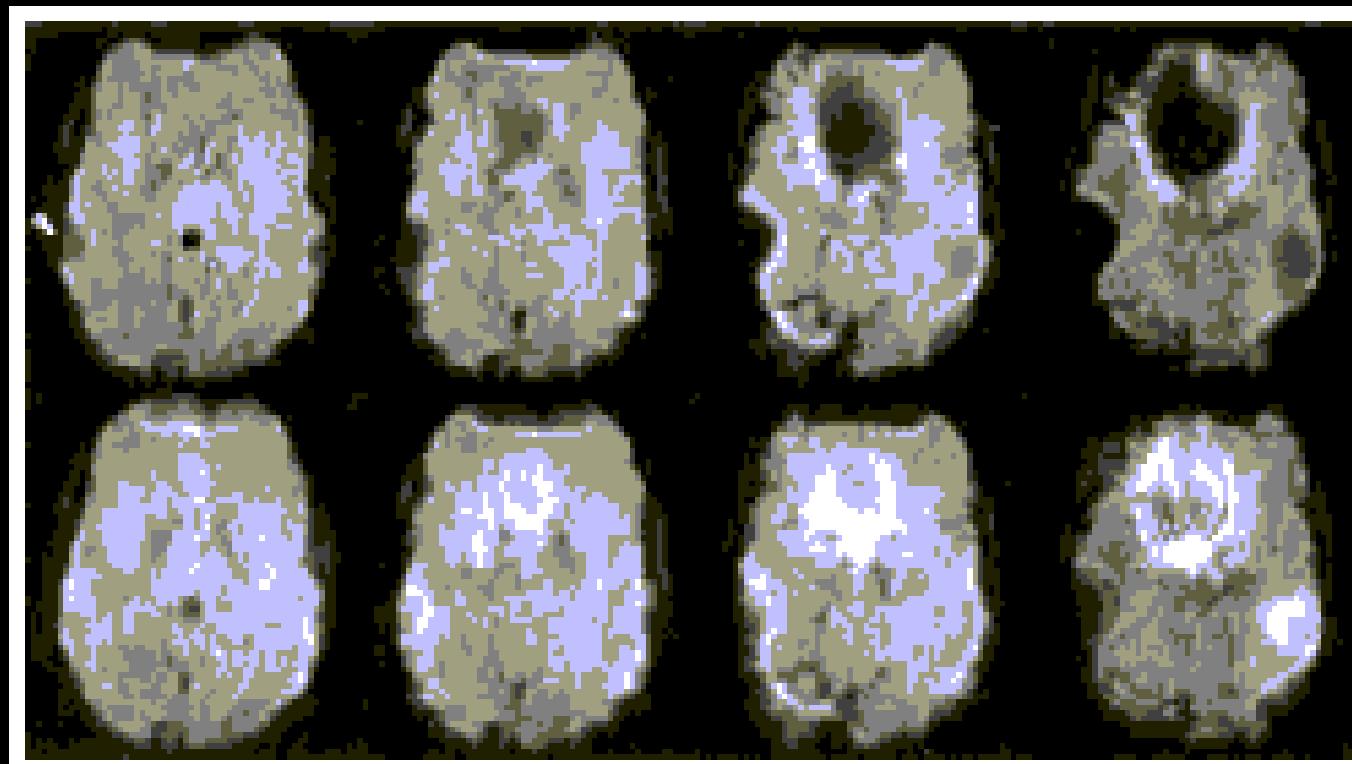






3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

Gary H. Glover*



- Contrast in fMRI

Hemodynamic Specificity

- The Hemodynamic Transfer Function

Location, Latency, Magnitude

- Best Results So Far

Temporal Resolution, Spatial Resolution

- Neuronal Activation Input Strategies

Block Design

Phase and Frequency Encoding

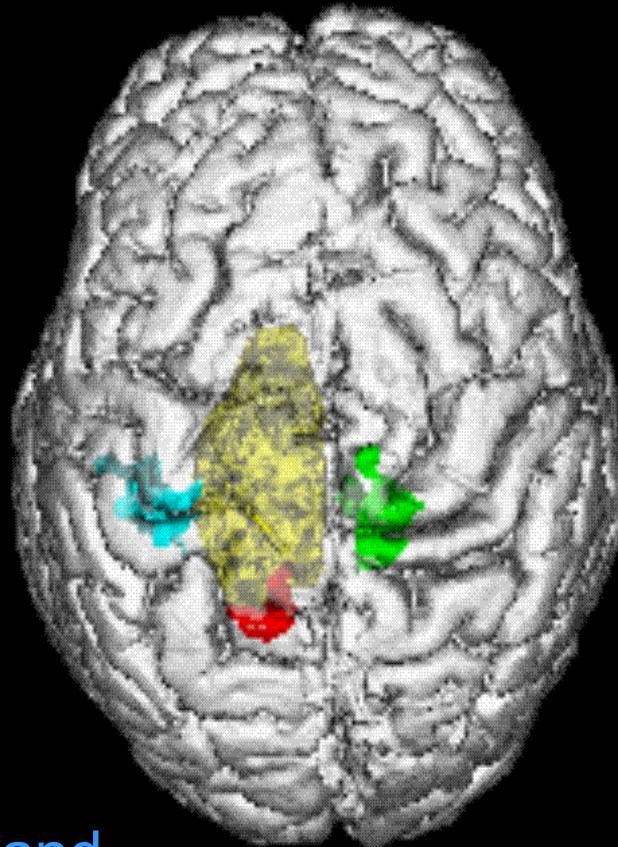
Orthogonal Designs

Parametric Designs

Event-Related Designs

Free Behavior Designs

Sensorimotor Mapping

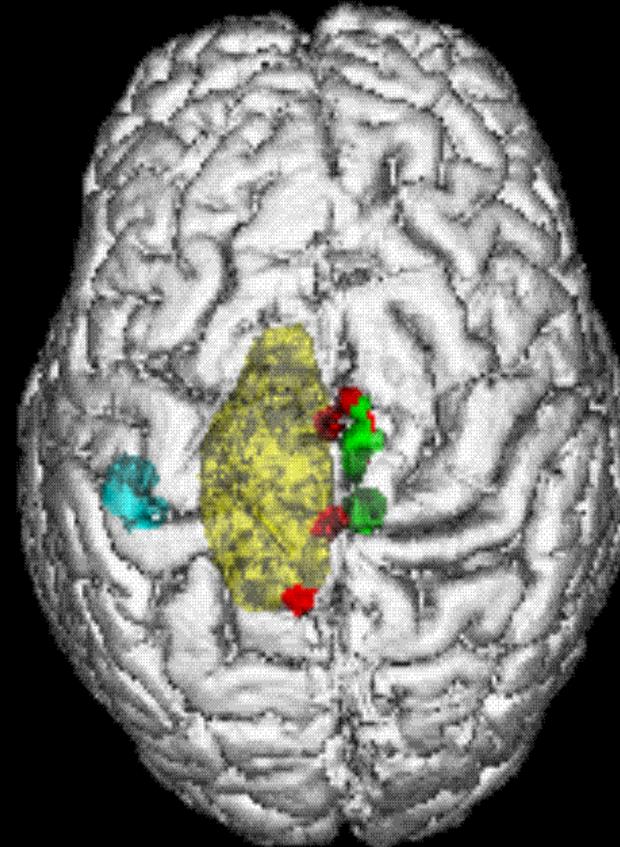


rt hand

rt foot

fM

R

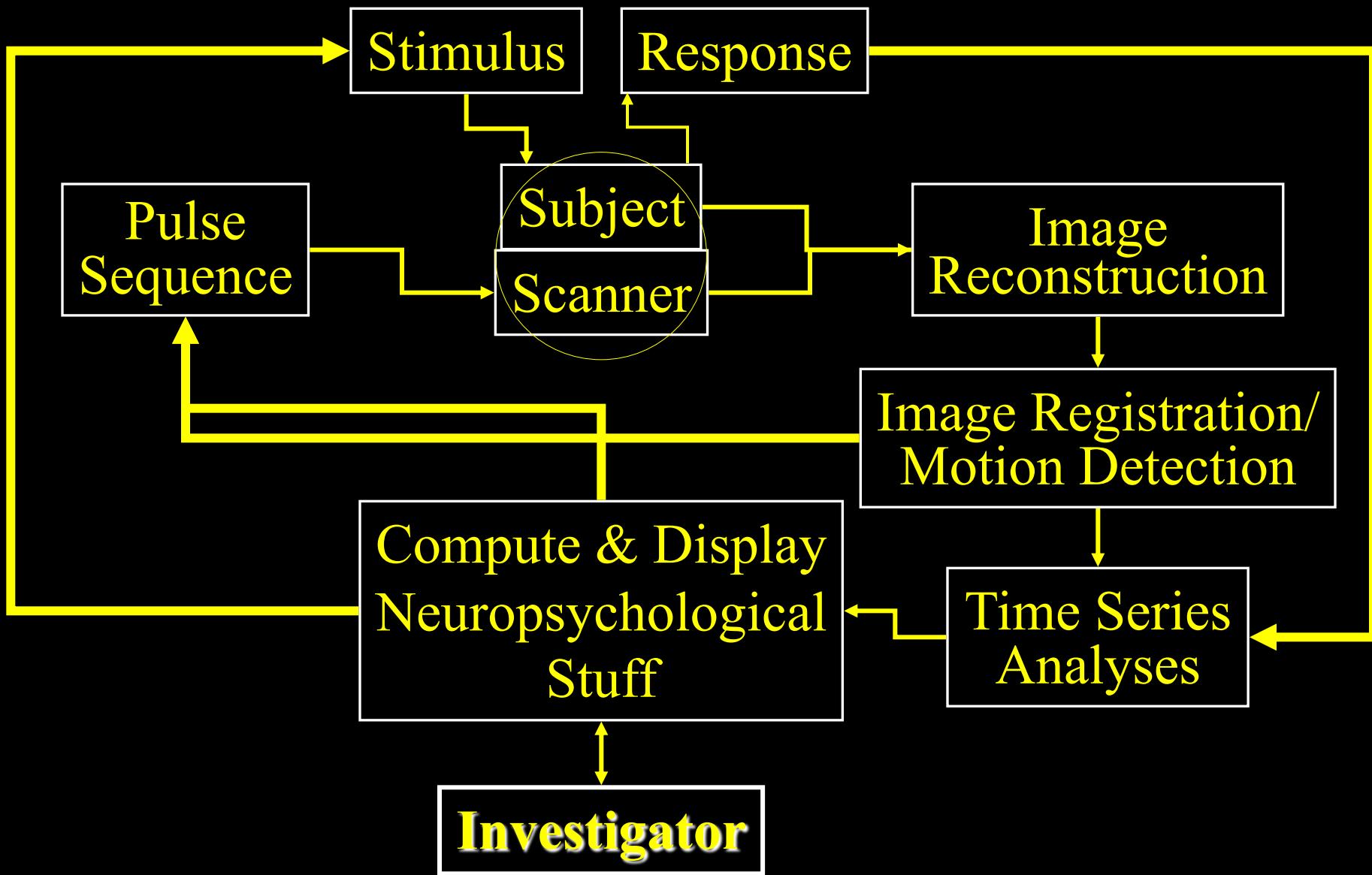


tumor

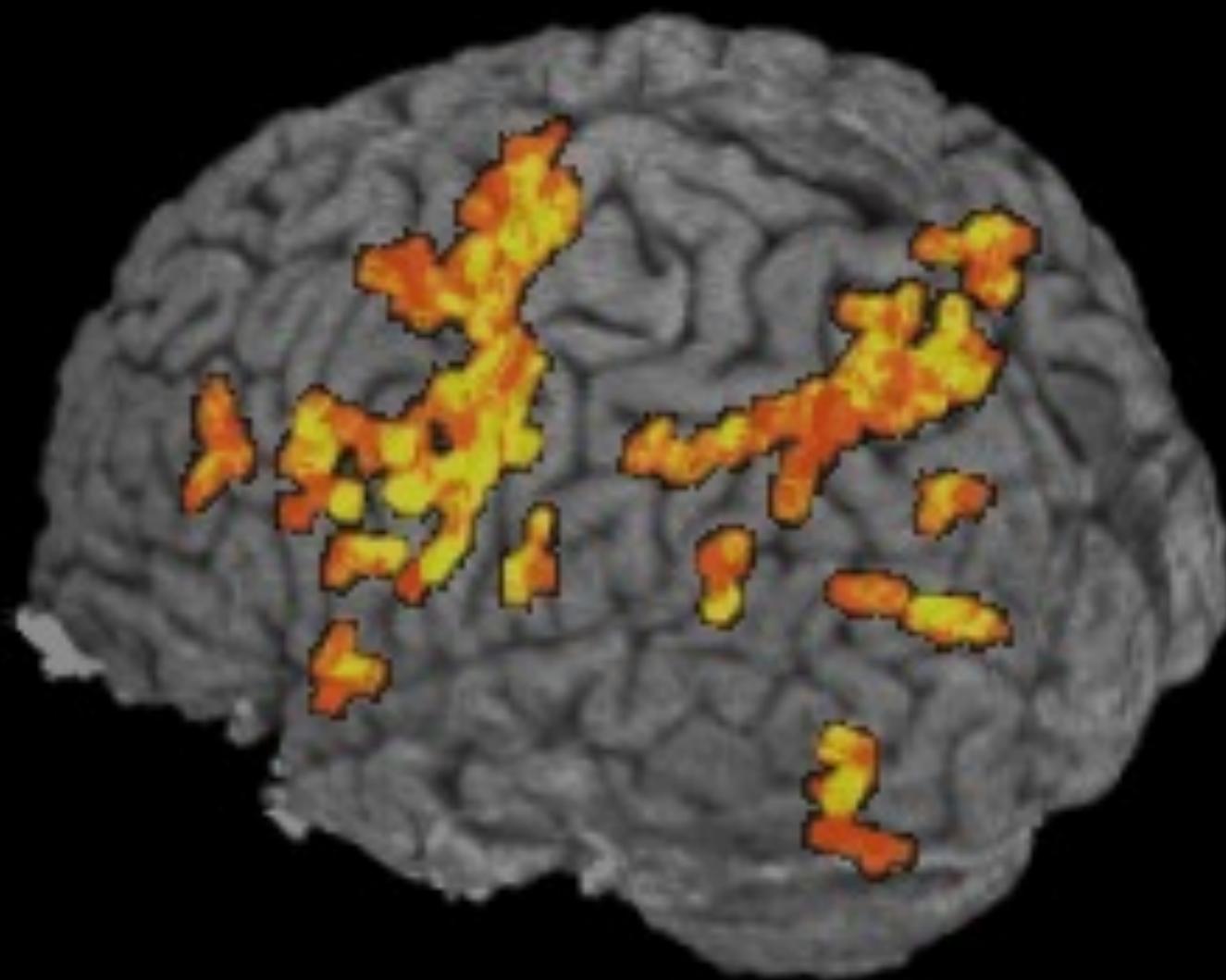
O-15 PET

lt foot

Processing Stream with Real Time fMRI



End of Acquisition



< 1 s to render

Blocked trials:
20 s on/20 s off
8 blocks

Blocks: 1 2 3 4 5 6 7 8

Color shows
through brain

Correlation > 0.45



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Functional Imaging Methods / 3T Group

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August, 2000