

Are You fMRI Experienced?

Peter A. Bandettini, Ph.D

Unit on Functional Imaging Methods
&
3T Neuroimaging Core Facility

Laboratory of Brain and Cognition
National Institute of Mental Health

- The experimental hypothesis
- Scanner variables
- Physiologic variables
- Subject interface variables
- Processing steps and variables

BORING

The only way to become experienced at fMRI is by doing it.

Technology

Methodology

Engineers

Statisticians

Physicists

Mathematicians

Neuroscientists

Physiologists

Clinicians

Interpretation

Applications

Past

Present

Future

Past

Present

Future

Technology

MRI	EPI	1.5T,3T, 4T	EPI on Clin. Syst. Nav. pulses	Diff. tensor	Mg ⁺	7T Venography SENSE
		Local Human Head Gradient Coils		Real time fMRI		
		ASL		Quant. ASL	Z-shim	
		Spiral EPI		Dynamic IV volume		
		BOLD		Multi-shot fMRI	Simultaneous ASL and BOLD	Baseline Susceptibility Current Imaging?

Methodology

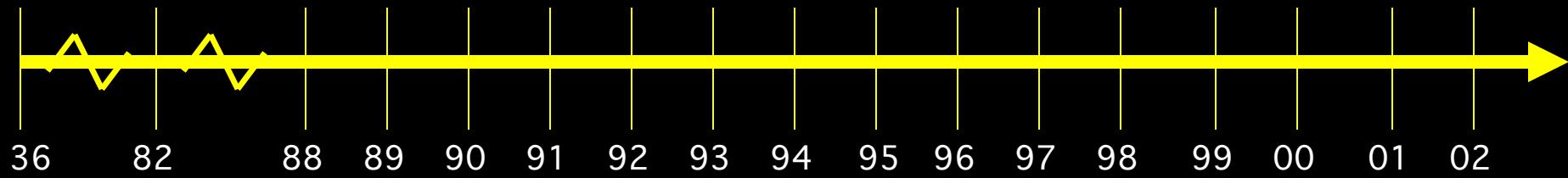
IVIM	Baseline Volume	Correlation Analysis		CO ₂ Calibration
		Motion Correction		
		Parametric Design		Multi-Modal Mapping
		Surface Mapping		
		Phase Mapping		Free-behavior Designs
		Linear Regression		Mental Chronometry
		Event-related		Deconvolution

Interpretation

Blood T2	Hemoglobin	BOLD models	PET correlation	
		B ₀ dep.	IV vs EV	
		TE dep	Pre-undershoot	PSF of BOLD
		Resolution Dep.		
		Post-undershoot		Extended Stim.
		SE vs. GE	CO ₂ effect	Linearity
		NIRS Correlation	Fluctuations	Metab. Correlation
		Veins	Inflow	Optical Im. Correlation
			Balloon Model	Electrophys. correlation

Applications

Volume - Stroke	△ Volume-V1	Complex motor		
		Language	Imagery	Memory
				Emotion
		Motor learning	Children	Tumor vasc.
		Presurgical	Attention	Drug effects
		V1, V2..mapping	Priming/Learning	Ocular Dominance
				Clinical Populations
		Plasticity	Face recognition	Performance prediction





L. Pauling, C. D. Coryell, (1936) “The magnetic properties and structure of hemoglobin, oxyhemoglobin, and carbonmonoxyhemoglobin.” Proc.Natl. Acad. Sci. USA 22, 210-216.

Thulborn, K. R., J. C. Waterton, et al. (1982).“Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field.” Biochim. Biophys. Acta. 714: 265-270.

S. Ogawa, T. M. Lee, A. R. Kay, D. W. Tank, (1990) “Brain magnetic resonance imaging with contrast dependent on blood oxygenation.” Proc. Natl. Acad. Sci. USA 87, 9868-9872.

R. Turner, D. LeBihan, C. T. W. Moonen, D. Despres, J. Frank, (1991). Echo-planar time course MRI of cat brain oxygenation changes. Magn. Reson. Med. 27, 159-166.

Functional MRI Methods

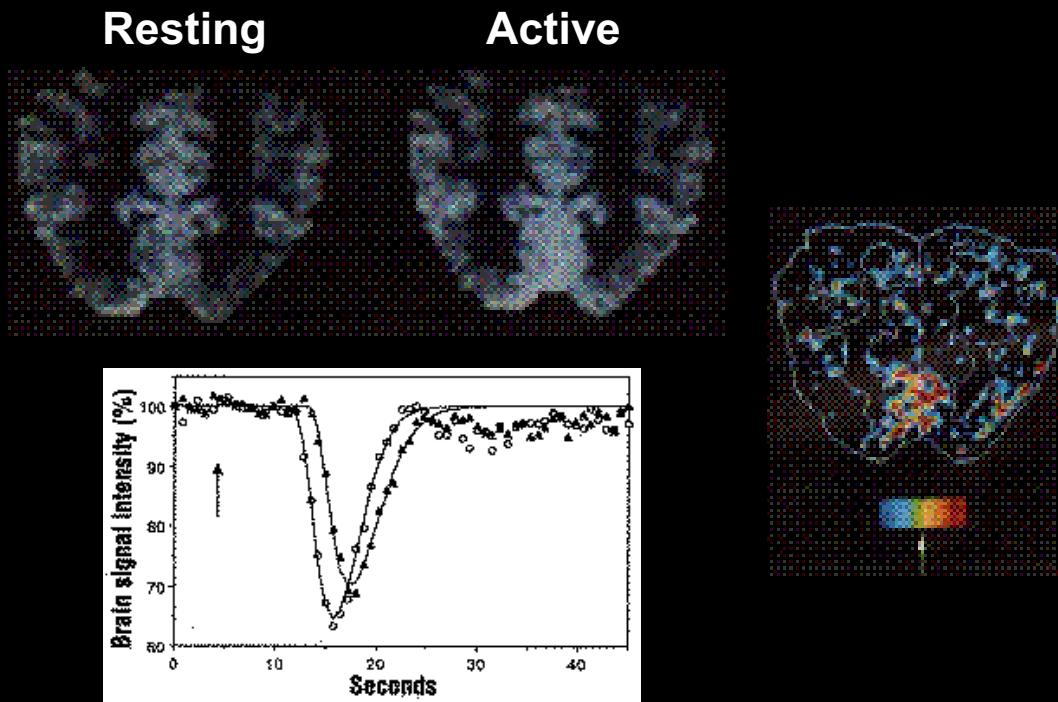
Blood Volume Imaging

BOLD Contrast

Arterial Spin Labeling

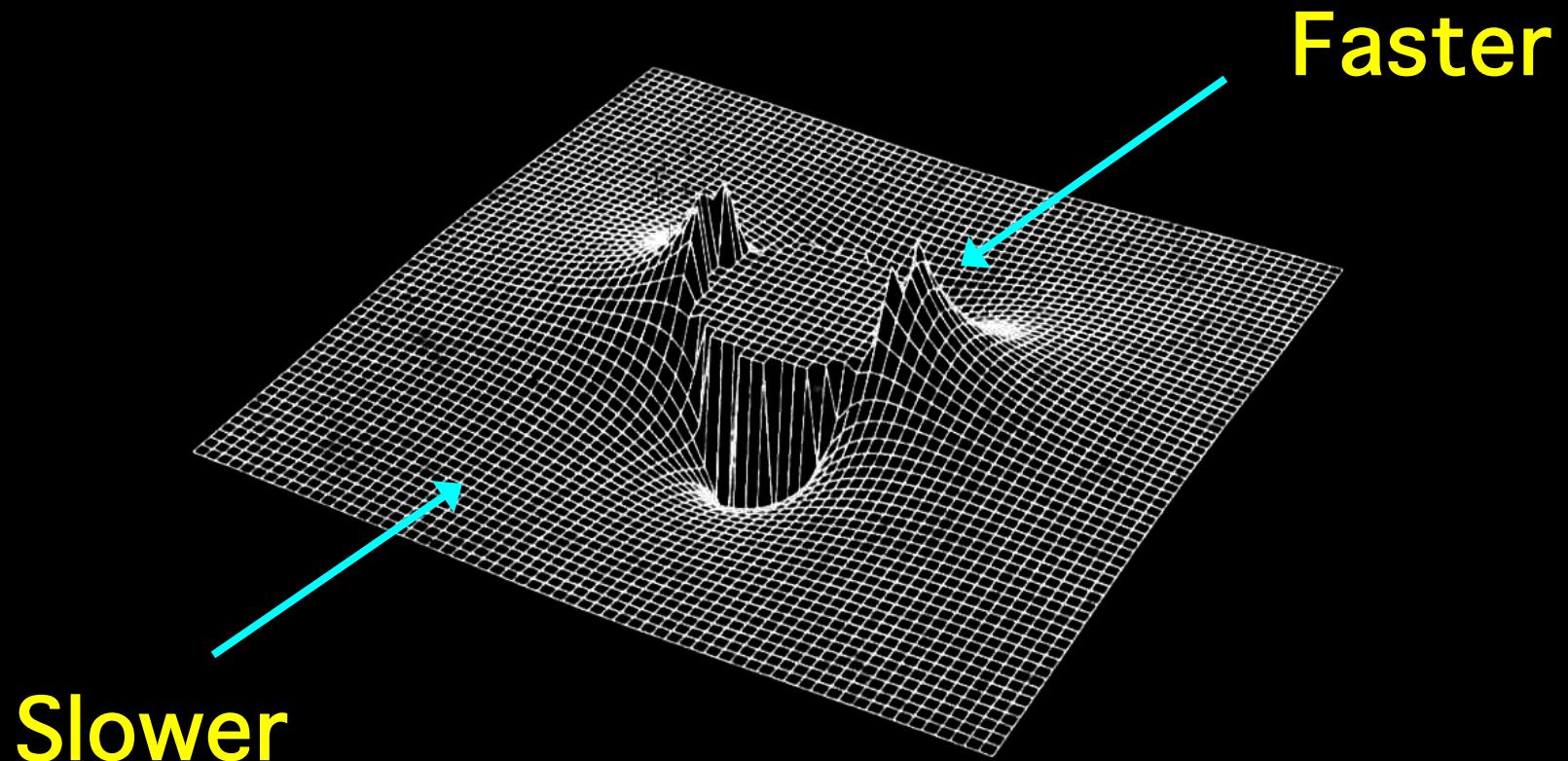
Blood Volume Imaging

Susceptibility Contrast agent bolus injection and time series collection of T2* or T2 - weighted images



Susceptibility Contrast

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



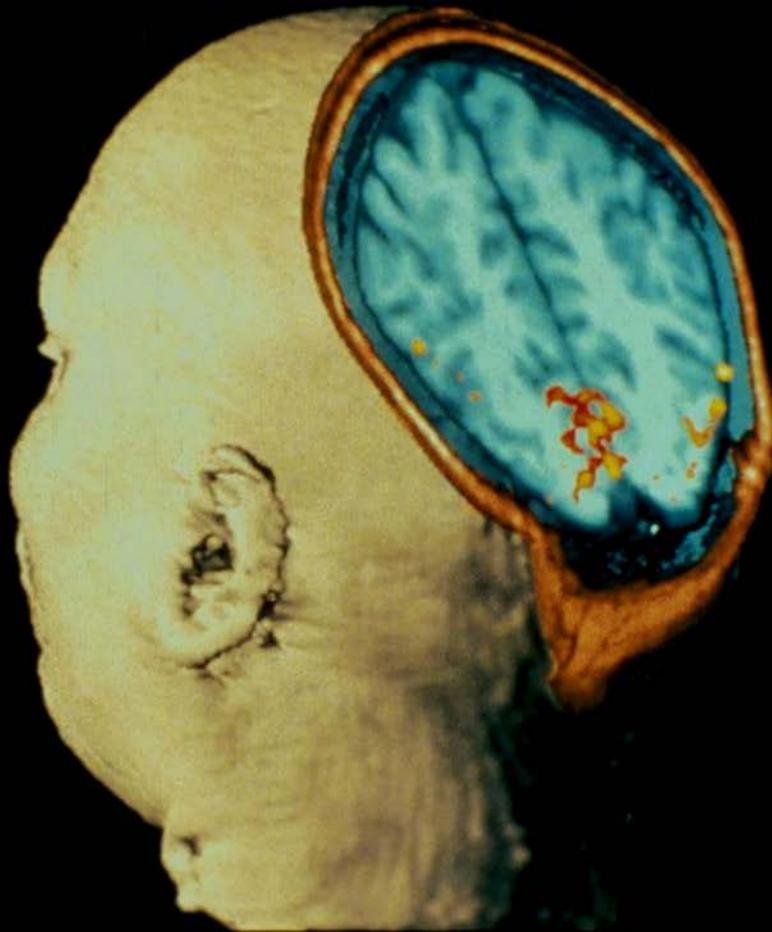
Blood Volume

**Photic
Stimulation**

**MRI Image showing
activation of the
Visual Cortex**

**From Belliveau, et al.
Science Nov 1991**

MSC - perfusion



Alternating Left and Right Finger Tapping



~ 1992

K. K. Kwong, et al, (1992) “Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation.” Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

S. Ogawa, et al., (1992) “Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. USA.” 89, 5951-5955.

P. A. Bandettini, et al., (1992) “Time course EPI of human brain function during task activation.” Magn. Reson. Med 25, 390-397.

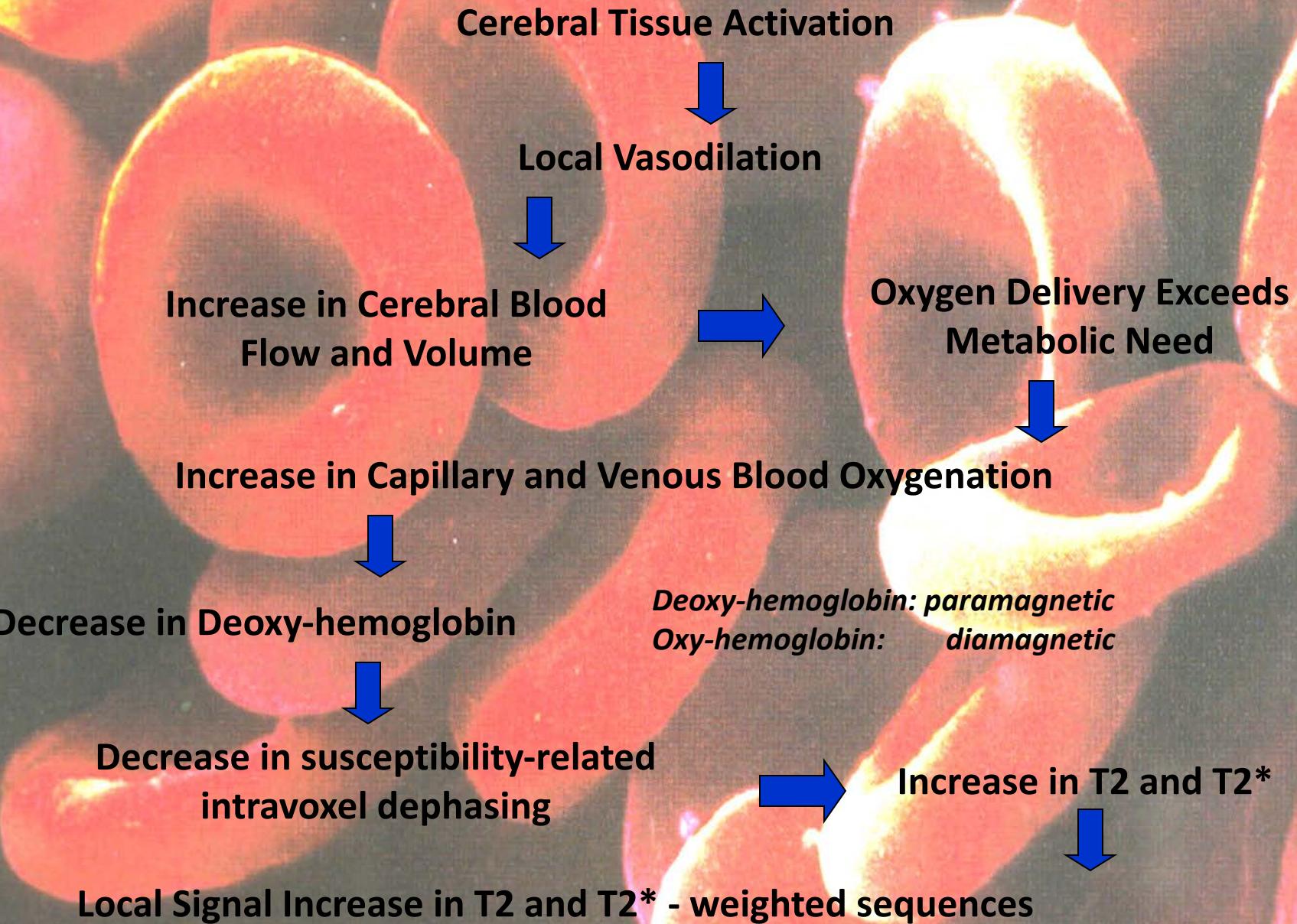
Blamire, A. M., et al. (1992). “Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging.” Proc. Natl. Acad. Sci. USA 89: 11069-11073.

Correlation analysis, Fourier analysis, t-test, f-test...
SPM, AFNI, brain voyager, fiasco, free surfer...



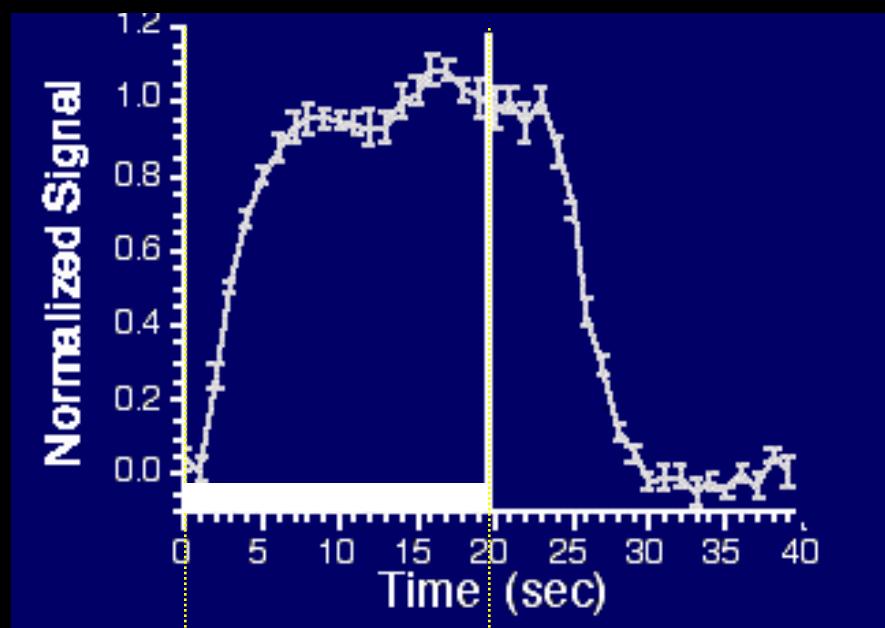
*Quality of results and importance of the findings depends on
type of question asked, experimental method, and analysis method...*

BOLD Contrast in the Detection of Neuronal Activity

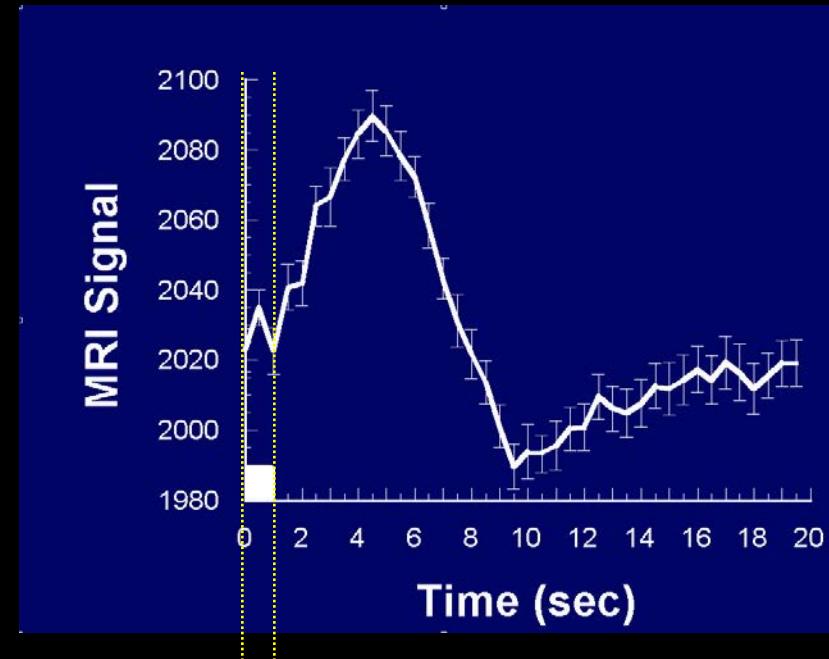


The BOLD Signal

Blood Oxxygenation Level Dependent (BOLD) signal changes

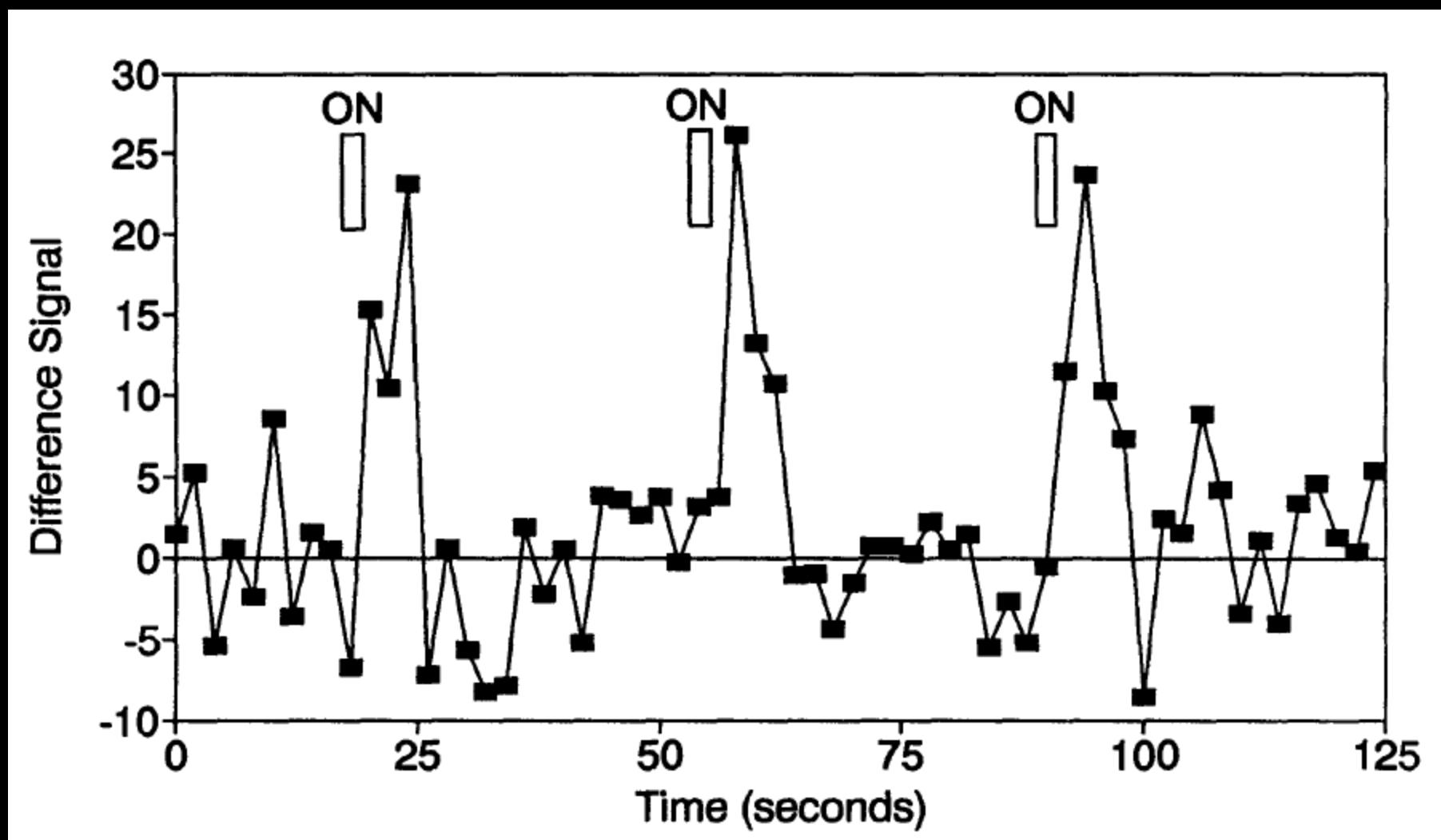


task



task

First Event-related fMRI Results



Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." Proc. Natl. Acad. Sci. USA 89: 11069-11073.

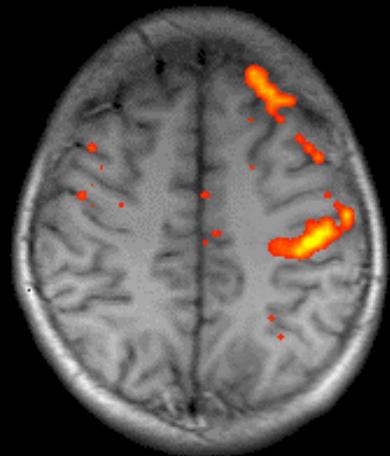
1991-1992



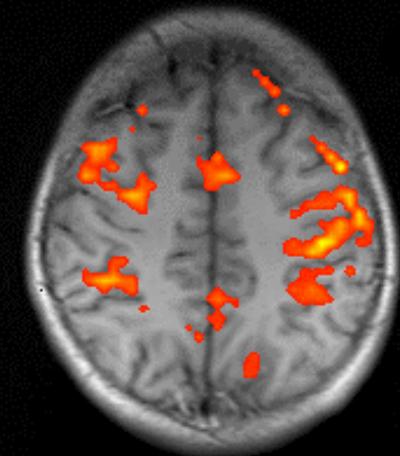
1992-1999



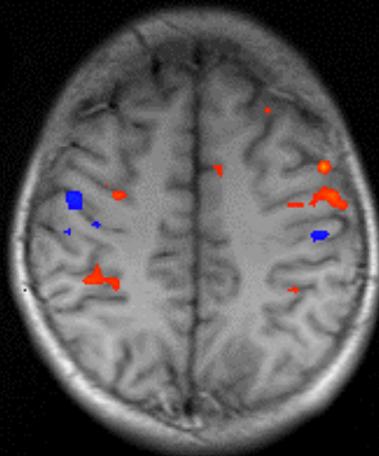
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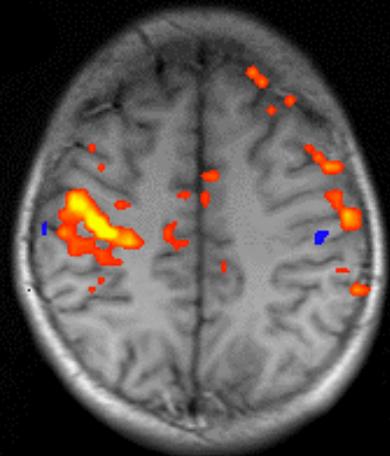
Complex Right



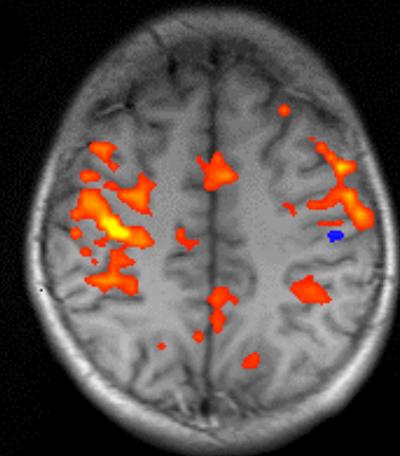
Imagined
Complex Right



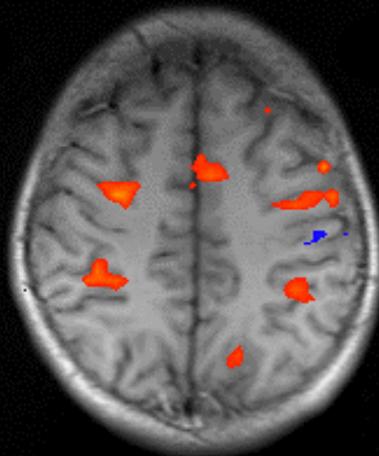
Simple Left



Complex Left

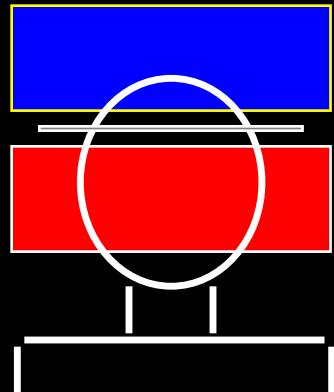


Imagined
Complex Left

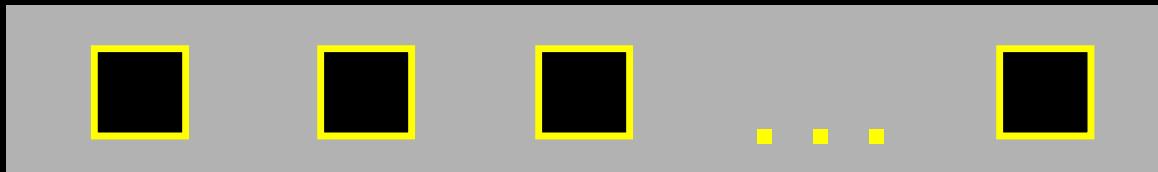
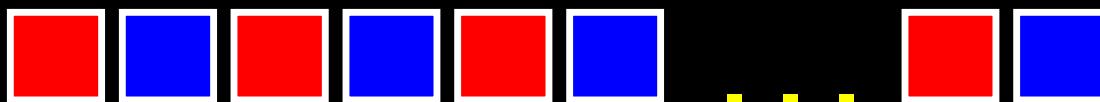
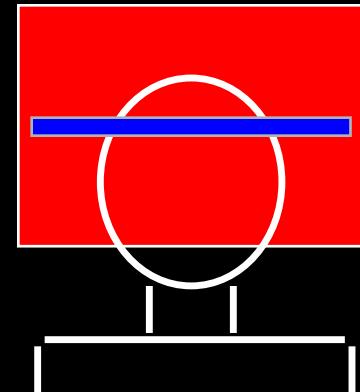


Blood Perfusion

EPISTAR

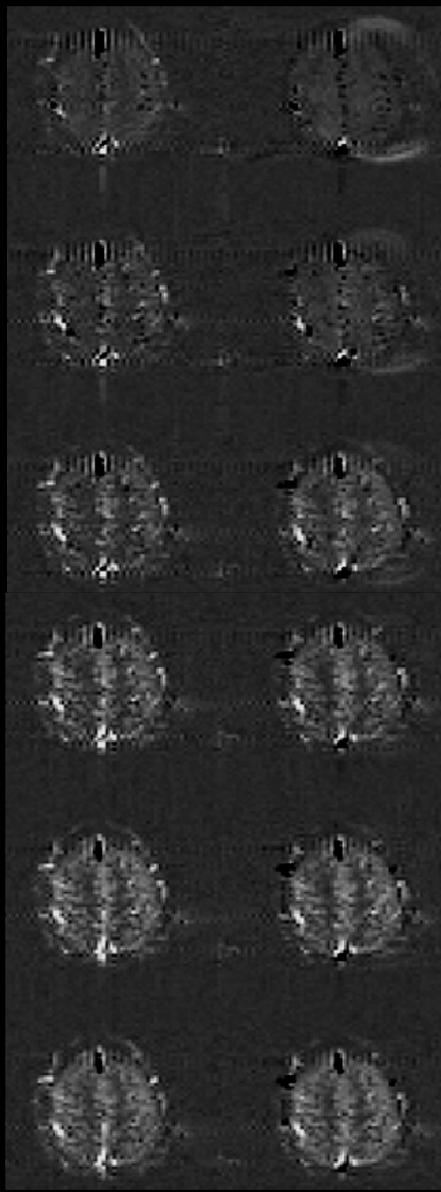


FAIR



TI (ms) FAIR EPISTAR

200



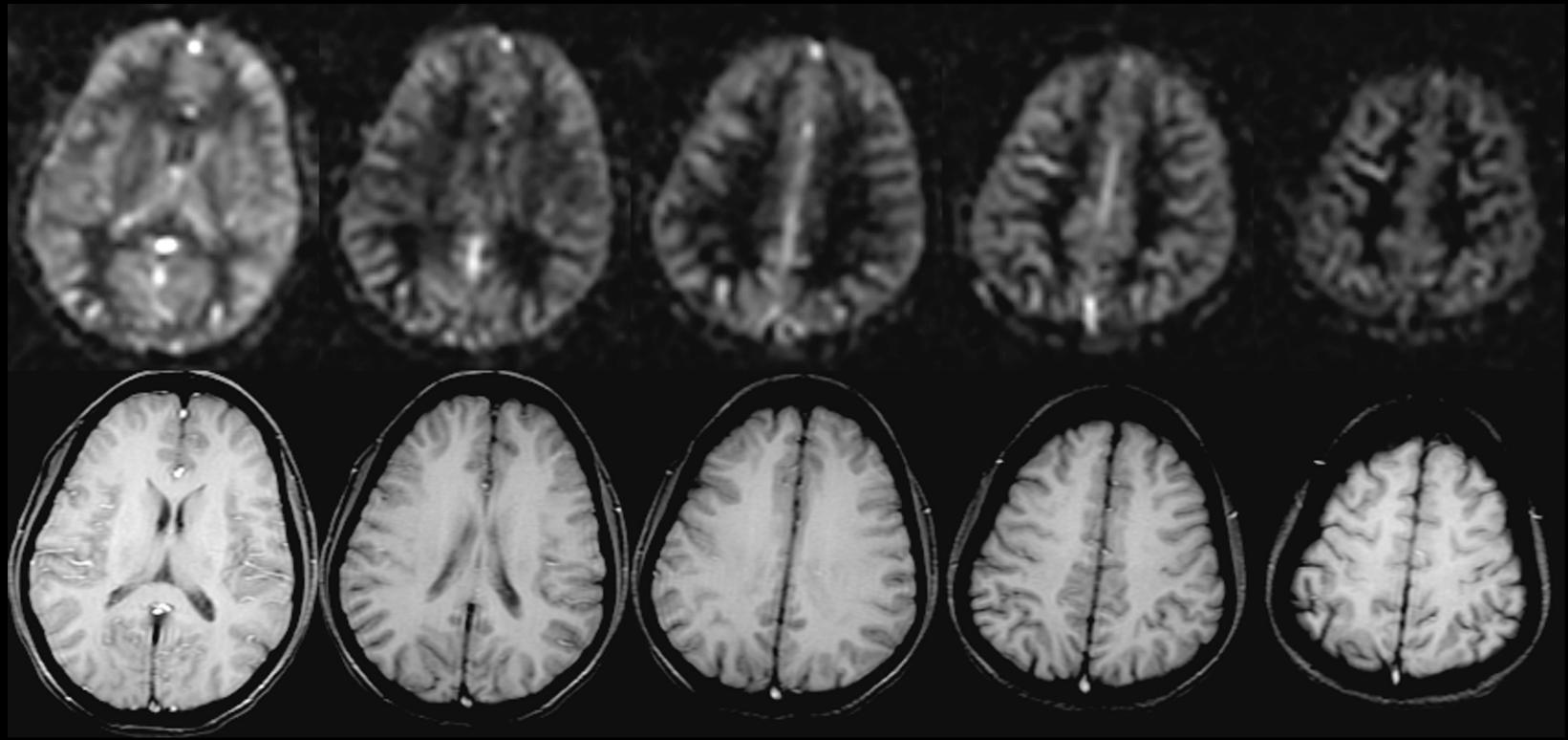
400

600

800

1000

1200



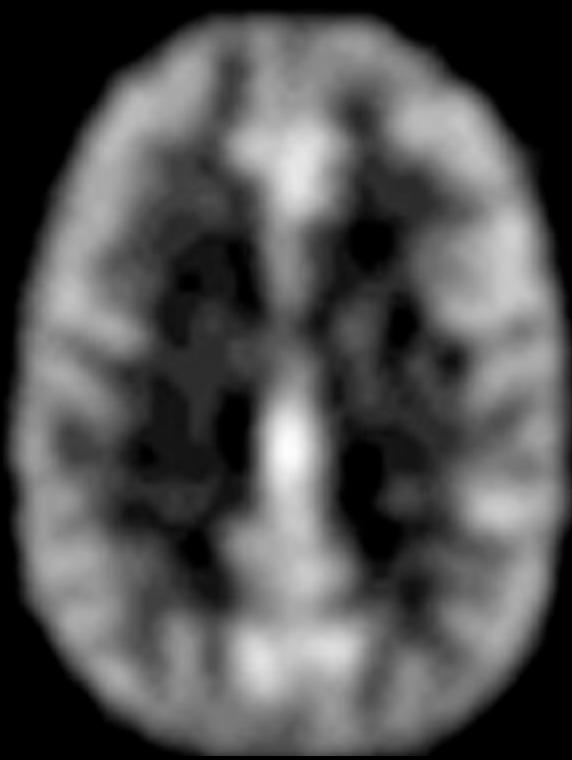
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." Proc. Natl. Acad. Sci. USA 89, 212-216.

Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging and signal targeting with alternating radiofrequency (EPISTAR)." Radiology 192, 1-8.

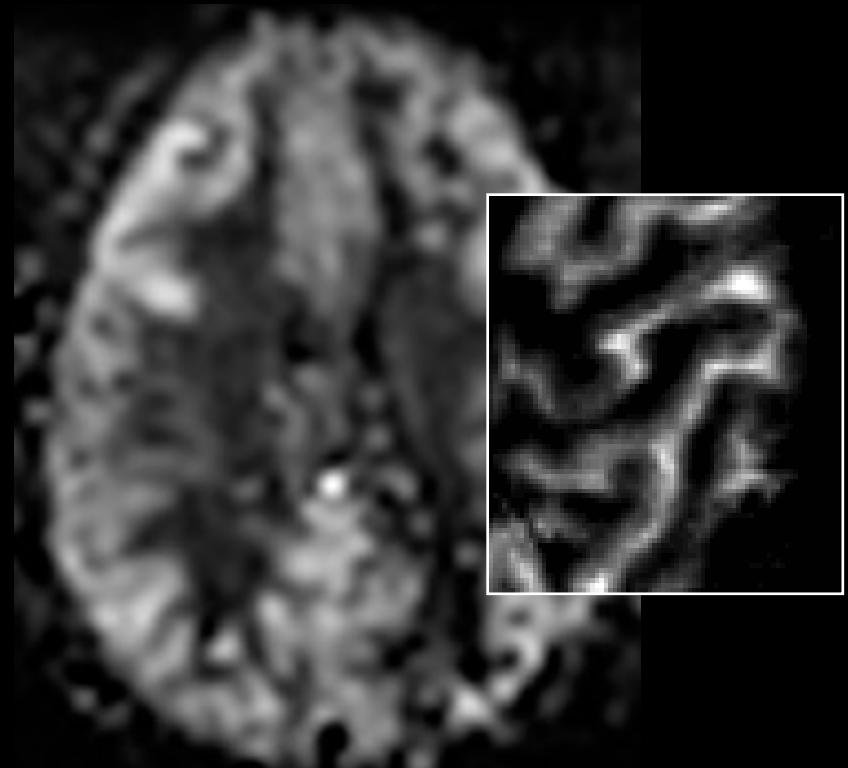
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." Magn. Reson. Med. 34, 293-301.

Kwong, K. K. et al. (1995) "MR perfusion studies with T1-weighted echo planar imaging." Magn. Reson. Med. 34, 878-887.

Comparison with Positron Emission Tomography



PET: H_2^{15}O



MRI: ASL

Refinements

BOLD Contrast Interpretation

Dynamics, Paradigm Design and Processing

Applications

Refinements

BOLD Contrast Interpretation

Dynamics, Paradigm Design and Processing

Applications

The Neuroscientists' Challenge:

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

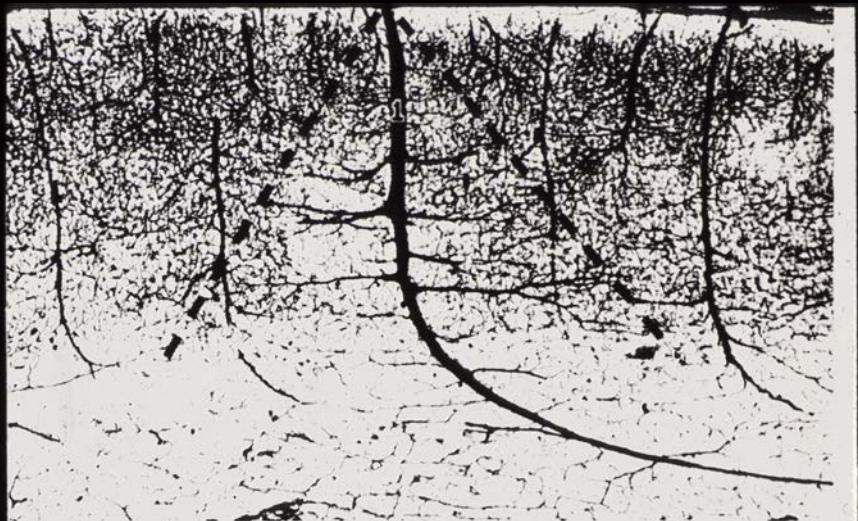
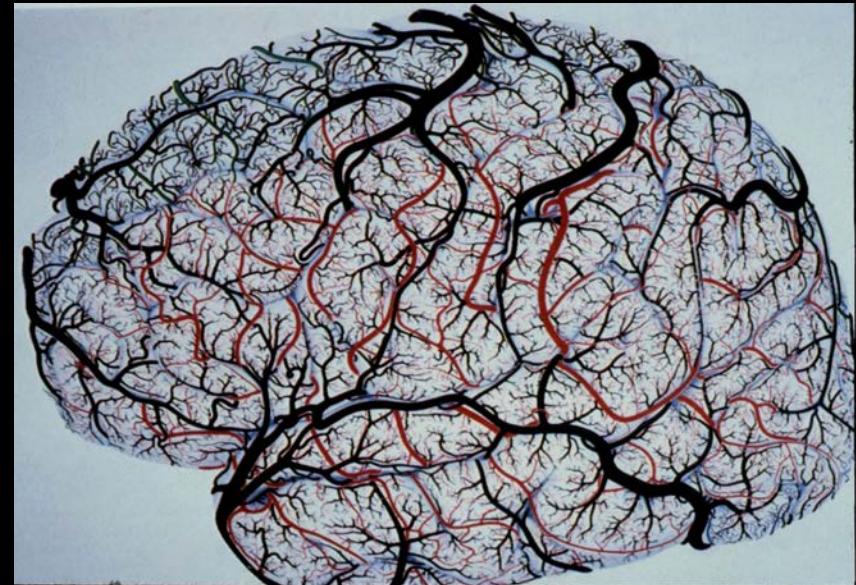
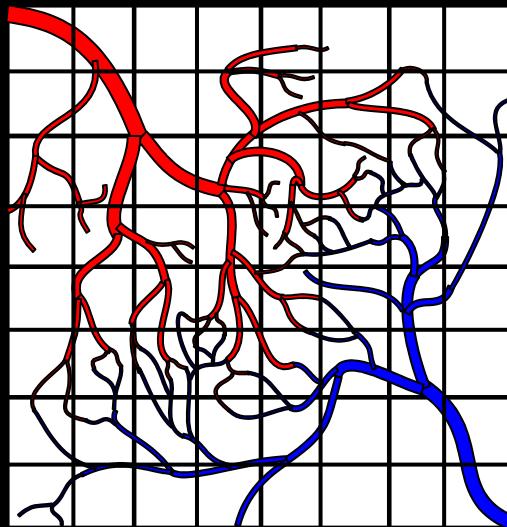


FIG. 43. Middle temporal gyrus. Female, 60 years. (1) Principal intracortical vein. The branches length regularly decreases from deep to superficial cortical regions, thus the vascular territory of the principal vein has a conical appearance (dotted line) ($\times 28$)



Neuronal
Activation



Measured
Signal

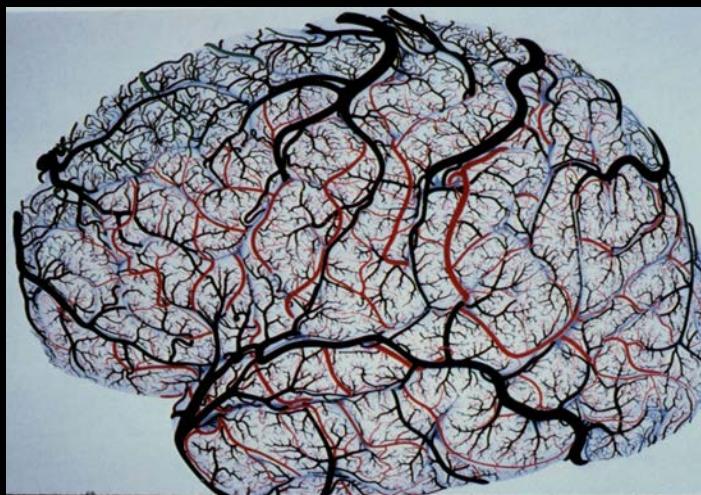
Hemodynamics

?

?

?

Noise



Technology

MRI	EPI	1.5T,3T, 4T	EPI on Clin. Syst. Nav. pulses	Diff. tensor	Mg ⁺	7T Venography SENSE
		Local Human Head Gradient Coils		Real time fMRI		
		ASL		Quant. ASL	Z-shim	
		Spiral EPI		Dynamic IV volume		
		BOLD		Multi-shot fMRI	Simultaneous ASL and BOLD	Baseline Susceptibility Current Imaging?

Methodology

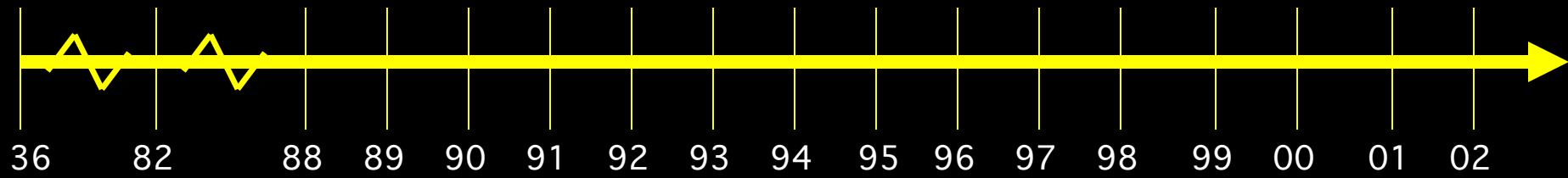
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		Event-related		Deconvolution

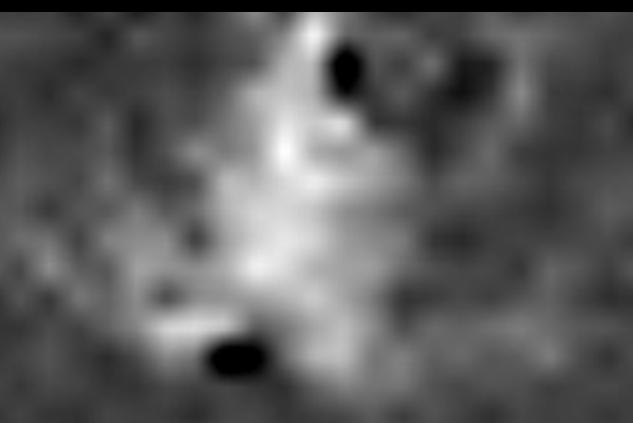
Interpretation

Blood T2	Hemoglobin	BOLD models	PET correlation	
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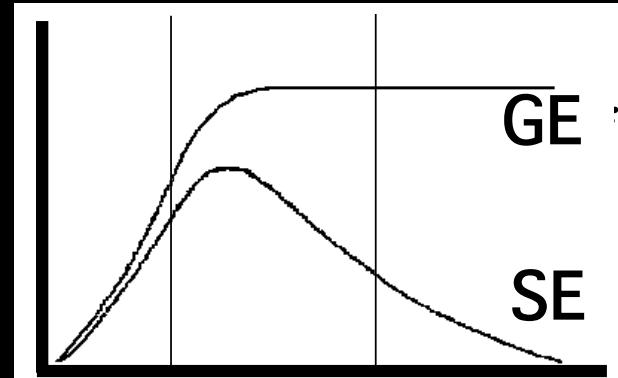
Applications

Volume - Stroke	△ Volume-V1	Complex motor		
		Language	Imagery	Memory
		Motor learning	Children	Tumor vasc. Drug effects
		Presurgical	Attention	Ocular Dominance
		V1, V2..mapping	Priming/Learning	Clinical Populations
		Plasticity	Face recognition	Performance prediction





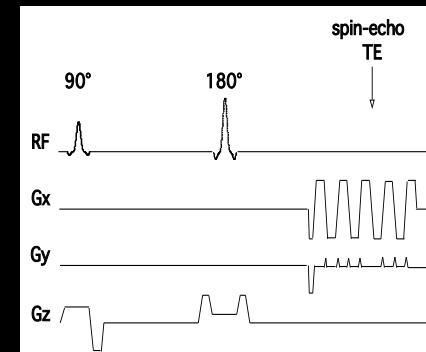
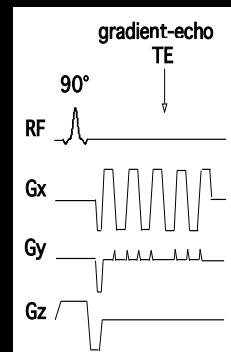
Contrast



2.5 to 3 μm 3 to 15 μm 15 to ∞ μm

compartment size

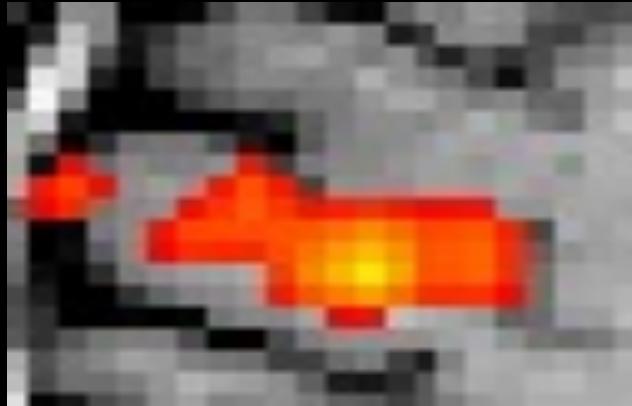
Gradient - Echo



Spin - Echo

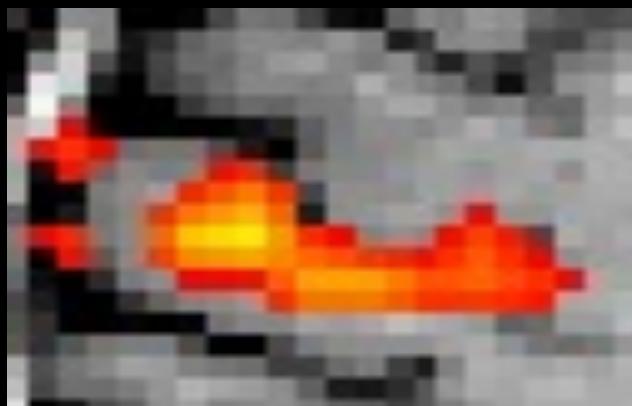
T1 - weighted

Flow weighted



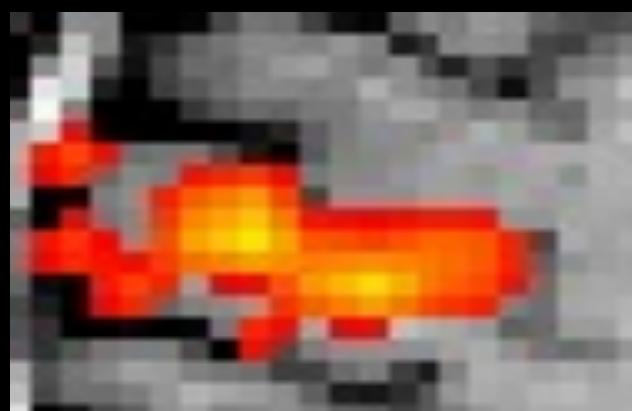
T2* weighted

BOLD weighted



T1 and T2* weighted

Flow and BOLD weighted



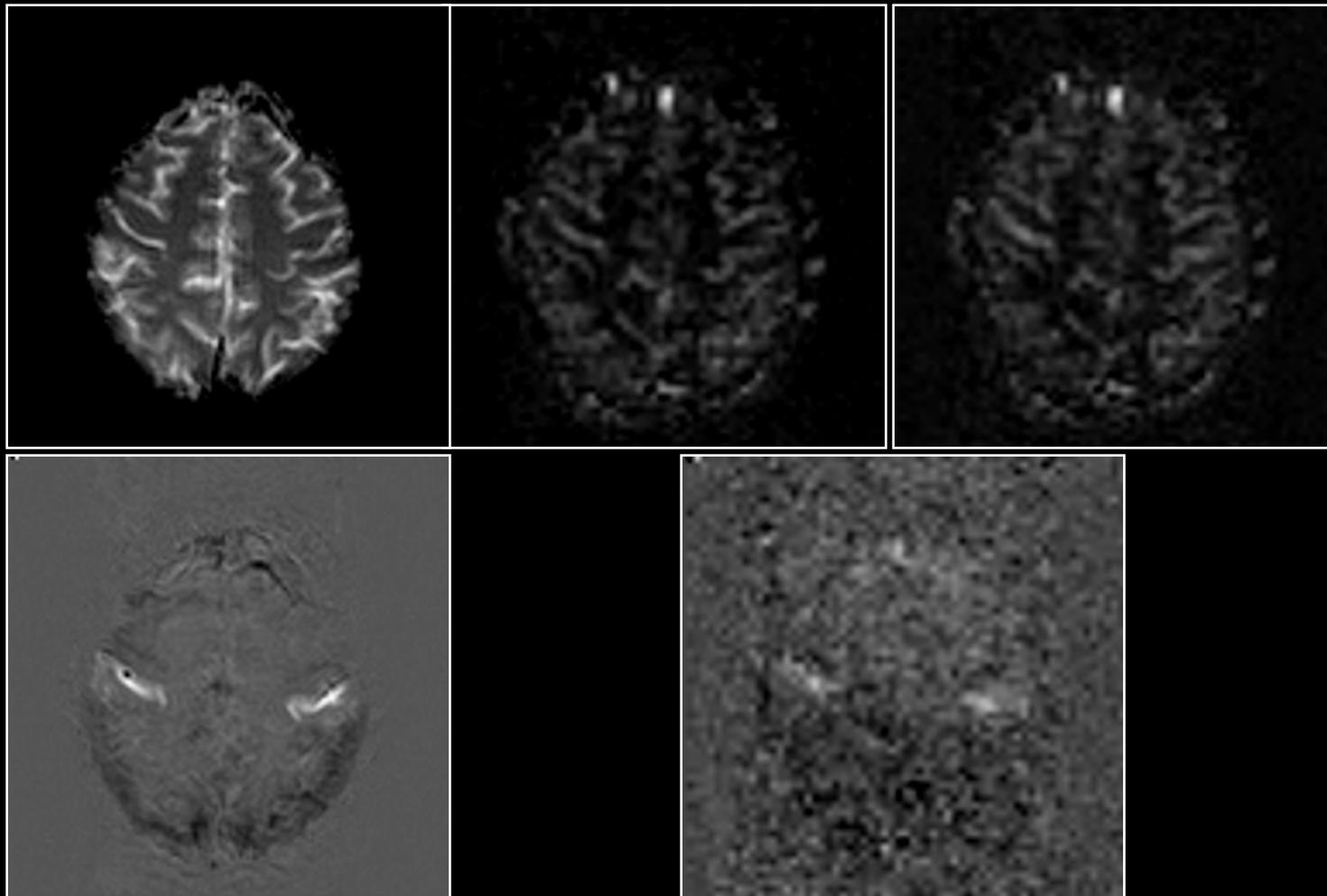
P. A. Bandettini, E. C. Wong, Echo - planar magnetic resonance imaging of human brain activation, *in* "Echo Planar Imaging: Theory, Technique, and Application" (F. Schmitt, M. Stehling, R. Turner, Eds.), p.493-530, Springer - Verlag, Berlin, 1997

BOLD

Rest

Perfusion

Activation



P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, in "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Anatomy



BOLD



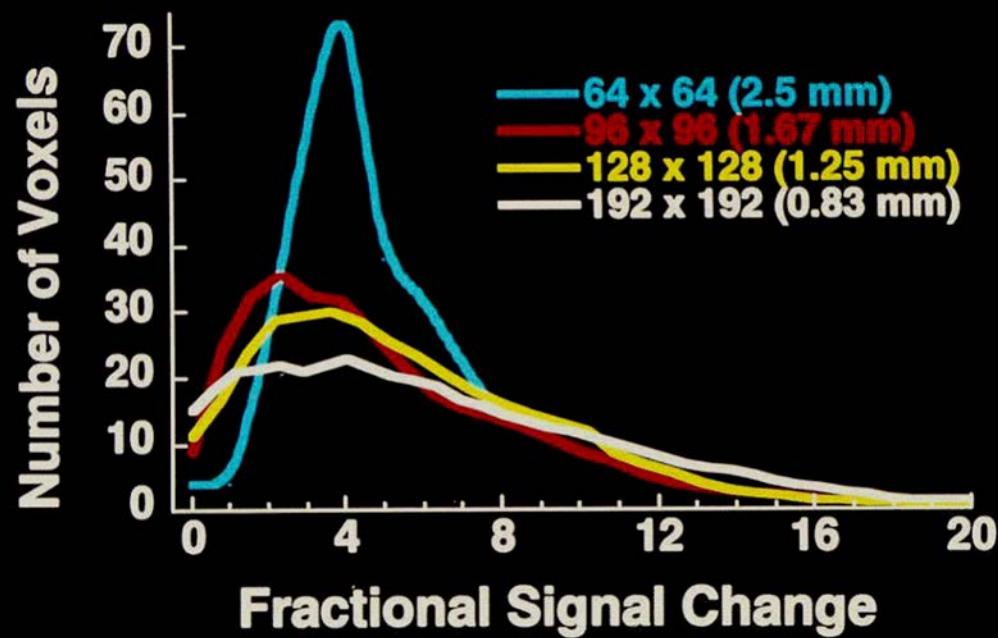
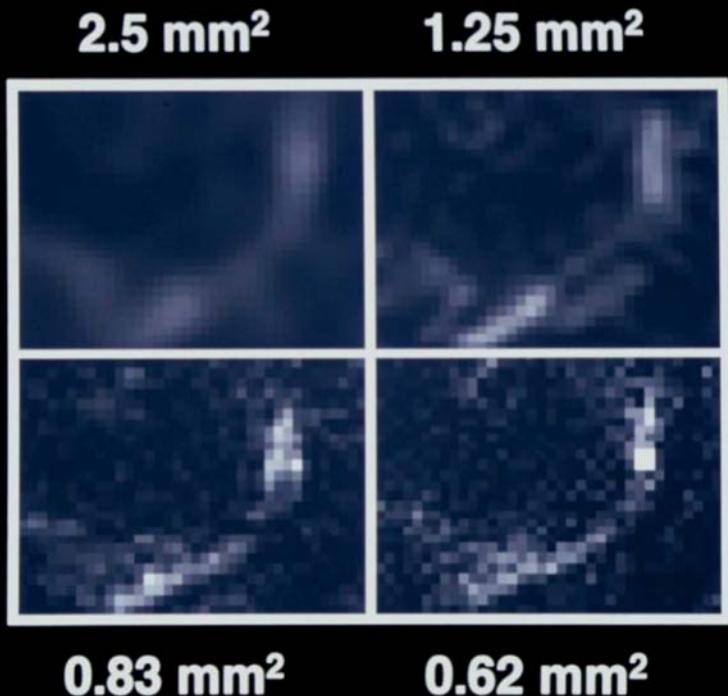
Perfusion



P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, in "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

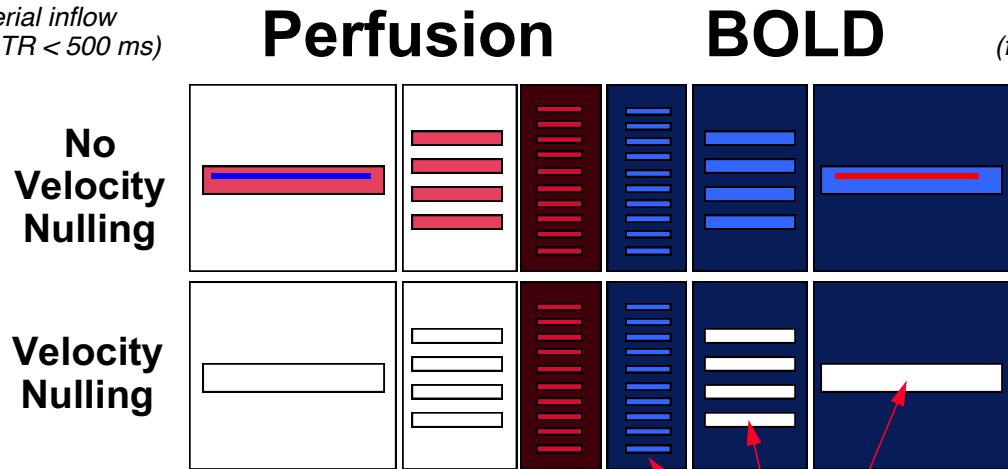
Partial k-space imaging

Fractional Signal Change



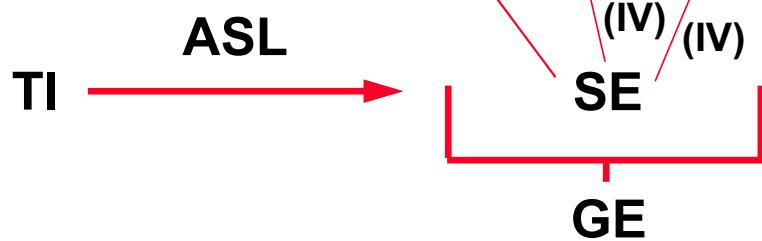
Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.

Arterial inflow
(*BOLD TR < 500 ms*)

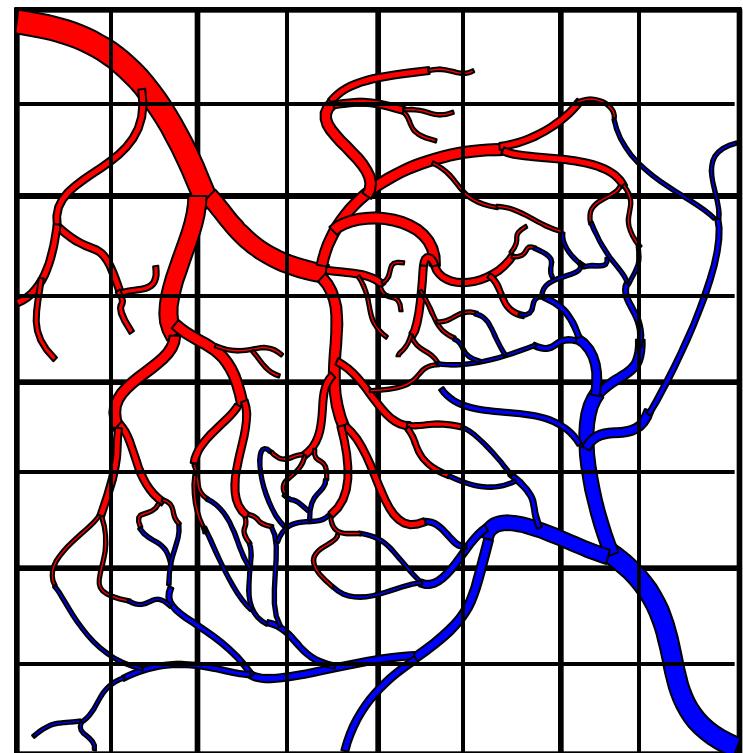


Venous inflow
(for ASL, w/ no VN)

Pulse Sequence
Sensitivity



Spatial
Heterogeneity



Refinements

BOLD Contrast Interpretation

Dynamics, Paradigm Design and Processing

Applications

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		ASL		Quant. ASL	Z-shim	
		BOLD		Dynamic IV volume		
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Methodology

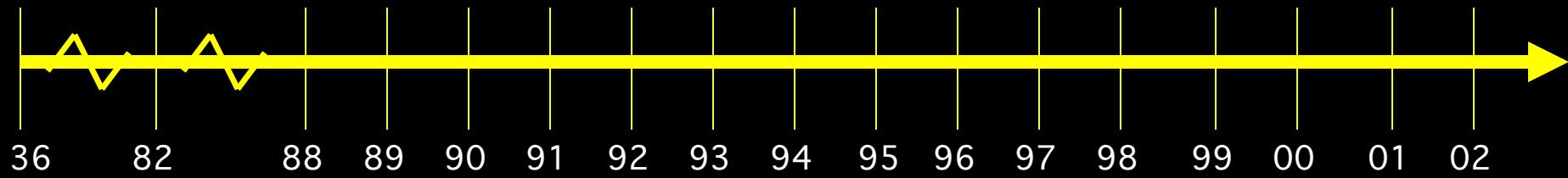
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Interpretation

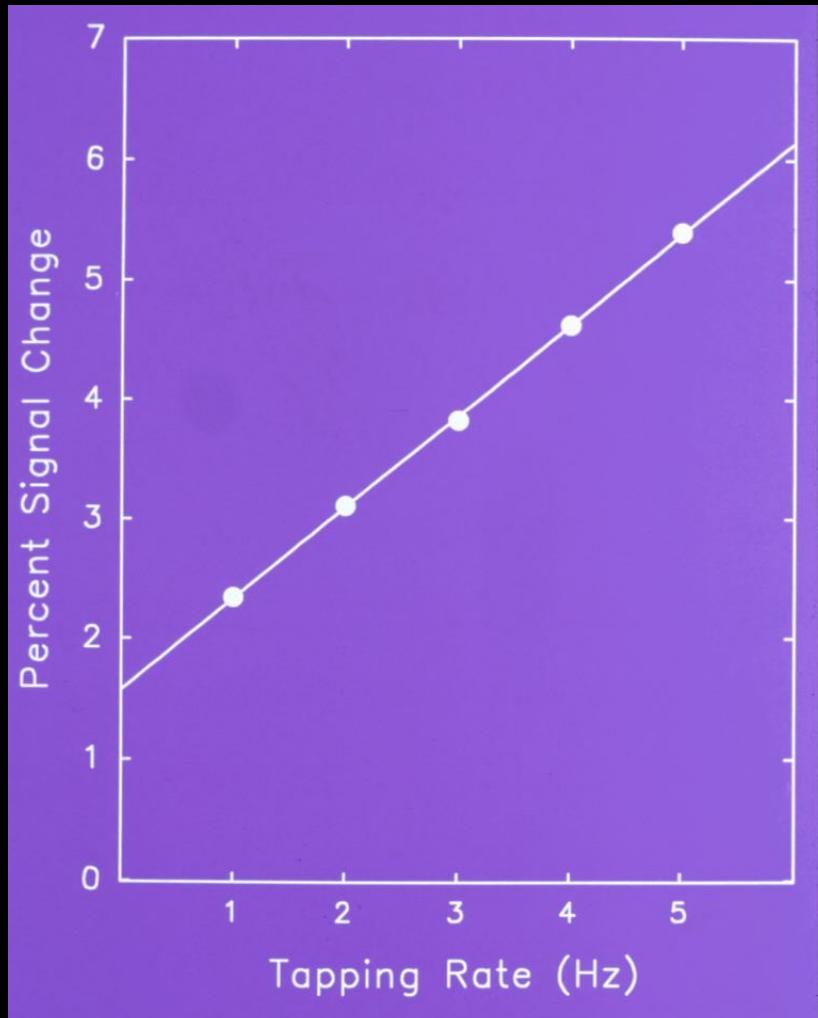
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	△ Volume-V1	Plasticity	Face recognition	Performance prediction

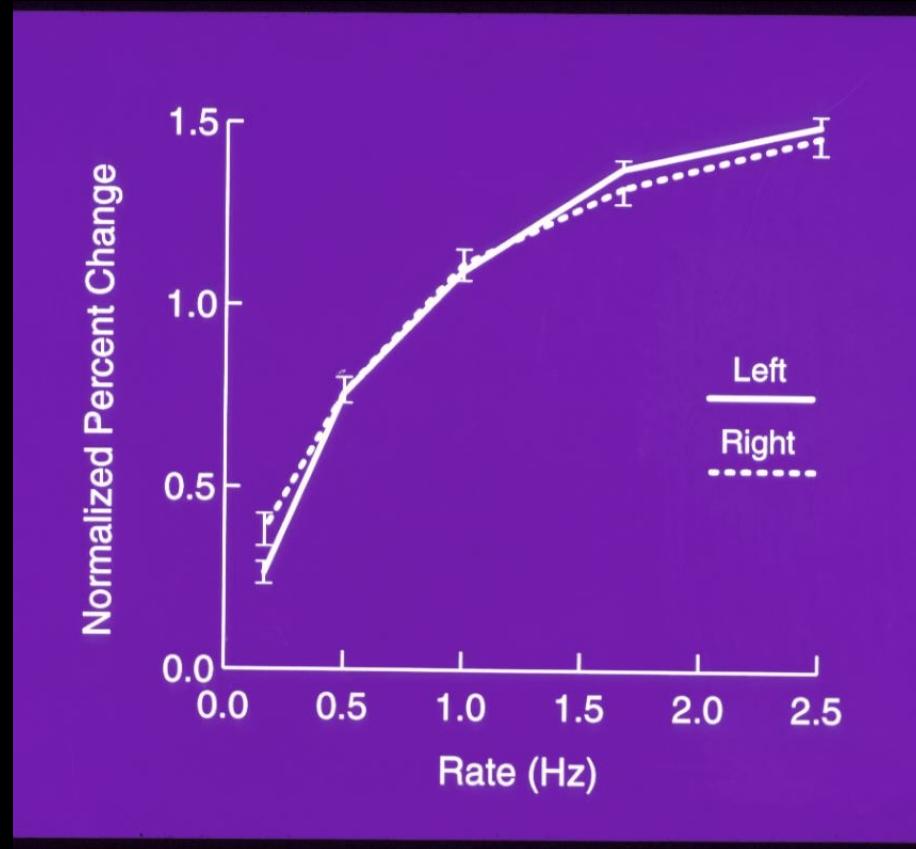


Motor Cortex



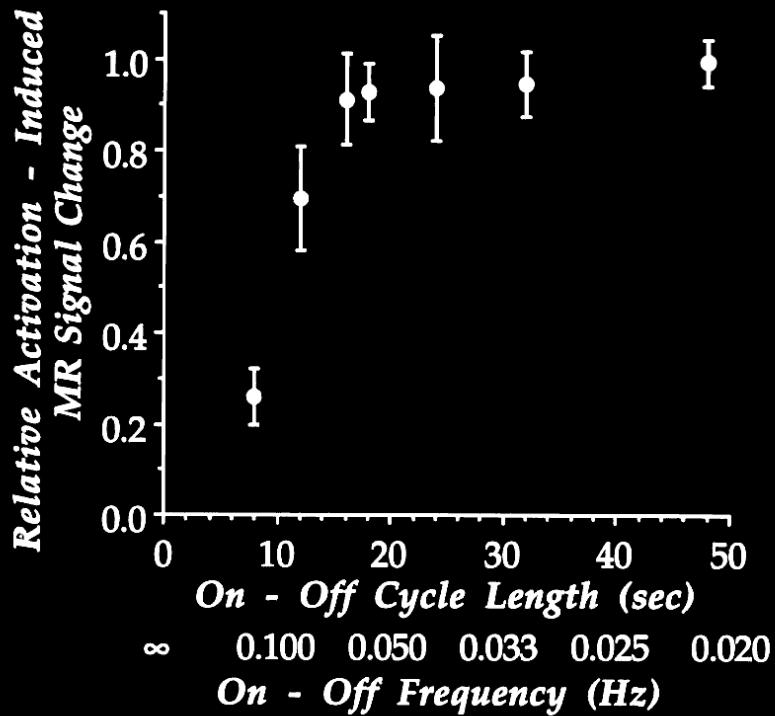
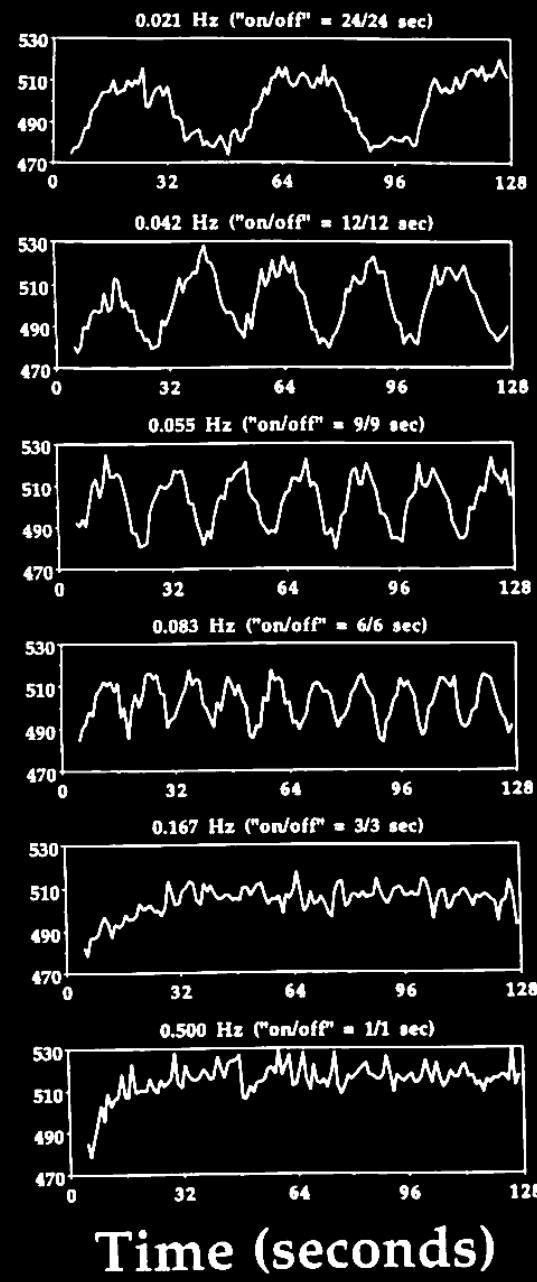
S. M. Rao et al, (1996) “Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex.” *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex



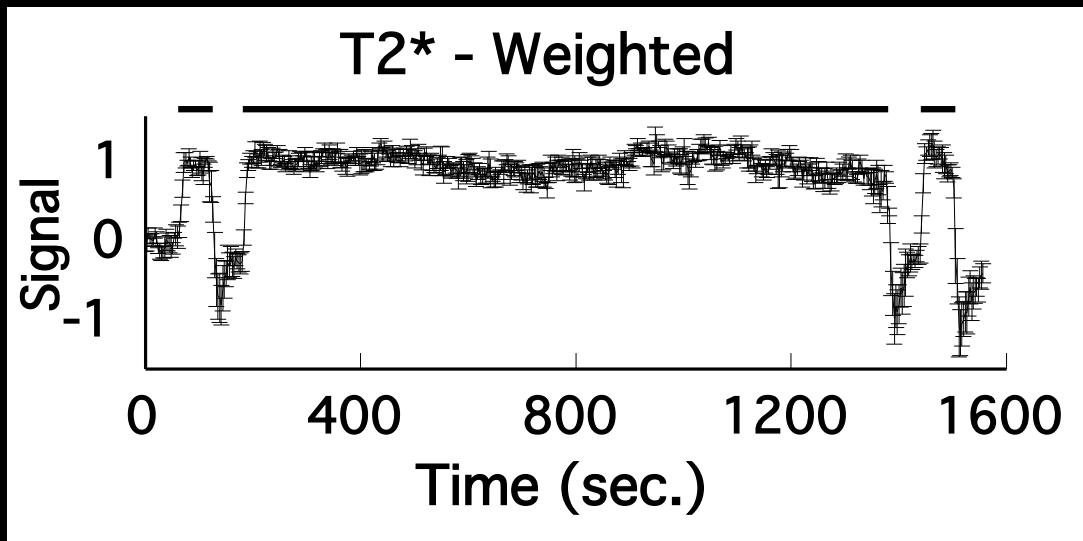
J. R. Binder, et al, (1994). “Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex.” *Cogn. Brain Res.* 2, 31-38

MRI Signal

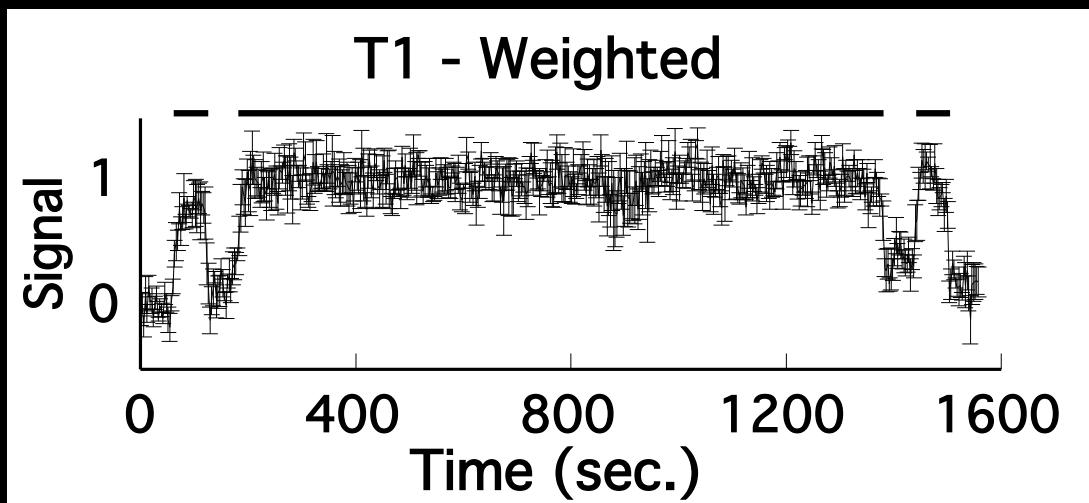


P. A. Bandettini, Functional MRI
temporal resolution in "Functional
MRI" (C. Moonen, and P. Bandettini.,
Eds.), p. 205-220, Springer - Verlag.,
1999.

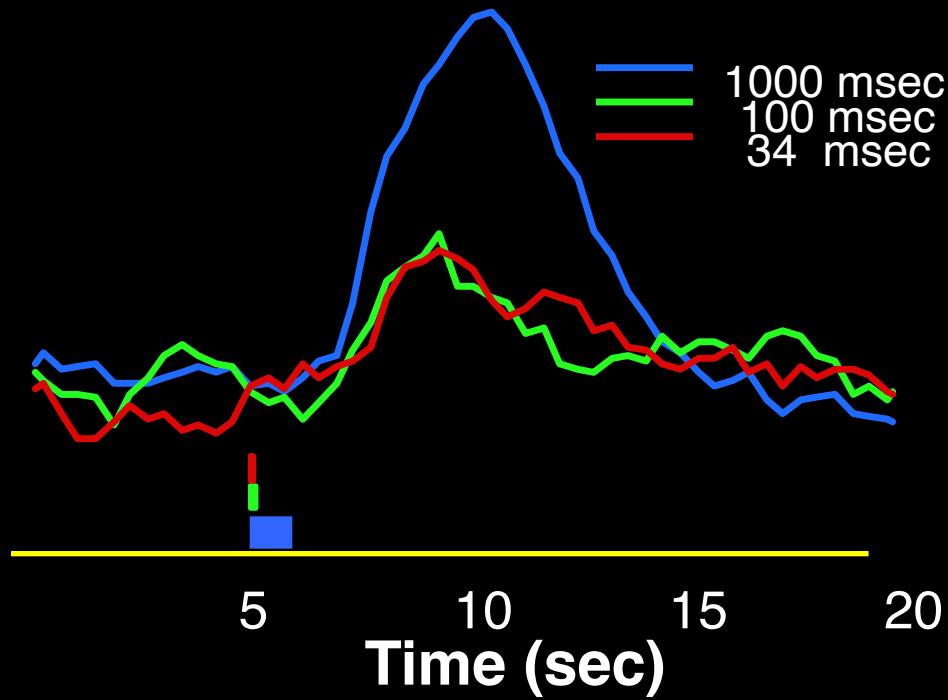
BOLD



Flow

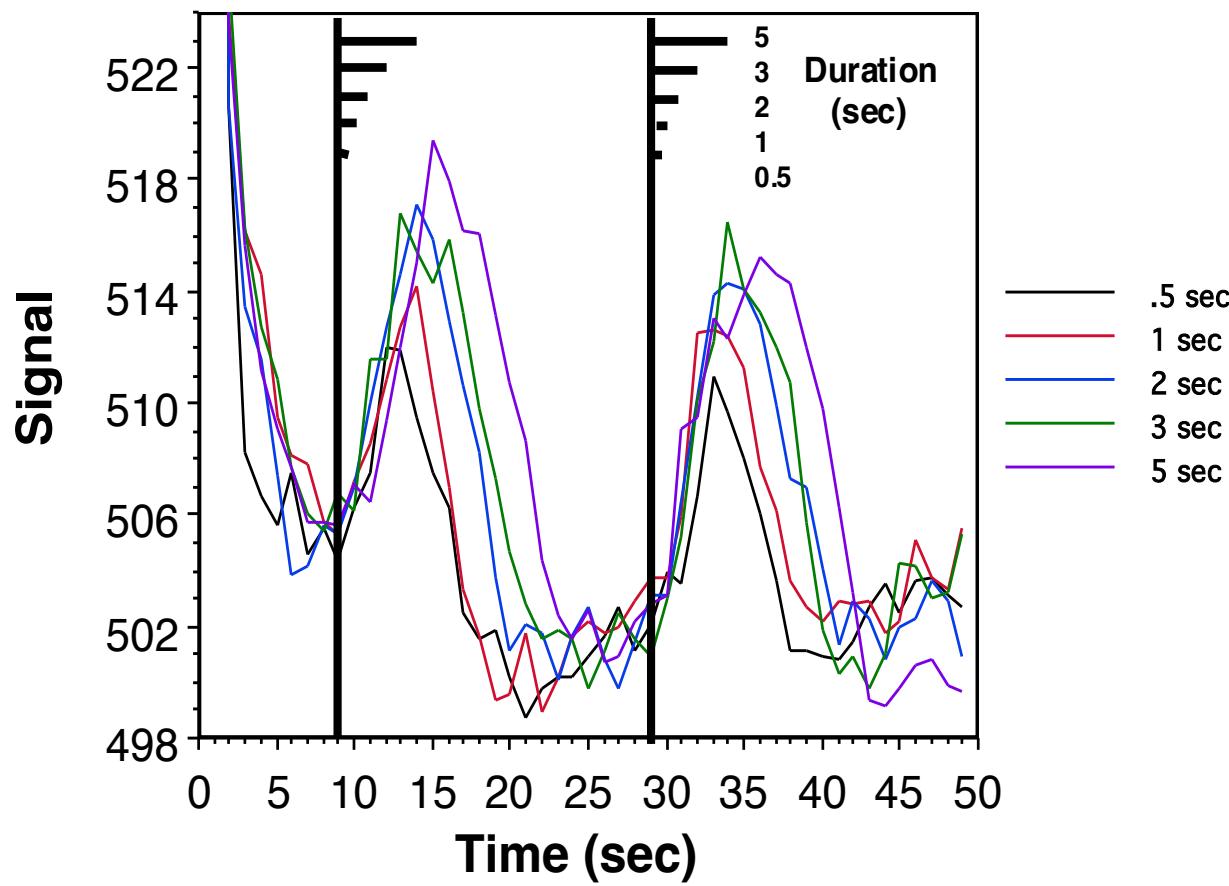


P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). “Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation.” *Human Brain Mapping* 5, 93-109.

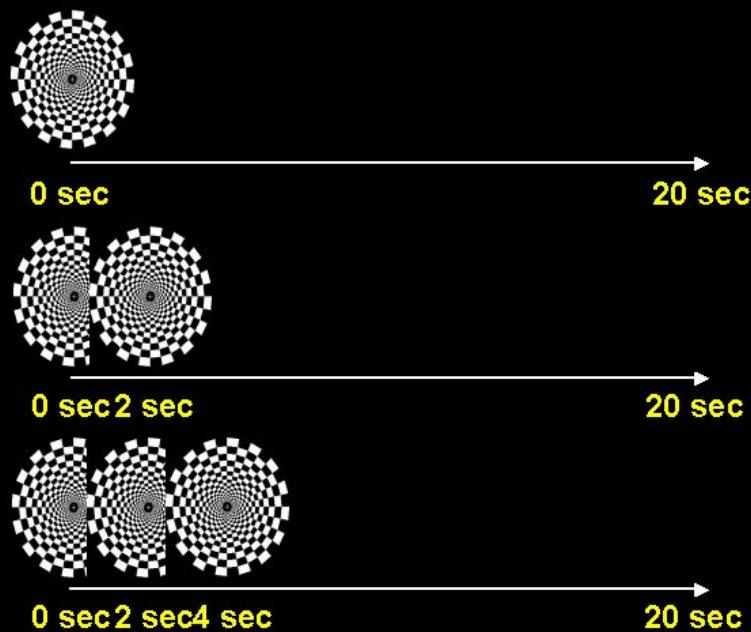


R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

Motor Cortex



Bandettini, et al., The functional dynamics of blood oxygenation level contrast in the motor cortex,
12'th Proc. Soc. Magn. Reson. Med., New York, p. 1382. (1993).

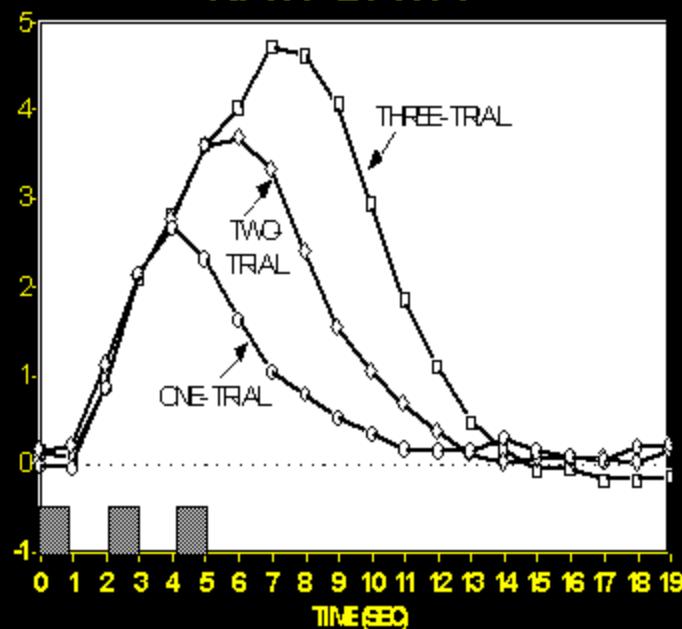


♦ Human Brain Mapping 5:329–340(1997)

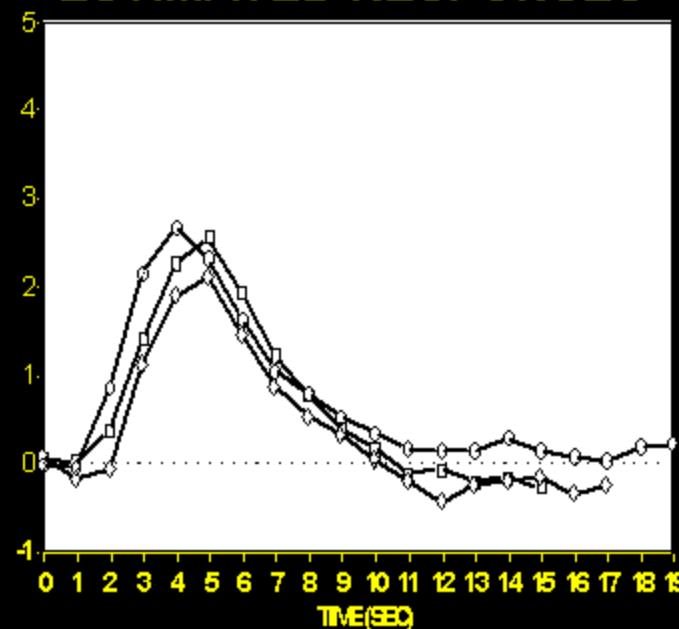
Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale* and Randy L. Buckner

RAW DATA



ESTIMATED RESPONSES



Neuronal Activation Input Strategies

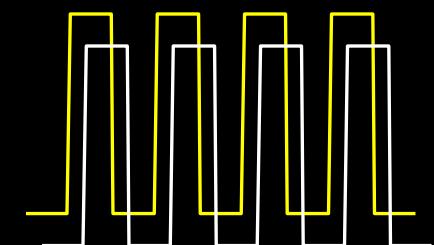
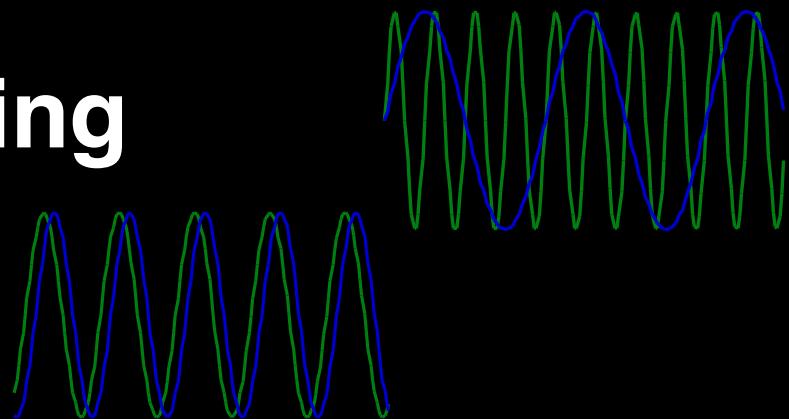
1. Block Design

2. Frequency Encoding

3. Phase Encoding

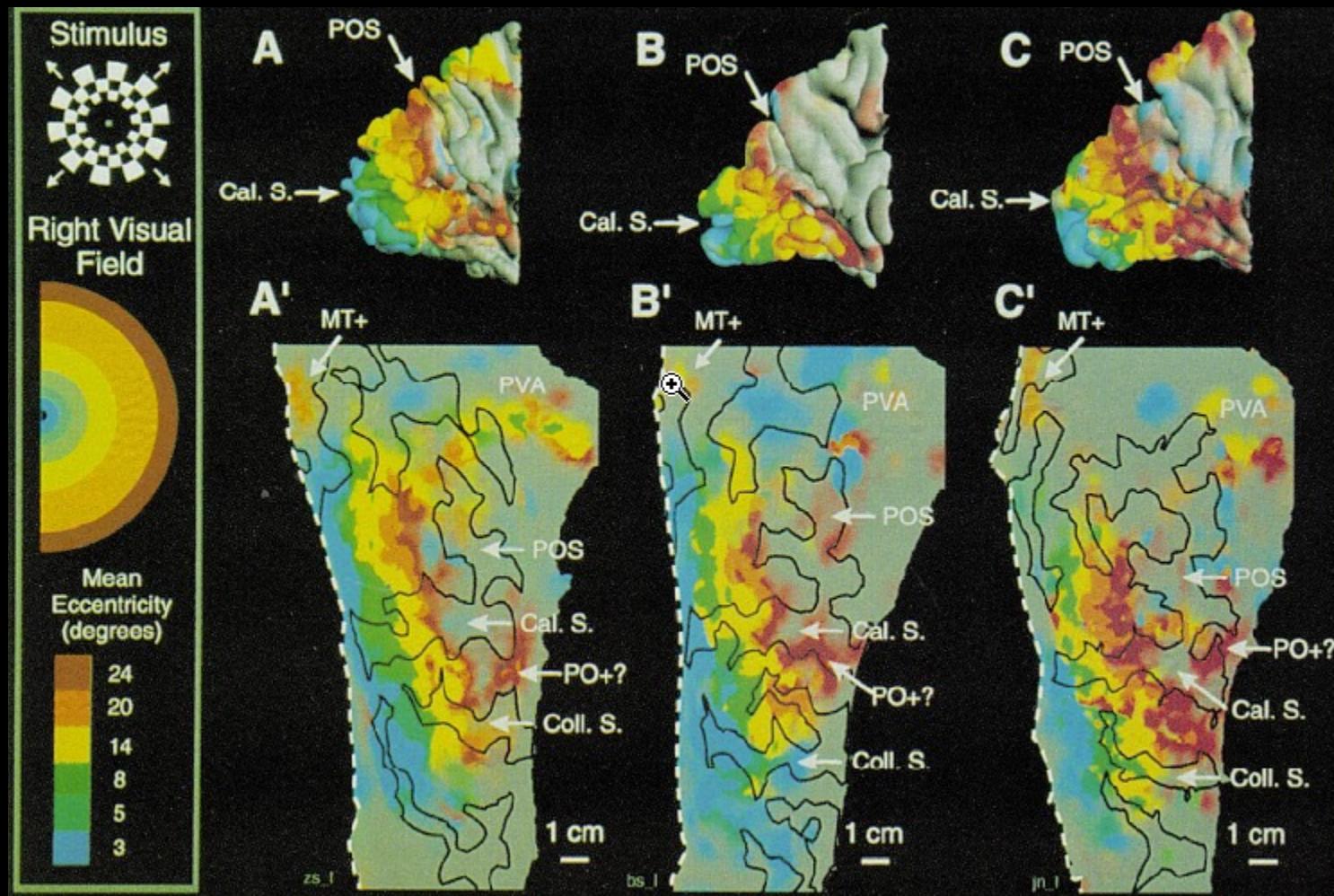
4. Event Related

5. Orthogonal Block Design

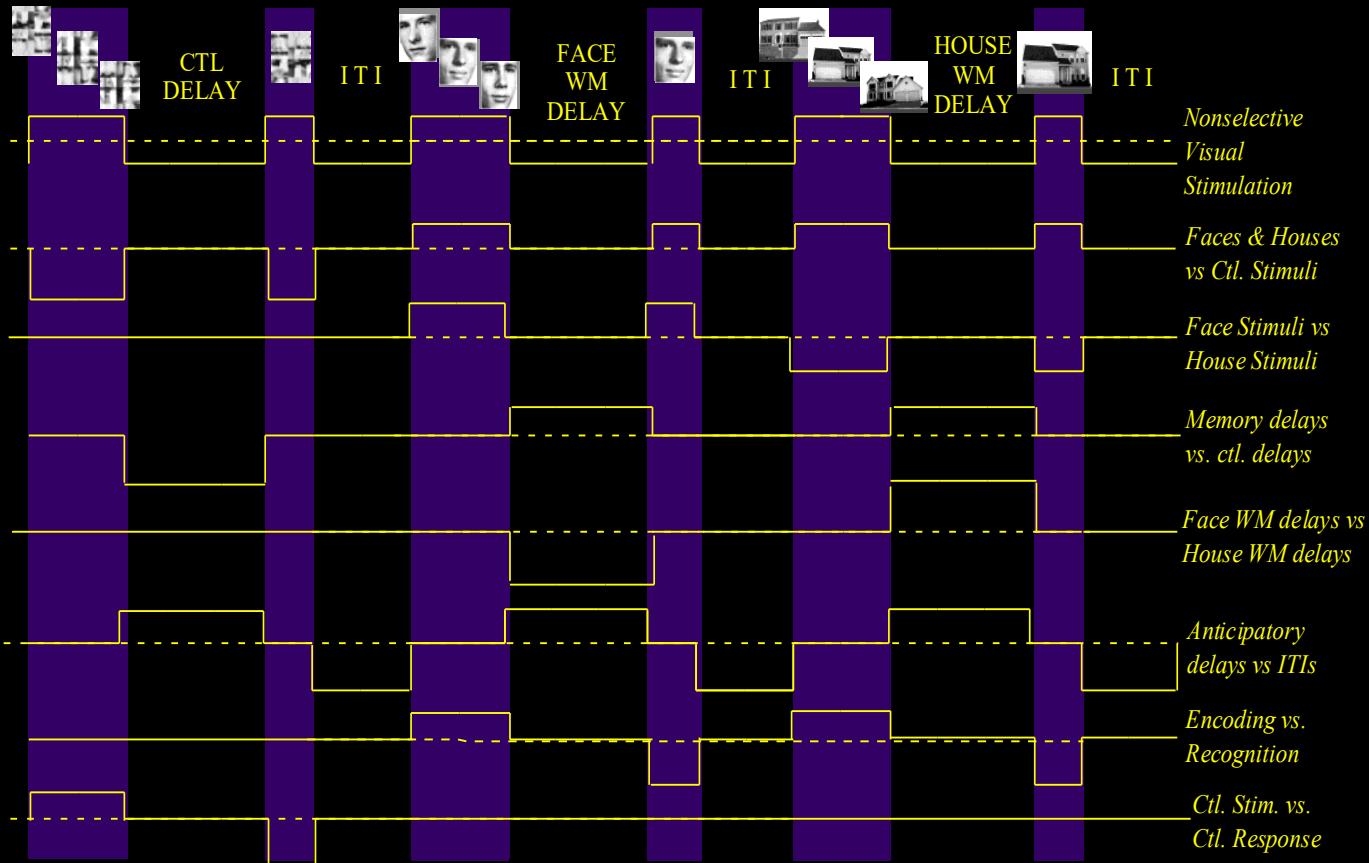


Mapping striate and extrastriate visual areas in human cerebral cortex

EDGAR A. DEYOE*, GEORGE J. CARMAN†, PETER BANDETTINI‡, SETH GLICKMAN*, JON WIESER*, ROBERT COX§,
DAVID MILLER¶, AND JAY NEITZ*



Example of a Set of Orthogonal Contrasts for Multiple Regression



Courtney, S. M., L. G. Ungerleider, et al. (1997). "Transient and sustained activity in a distributed neural system for human working memory." *Nature* 386(6625): 608-11.

Refinements

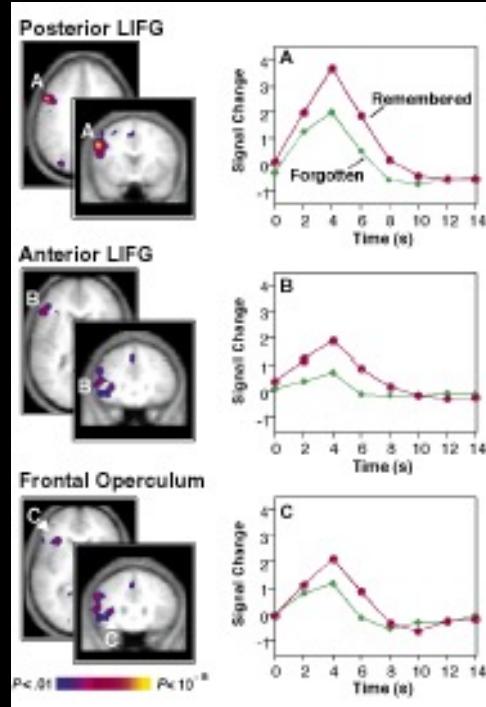
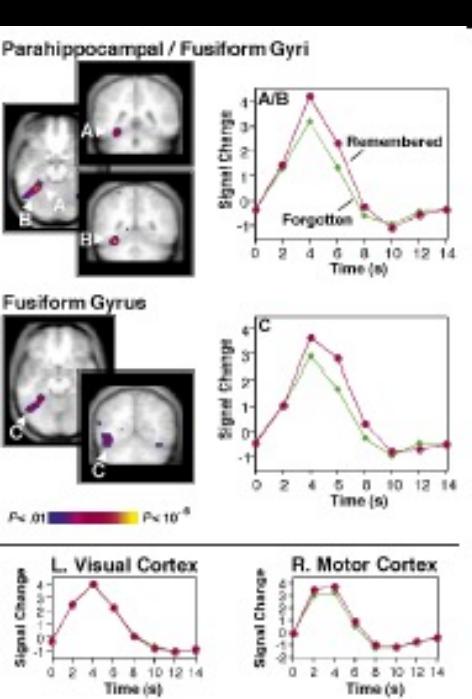
BOLD Contrast Interpretation

Dynamics, Paradigm Design and Processing

Applications

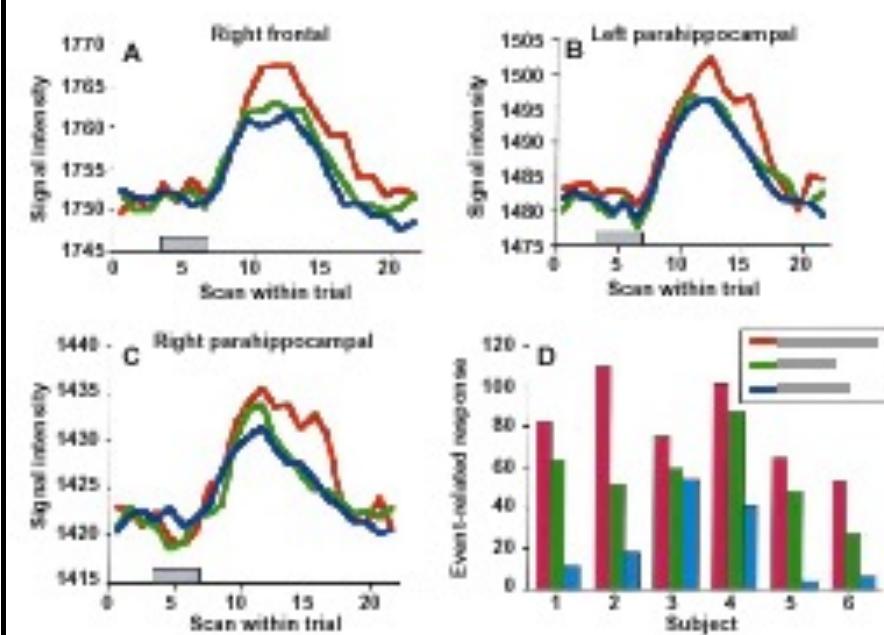
Building Memories: Remembering and Forgetting of Verbal Experiences as Predicted by Brain Activity

Anthony D. Wagner,* Daniel L. Schacter, Michael Rotte,†
Wilma Koutstaal, Anat Maril, Anders M. Dale, Bruce R. Rosen,
Randy L. Buckner



Making Memories: Brain Activity that Predicts How Well Visual Experience Will Be Remembered

James B. Brewer,* Zuo Zhao, John E. Desmond, Gary H. Glover,
John D. E. Gabrieli



Past

Present

Future

Technology

MRI	EPI	1.5T,3T, 4T	EPI on Clin. Syst.	Diff. tensor	Mg ⁺	7T
	Local Human Head Gradient Coils	Nav. pulses	Real time fMRI	Venography	SENSE	
	ASL	Spiral EPI	Quant. ASL	Z-shim	Baseline Susceptibility	
	BOLD	Multi-shot fMRI	Dynamic IV volume	Simultaneous ASL and BOLD	Current Imaging?	

Methodology

IVIM	Baseline Volume	Correlation Analysis	CO ₂ Calibration
		Motion Correction	
	Parametric Design	Surface Mapping	Multi-Modal Mapping
		Phase Mapping	Free-behavior Designs
	Linear Regression		Mental Chronometry

Interpretation

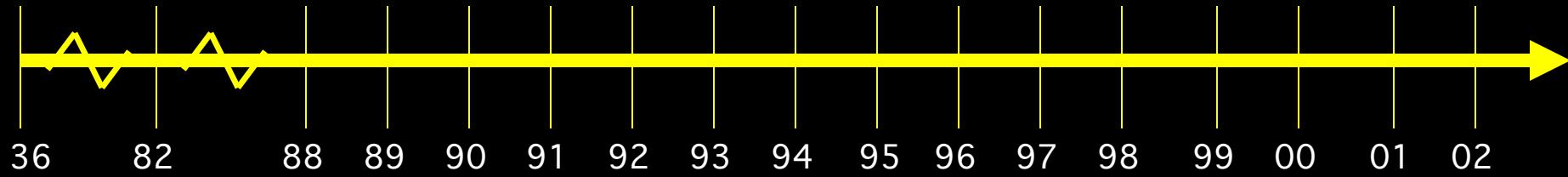
Blood T2	BOLD models	PET correlation	
	B ₀ dep.	IV vs EV	
	TE dep	Pre-undershoot	PSF of BOLD
		Resolution Dep.	
	SE vs. GE	Post-undershoot	Extended Stim.

Hemoglobin	CO ₂ effect	Linearity	Metab. Correlation
	NIRS Correlation	Fluctuations	Optical Im. Correlation
	Veins	Inflow	Balloon Model
			Electrophys. correlation

Applications

Volume - Stroke	Complex motor			
	Language	Imagery	Memory	Emotion
	Motor learning	Children	Tumor vasc.	Drug effects
	BOLD -V1, M1, A1	Presurgical	Attention	Ocular Dominance

△ Volume-V1	V1, V2..mapping	Priming/Learning	Clinical Populations	
		Plasticity	Face recognition	Performance prediction



Δ Neuronal Activity

Number of Neurons
Local Field Potential
Spiking Coherence
Spiking Rate

Δ Metabolism

Aerobic Metabolism

Anaerobic Metabolism

Δ Hemodynamics

Blood Volume

Deoxygenated Blood

Flow Velocity

Oxygenated Blood

Perfusion

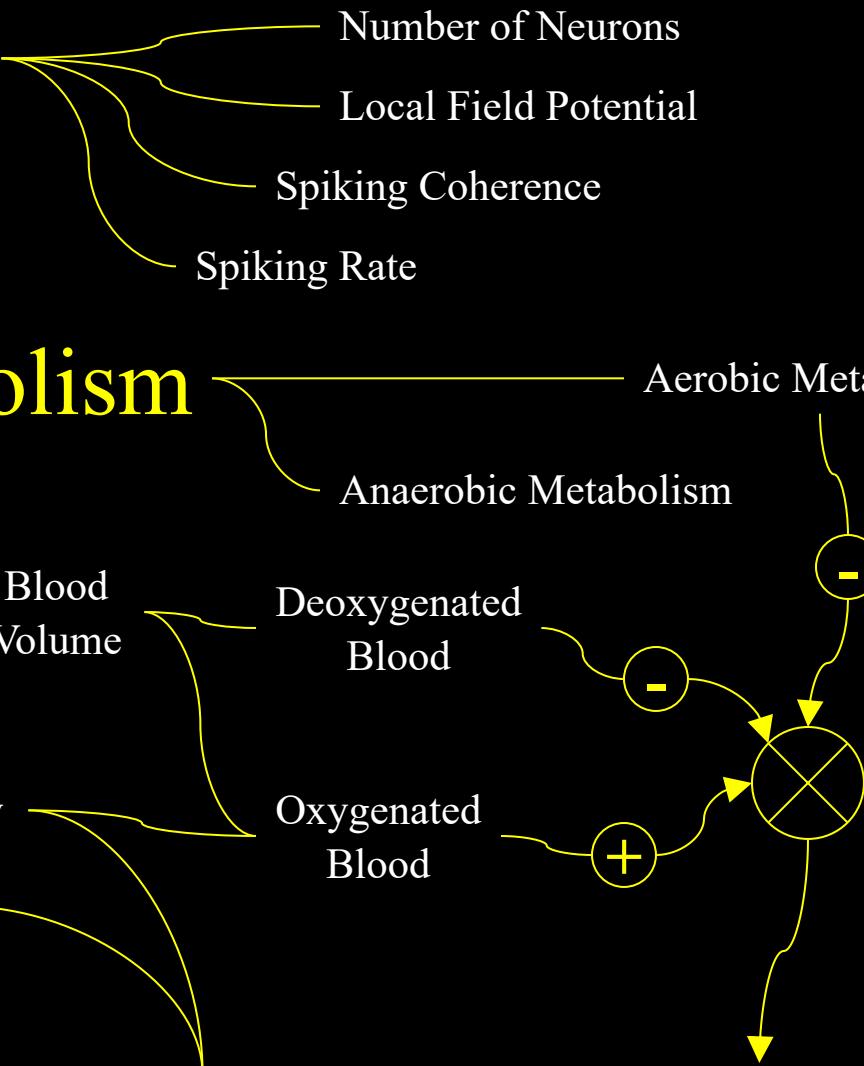
Δ BOLD Contrast

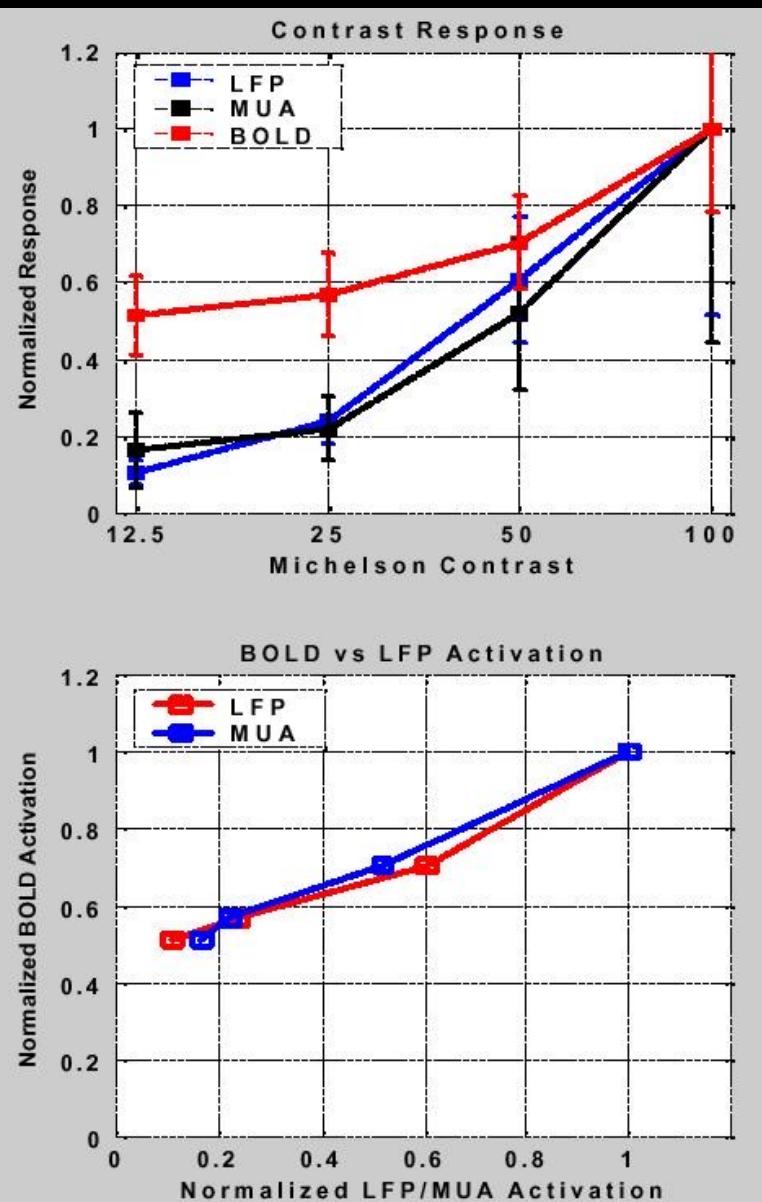
Δ Perfusion Contrast

Δ Inflow Contrast

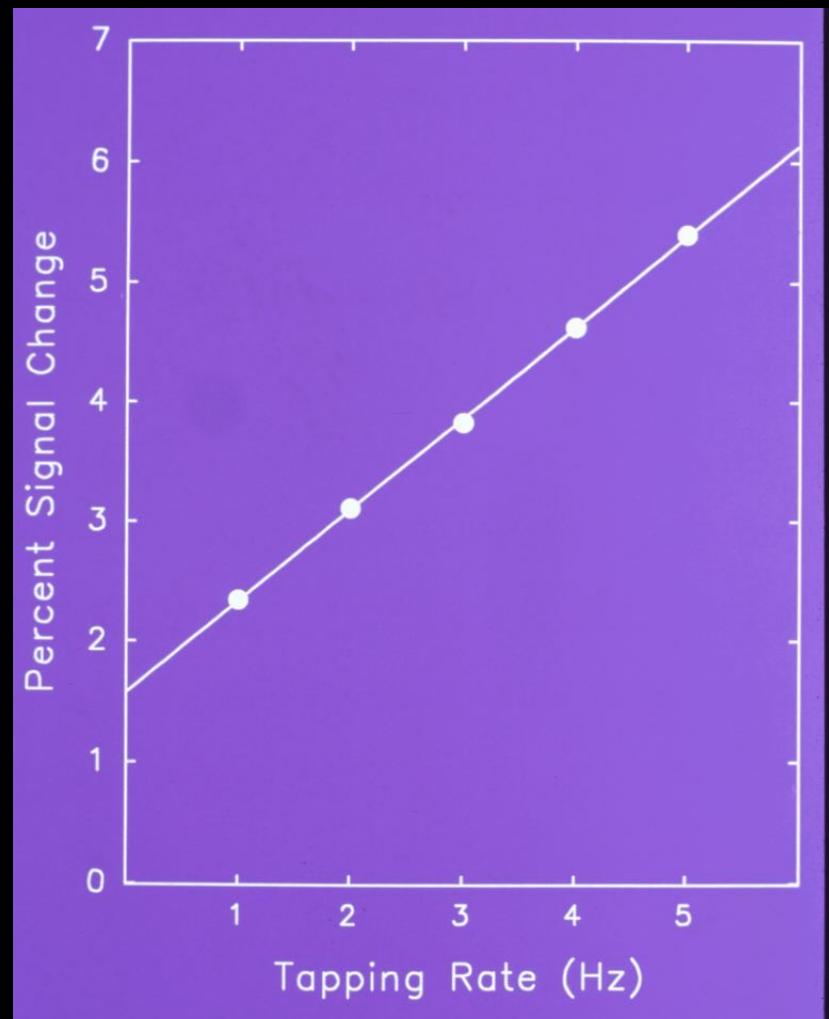
MRI Pulse Sequence

Δ Deoxy-Hb





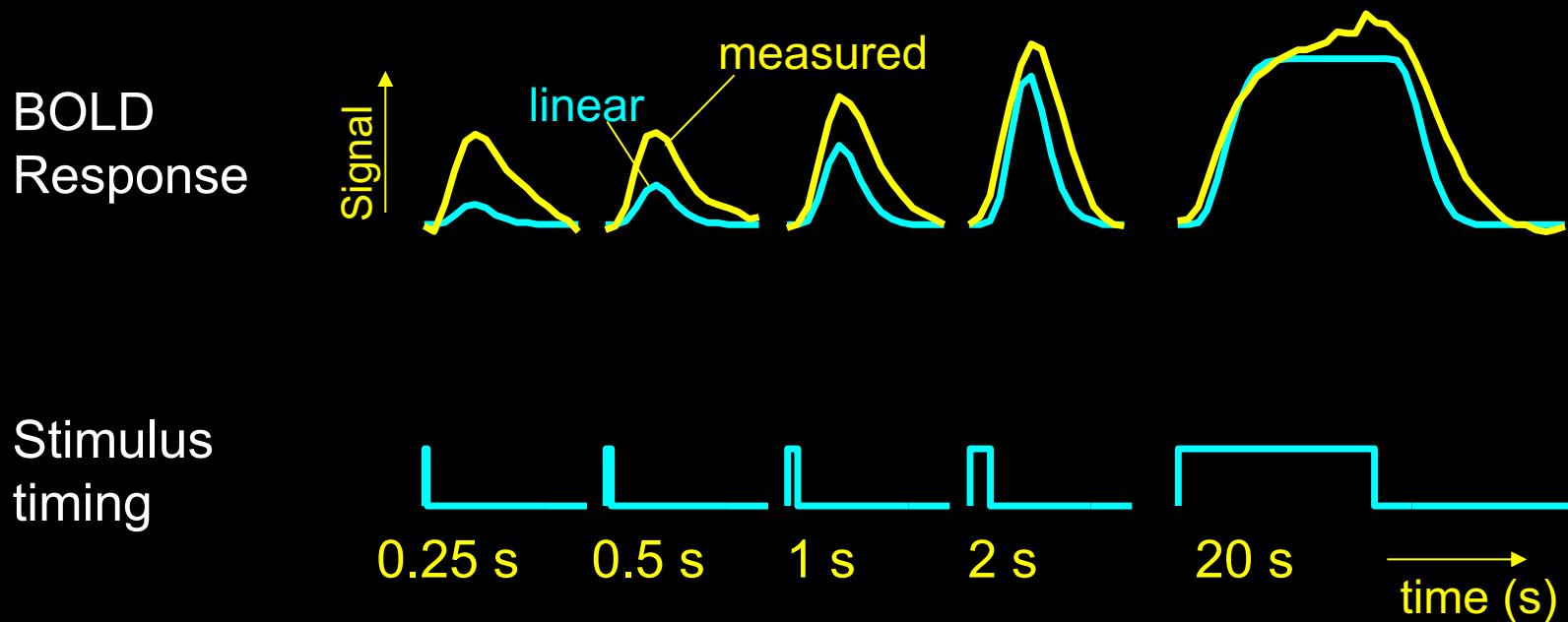
Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” *Nature*, 412, 150-157



S. M. Rao et al, (1996) “Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex.” *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

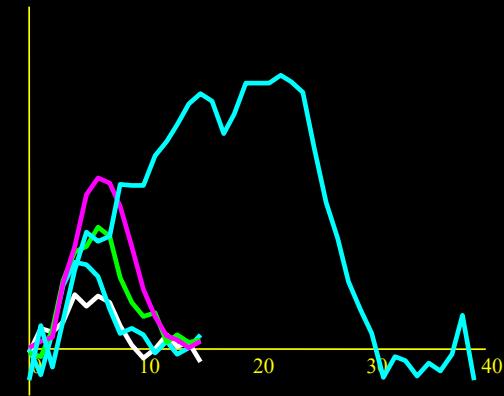
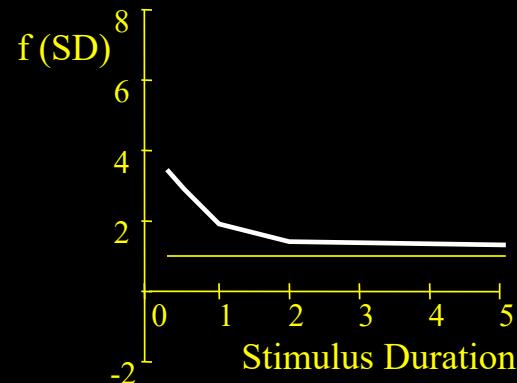
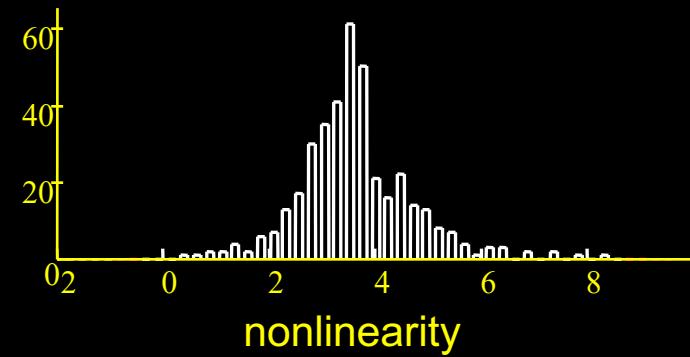
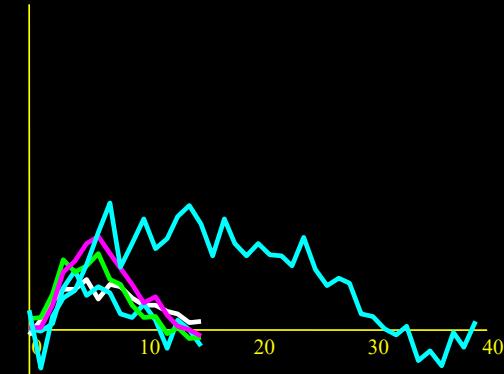
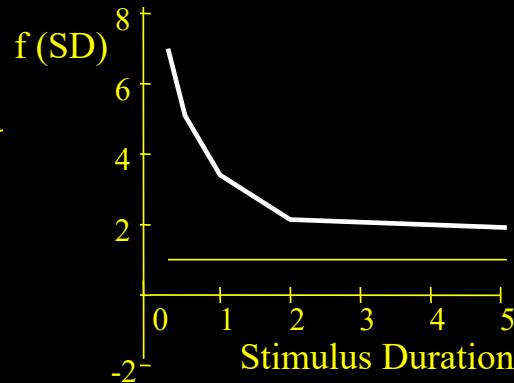
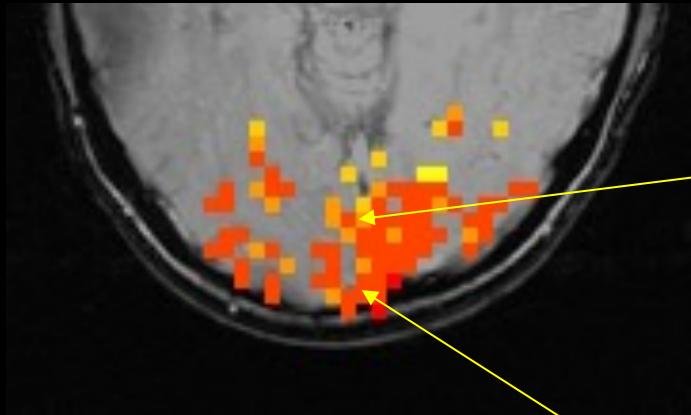
Dynamic Nonlinearity Assessment

Different stimulus “ON” periods



Brief stimuli produce larger responses than expected

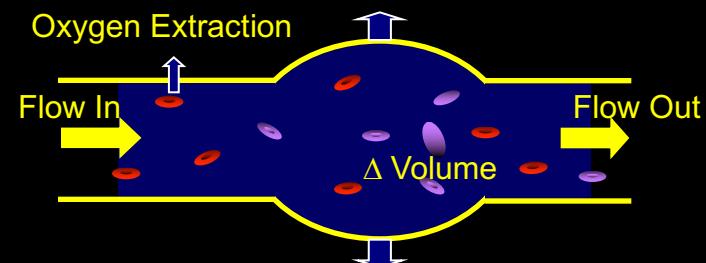
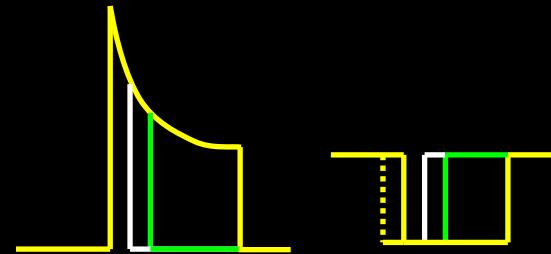
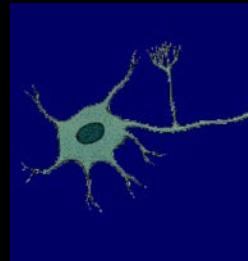
Spatial Heterogeneity of BOLD Nonlinearity



R. M. Birn, Z. Saad, P. A. Bandettini, (2001) “Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response.” *NeuroImage*, 14: 817-826.

Sources of this Nonlinearity

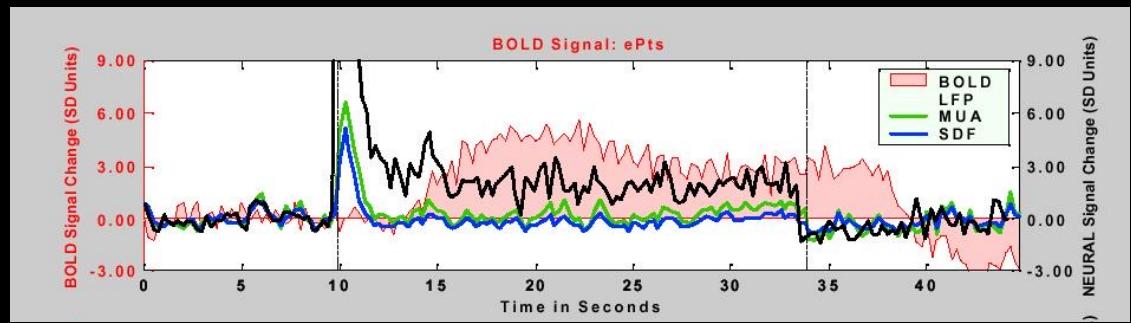
- Neuronal
- Hemodynamic
 - Oxygen extraction
 - Blood volume dynamics



BOLD Correlation with Neuronal Activity

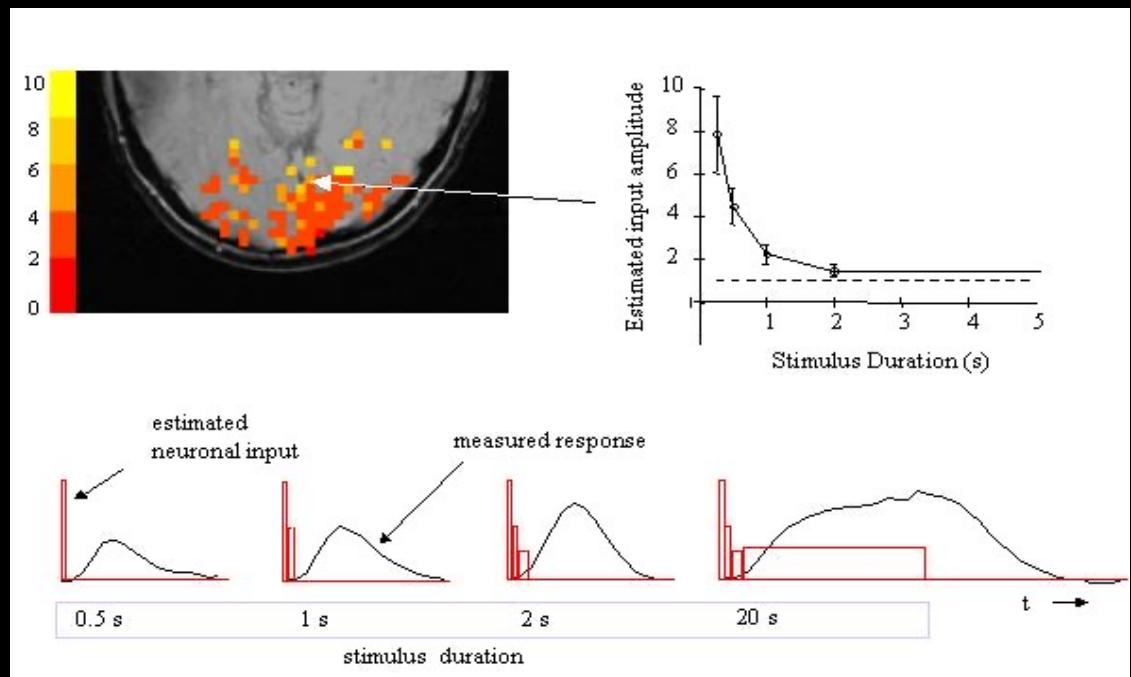
Logothetis et al. (2001)

“Neurophysiological investigation
of the basis of the fMRI signal”
Nature, 412, 150-157.



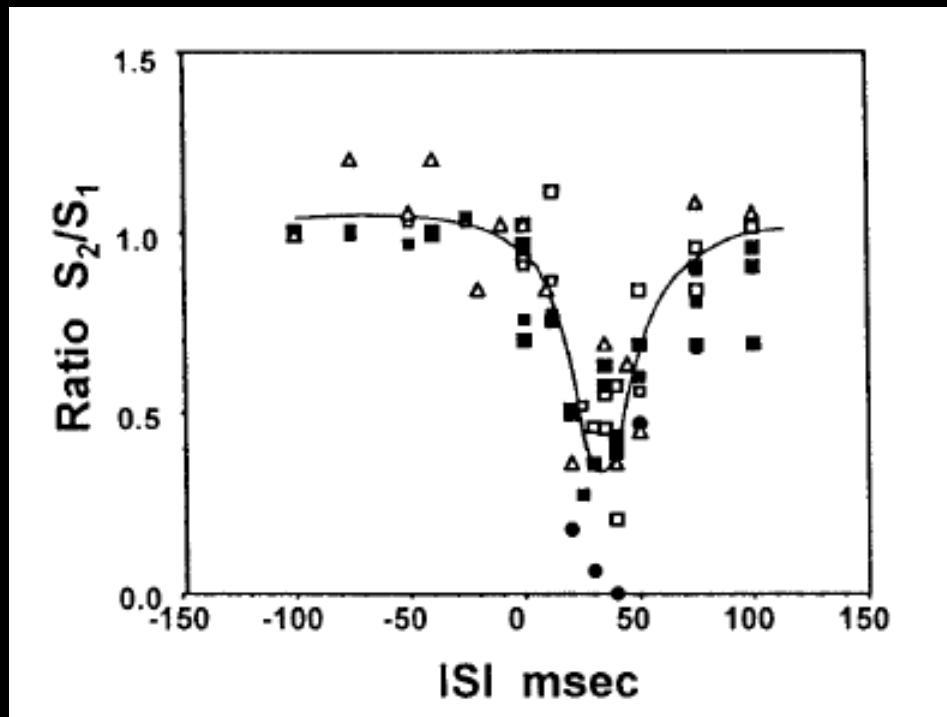
P. A. Bandettini and L. G.

Ungerleider, (2001) “From neuron
to BOLD: new connections.”
Nature Neuroscience, 4: 864-866.



An approach to probe some neural systems interaction by functional MRI at neural time scale down to milliseconds

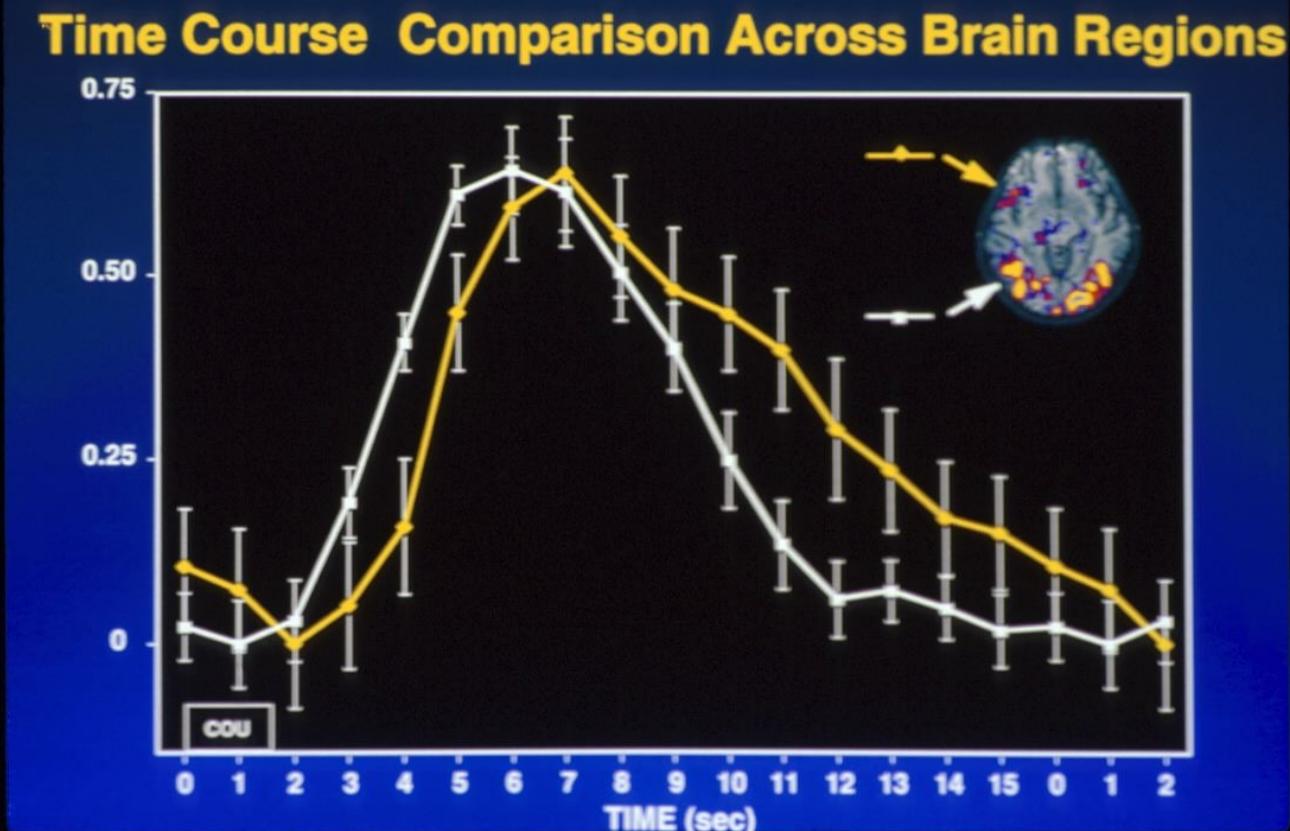
Seiji Ogawa^{†‡}, Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]



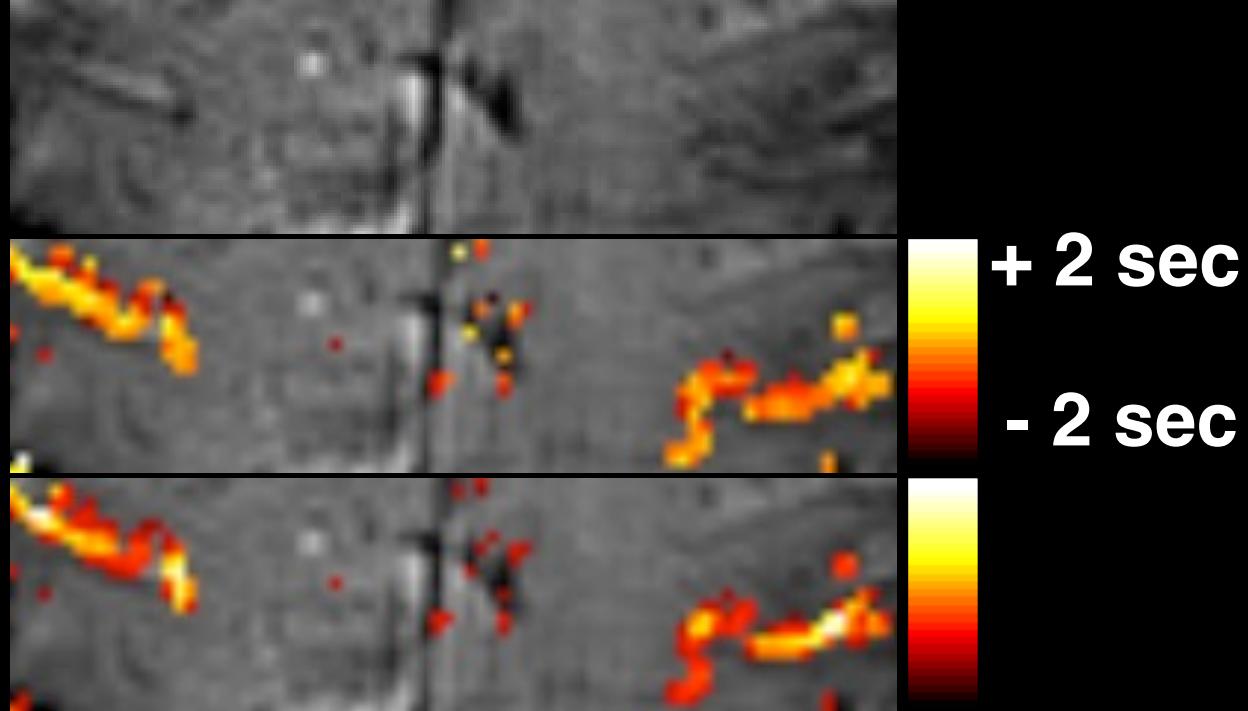
Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging

(neuroimaging/single trial/language/prefrontal)

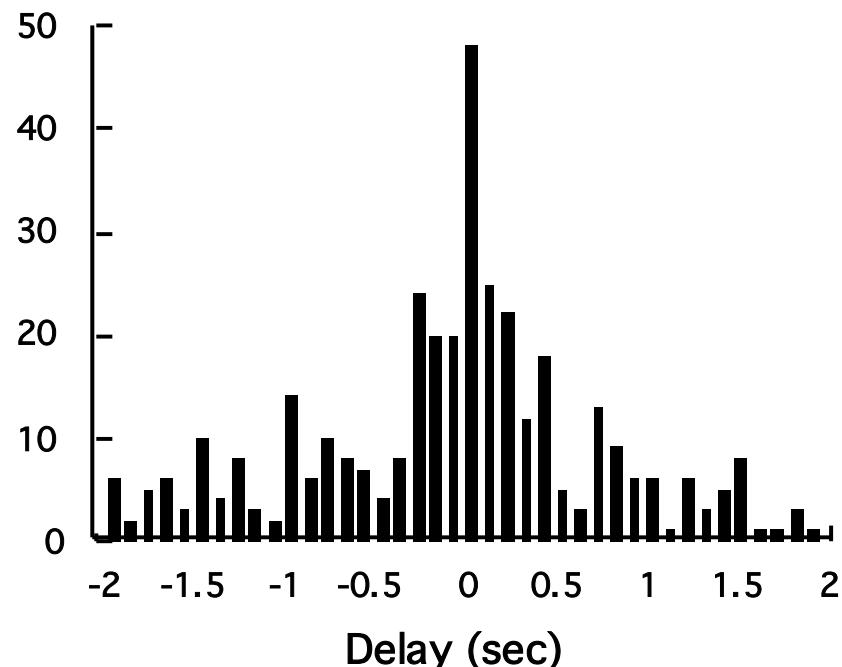
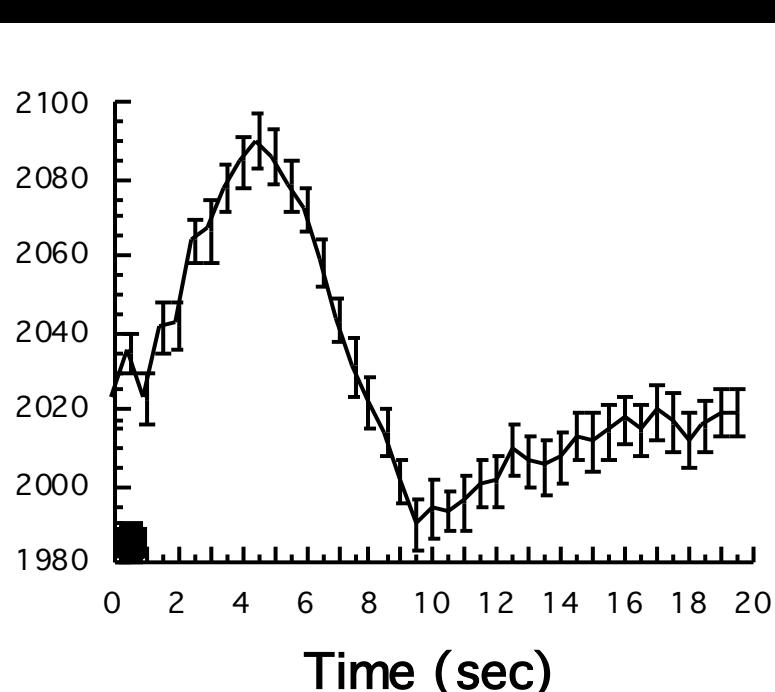
RANDY L. BUCKNER^{†‡§¶||}, PETER A. BANDETTINI^{†‡}, KATHLEEN M. O'CRAVEN^{†||}, ROBERT L. SAVOY^{†||},
STEVEN E. PETERSEN^{*++††}, MARCUS E. RAICHLE^{§++††}, AND BRUCE R. ROSEN^{†‡}



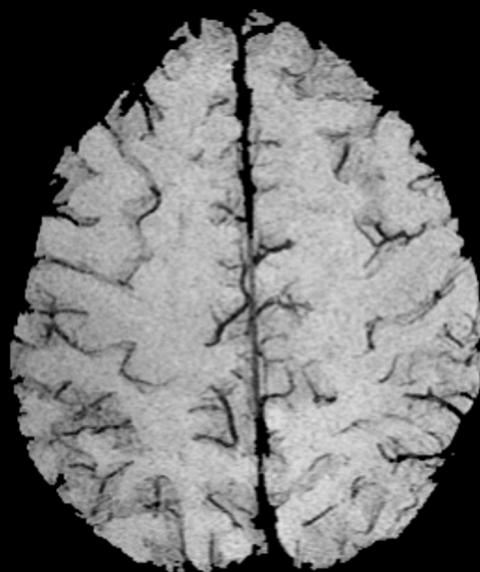
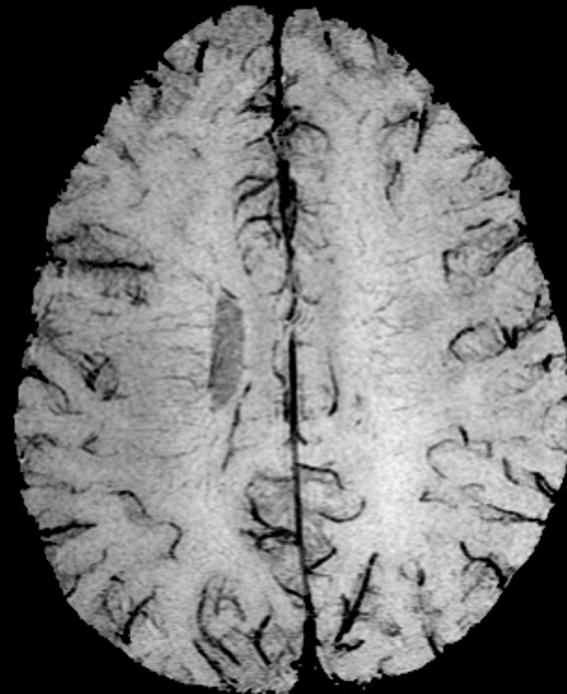
Latency

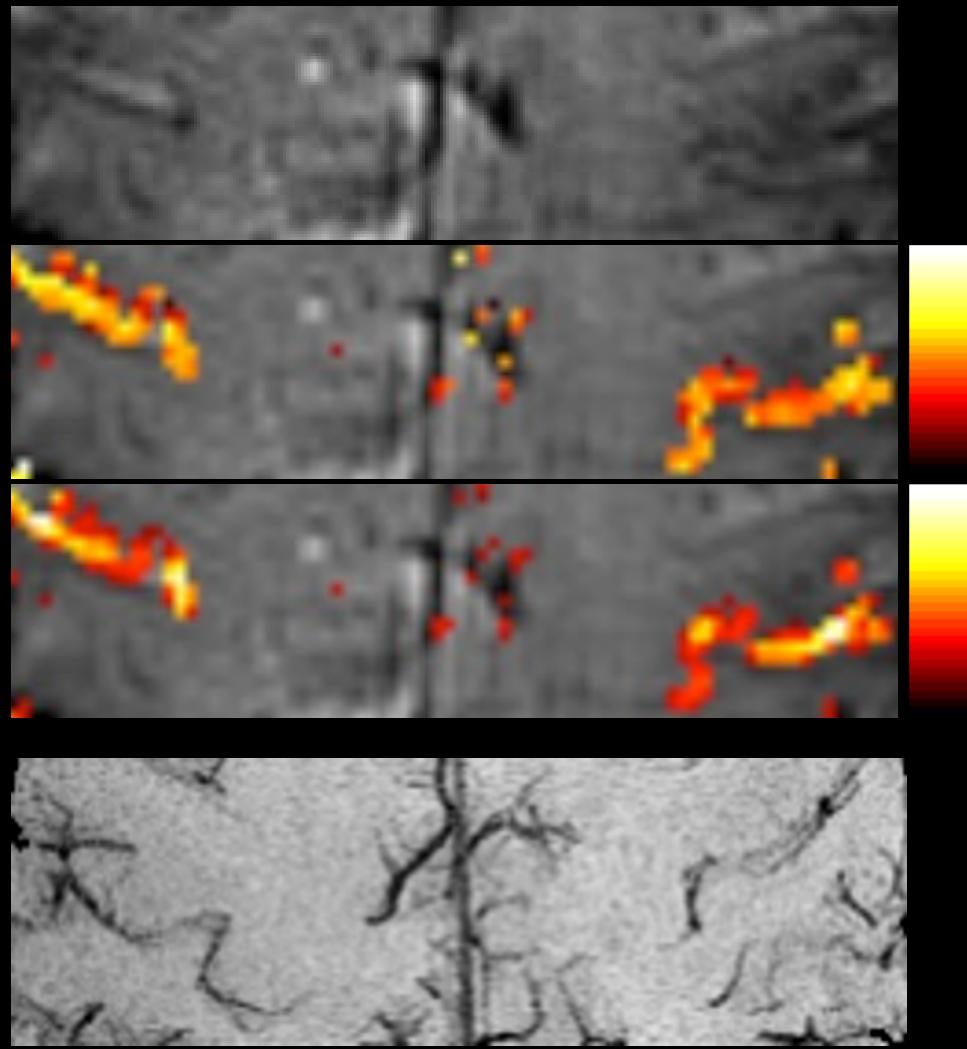


Magnitude



Venograms (3T)

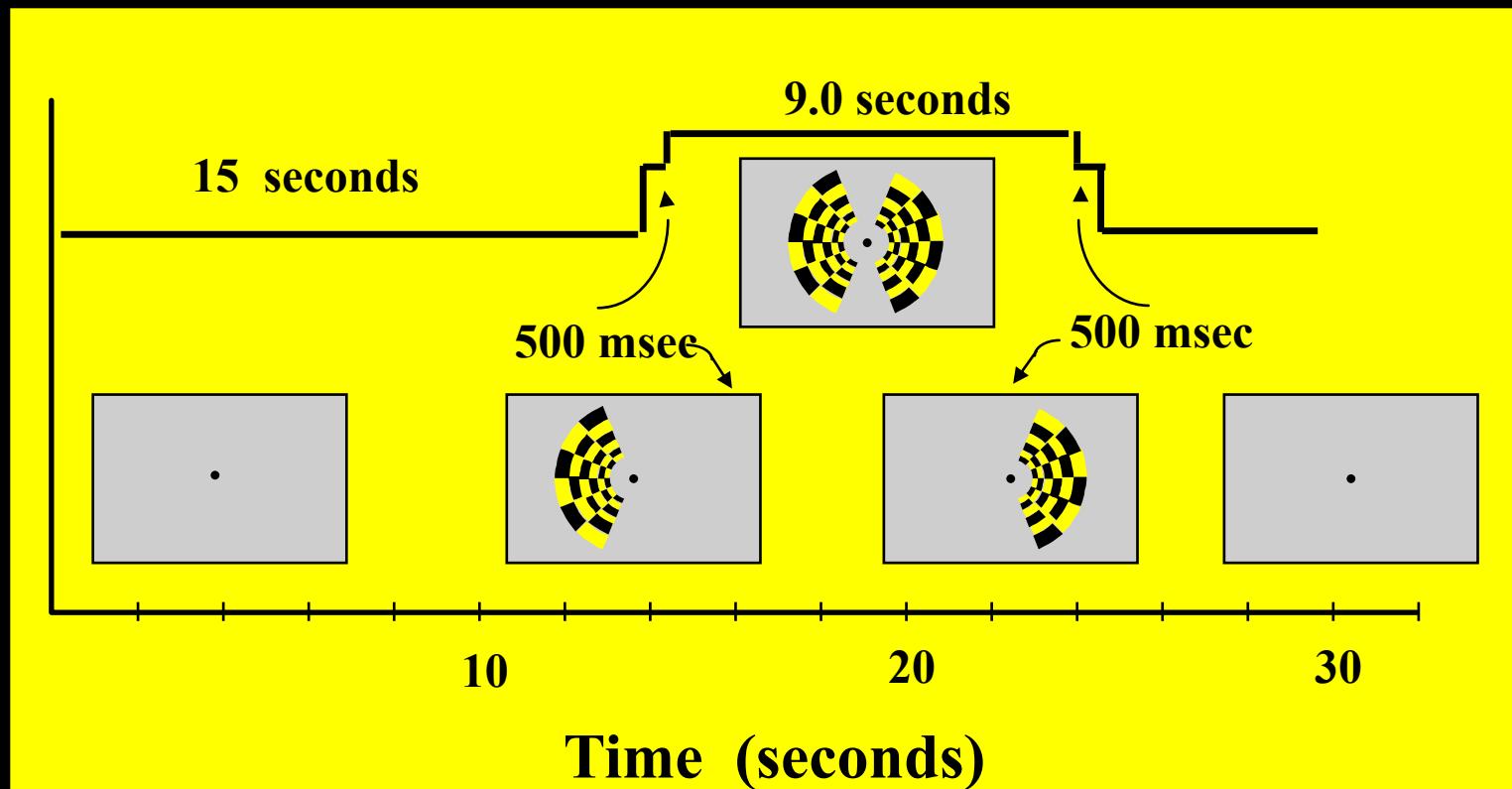


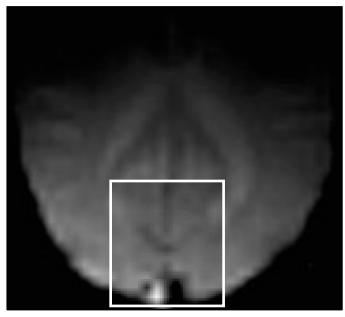


Hemi-Field Experiment

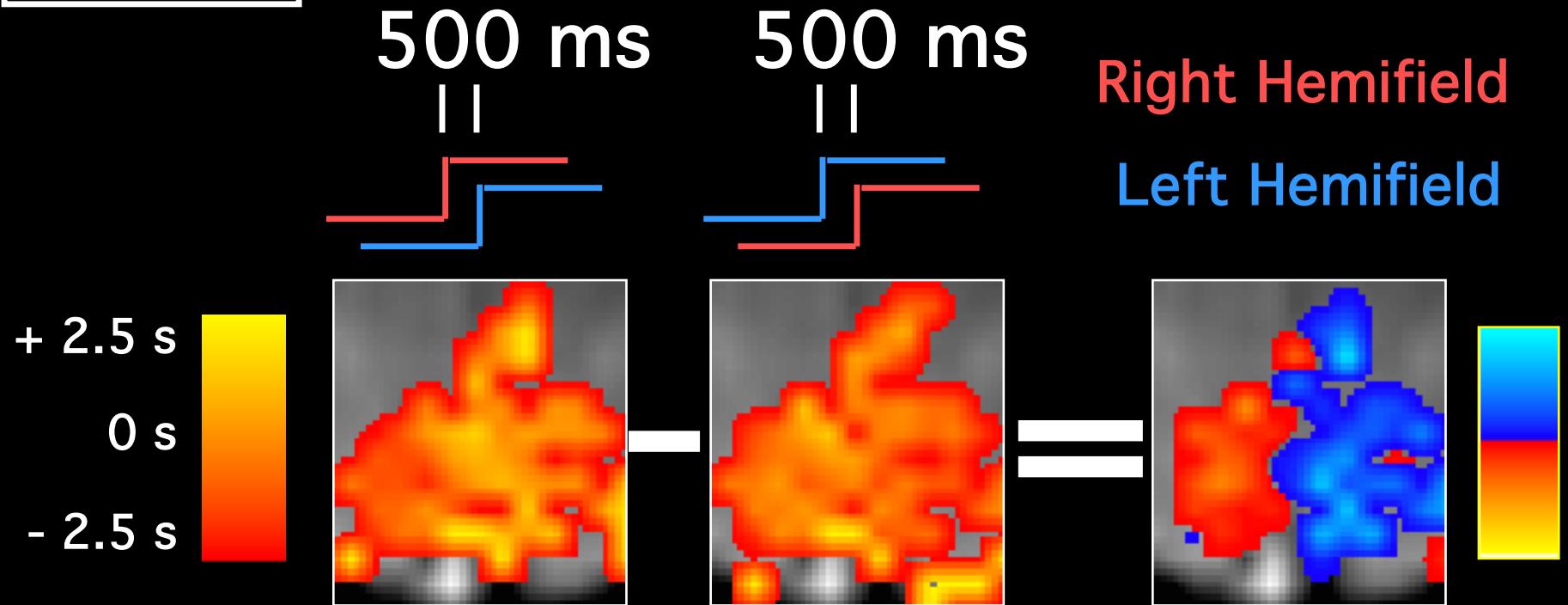
**Left
Hemisphere**

**Right
Hemisphere**





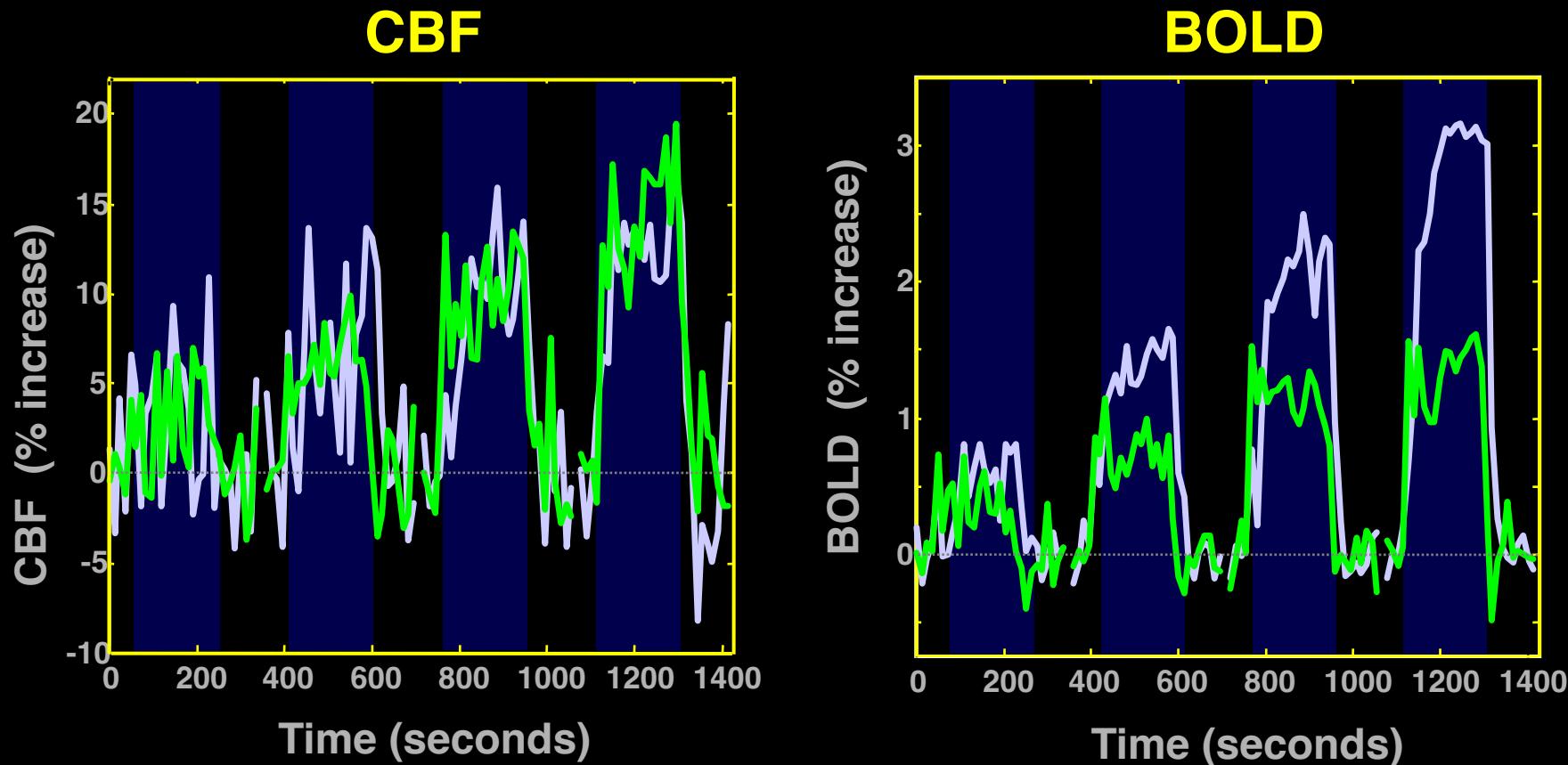
Calibration Techniques.....



Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

RICHARD D. HOGE^{*†}, JEFF ATKINSON*, BRAD GILL*, GÉRARD R. CRELIER*, SEAN MARRETT[‡], AND G. BRUCE PIKE*

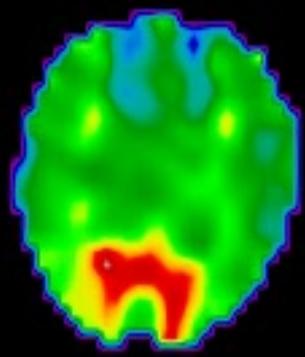
*Room WB325, McConnell Brain Imaging Centre, Montreal Neurological Institute, Quebec, Canada H3A 2B4; and [‡]Nuclear Magnetic Resonance Center, Massachusetts General Hospital, Building 149, 13th Street, Charlestown, MA 02129



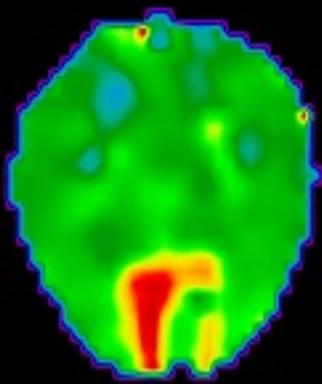
Simultaneous Perfusion and BOLD imaging during
graded visual activation and hypercapnia

N=12

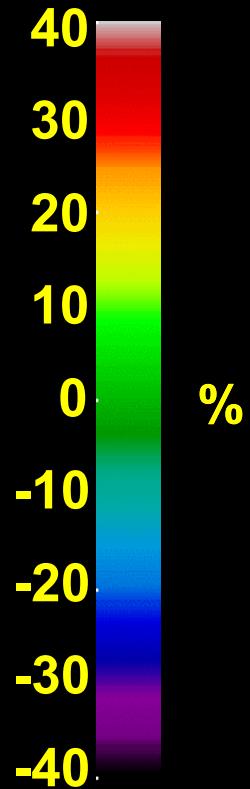
Computed CMRO₂ Changes



Subject 1



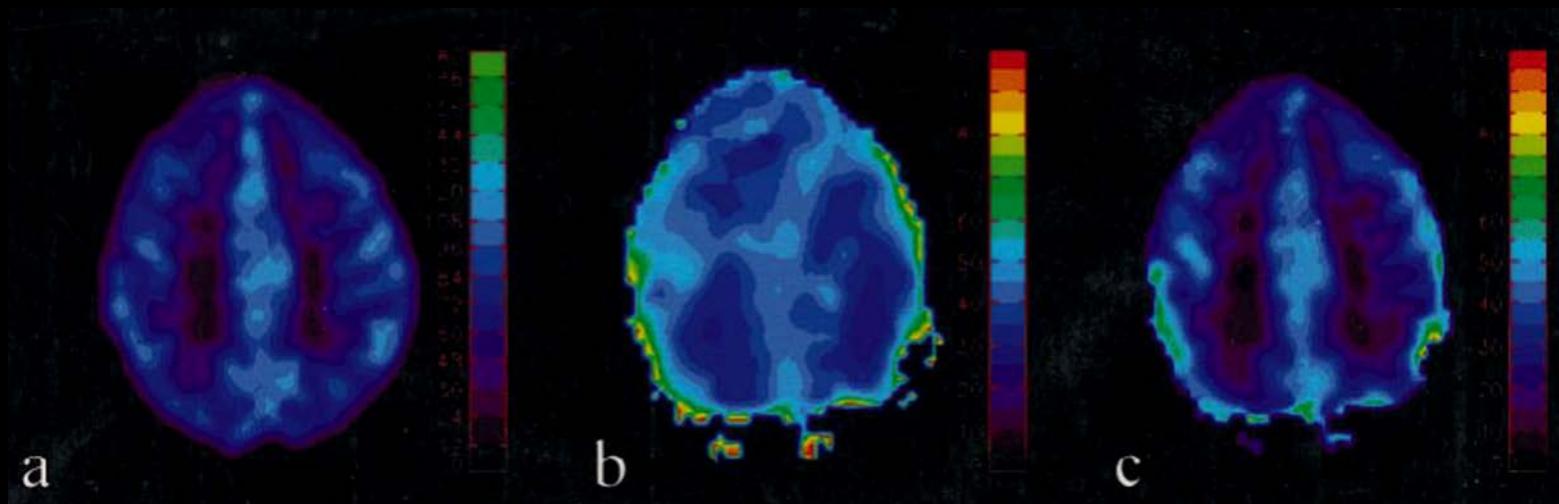
Subject 2



%

Quantitative measurements of cerebral metabolic rate of oxygen utilization using MRI: a volunteer study

Hongyu An,¹ Weili Lin,^{2*} Azim Celik³ and Yueh Z. Lee²

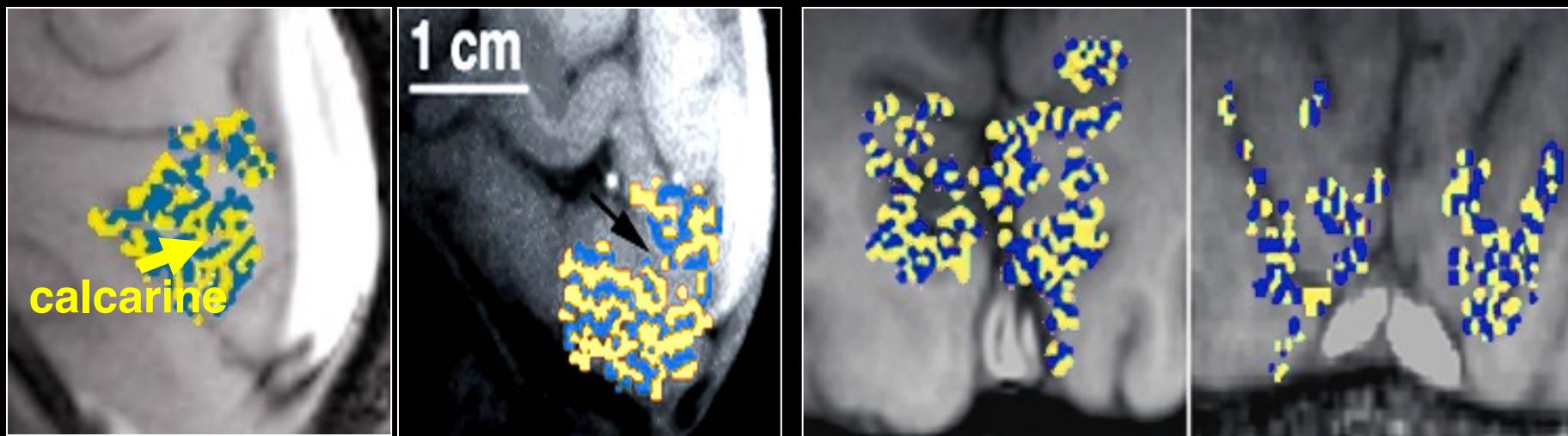


CBF

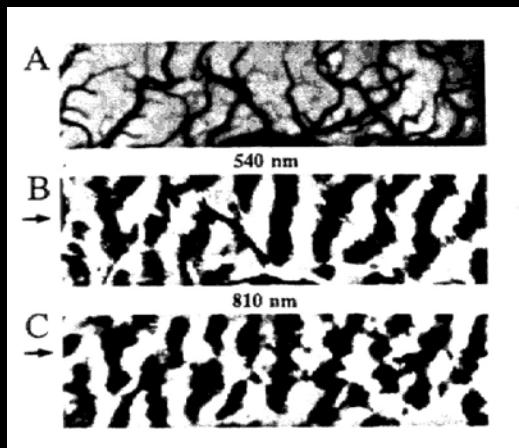
OEF

CMRO₂

Ocular Dominance Column Mapping using fMRI



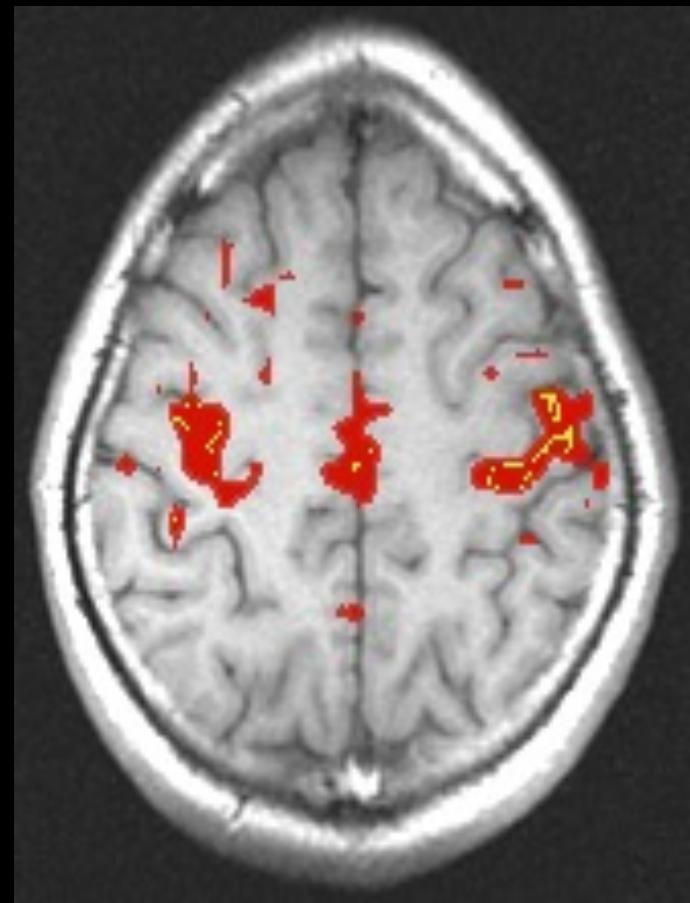
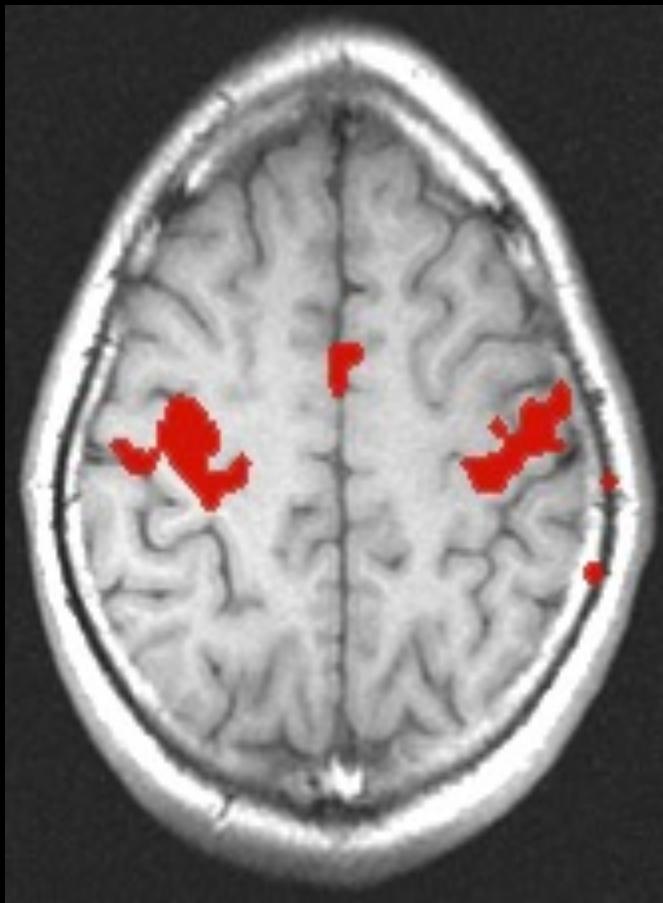
Menon, R. S., S. Ogawa, et al. (1997). "Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging." *J Neurophysiol* 77(5): 2780-7.



Optical Imaging

R. D. Frostig et. al, PNAS 87: 6082-6086, (1990).

Resting Hemodynamic Autocorrelations



B. Biswal *et al.*, MRM, 34:537 (1995)

Neuronal Activation Input Strategies

1. Block Design

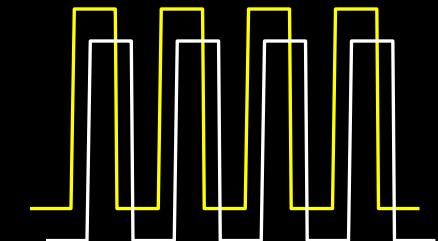
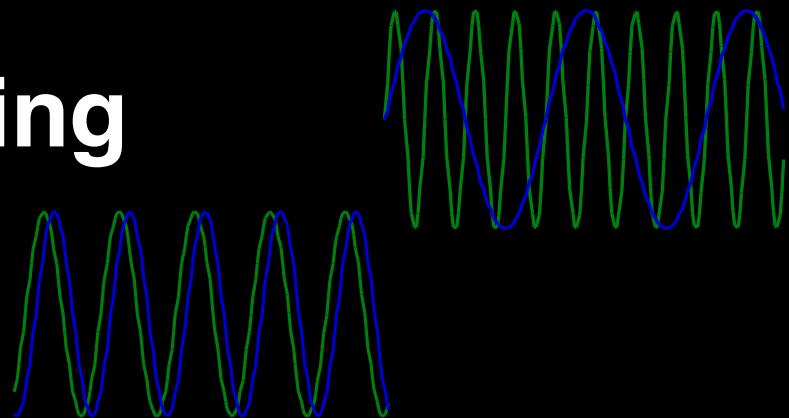
2. Frequency Encoding

3. Phase Encoding

4. Event Related

5. Orthogonal Block Design

6. Free Behavior Design

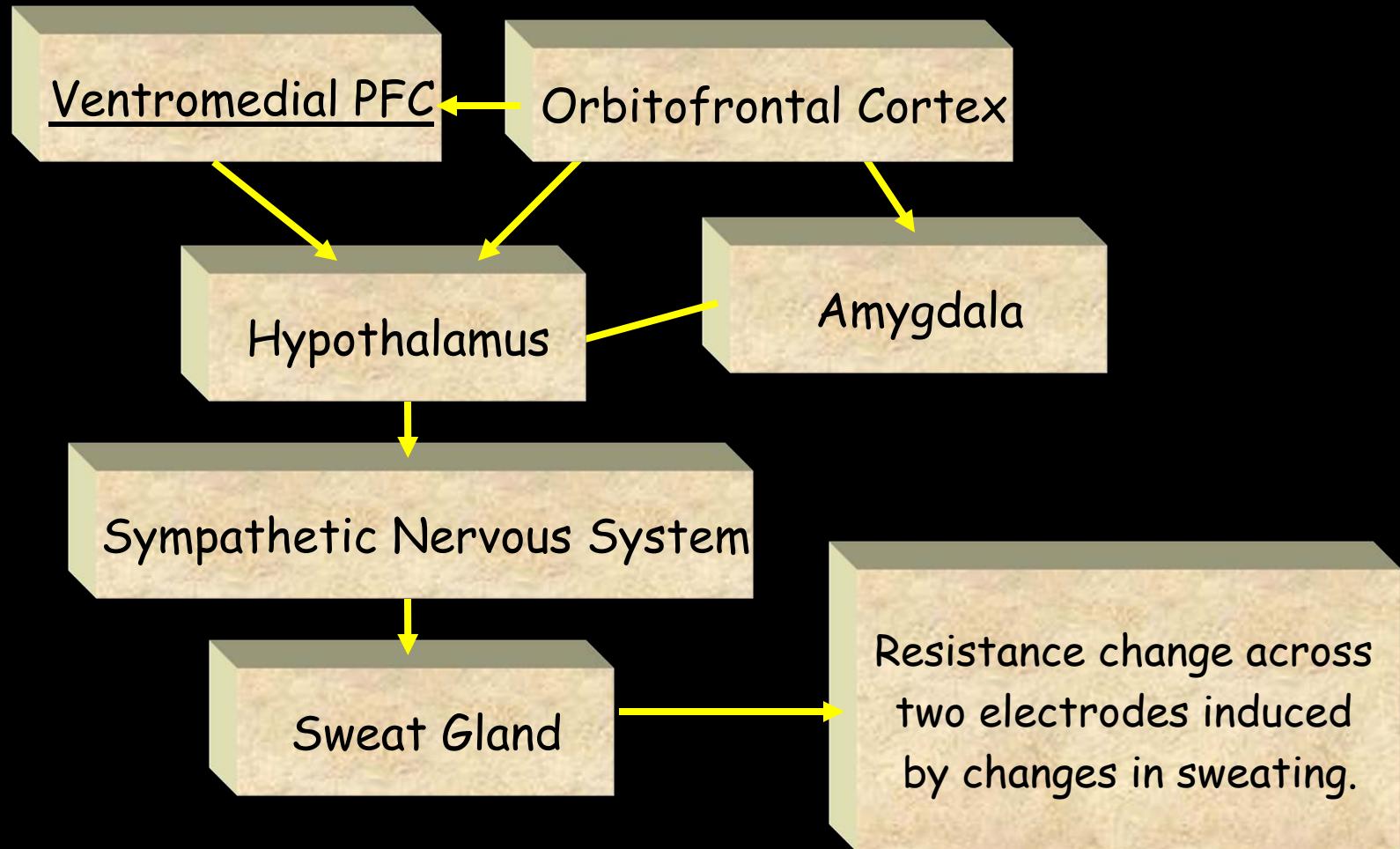


Free Behavior Design

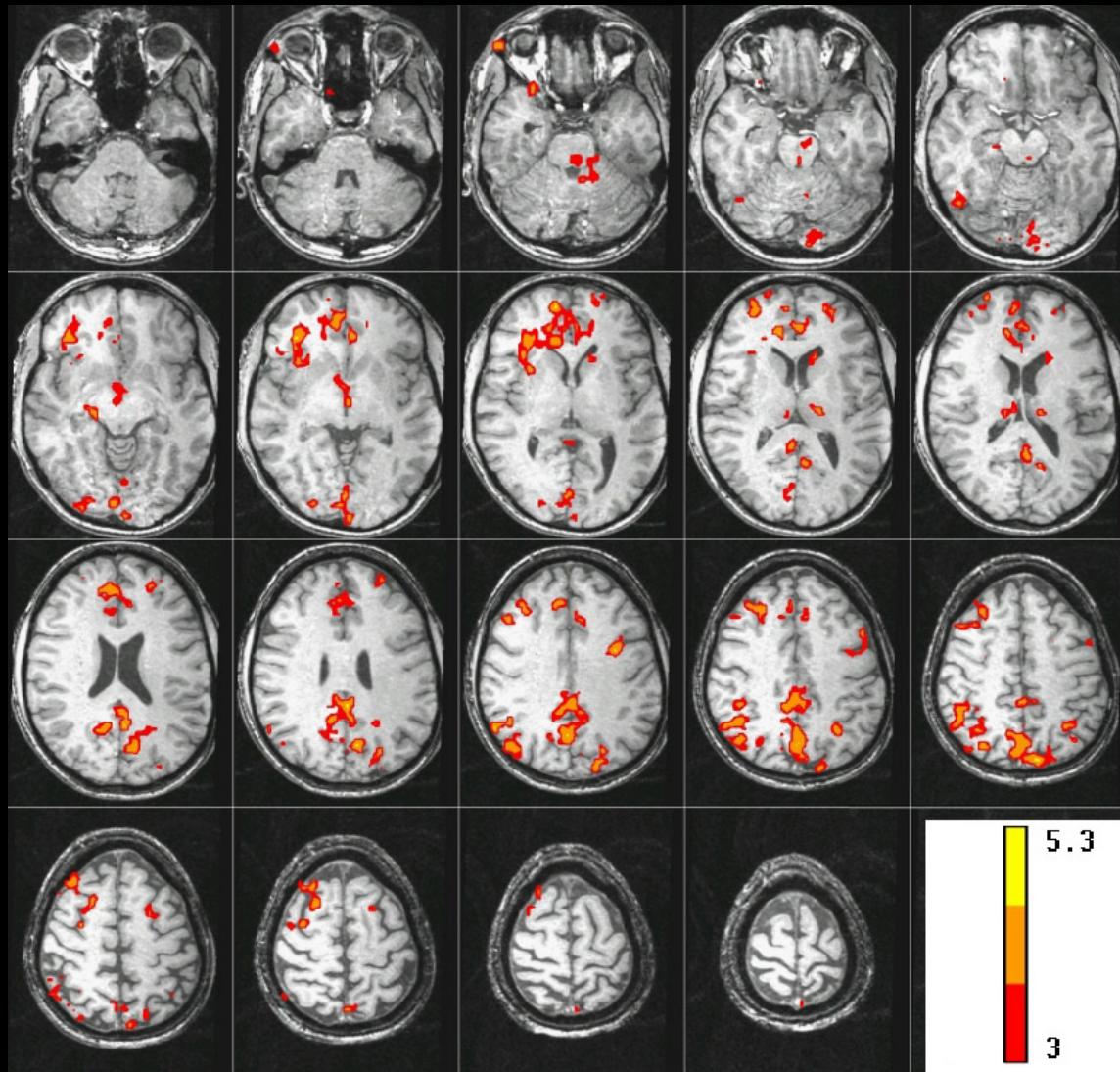
Use a continuous measure as a reference function:

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

The Skin Conductance Response (SCR)



Brain activity correlated with SCR during “Rest”



Past

Present

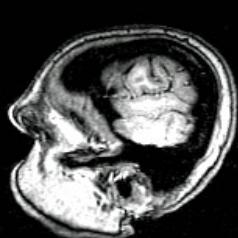
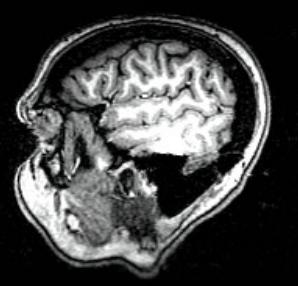
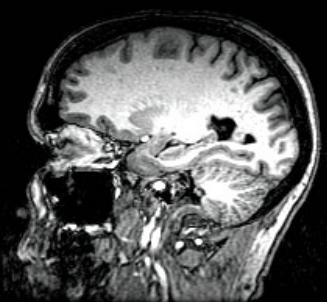
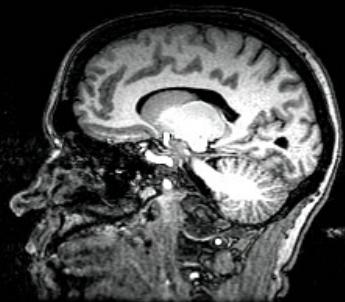
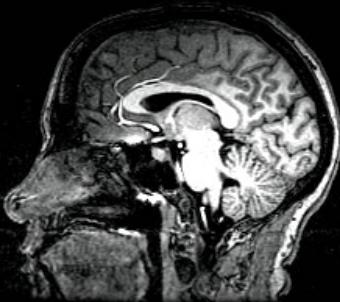
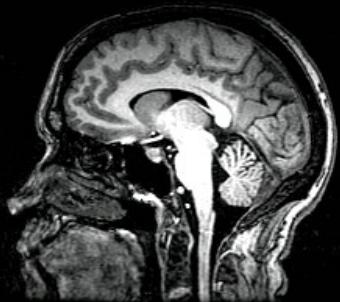
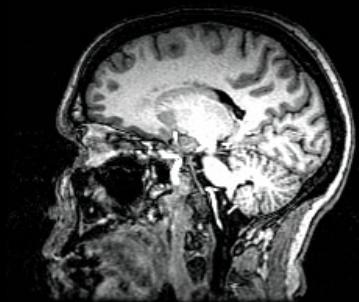
Future

Future

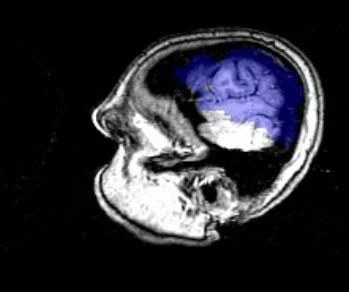
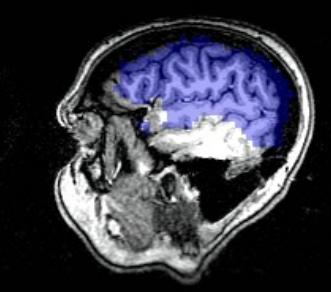
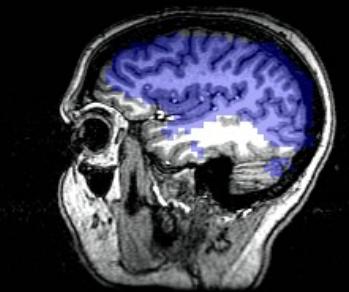
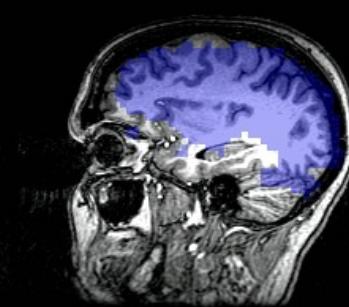
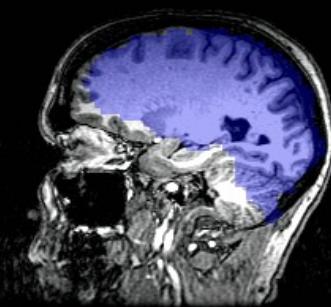
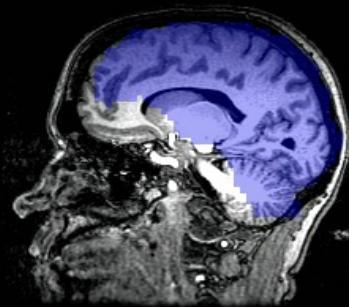
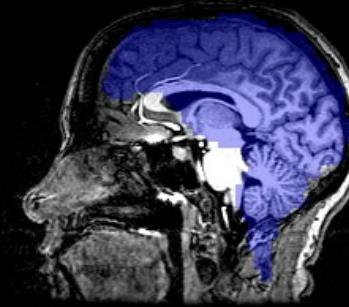
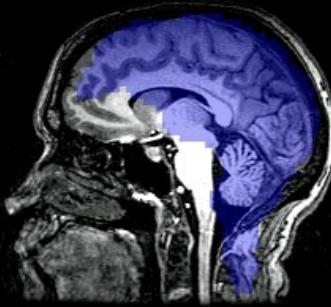
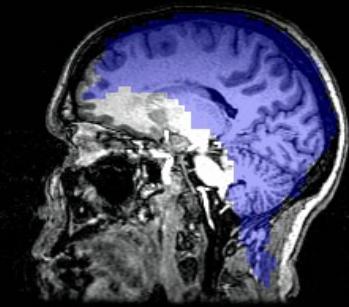
Imaging Methods

Implementation

- Shimming
- Acoustic Noise
- Multishot Techniques
- Increased Gradient Performance
- Higher Field Strengths
- Surface Coil Arrays
- Calibration / Quantification
- Embedded Functional Contrast
- Noise / Fluctuations
- Direct Neuronal Current Imaging
- Clinical Populations
- Neuronal, Vascular, and Metabolic Information

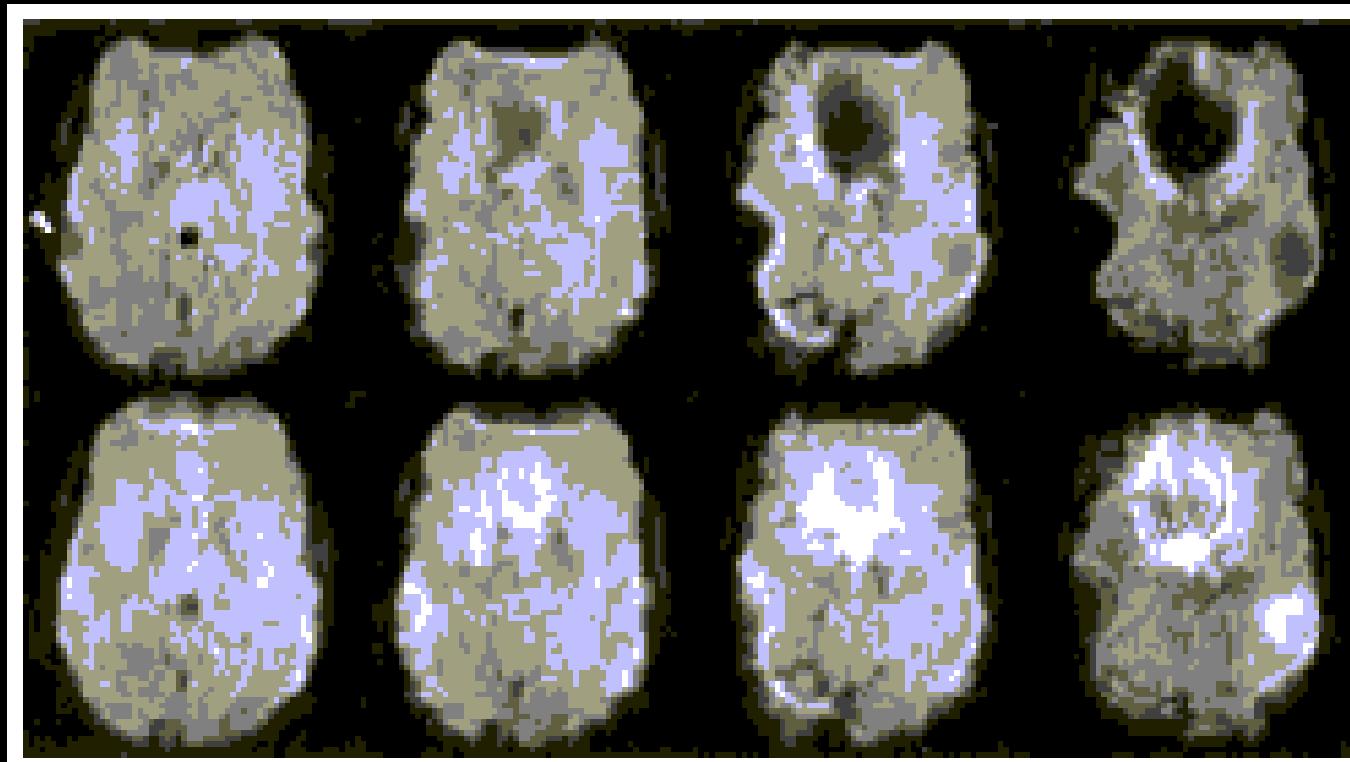






3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

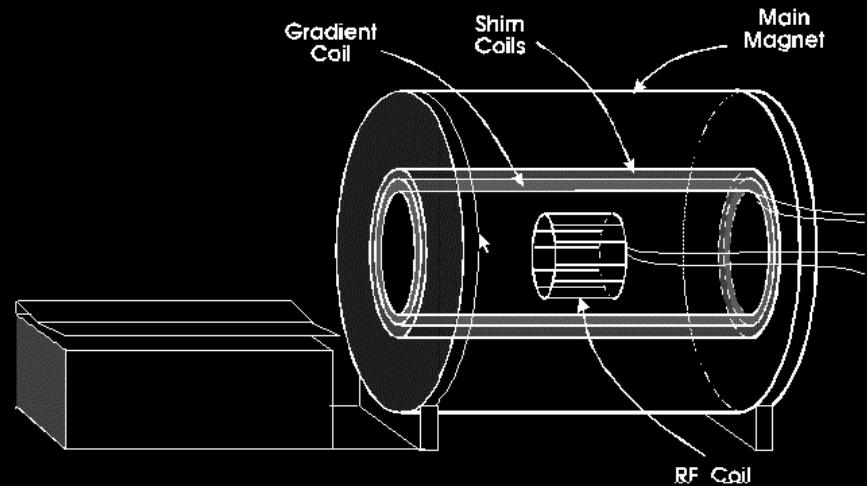
Gary H. Glover*



2 G/cm, 350 T/m/s



4 G/cm, 150 T/m/s



10 G/cm, 1000 T/m/s



Diffusion imaging
Faster imaging
Higher resolution

Neuronal Current Imaging

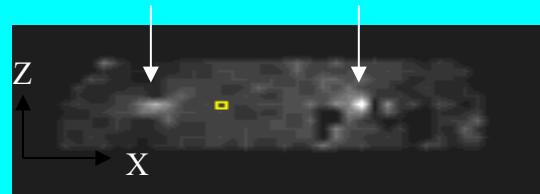
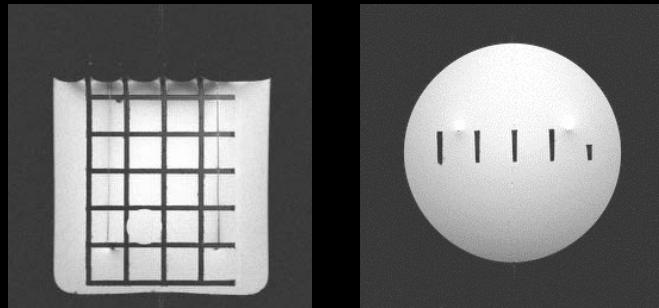
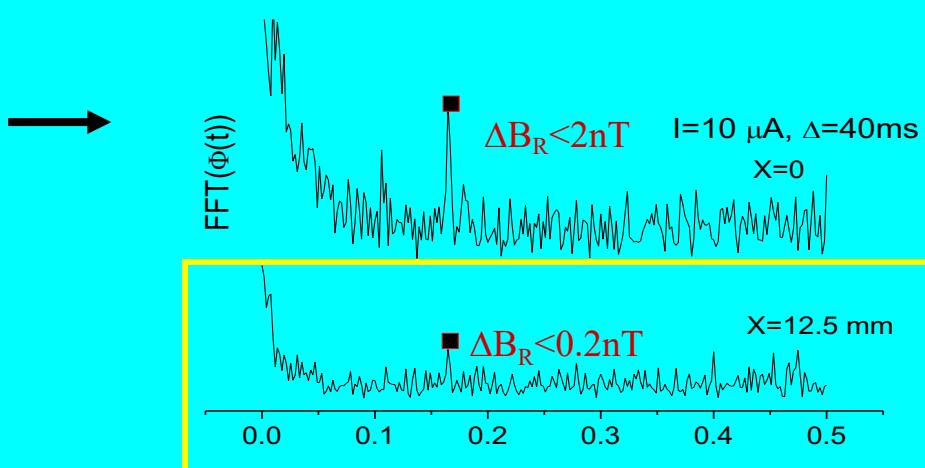


Figure 1



Functional Imaging Methods / 3T Group

Staff Scientists:

Sean Marrett

Jerzy Bodurka

Post Docs:

Rasmus Birn

Patrick Bellgowan

Ziad Saad

Graduate Student:

Natalia Petridou

Summer Student:

Dan Kelley

Program Assistant:

Kay Kuhns



August, 2000