

History and Prospects of fMRI and Human Brain Mapping

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods

<http://fim.nih.nih.gov>

Laboratory of Brain and Cognition

&

Functional MRI Facility

<http://fmrif.nih.nih.gov>



Technology

Magnet
RF Coils
Pulse Sequences

Methodology

Paradigm Design
Pre and Post Processing
Subject Interface
Data Display and Comparison

Increases
Decreases
Dynamics
Locations

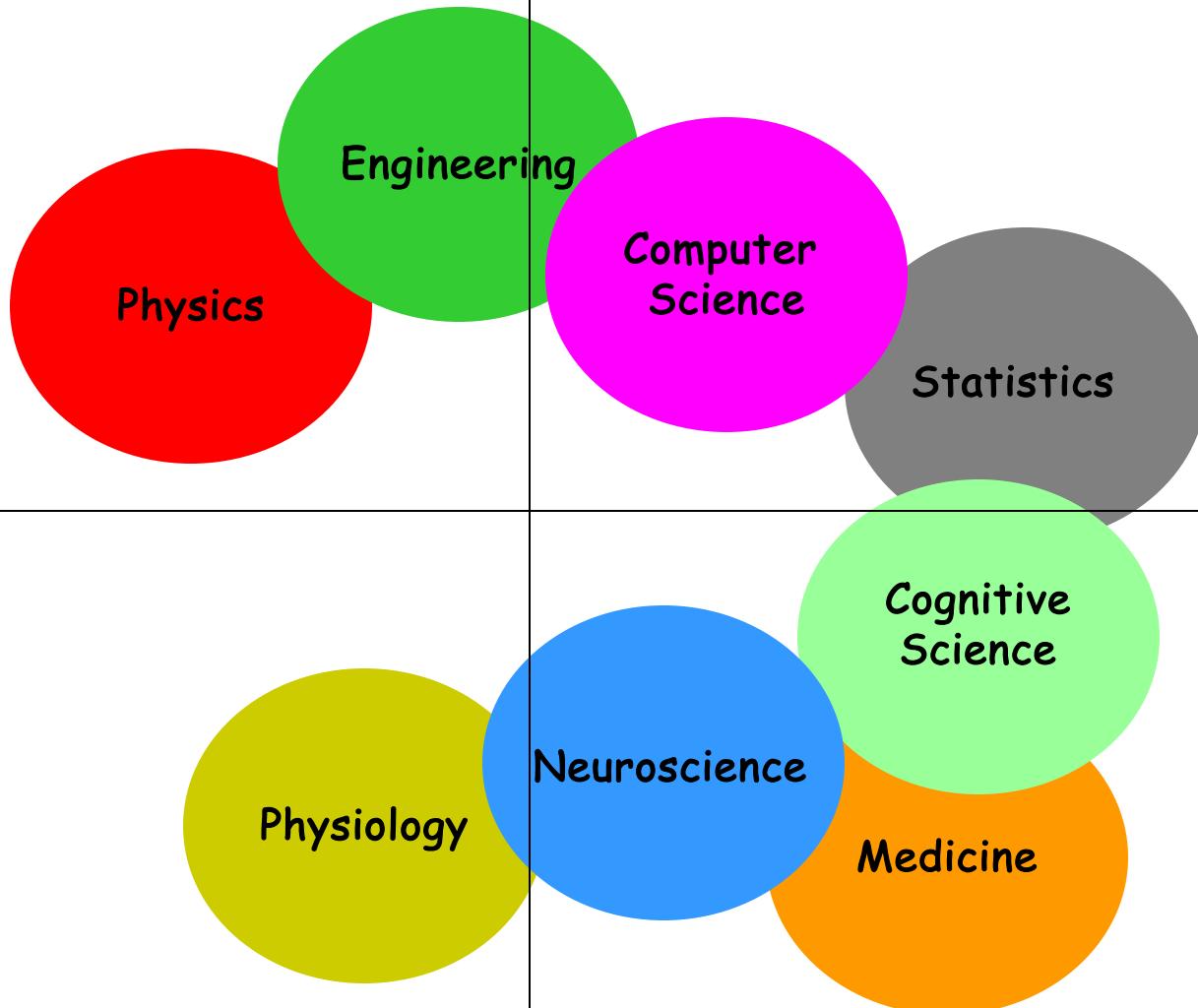
Neuroscience
Physiology
Genetics
Practical Clinical

Interpretation

Applications

Technology

Methodology



Interpretation

Applications

Technology

MRI	EPI	1.5T,3T, 4T	EPI on Clin. Syst.	Diff. tensor	Mg ⁺	7T	>8 channels
		Local Human Head Gradient Coils	Nav. pulses	Real time fMRI	Venography	SENSE	"vaso"
	ASL	Spiral EPI		Quant. ASL	Z-shim	Baseline Susceptibility	
	BOLD		Multi-shot fMRI	Dynamic IV volume	Simultaneous ASL and BOLD		Current Imaging?

Methodology

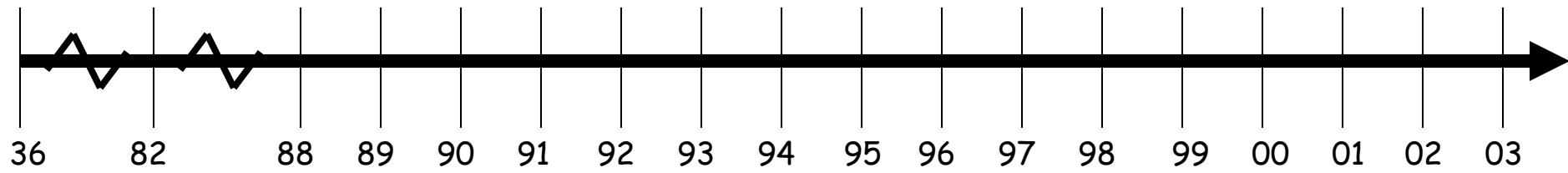
Baseline Volume	Correlation Analysis		CO ₂ Calibration	
	Motion Correction			Latency and Width Mod
	Parametric Design		Multi-Modal Mapping	
	Surface Mapping		ICA	Free-behavior Designs
IVIM	Phase Mapping		Mental Chronometry	Multi-variate Mapping
	Linear Regression			
	Event-related	Deconvolution	Fuzzy Clustering	

Interpretation

Blood T2	BOLD models	PET correlation		
	B ₀ dep.	IV vs EV	ASL vs. BOLD	Layer spec. latency
		Pre-undershoot	PSF of BOLD	
	TE dep	Resolution Dep.		Excite and Inhibit
		Post-undershoot	Extended Stim.	
	SE vs. GE	CO ₂ effect	Linearity	Metab. Correlation
Hemoglobin	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	Mirror neurons
	V1, V2..mapping	Priming/Learning	Ocular Dominance	
Δ Volume-V1		Clinical Populations		
	Plasticity	Face recognition	Performance prediction	



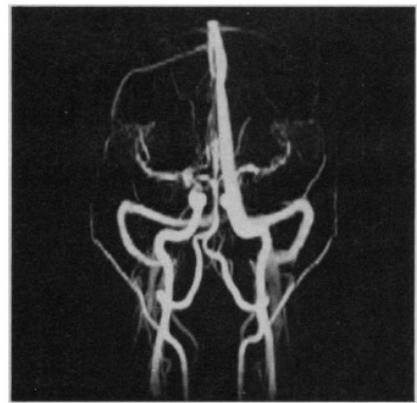
metabolic imaging (NAA)

Functional Magnetic Resonance Imaging in Medicine and Physiology

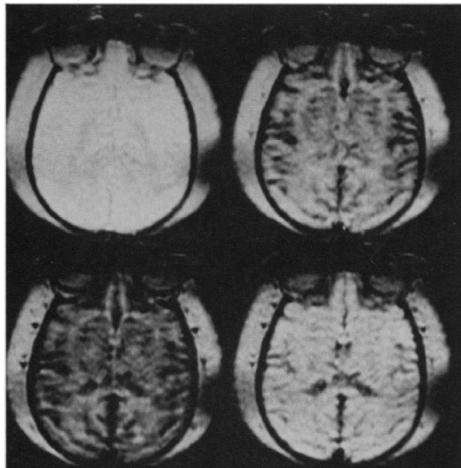
CHRIT T. W. MOONEN, PETER C. M. VAN ZIJL, JOSEPH A. FRANK,
DENIS LE BIHAN, EDWIN D. BECKER

(1990) *Science*, 250, 53-61.

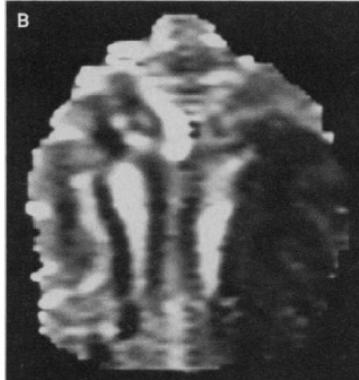
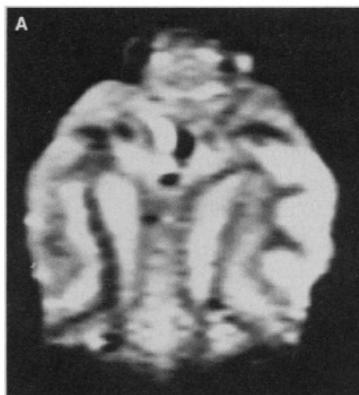
angiography



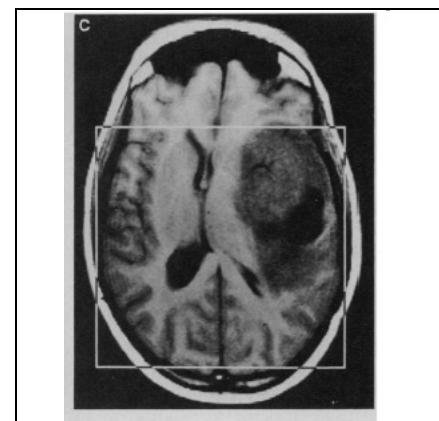
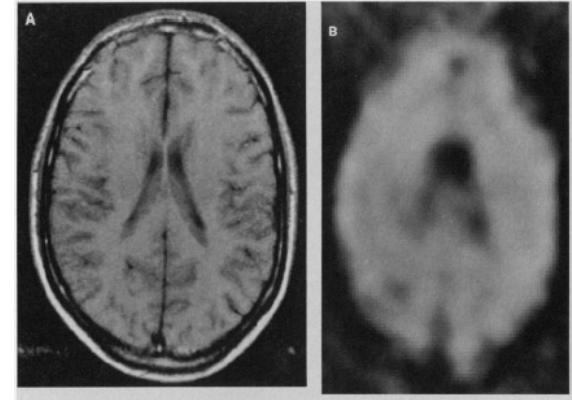
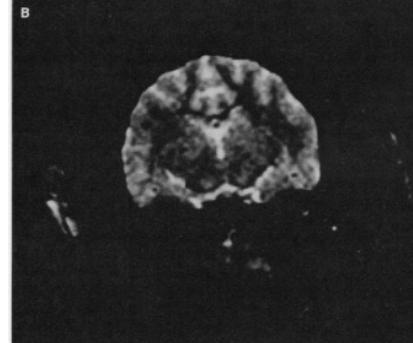
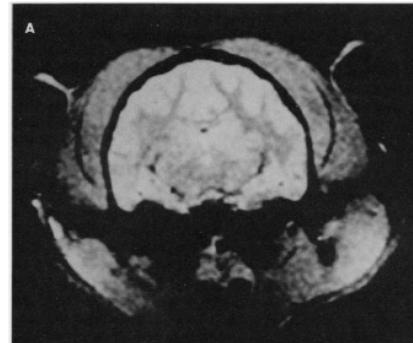
Gadolinium perfusion



Diffusion



magnetization transfer



NAA choline

creatine lactate

Pre 1992...

L. Pauling, C. D. Coryell, *Proc. Natl. Acad. Sci. USA* 22, 210-216, 1936.

K.R. Thulborn, J. C. Waterton, et al., *Biochim. Biophys. Acta.* 714: 265-270, 1982.

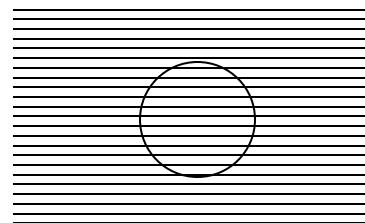
S. Ogawa, T. M. Lee, A. R. Kay, D. W. Tank, *Proc. Natl. Acad. Sci. USA* 87, 9868-9872, 1990.

Turner, R., Lebihan, D., Moonen, C. T. W., Despres, D. & Frank, J. *Magnetic Resonance in Medicine*, 22, 159-166, 1991.

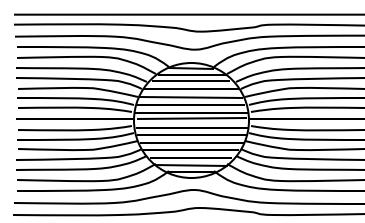


red blood cells

oxygenated



deoxygenated



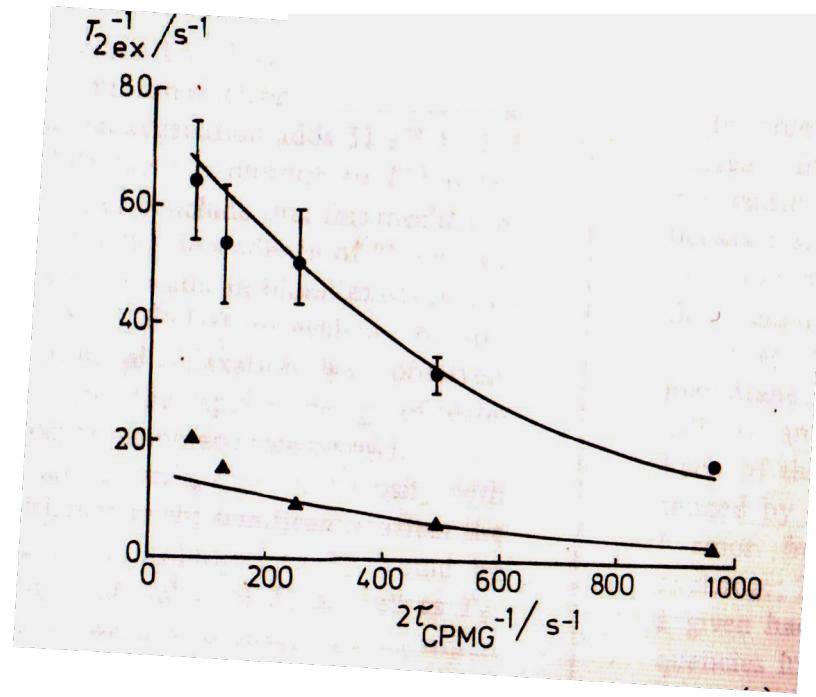
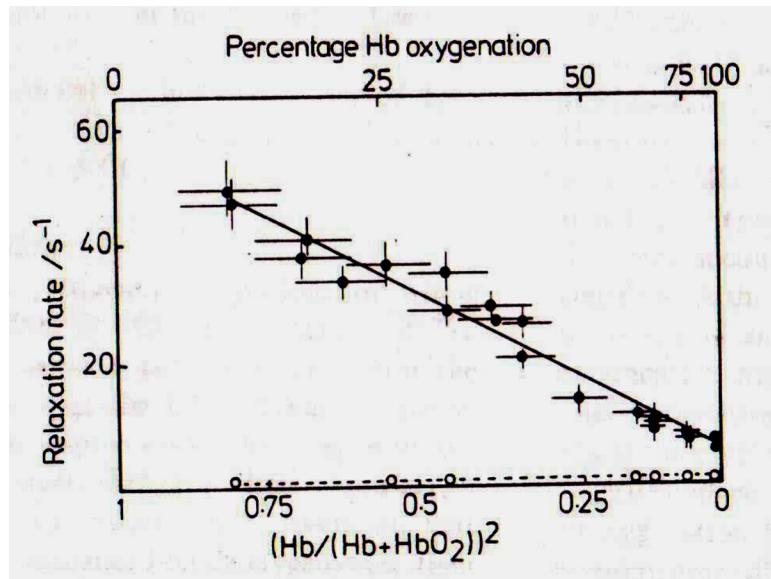
BBA 20122

OXYGENATION DEPENDENCE OF THE TRANSVERSE RELAXATION TIME OF WATER PROTONS IN WHOLE BLOOD AT HIGH FIELD

KEITH R. THULBORN, JOHN C. WATERTON *, PAUL M. MATTHEWS and GEORGE K. RADDA

Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU (U.K.)

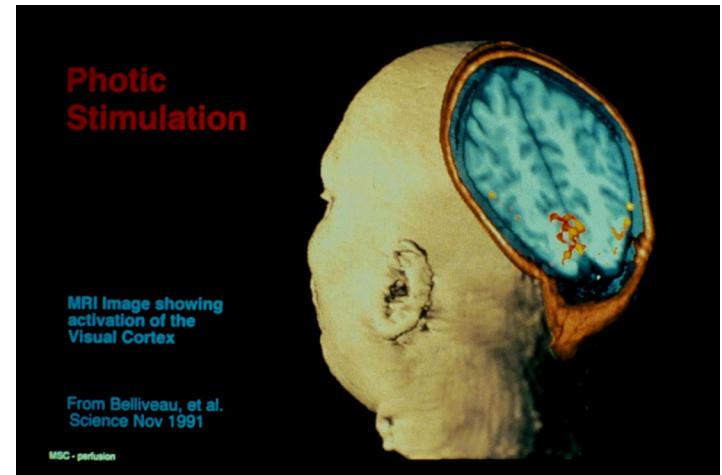
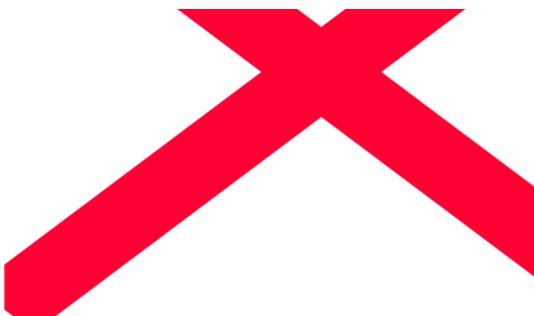
(Received August 4th, 1981)



Pre 1992...

Blood Volume Imaging

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



1992...BOLD

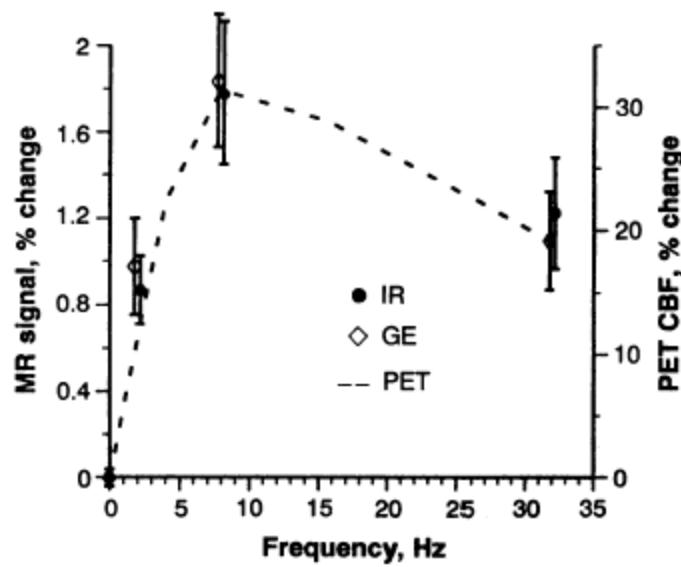
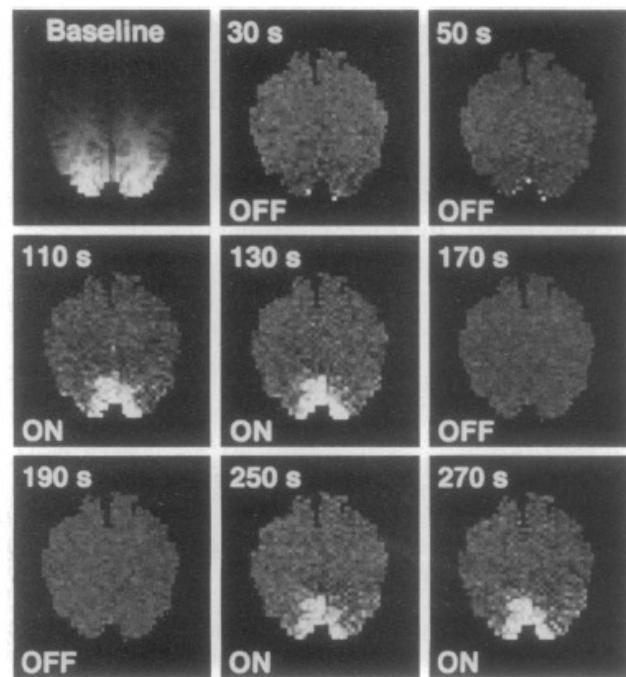
K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

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.

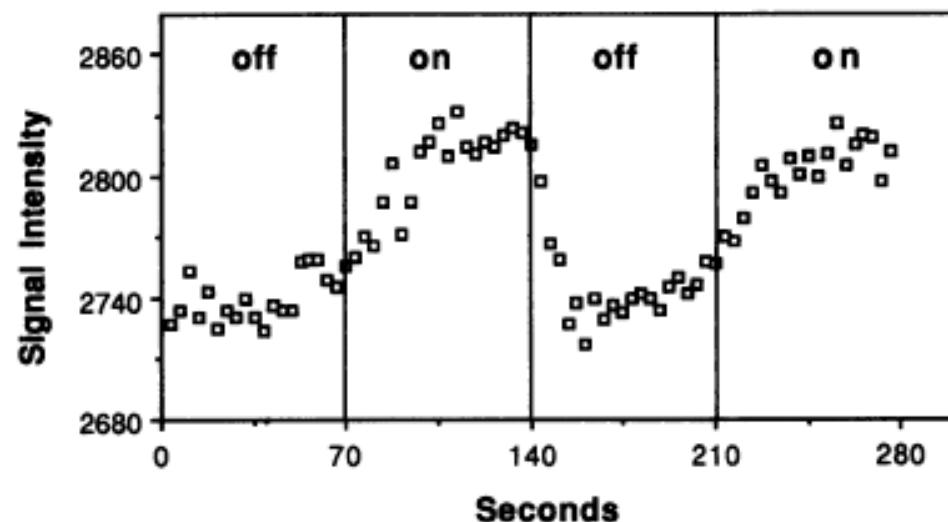
P. A. Bandettini, et al., (1992) "Time course EPI of human brain function during task activation." Magn. Reson. Med 25, 390-397.

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.

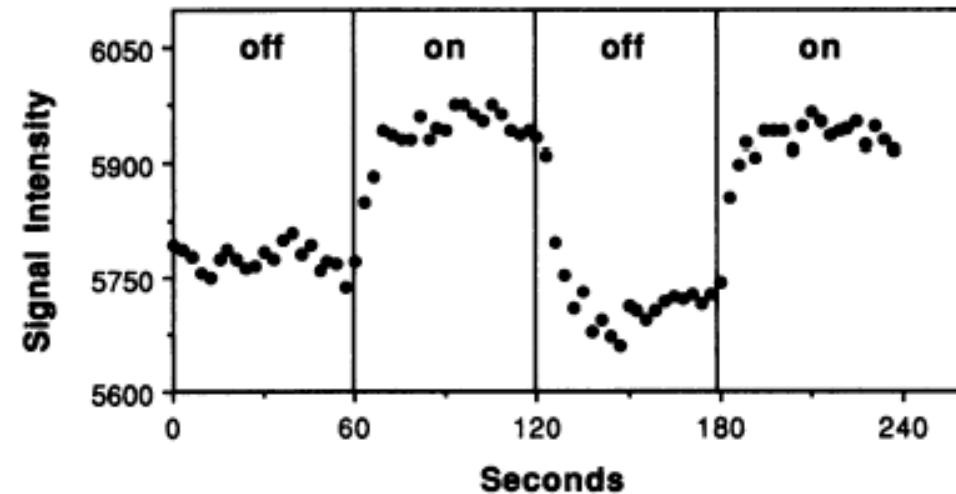
Frahm, J., et al (1992) "Dynamic MR Imaging of Human Brain Oxygenation During Rest and Photic-Stimulation." Journal of Magnetic Resonance Imaging, 2, 501-505.



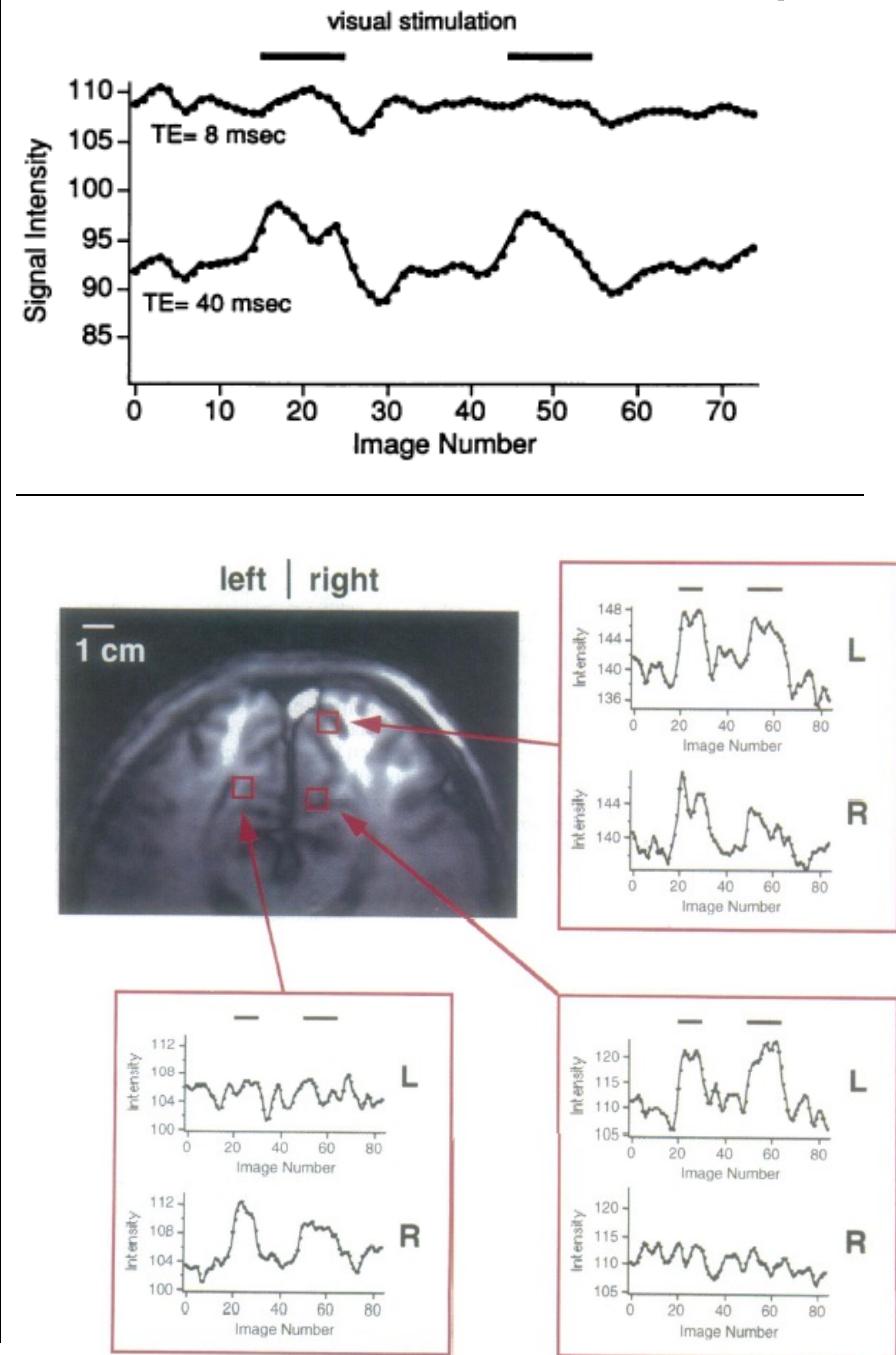
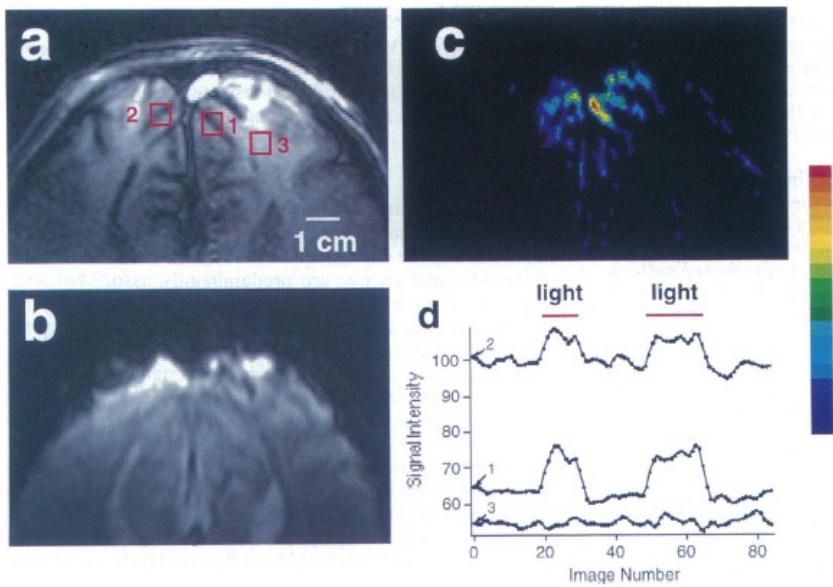
Photic Stimulation -- IR Images



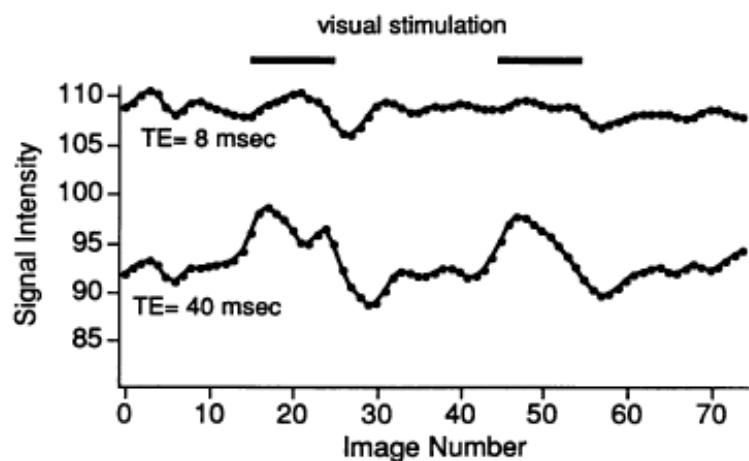
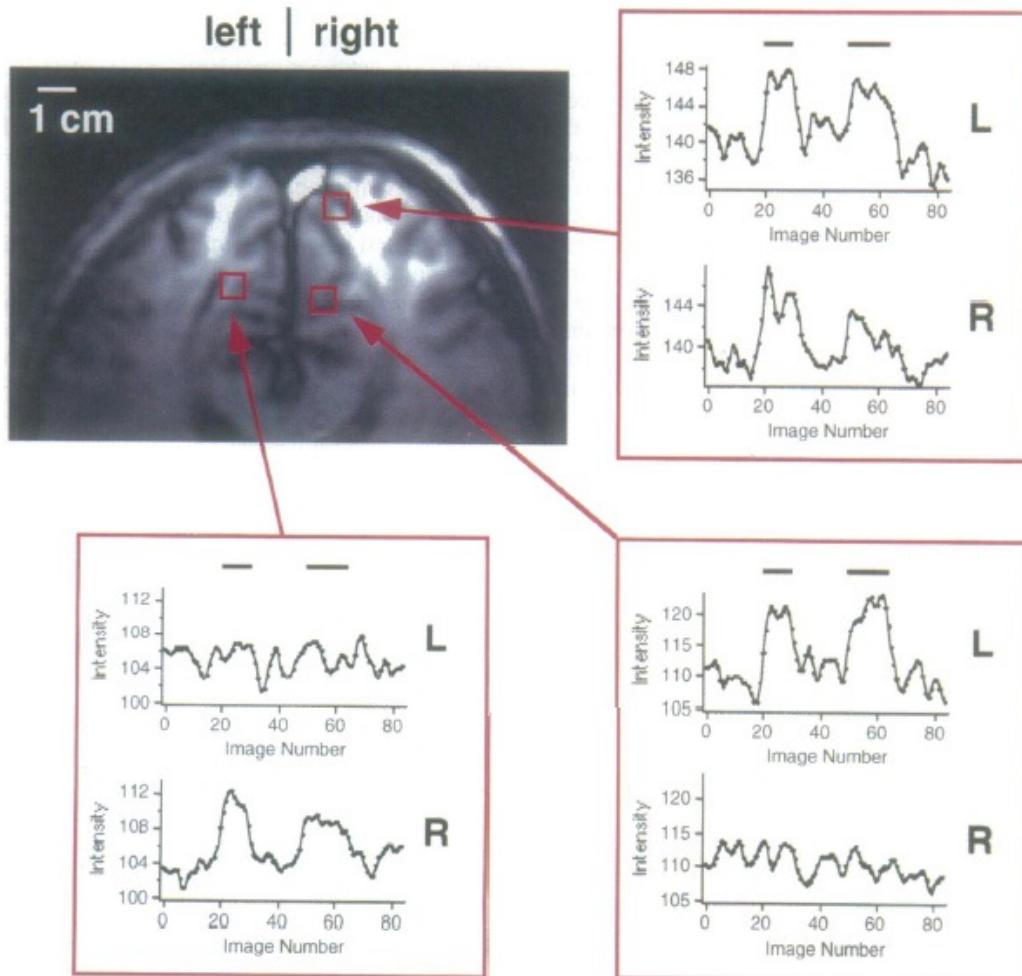
Photic Stimulation -- GE Images



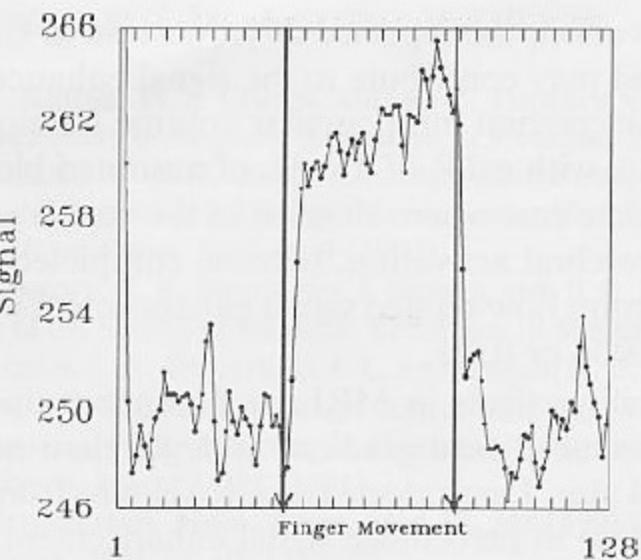
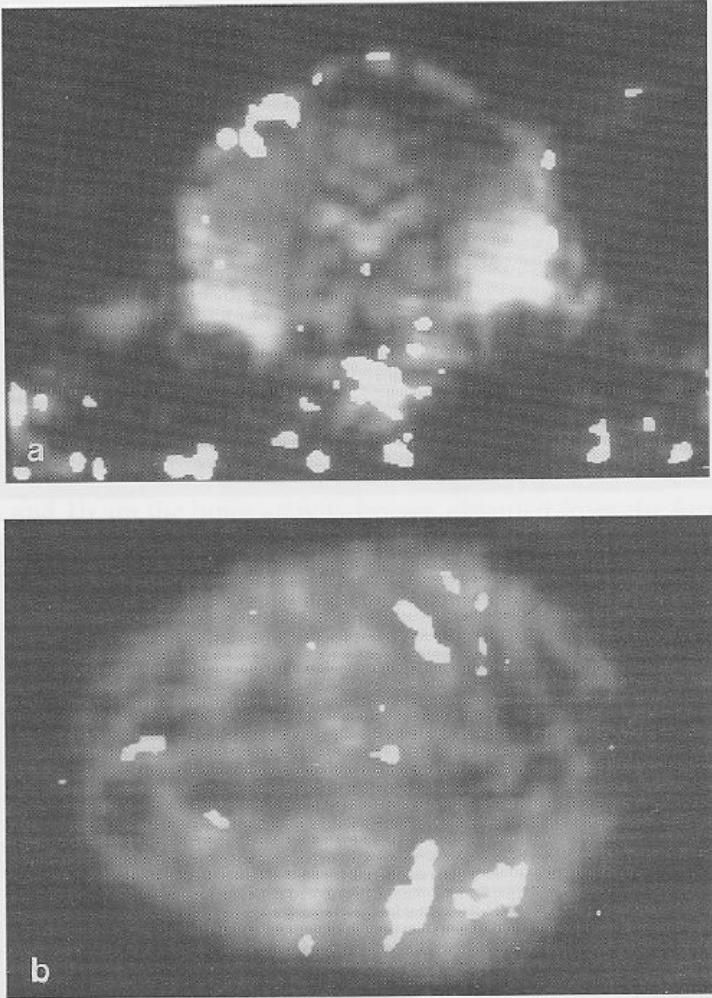
Ogawa et al.

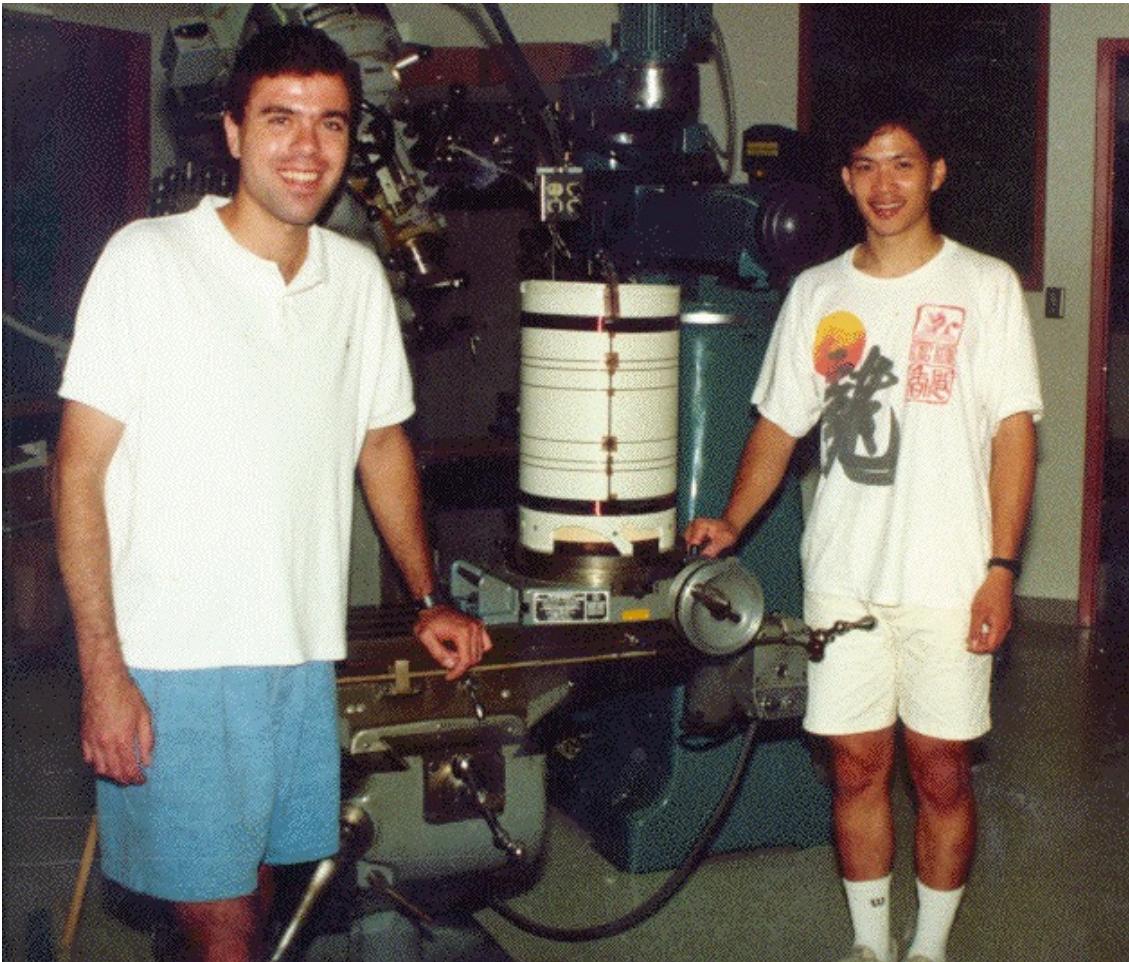


Ogawa et al.



Bandettini et al.



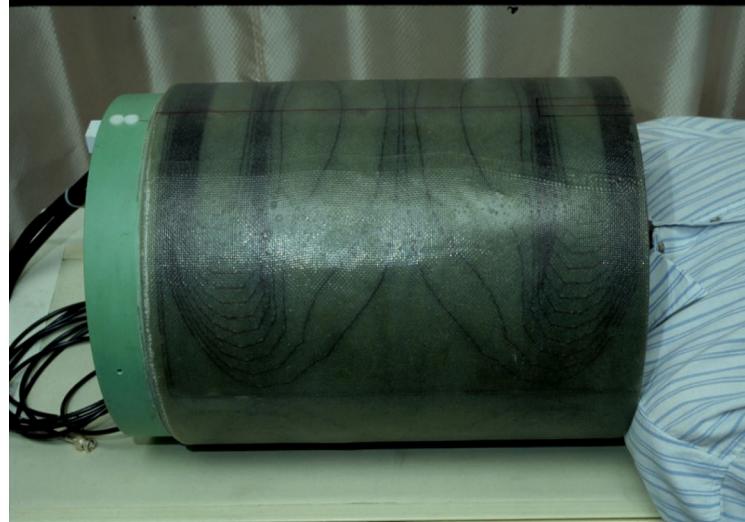


August, 1991

1991-1992

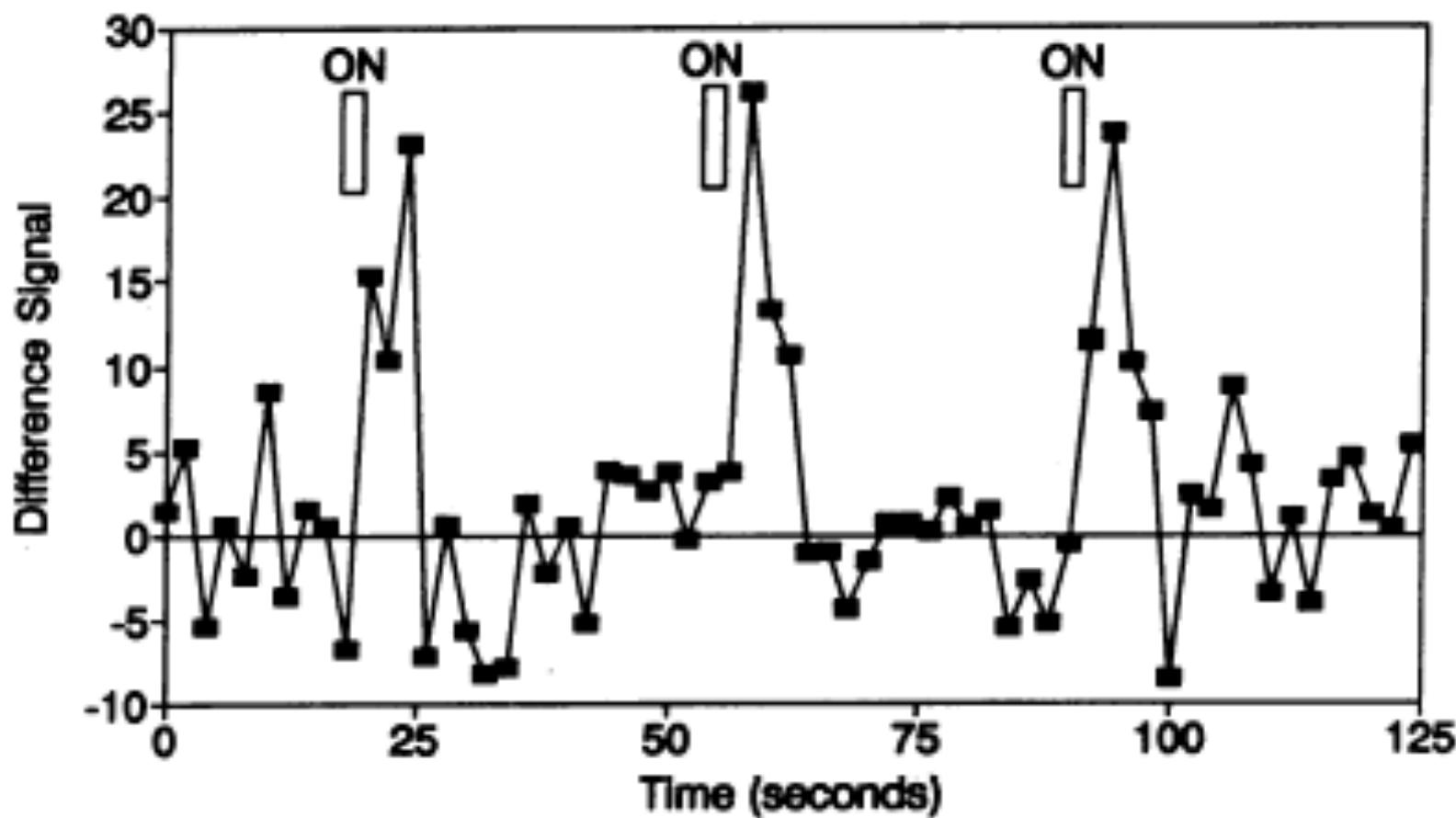


1992-1999





1991



1992...Perfusion using Arterial Spin Labeling

Proc. Natl. Acad. Sci. USA
Vol. 89, pp. 212–216, January 1992
Biophysics

Magnetic resonance imaging of perfusion using spin inversion of arterial water

(cerebral blood flow/adiabatic fast passage/hypercarbia/rat brain/cold injury)

DONALD S. WILLIAMS*, JOHN A. DETRE†‡, JOHN S. LEIGH†, AND ALAN P. KORETSKY*§

*Pittsburgh Nuclear Magnetic Resonance Center for Biomedical Research, and §Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA 15213; and †Metabolic Magnetic Resonance Research Center, Department of Radiology, and ‡Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104

Communicated by Mildred Cohn, September 19, 1991

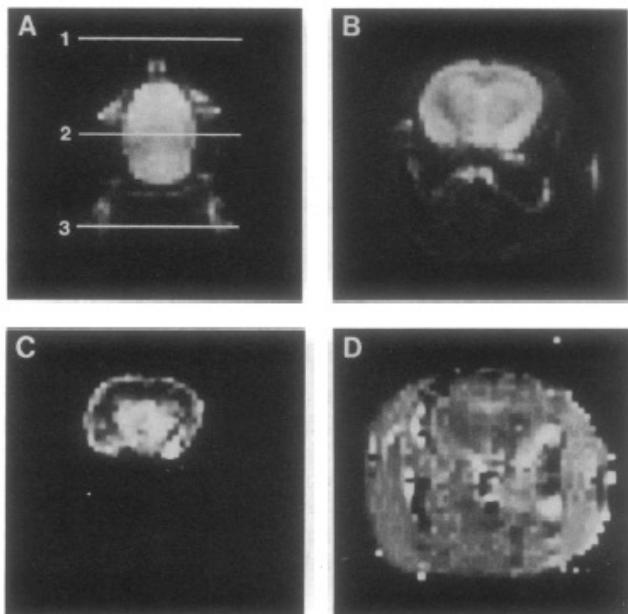


FIG. 2. (A) Coronal image of a rat head. The resonance planes for radiofrequency used for spin inversion by AFP for control and inversion images are indicated by 1 and 3, respectively, and plane 2 is the detection plane. (B) Control transverse image from the detection plane (plane 2 in A). (C) Difference image between control and inversion images. (D) $T_{1\text{app}}$ image.

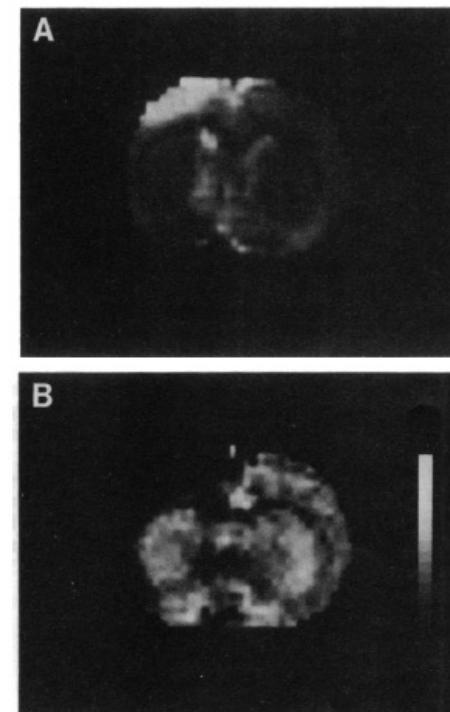
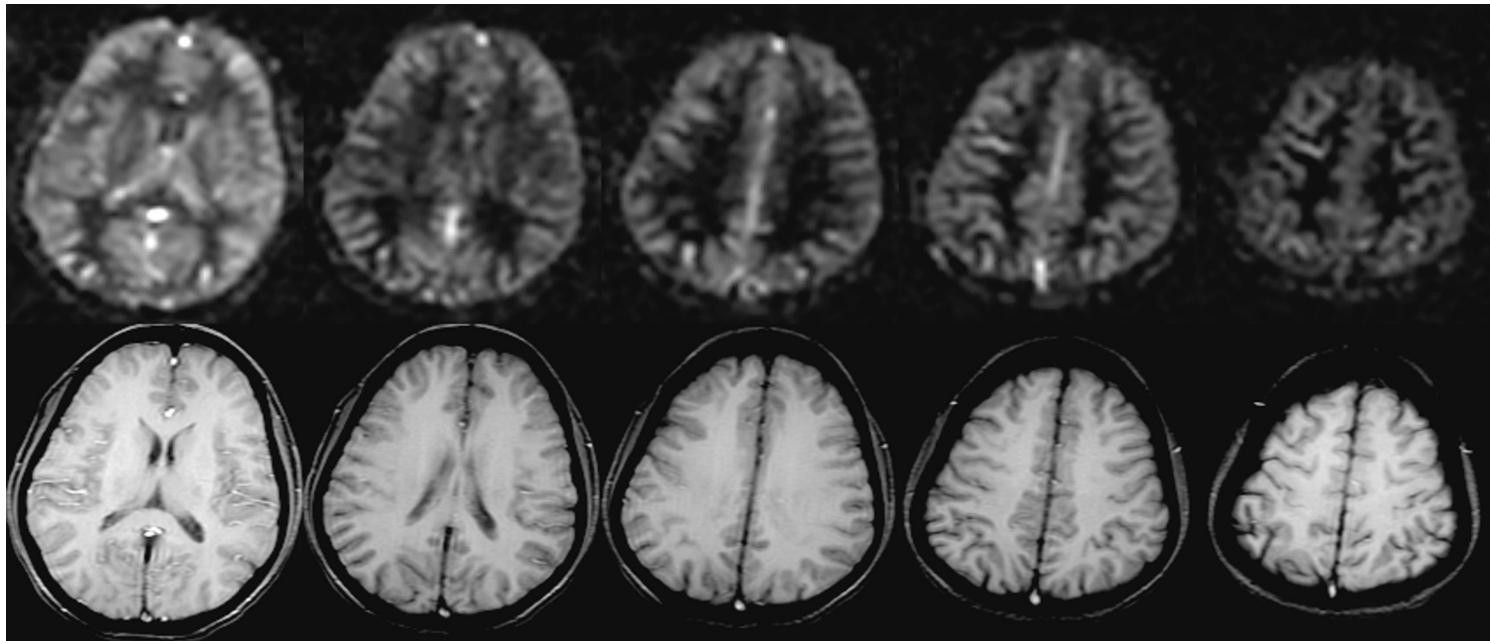


FIG. 5. Comparison of conventional MRI and perfusion imaging of a rat brain subjected to a regional cold injury. (A) Conventional T_2 -weighted image ($TE = 60$ ms, $TR = 2$ s). The injured region shows up as hyperintensity due to a longer T_2 . (B) Perfusion image of the same slice. The grey scale is from 0 to $6 \text{ ml}\cdot\text{g}^{-1}\cdot\text{min}^{-1}$. The injured region is dark due to low flow.



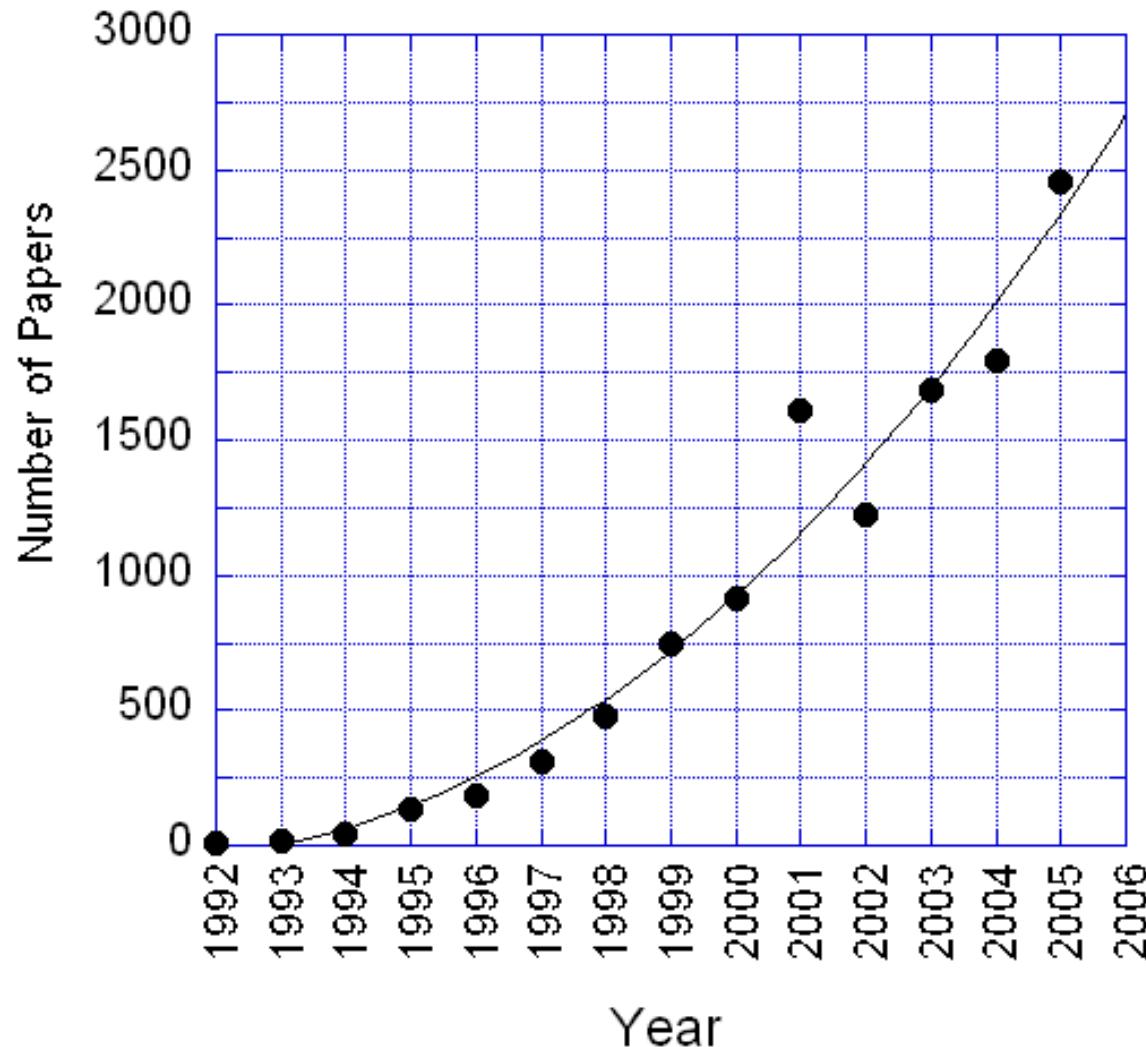
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." *Proc. Natl. Acad. Sci. USA* 89, 212-216.

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 (EPICSTAR)." *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.

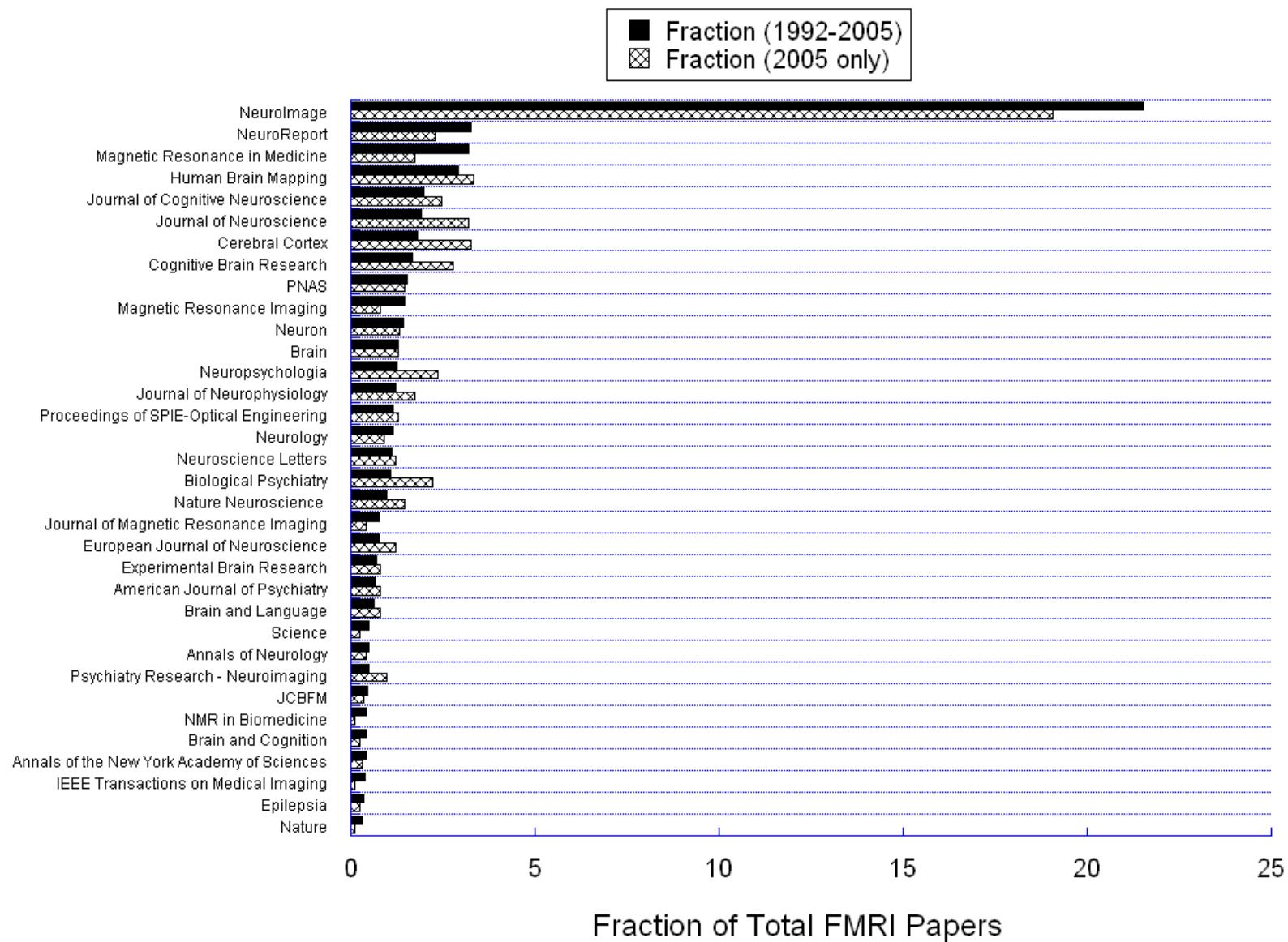
Kwong, K. K. et al. (1995) "MR perfusion studies with T1-weighted echo planar imaging." *Magn. Reson. Med.* 34, 878-887.

fMRI Papers Published per Year

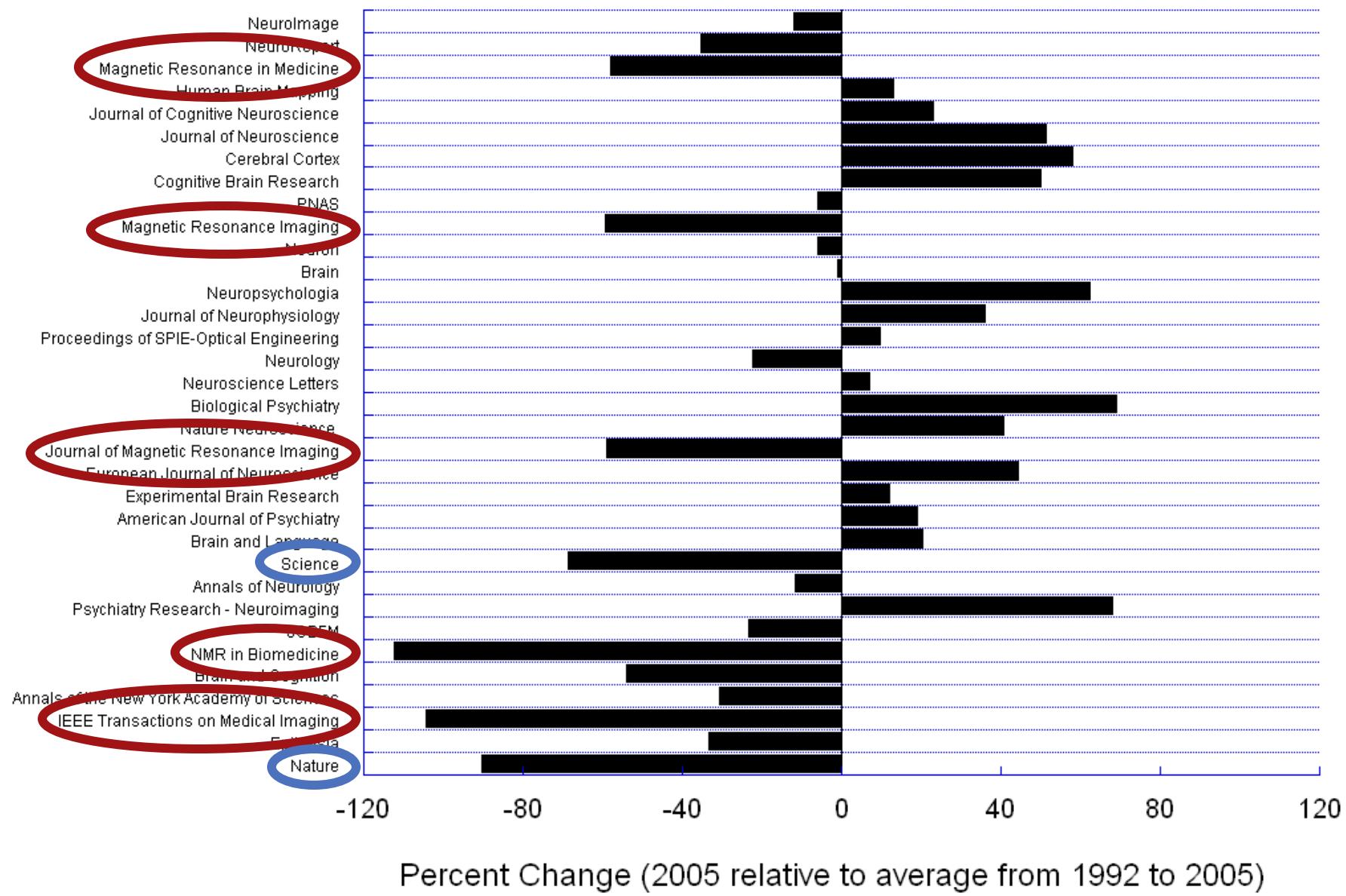


"fMRI" or "functional MRI"

Breakdown of fMRI papers by Journal



Percent Change in fMRI Publications of 2005 relative to Average (1992 - 2005) for Each Journal



Technology

Magnet
RF Coils
Pulse Sequences

Methodology

Paradigm Design
Pre and Post Processing
Subject Interface
Data Display and Comparison

Increases
Decreases
Dynamics
Locations

Neuroscience
Physiology
Genetics
Practical Clinical

Interpretation

Applications

Technology

8 to 96 Channel Coil Arrays
3 to 9.4 Tesla Field Strength
Sub-millimeter resolution
Novel Contrasts

Methodology

Calibration
Multi-variate mapping/classification
Multi-modal integration
Free Behavior task design
Resting state fluctuation assessment

Fluctuations
Dynamics
Cross - modal comparison

Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

Interpretation

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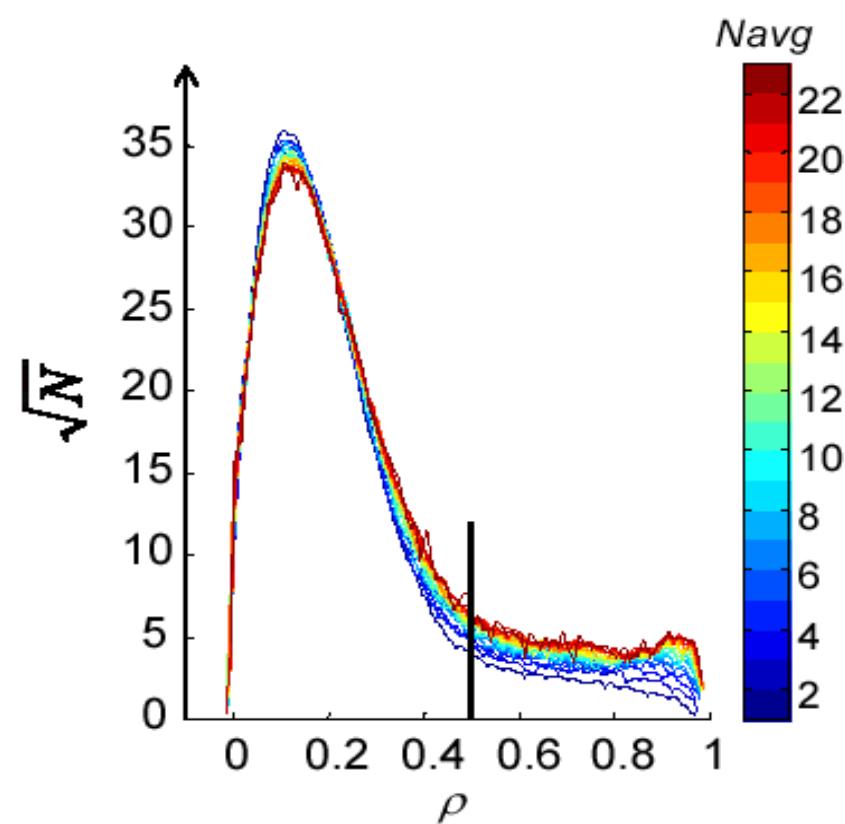
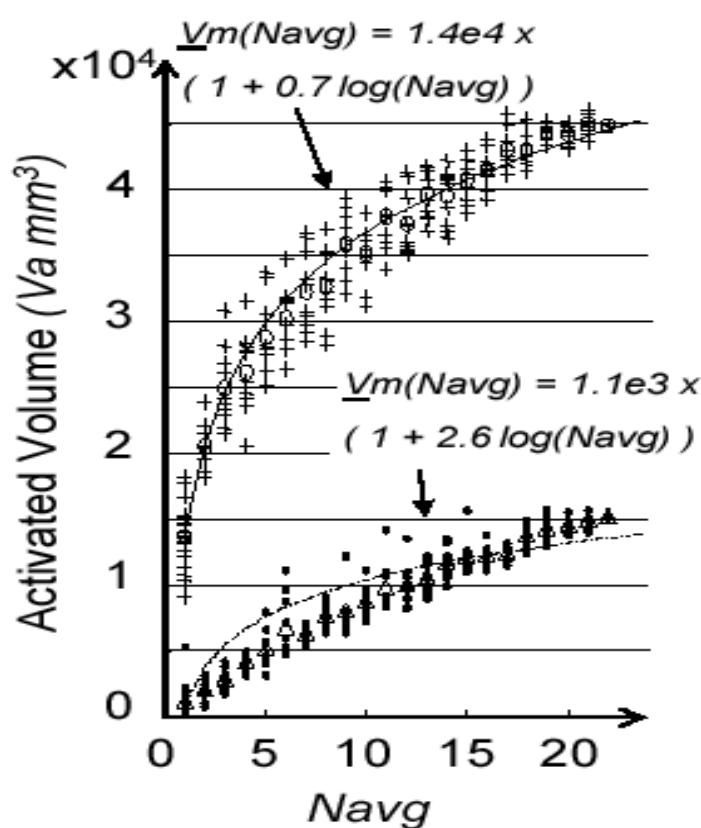
Fluctuations
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Cross - modal comparison

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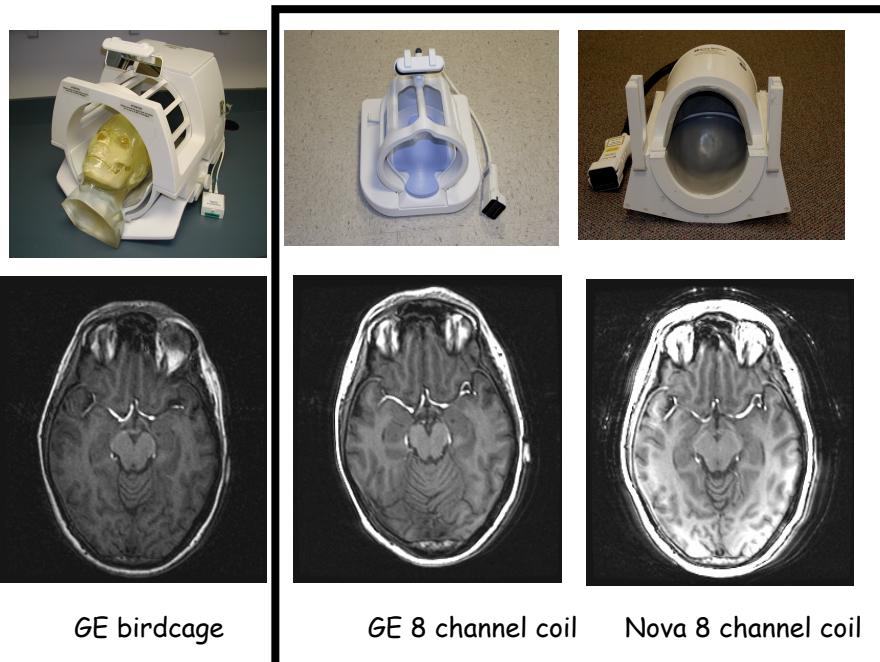
Technology



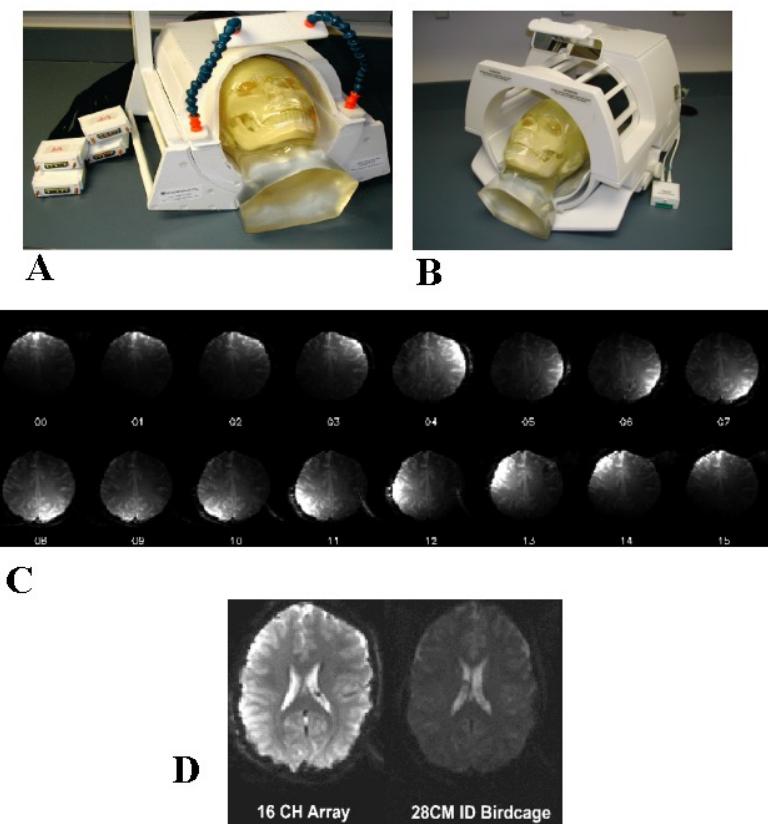
Z. S. Saad, K. M. Ropella, E. A. DeYoe, P. A. Bandettini, The spatial extent of the BOLD response. NeuroImage, 19: 132-144, (2003)

Technology

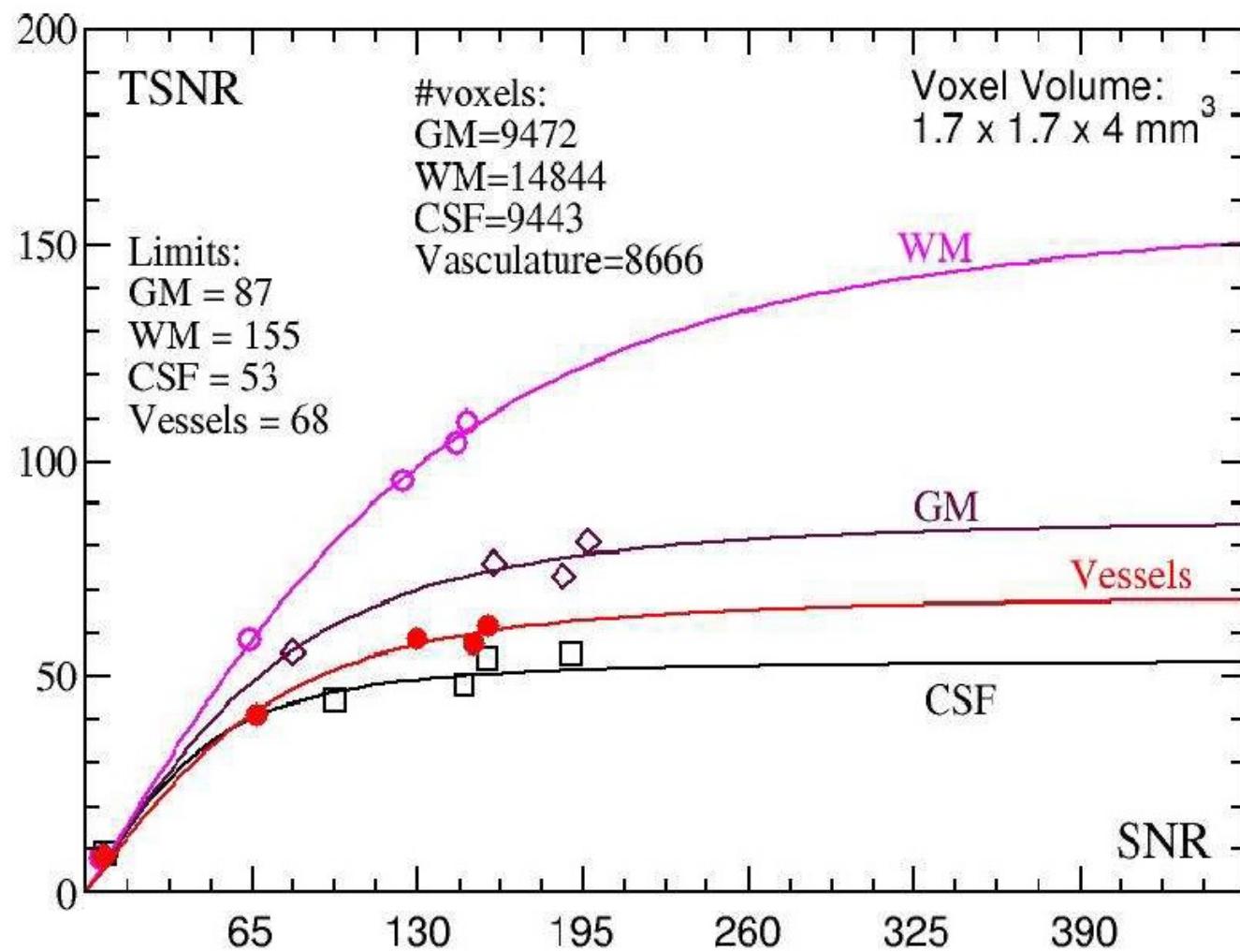
8 channel parallel receiver coil



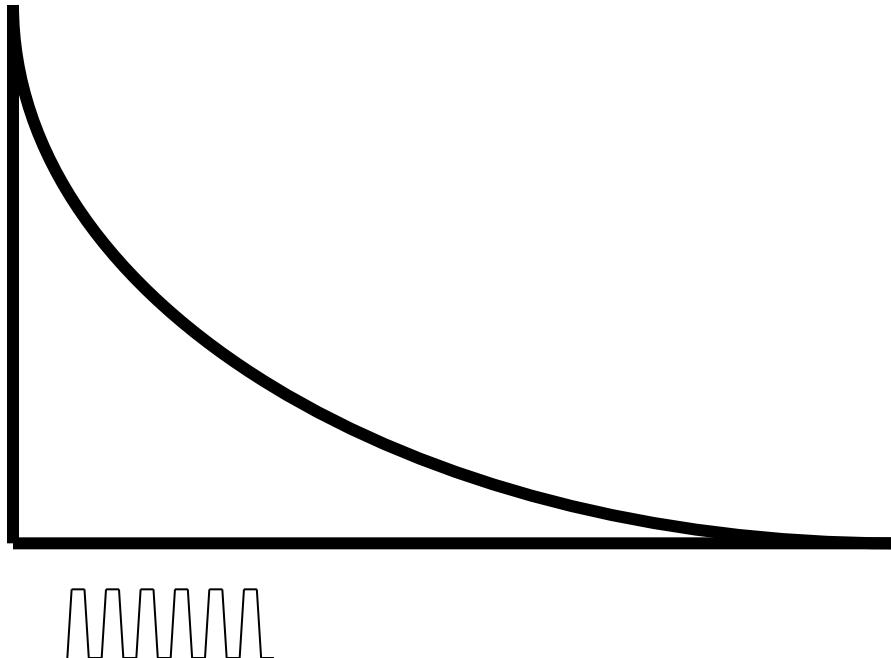
16 channel parallel receiver coil



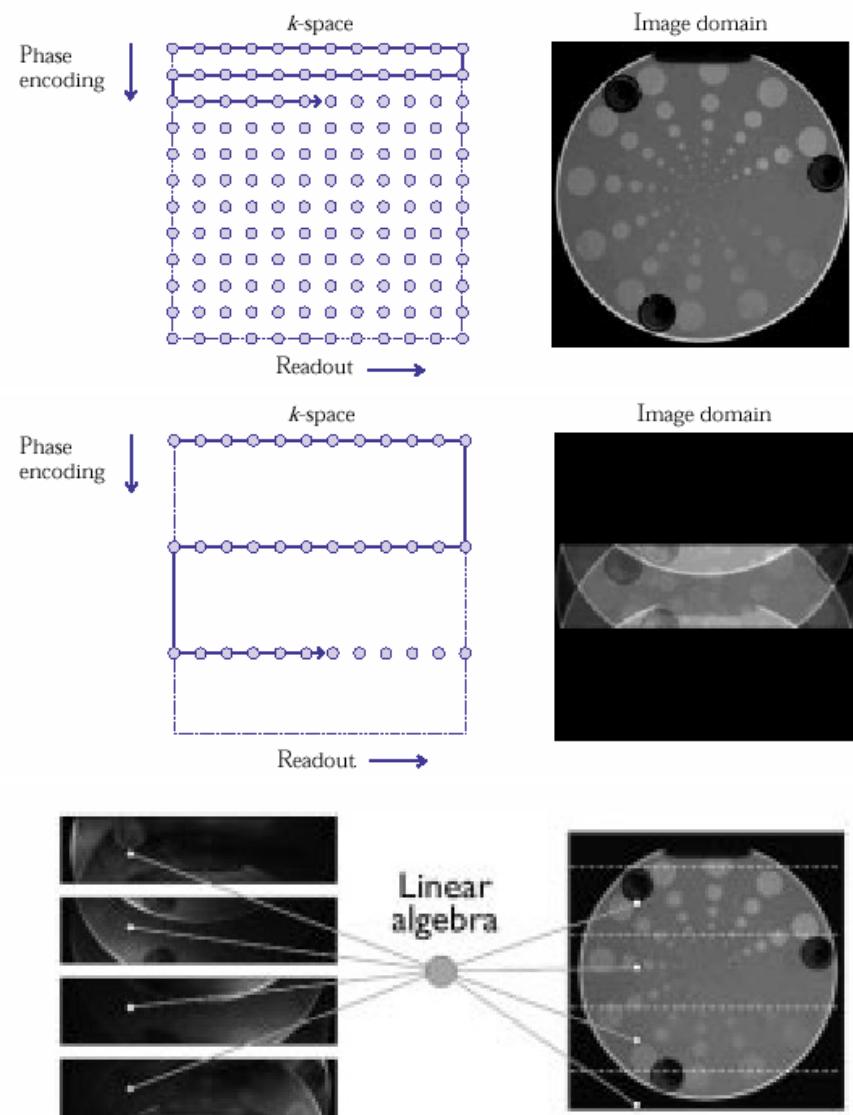
Technology



Technology

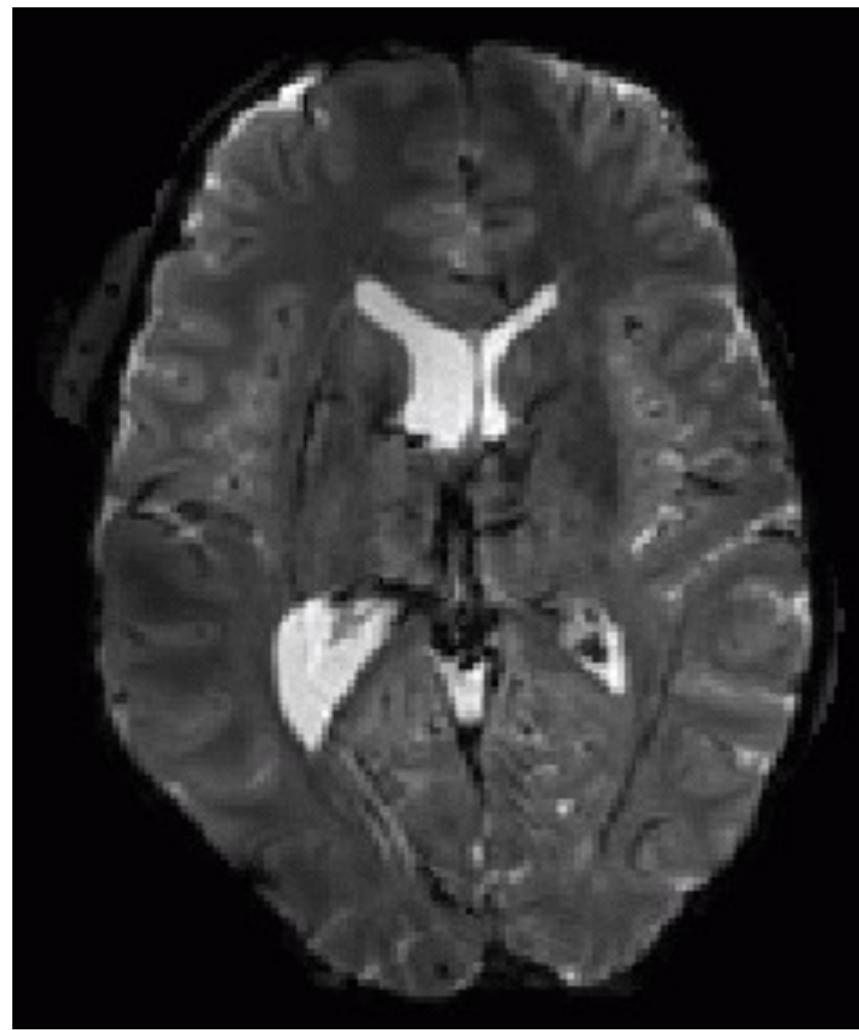


≈ 5 to 30 ms



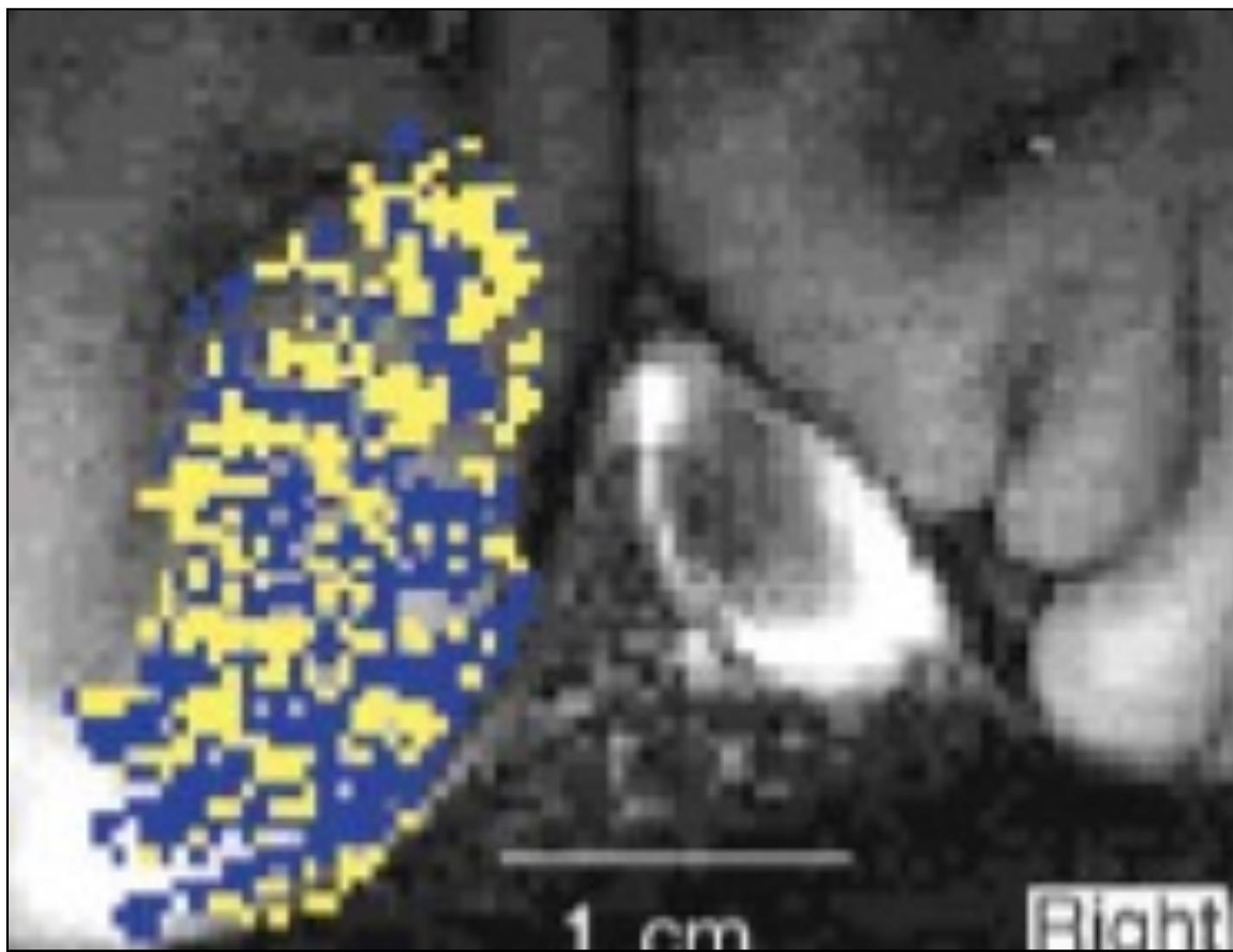
Pruessmann, et al.

Technology



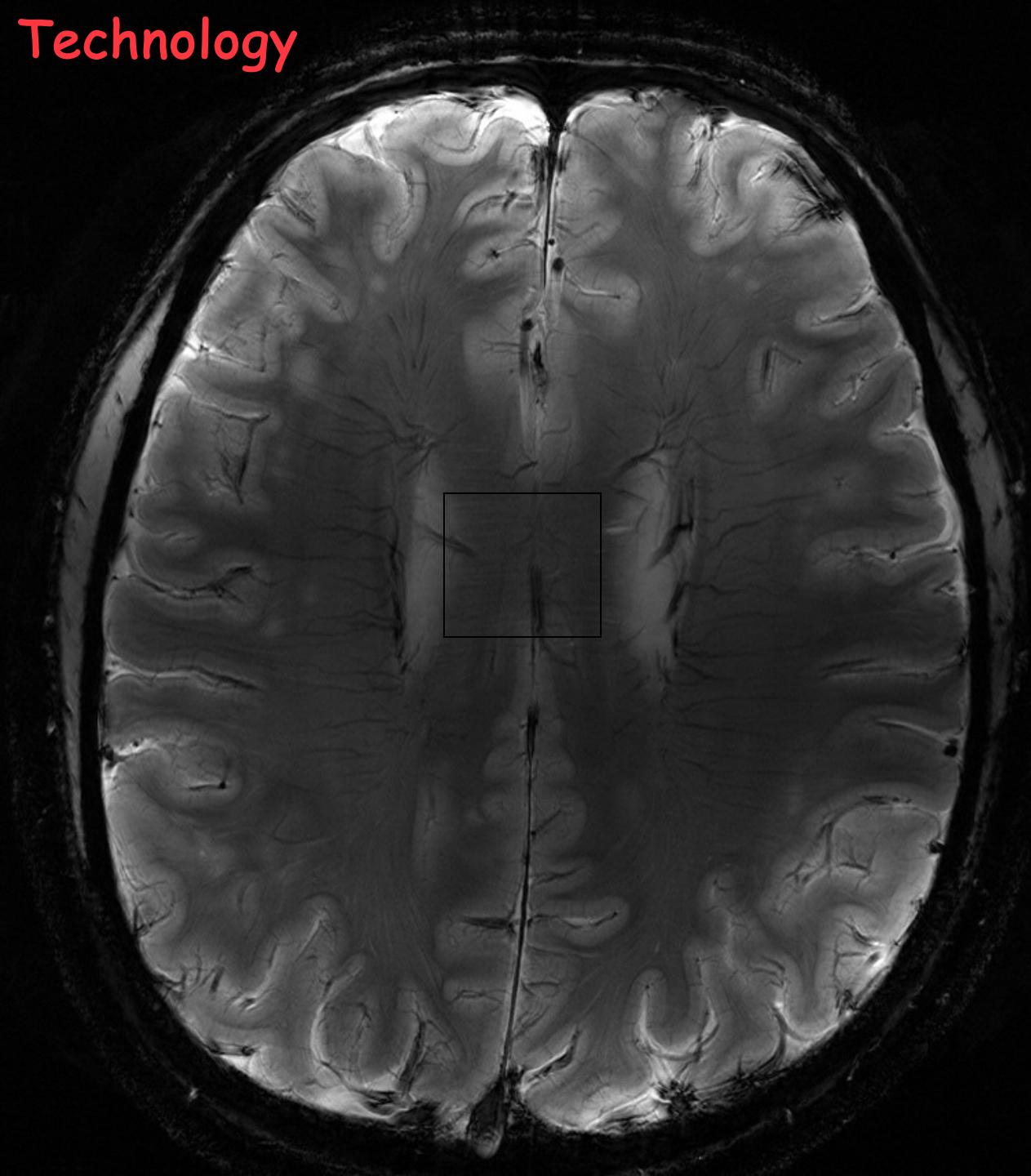
3T single-shot SENSE EPI using 16 channels: $1.25 \times 1.25 \times 2\text{mm}$

Technology



Cheng, et al. (2001) Neuron, 32:359-374

Technology

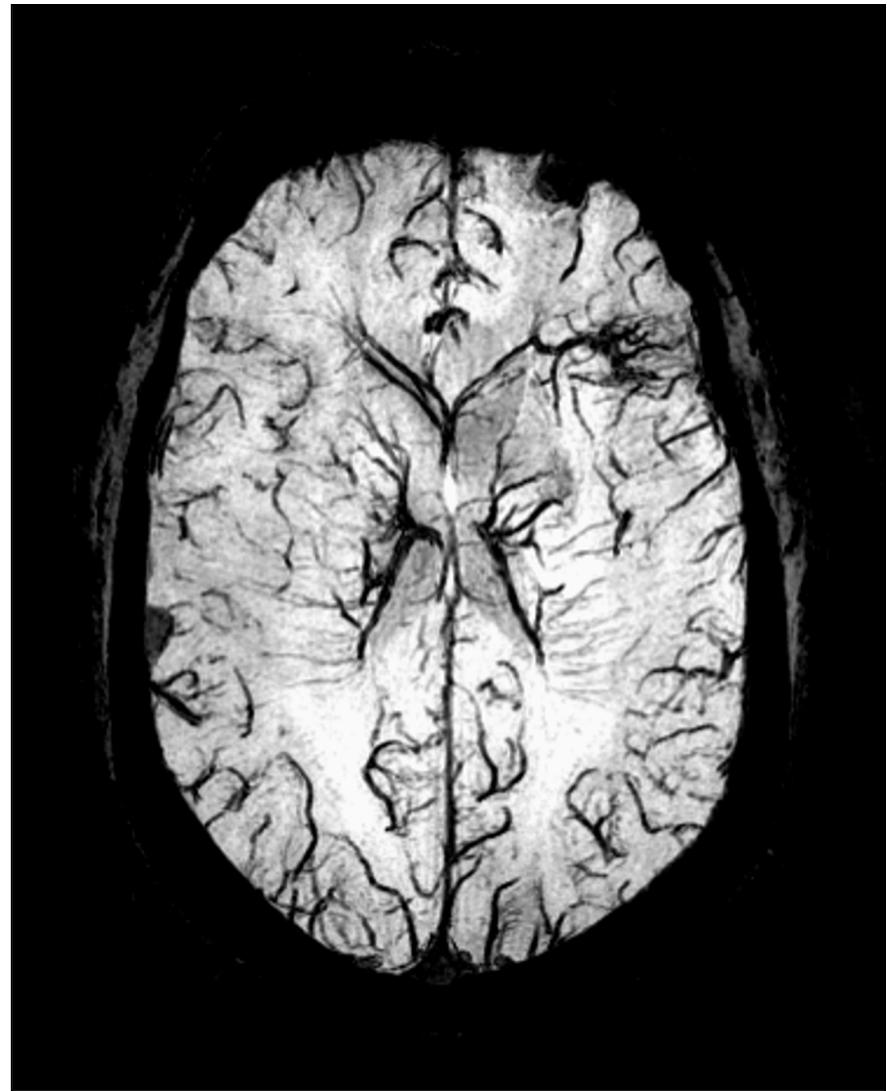
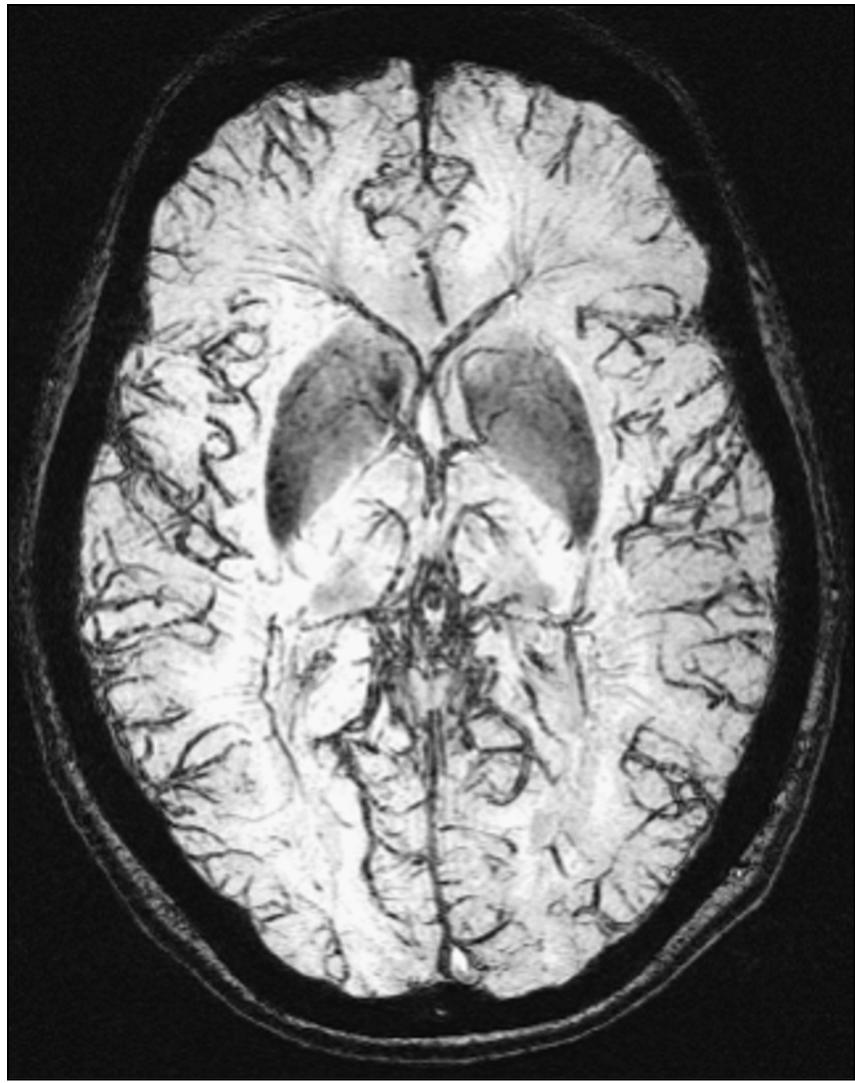


fiber bundles?

Courtesy Tie-Qiang
Li, NINDS

Technology

BOLD effect "SWI" highlights veins: 3 Tesla



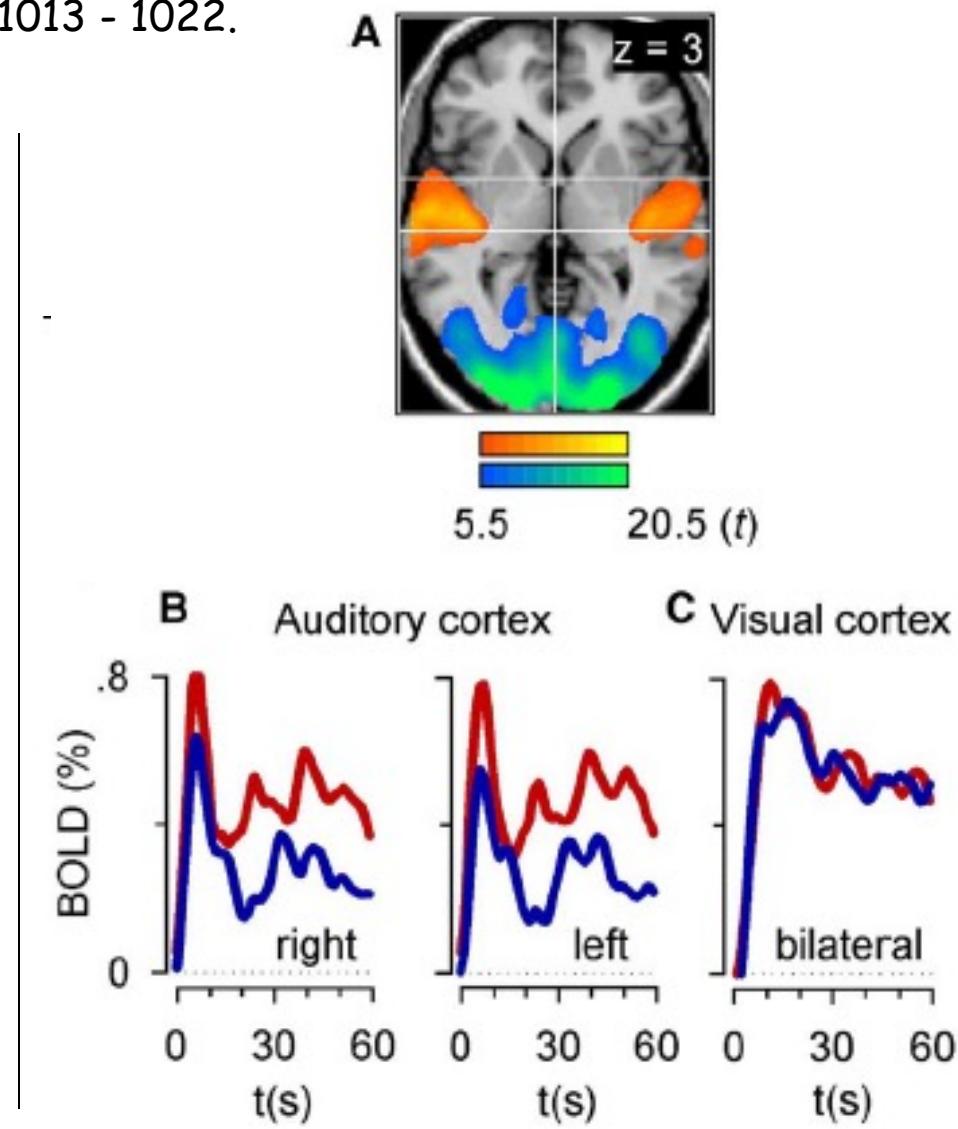
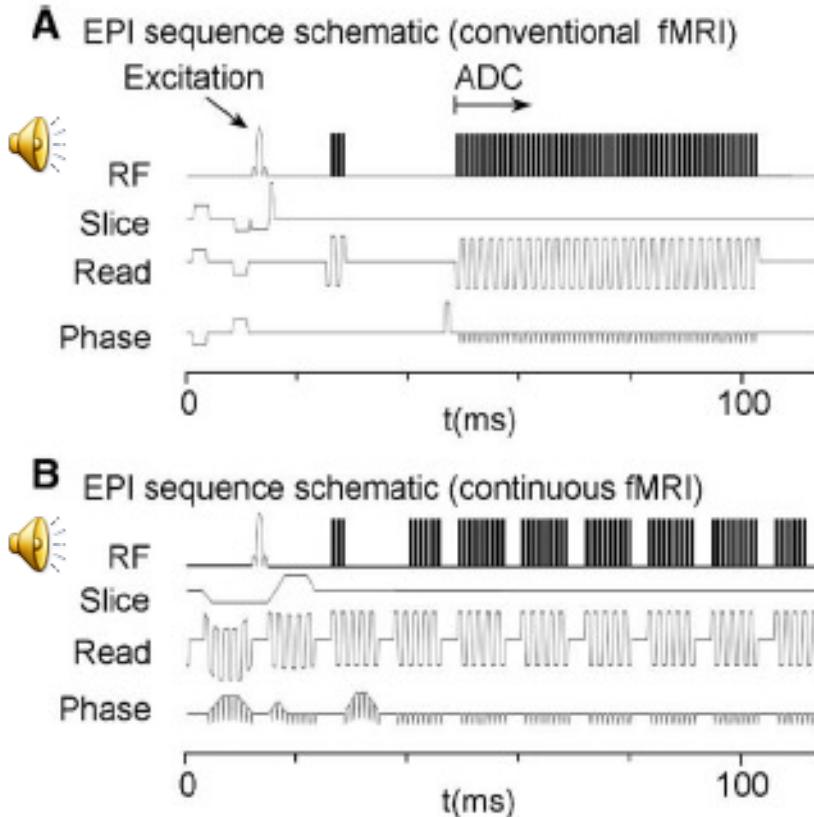
Bove-Bettis, et al (2004), SMRT

fMRI Contrast

- Volume (gadolinium)
- BOLD (GE and SE)
- Perfusion (ASL)
- ΔCMRO_2
- ΔVolume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

Technology

E. Seifritz et al, Enhancing BOLD response in the auditory system by neurophysiologically tuned fMRI sequence, NeuroImage, 29 (2006) 1013 - 1022.



Technology

8 to 96 Channel Coil Arrays
3 to 9.4 Tesla Field Strength
Sub-millimeter resolution
Novel Contrasts

Methodology

Calibration
Multi-variate mapping/classification
Multi-modal integration
Free Behavior task design
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Dynamics
Cross - modal comparison

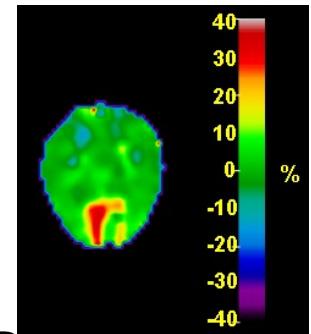
Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

Interpretation

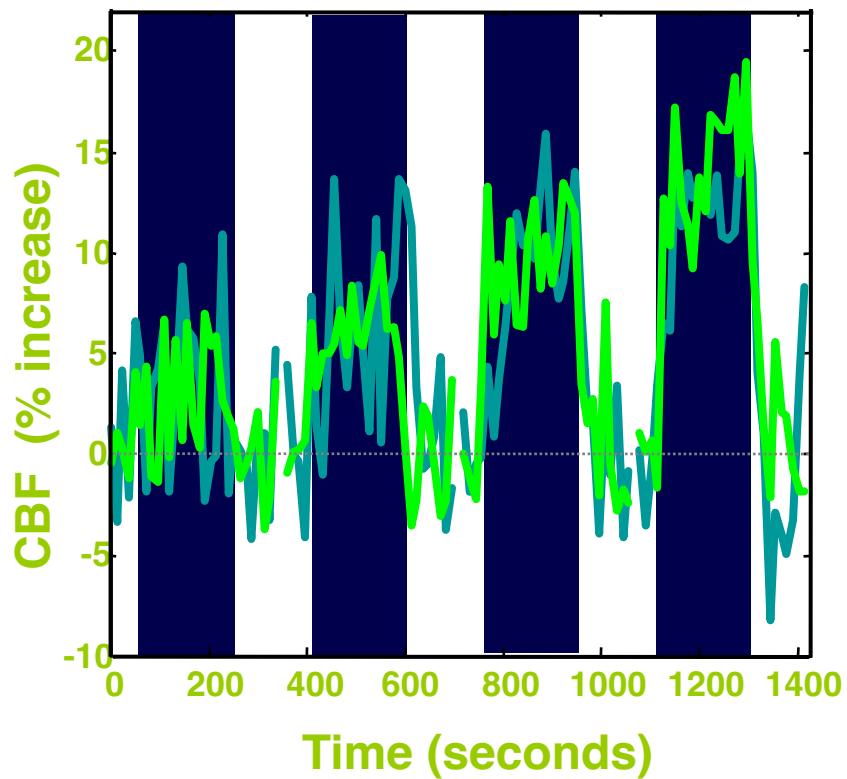
Applications

Methodology

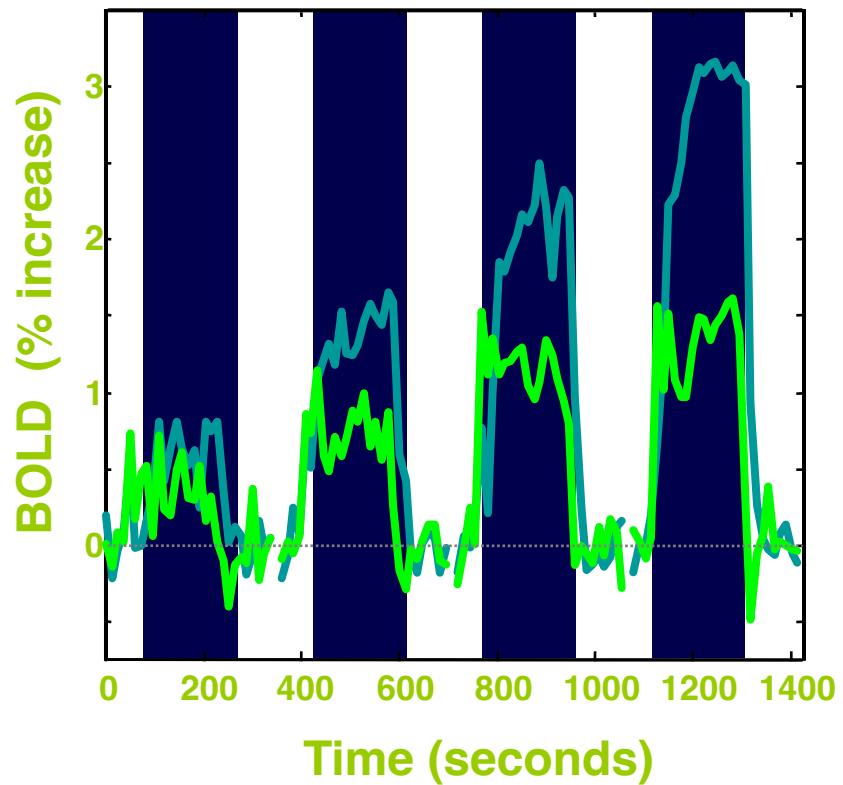
R. Hoge, et al. Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex, PNAS, 96, 9403-9408



CBF



BOLD



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

Methodology



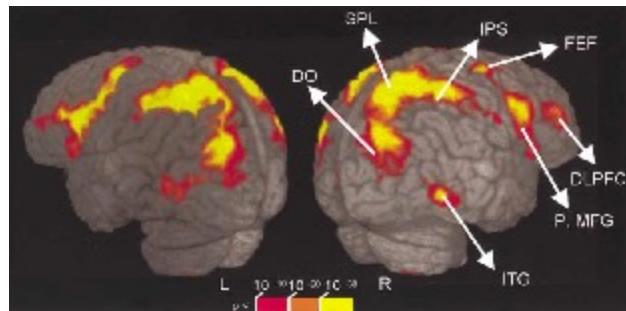
Mapping \leftrightarrow "Reading"

Methodology

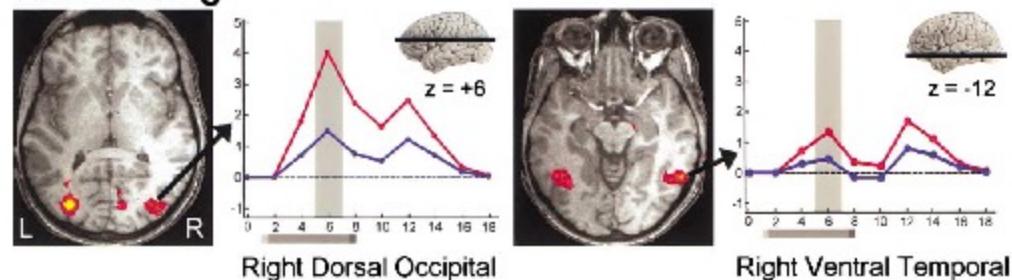
Neuron, Vol. 35, 975–987, August 29, 2002, Copyright ©2002 by Cell Press

Neural Correlates of Visual Working Memory: fMRI Amplitude Predicts Task Performance

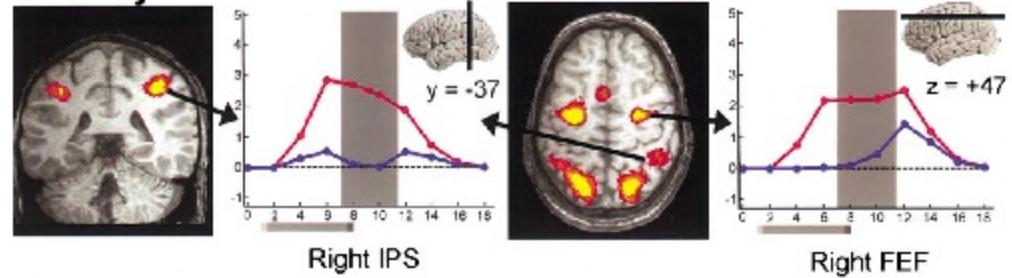
Luiz Pessoa,¹ Eva Gutierrez, Peter A. Bandettini,
and Leslie G. Ungerleider
Laboratory of Brain and Cognition
National Institute of Mental Health
National Institutes of Health
Bethesda, Maryland 20892



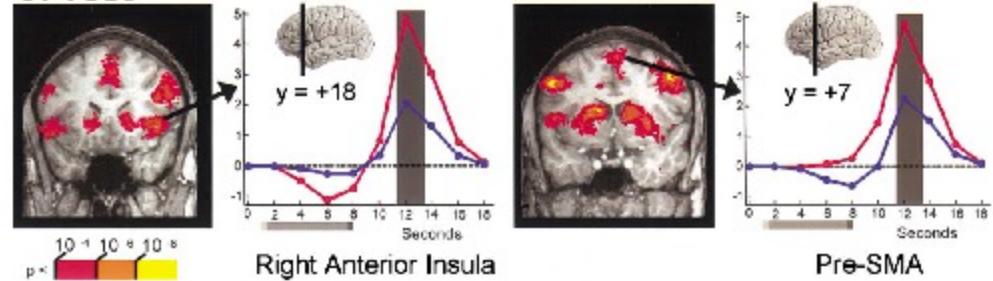
A. Encoding



B. Delay



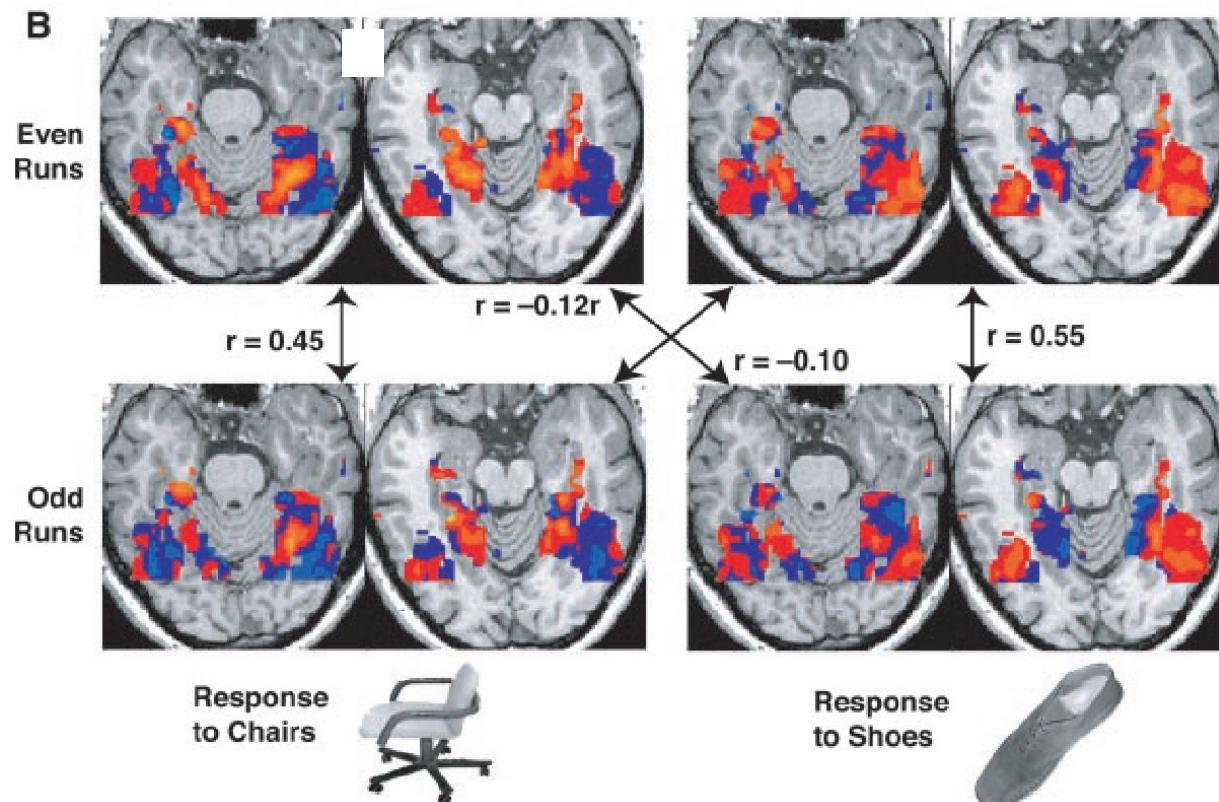
C. Test



Methodology

Ventral temporal category representations

Object categories are associated with distributed representations in ventral temporal cortex



Haxby et al. 2001

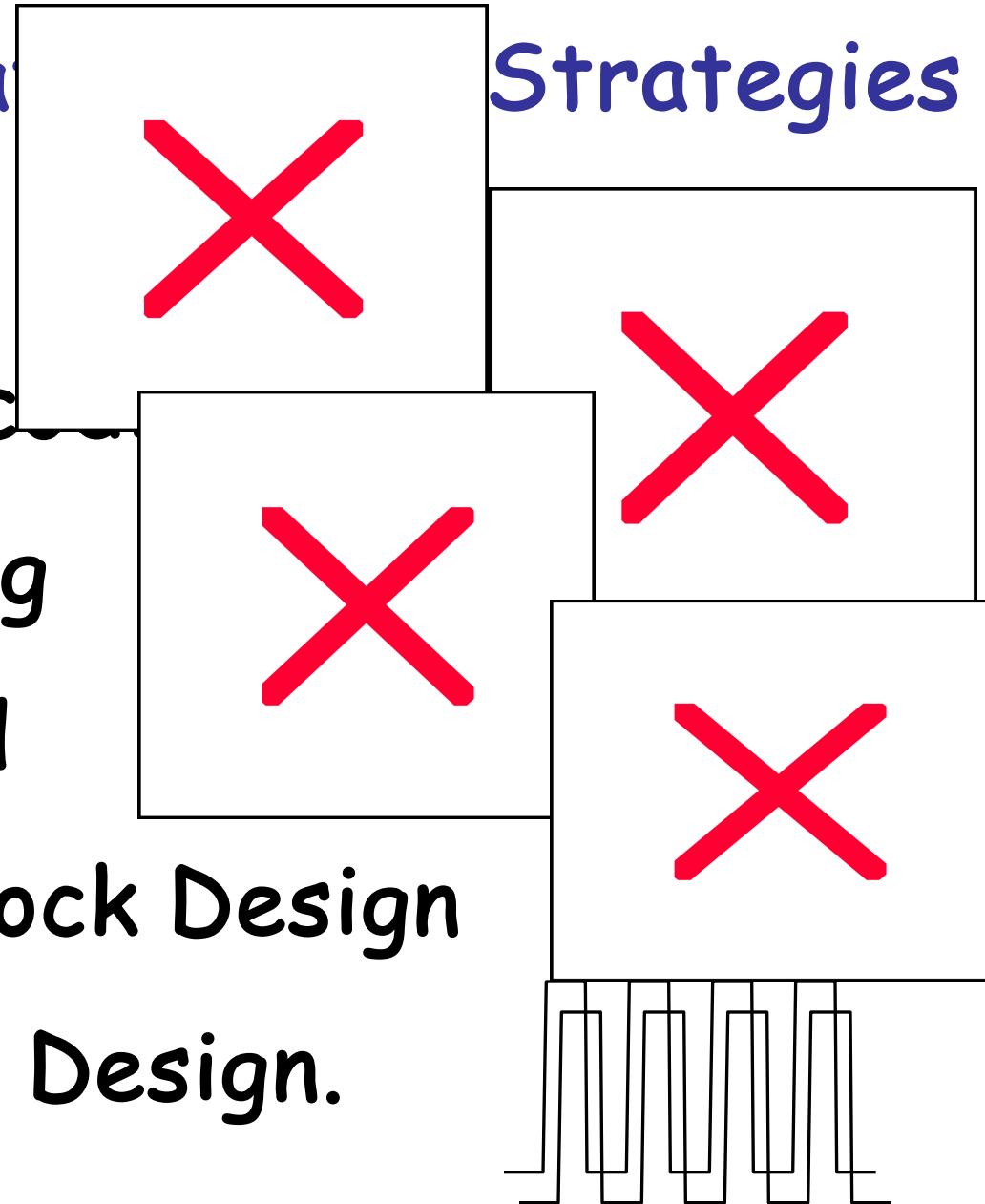
Pattern-recognition analysis of fMRI activity patterns

- Haxby et al. (2001)
- Cox & Savoy (2003)
- Carlson et al. (2003)
- Kamitani & Tong (2005)
- Haynes & Rees (2005)
- Kriegeskorte et al (2006)

Methodology

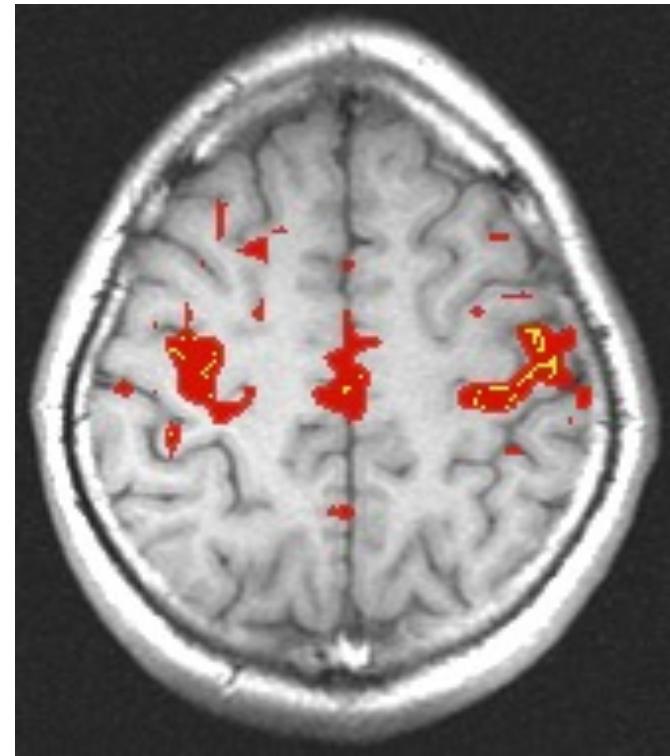
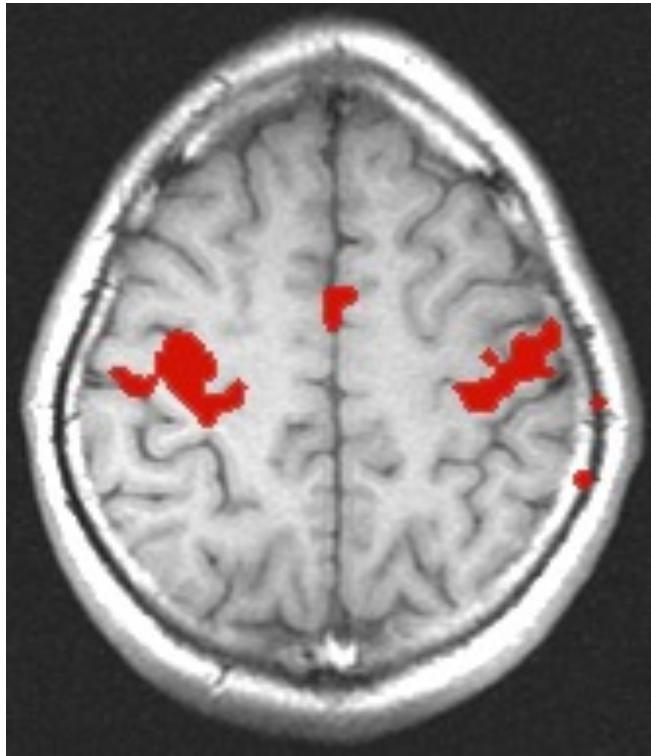
Neuronal Activation

1. Block Design
2. Frequency Encoding
3. Phase Encoding
4. Event-Related
5. Orthogonal Block Design
6. Free Behavior Design.



Methodology

Resting State Correlations



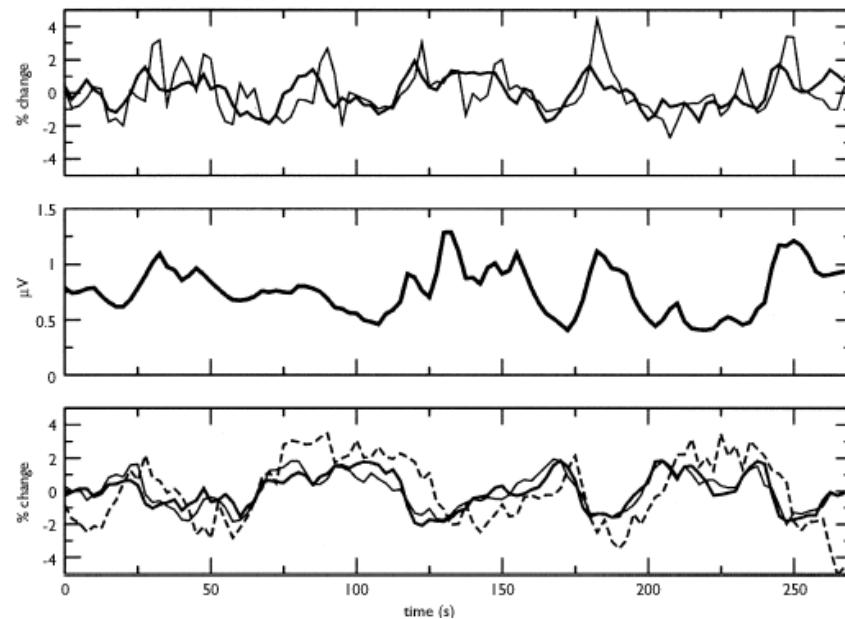
Activation:
correlation with reference function

Rest:
seed voxel in motor cortex

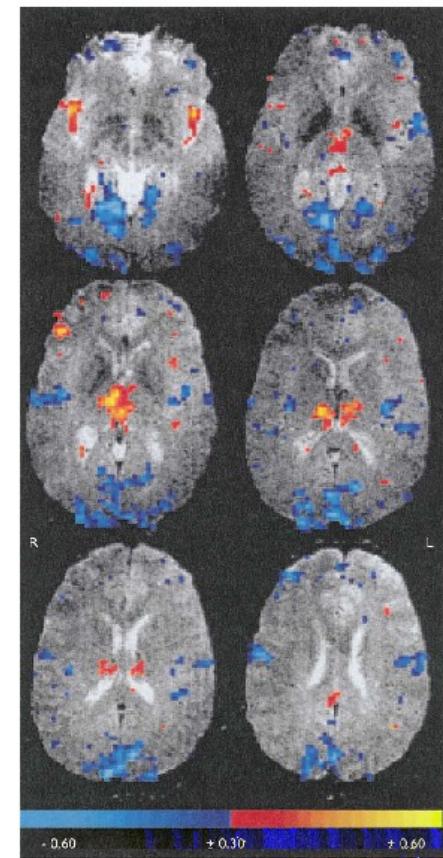
Methodology

BOLD correlated with 10 Hz power during "Rest"

Positive

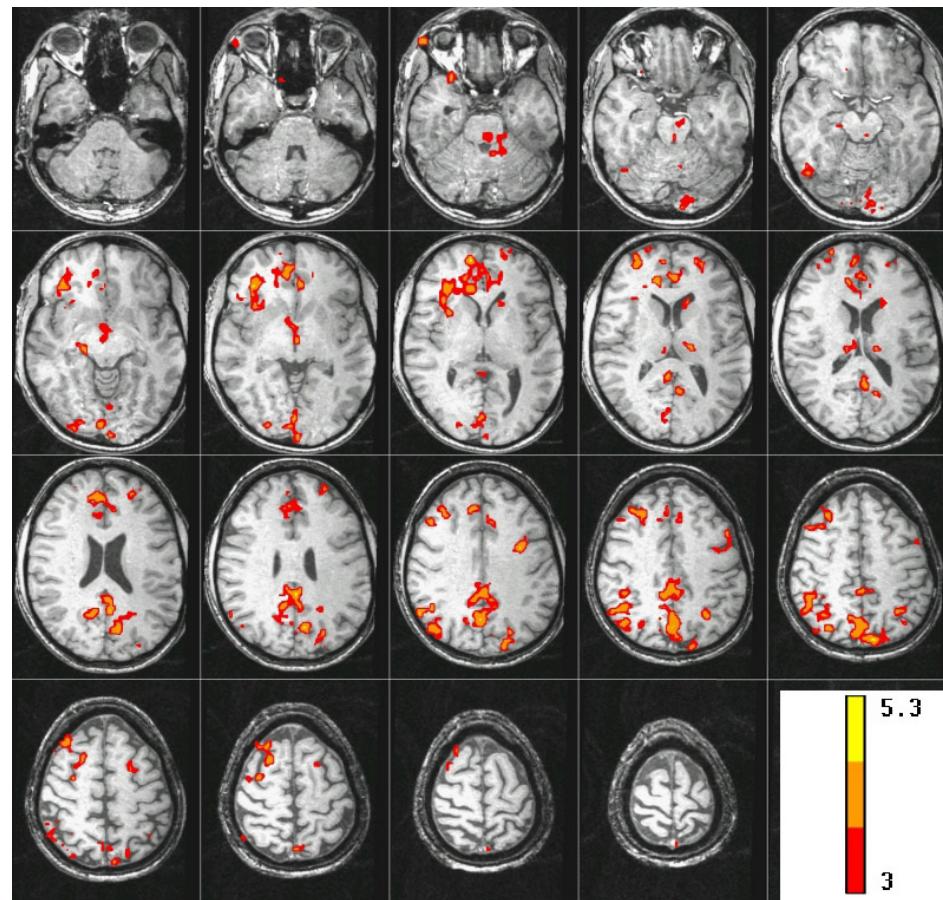


Goldman, et al (2002), Neuroreport



Methodology

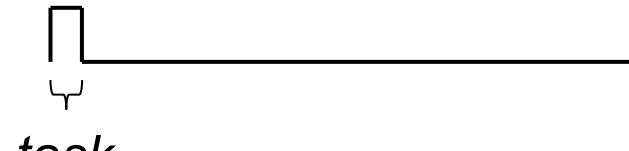
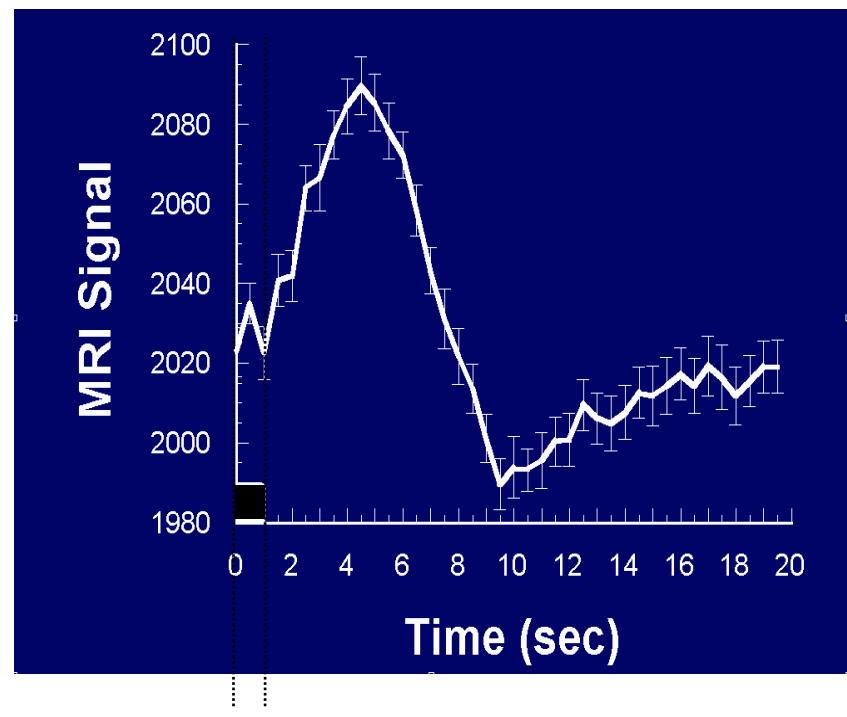
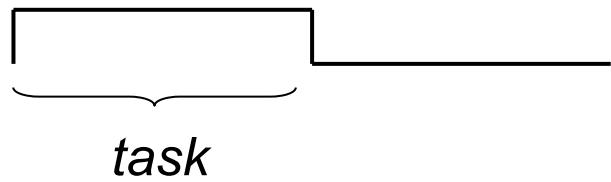
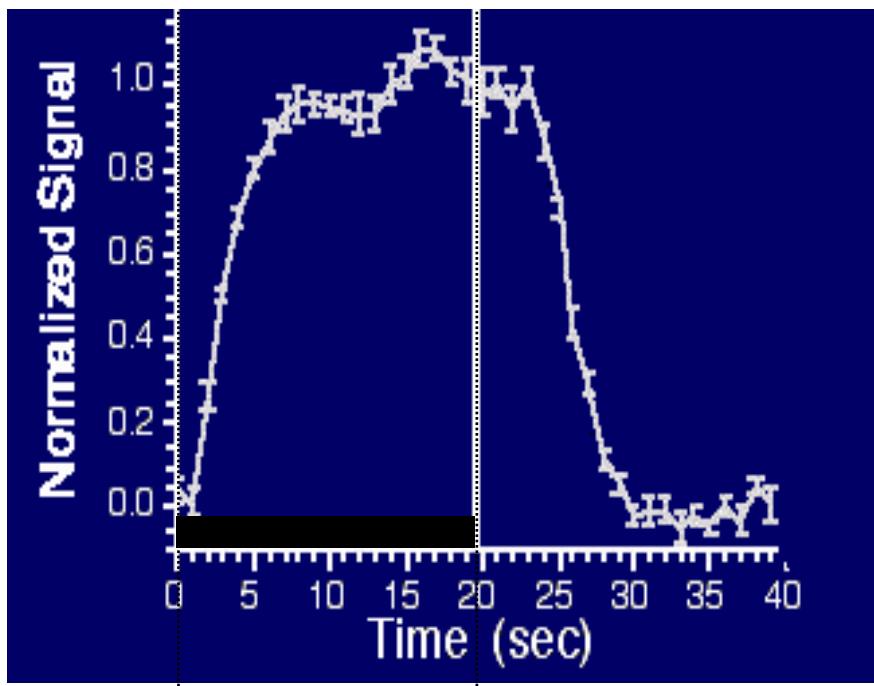
BOLD correlated with SCR during "Rest"



J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, *NeuroImage* 17: 1787-1806, (2002).

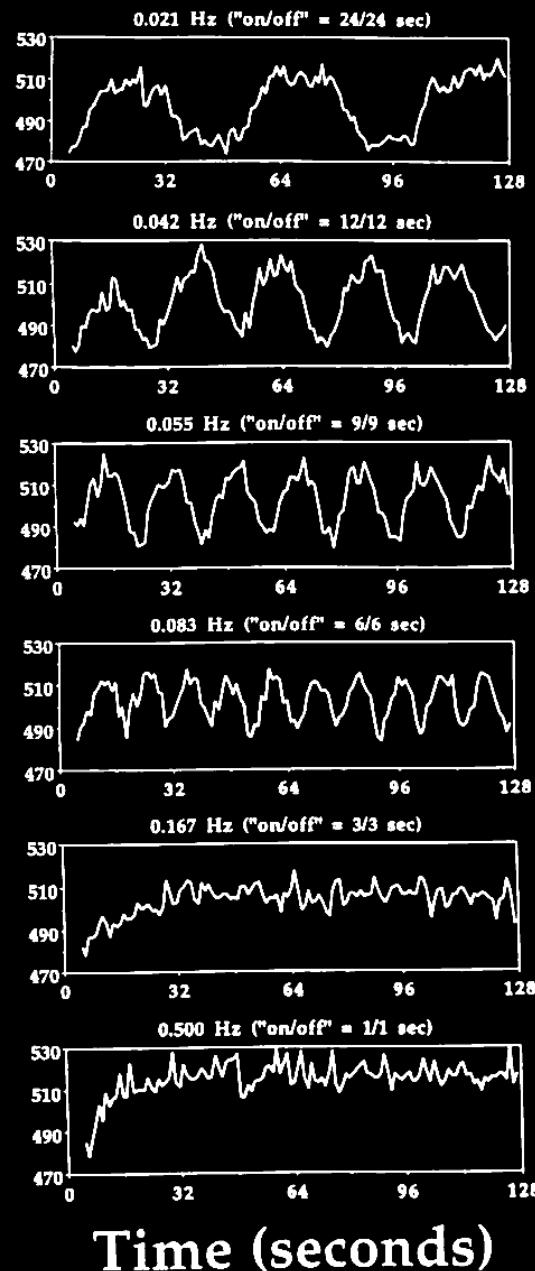
Methodology

Temporal Resolution

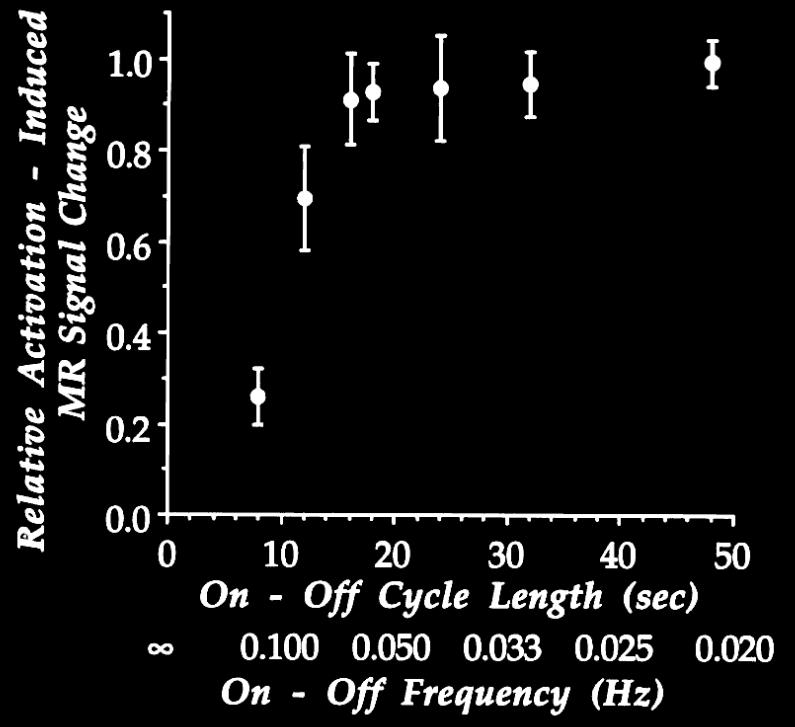


Methodology

MR Signal



Temporal Resolution

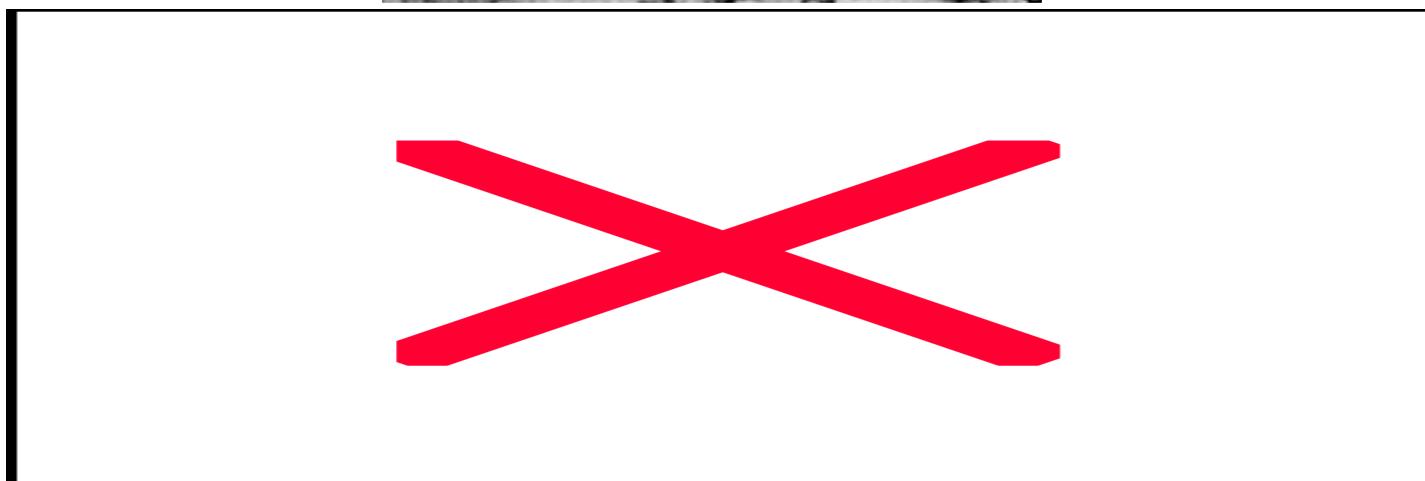
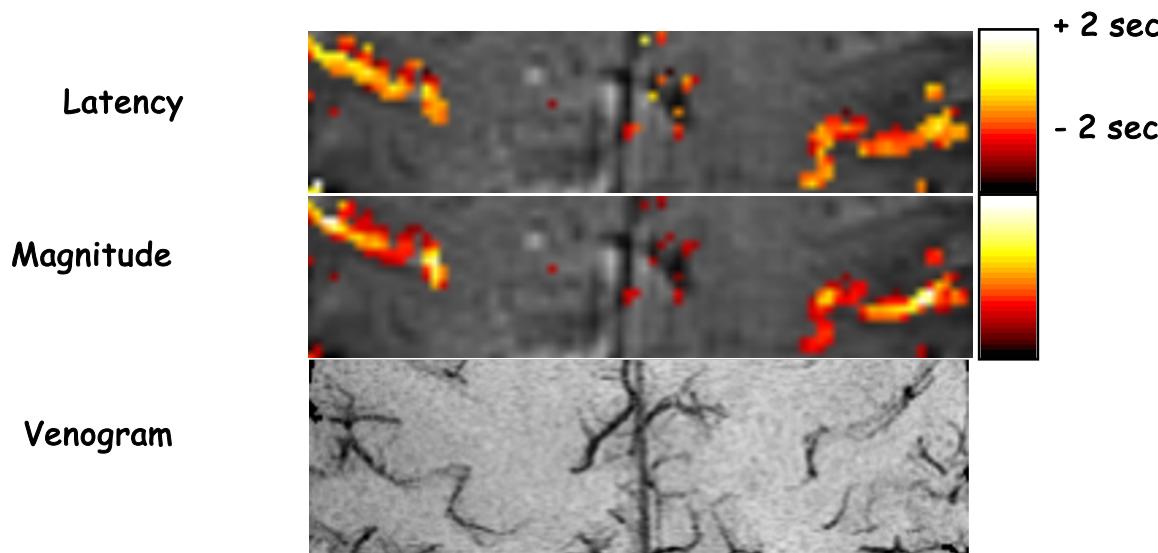


P. A. Bandettini, Functional MRI temporal resolution in "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag., 1999.

Methodology

Temporal Resolution

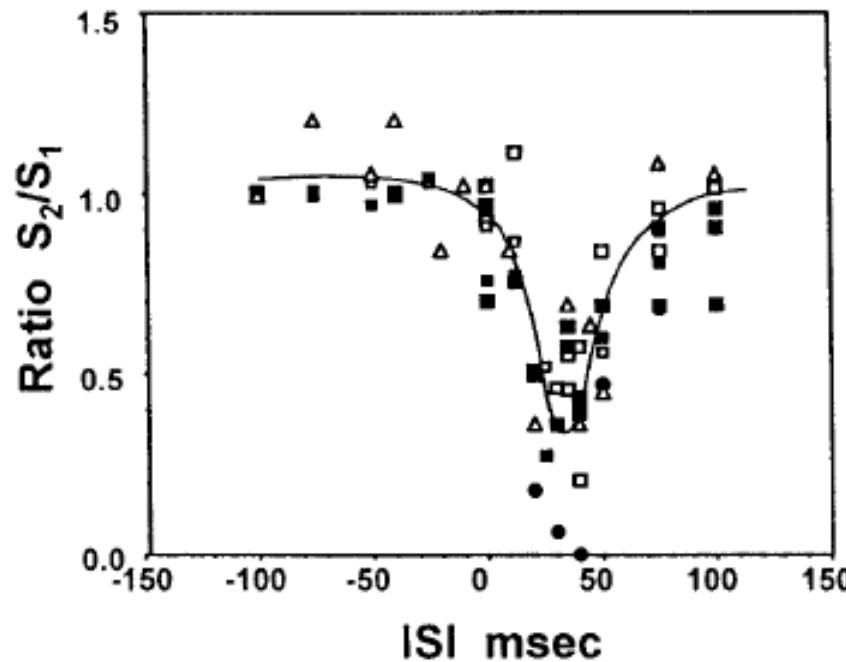
Latency Variation...



P. A. Bandettini, (1999) "Functional MRI" 205-220.

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[§]



Technology

8 to 96 Channel Coil Arrays
3 to 9.4 Tesla Field Strength
Sub-millimeter resolution
Novel Contrasts

Methodology

Calibration
Multi-variate mapping/classification
Multi-modal integration
Free Behavior task design
Resting state fluctuation assessment

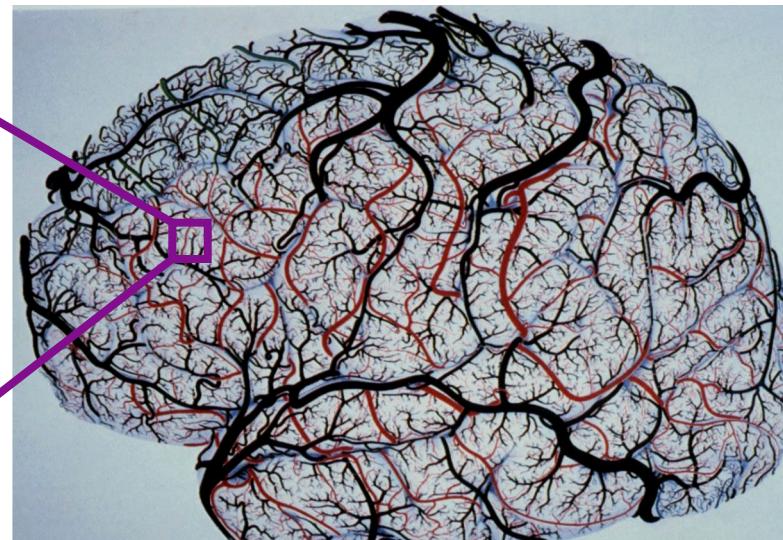
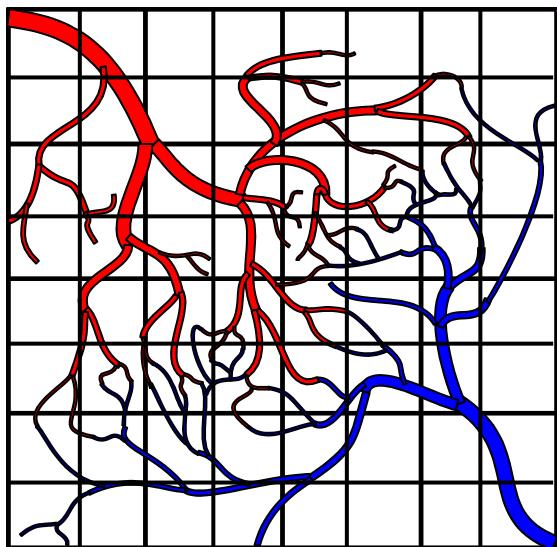
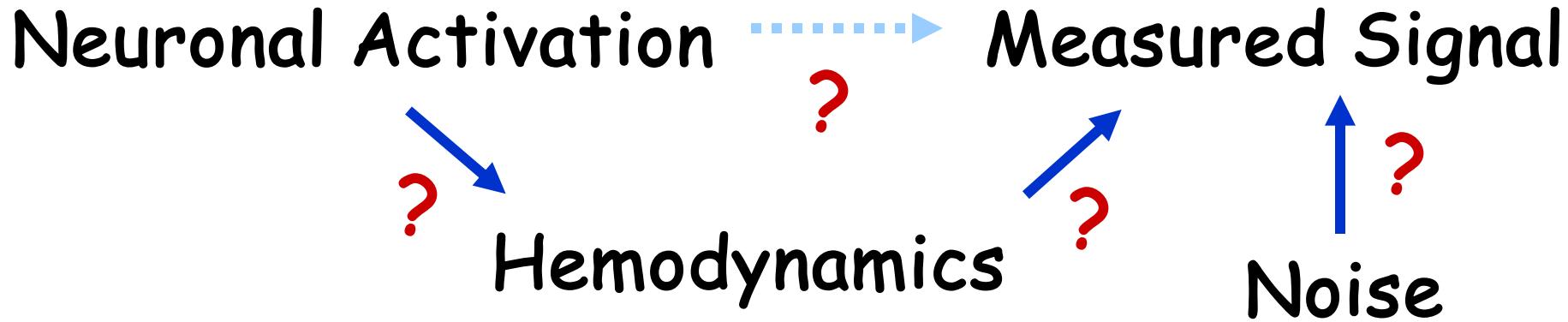
Fluctuations
Dynamics
Cross - modal comparison

Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

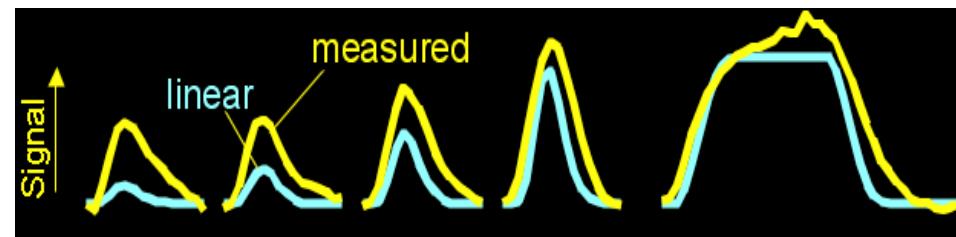
Interpretation

Applications

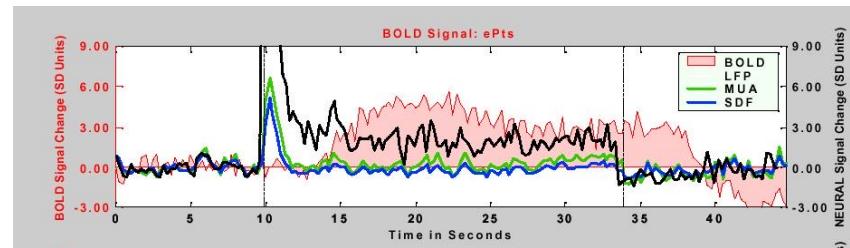
Interpretation



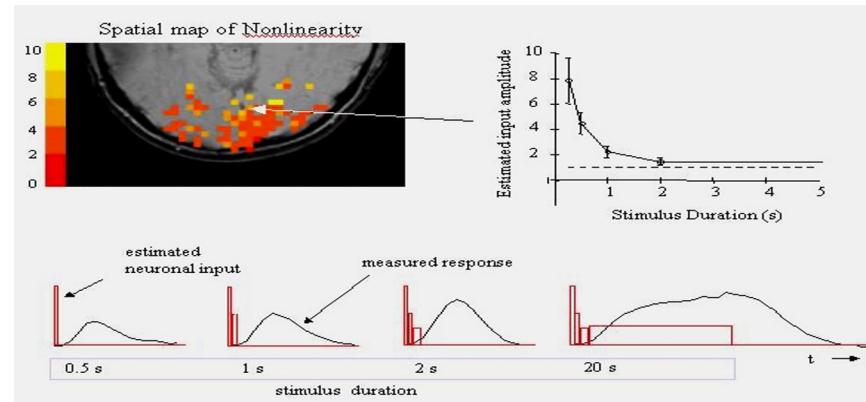
Interpretation



R. M. Birn, (2001) NeuroImage, 14: 817-826.



Logothetis et al. (2001) Nature, 412, 150-157.

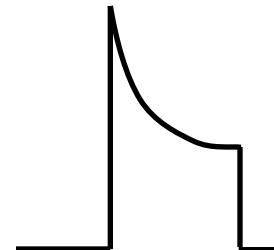
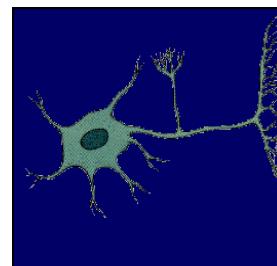


P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

Interpretation

Sources of this Nonlinearity

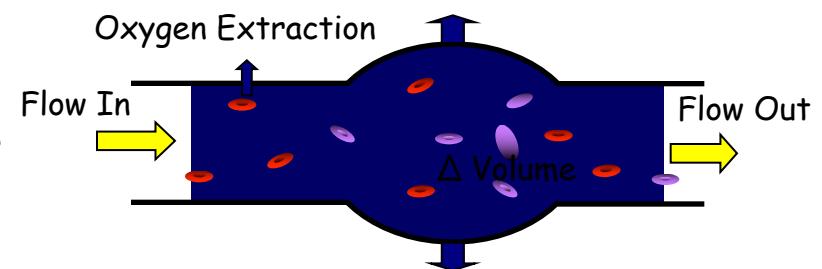
- Neuronal



- Hemodynamic

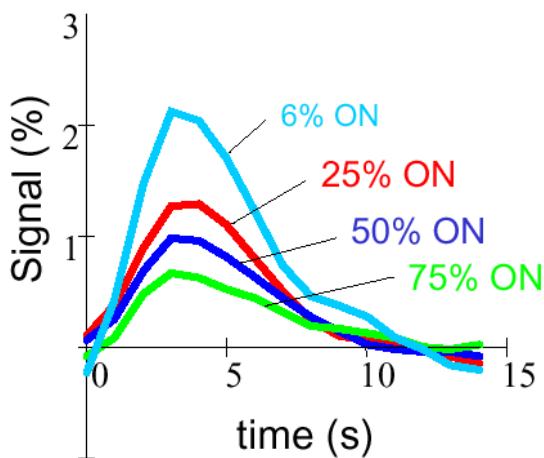
- Oxygen extraction

- Blood volume dynamics

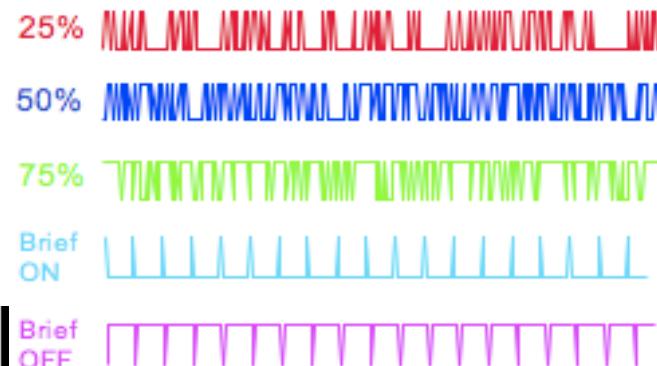
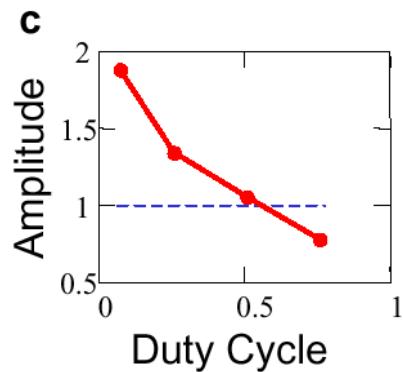
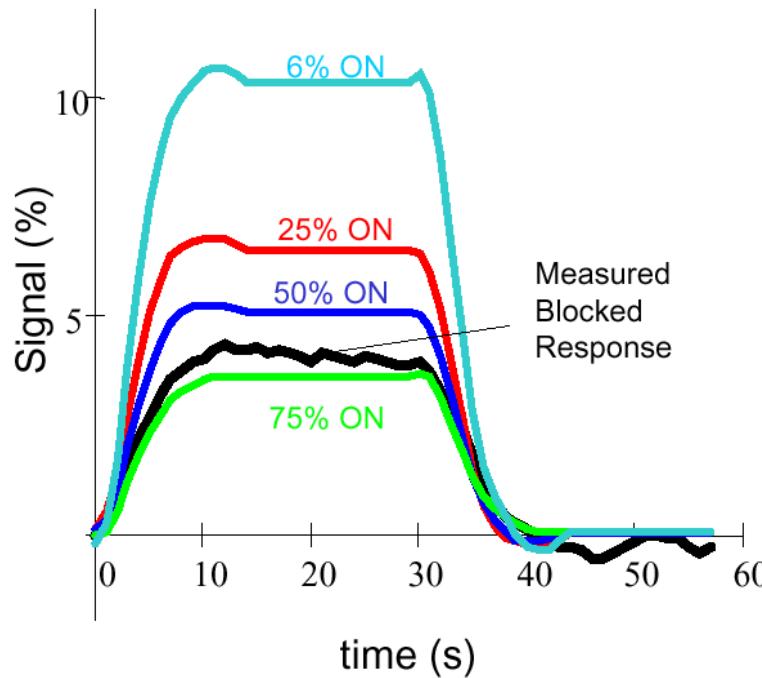


Interpretation Duty Cycle Effects

a Measured Event-related Responses



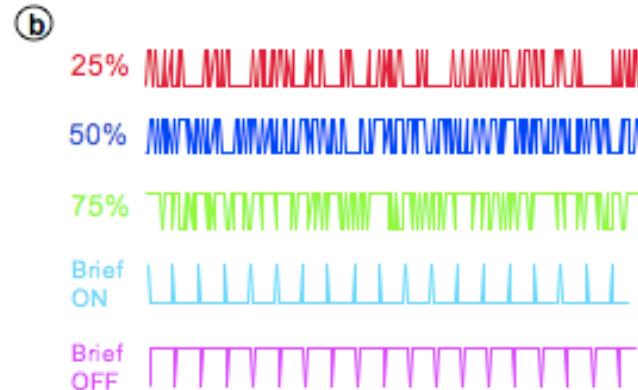
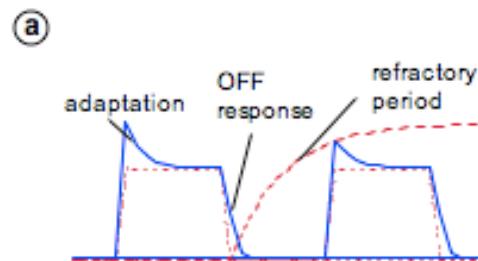
b Predicted Blocked Responses



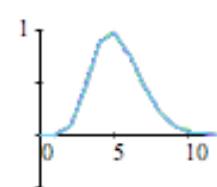
Interpretation

Linearity

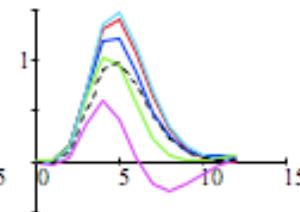
duty cycle effects



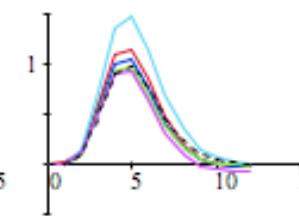
(c) Linear



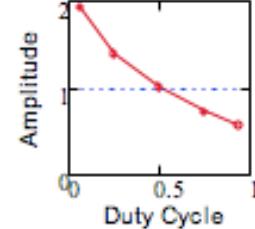
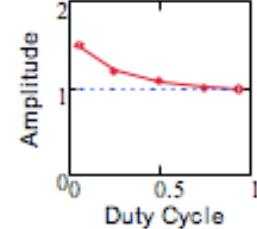
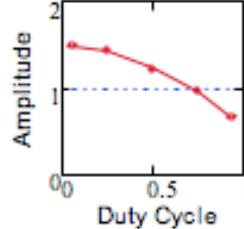
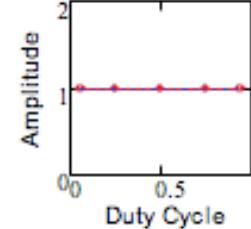
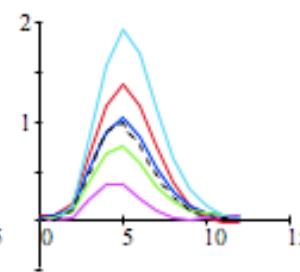
(d) Adaptation



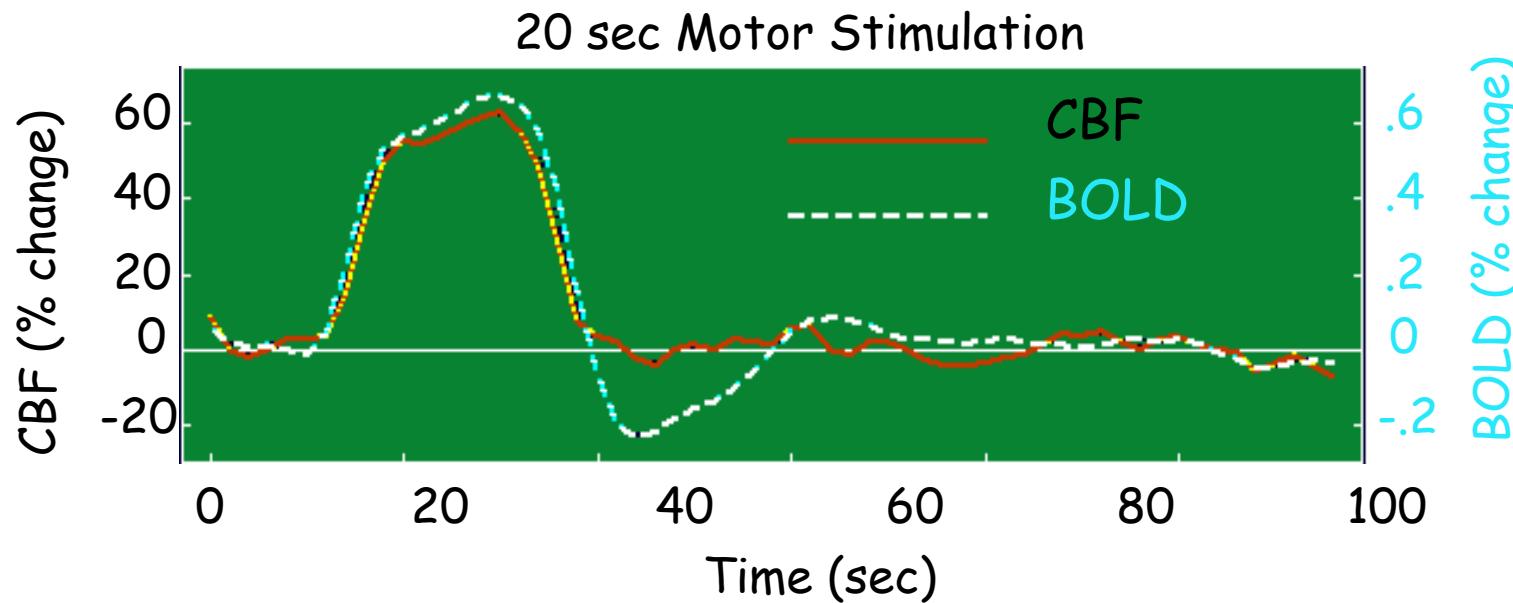
(e) Adaptation + refractory



(f) Adaptation + refractory + OFF response



BOLD post-stimulus undershoot



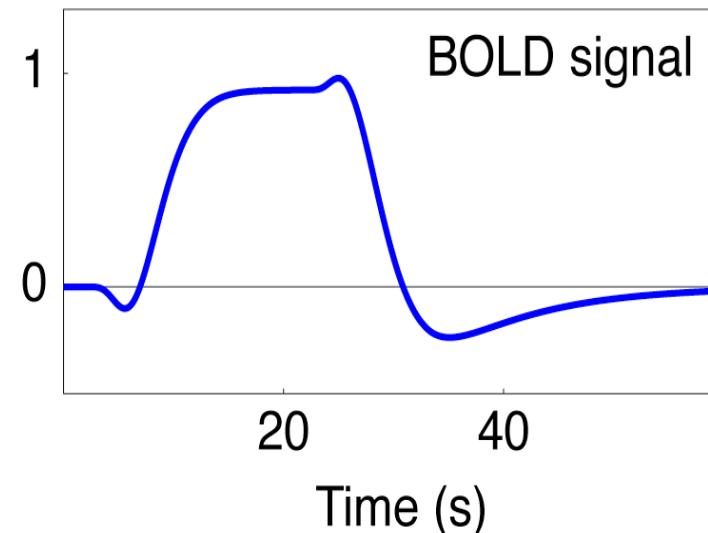
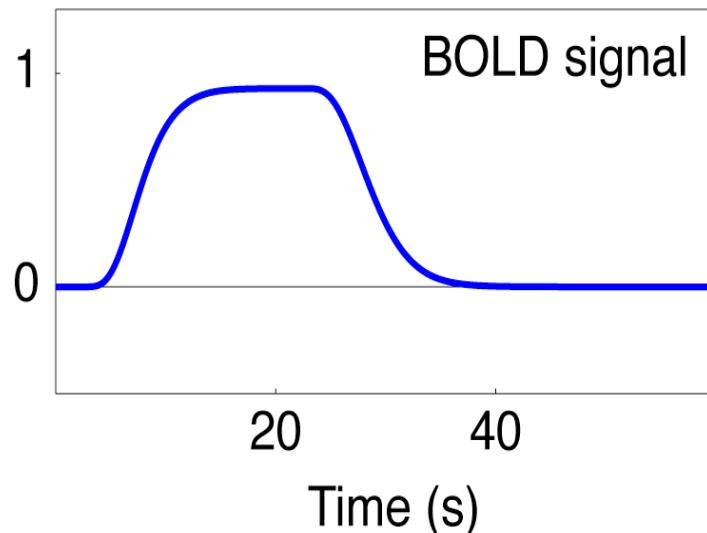
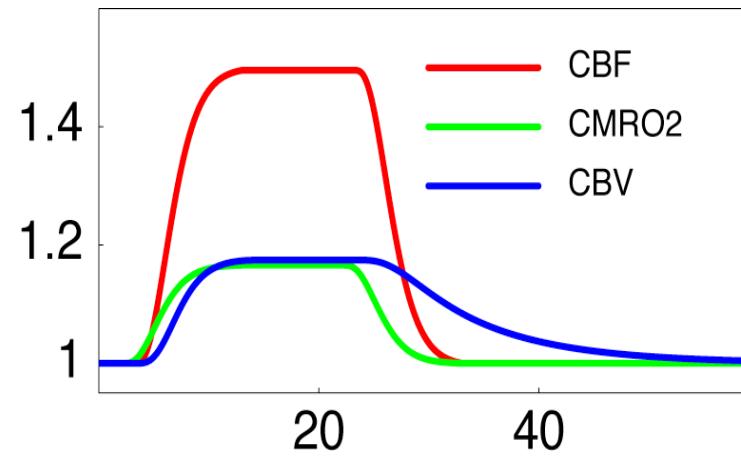
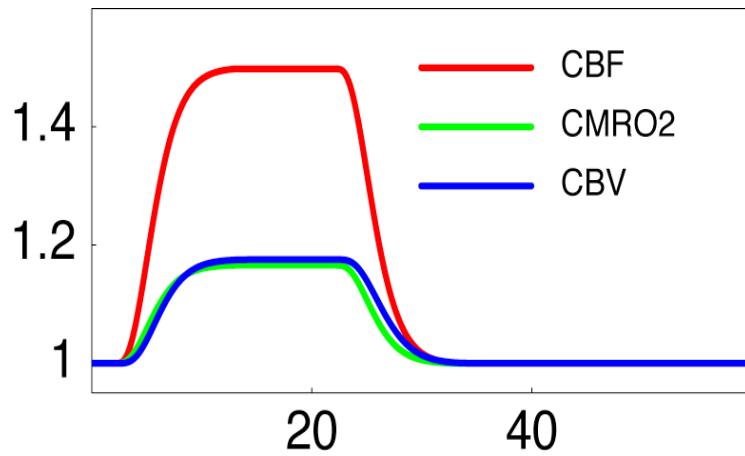
A BOLD undershoot without a CBF undershoot could be due to a slow return to baseline of either CBV or CMRO₂

Courtesy Rick Buxton

Interpretation

Post Undershoot

BOLD Signal Dynamics



Courtesy Rick Buxton

Technology

8 to 96 Channel Coil Arrays
3 to 9.4 Tesla Field Strength
Sub-millimeter resolution
Novel Contrasts

Methodology

Calibration
Multi-variate mapping/classification
Multi-modal integration
Free Behavior task design
Resting state fluctuation assessment

Fluctuations
Dynamics
Cross - modal comparison

Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

Interpretation

Applications

Applications

What fMRI Can Do

Understanding normal brain organization and changes

- networks involved with specific tasks (low to high level processing)
- changes over time (seconds to years)
- correlates of behavior (response accuracy, performance changes...)

Clinical research

- correlates of specifically activated networks to clinical populations
- presurgical mapping

What fMRI Might Do

Complementary use for clinical diagnosis

- utilization of clinical research results
- prediction of pathology

Clinical treatment and assessment

- drug, therapy, rehabilitation, biofeedback
- epileptic foci mapping
- drug effects

Non clinical uses

- complementary use with behavioral, anatomical, other modality results
- lie detection
- prediction of behavior tendencies
- brain/computer interface

Section on Functional Imaging Methods

Rasmus Birn
David Knight
Anthony Boemio
Nikolaus Kriegeskorte
Kevin Murphy
Monica Smith
Douglass Ruff
Joey Dunsmoor
Scott Phelps
Jon West



Functional MRI Facility

Kay Kuhns
Sean Marrett
Wen-Ming Luh
Jerzy Bodurka
Adam Thomas
James Hoskie

Karen Bove-Bettis
Ellen Condon
Sahra Omar
Alda Ottley
Paula Rowser
Janet Ebron

