

Are You fMRI Experienced?

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&
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

1.5T,3T, 4T

EPI

Local Human Head Gradient Coils

ASL

BOLD

EPI on Clin. Syst.

Nav. pulses

Spiral EPI

Multi-shot fMRI

Diff. tensor

Real time fMRI

Quant. ASL

Dynamic IV volume

Simultaneous ASL and BOLD

Mg⁺

Venography

Z-shim

7T

SENSE

Baseline Susceptibility

Current Imaging?

Methodology

Baseline Volume

IVIM

Correlation Analysis

Parametric Design

Surface Mapping

Phase Mapping

Linear Regression

Event-related

Motion Correction

Multi-Modal Mapping

Free-behavior Designs

Mental Chronometry

Deconvolution

CO₂ Calibration

Interpretation

Blood T2

Hemoglobin

BOLD models

B₀ dep.

TE dep

SE vs. GE

NIRS Correlation

Veins

PET correlation

IV vs EV

Pre-undershoot

Resolution Dep.

Post-undershoot

CO₂ effect

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Inflow

PET correlation

PSF of BOLD

Extended Stim.

Linearity

Fluctuations

Balloon Model

Metab. Correlation

Optical Im. Correlation

Electrophys. correlation

Applications

Complex motor Language

Imagery

Memory

Emotion

Motor learning

Children

Tumor vasc.

Drug effects

BOLD -V1, M1, A1

Presurgical

Attention

Ocular Dominance

Volume - Stroke

V1, V2..mapping

Priming/Learning

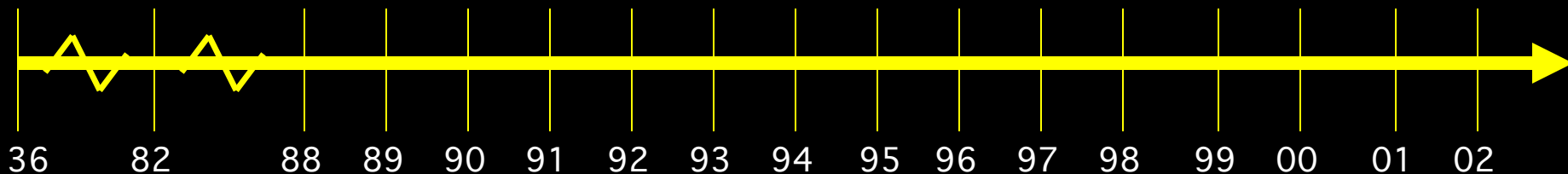
Clinical Populations

Δ Volume-V1

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

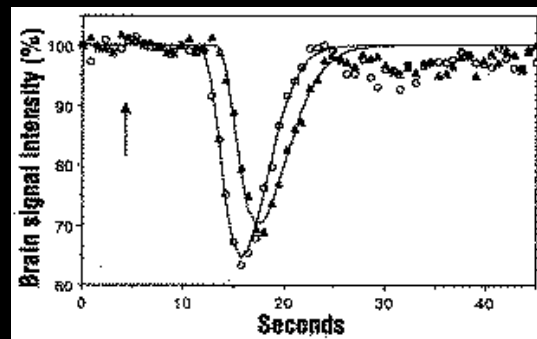
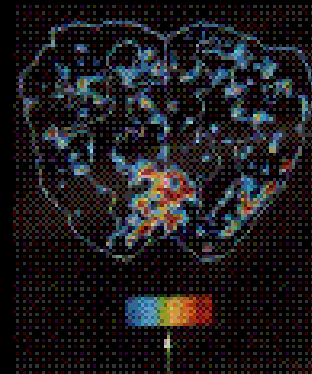
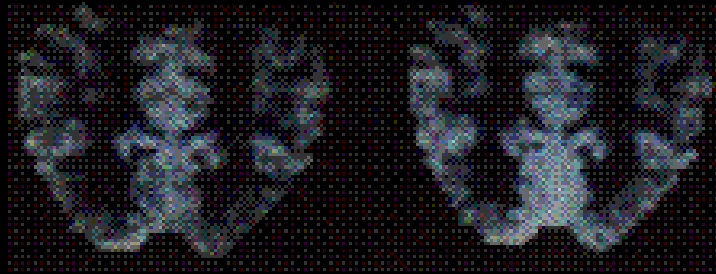
Arterial Spin Labeling

Blood Volume Imaging

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

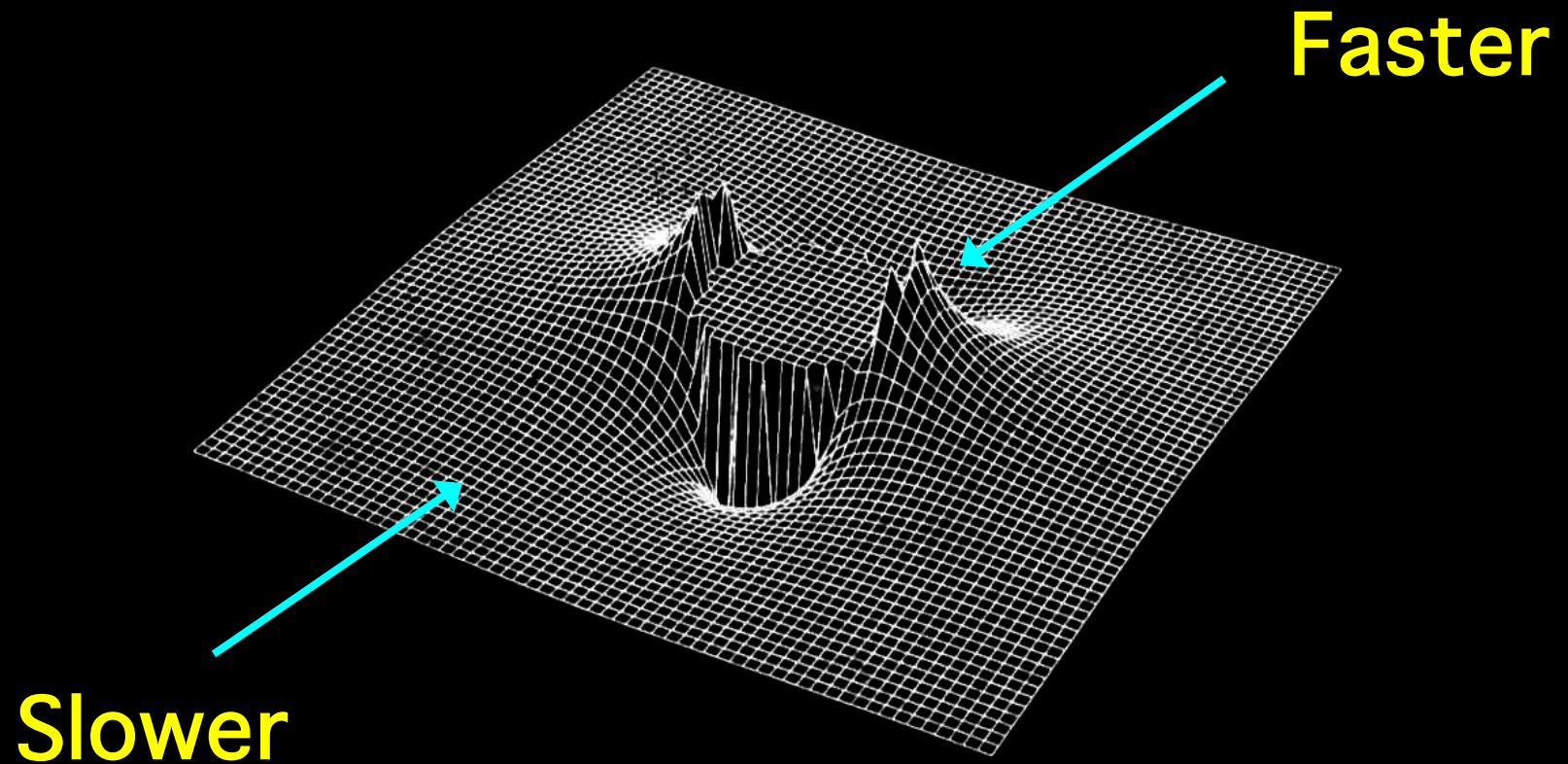
Resting

Active



Susceptibility Contrast

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

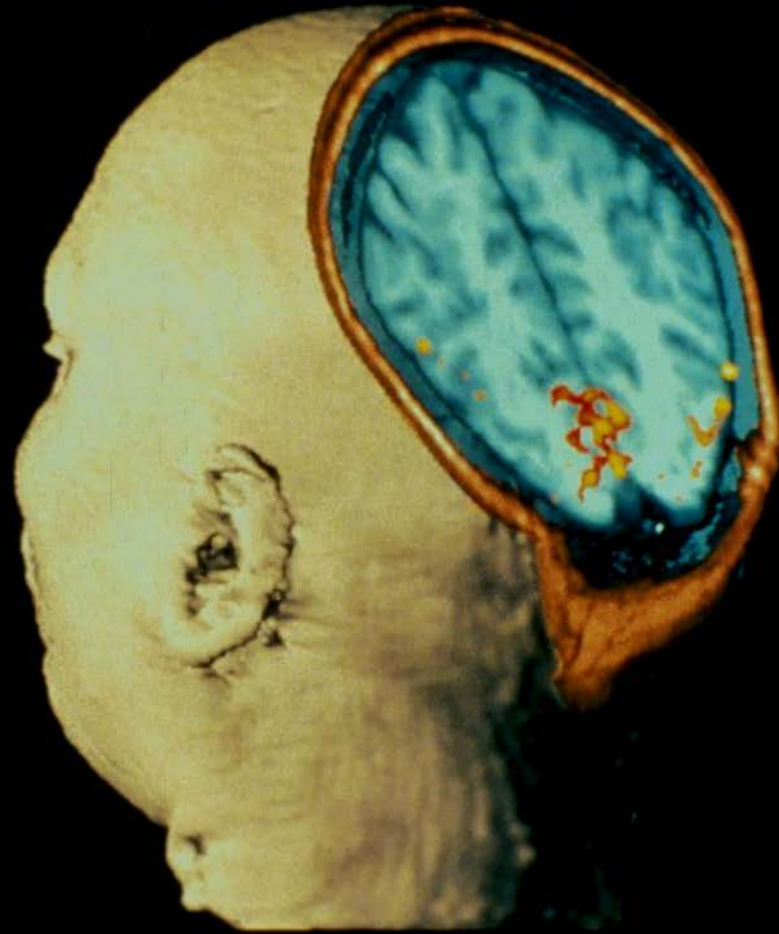


Blood Volume

**Photic
Stimulation**

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

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



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.

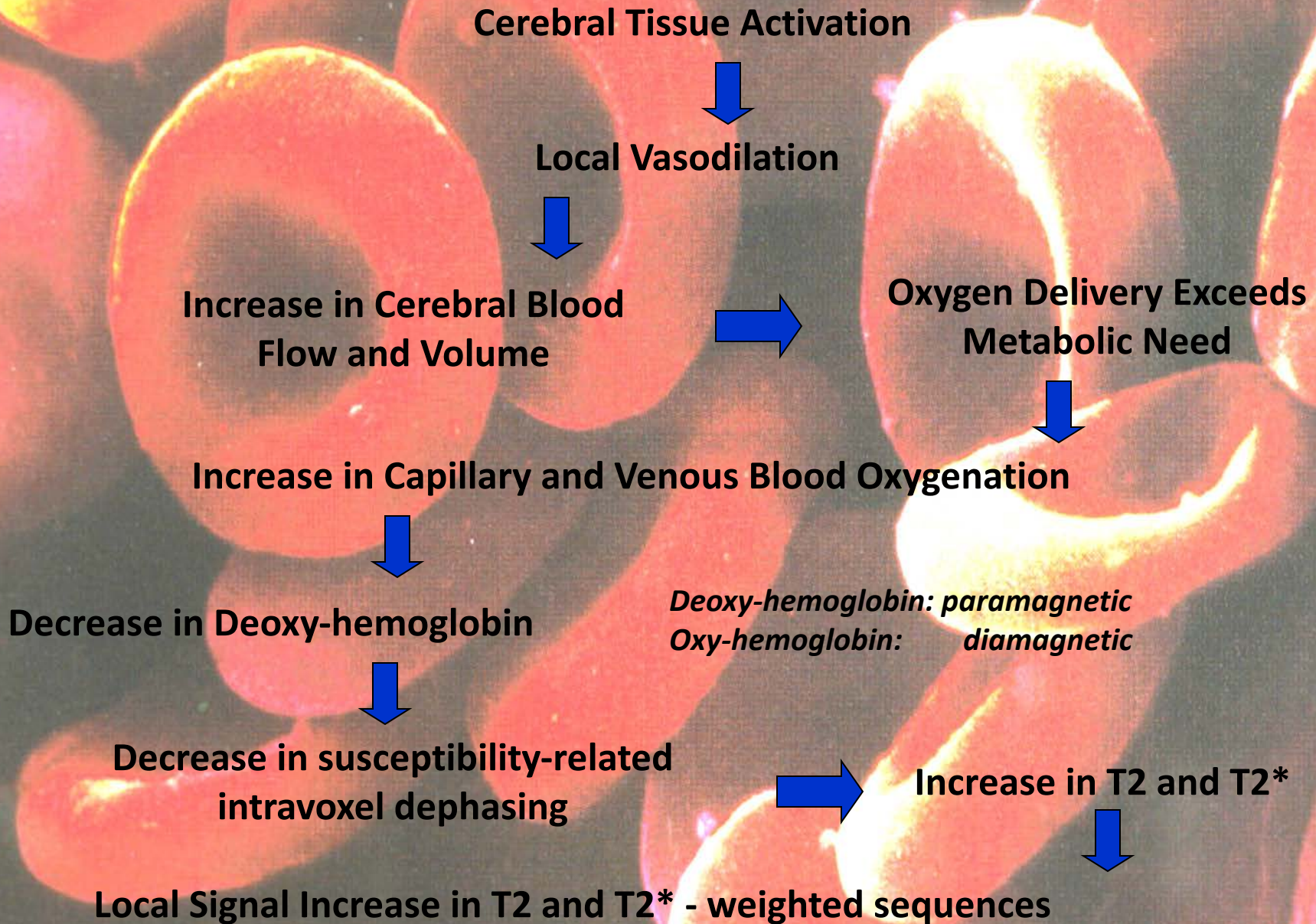
Blamire, A. M., et al. (1992). “Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging.” Proc. Natl. Acad. Sci. USA 89: 11069-11073.

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



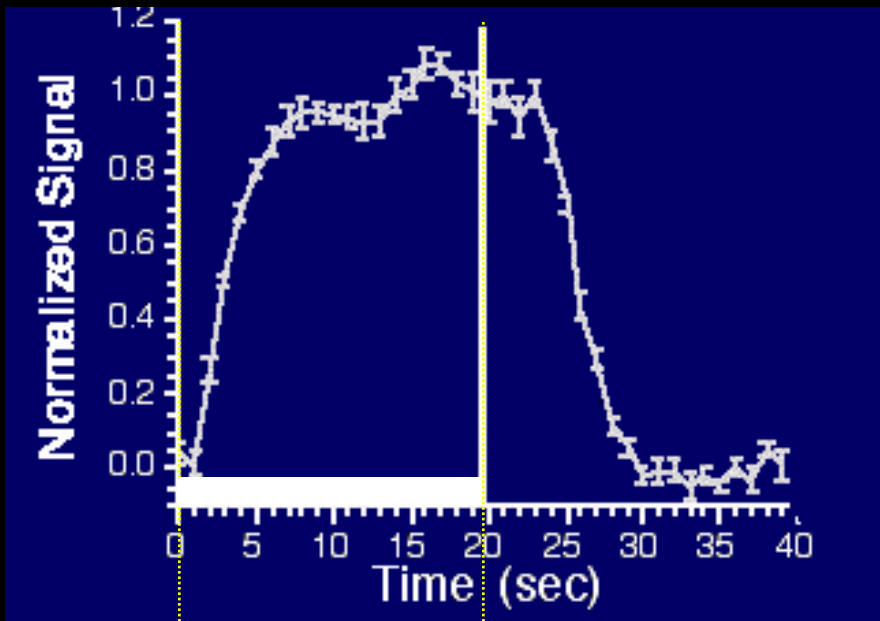
*Quality of results and importance of the findings depends on
type of question asked, experimental method, and analysis method...*

BOLD Contrast in the Detection of Neuronal Activity

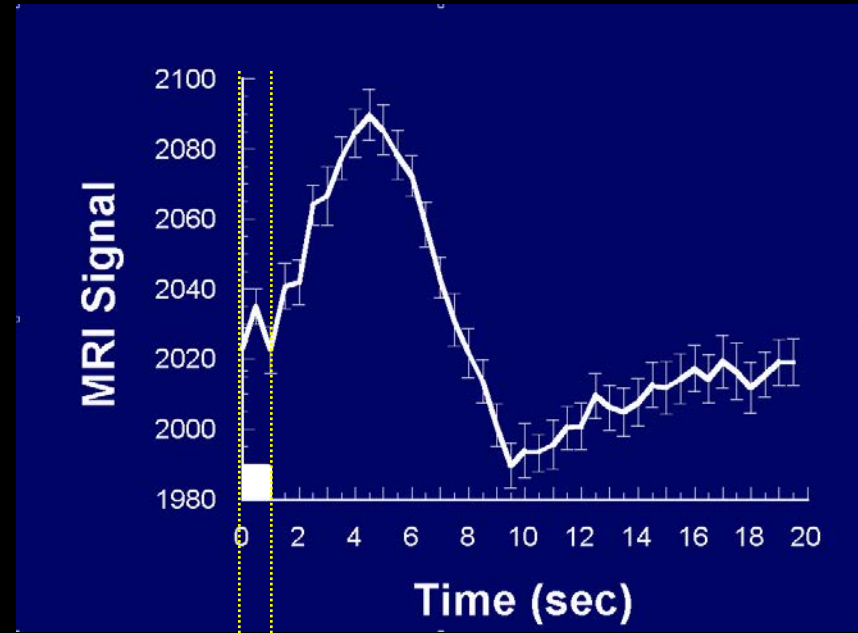


The BOLD Signal

Blood Oxygenation Level Dependent (BOLD) signal changes

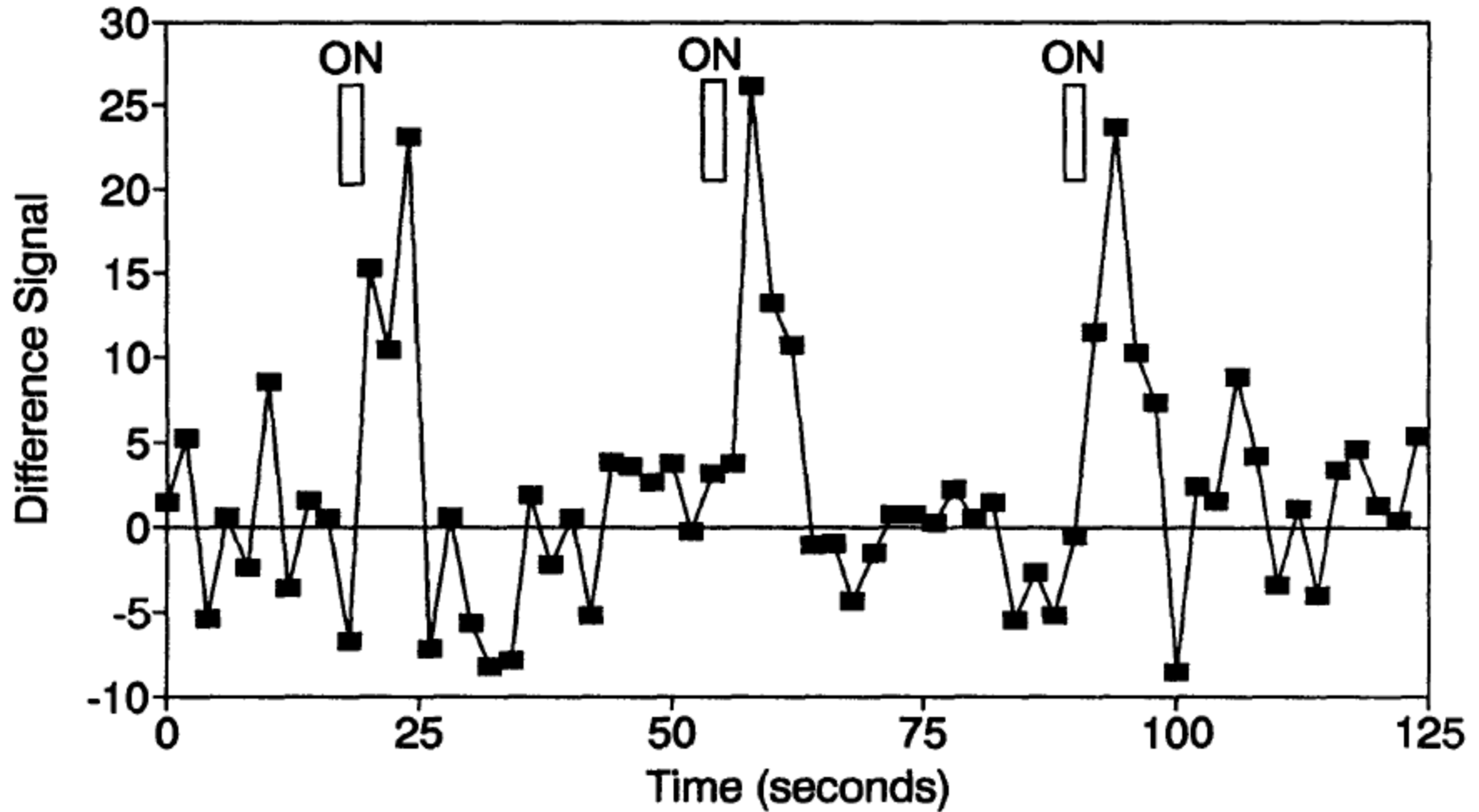


task



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.

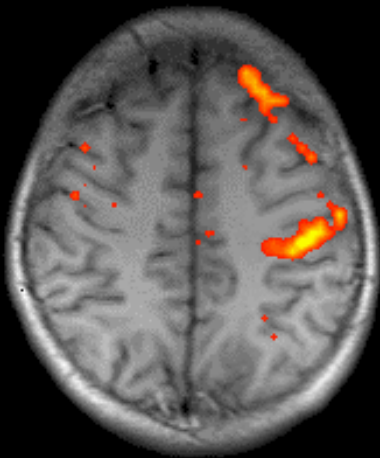
1991-1992



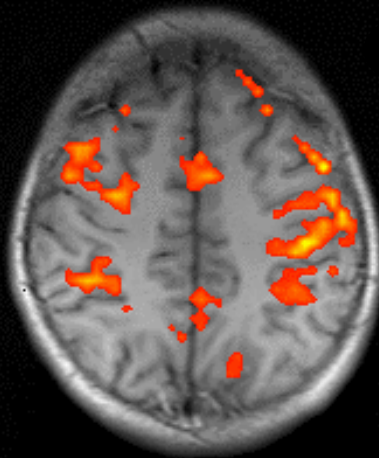
1992-1999



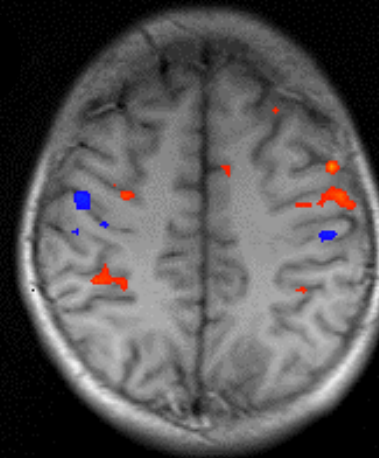
Simple Right



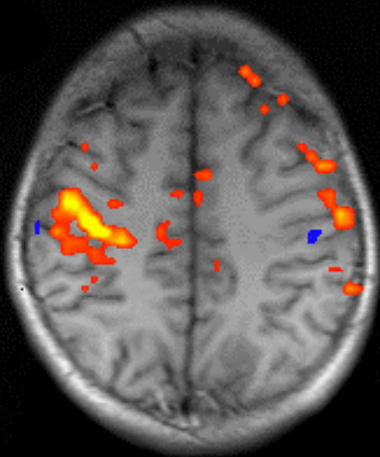
Complex Right



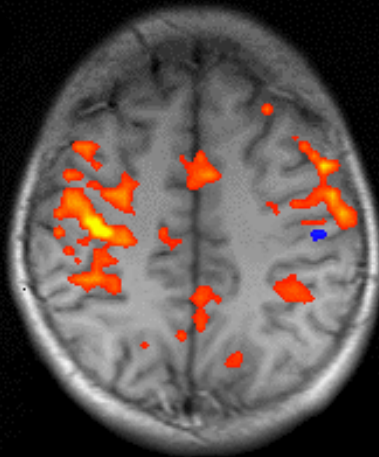
Imagined
Complex Right



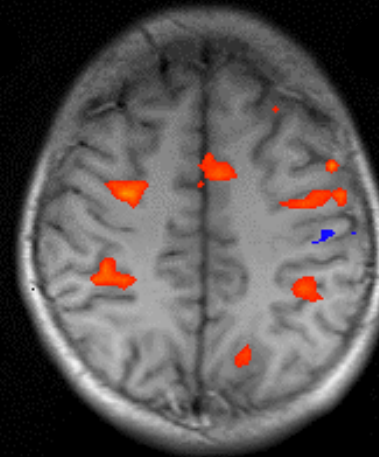
Simple Left



Complex Left

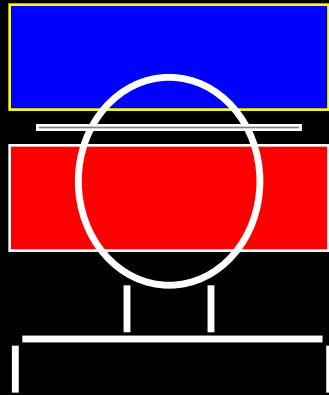


Imagined
Complex Left

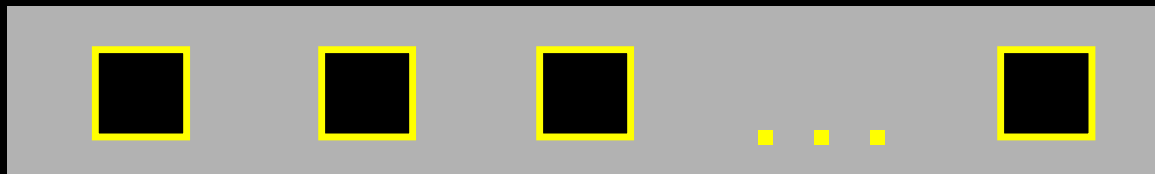
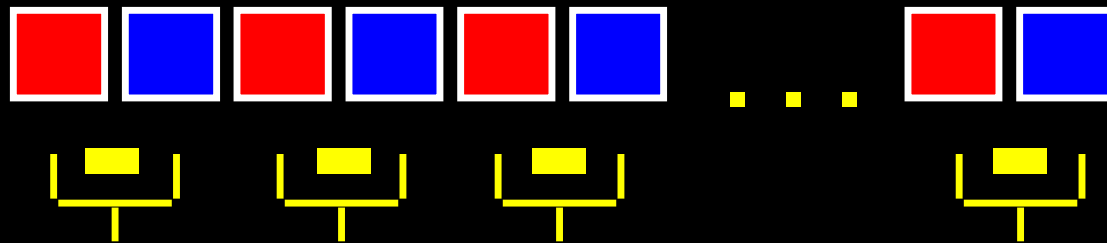
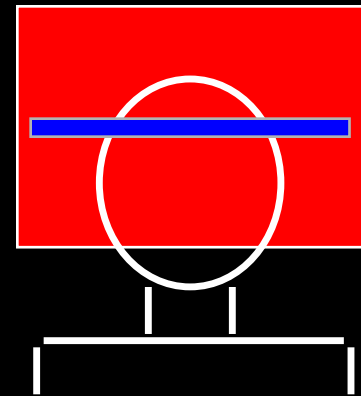


Blood Perfusion

EPISTAR



FAIR



**Perfusion
Time Series**

TI (ms)

FAIR

EPISTAR

200

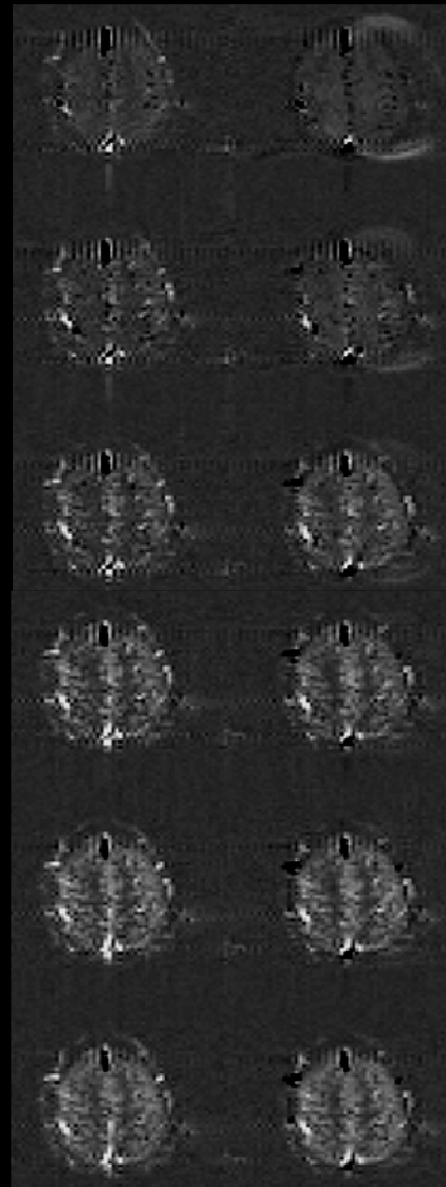
400

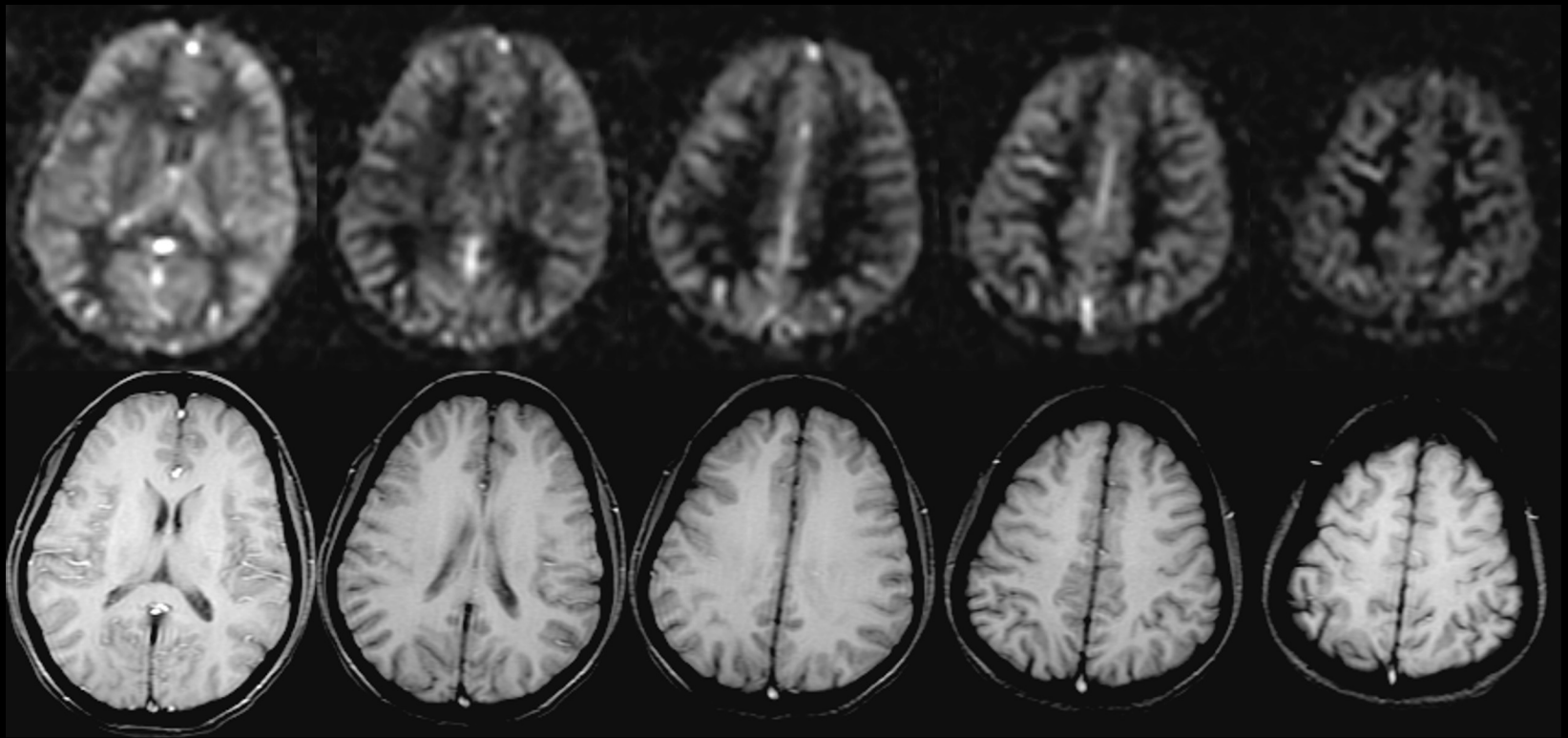
600

800

1000

1200





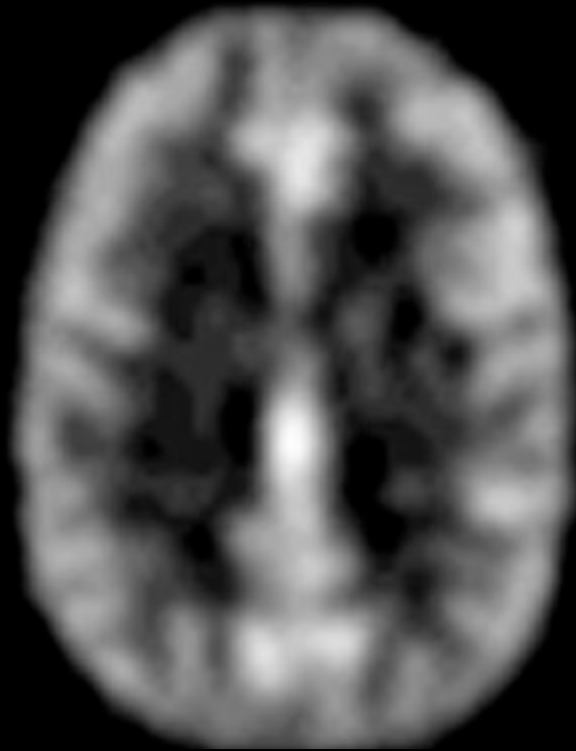
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." *Proc. Natl. Acad. Sci. USA* 89, 212-216.

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.

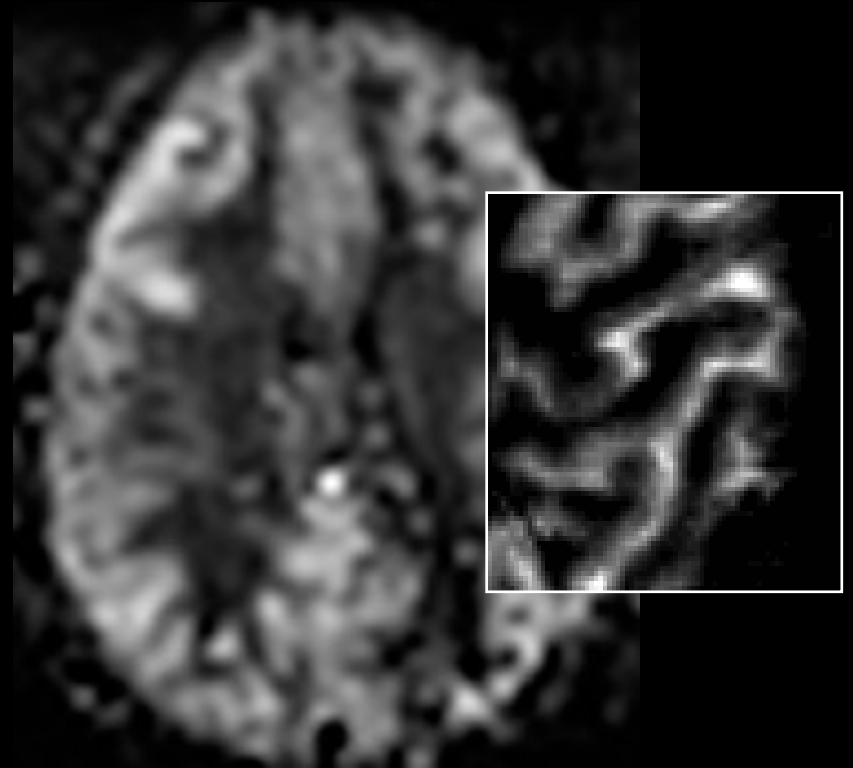
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." *Magn. Reson. Med.* 34, 293-301.

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

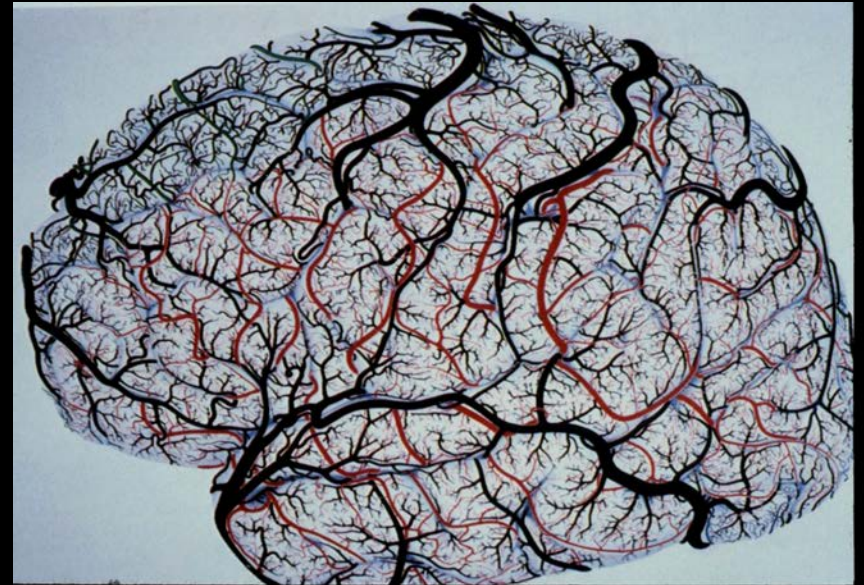
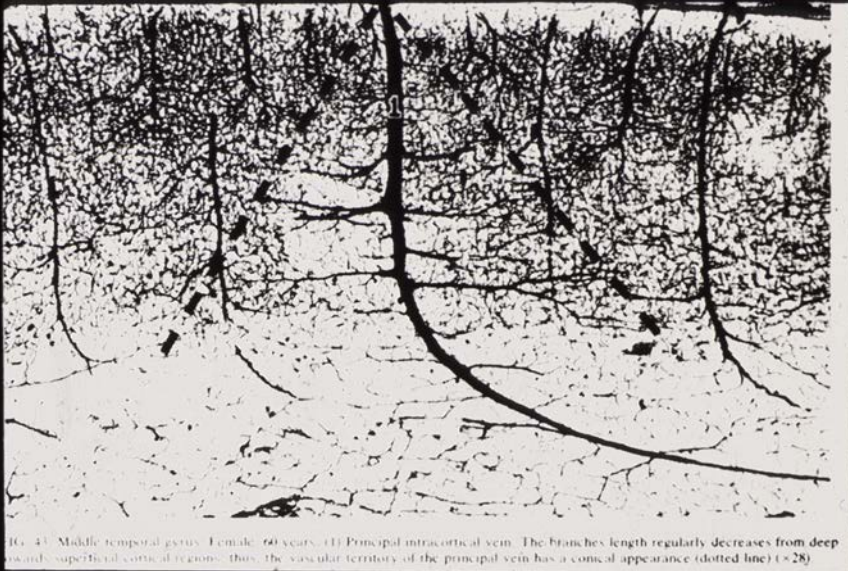
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Applications

The Neuroscientists' Challenge:

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

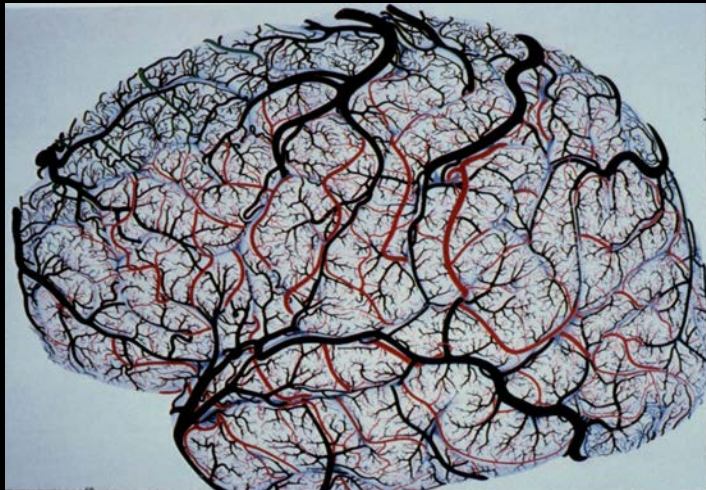


Neuronal
Activation



Measured
Signal

Hemodynamics



Noise

?

?

?



Technology

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1.5T,3T, 4T

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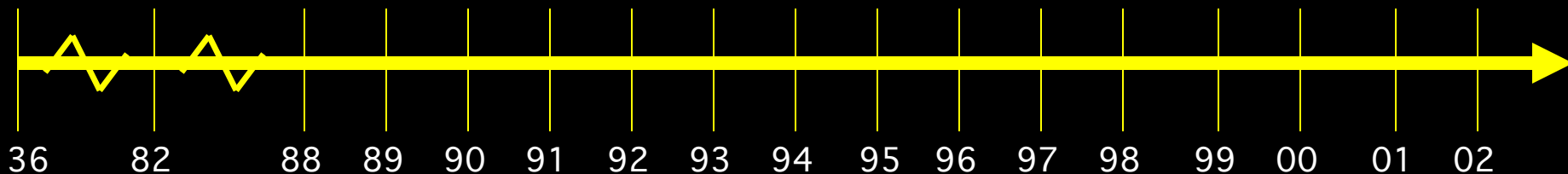
Clinical Populations

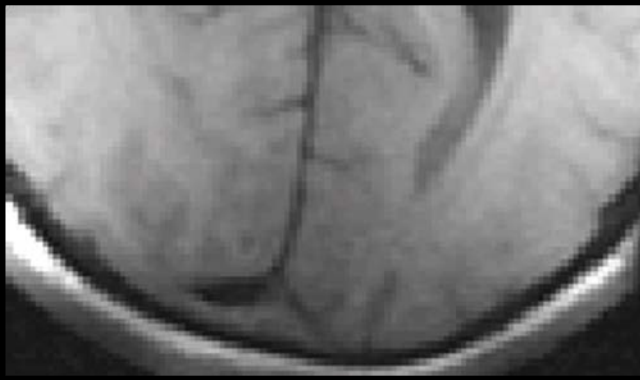
Δ Volume-V1

Plasticity

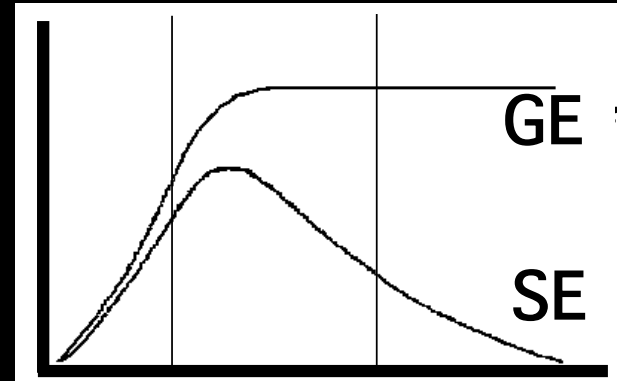
Face recognition

Performance prediction





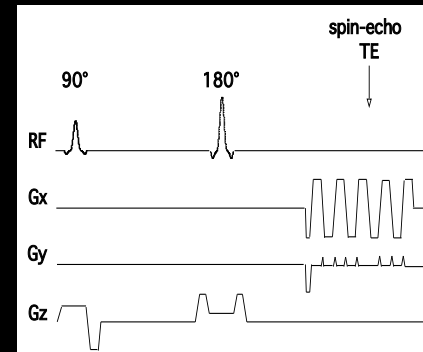
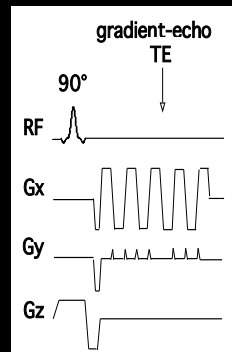
Contrast



2.5 to 3 μm 3 to 15 μm 15 to ∞ μm

compartment size

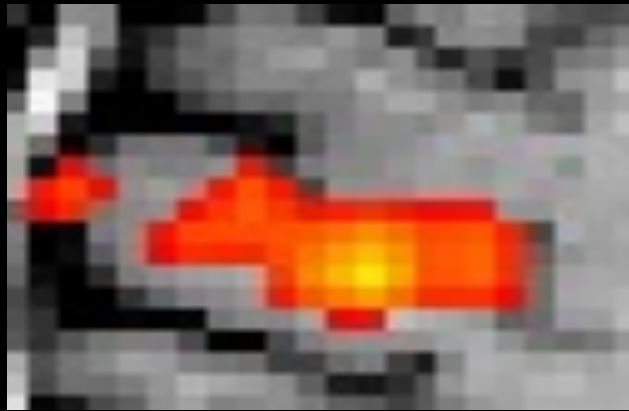
Gradient - Echo



Spin - Echo

T1 - weighted

Flow weighted



T2* weighted

BOLD weighted



T1 and T2* weighted

Flow and BOLD weighted



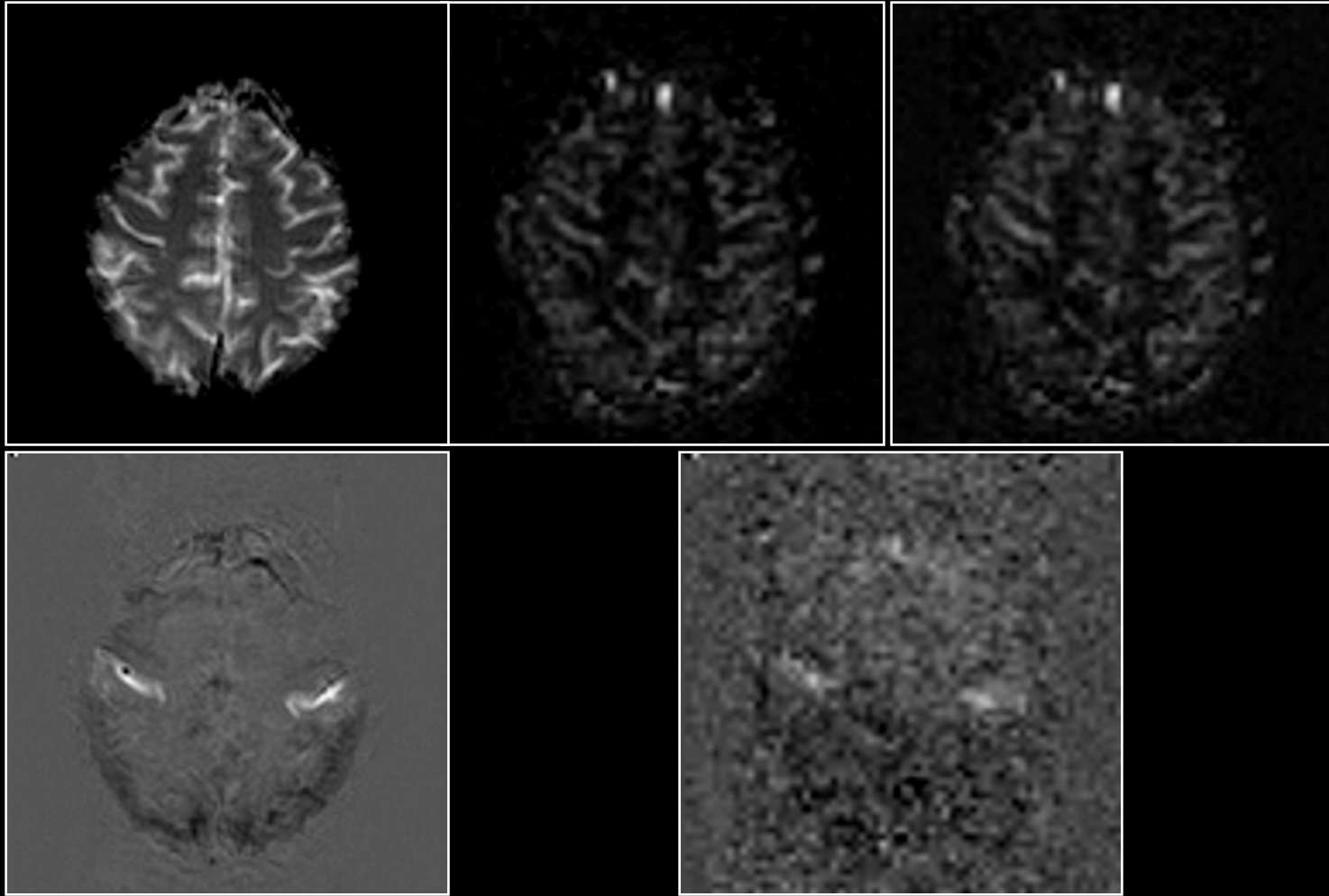
P. A. Bandettini, E. C. Wong, Echo - planar magnetic resonance imaging of human brain activation, in "Echo Planar Imaging: Theory, Technique, and Application" (F. Schmitt, M. Stehling, R. Turner, Eds.), p.493-530, Springer - Verlag, Berlin, 1997

Perfusion

BOLD

Rest

Activation

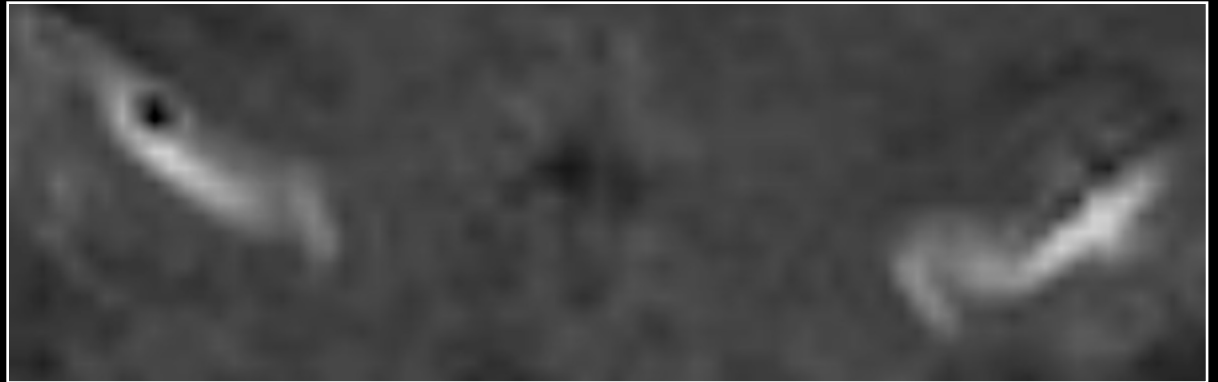


P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Anatomy



BOLD



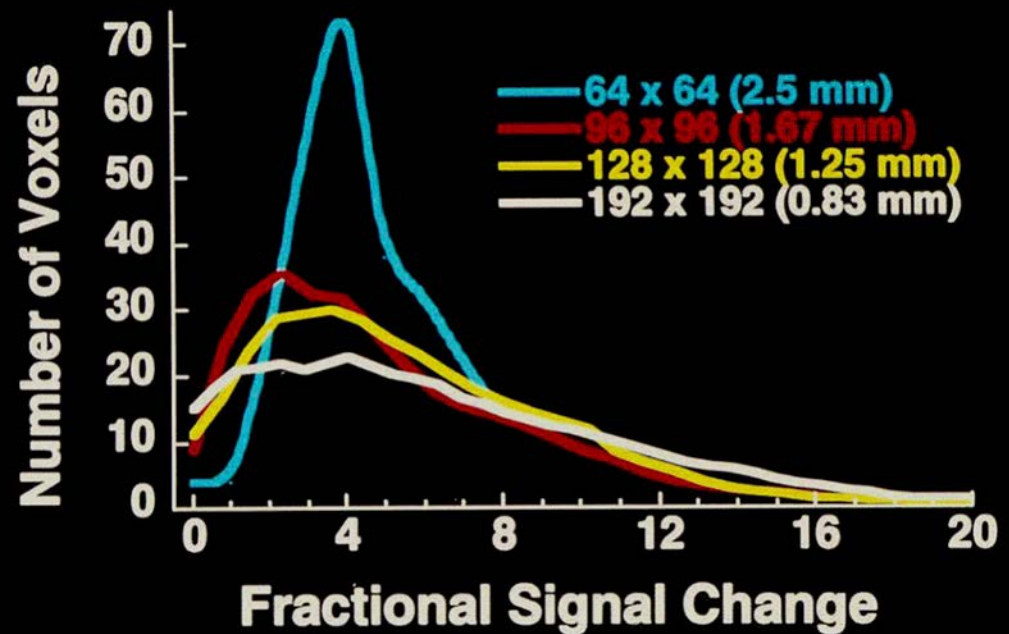
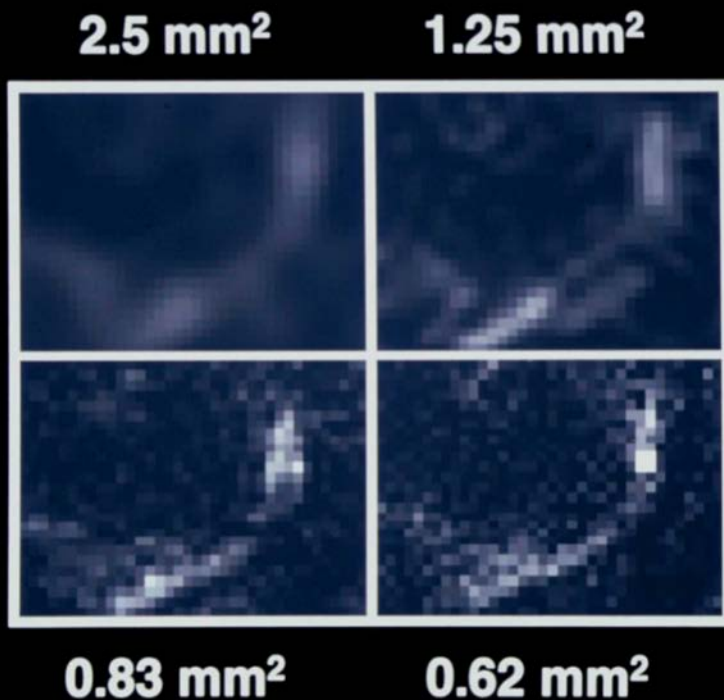
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P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

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)

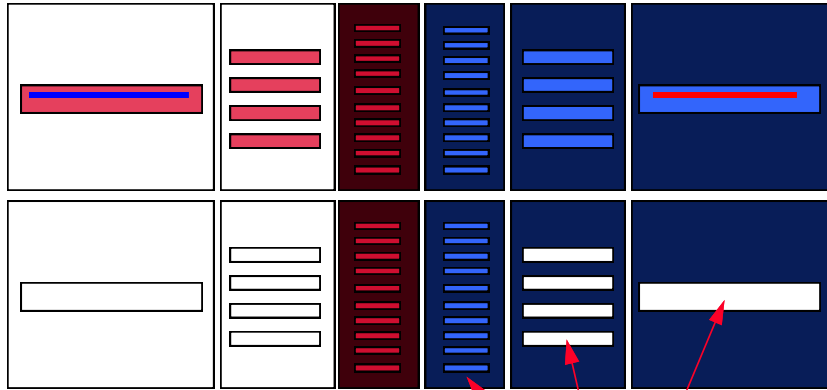
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BOLD

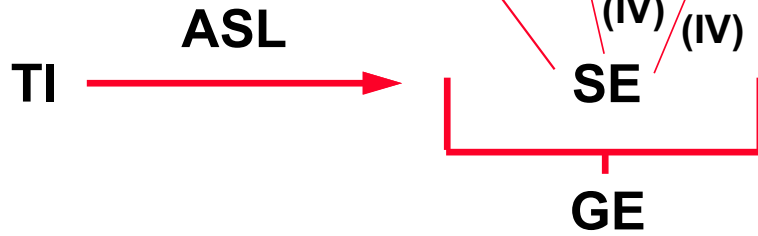
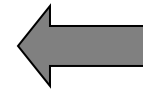
Venous inflow
(for ASL, w/ no VN)

No
Velocity
Nulling

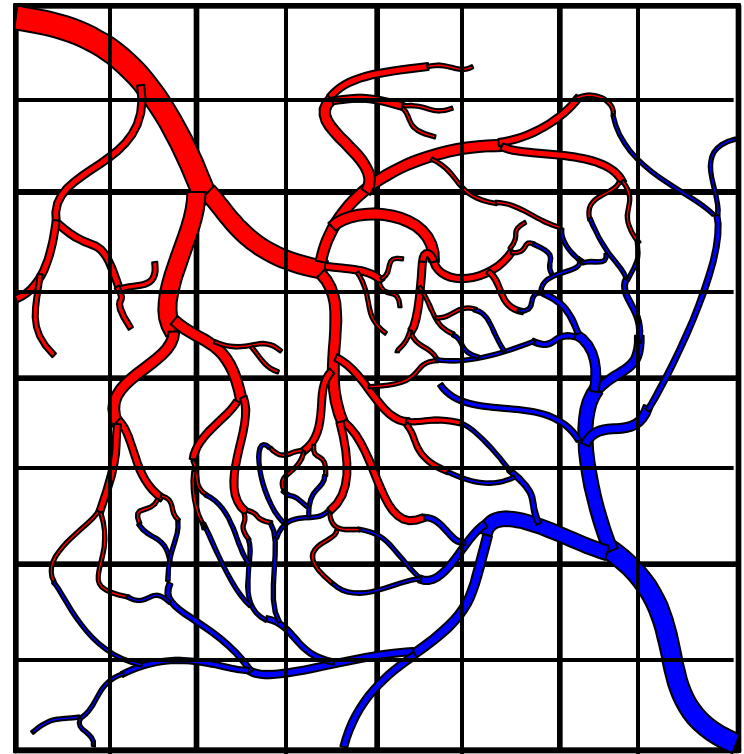
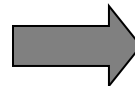
Velocity
Nulling



Pulse Sequence
Sensitivity



Spatial
Heterogeneity



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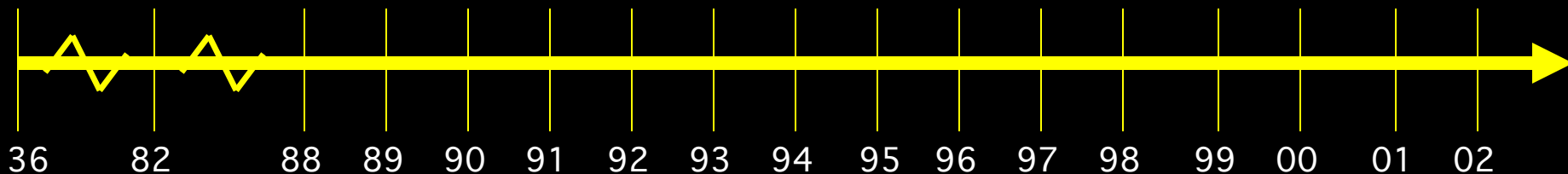
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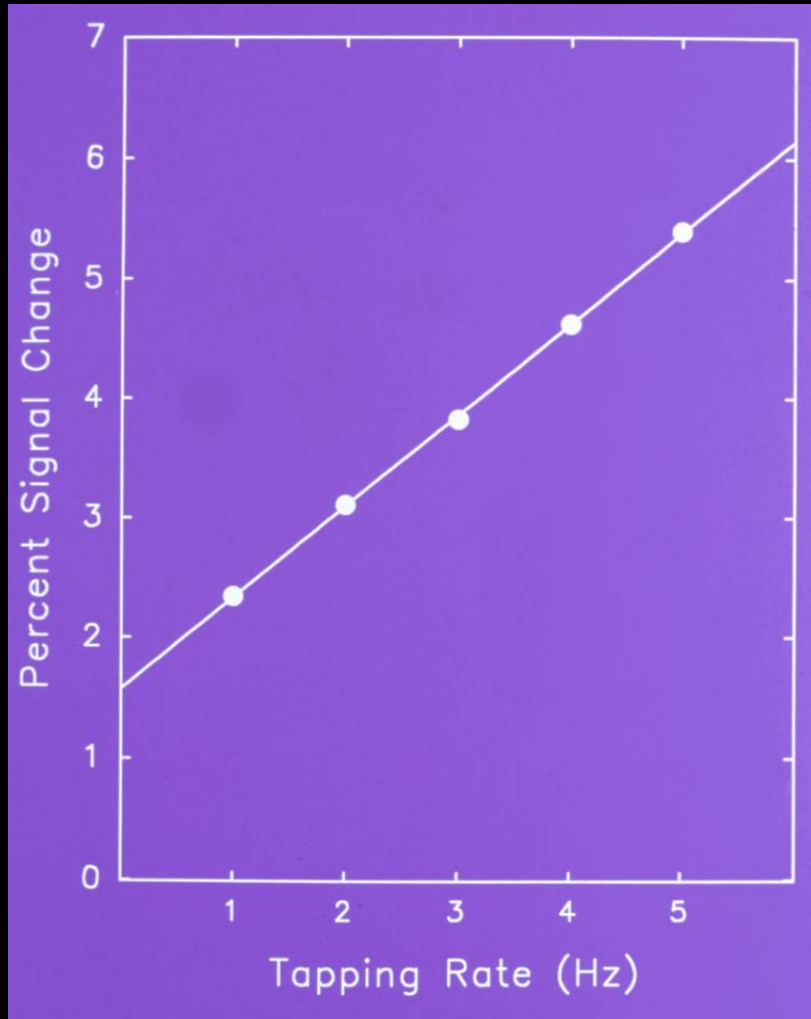
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Performance prediction

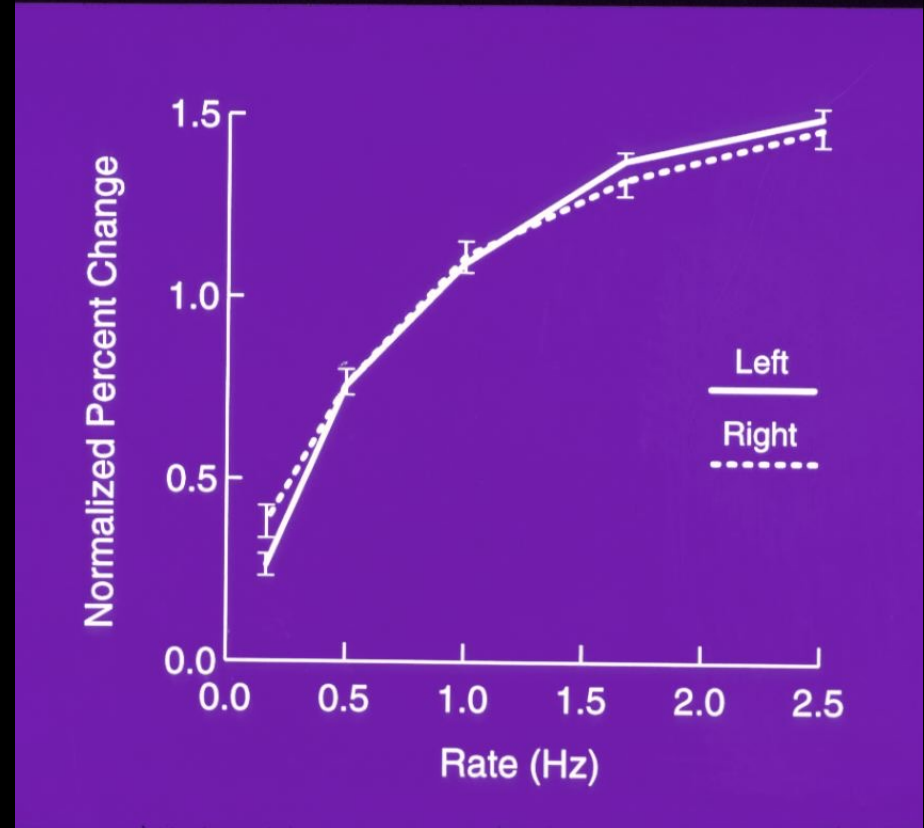


Motor Cortex



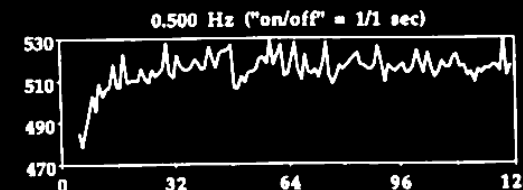
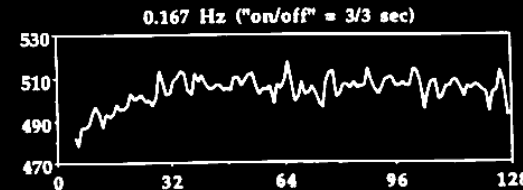
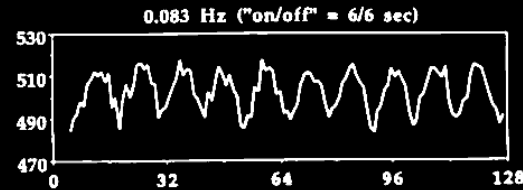
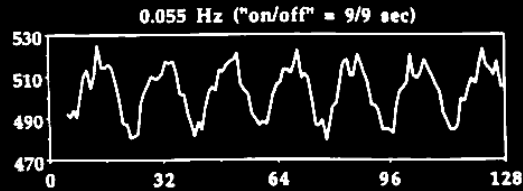
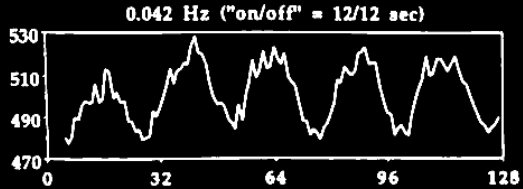
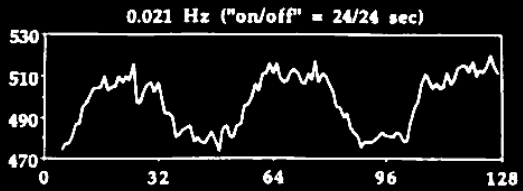
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex



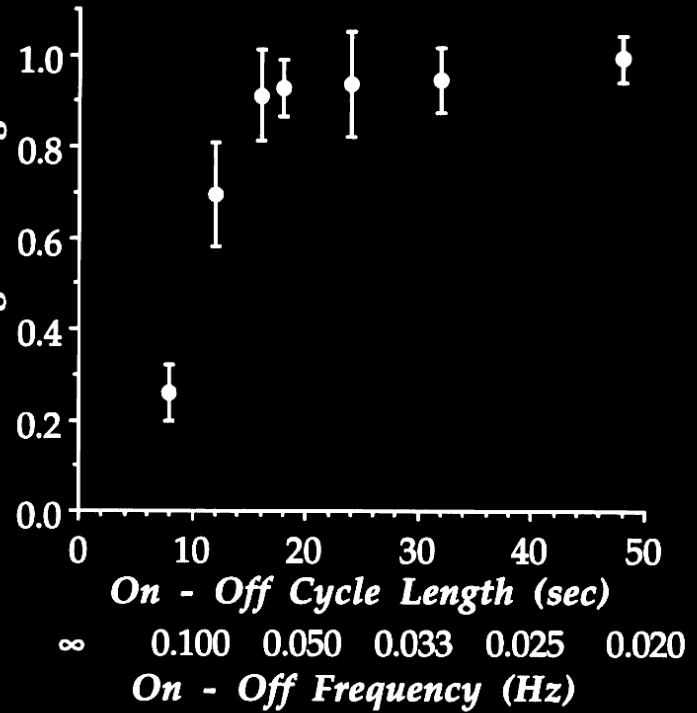
J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38

MRI Signal



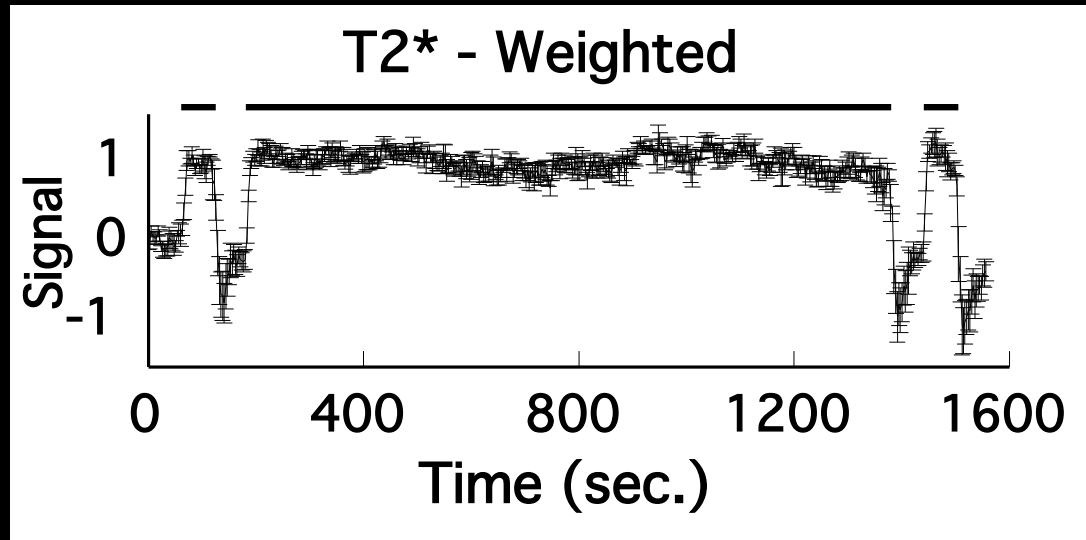
Time (seconds)

Relative Activation - Induced
MR Signal Change

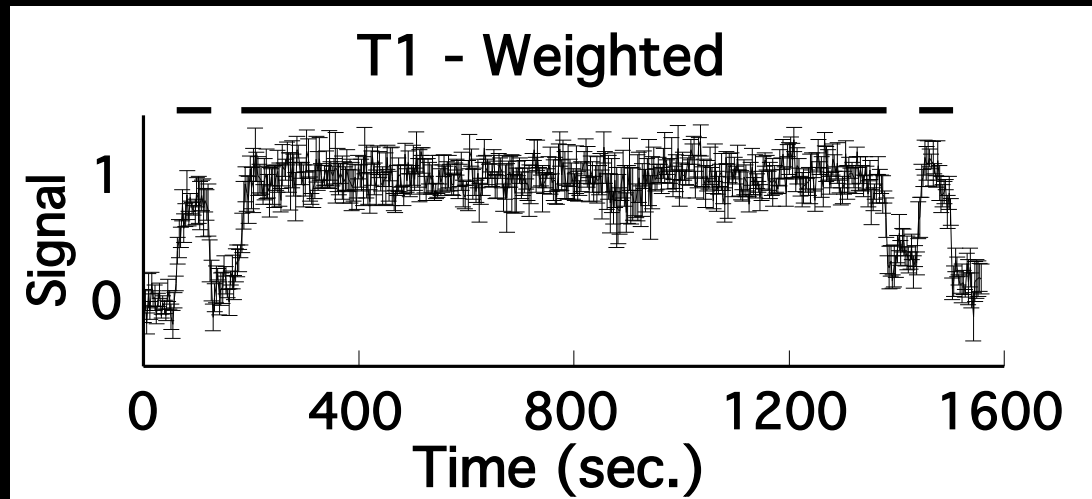


P. A. Bandettini, Functional MRI temporal resolution in "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag, 1999.

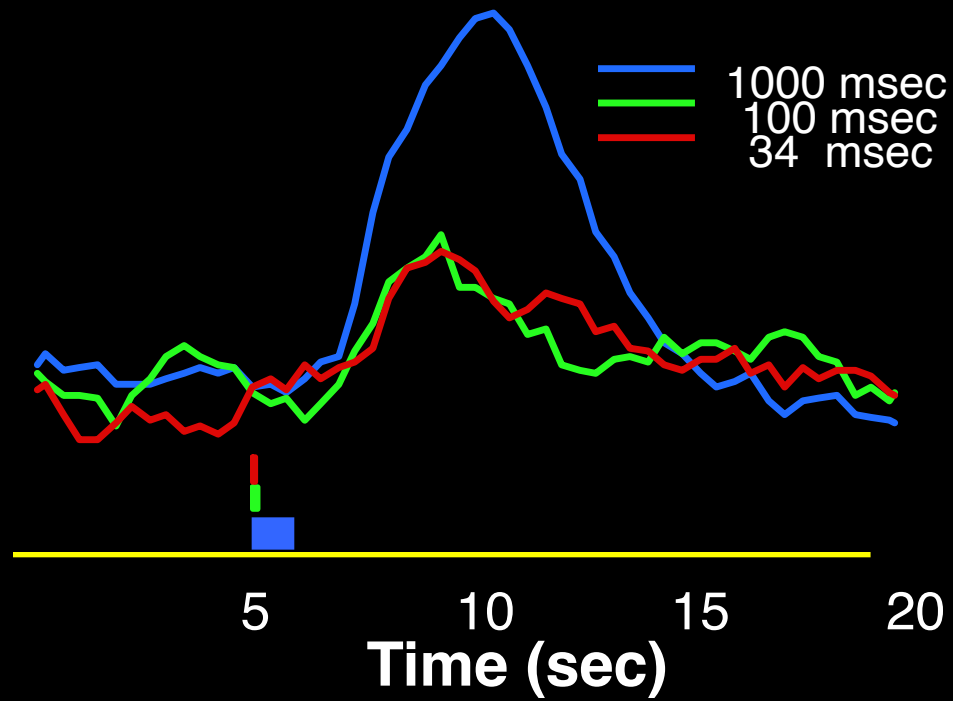
BOLD



Flow

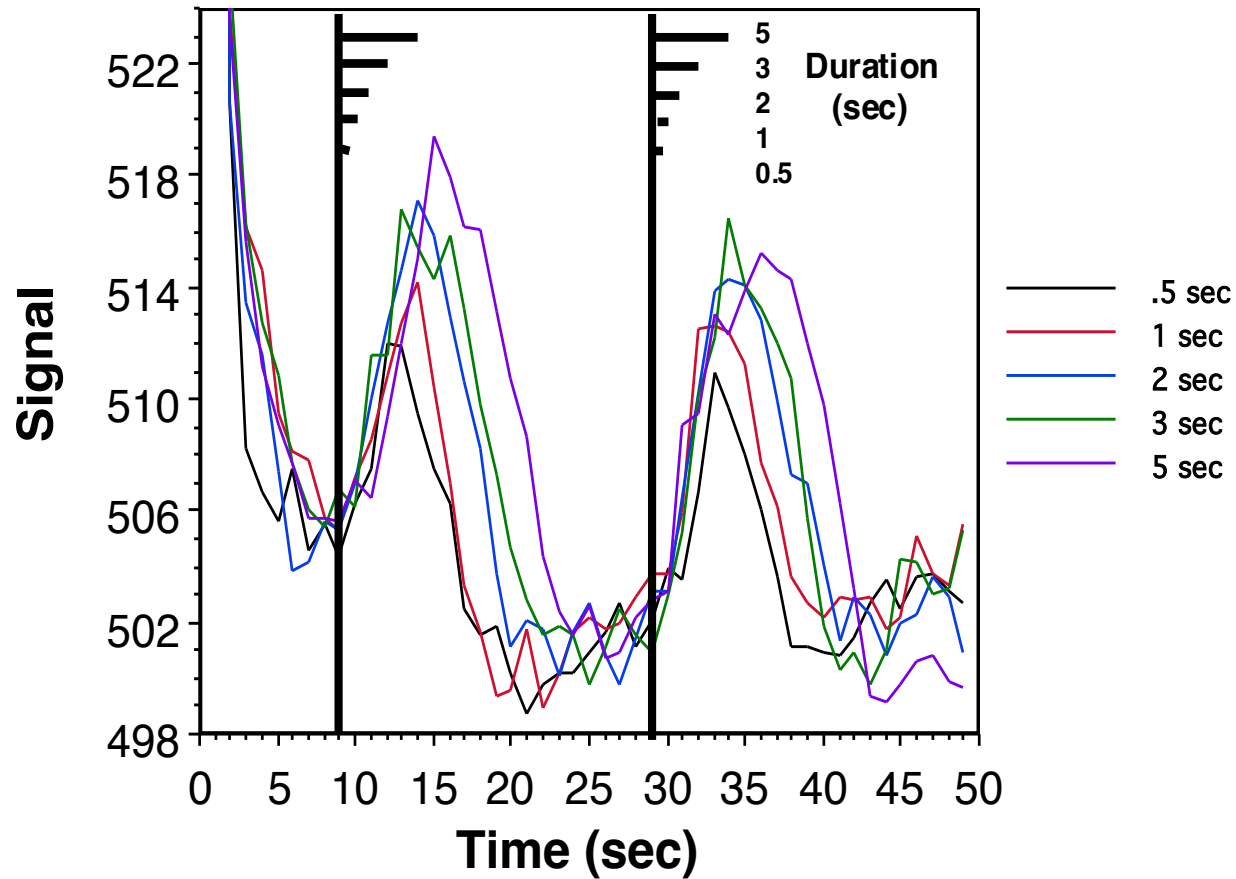


P. A. Bandettini, K. K. Kwong, T. L. Davis, R. B. H. Tootell, E. C. Wong, P. T. Fox, J. W. Belliveau, R. M. Weisskoff, B. R. Rosen, (1997). "Characterization of cerebral blood oxygenation and flow changes during prolonged brain activation." *Human Brain Mapping* 5, 93-109.



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], 3rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

Motor Cortex

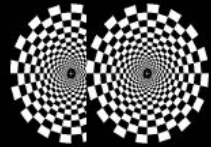


Bandettini, et al., The functional dynamics of blood oxygenation level contrast in the motor cortex, 12'th Proc. Soc. Magn. Reson. Med., New York, p. 1382. (1993).



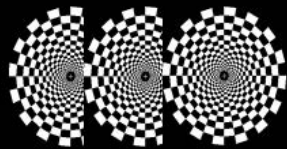
0 sec

20 sec



0 sec 2 sec

20 sec



0 sec 2 sec 4 sec

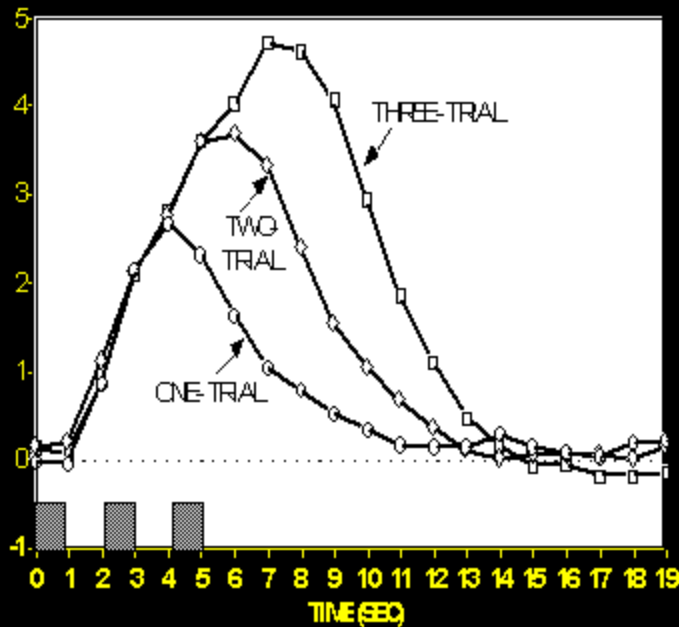
20 sec

♦ Human Brain Mapping 5:329-340(1997) ♦

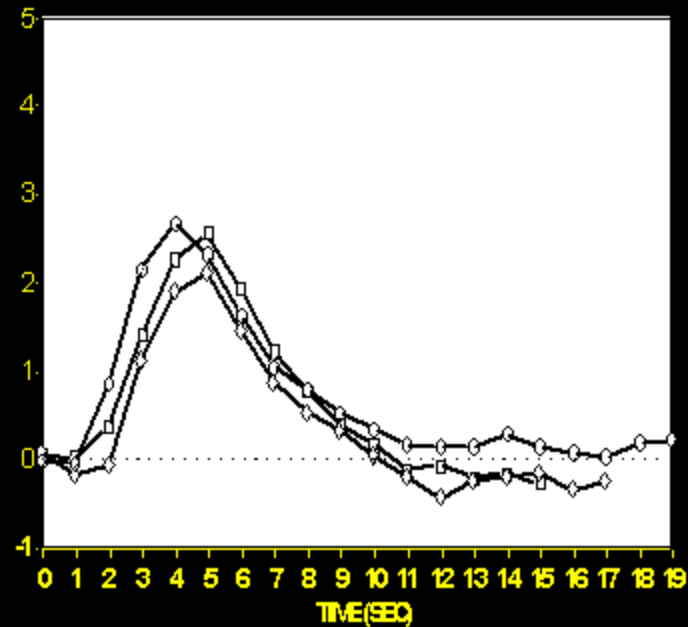
Selective Averaging of Rapidly Presented Individual Trials Using fMRI

Anders M. Dale* and Randy L. Buckner

RAW DATA



ESTIMATED RESPONSES



Neuronal Activation Input Strategies

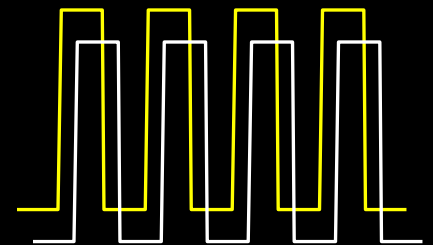
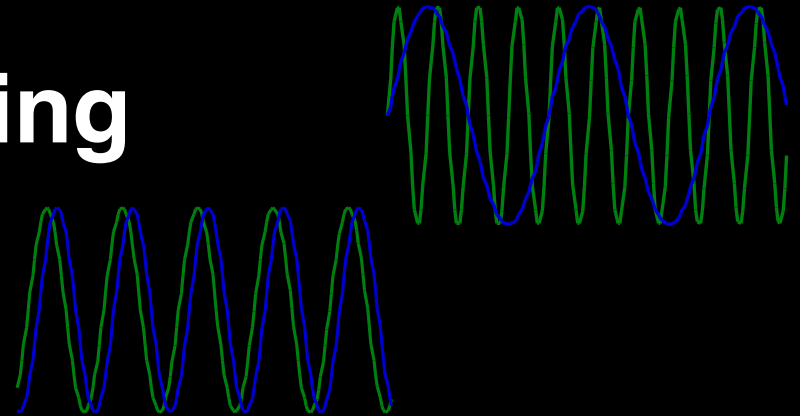
1. Block Design

2. Frequency Encoding

3. Phase Encoding

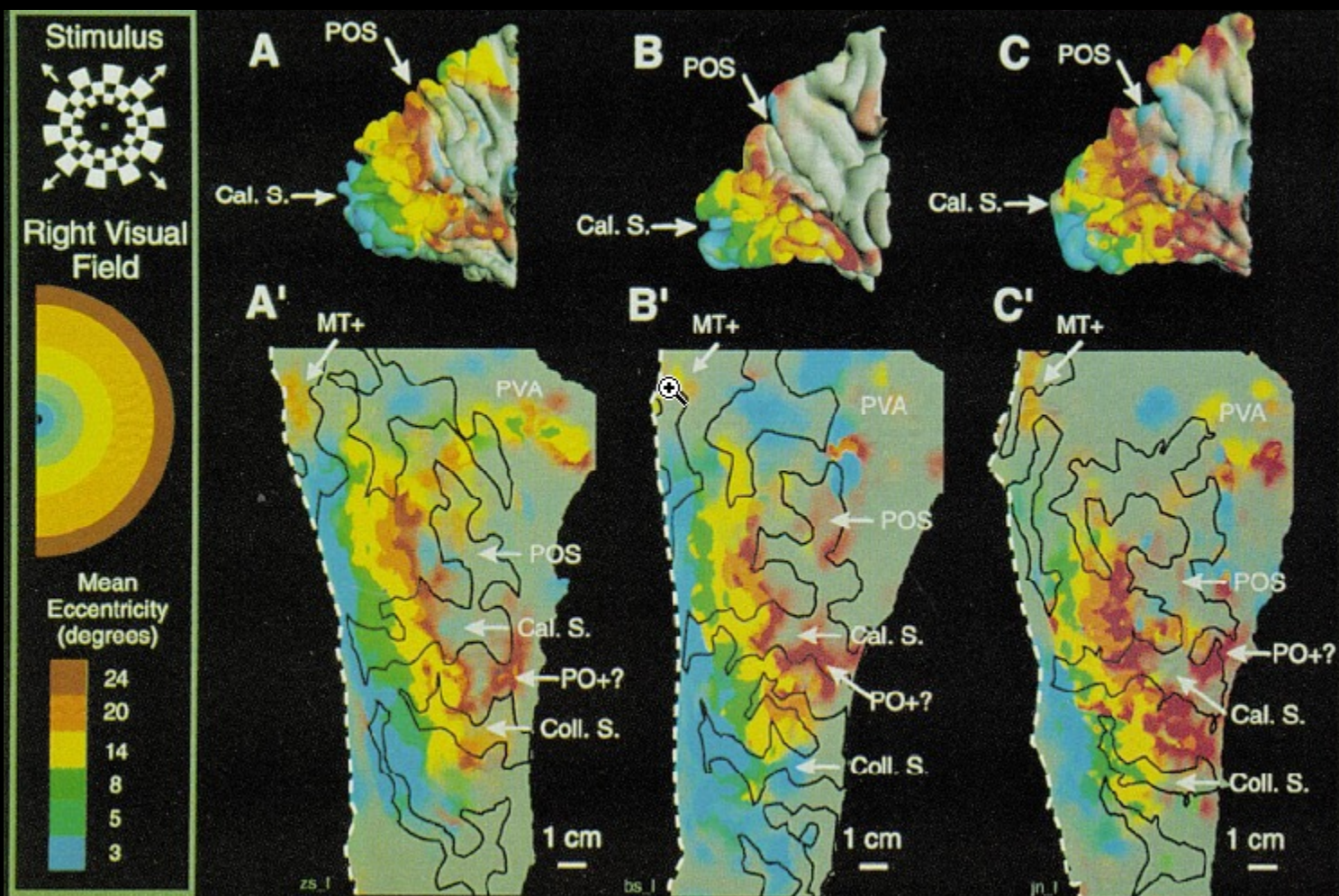
4. Event Related

5. Orthogonal Block Design

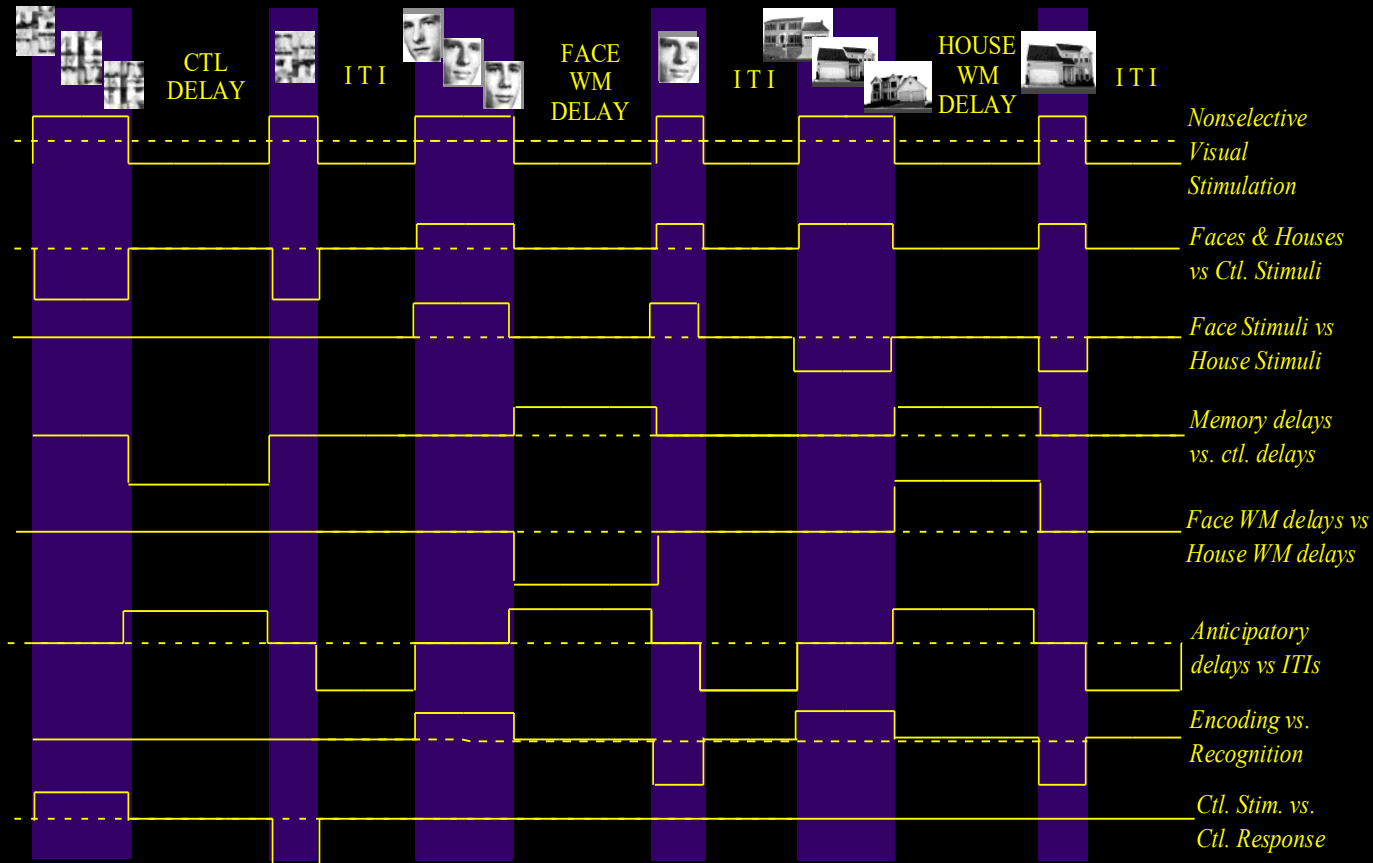


Mapping striate and extrastriate visual areas in human cerebral cortex

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

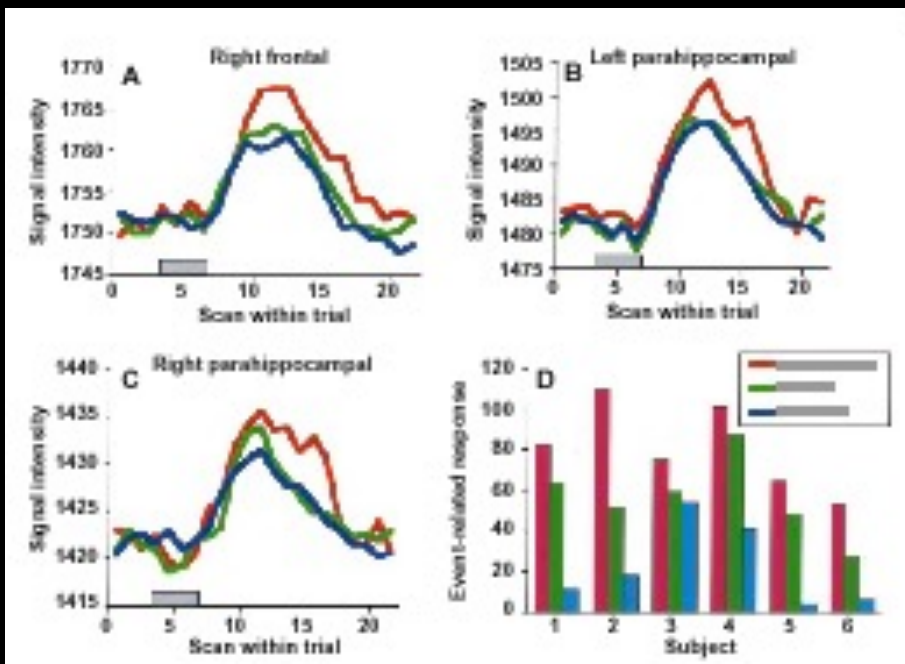
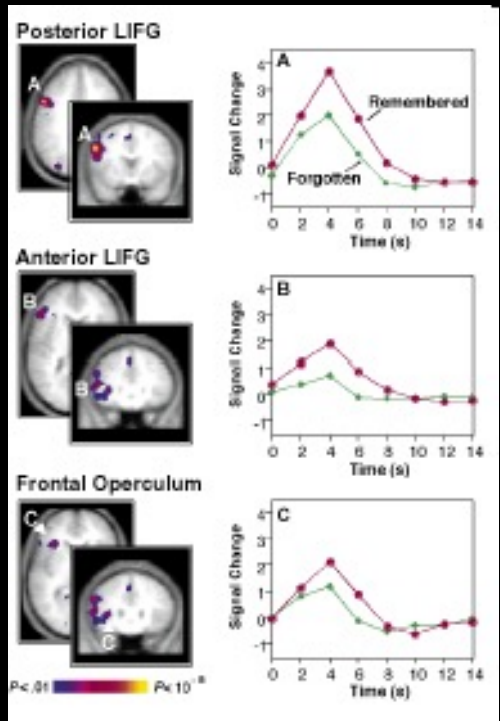
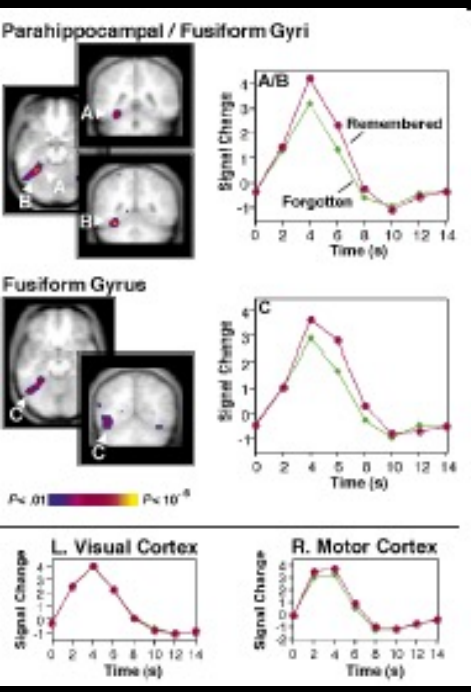
Applications

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



Science, Vol 281, August 1998

Past

Present

Future

Technology

MRI

1.5T,3T, 4T

EPI

Local Human Head Gradient Coils

ASL

BOLD

EPI on Clin. Syst.

Nav. pulses

Spiral EPI

Multi-shot fMRI

Diff. tensor

Real time fMRI

Quant. ASL

Dynamic IV volume

Simultaneous ASL and BOLD

Mg⁺

Venography

Z-shim

Baseline Susceptibility

7T

SENSE

Current Imaging?

Methodology

Baseline Volume

IVIM

Correlation Analysis

Parametric Design

Surface Mapping

Phase Mapping

Linear Regression

Event-related

Motion Correction

Multi-Modal Mapping

Free-behavior Designs

Mental Chronometry

Deconvolution

CO₂ Calibration

Interpretation

Blood T2

Hemoglobin

BOLD models

B₀ dep.

TE dep

SE vs. GE

NIRS Correlation

Veins

PET correlation

IV vs EV

Pre-undershoot

Resolution Dep.

Post-undershoot

CO₂ effect

NIRS Correlation

Inflow

Fluctuations

Balloon Model

PSF of BOLD

Extended Stim.

Linearity

Metab. Correlation

Optical Im. Correlation

Electrophys. correlation

Applications

Complex motor Language

Imagery

Memory

Emotion

Motor learning

Children

Tumor vasc.

Drug effects

BOLD -V1, M1, A1

Presurgical

Attention

Ocular Dominance

Volume - Stroke

V1, V2..mapping

Priming/Learning

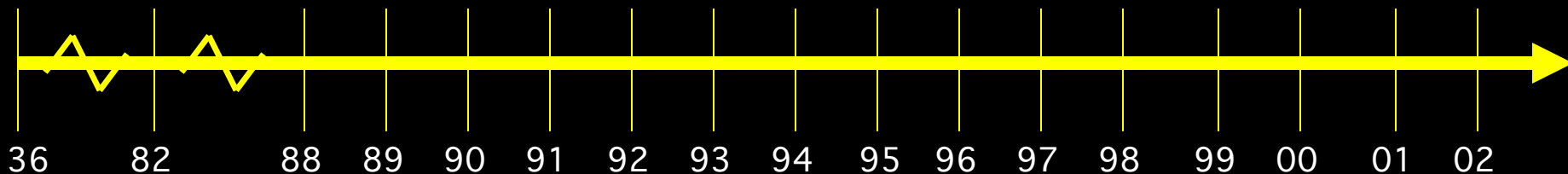
Clinical Populations

Δ Volume-V1

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

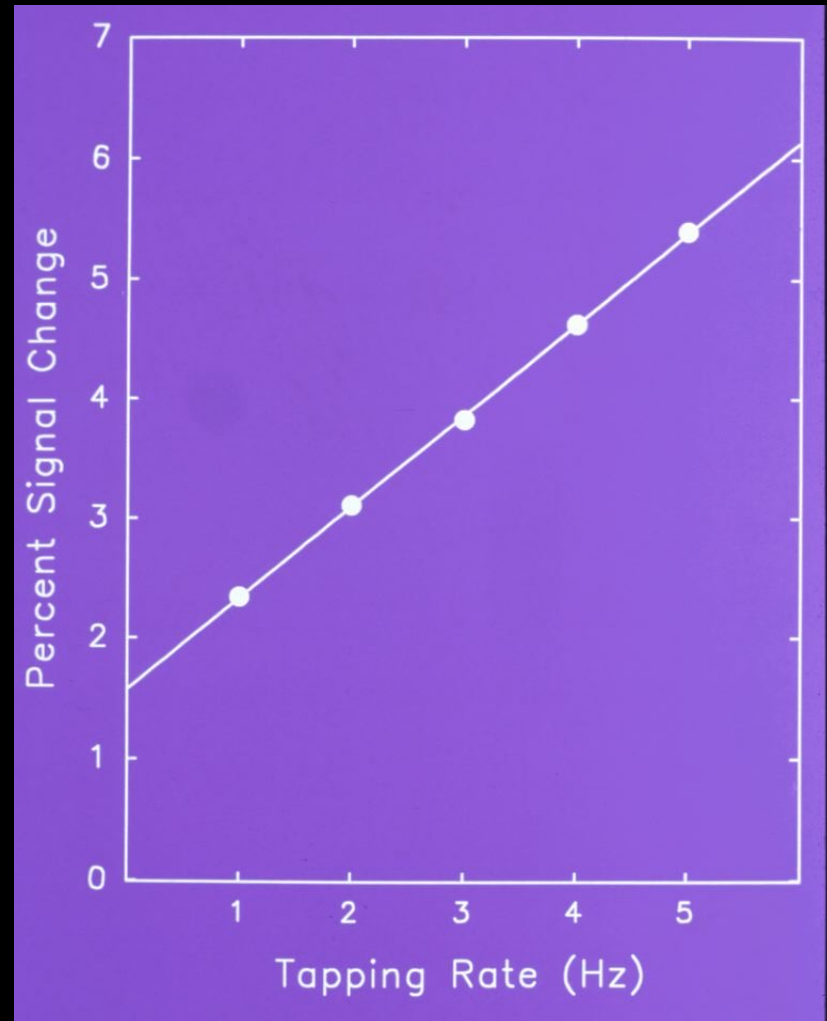
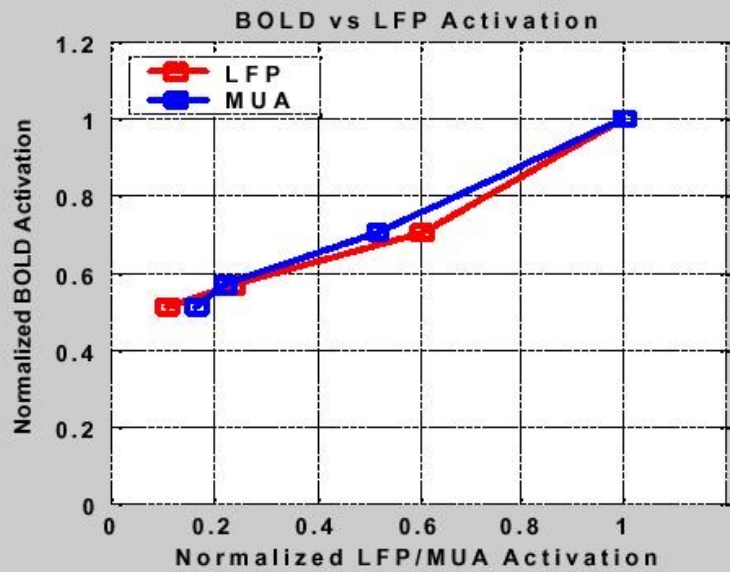
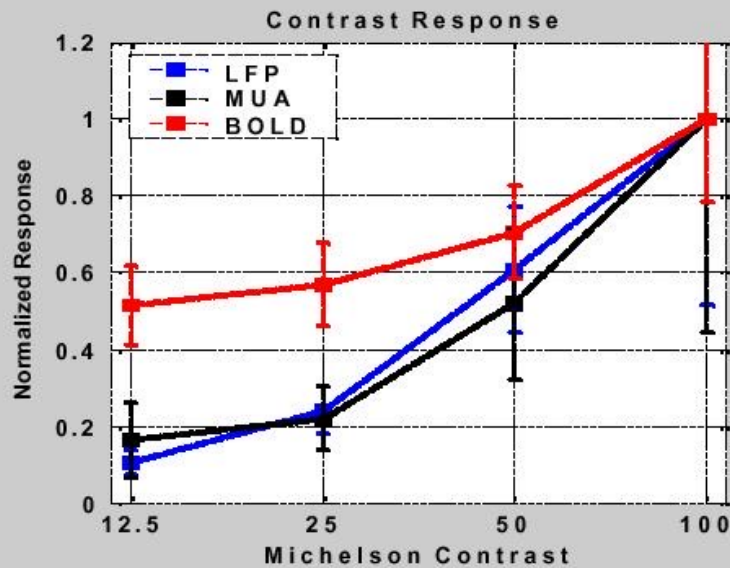
Δ Deoxy-Hb

-

-

+



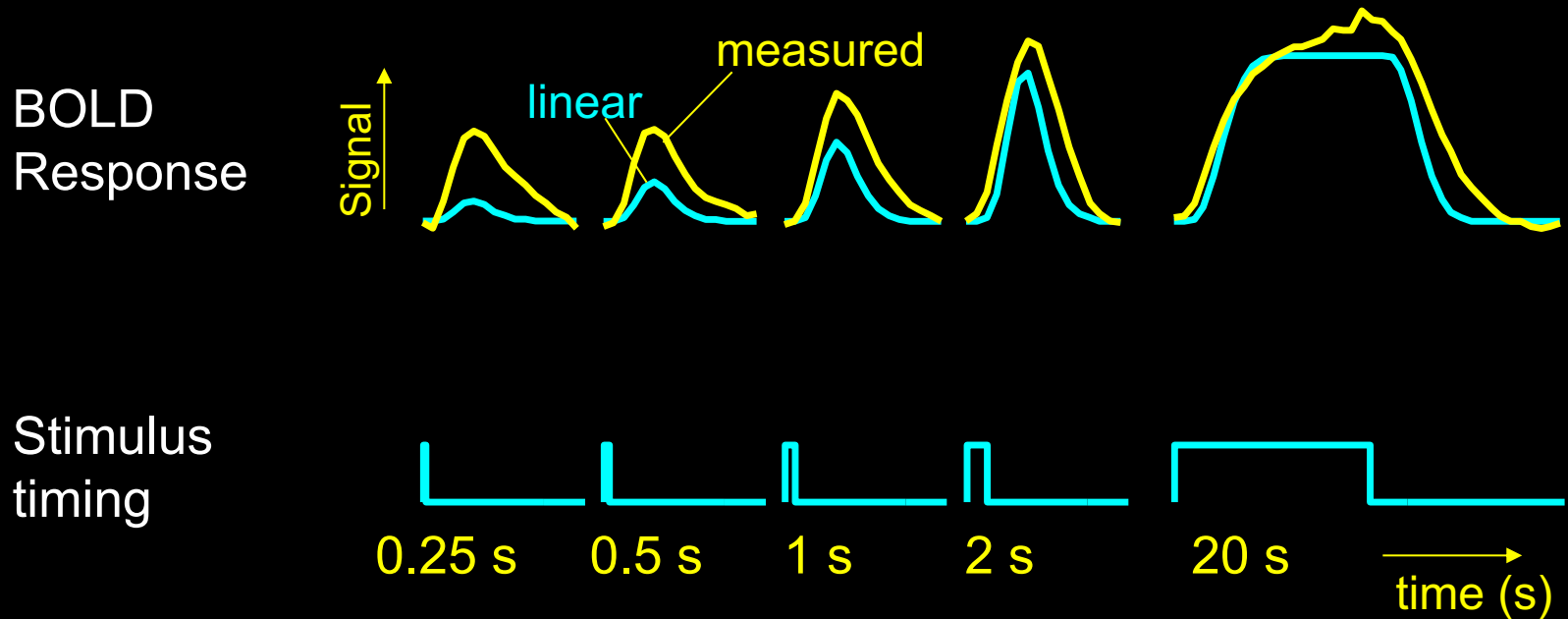


Logothetis et al. (2001) “Neurophysiological investigation of the basis of the fMRI signal” *Nature*, 412, 150-157

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.

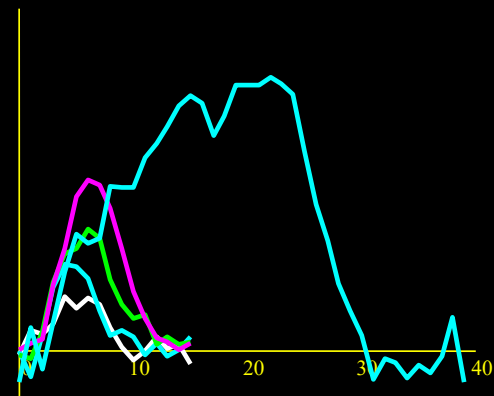
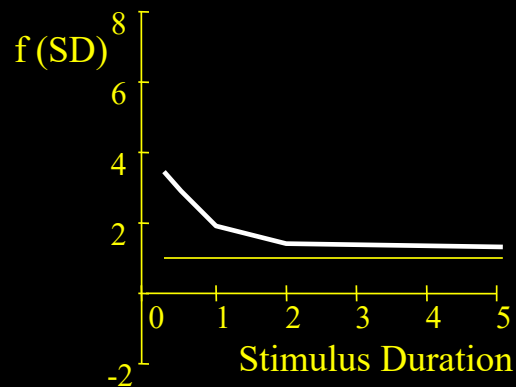
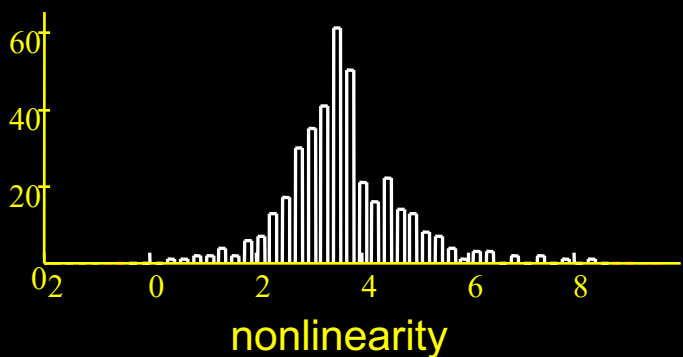
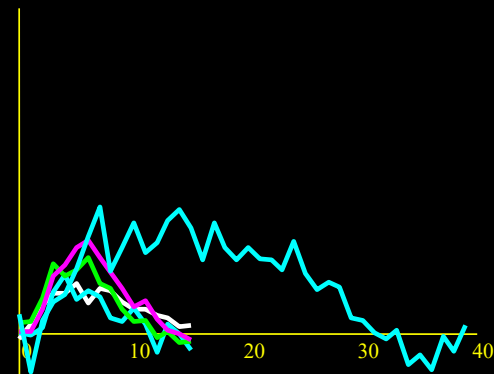
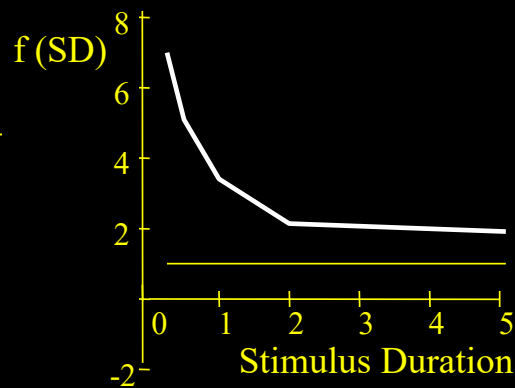
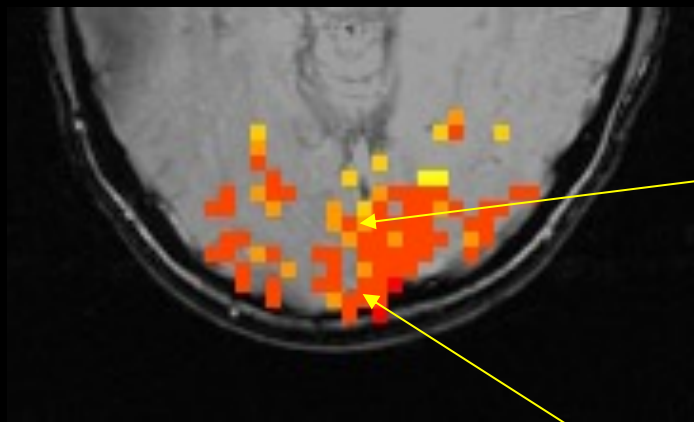
Dynamic Nonlinearity Assessment

Different stimulus “ON” periods



Brief stimuli produce larger responses than expected

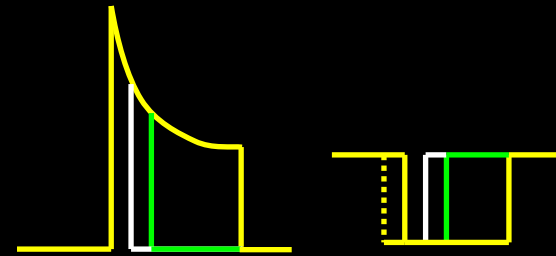
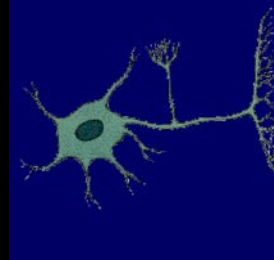
Spatial Heterogeneity of BOLD Nonlinearity



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

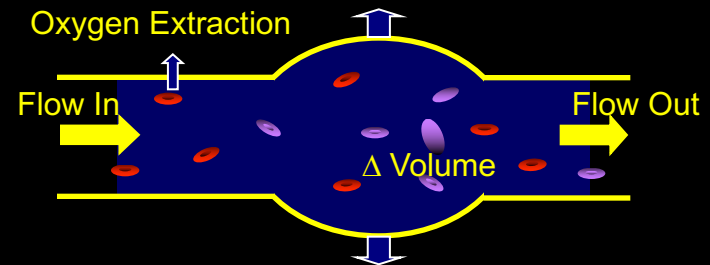
Sources of this Nonlinearity

- Neuronal



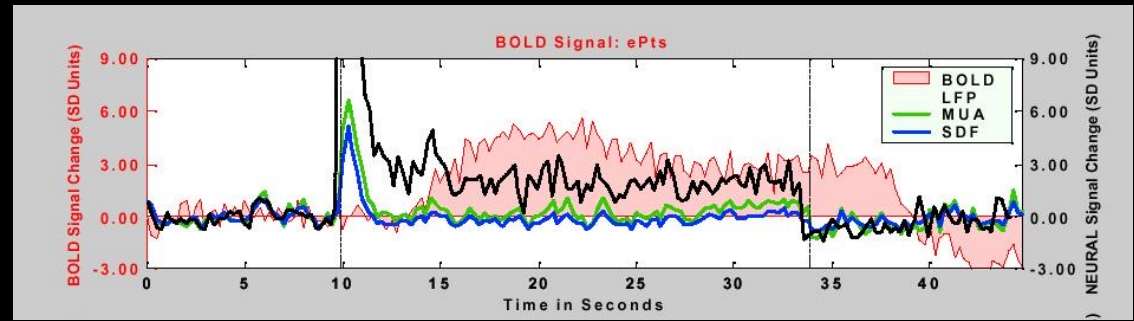
- Hemodynamic

- Oxygen extraction
- Blood volume dynamics

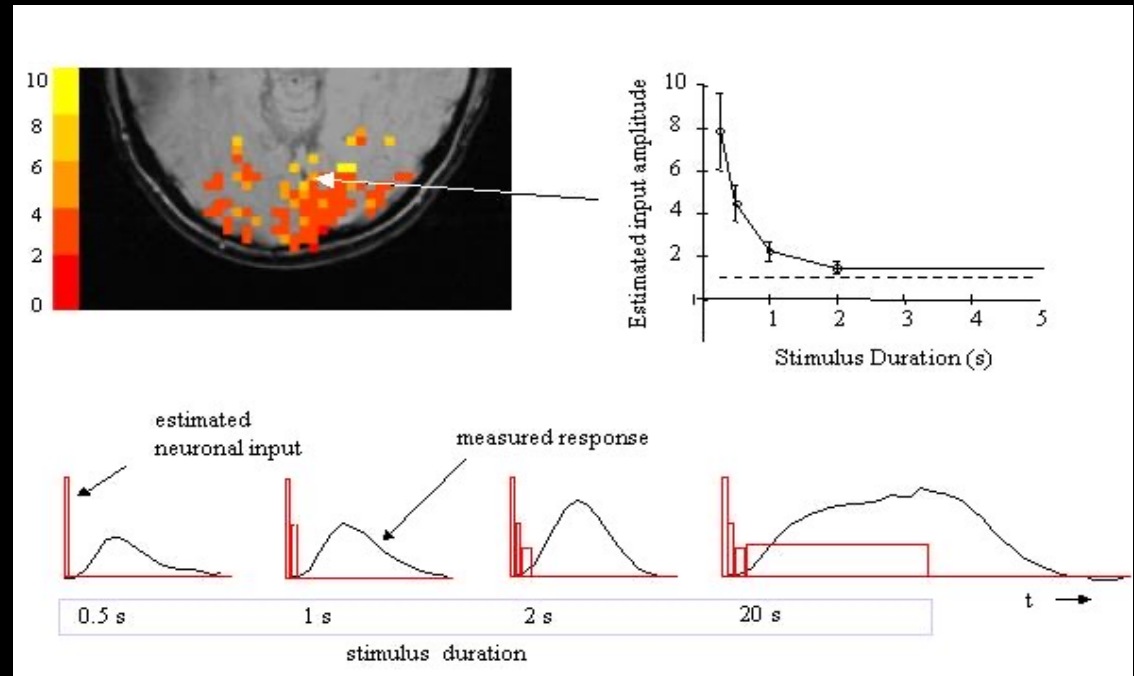


BOLD Correlation with Neuronal Activity

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

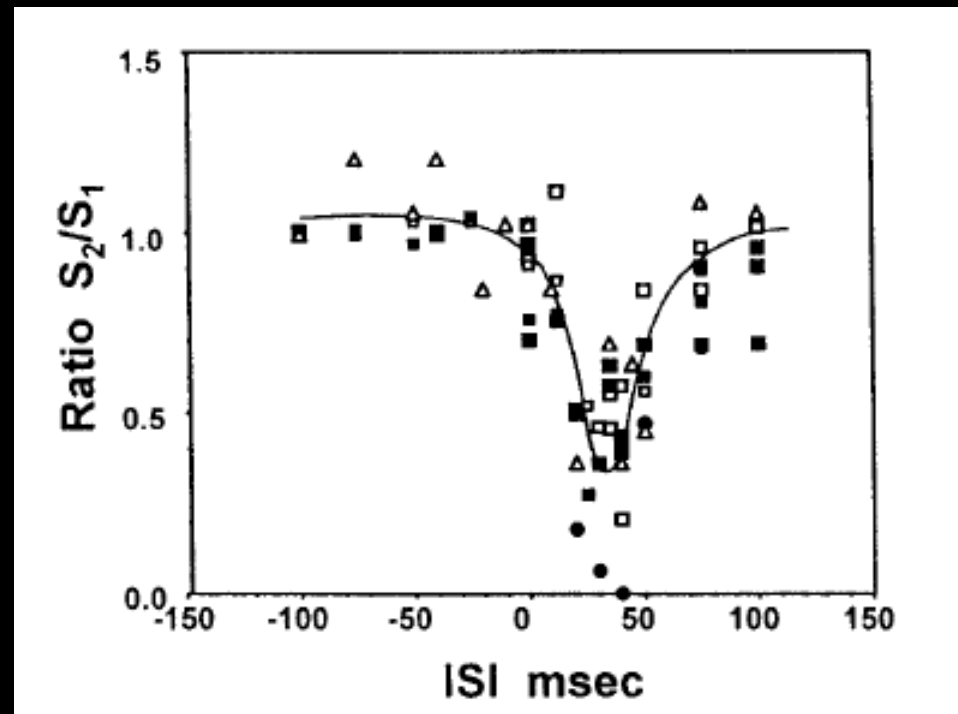


P. A. Bandettini and L. G. Ungerleider, (2001) “From neuron
to BOLD: new connections.”
Nature Neuroscience, 4: 864-866.



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[§]

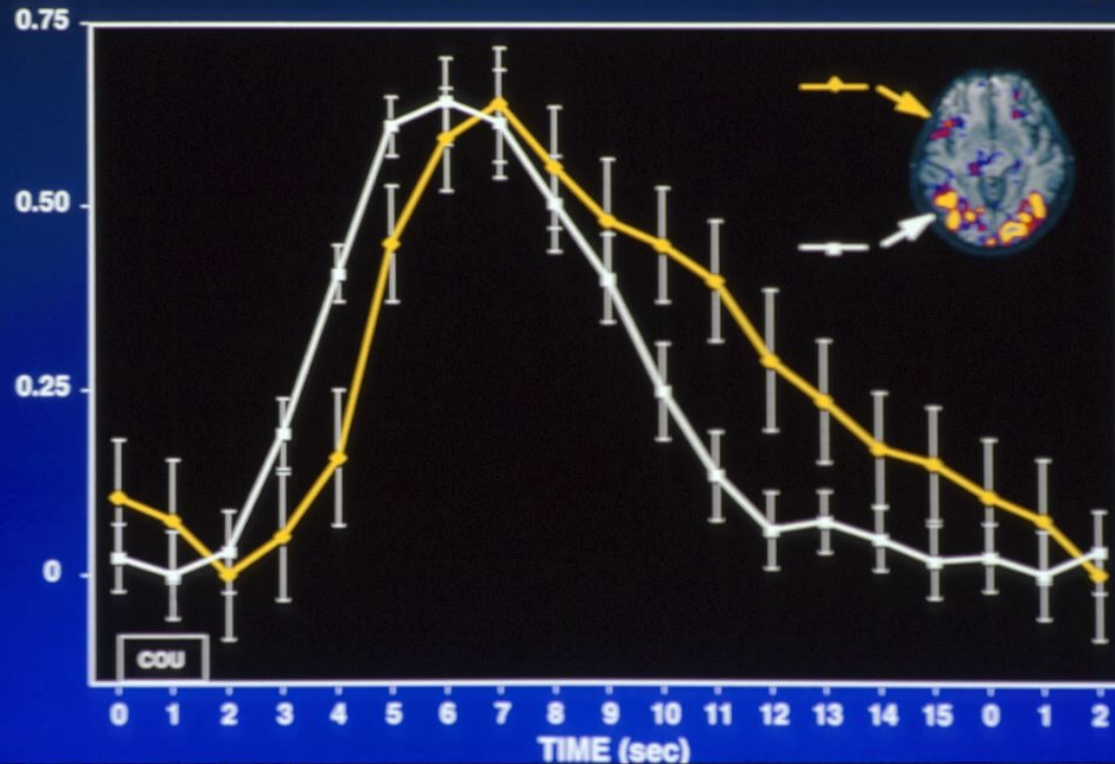


Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging

(neuroimaging/single trial/language/prefrontal)

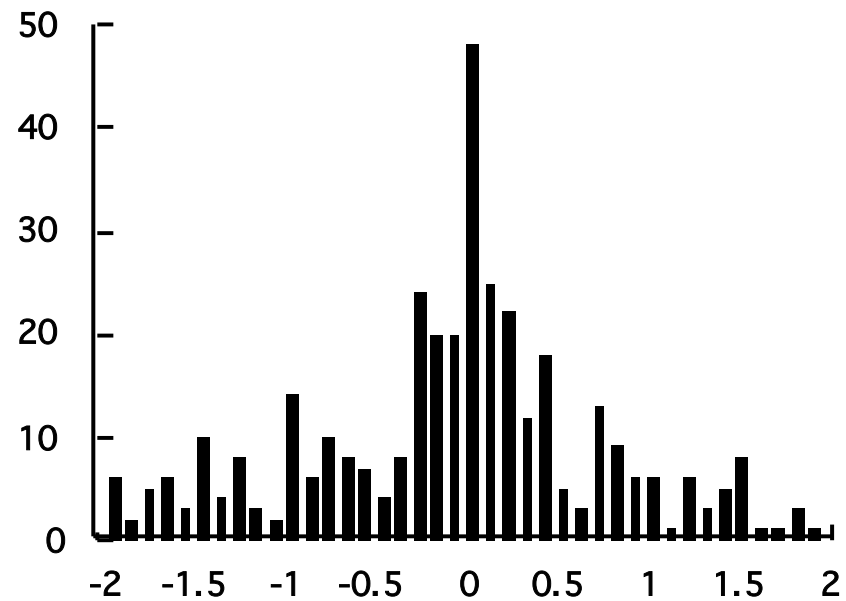
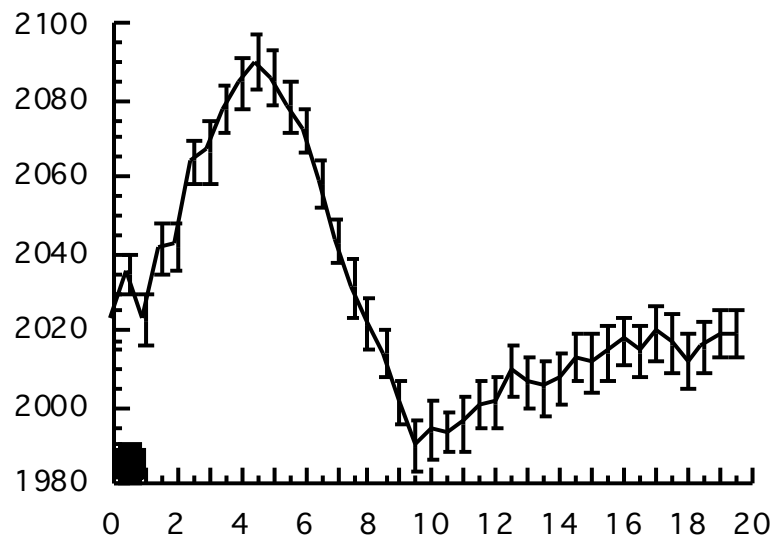
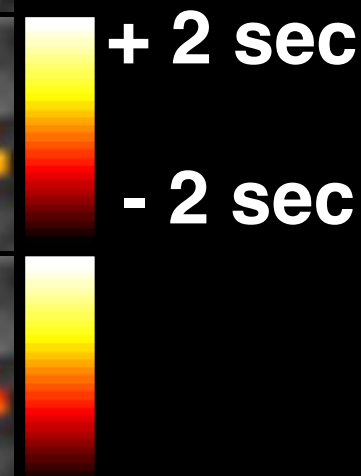
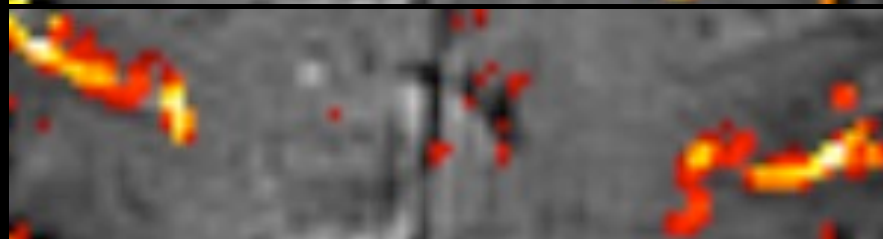
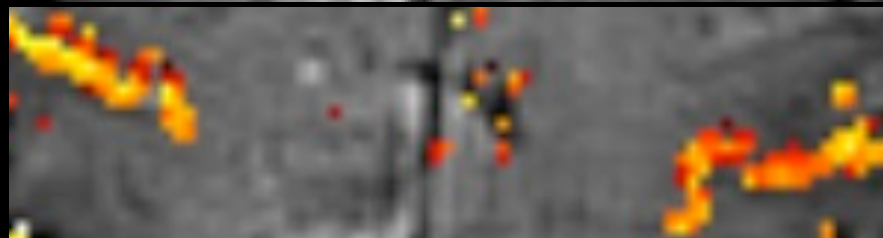
RANDY L. BUCKNER^{†‡§¶}, PETER A. BANDETTINI^{†‡}, KATHLEEN M. O'CRAVEN^{†||}, ROBERT L. SAVOY^{†||},
STEVEN E. PETERSEN^{**††}, MARCUS E. RAICHEL^{§**††}, AND BRUCE R. ROSEN^{†‡}

Time Course Comparison Across Brain Regions

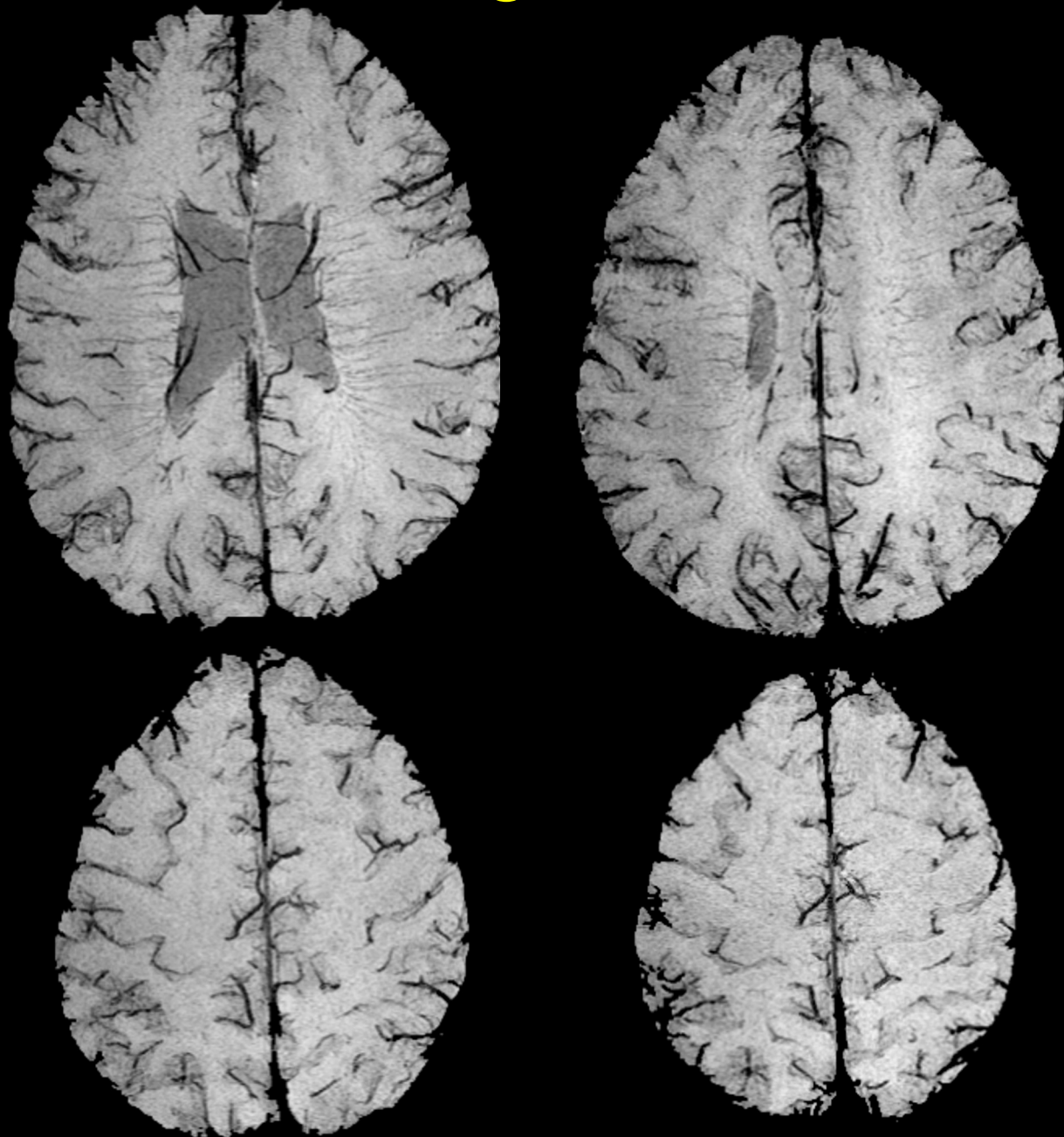


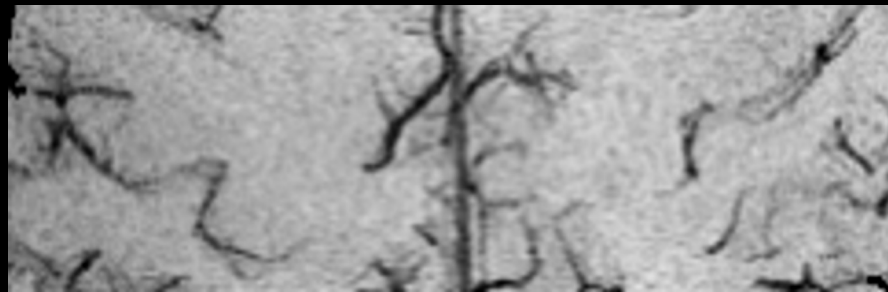
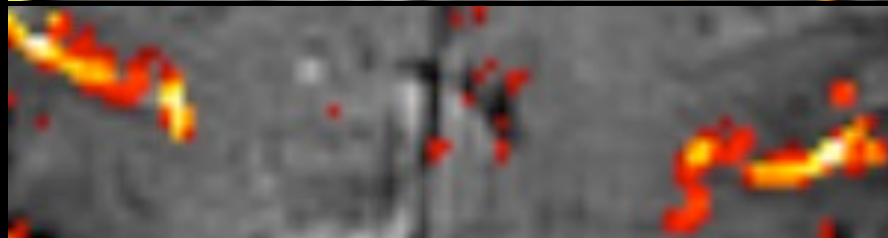
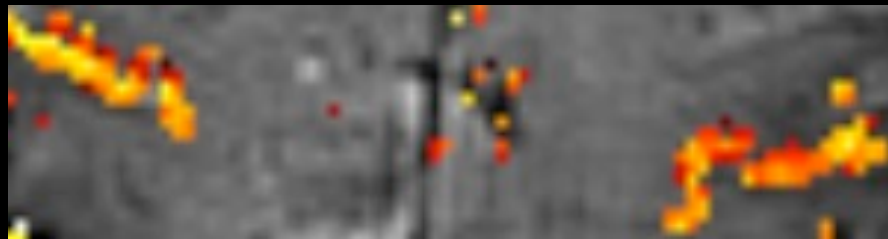
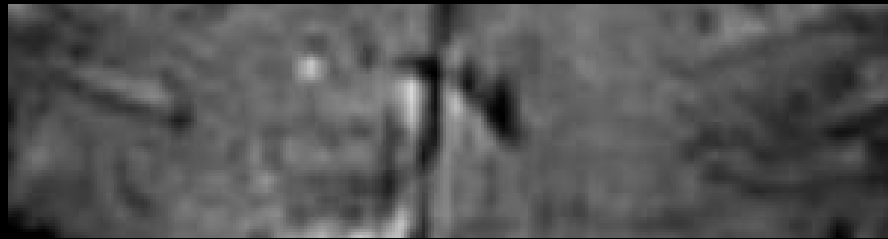
Latency

Magnitude



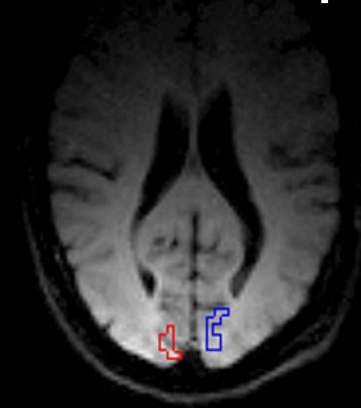
Venograms (3T)



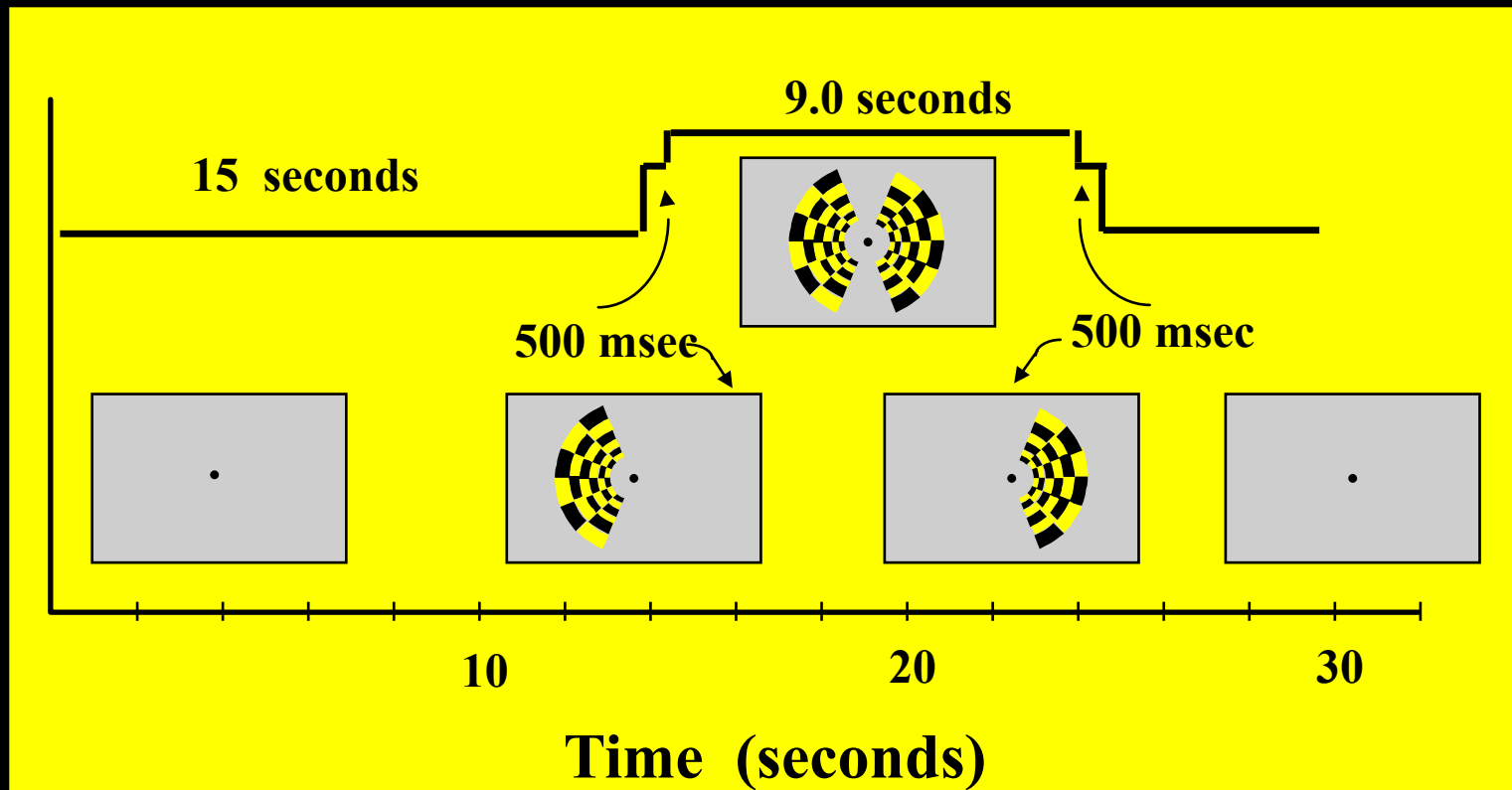


Hemi-Field Experiment

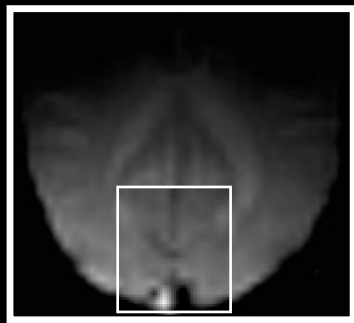
Left Hemisphere



Right Hemisphere

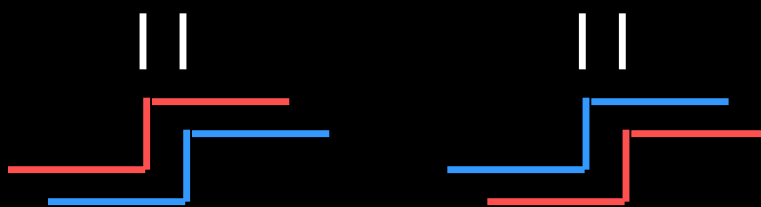


Calibration Techniques.....



500 ms

500 ms



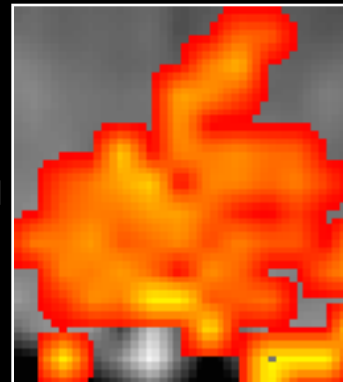
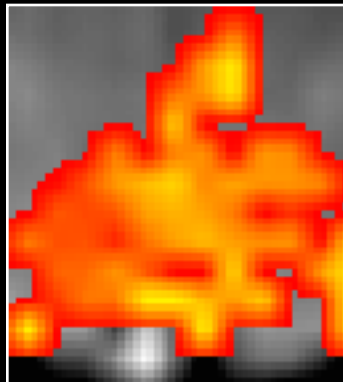
Right Hemifield

Left Hemifield

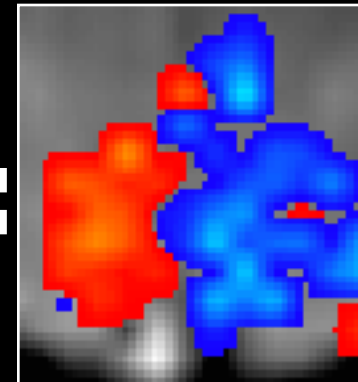
+ 2.5 s

0 s

- 2.5 s



=

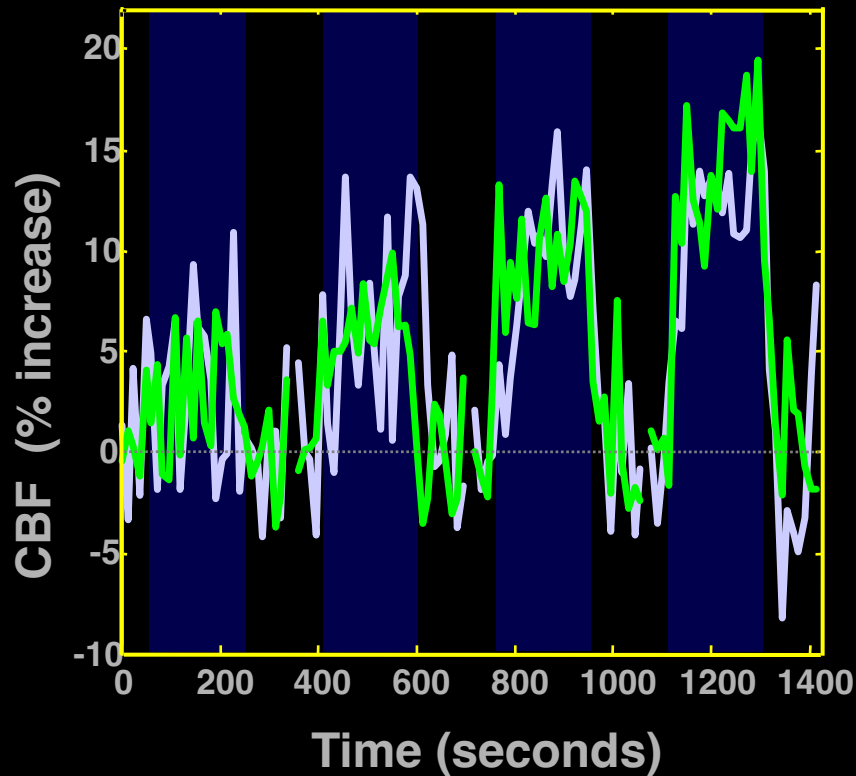


Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex

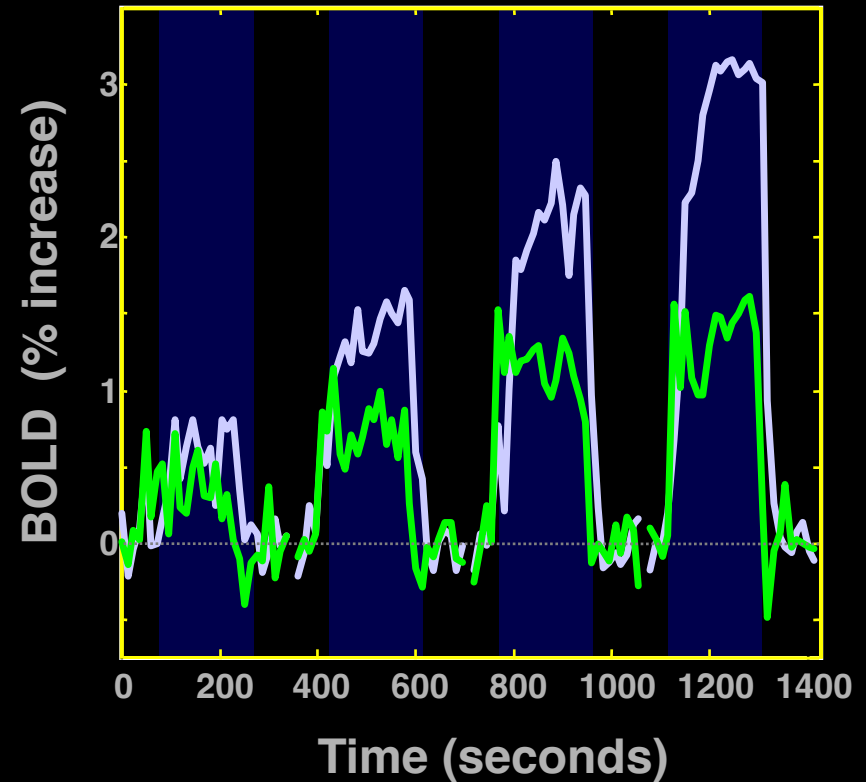
RICHARD D. HOGE^{*†}, JEFF ATKINSON^{*}, BRAD GILL^{*}, GÉRARD R. CRELIER^{*}, SEAN MARRETT[‡], AND G. BRUCE PIKE^{*}

^{*}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

CBF



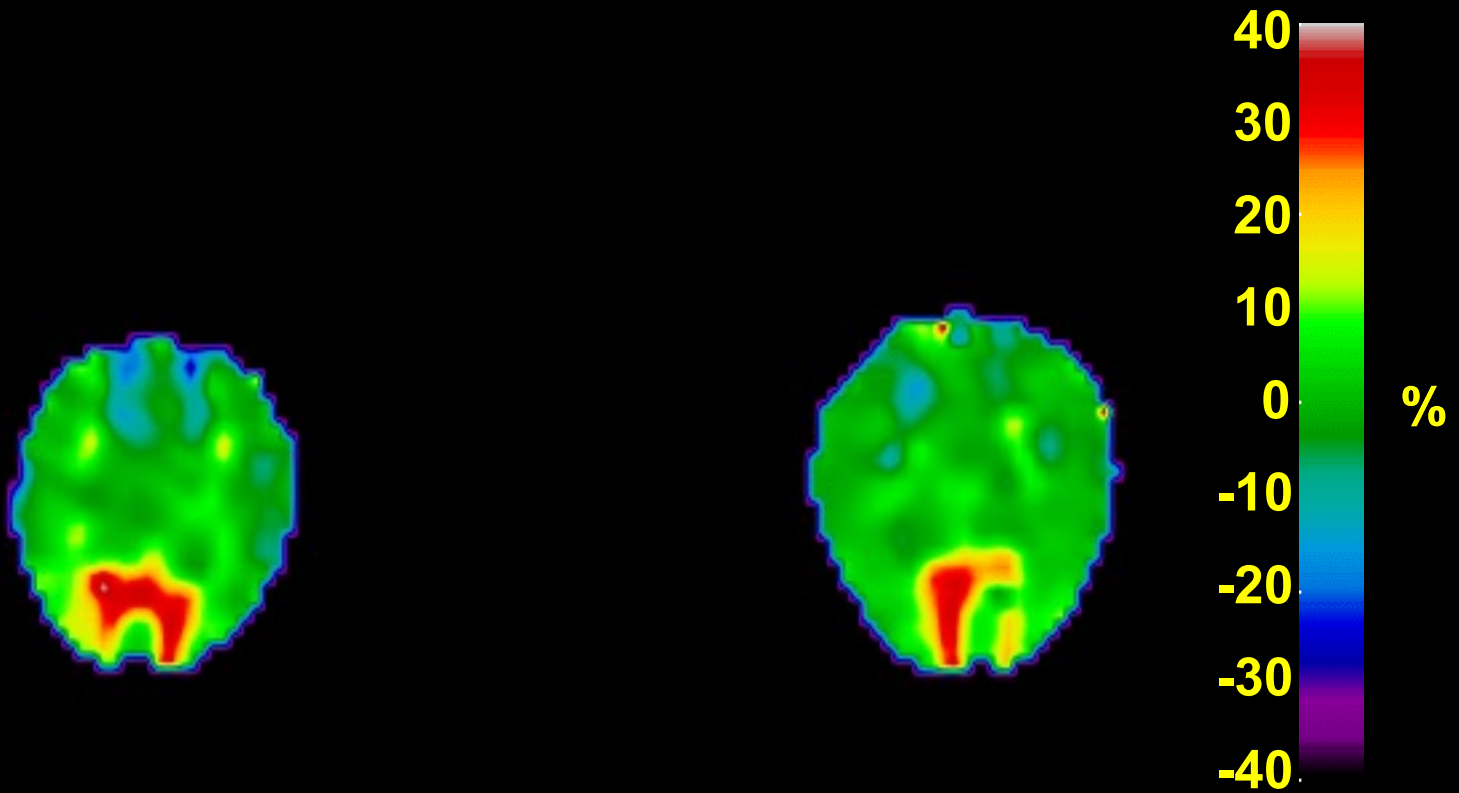
BOLD



Simultaneous Perfusion and BOLD imaging during
graded visual activation and hypercapnia

N=12

Computed CMRO₂ Changes

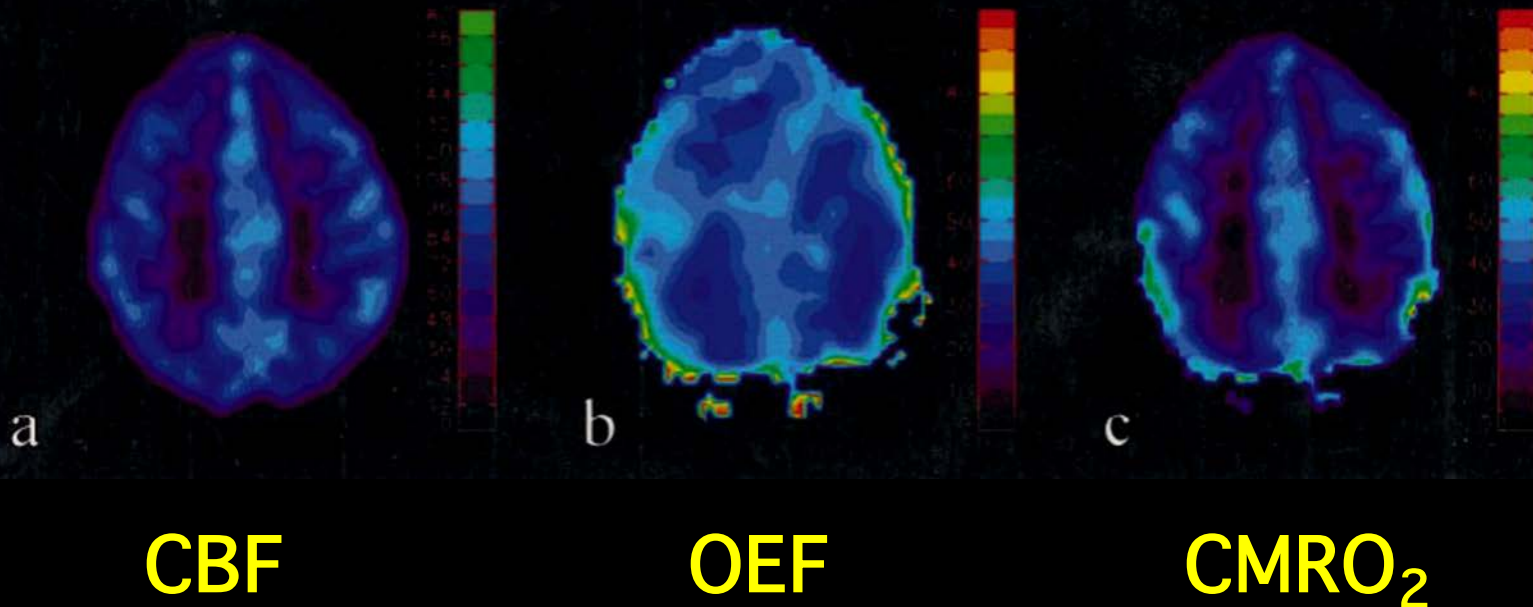


Subject 1

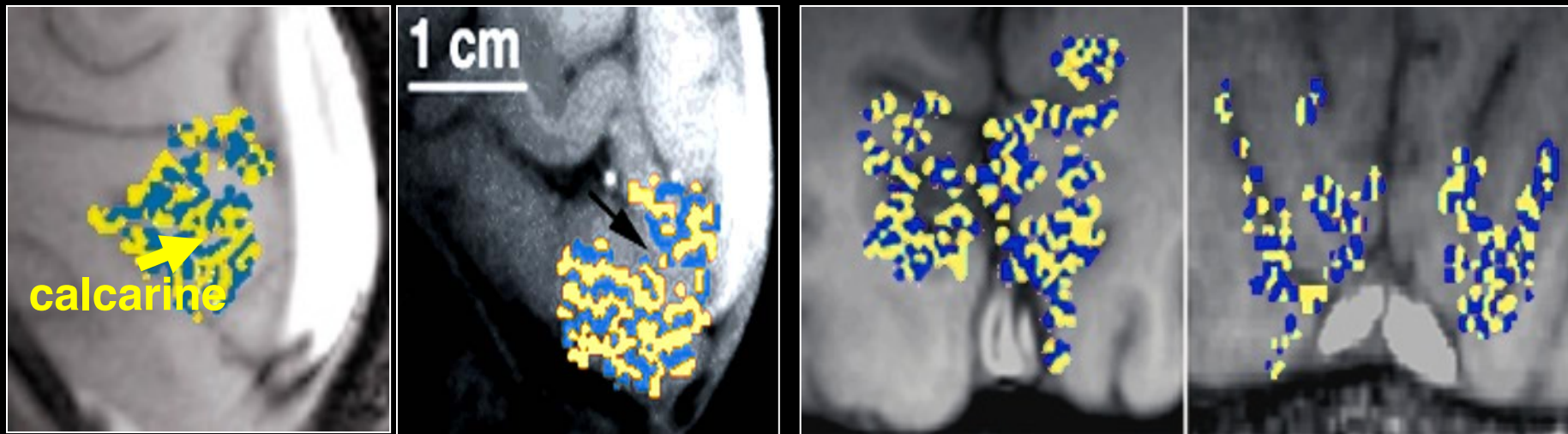
Subject 2

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

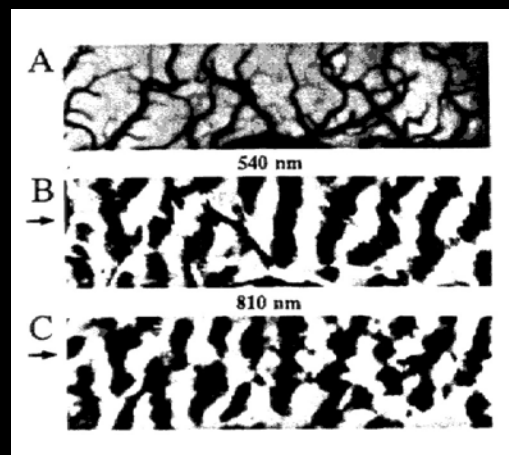
Hongyu An,¹ Weili Lin,^{2*} Azim Celik³ and Yueh Z. Lee²



Ocular Dominance Column Mapping using fMRI



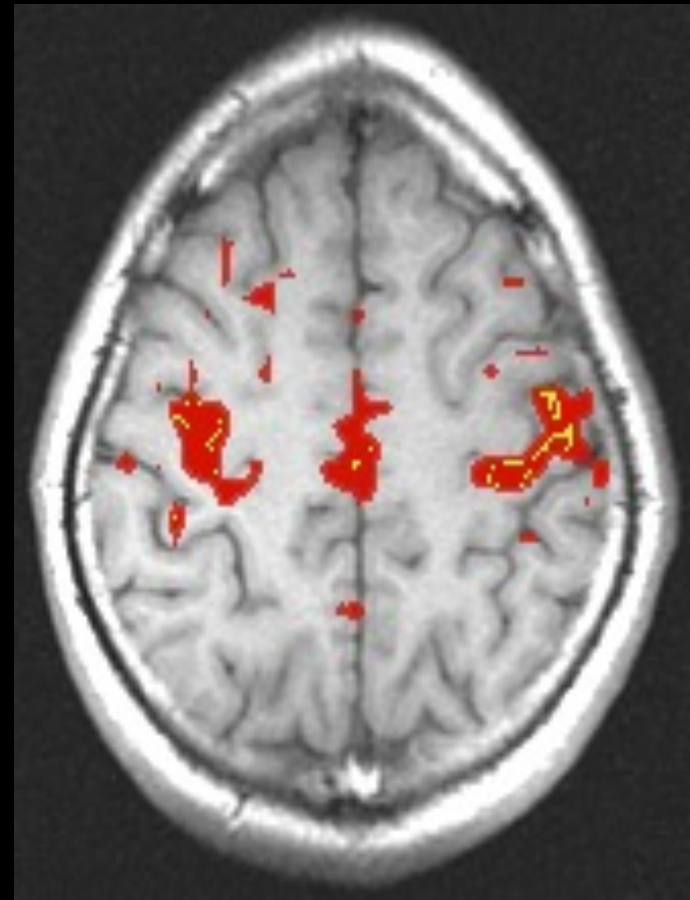
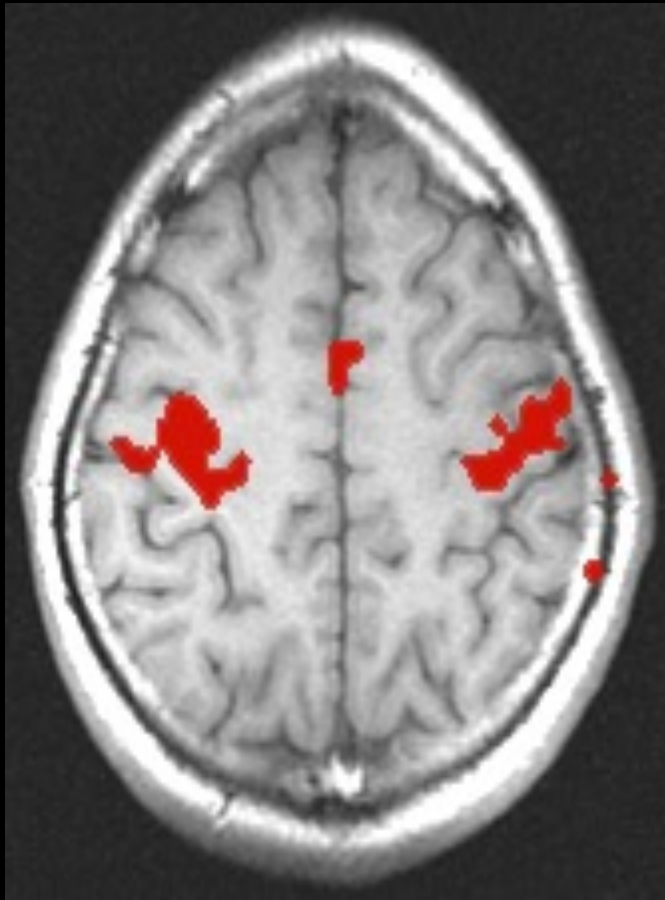
Menon, R. S., S. Ogawa, et al. (1997). "Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging." *J Neurophysiol* 77(5): 2780-7.



Optical Imaging

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

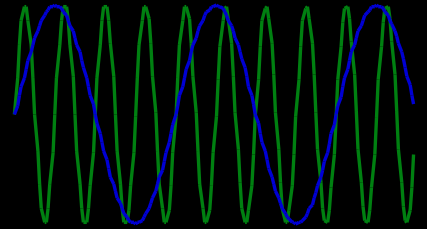
Resting Hemodynamic Autocorrelations



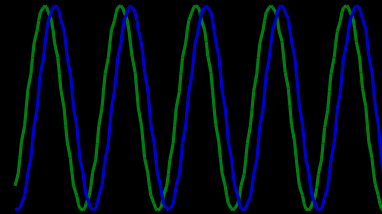
Neuronal Activation Input Strategies

1. Block Design

2. Frequency Encoding

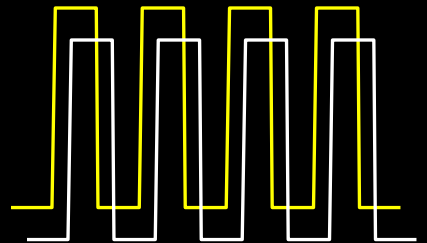


3. Phase Encoding



4. Event Related

5. Orthogonal Block Design



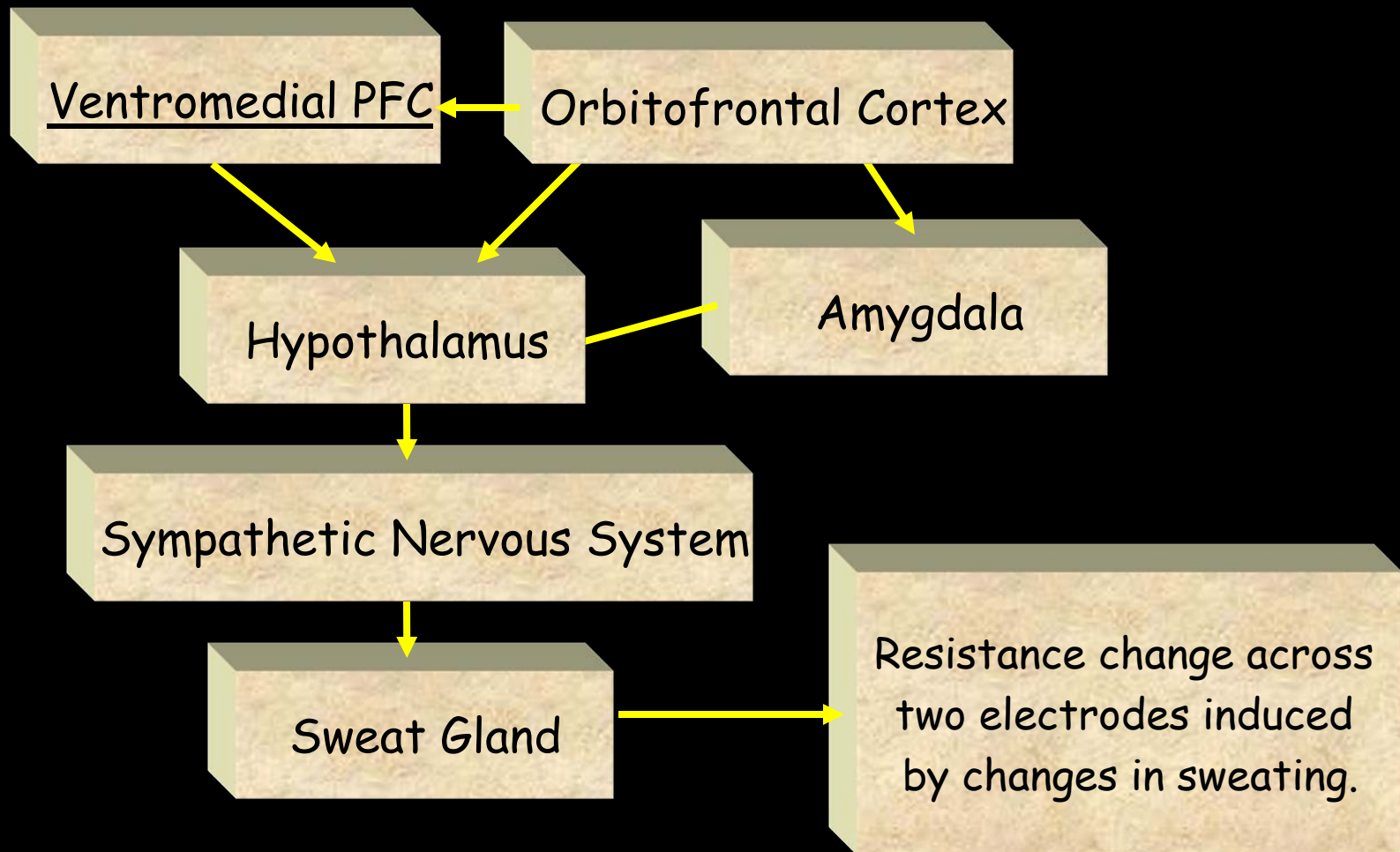
6. Free Behavior Design

Free Behavior Design

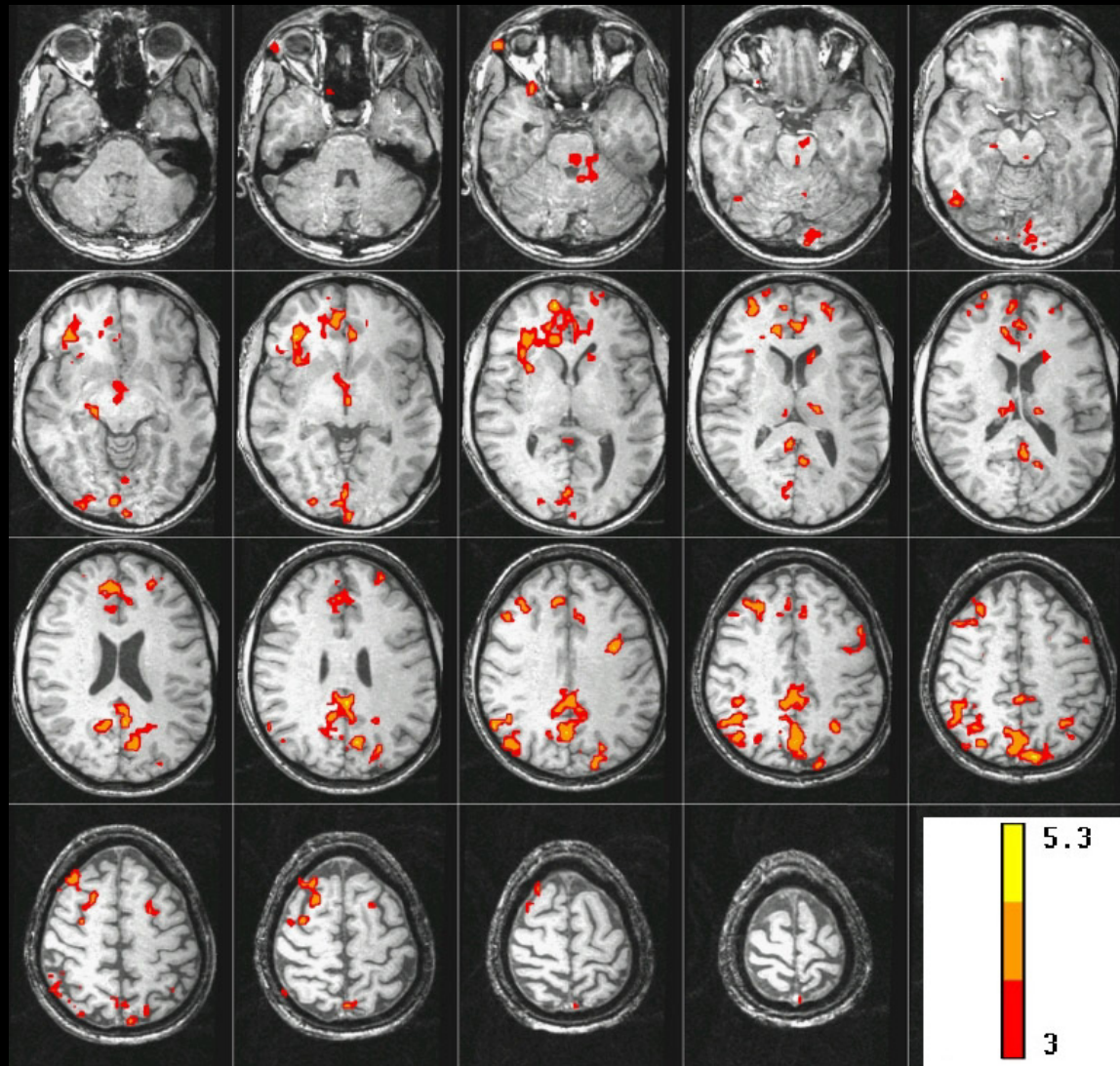
Use a continuous measure as a reference function:

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

The Skin Conductance Response (SCR)



Brain activity correlated with SCR during “Rest”



Past

Present

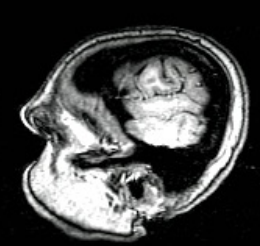
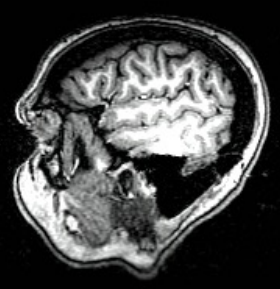
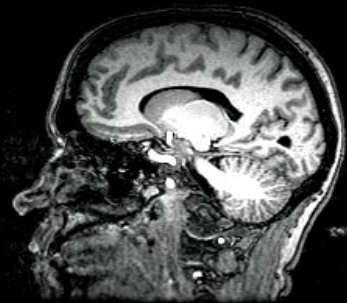
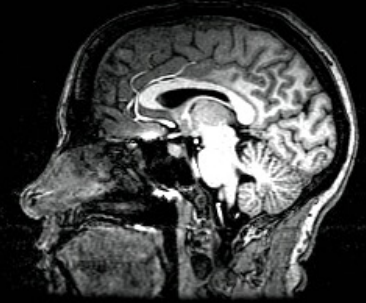
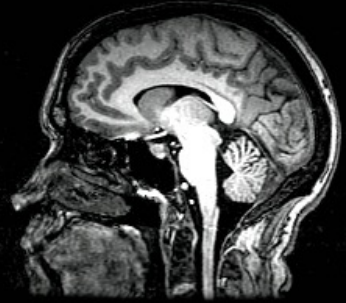
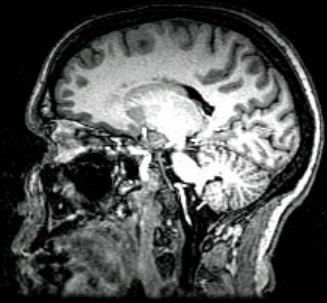
Future

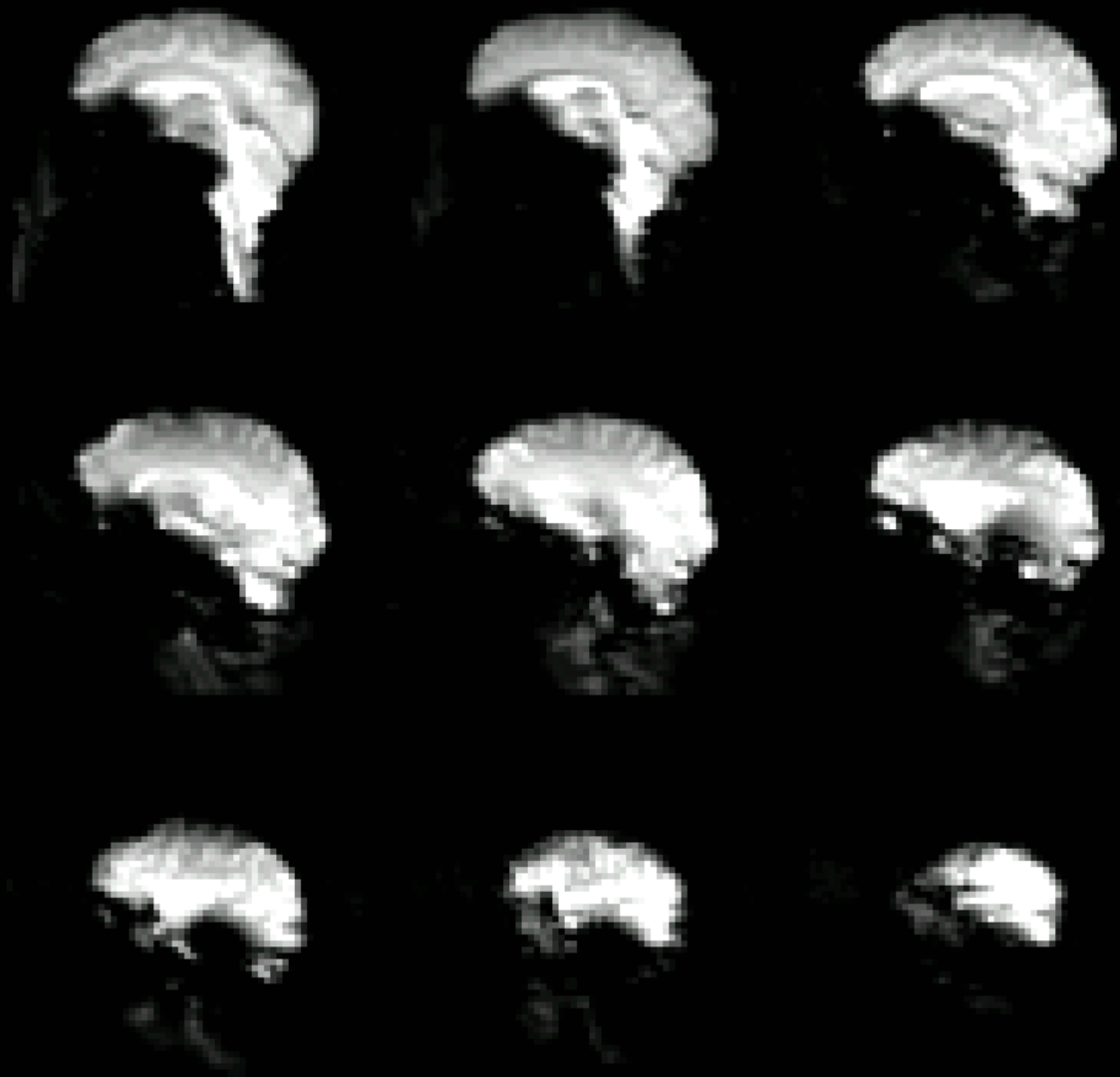
Future

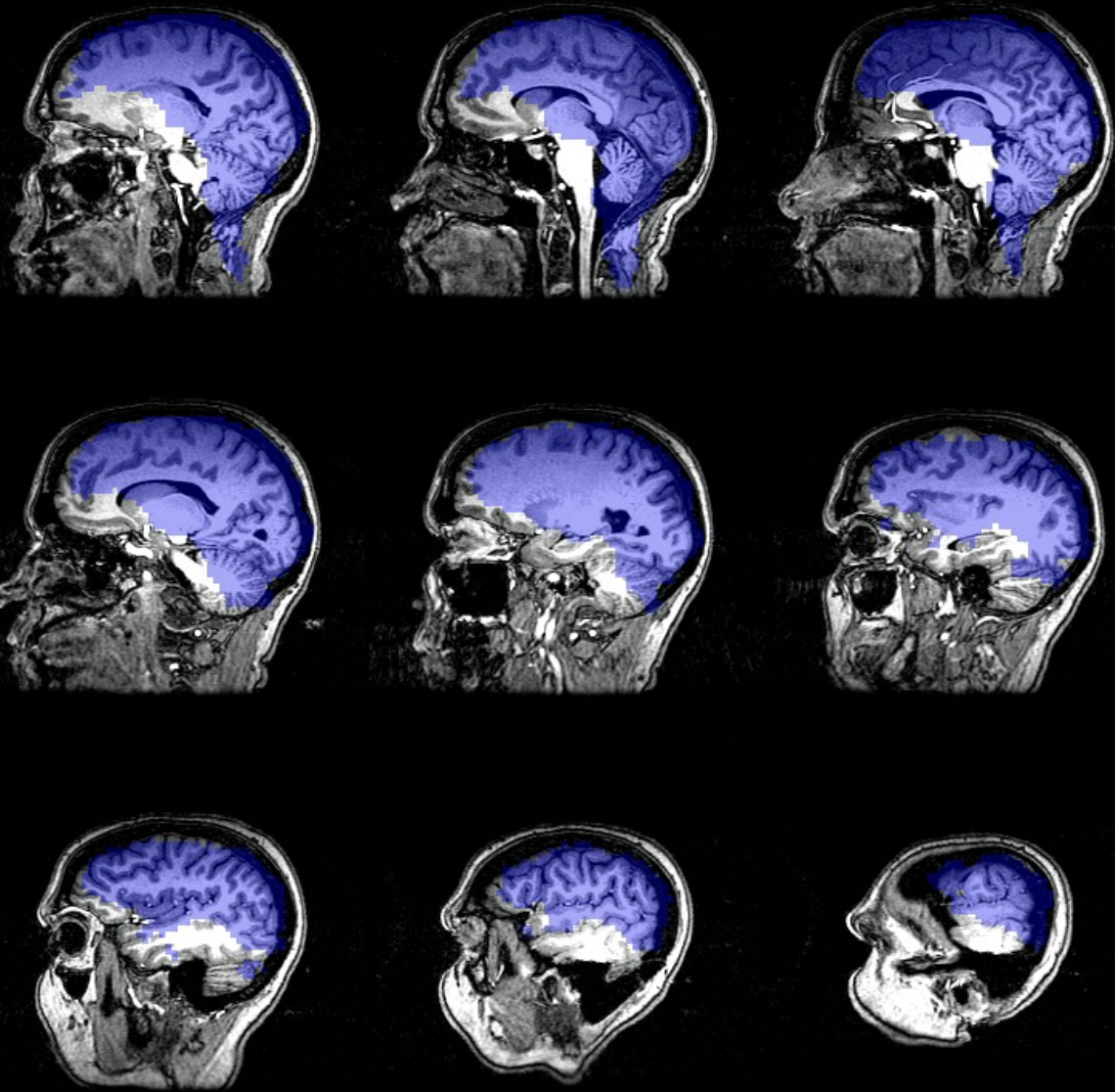
Imaging Methods

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

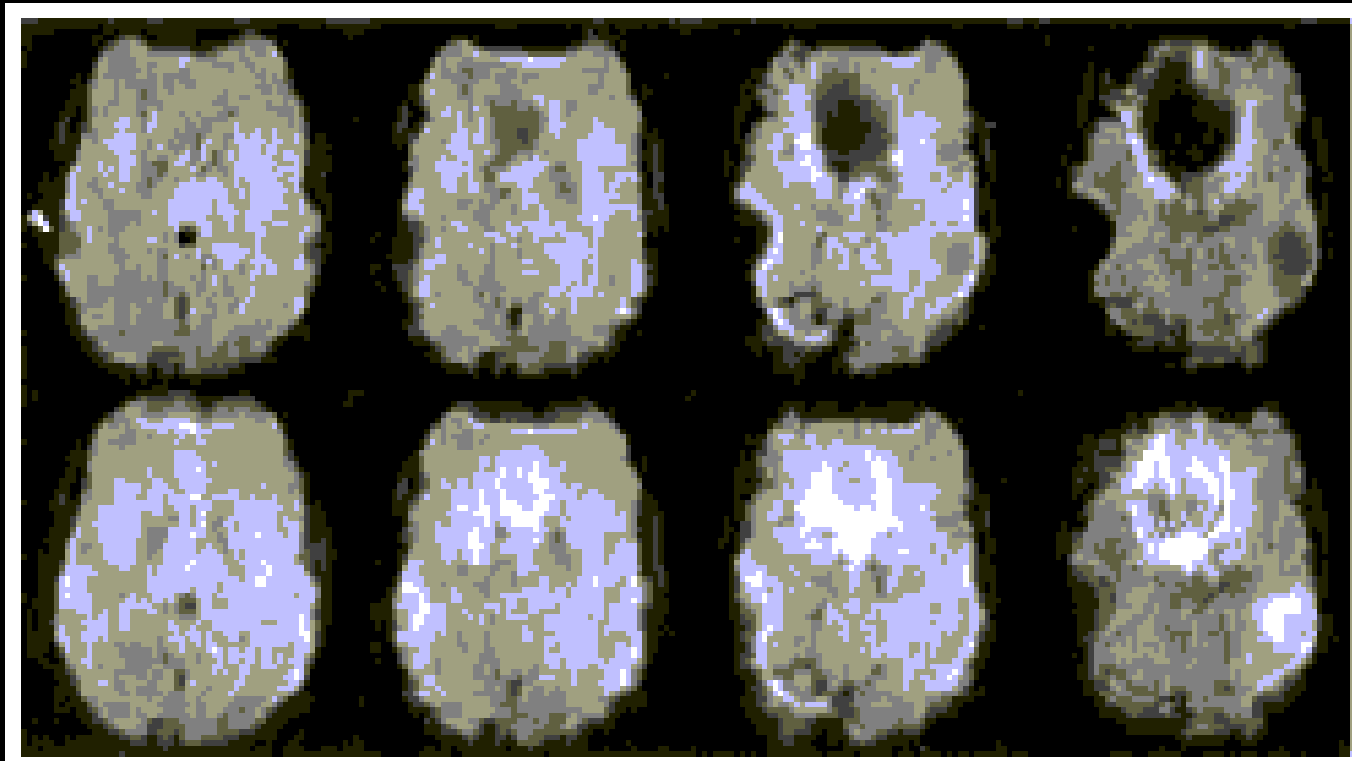






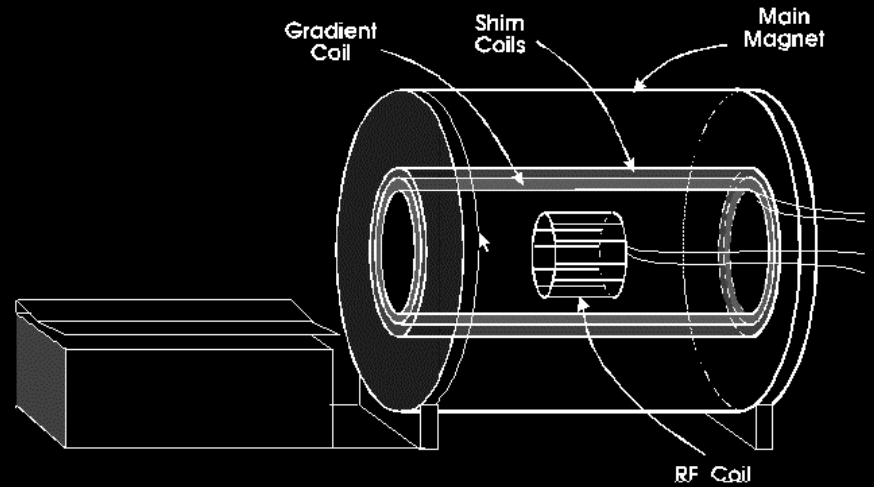
3D z-Shim Method for Reduction of Susceptibility Effects in BOLD fMRI

Gary H. Glover*



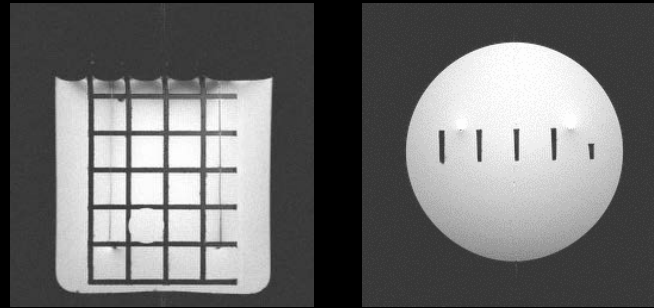
2 G/cm, 350 T/m/s

4 G/cm, 150 T/m/s



10 G/cm, 1000 T/m/s

Diffusion imaging
Faster imaging
Higher resolution



Neuronal Current Imaging

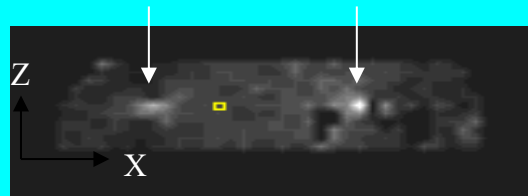
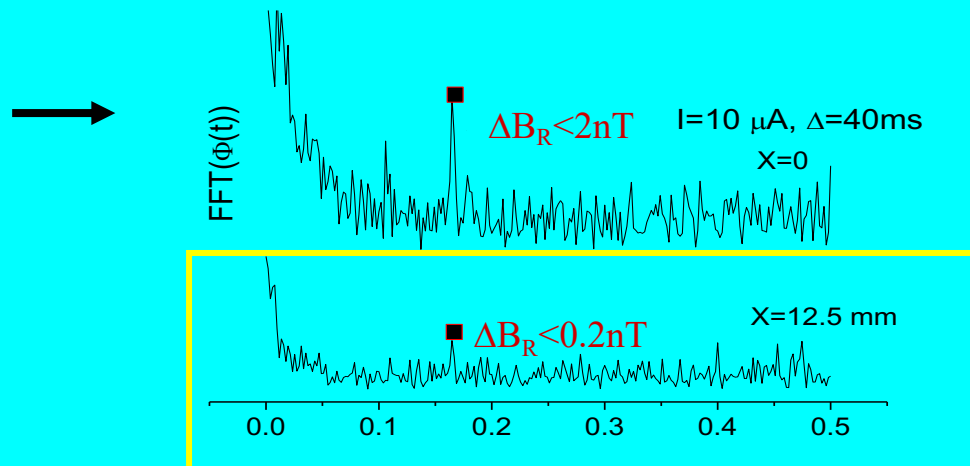


Figure 1



J. Bodurka, P. A. Bandettini. Toward direct mapping of neuronal activity: MRI detection of ultra weak transient magnetic field changes, Magn. Reson. Med. (in press).

Functional Imaging Methods / 3T Group

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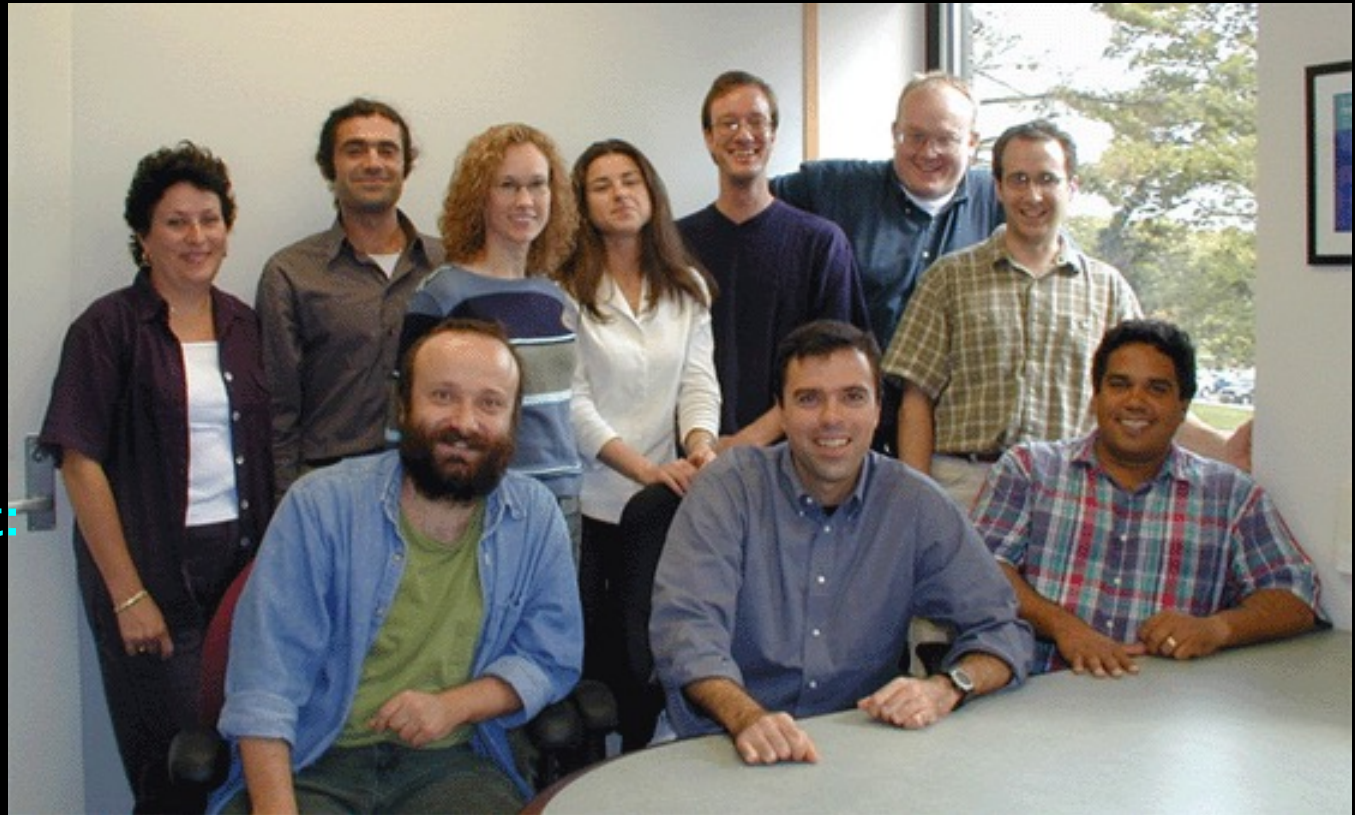
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August, 2000