How Much Neuronal Information Can We Extract With fMRI?

Advancing fMRI Utility

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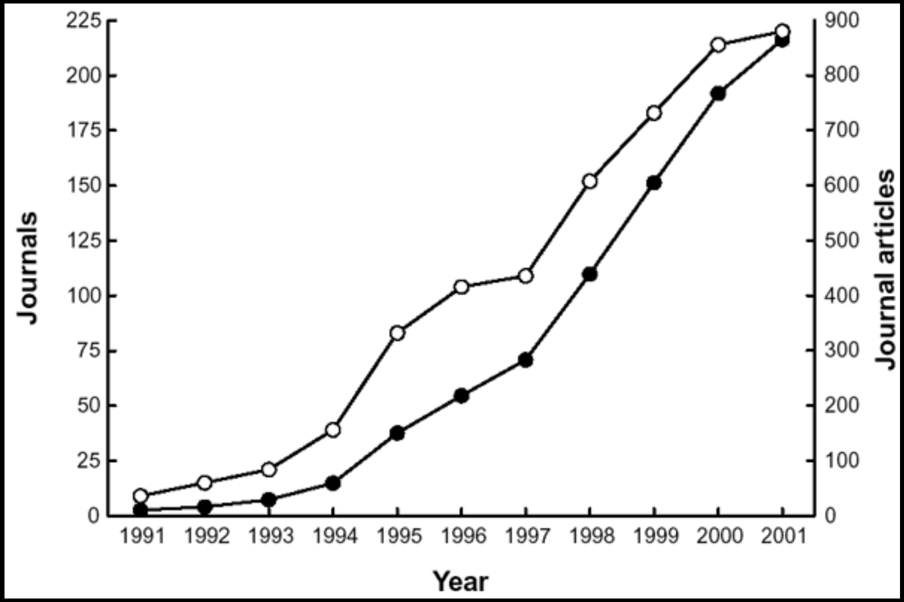
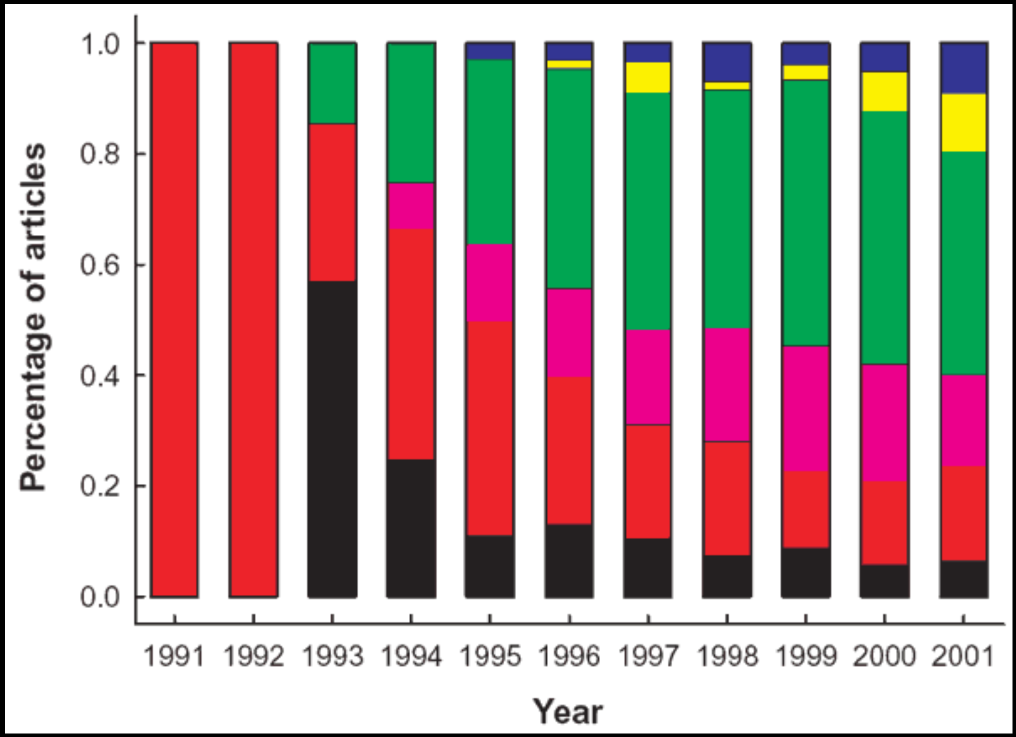
National Institute of Mental Health

NIMH National Institute of Mental Health

J. Illes, M. P. Kirschen,
J. D. E. Gabrielli,
Nature Neuroscience,
6 (3)m p.205



Motor (black)
Primary Sensory (red)
Integrative Sensory (violet)
Basic Cognition (green)
High-Order Cognition (yellow)
Emotion (blue)



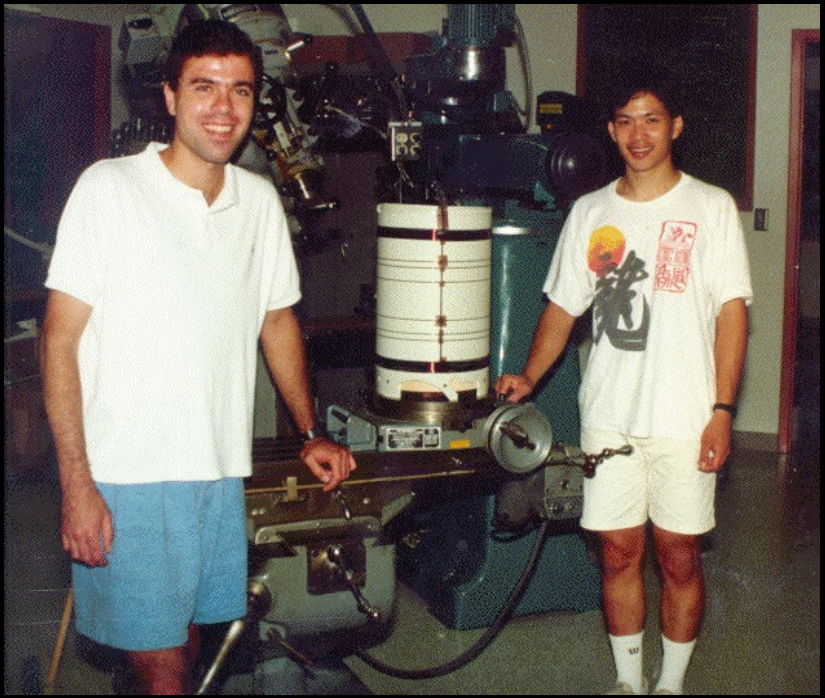
Most fMRI studies since 1992:

Minimum necessary:

- Whole Brain EPI
- Field strength of 1.5T or greater
- Basic stimulus delivery and feedback
- Software for image transfer, analysis, and display

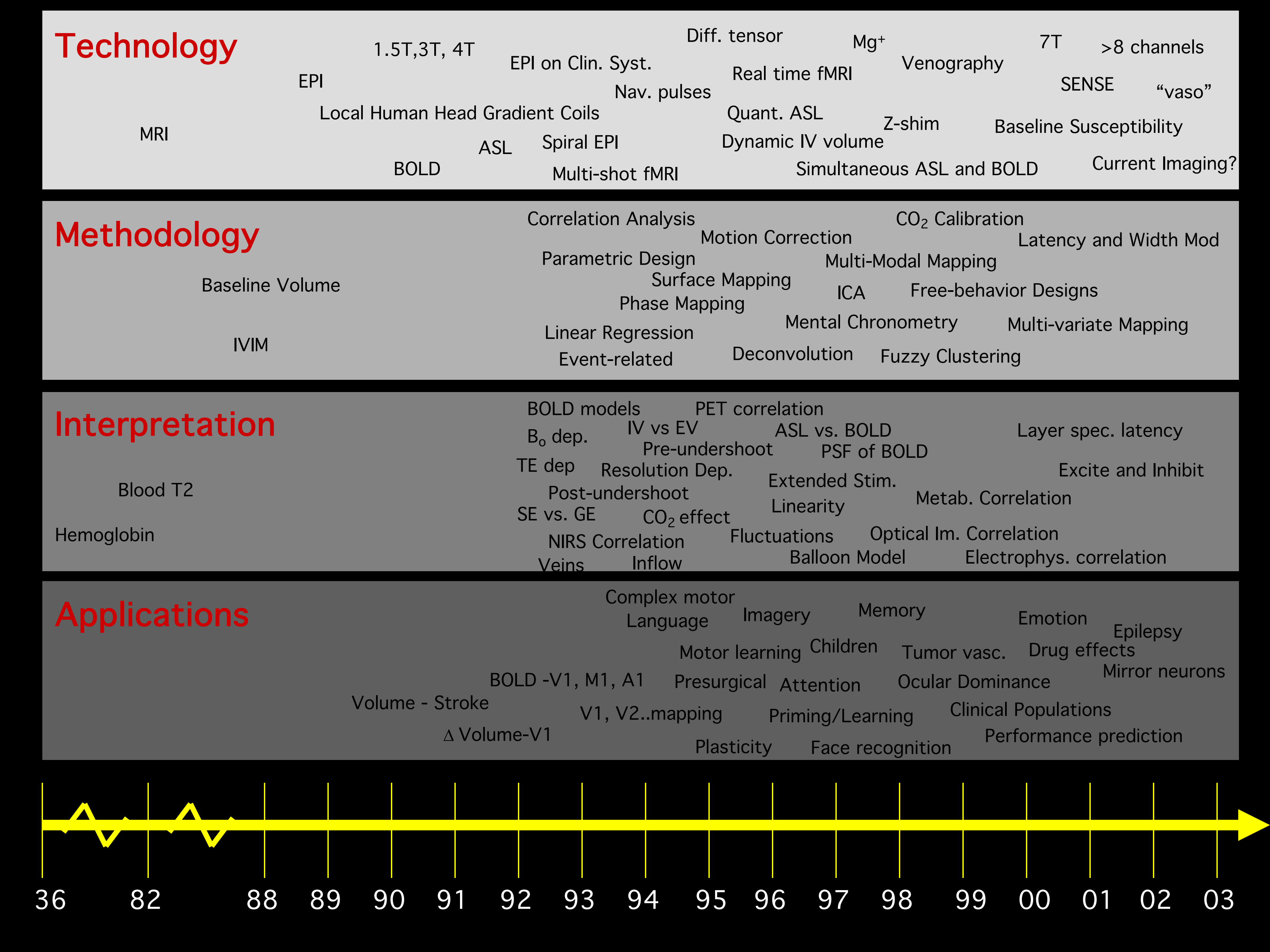
Typical advanced features:

- Higher resolution whole brain EPI, spiral, or multi-shot
- Field strength of 3T to 7T
- Quadrature and Surface coils (single, multiple)
- Susceptibility correction
- ASL (perfusion imaging)
- Multiple subject interface devices, including EEG, SCR, eye position.
- Multi-subject analysis, more rigorous statistics, more sophisticated display methods, exploratory analysis

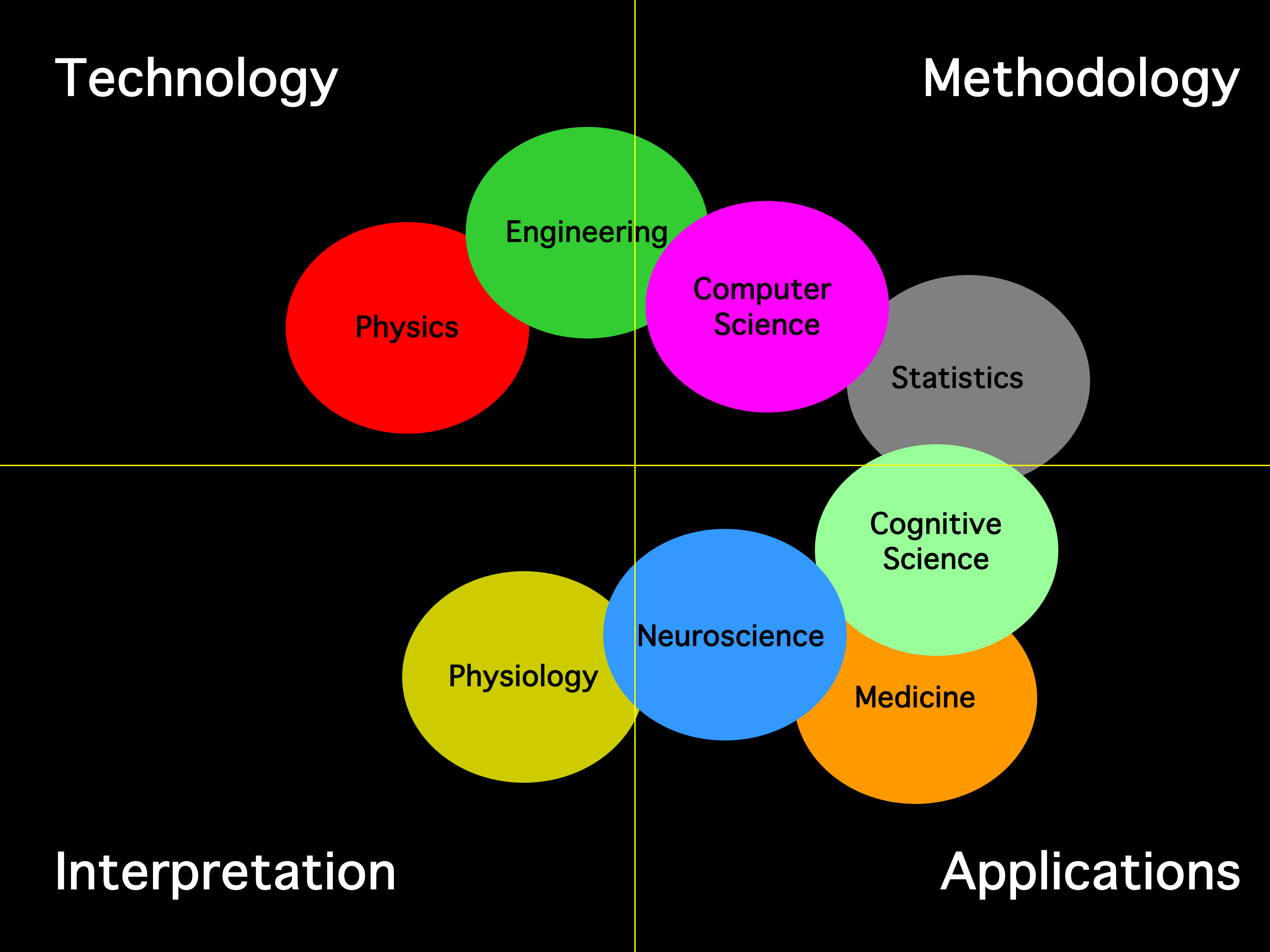


1991-1992

1992-1999



Technology
MRI
EPI
1.5T,3T, 4T
Local Human Head Gradient Coils
BOLD
ASL
EPI on Clin. Syst.
Spiral EPI
Multi-shot fMRI
Nav. pulses
Diff. tensor
Real time fMRI
Quant. ASL
Dynamic IV volume
Simultaneous ASL and BOLD
Mg+
Z-shim
Venography
7T
SENSE
Baseline Susceptibility
>8 channels
"vaso"
Current Imaging?
Methodology
Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Surface Mapping
Phase Mapping
Linear Regression
Event-related
Motion Correction
Multi-Modal Mapping
ICA
Mental Chronometry
Deconvolution
CO2 Calibration
Latency and Width Mod
Free-behavior Designs
Multi-variate Mapping
Fuzzy Clustering
Interpretation
Blood T2
Hemoglobin
BOLD models
Bo dep.
TE dep
SE vs. GE
Veins
IV vs EV
Pre-undershoot
Resolution Dep.
Post-undershoot
CO2 effect
NIRS Correlation
Inflow
PET correlation
ASL vs. BOLD
PSF of BOLD
Extended Stim.
Linearity
Fluctuations
Balloon Model
Optical Im. Correlation
Metab. Correlation
Layer spec. latency
Excite and Inhibit
Electrophys. correlation
Applications
Volume - Stroke
Δ Volume-V1
BOLD -V1, M1, A1
V1, V2..mapping
Complex motor
Language
Motor learning
Presurgical
Plasticity
Imagery
Children
Attention
Priming/Learning
Face recognition
Memory
Tumor vasc.
Ocular Dominance
Clinical Populations
Performance prediction
Emotion
Epilepsy
Drug effects
Mirror neurons
Performance prediction
36
82
88
89
90
91
92
93
94
95
96
97
98
99
00
01
02
03


Technology
Methodology
Engineering
Physics
Computer Science
Statistics
Cognitive Science
Neuroscience
Physiology
Medicine
Interpretation
Applications

What are the biggest unknowns/challenges?

1. Technology
2. Methodology
3. Interpretation

What are the biggest unknowns/challenges?

1. Technology

2. Methodology

3. Interpretation

Technology

- Field strength
- Signal to noise
- Resolution
- Shimming

Field strength

Plusses

-SNR proportional to Bo
-Contrast proportional to Bo

Minuses

-Susceptibility effects increase
-RF penetration problems
-SAR problems
-Fluctuations increase

Bottom Line

-SNR buys resolution when technology catches up
-Fluctuations may be increasingly interesting

Signal to noise

Methods to increase

- -Increase Bo
- -Smaller RF coils (arrays)
- -Reduce noise

Issue:

- -Temporal SNR is most important

More SNR…More "signal" is there…

The spatial extent of the BOLD response

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[b] *Department of Biomedical Engineering Marquette University, Milwaukee, WI 53233, USA*
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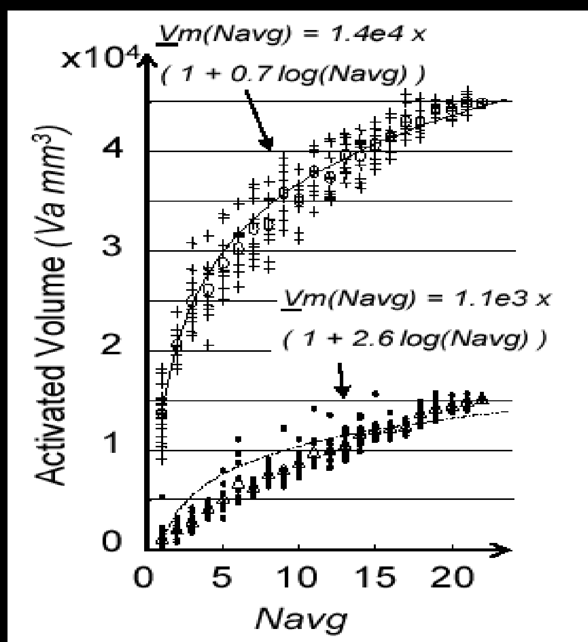
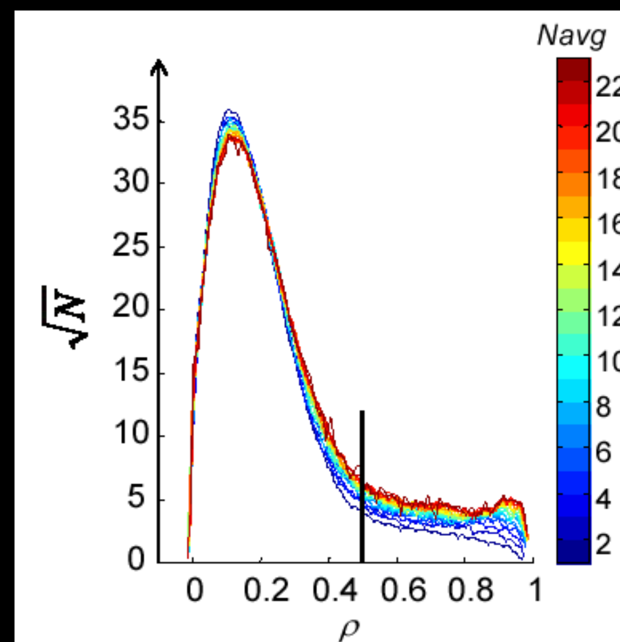
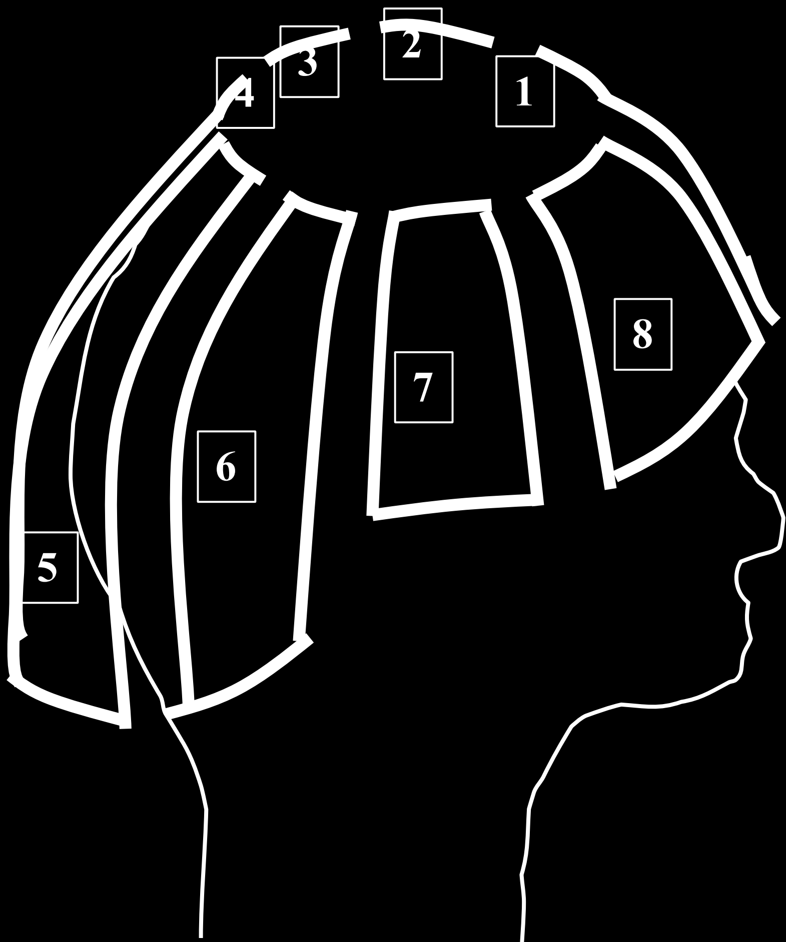
Received 16 August 2002; revised 29 October 2002; accepted 21 November 2002

NeuroImage





General concept



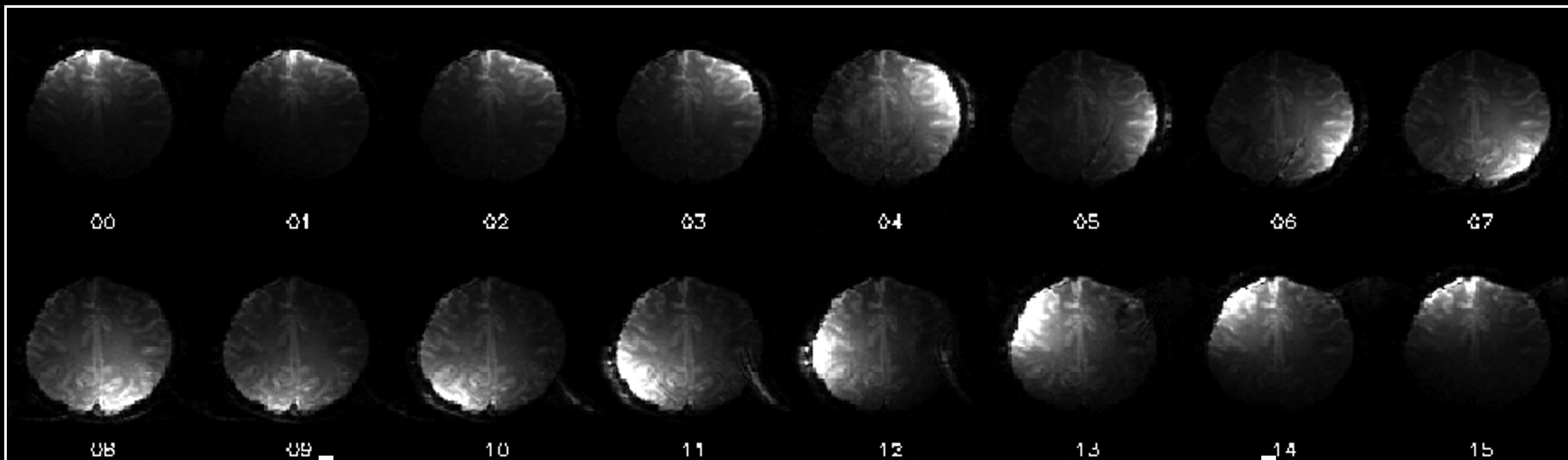
de Zwart et al. MRM 47:1218 (2002).

MRI Reception Hardware – 16 channels

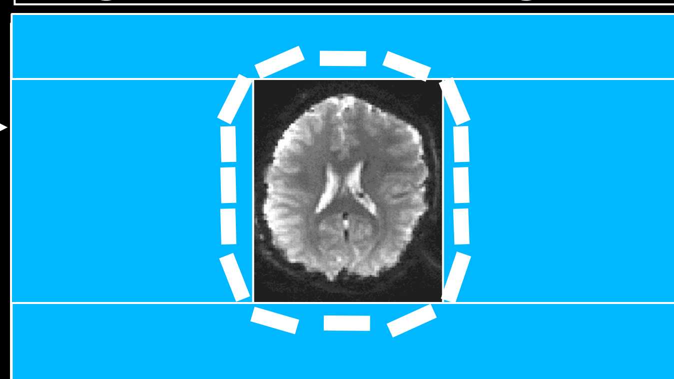
Built by Nova Medical Inc.

de Zwart et al. MRM 51:22 (2004).

Individual coil images

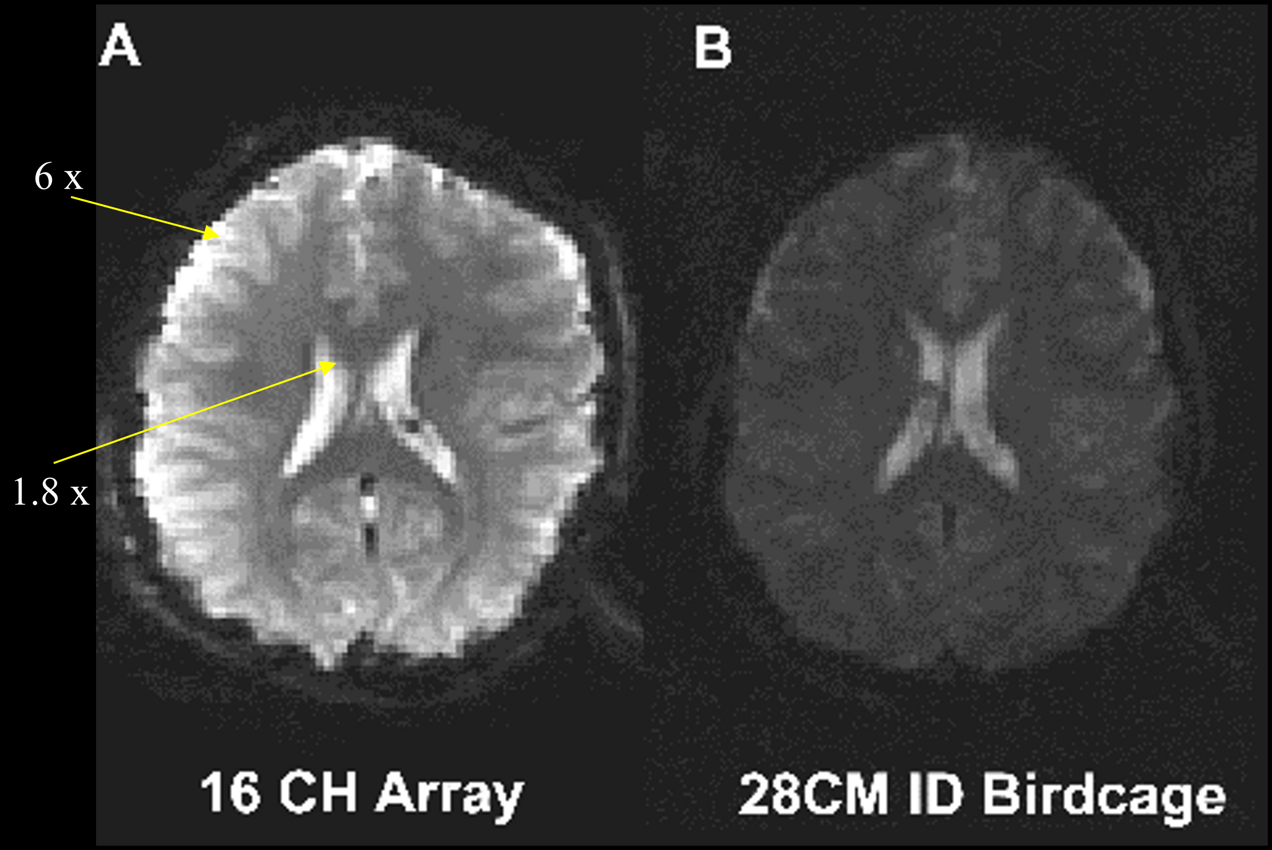


Single combined image



Experimental Data

SNR comparison



Both images are in the same scale.
Relative intensity corresponds to SNR.

3-fold SNR improvements

Experimental Data

TSNR comparison

1 channel (MAI coil) | 16 channel

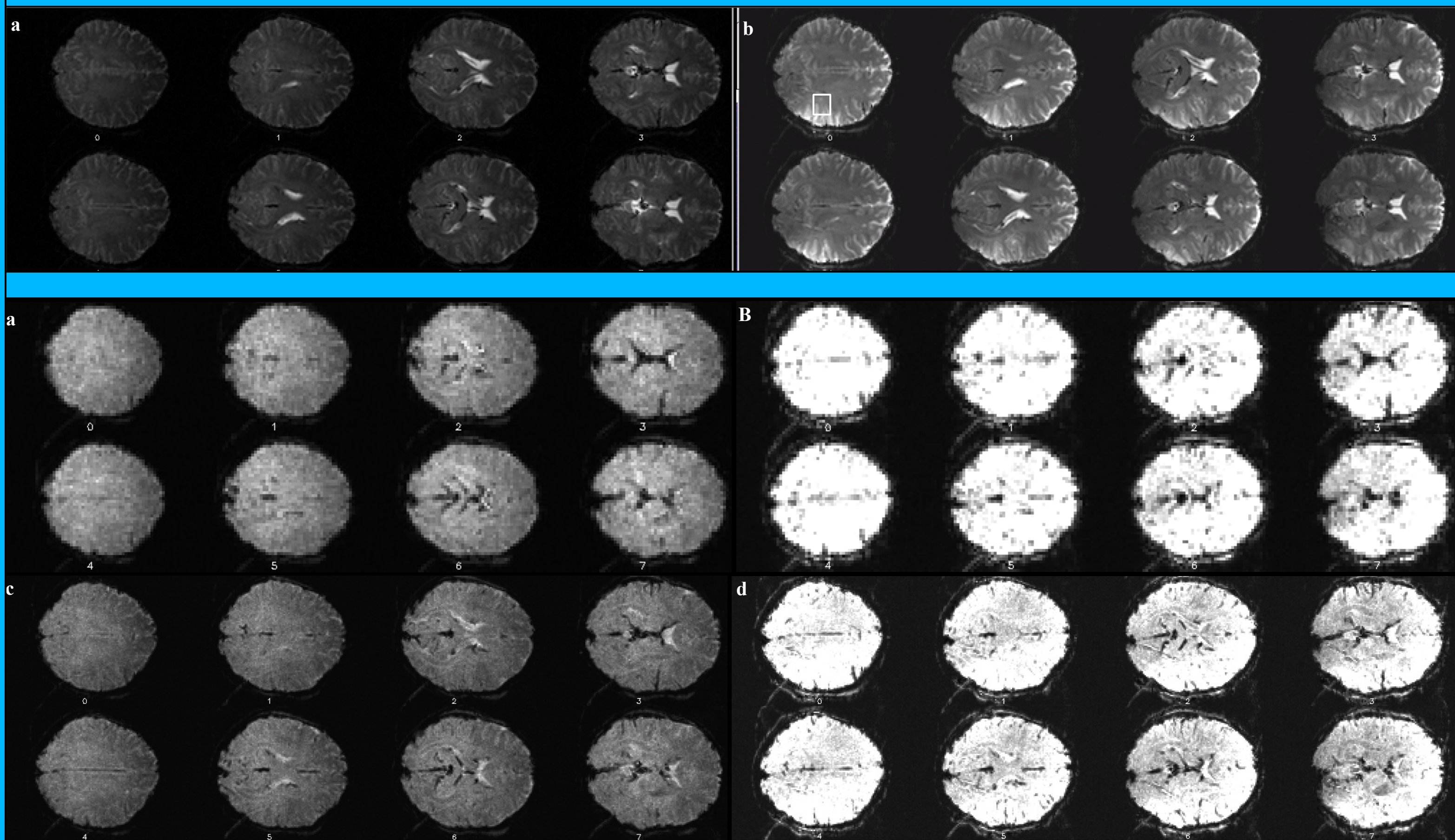
EPI

128x96

TSNR

64x48

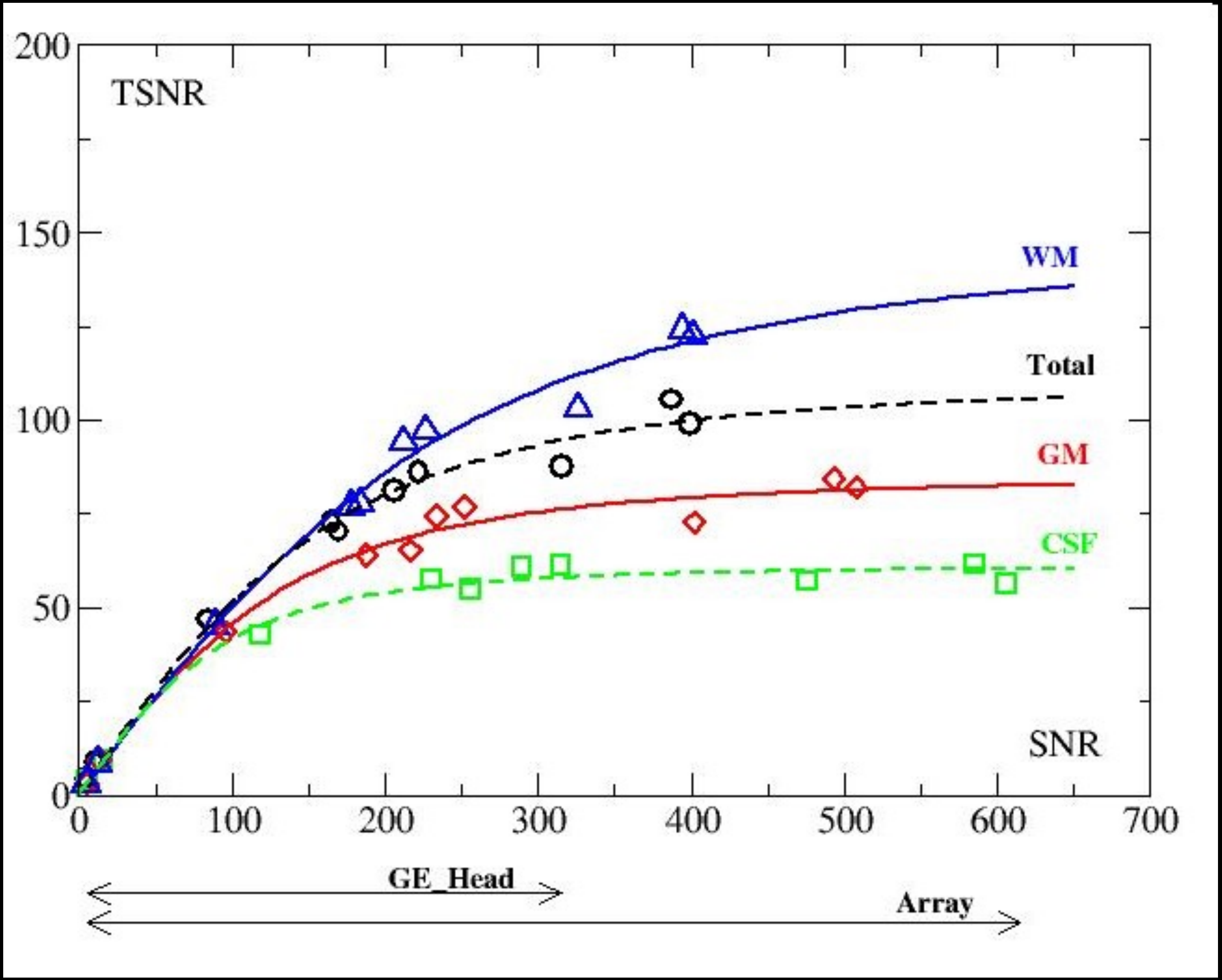
128x96



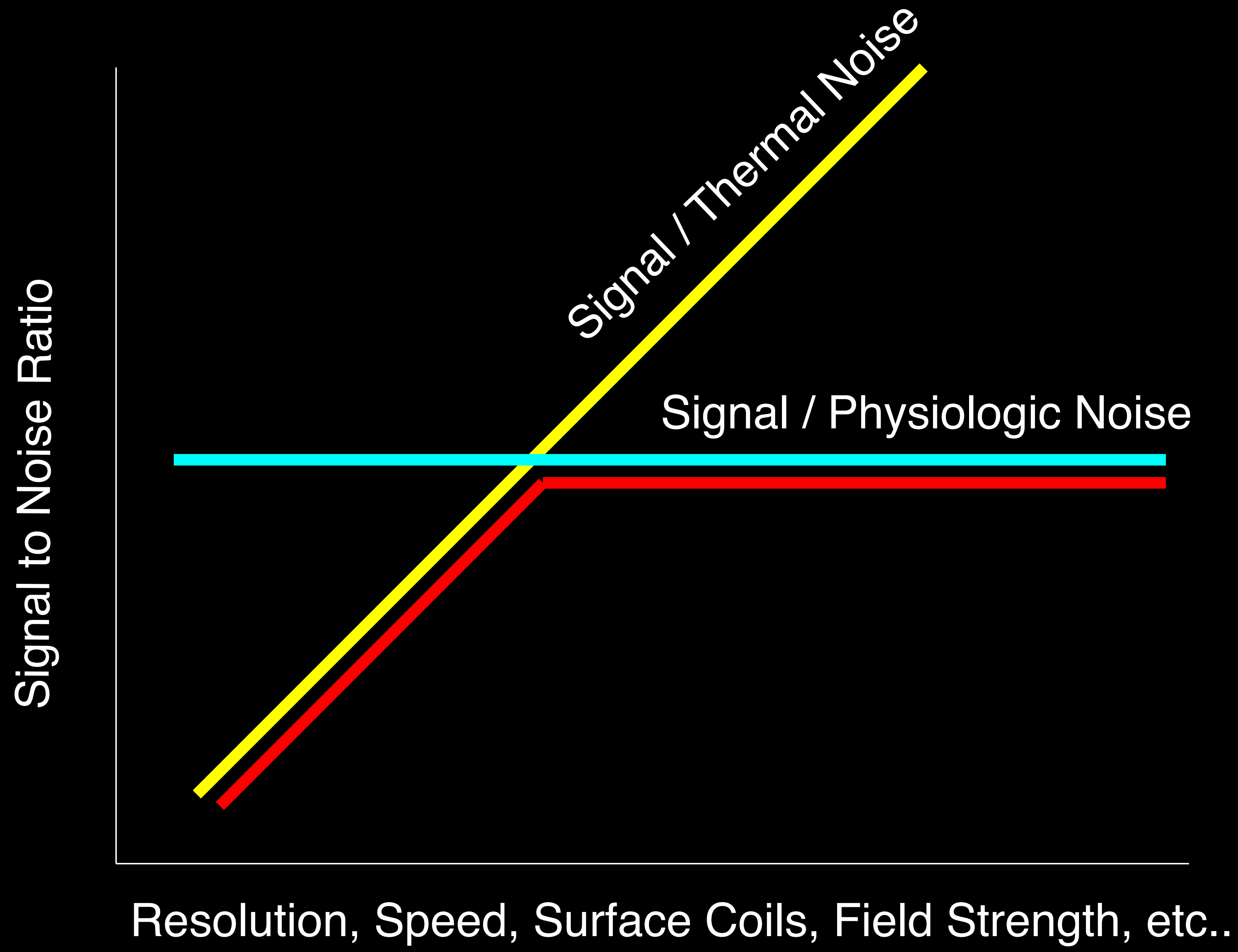
$TSNR_{16}/TSNR_{1}$:

ROI: 64x48 -> 1.98 +/- 0.52 128x96 -> 2.2 +/- 0.53

An average over all slices for both resolutions -> 1.7 +/- 0.3



Bodurka et al.



Signal to Noise Ratio
Signal / Thermal Noise
Signal / Physiologic Noise
Resolution, Speed, Surface Coils, Field Strength, etc..

Resolution

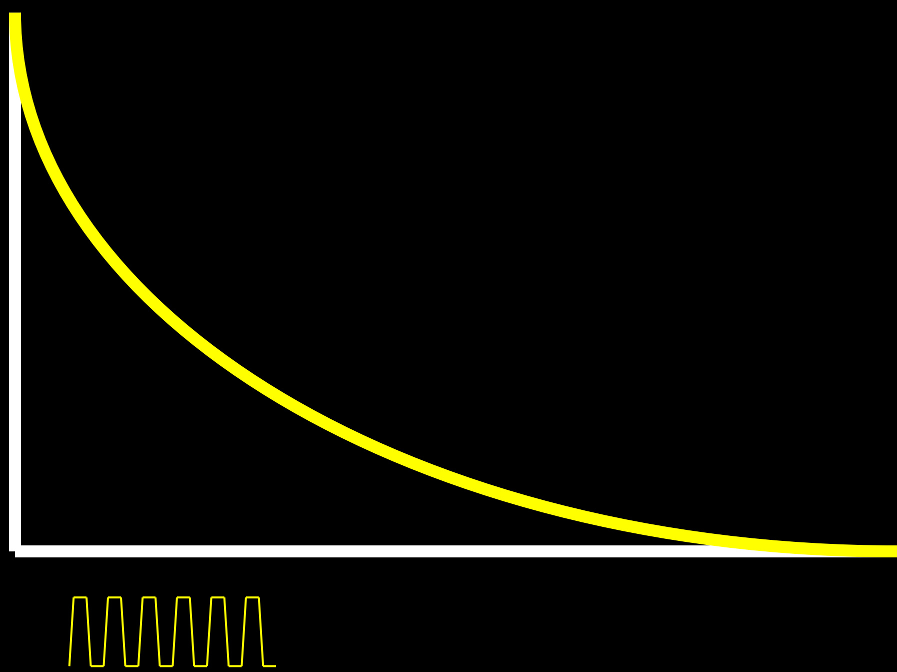
Methods to increase:

- -Faster sampling rate per image
- -Faster gradient switching
- -Longer readout window
- -Partial k-space
- -Multi-shot techniques
- -Parallel Imaging

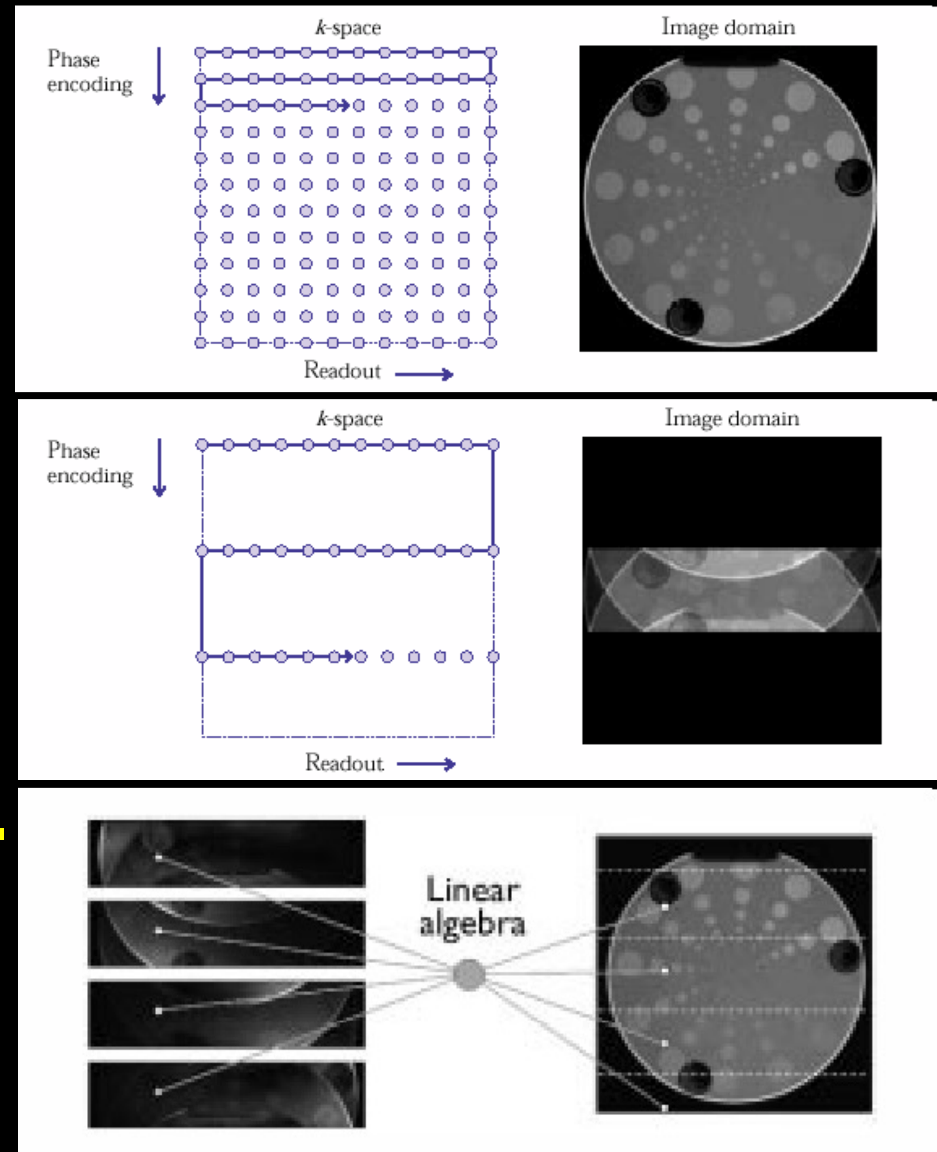
Bottom Line:

- -Up against limits in most methods
- -Multi-shot still problematic (time, stability)
- -Parallel imaging is most promising

SENSE Imaging



$\approx$ 5 to 30 ms

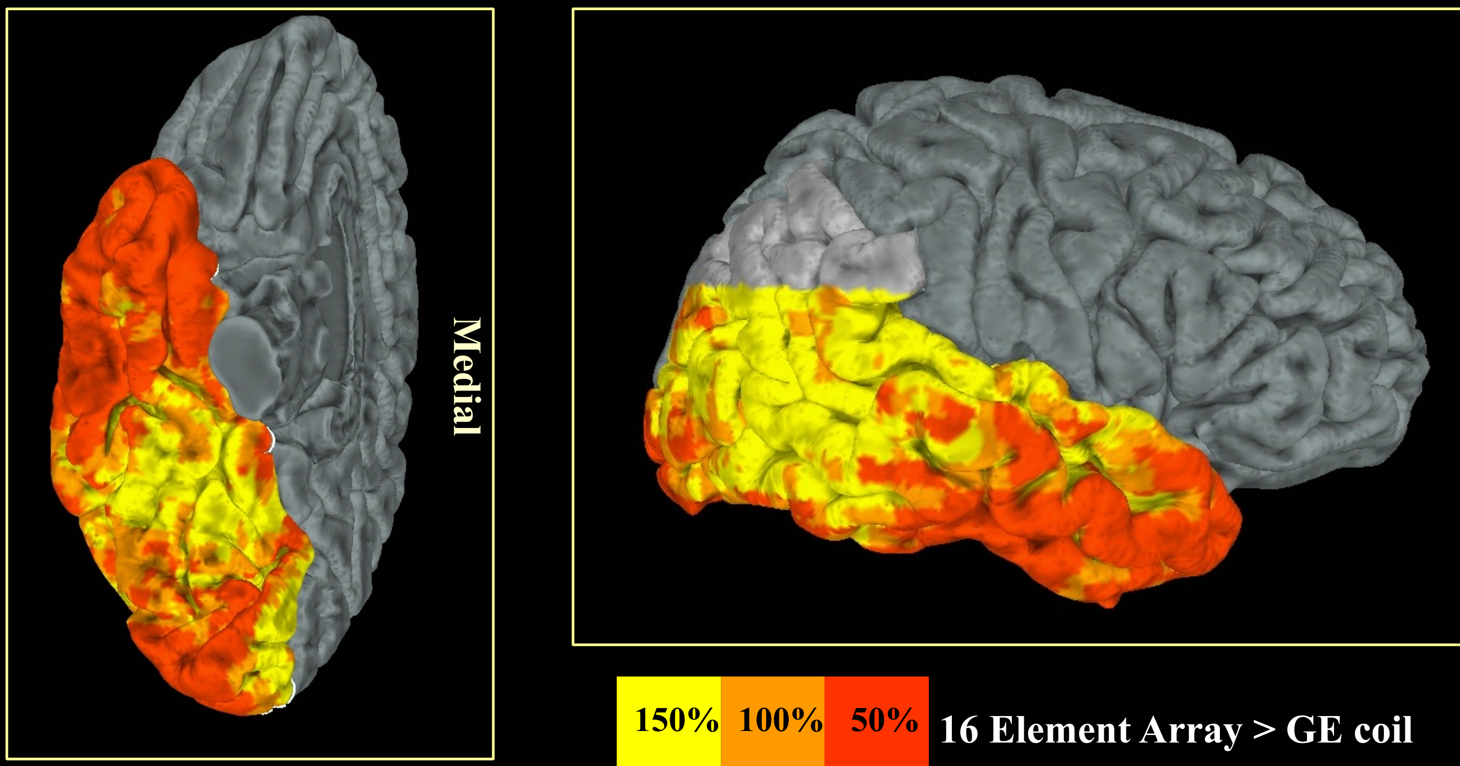


Pruessmann, et al.

Axial-oblique single shot SENSE EPI using 16-channel reception. 192x144 : 1.25x1.25x2mm

Average Temporal Signal-to-Noise ratio Comparison Between Coils

Anterior



Posterior

Shimming

A solvable problem:

- -more shim coils and/or coil designs
- -increased shim currents
- -higher resolution (fixes dropout)
- -shorter readout window (fixes distortion)
- -shim inserts
- -z-shim methods

Methodology

- Temporal resolution
- Spatial specificity
- Magnitude Calibration
- Multi-subject averaging/normalization at very high resolution
- Paradigm design
- Motion (very slow and motion correlated)
- Scanner acoustic noise effect removal
- Individual Map "Classification"
- Local pattern effect mapping and classification
- Exploratory analysis techniques (ICA, PCA..)
- Temporal fluctuations (removal and use)
- Simultaneous measures with fMRI
- Baseline susceptibility mapping
- Non-invasive blood volume imaging
- Multimodal integration
- Functional Connectivity mapping
- Real time fMRI
- Neuronal Current MRI

Methodology

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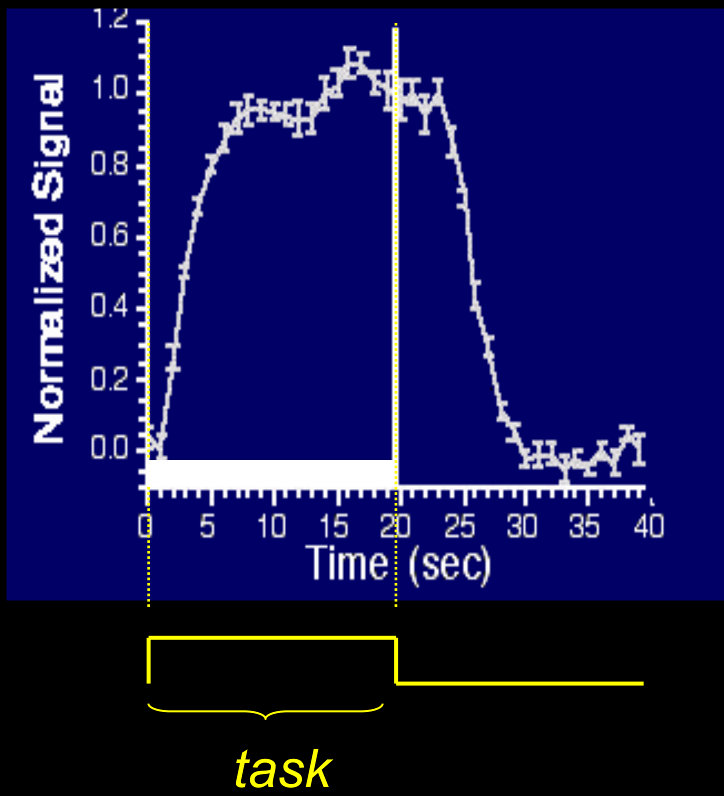
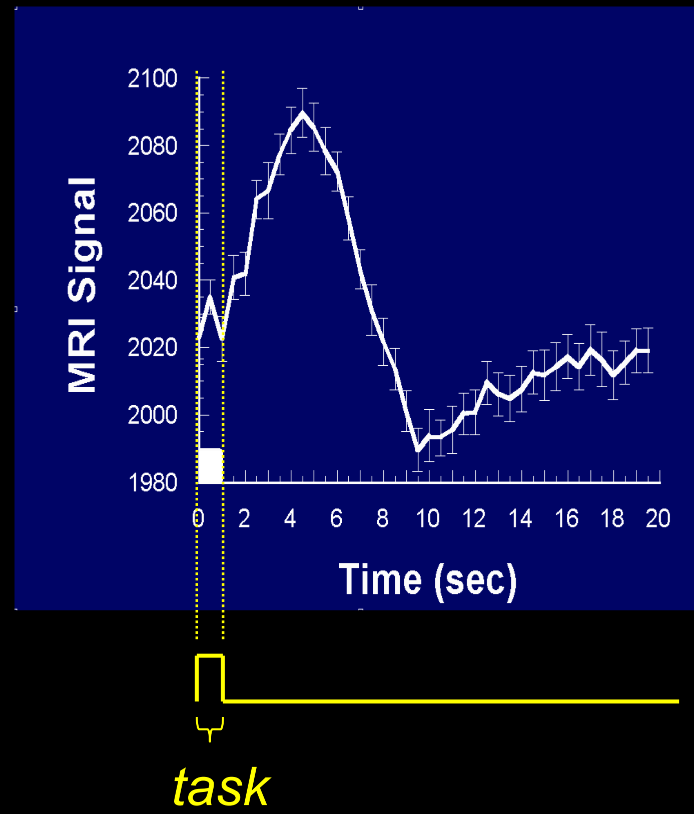
Temporal resolution



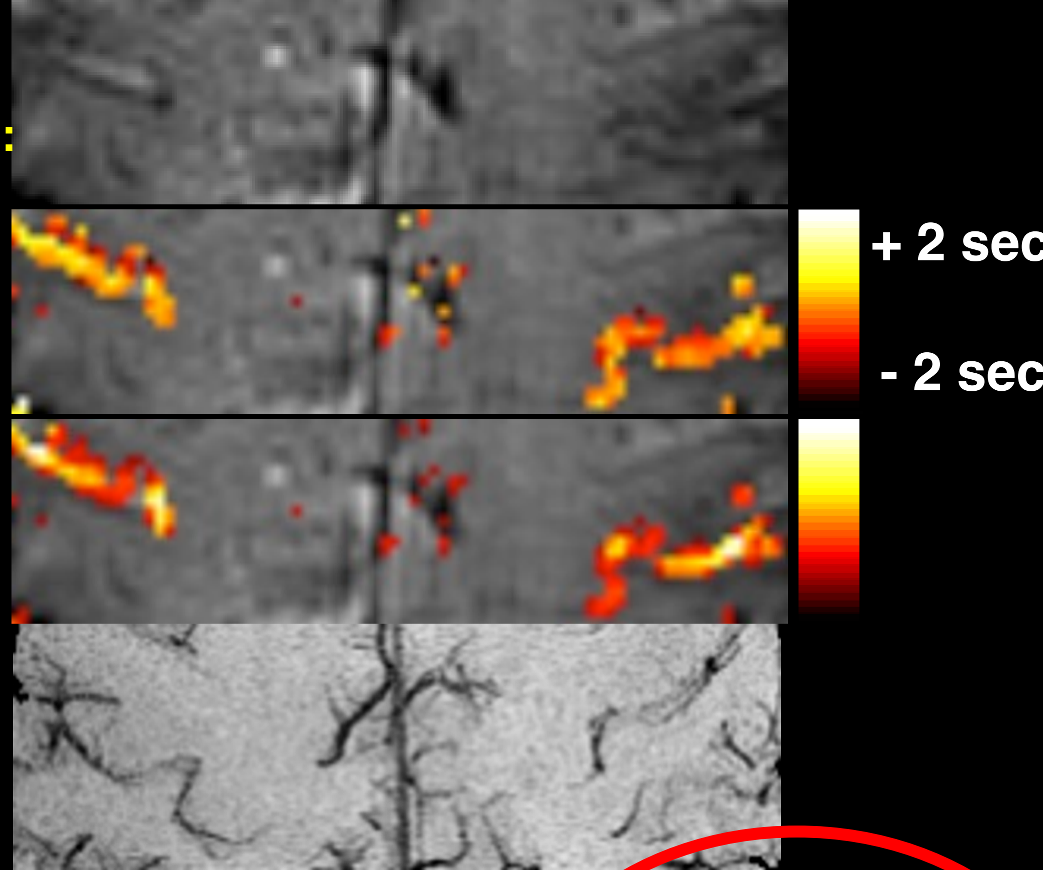


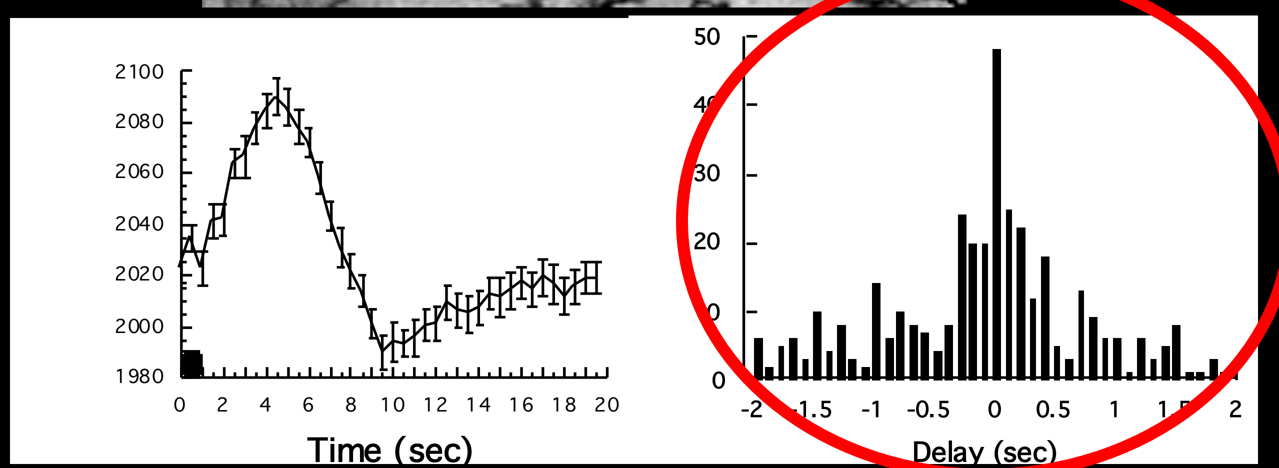
The major obstacle in BOLD contrast temporal resolution:

Latency

Magnitude

Venogram

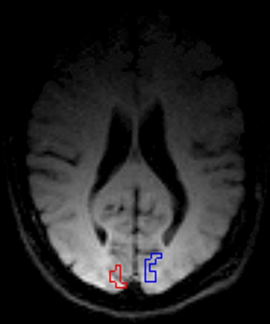




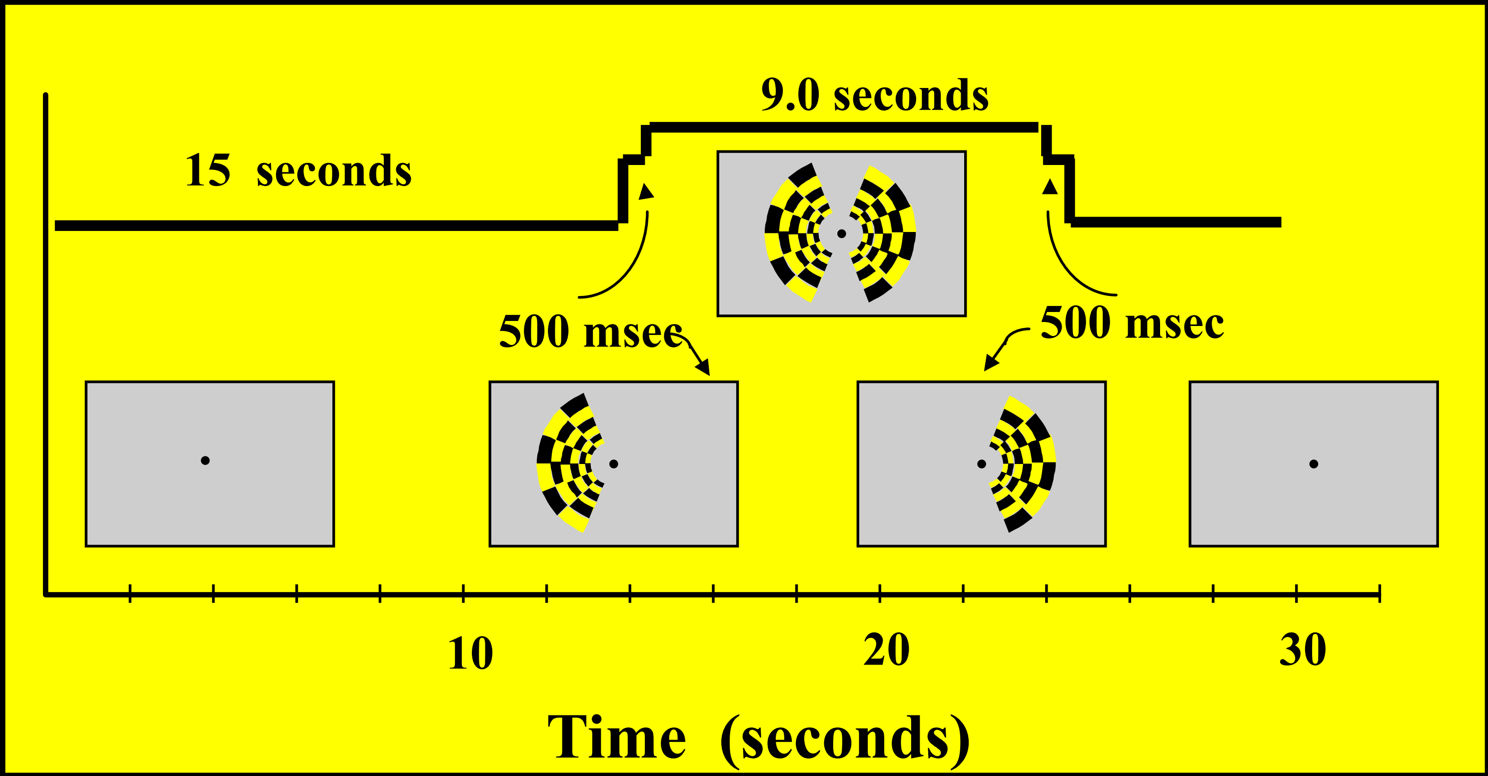
P. A. Bandettini, The temporal resolution of Functional MRI *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

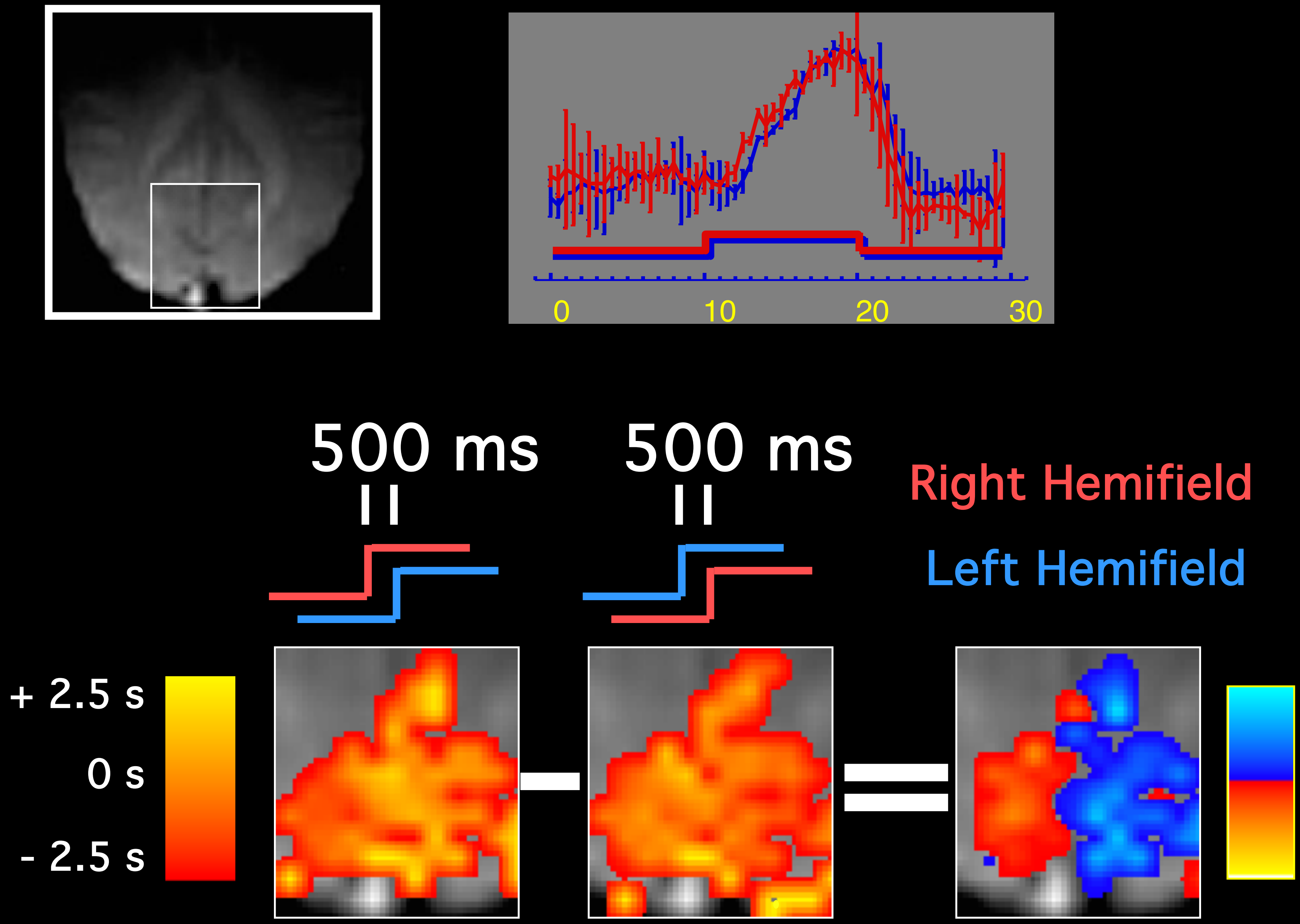
Hemi-Field Experiment

Right Hemisphere



Left Hemisphere





0
10
20
30
500 ms
=
500 ms
=
Right Hemifield
Left Hemifield
+ 2.5 s
0 s
- 2.5 s

Cognitive Neuroscience Application:

Understanding neural system dynamics through task modulation and measurement of functional MRI amplitude, latency, and width

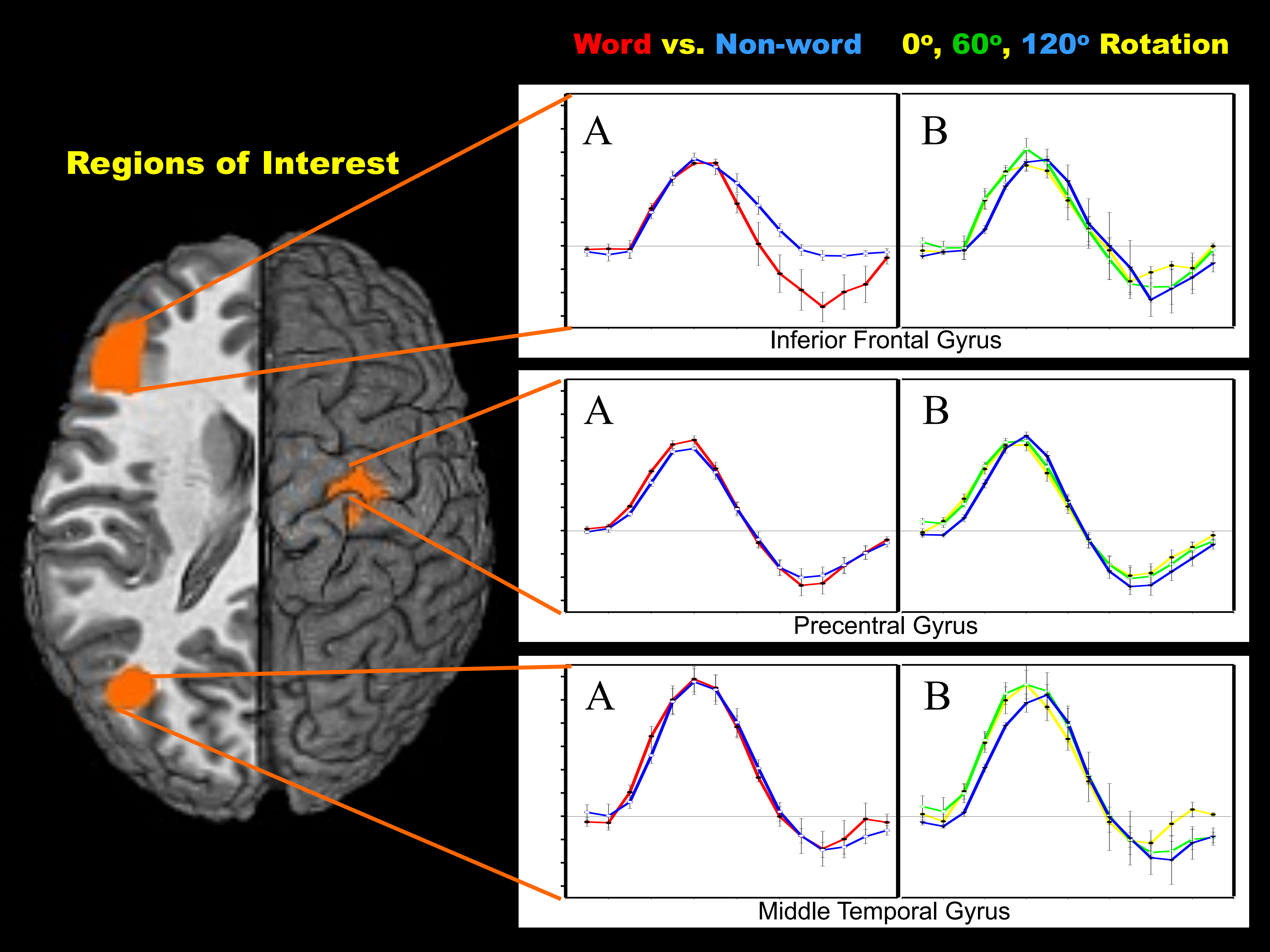
PNAS

P. S. F. Bellgowan*†, Z. S. Saad‡, and P. A. Bandettini*

*Laboratory of Brain and Cognition and ‡Scientific and Statistical Computing Core, National Institute of Mental Health, Bethesda, MD 20892

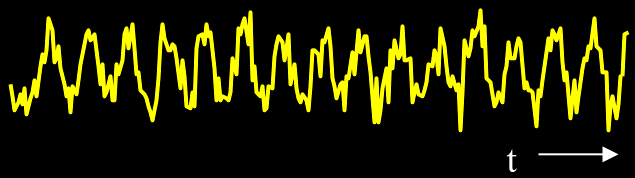
Communicated by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, December 19, 2002 (received for review October 31, 2002)

Rotational Delay	Lexical Delay: Words	Lexical Delay: Non-Words	Mean Reaction Time
0⁰	smudge	dierts	823 ms
60⁰	frolic	cuhlos	891 ms
120⁰	slouch	gedmus	1446 ms
Mean Reaction Time	986 ms	1219 ms	

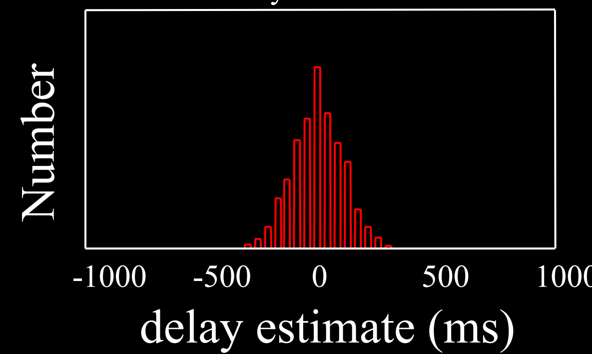

Word vs. Non-word
0º, 60º, 120º Rotation
Regions of Interest
A
B
Inferior Frontal Gyrus
A
B
Precentral Gyrus
A
B
Middle Temporal Gyrus

1 run:

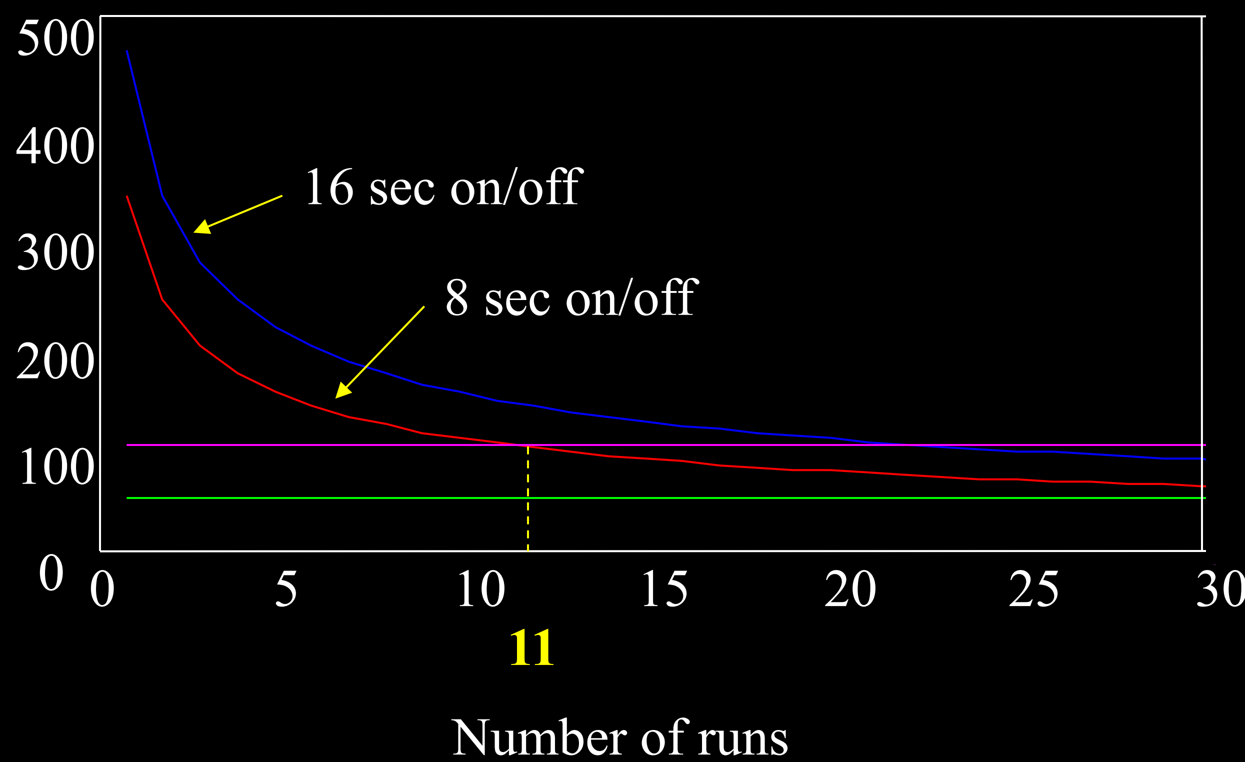
1% Noise
4% BOLD
256 time pts /run
1 second TR



σ_{delay} = 107ms



Smallest latency Variation Detectable (ms) (p < 0.001)

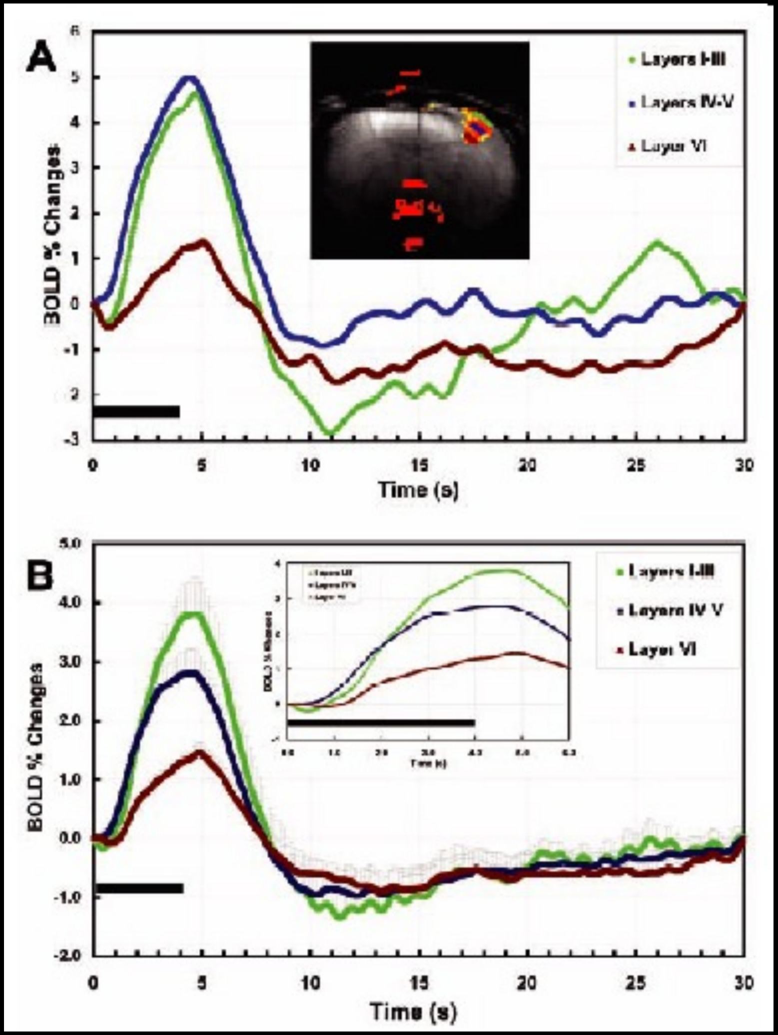


Laminar specificity of functional MRI onset times during somatosensory stimulation in rat

Afonso C. Silva* and Alan P. Koretsky

Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892

15182–15187 | PNAS | **November 12, 2002** | vol. 99 | no. 23



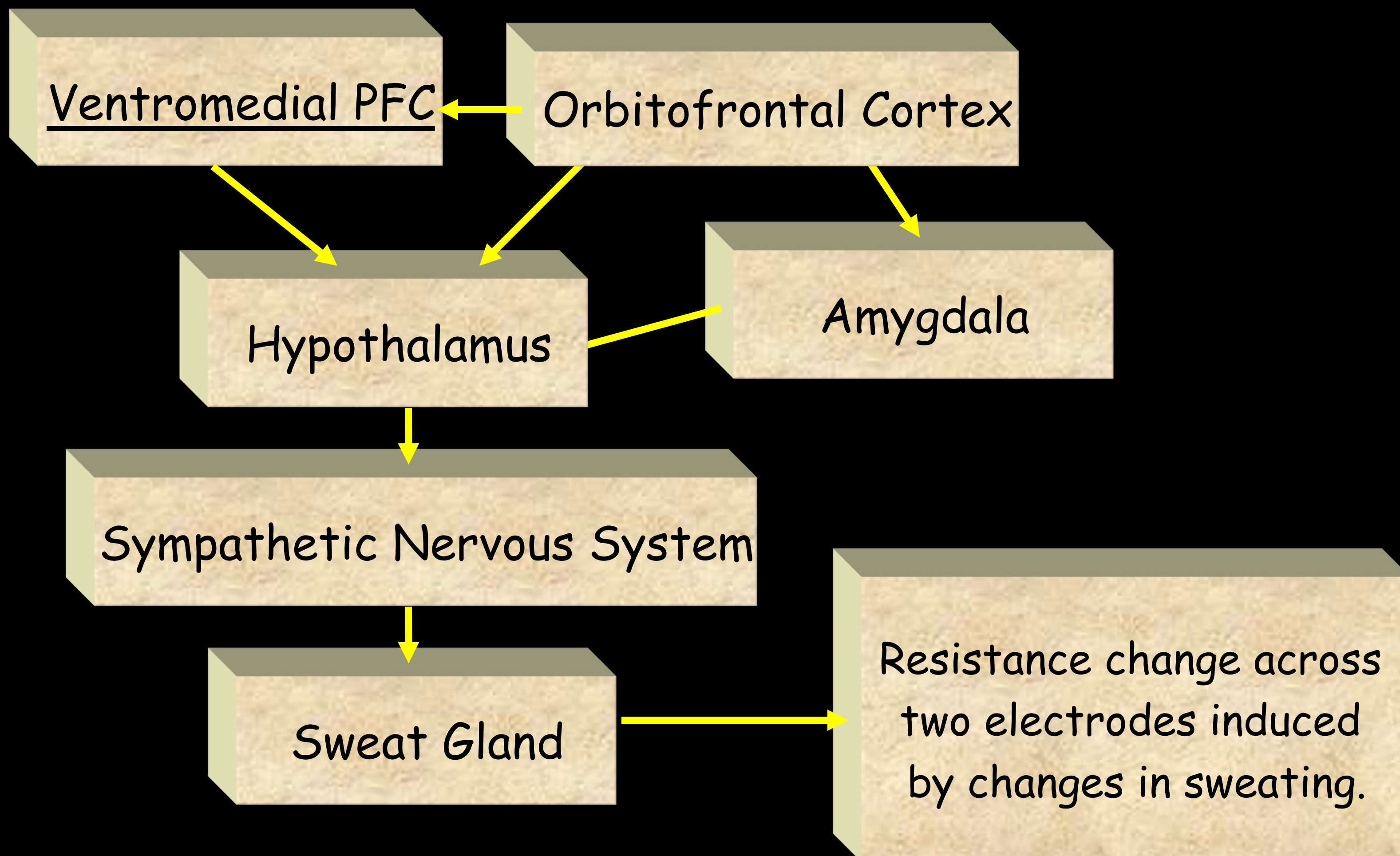
No calibration

11.7 T

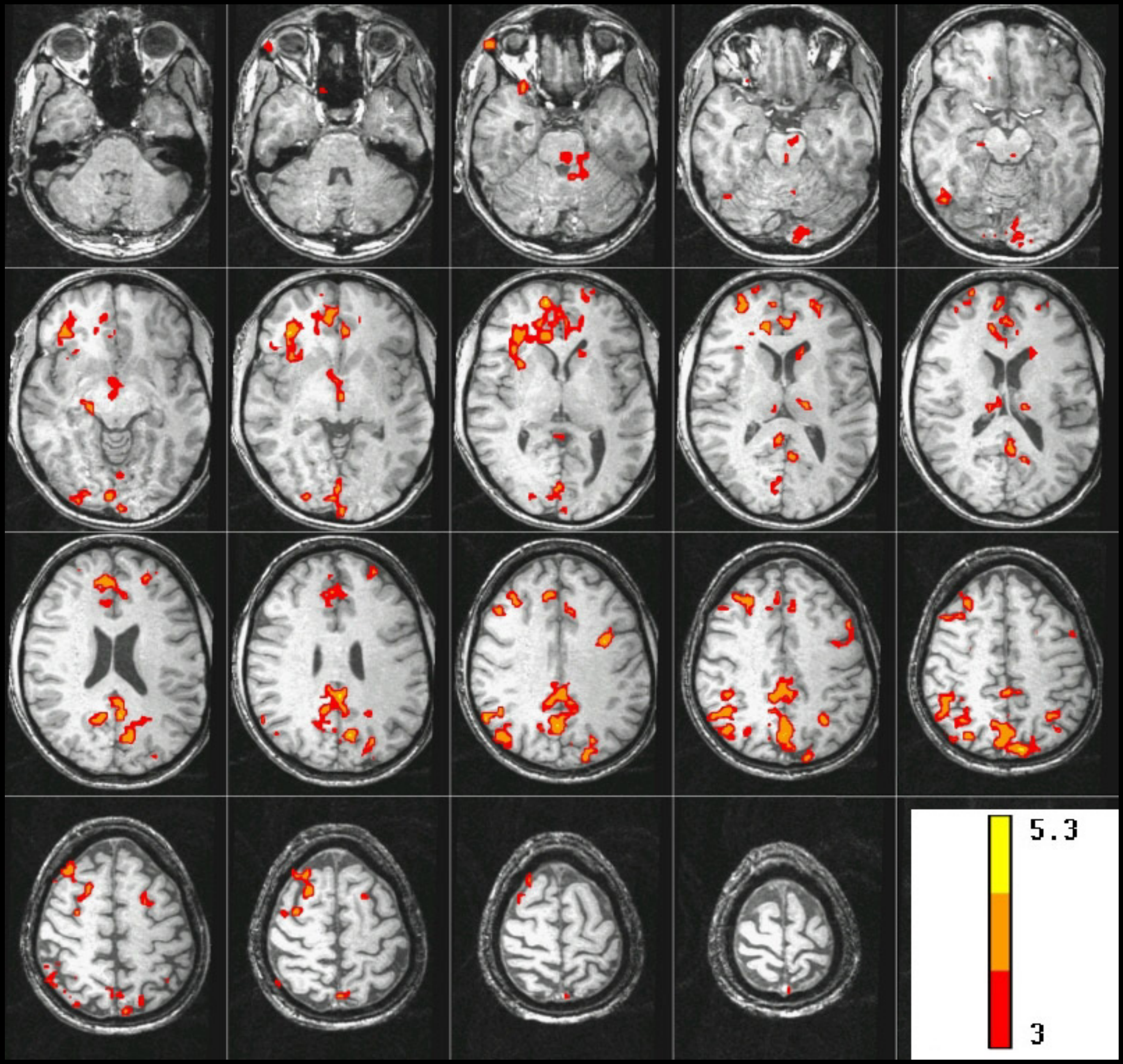
Paradigm Design

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

The Skin Conductance Response (SCR)



Brain activity correlated with SCR during "Rest"



J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, Task - independent functional brain activity correlation with skin conductance changes: an fMRI study. *NeuroImage 17: 1787-1806, (2002).*

Simultaneous EEG and fMRI of the alpha rhythm

Robin I. Goldman,[2,CA] John M. Stern,[1] Jerome Engel Jr[1] and Mark S. Cohen

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[CA,2]Corresponding Author and Address: rg2146@columbia.edu

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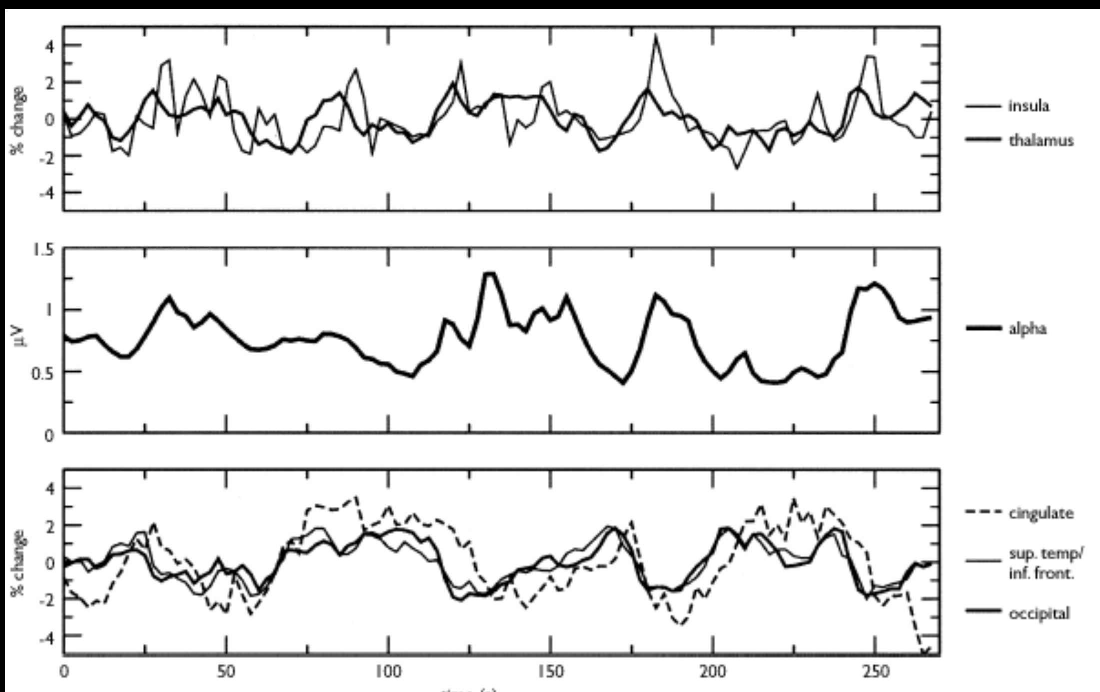
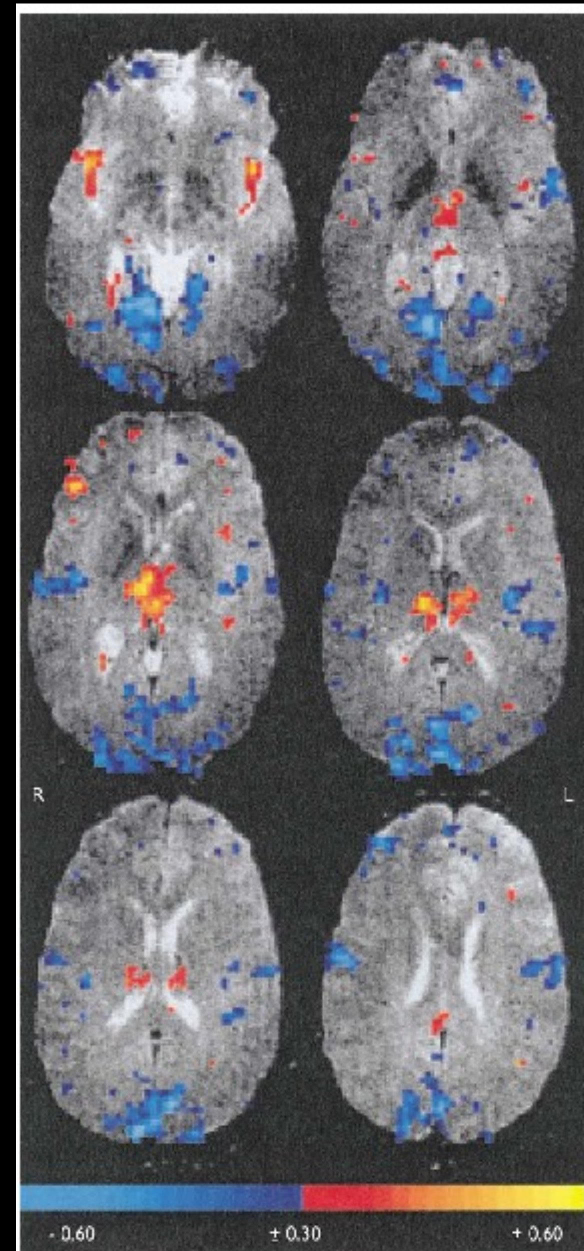




Motion (very slow and activation correlat

Very slow:

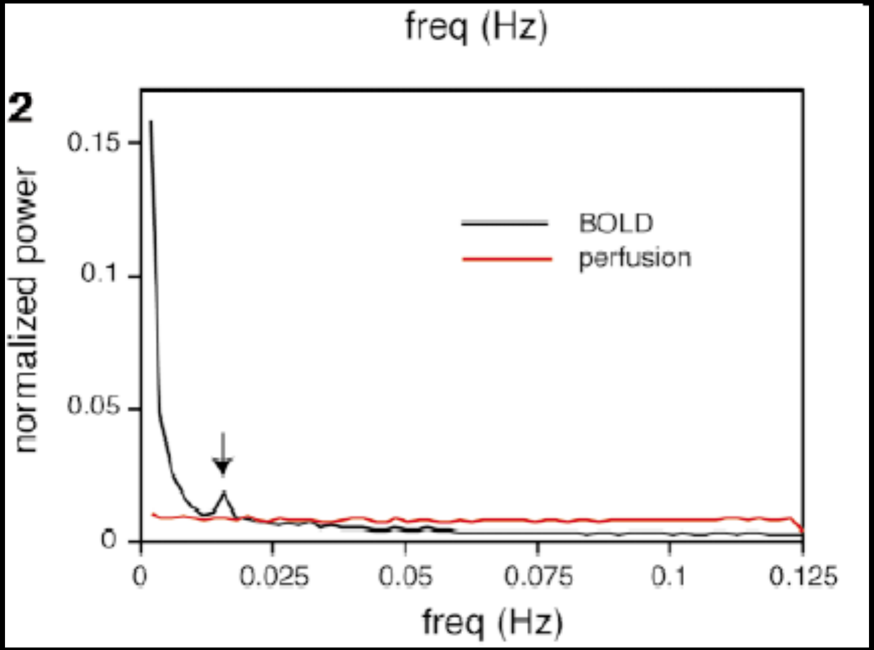
-a problem when looking at slow state changes

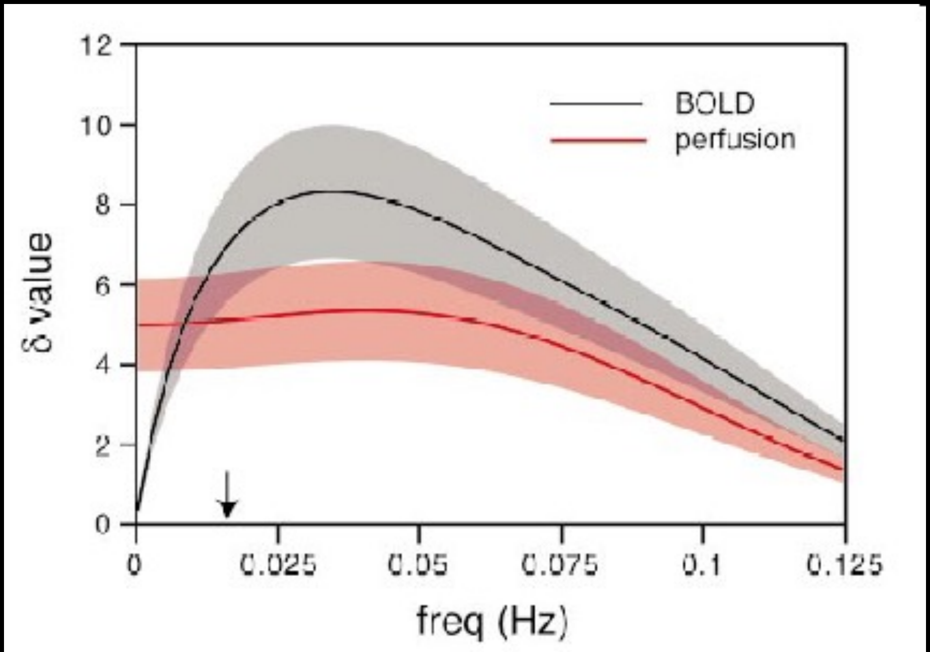
-one solution: ASL techniques

Activation correlated:

-separable from hemodynamic response

ASL Techniques show more temporal stability

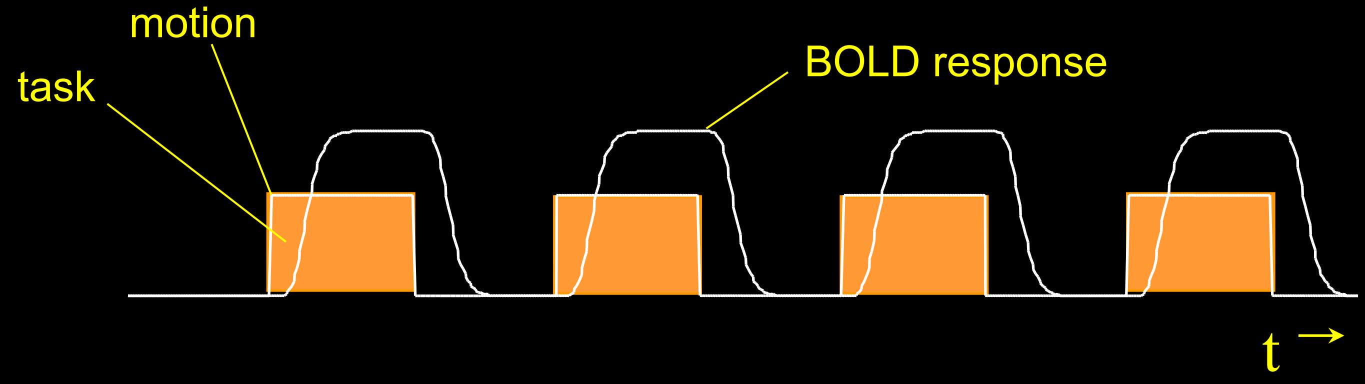




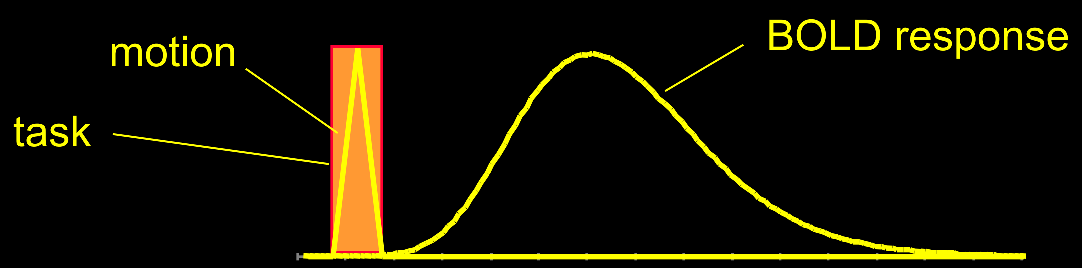
Experimental design and the relative sensitivity of BOLD and perfusion fMRI Aguirre GK, Detre JA, Zarahn E, Alsop DC, **NEUROIMAGE** 15 (3): 488-500 MAR 2002

fMRI during tasks that involve brief motion

Blocked Design

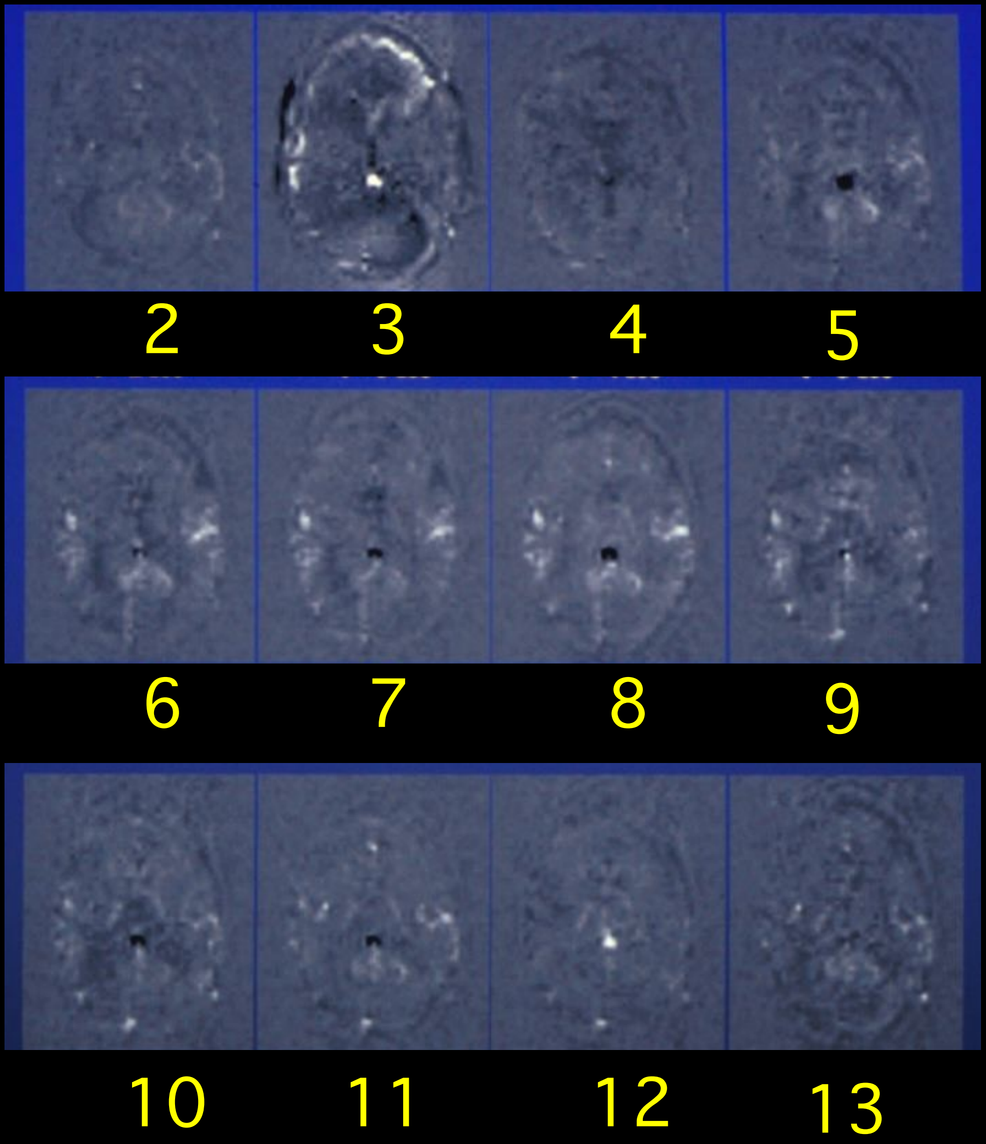


Event-Related Design



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

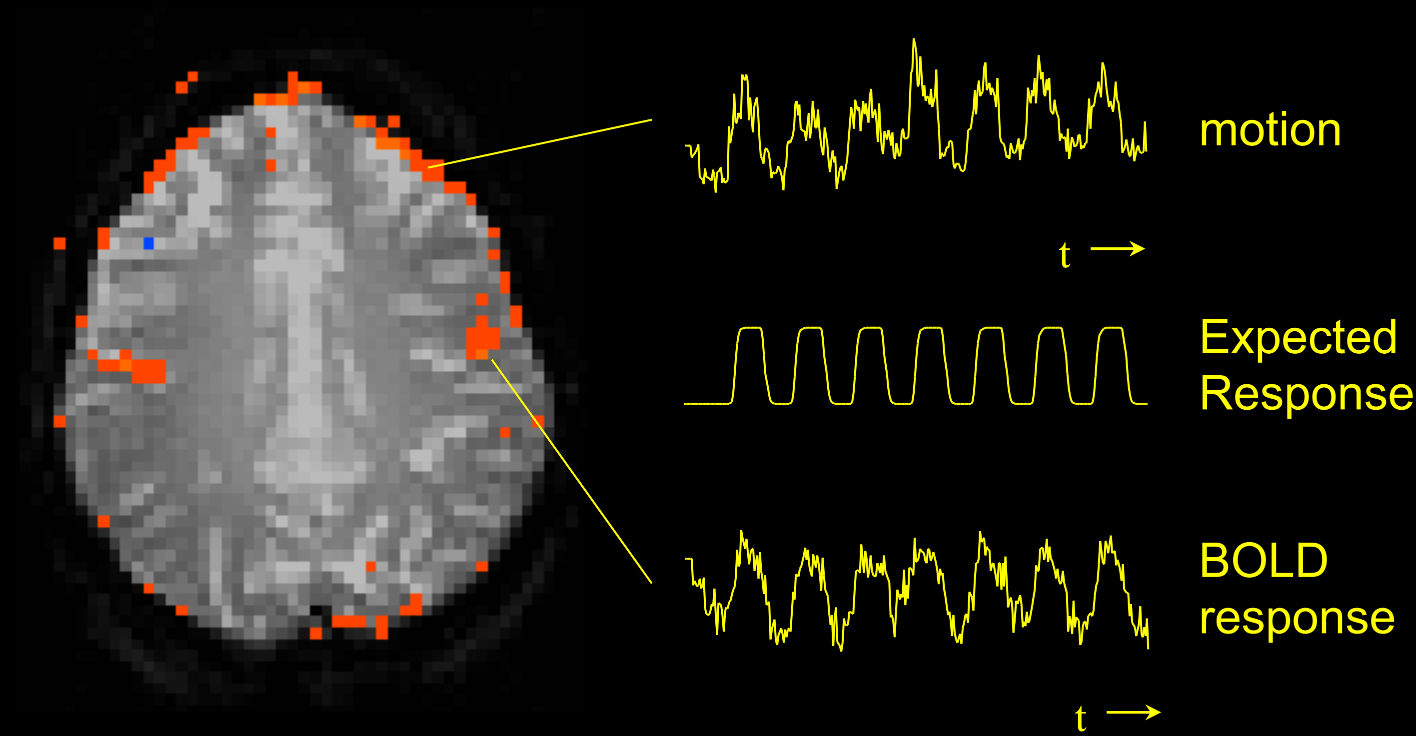
Overt Word Production



R. M. Birn, P. A. Bandettini, R. W. Cox, R. Shaker, Event - related fMRI of tasks involving brief motion. *Human Brain Mapping* 7: 106-114 (1999).

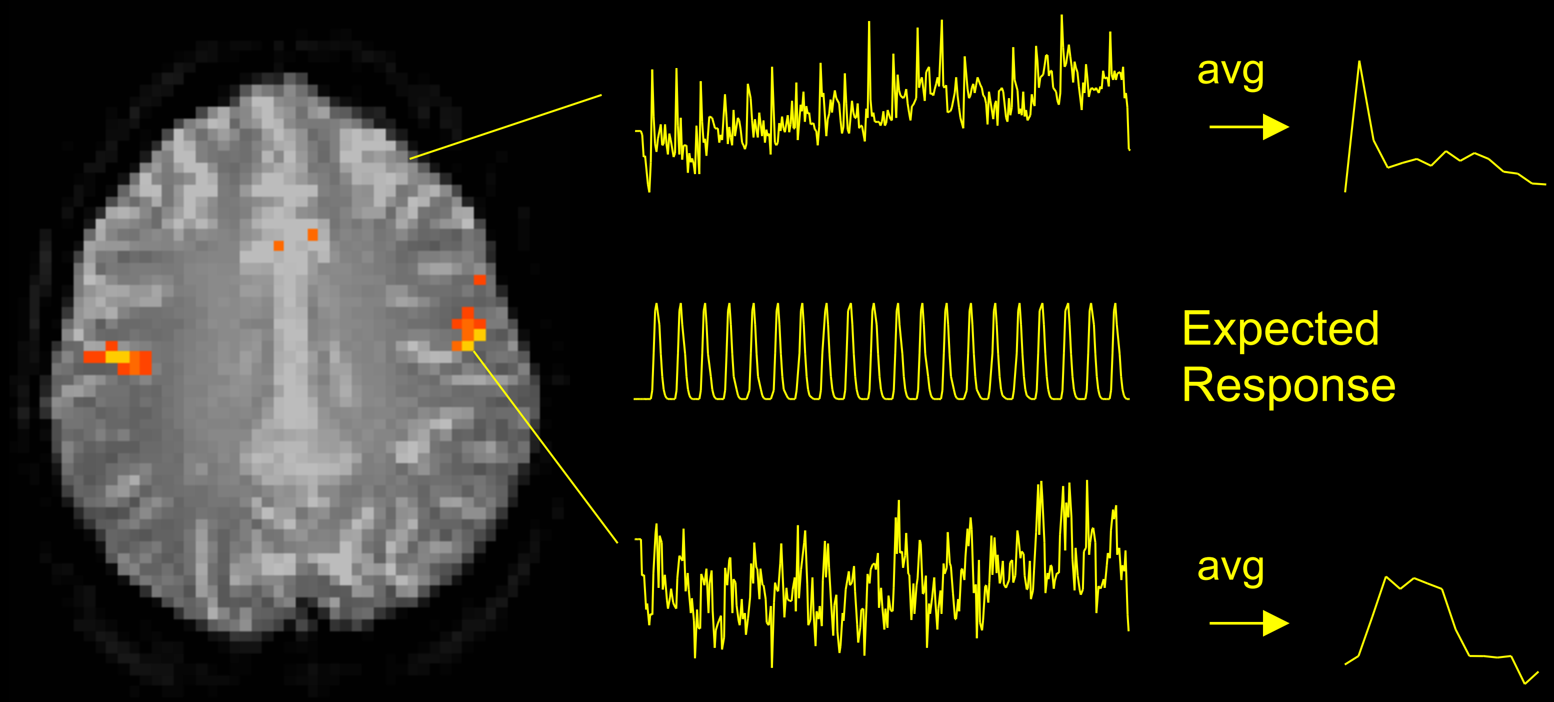
Speaking – Blocked design

R.M. Birn, et al. Human Brain Mapping 7(2), 106-114, 1999



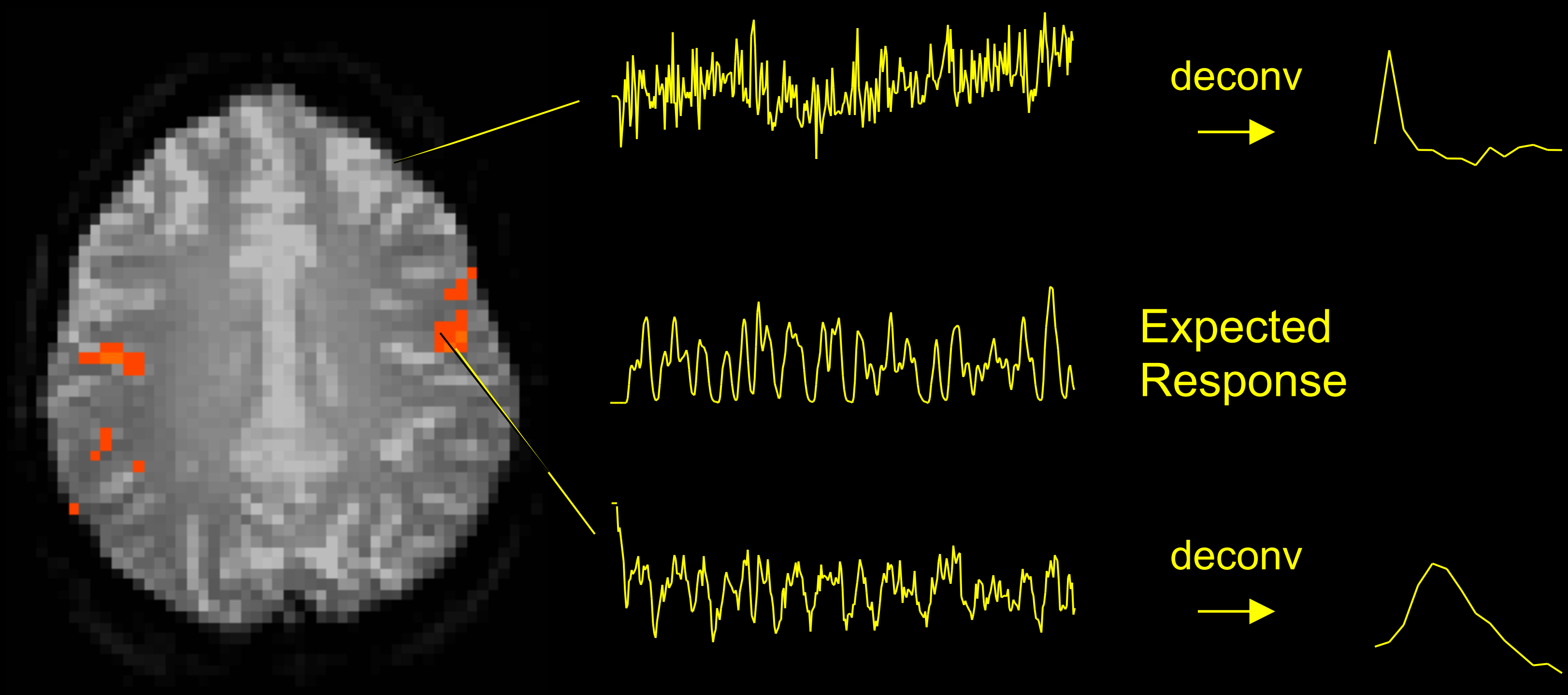
Speaking – Event related design

R.M. Birn, et al. Human Brain Mapping 7(2), 106-114, 1999



Variable ISI

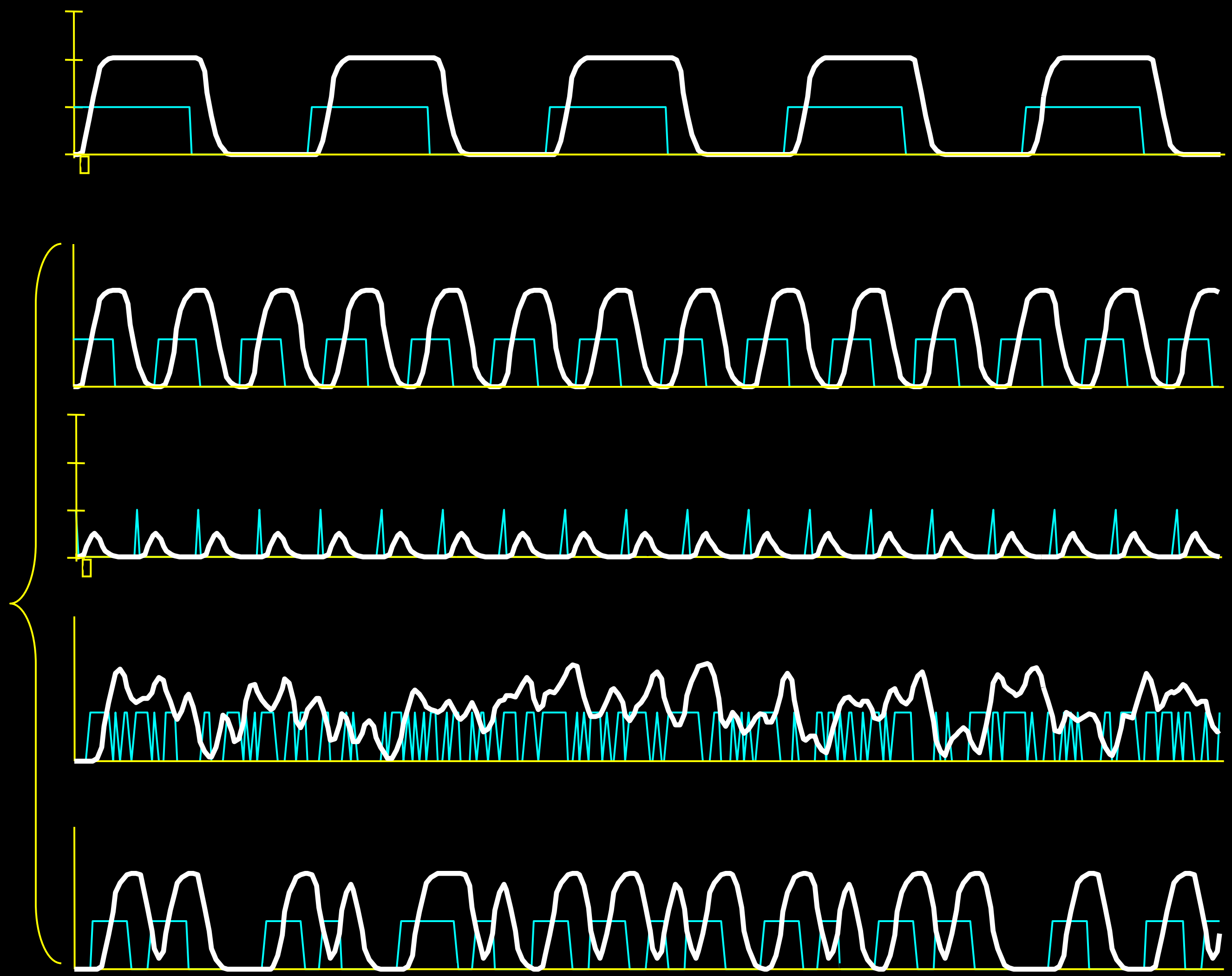
Speaking - ER-fMRI



Optimizing the stimulus paradigm

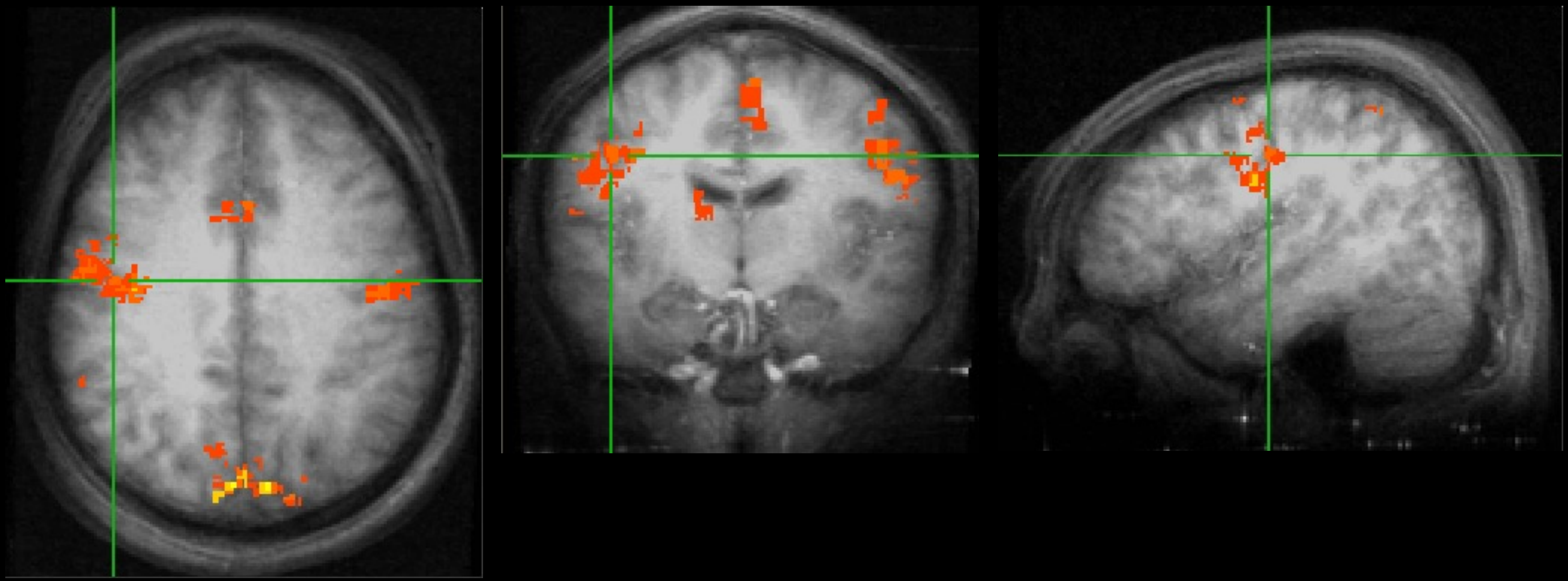
Blocked
(motion highly
correlated)

Blocked /
Event-Related
(low correlation
w/ motion)



Swallowing - Event-Related

M.K. Kern, R.M. Birn, S. Jaradeh, et al., Am J Physiol Gastrointest Liver Physiol, 280(4), G531-538, 2001.

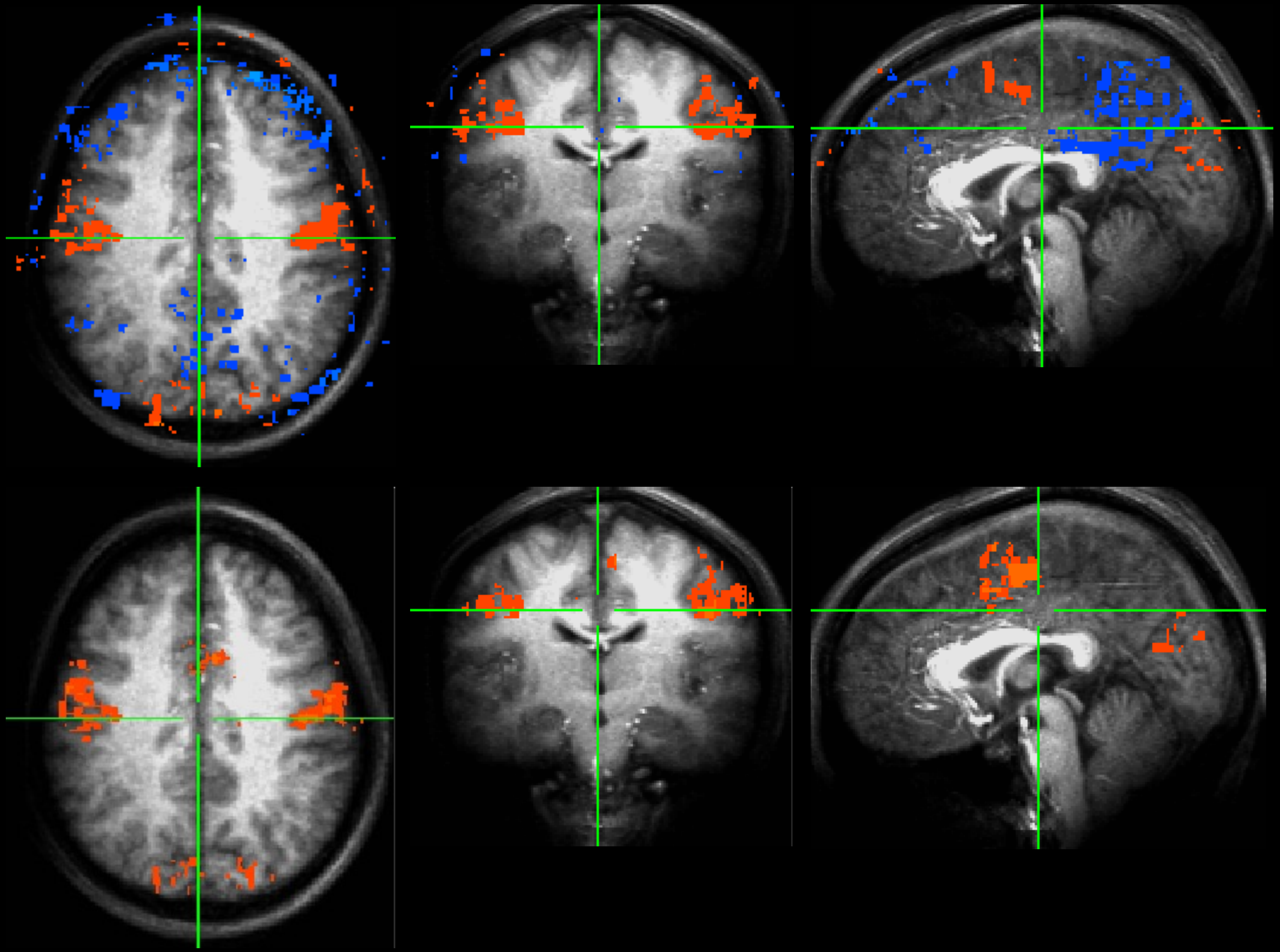


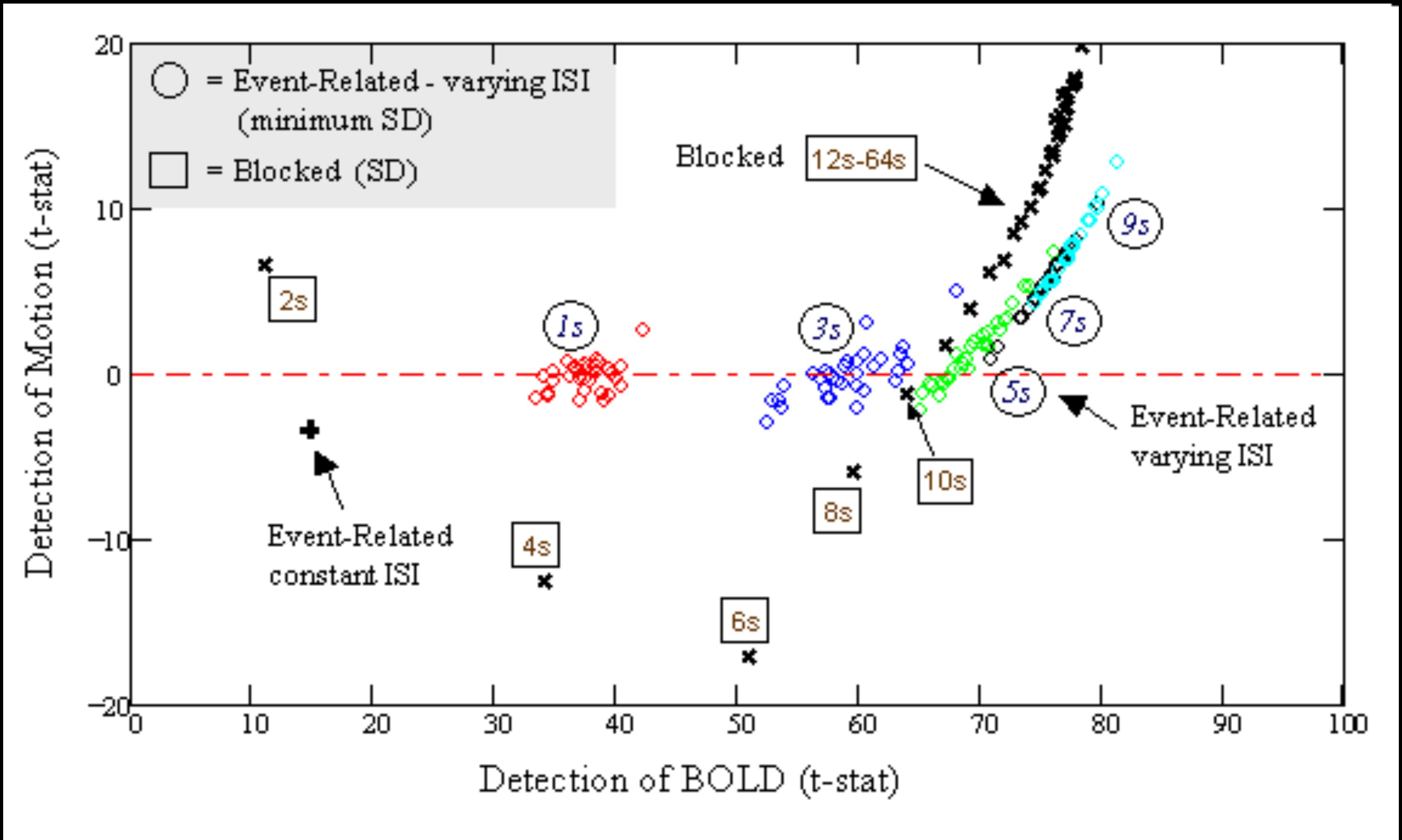
Facial muscle movement

R.M. Birn, et al. Human Brain Mapping 7(2), 106-114, 1999

Blocked design

Event - Related design





= Event-Related - varying ISI (minimum SD)
= Blocked (SD)
Blocked
12s-64s
2s
1s
3s
5s
7s
9s
4s
6s
8s
10s
Event-Related constant ISI
Event-Related varying ISI
Detection of Motion (t-stat)
Detection of BOLD (t-stat)
20
10
0
−10
−20
0
10
20
30
40
50
60
70
80
90
100

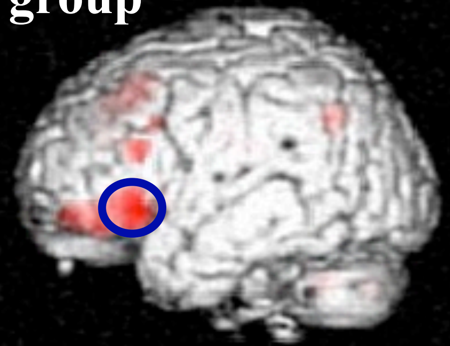
Individual Map “Classification”

The issue: We can make inferences about groups when averaging individual maps, but can we make inferences which group an individual belongs to?

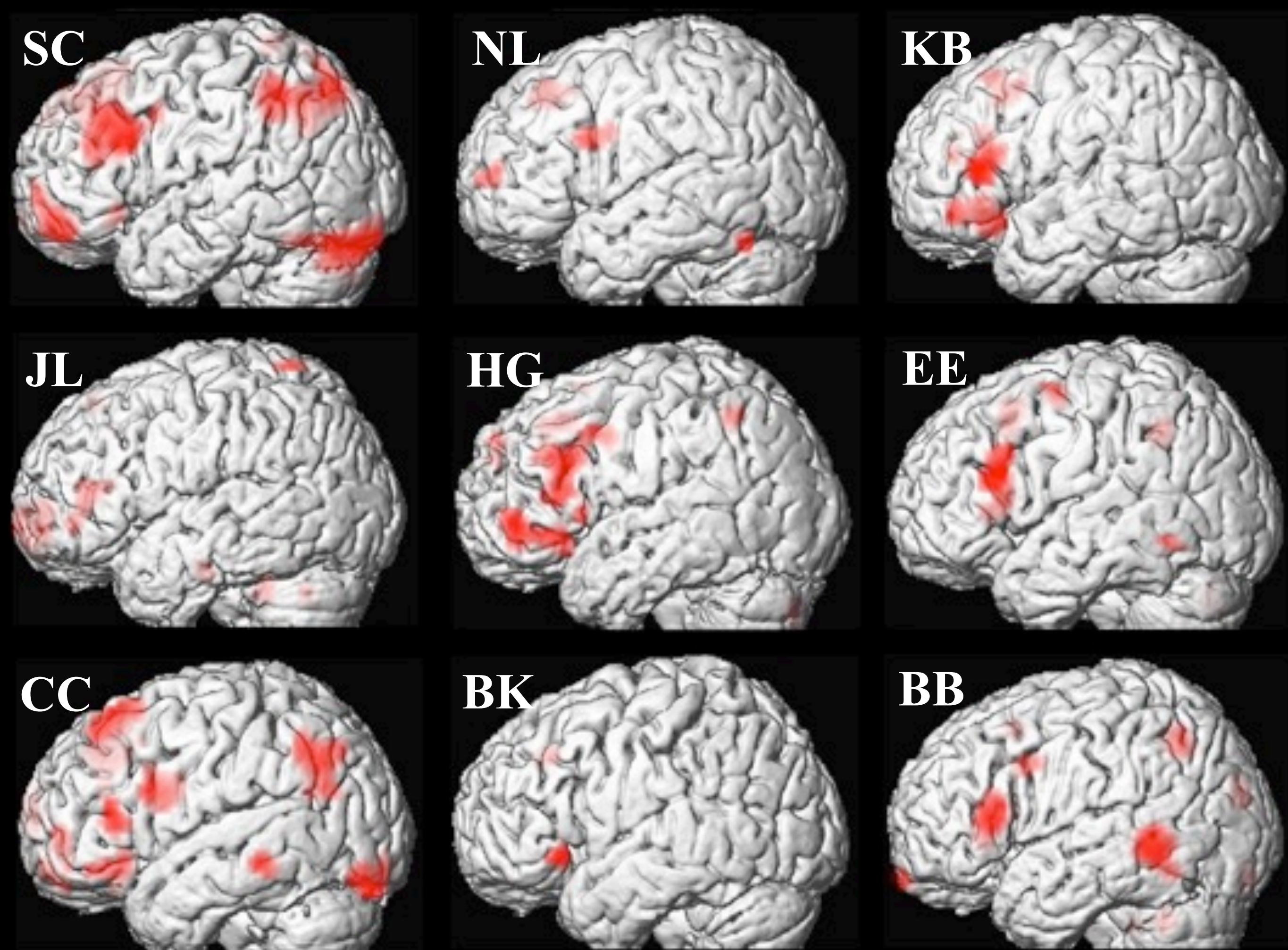
Not yet. Requires extensive classification techniques.

Extensive Individual Differences in Brain Activations During Episodic Retrieval

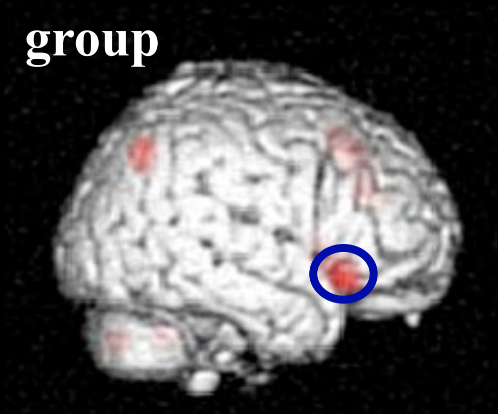
Miller et al., 2002



Individual activations from the left hemisphere of the 9 subjects



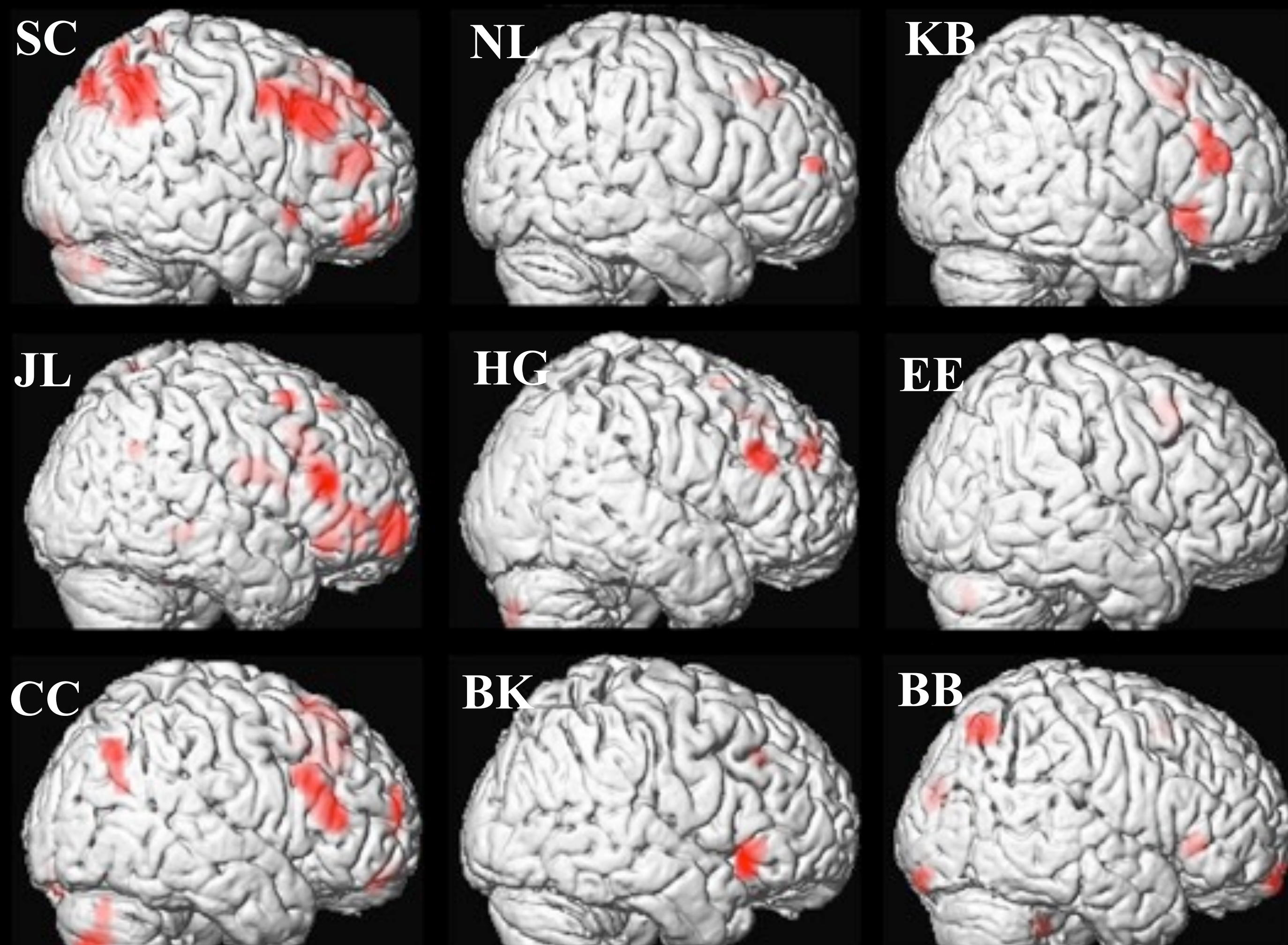
Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University



Extensive Individual Differences in Brain Activations During Episodic Retrieval

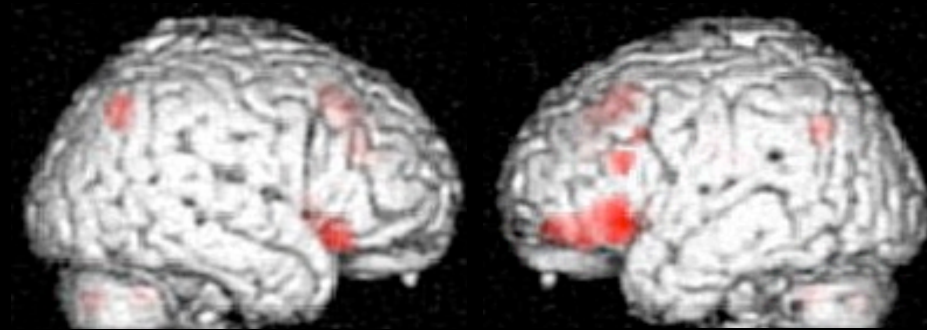
Miller et al., 2002

Individual activations from the right hemisphere of the 9 subjects

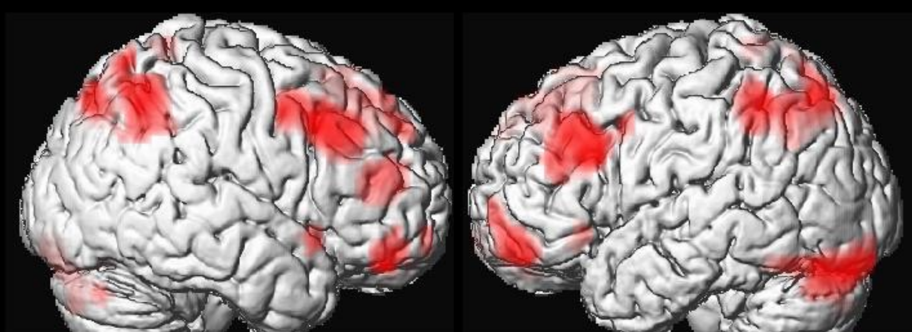


Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University

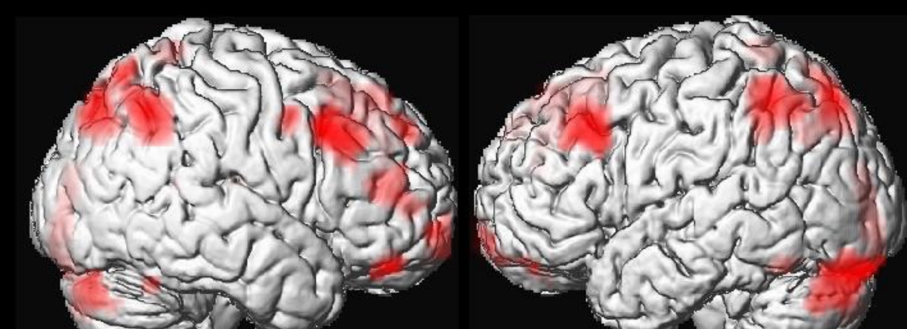
These individual patterns of activations are stable over time



Group Analysis of Episodic Retrieval



Subject SC

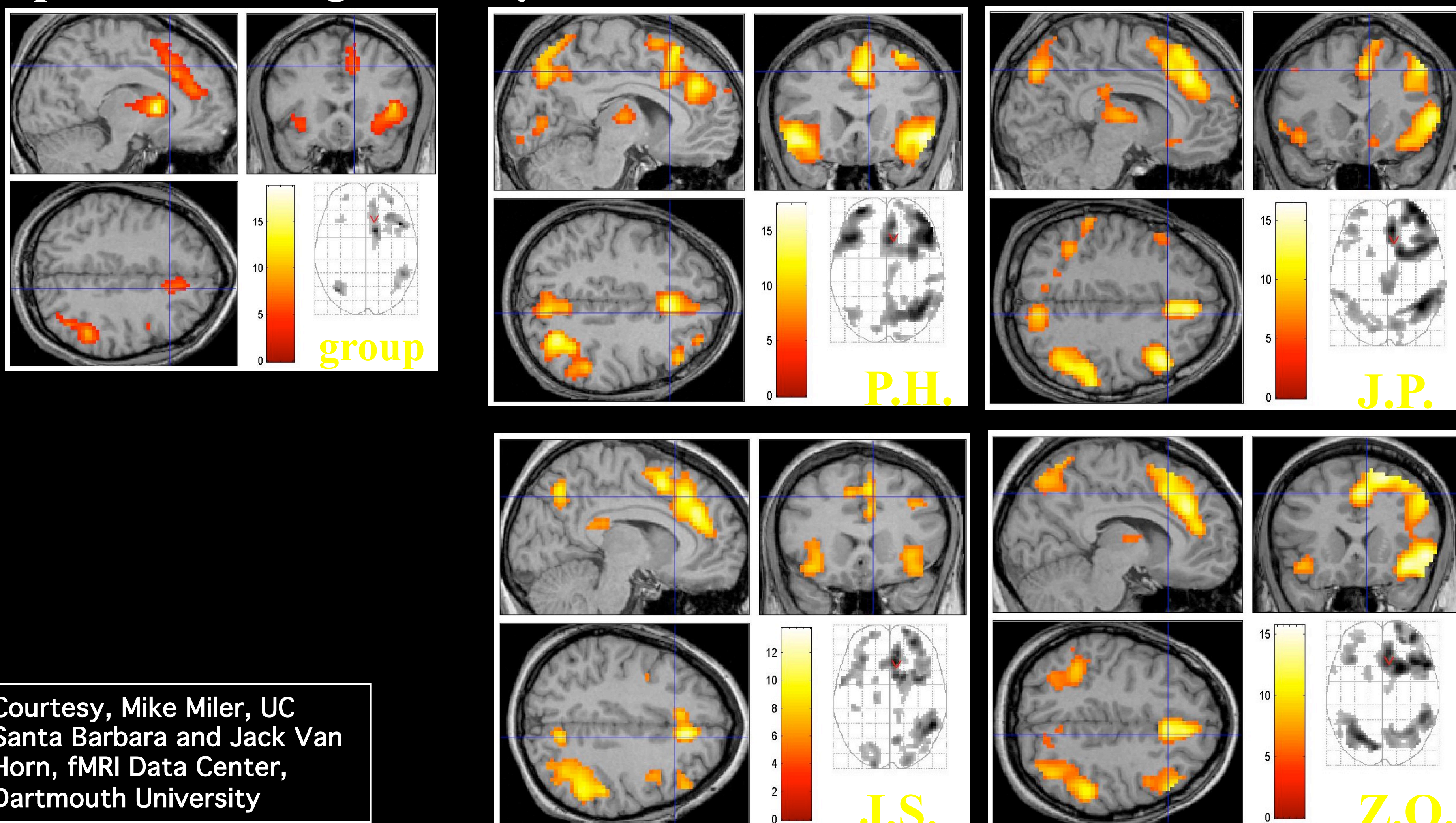


Subject SC 6 months later

Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University

Individual patterns of activity are much more consistent across subjects for other retrieval tasks.

spatial working memory



Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University

Local Pattern Effect
Classification and Mapping

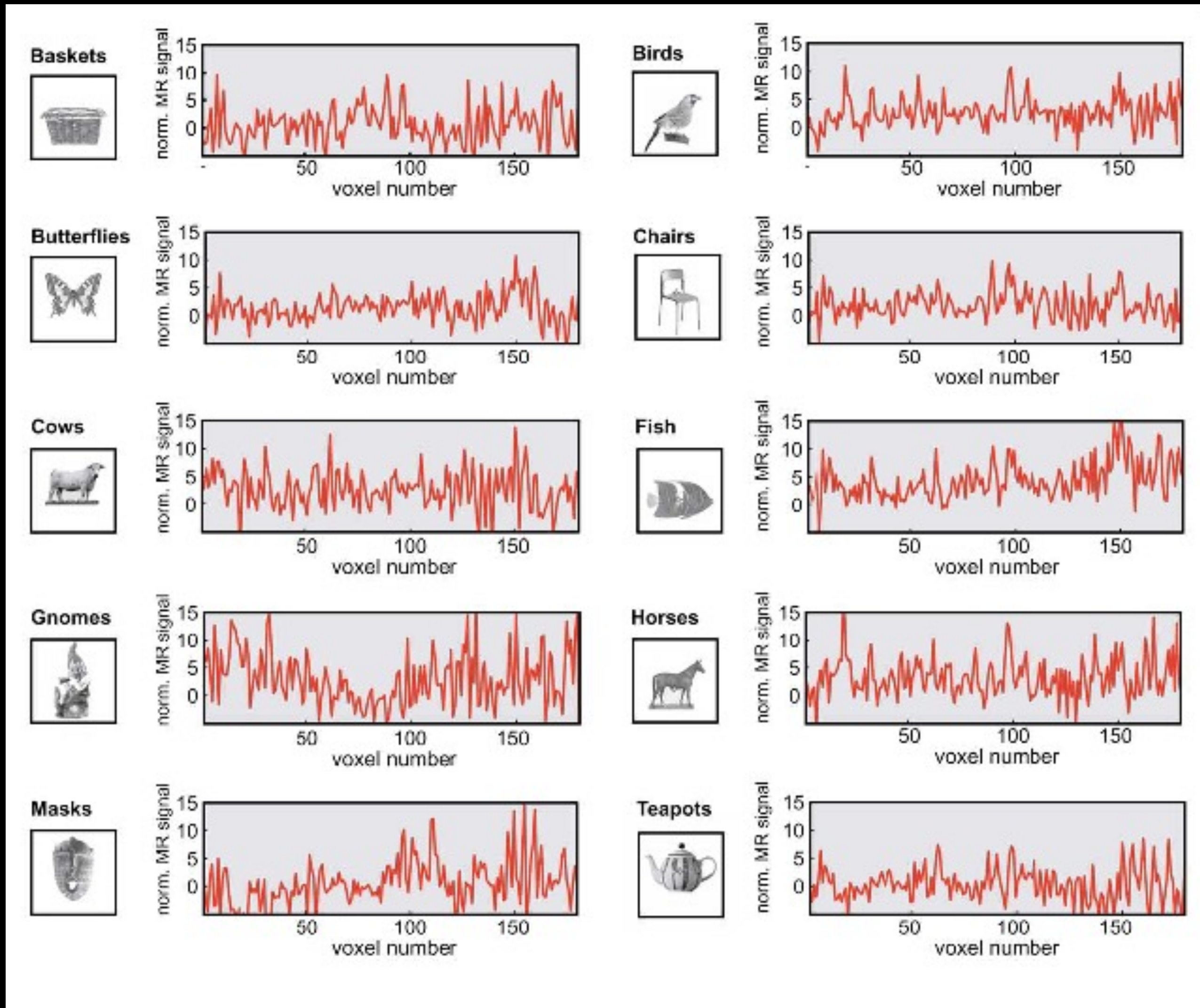
Functional magnetic resonance imaging (fMRI) "brain reading": detecting and classifying distributed patterns of fMRI activity in human visual cortex

David D. Cox[a,b,*] and Robert L. Savoy[a,b,c]

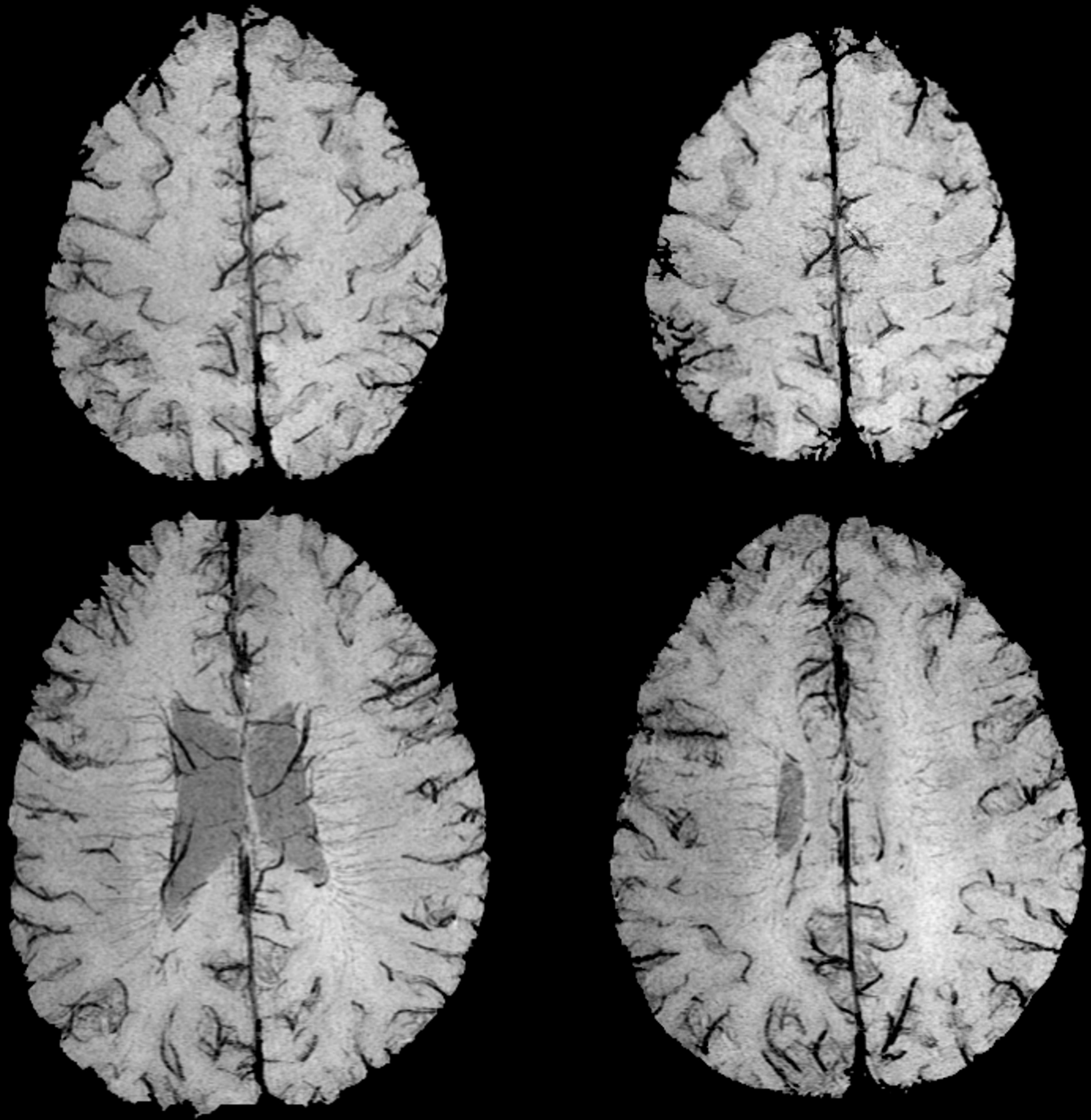
[a] Rowland Institute for Science, Cambridge, MA 02142, USA
[b] Athinoula A. Martinos Center for Structural and Functional Biomedical Imaging, Charlestown, MA 02129, USA
[c] HyperVision, Inc., P.O. Box 158, Lexington, MA 02420, USA

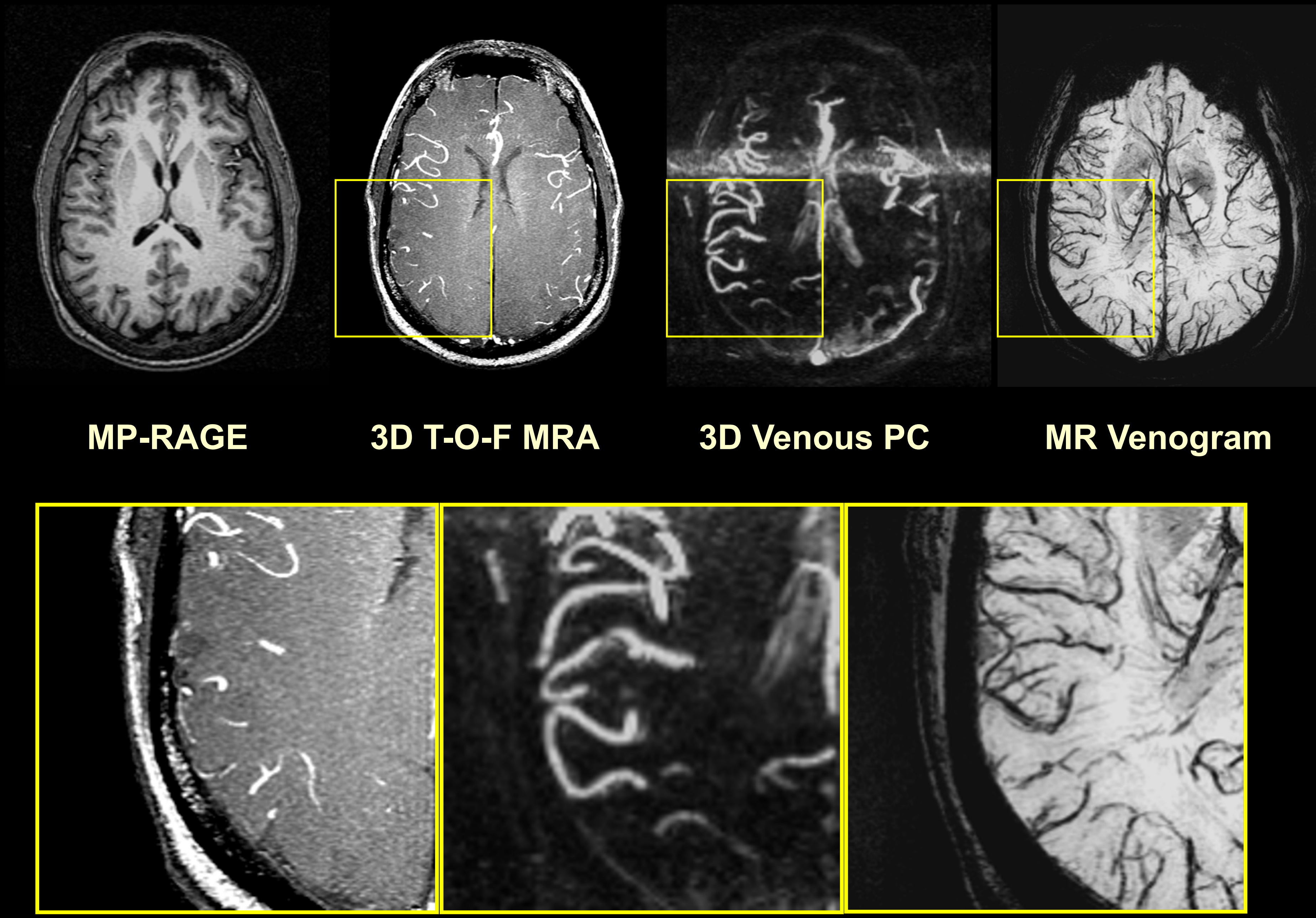
Received 15 July 2002; accepted 10 December 2002

NEUROIMAGE 19 (2): 261-270 Part 1 JUN 2003

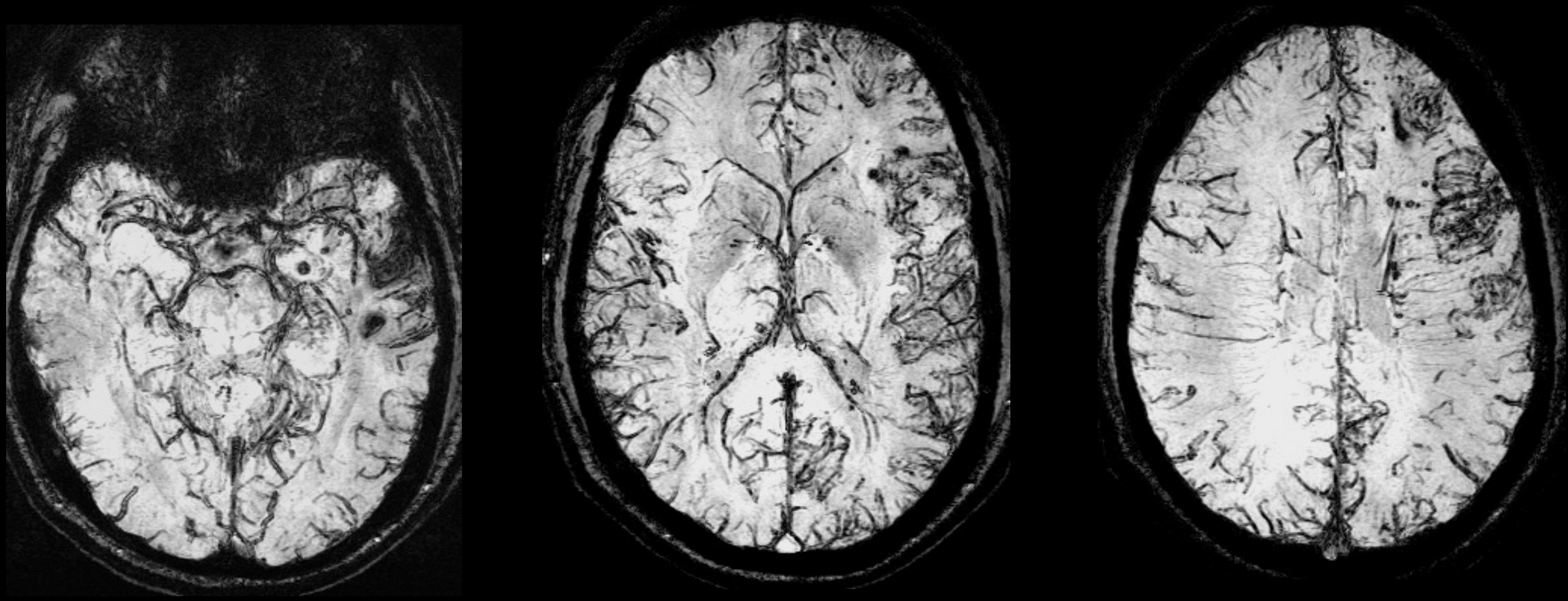


Baseline susceptibility mapping





MP-RAGE
3D T-O-F MRA
3D Venous PC
MR Venogram



Direct Neuronal Current Imaging?

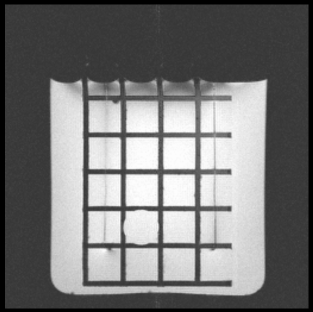
Toward Direct Mapping of Neuronal Activity: MRI Detection of Ultraweak, Transient Magnetic Field Changes

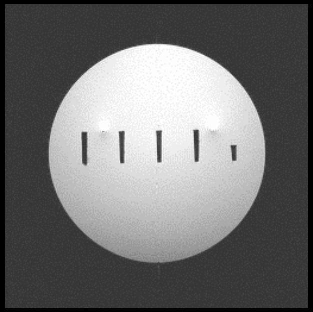
Jerzy Bodurka[1*] and Peter A. Bandettini[1,2]

- Preliminary models suggest that magnetic field changes on the order of 0.1 to 1 nT are induced (at the voxel scale) in the brain.

- These changes induce about a 0.01 Hz frequency shift or 0.09 deg (@ TE = 30 ms) phase shift.

- Question: Is this detectable?





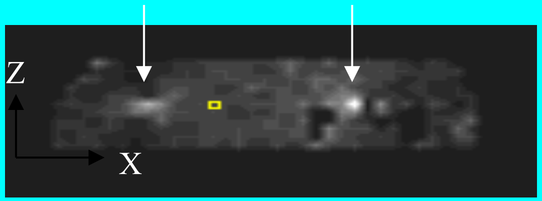
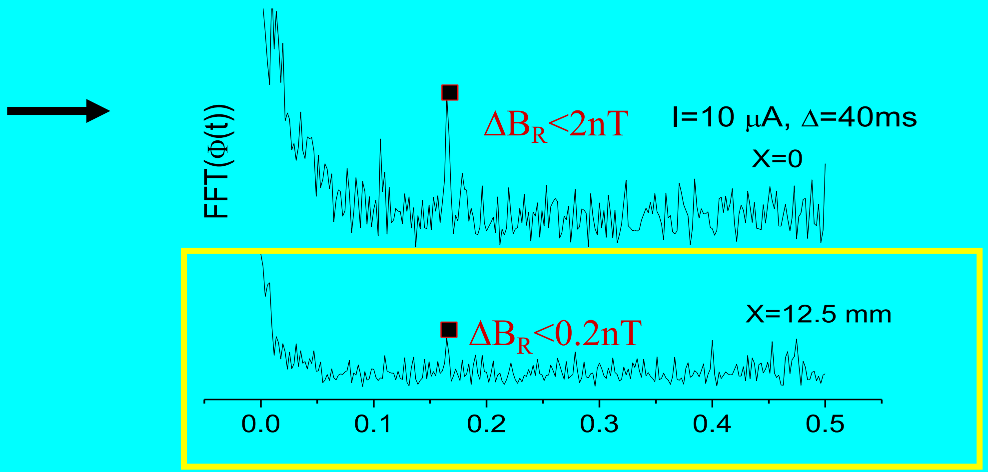
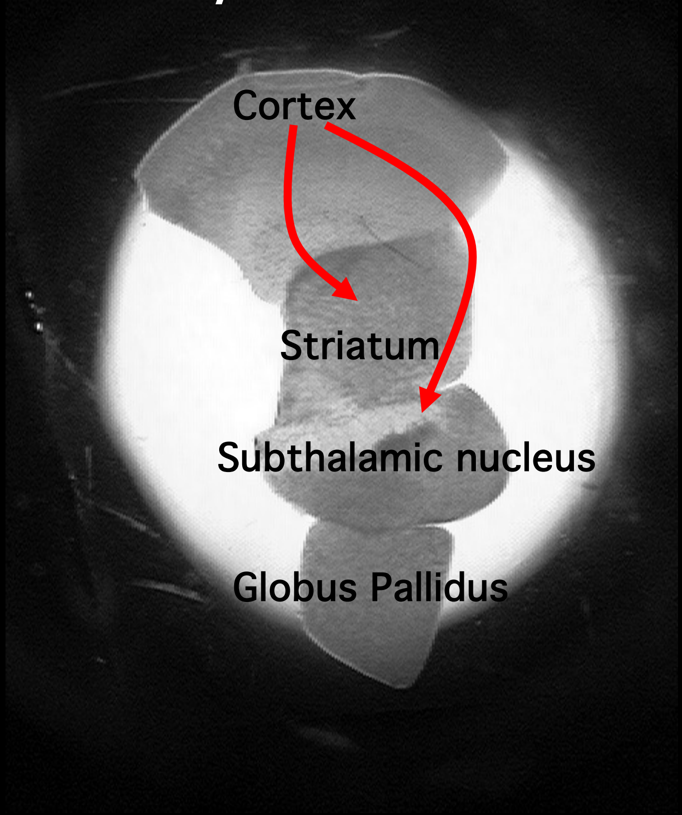

Z
X

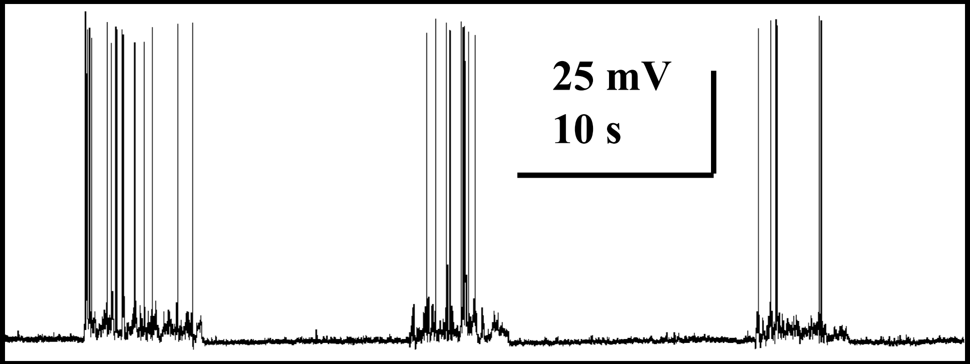
Figure 1


FFT(Φ(t))
ΔB_R<2nT
I=10 μA, Δ=40ms
X=0
ΔB_R<0.2nT
X=12.5 mm
0.0
0.1
0.2
0.3
0.4
0.5

In Vitro Results

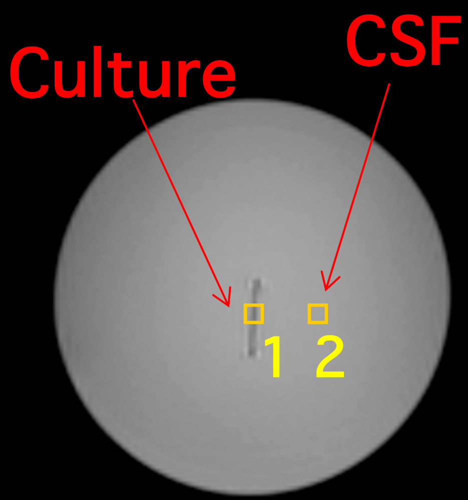
Newborn rat brains have been found to exhibit spontaneous and synchronous firing at specific frequencies



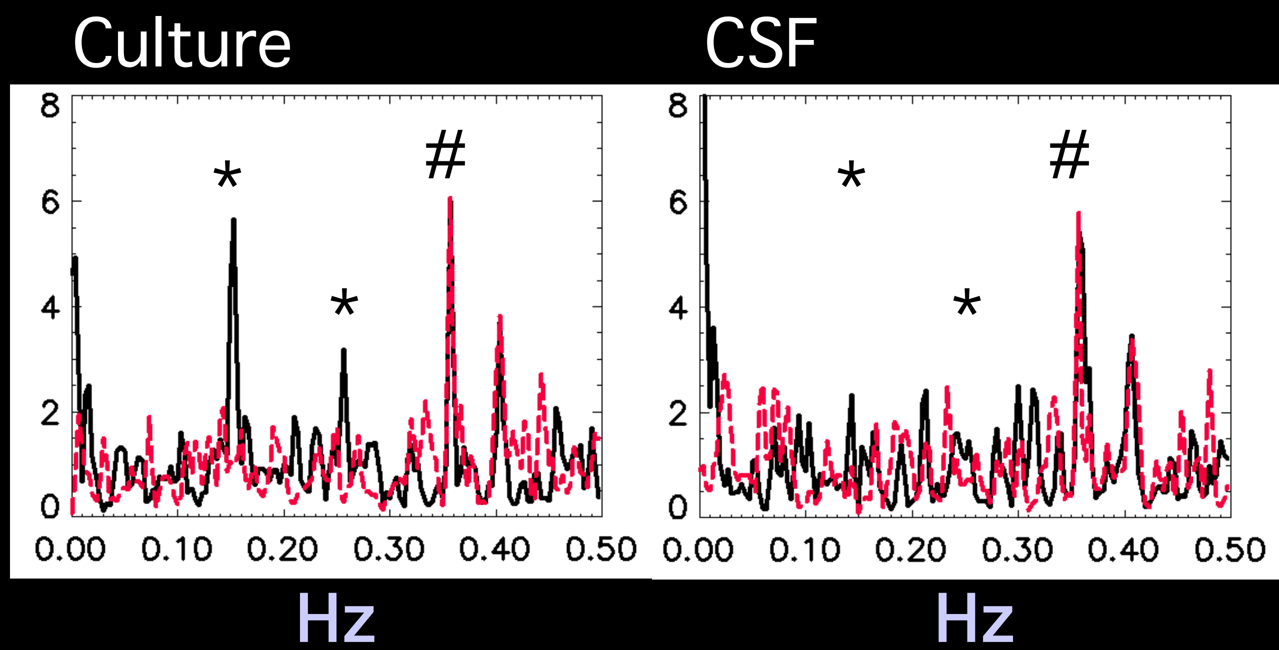


Plenz, D. and S.T. Kital. Nature, 1999. **400**: p. 677-682.

Results



FSE image



Active state: 10 min, Inactive state: 10 min after TTX admin.

*: activity

#: scanner pump frequency

Petridou et al.

What are the biggest unknowns/challenges?

1. Technology

2. Methodology

3. Interpretation

Interpretation

- Linearity / proportionality
- Hemodynamic vs. Neuronal effects
- Resting state (fluctuations and DC)
- Neuronal inhibition / excitation effects
- Negative signal changes
- HRF latency, magnitude, pre and post undershoot
- T2, T2*, T1, diffusion, and Mo changes
- Differences across modalities (location, timing)

Interpretation

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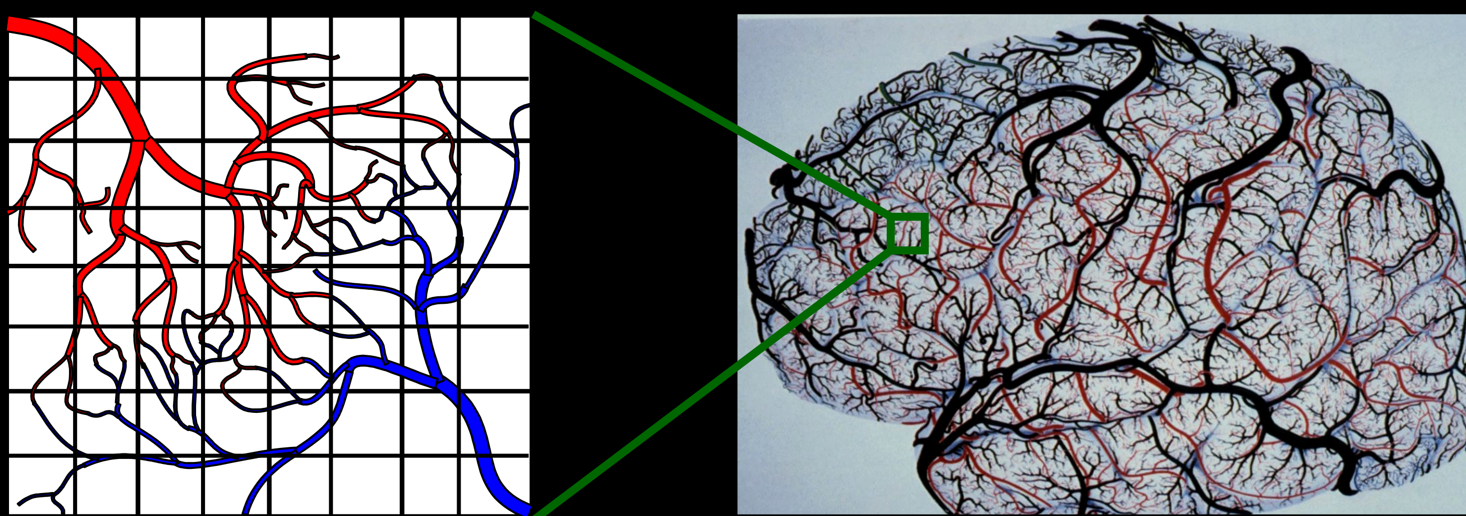
- Differences across modalities (location, timing)

The Problem

Neuronal Activation ? Measured Signal

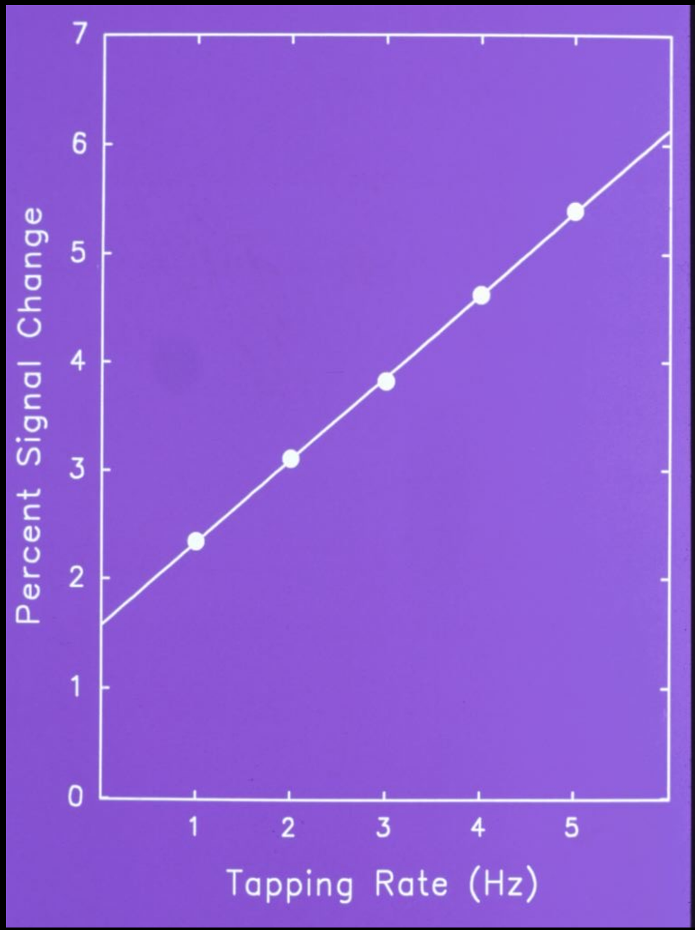
? Hemodynamics ?

? Noise



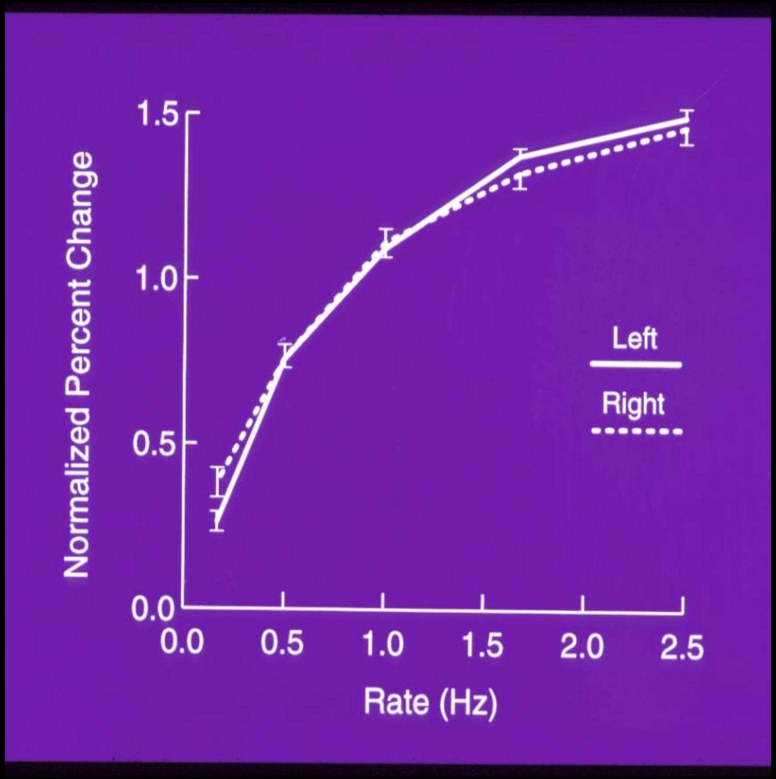
Linearity / proportionality

Motor Cortex



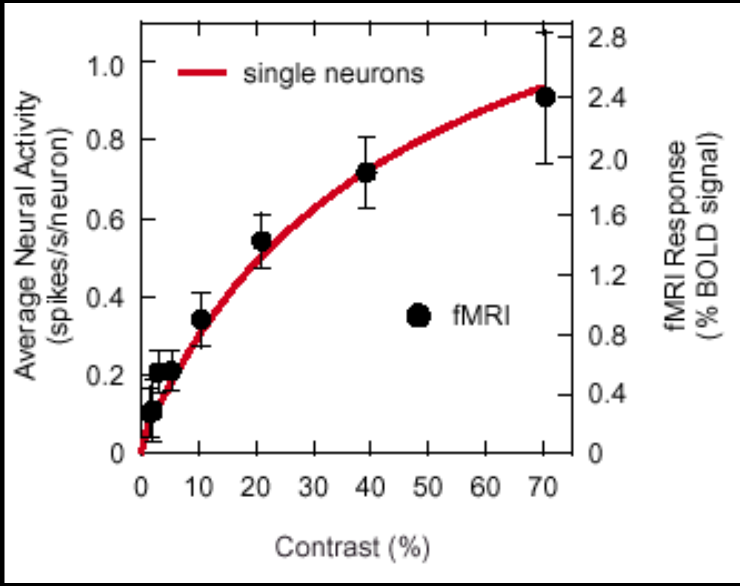
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

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

fMRI responses in human V1 are proportional to average firing rates in monkey V1



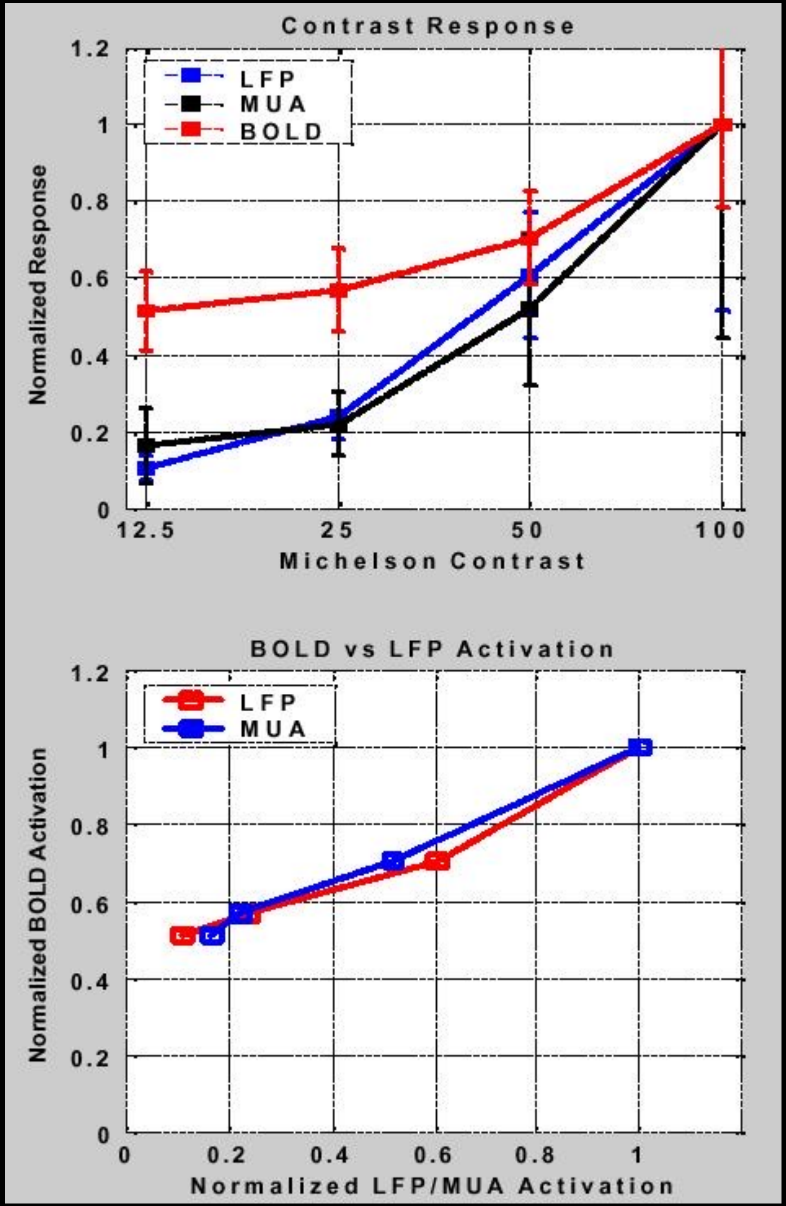
Heeger, D. J., Huk, A. C., Geisler, W. S., and Albrecht, D. G. 2000.Spikes versus BOLD: What does neuroimaging tell us about neuronal activity? *Nat. Neurosci.* **3:** 631–633.

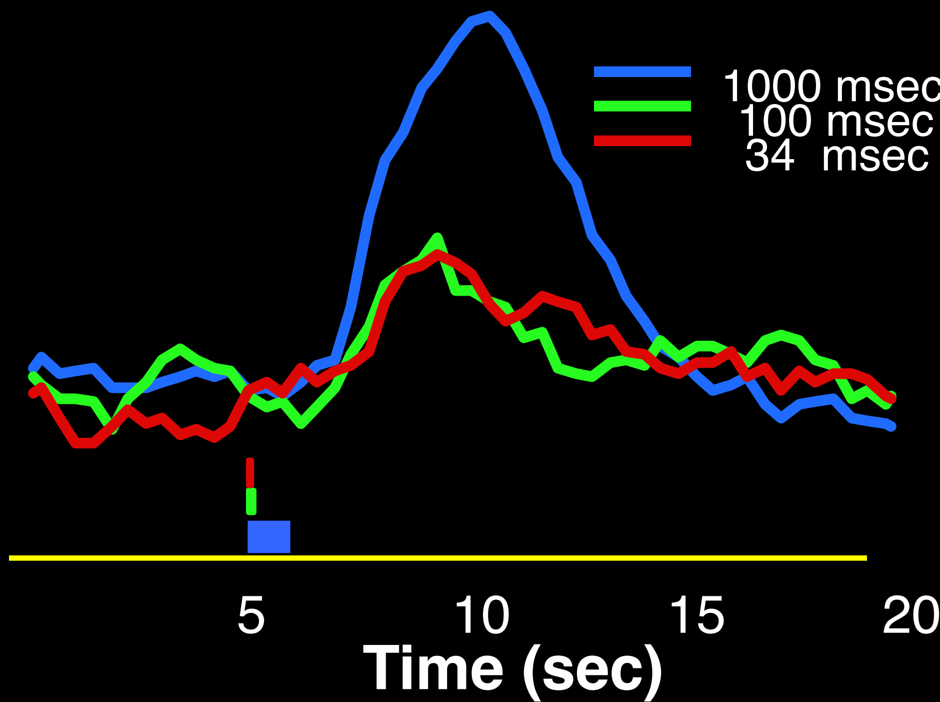
0.4 spikes/sec -> 1% BOLD

Rees, G., Friston, K., and Koch, C. 2000. A direct quantitative relationship between the functional properties of human and macaque V5. *Nat. Neurosci.* **3:** 716–723.

9 spikes/sec -> 1% BOLD

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

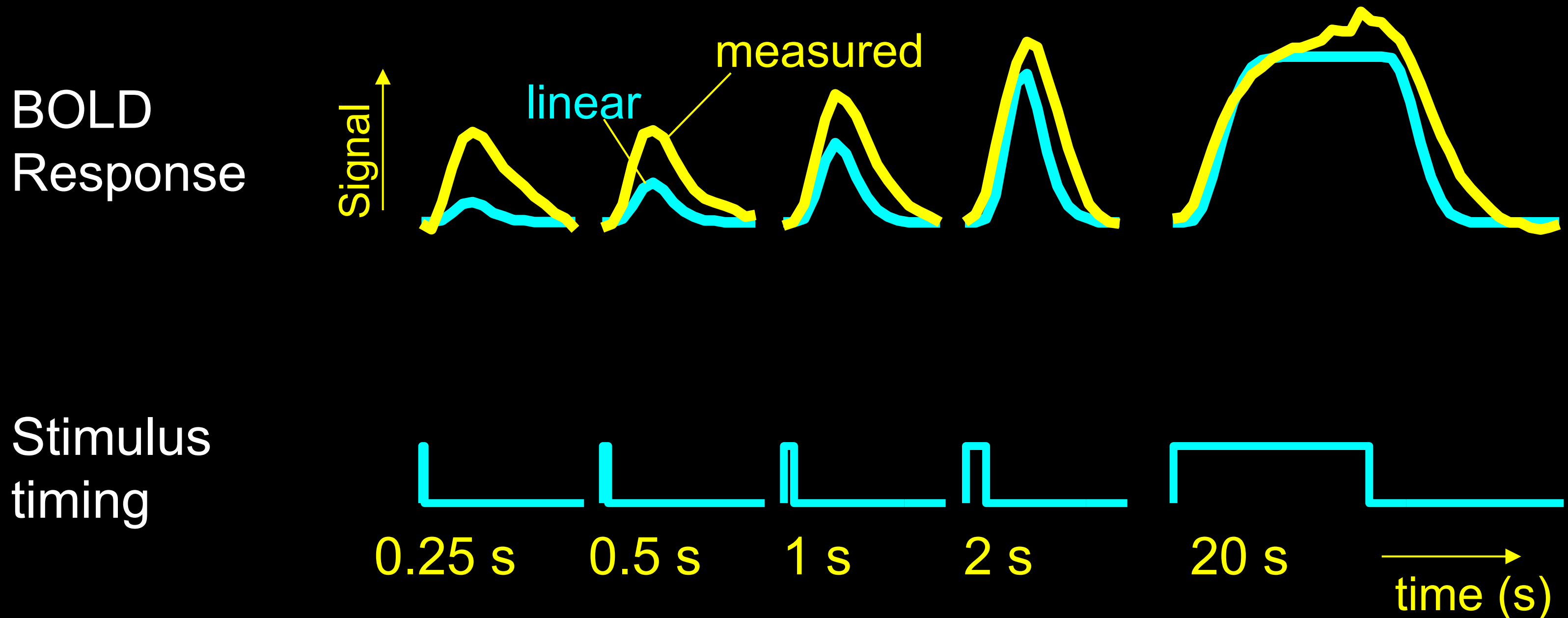




R. L. Savoy, et al., Pushing the temporal resolution of fMRI: studies of very brief visual stimuli, onset variability and asynchrony, and stimulus-correlated changes in noise [oral], 3'rd Proc. Soc. Magn. Reson., Nice, p. 450. (1995).

Dynamic Nonlinearity Assessment

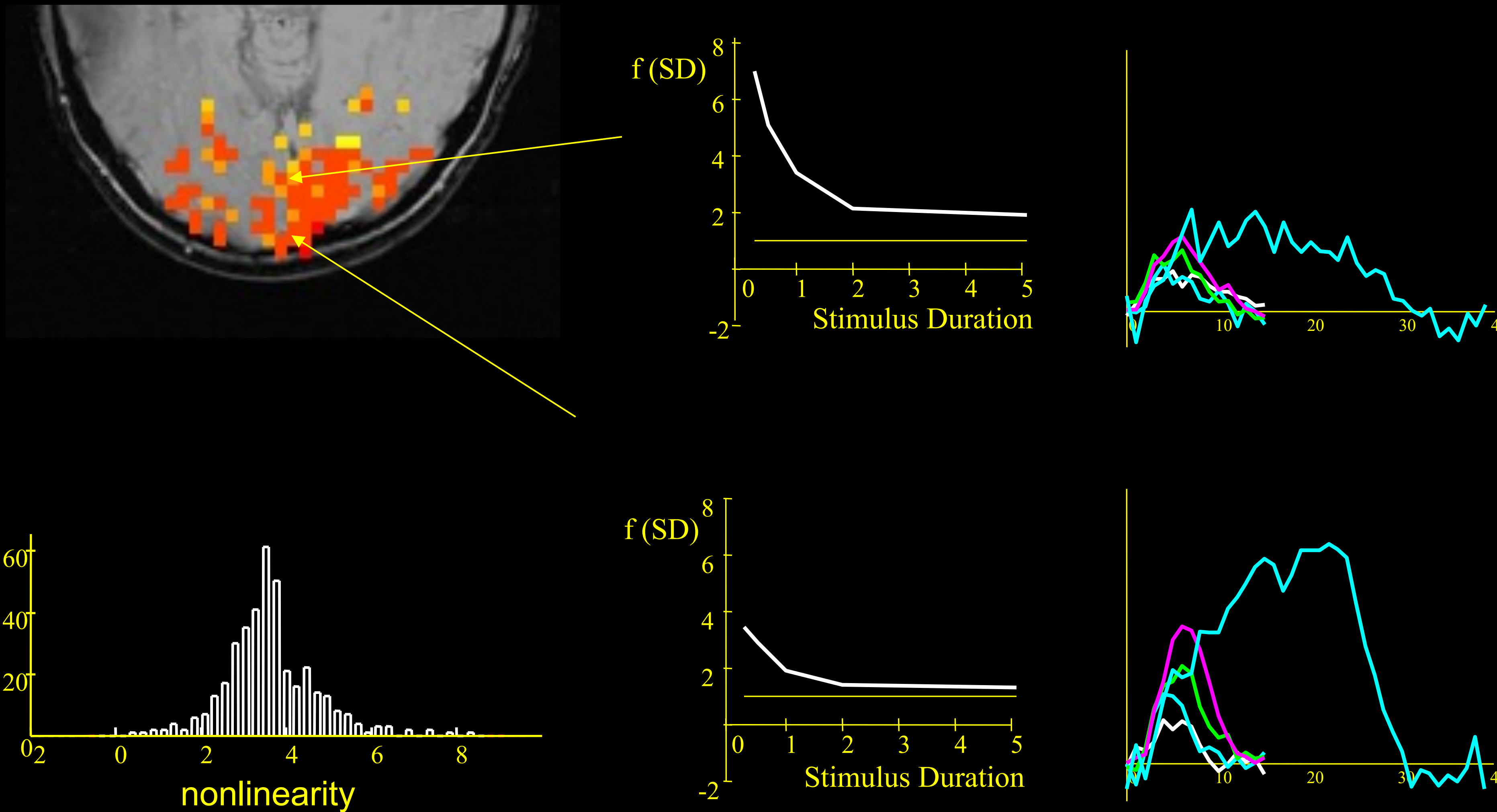
Different stimulus "ON" periods



Brief stimuli produce larger responses than expected

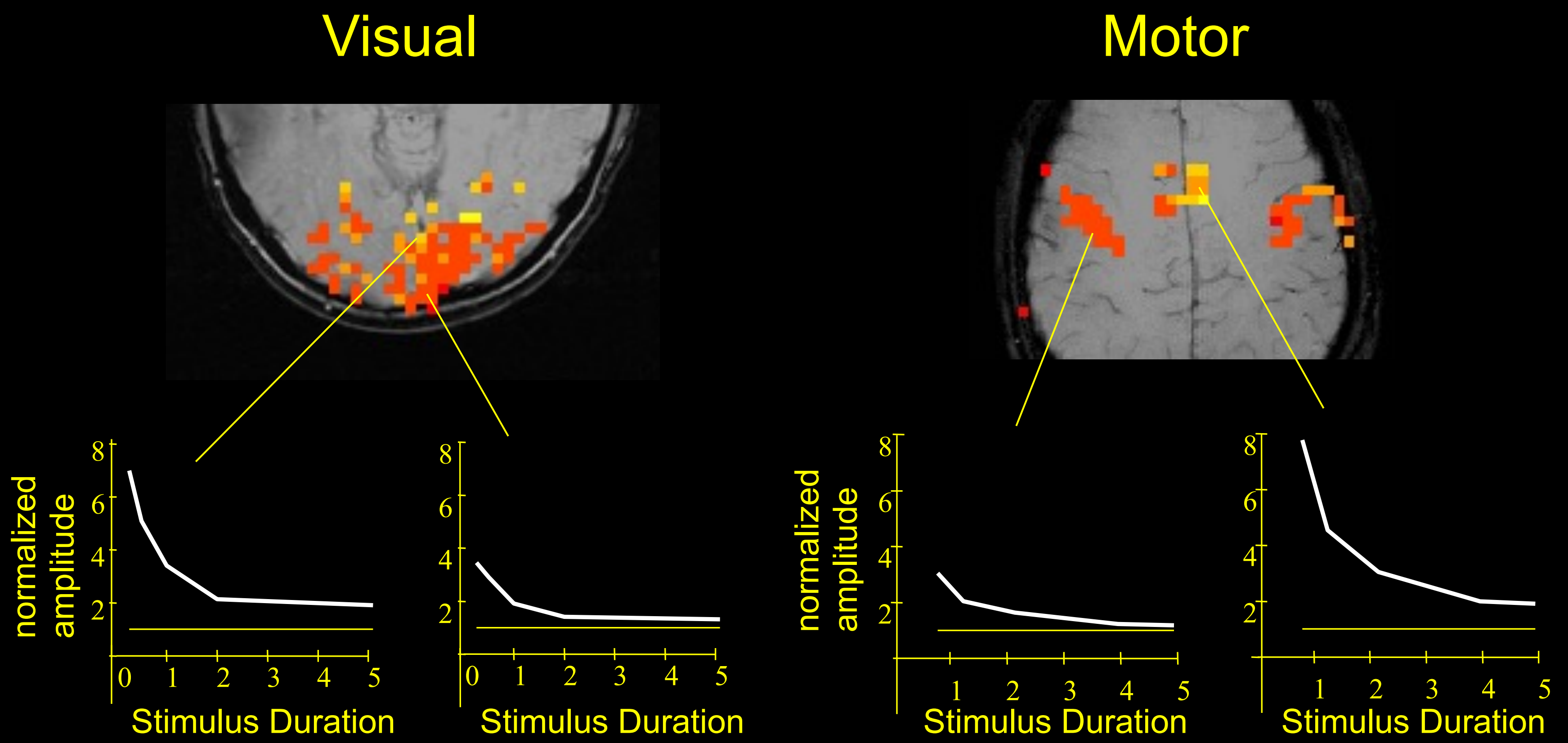
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." ***NeuroImage*****, 14: 817-826.**

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.

Spatial variation of linearity



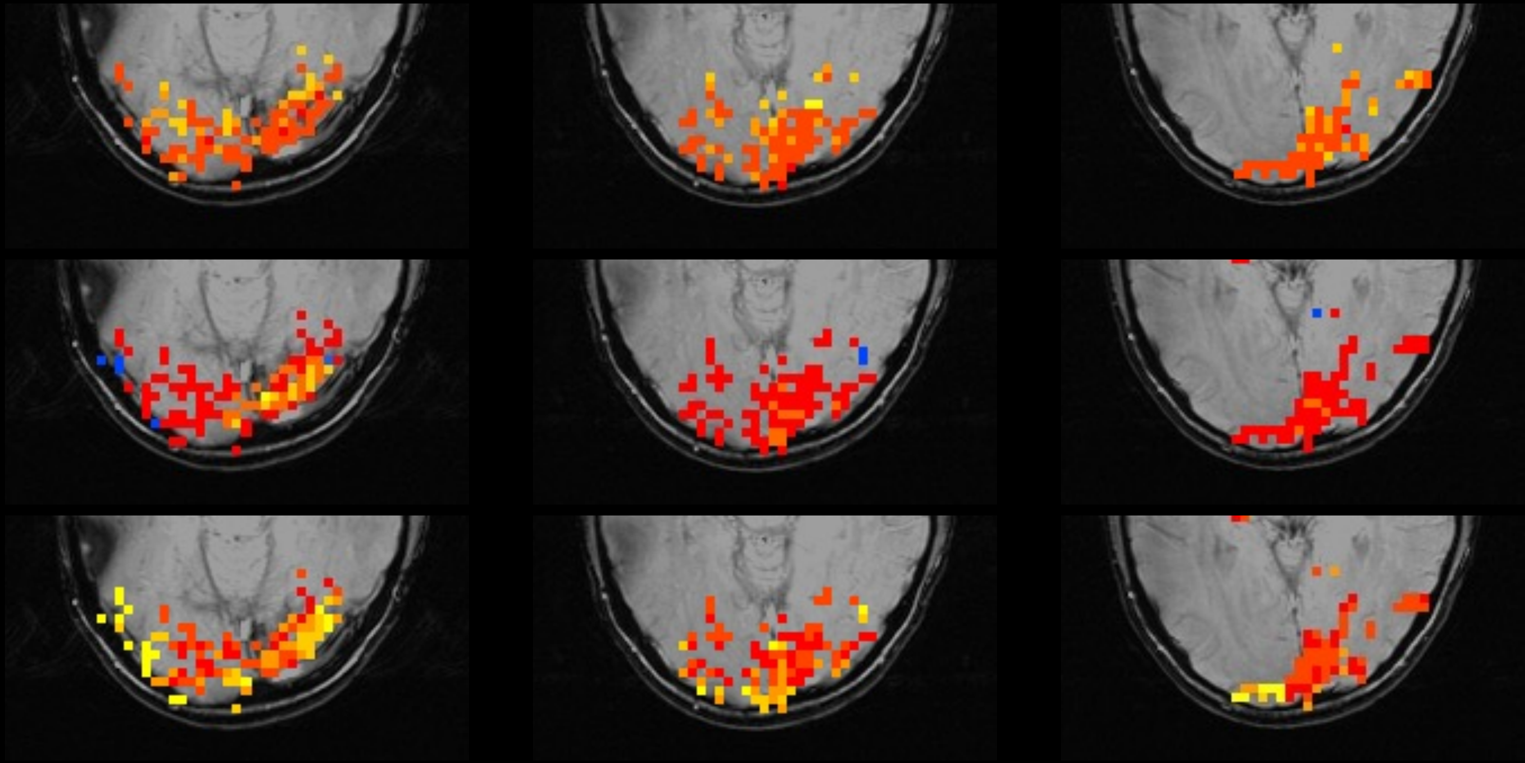
R.M. Birn, et al. Neuroimage 14, 817-26, 2001

Results – visual task

Nonlinearity

Magnitude

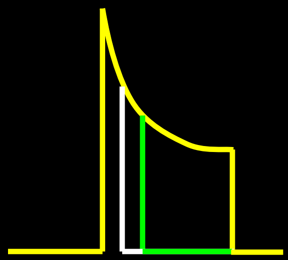
Latency



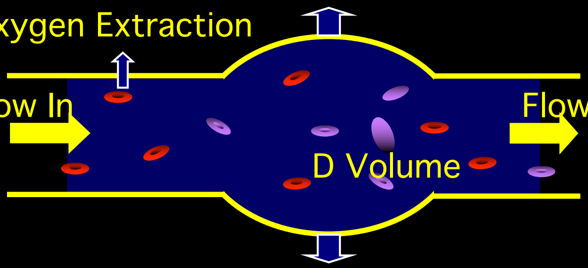
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

Sources of this Nonlinearity

- Neuronal

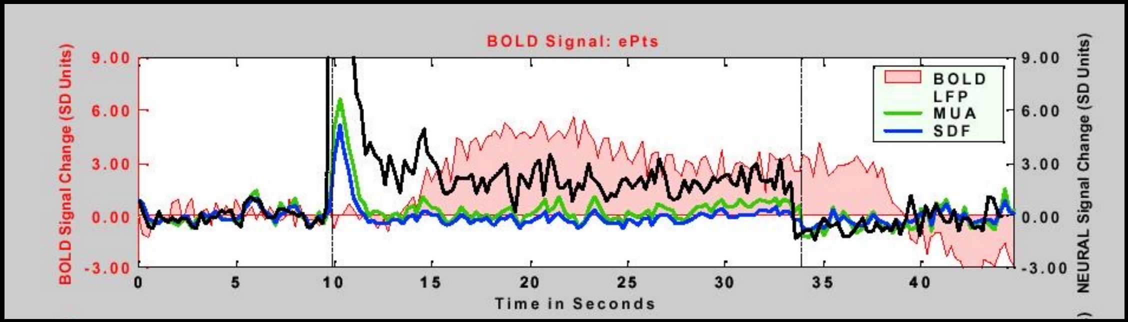


- Hemodynamic
  - Oxygen extraction
  - Blood volume dynamics

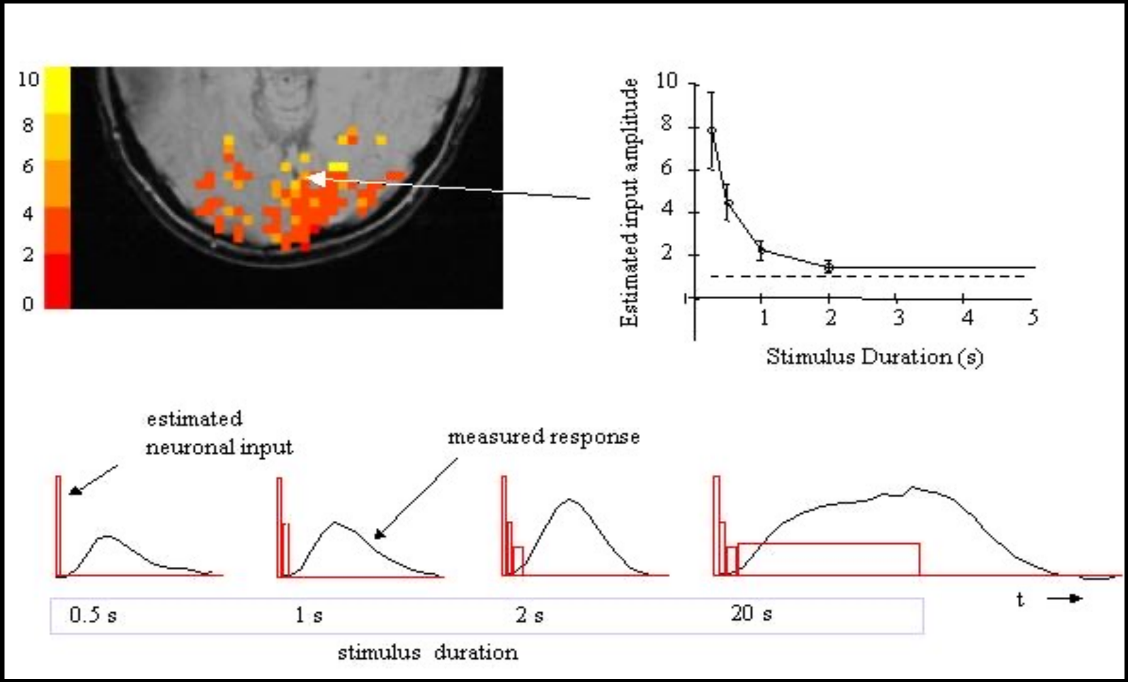


BOLD Correlation with Neuronal Activity

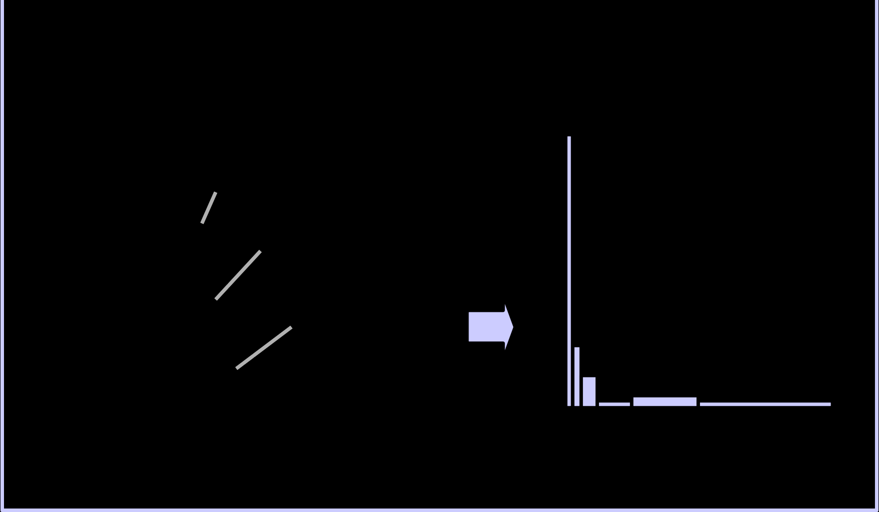
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157.



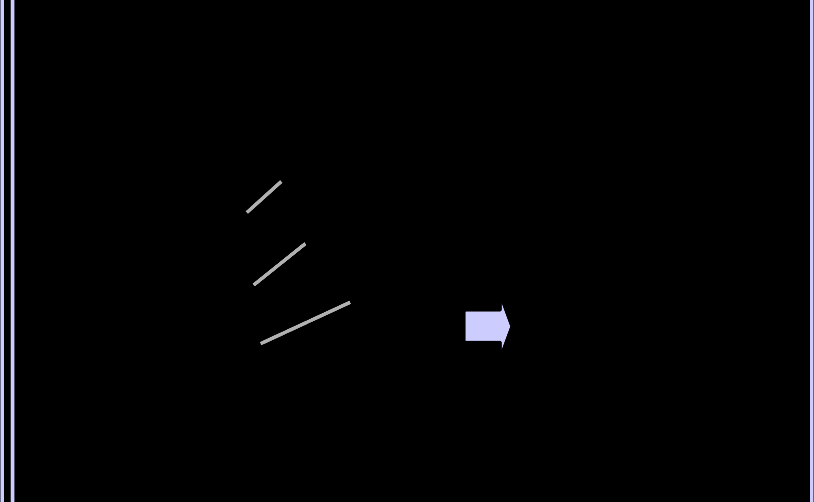
P. A. Bandettini and L. G. Ungerleider, (2001) "From neuron to BOLD: new connections." Nature Neuroscience, 4: 864-866.



Stationary grating



Contrast-reversing checkerboard



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