

# Recent Advances in Functional MRI

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods

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

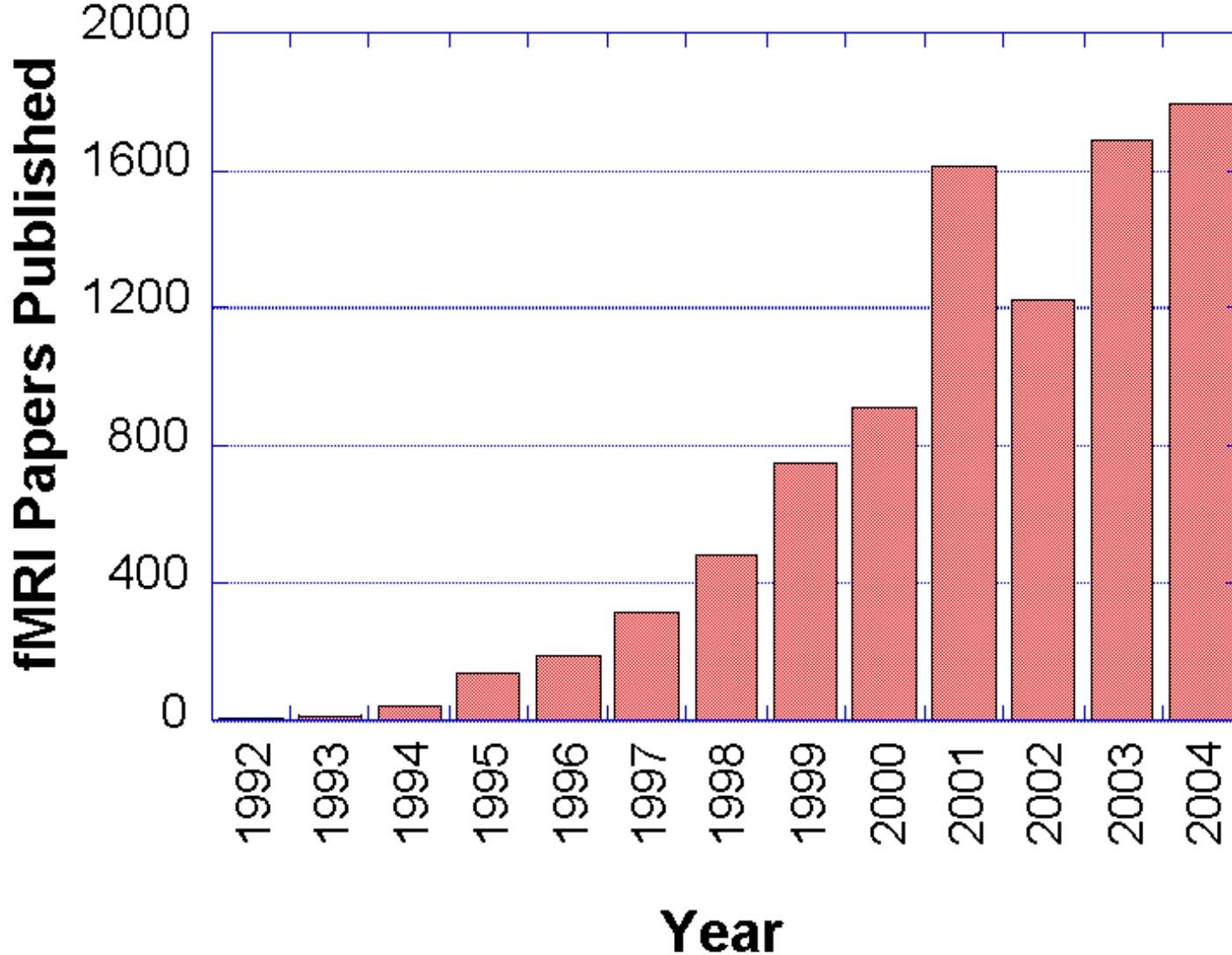
Laboratory of Brain and Cognition

&

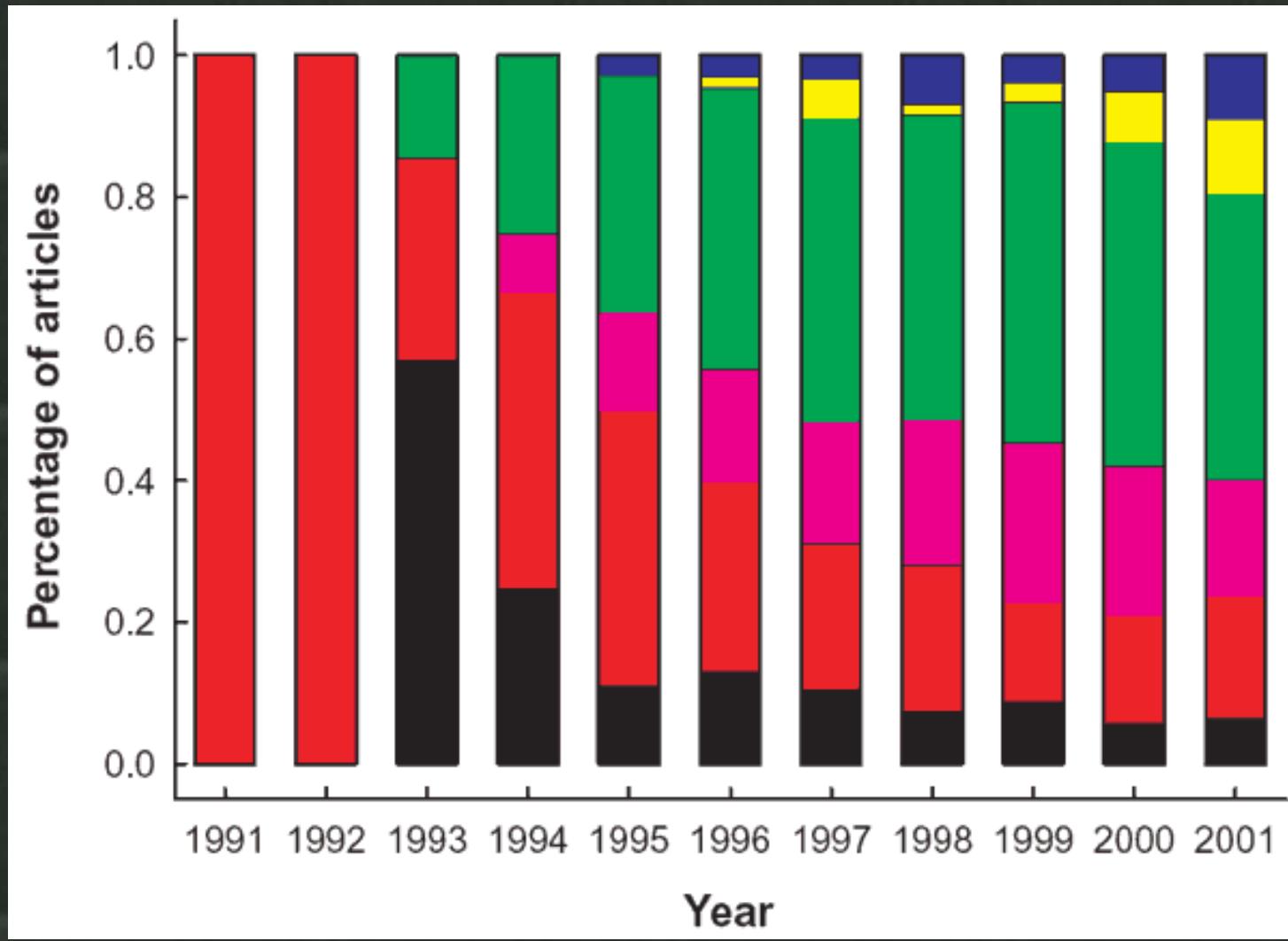
Functional MRI Facility

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





"fMRI" or "functional MRI"



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

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

Technology

Methodology

Engineering

Physics

Computer  
Science

Statistics

Cognitive  
Science

Medicine

Physiology

Neuroscience

Interpretation

Applications

Technology

Methodology

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Applications

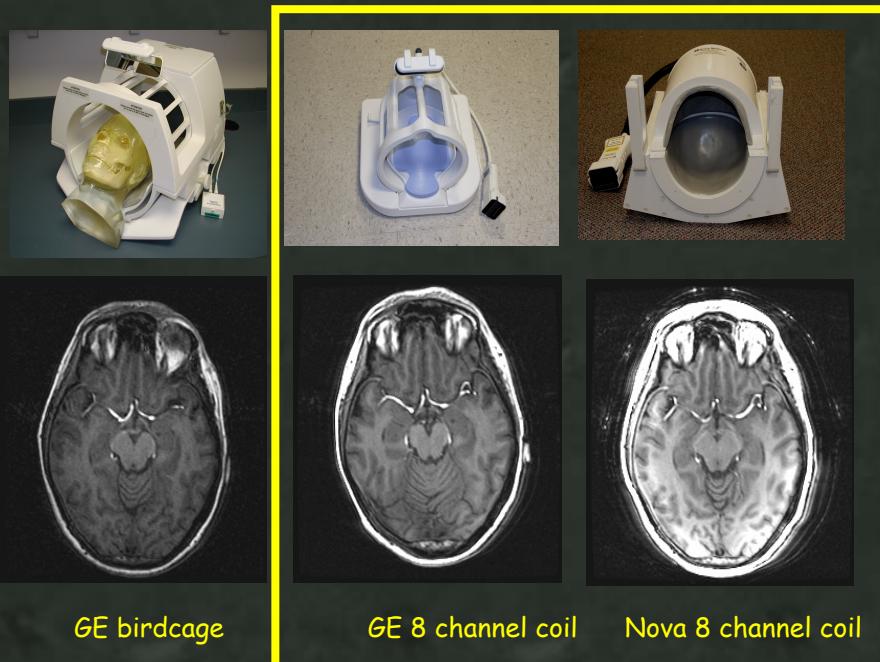
# Technology

- Parallel Acquisition
- SENSE Imaging
- High Fields

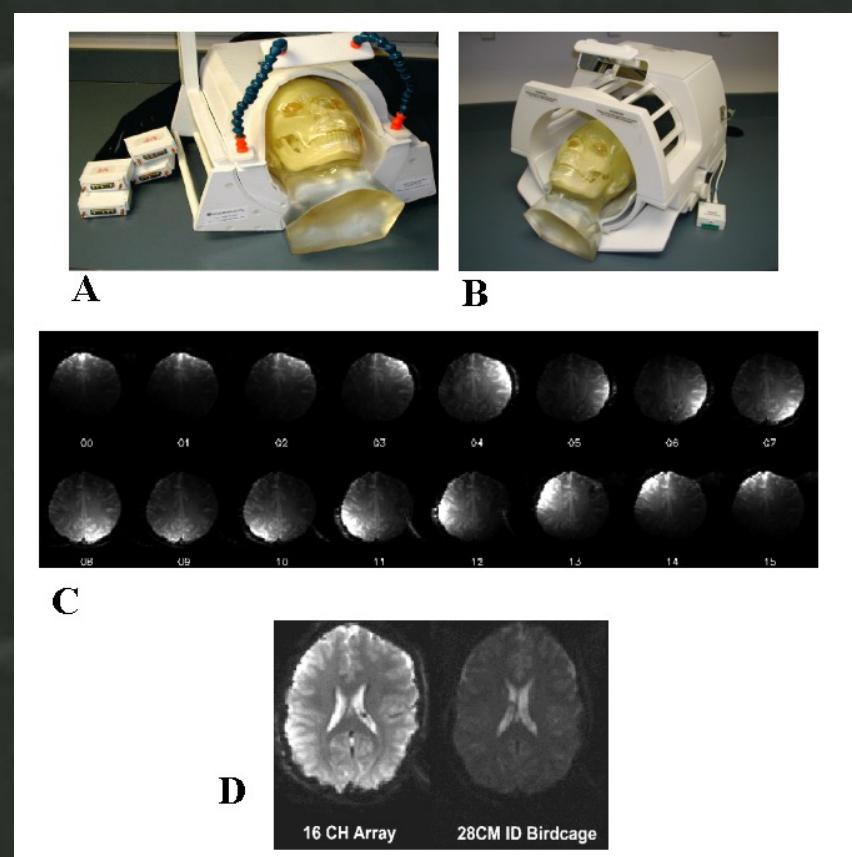
# Technology

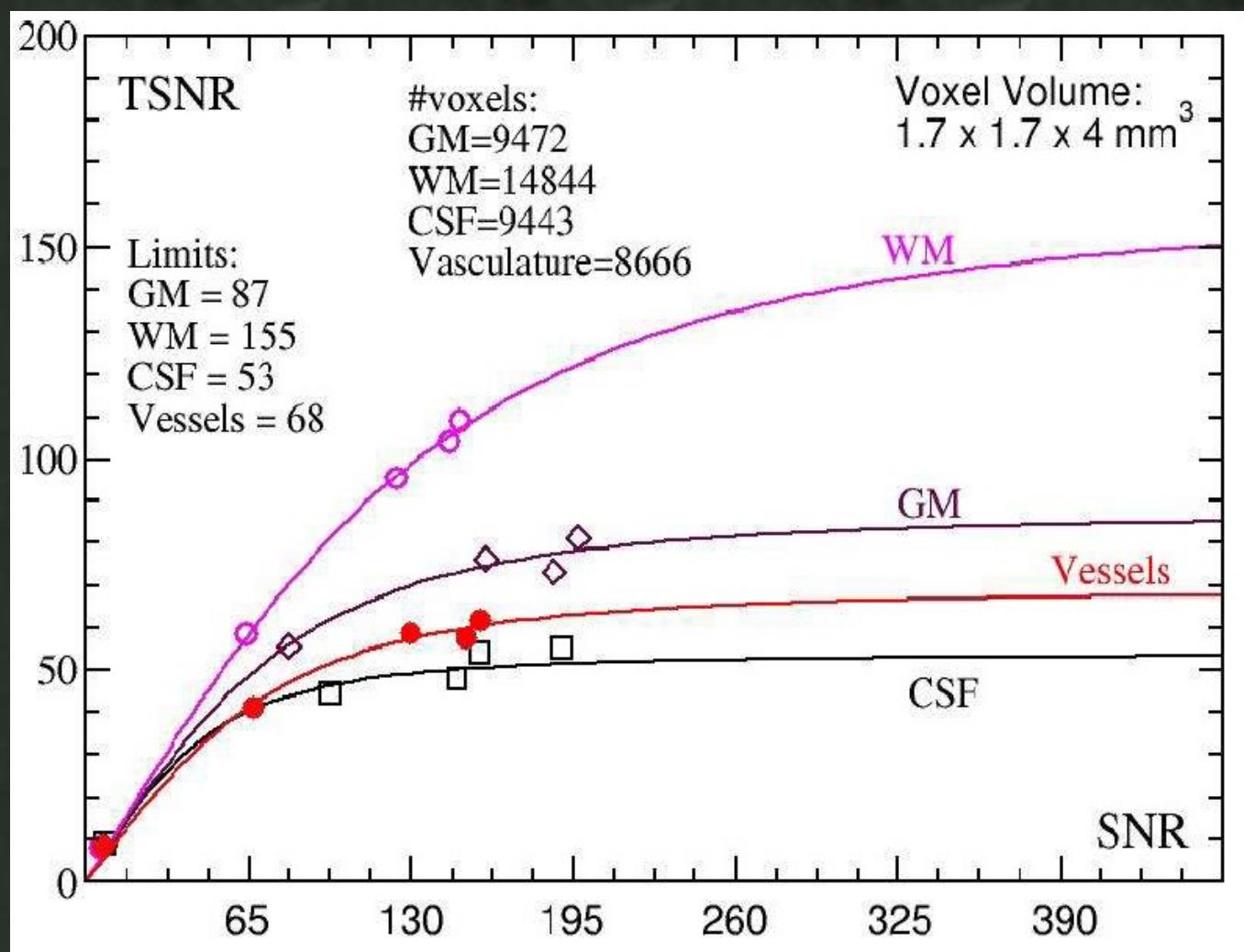
# Parallel Acquisition

8 channel parallel receiver coil

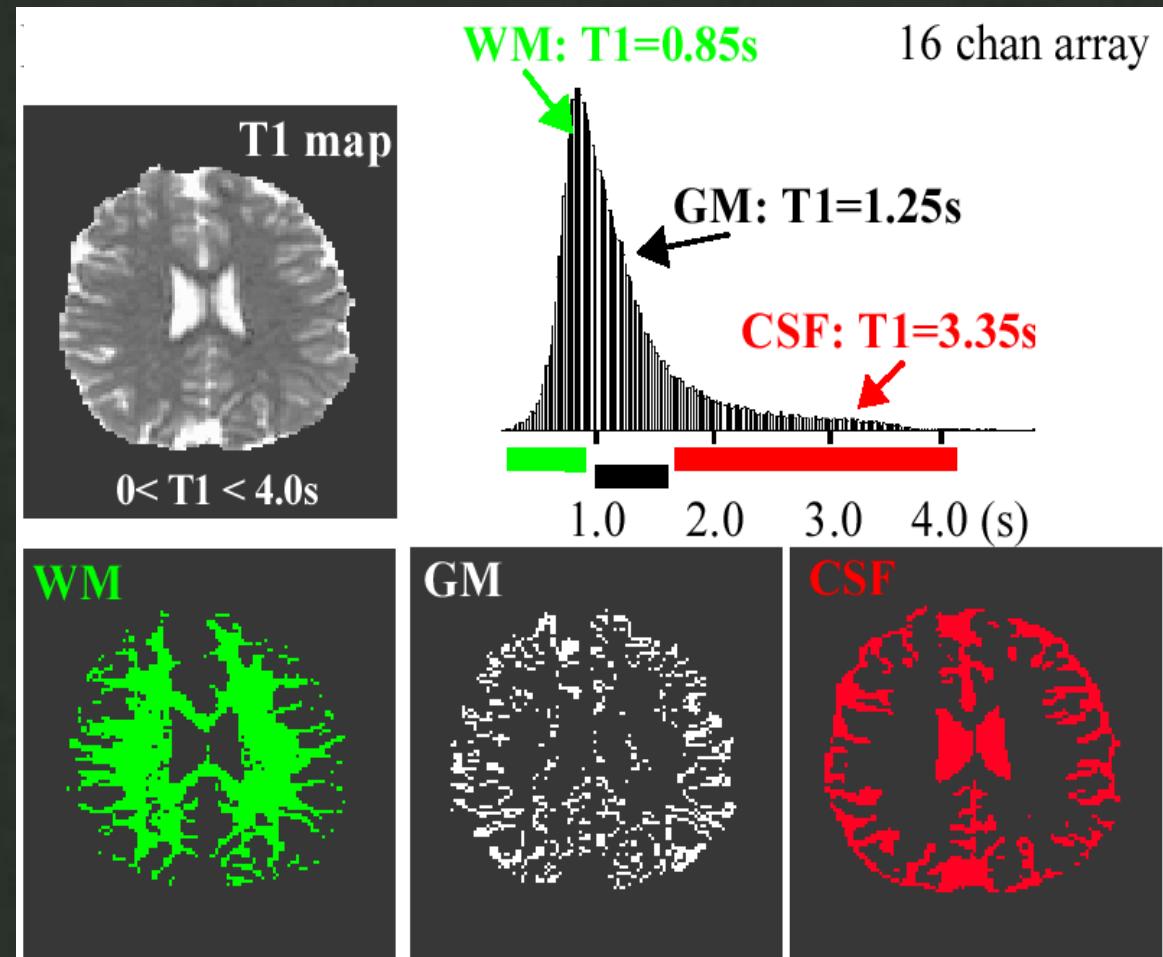
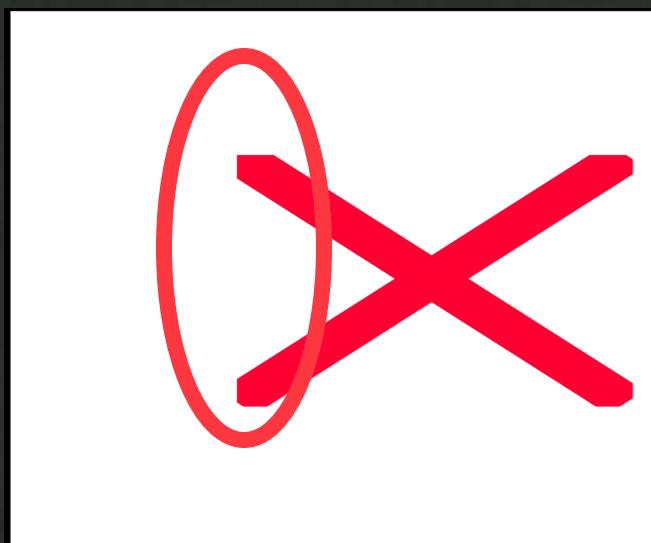


16 channel parallel receiver coil





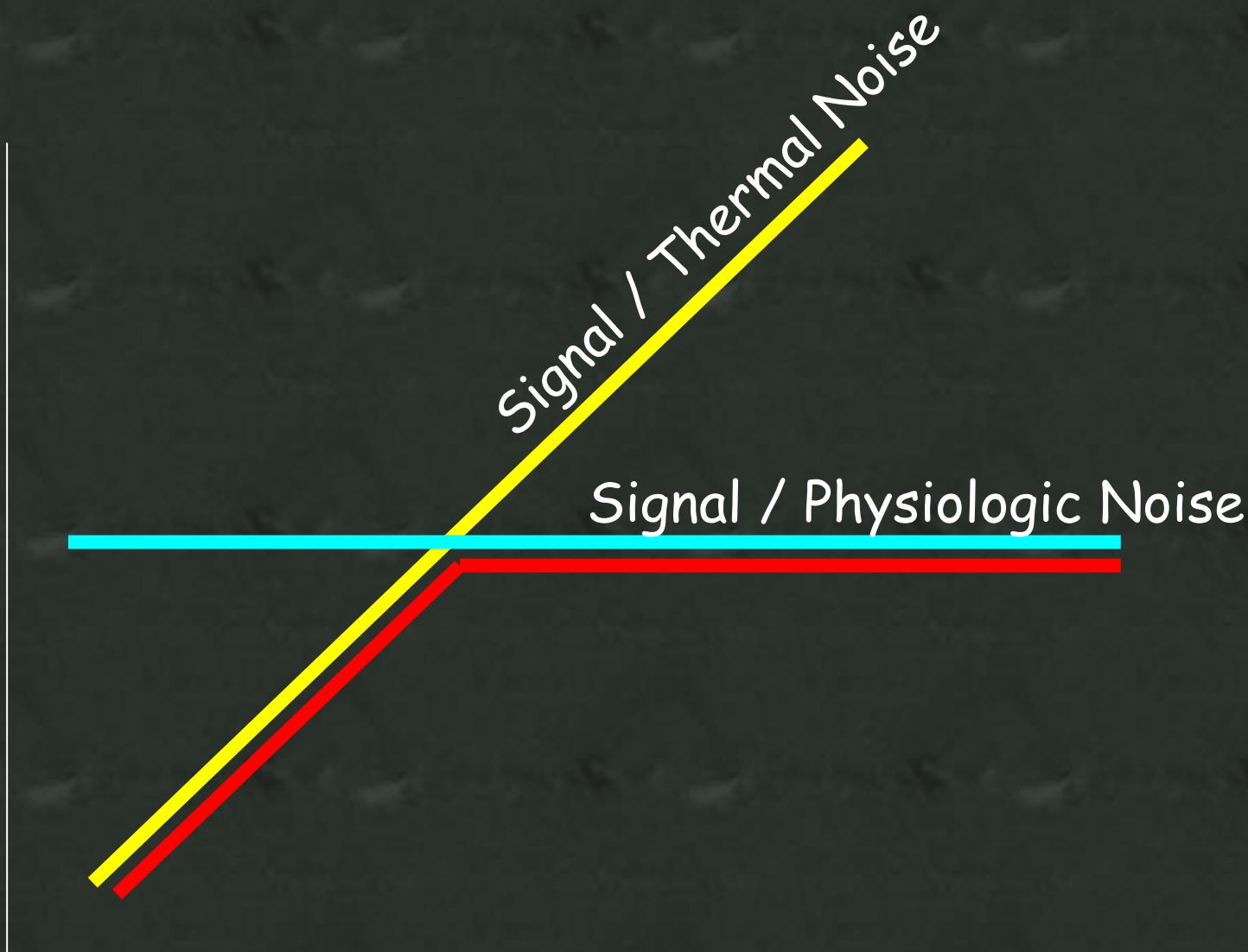
## Segmentation using EPI Transient



# Technology

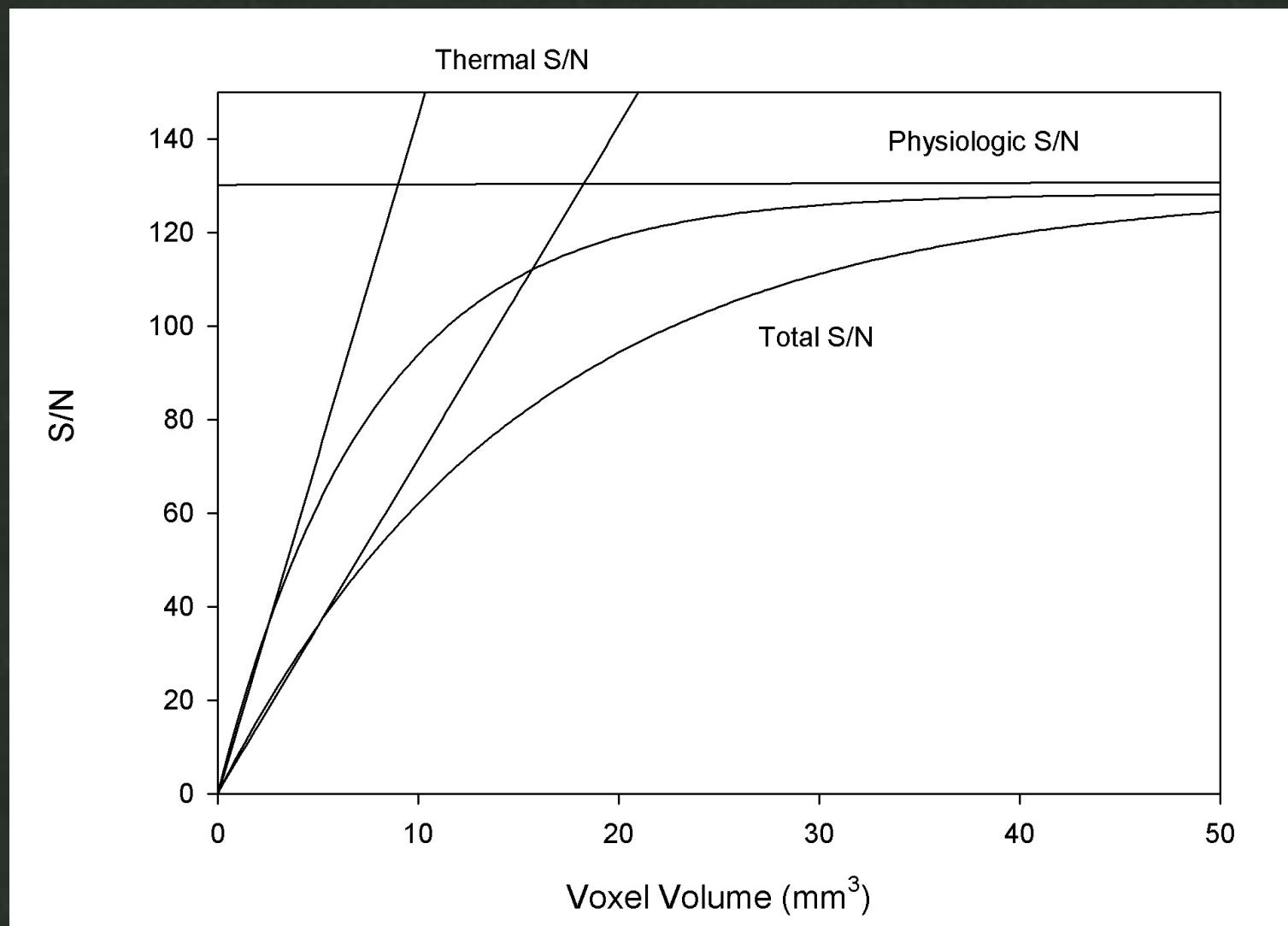
# Parallel Acquisition

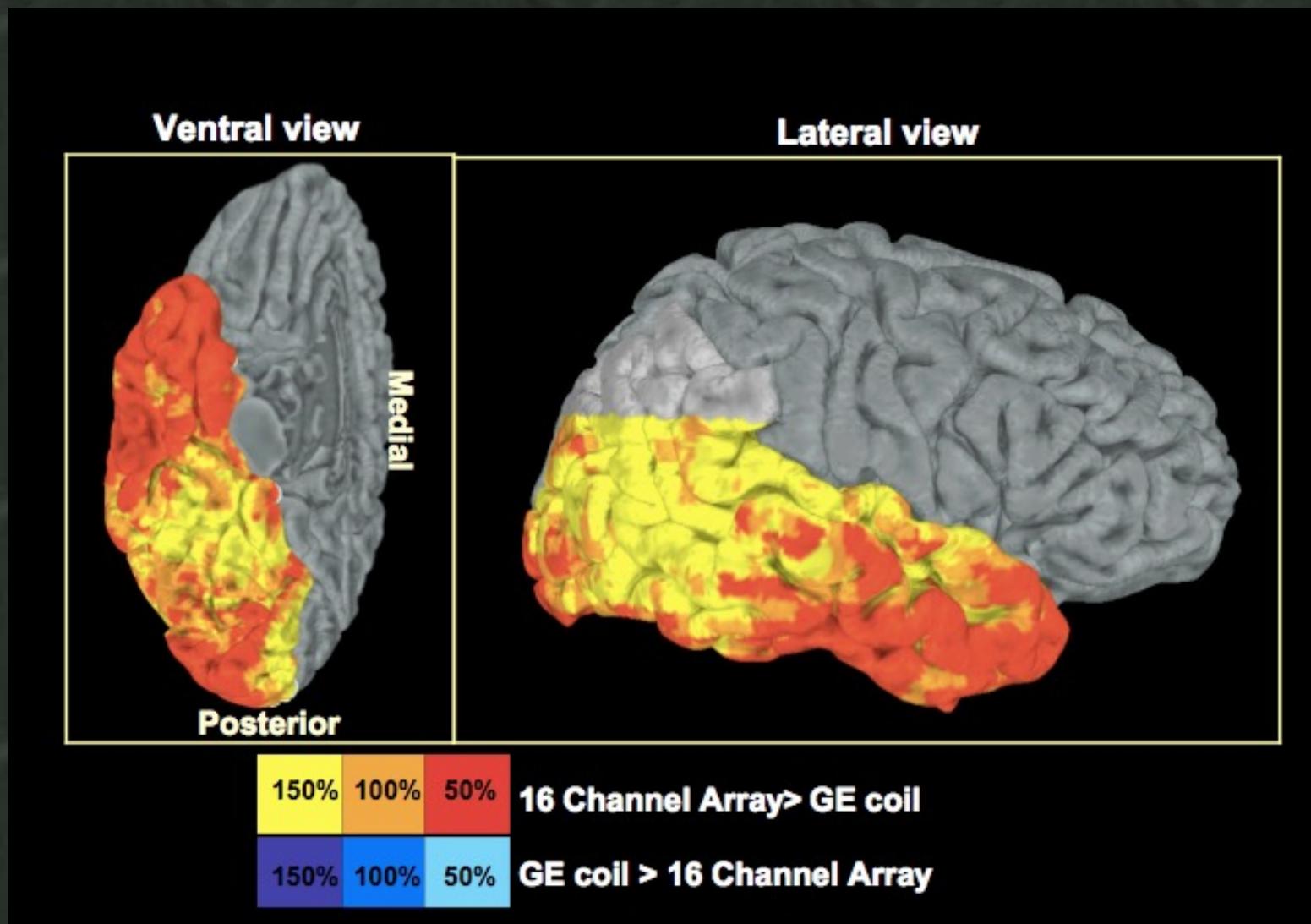
Signal to Noise Ratio



Resolution, Speed, Surface Coils, Field Strength, etc..

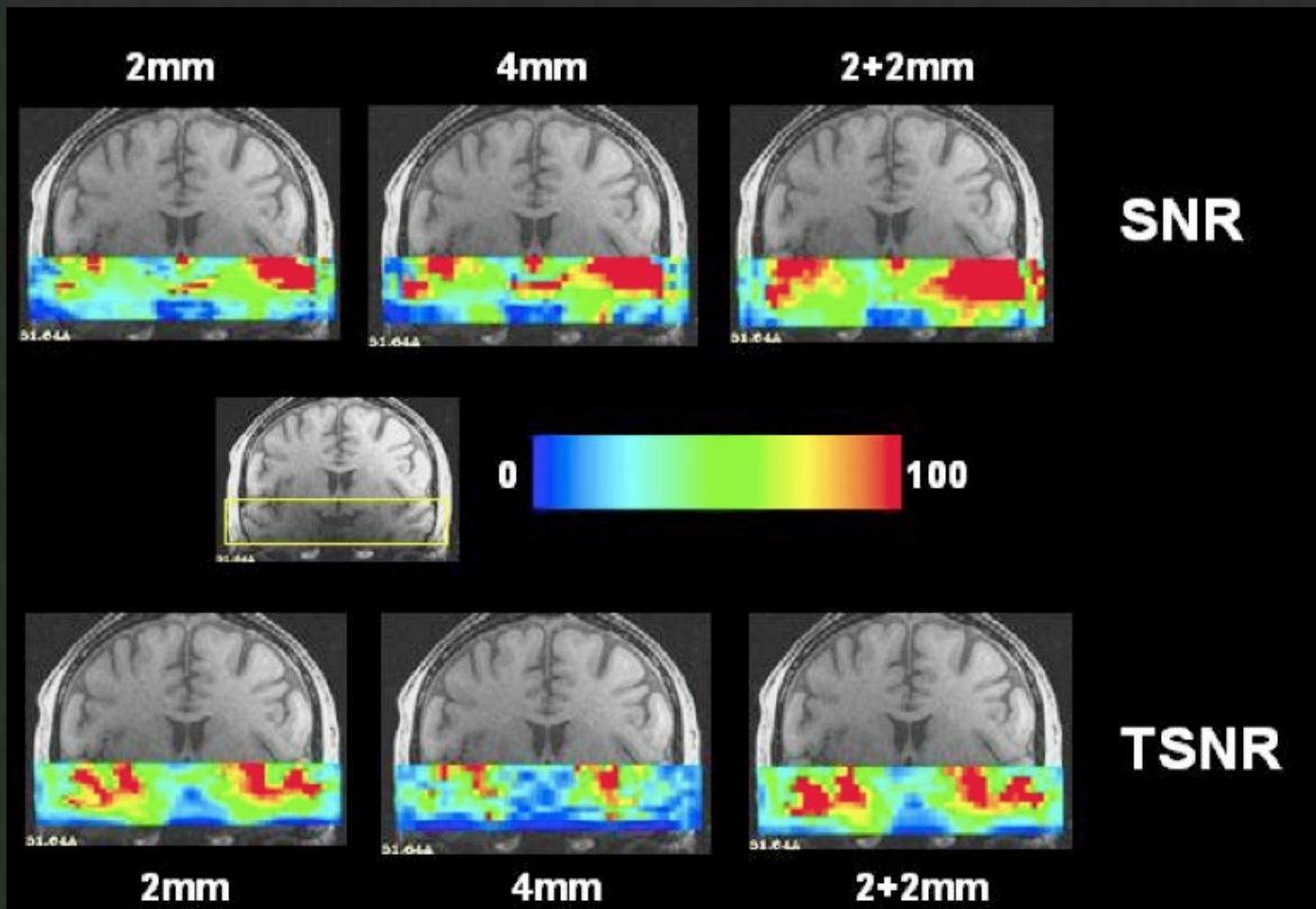
## Simulated gains in TNSR with doubling sensitivity





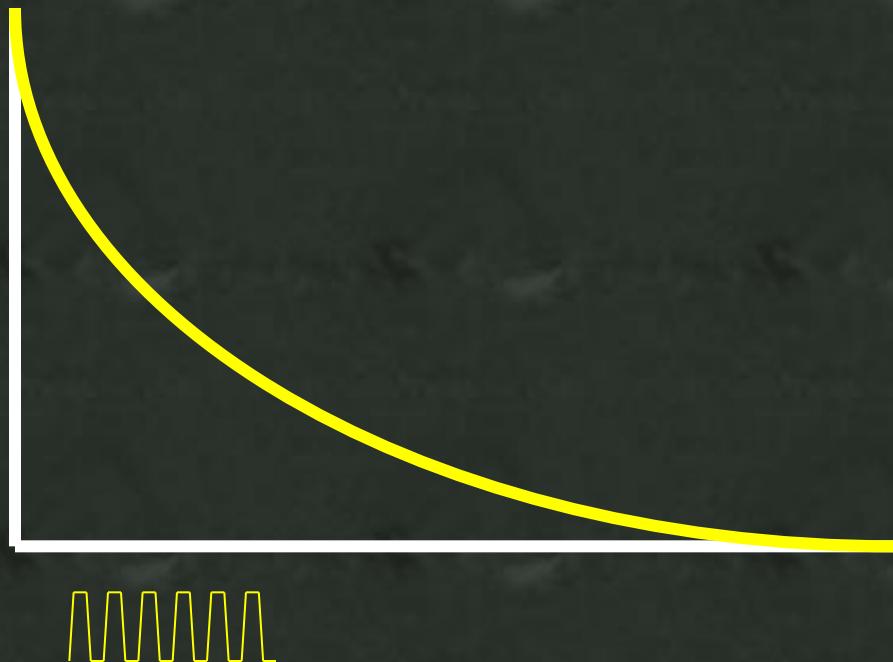
# Technology

# Parallel Acquisition

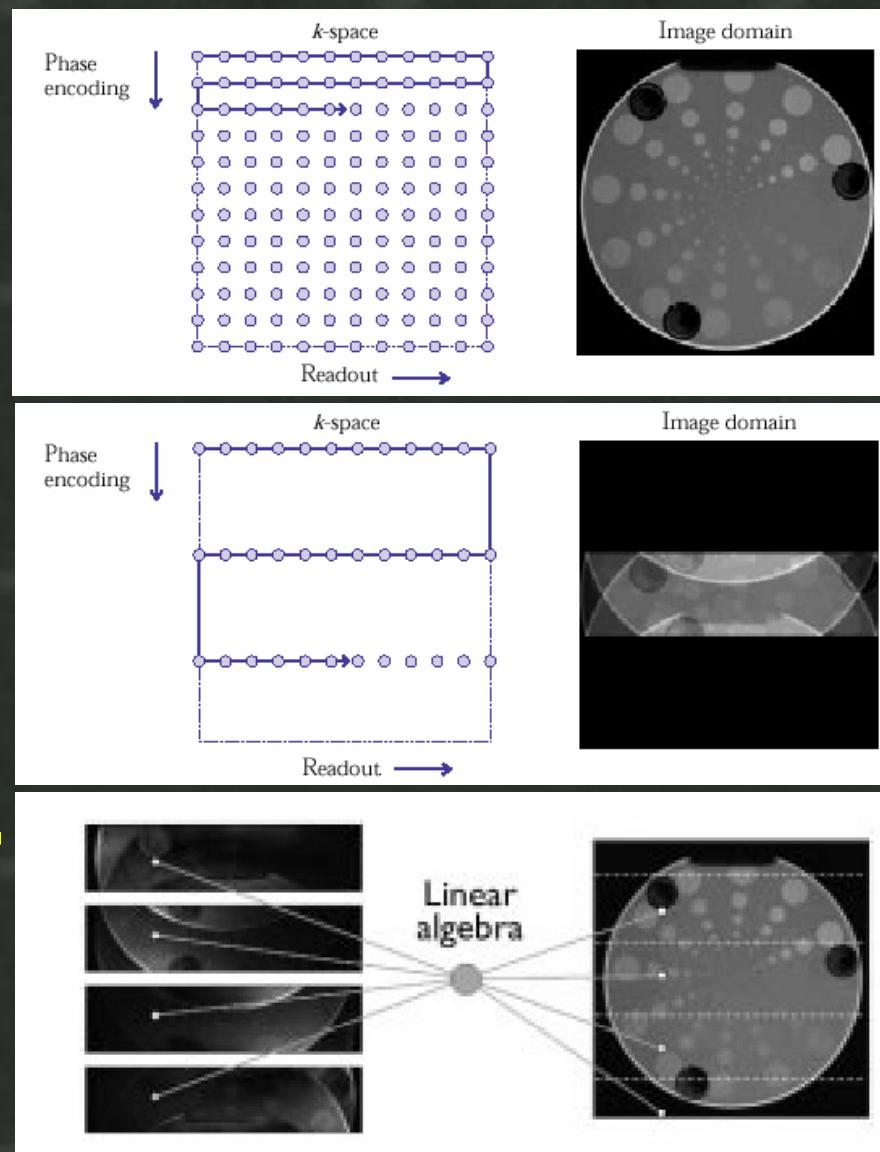


# Technology

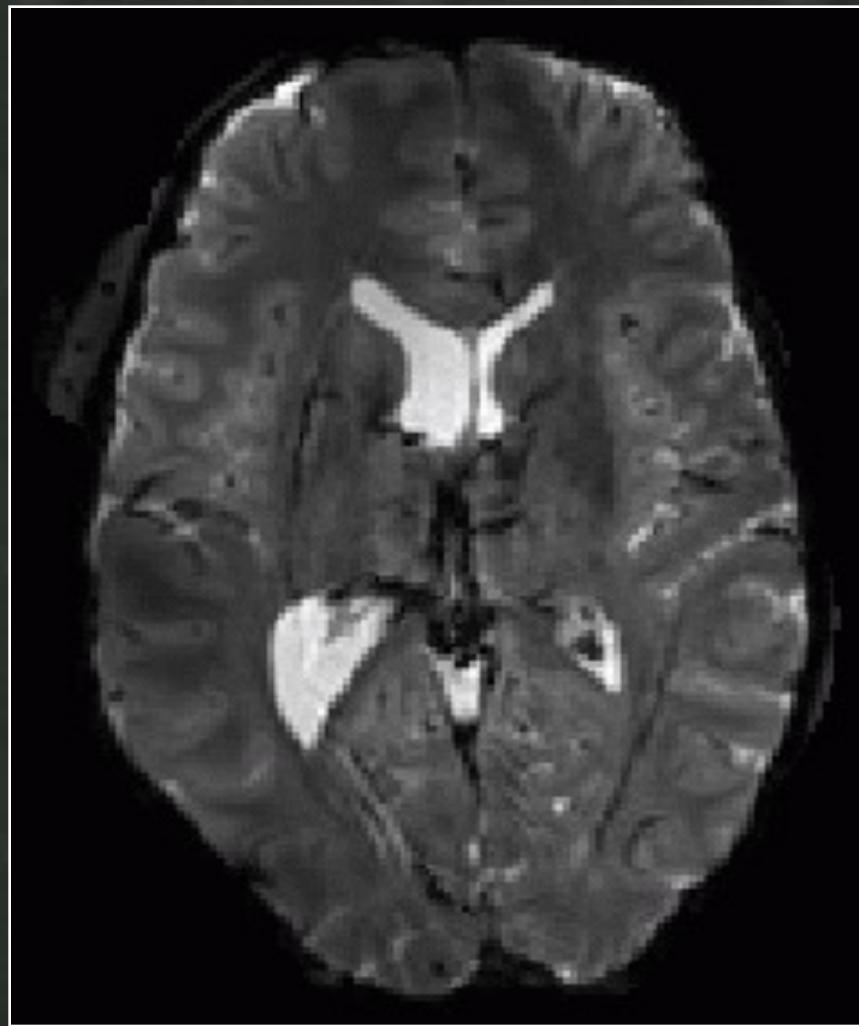
# SENSE Imaging



$\approx 5$  to  $30$  ms



Pruessmann, et al.



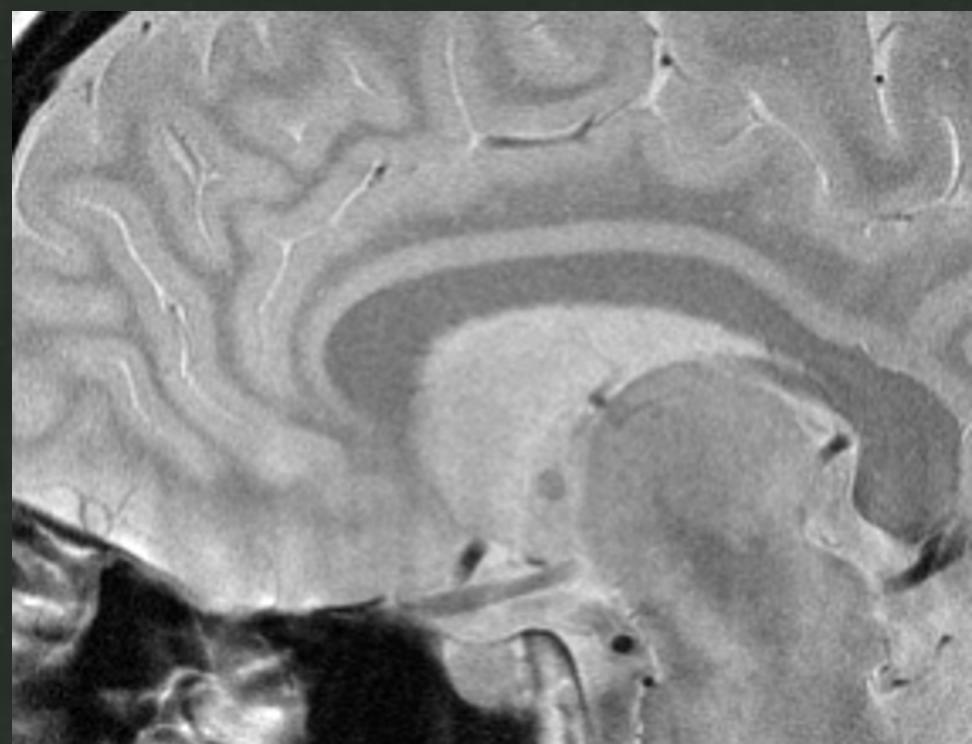
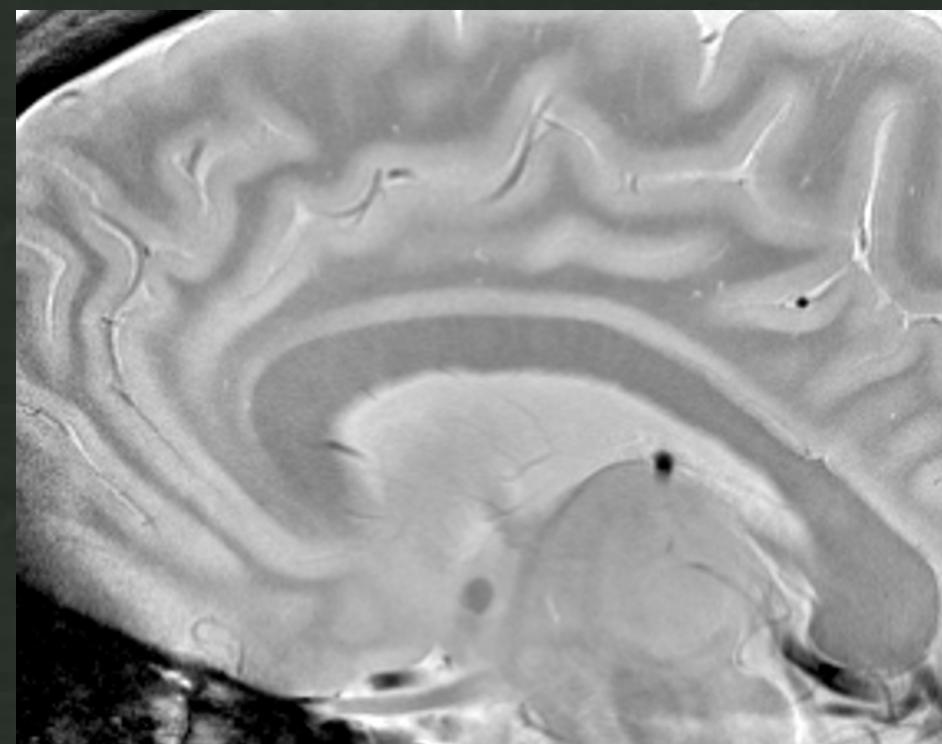
3T single-shot SENSE EPI using 16 channels:  $1.25 \times 1.25 \times 2\text{mm}$

# Technology

High Fields

7T head coil

3T head coil



TSE, 11 echoes, 7 min exam, 20cm FOV, 512x512 (0.4mm x 0.4mm), 3mm thick slices.

7T

white matter SNR = 65

Gray matter SNR = 76

3T

white matter SNR = 26

Gray matter SNR = 34

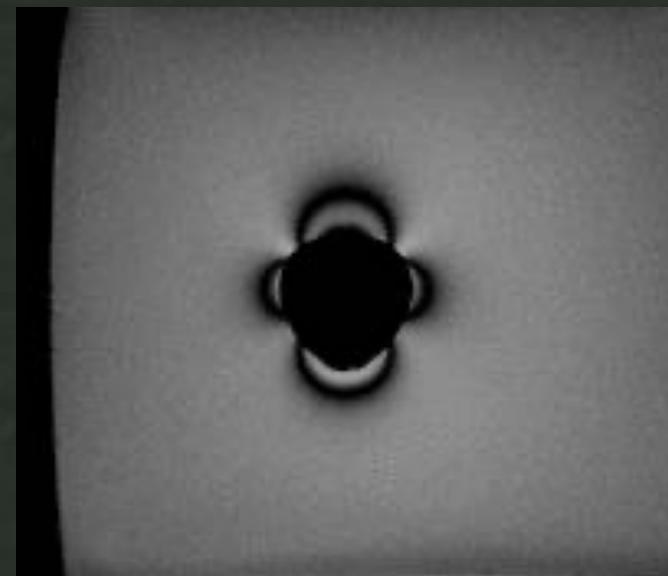
Courtesy Larry Wald

# Technology

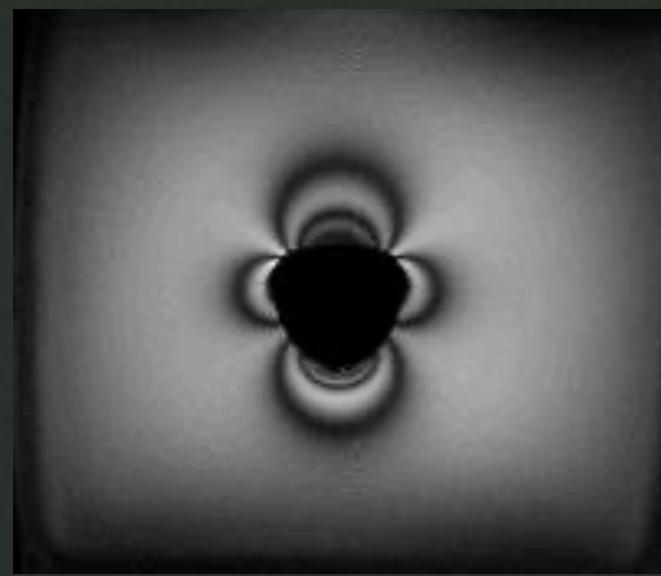
# High Fields

Susceptibility field (in Gauss) increases w/  $B_0$

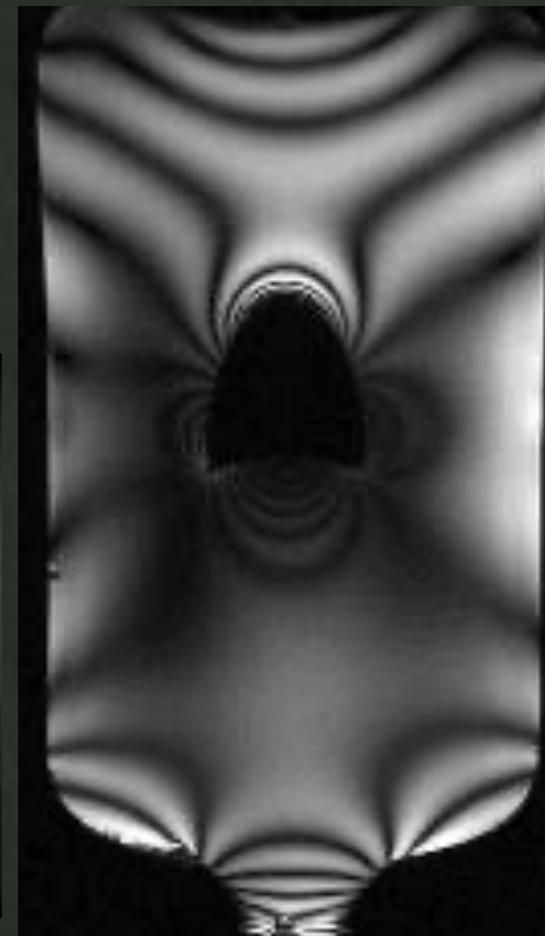
Ping-pong ball in  $H_2O$ :  
Field maps (DTE = 5ms), black lines spaced by  
0.024G (0.8ppm at 3T)



1.5T



3T



7T

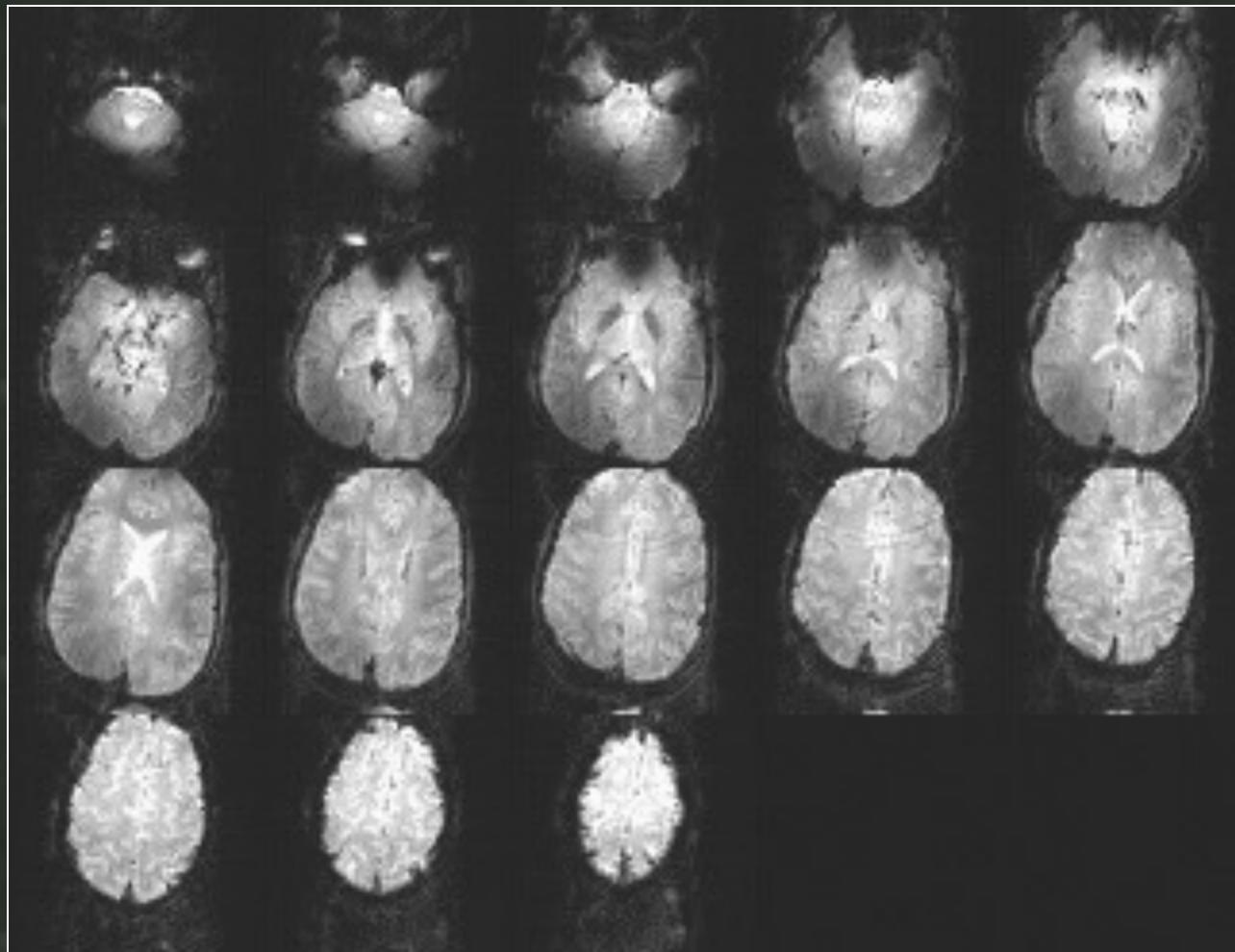
# 7T: Single Shot whole head EPI

3mm isotropic

single shot EPI, 7T.

64x64, 19cm FOV(3mm  
resolution), 3mm slice.

TE=20ms



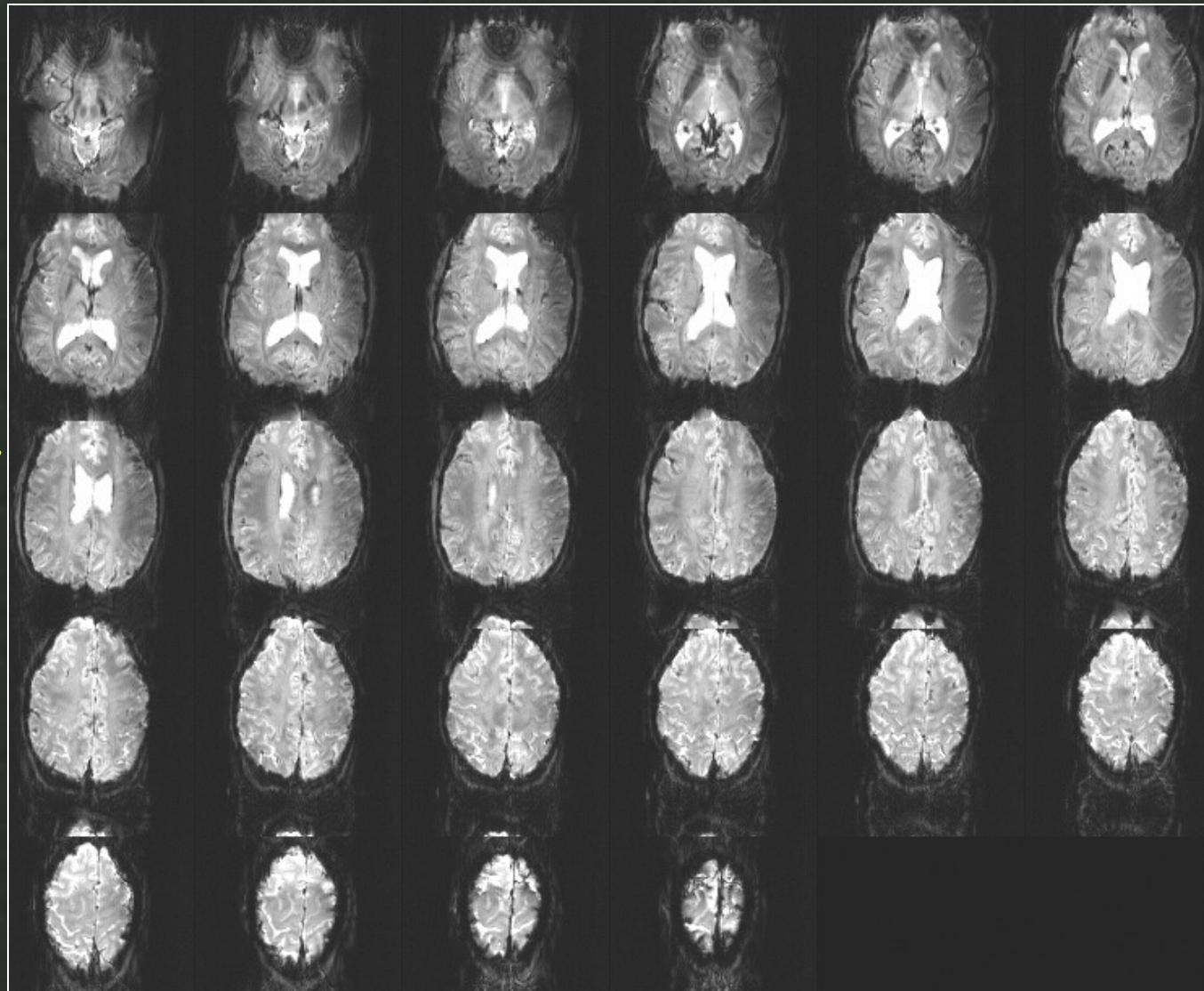
# 7T: Single Shot whole head EPI

1.5mm inplane

single shot EPI, 7T.

128x128, 20cm FOV  
(1.5mm resolution),  
2mm slice,

TE = 20ms



Courtesy Larry Wald

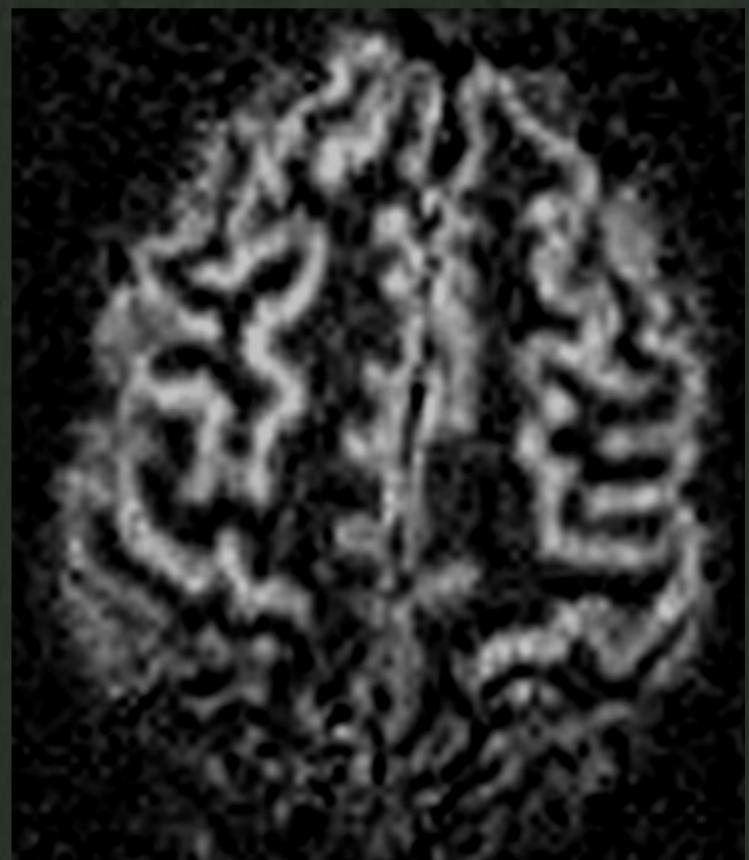
## 7T Blood flow and BOLD based fMRI

Longer T1 means better ASL...

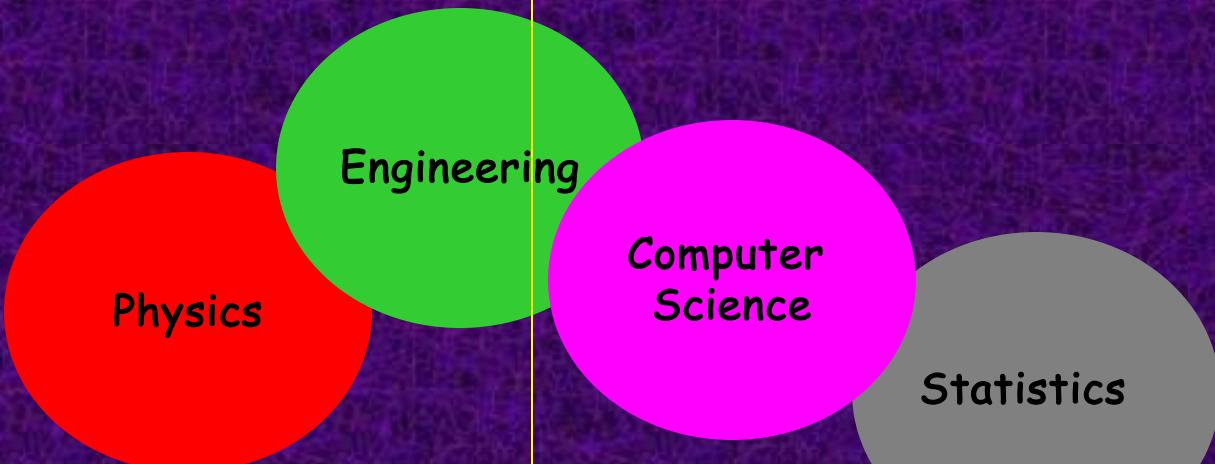
6 minute pulse Arterial Spin Labeling blood flow image

1.56mm x 1.56mm x 4mm

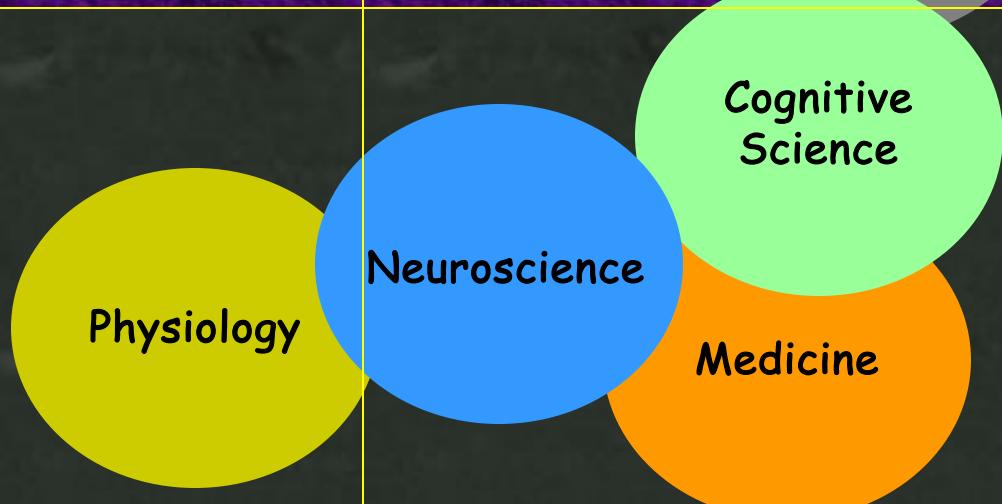
(3T typical resolution: 3mmx 3mm x 5mm)



# Technology



# Methodology



# Interpretation

# Applications

# Methodology

- New Contrasts
- Paradigm Designs
- Temporal Resolution
- Spatial Resolution
- Processing Methods

# fMRI Contrast

- Volume (gadolinium)
- BOLD
- Perfusion (ASL)
- $\Delta\text{CMRO}_2$
- $\Delta$ Volume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

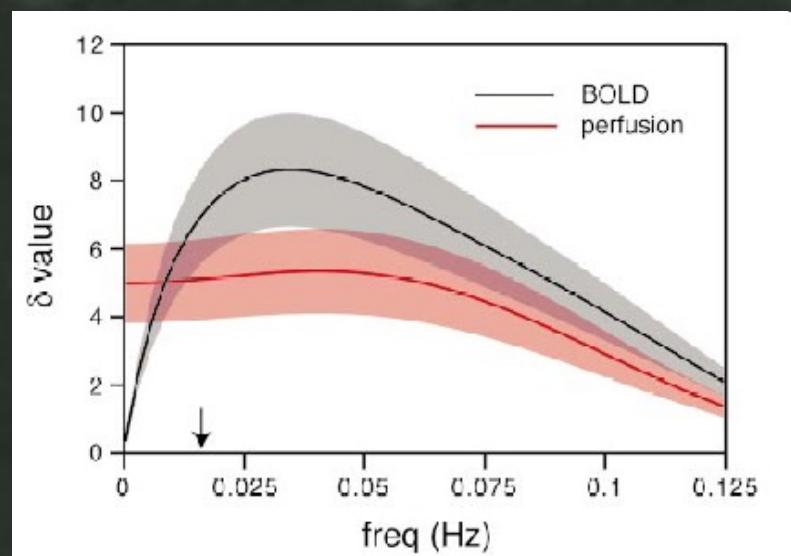
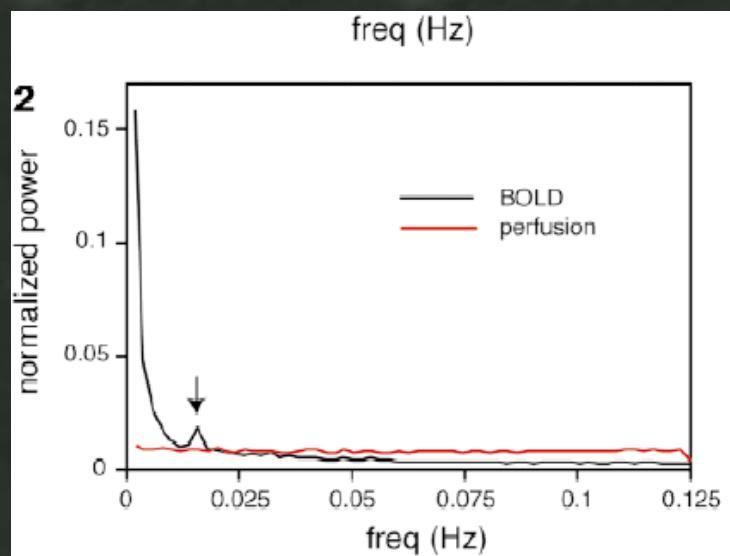
# fMRI Contrast

- Volume (gadolinium)
- BOLD
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- $\Delta\text{CMRO}_2$
- $\Delta\text{Volume}$  (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

# Methodology

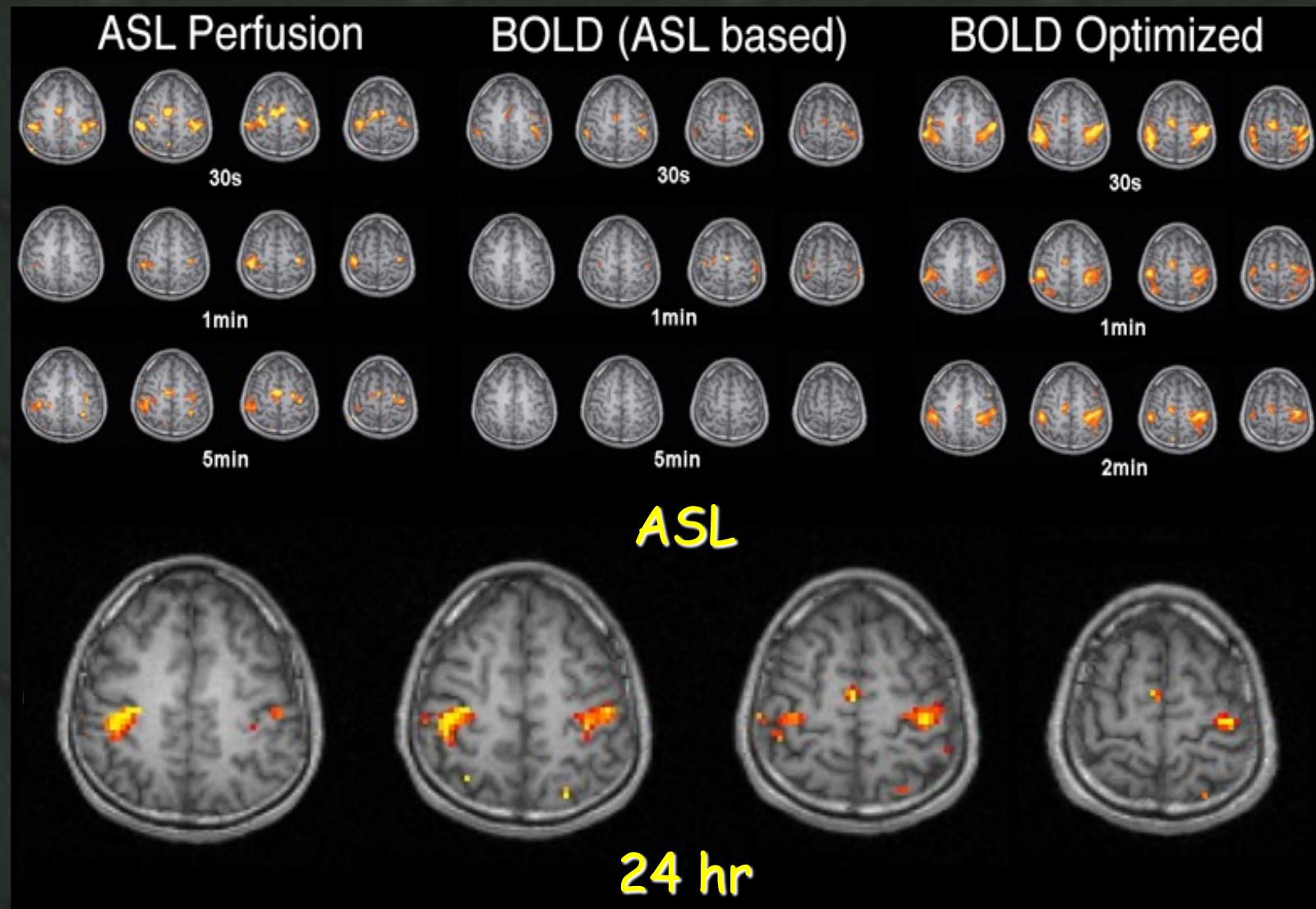
# New Contrasts Perfusion (ASL)

Better than BOLD for long duration activation...



GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

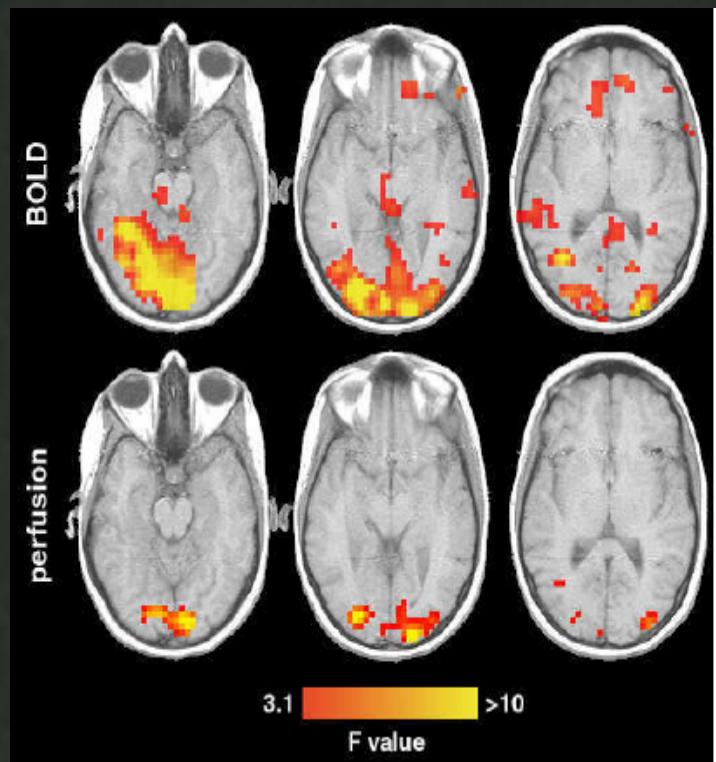
# Perfusion vs. BOLD: Low Task Frequency



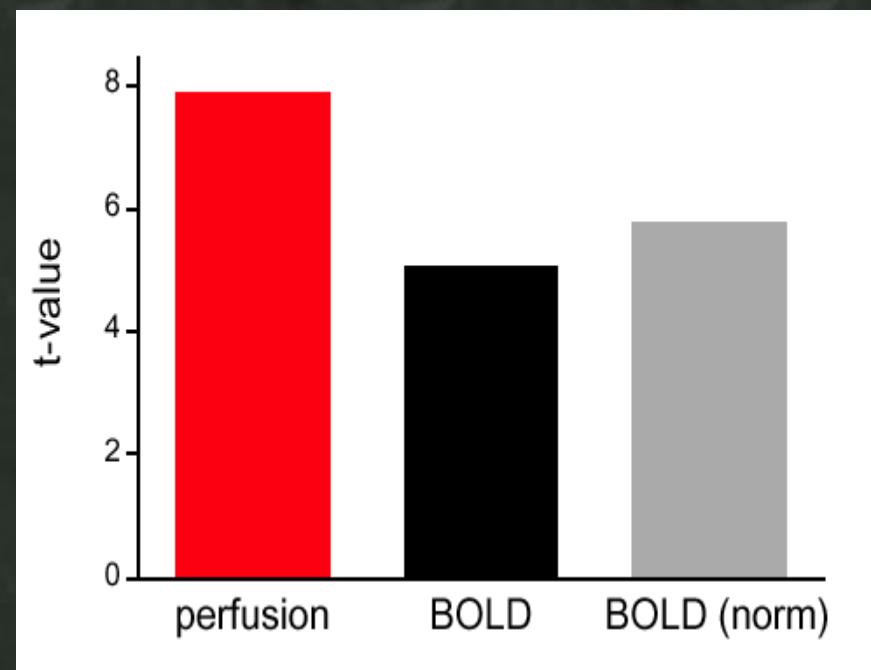
# Methodology

# New Contrasts Perfusion (ASL)

ASL Perfusion fMRI vs. BOLD  
*Improved Intersubject Variability vs. BOLD*



Single Subject

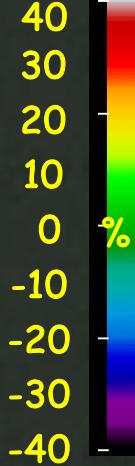


Group (Random Effects)

# Methodology

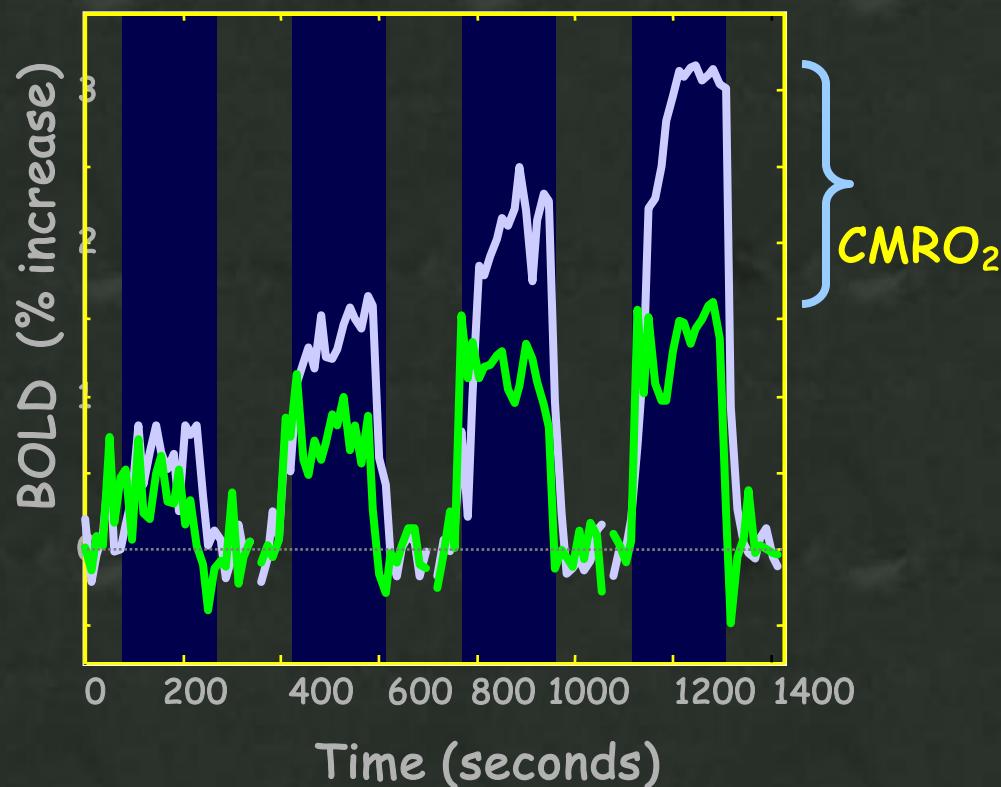
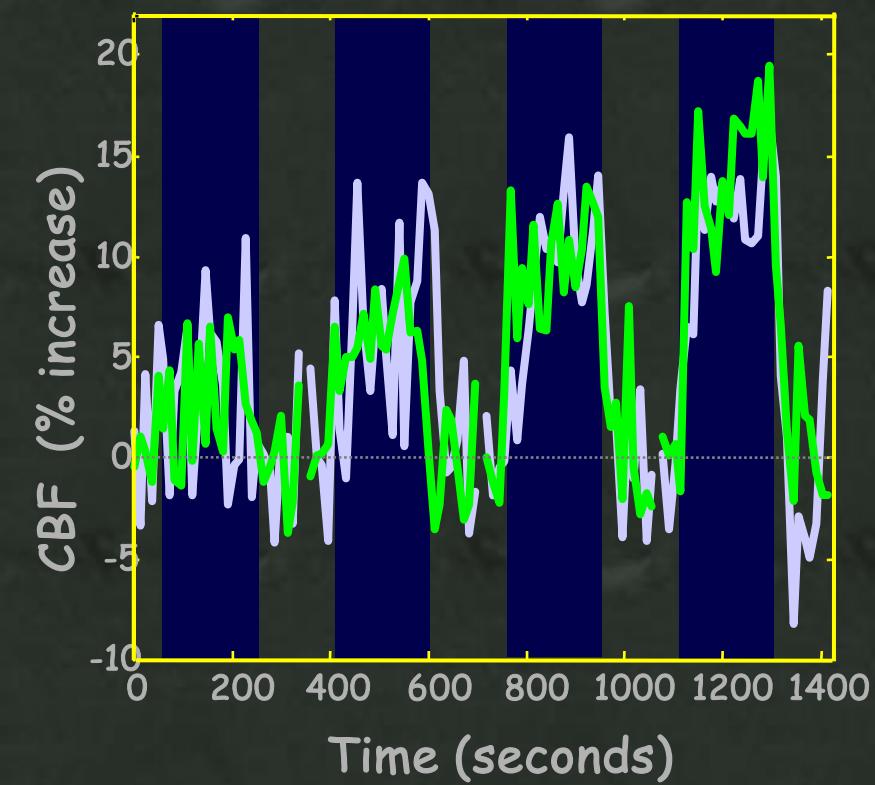
New Contrasts

$$\Delta CMRO_2$$



BOLD

CBF

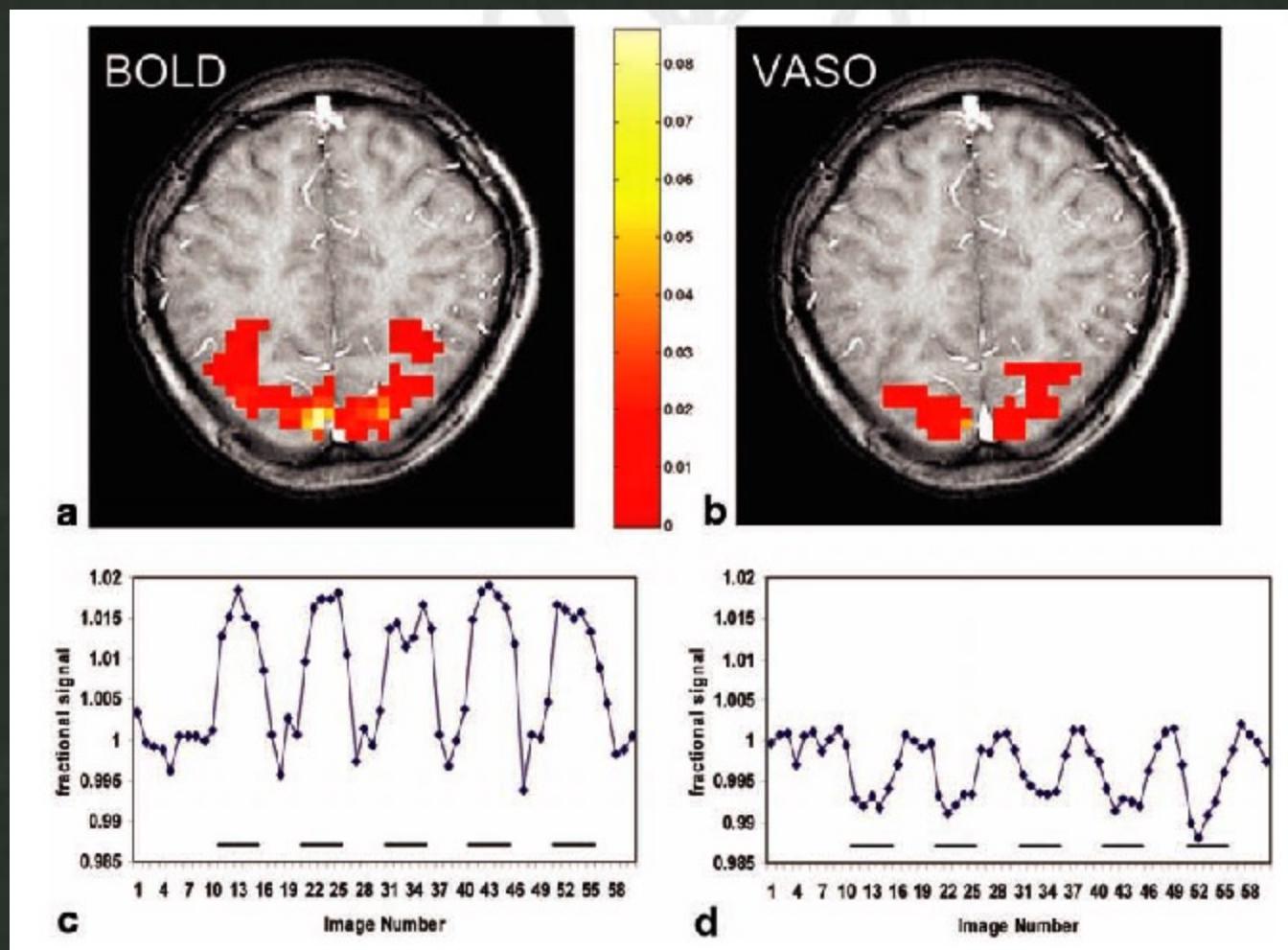


CMRO<sub>2</sub>

Simultaneous Perfusion and BOLD imaging during  
graded visual activation and hypercapnia

Hoge et al, PNAS 96:  
9403-9408 (1999)

VASO



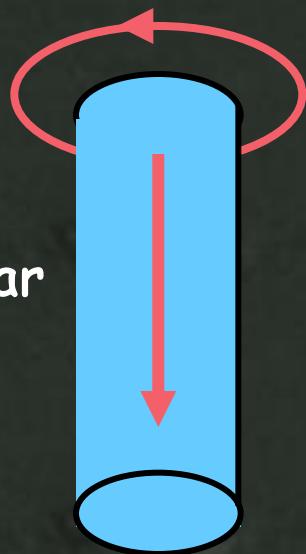
Lu et al, MRM 50 (2): 263-274 (2003)

# Methodology

# New Contrasts

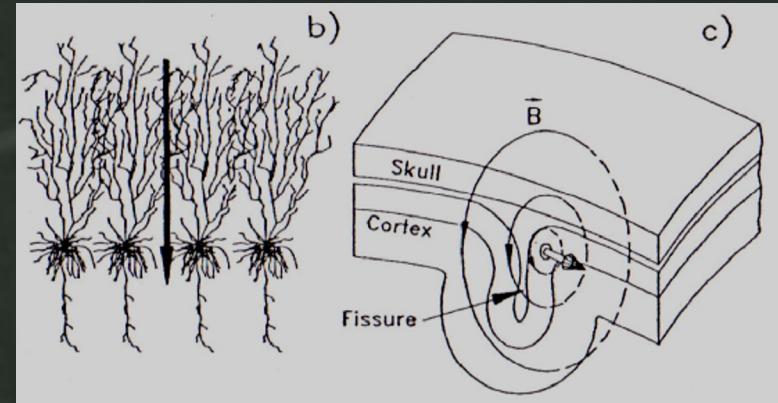
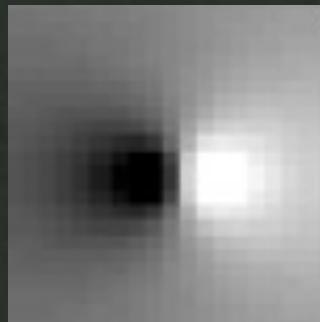
## Neuronal Currents

Magnetic Field



Intracellular  
Current

Surface Fields



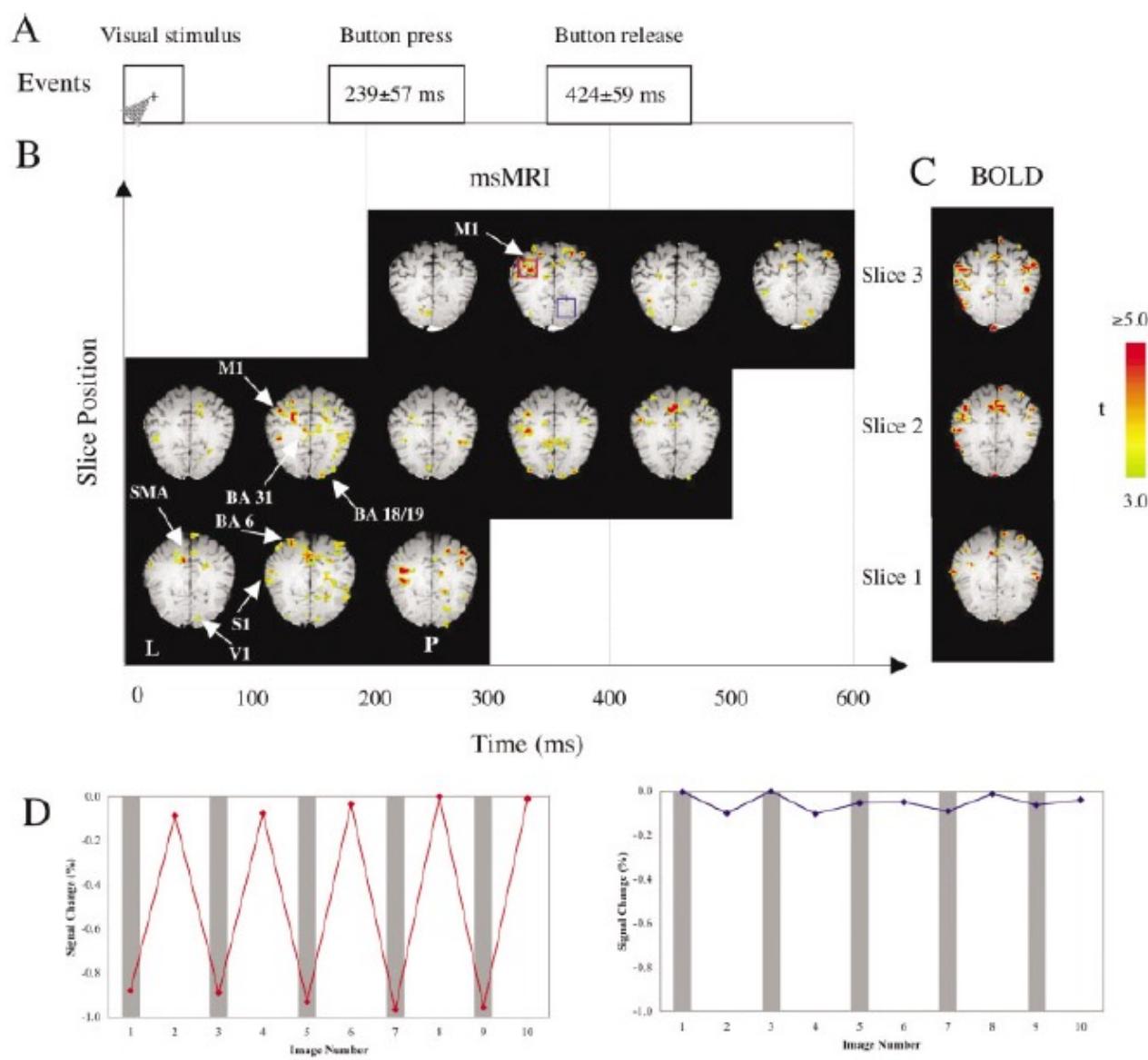
100 fT at on surface of skull

And 0.2 nT near source

# Methodology

# New Contrasts

## Neuronal Currents



J. Xiong, P. T. Fox, J.-H. Gao, *Direct MRI Mapping of neuronal activity*.  
Human Brain Mapping, 20: 41-49, (2003)

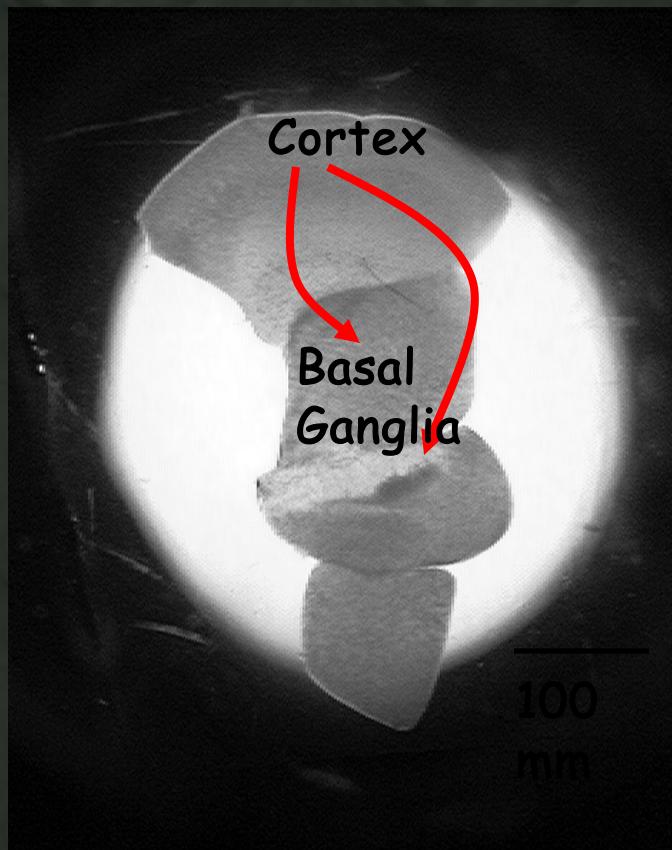
# Methodology

# New Contrasts

## Neuronal Currents

### In Vitro Results

Organotypic (*no blood supply or hemoglobin traces*) sections of newborn-rat somato-sensory Cortex, or somato-sensory Cortex & Basal Ganglia



- Size: in-plane:~1-2mm<sup>2</sup>, thickness: 60-100μm
- Neuronal Population: 10,000-100,000
- Spontaneous synchronized activity < 2Hz
- Epileptiform activity
- Spontaneous beta freq. activity (20-30Hz)
- Network Activity Range: ~ 0.5-15μV

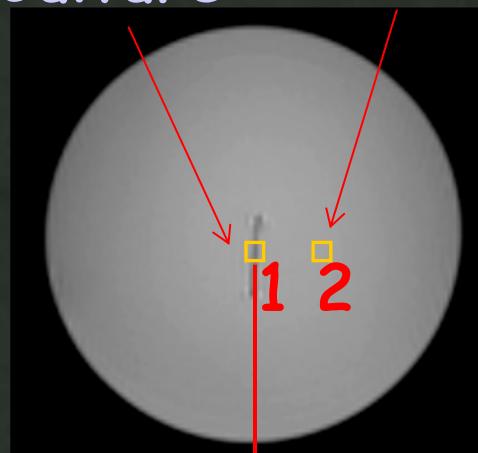
# Methodology

# New Contrasts

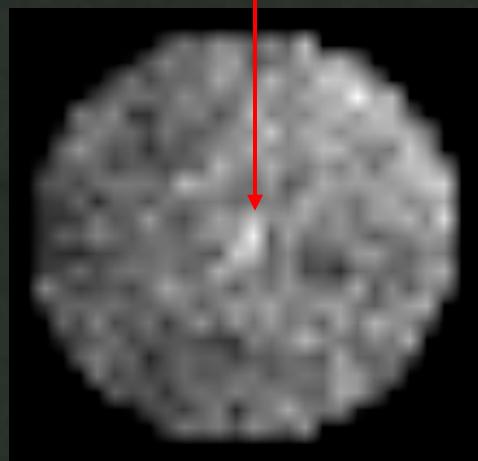
## Neuronal Currents

Culture

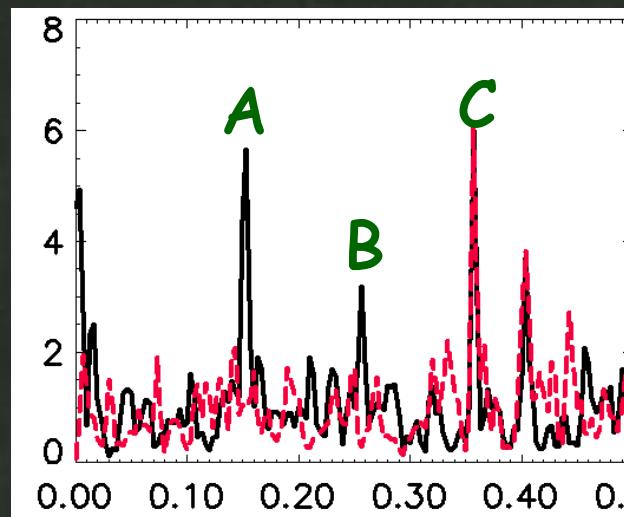
ACSF



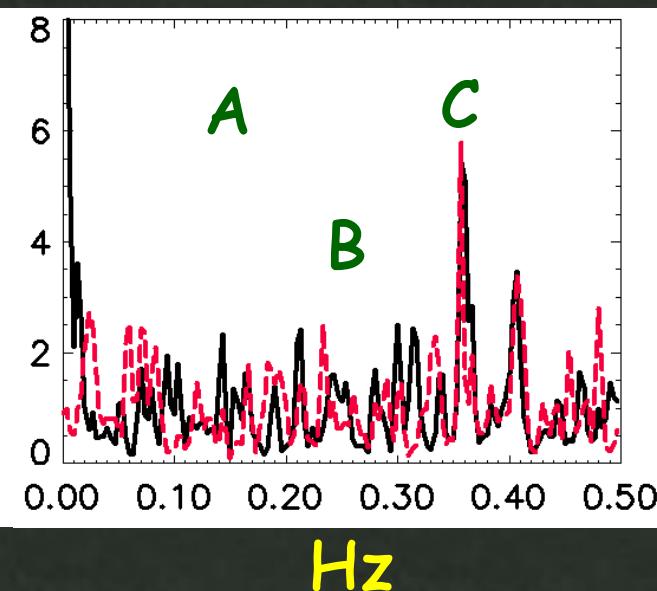
0.15Hz map



1: culture



2: ACSF

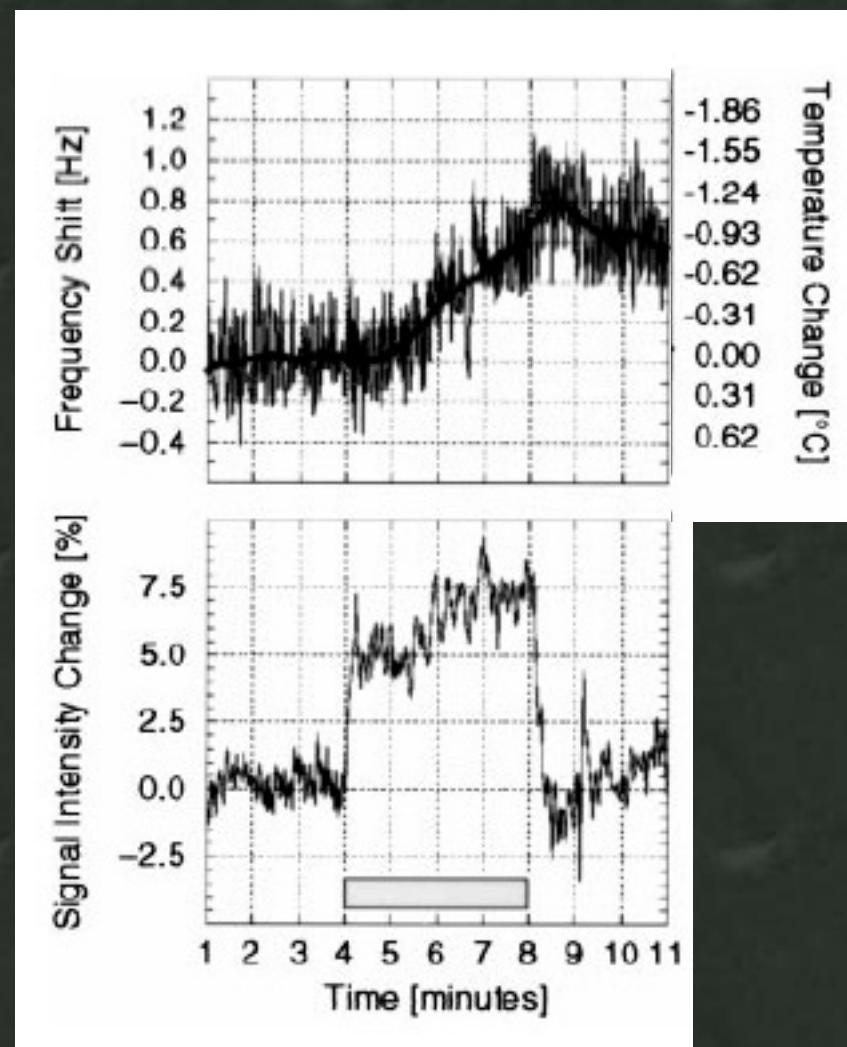


Active condition: black line  
Inactive condition: red line

- A: 0.15 Hz activity, on/off frequency
- B: activity
- C: scanner noise (cooling-pump)

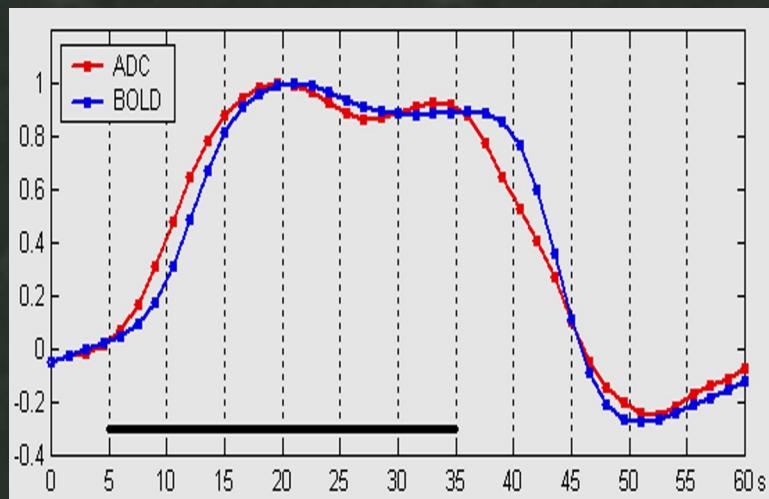
# Methodology

# New Contrasts Temperature



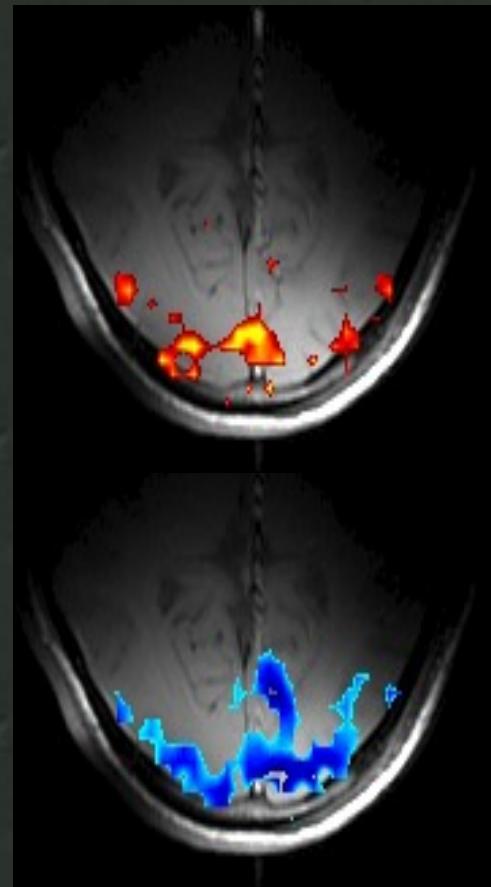
Yablonski, et al. PNAS 97: 7603-7608 (2000).

# Methodology



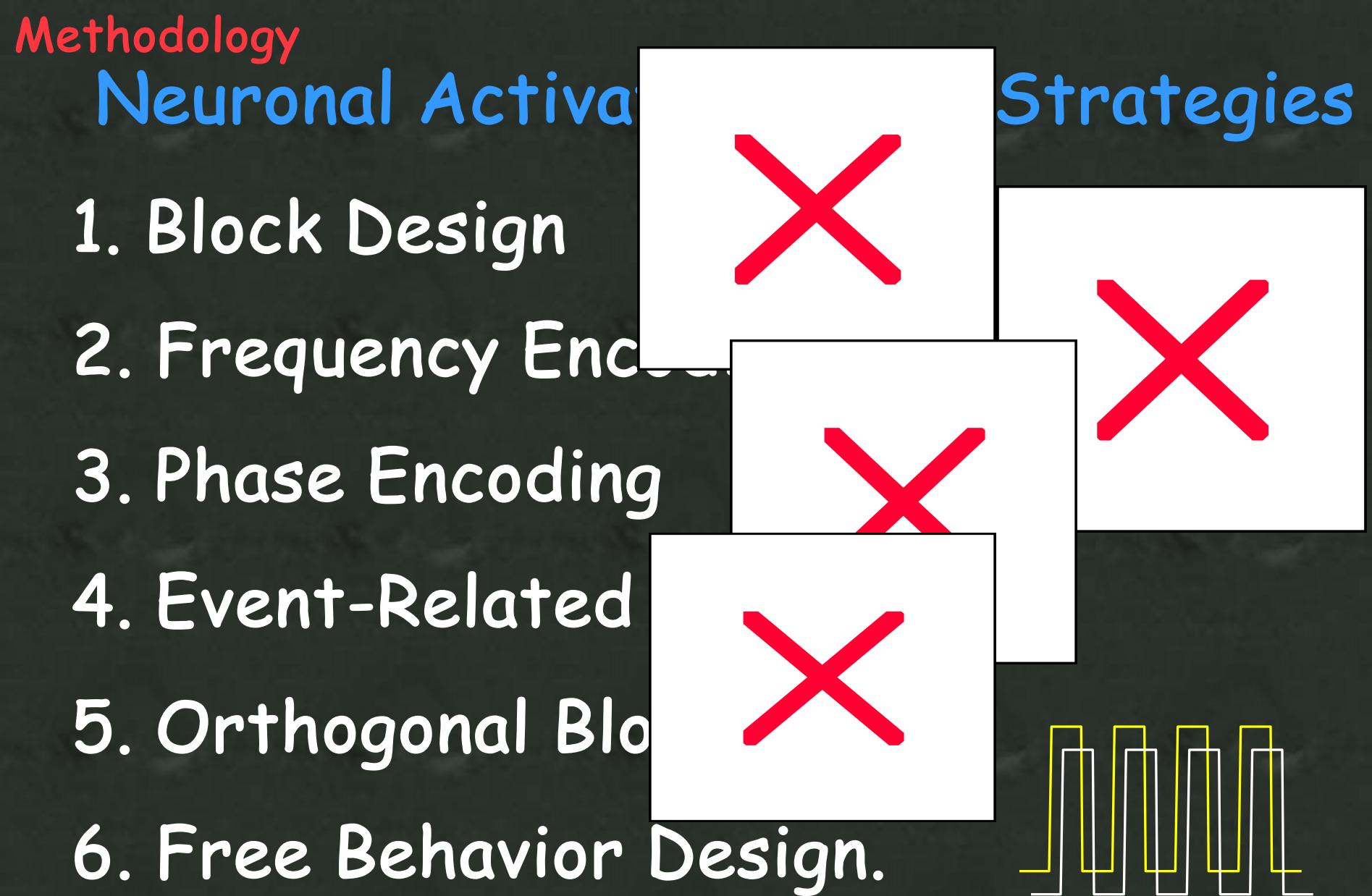
ADC increase precedes BOLD increase

Gangstead and Song, MRM  
48, 385-388, 2002



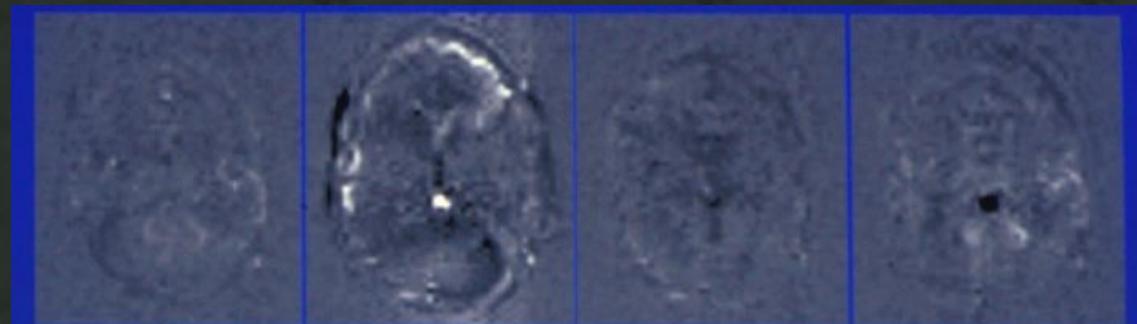
Song et al., NeuroImage, 20,  
955-961, 2003.

# New Contrasts Diffusion Coefficient



# Methodology

## Overt Word Production



2

3

4

5



6

7

8

9



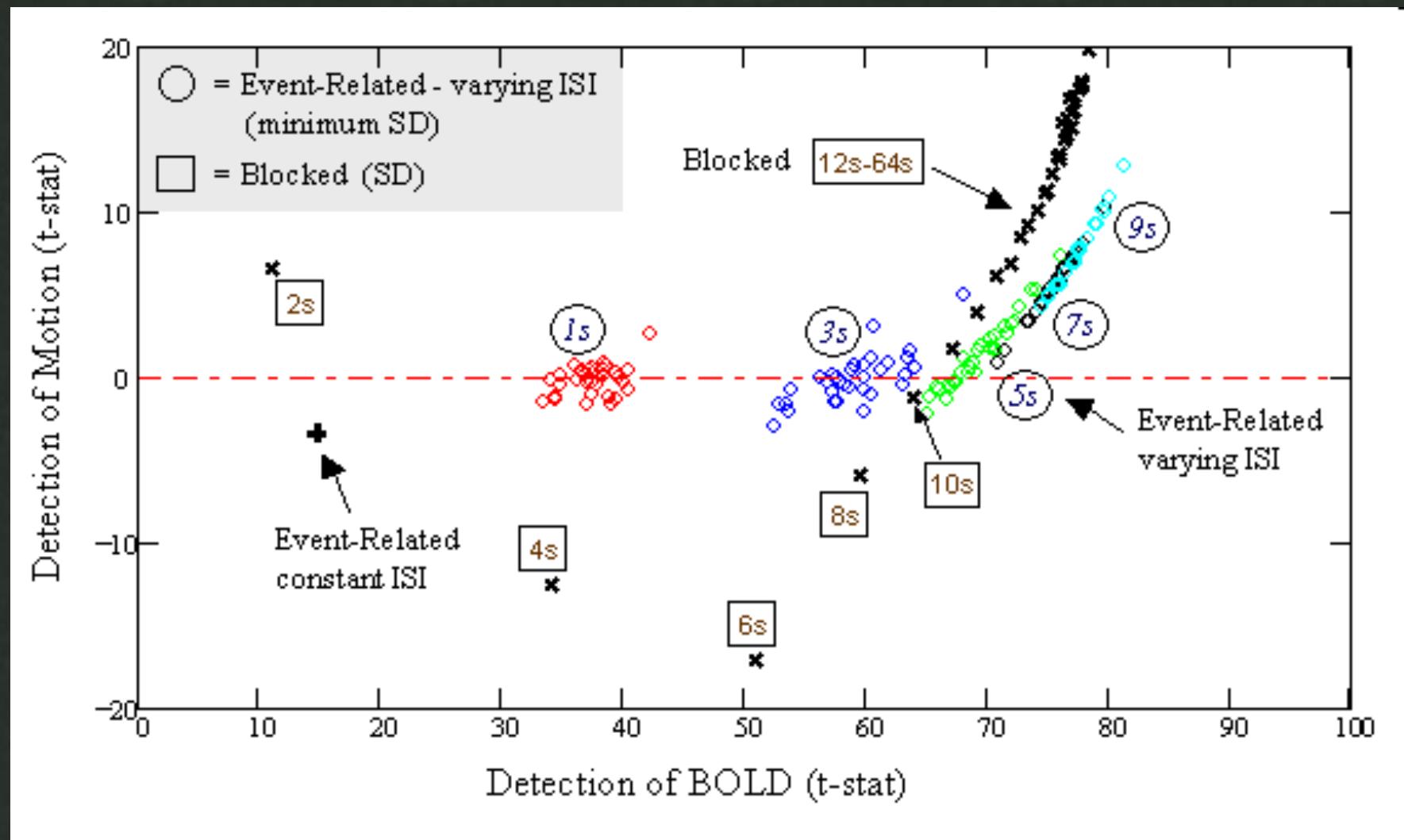
10

11

12

13

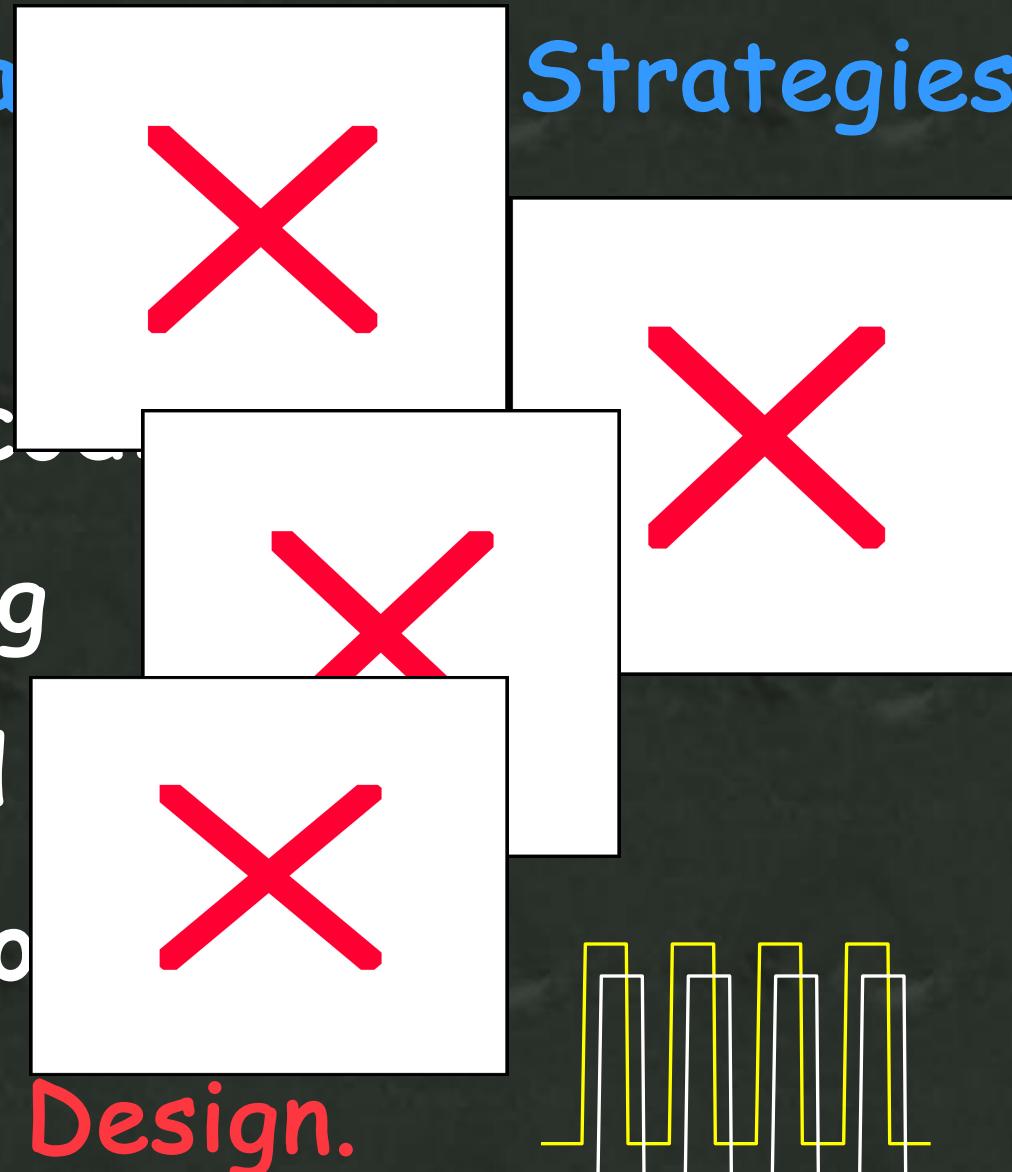
# Methodology



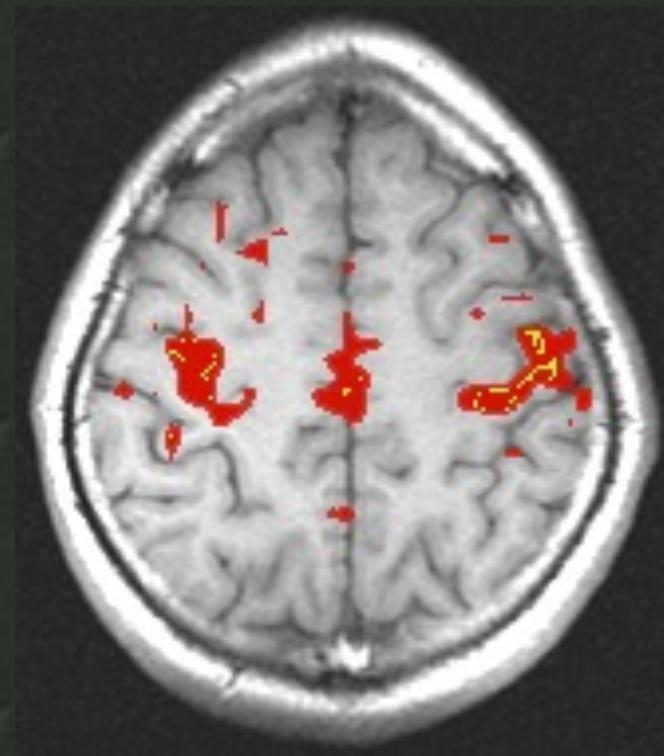
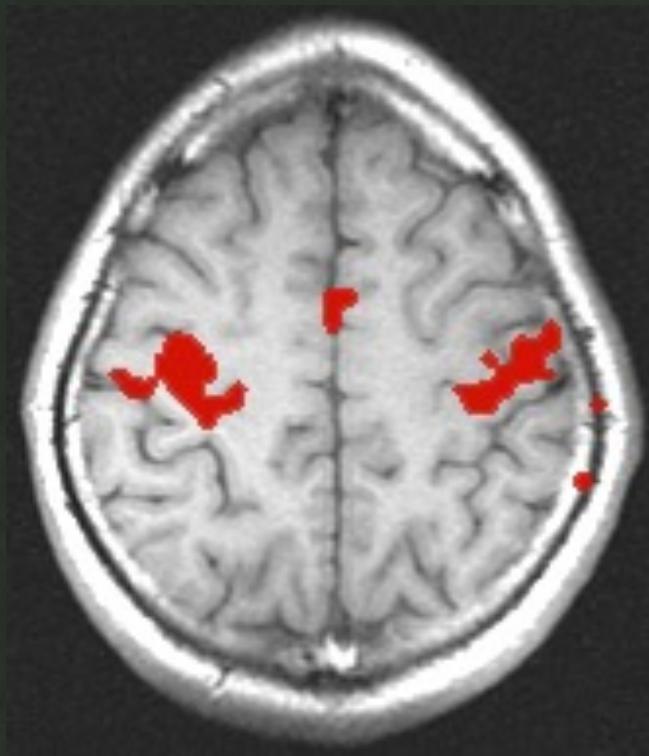
# Methodology

## Neuronal Activation Strategies

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



## Resting State Correlations



Activation:  
correlation with reference function

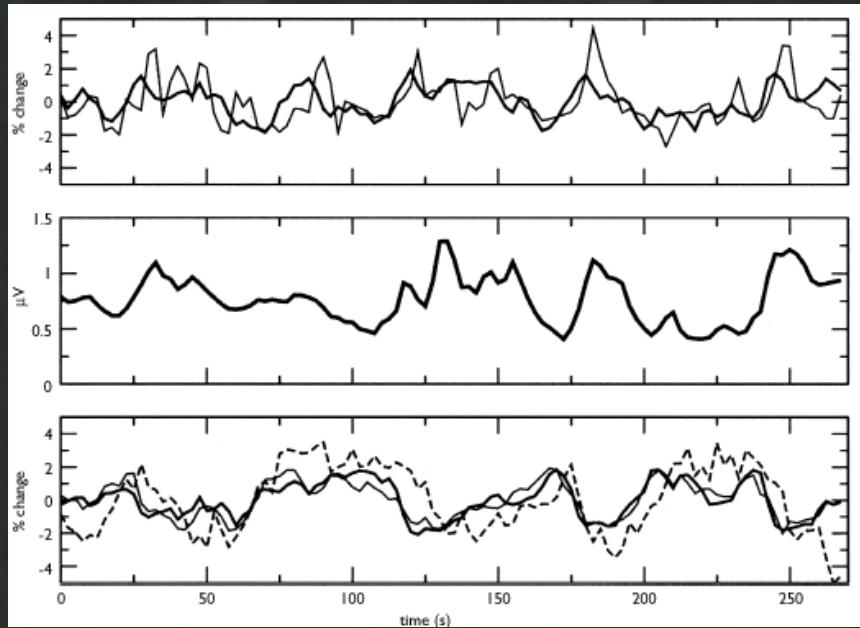
Rest:  
seed voxel in motor cortex

BOLD correlated with 10 Hz power during "Rest"

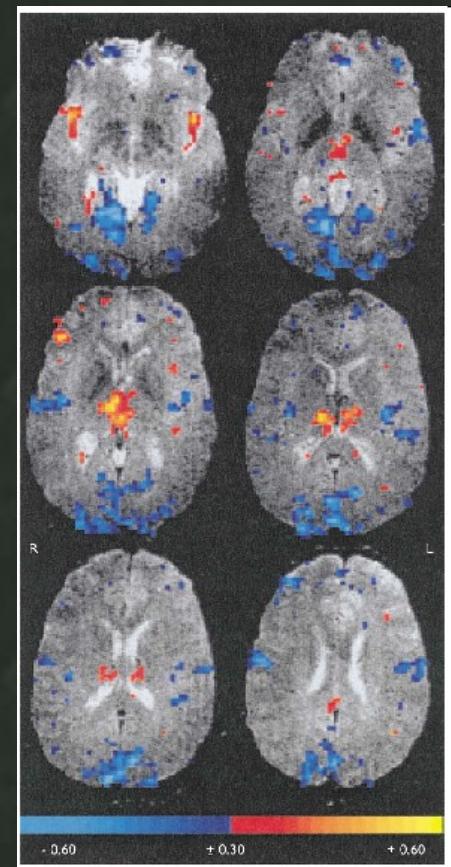
Positive

10 Hz power

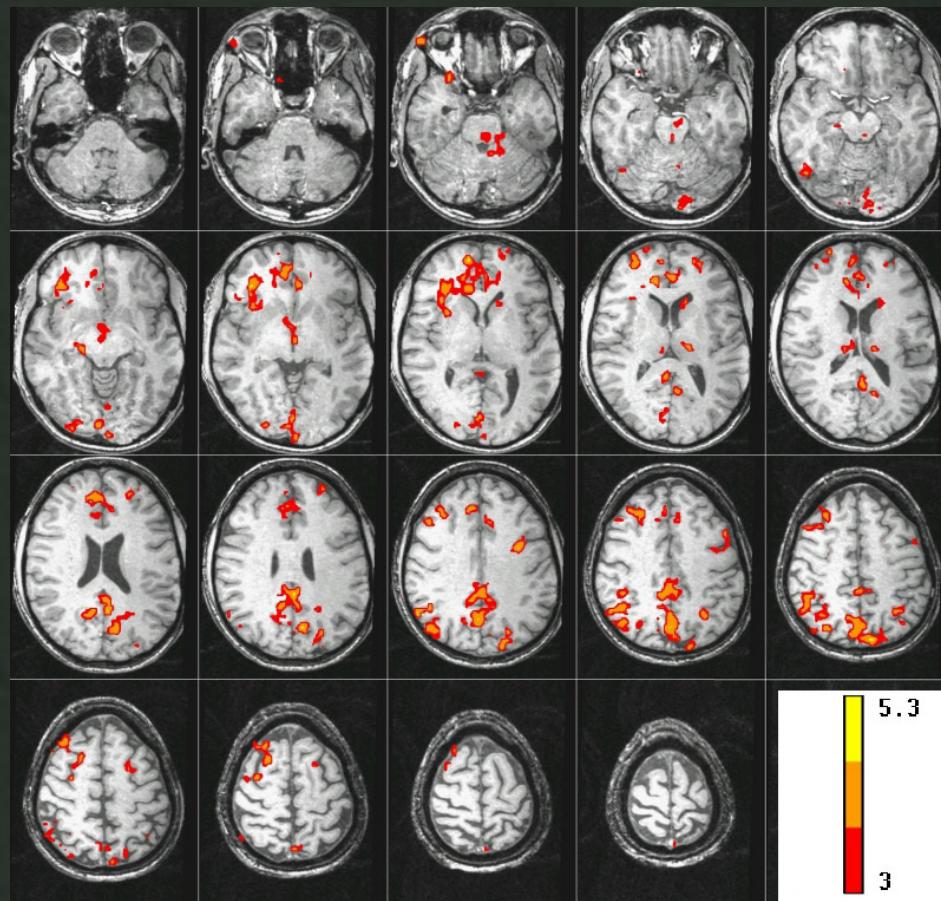
Negative



Goldman, et al (2002), Neuroreport

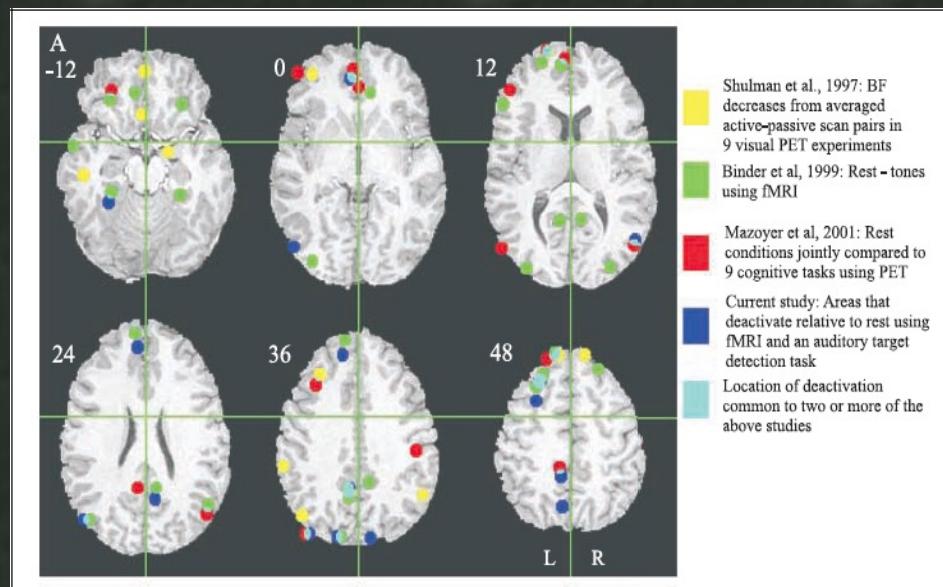
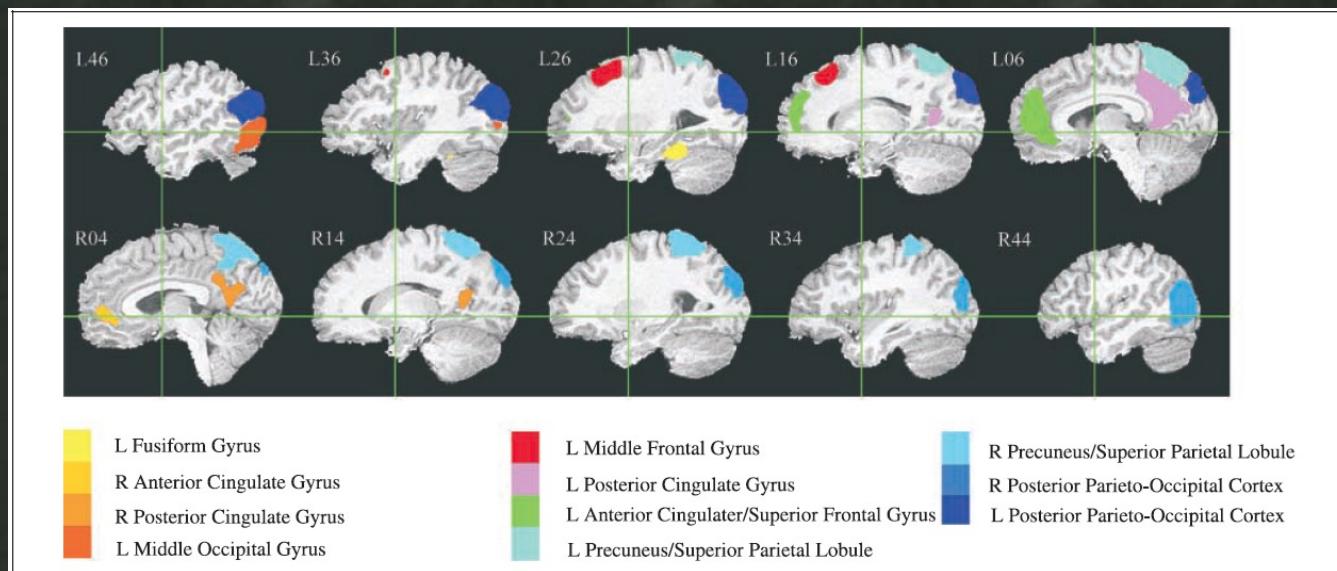


BOLD correlated with SCR during "Rest"



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

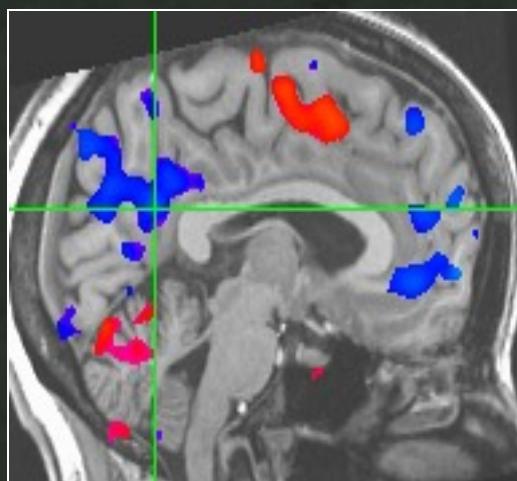
## Regions showing decreases during cognitive tasks Free Behavior



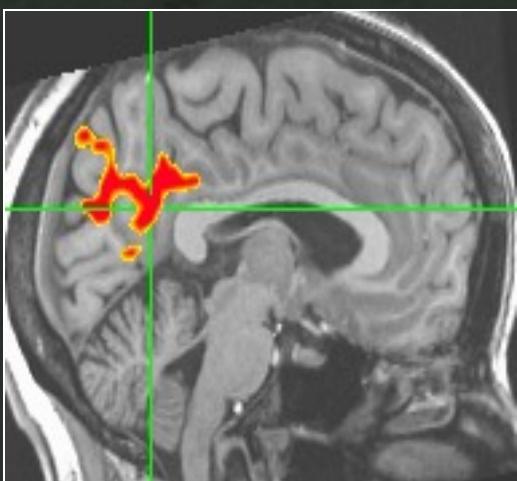
# Methodology

NAIS

Free Behavior



Lexical Task



ROI



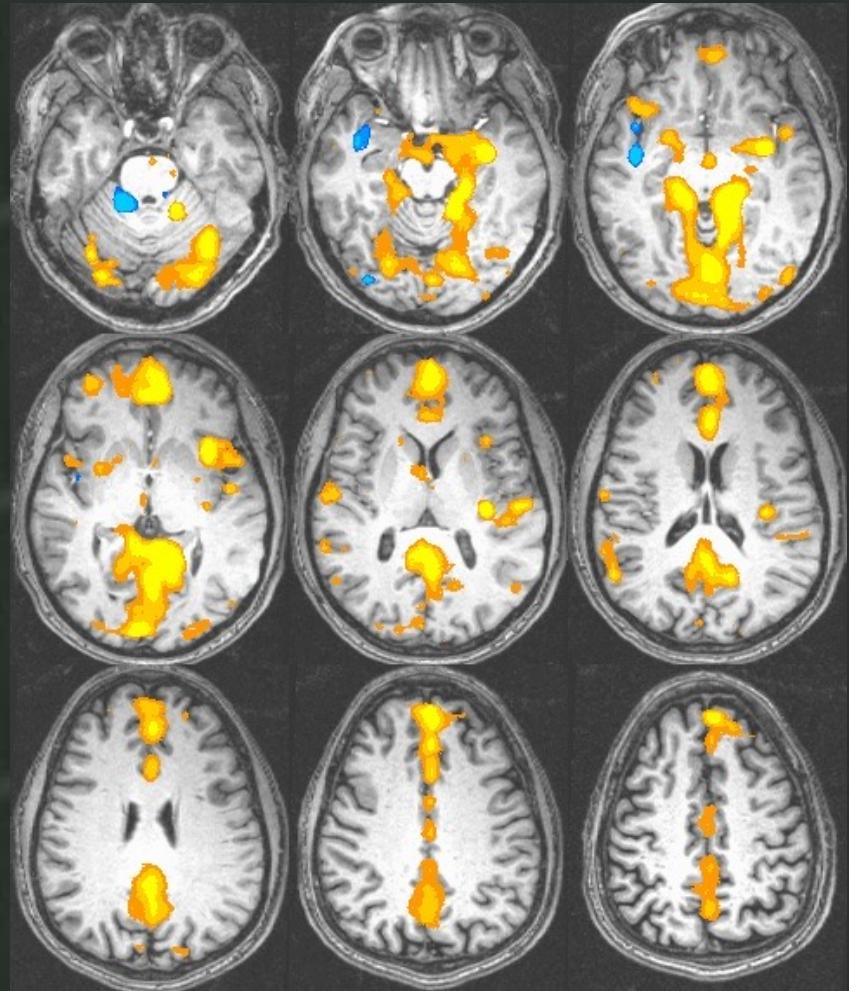
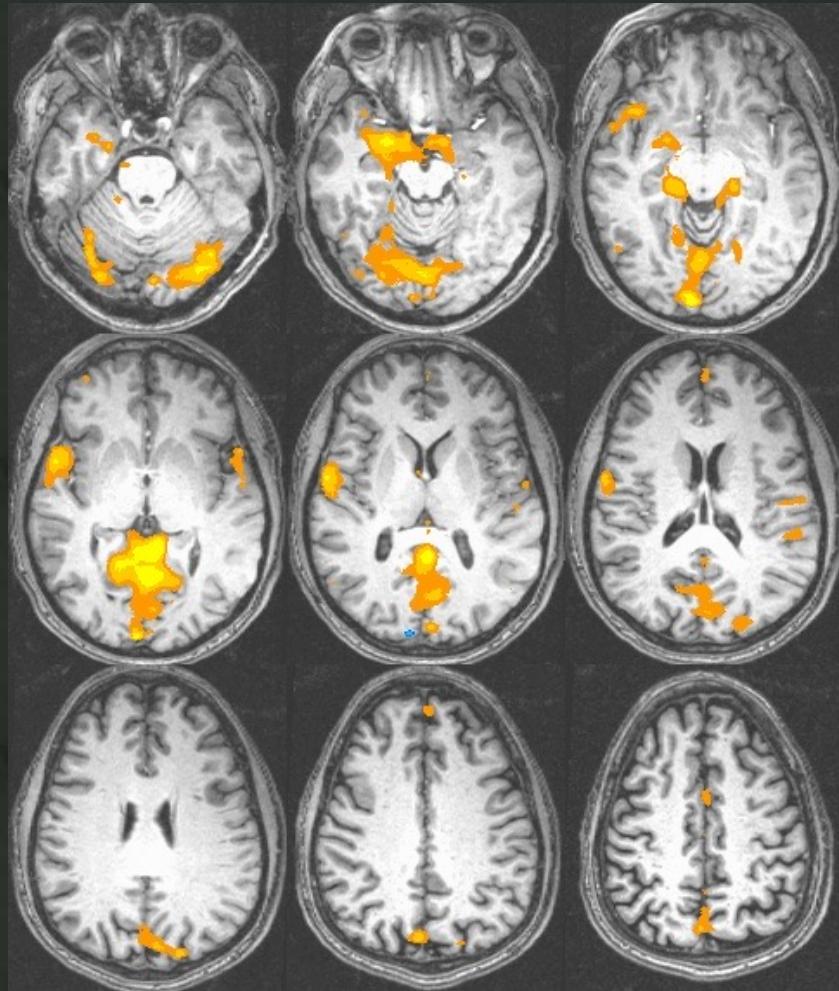
Functional  
Connectivity

# Methodology

NAIS

Free Behavior  
Left

Right



Brain regions showing strong correlation with left and right amygdala activity.

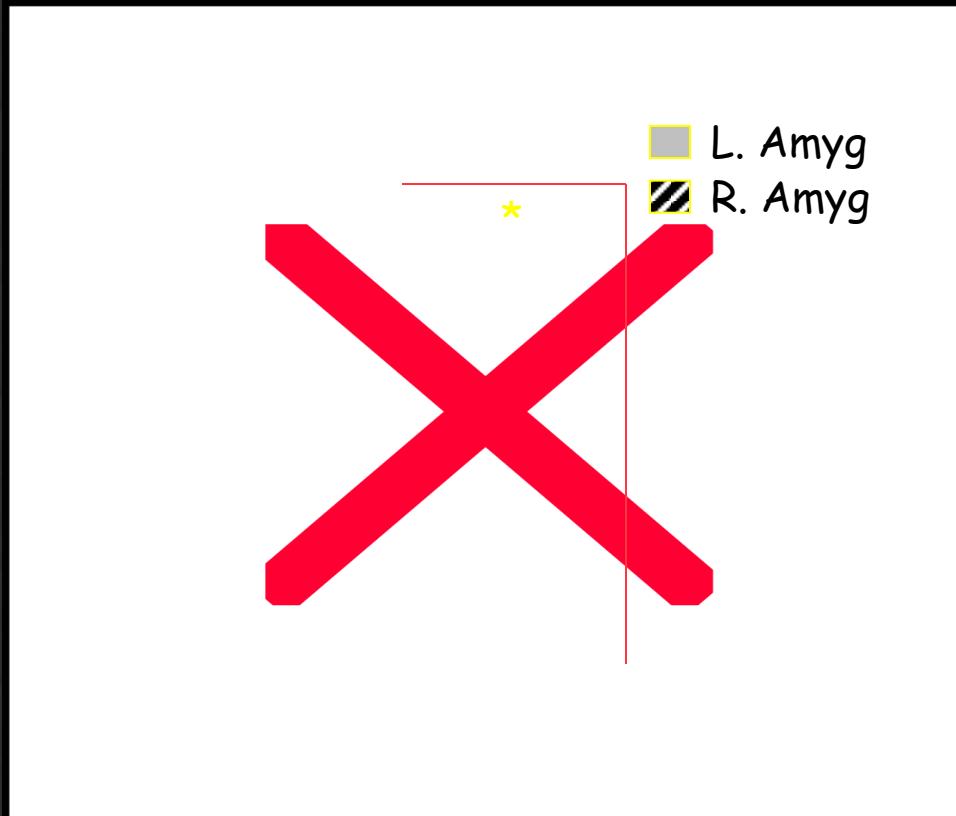
D. Knight, H. Nguyen

# Methodology

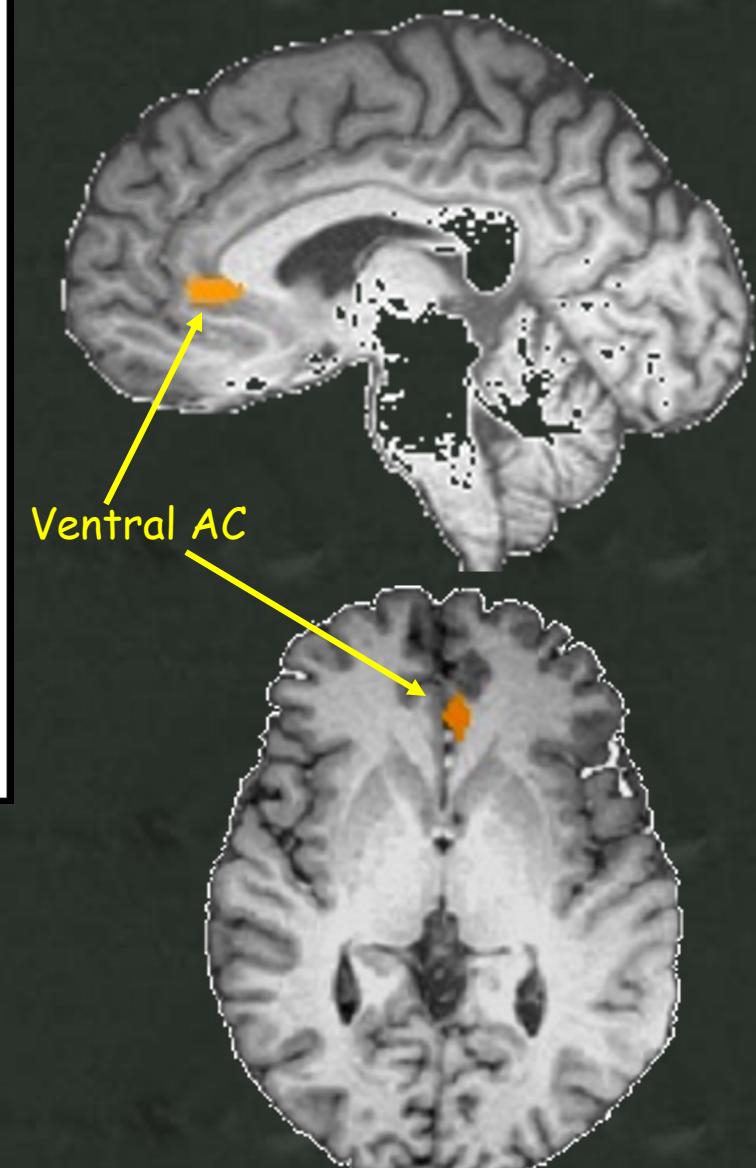
NAIS

Free Behavior

Fit coefficient



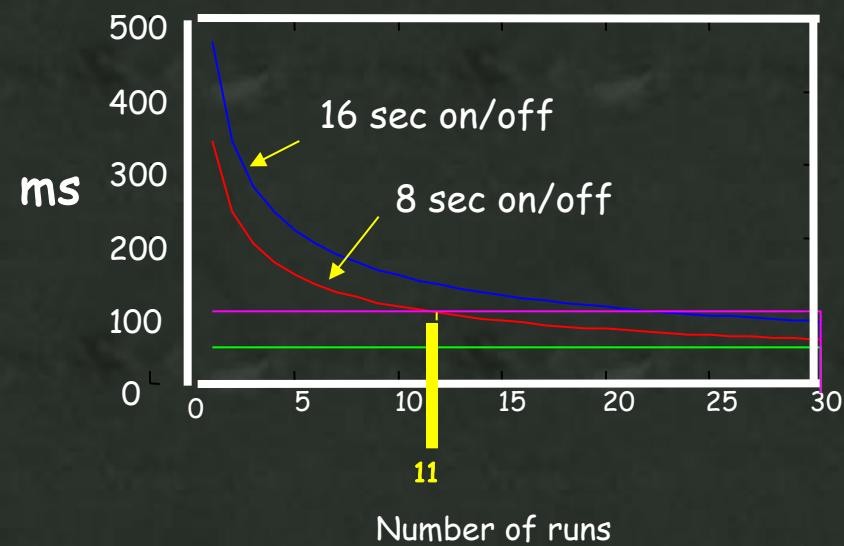
Fit coefficient comparing similarity of ventral AC activity with left and right amygdala activity. Activity within the ventral AC was more strongly associated with left than right amygdala activity.



# Methodology

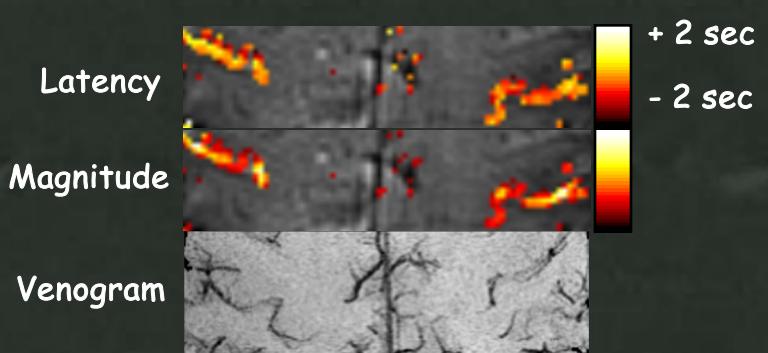
# Temporal Resolution

In an ideal world... no latency variation



R. Birn

Latency Variation...



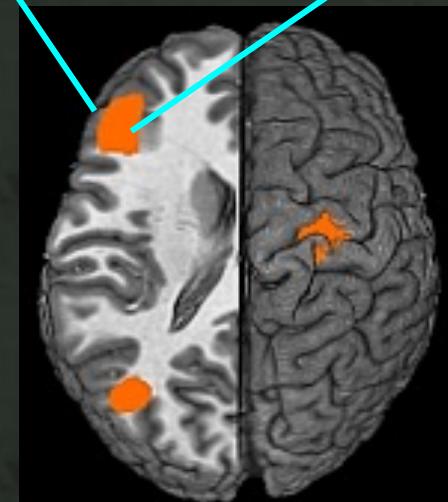
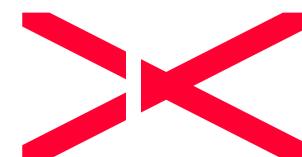
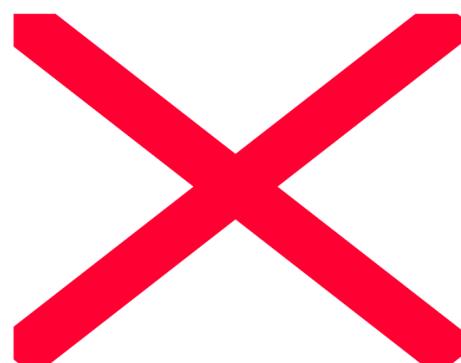
P. A. Bandettini, (1999) "Functional MRI" 205-220.

# Methodology

# Temporal Resolution

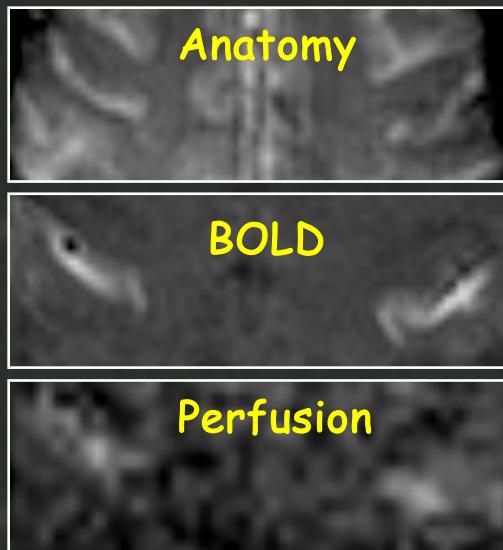
Word vs. Non-word

0°, 60°, 120° Rotation



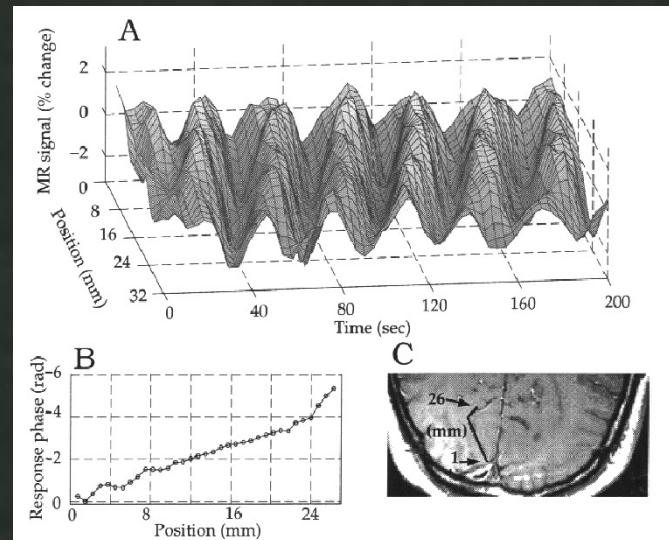
# Methodology

# Spatial Resolution



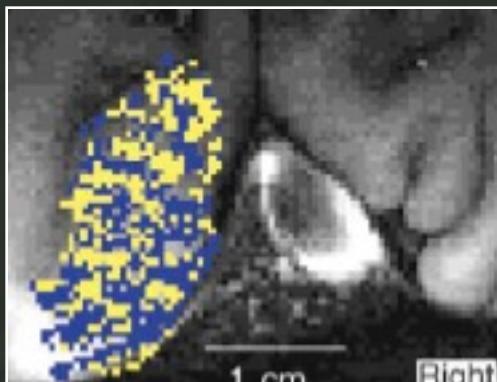
P. A. Bandettini, (1999) "Functional MRI" 205-220.

PSF FWHM = 3.5mm



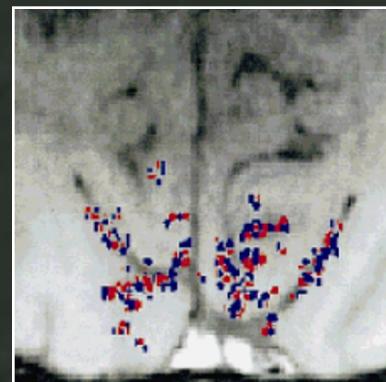
S.A. Engel, et al. Investigative Ophthalmology & Visual Science 35 (1994) 1977-1977.

0.47 x 0.47 in plane resolution



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

0.54 x 0.54 in plane resolution



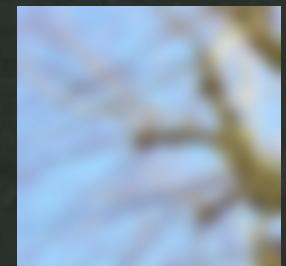
Multi-shot with navigator pulse

Menon et al, (1999) MRM 41 (2): 230-235

# Methodology

# Processing Methods

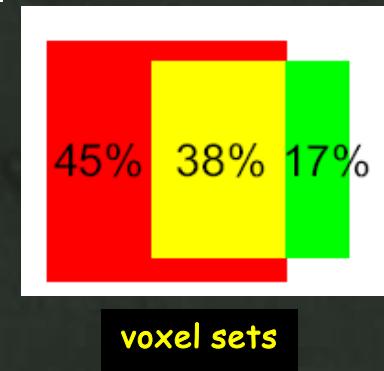
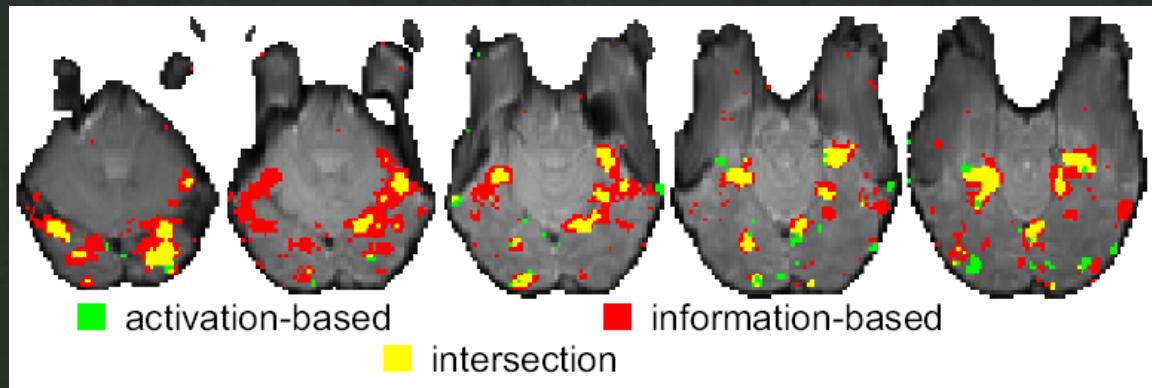
*Activation-based* mapping: data smoothing  
(classical approach)



*Information-based* mapping: local multivariate analysis

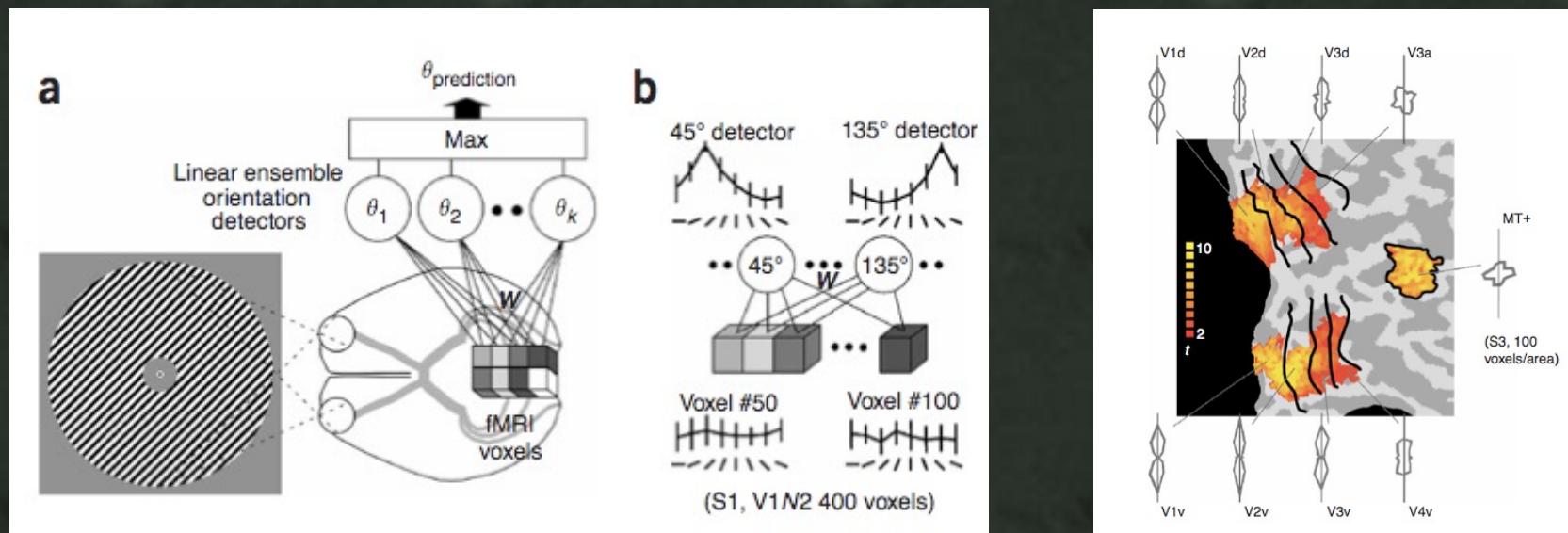


volume scanned with MANCOVA searchlight →

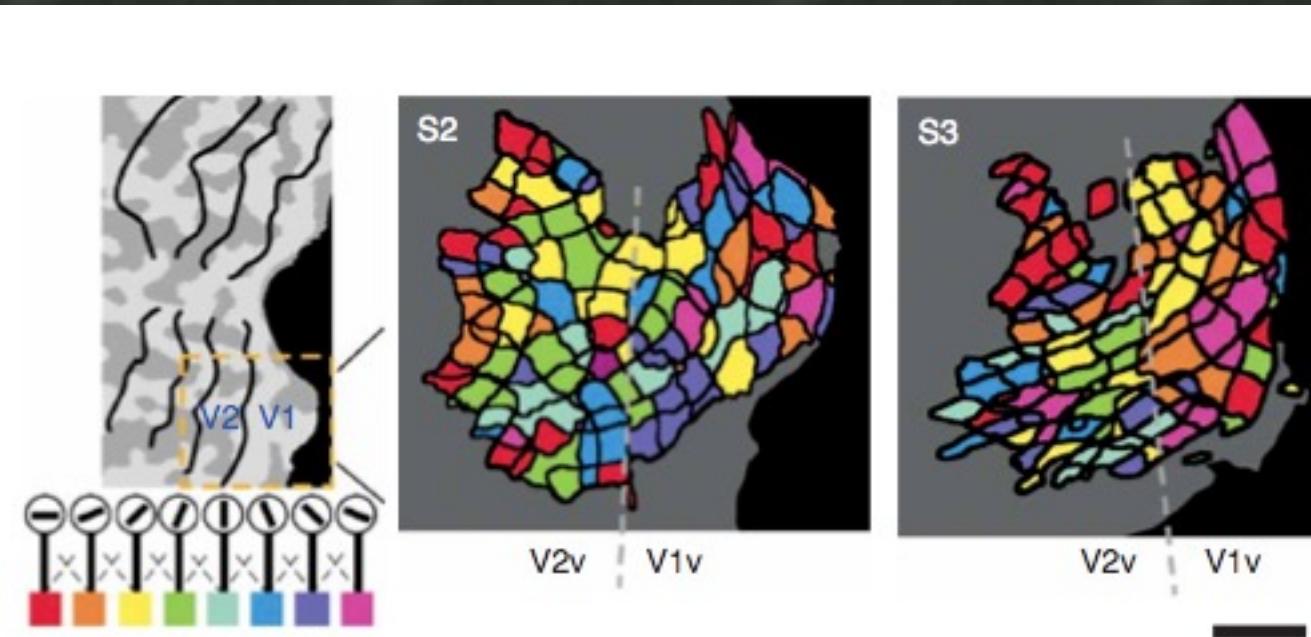


# Methodology

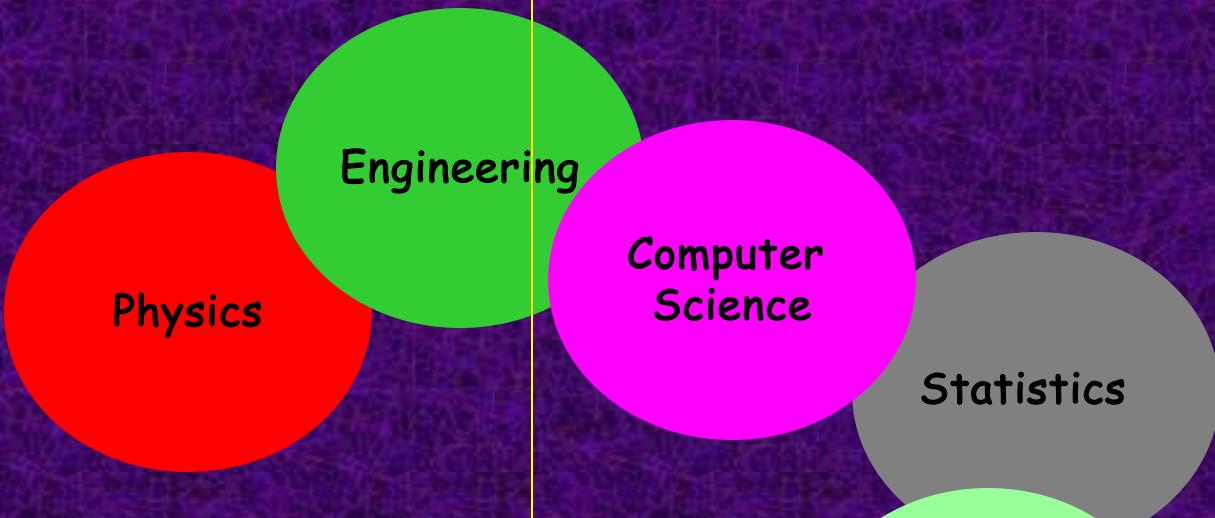
# Processing Methods



Y. Kamatani and F. Tong,  
Nature Neuroscience, 8,  
679-685.

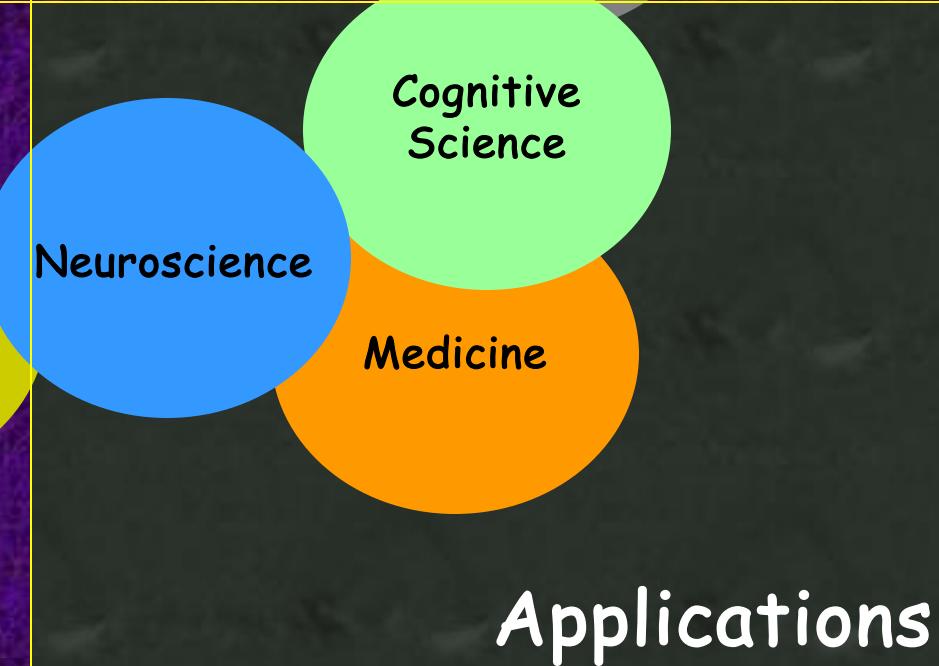


Technology



Interpretation

Methodology

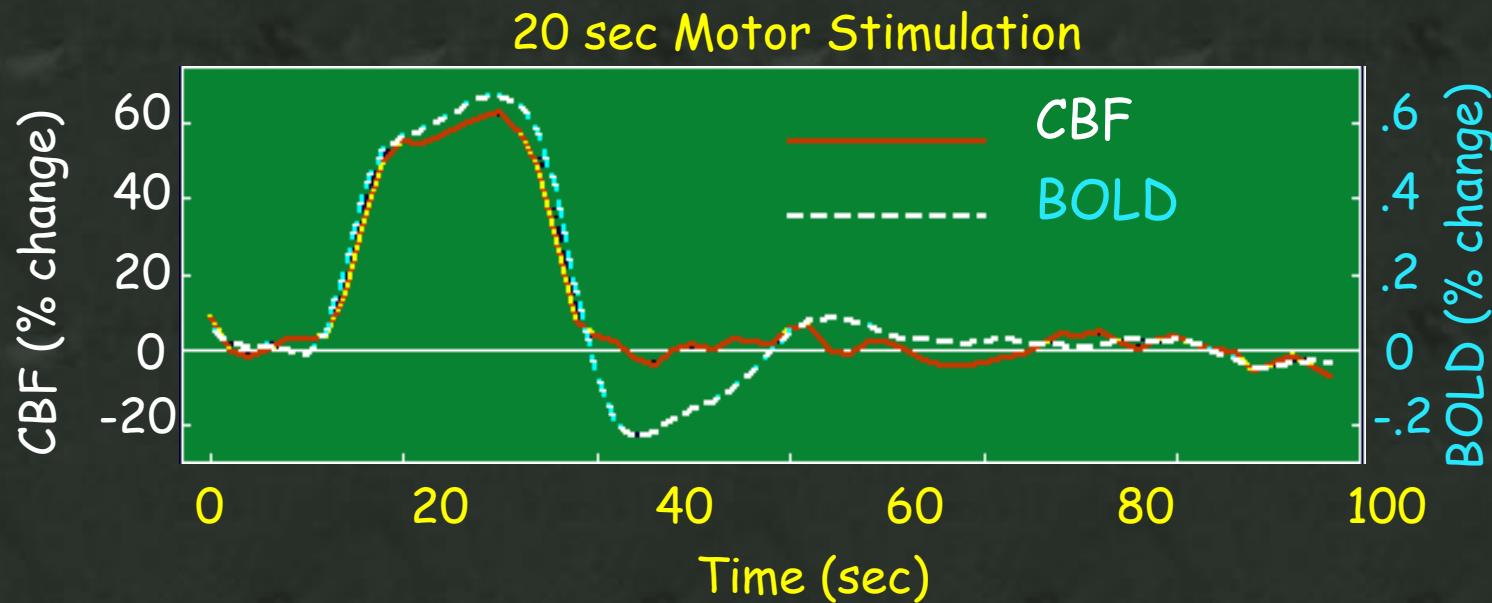


Applications

# Interpretation

- Post Undershoot
- Linearity
- Local Field Potentials vs Spiking
- Inhibition and Decreases

# BOLD post-stimulus undershoot



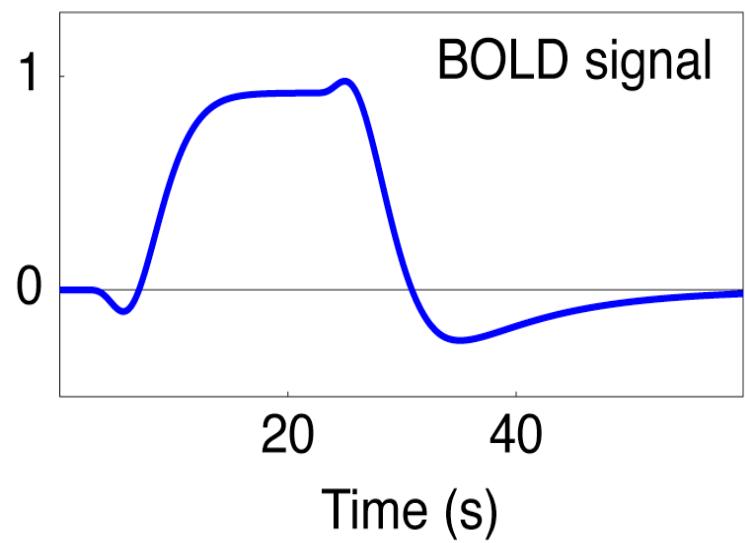
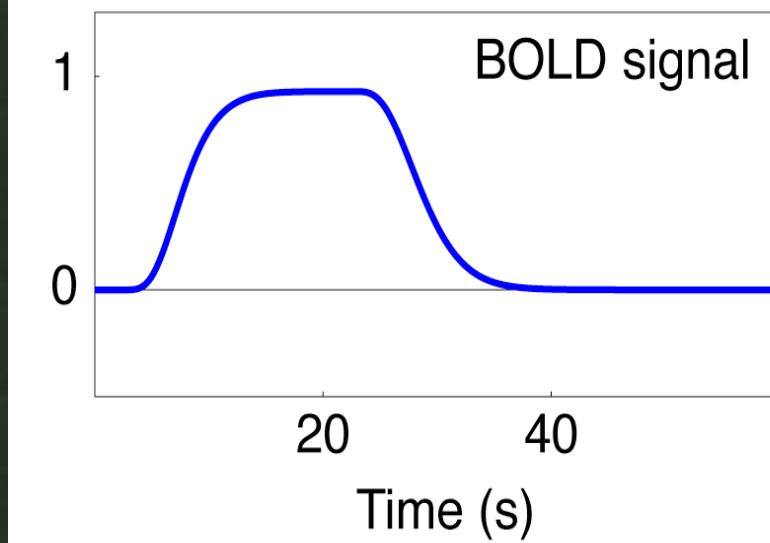
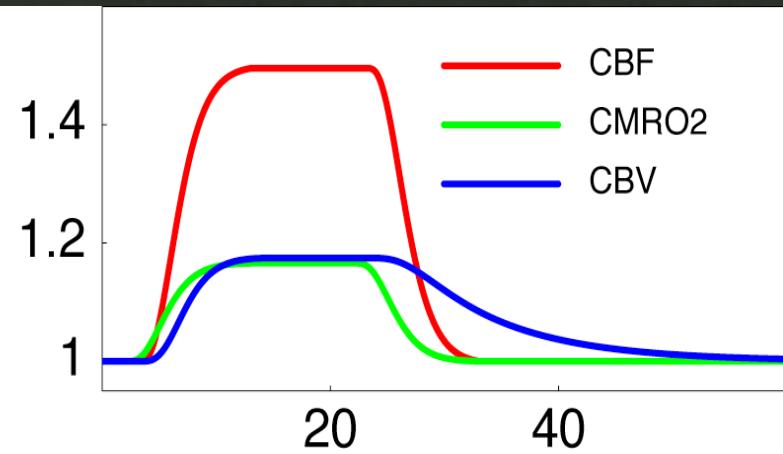
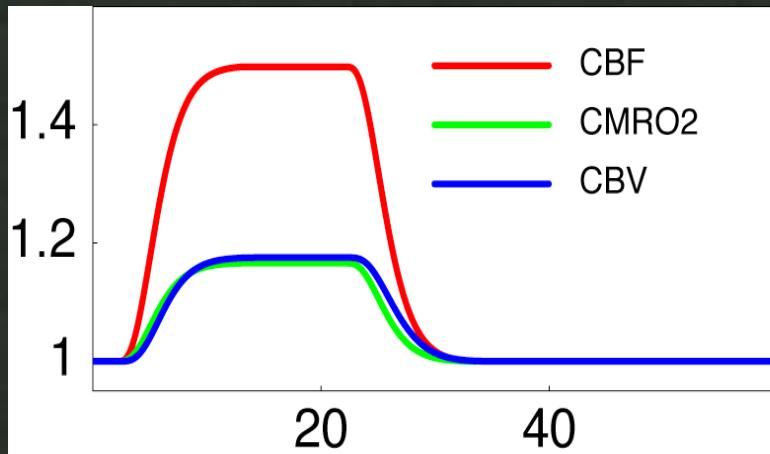
A BOLD undershoot without a CBF undershoot could be due to a slow return to baseline of either CBV or CMRO<sub>2</sub>

Courtesy Rick Buxton

Interpretation

Post Undershoot

# BOLD Signal Dynamics

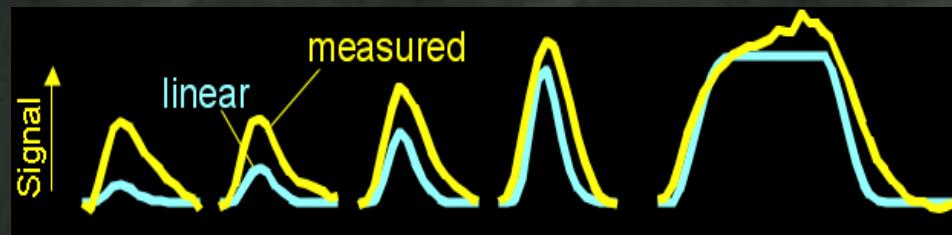


Courtesy Rick Buxton

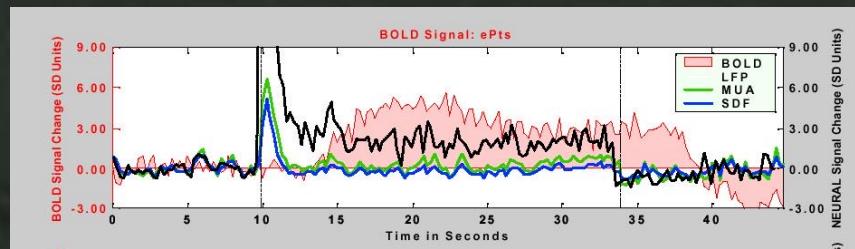
# Interpretation

# Linearity

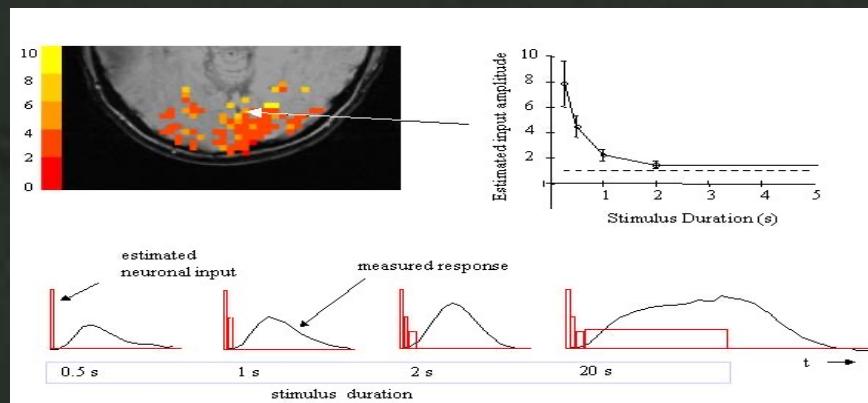
Increases: linearity



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



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



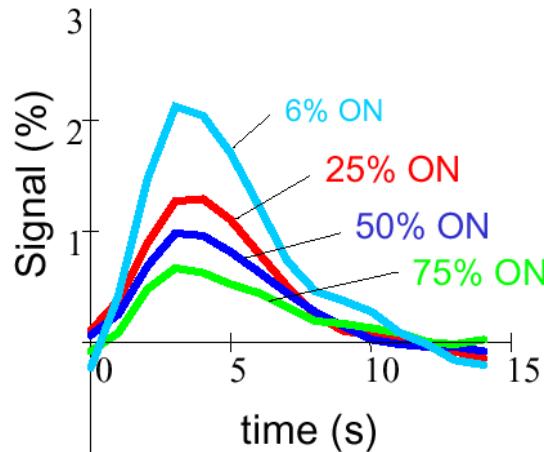
P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

# Interpretation

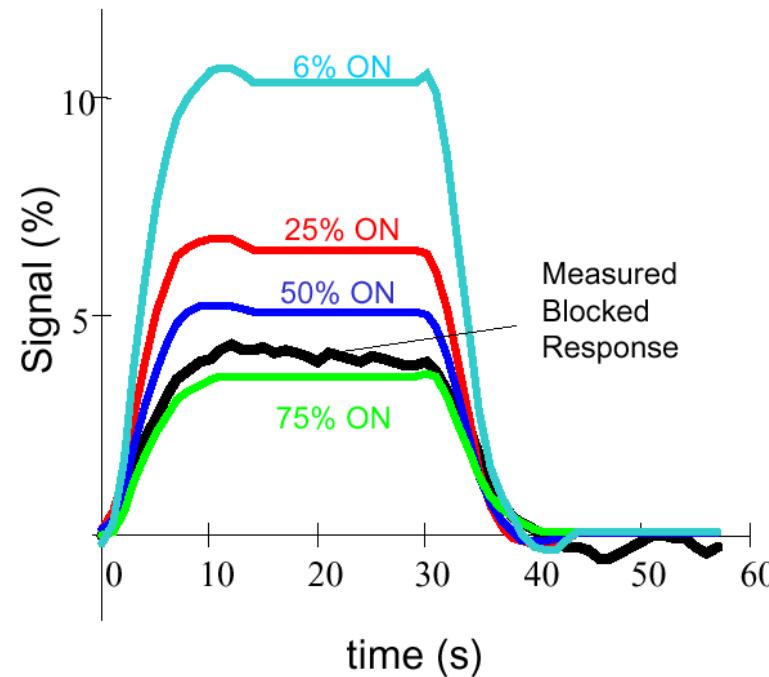
## Increases: duty cycle

# Linearity

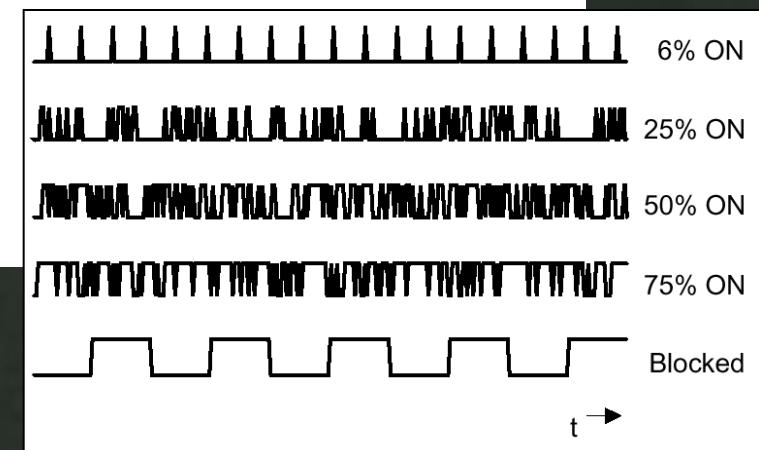
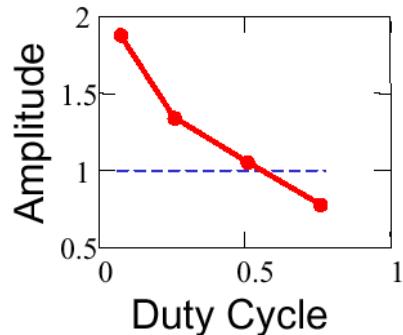
**a** Measured Event-related Responses



**b** Predicted Blocked Responses



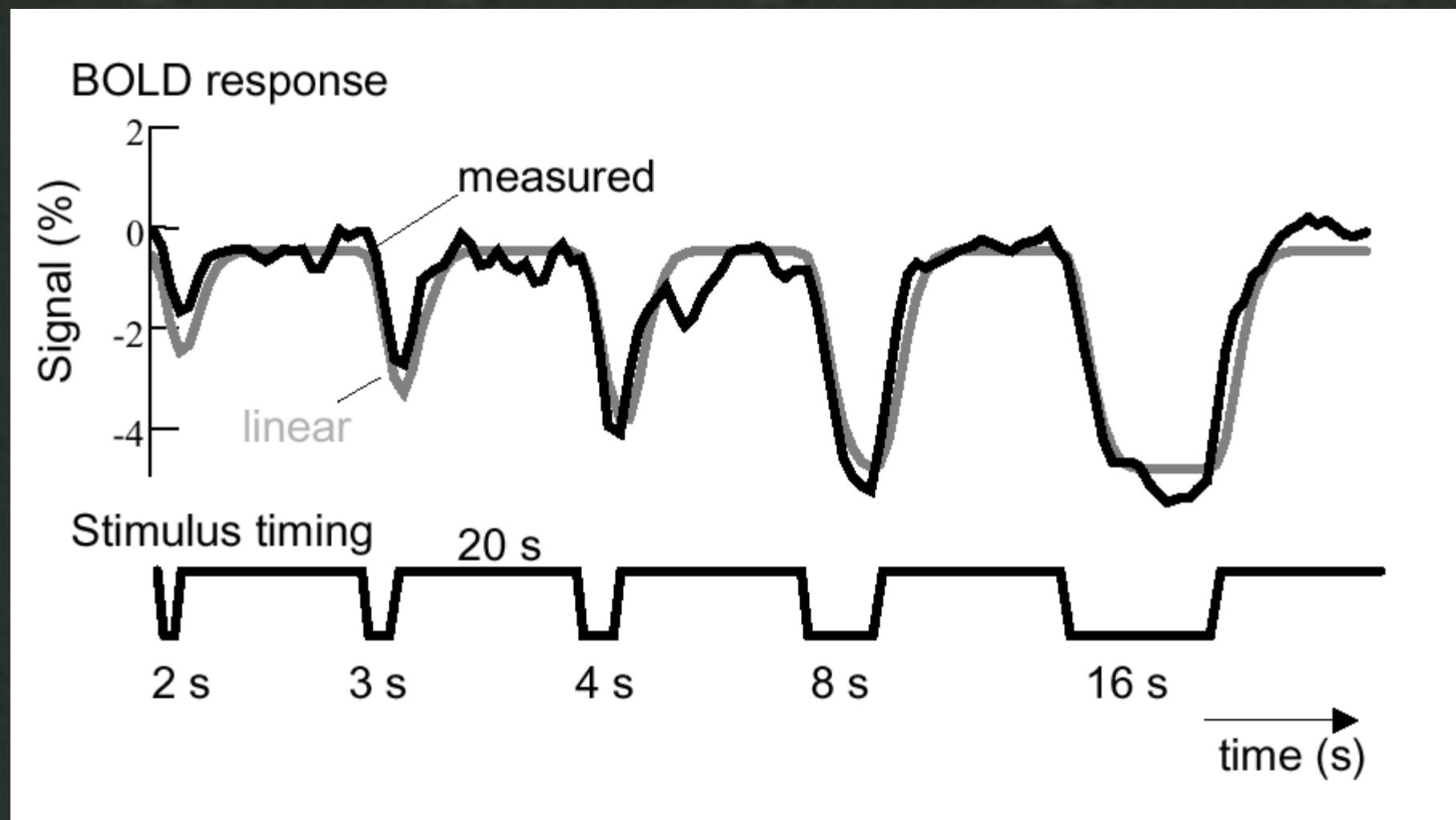
**c**



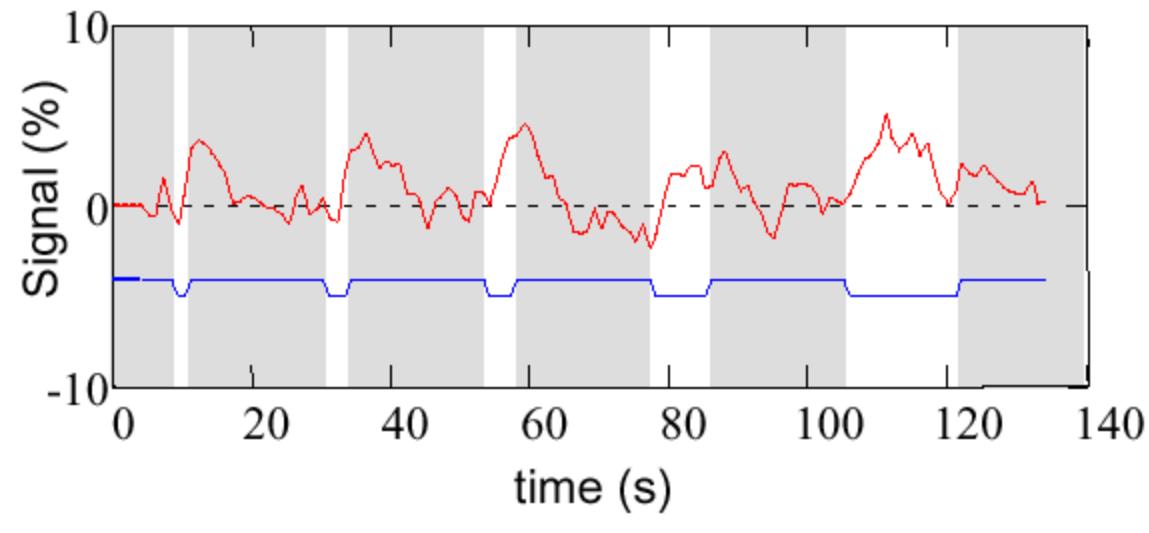
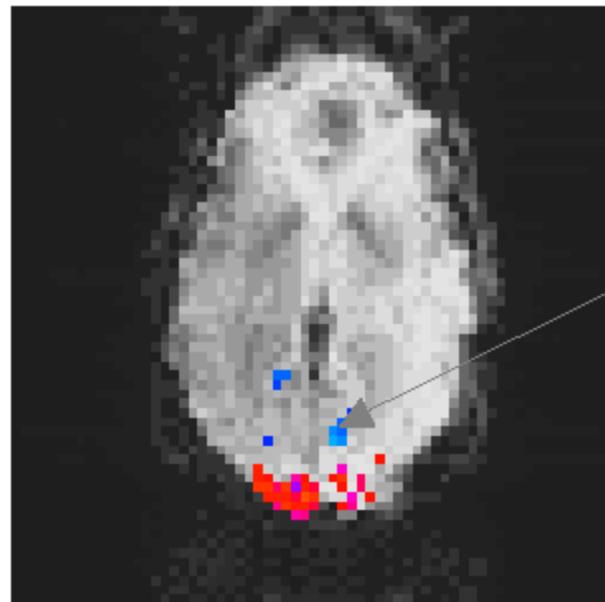
# Interpretation

# Linearity

Decreases: linearity



We also see increases during stimulus cessation...

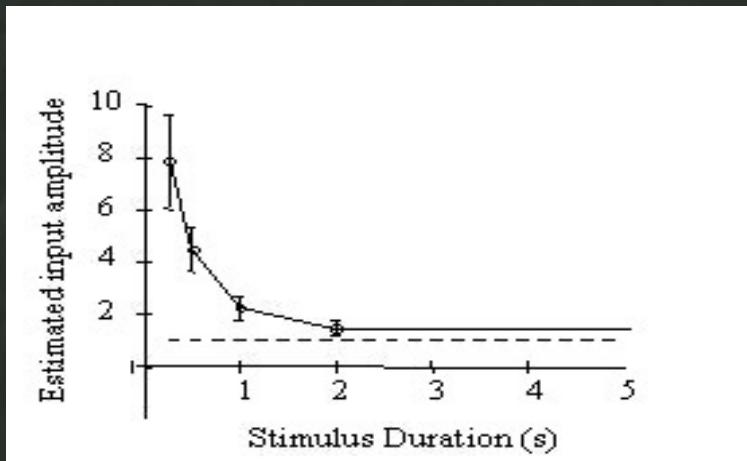


Visual stimulation

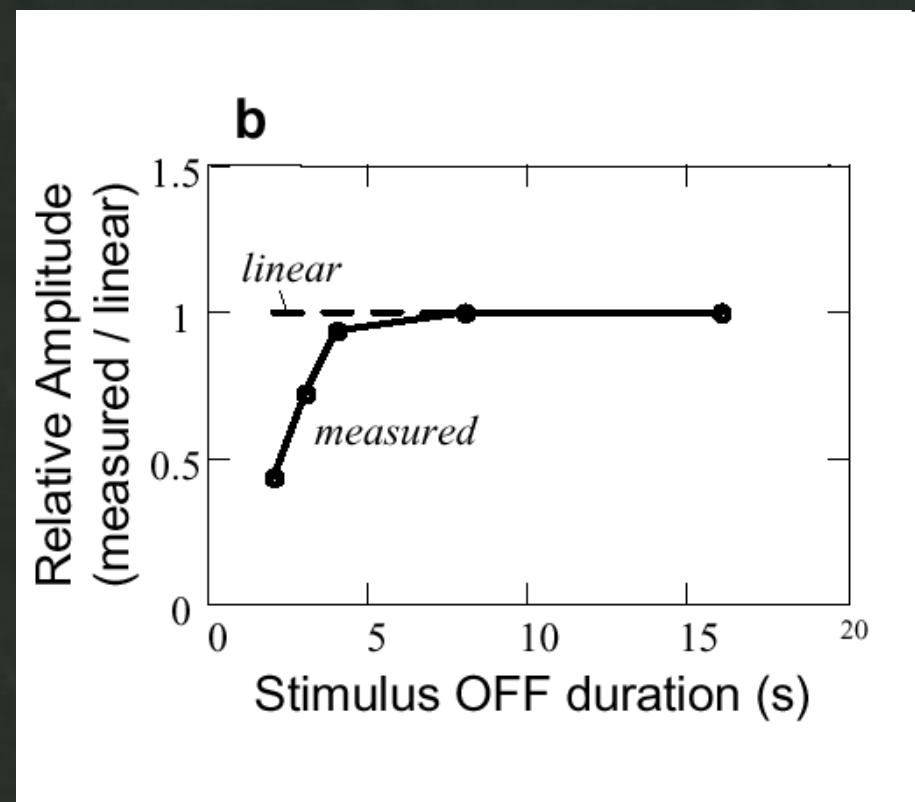
# Interpretation

# Linearity

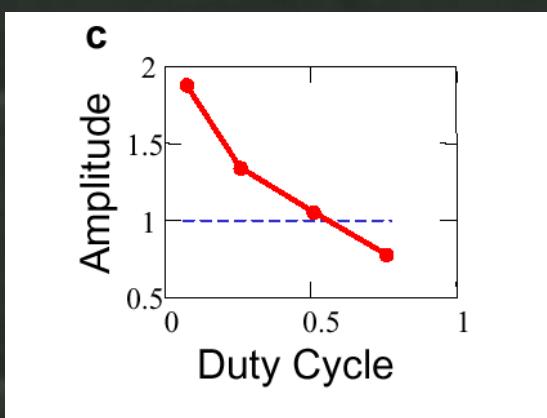
Increase: duration on



Decrease: duration off

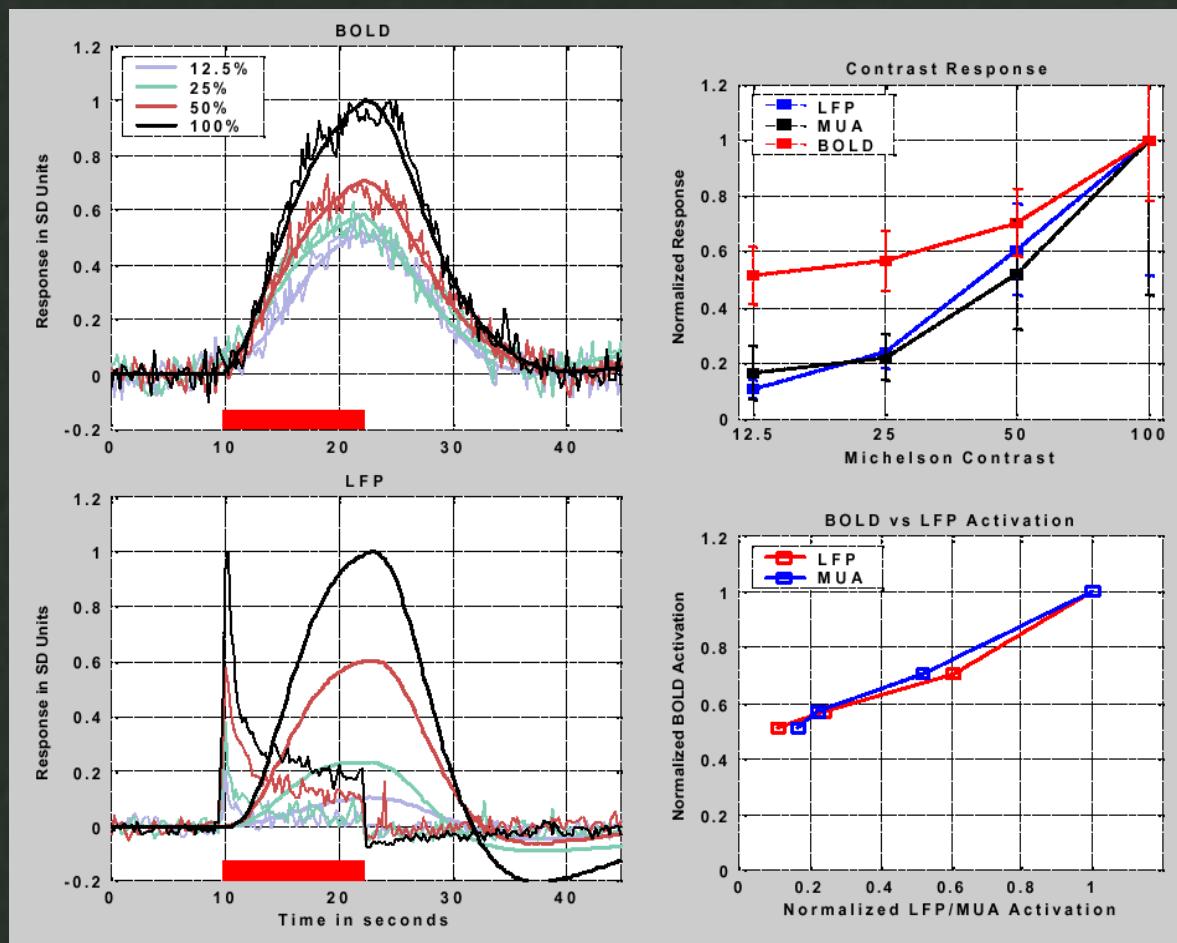


Increase: duty cycle



# Interpretation

# LFP vs Spiking

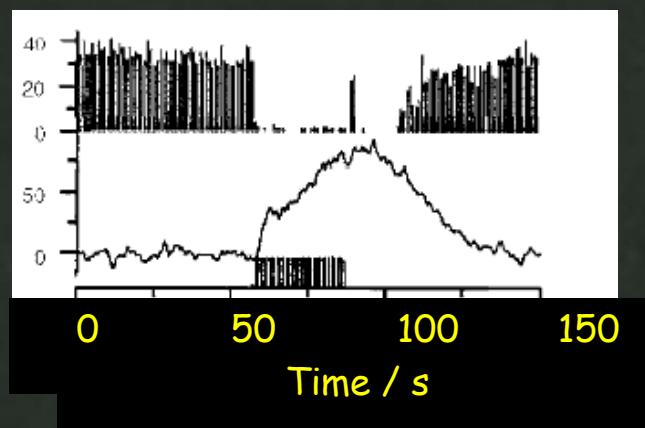


Logothetis et al. (2001) Nature, 412, 150-157

# Interpretation

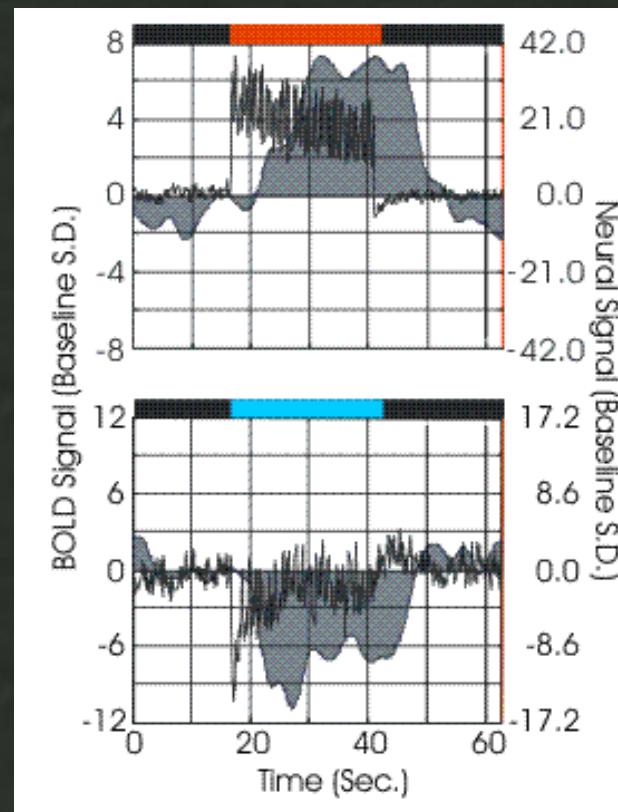
# Inhibition and Decreases

Inhibition



Mathiesen, et al (1998), J Physiol  
512.2:555-566

Neg. BOLD



Schmucl et al. (2003)  
OHBM, 308

Technology

Methodology

Engineering

Physics

Computer  
Science

Statistics

Cognitive  
Science

Physiology

Neuroscience

Medicine

Interpretation

Applications

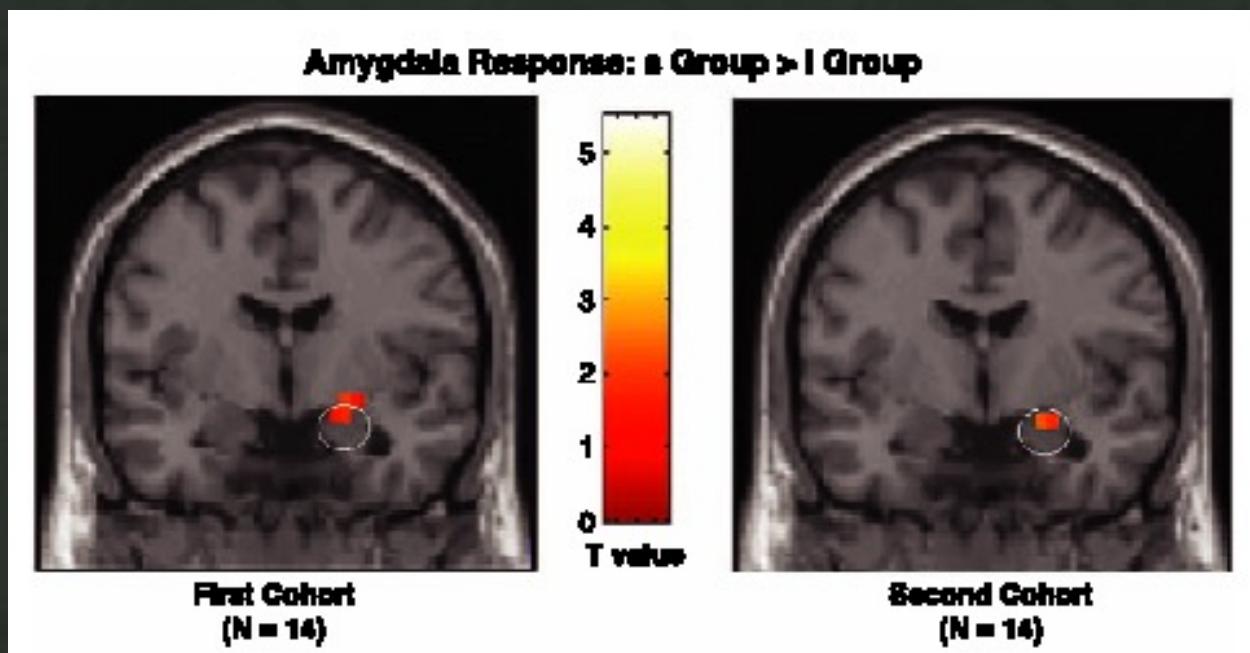
# Applications

- Real Time Feedback
- Clinical Applications

Comparison of two groups of *normal* individuals with differences in the Serotonin Transporter Gene

## Serotonin Transporter Genetic Variation and the Response of the Human Amygdala

Ahmad R. Hariri,<sup>1</sup> Venkata S. Mattay,<sup>1</sup> Alessandro Tessitore,<sup>1</sup>  
Bhaskar Kolachana,<sup>1</sup> Francesco Fera,<sup>1</sup> David Goldman,<sup>2</sup>  
Michael F. Egan,<sup>1</sup> Daniel R. Weinberger<sup>1\*</sup>



# Highest Citation Rate as of December 2004

Rank	Cit./Yr.	Tot. Cit.	Yr. Pub.	Authors	Journal, Vol, Pages	Type	Title
1	114	1485	1992	K. K. Kwong, J. W. Belliveau, et al.	PNAS,89,5675-5679	M	Dynamic Magnetic-Resonance-Imaging of Human Brain Activity During Primary Sensory Stimulation
2	112	448	2001	N. K. Logothetis, J. Pauls, et al.	Nature,412,150-157	I	Neurophysiological investigation of the basis of the fMRI signal
3	101	507	2000	R. Cabeza and L. Nyberg	Journal of Cog. Neuro,12,1-47	A	Imaging cognition II: An empirical review of 275 PET and fMRI studies
4	84	1095	1992	S. Ogawa, D. W. Tank, et al.	PNAS,89,5951-5955	M	Intrinsic Signal Changes Accompanying Sensory Stimulation - Functional Brain Mapping with Magnetic-Resonance-Imaging
5	82	655	1997	N. Kanwisher, J. McDermott et al.	Journal of Neuroscience,17,4302-4311	A	The fusiform face area: A module in human extrastriate cortex specialized for face perception
6	71	857	1993	P. A. Bandettini, A. Jesmanowicz, et al.	MRM,30,161-173	M	Processing Strategies for Time-Course Data Sets in Functional MRI of the Human Brain
7	67	336	2000	G. Bush, P. Luu et al.	TICS,4,215-222	A	Cognitive and emotional influences in anterior cingulate cortex
8	60	419	1998	C. S. Carter, T. S. Braver, et al.	Science,280,747-749	A	Anterior cingulate cortex, error detection, and the online monitoring of performance
9	58	231	2001	M. F. Egan, T. E. Goldberg et al.	PNAS,98,6917-6922	A	Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia
10	57	458	1997	J. D. Cohen, W. M. Perlstein, et al.	Nature,388,604-608	M/A	Temporal dynamics of brain activation during a working memory task
11	57	509	1996	R. W. Cox	Comp. and Biomed. Res, 29,162-173	M	AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages
12	55	497	1996	A. Martin, C. L. Wiggs, et al.	Nature,379,649-652	A	Neural correlates of category-specific knowledge
13	53	745	1991	J. W. Belliveau, D. N. Kennedy, et al.	Science,254,716-719	M	Functional Mapping of the Human Visual-Cortex by Magnetic-Resonance-Imaging
14	53	691	1992	P. A. Bandettini, E. C. Wong, et al.	MRM, 25,390-397	M	Time Course Epi of Human Brain-Function During Task Activation
15	52	523	1995	M. I. Sereno, A. M. Dale, et al.	Science,268,889-893	M/A	Borders of Multiple Visual Areas in Humans Revealed by Functional Magnetic-Resonance-Imaging
16	50	348	1998	A. D. Wagner, D. L. Schacter, et al.	Science,281,1188-1191	A	Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity
17	50	348	1998	P. J. Whalen, S. L. Rauch et al.	Journal of Neuroscience,18,411-418	A	Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge
18	48	428	1996	K. J. Worsley, S. Marrett, et al.	Human Brain Mapping,4,58-73	M	A unified statistical approach for determining significant signals in images of cerebral activation
19	47	233	2000	M. Corbetta, J. M. Kincade, et al.	Nature Neuroscience,3,292-297	A	Voluntary orienting is dissociated from target detection in human posterior parietal cortex
20	44	174	2001	J. O'Doherty, M. L. Kringelbach, et al.	Nature Neuroscience,4,95-102	A	Abstract reward and punishment representations in the human orbitofrontal cortex
21	44	87	2003	M. F. Egan, M. Kojima, et al.	Cell,112,257-269	A	The BDNF val66met polymorphism affects activity-dependent secretion of BDNF and human memory and hippocampal function
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23	43	427	1995	R. B. H. Tootell, J. B. Reppas, et al.	Journal of Neuroscience,15,3215-3230	M/A	Functional-Analysis of Human Mt and Related Visual Cortical Areas Using Magnetic-Resonance-Imaging
24	42	419	1995	B. A. Shaywitz, S. E. Shaywitz, et al.	Nature,373,607-609	A	Sex-Differences in the Functional-Organization of the Brain for Language
25	42	418	1995	K. J. Worsley and K. J. Friston	Neuroimage,2,173-181	M	Analysis of Fmri Time-Series Revisited - Again
26	41	446	1994	L. Pellerin and P. J. Magistretti	PNAS,91,10625-10629	I	Glutamate Uptake into Astrocytes Stimulates Aerobic Glycolysis - a Mechanism Coupling Neuronal-Activity to Glucose-Utilization
27	40	359	1996	H. C. Breiter, N. L. Elcock, et al.	Neuron,17,875-887	A	Response and habituation of the human amygdala during visual processing of facial expression
28	40	319	1997	J. R. Binder, J. A. Frost, et al.	Journal of Neuroscience,17,353-362	A	Human brain language areas identified by functional magnetic resonance imaging
29	40	317	1997	T. S. Braver, J. D. Cohen, et al.	Neuroimage,5,49-62	M/A	A parametric study of prefrontal cortex involvement in human working memory
30	39	393	1995	M. Desposito, J. A. Detre, et al.	Nature,378,279-281	A	The Neural Basis of the Central Executive System of Working-Memory
31	39	391	1995	K. J. Friston, A. P. Holmes, et al.	Neuroimage,2,45-53	M	Analysis of Fmri Time-Series Revisited
32	39	348	1996	G. M. Boynton, S. A. Engel, et al.	Journal of Neuroscience,16,4207-4221	I	Linear systems analysis of functional magnetic resonance imaging in human V1
33	39	348	1996	D. Malonek and A. Grinvald	Science,272,551-554	I/A	Interactions between electrical activity and cortical microcirculation revealed by imaging spectroscopy: Implications...
34	38	384	1995	A. Karni, G. Meyer, et al.	Nature,377,155-158	A	Functional MRI Evidence for Adult Motor Cortex Plasticity During Motor Skill Learning
35	38	114	2002	M. Corbetta and G. L. Shulman	Nature Rev. Neuroscience,3,201-215	A	Control of goal-directed and stimulus-driven attention in the brain
36	38	455	1993	S. Ogawa, R. S. Menon, et al.	Biophysical Journal,64,803-812	I	Functional Brain Mapping by Blood Oxygenation Level-Dependent Contrast Magnetic-Resonance-Imaging...
37	38	303	1997	S. M. Courtney, B. G. Ungerleider, et al.	Nature,386,608-611	M/A	Transient and sustained activity in a distributed neural system for human working memory
38	37	185	2000	J. V. Haxby, E. A. Hoffman et al.	TICS,4,223-233	A	The distributed human neural system for face perception
39	37	443	1993	S. M. Rao, J. R. Binder, et al.	Neurology,43,2311-2318	A	Functional Magnetic-Resonance-Imaging of Complex Human Movements
40	37	368	1995	R. L. Buckner, S. E. Petersen, et al.	Journal of Neuroscience,15,12-29	A	Functional Anatomical Studies of Explicit and Implicit Memory Retrieval Tasks
41	37	365	1995	S. D. Forman, J. D. Cohen, et al.	MRM,33,636-647	M	Improved Assessment of Significant Activation in Functional Magnetic-Resonance-Imaging (fMRI) - Use of a Cluster-Size Threshold
42	36	181	2000	J. B. Hopfinger, M. H. Buonocore et al.	Nature Neuroscience,3,284-291	A	The neural mechanisms of top-down attentional control
43	36	253	1998	W. M. Kelley, F. M. Miezin, et al.	Neuron,20,927-936	A	Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding
44	36	249	1998	M. Corbetta, E. Akbudak, et al.	Neuron,21,761-773	A	A common network of functional areas for attention and eye movements
45	35	317	1996	S. M. Courtney, L. G. Ungerleider, et al.	Cerebral Cortex,6,39-49	A	Object and spatial visual working memory activate separate neural systems in human cortex
46	34	344	1995	J. B. Demb, J. E. Desmond, et al.	Journal of Neuroscience,15,5870-5878	A	Semantic Encoding and Retrieval in the Left Inferior Prefrontal Cortex - A Functional MRI Study of Task-Difficulty and Process Specificity
47	34	271	1997	A. M. Dale and R. L. Buckner	Human Brain Mapping,5,329-340	M	Selective averaging of rapidly presented individual trials using fMRI
48	34	203	1999	K. J. Friston, A. P. Holmes, et al.	Neuroimage,10,385-396	M	Multisubject fMRI studies and conjunction analyses
49	33	200	1999	M. Botvinick, L. E. Nystrom, et al.	Nature,402,179-181	A	Conflict monitoring versus selection-for-action in anterior cingulate cortex
50	33	231	1998	S. M. Courtney, L. Petit, et al.	Science,279,1347-1351	A	An area specialized for spatial working memory in human frontal cortex

Keywords "fMRI" or "functional MRI"

M = Methods, I = Interpretation, A= Applications

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