Neuronal Correlates of BOLD

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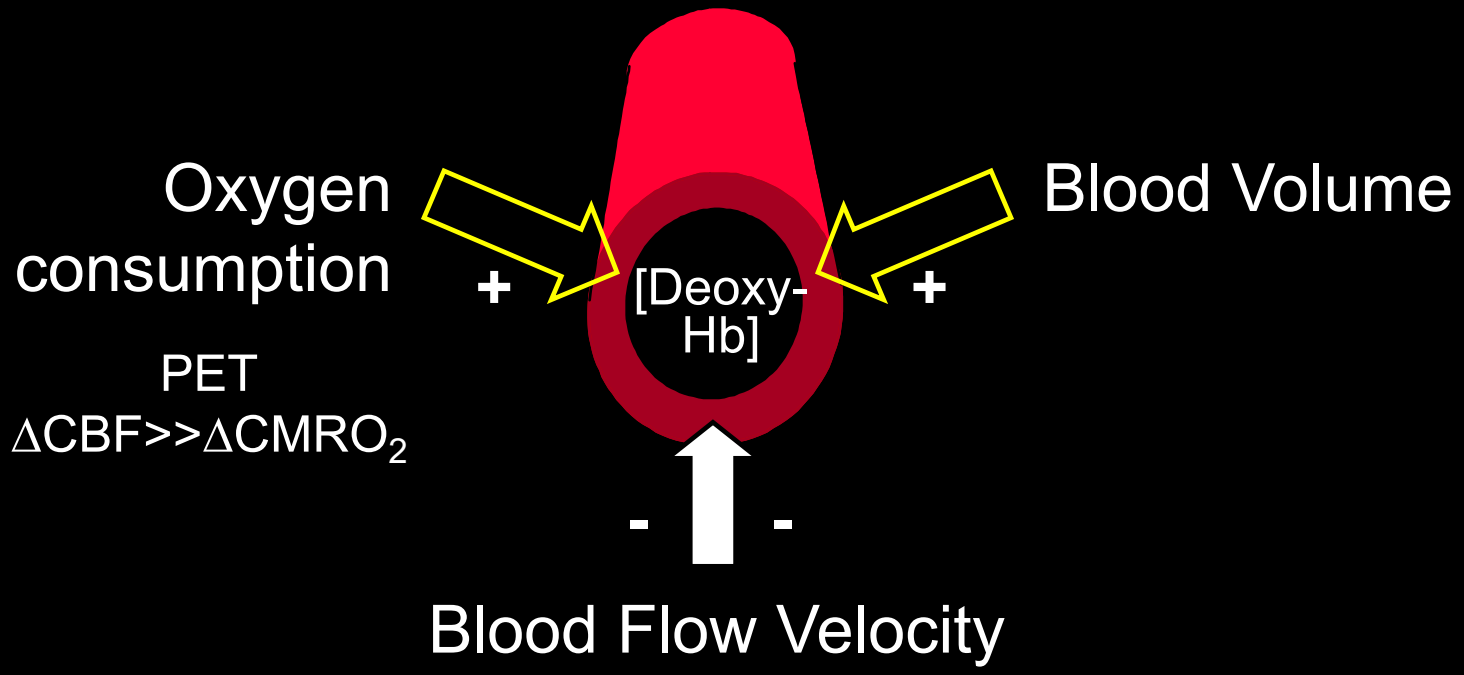
&
Functional MRI Facility

Laboratory of Brain and Cognition
National Institute of Mental Health

The vascular response

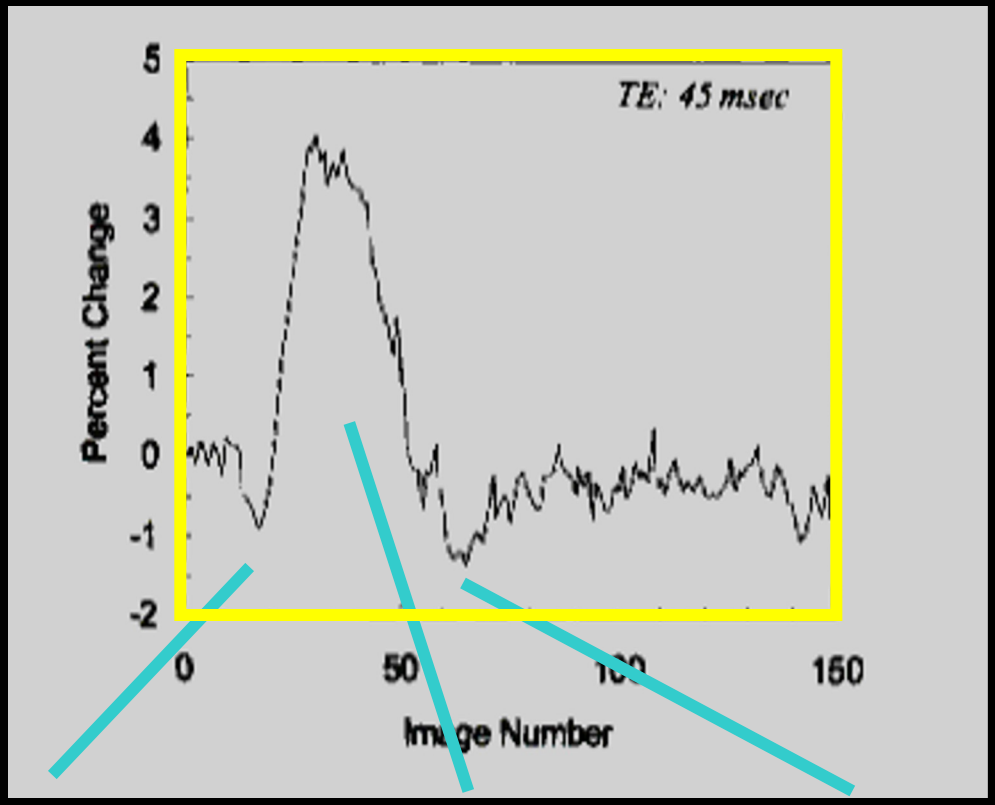
Factors influencing
[Deoxy-Hb] concentration



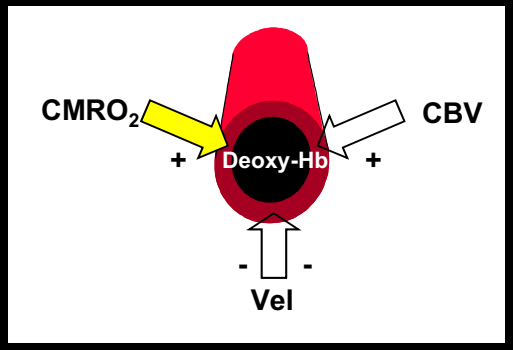
PET
$\Delta CBF >> \Delta CMRO_2$

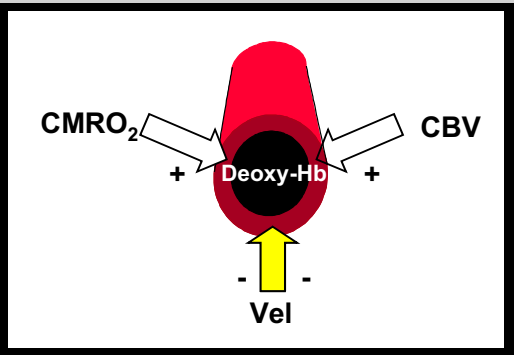
Courtesy of Arno Villringer

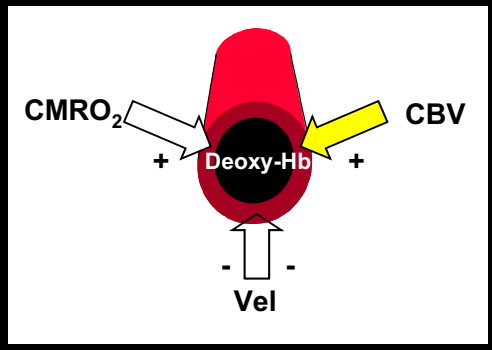
Time course of BOLD signal



Yacoub E, Le TH, Ugurbil K, Hu X (1999) Magn Res Med 41(3):436-41







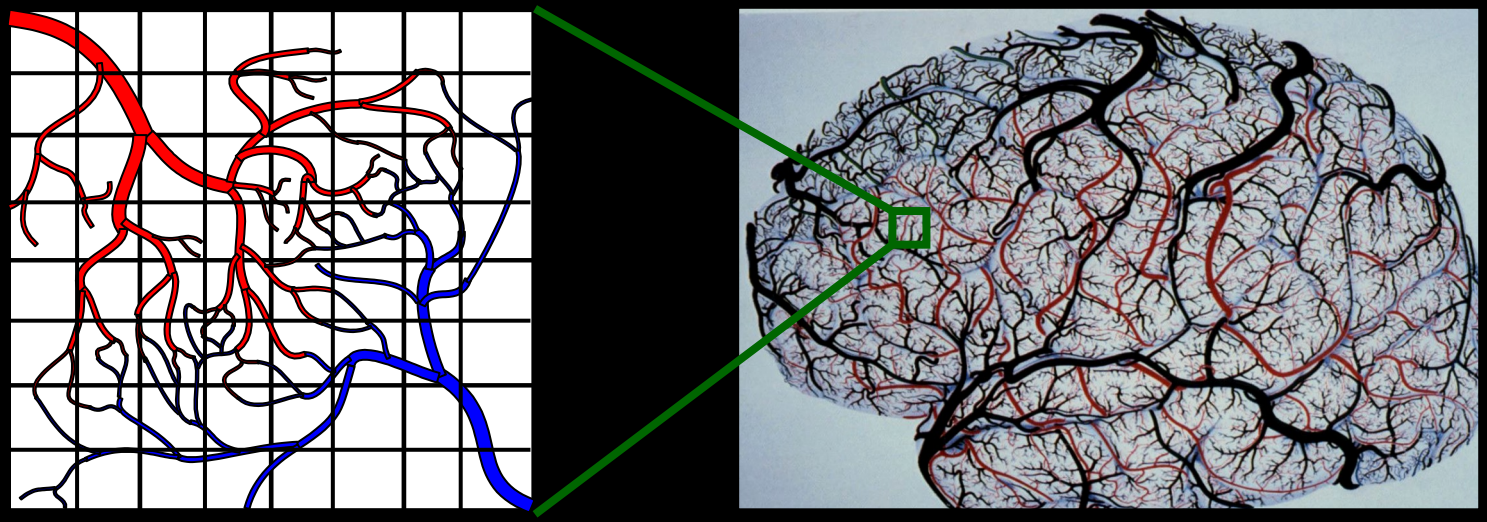
Courtesy of Arno Villringer

The Problem

Neuronal Activation ⇢ Measured Signal

Neuronal Activation → ? → Hemodynamics → ? → Measured Signal

Noise → ? → Measured Signal

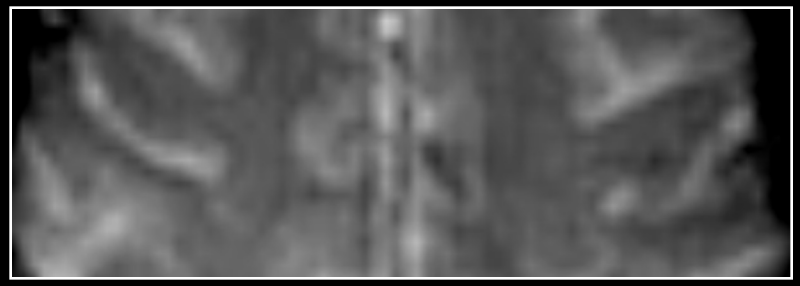


What we observe

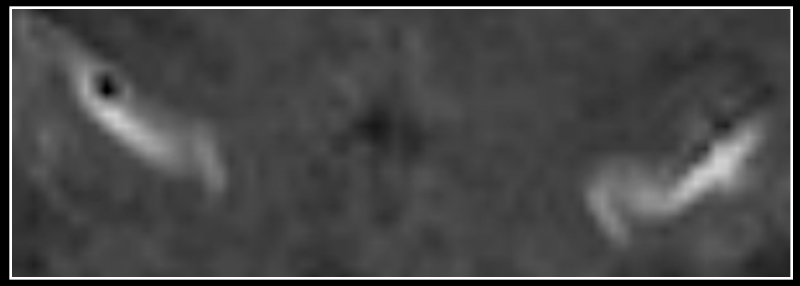
- Magnitude
- Location
- Parametric Manipulation
- Latency
- Fluctuations

Location

Anatomy

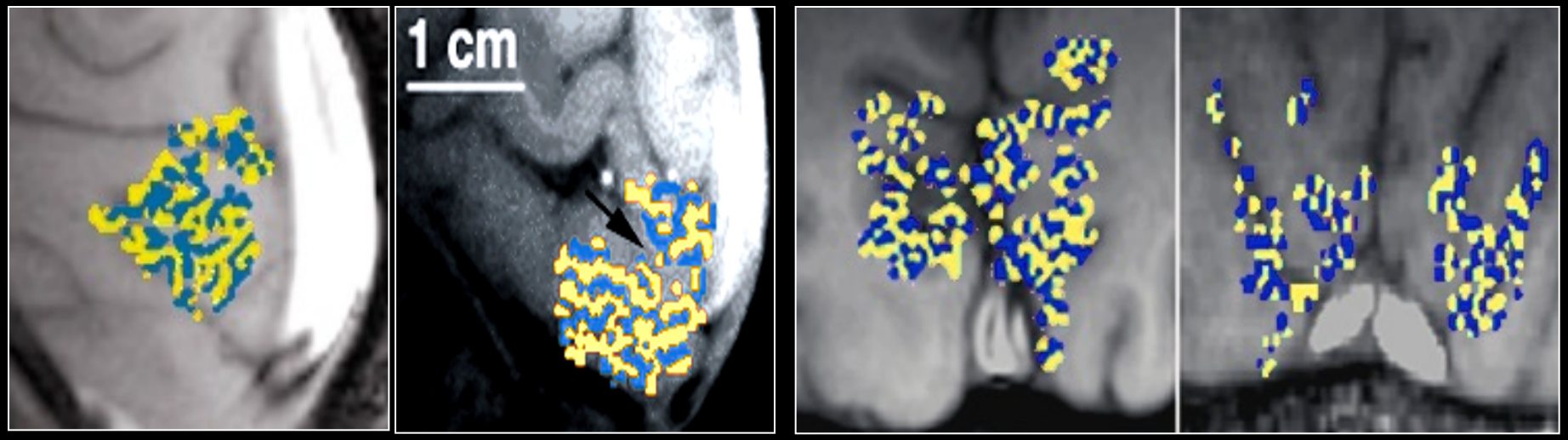


BOLD

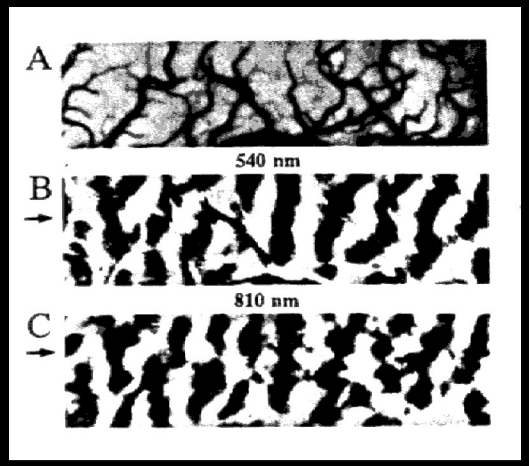


Perfusion

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).

The spatial extent of the BOLD response

Ziad S. Saad,[a,b,*] Kristina M. Ropella,[b] Edgar A. DeYoe,[c] and Peter A. Bandettini[a]

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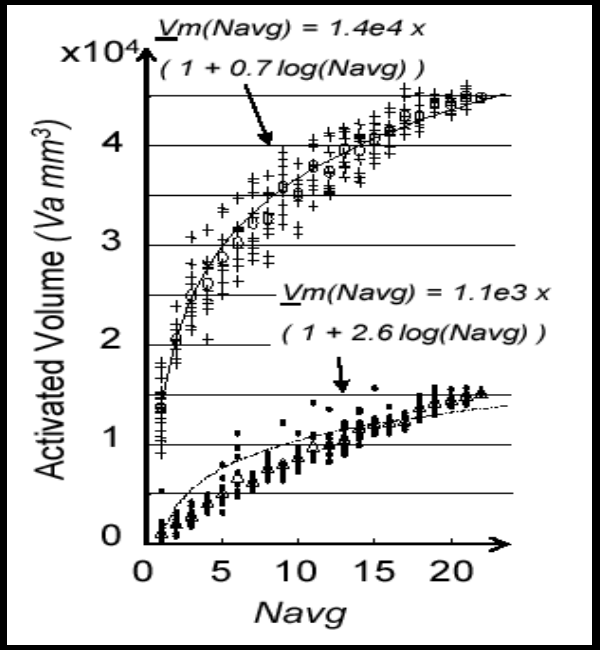
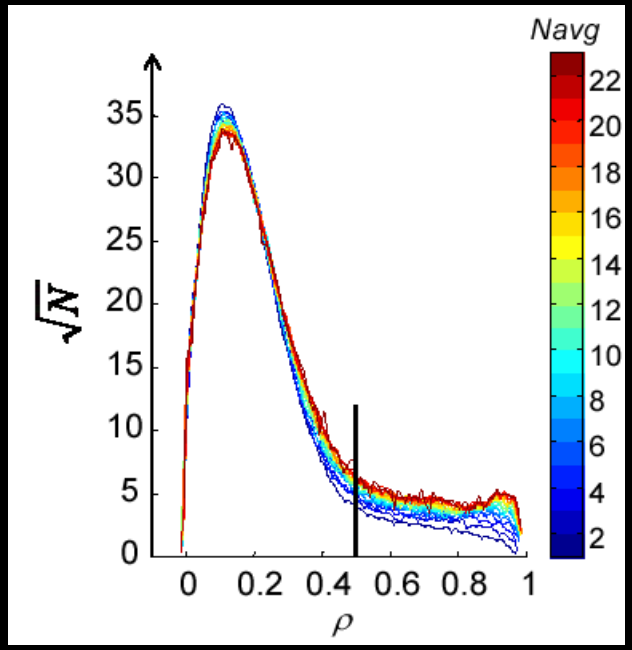
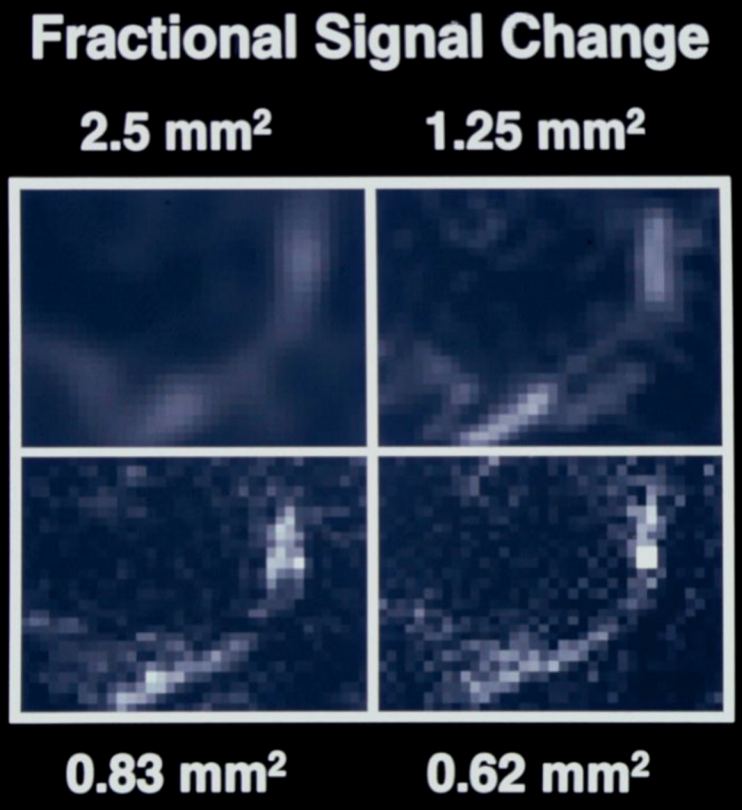
Received 16 August 2002; revised 29 October 2002; accepted 21 November 2002

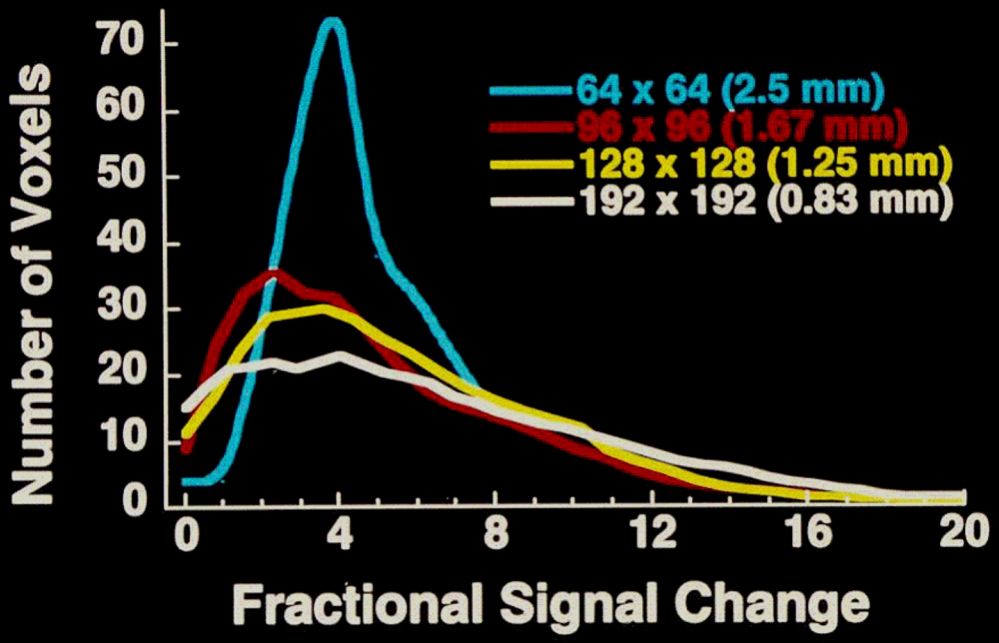
NeuroImage, **19:** 132-144, (2003).





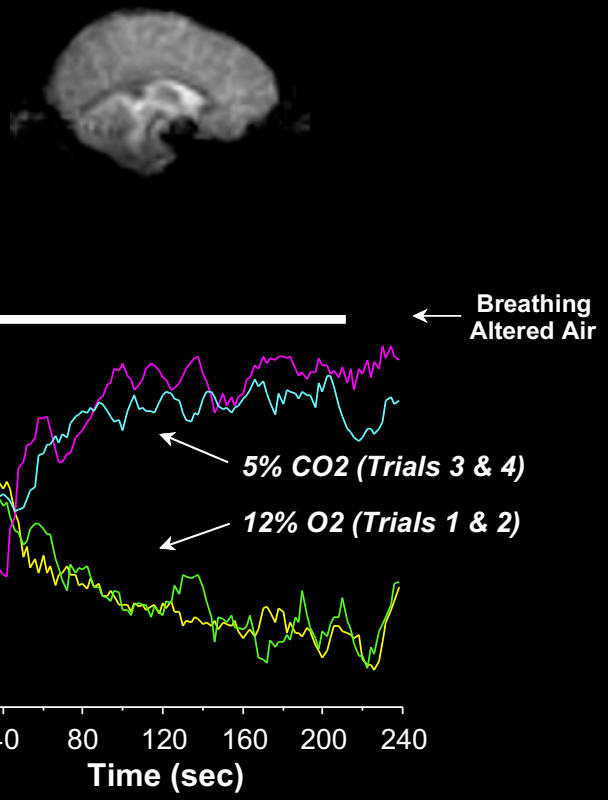
Magnitude

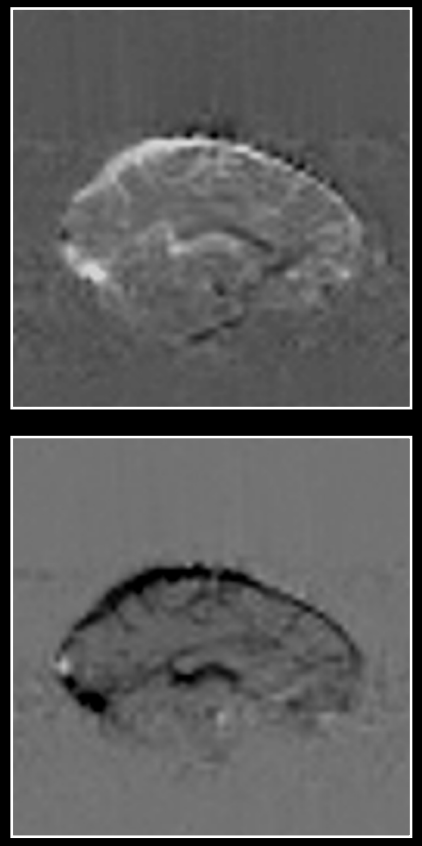




Jesmanowicz, P. A. Bandettini, J. S. Hyde, (1998) "Single shot half k-space high resolution EPI for fMRI at 3T." *Magn. Reson. Med.* 40, 754-762.

Hemodynamic Stress Calibration





P. A. Bandettini, E. C. Wong, A hypercapnia - based normalization method for improved spatial localization of human brain activation with fMRI. *NMR in Biomedicine* 10, 197-203 (1997).

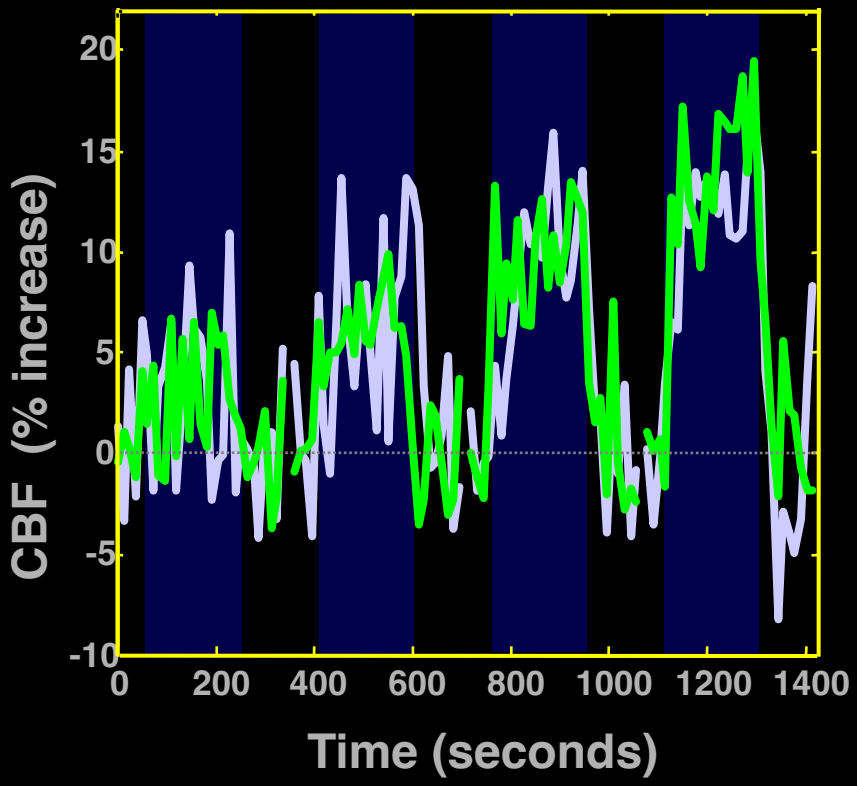
Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 9403–9408, August 1999
Neurobiology

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

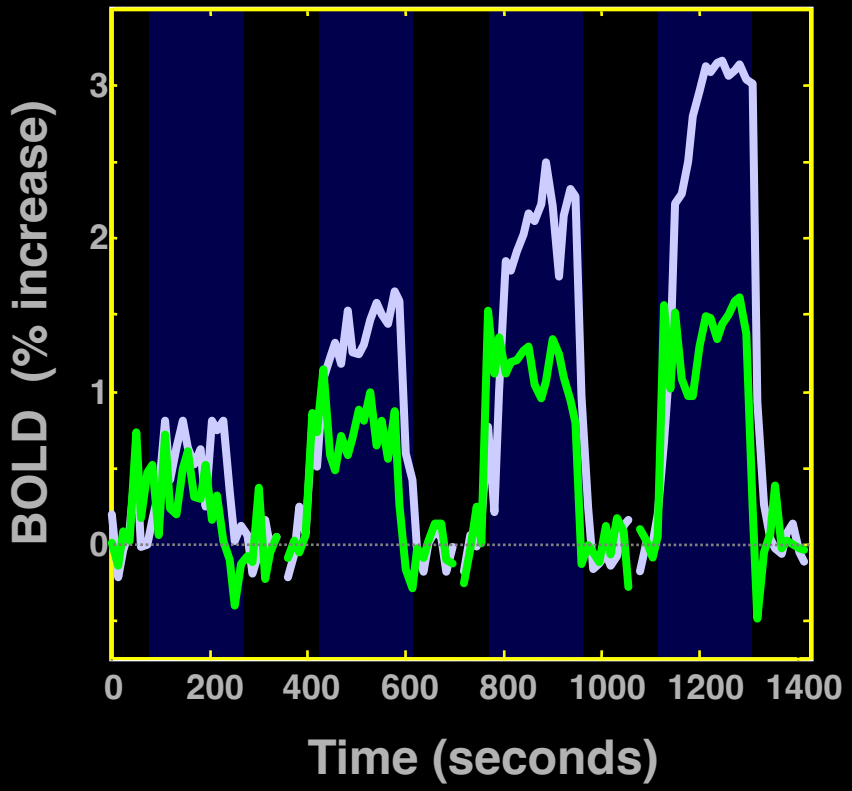
RICHARD D. HOGE*†, JEFF ATKINSON*, BRAD GILL*, GÉRARD R. CRELIER*, SEAN MARRETT‡, AND G. BRUCE PIKE*

*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



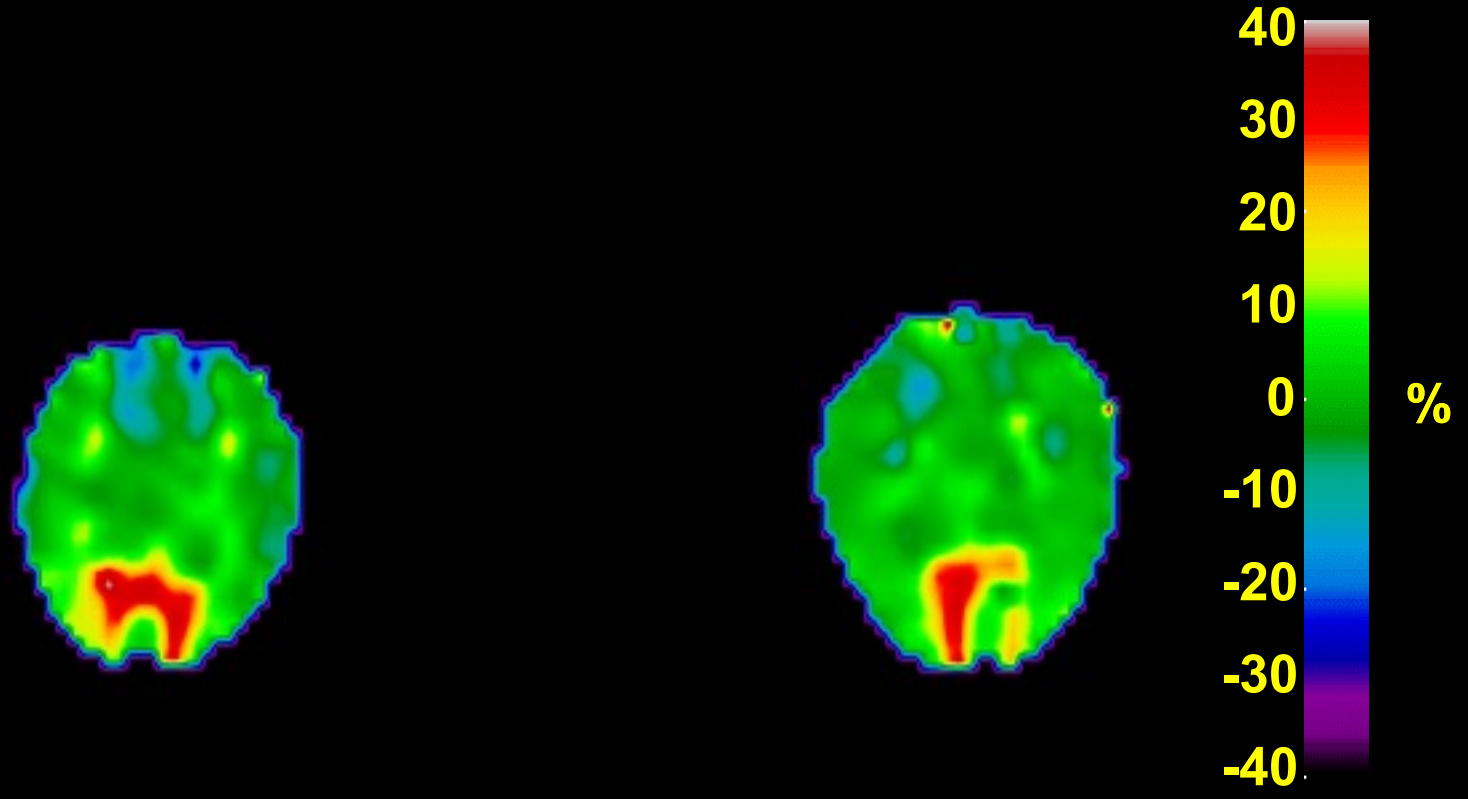
BOLD



Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

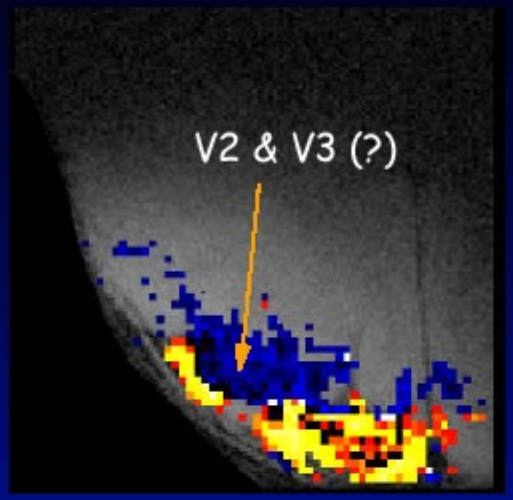
N=12

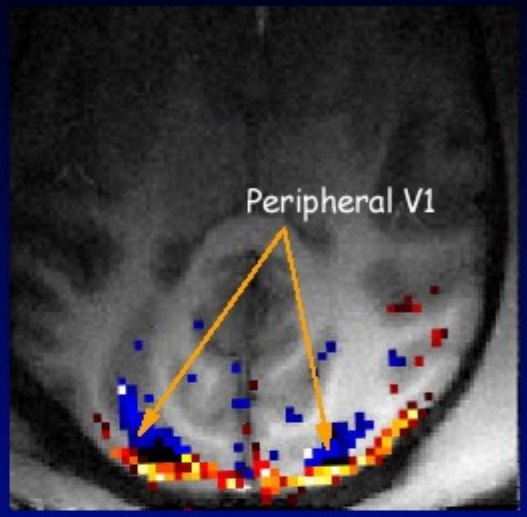
Computed $CMRO_2$ Changes

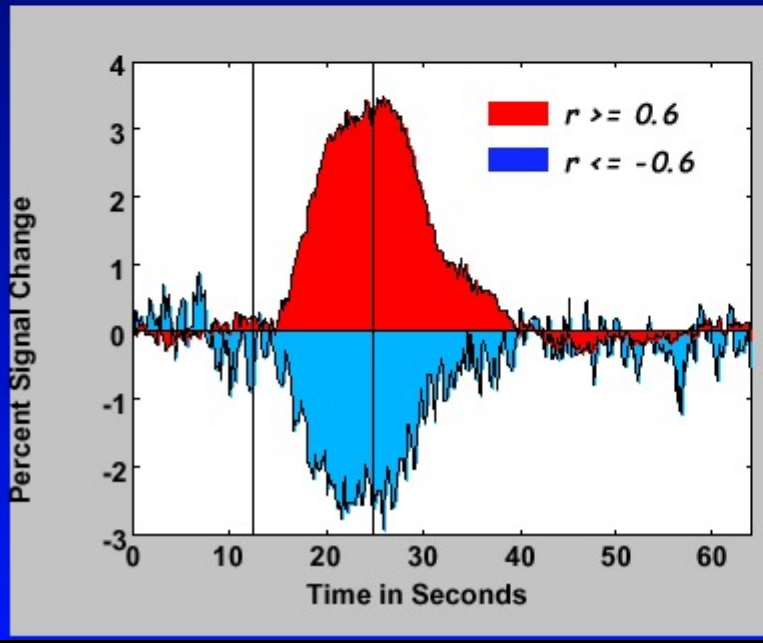


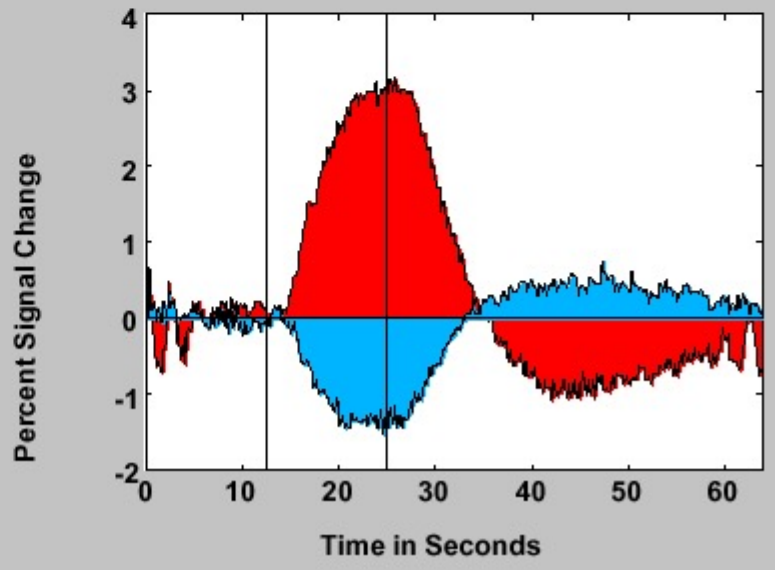
R. Hoge et al.

Negative BOLD effect





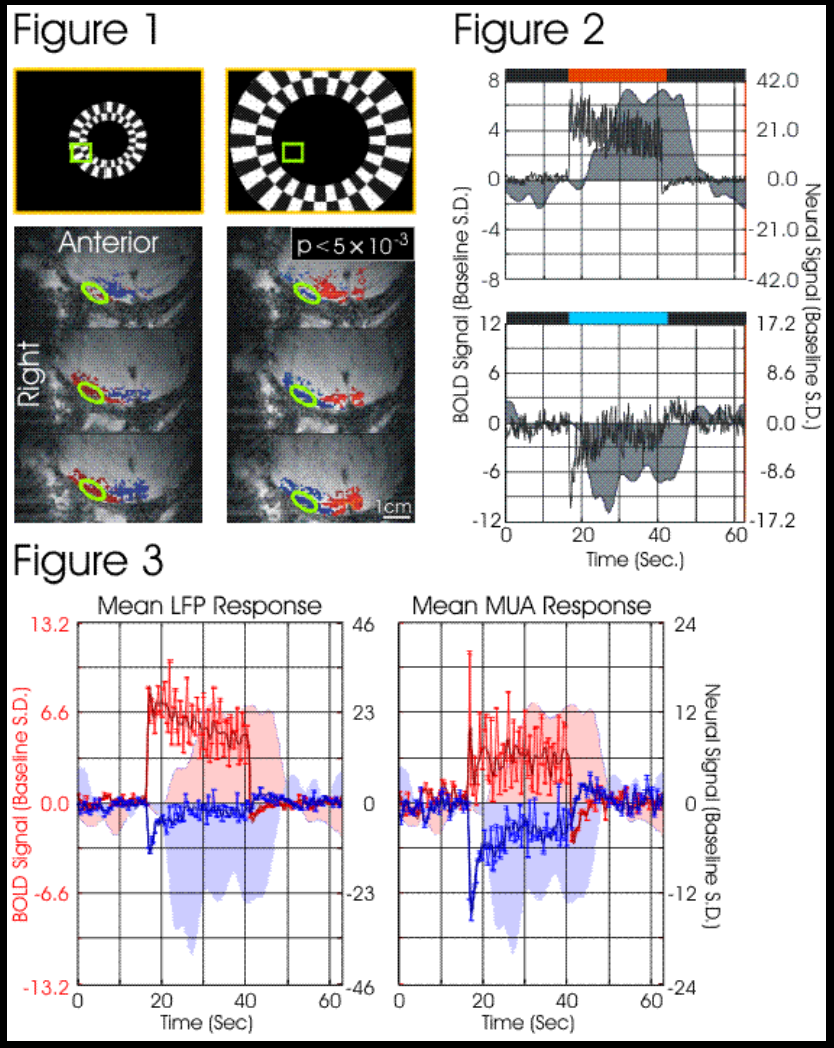




HBM 2003
Poster number: 308

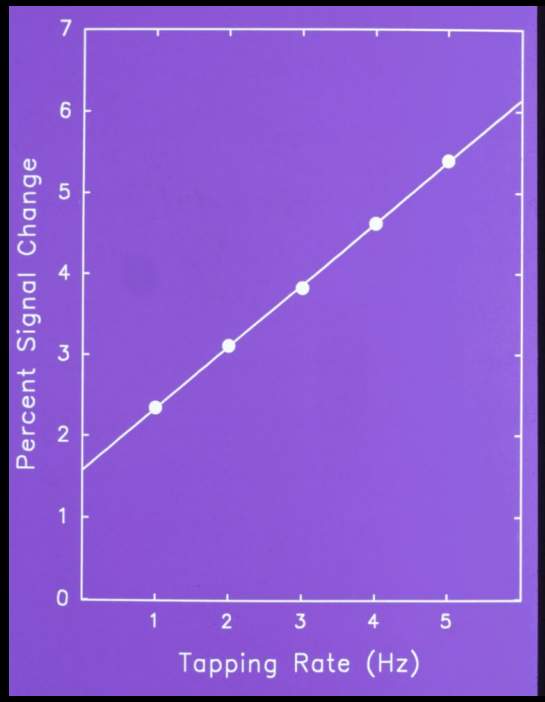
The Negative BOLD Response in Monkey V1 Is Associated with Decreases in Neuronal Activity

Amir Shmuel*†, Mark Augath, Axel Oeltermann, Jon Pauls, Yusuke Murayama, Nikos K. Logothetis



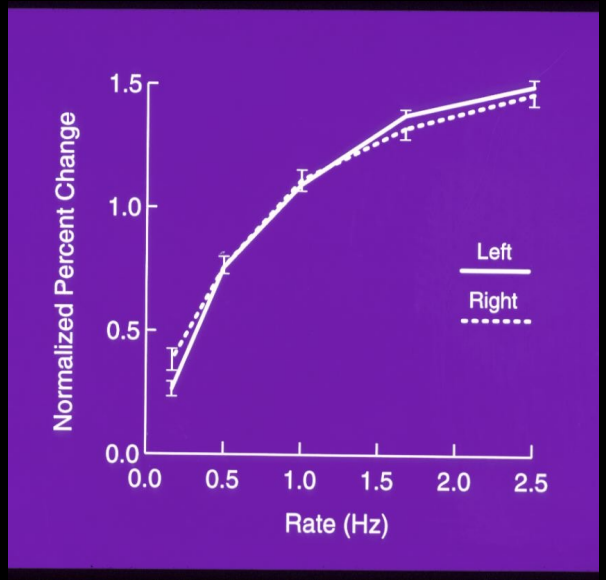
Parametric Manipulation

Motor Cortex



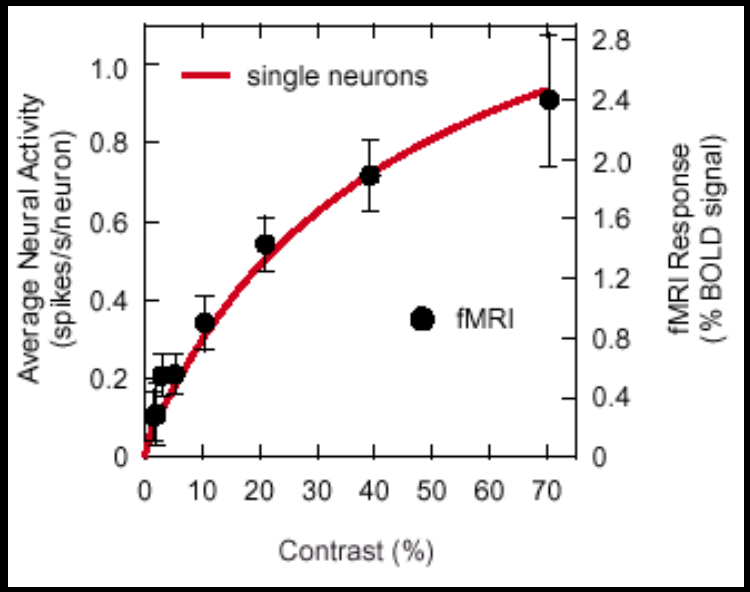
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

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

Magnetic Resonance in Medicine 41:469–473 (1999)

Simultaneous Recording of Evoked Potentials and T_2^*-Weighted MR Images During Somatosensory Stimulation of Rat

Gerrit Brinker, Christian Bock, Elmar Busch, Henning Krep, Konstantin-Alexander Hossmann, and Mathias Hoehn-Berlage

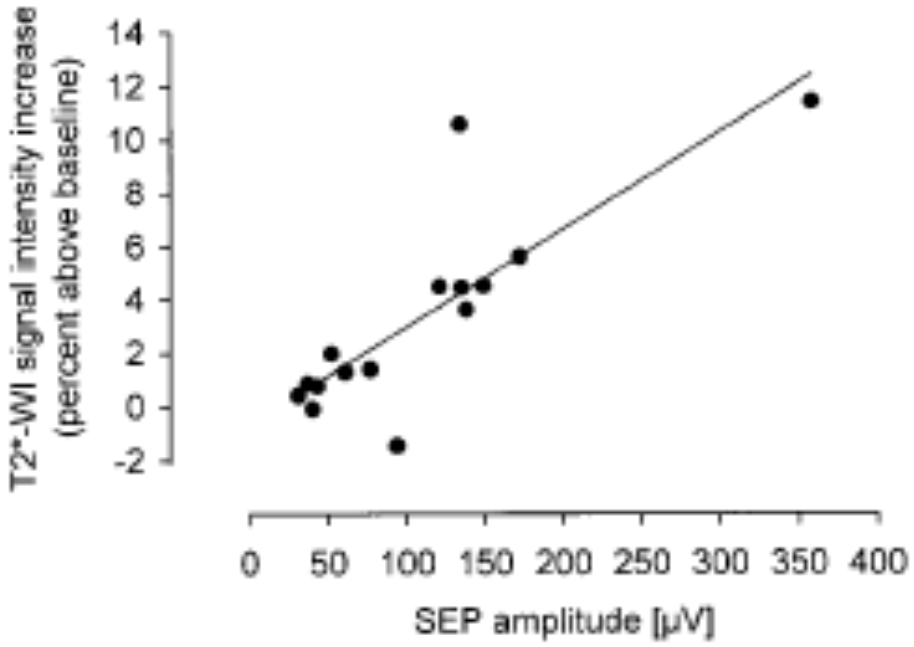


FIG. 3. Correlation of the increase of T_2^*-weighted imaging signal intensity with the peak-to-peak amplitude of the somatosensory evoked potential (SEP) during forepaw stimulation at increasing frequencies (data are from one individual animal; $r = 0.82$).

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[§]

[†]Bell Laboratories, Lucent Technologies, Murray Hill, NJ 07974; and [§]Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455

11026–11031 PNAS **September 26, 2000** vol. 97 no. 20

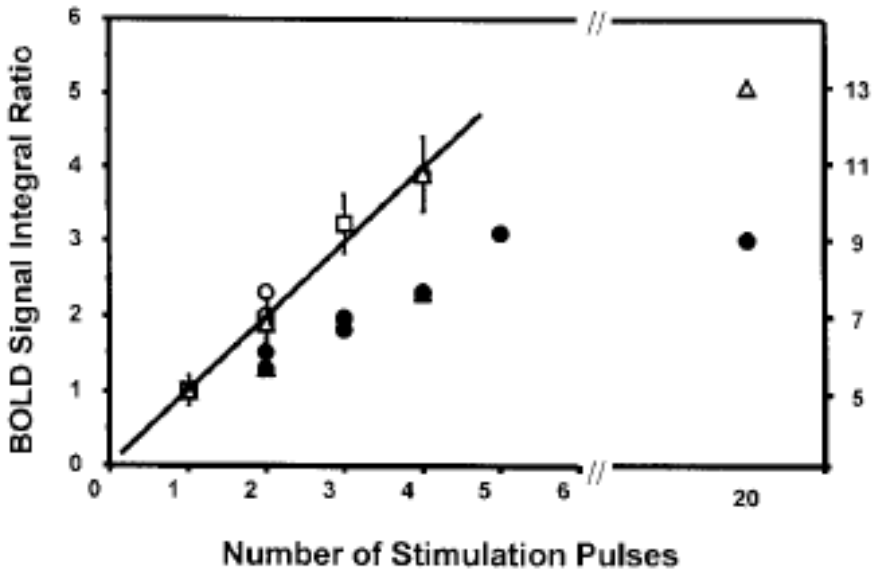


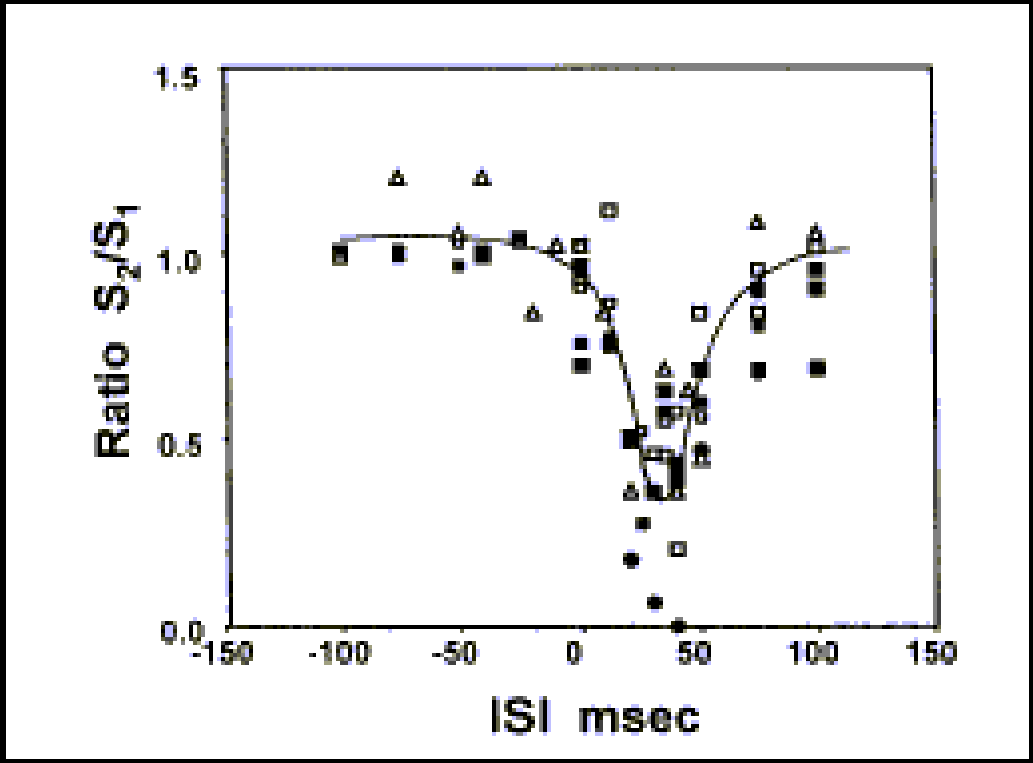
Fig. 2. BOLD responses to a number of stimulation pulses (Paradigm I) given to the rat forepaw. BOLD signal integrals (height times width at half height) relative to the signal by single stimulus (300-μsec-wide current pulse at 0.4 to 0.8 mA) are plotted as a function of the number of stimuli administered. The open symbols are those measured with 620 msec ISI. The error bars indicate the possible ranges of the uncertainty in estimating the normalized values of BOLD signal changes (four rats). The filled symbols are those with 310 msec ISI (two rats).

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

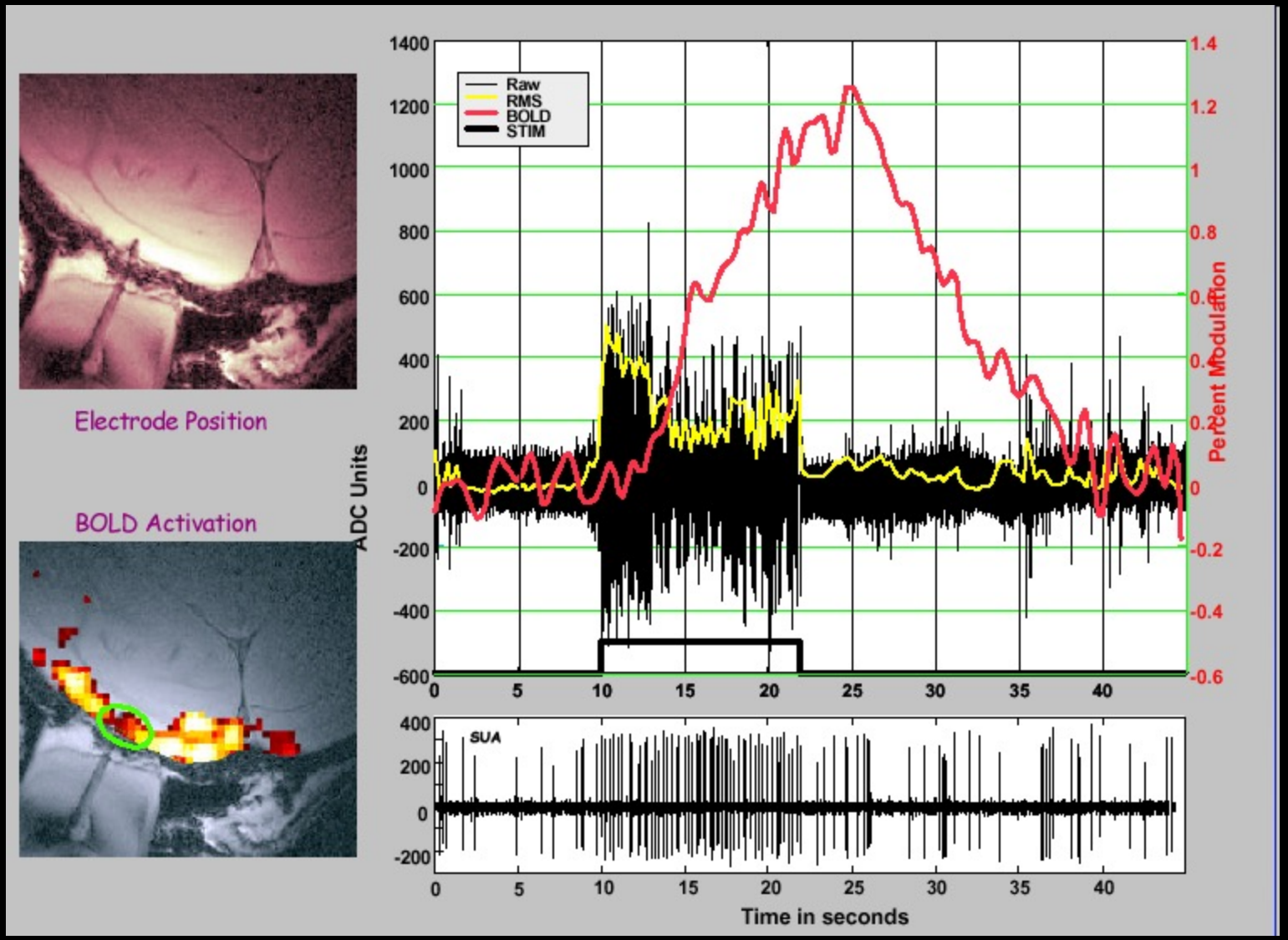
Seiji Ogawa[†‡], Tso-Ming Lee[†], Ray Stepnoski[†], Wei Chen[§], Xiao-Hong Zhu[§], and Kamil Ugurbil[§]

[†]Bell Laboratories, Lucent Technologies, Murray Hill, NJ 07974; and [§]Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN 55455

11026–11031 PNAS **September 26, 2000** vol. 97 no. 20



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



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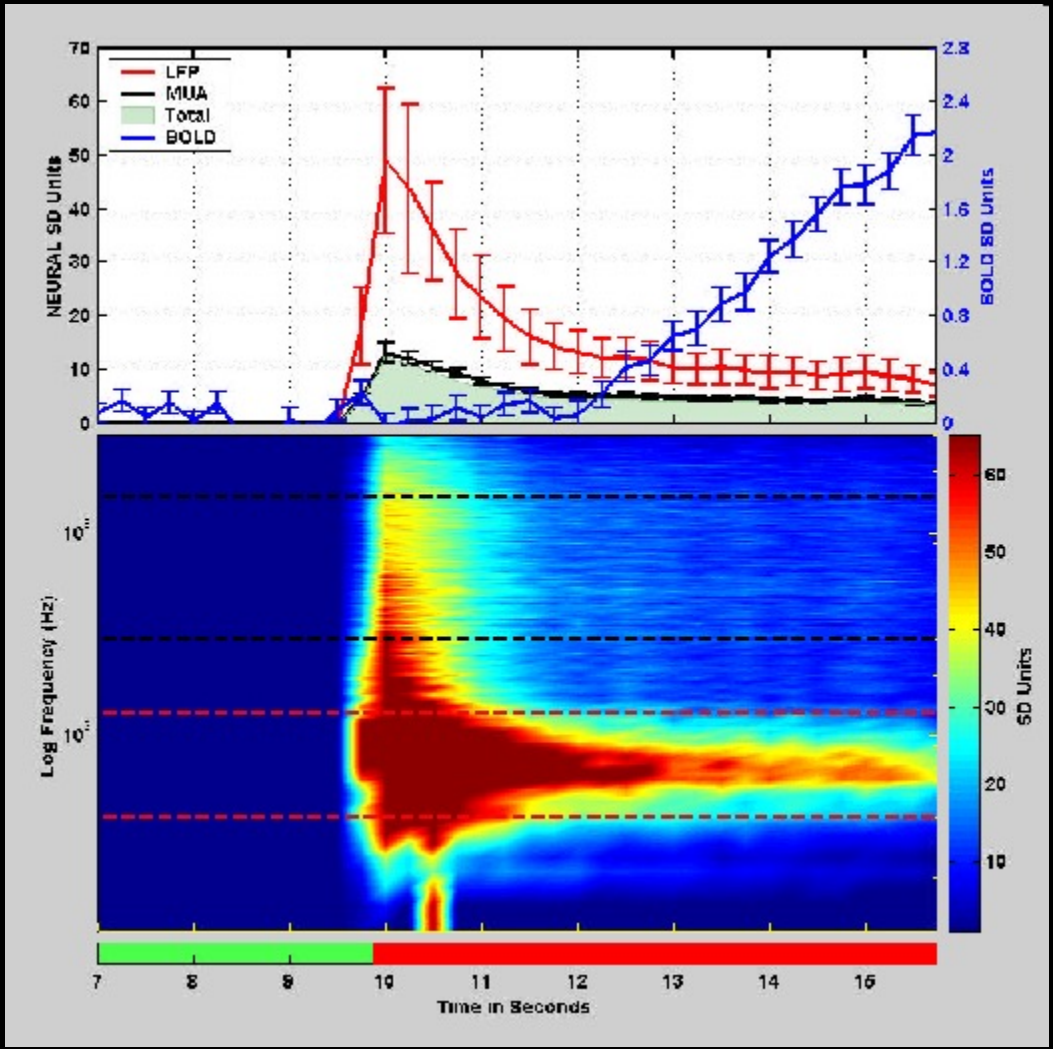


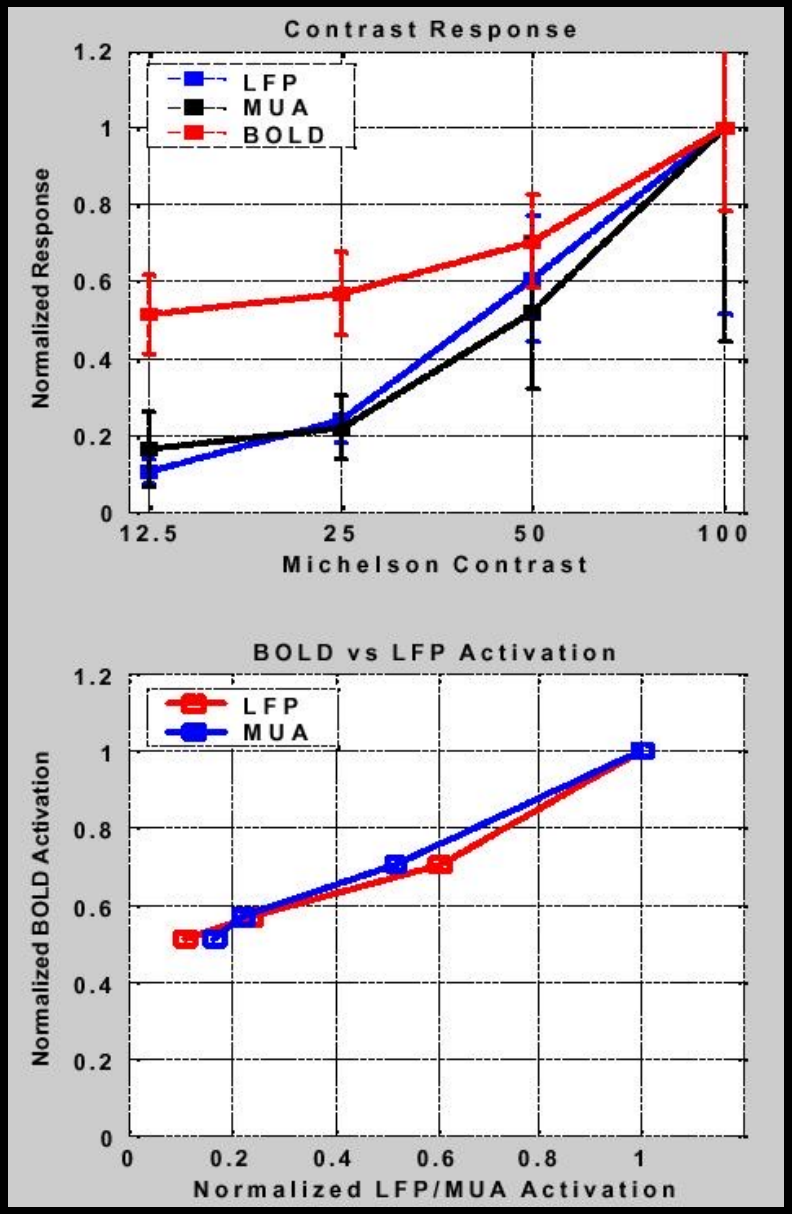
The Journal of Neuroscience, May 15, 2003 • 23(10):3963–3971 • 3963

The Underpinnings of the BOLD Functional Magnetic Resonance Imaging Signal

Nikos K. Logothetis
Max Planck Institute for Biological Cybernetics, 72076 Tuebingen, Germany

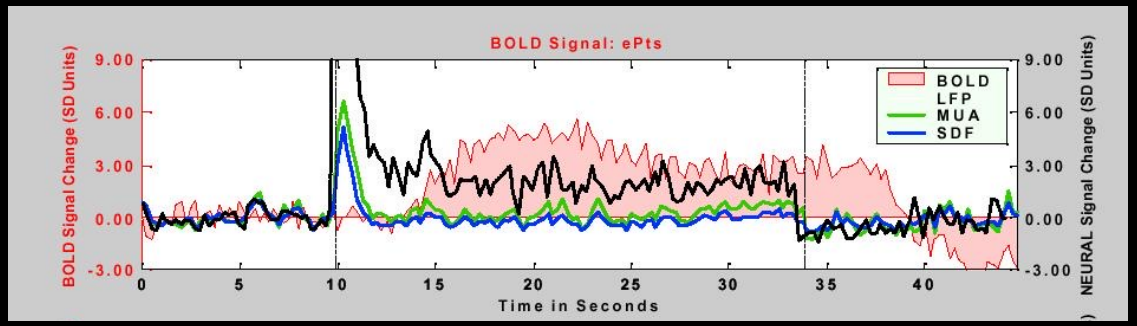
In summary, MUA mostly represents the spiking of neurons, with single-unit recordings mainly reporting on the activity of the projection neurons that form the exclusive output of a cortical area. LFPs, on the other hand, represent slow waveforms, including synaptic potentials, afterpotentials of somatodendritic spikes, and voltage-gated membrane oscillations, that reflect the input of a given cortical areas as well as its local intracortical processing, including the activity of excitatory and inhibitory interneurons.

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

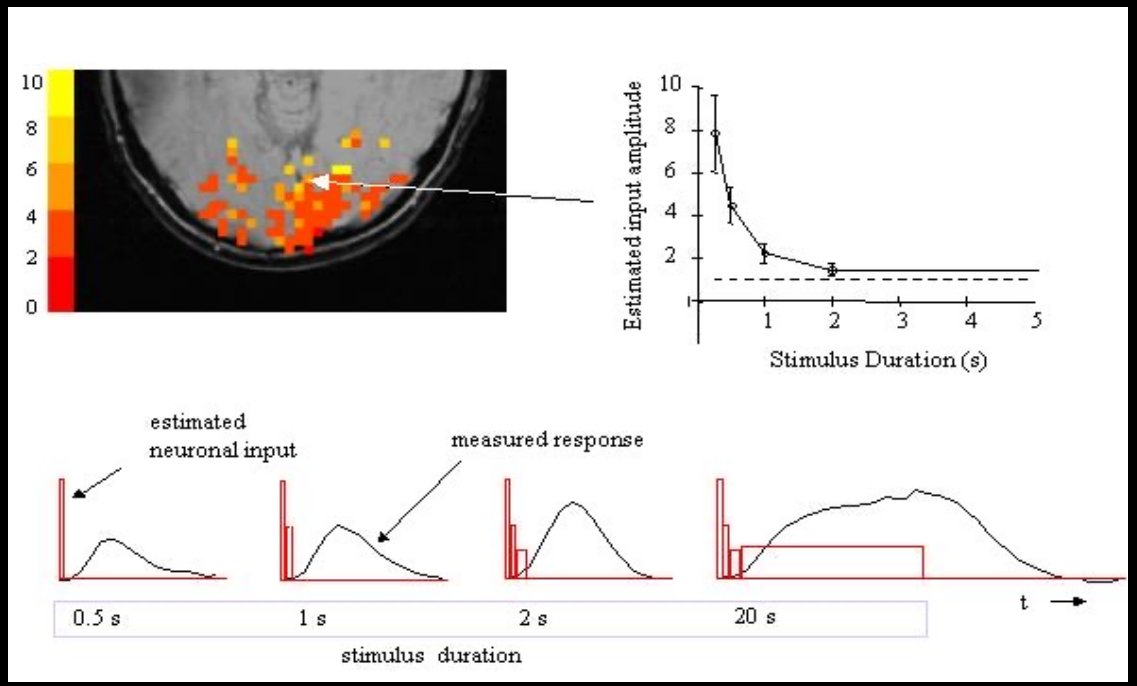


BOLD Correlation with Neuronal Activity

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.



Evidence that inhibitory input produces increased blood flow

Journal of Physiology (1998), 512.2, pp.555–566

Modification of activity-dependent increases of cerebral blood flow by excitatory synaptic activity and spikes in rat cerebellar cortex

Claus Mathiesen*†, Kirsten Caesar*, Nuran Akgören* and Martin Lauritzen*‡

**Department of Medical Physiology, The Panum Institute, University of Copenhagen, †NeuroSearch A/S, Glostrup and ‡Department of Clinical Neurophysiology, Glostrup Hospital, Denmark*

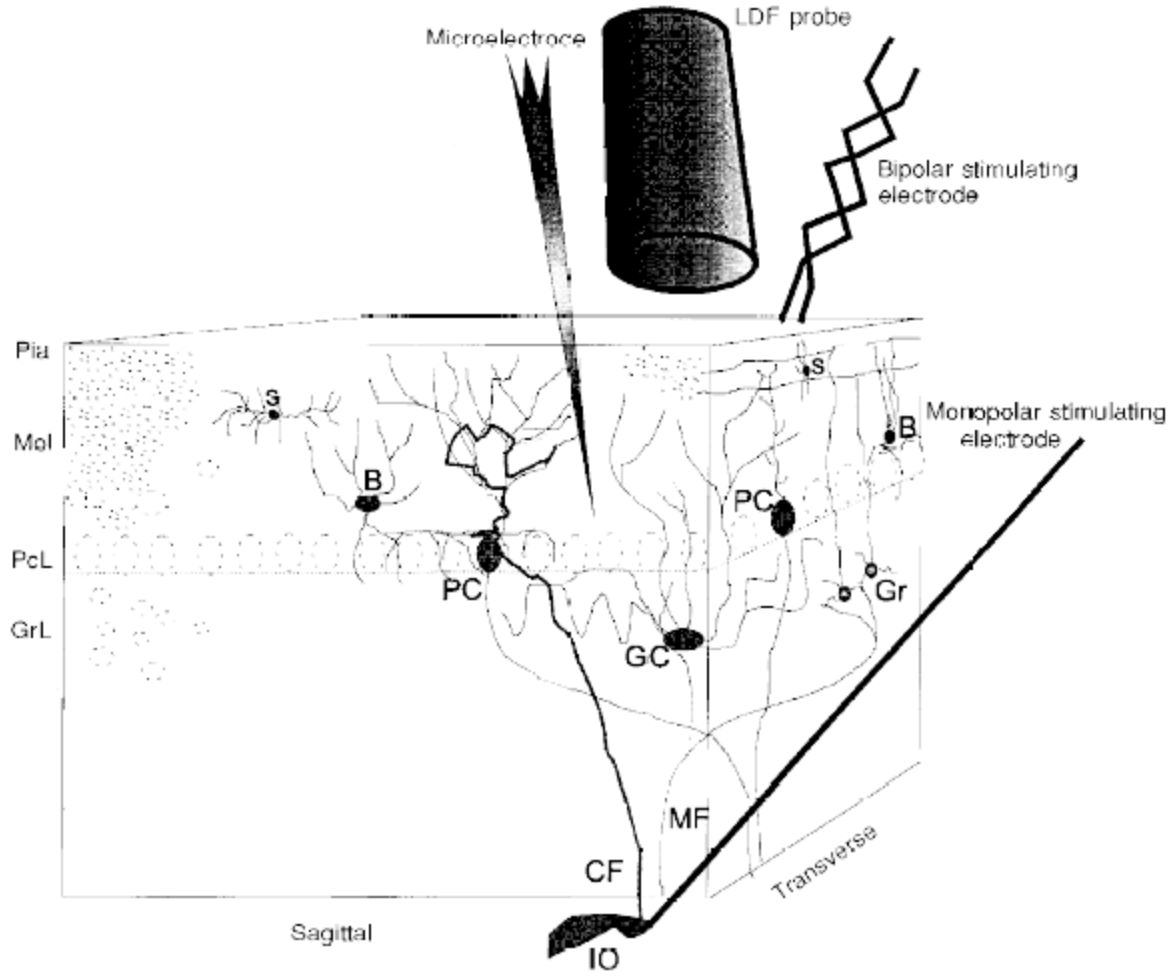
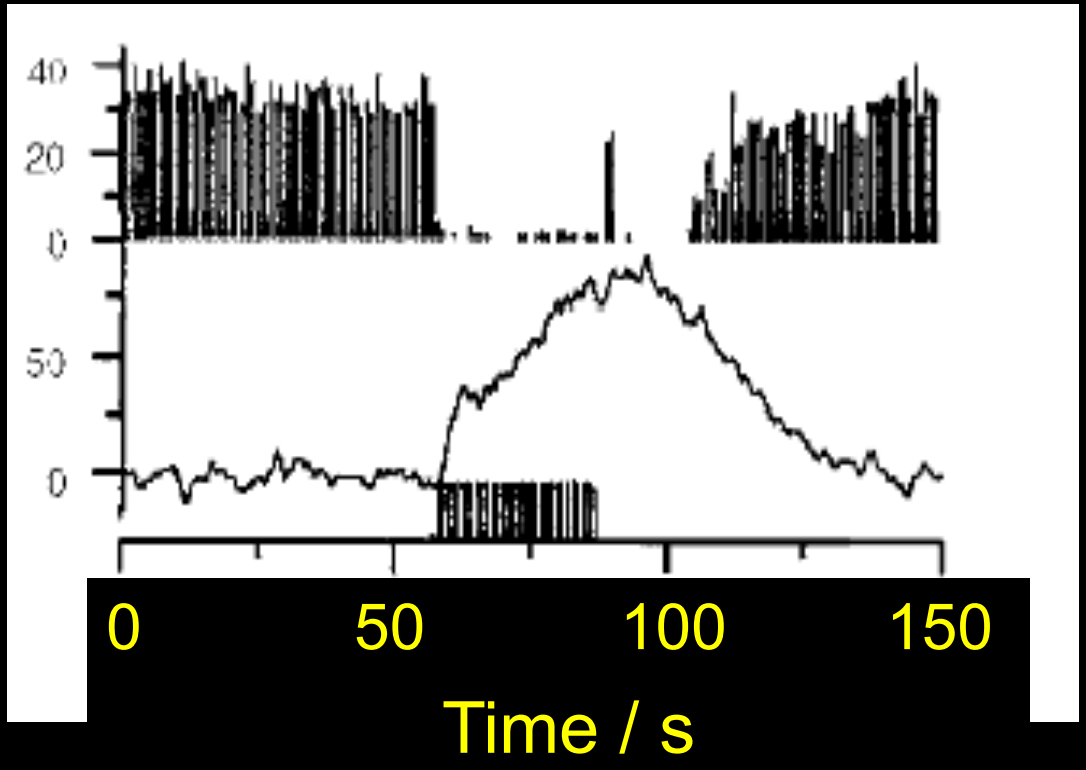


Figure 1. Schematic three-dimensional drawing of experimental set-up, including neurones of interest and position of laser Doppler probe, stimulating and recording electrodes

The positions of the three cerebellar layers, molecular (Mol, with a thickness of 400 μm), Purkinje cell (PcL, about 100 μm) and granular (GrL, 400–500 μm), are indicated. The molecular layer contains granule cell axons, called parallel fibres, the dendrites of Purkinje cells, stellate cells (S) and basket cells (B). The granule cell layer contains granule cells (Gr) and Golgi cells (GC). The superficial parallel fibres were stimulated by a bipolar stimulating electrode, while climbing fibres (CF) were stimulated by a monopolar electrode lowered into the caudal part of the inferior olive (IO). Field potentials and single unit spike activity were recorded with a glass microelectrode. CBF was recorded by a laser Doppler flowmetry (LDF) probe located 0·3–0·5 mm above the pial surface (Pia).

Divergence of spike rate and blood flow during parallel fiber stimulation



Mathiesen, Caesar, Akgören, Lauritzen (1998), J Physiol 512.2:555-566

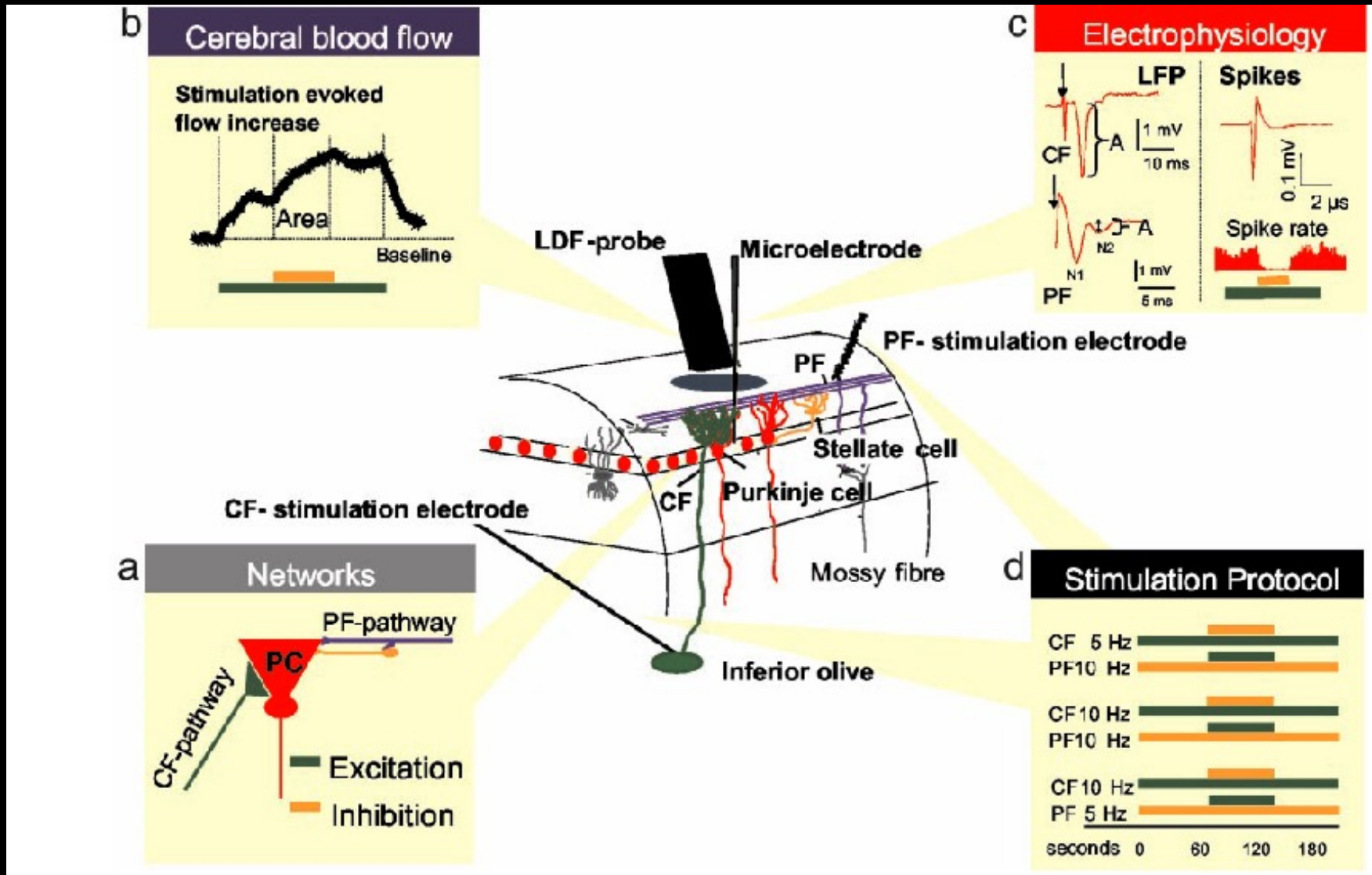
It gets more complicated...

Context sensitivity of activity-dependent increases in cerebral blood flow

Kirsten Caesar*, Lorenz Gold*, and Martin Lauritzen*†‡

*Department of Medical Physiology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, 2000 Copenhagen N, Denmark; and †Department of Clinical Neurophysiology, Glostrup Hospital, 2600 Glostrup, Denmark

PNAS | **April 1, 2003** | vol. 100 | no. 7 | **4239–4244**


b
Cerebral blood flow
Stimulation evoked flow increase
Area
Baseline
c
Electrophysiology
LFP
Spikes
CF
A
1 mV
10 ms
0.1 mV
2 µs
Spike rate
N2
N1
PF
5 ms
LDF-probe
Microelectrode
PF- stimulation electrode
PF
Stellate cell
CF
Purkinje cell
CF- stimulation electrode
Mossy fibre
Inferior olive
a
Networks
PF-pathway
PC
CF-pathway
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d
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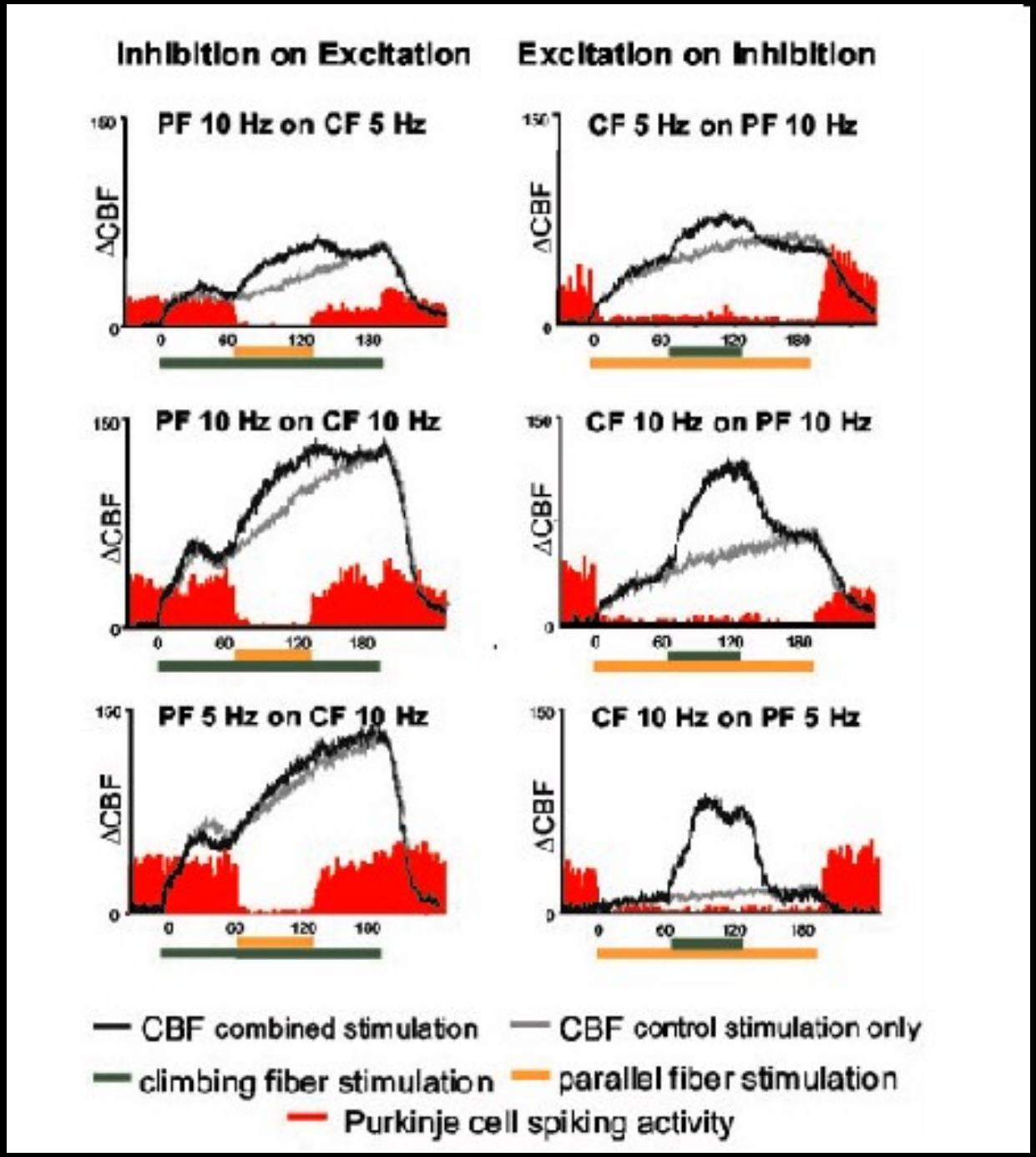
PF10 Hz
CF10 Hz
PF10 Hz
CF10 Hz
PF 5 Hz
seconds 0 60 120 180


Inhibition on Excitation
Excitation on Inhibition
PF 10 Hz on CF 5 Hz
CF 5 Hz on PF 10 Hz
PF 10 Hz on CF 10 Hz
CF 10 Hz on PF 10 Hz
PF 5 Hz on CF 10 Hz
CF 10 Hz on PF 5 Hz
ΔCBF
CBF combined stimulation
CBF control stimulation only
climbing fiber stimulation
parallel fiber stimulation
Purkinje cell spiking activity

?!

NEUROIMAGE **6**, 270–278 (1997)
ARTICLE NO. NI970300

Characterizing the Relationship between BOLD Contrast and Regional Cerebral Blood Flow Measurements by Varying the Stimulus Presentation Rate

Geraint Rees, A. Howseman, O. Josephs, C. D. Frith, K. J. Friston, R. S. J. Frackowiak, and R. Turner

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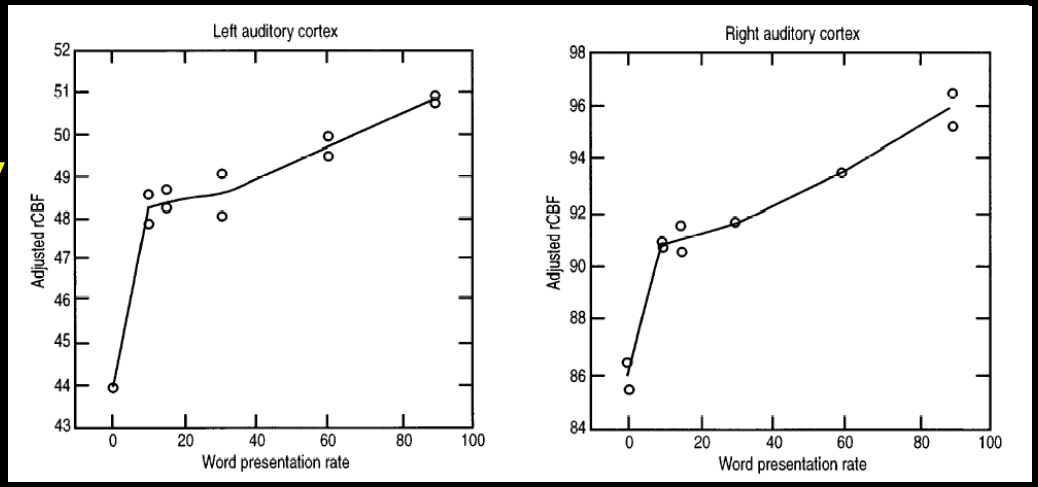
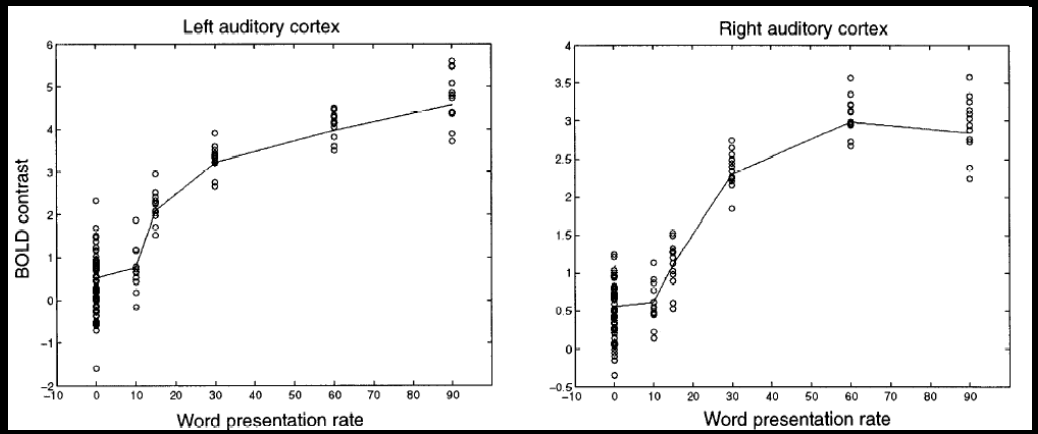
Flow modulation is not necessarily the same as BOLD modulation





Mediators of neurovascular coupling

There is **not just one** coupling mechanism.

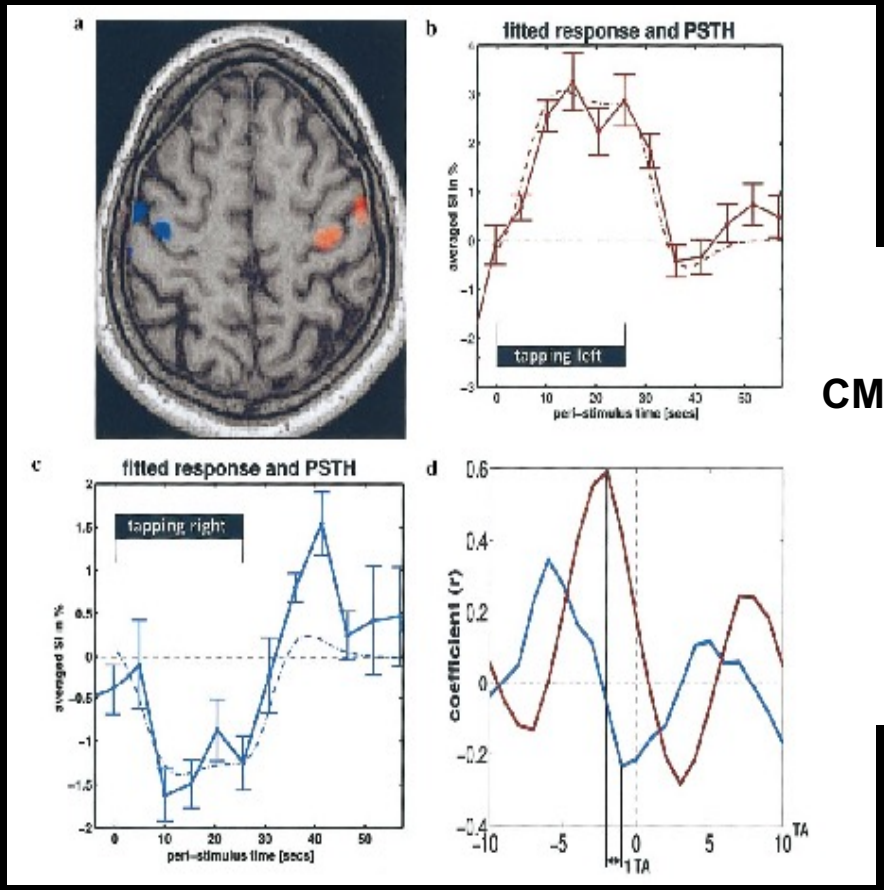
NO is a mediator in the cerebellar cortex, but only a permissive factor in the somatosensory cortex

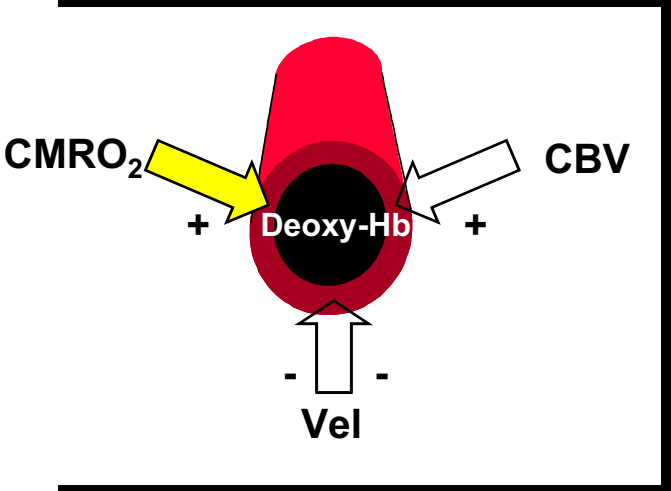
Astrocytes may link synaptic activity to vascular response via Glutamate-induced Ca elevation and release of vasodilators at perivascular endfeets

Metabolic factors (adenosine, pH, lactate, CO_2) may act posthoc for finer long-term adjustment (not much relevance for BOLD!?)

Courtesy of Arno Villringer

Negative BOLD in carotid artery disease

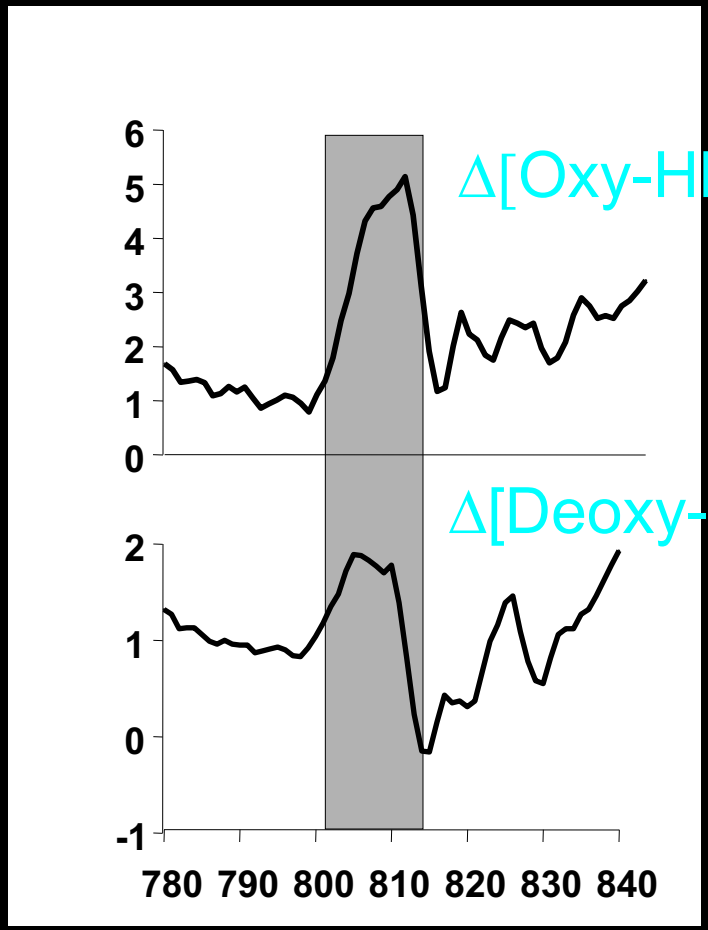


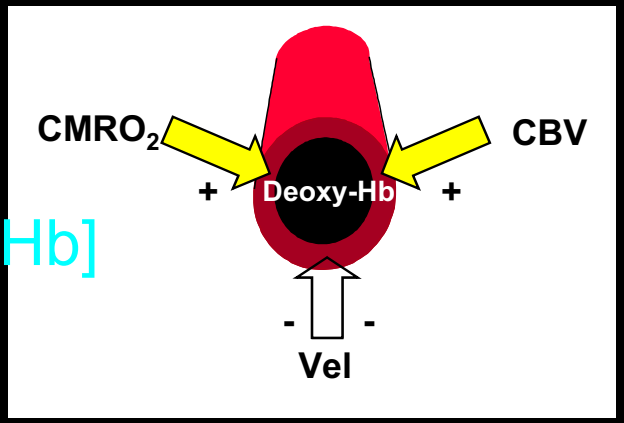


Röther et al. NeuroImage 2002

Courtesy of Arno Villringer

Increase in deoxy-Hb and oxy-Hb during focal seizure





Courtesy of Arno Villringer

Altered neurovascular coupling: Pathology, drugs

Pathologic state / Drug	**Reference**
Carotid occlusion	Röther et al. 2002
Transient global ischemia	Schmitz et al. 1998
Penumbra of cerebral ischemia	Mies et al. 1993, Wolf et al. 1997
Subarachnoid hemorrhage	Dreier et al. 2000
Trauma	Richards et al. 2001
Epilepsy	Fink et al. 1996, Brühl et al. 1998, von Pannwitz et al. 2002
Alzheimer´s disease	Hock et al. 1996, Niwa et al. 2000
Theophylline	Ko et al. 1990, Dirnagl et al. 1994
Scopolamine	Tsukada et al. 1998

Courtesy of Arno Villringer

BOLD correlates with de-synchronization of MEG signal ...

NeuroImage **16,** 103–114 (2002)
doi:10.1006/nimg.2001.1050, available online at http://www.idealibrary.com on IDEAL®

Task-Related Changes in Cortical Synchronization Are Spatially Coincident with the Hemodynamic Response

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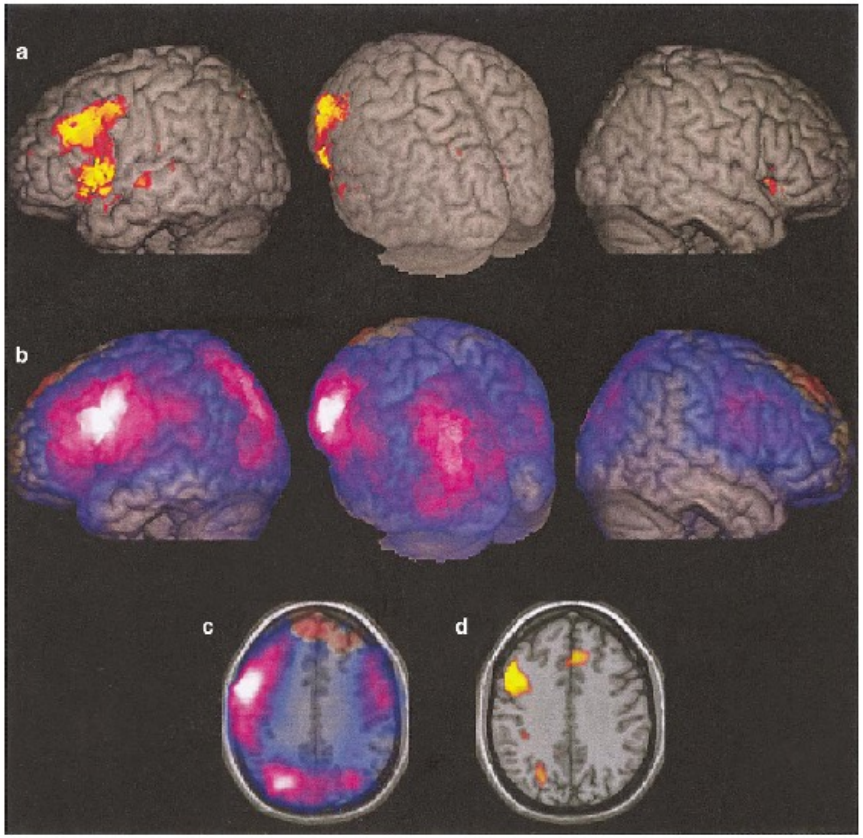


FIG. 2. The results of the group fMRI experiment and the group MEG experiment for the letter fluency task, superimposed on a template brain. The color scales are as described in the legend of Fig. 1. (a) Group fMRI data. Only those clusters significant at $P < 0.05$ (corrected) are shown. (b) The peak group SAM image. This shows the peak power increase or decrease at each voxel in the brain, irrespective of which frequency band the power change occurred in. This image can be thought of as an amalgam of Figs. 1b to 1f. (c) The peak group SAM data superimposed on a slice through the template brain at an MNI Z coordinate of +36. The image shows bilateral, but strongly left biased, activation within the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex. (d) The group fMRI data superimposed on the $Z = +36$ slice. Note the left DLPFC and left posterior parietal activation which match the group SAM results. However, there is also a small cluster in a more anterior portion of the parietal lobe, and another in the medial frontal gyri, which are visible in the group fMRI data but not in the group MEG data.

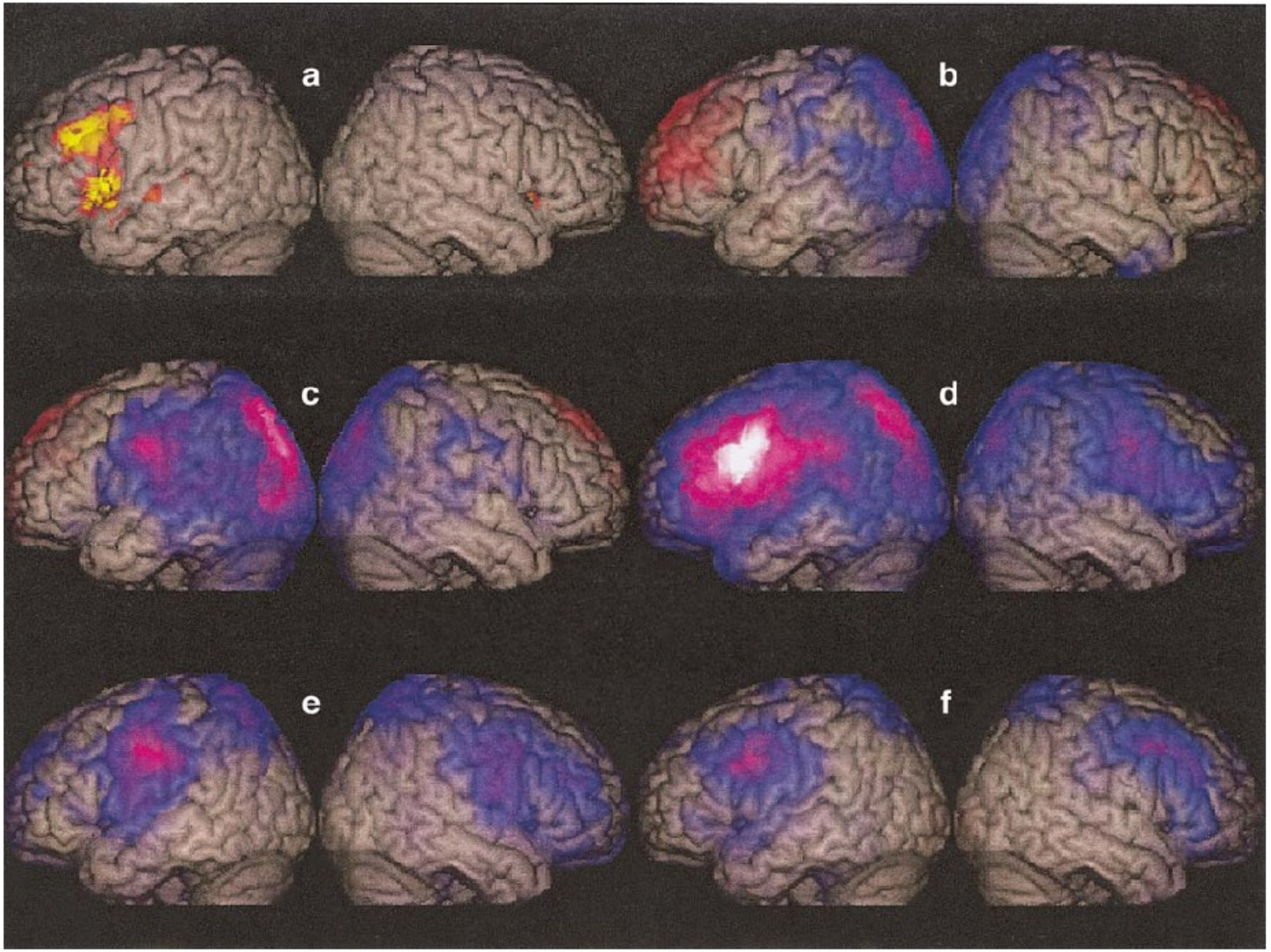
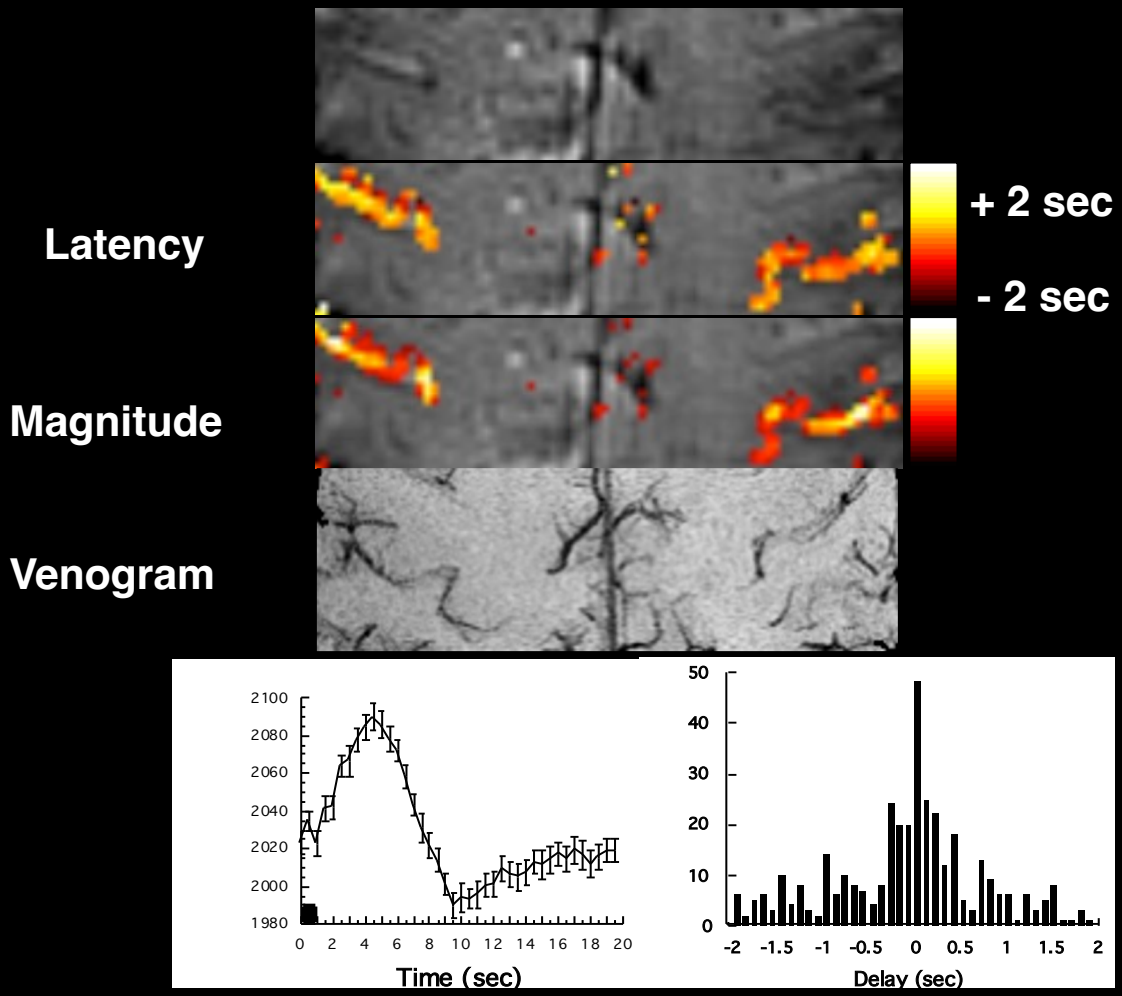


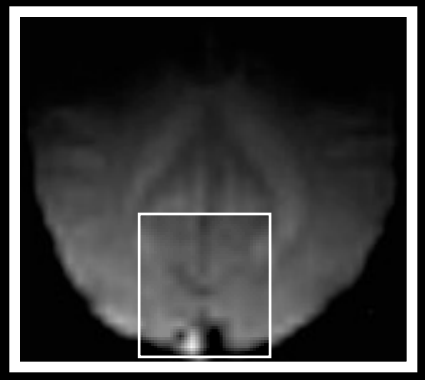
FIG. 1. The results of the group fMRI experiment and the group MEG experiment for the covert letter fluency task, superimposed on a template brain. (a) Group fMRI data. Only those clusters significant at $P < 0.05$ (corrected) are shown. The red–orange–yellow color scale depicts increasing BOLD amplitude. (b–f) The results of the group SAM analysis of the MEG data. Increases in signal power in the Active phase, compared to the Passive baseline are shown using a red–orange–yellow color scale. Decreases in signal power in the Active phase are shown using a blue–purple–white color scale. The power changes are in the following frequency bands (b) 1–10 Hz; (c) 5–15 Hz; (d) 15–25 Hz; (e) 25–35 Hz; and (f) 35–45 Hz.

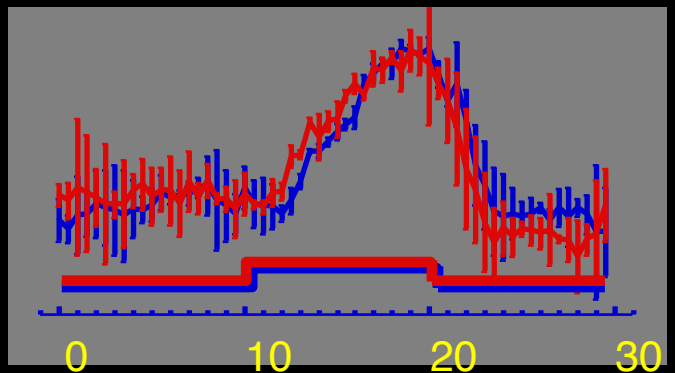
Latency and Width

Latency and Width



Timing Modulation (calibration)





500 ms

500 ms

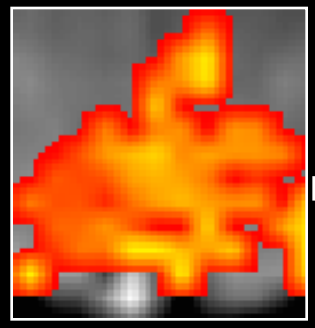
Right Hemifield

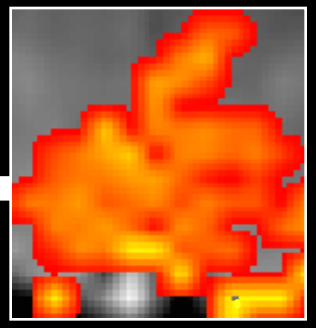
Left Hemifield

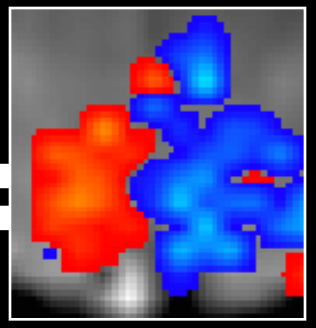
+ 2.5 s

0 s

- 2.5 s







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

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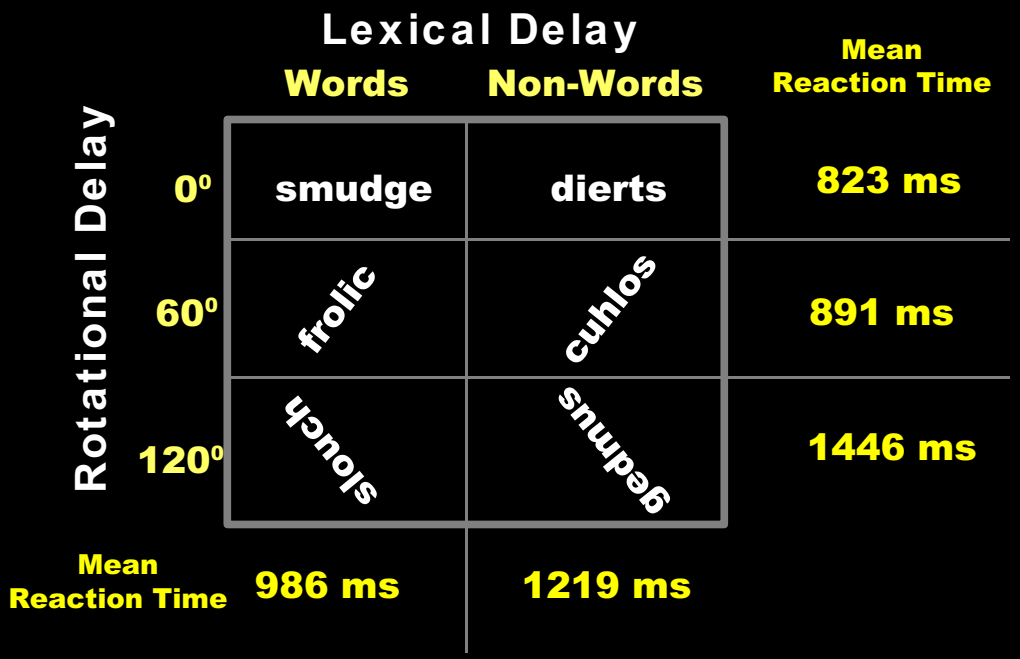
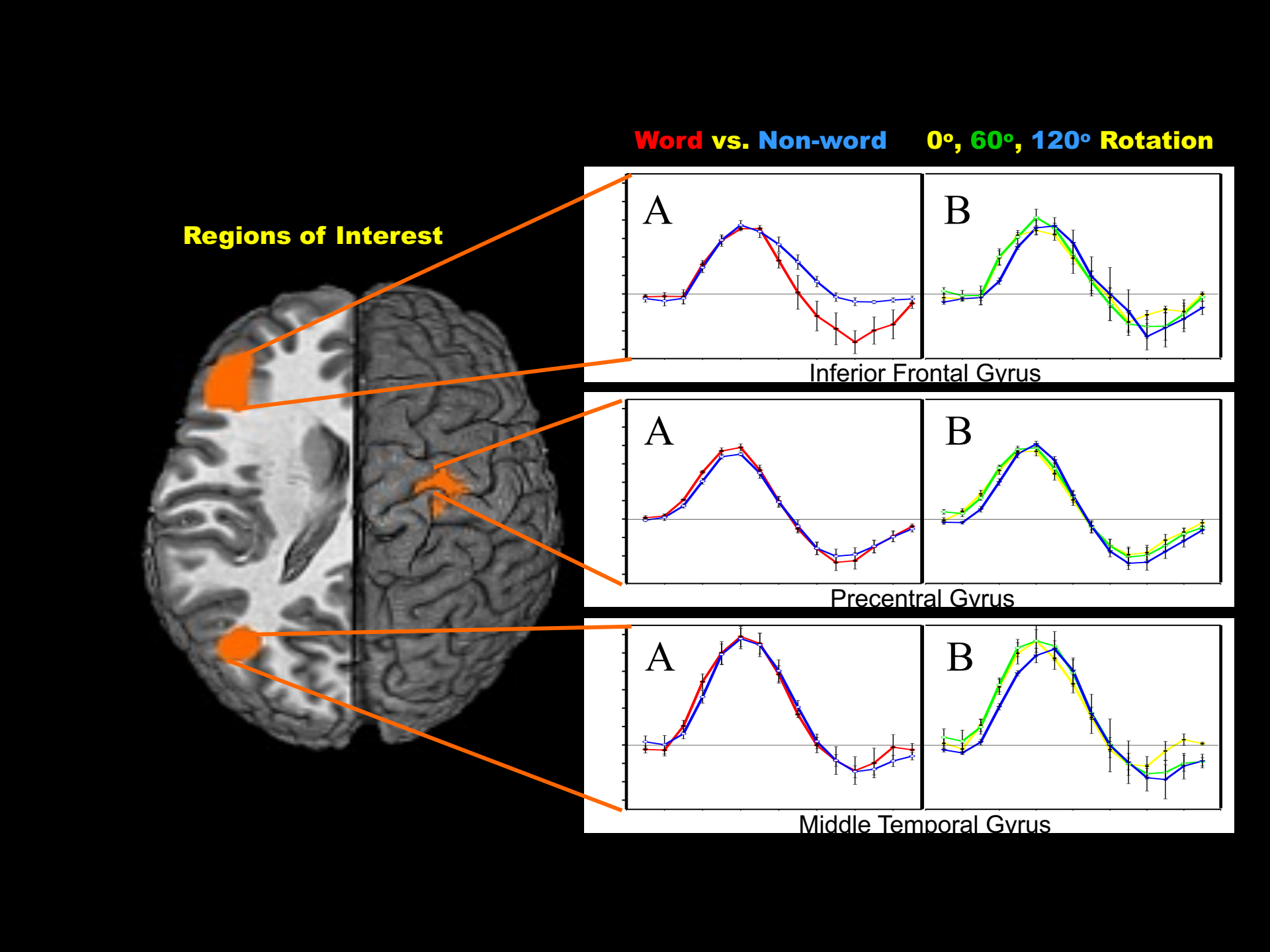
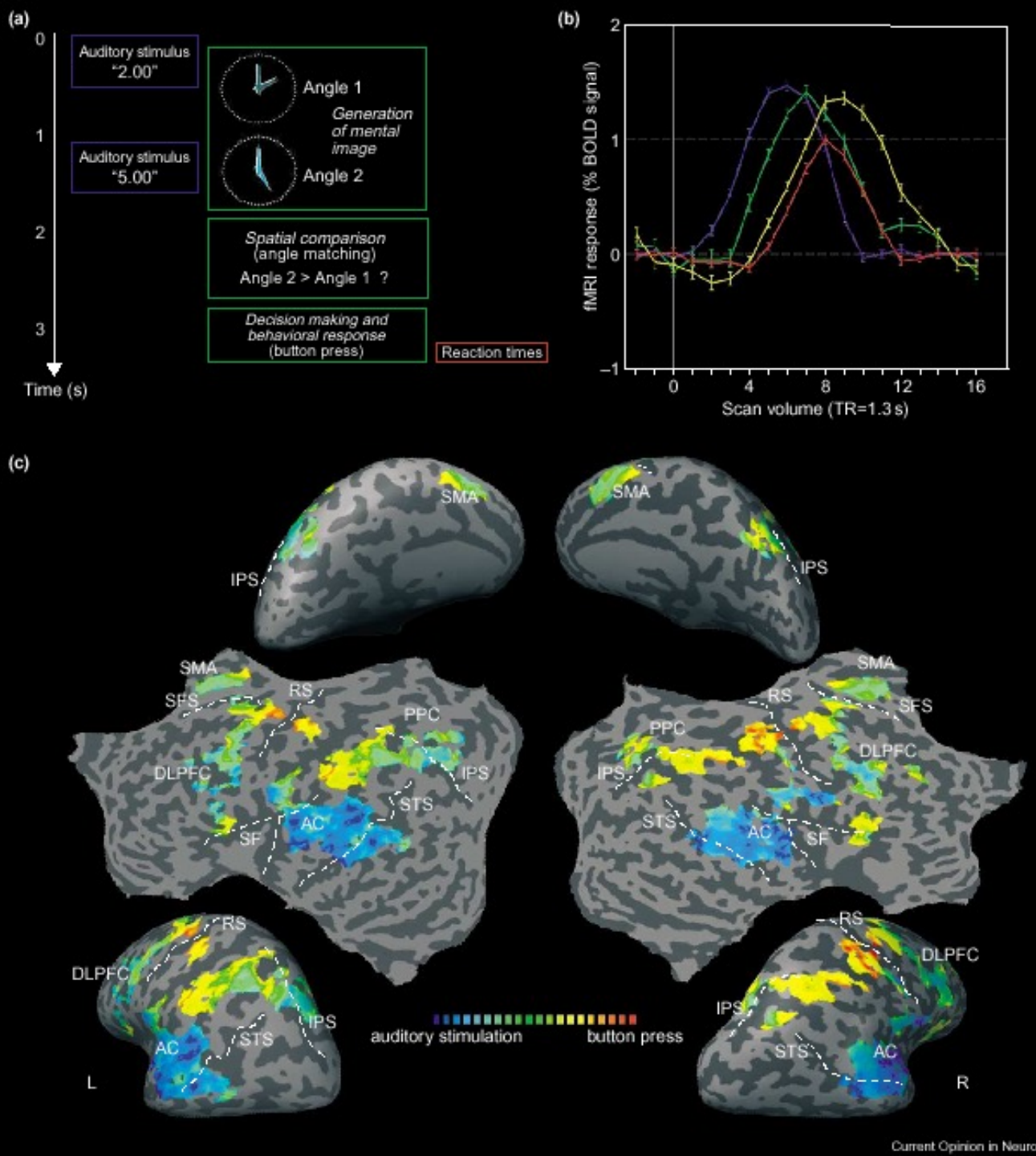
Communicated by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, December 19, 2002 (received for review October 31, 2002)

Proc. Nat'l. Acad. Sci. USA **100**, 1415-1419 (2003).




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

No calibration



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

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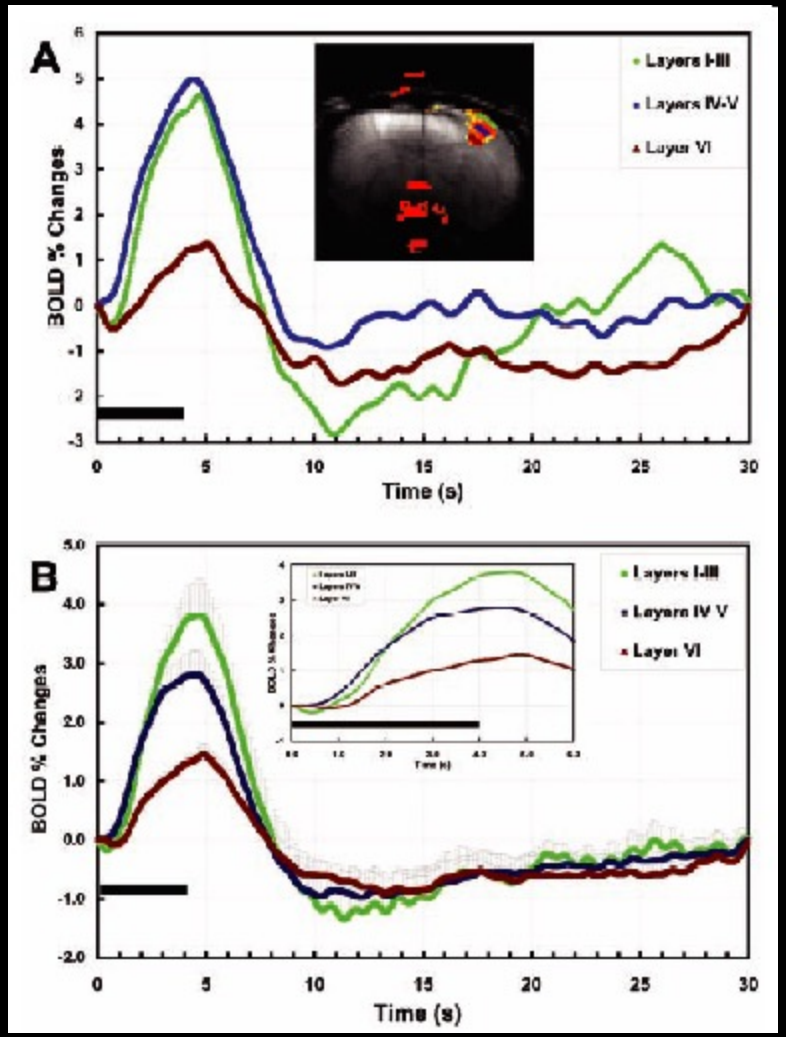
5182–15187 | PNAS | **November 12, 2002** | vol. 99 | no. 231



No calibration

11.7 T

Baseline Modulation...

Quarterly Reviews of Biophysics **35**, 3 (2002), pp. 287–325. © 2002 Cambridge University Press
DOI: 10.1017/S0033583502003803 Printed in the United Kingdom

Biophysical basis of brain activity: implications for neuroimaging

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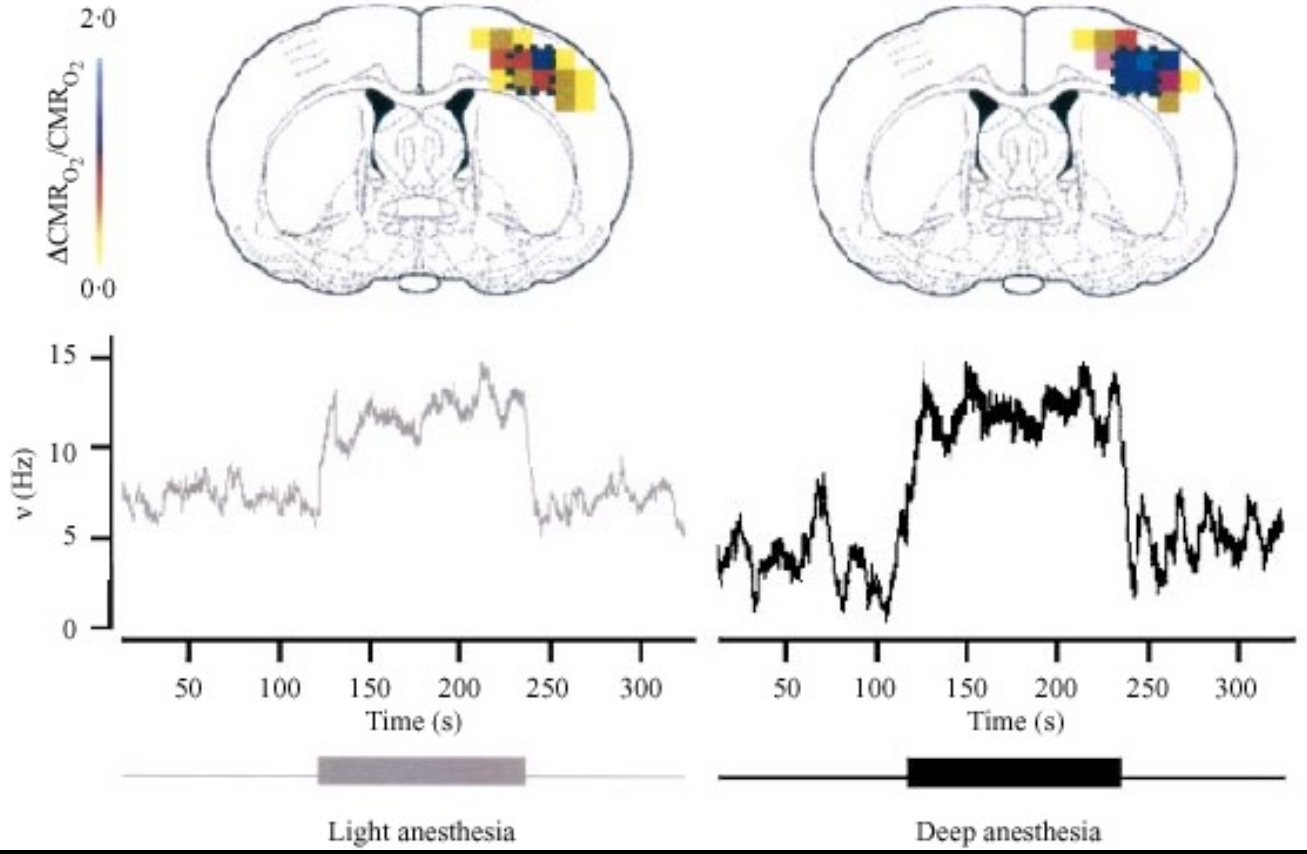
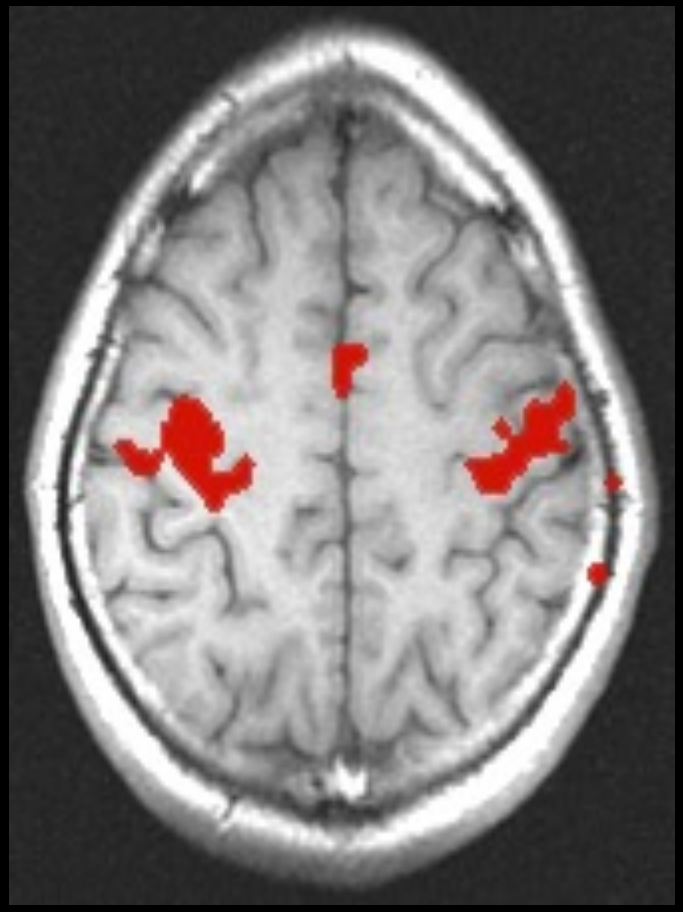
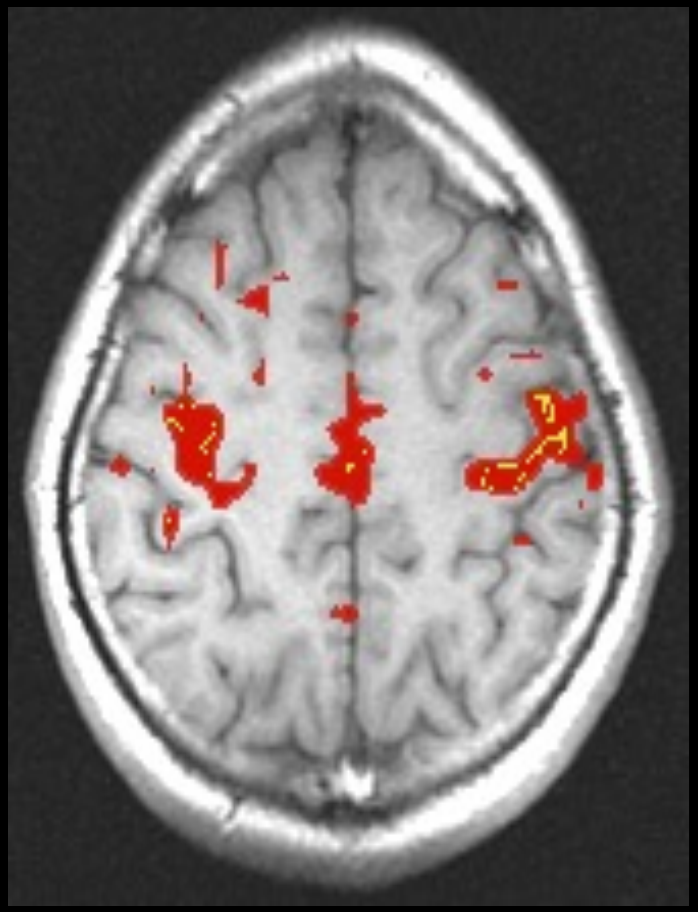


Resting State Fluctuations





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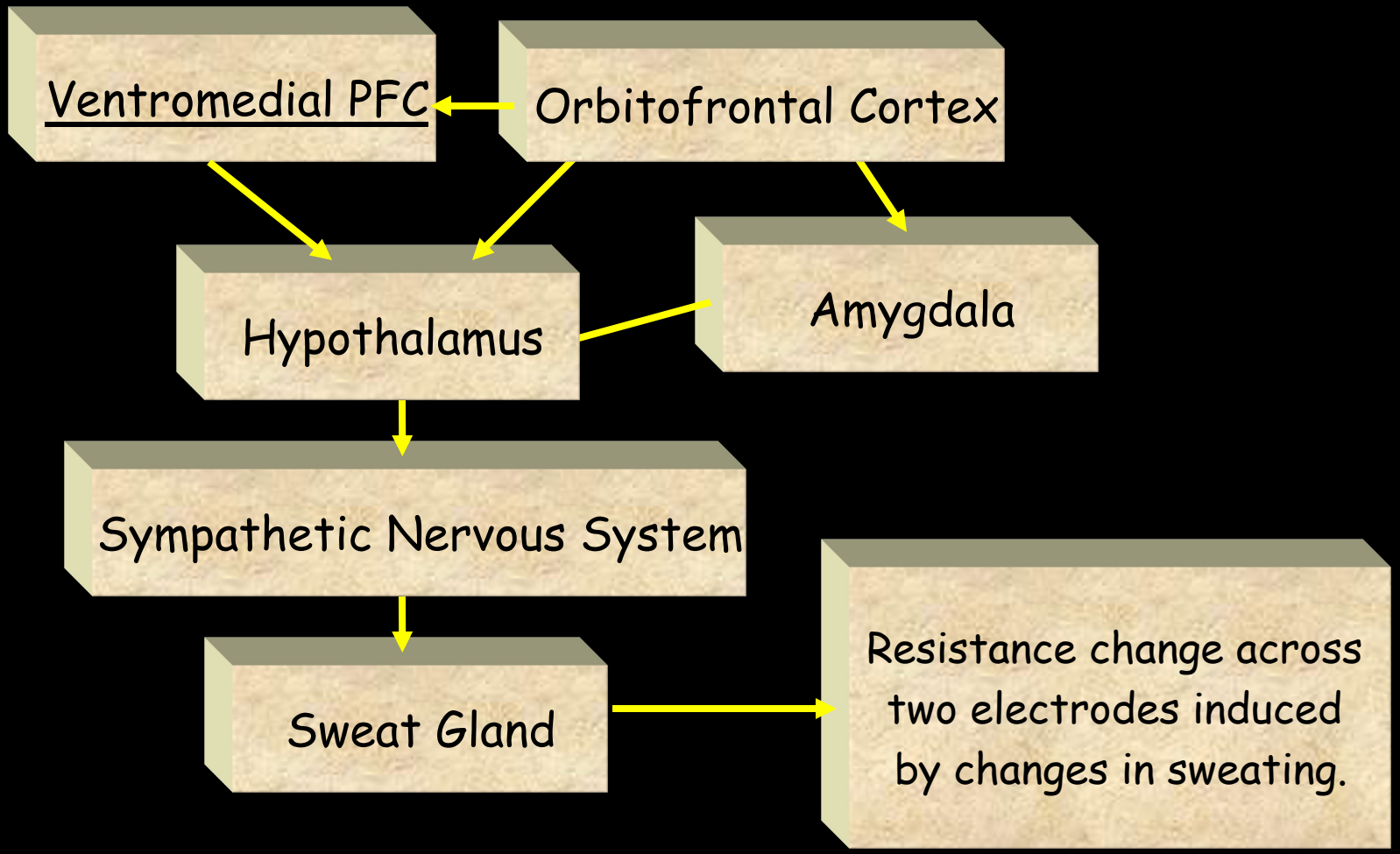
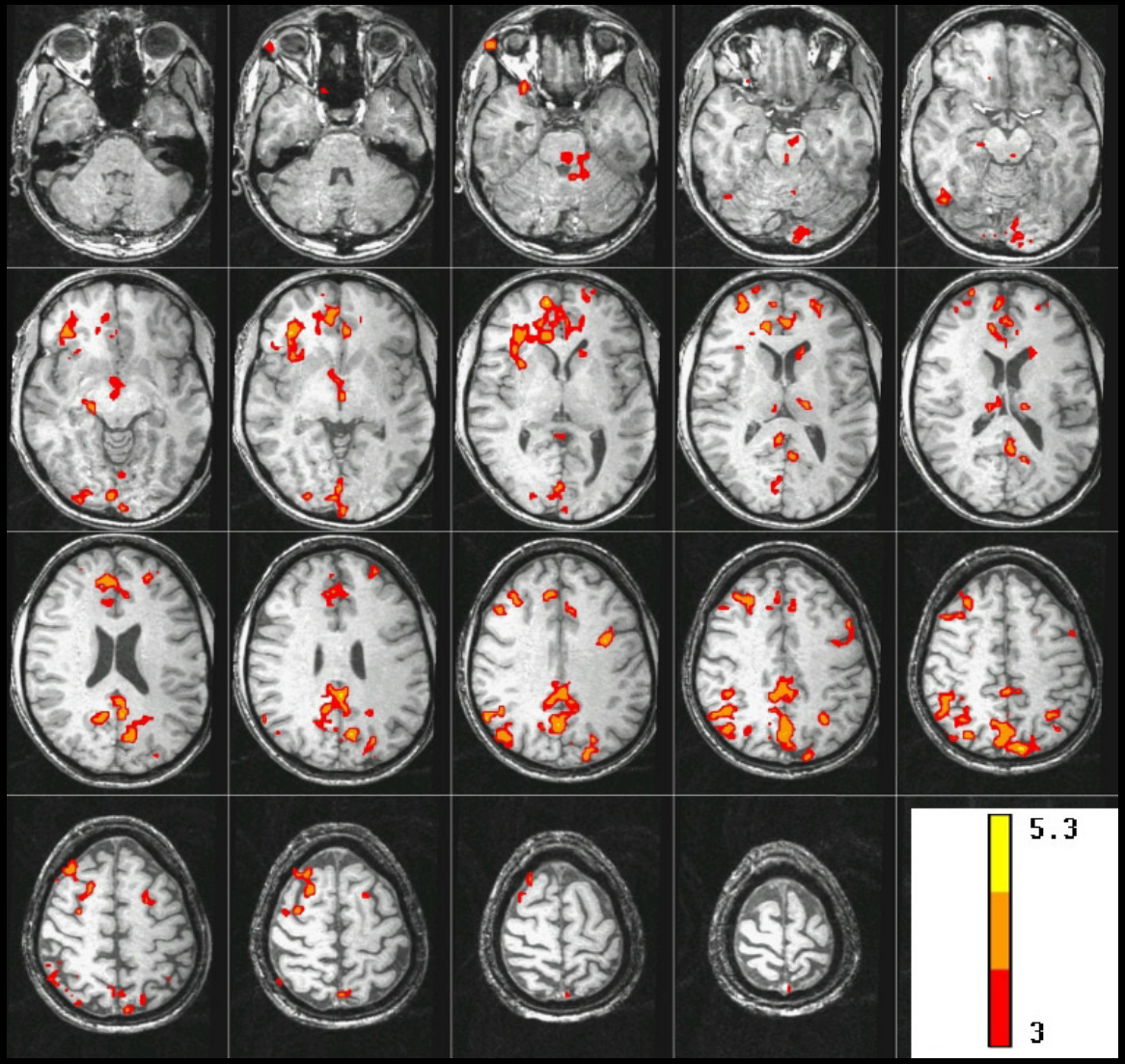
The Skin Conductance Response (SCR)



Brain activity correlated with SCR during “Rest”



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Simultaneous EEG and fMRI of the alpha rhythm

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Received 28 October 2002; accepted 30 October 2002

DOI: 10.1097/01.wnr.0000047685.08940.d0