Fifteen Years of 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

1991

Five Key Factors For The Emergence of Functional MRI

1. Magnetic properties of red blood cells
2. Activation related hemodynamic changes
3. Spatial scale of brain activation
4. Echo Planar Imaging
5. Prevalence of MRI scanners

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Magnetic Properties of Blood

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

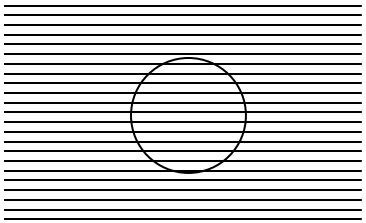
K.R. Thulborn, J. C. Waterton, et al., *Biochim. Biophys. Acta. 714: 265-270*, **1982**.

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

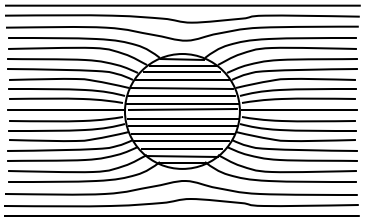
Turner, R., Lebihan, D., Moonen, C. T. W., Despres, D. & Frank, J. *Magnetic Resonance in Medicine,* 22, 159-166, **1991.**

red blood cells

oxygenated



deoxygenated



Biochimica et Biophysica Acta, 714 (1982) 265–270
Elsevier Biomedical Press

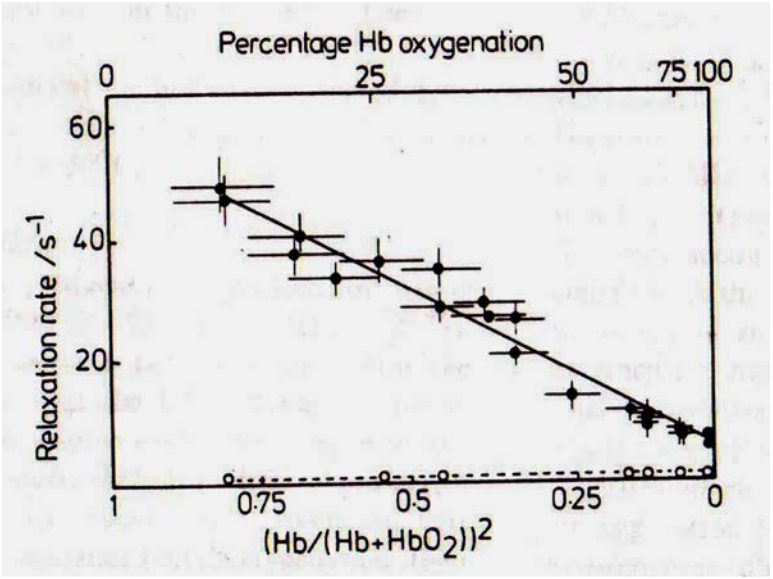
BBA 20122

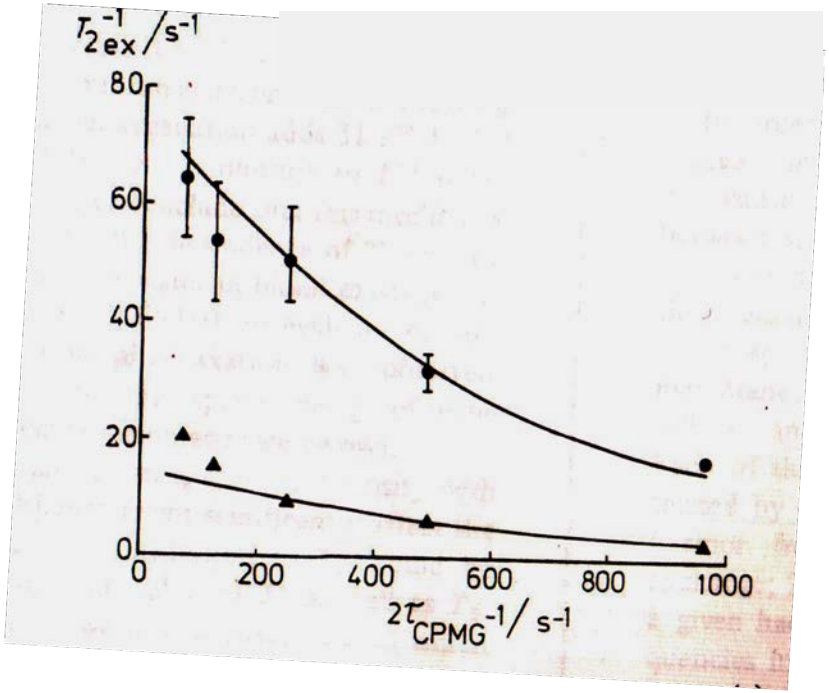
OXYGENATION DEPENDENCE OF THE TRANSVERSE RELAXATION TIME OF WATER PROTONS IN WHOLE BLOOD AT HIGH FIELD

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

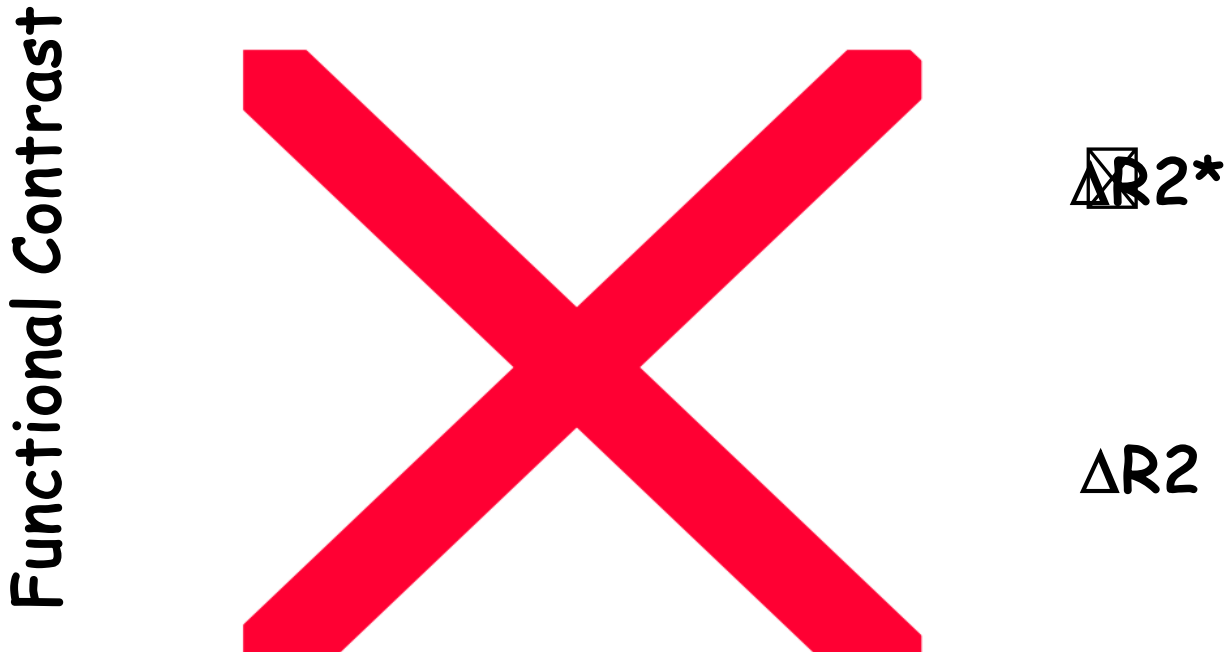
Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU (U.K.)

(Received August 4th, 1981)





Spin echo vs. Gradient echo



compartment radius:	< 3 µm	3 to 15 µm	> 15 µm

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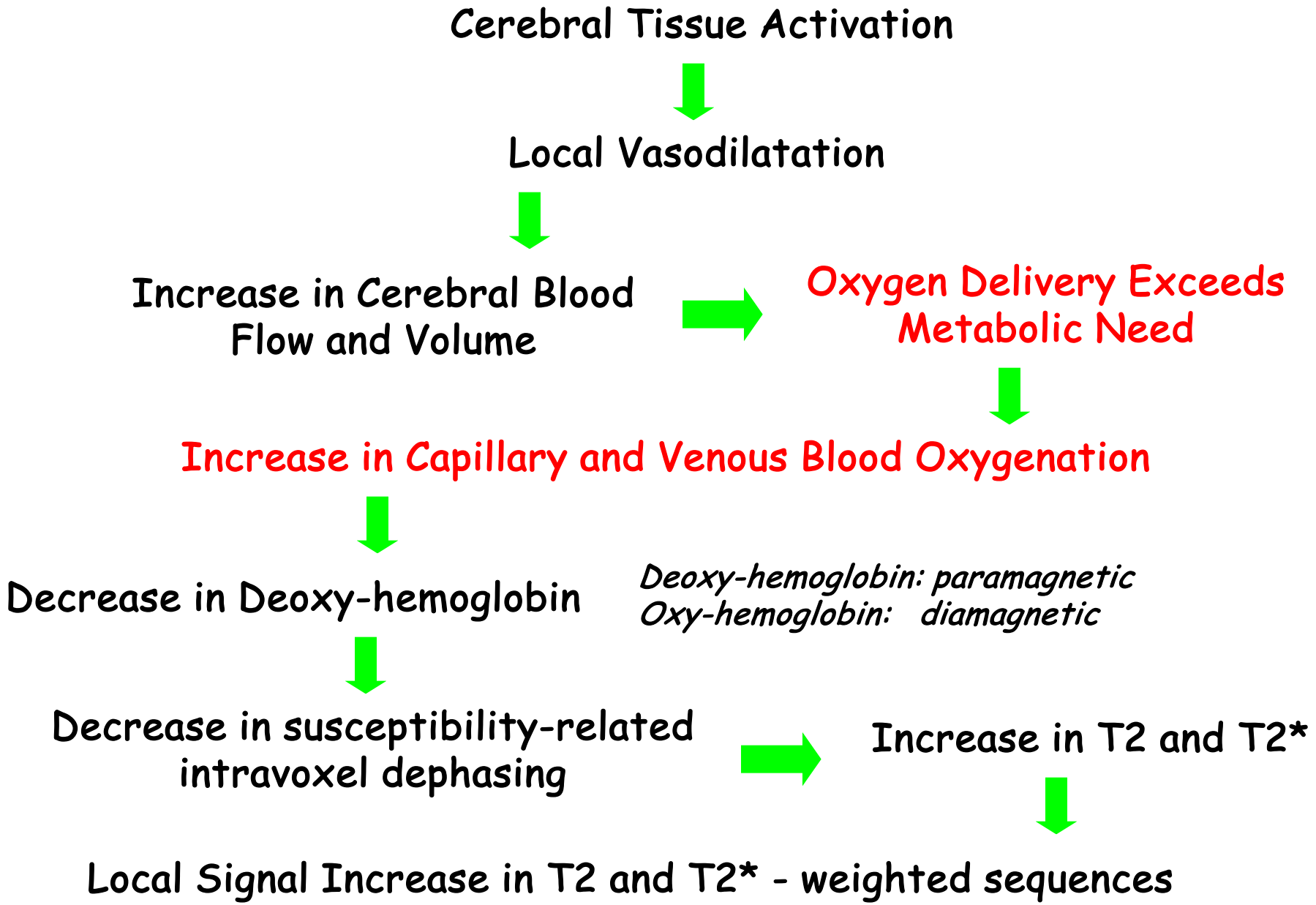
Cerebral Tissue Activation
Local Vasodilatation
Increase in Cerebral Blood Flow and Volume
Oxygen Delivery Exceeds Metabolic Need
Increase in Capillary and Venous Blood Oxygenation
Decrease in Deoxy-hemoglobin
Deoxy-hemoglobin: paramagnetic
Oxy-hemoglobin: diamagnetic
Decrease in susceptibility-related intravoxel dephasing
Increase in T2 and T2*
Local Signal Increase in T2 and T2* - weighted sequences

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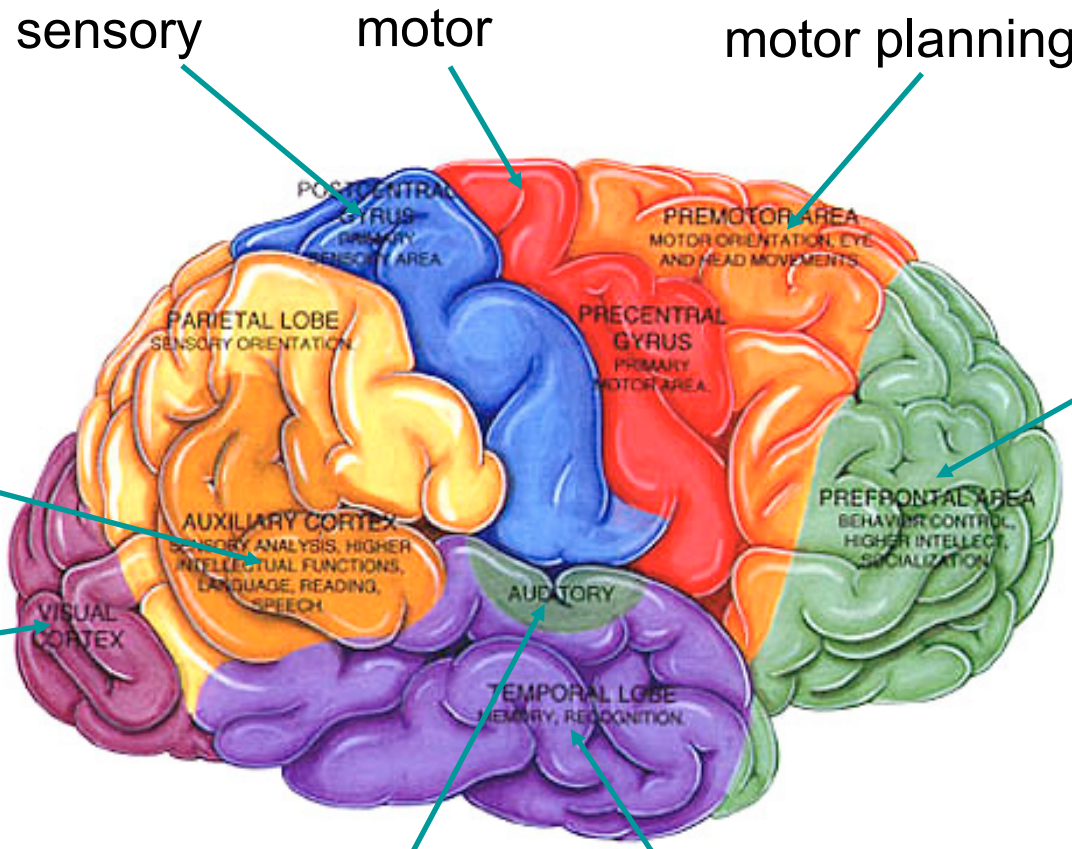
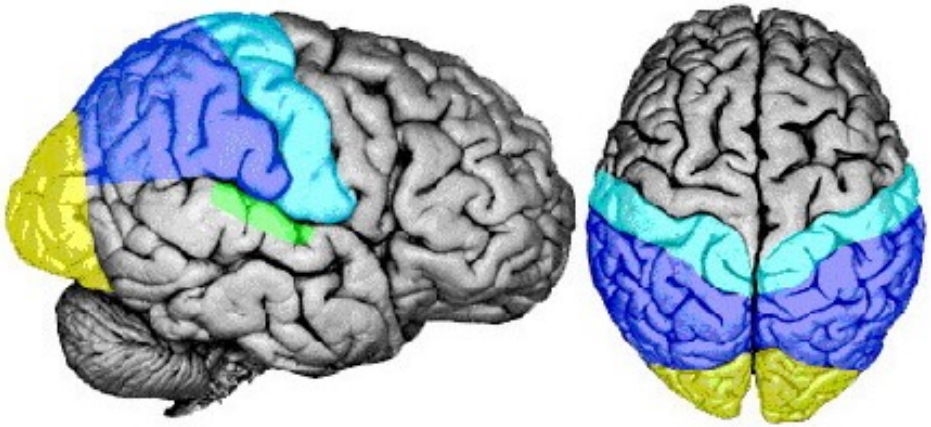
Brain Function



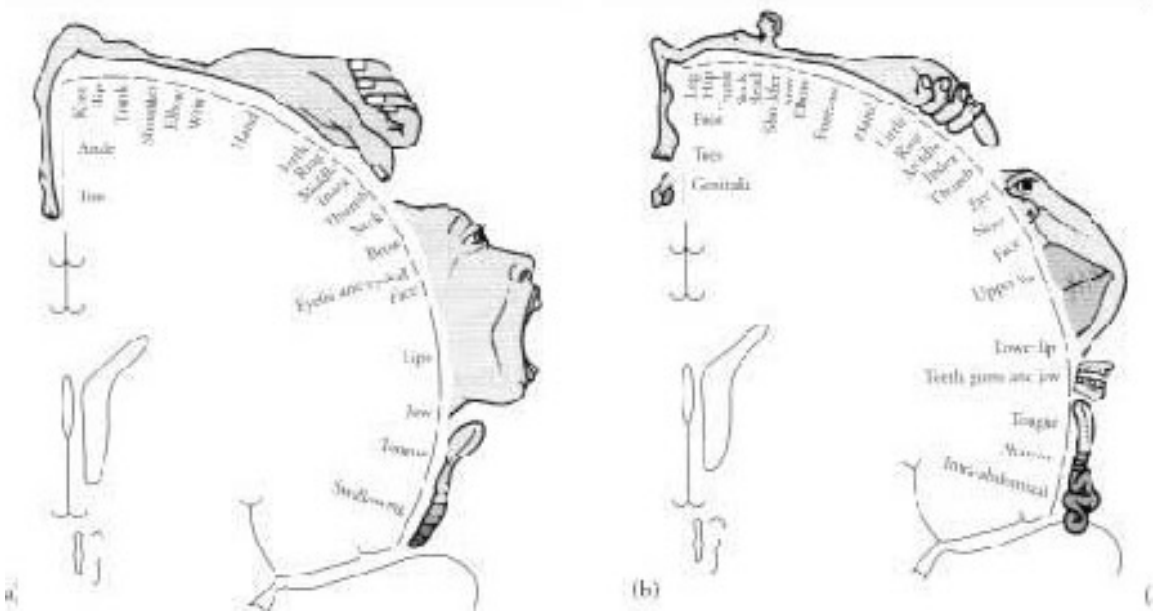


Parietal/ Somatosensory

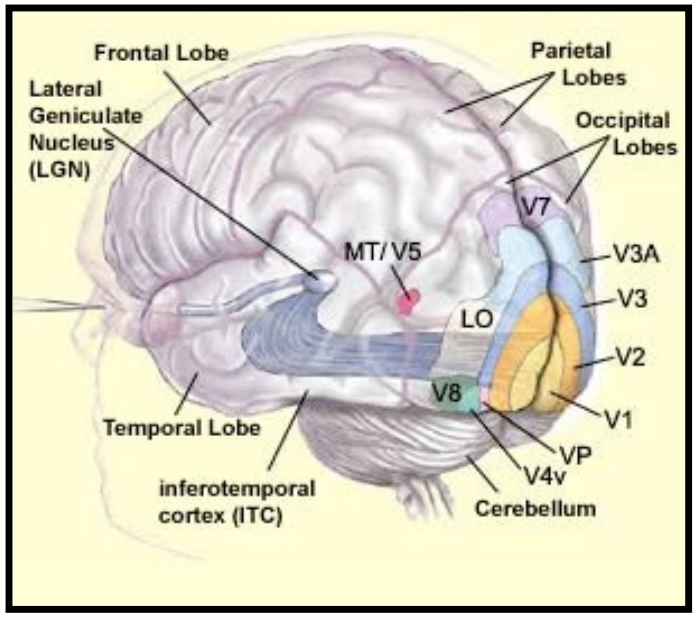
Occipital/Vision

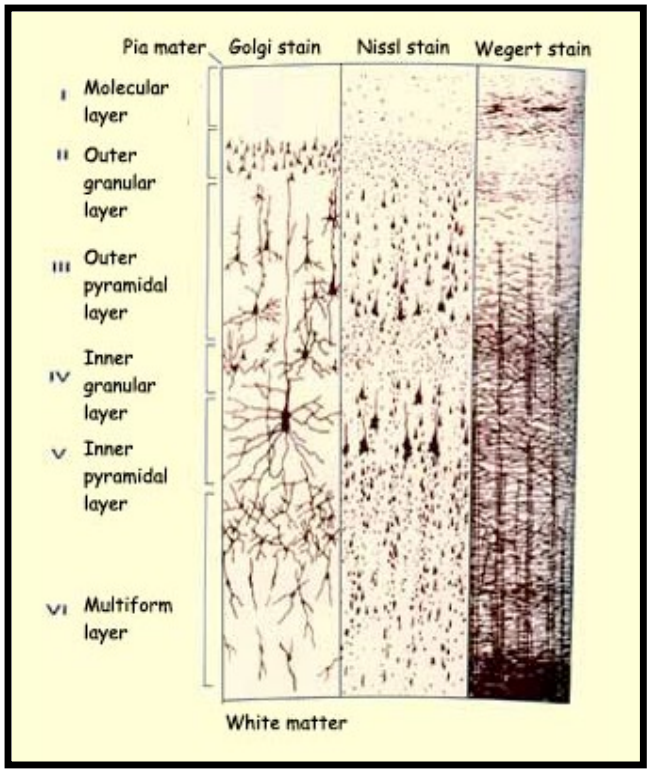
Parietal/ Association Area

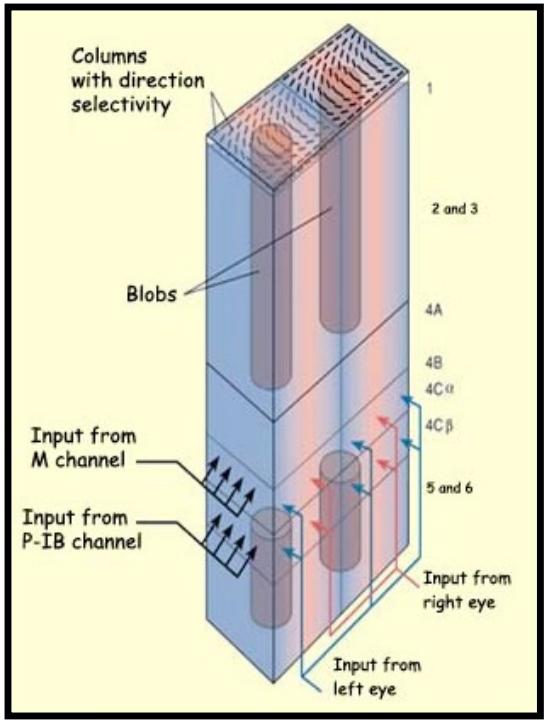
Auditory



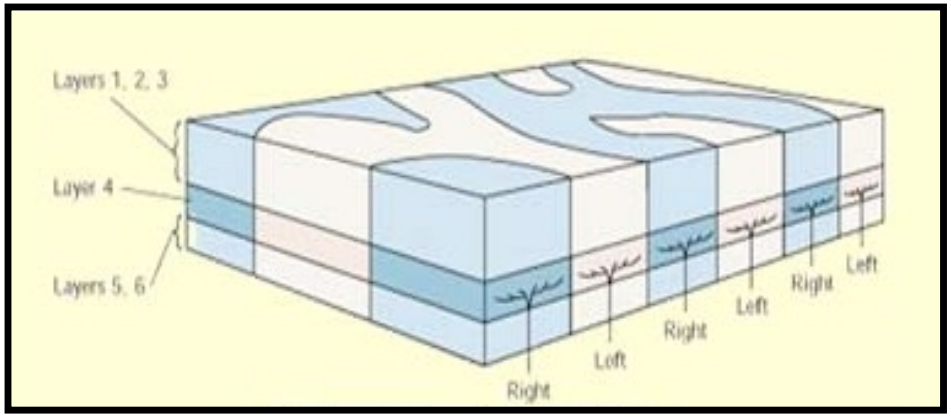
Visual Cortex Organization



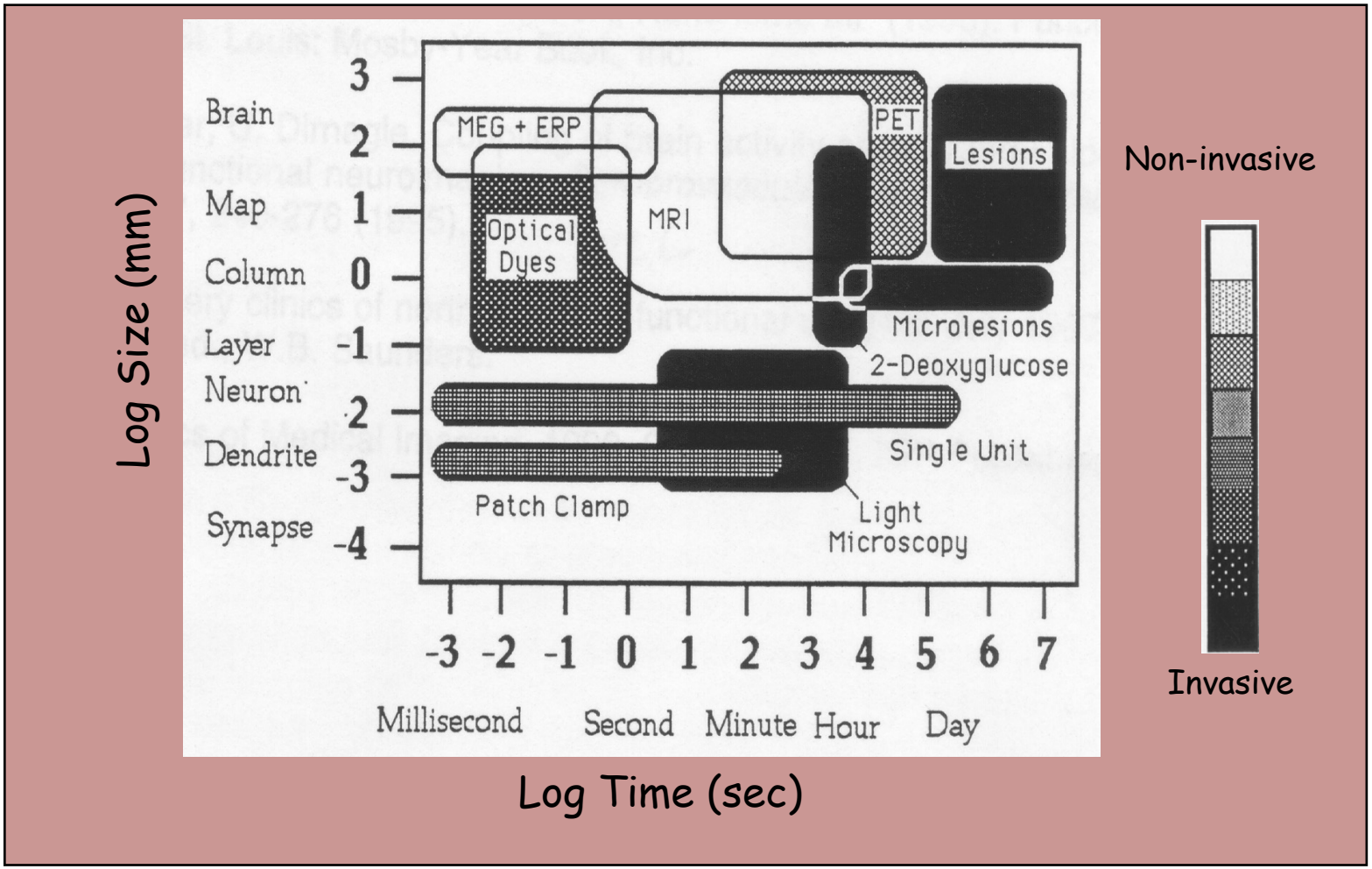




http://www.thebrain.mcgill.ca



Functional Neuroimaging Techniques



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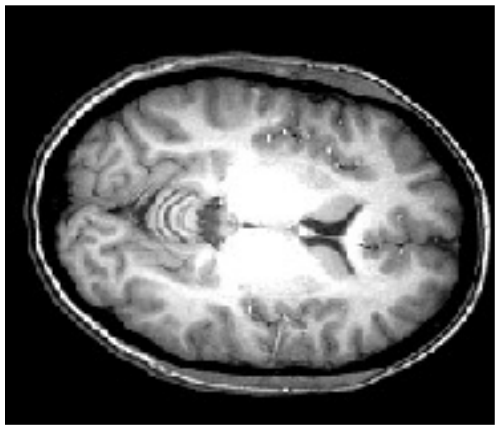
MRI vs. fMRI

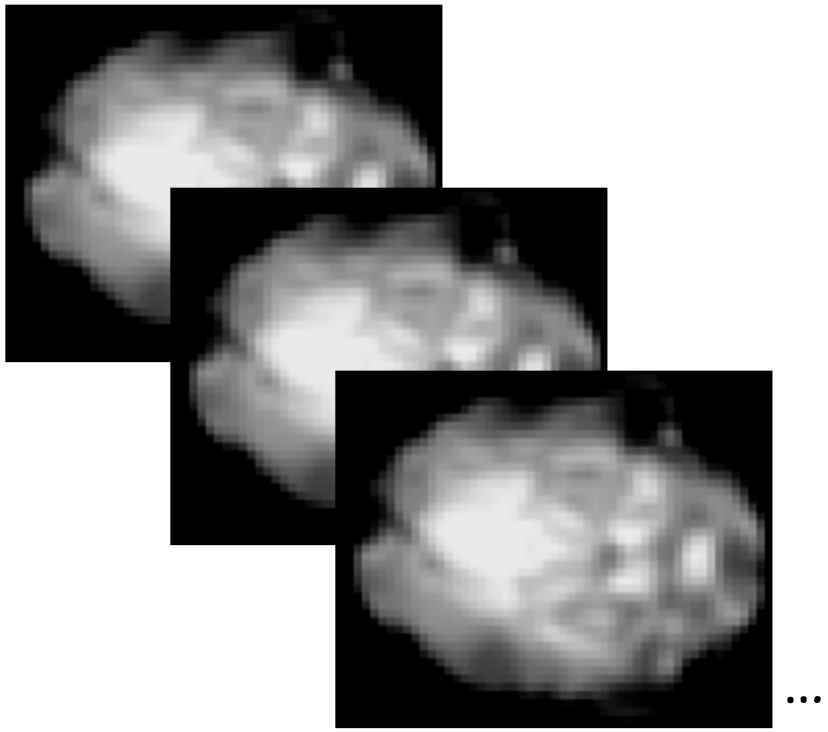
MRI

high resolution
(1 mm)



one image

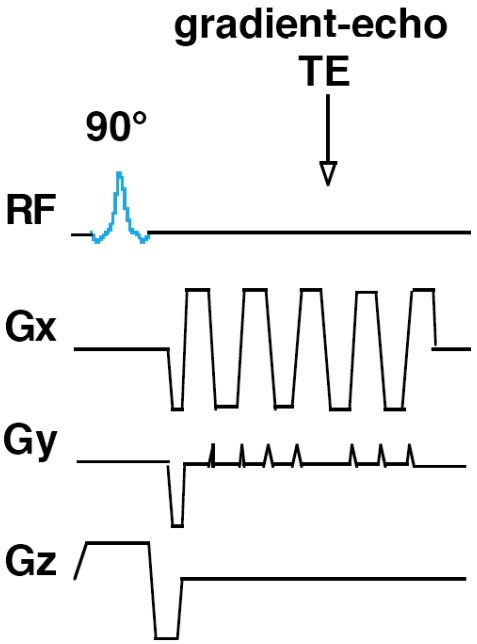
fMRI

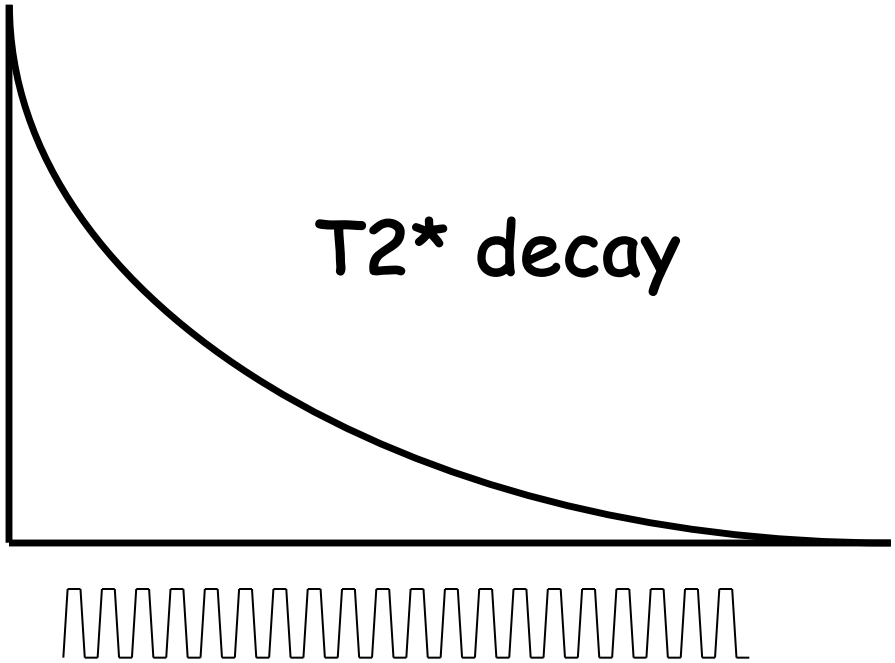


...

many images
(e.g., every 2 sec for 5 mins)

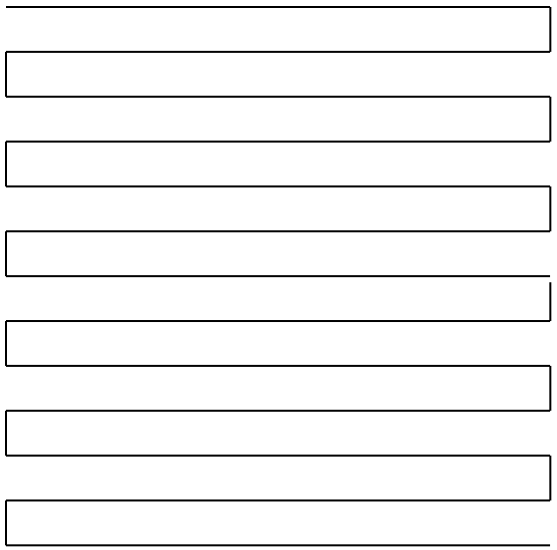
Single Shot Echo Planar Imaging (EPI)





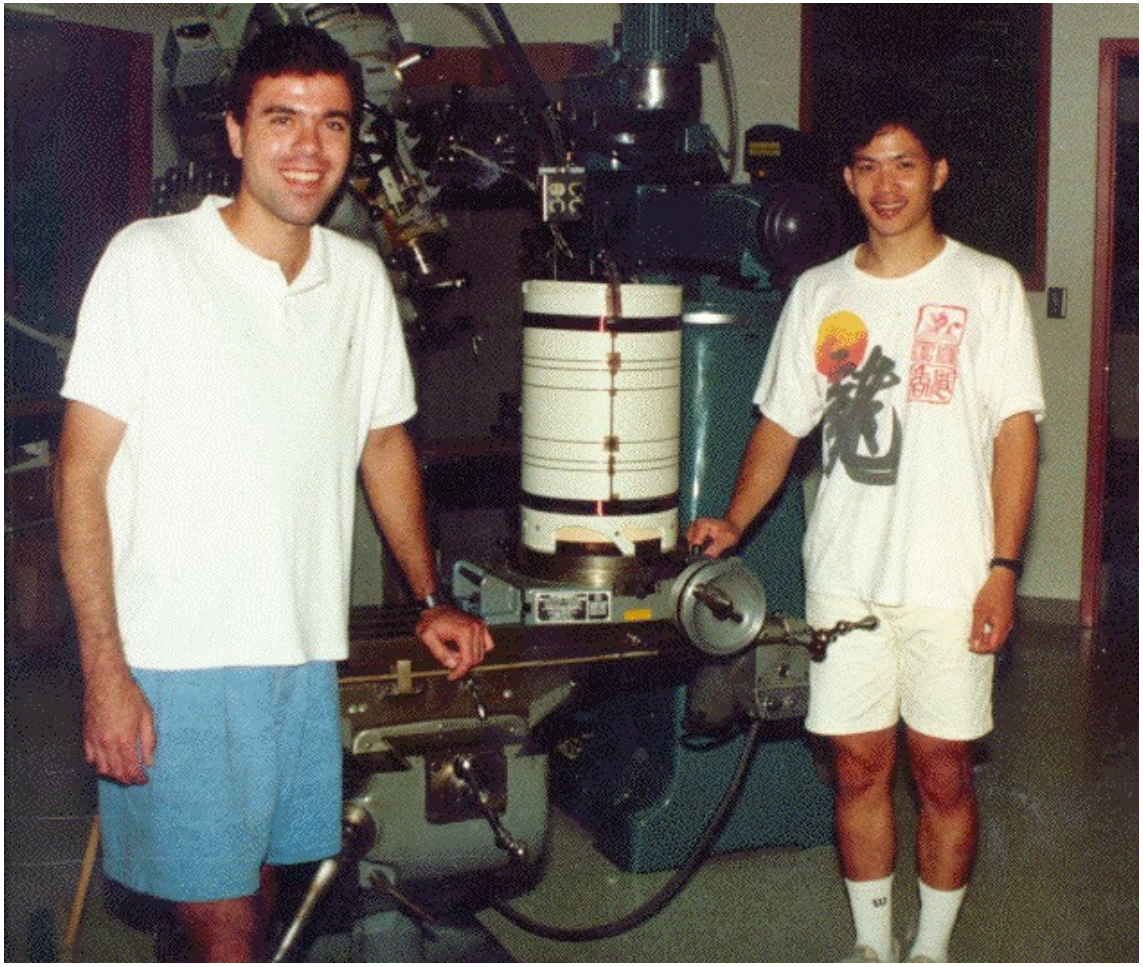
EPI Readout Window

≈ 20 to 40 ms



Approximate EPI Timeline

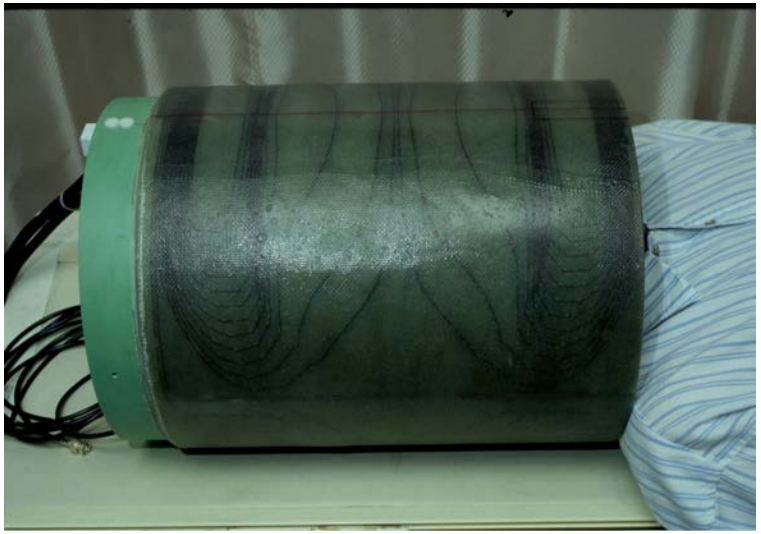
1976 P. Mansfield conceives of EPI
1989 EPI of humans emerges on a handful of scanners
3 x 3 x 3-10 mm^3
1989 ANMR retrofitted with GE scanners for EPI
1991 Home built head gradient coils perform EPI
1996 EPI is standard on clinical scanners
2000 Gradient performance continues to increase
2002 Parallel imaging allows for higher resolution EPI
2006 1.5 x 1.5 x 1.5 mm^3 single shot EPI possible



August, 1991

1991-1992

1992-1999



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Technology

Magnet
RF Coils
Pulse Sequences

Methodology

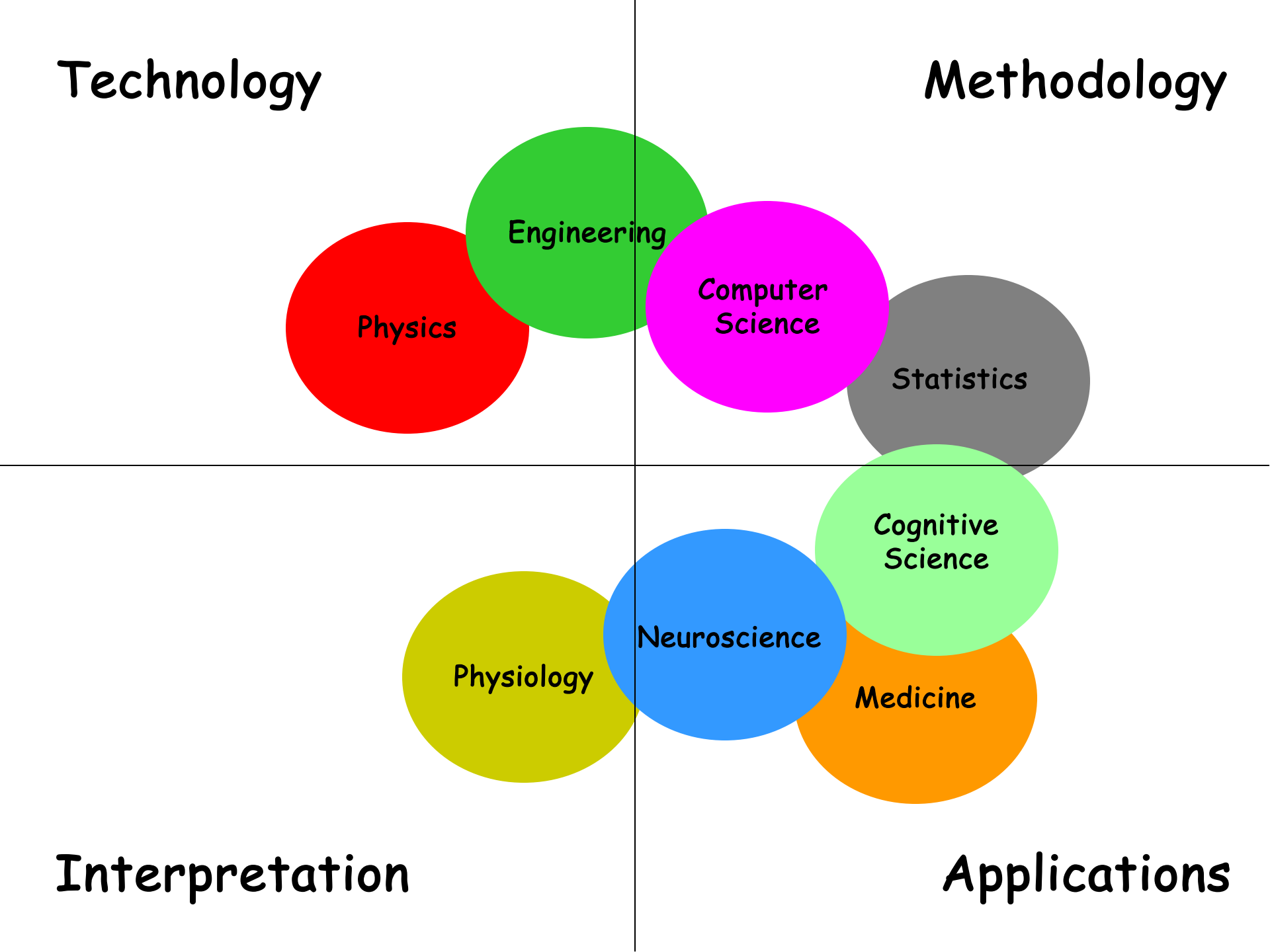
Paradigm Design
Pre and Post Processing
Subject Interface
Data Display and Comparison

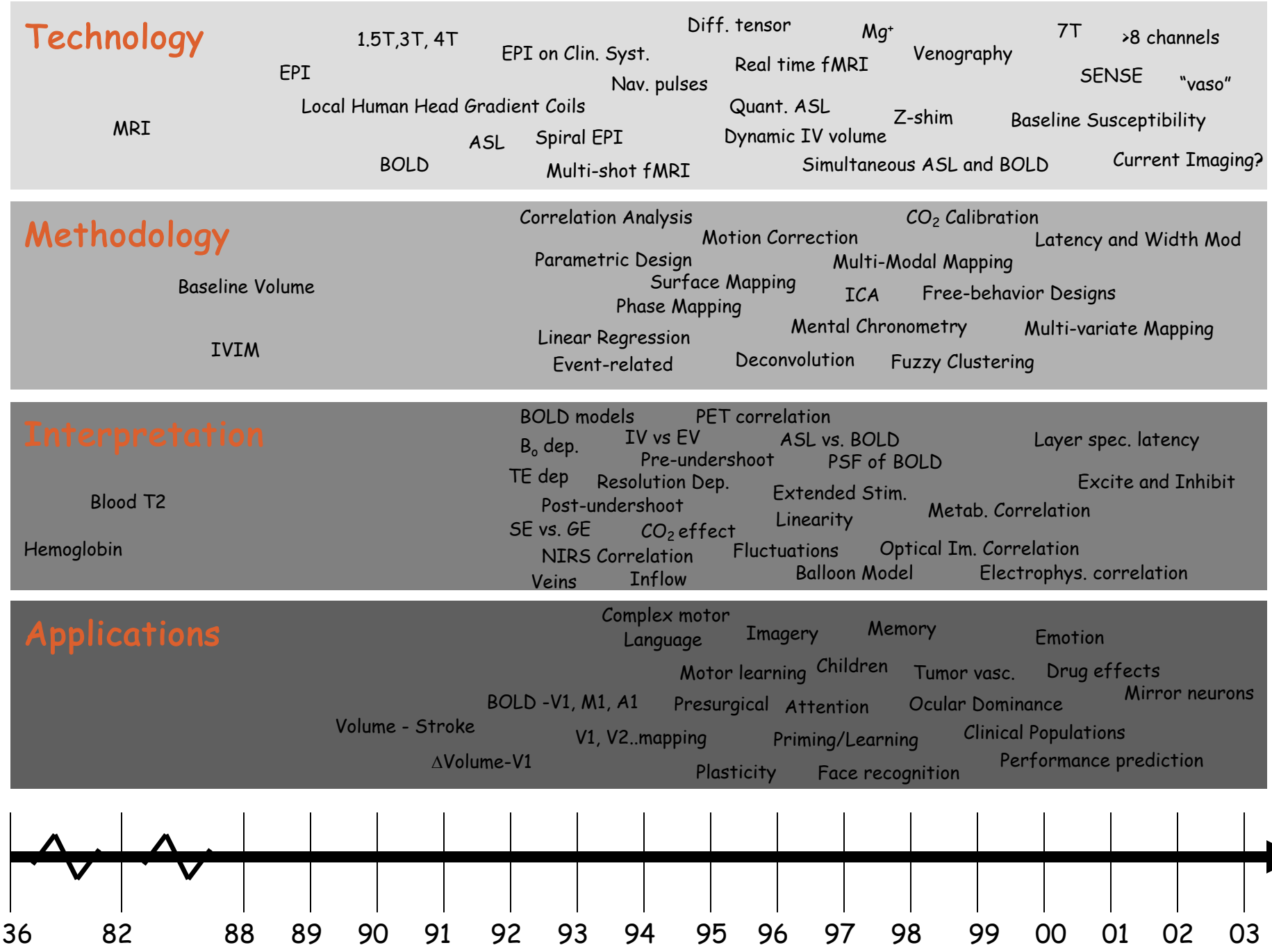
Interpretation

Increases
Decreases
Dynamics
Locations

Applications

Neuroscience
Physiology
Genetics
Practical Clinical


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

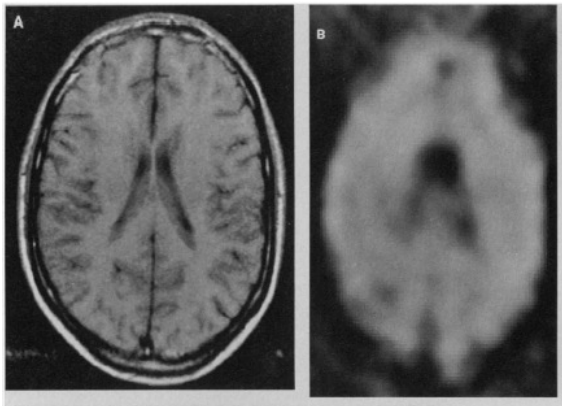

Technology
1.5T,3T, 4T
Diff. tensor
Mg+
7T
>8 channels
EPI on Clin. Syst.
Venography
EPI
Real time fMRI
SENSE
Nav. pulses
"vaso"
Local Human Head Gradient Coils
Quant. ASL
Z-shim
MRI
Baseline Susceptibility
ASL
Spiral EPI
Dynamic IV volume
BOLD
Multi-shot fMRI
Simultaneous ASL and BOLD
Current Imaging?
Methodology
Correlation Analysis
CO_2 Calibration
Motion Correction
Latency and Width Mod
Parametric Design
Multi-Modal Mapping
Baseline Volume
Surface Mapping
ICA
Free-behavior Designs
Phase Mapping
Mental Chronometry
Multi-variate Mapping
Linear Regression
IVIM
Event-related
Deconvolution
Fuzzy Clustering
Interpretation
BOLD models
PET correlation
IV vs EV
ASL vs. BOLD
Layer spec. latency
B_0 dep.
Pre-undershoot
PSF of BOLD
TE dep
Resolution Dep.
Excite and Inhibit
Extended Stim.
Blood T2
Post-undershoot
Metab. Correlation
Linearity
SE vs. GE
CO_2 effect
Hemoglobin
NIRS Correlation
Fluctuations
Optical Im. Correlation
Veins
Inflow
Balloon Model
Electrophys. correlation
Applications
Complex motor
Language
Imagery
Memory
Emotion
Motor learning
Children
Tumor vasc.
Drug effects
Mirror neurons
BOLD -V1, M1, A1
Presurgical
Attention
Ocular Dominance
Volume - Stroke
V1, V2..mapping
Priming/Learning
Clinical Populations
ΔVolume-V1
Performance prediction
Plasticity
Face recognition
36
82
88
89
90
91
92
93
94
95
96
97
98
99
00
01
02
03

Functional Magnetic Resonance Imaging in Medicine and Physiology

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

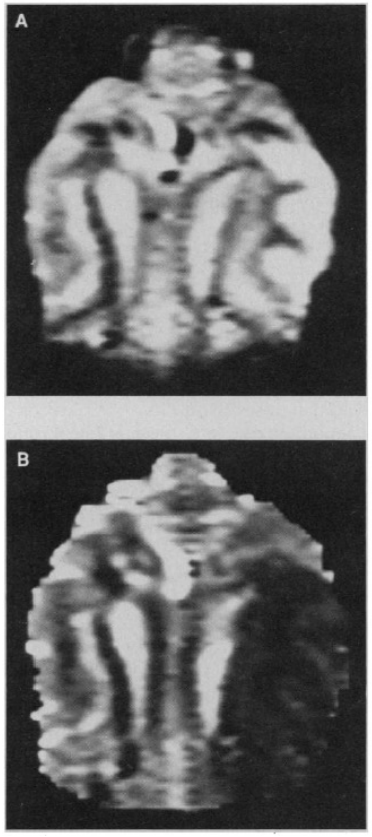
(1990) *Science*, 250, 53-61.

metabolic imaging (NAA)

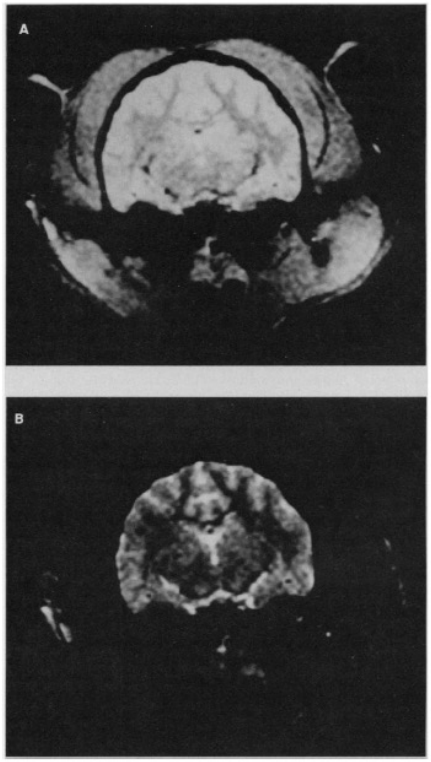


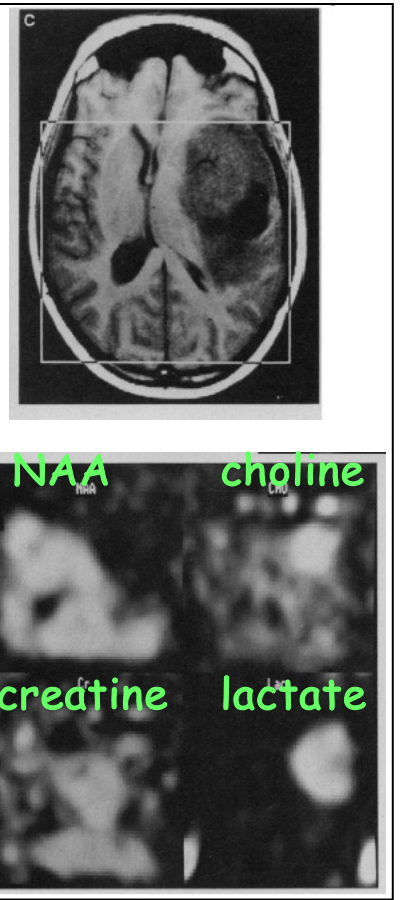
angiography

Diffusion

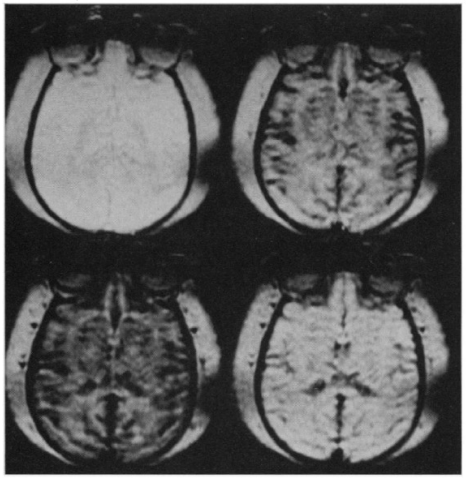


magnetization transfer





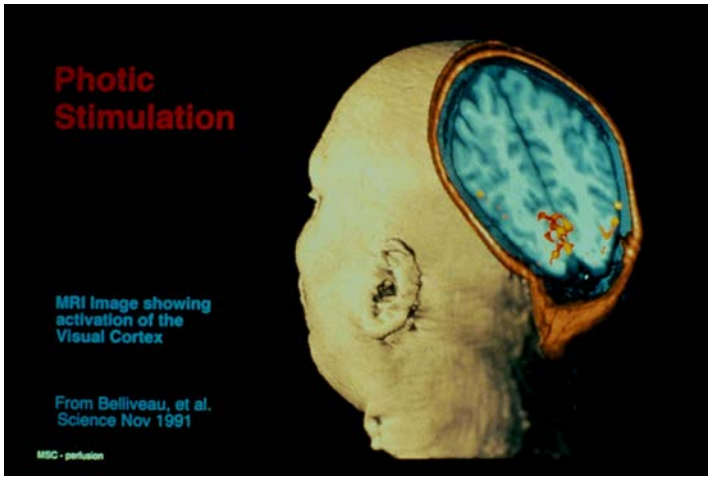
Gadolinium perfusion



Pre 1992…

Blood Volume Imaging

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



1992…BOLD

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

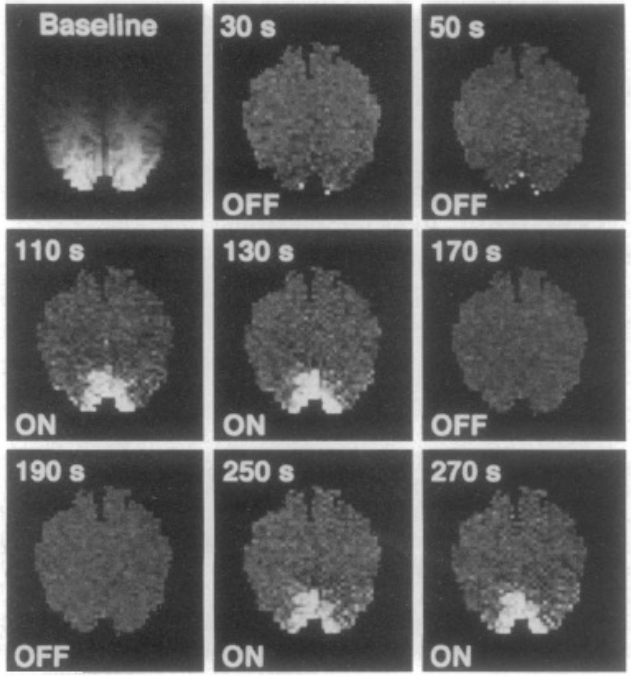
S. Ogawa, et al., (1992) "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging." **Proc. Natl. Acad. Sci. USA. 89, 5951-5955.**

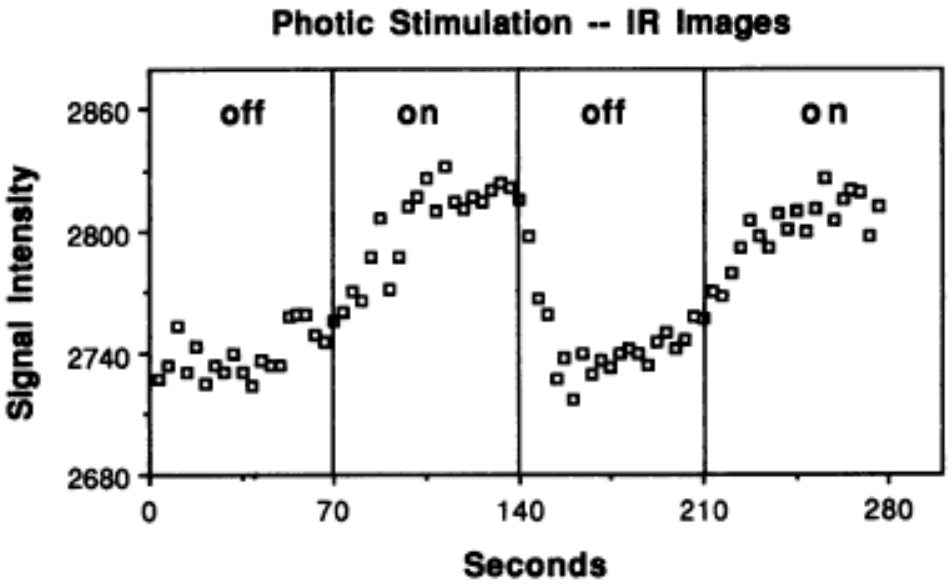
P. A. Bandettini, et al., (1992) "Time course EPI of human brain function during task activation." **Magn. Reson. Med 25, 390-397.**

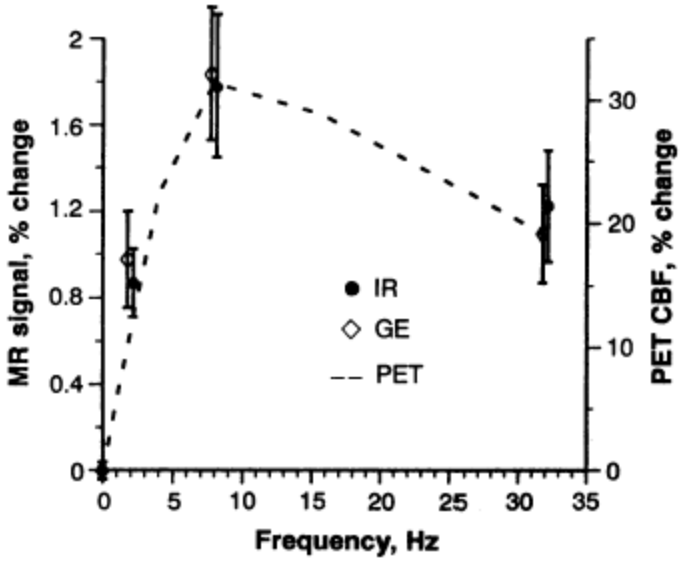
Blamire, A. M., et al. (1992). "Dynamic mapping of the human visual cortex by high-speed magnetic resonance imaging." **Proc. Natl. Acad. Sci. USA 89: 11069-11073.**

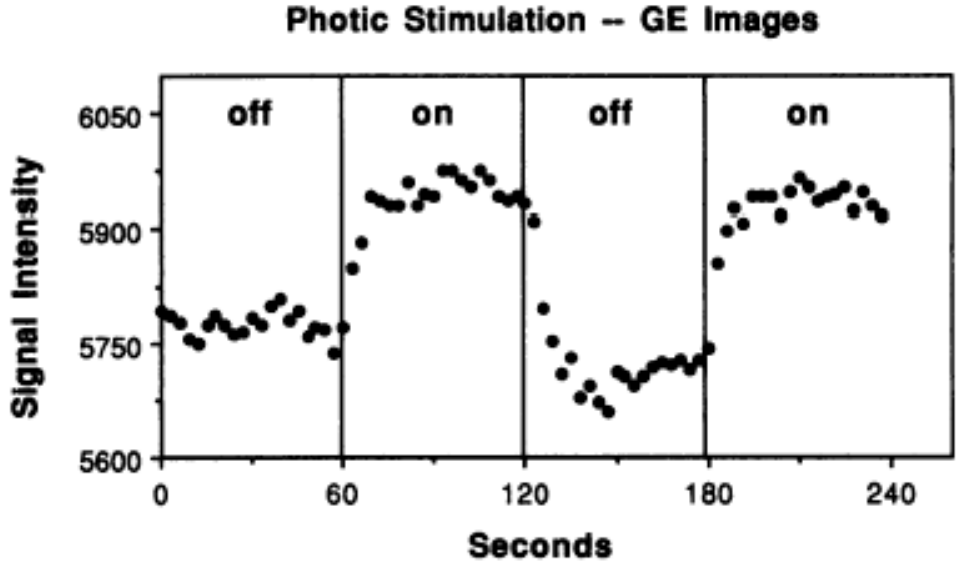
Frahm, J., et al (1992) "Dynamic MR Imaging of Human Brain Oxygenation During Rest and Photic-Stimulation." **Journal of Magnetic Resonance Imaging, 2, 501-505.**

Kwong et al.

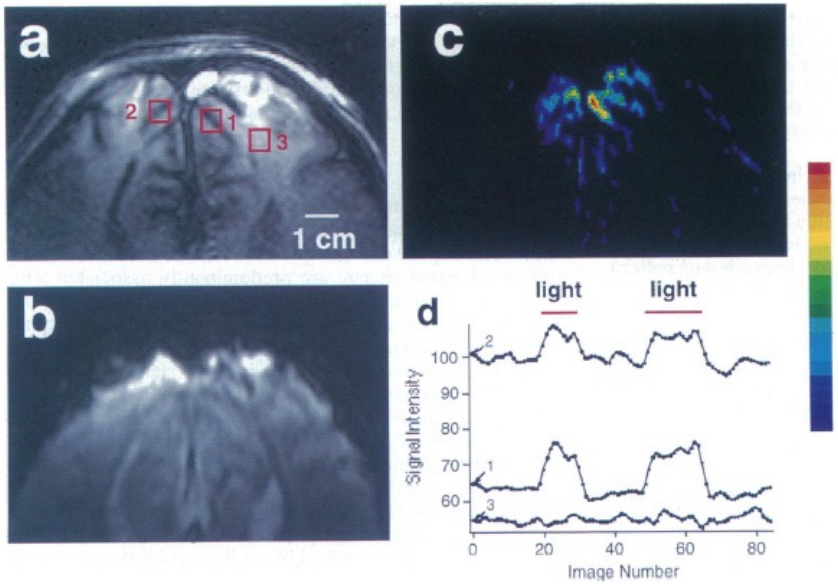

Baseline
30 s
OFF
50 s
OFF
110 s
ON
130 s
ON
170 s
OFF
190 s
OFF
250 s
ON
270 s
ON

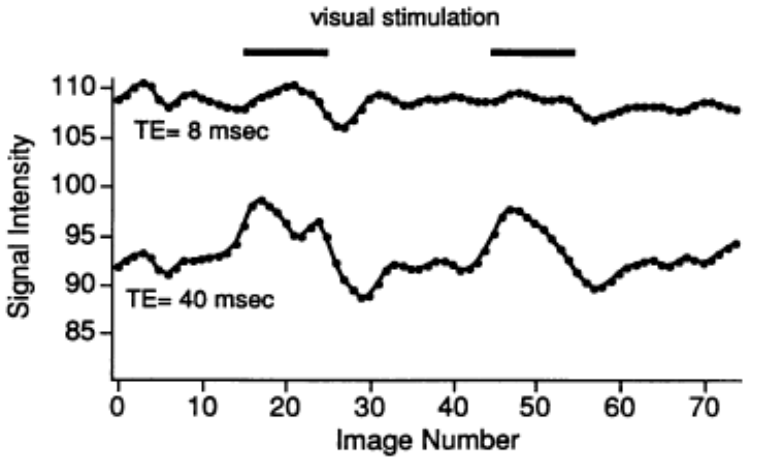

Photic Stimulation -- IR Images
Signal Intensity
2860
2800
2740
2680
off
on
off
on
0
70
140
210
280
Seconds

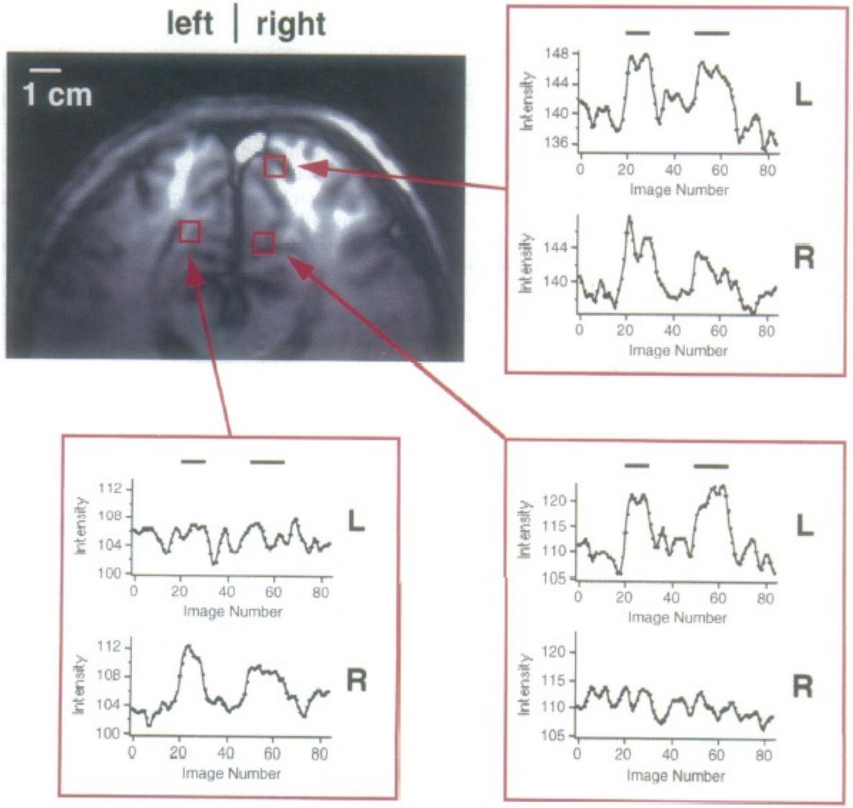

MR signal, % change
PET CBF, % change
2
1.6
1.2
0.8
0.4
0
30
20
10
0
IR
GE
PET
0
5
10
15
20
25
30
35
Frequency, Hz


Photic Stimulation -- GE Images
Signal Intensity
6050
5900
5750
5600
off
on
off
on
0
60
120
180
240
Seconds

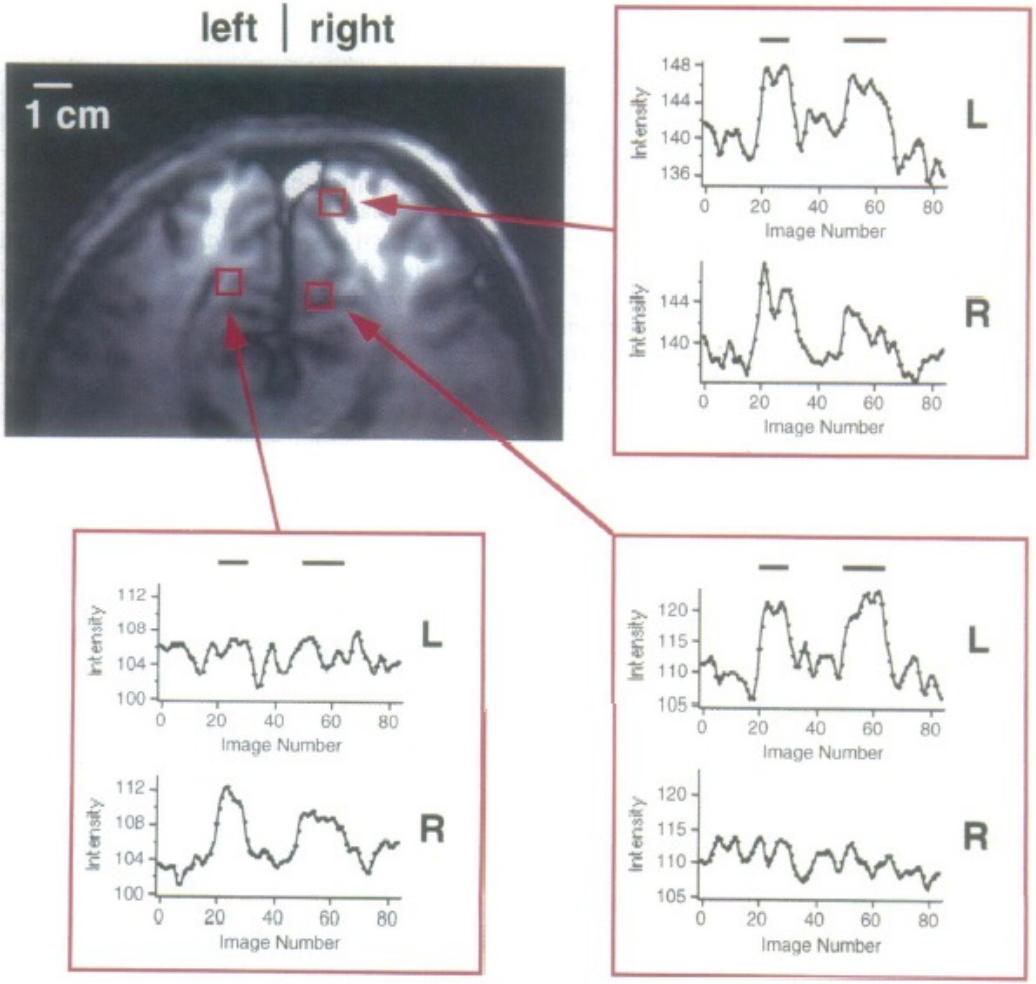
Ogawa et al.

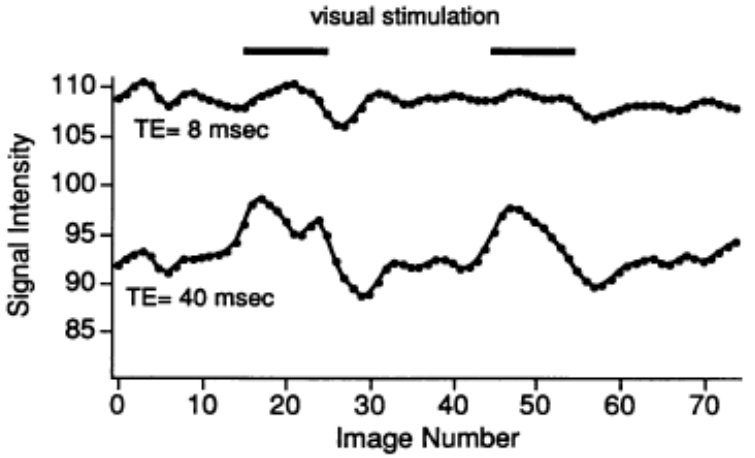

a
2
1
3
1 cm
c
b
d
light
light
Signal Intensity
100
90
80
70
60
2
1
3
0
20
40
60
80
Image Number


visual stimulation
110
105
100
95
90
85
TE= 8 msec
TE= 40 msec
Signal Intensity
0
10
20
30
40
50
60
70
Image Number

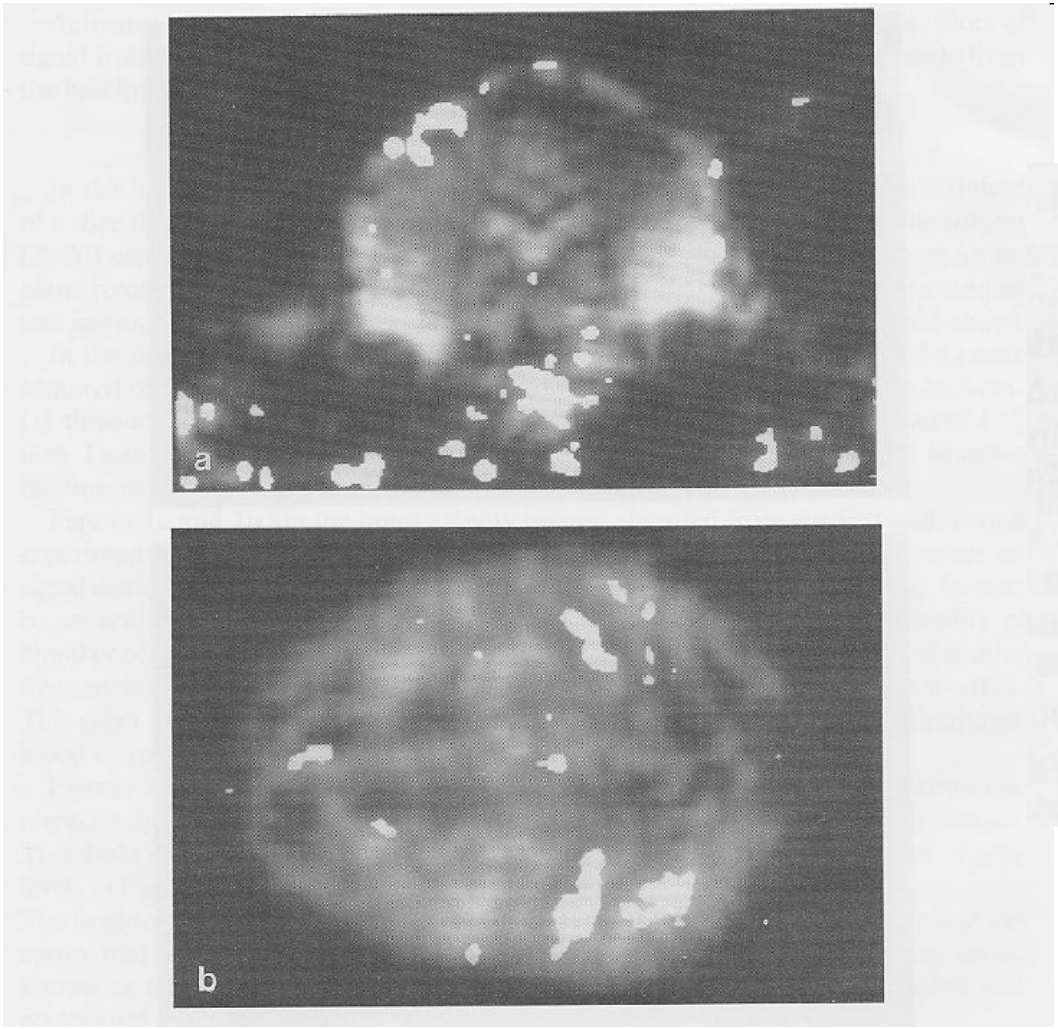

left | right
1 cm
Intensity
148
144
140
136
L
R
0
20
40
60
80
Image Number
112
108
104
100
120
115
110
105

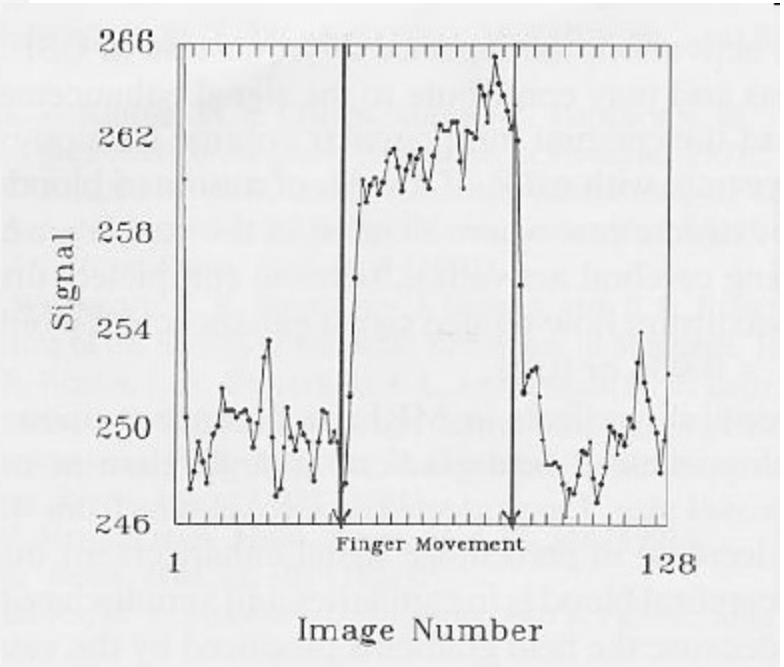
Ogawa et al.


left | right
1 cm
Intensity
Image Number
L
R
148
144
140
136
112
108
104
100
120
115
110
105
0
20
40
60
80


visual stimulation
TE= 8 msec
TE= 40 msec
Signal Intensity
Image Number
110
105
100
95
90
85
0
10
20
30
40
50
60
70

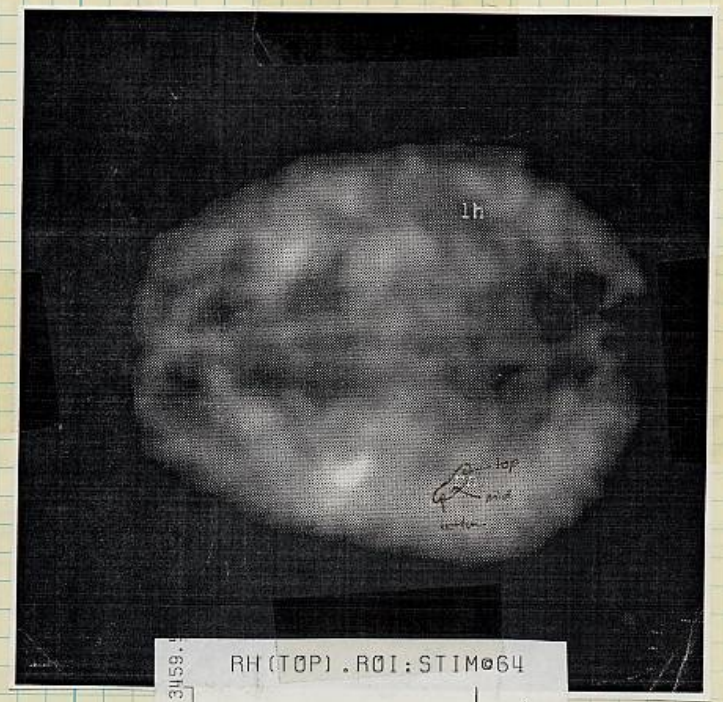
Bandettini et al.

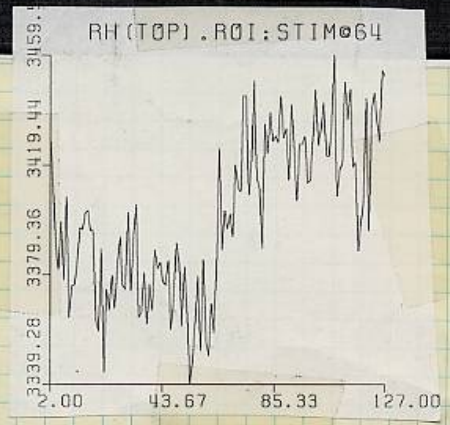




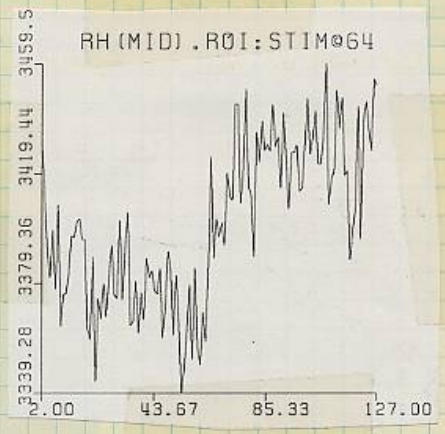
9-16-91 Results from dH61 (sig ↑ upon stim?!!)

Experiment 1: Rest until 63 then move right fingers

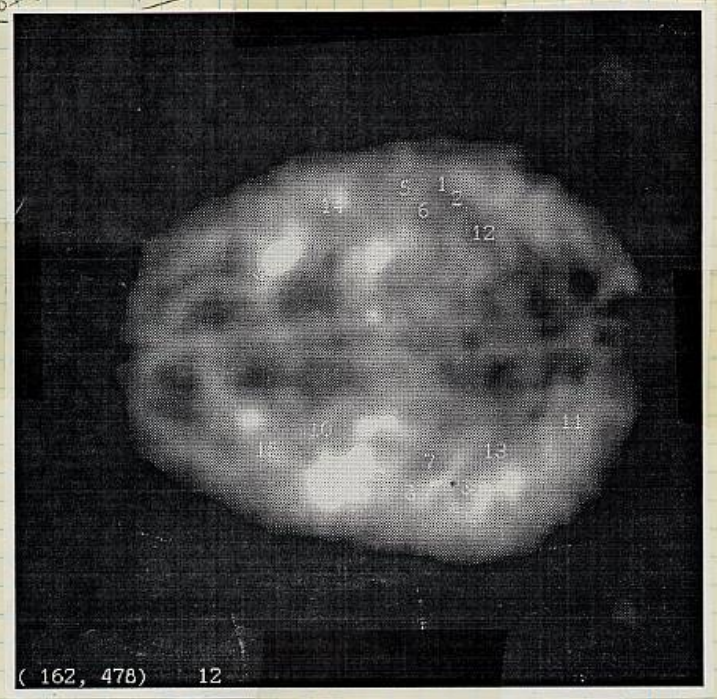




9-16-91



ROI's from p17



9-16-91

Finally, a difference image in which the average of the first 64 images (no movement) is subtracted from the last 64 images (movement of right hand.

Right-Hand Movement

Axial

T2wt

Results.

20 cm / 64

.3125 cm

= 3.125 mm

15/20 15/2

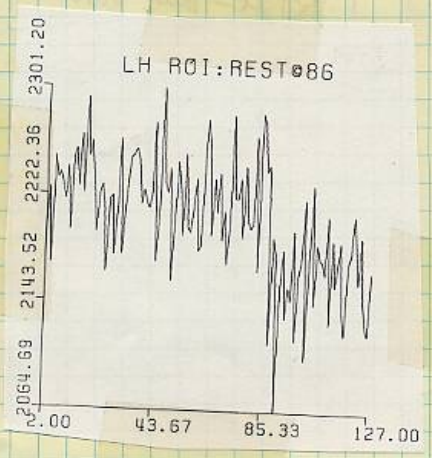
Brightest area is an indicator of largest signal increase when the right hand was stimulated (fingers moved) → exactly corresponds to region of motor cortex and sensory and supplementary motor cortex as well that is associated with right hand movement.

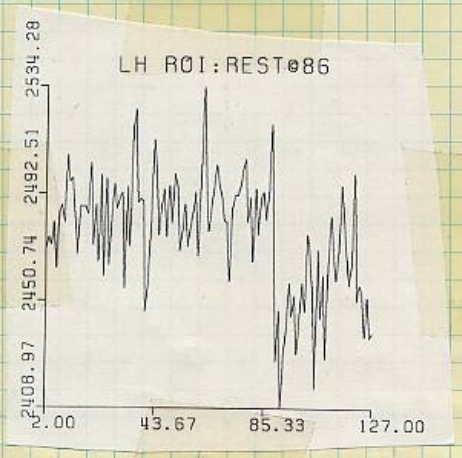
9-16-91

Results from experiment #2

Experiment #2 consisted of moving the left hand and then stopping the movement after 86 images.

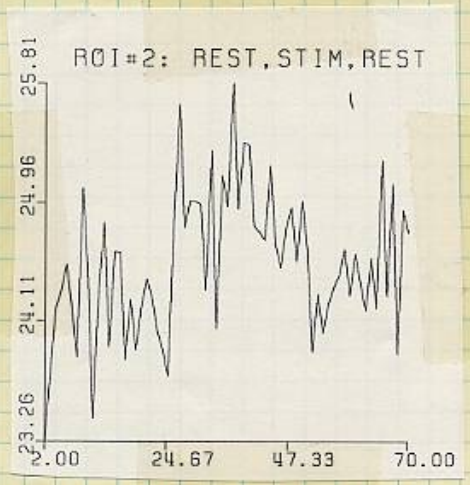
LH ROI From 1/4





9-16-91 Experiment #3

Rest for 24 images, Move both hands for 24, then rest For 24.



Rough Theory of what is going on here:

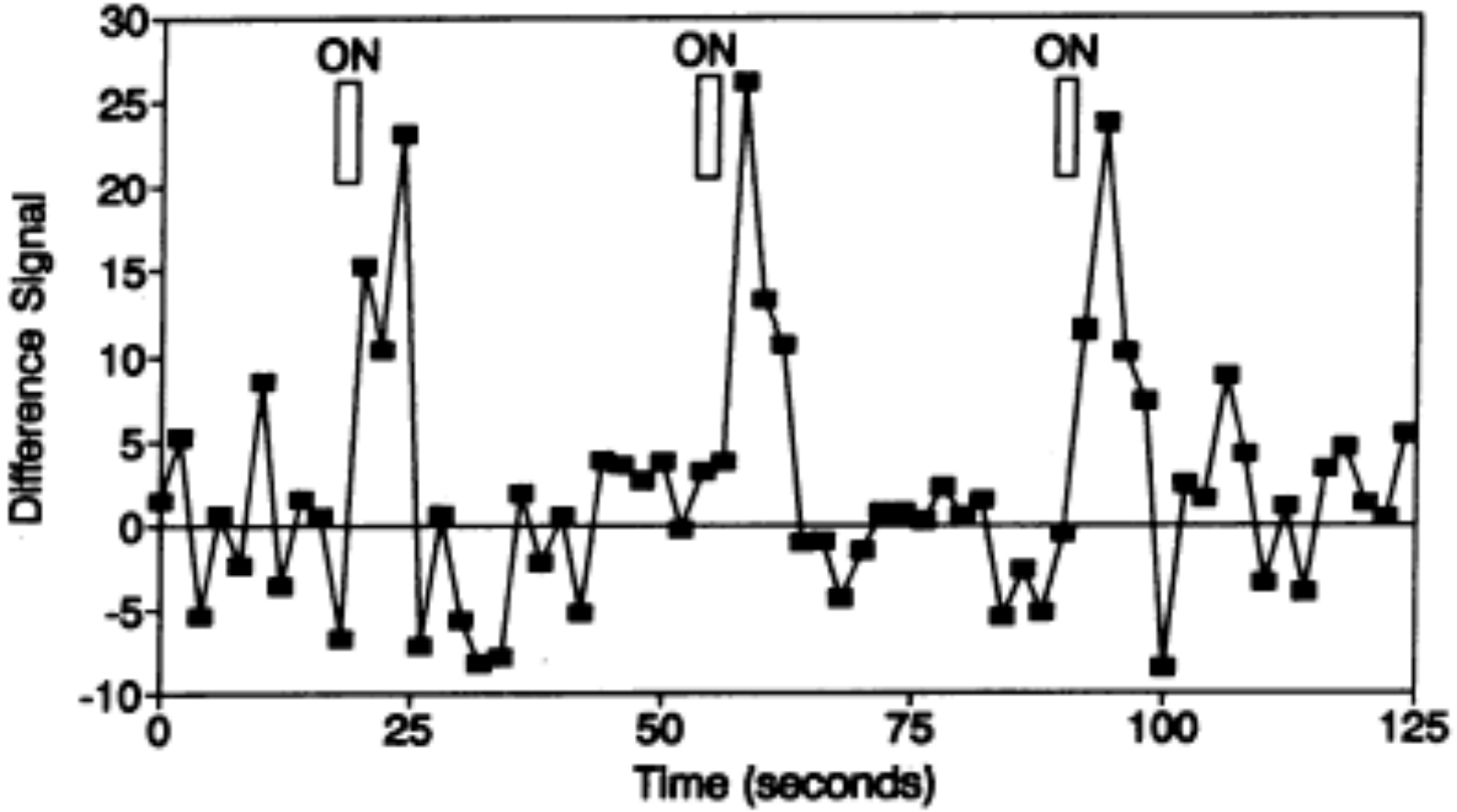
stim nerve → move hand → ↑CO_2 ↑H^+ ↓O_2 in tissue → capillary and vein dilation → ↑ Blood flow → ↓ deoxy at site

↑ signal due to ↓ susceptibility ⇐ Stop stim ← ↑O_2 ↓CO_2 ↓H^+ in tissue ← vaso constriction + cap. ← decreased blood flow ← ↑C_6 deoxyHb at steady state

Question: Relationship between flow volume and bulk susceptibility in capillaries.

1991

Blamire et al.



1992…Perfusion using Arterial Spin Labeling

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

Magnetic resonance imaging of perfusion using spin inversion of arterial water

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

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

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

Communicated by Mildred Cohn, September 19, 1991

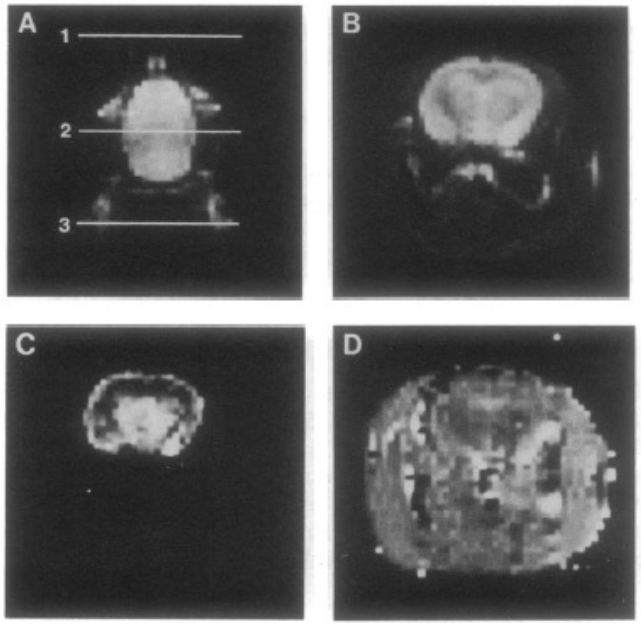


FIG. 2. (*A*) Coronal image of a rat head. The resonance planes for radiofrequency used for spin inversion by AFP for control and inversion images are indicated by 1 and 3, respectively, and plane 2 is the detection plane. (*B*) Control transverse image from the detection plane (plane 2 in *A*). (*C*)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

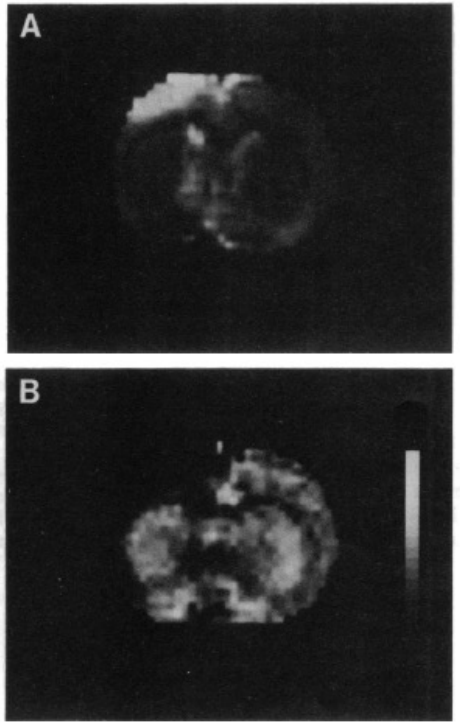
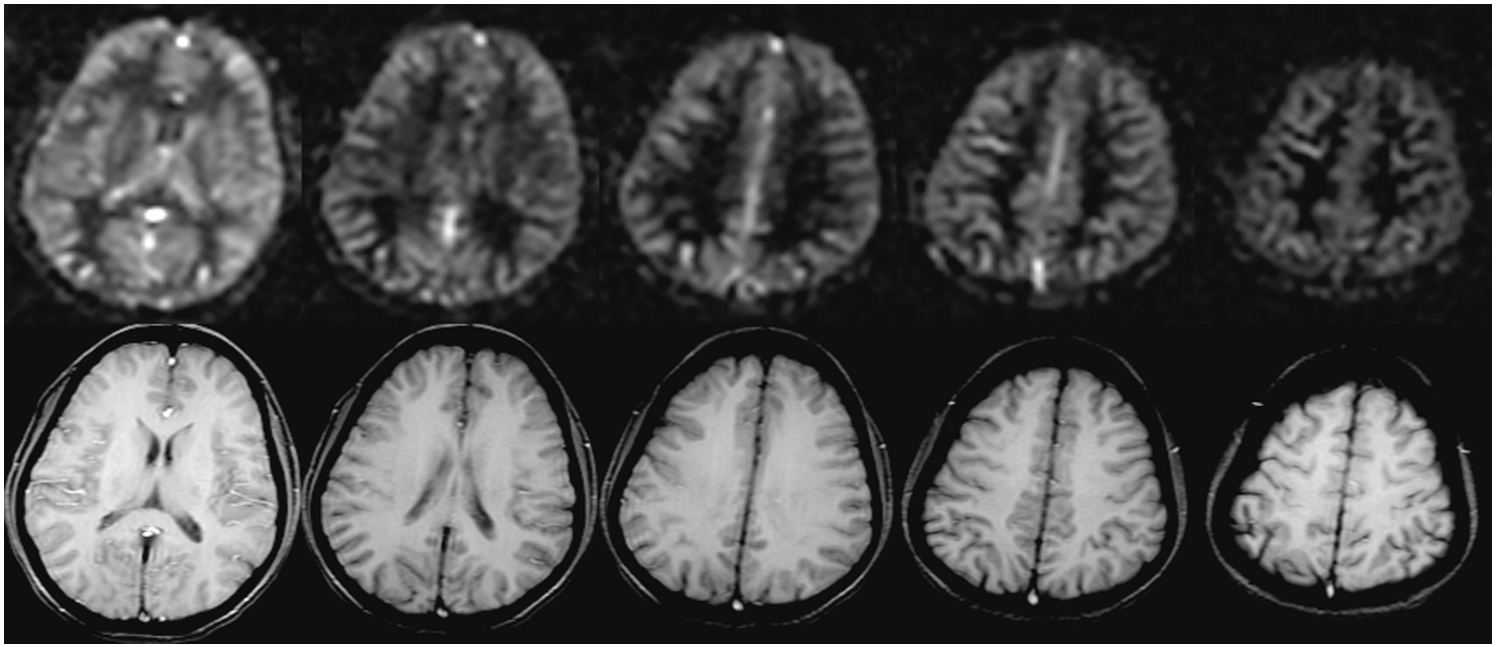


FIG. 5. Comparison of conventional MRI and perfusion imaging of a rat brain subjected to a regional cold injury. (*A*) Conventional T_2-weighted image (TE = 60 ms, TR = 2 s). The injured region shows up as hyperintensity due to a longer T_2. (*B*) Perfusion image of the same slice. The grey scale is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



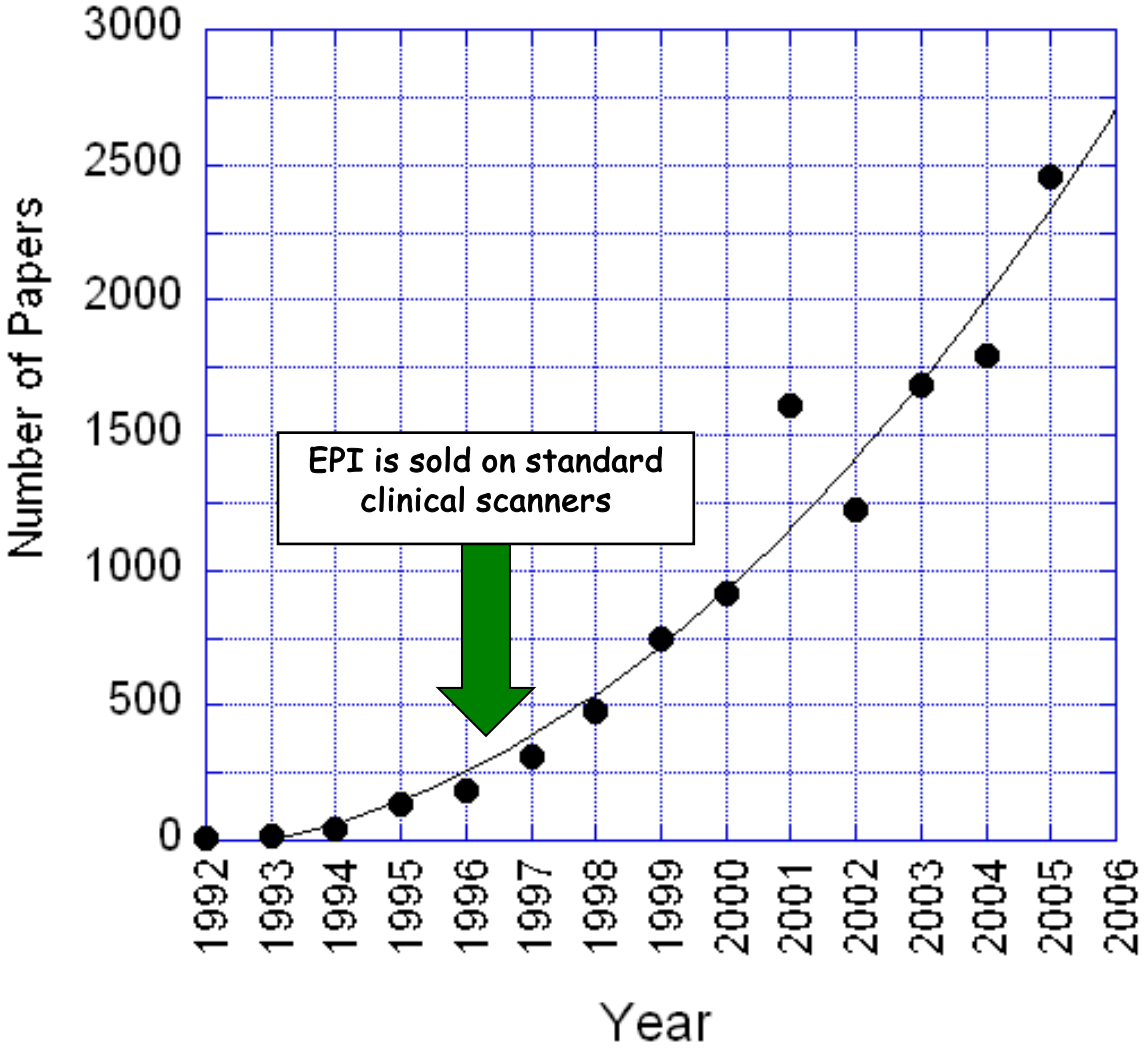
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." **Proc. Natl. Acad. Sci. USA 89, 212-216.**

Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR)." **Radiology 192, 1-8.**

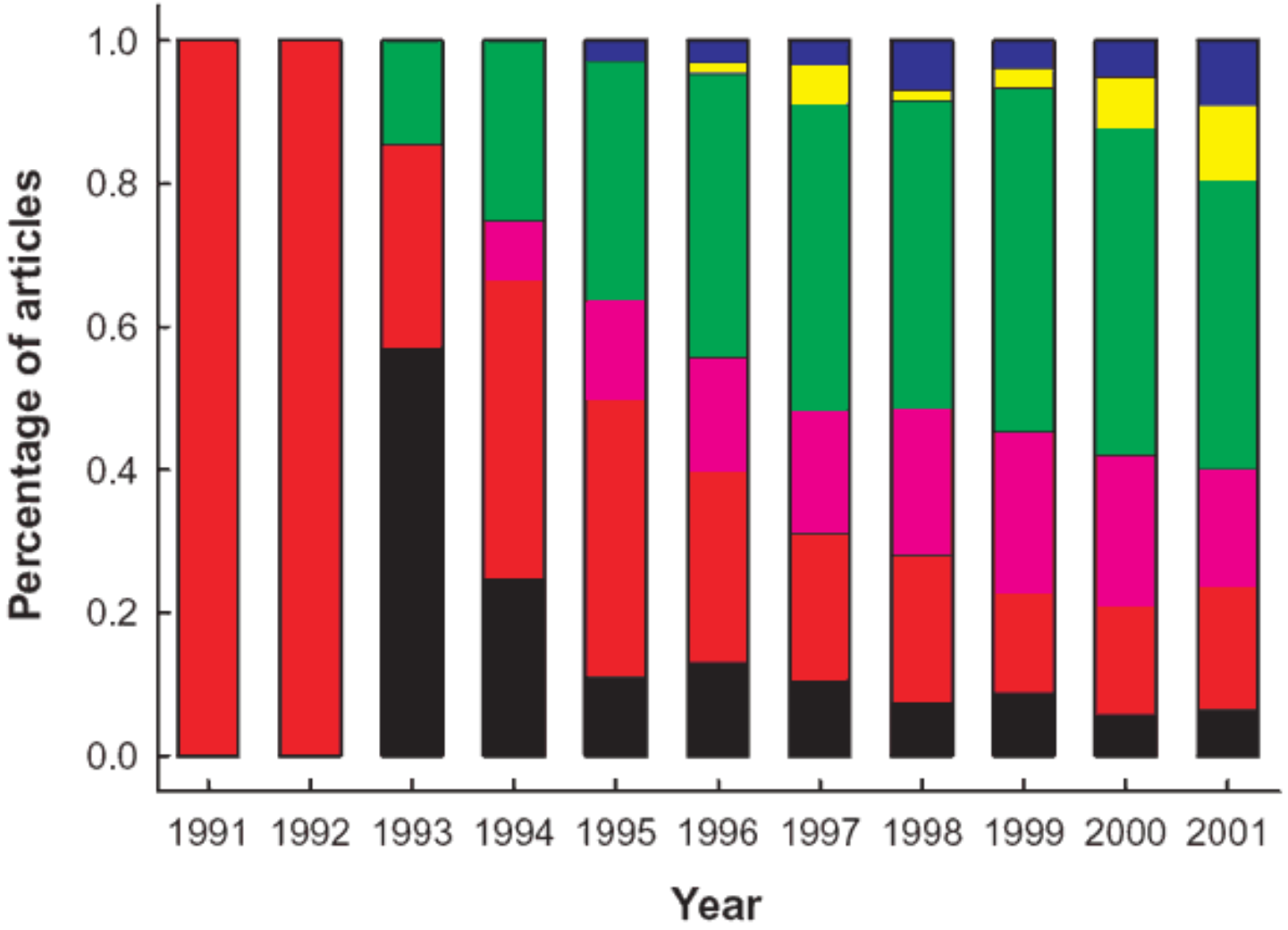
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." **Magn. Reson. Med. 34, 293-301.**

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

fMRI Papers Published per Year



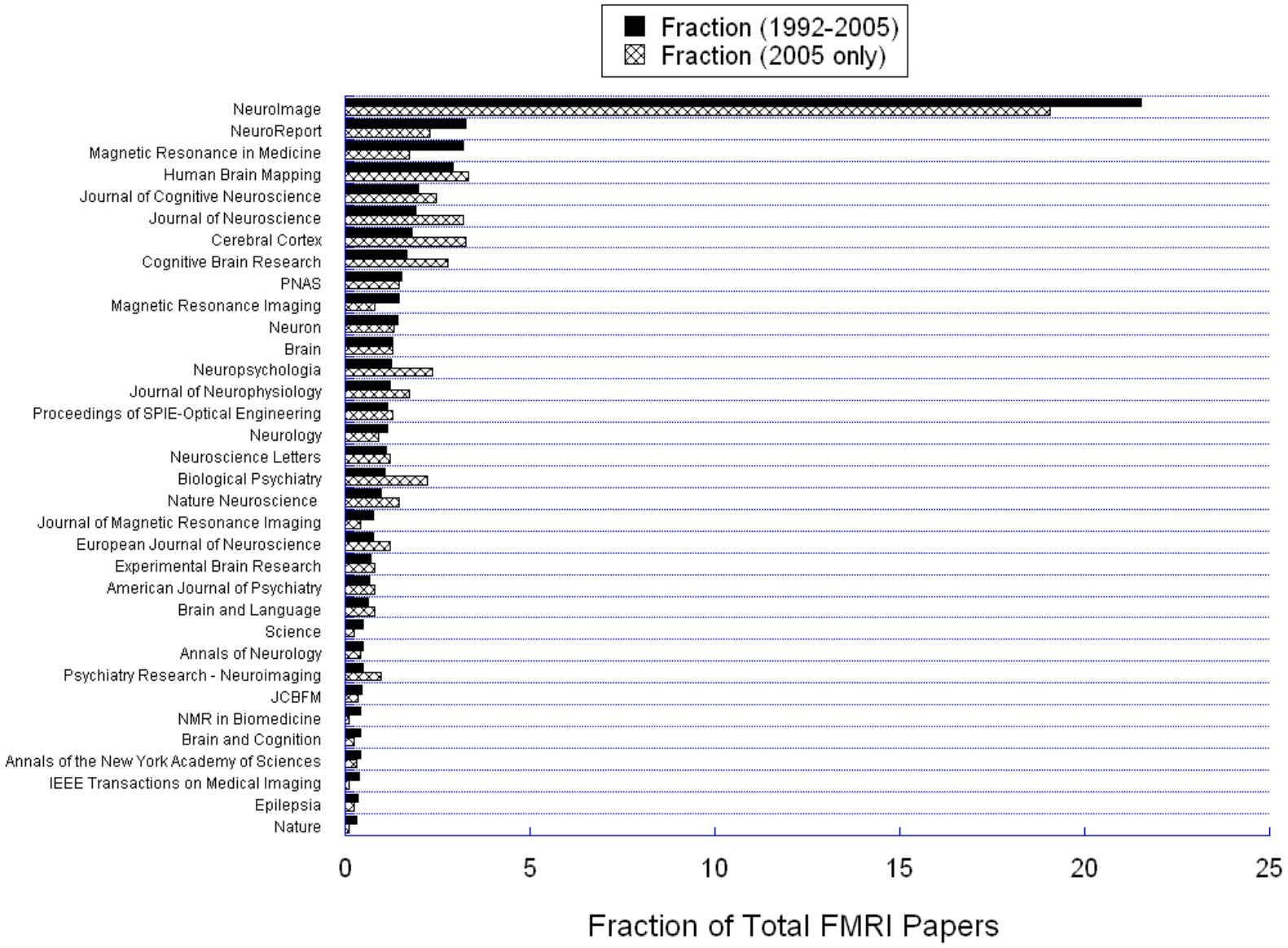
"fMRI" or "functional MRI"

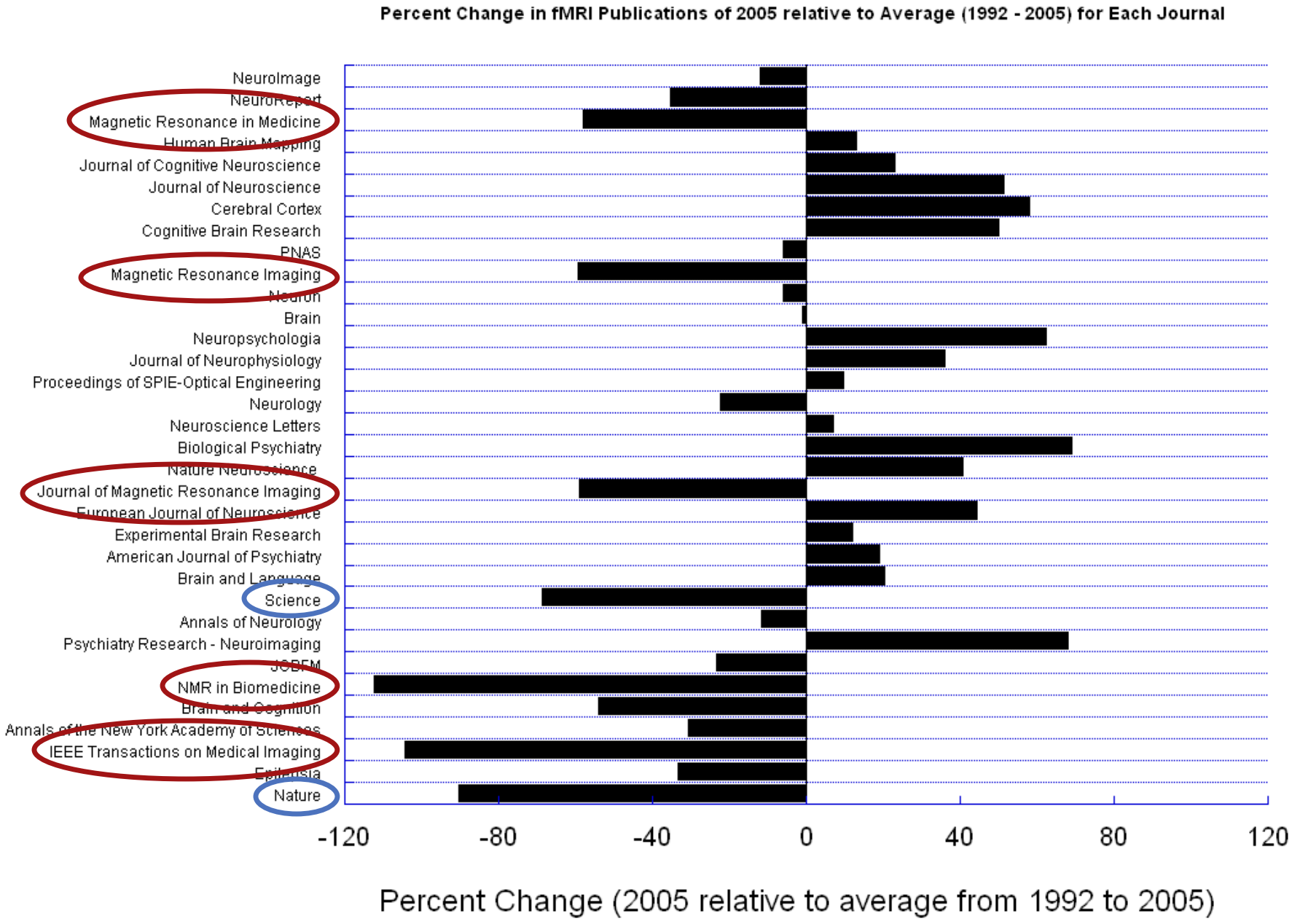


Motor (black)
Primary Sensory (red)
Integrative Sensory (violet)
Basic Cognition (green)
High-Order Cognition (yellow)
Emotion (blue)

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

Breakdown of fMRI papers by Journal




Percent Change in fMRI Publications of 2005 relative to Average (1992 - 2005) for Each Journal
NeuroImage
NeuroReport
Magnetic Resonance in Medicine
Human Brain Mapping
Journal of Cognitive Neuroscience
Journal of Neuroscience
Cerebral Cortex
Cognitive Brain Research
PNAS
Magnetic Resonance Imaging
Neuron
Brain
Neuropsychologia
Journal of Neurophysiology
Proceedings of SPIE-Optical Engineering
Neurology
Neuroscience Letters
Biological Psychiatry
Nature Neuroscience
Journal of Magnetic Resonance Imaging
European Journal of Neuroscience
Experimental Brain Research
American Journal of Psychiatry
Brain and Language
Science
Annals of Neurology
Psychiatry Research - Neuroimaging
JOBFM
NMR in Biomedicine
Brain and Cognition
Annals of the New York Academy of Sciences
IEEE Transactions on Medical Imaging
Epilepsia
Nature
-120
-80
-40
0
40
80
120
Percent Change (2005 relative to average from 1992 to 2005)

Technology

Magnet
RF Coils
Pulse Sequences

Methodology

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

Interpretation

Increases
Decreases
Dynamics
Locations

Applications

Neuroscience
Physiology
Genetics
Practical Clinical

Technology

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

Methodology

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

Fluctuations
Dynamics
Cross - modal comparison

Interpretation

Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

Applications

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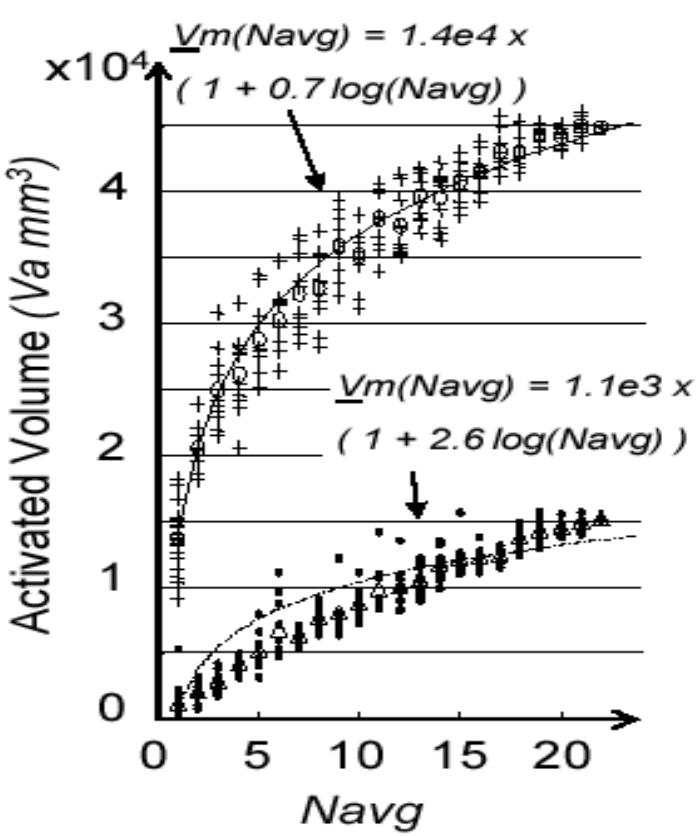
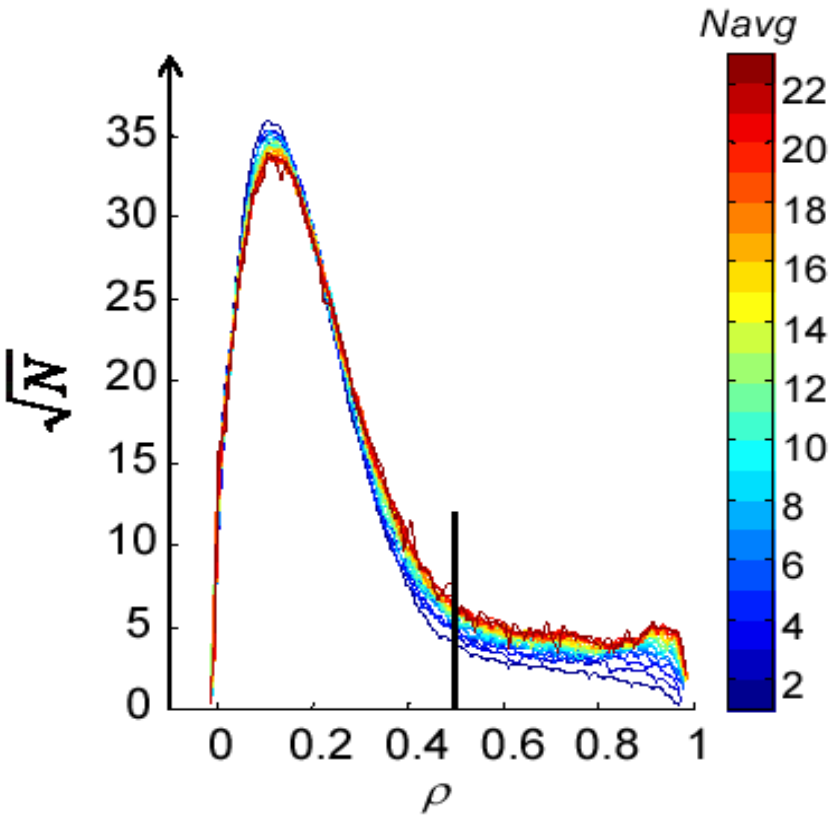
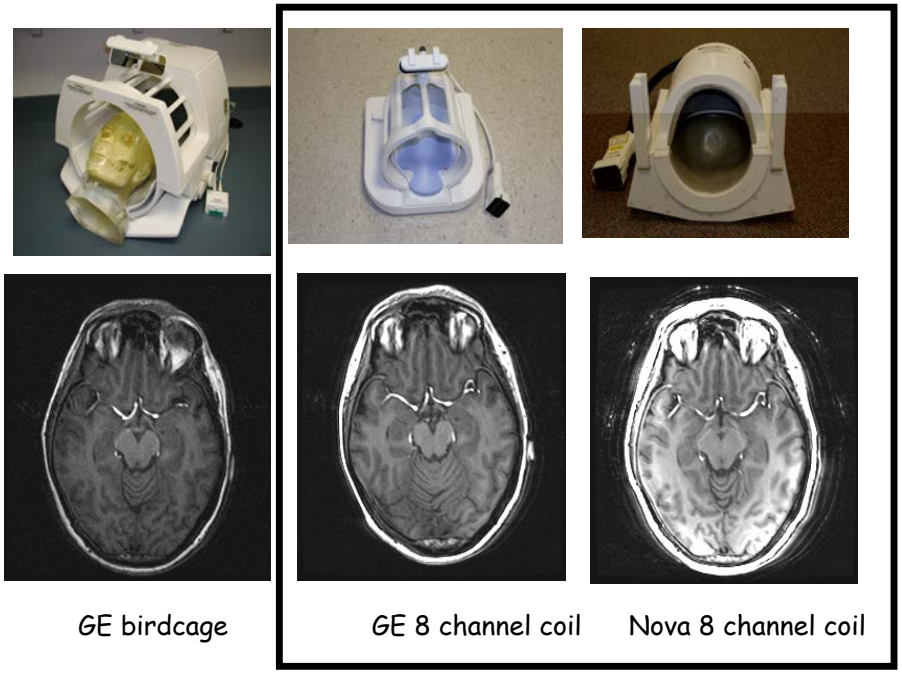




Z. S. Saad, K. M. Ropella, E. A. DeYoe, P. A. Bandettini, The spatial extent of the BOLD response. NeuroImage, 19: 132-144, (2003)

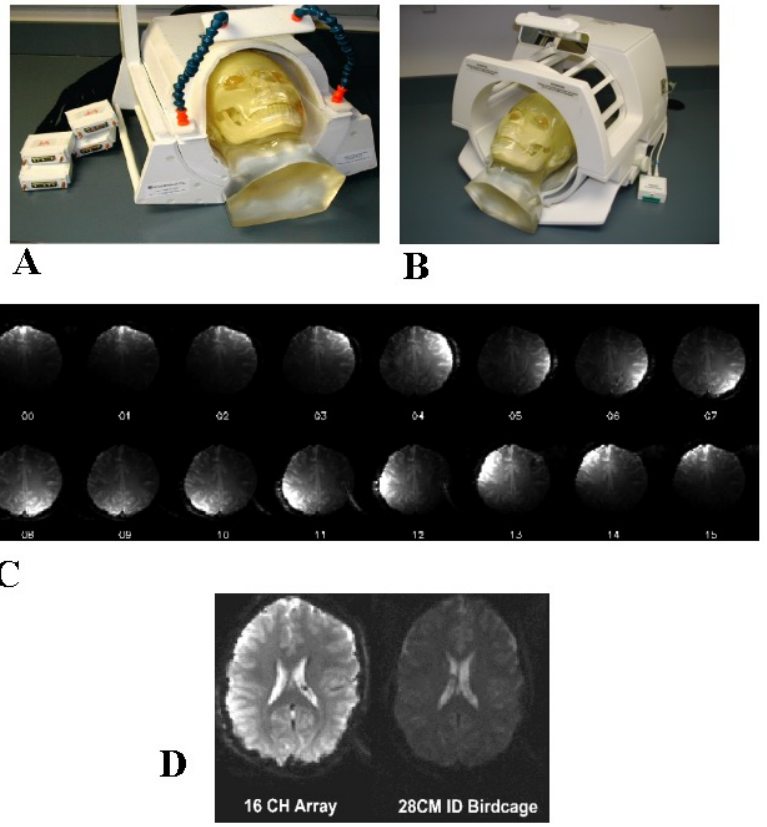
Technology

8 channel parallel receiver coil



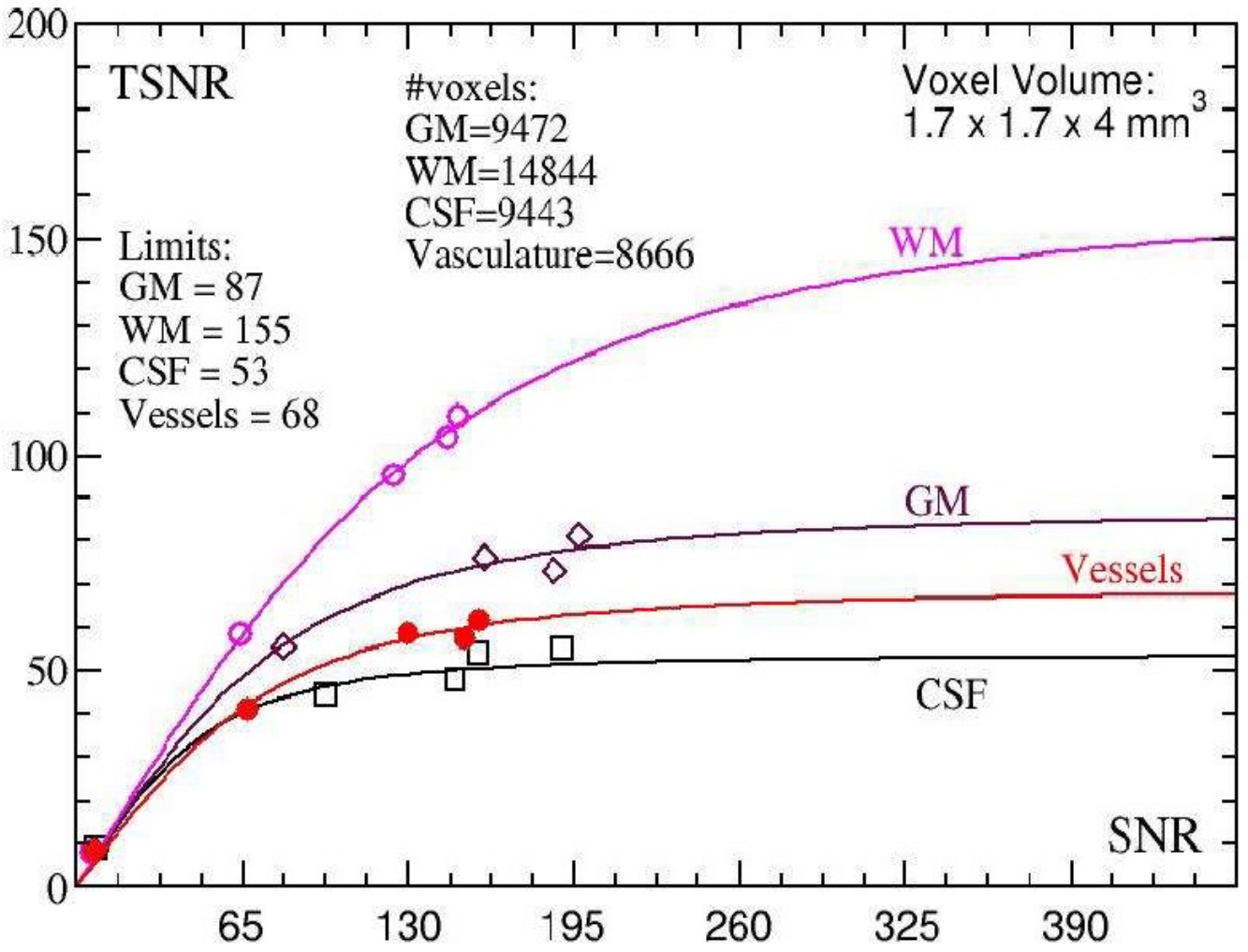
GE birdcage | GE 8 channel coil | Nova 8 channel coil

16 channel parallel receiver coil



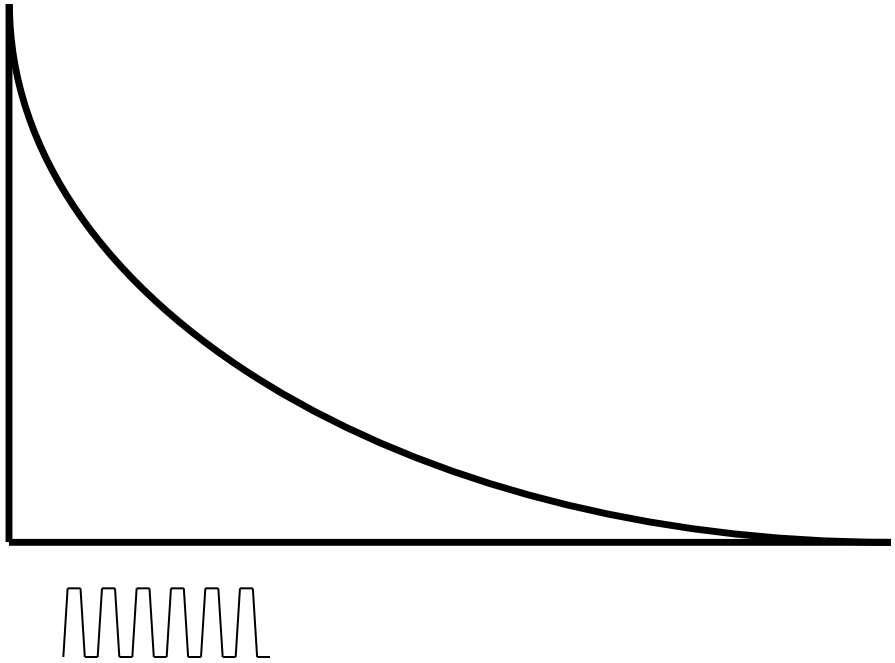
J. Bodurka, et al, Magnetic Resonance in Medicine 51 (2004) 165-171.

Technology

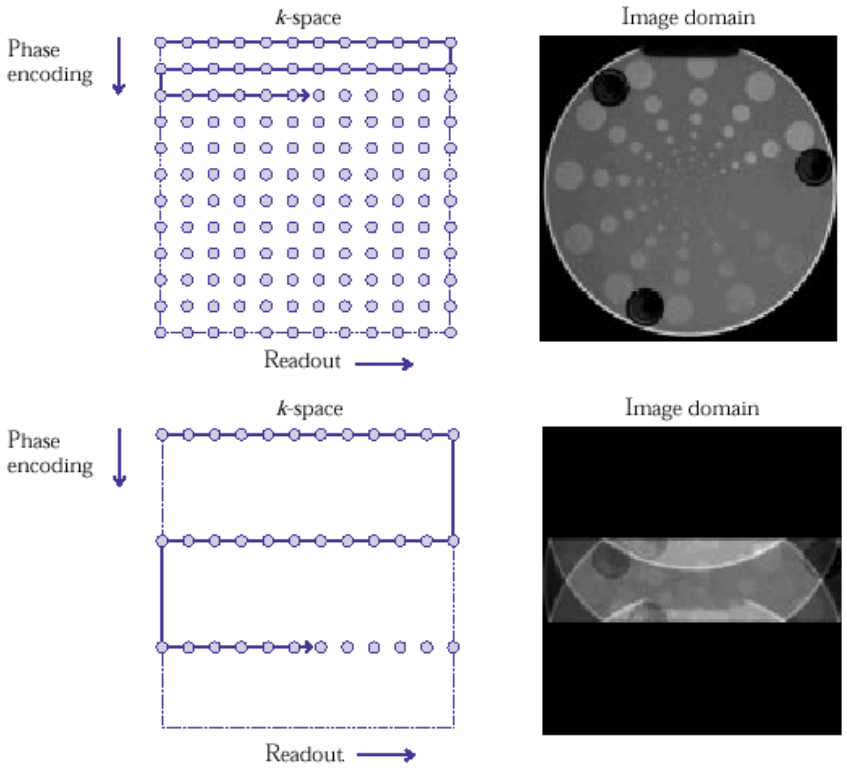


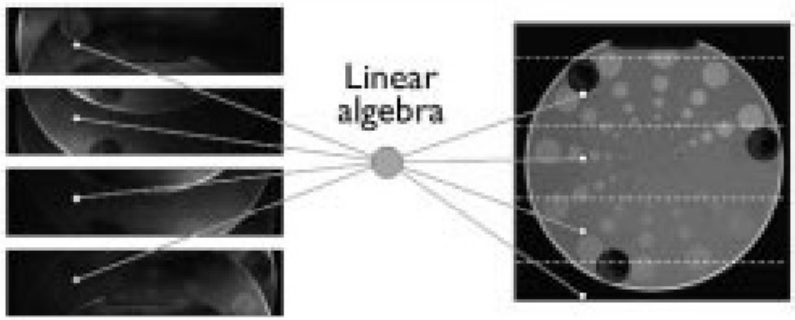
J. Bodurka

Technology



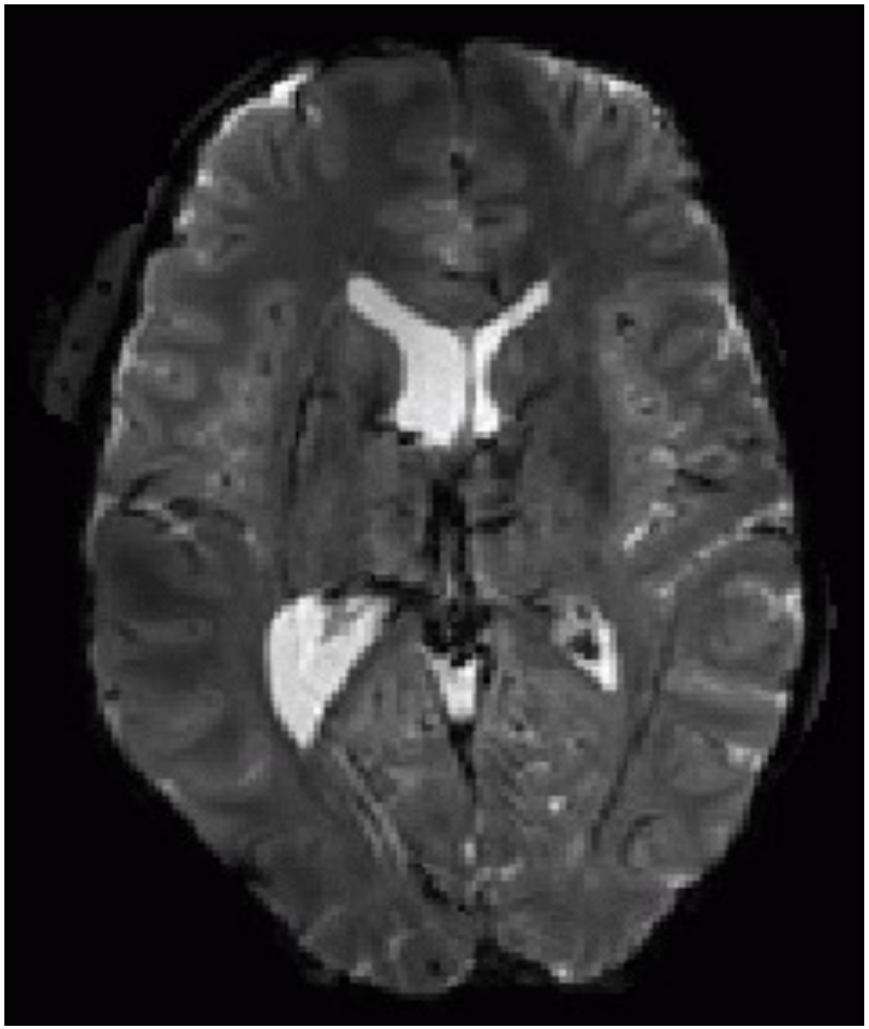
≈ 5 to 30 ms





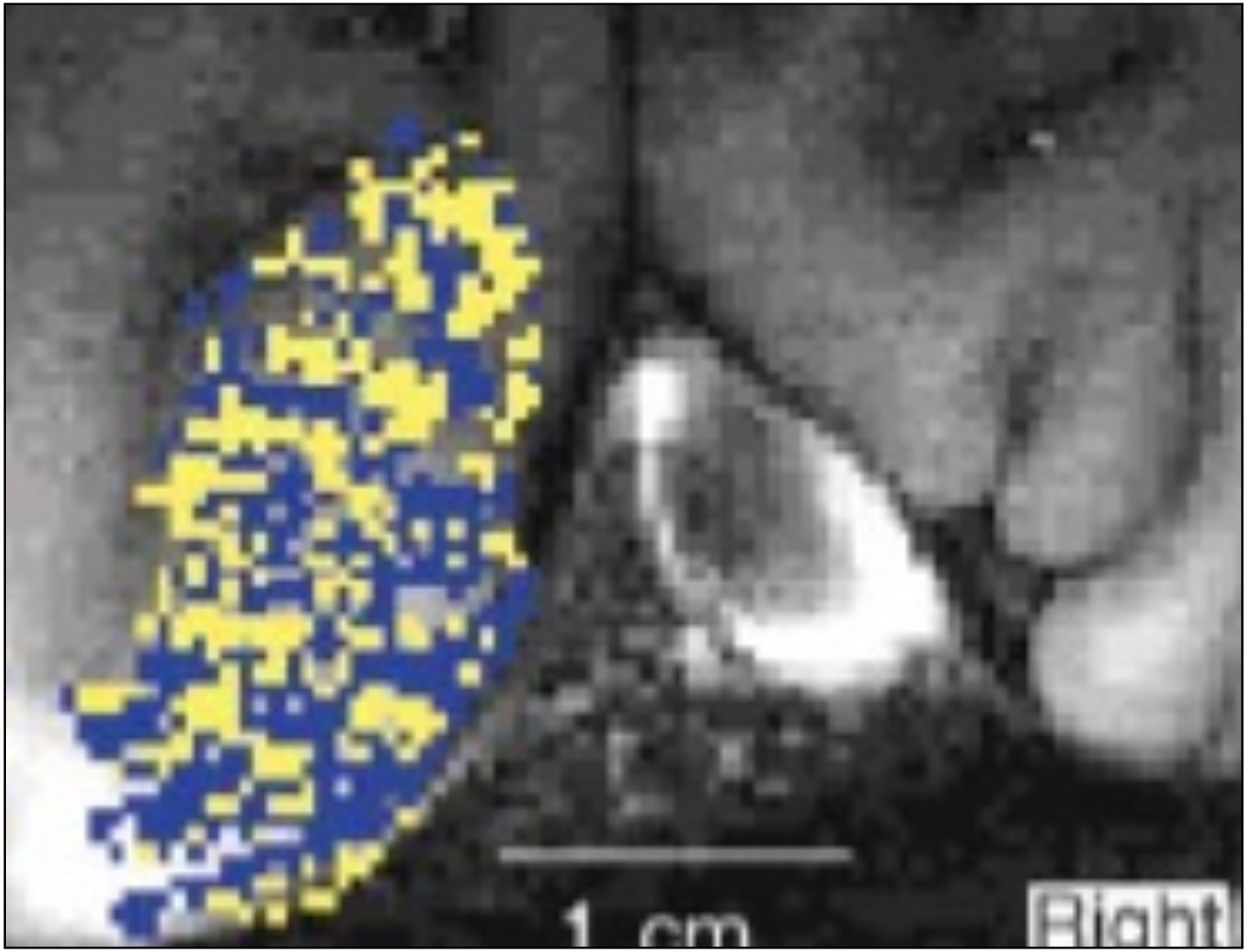
Pruessmann, et al.

Technology



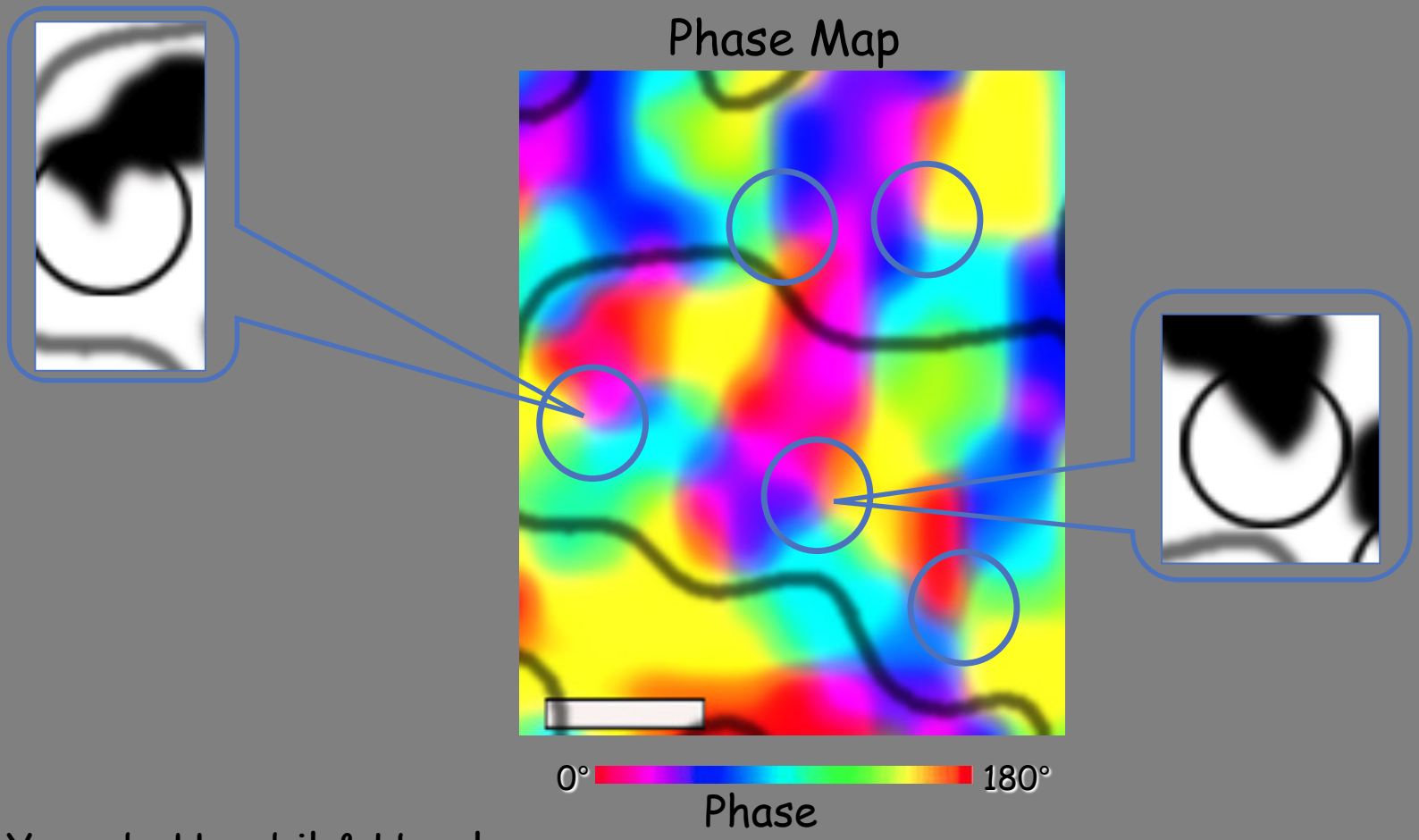
3T single-shot SENSE EPI using 16 channels: 1.25x1.25x2mm

Technology



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

Orientation Columns in Human V1 as Revealed by fMRI at 7T

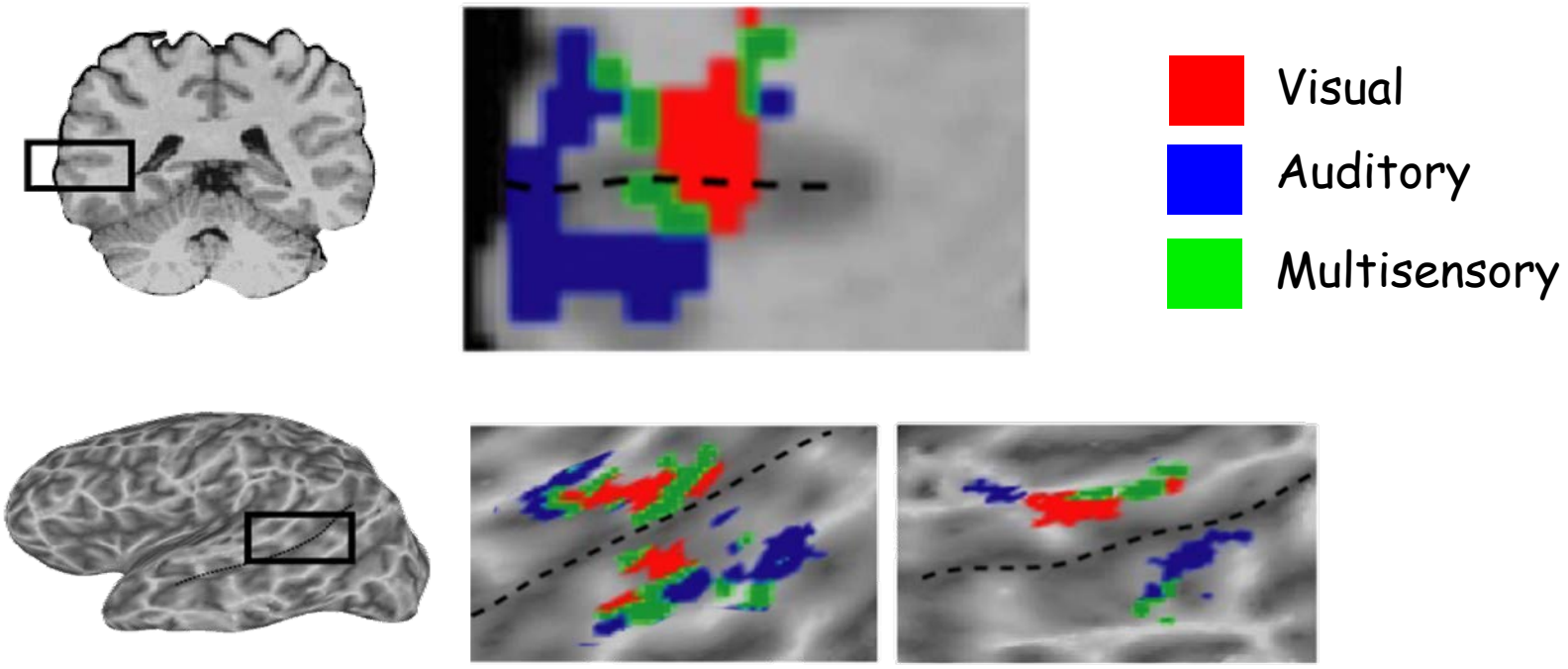


Yacoub, Ugurbil & Harel
University of Minnesota / CMRR
HBM 2006: Thursday, June 15, 2006 at 9:30

Scalebar = 0.5 mm

Multi-sensory integration

M.S. Beauchamp et al.,

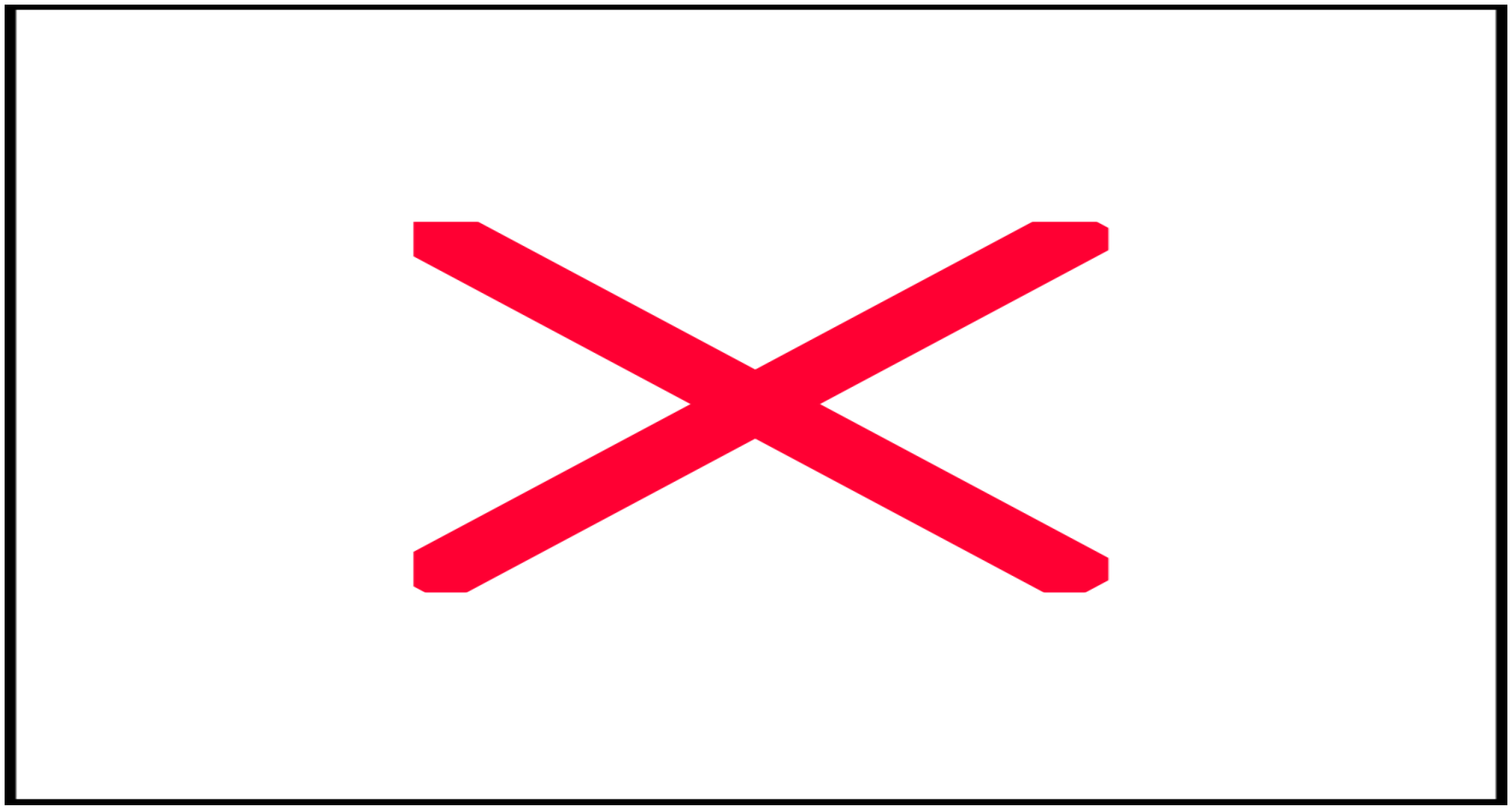


Technology

fiber bundles?

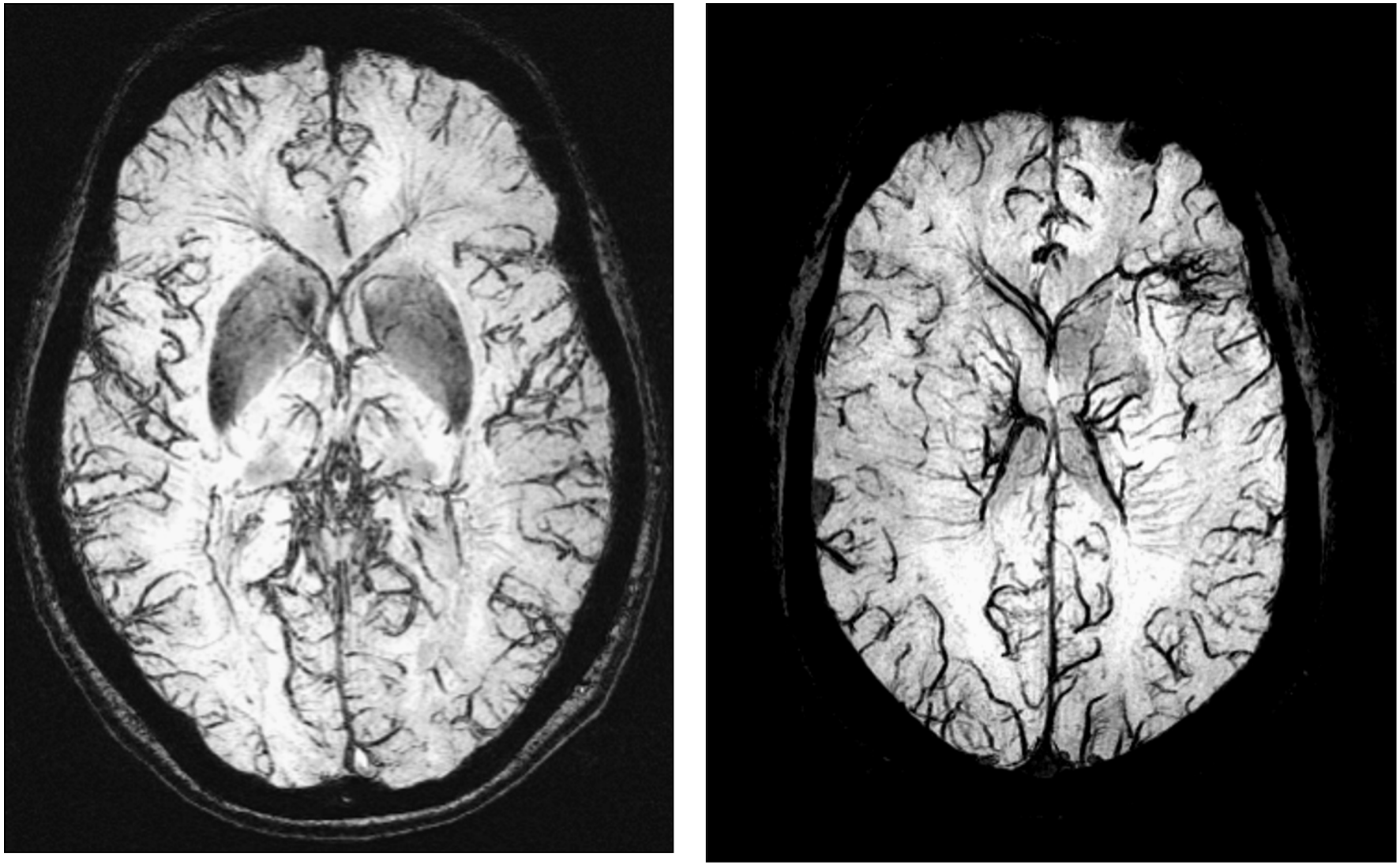
Courtesy Tie-Qiang Li, NINDS

Progression of Human MRI Scanner Field Strength



Technology

BOLD effect "SWI" highlights veins: 3 Tesla



Bove-Bettis, et al (2004), SMRT

fMRI Contrast

- Volume (gadolinium)
- BOLD (GE and SE)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Diffusion coefficient
- Temperature

Technology

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

Methodology

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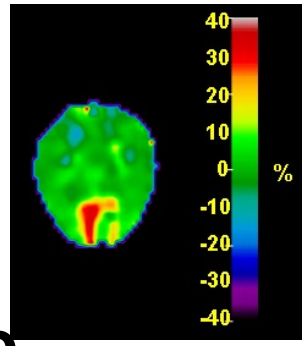
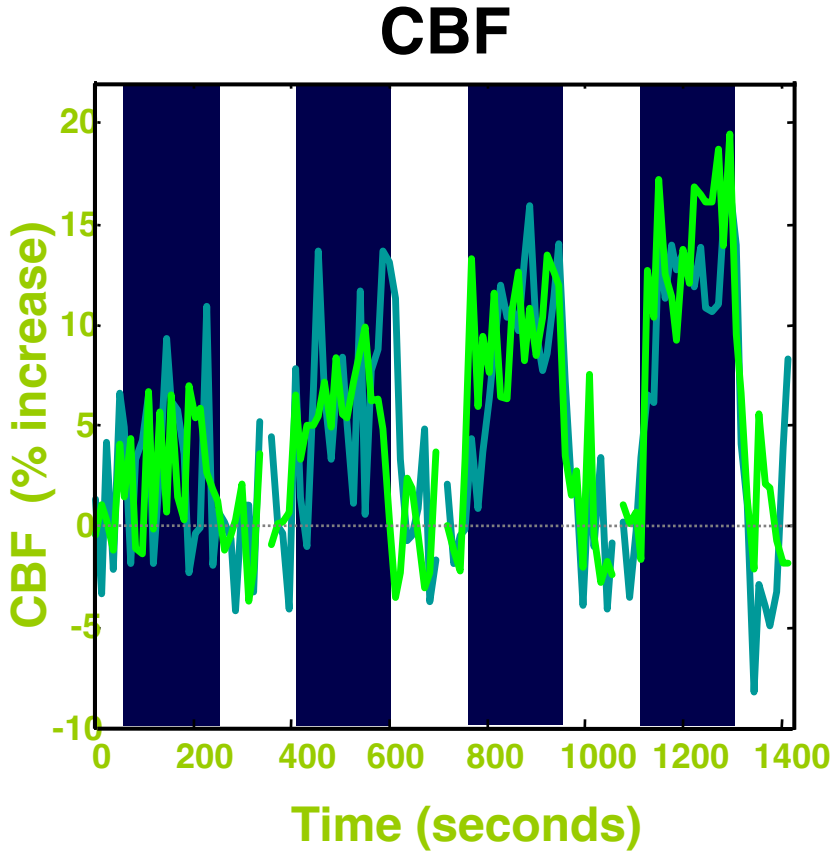
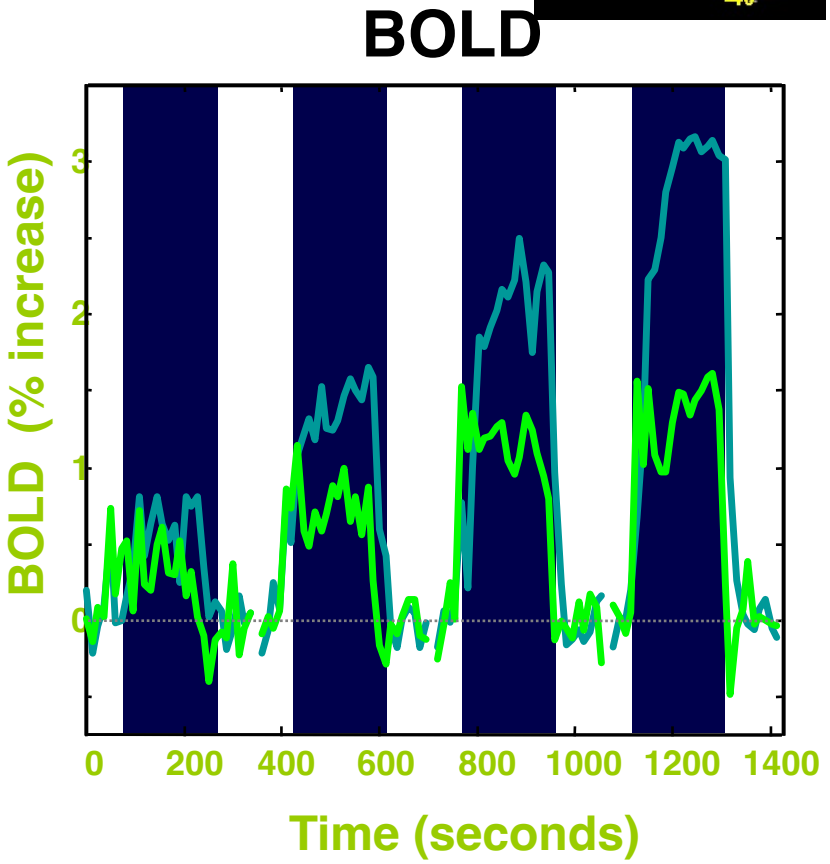
R. Hoge, et al. **Linear coupling between cerebral blood flow and oxygen consumption in activated human cortex**, PNAS, 96, 9403-9408







Simultaneous Perfusion and BOLD imaging during graded visual activation and hypercapnia

N=12

Methodology

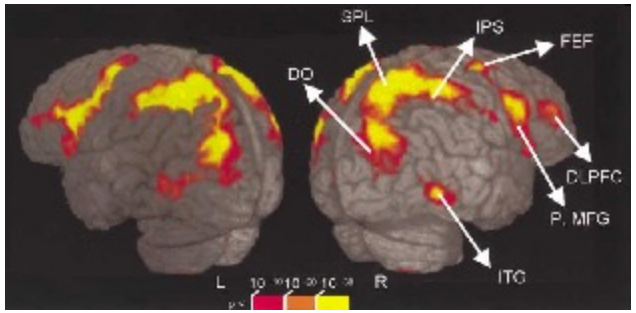
Mapping ⟷ "Reading"

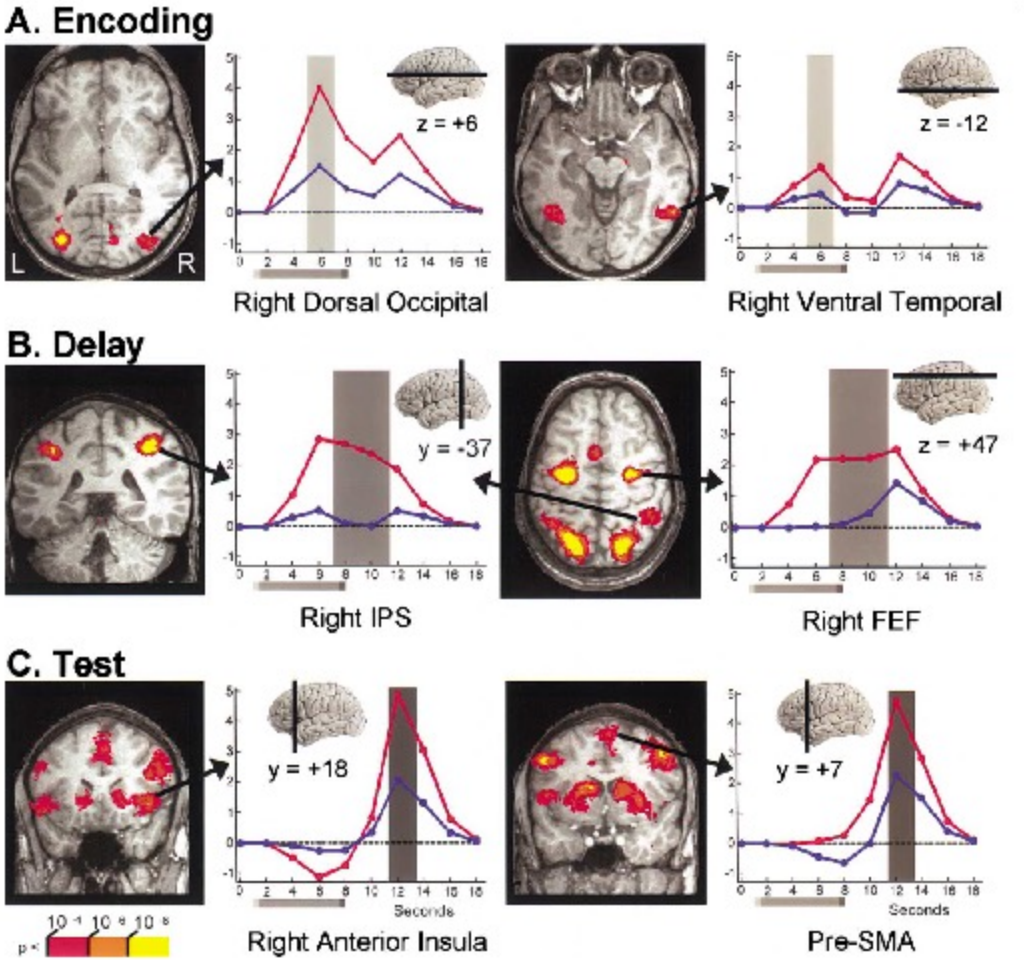
Methodology

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

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

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

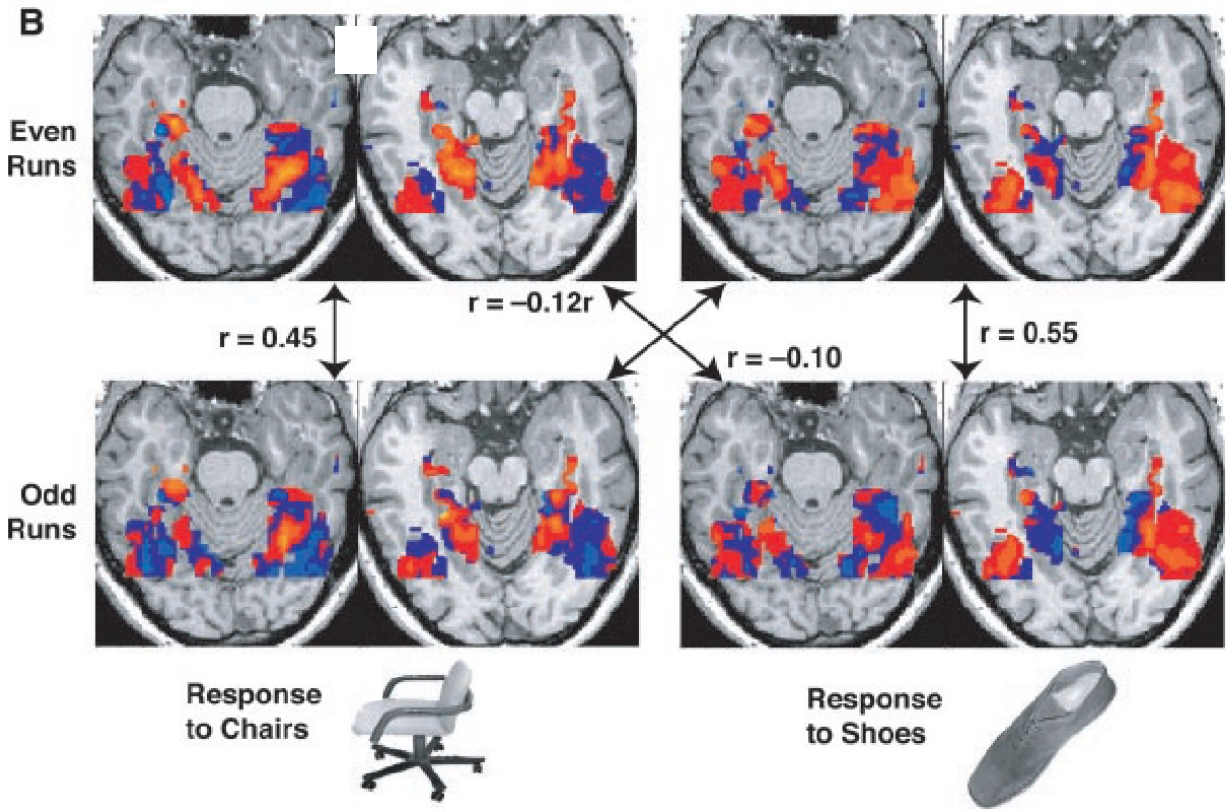




Methodology

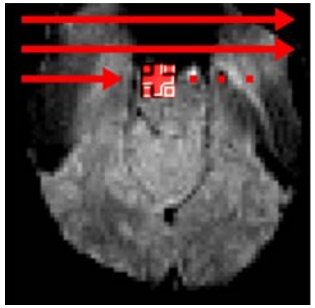
Ventral temporal category representations

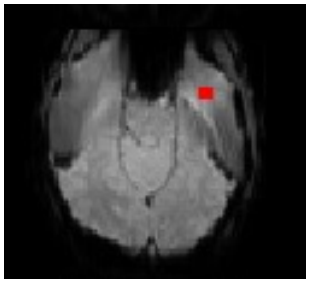
Object categories are associated with distributed representations in ventral temporal cortex

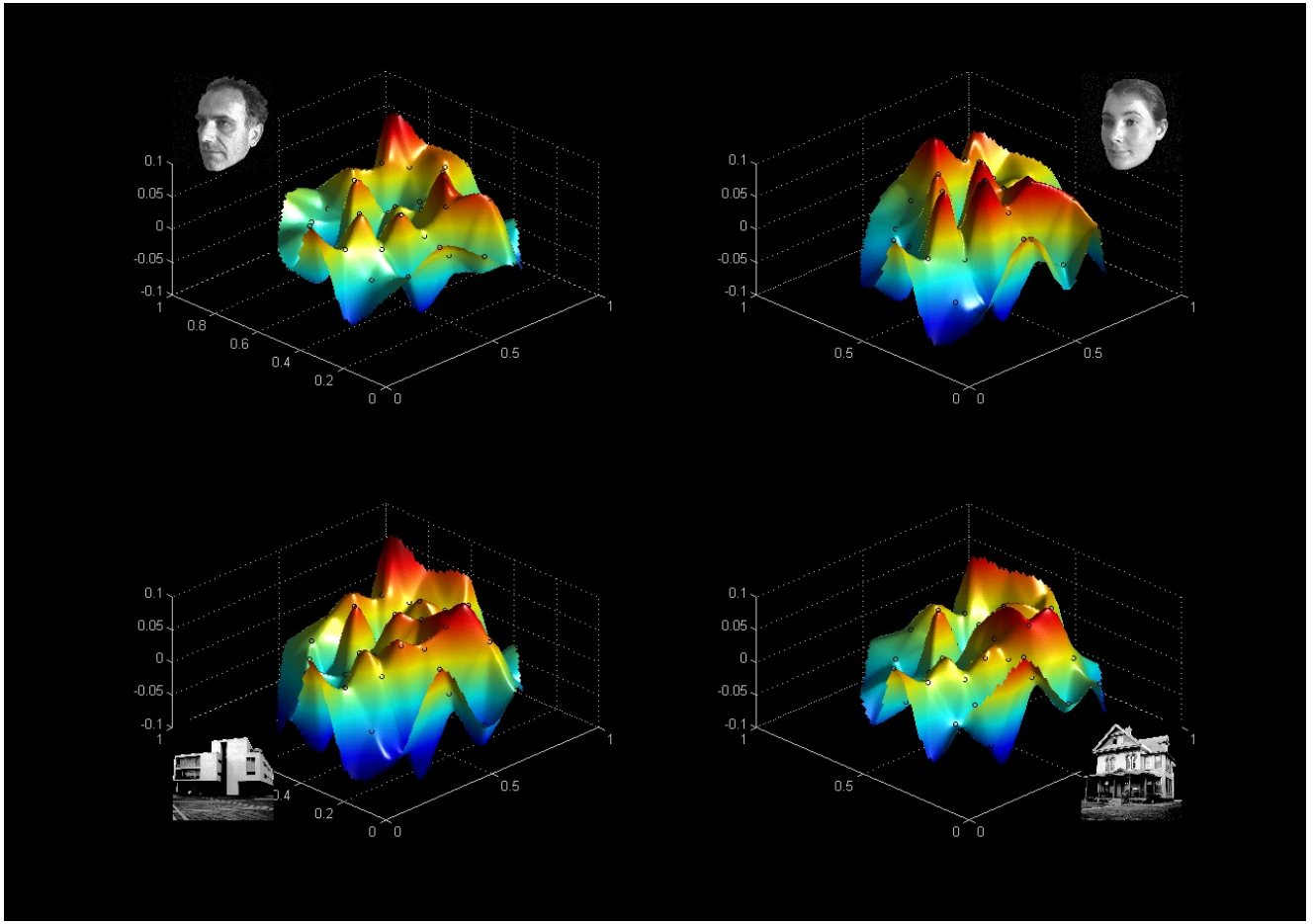


Haxby et al. 2001

Multivariate Analysis:
looking for differences in pattern







Niko Kriegeskorte, NIH

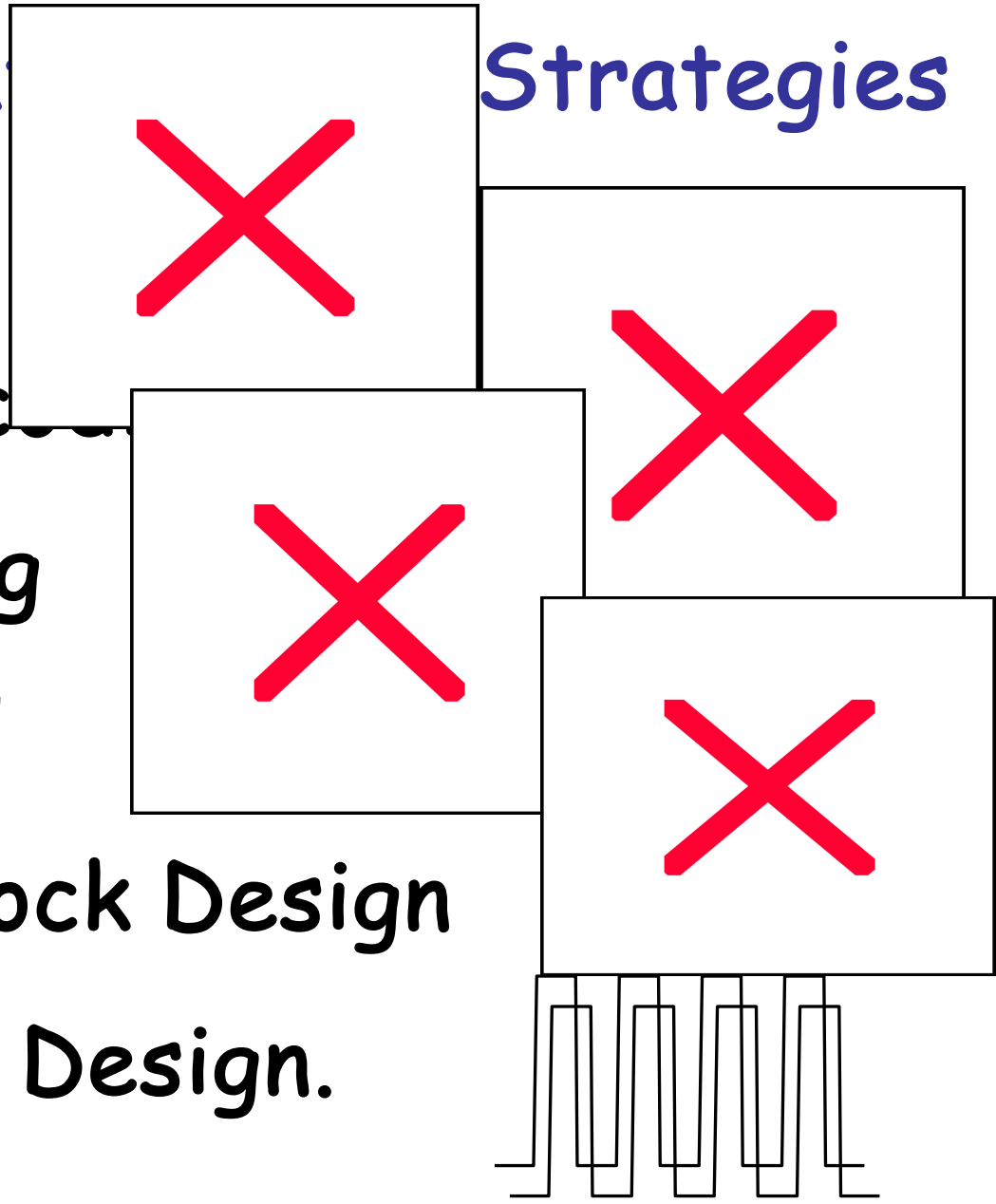
Pattern-recognition analysis of fMRI activity patterns

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

Methodology

Neuronal Activa Strategies

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



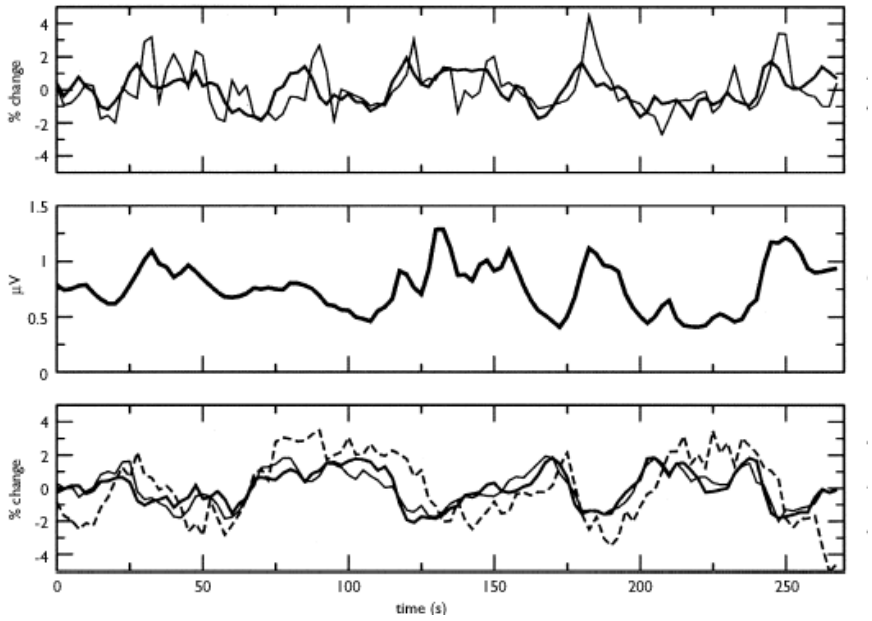
Methodology

BOLD correlated with 10 Hz power during "Rest"

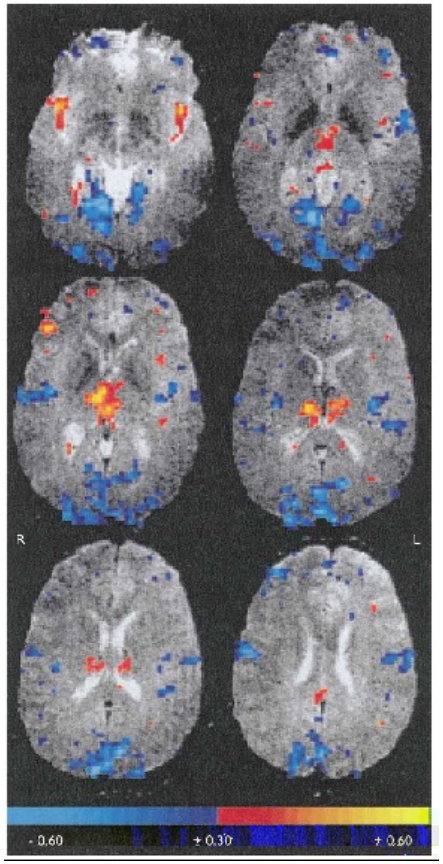
Positive

10 Hz power

Negative

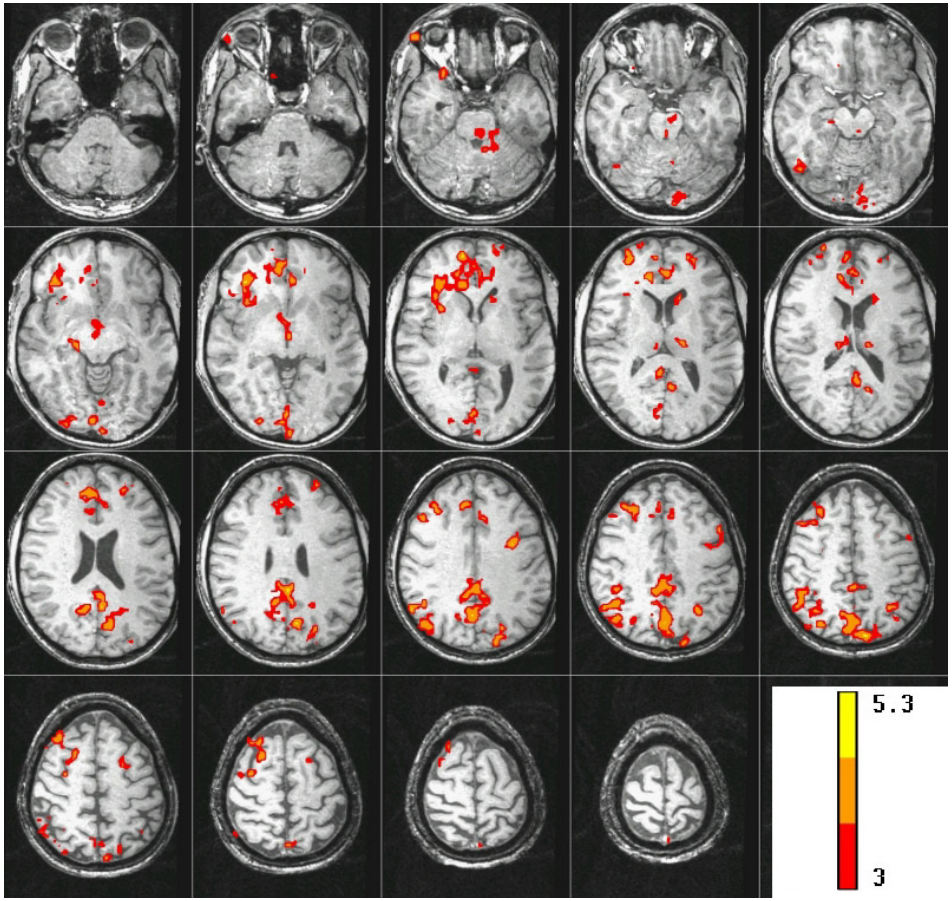


Goldman, et al (2002), Neuroreport



Methodology

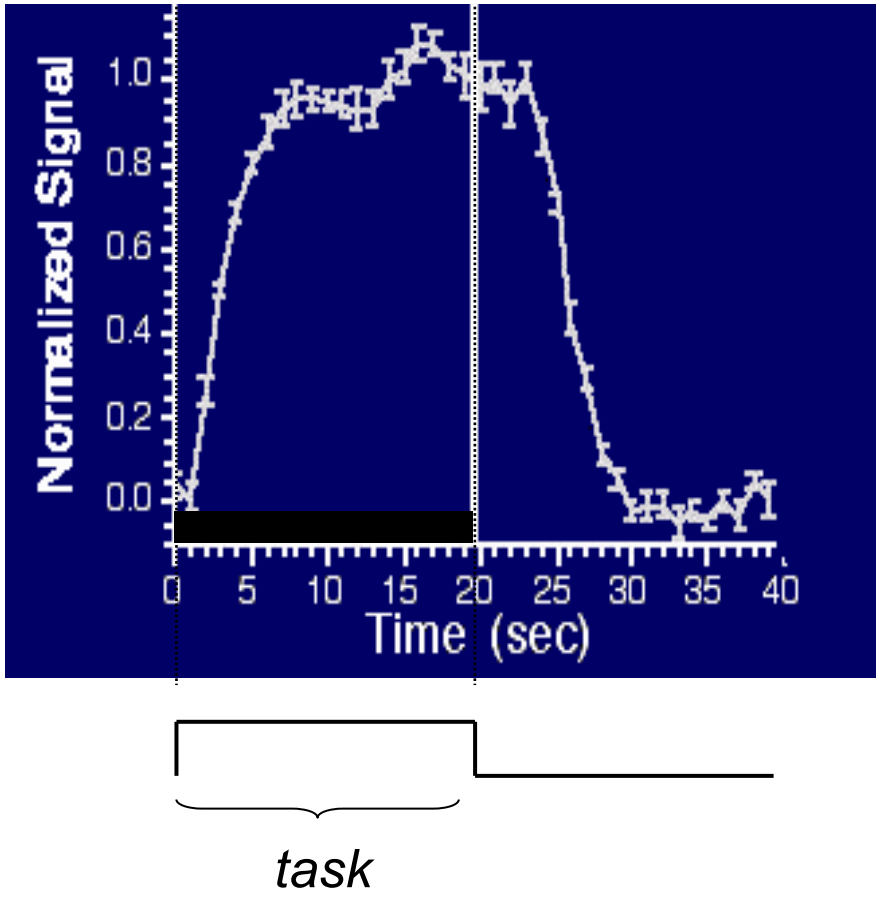
BOLD correlated with SCR during "Rest"

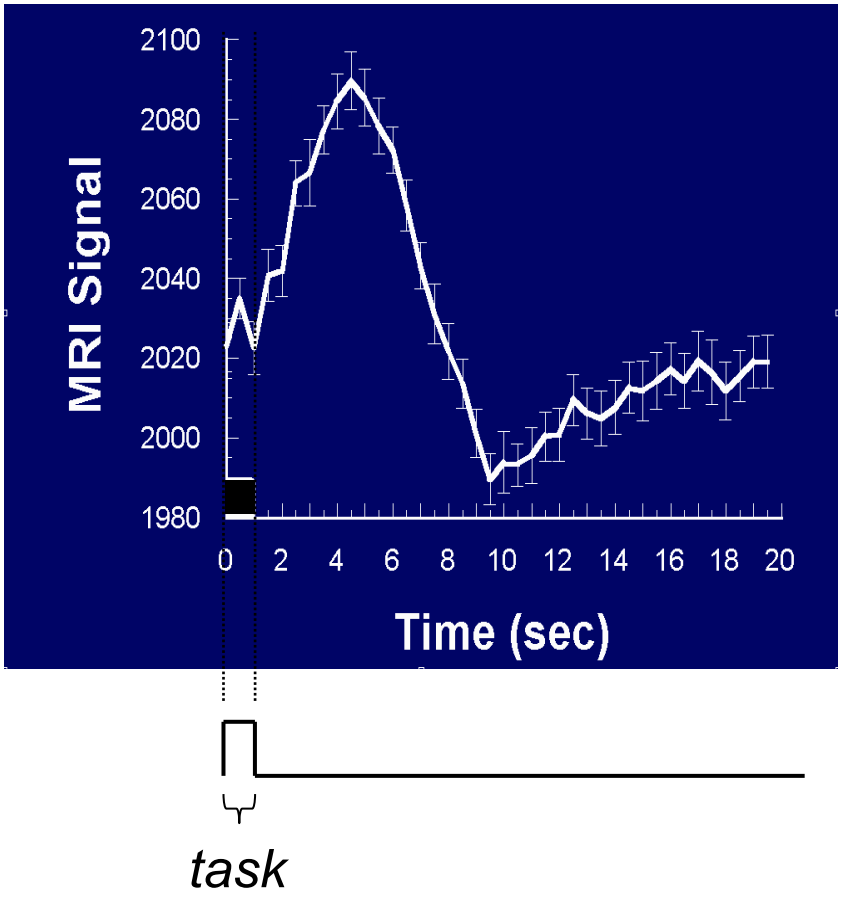


J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, *NeuroImage* **17**: *1787-1806, (2002).*

Methodology

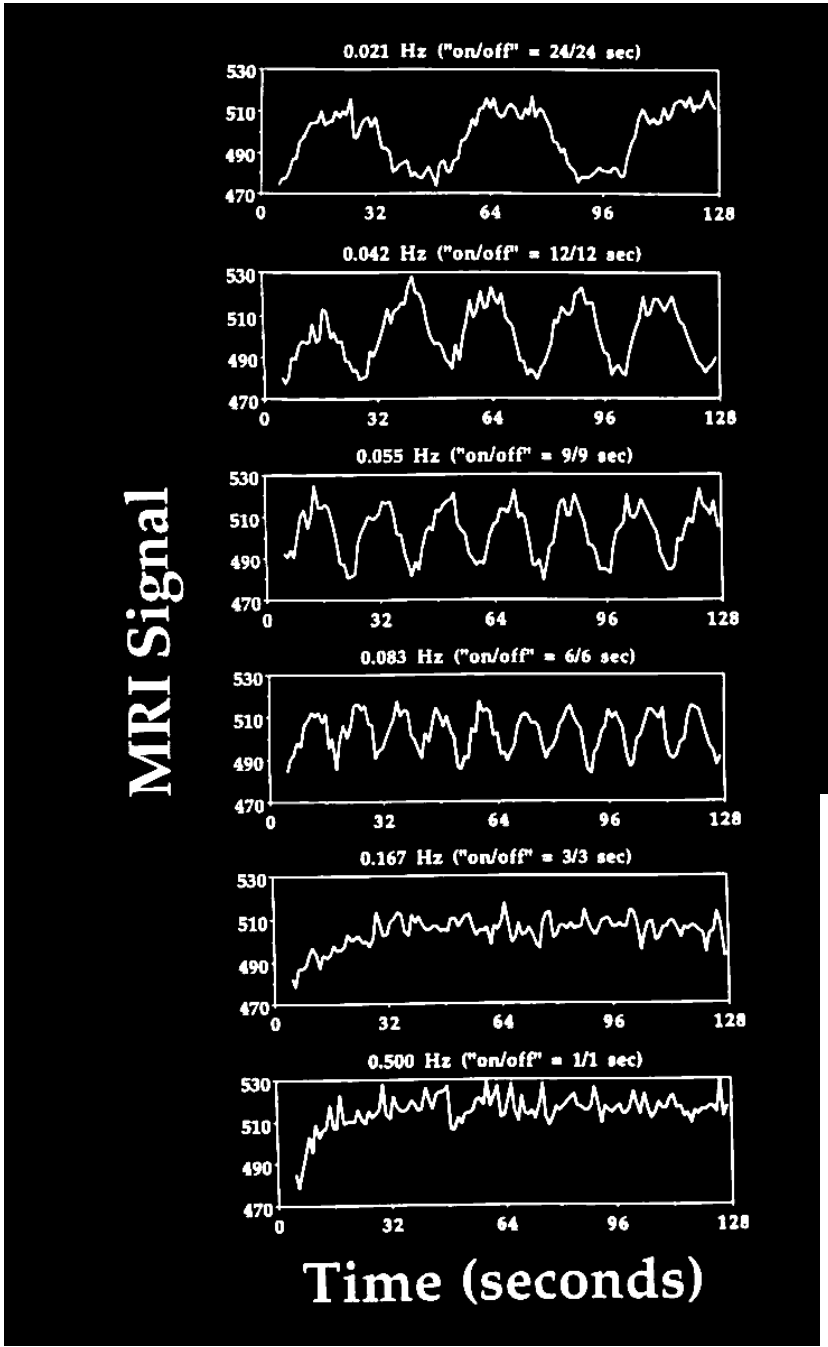
Temporal Resolution

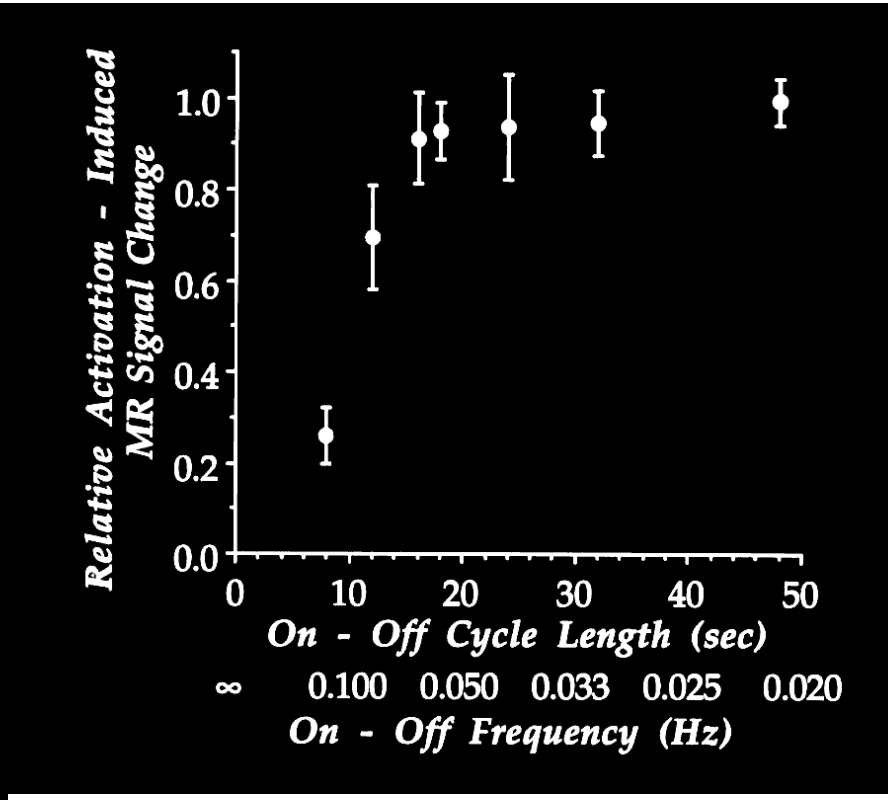




Methodology

Temporal Resolution



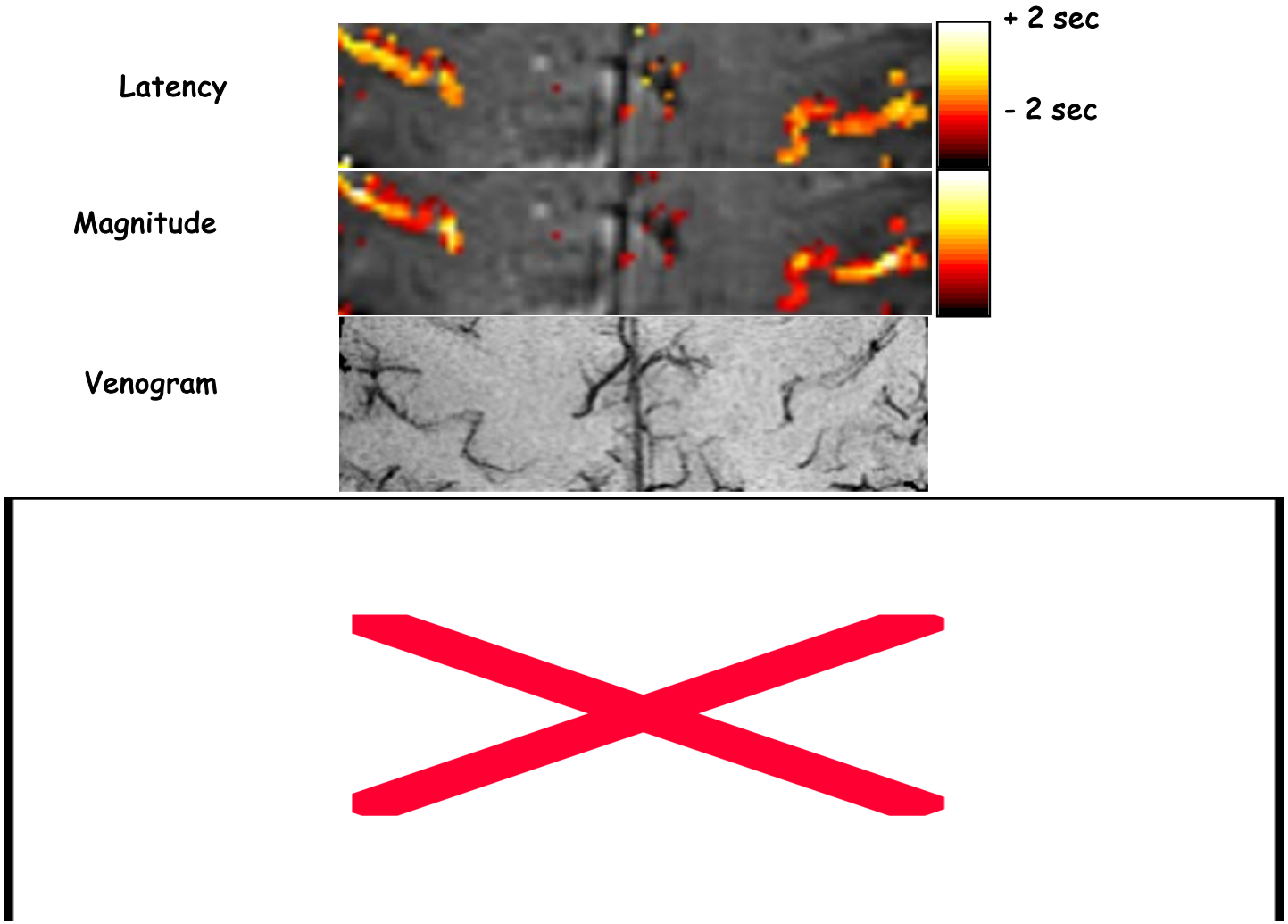


P. A. Bandettini, Functional MRI temporal resolution *in* "Functional MRI" (C. Moonen, and P. Bandettini., Eds.), p. 205-220, Springer - Verlag,. 1999.

Methodology

Temporal Resolution

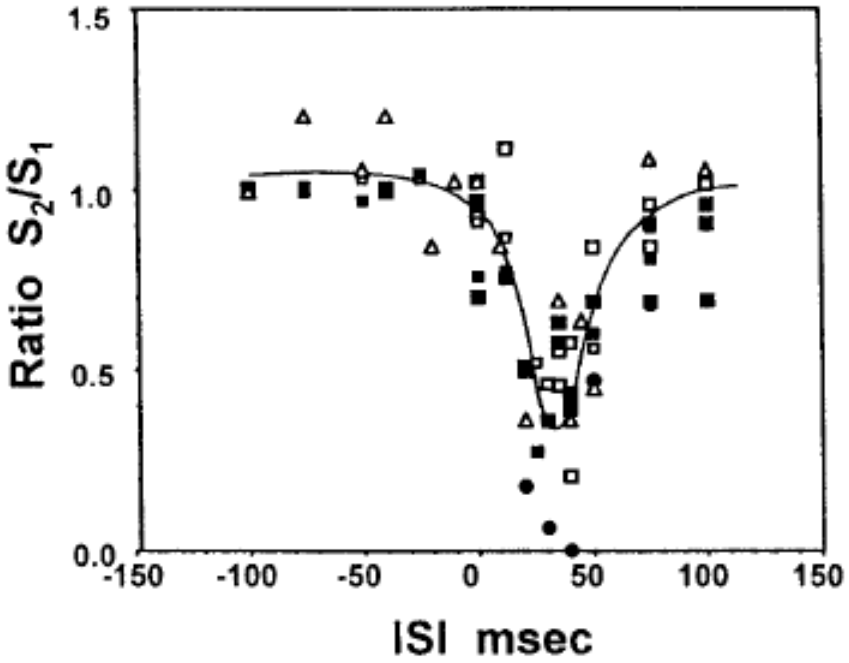
Latency Variation…



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

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

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



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

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

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Multi-modal integration
Free Behavior task design
Resting state fluctuation assessment

Fluctuations
Dynamics
Cross - modal comparison

Interpretation

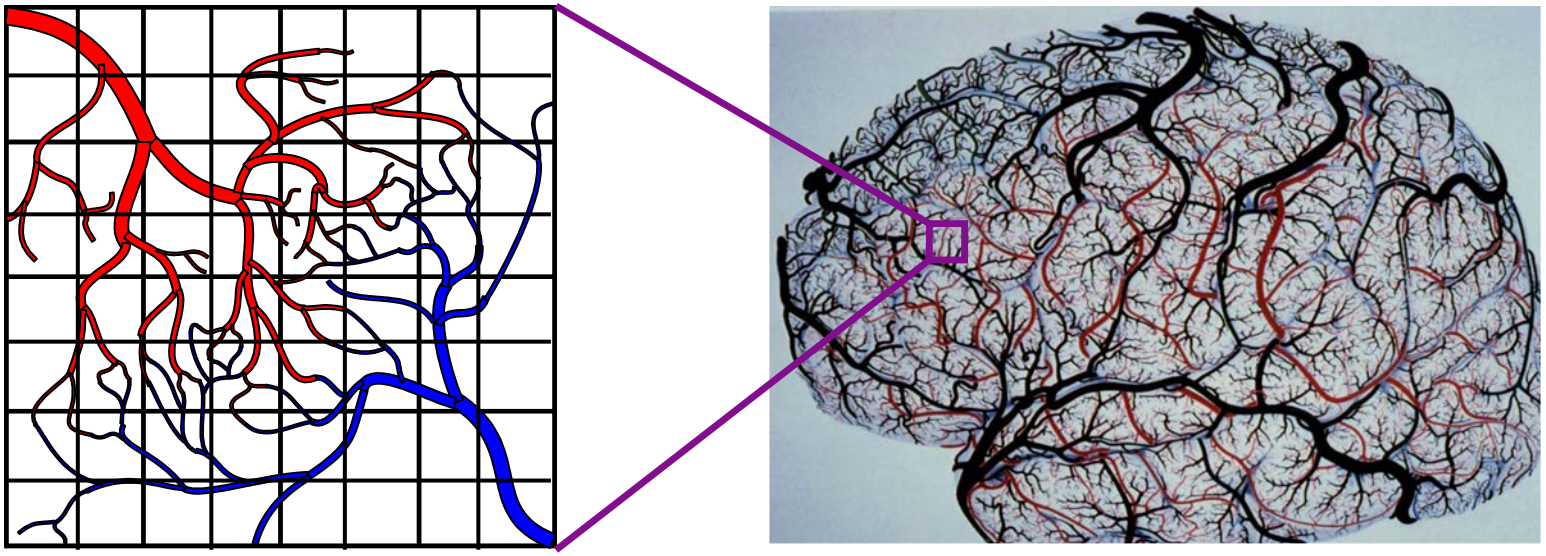
Basic Neuroscience
Behavior correlation/prediction
Pathology correlation

Applications

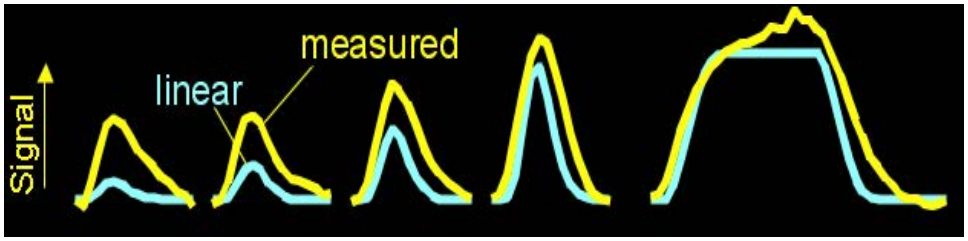
Interpretation

Neuronal Activation ? Measured Signal

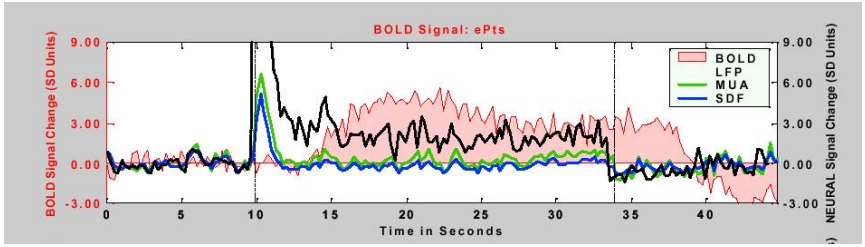
? Hemodynamics ? Noise ?



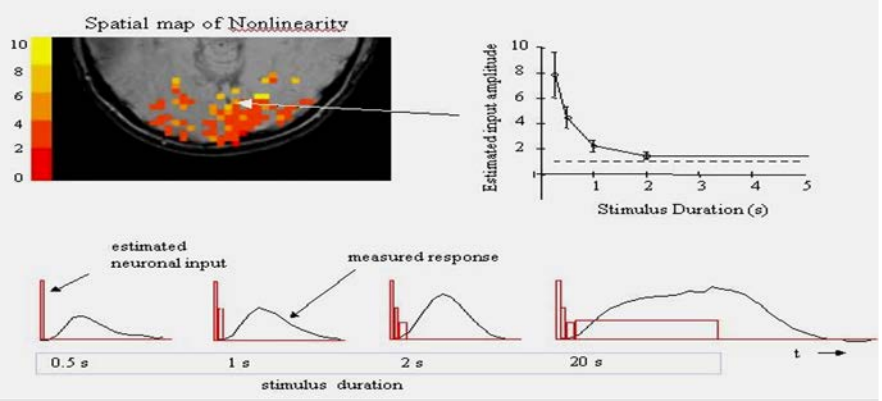
Interpretation



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



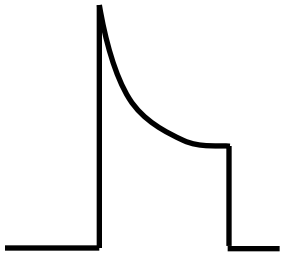
Logothetis et al. (2001) Nature, 412, 150-157.



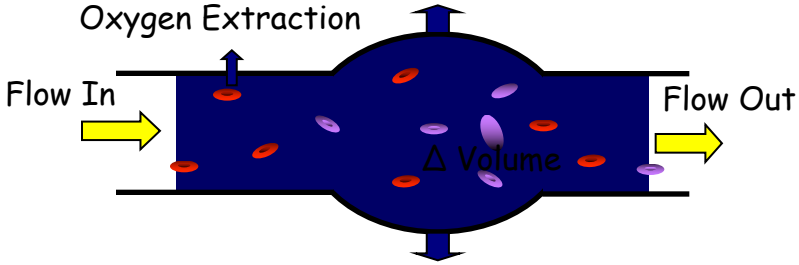
P. A. Bandettini et al, (2001) Nature Neuroscience, 4: 864-866.

Sources of this Nonlinearity

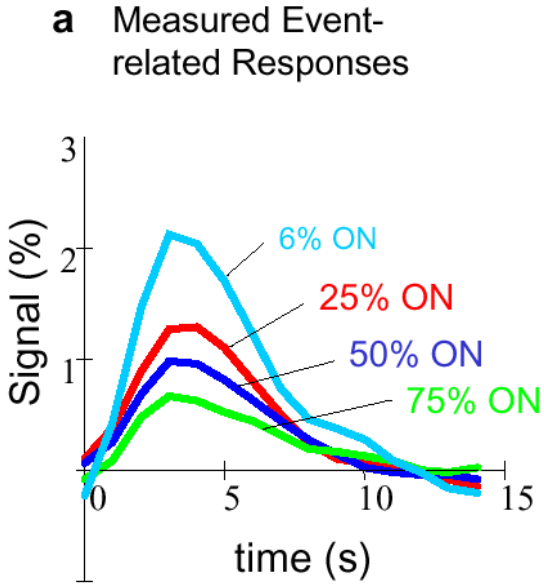
- Neuronal

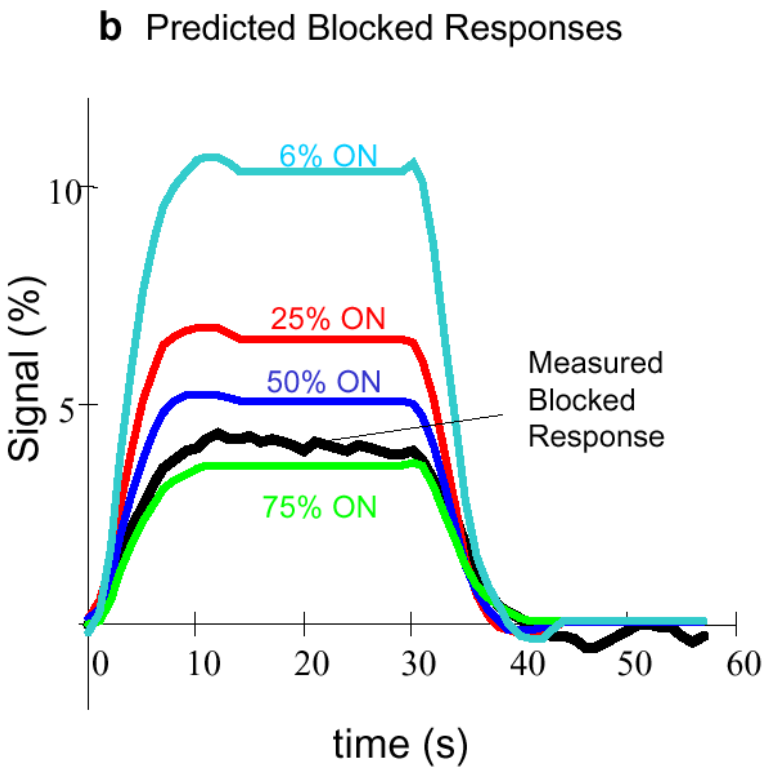


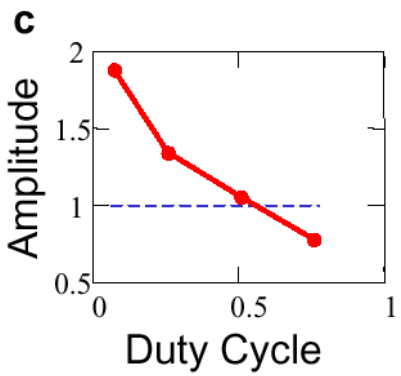
- Hemodynamic
  - -Oxygen extraction
  - -Blood volume dynamics

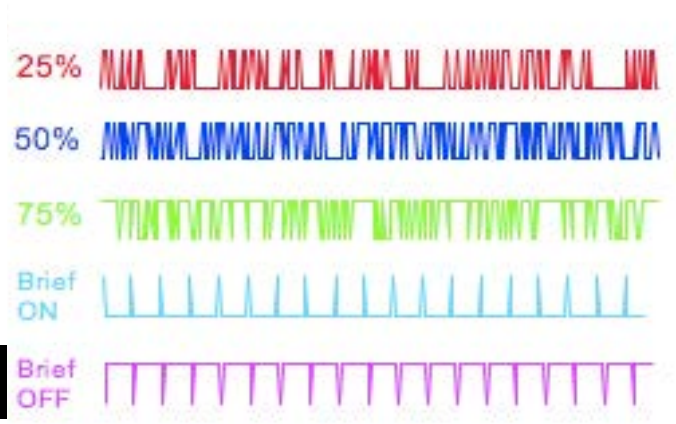


Interpretation Duty Cycle Effects

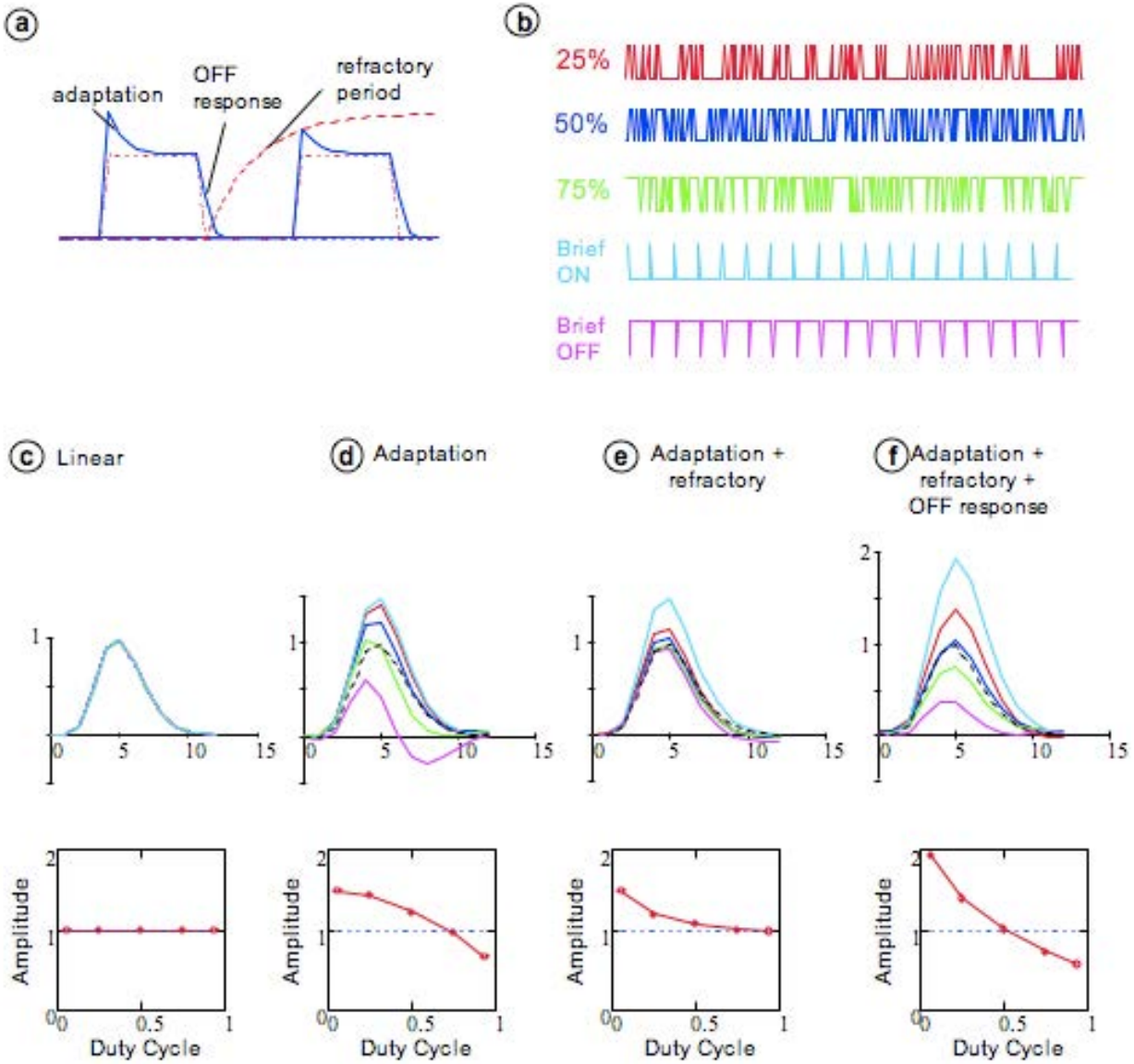




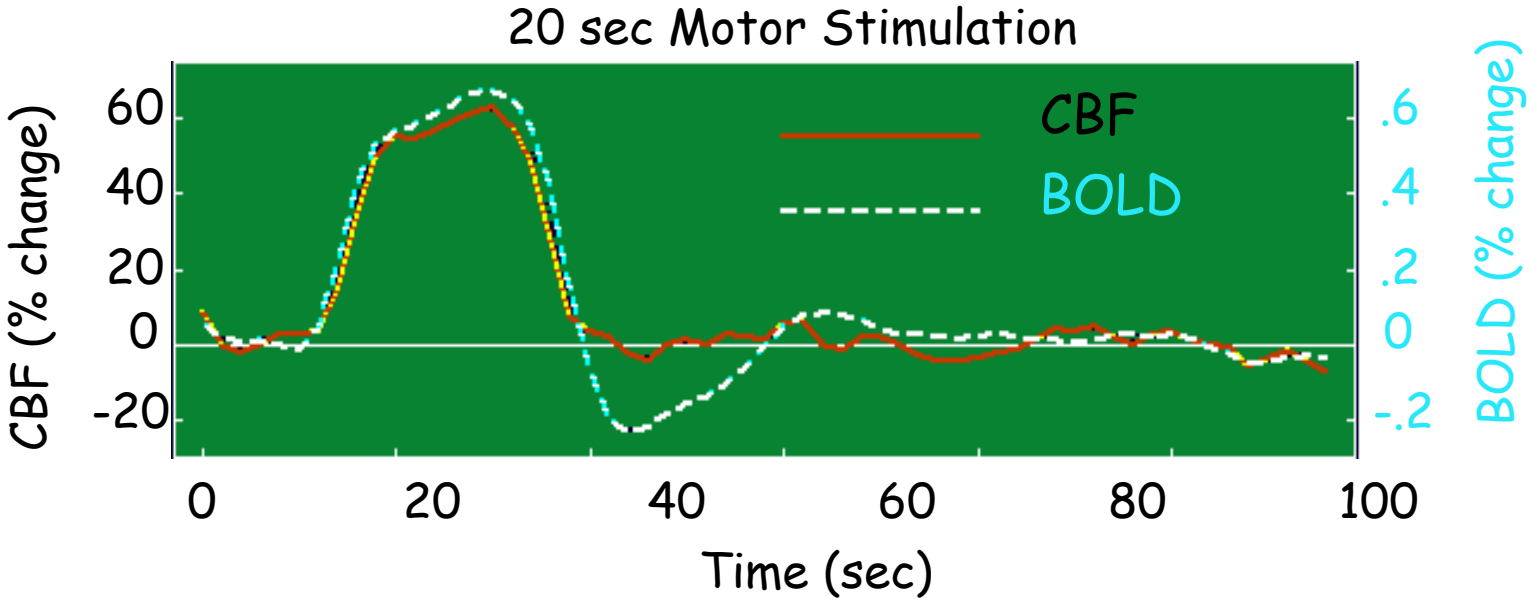




duty cycle effects



BOLD post-stimulus undershoot



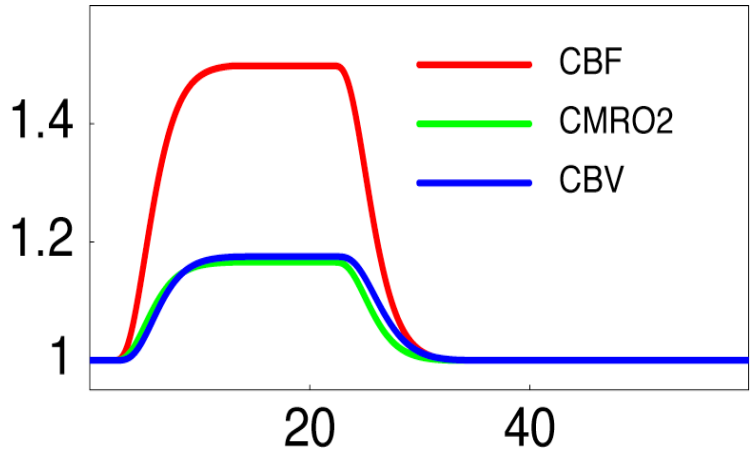
A BOLD undershoot without a CBF undershoot could be due to a slow return to baseline of either CBV or $CMRO_2$

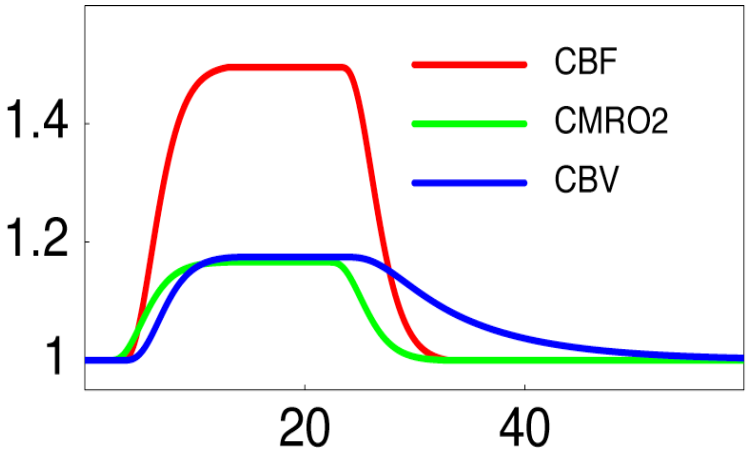
Courtesy Rick Buxton

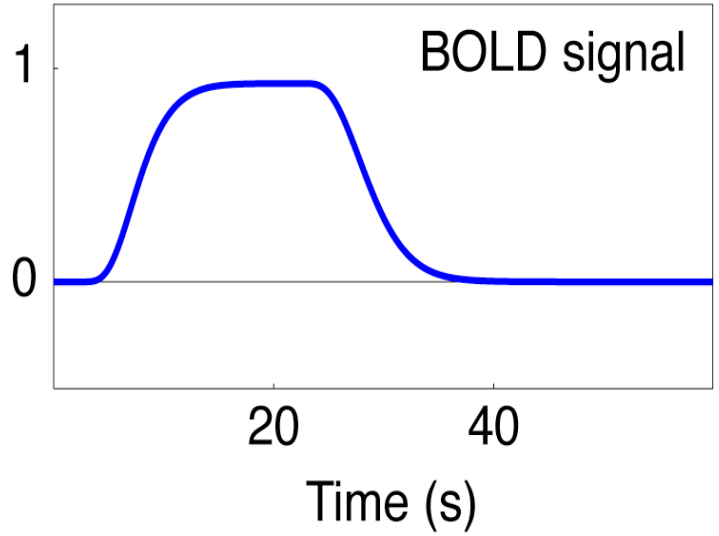
Interpretation

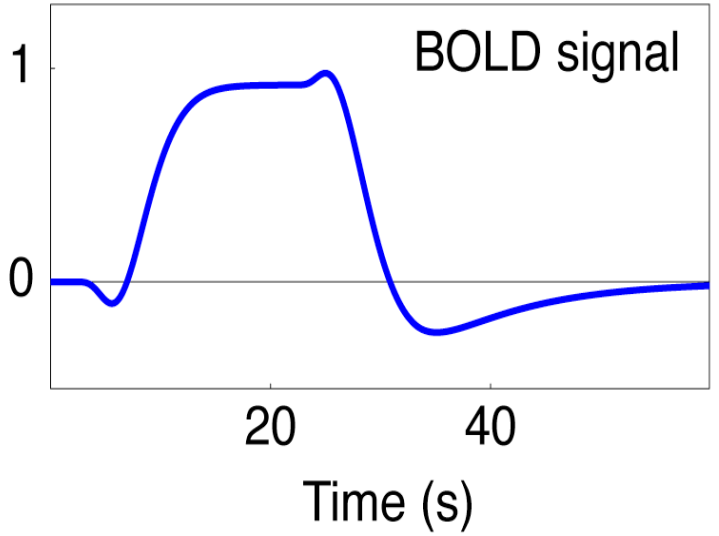
Post Undershoot

BOLD Signal Dynamics









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Applications

What fMRI Can Do

Understanding normal brain organization and changes

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

Clinical research

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

What fMRI Might Do

Complementary use for clinical diagnosis

- -utilization of clinical research results
- -prediction of pathology

Clinical treatment and assessment

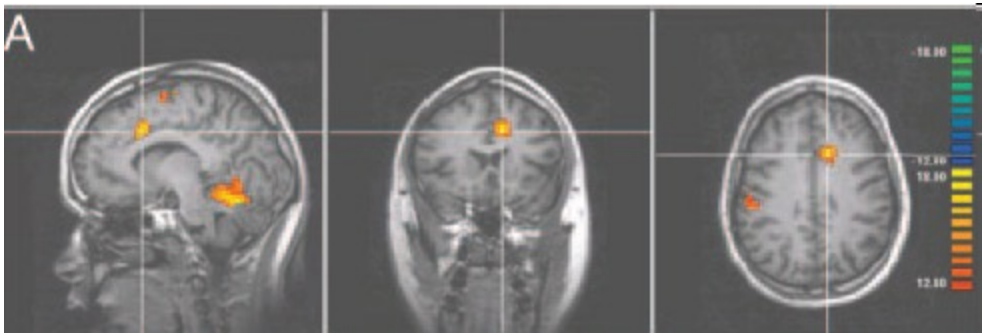
- -drug, therapy, rehabilitation, biofeedback
- -epileptic foci mapping
- -drug effects

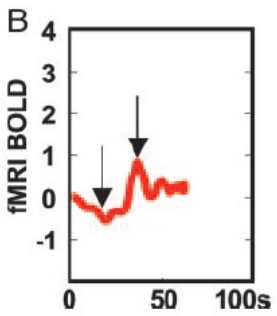
Non clinical uses

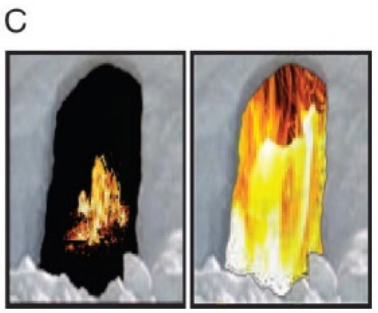
- -complementary use with behavioral, anatomical, other modality results
- -lie detection
- -prediction of behavior tendencies
- -brain/computer interface

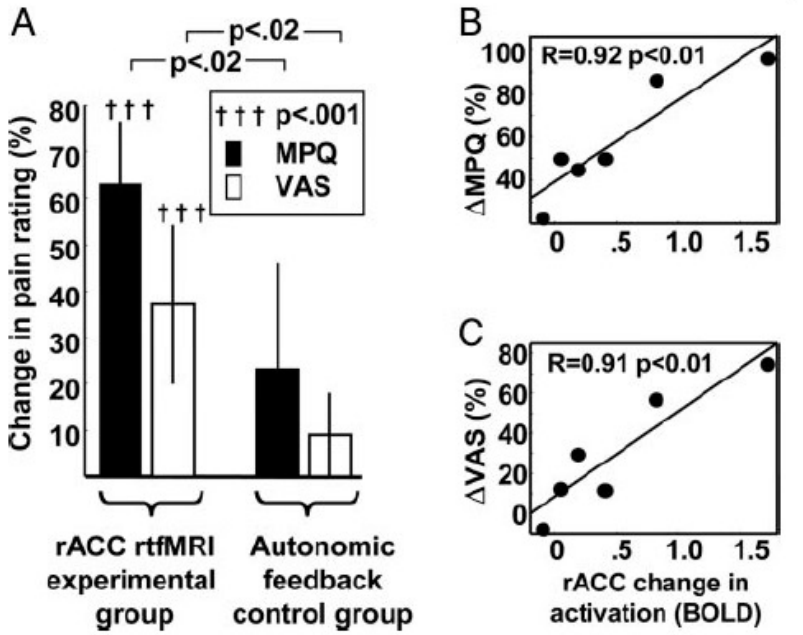
Applications

Real time fMRI feedback to reduce chronic pain









Control over brain activation and pain learned by using real-time functional MRI, R. C. deCharms, et al. PNAS, 102; 18626-18631 (2005)

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