fMRI in Perspective

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods
Laboratory of Brain and Cognition
http://fim.nimh.nih.gov

&

Functional MRI Facility
http://fmrif.nimh.nih.gov

Functional MRI

- **27 years since the first results.**
- **Currently, over 4,000 fMRI papers published per year.**
- **Over 52,000 fMRI papers published in total.**
- **At the interface of a wide range of disciplines.**

- **Noninvasive, fast, whole brain, high-resolution.**
- **Major impact on our understanding of human brain functional organization**
- **Wide range of disorders studied…**
- **No major clinical application yet**

	Day	Date	Bldg	Time	Topic	Lecturer
1	Friday	6/1/2018	Bldg 35A Rm 620/630	2:00 PM	Introduction to Course Topics & History Basics of fMRI	Peter Bandettini
2	Monday	6/4/2018	Bldg 40 1201/1203	2:00 PM	Neuroimaging and Neuromodulation at the NIH	Sean Marrett
3	Wednesday	6/6/2018	Bldg 40 1201/1203	2:00 PM	Nuts and Bolts of MRI and fMRI scanning	Vinai Roopchansinch
4	Friday	6/8/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Advanced MRI and fMRI Acquisition Methods	Andy Debyshire
5	Monday	6/11/2018	Bldg 40 1201/1203	2:00 PM	The chalenges and oppportunities of data sharing	Adam Thomas
6	Wednesday	6/13/2018	Bldg 40 1201/1203	2:00 PM	Real time fMRI	Michal Ramot
	Friday	6/15/2018			ISMRM and OHBM	
	Monday	6/18/2018			ISMRM and OHBM	
	Wednesday	6/20/2018			ISMRM and OHBM	
	Friday	6/22/2018			ISMRM and OHBM	
7	Monday	6/25/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Minimizing noise during fMRI acquisition	Dan Handwerker
8	Wednesday	6/27/2018	Bldg 40 1201/1203	2:00 PM	Understanding Visual Processing with fMRI	Elisha Merriam
9	Friday	6/29/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Assessing individual differences with fMRI	Emily Finn
10	Monday	7/2/2018	Bldg 40 1201/1203	2:00 PM	Resting State fMRI	Catie Chang
	Wednesday	7/4/2018			Independence Day	
11	Friday	7/6/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Predicting Performance with fMRI	David Jangraw
12	Monday	7/9/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Multivariate pattern analysis of fMRI data	Martin Hebart
13	Wednesday	7/11/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Encoding and decoding models	Francisco Pereira
14	Friday	7/13/2018	Bldg 40 1201/1203	2:00 PM	Multi-echo EPI for task-based and resting-state fMRI	Javier Gonzalez-Castillo
15	Monday	7/16/2018	Bldg 40 1201/1203	2:00 PM	High Field and High Resolution Structural and Functional MRI	Renzo Huber
16	Wednesday	7/18/2018	Bldg 40 1201/1203	2:00 PM	Layer specific fMRI	Renzo Huber
17	Friday	7/20/2018	Bldg 40 1201/1203	2:00 PM	EEG/fMRI and the study of Language	Peter Molfese
18	Monday	7/23/2018	Bldg 40 1201/1203	2:00 PM	Pharmacologic fMRI	Jen Evans
19	Wednesday	7/25/2018	Bldg 40 1201/1203	2:00 PM	Neurdegegerative disorders	Silvina Horovitz
20	Friday	7/27/2018	Bldg 40 1201/1203	2:00 PM	fMRI of pain	Lauren Atlas
21	Monday	7/30/2018	Bldg 40 1201/1203	2:00 PM	Perfusion Imaging	Lalith Talagala
22	Wednesday	8/1/2018	Bldg 40 1201/1203	2:00 PM	PET for Precision Medicine and Drug Development	Bob Innis
23	Friday	8/3/2018	Bldg 40 1201/1203	2:00 PM	Magnetoencephalography (MEG)	Fred Carver
24	Monday	8/6/2018	Bldg 40 1201/1203	2:00 PM	Imaging Changes in Brain Anatomy	Cibu Thomas
25	Wednesday	8/8/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Neuromodulation methods	Bruce Luber
26	Friday	8/10/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Efficient Modeling through Information Sharing	Gang Chen
27	Monday	8/13/2018	Bldg 40 1201/1203	2:00 PM	T1 Contrast, MPRAGE and MT	Peter van Gelderen
28	Wednesday	8/15/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Studying CNS diseases with advanced MRI	Pascal Sati
29	Friday	8/17/2018	Bldg 40 1201/1203	2:00 PM	Quantitative MRI	Govind Bhagavatheeshwaran
30	Monday	8/20/2018	Bldg 40 1201/1203	2:00 PM	Imaging Stroke and Traumatic Brain Injury	Lawrence Latour
31	Wednesday	8/22/2018	Bldg 49 Rm 1A51/1A59	2:00 PM	Diffusion MRI: Basics and Limits	Joelle Sarlls & Carlo Pierpaoli
32	Friday	8/24/2018	Bldg 40 1201/1203	2:00 PM	Depression and Multimodal Neuroimaging	Allison Nugent
33	Monday	8/27/2018	Bldg 40 1201/1203	2:00 PM	Anatomical and Functional Neuroimaging in Animal Models	Afonso Silva
34	Wednesday	8/29/2018	Bldg 40 1201/1203	2:00 PM	Genetics and Neuroimaging: How to analyze imaging data and SNPs	Yin Yao
35	Friday	8/31/2018	Bldg 40 1201/1203	2:00 PM	The Future of NeuroImaging and Course Conclusion	Peter Bandettini

fMRI in Perspective

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

Where are we going?

Ultimate limits and applications?

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

Where are we going?

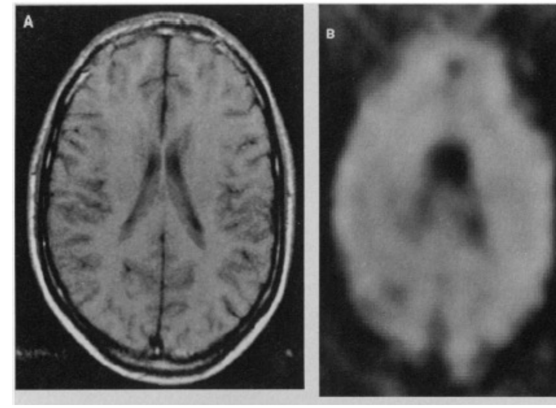
Ultimate limits and applications?

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

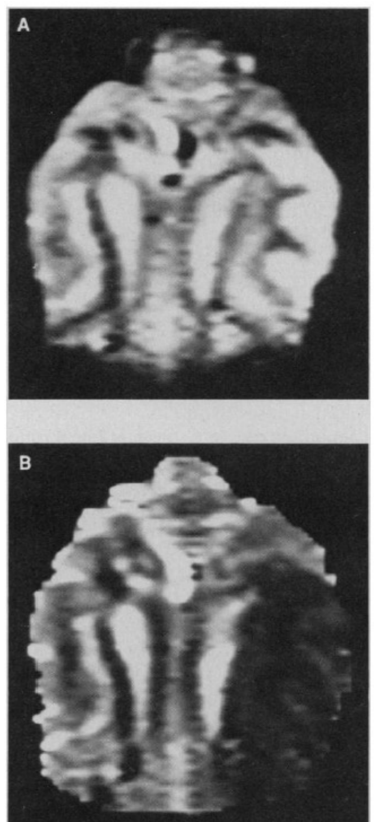
(1990) *Science*, 250, 53-61.

metabolic imaging (NAA)

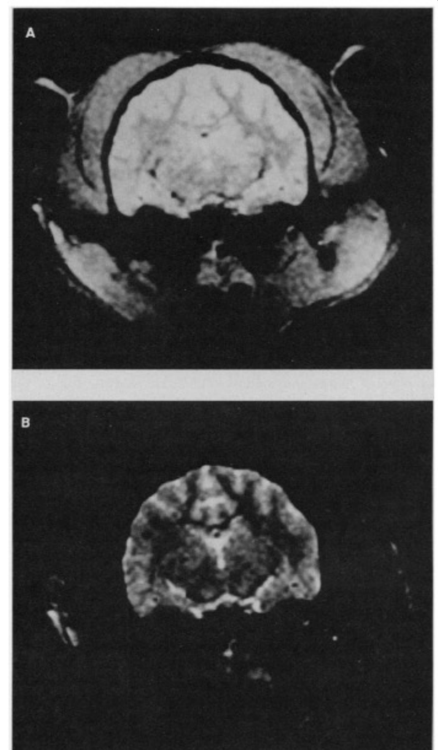


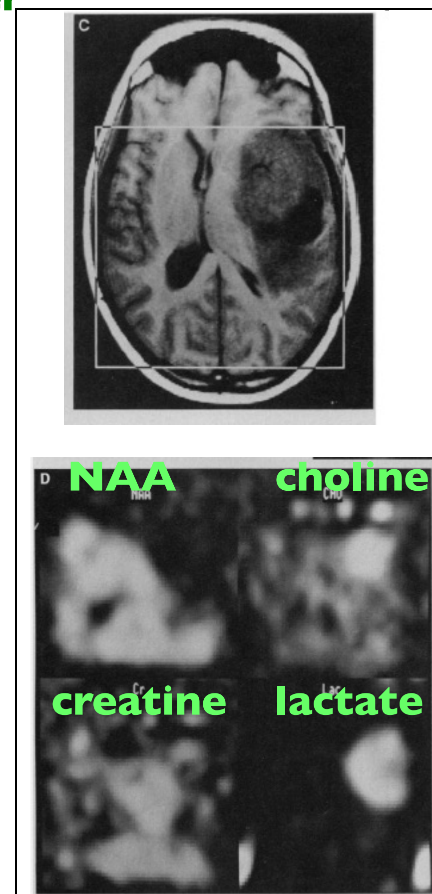
angiography

Diffusion

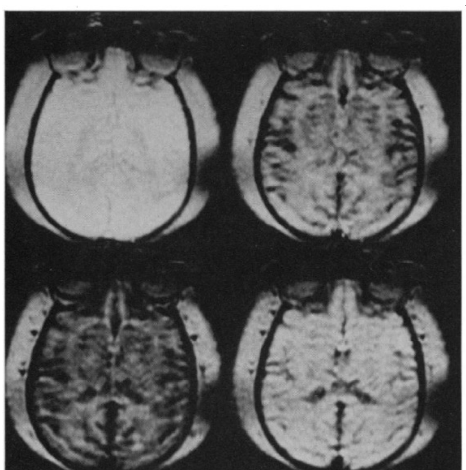


magnetization transfer



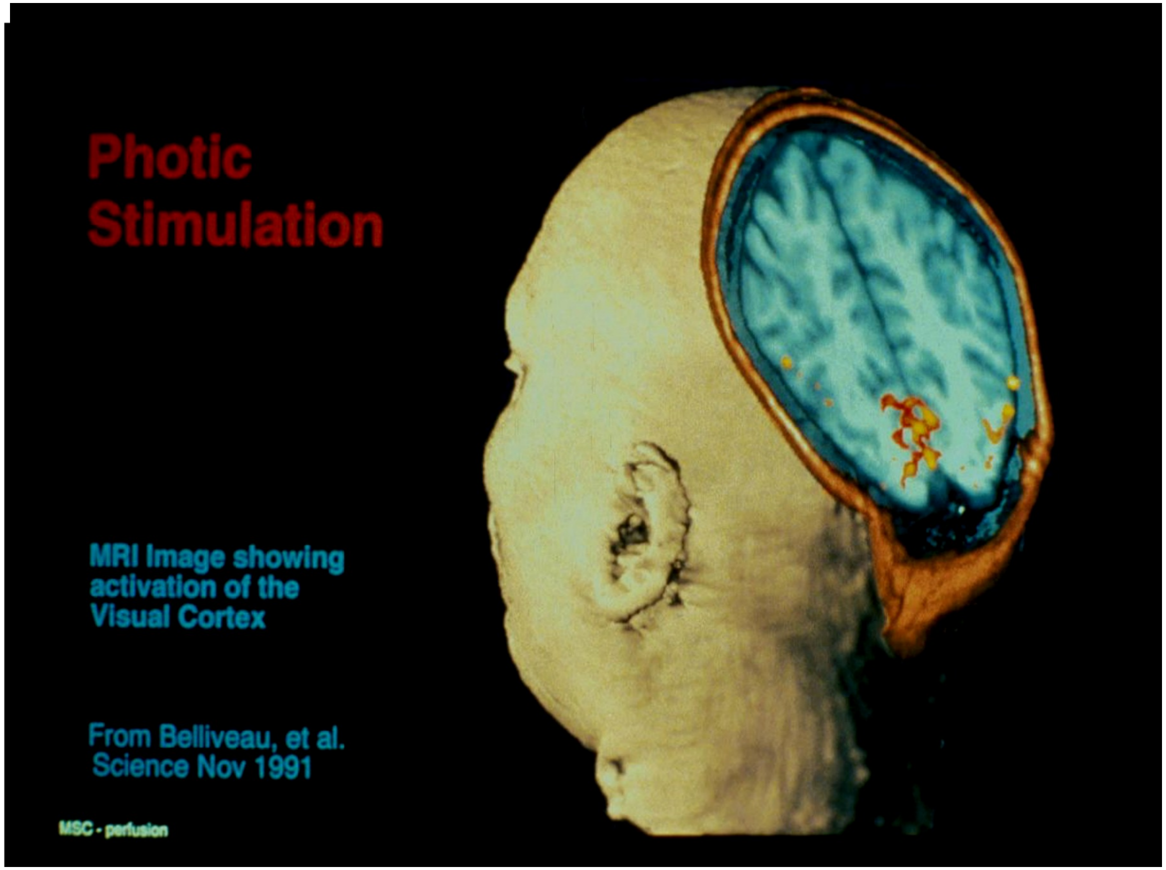


Gadolinium perfusion



The First Functional MRI Results (MGH & Jack Belliveau - 1991)

- Bolus injection of a susceptibility contrast agent.
- Time series collection of T2 - weighted images.



Fundamental Work towards BOLD contrast :

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

(Blood susceptibility changes with oxygenation)

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

(Blood T2 is proportional to oxygenation & mechanism is bulk susceptibility)

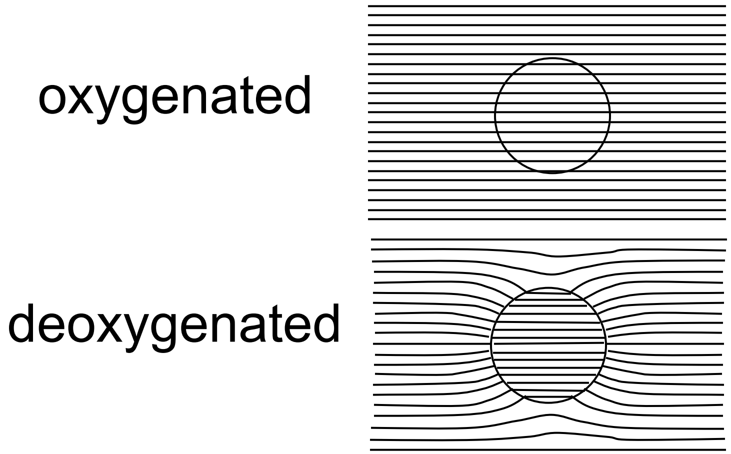
S. Ogawa, T. M. Lee, A. R. Kay, D.W.Tank, *Proc. Natl.Acad. Sci. USA 87, 9868-9872*, **1990**.

(T2 and T2 modulation in vessels in living rat brains with oxygenation changes)*

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

(T2 modulation with cat brain with oxygenation changes)*

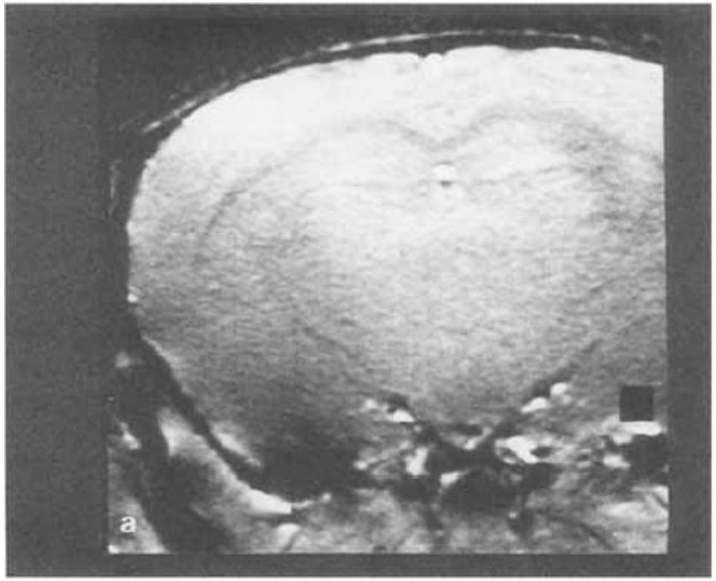
red blood cells



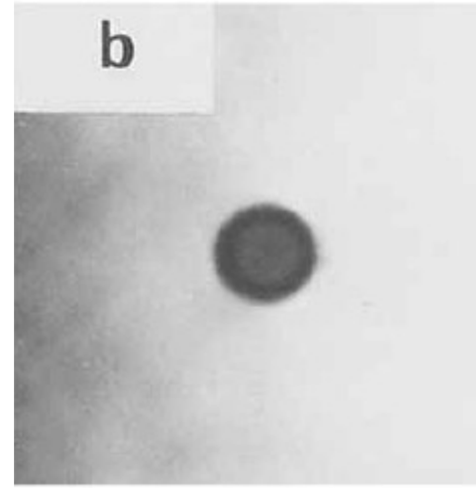
in vivo

in vitro

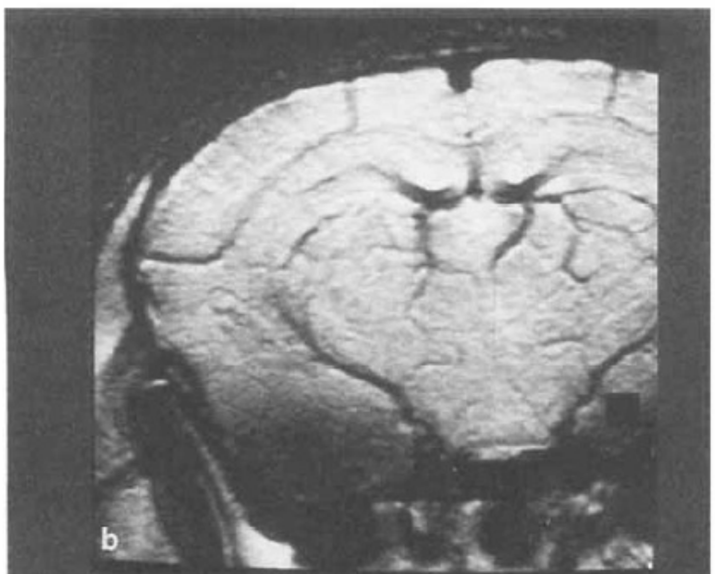
100% O_2



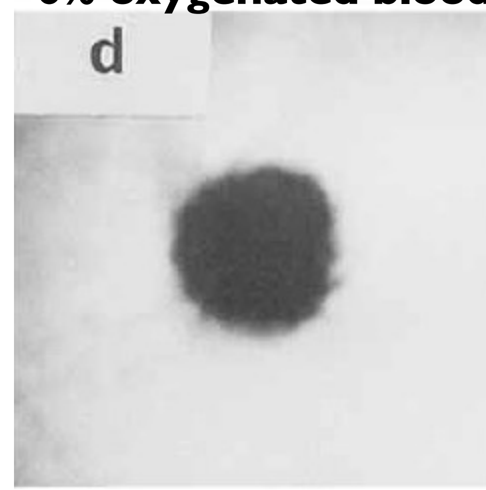
100% oxygenated blood



20% O_2



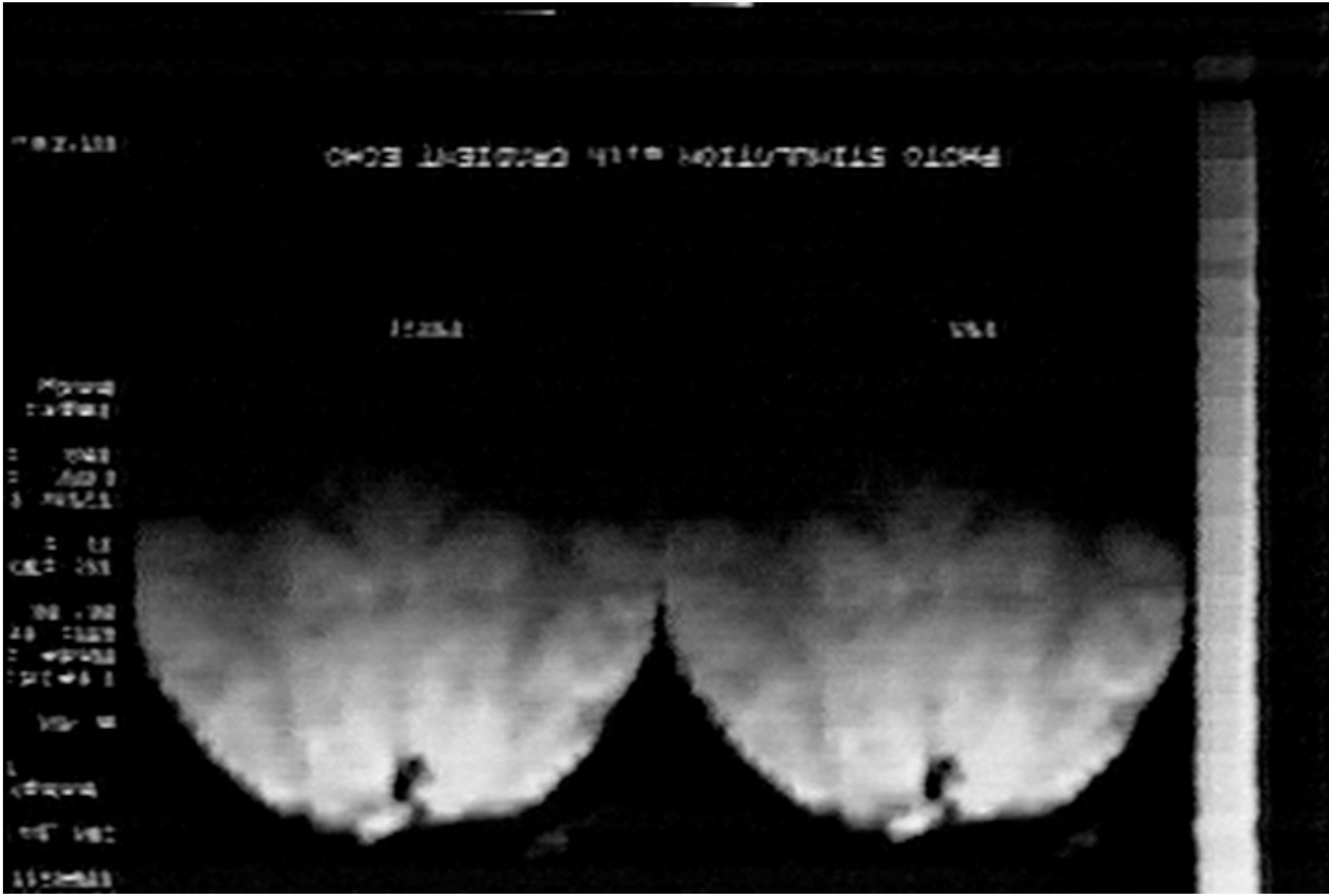
0% oxygenated blood



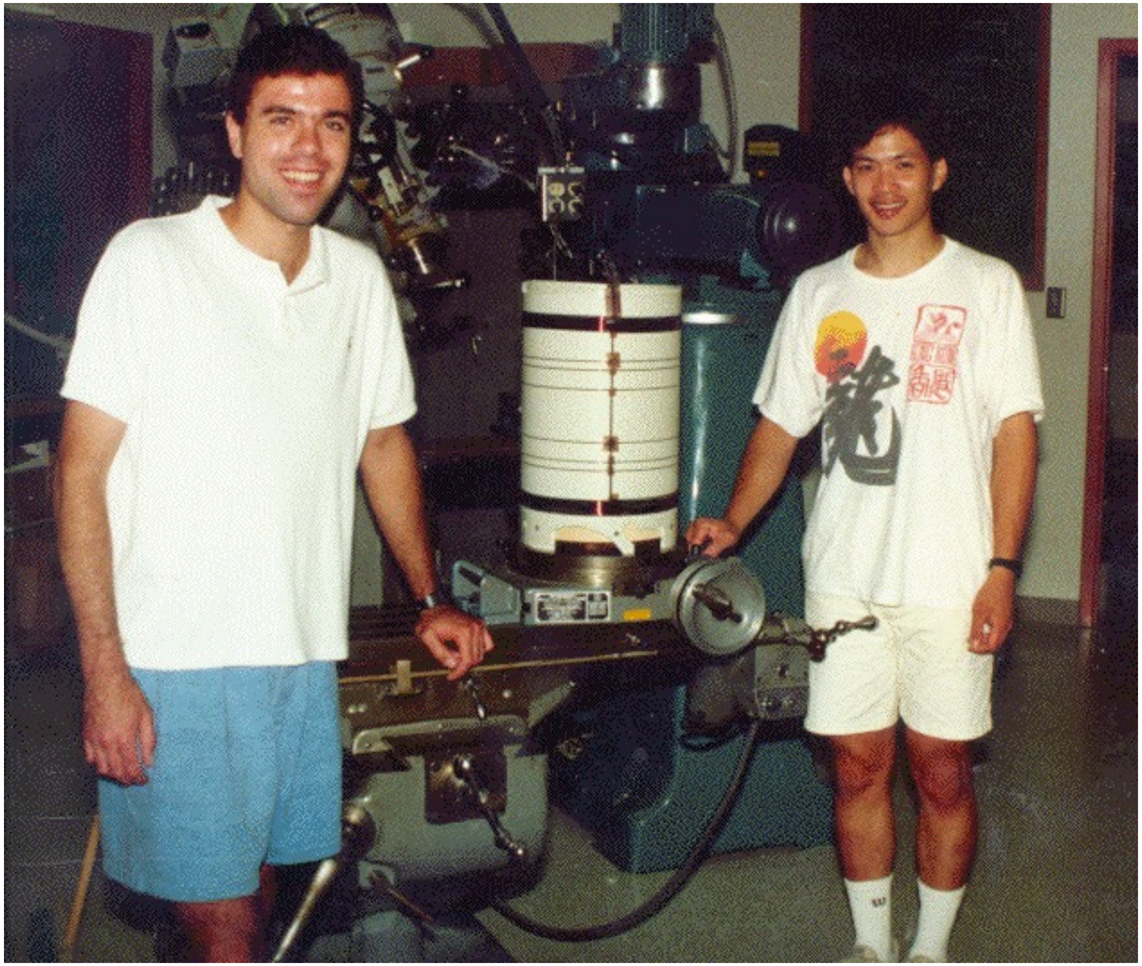
S. Ogawa, T.-M. Lee, A. S. Nayak, P. Glynn, Magn. Reson. Med, 14, 68-78 (1990)

The video that started it all.

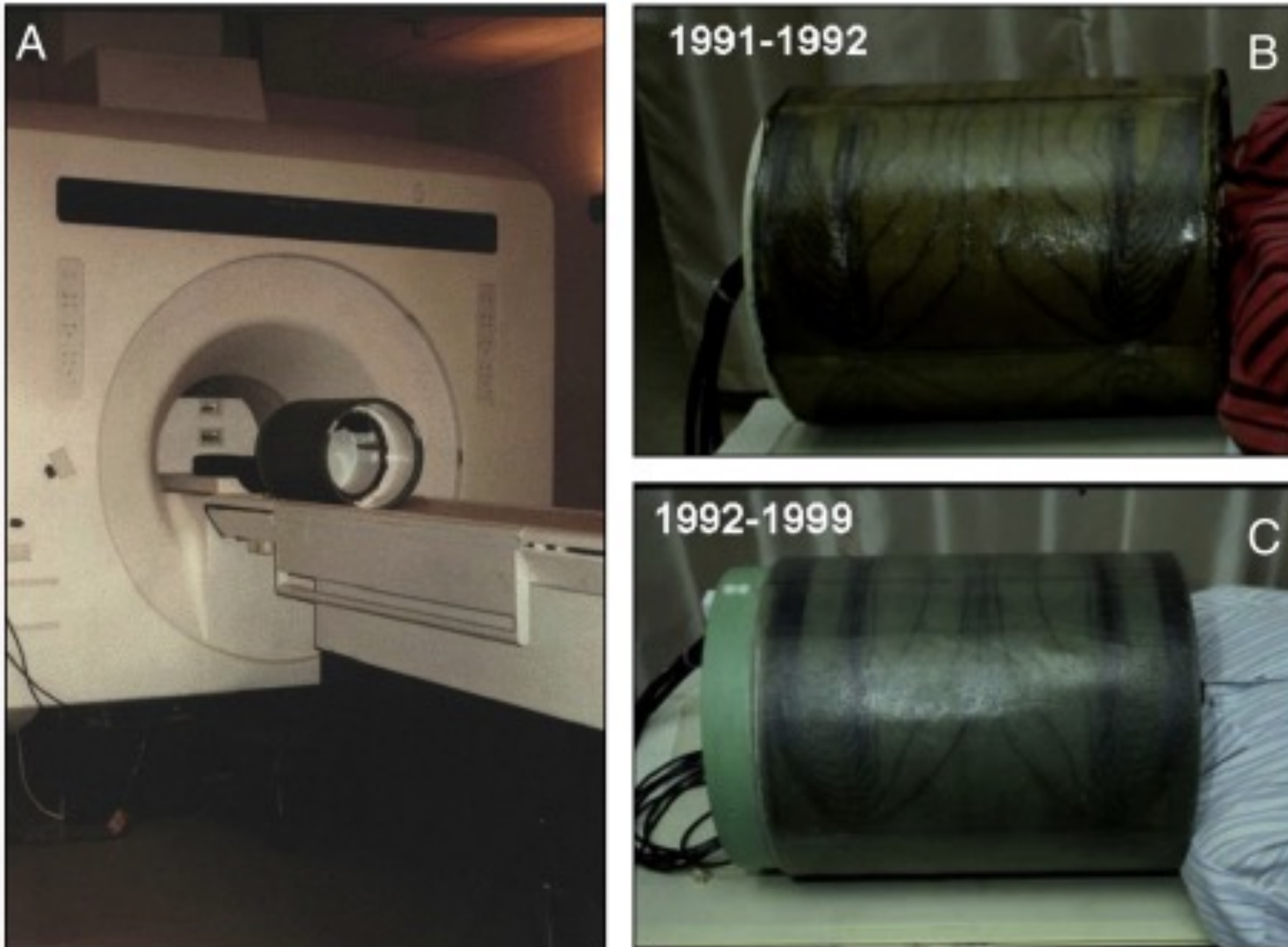
Aug 12, 1991: Tom Brady Plenary Lecture at SMRM, San Francisco



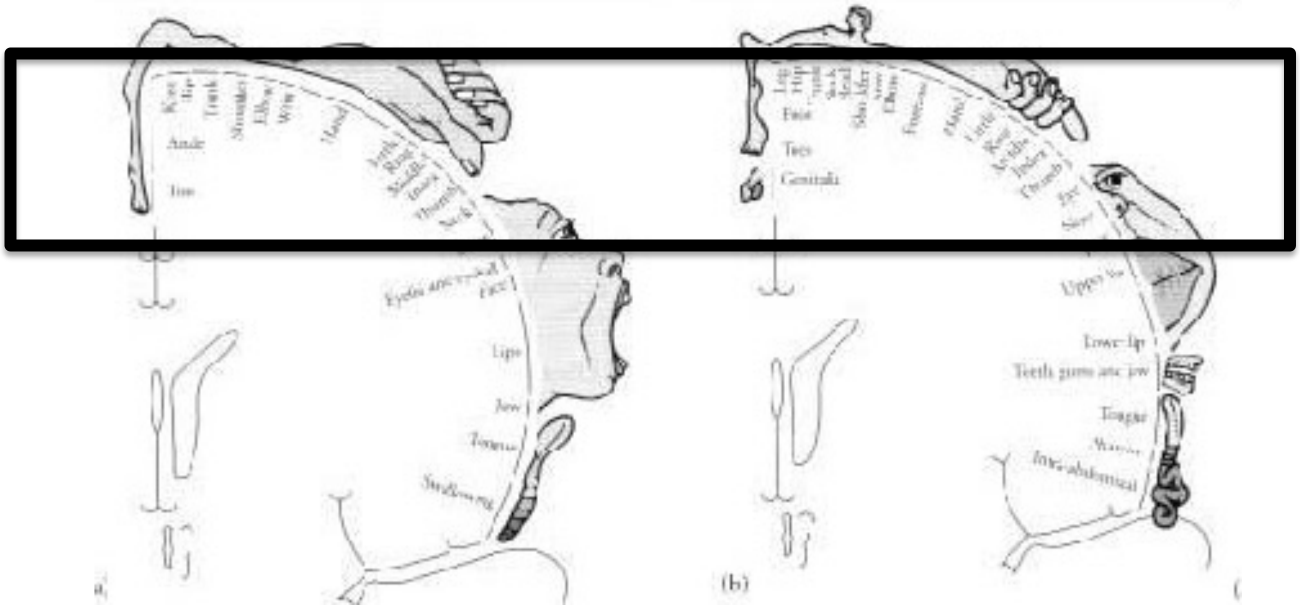
just before that meeting…



August, 1991


A
1991-1992
B
1992-1999
C

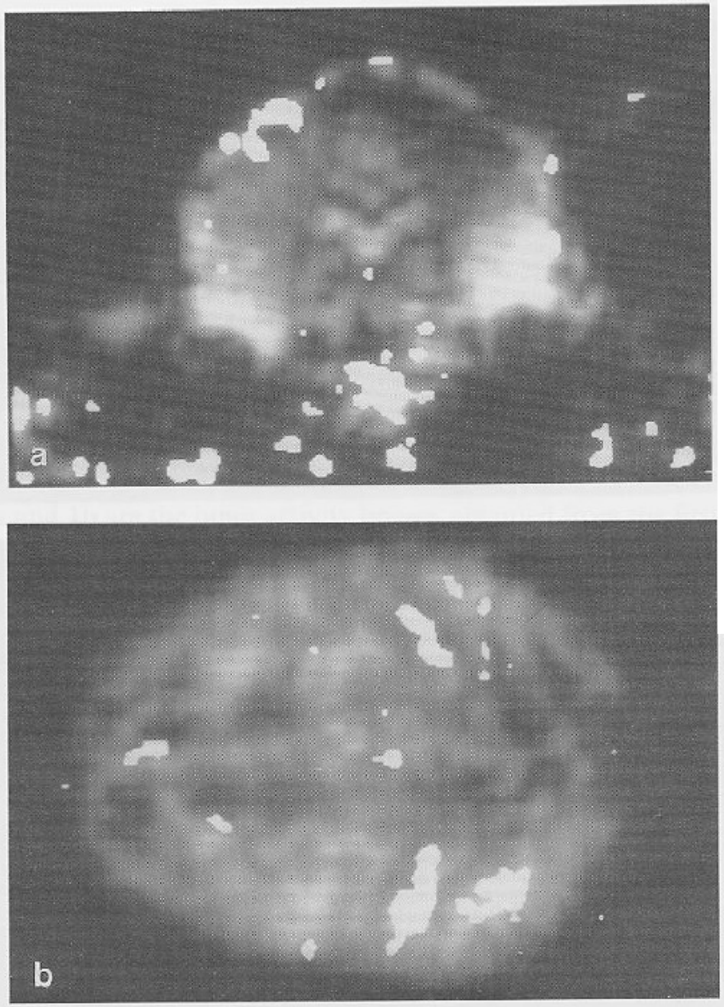
Initially could only do one slice…

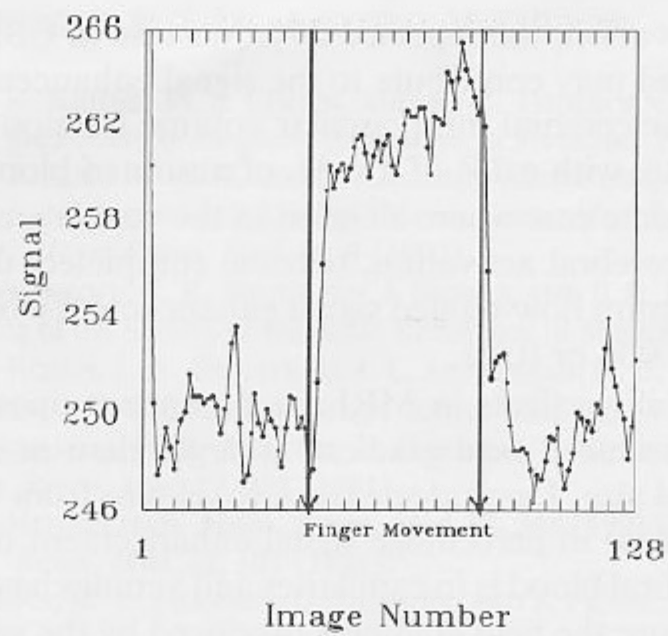


2.5 cm !

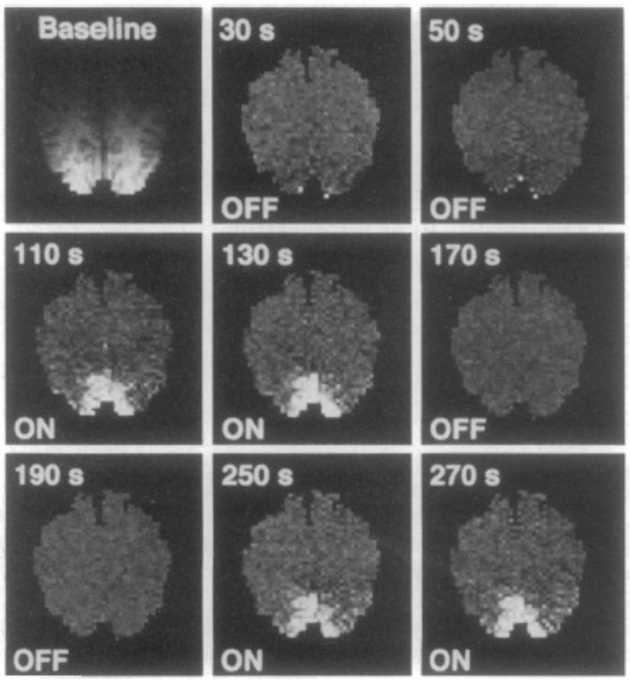
TR = 2 sec
TE = 50 ms
One slice
In plane 3.75 x 3.75

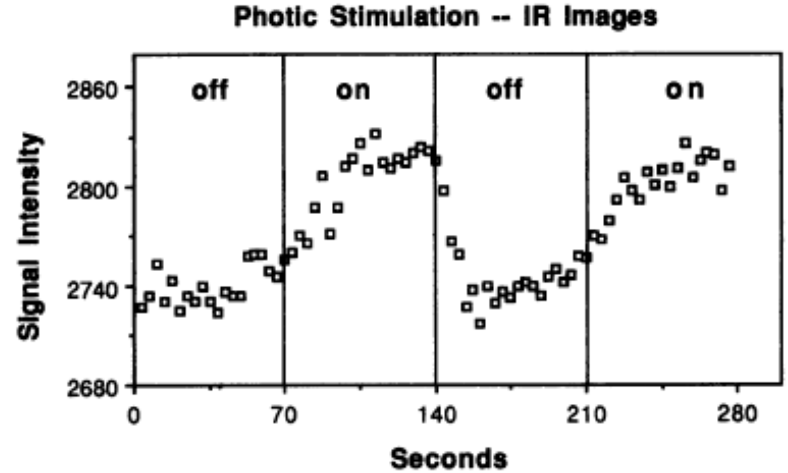
1991

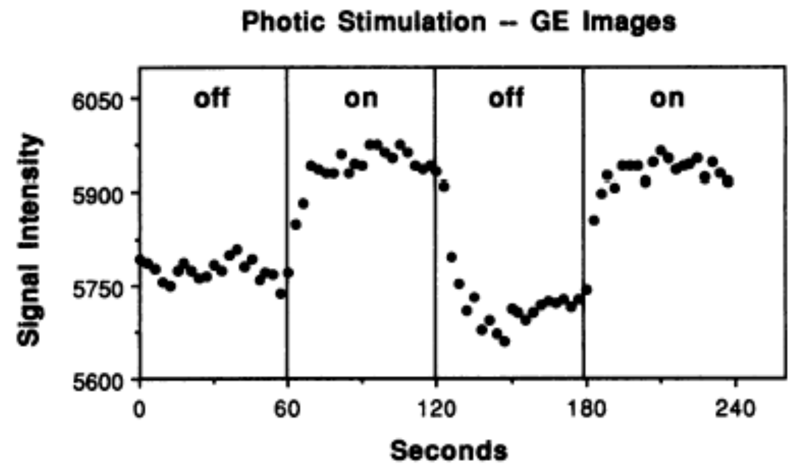


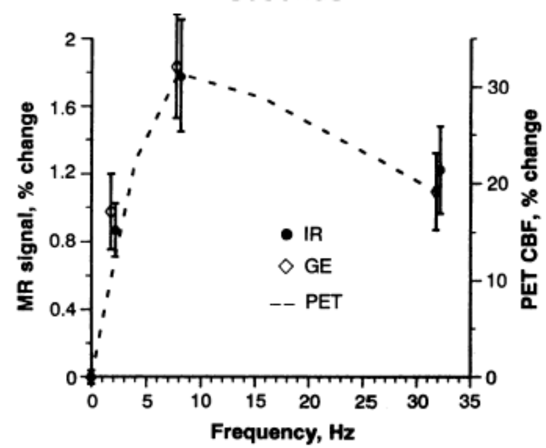


P. A. Bandettini, et al., (1992)
"Time course EPI of human brain function during task activation."
Magn. Reson. Med 25, 390-397.



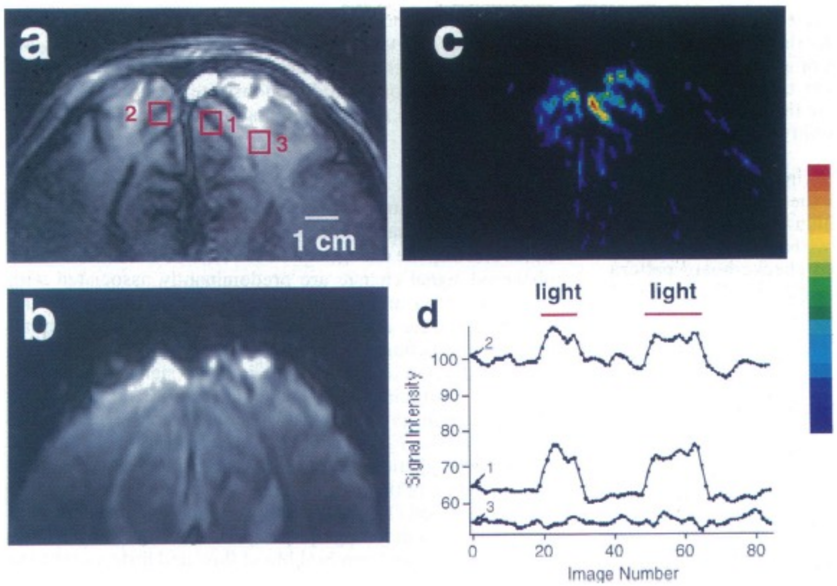


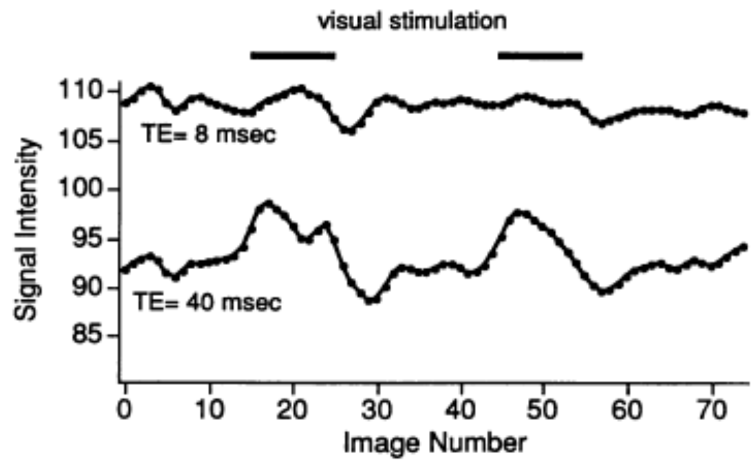


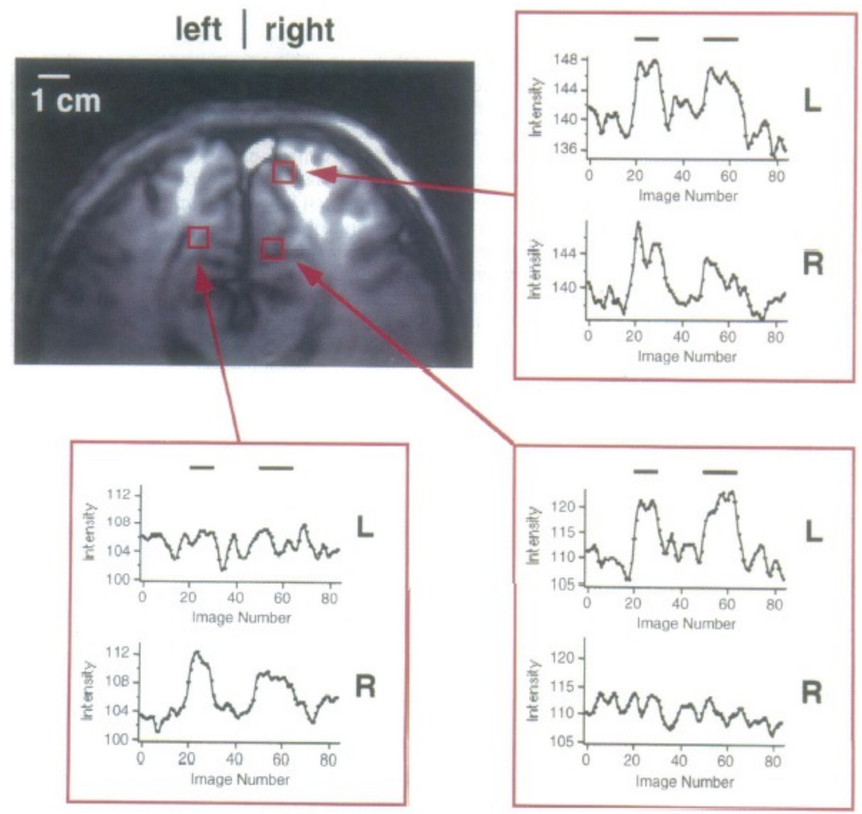


K. K. Kwong, et al, (1992) "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. 89, 5675-5679.

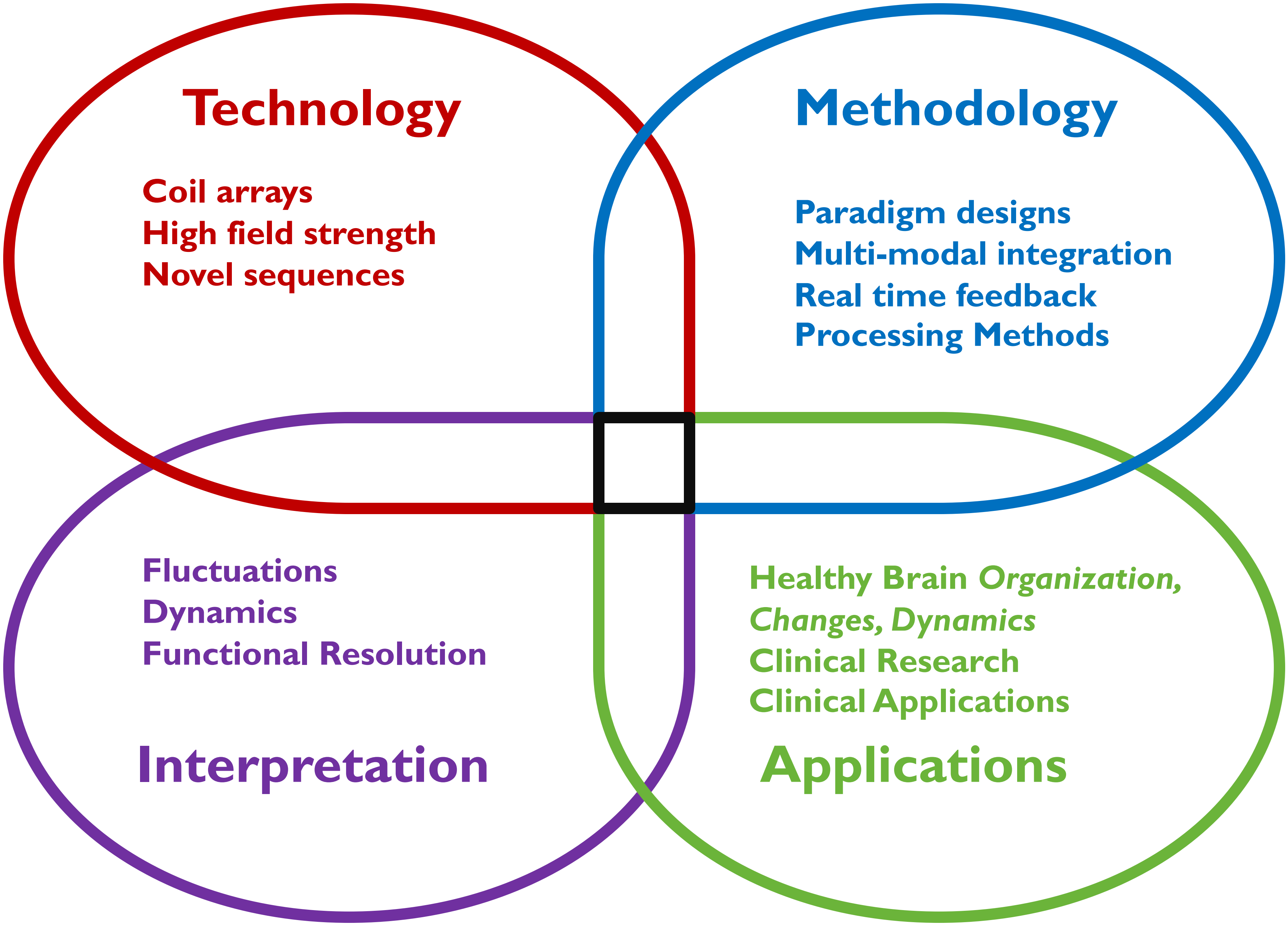
Multi-shot results at 4T, U. Minnesota.







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.


Technology
Coil arrays
High field strength
Novel sequences
Methodology
Paradigm designs
Multi-modal integration
Real time feedback
Processing Methods
Fluctuations
Dynamics
Functional Resolution
Interpretation
Healthy Brain *Organization, Changes, Dynamics*
Clinical Research
Clinical Applications
Applications

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

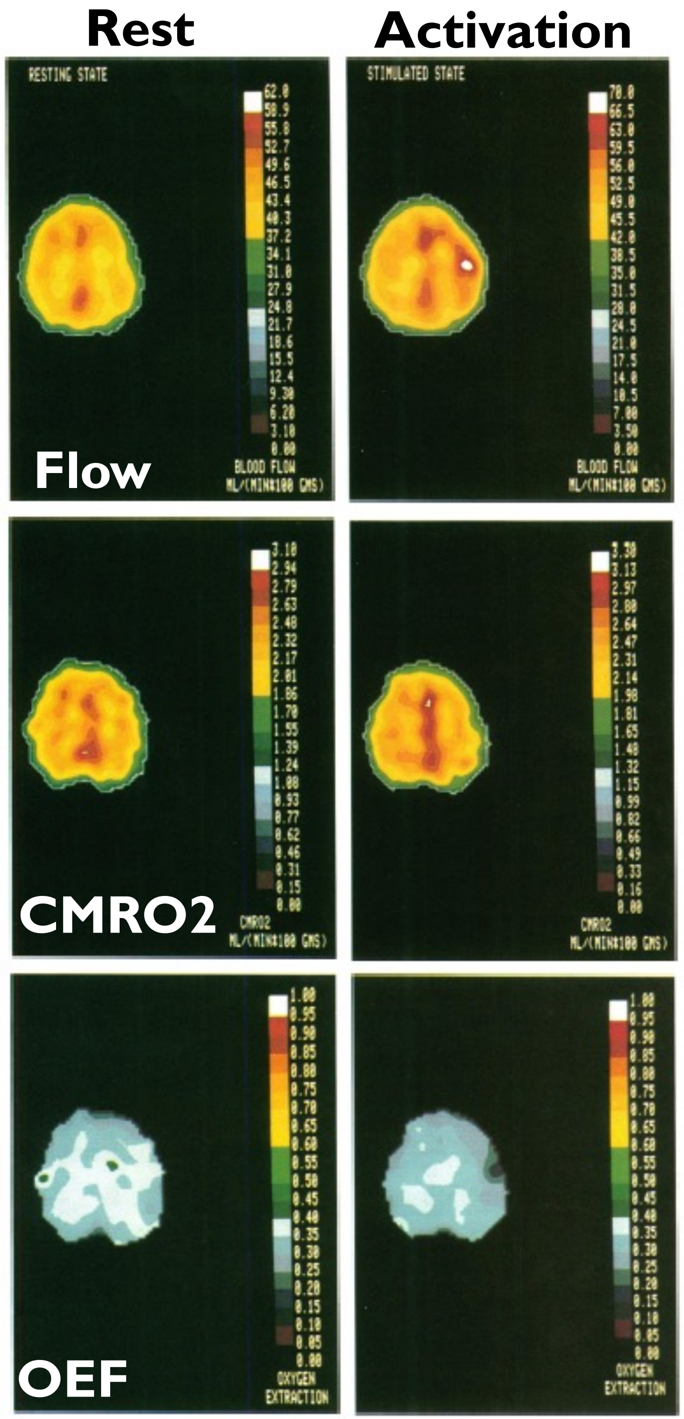
Where are we going?

Ultimate limits and applications?

First Challenges…

- Prove it's meaningful
- Characterize it
- Improve it

Mechanisms of BOLD



Proc. Natl. Acad. Sci. USA
Vol. 83, pp. 1140–1144, February 1986
Neurobiology

Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects

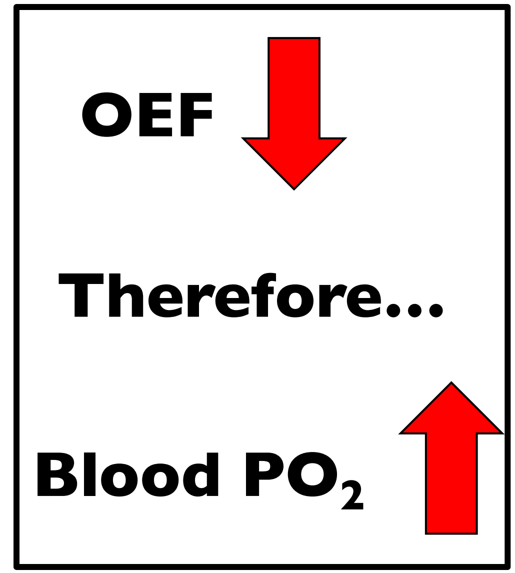
(positron emission tomography)

Peter T. Fox*†‡ and Marcus E. Raichle*†

*Department of Neurology and Neurological Surgery (Neurology), †Department of Radiology (Radiation Sciences), and The McDonnell Center for Studies of Higher Brain Function, Washington University School of Medicine, St. Louis, MO 63110

Communicated by Oliver H. Lowry, October 7, 1985

Fig. 1. Physiological uncoupling of brain blood flow and metabolism. (*Left*) Resting-state measurements. (*Right*) Stimulated-state measurements (unilateral vibrotactile stimulation of the fingers). All images are from a single subject's scanning session and pass through the same brain plane. Color scales are linear with the maxima set at a fixed multiple (1.6) of the global average, to facilitate visual comparisons (16). During specific somatosensory stimulation a marked focal increase in CBF (29% of mean, nine subjects, three trials per subject) was produced in the contralateral sensorimotor cortex. The observed increase in the $CMRo_2$ was much smaller (5% of mean, nine subjects, three trials per subject) and failed to attain significance. This physiological uncoupling of CBF and $CMRo_2$ flow produced a highly significant decrease in the local OEF (−19% of mean), indicating that tissue Po_2 (and probably pH) rose during stimulation. Note that, although the data were analyzed as contralateral/ipsilateral ratios (see text and Tables 1–4), the disparity between blood flow and metabolism was evident from the raw data and was not dependent on a particular strategy of analysis.



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

↓

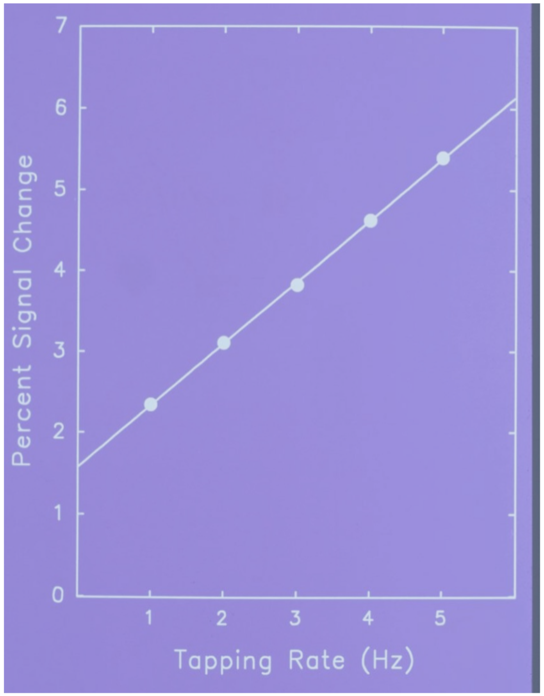
Decrease in susceptibility-related intravoxel dephasing → **Increase in T2 and T2***

↓

Local Signal Increase in T2 and T2* - weighted sequences

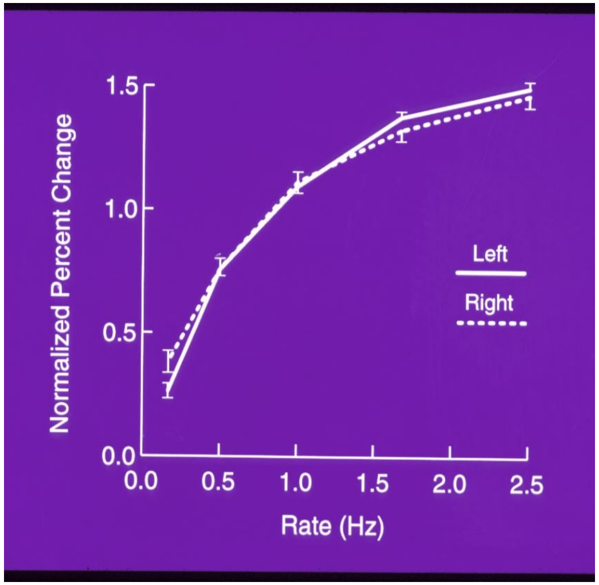
Parametric Manipulation

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.

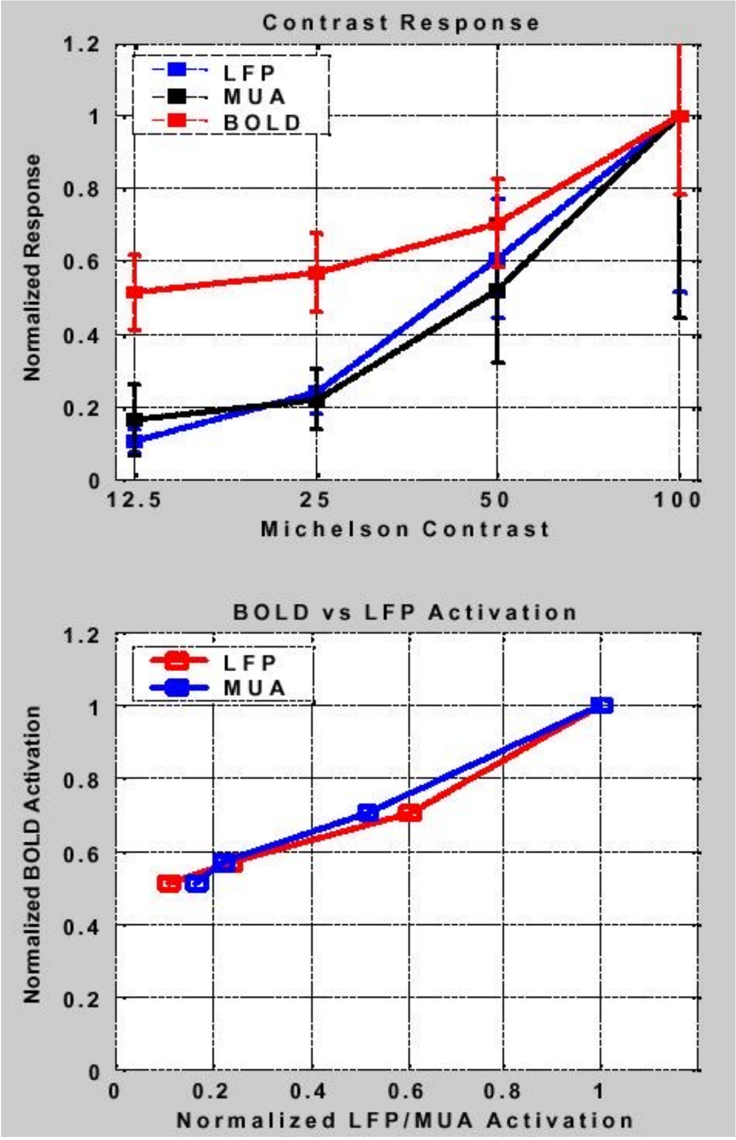
Auditory Cortex



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

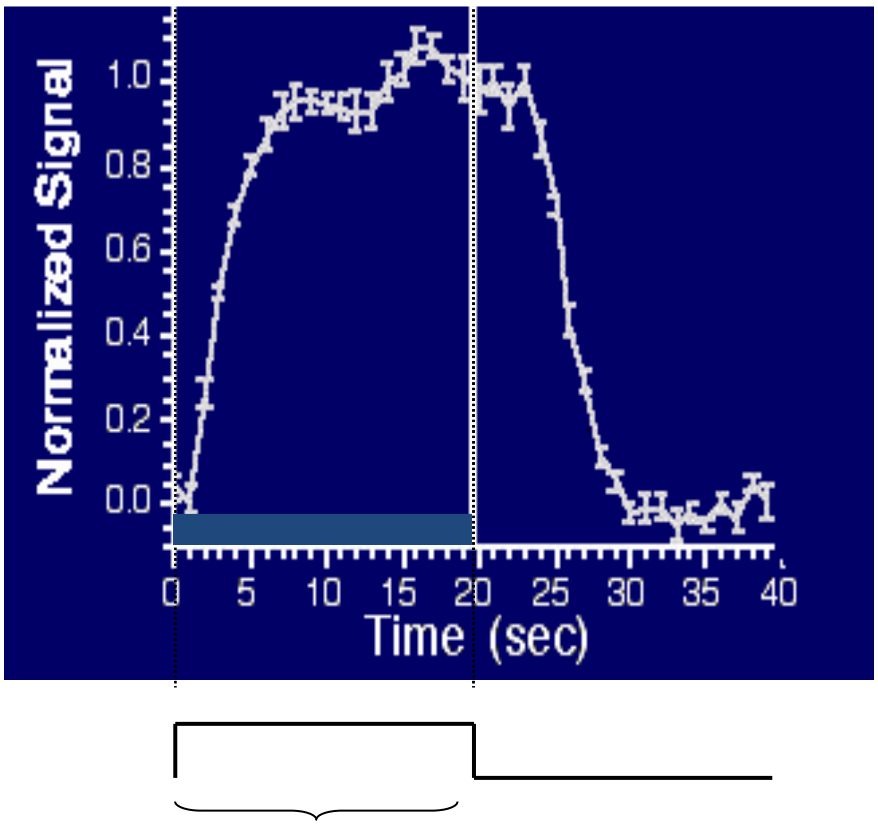
Prove it's Meaningful

Mechanisms of BOLD: Neuronal Correlates

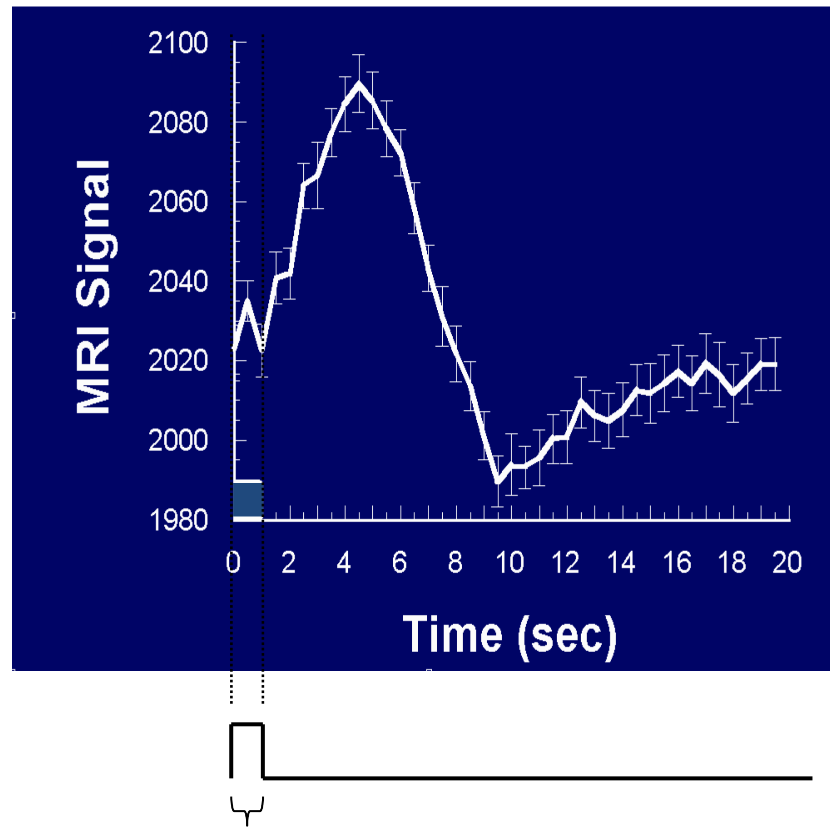


Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

Dynamic Characteristics of BOLD

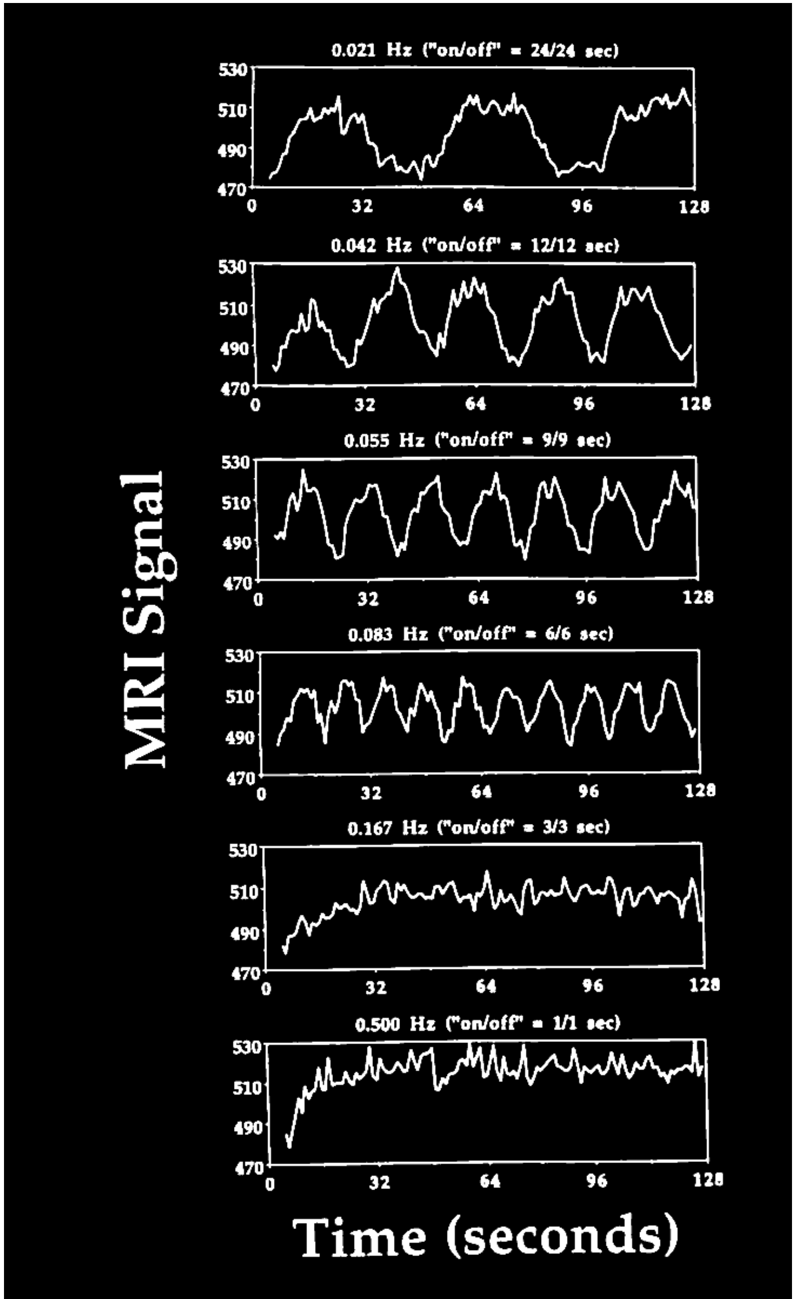


task

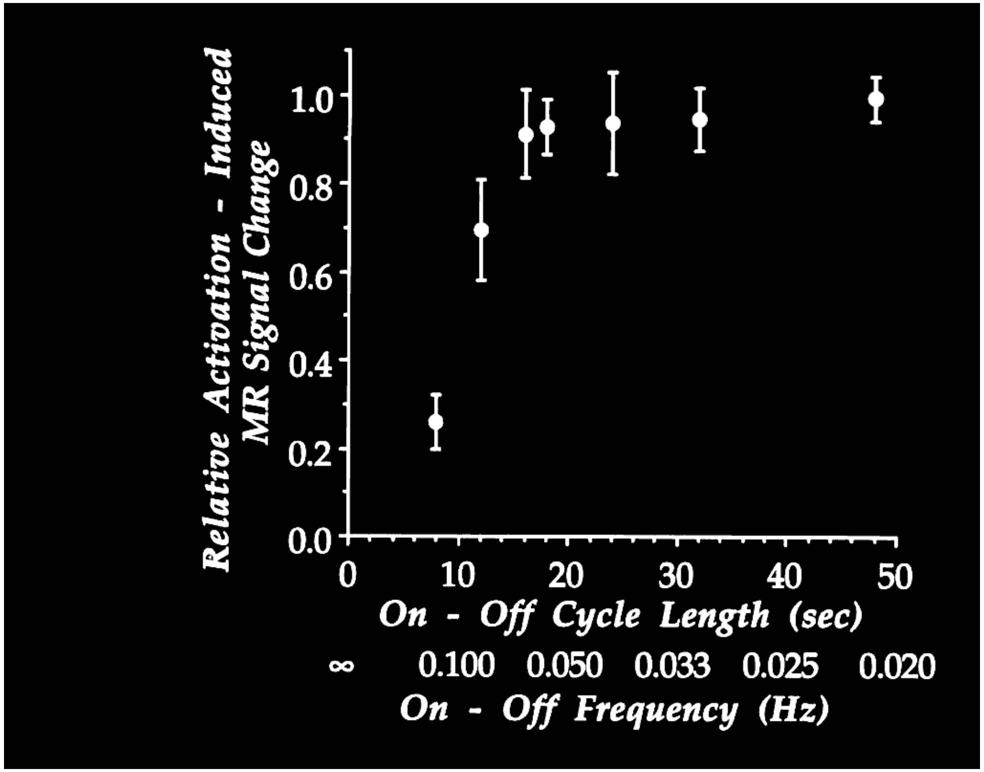


task

Dynamic Characteristics of BOLD



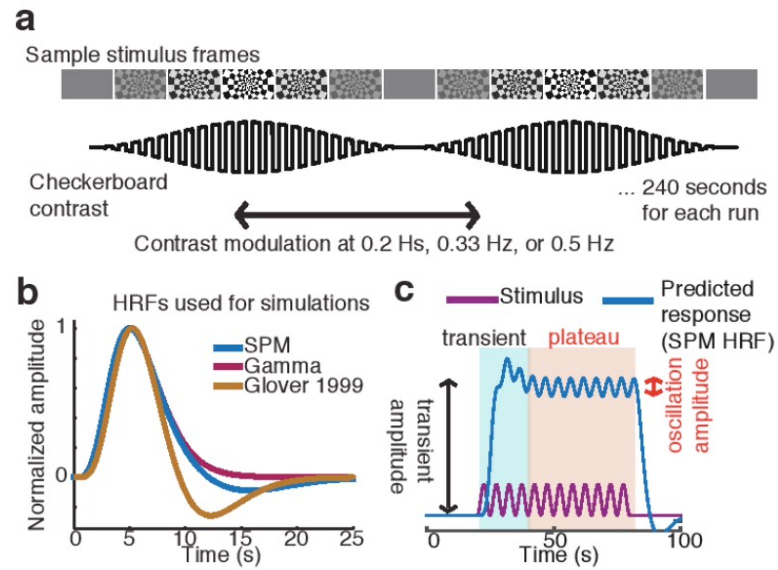
How rapidly can one switch on and off?

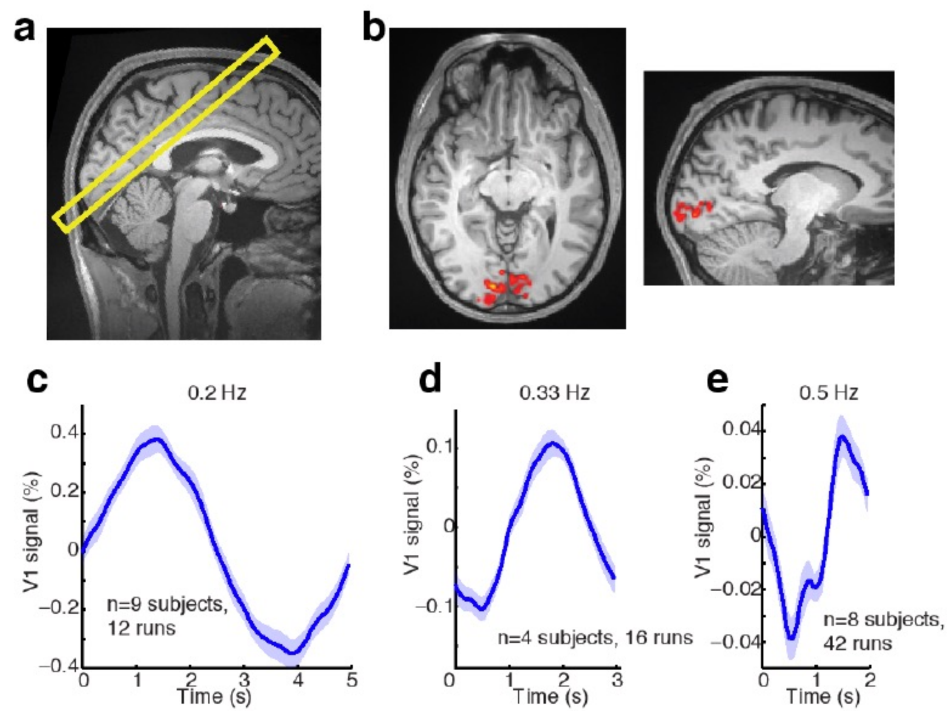


P. A. Bandettini,, Functional MRI using the BOLD approach: dynamic characteristics and data analysis methods, in "Diffusion and Perfusion: Magnetic Resonance Imaging" (D. L. Bihan, Ed.), p.351-362, Raven Press, New York, 1995.

Characterize It

Recently, even faster driven oscillations (0.5Hz…*and potentially 0.75 Hz*) were detected…

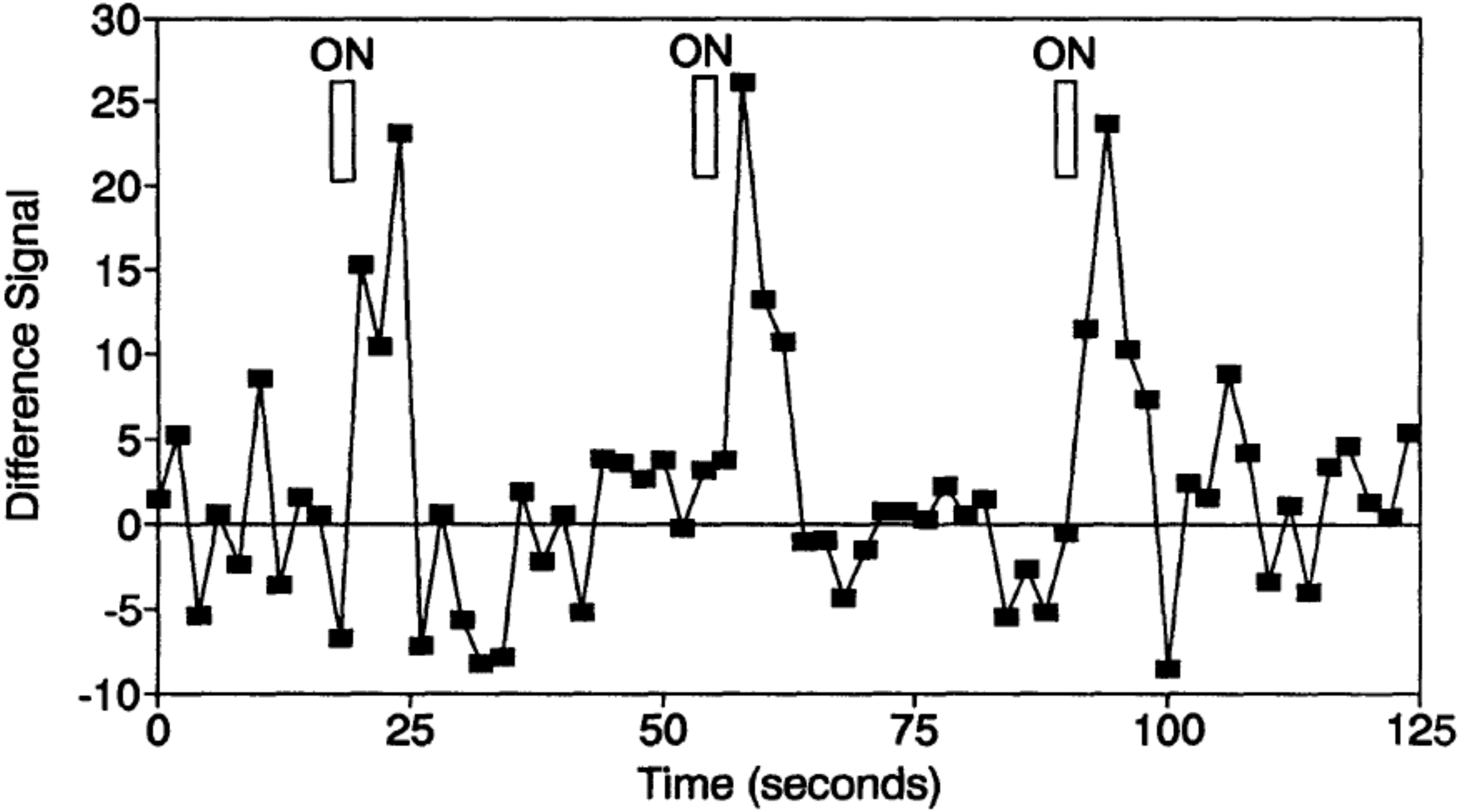




Lewis, et al. PNAS 2016

Dynamic Characteristics of BOLD

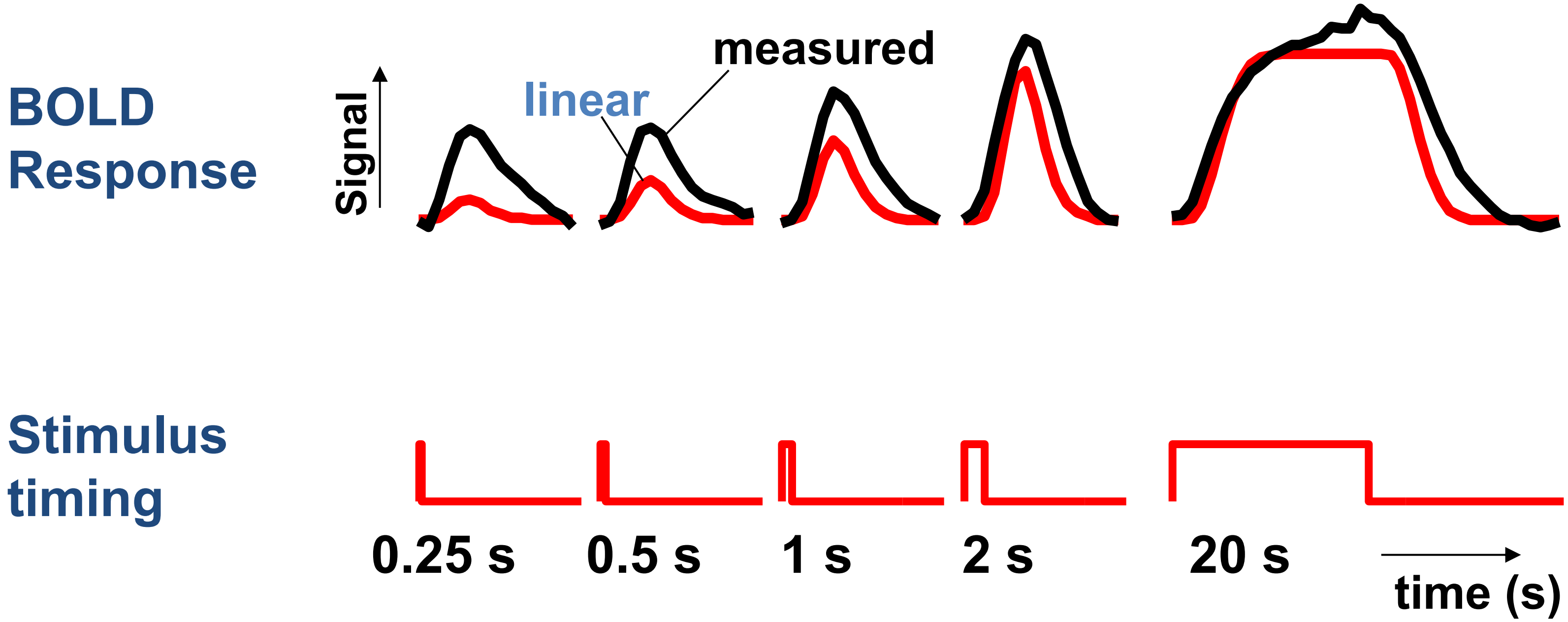
The first event-related study.



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.**

Dynamic Characteristics of BOLD

Different stimulus "ON" periods

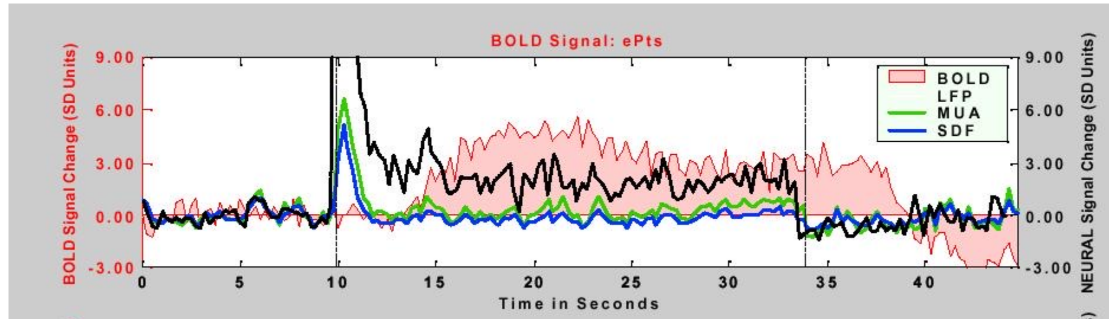


Brief stimuli produce larger responses than expected

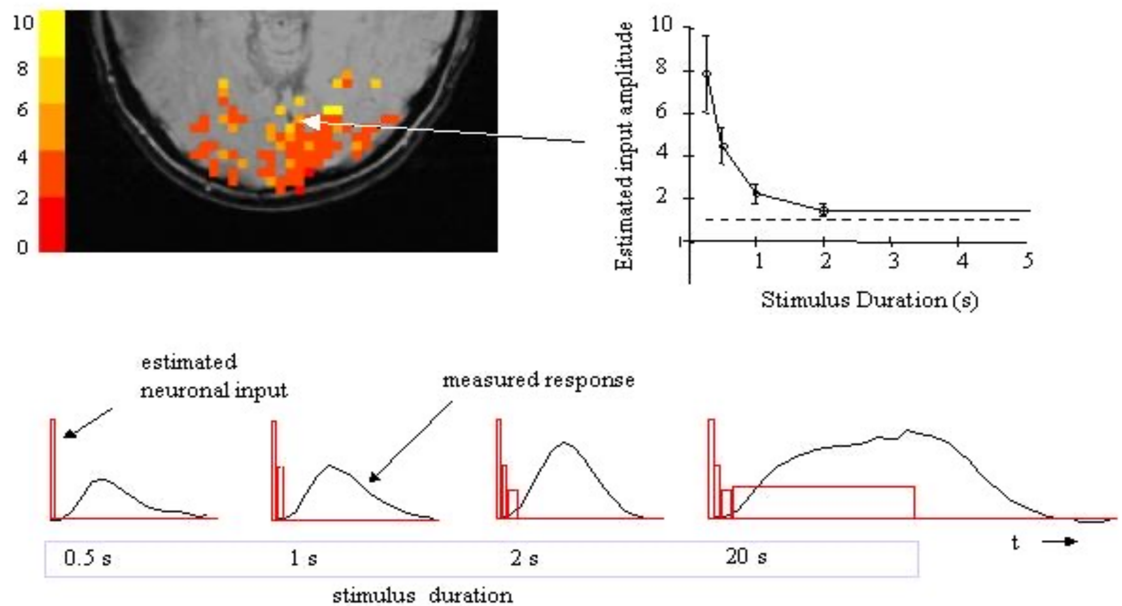
R. M. Birn, Z. Saad, P. A. Bandettini, (2001) "Spatial heterogeneity of the nonlinear dynamics in the fMRI BOLD response." *NeuroImage*, 14: 817-826.

BOLD Correlation with Neuronal Activity

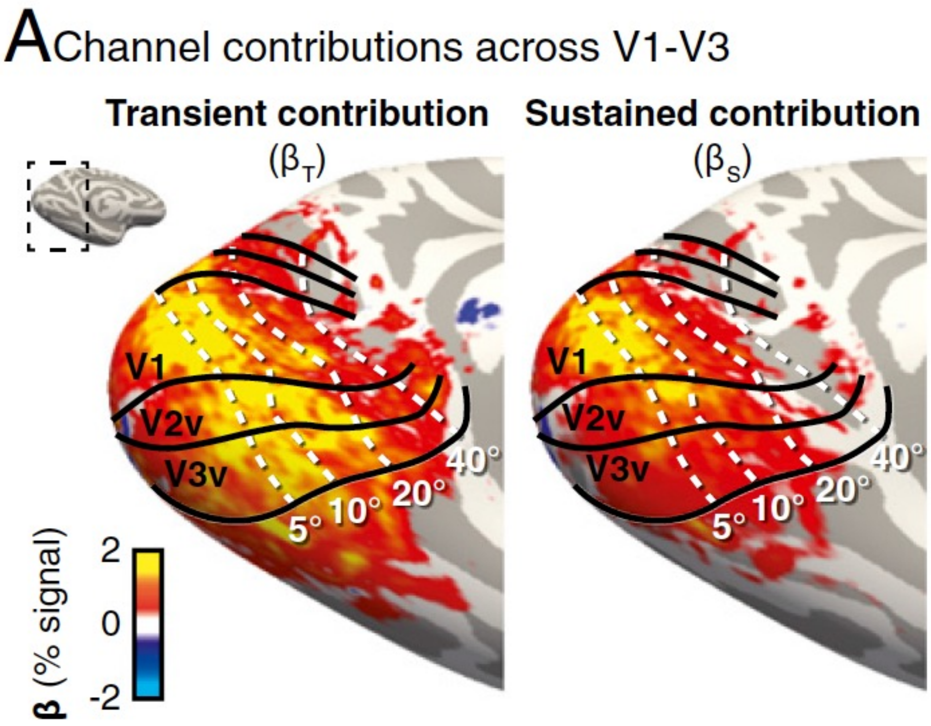
Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157.



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



Characterize It



Stigliani, A., Jeska, B., and Grill-Spector, K. et Encoding model of temporal processing in Human visual cortex, E11047–E11056 PNAS 2017

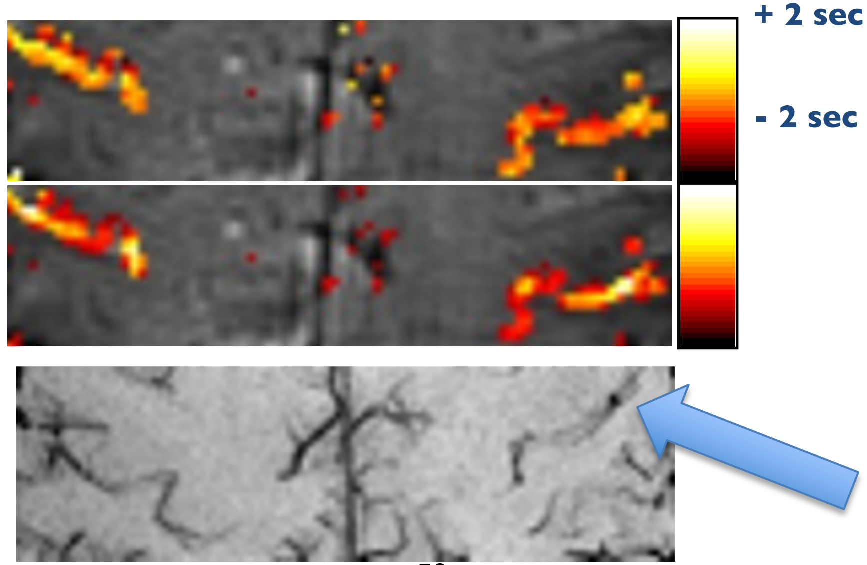
Characterize It

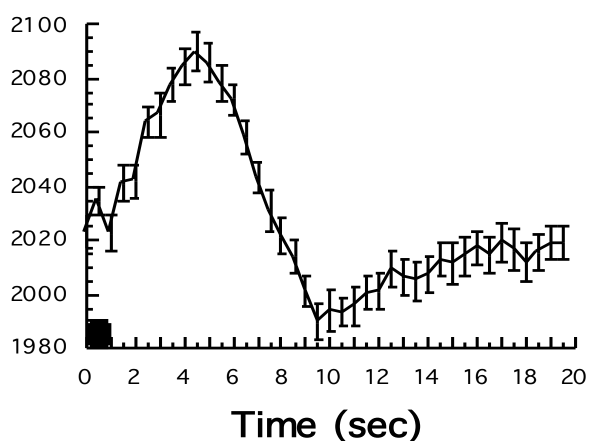
Latency Variation... DRAINING VEIN EFFECTS!

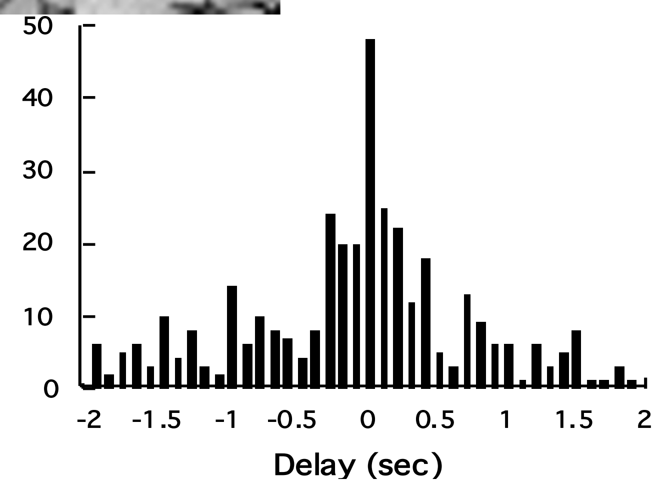
Latency

Magnitude

Venogram

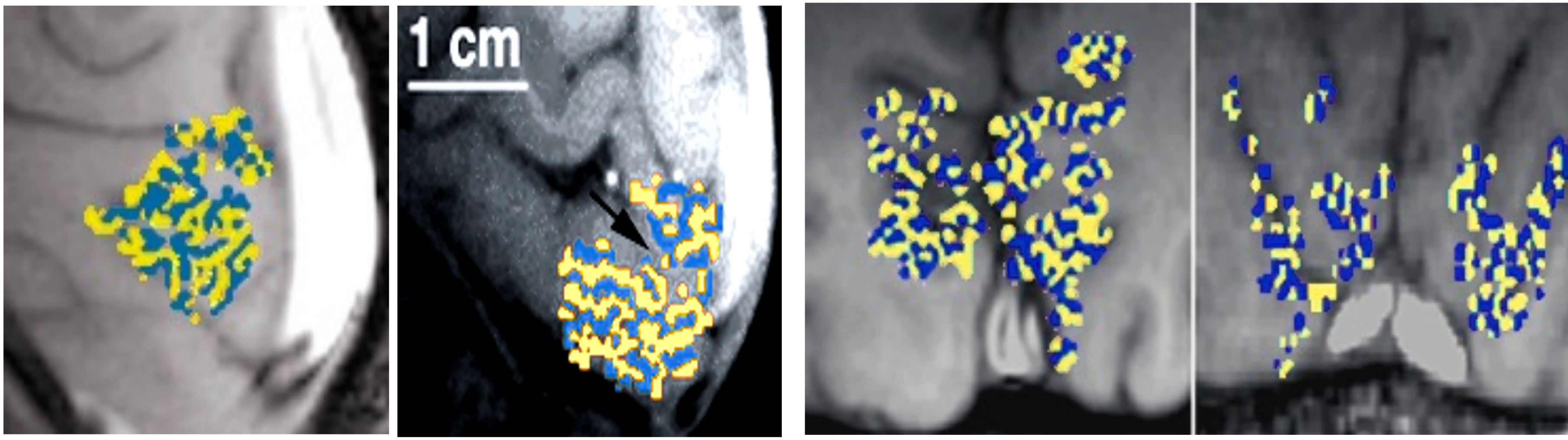






P.A. Bandettini, (1999) "Functional MRI" 205-220.

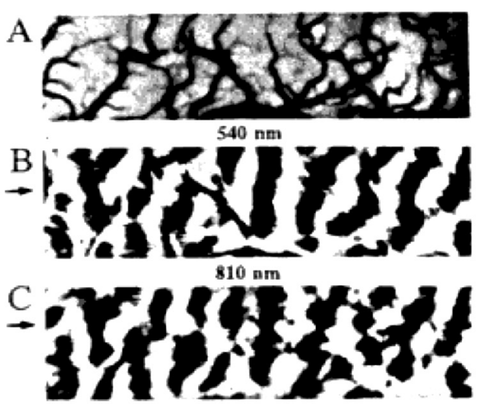
Ocular Dominance Column Mapping



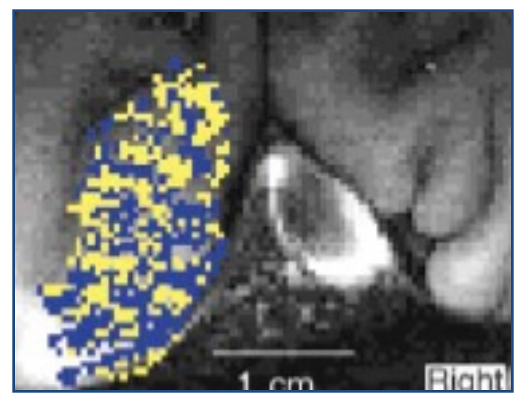
Menon, R. S., S. Ogawa, et al. (1997). J Neurophysiol 77(5): 2780-7.

0.54 x 0.54 in plane resolution

Optical Imaging



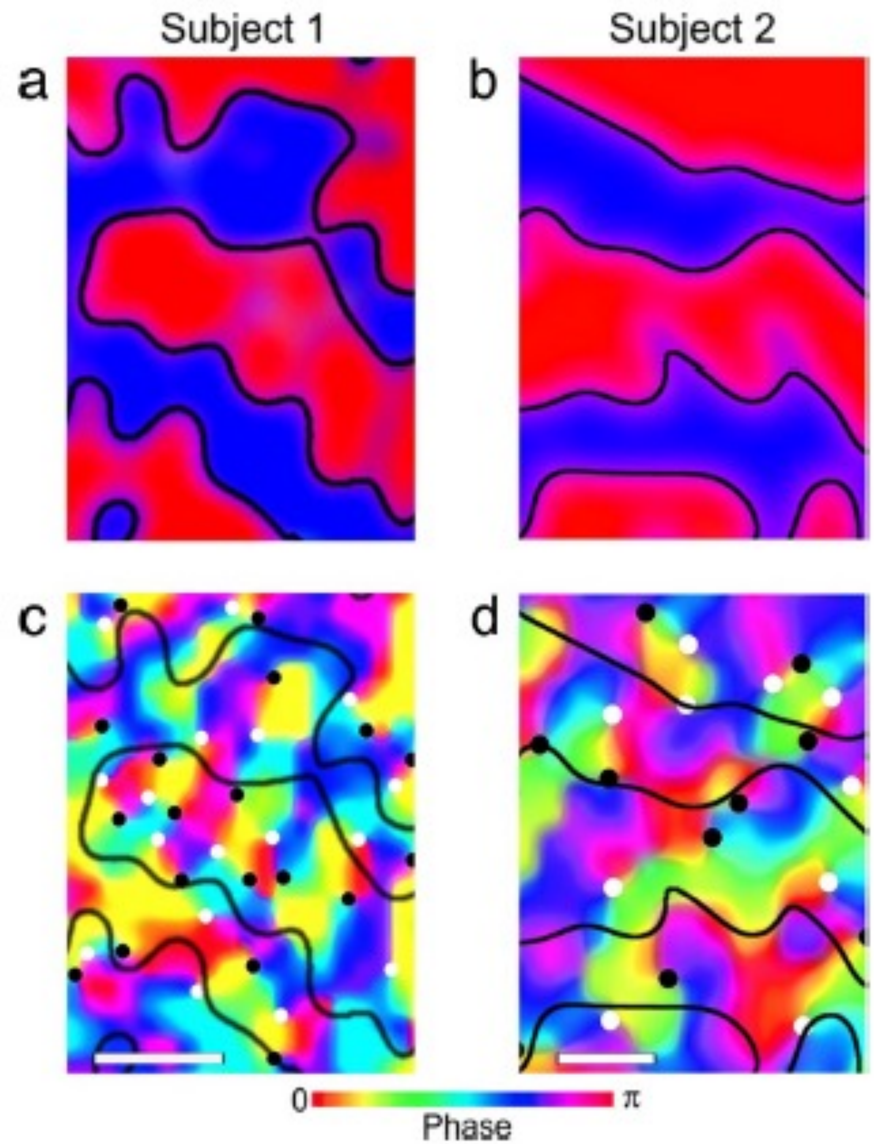
R. D. Frostig et. al, PNAS 87: 6082-6086, (1990).



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

0.47 x 0.47 in plane resolution

Characterize It



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

Yacoub et al. PNAS 2008

First Opportunities…

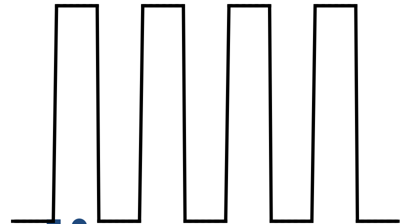
- New Contrasts
- New Paradigms
- New Processing Methods
- New Applications

fMRI Contrast

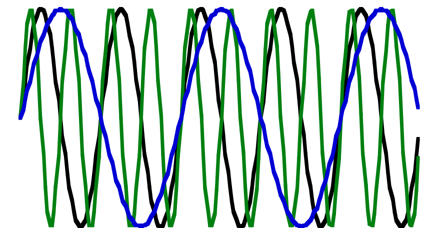
• Volume (gadolinium)	1991
• BOLD (GE and SE)	1992
• Perfusion (ASL)	1992
• $\Delta CMRO_2$	1998
• ΔVolume (VASO)	2001
• Neuronal Currents?	
• Diffusion coefficient?	
• Temperature?	
• Elastography?	

Neuronal Activation Input Strategies

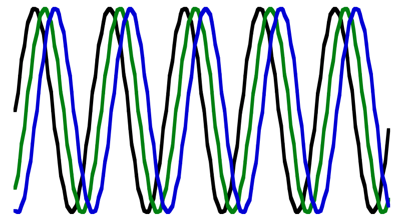
1. Block Design



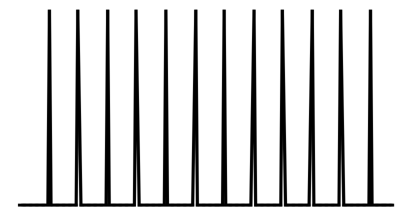
2. Frequency Encoding



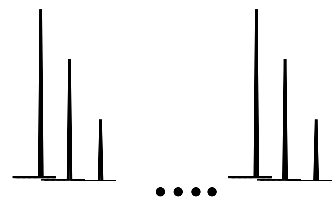
3. Phase Encoding



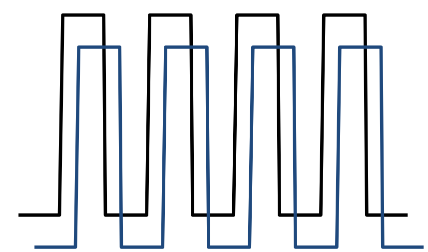
4. Event-Related



5. fMRI adaptation



6. Orthogonal Block Design

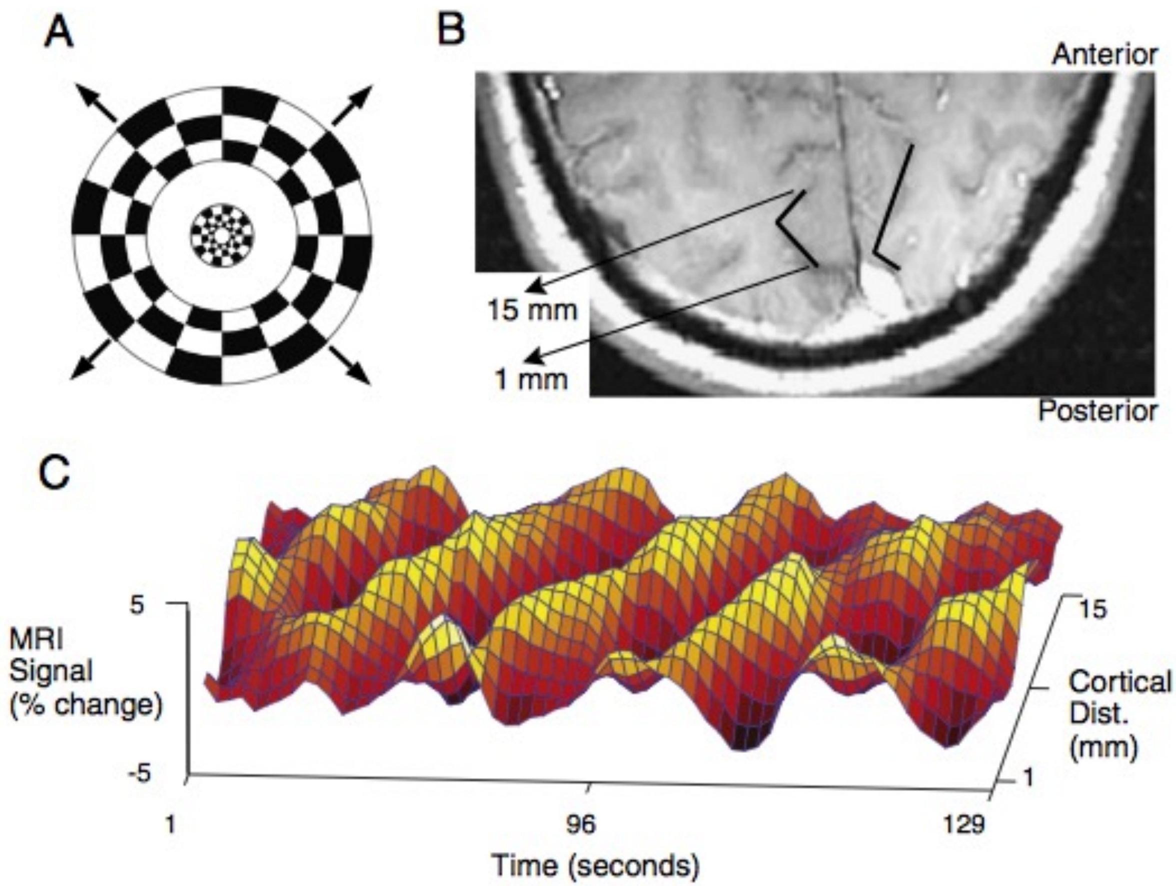


7. Free Behavior Design.

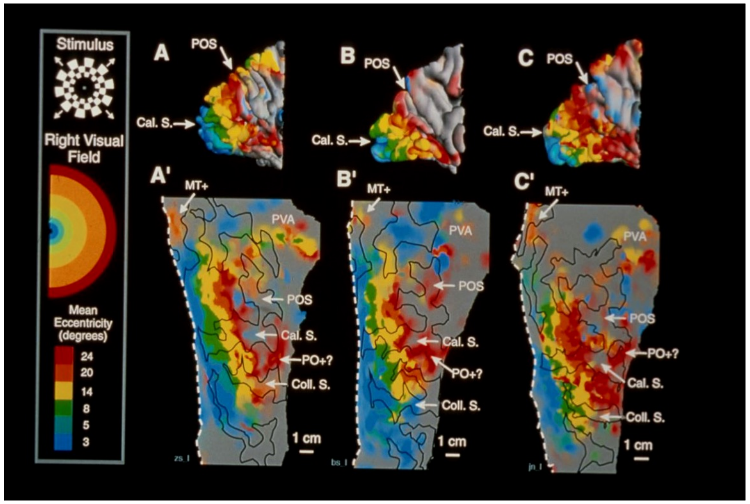
Phase encoding: Retinotopy

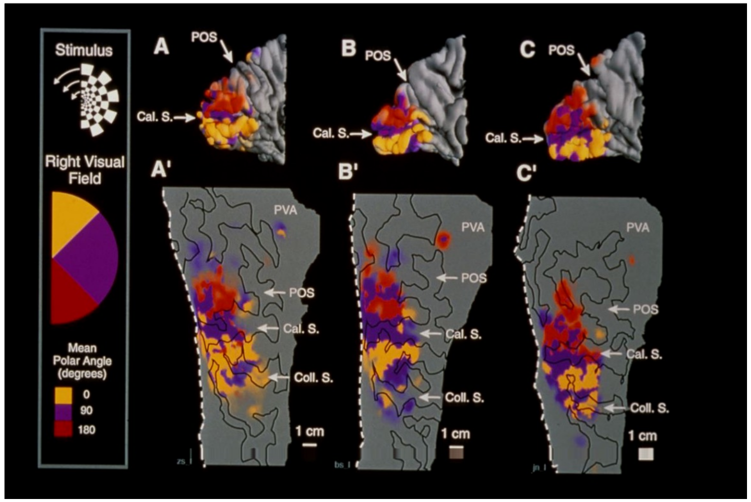
NATURE · VOL 369 · 16 JUNE 1994

Stephen A. Engel
David E. Rumelhart
Brian A. Wandell
Department of Psychology,
Adrian T. Lee
Gary H. Glover
Department of Radiology,
Eduardo-Jose Chichilnisky
Neuroscience Program,
Michael N. Shadlen
Department of Neurobiology,
Stanford University, Stanford,
California 94305, USA



Phase encoding: Retinotopy





Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 2382–2386, March 1996
Neurobiology

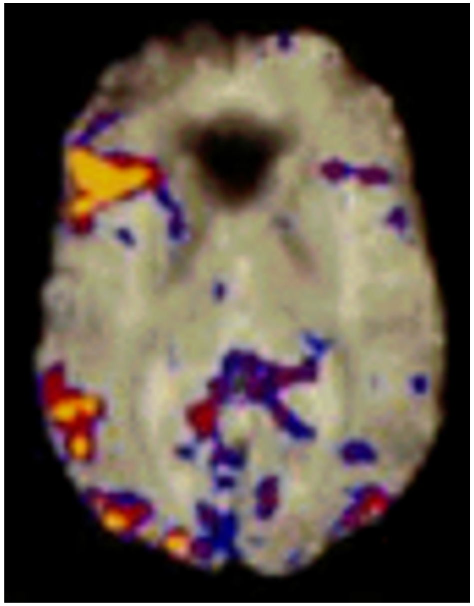
Mapping striate and extrastriate visual areas in human cerebral cortex

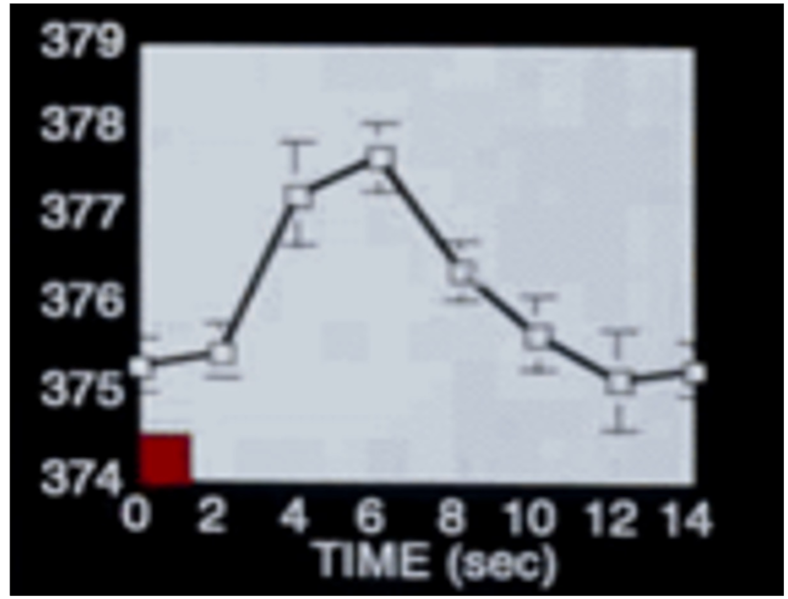
EDGAR A. DEYOE[*], GEORGE J. CARMAN[†], PETER BANDETTINI[‡], SETH GLICKMAN[*], JON WIESER[*], ROBERT COX[§], DAVID MILLER[¶], AND JAY NEITZ[*]

[*]Department of Cellular Biology and Anatomy, and Biophysics Research Institute, The Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226; [†]The Salk Institute for Biological Studies, La Jolla, CA 92037; [‡]Massachusetts General Hospital–NMR Center, Charlestown, MA 02129; [§]Biophysics Research Institute, The Medical College of Wisconsin, Milwaukee, WI 53226; and [¶]Brown University, Providence, RI 02912

Communicated by Francis Crick, The Salk Institute for Biological Sciences, San Diego, CA, November 14, 1995 (received for review August 2, 1995)

First Event-Related Study of Cognition





Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 14878–14883, December 1996
Neurobiology

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

(neuroimaging/single trial/language/prefrontal)

RANDY L. BUCKNER[†‡§¶], PETER A. BANDETTINI[†‡], KATHLEEN M. O'CRAVEN[†‖], ROBERT L. SAVOY[†‖], STEVEN E. PETERSEN[**††], MARCUS E. RAICHLE[§**††], AND BRUCE R. ROSEN[†‡]

[†]Department of Radiology, Massachusetts General Hospital Nuclear Magnetic Resonance Center, Charlestown, MA 02129; [‡]Harvard University Medical School, Boston, MA 02115; [‖]Rowland Institute, Cambridge, MA 02142; and [**]Departments of Neurology and Neurosurgery and McDonnell Center for the Study of Higher Brain Function, and Departments of [§]Radiology and [††]Anatomy and Neurobiology, Washington University Medical School, St. Louis, MO 63110

Contributed by Marcus E. Raichle, September 4, 1996

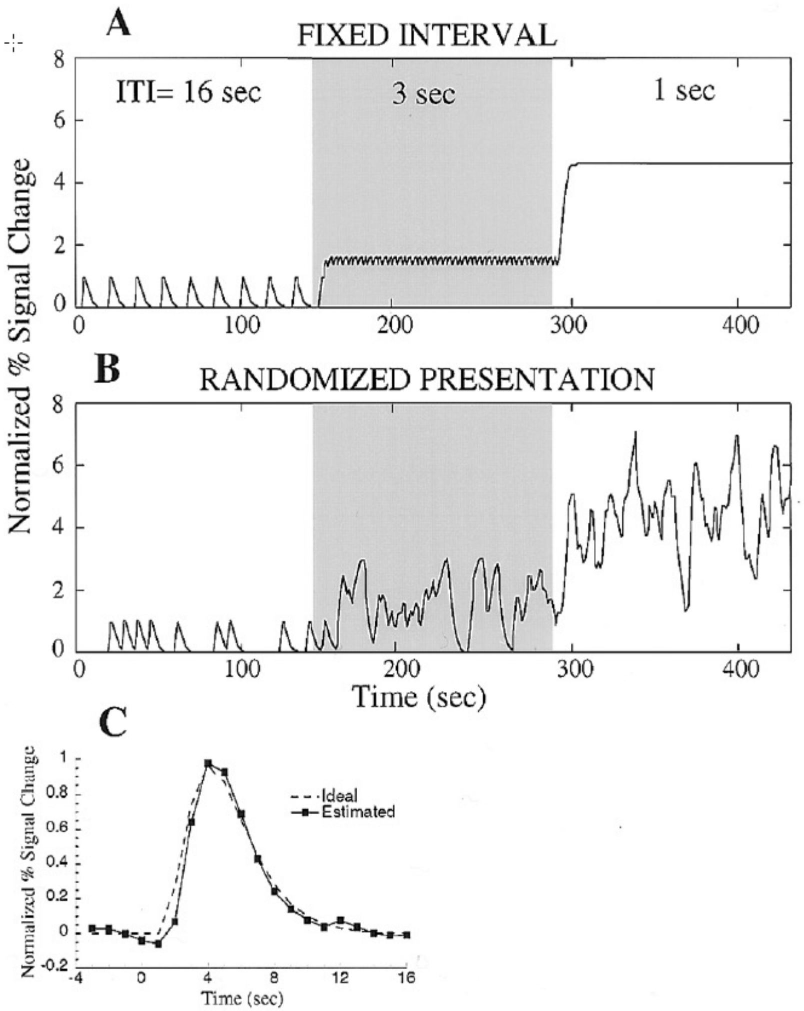
Jittered Event-Related Designs

NeuroRepor t9, 3735–3739 (1998)

Randomized event-related experimental designs allow for extremely rapid presentation rates using functional MRI

Marc A. Burock,[1,2] Randy L. Buckner,[3] Marty G. Woldorff,[4] Bruce R. Rosen[1] and Anders M. Dale[1,CA]

[1]Massachusetts General Hospital, Nuclear Magnetic Resonance Center, Bldg 149, 13th Street, Charlestown, MA 02129; [2]Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA 02129; [3]Washington University, Department of Psychology, St. Louis, MO 63130; [4]University of Texas Health Science Center, Research Imaging Center, San Antonio, TX 78284, USA



New Paradigms

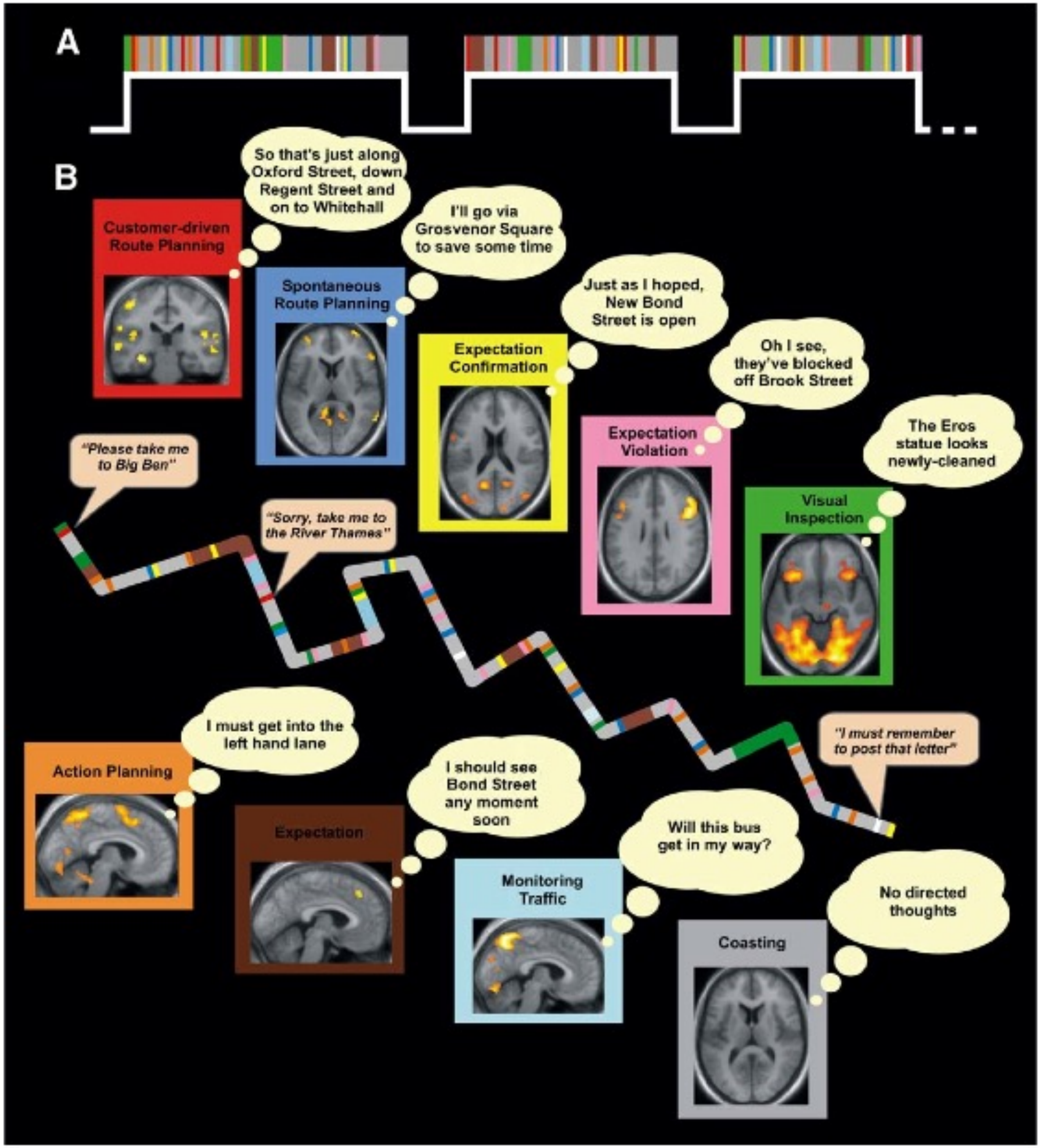
Free Behavior Designs

Category	Definition	Mean number of occurrences (SD)
Customer-driven Route Planning	Planning a route to a given destination	16.6 (1.8)
Subtypes: Initial plan	Planning from the initial request	6.8 (0.8)
Change in plan	Planning after an en route request from a customer to alter the destination	9.8 (1.0)
Spontaneous Route Planning	Further planning en route, independent of customers	34.3 (10.9)
Subtypes: Filling in	Planning the next stage of the journey	17.7 (6.6)
Re-planning	Altering the current plan to adapt to the environment	16.7 (5.7)
Action Planning	Planning future movements with the vehicle	45.8 (15.1)
Expectation Confirmation	Detecting the presence of an expected environmental feature	28.6 (9.9)
Expectation Violation	Detecting the absence of an expected environmental feature	31.6 (10.5)
Expectation	Looking out for the next expected environmental feature	24.5 (8.5)
Visual Inspection	Visual inspection of an environmental feature	36.0 (11.8)
Monitoring Traffic	Watching moving traffic in the environment	11.4 (5.9)
Coasting	Navigating automatically without any directed thoughts	25.8 (7.5)
Customers' Navigationally-Irrelevant Statements	Navigationally-irrelevant statements by customers, (a control for Customer-driven Route Planning)	6.6 (0.9)

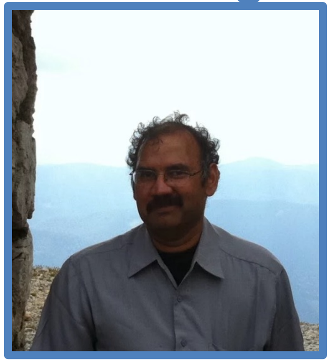
Thoughts, behaviour, and brain dynamics during navigation in the real world. Hugo J. Spiers and Eleanor A. Maguire, NeuroImage, 31 (2006), 1826-1840.

New Paradigms

Thoughts, behaviour, and brain dynamics during navigation in the real world. Hugo J. Spiers and Eleanor A. Maguire, NeuroImage, 31 (2006), 1826-1840.



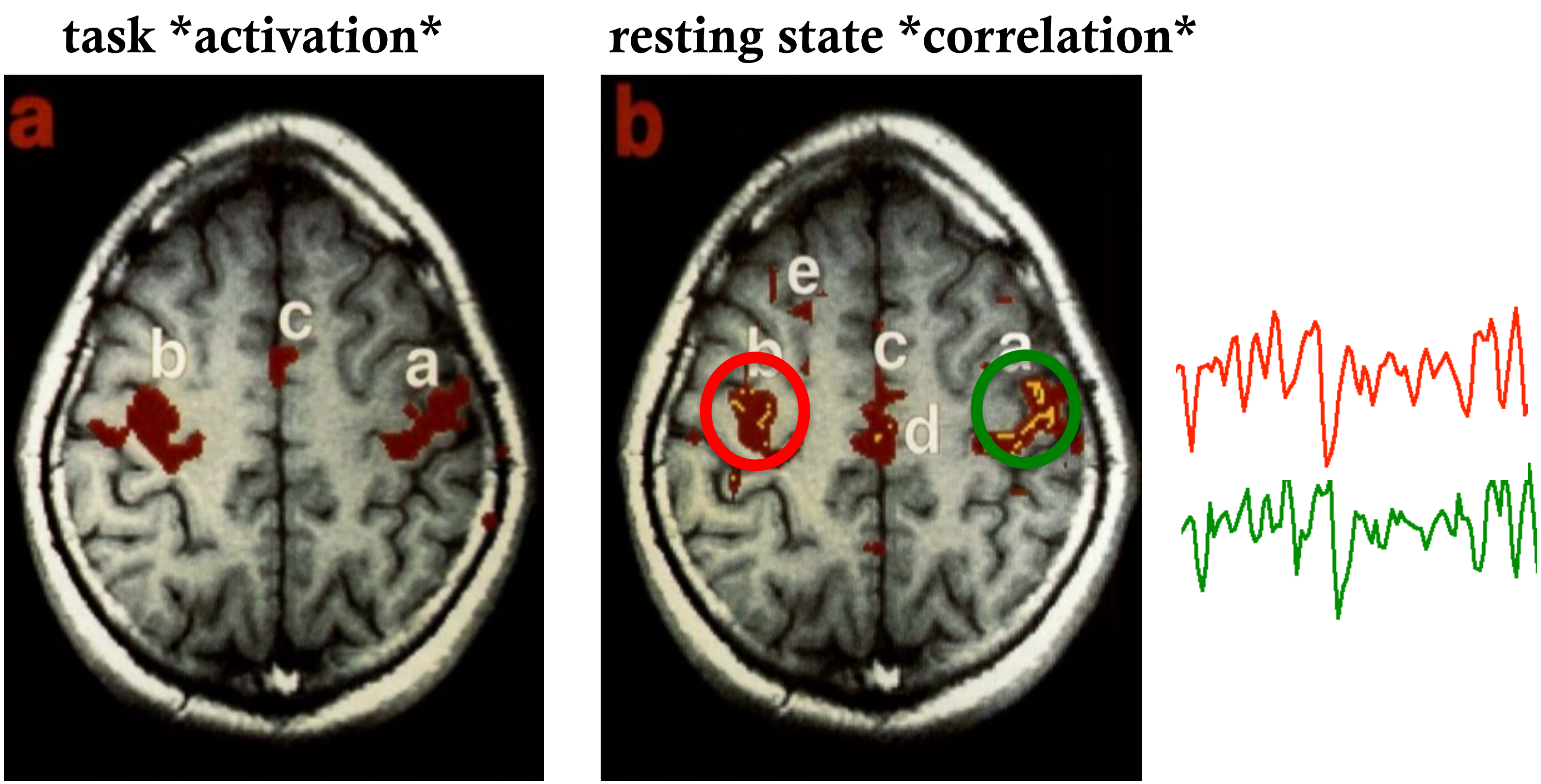
New Paradigms



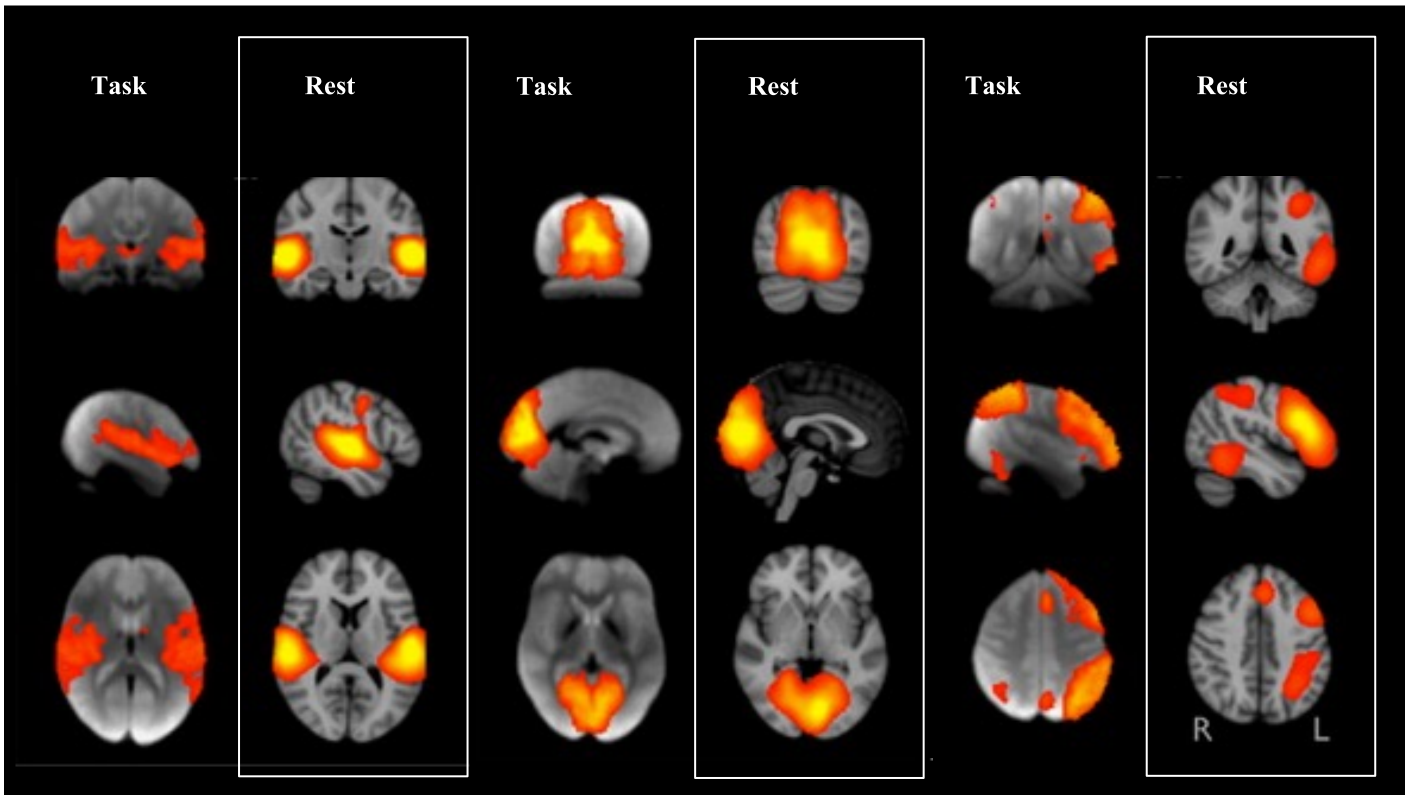
Functional Connectivity in the Motor Cortex of Resting Human Brain Using Echo-Planar MRI

Bharat Biswal, F. Zerrin Yetkin, Victor M. Haughton, James S. Hyde

Mag. Res. Med. 1995, ~5300 citations



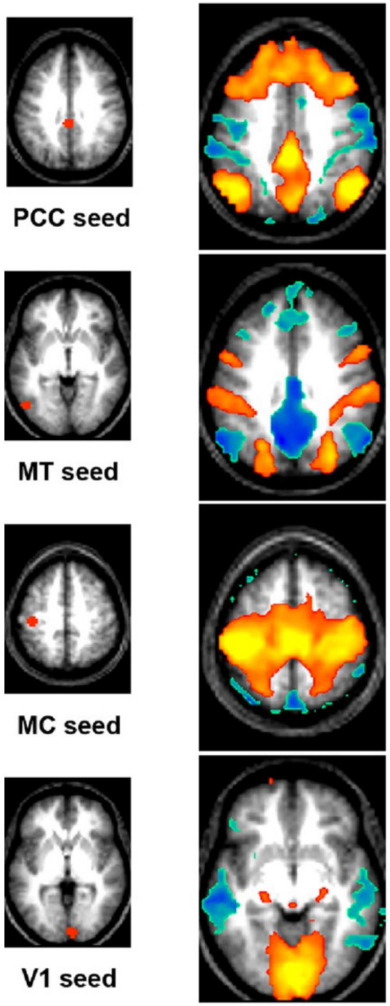
Resting-state "networks" closely resemble task-activated networks



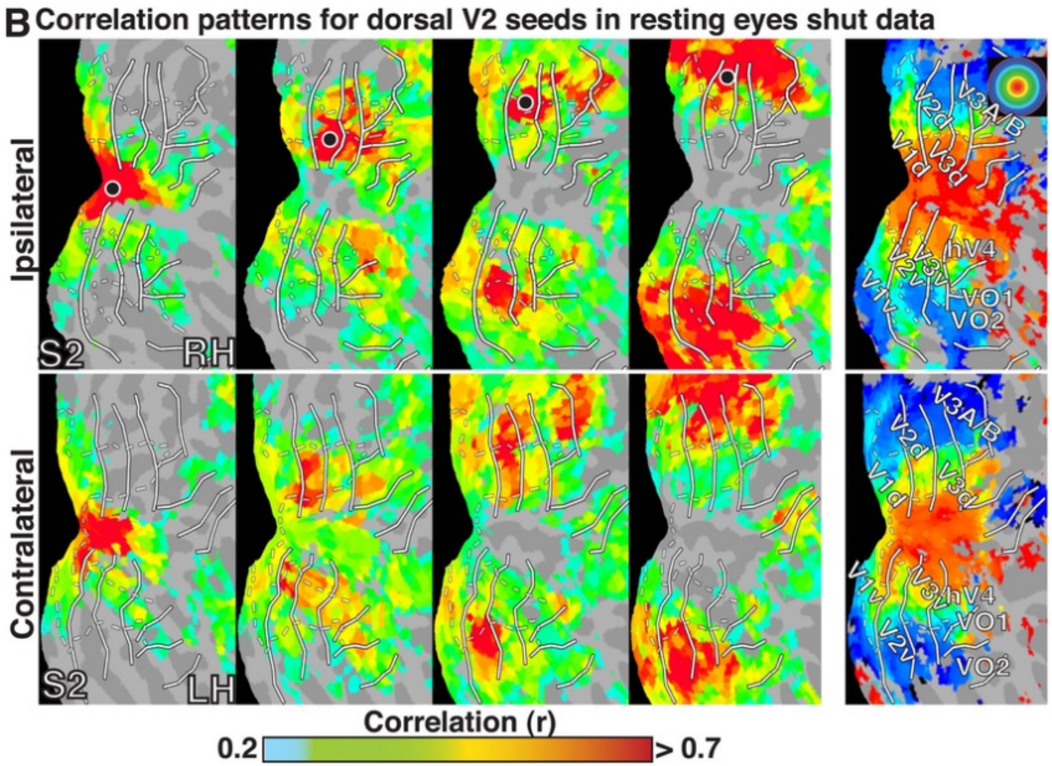
Smith et al, 2009

-> Suggests we may be able to map multiple functional networks without needing tasks

Seed-based resting state correlation reveals retinotopy



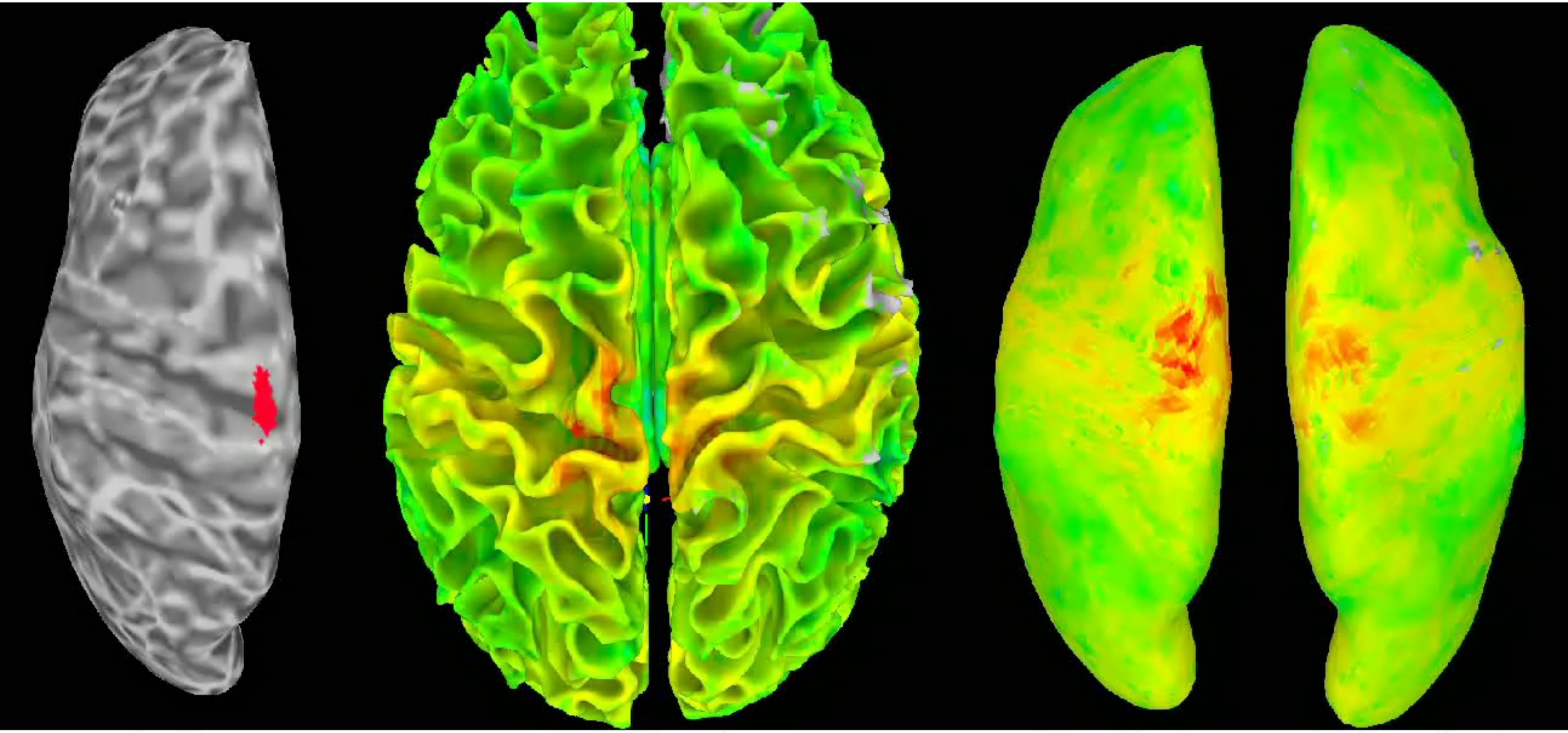
Fox et al. 2009



Arcaro et al., 2015

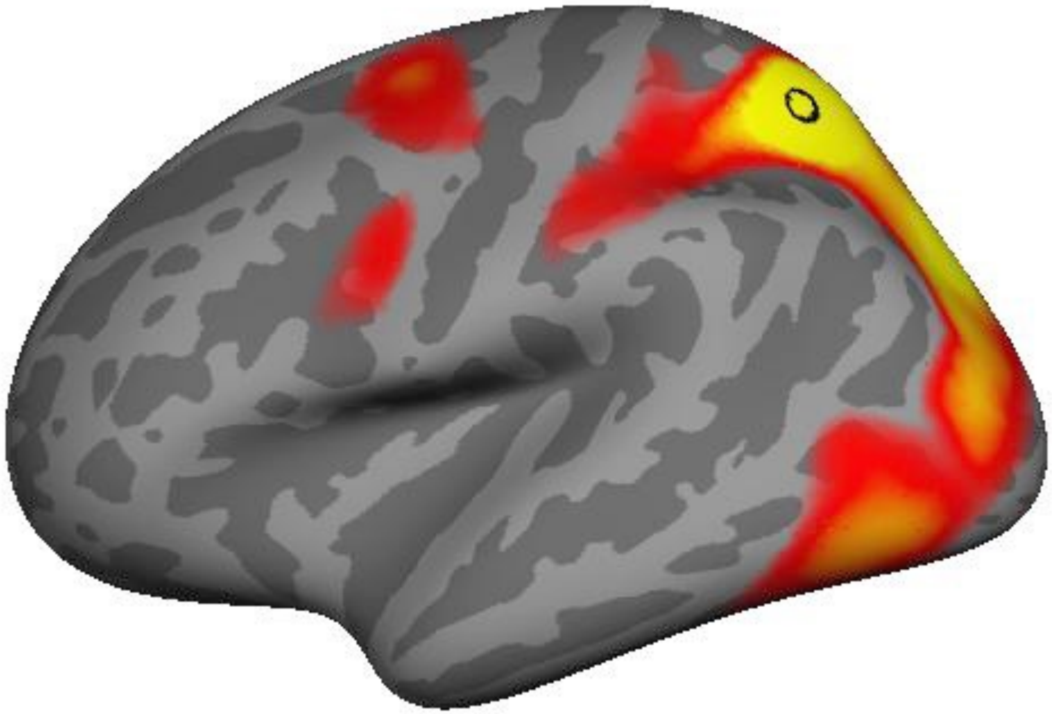
Sliding Seed-based Correlation Movies

Relative correlation strength pattern obtained with a systematically shifted seed region



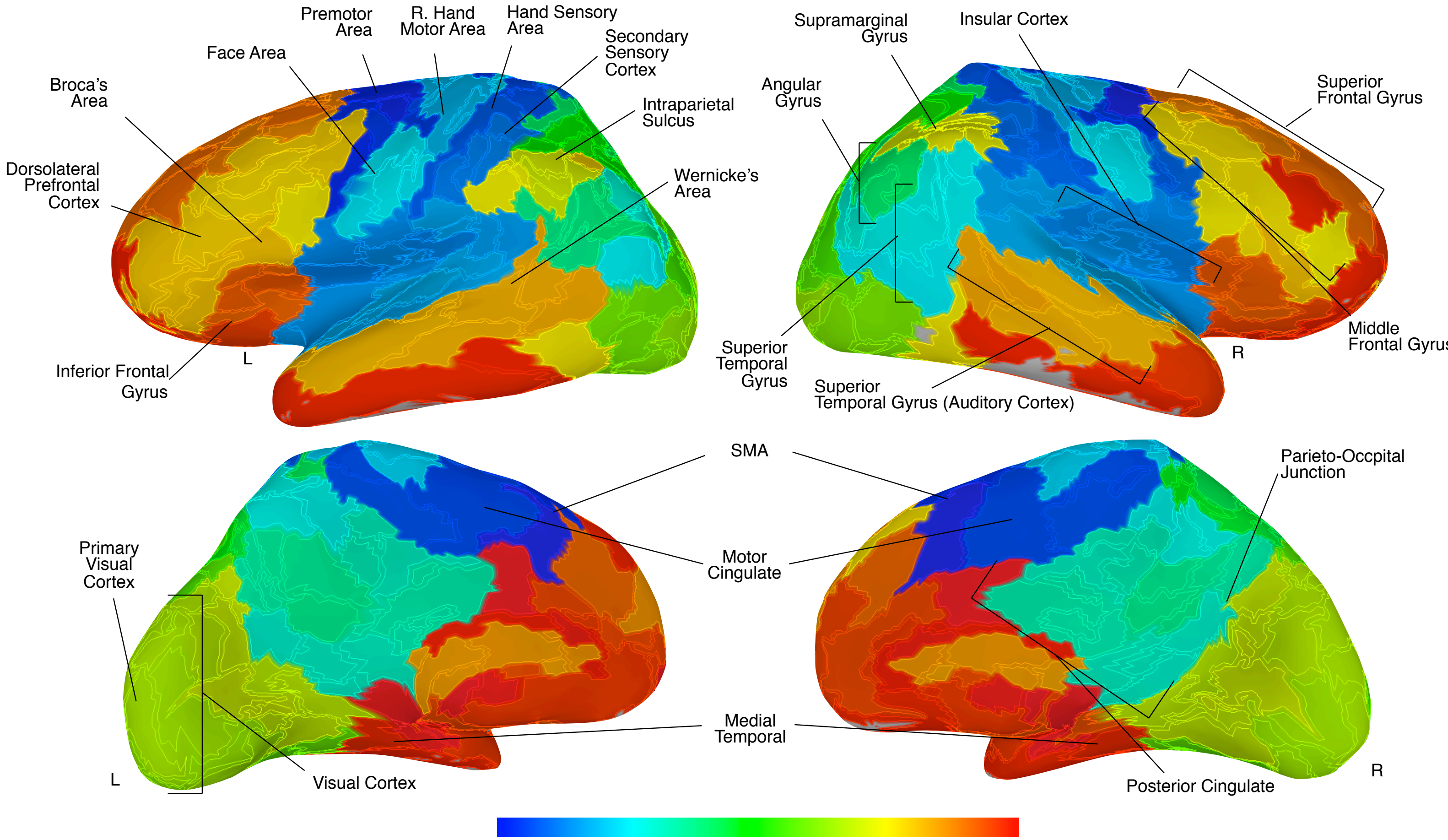
Seed 1 GM/WM Boundary LH (seed hemi) RH (contra hemi)

Sliding Seed-based Correlation Movies



Buckner et al. 2013

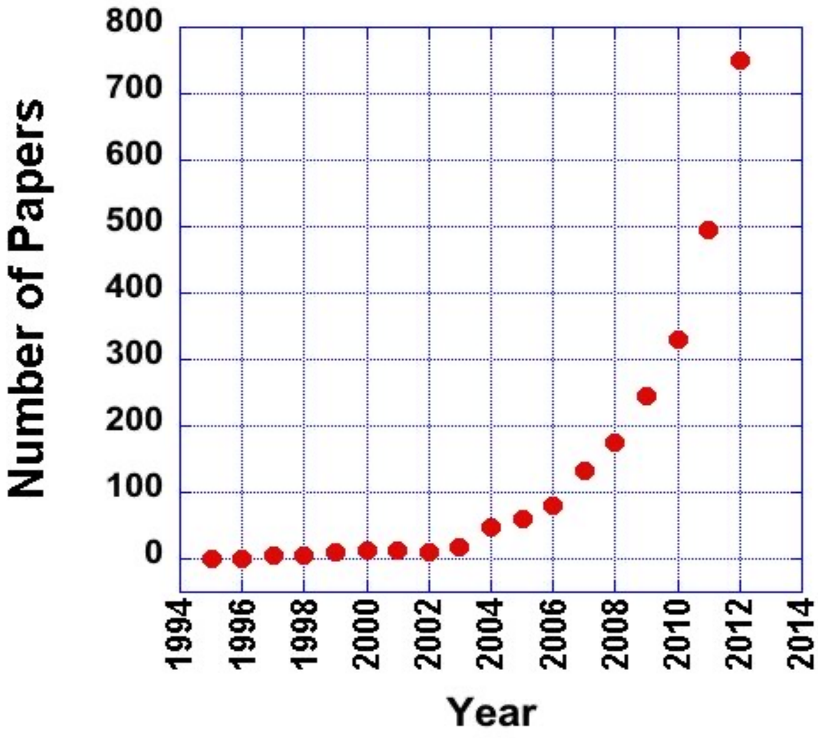
Whole brain connectivity patterns from resting state signal



Khundu et al.

Resting State Fluctuations and Connectivity Assessment

Resting state fMRI



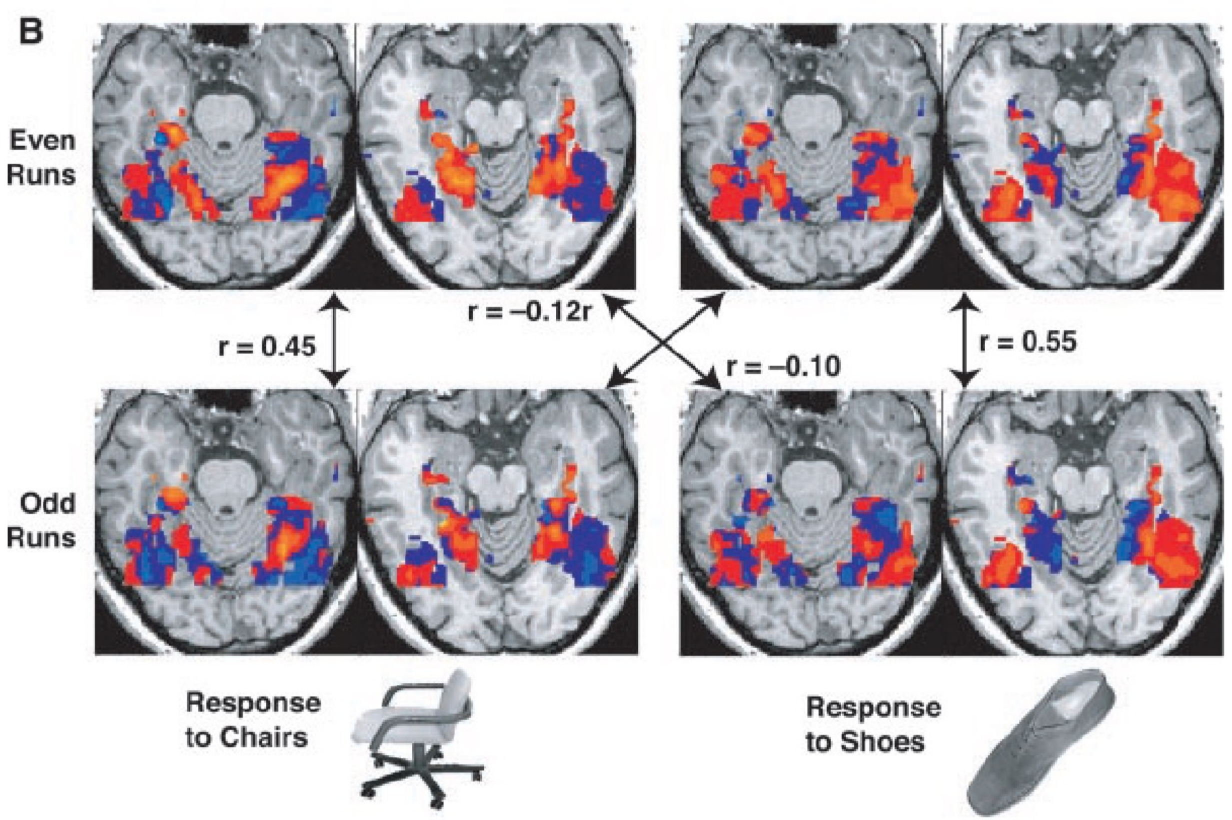
From Blobs to Information-rich Patterns

Multivariate Assessment

Distributed and Overlapping Representations of Faces and Objects in Ventral Temporal Cortex

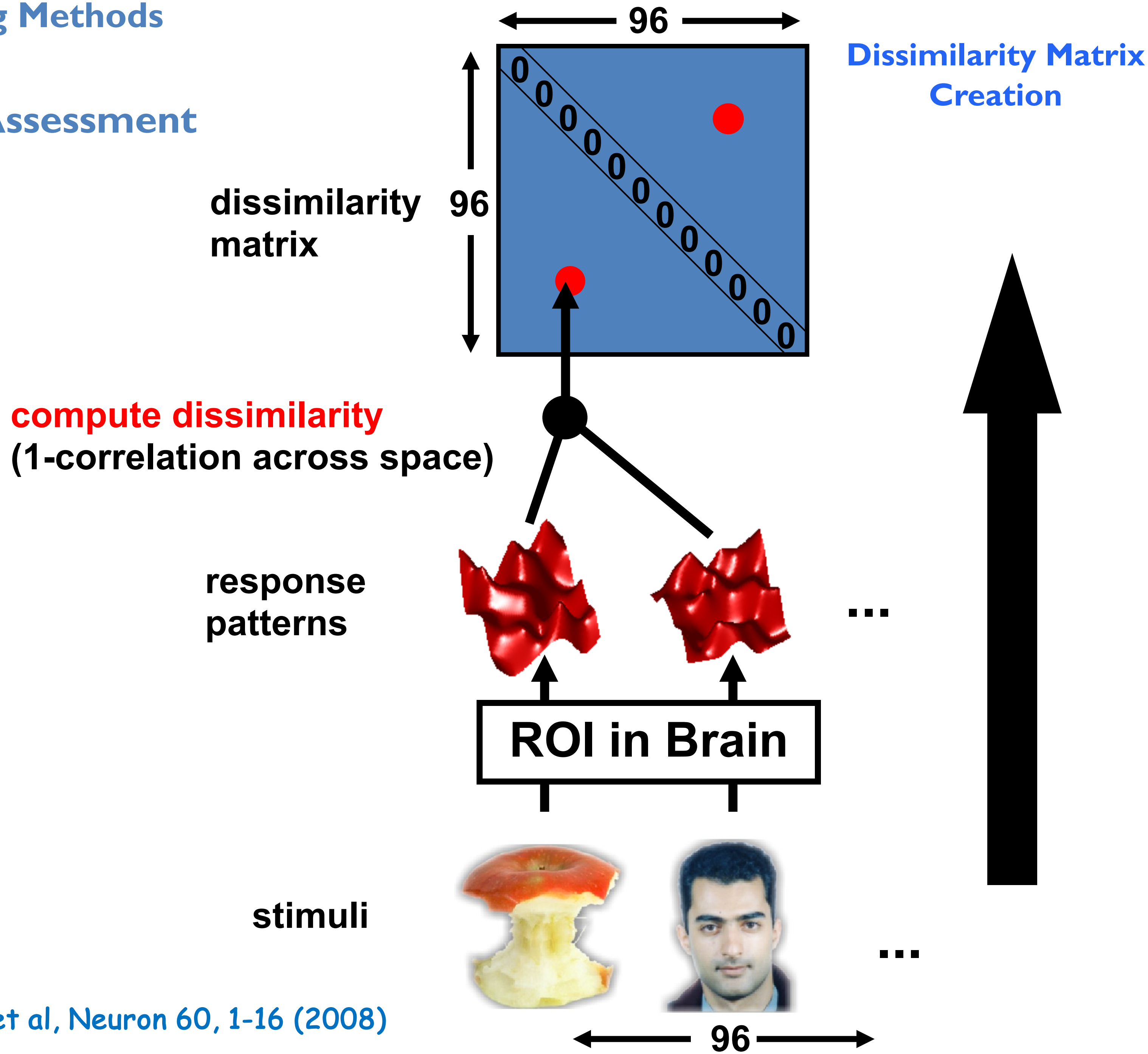
James V. Haxby,[1*] M. Ida Gobbini,[1,2] Maura L. Furey,[1,2]
Alumit Ishai,[1] Jennifer L. Schouten,[1] Pietro Pietrini[3]

SCIENCE VOL 293 28 SEPTEMBER 2001



New Processing Methods

Multivariate Assessment



N. Kriegeskorte, et al, Neuron 60, 1-16 (2008)

Multivariate Assessment

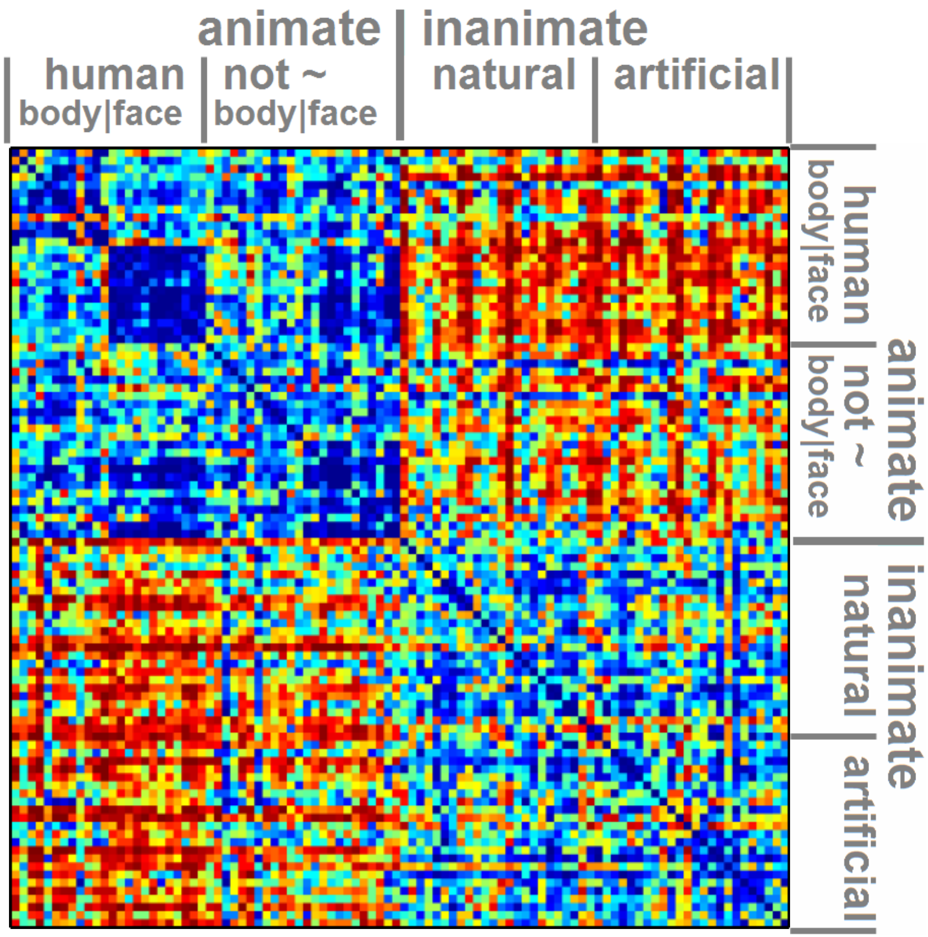
Visual Stimuli

New Processing Methods

Multivariate Assessment

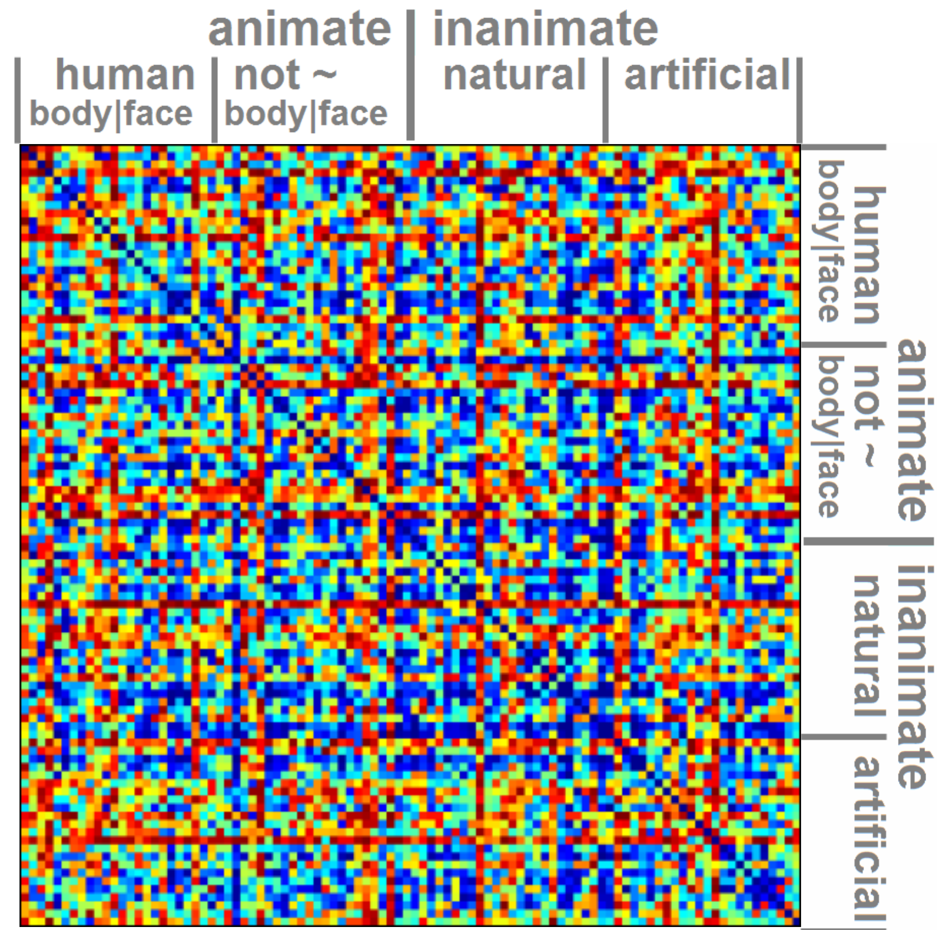
Human IT

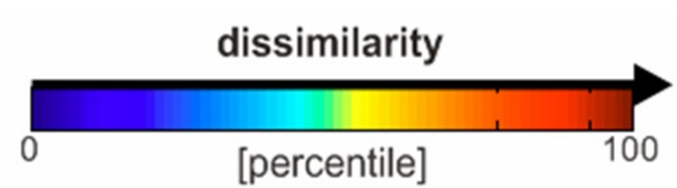
(1000 visually most responsive voxels)



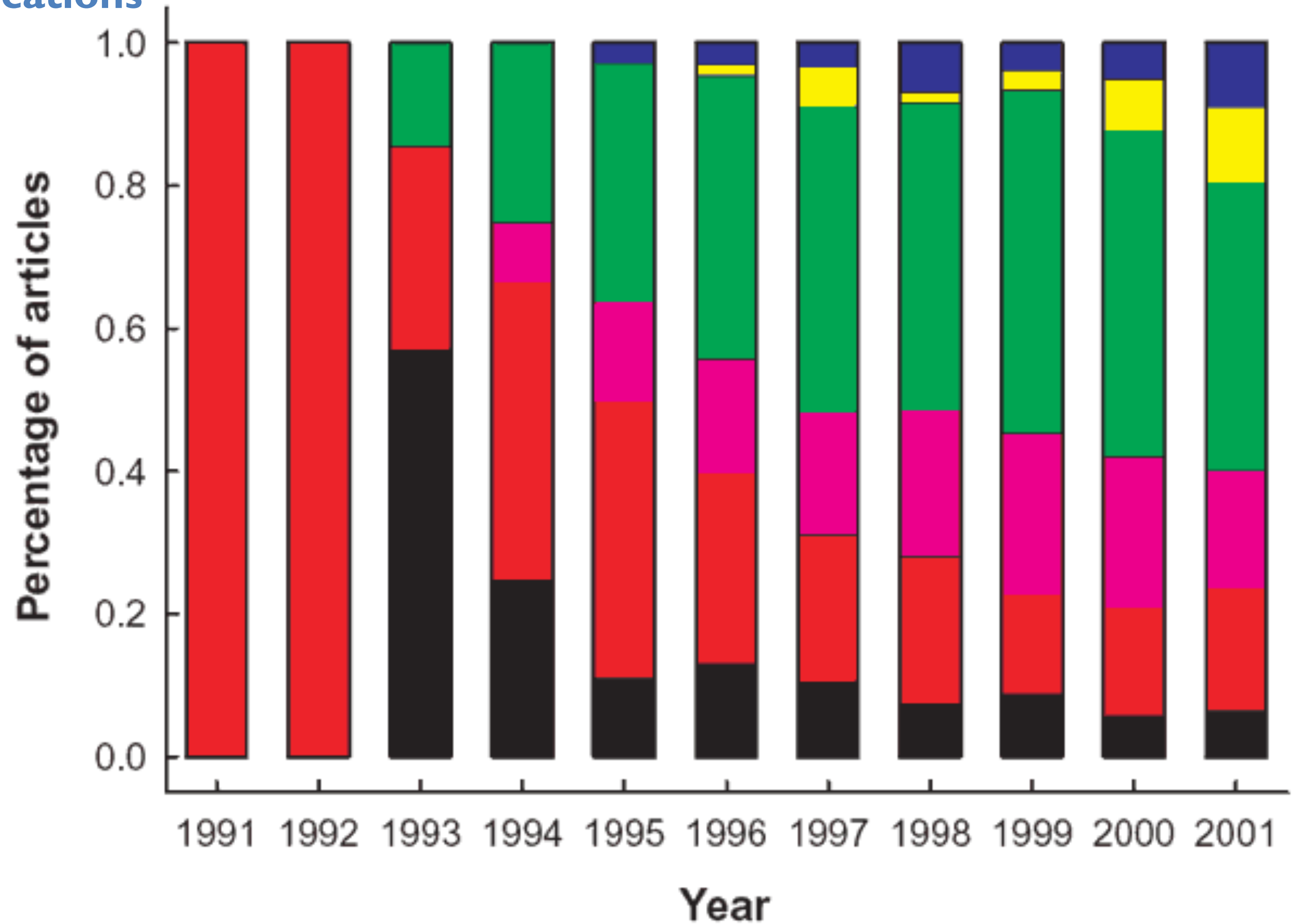
Human Early Visual Cortex

(1057 visually most responsive voxels)



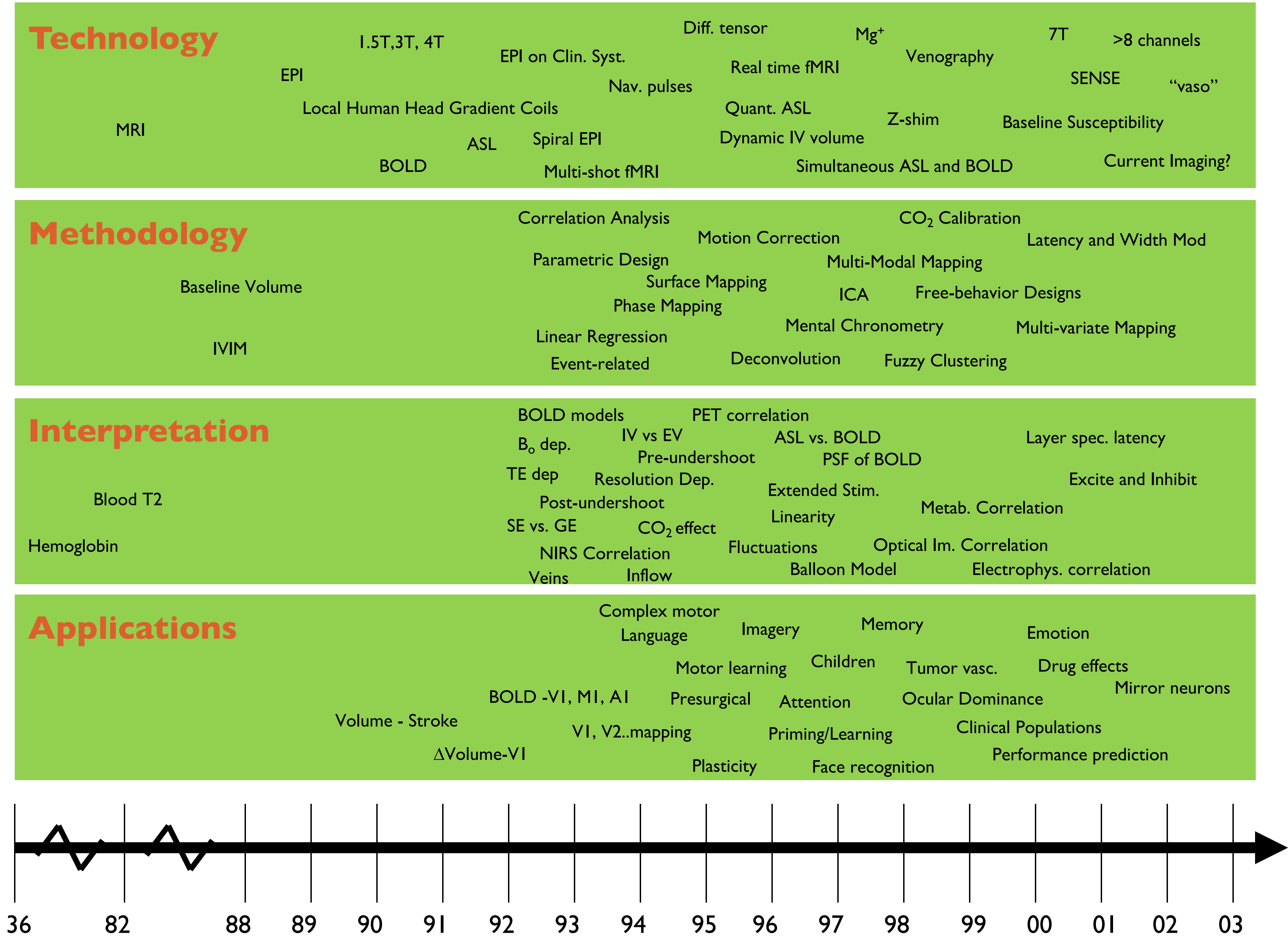


New Applications



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
MRI
EPI
1.5T,3T, 4T
Local Human Head Gradient Coils
BOLD
ASL
EPI on Clin. Syst.
Spiral EPI
Multi-shot fMRI
Nav. pulses
Diff. tensor
Real time fMRI
Quant. ASL
Dynamic IV volume
Simultaneous ASL and BOLD
Mg^+
Venography
Z-shim
7T
SENSE
Baseline Susceptibility
>8 channels
"vaso"
Current Imaging?
Methodology
Baseline Volume
IVIM
Correlation Analysis
Parametric Design
Surface Mapping
Phase Mapping
Linear Regression
Event-related
Motion Correction
Deconvolution
Mental Chronometry
ICA
Multi-Modal Mapping
CO_2 Calibration
Free-behavior Designs
Fuzzy Clustering
Latency and Width Mod
Multi-variate Mapping
Interpretation
Blood T2
Hemoglobin
BOLD models
B_o dep.
TE dep
Post-undershoot
SE vs. GE
NIRS Correlation
Veins
Inflow
IV vs EV
Pre-undershoot
Resolution Dep.
CO_2 effect
PET correlation
ASL vs. BOLD
PSF of BOLD
Extended Stim.
Linearity
Fluctuations
Balloon Model
Metab. Correlation
Optical Im. Correlation
Electrophys. correlation
Layer spec. latency
Excite and Inhibit
Applications
Volume - Stroke
ΔVolume-V1
BOLD -V1, M1, A1
V1, V2..mapping
Complex motor
Language
Motor learning
Presurgical
Plasticity
Imagery
Children
Attention
Priming/Learning
Face recognition
Memory
Tumor vasc.
Ocular Dominance
Clinical Populations
Performance prediction
Emotion
Drug effects
Mirror neurons
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Volume 62, Issue 2, August 15, 2012

ELSEVIER

NeuroImage

Editor-in-Chief
Peter Bandettini

Special Issue
20 Years of fMRI: The Science and the Stories

Available online at www.sciencedirect.com
SciVerse ScienceDirect

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

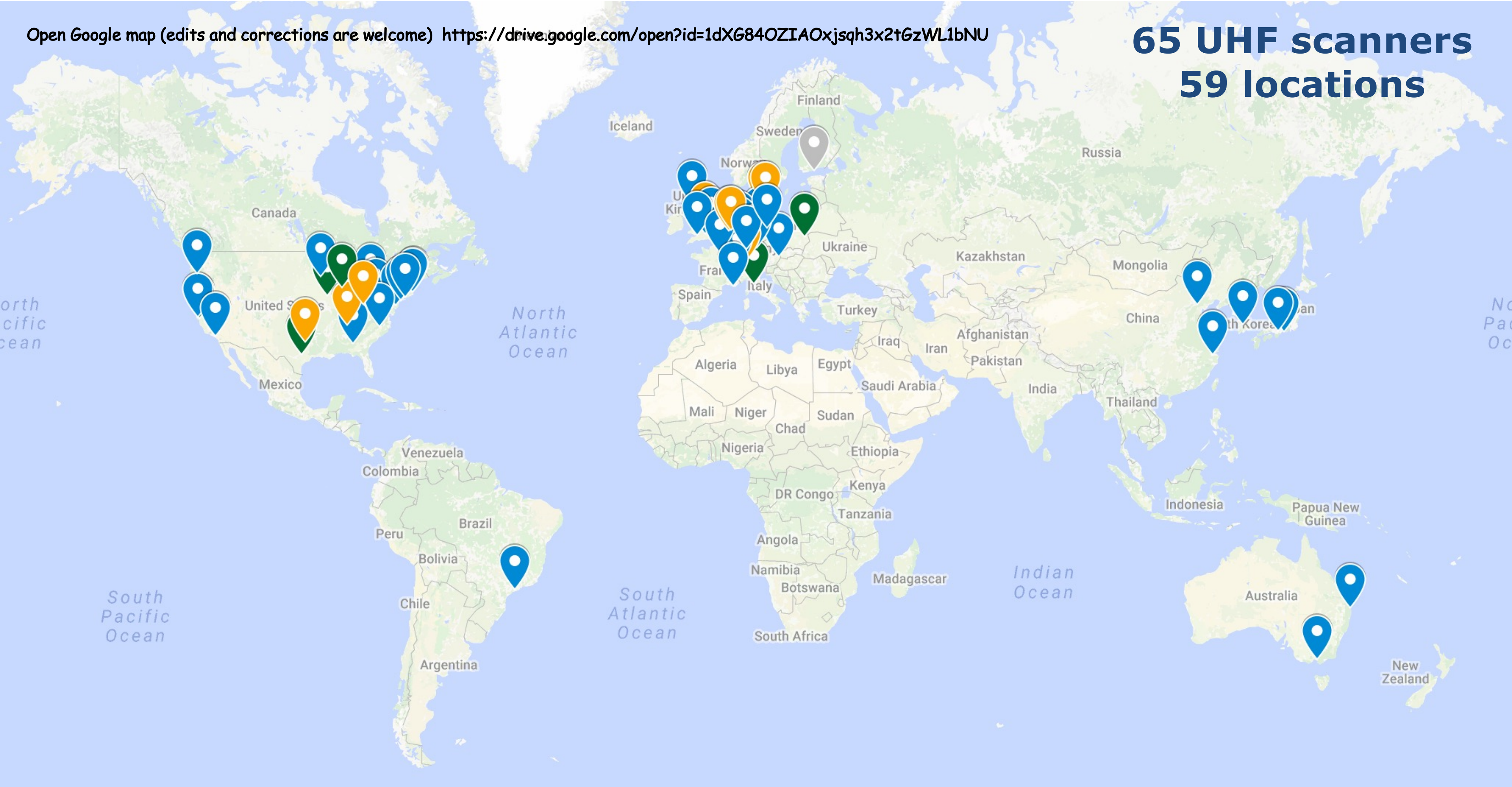
Where are we going?

Ultimate limits and applications?

….after 26 years, *what has improved?*

- Image quality, temporal stability, sensitivity, resolution and speed.
- Implementation, standardization in in acquisition, processing, and display
- Many different processing methods available: *Multivariate decoding, encoding, pattern effect mapping, machine learning, cross subject correlation, and dynamic resting state connectivity analyses* have opened up new insights and directions.
- Artifacts are better understood, and more fully removed
- Underlying neuronal correlates of fMRI are better established
- Resting state fMRI has exploded
- Large pooled datasets have catalyzed meta-analysis, transparency, new methods, reproducibility, and biomarker discovery
- Individual assessment in fMRI is growing
- Standard resolution used has increased
- Multimodal integration
- More groups, better questions.
- More high field scanners (>60 7T's)

7T+ human scanners worldwide



How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

Where are we going?

Ultimate limits and applications?

What has NOT improved…

- **Still struggling with subject motion and breathing**
- **Temporal SNR still limited by physiologic fluctuations**
- **Still struggling with HRF characterization and normalization**
  -*spatially variable BOLD latency & magnitude*
  -spatially variable HRF
- **Spatial resolution of fMRI has reached a theoretical limit due to hemodynamics.**
- **FMRI is still not used clinically** *(effect size/noise << 10)*
- **Vendors still have not focused fMRI** *(no clear clinical applications yet)*
- **Scanners are still loud and confining**
- **MRI is still extremely expensive**
- **Still using 2.5 mm^3 voxels for most studies**
- **We don't understand "connectivity" as inferred by correlation**
- **We don't understand source of resting state fluctuations or biologic purpose that resting state serves**
- **Shimming (reducing Bo inhomogeneities) is still an issue** *(especially for high field fMRI using echo planar imaging)*
- **Db/dt limit (gradient switching) is still an issue**
- **Large databases are not curated well enough …or methods are not sophisticated enough to deal with variability of large databases.**

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

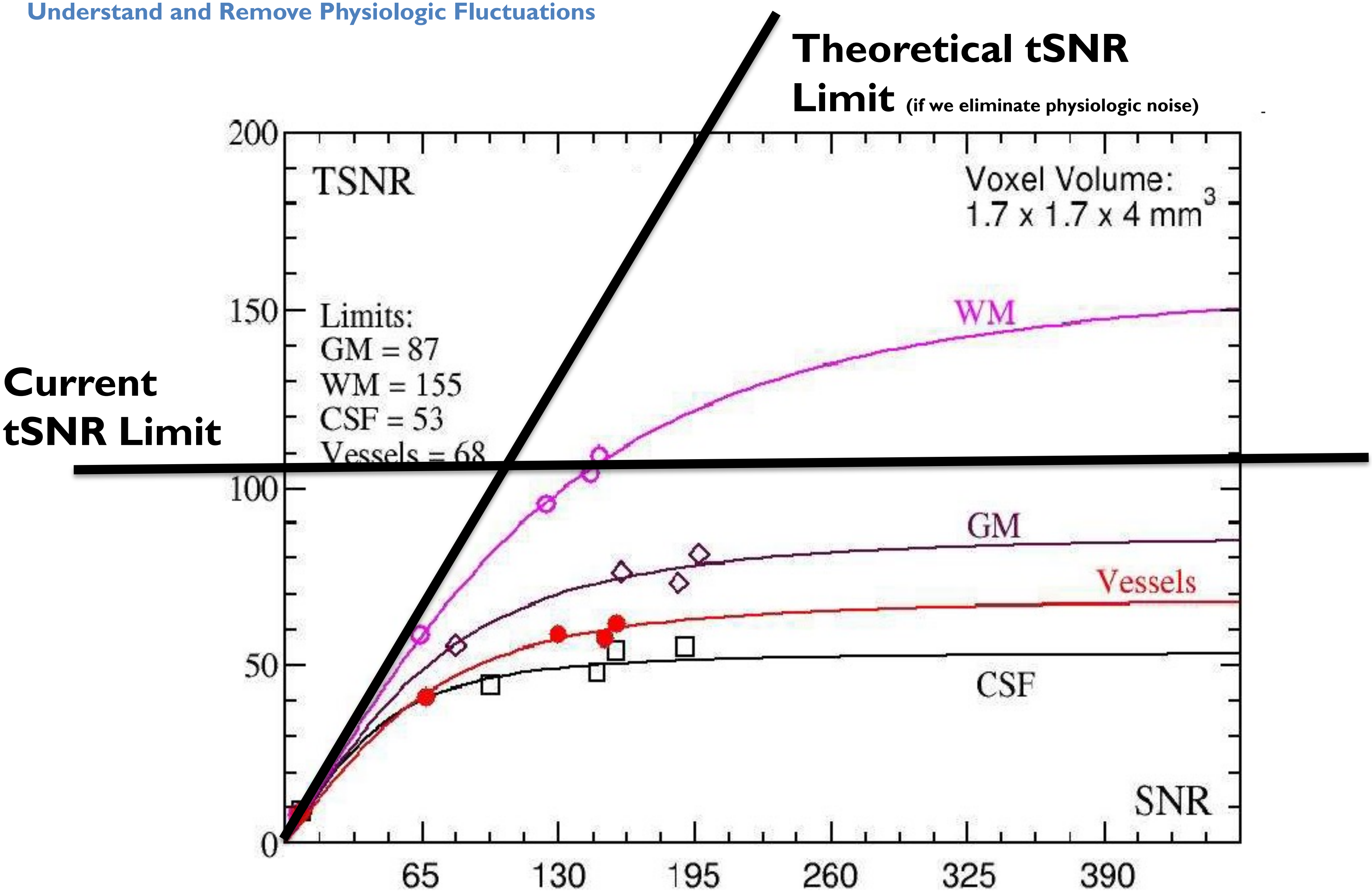
Where are we going?

Ultimate limits and applications?

A few Current Challenges…

Generally to maximize the interpretability and utility of the fMRI signal

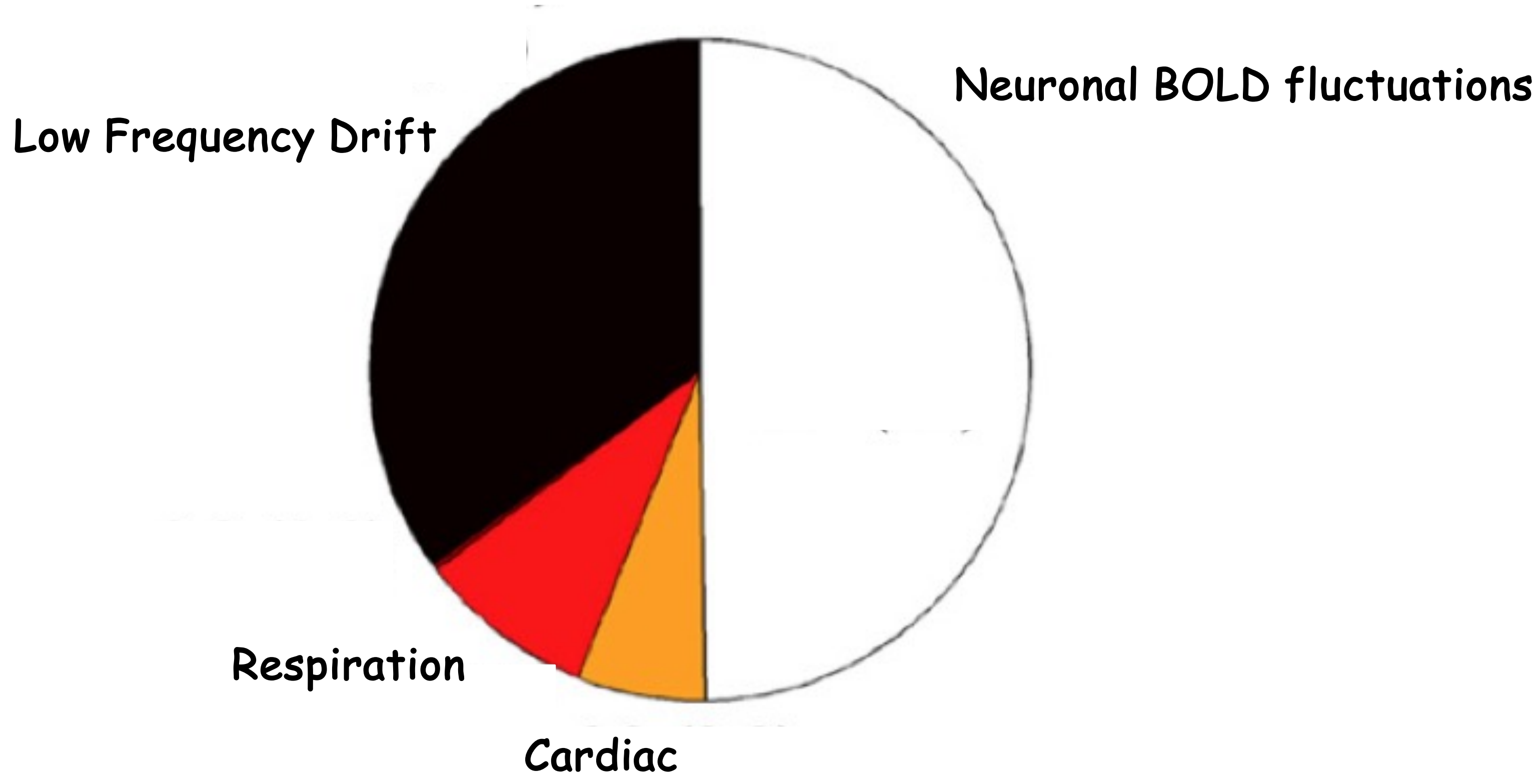
- **Completely remove fluctuations and variability.**
- **Create a pipeline for robust individual assessment.**
- **High resolution mapping impervious to vascular variations.**



J. Bodurka, F. Ye, N Petridou, K. Murphy, P. A. Bandettini, Mapping the MRI voxel volume in which thermal noise matches physiological noise – implications for fMRI. *NeuroImage,* 34, 542-549 (2007)

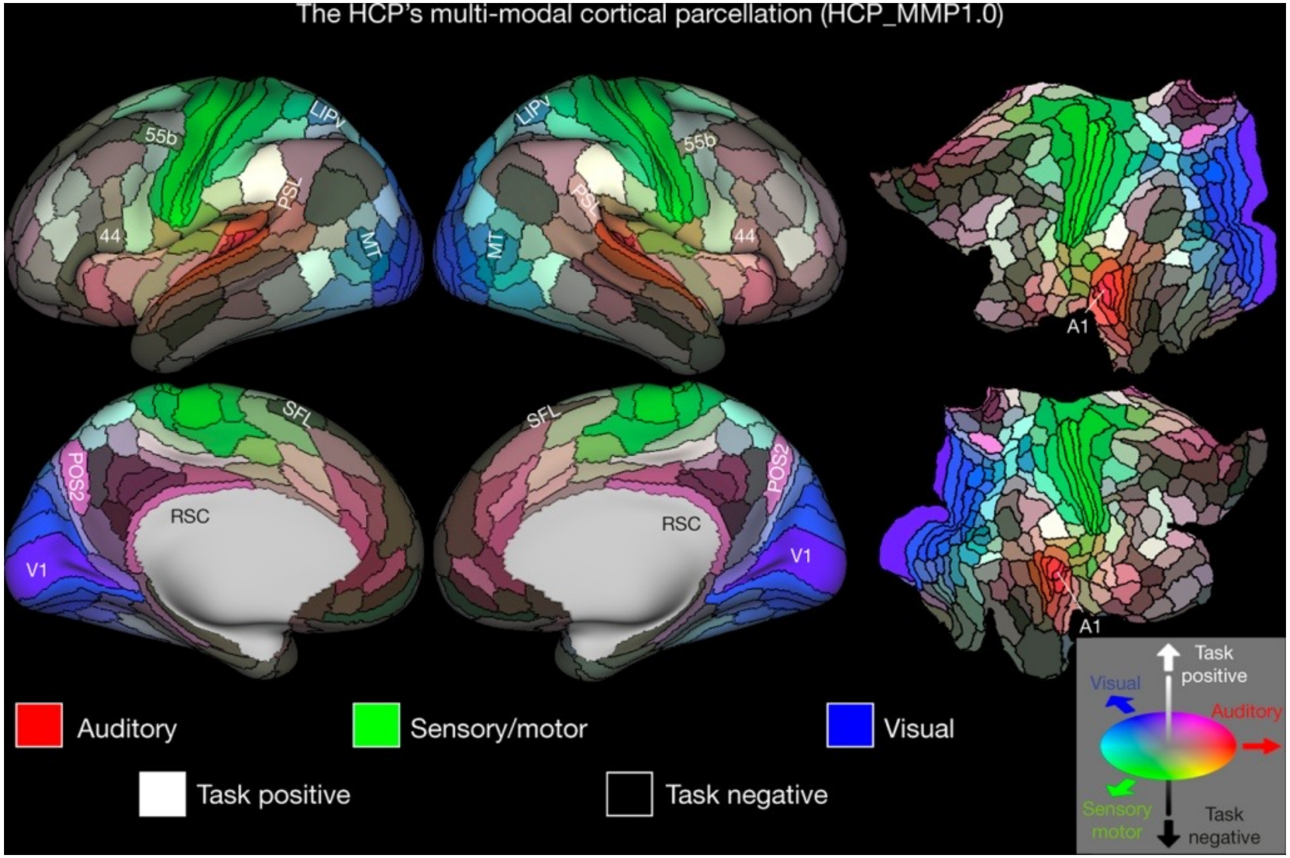
Components of fMRI Fluctuations

From an ROI



Bianciardi et al. Magnetic Resonance Imaging 27: 1019-1029, 2009

The HCP’s multi-modal parcellation, version 1.0 (HCP_MMP1.0)

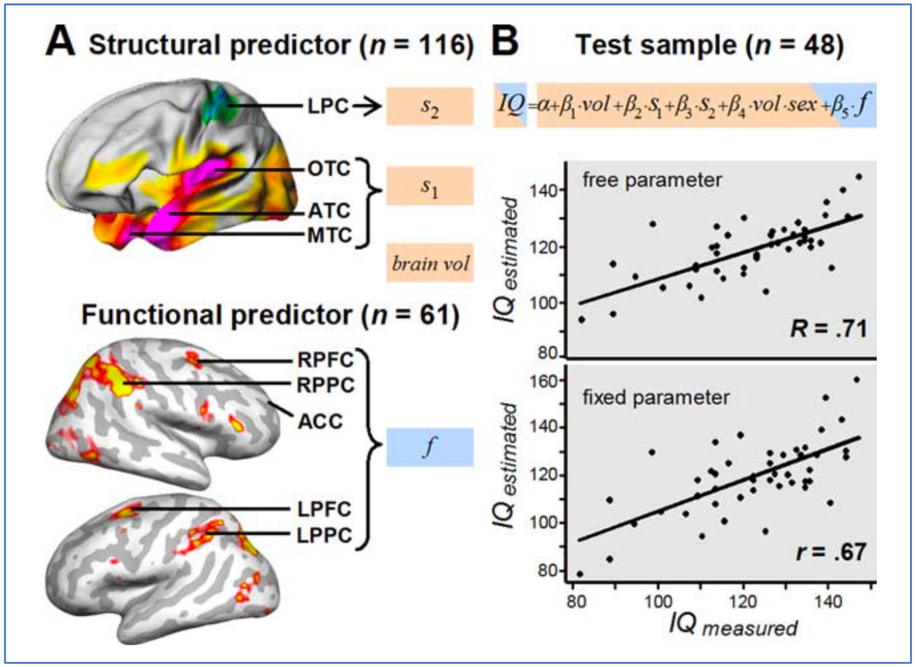


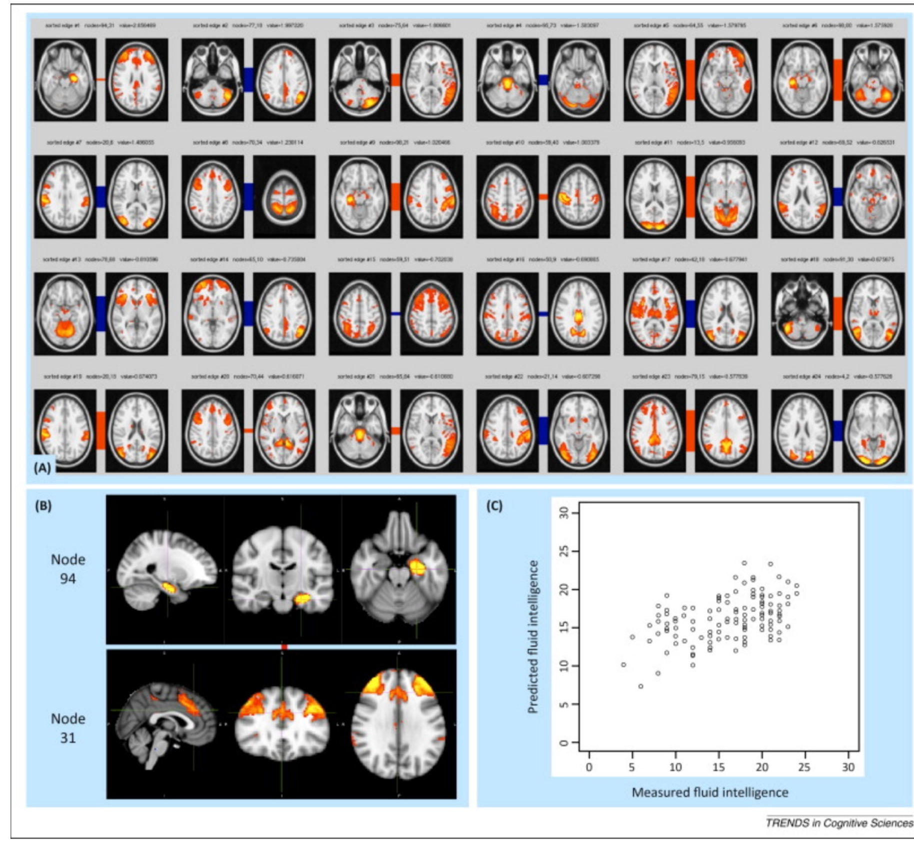
M F Glasser *et al. Nature* 1–8 (2016) doi:10.1038/nature18933

nature

Structural, Functional, and Connectivity for Individual Assessment

Fluid Intelligence..



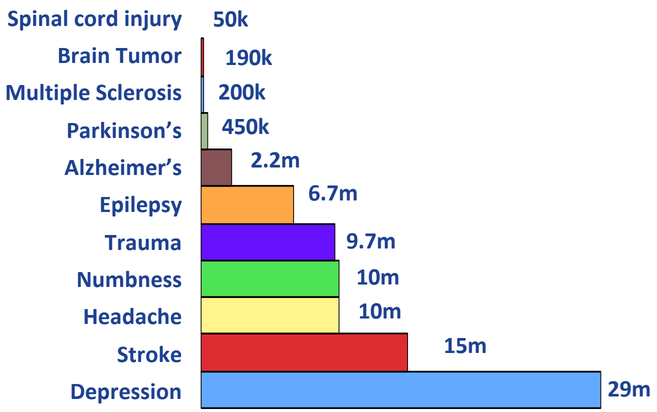


Multiple Bases of Human Intelligence Revealed by Cortical Thickness and Neural Activation, Choi et al, The Journal of Neuroscience, October 8, 2008 • 28(41):10323–10329

Functional Connectomics from Resting State Data, Smith. et al, Trends in Cognitive Sciences (2013) 17(12), pp. 666-682

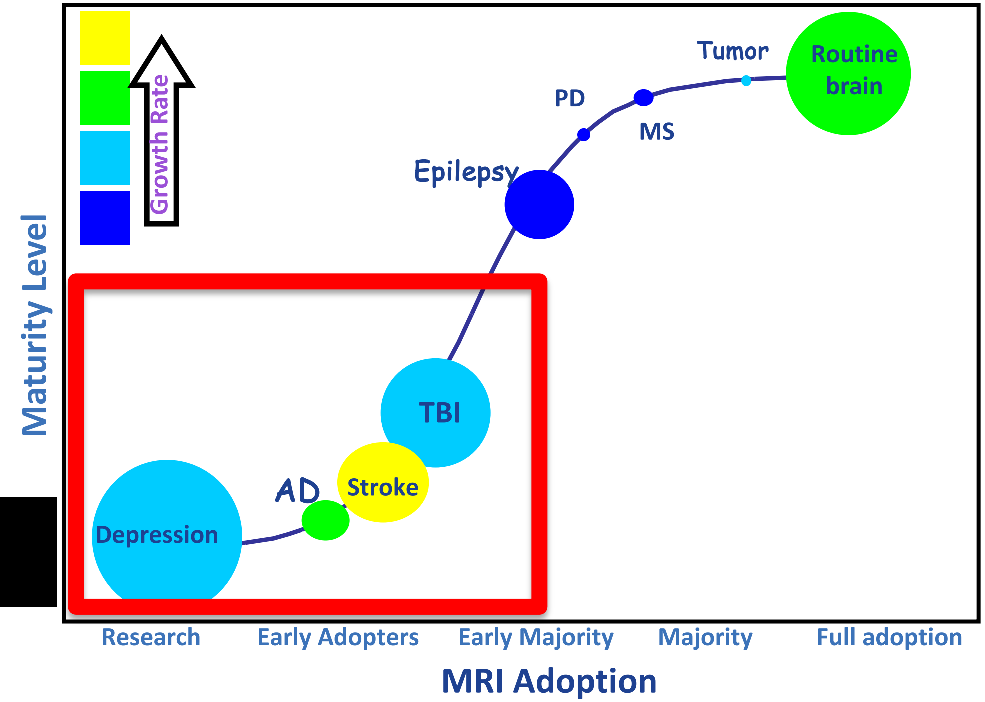
Neuro-MRI Potential Clinical Impact

Incidence



Number of newly-diagnosed people per year.
Corresponds to bubble sizes in growth chart.

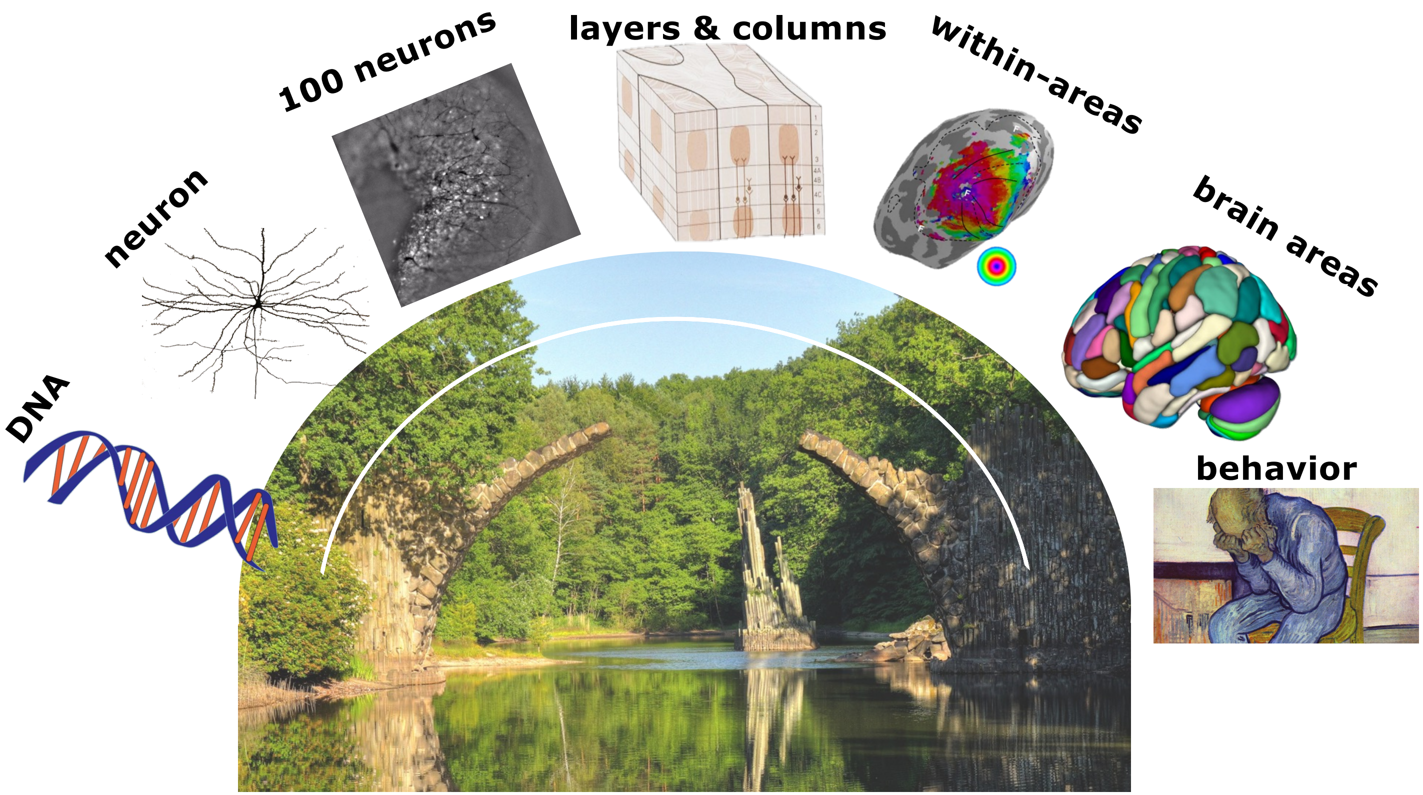
Growth Potential



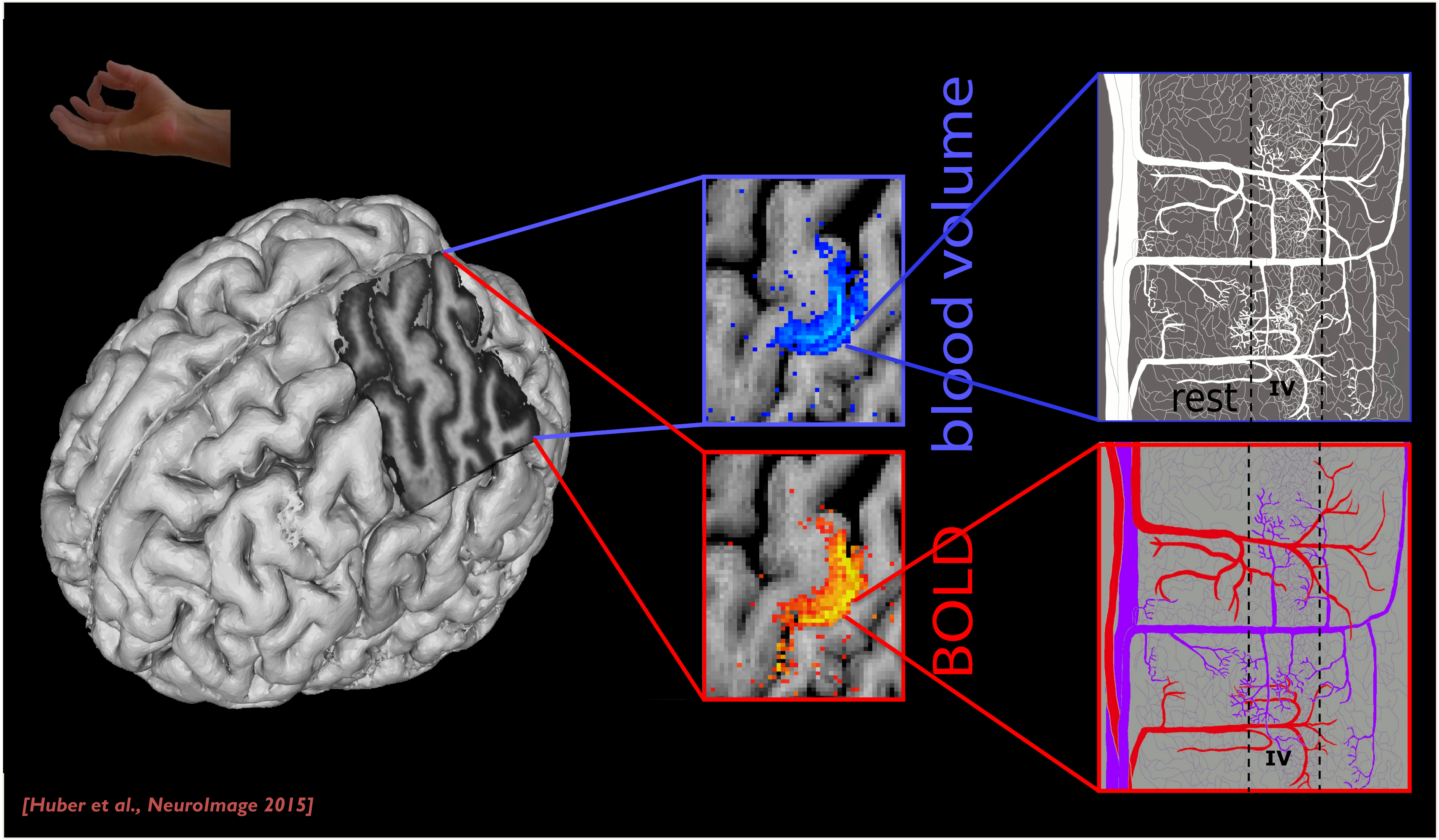
Neuropsychiatric disorders have the most growth potential for imaging

Courtesy: Scott Hinks, GE Medical Systems

bridging the scales in neuroscience

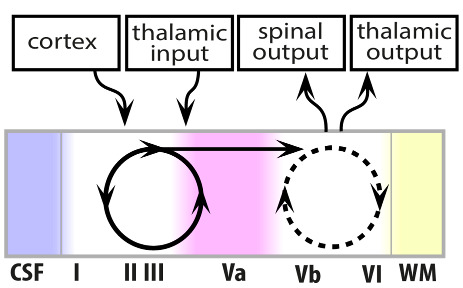


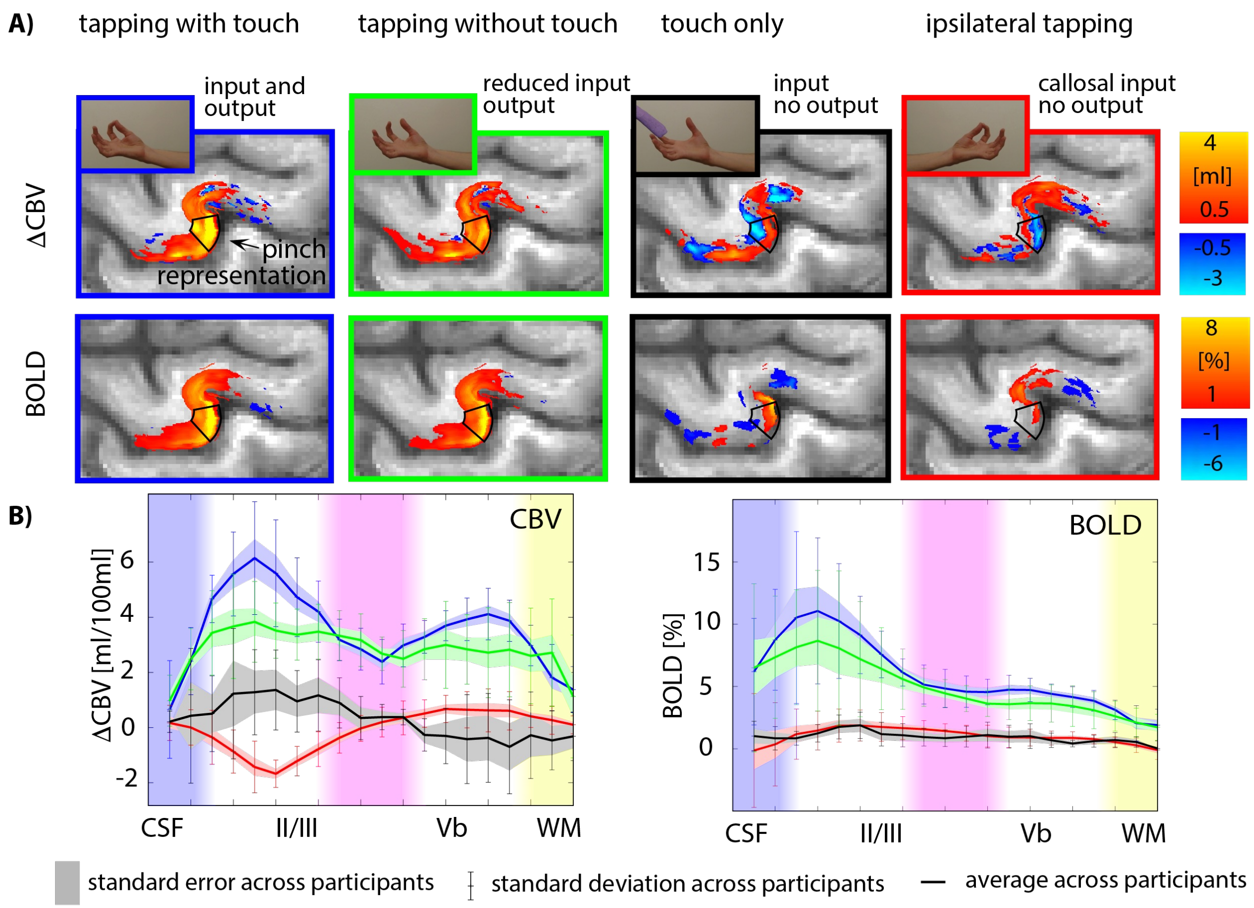
VASO vs. BOLD Specificity



Experimental Results using VASO

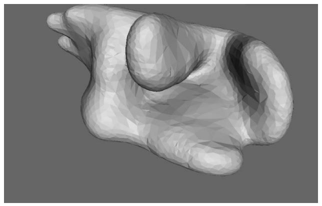
A) expected M1 circuitry based on Mao et al. 2011 and Weiler et al. 2008

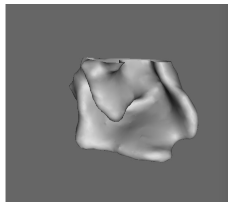




Huber, L. et al. Neuron (in press)

Layer-dependent fMRI in “cognitive” area DLPFC

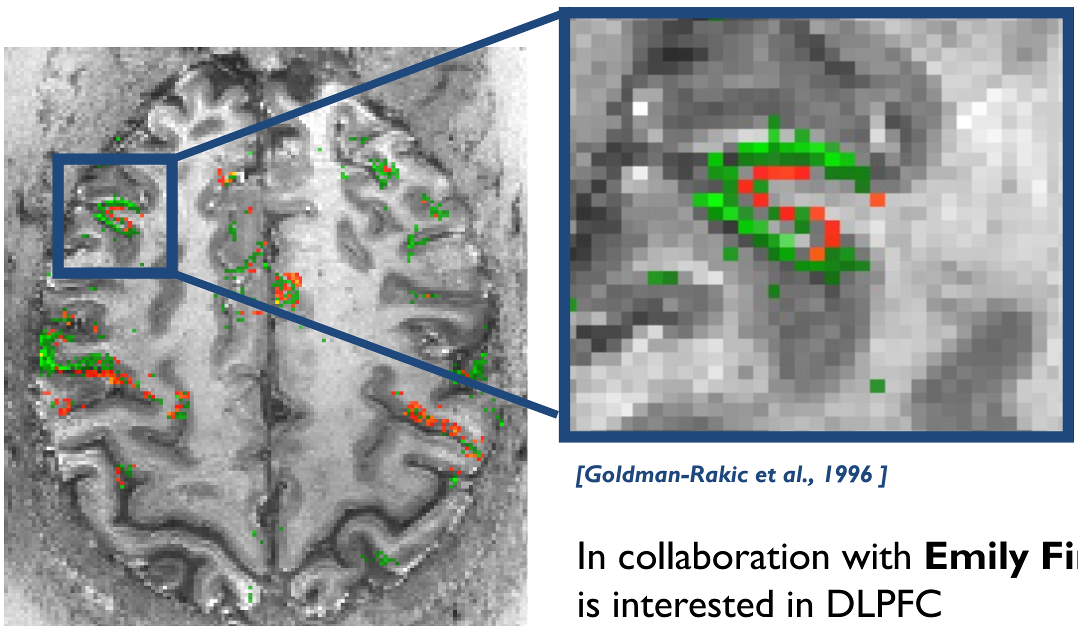




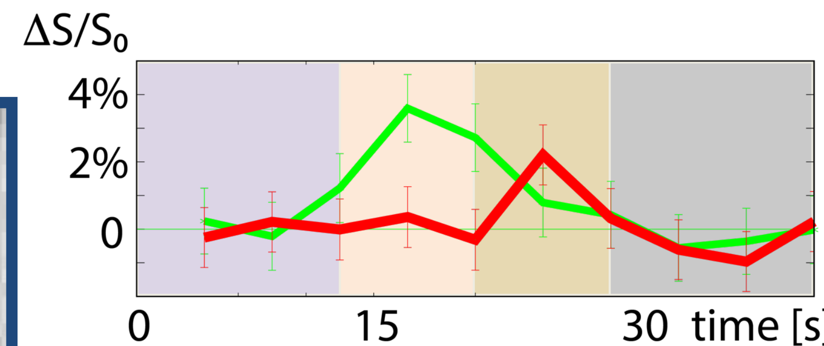
Task: alphabetize remember

[D’Esposito et al., 1999]

signal slope after response “output” mental alphabetizing



[Goldman-Rakic et al., 1996]



superfical layer: alphabetizing

deeper layer: output, response

N=5 participants

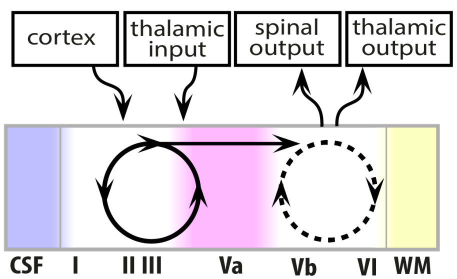
7T, 32ch. Nova
resol. 0.9 mm,
FLASH-GRAPPA,
partial Fourier 6/8
24 slices

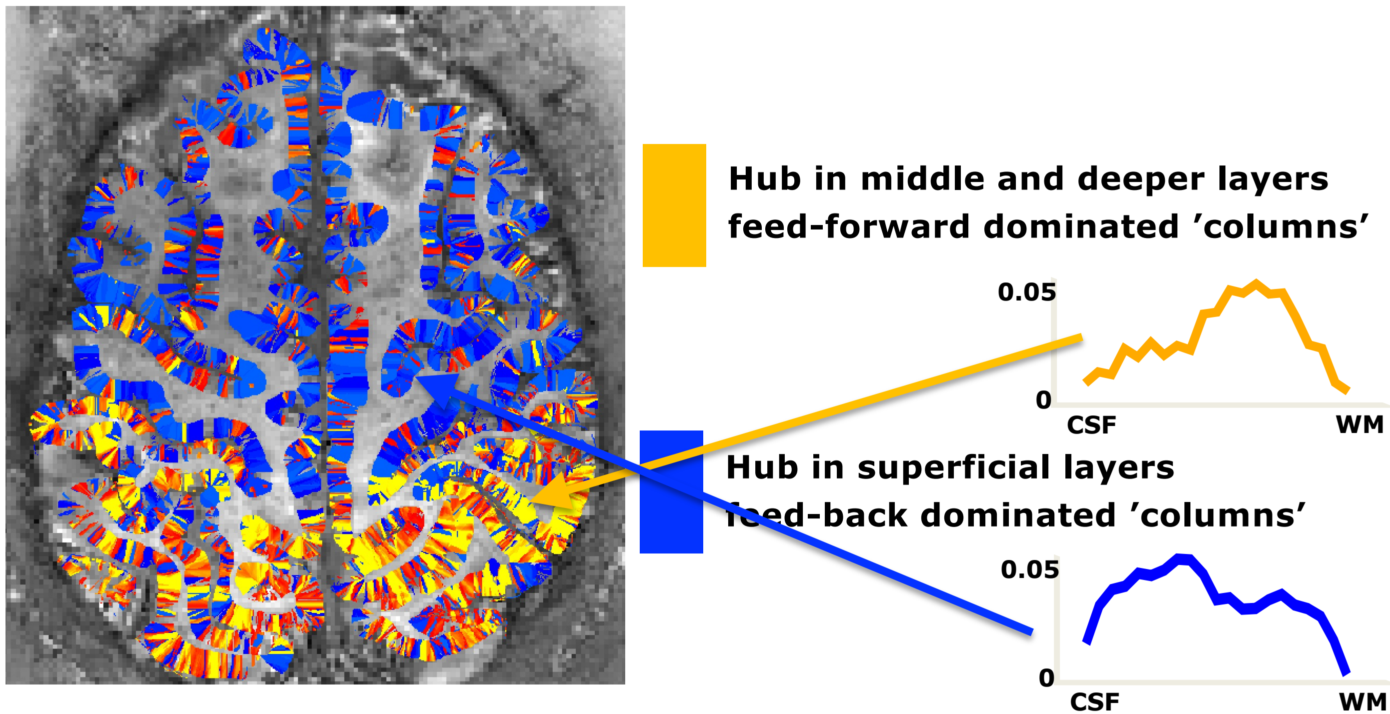
In collaboration with **Emily Finn**, who is interested in DLPFC

Resting State Correlation within Layers

Hubness: functional connectivity strengths of one layer to all other layers in each column

A) expected M1 circuitry based on
Mao et al. 2011 and Weiler et al. 2008



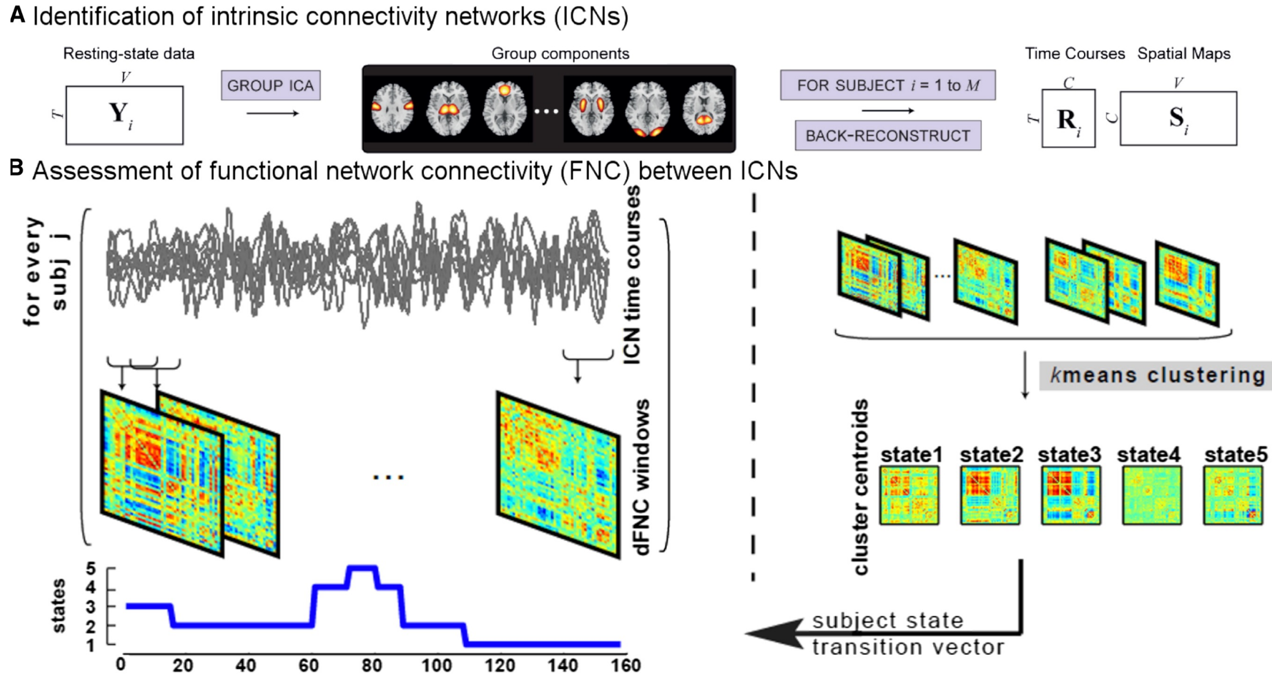


Huber, L. et al. Neuron (in press)

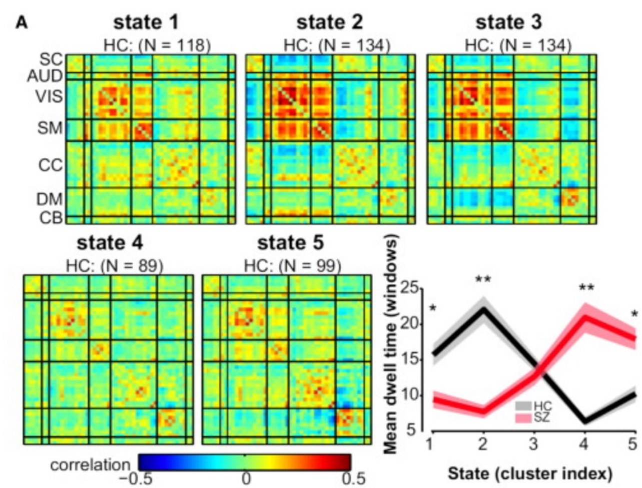
Current Opportunities…

- **Processing methods**
- **Acquisition methods**
- **Big Data Analysis**

Those with Schizophrenia have Different Resting State Dynamics



Five States…Dwell time is different in those with Schizophrenia



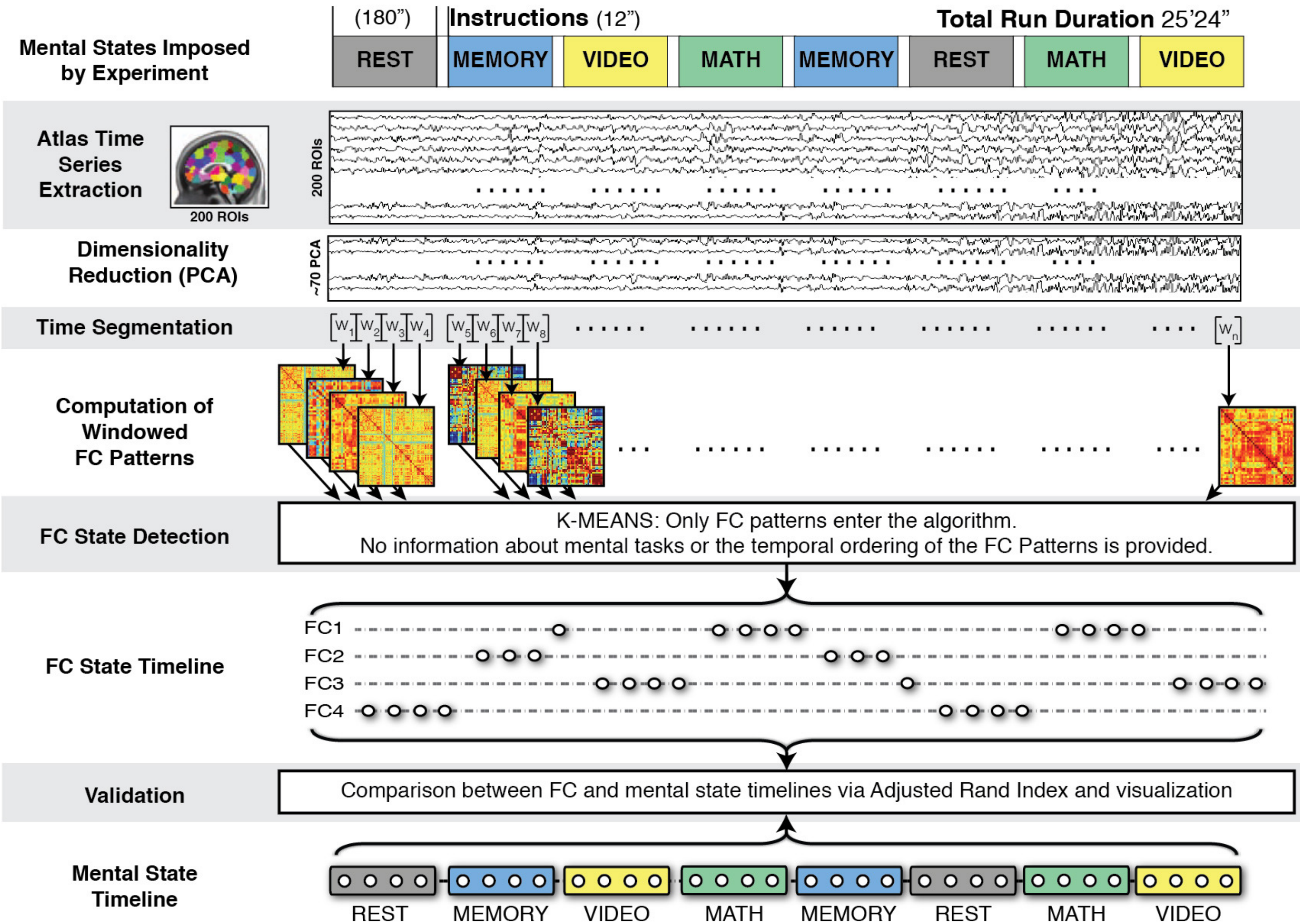
Neuron
Volume 84, Issue 2, 22 October 2014, Pages 262-274

Perspective

The Chronnectome: Time-Varying Connectivity Networks as the Next Frontier in fMRI Data Discovery

Vince D. Calhoun [1, 2], Robyn Miller [1], Godfrey Pearlson [4], Tulay Adalı [3]

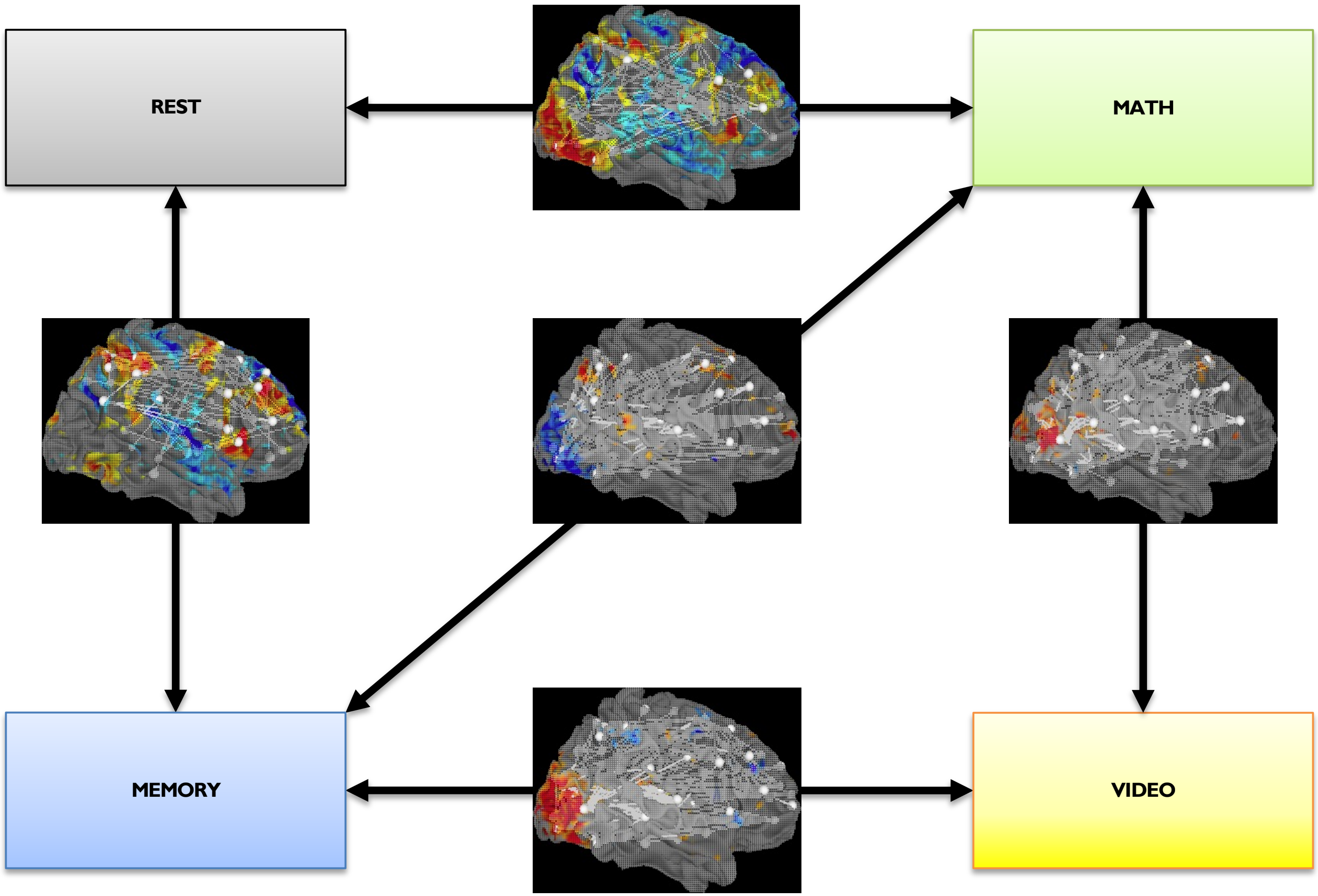
Connectivity – Based Ongoing Task Decoding



Nearly 100% Accurate for subjects who were most engaged.

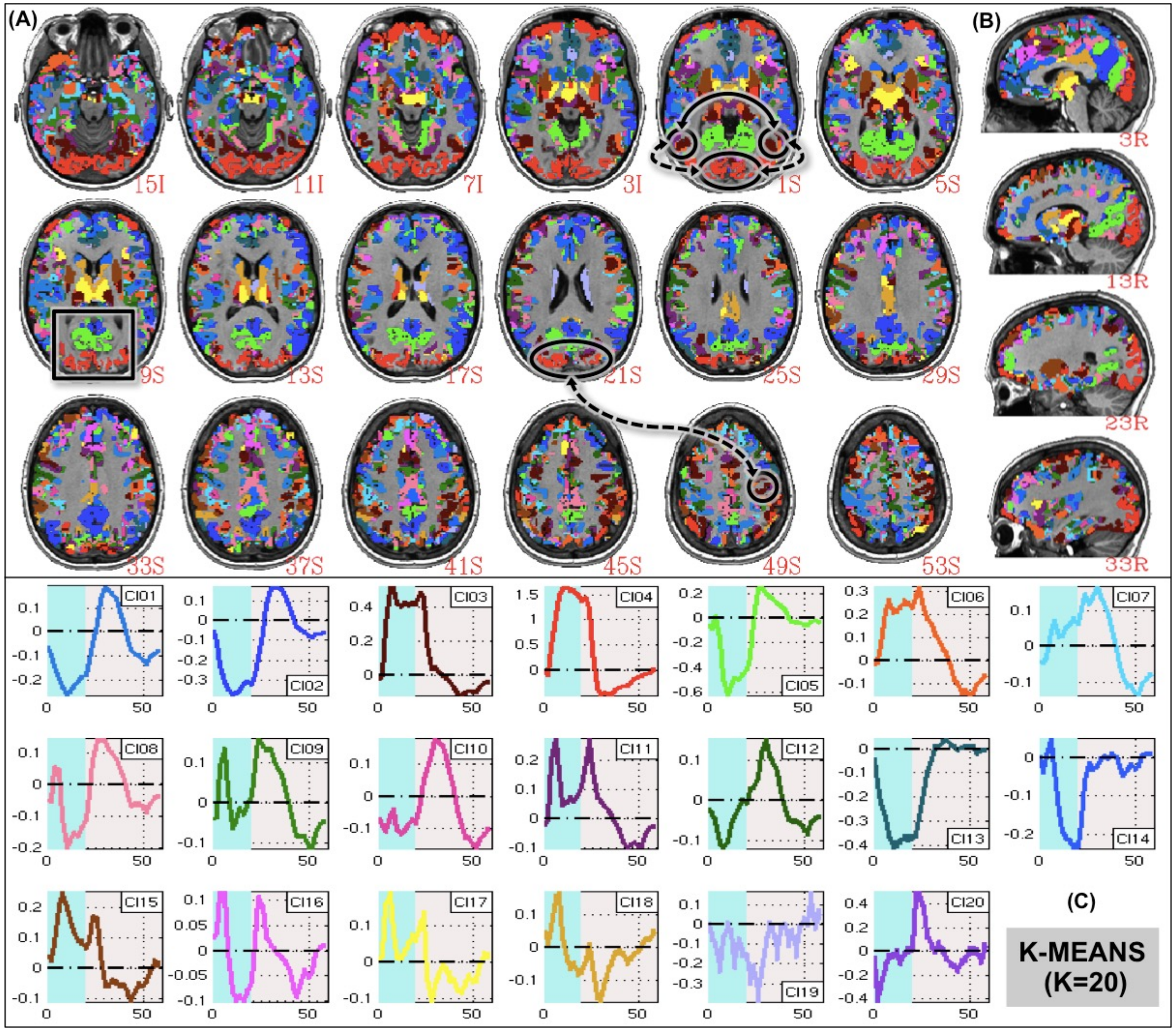
Gonzalez-Castillo et al., PNAS 2015

Informative Connectivity Changes were more extensive than magnitude changes *(3 min window)*



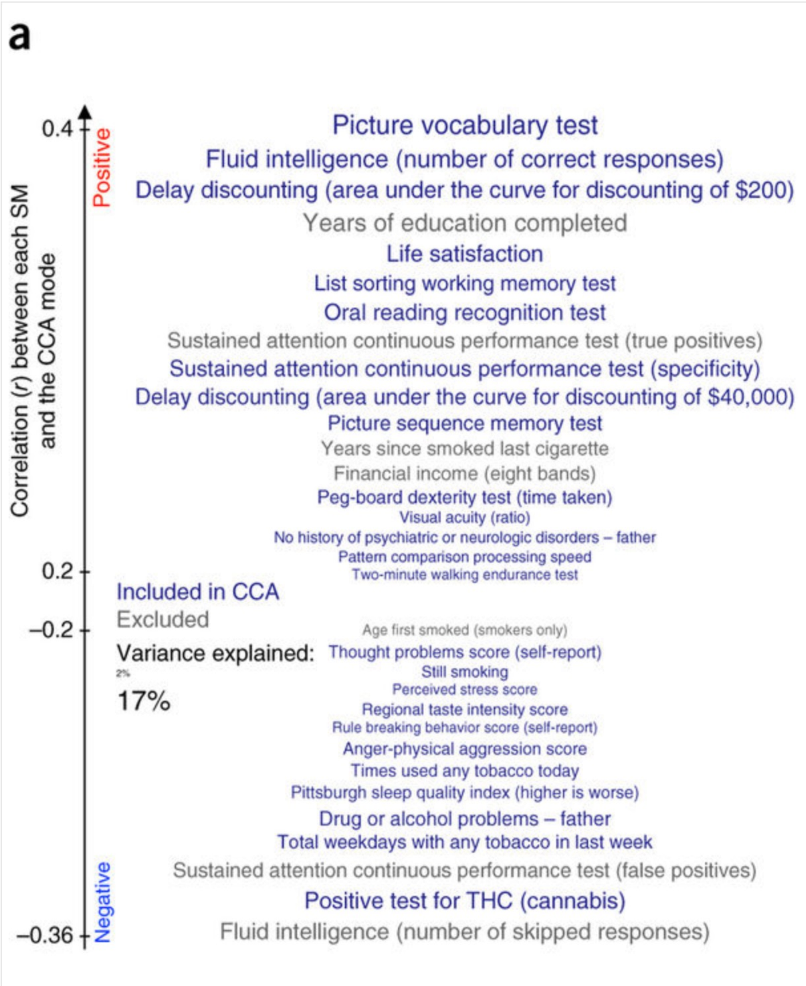
Gonzalez-Castillo et al., PNAS 2015

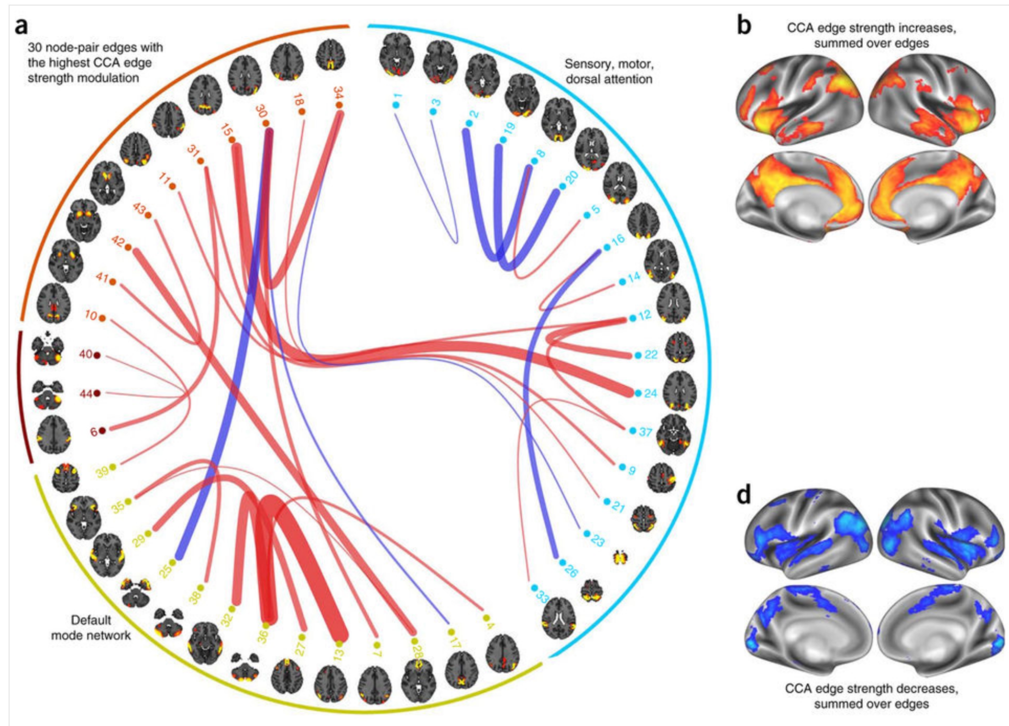
Massive time-locked averaging & model free analysis
= *whole brain activation with a simple task*



J. Gonzalez-Castillo, Z. Saad, D. A. Handwerker, S. J. Inati, N. Brenowitz, P. A. Bandettini, Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis. Proceedings of the National Academy of Sciences 109, 14: pp. 5487-5492 (2012)

Specific Networks are Correlated with Subject Measures





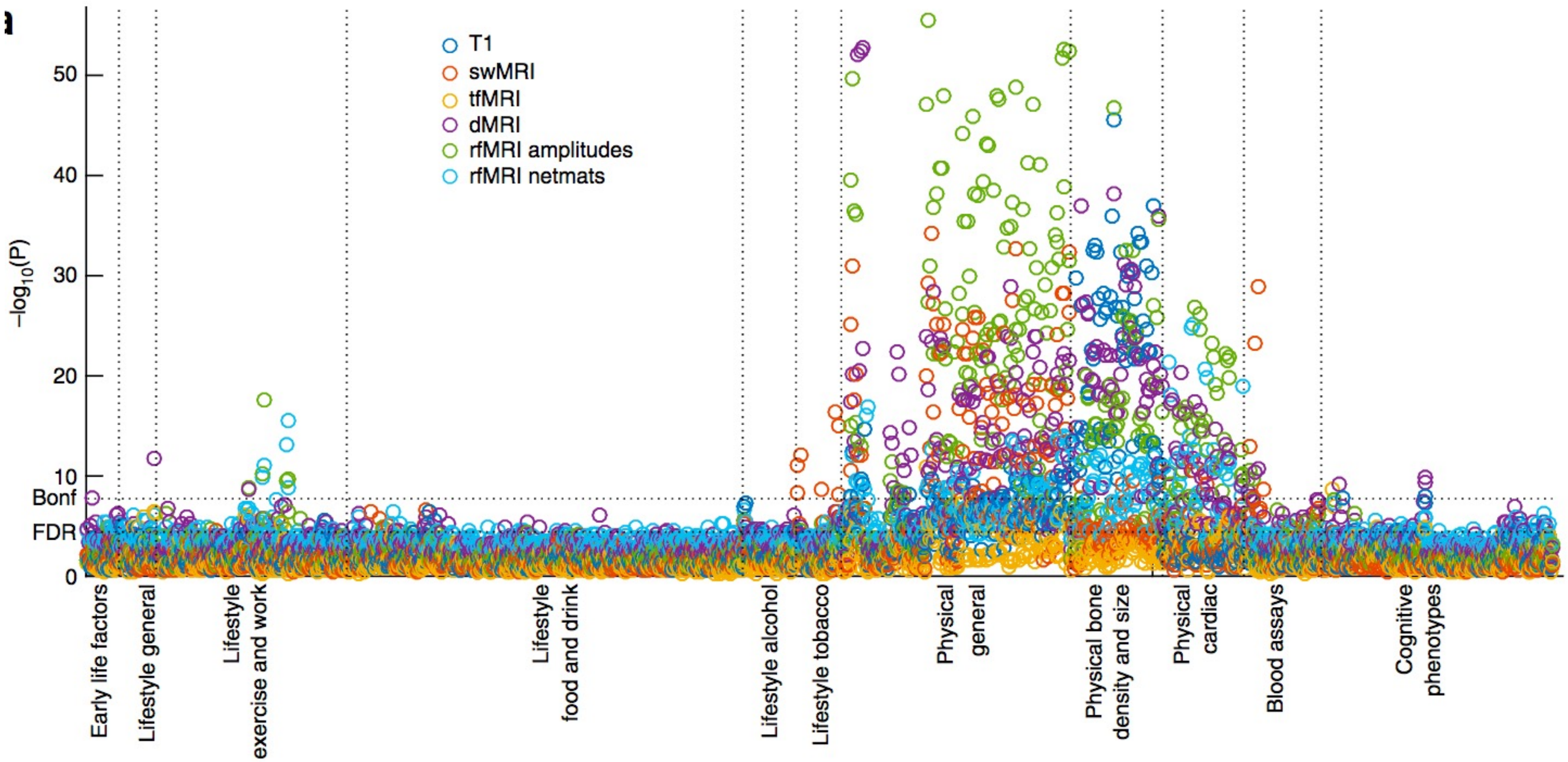
A positive-negative mode of population covariation links brain connectivity, demographics and behavior

Stephen M Smith, Thomas E Nichols, Diego Vidaurre, Anderson M Winkler, Timothy E J Behrens, Matthew F Glasser, Kamil Ugurbil, Deanna M Barch, David C Van Essen & Karla L Miller

Nature Neuroscience **18**, 1565–1567 (2015) | doi:10.1038/nn.4125

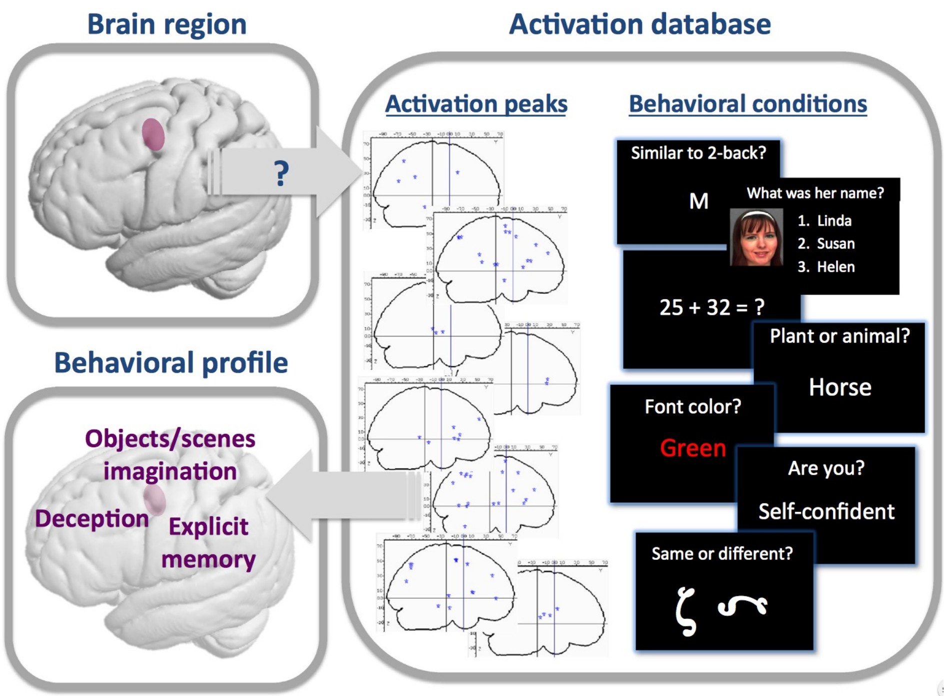
Received 12 June 2015 | Accepted 01 September 2015 | Published online 28 September 2015

UK Biobank: 5000 subjects analyzed…plan for 100,000 subjects.



Multimodal population brain imaging in the UK Biobank prospective epidemiological study, Miller et al. Nature Neuroscience, 19, 2016

Creating a behavioral profile for each region



Brain Map or NeuroSynth

Genon, S, et al. How to characterize the function of a brain region. TICS, 22, 2018

Current Challenges and Opportunities:

Challenges

- Remove Fluctuations & Sources of Variability
  - **Physiologic Fluctuations**
  - **BOLD HRF variability.**
  - **Scanner and pulse sequence variability**
- Develop pipeline for Individual Assessment
  - **Develop fMRI-based *Biomarkers* from large data sets**
  - **Universal parcellation scheme for resting state analysis**
- High Resolution
  - **Whole brain high resolution method that is impervious to veins**
  - **Compare high resolution data** *(blobs – yes, columns and layers – not yet)*

Opportunities

- Processing and Modeling Methods
  - **Machine learning and deep learning approaches…big data.**
  - **Create better computational models to describe data.**
  - **Further information extraction from the time series**

    dynamic resting state, activation dynamics and latencies, activation-based correlation changes, subtle non-canonical signal changes.
- Acquisition
  - **Potential contrast mechanisms** *(diffusion, elastography, currents…).*
  - **Real time feedback fMRI for behavioral modification.**

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

Where are we going?

Ultimate limits and applications?

Technology

Methodology

Local Gradient Coils

Standardized Parcellation

More detail: layers, columns, pattern effects

Machine Learning

Multiple simultaneous contrasts

Computational Models rather than description

Compressed sensing, fingerprinting…

Massive Well Curated Databases

Noise Characterization and Removal

Real time feedback fMRI

More precise BOLD – neuronal activity comparisons

Neuromodulation effects on connectivity

Biomarker Discovery

Individual rather than Group Assessment

Interpretation

Applications

How did this all begin?

First challenges and opportunities.

What has improved?

What has not improved?

Current challenges and opportunities.

Where are we going?

Ultimate limits and applications?

Ultimate fMRI limits?

- **What is solvable?**
  - ✓ **Physiologic noise removal**
  - ✓ **Achieving nearly perfect shim**
  - ✓ **Basis and purpose of resting state signal and connectivity**
  - ✓ **Hemodynamic variability in magnitude and phase**
  - ✓ **Vendor, scanner, upgrade, pulse sequence variability for large data sets**
  - ✓ **Universal Parcellation Scheme**
  - ✓ **Cryogen-free scanners up to 7T**
  - ✓ **Silent fMRI sequences – or improved noise cancellation**

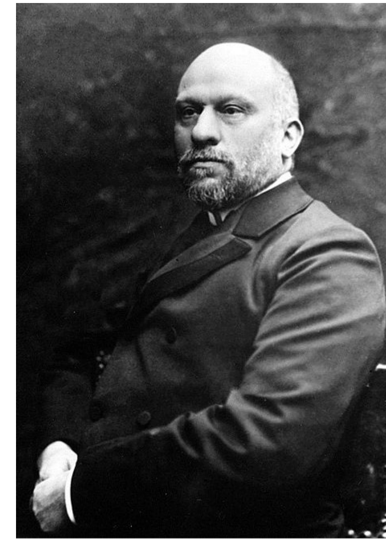
- **What may become Common practice?**
  - ✓ **Sub – mm functional resolution for whole brain**
  - ✓ **Simultaneous multiple hemodynamic contrasts**
  - ✓ **Quantitative baseline fMRI- based $CMRO_2$ mapping**
  - ✓ ***Database research:* normal, cross disease, longitudinal, and multimodal - for biomarker discovery**
  - ✓ **Naturalistic paradigms**

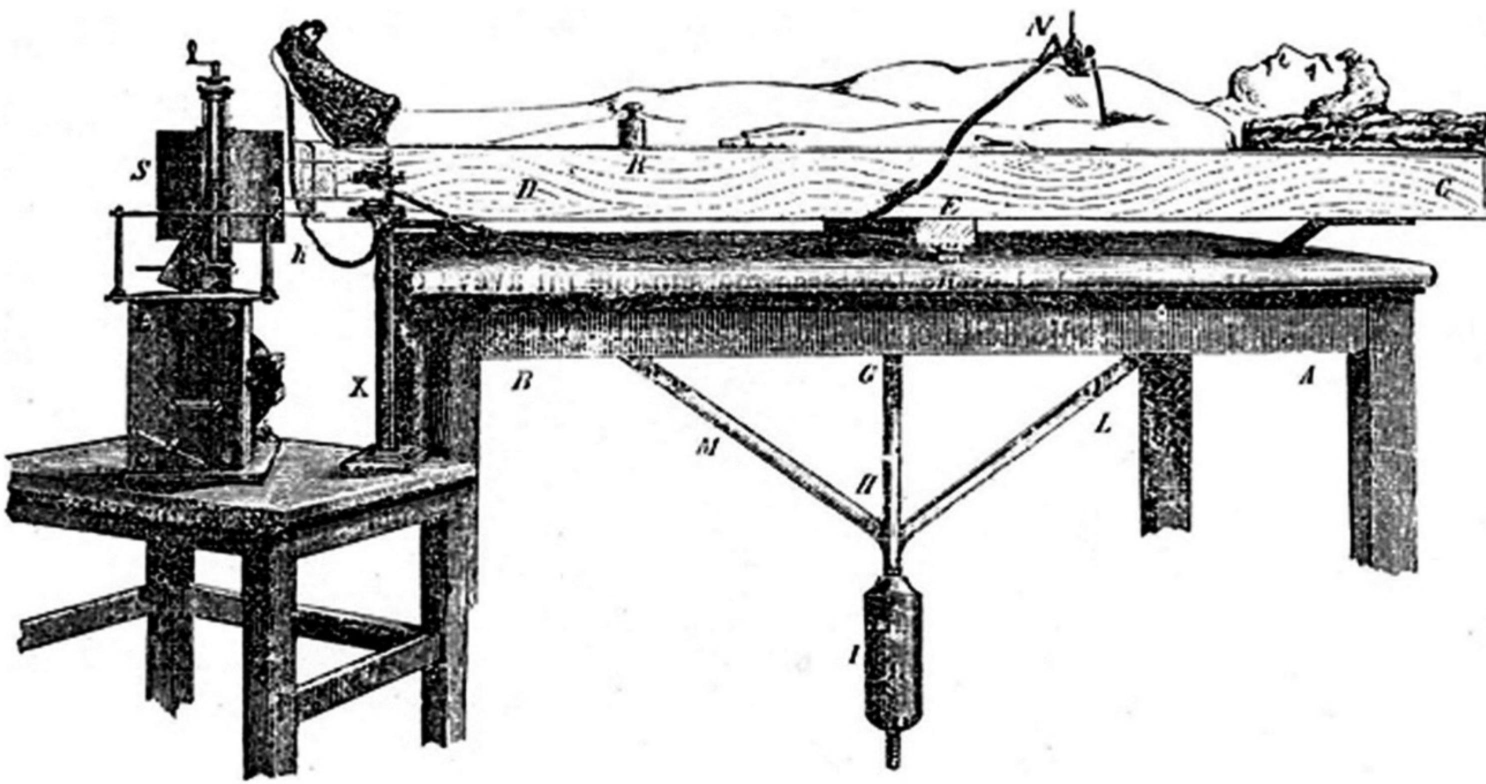
- **Applications:**
  - ✓ **Individual fMRI-based "stress-test" for psychiatric or neurologic testing**
  - ✓ **Real time fMRI feedback for behavior or perception modification**
  - ✓ **Pre-surgical Mapping**
  - ✓ **Rapid biomarker based fMRI screening**

What could change everything?

- Room temperature superconductors
- Direct neuronal contrast with MRI is discovered/developed
- Breakthrough in function-specific contrast agents (labelled agents or nano-particles)
- One powerful and unique clinical application of fMRI

1880's: Angelo Mosso's balance





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Post Bac IRTA's:

Harry Hall

Natasha Topolski

Data Sharing Team

Adam Thomas

John Rodgers-Lee

Dylan Nielson

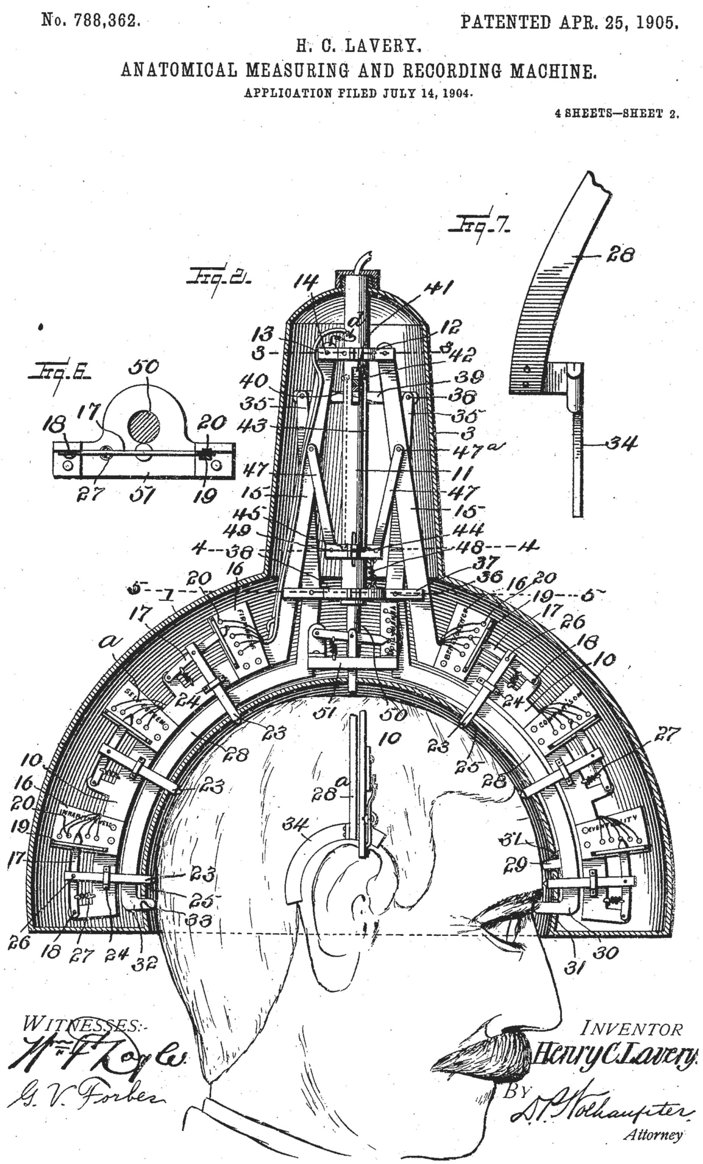
Machine Learning Team

Francisco Pereira

Charles Zheng

Patrick McClure

Brain Assessment… c. 1905



Early Resting State Apparatus

*** Not FDA-Approved***