# What fMRI Can, Can't, and Might Do


Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods

Laboratory of Brain and Cognition

http://fim.nimh.nih.gov

&

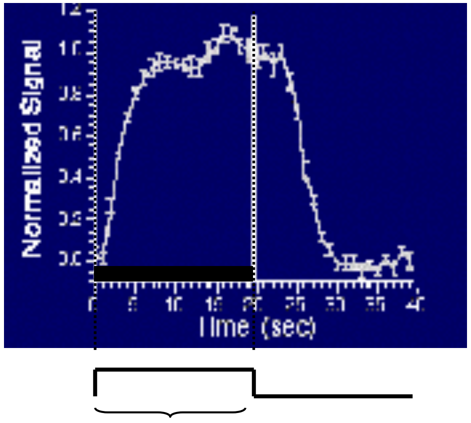
Functional MRI Facility

ttp://fr

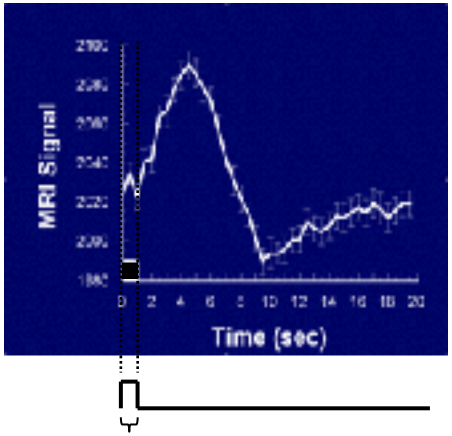
# Overview of fMRI

**Functional Contrast:**

Blood volume
Blood flow/perfusion
Blood oxygenation




task




task

**Spatial resolution:**

Typical: 3 $mm^3$
Upper: 0.5 $mm^3$

**Temporal resolution:**

Minimum duration: < 16 ms
Minimum onset diff: 100 ms to 2 sec

**Sensitivity:**

tSNR = 40/1 to 120/1
fCNR = 1/1 to 6/1

**Interpretability issues:**

# How fMRI is Currently Being Used

## Research Applications

-map networks involved with specific behavior or stimuli

-characterize changes over time (seconds to years)

-group or individual characterization

## Clinical Research

-clinical population characterization (probe task or resting state)

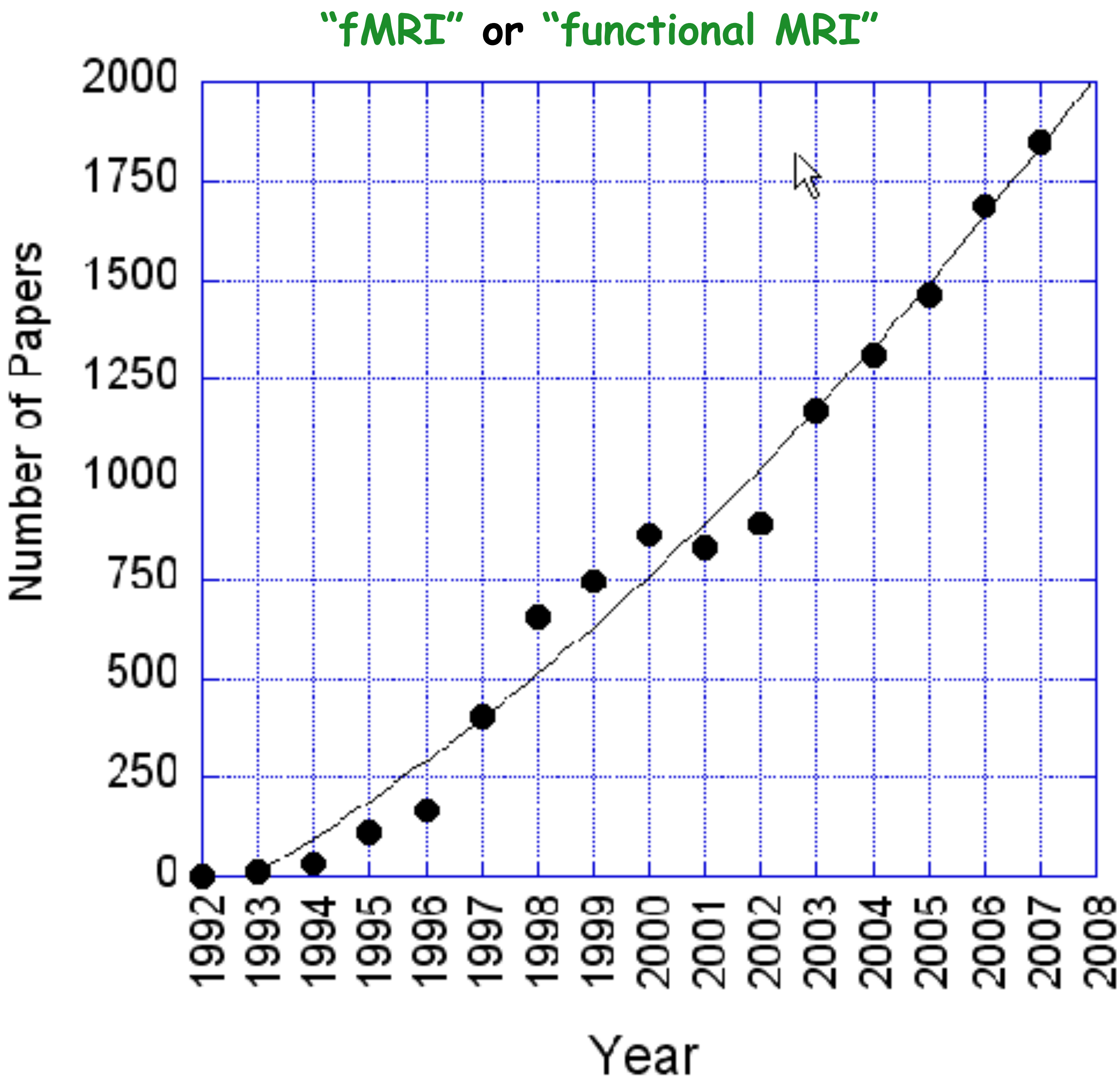
-assessment of recovery and plasticity

-attempts to characterize (classify) individuals

## Clinical Applications

-presurgical mapping (CPT code in place as of Jan, 2007)

# Scopus: Articles or Reviews Published per Year



# What fMRI Can't Do

## What some would argue are shortcomings with fMRI

- Too low SNR vs subject/patient limits of compliance (about 2 hours)
- Requires motivated subjects/patients (motion sensitivity)
- Too low spatial resolution (each voxel has several million neurons)
- Any higher resolution than 3 $mm^3$ lost with subject averaging.
- Too low temporal resolution (hemodynamics are variable and sluggish)
- Too inconsistent activation patterns
- Anatomical images for fMRI are low quality (dropout/distortion)
- Requires a task (BOLD cannot look at baseline maps).
- Too confined space and high acoustic noise (environment non-optimal).

# What fMRI Can't Do

## What some would argue are shortcomings with fMRI

- Too low SNR vs subject/patient limits of compliance (about 2 hours)
- Requires motivated subjects/patients (motion sensitivity)
- Too low spatial resolution (each voxel has several million neurons)
- Any higher resolution than 3 $mm^3$ lost with subject averaging.
- Too low temporal resolution (hemodynamics are variable and sluggish)
- Too inconsistent activation patterns
- Anatomical images for fMRI are low quality (dropout/distortion)
- Requires a task (BOLD cannot look at baseline maps).
- Too confined space and high acoustic noise (environment non-optimal).

# What fMRI Can't Do

## What some would argue are shortcomings with fMRI

- Too low SNR vs subject/patient limits of compliance (about 2 hours)
- Higher field strength, multi-channel, temporal processing (15 min)
- Requires motivated subjects/patients (motion sensitivity)
- Real time fMRI, improved motion correction, navigator pulses
- Too low spatial resolution (each voxel has several million neurons)
- FMRI-adaptation paradigms, smallest functional unit about 0.5mm anyway
- *Any higher resolution than 3 $mm^3$ lost with subject averaging.*
- Spatial averaging becoming a bit less common.
- Too low temporal resolution (hemodynamics are variable and sluggish)
- Paired pulse paradigms, timing modulation w/ latency comparison (<100 ms)
- Too inconsistent activation patterns
- Not typically due to low SNR. Subject differences – good problem.
- *Anatomical images for fMRI are low quality (dropout/distortion)*
- SENSE, multi-channel, and Bo correction can help.
- Requires a task (BOLD cannot look at baseline maps).
- Calibration methods getting much better. Baseline info is coming.
- Too confined space and high acoustic noise (environment non-optimal).
- Strategies around this. Vendors learning how to dampen sound.

## Technology

- Coil arrays
- High field strength
- High resolution
- Novel functional contrast

## Methodology

- Functional Connectivity Assessment
- Multi-modal integration
- Pattern classification
- Real time feedback
- Task design (fMRIa…)

- Fluctuations
- Dynamics
- Spatial patterns

## Interpretation

- Basic Neuroscience
- Behavior correlation/prediction
- Pathology assessment

## Applications

## Major Directions of fMRI Advancement:

(technology) Increased sensitivity and resolution

(interpretation) Physiologic Fluctuations

(methodology) “Pattern effect”, fMRI “decoding”

(applications) Real time fMRI

## Technology

Coil arrays
High field strength
High resolution
Novel functional contrast

## Methodology

Functional Connectivity Assessment
Multi-modal integration
Pattern classification
Real time feedback
Task design (fMRIa…)

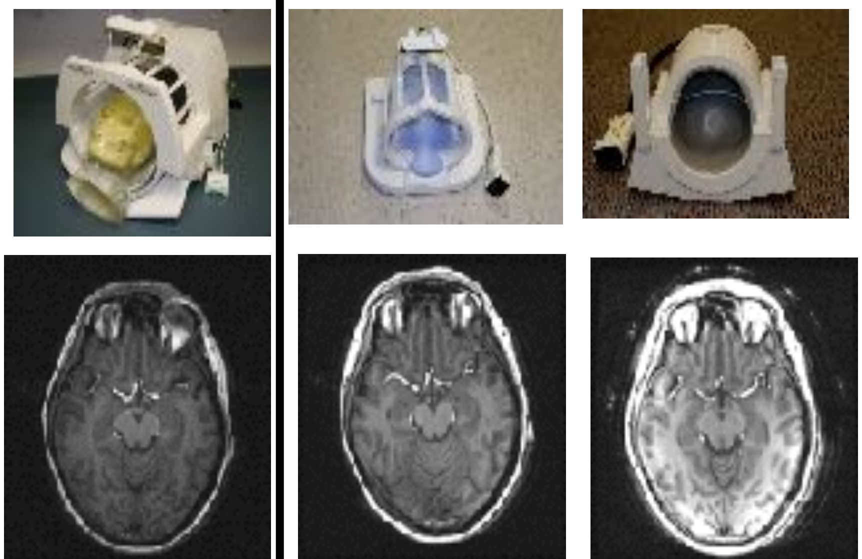
Fluctuations
Dynamics
Spatial patterns

## Interpretation

Basic Neuroscience
Behavior correlation/prediction
Pathology assessment

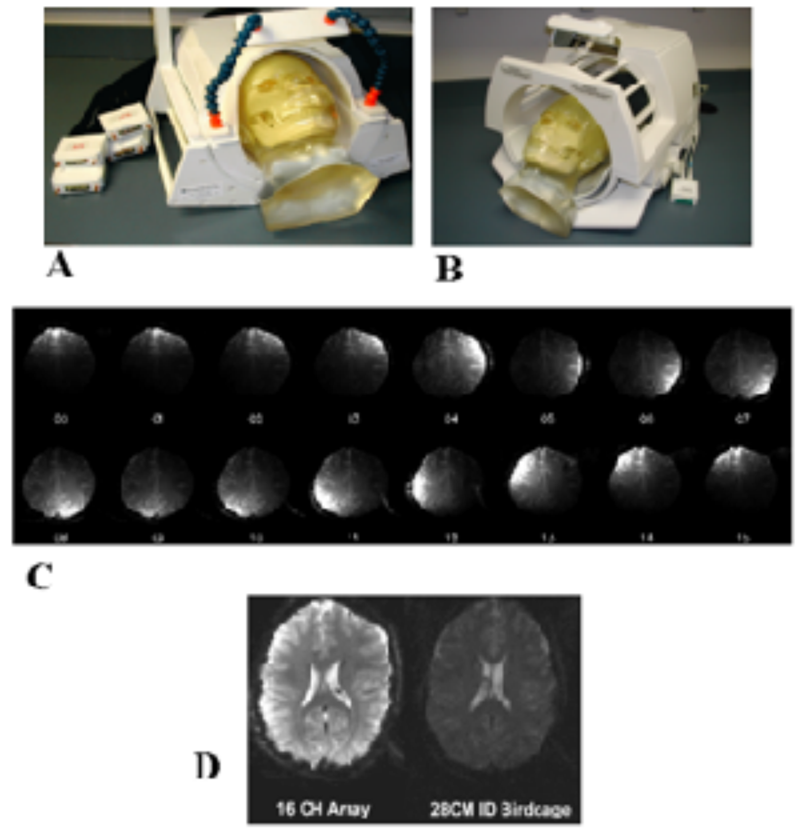
## Applications

## 8 channel parallel receiver coil

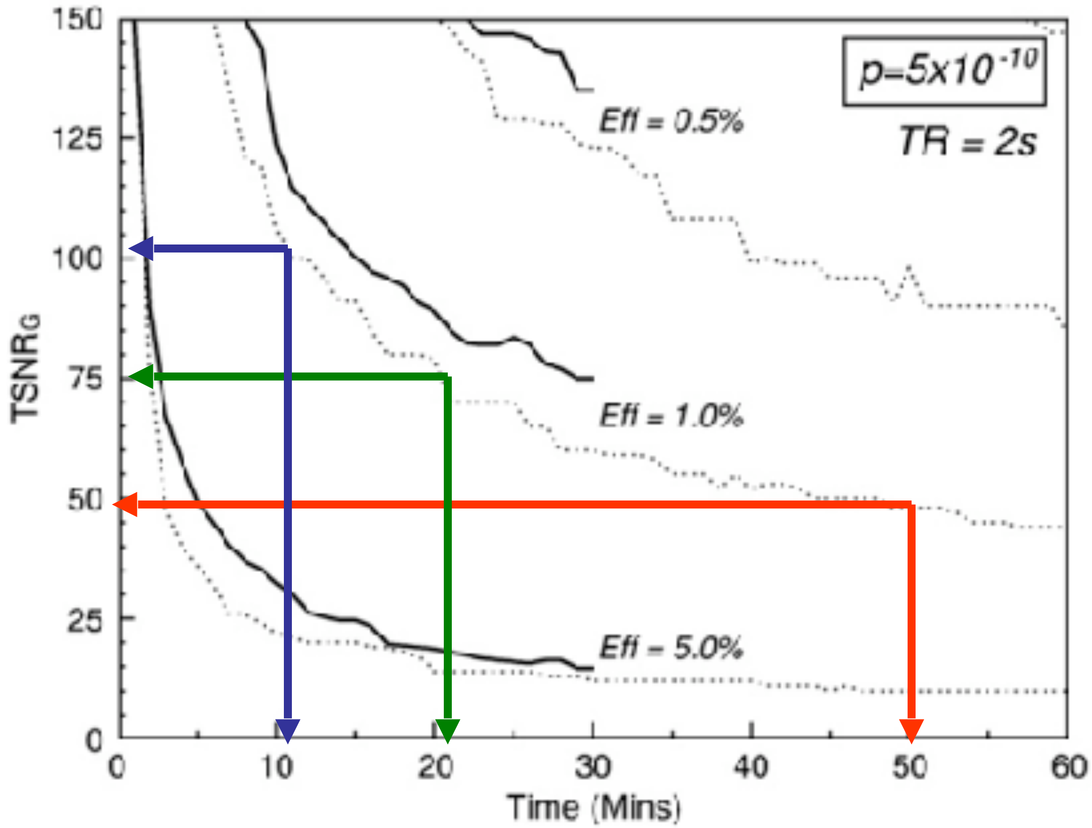


GE birdcage | GE 8 channel coil | Nova 8 channel coil

## 16 channel parallel receiver coil

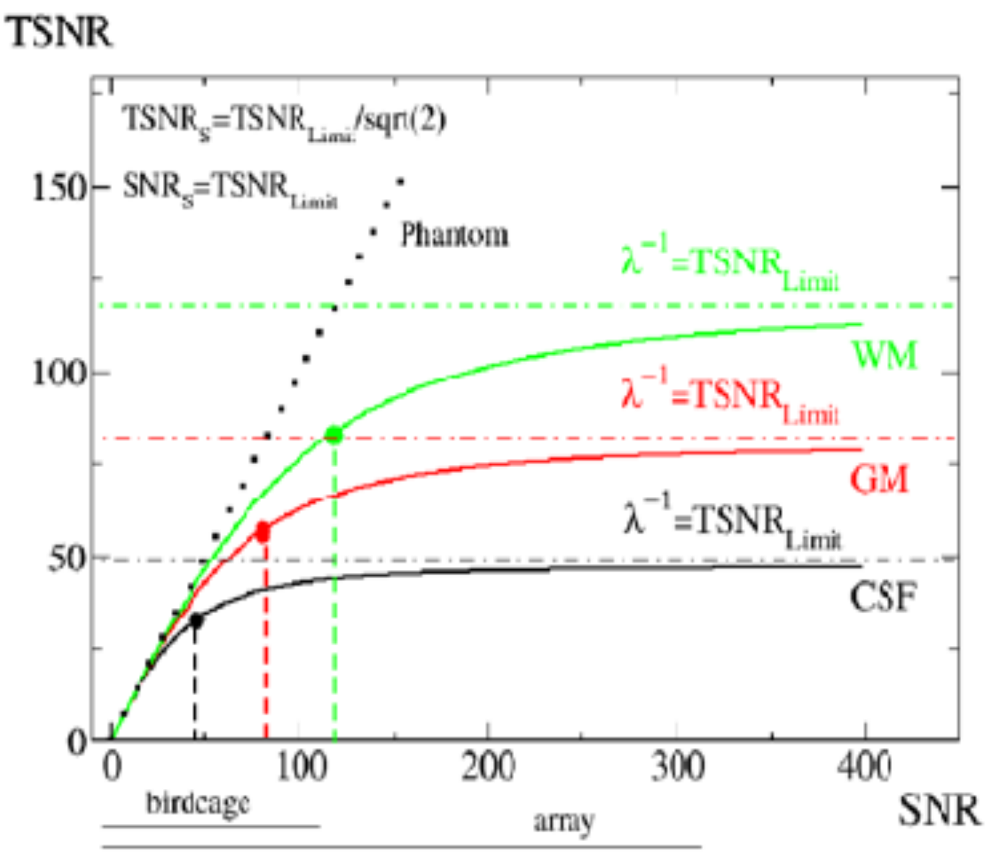



J. Bodurka, et al, Magnetic Resonance in Medicine 51 (2004) 165-171.




K. Murphy, J. Bodurka, P. A. Bandettini, How long to scan? The relationship between fMRI temporal signal to noise and the necessary scan duration. NeuroImage, 34, 565-574 (2007)

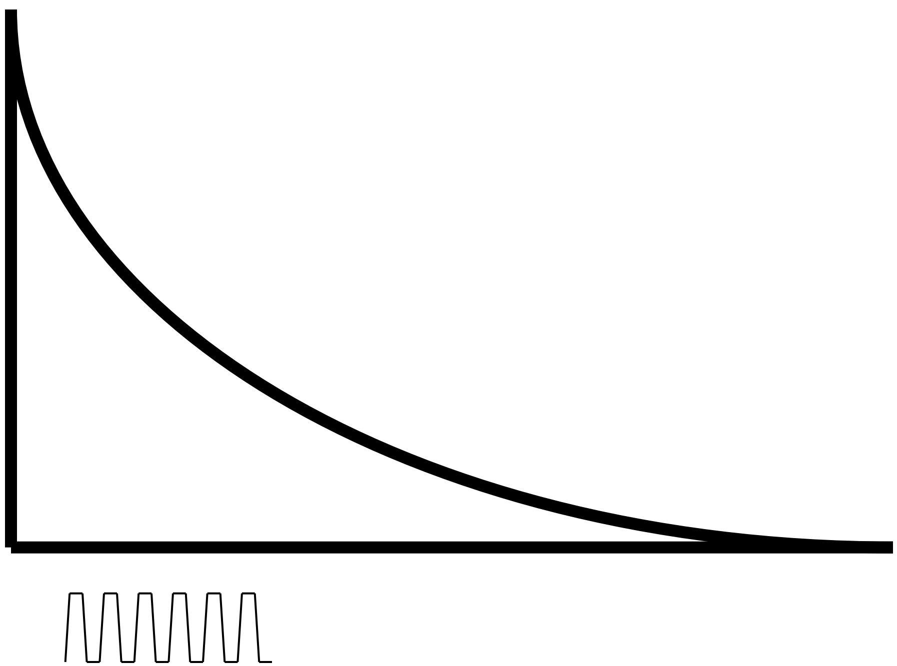
## Temporal Signal to Noise Ratio (TSNR) vs. Signal to Noise Ratio (SNR)



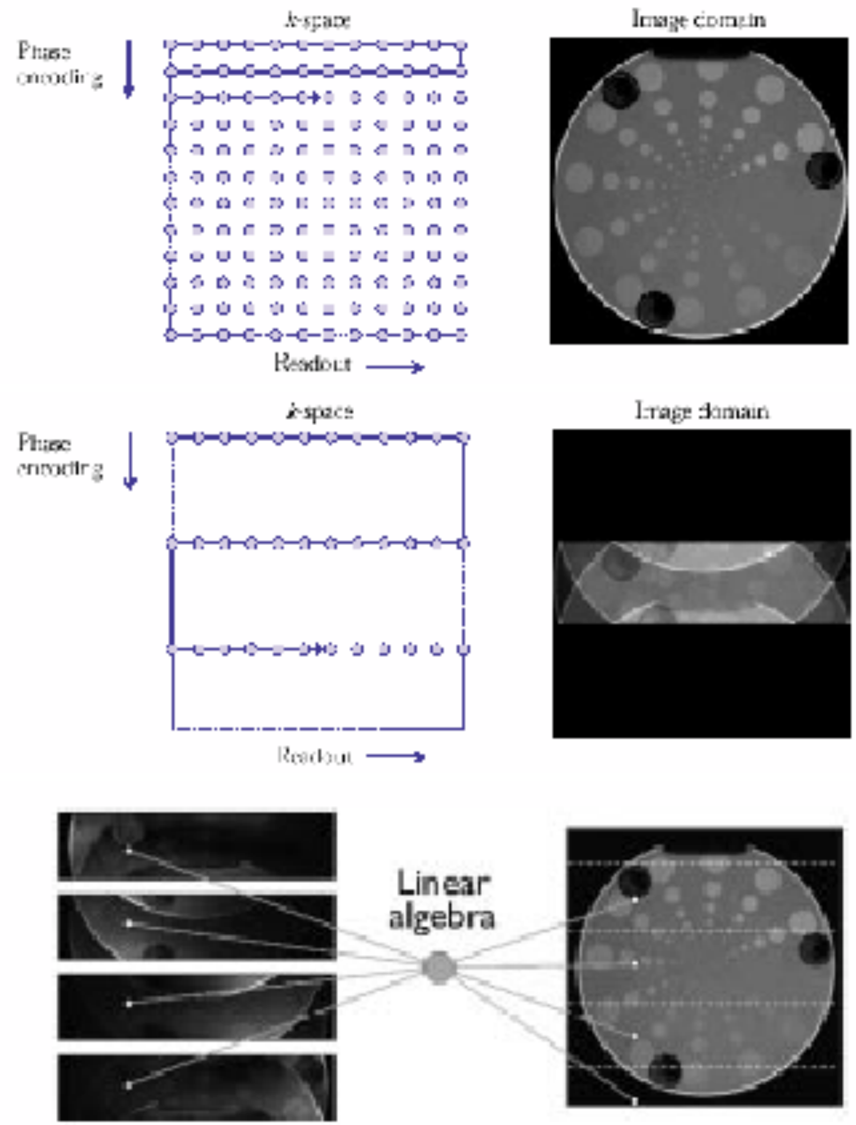

suggested voxel volume

| | |
|---|---|
| 3T, birdcage: | 2.5 $mm^3$ |
| 3T, 16 channel: | 1.8 $mm^3$ |
| 7T, 16 channel: | 1.4 $mm^3$ |

J. Bodurka, F. Ye, N Petridou, K. Murphy, P. A. Bandettini, NeuroImage, 34, 542-549 (2007)

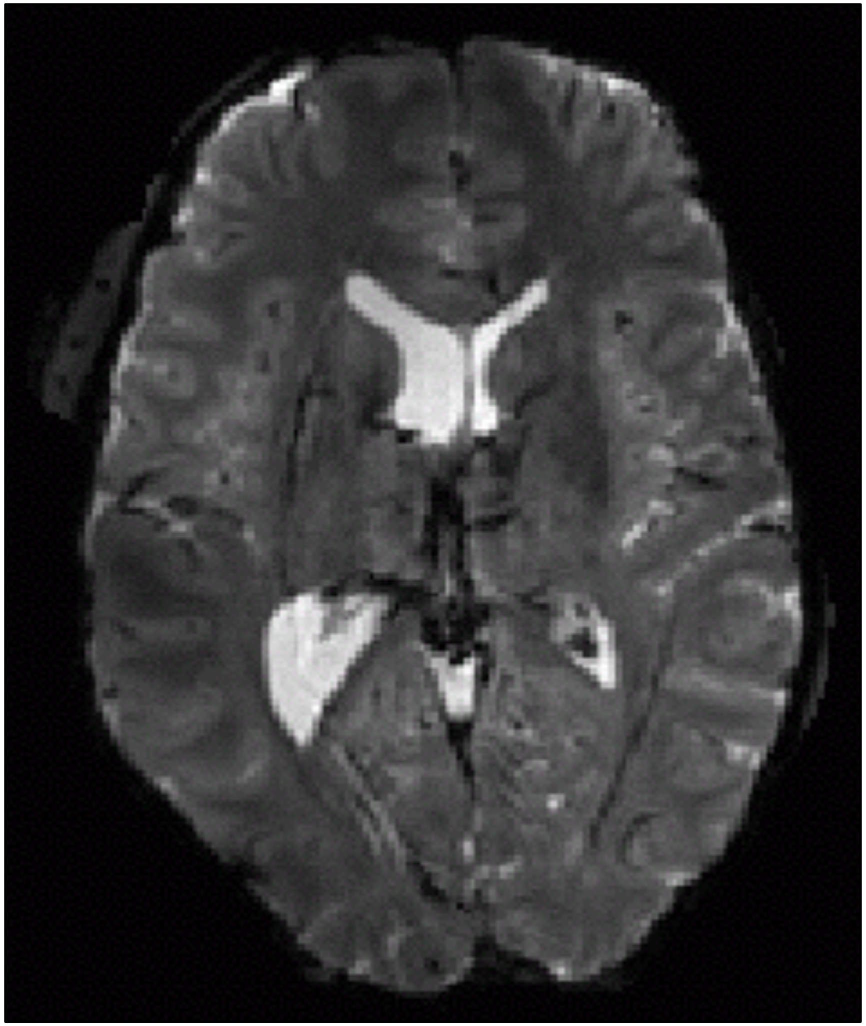


≈ 5 to 30 ms



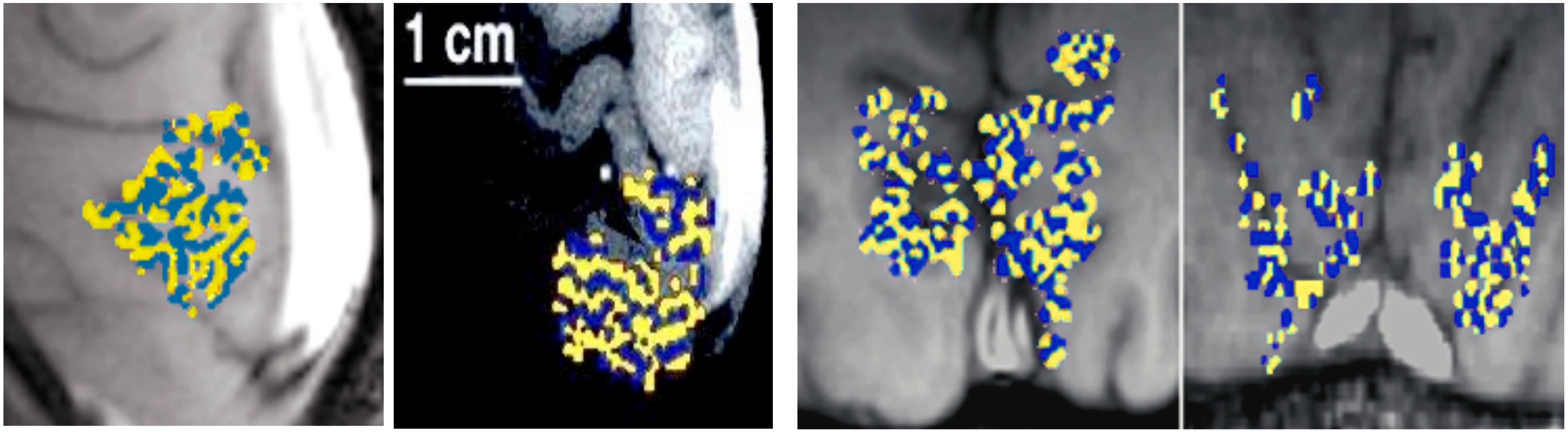

Pruessmann, et al.

# Technology

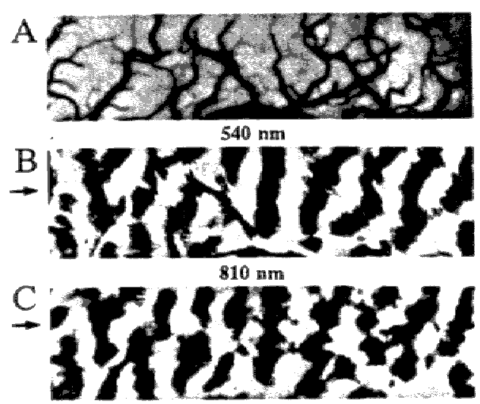


3T single-shot SENSE EPI using 16 channels: 1.25x1.25x2mm

# Ocular Dominance Column Mapping using fMRI




**Menon, R. S., S. Ogawa, et al. (1997). "Ocular dominance in human V1 demonstrated by functional magnetic resonance imaging." J Neurophysiol 77(5): 2780-7.**

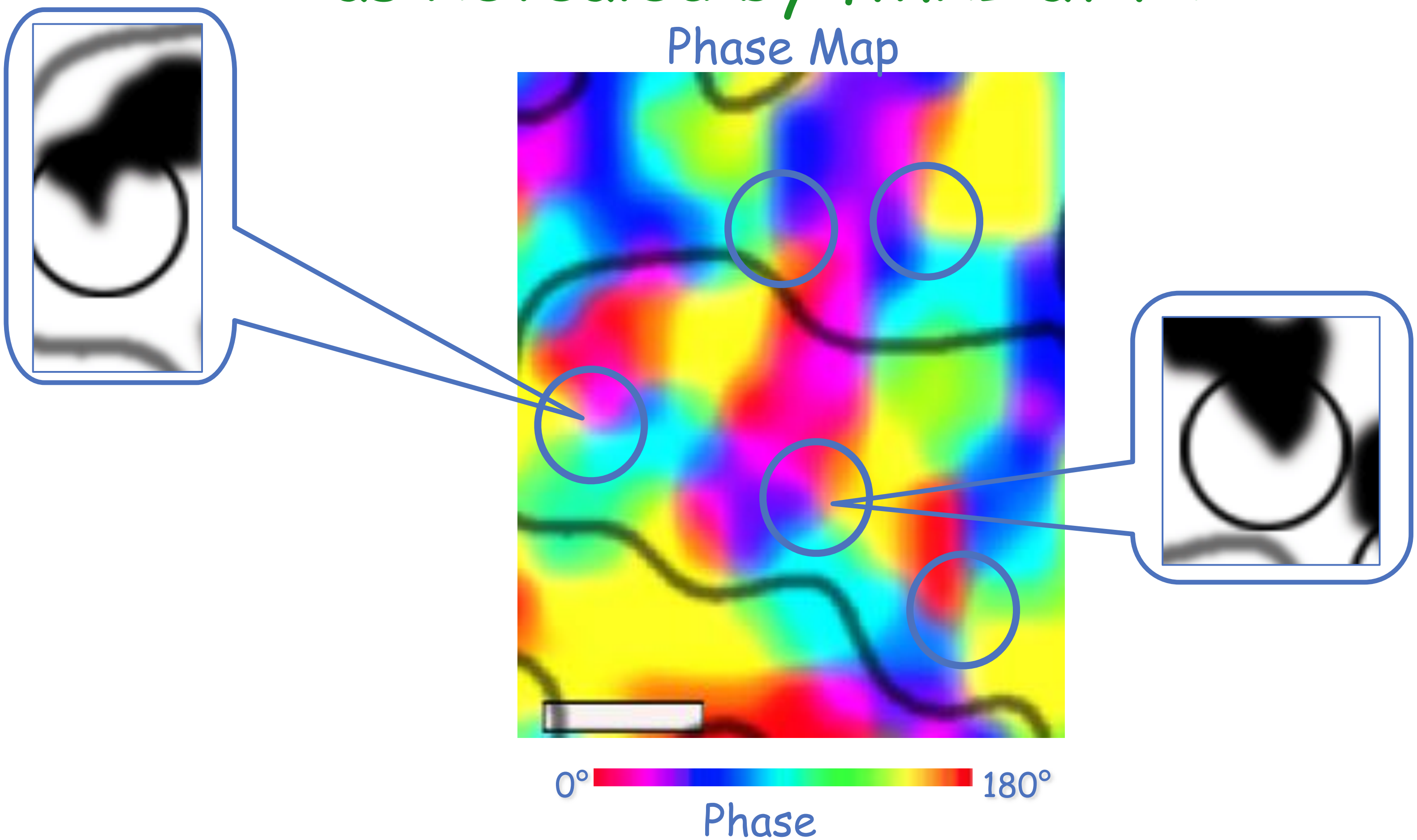



Optical Imaging

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

Technology

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




Yacoub, Ugurbil & Harel

Scale bar = 0.5 mm

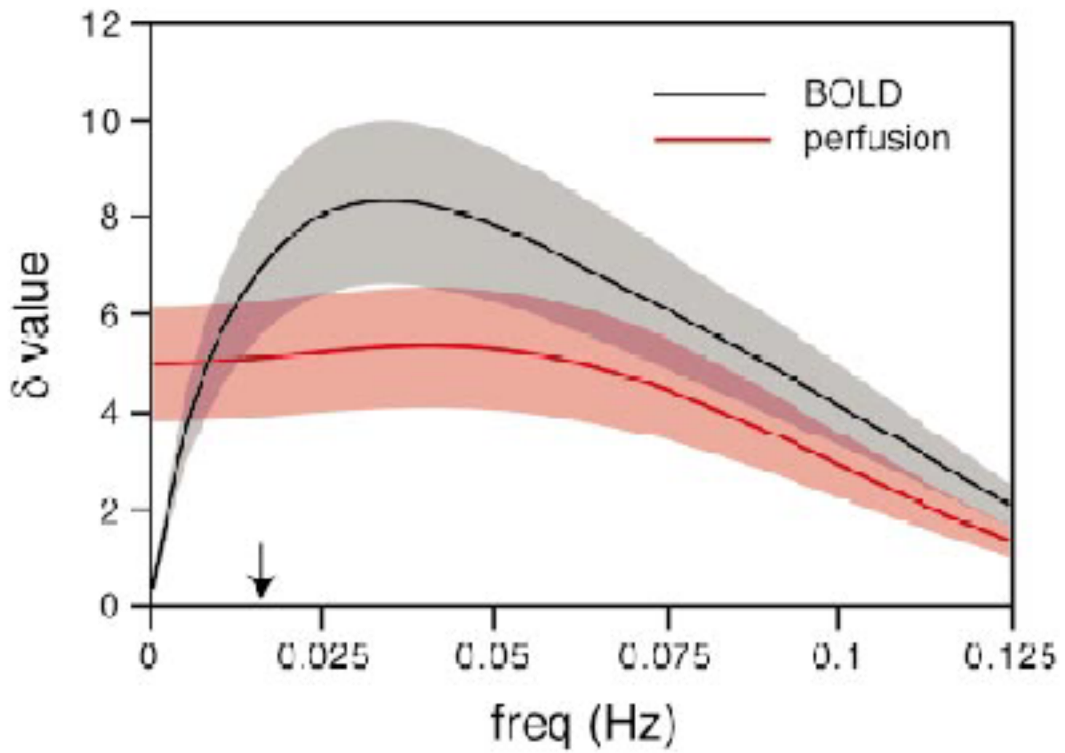
# fMRI Contrast

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

# Technology

## Perfusion (ASL)

**Better than BOLD for long duration activation…**




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

## Technology

- Coil arrays
- High field strength
- High resolution
- Novel functional contrast

## Methodology

- Functional Connectivity Assessment
- Multi-modal integration
- Pattern classification
- Real time feedback
- Task design (fMRIa…)

- Fluctuations
- Dynamics
- Spatial patterns

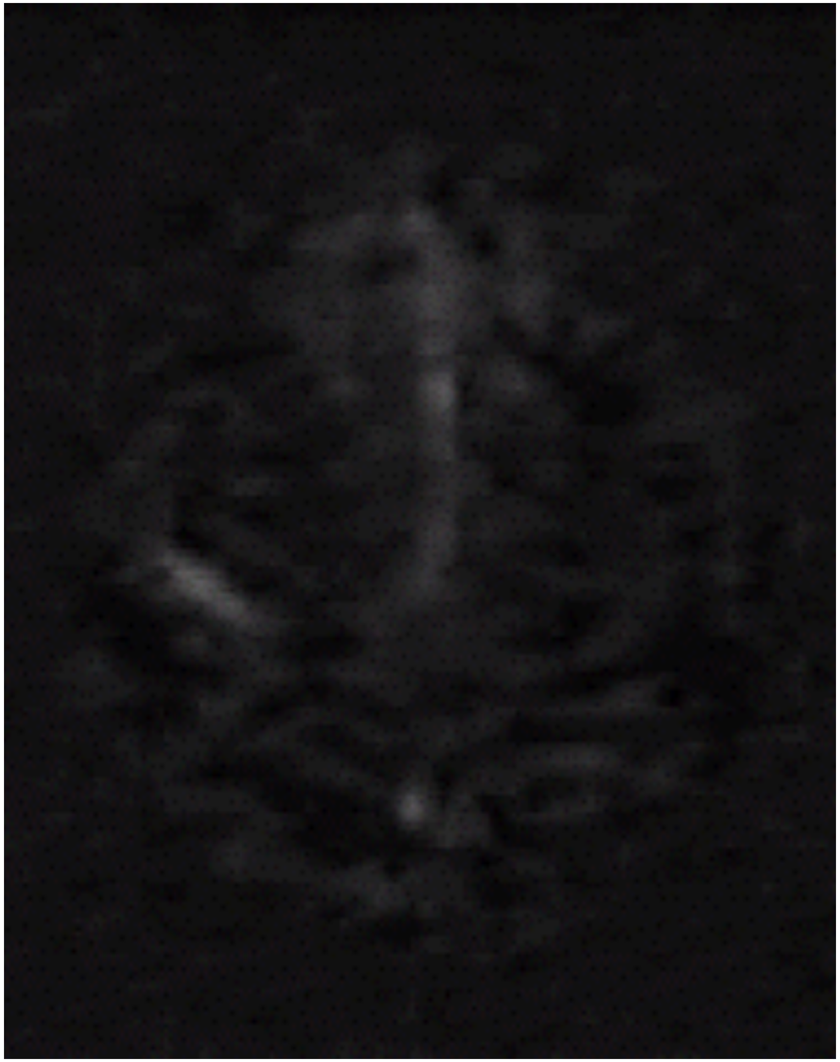
## Interpretation

- Basic Neuroscience
- Behavior correlation/prediction
- Pathology assessment

## Applications

## Methodology

## Beyond Mapping

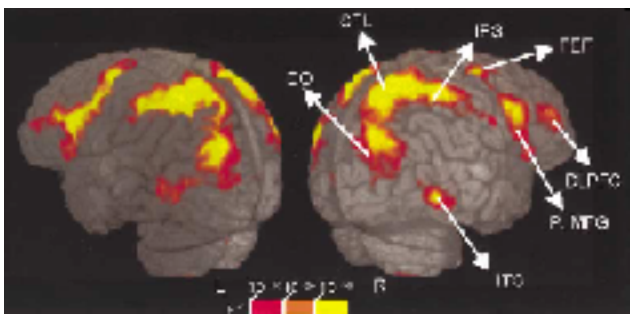


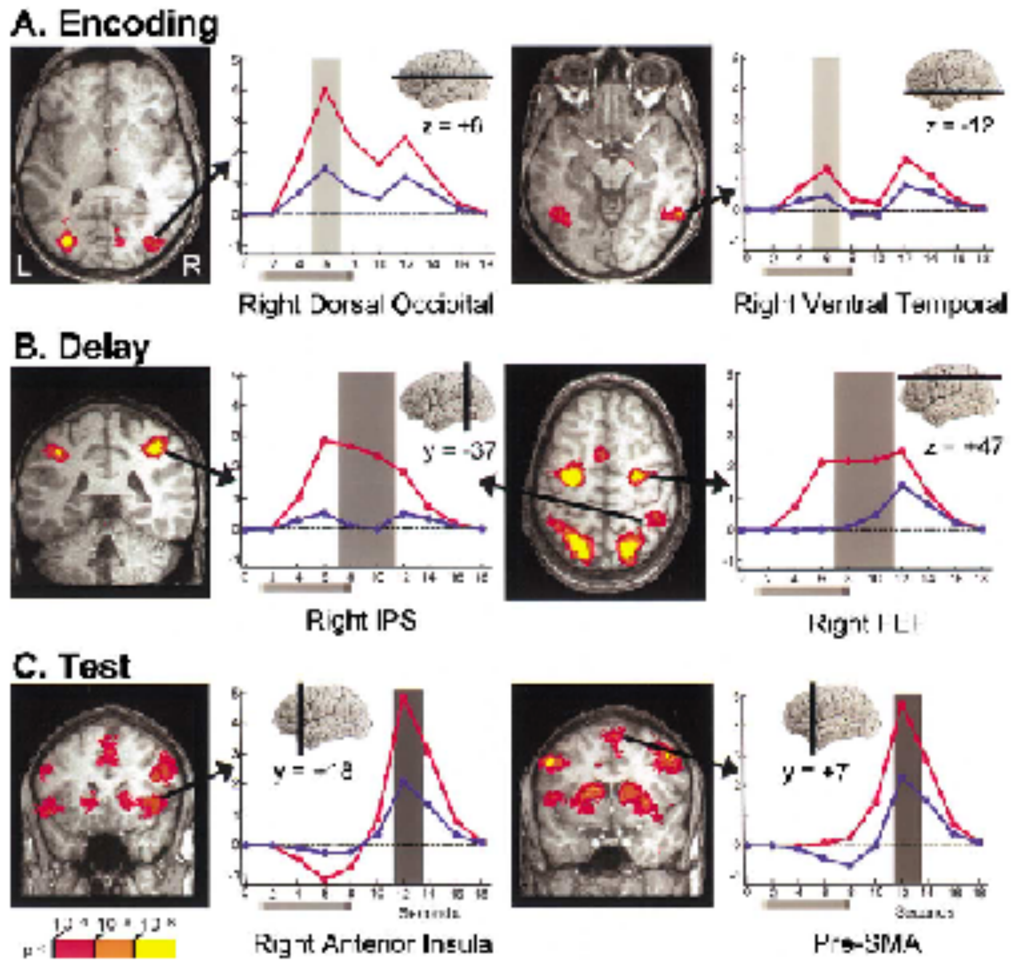
# Mapping ⟷ "Reading"

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

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

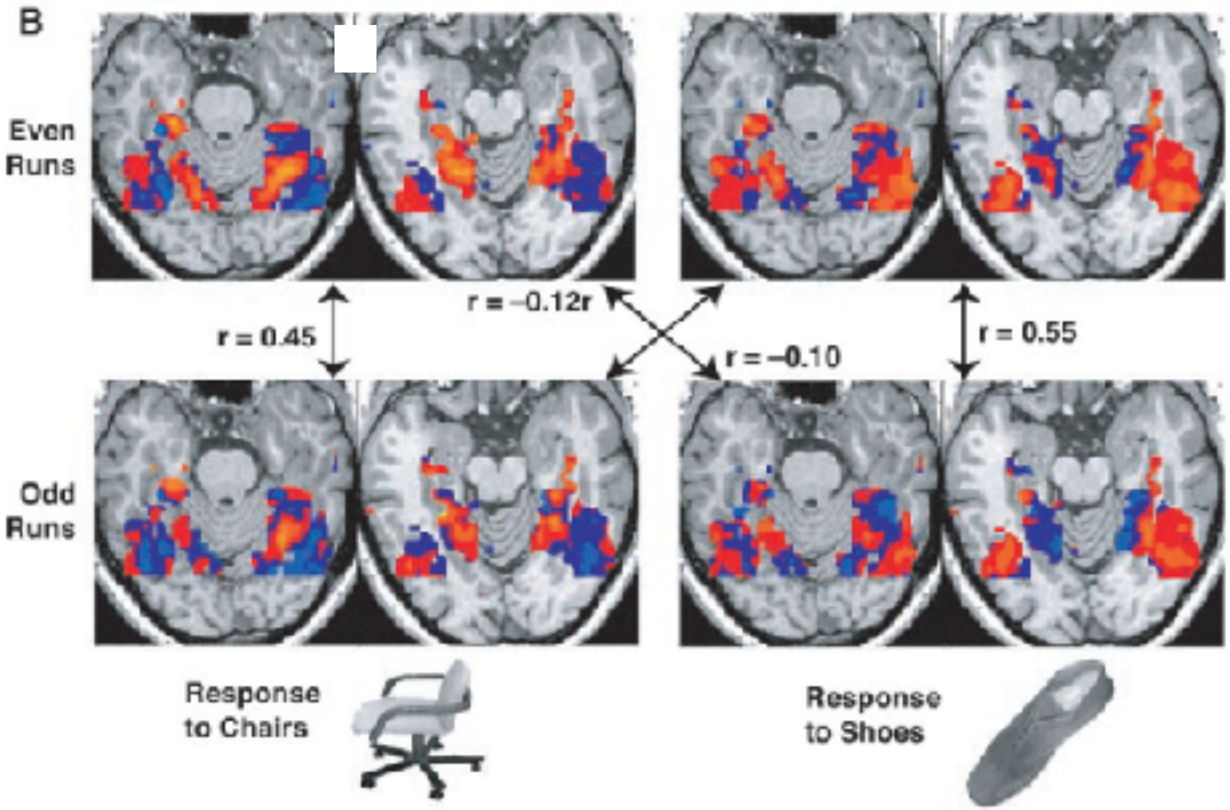
**Luiz Pessoa,[1] Eva Gutierrez, Peter A. Bandettini, and Leslie G. Ungerleider**
Laboratory of Brain and Cognition
National Institute of Mental Health
National Institutes of Health
Bethesda, Maryland 20892



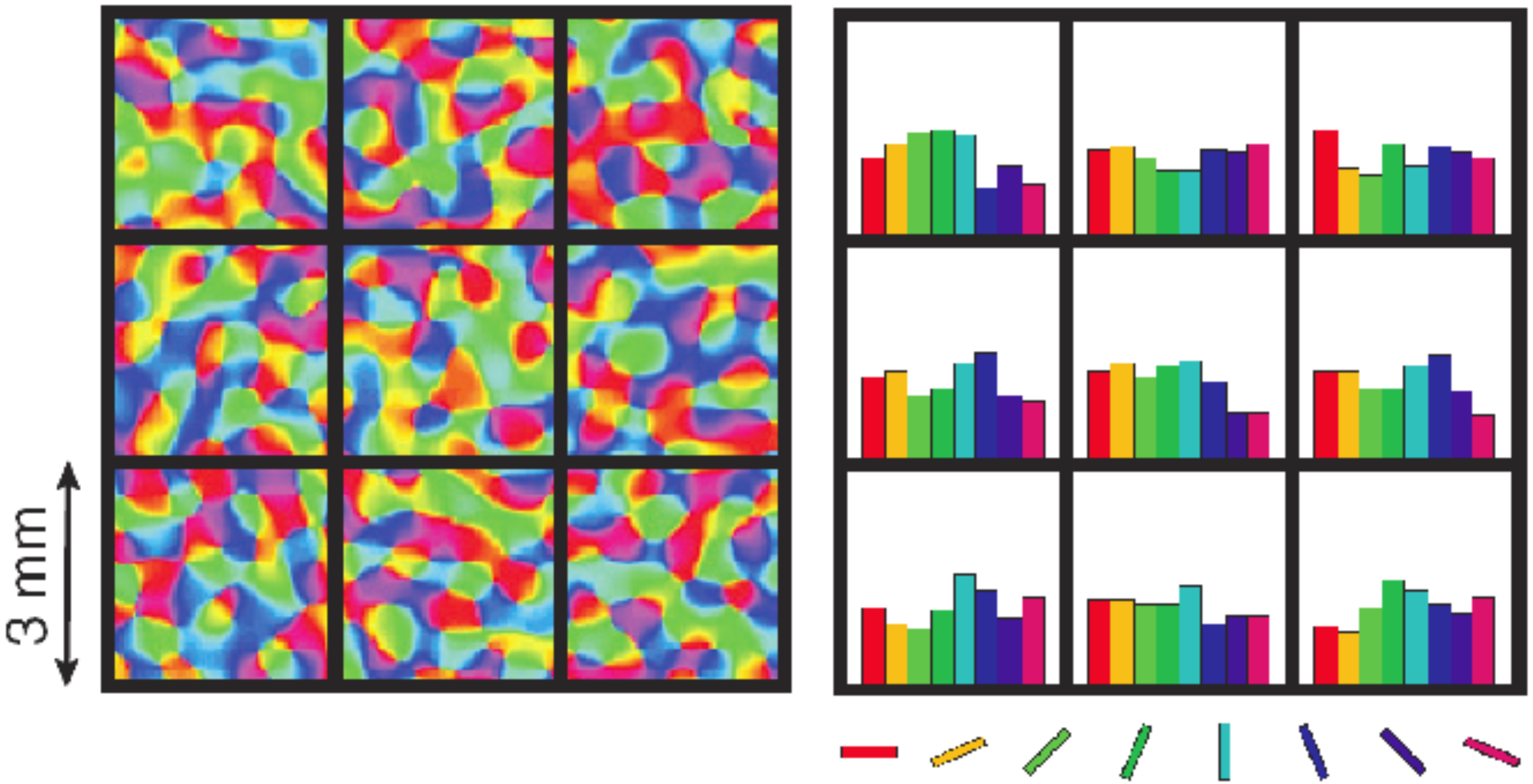



# Ventral temporal category representations

Object categories are associated with distributed representations in ventral temporal cortex

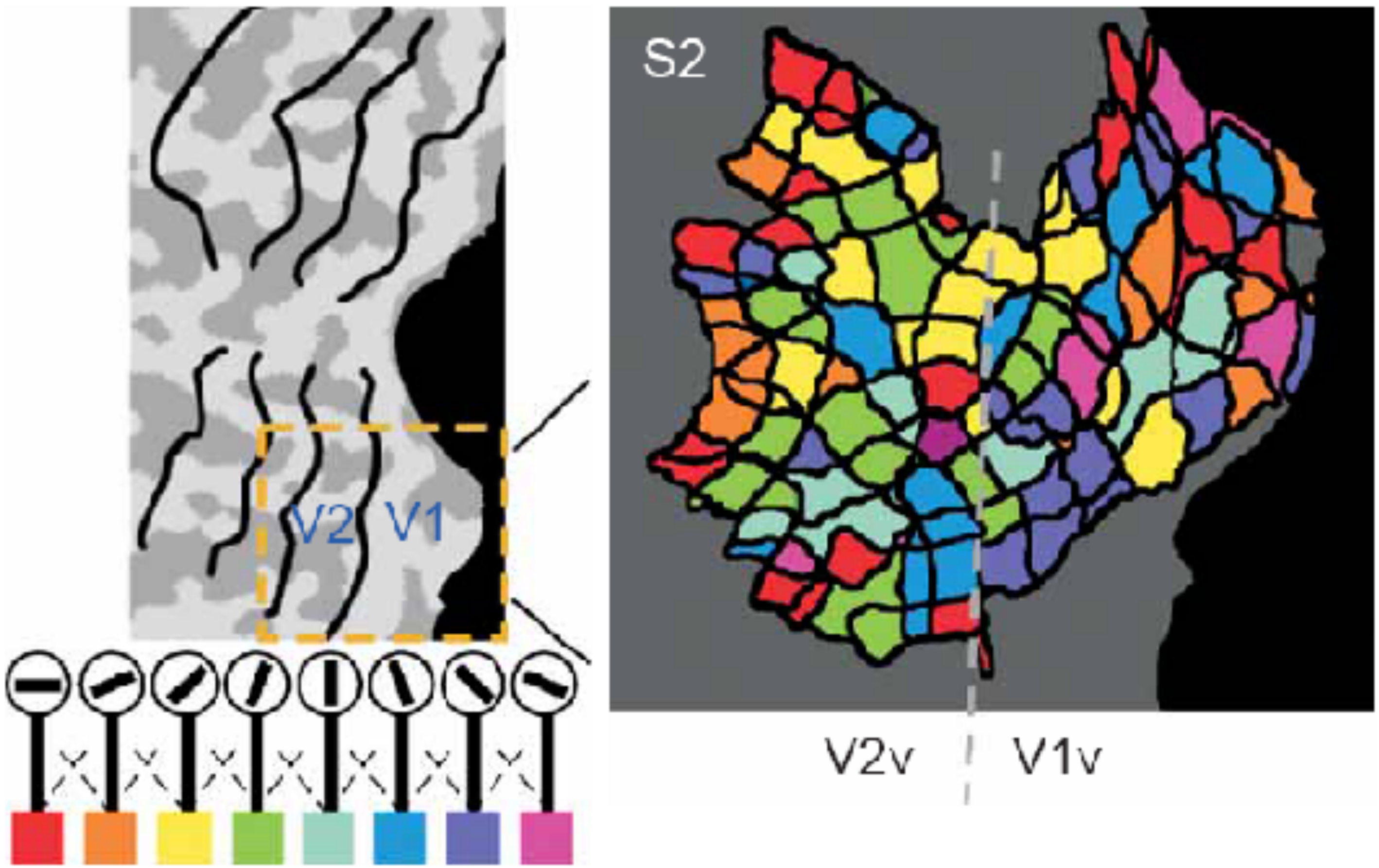



**Haxby et al. Science, 2001**




Boynton (2005), News & Views on Kamitani & Tong (2005) and Haynes & Rees (2005)

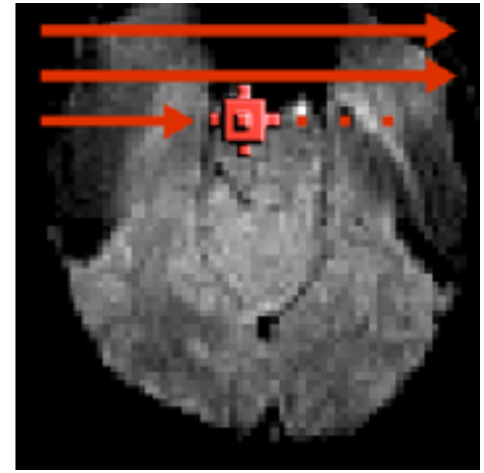
# Lower spatial frequency clumping



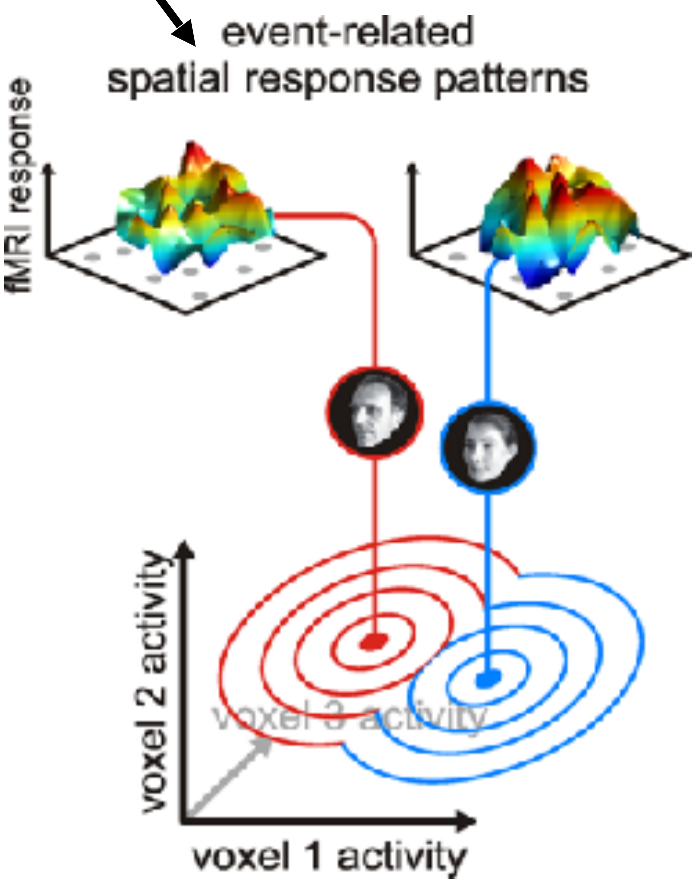

Kamitani & Tong (2005)

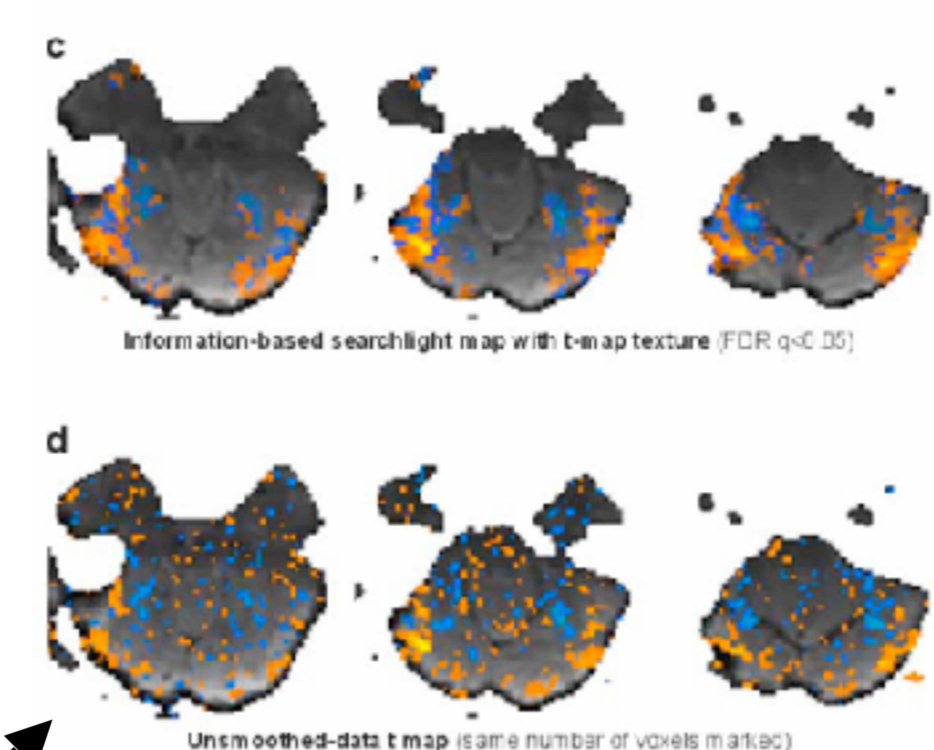
# Pattern Information Mapping

"searchlight" ROI



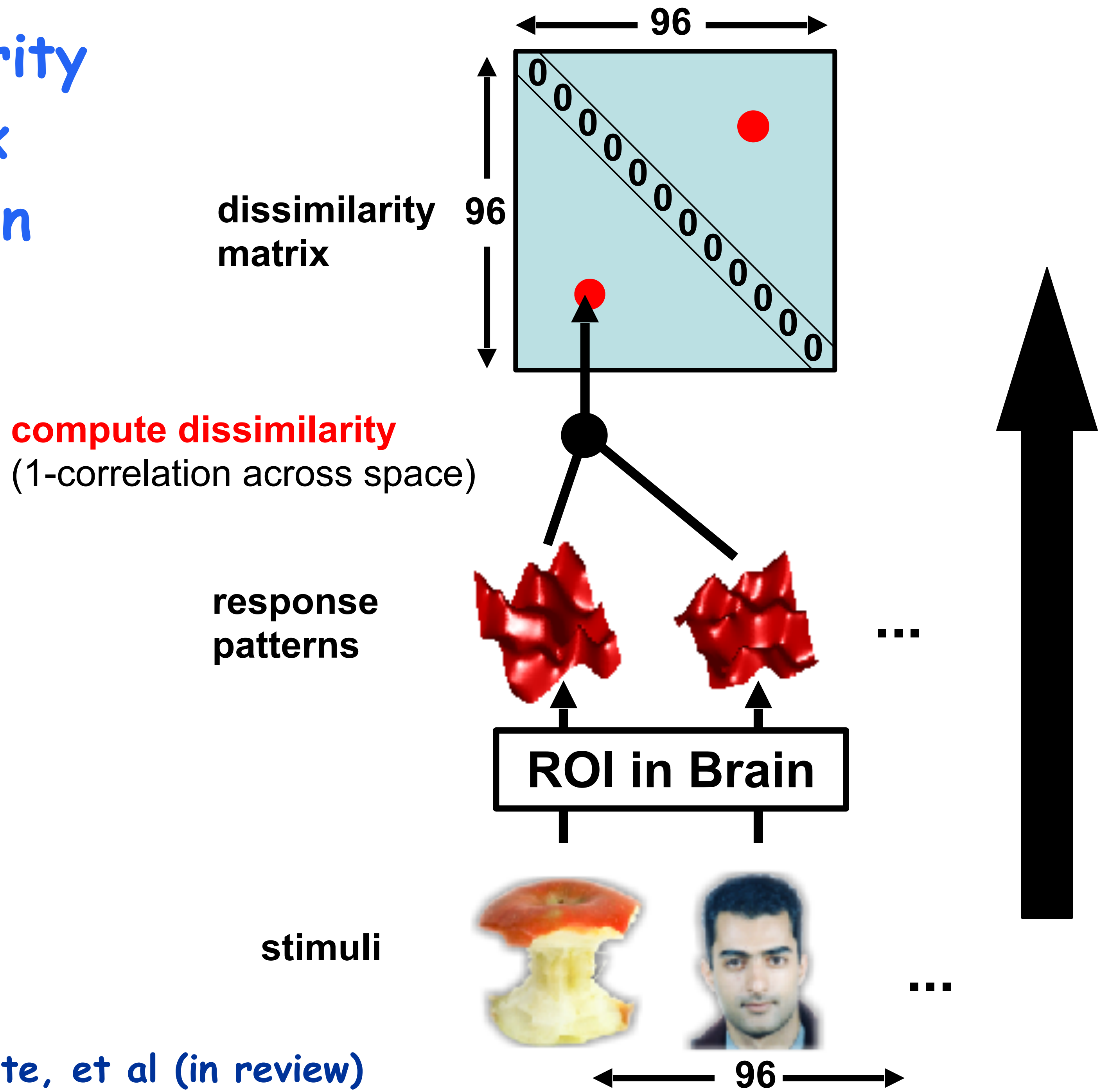
From fixed ROI




N. Kriegeskorte, R. Goebel, P. Bandettini, Proc. Nat'l. Acad. Sci. USA, 103, 3863-3868 (2006)

# Dissimilarity Matrix Creation

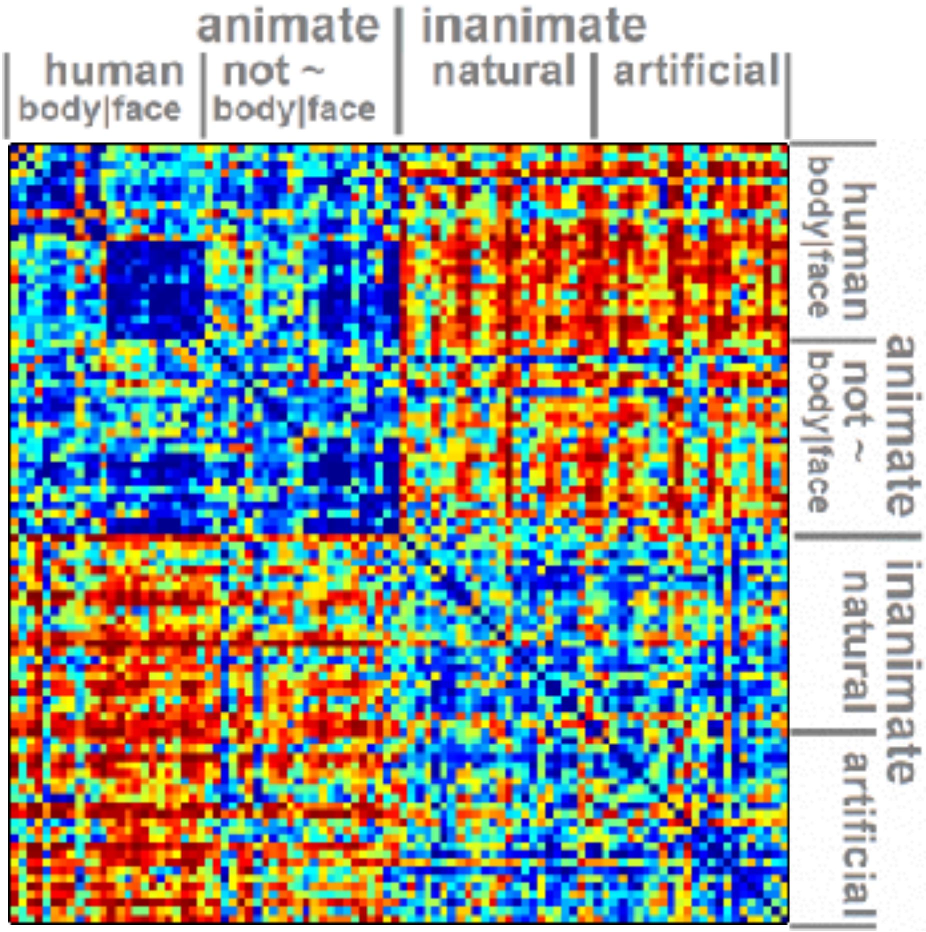



N. Kriegeskorte, et al (in review)

# Visual Stimuli

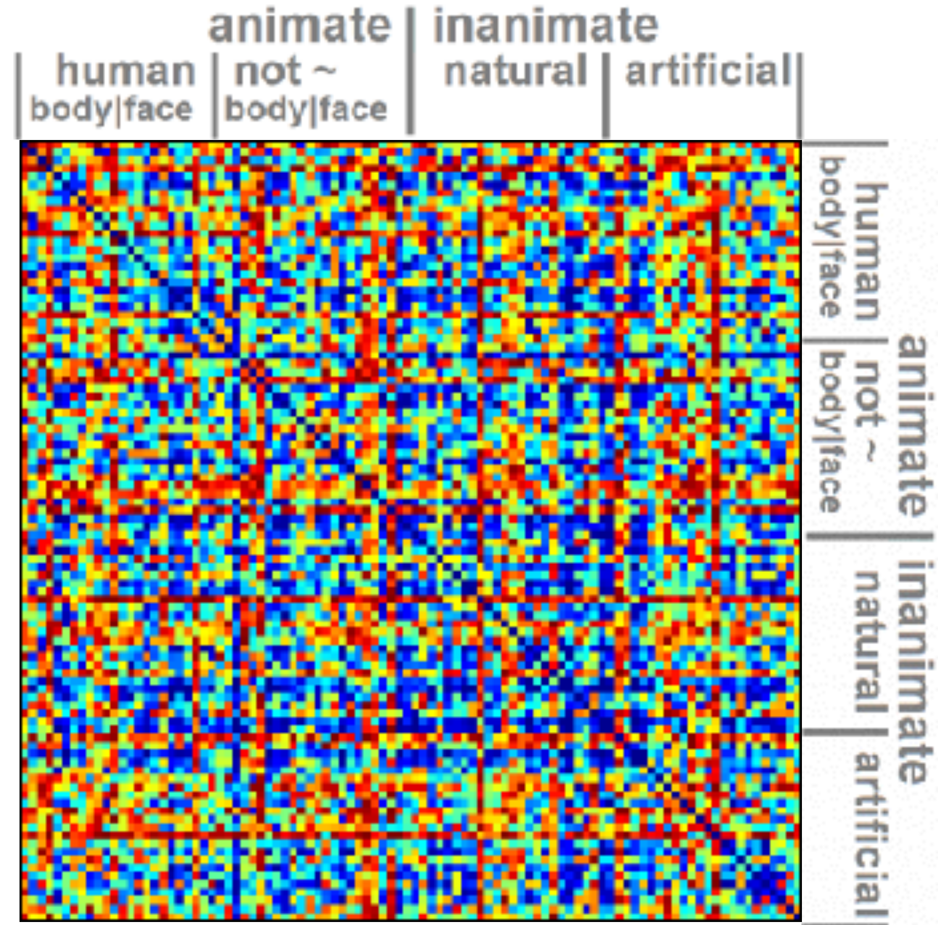
# Human IT

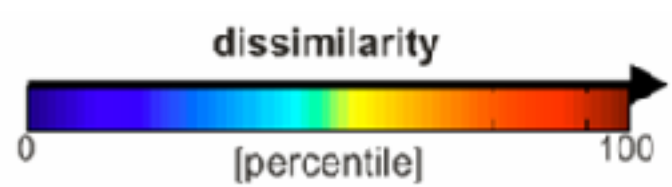
(1000 visually most responsive voxels)




# Human Early Visual Cortex

(1057 visually most responsive voxels)



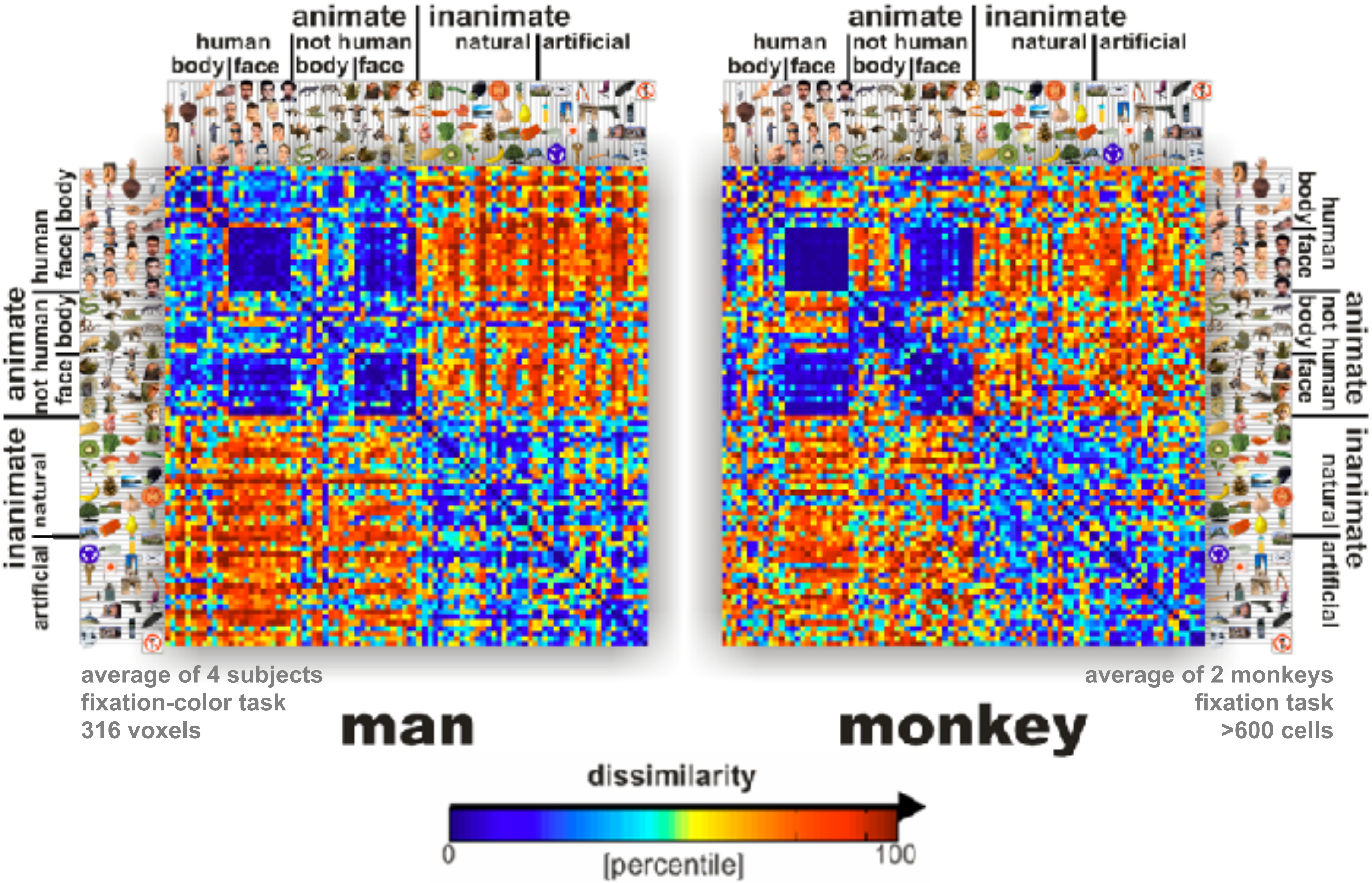
# Monkey-Human Comparison Procedure

**Human**

- fMRI in four subjects
  (repeated sessions,
  >12 runs per subject)
- "quick" event-related design
  (stimulus duration: 300ms,
  stimulus onset asynchrony: 4s)
- fixation task
  (with discrimination of fixation-point color changes)
- occipitotemporal measurement slab
  (5-cm thick)
- small voxels ($1.95 \times 1.95 \times 2 mm^3$)
- 3T magnet, 16-channel coil (SENSE, acc. fac. 2)

**Monkey** (Kiani et al. 2007)

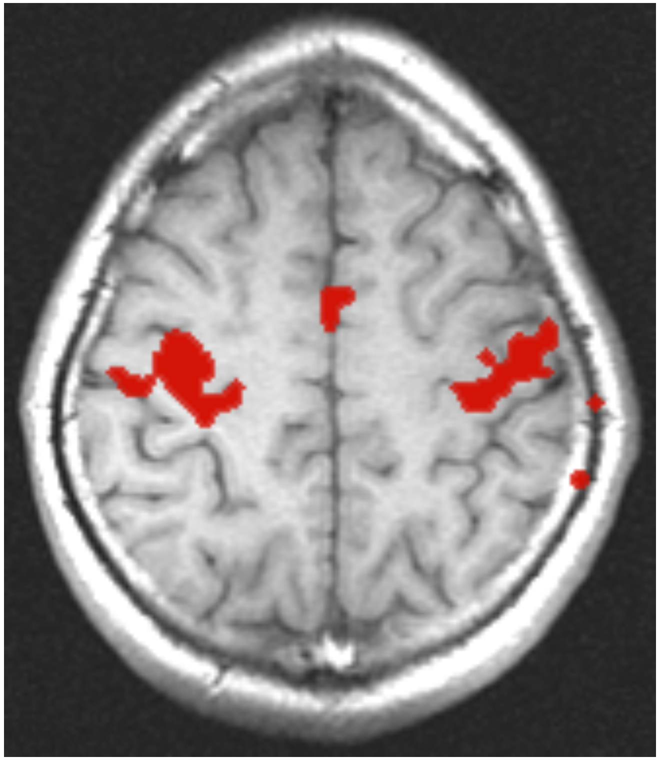
- single-cell recordings in two monkeys
- rapid serial presentation
  (stimulus duration: 105ms)
- fixation task
- electrodes in anterior IT
  (left in monkey 1, right in monkey 2)
- 674 cells total
- windowed spike count
  (140-ms window starting 71ms after stimulus onset)



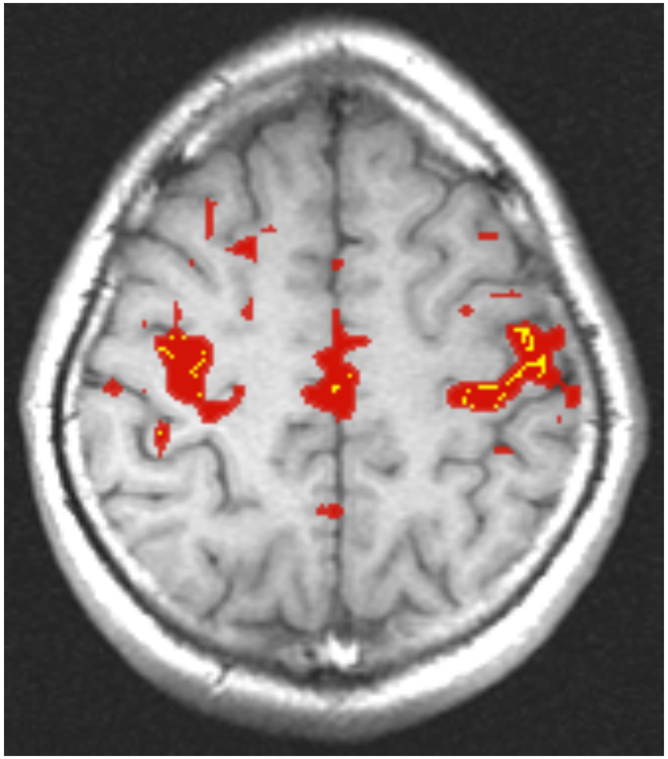

N. Kriegeskorte, et al (in review)

# Methodology

## Resting State Correlations



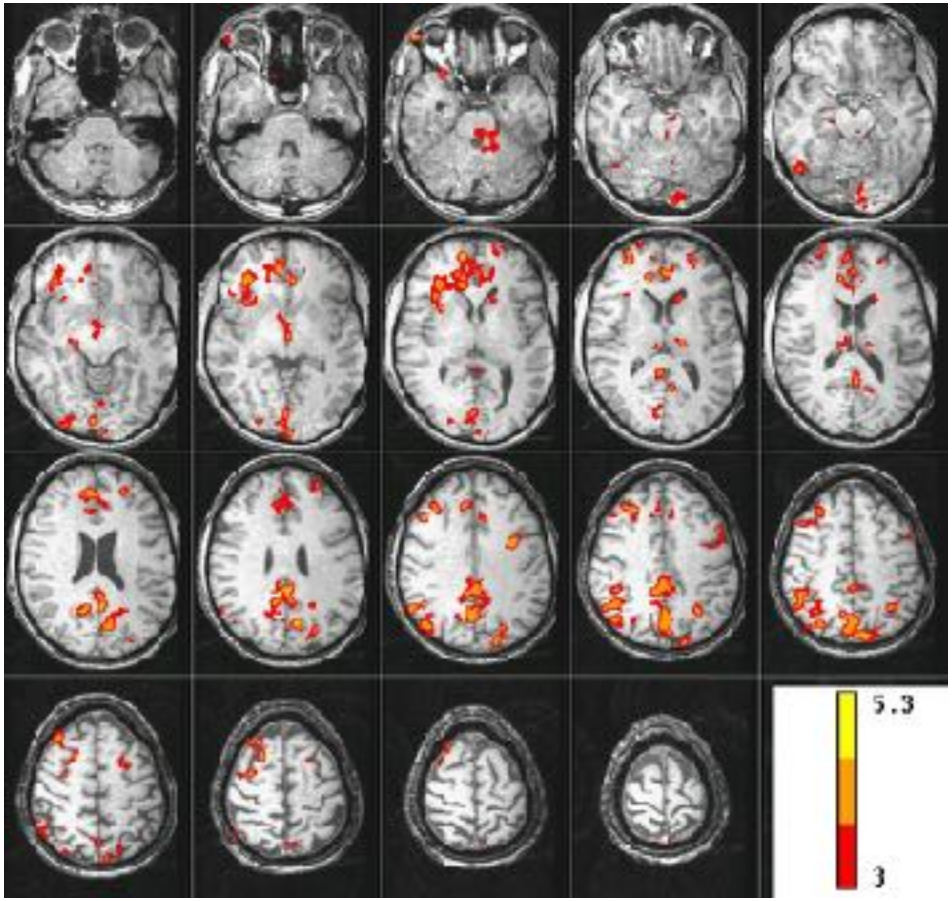
Activation:
correlation with reference function



Rest:
seed voxel in motor cortex

B. Biswal et al., MRM, 34:537 (1995)

# BOLD correlated with SCR during "Rest"



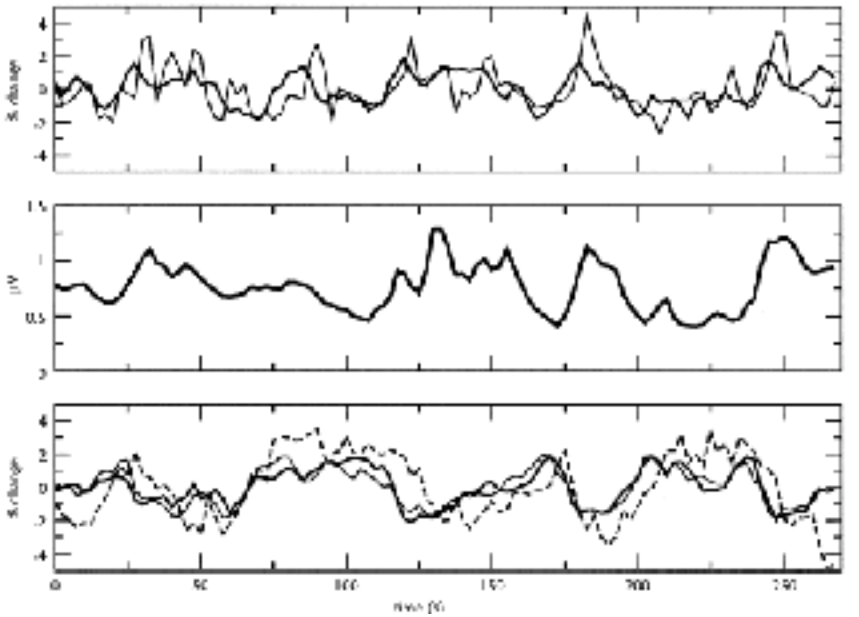

J. C. Patterson II, L. G. Ungerleider, and P. A Bandettini, NeuroImage 17: 1787-1806, (2002).

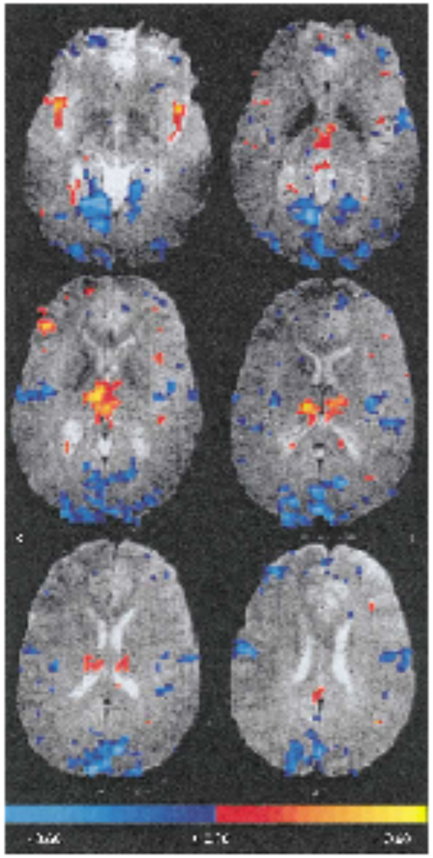
# BOLD correlated with 10 Hz power during “Rest”

Positive

10 Hz power

Negative



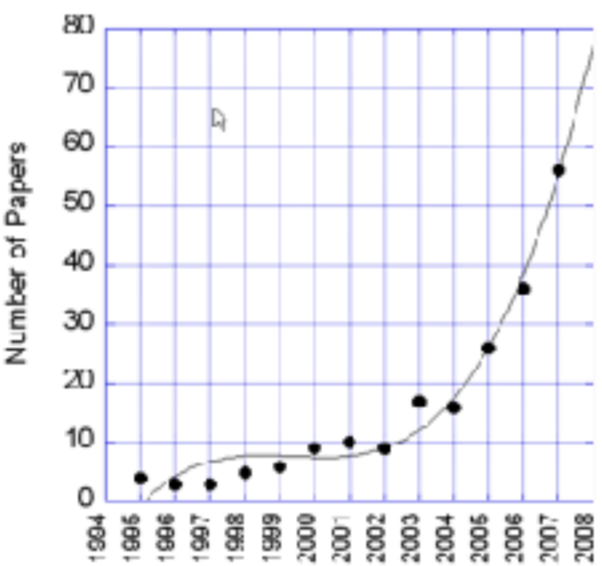


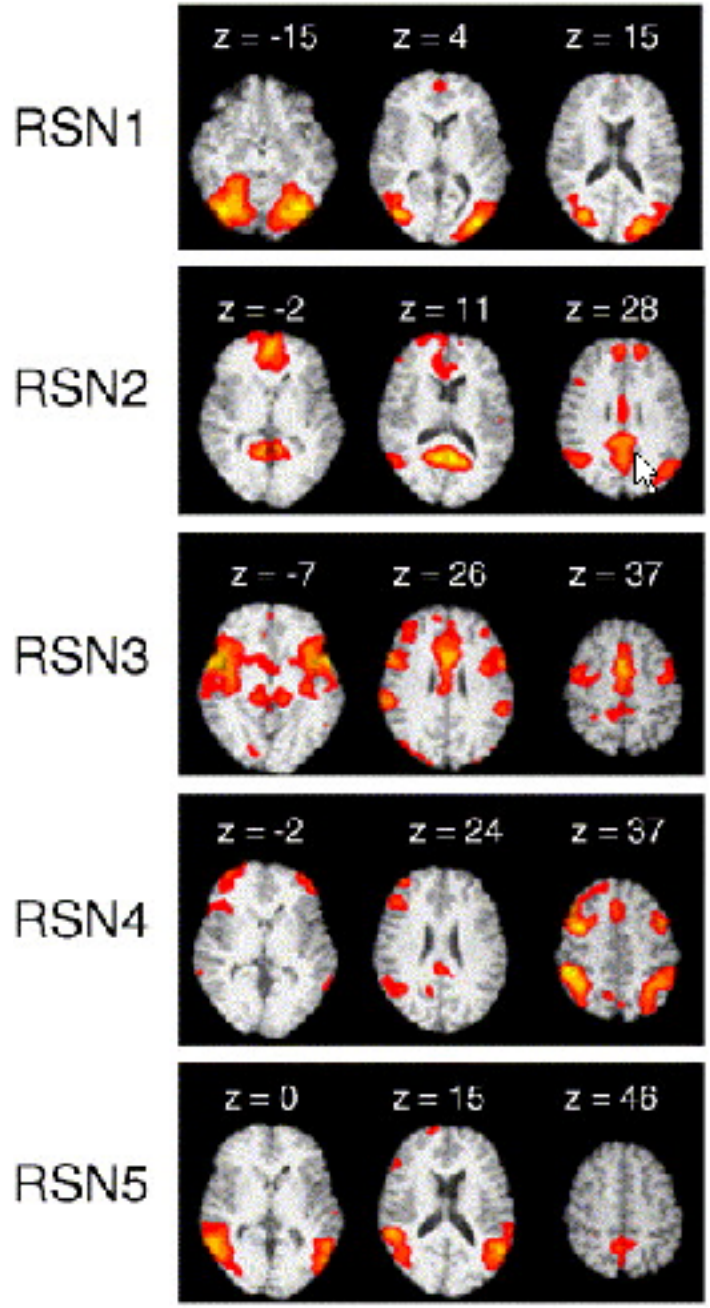
**Goldman, et al (2002), Neuroreport**

# Methodology

## Resting state networks identified with ICA

M. DeLuca, C.F. Beckmann, N. De Stefano, P.M. Matthews, S.M. Smith, fMRI resting state networks define distinct modes of long-distance interactions in the human brain. NeuroImage, 29, 1359-1367



## Technology

Coil arrays
High field strength
High resolution
Novel functional contrast

## Methodology

Functional Connectivity Assessment
Multi-modal integration
Pattern classification
Real time feedback
Task design (fMRIa…)

Fluctuations
Dynamics
Spatial patterns

## Interpretation

Basic Neuroscience
Behavior correlation/prediction
Pathology assessment

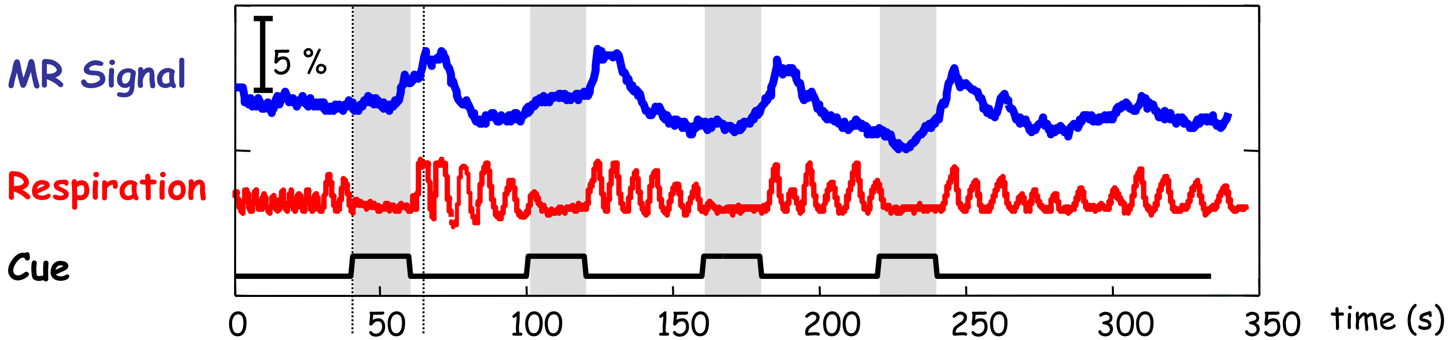
## Applications

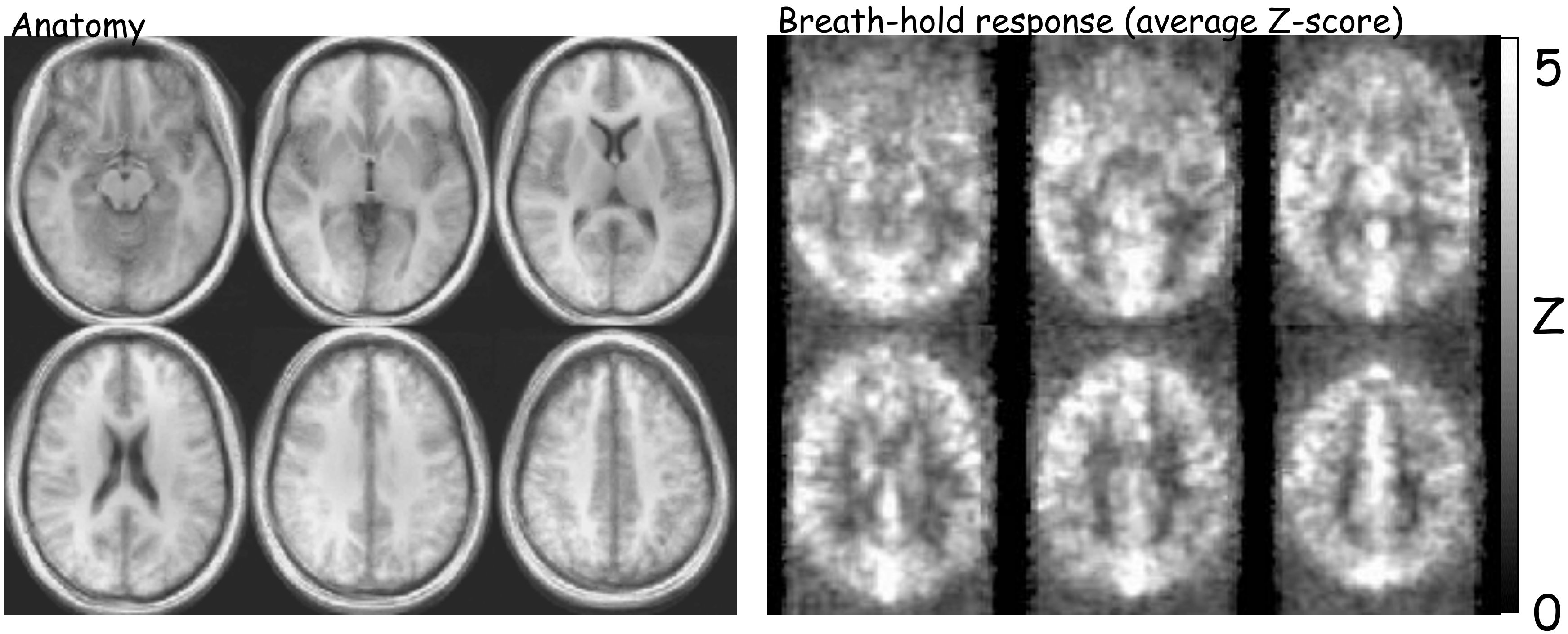
## Sources of time series fluctuations:

- Blood, brain and CSF pulsation
- Vasomotion
- Breathing cycle ($B_0$ shifts with lung expansion)
- Bulk motion
- Scanner instabilities
- Changes in blood $CO_2$ (changes in breathing)
- Spontaneous neuronal activity

# Breath-holding

Group Maps (N = 7)

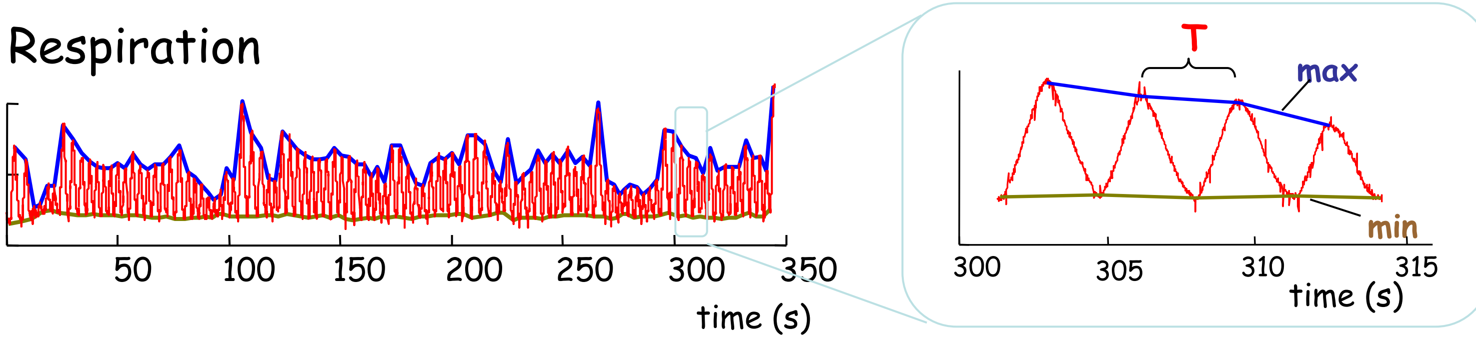


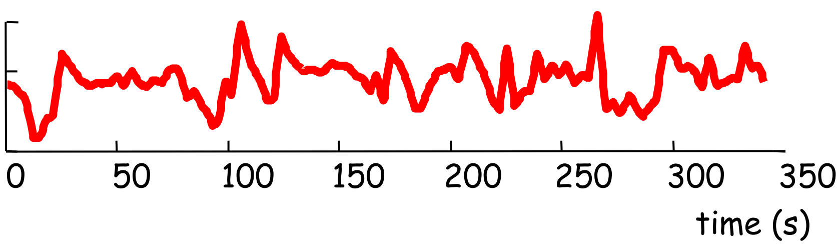

R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, NeuroImage, 31, 1536-1548

# Estimating respiration volume changes

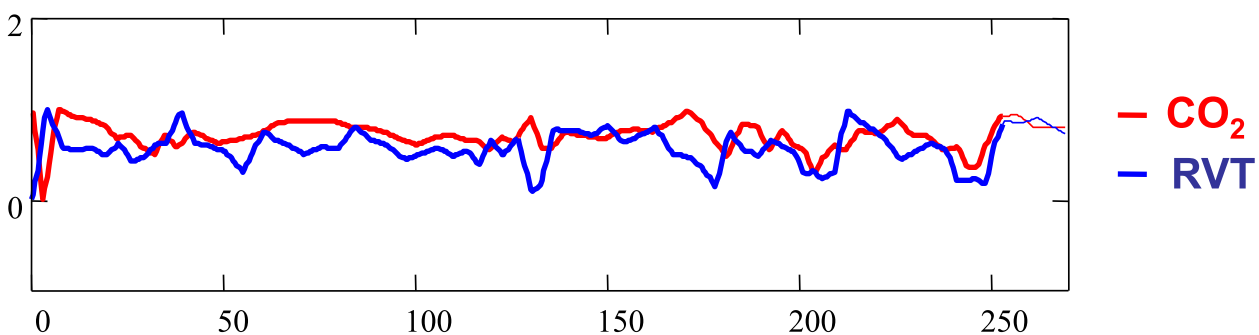
Respiration

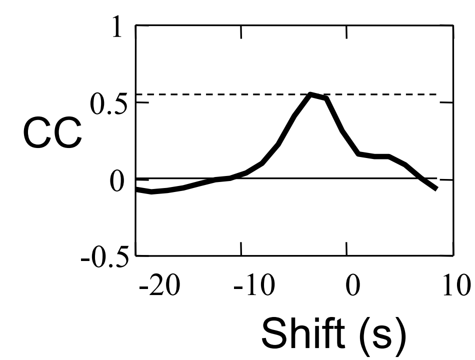



Respiration Volume / Time (**RVT**)




$$\mathbf{RVT} = \frac{\text{max} - \text{min}}{T}$$

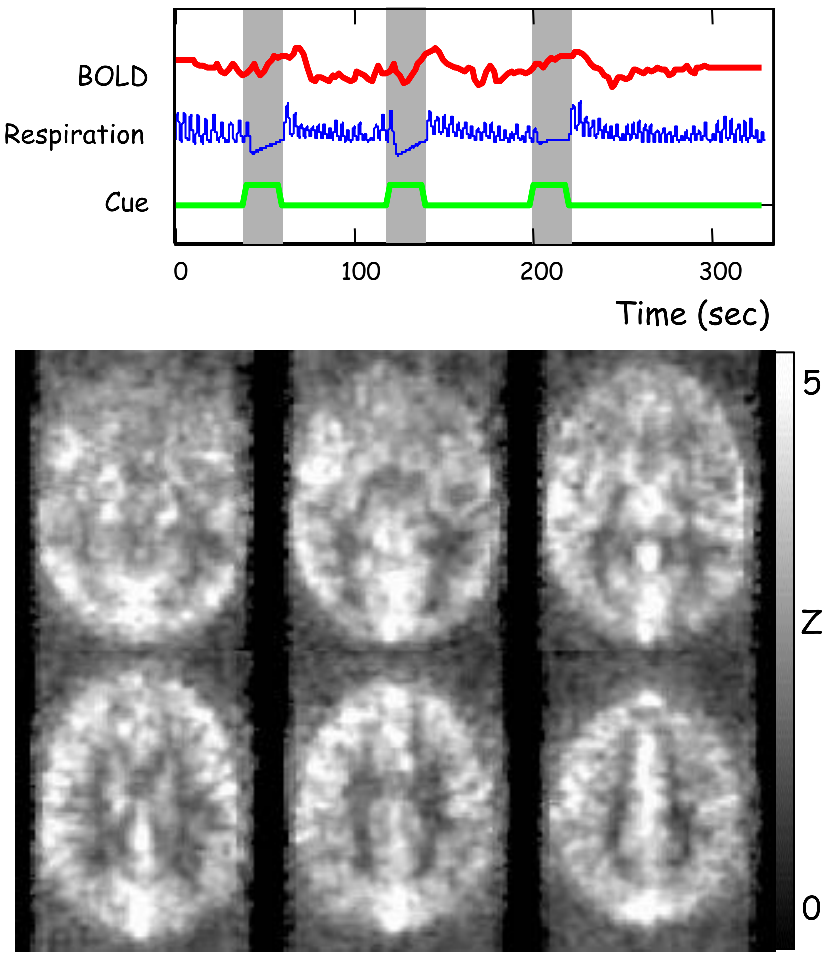



**RVT precedes end tidal $CO_2$ by 5 sec.**

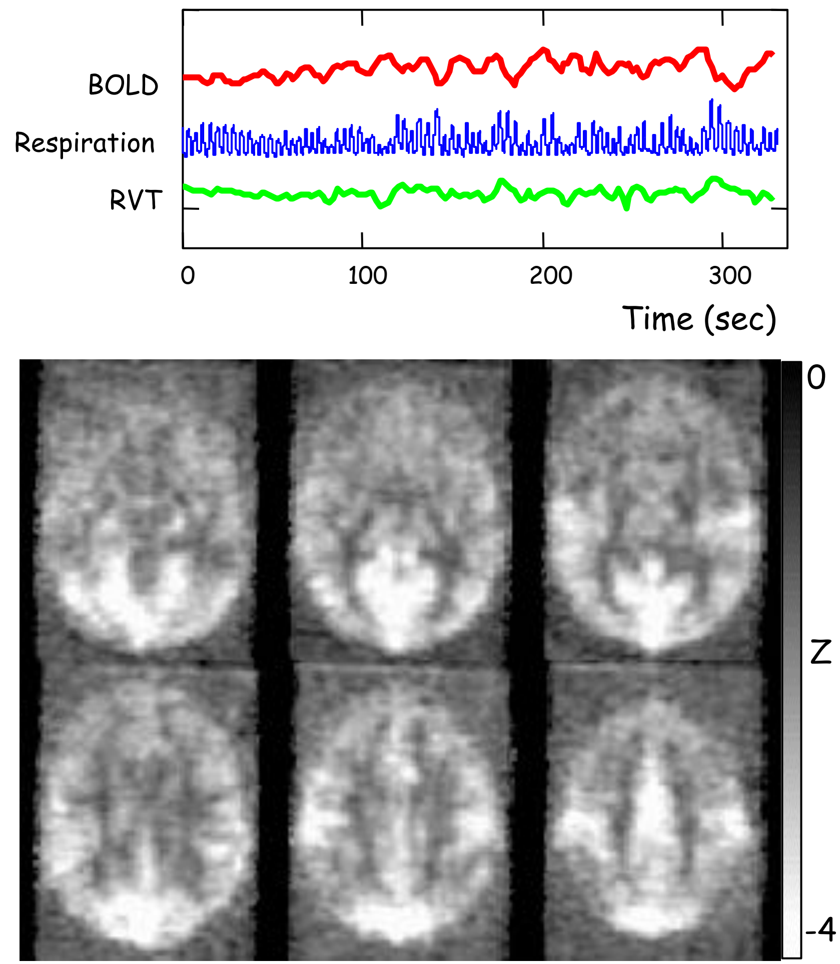
# Respiration induced signal changes

## Breath-holding



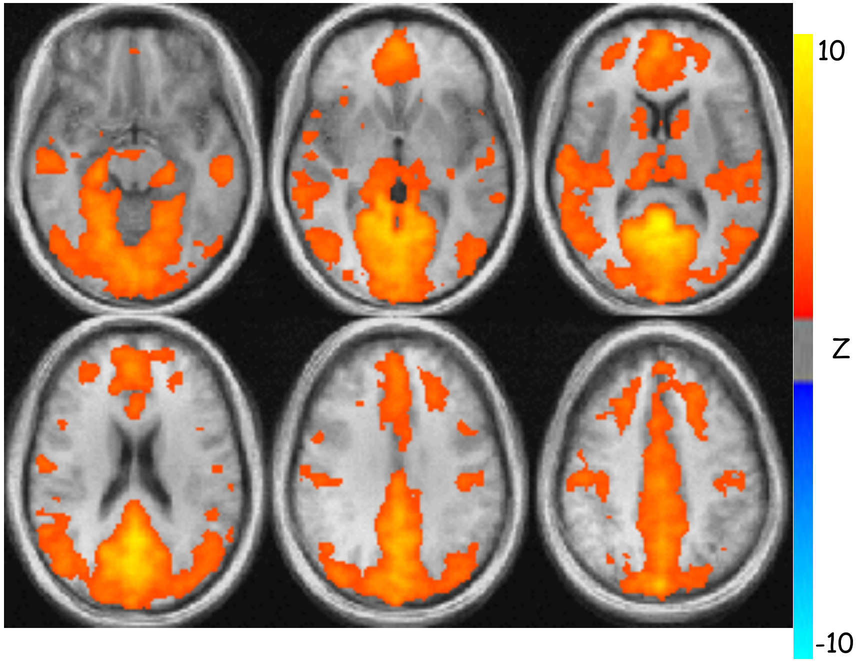

(N=7)

## Rest



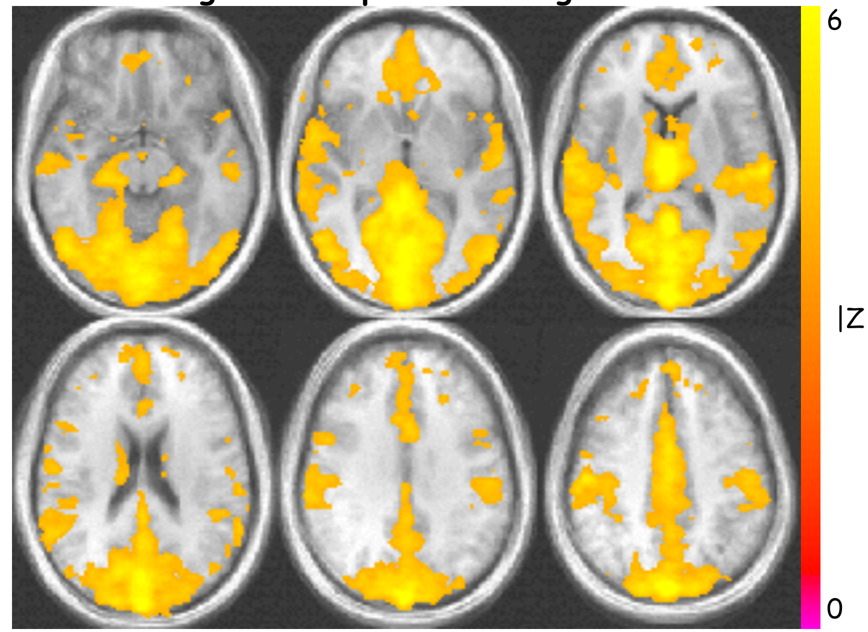

R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, NeuroImage, 31, 1536-1548 (2006)

Resting state correlation with RVT signal

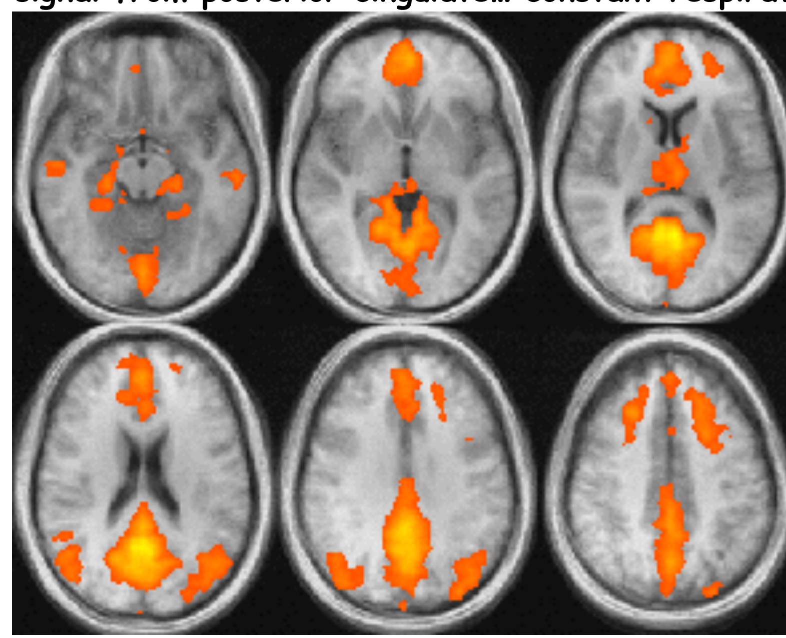



R.M. Birn, J. A. Diamond, M. A. Smith, P. A. Bandettini, NeuroImage, 31, 1536-1548

Resting state correlation with signal from posterior cingulate

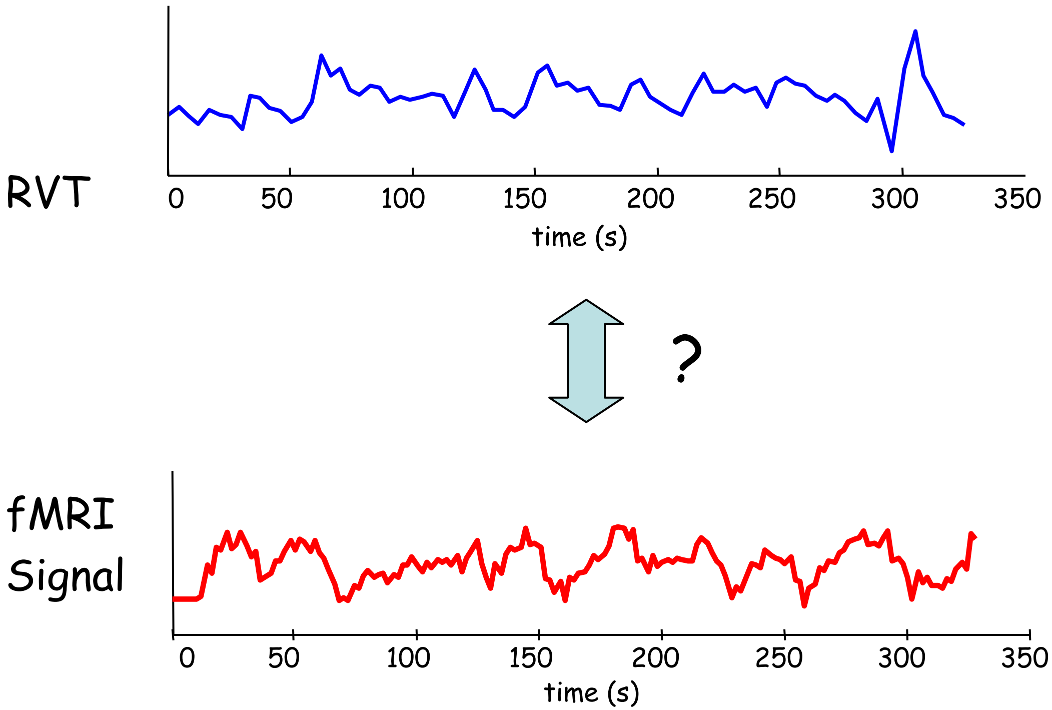



Resting state correlation with signal from posterior cingulate… constant respiration



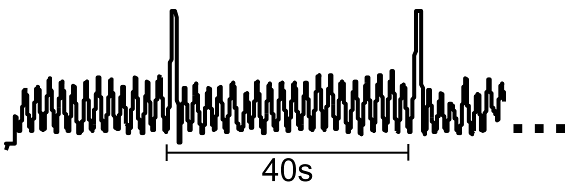
# Respiration Changes vs. BOLD

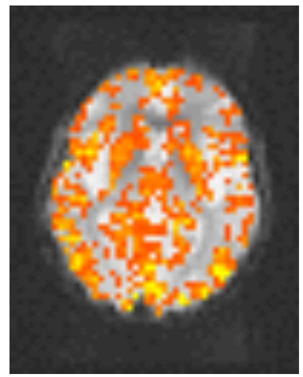
How are the BOLD changes related to respiration variations?

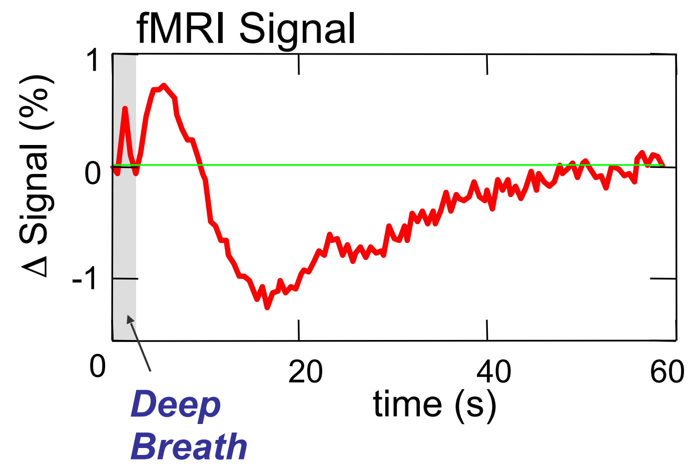


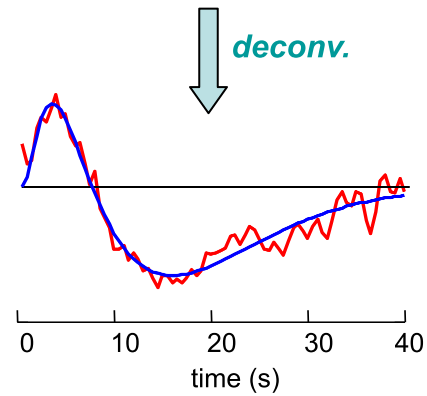
# fMRI response to a single Deep Breath

*Respiration*





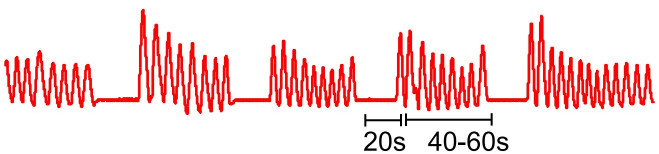

Respiration Response Function (**RRF**)

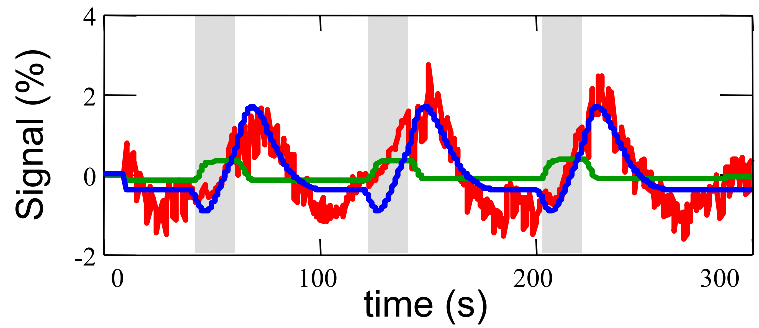
$$RRF(t) = 0.6\, t^{2.1} e^{-\frac{t}{1.6}} - 0.0023\, t^{3.54} e^{-\frac{t}{4.25}}$$

R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, NeuroImage, (in press)

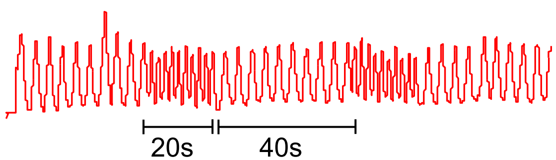
Respiration response function predicts BOLD signal associated with breathing changes better than activation response function.

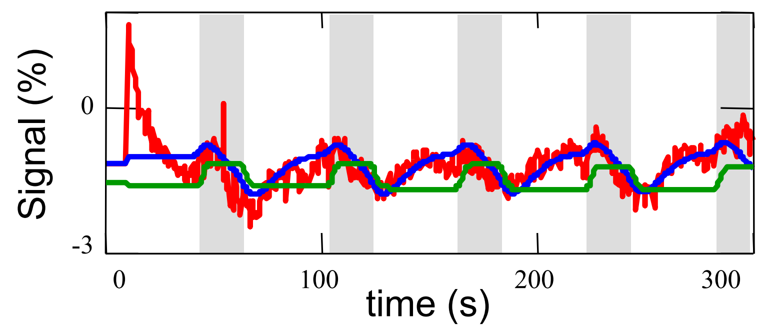
## Breath-holding



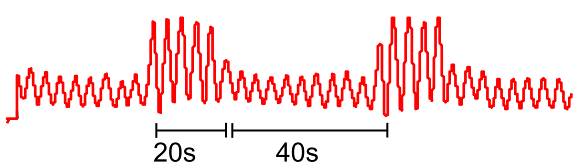



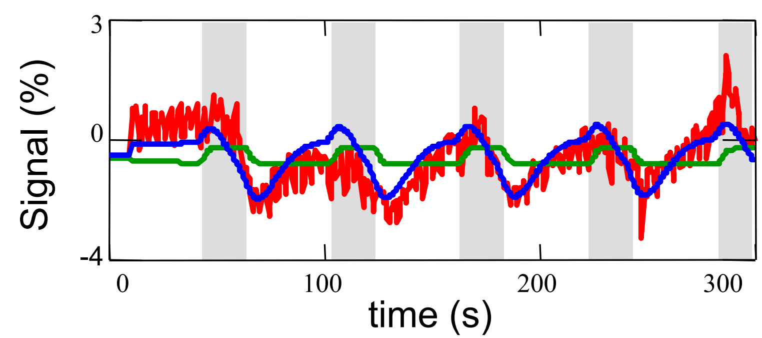

## Rate Changes



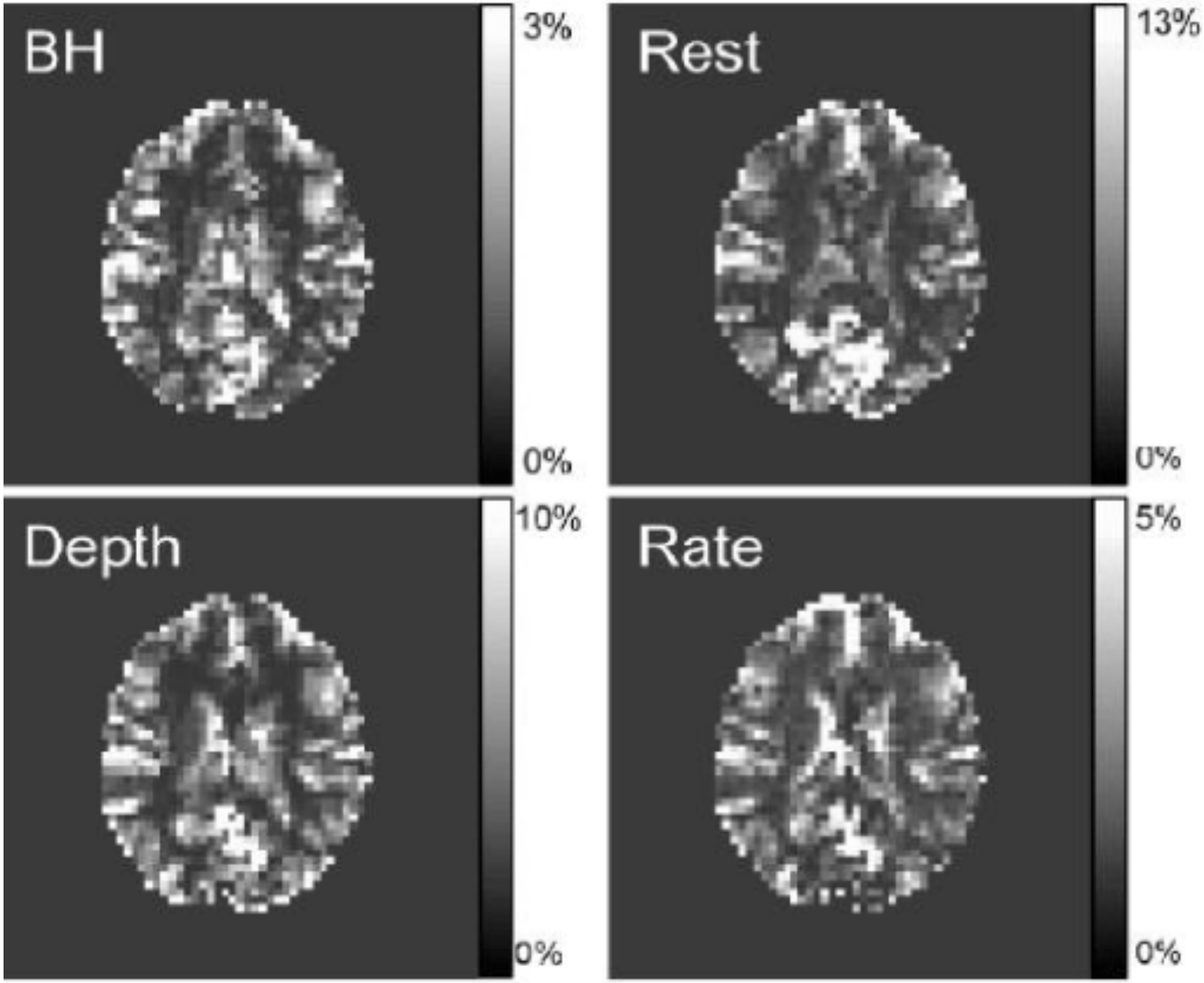




## Depth Changes



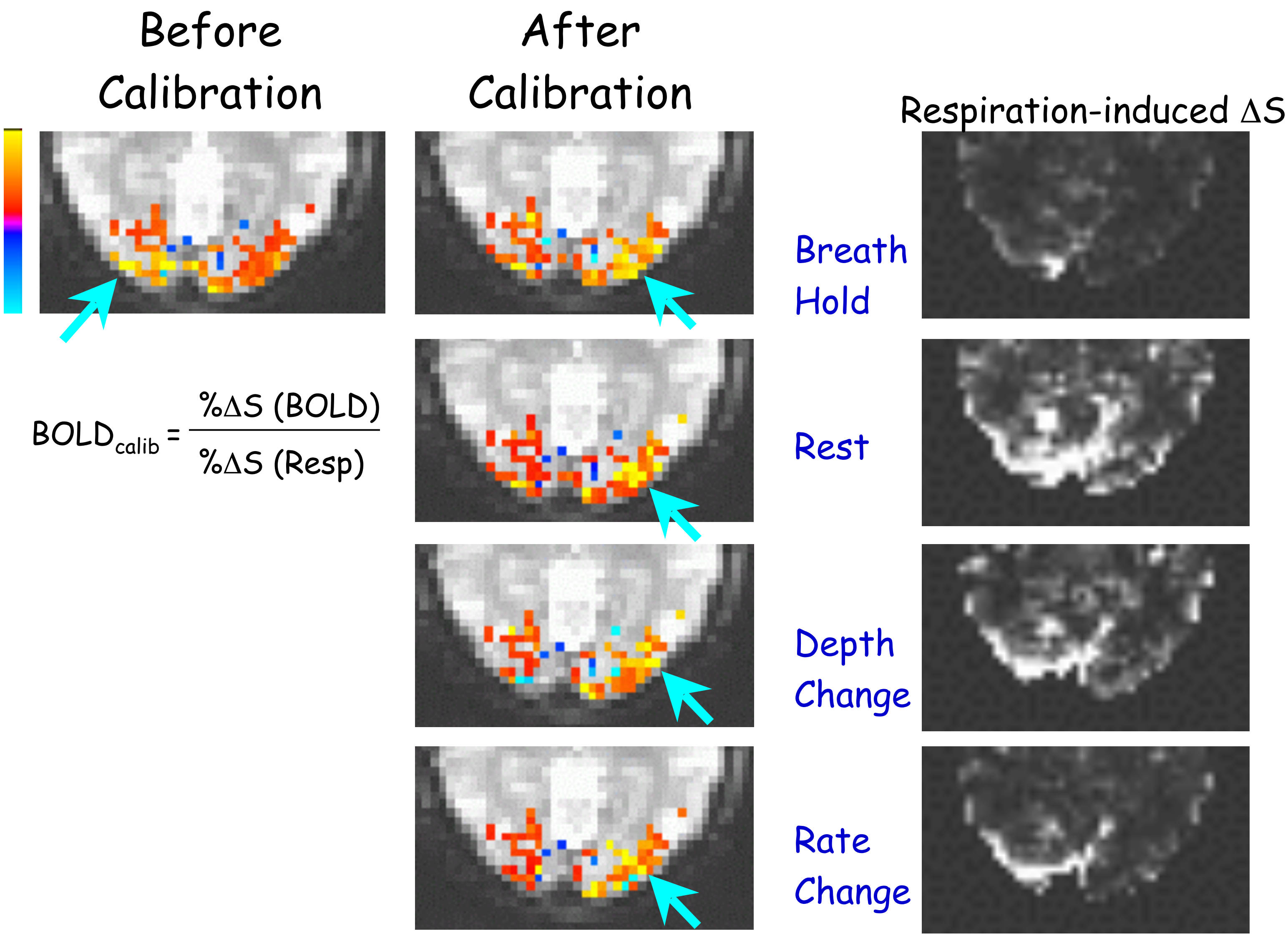




R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, NeuroImage, (in press)




R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, NeuroImage, (in press)

# BOLD magnitude calibration

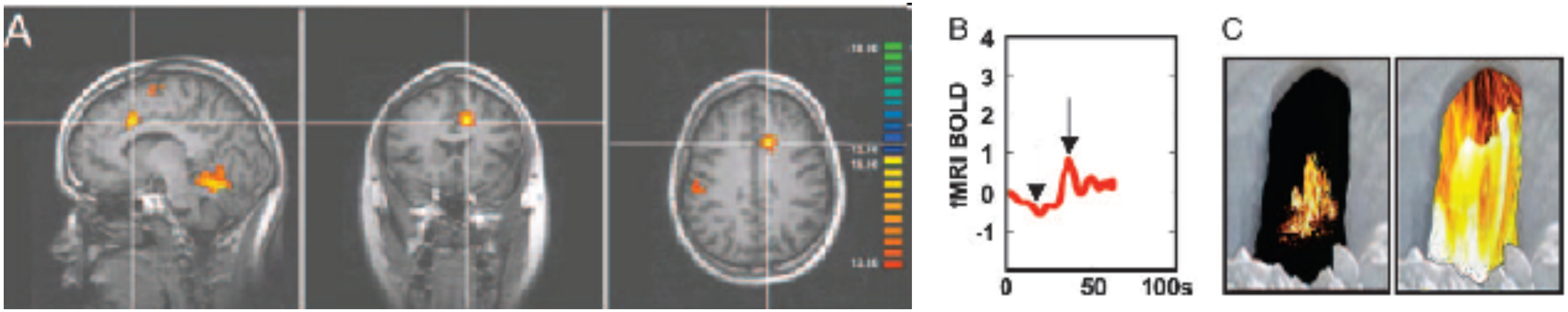


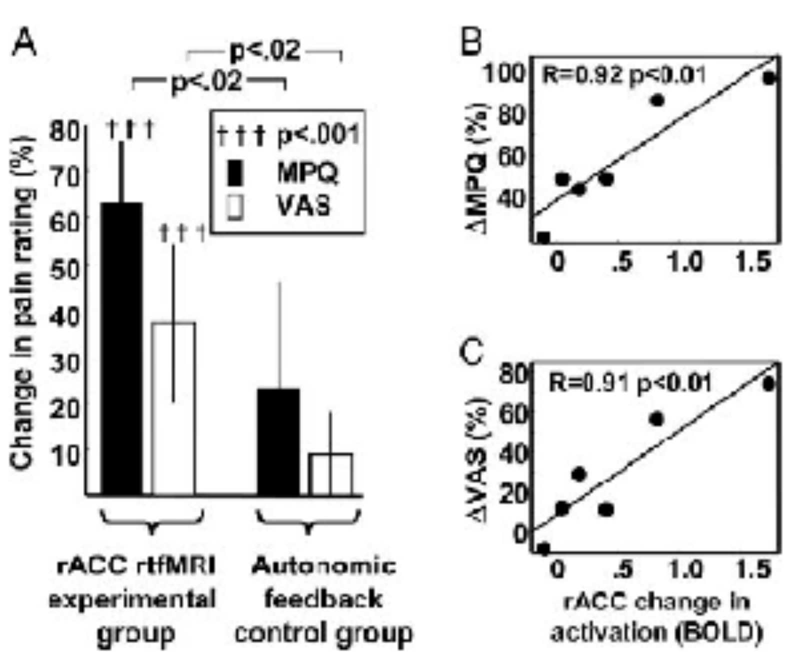

$$BOLD_{calib} = \frac{\%\Delta S\ (BOLD)}{\%\Delta S\ (Resp)}$$

R.M. Birn, M. A. Smith, T. B. Jones, P. A. Bandettini, NeuroImage, (in press)

# Applications

**Real time fMRI feedback from Anterior Cingulate Cortex 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)**

# How most fMRI studies are performed

**MRI parameters:**

1.5T - 3T, 64 x 64 matrix, 3mm x 3mm x 5mm voxel size, whole brain, TR = 2 sec.

**Paradigm:**

Block design or event-related, single or multiple conditions.

**Analysis:**

Motion correct, multi-regression, spatial smoothing and spatial normalization, standard classical statistical tests, multi-subject averaging.

**Hypothesis:**

A region or network of regions show modulation with a task. This modulation is unique to the task and/or population.

# How fMRI might be be performed

**MRI parameters:**

3T - 11.7T, 256 x 256 matrix, 0.5 x 0.5 x 0.5 voxel size, whole brain TR = 1sec or select slab TR = 100 ms.

**Paradigm:**

Natural, continuous, fMRI-adaptation, or no stimuli/task. Simultaneous multi-modal, or multiple contrast measurements.

**Analysis:**

Motion correct, dynamic Bo-field correction, no spatial or temporal smoothing, machine learning algorithms, pattern classification, hemodynamic parameter assessment - calibration, correlation with behavior.

**Hypothesis:**

Similar to previous but using the high resolution patterns, fluctuations, dynamics, and contrast mechanisms that we are still figuring out how to interpret and extract.

# What fMRI Might Do

Complementary use for clinical use

- usage of clinical research findings for more effective diagnoses, prediction, characterization, and/or intervention

Clinical treatment and assessment of therapy

- better understanding of the specific pathology mechanism
- drug effect assessment
- assessment of therapy progress, biofeedback
- epileptic foci mapping
- neurovascular physiology assessment

Non clinical uses

- lie detection
- prediction of behavior tendencies
- brain/computer interface

## Section on Functional Imaging Methods

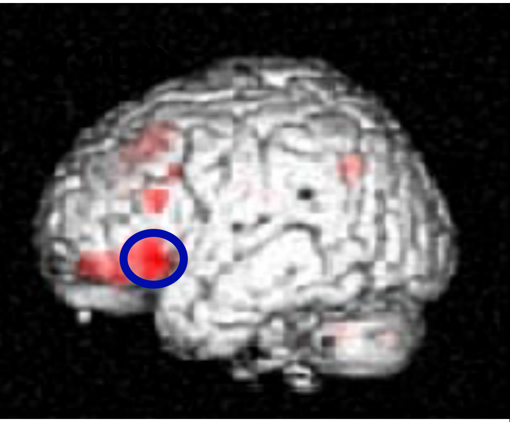
| | |
|---|---|
| Rasmus Birn | staff scientist |
| Anthony Boemio | post doc |
| Justin Edmands | system admin |
| Dan Handwerker | post doc |
| Tyler Jones | post bac IRTA |
| Youn Kim | post bac IRTA |
| Niko Kriegeskorte | post doc |
| Marieke Mur | student IRTA |
| Kevin Murphy | post doc |
| Alissa Par | post bac IRTA |
| Vikas Patel | system admin |
| Dorian Van Tassell | program assistant |

| | |
|---|---|
| Javier Castillo-Gonzalez | Summer Student |
| Jason Diamond | Howard Hughes Fellow |
| Thomas Gallo | Summer Student |
| Hauke Heekeren | post doc |
| David Knight | post doc |
| Ilana Levy | post bac IRTA |
| Marta Maieron | visiting fellow |
| Hanh Nguyen | post bac IRTA |
| Natalia Petridou | student IRTA |
| Douglass Ruff | post bac IRTA |
| Monica Smith | post bac IRTA |
| August Tuan | post bac IRTA |

## Functional MRI Facility

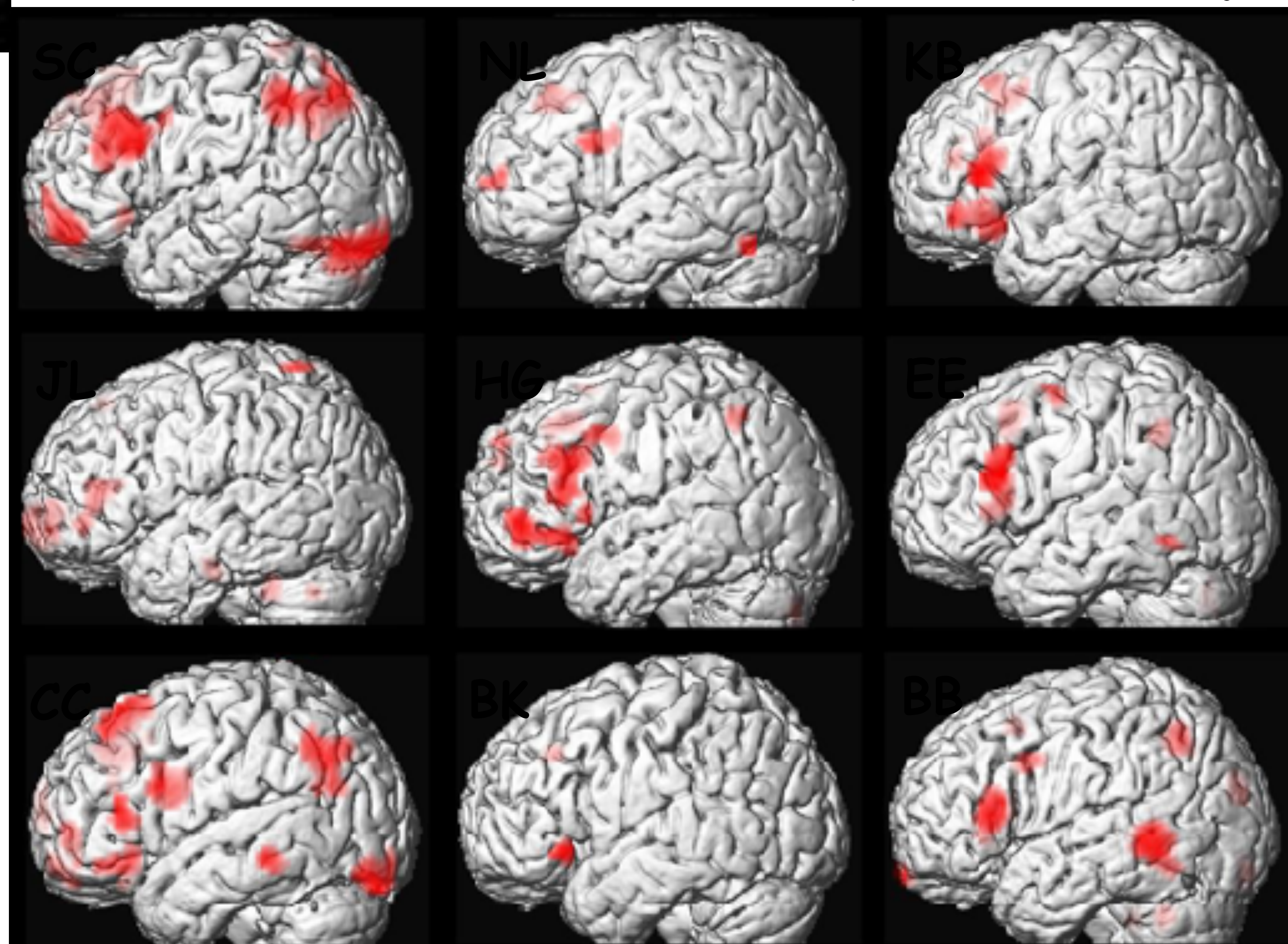
| | |
|---|---|
| Jerzy Bodurka | staff scientist |
| Ellen Condon | technologist |
| Janet Ebron | technologist |
| Kenny Kan | technologist |
| Kay Kuhns | admin. lab manager |
| Wenming Luh | staff scientist |
| Sean Marrett | staff scientist |
| Marcela Montequin | technologist |
| Sandra Moore | technologist |
| Sahra Omar | technologist |
| Alda Ottley | technologist |
| Paula Rowser | technologist |
| Adam Thomas | system admin |

| | |
|---|---|
| Karen Bove-Bettis | technologist |
| James Hoske | technologist |

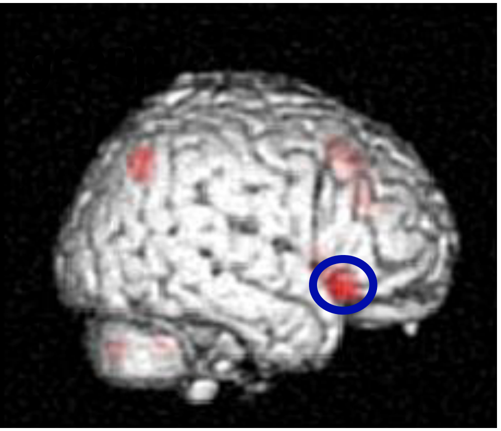


# Individual Differences in Brain Activations During Episodic Retrieval
## Miller et al., 2002

Individual activations from the left hemisphere of the 9 subjects

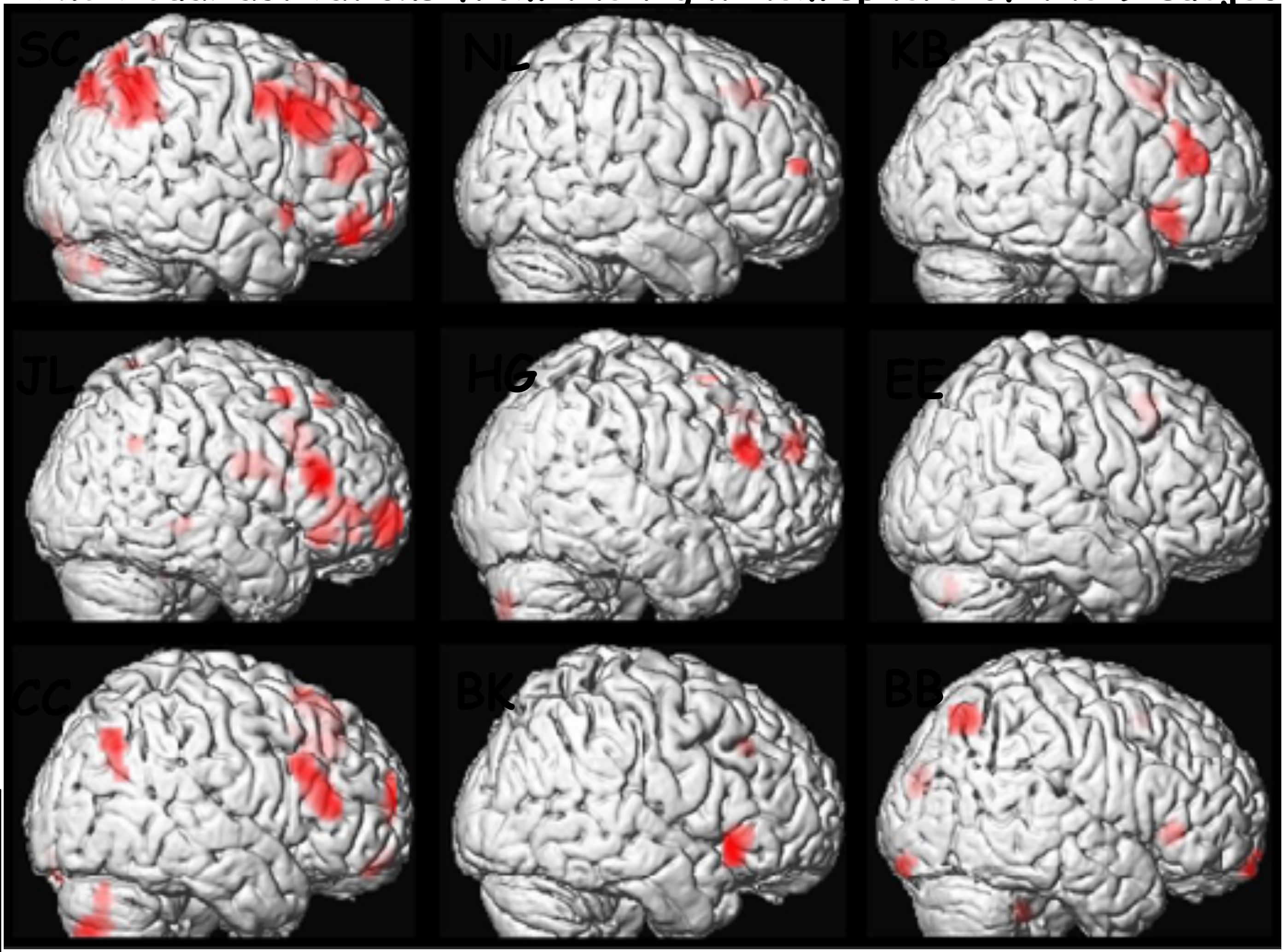



Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University



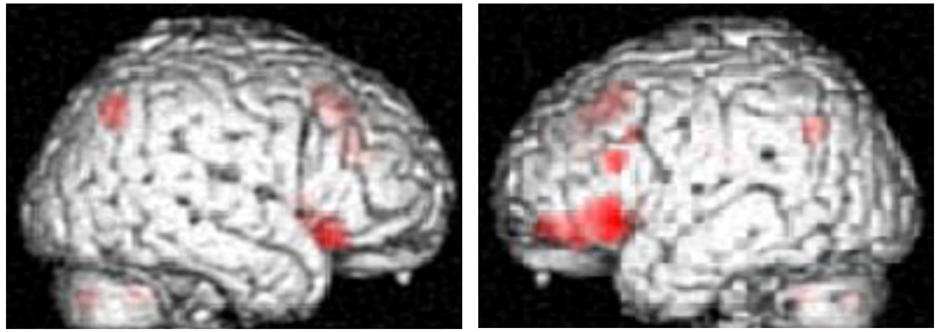
# Individual Differences in Brain Activations During Episodic Retrieval
# Miller et al., 2002

Individual activations from the right hemisphere of the 9 subjects

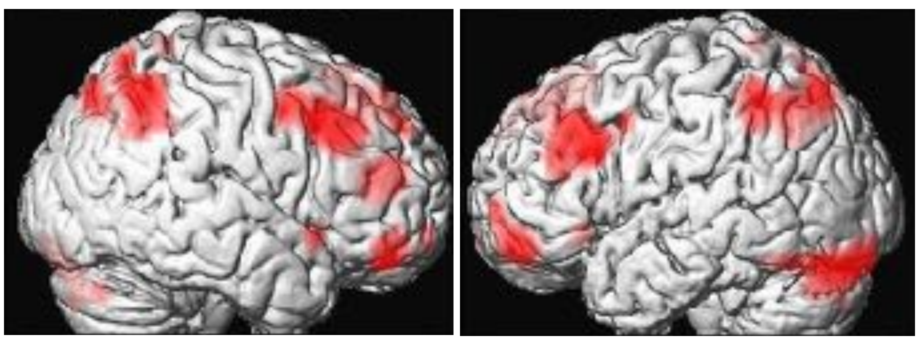



Courtesy, Mike Miler, UC Santa Barbara and Jack Van Horn, fMRI Data Center, Dartmouth University

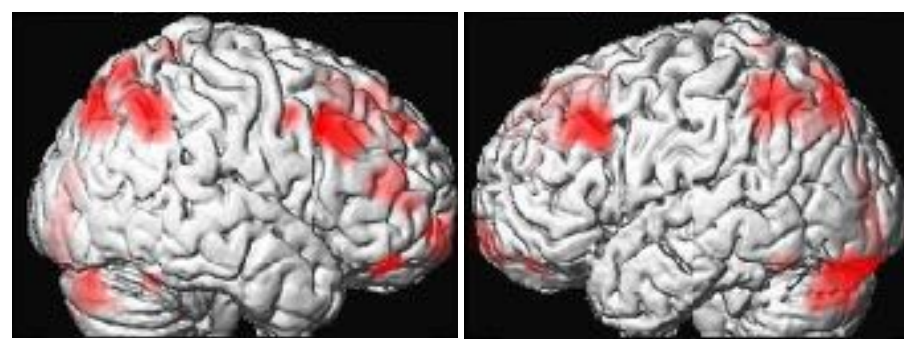
# These individual patterns of activations are stable over time



Group Analysis of Episodic Retrieval



Subject SC



Subject SC 6 months later

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