Contentious Issues in fMRI

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

FMRIF fmrif.nimh.nih.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NATIONAL INSTITUTES OF HEALTH

NIMH National Institute of Mental Health

FIM fim.nimh.nih.gov

- The Undershoots
- Negative signal changes
- Relationship to neuronal activity
- Linearity
- Temporal precision
- fMRI contrast mechanisms and sequences
- Analysis circularity issue
- How to handle high resolution
- Basis of the decoding signal
- How to best process/interpret resting state

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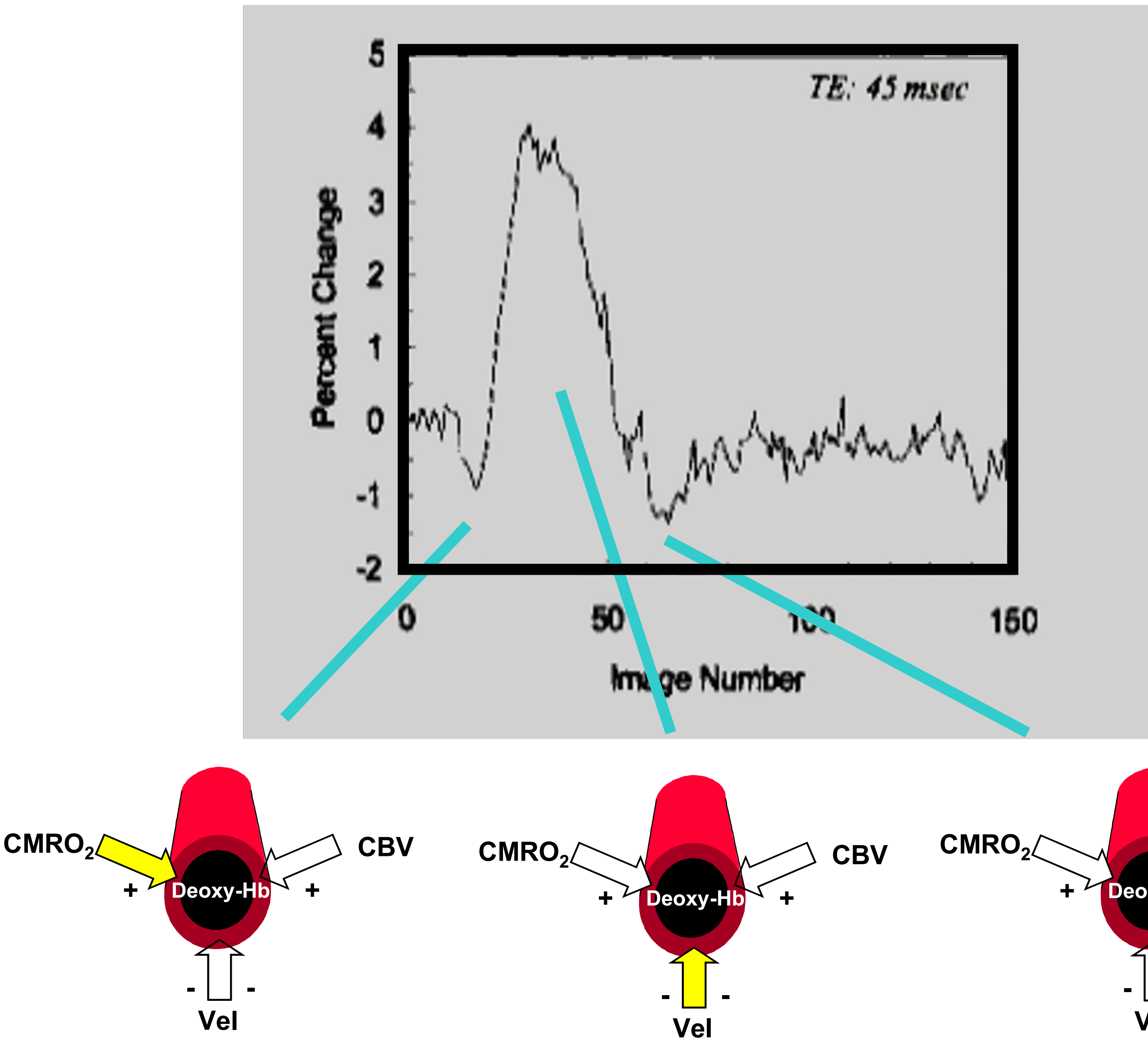
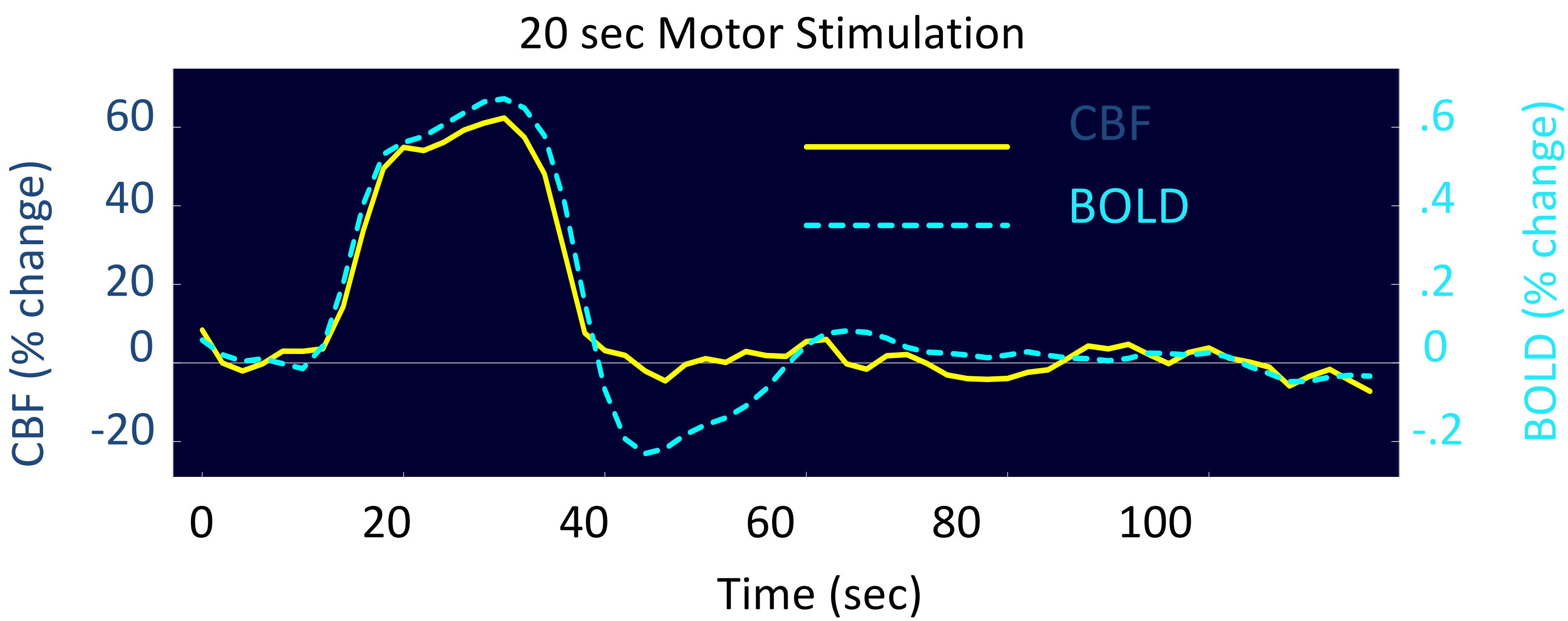
The Undershoots



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

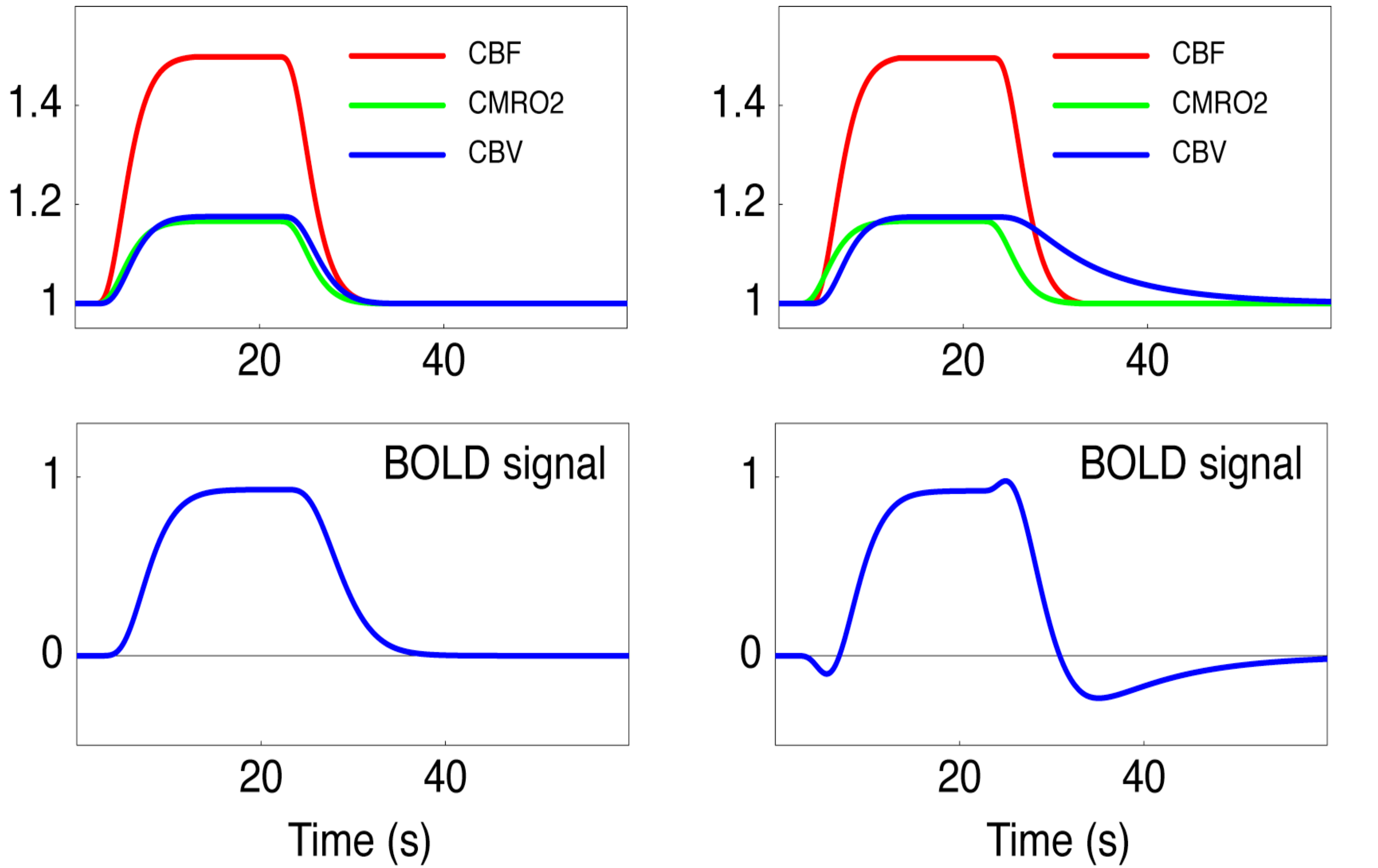
Courtesy of Arno Villringer

BOLD post-stimulus undershoot



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

BOLD Signal Dynamics



Courtesy Rick Buxton

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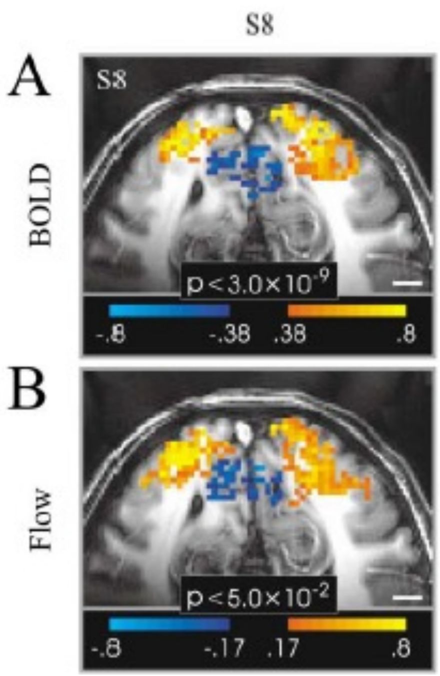
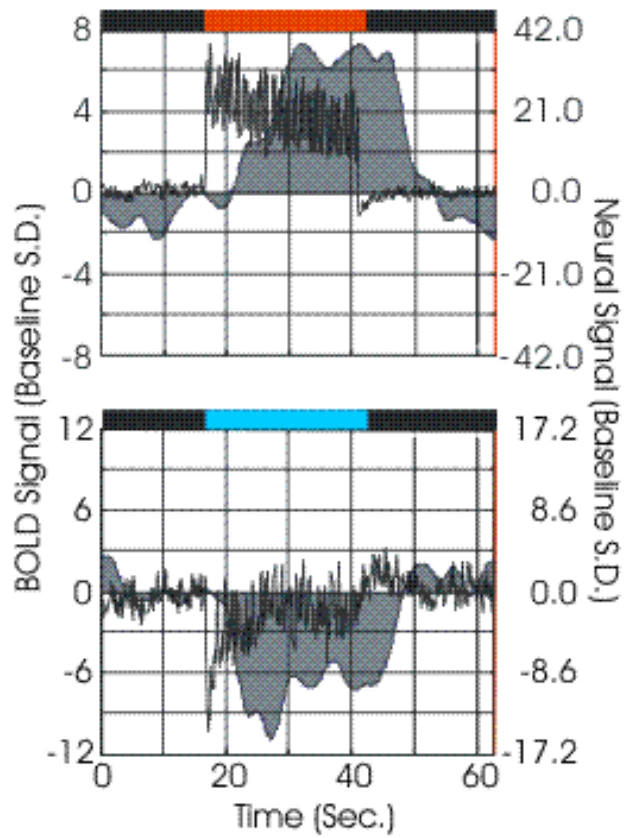
Negative Signal Change

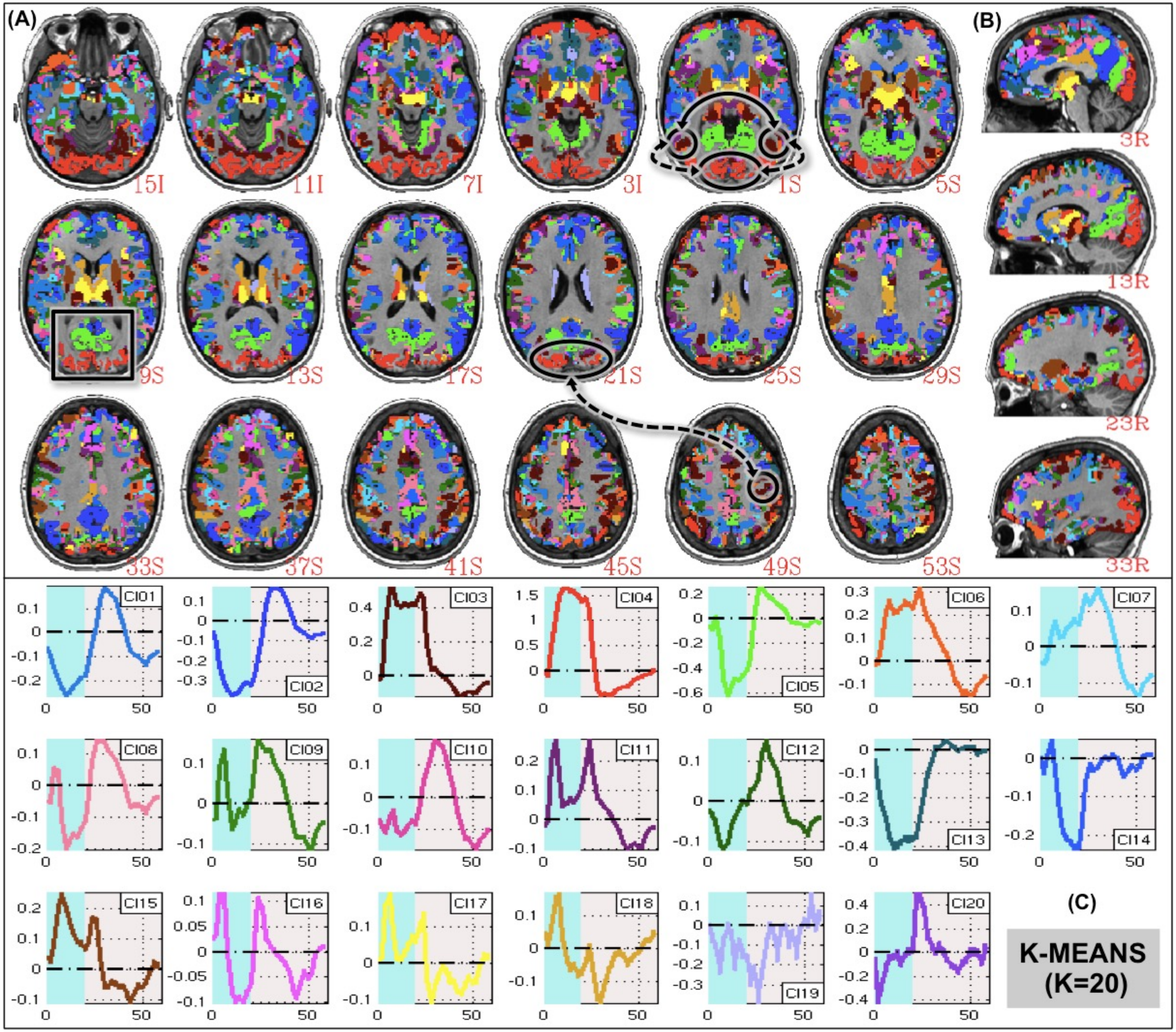


Neg. BOLD

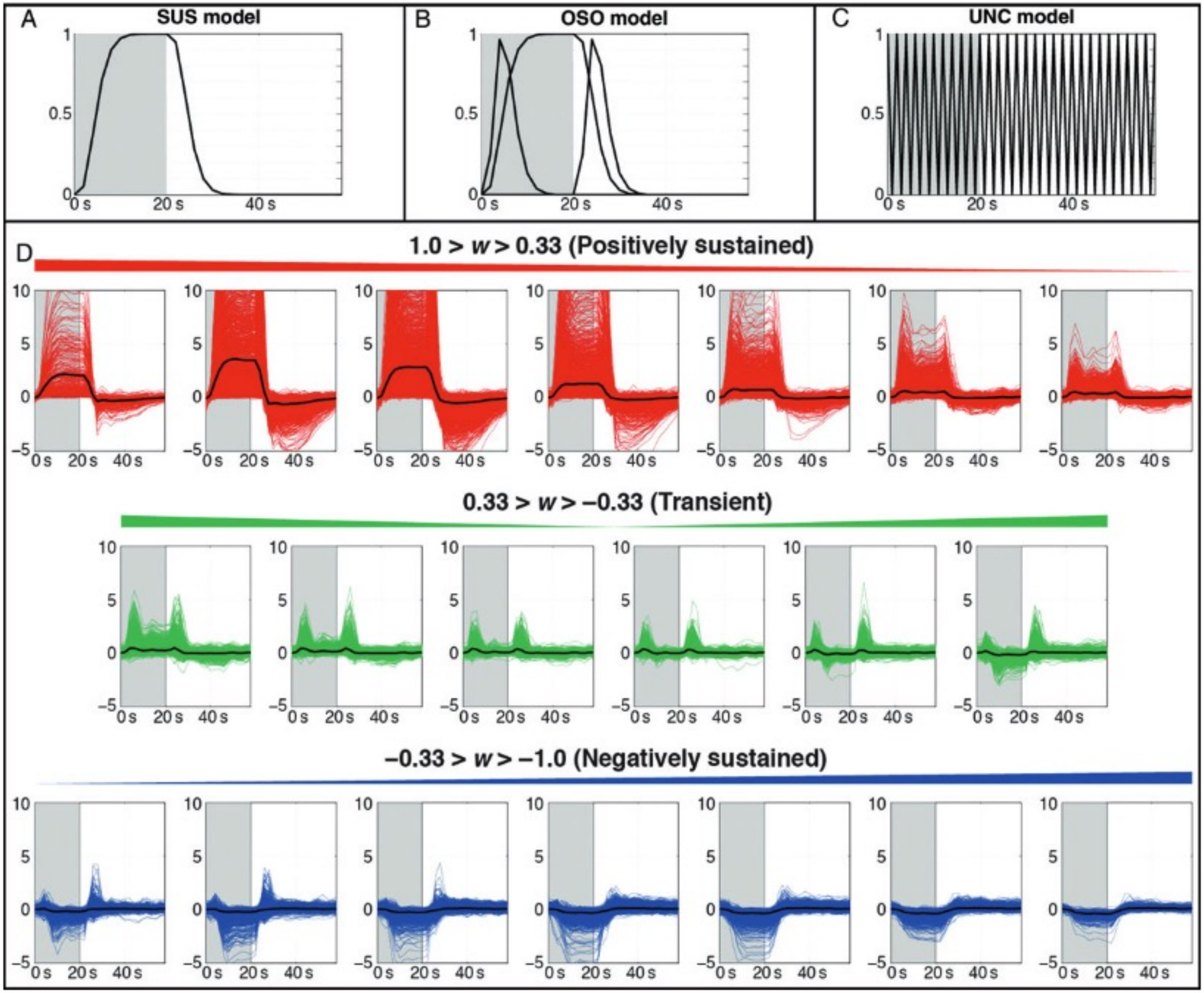


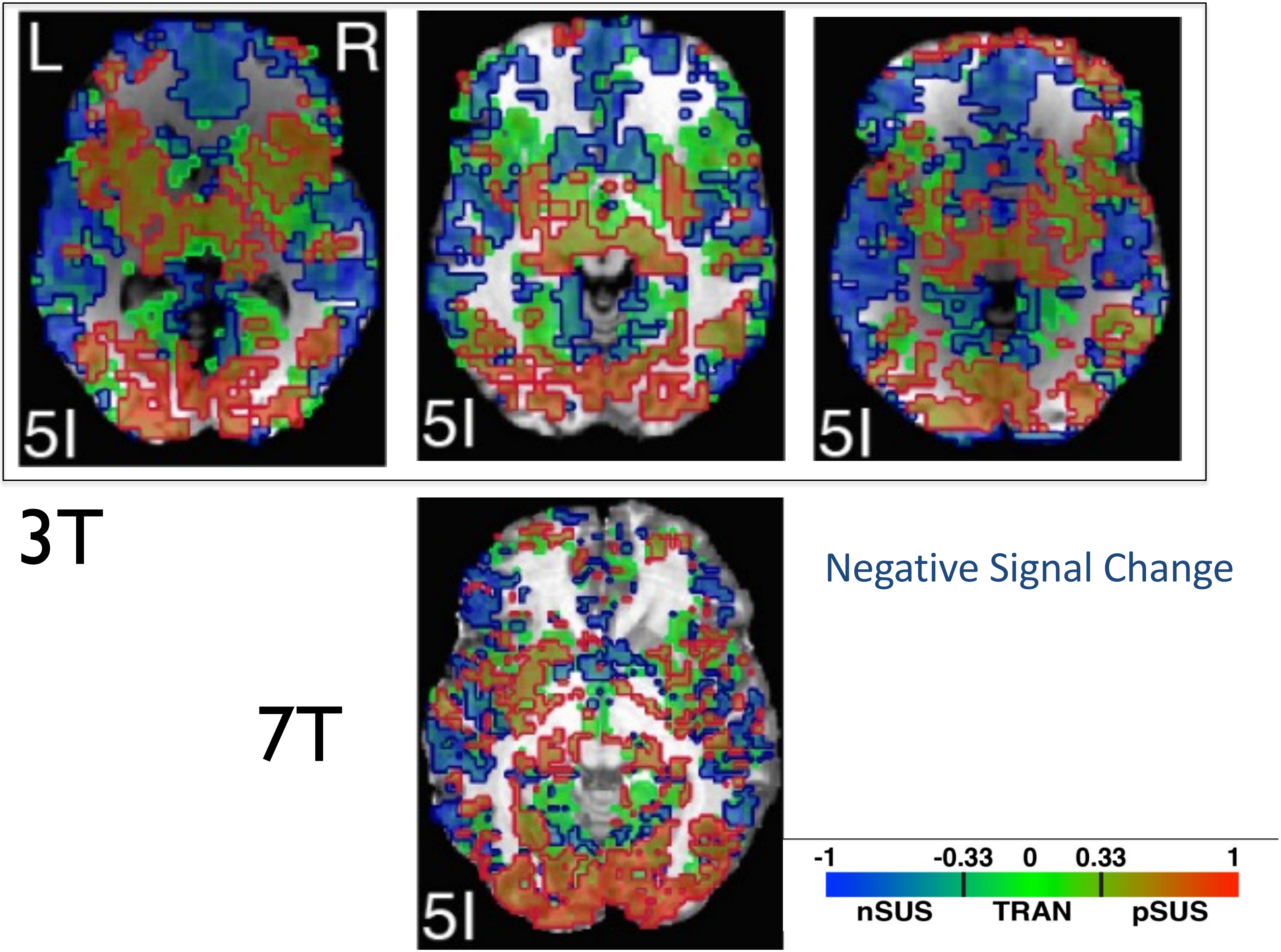
Schmuel et al. (2002) Neuron, Vol. 36, 1195–1210

Negative Signal Change



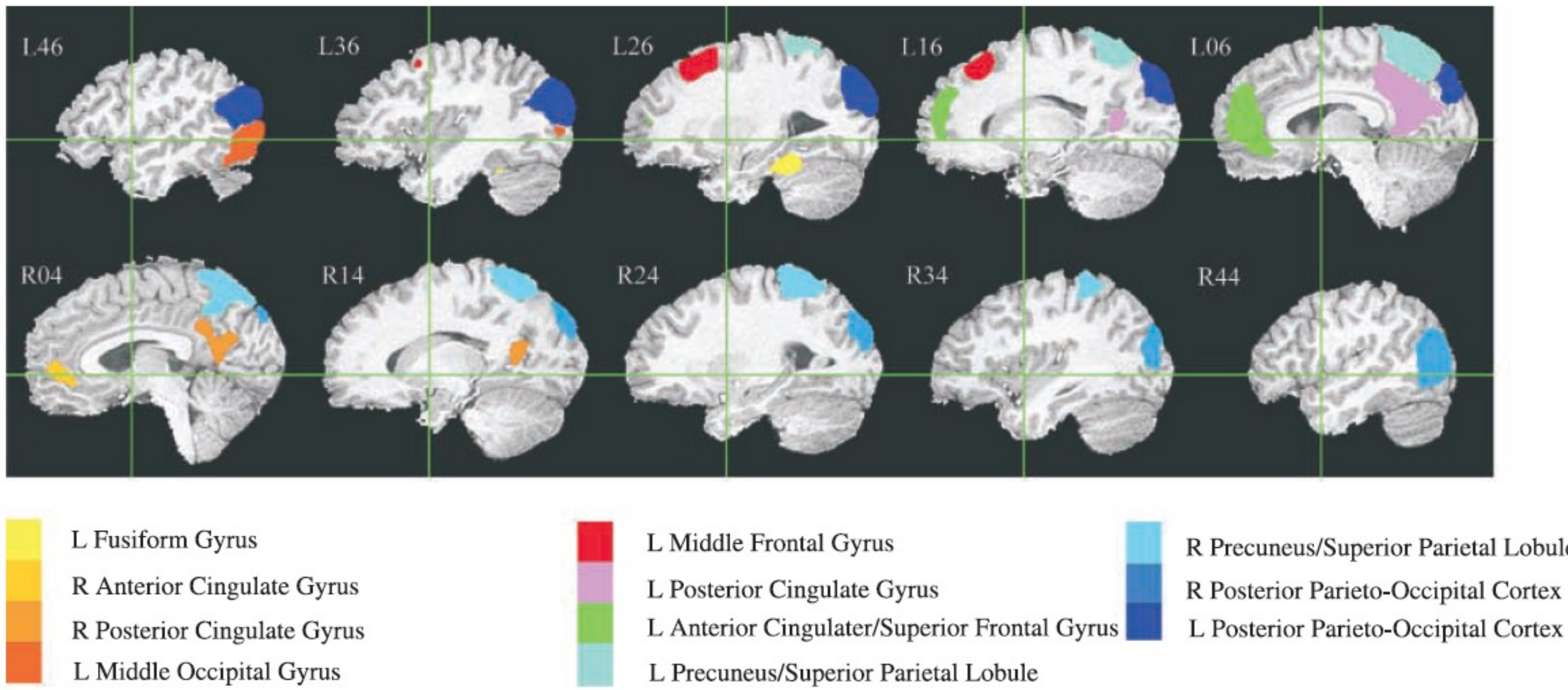
Negative Signal Change




L
R
5I
5I
5I
3T
7T
5I
Negative Signal Change
-1
-0.33
0
0.33
1
nSUS
TRAN
pSUS

Negative Signal Change

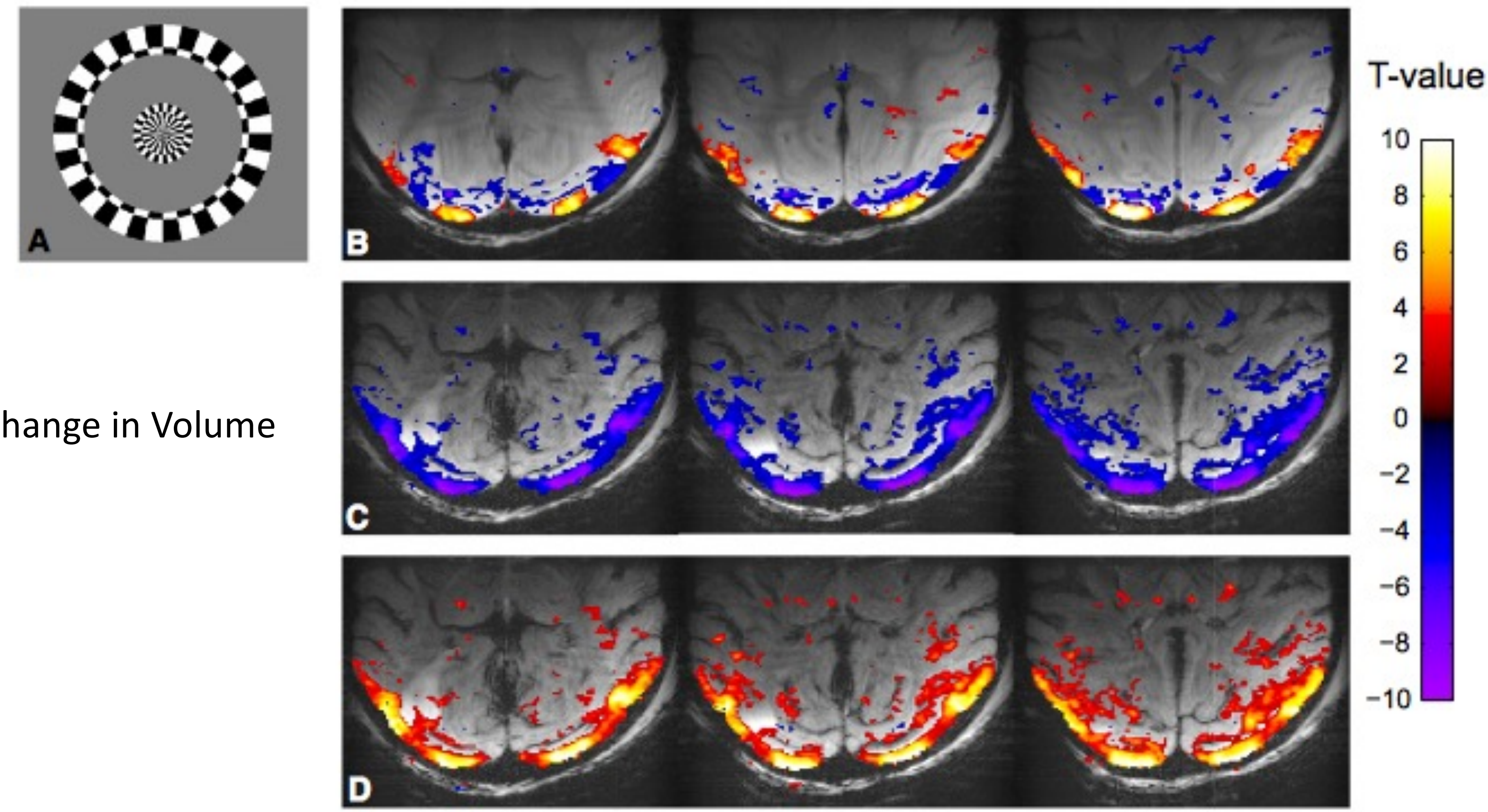
Regions showing negative signal changes during cognitive tasks



McKiernan, et al (2003), Journ. of Cog. Neurosci. 15 (3), 394-408

Change in BOLD

Change in Volume



J. Goense, et al. Neuron, 76, 629-639 (2012)

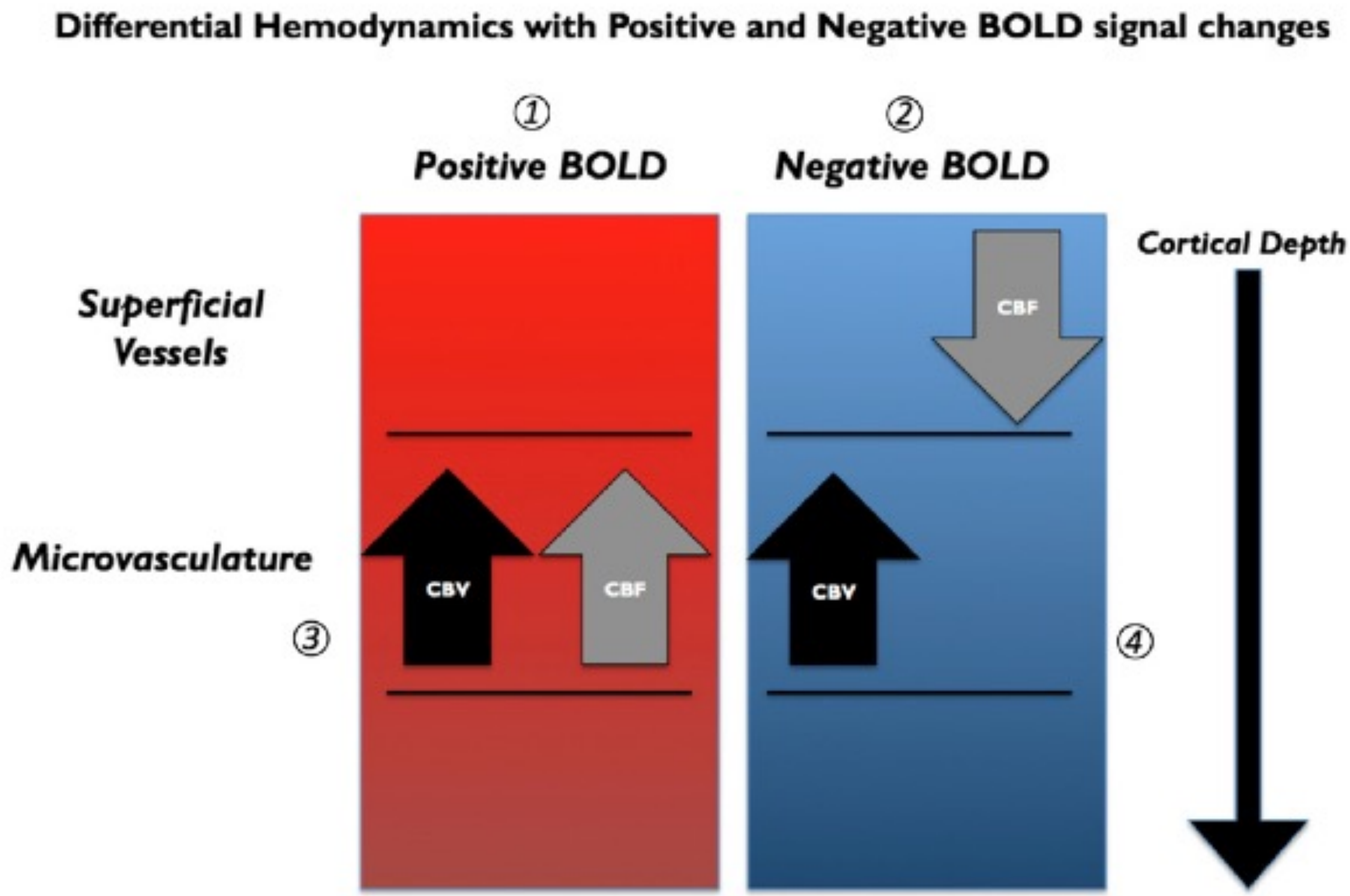


Figure 1. Summary of Conclusions
(1) Regions showing positive BOLD responses had, as expected, increases in CBV and CBF. (2) Adjacent regions that showed a negative BOLD response corresponded to a decrease in CBF *yet an increase in CBV*. (3) With regard to layer specificity, for positive BOLD responses, CBF and CBV increased in the center layers. (4) *For negative BOLD responses, CBF decreased near the surface but CBV increased in the center layers*. So, not only do the underlying hemodynamic mechanisms differ between positive and negative signal changes, but they apparently also vary across layers.

P. A. Bandettini, Neuron, 76, 468-469 (2012)

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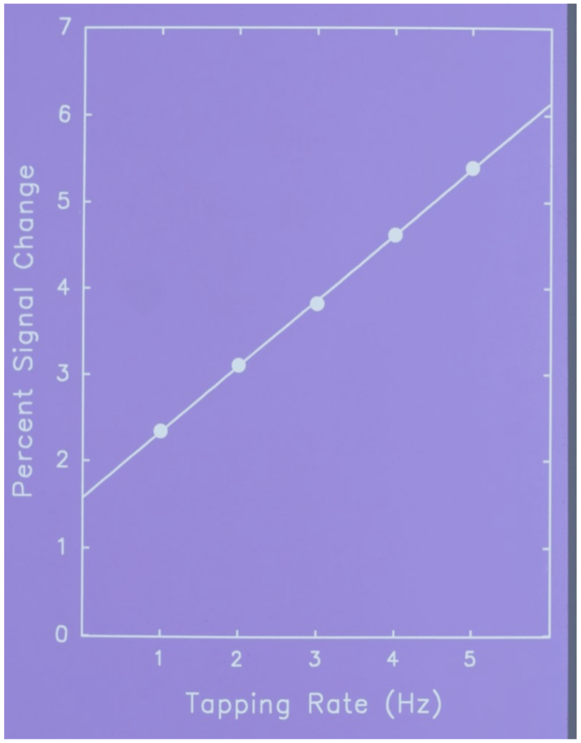
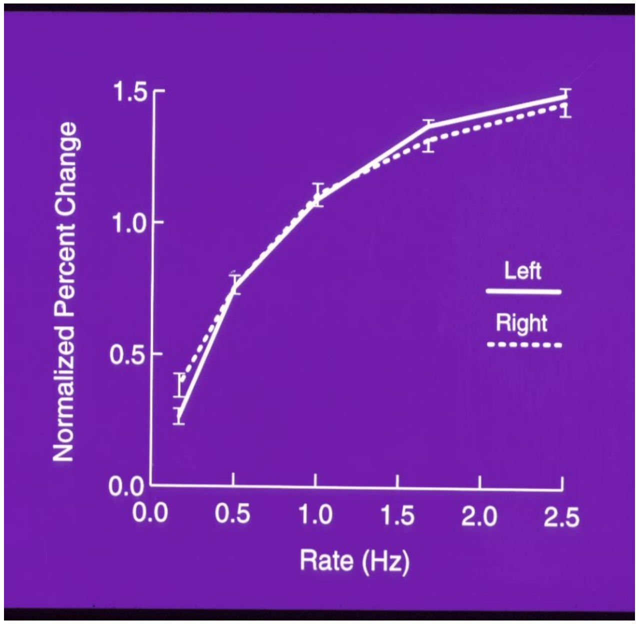
Parametric Manipulation

Motor Cortex



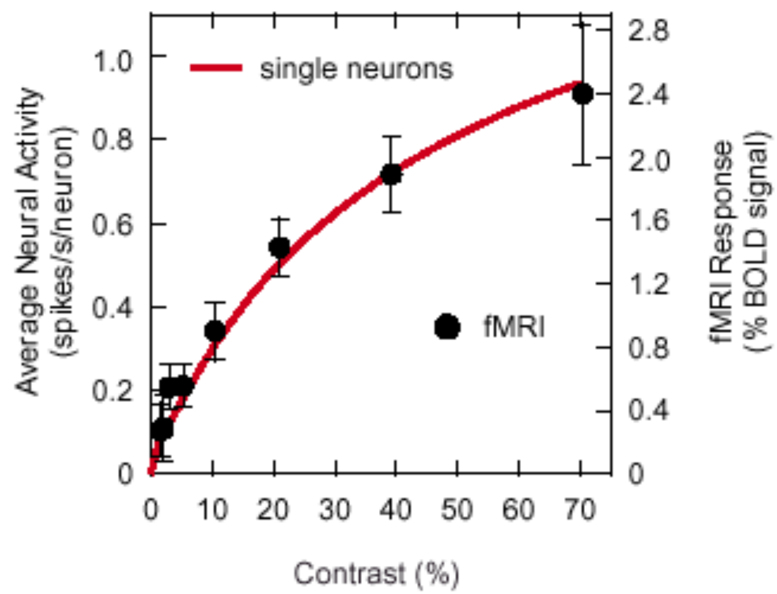
S. M. Rao et al, (1996) "Relationship between finger movement rate and functional magnetic resonance signal change in human primary motor cortex." *J. Cereb. Blood Flow and Met.* 16, 1250-1254.

Auditory Cortex



J. R. Binder, et al, (1994). "Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex." *Cogn. Brain Res.* 2, 31-38

fMRI responses in human V1 are proportional to average firing rates in monkey V1



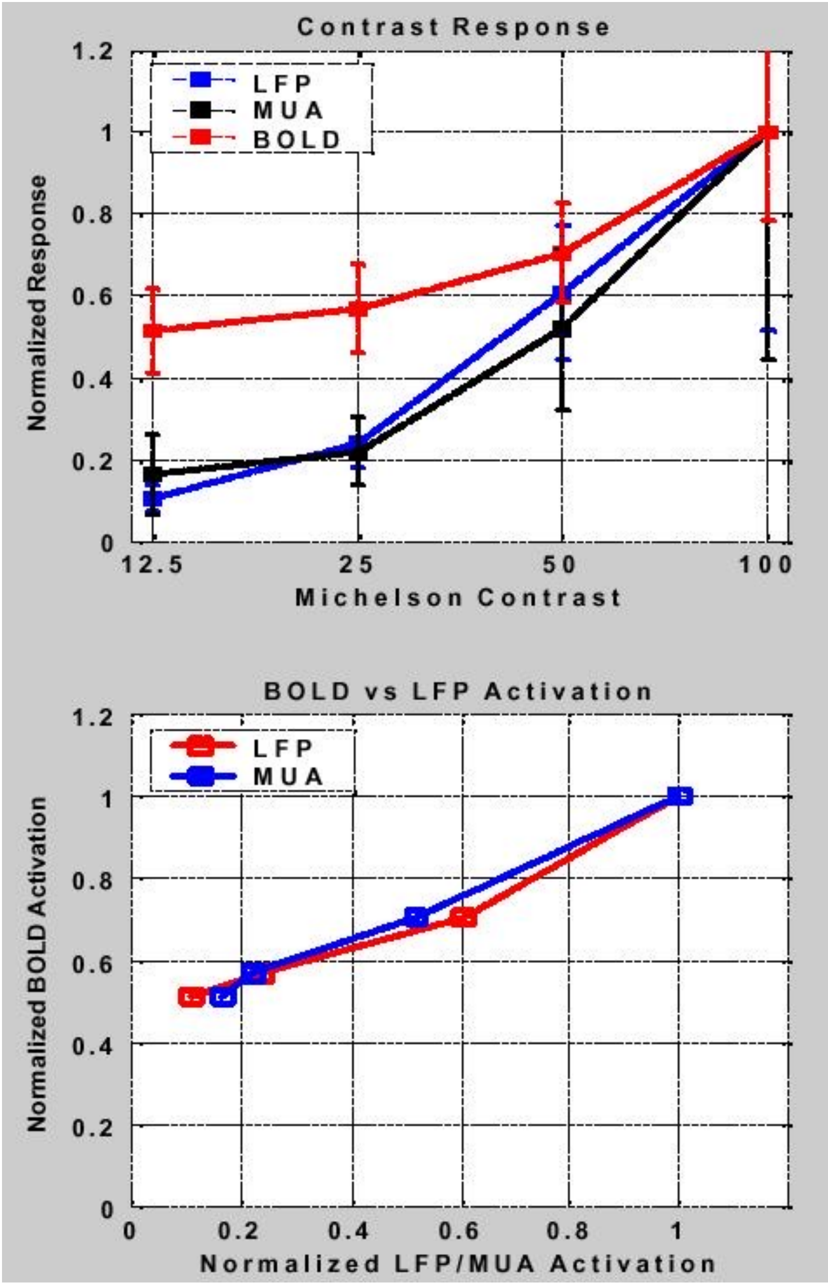
Heeger, D. J., Huk, A. C., Geisler, W. S., and Albrecht, D. G. 2000.Spikes versus BOLD: What does neuroimaging tell us about neuronal activity? *Nat. Neurosci.* **3:** 631–633.

0.4 spikes/sec -> 1% BOLD

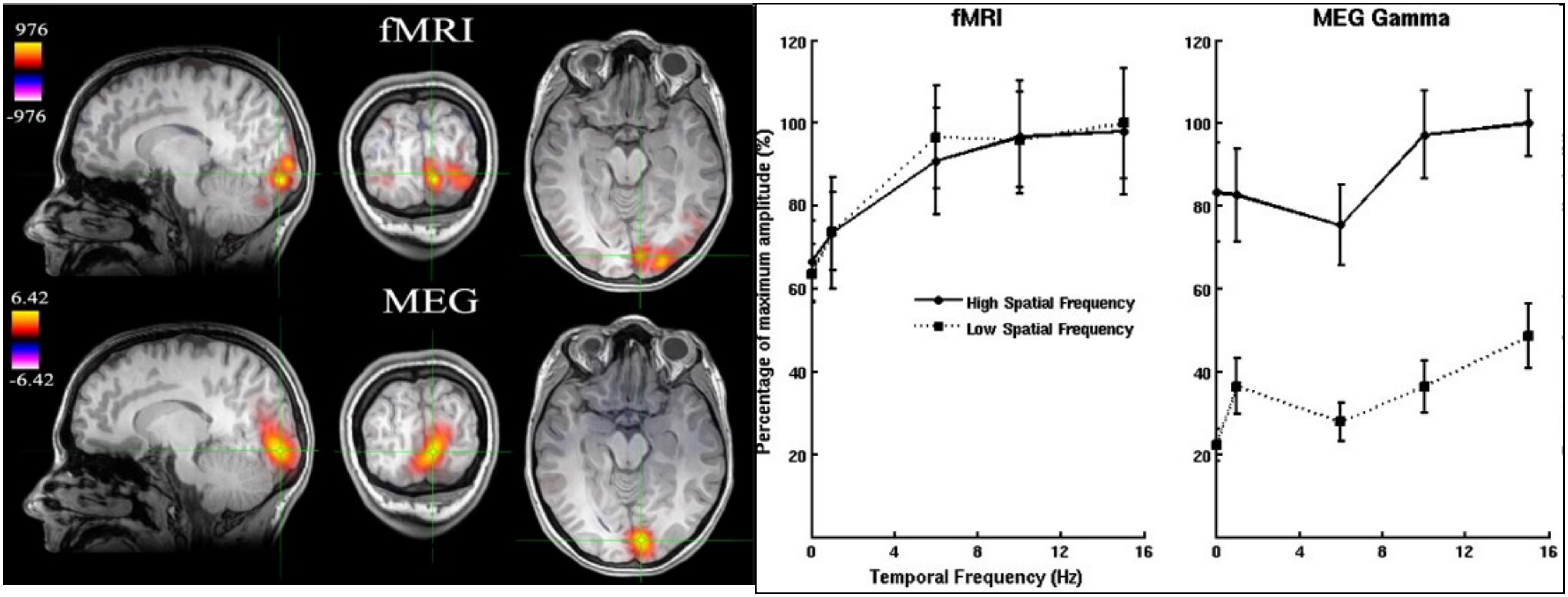
Rees, G., Friston, K., and Koch, C. 2000. A direct quantitative relationship between the functional properties of human and macaque V5. *Nat. Neurosci.* **3:** 716–723.

9 spikes/sec -> 1% BOLD

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



Relationship to Neuronal Activity



Muthukumaraswamy, S. D., Singh, K. D. (2008)
NeuroImage 40 (4), pp. 1552-1560

Vol 457|22 January 2009|doi:10.1038/nature07664 nature

LETTERS

Anticipatory haemodynamic signals in sensory cortex not predicted by local neuronal activity

Yevgeniy B. Sirotin[1] & Aniruddha Das[1,2,3,4,5,6]

NeuroImage 55 (2011) 1409–1412

Contents lists available at ScienceDirect

NeuroImage

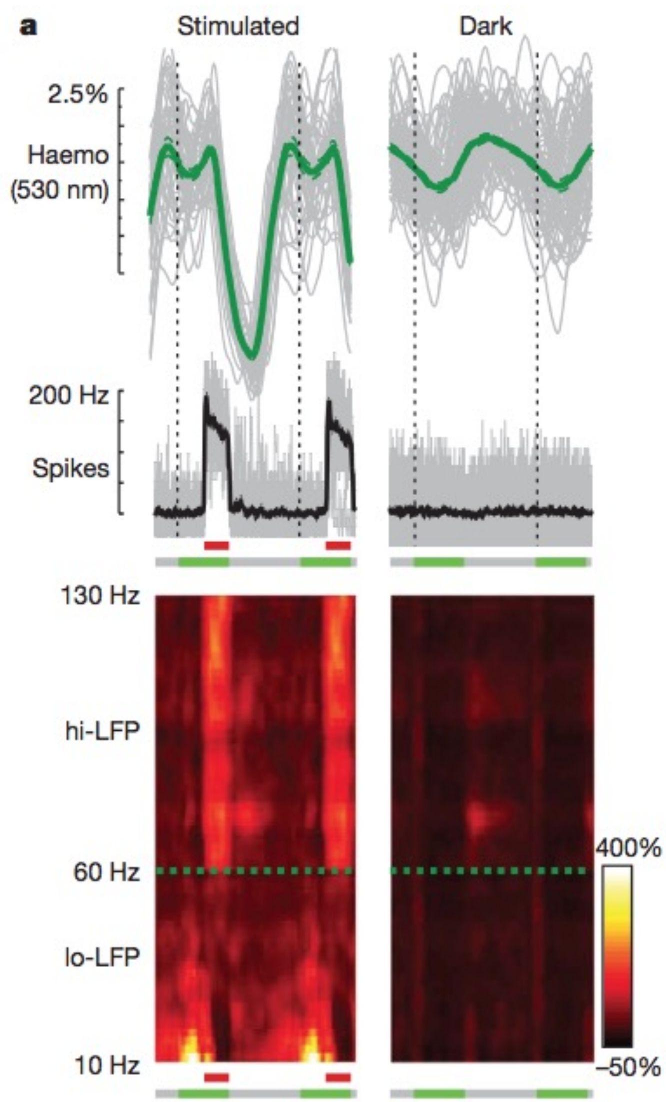
journal homepage: www.elsevier.com/locate/ynimg

Comments and Controversies

Hemodynamic signals not predicted? Not so: A comment on Sirotin and Das (2009)

Daniel A. Handwerker [a], Peter A. Bandettini [a,b,*]

[a] Section on Functional Imaging Methods, Laboratory of Brain and Cognition, National Institute of Mental Health, NIH, USA
[b] Functional MRI Facility, National Institute of Mental Health, NIH, USA



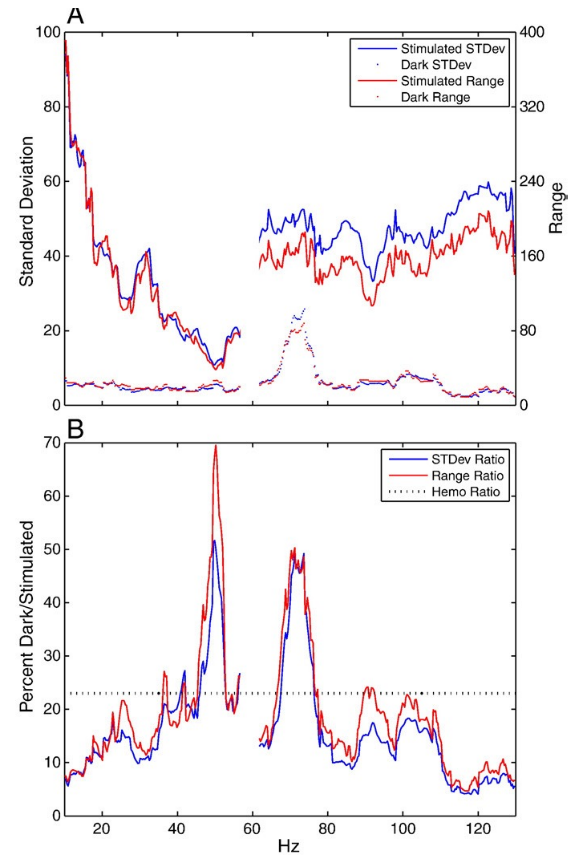
frontiers in NEUROENERGETICS

OPINION ARTICLE
published: 02 June 2010
doi: 10.3389/fnene.2010.00002

Neurovascular uncoupling: much ado about nothing

Nikos K. Logothetis[1,2*]

[1] Max Planck Institute for Biological Cybernetics, Tuebingen, Germany
[2] Division of Imaging Science and Biomedical Engineering, University of Manchester, Manchester, UK
*Correspondence: nikos.logothetis@tuebingen.mpg.de



In Serotin et al, there was a hemodynamic response where ***no*** neuronal activity was seen.

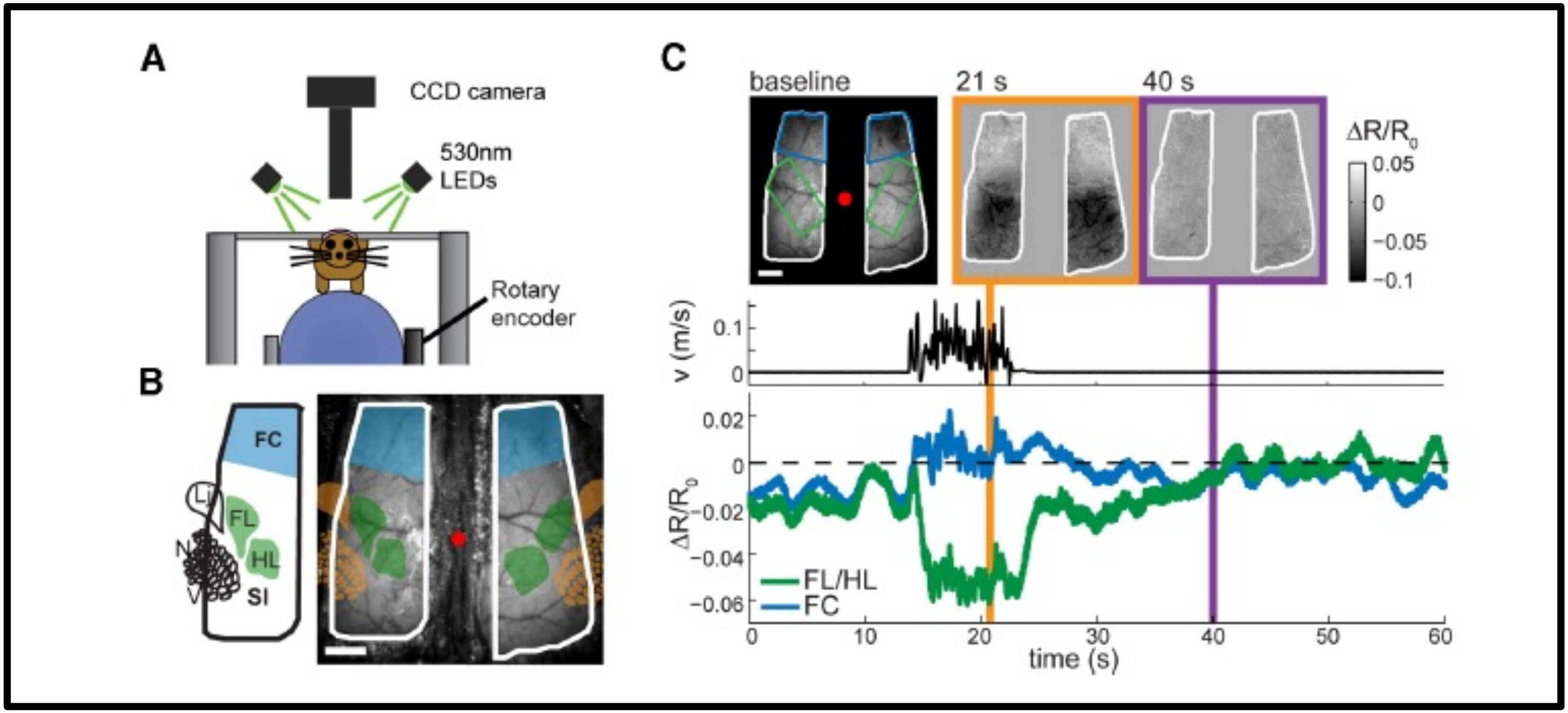
In Huo e al, there was no hemodynamic response where neuronal activity ***was*** seen.

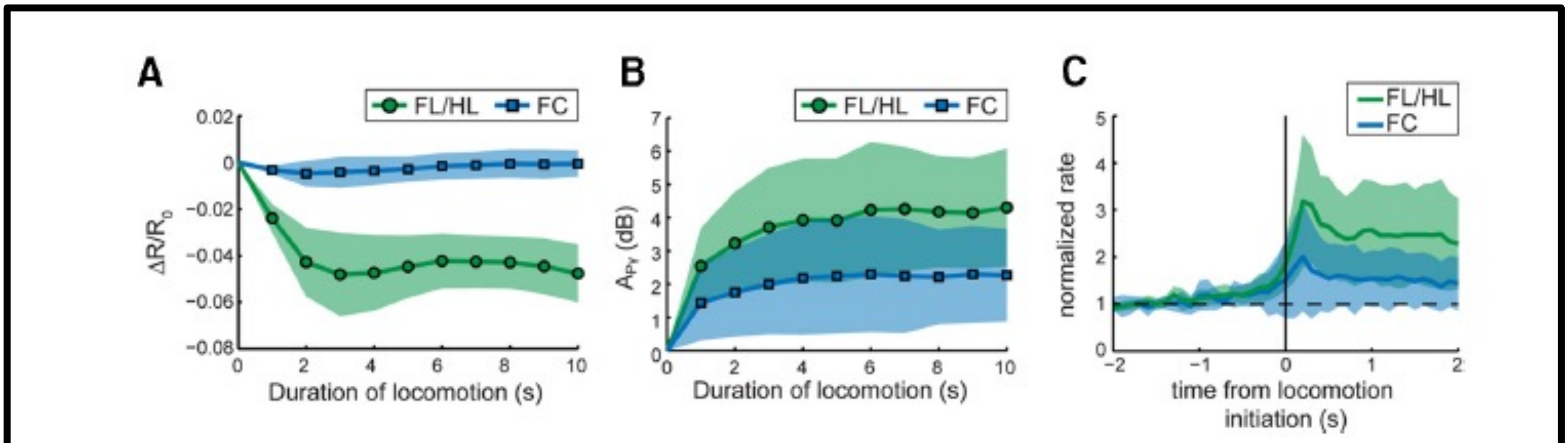
The Journal of Neuroscience, August 13, 2014 • 34(33):10975–10981 • **10975**

Systems/Circuits

Neurovascular Coupling and Decoupling in the Cortex during Voluntary Locomotion

Bing-Xing Huo (霍冰星),[1] Jared B. Smith,[1] and Patrick J. Drew[1,2]
[1]Center for Neural Engineering, Department of Engineering Science and Mechanics, and [2]Department of Neurosurgery, Pennsylvania State University, University Park, Pennsylvania 16802


A
CCD camera
530nm LEDs
Rotary encoder
B
FC
Li
FL
HL
N
V
SI
C
baseline
21 s
40 s
ΔR/R0
0.05
0
−0.05
−0.1
v (m/s)
0.1
0
ΔR/R0
0.02
0
−0.02
−0.04
−0.06
FL/HL
FC
0
10
20
30
40
50
60
time (s)


A
FL/HL
FC
0.02
0
-0.02
-0.04
-0.06
-0.08
ΔR/R0
0
2
4
6
8
10
Duration of locomotion (s)
B
FL/HL
FC
7
6
5
4
3
2
1
0
APγ (dB)
0
2
4
6
8
10
Duration of locomotion (s)
C
FL/HL
FC
5
4
3
2
1
0
normalized rate
−2
−1
0
1
2
time from locomotion initiation (s)

Aside from some of the technical issues for both studies, both look at measures of blood volume and not the fMRI signal – specifically BOLD.

….“absence of **evidence is not evidence** of absence”

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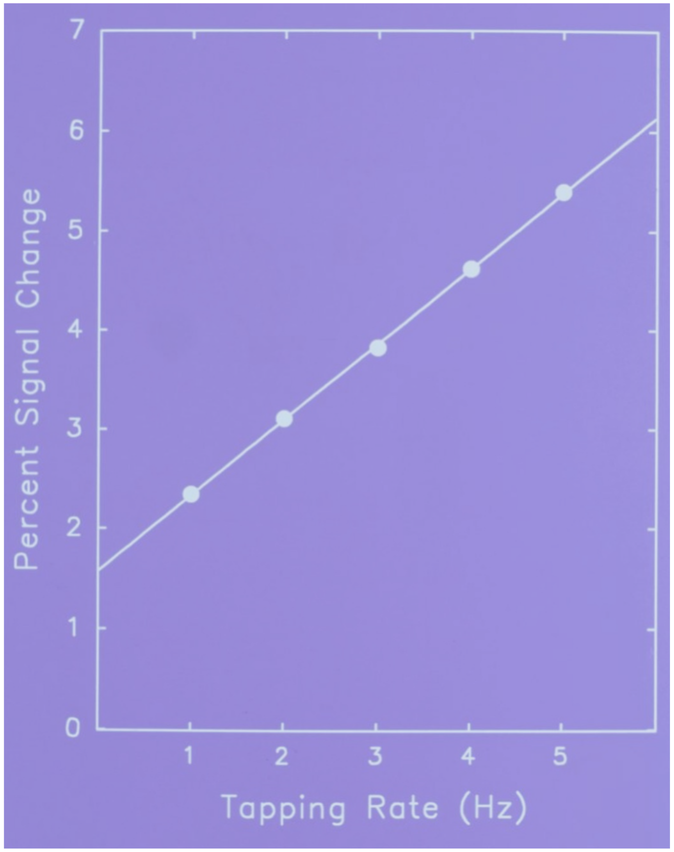
Linearity



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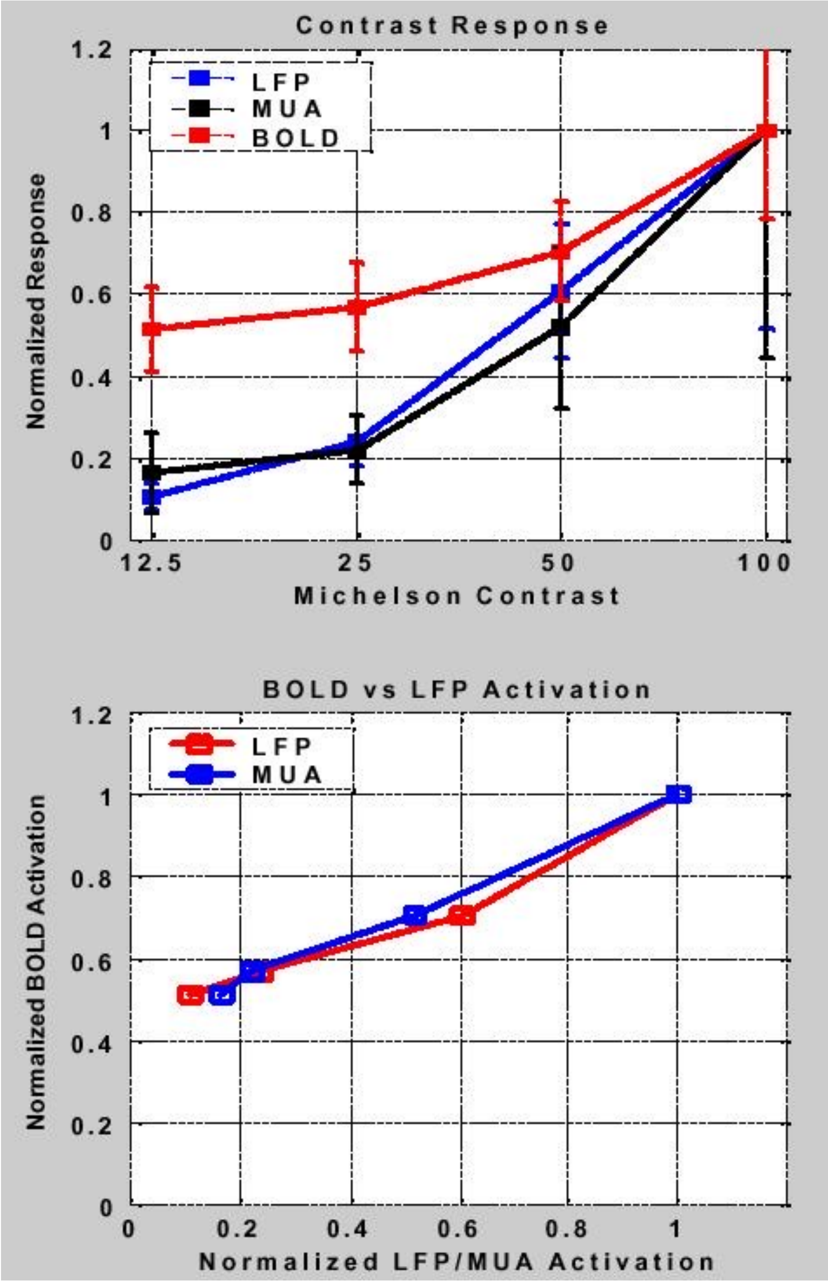
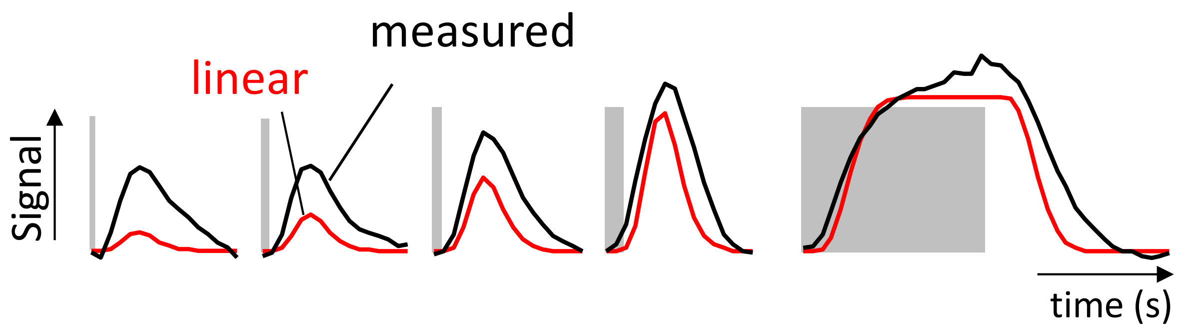
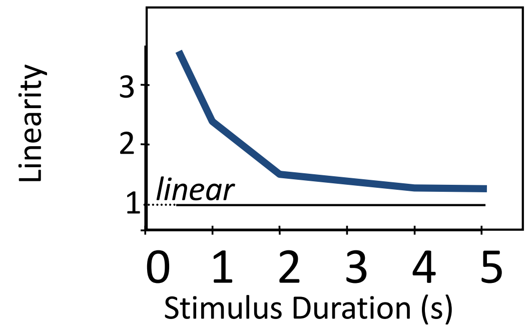


Logothetis et al. (2001) "Neurophysiological investigation of the basis of the fMRI signal" Nature, 412, 150-157

Linearity

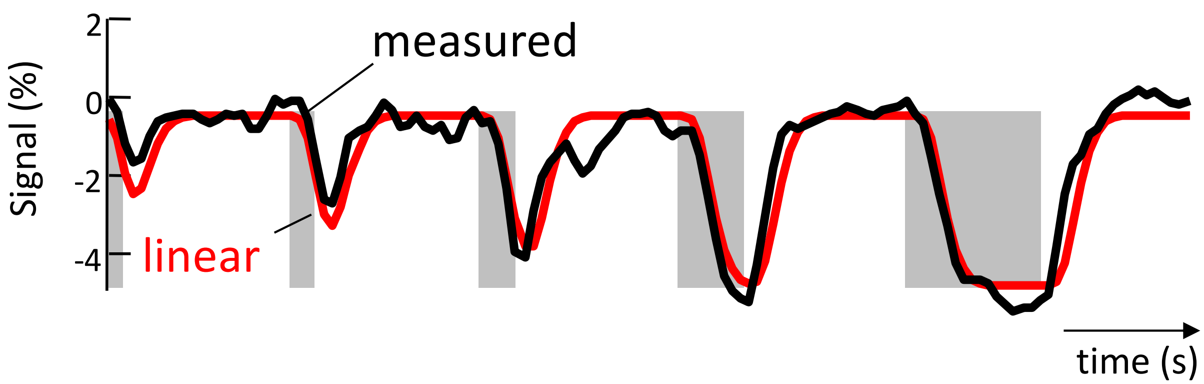
Brief "on" periods produce larger increases than expected.

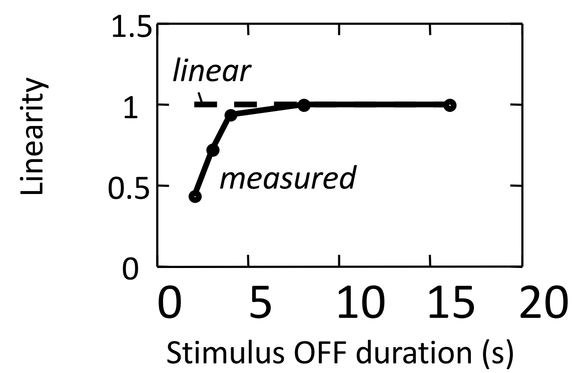




R. M. Birn, Z. Saad, P. A. Bandettini, NeuroImage, 14: 817-826, (2001)

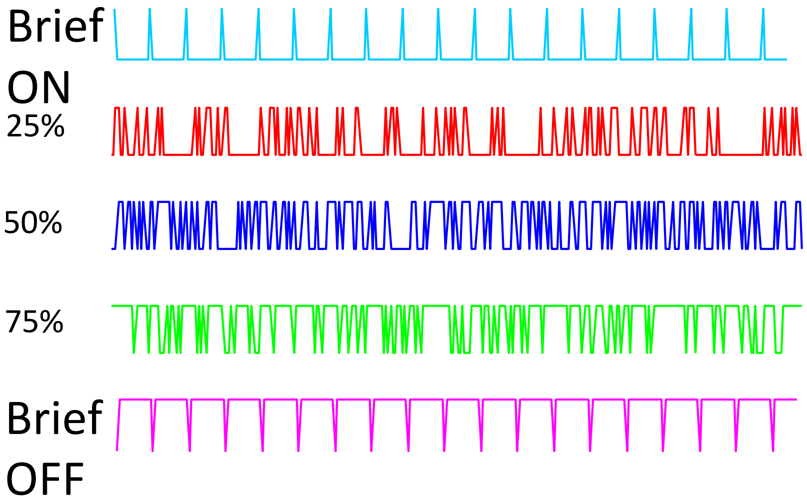
Brief "off" periods produce smaller decreases than expected.

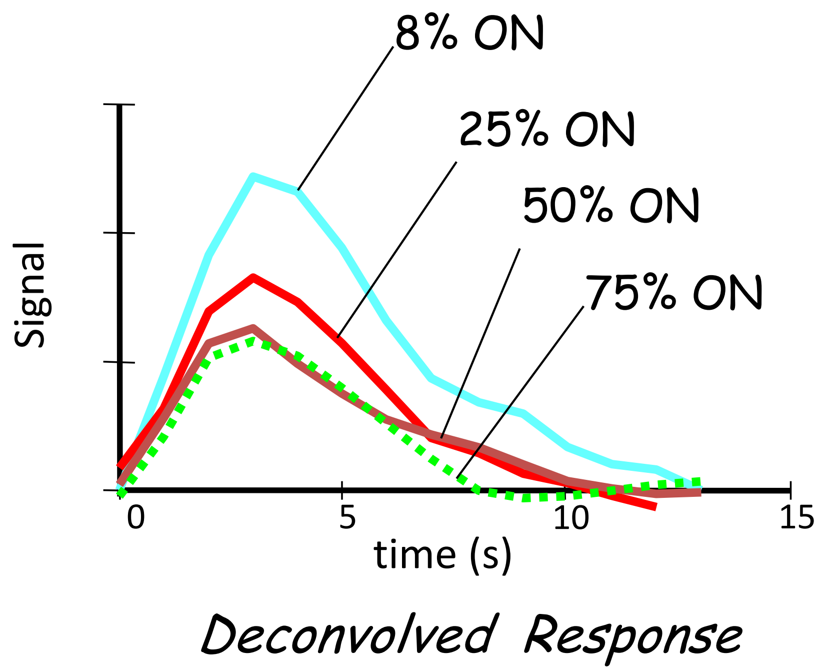


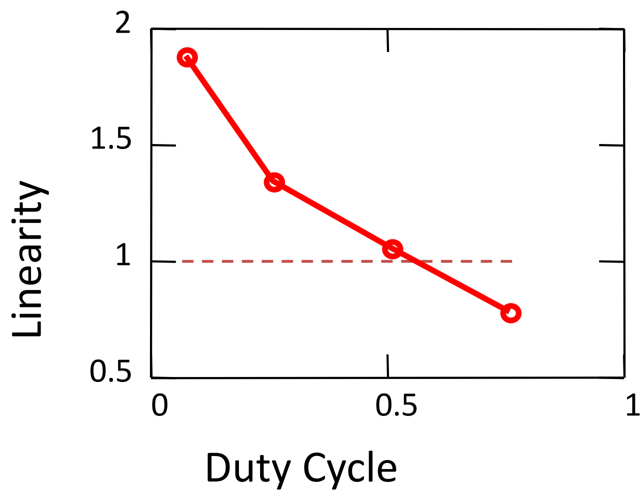


R.M. Birn, P. A. Bandettini, NeuroImage, 27, 70-82 (2005)

Varying the Duty Cycle







R.M. Birn, P. A. Bandettini, *NeuroImage*, 27, 70-82 (2005)

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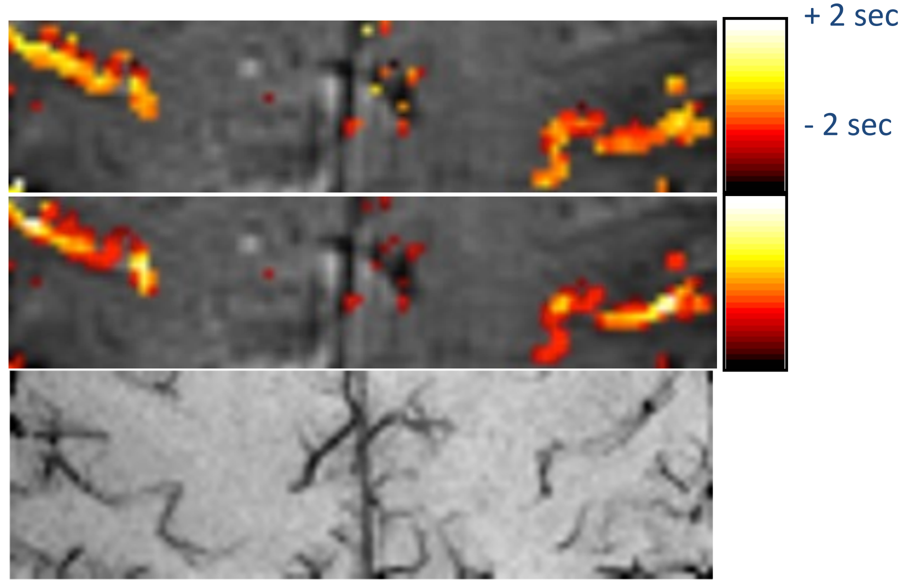
Methodology

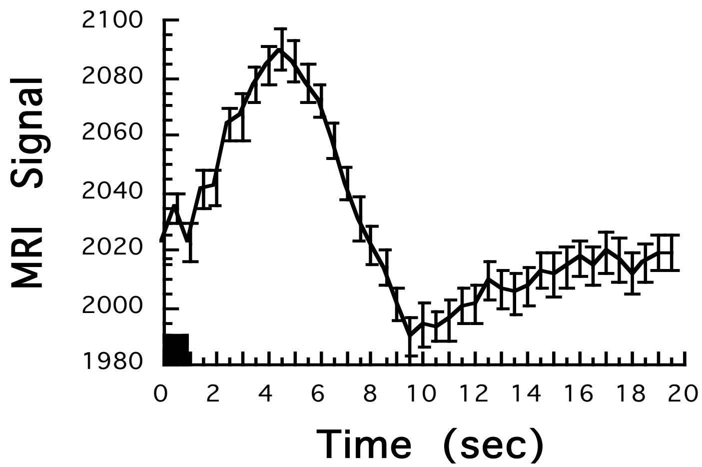
Latency Variation...

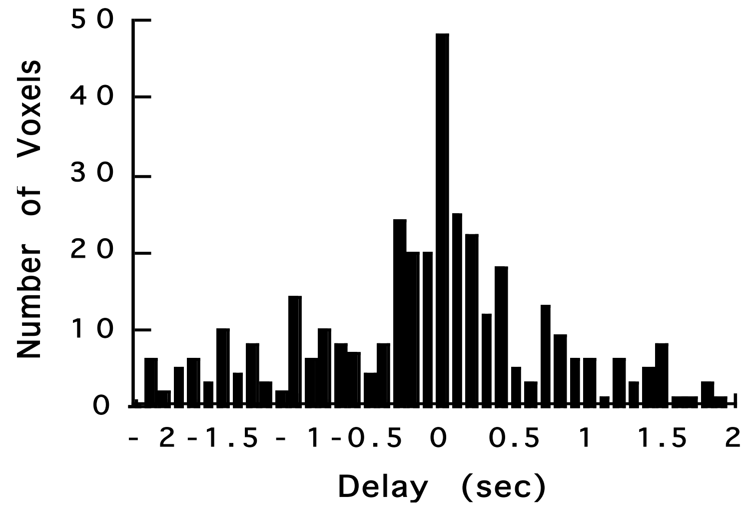
Latency

Magnitude

Venogram







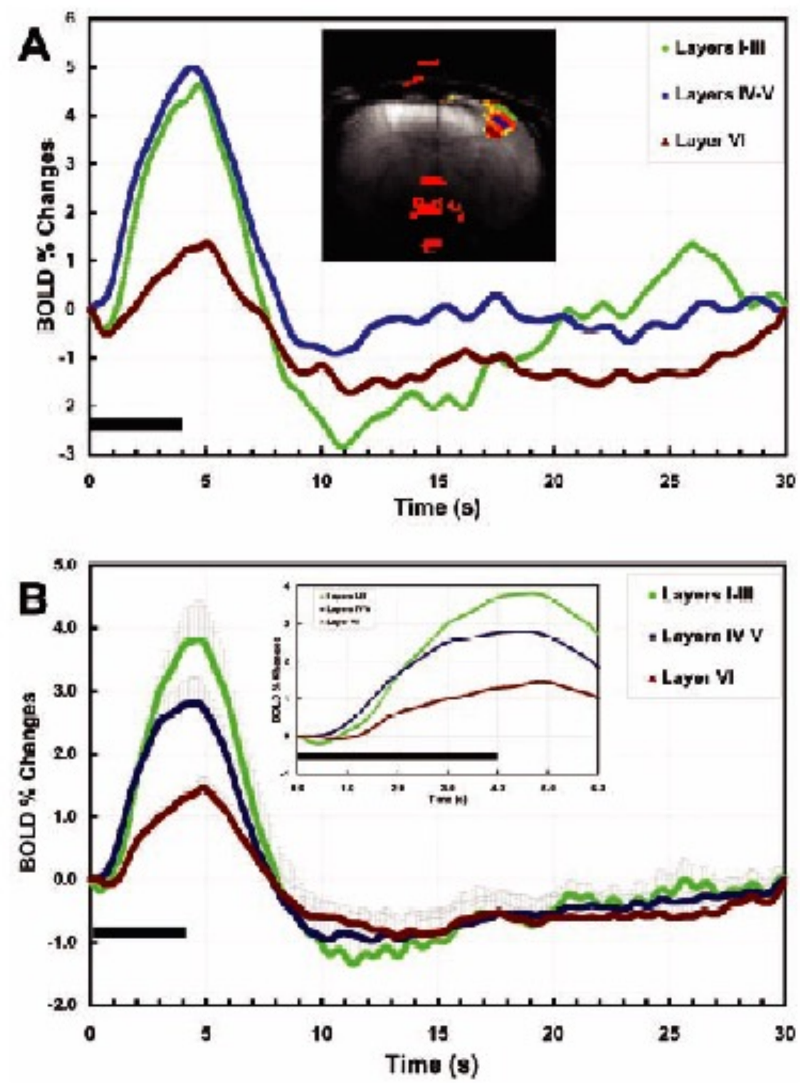
P. A. Bandettini, (1999) "Functional MRI" 205-220.

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

Afonso C. Silva* and Alan P. Koretsky

Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892

15182–15187 | PNAS | November 12, 2002 | vol. 99 | no. 23



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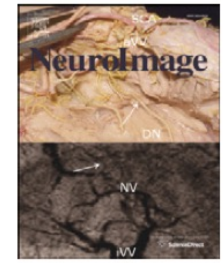
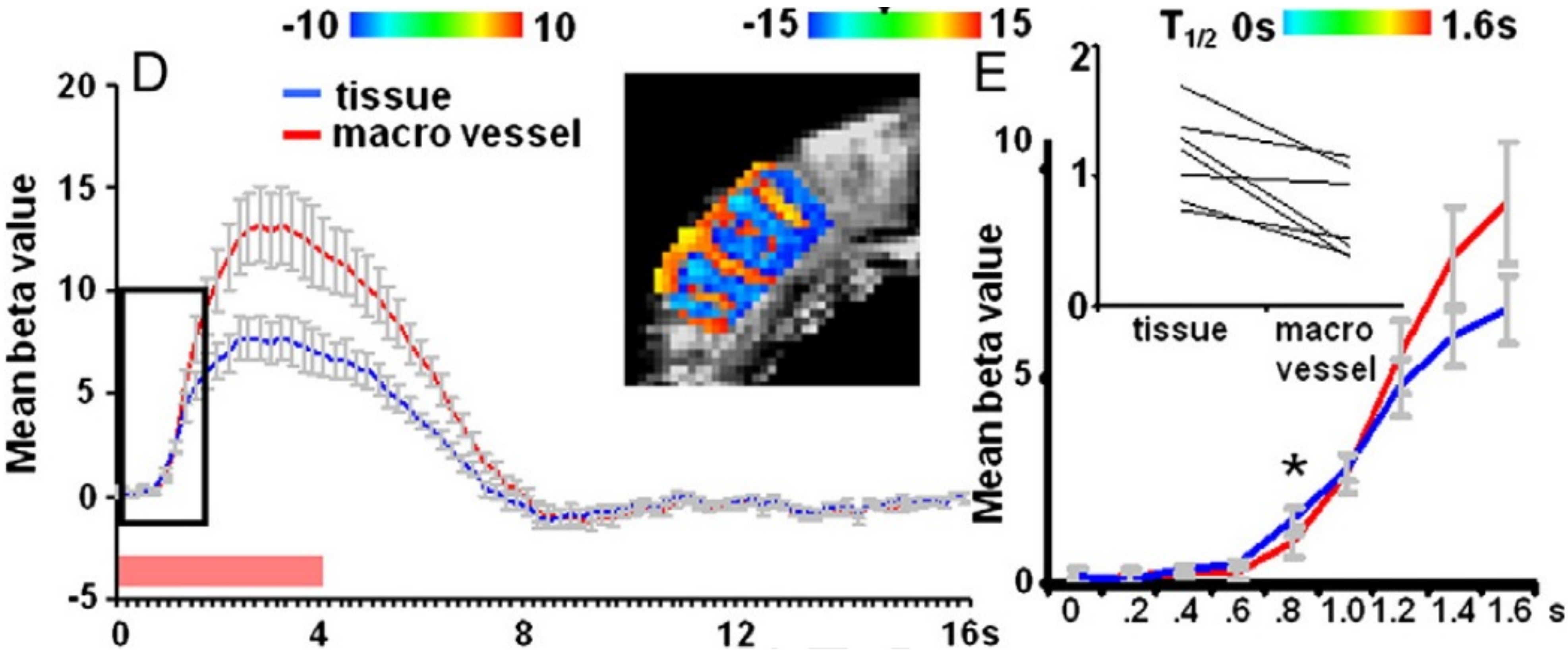


Direct imaging of macrovascular and microvascular contributions to BOLD fMRI in layers IV–V of the rat whisker–barrel cortex

Xin Yu [a], Daniel Glen [b], Shumin Wang [a,1], Stephen Dodd [a], Yoshiyuki Hirano [a], Ziad Saad [b], Richard Reynolds [b], Afonso C. Silva [a], Alan P. Koretsky [a,*]



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Journal of Cerebral Blood Flow & Metabolism (2010) 30, 1551–1557

www.jcbfm.com

Review Article

Everything you never wanted to know about circular analysis, but were afraid to ask

Nikolaus Kriegeskorte[1], Martin A Lindquist[2], Thomas E Nichols[3,4,5], Russell A Poldrack[6] and Edward Vul[7,8]

Over the past year, a heated discussion about 'circular' or 'nonindependent' analysis in brain imaging has emerged in the literature. An analysis is circular (or nonindependent) if it is based on data that were selected for showing the effect of interest or a related effect. The authors of this paper are researchers who have contributed to the discussion and span a range of viewpoints. To clarify points of agreement and disagreement in the community, we collaboratively assembled a series of questions on circularity herein, to which we provide our individual current answers in <– 100 words per question. Although divergent views remain on some of the questions, there is also a substantial convergence of opinion, which we have summarized in a consensus box. The box provides the best current answers that the five authors could agree upon.

Key definitions

Selective analysis

An analysis is “selective” when a subset of the data is first selected from the full data set before performing secondary analyses on the selected data only. For example, subsets of voxels are often selected in neuroimaging research, single cells are selected in single-unit neurophysiological studies and waveforms are selected in MEG and EEG research. (More generally, an analysis is also selective if the data channels, e.g. voxels, are differentially weighted for further analysis.)

Circular analysis

A circular analysis is a selective analysis, in which the biases incurred by selection are not taken into account. Because data always contain noise, the selected subset will never be determined by true effects only. Even in the absence of any true effects, the selected data will show the tendencies they were selected for. One way to avoid circularity is to analyze the selected sites (i.e. voxels or neurons) using independent data (e.g. a replication of the experiment). Effects, but not noise, will replicate. The results, thus, will reflect actual effects at the selected sites, without bias due to the influence of noise on the selection.

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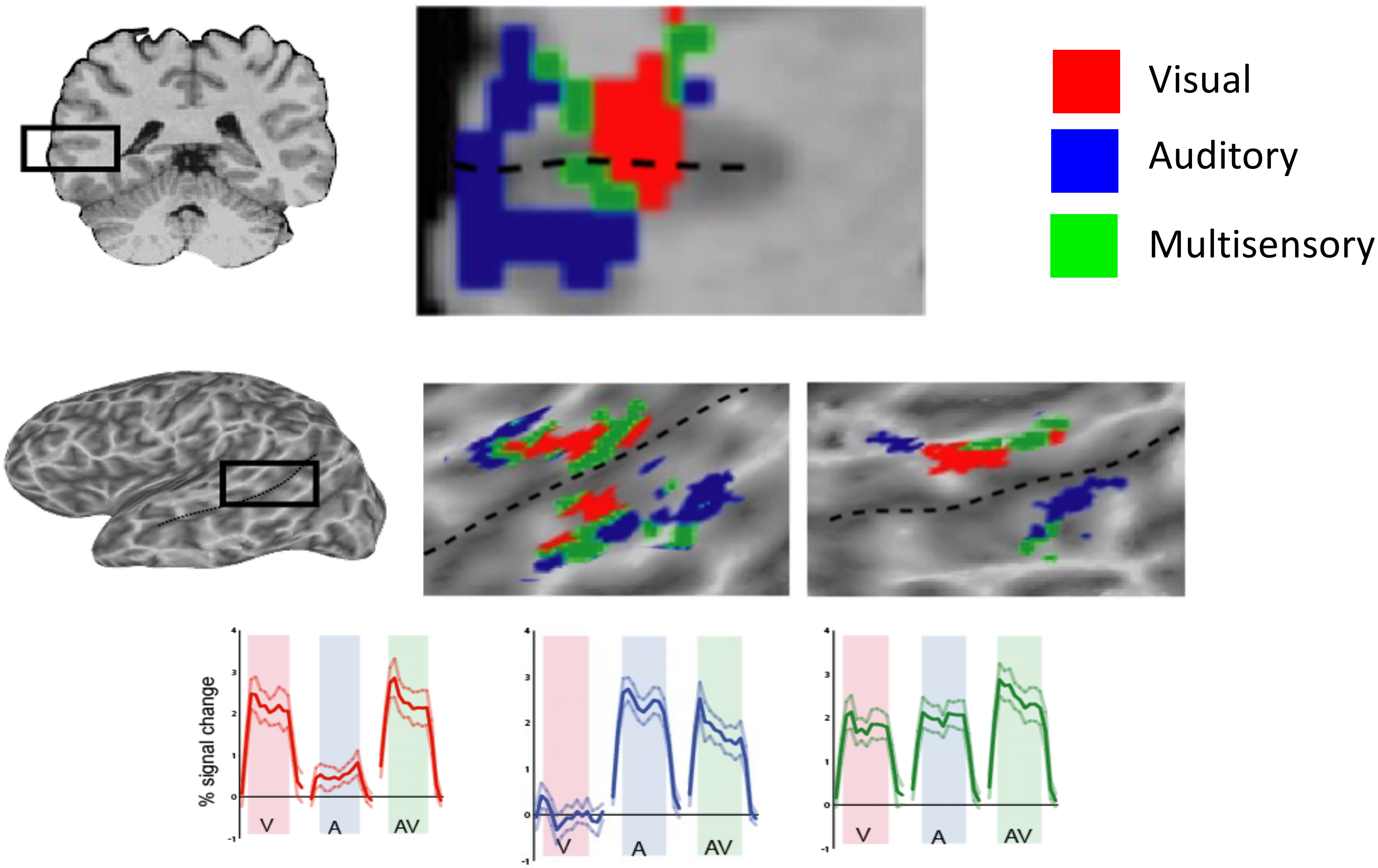
Multi-sensory integration

M.S. Beauchamp et al.,



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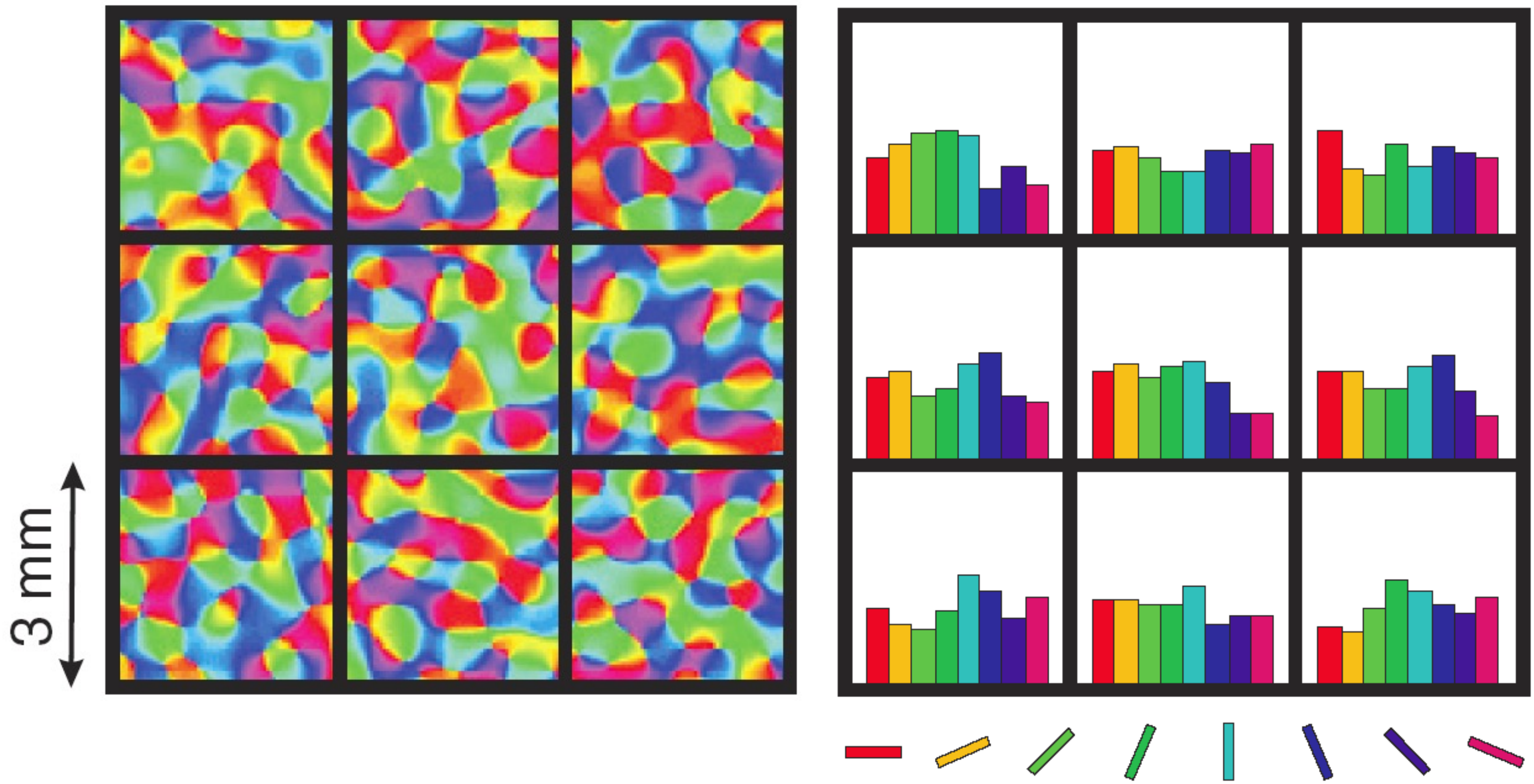
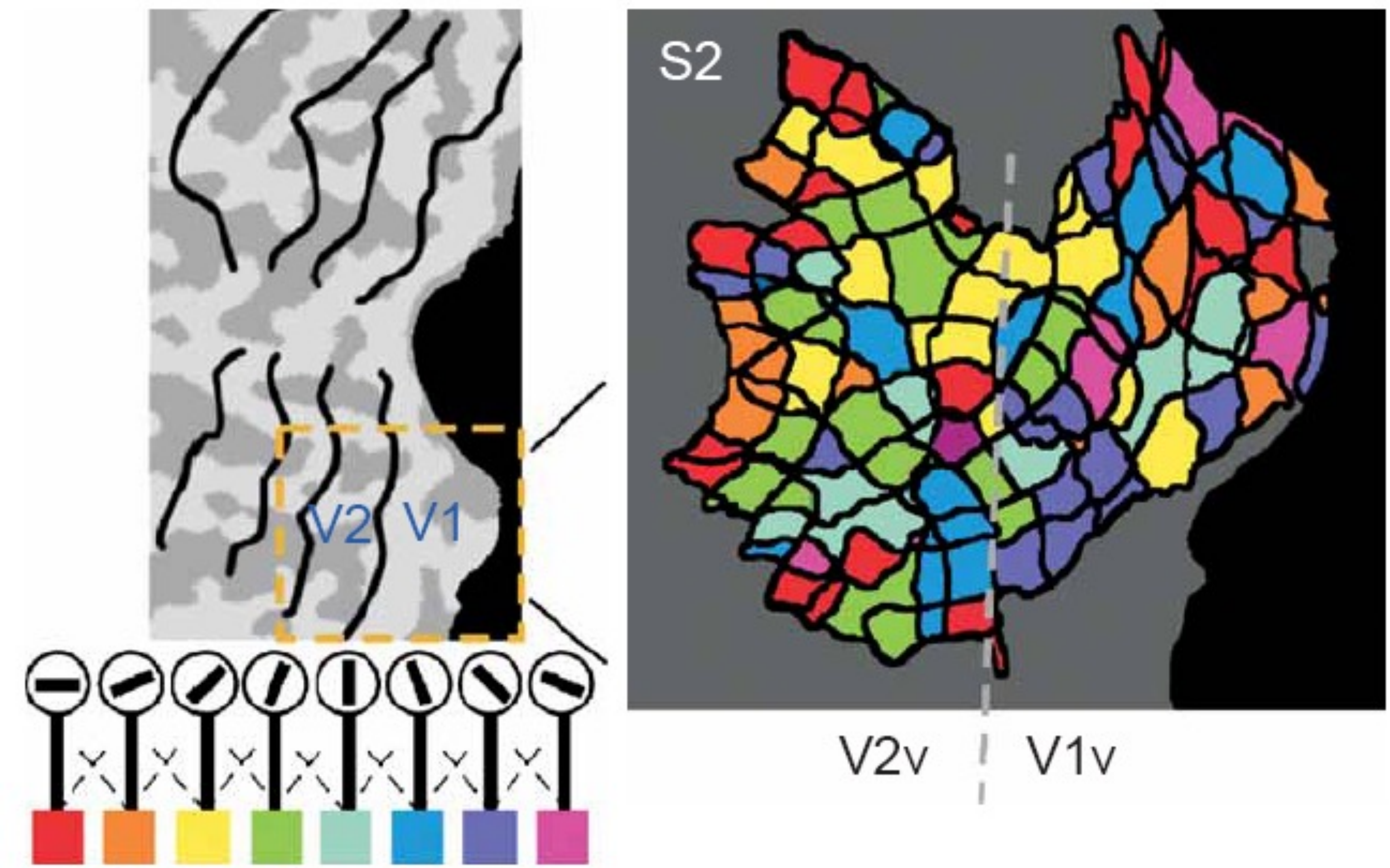


Boynton (2005), News & Views on Kamitani & Tong (2005) and Haynes & Rees (2005)

Lower spatial frequency clumping



Kamitani & Tong (2005)

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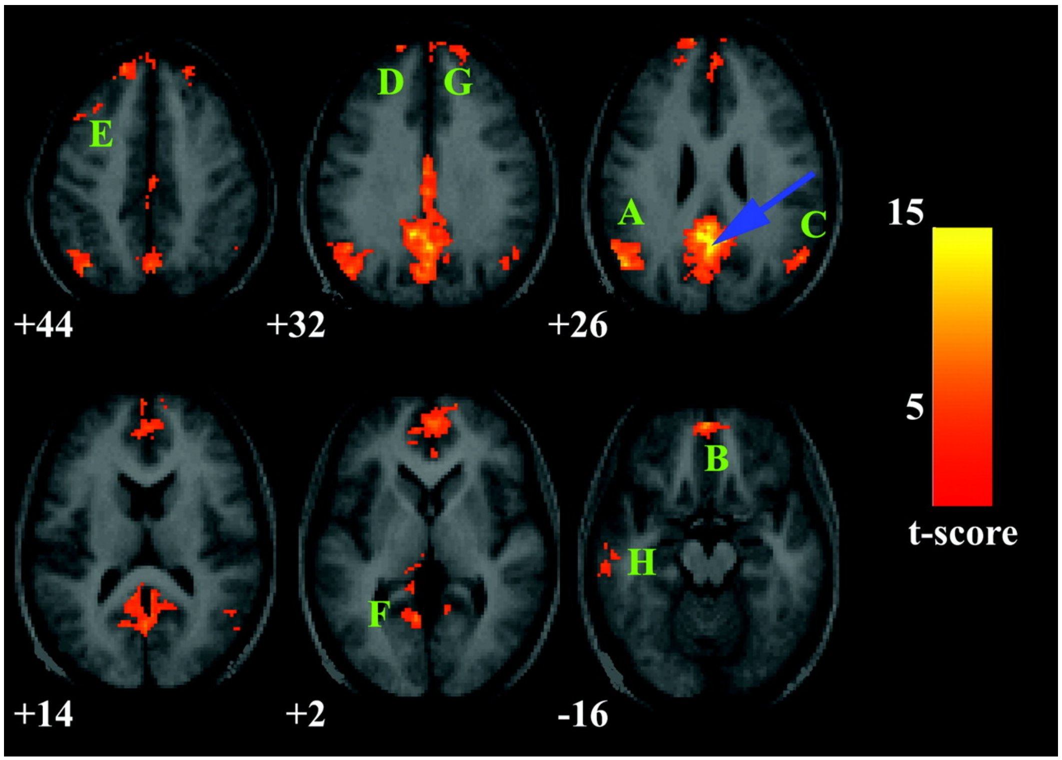
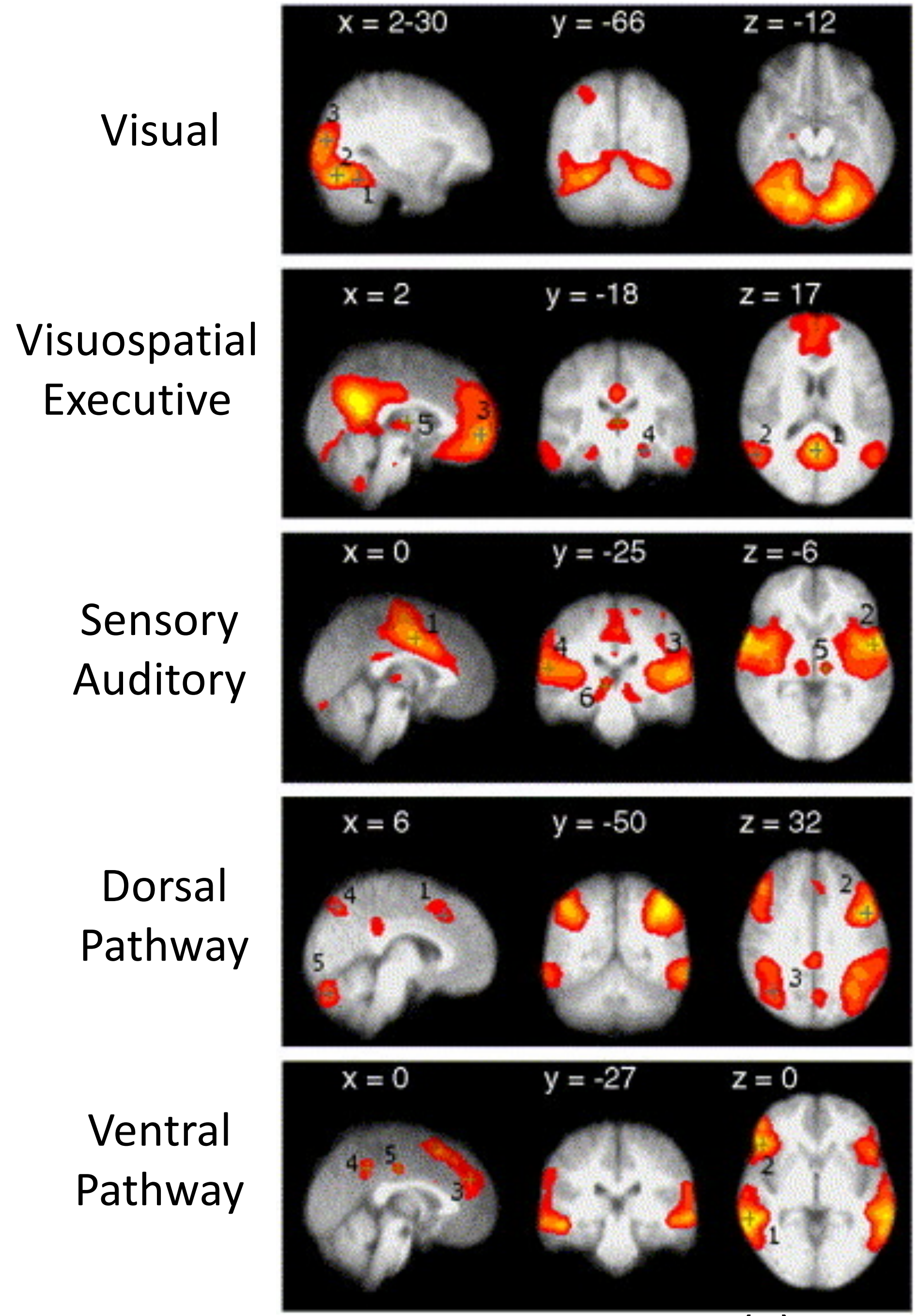
Seed Voxel

Seed Based Correlation from the Posterior Cingulate Cortex (PCC)



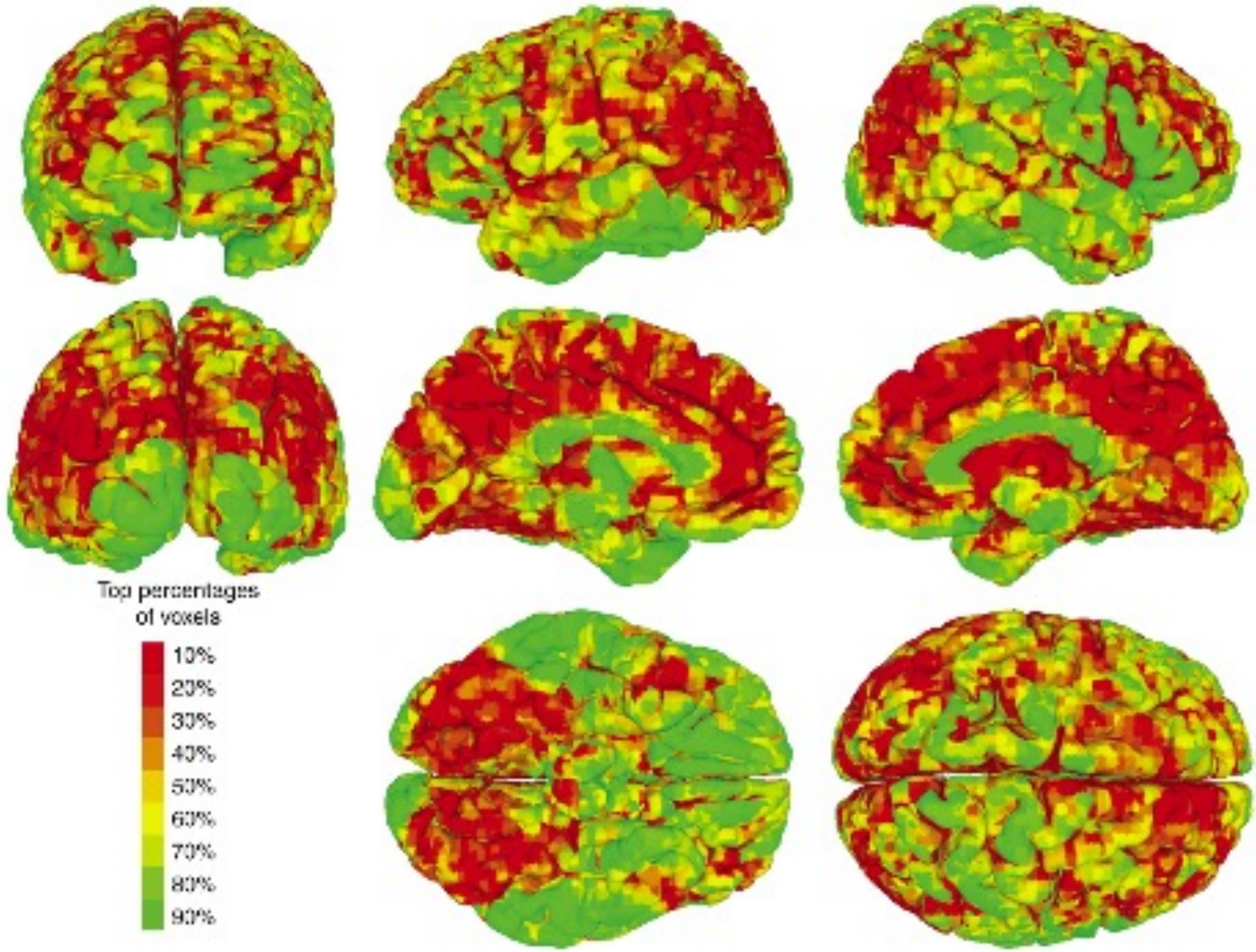
Greicius M D et al. PNAS 2003;100:253-258

ICA



De Luca, Neuroimage 29(4) 2006

Hub Maps

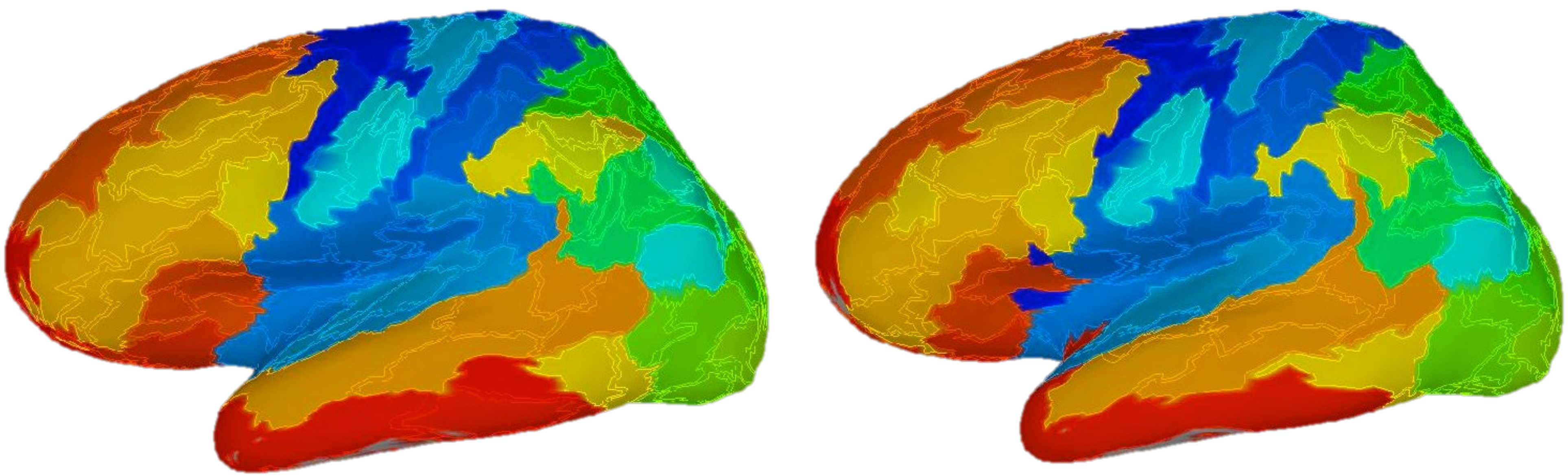


Identifying the brain's most globally connected regions,
M. W. Cole, S. Pathak, W. Schneider, NeuroImage 49, 2010, 3132-3148

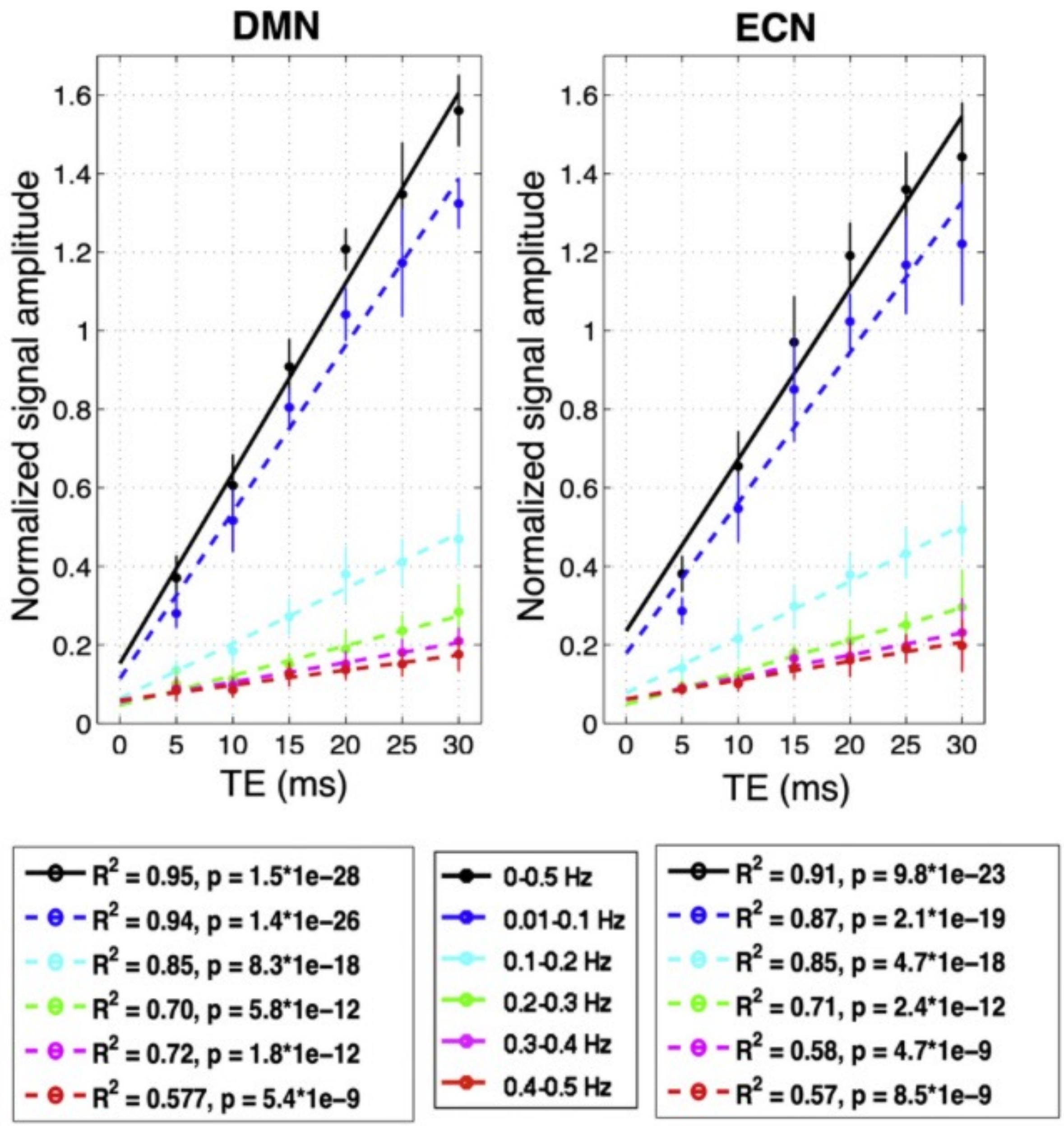
Test-retest of **group** clustering at 350 clusters

Rest 1

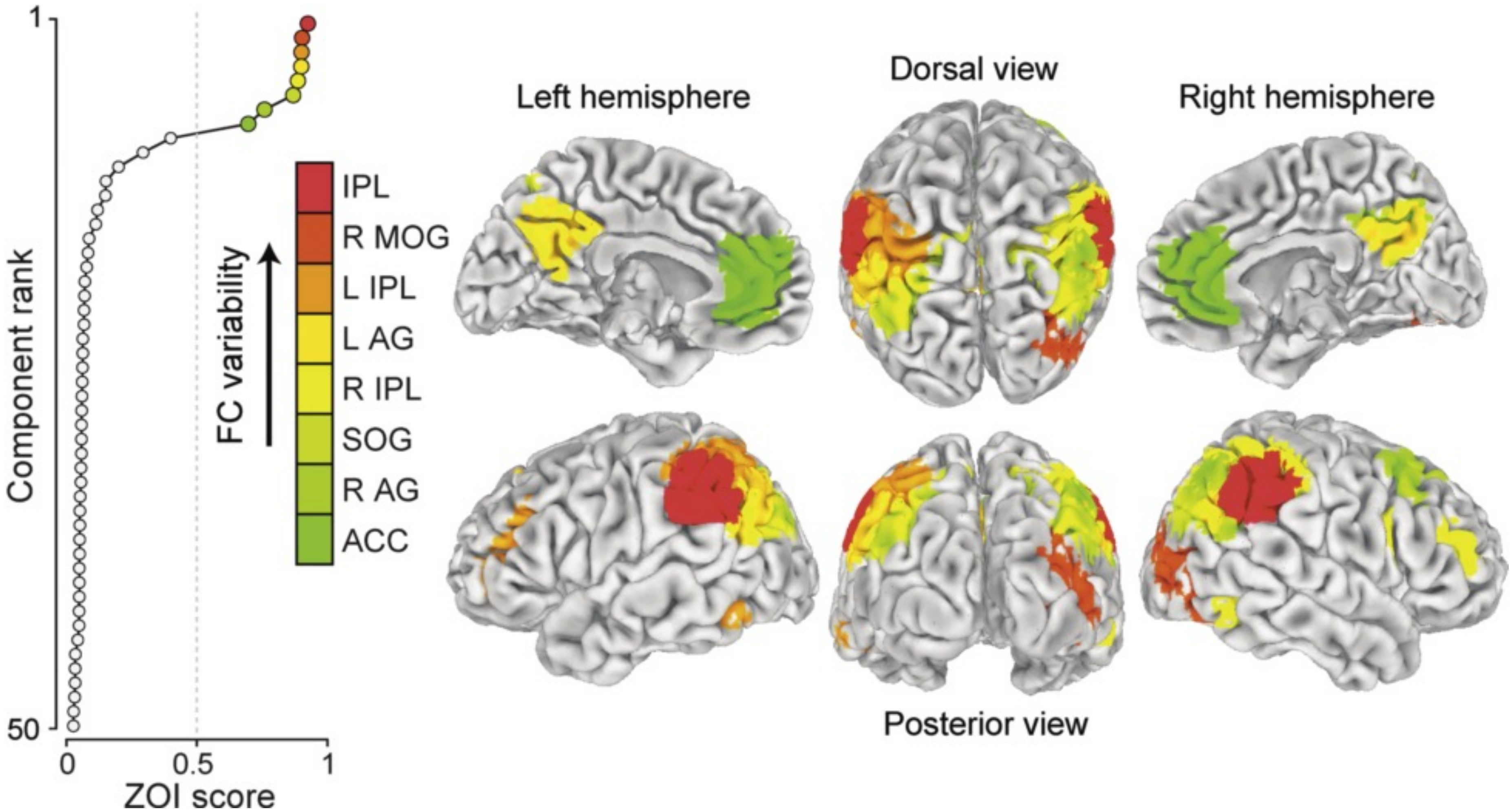
Rest 2
(color matched to Rest 1)



J. E. Chen and G. H. Glover, BOLD fractional contribution to resting-state functional connectivity above 0.1 Hz NeuroImage 107 (2015) 207–218



Spatial Distribution of Short Term FC Stability (II)



ZONE OF INSTABILITY: Set of Intrinsic Connectivity Networks with the most variable FC based on approx. 6 min long rest scans acquired on a group of 405 young adults and using a window length of 44 seconds.

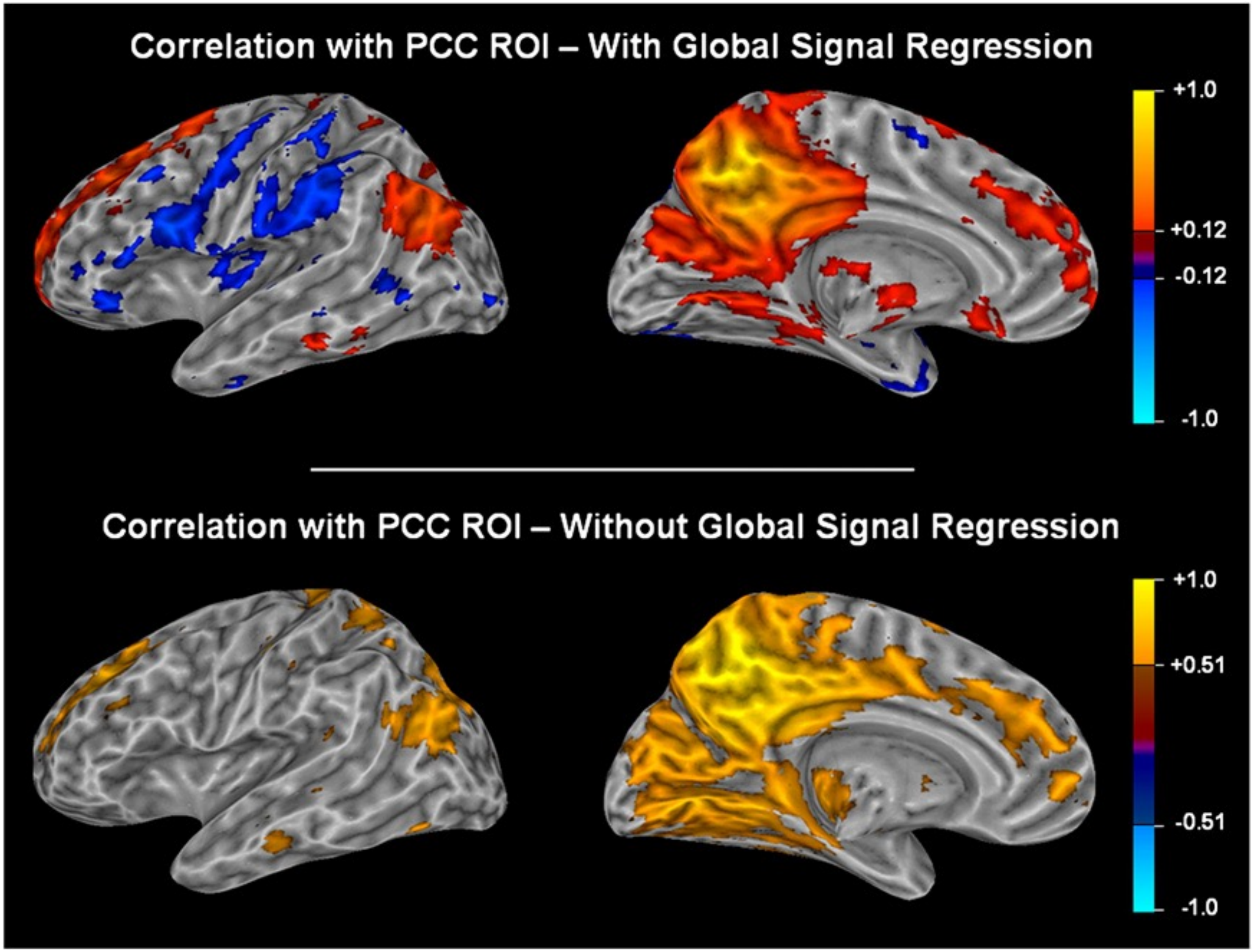
Allen et al. Cerebral Cortex 2014

Two other issues with imaging resting state fluctuations:

1. Global signal correction or not?

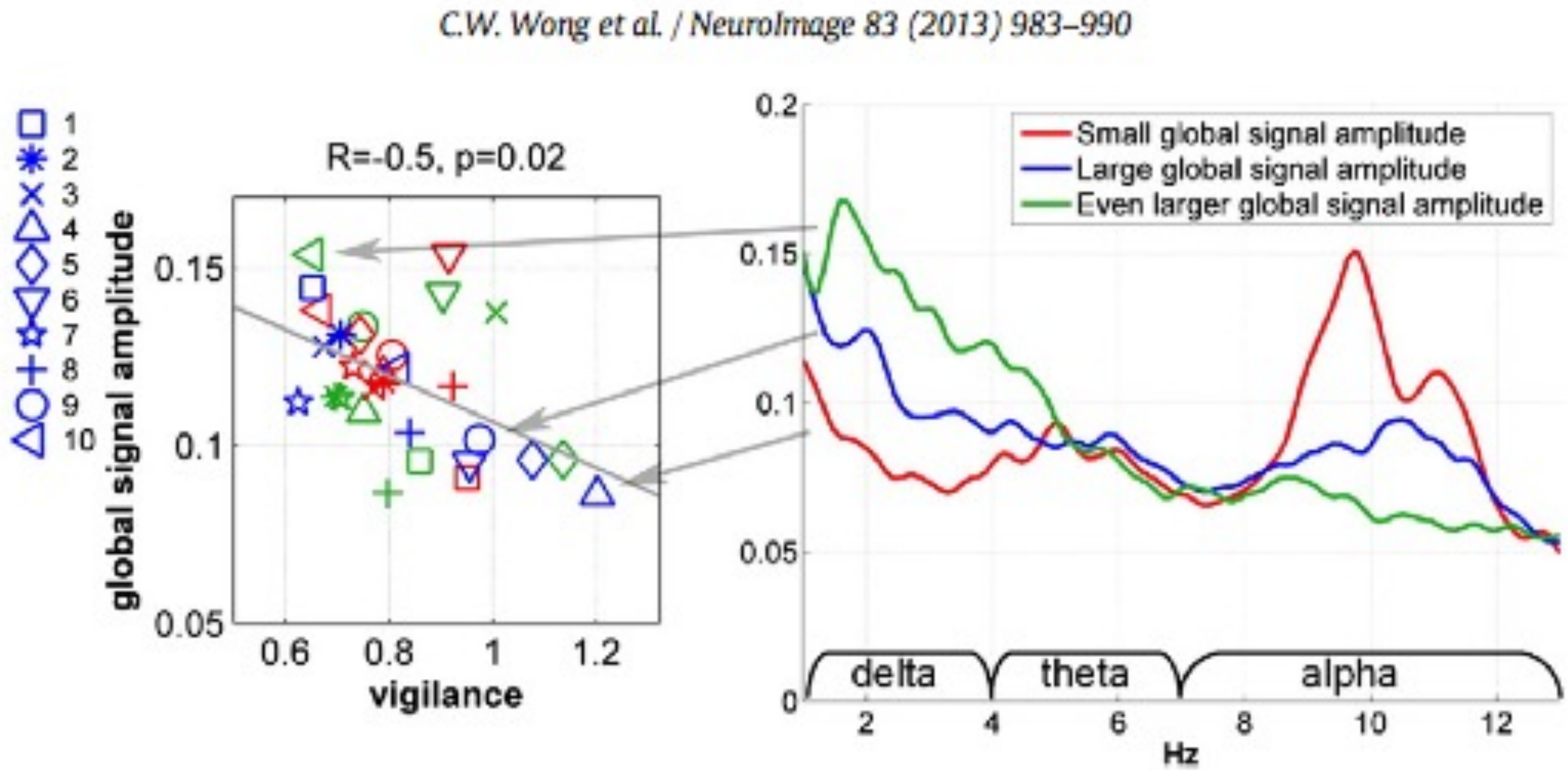
2. Short range correlations may be scanner-related.

The issue of global signal regression



K. Murphy, R. M. Birn, D. A. Handwerker, T. B. Jones, P. A. Bandettini, NeuroImage, 44, 893-905 (2009)

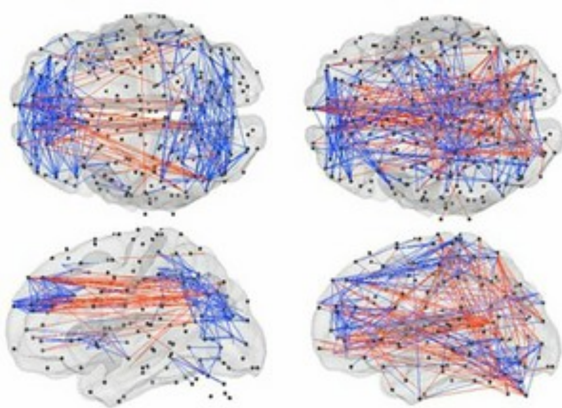
Global signal is an indicator of vigilance…



Movement during brain scans may lead to spurious patterns

Virginia Hughes

16 January 2012



Ties that blind: Correcting brain imaging data for head movements makes long-range connections (red) stronger, and short-range connections (blue) weaker, especially in children (left) more than in adults (right).

Head movements taint the results of many brain imaging studies, particularly those analyzing children or individuals with autism. That's the sobering message from two independent studies published over the past few months in *NeuroImage*[1,2].

Both reports analyze so-called 'resting-state functional connectivity' studies: the increasingly popular five-minute brain scans that measure synchrony between different regions when the brain is at rest.

Together, they call into question high-profile findings published in the past couple of years showing that short-range connections in the brain start off strong in children and weaken over the course of typical development, while long-range connections begin weak in children and strengthen over time.

In a study published 14 October, researchers reanalyzed data from several of their own functional connectivity studies after correcting for head motion and found that this maturation pattern usually disappears once head motion is taken into account.

"It really, really, really sucks. My favorite result of the last five years is an artifact," says lead investigator Steve Petersen, professor of cognitive neuroscience at Washington University in St. Louis.

It's unclear how many published results head motion has skewed, and whether this changes the bottom-line conclusions. But many researchers are concerned.

"It's going to impact some findings with regard to the robustness, but whether it completely wipes out the findings that are out there is another question," says Damien Fair, assistant professor of behavioral neuroscience and psychiatry at Oregon Health and Science University. "It is going to require folks to reanalyze their data, controlling for these new ways of examining motion."

Insidious artifact:

The new analyses also challenge some studies showing that the brains of people with autism and other neurodevelopmental disorders have excessive short-range and weak long-range connections.

Functional imaging studies may be marred by head motion

Virginia Hughes

7 September 2011

Head strong: Movements of the head can affect activity in the default network, a brain circuit that has been tied to autism.

Signatures of brain activity found in individuals with autism could simply be the result of squirmy volunteers, according to a report published 23 July in *Neuroimage*[1]. The study found that even small head movements inside of a brain scanner can affect results.

The first rule of brain scanning is to keep the participant's head as still as possible, because movement can confound the fast-changing measurements of neural activity. But it's impossible for any participant, and especially a child with autism, to keep perfectly still.

In the new study, Randy Buckner and colleagues investigated whether head movements affect data gleaned from resting-state functional magnetic resonance imaging (fMRI). This technique, which is getting more and more popular among autism researchers, measures synchrony between brain regions while a participant lies passively in the scanner for five to ten minutes.

Scanning 1,000 healthy adults, the researchers found that, for most brain circuits, head movement does not affect variations in brain activity. There are a few notable exceptions, however.

Head motion is associated with decreased synchrony in the default network, a brain circuit that is most active during daydreaming and sleeping, and quiet during explicit tasks. Movement is also associated with increased synchrony between nearby brain regions. Both of these brain signatures have cropped up in imaging studies of individuals with autism.

To avoid this potential pitfall, the researchers emphasize the importance of reminding participants to stay still, and suggest using attached helmets that keep the head immobilized.

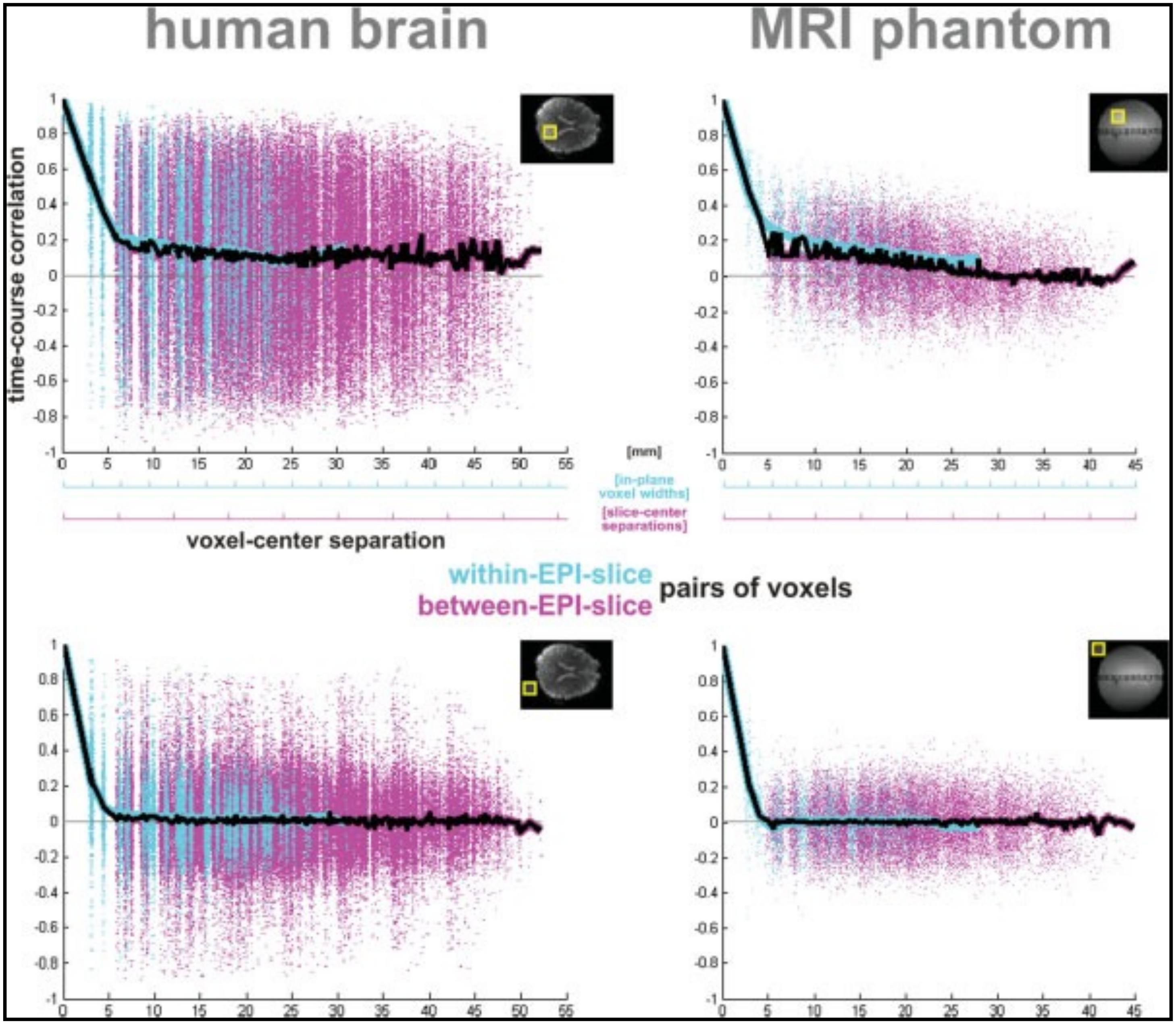
These strategies won't help other causes of head movements, however, such as swallowing and jaw-clenching. For these, the researchers suggest using certain types of data analyses that correct for motion[2].

References:

1: Van Dijk K.R. *et al. Neuroimage* Epub ahead of print (2011) PubMed

2: Jo H.J. *et al. Neuroimage* **52**, 571-582 (2010) PubMed

The issue of correlation across voxels due scanner instabilities



N. Kriegeskorte, J. Bodurka, P. Bandettini, International Journal of Imaging Systems and Technology, 18 (5-6), 345-349 (2008)

Best Acquisition for best signal to noise & artifact?

- Multi-echo?
- Multi-band with short TR?

- The Undershoots
- Negative signal changes
- Relationship to neuronal activity
- Linearity
- Temporal precision
- fMRI contrast mechanisms and sequences
- Analysis circularity issue
- How to handle high resolution
- Basis of the decoding signal
- How to best process/interpret resting state

The Future…

Where are we now…after 20 years?

- Technology is more sophisticated
  (hardware, computers, software)
- Images are better
  (SNR, acquisition speed, resolution)
- Easier to implement
  (what was cutting edge is now routine)
- Data are more interpretable
  (we understand it better and trust it more)
- More groups working with fMRI
- Wider applications
  (growth $\propto$ utility)
- Resting state has exploded.
  (robust results being found, processing improving)

Technology

- Magnet
- RF Coils
- Gradients
- Pulse Sequences

Methodology

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

Interpretation

- Increases
- Decreases
- Dynamics
- Locations
- Fluctuations

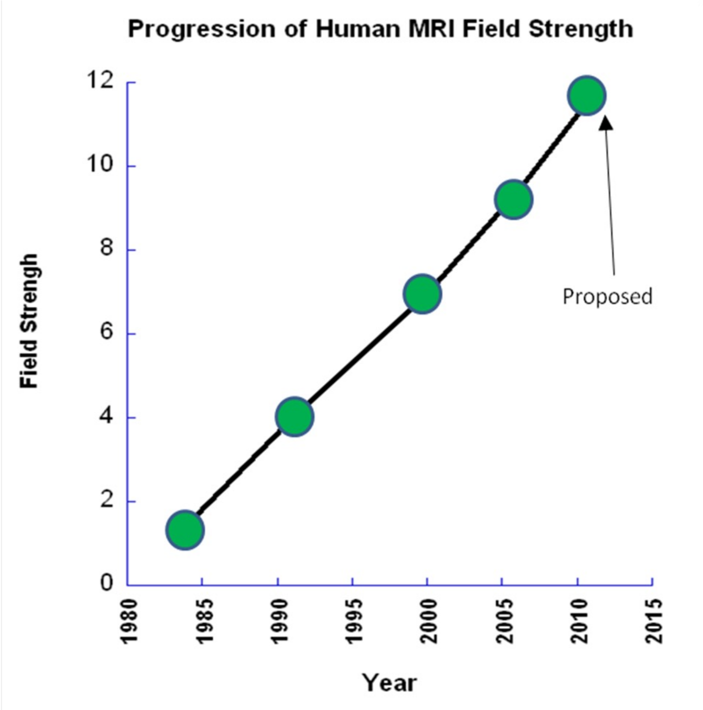
Applications

- Neuroscience
- Physiology
- Genetics
- Clinical
- Law
- Marketing
- Entertainment

Magnet

Currently:

- We have about 50 7T scanners and almost one 11.7T scanner



In 5 years:

- Two 11.7T scanners (no higher fields)
- 3T will almost completely replace 1.5T for most clinical imaging
- The number of 7T scanners will plateau.

In 10 years:

- Four 11.7T scanners (perhaps one 15.0 T)

RF Coils

Currently:

- Most use 8 to 32 channel receive only.

5 Years:

- Most will use 32 to 64 channel receive only & 8 channel excite.
- Cutting edge will be 128 channel receive and 8 channel excite.

10 Years:

- Most will use 32 to 64 channel receive only & 16 channel excite.
- Cutting edge will be 512 channel receive and 64 channel excite.

Gradients & shims

Currently:

- Most use 6 Gauss/cm & 3'rd order shims
- Rise time determined by biologic limits
- Cutting edge: 30 Gauss/cm for Diffusion Imaging (DSI).

5 Years:

- Most will use 6 to 12 Gauss/cm. No change in rise time.
- More local gradient coils (30 Gauss/cm) for head-only imaging. (Rise time can be a bit faster)
- Non-orthogonal shims implemented.

10 Years:

- Most will use 6 to 20 Gauss/cm. No change in rise time.
- Cutting edge will be 512 channel receive and 64 channel excite.
- Shim will be subject specific and essentially solved by a combination of higher order shims, local non-orthogonal shims and passive shims.

Pulse Sequences

Currently:

- 2 mm isotropic EPI is common. Many still use 3 mm isotropic.
- Cutting edge: 128 slices in 2 sec, 1 mm isotropic, single shot EPI

5 Years:

- 1.5 mm isotropic, 128 slices in 2 sec, will be commonly used.
- Multi-echo will be more commonly used.
- Cutting edge will be compressed sensing strategies for fMRI.
- Cutting edge will also be 100 um single shot EPI.
- Integration of acquisition and goal directed analysis (real time calibration, multi-contrast fusion, etc..)

10 Years:

- 1.5 mm isotropic, 128 slices in 2 sec, will be commonly used.
- Embedded contrast (i.e. multi-echo, simultaneous flow/BOLD/volume) will be more common as this will be critical for specific information extraction.

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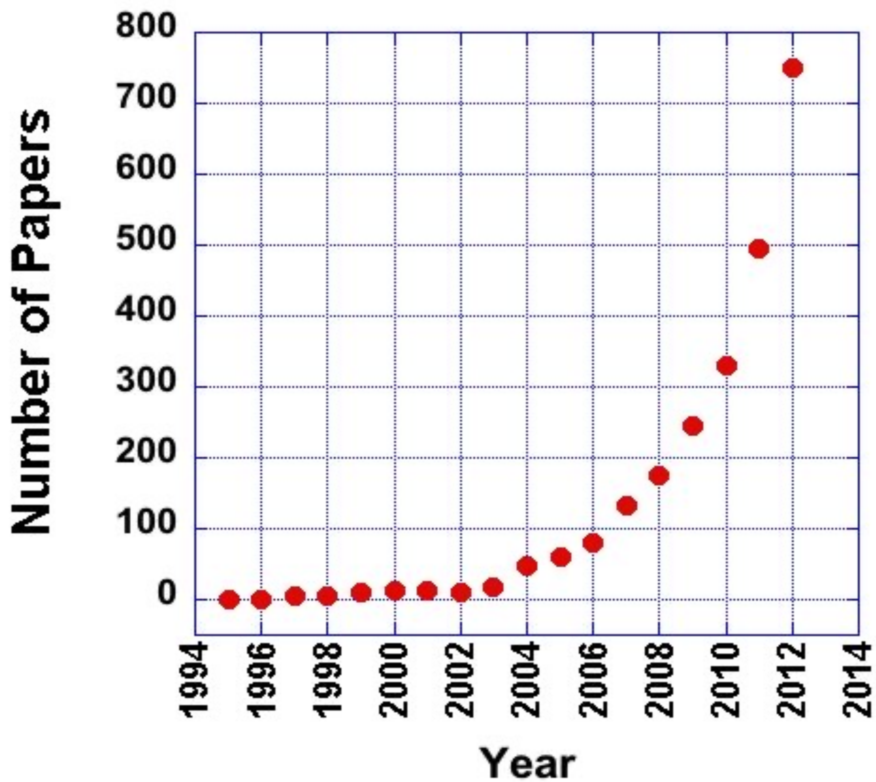
Most exciting trends in Methodology

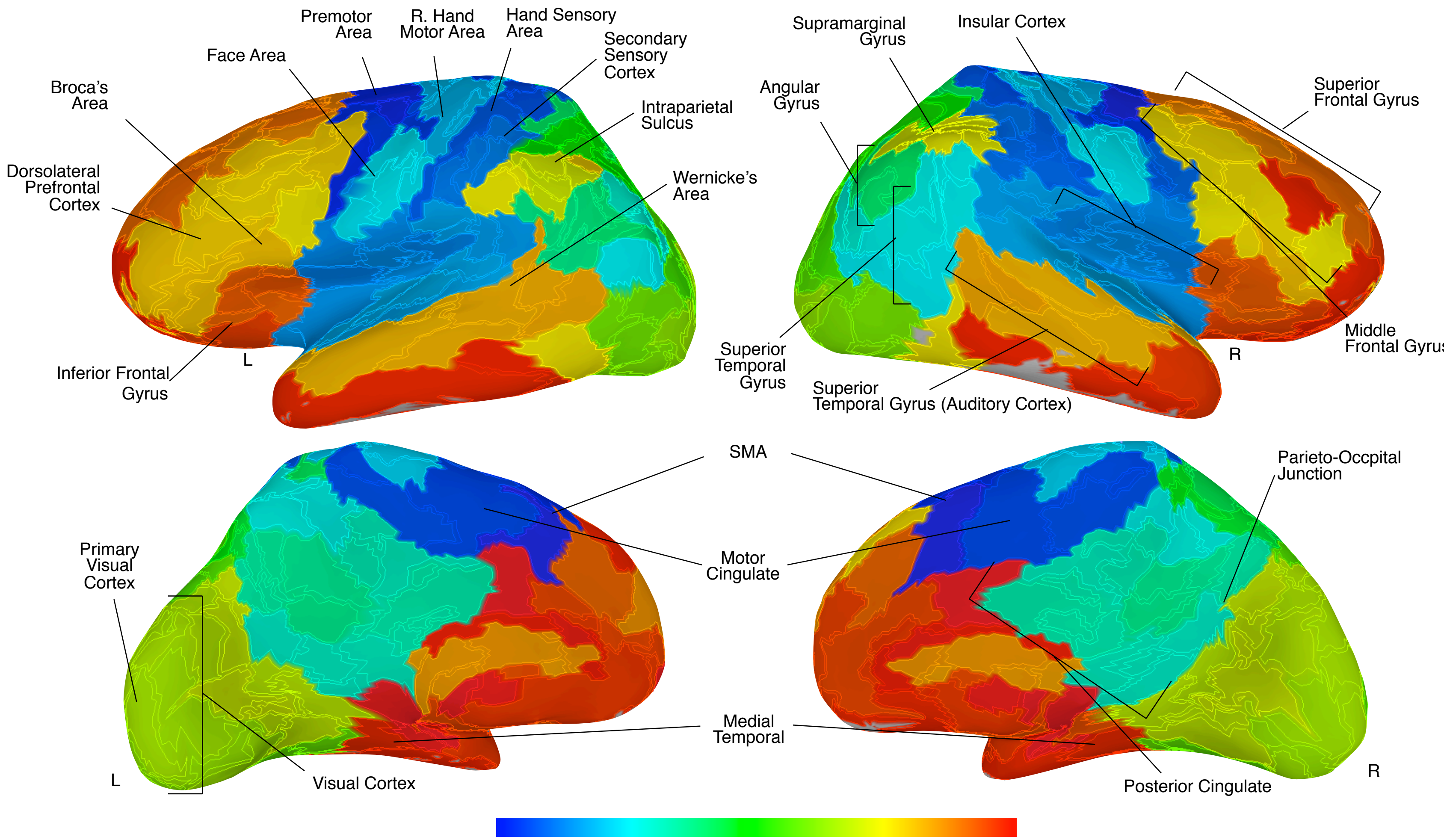
- •Resting State Fluctuations and Connectivity Assessment
- •Multivariate assessment and Machine Learning
- •Natural stimuli and performance in scanner
- •From Populations to Individuals …classification
- •Real time fMRI and multi-modal with feedback
- •Using more of the more subtle signal changes

Resting State Fluctuations and Connectivity Assessment

Resting state fMRI



Whole brain connectivity patterns from resting state signal

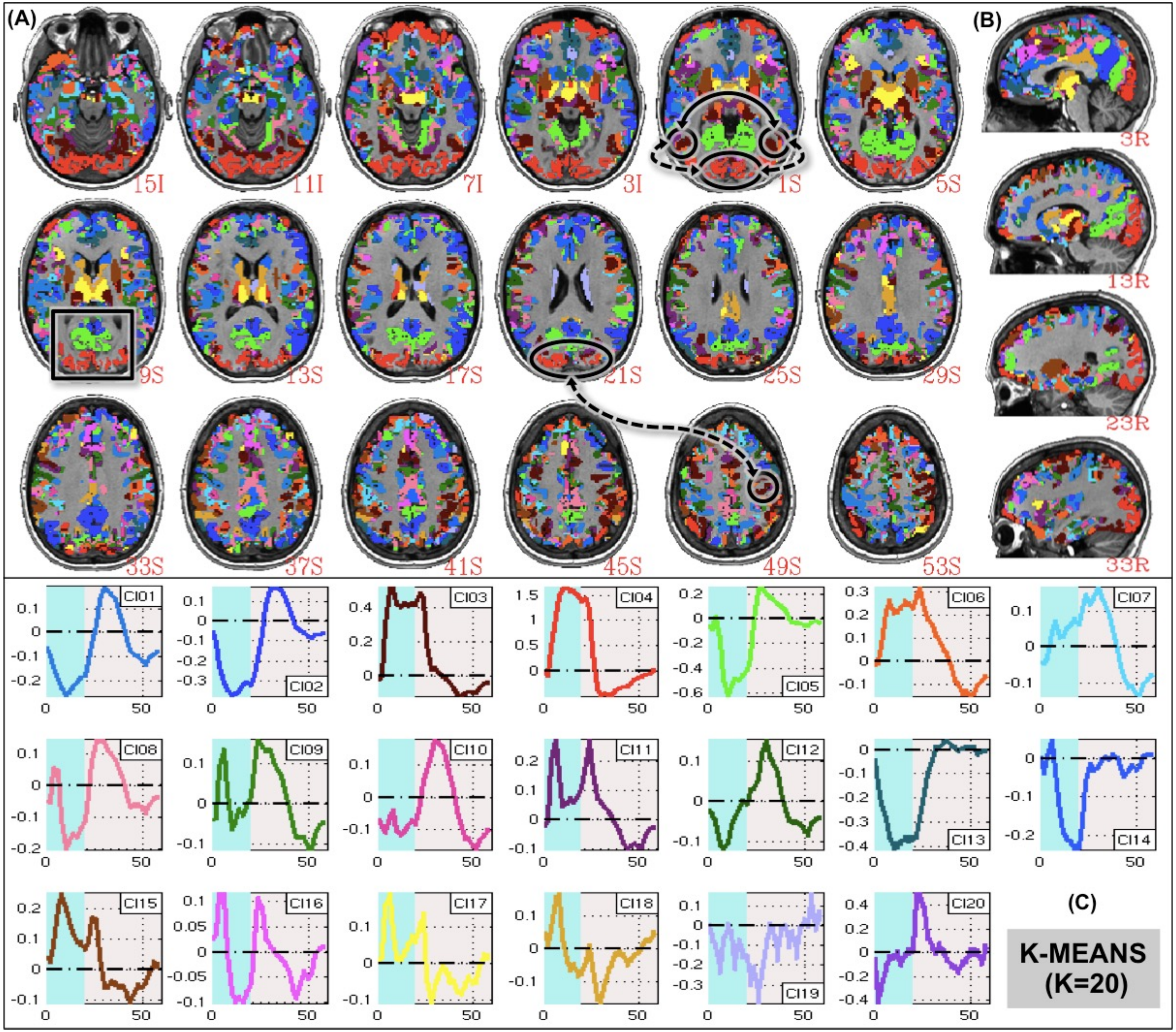


Reconstructing dynamic movies

Presented clip

Clip reconstructed from brain activity

Nishimoto et al (2011). Current Biology.


(A)
15I
11I
7I
3I
1S
5S
9S
13S
17S
21S
25S
29S
33S
37S
41S
45S
49S
53S
(B)
3R
13R
23R
33R
CI01
CI02
CI03
CI04
CI05
CI06
CI07
CI08
CI09
CI10
CI11
CI12
CI13
CI14
CI15
CI16
CI17
CI18
CI19
CI20
(C)
K-MEANS
(K=20)

Neuron
Article

A Continuous Semantic Space Describes the Representation of Thousands of Object and Action Categories across the Human Brain

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http://dx.doi.org/10.1016/j.neuron.2012.10.014

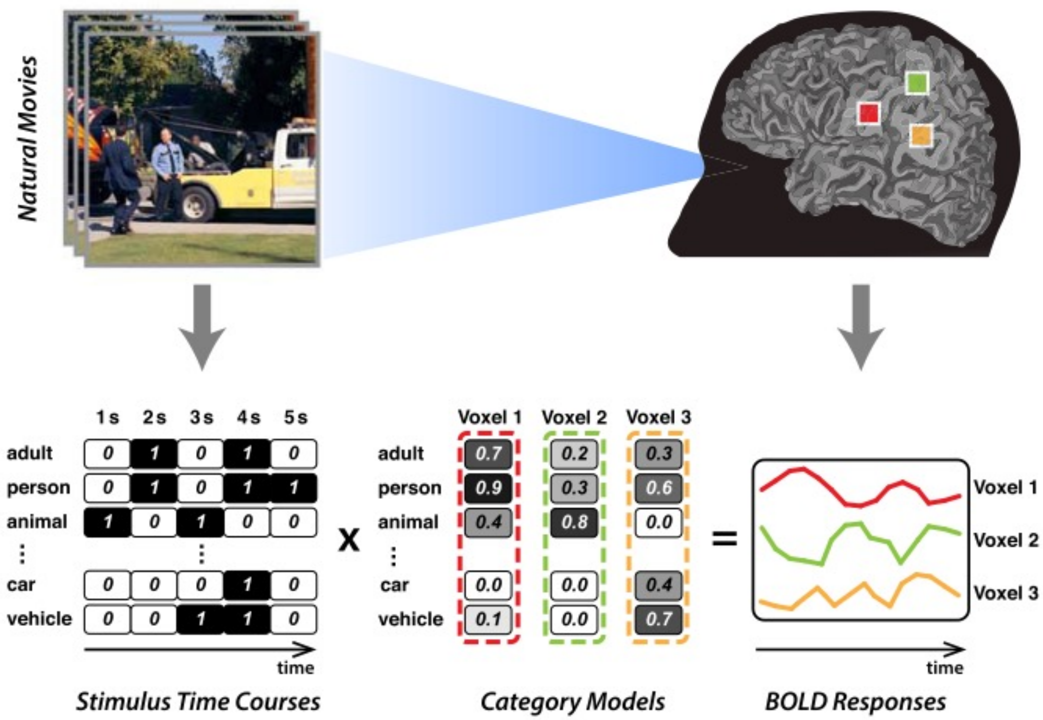

Figure 1. Voxelwise category encoding model. To construct the basis for the category model, the salient object and action categories in each 1 second epoch of movies were labeled using 1705 unique terms from the WordNet lexicon (Miller, 1995). The stimulus time courses were constructed in matrix form, with rows and columns representing distinct categories and epochs, respectively. Regularized linear regression was used to describe individual voxel responses as a weighted sum of these time courses. The fit model weights characterize the category responses of individual voxels to the corresponding object and action categories.

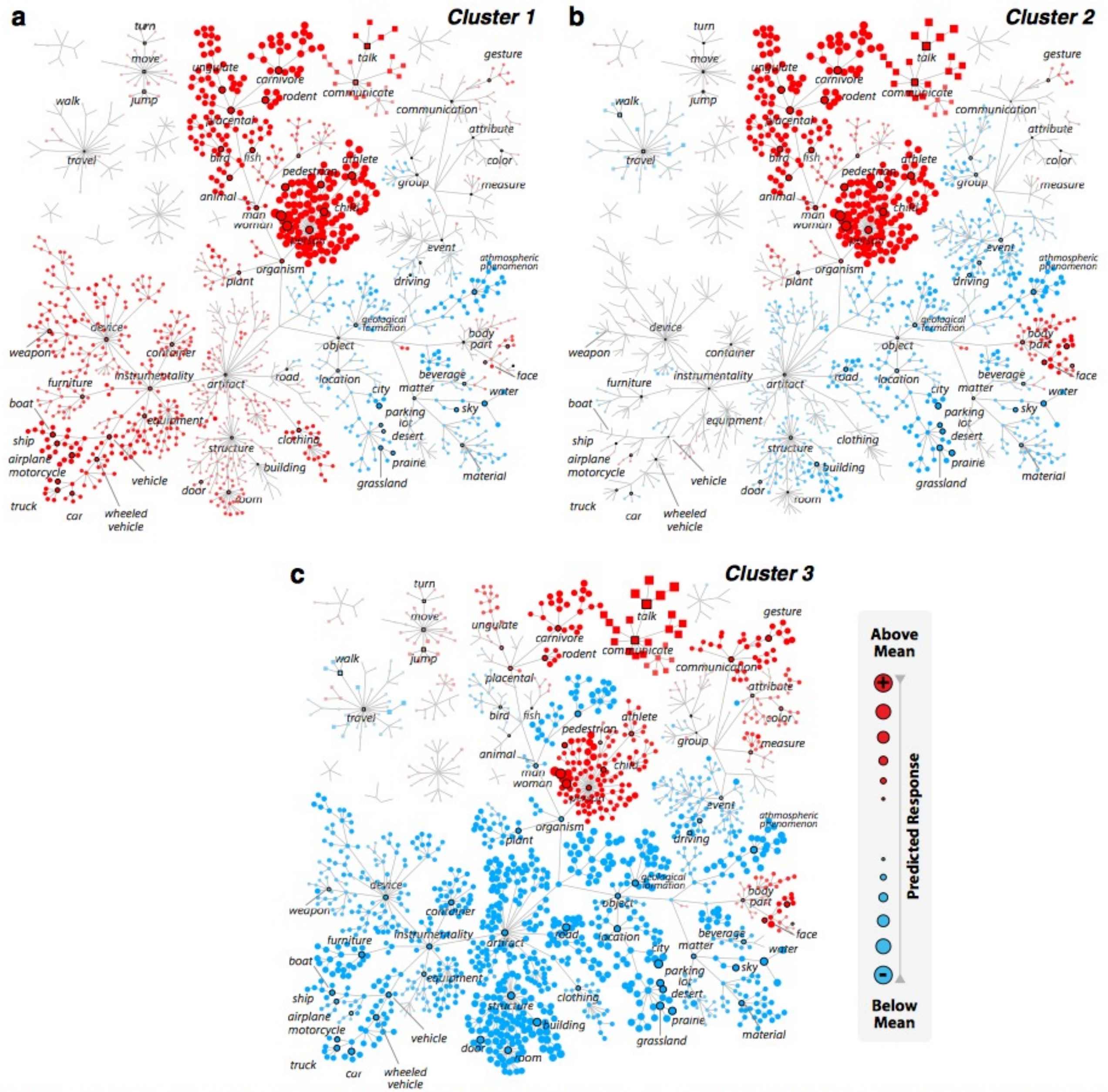

Figure 5. The cluster centers. Spectral clustering analysis among FFA voxels reveals three functional subdomains. ***a–c***, Mean tuning profiles across voxels within each cluster are shown using a series of graphs for object (main tree, circular vertices) and action (smaller trees, square vertices) categories. Subsets of the categories are labeled to orient the reader. The size of each vertex indicates the magnitude, whereas its color indicates the sign (red represents +; blue represents −) of the category response (see legend). ***a***, Responses of the first cluster are strongly enhanced by humans and animals and weakly enhanced by man-made instruments, including vehicles ($p < 0.05$, Monte Carlo test, FDR corrected). ***b***, Responses of the second cluster are strongly enhanced by humans and animals ($p < 0.05$) and weakly enhanced by body parts and communication verbs, including primary faces (faces that are the most salient object in the scene). ***c***, Responses of the third cluster are strongly enhanced by humans, placental mammals, communication verbs, gestures (i.e., facial gestures), and faces but strongly suppressed by man-made artifacts, particularly structures, such as buildings and rooms ($p < 0.05$). Responses of all three clusters are suppressed by many natural objects, such as geological landscapes and natural materials ($p < 0.05$).

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Interesting Directions in Interpretation

Dynamics of resting state

Global resting state signal

Whole brain activation

Non-typical hemodynamic shapes

Post undershoot

Biomarker development

Layer and column dependent activation

Flow vs BOLD vs Volume

CMRO2 calibration

Baseline CMRO2

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Most exciting trends in Applications

- From Populations to Individuals

- Longitudinal fMRI / MRI studies over multiple time scales

- Clinical Use:

  Current: pre-surgical mapping, "locked-in" patients
  Future: psychiatric assessment, behavioral prediction, drug effects, neurologic assessment,
  differential diagnosis of PTSD vs TBI, recovery/plasticity assessment, therapy with real-time feedback, continuous attention determination

For the Individual:

- psychiatric assessment behavioral prediction
- drug effects
- neurologic assessment
- differential diagnosis of PTSD vs. TBI
- recovery/plasticity assessment
- therapy with real-time feedback

The challenge:

- Effect size / variability > 10
- Classification and modeling can improve this ratio…depending on the question being asked.

In 20 years

Technology

Field Strength -7T most common,
-19 T human scanner in place
-wearable 1.5T scanner helmet
-ultra low (Larmor = brain frequencies)
RF Coils -128+ arrays common, flexible, highly configurable, micro-coils
Gradients – Flexible, wearable, up to 100 G/cm
Shim – Solved.
Pulse Sequences -automated optimization based on menu of what's desired
-multiple simultaneous contrast and synthetic contrasts the norm
Image resolution -50 um common, 10 um doable

Methodology

Real time
Fully automated real time scanning, analysis, and assessment
Wireless, comprehensive subject interface
-eeg, nano-electrode implants
-nerve transmission
-temperature
-muscle tension
-eye position
-respiration, CO2, heart, blood pressure
-hormone level
-GSR
Optogenetics
Focused acoustic activation and other stimulation methods
3D coordinate system in decline, new network-based system

Interpretation

We will be using every aspect of signal:
-magnitude
-undershoot
-fluctuations at each frequency and phase
-transients
-rise time
-fall time
-refractivity
-slow trends
-NMR phase

We will have full calibration
-metabolism will be routine

All non-neuronal noise will be completely removed

Applications

Neuroscience
Physiology
Genetics
Psychotherapy
Physical therapy
Education (track myelin and grey matter changes)
Lie detection (motivation, sincerity & bias detection)
Biofeedback for self improvement
Job testing and screening
Amusement park rides
Brain-Interfaced Video games
Communication enhancement
Brain Computer interface guidance
(where to put the nano-electrodes and nano-stimulators)
MRI scan part of routine checkup

Resting state will completely outstrip activation related