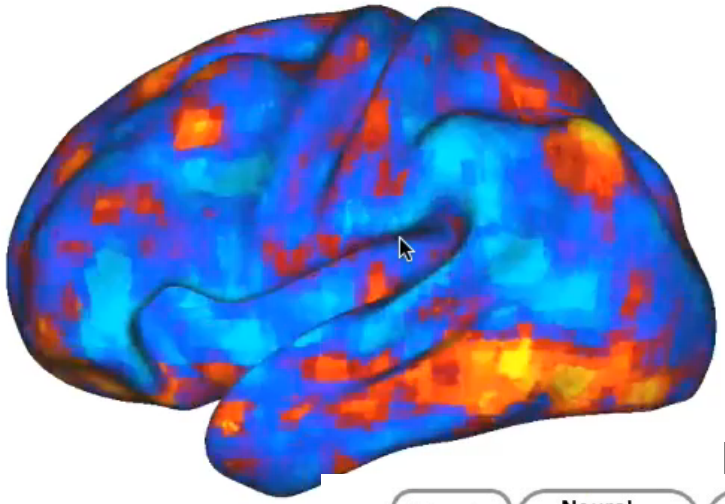
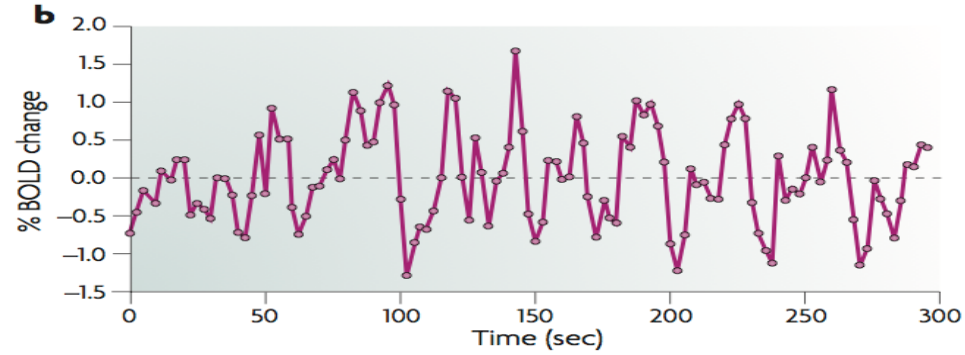
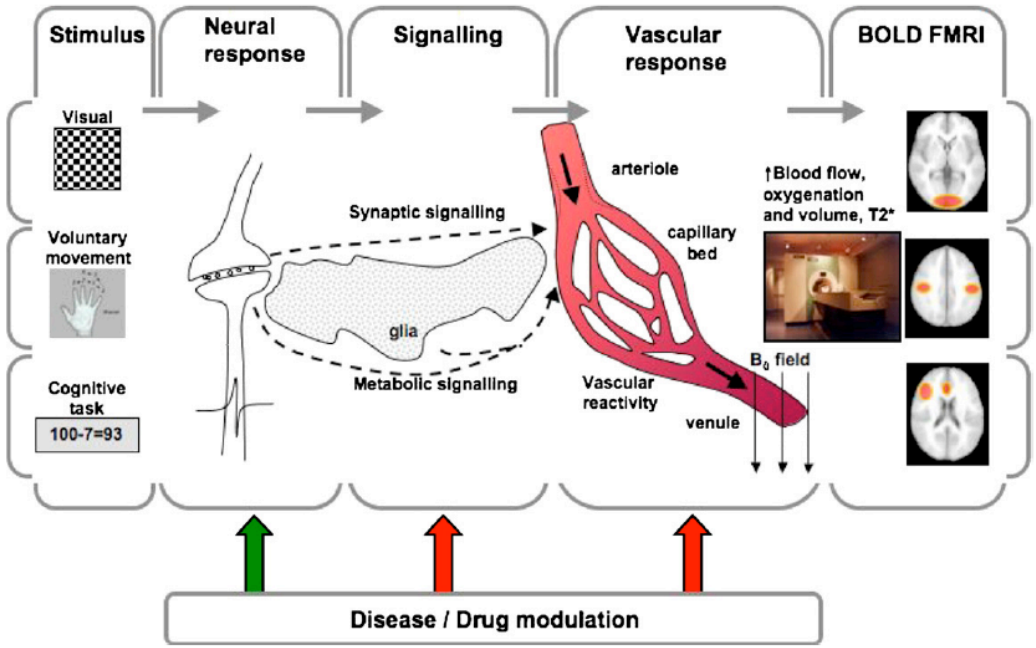
Neurovascular Factors in Resting-State fMRI

Thomas Liu
Center for Functional MRI
University of California San Diego

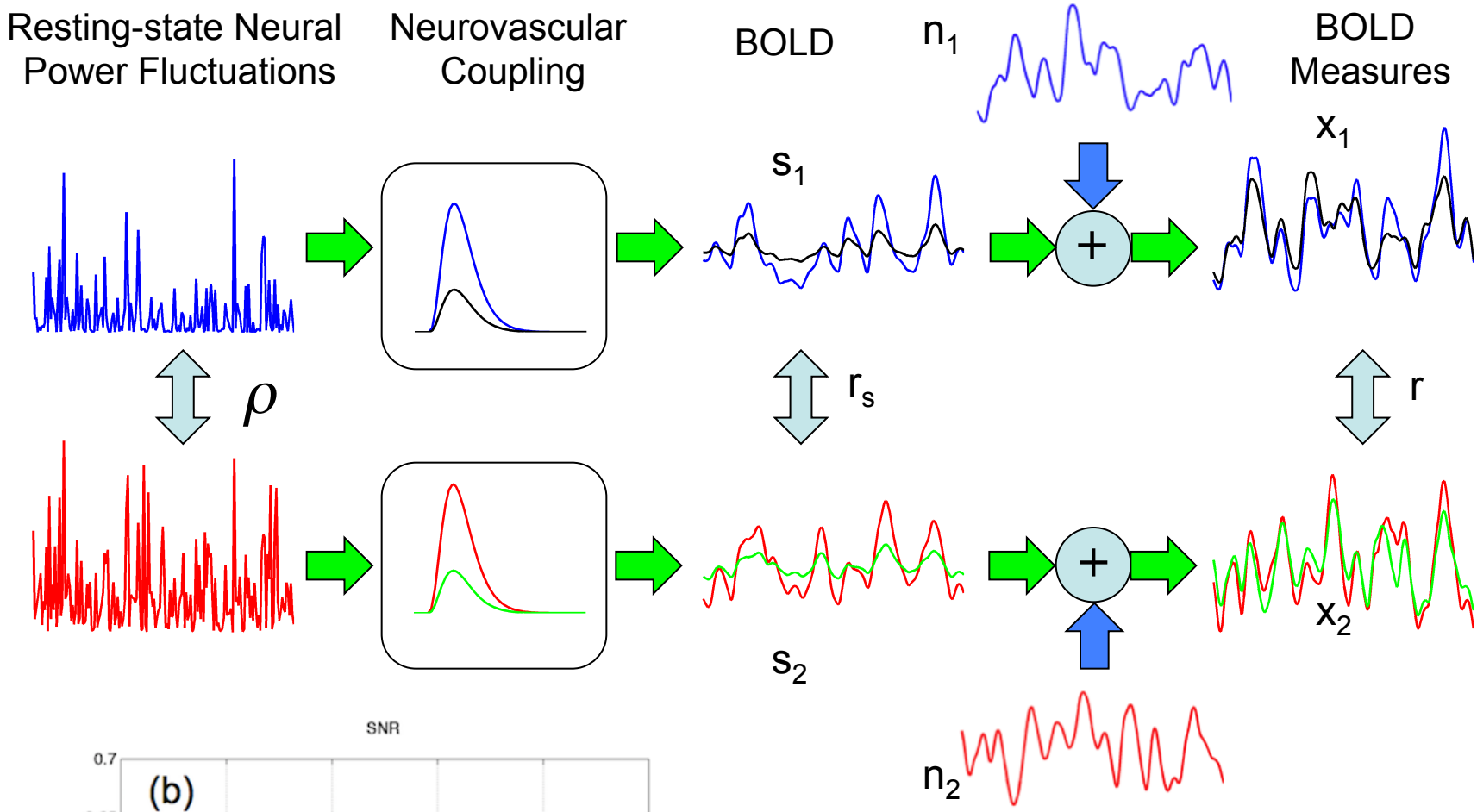
Resting-State fMRI

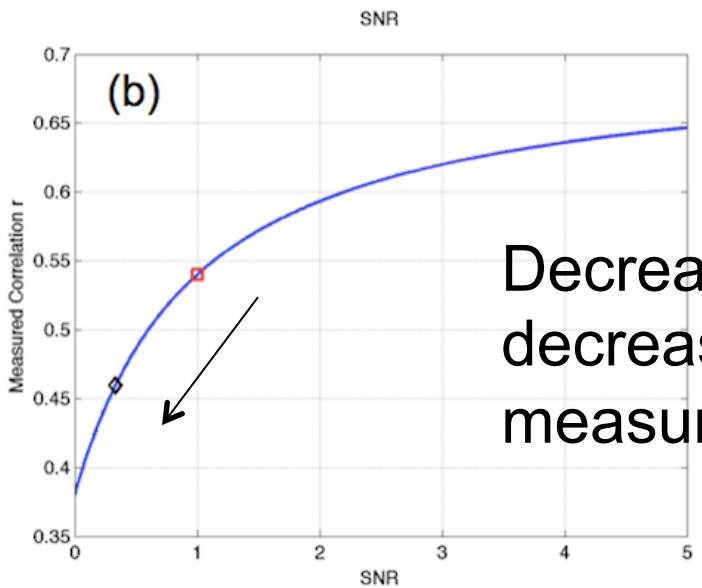






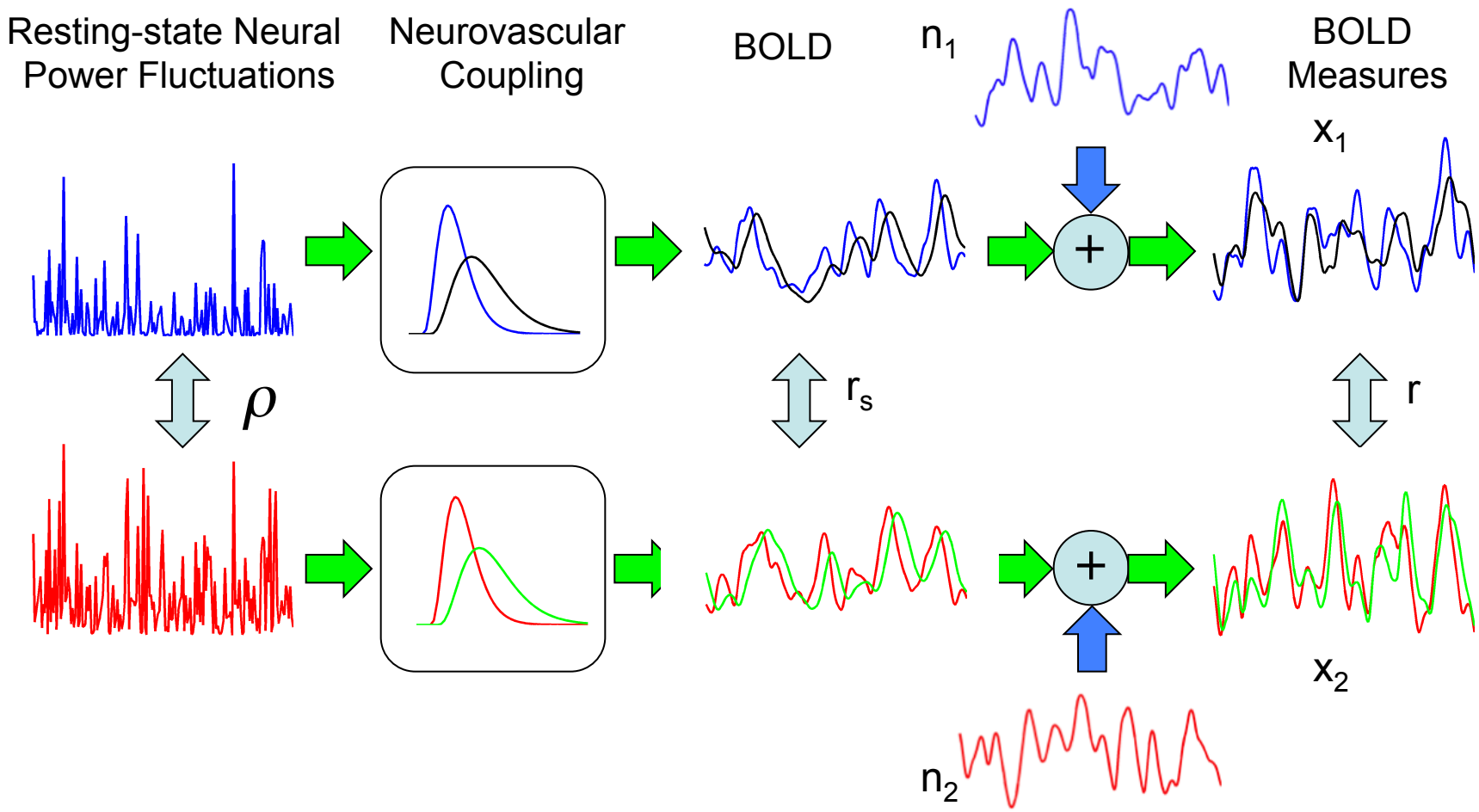
Fox and Raichle 2005; Iannetti and Wise 2007; http://www.youtube.com/watch?v=VaQ66lDZ-08&feature=plcp





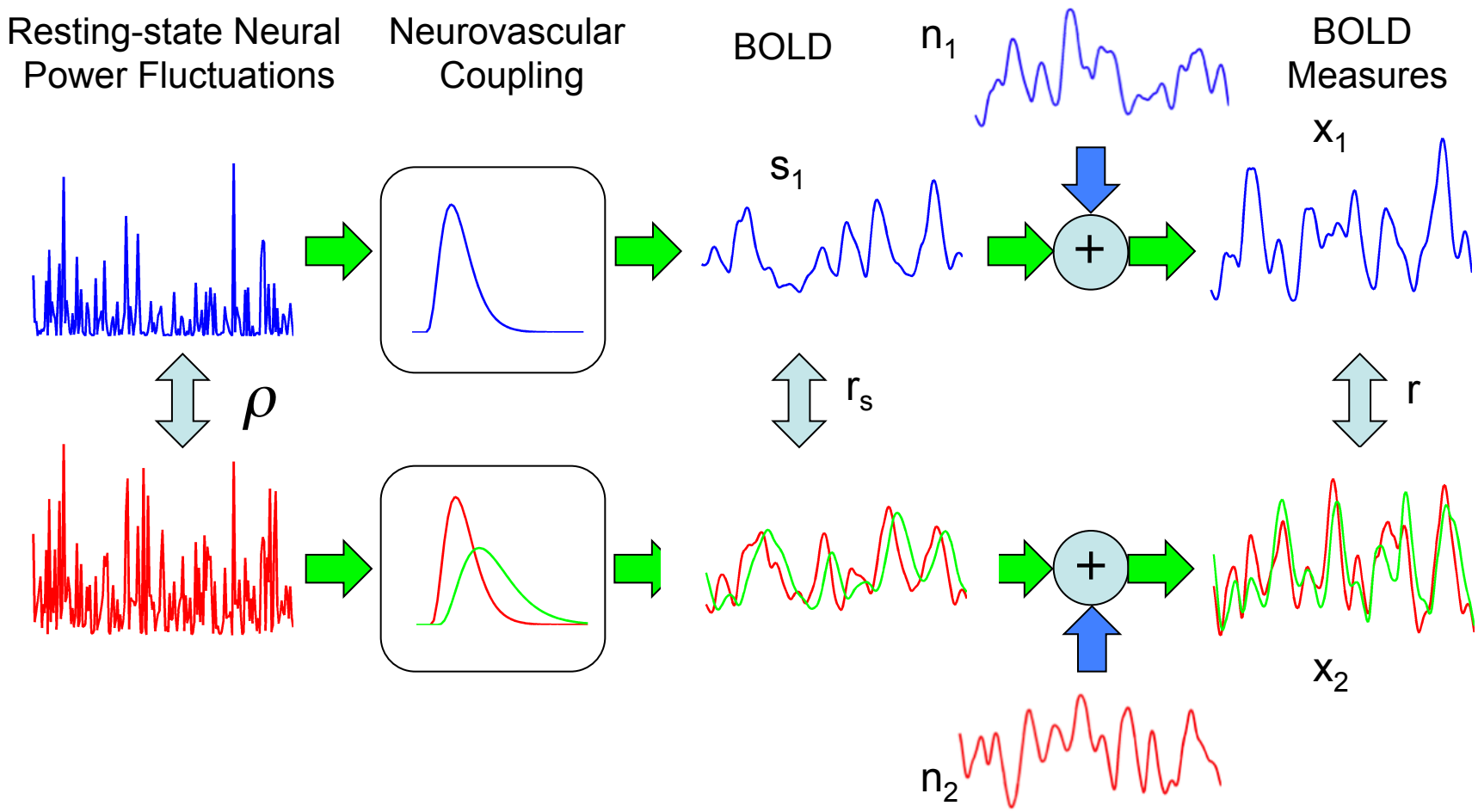
Decrease in HDR amplitudes leads to a decrease in correlation between BOLD measures of 0.54 to 0.41.

Liu, NIMG 2013



Broadening of both hemodynamic response functions leads to a decrease in correlation between the BOLD measures of 0.54 to 0.34.

Liu, NIMG 2013



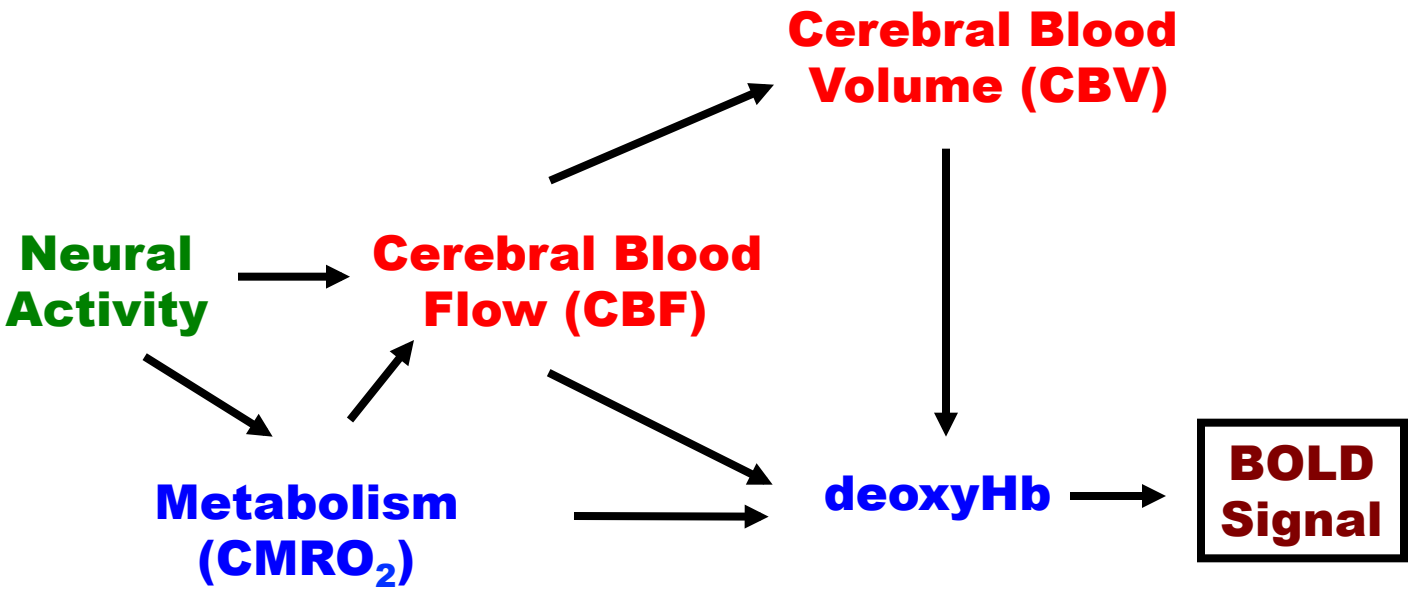
Broadening of the lower hemodynamic response function (red to green) leads to a decrease in correlation between the BOLD measures of 0.54 to 0.17.

Liu, NIMG 2013

Approaches and Issues

- Arguments based on BOLD signal model and prior observations.
- Comparing effects across networks.
- Calibrated fMRI
- Global Signal Effects
- Multimodal Experiments

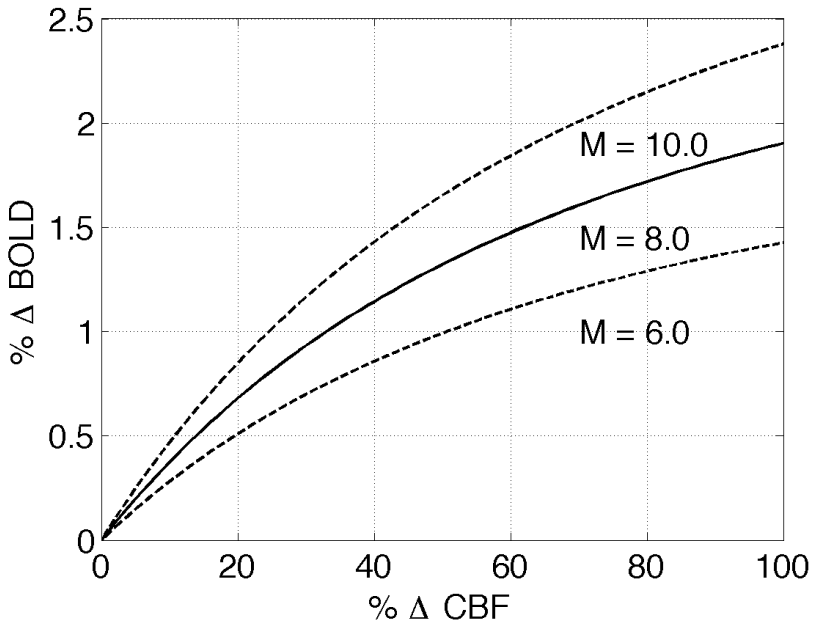
BOLD Signal Model

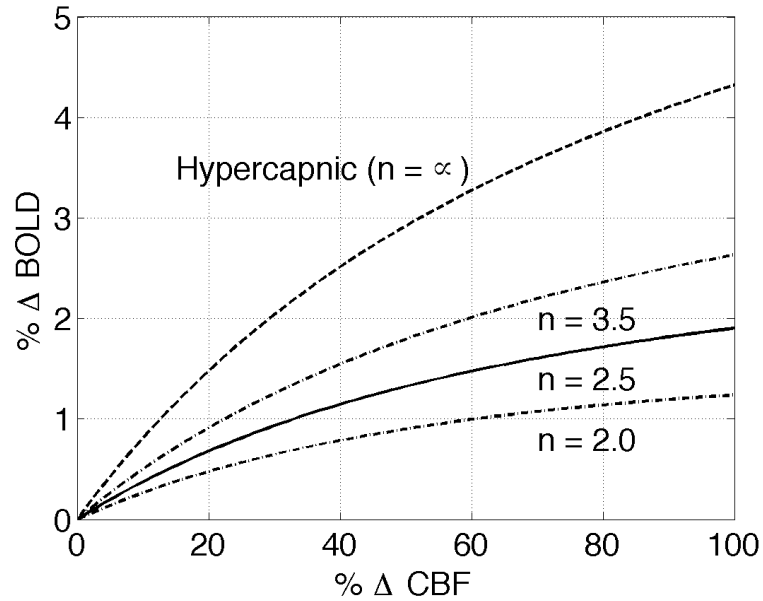


$$\frac{\Delta BOLD}{BOLD_0} \approx M\left(1 - f^{\alpha-\beta} m^{\beta}\right)$$

$$f = \frac{CBF}{CBF_0}; \quad m = \frac{CMRO_2}{CMRO_{2,0}}$$

$$\frac{\Delta BOLD}{BOLD_0} \approx M\left(1 - f^{\alpha-\beta} m^{\beta}\right)$$





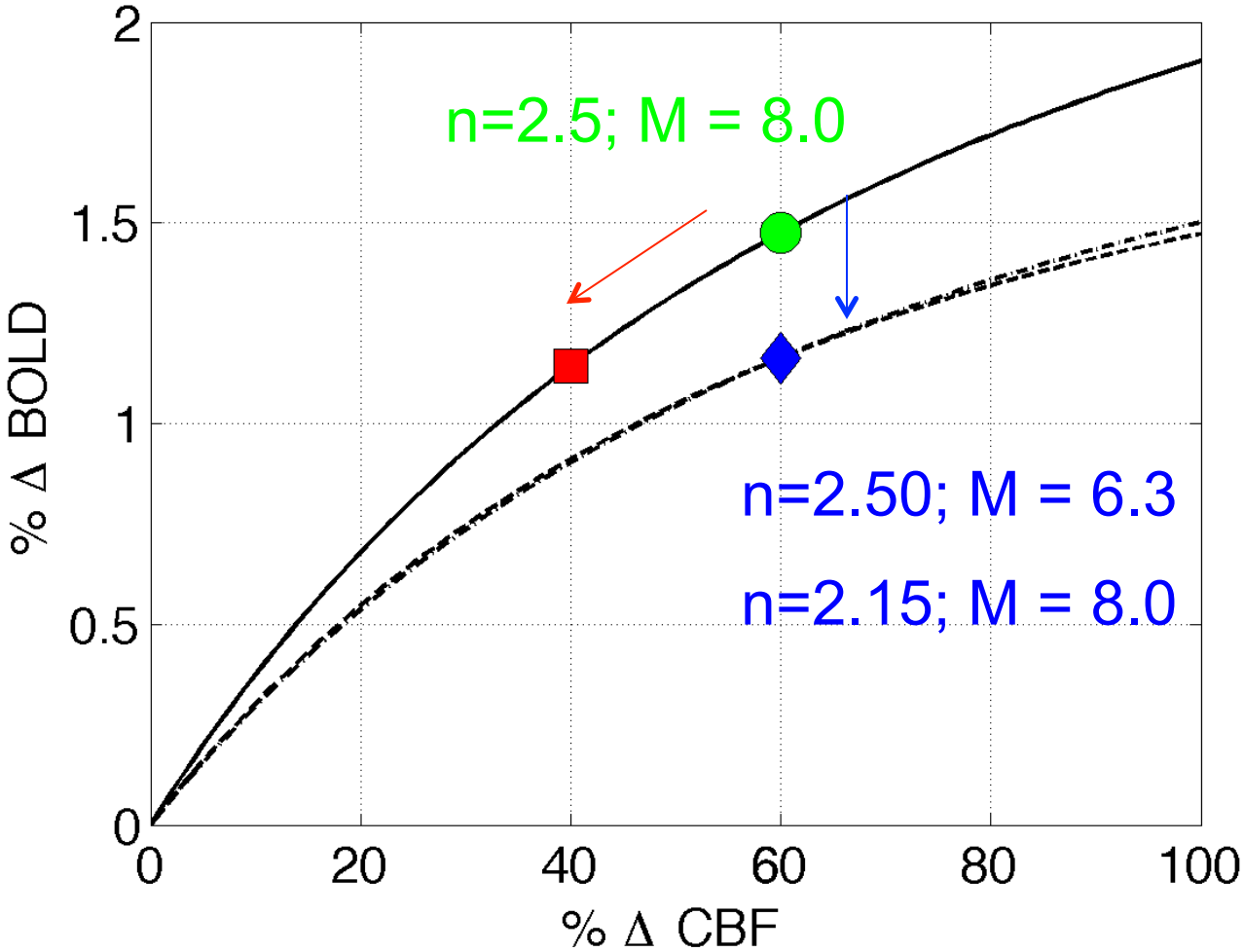
Maximal BOLD signal

$$M = TE \cdot A \cdot CBV_0 \cdot [dHb_0]^{\beta}$$

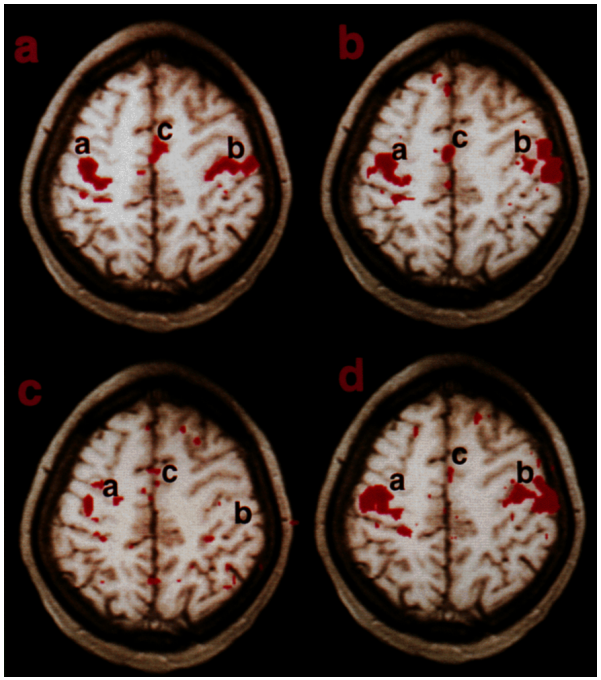
CBF/CMRO$_2$ Coupling Factor

$$n = \frac{\%\Delta CBF}{\%\Delta CMRO_2} = \frac{f-1}{m-1}$$

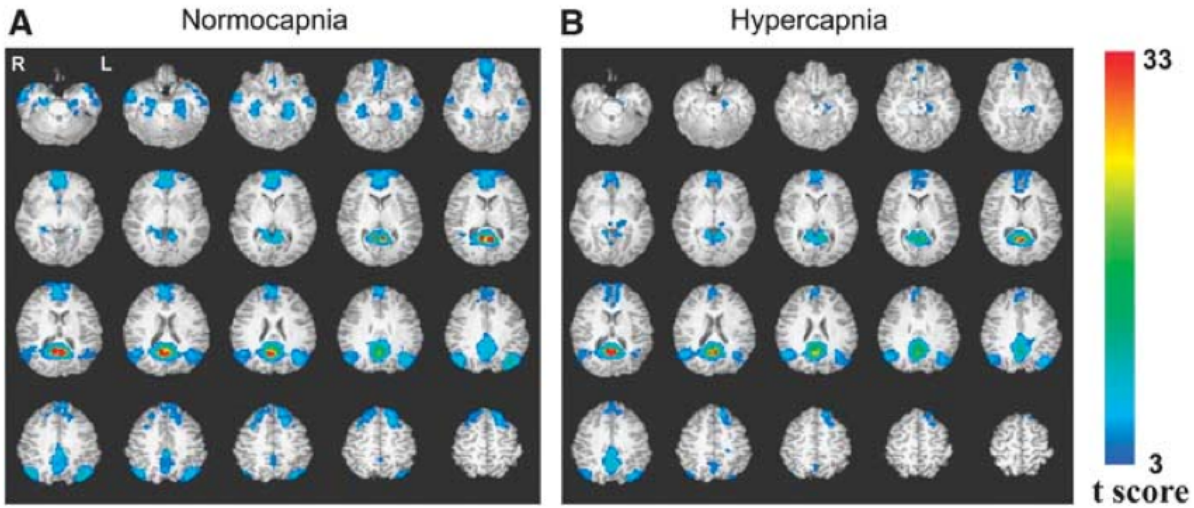
Different ways to accomplish the same change in BOLD



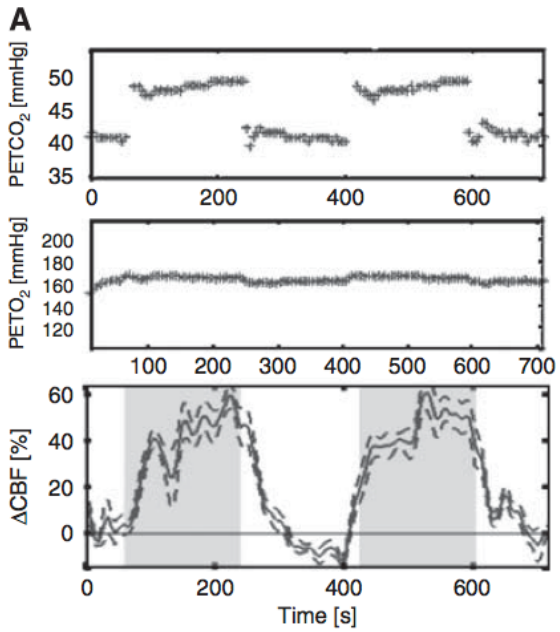
Case Study: Effects of Hypercapnia on Functional Connectivity



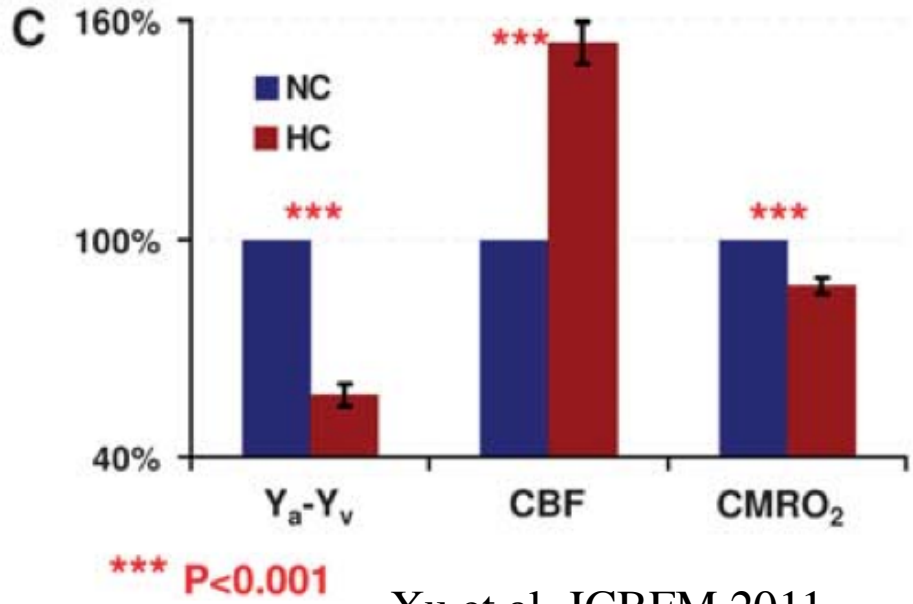
Biswal et al, JCBFM 1997



Xu et al, JCBFM 2011



Chen and Pike, JCBFM, 2010

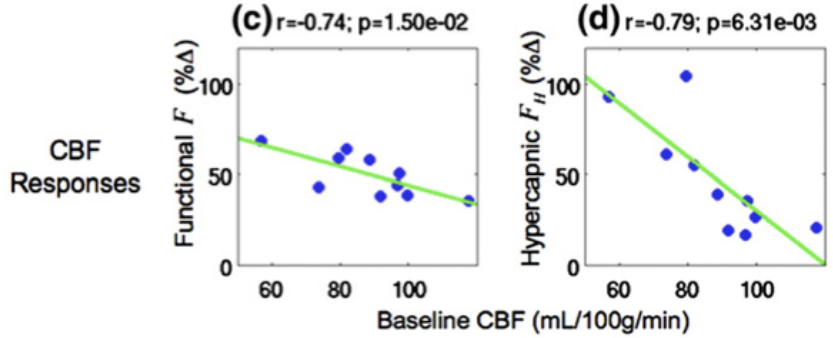


Xu et al, JCBFM 2011

CBF_0 ⇧ → dHB_0 ⇩ → M ⇩ → BOLD ⇩

$CMRO_{2,0}$ ⇩ ?

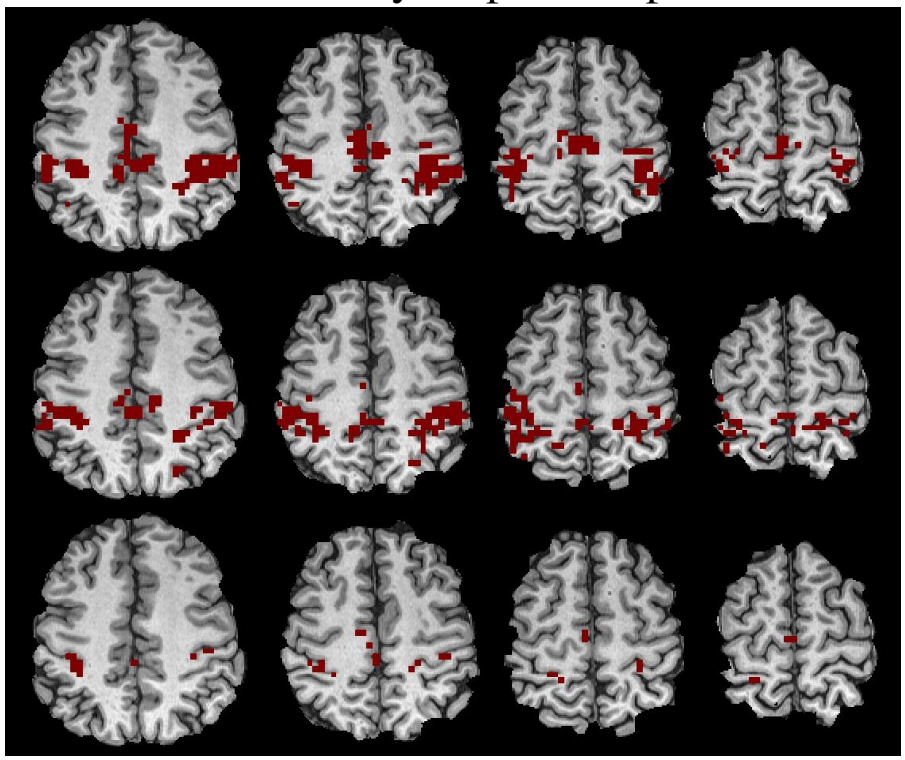
ΔCBF ⇩ → BOLD ⇩

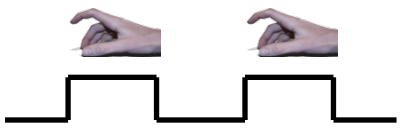


Liau et al NIMG 2009

Case Study: Effects of Caffeine on Functional Connectivity

Functional connectivity maps for representative subject



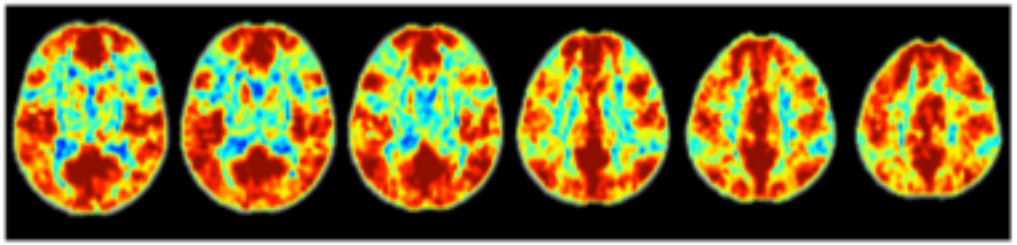


Activation Map

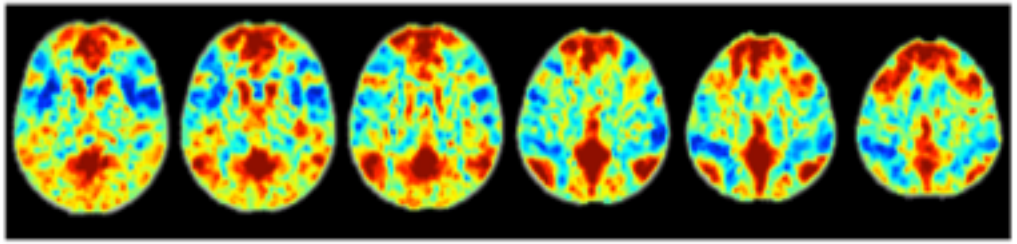
Rest

Rest 

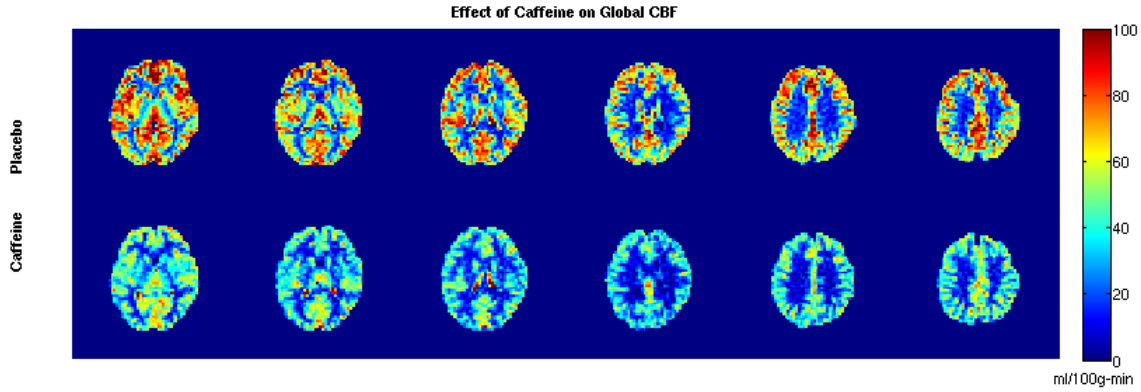
pre-dose



post-dose

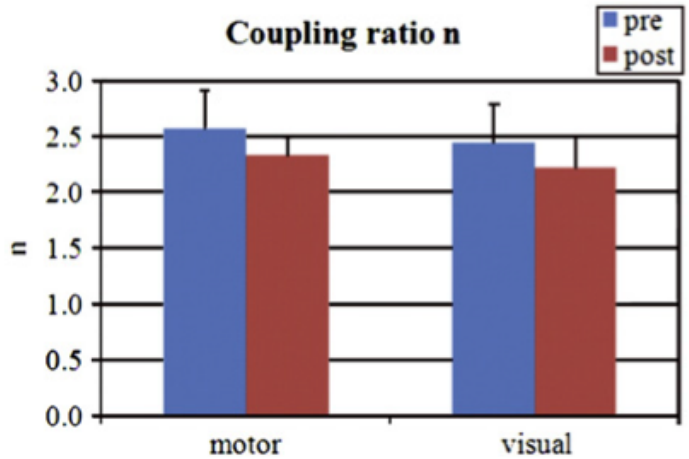


Wong et al; NIMG 2012;, Rack-Gomer et al, NIMG, 2009



$CBF_0 \Downarrow \longrightarrow dHB_0 \Uparrow \longrightarrow M \Uparrow \longrightarrow BOLD \Uparrow$

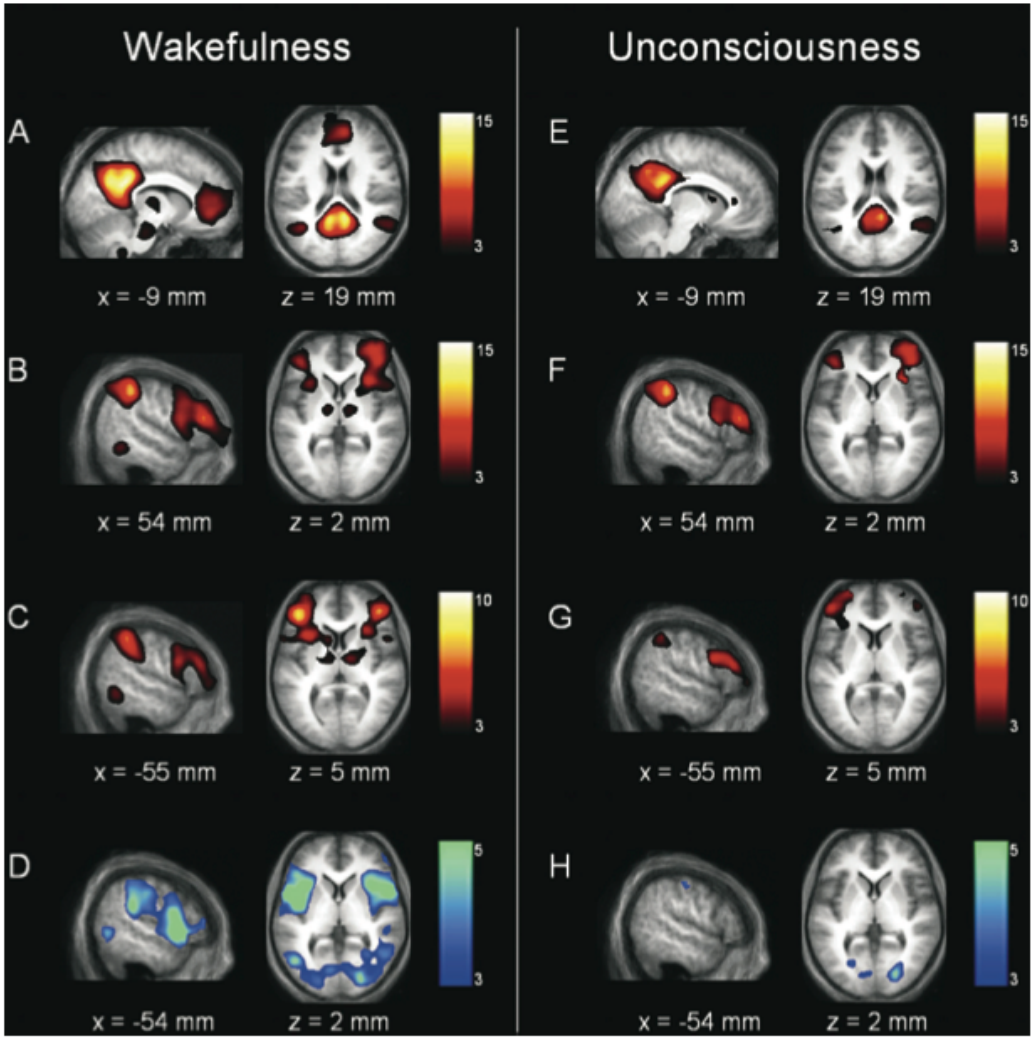
$CMRO_{2,0} \Uparrow$? $\nearrow dHB_0$

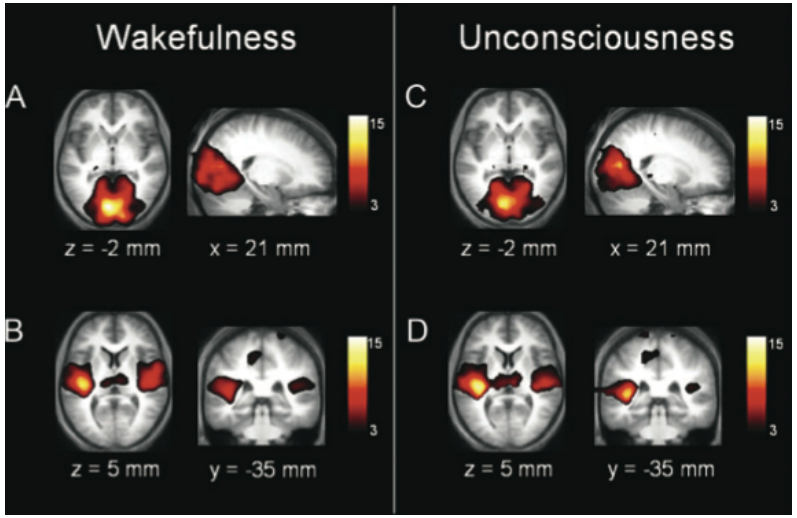


$n \Downarrow \longrightarrow BOLD \Downarrow$

Chen and Parrish 2009; Rack-Gomer et al, NIMG, 2009; Griffeth et al 2011; Xu et al ISMRM2014, p. 4168

Case Study: Effects of Propofol

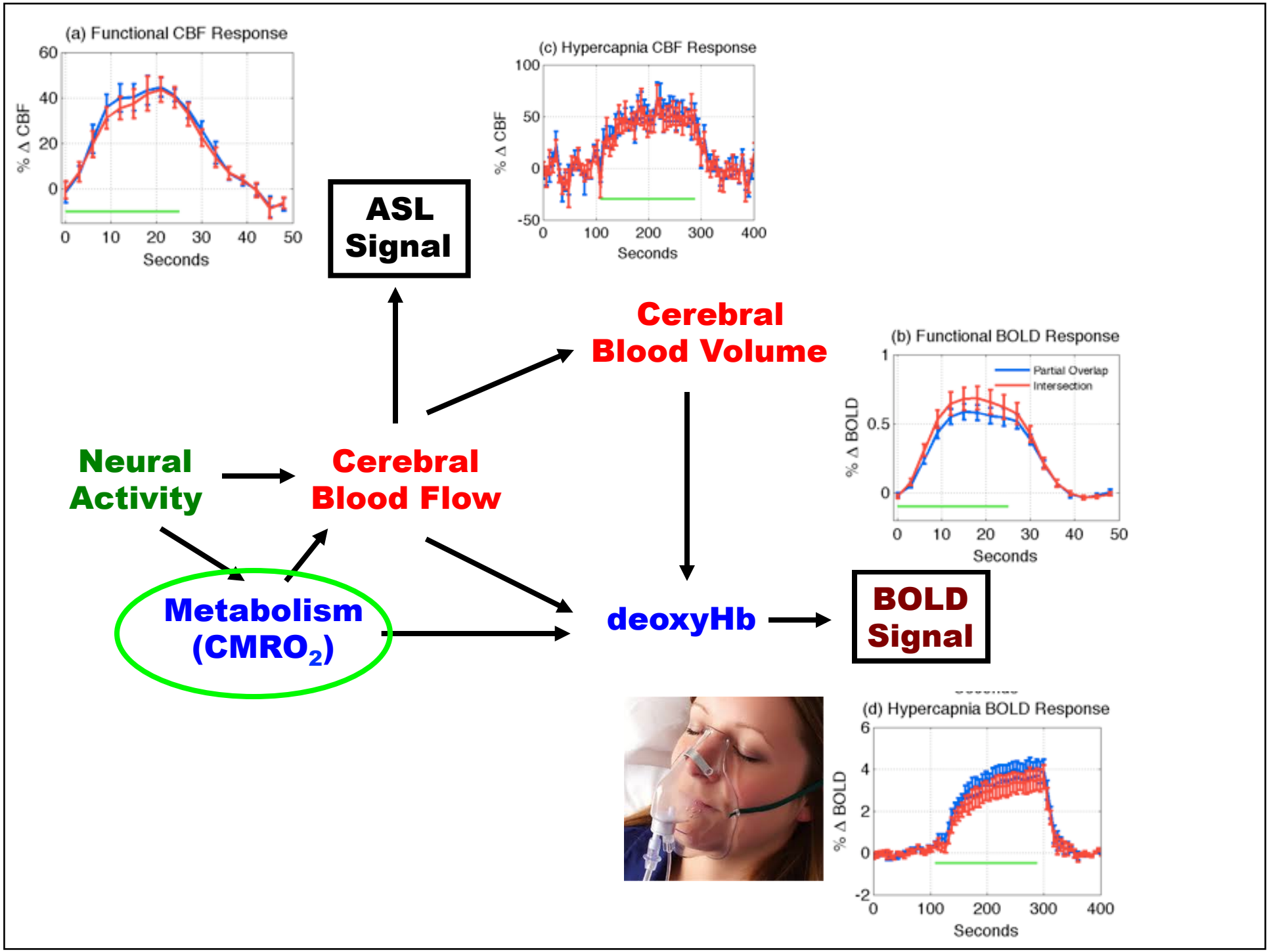




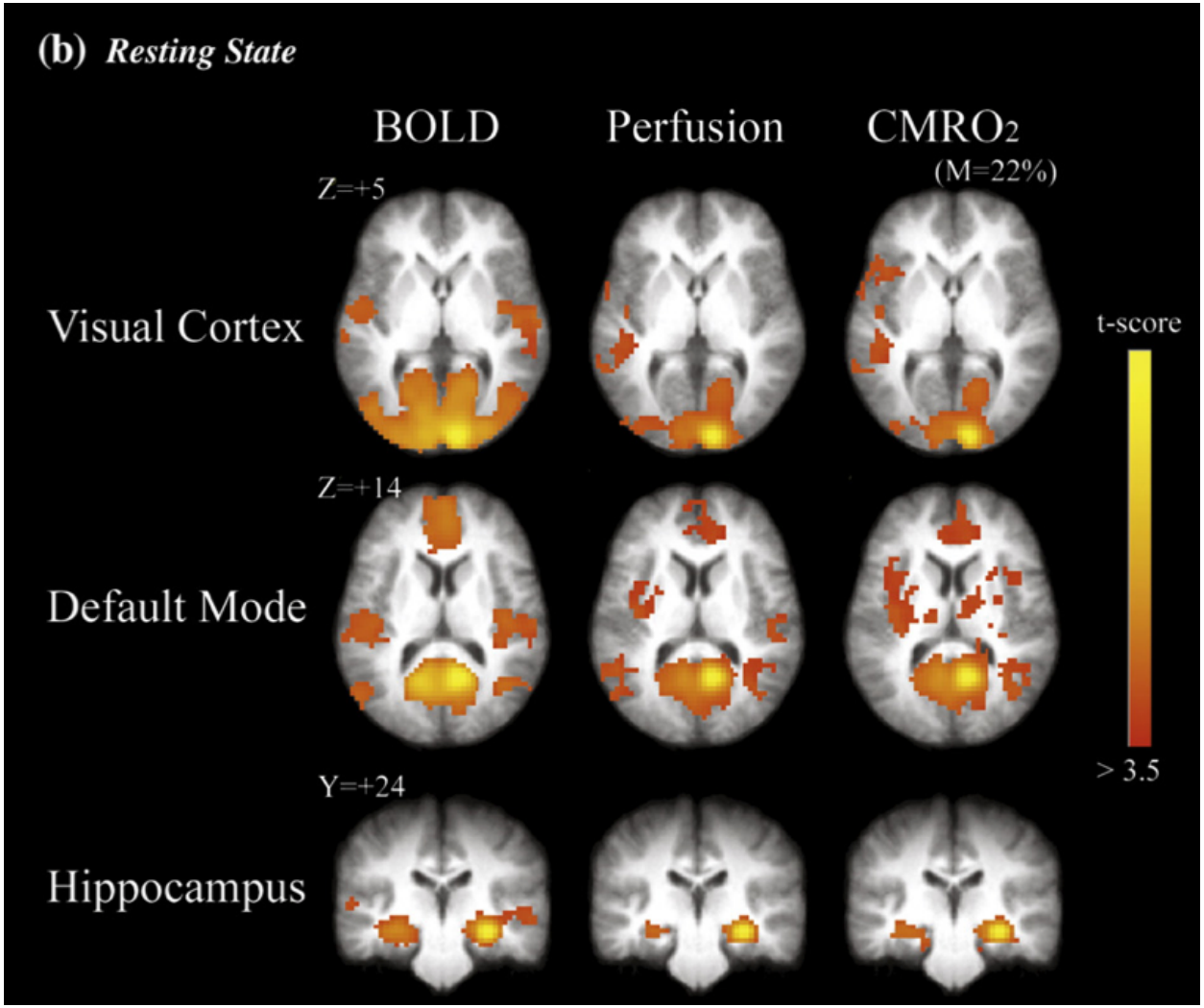
Connectivity reduced in frontoparietal network, but not in auditory and visual networks.

Also, prior studies indicate propofol does not alter either CBF response or flow-metabolism coupling

Boveroux et al 2010

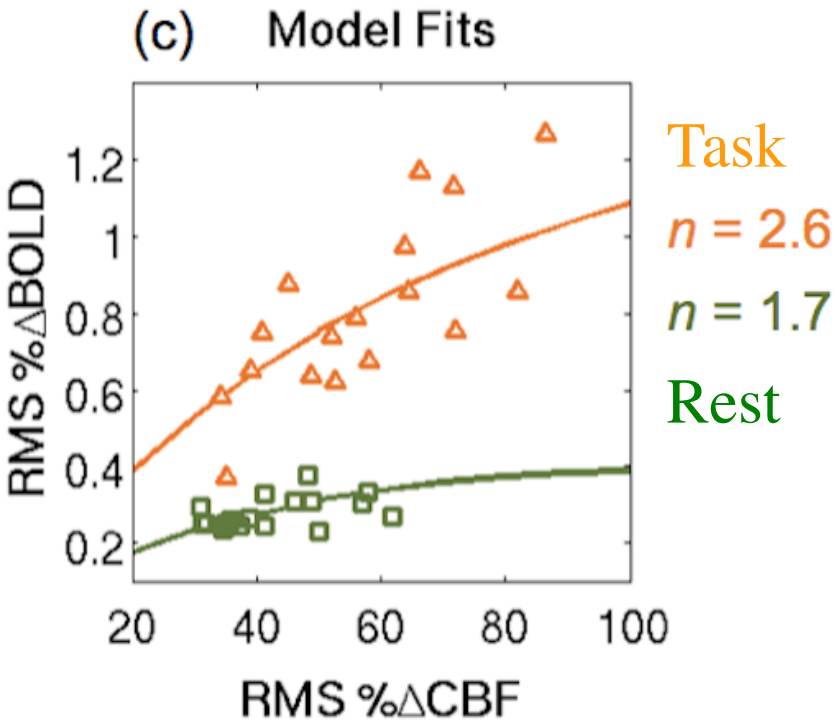

(a) Functional CBF Response
% Δ CBF
Seconds
(c) Hypercapnia CBF Response
% Δ CBF
Seconds
ASL Signal
Cerebral Blood Volume
(b) Functional BOLD Response
Partial Overlap
Intersection
% Δ BOLD
Seconds
Neural Activity
Cerebral Blood Flow
Metabolism ($CMRO_2$)
deoxyHb
BOLD Signal
(d) Hypercapnia BOLD Response
% Δ BOLD
Seconds

Calibrated fMRI of Resting-state Connectivity



Wu et al, NIMG 2009

Calibrated fMRI of Resting-state Measures



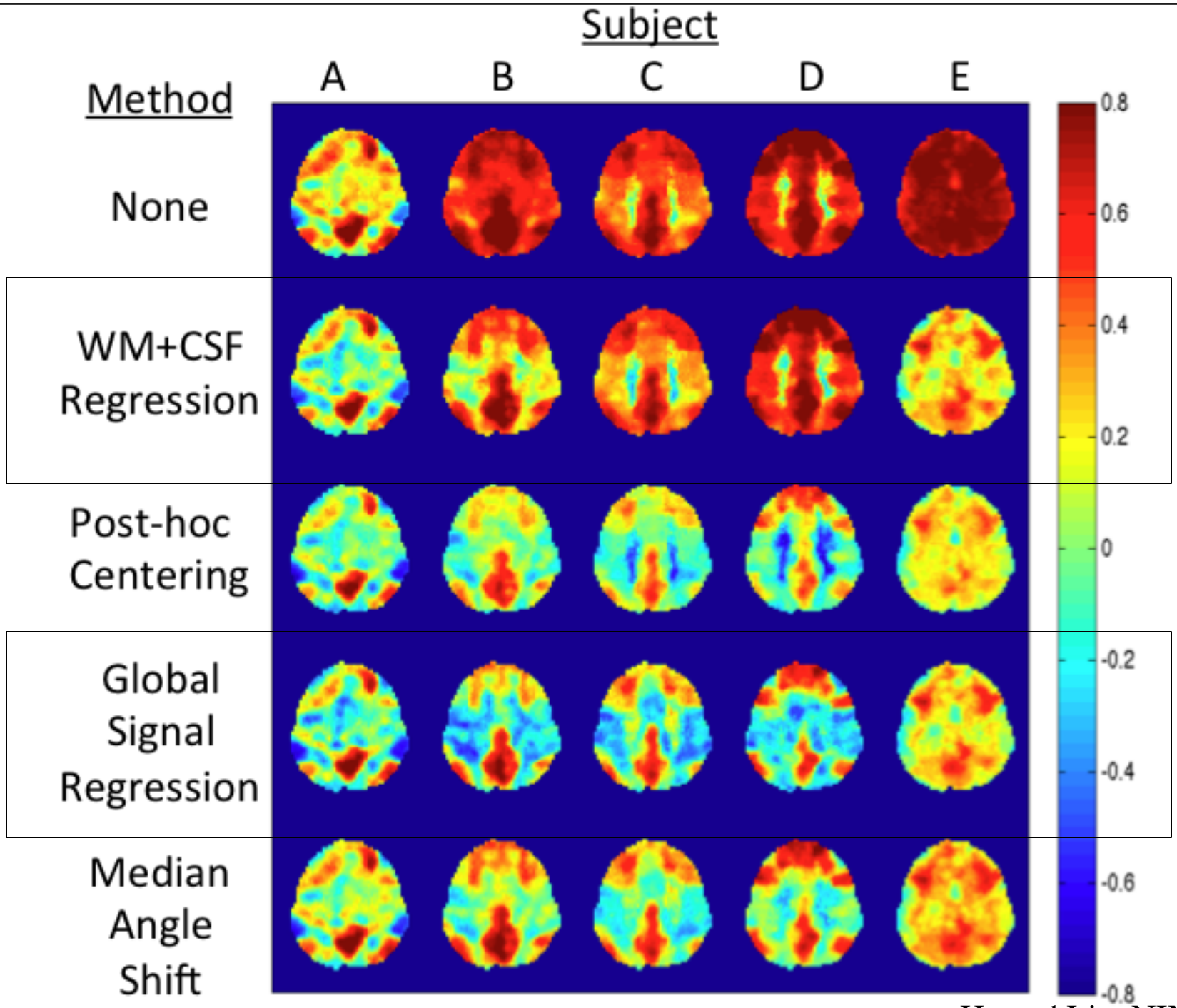
$$\left(\frac{CMRO_2}{CMRO_{20}}\right)^{\beta} = \left(\frac{CBF}{CBF_0}\right)^{\beta-\alpha}\left[1-\left(\frac{\Delta BOLD/BOLD_0}{M}\right)\right]$$

As BOLD signals get smaller

$$\left(\frac{CMRO_2}{CMRO_{20}}\right) \rightarrow \left(\frac{CBF}{CBF_0}\right)^{1-\frac{\alpha}{\beta}}$$

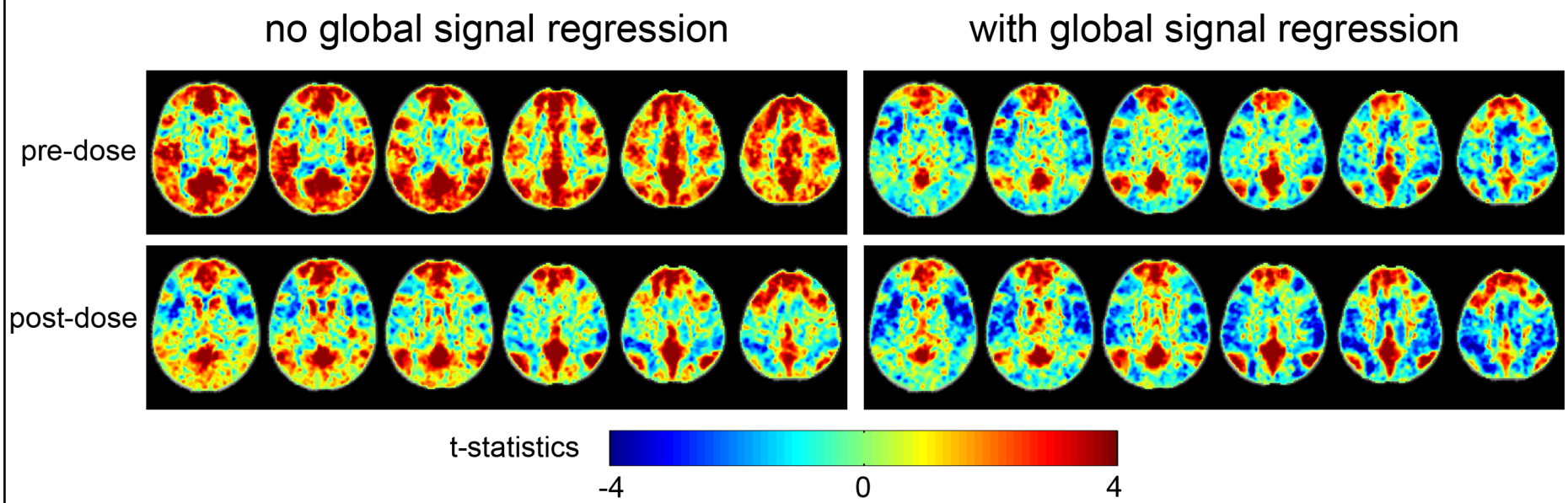
$CMRO_2$ estimates are driven primarily by the CBF measures

Restom et al 2008; Rack-Gomer 2011



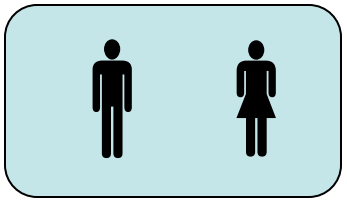
He and Liu, NIMG 2012

How global signal regression can alter interpretation of an experiment



Wong et al, NIMG 2012

Case Study: Effects of Caffeine Revisited



4 6

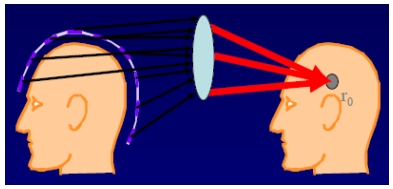
PRE

Caffeine

OR

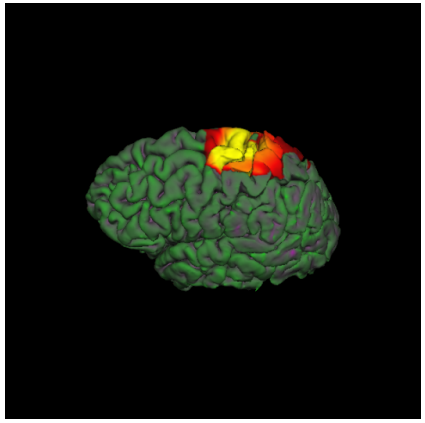
Placebo

POST

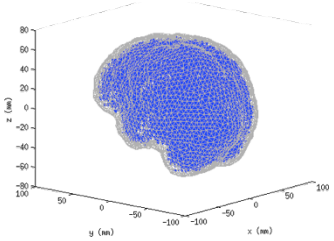


Inverse Model

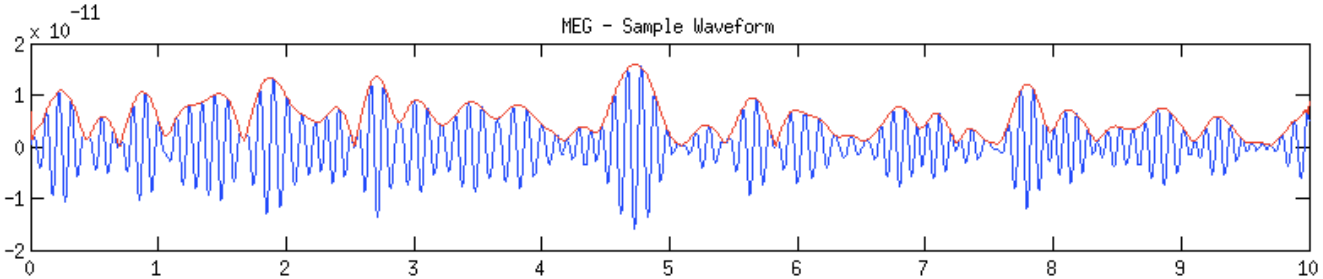
Forward Model

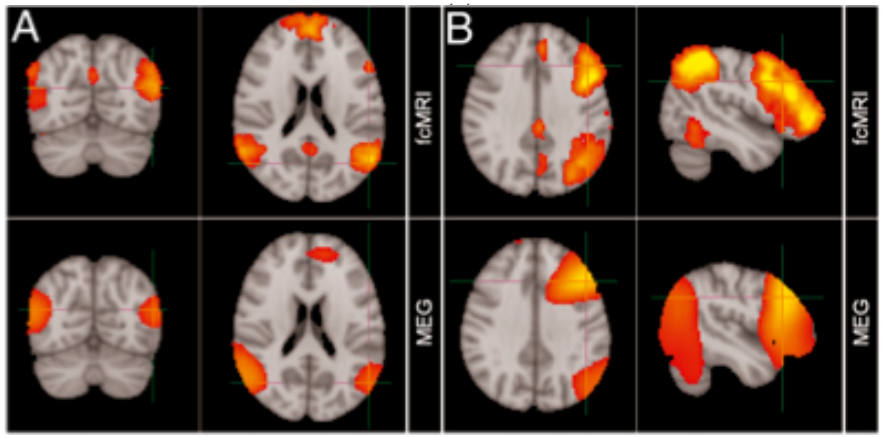


Sensor Space

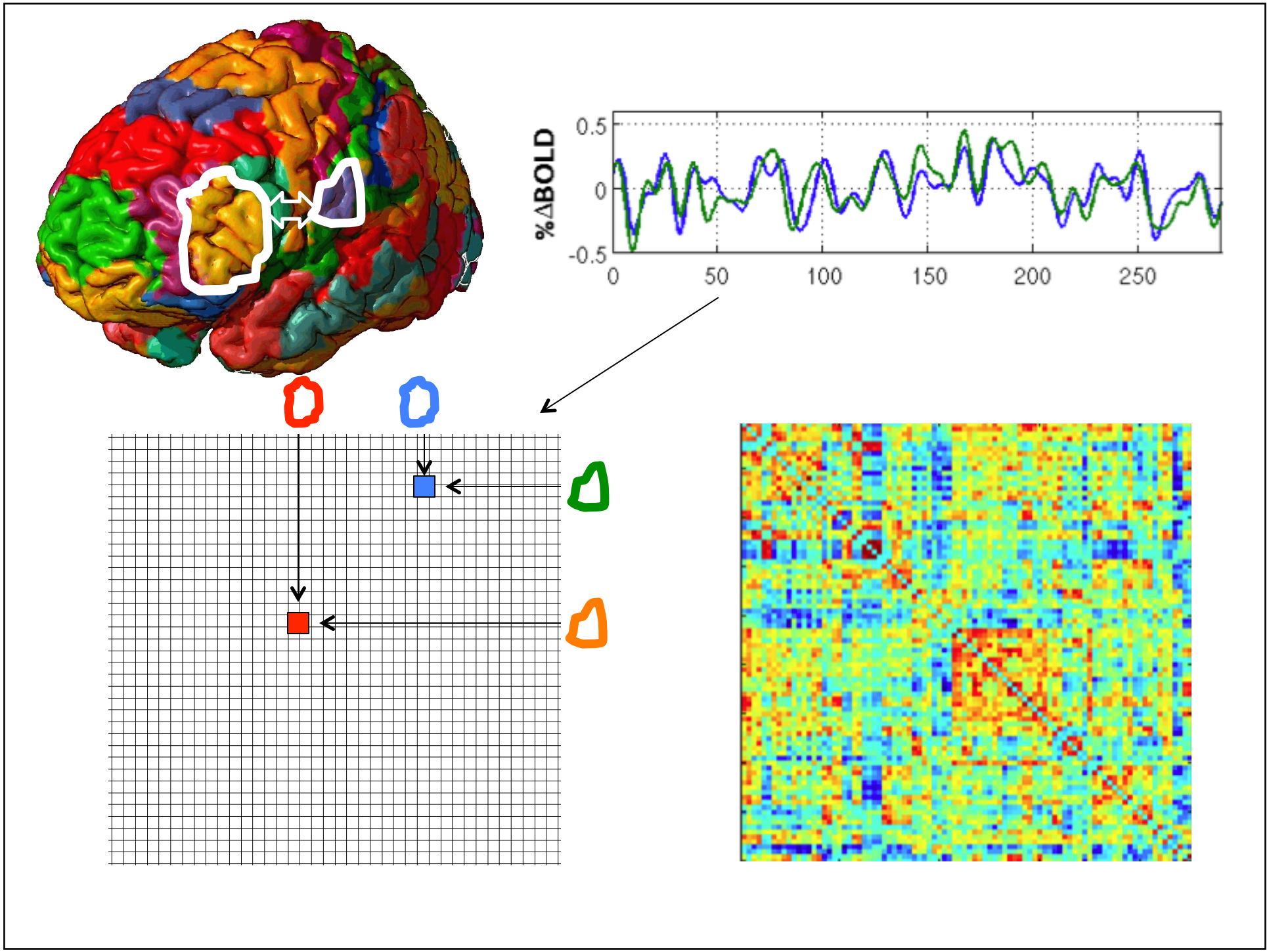


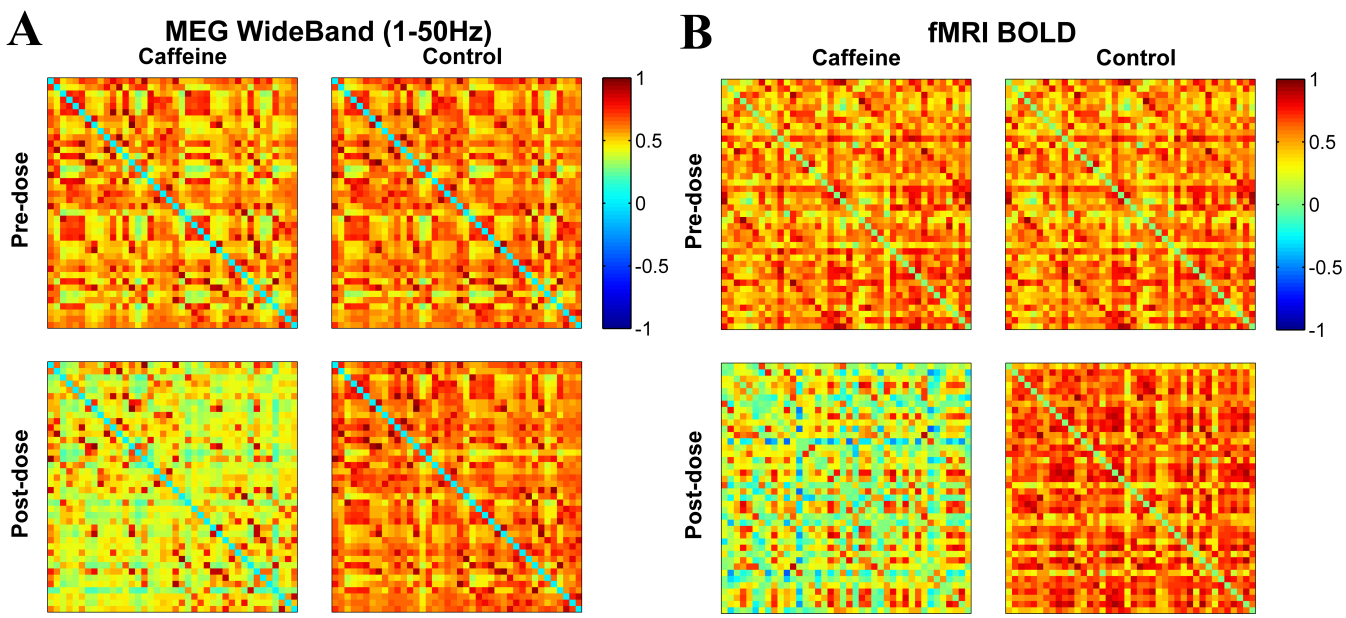
Source Space



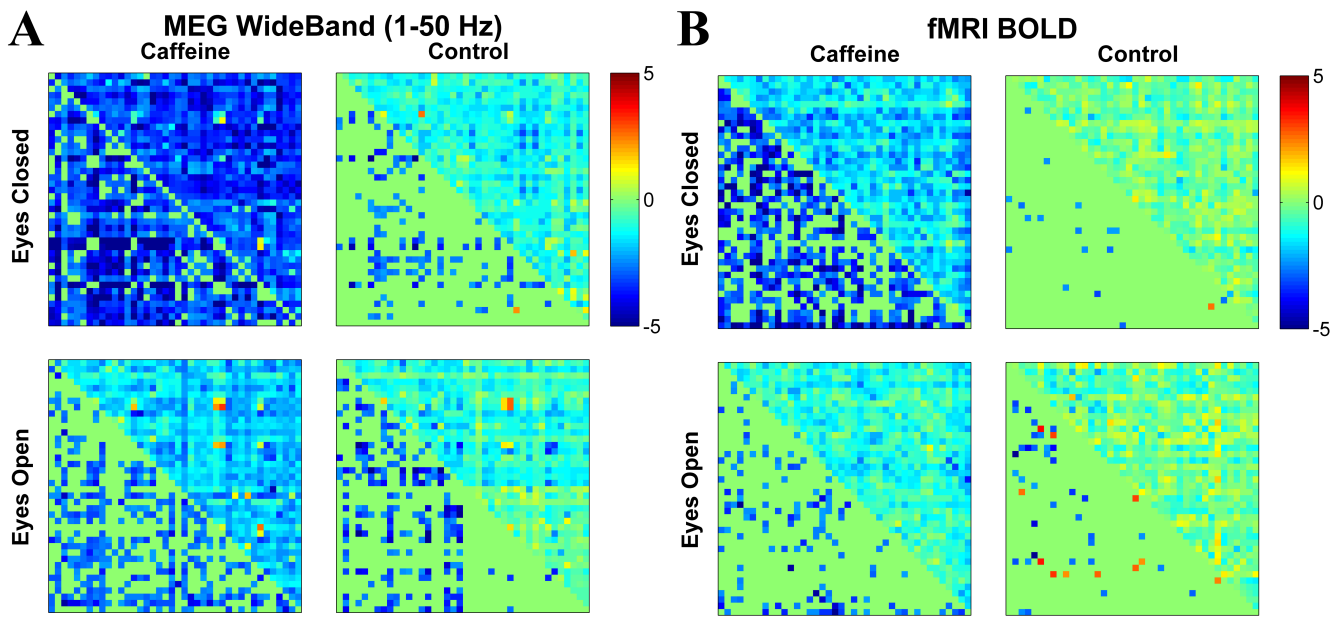


Brookes et al 2011


%ΔBOLD
0.5
0
-0.5
0
50
100
150
200
250

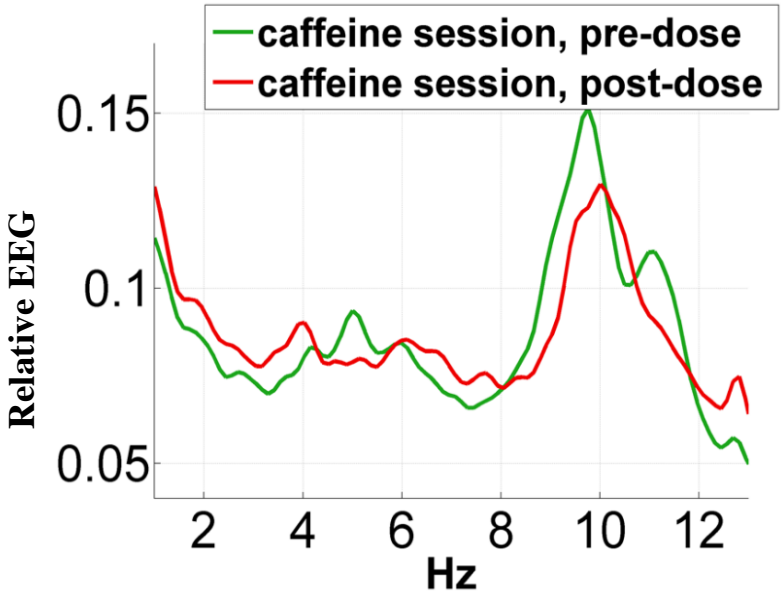


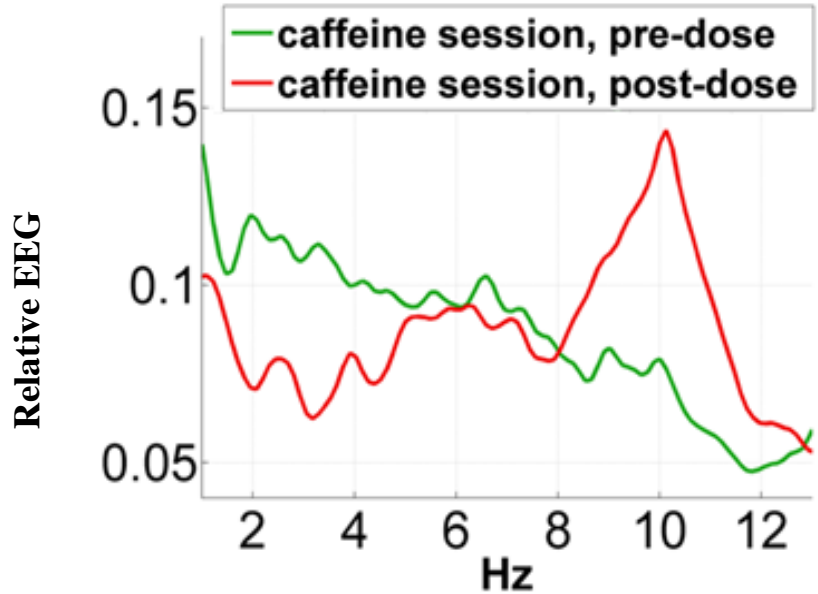
Single Subject Analysis

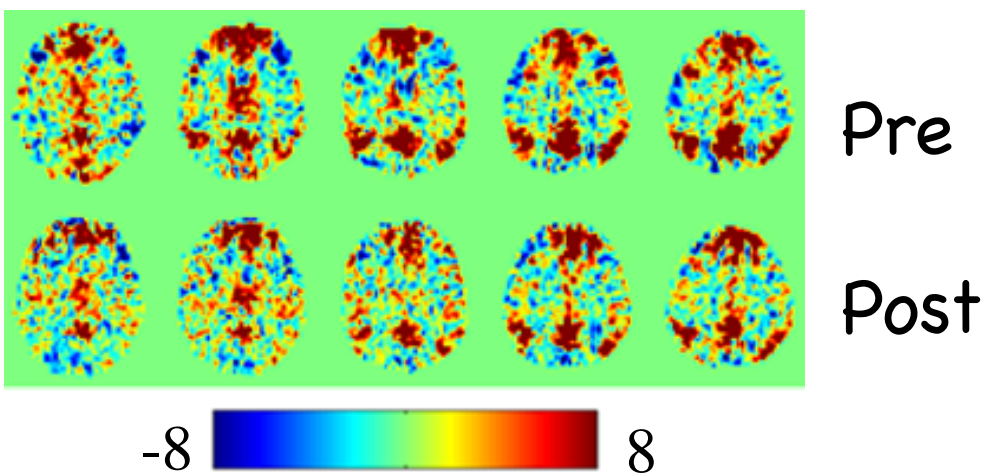


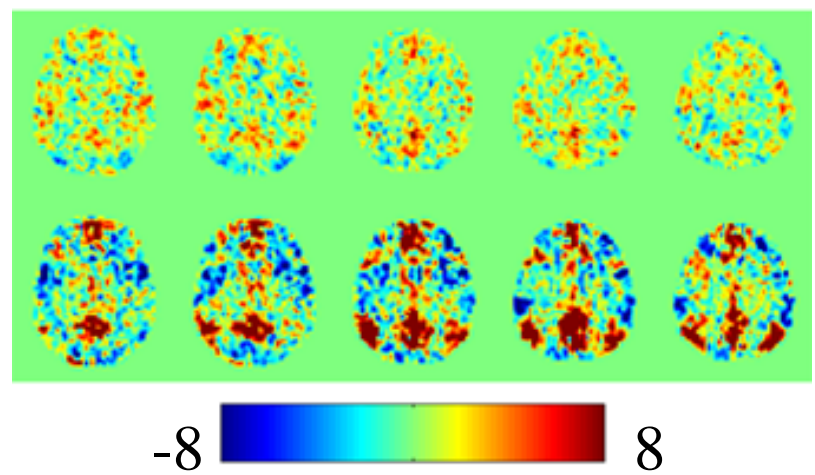
Group Analysis

Tal et al, Front. Hum. Neurosci. 2013









Higher vigilance -> lower GS -> more anticorrelation

Summary

- Most rs-fMRI studies use the BOLD signal.
- Changes in BOLD functional connectivity can be difficult to interpret on their own.
- The use of prior observations and BOLD signal models can help to distinguish between vascular and neural effects.
- However, in some cases multimodal measures are needed to determine the primary causes.
- Some preprocessing approaches, such as global signal regression, should be used with caution as they can mask the effect of interest.

Acknowledgements

Hongjian He
Valur Olafsson
Anna Leigh Rack-Gomer
Khaled Restom
Omer Tal
Alec Wong
Rick Buxton
Valerie Griffeth
Eric Wong

Mithun Diwakar
Mingxiong Huang

Markus Plank
Howard Poizner
Joe Snider

NATIONAL INSTITUTES OF HEALTH

ONR
Office of Naval Research