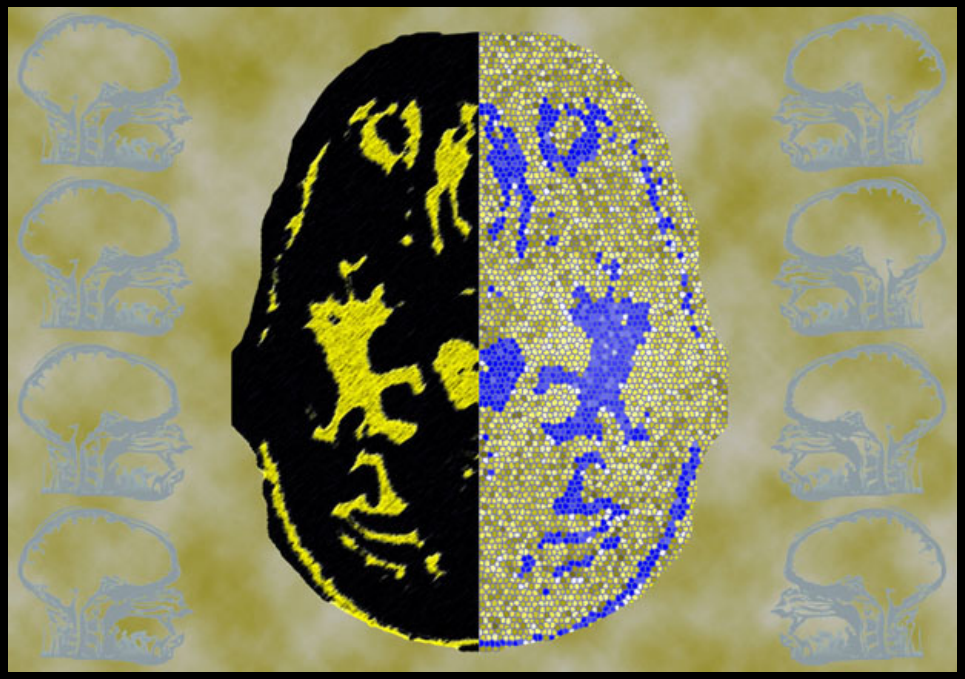
Characterizing task-related interactions between brain regions with fMRI

Beta Series Correlation & Psychophysiological Interaction Approaches



Jesse Rissman

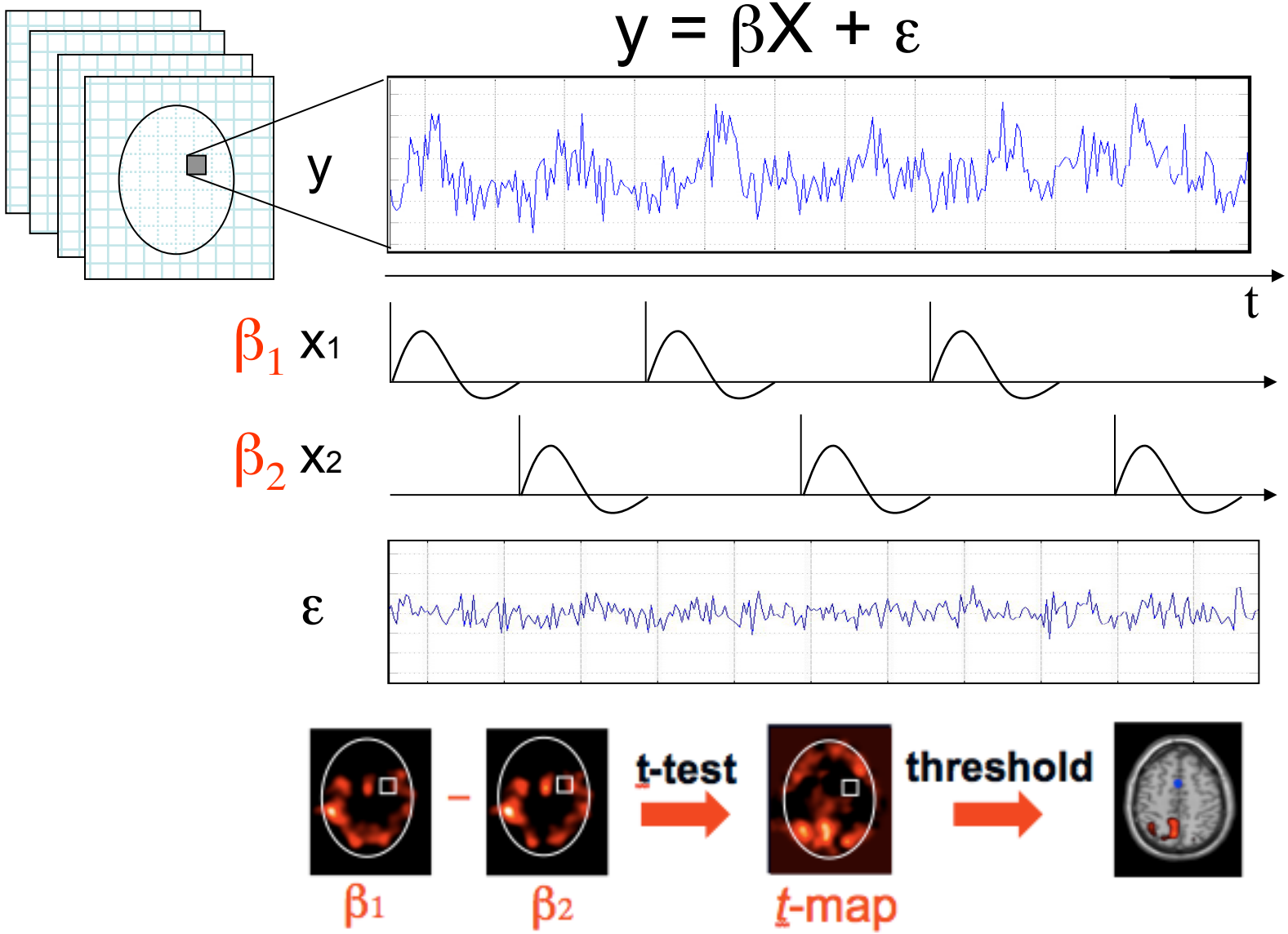
NITP Summer Course 2013

UCLA

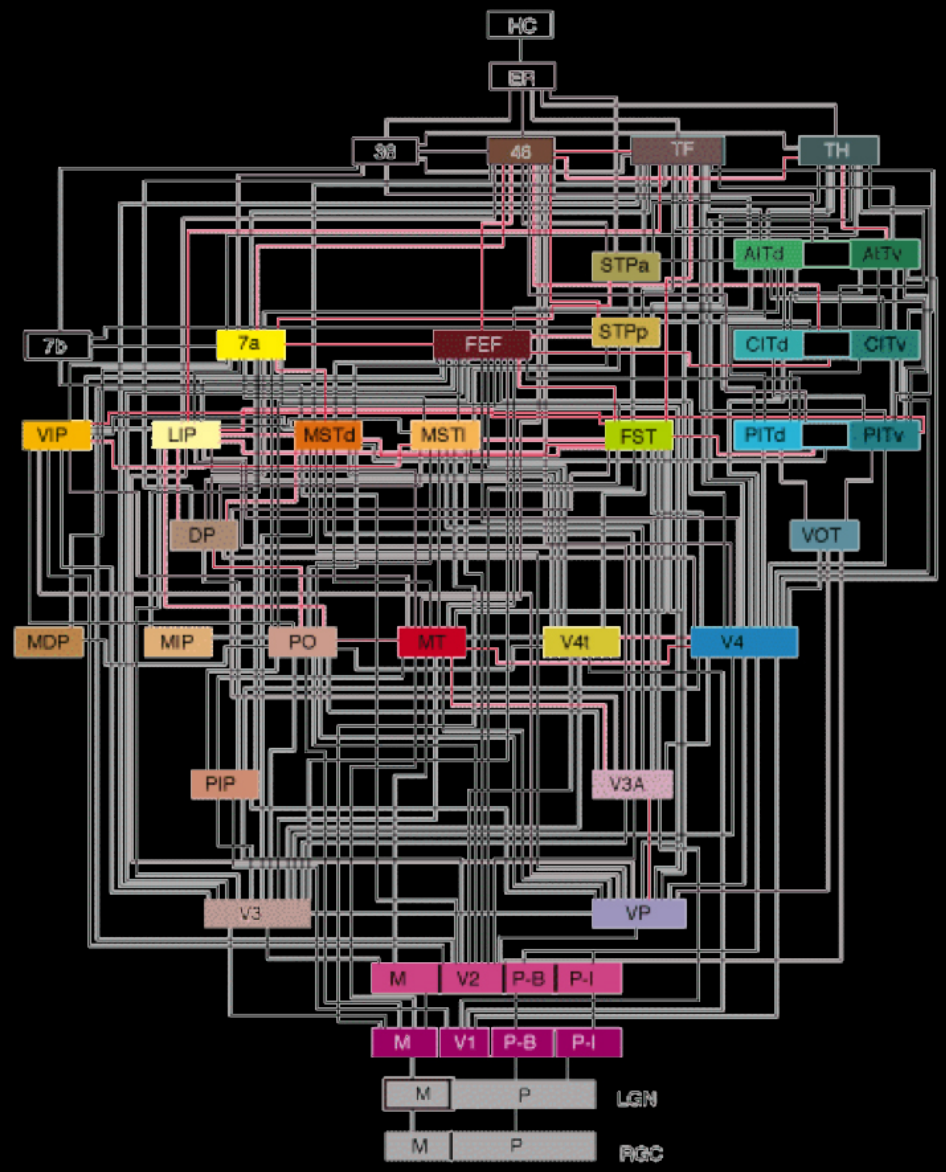
Mapping brain function with fMRI:

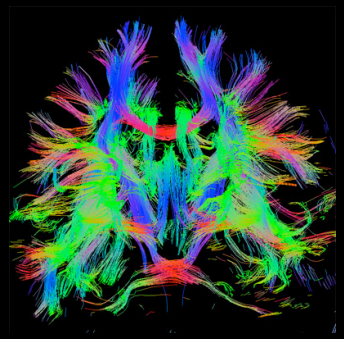
Traditional univariate GLM approach to functional localization

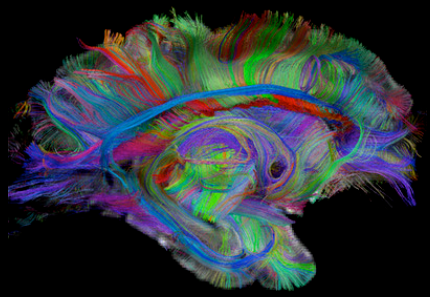
$$y = \beta X + \varepsilon$$



But brain regions do not act in isolation...



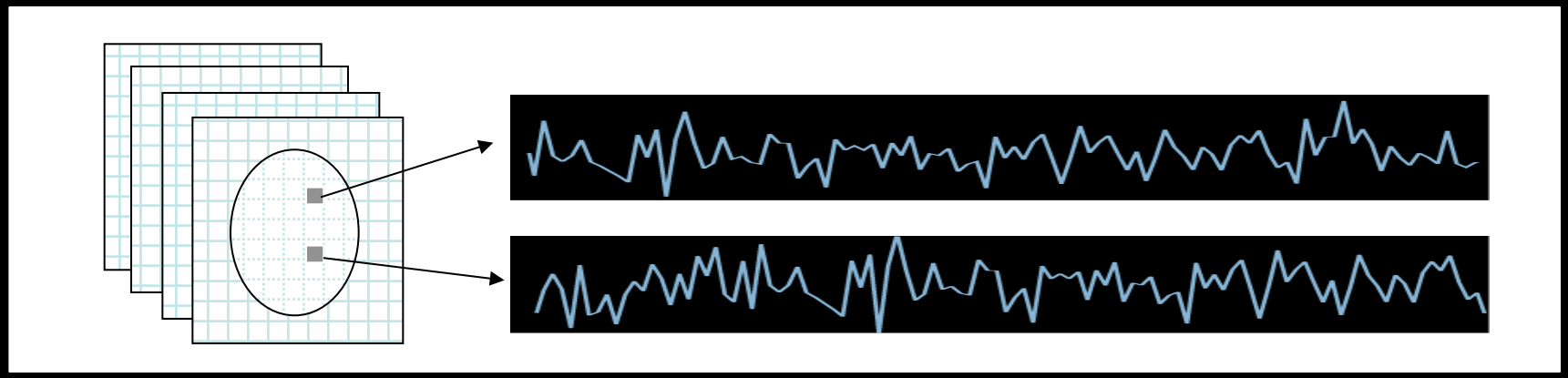




Felleman & Van Essen, 1991

Mapping brain function with fMRI:

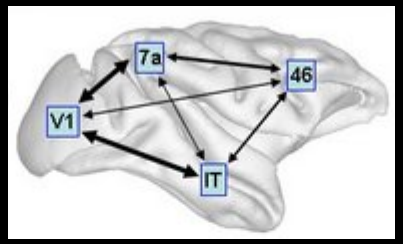
Functional connectivity approach



- Early functional connectivity analyses examined temporal correlations during the resting state (e.g., Biswal et al., 1995)
  - This approach continues to an extremely useful assay of inter-regional coupling
- Later studies began to examine <u>task-dependent</u> modulation of inter-regional coupling
  - Attending to motion vs. not attending to motion (Friston et al., 1997)
  - 2-back vs. 0-back working memory task (Lowe et al., 2000)
  - Listening to continuous speech vs. resting (Hampson et al., 2002)
- A growing collection of methods have been developed to extract information about functional interactions from fMRI data

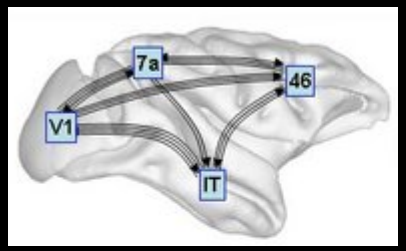
Types of connectivity

Functional Connectivity

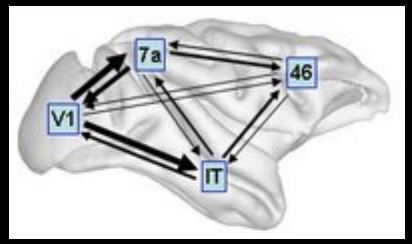


Documenting the correlation between spatially remote neurophysiological events

Structural Connectivity



Effective Connectivity



Characterizing the influence that one neuronal system exerts over another

- Data-driven / exploratory
  - Bivariate approaches
    - Timeseries correlations
    - Beta series correlations
    - Psychophysiological interactions (PPI)
  - Multivariate approaches
    - PCA, ICA, PLS

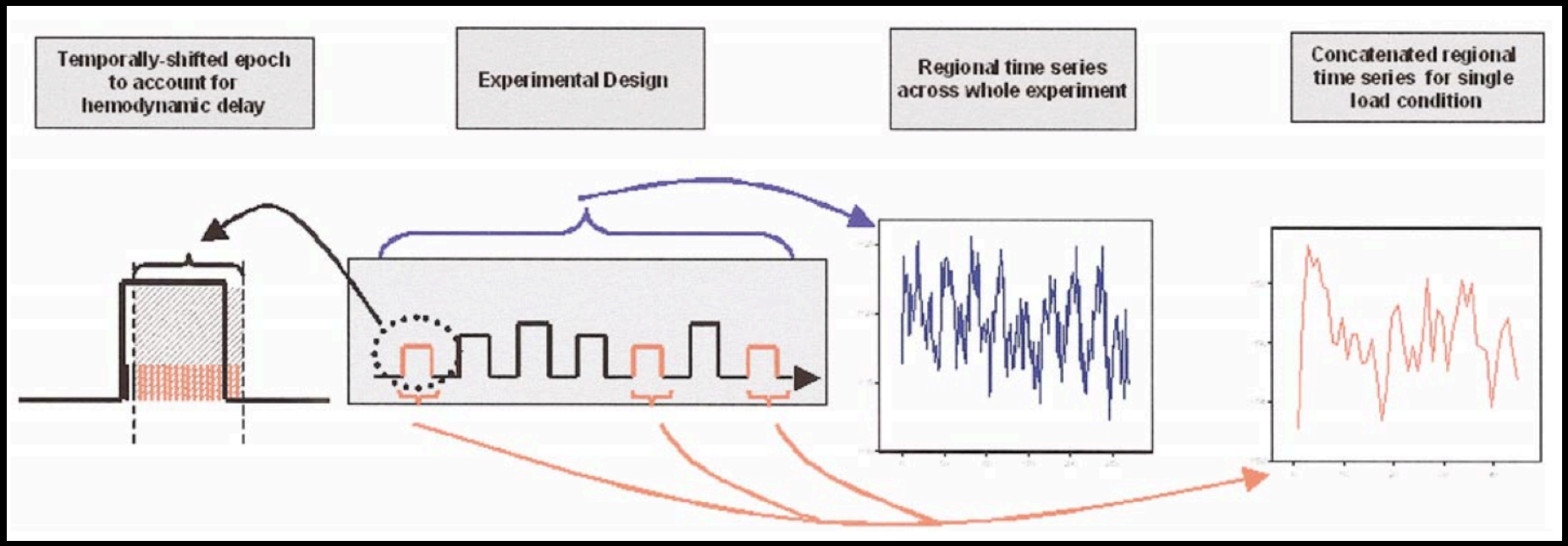
- Hypothesis-driven / model-based
  - Structural equation modeling (SEM)
  - Dynamic causal modeling (DCM)
  - Granger causality

[figures adapted from Sporns (2007), *Scholarpedia*]

Functional connectivity

Time series correlations

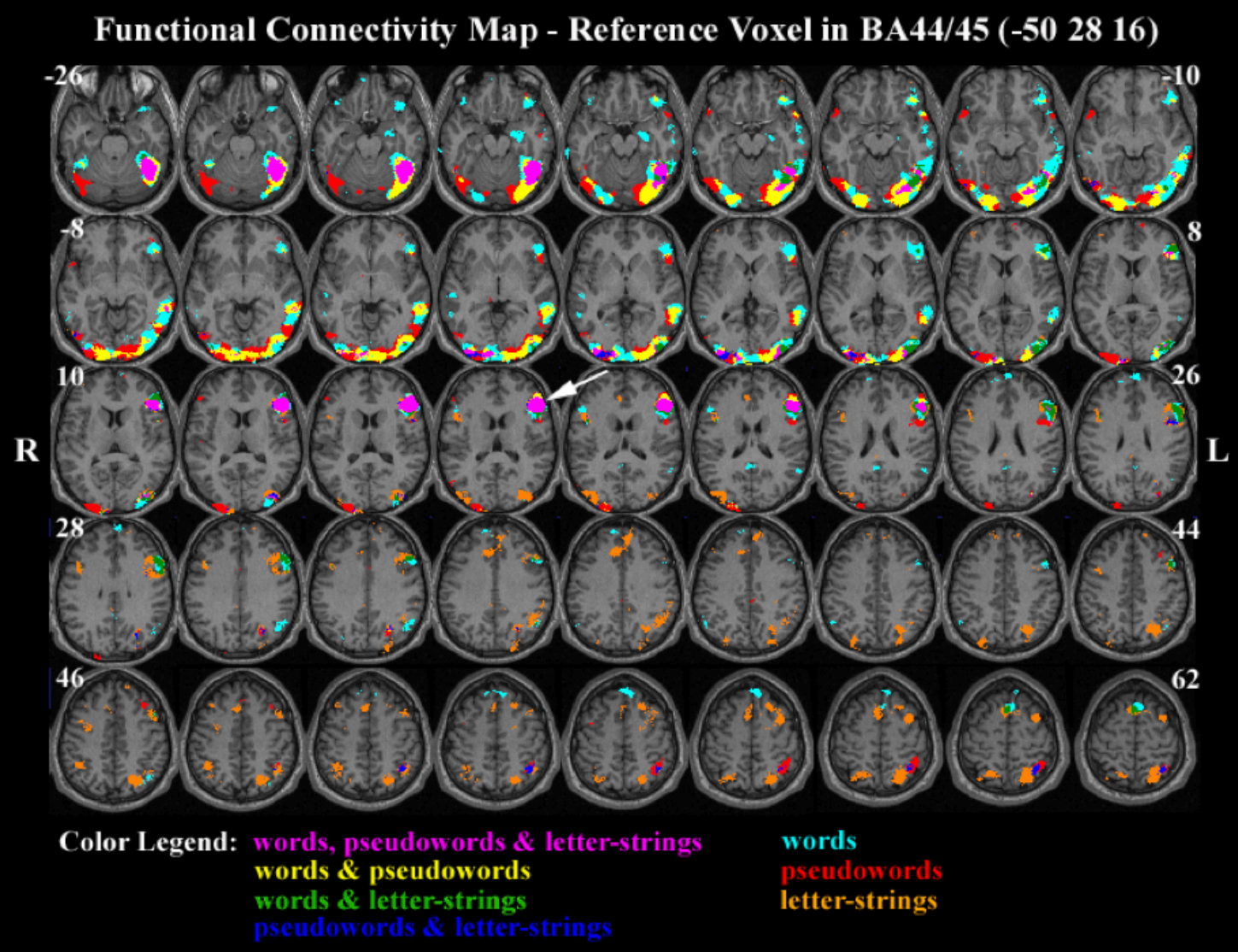
- Similar to resting state analyses, except that correlations are computed on data collected during task performance
  - *Generally requires that experiment utilizes a block design*



Honey et al. (2002), *NeuroImage*

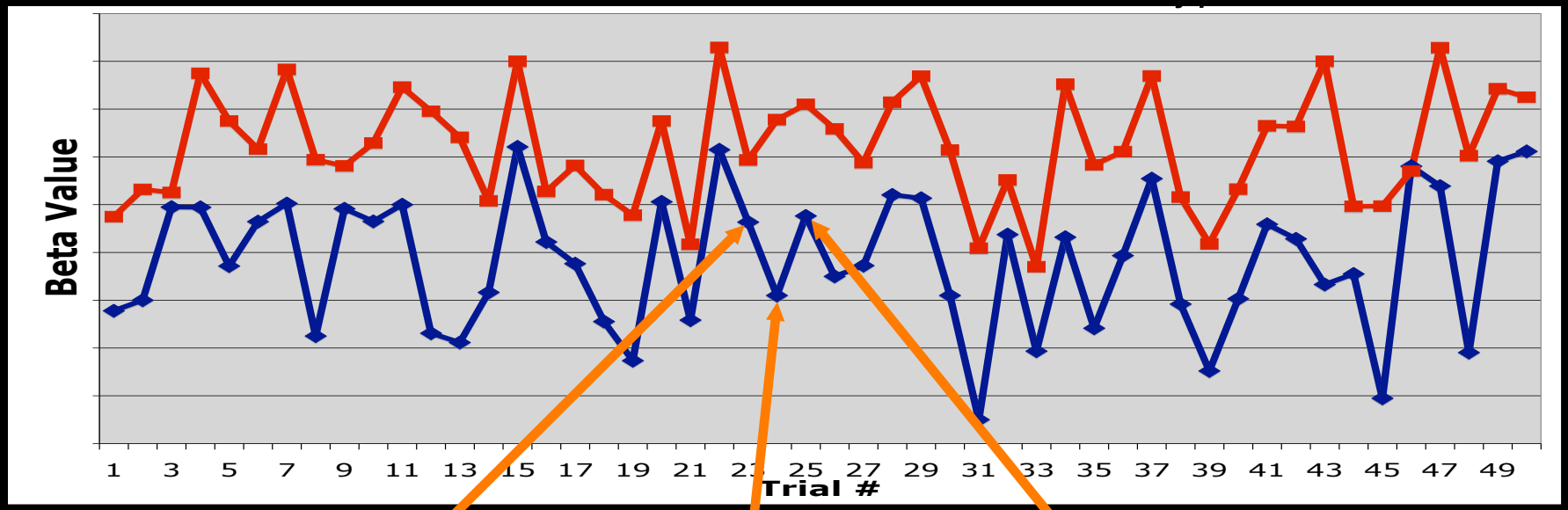
Functional connectivity

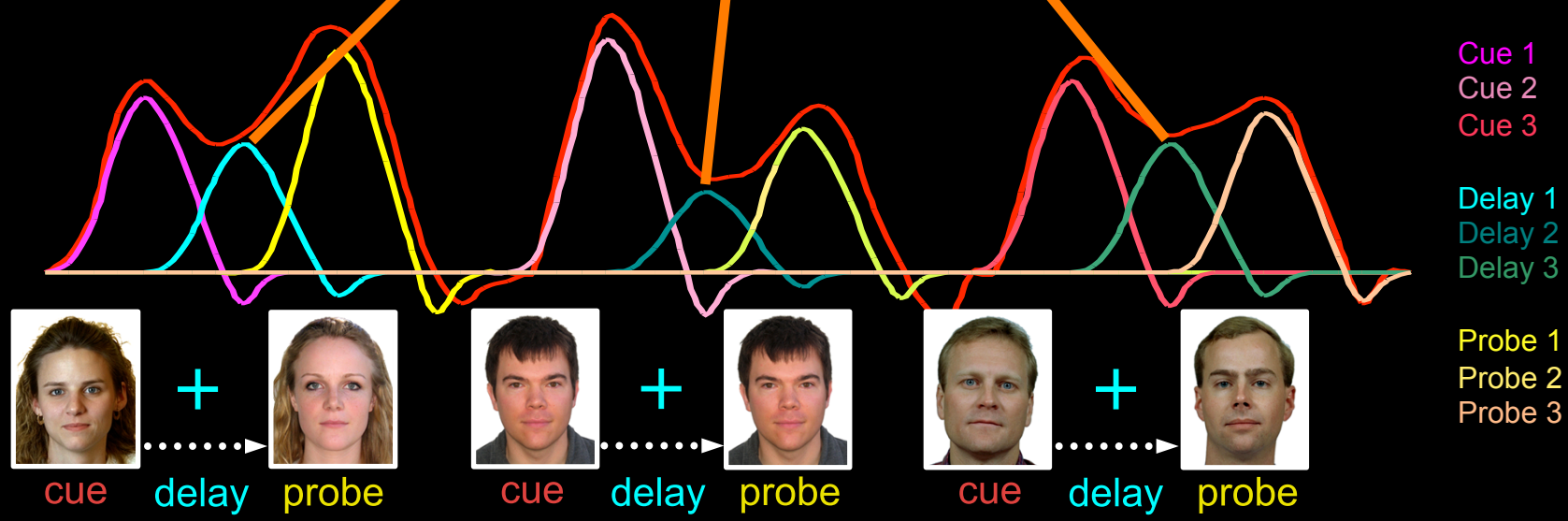
Time series correlations



Bodke et al. (2001), *Neuron*

Measuring functional connectivity during distinct task stages:
Beta series correlation analysis





Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

Beta series correlations:

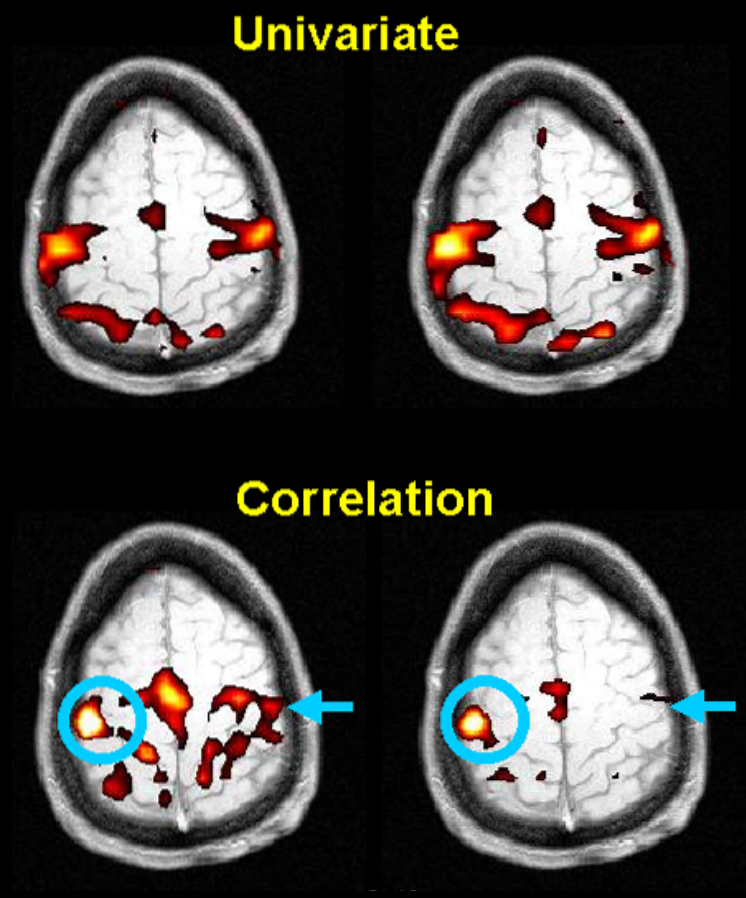
Methodological validation

- Beta series correlation analysis method applied to simple bimanual motor task.
- In the **Right-then-Left** condition, subjects played a sequence of 4 keystrokes with their right hand and then played a different sequence with their left.
- In the **Interleaved** condition, subjects played 8 keystrokes alternating between hands – a task requiring increased bimanual coordination.
- Hypothesis: The Interleaved condition should induce more inter-hemispheric cross-talk between motor regions.

Beta series correlations:

A meaningful metric of inter-regional coupling?

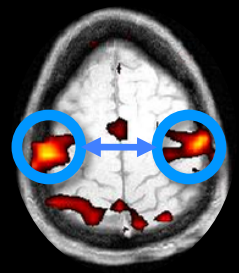
Bimanual coordination **One hand at a time**

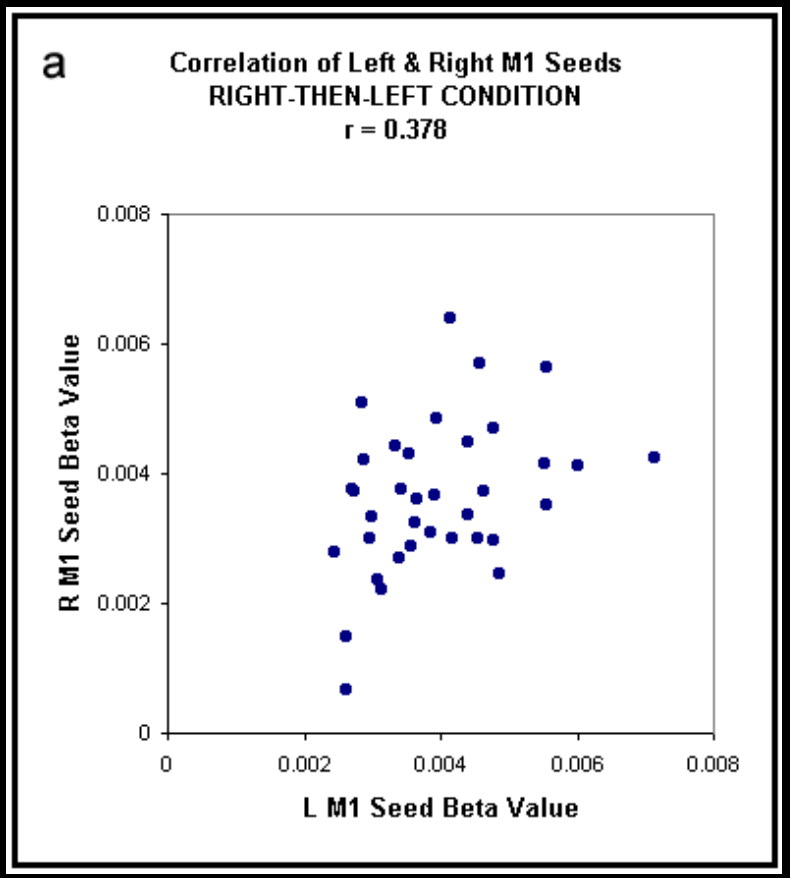


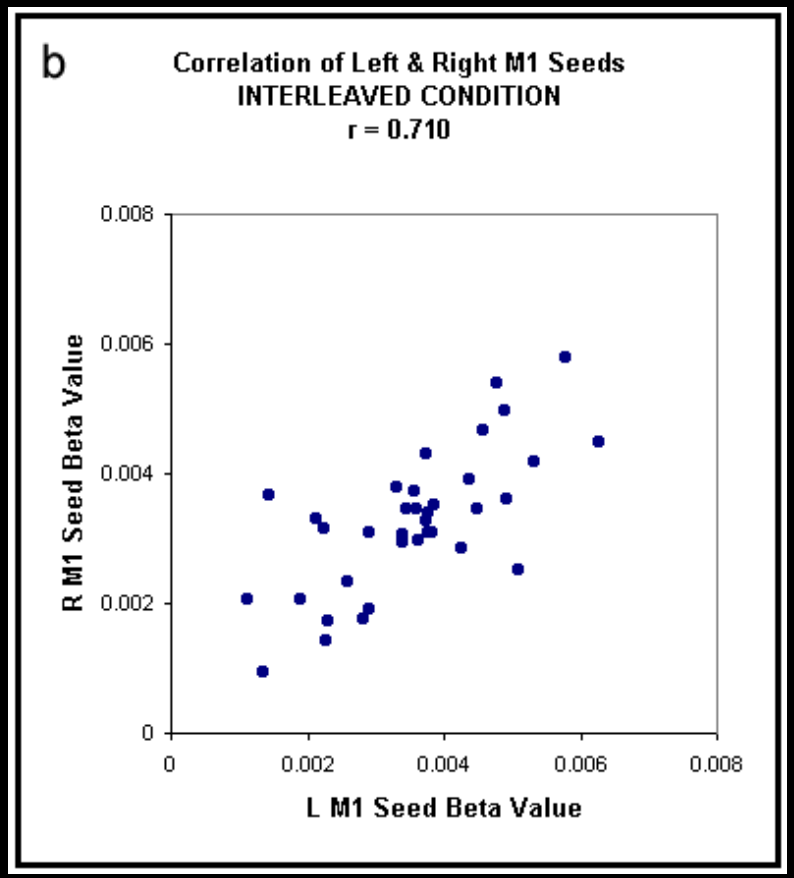
Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

Beta series correlations:

A meaningful metric of inter-regional coupling?







Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

Beta series correlation analysis applied to a basic visual working memory task

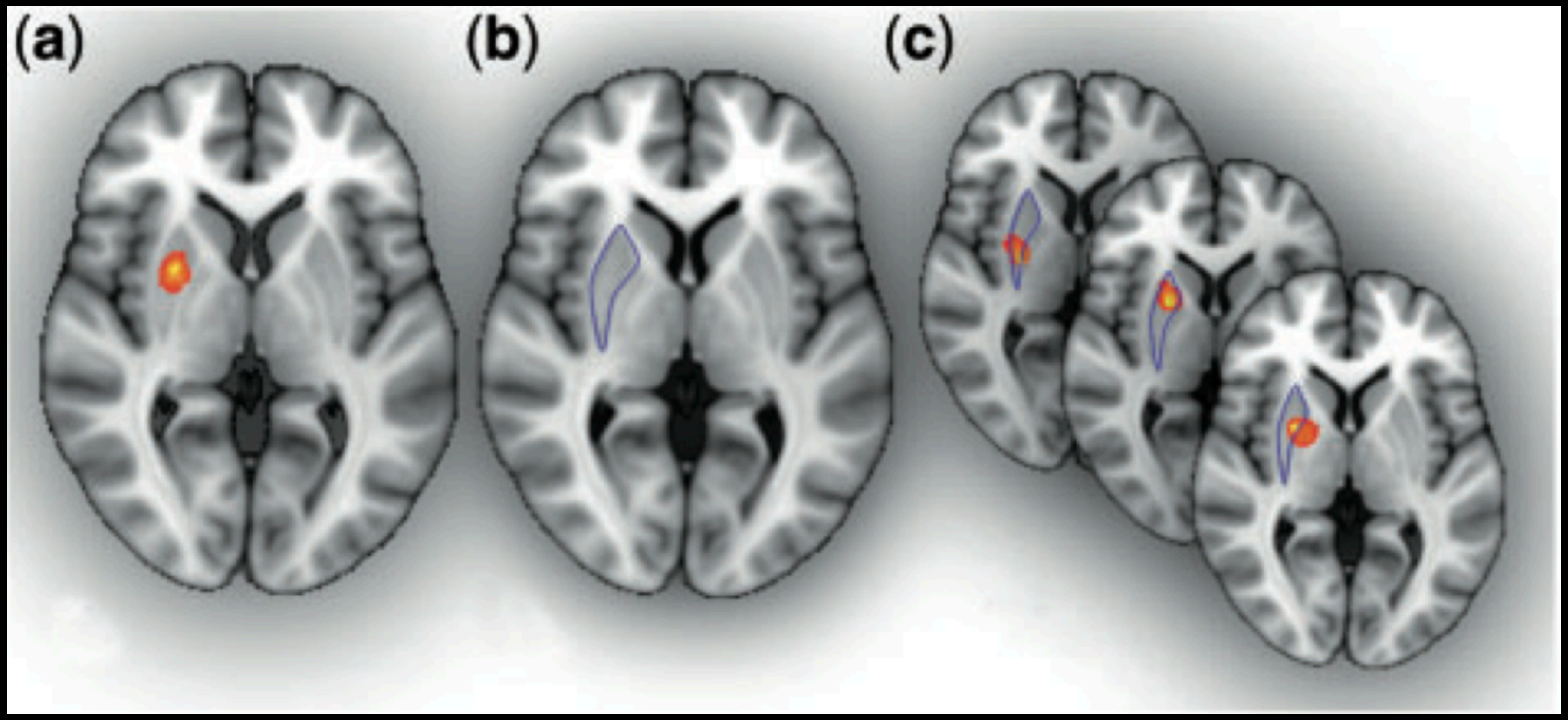
- Hypothesis: Frontoparietal regions interact with neural ensembles in inferotemporal cortex to keep behaviorally-relevant visual representations active
- Analysis performed on fMRI data from 17 subjects
- Task: maintain a single face across a 7-8 sec delay period

right fusiform face area (FFA) "seed"

Which brain regions are most strongly correlated with this seed region during face maintenance?

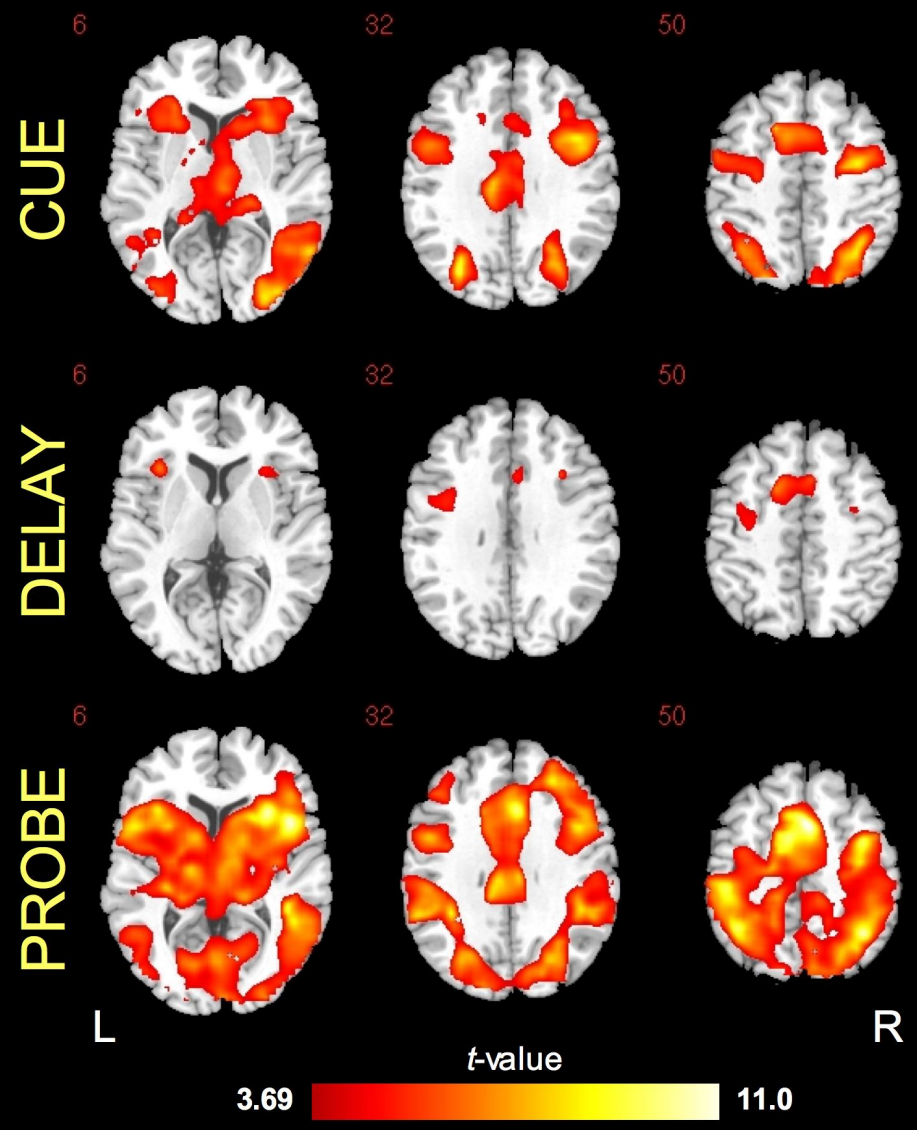
Side note: Defining a good seed ROI

Group-defined, anatomically-defined, or individually-defined?

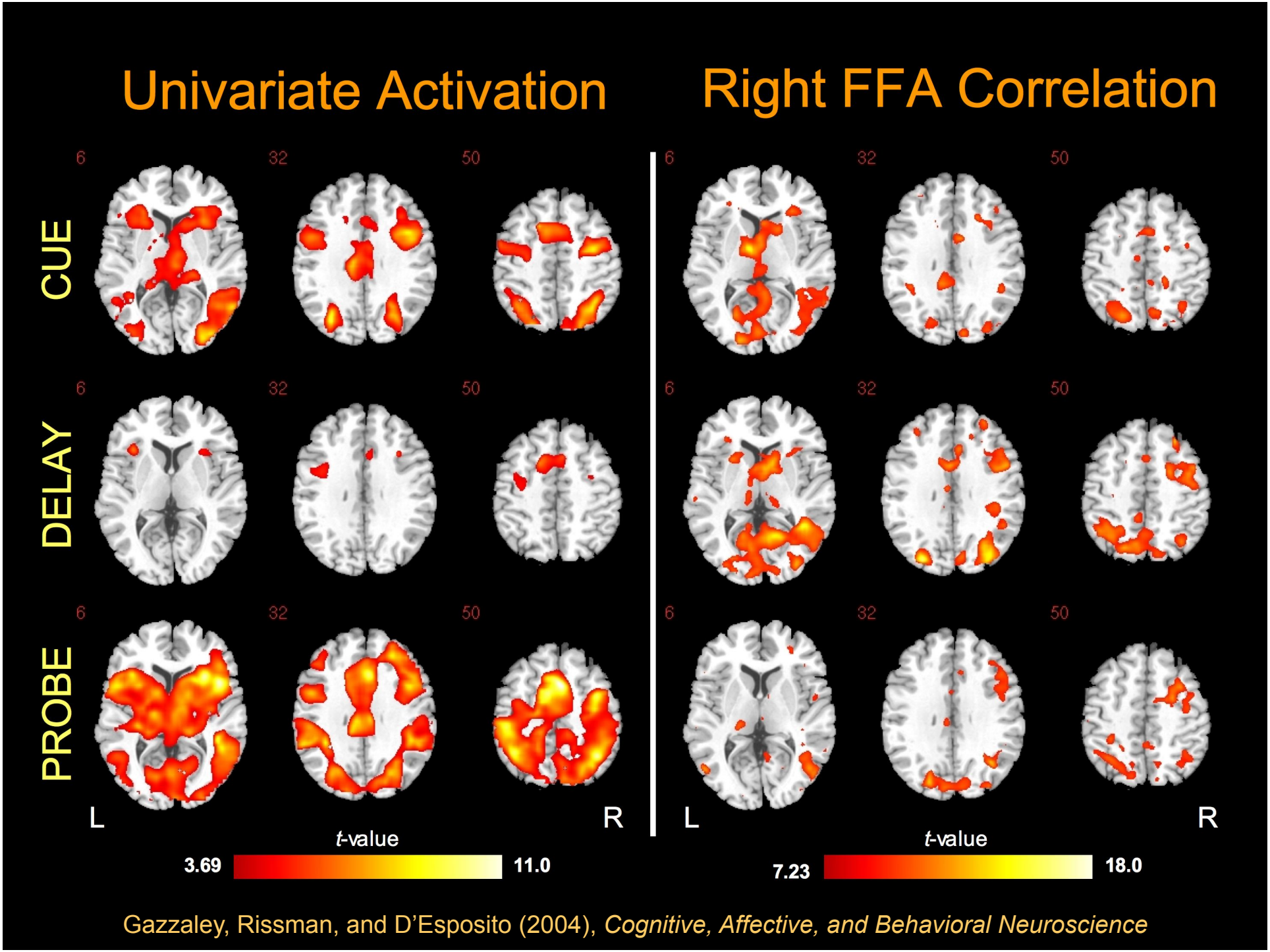


O'Reilly et al. (2012) *SCAN*

Univariate Activation

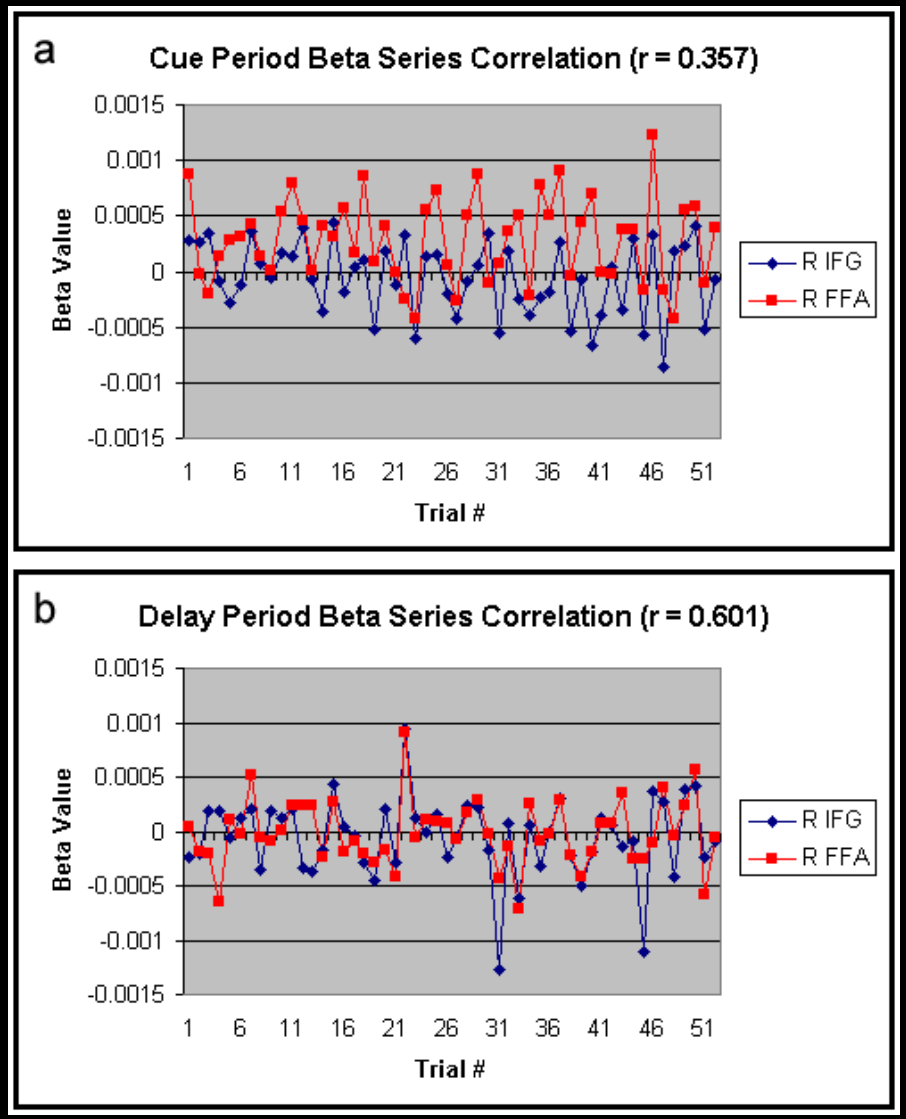


Gazzaley, Rissman, and D'Esposito (2004), *Cognitive, Affective, and Behavioral Neuroscience*



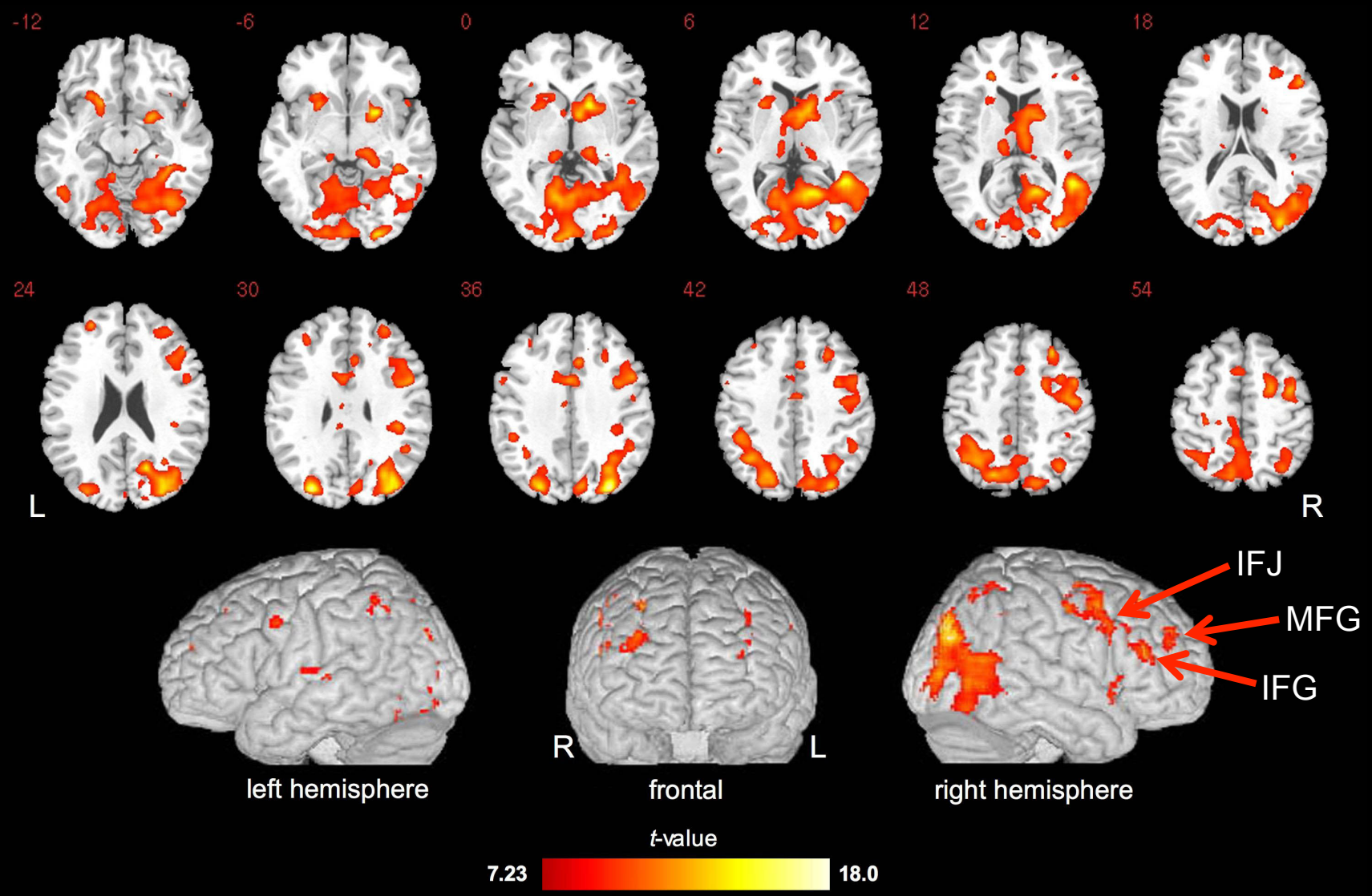
Gazzaley, Rissman, and D'Esposito (2004), *Cognitive, Affective, and Behavioral Neuroscience*

Higher mean activity does not necessarily imply higher connectivity



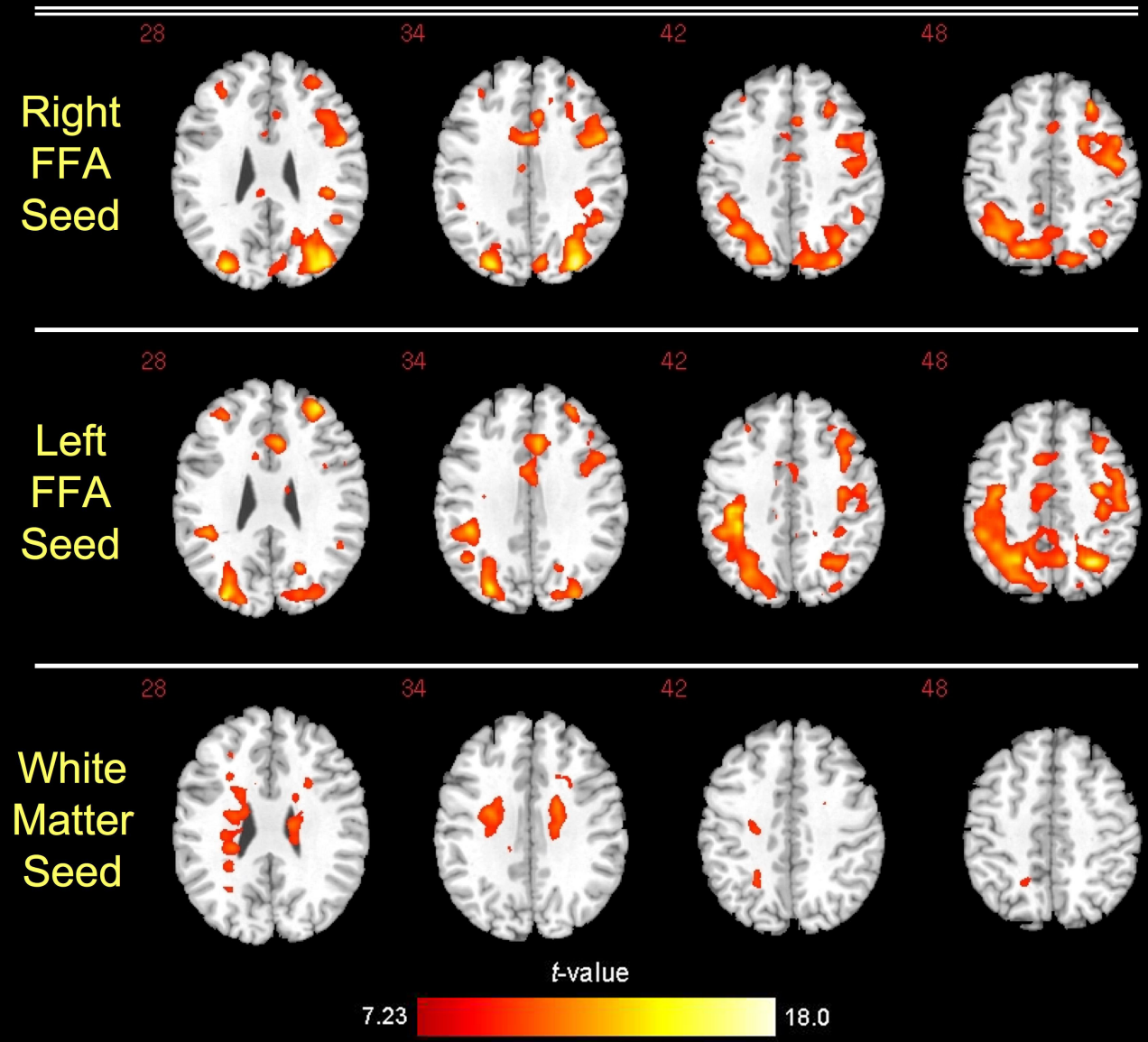
Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

Visual WM maintenance network:
Delay period connectivity with FFA seed



Gazzaley, Rissman, and D'Esposito (2004), *Cognitive, Affective, and Behavioral Neuroscience*

Delay Network Maps

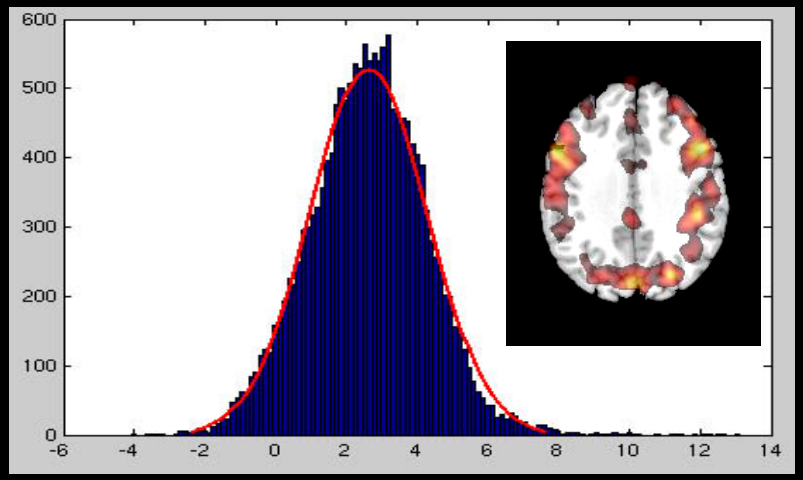


Gazzaley, Rissman, and D'Esposito (2004), *Cognitive, Affective, and Behavioral Neuroscience*

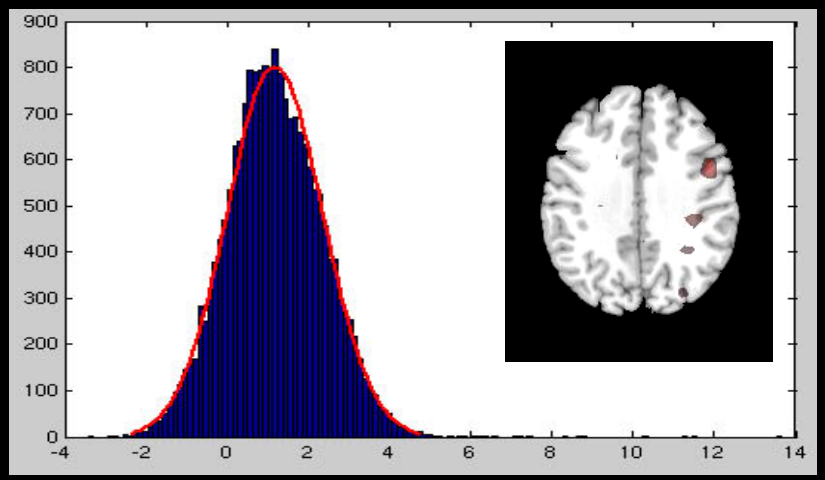
A few methodological considerations

- Across-subject differences in global correlation magnitudes

High Magnitude Subject



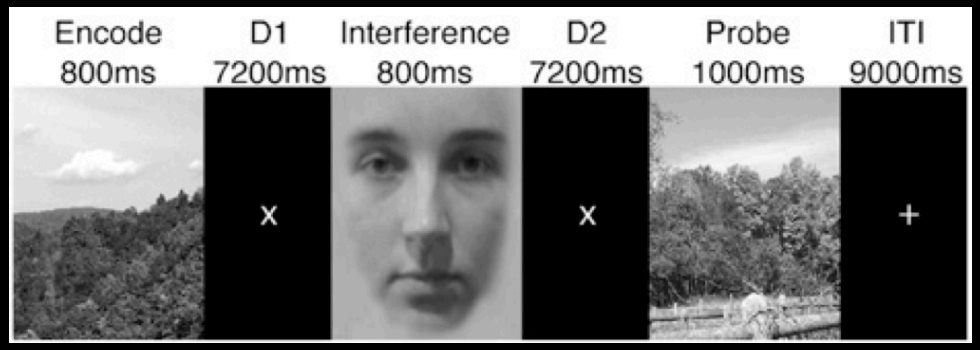
Low Magnitude Subject



- Potential solutions
  - -- Regress out global signal or signal from “noise” region (e.g., ventricle)
  - -- Contrast correlation maps with control condition
  - -- Ensure that outliers are not present in the seed’s beta series

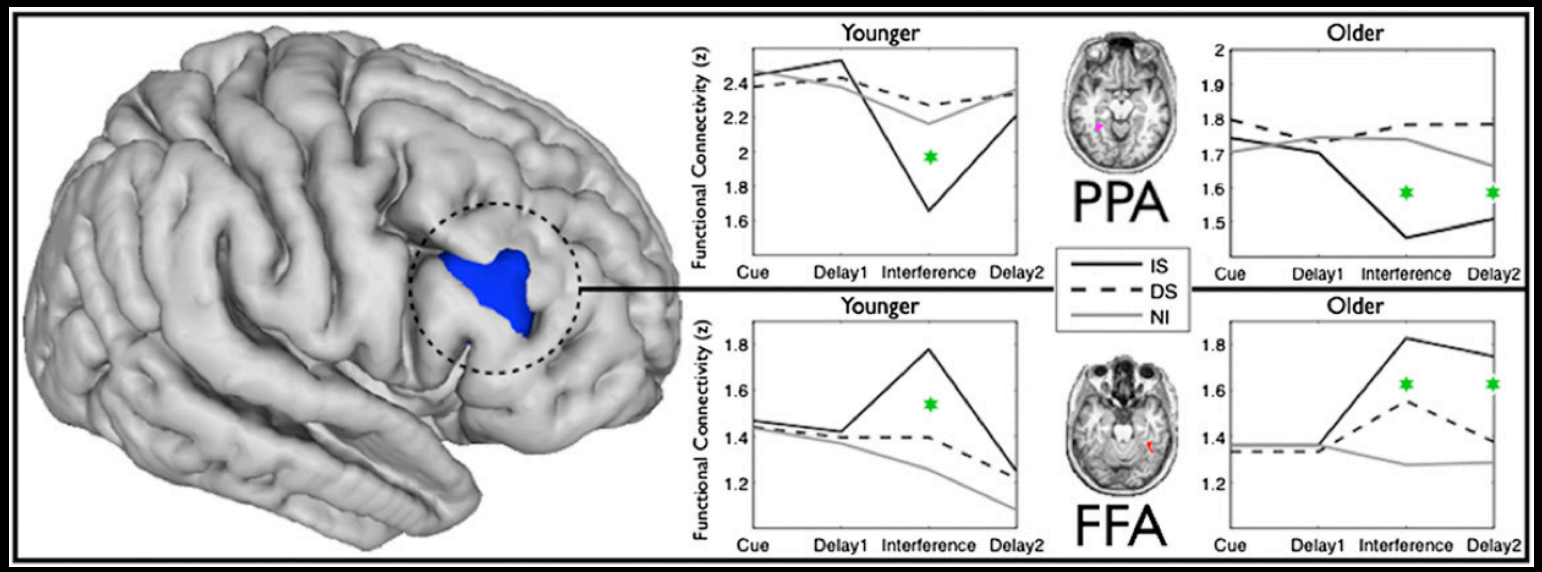
Another example application:

Age-related changes in prefrontal coupling



<u>3 task conditions</u>:

- Interrupting stimulus (IS): *make judgment about face (male over 40?)*
- Distracting stimulus (DS): *ignore face; no decision required*
- No interference (NI): *no face stimulus presented*

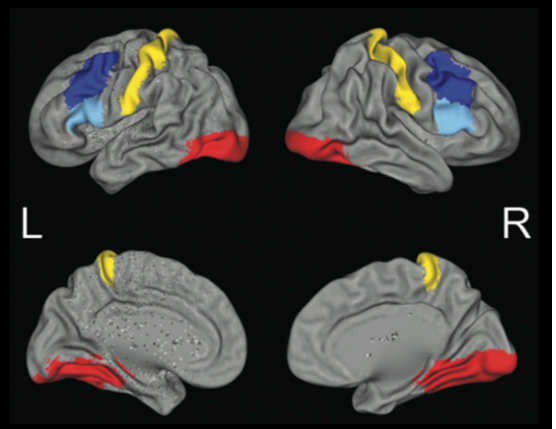


Older adults failed to reestablish connectivity following interruptions!

Clapp et al. (2011), *PNAS*

Another example application:

Sustaining a similar level of fronto-posterior connectivity from encoding to delay period leads to improved working memory performance



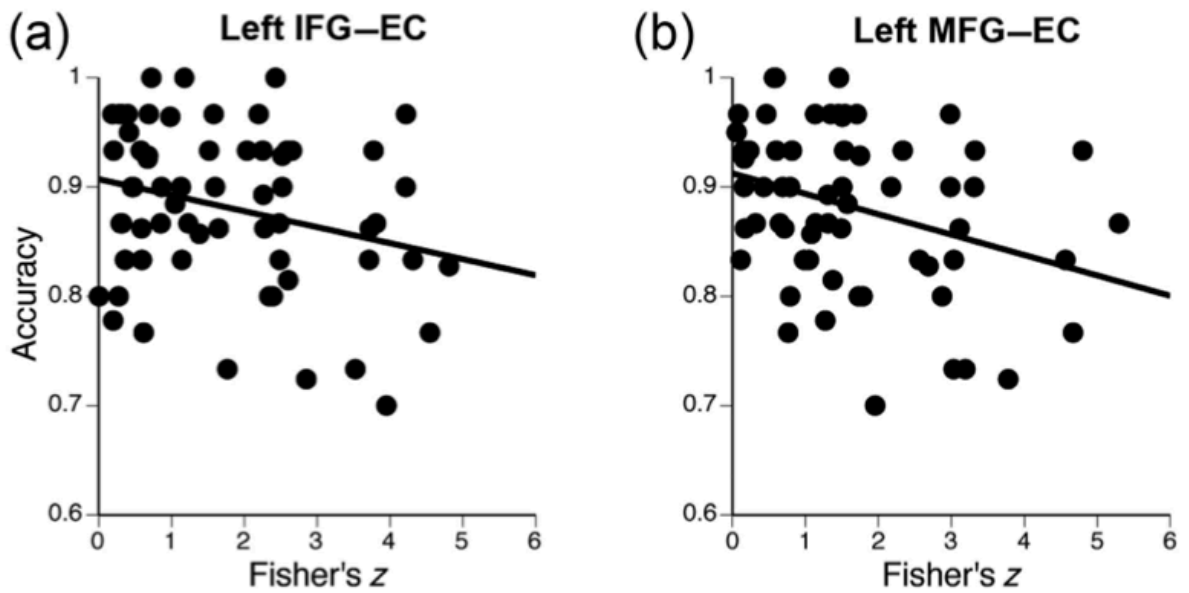


Figure 4. Connectivity Similarity relationships with behavior. Connectivity Similarity was comparably associated with accuracy for the (*a*) left IFG–EC and (*b*) left MFG–EC pairs. Note that the Connectivity Similarity metric is a difference score, thus smaller values are indicative of greater similarity.

Cohen et al. (2012), *Cerebral Cortex*

Pros & cons of beta series correlation method

- Pros:
  - Can examine how functional interactions between regions evolve over the course of a multi-stage trial
  - Relatively simple to implement (demo to follow)

- Cons:
  - Cannot determine whether inter-regional correlations reflect direct or indirect communication
  - Single trial activity estimates can be quite noisy
  - Serially-positioned HRF-convolved regressors may not provide ideal fit to data
  - Not ideal for rapid, jittered event-related designs
    - But might work with modified GLM model (Mumford et al., 2012)

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Deconvolving BOLD activation in event-related designs for multivoxel pattern classification analyses

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ABSTRACT

Use of multivoxel pattern analysis (MVPA) to predict the cognitive state of a subject during task performance has become a popular focus of fMRI studies. The input to these analyses consists of activation patterns corresponding to different tasks or stimulus types. These activation patterns are fairly straightforward to calculate for blocked trials or slow event-related designs, but for rapid event-related designs the evoked BOLD signal for adjacent trials will overlap in time, complicating the identification of signal unique to specific trials. Rapid event-related designs are often preferred because they allow for more stimuli to be presented and subjects tend to be more focused on the task, and thus it would be beneficial to be able to use these types of designs in MVPA analyses. The present work compares 8 different models for estimating trial-by-trial activation patterns for a range of rapid event-related designs varying by interstimulus interval and signal-to-noise ratio. The most effective approach obtains each trial's estimate through a general linear model including a regressor for that trial as well as another regressor for all other trials. Through the analysis of both simulated and real data we have found that this model shows some improvement over the standard approaches for obtaining activation patterns. The resulting trial-by-trial estimates are more representative of the true activation magnitudes, leading to a boost in classification accuracy in fast event-related designs with higher signal-to-noise. This provides the potential for fMRI studies that allow simultaneous optimization of both univariate and MVPA approaches.

Psychophysiological interactions (PPI)

- Bilinear model of how a psychological context A changes the influence of area B on area C :

$$B \times A \rightarrow C$$

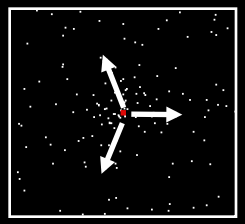
- A PPI corresponds to a difference in regression slopes for different contexts

- Seed-based approach
  - PPI effects computed voxel-by-voxel across entire brain

Friston et al. (1997), *NeuroImage*

[slide adapted from K.E. Stephan]

Psychophysiological interactions (PPI)



Stimulus factor		Task factor: Task A, NO ATTENTION	Task B, ATTENTION
Stim 1	STATIC DOTS	T_A/S_1	T_B/S_1
Stim 2	MOVING DOTS	T_A/S_2	T_B/S_2

GLM of a 2x2 factorial design:

$$y = (T_A - T_B)\beta_1 + (S_1 - S_2)\beta_2 + (T_A - T_B)(S_1 - S_2)\beta_3 + e$$

- $(T_A - T_B)\beta_1$ ← main effect of task
- $(S_1 - S_2)\beta_2$ ← main effect of stim. type
- $(T_A - T_B)(S_1 - S_2)\beta_3$ ← interaction

- Replace one main effect in the GLM by the time series of an area that shows this main effect
- e.g., swap out the main effect of stimulus type with the time series of area V1

$$y = (T_A - T_B)\beta_1 + V1\beta_2 + (T_A - T_B)V1\beta_3 + e$$

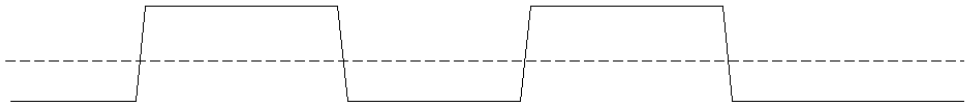
- $(T_A - T_B)\beta_1$ ← main effect of task
- $V1\beta_2$ ← V1 time series ≈ main effect of stim. type
- $(T_A - T_B)V1\beta_3$ ← psycho-physiological interaction

Friston et al. (1997), *NeuroImage*

[slide adapted from K.E. Stephan]

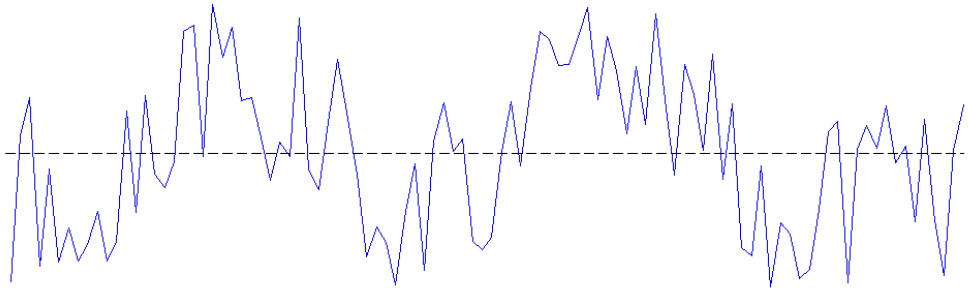
Psychophysiological interactions (PPI)

PSY main effect (task variable)

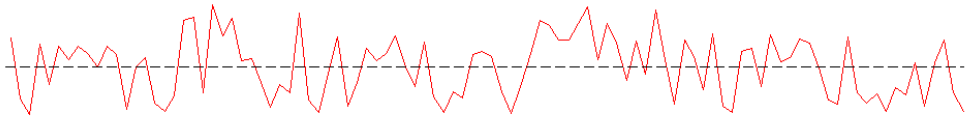


.*

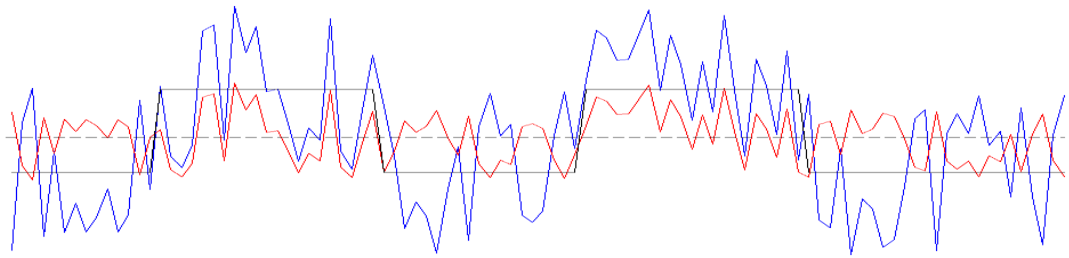
PHYS main effect (time series from seed region)



PPI = PSY.*PHYS



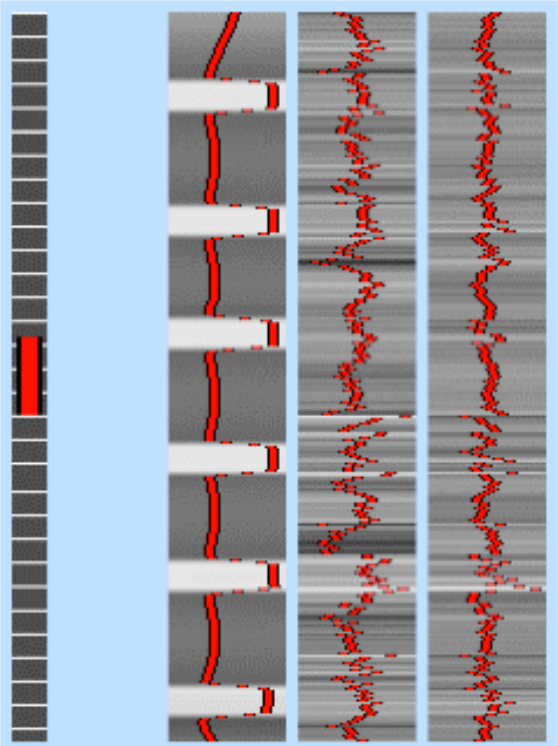
Overlay:



[slide from J. O'Reilly]

Psychophysiological interactions (PPI)

Figure 2. Design for a PPI analysis

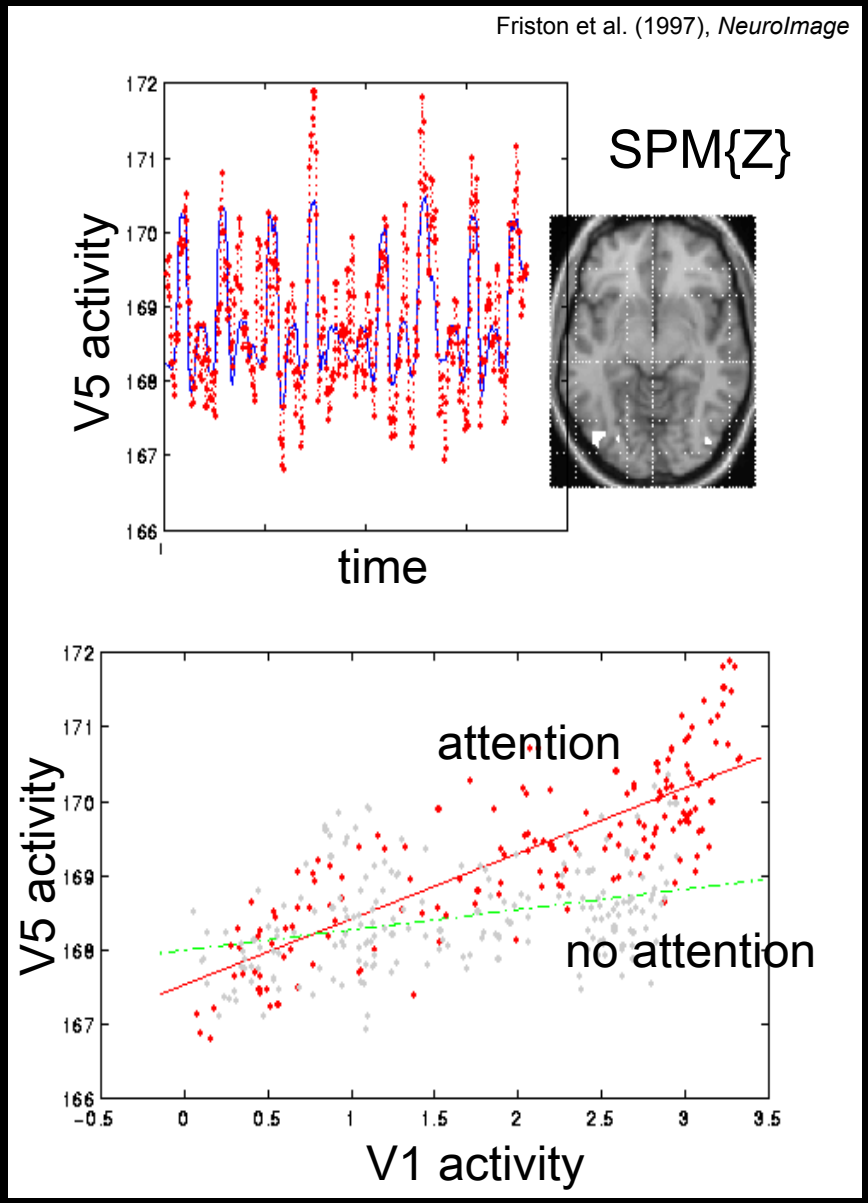


C1	PSY	1	0	0
C2	PHYS	0	1	0
C3	PPI	0	0	1

The design contains regressors for the main effects PSY and PHYS, and for the PPI interaction.

[slide from J. O'Reilly]

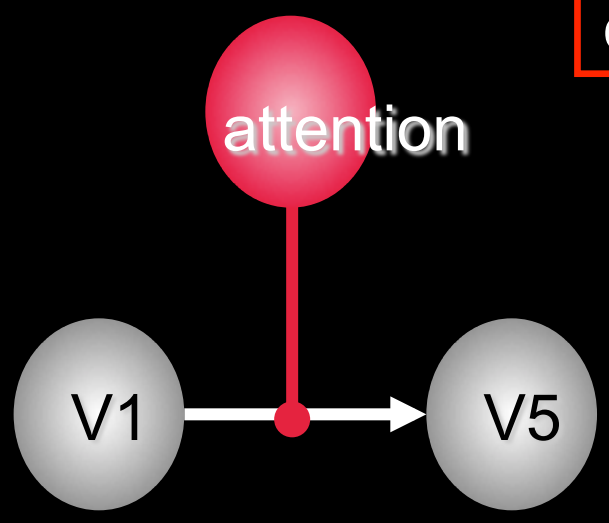
Psychophysiological interactions (PPI)

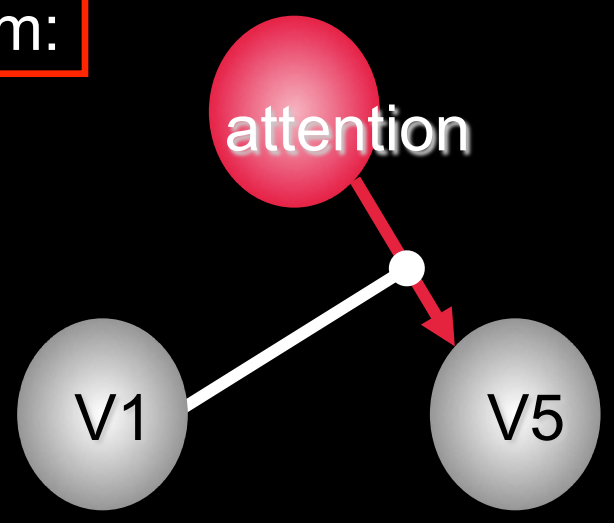


Psychophysiological interactions (PPI)

$$
\begin{aligned}
y = \; & (T_A - T_B)\,\beta_1 \\
& + V1\beta_2 \\
& + (T_A - T_B)\,V1\beta_3 \\
& + e
\end{aligned}
$$

Two possible interpretations of the PPI term:

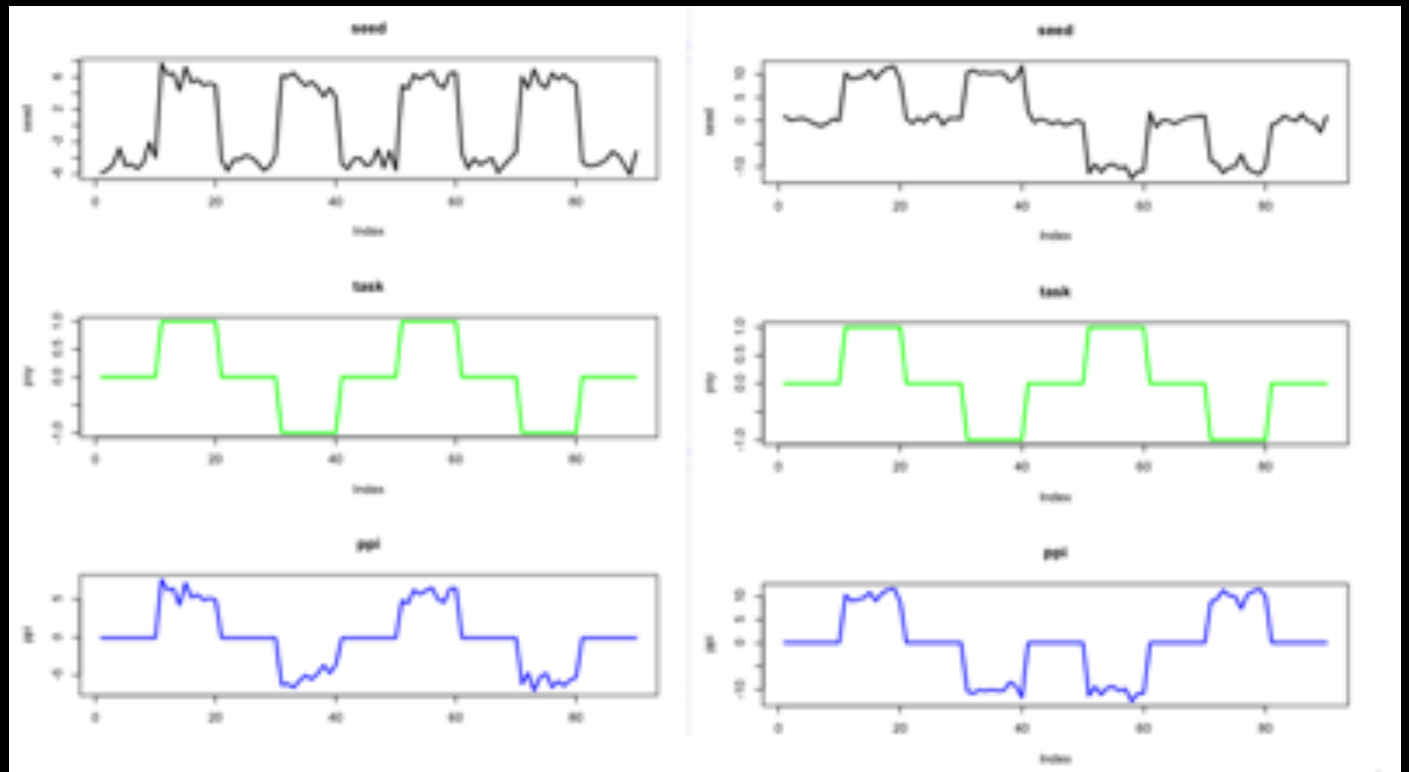




[slide adapted from K.E. Stephan]

Important caveat:

PPI analysis will be underpowered if PSY regressor is strongly correlated with PPI regressor

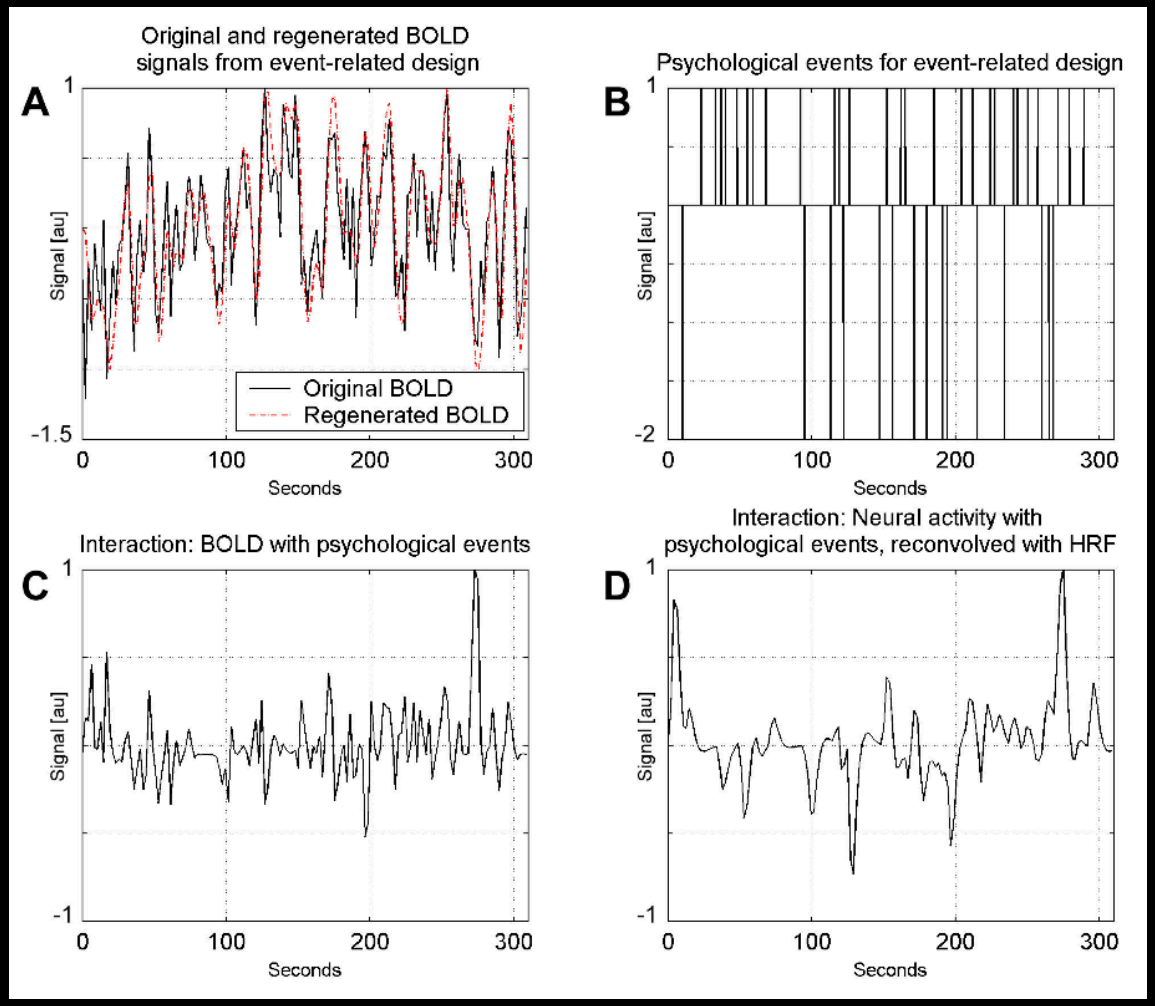


Corr(seed,ppi) = 0.05
Corr(psy,ppi) = 0.97
Corr(seed,psy) = 0.03

Corr(seed,ppi) = 0.02
Corr(psy,ppi) = 0.01
Corr(seed,psy) = 0.02

PPI on event-related fMRI data

The importance of hemodynamic deconvolution



$$(A \otimes HRF) \times (B \otimes HRF) \neq (A \times B) \otimes HRF$$

Gitelman et al. (2004), *NeuroImage*

A helpful overview of PPI:

http://www2.fmrib.ox.ac.uk/Members/joreilly/what-is-ppi/

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Tools of the trade: psychophysiological interactions and functional connectivity

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Psychophysiological interactions (PPIs) analysis is a method for investigating task-specific changes in the relationship between activity in different brain areas, using functional magnetic resonance imaging (fMRI) data. Specifically, PPI analyses identify voxels in which activity is more related to activity in a seed region of interest (seed ROI) in a given psychological context, such as during attention or in the presence of emotive stimuli. In this tutorial, we aim to give a simple conceptual explanation of how PPI analysis works, in order to assist readers in planning and interpreting their own PPI experiments.

Keywords: psychophysiological interactions; PPI; functional connectivity; resting state

The gPPI Toolbox:

http://www.nitrc.org/projects/gppi/

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Technical Note

A generalized form of context-dependent psychophysiological interactions (gPPI): A comparison to standard approaches

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Pros & cons of PPI analysis

- Pros:
  - Provides useful exploratory assay of how a given region's connectivity with the rest of the brain is modulated by task context
  - Easy to implement (FSL demo to follow)

- Cons:
  - Can only model contributions from a single area
  - PPI regressor may be highly correlated with psychological task regressor, reducing power
    - Factorial designs help avoid this problem!
  - Limited causal interpretability