Characterizing task-related interactions between brain regions with fMRI

Beta Series Correlation & Psychophysiological Interaction Approaches

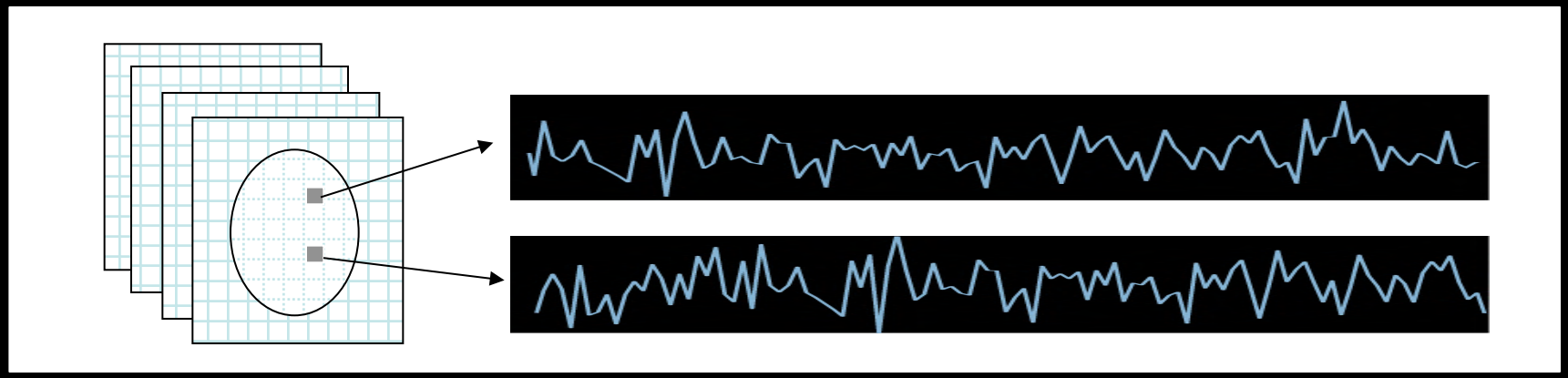
Jesse Rissman & Agatha Lenartowicz

NITP Summer Course 2012

UCLA

Mapping brain function with fMRI:

Functional connectivity approach

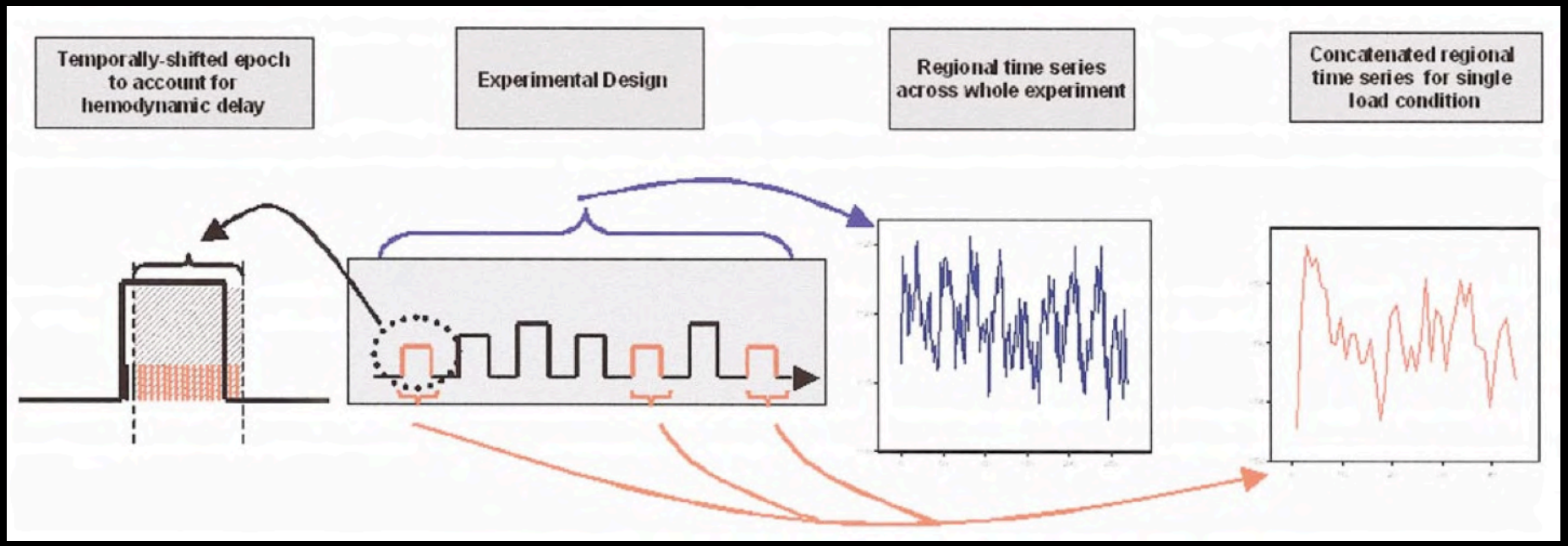


- Early functional connectivity analyses examined temporal correlations during the resting state (e.g., Biswal et al., 1995)
  - This approach continues to an extremely useful assay of inter-regional coupling
- Later studies began to examine <u>task-dependent</u> modulation of inter-regional coupling
  - 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

Functional connectivity

Time series correlations

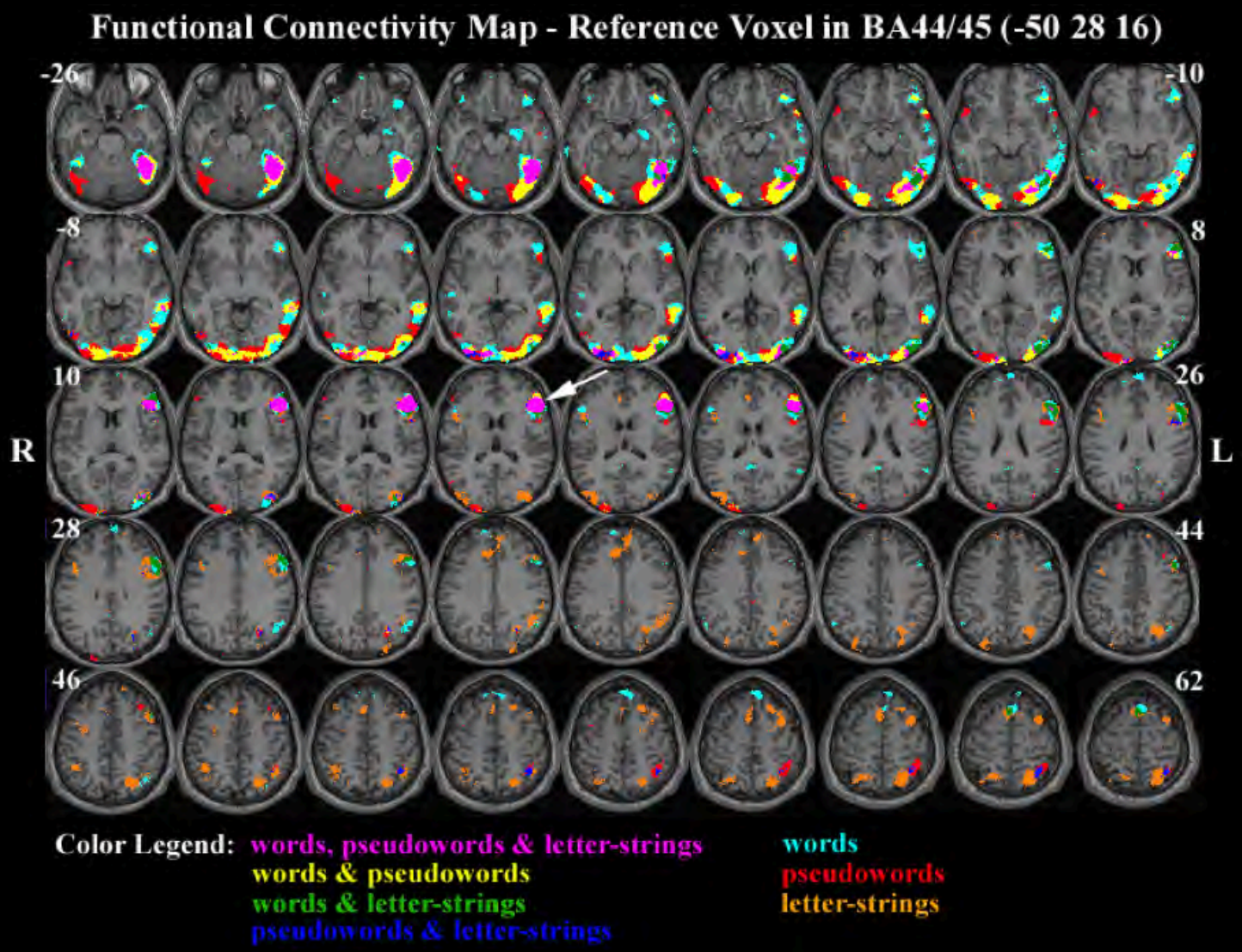
- Similar to resting state analyses, except that correlations are computed on data collected during task performance
  - *Generally requires that experiment utilizes a block design*



Honey et al. (2002), *NeuroImage*

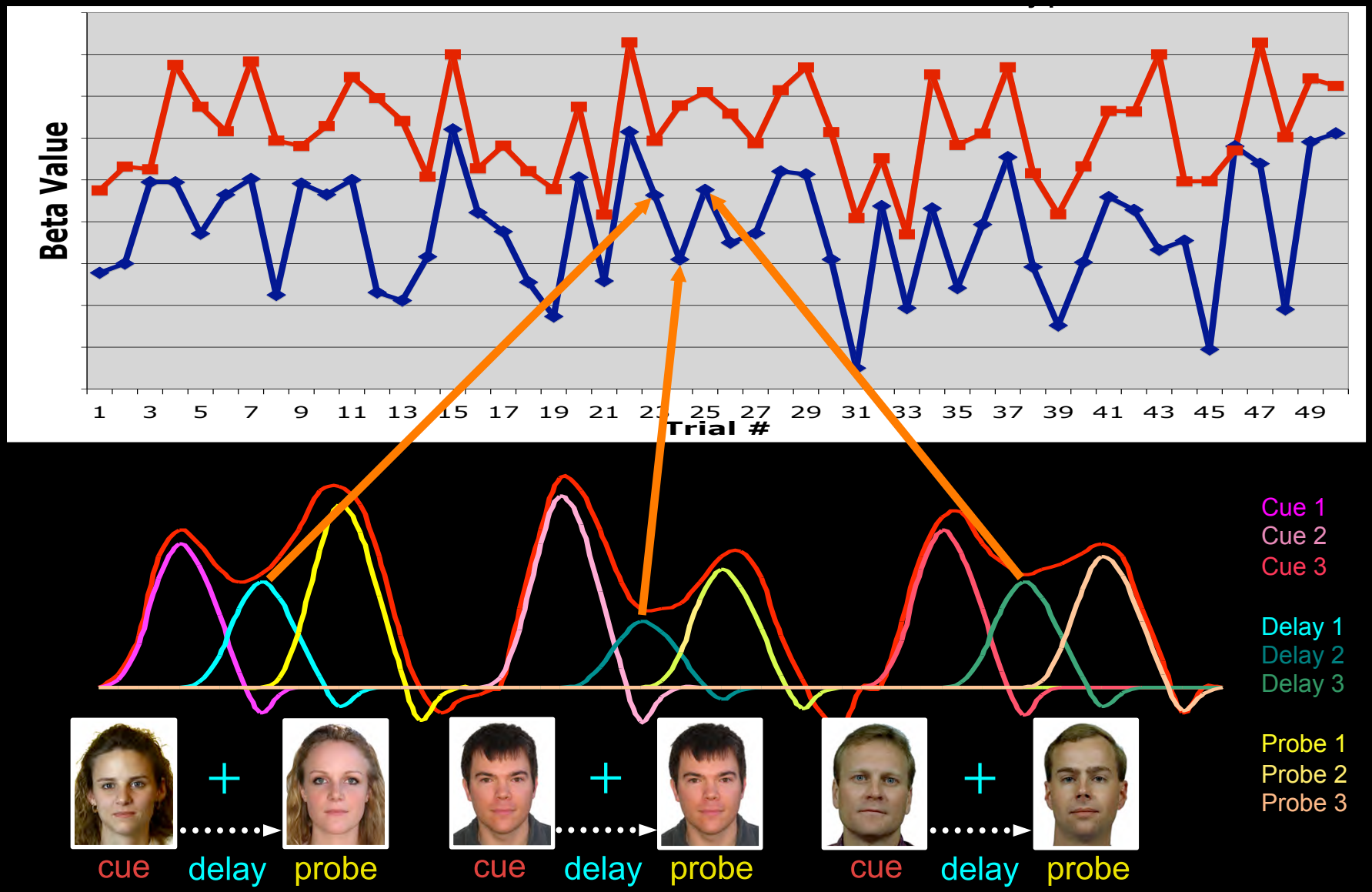
Functional connectivity

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:

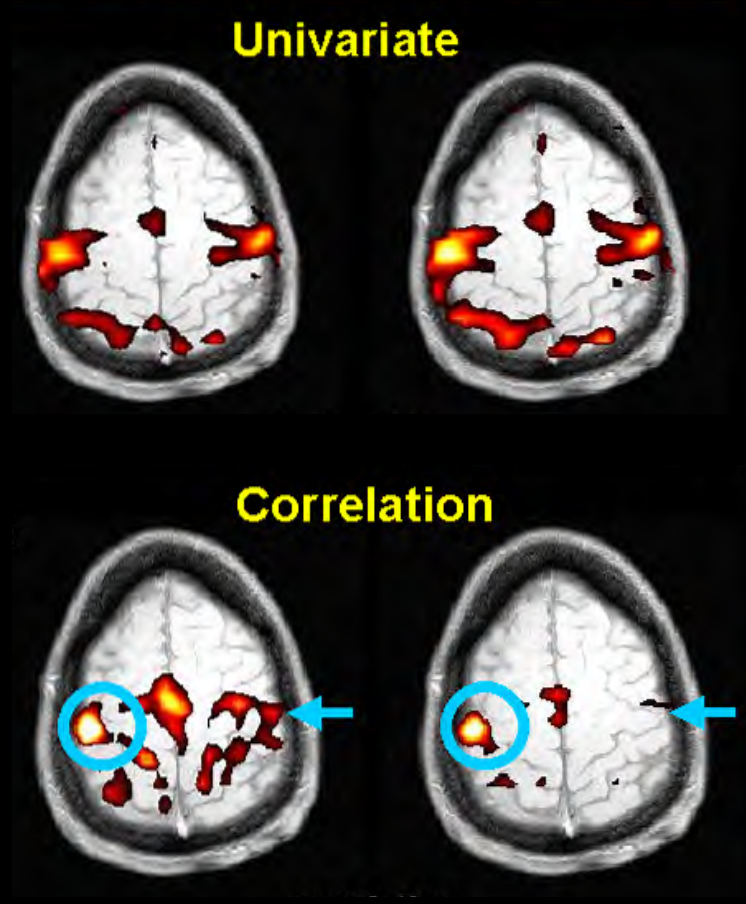
Methodological validation

- 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?

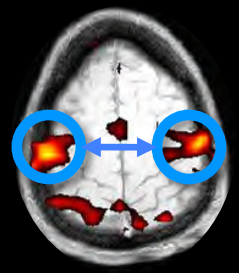
Bimanual coordination | **One hand at a time**

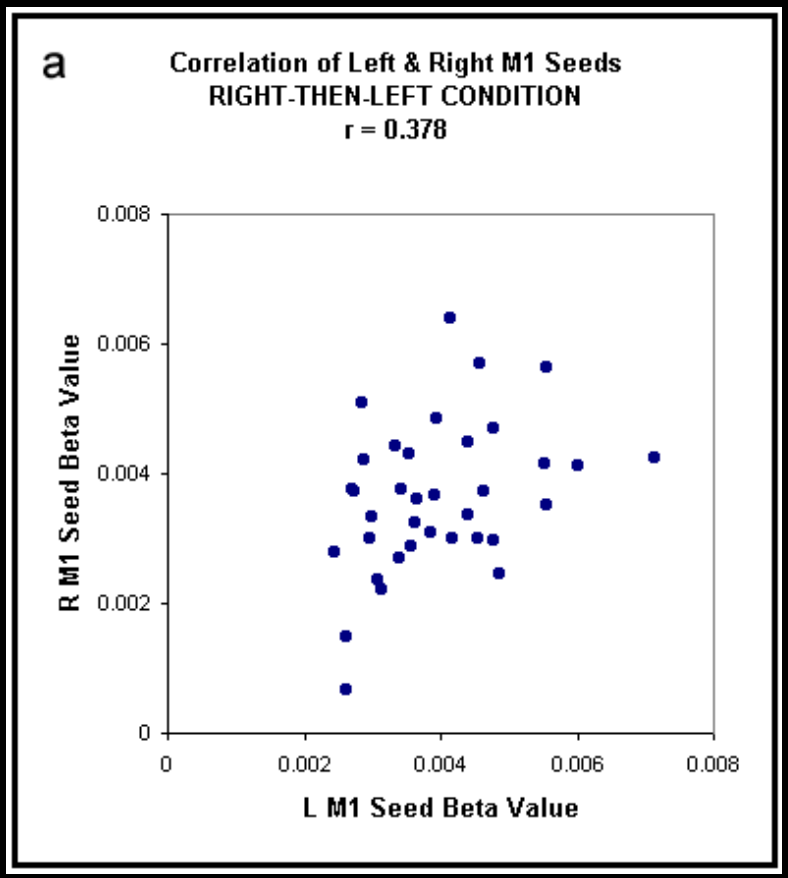


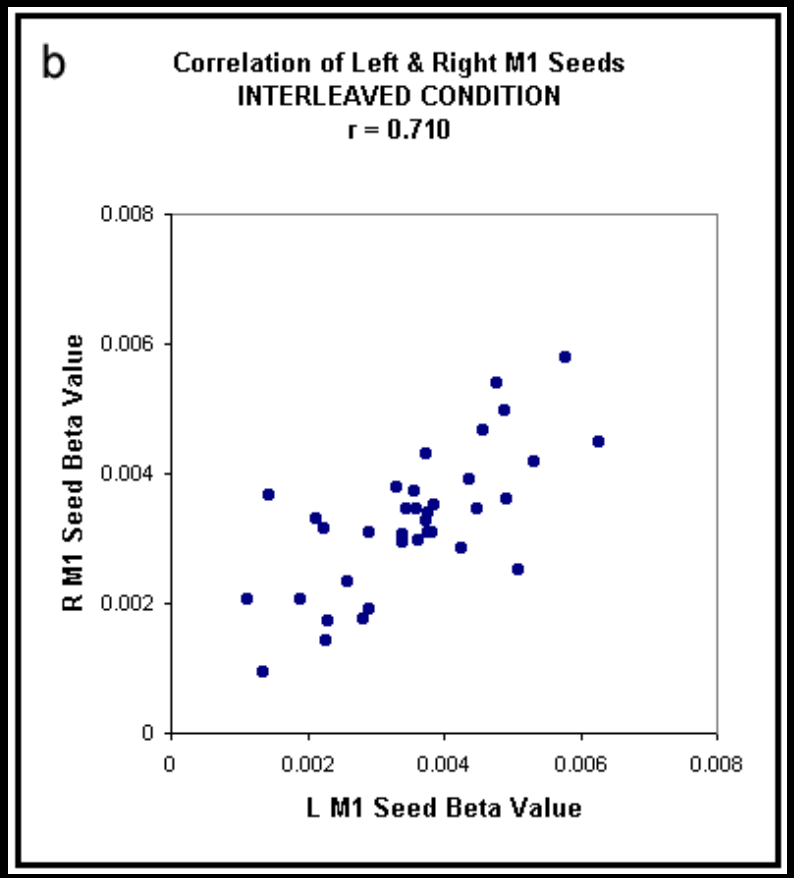
Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

Beta series correlations:

A meaningful metric of inter-regional coupling?







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

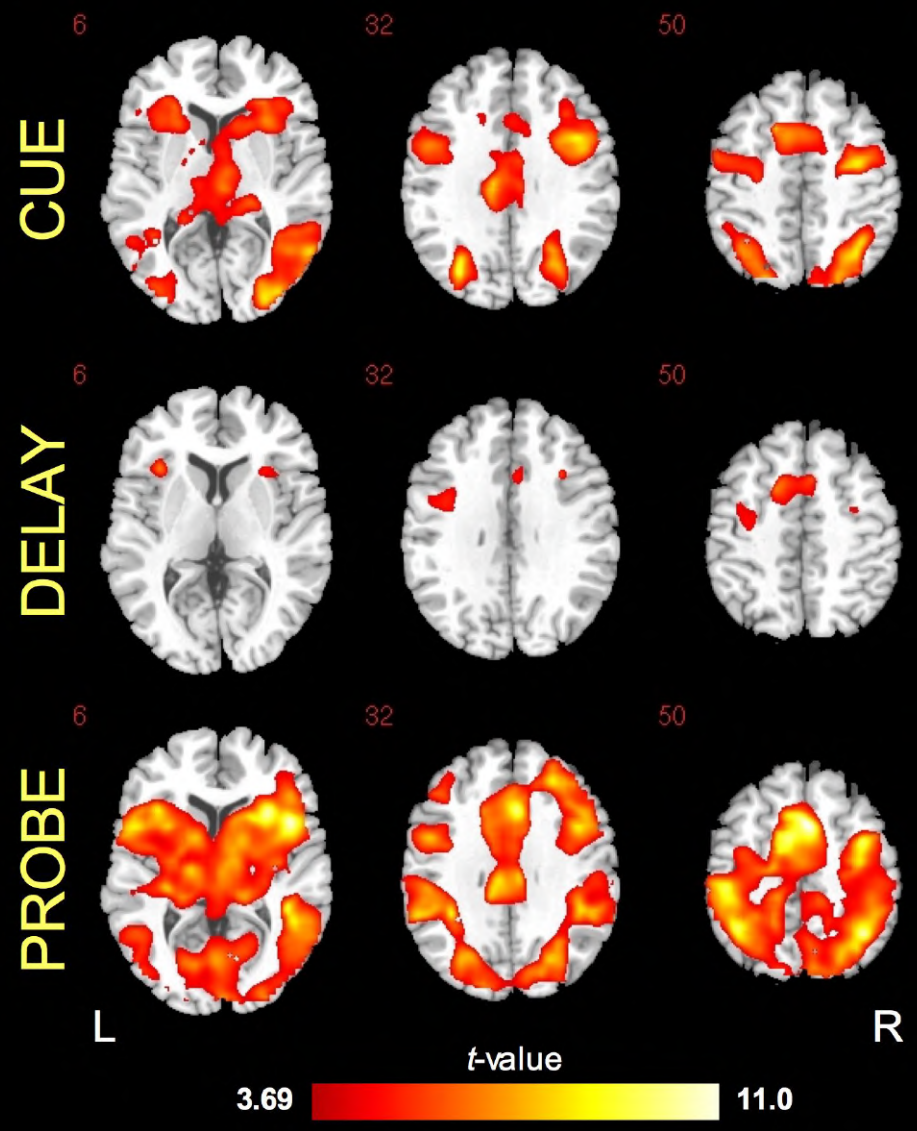
Beta series correlation analysis applied to a basic visual working memory task

- 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

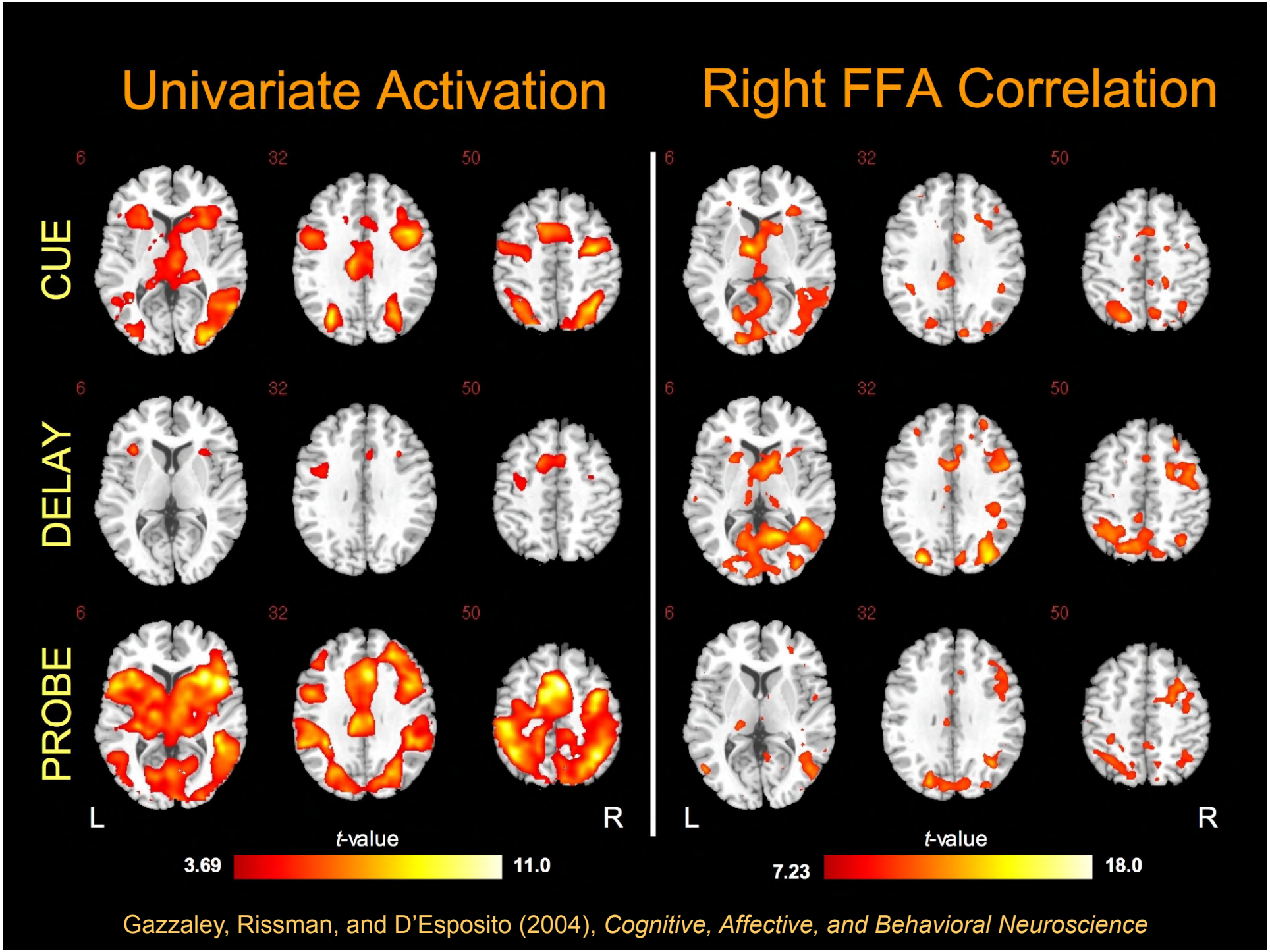
right fusiform face area (FFA) "seed"

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

Univariate Activation



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



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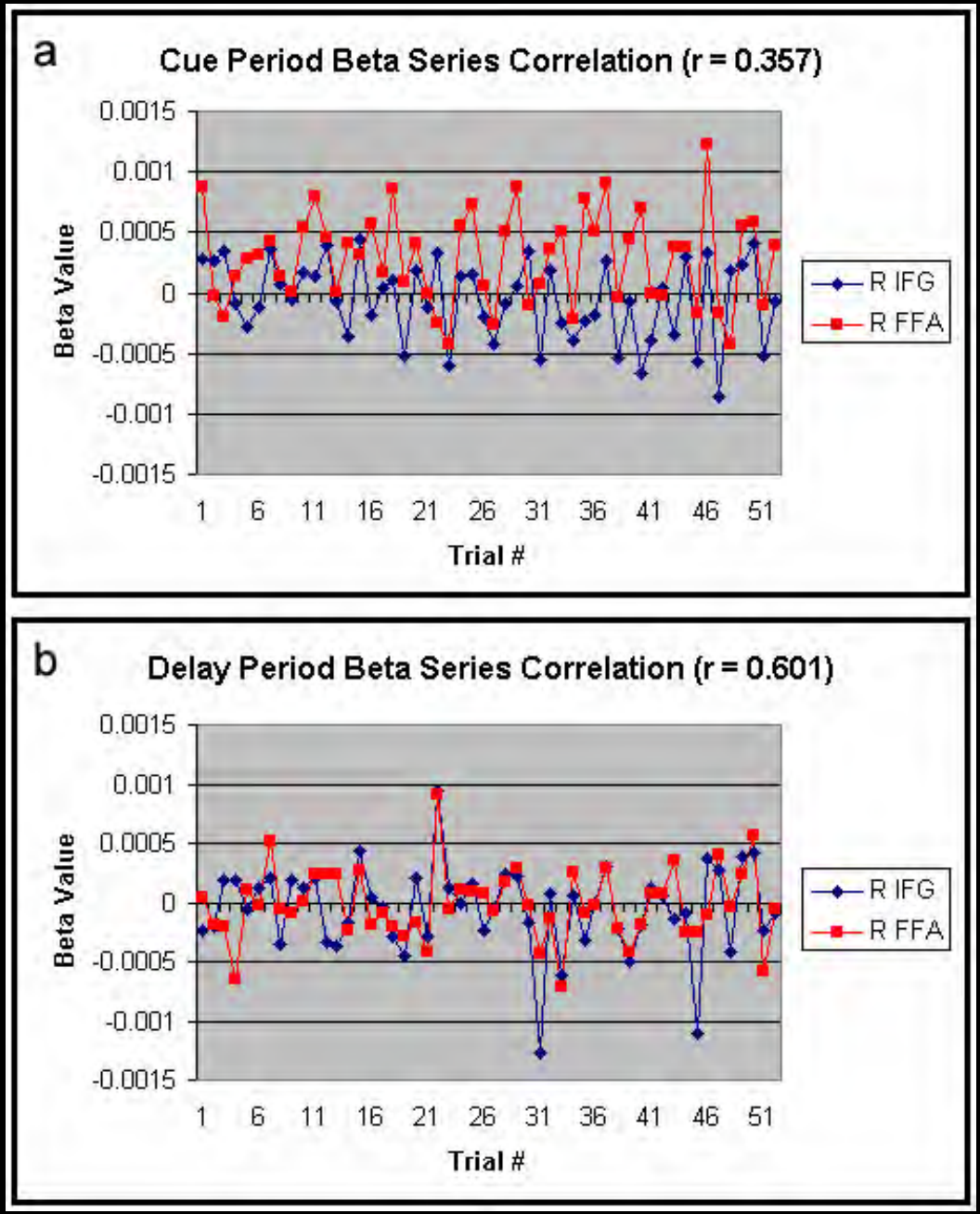
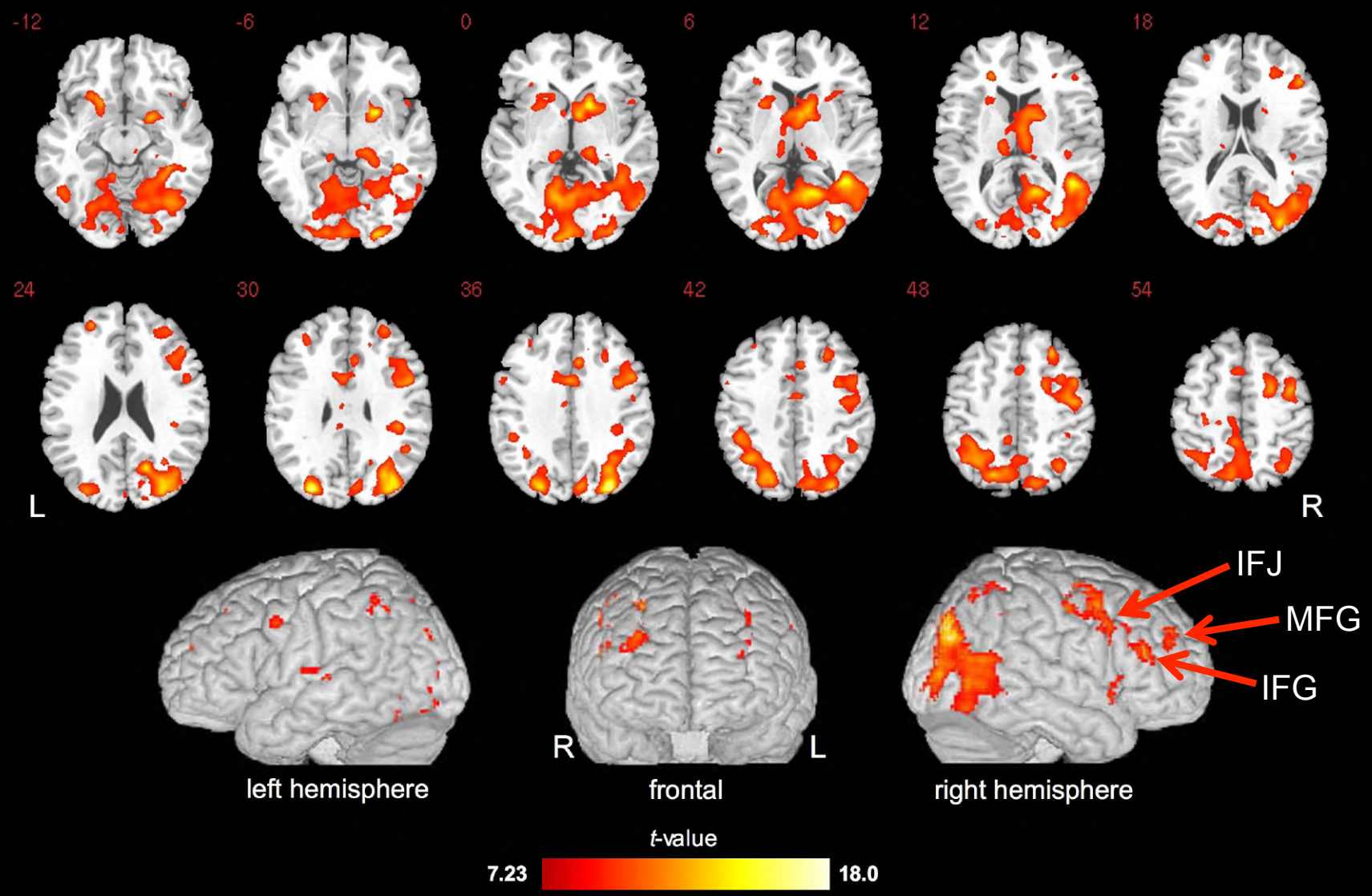


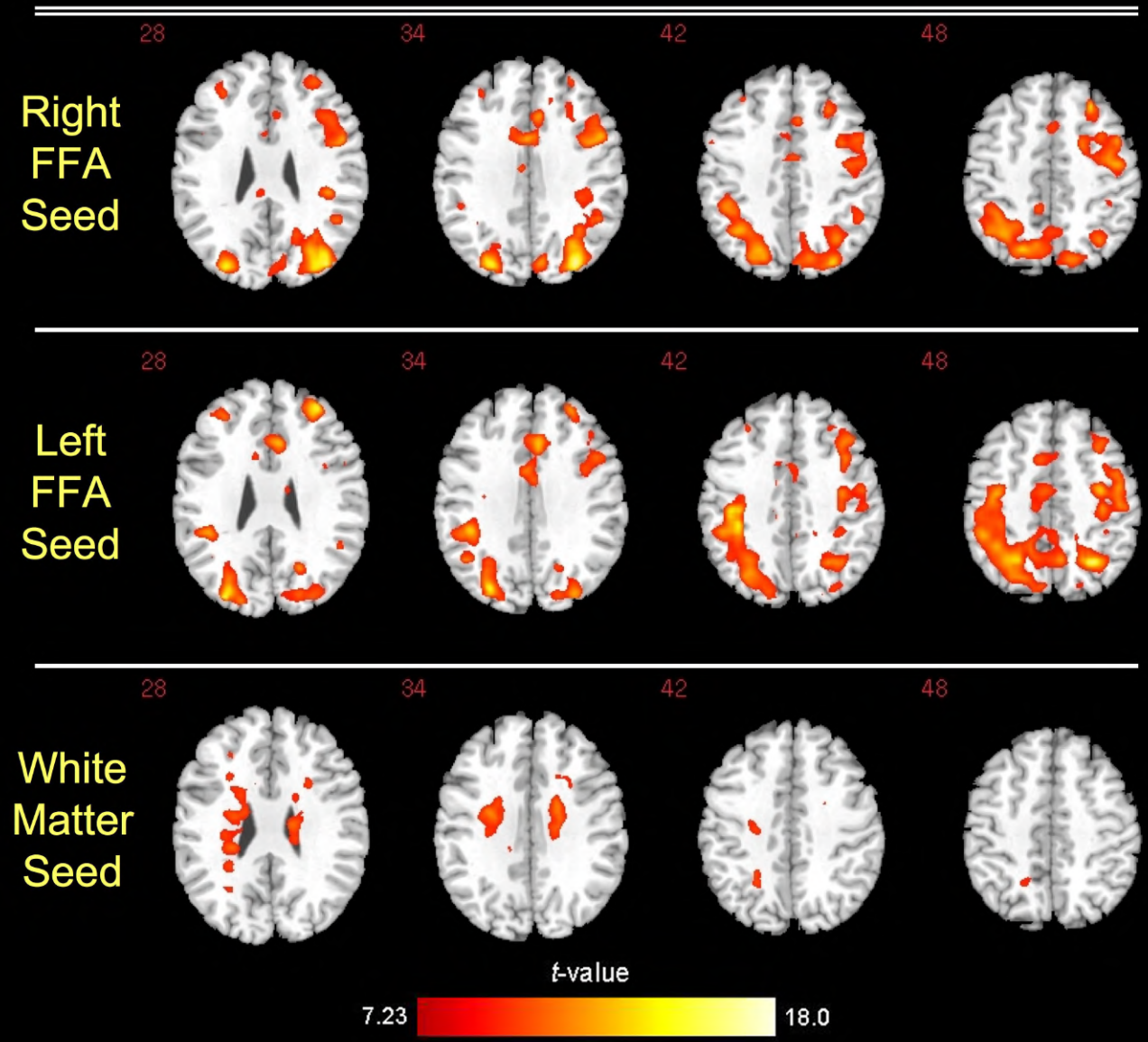
Rissman, Gazzaley, and D'Esposito (2004), *NeuroImage*

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*

Working Memory: Stage-specific neuronal contributions

Subsets of prefrontal neurons in the area of the principal sulcus:

1) are activated phasically in the presence of a visual stimulus,
2) are activated tonically during the delay period over which the stimulus is kept on-line
3) show phasic reactivation in relation to the initiation of a memory-guided response

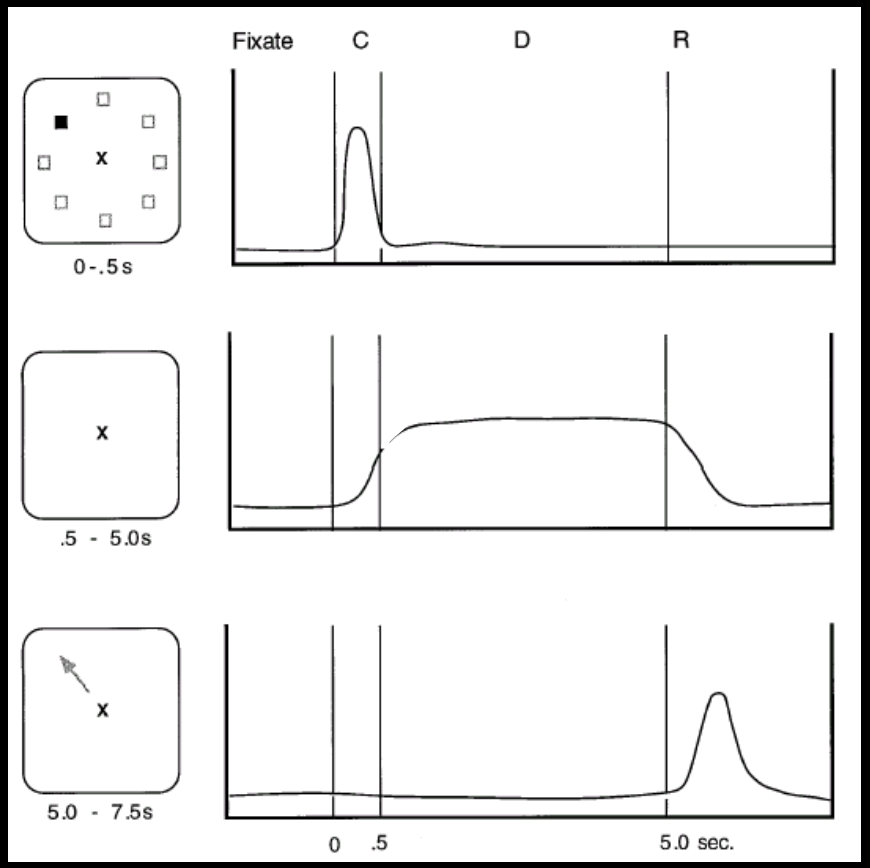
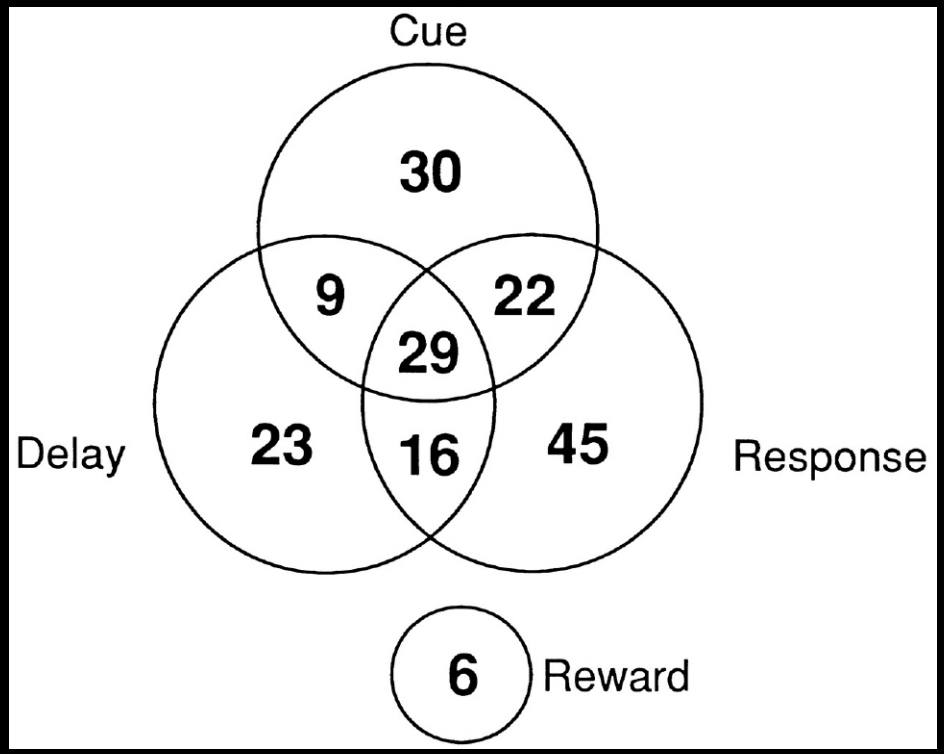


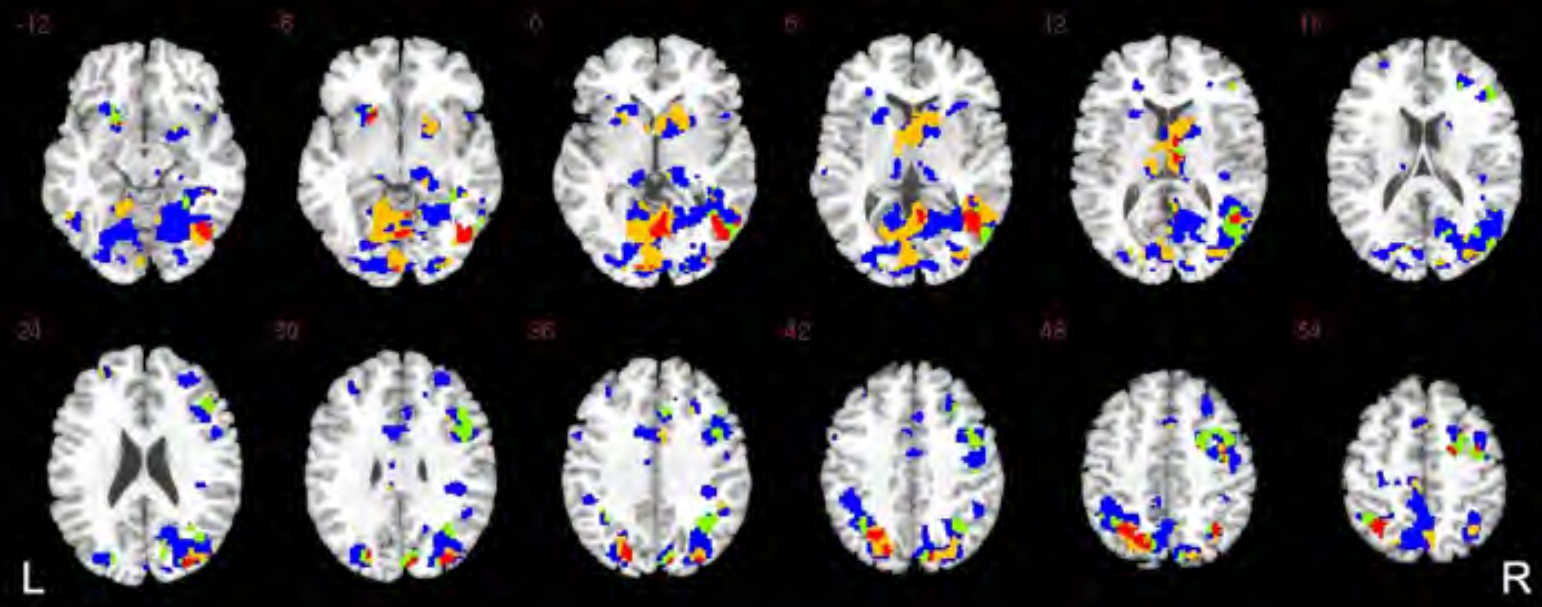
Figure from Goldman-Rakic, 1996

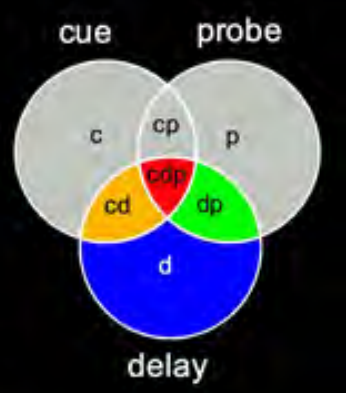
# of Neurons Exhibiting Task-Related Activity in an ODR Task



Funahashi and Inoue, 2000

Delay Network Subcategories: Right FFA seed

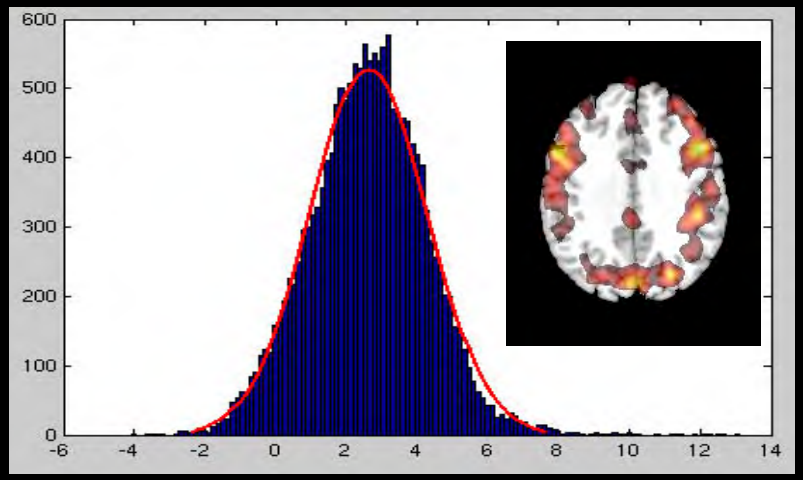




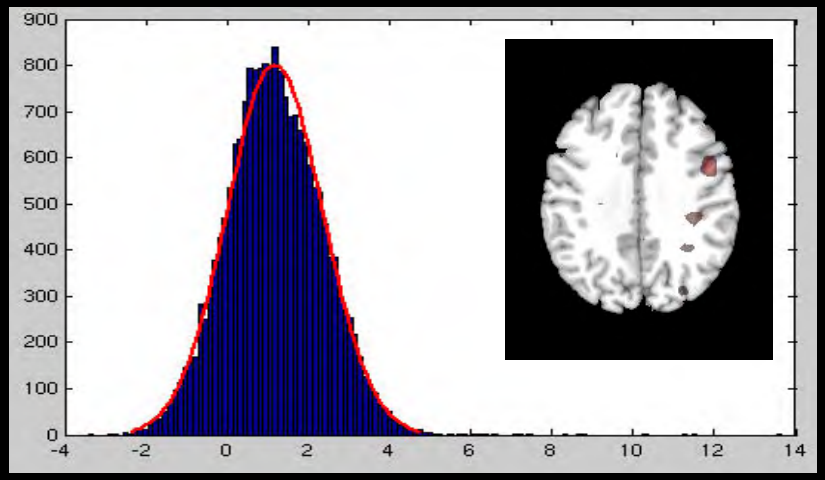
A few methodological considerations

- Across-subject differences in global correlation magnitudes

High Magnitude Subject



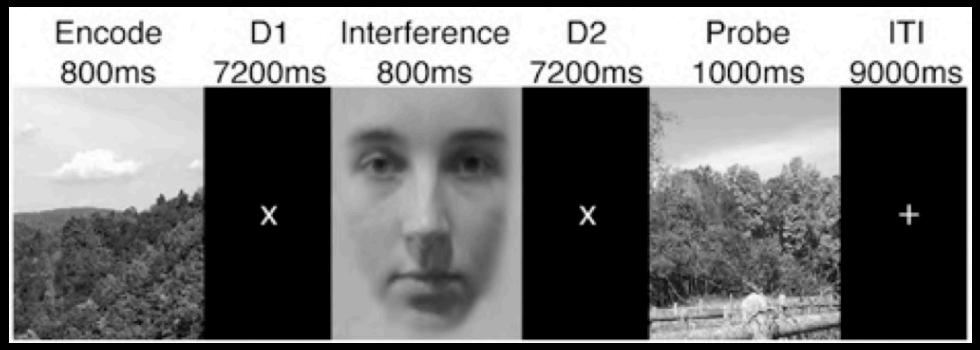
Low Magnitude Subject



- 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

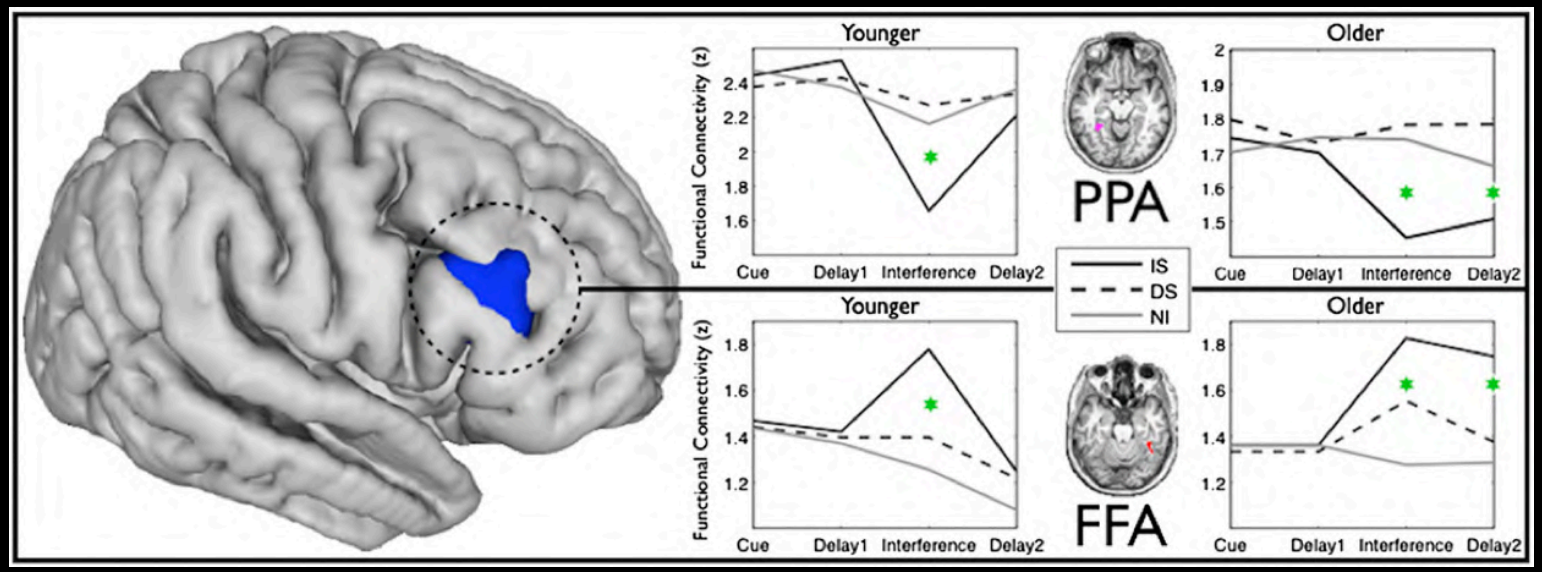
Another example application:

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*

Other recent applications of the beta series correlation analysis approach

- Persistence of emotional memories (Ritchey et al., *Cerebral Cortex* 2008)
  - Increased connectivity between amygdala and hippocampus during encoding predicts increased temporal durability of emotional memories
- Cognitive control in schizophrenia (Yoon et al., *Am J Psychiatry* 2008)
  - Diminished connectivity between DLPFC and task-relevant brain regions
- Drug effects on locus coeruleus function (Minzenberg et al., *Science* 2009)
  - Modafinil increases (negative) functional coupling between PFC and LC
- Emotional regulation in depression (Heller et al., *PNAS* 2010)
  - Decreased NAcc activity in depressed individuals is related to diminished connectivity between NAcc and PFC
- Individual differences in financial risk-taking (Samanez-Larkin et al., *J Neurosci* 2010)
  - Individuals with reduced connectivity between the NAcc and PFC made more risk-seeking mistakes

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 available online)

- Cons:
  - 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., 2011)
  - Cannot determine whether inter-regional correlations reflect direct or indirect communication

Psychophysiological interaction (PPI)

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

$$B \times A \rightarrow C$$

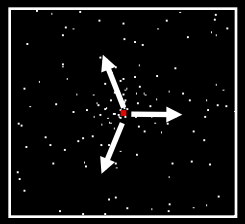
- A PPI corresponds to a difference in regression slopes for different contexts

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

Friston et al. (1997), *NeuroImage*

[slide adapted from K.E. Stephan]

Psychophysiological interaction (PPI)



Stimulus 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:

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

main effect of task

main effect of stim. type

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

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

main effect of task

V1 time series ≈ main effect of stim. type

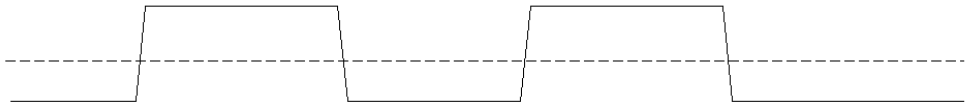
psycho-physiological interaction

Friston et al. (1997), *NeuroImage*

[slide adapted from K.E. Stephan]

Psychophysiological interaction (PPI)

PSY main effect (task variable)



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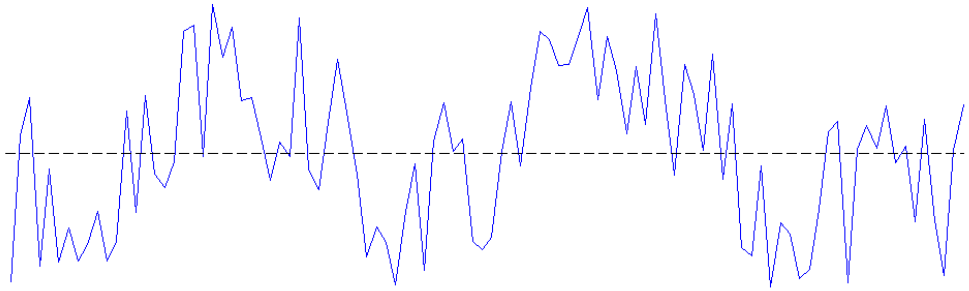
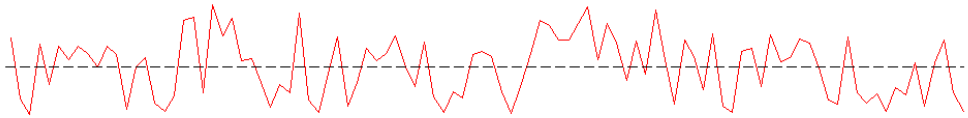
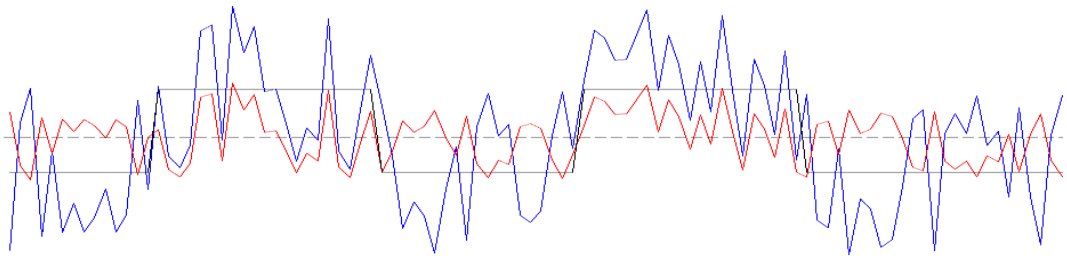
PHYS main effect (time series from seed region)



PPI = PSY.*PHYS

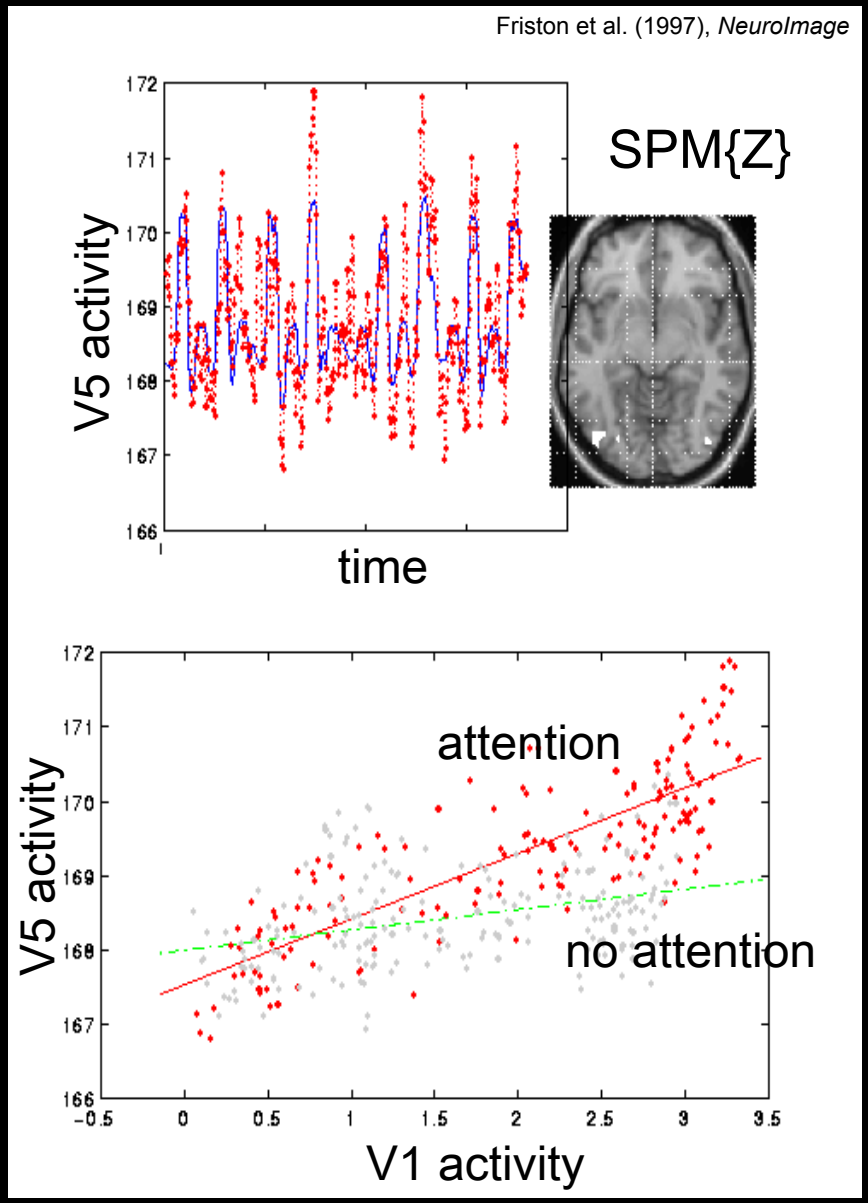


Overlay:



[slide adapted from J. O'Reilly]

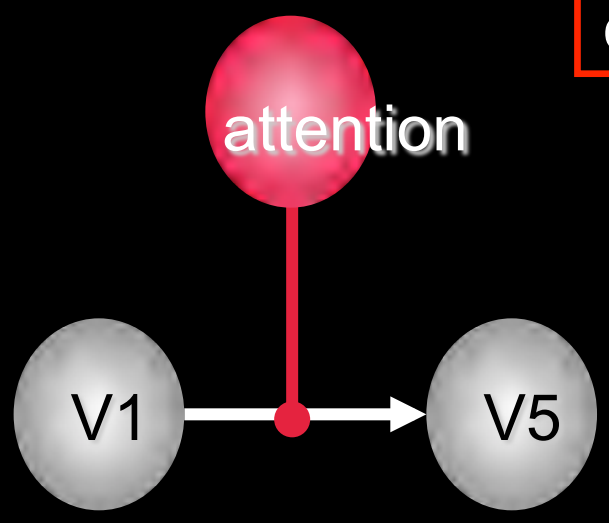
Psychophysiological interaction (PPI)

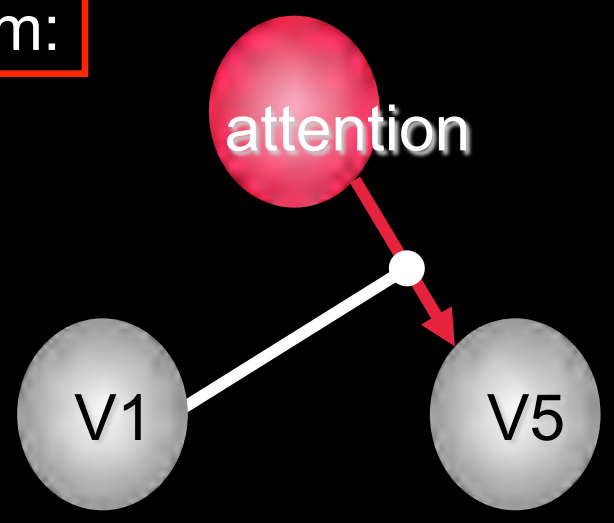


Psychophysiological interaction (PPI)

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

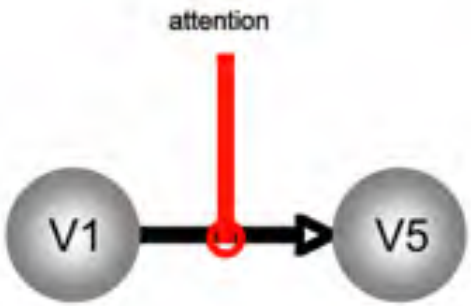
Two possible interpretations of the PPI term:

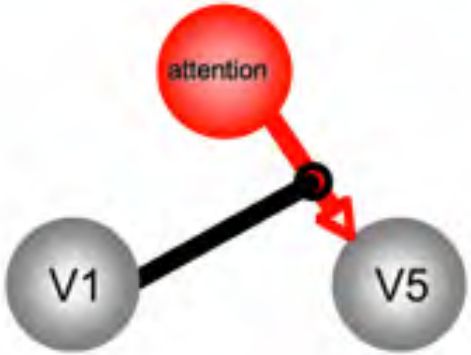


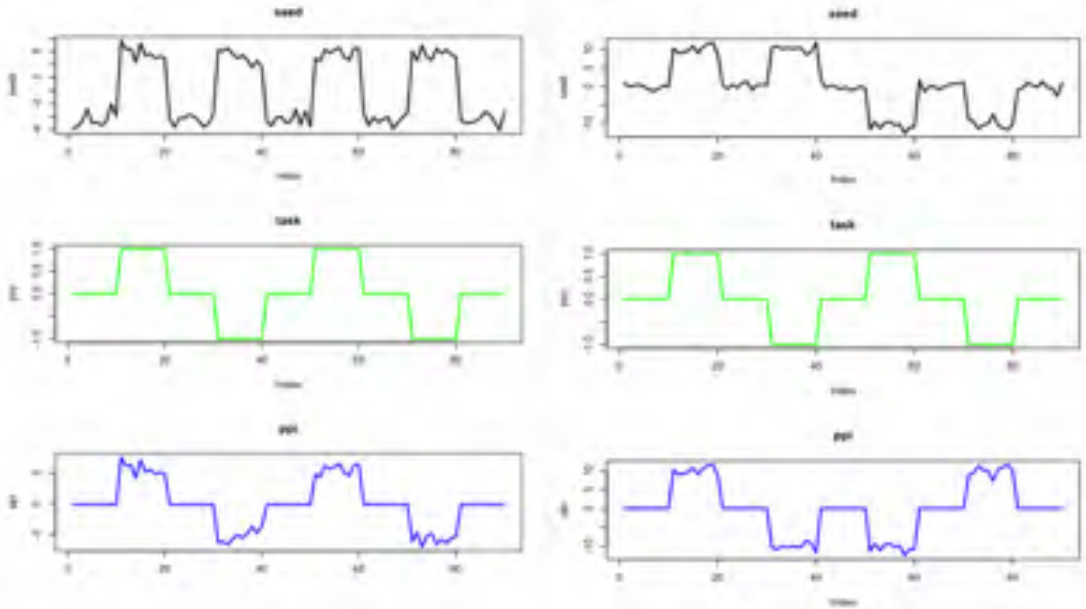


[slide adapted from K.E. Stephan]

Some problems... interpretation and collinearity (not very powerful in event-related designs)





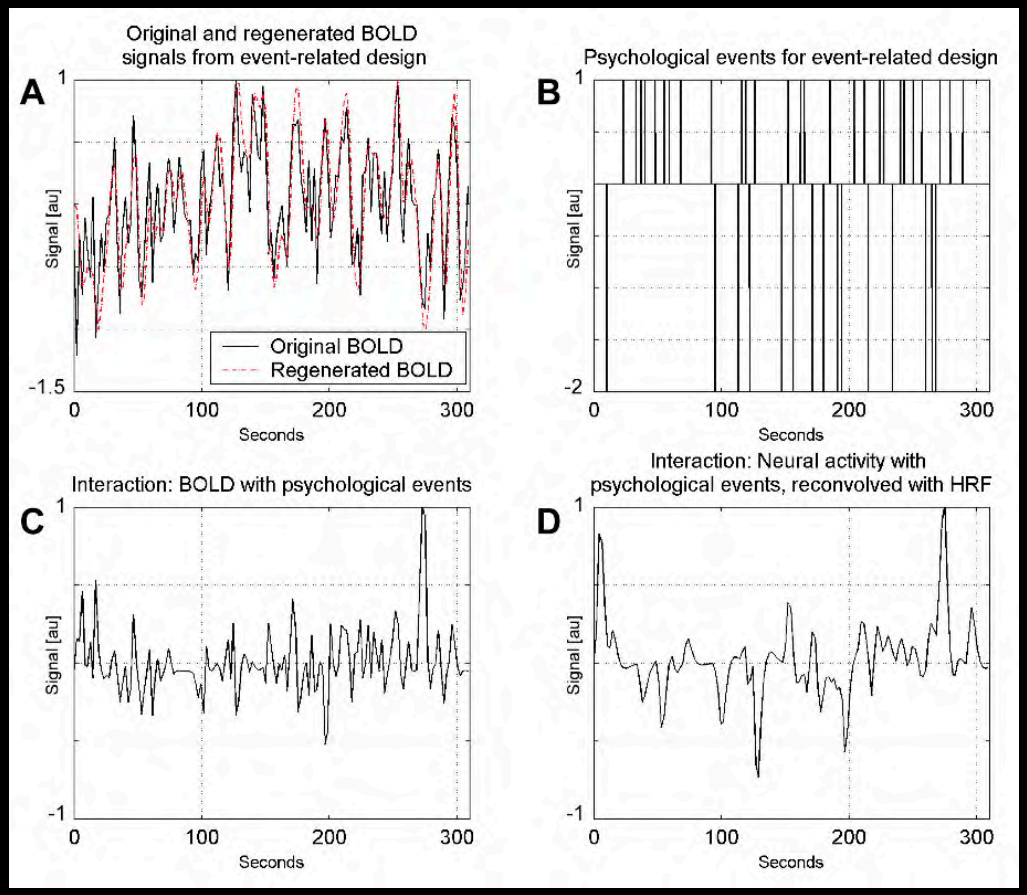


Corr(seed,ppi) = 0.05
Corr(psy,ppi) = 0.97
Corr(seed,psy) = 0.03

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



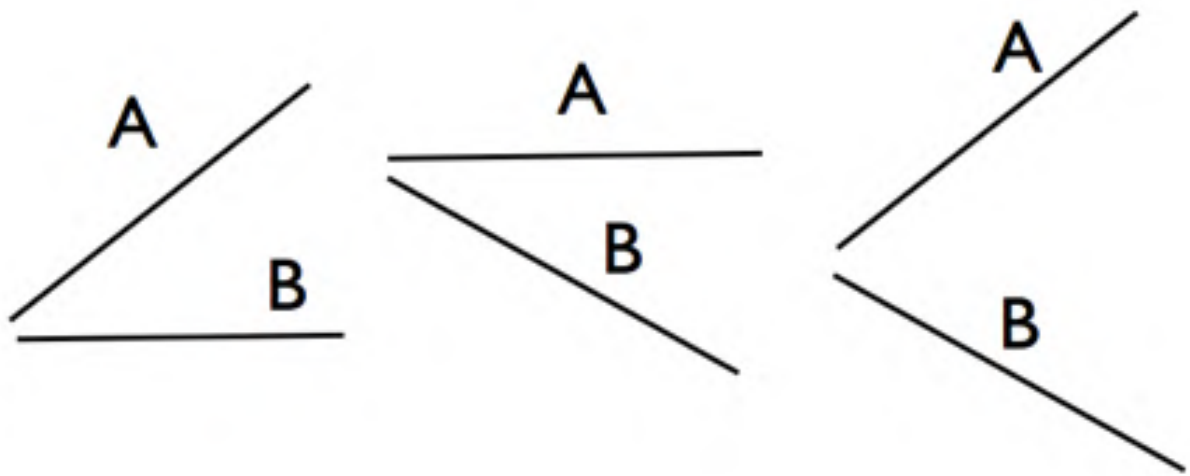
$$(A \otimes HRF) \times (B \otimes HRF) \neq (A \times B) \otimes HRF$$

Gitelman et al. (2004), *NeuroImage*

A different model for PPI...

How can you get the individual slopes from the model?

y = b0 + b1*(A-B) + b2*seed + b3*(A-B)*seed + error
model assumes centering around slope of seed vs y



A different model for PPI...

How can you get the individual slopes from the model?

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model assumes centering around slope of seed vs y

VS

y = b0 + b1*A + b2*B + b3*seed + b4*A*seed + b5*B*seed + error

To test for slope diff: b4-b5 [0 0 0 0 1 -1]
To test for pos slope on A: b3+b4 [0 0 0 1 1 0]
To test for pos slope on B: b3+b5 [0 0 0 1 0 -1]

Jeanette Mumford developed this model

doi:10.1093/scan/nss055 SCAN (2012) 7, 604–609

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

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 this afternoon)

- 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