How I Learned to Stop Worrying and ~~Love~~ Use DCM

Derek Evan Nee, PhD
Helen Wills Neuroscience Institute

Assessing Changes in Connectivity

- **Functional connectivity** – statistical interdependency between regions

- **Effective connectivity** – directed influence of one region upon another

Task-Based Connectivity Tools

Functional Connectivity

- Time series correlation
- Beta Series
- Psychophysiological interaction (PPI)

Effective Connectivity

- Granger Causality
- Structural Equation Modeling (SEM)
- Dynamic Causal Modeling (DCM)

See McIntosh & Misic, 2013, Annu Rev Psychology for a review

Exploratory vs Confirmatory

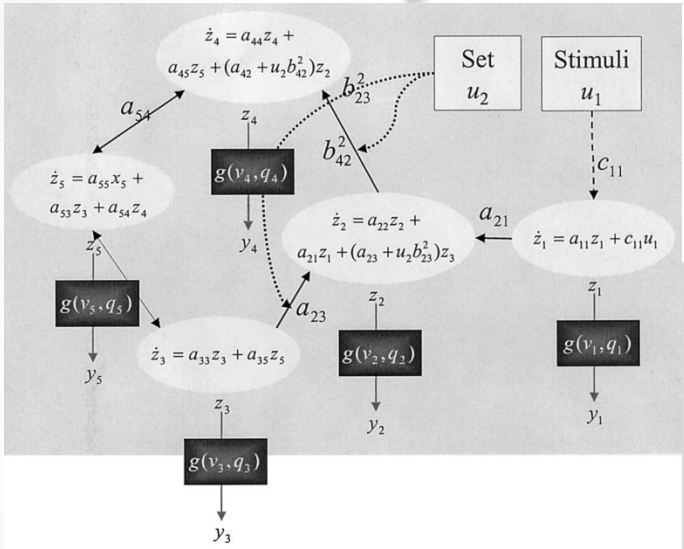
One (or more) seed regions

- Time series correlation
- Beta Series
- PPI
- Granger Causality

All regions known/hypothesized

- SEM
- DCM

Why Not DCM?



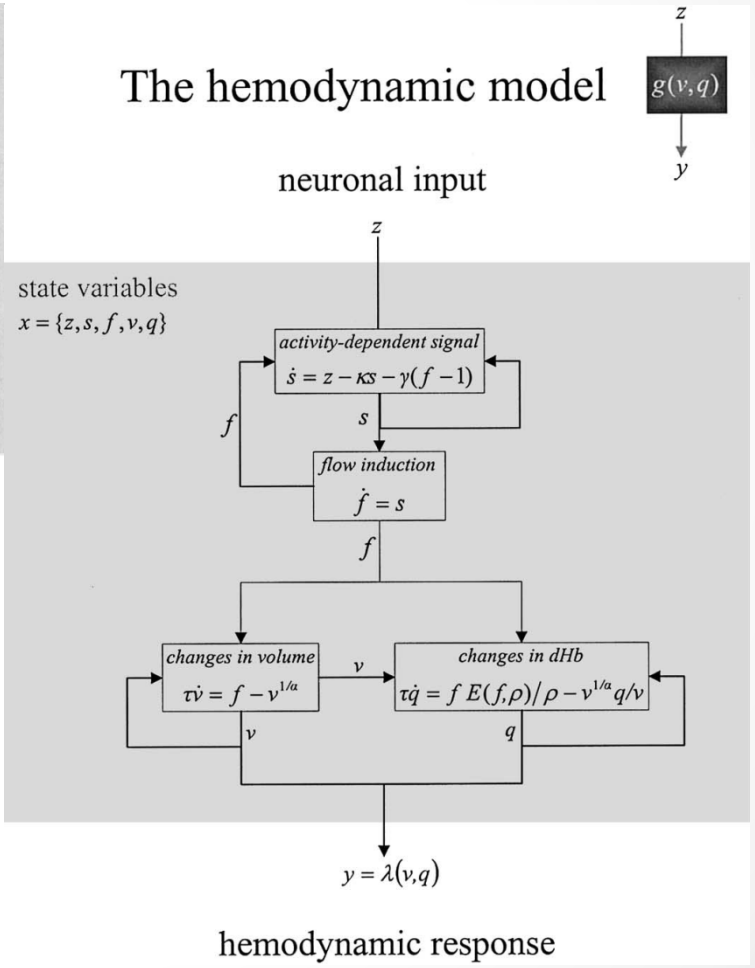
latent connectivity induced connectivity

$$\begin{bmatrix}\dot{z}_1\\ \vdots\\ \dot{z}_5\end{bmatrix} = \left\{\begin{bmatrix} a_{11} & \cdots & 0\\ a_{21}\ a_{22}\ a_{23} & & \\ \vdots\ \ a_{33}\ \ a_{35}\\ a_{42}\ \ a_{44}\ a_{45}\\ 0\ \cdots\ a_{53}\ a_{54}\ a_{55}\end{bmatrix} + u_2\begin{bmatrix}0 & \cdots & 0\\ & b^2_{23} & \\ \vdots & \ddots & \vdots\\ b^2_{42} & & \\ 0 & \cdots & 0\end{bmatrix}\right\}\begin{bmatrix}z_1\\ \vdots\\ z_5\end{bmatrix} + \begin{bmatrix}c_{11} & 0\\ \vdots & \vdots\\ 0 & 0\end{bmatrix}\begin{bmatrix}u_1\\ u_2\end{bmatrix}$$

Forward, backward & self

$$\dot{z} = (A + \sum_j u_j B^j)z + Cu$$

The bilinear model



Friston, 2003, NeuroImage

Why Not DCM?

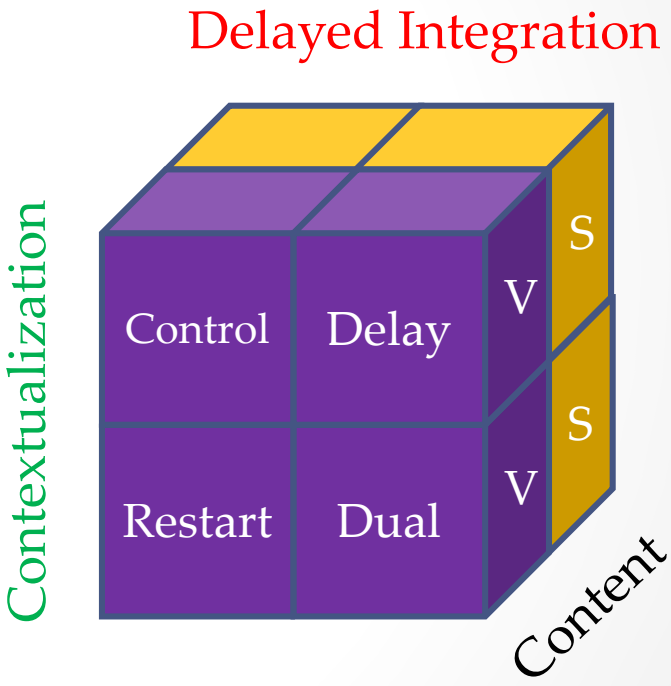
- Not exploratory
  - Need Model(s)
    - **Regions**, Inputs, Connections
- Model-dependent
  - Parameters estimates change dramatically based on model structure
- Computationally expensive

Questions to ask

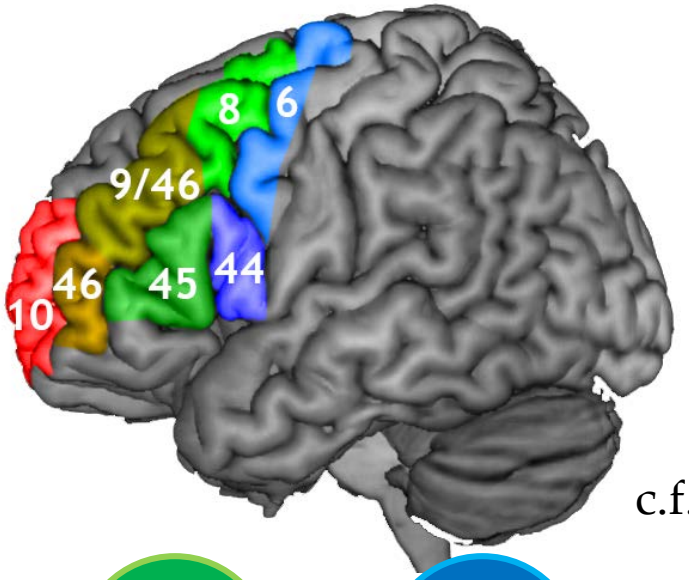
- Can I answer my question with any other (simpler) method?
- Can I believe the answer that DCM gives me?
- (Do I have a lot of time to spend on this?)

Case Study


TASK
SUB-TASK
TASK


Delayed Integration
Contextualization
Control
Delay
Restart
Dual
V
S
V
S
Content

Hypothesis



Spatial

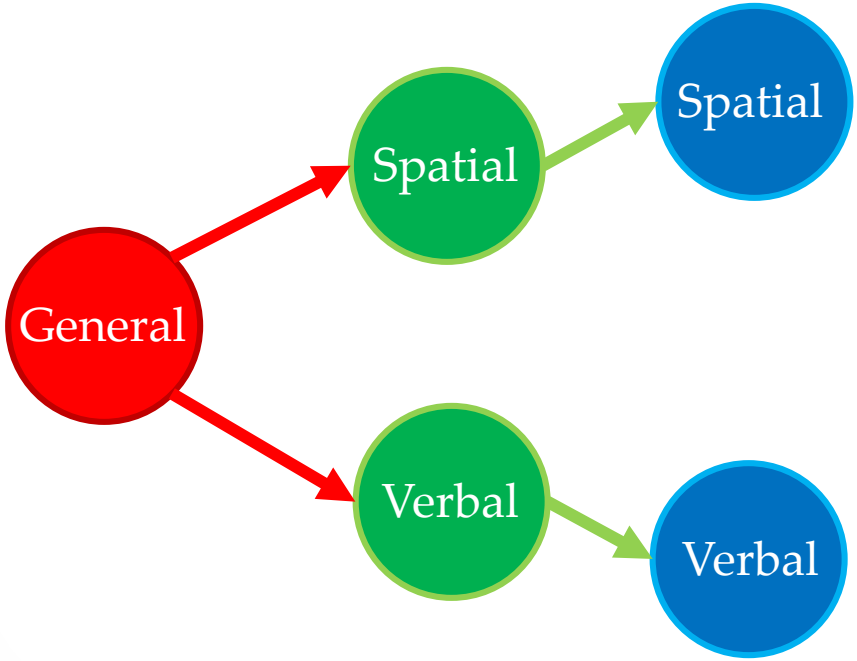
Object

c.f. Nee et al., 2013, Cereb Cortex

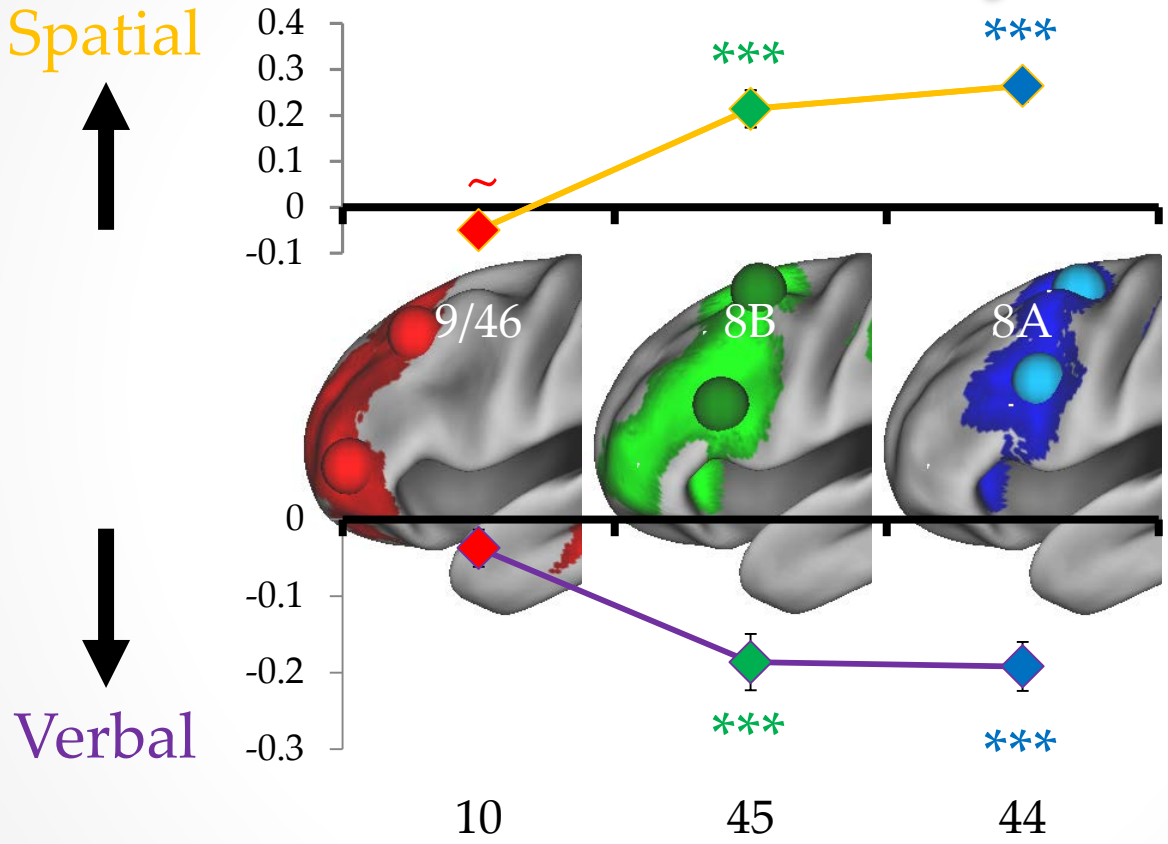
Abstract → Concrete

c.f. Badre & D'Esposito, 2009, Nat Rev Neurosci

Testing Hierarchy



Converging Content Sensitivity



~ $p < 0.05$ uncorrected
*** $p < 0.0005$ corrected

Questions to ask

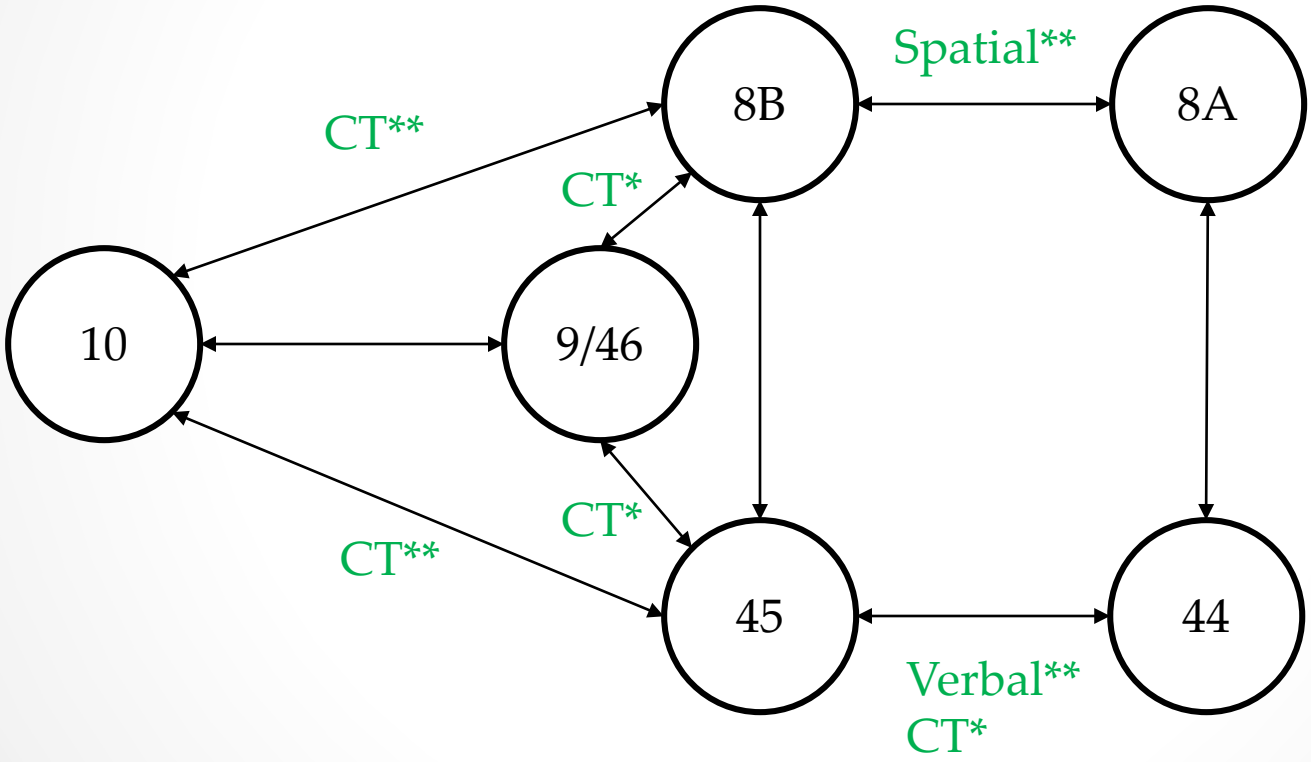
- **Can I answer my question with any other (simpler) method?**

- Can I believe the answer that DCM gives me?

Simplest Test: Time Series Correlations

- For each ROI (and subject)
  - Whiten and high-pass filter time-series
  - Extract (time-shifted) TRs associated with each block and concatenate by condition
  - Regress out stimuli
  - Calculate inter-regional correlations by condition
  - Look for differences in correlations as a function of condition

Simplest Test: Time Series Correlations



Simplest Test: Upshot

- Differences exist suggesting that there are changes in functional connectivity
- Direction of influences is unclear
- Paves way for more complex approach

Choosing an Effective Method

- Granger causality?
  - Personal bias that inter-regional time-based information is mostly meaningless in fMRI (YMMV)
- DCM?
  - No thanks (c.f. why not DCM?)
- SEM it is!

Why SEM?

- Models are essentially series of regression equations
  - Can understand this!

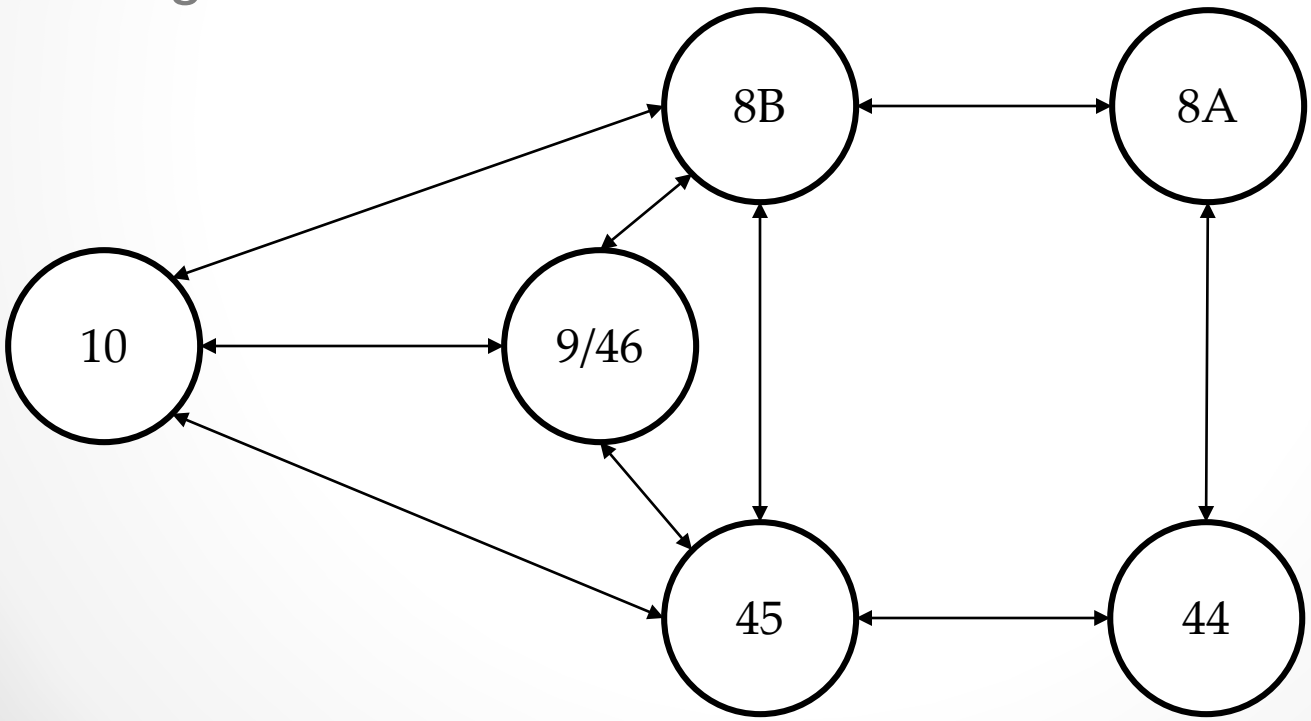
- Less assumptions than other effective connectivity methods

SEM Implementation

- 1dSEMr
  - (http://afni.nimh.nih.gov/sscc/gangc/SEMr.html)
  - Chen et al., 2011, Comp Biol med
- Inputs
  - Correlation matrix
  - Path model(s)

Why Not SEM?

- Not all models are identifiable
  - Multiple potential ways to account for inter-regional correlations



Why Not SEM?

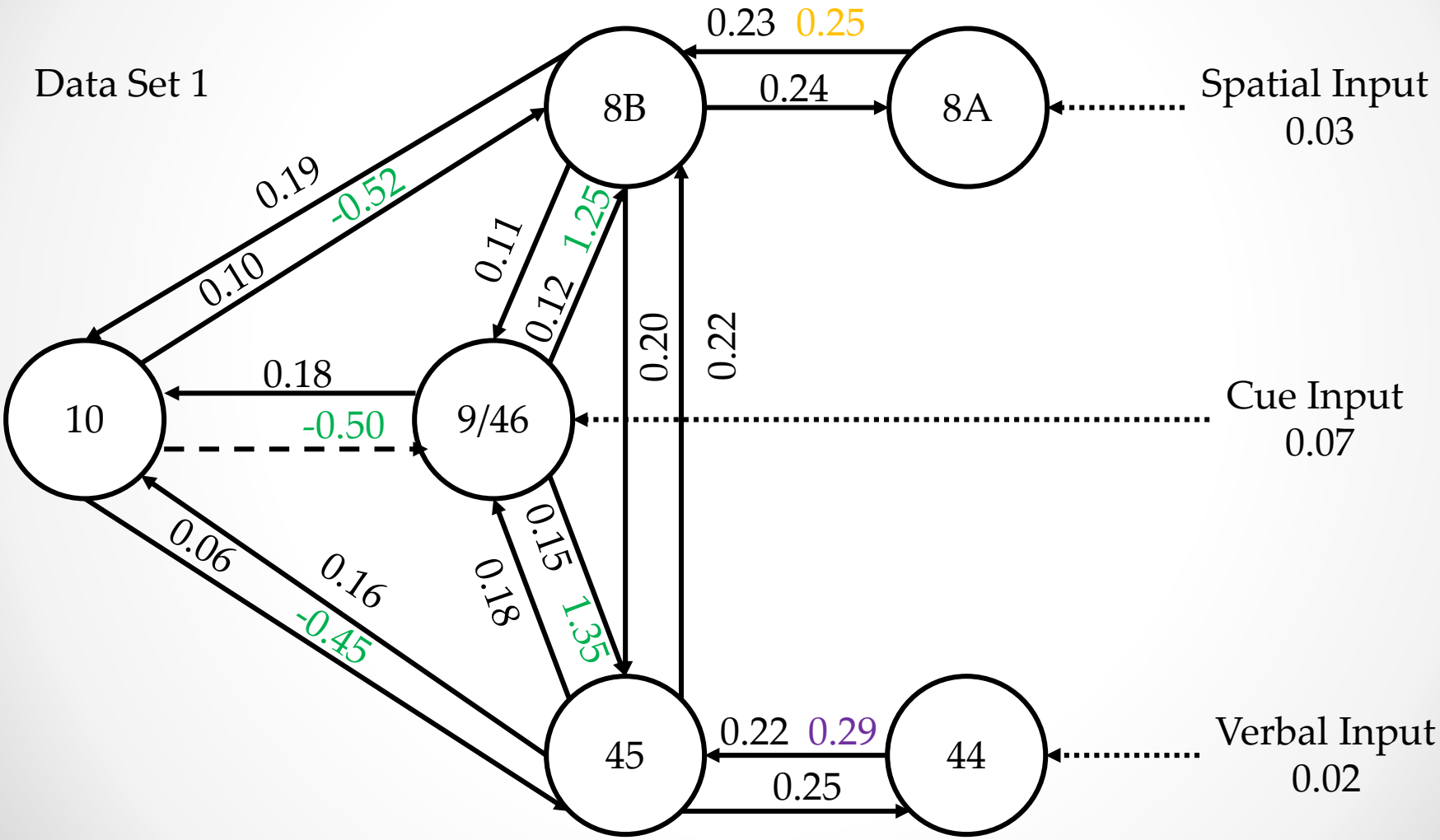
- Not all models are identifiable
  - Multiple potential ways to account for inter-regional correlations
- Models that I could compare were severely limited
- Significant path changes by condition that were observed were small and did not seem to match observations based on times series correlations

Questions to ask

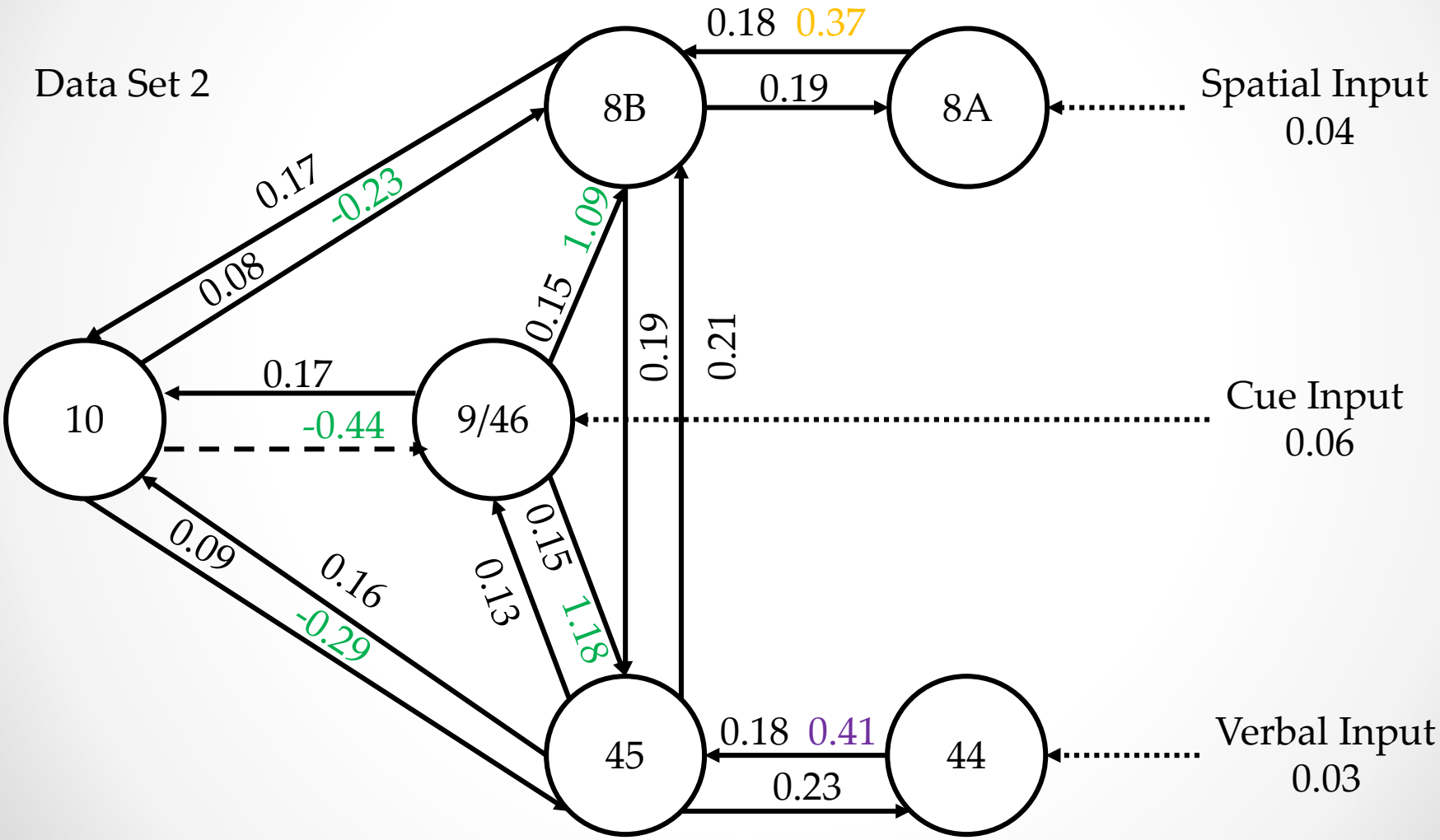
- Can I answer my question with any other (simpler) method?
  - No…

- **Can I believe the answer that DCM gives me?**

Prefrontal Dynamics



Prefrontal Dynamics



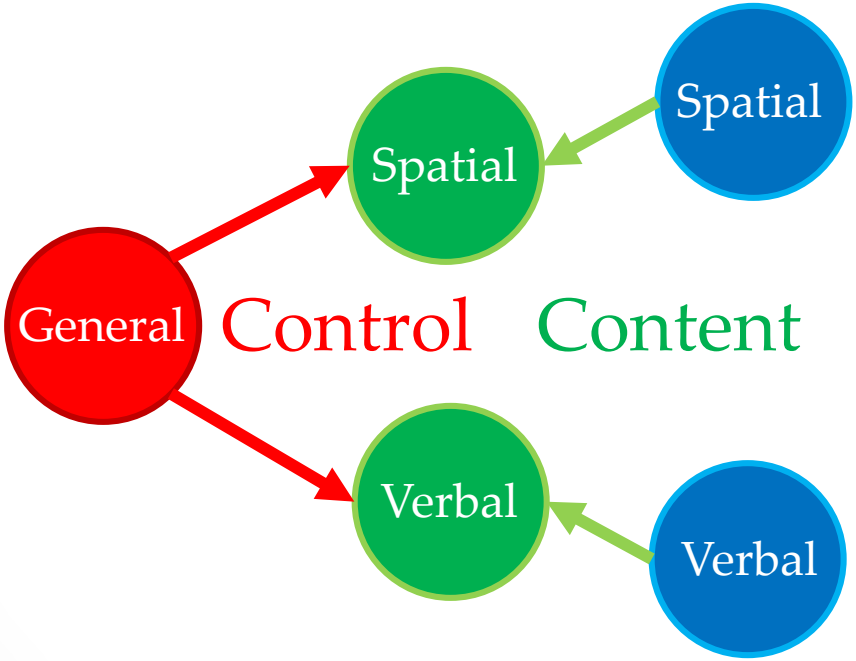
DCM Robustness

- >40 parameters estimated
- Only 1 parameter significant in one data set and not the other
- Similar pattern observed for at least a dozen models that I examined in this way
- Observed modulations by connectivity matched time series correlation

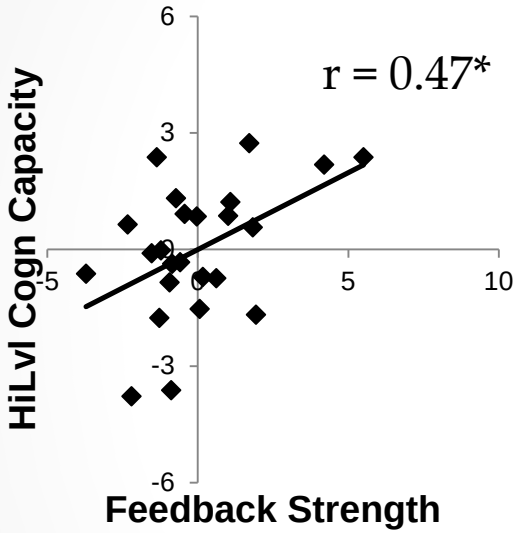
Questions to ask

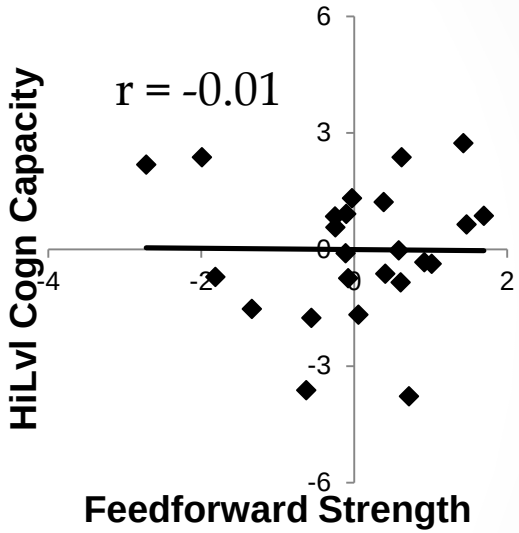
- Can I answer my question with any other (simpler) method?
  - No…
- Can I believe the answer that DCM gives me?
  - I'm not sure that DCM computes what it purports to compute, but it does appear to compute whatever it is it computes robustly

Conclusions



Modulatory Strength and Cognitive Ability





Significant after robust regression and after removal of 2 low cognitive capacity individuals

Top-down control predicts better higher-level cognitive ability

Summary

- DCM is a complex and time-consuming investment
- Explore precursors and alternatives
- Check robustness
- Profit