



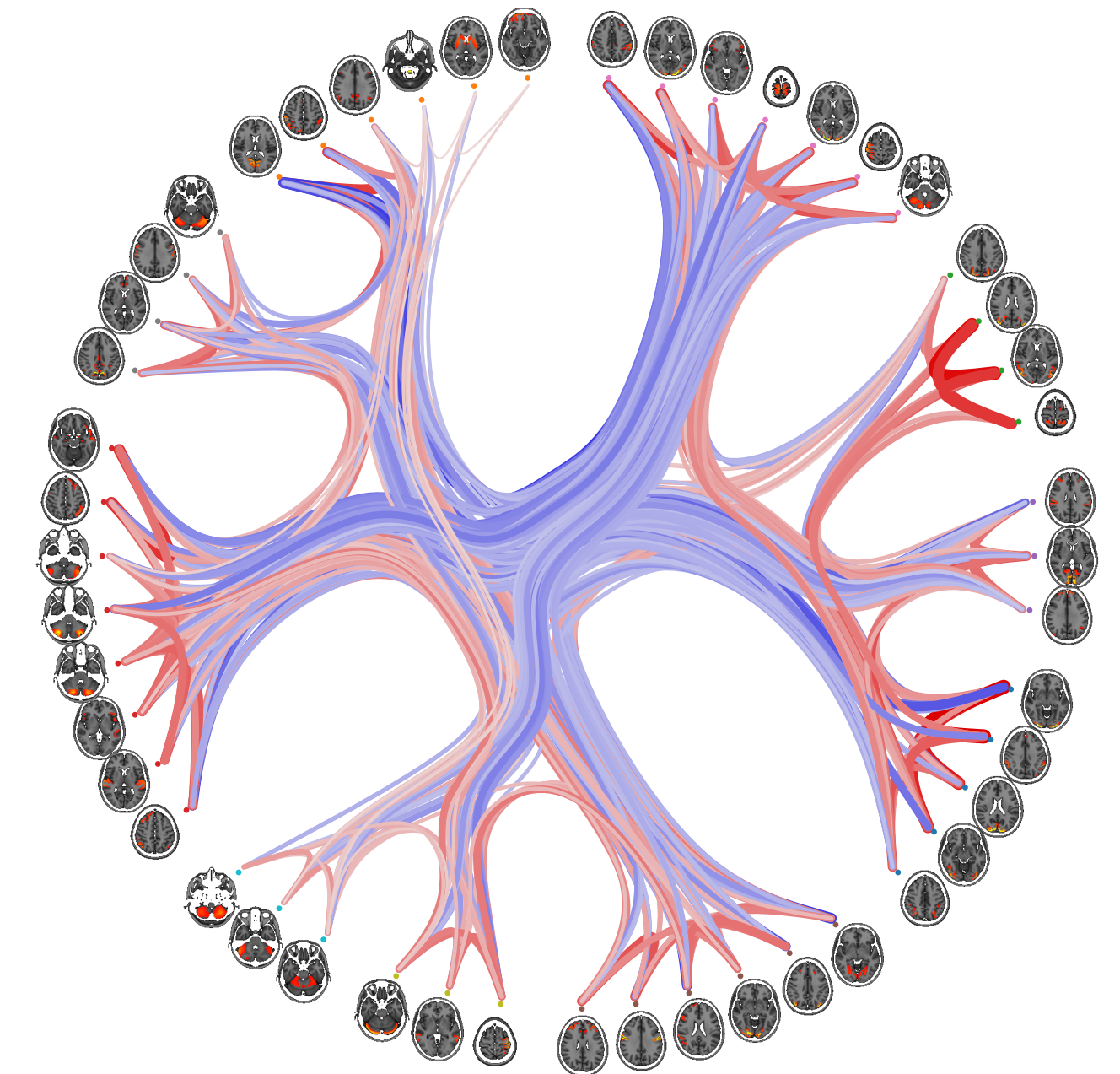
# Resting-State fMRI: Network Modelling and FSLNets

FSL Course 2026

25 June, Bordeaux, France

# Network modelling analysis

- **Characteristics of Resting State Networks (RSNs)**
- **Additional notes on preprocessing**
- Network modelling analysis
- Methods comparisons and considerations

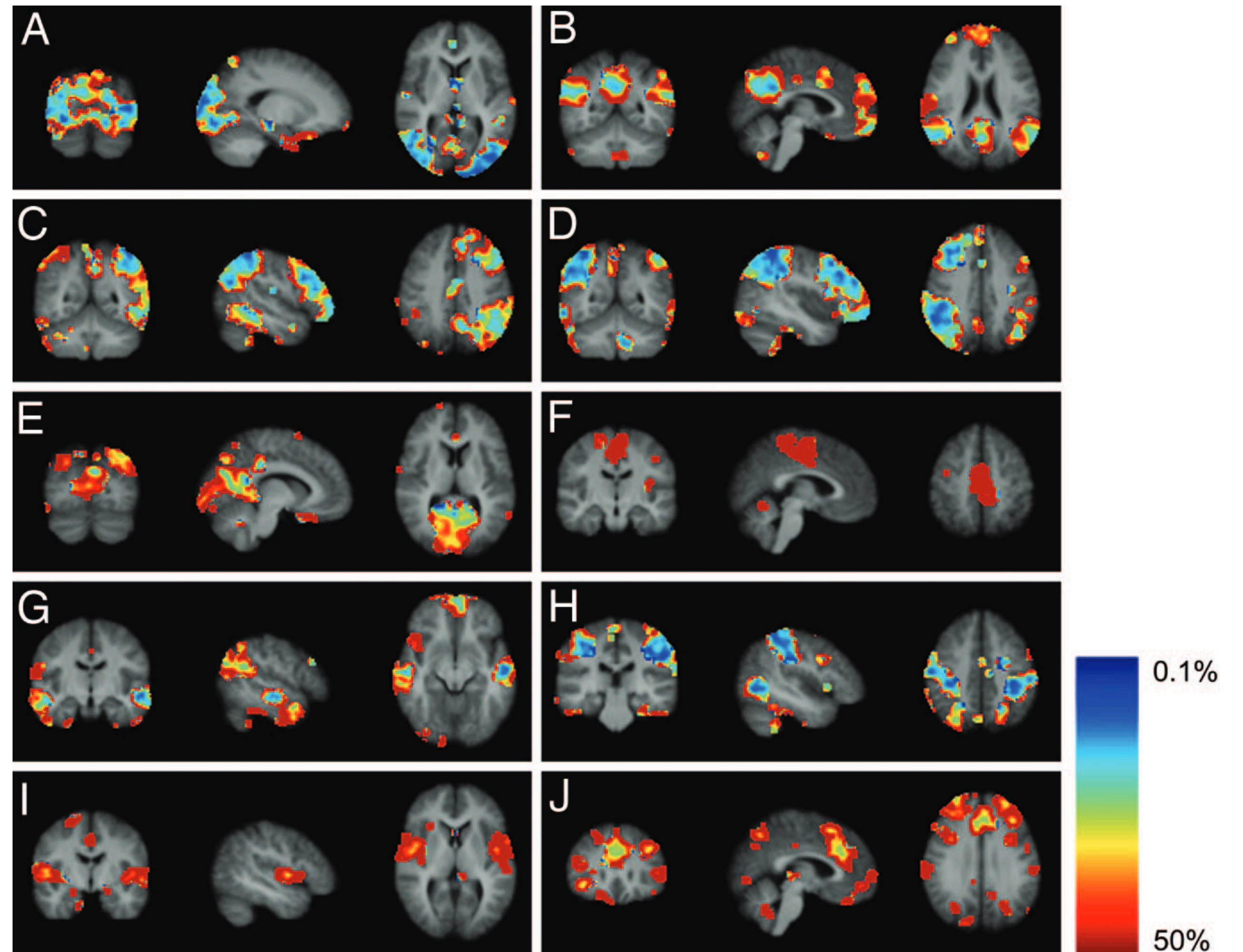




# Characteristics of Resting State Networks (RSNs)

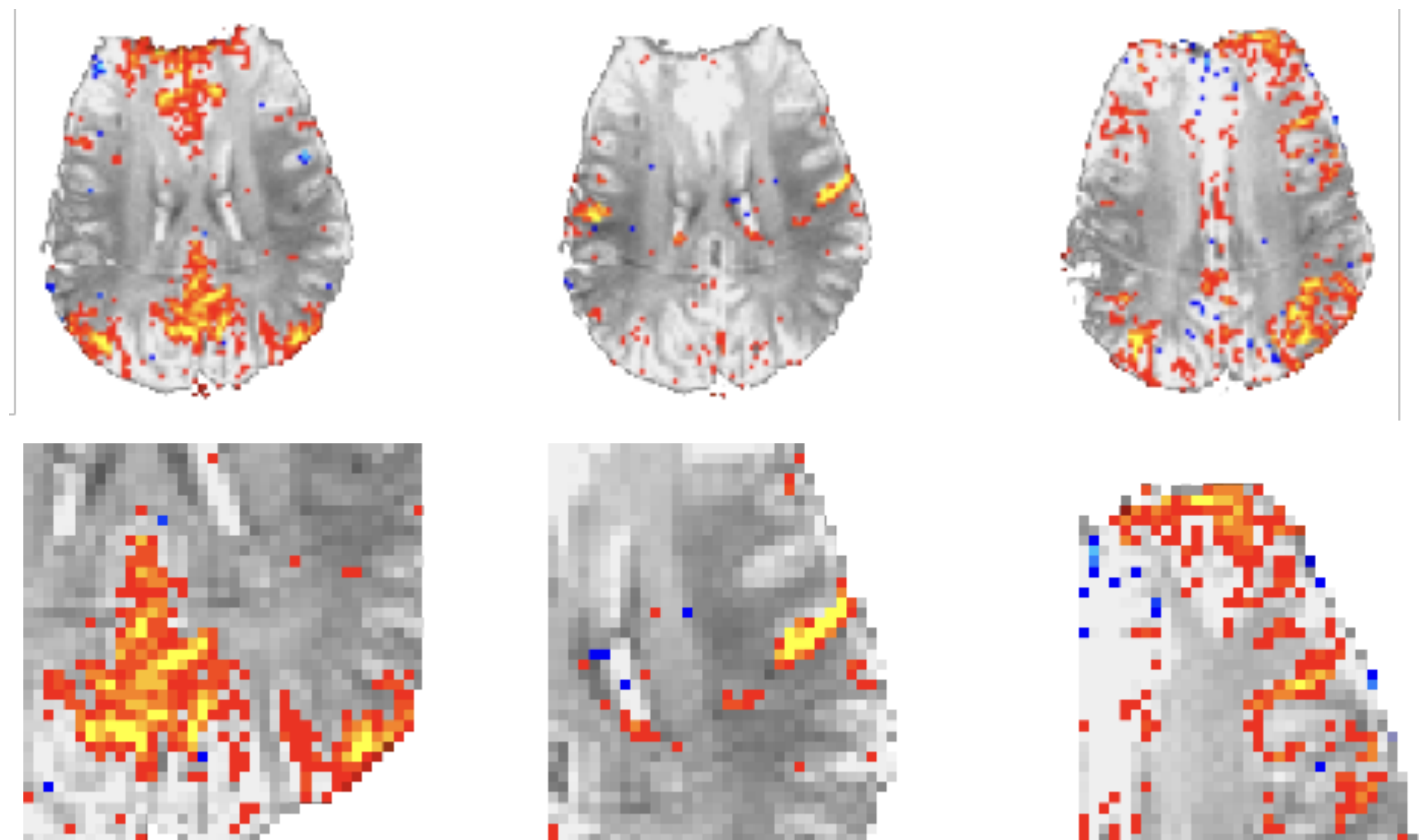
# Replicable networks

Large-scale inherent organisation is reproducibly found across studies and approaches



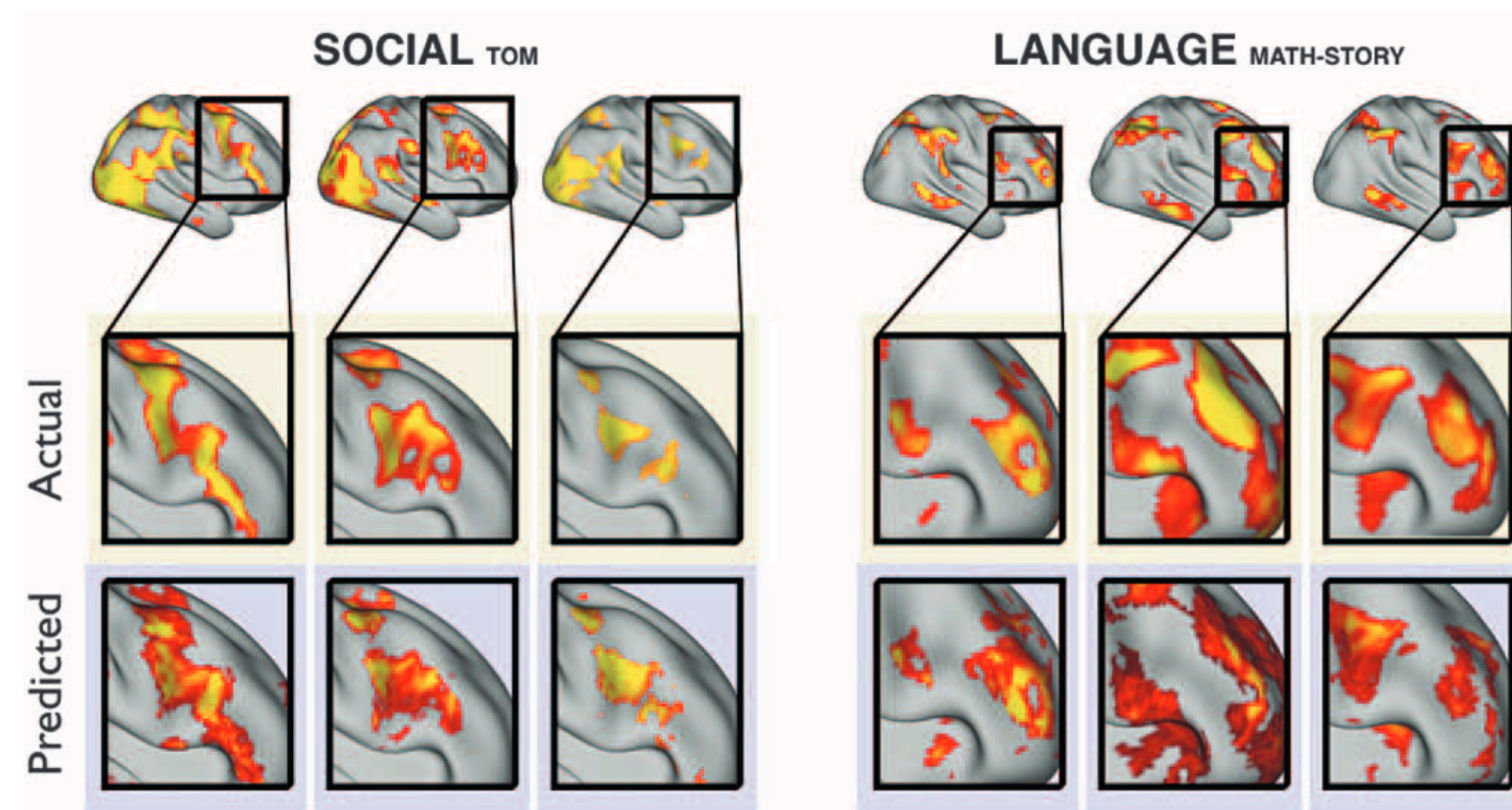
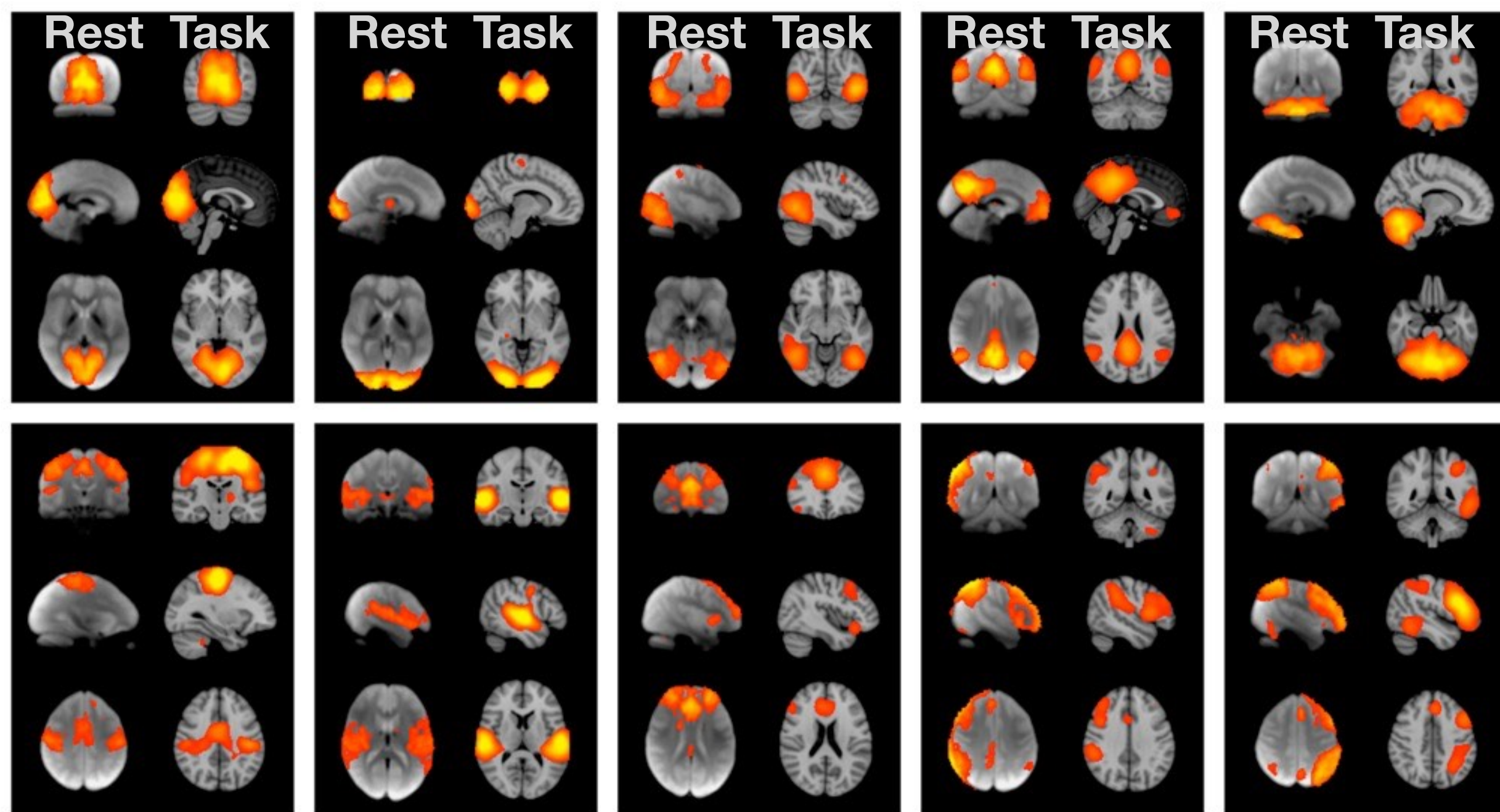
# Grey matter networks

Resting state network structure is localised in grey matter



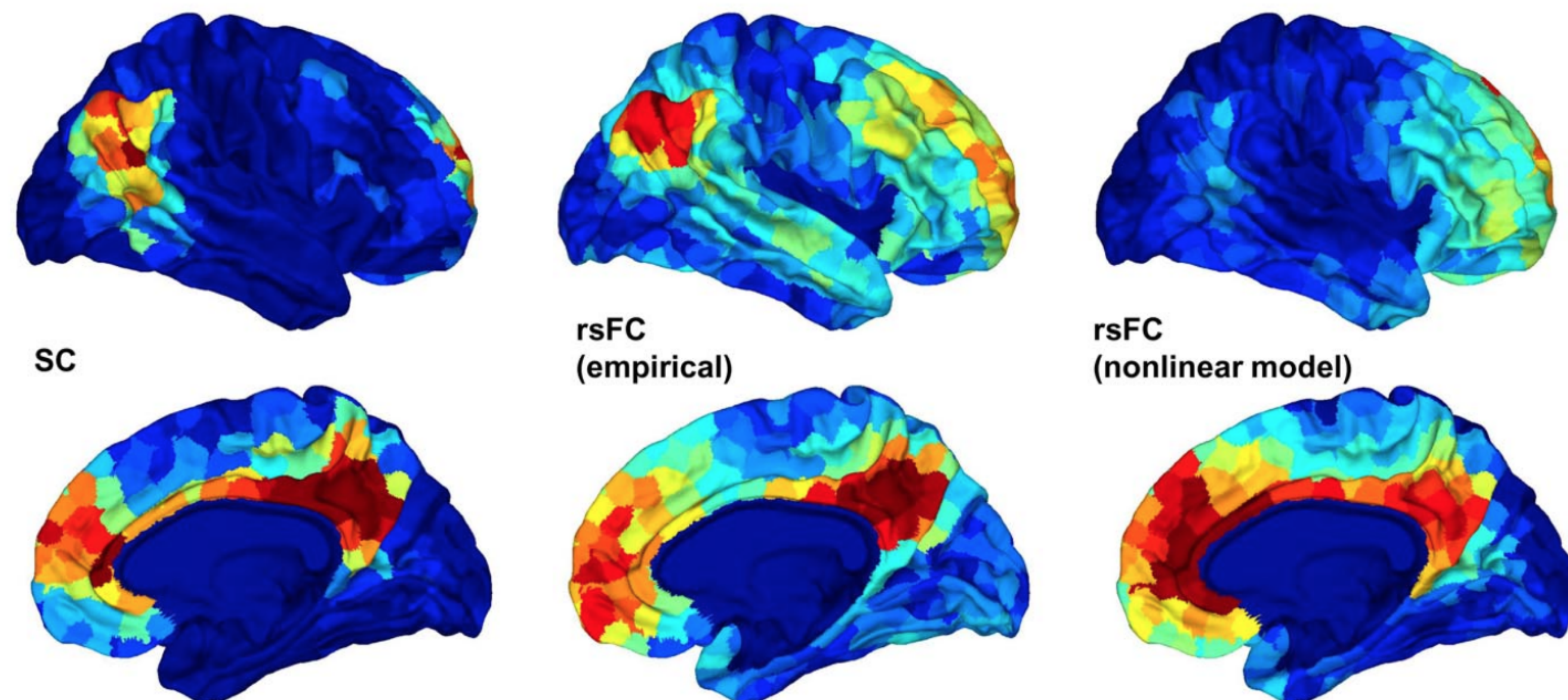
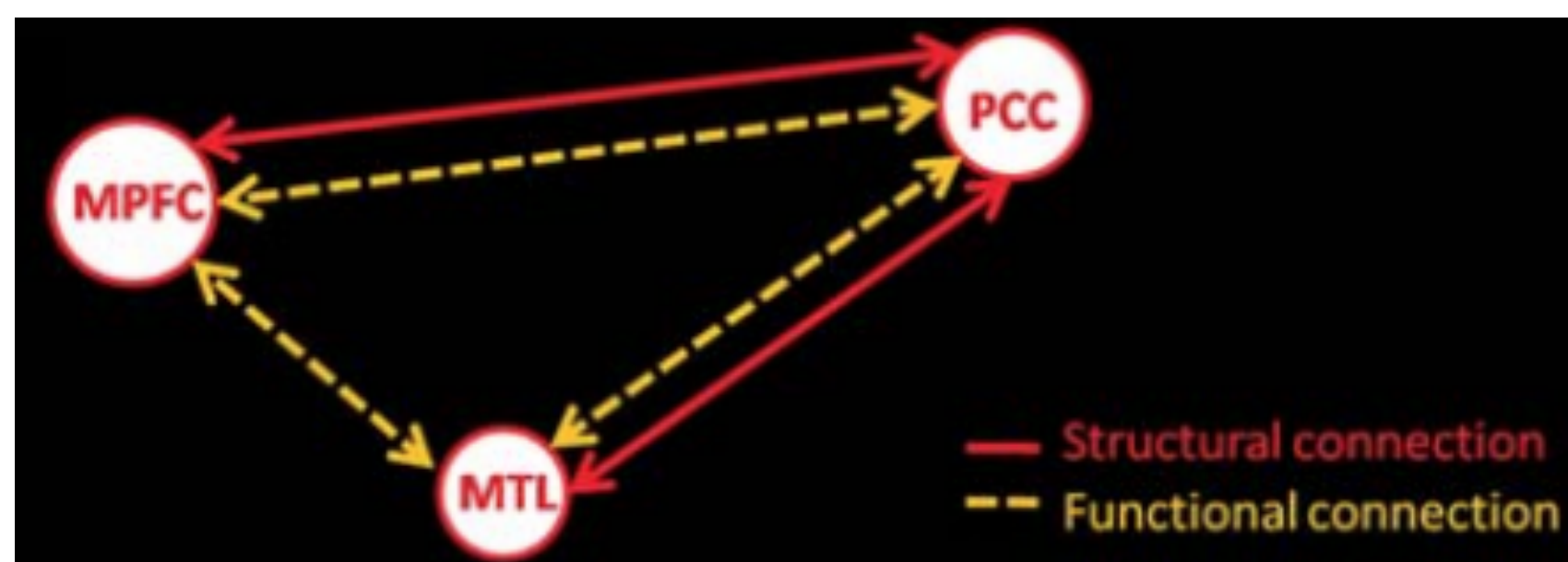
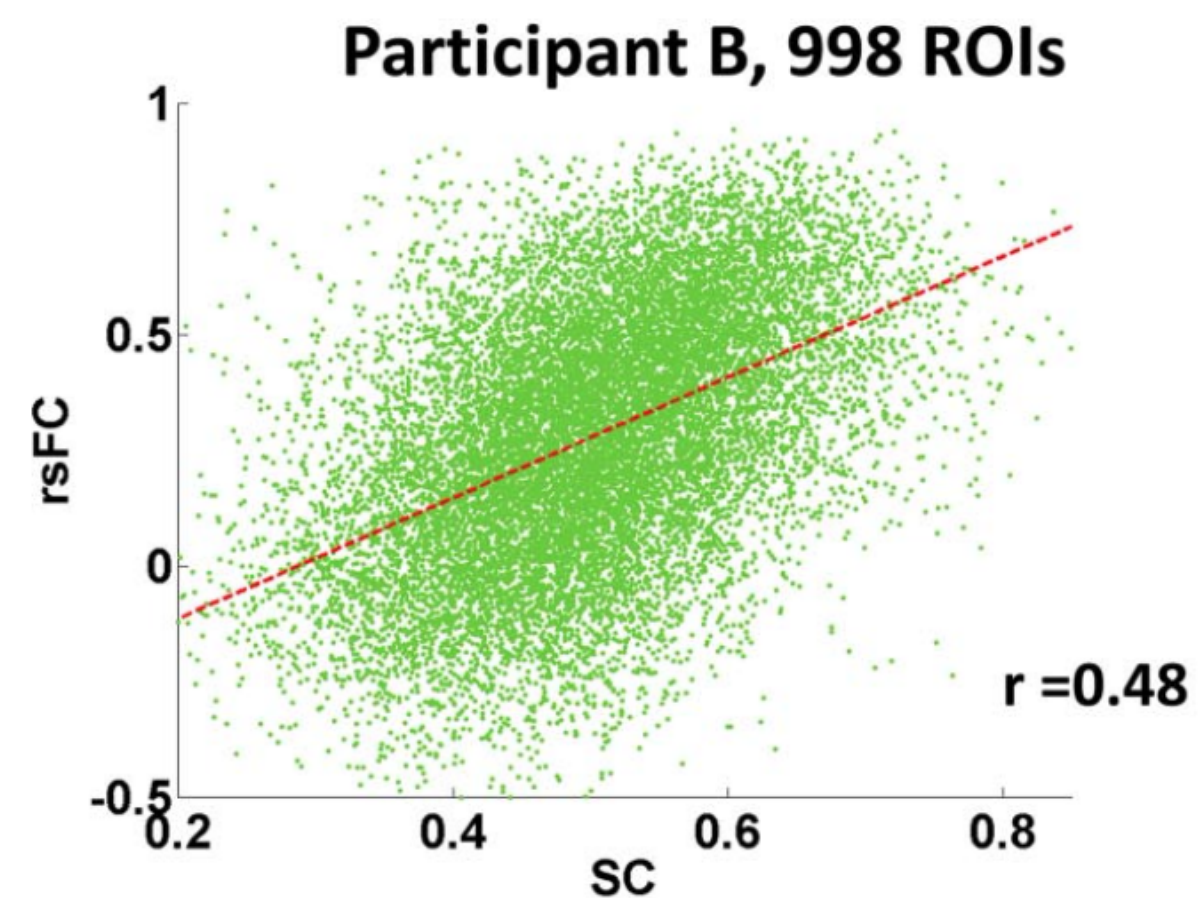
# Relationship to task

Resting state networks are similar to task activation patterns at group and single subject level

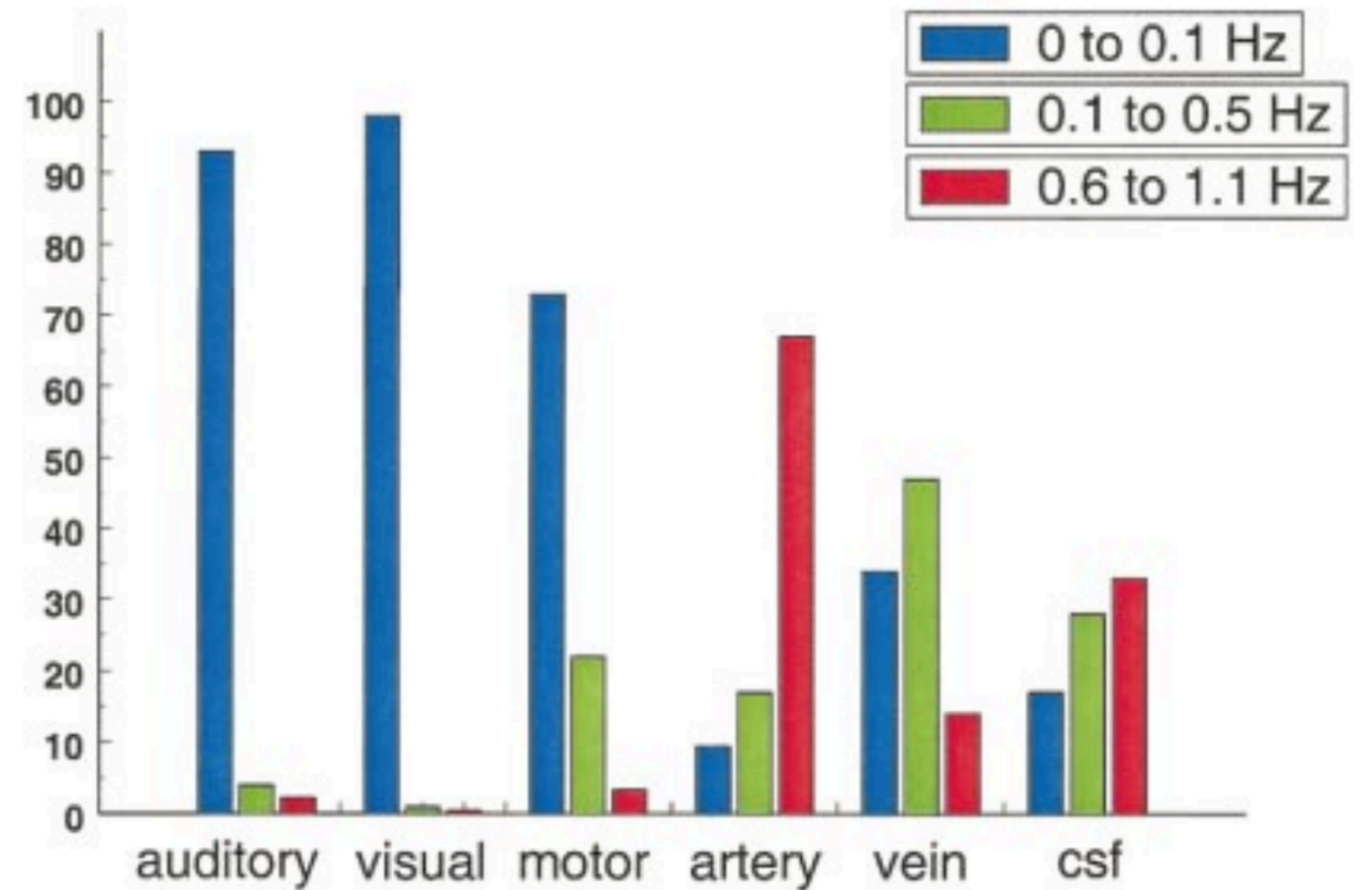
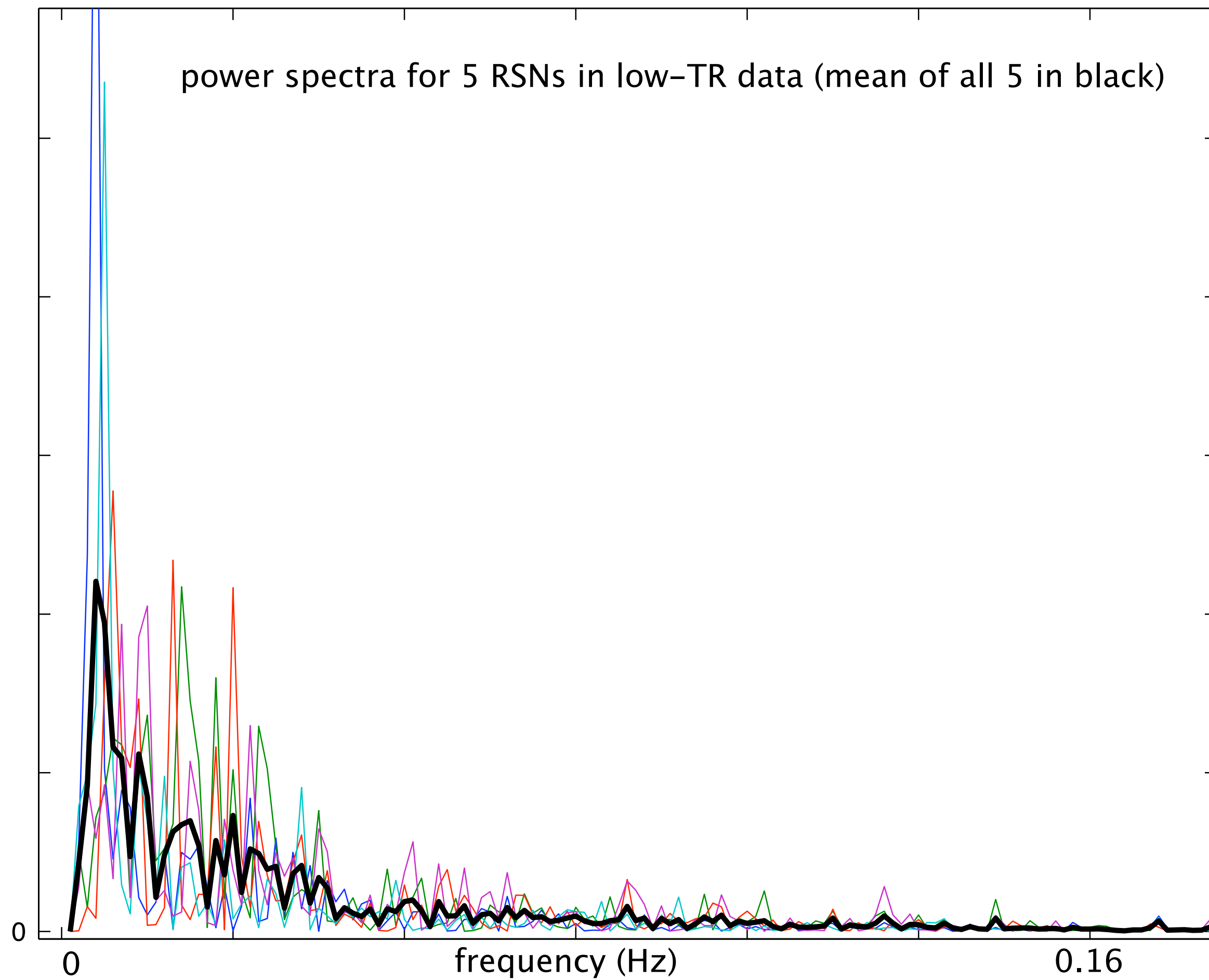


# Functional vs structural connectivity

Functional connectivity is related to structural connectivity

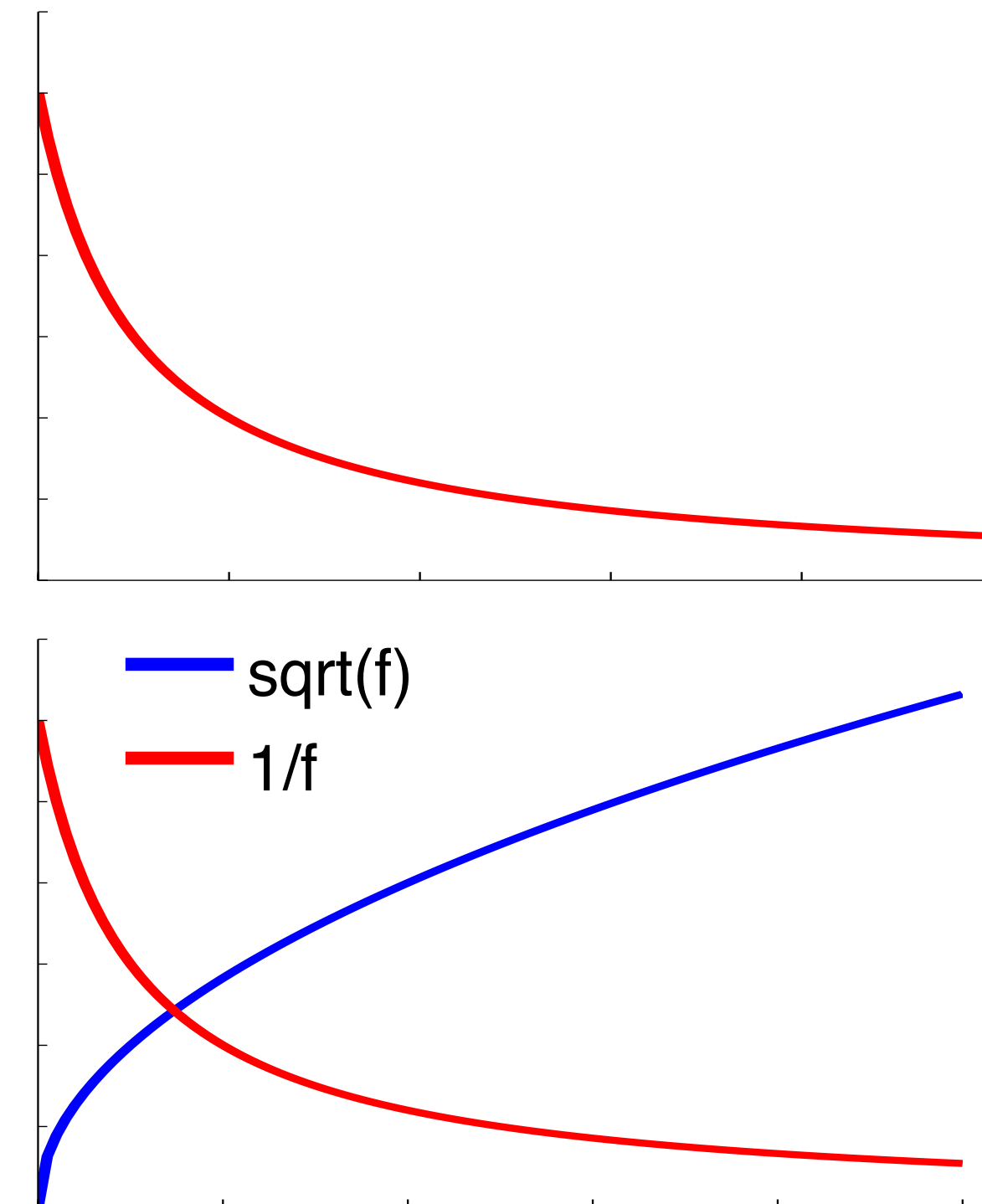


# Low frequency fluctuations?



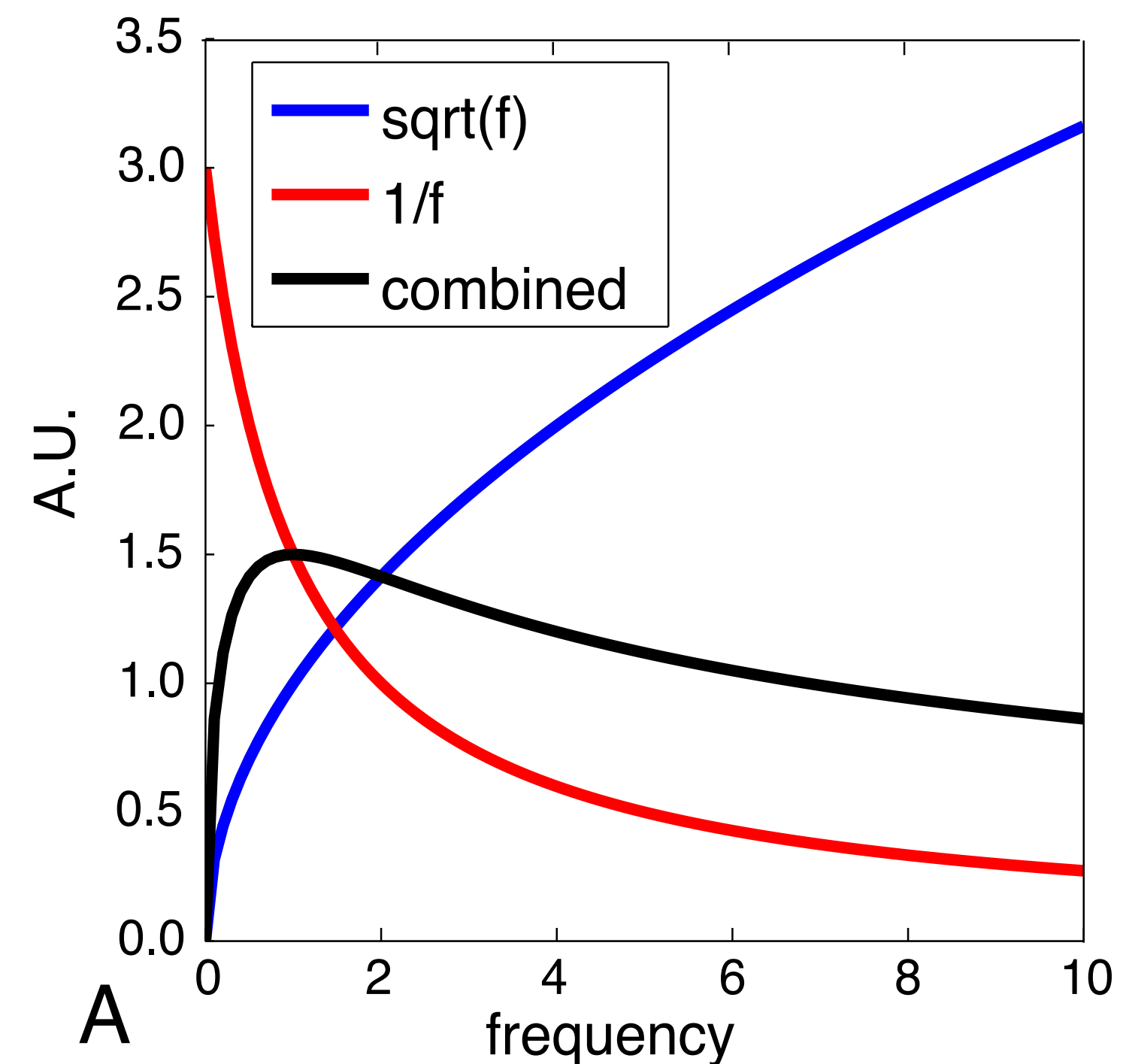
# Low frequency fluctuations?

- BOLD decreases as  $1/f$
- Degrees of freedom increase as  $\text{sqrt}(f)$



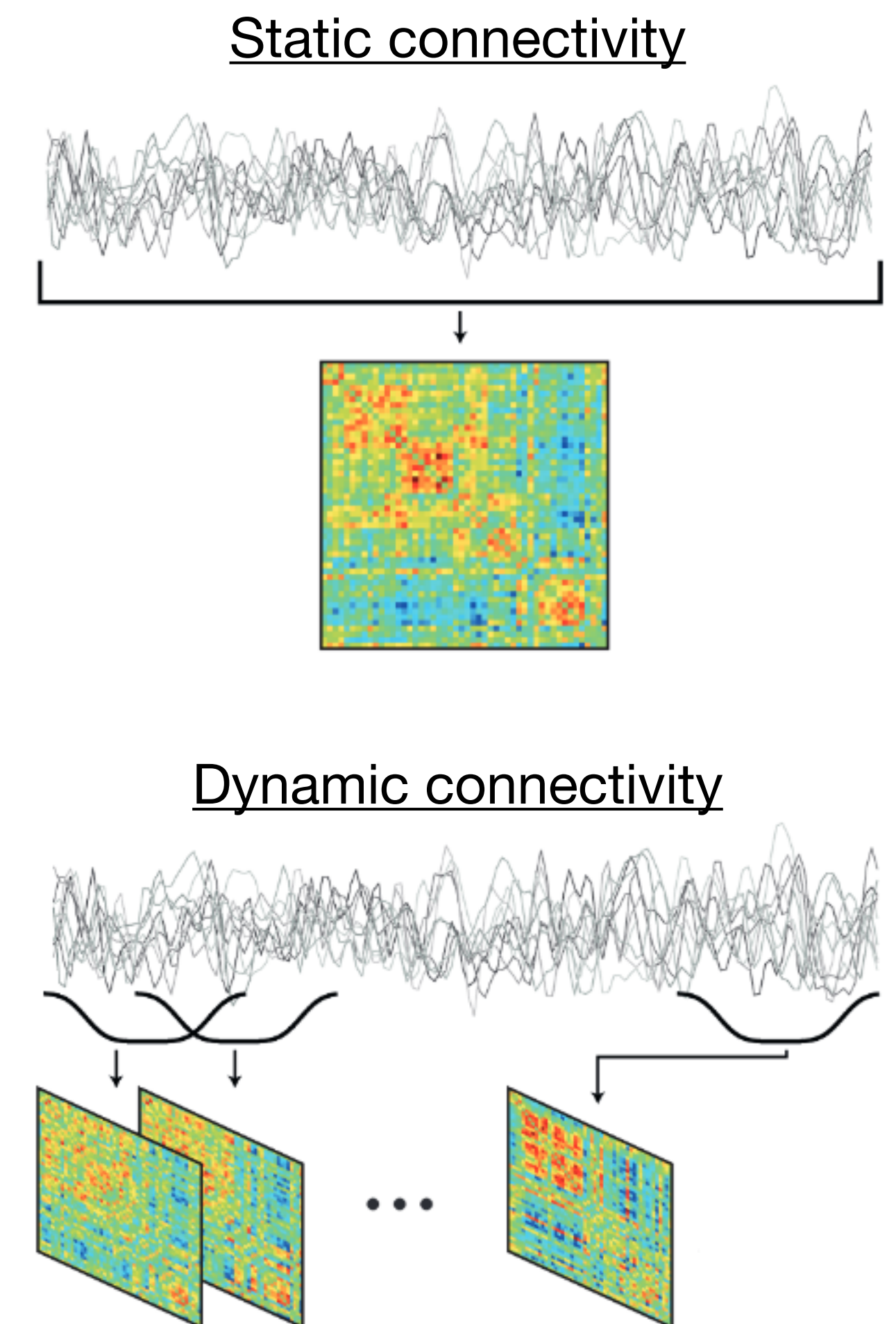
# Low frequency fluctuations?

- BOLD decreases as  $1/f$
- Degrees of freedom increase as  $\text{sqrt}(f)$
- Combined effect contributes to RSN estimation across frequency range!



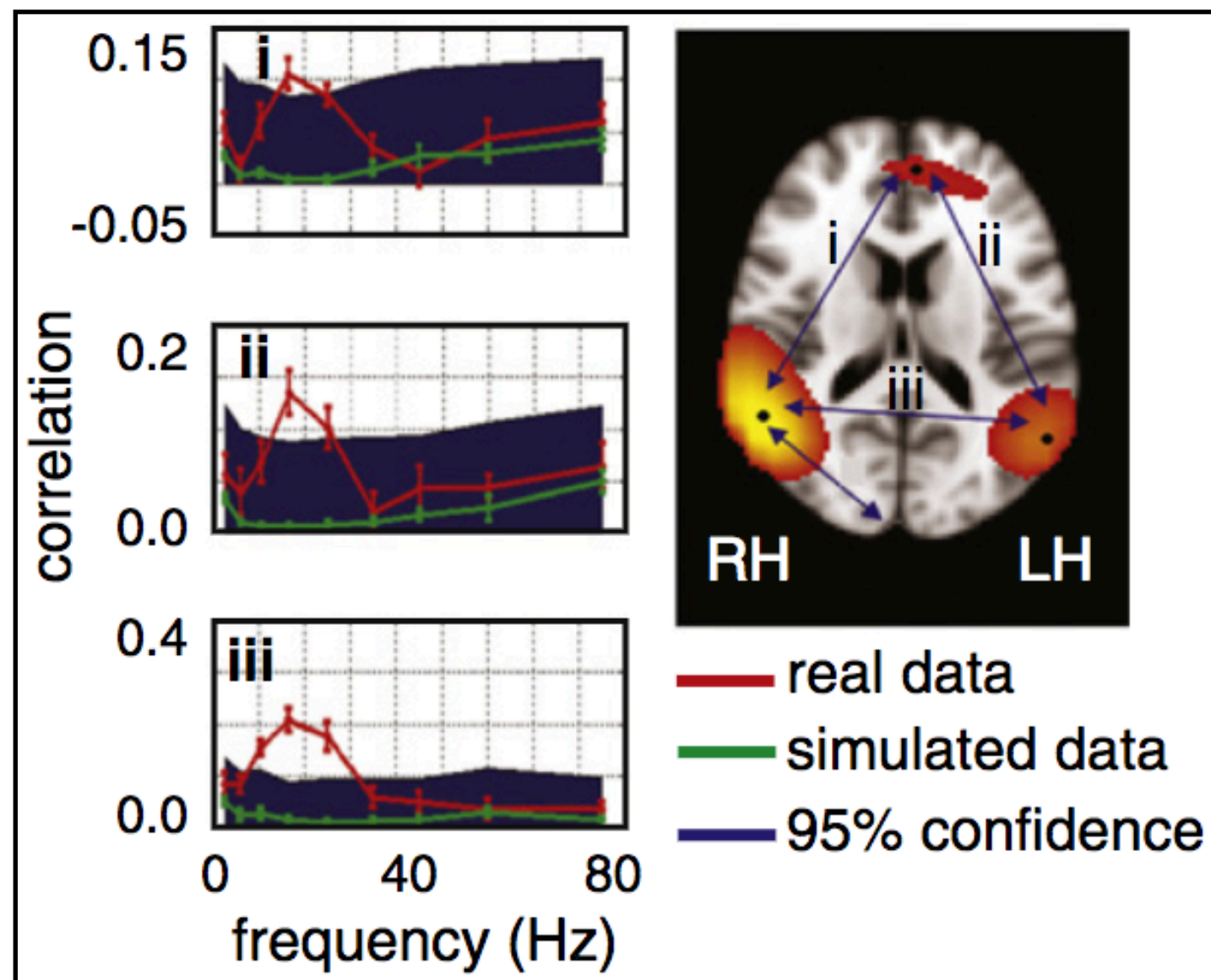
# Static versus dynamic connectivity

- Most connectivity measures are static (based on the full resting state scan)
- Dynamic connectivity is like to occur (changes over time)
- Static connectivity measures reflect average across dynamic states
- Dynamic connectivity measures are challenging (in terms of noise influences, significance testing)

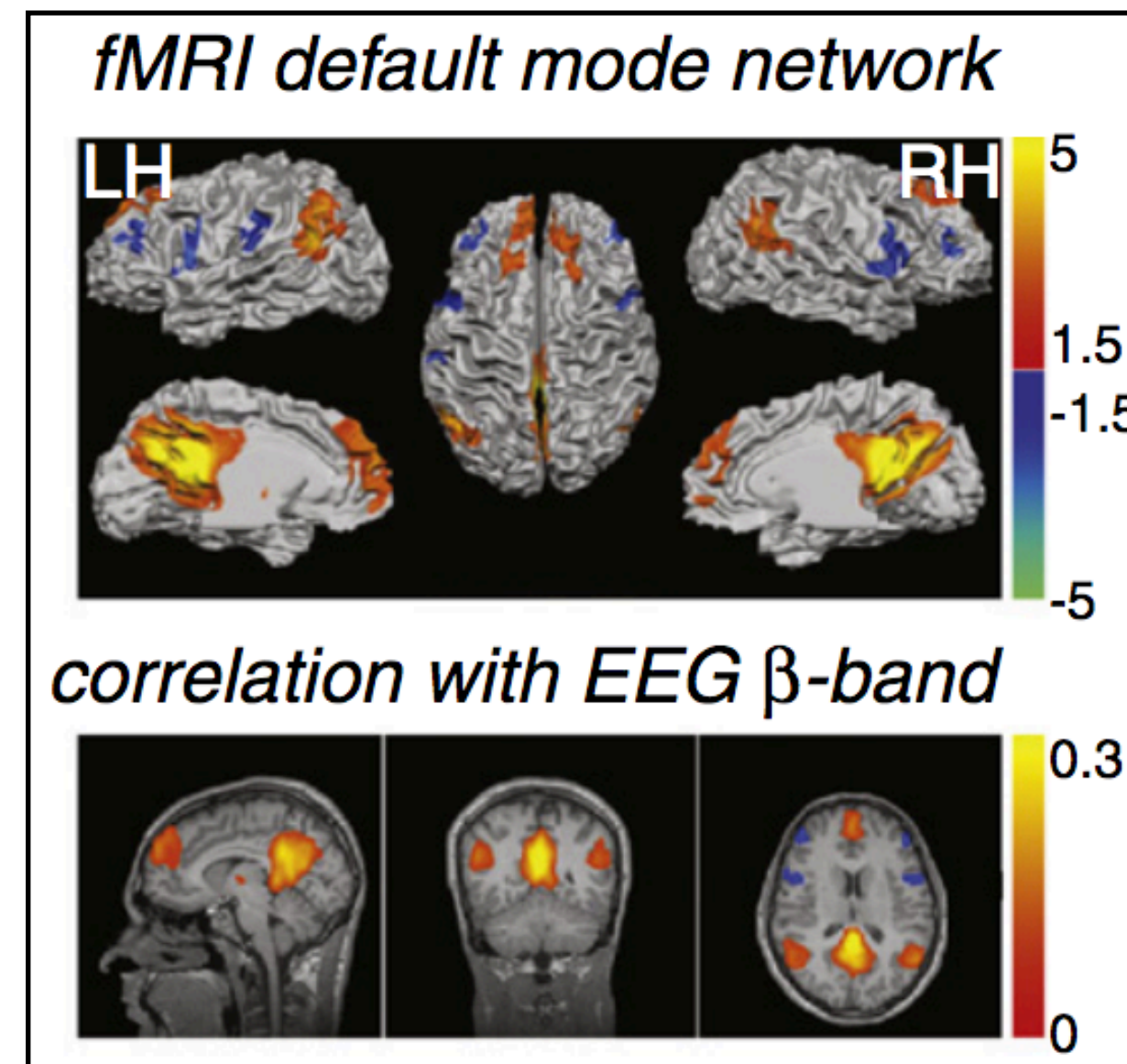


# Electrophysiology of BOLD connectivity

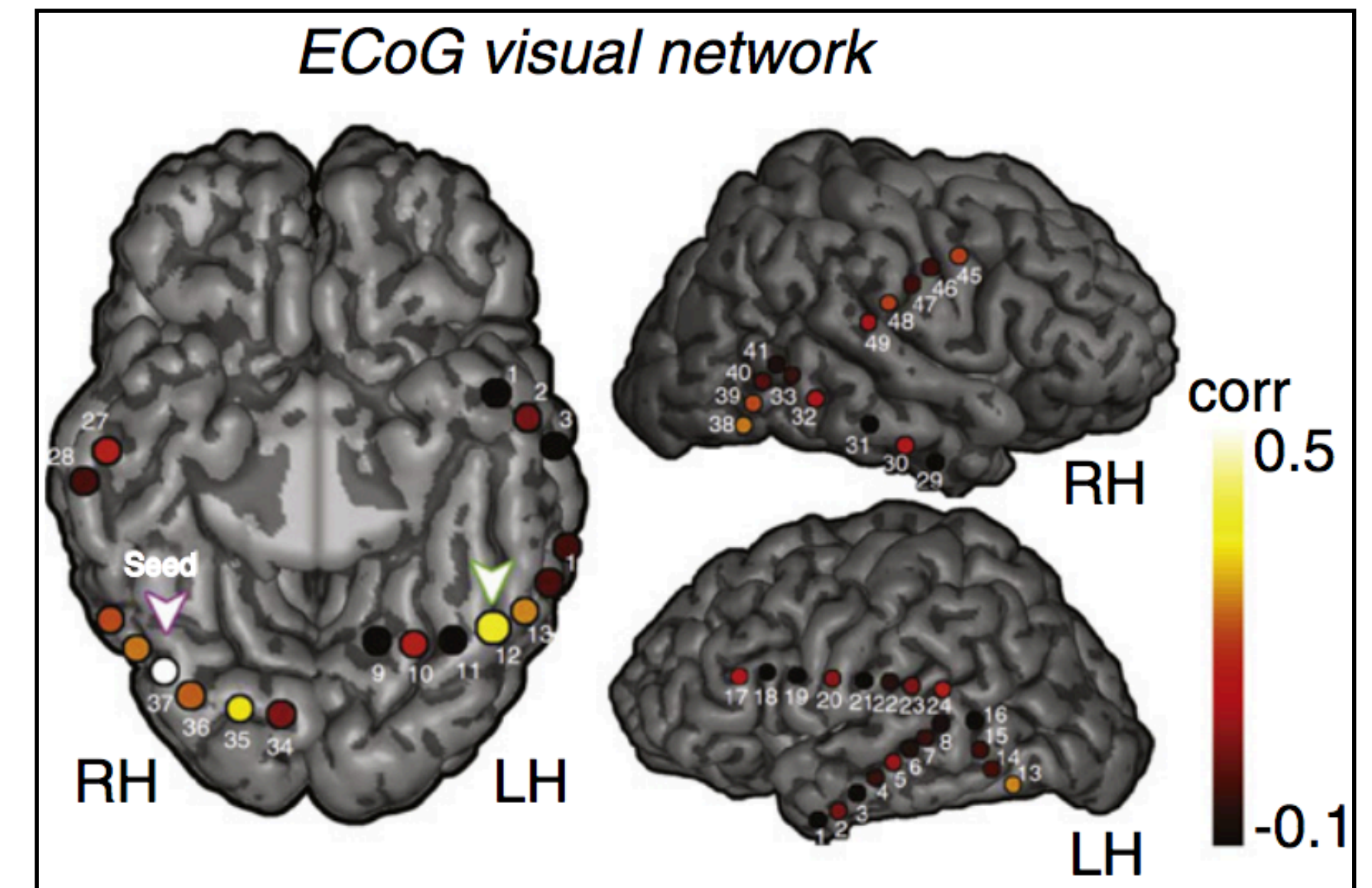
## MEG



## EEG

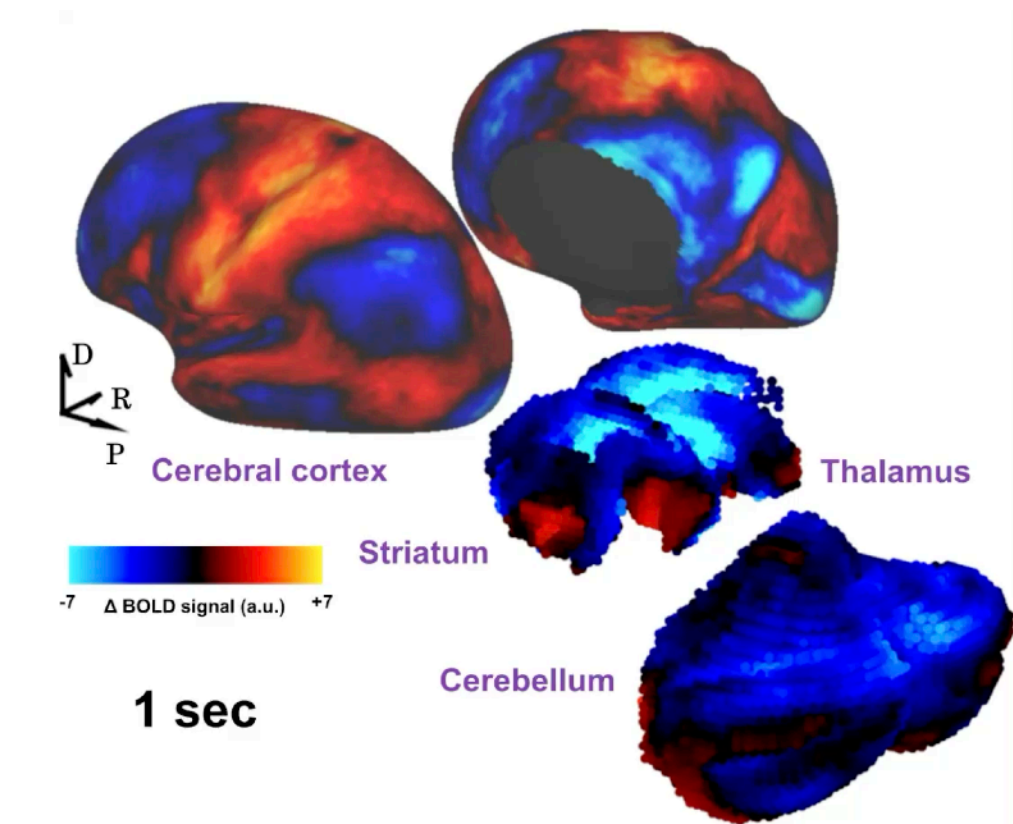
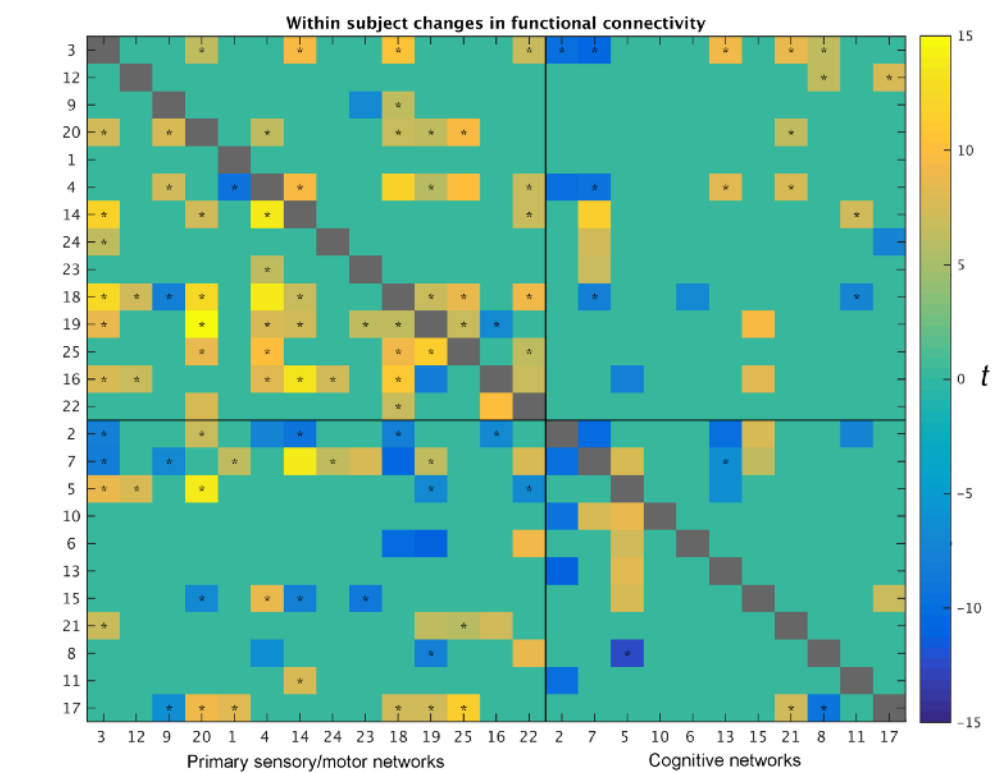
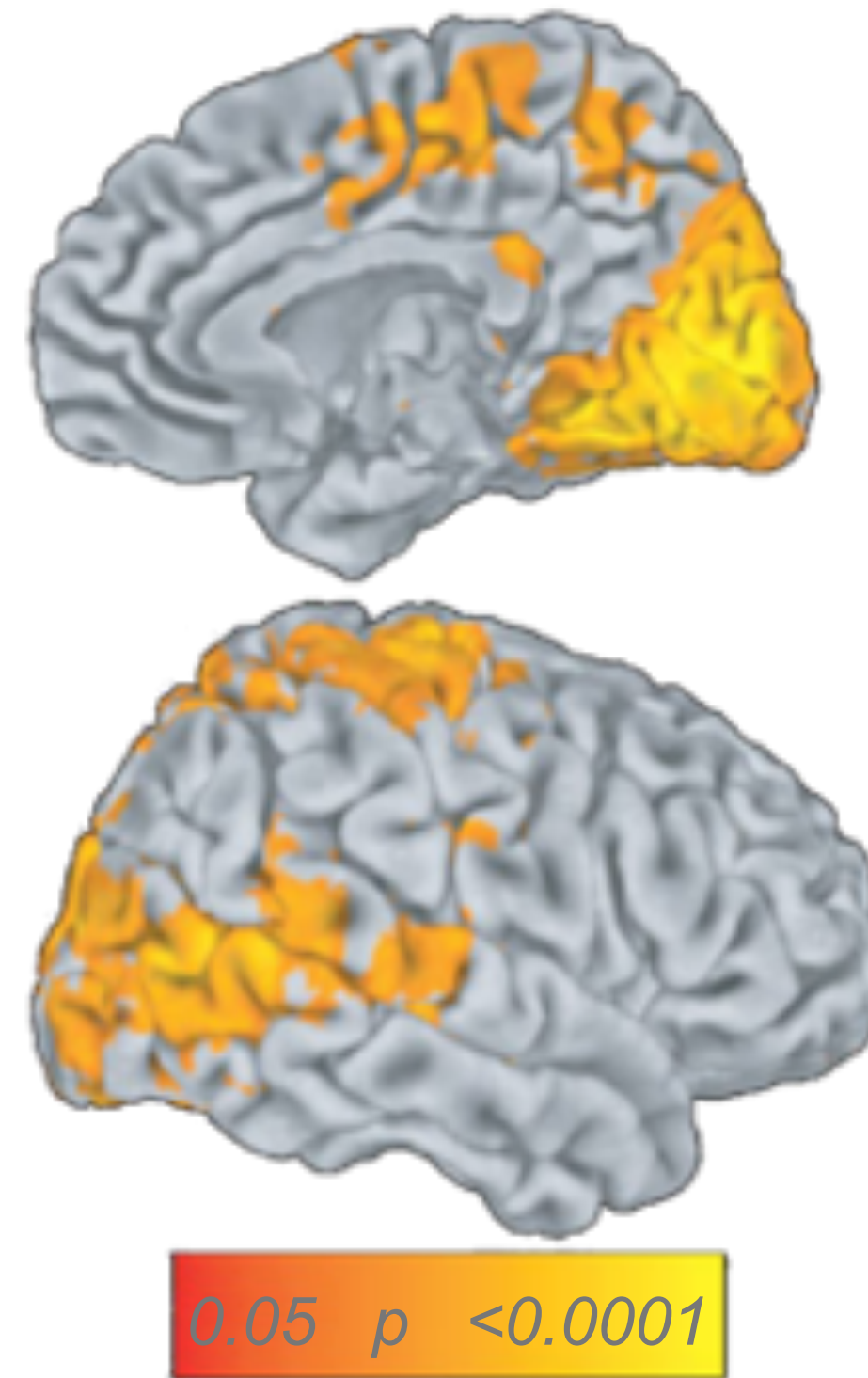
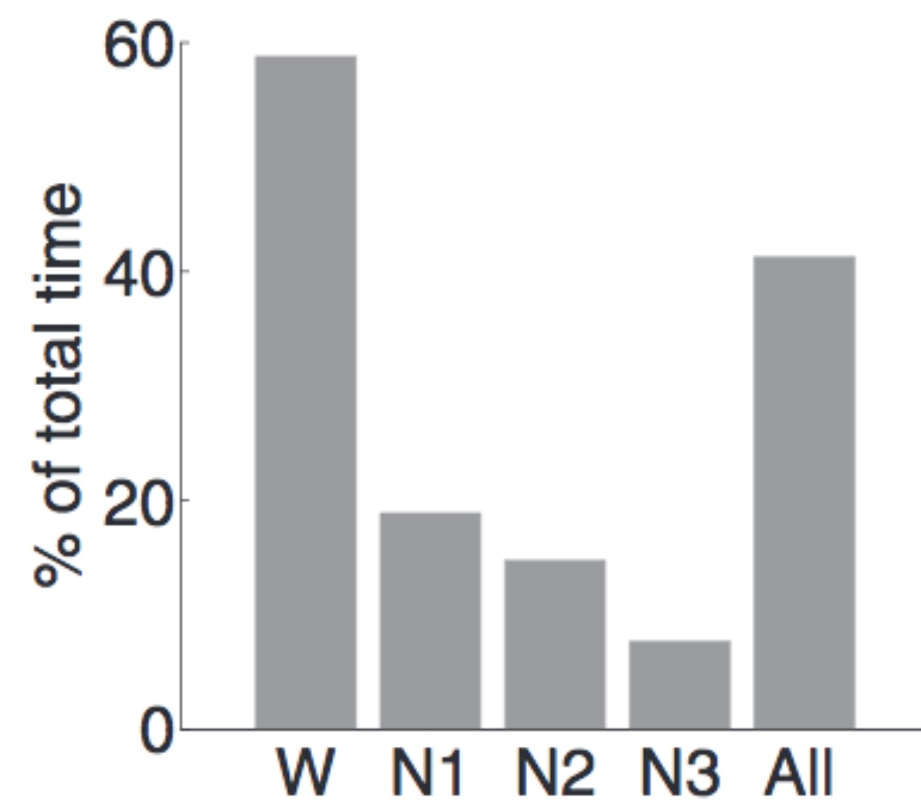
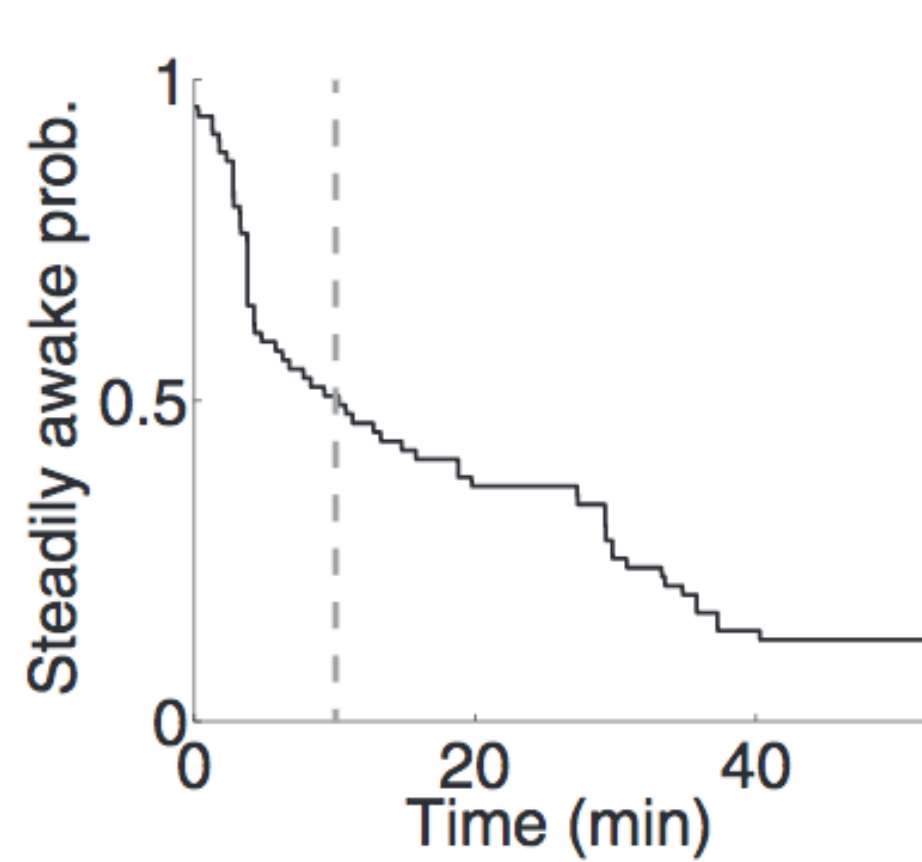


## ECoG



# Arousal

- Subjects fall asleep
- Changes in BOLD amplitude
- Related changes in correlation



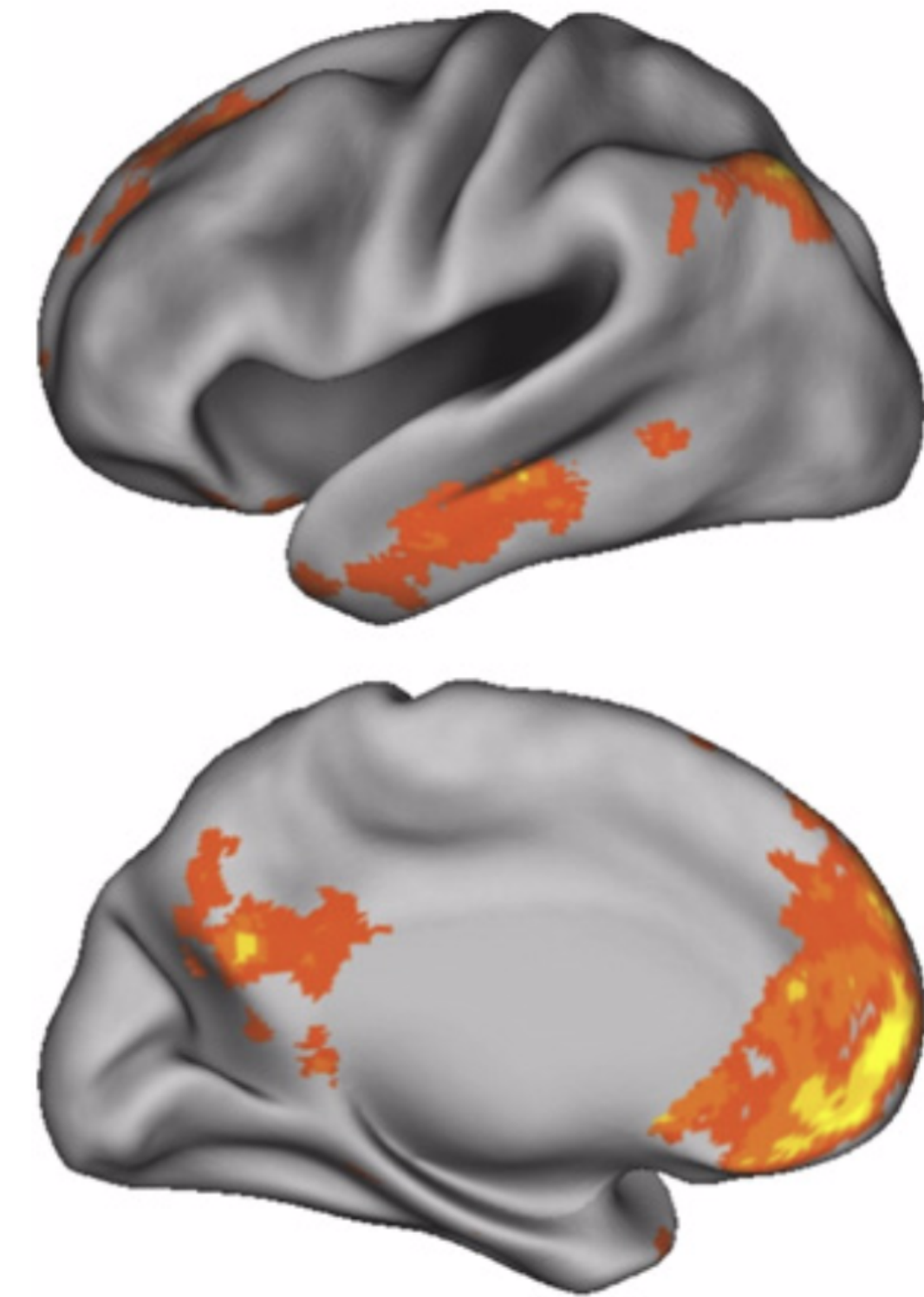


Additional notes on preprocessing

# Careful cleanup required

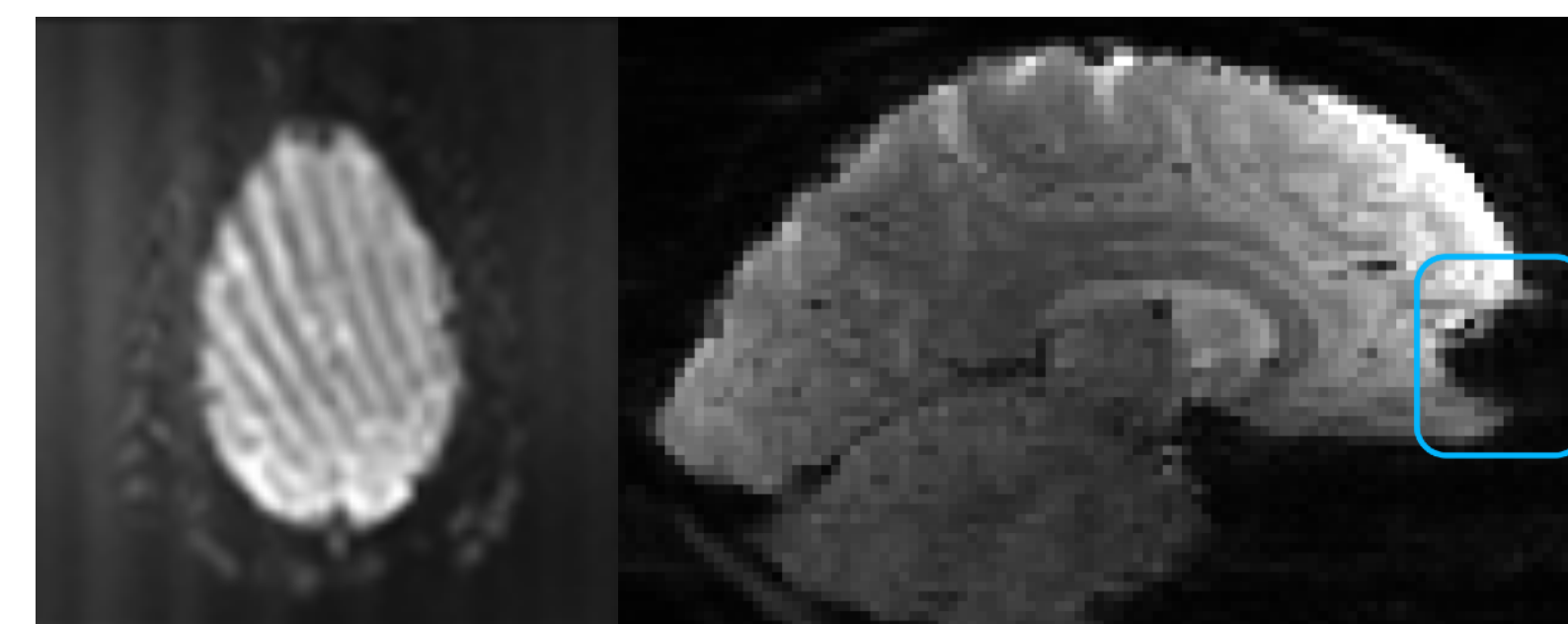
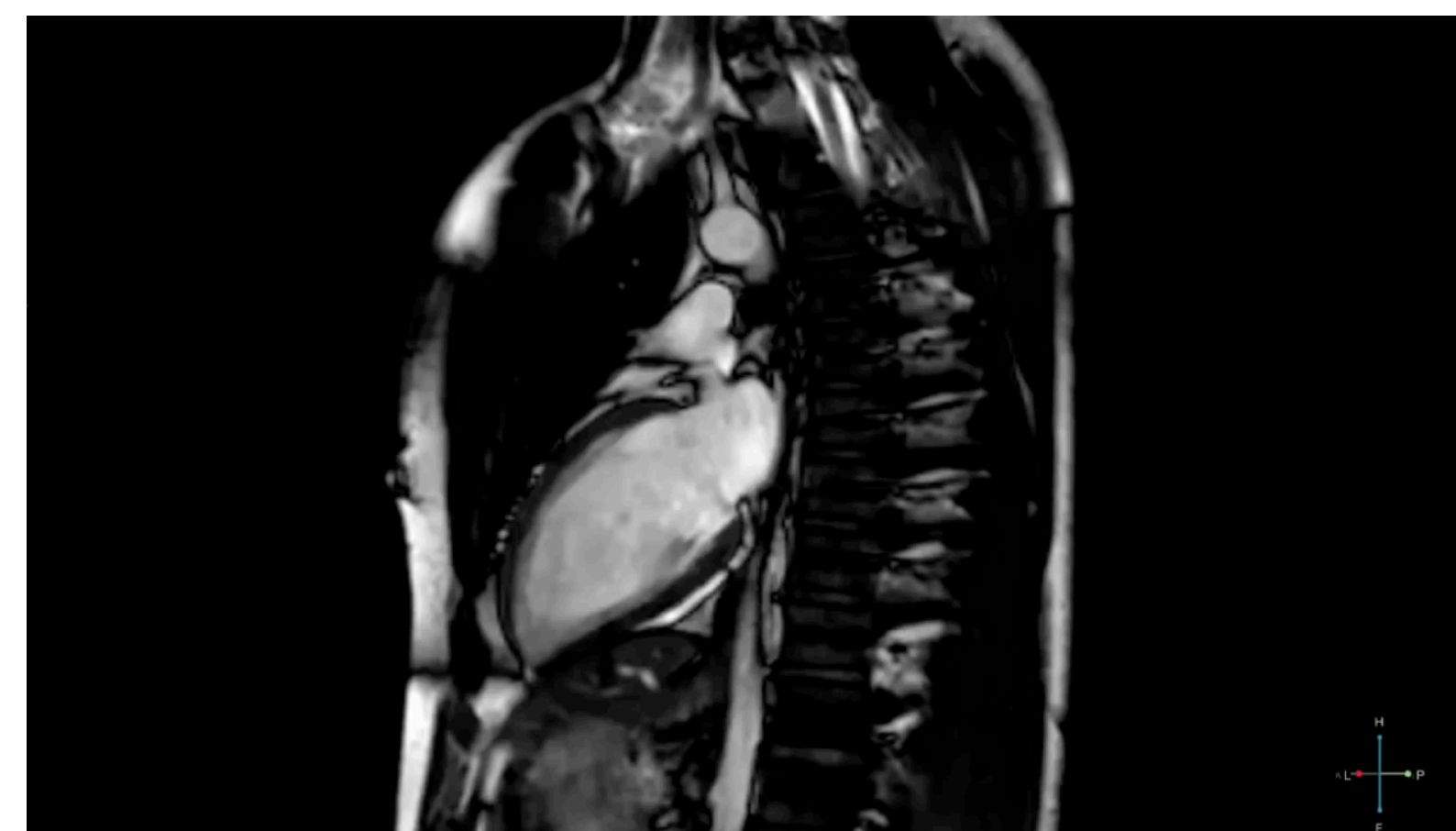
- Structured artefacts much more of a problem for rfMRI than task-fMRI
- No model of expected activation
- Instead based on correlating timeseries with each other

Low motion > high motion



# Noise sources

- Head motion
- Cardiac & breathing cycles
- Scanner artefacts





# Preprocessing overview

## Conventional preprocessing steps

Motion & distortion correction

Slice timing correction

High pass temporal filtering

Spatial smoothing

Registration

## Noise reduction steps (use at least one of these)

Nuisance regression

Low pass temporal filtering

Volume censoring

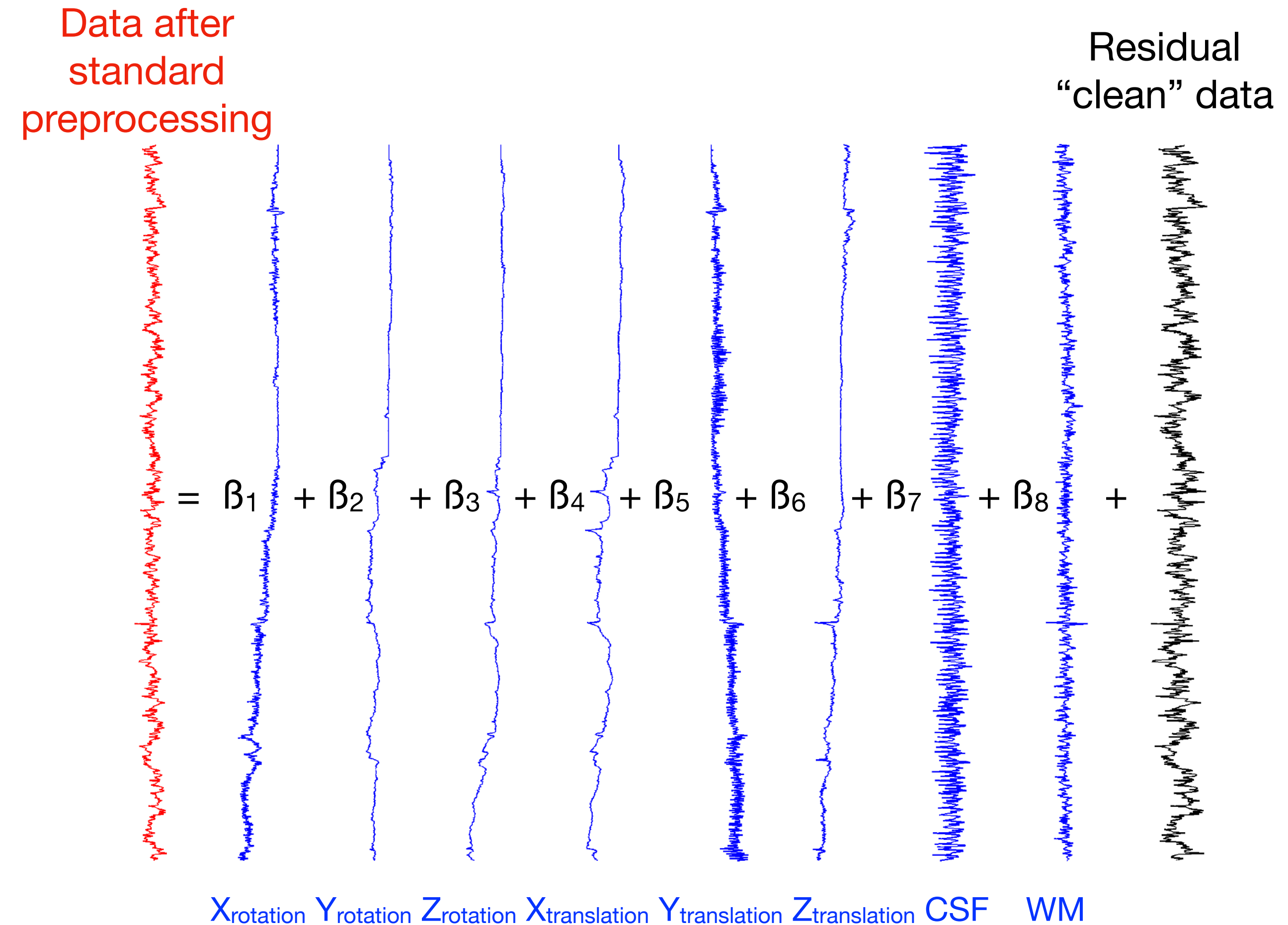
Global signal regression

ICA-based clean-up

Physiological noise regression

# Regressing out noise

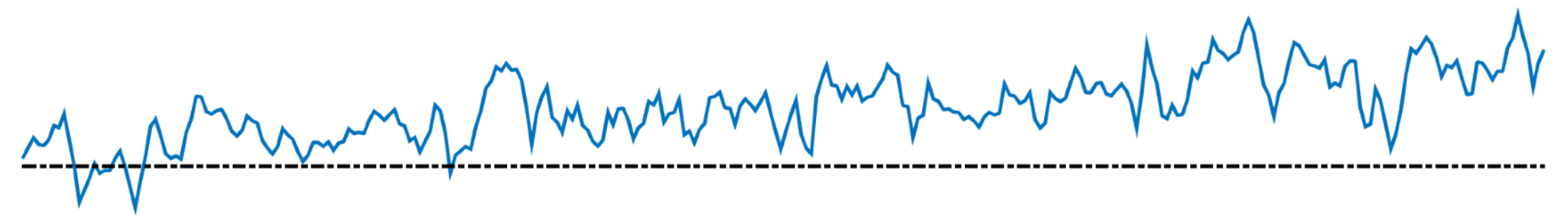
- Head motion parameters
- White-matter / CSF
- Use GLM to remove nuisance timeseries
- Perform analysis on residuals
- “CompCor” method (PCA-based)



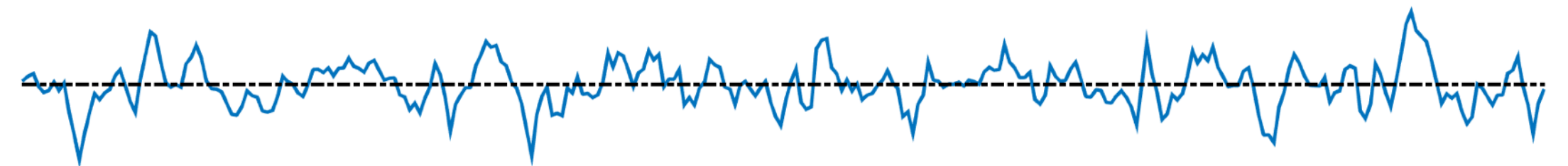
# Lowpass temporal filtering

- E.g., common to remove frequencies  $> 0.1\text{Hz}$
- May remove useful signal
- Not guaranteed to remove much artefact
- Lowpass side might create “shadow” RSNs -> use carefully if needed

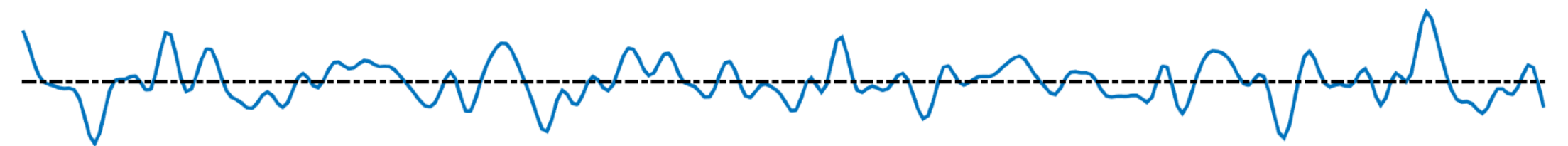
Original BOLD data



Highpass filtered data ( $>0.01\text{ Hz}$ )

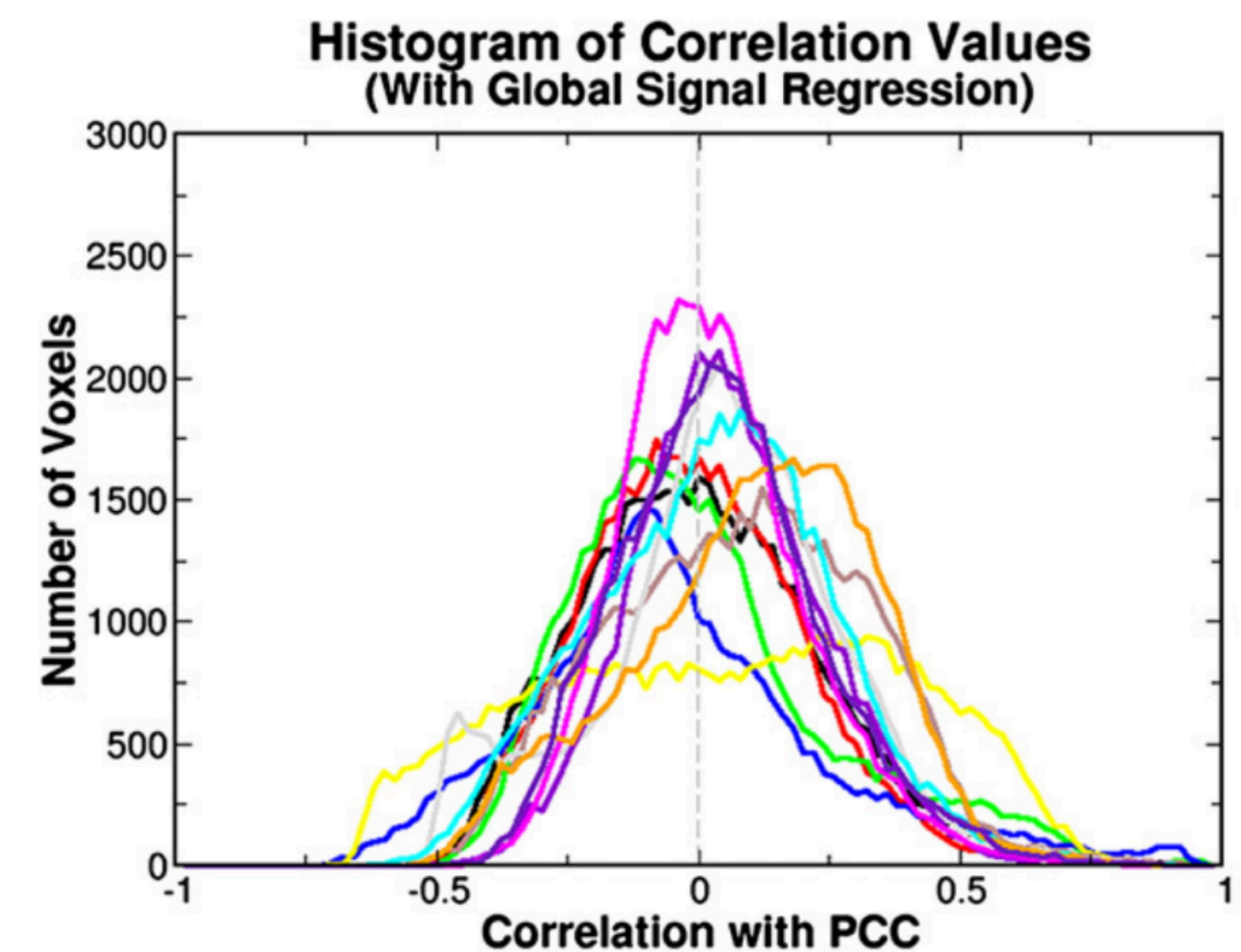
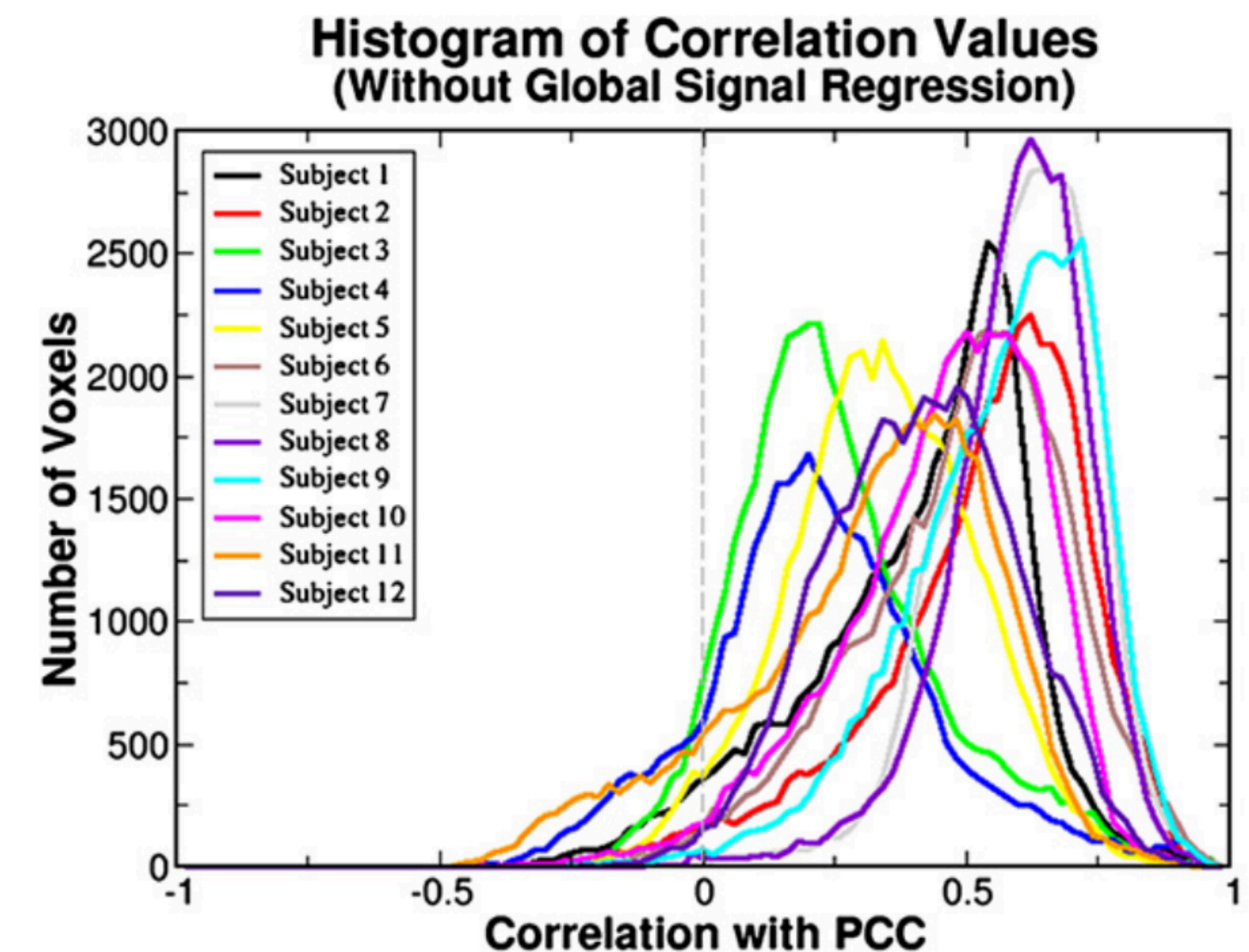


Bandpass filtered data ( $0.01 - 0.1\text{ Hz}$ )

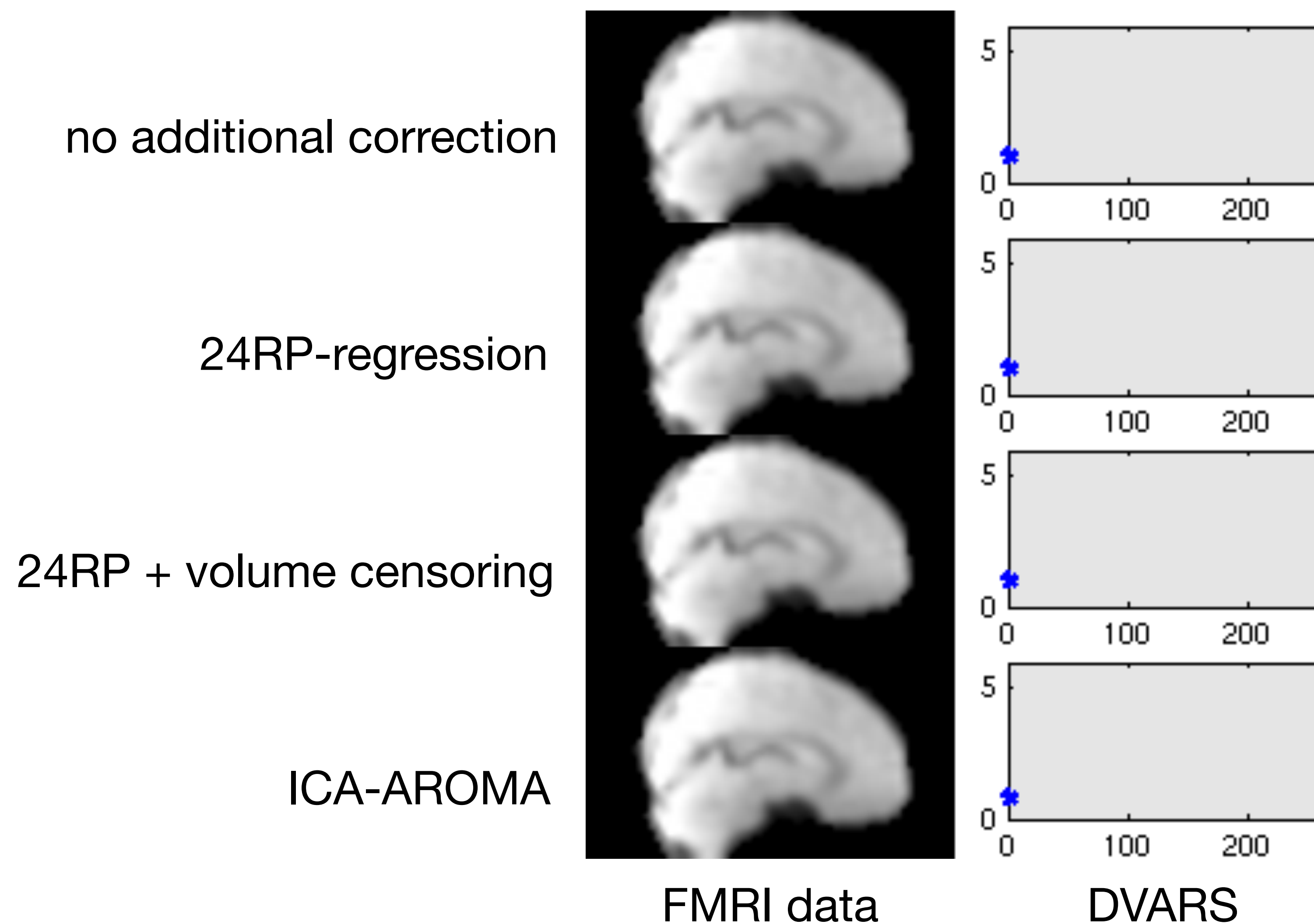


# Global signal regression

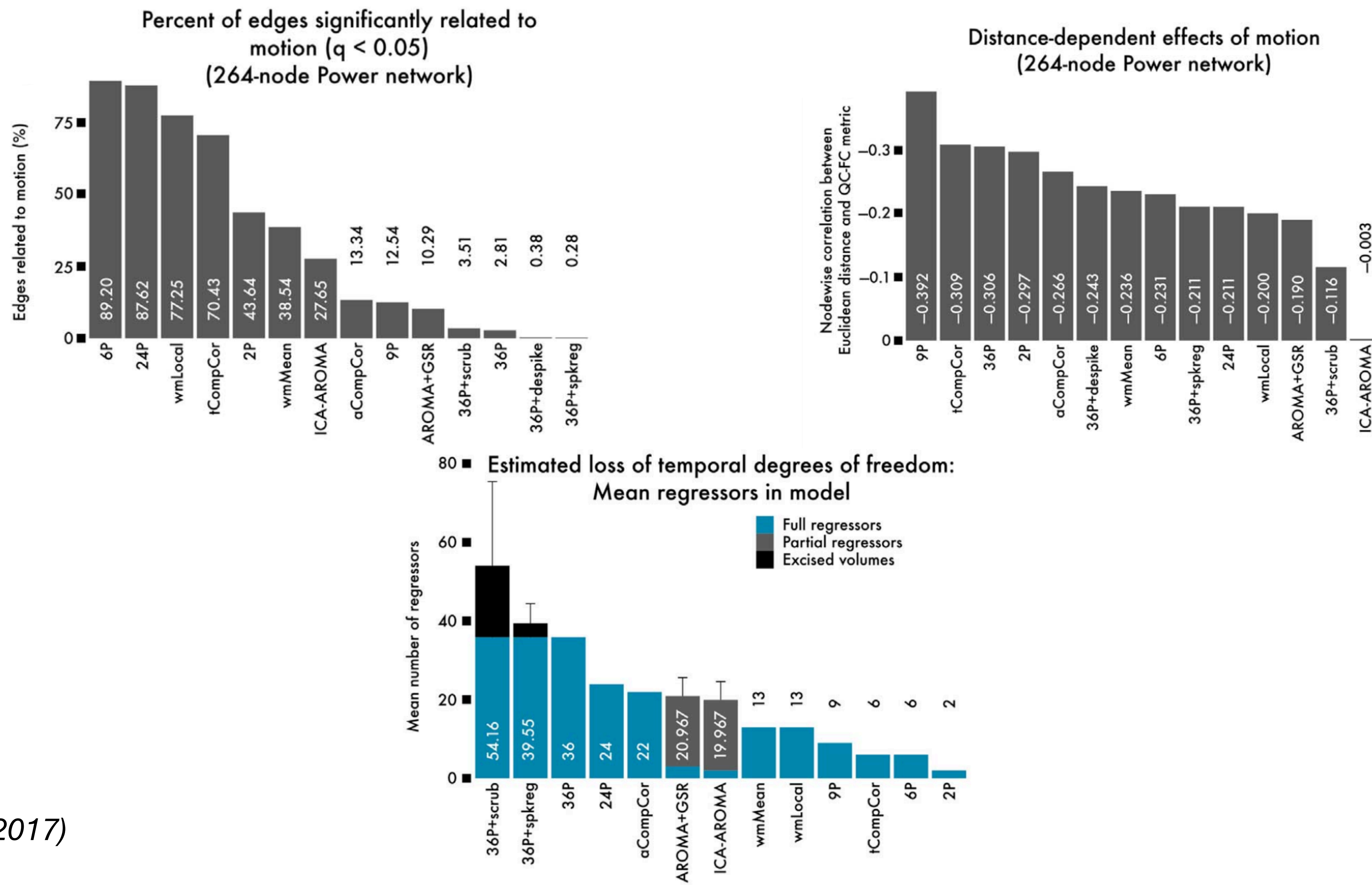
- Regress out mean timeseries across all voxels (or all grey matter voxels)
- Shifts connectivity values to be zero mean
- Therefore, more negative correlations
- Not necessary if using partial correlation



# Clean-up comparison



# Clean-up comparison



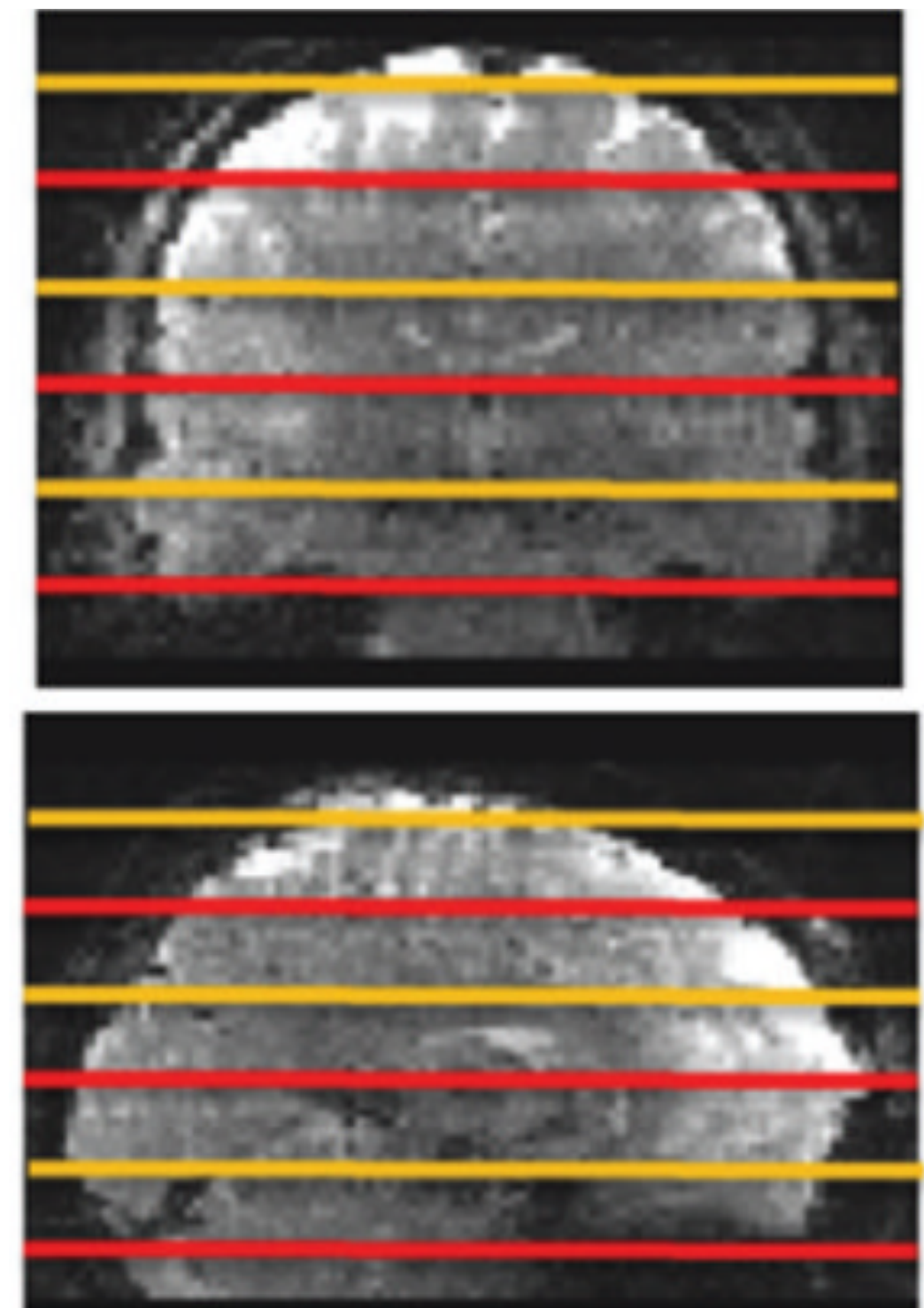


# Preprocessing advice

- Read up on the latest literature
- Nuisance regression is not enough
- Low-pass filtering is not enough & often not necessary when using other approaches -> might introduce other issues too
- Use ICA-based methods and/or volume censoring
- Use physiological noise regression when interested in brainstem or other vulnerable brain regions
- Don't use global signal regression (or if you must, show results with and without to assess GSR's impact)

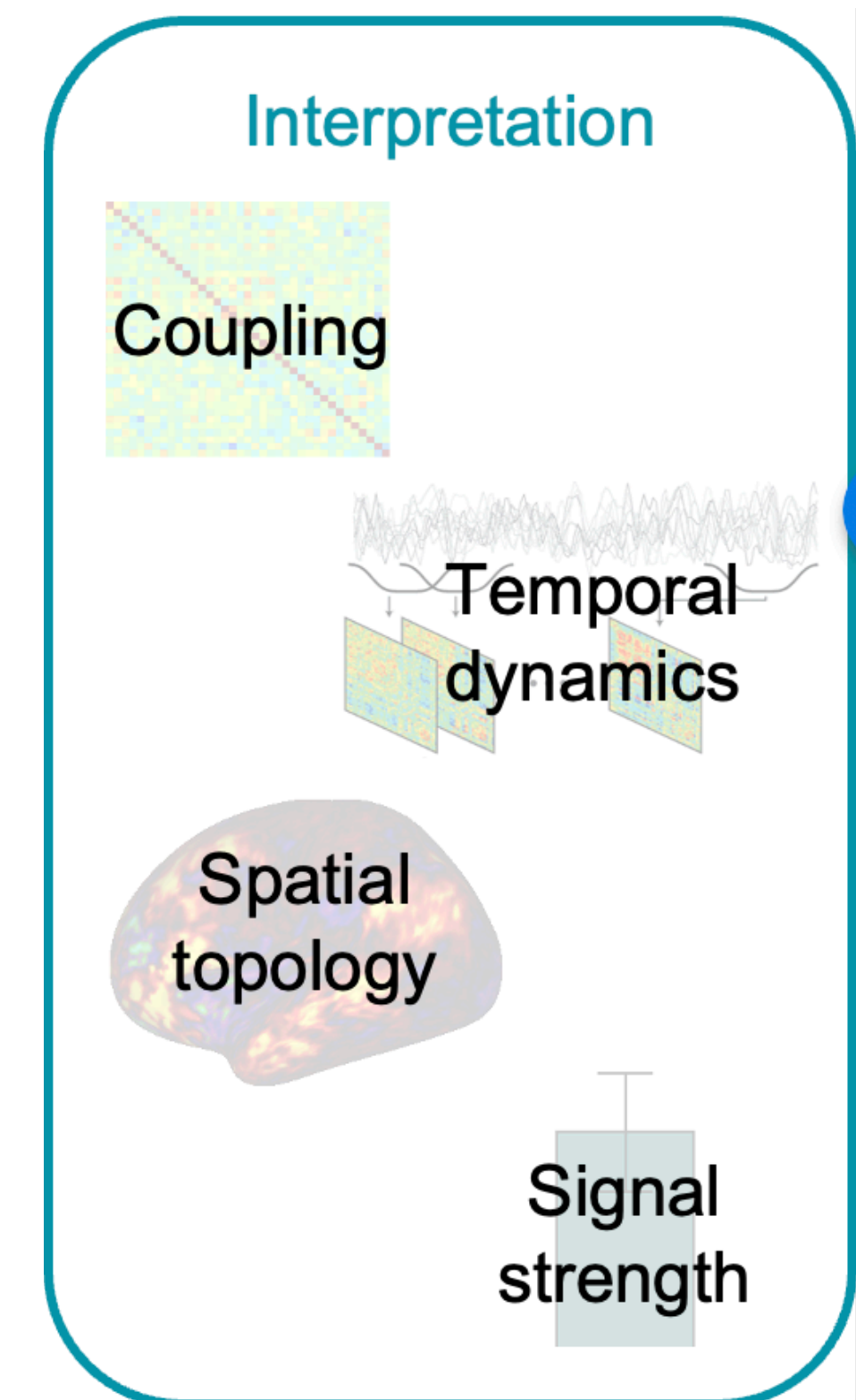
# Data acquisition advice

- Just a guide, may vary depending on study aims!
- Whole brain coverage, voxelsize: 2 - 3 mm
- Scan duration:
  - 15-20 minutes per scan
  - Potentially multiple scans
- Repetition time: ideally close to 1 second (multiband/ multiplexed imaging)
- Paradigm: eyes open, fixation cross



# Analysis method advice

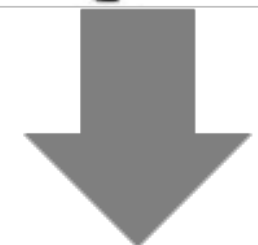
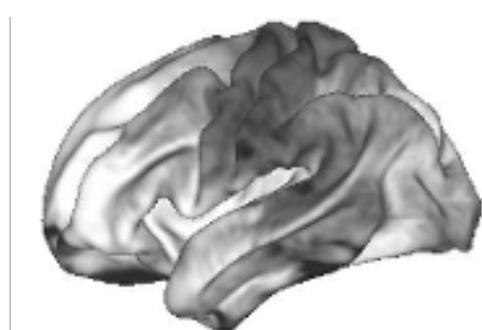
- Don't do the same thing that your lab always does without further consideration
- Do think about your study and hypotheses
  - Brain areas will inform spatial summary
  - Expected change will inform feature type
- Ok to test multiple dimensionalities (e.g., ICA) without looking at final statistical results
- If possible, compare results across multiple brain representations





# Resting state big picture

# The many options of resting state



**Gradients**  
[\(Margulies et al, 2016\)](#)

**ICA**  
[\(Beckmann et al, 2005\)](#)

**Periodic Waves**  
[\(Abbas et al, 2019\)](#)

**Hidden Markov**  
[\(Vidaurre et al, 2018\)](#)

**Connectome**

**Your favorite**

**PROFUMO**  
[\(Harrison et al, 2015\)](#)

**Precision Maps**  
[\(Gordon et al, 2017\)](#)

**Coactivation**  
[\(Liu et al, 2018\)](#)

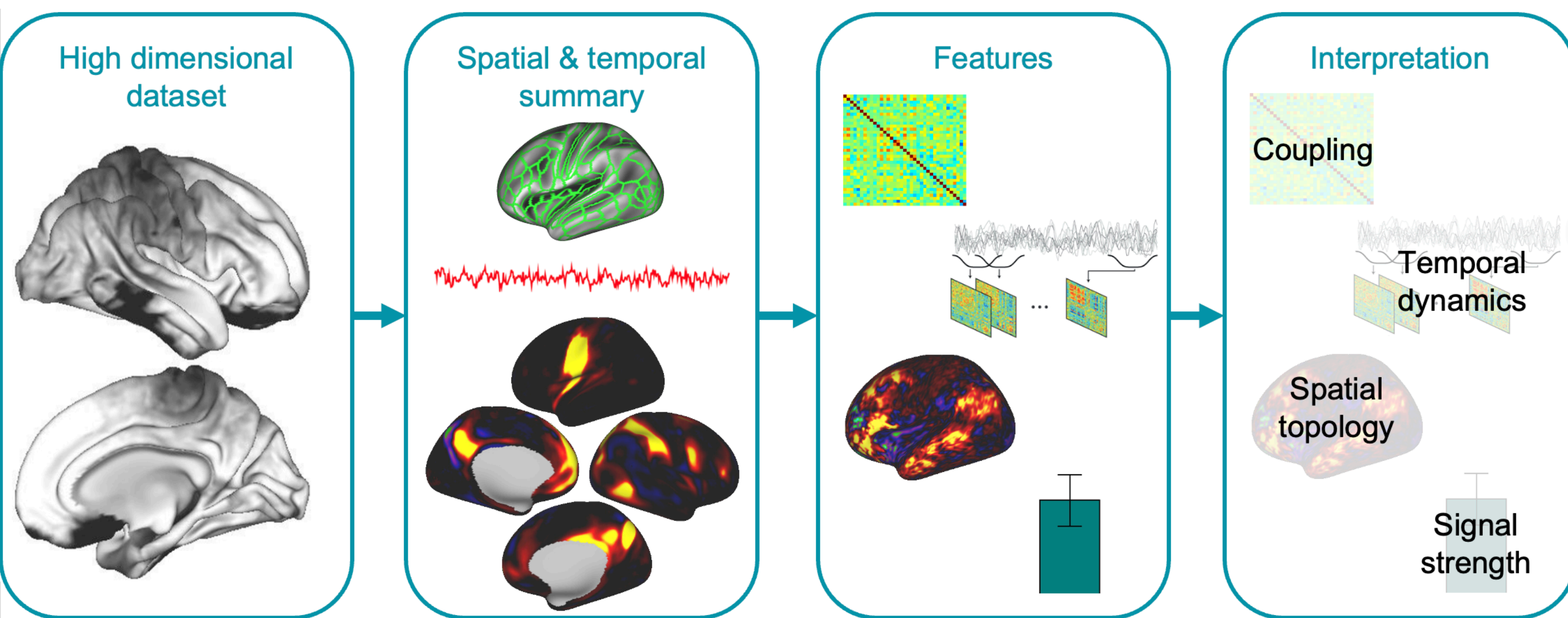
**Windowing**  
[\(Allen et al, 2014\)](#)

**Causal modeling**  
[\(Friston et al, 2003\)](#)

**Amplitudes**  
[\(Zou et al, 2008\)](#)

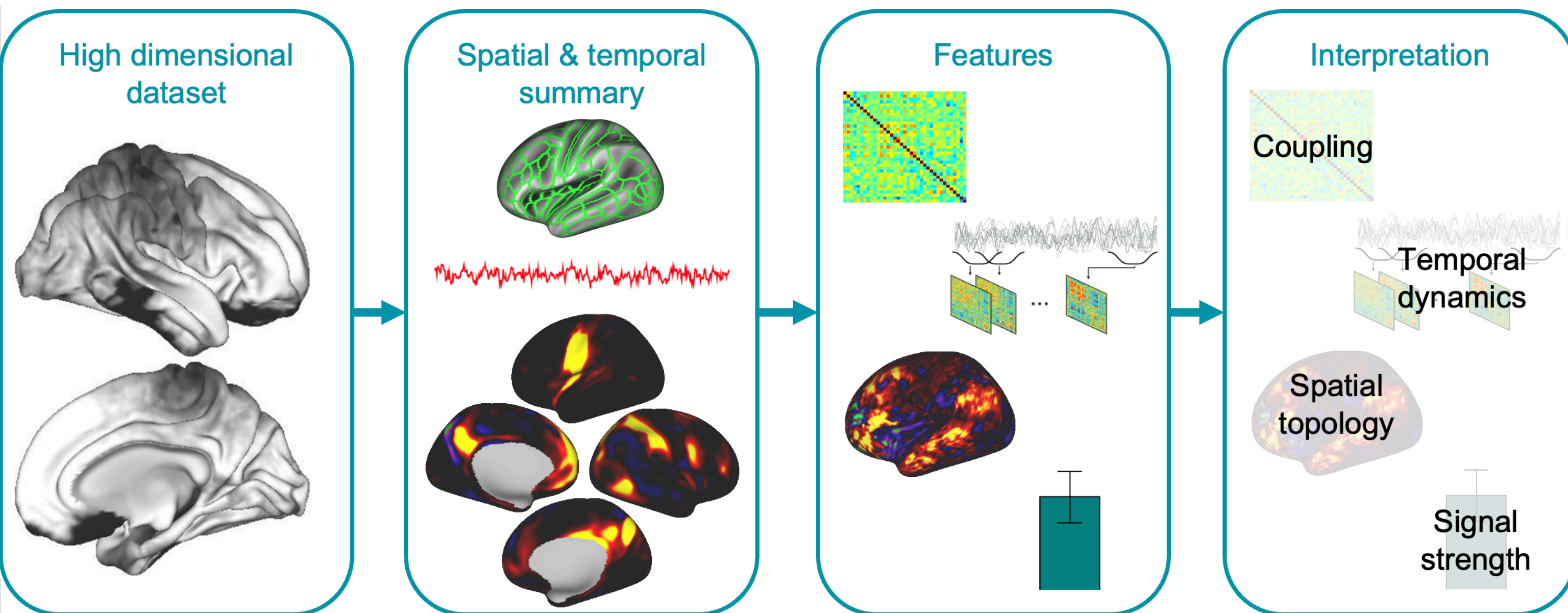
# Why more than one tool?

## “Brain representations”



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## “Brain representations”



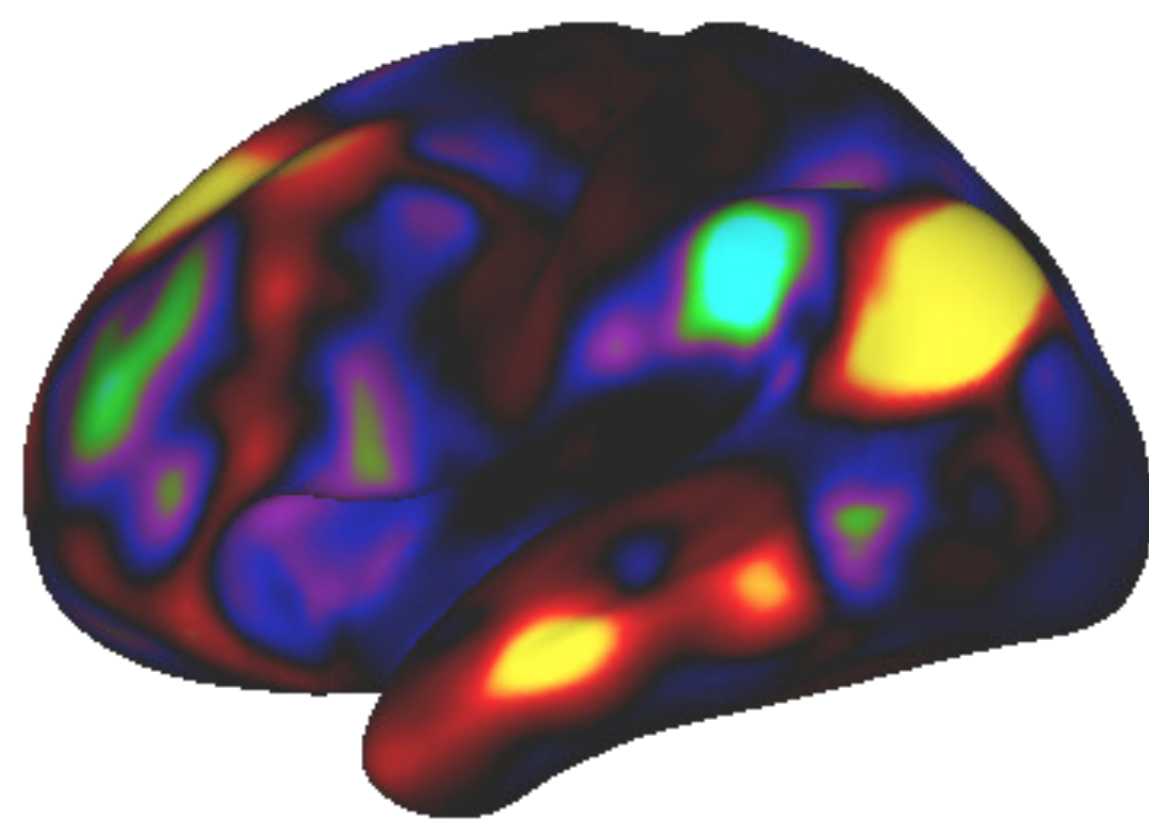
### Which tool to use?

What parts of the brain are interesting in your study?

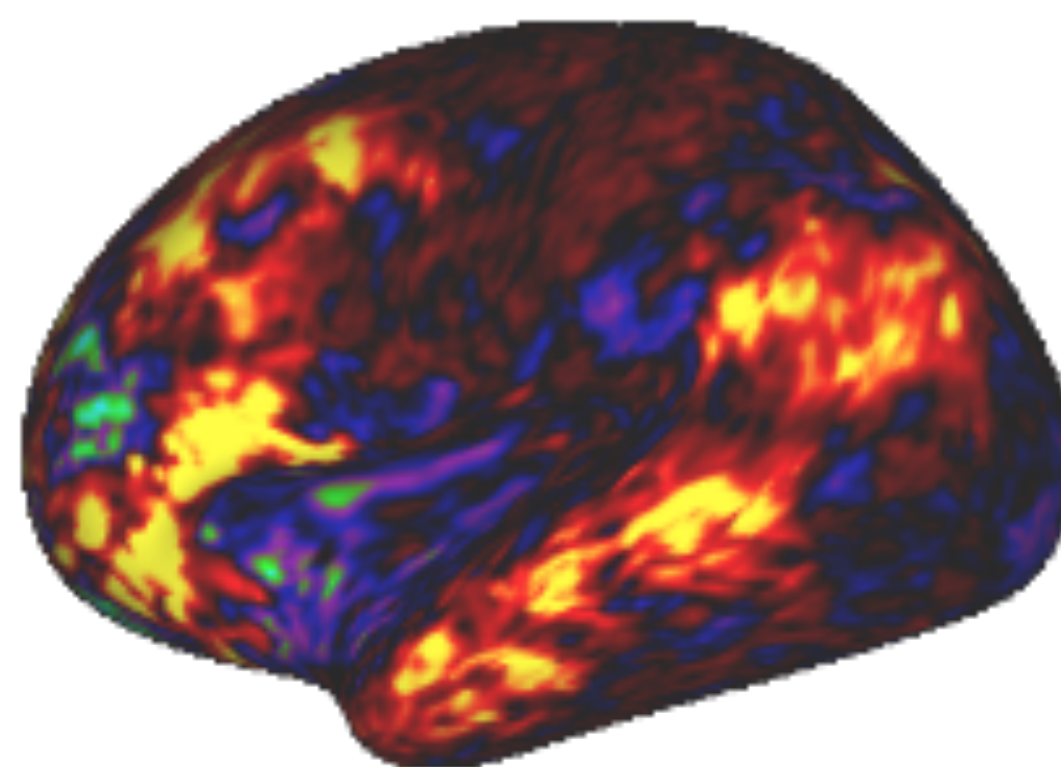
What type of change do you expect (e.g., strength/ shape/ connection)?

How much power do you have?

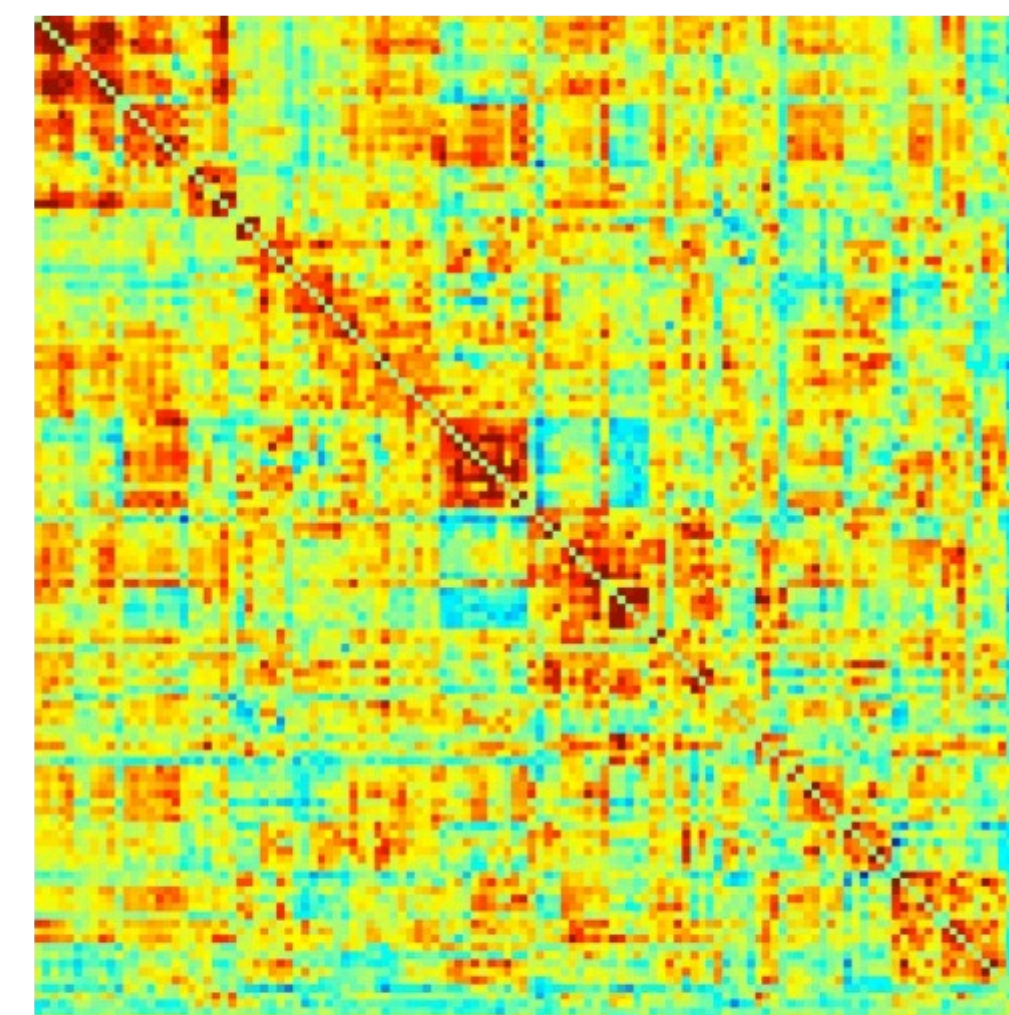
# Options within FSL



**ICA + dual regression  
(Melodic)  
Yesterday**



**Probabilistic Modes  
(PROFUMO)  
Tomorrow**



**Network modeling  
(FSLnets)  
Today**

Time for a break!





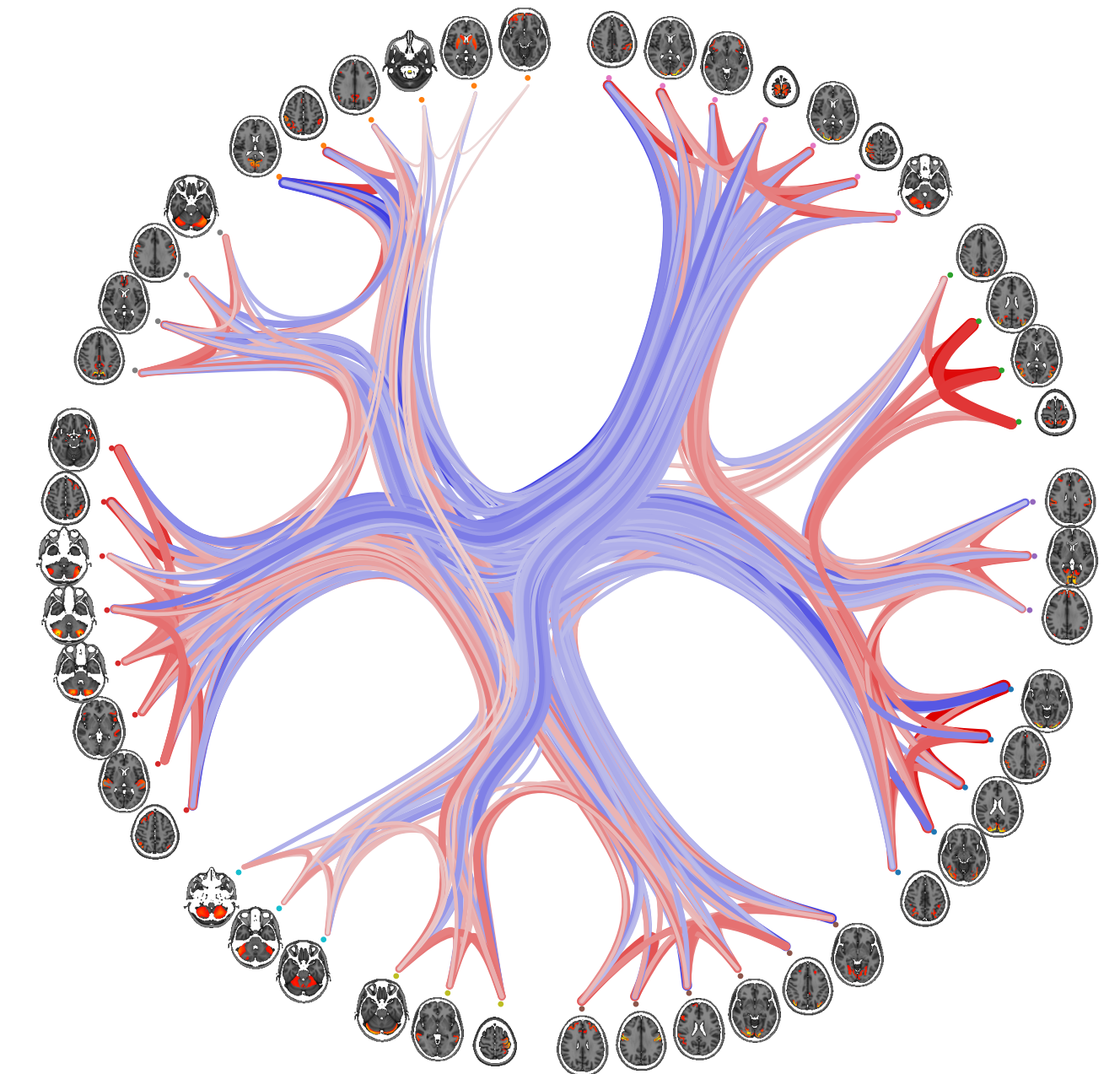
# Resting-State fMRI: Network Modelling and FSLNets

FSL Course 2026

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# Network modelling analysis

- Characteristics of Resting State Networks (RSNs)
- Additional notes on preprocessing
- **Network modelling analysis**
- **Methods comparisons and considerations**

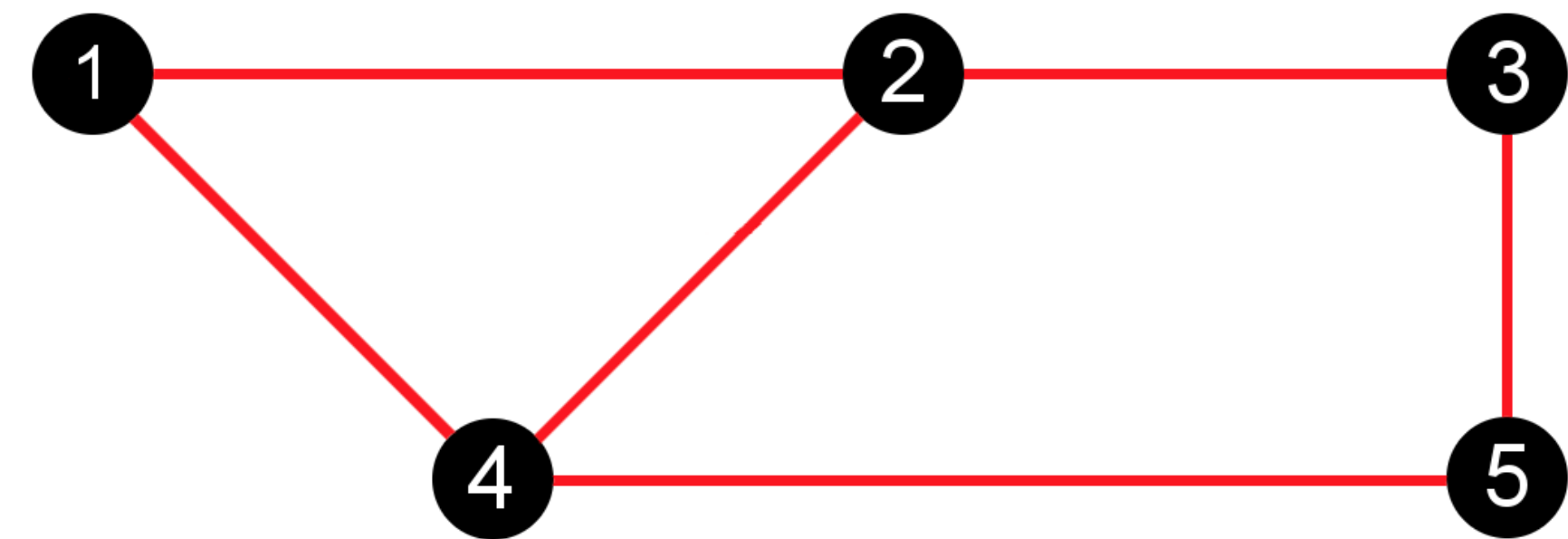




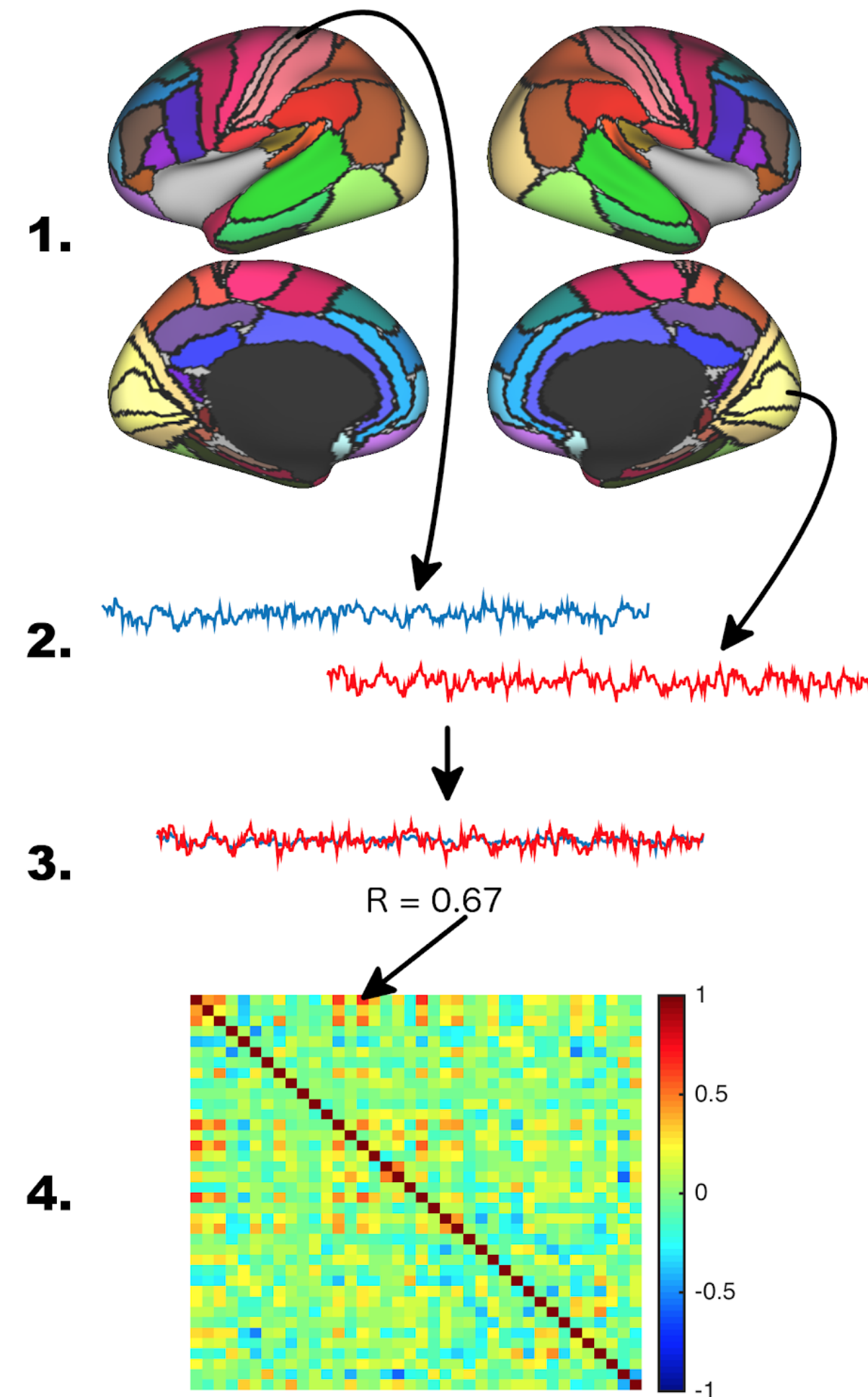
# Network Modelling analysis

# Glossary

- Node = functional brain region
  - Contiguous nodes = interconnected 'blobs'
  - Non-contiguous nodes = e.g. bilateral
- Parcellation = separation of all voxels into a set of nodes
  - Hard parcellation = binary regions
  - Soft parcellation = weighted regions
- Edge = connection between nodes
- Connectomics = mapping all connections between all brain regions



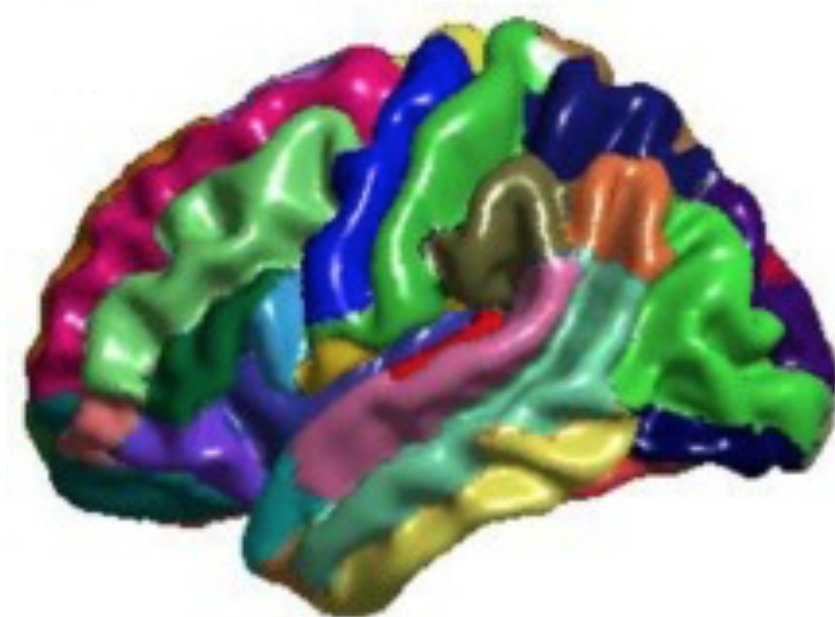
# Analysis steps



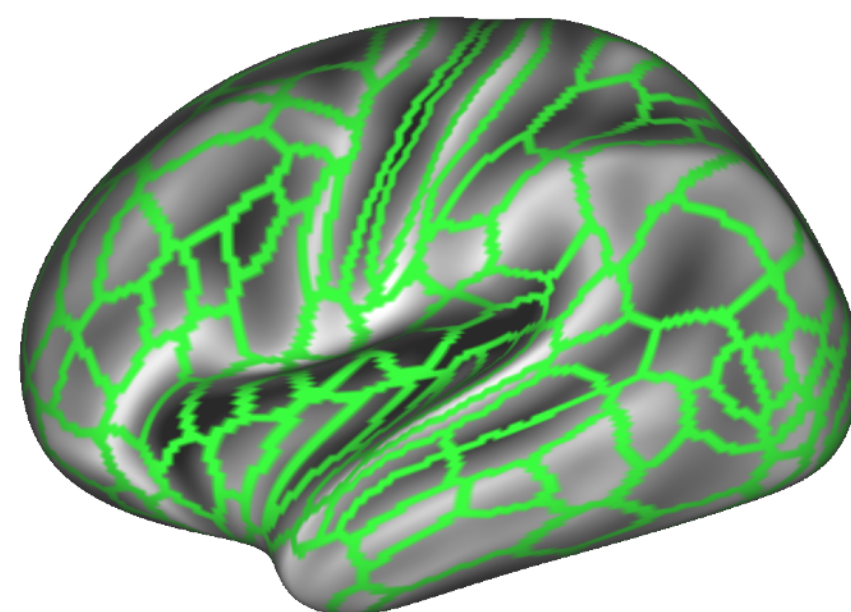
- Node definition
- Timeseries extraction
- Edge calculation
- Network matrix
- Group analysis

# Node definition

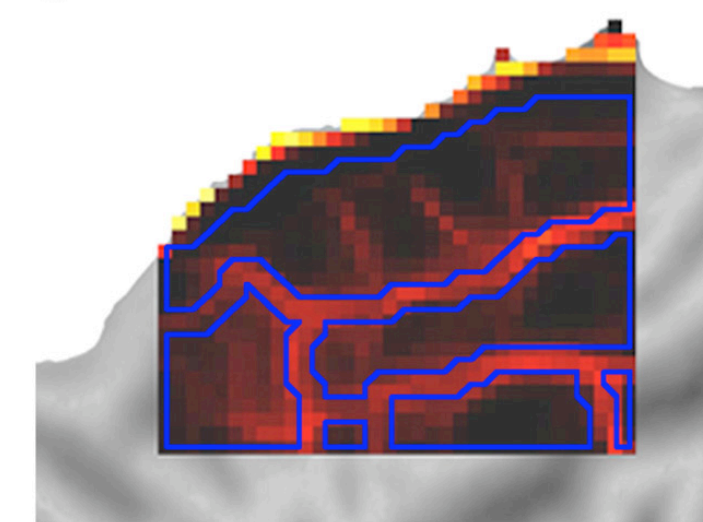
Anatomical atlases



Functional atlases



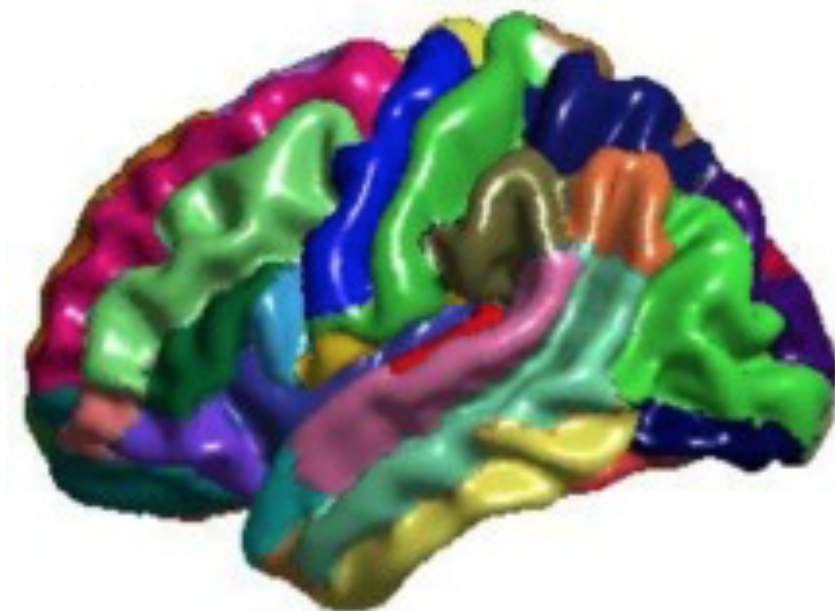
Data-driven parcellation



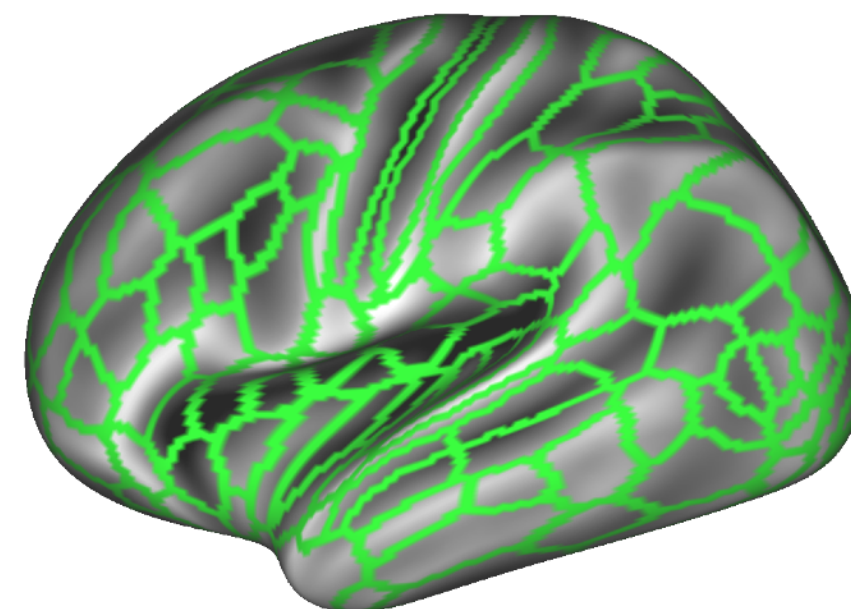
# Node definition

## Anatomical atlases

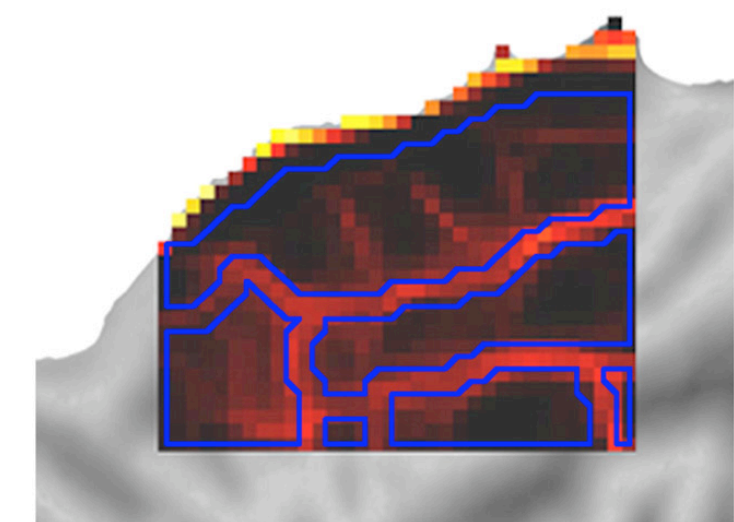
- Harvard-Oxford/ AAL
- Avoid if possible because typically based on small number of subjects and not a good estimation of functional boundaries



## Functional atlases



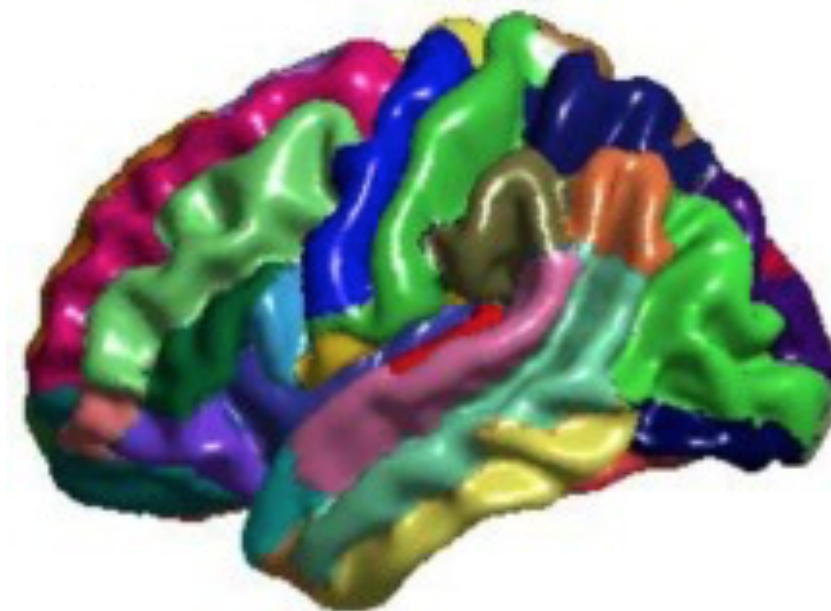
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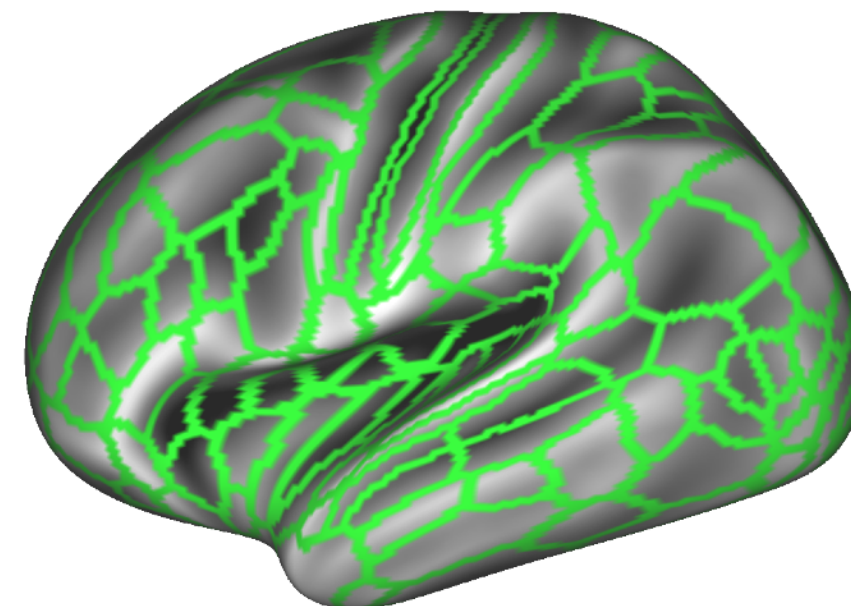
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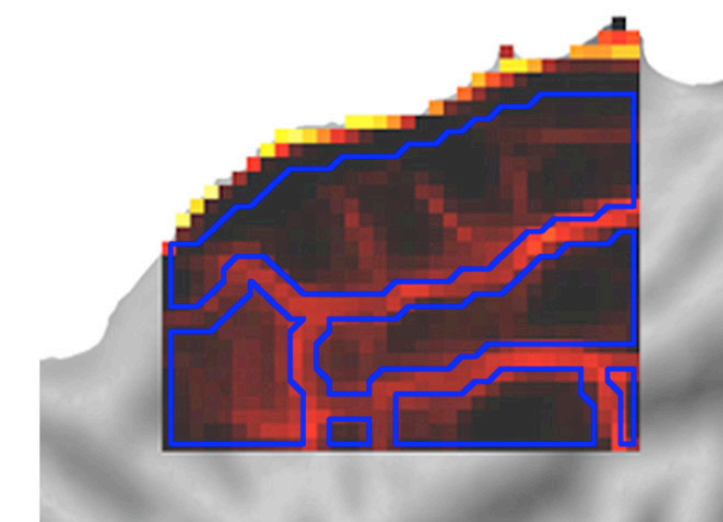


## Functional atlases

- Yeo 2011/ Glasser 2016
- Many good functional atlases available, though few comparison studies
- How to map onto individuals is very important



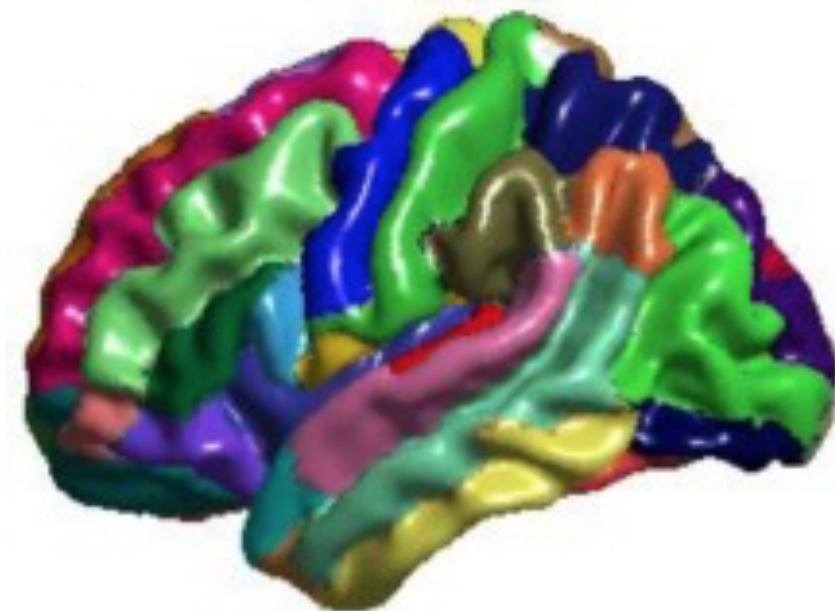
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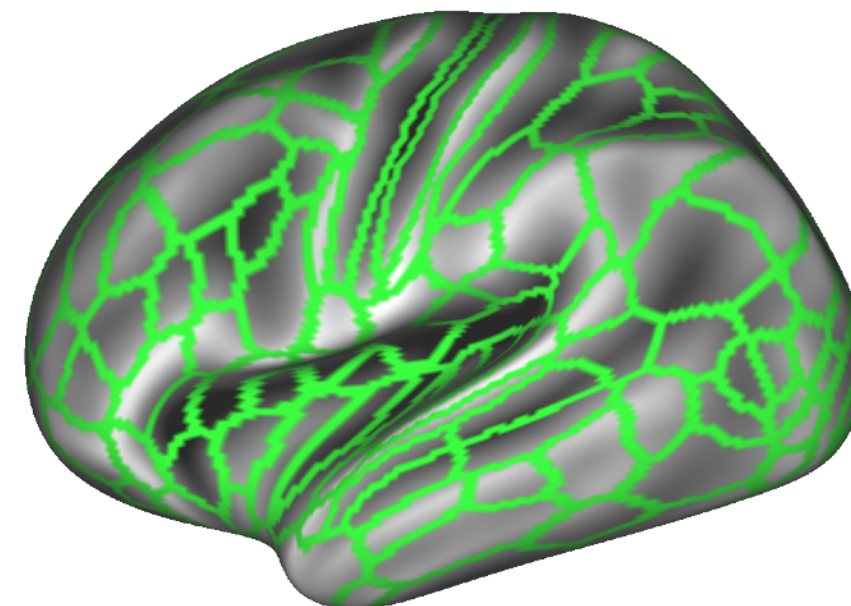
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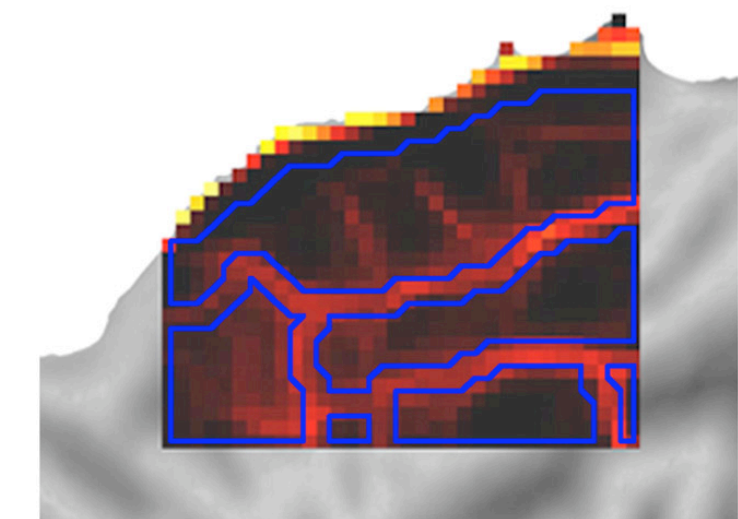
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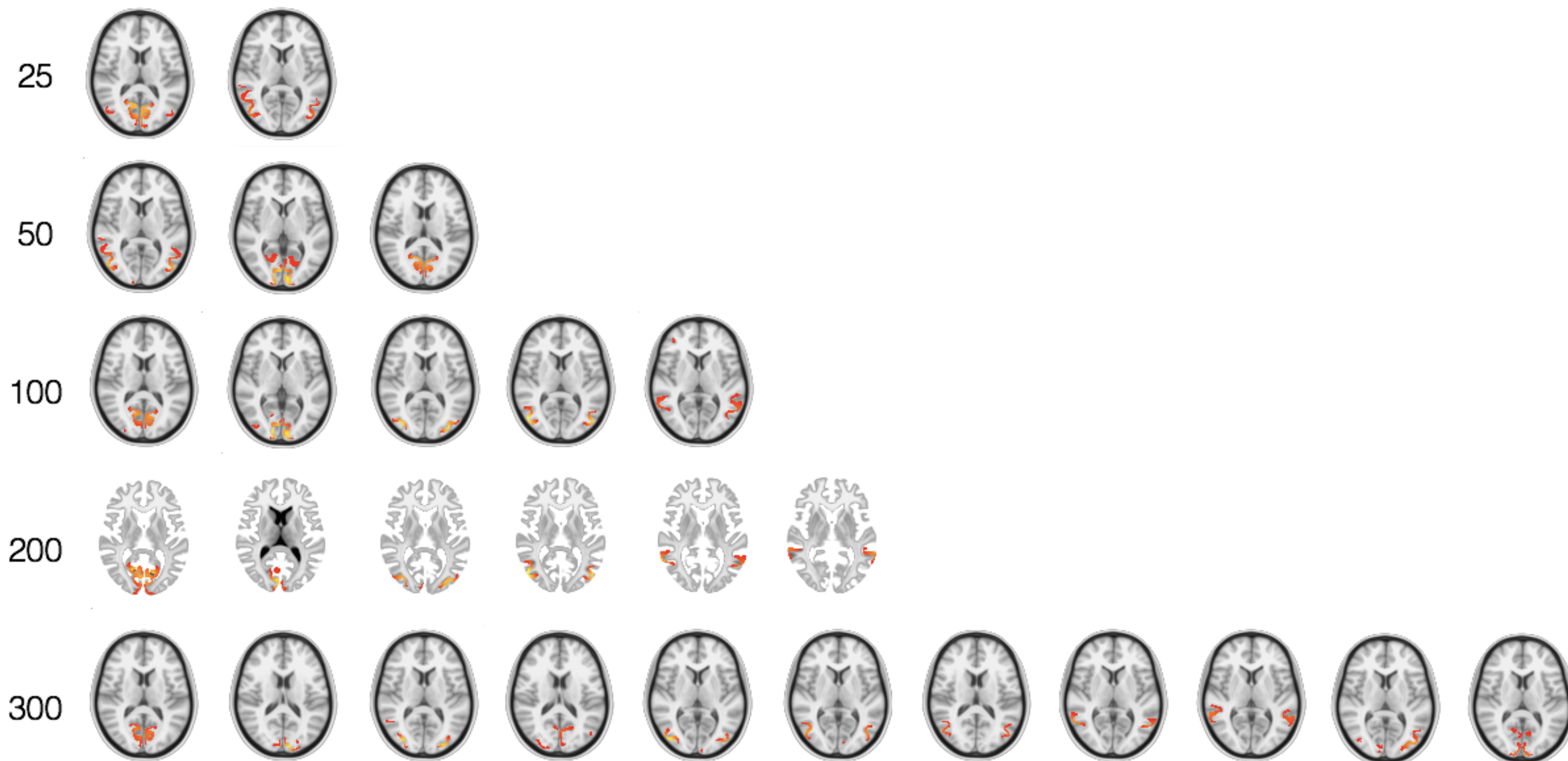


## Data-driven parcellation

- ICA/ Clustering/ Gradients
- Estimate parcellation from the same dataset used for further analyses
- How to map group parcellation onto individuals very important



# ICA for parcellation



# Timeseries extraction

## Hard parcellation:

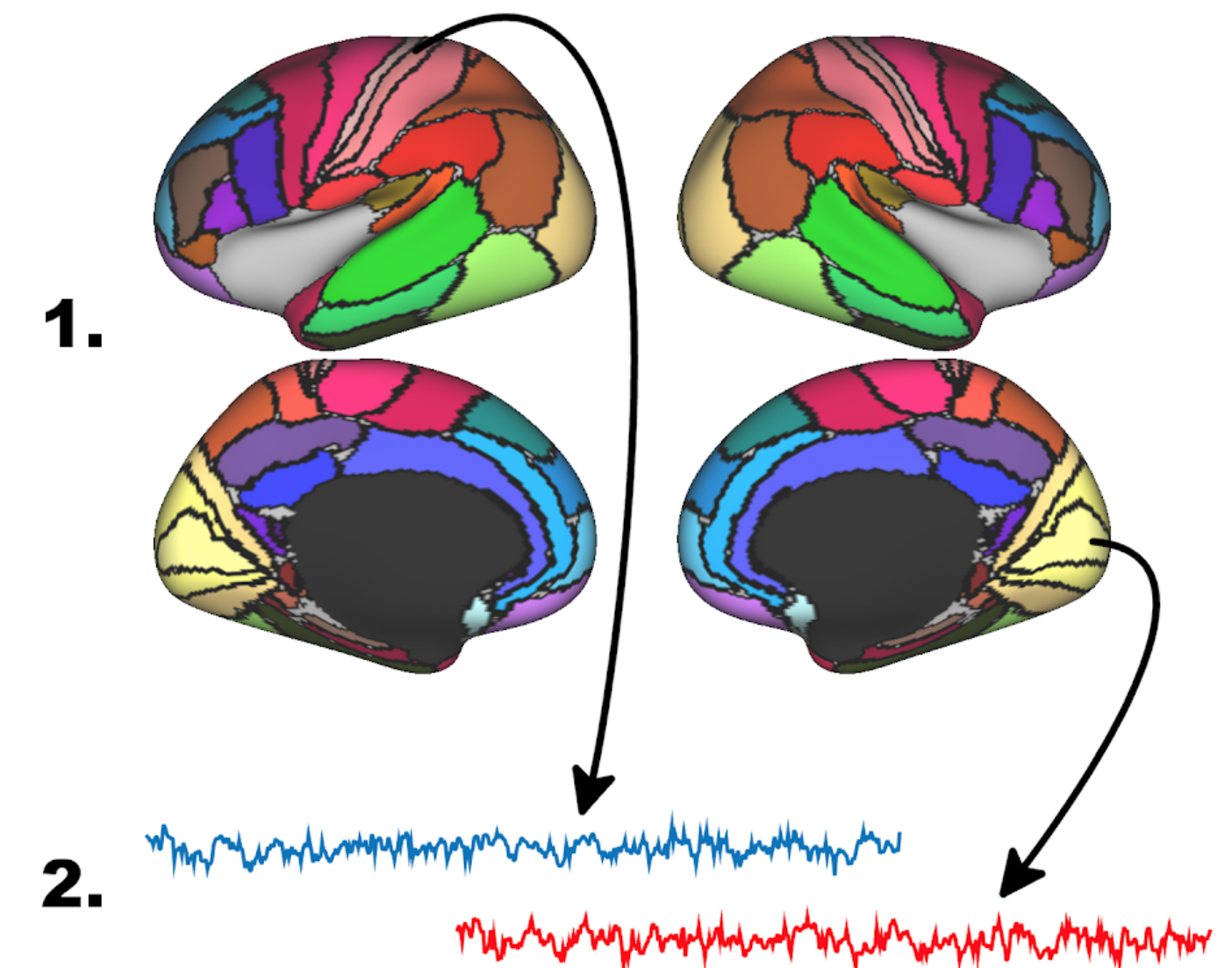
- Masking (mean timeseries)
- Eigen timeseries (PCA)
- Using multilayer classifier

## ICA (soft parcellation):

- Dual regression/ back projection

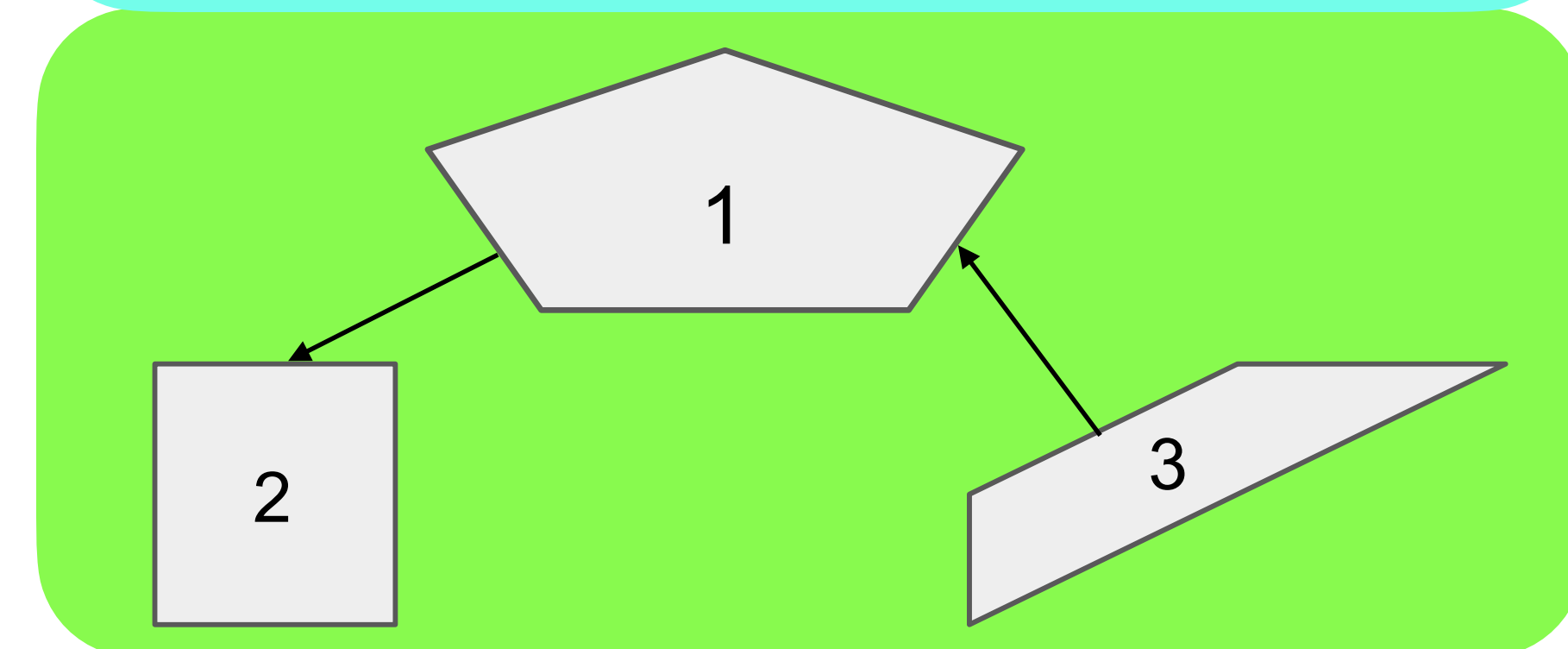
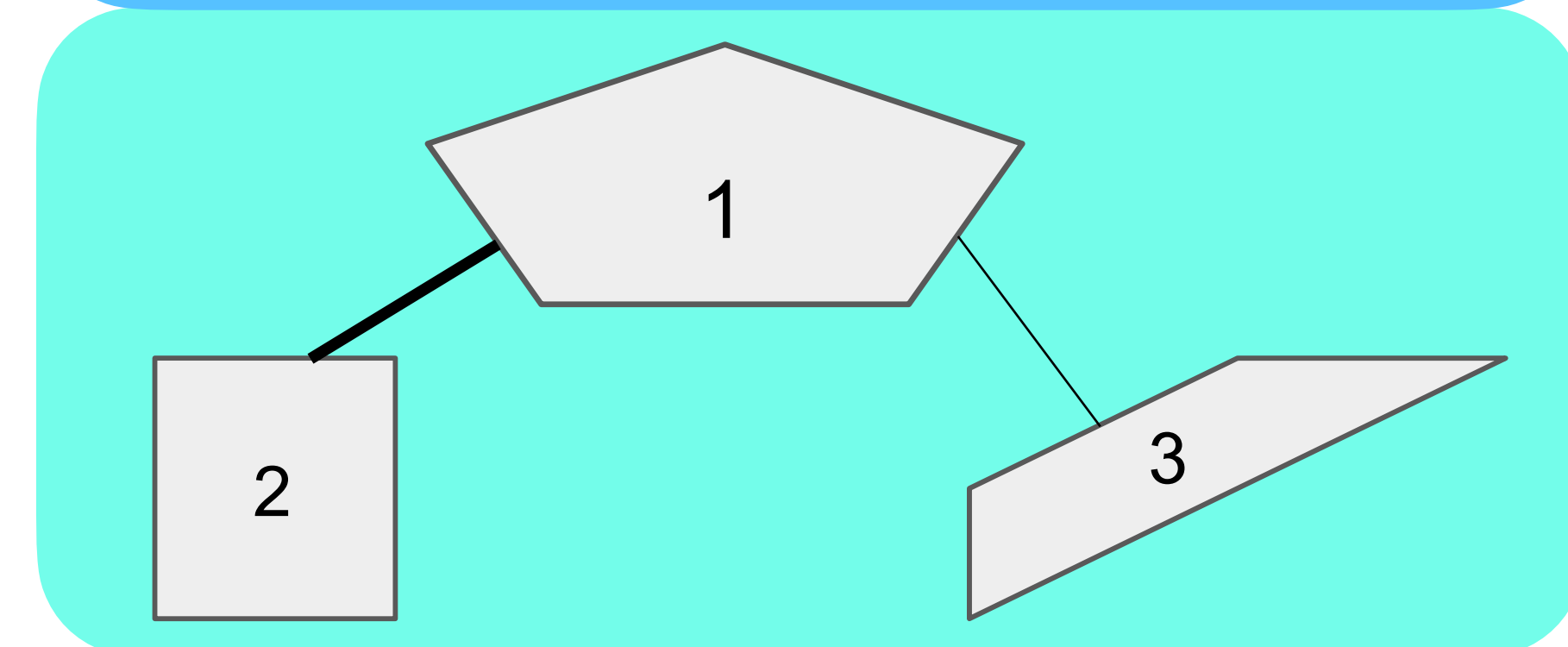
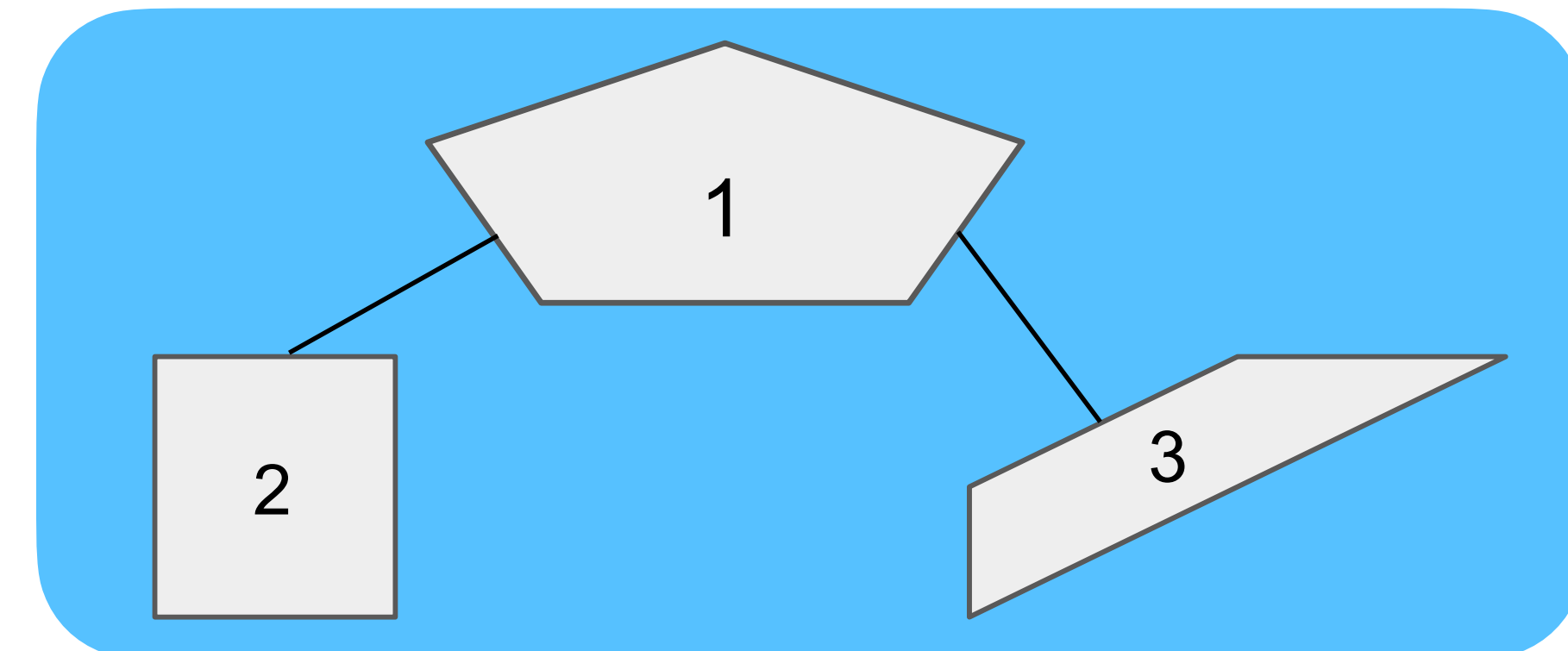
## Alternative:

- Hierarchical estimation of group & subject
- e.g. PROFUMO



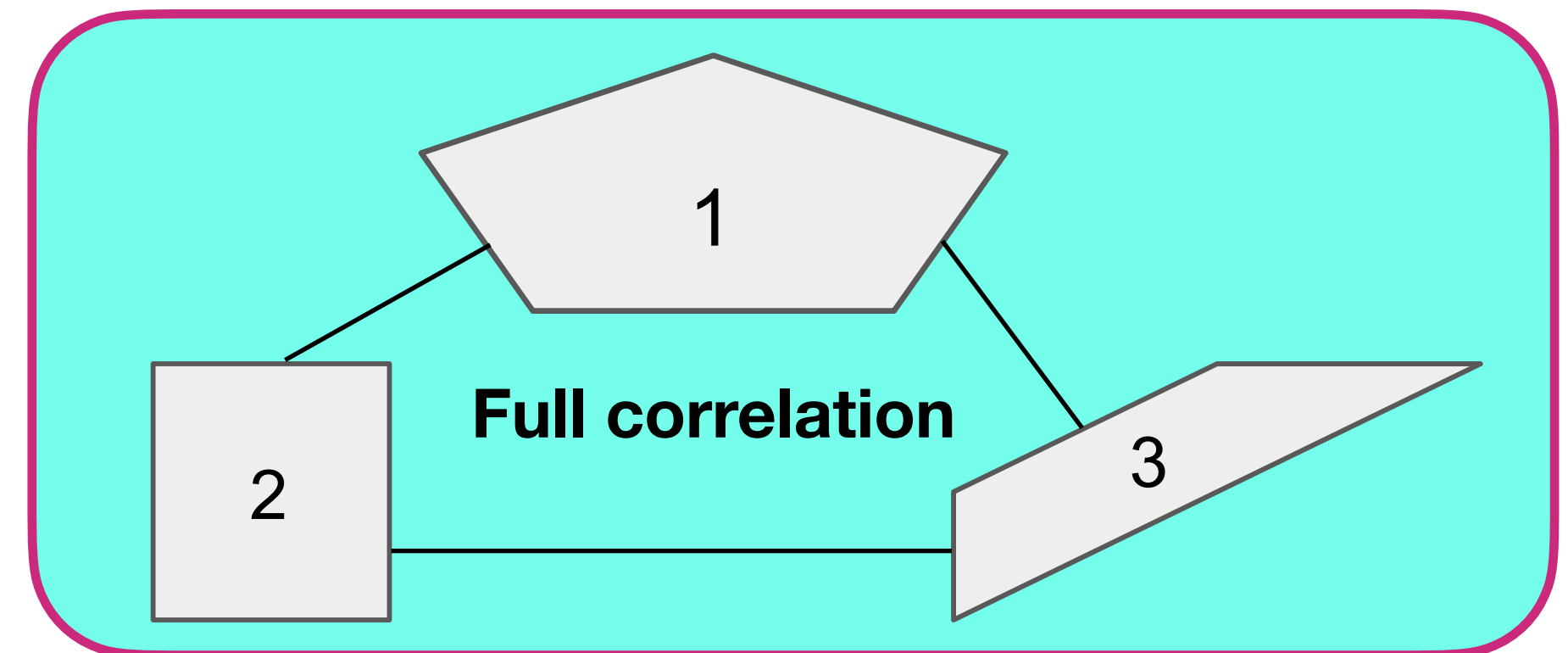
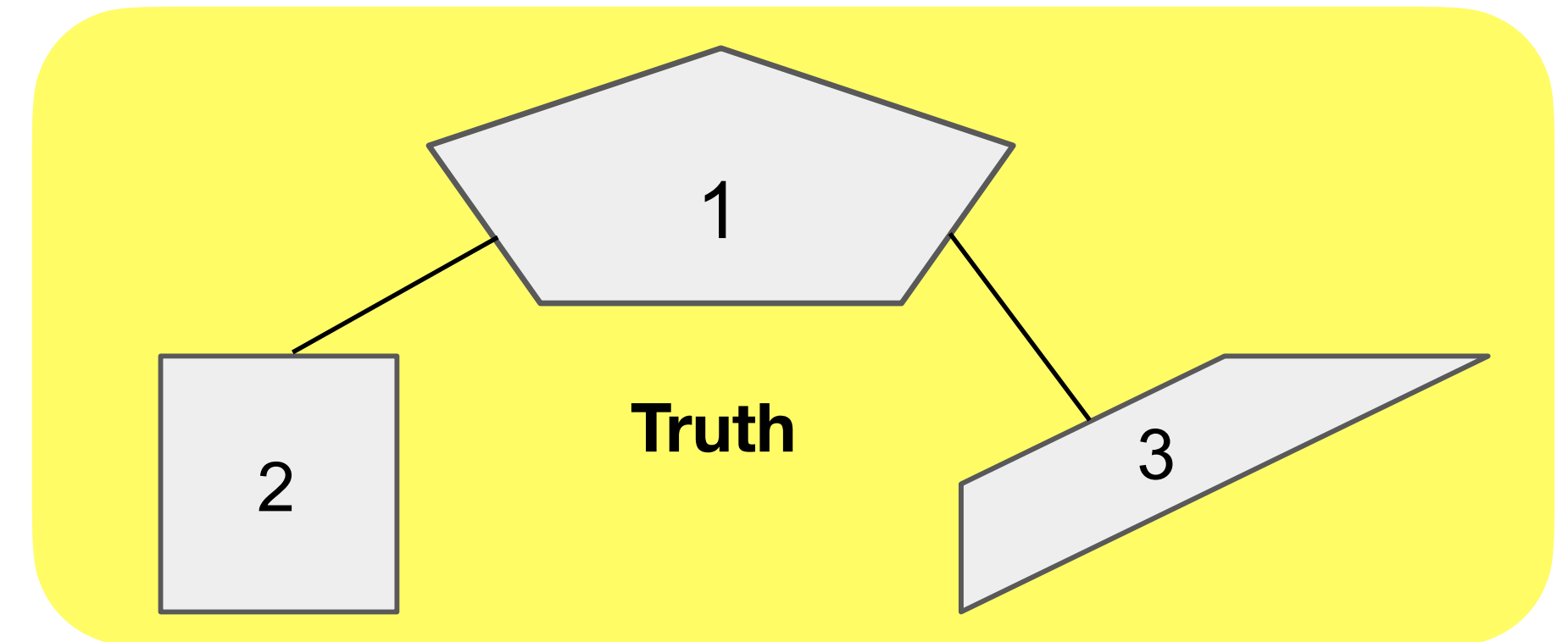
# Edge calculation

- Presence/ absence of edges
- Strength of edges
- Directionality of edges



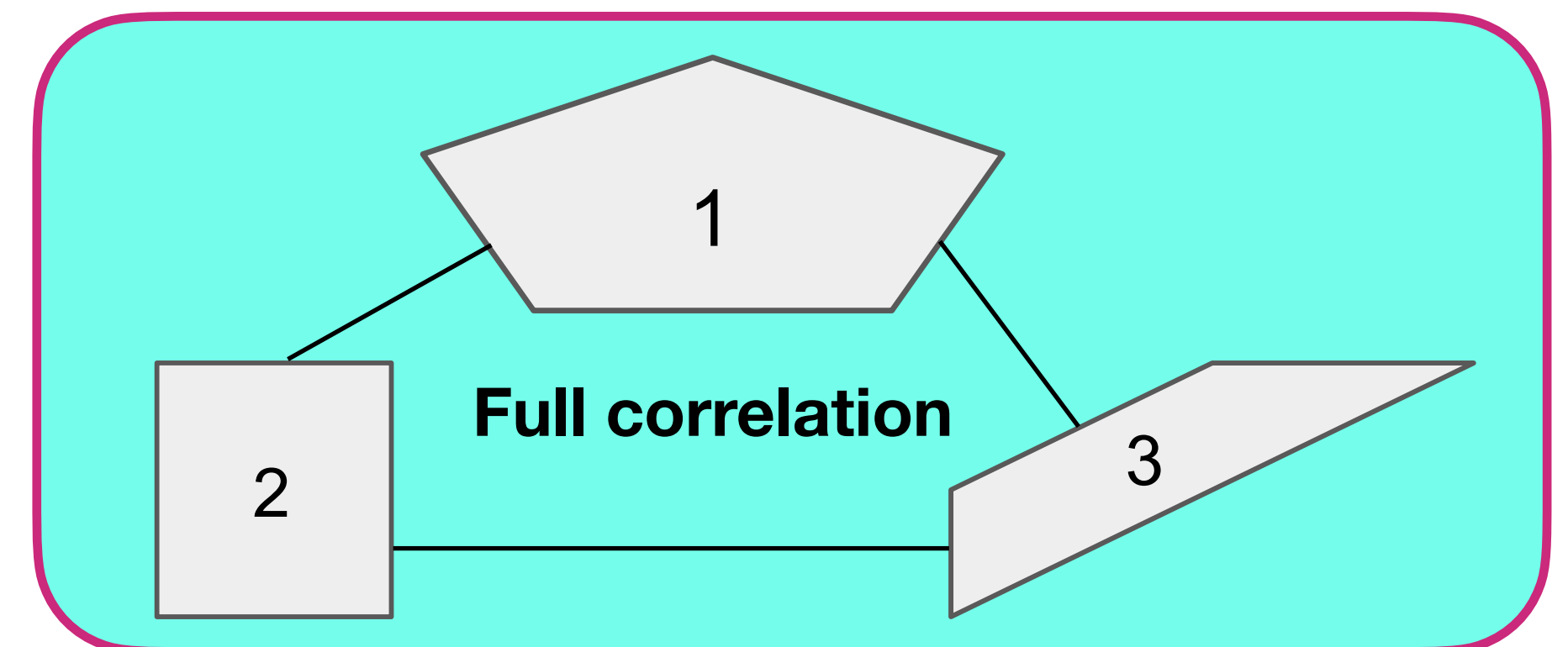
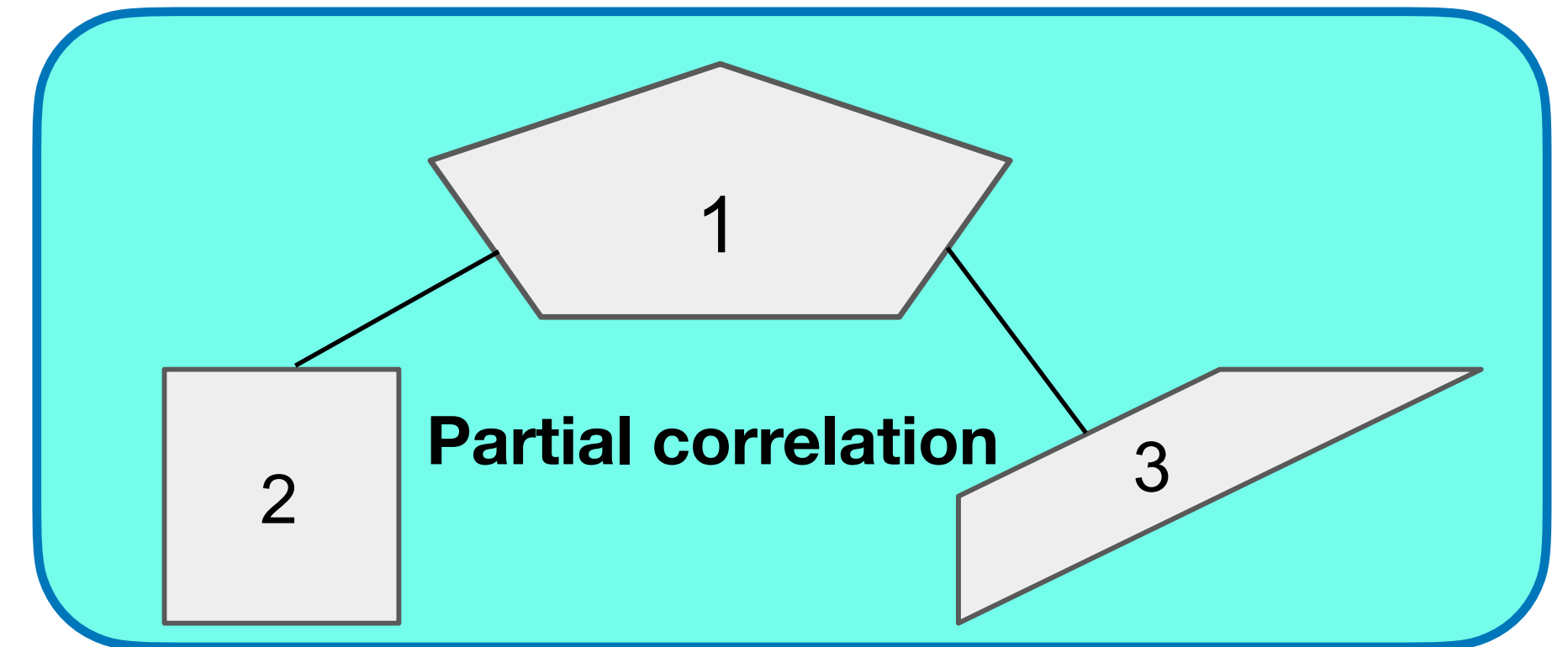
# Direct versus indirect connections

- Correlation between 2 and 3 will exist
- Therefore full correlation will incorrectly estimate connection 2-3
- 2-3 is an indirect connection



# Partial correlation

- Before correlating 2 and 3, first regress 1 out of both (“orthogonalise wrt 1”)
  - If 2 and 3 are still correlated, a direct connection exists
- More generally, first regress all other nodes’ timecourses out of the pair in question
  - Equivalent to the inverse covariance matrix

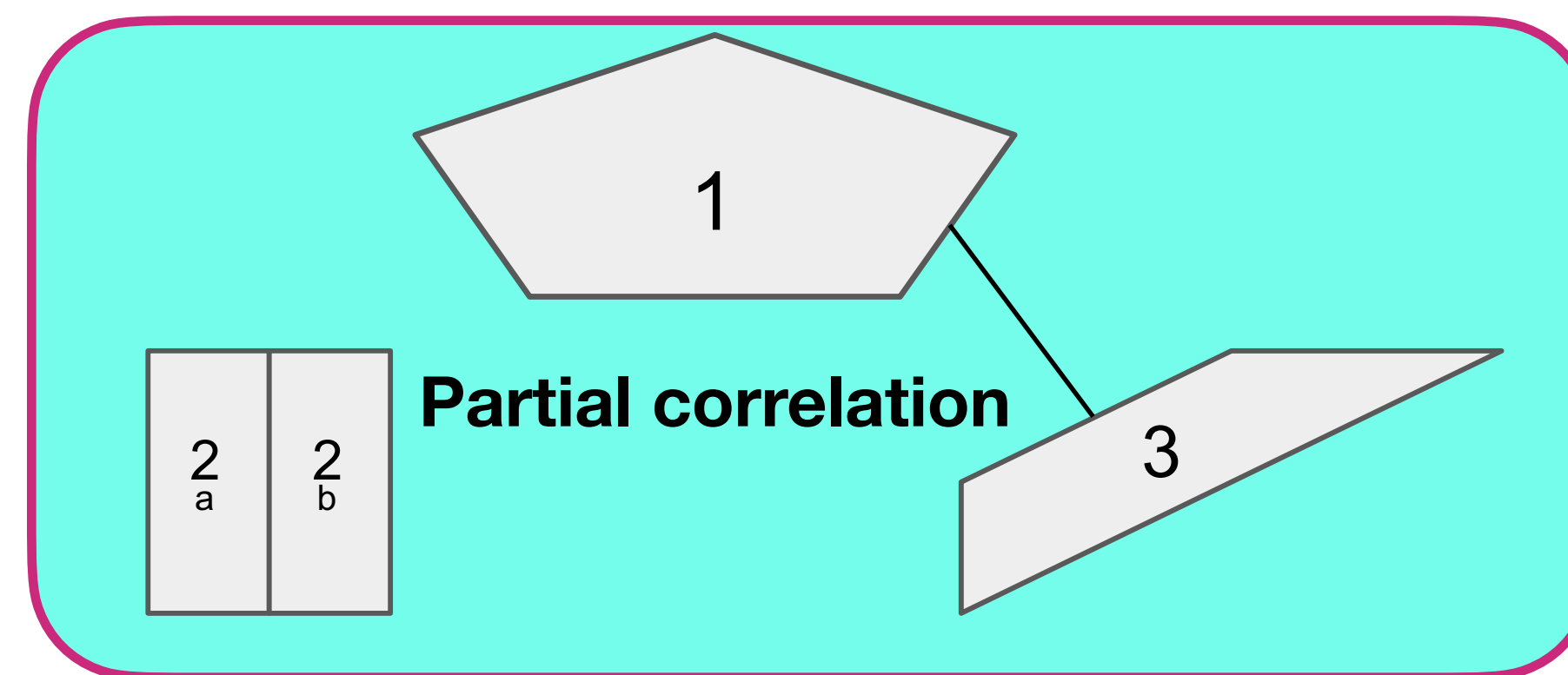
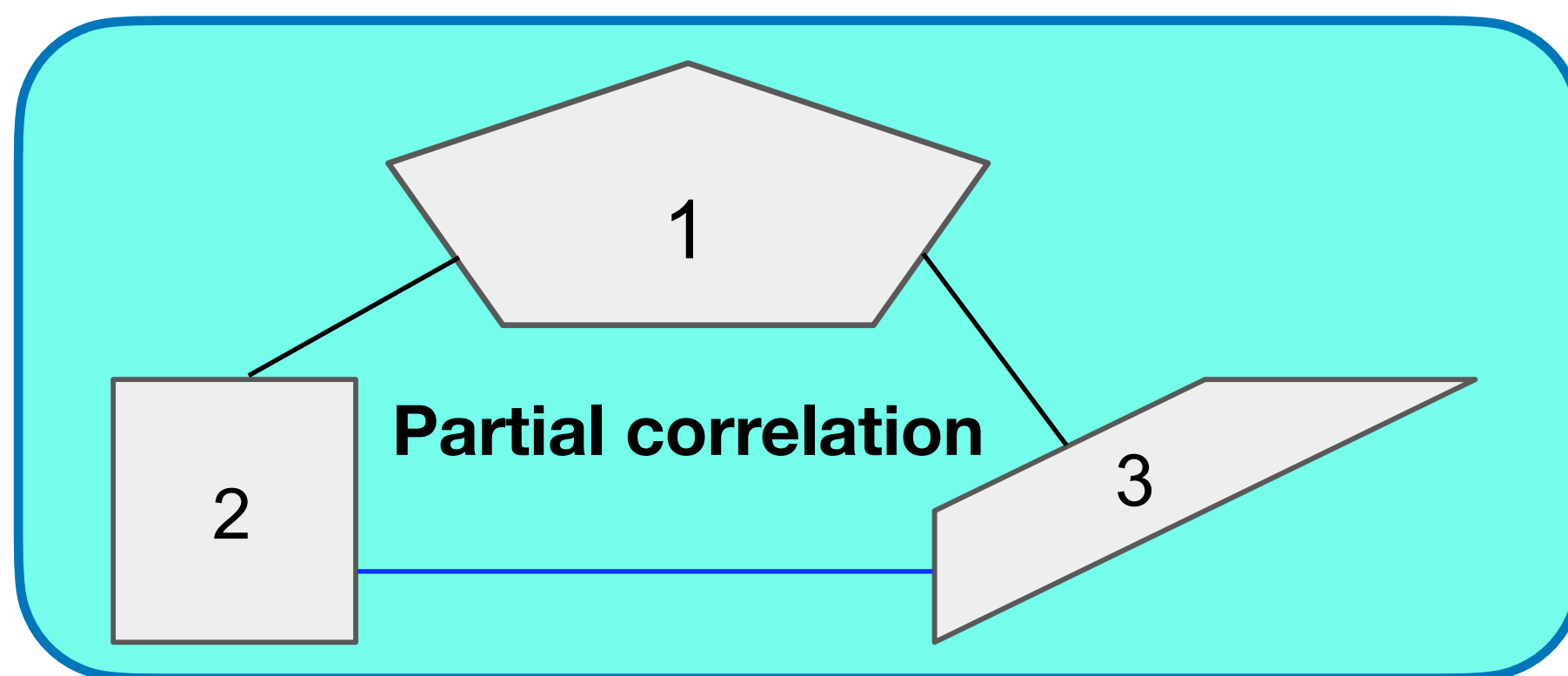
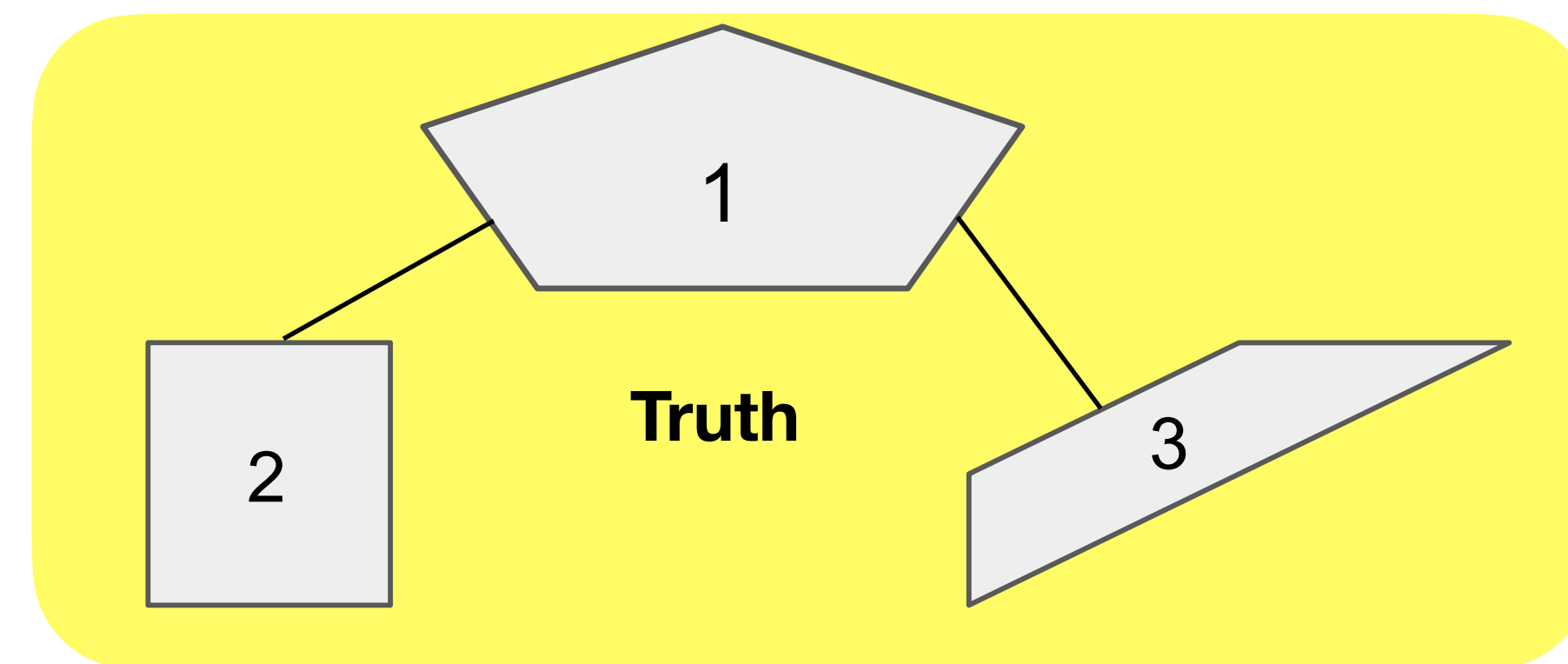
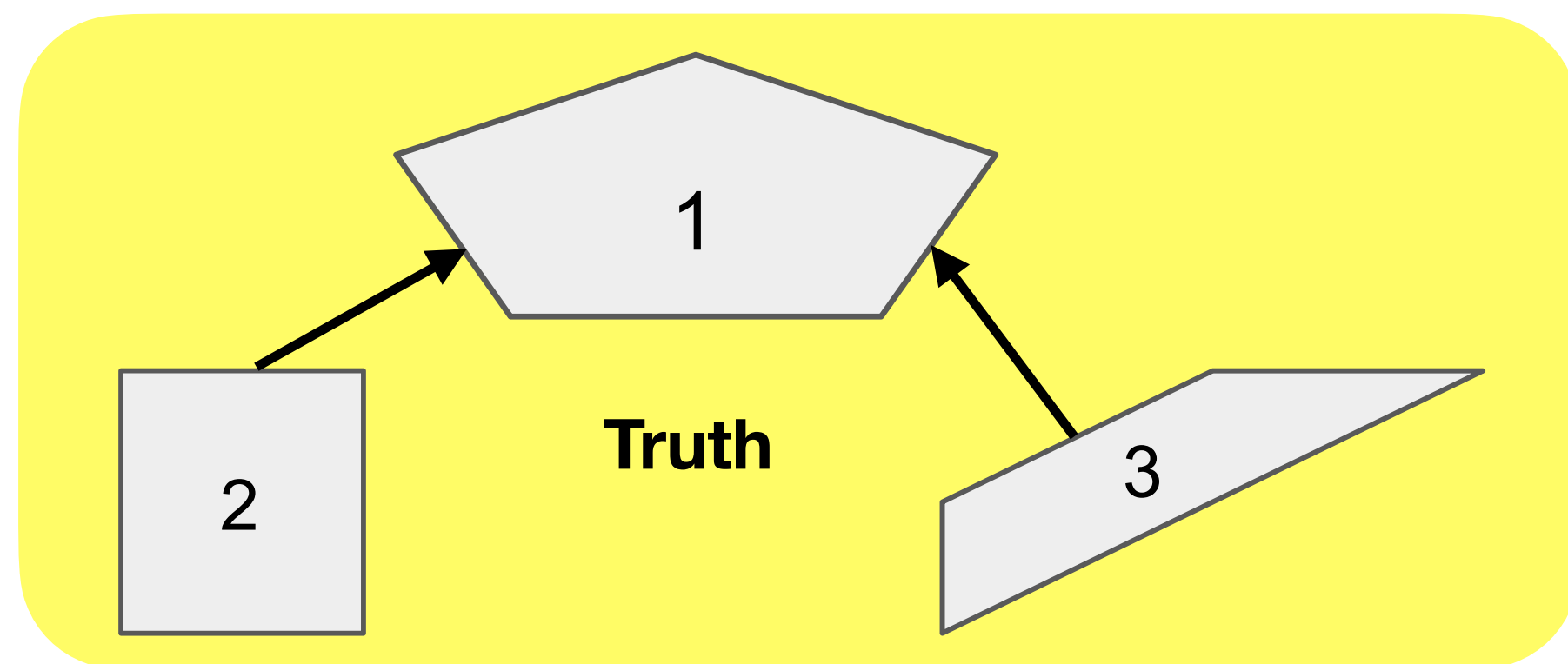




# Regularisation

- Urgh! If you have 200 nodes and 100 timepoints, this is impossible!
- A problem of DoF - need large #timepoints - #nodes
- When inverting a “rank-deficient” matrix it is common to aid this with some mathematical conditioning, e.g. force it to be sparse (force low values that are poorly estimated to zero)
- Regularised partial correlation (such as ICOV, Ridge)
- But still important to maximise temporal degrees of freedom

# Need to carefully define nodes

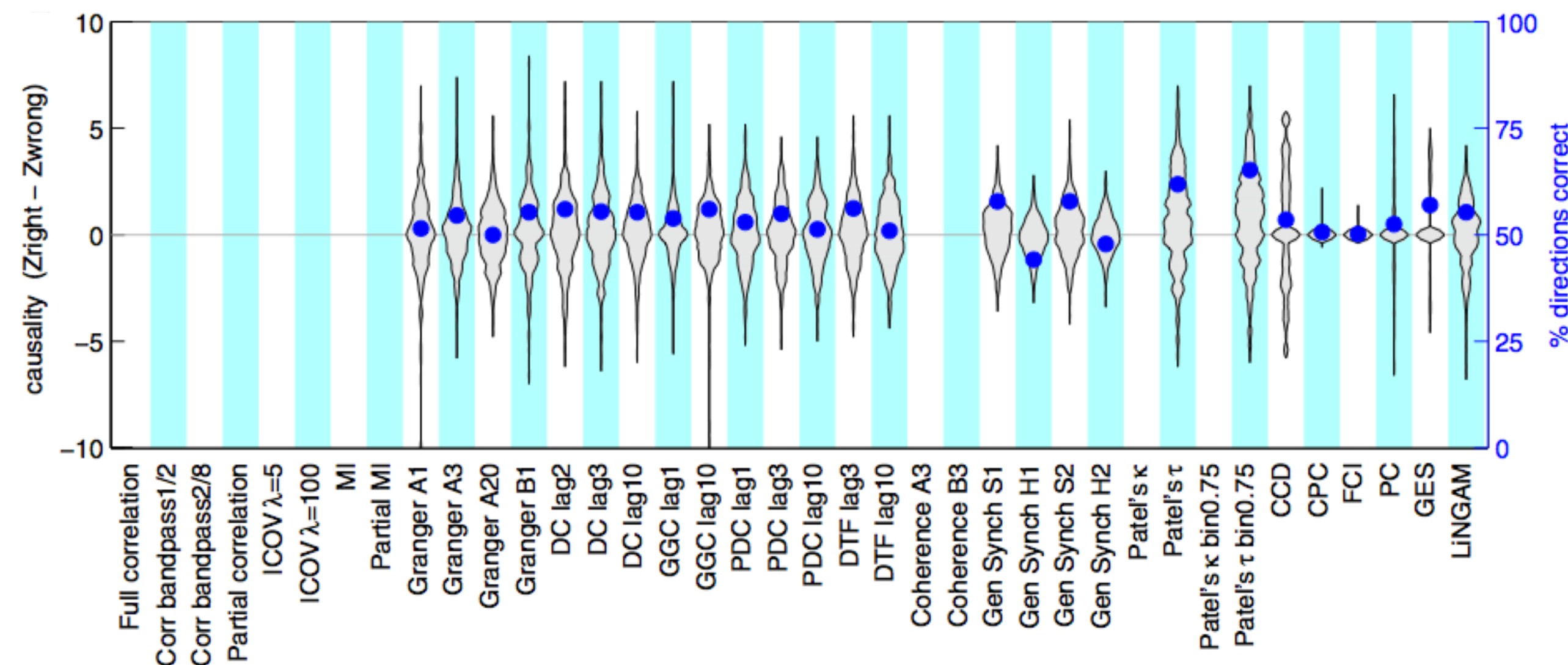


Berkson's paradox = false positive (2-3)

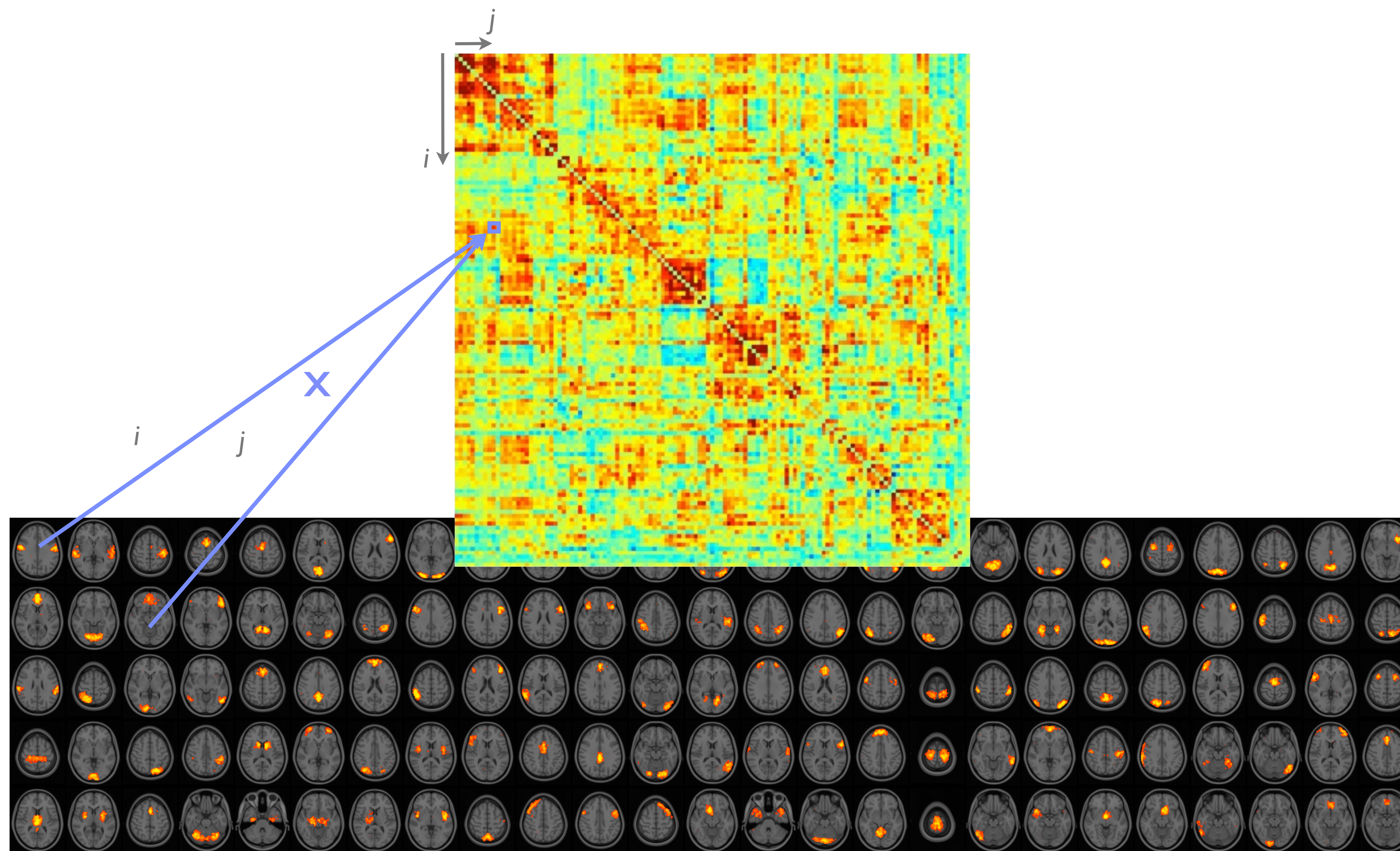
Over-splitting = false negative (1-2)

# Directionality of edges

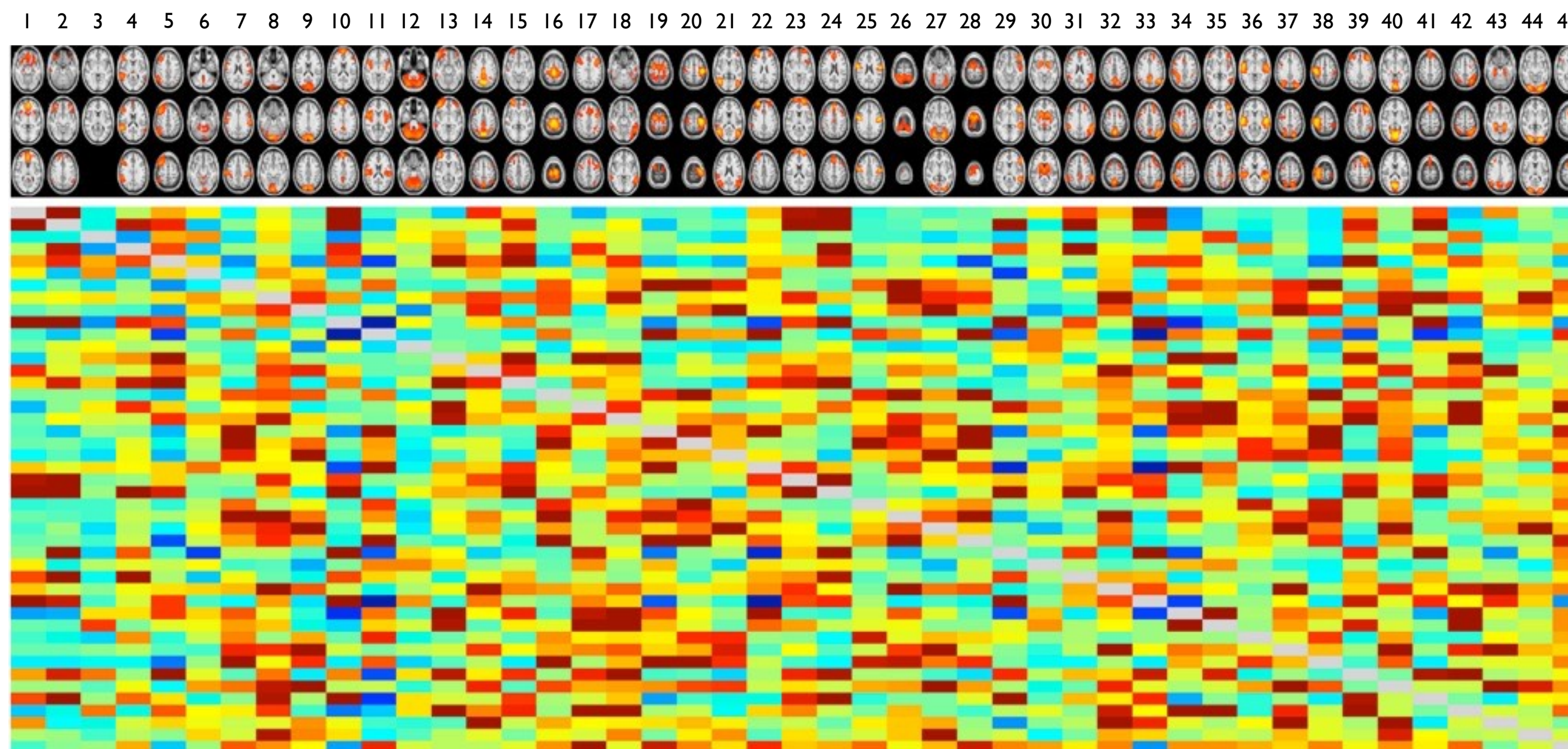
- Directionality is hard to estimate in BOLD data
- Don't use lag-based methods such as Granger causality
- Perhaps directionality is oversimplistic view of neural connectivity (particularly in resting-state)?



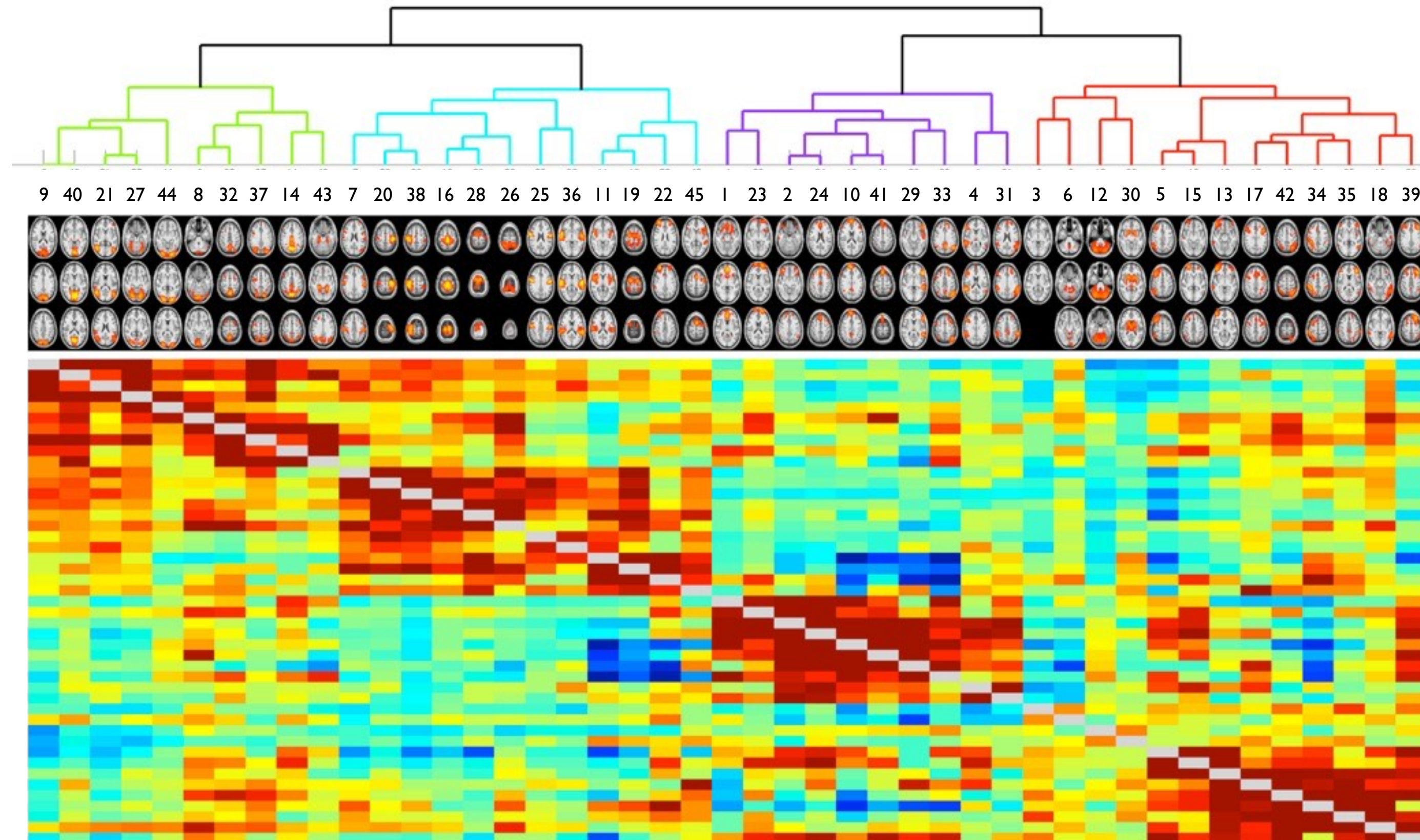
# Building a network matrix



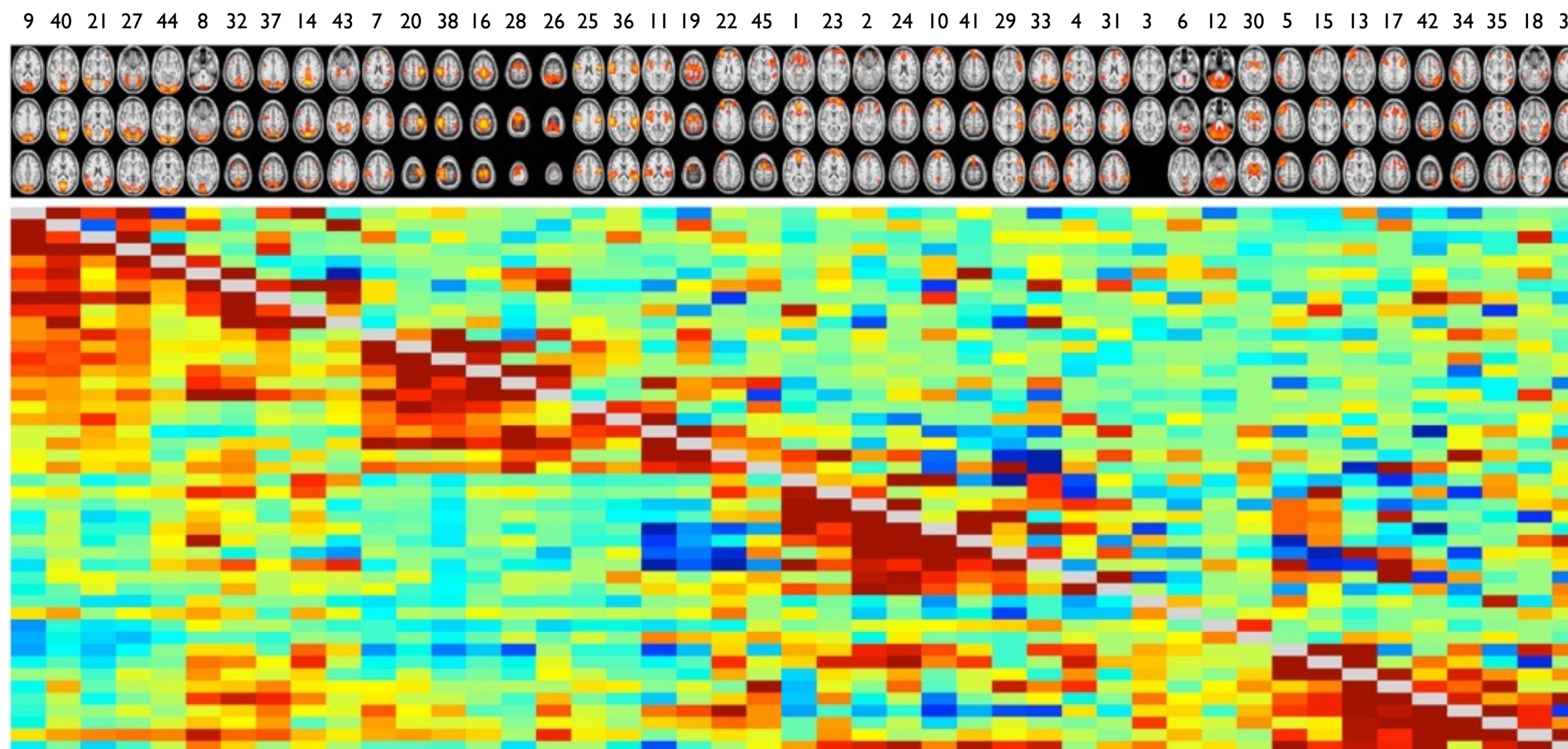
# Network matrix



# Hierarchical clustering



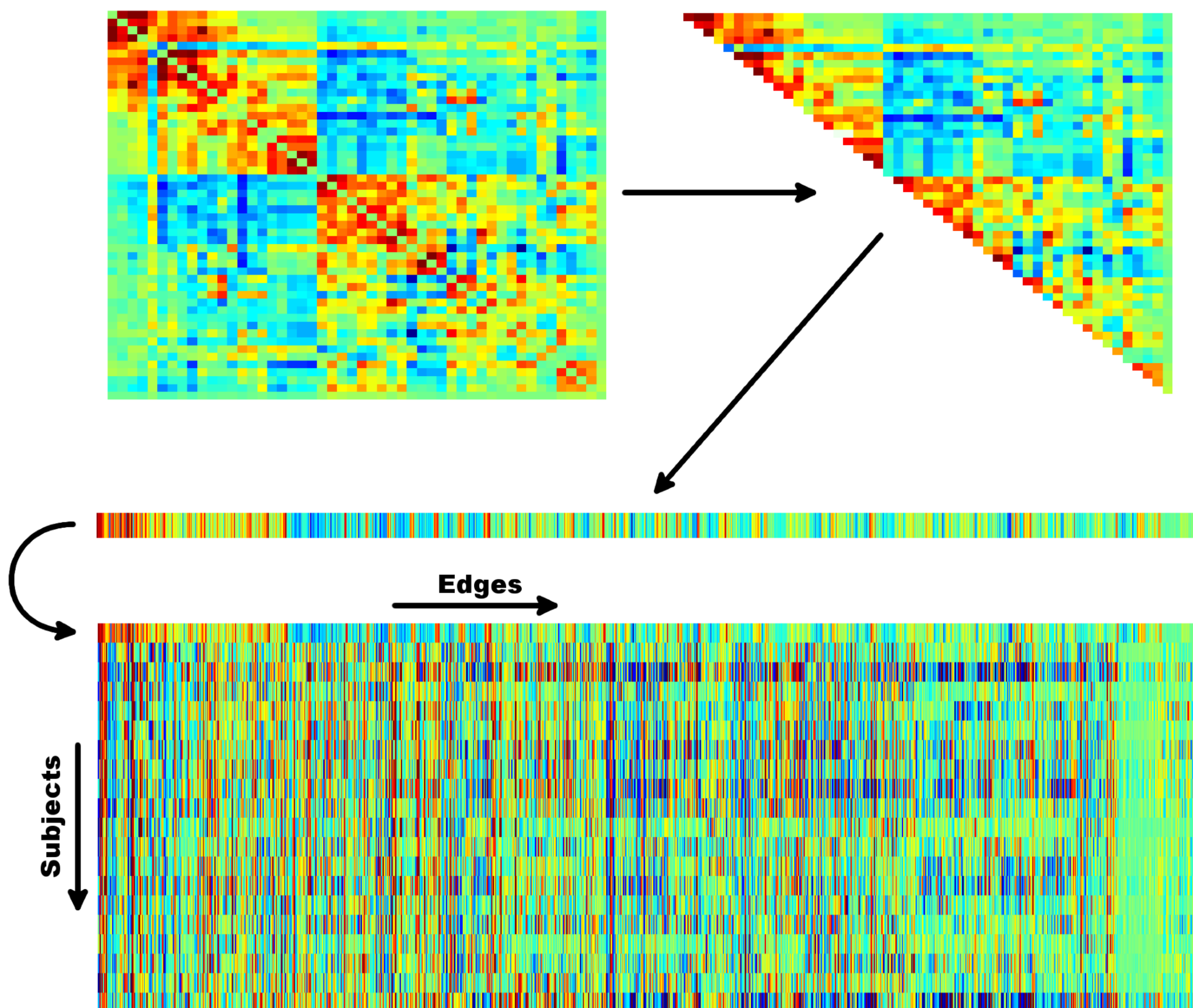
# Partial correlation is sparser than full



Full correlation matrix

Partial correlation matrix

# Group analysis



- Calculate network matrix for each subject
- Combine all network matrices into one
- Perform group-level comparisons:
  - Univariate tests for each edge (GLM)
  - Multivariate prediction methods (SVM)



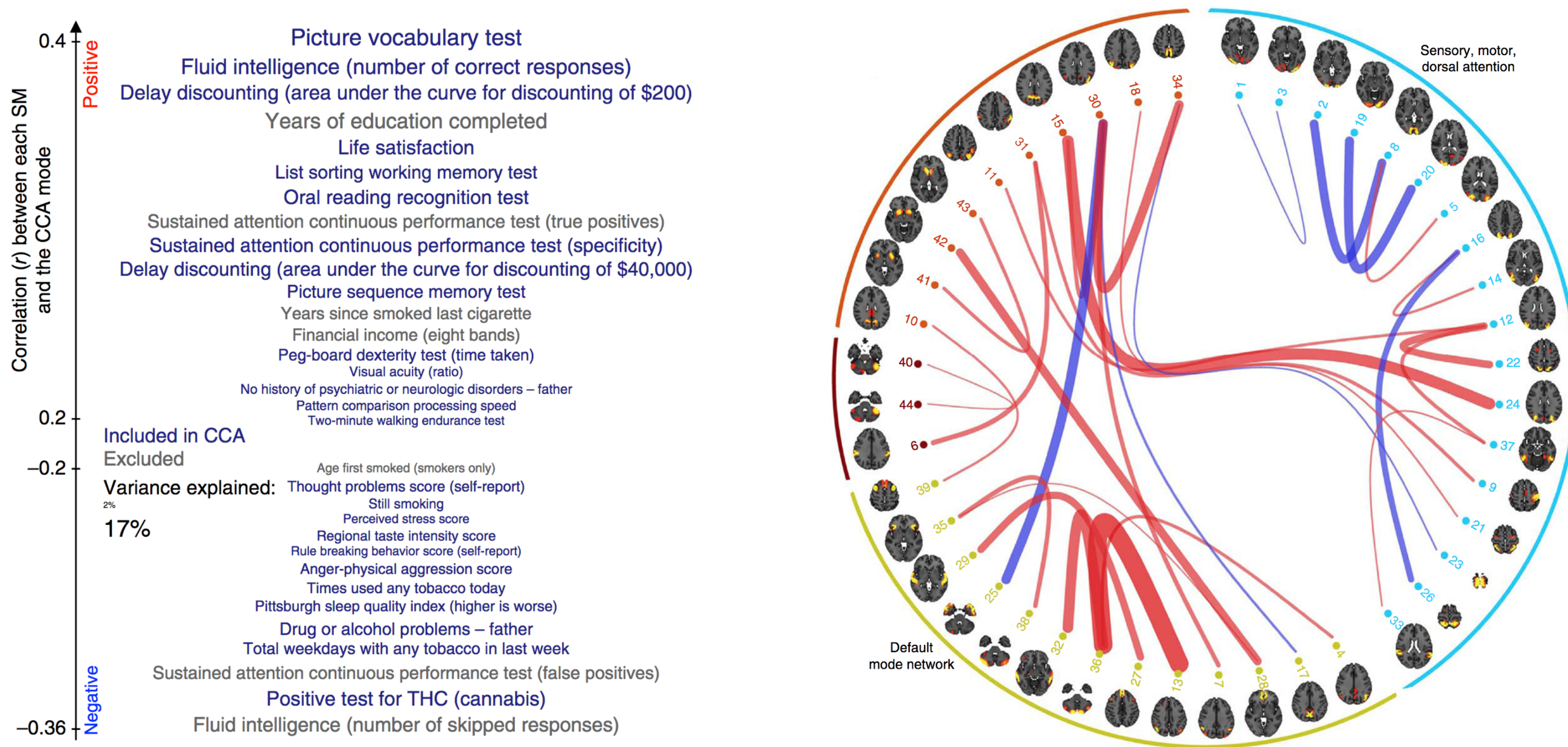
# FSLnets

- Python tool

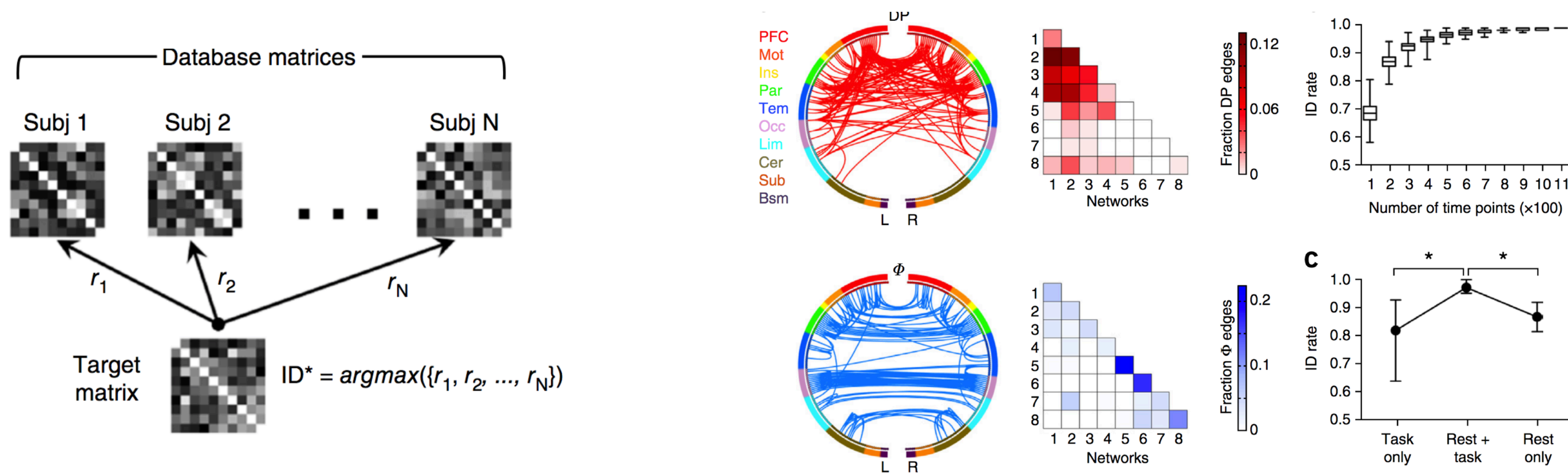


- This practical will be a bit different from other practicals

# Example: positive-negative mode



# Example: connectivity fingerprint

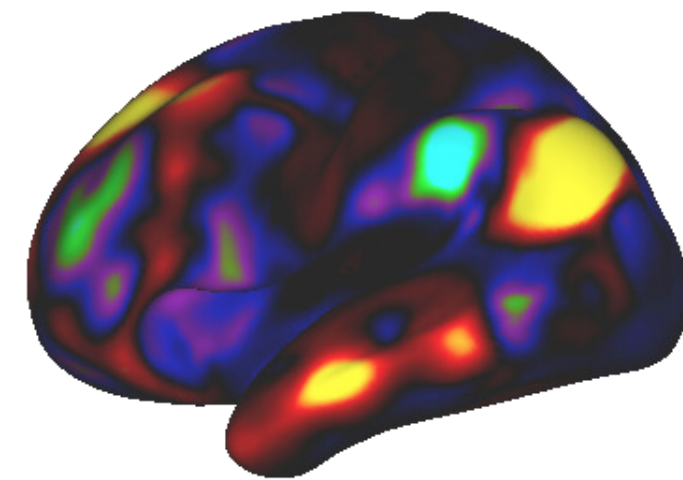




# Comparison of methods

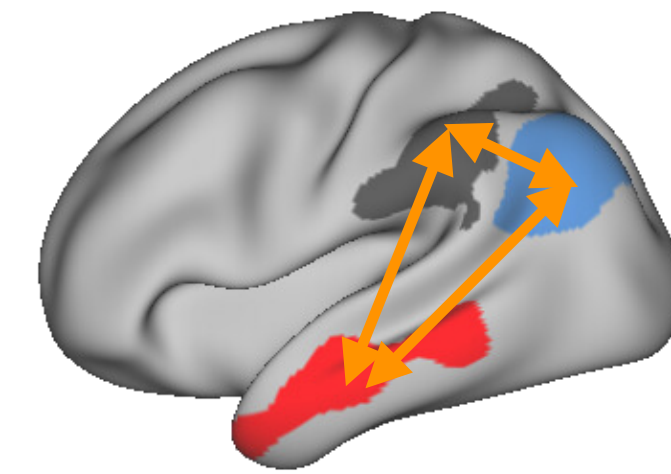
# Overview of resting state methods

## Voxel-based



- Seed-based correlation analysis
- Independent component analysis
- Amplitude of low frequency fluctuations
- Regional homogeneity

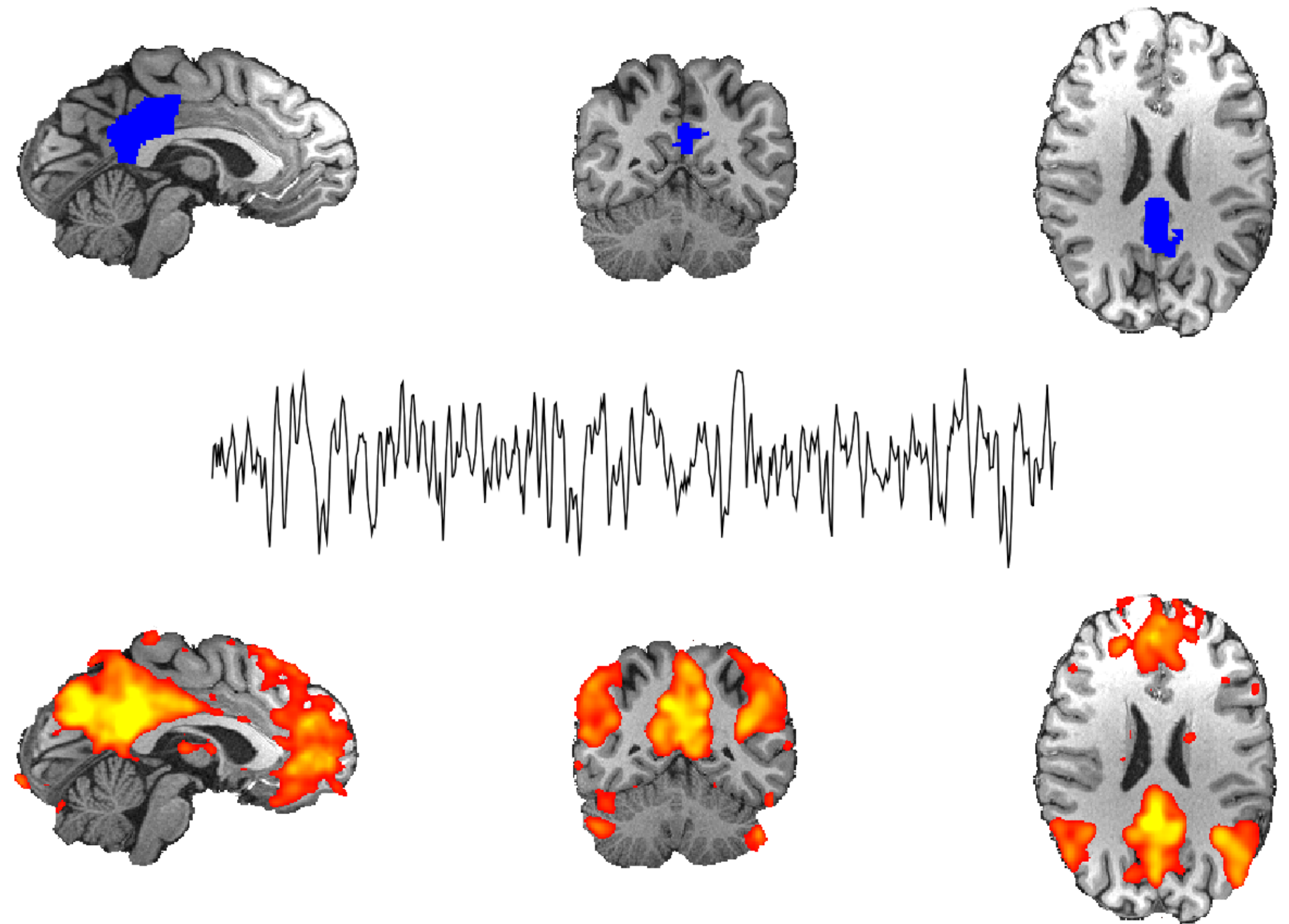
## Node-based



- Network modelling analysis
- Graph theory analysis
- Dynamic causal modelling
- Non-stationary methods

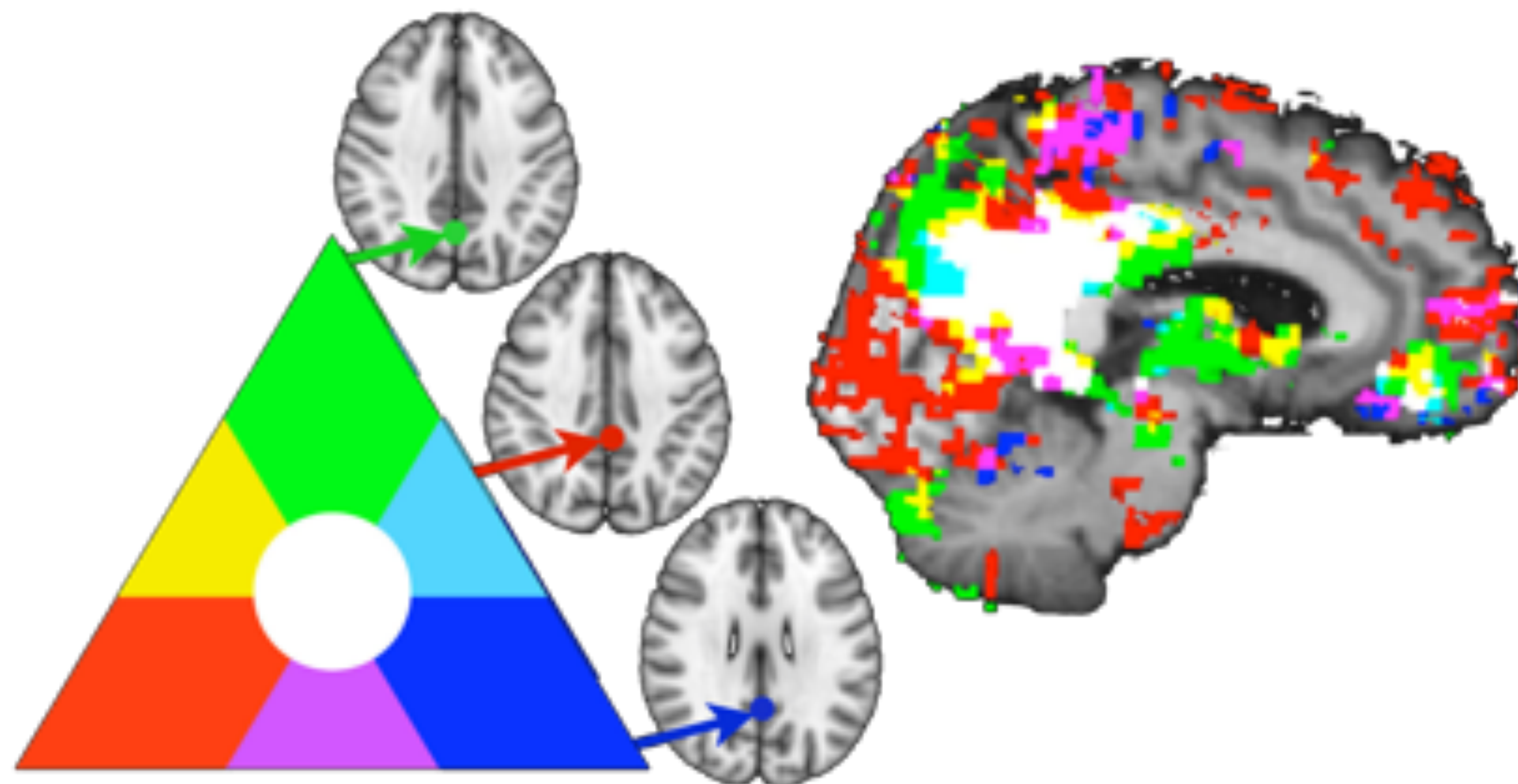
# Seed-based correlation

- Easy to interpret
- No correspondence problem
- Seed-selection bias
- Only models seed-effect (ignoring complex structure & noise)



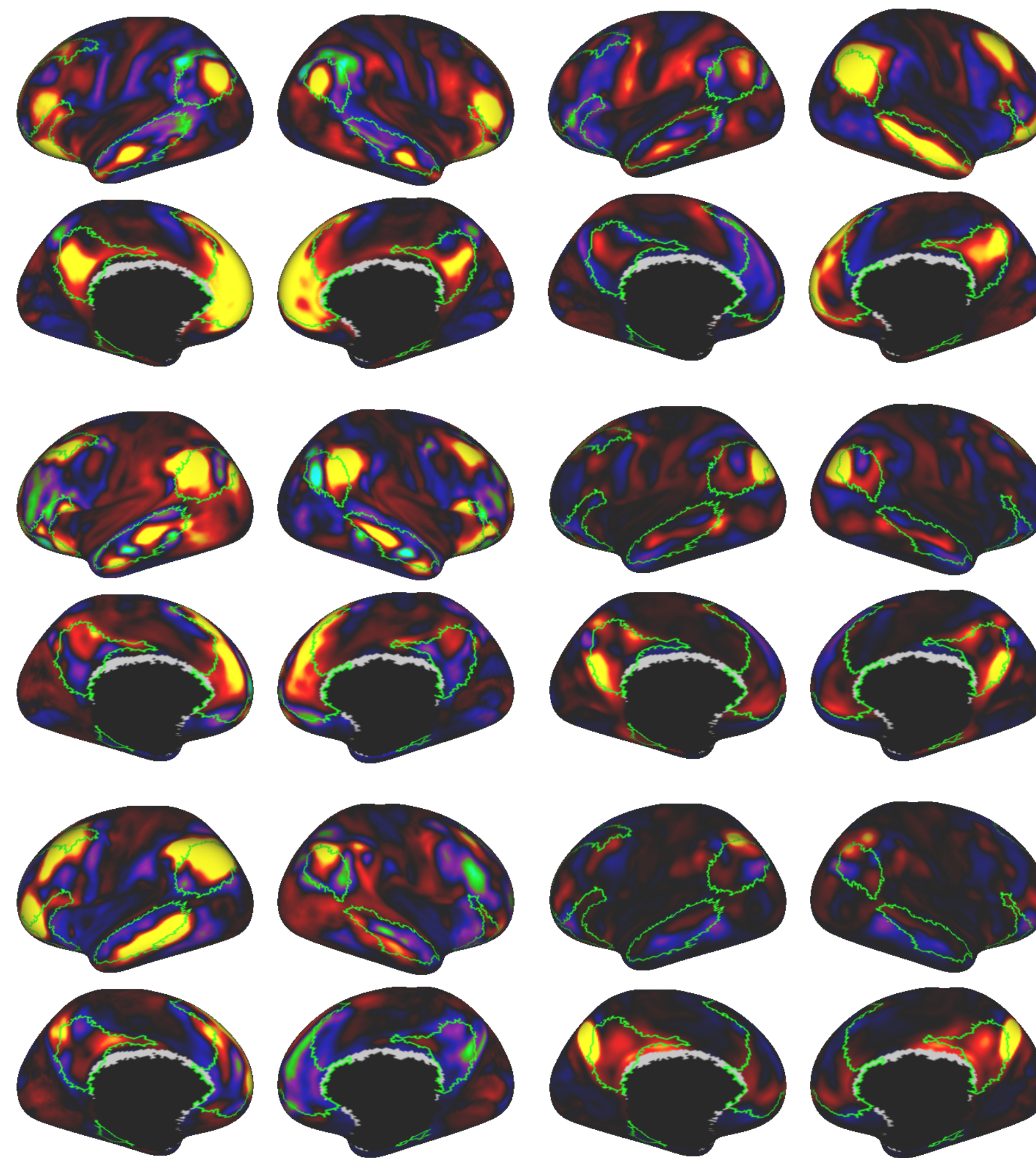
# Seed-selection bias

Seed-based correlation results are strongly influenced by small changes in seed location



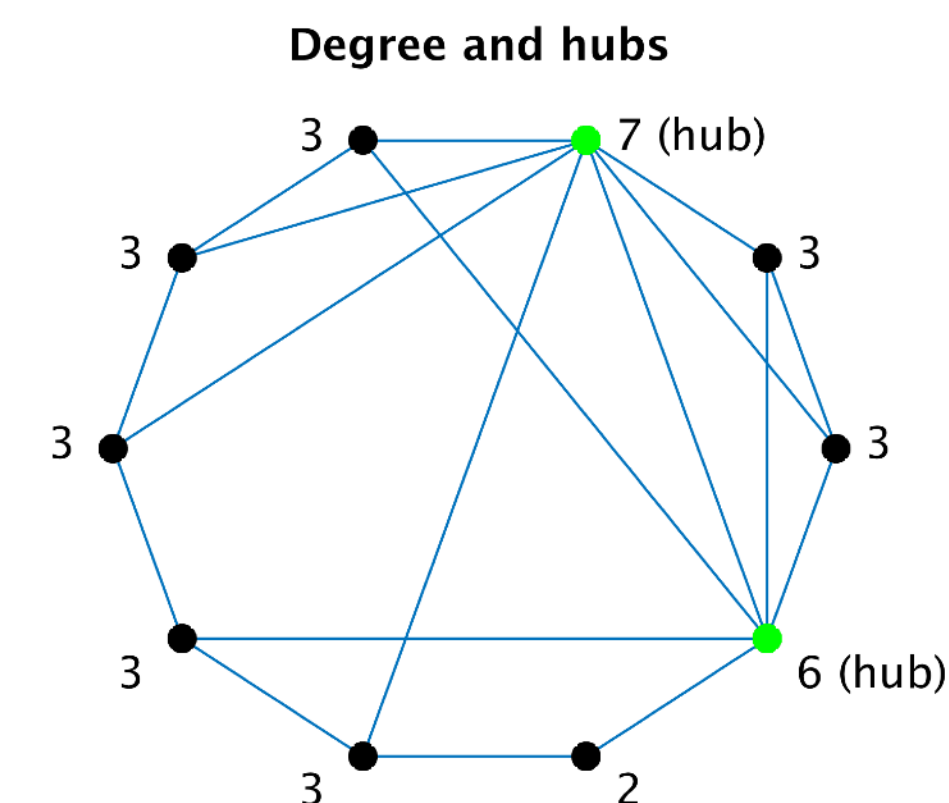
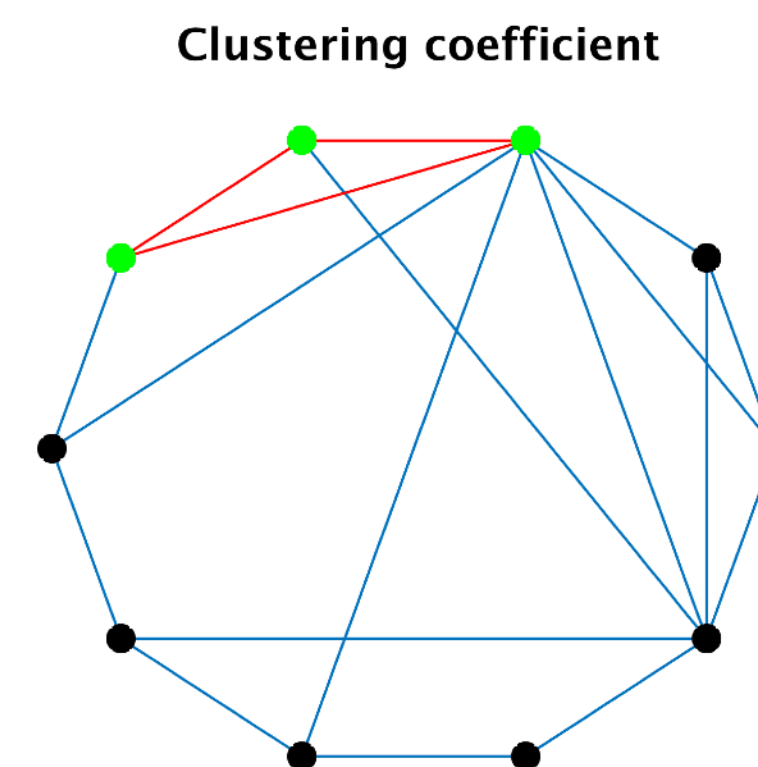
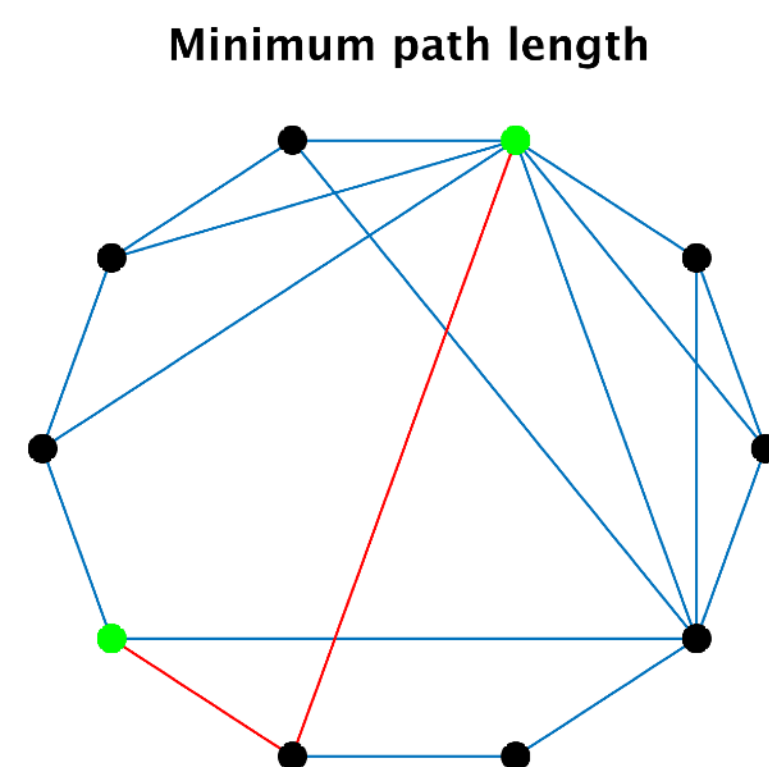
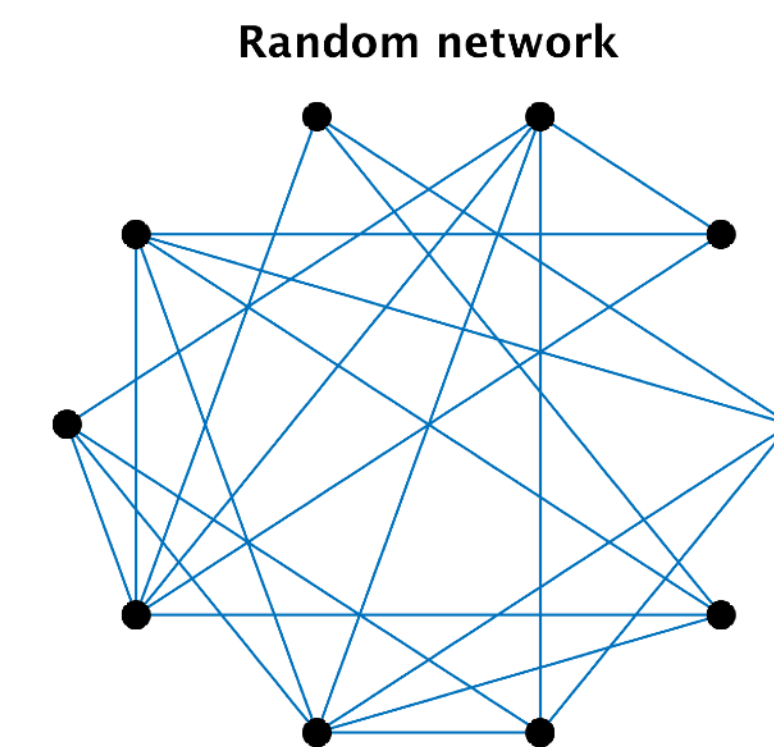
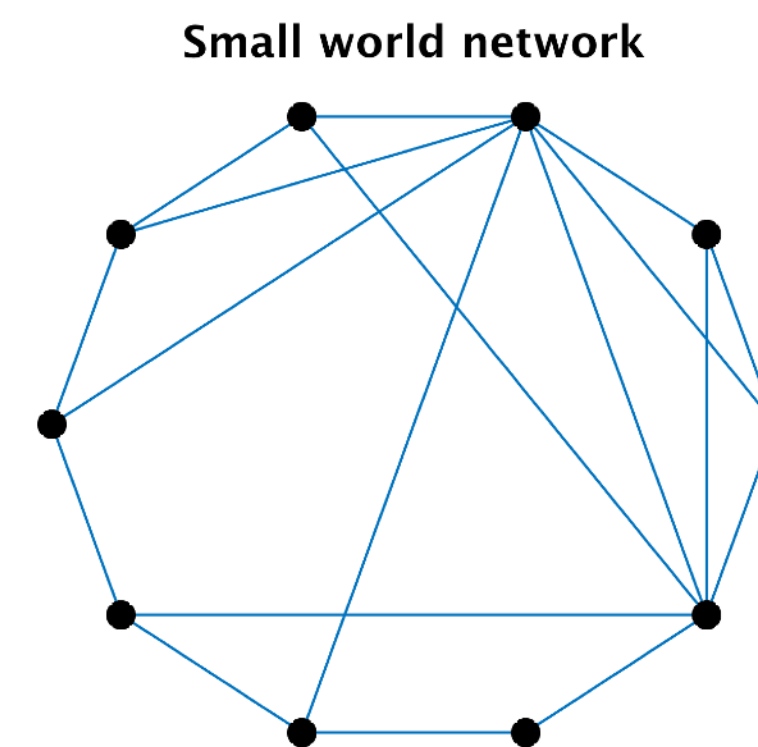
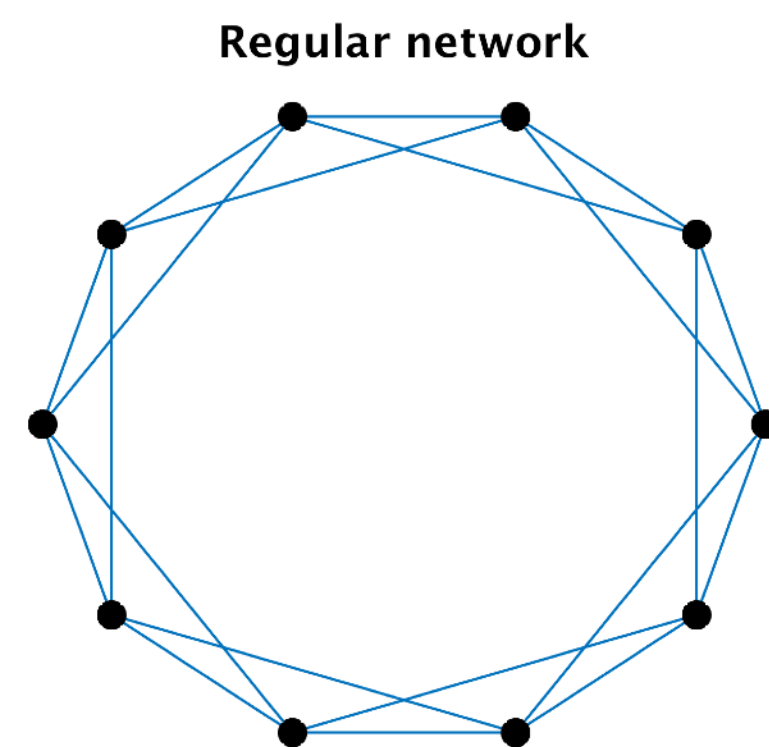
# ICA

- Multivariate: decompose full dataset
- Test for shape & amplitude
- Can be hard to interpret
- No control over decomposition (may not get breakdown you want)



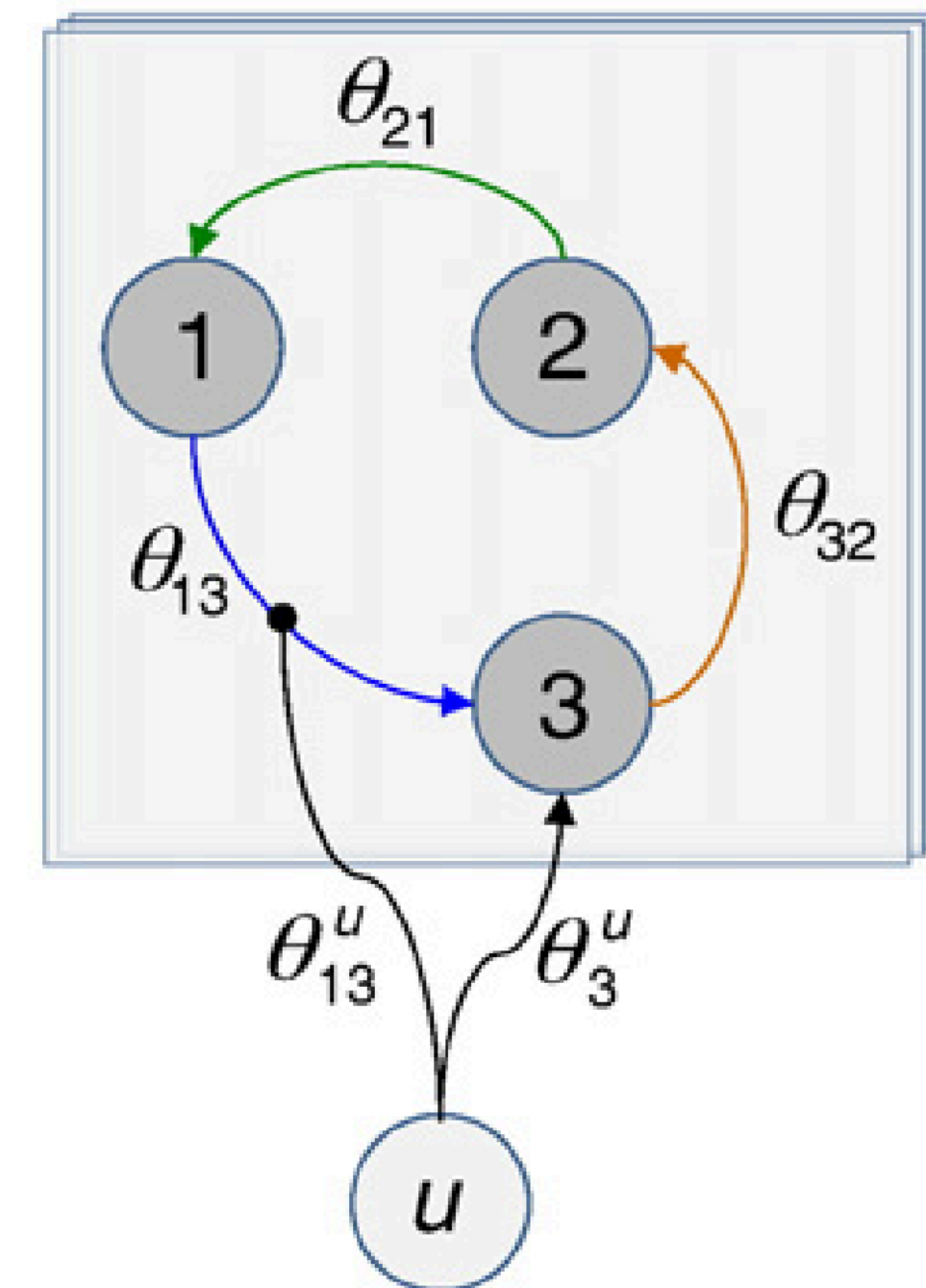
# Graph theory

- Simple summary measures (derived from network matrix)
- Network matrix often binarised
- Difficult to meaningfully interpret (abstract and far removed from data)



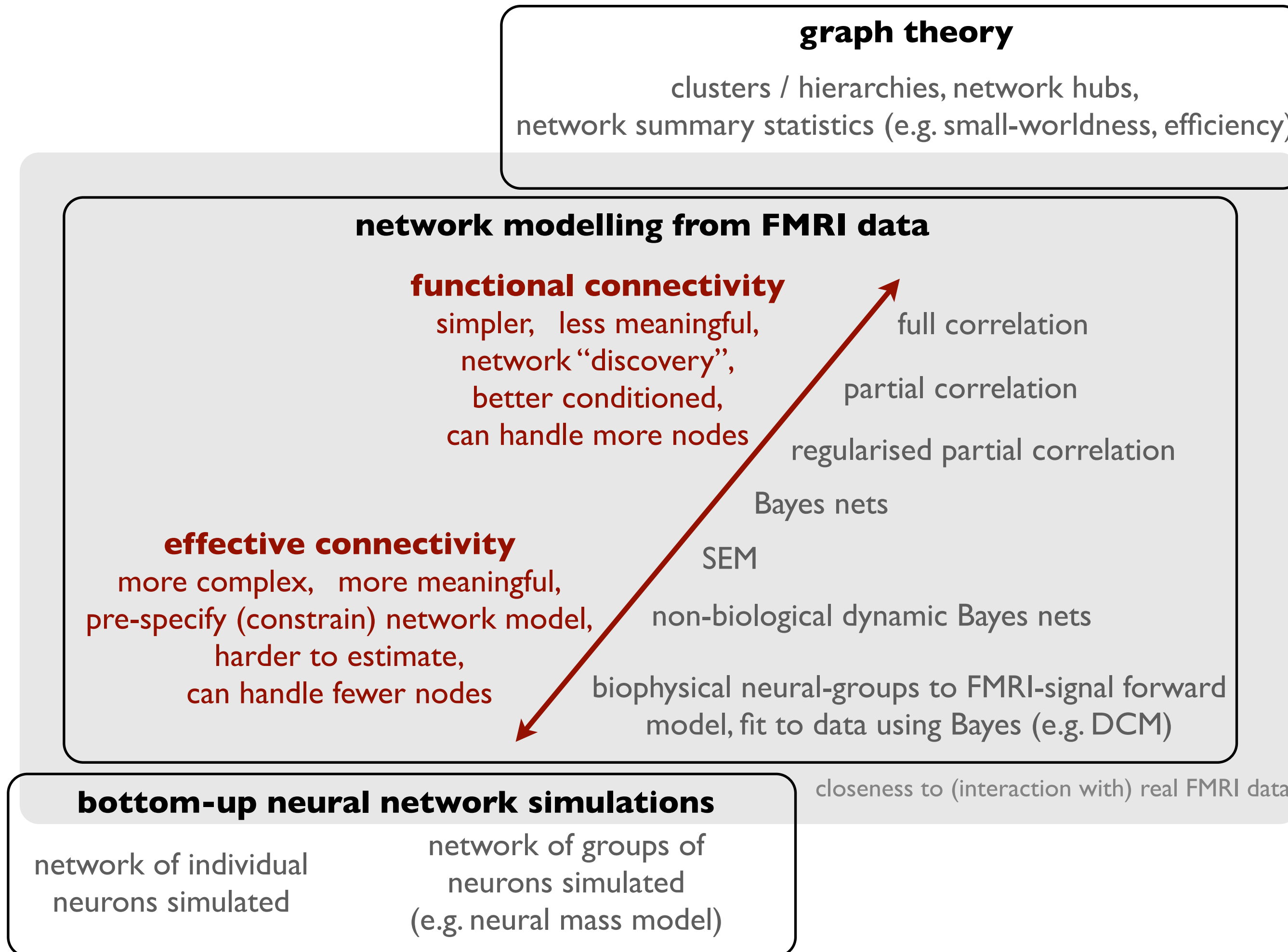
# Dynamic causal modelling

- Directional interpretation (effective connectivity)
- Biophysical model
- Assumes HRF homogeneity
- Limited model comparisons

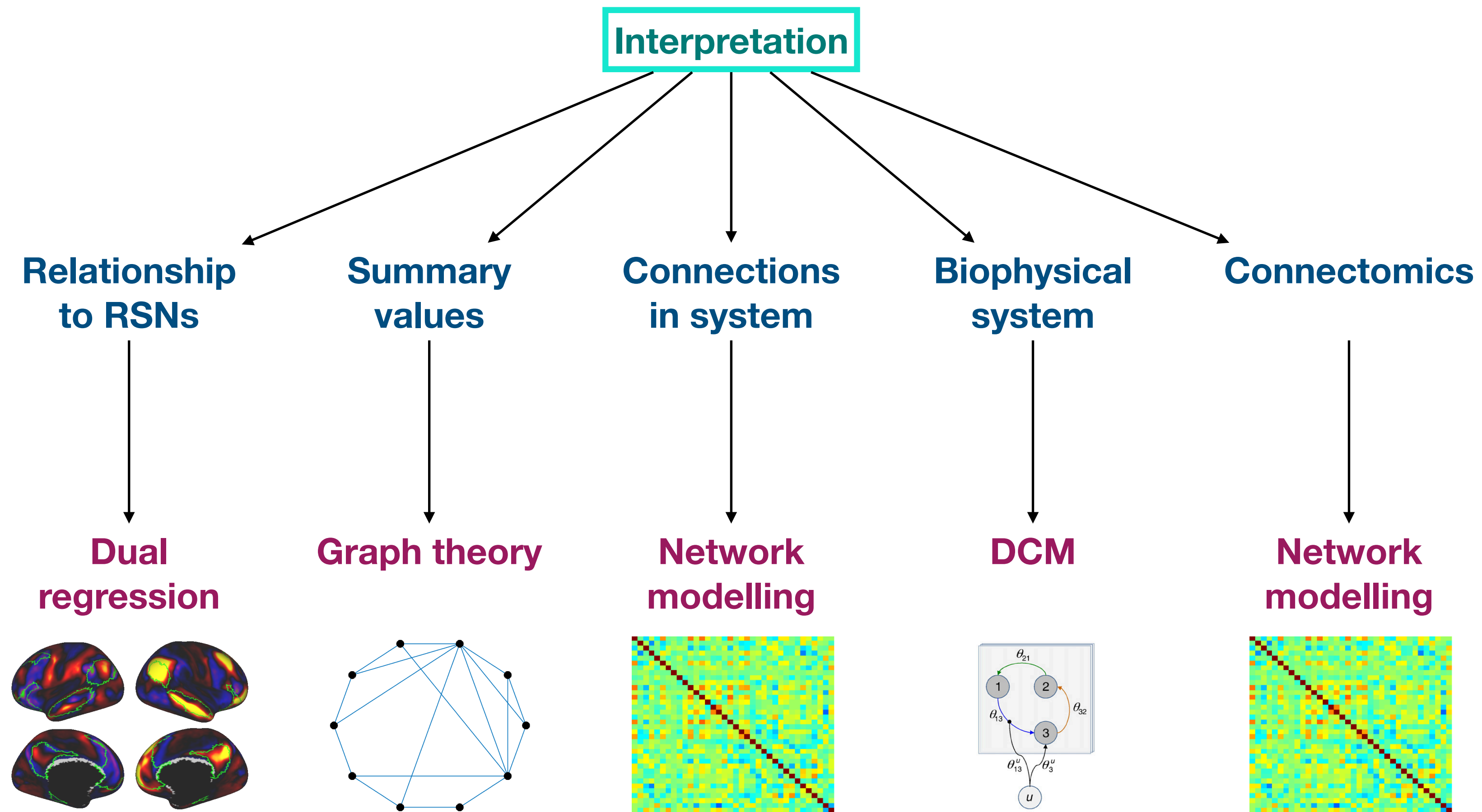




# Overview of node-based methods



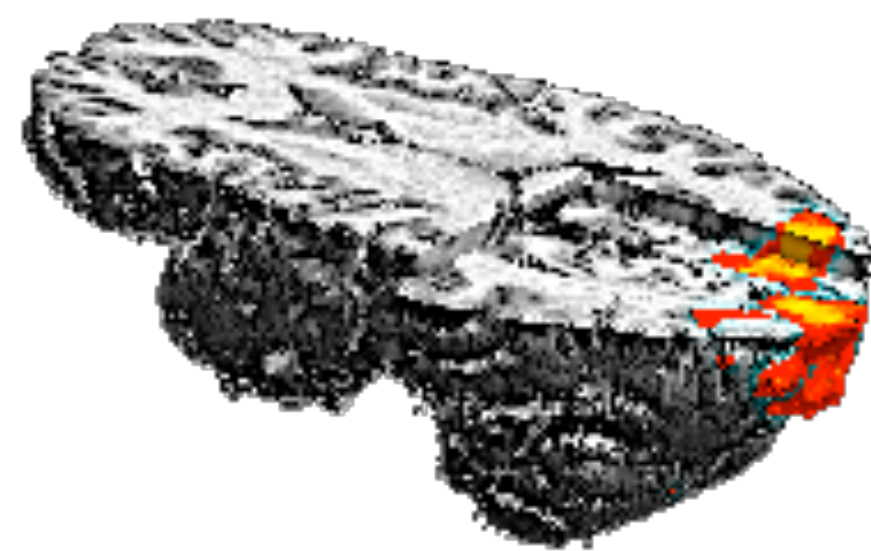
# Which method to choose?



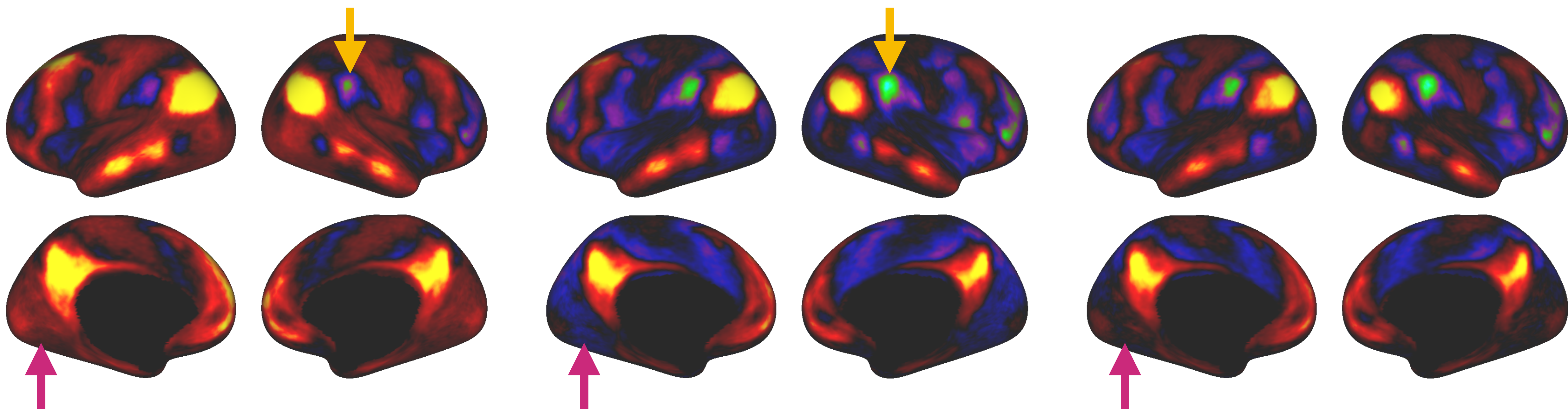


**Thank you!**

That's all folks



# GSR effects & alternative



PCC correlation  
spatial ICA cleanup

PCC correlation  
spatial ICA cleanup + **GSR**

PCC correlation  
spatial ICA cleanup + **temporal ICA cleanup**

# Even more choices...

- How to define the nodes?
  - Schaefer, Glasser, Gordon, Power, [...]
  - Data driven, task localizer, [...]
- How many nodes?
  - 10, 100, 1000, [...]
  - Combining bilateral, combining modules, [...]
- How to calculate the edges?
  - Pearson, partial correlation, covariance, [...]
  - Regularization, tangent projection, [...]
- How to relate edges to question of interest?
  - Mass univariate, prediction, normative modeling, [...]
  - Multiple comparison correction, network statistics, [...]

