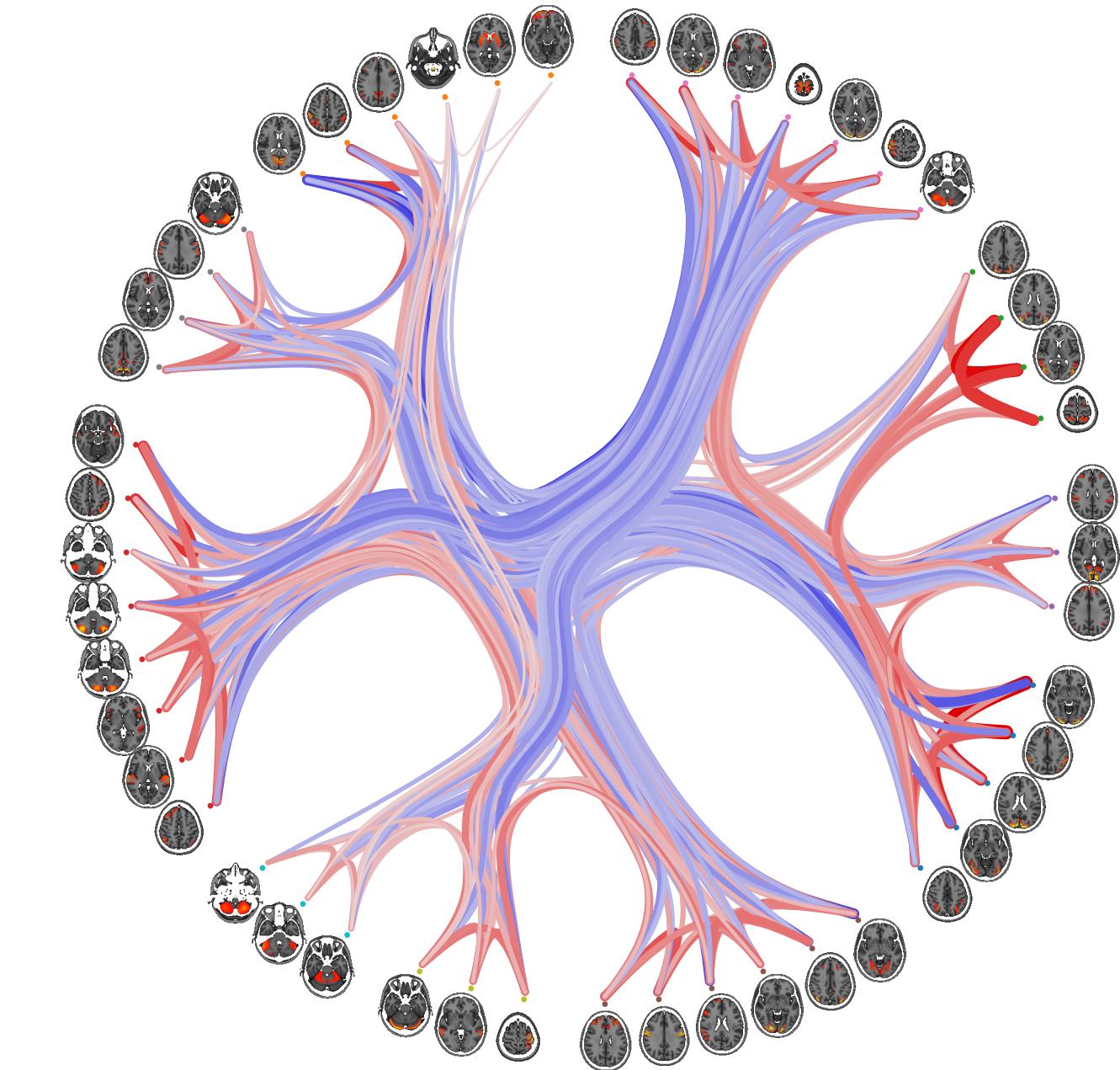
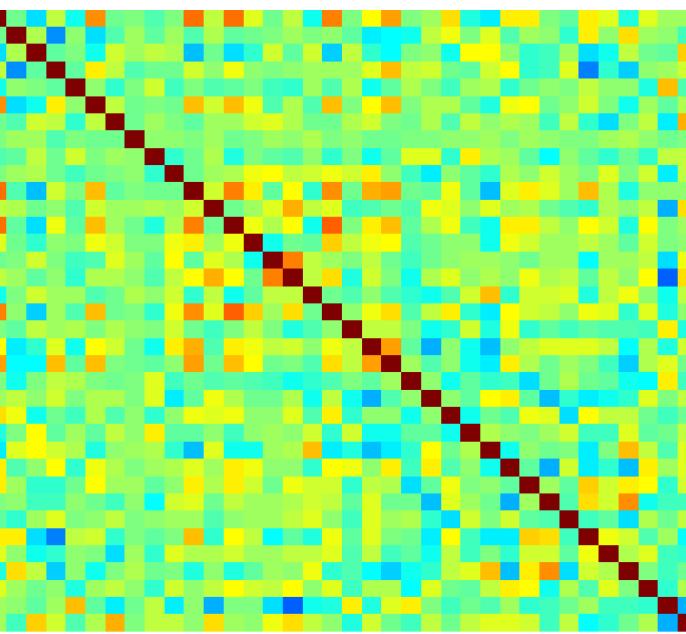


# Network modelling analysis

## 脑网络分析

- Resting state data characteristics 静息态数据特征
- Preprocessing 预处理
- Network modelling analysis 网络建模
- Methods comparisons and considerations 方法比较和注意事项

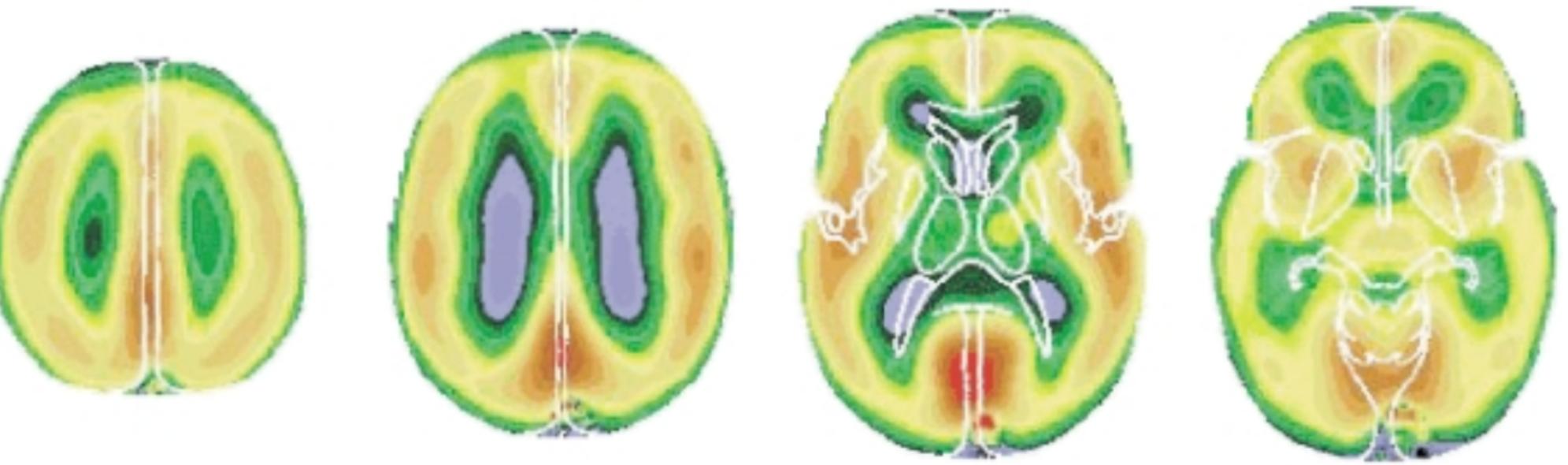


# Energy consumption in the brain

## 大脑的能量消耗

- Brain < 2% body weight but consumes ~20% of total energy  
大脑重量约占身体的<2%,但却消耗约20%的总能量
- estimated 60-80% of this energy used to support communication between cells  
约60-80%的能量用于细胞间的交流
- task-evoked activity accounts for ~1%  
任务诱发的脑活动约占1%

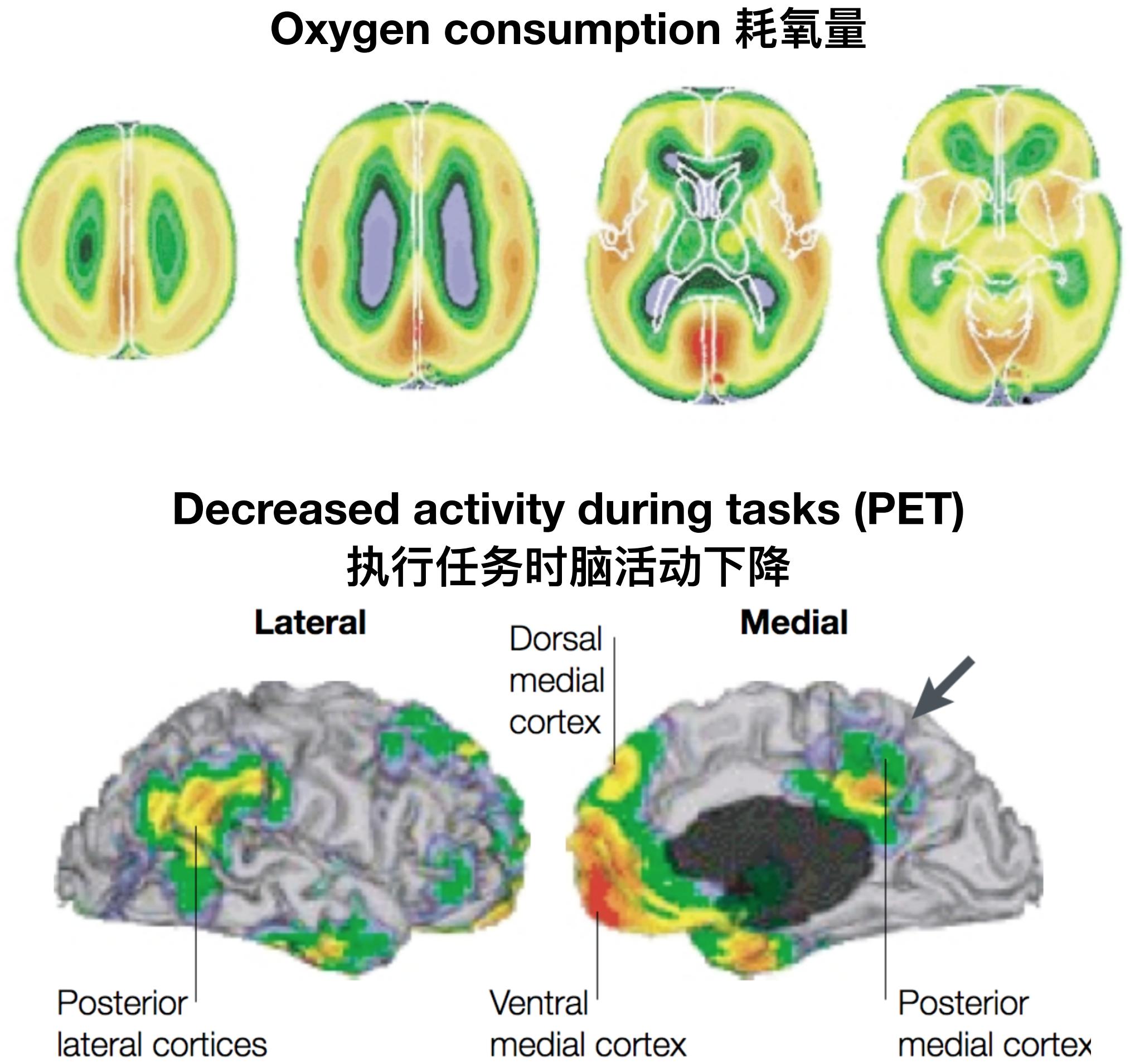
Oxygen consumption 耗氧量



# Energy consumption in the brain

## 大脑的能量消耗

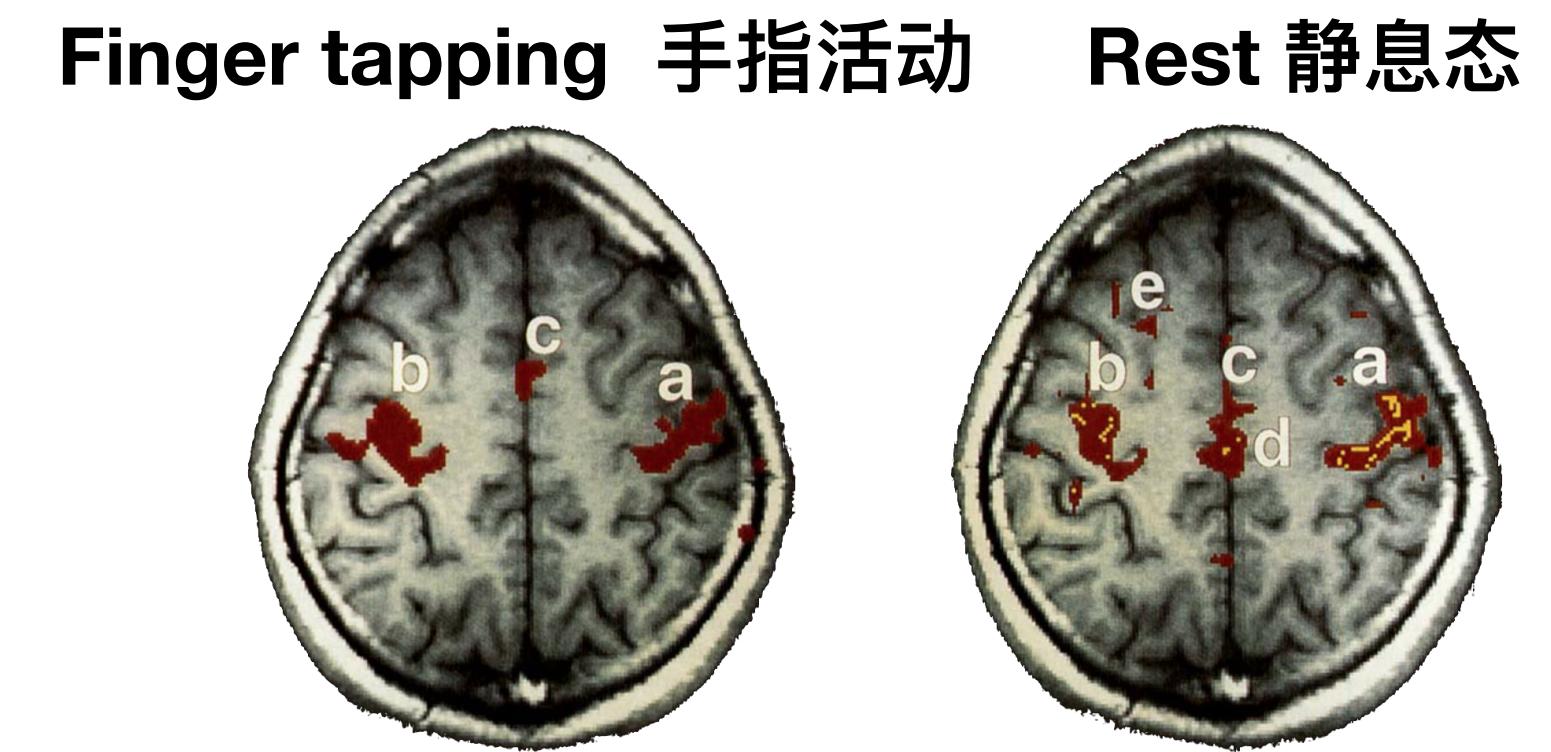
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# Why study the brain at rest?

为什么研究大脑的静息态

- Localisation versus connectivity 定位与连接
- Understand the inherent functional organisation of the brain 了解大脑固有的功能活动

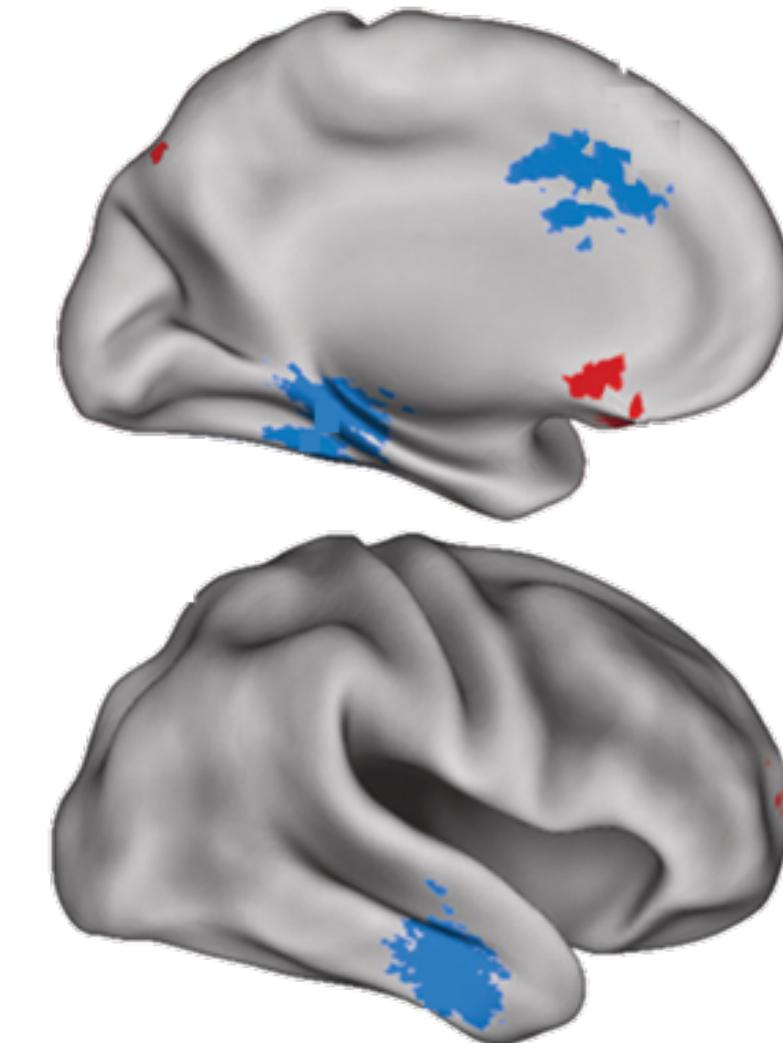
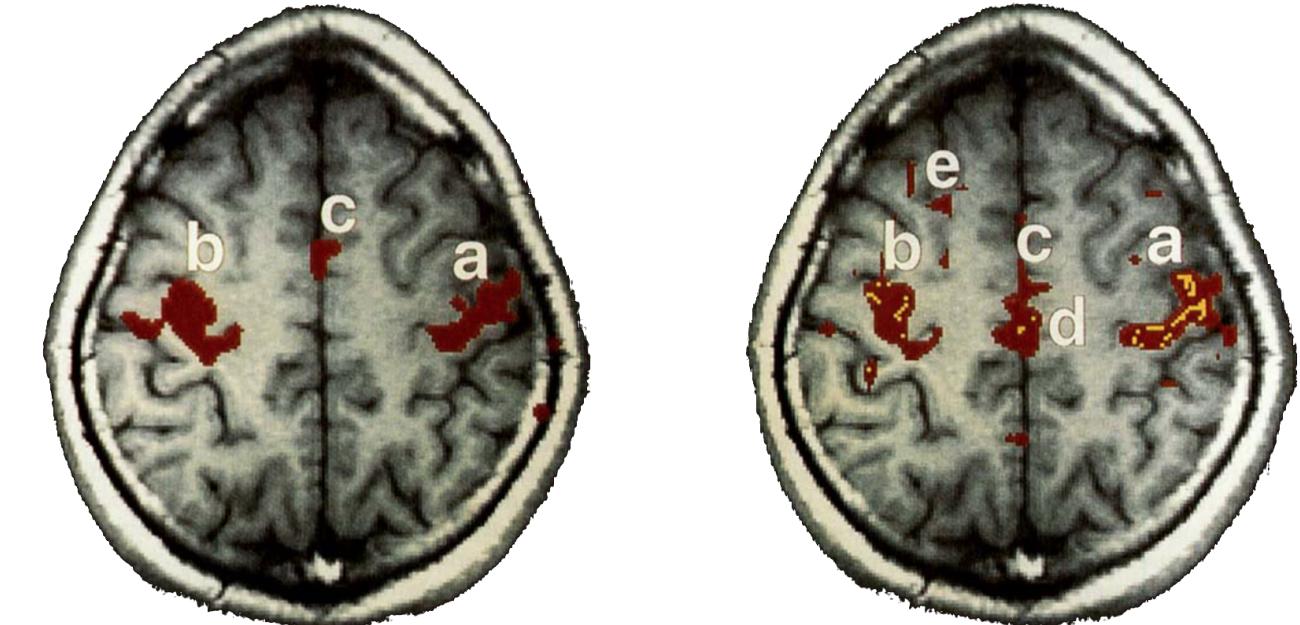


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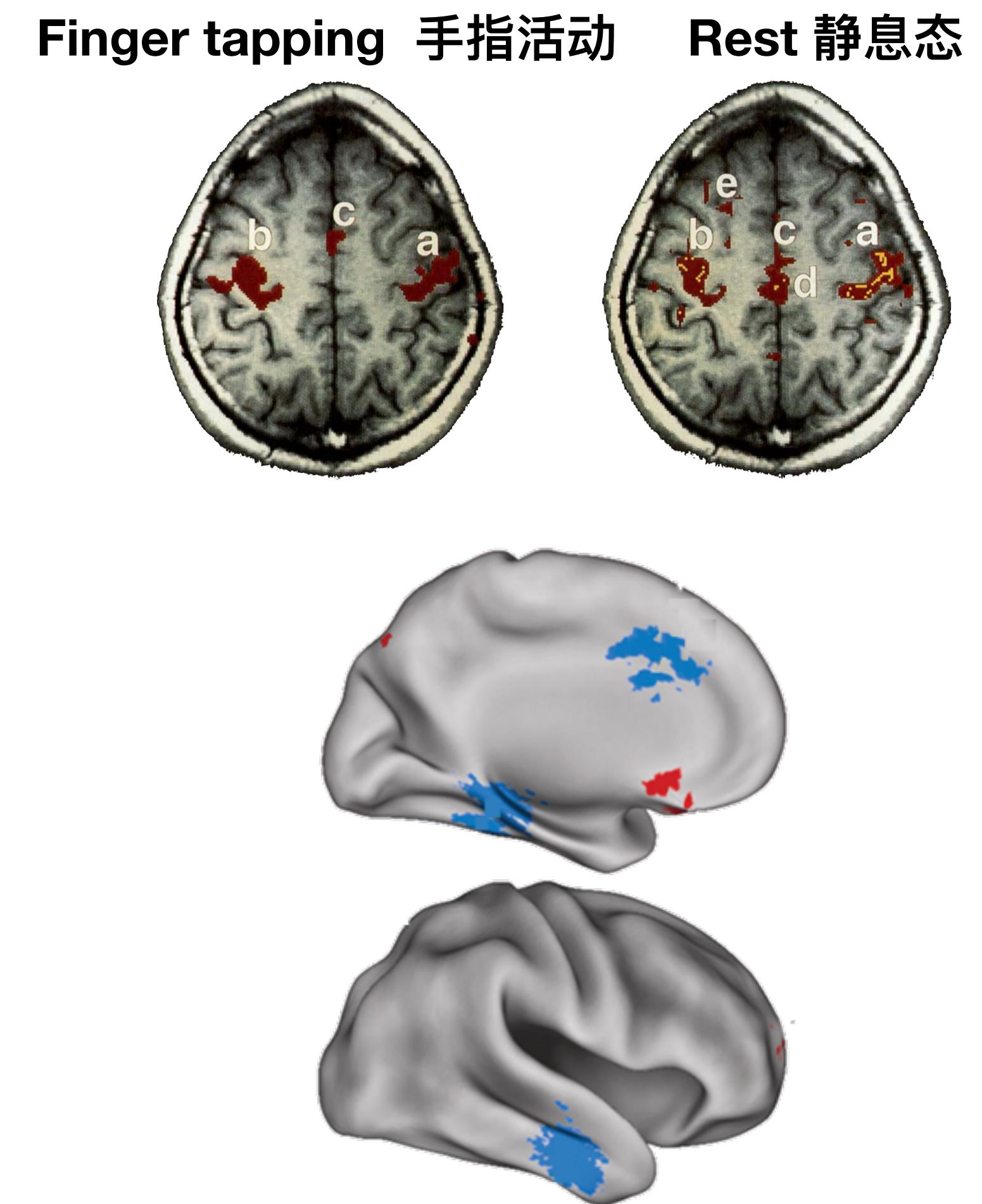
Finger tapping 手指活动 Rest 静息态



# Why study the brain at rest?

## 为什么研究大脑的静息态

- Localisation versus connectivity 定位与连接
- Understand the inherent functional organisation of the brain 了解大脑固有的功能活动
- Clinical/ cognitive biomarker 临床/认知标记
- Pragmatic benefits: can be done in any population, with relatively little setup and expertise required 实用的优点：可以在任何人群中完成，只需要相对较少的设置和专业知识





# Resting state data analysis

## 静息态数据分析

- Many different methods available for analysis  
可用许多不同的分析方法
- All have one assumption in common: 它们共同的假设:
- i.e. Definition of functional connectivity is based on a statistical dependency between time series  
功能连接的定义是基于时间序列之间的统计依赖性
- Differences between methods lie in the way these similarities are estimated and/or represented  
方法之间的差异在于估计和/或表示这些相似性的方式

If two brain regions show similarities in their **BOLD** timeseries, they are functionally connected

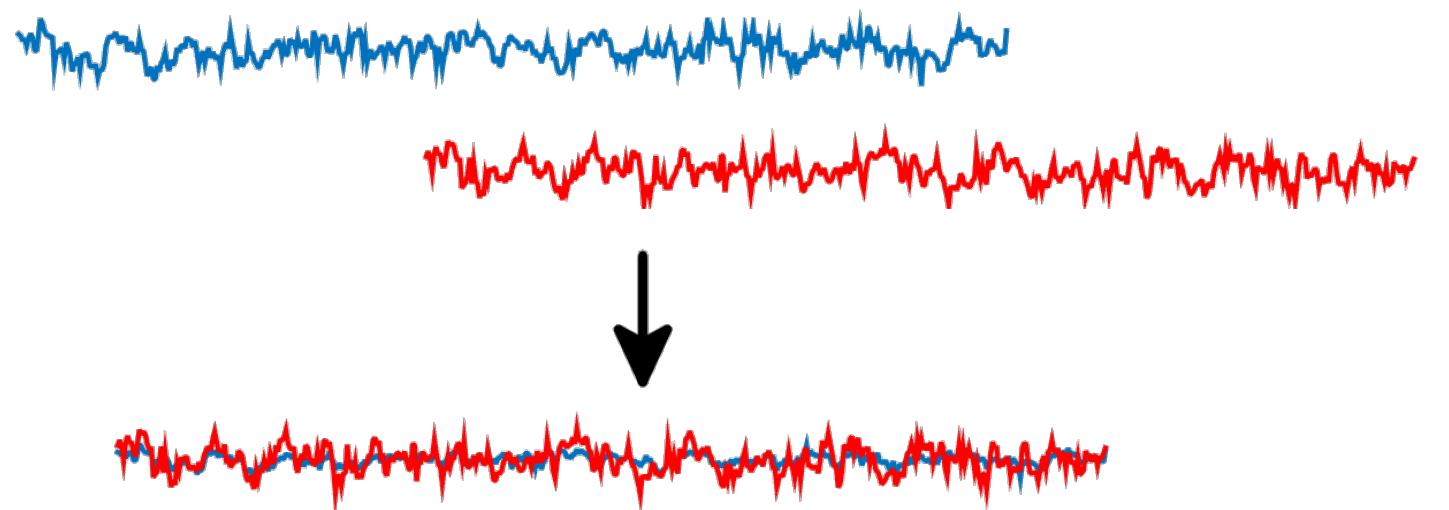
如果两个大脑区域在其**BOLD**时间序列中显示出相似性，则它们在功能上是相互关联的



# Types of connectivity

## 连接的类型

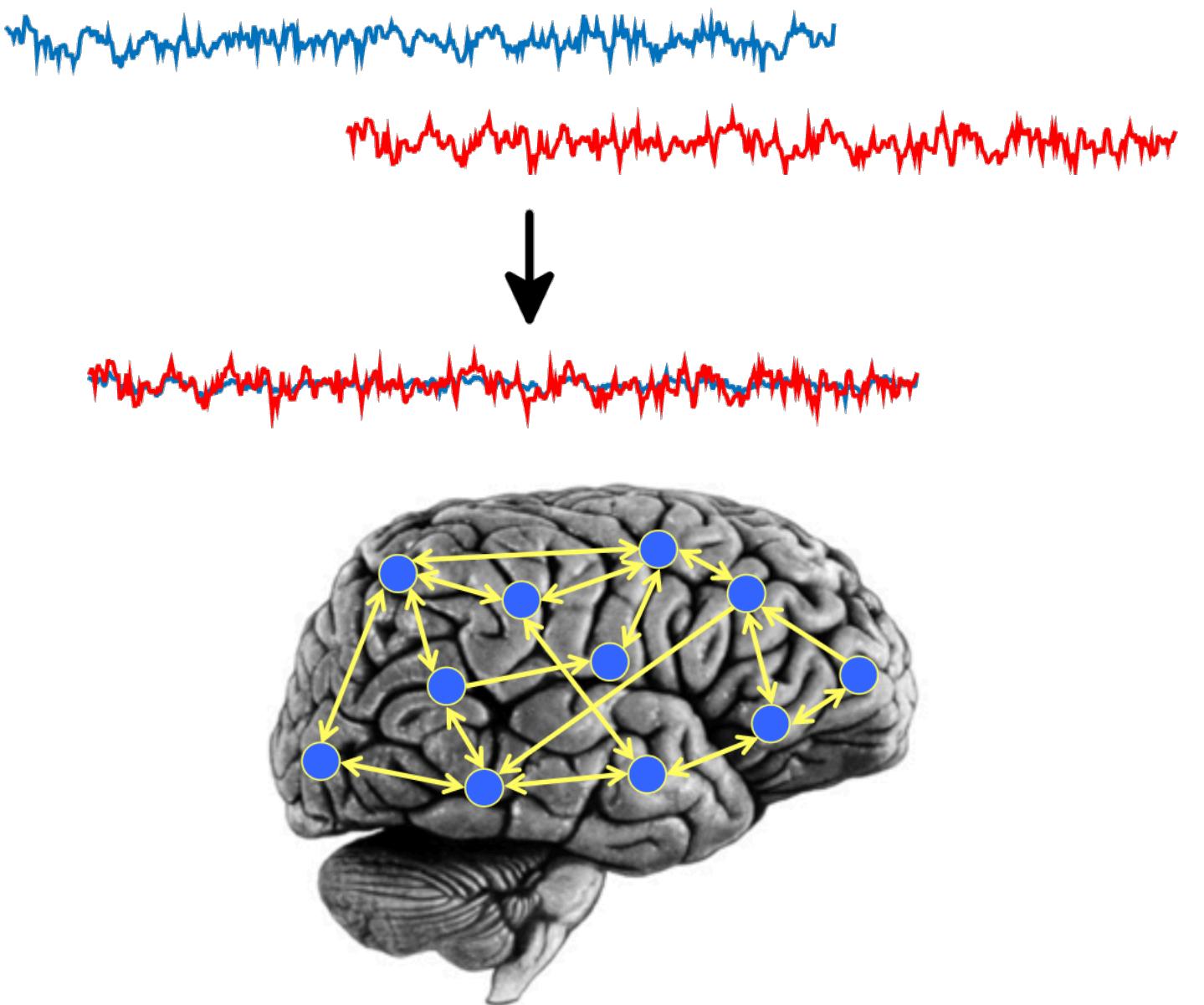
- Functional connectivity 功能连接
  - Statistical dependency 统计依赖性
- Effective connectivity 有效连接
  - Directional influence 方向的影响
- Anatomical (structural) connectivity 结构连接
  - Presence of a white matter tract 白质纤维束



# Types of connectivity

## 连接的类型

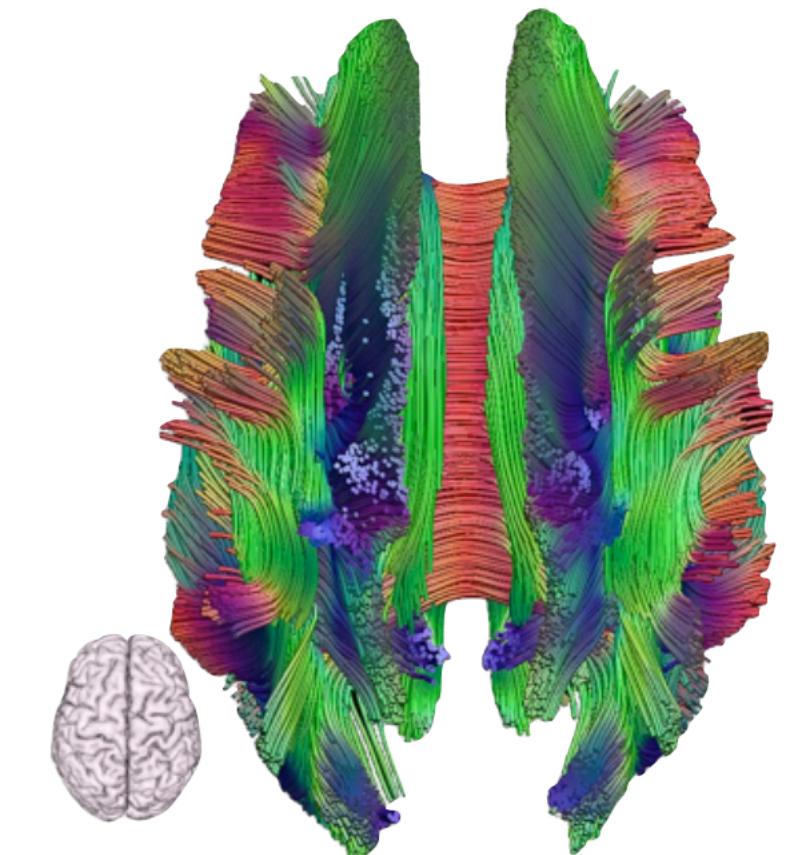
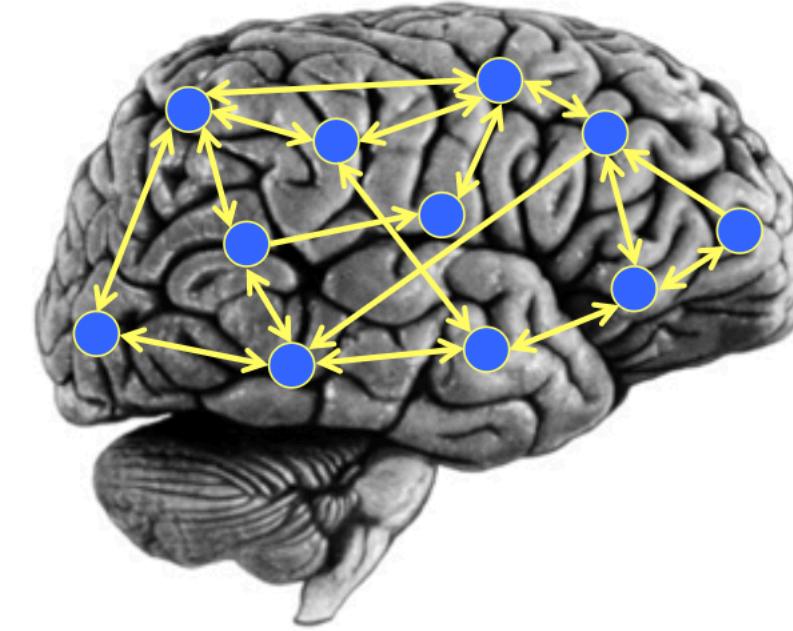
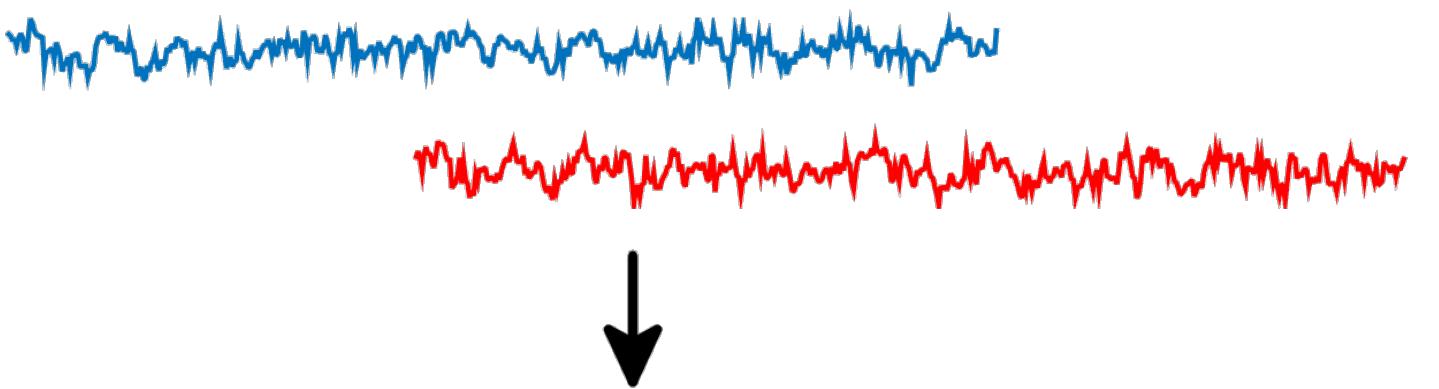
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# Data characteristics

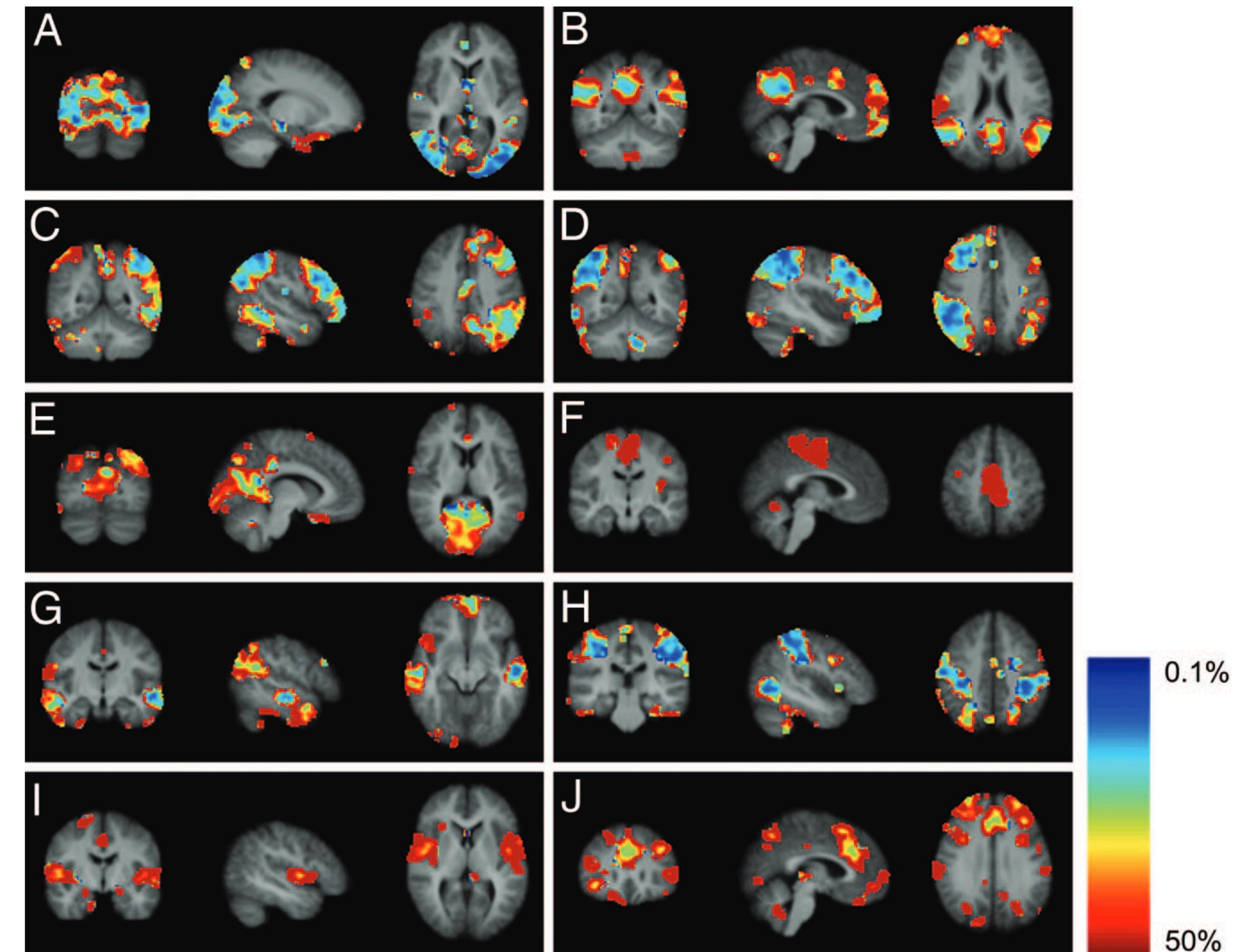
# 数据特征

# Replicable networks

可重复的网络

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

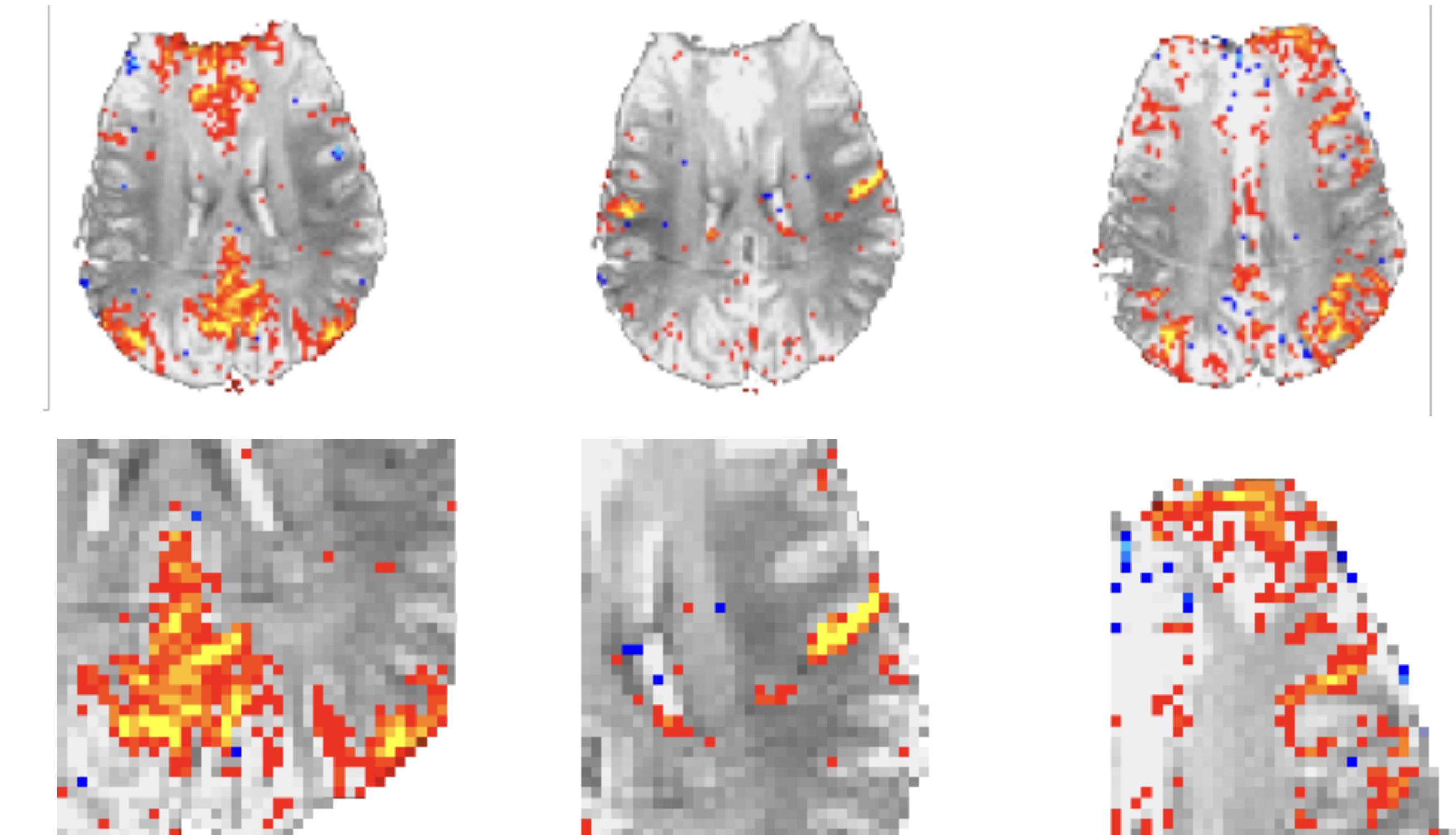
多种研究和方法可重复地发现脑内存在大规模的固有组织



# Grey matter networks

灰质网络

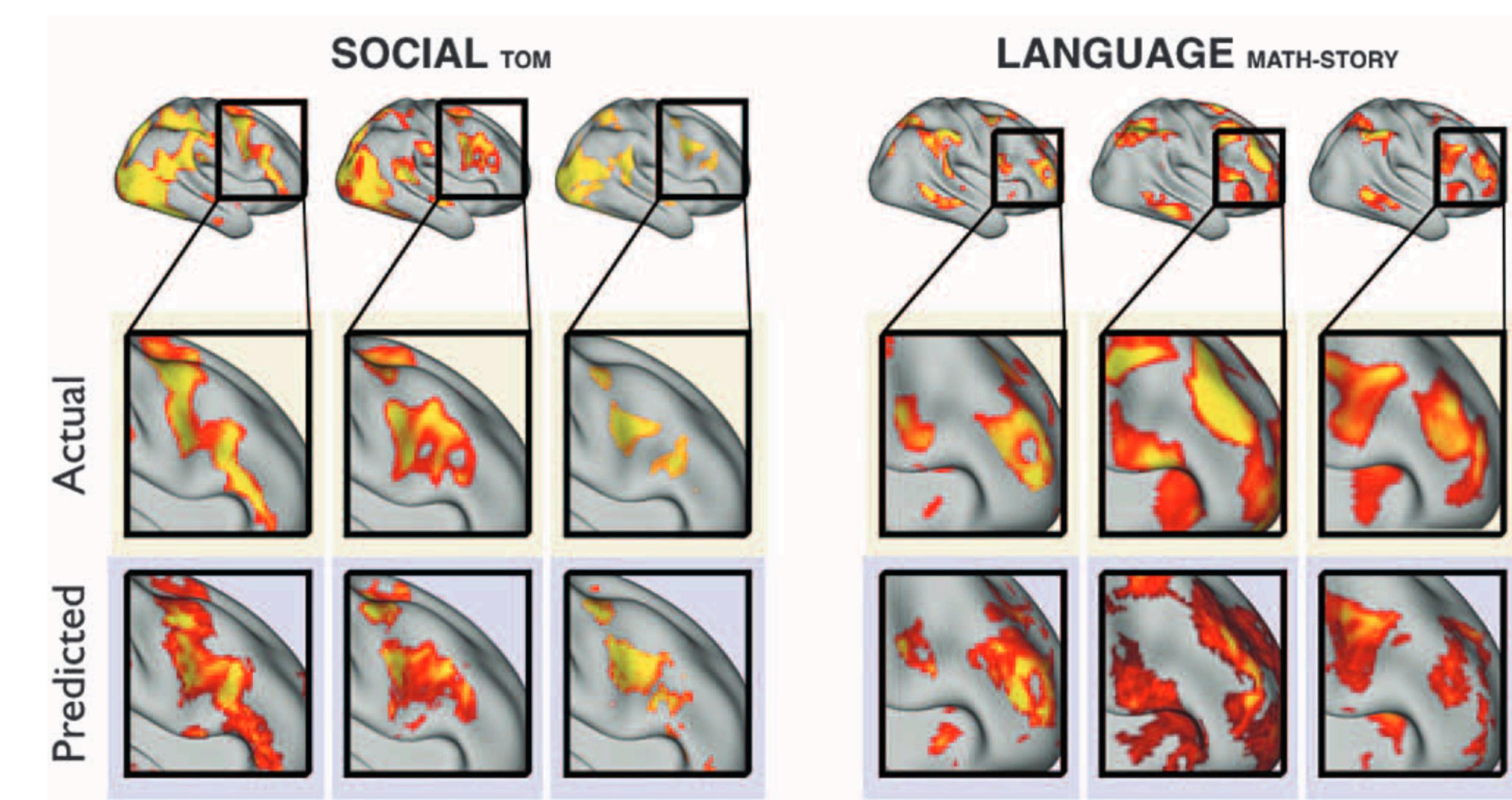
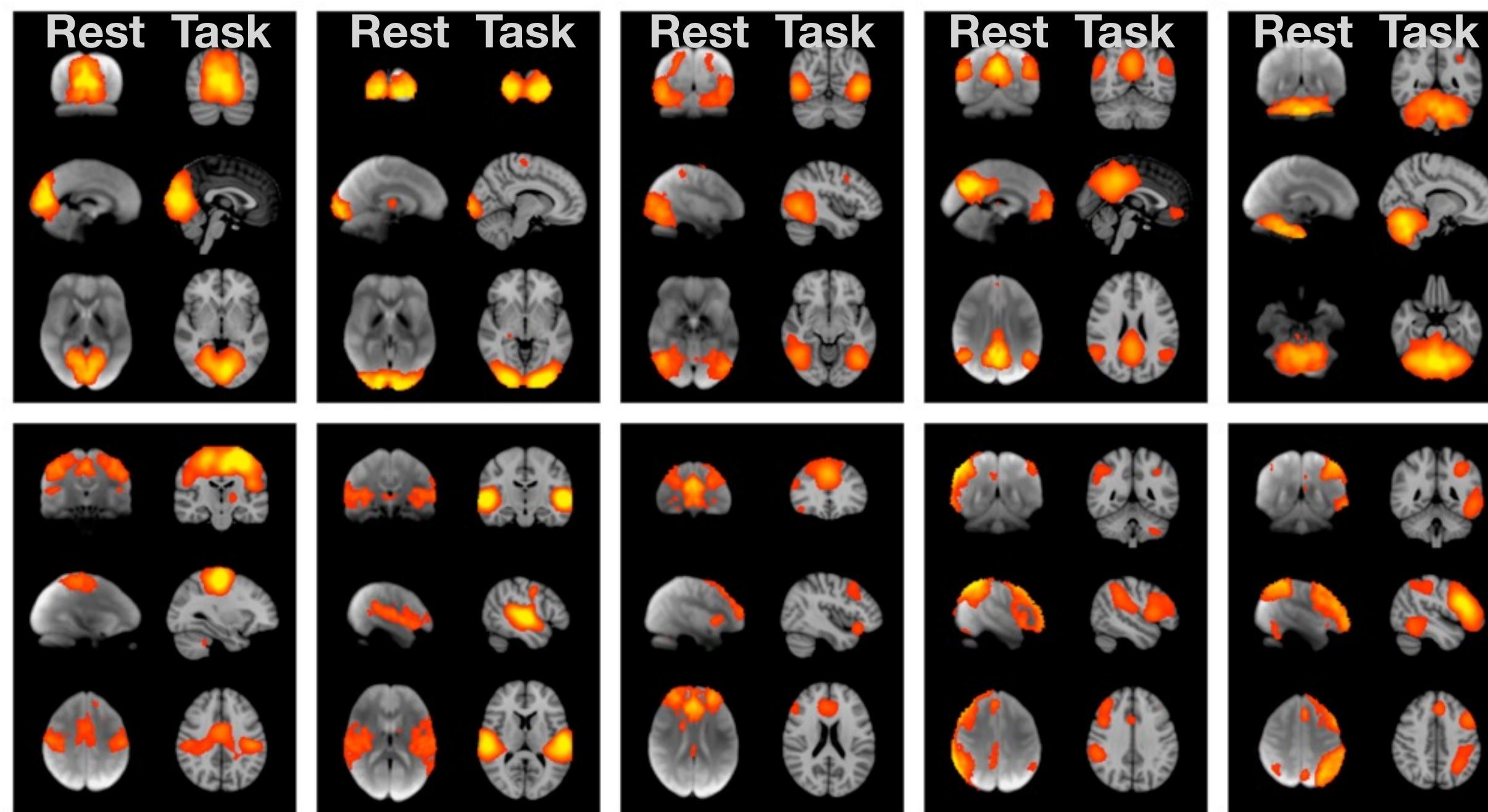
Resting state network structure  
is localised in grey matter  
静息态网络结构位于灰质内



# Relationship to task 与任务的关系

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

静息态网络类似于组和单个被试的任务激活模式

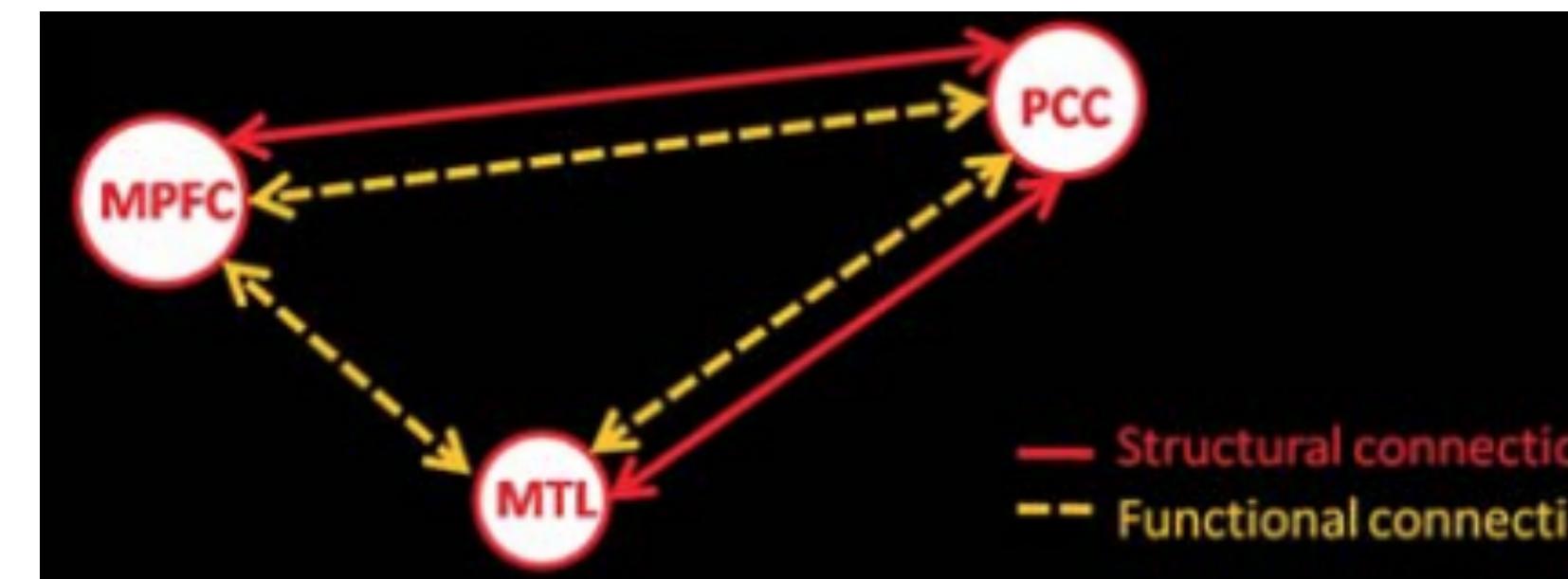


# Functional vs structural connectivity

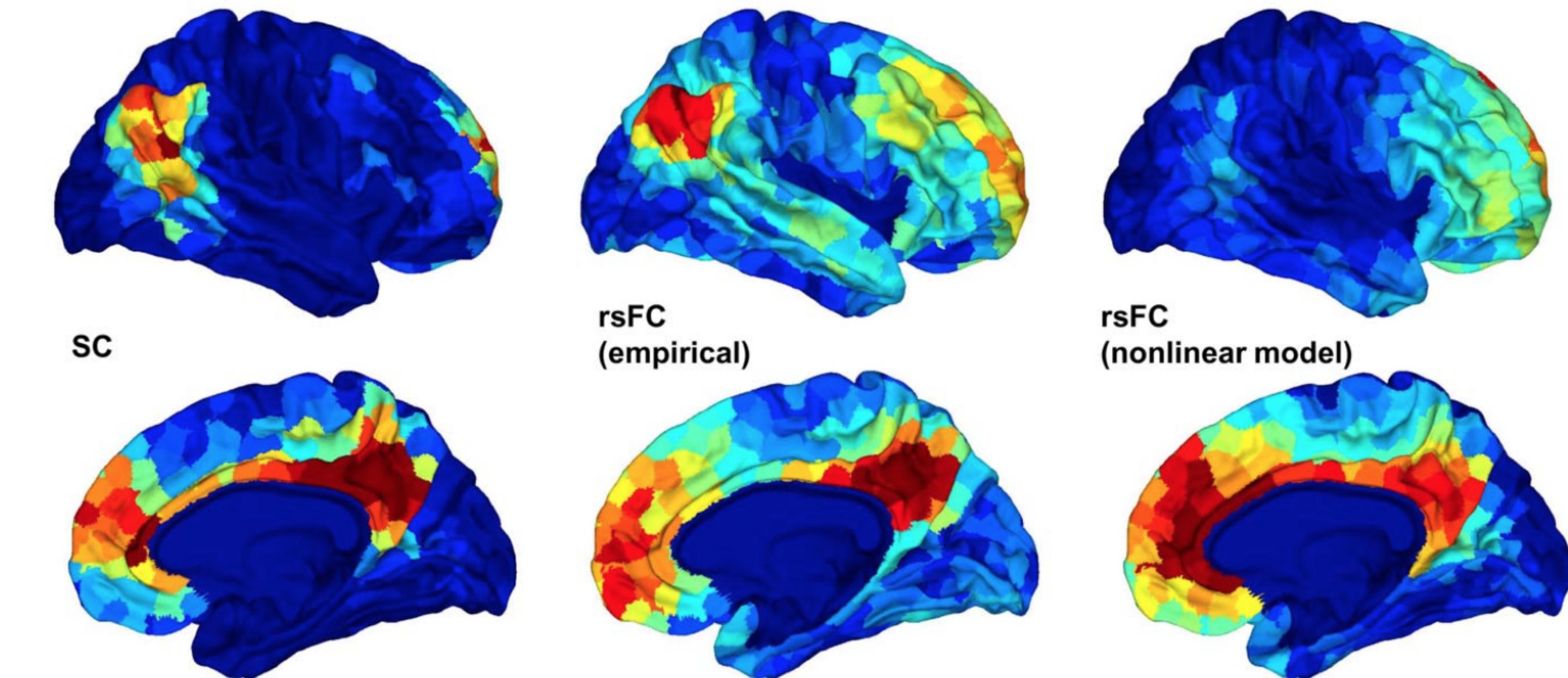
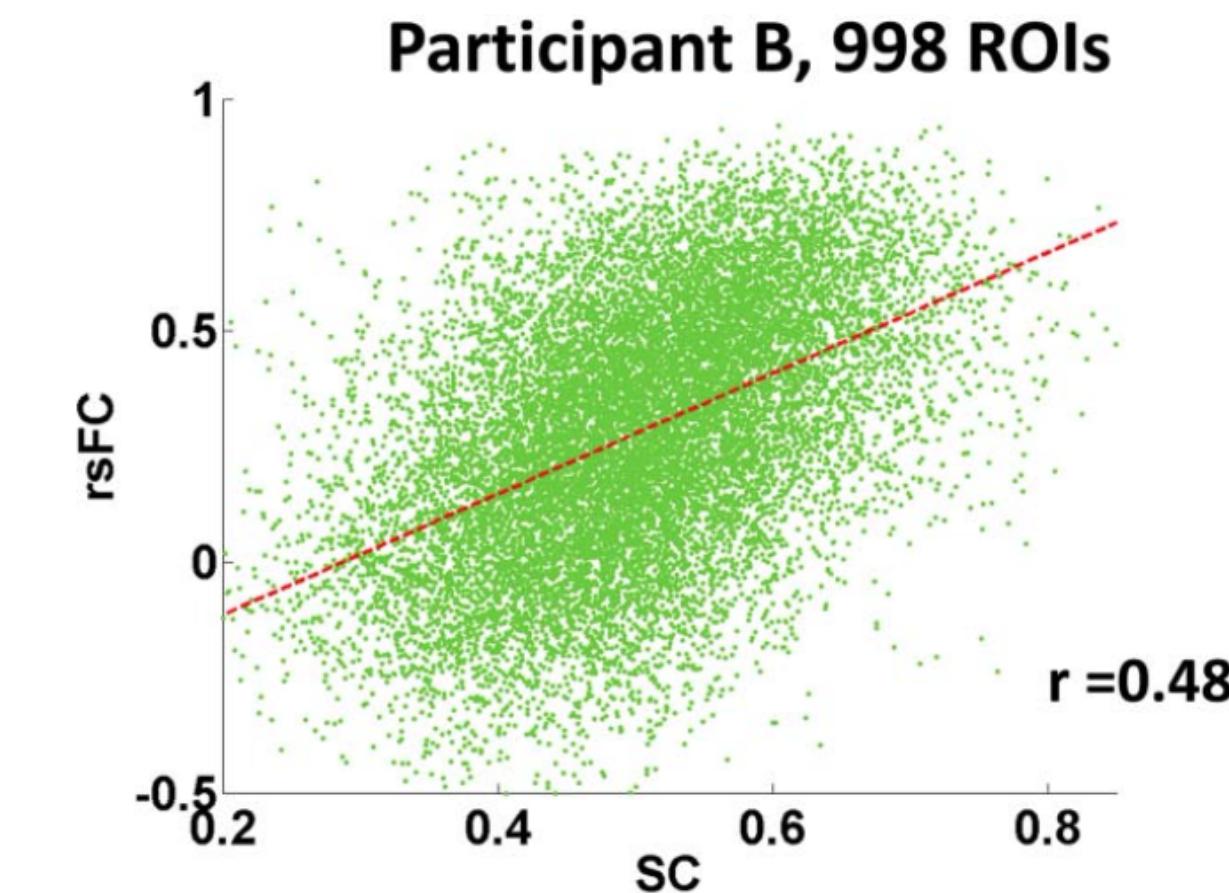
## 功能和结构连接

Functional connectivity is related to structural connectivity

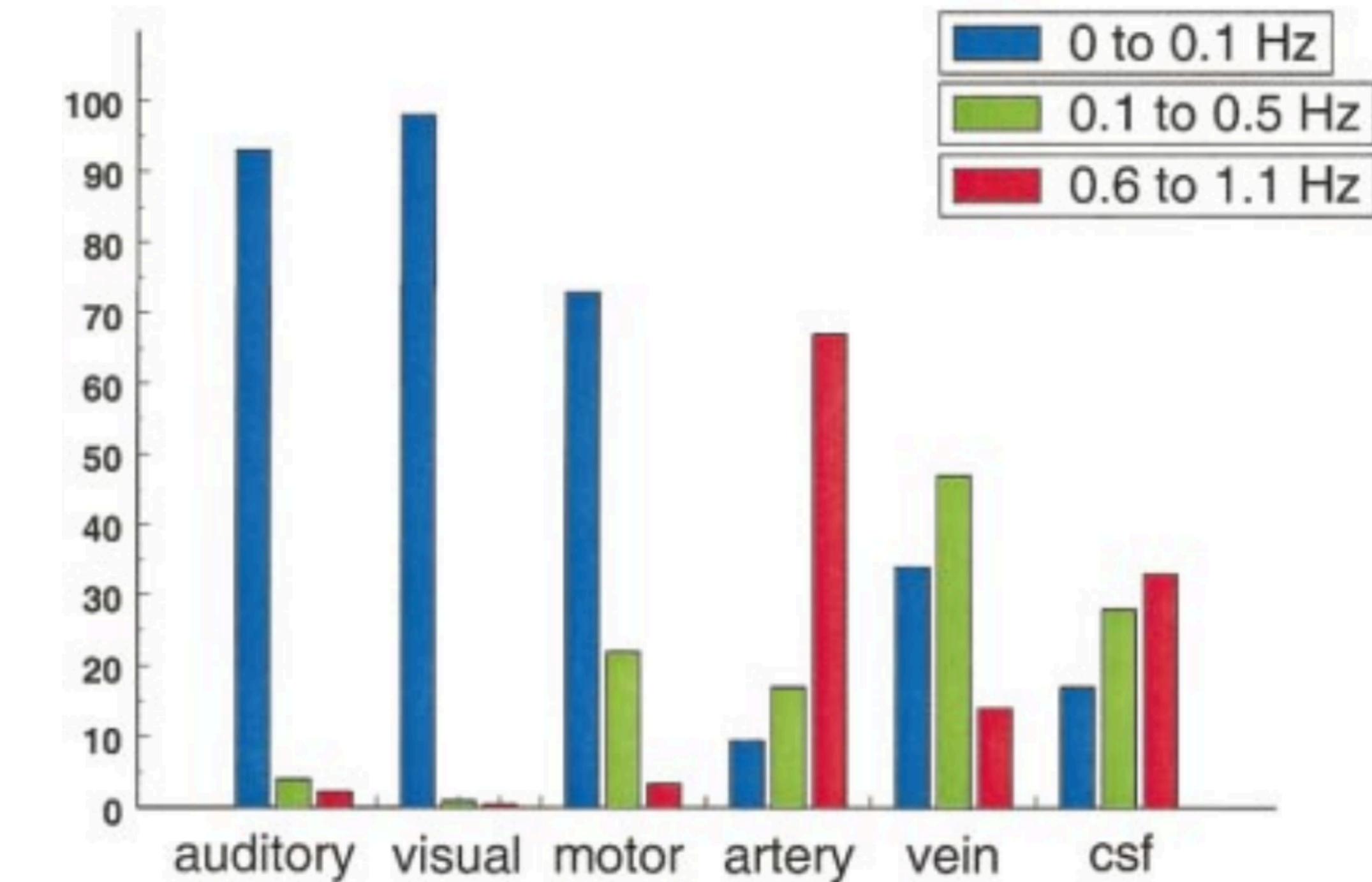
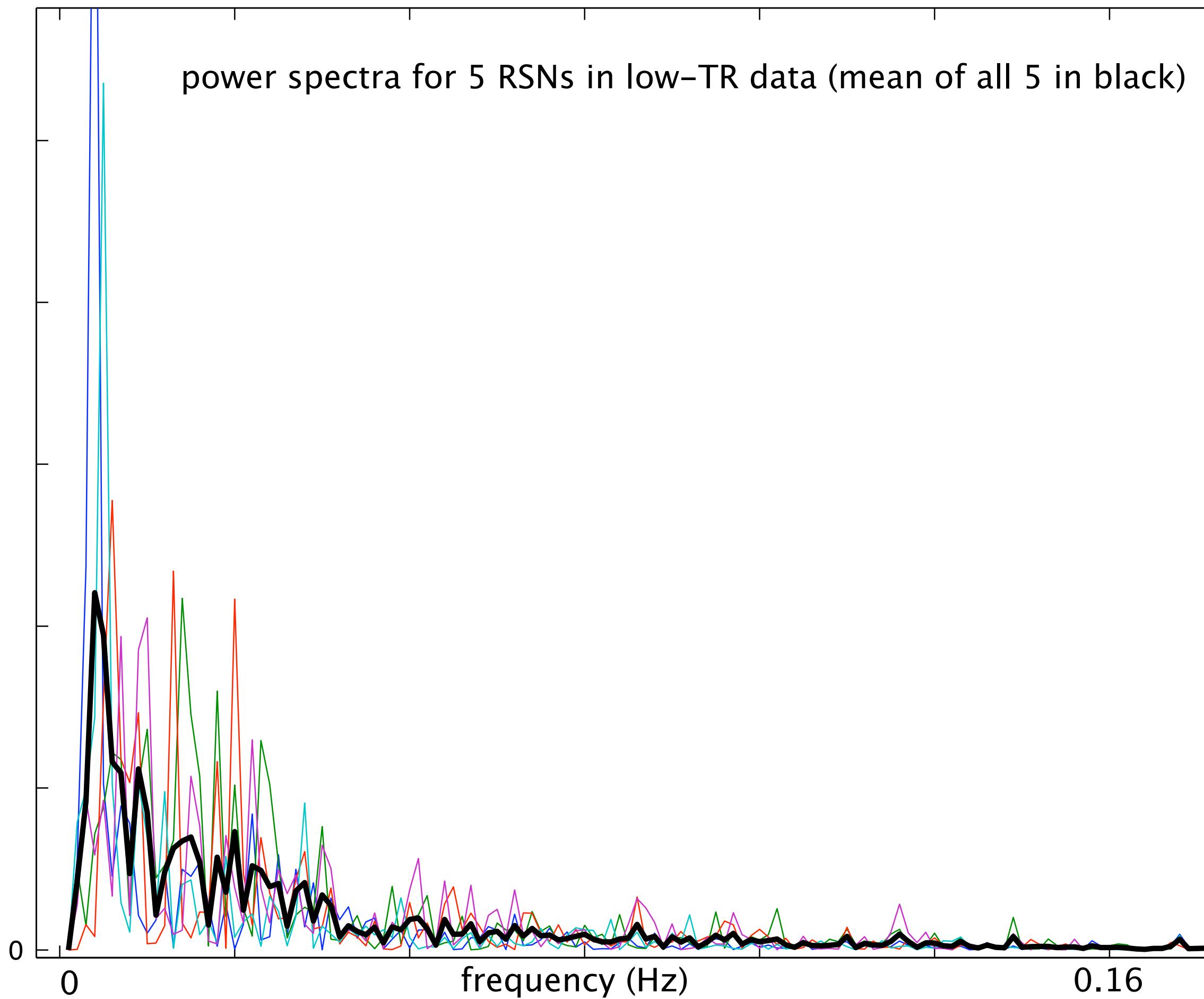
功能连接与结构连接有关



Honey et al (2009), Damoiseaux & Greicius (2009)



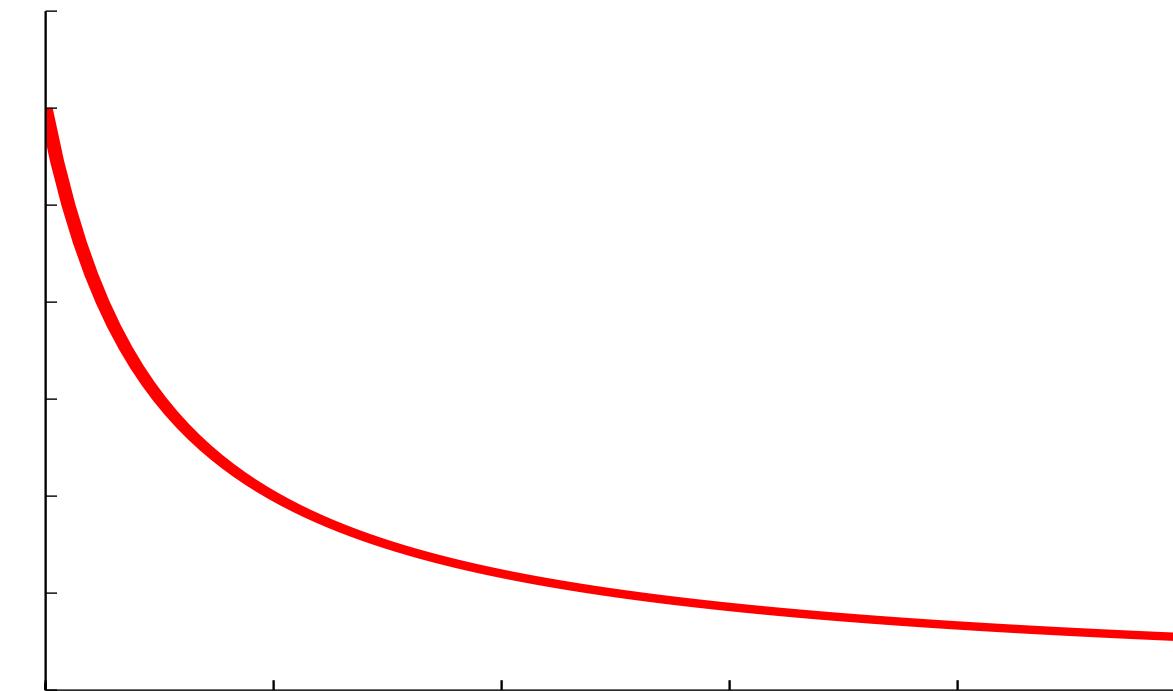
# Low frequency fluctuations? 低频波动振幅?



# Low frequency fluctuations? 低频波动振幅?

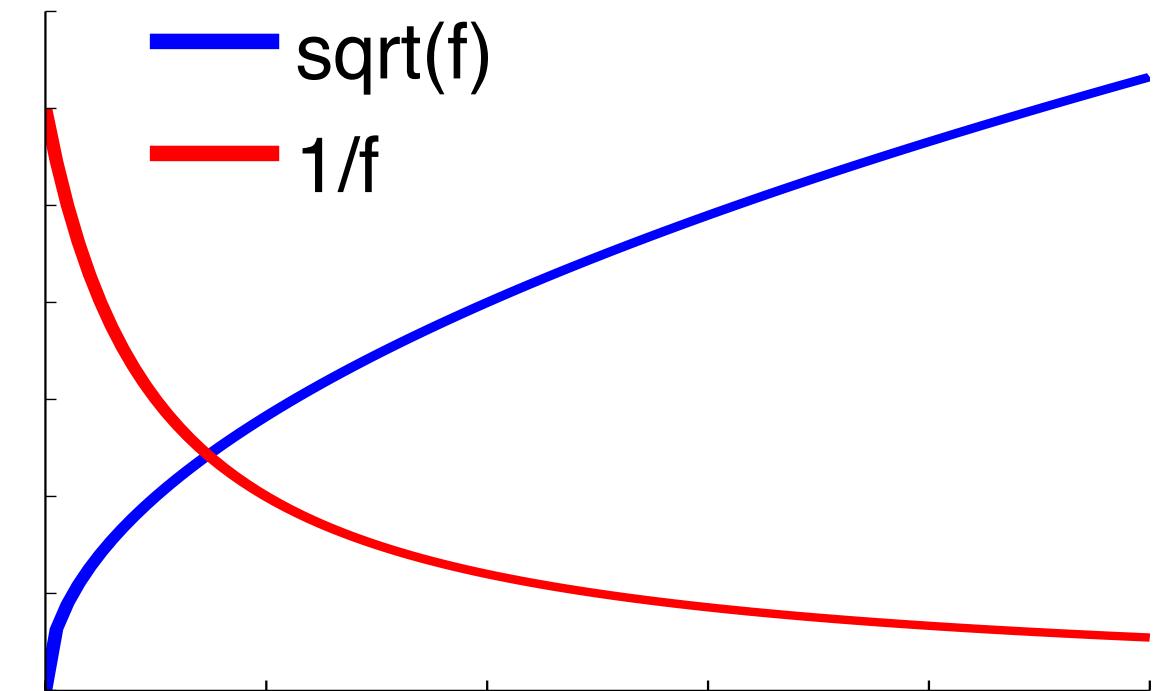
- BOLD decreases as  $1/f$

*BOLD降低*  $1 / f$



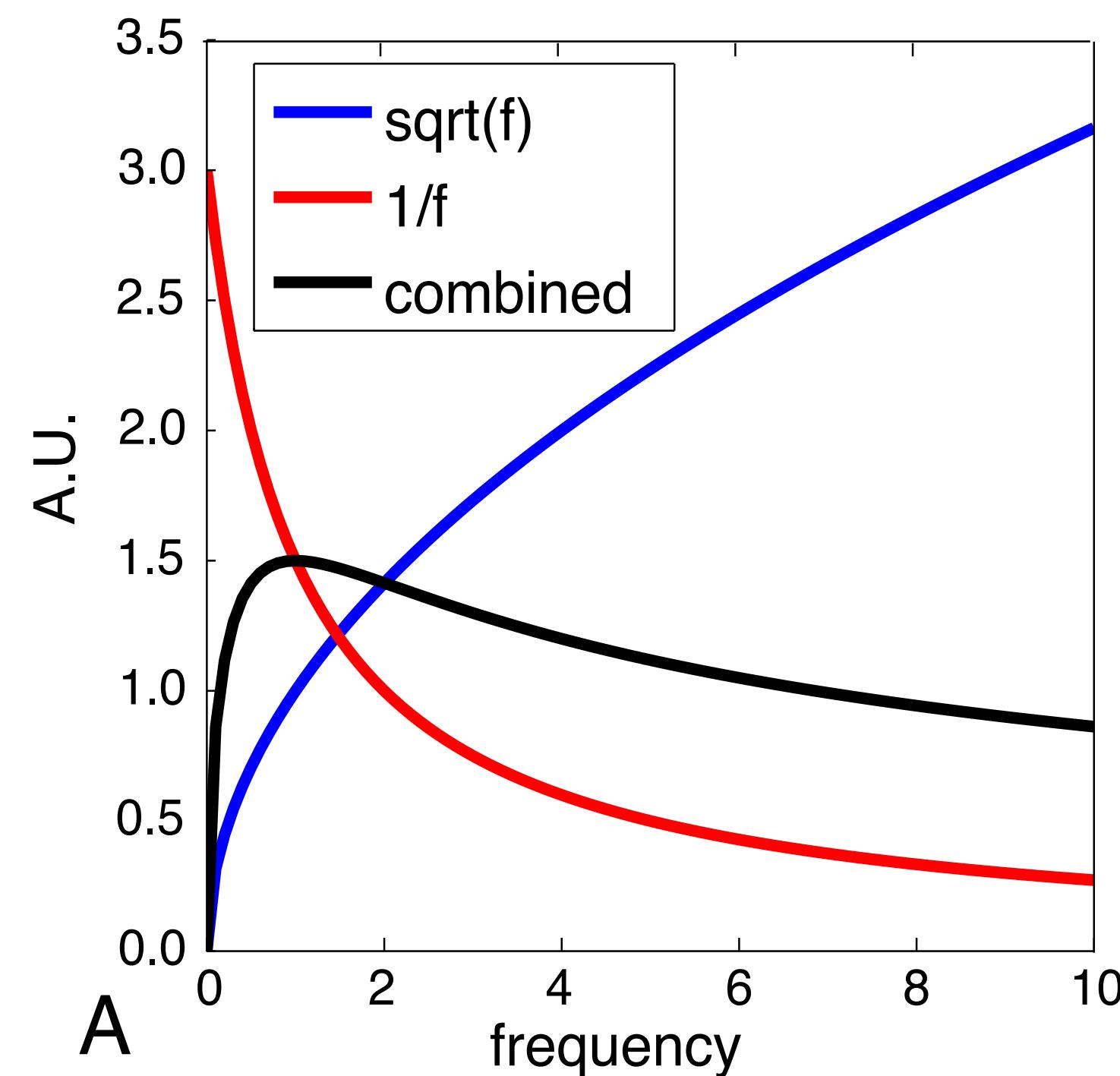
- Degrees of freedom increase as  $\sqrt{f}$

自由度增加为  $\sqrt{f}$



# Low frequency fluctuations? 低频波动振幅?

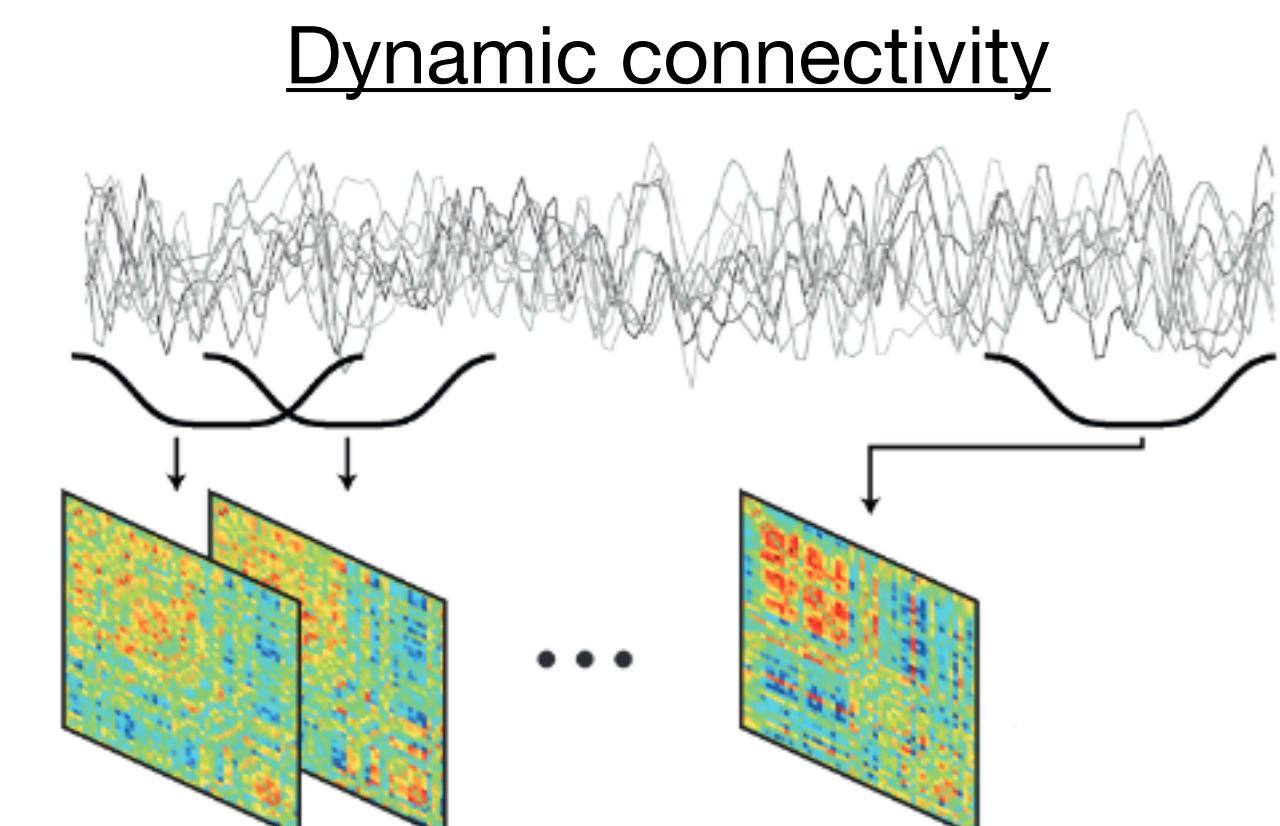
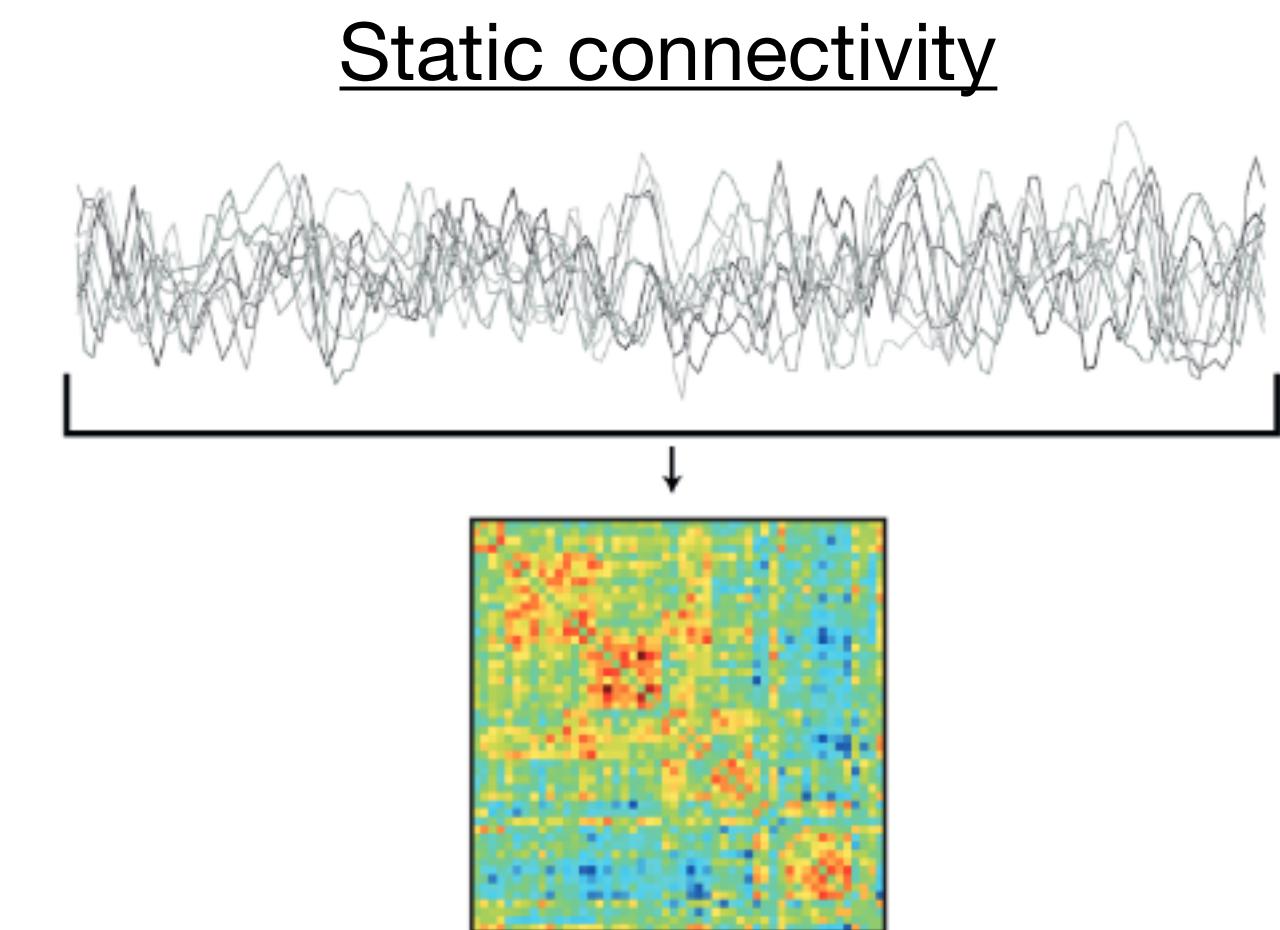
- BOLD decreases as  $1/f$   
*BOLD降低 $1/f$*
- Degrees of freedom increase as  $\sqrt{f}$   
*自由度增加为 $\sqrt{f}$*
- Combined effect contributes to RSN estimation across frequency range!  
*联合效应有助于跨频率范围的RSN估计!*



# Static versus dynamic connectivity

## 静态与动态连接

- Most connectivity measures are static (based on the full resting state scan) 大多数连接度量是静态的 (基于完全静止状态扫描)
- Dynamic connectivity is like to occur (changes over time) 动态连接似乎会发生 (随时间变化)
- Static connectivity measures reflect average across dynamic states 静态连接度量反映了动态的平均值
- Dynamic connectivity measures are challenging (in terms of noise influences, significance testing) 动态连接测量具有挑战性 (在噪声和显著性检验方面)



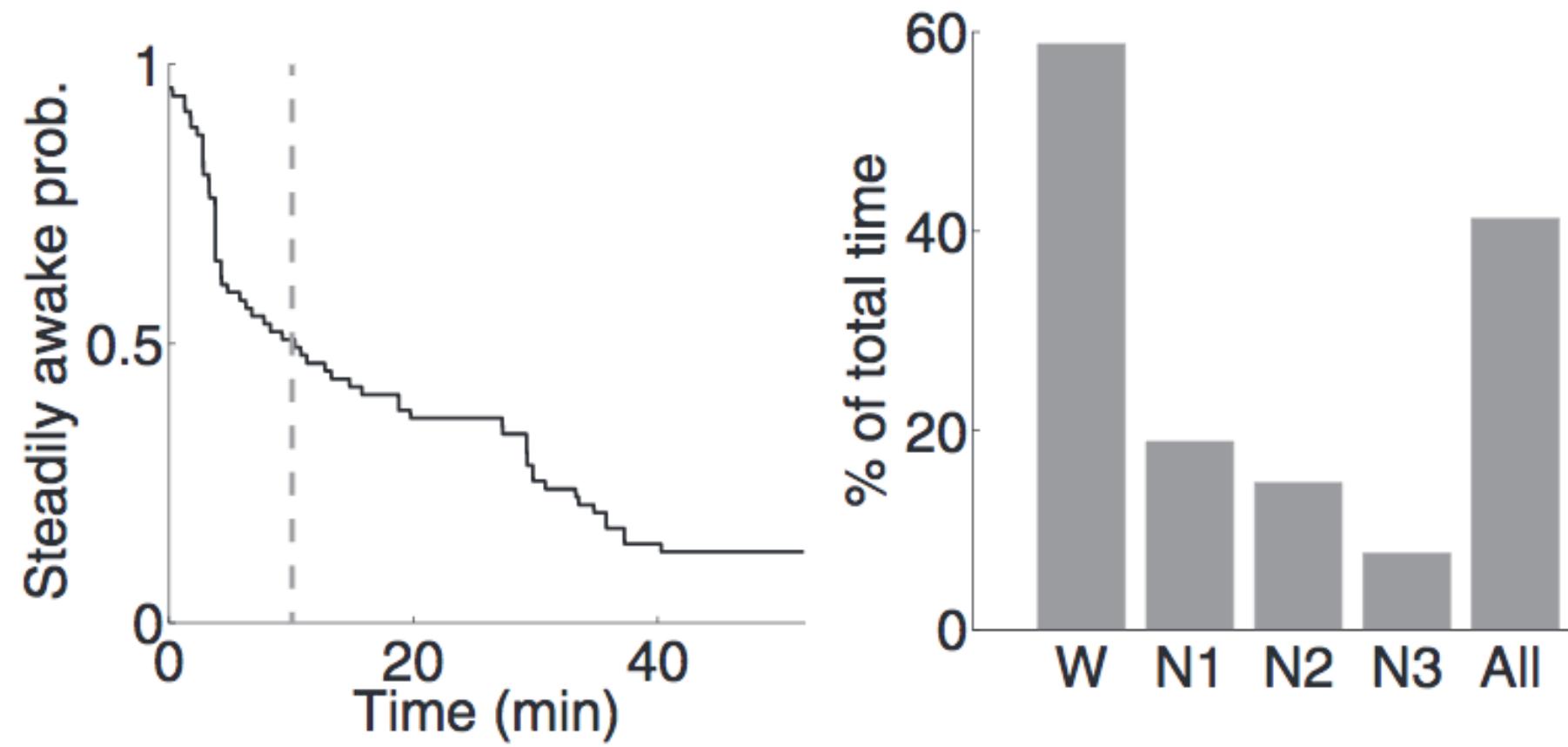


# Arousal 觉醒

- Subjects fall asleep 受试者入睡

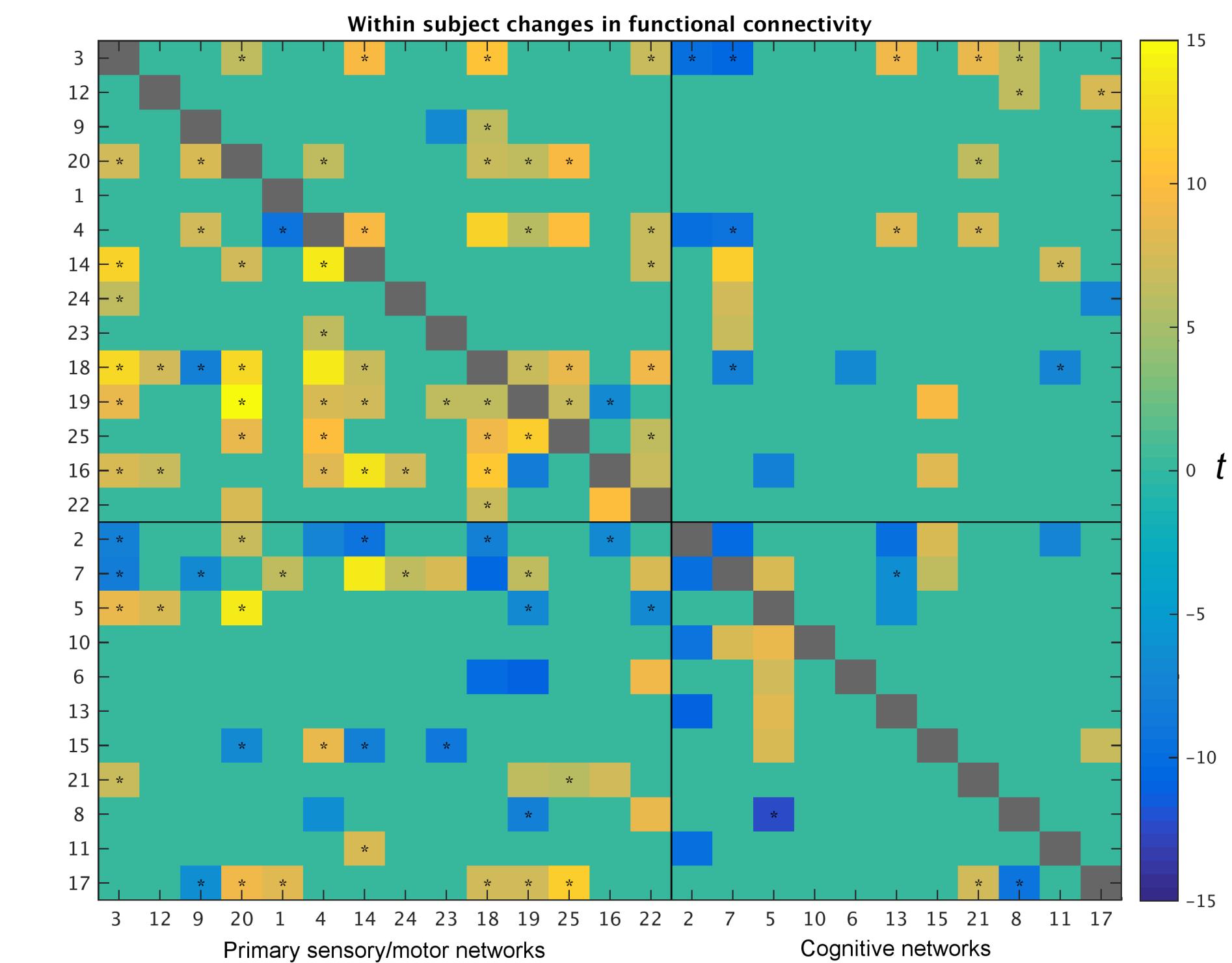
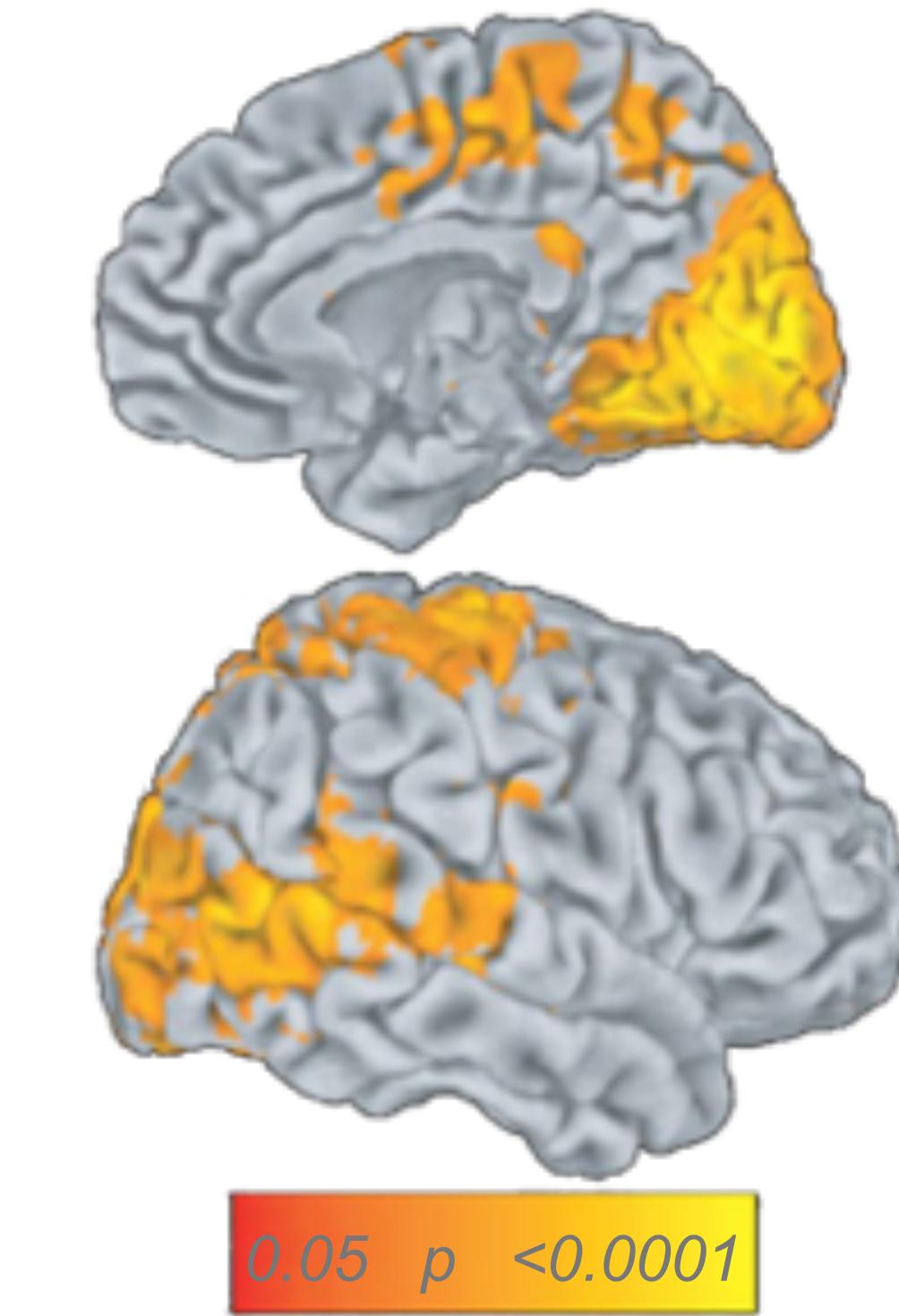
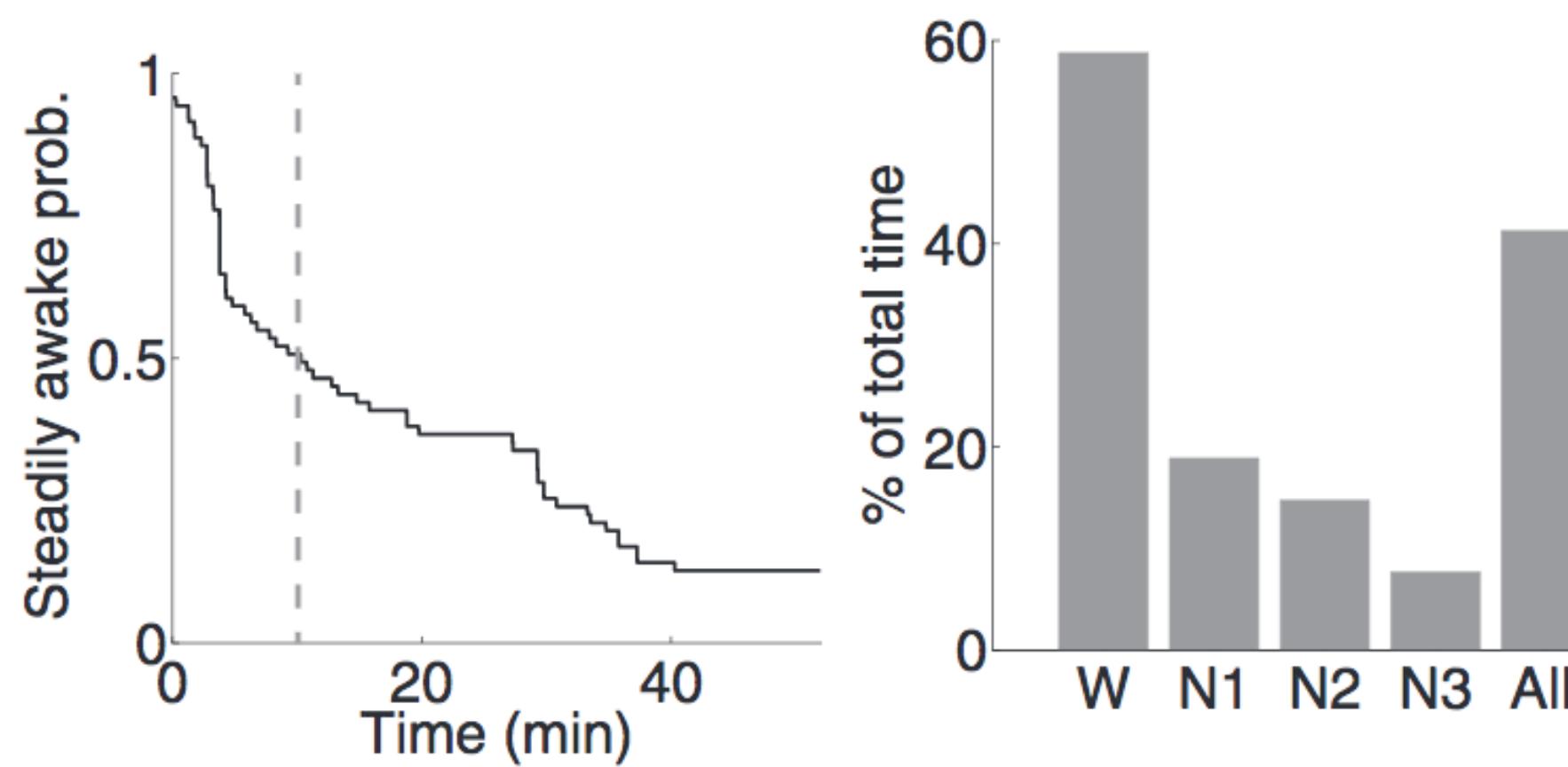
# Arousal 觉醒

- Subjects fall asleep 受试者入睡



# Arousal 觉醒

- Subjects fall asleep 受试者入睡
- Changes in BOLD amplitude BOLD幅度的变化
- Related changes in correlation 相关性变化





# Preprocessing

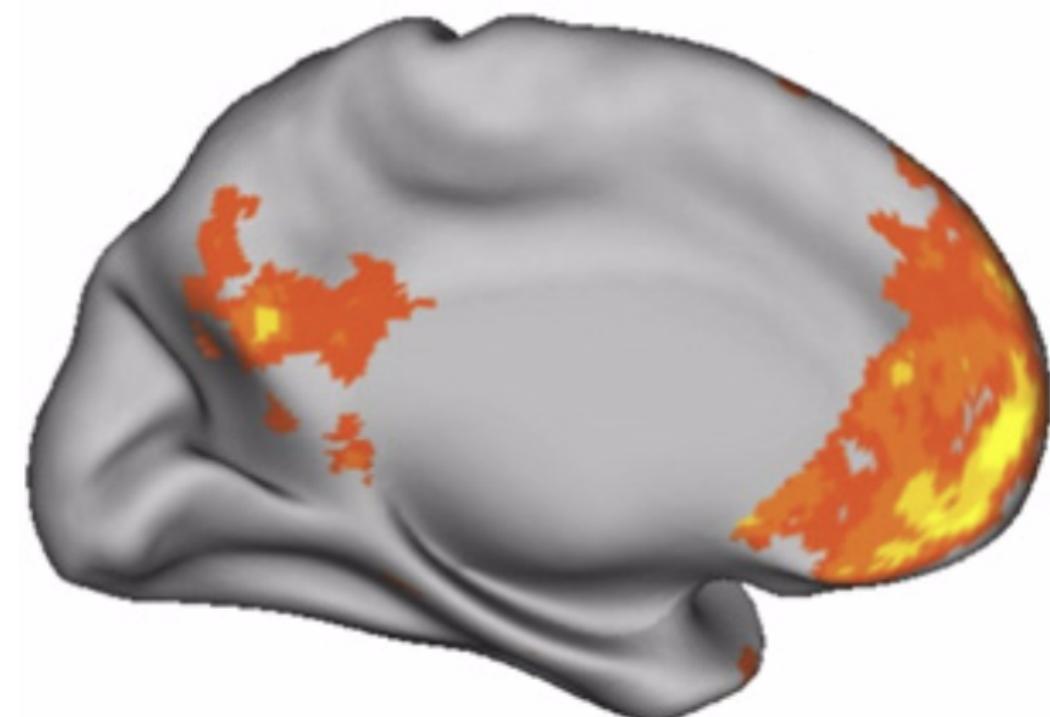
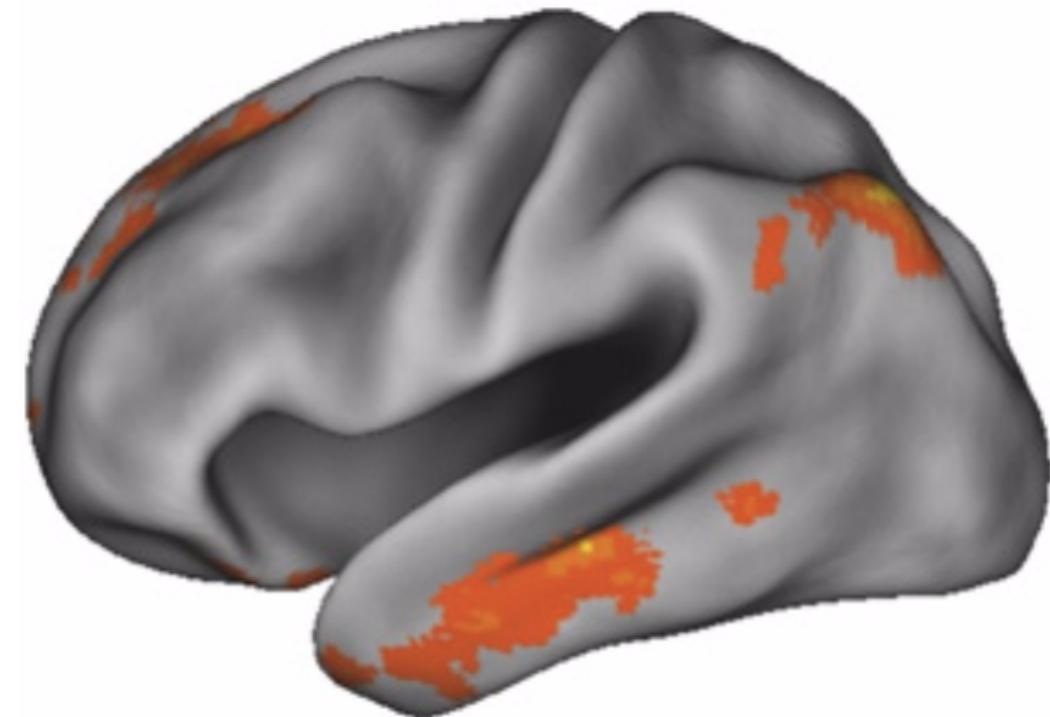
# 预处理

# Careful cleanup required

需要仔细去噪

- Structured artefacts much more of a problem for rfMRI than task-fMRI rfMRI比task-fMRI存在更多的人为因素
- No model of expected activation 没有预期激活的模型
  - Instead based on correlating timeseries with each other 而是基于将时间序列相互关联

Low motion > high motion

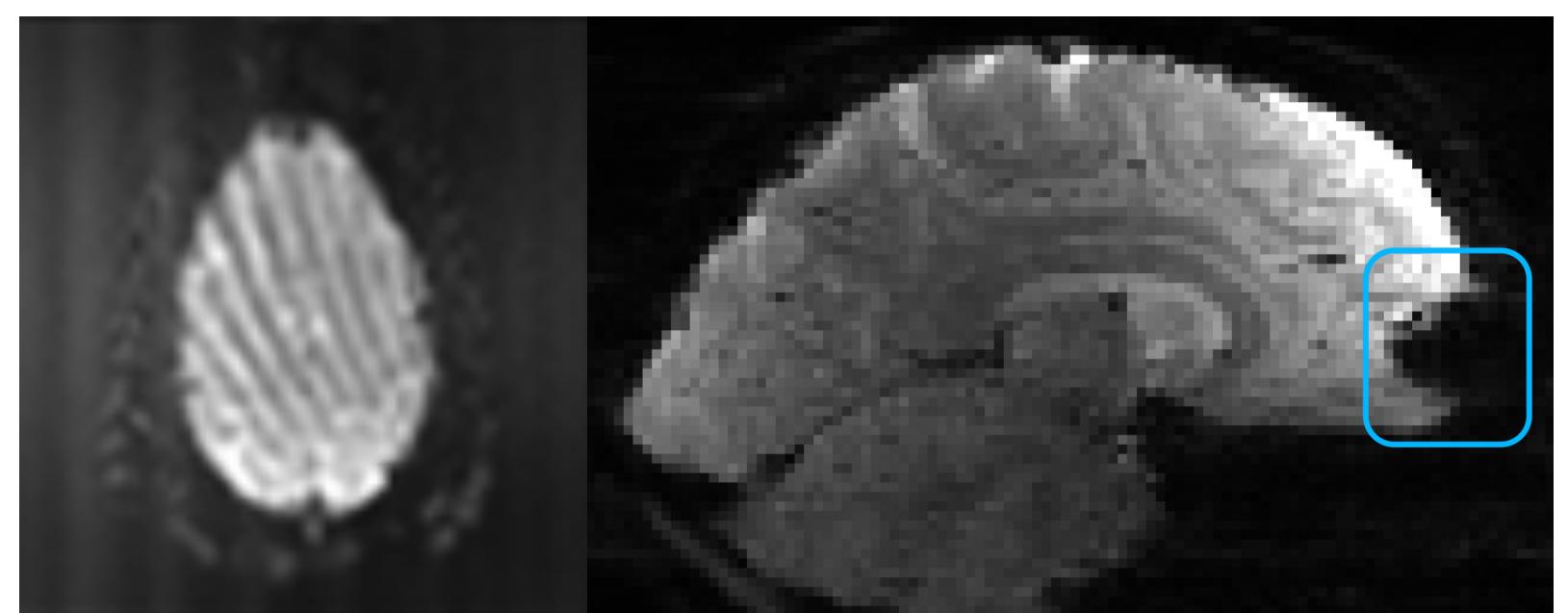
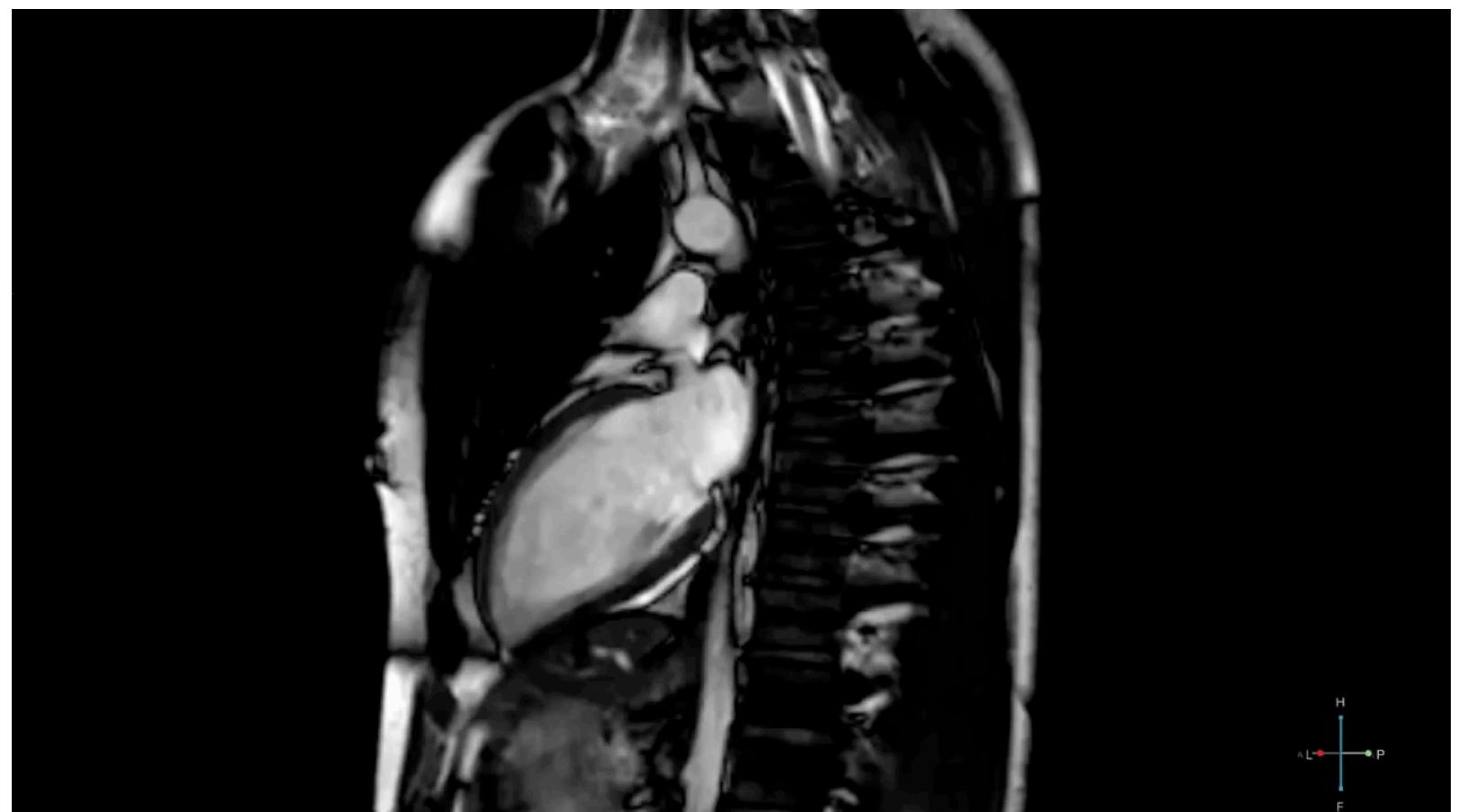




# Noise sources

## 噪声来源

- Head motion 头动
- Cardiac & breathing cycles 心跳和呼吸周期
- Scanner artefacts 扫描仪噪声





# Preprocessing overview

## 预处理概述

头动&失真校正

### Conventional preprocessing steps

Motion & distortion correction

Slice timing correction

高通滤波

High pass temporal filtering

Spatial smoothing

配准

Registration

常规预处理步骤

时间层校正

空间平滑

噪声回归

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

Nuisance regression

Low pass temporal filtering

全脑检查

Volume censoring

Global signal regression

降噪步骤 (至少使用其中之一)

低通滤波

ICA降噪

ICA-based clean-up

全脑信号回归

去除生理噪声

Physiological noise regression



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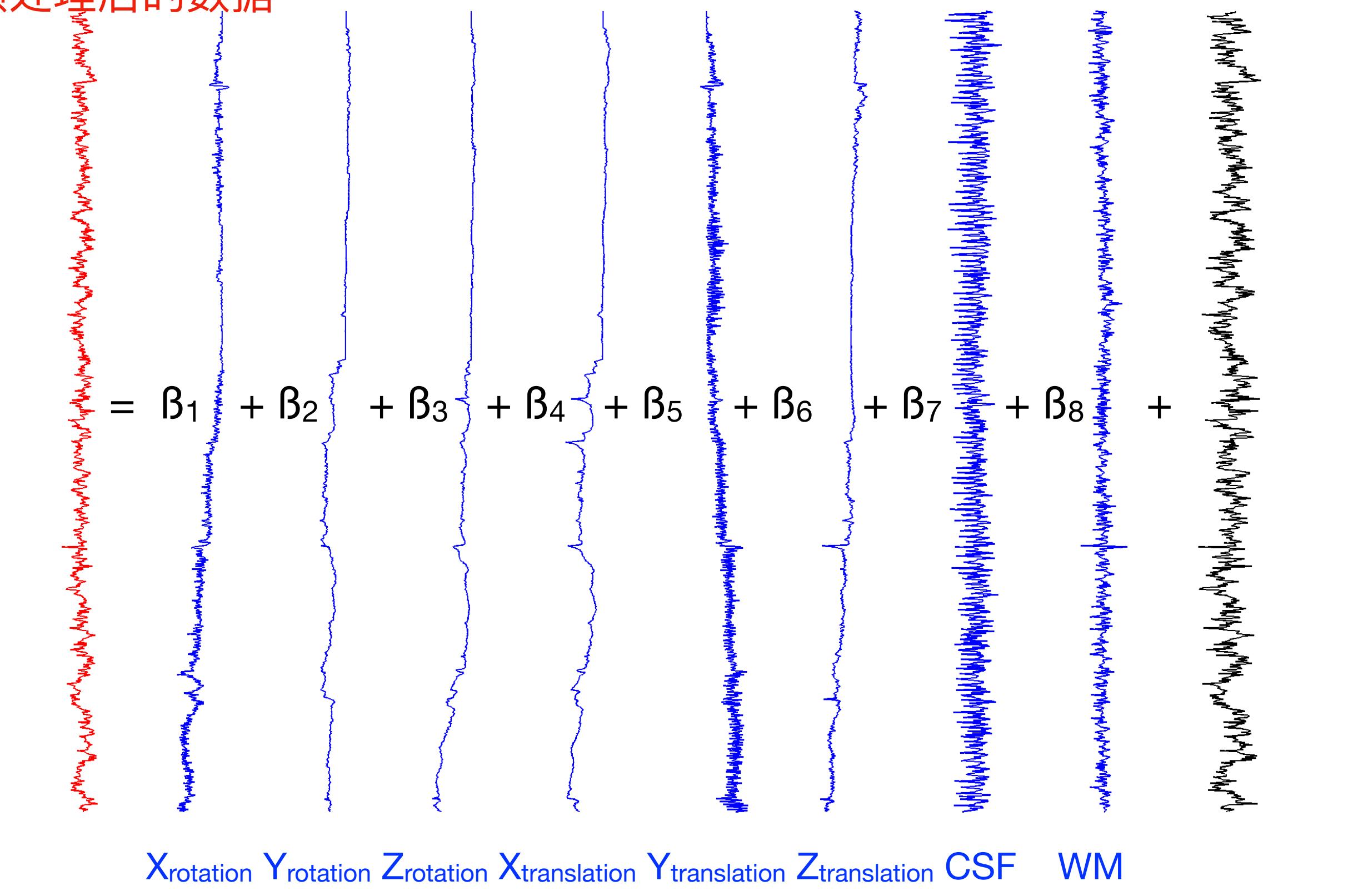
Physiological noise regression

# Nuisance regression

## 噪声回归

- Head motion parameters (头动参数)
- White-matter / CSF (白质/脑脊液)
- Use GLM to remove nuisance timeseries (GLM去除噪声时间序列)
- Perform analysis on residuals (残差分析)
- “CompCor” method (PCA-based) (“CompCor”方法 (基于PCA) )

Data after  
standard  
preprocessing  
标准预处理后的数据

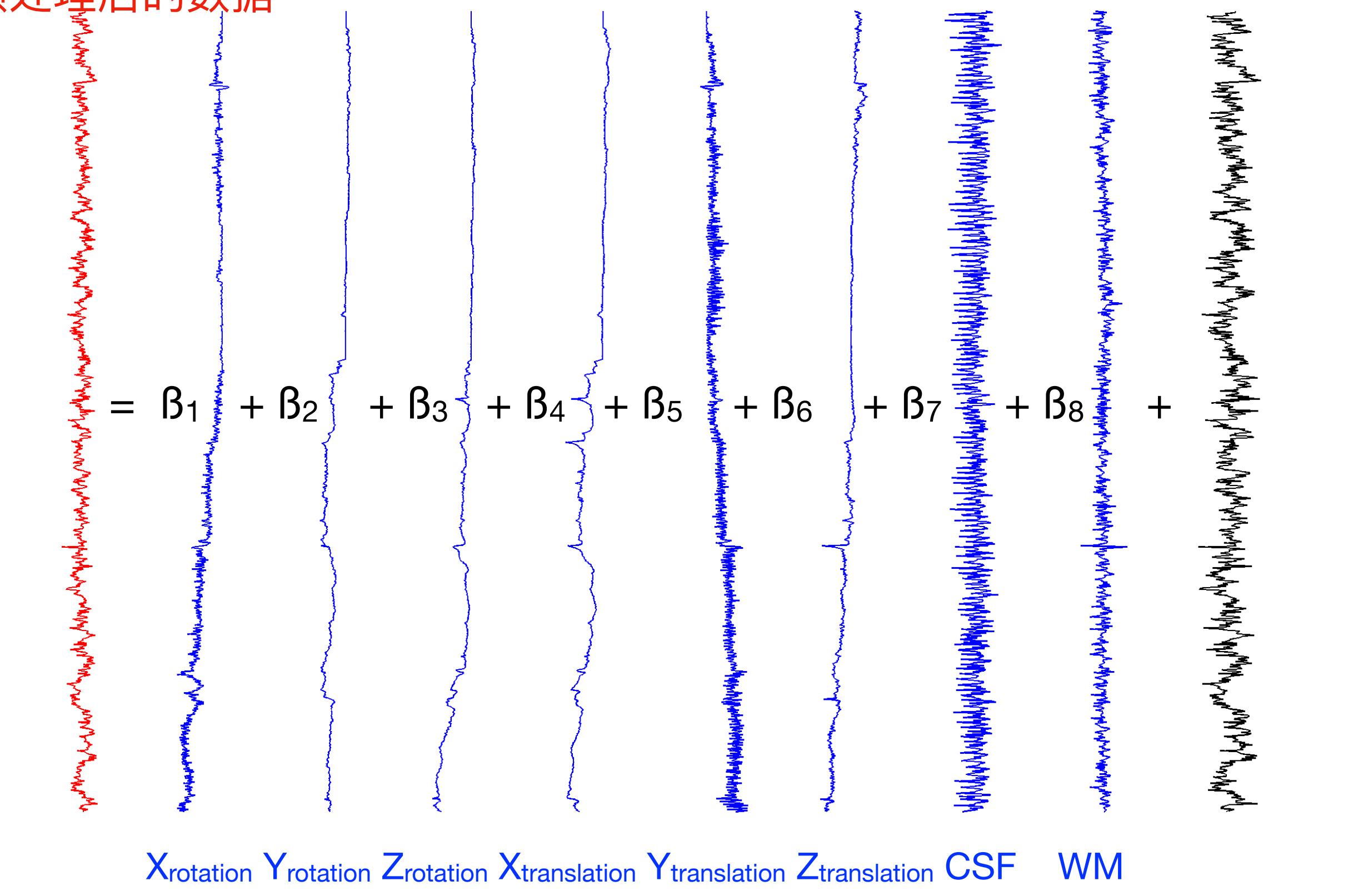


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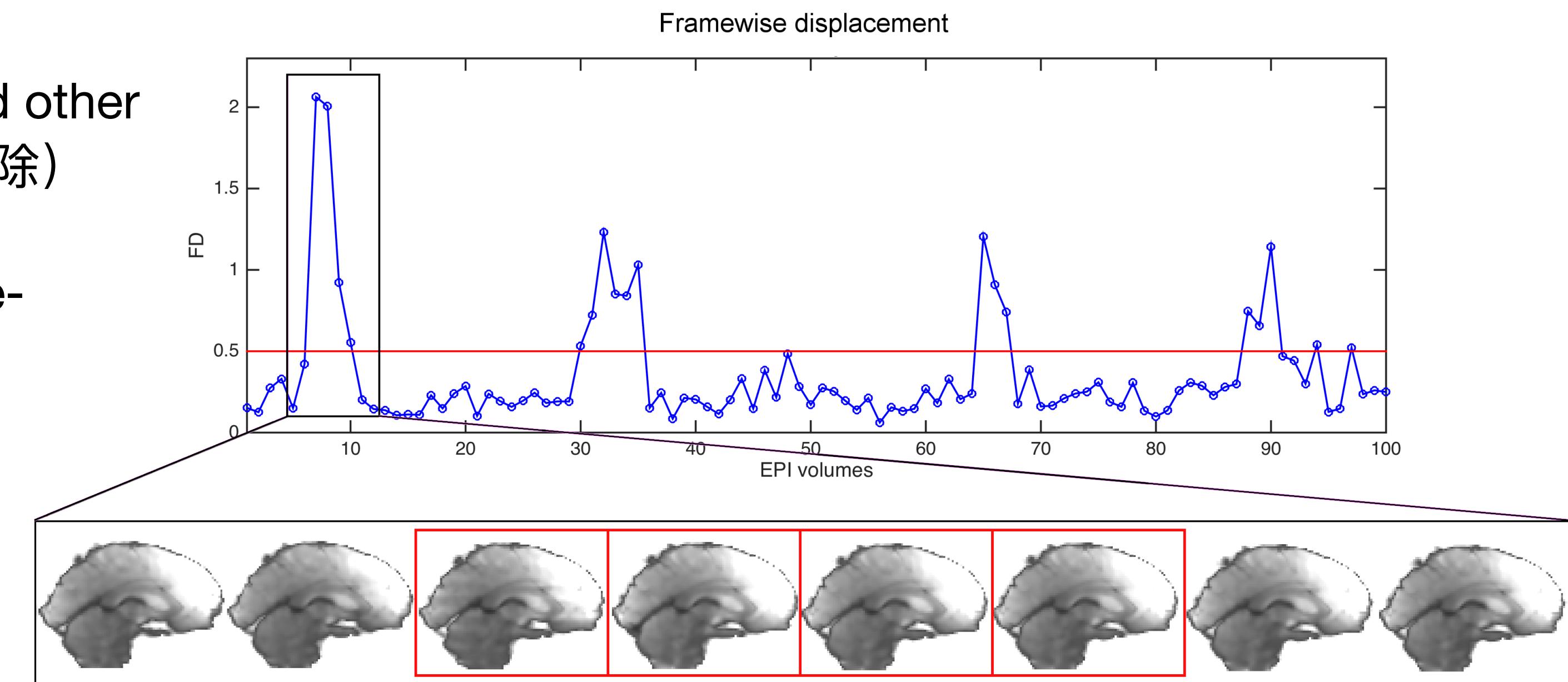
Data after  
standard  
preprocessing  
标准预处理后的数据



# Volume censoring

## 大脑检查

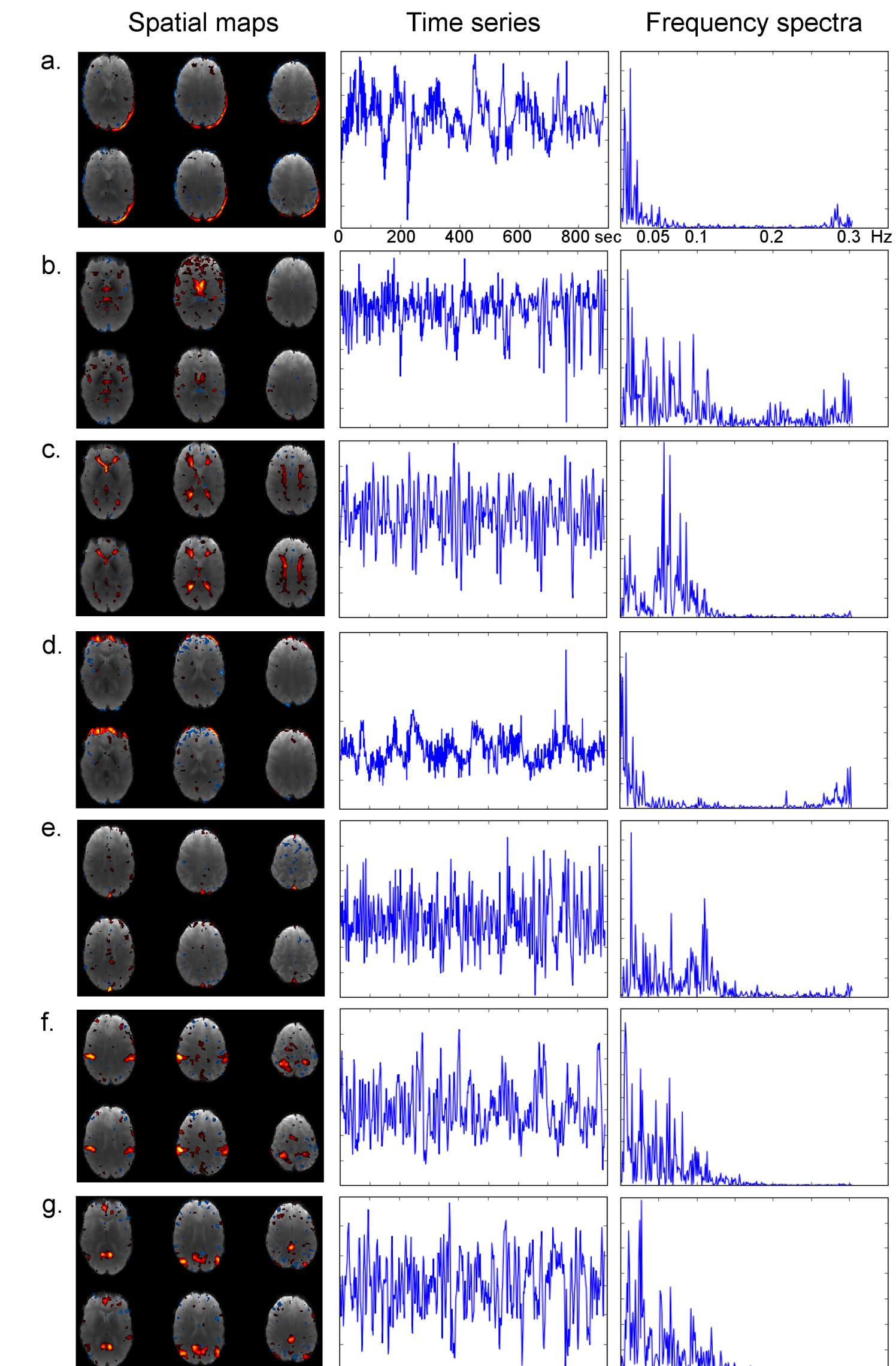
- Remove volumes with high motion (移除头动较大的图像)
- Very effective to fully remove large motion effects (移除头动较大的体素效果很好)
- But, does not remove small motion effects and other noise sources (头动小的以及其他噪声不要移除)
- Also known as scrubbing, spike regression, de-spiking  
也称为去噪, 尖峰回归, 去尖峰



# ICA based cleanup

## ICA降噪

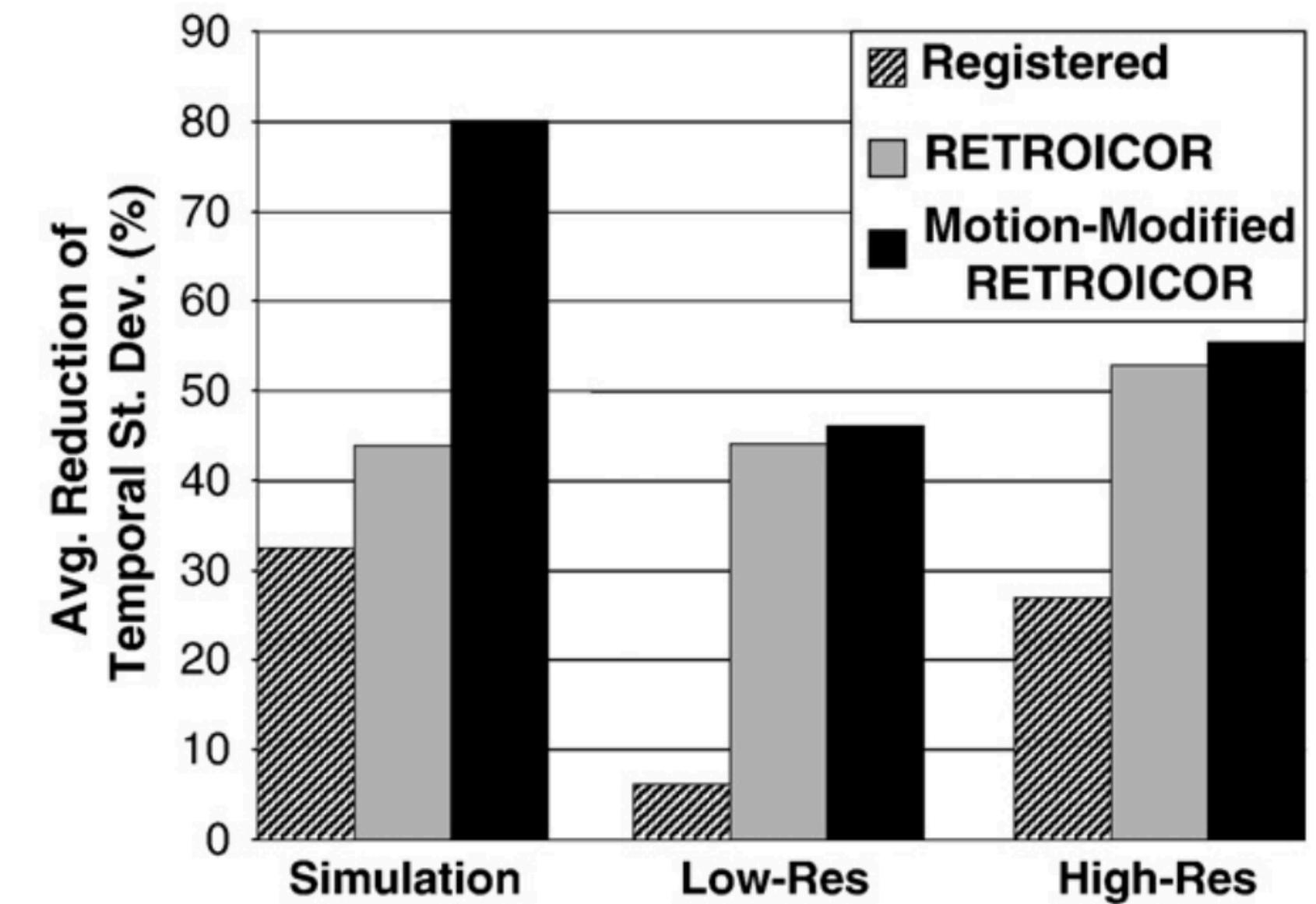
- Semi-Automatic labelling methods available (ICA-FIX, ICA-AROMA)  
半自动标记的方法 (ICA-FIX, ICA-AROMA)
- Removes most types of artefacts (motion, physiology, scanner)  
删除大多数类型的噪声 (头动、生理、扫描设备)
- But, does not capture global (spatially extended) noise  
但是，不会删除全局（空间扩展）噪声



# Physiological noise regression

## 去除生理噪声

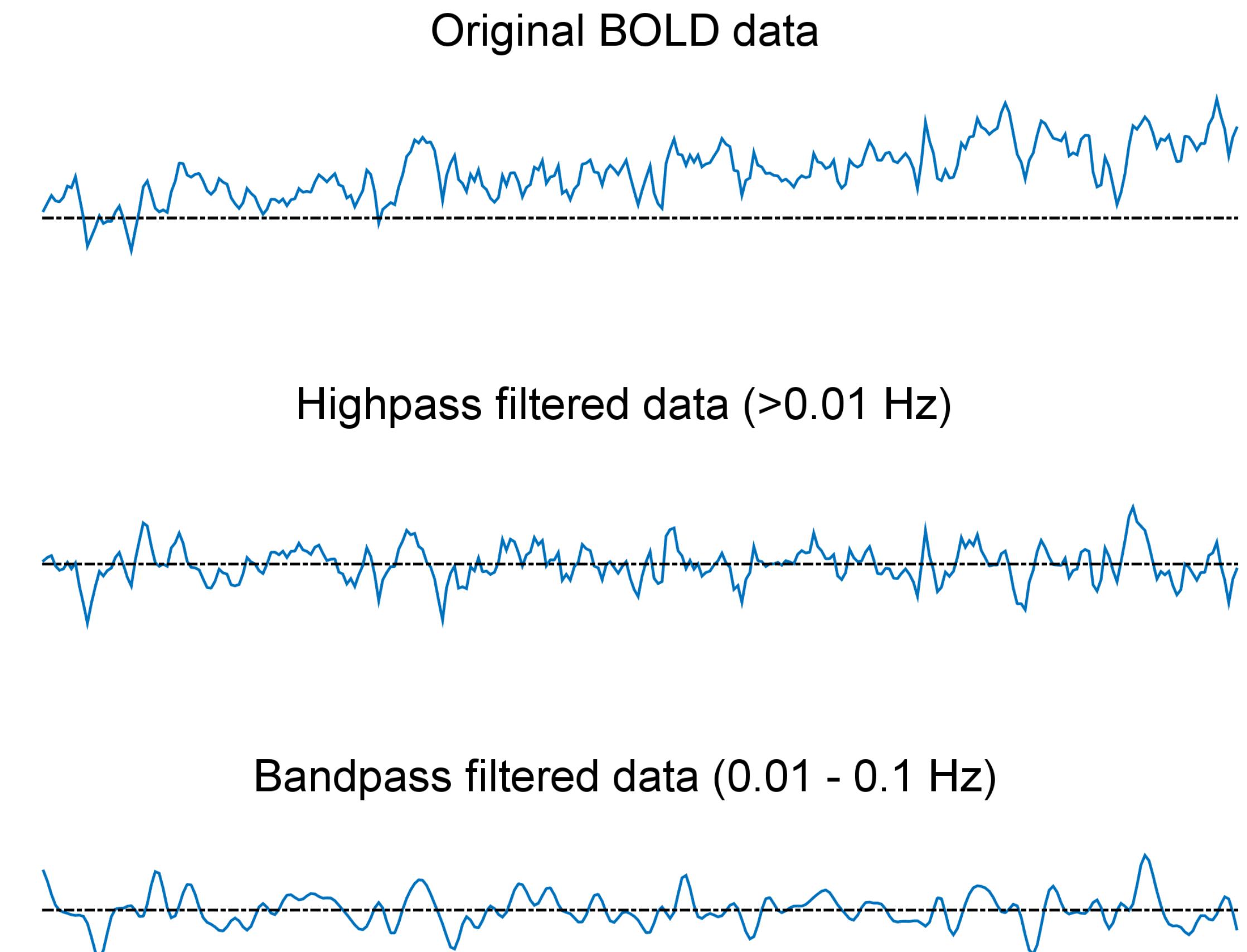
- PNM, RETROICOR
- Requires physiological measurements during scan 在扫描期间需要生理信号测量
- Generates regressors based on physiological data 基于生理数据生成回归量



# Lowpass temporal filtering

## 低通时间滤波

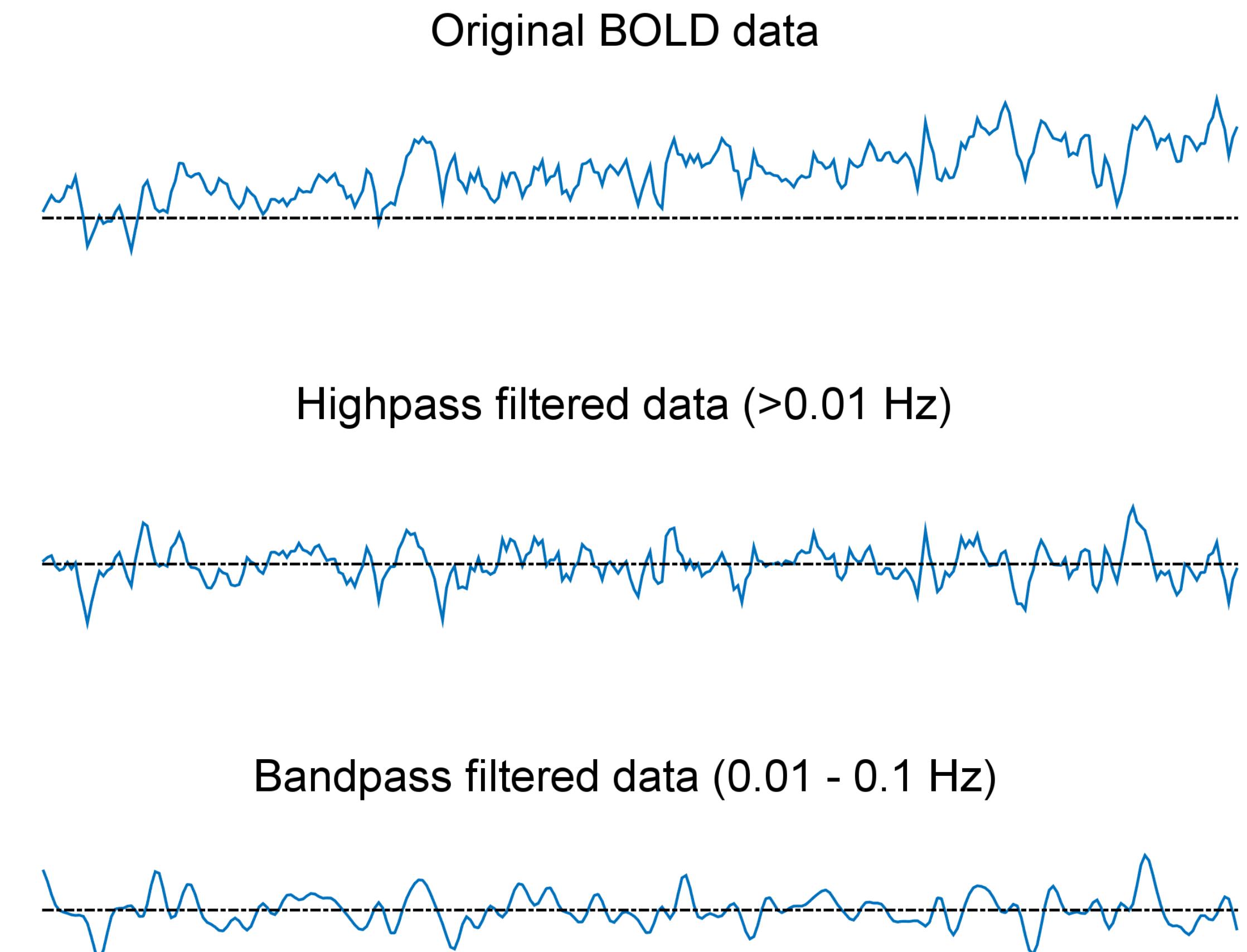
- E.g., common to remove frequencies  $> 0.1\text{Hz}$   
通常去除 $> 0.1\text{Hz}$ 的频率
- May remove useful signal  
可能会删除有用信号
- Not guaranteed to remove much artefact  
不能保证删除很多噪声



# Lowpass temporal filtering

## 低通时间滤波

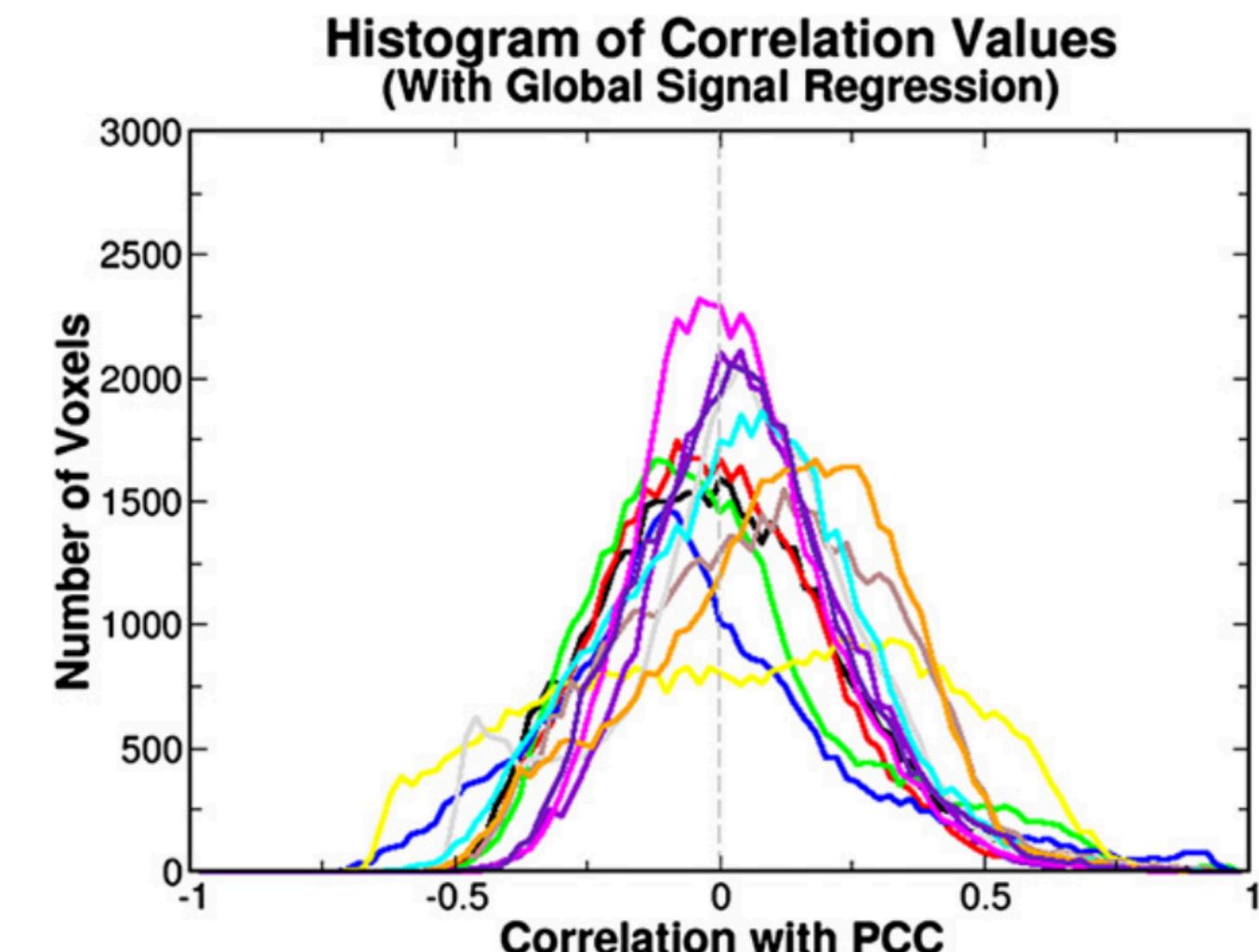
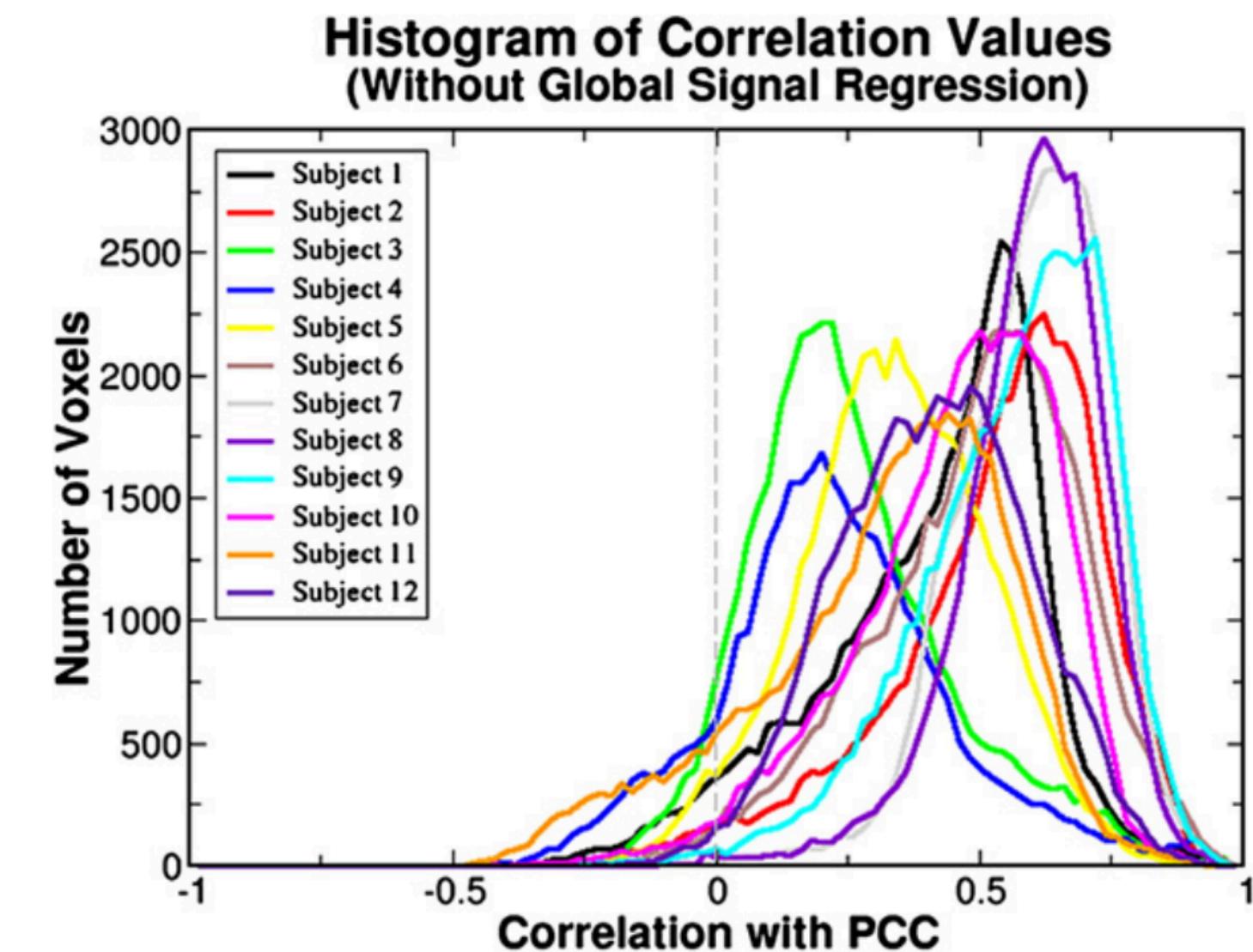
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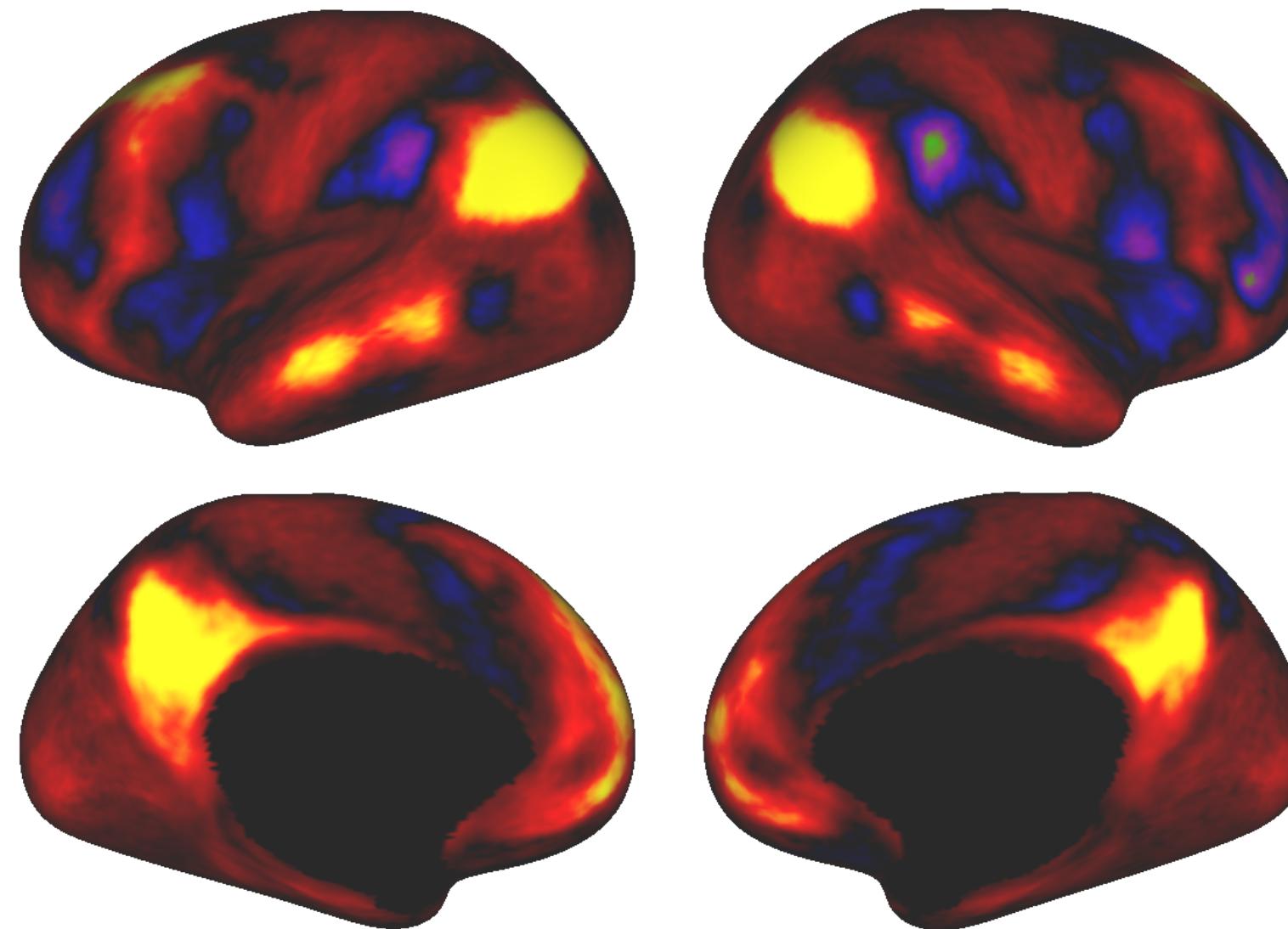
# Global signal regression

## 去除全脑信号

- Regress out mean timeseries across all voxels (or all grey matter voxels)  
回归所有体素（或所有灰质体素）的平均时间序列
- Shifts connectivity values to be zero mean  
将连通性值转换为零均值
- Therefore, more negative correlations  
因此，存在更多的负相关
- Not necessary if using partial correlation  
如果使用偏相关则不必要

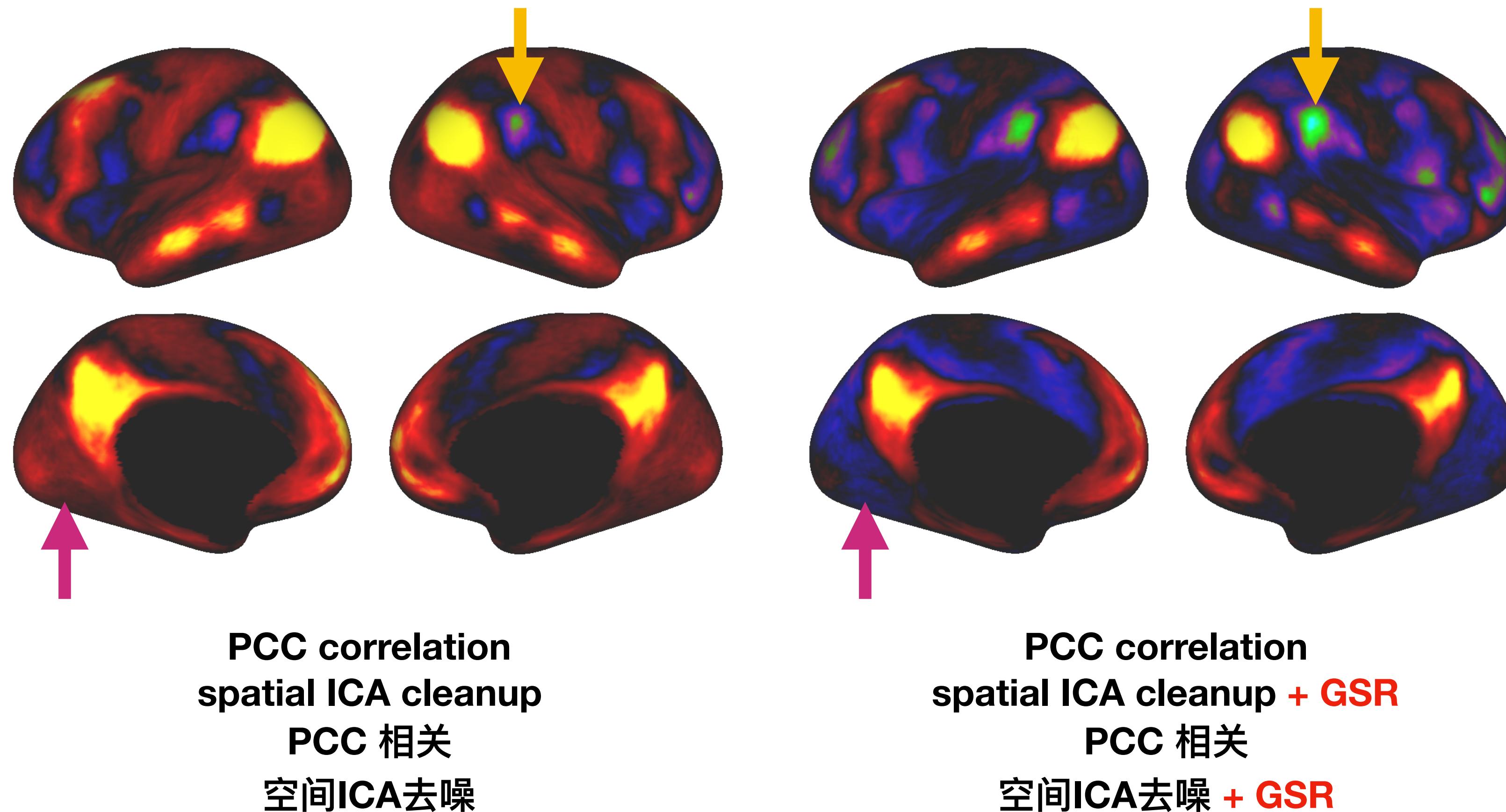


# GSR effects & alternative 去除全脑信号效应和替代方法

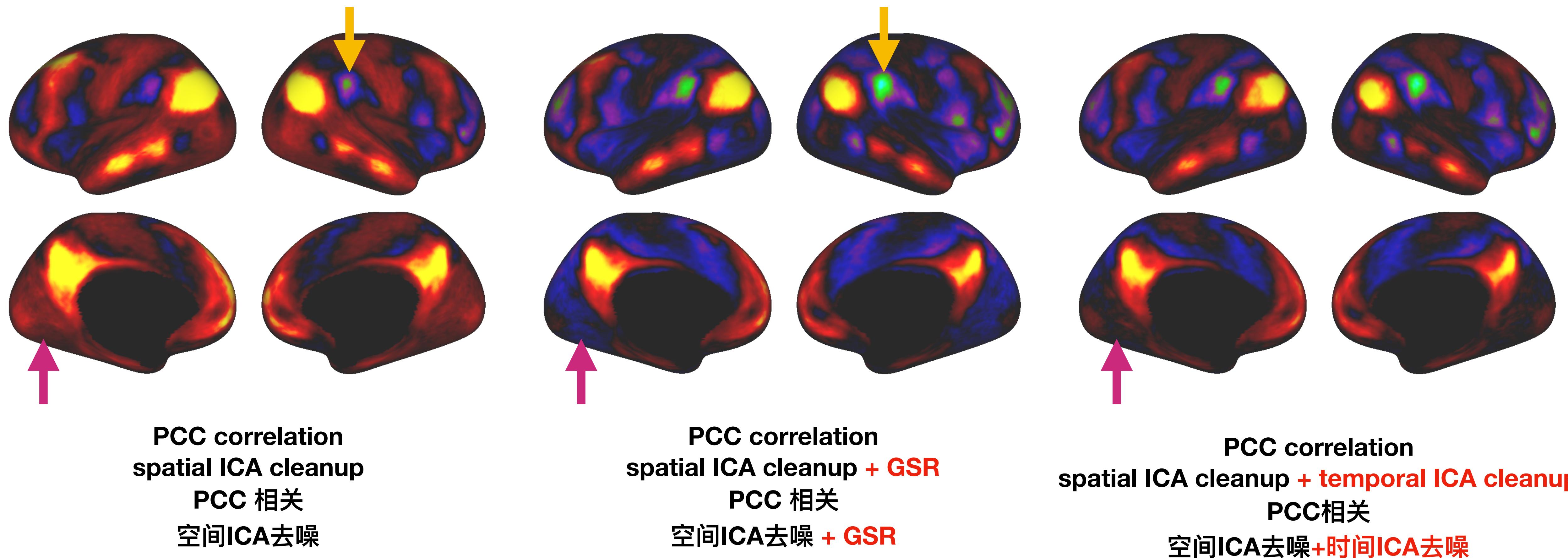


PCC correlation  
spatial ICA cleanup  
PCC 相关  
空间ICA去噪

# GSR effects & alternative 去除全脑信号效应和替代方法



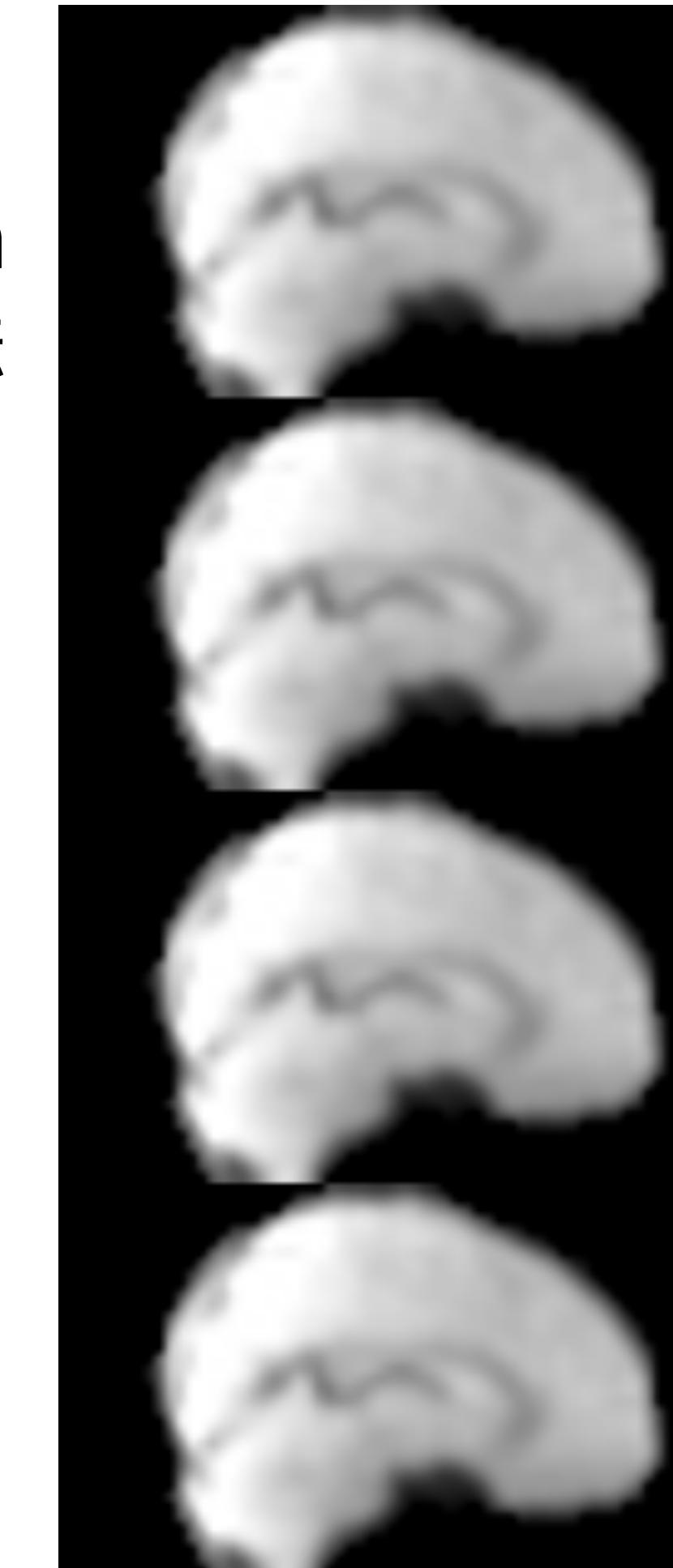
# GSR effects & alternative 去除全脑信号效应和替代方法



# Clean-up comparison

## 去噪比较

no additional correction  
没有使用其他校正方法

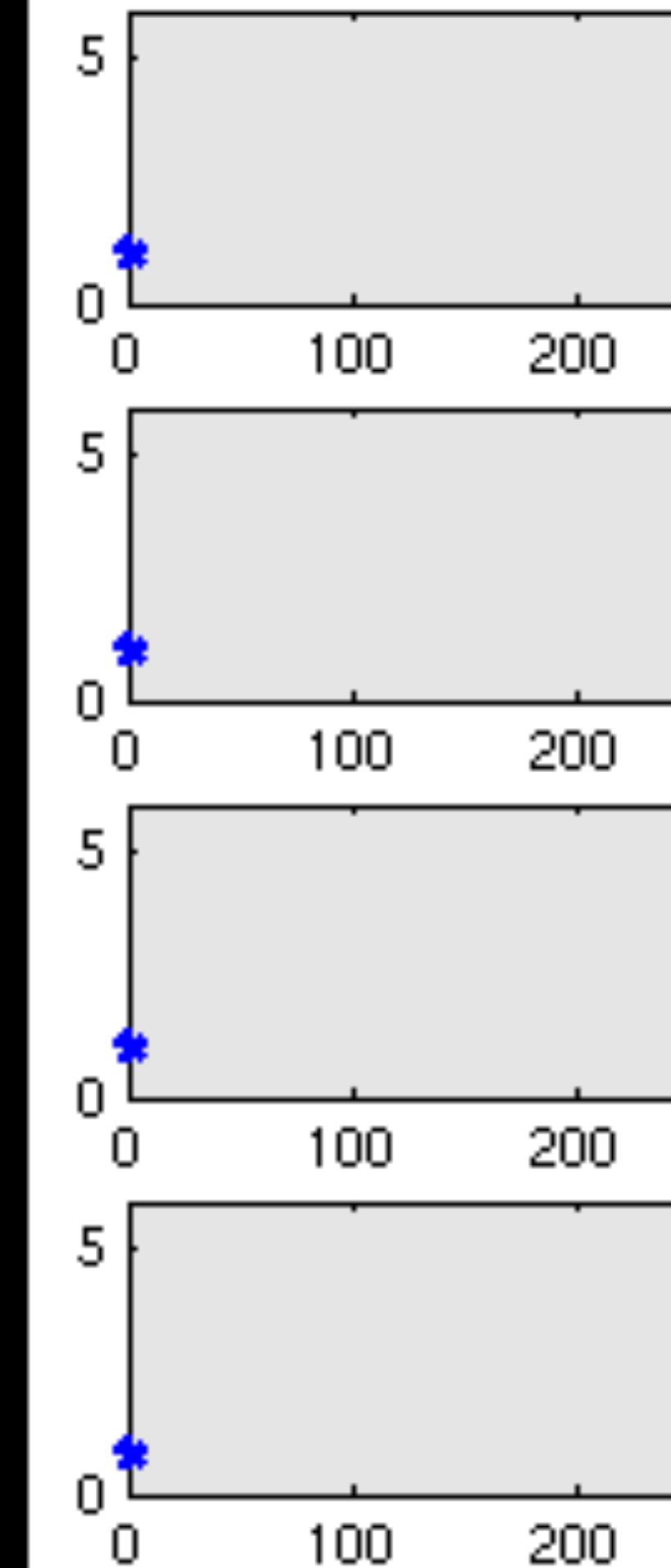


24RP-regression  
24RP校正

24RP + volume censoring  
24RP+体素检查

ICA-AROMA

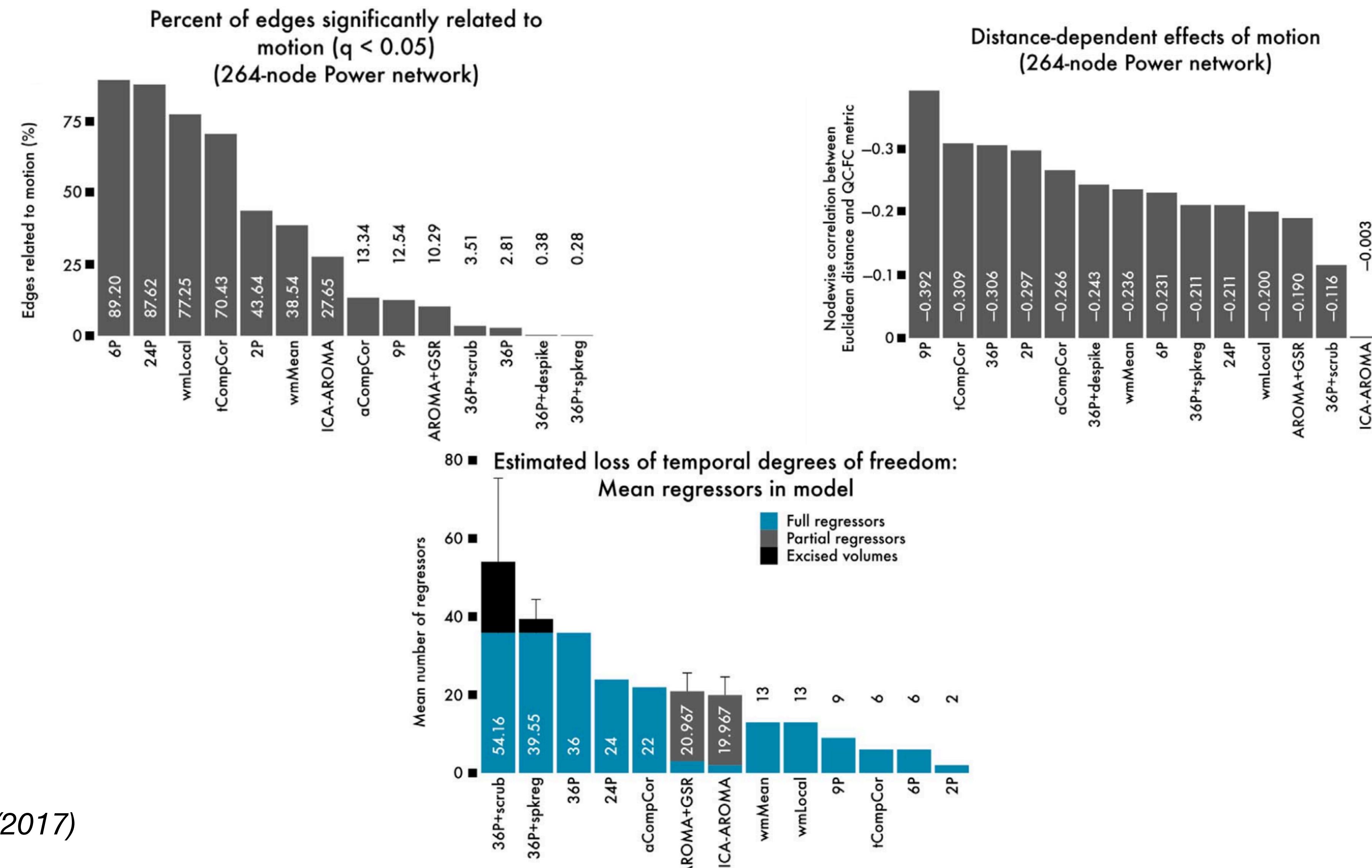
FMRI data



DVARS

# Clean-up comparison

## 去噪比较





# Preprocessing advice

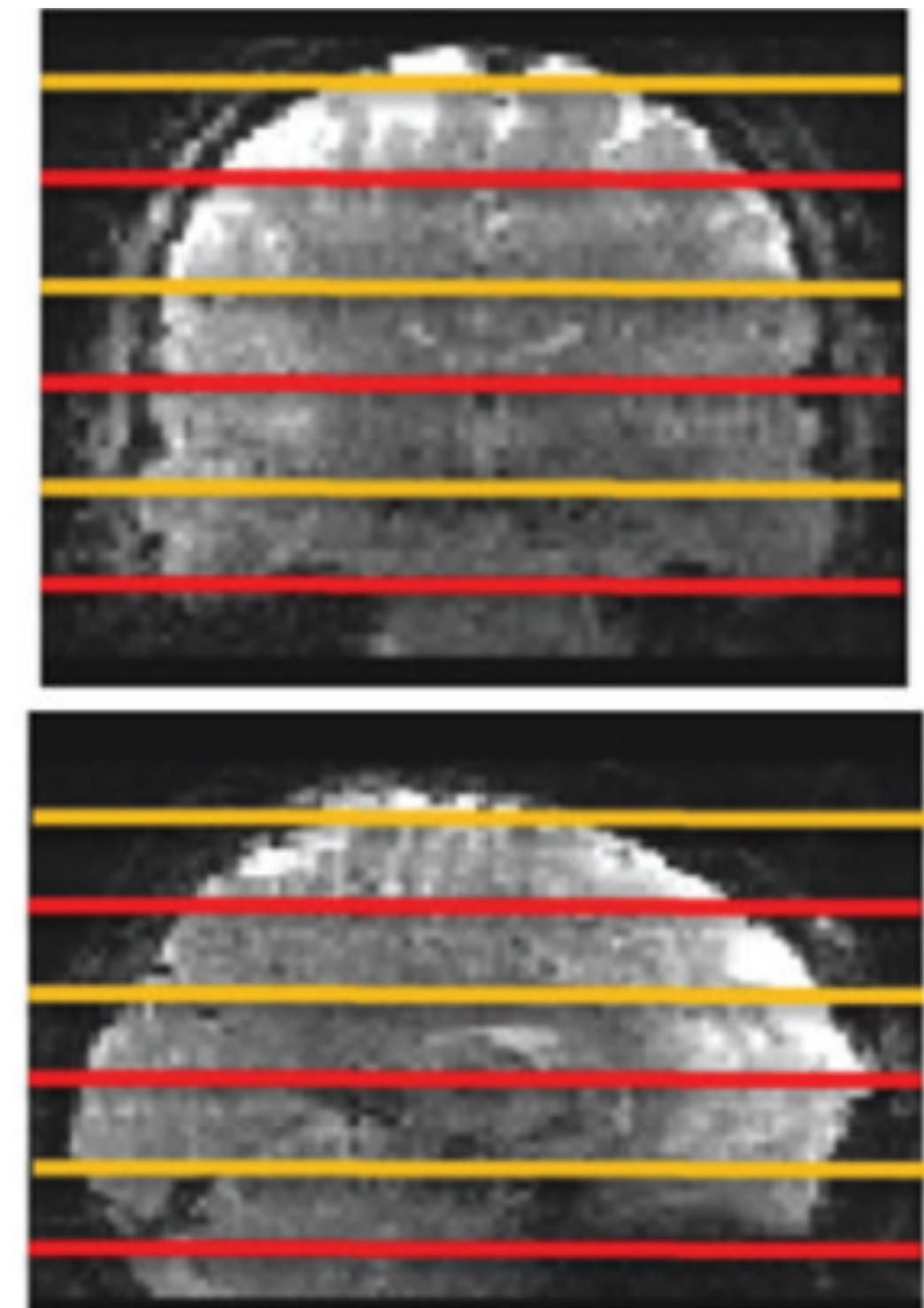
## 预处理建议

- Read up on the latest literature 阅读最新文献
- Nuisance regression is not enough 噪声回归是不够的
- Low-pass filtering is not enough & often not necessary when using other approaches 低通滤波是不够的，在使用其他方法时通常不需要
- Use ICA-based methods and/or volume censoring  
使用基于ICA的方法和/或全脑检查
- Use physiological noise regression when interested in brainstem or other vulnerable brain regions 当对脑干或其他敏感的大脑区域感兴趣时，使用生理噪声回归
- Don't use global signal regression 不要回归全脑信号

# Data acquisition advice

## 数据采集建议

- Just a guide, may vary depending on study aims!  
只是一个建议，可能会根据研究目标而有所不同！
- Whole brain coverage, voxel size: 2 - 3 mm  
全脑覆盖，体素大小：2-3毫米
- Scan duration: 扫描持续时间
  - 10-15 minutes per scan 每次扫描10-15分钟
  - Potentially multiple scans 可以多次扫描
- Repetition time: ideally close to 1 second (multiband/  
multiplexed imaging) 重复时间：理想情况下接近1秒（多频段/多路复用成像）
- Paradigm: eyes open, fixation cross 范式：睁眼，固定十字架
- Auxiliary data: physiology, sleep 辅助数据：生理，睡眠





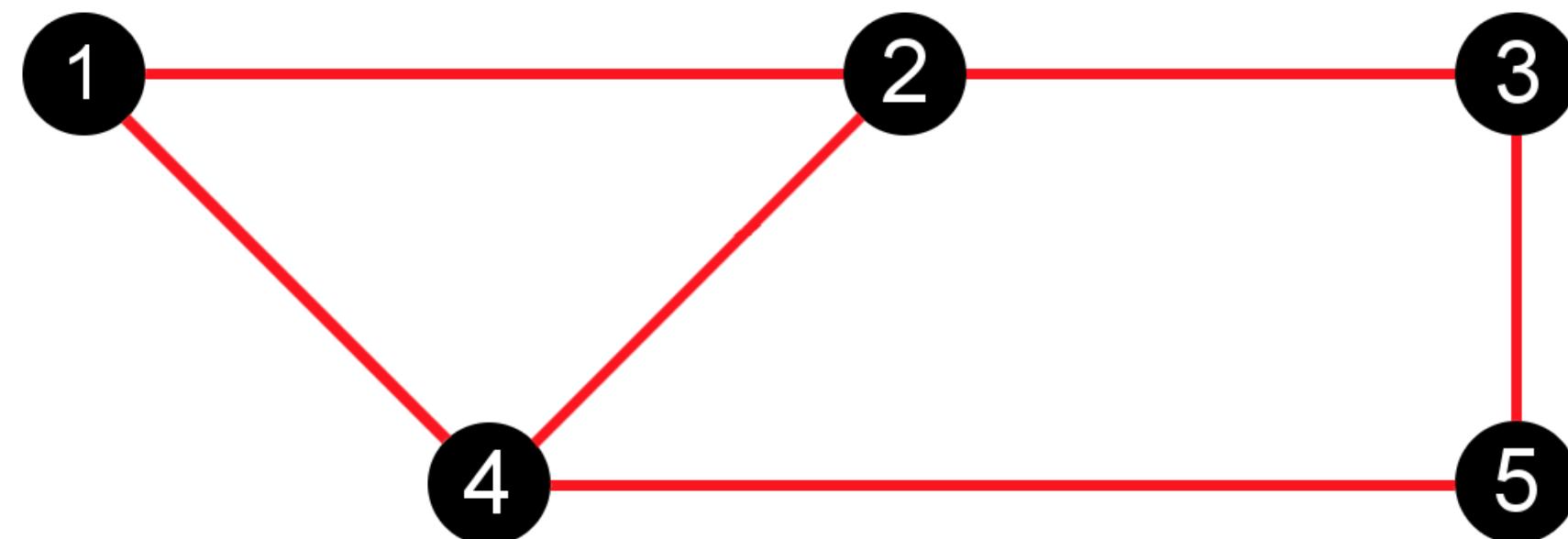
# **Network modelling analysis**

## **网络建模分析**

# Glossary

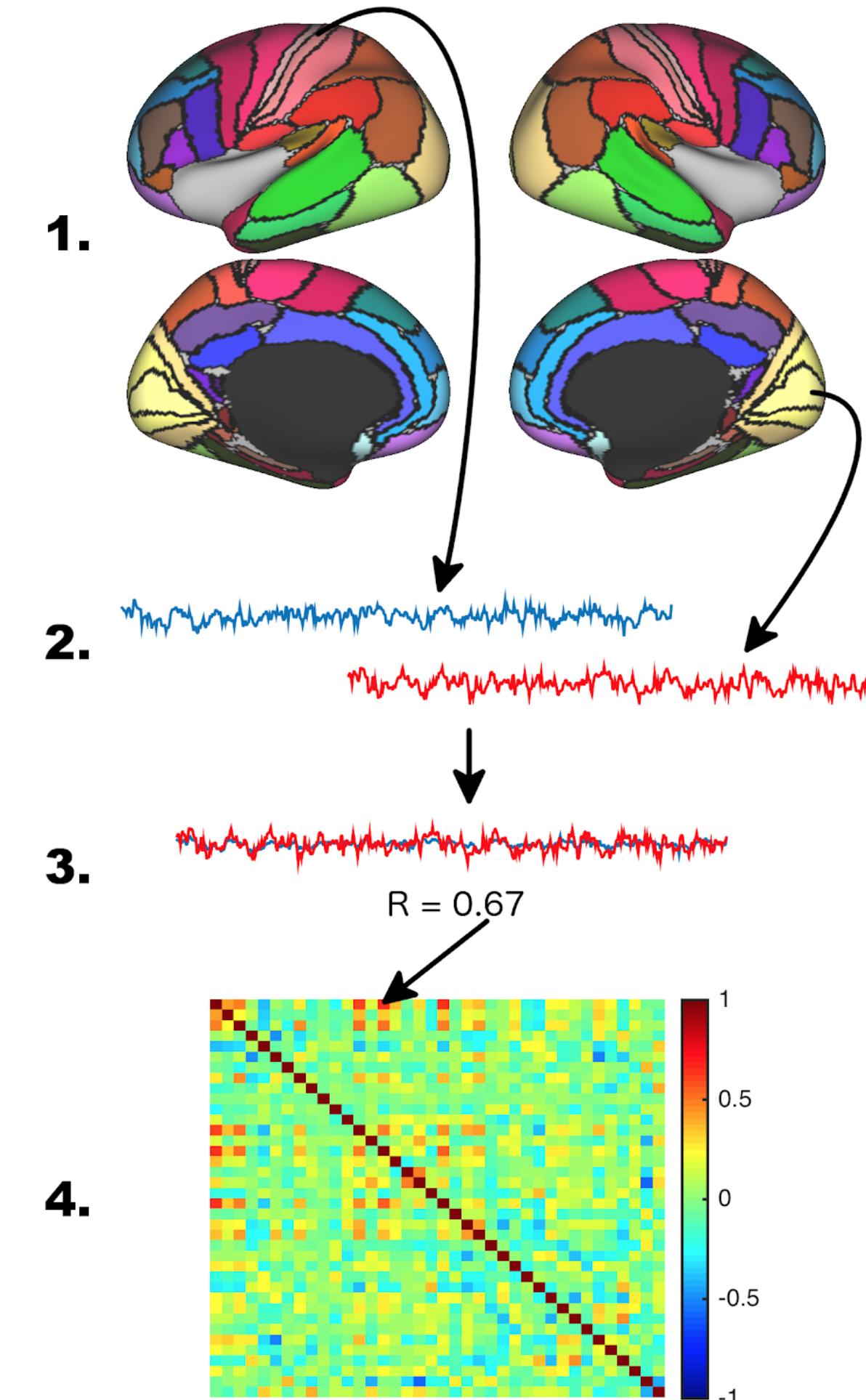
## 词汇表

- Node = functional brain region 节点=功能性大脑区域
  - Contiguous nodes = interconnected ‘blobs’ 连续节点=互连‘节点’
  - Non-contiguous nodes = e.g. bilateral 非连续节点=例如双边
- Parcellation = separation of all voxels into a set of nodes
- 分区 = 将所有体素分离为一组节点
  - Hard parcellation = binary regions 二进制区域
  - Soft parcellation = weighted regions 加权区域
- Edge = connection between nodes 边缘=节点之间的连接
- Connectomics = mapping all connections between all brain regions  
连接组 = 映射所有大脑区域之间的所有连接



# Analysis steps

## 分析步骤



- Node definition 节点定义
- Timeseries extraction 时间序列提取
- Edge calculation 边缘计算
- Network matrix 网络矩阵
- Group analysis 组分析

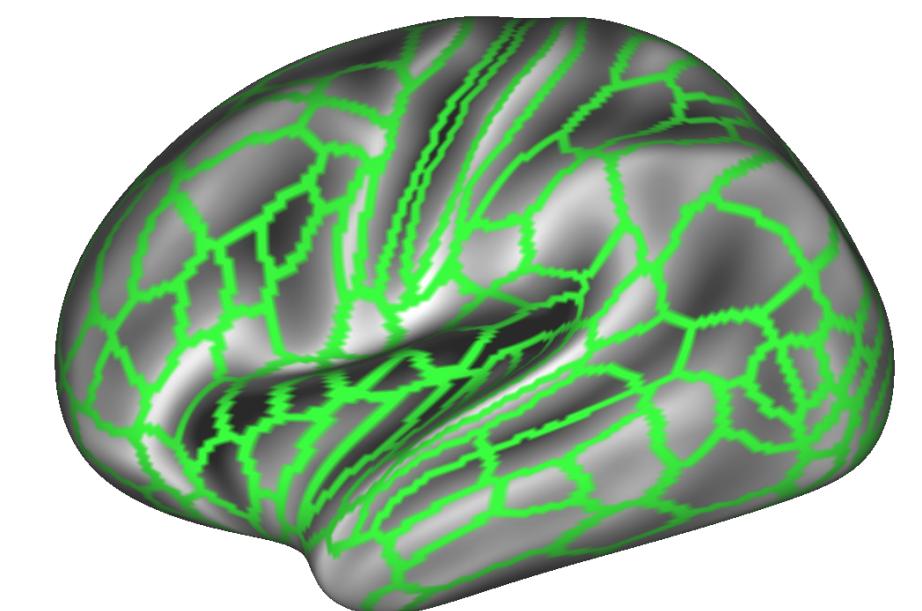
# Node definition

## 节点定义

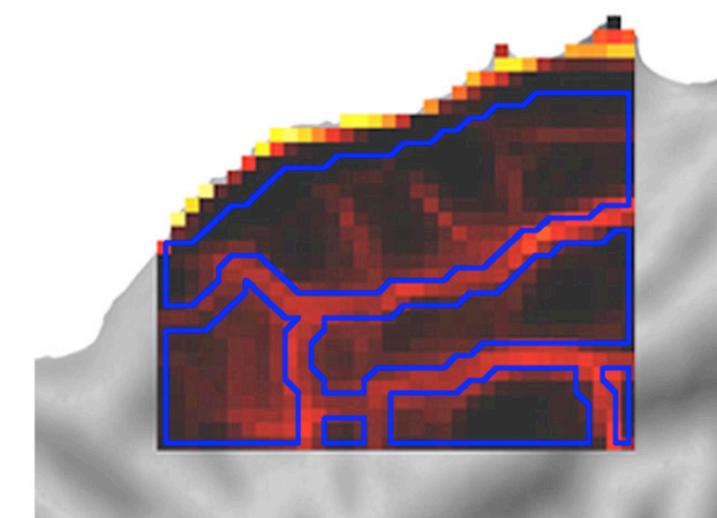
Anatomical atlases  
结构模板



Functional atlases  
功能模板



Data-driven parcellation  
数据驱动分区

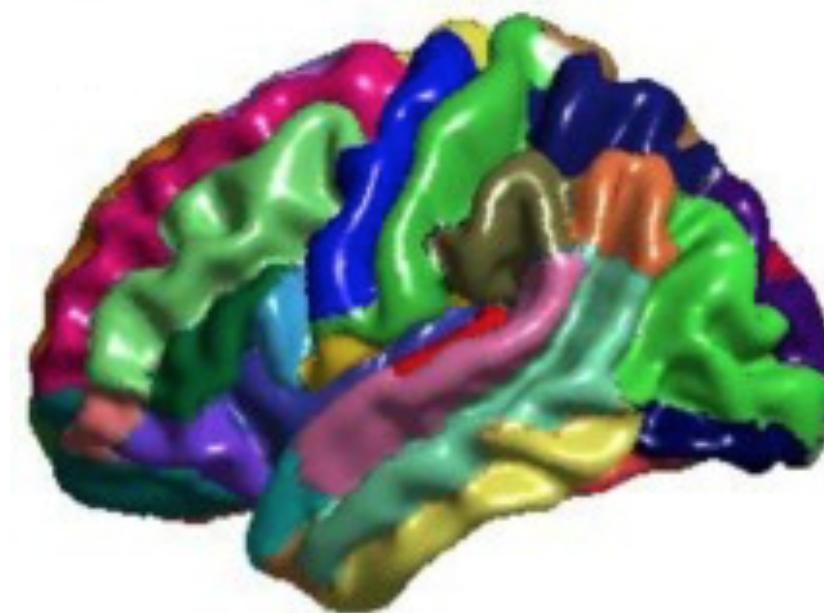


# Node definition

## 节点定义

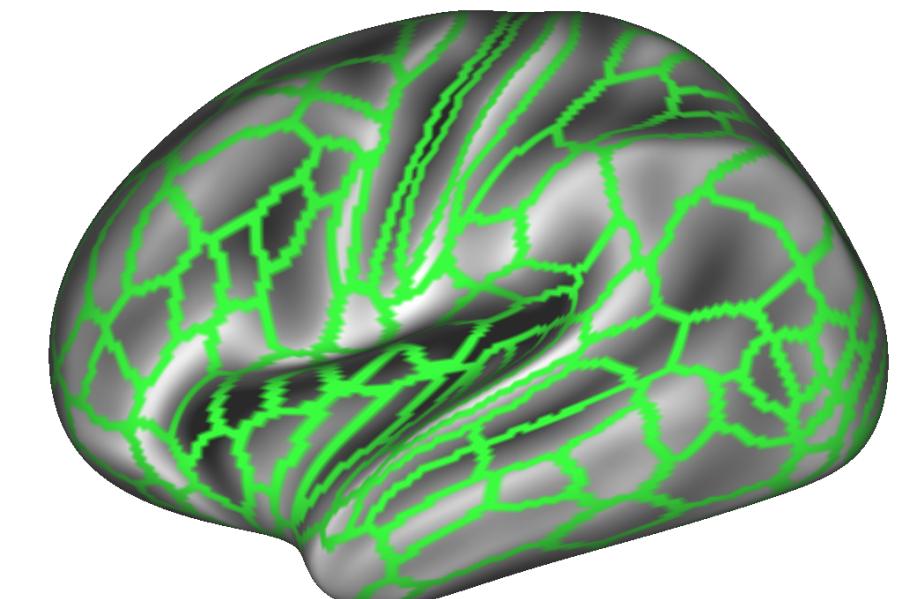
### Anatomical atlases

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

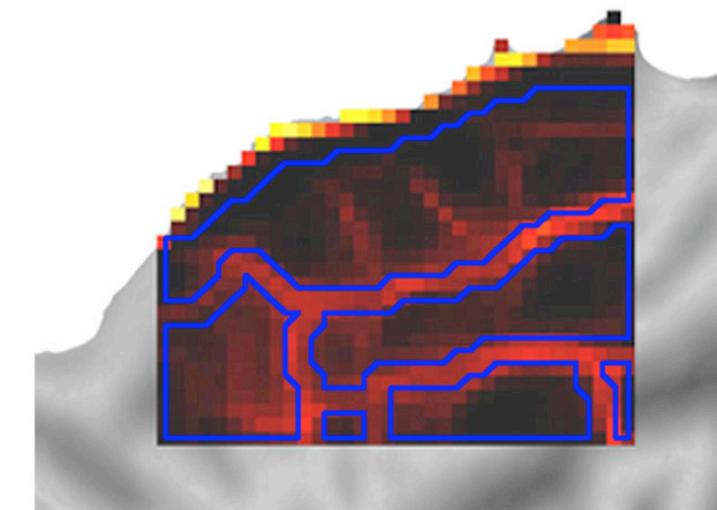


### Functional atlases

尽可能避免，因为通常基于少量被试，对功能边界不能良好的估计



### Data-driven parcellation

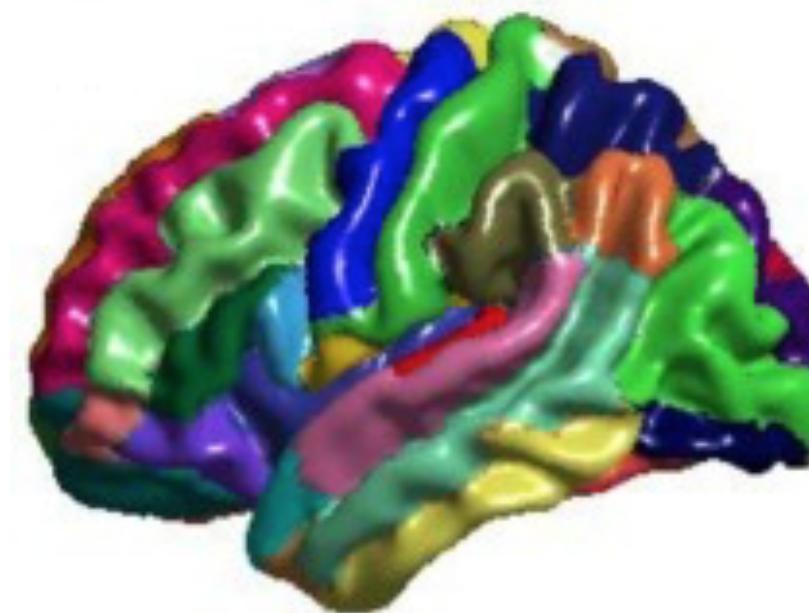


# Node definition

## 节点定义

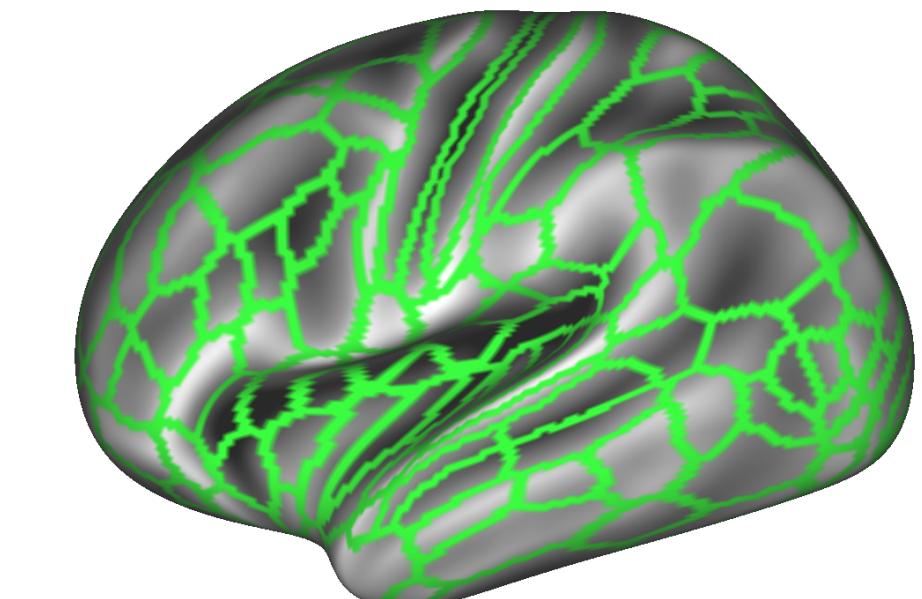
### Anatomical atlases

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



### Functional atlases

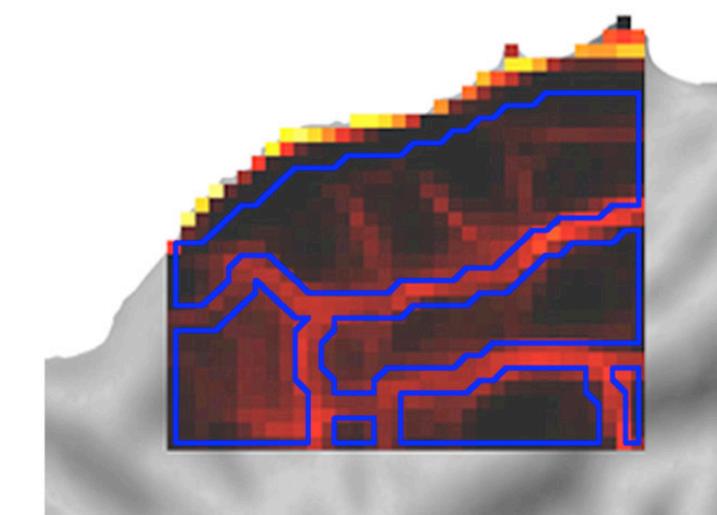
- Yeo 2011/ Glasser 2016
- Many good functional atlases available, though few comparison studies
- How to map onto individuals is very important



### Data-driven parcellation

虽然很少有比较研究，但可以使用许多功能良好的模板

如何映射到个体空间是非常重要的

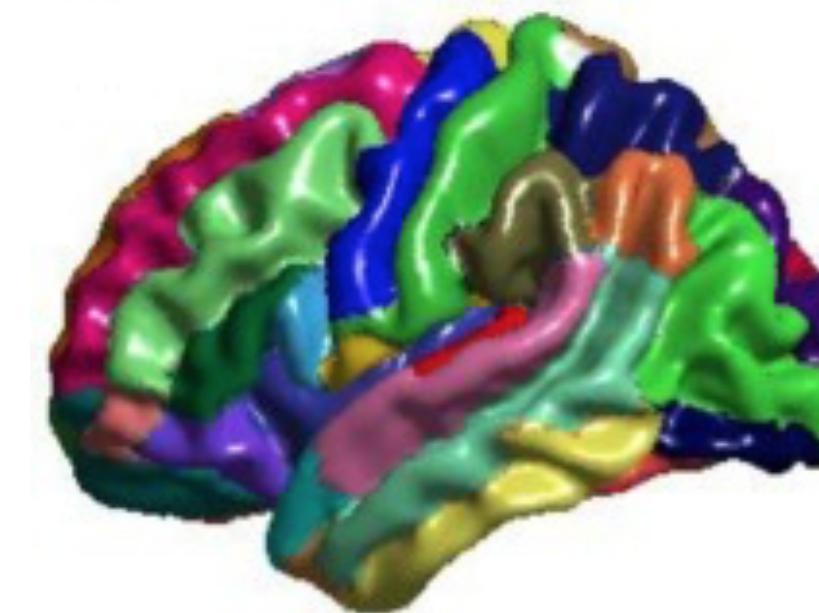


# Node definition

## 节点定义

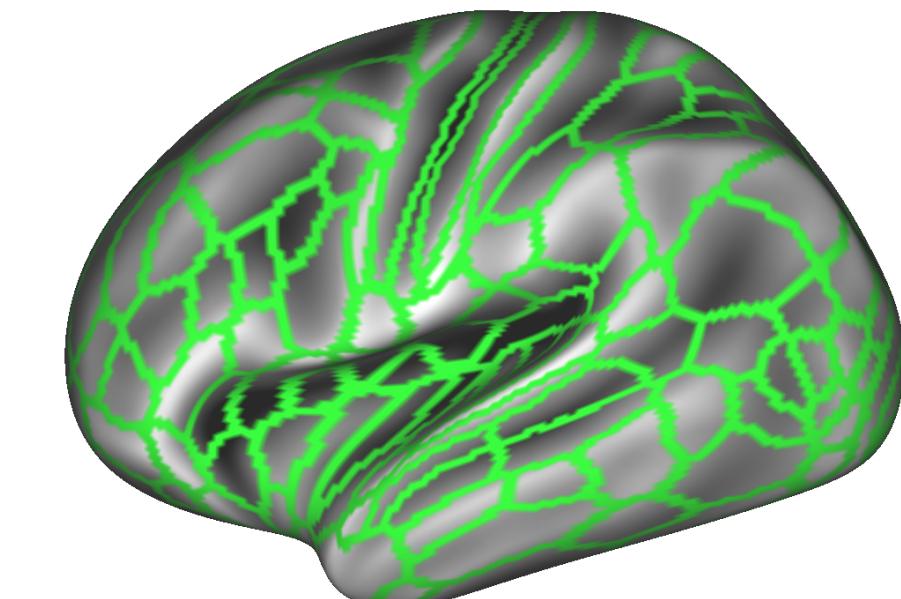
### Anatomical atlases

- Harvard-Oxford/ AAL
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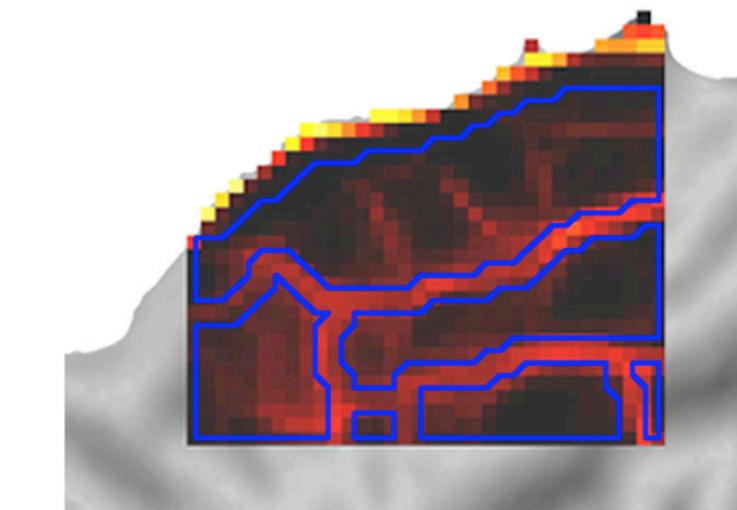
### Functional atlases

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



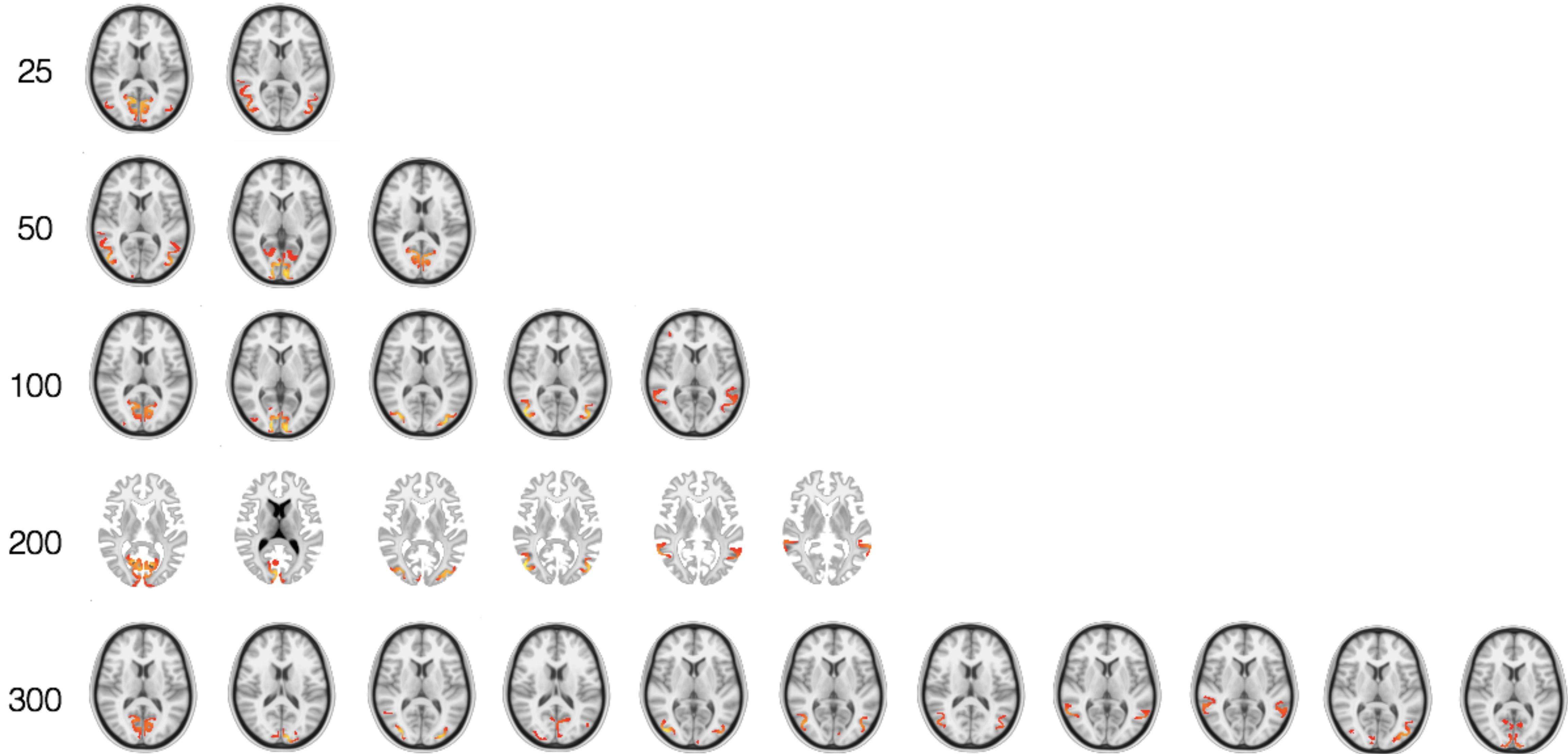
### Data-driven parcellation

- ICA/ Clustering/ Gradients
- Estimate parcellation from the same dataset used for further analyses  
从用于进一步分析的相同数据集中估算分区
- How to map group parcellation onto individuals very important  
如何将组分割映射到个体非常重要



# ICA for parcellation

## ICA分区



# Timeseries extraction

## 时间序列提取

### Hard parcellation:

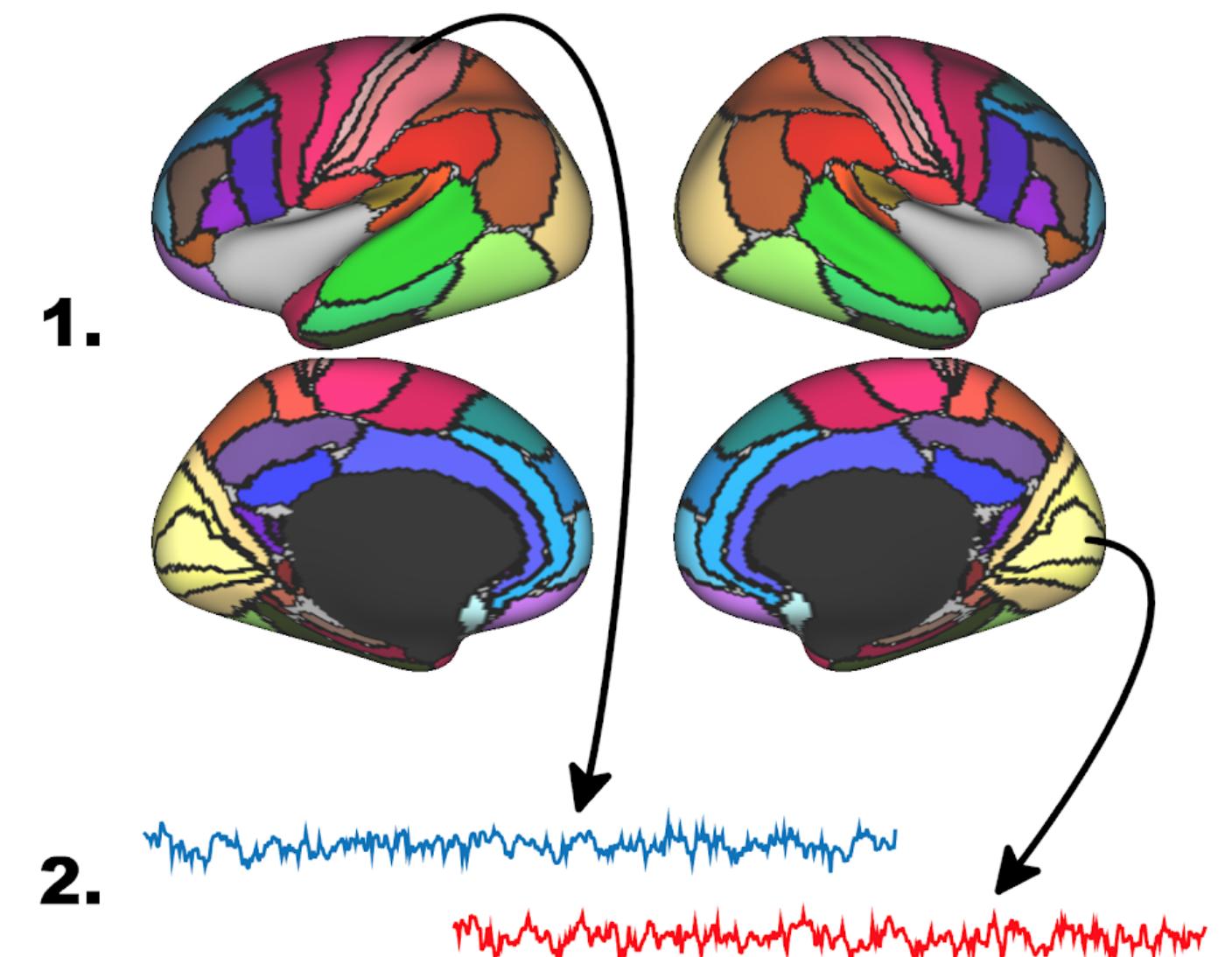
- Masking (mean timeseries) 掩板 (平均时间序列)
- Eigen timeseries (PCA) 特征时间序列 (PCA)
- Using multilayer classifier 使用多层分类器

### ICA (soft parcellation):

- **Thresholded** dual regression/ back projection  
阈值双重回归/反投影

### Alternative: 其他

- Hierarchical estimation of group & subject 组、个体的分层估计
- e.g. PROFUMO

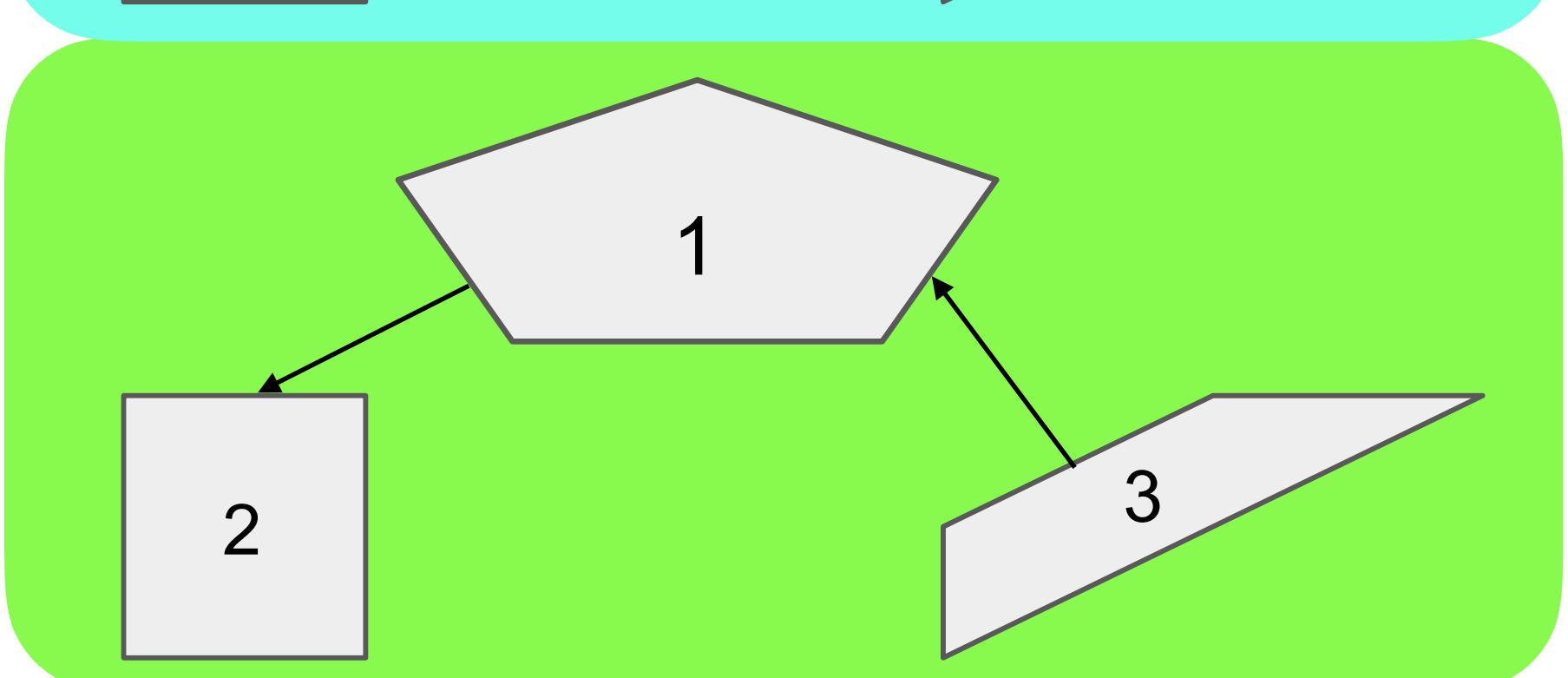
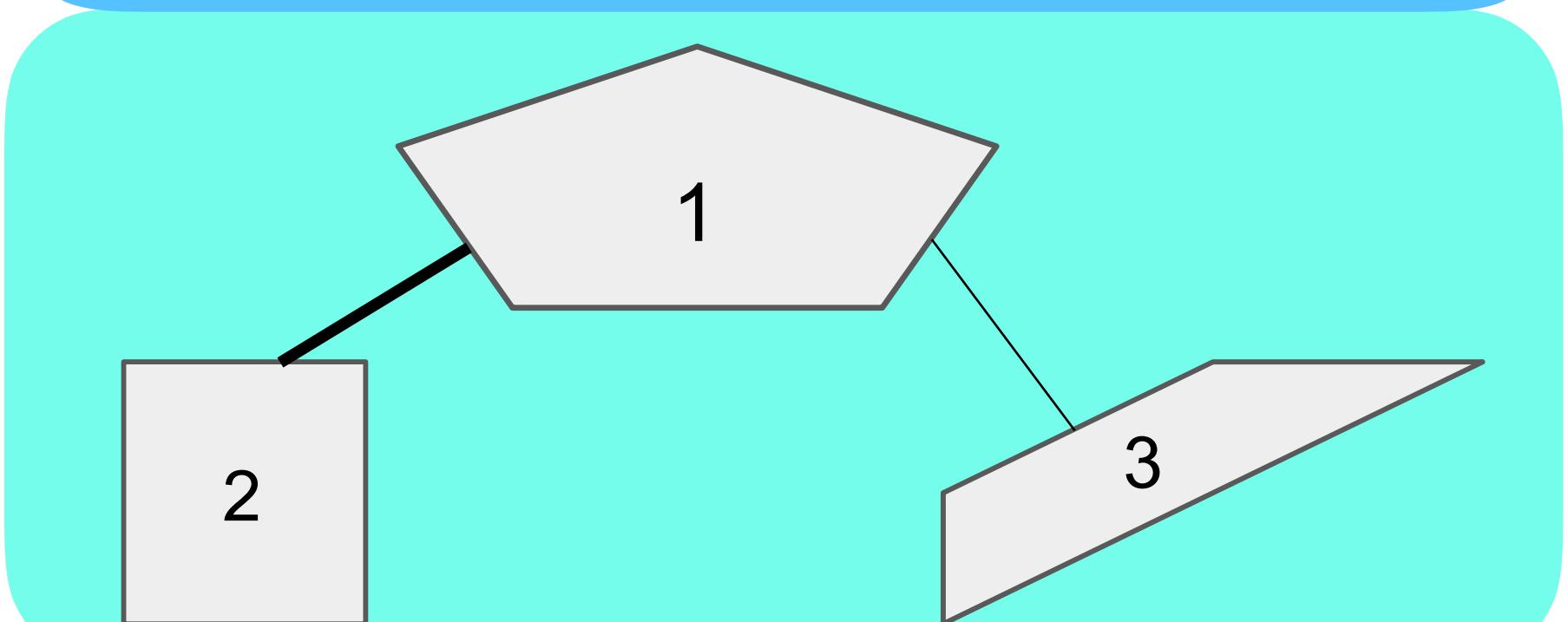
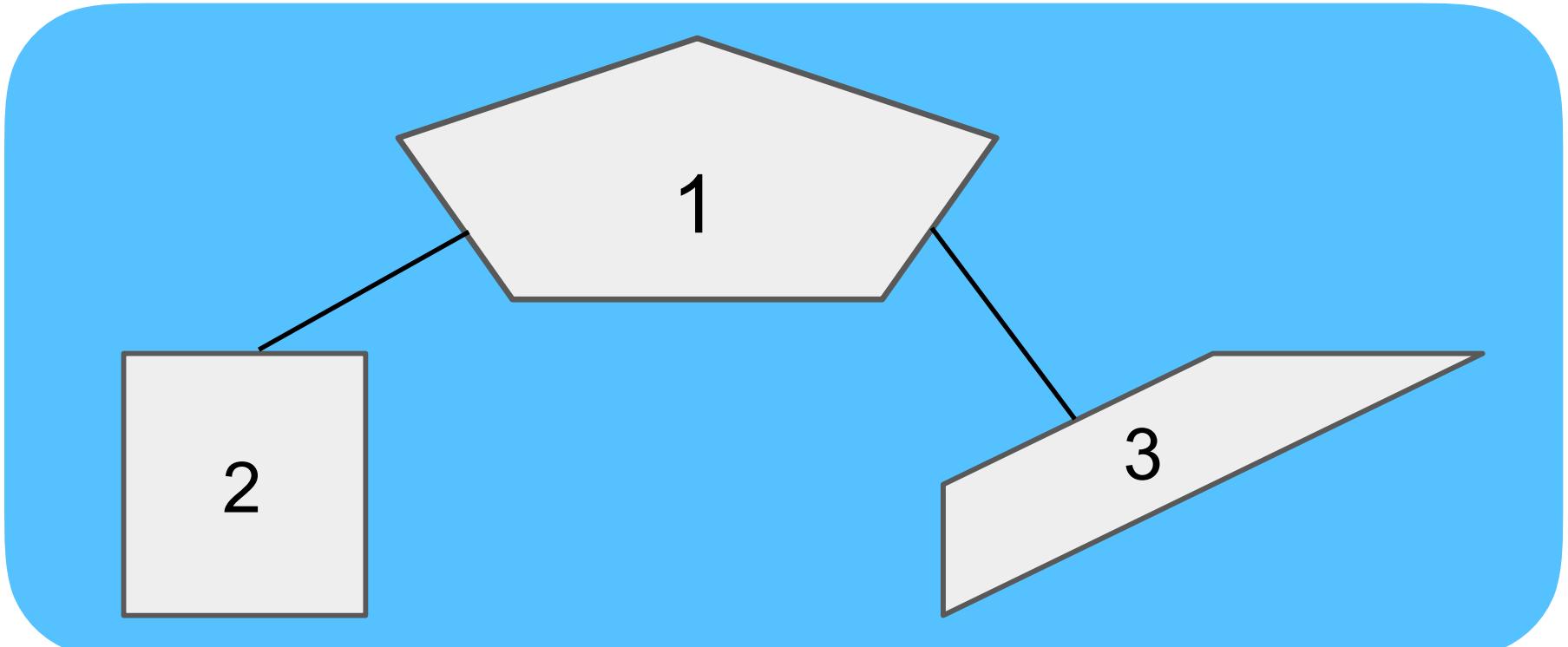




# Edge calculation

## 边缘计算

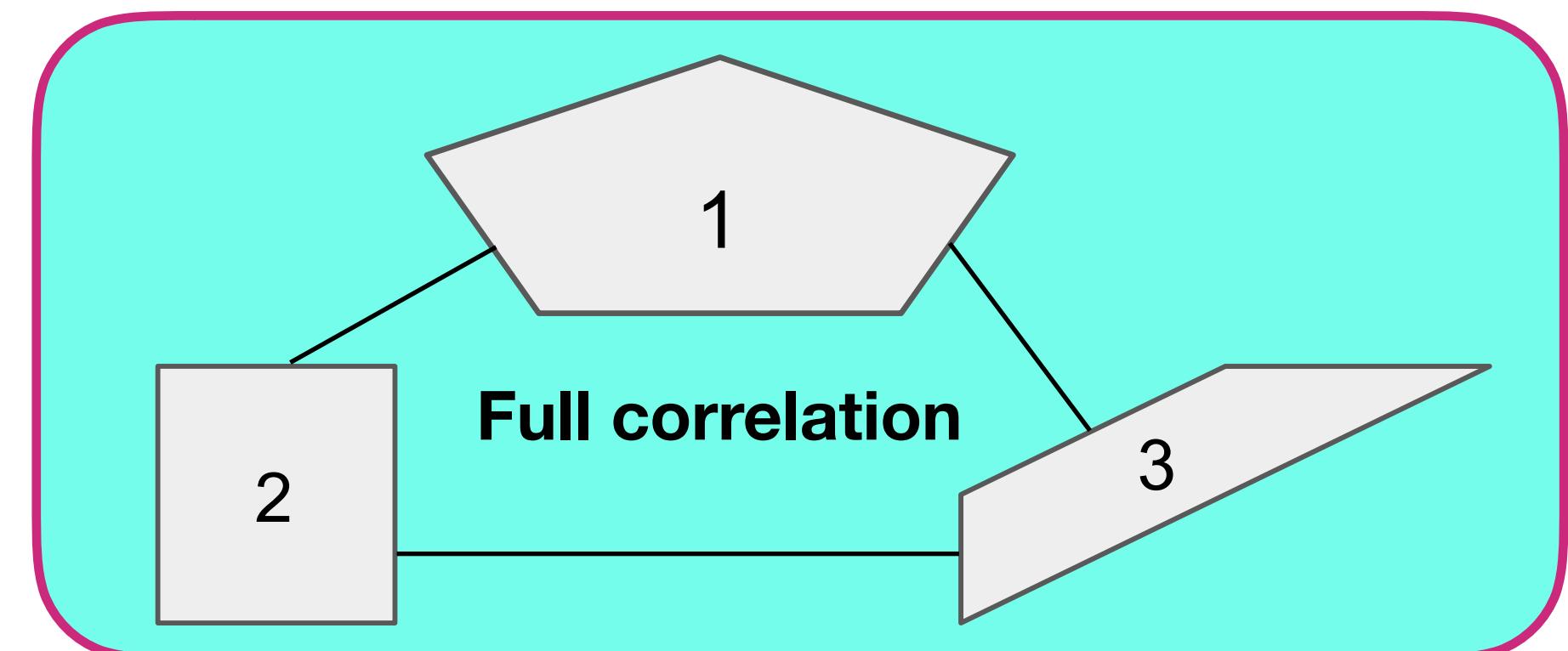
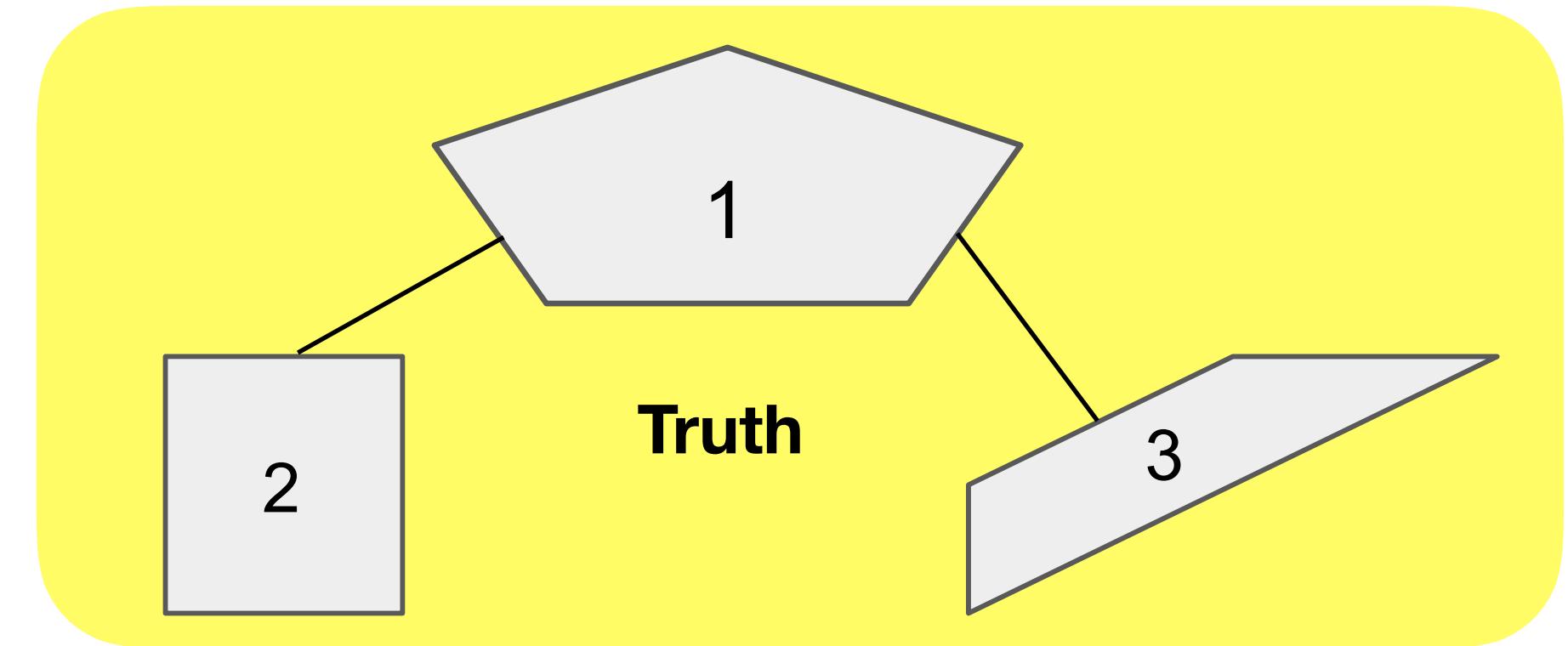
- Presence/ absence of edges 存在/不存在边缘
- Strength of edges 边缘强度
- Directionality of edges 边缘的方向性



# Direct versus indirect connections

## 直接连接与间接连接

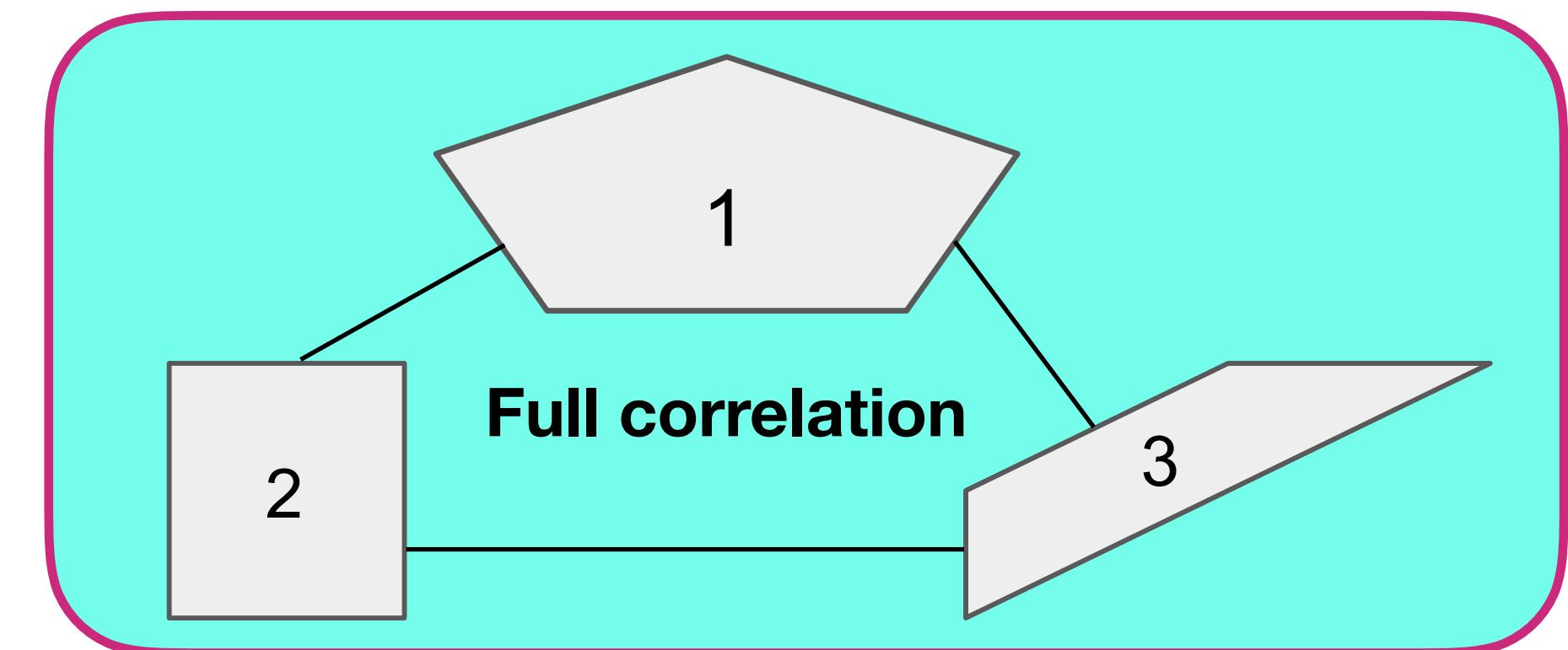
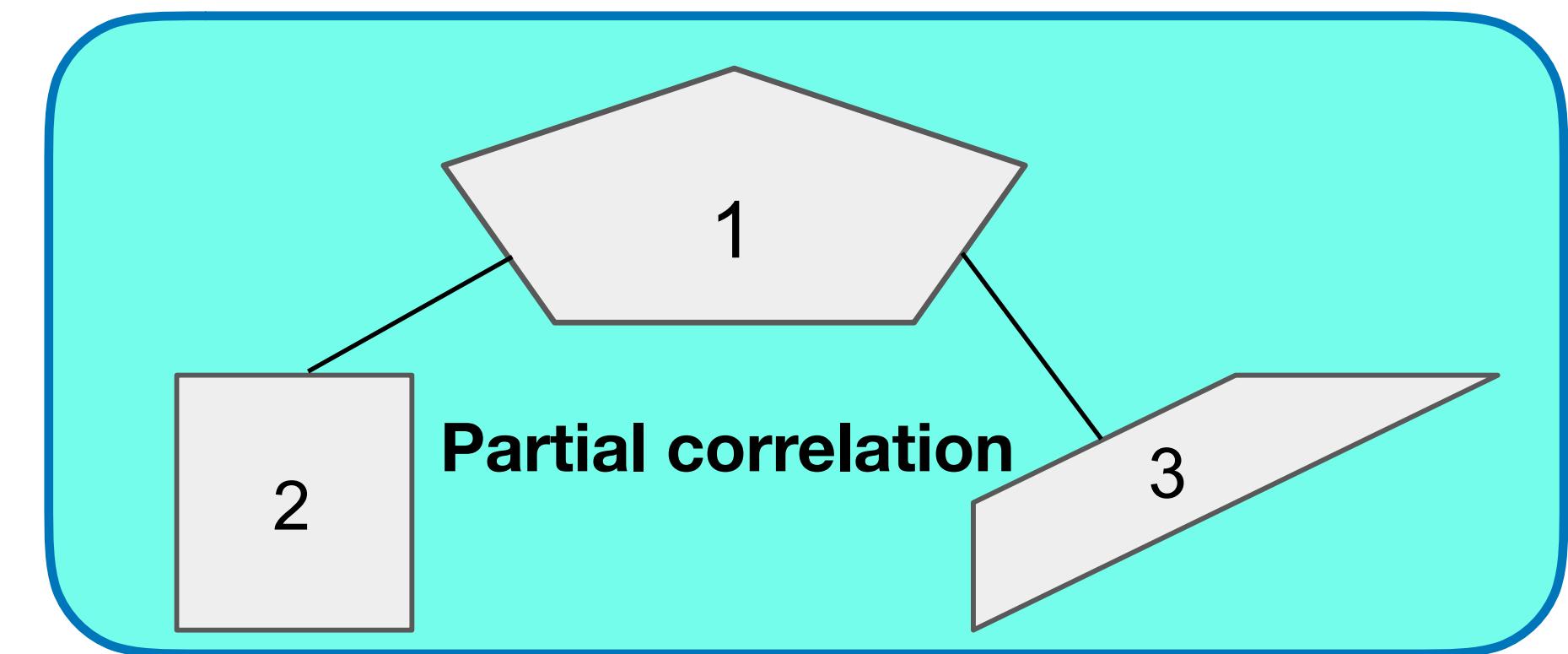
- Correlation between 2 and 3 will exist  
2和3之间存在相关性
- Therefore full correlation will  
incorrectly estimate connection 2-3  
因此，完全相关将错误地估计连接2-3
- 2-3 is an indirect connection  
2-3是间接连接



# Partial correlation

## 偏相关

- Before correlating 2 and 3, first regress 1 out of both (“orthogonalise wrt 1”) 在关联2和3之前，首先从两者中回归1 (“正交wrt 1”)
  - If 2 and 3 are still correlated, a direct connection exists 如果2和3仍然相关，则存在直接连接
- More generally, first regress all other nodes’ timecourses out of the pair in question 更一般地说，首先从所讨论的对组中回归所有其他节点的时间序列
  - Equivalent to the inverse covariance matrix 等效于逆协方差矩阵





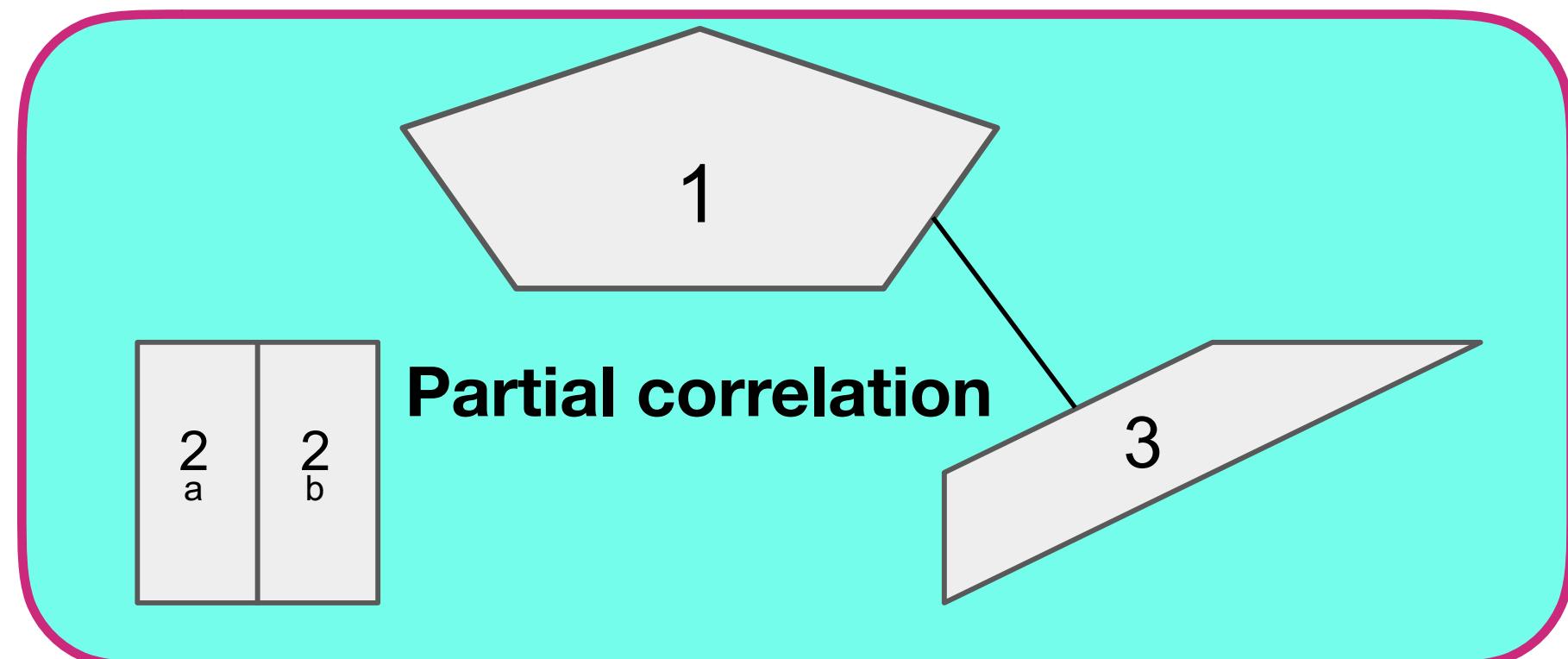
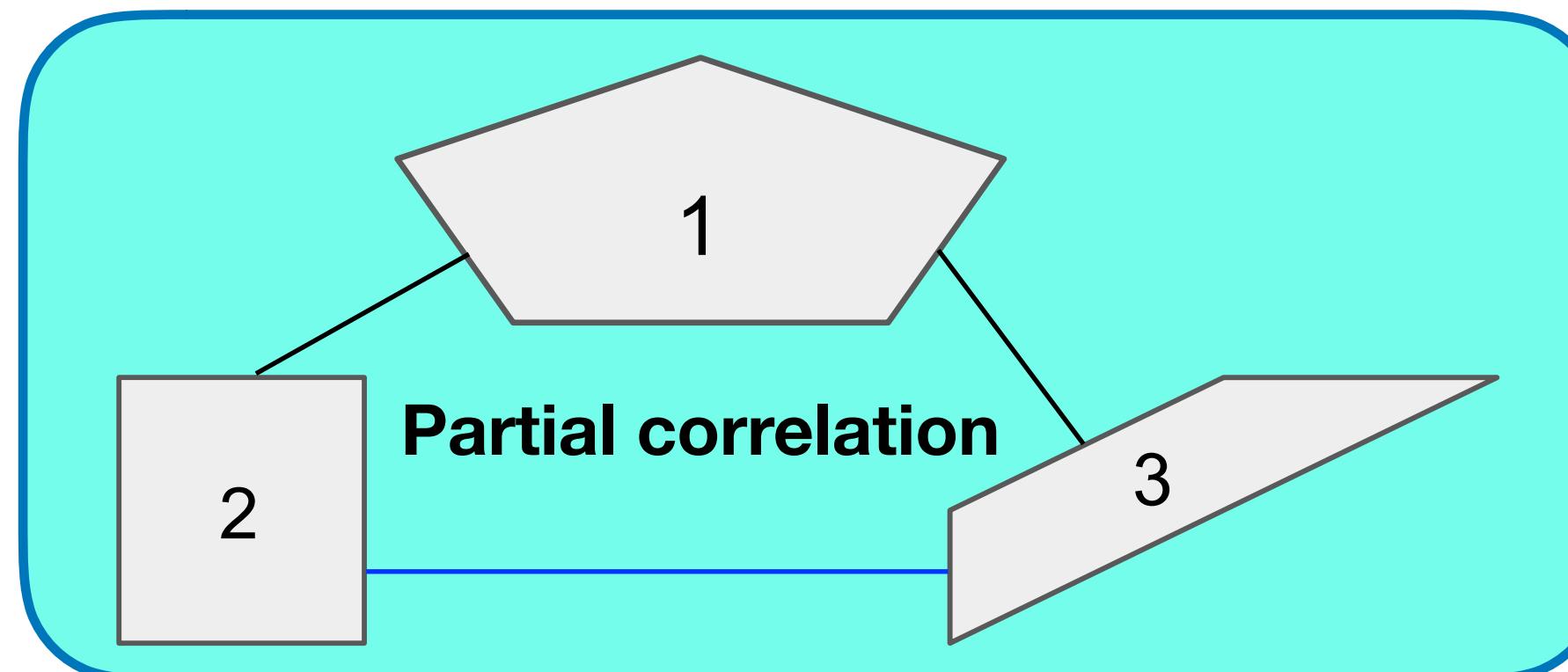
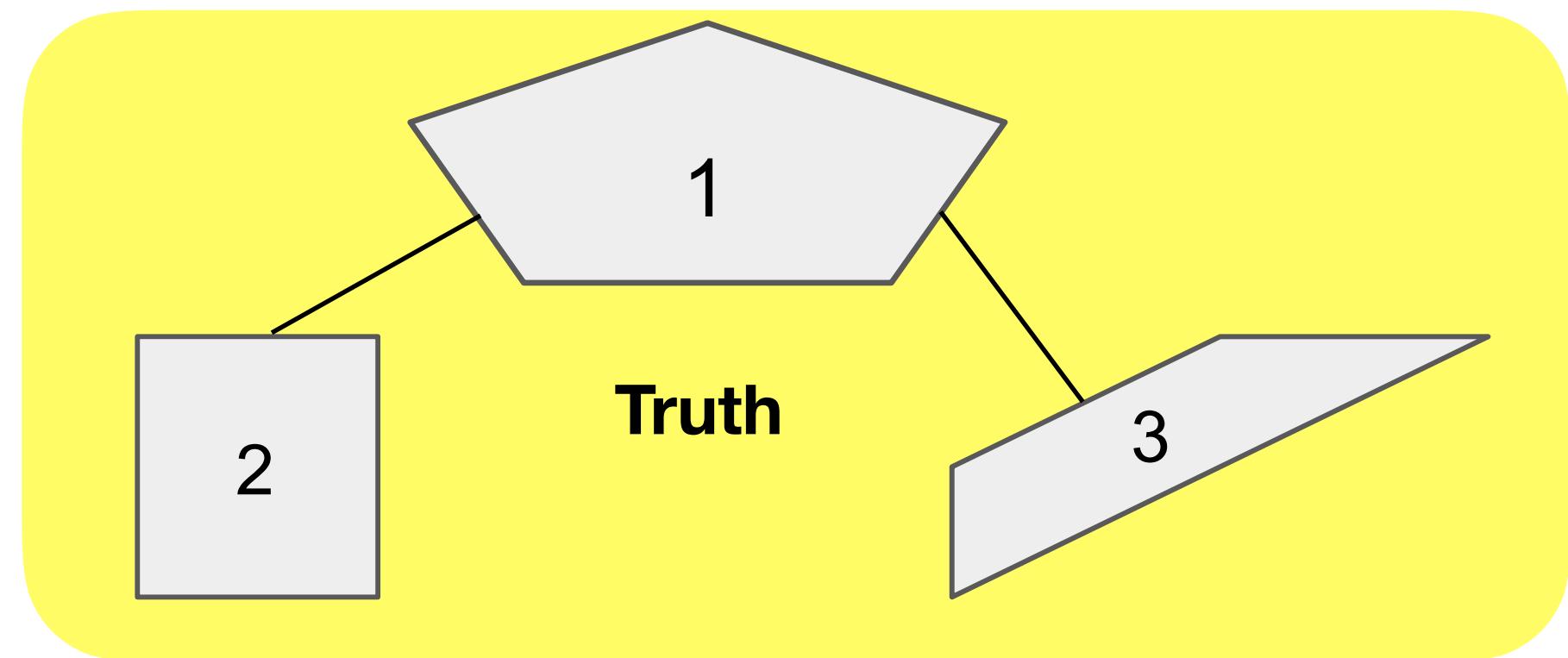
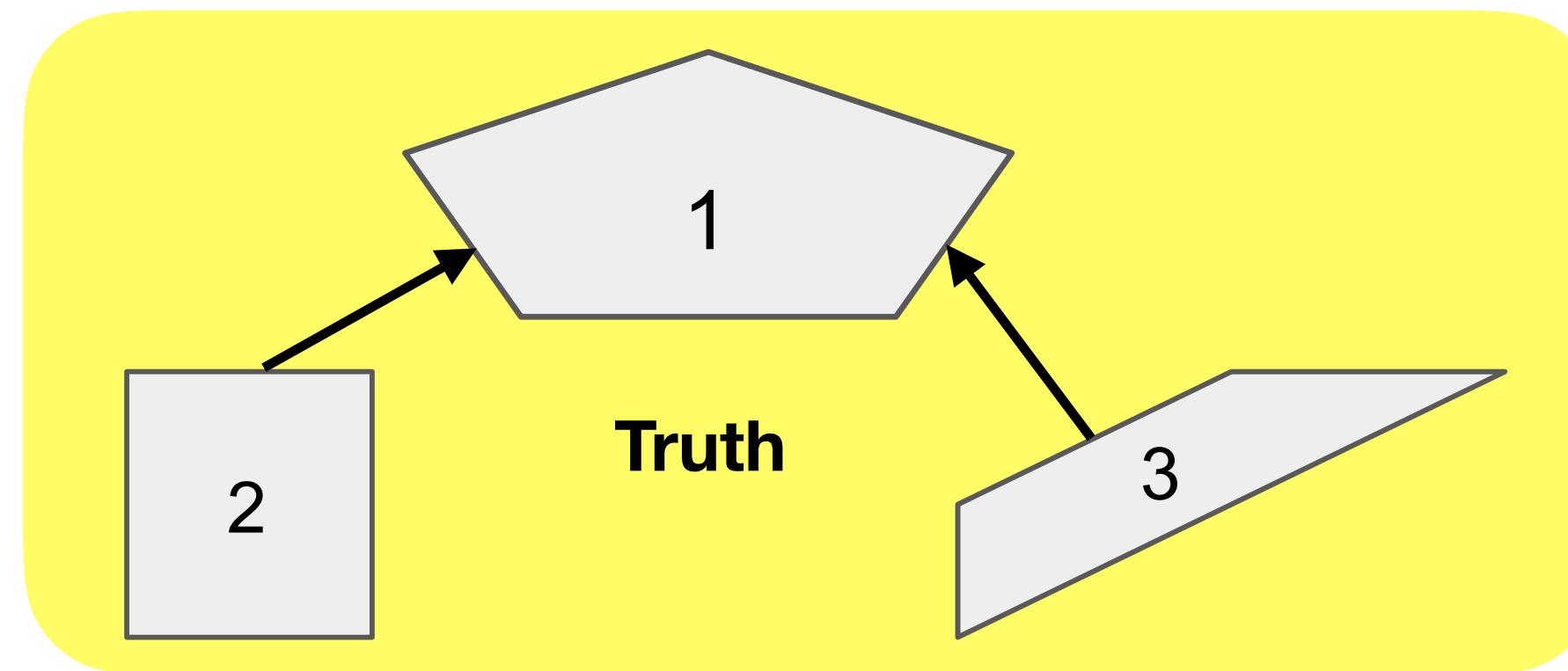
# Regularisation

## 正规化

- Urgh! If you have 200 nodes and 100 timepoints, this is impossible! Urgh!  
如果你有200个节点和100个时间点，这是不可能的！
- A problem of DoF - need large #timepoints - #nodes DoF的问题 - 需要大的#时间点 - #节点
- 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)  
当反转“秩不足”矩阵时，通常用一些数学条件来辅助它，例如，强制它稀疏（强制估计为零的低值）
- Regularised partial correlation (such as ICOV, Ridge) 正则化的偏相关 (如ICOV, Ridge)
- But still important to maximise temporal degrees of freedom 但是最大化时间自由度仍然很重要

# Need to carefully define nodes

需要仔细定义节点



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

伯克森悖论=误报 (2-3)

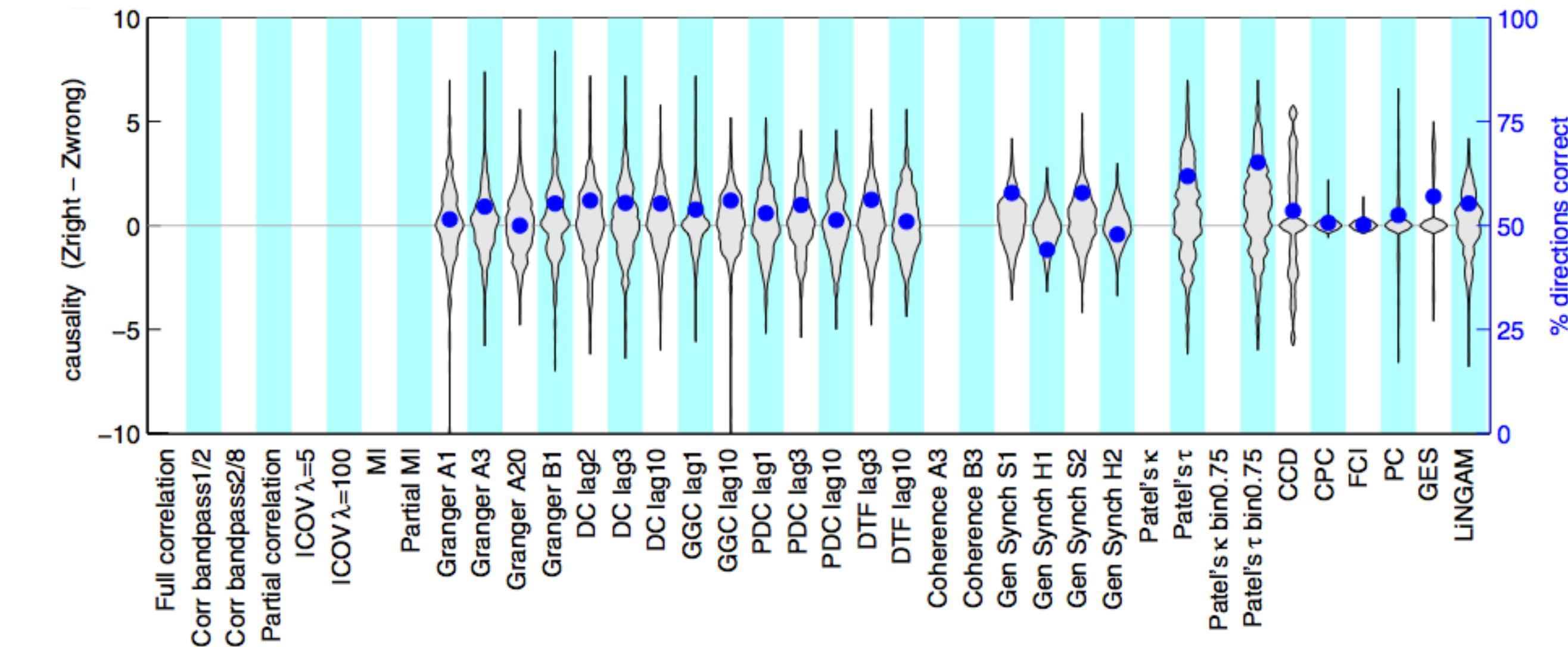
Over-splitting = false negative (1-2)

过度拆分=假阴性 (1-2)

# Directionality of edges

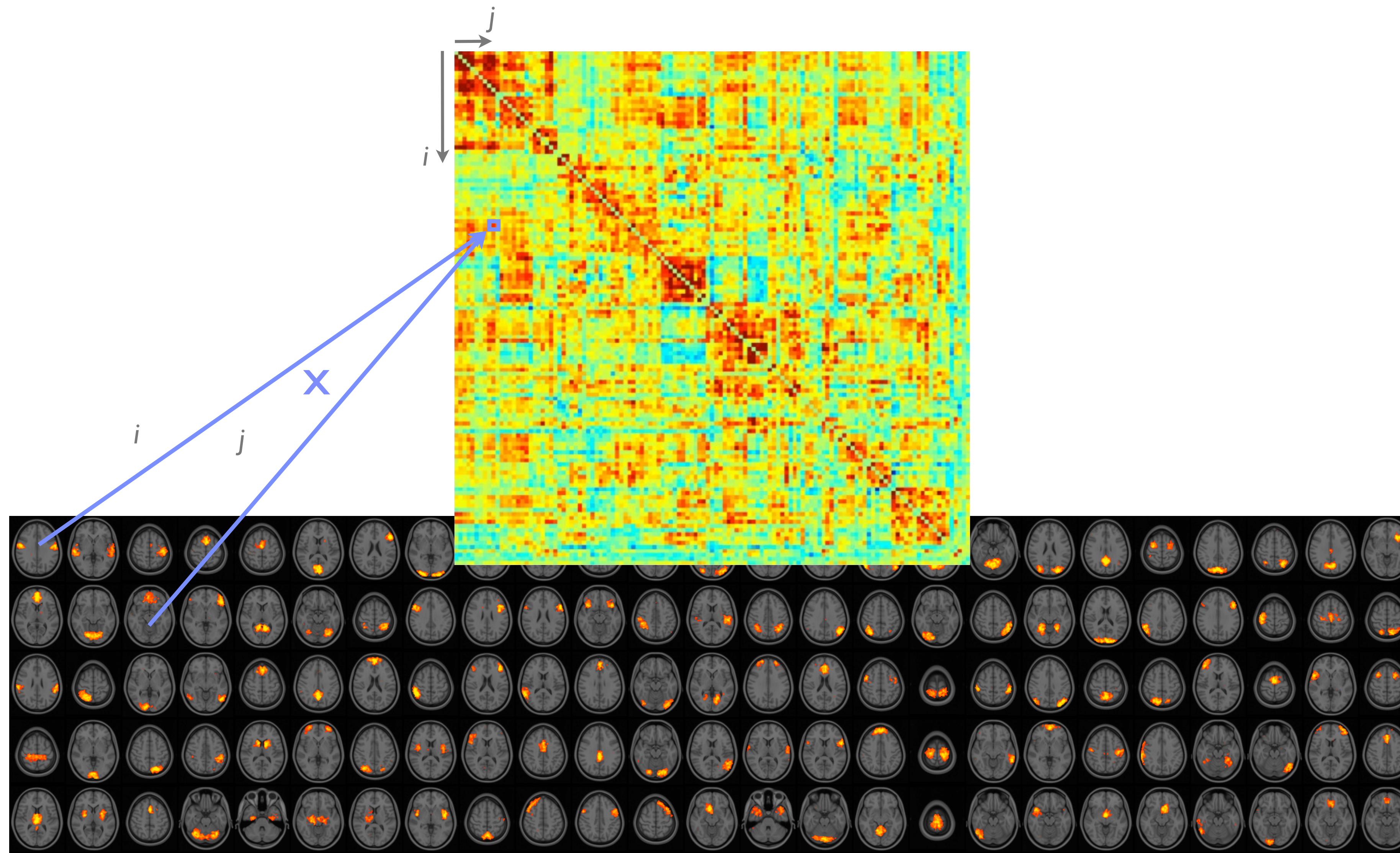
## 边缘的方向性

- Directionality is hard to estimate in BOLD data 在BOLD数据中难以估计方向性
- Don't use lag-based methods such as Granger causality  
不要使用基于事后的方法，例如格兰杰因果关系
- Perhaps directionality is oversimplistic view of neural connectivity (particularly in resting-state)?  
也许方向性是神经连接过于简单的观点（特别是在静止状态下）？



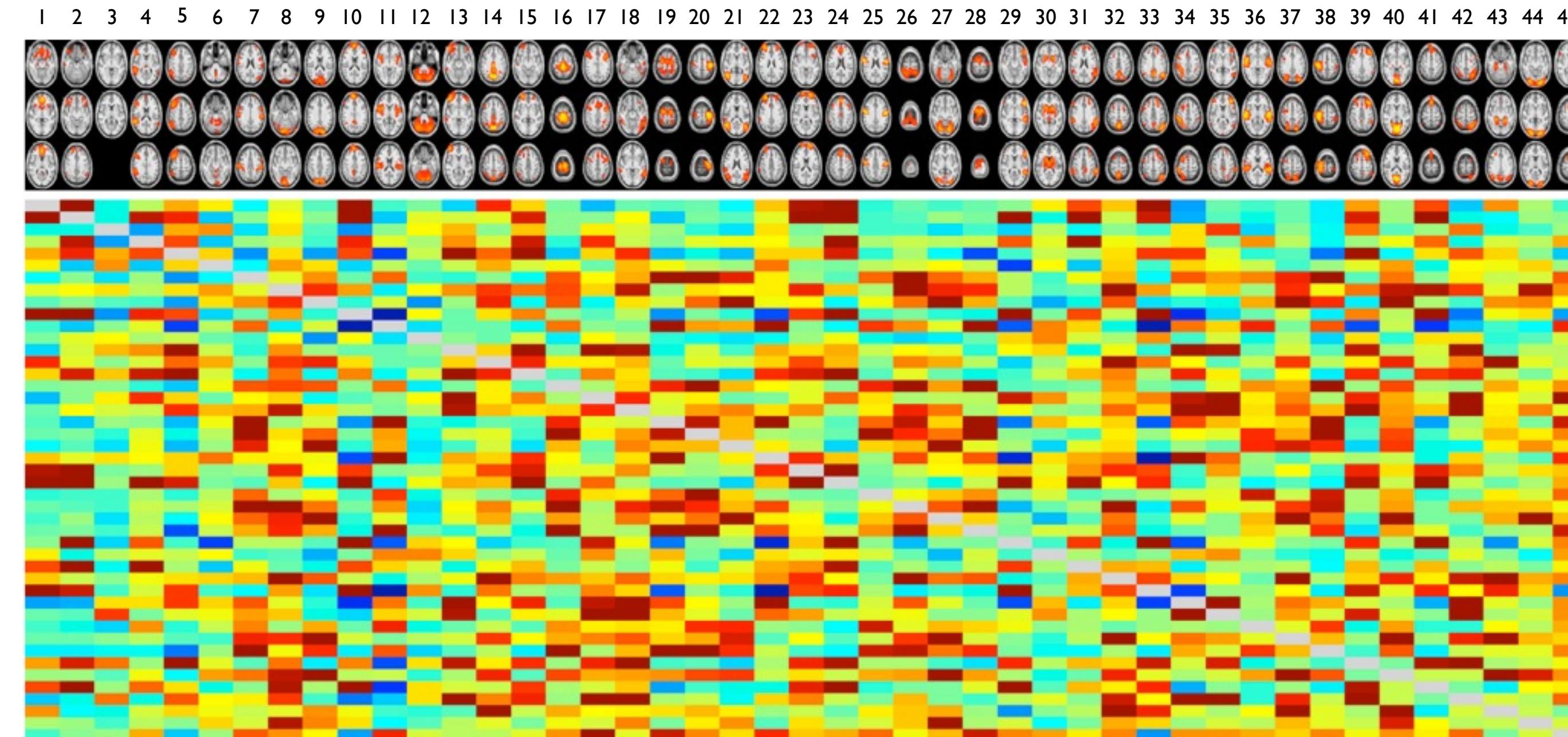
# Building a network matrix

构建网络矩阵



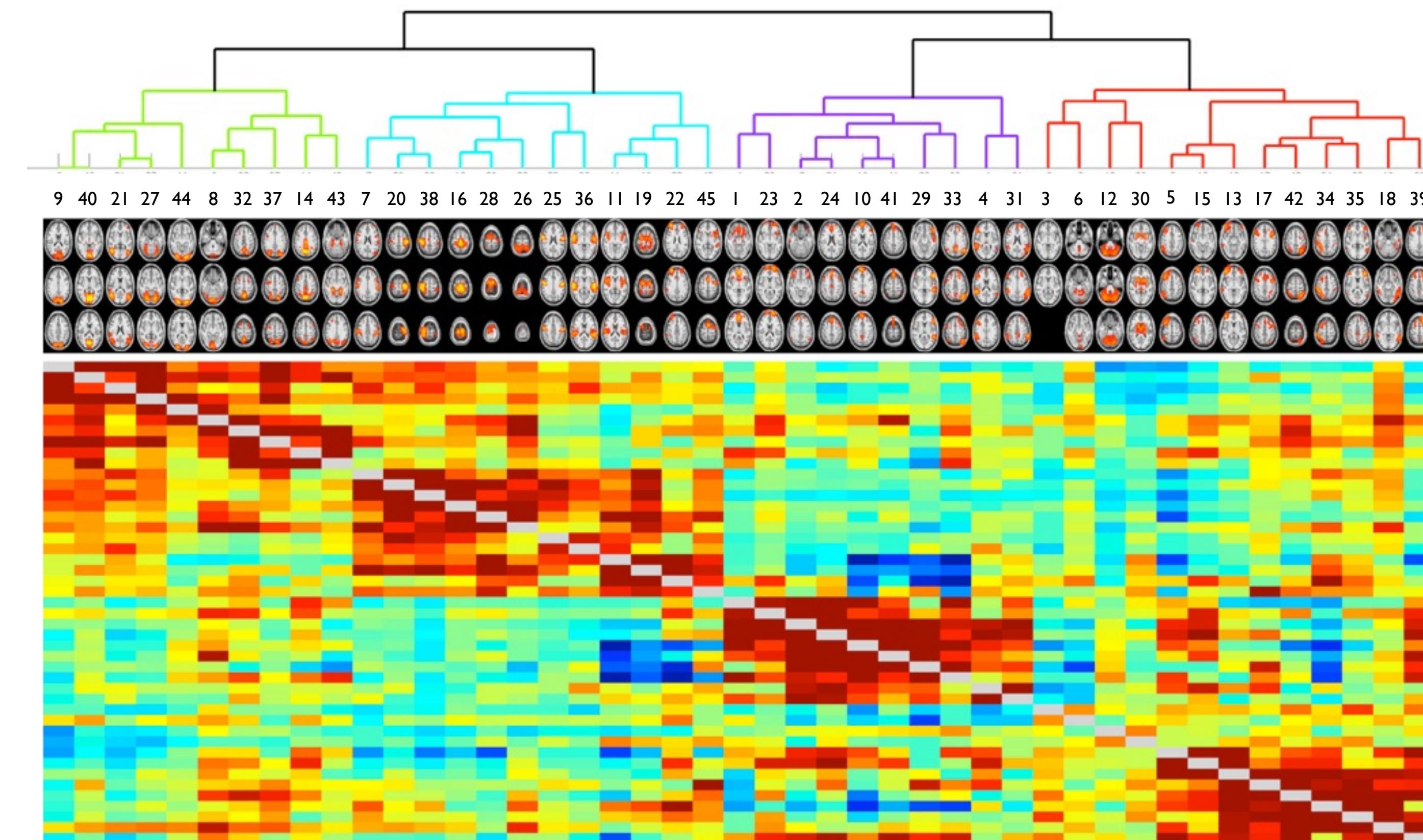
# Network matrix

网络矩阵



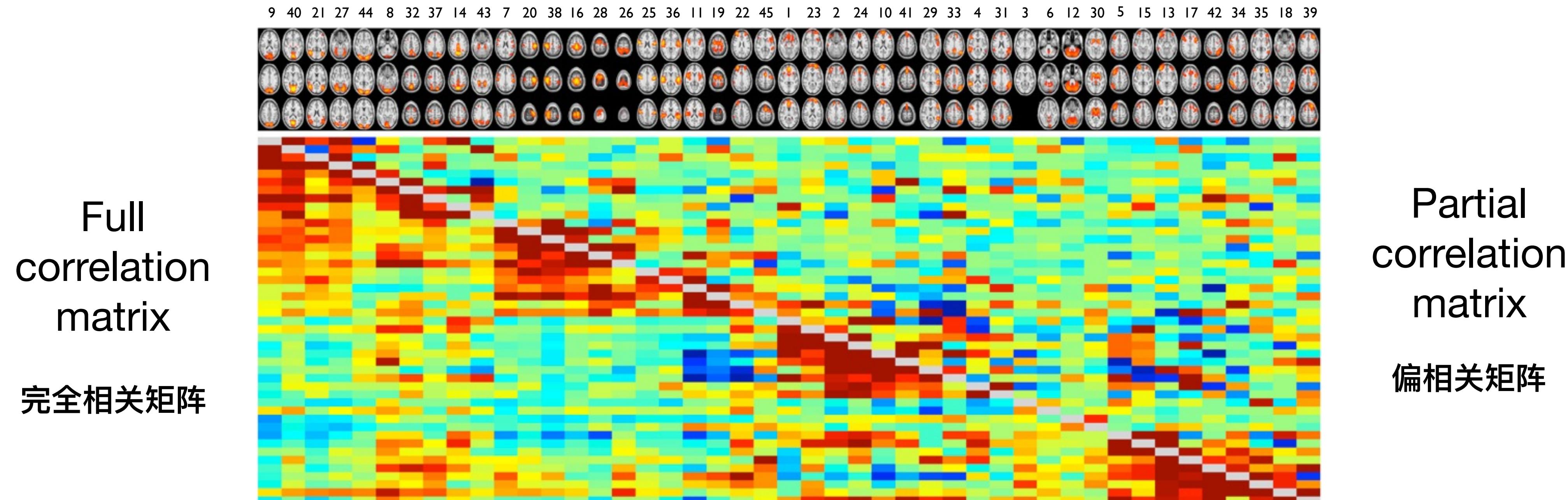
# Hierarchical clustering

分层聚类



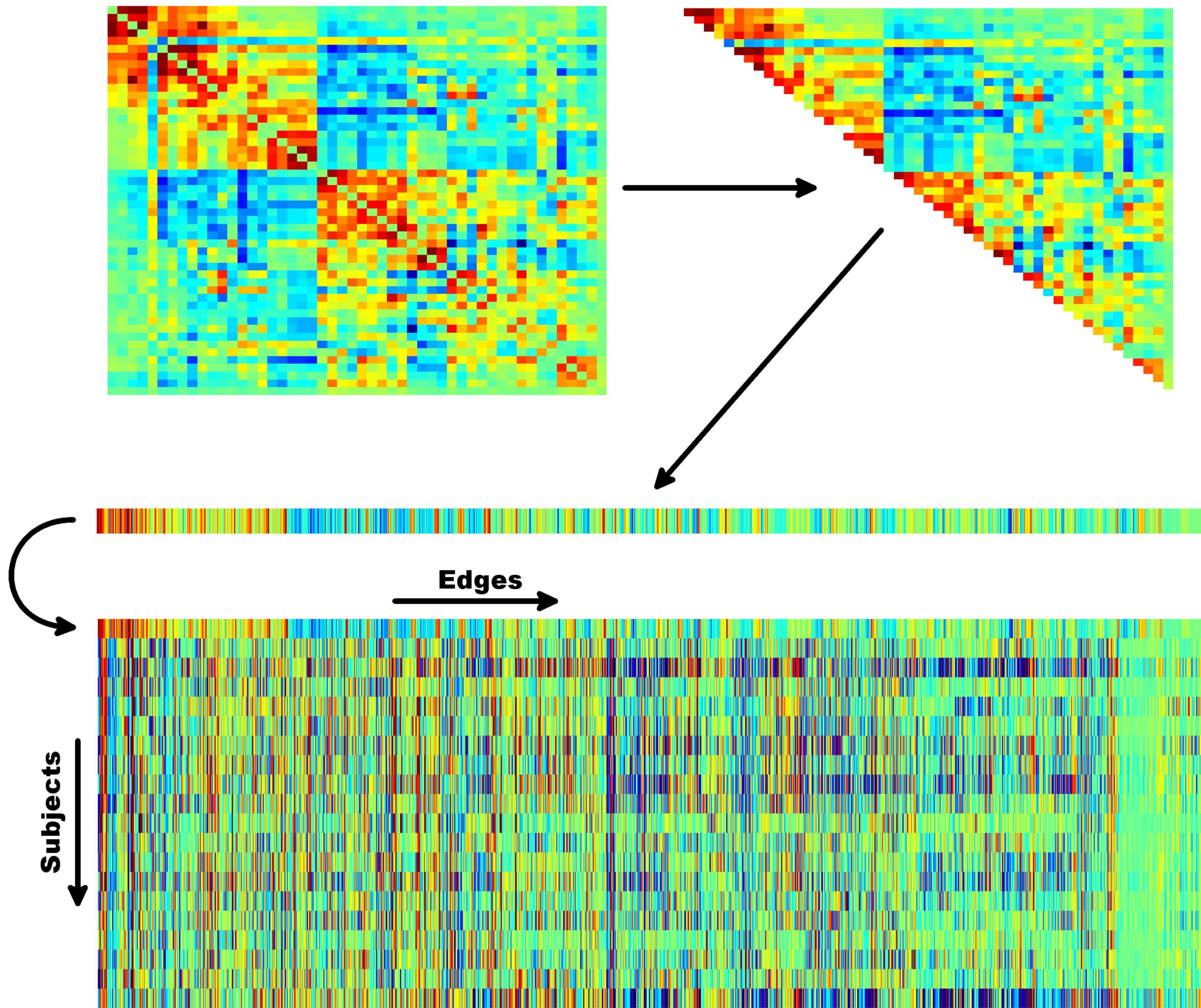
# Partial correlation is sparser than full

部分相关比完全相关更少见



# Group analysis

## 组分析



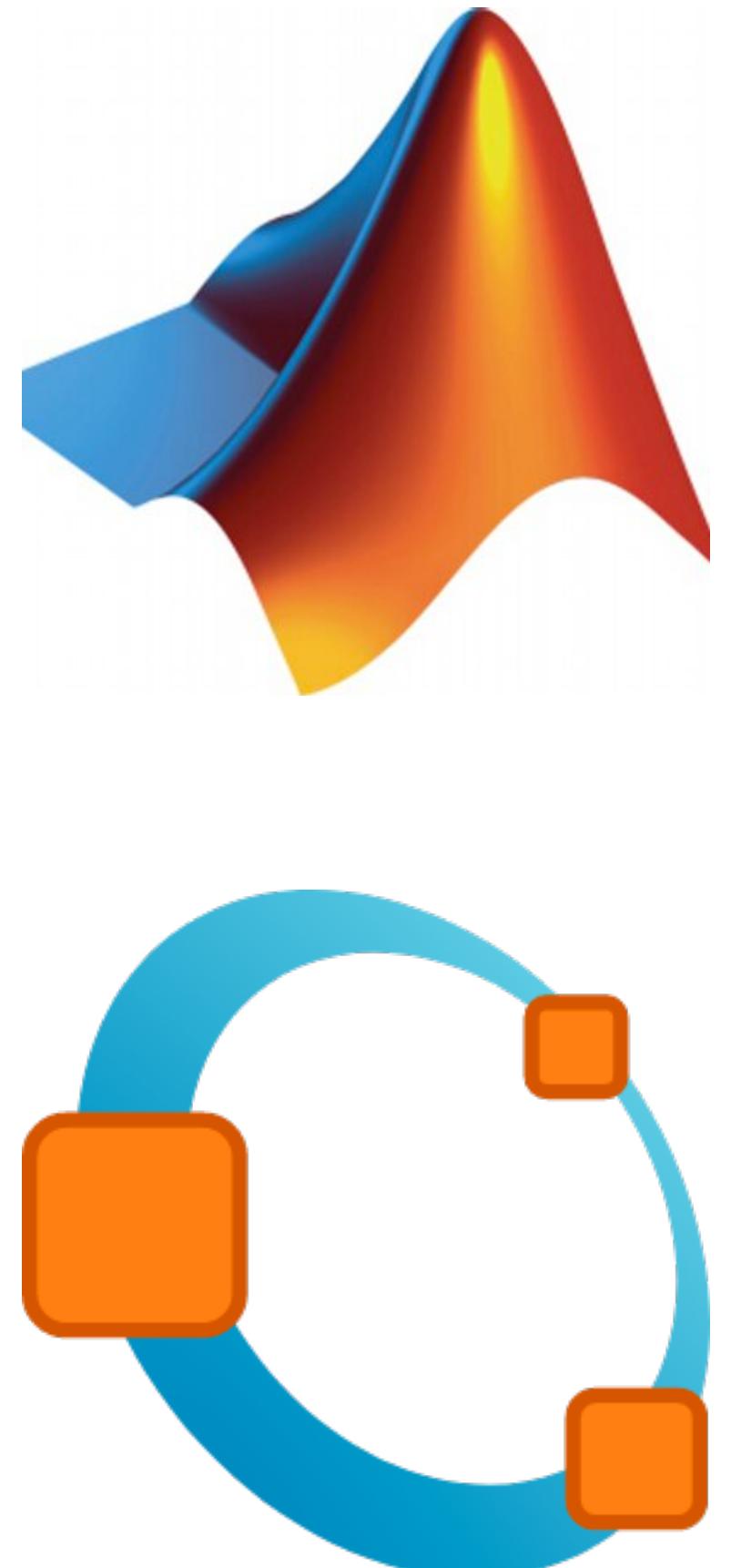
- Calculate network matrix for each subject 计算每个被试的网络矩阵
- Combine all network matrices into one 将所有网络矩阵合并为一个
- Perform group-level comparisons: 组分析
  - Univariate tests for each edge (GLM) 每条边的单变量测试 (GLM)
  - Multivariate prediction methods (SVM) 多变量预测方法 (SVM)



# FSLnets

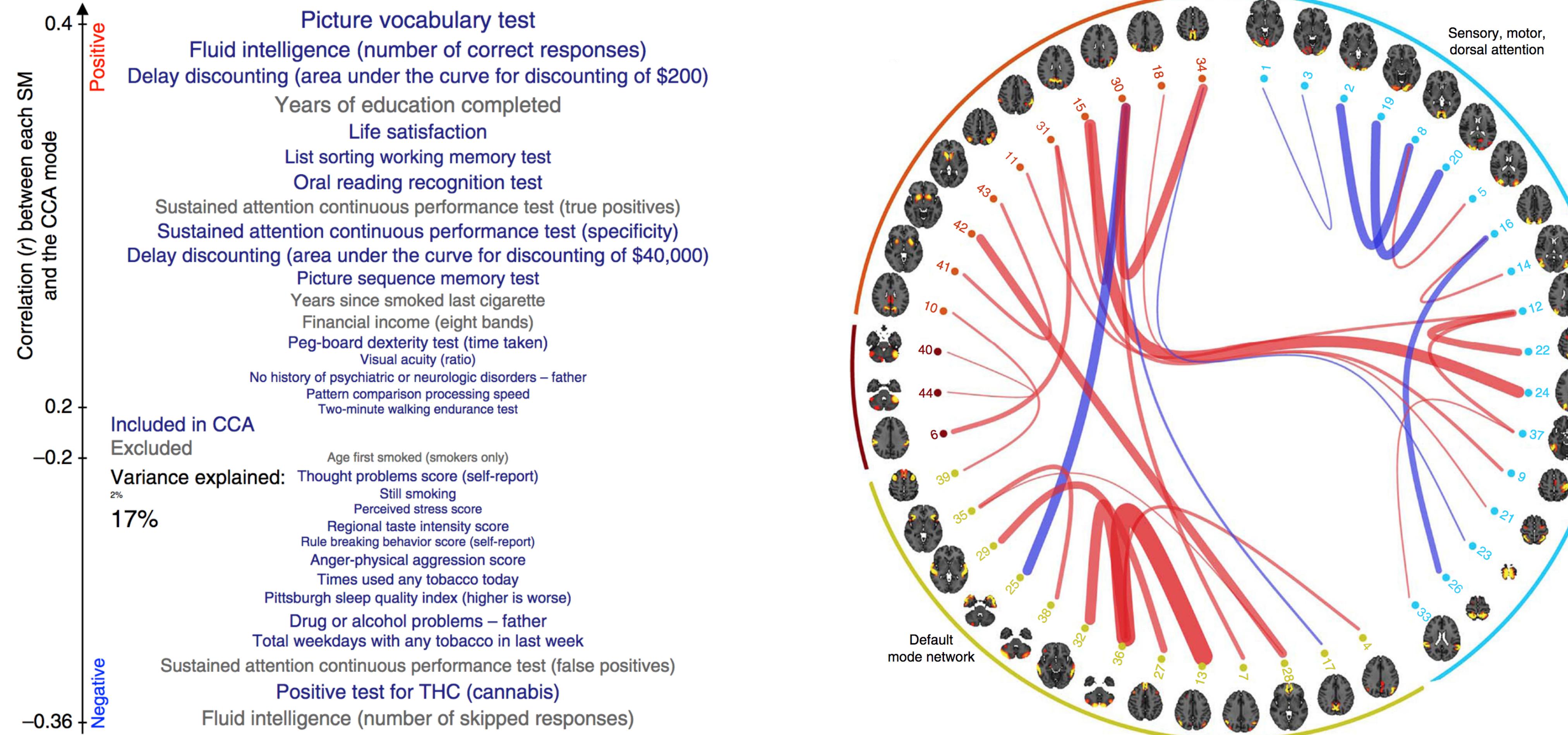
## fsl网络分析

- Currently uses Matlab or Octave 目前使用Matlab或Octave
- Therefore this practical will be a bit different from other practicals 因此，这种分析方法与其他方法略有不同
- More information and download here: 更多信息及下载地址：<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets>



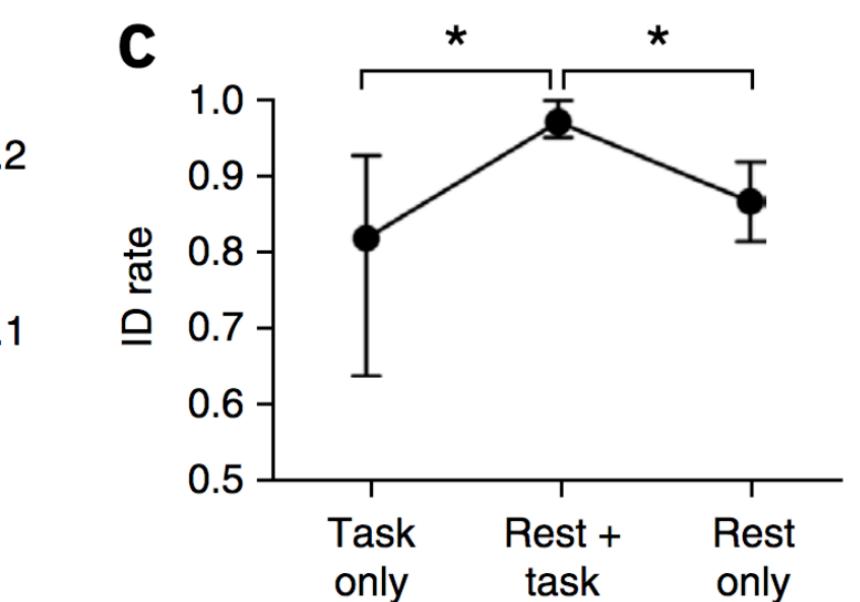
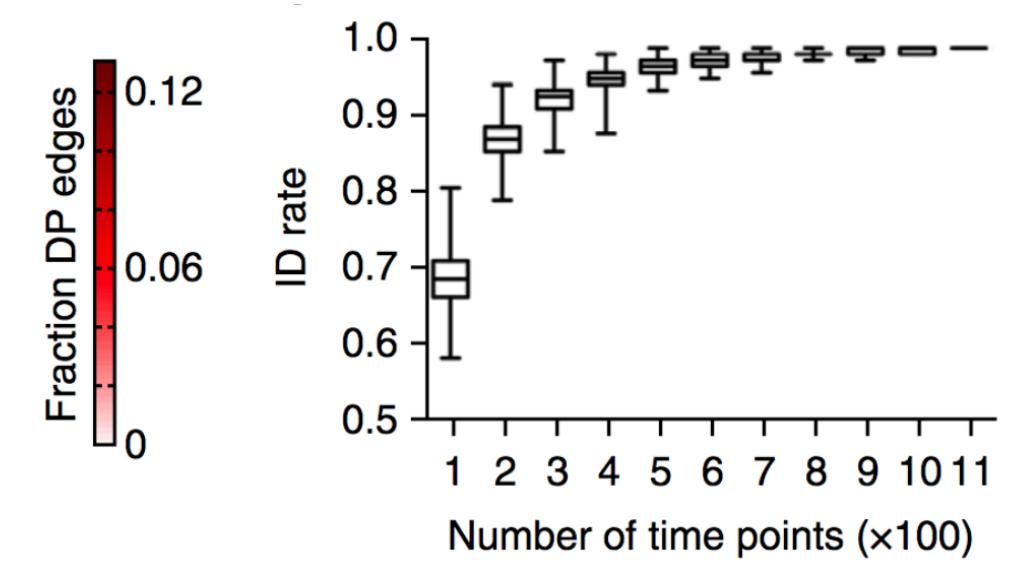
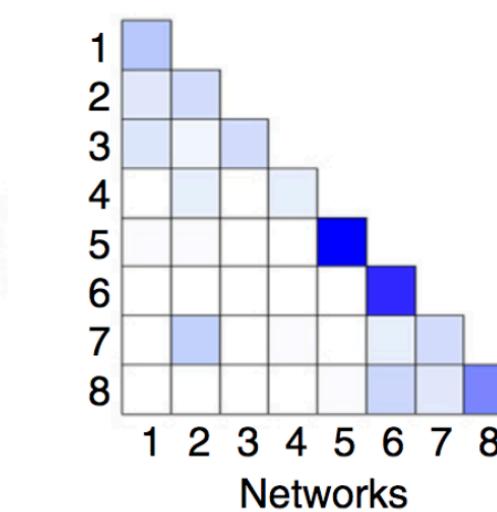
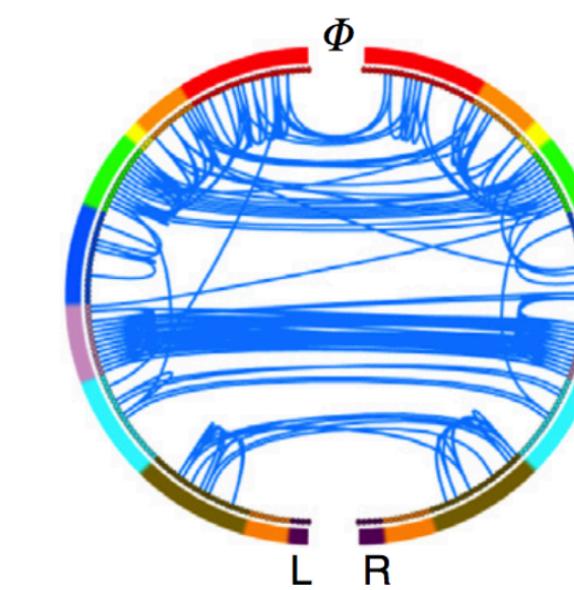
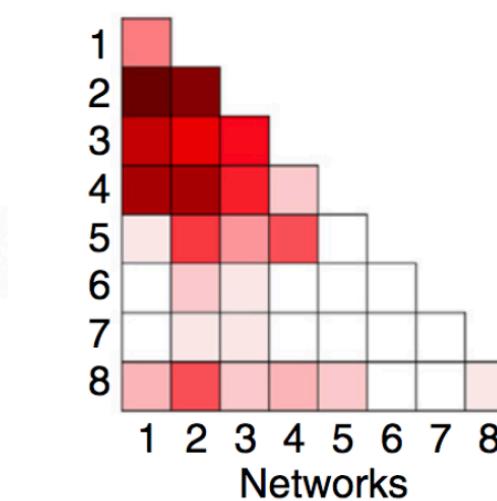
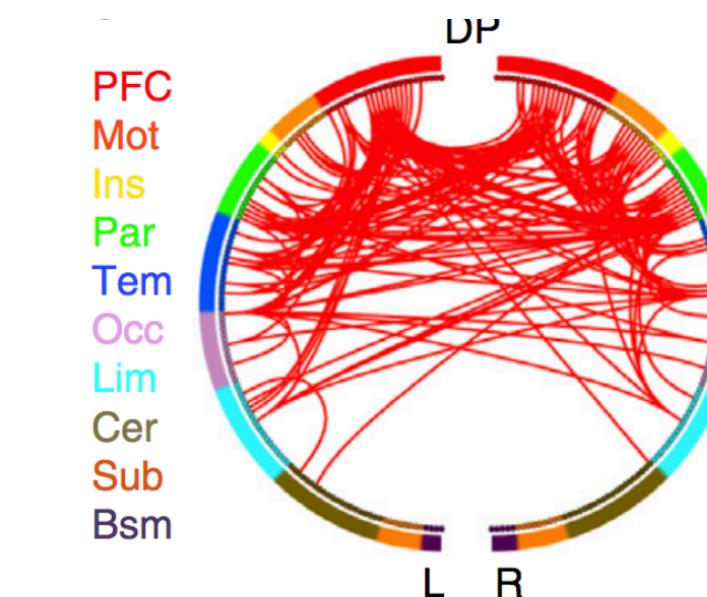
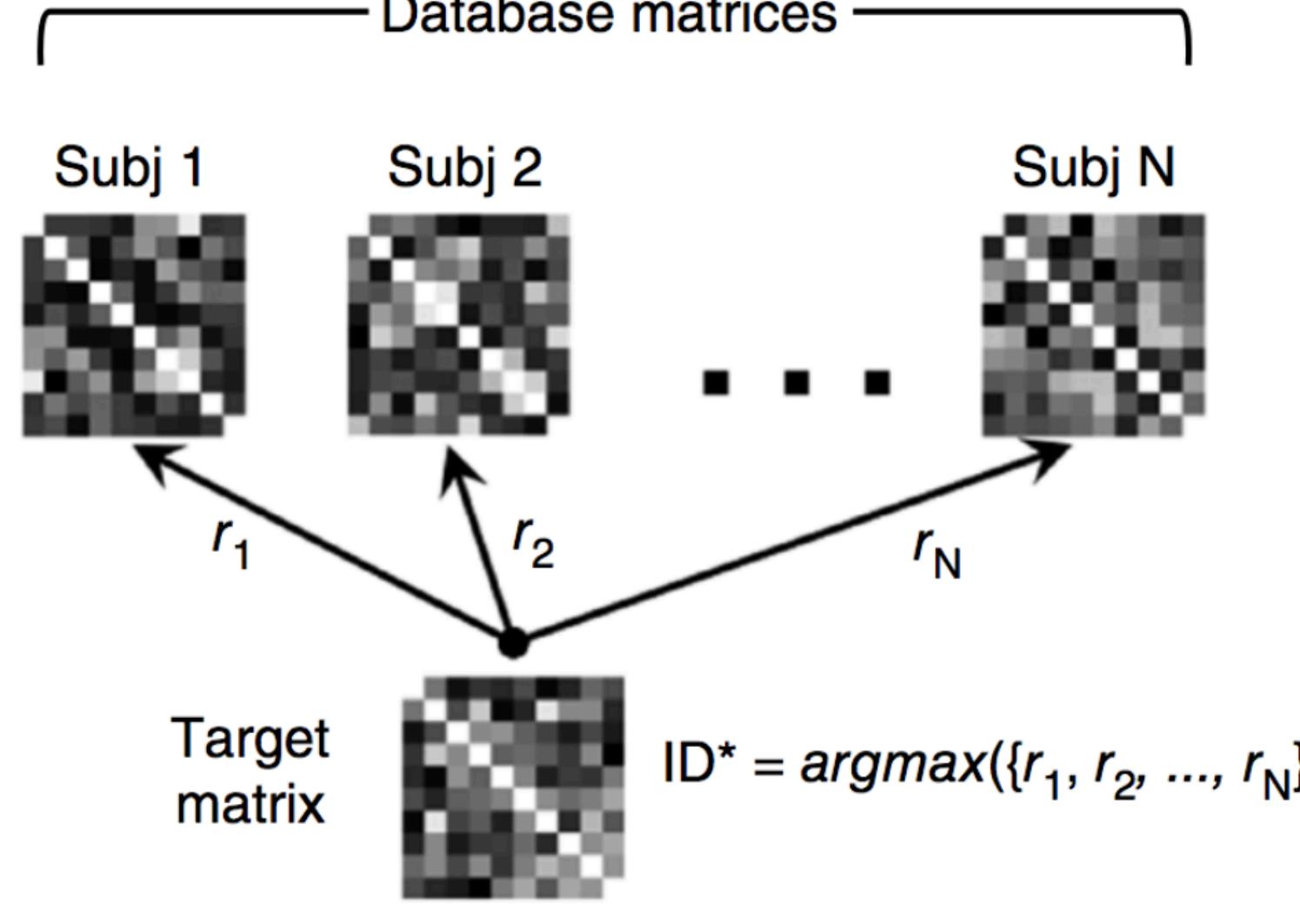
# Example: positive-negative mode

例如：正负模式



# Example: connectivity fingerprint

示例：脑连接的指纹图谱



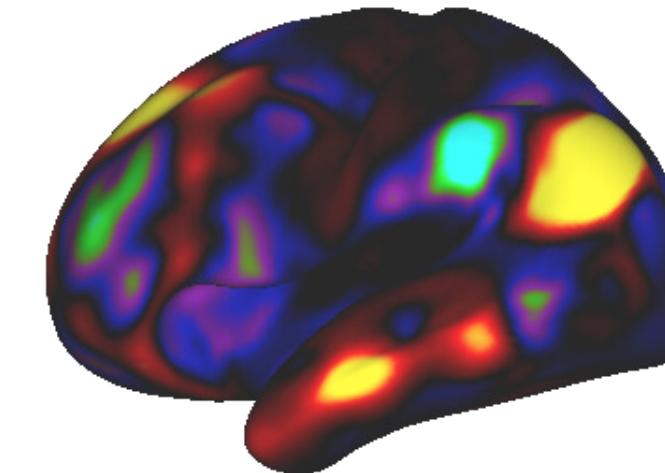


# Comparison of methods

# 方法比較

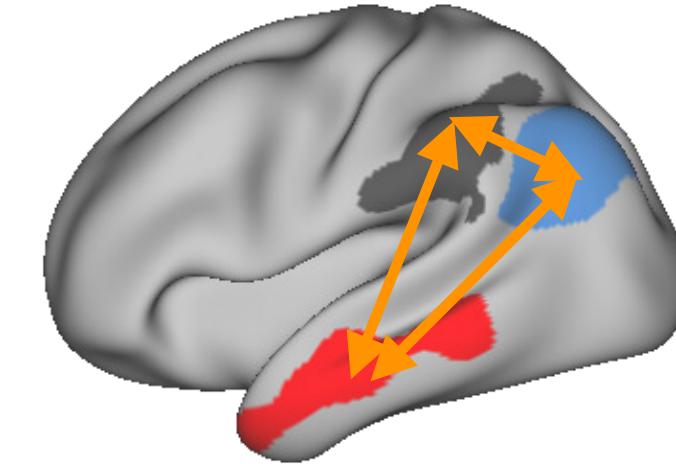
# Overview of resting state methods

## 静息态方法的概况



### Voxel-based 基于体素

- Seed-based correlation analysis 基于种子点的相关分析
- Independent component analysis 独立成分分析
- Amplitude of low frequency fluctuations 低频波动的幅度
- Regional homogeneity 局部一致性



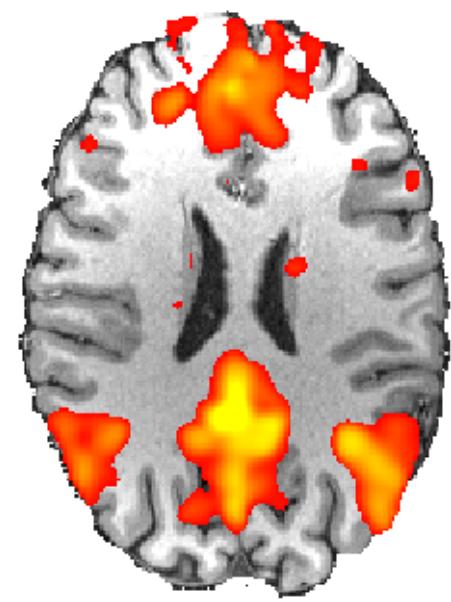
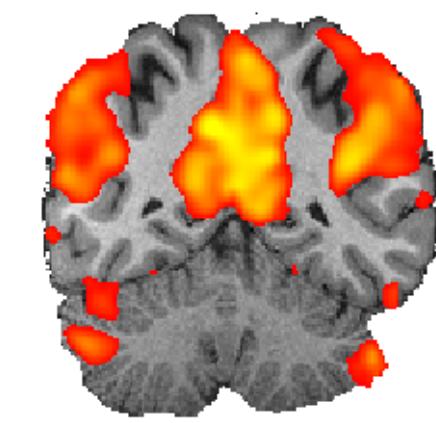
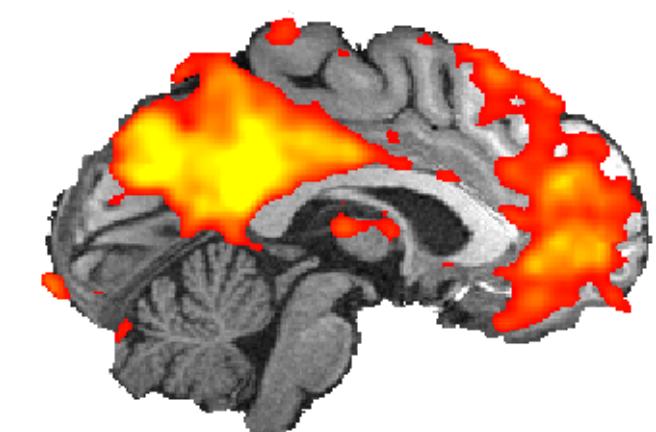
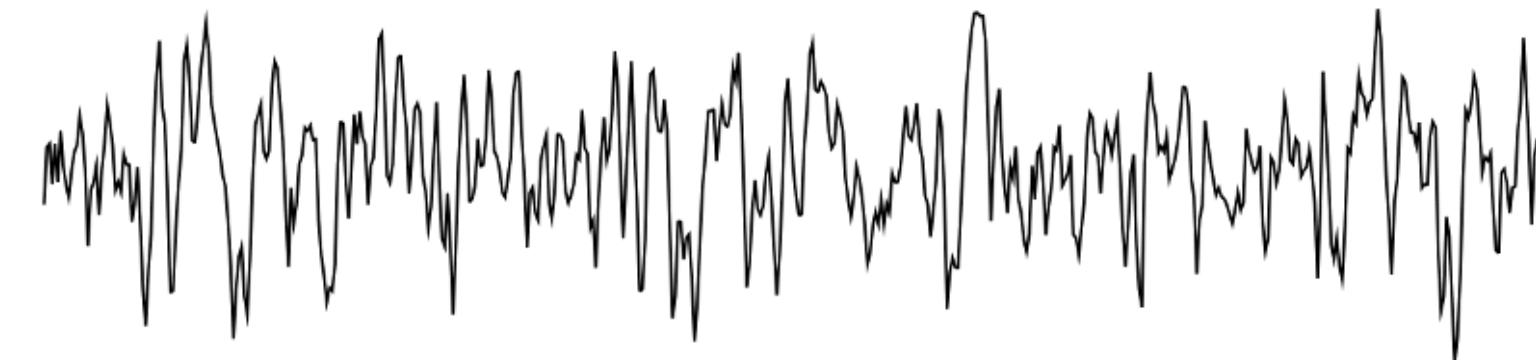
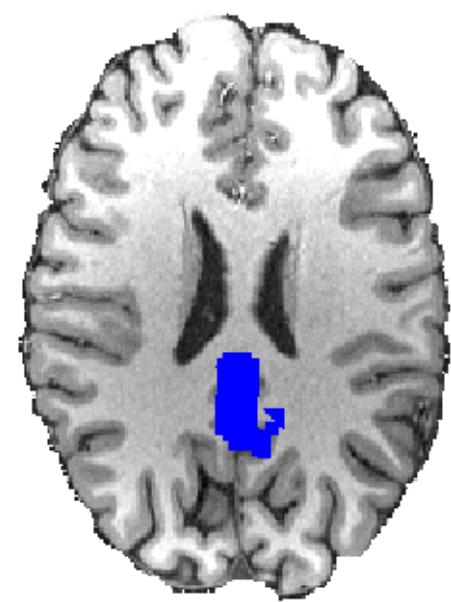
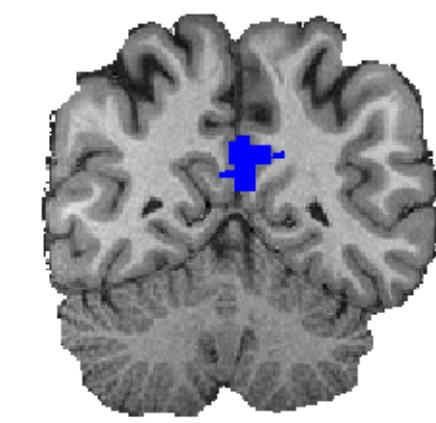
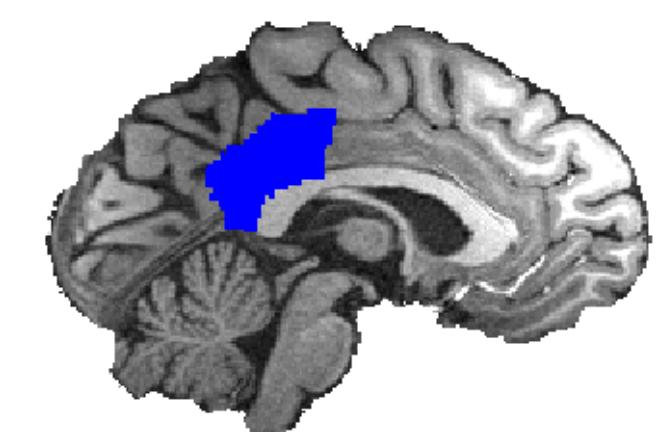
### Node-based 基于节点

- Network modelling analysis 网络建模分析
- Graph theory analysis 图论分析
- Dynamic causal modelling 动态因果建模
- Non-stationary methods 非稳定的方法

# Seed-based correlation

基于种子点的相关分析

- Easy to interpret 易于解释
- No correspondence problem 没有一致性问题
- Seed-selection bias 种子点选择偏差
- Only models seed-effect (ignoring complex structure & noise) 只模拟种子点效应 (忽略复杂的结构和噪音)

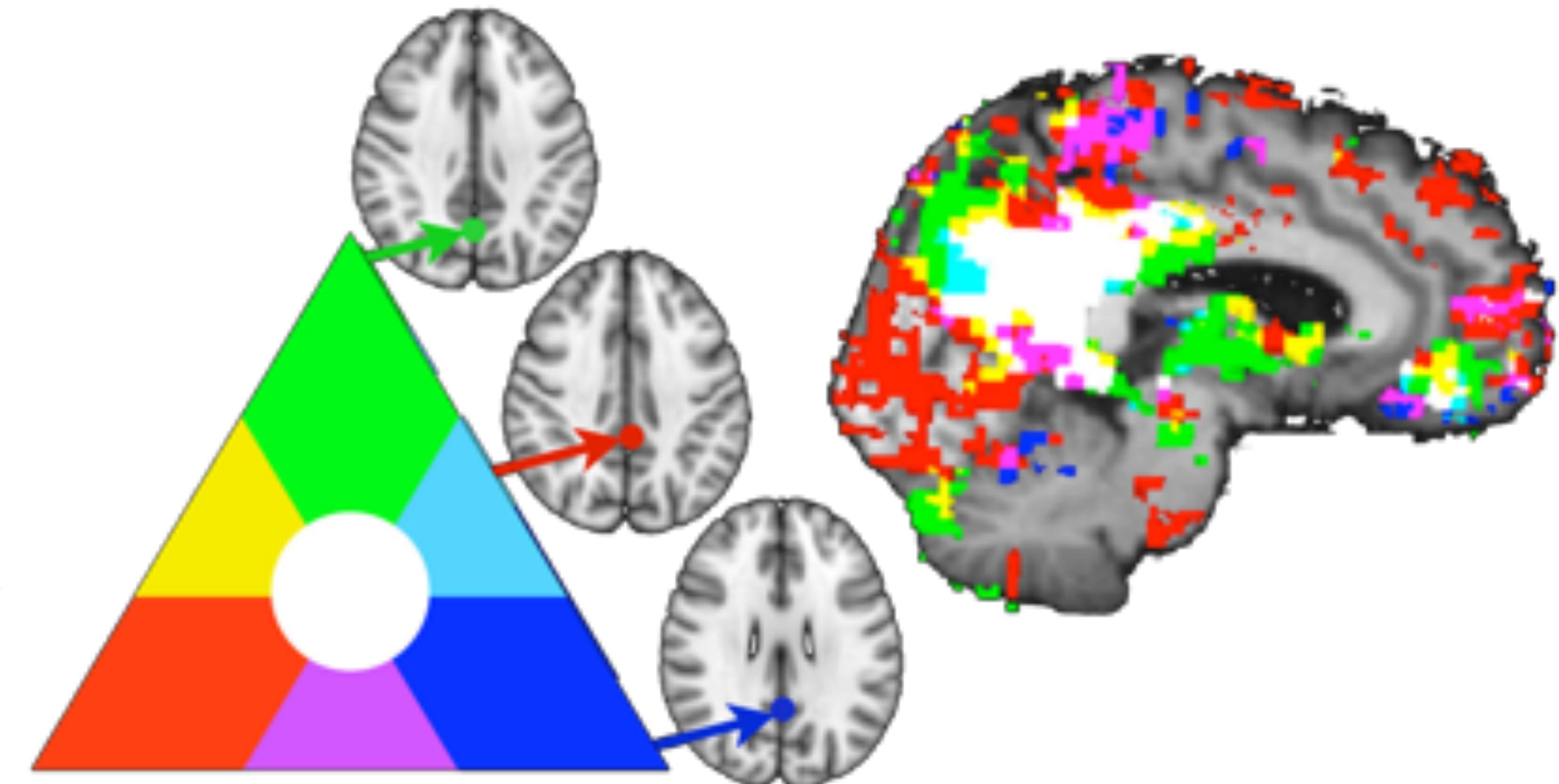


# Seed-selection bias

种子点选择偏差

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

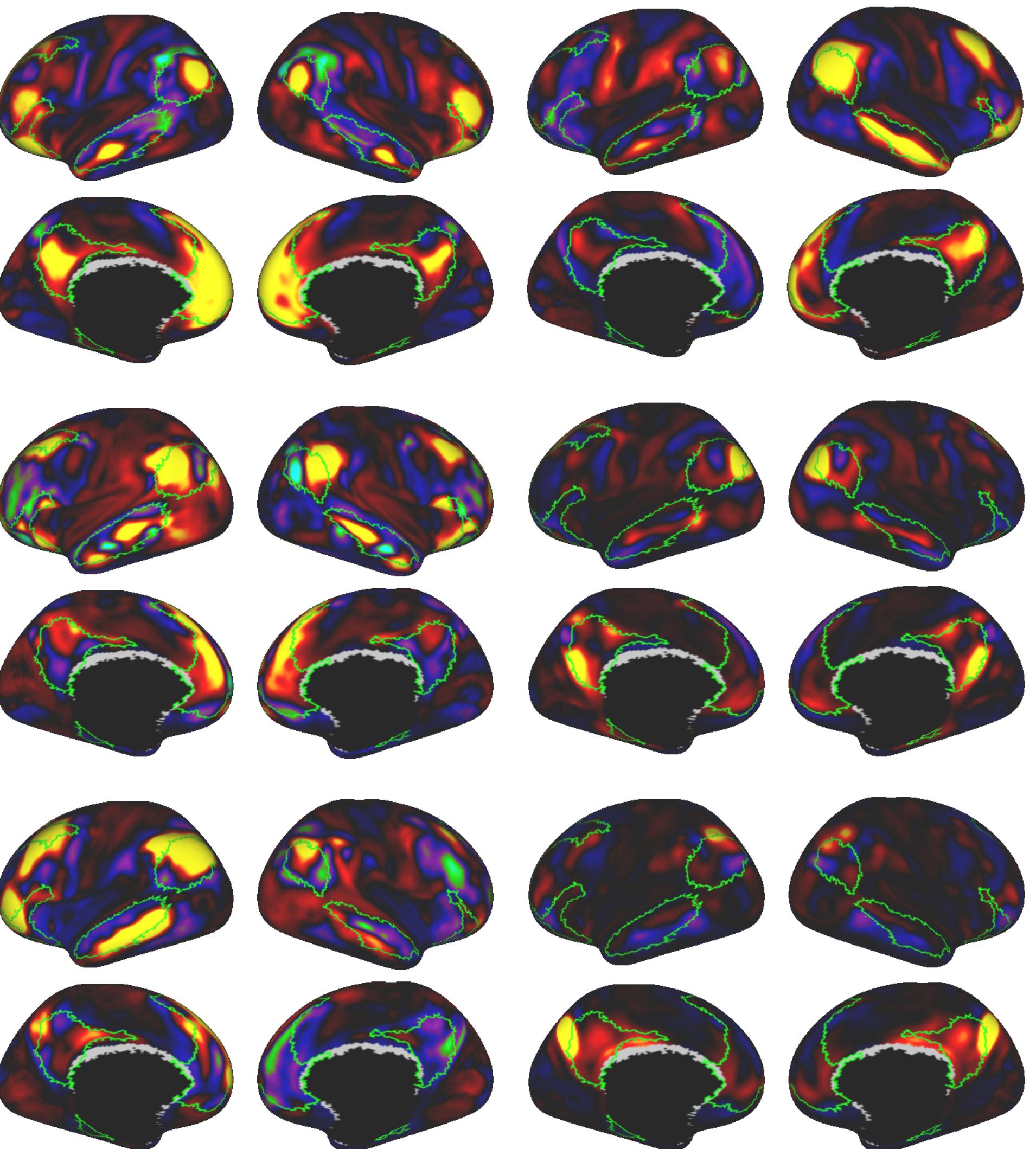
基于种子的相关结果受种子位置的微小变化的强烈影响



# ICA

## 独立成分分析

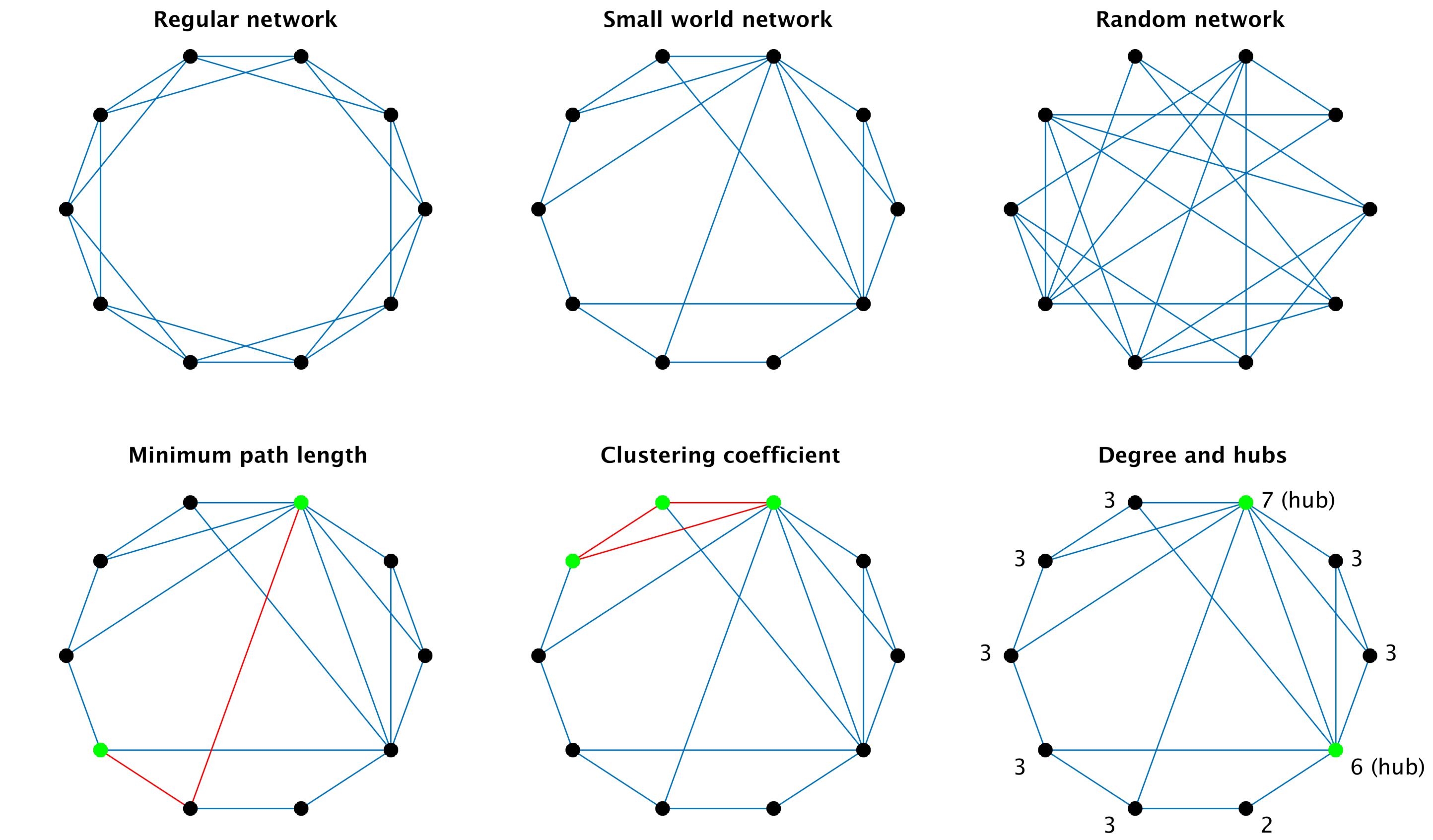
- Multivariate: decompose full dataset  
多变量：完全分解数据集
- Test for shape & amplitude  
测试形状和振幅
- Can be hard to interpret 可能难于解释
- No control over decomposition (may not get breakdown you want)  
成分无法分解（可能无法获得您想要的）



# Graph theory

## 图论

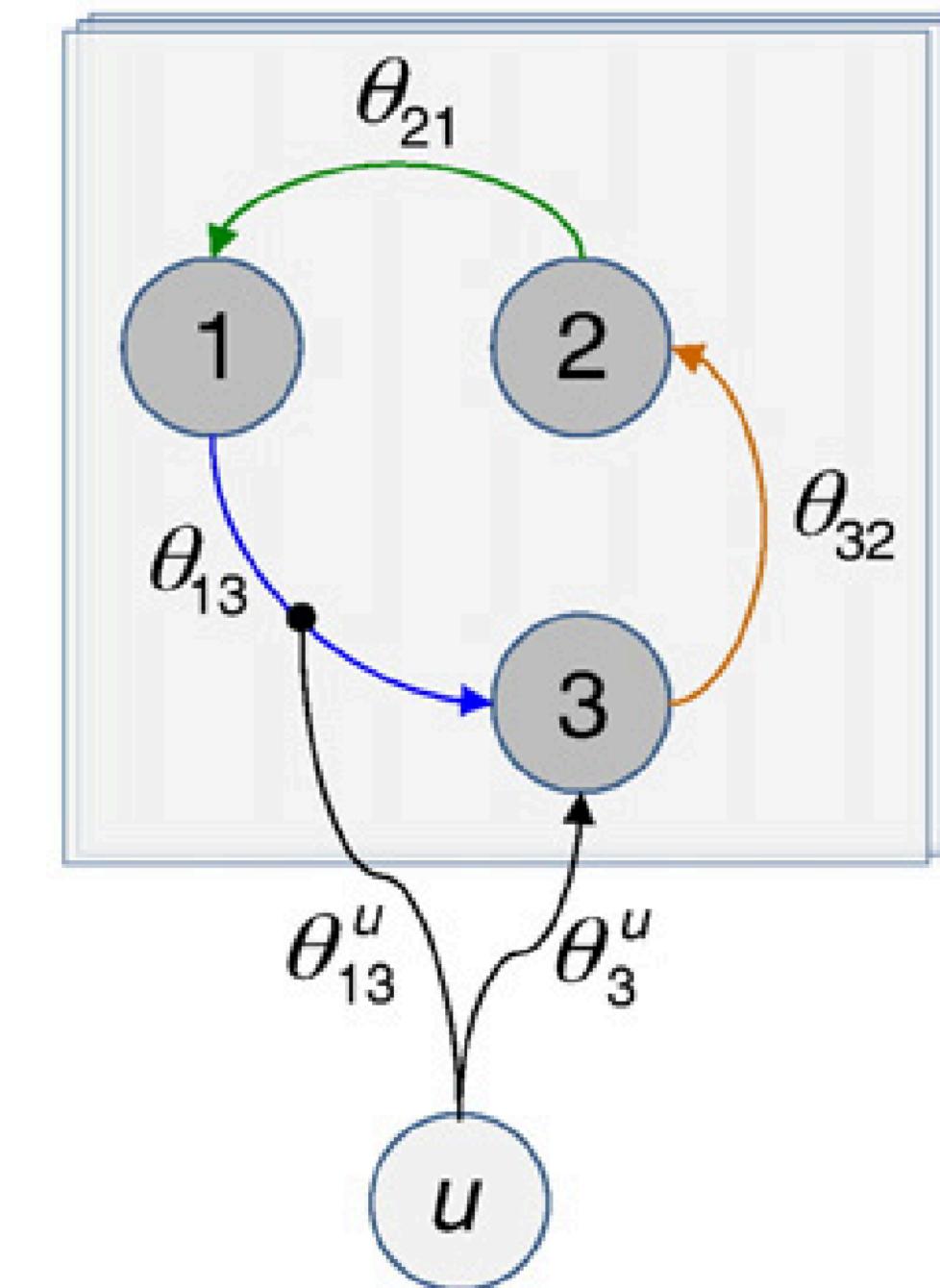
- Simple summary measures (derived from network matrix) 简单的汇总方法 (源自网络矩阵)
- Network matrix often binarised 网络矩阵经常被二进制化
- Difficult to meaningfully interpret (abstract and far removed from data) 很难有意义地解释 (抽象和远离数据)



# Dynamic causal modelling

## 动态因果模型

- Directional interpretation (effective connectivity)  
定向解释 (有效连接)
- Biophysical model 生物物理模型
- Assumes HRF homogeneity 假设HRF同质性
- Limited model comparisons 有限的模型比较

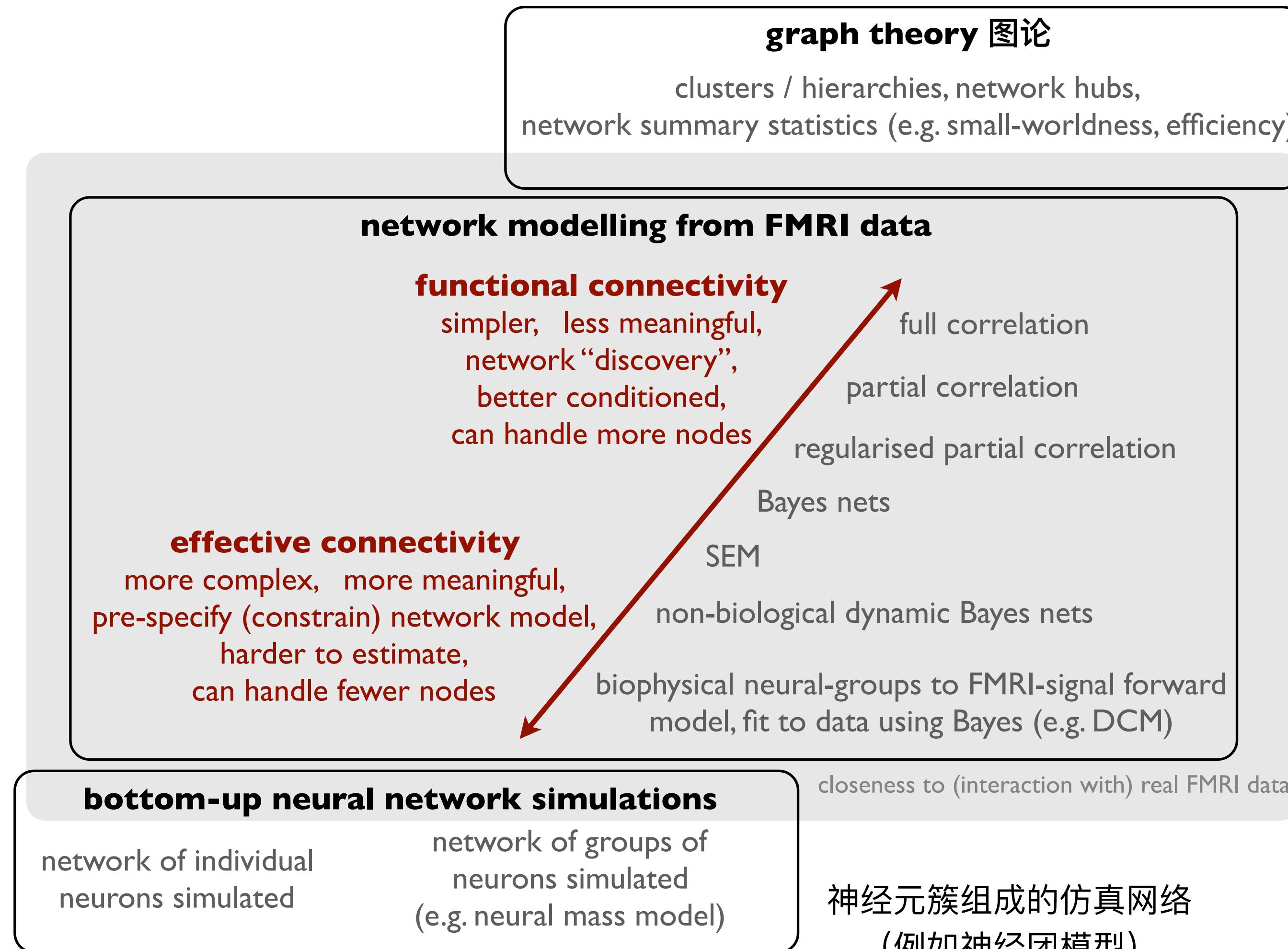


# Overview of node-based methods

## 基于节点的方法概述

**有效性连接**  
更复杂，更有意义，  
预先设定（限制）网络模型，  
更难预测模型，  
可以处理较少节点

**由下至上的神经网络仿真**  
单个神经元组成的仿真网络



集群/层次结构，网络节点  
网络统计方法（小世界、有效性）

FMRI数据的网络建模

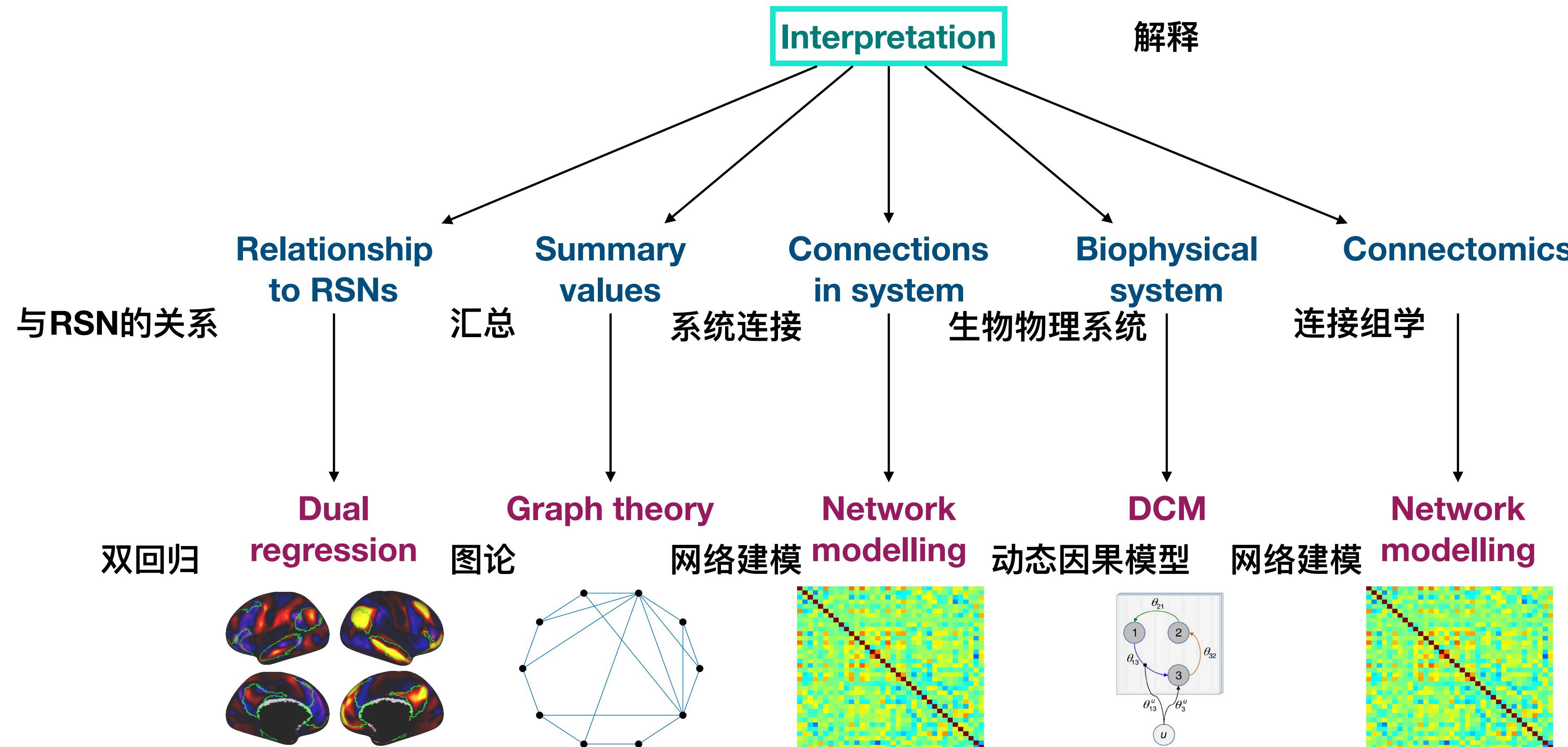
**功能连接**  
更简单，较少意义，  
网络“发现”，  
条件更好，  
可以处理更多节点

完全相关  
偏相关  
正则化的偏相关  
贝叶斯网络  
结构方程模型  
非生物动态贝叶斯网

生物物理神经组到FMRI  
信号正向模型，适合使用  
贝叶斯（例如DCM）的数据

# Which method to chose?

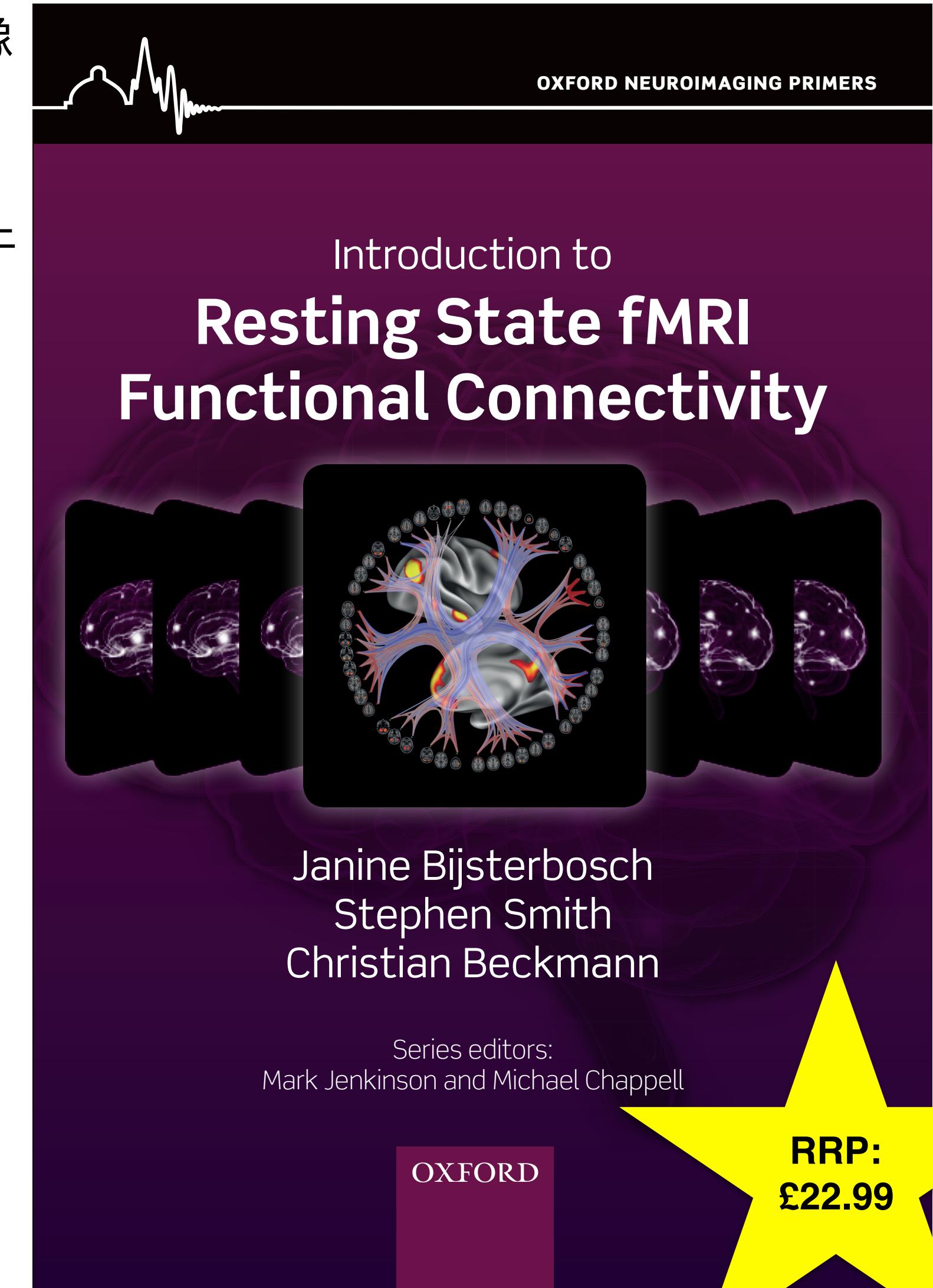
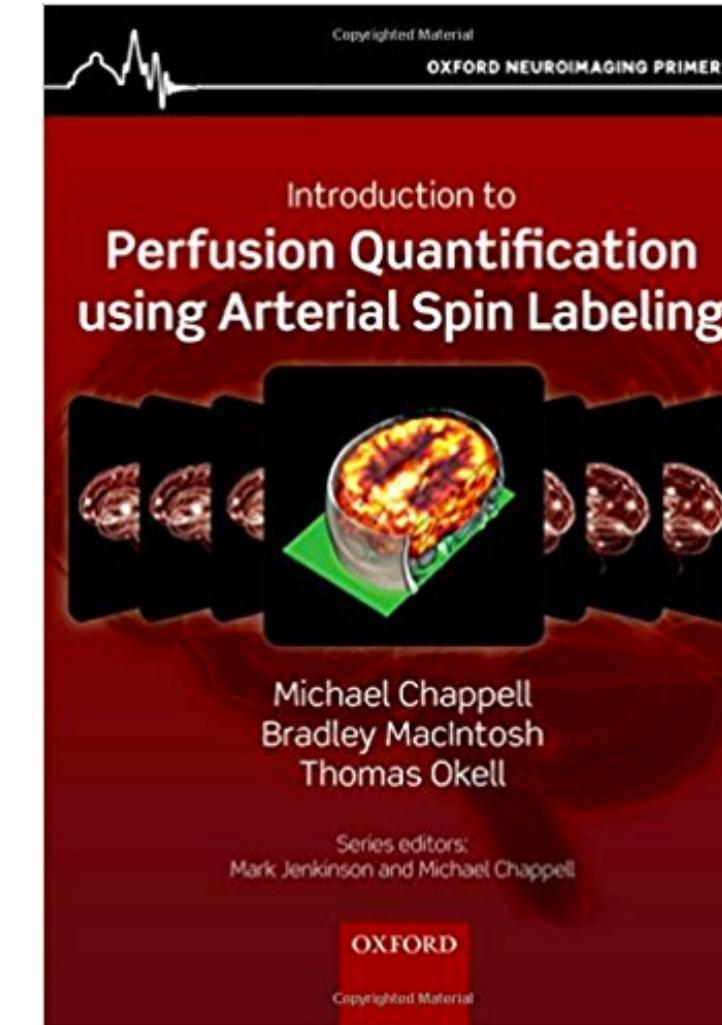
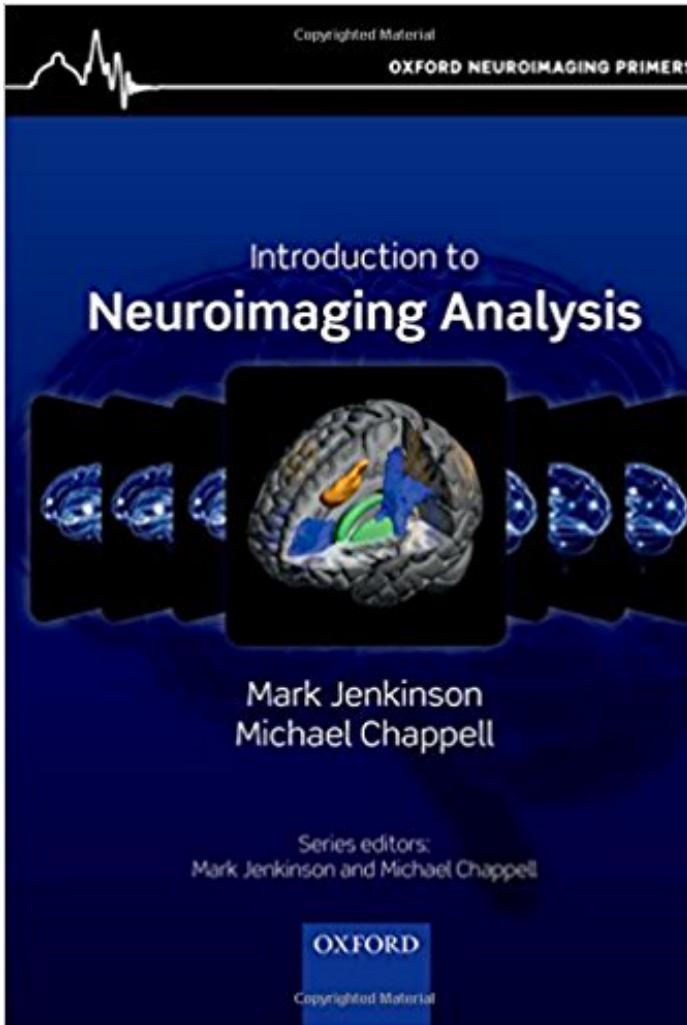
## 选择哪种方法?





# The book

- Part of a series of Oxford Neuroimaging Primers —系列牛津神经影像引物的一部分
- Available from Amazon and Oxford University Press 可从亚马逊和牛津大学出版社获得
- Free material available on primer website: <http://www.neuroimagingprimers.org/>
- Please consider writing a book review on Amazon





That's all folks

