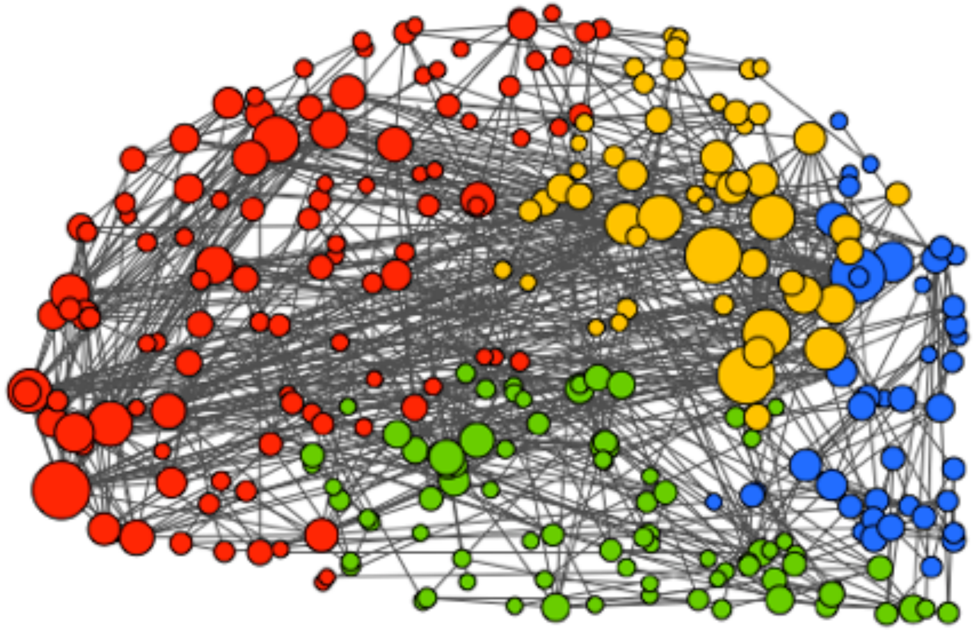

Network analyses for fMRI

Petra Vertes – 24th January 2012

Brain Mapping Unit
Behavioural and Clinical Neuroscience Institute
University of Cambridge

Acknowledgements

- Ed Bullmore
- Aaron Alexander-Bloch
- Sophie Achard
- Carsten Giessing
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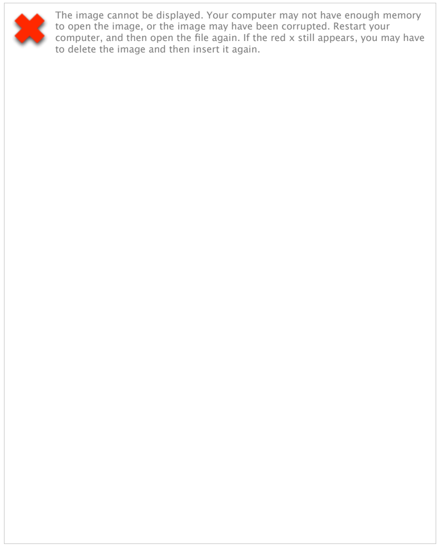
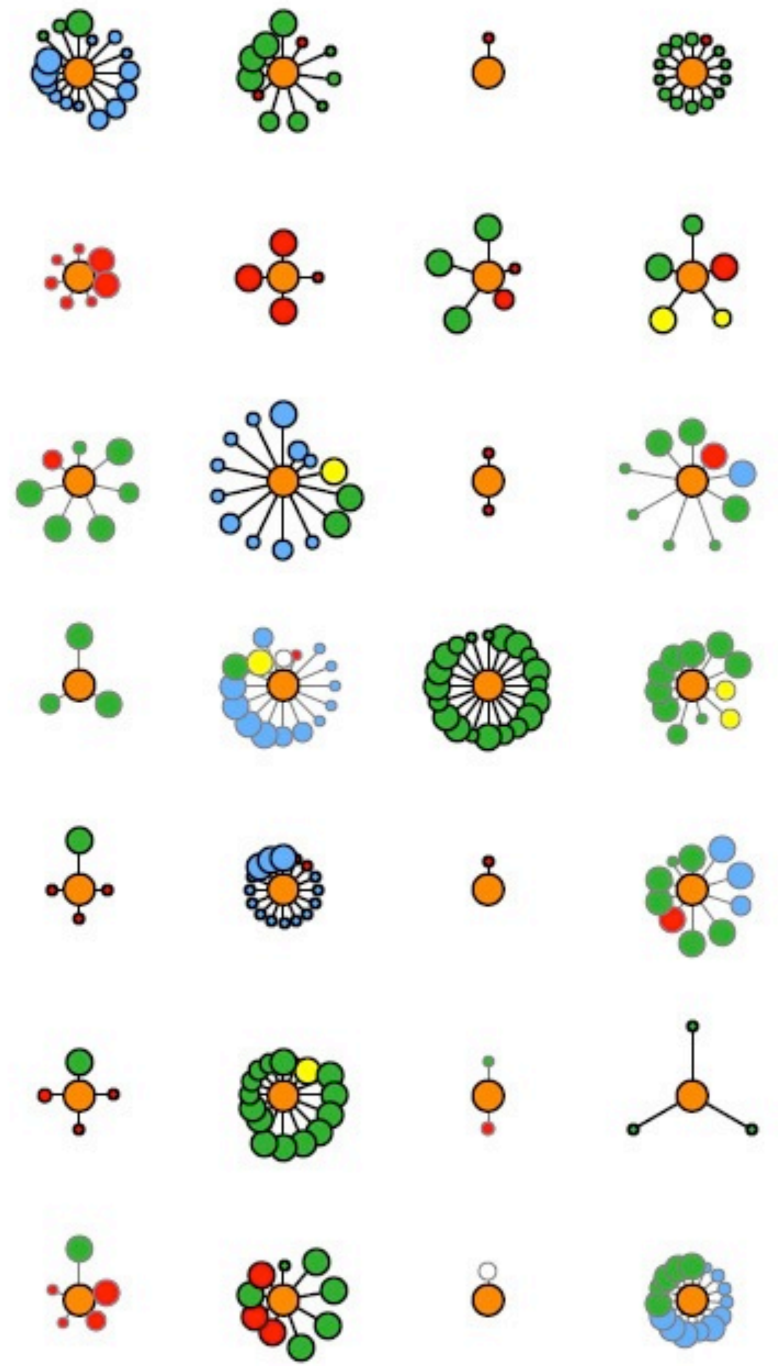


Overview

- Introduction to networks:
  - Defining a network
  - Representing a network
  - Network measures

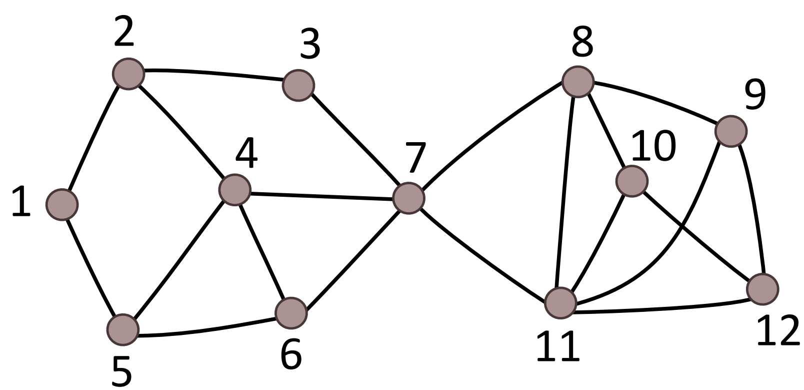
- Brain functional networks:
  - How are they constructed
  - What do they tell us?



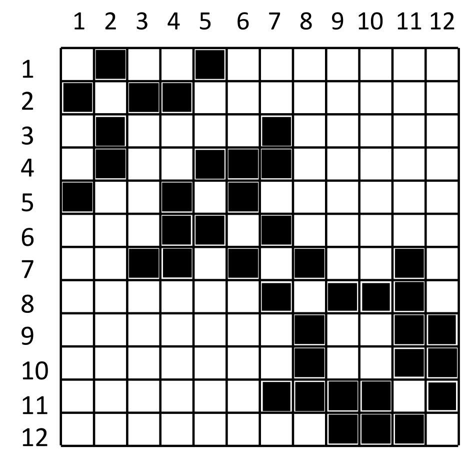
Defining a Real-World Network

- Nodes:
  - Individuals
  - Groups of people
- Edges:
  - Simple
  - Weighted
  - Directed

Representing a Network



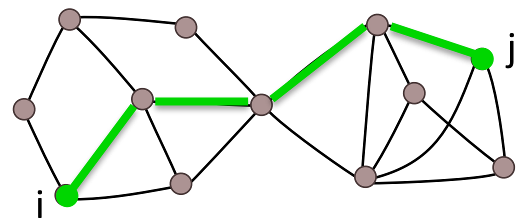
Spatial embedding



Adjacency matrix

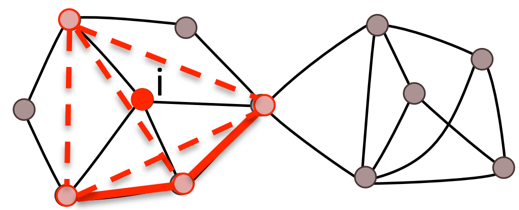
Characterizing a Network

Path Length
(or Efficiency)



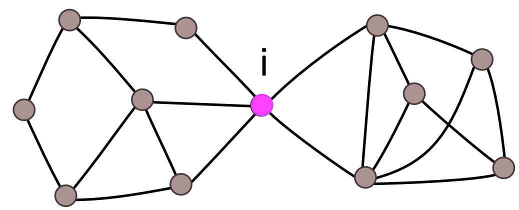
$$L_{i,j} = 4 \qquad E = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{L_{i,j}}$$

Clustering



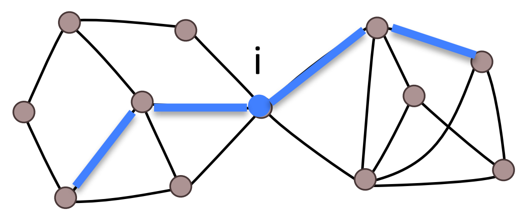
$$C_i = \frac{2}{6} = \frac{\text{Links between 'friends'}}{\text{Total possible number}}$$

Degree (Hubs)



$$d_i = 5$$

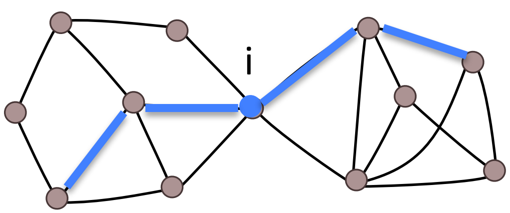
Betweenness
Centrality

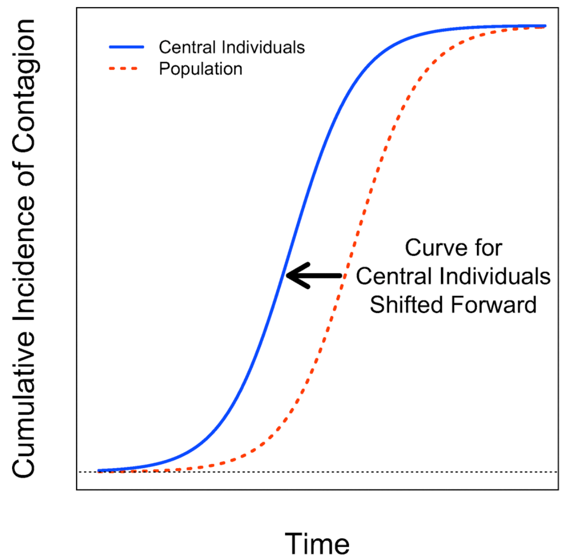


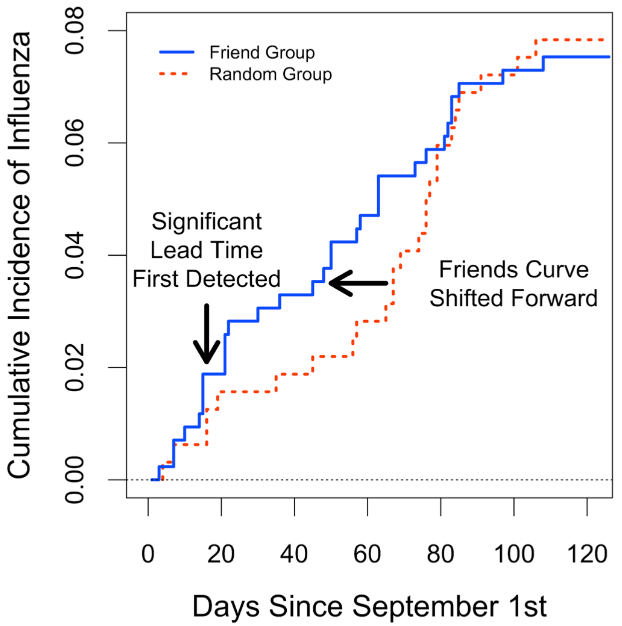
$$BC_i = high$$

Central Individuals are Early Adopters

High betweenness centrality



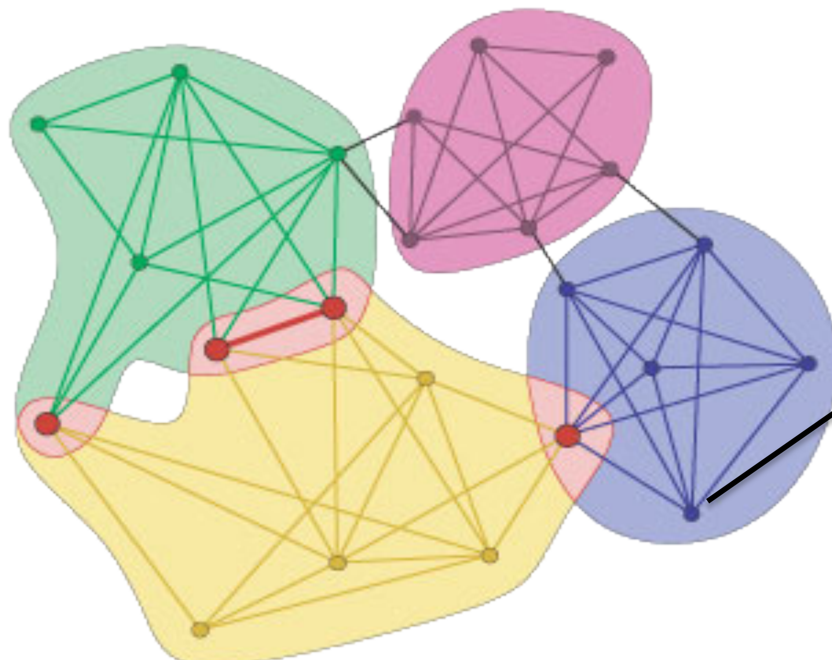




Christakis & Fowler, 2010

Modularity

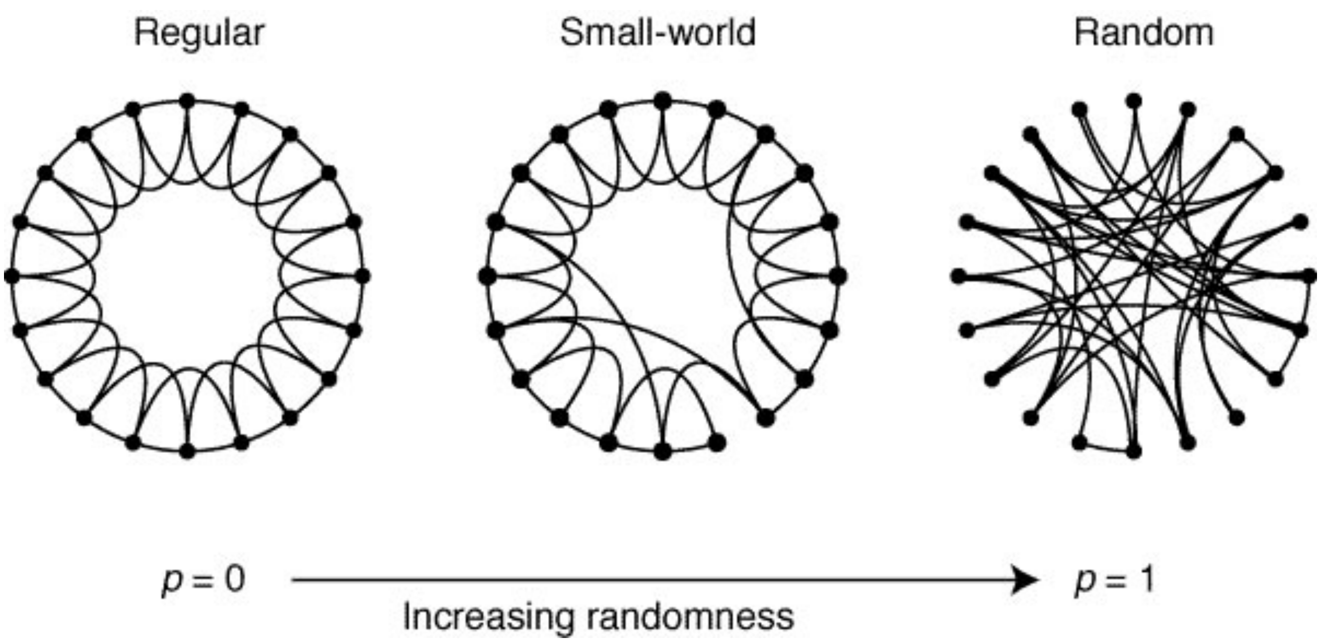
M = Fraction of within-module connections compared to what is expected by chance (for the optimal partition).



Infer function of less well-known nodes based on their module?

Girvan & Newman (2002) PNAS

Small- World Networks:

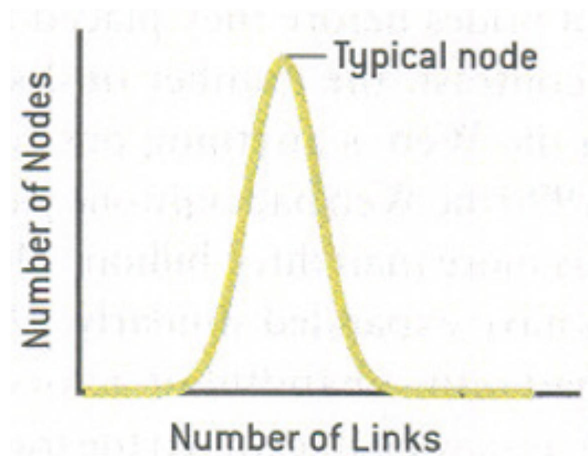


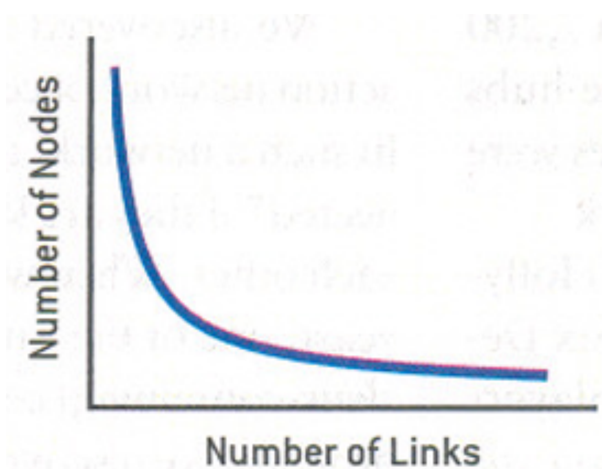
High C

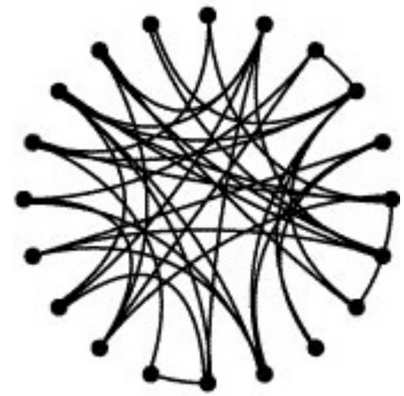
Low L

Watts & Strogatz (1998) Nature

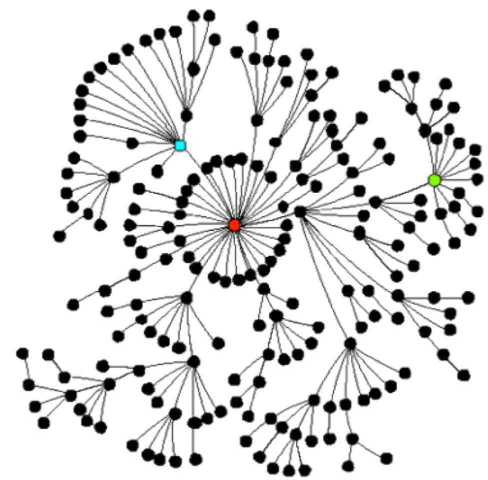
Degree Distribution







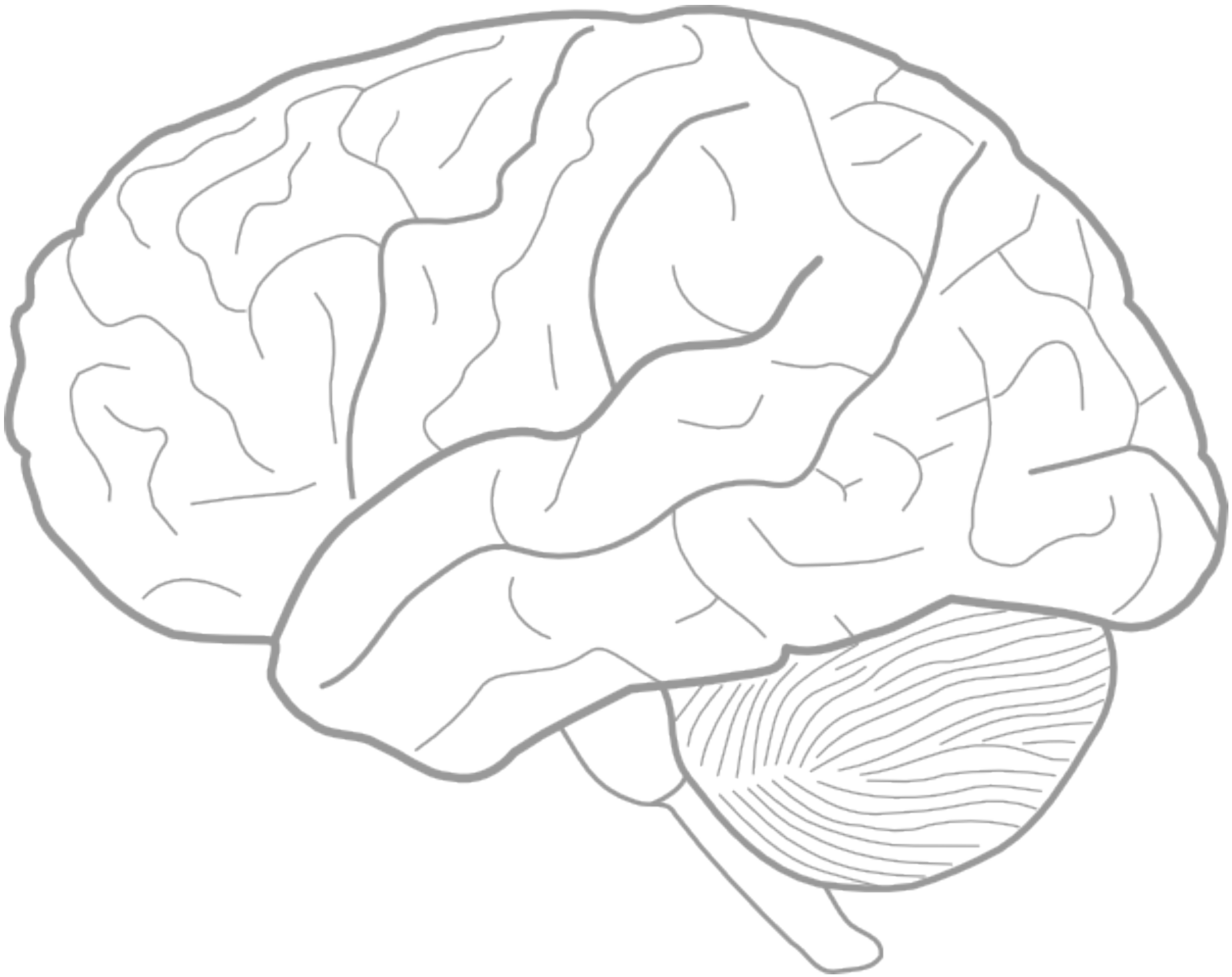
Random Network



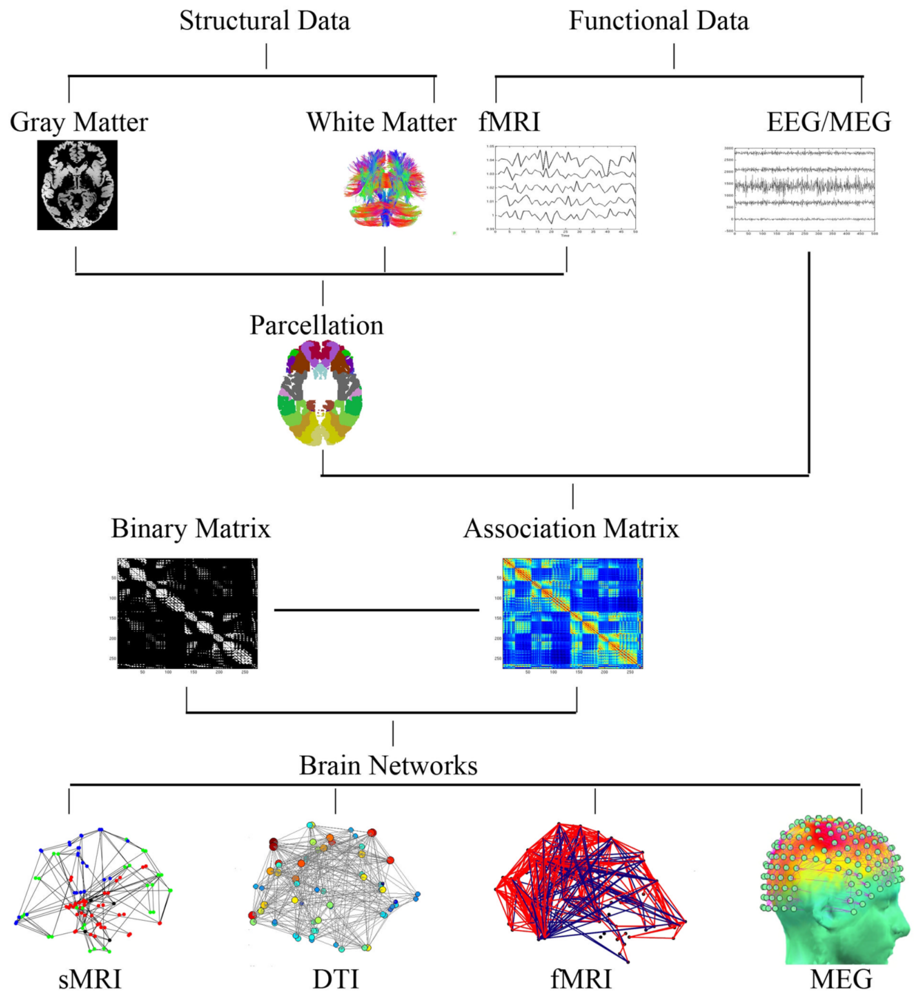
Scale-free Network

Barabasi & Albert (1999) Science

What about brain networks?



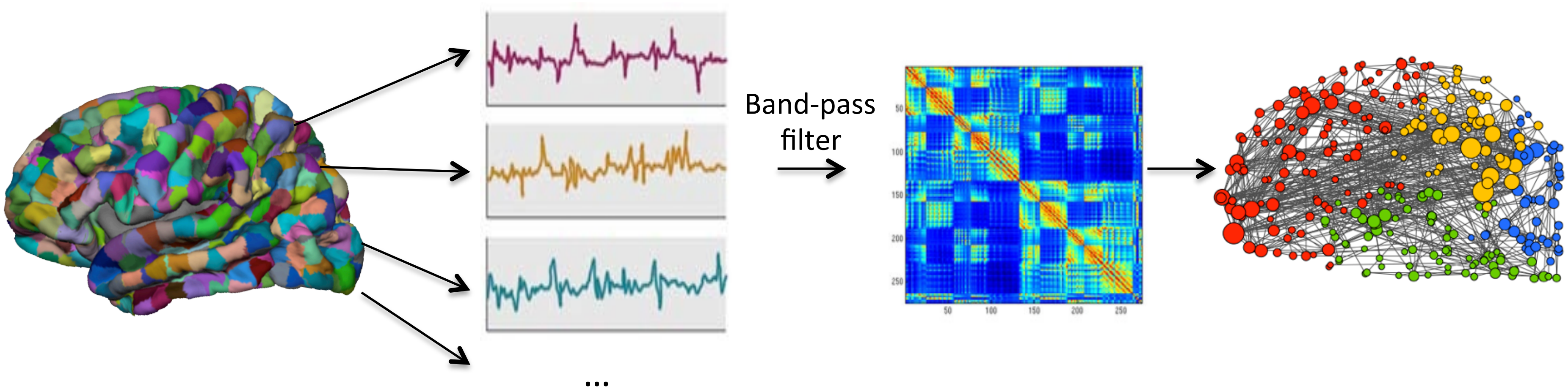
Brain networks and modalities



Bassett & Bullmore (2009) Curr Opin Neurol 2009

Network analyses of fMRI

1. 2. 3. 4.



Parcellation

fMRI time series for each region

Matrix of similarity (correlation) between Time series

Network construction

Network Construction

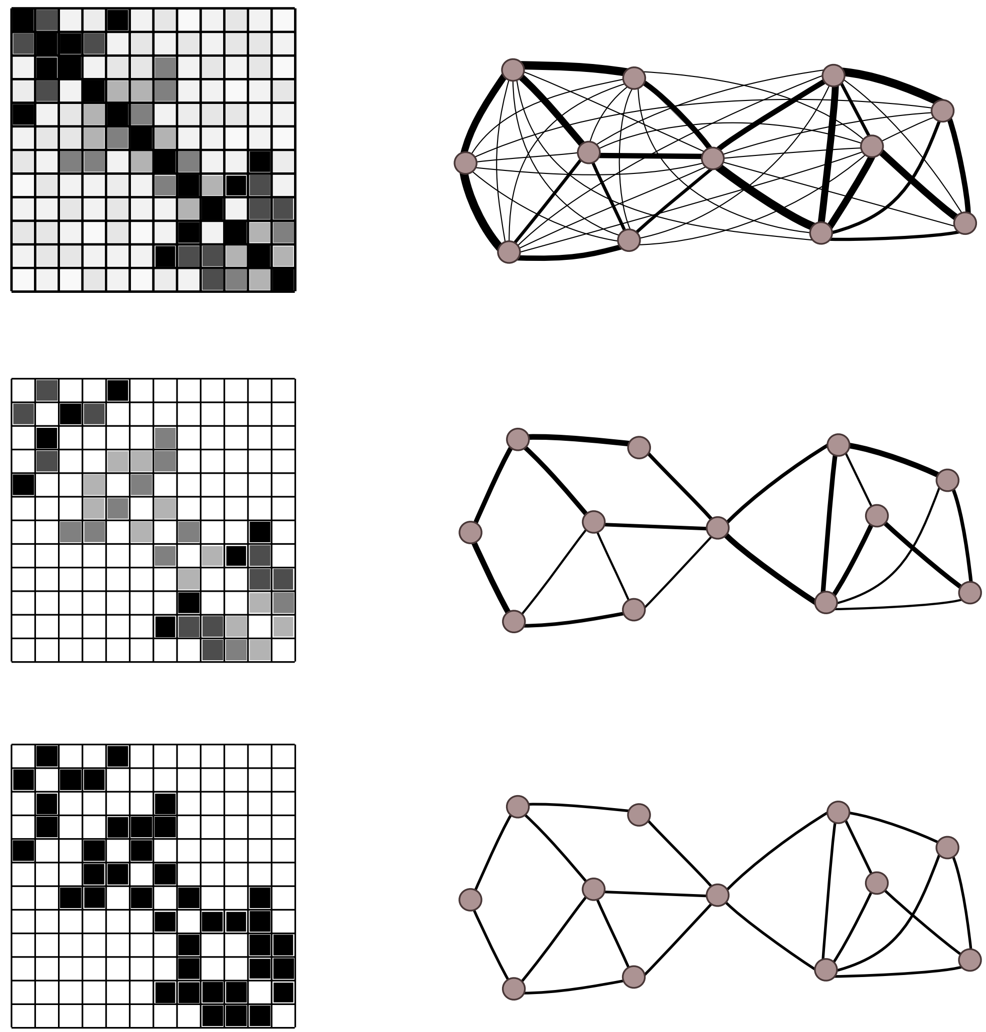
Weighted, Undirected

threshold

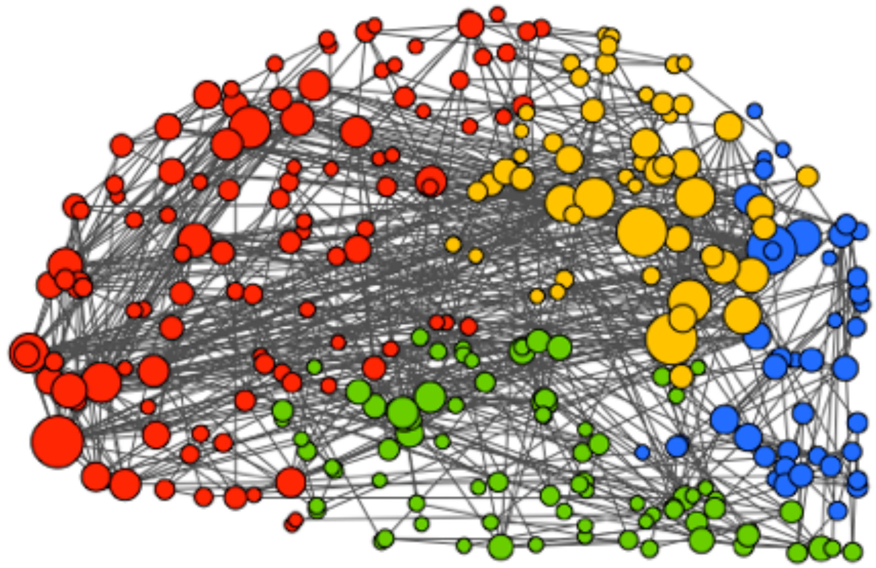
Weighted, Undirected

binarize

Unweighted, Undirected



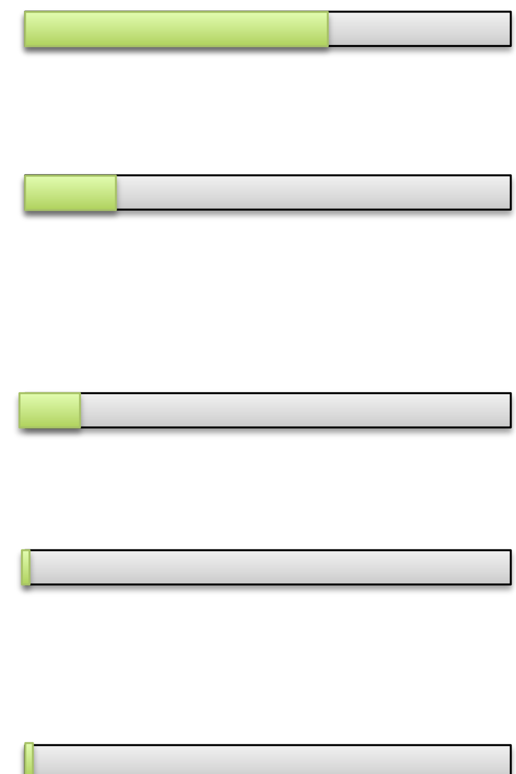
What now?



Aims of brain network analyses:

Optimistic progress bars

1. Describe healthy brain networks
2. Help understand the disease
   - How does it actually affect the brain?
3. Help measure the effect of drugs
4. Help diagnose disease
5. Help predict disease or recovery
   - Will the coma patient wake up?



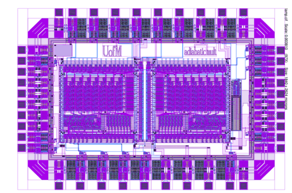
1. Describing healthy brain networks

Optimistic progress bars

Describing healthy brain networks

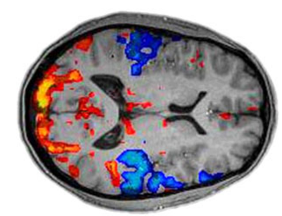
Small-world

- high clustering
- short path length or high efficiency



Cost-efficient

- high efficiency for relatively low connection cost

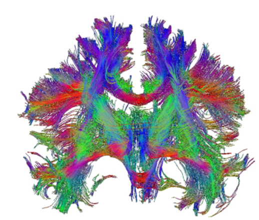


Hubby

- fat-tailed degree distributions

Modular

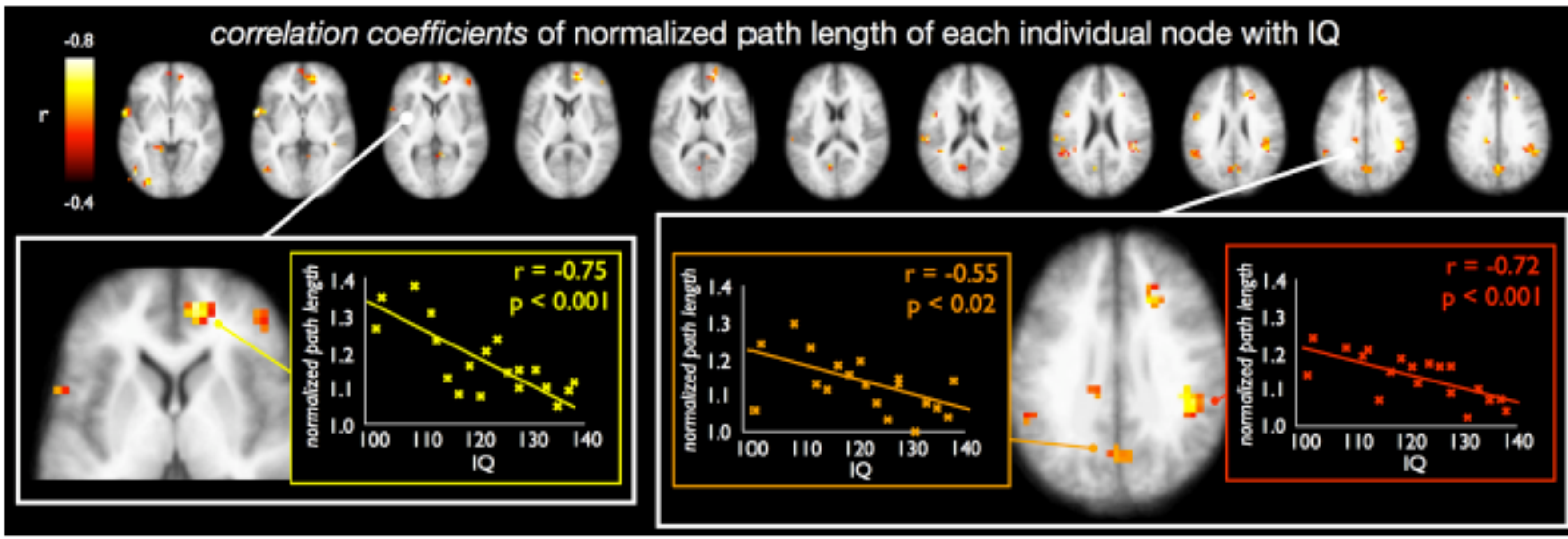
- nodes are more densely connected to other nodes in the same module than to nodes in other modules



Bullmore & Sporns (2009) Nat Rev Neurosci
Bassett et al (2010) PloS Comp Bio

Linking structure and function

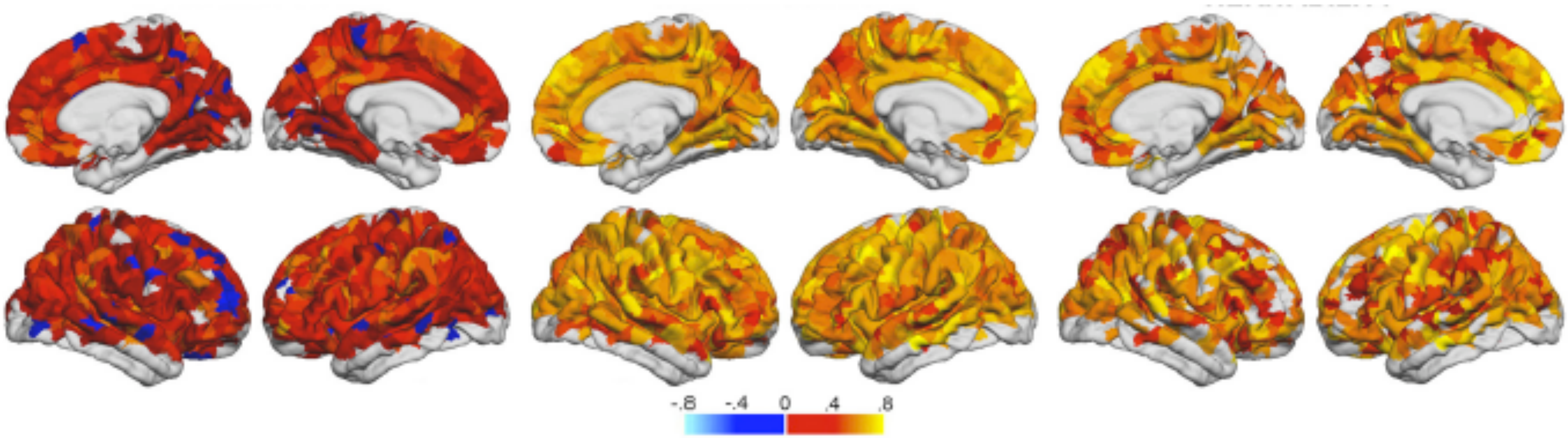
Greater efficiency (or shorter path length) of human brain networks is correlated with higher IQ:



Van den Heuvel et al (2009) J Neurosci

Li et al (2009) PLoS Comp Biol

Heritability of Brain networks



Similarity of
Non-identical Twins

Similarity of
Identical Twins

Heritability

High heritability (60-70%) means that network cost-efficiency is under strong genetic control

Fornito et al (2011) J Neurosci

2. Understanding disease

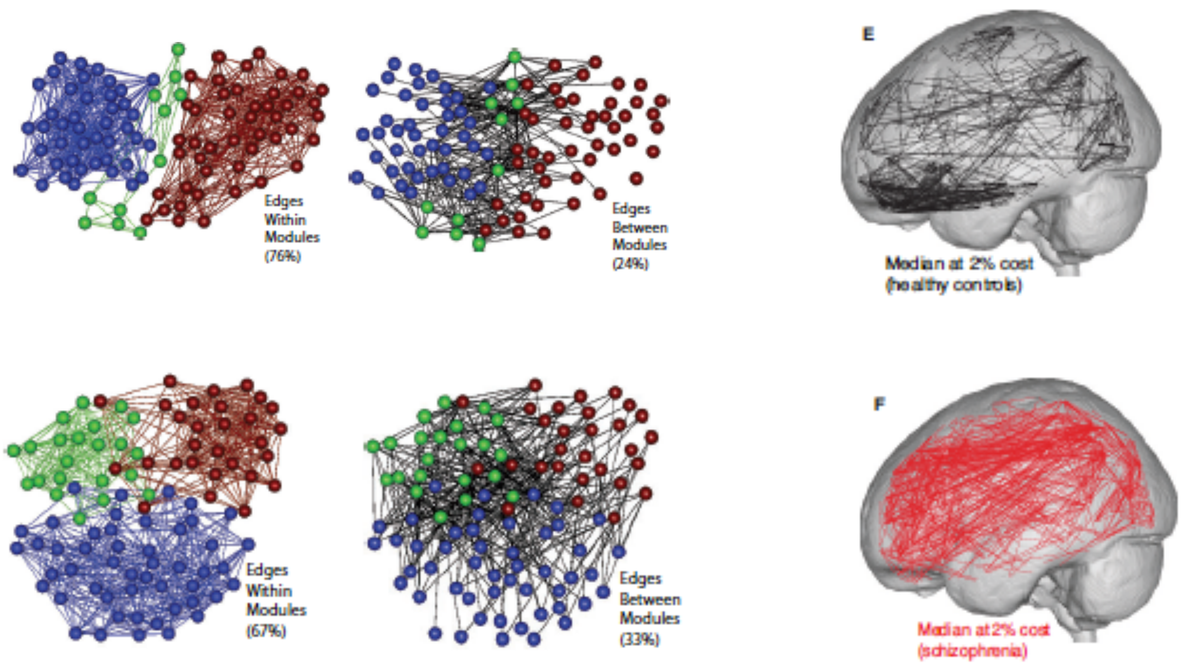
Optimistic progress bars

Schizophrenia as a disorder of brain networks

Brain functional networks in schizophrenia are slightly more random: less economically wired and less modular

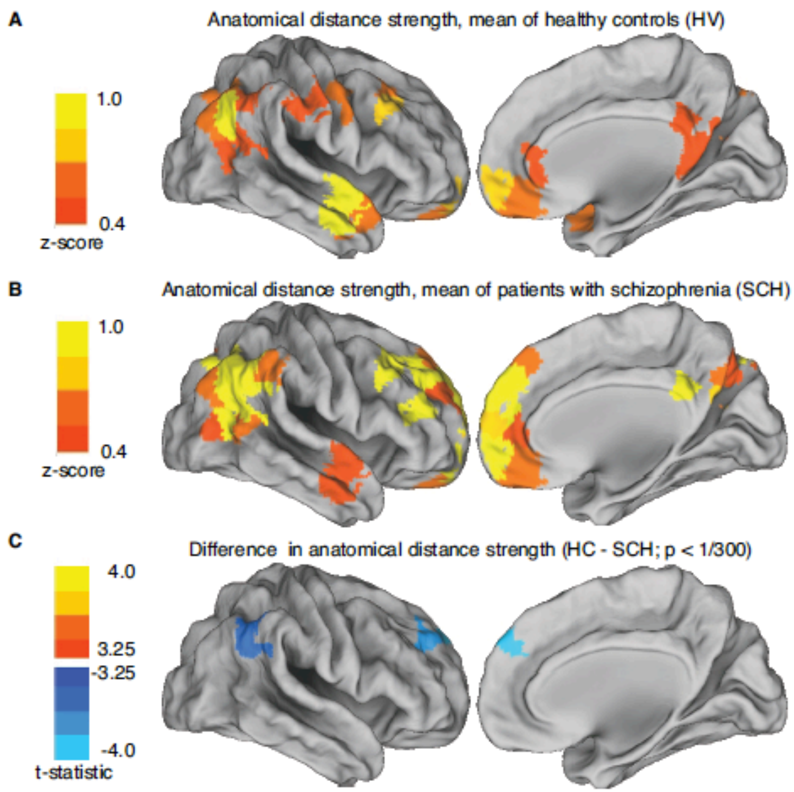
Healthy Volunteers

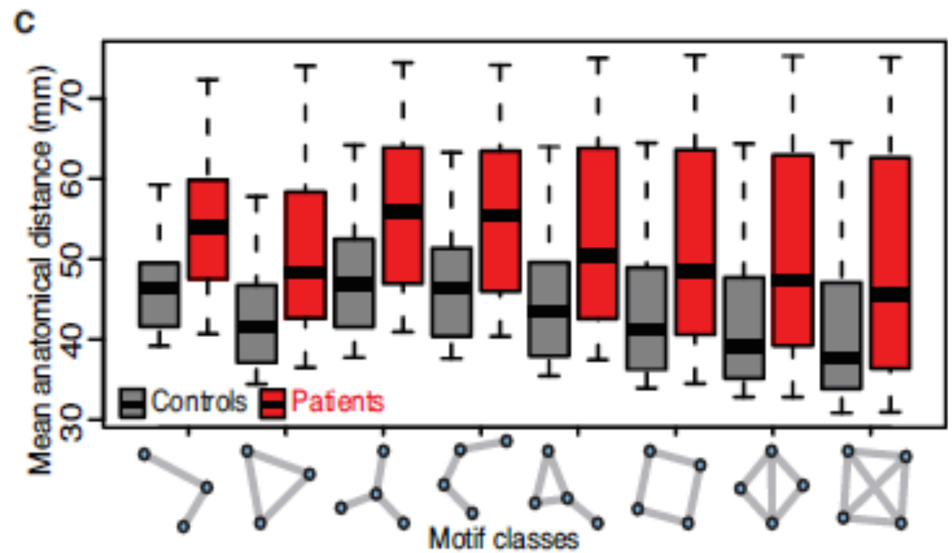
Participants with Schizophrenia



Alexander-Bloch et al (2010) Front Sys Neurosci

Zooming-in on topological differences in schizophrenia





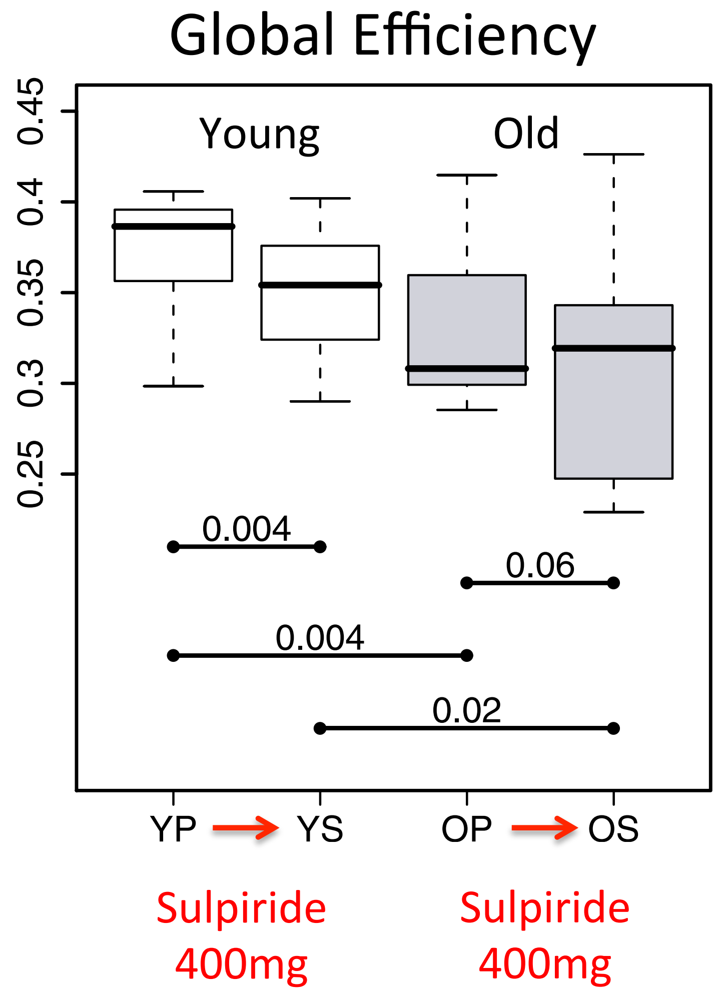
Alexander-Bloch et al (2011) Cereb Cortex (in press)

3. Measuring the effect of drugs

Optimistic progress bars

The effect of Sulpiride on healthy volunteers

Sulpiride significantly reduces the Global Efficiency of healthy brain networks, counteracting the subtle randomization observed in schizophrenia



Achard & Bullmore (2007) PLoS Comp Bio

Relating drugs, networks and behaviour

18 right-handed smokers were measured two times in an fMRI scanner:

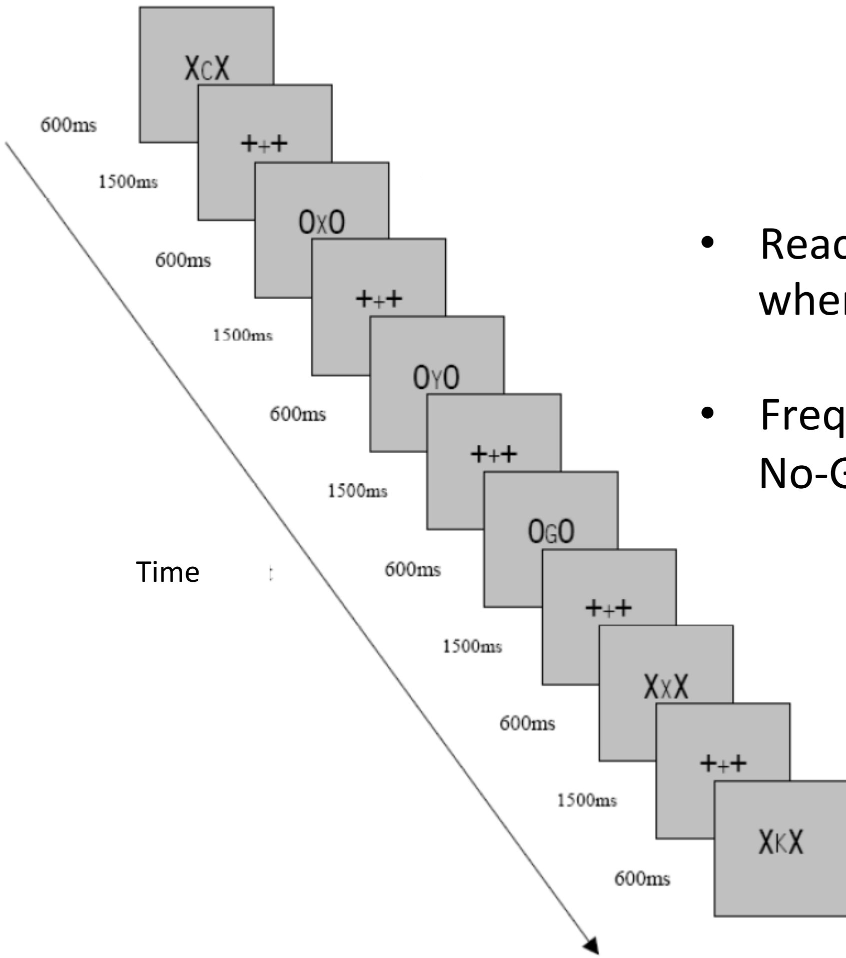
- placebo
- 4 mg nicotine gum (Nicorette®)

Subjects smoked 16 cigarettes on average per day (sd=8.58) for on average 10 years (minimum 3 years, sd=24). Fagerström Nicotine Dependence Scale: mean 3.4 (sd=2.3, weak nicotine dependence).

Last nicotine intake: 2 hours before

Giessing et al (2011) in review

Continuous performance task:



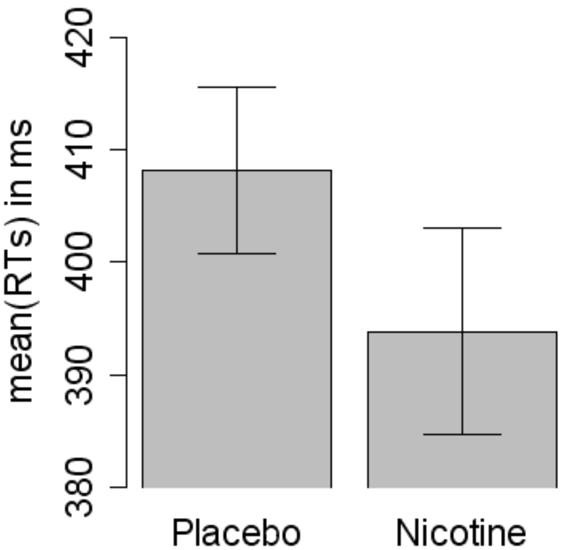
- Reaction time on button-press for 'Go' trials where the central symbol is C, G, D, W, K, or Y

- Frequency of No-Go errors: button-press for No-Go trials where the central symbol is X, O

Giessing et al (2011) in review

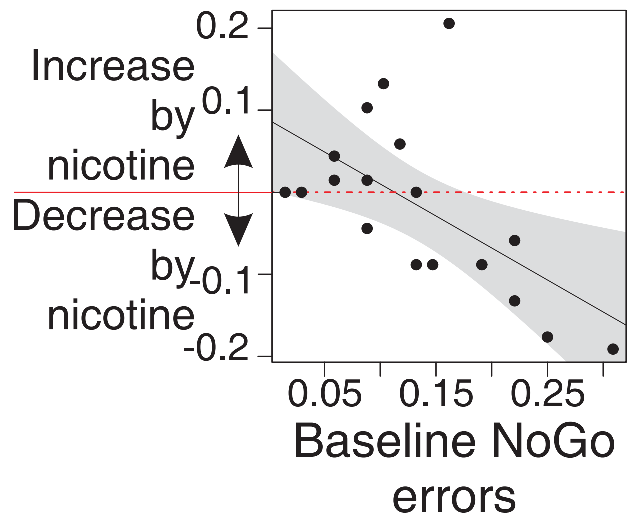
Significant main effect of Nicotine

Nicotine reduces reaction times for Go trials



Means and SEMs
permutation test $p<0.05$

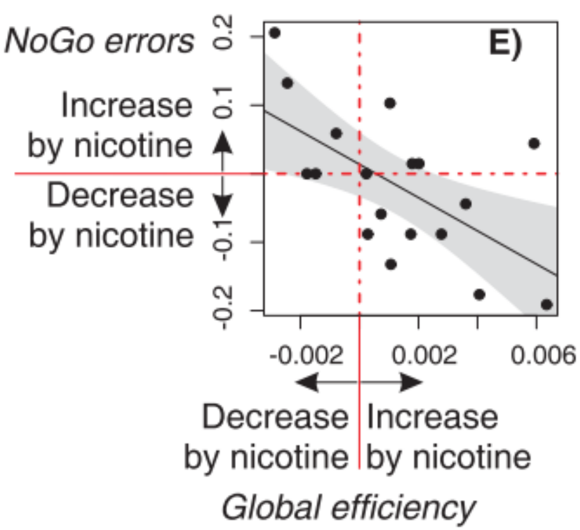
Nicotine reduces NoGo errors in error-prone subjects



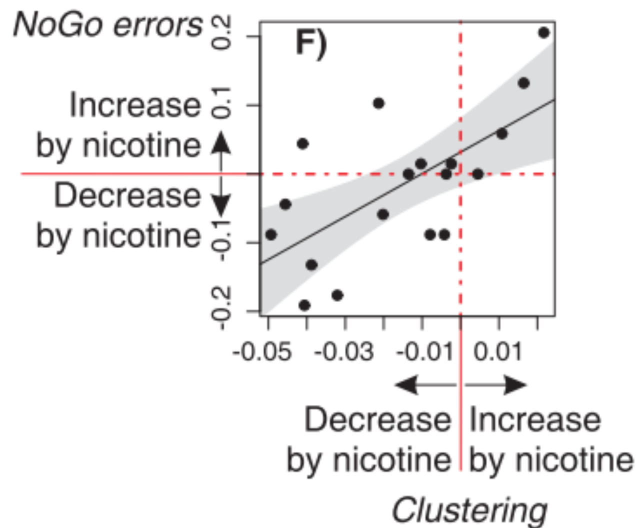
Giessing et al (2011) in review

Network-effects of Nicotine

Nicotine tends
to increase
Global Efficiency

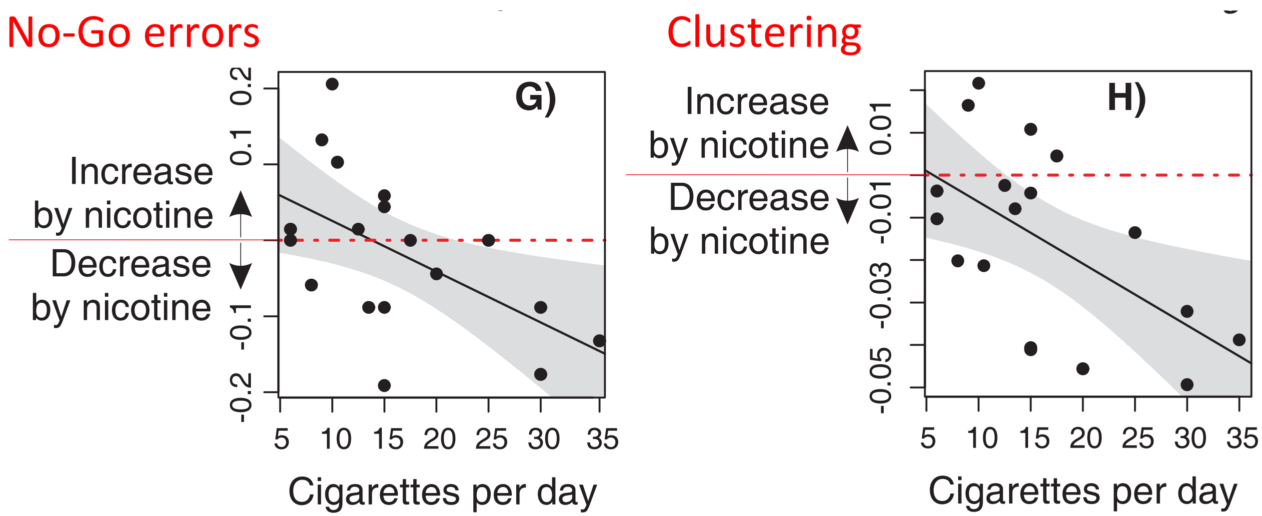


Nicotine tends
to decrease
Clustering



Giessing et al (2011) in review

Dependence-dependence



Giessing et al (2011) in review

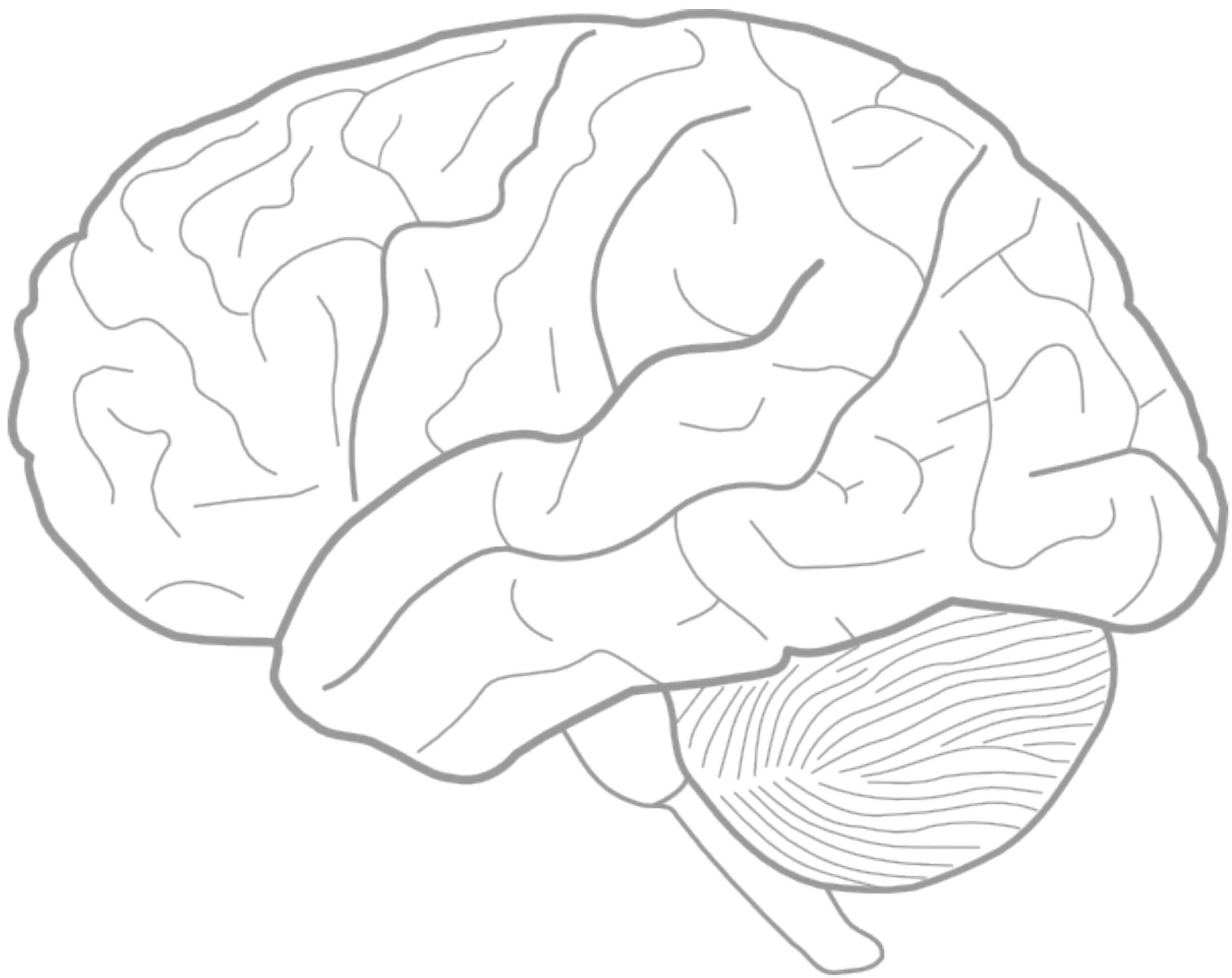
Challenges for fMRI network analysis

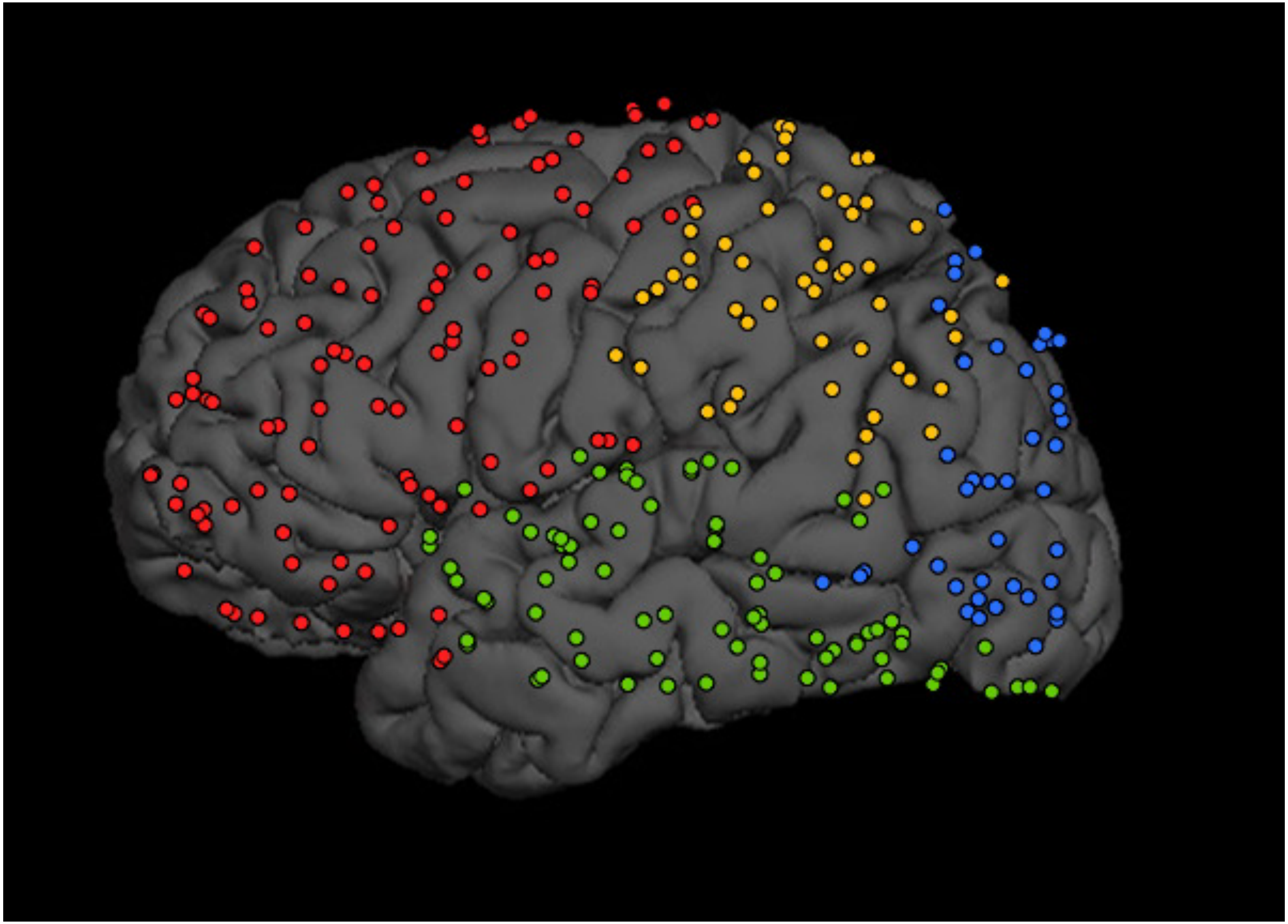
1. Methodological issues:
   - Preprocessing
   - Differentiating neuronal effect and confounding vascular effect

2. Sensitivity of network measures:
   - Group differences for less severe diseases
   - Diagnosis of individuals

3. Differentiating disease profiles:
   - Increased E: with high IQ, with Nicotine, in schizophrenia…
   - Decreased E: with age, in Alzheimer’s disease, with Sulpiride…

Any Questions?





Search for “twitterbrain” on YouTube