Human brain graphs

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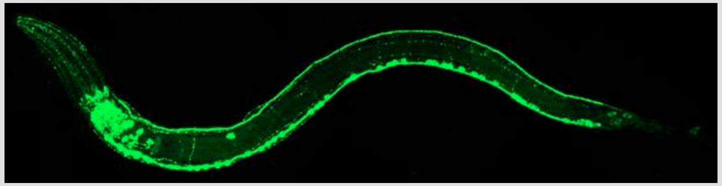
gsk

The state of the art?

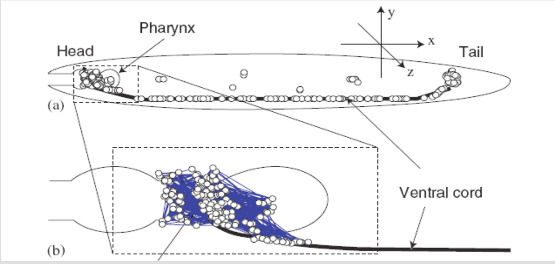
North America circa 1730

The small world of the worm's brain

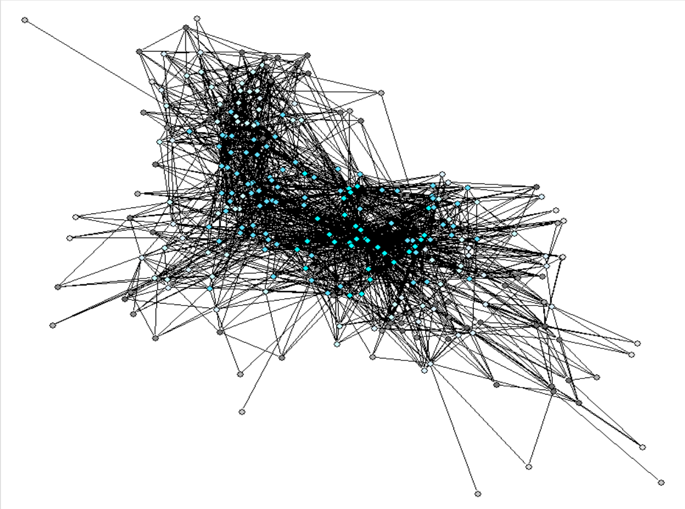
Caenorhabditis elegans



Anatomy (277 neurons, 7000 synapses)



Topology (277 nodes, 7000 edges)

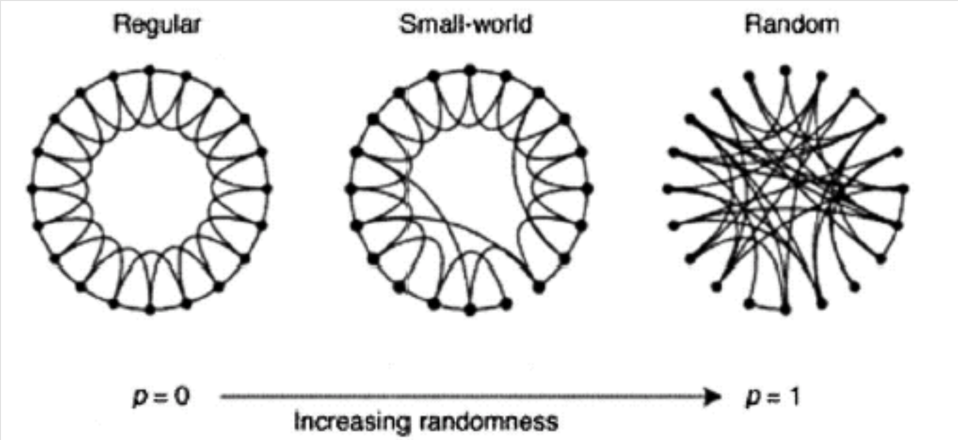


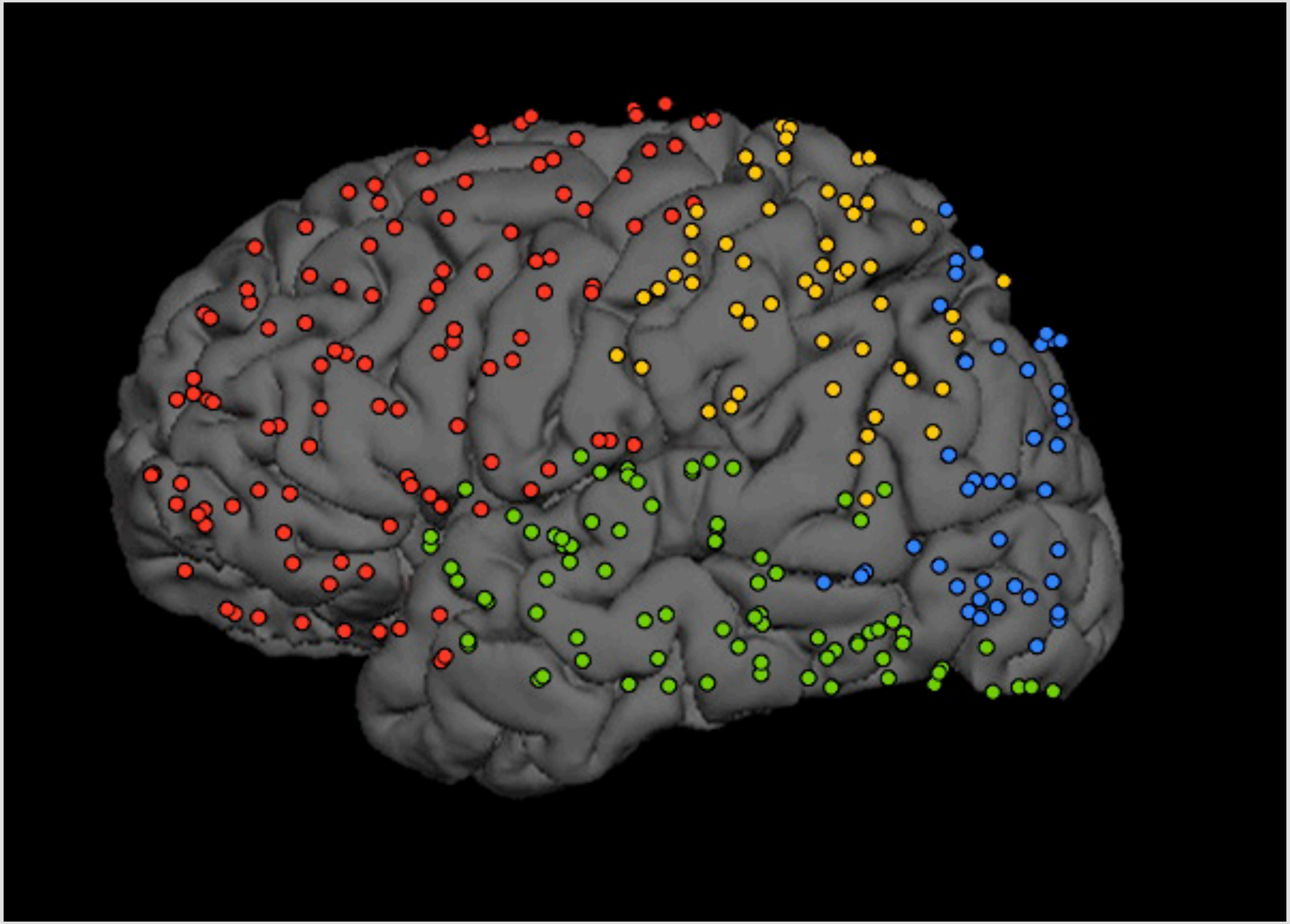
- Small-world
  - *High clustering or cliquishness of connections between neighboring nodes*
  - *Short path length or high efficiency of communication between any pair of nodes*

- Cost-efficient

  ~40% maximum efficiency of information transfer for only ~4% maximum connection cost

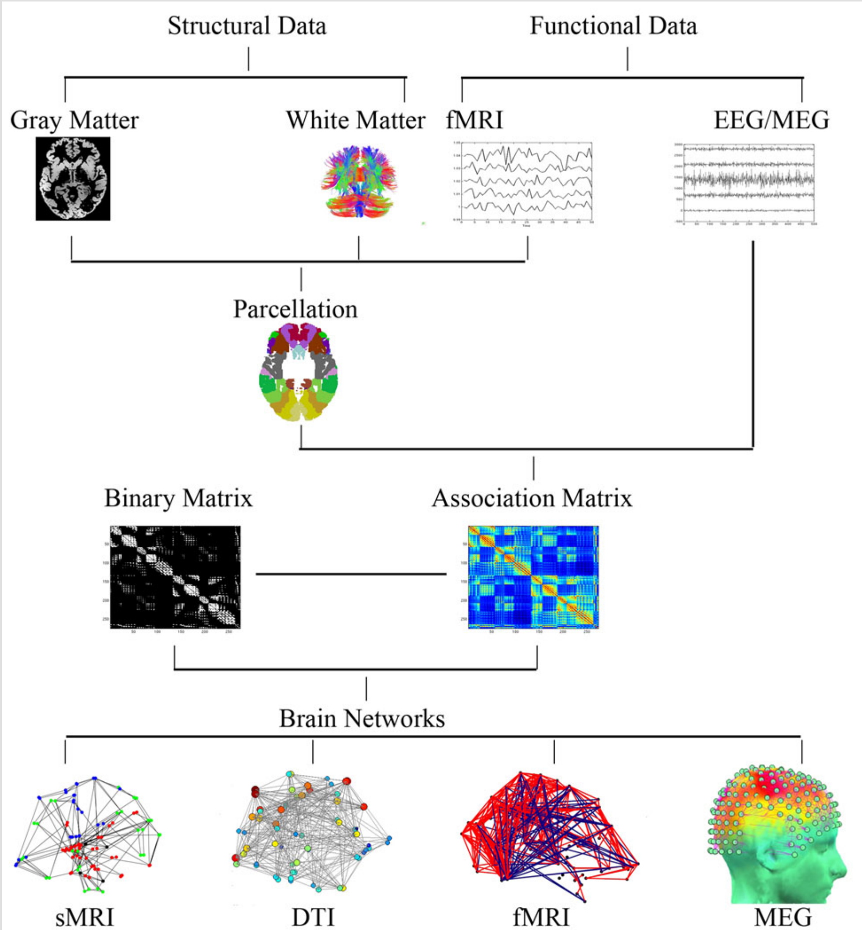
Watts & Strogatz (1998) *Nature;* Latora & Marchiori (2001) *Phys Rev Lett*





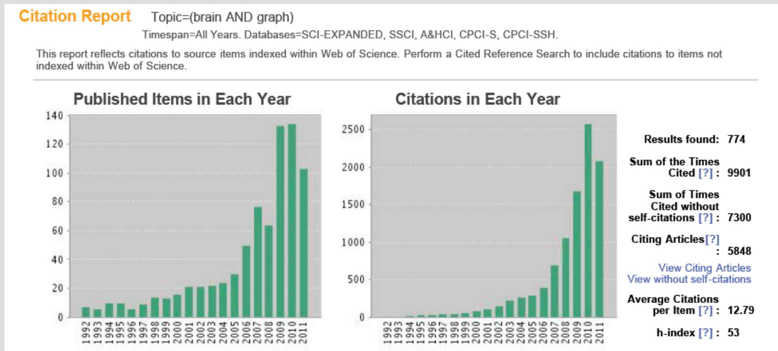
Vertes et al (2011) *YouTube*
(search on neuro tweets)

From neuroimaging to human brain graphs v1.0



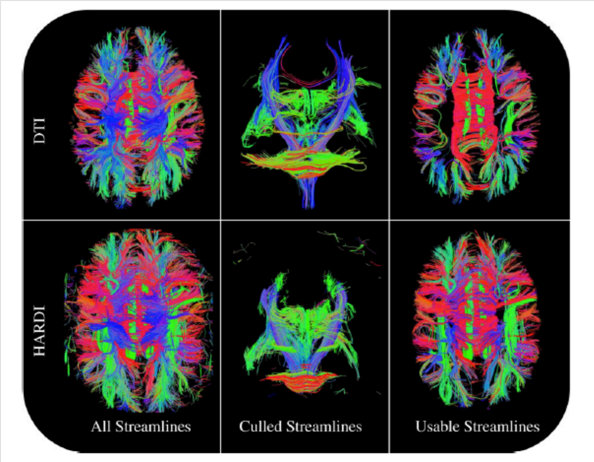
1. Estimate an association matrix from the data
   - What are the nodes?
   - What metric of connectivity?
2. Generate an adjacency matrix from the association matrix
   - What are the edges?
3. Measure topological properties of each graph and compare between graphs

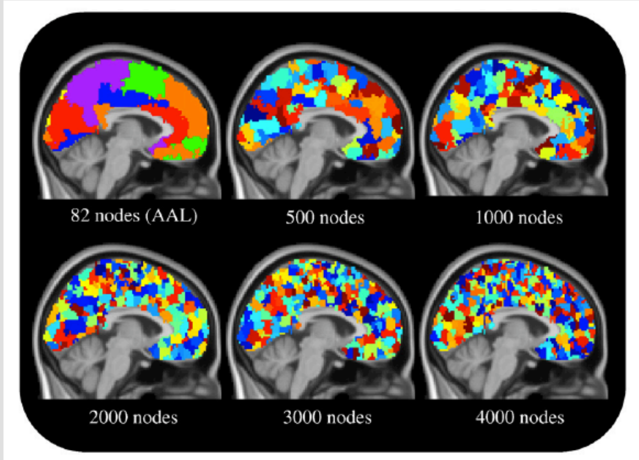
Binary undirected graphs predominate currently but are almost certainly not optimal

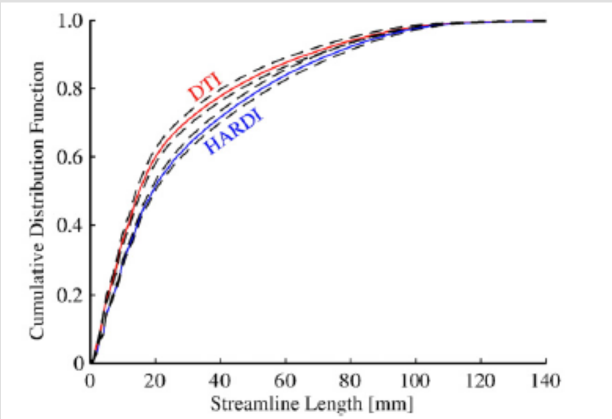


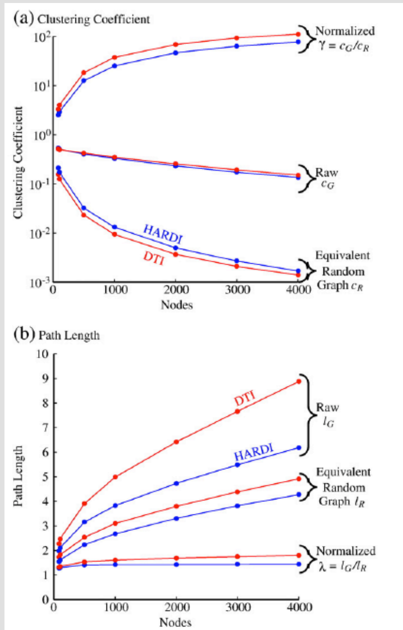
Bassett & Bullmore (2010) *Curr Op Neurol;* Bullmore & Bassett (2011) *Annu Rev Clin Psychol*

What are the nodes?





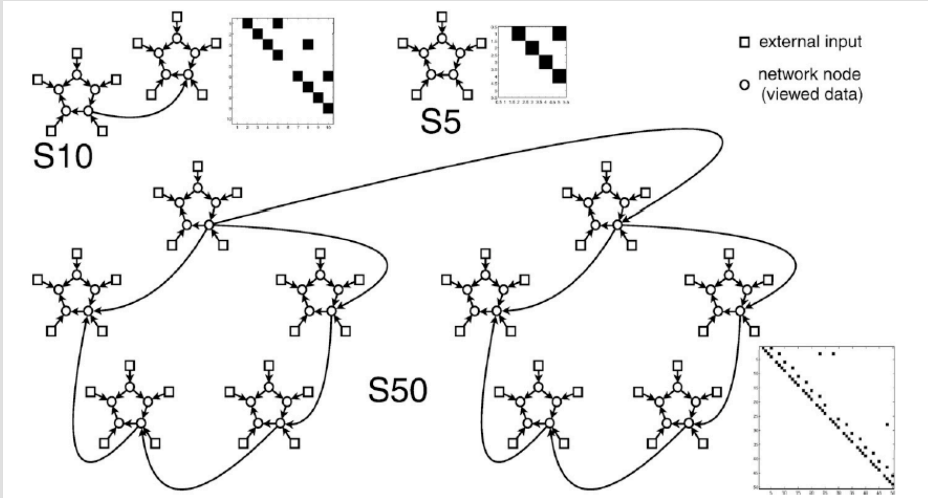


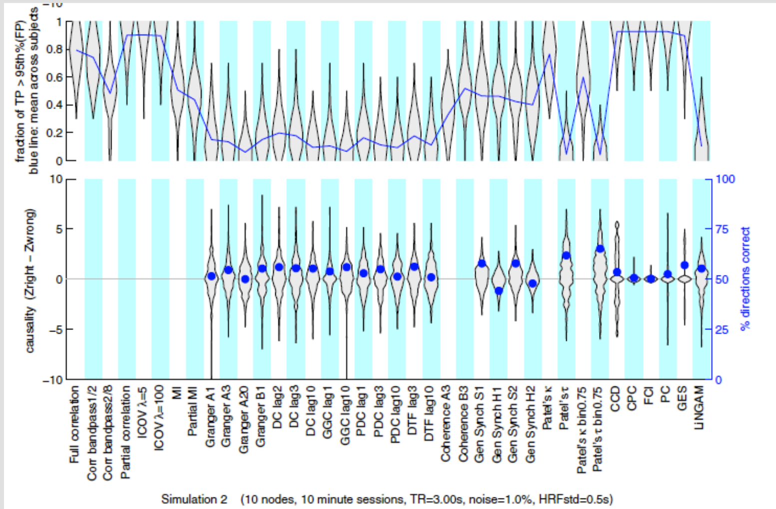


Zalesky et al (2010) Neuroimage

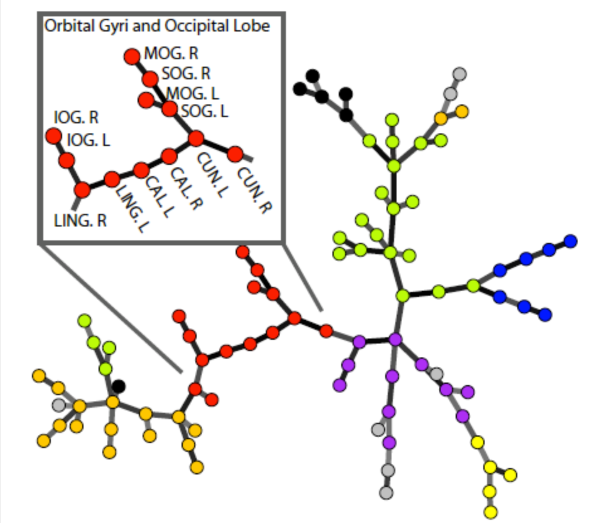
What connectivity metric?

- Functional, symmetric, non-causal
  - Correlation, partial correlation…
  - Will generate undirected graphs
- Effective, asymmetric, causal
  - Granger causality, DCM…
  - Will generate directed graphs
- Frequency-specific, narrow-band
  - Coherence, partial coherence (Fourier)
  - Wavelet correlations
  - Will generate a graph per frequency band
- Sensitivity to nonlinear interactions
  - Mutual information
  - Phase synchronization
  - Synchronization likelihood



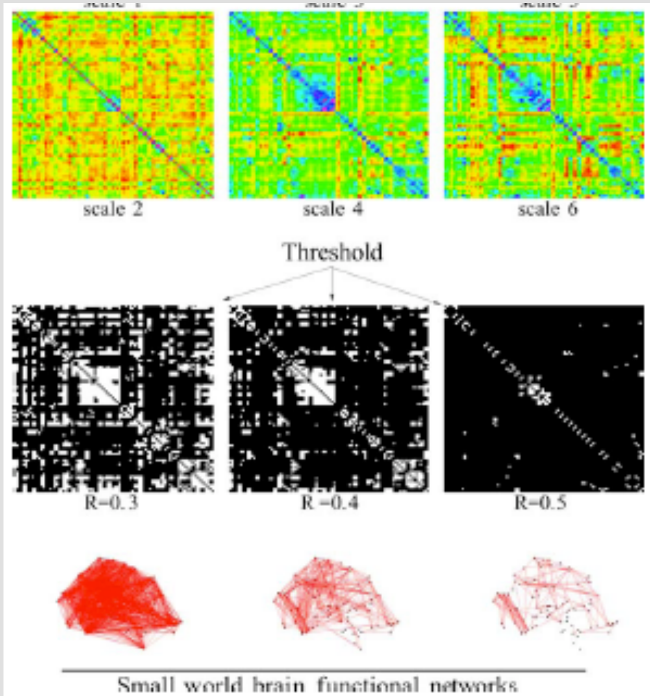


Smith et al (2010) *NeuroImage*



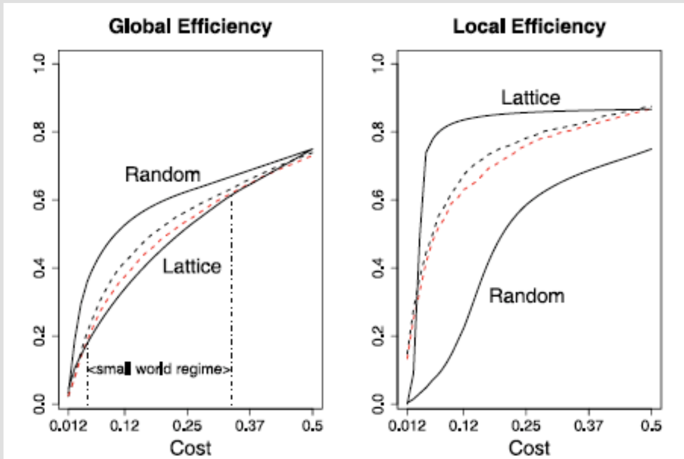
What are the edges?

Dependency on threshold and connection density



- Global hard thresholding is the simplest way to define binary or unweighted edges from an association matrix
  - Minimum spanning trees and other graph construction algorithms can be used to force full connectedness at sparsest cost

- Changing threshold changes connection density and network parameters will change accordingly
  - Explore network properties over a range of costs
  - Or define a unique threshold, for example, by controlling type 1 error (FDR)



Achard et al (2006) *J Neurosci*

Achard & Bullmore (2007) *PLoS Comp Biol*

Many properties are broadly conserved across many scales and kinds and species of brain graphs

Small worldness

- high clustering
- short path length or high efficiency

Cost-efficiency

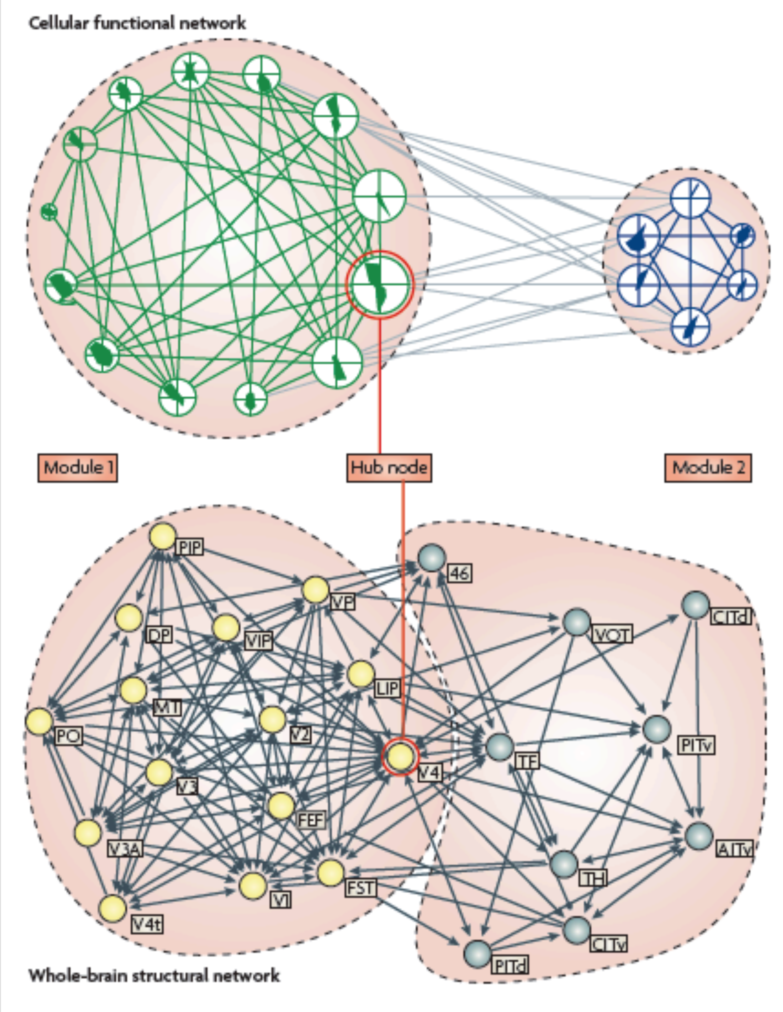
- high efficiency of information transfer for relatively low connection cost

Hub nodes

- fat-tailed degree distributions

Modularity

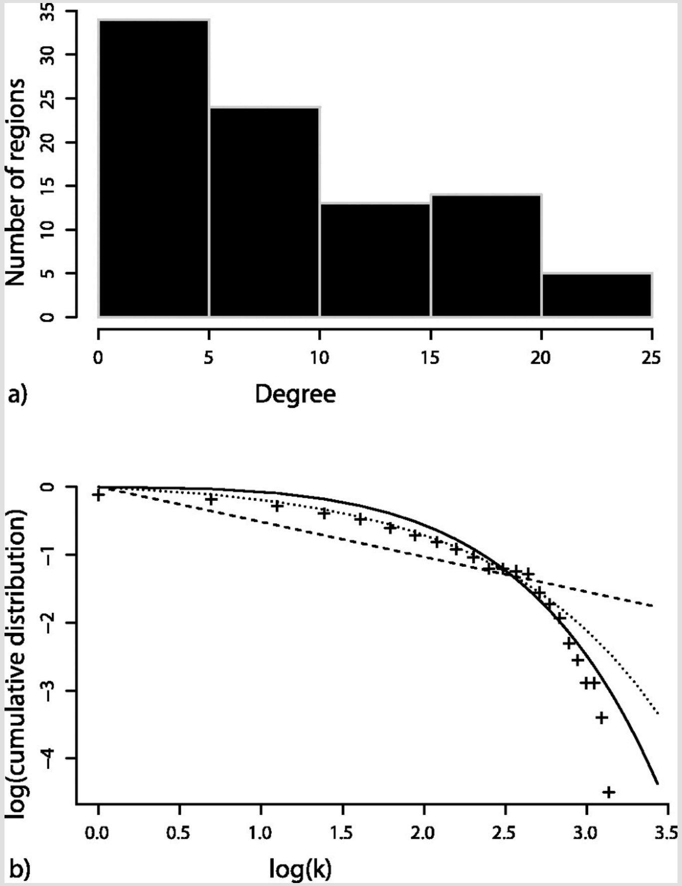
- nodes are more densely connected to other nodes in the same module than to nodes in other modules

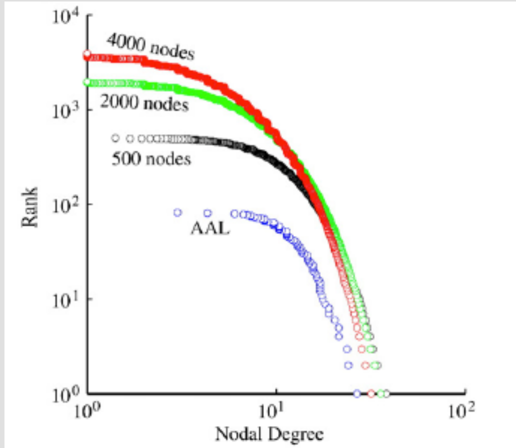


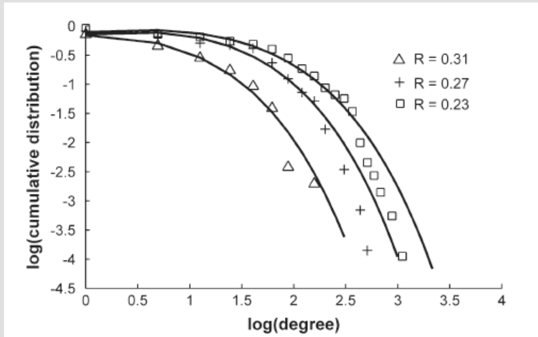
Bullmore & Sporns (2009) *Nat Rev Neurosci*

Sporns et al (2007) *PLoS ONE;* Yu et al (2008) *Cereb Cortex;* Meunier et al (2010) *Front Neurosci*

The degree distribution of brain graphs is typically *not* a power law



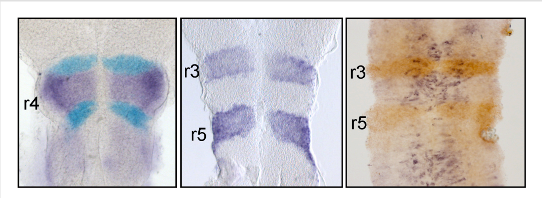


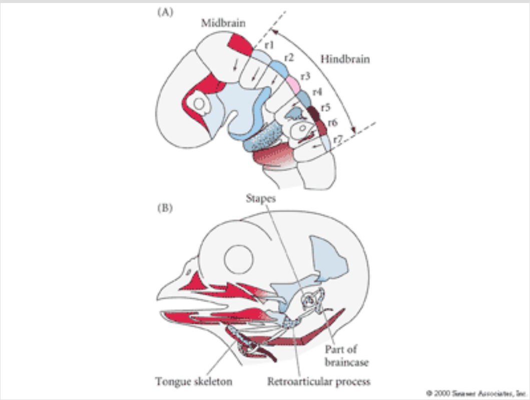


Functional MRI
Achard et al (2006) *J Neurosci*

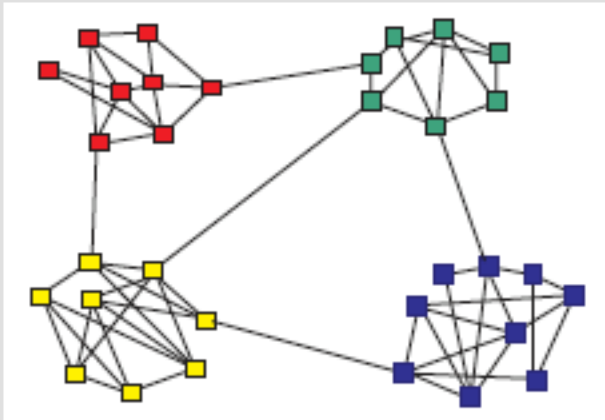
Structural MRI, Diffusion MRI
He et al (2007) *Cereb Cortex*
Zalesky et al (2010) *Neuroimage*

There are many meanings of “modularity” in neuroscience: (how) are they related?





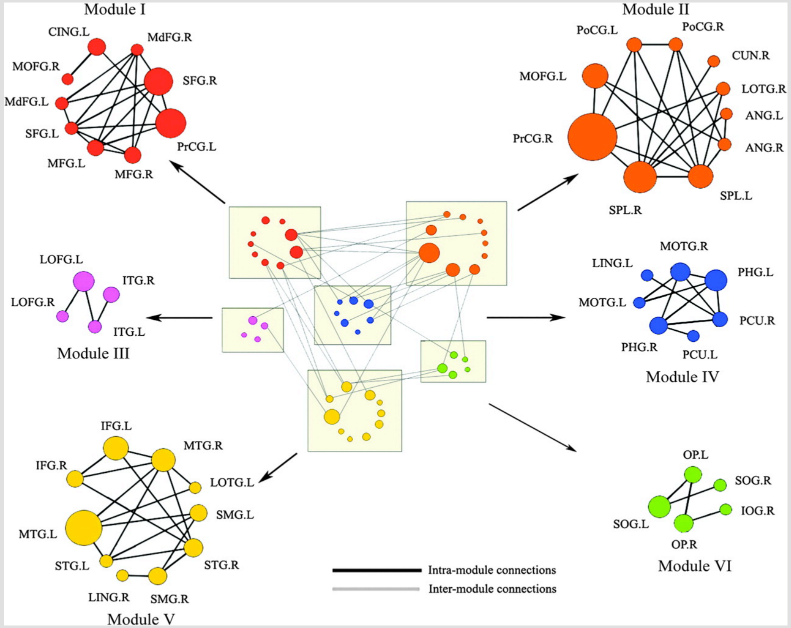
Developmental

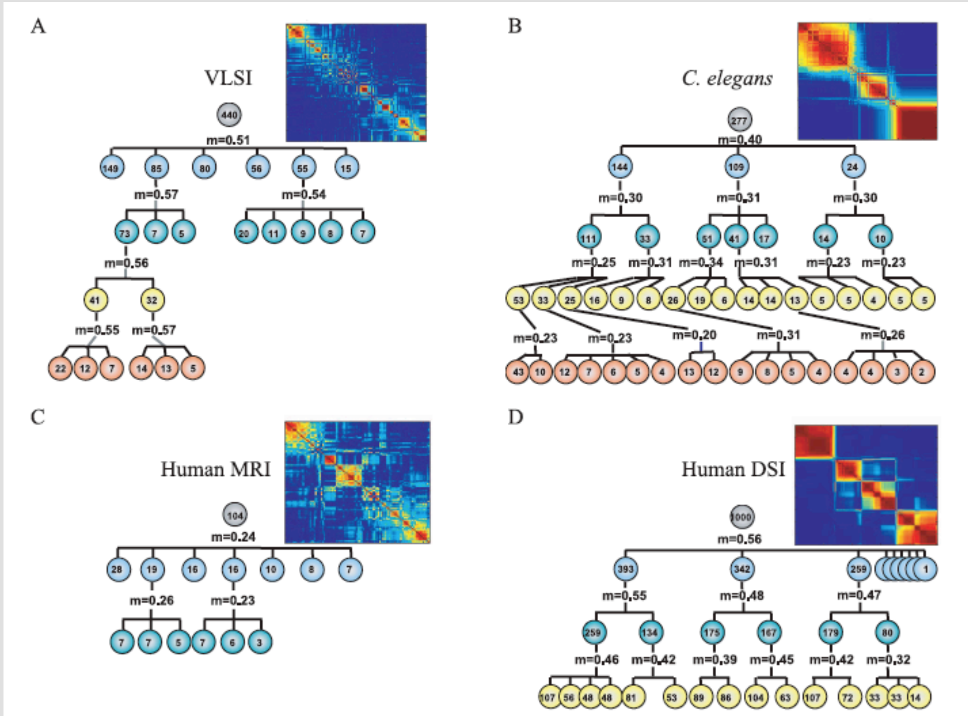


Topological

Psychological

Human brain graphs and other information processing networks are hierarchically modular





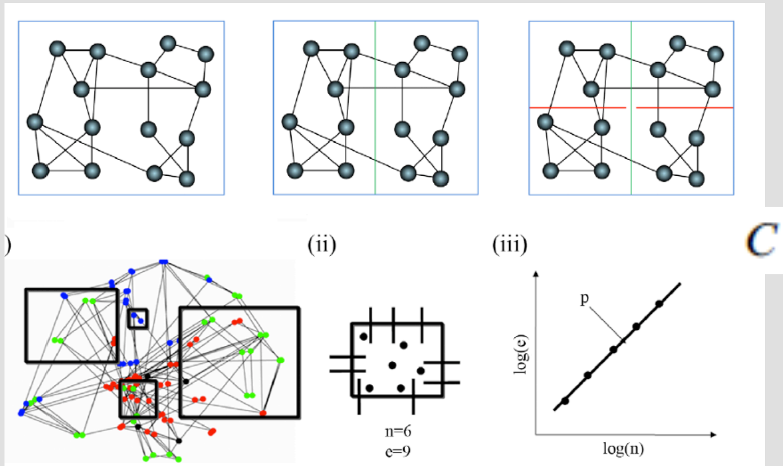
Nodes in the same module are often, but not always, anatomical as well as topological neighbours: so intra-modular edges will be shorter distance than inter-modular edges

Brain graphs typically have modules within modules

Meunier et al (2010) *Front Neurosci*; Bassett et al (2010) *PLoS Comp Biol;* Chen et al (2008) *Cereb Cortex*

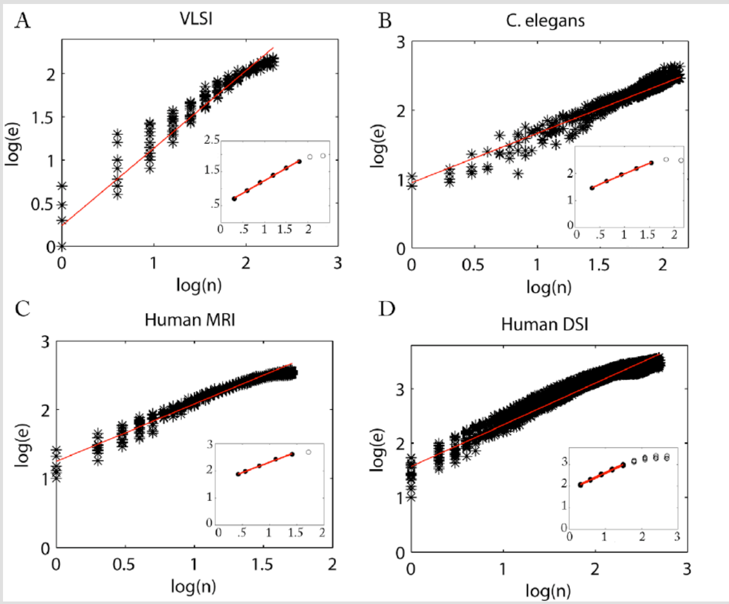
Rentian and allometric scaling in brains

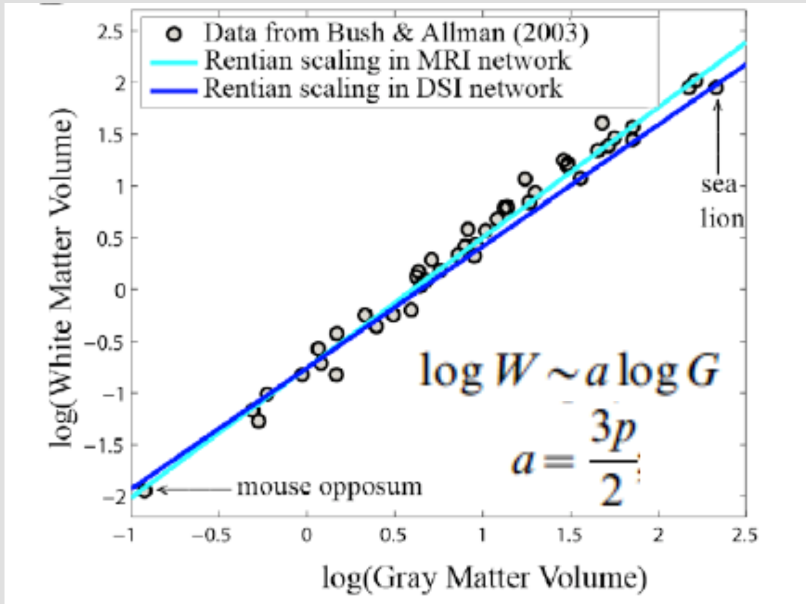
Bassett et al (2010) *PLoS Comp Biol*



Rent's rule

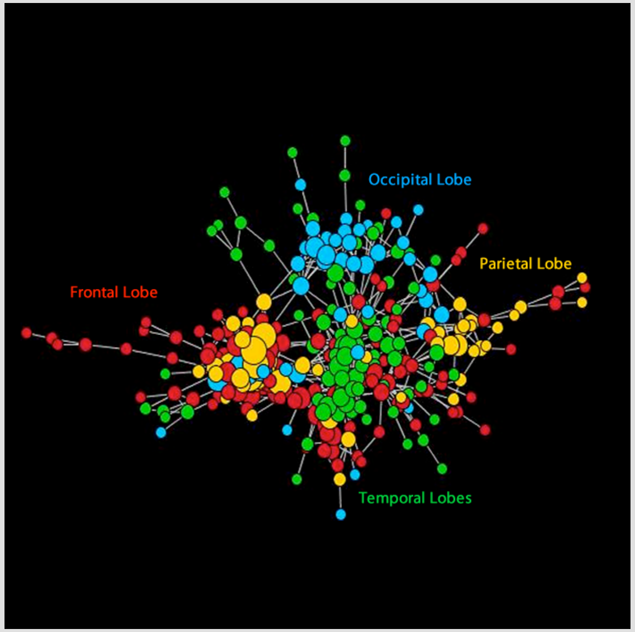
$$C = k\,N^{p}$$

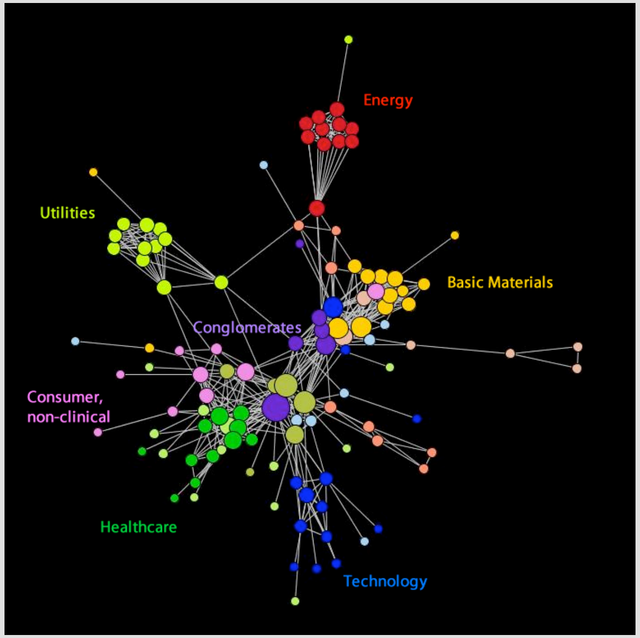


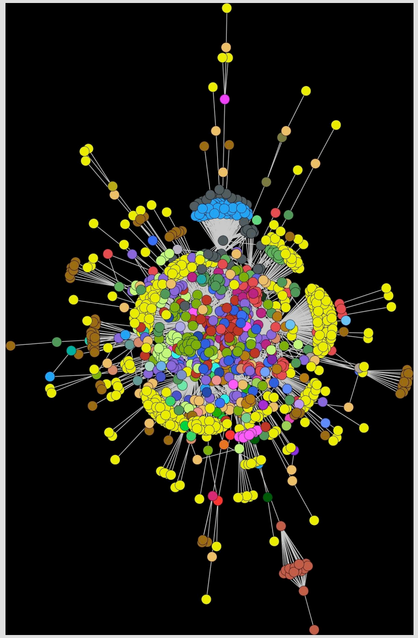


Allometric scaling of mammalian brains is approximated by Rentian scaling of human brain

What's special and what's not so special about human brains compared to other information networks?



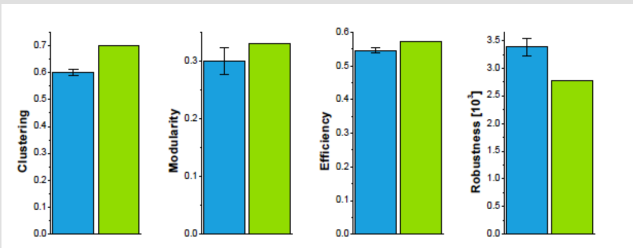




Human Brain Network
Resting state FMRI

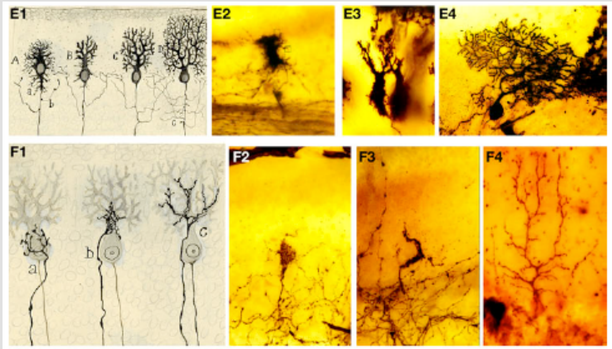
Economic Network
New York Stock Exchange

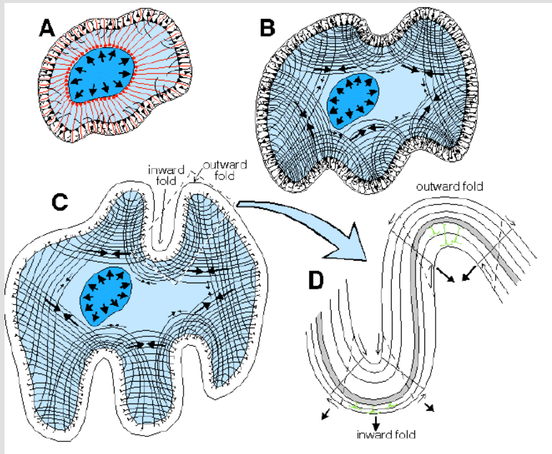
Social Network
Twitter #gadaffi

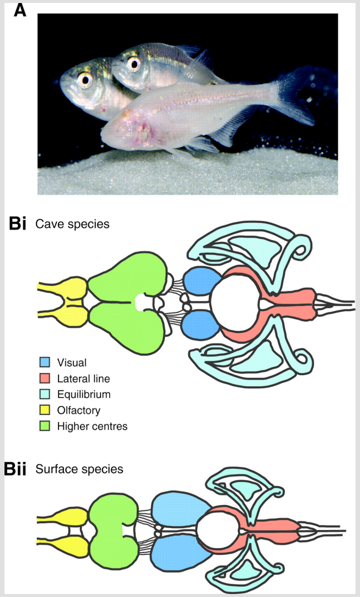


Vertes et al (2011) *Front Sys Neurosci*

"Back to anatomy": considering the costs of spatially embedded and metabolically expensive brain networks







Cajal's economical principle:

"We realized that all of the various conformations of the neuron and its various components are simply morphological adaptations governed by laws of conservation for time, space, and material."

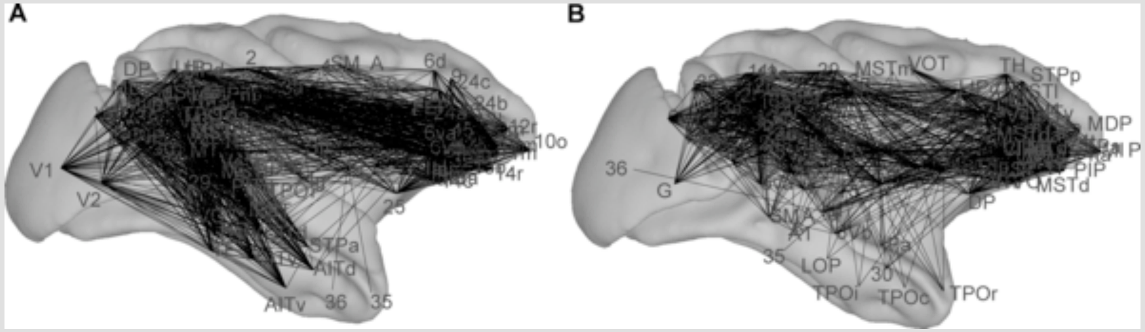
Increasing awareness also of the metabolic or energy costs of the nervous system and the biological drive to control metabolic as well as material costs of brains

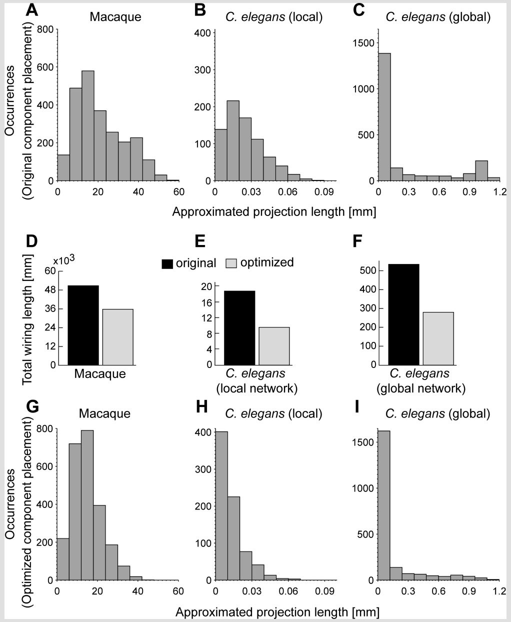
Human brain has ~2% of total body mass and spends ~20% of total energy budget

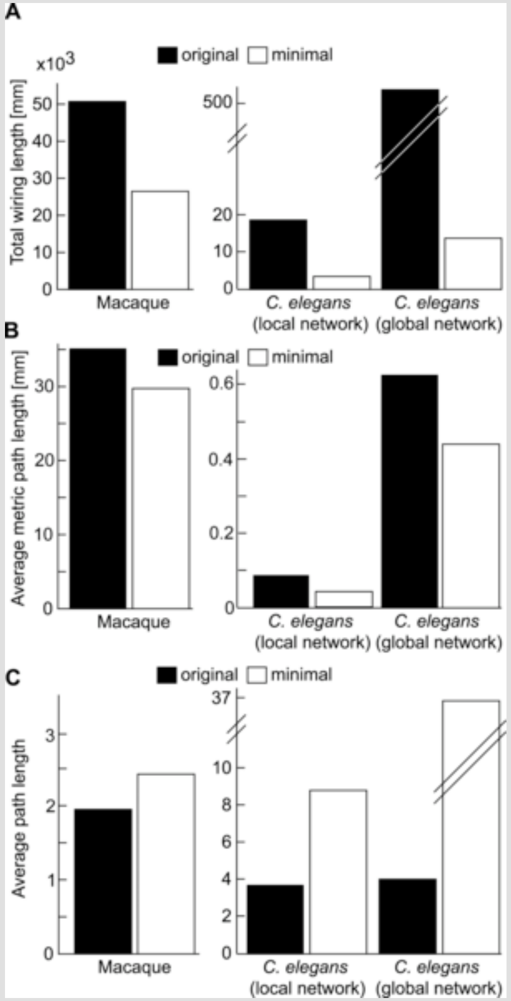
Van Essen (1997) *Nature*
Niven & Laughlin (2008) *J Exp Biol*
Garcia-Lopez (2010) *Front Neuroanatomy*

Brain networks are economically wired but do not strictly minimize wiring cost

Original Macaque Minimal

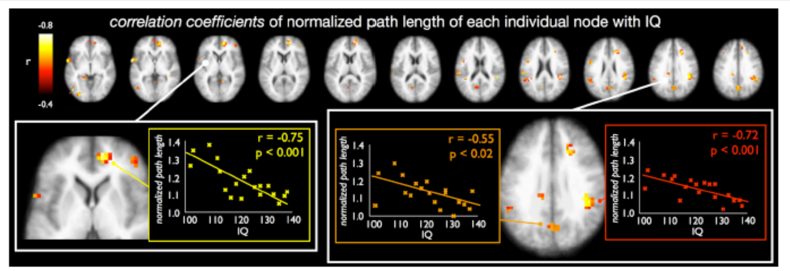


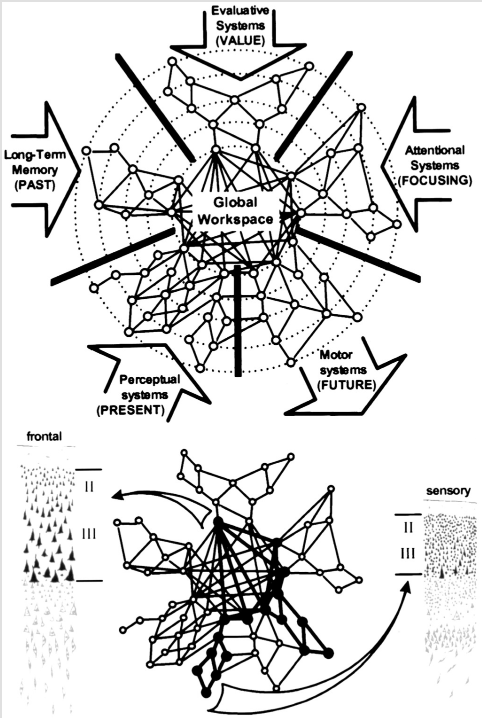




Kaiser & Hilgetag (2006) *PLoS Comp Biol*

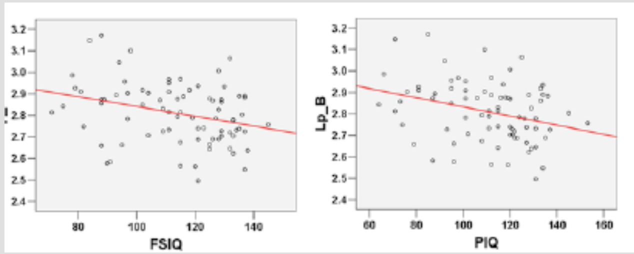
Expensive integrative connections may be "worth it" for extra cognitive capacity





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

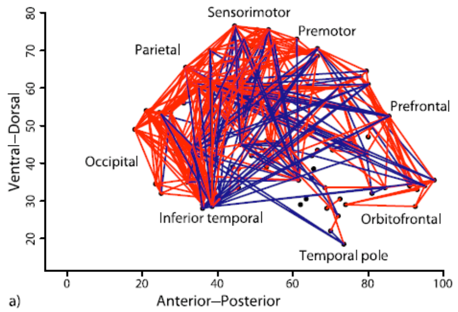
Van den Heuvel et al (2009) *J Neurosci*; Li et al (2009) *PLoS Comp Biol;* Bassett et al (2010) *PLos Comp Biol*;



- Global (neuronal) workspace theory predicts integrative networks will be required for conscious, effortful processing

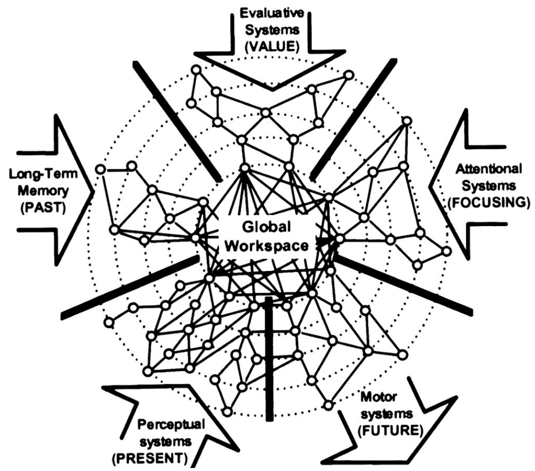
Dehaene et al (1998) *Proc Natl Acad Sci*
Baars (1993) *A cognitive theory of consciousness*

Cartoon interpretation of economical small-world architecture in terms of cognitive processes



High efficiency
Short path length
(Higher cost)

High clustering
Modularity
(Lower cost)



Integrated processes

General – eg "executive"
Isotropic (IQ)
Distributed
Conscious
Effortful

Segregated processes

Specialised – eg face vision
Encapsulated
Localised
Unconscious
Automatic

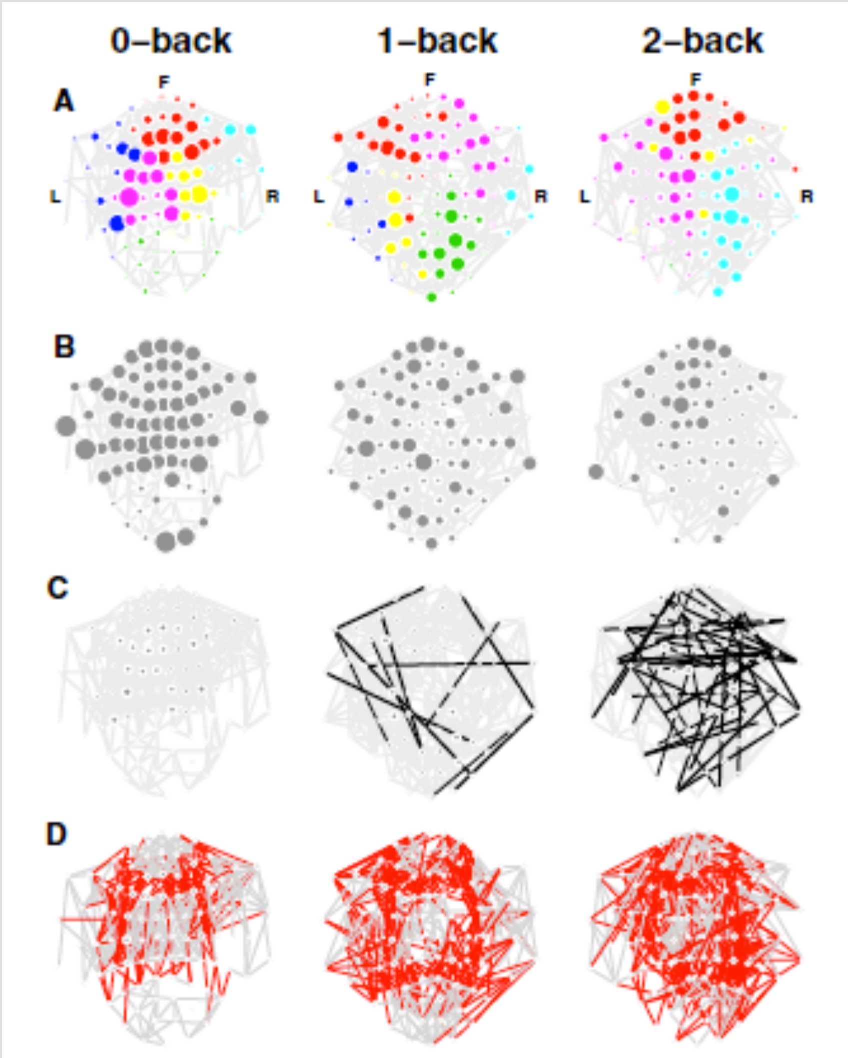
Working memory load "breaks modularity" and drives workspace configuration of functional brain networks

Modules

Clustering

Long-distance edges

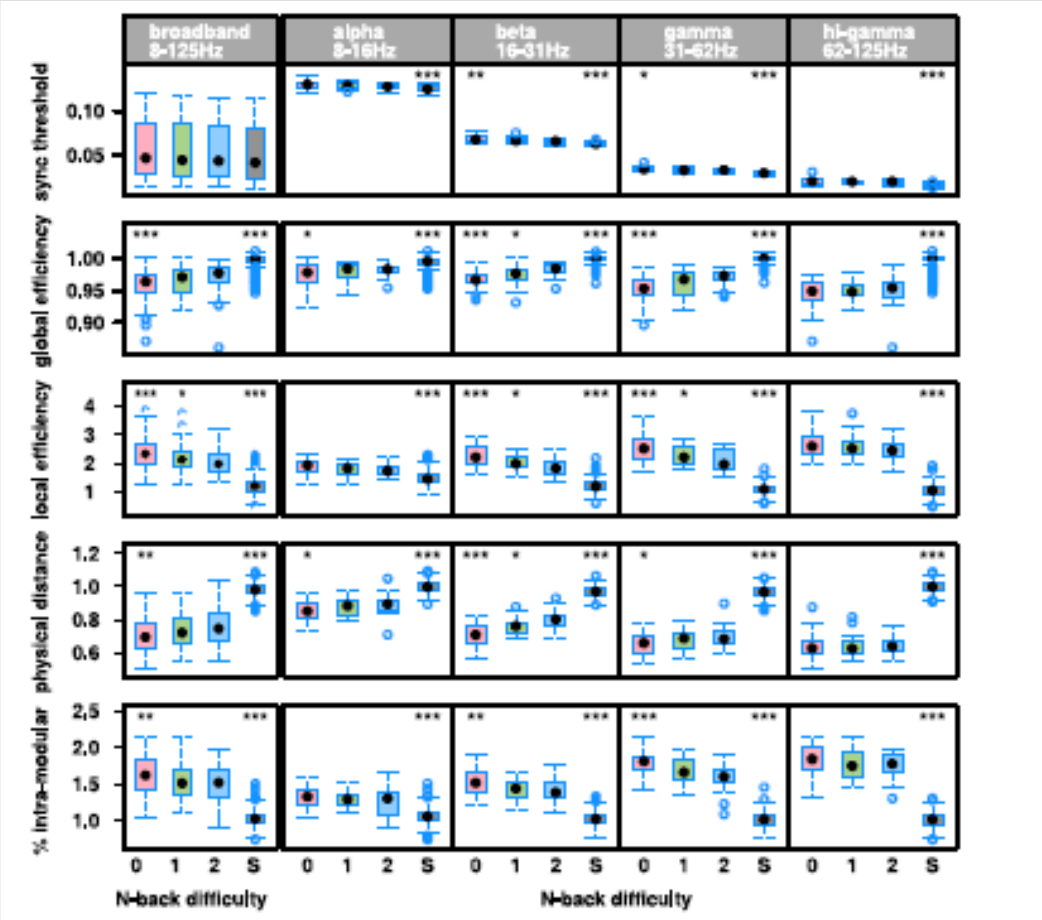
Inter-modular edges

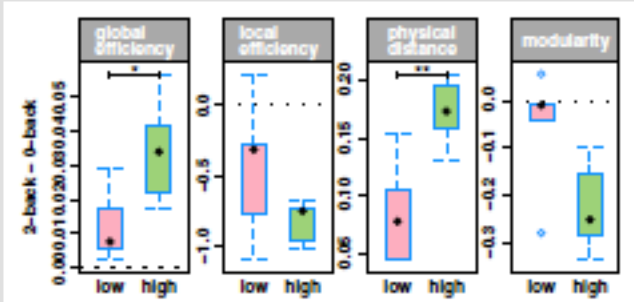


β-band frequency networks recorded using MEG in healthy volunteers performing N-back working memory task

Kitzbichler et al (2011) *J Neurosci*

Task difficulty-related MEG network changes are clearest in beta and gamma intervals

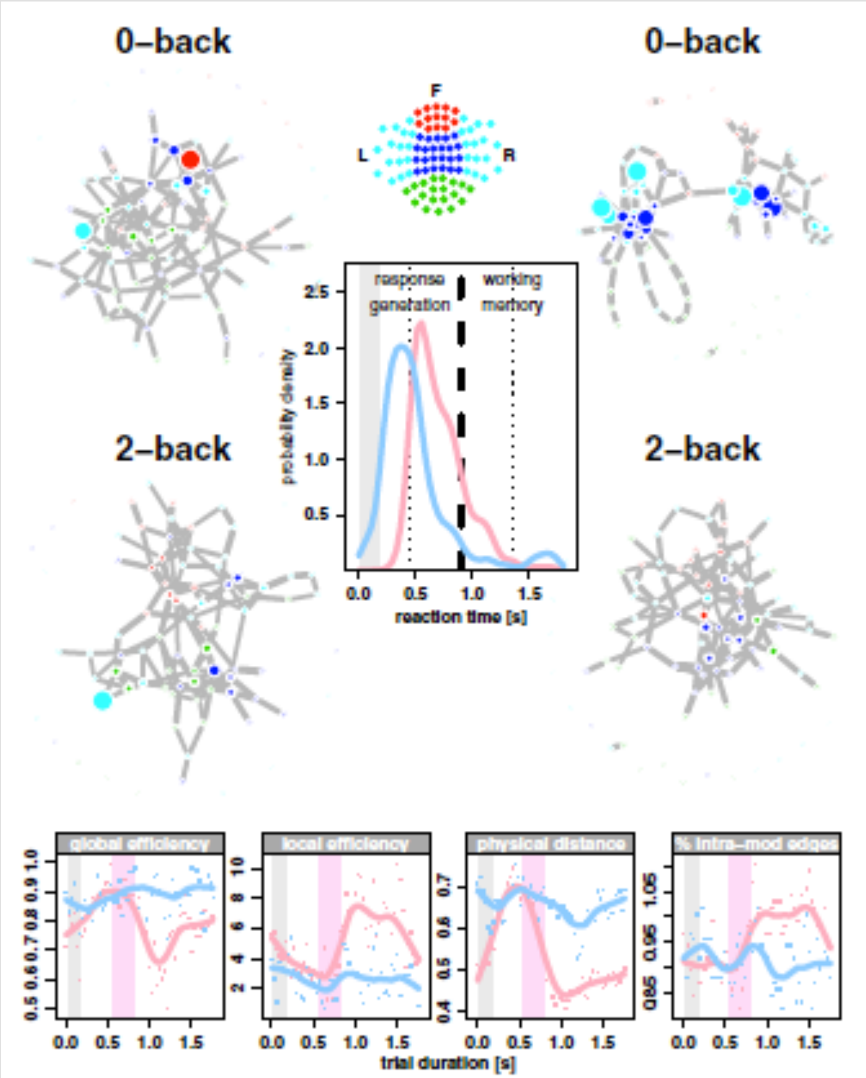




High performing individuals show greater task-related changes in beta band networks

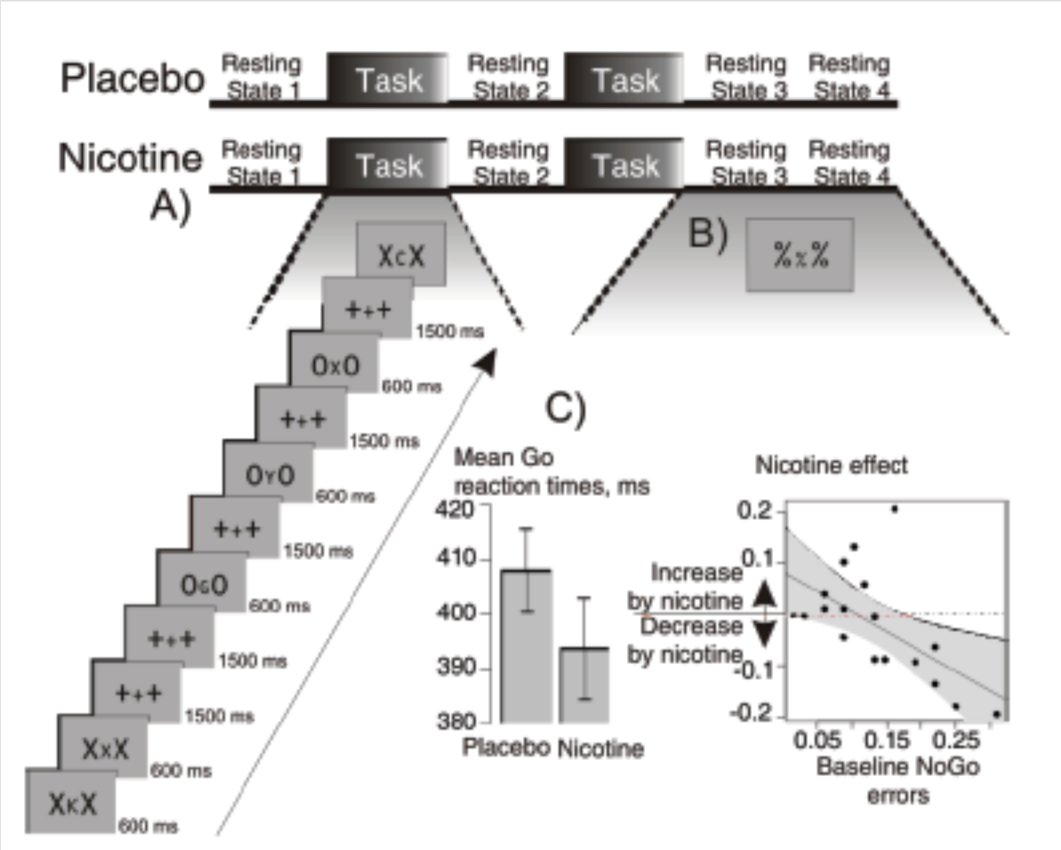
Kitzbichler et al (2011) *J Neurosci*

Functional brain networks rapidly "relax" from workspace configuration when cognitive effort is reduced



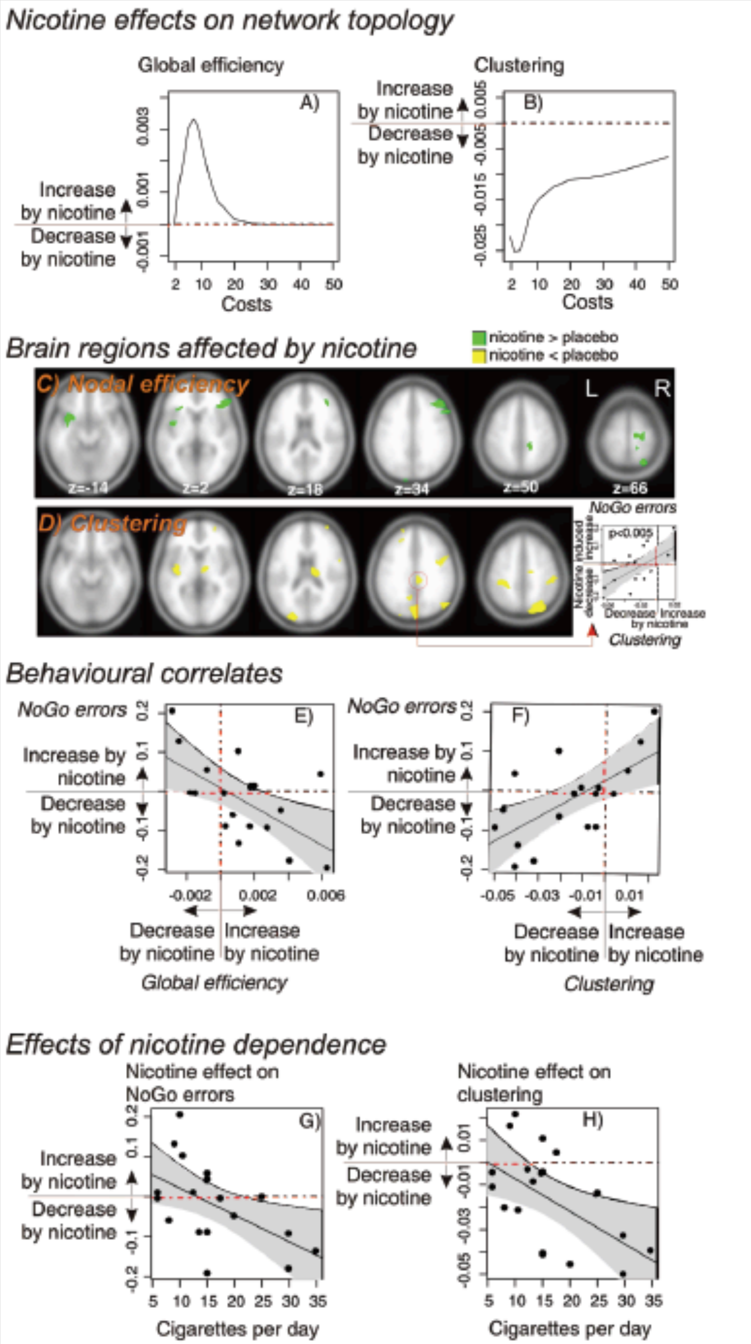
Kitzbichler et al (2011) *J Neurosci*

What are the effects of an attention-enhancing drug on fMRI network configuration?

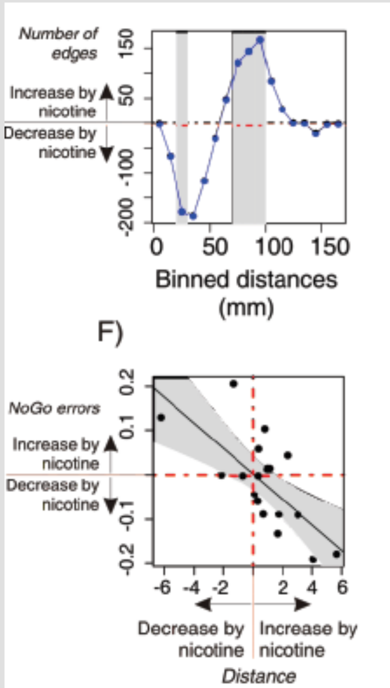


Temporarily abstinent cigarette smokers have impaired attentional performance which is restored by nicotine replacement

Giessing et al (2011) *in review*

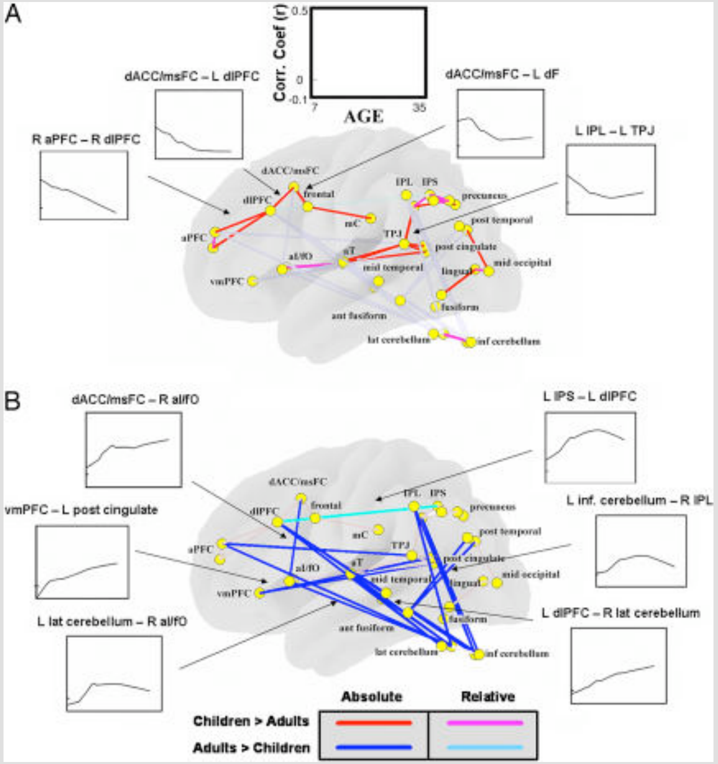


Nicotine enhances attentional performance as it increases network efficiency and connection cost (especially in most frequent smokers)



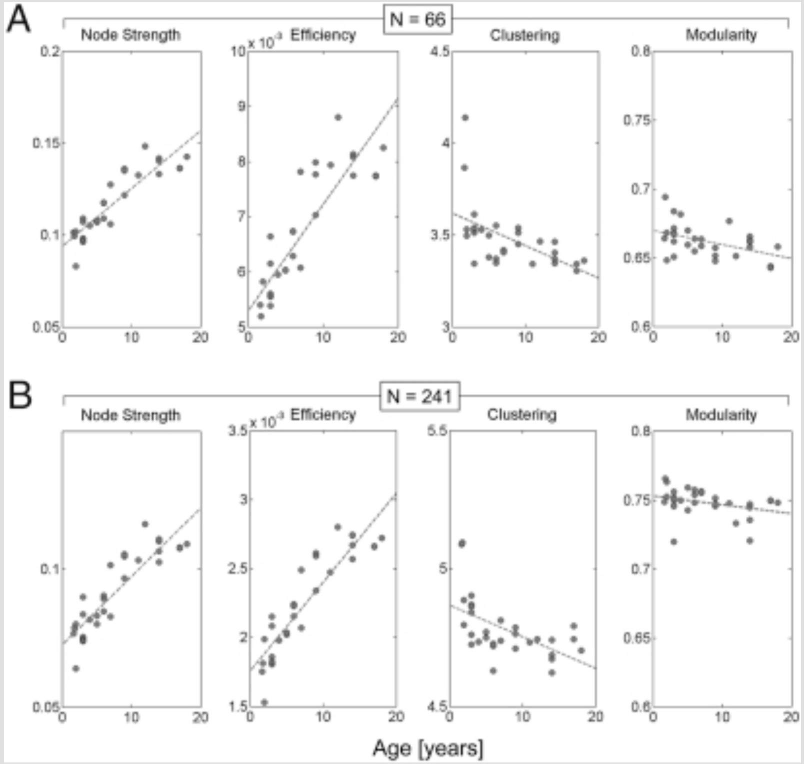
Giessing et al (2011) *in review*

Normal brain development is associated with changes in network efficiency and connection cost



Functional MRI networks

Connection distance increases with age



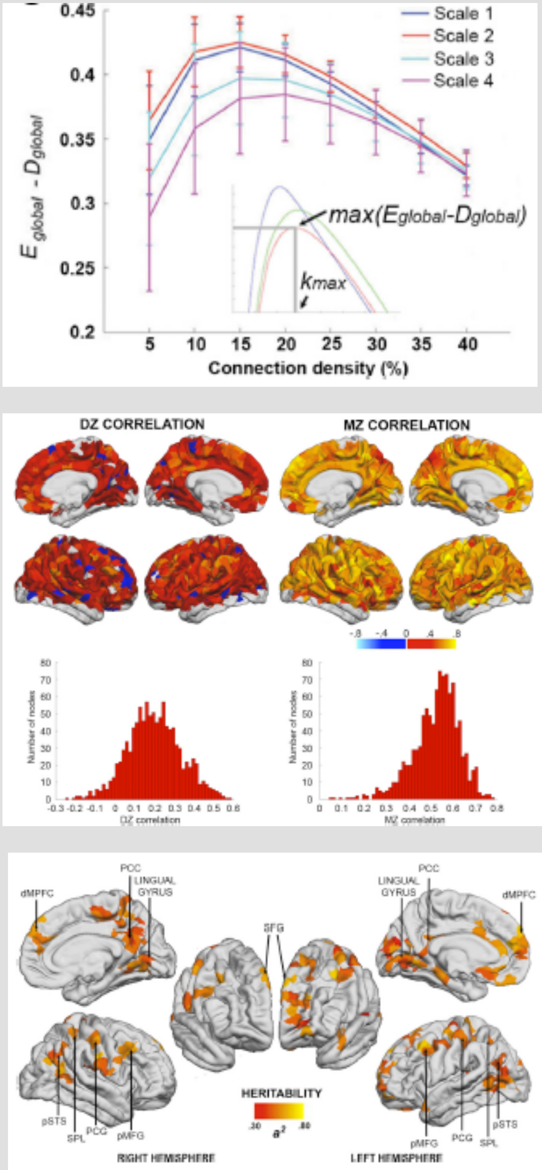
Anatomical DTI networks

Topological efficiency increases with age

Fair et al (2007) *Proc Natl Acad Sci*

Hagmann et al (2010) *Proc Natl Acad Sci*

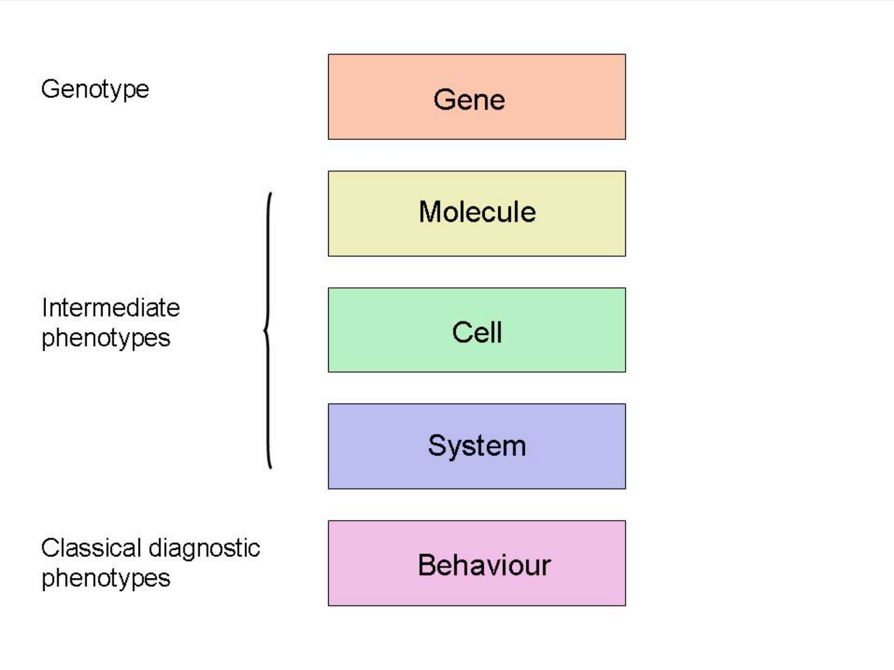
A simple way of measuring cost-efficiency and its heritability in human fMRI networks



- Trade-off between topological efficiency and wiring cost (connection distance) was measured in 20 MZ and 20 DZ twin pairs
- Global cost-efficiency was heritable ~0.6 and nodal cost-efficiency was heritable ~0.8 in symmetrical cortical regions
- Necessary but not sufficient for competitive selection hypothesis - brain networks are naturally selected by competitive criteria of minimising cost and maximising efficiency

Fornito et al (2011) *J Neurosci*

What do we need to explain in psychiatry and how does any of this help us?



- We need to explain a lot
- Most disorders are heritable with few specific causative genes yet identified
- Many disorders are developmental in origin but links to normal brain development are tenuous
- Access to molecular and especially cellular phenotypes in humans has been limited
- Classical diagnostic syndromes are not biologically defined and increasingly controversial

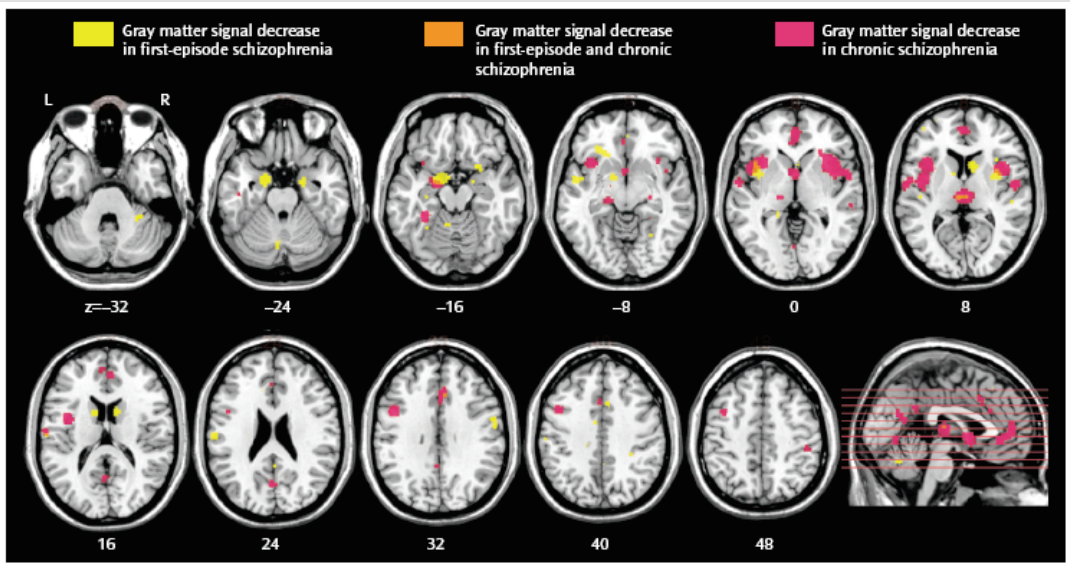
What does the brain look like in schizophrenia?

~1000 patients, 27 voxel-based morphometry studies

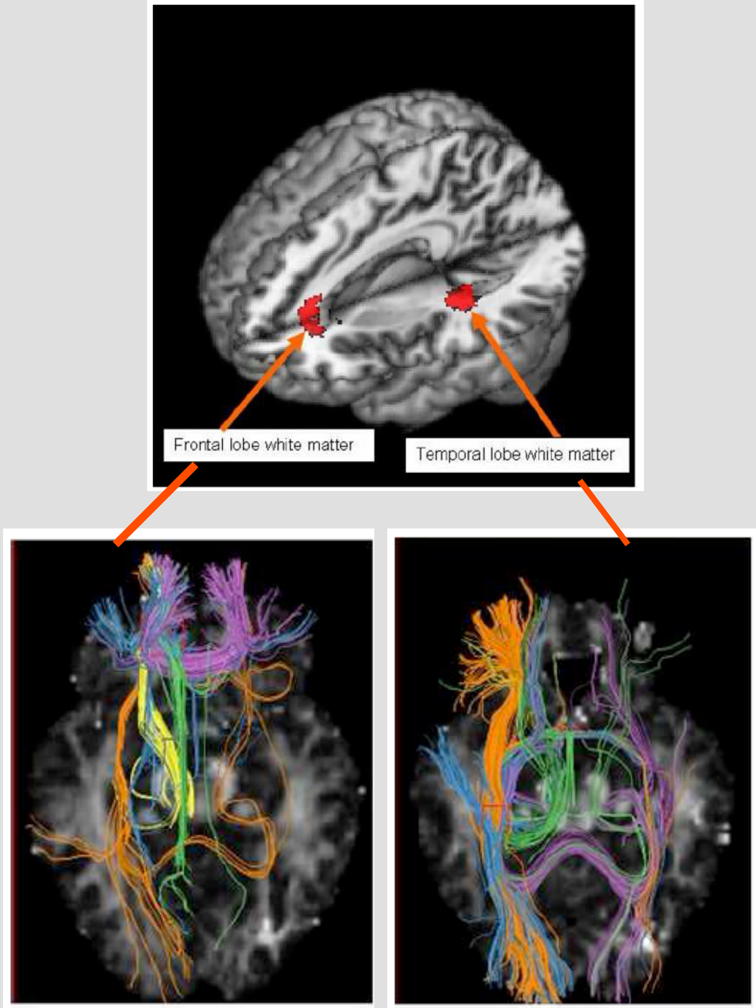
• Grey matter deficits distributed in medial temporal lobe, insula, medial and lateral prefrontal cortex, thalamus

• White matter deficits too

~400 patients, 15 DTI studies



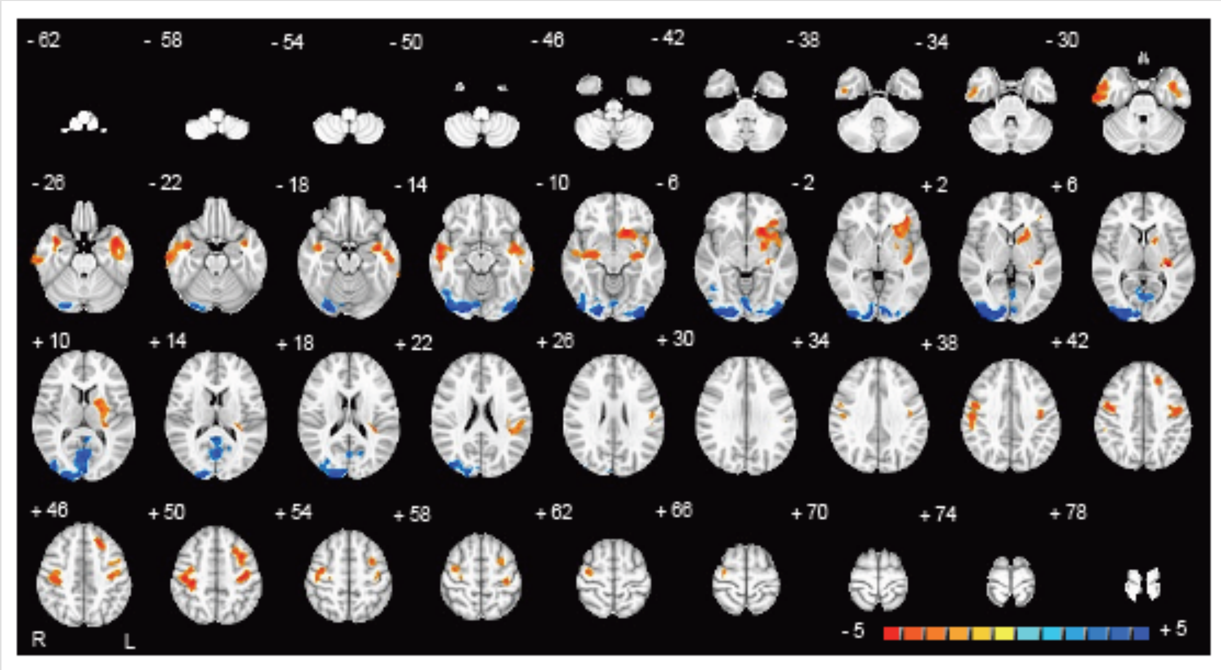
Gray Matter, MRI



Ellison-Wright et al (2008) *Am J Psychiatry*
Ellison-
Wright et al (2009) *Schiz Res*
Glahn et al (2008) *Biol*
Psychiatry

White Matter, DTI

What does the brain look like in autism?



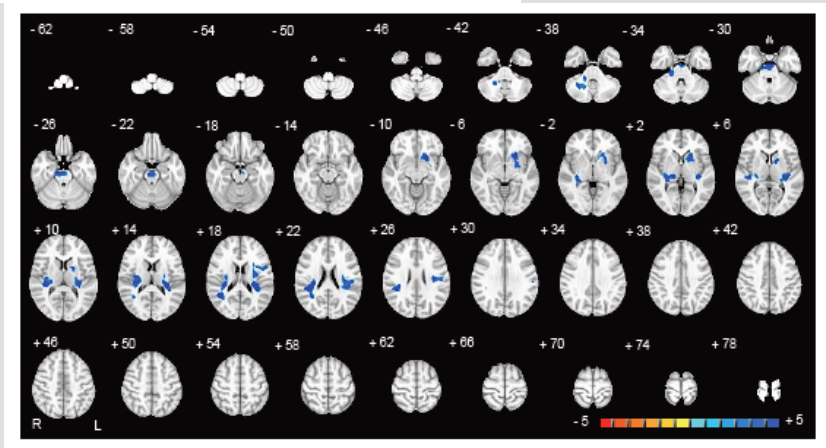
~100 patients, 100 healthy volunteers; study in London, Oxford & Cambridge

1 VBM

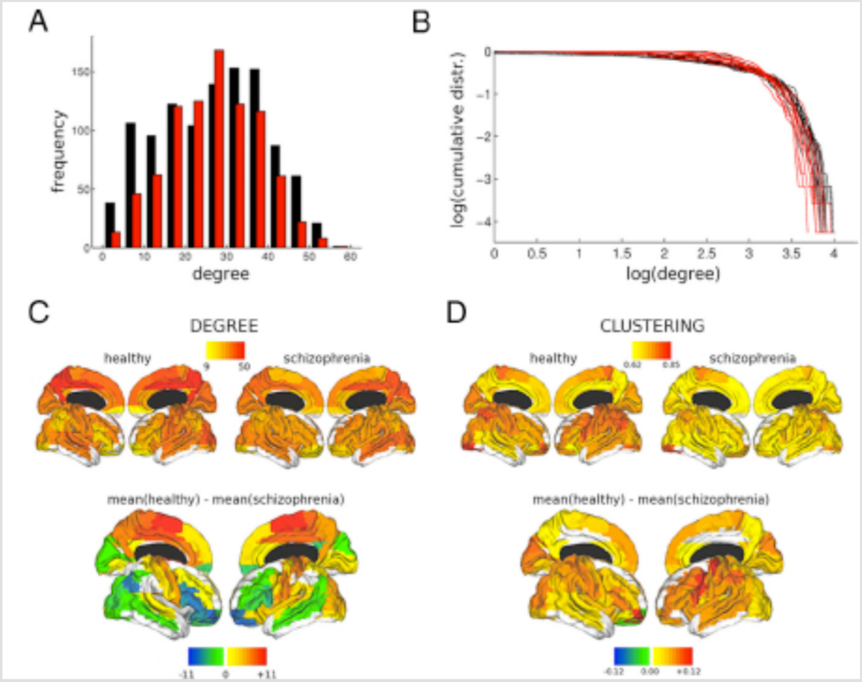
• Grey matter volume deficits in occipital cortex; grey matter excesses in basal ganglia, medial and lateral temporal cortex, premotor and prefrontal cortex

• White matter deficits too

Ecker et al (2011) *Archives Gen Psychiatry*



Topological abnormalities of brain graphs in schizophrenia



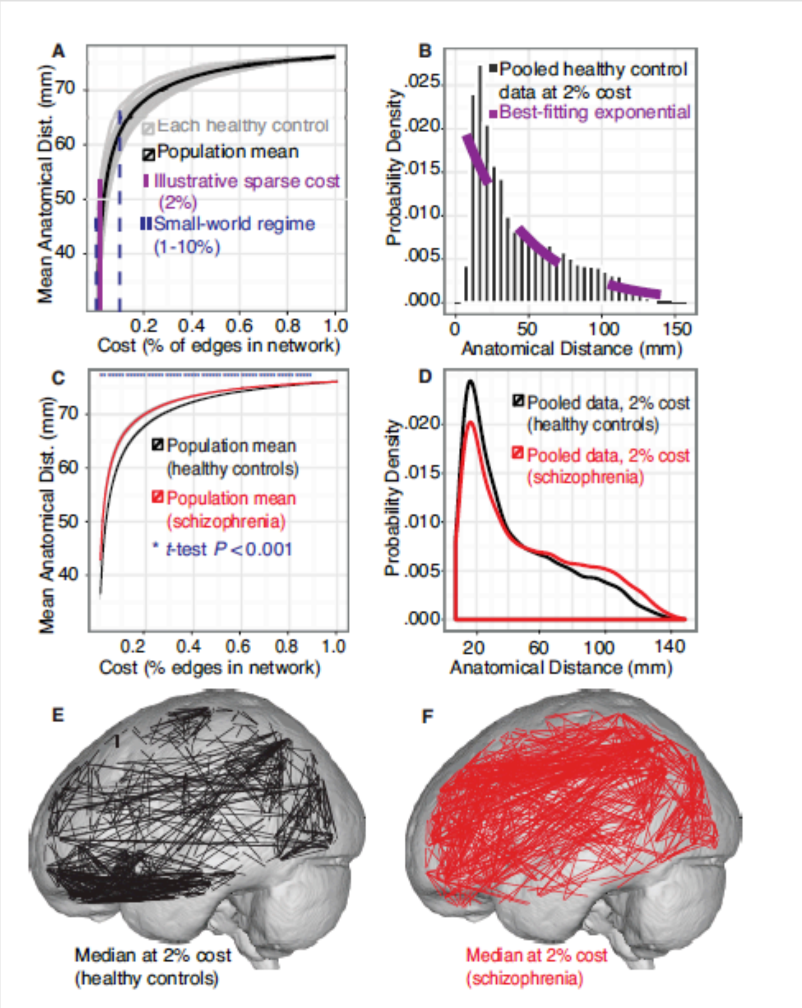
Brain functional networks in schizophrenia are:

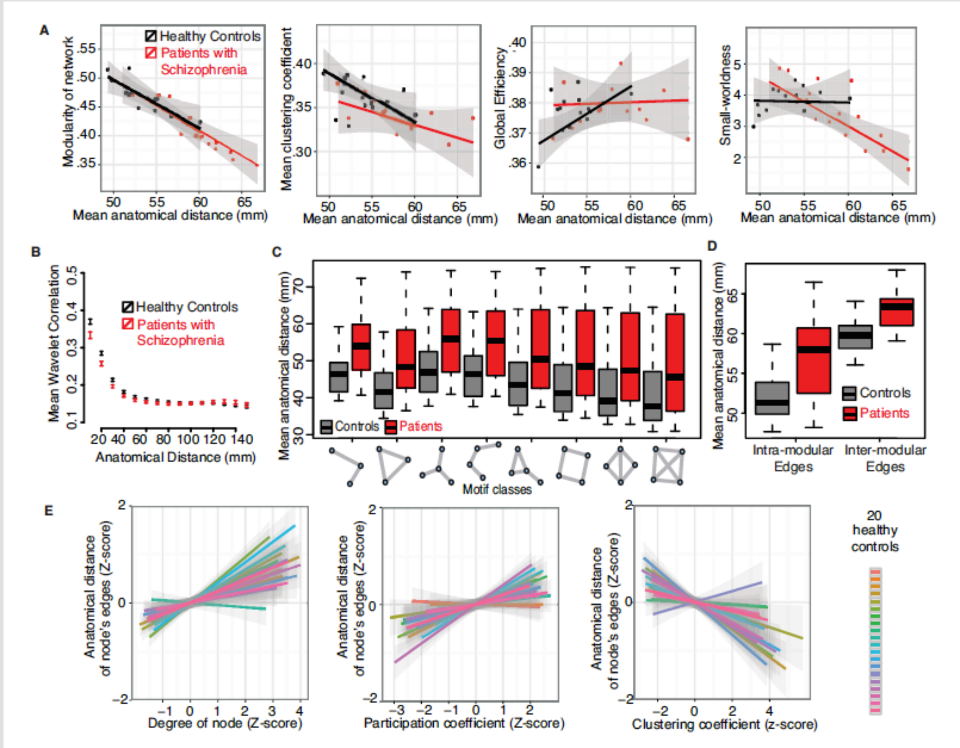
less clustered, lower modularity and less hub-dominated than healthy volunteers

maybe more robust to random attack

Lynall et al (2010) *J Neurosci*; Alexander-Bloch et al (2010) *Frontiers Sys Neurosci*

How do spatial and topological network properties interact in health and schizophrenia?

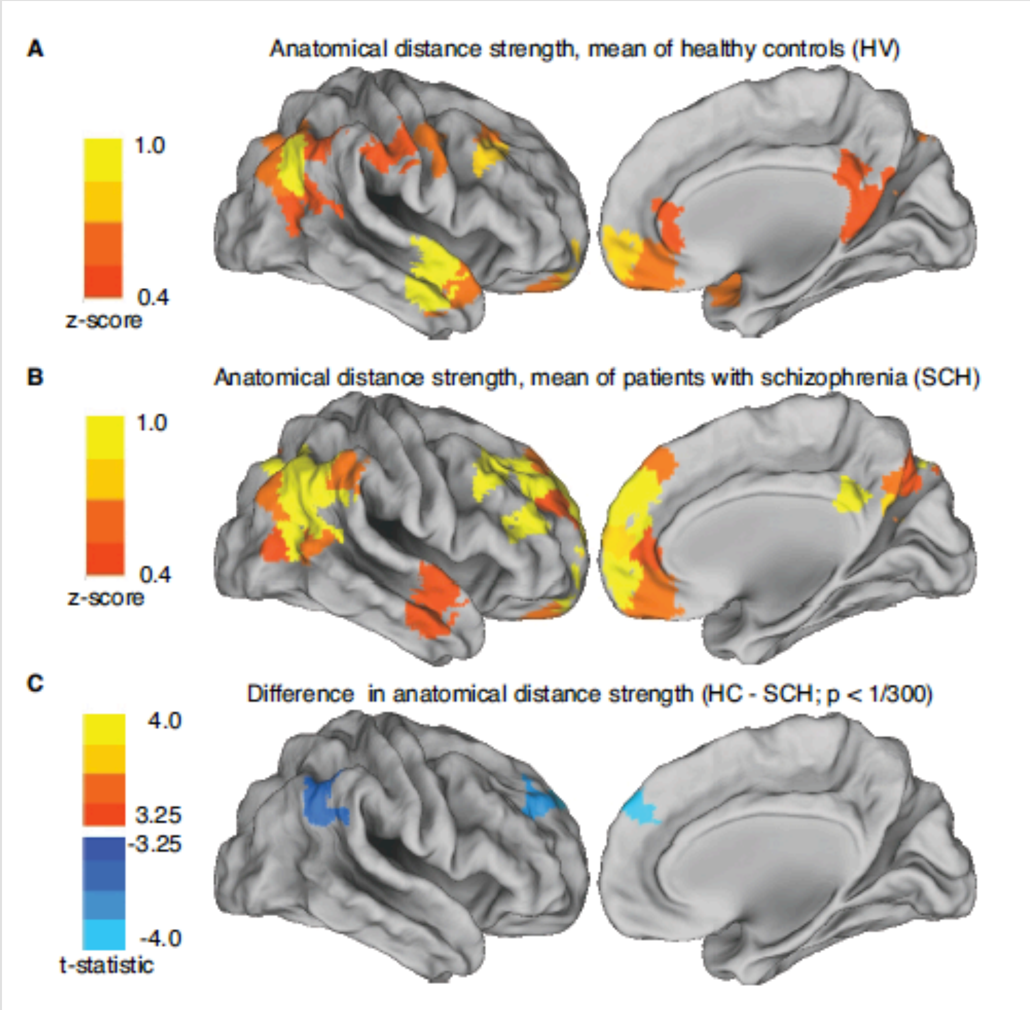




Schizophrenia networks are less economically wired but not proportionally more efficient

Alexander-Bloch et al (2011) *in review*

Connection distance abnormalities in schizophrenia are localised to a set of long-distance connector hubs



Alexander-Bloch et al (2011) *in review*

Conclusions

- Graph theoretical analysis of human networks derived from neuroimaging data is at an early stage of technical development and growing rapidly
- Hypothetically, brain networks may “negotiate a trade-off” between minimization of connection cost and maximization of efficiency (or other advantageous but expensive topological properties)
- Recent data show that cost-efficiency trade-offs in brain networks are heritable and can be renegotiated dynamically in response to changing cognitive demands, pro-cognitive drug challenge, and (maybe also) in the course of normal development
- Schizophrenia – a neurodevelopmental disorder – is characterised by related abnormalities of connection distance and network topology which are located most clearly in a set of long-distance connector hubs

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