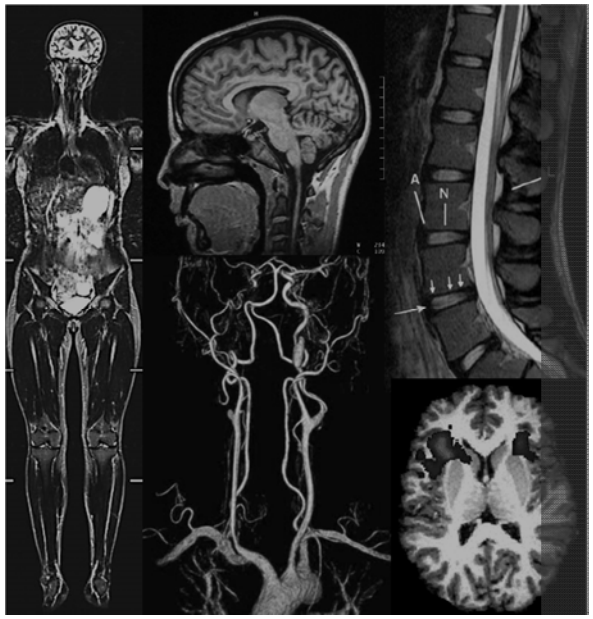

腦網路連結分析
A Course of MRI

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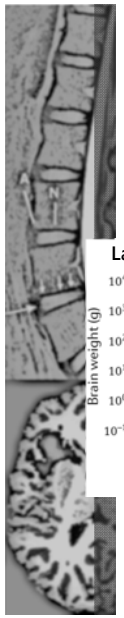
本週課程內容

- 腦網路連結(connectivity & network)
- 結構性與功能性連結關係(structural/functional connectivity)
- 複雜網路：圖學理論(graph theory)

腦網路連結

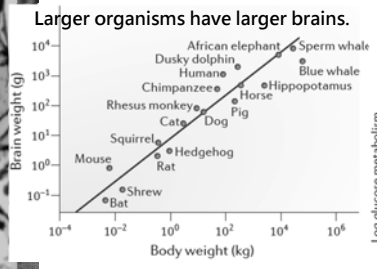
Brain connectivity & networks



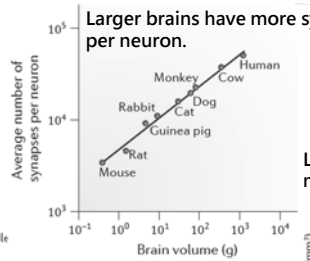
Brain networks

- Allometric scaling laws

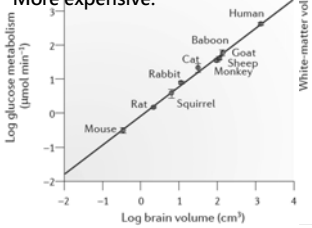
Larger organisms have larger brains.



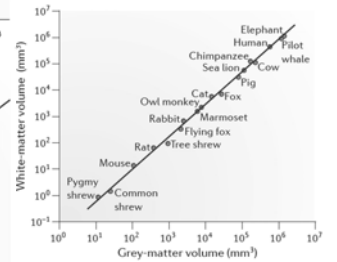
Larger brains have more synapses per neuron.



Larger brains are metabolically More expensive.



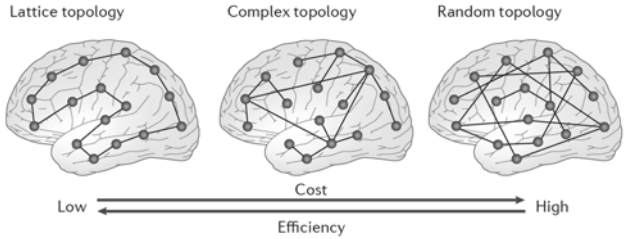
Larger brains have disproportionately more white matter than grey matter.



Bullmore et al., Nature Reviews Neuroscience, 13: 336-349, 2012.

Human brain networks Wiring costs ⇔ efficiency

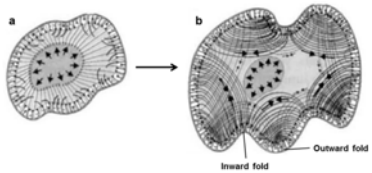
- Clusters of lattice-like short-distance connections between spatially neighboring nodes
- Nodes aggregated topologically and anatomically as modules → minimize wiring cost
- Topologically direct interconnections between spatially remote brain regions → increase efficiency of information processing



Bullmore et al., Nature Reviews Neuroscience, 13: 336-349, 2012.

Cortical folding and connectivity

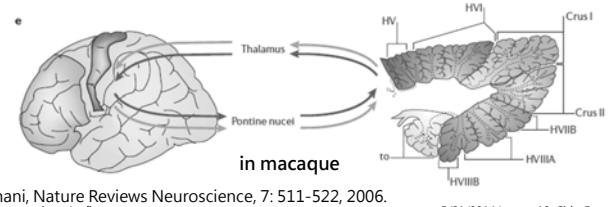
- The Tension-based Theory of Cortical Morphogenesis
- Tension-based folding
  - Pathways should mainly connect brain regions within cortical gyri rather than across sulci.
  - Denser pathways should exhibit white-matter trajectories that are straighter than those of less-dense pathways.
  - Variations in connectivity should become expressed in variations of gyrification or of the placement of gyri and sulci across the cortical surface.



- ✓ Bullmore et al., Nature Reviews Neuroscience, 13: 336-349, 2012.
- ✓ DC Van Essen, Nature, 385: 313-318, 1997.

Structural connectivity

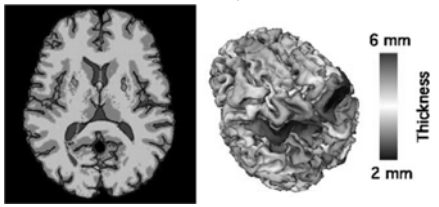
- Invasive tracer methods (for nonhuman species)
  - Tracing of axonal projections with transneuronal tracers
  - Effective tracers require antemortem injections
- Non-invasive methods
  - Significant correlations in cortical thickness
  - Diffusion MRI and tractography



N Ramnani, Nature Reviews Neuroscience, 7: 511-522, 2006.

Cortical thickness correlations

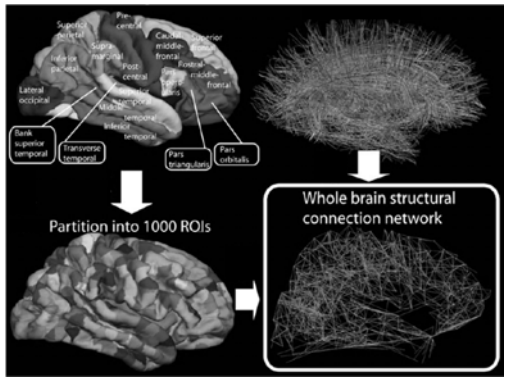
- The possible biological nature
  - the size, density and arrangement of cells (neurons and glial cells)
  - the mutually trophic influences
  - the contribution of heredity
  - common experience-related plasticity
- Inter-correlated regions may be a part of functional, neuroanatomically interconnected systems.



- ✓ Lerch et al., Neuroimage, 31: 993-1003, 2006.
- ✓ He et al., Cereb Cortex, 17: 2407-2419, 2007.

Diffusion MR tractography

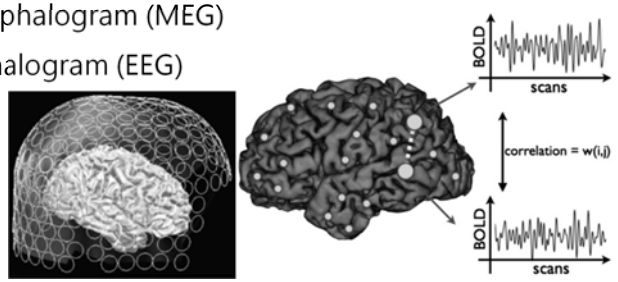
- Nodes: brain regions
  - AAL, CMA, Brodmann…
- Edges: fiber connections
  - DSI, DTI
- Network = nodes + edges



Hagmann et al., Plos Biology, 6(7): e159, 2008.

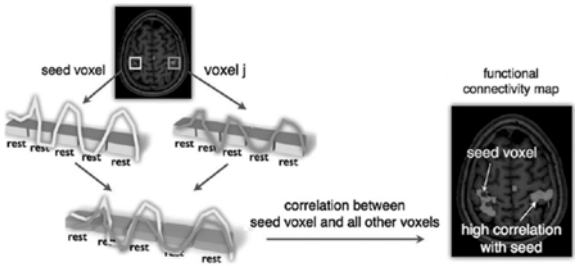
Functional connectivity

- Statistical dependence **(correlations, coherence, ICA,…)**
- Functional MRI
  - Correlations in inter-regional BOLD signal
- Magnetoencephalogram (MEG)
- Electroencephalogram (EEG)



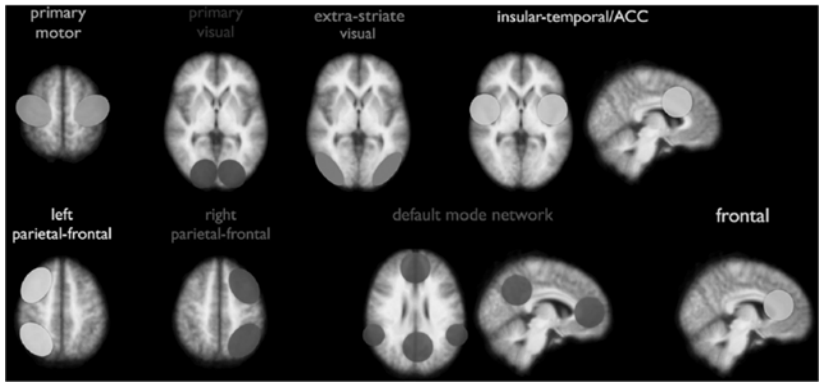
Resting-state networks (RSN) **(Biswal, 1995, 1997)**

- "Our brain is never idle even when we are at rest."
- Spontaneous fluctuation patterns of cortical regions
- Without task-specific bias, correlates with task performance



Martijn et al., Europ Neuropsychopharmacology, 20: 519-534, 2010.

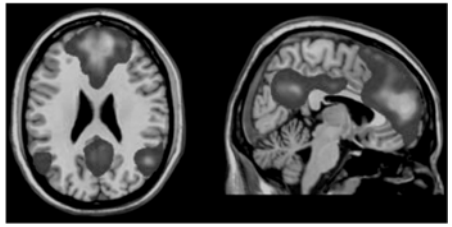
Resting-state networks



Martijn et al., Europ Neuropsychopharmacology, 20: 519-534, 2010.

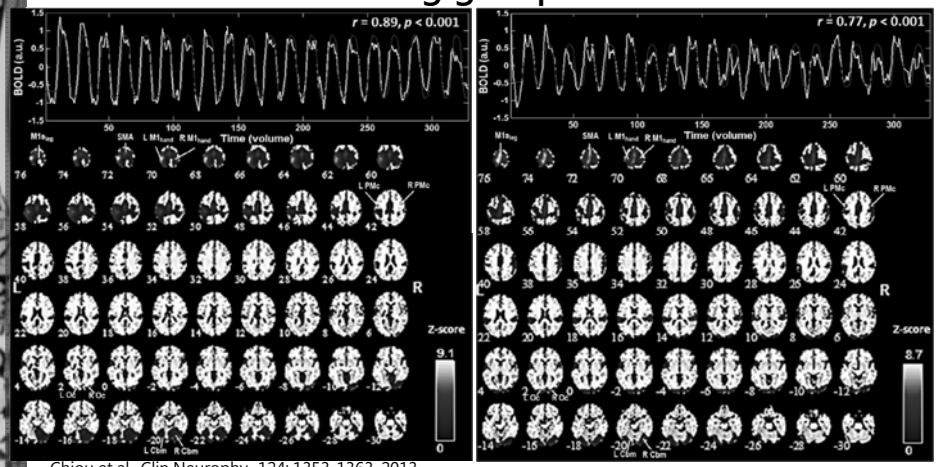
Default mode network (DMN)

- Including brain regions
  - Posterior cingulate cortex (PCC)
  - Precuneus
  - Inferior parietal cortex (IPC)
  - Dorsal and ventral areas of the medial prefrontal cortex (MPFC)
  - Medial temporal lobe (MTL)
- Functions
  - Internally mental processes
  - Deactivation during tasking



- Harrison et al., PNAS, 105(28): 9781-9786, 2008.
- Greicius et al., Cereb Cortex, 19: 72-78, 2009.

Motor networks using group-ICA



Chiou et al., Clin Neurophy., 124: 1353-1363, 2013.

結構性與功能性連結關係

structural/functional connectivity

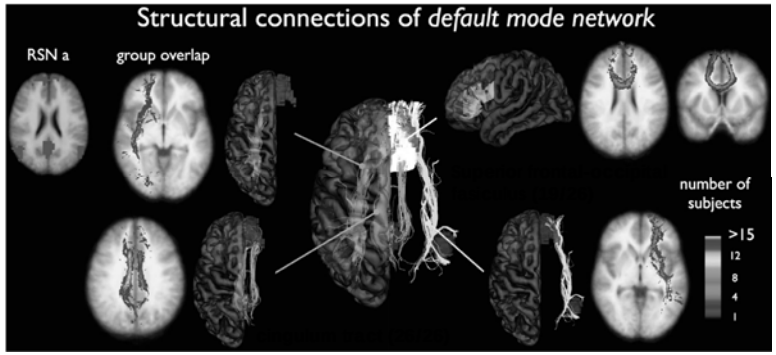
Structural vs. functional connectivity

- The structural fiber connectivity is the basis of the synchronization of neuronal activity between anatomically separated brain regions.
- The functional connectivity between RSN regions suggests the existence of direct anatomical pathways between these brain areas to facilitate this high level of ongoing interregional communication during rest.

Van den Heuvel. Human Brain Mapping, 30(10): 3127-3141, 2009.

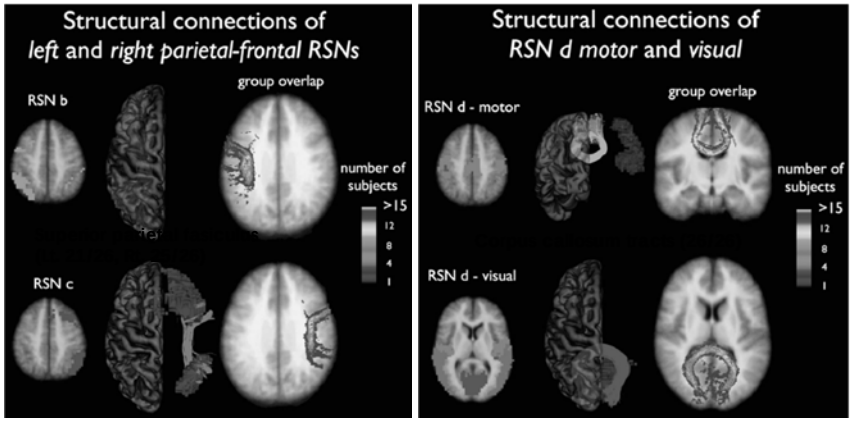
Anatomical pathways of DMN

- The seed ROIs are selected based on the functional DMN.



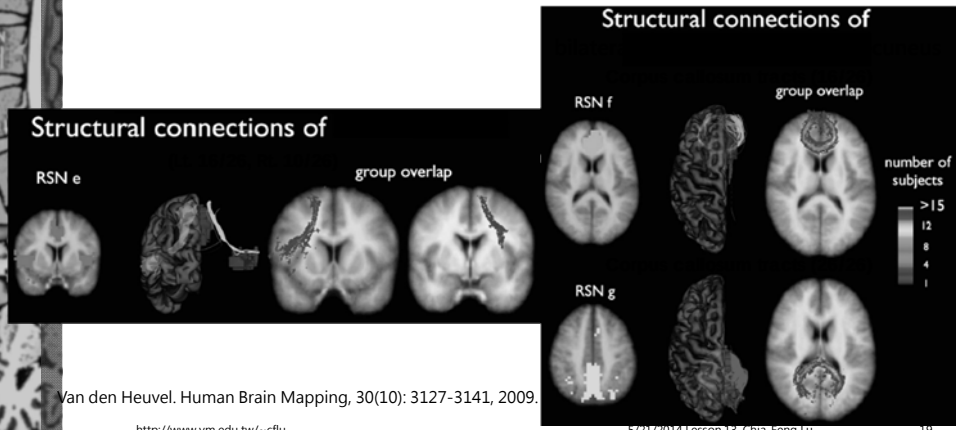
Van den Heuvel. Human Brain Mapping, 30(10): 3127-3141, 2009.

Anatomical pathways of RSN



Van den Heuvel. Human Brain Mapping, 30(10): 3127-3141, 2009.

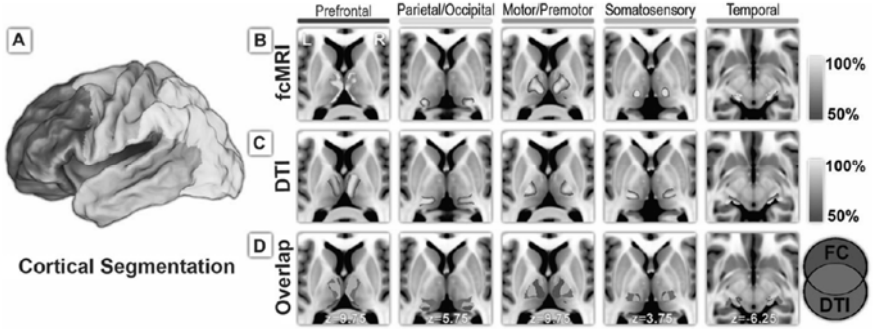
Anatomical pathways of RSN



Van den Heuvel. Human Brain Mapping, 30(10): 3127-3141, 2009.

Connectivity of thalamocortical system

- Structural DTI versus resting-state fMRI

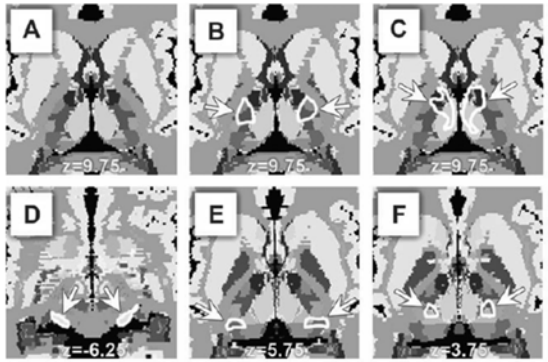


Zhang et al., Cereb Cortex, 20: 1187-1197, 2010.

Imaging results versus histology

Motor/premotor Cortex (VL, VLP)

Prefrontal Cortex (MB, VA)



Atlas Color	Principal Cortical Target
Mediodorsal (MD)	Frontal eye field; Orbitofrontal; Lateral Frontal; Medial Frontal
Anterior group (AV; AM; AD)	Cingulate; Retrosplenial; Anterior Limbic
Ventral Anterior (VA)	Diffuse Prefrontal and Cingulate
Ventral Lateral (VL)	Mainly Premotor
Ventral Lateral Posterior (VLP)	*Mainly Motor*
Ventral Posterior Lateral (VPL)	SI (BA3,2,1); SII
Anterior Pulvinar	Brodmann Area 5
Lateral Pulvinar	Parietotemporal and diffuse to Occipital
Medial Pulvinar	Superior Temporal Gyrus
Lateral Geniculate Nucleus (LGN)	Striate Area
Medial Geniculate Nucleus (MGN)	Auditory Cortex (AI; AII)

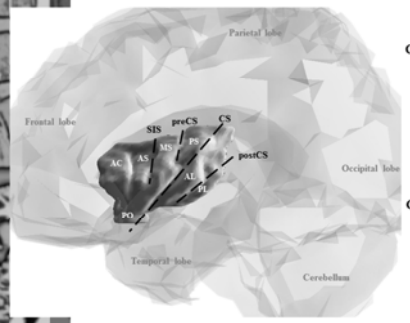
Temporal cortex (MGN)

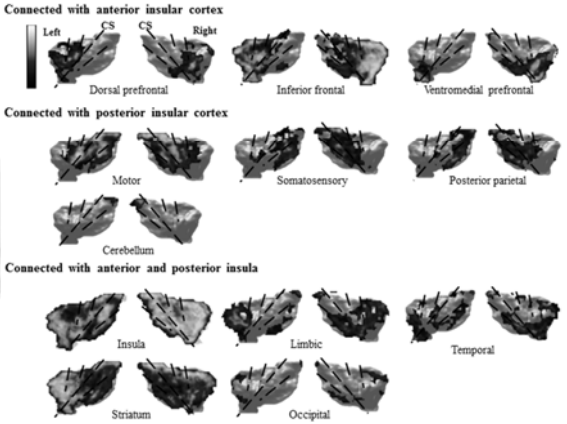
Parietal/occipital Cortex (lateral pulvinar)

Somatosensory cortex (anterior pulvinar)

Zhang et al., Cereb Cortex, 20: 1187-1197, 2010.

Structural Connectivity of insula

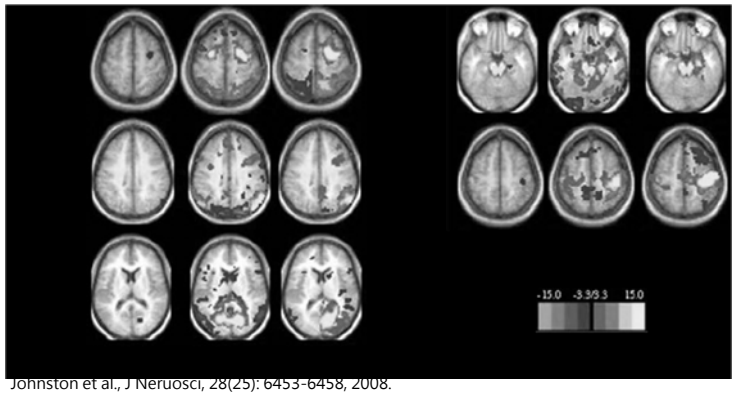




Lu et al., 2013 OHBM.

Evidences from corpus callosotomy

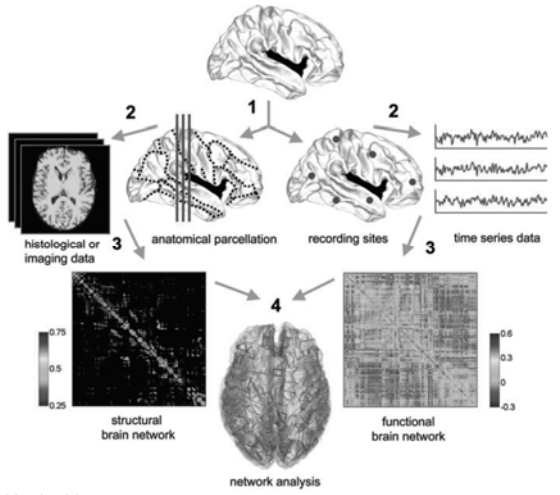
- Loss of resting interhemispheric functional connectivity



Johnston et al., J Neruosci, 28(25): 6453-6458, 2008.

Brain networks

- Greater than the sum of its parts: combining structural and functional connectivity.



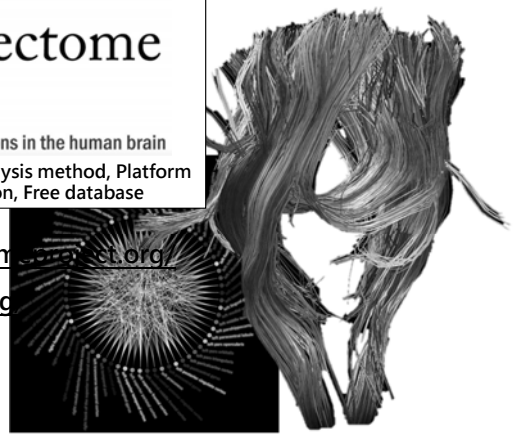
Olaf Sporns. Ann NY Acad Sci 1224:109-125, 2011.

HUMAN Connectome PROJECT

Mapping structural and functional connections in the human brain

Phase I (2010 - mid-2012): **Hardware, Analysis method, Platform**
Phase II (mid-2012 - 2015): **Data acquisition, Free database**

- http://www.humanconnectom[illegible]ct.org/
- http://humanconnectome.org

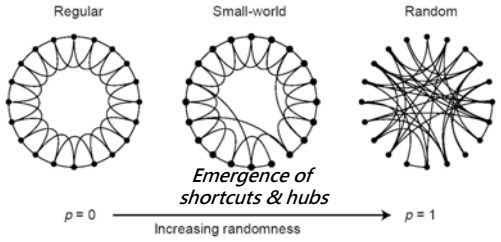


複雜網路：圖學理論

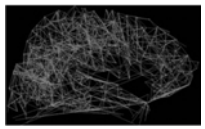
Complex networks: Graph theory

Complex networks

- Brain have a small-world architecture.



Complex networks
- **Social network**
- **WWW internet**
- **Biological system**
- **Brain network**



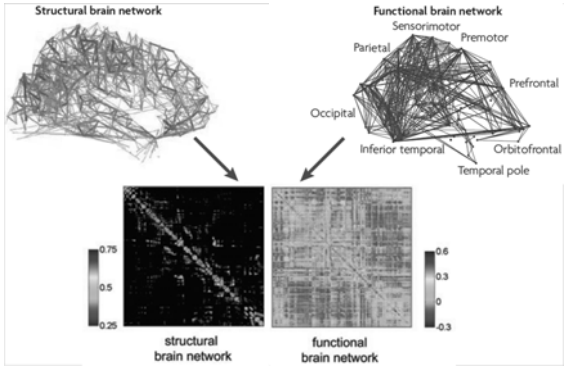
- ➢ *High local clustering* ➢ *Local segregation*
- ➢ *Low separation* ➢ *Global integration*

high signal-propagation speed, computational power, and synchronizability

Watts DJ, Strogatz SH, *Nature* 393:440-442, 1998.

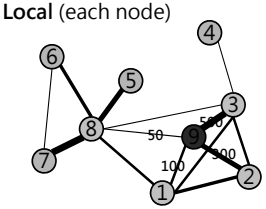
Network construction

- **Nodes**
  - Cortical regions
- **Edges**
  - Cortical thickness correlations
  - Fiber connections
  - Functional connectivity

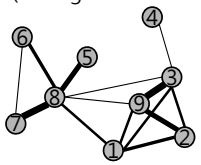


Graph theory: topological properties

Local (each node)



Global (average over all nodes)

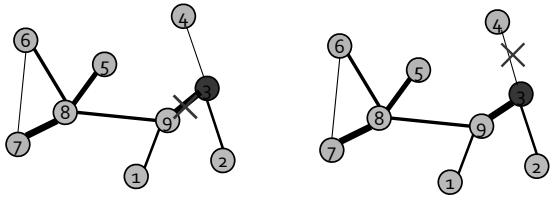


- **degree** (the number of neighbors)
  e.g. degree of node 9 = 4
- **strength** (the connected fiber number*FA)
  e.g. strength of node 9 = (50+100+300+500)/4 = 237.5
- **clustering coefficient** (the connection between neighbors, [0~1])
  e.g. clustering coefficient of node 9 = 5/6 = 0.83
- **path length (separation)** (the minimal steps for connection)
  e.g. path length from node 9 to node 6 = 2 steps (9 → 8 → 6)

Salvador et al, *Philos Trans R Soc Lond B Biol Sci*, 360, 937-946, 2005

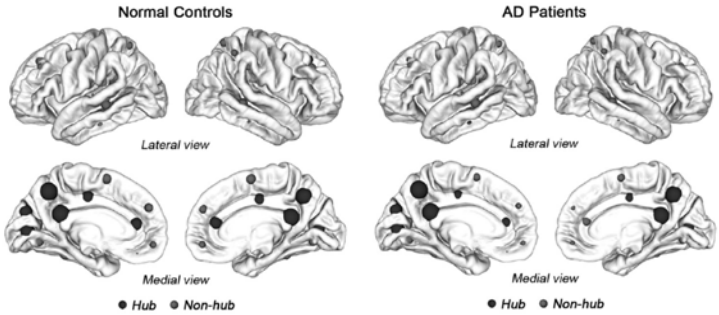
Network properties

- The topological observations can reveal a "hidden" or "high-level" relations between nodes.



Network hubs

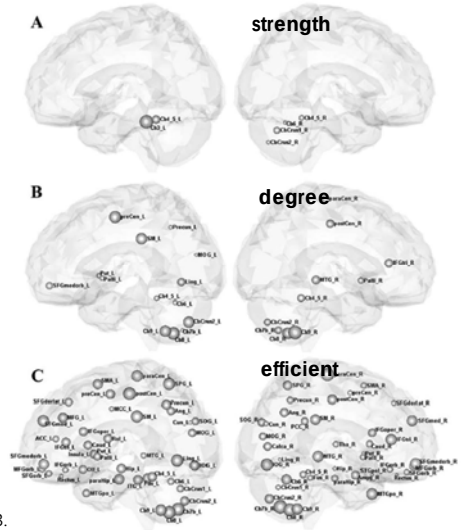
- The hub can be defined as the brain regions with high nodal efficiency (larger than mean + std).



Lo et al.. J NeuroSci, 30(50):16876-16885, 2010.

MSA-C

- The dominant cerebellar atrophy can cause the alteration of whole-brain effeciency.
- Network properties correlate with ataxia score in MSA-C.



Lu et al., Movement Disord, 28(3):362-369, 2013.

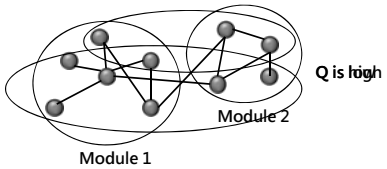
Modular structure of brain

- The modular organization is a possible partition of a network.

Modularity, Q

$$Q = \frac{1}{2m}\sum_{C\in P}\sum_{i,j\in C}\left[e_{ij} - \frac{k_i k_j}{2m}\right]$$

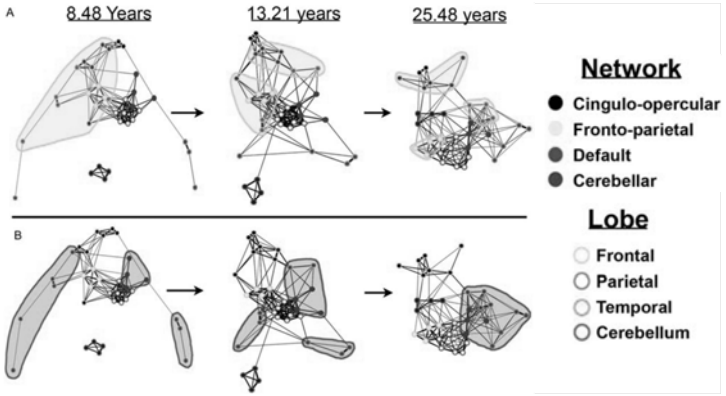
m: the total number of edges
C: the modules of the partition P



- *Densely connected groups of nodes in a module*
- *Sparser connections between modules*

Newman MEJ. Proceedings of the National Academy of Sciences 103: 8577-8582, 2006.

Functional brain networks develop from a local to distributed organization



Video S1

Fair et al.. Plos Comput Biology, 5(5):e1000381, 2009.

THE END

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