Graph theoretical analysis of functional connectivity: 'Small-world' properties of the brain correlate with cognitive performance.

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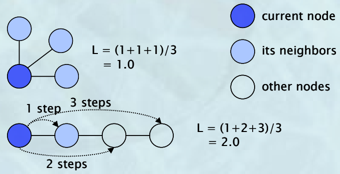
The functioning brain is a network of connected brain areas. Such networks may be mathematically described using graph theoretical analysis. From background EEG we calculated a measure of connectivity (Synchronization Likelihood) between each pair of electrodes. By applying a threshold to the resulting connectivity matrix, a {0,1} valued graph is created. From the graph, **clustering coefficient** and average **path length** can be determined (see box below left). It was tested whether individual differences in these descriptive parameters are heritable and predict differences in cognitive performance (subscales of the **WAIS**).

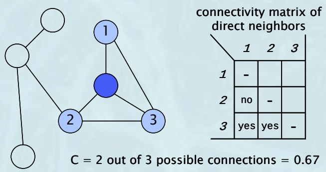
Graph theory mathematically describes networks of connected nodes and has been used to describe social groups, computer networks (e.g., the WWW), and power grids. **Path length (L)** is the average number of steps between all possible pairs of nodes.

Clustering coefficient (C) is the probability that a node's direct neighbours, that is, those nodes that are one step removed, are connected amongst each other, i.e., they form a cluster.

L (path length) is the average number of steps from the current node to all other nodes.

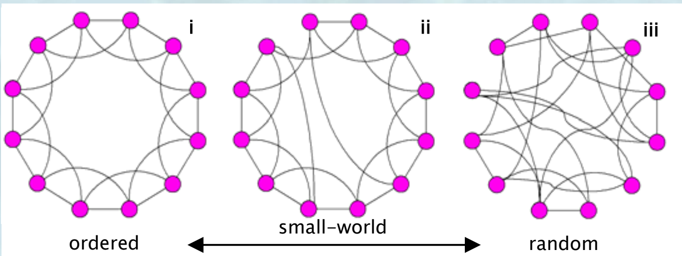


C (clustering) describes connectivity between the nodes neighboring the current node.



C = 2 out of 3 possible connections = 0.67

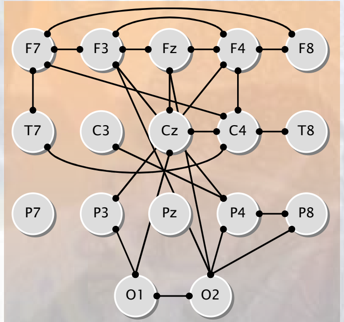
'**Small World**' refers to a phenomenon found in networks such as human society: although one is mostly befriended with people living close by, only a few distant friends or friends of friends are necessary to reach the whole world in an estimated 6 steps (the so-called *Six degrees of separation*). Watts and Strogatz (1998) have shown that networks which are locally and regularly connected have high C but long L (i). Those with totally random connectivity have low C but short L (iii). 'Small-world' networks are formed by interspersing an ordered network with a few long-range random connections, combining high C with short L (ii). The brain may work like this.



Participants were a population based sample of 732 adult twins and siblings from the Netherlands Twin Registry.

WAIS data of a randomly selected subset of 280 genetically unrelated subjects (i.e., one per family) were used to calculated correlations with C and L.

Eyes closed resting EEG was collected at F7 F3 Fz F4 F8, T7 C3 Cz C4 T8, P7 P3 Pz P4 P8, O1 and O2 and sampled at 250 Hz with. Four artifact free 16 s epochs were selected for each subject. Each epoch was filtered in the frequency bands **theta** (4-8 Hz), **alpha-1** (8-10 Hz), **alpha-2** (10-13 Hz), **beta-1** (13-18 Hz), and **beta-2** (18-25 Hz).



Actual example of a graph derived from EEG activity

Connectivity in each of the frequency bands was determined with **Synchronization Likelihood (SL)**, a measure of combined linear and non-linear synchronization between signals. For each subject a 17 x 17 connectivity matrix of SL values was calculated, the average SL value subtracted to correct for individual differences in overall SL, and converted to a {0, 1} graph by applying a threshold where a 0 represents absence of connection. The threshold was fixed for all subjects such that the mean number of connections per node was three. From these, C and L were determined for each subject.

Heritability was estimated by comparing monozygotic twin correlations to dizygotic and sibling correlations using Structural Equation Modeling.

Heritability is the percentage of individual variation attributed to genes. C and L in all frequency bands show substantial and significant heritability. The variable zscore(C) - zscore(L) may serve to represent the 'small-world' properties of an individual's functional network and also shows substantial heritability.

Table: heritability of C, L, and 'small-world variable' C minus L

	C	L	zscore(C) - zscore(L)
theta	**54%**	**40%**	**54%**
alpha-1	**64%**	**62%**	**64%**
alpha-2	**66%**	**47%**	**57%**
beta-1	**82%**	**49%**	**67%**
beta-2	**73%**	**54%**	**69%**

Bold is significant

The **correlation** of zscore(C) - zscore(L) with Verbal Comprehension reached significance for the theta, beta-1, and beta-2 bands.

Table: Correlations of C & L with cognitive peformance measures corrected for age, sex, and overall band power.

	Verbal Comprehension	Working Memory	Perceptual Organization	Perceptual Speed
zscore(C) - zscore(L)				
theta	**0.16**	0.08	-0.02	0.02
alpha-1	0.08	0.05	-0.05	0.12
alpha-2	0.06	-0.03	-0.05	0.05
beta-1	**0.20**	0.07	0.07	0.03
beta-2	**0.14**	0.00	-0.04	-0.04

Bold is significant

Conclusions

- Graph theory provides useful tools for describing functional brain connectivity.
- Graph theoretical descriptors Clustering and Path Length are heritable traits, and are therefore firmly rooted in human biology.
- Efficient brains with Small-world like properties are associated with increased performance on verbal comprehension.