

# Increased Cost Efficiency of Economical Brain Structural Networks in the Early Developing Brain

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**Introduction:** Brain networks are the graph representation of brain regional connectivity which is typically estimated as the correlation between regional measures of brain structure and function using imaging analysis techniques [1]. Recent studies have shown that brain anatomical and functional networks as studied with MRI, EEG, MEG, and functional MRI often exhibit so called small-world network properties, i.e., these brain networks have dense, clustered local connectivity and relatively few long-range connections, which are topologically in between of regular lattices and random graphs [1, 2]. The small world structure is an optimal and economical model for brain networks to support rapid synchronization and information transfer with minimal rewiring cost, as well as to balance between local processing and global integration of information. The small world characteristics of brain networks might be the evolutionary result of brain development and have been competitively selected to solve the economic problem of optimizing the brain information processing [3]. To test the hypothesis that the economical brain networks have been competitively selected, as well as to confirm previous findings that brain networks have economical properties, we studied the efficiency and cost of brain structural networks derived from longitudinal MRI data of healthy pediatric subjects between 2 weeks and 2 years of age.

**Materials and methods:** Twenty eight subjects (18 female/10 male) participated in this study, each of them having 3 structural brain MRI images scanned at the gestational age of  $41\pm 1$ ,  $95\pm 3$ , and  $144\pm 7$  weeks, referred to as postnatal age of two weeks, one year and two years, respectively. All subjects were imaged while asleep; no sedation was used. For each subject, T1 and T2 brain images were collected using a 3T Siemens scanner. The longitudinal images of each subject were first skull stripped, brain tissue segmented [4], and spatially normalized to a standard template space with a longitudinal image registration algorithm [5] that can measure temporal changes accurately. From the resulting deformation fields, tissue density maps were computed to represent the local brain volume changes relative to the selected template voxel-wisely. From the tissue density maps, regional brain volume measures were obtained for 90 brain regions using an anatomically labeled brain template [6]. The effect of total brain volume size was removed by normalizing the regional brain volume measures with the intracranial volume.

The brain structural connectivity was defined as statistical association in volume measures between brain regions, which was statistically measured by the Pearson correlation coefficient across subjects. Three interregional correlation matrices, each corresponding to one time point, were computed based on 28 subjects. Brain structural networks with various sparsity were constructed by thresholding the correlation matrices, which allows us to focus on the topology of relatively sparse networks with the strongest structural connections [1]. The choice of the threshold value has a critical effect on the topology of the resulting networks, which was addressed by estimating and integrating the network efficiency over a range of correlation thresholds equivalent to costs of networks in the range of 0.05 to 0.5 [3].

The global and local efficiency of information processing as a function of cost in these brain structural networks were measured. The *cost of a network* measures how expensive to build the network, defined as the total number of edges in the network, divided by the maximum possible number of edges [1]. The *efficiency* was defined as a function of the minimum path length between regions. Specially, the *global efficiency* measures the efficiency of parallel information transfer in the network, defined as the inverse of the harmonic means of the minimum of absolute path length between each pair of regions, while the *local efficiency* quantifies the efficiency of information transfer between sub-networks, defined as the inverse of the harmonic means of the minimum of absolute path length between each pair of regions within the sub-network associated with each node in the network. The average of the local efficiencies over all nodes was used to estimate the mean local efficiency of the network. The *cost efficiency* defined as the difference between global efficiency and cost was also measured. The network with positive cost efficiency is referred to as an *economical network*. To diagnosis of the small world properties of the brain structural networks, the comparable regular lattices and random graphs (1000 at each cost) were generated over the same range of network costs [1]. In the case of a small world network, the global efficiency is greater than a comparable lattice but less than a random graph, and the local efficiency is greater than a random graph but less than a lattice [2].

**Results:** Three groups of brain structural networks, one for each age group, were constructed corresponding to different network cost (sparsity). As shown in the left column of Fig. 1, economical networks are observed in all the groups and the cost efficiency continue to increase steadily from 2 weeks to 2 years over a wide range of network cost. The increase of the cost efficiency is statistically significant with p-values of  $1.0\text{e-}13$  for networks of 2 week vs. one year old, and  $1.0\text{e-}11$  for 1 year vs. 2 year old. As expected efficiency monotonically increase as a function of cost in all the networks, as shown in the middle and right column of Fig. 1; however, the networks of the group of 2 week old do not have the small world properties. The characteristically small world behavior of the brain networks becomes observable in the group of 1 year old, and consistently presents in the group of 2 year old for low-cost to medium-cost networks.

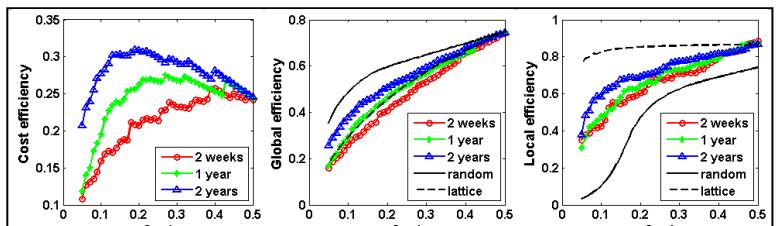


Fig. 1. Cost efficiency (left), global (middle) and local efficiency (right) as a function of cost (x-axis) for brain networks. Global and local efficiency of random graphs and regular lattice are also shown in the middle and right column for comparison purpose.

**Discussion and conclusions:** These findings suggest that the brain structural networks are economical, even at very early brain development stage of 2 weeks, and their cost efficiency increases steadily and significantly with the brain development from 2 weeks to 2 years. The brain structural networks at early brain development stages do not necessarily have small world network prosperities, albeit they gradually develop to small world networks as observed in network studies of adult brains [1]. The dynamic property of brain structural network development also reflects that the brain functional development with increased capability of information processing. This first study of its kind provides a strong support for the hypothesis that the characteristics of brain networks have been competitively selected to solve the economic problem of optimizing the brain information processing.

## References:

1. Stam, C. and J. Reijneveld, *Graph theoretical analysis of complex networks in the brain*. Nonlinear Biomedical Physics, 2007. 1(1): p. 3.
2. Watts, D.J. and S.H. Strogatz, *Collective dynamics of 'small-world' networks*. Nature, 1998. 393: p. 440-442.
3. Bassett, D.S. and E. Bullmore, *Small-world brain networks*. Neuroscientist, 2006. 12: p. 512 - 523.
4. Shi, F., et al., *Neonate brain MRI segmentation using subject-specific probabilistic atlas*, in *SPIE medical Imaging*. 2009: Lake Buena Vista, FL.
5. Shen, D. and C. Davatzikos, *Measuring Temporal Morphological Changes Robustly in Brain MR Images Via 4-Dimensional Template Warping*. NeuroImage, 2004. 21(4): p. 1508-1517.
6. Tzourio-Mazoyer, N., et al., *Automated Anatomical Labeling of Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain*. NeuroImage, 2002. 15(1): p. 273-289.