Mapping the development of the human connectome

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Introduction

From birth to early adulthood the brain undergoes dramatic modifications, with neuronal loss, dendritic proliferation and axonal growth followed by reductions in synaptic plasticity, axonal pruning and myelination [1,2]. These processes result in gyral folding, regional specification and ultimately network optimization. The most dramatic change observed with standard neuroimaging techniques is the progressive, sequential and stereotyped myelination process, resulting in decreased white matter T2 signal and decreased Apparent Diffusion Coefficients (ADCs). However, these modifications have been almost exclusively described at the regional level and changes beyond age 2 years are subtle. In the present study we investigate the sequential myelination of individual connections using high b-value diffusion imaging with tractography to determine the effect on brain network topology.

Material and Methods

30 participants, with age ranging between 1.5 and 18 years, were scanned on a 3T system with whole brain high-resolution T1 weighted imaging, Q-ball diffusion MRI (2x2x2mm voxels, b-value of 3000 s/mm^2, 60 diffusion gradient directions). The latter was reconstructed with the standard q-ball algorithm [3]. Structural connectivity (SC) matrices were computed in a five step process identical to that described in [4]: (1) q-ball imaging and high resolution T1-weighted MRI acquisition of the brain, (2) segmentation of white and gray matter, (3) white matter tractography, (4) segmentation of the cortex and deep gray structures into 258 ROIs covering hemispheric cortex and deep gray nuclei (5) network construction by computing the SC (using the average 1/ADC of the pathway connecting any pair of ROIs). The anatomical positions of the ROIs are in register across subjects, allowing for averaging across individual networks. From the connectome of these 30 participants we looked at the evolution of several network measure across age. In particular we investigated "Global Efficiency", "Modularity", "Clustering", "Path Length" and "Small World Index" computed over the 1/ADC weighted network, the details of the computation are available at [5]. We also considered the speed of ADC change for edges connecting a specific node (i.e. ROI) by using a logarithmic interpolation scheme across subjects and defined the speed as the difference between the extremes of age, i.e. 2 and 17. More precisely the fitted model is: $ADC(t) = a \log(t) + b$ and $ADC_{speed}=ADC(t=2) - ADC(t=17)$. The node (ROI) speed is then the average ADC_{speed} over all the connected edges.

Results

We found that global efficiency ($r = 0.51$, $p<0.005$) significantly increases with age, while modularity ($r = -0.43$, $p<0.02$), clustering ($r = -0.44$, $p<0.02$) and path length decrease over the investigated age range. Furthermore the small world index ($r = -0.48$, $p< 0.01$) also decreases during that period (Figure 1). We also found that the speed of ADC change is not uniform over the brain. Typically primary motor cortex changes slowly whereas association cortices are faster in their change. The cortices that change the fastest during this age period are the orbito-frontal cortices and the parieto-temporal junction.

Discussion

There is good evidence that 1/ADC is a good measure of the level of myelination and we expect that the later is reflective of connection efficacy. Using this model we observe significant change in global efficency, which is a measure of functional integration. The later seems to be due to the maturation of the long association pathways, thus shortening the path length and also some functional pruning (through differential myelination) of short U-fibers, directly affecting clustering and modularity. These combined effects are naturally reflected in the small world index that decreases. In other words the brain moves progressively from a multi-lattice like network to a more largely integrated and efficient network. We also found that the myelination change is most dramatic during the period 2 to 18 year on connections that are connecting association cortex like the frontal, parietal and inferior temporal regions whereas myelination is slowest in connections linking primary visual motor and auditory cortex that are likely already myelinated soon after birth. Even more dramatic, are the high myelination speeds of the orbitofrontal cortex and the temporo-parietal junction suggesting that the efficency of these areas is rapidly catching up to other brain areas.

Figure 1

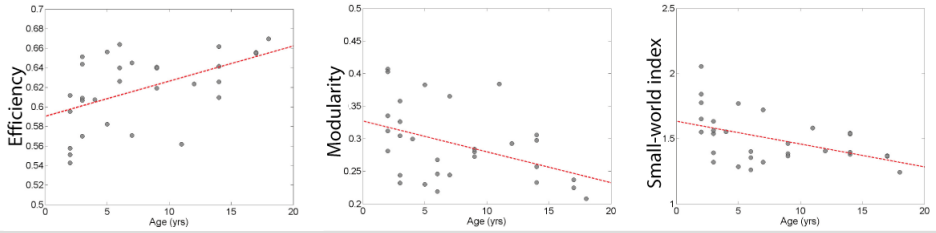
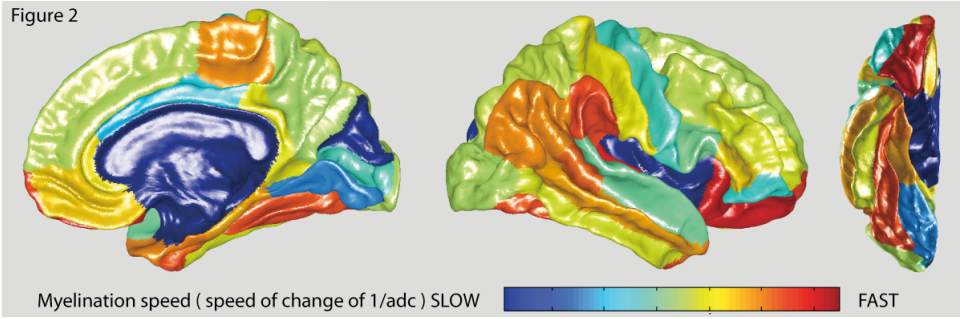


Figure 2



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