Maturation of the Structural Connectome: A Network-Driven Approach

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Introduction. Improved understanding of how the human brain is "wired," at least on a macroscale, may become possible due to the newly emerging field of *MRI connectomics*. However, mapping the rapidly developing newborn brain networks poses challenges, since atlases and templates commonly used for brain *parcellation* might not match with function and anatomy during early brain development [1]. The *purpose* of this study was to examine the maturational changes of the cortical connectome in subjects across the age spectrum, from premature neonates to term-born neonates, six-month-old infants, and adults using a template-free network-driven analysis of white matter connectivity.

Methods. Diffusion MRI was performed in 8 prematurely born neonates (gestational age (GA) at birth 27-30 weeks, GA at scan 31-40 weeks), 8 term-born neonates, and 10 six-month-old infants; the two latter groups had transient encephalopathy at birth but no clinical or imaging evidence of brain injury. Seven healthy adults (age 24-31 years) were included to represent the mature brain. The subjects were scanned on a 3T MR scanner using SE EPI with a FOV=24-25.6 cm, 128×128, slice thickness 1.8-2 mm, 30 directions, b=600 s/mm^2 for preterm babies, b=700 s/mm^2 for term and six-month-olds, and b=1000 s/mm^2 for adults.

To assess structural networks, the "baby connectome" framework was employed [2], which included data quality assurance, deterministic whole-brain streamline fiber tractography (Fig. 1A), and template-free parcellation of the brain surface based on *equal area sphere partitioning*. The number of nodes was chosen to be 100 based on the network-driven method for determining the optimal number of nodes in six-month-old infants [3]. The resulting networks (Fig. 1B) were assessed using the Brain Connectivity Toolbox [4]. We determined the optimal number of modules for each subject by maximizing network modularity. To identify modules, the spectral community detection algorithm was applied [5].

Results and Discussion. We observed increasing brain network *integration* and decreasing *segregation* with age in term-born subjects (Fig. 2), consistent with previous findings in the late developing human brain [6]. We were able to extend the age span to include younger babies by employing a template-free parcellation of the cortex into equal area nodes, which is more flexible than atlas-based approaches and suits the rapidly growing brain.

The optimal number of modules was relatively consistent in all groups: 5-6 modules in the preterm group, 5-7 modules in the term-born neonates, 5-8 modules in the six-month-old infants, and 5-7 modules in the adults. In Figure 1C, we selectively show the obtained network-driven segmentation of the cortex into five modules for subjects from all age groups that showed a similar pattern. It should be emphasized that the equal area nodes were grouped into modules without any prior anatomical information – an important step toward a fully network-driven registration and analysis of brain connectivity.

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References. [1] Fan Y et al (2011) Neuroimage 54:1862-71. [2] Tymofiyeva O et al (2012) PLoS ONE 7(2):e31029. [3] Tymofiyeva O et al (2012) Proc OHBM, #680. [4] Rubinov M & Sporns O (2010) NeuroImage 52:1059-69. [5] Newman MEJ (2006) PNAS 103:8577-82. [6] Hagmann et al (2010) PNAS 107:19067-72.

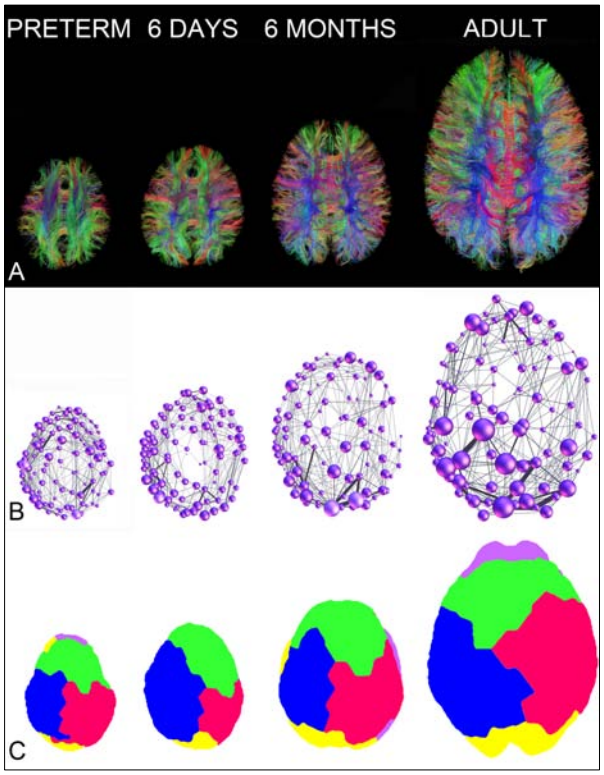

Fig 1. Maturation of the "baby connectome": examples at four different ages. A) Tractograms. B) Brain networks. C) Network-driven segmentation of the cortex into five modules.

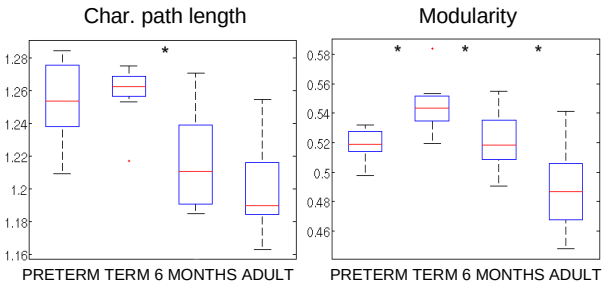

Fig 2. Group analysis of the scaled characteristic path length (measure of integration) and maximized modularity (measure of segregation). *p<0.05.