Brain without Anatomy: Construction and Comparison of Fully Network-Driven Diffusion MRI Connectomes

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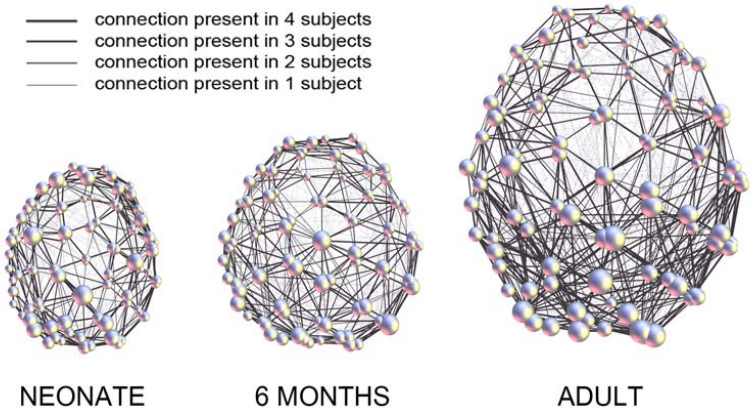
Purpose. MRI connectomics treats the brain as a network and can provide new information about its efficiency and mechanisms of disruption.[1] To define network nodes, the brain is usually registered to a standardized anatomical atlas based on Brodmann's areas. This approach does not account for inter-subject variability and can be especially problematic when studying brain maturation or cerebral reorganization after brain damage (plasticity). The recently proposed "baby connectome" approach to study structural connectivity is based on an atlas-free equal-area parcellation scheme and is not constrained by anatomy.[2-4] While the approach allows for comparison of global network measures, local comparison of specific nodes and connections has not yet been possible. The purpose of this study is to develop a framework for fully network-driven construction and connection-wise comparison of diffusion MRI-based brain networks.

Methods. Four term-born neonates, four six-month old infants, and four adults were scanned on a 3T GE MR scanner using SE EPI diffusion MRI with a FOV=24-25.6cm, 128x128 matrix, 1.8-2mm slice, 30 directions, b=700s/mm^2 for infants and b=1000s/mm^2 for adults. The neonates and infants had transient encephalopathy at birth but no clinical or imaging evidence of brain injury. To estimate the method's reproducibility, one 6-month-old subject and one adult were scanned twice. The following steps were performed to construct and compare atlas-free brain networks. ***Step 1.*** Defining all-to-all cortical connections ("dense connectome") by using the results of deterministic whole-brain streamline fiber tractography performed using Diffusion Toolkit. ***Step 2.*** Automated atlas-free parcellation of the cortical surface into N equal-area nodes.[2] The optimal number of nodes N was determined by the finest parcellation at which the largest connected component still represents the whole brain.[4] ***Step 3.*** Calculation of the NxN network by combining the dense connectome entries, followed by binarization at threshold=1 streamline. ***Step 4.*** Network alignment using a matrix alignment algorithm with simulated annealing.[5] It aligns two matrices by reordering nodes in one of the matrices. For each iteration, a distance metric between the two matrices was calculated and minimized. ***Step 5.*** Finding the cohort's most "common" brain network by pair-wise alignment of networks and calculating the Pearson correlation coefficient. The network with the highest average correlation coefficient was chosen as the "common brain". ***Step 6.*** Calculating the average brain network by aligning all networks to the "common brain" and adding up connections; this can be followed by connection-wise comparison and statistical analysis.

Results and Discussion. At N=95 nodes all twelve subjects had just one largest connected component covering the whole brain. The correlation coefficients after pair-wise network alignment ranged from 0.613 to 0.668 (mean 0.640, std 0.018). The figure to the right demonstrates the average brain networks for the three age groups, mapped onto the anatomy of the corresponding "common" brain. Thicker lines represent connections present in more subjects. Correlation coefficients for the aligned test-retest networks in the 6-month-old subject and adult were 0.745 and 0.704 respectively. While being less than 1 due to the specifics of the parcellation and noise, statistically these values were significantly higher than inter-subject values.



Conclusion. Through the abstraction from the anatomy, the developed framework allows for unbiased construction and connection-wise comparison of diffusion MRI-based brain networks. Brain alignment is performed in the network domain and, therefore, can be applied to subjects at any stage of development with any potential anatomical abnormalities.

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References. [1] Hagmann P et al (2010) J Neurosci Methods. 194(1):34-45. [2] Tymofiyeva O et al (2012) PLoS ONE 7(2):e31029. [3] Tymofiyeva O et al (2013) PLoS ONE 8(5):e63310. [4] Ziv E et al (2013) PLoS ONE (in press). [5] Rubinov M & Sporns O (2010) NeuroImage 52:1059-1069.