Changes of microstructural correlation of white matter tracts with human brain development

Virendra Mishra[1], Hua Cheng[2], Gaolang Gong[3], Yan Daniel Zhao[4], Yong He[3], Qi Dong[3], and Hao Huang[1]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [2]*Imaging Center, Beijing Children's Hospital, Beijing, China, People's Republic of,* [3]*State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China, People's Republic of,* [4]*Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, Texas, United States*

Introduction

DTI-derived metrics, including fractional anisotropy (FA), mean diffusivity (MD), axial (AxD) and radial diffusivity (RD) have been recently used to characterize the microstructural development of human brain white matter (e.g. 1-5). While the general increase of FA and general decrease of diffusivities including MD, AxD and RD of white matter are commonly found in the literature (e.g. 1-4), how microstructural correlations of major white matter tracts change during development remains unclear. In this study, we hypothesized that the microstructural correlations of different white matter tracts undergo significant change in terms of correlation maps and the microstructural correlation pattern represented by dendrograms (5) is reshuffled during brain development. DTI data of 26 neonates and 28 adolescents were acquired. Left and right cingulum in cingulate gyrus (CGC-L and CGC-R), left and right cingulum to hippocampus (CGH-L and CGH-R), left and right inferior fronto-occipital fasciculus (IFO-L and IFO-R), left and right cortico-spinal tracts (CST-L and CST-R), forceps major (Fmajor) and forceps minor (Fminor) of corpus callosum (CC) were traced individually for all 54 subjects. These tracts were chosen as they can be consistently traced in neonate brains and cover major tract groups, namely limbic, projection, association and callosal tract groups, each of which is related to a specific brain function.

Methods

Subjects and data acquisition: DTI data of 26 normal neonates (14 M and 12 F; 40.1±2.0 gestational weeks) and 28 normal adolescents (15 M and 13F; age 12.0±2.3; age range 9.1 to 16 years) were acquired from Philips 3T scanners of two institutions with identical imaging protocol. Both neonates and adolescents were recruited in either institution to minimize the data difference between the neonate and adolescent group caused by systematic bias of the scanner. DTI data were acquired using a single-shot EPI with SENSE. The image parameters were: resolution=2x2x2 mm, 30 directions; b=1000 sec/mm^2, repetition=2. *Measurements of DTI metrics of different tracts:* 10 major white matter tracts, CGC-L/R, CGH-L/R, CST-L/R, IFO-L/R, Fmajor and Fminor, were traced following the protocol in the literature (6). The traced tracts of a typical neonate and adolescent brain are shown in Fig. 1. With traced tracts as binary masks, the tract-level DTI metrics were measured. *Microstructural correlation analysis:* Non-parametric spearman's rank correlation was used to compute pair-wise correlation of DTI metric of two tracts, generating FA, MD, AxD and RD correlation matrix with each matrix containing 45 independent correlation values. All of the 4 correlation matrices were tested to see if they significantly differ from identity matrix or homogeneous matrix. A paired t-test was computed on the 45 correlation values for each DTI metric to see if the correlation strength differs significantly between two groups. For correlation matrix of each DTI metric, hierarchical clustering methods were used to characterize the patterns of inter-tract correlation with dendrograms.

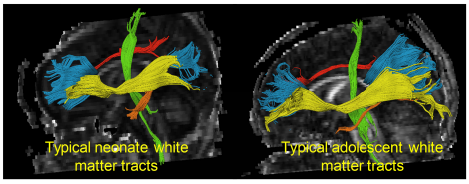
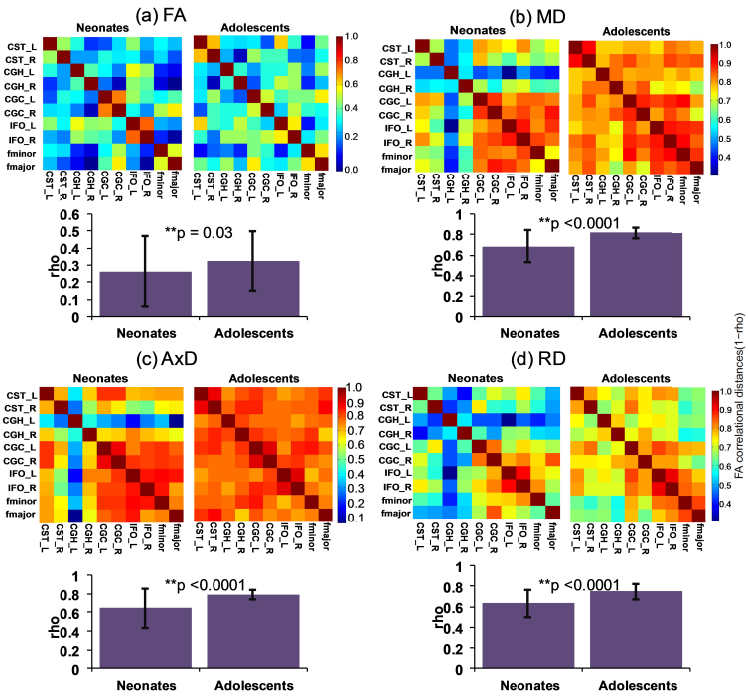


Fig. 1: Typical neonate (left) and adolescent (right) white matter tracts. Different colors indicate different tracts. Red: CGC; orange: CGH; blue: Fmajor and Fminor; green: CST; yellow: IFO.

Results

DTI metric changes from neonates to adolescents: All four DTI metrics change significantly (corrected p<0.05) for all tracts. *Microstructural correlation changes of white matter tracts:* All the four correlation matrices for both groups are significantly different from identity or homogeneous matrix (p<0.05). Fig. 2 shows the correlation maps from FA (Fig. 2a), MD (Fig. 2b), AxD (Fig. 2c) and RD (Fig. 2d) measurements of 10 tracts for neonates and adolescents. Statistically significant increases of inter-tract correlation strength (rho) from FA, MD, AxD and RD measurements were found, indicating stronger microstructural inter-tract correlations are built up during the development. Moreover, despite that homologous tracts are paired together in both neonate and adolescent groups (Fig. 3), the dendrograms of adolescents and neonates based on tract-level FA measurements indicate the hierarchy of the tract correlations is different between the two groups. Specifically, the most tightly correlated tracts change from CGC-L/R and IFO-L/R to CST-L/R and Fmajor/Fminor from neonates to adolescents.



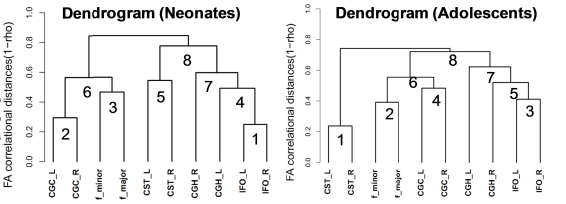


Fig. 2 (left): Matrices of correlation values from FA (a), MD (b), AxD (c) and RD (d) measurements of 10 white matter tracts for neonate and adolescent group. The correspondent bar plots indicating mean and standard deviation of the correlation strength (rho) are also displayed beneath the correlation matrix of each panel.

Fig. 3 (right): Dendrogram of correlations from tract-level FA measurements of neonate and adolescent group.

Conclusion and discussion

Microstructural changes were investigated with tract-level FA, MD, AxD and RD measurements and inter-tract correlation analysis. Stronger and enhanced microstructural inter-tract correlations are built up during development from neonates to adolescents. The linkage pattern of the major tracts also differs with the dendrograms of two groups due to brain development. These changes of microstructural correlations between neonates and adolescents suggest inhomogeneous but organized axonal development which causes the reshuffled inter-tract correlation pattern while keeping homologous tracts tightly correlated. It opens a new perspective to study axonal connectivity development and adds a new window to investigator atypical brain development due to neurological or psychiatric disorders. Data from more subjects from both groups will be added to increase the statistical power.

References: [1] Lebel C et al (2008) Neuroimage 40: 1044. [2] Gao W et al (2009) AJNR 30: 290-296. [3] Giorgio A et al (2010) 49: 94-103. [4] Westlye LT et al (2010) Cereb Cortex 20: 2055-2068. [5] Wahl M et al (2010) Neuroimage 51: 531-541. [6] Wakana, S et al (2007) Neuroimage 36:630 **Acknowledgement:** This study is sponsored by NIH MH 092535 and NIH EB009545.