BRAIN DEVELOPMENT IN PRETERM AND TERM NEONATES ASSESSED BY WHITE MATTER MODEL OF DIFFUSION KURTOSIS IMAGING WITH TRACT-BASED SPATIAL STATISTICS ANALYSIS

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Target audience

Researchers engaged in MRI applications, pediatric researchers and clinicians may be interested in this study.

Introduction

During the late period of the last trimester of human gestation, white matter undergoes rapid changes [1]. Documenting the developmental changes in white matter at this stage is important for understanding the early development of human brains. Recently, white matter model of diffusion kurtosis imaging (DKI) was proposed based on two compartments [2]. The derived parameters, such as intra-axonal diffusivity (D_{axon}), axial diffusivity ($\lambda_{e,//}$), and radial diffusivity ($\lambda_{e,\perp}$) and tortuosity (α) of the extra-axonal space, provide diffusion information in intra-axon and extra-axon space. In this study, we aimed to investigate the white matter microstructural changes in preterm and term neonates using the DKI white matter model and tract-based spatial statistics (TBSS) analysis.

Methods

In this study, 38 neonates with postmenstrual ages (PMA) of 33 - 42 weeks were examined, including 19 preterm neonates (6 females, mean PMA = 35.57 ± 0.94 weeks, PMA range: 33.57 – 36.86 weeks) and 19 term neonates (6 females, PMA = 39.86 ± 1.63 weeks, PMA range: 37.57 – 42.71 weeks). Subjects underwent MRI at a mean age of 9.58 ± 4.95 days after birth. There were no significant differences in sex, or postnatal age between term group and preterm group. Parents were informed with the goals and risks of MRI canning and requested written consent before enrollment. Subjects who were confirmed or suspected to have congenital malformations of central nervous system, congenital infections, metabolic disorders, abnormal appearances in conventional MRI were all excluded. The neonates were all sedated with oral chloral hydrate (25 - 50 mg/kg) before scanning. The 3D magnetization prepared rapid gradient echo T1 weighted images, fast spin echo T2 weighted images and DKI by single short DW-EPI sequence were performed in a 3T scanner (Signa HDxt, General Electric Medical System, Milwaukee, WI, USA) with 8-channel RF head coil. DKI was carried out by 25 gradient directions, TR/TE = 4000/106.6 ms, slice thickness = 5 mm without gap, field of view = 180 × 180 mm^2, matrix size = 128 × 128, b value = 500, 1000, 1500, 2000, 2500 s/mm^2. Each DKI scanning took 8 minutes 44 seconds. DKI tensors were estimated using constrained linear least squares [3] after artifacts rejection. Diffusivity and kurtosis tensors were used to calculate various parameters in the DKI white matter model. Differences of D_{axon}, $\lambda_{e,//}$, $\lambda_{e,\perp}$, and α between two groups were analyzed using TBSS [4]. Linear and nonlinear registrations were used to align extra-axonal fractional anisotropy (FA_e) images of all subjects to the target image and affine the aligned images into 1×1×1 mm^3 space [5]. Then the mean FA_e image and its skeleton were created. The aligned FA_e image of each subject was projected onto the mean FA_e skeleton (threshold = 0.1). Voxel-wise cross-subject statistics analysis was performed to assess differences of α, D_{axon}, $\lambda_{e,//}$, and $\lambda_{e,\perp}$ values between term group and preterm group by applying unpaired t test for multiple comparisons. All tests were taken to be significant at $p < 0.05$ after family-wise error rate (FWE) correction with threshold-free cluster enhancement (TFCE). Changes of derived parameters with PMA were analyzed using Spearman-rho correlation on Matlab (Mathworks, Natick, MA, USA).

Results

Differences in various DKI white matter model parameters between preterm group and term group were shown in Fig. 1 (a). Significant increase of α and decrease of $\lambda_{e,\perp}$ were found in almost all the skeleton areas of white matter, except part of genu of corpus callosum (GCC) and body of corpus callosum (BCC). D_{axon} increased with PMA in posterior limb of internal capsule (PLIC), splenium of corpus callosum (SCC), and GCC. Differences of $\lambda_{e,//}$ between term group and preterm group in PLIC, SCC, and GCC were not significant. Regression analysis illustrated significant age-related changes in white matter (Fig. 1 (b)).

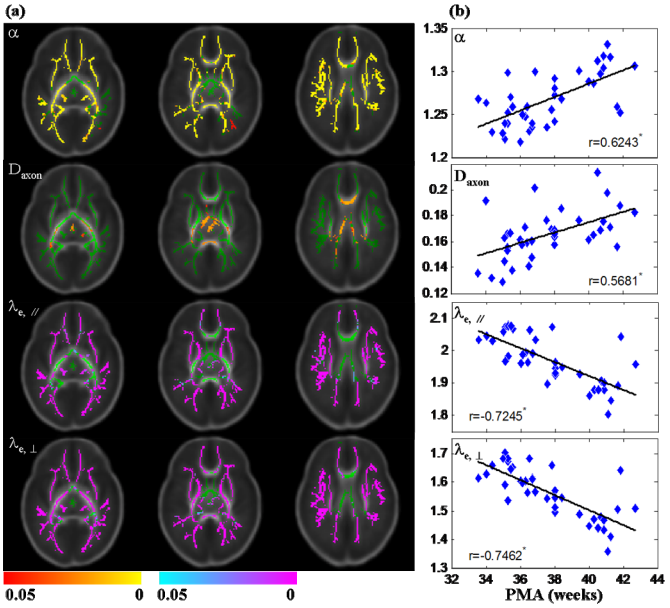

Fig. 1. Developmental changes of white matter model parameters assessed using (a) TBSS and (b) correlation analysis. Mean FA_e skeleton was shown in green. Significant increase with PMA was shown in warm color. Significant decrease with PMA was shown in cool color. In (b), the scatter plots were the mean values of the whole skeleton, analyzed using Spearman-rho correlation. *: $p < 0.001$.

Discussion

The results demonstrated that diffusivity decreased in extra-axonal space and increased in intra-axonal space. In GCC and BCC, significant increase of D_{axon} without significant changes of $\lambda_{e,//}$, and $\lambda_{e,\perp}$ reflected that changes in these cellular environments likely resulted from the increase of alignment, caliber and number of axons. In PLIC and SCC, more restrictions reduced the diffusivity in radial direction. There were counteracting physiological changes on the axial diffusivity in extra-axonal space, with a reduction in total water and increase of restrictions countered by an increase in alignment of fibers.

Conclusion

In this study, we demonstrated the changes of white matter diffusion properties in preterm and term neonates using DKI white matter model with TBSS analysis. The derived diffusivity and kurtosis parameters will be valuable to our understanding the white mater changes, both in intra-axon and extra-axon space, during early brain development.

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References

1. Hüppi PS, Warfield S, Kikinis R, et al. Quantitative magnetic resonance imaging of brain development in premature and mature newborns. Ann Neurol. 1998; 43(2):224-235.

2. Fieremans E, Jensen JH, Helpern JA. White matter characterization with diffusional kurtosis imaging. Neuroimage. 2011; 58(1):177-188.

3. Tabesh A, Jensen JH, Ardekani BA, et al. Estimation of tensors and tensor-derived measures in diffusional kurtosis imaging. Magn Reson Med. 2011; 65(3):823-836.

4. S Smith SM, Jenkinson M, Johansen-Berg H, et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. Neuroimage. 2006; 31(4):1487-1505.

5. Ball G, Counsell SJ, Anjari M, et al. An optimised tract-based spatial statistics protocol for neonates: applications to prematurity and chronic lung disease. Neuroimage. 2010; 53(1):94-102.