THE VARIATION OF WHITE MATTER TRACT IN NEONATES WITH MILD HYPOXIC-ISCHEMIC INJURY:A DIFFUSION TENSOR IMAGE ANALYSIS BY TRACT-BASED SPATIAL STATISTICS (TBSS)

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Introduction

Mild hypoxic-ischemic (HI) injury is becoming the major type in neonatal brain diseases, especially in preterm, and is often correlated to later anomalies in school age, such as behavioral problems, amblyopia, delays in language acquisition and other cognition impairments [1-3]. Diffusion tensor image (DTI) can highlight microstructural abnormalities which are not evident on conventional MRI, and tract-based spatial statistics (TBSS) provides an objective and powerful method for DTI data analyzing [4, 5]. The aim of this study is to use TBSS to test the voxel-wise differences in fractional anisotropy (FA), λ_1, λ_2, λ_3 between normal and mild HI neonatal brains.

Methods

This study was approved by the local institutional review board. The neonates were all sedated (oral chloral hydrate, 25-50 mg/kg) before MRI scanning. 41 full term neonates (17 neonates with mild HI injury, 24 neonates as normal control) with mean postmenstrual ages (PMA) of 39.51±1.77weeks (range of 37-42weeks) and 31 preterm neonates (11 neonates with mild HI injury, 20 neonates as normal control) with PMA mean of 35.31±0.95weeks (range of 33-36 weeks) underwent MRI within 28 days after birth. In this study, the three-dimensional magnetization prepared rapid gradient echo (3D-MPRAGE) T1 weighted images (T1WIs), fast spin echo (FSE) T2 weighted images (T2WIs) and DTI by single shot echo planar sequence were performed in a 3T scanner (GE, Signa HDxt,) with 8-channel head coil. DTI was performed by 35 directions, b value=1000s/mm^2, SENSE factor = 2, TR/TE=5500/95ms, slice thickness= 4 mm without gap, field of view = 180mm×180mm, matrix = 256×256, voxel size= 0.70×0.70×4mm^3. The analysis of DTI data was performed using the general linear model implemented in FMRIB's Software Library (FSL) [6]. Extracted brain images were acquired using Brain Extraction Tool (BET, package in the FSL) [7]. FMRIB's Diffusion Toolbox (FDT) [8] was used to carry out eddy current correction. FA, λ1, λ2, λ3 of the diffusion tensor were calculated. TBSS [4] was used to align FA images of all subjects to the target image (a representative FA image) and affine the aligned images into 1×1×1 mm^3 MNI152 standard space. Then the mean FA image and its skeleton were created. The aligned FA image of each subject was projected onto the mean FA skeleton (threshold = 0.2). The resulting FA skeleton images fed into voxel-wise cross-subject statistics. The differences of FA, λ1, λ2, λ3, MD values between mild HI group and control group were tested by using TBSS in preterm and full term neonates separately. All tests were taken to be significant at $p<0.05$.

Results

Mild HI injuries were defined by clinical diagnosis and manifested as the punctate white matter injury with hyperintensity in T1WIs and hypointensity in T2WIs and watershed white matter injury with hypointensity in T1WIs and hyperintensity in T2WIs. The demographic characteristics were matched between mild HI group and normal group both in preterm and full term neonates.

The differences of FA, λ1, λ2, λ3 values between mild HI and normal neonates were showed by TBSS maps respectively in preterm group (left part of Fig.1) and term group (right part of Fig.1). The results of TBSS mainly showed significantly decreased FA and increased λ2, λ3 in multiple white matter tracts ($p<0.05$). These differences of DTI indexes between the mild HI and normal neonates were mainly located in cerebral peduncle (CP), posterior limb of internal capsule (PLIC) and corona radiata (CR) both in full term and preterm groups. Moreover, the additional regions with above changes of DTI indexes in full term neonates were exhibited in external capsule (EC) and splenium of the corpus callosum (SCC) mainly. In TBSS maps of λ1, the irregularly increased and decreased regions were found in some discrete white matters.

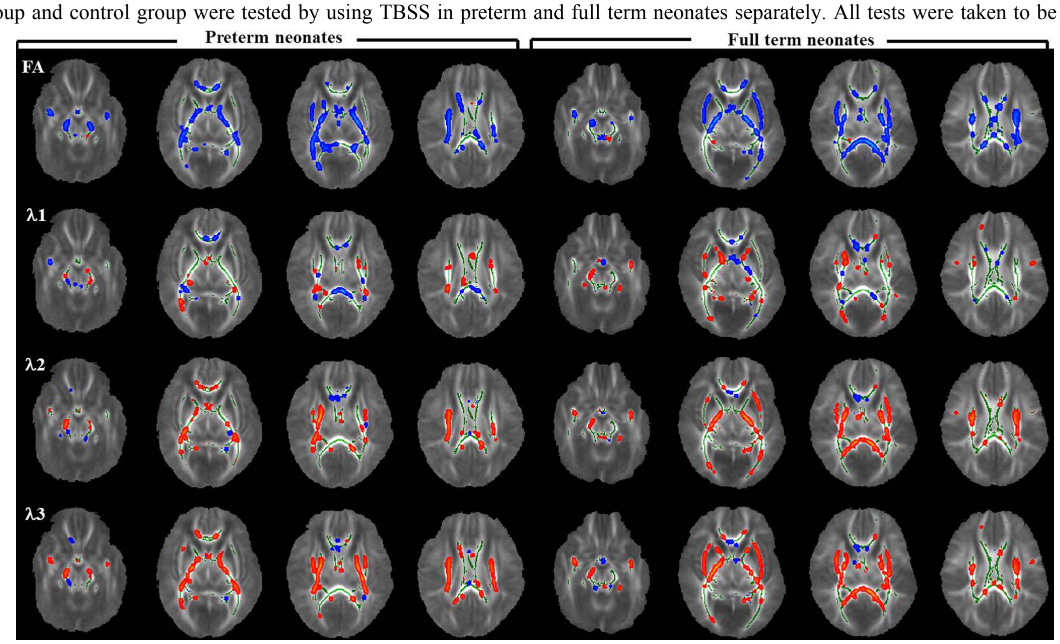

Fig.1 Differences of FA, λ1, λ2, λ3 values revealing by TBSS between mild HI and normal neonates in preterm and term groups. Blue regions showed where DTI indexes significantly decreased ($p<0.05$) in mild HI neonates relative to normal neonates. Red regions showed where DTI indexes significantly increased ($p<0.05$) in mild HI neonates relative to normal neonates. Green regions represented the mean FA skeleton.

Discussion & Conclusions

In this study, we demonstrated multiple white matter tracts damage in neonates with mild HI injury by using TBSS of DTI indexes. The decreased FA with increased λ2, λ3 in above white matter tracts may reflect increased diffusion perpendicular to white matter fibers, mainly due to deficits or delays in myelination. Some sites of white matter with myelin development after PMA of 42 weeks, such as EC and SCC in full term neonates, CR in preterm neonates, also presented increased radial diffusion. It suggested that the mild HI injury might also affect white matter premyelination. The injury of white matter tract along the corticospinal tract (from CP to CR) was observed in both preterm and term neonates with mild HI injury, which might cause motor impairment later. The additional sites of mild HI injury in EC and SCC might be related to worse performance on coordination and integration of motor, vision and sensation in full term infants. The different damage locations between preterm and full term neonates reflected the different vulnerability determined by the stage of brain maturation. This is the first study to explore white matter injury in both preterm and term neonatal brains with mild HI injury by using TBSS for DTI data analyzing. TBSS, as an objective and sensitive method, can reveal multiple white matter microstructural abnormalities in mild HI neonatal brains.

Acknowledgements: The authors would like to thank Drs. He Wang, Zhikui Xiao and Guang Cao from Applied Science Lab, GE Healthcare for their technical assistance. This study was supported by a grant from National Natural Science Foundation of China (No. 30970797 to JY).

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