WHITE MATTER DEVELOPMENT IN PRETERM INFANTS AT TERM EQUIVALENT AGE: ASSESSMENT USING TBSS

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Introduction

Preterm infants have an increased risk of future neurodevelopmental impairment that is correlated with the degree of prematurity at birth. [1] Diffusion tensor imaging (DTI) enables the visualization and quantitative characterization of white matter *in vivo*. Especially tract-based spatial statistics (TBSS) performed spatial normalization for group analyses in brain white matter. Our aim was to compare serial diffusion tensor imaging (DTI) data from preterm infants without apparent brain abnormalities on magnetic resonance imaging with those from term controls and to investigate the white matter (WM) region associated with neuromotor outcomes.

Methods.

Subjects : We obtained serial DTIs from 21 preterm infants at term-equivalent age and 1 year of corrected age. As controls, 15 term neonates and 20 newly recruited term infants aged 1 year underwent DTI. Clinical details of the infants are given in **Table 1**.

Image Acquisition : DTIs were obtained using 3T MRI (Verio;Siemens, Germany) with a Siemens matrix coil. DTI parameters were substituted as follows : B=0 and 800s/mm2 and TR/TE = 10,100/76 ms, number of diffusion gradient directions = 30, number of exc itations = 2, Flip angle = 90°, Voxel size = 1.8x1.8x1.8mm, FOV = 230mm. The scanni ng times for the DTI sequenceswas 10min 18s.

Data analysis : TBSS was performed according to our previous method.[2] The diffusio n-weighted images were processed with the FMRIB Software Library (FSL v4.1.7: ww w.fmrib.ox.ac.uk/fsl) [3] . The DTI data were first corrected for eddy-current-induced sp atial distortion, and the images were brain extracted using the Brain Extraction Tool [4]. FA, MD and RD maps were calculated using FMRIB Diffusion Toolbox. All FA images were aligned to a target in a common space by using an optimized TBSS protocol for ne onates [5]. Voxelwise analysis was performed to assess the relationship between FA, M D and RD and clinical variables using the randomize tool. Threshold-free cluster enhanc ement (TFCE) was used in the analysis. [6]

ROIs :To investigate the relationship between the FA and clinical parameter, we selected the ROI from a FA map. (1) Corpus callosum, (2) Posterior limb of internal capsule, (3) Optic radiation.

Table 1. . Characteristics of all subjects.

Variables	Preterm	Term	
	Serial DTIs (*n*=21)	DTIs in neonates (*n*=15)	DTIs at 1 year of age (*n*=20)
Gestational age, weeks	28^{+1} (2^{+6})	38^{+1} (2^{+0})	38^{+6} (1^{+6})
Birth weight, g	1,112 (397)	3,146 (631)	3,204 (509)
Male	10 (47.6)	6 (40.0)	10 (50)
Age at DIT, weeks	38^{+6}	39^{+3}	NA

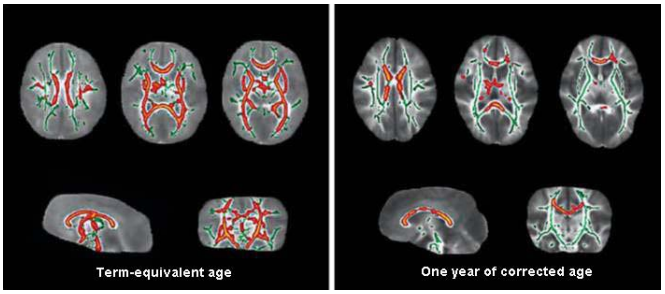

Figure 1. Comparisons of the mean FA maps between the preterm and term infants. At the TEA, the FA value across all of the white matter was lower in the preterm infants than in the term infants. (*Left*) However, at 1 year of corrected age, the CC was the only area to exhibit a reduced FA value in the preterm infants compared with the term infants. (*Right*) (*p*=0.01)

Results

Figure 1. show red-yellow regions showing reduced FA in preterm infants compared to full-term infants ($p<0.01$; TFCE-corrected). At term-equivalent age, the FA values were lower for the entire WM in the preterm infants compared with the term infants, however, at 1 year of corrected age, these differences were absent **(Fig. 1: Left)**. Only the FA value in the CC was lower in the preterm infants than in the term infants at 1 year of corrected age **(Fig. 1 ; Right).** FA values of full-term infants were significantly higher than FA values of preterm infants for corpus callosum**. (Table 2) Figure 2.** Shows FA value in the corpus callosum positively correlated with the gestational age. (r2=0.115, p<0.001)

Discussion

The present study is the first to compare serial DTI data between preterm and term infants. We found that the entire WM development was delayed in the preterm infants compared with the term infants at term equivalent age, but by 1 year of corrected age, the WM development of the preterm infants had reached the development level of the term infants, with the exception of the corpus callosum. The CC of the preterm infants was consistently underdeveloped compared with that of the term controls. The FA in the CC well reflected the degree of motor function in infants without apparent brain abnormalities..

References : 1. Wood NS, et al. *Arch Dis Child Fetal Neonatal Ed.* 90(2):F134-F140 (2005) **2**. Shim SY, et al. *Neonatology* 102:309-315. (2012) **3**. Smith, S.M, et al. *Neuroimage.* 23Suppl 1:S208-19 (2004) **4**. Smith, S.M, et al. *Hum BrainMapp*. 17(3):143-55.(2002) **5**. Ball G et al. *Neuroimage* 2010; 53: 94 –102. **6.** Smith, S.M, et al. *Neuroimage*. 44:83-98 (2009).

Table 2. Comparison of DTI parameters between preterm and full-term infants.

	DTI at term age (*n*=36)			DTI at 1 year of age (*n*=41)		
	Preterm (*n*=21)	Term (*n*=15)	*P*-value	Preterm (*n*=21)	Term (*n*=20)	*P*-value
FA						
CC	0.29 (0.09)	0.34 (0.04)	0.003	0.48 (0.06)	0.53 (0.04)	0.003
PLIC	0.36 (0.03)	0.39 (0.04)	0.006	0.85 (0.05)	0.86 (0.07)	0.760
Optic radiation	0.32 (0.04)	0.36 (0.04)	0.008	0.53 (0.03)	0.54 (0.02)	0.114
ADC ($10^{-3}mm^2/s$)						
CC	1.50 (0.11)	1.49 (0.12)	0.821	1.31 (0.11)	1.28 (0.08)	0.212
PLIC	1.10 (0.04)	1.05 (0.05)	0.004	0.96 (0.05)	0.94 (0.09)	0.111
Optic radiation	3.24 (0.21)	3.00 (0.18)	0.004	2.32 (0.10)	2.31 (0.16)	0.910

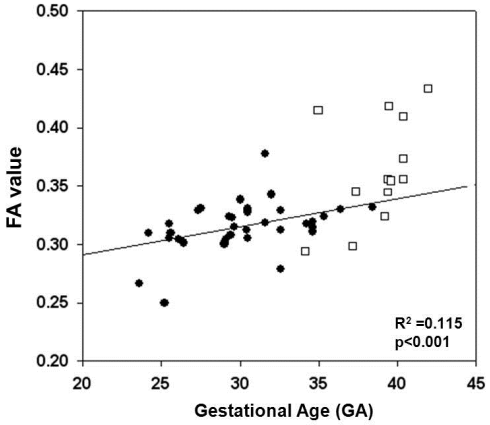

Fig 2. Graph demonstrating correlation between FA value and GA in corpus callosum. Black circles and hollow squares indicate preterm infants and term infants, respectively.