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

Jeong Hye Jin[1], Shim So-Yeon[2], Jeong Joon-Sup[1], Oh Se-Hong[1], Park Sung-Yeon[1], Kim Young-Bo[1], and Cho Zang-Hee[1]

[1]*Neuroscience Research Institute, Gachon university, Namdong-gu, Incheon, Korea,* [2]*Department of Pediatrics, Gachon University Gil Hospital, Namdong-gu, Incheon, Korea*

PURPOSE : 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 analysis in brain white matter. In this study, we performed analyses of white matter development between full-term infants and preterm infants at equivalent age using TBSS.

METHOD : ***Subjects :*** We studied 54 infants who were obtained on 12 full-term control infant and 42 preterm infants at term-equivalent age. Clinical details of the infants are given in **Table 1.** ***MRI acquisition :*** We used a conventional 3.0T MRI (Verio, Siemens) using Siemens matrix coil. The DTI sequence parameters were as follows : b = 0 and 700 s/mm^2, TR/TE = 6600/74 ms, number of diffusion gradient directions = 30, number of excitations =2, FOV = 230 mm, matrix = 128x128, slice thickness = 1.8 mm, voxel =1.8 x 1.8 x 1.8 mm, Flip angle = 90 °. The scanning time for the DTI sequence was 7min 36seconds. ***Image analysis :*** The diffusion weighted images were processed with FMRIB Software Library (FSL v4.1.4: www.fmrib.ox.ac.uk/fsl).[2] The DTI data were first corrected for eddy-current-induced spatial distortion, and the images were brain extracted using the Brain Extraction Tool.[3] Individual FA and ADC maps and eigenvalue maps (λ_1, λ_2, and λ_3) were generated. Voxel-wise Statistical analysis of FA (or ADC) was performed with TBSS for neonates.[4] A correction for multiple comparisons and cluster formation was conducted with threshold-free cluster enhancement (TFCE).[5] Voxels with p=0.05 (TFCE-corrected) were considered significantly different. ***ROIs :*** Five additional regions of interests (ROIs) were chosen from a TBSS-generated skeleton FA-slice : (1) Corpus callosum, (2) Interior limb of internal capsule, (3) Posterior limb of internal capsule, (4) Optic radiation, (5) Cerebral peduncle. Two researchers drew ROIs, and no significant differences were found either between observers (p = 0.78) or between test-retest (p = 0.45).

RESULTS: Figure 1. show red-yellow regions showing reduced FA in preterm infants compared to full-term infants (p<0.01; TFCE-corrected). Group-wise voxel-based comparisons between full-term infants and preterm infants revealed significantly decreased FA values in preterm infants at term equivalent age. FA values of full-term infants were significantly higher than FA values of preterm infants for all investigated 5 ROIs**. (Table 2) Fig 2.** Shows FA value in the corpus callosum positively correlated with the gestational age. (r^2=0.115, p<0.001)

CONCLUSION: The comparison of FA map between preterm infants and full term infants at term equivalent age revealed significantly reduces in FA map corresponding to the cerebral white matter. FA values in the CC decreased in preterm infants and were positively correlated with gestational age at birth. We show that growth of white matter is gestation dependent. Longitudinal study is needed to define the catch-up growth in preterm infants.

Table 1. Characteristics of all subjects.

	All subjects (n=54)	
	Full-term infant (n=12)	Preterm infant (n=42)
Male, n	5 (41.7%)	22 (52.3%)
Birth weight, g	3100 (2800 - 4000)	1482 (850 - 2800)
GA, weeks	38^{+4} (37^{+2} ~ 40^{+4})	31^{+3} (22^{+4} ~ 35^{+4})
PMA at MRI, weeks	40^{+2} (38^{+0} ~ 42^{+4})	38^{+4} (35^{+6} ~ 41^{+2})

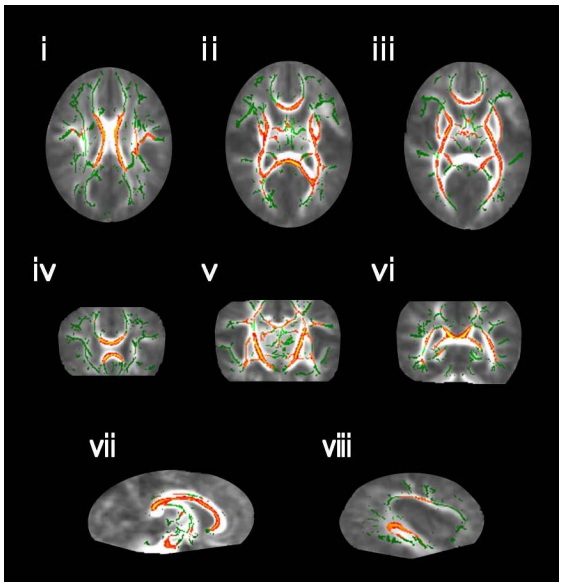

Fig 1. TBSS analysis of FA map. mean FA skeleton (green) overlaid on mean FA map in axial (i-iii), coronal (iv-vi) and sagittal (vii–viii) plane. Areas in red-yellow represent voxels where the FA was significantly lower in the preterm infants. (*p<0.01;* TFCE-corrected)

REFERENCE: 1. Wood NS, et al. *Arch Dis Child Fetal Neonatal Ed.* 90(2):F134-F140 (2005), **2**. Smith, S.M, et al. *Neuroimage*. 23Suppl 1:S208-19 (2004) **3**. Smith, S.M, et al. *Hum BrainMapp*. 17(3):143-55.(2002) **4**. Ball G et al. *Neuroimage* 2010; 53: 94 –102. **5**. Smith, S.M, et al. *Neuroimage*.31(4):1487-505 (2006).

Acknowledgements :

This study was supported by a grant of the Korea Health technology R&D Project, Ministry of Health & Welfare, R epublic of Korea. (A090084)

Table 2. Comparison of mean FA and mean ADC between preterm infants and full-term infants.

	Preterm infants (n=42)	Full term infants (n=12)	p-value
FA			
Corpus callosum	0.3183 (0.0316)	0.3572 (0.0410)	0.002
ALIC	0.2618 (0.0448)	0.3181 (0.0521)	0.001
PLIC	0.3452 (0.0286)	0.3979 (0.0402)	< 0.001
Optic radiation	0.3207 (0.0437)	0.3757 (0.0566)	0.001
Cerebral peduncle	0.3865 (0.0487)	0.4823 (0.0753)	<0.001
ADC (10^{-3} mm^2/s)			
Corpus callosum	1.5040 (0.1018)	1.4758 (0.1021)	0.004
ALIC	2.5741 (0.1548)	2.2669 (0.1391)	< 0.001
PLIC	1.1006 (0.0611)	1.0282 (0.0408)	< 0.001
Optic radiation	3.2275 (0.2386)	2.9532 (0.1464)	0.001
Cerebral peduncle	3.0628 (0.4502)	2.6281 (0.2357)	0.003

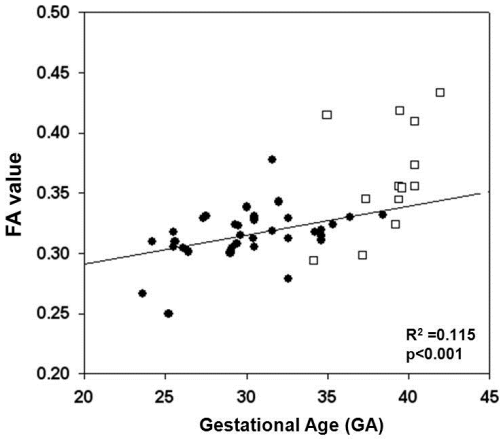

Fig 2. Graph demonstrating correlation between FA value and GA in corpus callosum. Black circles and hollow squares indicate preterm infants and term infants, respectively.