Abnormal White Matter and Gray Matter Maturation in Premature Neonates with Periventricular Hemorrhagic Infarction: A Diffusion Tensor Imaging Study

A. Garg[1,2], J. I. Berman[1], D. Xu[1], S. Veeraraghavan[1], S. L. Bonifacio[3], H. C. Glass[3,4], D. B. Vigneron[1], A. J. Barkovich[1,3], and P. Mukherjee[1]

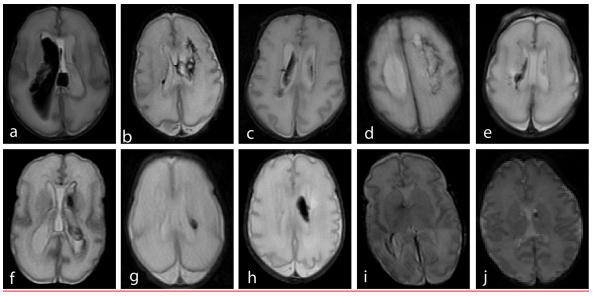
[1]Radiology and Biomedical Imaging, UCSF, San Francisco, California, United States, [2]Neuroradiology, AIIMS, New Delhi, India, [3]Pediatrics, UCSF, San Francisco, California, United States, [4]Neurology, UCSF, San Francisco, California, United States

Introduction

Periventricular hemorrhagic infarct (PVHI) is among the most devastating injuries suffered by prematurely born infants. In PVHI (formerly called Grade 4 intraventricular hemorrhage), an intraventricular vein that drains smaller veins from the surrounding white matter is occluded, resulting in venous infarction with hemorrhage [1]. DTI has become a useful imaging technique to identify maturational trends reflecting microstructural changes in white matter (WM) & gray matter (GM) of the developing brain [2-4] and has been shown to detect microstructural injury, even in normal appearing neonatal WM [5]. However, there have been no reports of abnormal microstructural maturation in GM with DTI. Furthermore, there have been no prior DTI studies of PVHI. In this study, we hypothesize that, in prematurely born neonates with PVHI, DTI would be able to detect abnormal microstructural development in WM and GM that appear normal on conventional T1-weighted and T2-weighted MR imaging.

Materials and methods

Ten preterm neonates with imaging findings of PVHI, and 10 age-matched preterm healthy neonates without imaging evidence of brain injury and normal neurological outcome at 1-year of age were prospectively enrolled. The patients and controls were age-matched for gestational age at birth and age at time of MR scan. We compared DTI parameters of directionally averaged diffusion coefficient (D_{av}), fractional anisotropy (FA), and the maximum, intermediate, and minimum eigenvalues ($\lambda1$, $\lambda2$ and $\lambda3$ respectively) in 6 cerebral cortical regions, 2 deep GM regions and 6 WM regions between the 2 groups.



Results

The figure at right shows axial T2-weighted images of the varying extent of hemorrhages in these ten cases of PVHI. Compared to normal controls, the PVHI group showed significantly higher FA values in the frontal (P = 0.004) and temporal (P = 0.043) cortical regions, while occipital cortex showed a trend towards higher value (P = 0.065). No significant differences were seen in the D_{av} values in the other cortical and deep gray matter regions. Across serial examinations with correction for repeated measures, PVHI patients showed statistically significant increases in $\lambda1$ in temporal (P = 0.003) cortex, while frontal (P = 0.13) and occipital (P= 0.083) cortex showed a trend towards higher values.

The PVHI group had significantly lower FA values in normal-appearing low centrum semiovale (LCS, P <0.001), high centrum semiovale (HCS, P = 0.008), and splenium of the corpus callosum (P = 0.002). PVHI patients showed statistically significant increases in D_{av} in the normal-appearing LCS (P = 0.005), and splenium of the corpus callosum (P = 0.003), while HCS (P = 0.123) showed a trend towards higher D_{av} values. Table 1 shows DTI parameters in various GM and WM regions in patients and controls.

	FA			ADC (10^{-3} mm^2/sec)		
	Controls	**PVHI**	**P Value**	**Controls**	**PVHI**	**P Value**
ALIC	0.277±0.020	0.277±0.032	1.000	1.364±0.046	1.315±0.059	0.089
PLIC	0.444±0.025	0.419±0.053	0.481	1.194±0.049	1.170±0.053	0.190
Genu	0.510±0.034	0.474±0.066	0.218	1.305±0.063	1.310±0.060	0.971
Splenium	0.559±0.028	0.481±0.061	**0.002**	1.226±0.044	1.355±0.115	**0.003**
High CS	0.139±0.008	0.123±0.014	**0.008**	1.843±0.085	1.909±0.105	0.123
Low CS	0.173±0.008	0.143±0.018	**0.001**	1.610±0.081	1.768±0.143	**0.005**
Frontal Ctx	0.246±0.015	0.270±0.020	**0.004**	1.231±0.025	1.211±0.039	0.065
Temporal Ctx	0.218±0.020	0.246±0.032	**0.043**	1.219±0.054	1.263±0.103	0.393
Parietal Ctx	0.226±0.020	0.219±0.015	0.604	1.194±0.049	1.179±0.048	0.278
Occipital Ctx	0.231±0.025	0.253±0.019	0.065	1.213±0.029	1.192±0.051	0.604
Pre Cen Ctx	0.170±0.014	0.161±0.030	0.165	1.112±0.036	1.144±0.041	0.089
Post Cen Ctx	0.161±0.016	0.155±0.031	0.280	1.129±0.095	1.170±0.062	0.393
Len Nuc	0.102±0.010	0.108±0.005	0.211	1.357±0.060	1.326±0.038	0.133
Thalamus	0.136±0.011	0.139±0.009	0.604	1.274±0.036	1.254±0.048	0.165

Discussion

DTI in PVHI reveals abnormal microstructural maturation of gray matter and white matter in regions that appear normal on conventional MR imaging. This implies that the abnormal development and injury due to PVHI extends well beyond that detected by conventional anatomic imaging techniques. Late maturing white matter regions (high- and low-centrum semiovale) and cortical regions (frontal, occipital, and temporal cortex) regions are more affected compared to earlier maturing regions such as the posterior limb of the internal capsule or the pre- and post-central cortex.

Conclusion

The increased cortical FA and decreased WM FA in the affected regions, as well as the pattern of alteration of the diffusion tensor eigenvalues, suggest delayed development as the etiology of the observed microstructural changes of gray matter and white matter in PVHI.

References& Acknowledgements: [1] Papile at al. J Pediatr 1978:93;834-836 [2] Partridge SC et al. Neuroimage 2004;22:1302-1314 [3] Deipolyi AR et al. Neuroimage 2005;27:579-586 [4] Gupta RK et al. J Neurosci Res 2005;81:172-178 [5] Huppi PS et al. Pediatrics 2001;107:455-460. This study was made possible by Grant Number UL RR024131-01 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and NIH Roadmap for Medical Research and NIH grants NS35902 and NS046432. A.G. is supported by the "Overseas Associateship Award" from the Department of Biotechnology, India. H.C.G. is supported by the NINDS Neurological Sciences Academic Development Award (NS01692).