DTI is more sensitive to detect effects of hypercapnia on white matter development in ELBW infants than conventional MRI

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Introduction

Cerebral white matter injury is very common in extremely low birth-weight (ELBW) infant survivors of intensive care and is associated with poor long-term neurological outcomes including cerebral palsy, learning disabilities, epilepsy, and mental retardation. In ELBW infants, the immature development and regulation of the vascular supply of the white matter suggests a very small margin of safety. White matter may be vulnerable to hypoxic-ischemic injury or other events such as hyperperfusion induced by permissive hypercapnia (a common ventilation strategy used with ELBW infants which allows PaCO2 to be relatively higher than normal to prevent injury to the fragile lung). PaCO2 is a potent regulator of cerebral blood flow (CBF), and hypercapnia (PaCO2 >45 mm Hg) causes vasodilation, increases CBF, and may affect the developing white matter. While overt white matter injury such as periventricular leukomalacia (PVL) can be easily detected by conventional MRI, subtle white matter injury may not be apparent and advanced MRI methods sensitive to white matter such as diffusion tensor imaging (DTI) may provide more information on the effects of hypercapnia. In this study, we used DTI in addition to conventional MRI to evaluate two groups of ELBW infants: one was randomized to permissive hypercapnia ventilation during the first week of life, and the other was randomized to normocapnic ventilation.

Methods

Twenty-eight ELBW infants with birth weight 401-1000 g (gestational age < 30 weeks) were recruited and randomized to hypercapnic ventilation (50-60 mm Hg, N=14) or normocapnic ventilation (35-45 mm Hg, N=14) during the first week of life. MRI examinations were performed at term-equivalent age for each on a 1.5 Tesla Philips Achieva scanner with an 8-channel SENSE coil. No sedation was used. The infants were fed ~30 minutes before the MRI and were swaddled in warm sheets, and a MRI-compatible MedVac Infant Immobilizer was used to restrict movement during the scan. A neonatal brain MRI protocol was used which includes sequences such as sagittal T1-weighted, axial T2-weighted, axial diffusion weighted, and axial T2*-weighted gradient echo or axial susceptibility weighted imaging with minimum intensity projection reconstruction. A single-shot gradient echo EPI diffusion weighted imaging sequence with b=800s/mm^2 and diffusion gradients uniformly distributed in 15 directions was used for the DTI data acquisition. After the scan, MRI images were exported to the institutional PACS system and were independently evaluated by two experienced neuroradiologists to score the white matter development. The scoring consists of five components: white matter signal intensity, volume of periventricular white matter, presence of cyst, ventricular dilation, and corpus callosum thickness (adopted from Reference 1), with each component scored from 1 to 4, corresponding to normal, mild, moderate, and severely abnormal, respectively. The overall score was the sum of the five scores and the scores from the two neuroradiologists were averaged. For DTI data analysis, fractional anisotropy (FA) and mean diffusivity (MD) maps were calculated and exported to a workstation with MATLAB for region of interest (ROI) analysis. Regions were drawn on the FA maps to include as many voxels as possible for each white matter structure and to exclude all edge voxels to minimize partial volume effects. Average FA and MD values for each main white matter structure in each subject were calculated. The MRI scores and DTI parameters were compared between subjects with or without permissive hypercapnia by an unpaired two-sample t-test.

Results

The number of subjects with abnormal white matter (defined as overall score ≥6) was higher in the hypercapnic group (N=9) than the normocapnic group (N=6). However, the overall white matter scores were not significantly different between groups (7.38±3.21 vs 7.14±2.78, p=0.85). The scores for each of the 5 components were also not significantly different between the groups. Some of the DTI results are illustrated in Figure 1. The DTI-measured FA values were lower in the genu and splenium of the corpus callosum for the comparison of hypercapnic to normocapnic subjects (0.52±0.10 vs 0.55±0.07, and 0.50±0.13 vs 0.59±0.09, respectively), while the DTI measured MD values were higher in in the genu and splenium for the hypercapnic subjects (1.38±0.11 vs 1.32±0.09, and 1.38±0.22 vs 1.22±0.10 10^{-3} mm^2/s, respectively). The MD difference in splenium was significantly different (p=0.03); the FA and MD values in other white matter regions were not significantly different between hypercapnic and normocapnic subjects

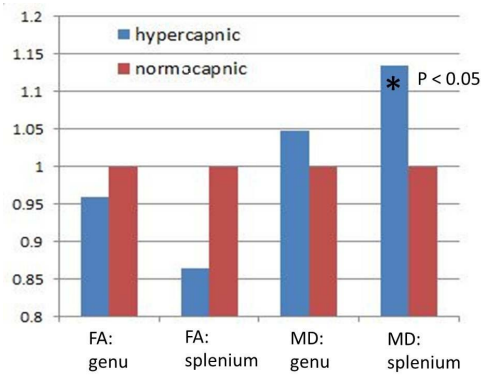

Figure 1:

Comparison of DTI parameters in the genu and splenium for the two groups. The FA and MD values for the normocapnic group are normalized to 1.

Discussion

We used both conventional MRI and DTI to evaluate the effects of permissive hypercapnia on white matter development at term-equivalent age in ELBW infants. The conventional MRI, which was the clinical neonatal brain protocol, was graded for white matter injury/development. Although the number of subjects with abnormal white matter was higher for the hypercapnic group, the average score for this group was not significantly different from that in the normocapnic group. DTI analysis revealed lower FA values and higher MD values in the genu and splenium of hypercapnic subjects, and the MD values in splenium were significantly different between the hypercapnic and normocapnic infants, similar to a pattern of delayed myelination. These results suggest that hypercapnia may have unfavorable effects on the white matter development of ELBW infants, and DTI may be more sensitive to detect these effects.

Reference

1. Woodward LJ et al, the New England Journal of Medicine 2006: 355; 685-694

Acknowledgements

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