Delayed maturation of the cortico-spinal tract of premature newborns: a preliminary study with quantitative DTI-based tractography

J. Dubois[1], F. Lazeyras[2], M. Perrin[3], Y. Cointepas[3], C. Borradori-Tolsa[1], S. Sizonenko[1], and P. Huppi[1]

[1]Department of Pediatrics, Geneva University Hospitals, Geneva, Switzerland, [2]Department of Radiology, Geneva University Hospitals, Geneva, Switzerland, [3]Service Hospitalier Frederic Joliot, CEA, Orsay, France

Introduction

Prematurity is an important cause of neurodevelopmental delay, even in preterm infants without overt brain lesions. As alterations in the organization and maturation of cerebral white matter can affect the cortical functional development, the quantitative evaluation of the development of fiber fascicles can provide important insights on the neurological outcome. Diffusion tensor imaging (DTI) then appears as the most adequate technique, as it provides valuable information on the brain tissue microstructure non-invasively [1]. Recently, the effect of prematurity on the cortico-spinal tract maturation has been outlined by comparing DTI measurements of preterm and term newborns with equivalent gestational age (GA), with an approach by regions-of-interest [2] and a voxel-by-voxel method [3]. Tractography has also been used to precisely segment this immature fiber bundle and highlight age-related differences in its local maturation in preterm newborns at birth and at term [4]. In this study, such approach was used to map the effect of prematurity in the developing cortico-spinal tract, in the internal capsule and centrum semiovale, by comparing diffusion indices of normal preterm and term newborns.

Materials and Methods

Subjects Five preterm (PT) newborns (GA at birth: 28.7±0.4 weeks) were compared to five control fullterm (FT) newborns (GA at birth: 40±1 weeks) at term-equivalent age (PT: 40.7±0.6w, FT: 40.5±1w).

DTI acquisition The acquisition was performed on a 1.5T MRI system (Philips Medical Systems), using a circulary polarised head coil and a diffusion-weighted EPI sequence (b=700s.mm^{-2}, 6 directions of the diffusion gradients, 3 averaging, TE/TR=65ms/4.45s). Axial slices covering the whole brain were imaged, with a spatial resolution interpolated to 1.56x1.56x3mm^3 at reconstruction.

Data post-processing Data processing was performed using BrainVISA software [5]. The DW images were corrected for the geometric distortions due to eddy currents [6], and the diffusion tensor was estimated on a pixel-by-pixel basis. Maps of mean (<D>), longitudinal ($\lambda_{//}$) and transverse ($\lambda_{\perp}$) diffusivities, and of fractional anisotropy (FA) were calculated. For each newborn, the cortico-spinal tract was tracked in 3D using regularized particle trajectories [7], with tractography "seeds" and selection regions [8] positioned on the color-coded (RGB) directionality maps at the level of the posterior limb of the internal capsule, the low and high centrum semiovale. The propagation mask excluded voxels with low FA (<0.1) or high <D> (>2.10^{-3}mm^2.s^{-1}), and a 30° maximum curvature angle was used.

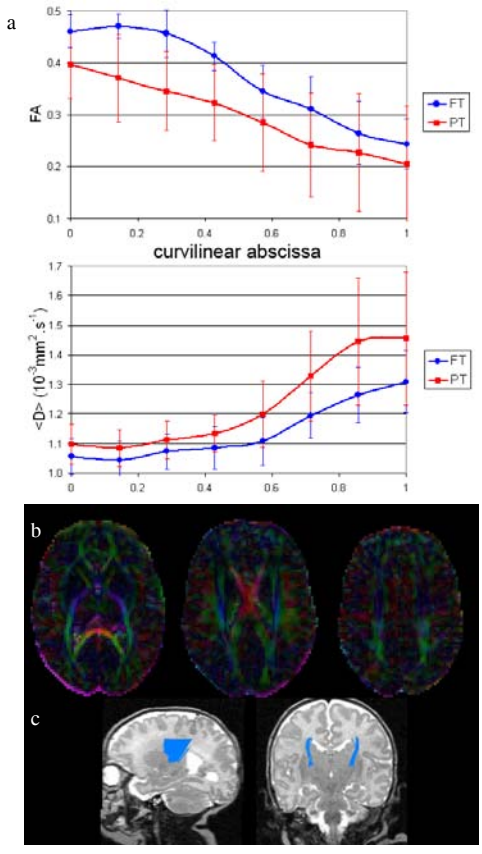

Figure 1: FA and <D> quantification for the fullterm (FT) and preterm (PT) groups along the cortico-spinal tract (a), between the internal capsule (abscissa=0) and the high centrum semiovale (abscissa=1), which are represented on the RGB map (b) and were delineated by tractography (c).

Evaluation of the cortico-spinal tract maturation The tract maturation was assessed for each newborn by quantifying the diffusion indices along the tracked fibers between the internal capsule and the centrum semiovale (with a curvilinear abscissa ranging from 0 to 1, over a tract length measuring approximately 2cm). The resulting curves were compared qualitatively across the two groups.

Results

Cortico-spinal tract tractography Despite its low myelination, the bundle was reconstructed in 3D for all newborns in its upper portion (between the posterior limb of the internal capsule and the high centrum semiovale, Figure 1c), but the tracking was erroneous in the lower portion, in the midbrain below the cerebral peduncles.

Cortico-spinal tract maturation In both groups, we observed higher FA and lower <D> in the internal capsule in comparison with the centrum semiovale (Figure 1a), because these regions present different degree of myelination, fiber density and organization.

Effect of prematurity on the tract maturation In the preterm group, FA was reduced at each location of the tract (Figure 1a), and <D> was increased in the centrum semiovale (curvilinear abscissa>0.5). In terms of tensor eigenvalues, higher $\lambda_{\perp}$ was observed in the whole tract, whereas $\lambda_{//}$ was respectively lower below the centrum semiovale, and higher above. These results were not significant because of the small size of the two groups. Thus the maturation of the cortico-spinal tract differs qualitatively between preterm at term and fullterm newborns, and two distinct effects of prematurity on diffusion parameters seem to be involved along the tract. In preterm newborns, the tract may be less organized, compacted and myelinated at the level of the internal capsule, while the tissue water content may be larger in the centrum semiovale due to a reduced density in cells and membranes.

Discussion and Conclusion

These preliminary results indicate that prematurity delays the maturation of the cortico-spinal tract, at term-equivalent age and even without overt lesion, in a white matter region which is particularly sensitive to early injury and may relate to the cerebral motor developmental difficulties observed in preterm infants. These results should be confirmed over a larger cohort of newborns with an improved acquisition protocole (higher spatial resolution and number of diffusion gradient directions), as such consequences of prematurity were previously only shown with concomitant T2 hyperintensities [9].

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