Comparative DTI study of preterm and normal newborns : SPM and ROI analyses

P. Scifo[1,2], C. Baldoli[2,3], S. Pontesilli[2,3], F. Navarra[1,2], R. Scotti[2,3], A. Poloniato[4], G. Scotti[2,3], and F. Fazio[1]

[1]Nuclear Medicine, Scientific Institute H San Raffaele, Milan, Italy, [2]CERMAC, Università Vita-Salute San Raffaele, Milan, Italy, [3]Neuroradiology, Scientific Institute H San Raffaele, Milan, Italy, [4]Pediatrics, Scientific Institute H San Raffaele, Milan, Italy

Introduction:

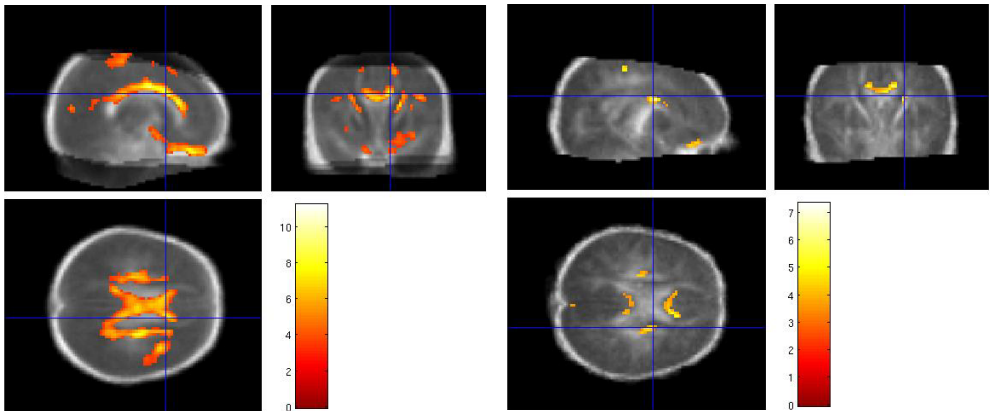
The prenatal period and the first months of life are crucial for myelination with important microstructural changes in the brain [1]. The study of these first stages of brain development are particularly interesting for the comprehension of brain maturation and connectivity. Comparisons between groups of normal subjects and preterm newborns have been presented [2] but few studies have been performed looking at changes along time. In this work, we show a comparative DTI study between a group of normal newborns and a group of preterm newborns these last acquired three times, at different stages of development. Analysis have been performed both on voxel-by-voxel basis and on ROIs. Results have been compared.

Materials and methods:

Two groups of subjects have been studies: a) 20 normal subjects, born at term, studied within the first 4 days of life; b) 15 preterm newborns (within 28-33 weeks of gestational age, GA), without any evident white matter injuries on conventional MR examinations. MR acquisitions were performed once for normal subjects and three times for preterm infants (*stage1,* early after birth, *stage2,* 41st week GA, and *stage3,* during the second month of life). During the examinations, infants were spontaneously asleep without sedation. MR acquisitions were performed on a 1.5 Tesla scanner (Philips, Intera) and included a clinical examination (T1, T2) and DTI acquisitions (DW-EPI, 15 directions for diffusion gradients, b-value=700s/mm^2, voxel size=2x2x3.5mm^3). Fractional Anisotropy (FA) maps were calculated using Brainvisa software [http://brainvisa.info]. For ROI analysis the regions were placed on FA maps in several white matter structures by 3 different experts. Mean and standard deviations have been calculated for all the ROIs first for each subject and then within the four groups (Normal subjects, preterms *stage 1*, preterms *stage 2,* preterms *stage 3*). Voxel-by-voxel analysis was performed using SPM5. To compare subjects, DTI images were normalised first to a template of babies [3], then DTI(b=0) template were created with the subjects' normalised images. The original data were then re-normalised to these new templates. Transformation parameters calculated for DTI(b=0) data were then applied to the FA maps. Statistical analysis was conducted comparing the group of normal subjects with the group of preterms at the three different stages.

Results:

In the figure, results of the SPM group-based FA analysis have been superimposed to the FA template. On the left, regions of significant differences between normal subjects and preterm at *stage2*. On the right, regions of significant differences between normal subjects and preterms at *stage3*.



Discussion and conclusions:

SPM analysis indicates that, with respect to normal subjects, in preterm newborns myelination process is delayed. Specifically, the comparison between normal subjects and preterms at *stage2* shows strongly significant differences in the myelination mainly localised in corpus callosus, subcortical Rolandic white matter and internal capsules. This means that, although at the same corrected age, the myelination process in preterms is not as developed as in normal subjects. Nevertheless, the comparison between normal subjects and the preterms at *stage3*, shows that the significant regions of difference are dramatically decreased and mainly located in corpus callosum and internal capsules. This means that in preterm newborn, even with a delay, the myelination seems to proceed quite normally.

Preliminary ROI analysis shows congruent results. Significant differences between normal subjects and preterms at *stage2* have been found in corpus callosum and subcortical Rolandic white matter tracks. On the other hand, comparison between normal subjects and preterms at *stage3* shows significant difference mainly in internal capsules.

In conclusion, the comparison between normal subjects and preterms studies acquired at different stages of development enables to follow the maturation process of the immature brains along time.

The congruency between the SPM and ROI analyses is another important point of this study. SPM analysis is usually considered to be an objective statistical analysis but with a critical point related to the normalisation step. In particular in infants, with weak contrasted images and immature brains, this step might fail to overlap correspondent regions. On the other hand, ROI analysis, where no normalisation step has to be applied, is usually considered to be critical as it is operator's dependent. The comparison between these two analyses and the congruence of the results is then important to guarantee the goodness of the two procedures.

References:[1] Huppi et al., Semin. Fetal Neonat Med, 2006;11(6):489-497; [2] Yoo et al, Invest Radiol, 2005, 40(2) :110-5 ; [3] Dehaene et al., Science. 2002;6;298(5600):2013-5; [4] Partridge et al, Neuroimage, 2004; 22:1302-1314.