Longitudinal fMRI and DTI study of brain development in preterm newborns

P. Scifo[1,2], C. Baldoli[2], V. Blasi[2], S. Pontesilli[2], R. Scotti[2], G. Scotti[2], and F. Fazio[1]
[1]Nuclear Medicine, San Raffaele Scientific Institute, Milan, Italy, [2]CERMAC, San Raffaele Scientific Institute, 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 in the same group of subjects looking at changes along time. In this work, we show a longitudinal DTI and fMRI study on preterm newborns. Three acquisitions, at different stages of development, have been compared to see the main changes in myelination and cognitive functions in this critical period of life.

Materials and methods:
The group of subjects included in this work were born at 28-33 weeks of gestational age (GA) and they had no evident white matter injuries on conventional MR examinations. MR acquisitions were performed early after birth (*stage1*), at term (41st weeks GA, *stage2*) and during the second month of life (*stage3*). 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), DTI acquisitions (DW-EPI, 15 directions for diffusion gradients, b-value=700s/mm^2, voxel size=2x2x3.5mm^3) and two fMRI scans (GE-EPI, TR/TE=2200/40ms). fMRI protocol consisted in a block-design paradigm (60 volumes) in which during the activation condition children listened to a story. Fractional Anisotropy (FA) maps were calculated using Brainvisa software [http://brainvisa.info]. Statistical analyses were performed using SPM2. Images were normalised first to a template of babies [3], then a T2 (for DTI) and EPI template were created with the subjects' normalised images. The original data were then re-normalised to these new templates. Transformation parameters calculated for T2 images were then applied to the FA maps. Statistical analysis of DTI data was conducted comparing the groups of subjects at the three different stages. fMRI data were analysed only as single subjects due to the high variability of results.

Results:
DTI data have shown more consistent results than fMRI. In fig.1 results of group-based FA analysis have been superimposed to the FA template. On the left, regions of significant differences between *stage2* and *stage1*. On the right, regions of significant differences between *stage3* and *stage2*. In fMRI data, single subject analysis showed congruent activations only in few subjects: acoustic activations were found in one subject of *stage1*, in 3 subjects of *stage2* (see for example fig.2) and in 2 subjects of *stage3*. Activations in the Broca's area were found in 2 subjects of *stage2* and in 2 of *stage3*.

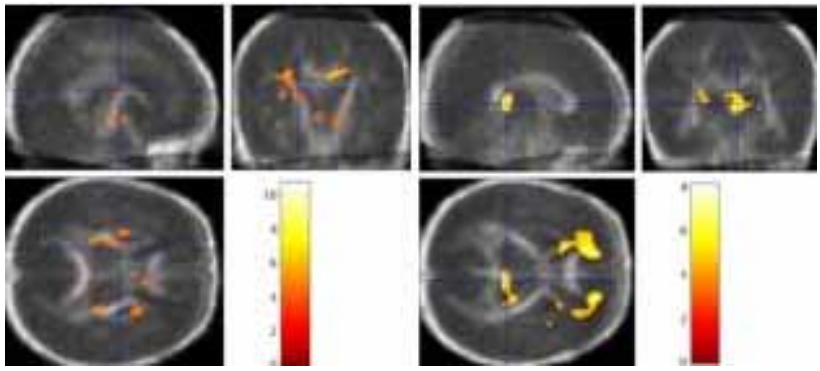

Figure 1

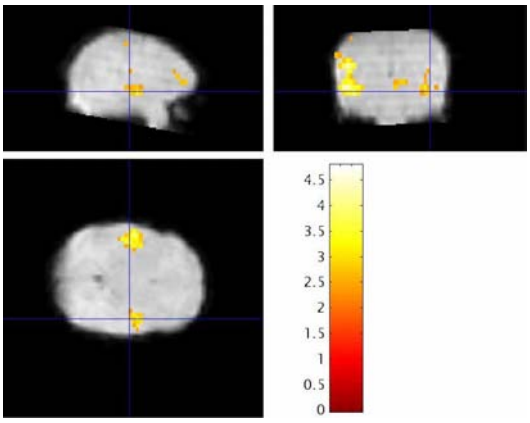

Figure 2

Discussion and conclusions:
DTI data indicate that in the preterm period a significant increase in FA is localised mostly in the anterior region of corpus callosum and the external capsule. During the first month more frontal regions are involved. fMRI data showed low image contrast due to the different composition of the brain in this first stage of life. fMRI analysis showed high variability among subjects: positive and negative activations or even absence of activations. Critical aspects in acquisitions, such as MR parameters, device for auditory stimulation, slept subjects have to be considered. Nevertheless, variability in hemodynamic response might be related to the incomplete myelinisation of newborns [4]. Further researches focusing on new models of hemodynamic response for newborns and optimised MR acquisition parameters will be necessary to overcome these problems.

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References:
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