Evidence of thalamocortical fibers maturation in early human brain development assessed by diffusion tensor imaging

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INTRODUCTION

Several authors have shown that brain maturation may be evidenced *in vivo* in newborns using diffusion tensor imaging (DTI) (1-4). However, these studies were based on measurements in pre-defined regions of interest (ROI), which introduce a bias due to a priori hypotheses about the localization of maturational changes. Therefore we used a voxel-based approach, as known as statistical parametric mapping (SPM), to detect maturational changes in a population of preterm and term newborns, without prior prescription of the brain area to be analyzed.

MATERIALS AND METHODS

Forty eight prematurely born infants (between 25 3/7 and 34 2/7 weeks) and seventeen term newborns (between 37 6/7 and 40 4/7) were imaged without sedation between 34 2/7 and 41 1/7 weeks gestational age, in accordance to a research protocol approved by the institutional review board at our medical center. All of the infants included in this study had normal Brain MRI.

MR scans were performed at 1.5 T on a Philips Achieva scanner with 2.3 mm slice thickness, TR=5888 ms, TE= 92 ms, FOV= (220 mm)^{2,} 32 non-collinear diffusion-sensitizing gradient directions with diffusion sensitivity b=600 s/mm^2, no average, and an in-plane resolution of 2mmx2mm. Total DTI scan time was 3'32" for 45 contiguous slices yielding full brain coverage. A vacuum-rigidified pillow was used to reduce movements during MRI acquisition

Patients with visible motion artifacts in the b=0 image, or in more than 10 different diffusion-weighted images, were removed from the study. In the remaining patients, directions with visible motion artifacts were removed, and the remaining images were realigned using the diffusion toolbox of SPM2 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). The DTI toolbox was then used to compute apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps. To exclude patients with motion-related artifacts not visible with visual inspection of each of the 32 directions, we performed a voxel-by-voxel two sample t-test on FA and ADC map with SPM2, each patient against the rest of the group. Subjects with significant differences (clusters of more than 100 voxels with corrected P value < 0.05) were rejected from the study. When the effect of removing the corrupted directions was more than 5% in a motion-free dataset, the patient was removed from the study.

Each FA and ADC volume was normalized to the same anatomical space with SPM2. The template created for this purpose consisted of the b=0 image of a normal term patient included in the study. Finally, all individually normalized ADC and FA data sets were smoothed by convolving them with isotropic 5mm FWHM (full width at half maximum) Gaussian kernels. An F statistic was computed at each voxel to test for a linear relationship between the patient's age and ADC or FA. Regions of more than 50 voxels attaining a corrected P value < 0.05 were considered as statistically significant.

RESULTS

Twenty-two premature were removed from the study, 5 because of movements during B0 acquisition and 17 because of visible motion artifacts in more than 10 directions. Nine term newborns where removed from the study, 3 because of movements during B0 acquisition and 6 because of visible motion artifacts in more than 10 directions. Amongst the 34 newborns left (26 premature and 8 term newborns), 18 had movements causing image corruption in at least one direction. Amongst the 32 directions acquired, we had to remove 1 direction in 1 patient, 2 directions in 3 patients, 3 directions in 4 patients, 4 directions in 4 patients, 5 directions in 4 patients, 7 directions in 1 patient and 9 directions in one patient. Four more patients were removed from the study because of motion related artifacts revealed by the two-sample t-test, and two others because FA was too much affected by the removal of corrupted directions, according to the above mentioned criterion.

As illustrated by figure 1, statistical analysis of data from the 28 remaining patients revealed a highly significant positive association between age and FA in prefrontal white matter, pre-rolandic motor cortex, corona radiata, centrum semi ovale, internal capsule, optic radiation and thalami. No significant association was found with ADC.

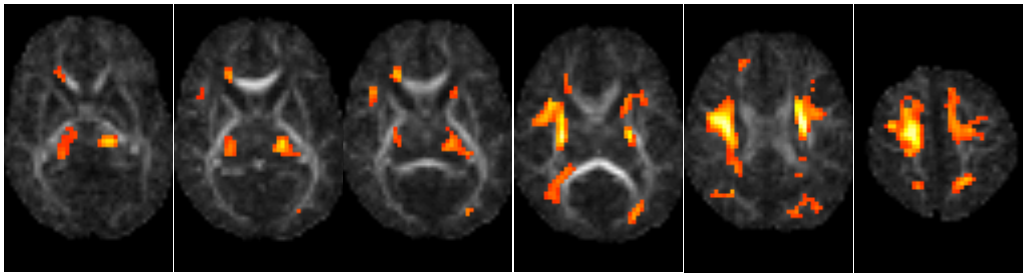

Figure 1: Areas of significant linear increase of FA with age in a population of 28 newborns. Threshold set at $P_{corrected}$<0.05. Color overlay on FA image of one patient used as template.

CONCLUSION

This study demonstrates that, besides regions previously identified using ROI analyses, i.e. motor and somatosensory tracts, optic radiation and corpus callosum (1-4), significant maturational changes also occur in the thalamus, between 34 and 41 weeks gestational age. The latter findings suggest that thalamocortical pathways, which are known to appear between 20-23 weeks gestational age in the fetus (5), may undergo significant maturational changes between 34 and 41 weeks.

Despite motion artifacts inherent to sedation-free imaging in newborns, we could obtain highly significant results by selectively eliminating severely corrupted images, and realigning the remaining datasets.

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