Assessment of structural and functional maturation of the optic radiations in infants using DTI-based fiber-tracking and Event-Related Potentials

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Introduction

Brain white matter myelination is a long process which progresses at different rates depending on location [1]. The optic radiations are known to myelinate during the first postnatal months, as vision is one of the earliest brain function acquired after birth. DTI provides a non invasive *structural* evaluation of the bundles organization and maturation, through quantification of water diffusion parameters [2-4]. On the other hand, Event-Related Potentials (ERPs) have been used to monitor the *functional* maturation of the visual system [5]. The aim of this preliminary study was to evaluate in healthy infants the feasibility to quantitatively assess fiber maturation *along* the optic radiations, as delineated using DTI-based fiber tracking, and to correlate the structural maturation with the functional maturation using visual ERPs.

Material and Methods

Structural maturation: *DTI acquisition*: The study was performed on 8 non-sedated healthy babies (mean age 13.4±2.7 weeks), under a protocol approved by our Institutional Ethical Committee. Acquisition was realized on a 1.5T MRI system (Signa LX, GEMS, USA) with maximum gradient amplitude of 22mT.m^{-1} using a birdcage head coil. 30 interleaved axial slices covering the whole brain were acquired with a diffusion-weighted spin echo single-shot EPI sequence (slice thickness = 2.5mm, FOV = 24cm, matrix = 128x128, b = 0 and 700s.mm^{-2}, TE = 89.6ms, TR = 13.8s). Diffusion gradient pulses were applied in 15 directions, resulting in a total acquisition time of 3min40s. For comparison, adults were also scanned (slice thickness = 3.5mm, 3 averagings). *Data processing*: Geometric distortions due to eddy currents were first corrected referring to the T2 image and images were realigned in the plane of anterior/posterior commissures. The diffusion tensor parameters were estimated in each voxel using Brainvisa software [6]. Maps of apparent diffusion coefficient (ADC), fractional anisotropy (FA) and FA-weighted color-coded directionality (RGB) were generated. Optic radiations (OR) were identified in individual slices and tracked using the FACT algorithm [7], between the lateral geniculate nucleus (LGN) and the occipital pole (FA > 0.1, curvature angle < 60°). *Quantification of maturation*: FA and ADC were quantified along the tracked OR using a curvilinear abscissa interpolated every 0.6mm (s = 0 and 1 respectively for the LGN and the occipital end of the tracked OR). FA and ADC were also averaged over the whole tracts and over 3 segments of the tracts (anterior, middle and posterior). Functional maturation: *ERPs acquisition*: Electrical activity was recorded with a high-density recording system (65 electrodes) in 5 of the babies, looking at attractive visual stimuli (faces) presented every 1.5s. *Data post-processing*: Responses from all stimuli were averaged, and the latency of the maximum of the first visual positive wave (P1) was determined from the occipital electrodes. In order to correct for the different brain shape and bundle size across babies, an index of the visual response speed, called "apparent conduction speed" (ACS), was calculated (inverse of P1 latency normalized to the length of the tracked OR). Anatomical and functional correlation: Diffusion measurements (FA and ADC) and ACS were plotted against age. Statistical correlations were assessed by calculating non-parametric Spearman rank coefficients ($p<0.05$). Besides, the relationship between FA and ACS was assessed.

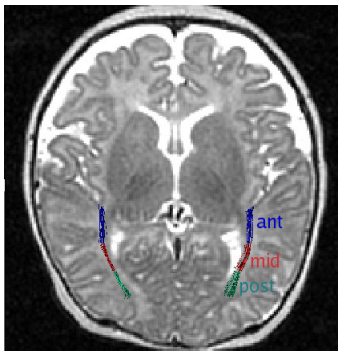

Figure 1: Tracked optic radiations of a 17w old baby, splitted in three segments (anterior, middle and posterior)

Results

OR *structural* maturation: Despite incomplete myelination, the OR could be tracked (Figure 1). FA and ADC averaged over the whole tracts were respectively larger and smaller in adults than babies (0.60 vs 0.37; 0.9 vs 1.28.10^{-3}mm^2.s^{-1}). Whereas FA did not vary much along the tract in adults (range 0.5-0.7, lower values at both extremities), a "humped" pattern with a decreased FA in the tract middle segment was observed for 6 babies (FA range 0.2-0.5, Figure 2, arrow), with some variability in the details of the FA topographical pattern across babies. Significant correlations were found between FA and age for the whole tract and the middle segment (Figure 3). In the other segments, the trend was not significant, probably because of the small number of babies. Mean FA change per week of age was 2.4% of mean FA over babies (range: 2-3%). Visual *functional* maturation: Mean P1 latency and ACS were respectively 142ms and 0.26mm.ms^{-1} over babies (range: 120-160ms; 0.21-0.32mm.ms^{-1}). In this small group of infants (n = 5), neither the P1 latency nor the ACS were significantly correlated with age; however, the correlation was significant in a larger group of 8 infants (data not shown). Moreover, the ACS was significantly correlated to the averaged FA over the OR anterior segment (Figure 4).

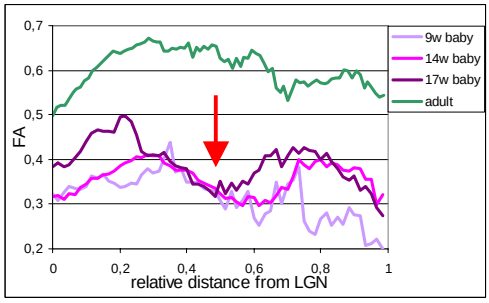

Figure 2: FA as function of curvilinear abscissa along the tracked OR (s=0: LGN, s=1: occipital end) for 3 babies of different age (9, 14 and 17 weeks) and an adult.

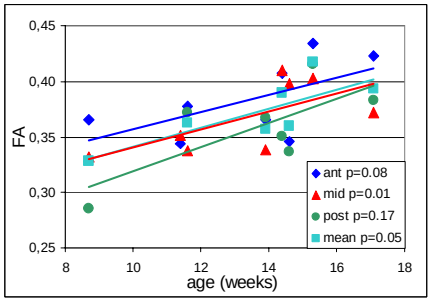

Figure 3: FA linear regression with babies' age in the 3 segments of OR and on average on the whole tract

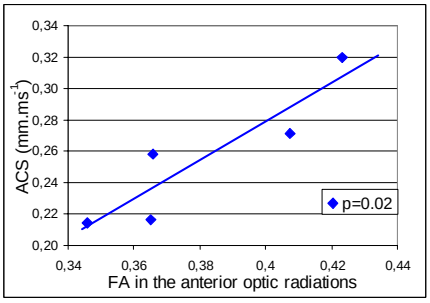

Figure 4: Linear regression of "apparent conduction speed" with averaged FA in the anterior segment of OR

Discussion and Conclusion

We evaluated the structural maturation of the optic radiations in babies using fiber tracking and a quantitative analysis of FA along the tract, from the LGN to the tract occipital end. The "humped" pattern observed in babies could reflect fiber maturation and myelination progressing at both fronts of the tracts, originating respectively from geniculocortical-bound and corticogeniculate-bound fibers [8], although partial volume effects with cortico-spinal fluid in the OR middle segment can not be entirely excluded. Besides, we evaluated the functional maturation of visual response by measuring the P1 latency with ERPs. The "apparent conduction speed" seemed mainly correlated to the FA measured in the OR anterior segment, which would support the hypothesis that myelination proceeds from the center to the periphery in the fibers conducting the information (the geniculocortical ones). This has to be validated in a larger group of infants. These preliminary results suggest that the structural maturation of the optic radiations can be quantitatively assessed along the fibers using DTI, offering a powerful approach to study interactions between myelination and post-natal environment on functional visual maturation [9] when combined with functional ERPs.

References [1] Yakovlev *et al*, in Regional development of the brain in early life, 1967, 3-69. [2] Neil et al NMR in Biomed 2002, 15:543-522. [3] Neil *et al* Radiology 1998, 15:57-66. [4] Huppi *et al* Pediatr Res 1998, 44:584-590. [5] McCulloch *et al* Vision Res 1999, 39:3673-3680. [6] Cointepas *et al* Neuroimage 2003, 19:S810, http://brainvisa.info/. [7] Mori *et al* Ann Neurol 1999, 45:265-269. [8] McCart *et al* Brain Res 1994, 653:351-356. [9] Demerens *et al* PNAS 1996, 93:9887-9892.