Quantification and classification of white matter bundles maturation in healthy babies with DTI and fiber tracking

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Introduction

Brain white matter myelination is a long process which starts before birth and continues during childhood, and progresses at different rates depending on location [1]. The potential of DTI for monitoring non invasively the bundles organization and maturation in newborns and children has been outlined [2-4], since the increase in water diffusion anisotropy with age relies on fibers arrangement and myelination. In a previous report [5], the feasibility of reliable fiber tracking was assessed in healthy babies with incompletely myelinated fibers. In this study, our aims were to evaluate the potential of fiber tracking for quantifying diffusion parameters over fiber bundles, and to propose a non invasive classification of the tracts maturation in infants.

Material and Methods

Data acquisition: The study was performed on 10 non-sedated healthy babies (mean age 13.7±2.5 weeks), under a protocol approved by the Institutional Ethical Committee. Acquisition was realized on a 1.5T MRI system (Signa LX, GEMS, USA) with maximum gradients amplitude of 22mT.m^{-1}, and using a birdcage head coil. A diffusion-weighted spin echo single-shot EPI technique was implemented. 30 interleaved axial slices covering the whole brain were imaged (slice thickness = 2.5mm, FOV = 24cm, matrix = 128x128, b = 0 and 700s.mm^{-2}, TE = 89.6ms, TR = 13.8s). Diffusion gradients were applied in 15 directions without repetitions, leading to a total acquisition time of 3min40s. For comparison, adults were also scanned (slice thickness = 3.5mm, 3 averaging). 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. Individual white matter bundles were identified and tracked using the FACT algorithm [7], with constraints: FA > 0.1, curvature angle < 45°/60°. In order to increase the reliability of bundles tracking, fibers were selected only when crossing specific regions. FA and ADC were quantified on average over sections of the bundles, after fibers were splitted between specific regions. For comparison, the same parameters were also evaluated in regions of interest (ROIs) manually positioned on bundles. Classification of bundles maturation: First, the ratio between mean FA over babies and mean FA over adults was calculated for each bundle, in order to normalize for different bundles geometry and compacity. Differential bundles maturation was assessed by comparison of each ratio to the averaged ratio over bundles. Second, for each bundle, evolution of FA with both babies' age and age corrected to term was assessed; in the case of statistically significant linear regression, the change rate per week of age was normalized by mean FA over babies. The bundles were classified by comparing these normalized change rates.

Results

Bundles identification: Several white matter fascicles were identified in 2D [corpus callosum (1) genu (1a), splenium (1b), body (1c), middle cerebellar peduncles (2), spino-thalamic tract (3), cortico-spinal tract (4) (in the mid-brain (5), the cerebral peduncles (6), the posterior limb of the internal capsule (7), the low (8) and high (9) centrum semiovale), anterior limb of the internal capsule (10), external capsule (11), optic (12) and acoustic (13) radiations, superior (14) and inferior (15) longitudinal fasciculi, uncinate fasciculi (16), cingulum (17)] and tracked in 3D (except bundle 17). Figure 1 presents examples of tracts sections for a 17w old baby. The cortico-spinal tract was constrained to pass through regions 5 to 9 and was splitted in four parts (5-6, 6-7, 7-8, 8-9). Bundles 15 and 16 were splitted in two (15a, 15b: temporal and occipital regions; 16a, 16b: frontal and temporal regions). Bundles 2, 13 and 14 could not be reproducibly splitted over babies so the quantitative analysis was not performed for these bundles. FA quantification: In both babies and adults, analysis over splitted tracts led to lower FA and higher ADC measurements compared to analysis by ROIs, because quantification was performed in a bigger volume of interest. Mean FA over babies and adults were respectively of 0.39 and 0.53 on average over bundles (respective ranges across bundles: 0.28-0.56 and 0.4-0.68). FA ratio between babies and adults was 0.74 on average over bundles (range: 0.68-0.94, Figure 2). The most mature bundles were the corpus callosum, parts of the cortico-spinal tract (4, 6-8) and the external capsule. The less mature bundles were the spino-thalamic tract, the corona radiata, the optic radiations and the inferior longitudinal fasciculus. FA evolution with age: Significant FA correlations with age were found in most bundles (Figure 3). Normalized change rate was 2.1% on average over bundles (range: 1.1-2.8%, Figure 2). Correlations were found to be more significant with age than with corrected age for all bundles except for the corpus callosum body and parts of the cortico-spinal tract (5-7). The corpus callosum body, the spino-thalamic and the cortico-spinal (4-8) tracts, the external capsule, the optic radiations and the inferior longitudinal fasciculus in the occipital region appear to mature the fastest.

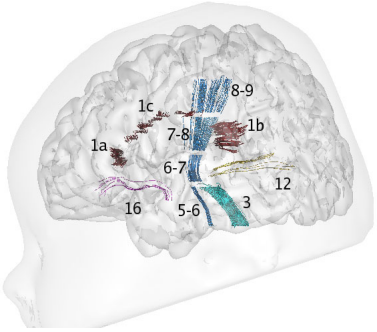

Figure 1: Examples of splitted tracts

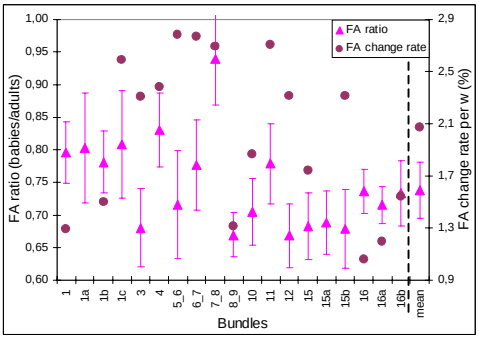

Figure 2: FA ratio between babies and adults (with standard deviations over babies normalized by mean FA over adults) and FA normalized change rate per week of age (in %)

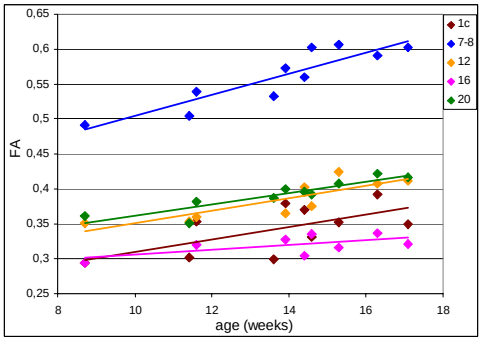

Figure 3: Examples of FA linear regression with babies' age

Discussion and Conclusion

We assessed the potential of fiber tracking for diffusion parameters quantification in white matter bundles and applied this method to compare the maturation of some commissural, projection and association fibers in infants. The results are in good agreement with the known stages of myelination. For example, the cortico-spinal tract, below the low centrum semiovale, which is known to mature early, has a higher FA ratio than other bundles and still presents a rapid change in FA. On the contrary, the corona radiata is not mature yet and FA does not clearly evolve over the considered range of age. Besides, the maturation occurs faster for the occipital region than for the temporal and frontal regions. The proposed approach provides a non invasive partial classification of bundles maturation. The role of post-natal environment on maturation can be investigated through the comparison of age and corrected age. Nevertheless, the respective roles of myelination and of other maturational processes (compaction …) on FA evolution with age are still not widely known; this might explain why the FA ratio in the optic radiations is low whereas this bundle is known to myelinate during the first postnatal months.

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