Tracking healthy babies' white matter fibers despite low anisotropy: a feasibility study

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Introduction

Brain white matter myelination is a long process which starts well before birth and continues during childhood. Post-mortem studies have highlighted that myelination progresses in a caudo-rostral way at different rates depending on location. Although important variations in T1 and T2 during childhood [1] underline the long-lasting myelination process, some of the fiber bundle connection networks are already in place in the fetal and neonatal brains, though not necessarily functional. In this context the potential of DTI which may monitor fiber bundle organization well before myelination appears tremendous [2]. Water diffusion anisotropy has been observed in the white matter of human premature babies [3] and in young animals [4] at a stage where fibers are not or poorly myelinated, pointing out that fiber bundles seem to be early organized. The degree of anisotropy is lower than in adults and increases with myelination. This lower degree of anisotropy might impair fiber tracking algorithms which have been used, so far, only in older children and adults with fully myelinated brains. In this first study, our aim was to assess the feasibility of reliable fiber tracking in healthy babies with incompletely myelinated fibers and thus, low diffusion anisotropy.

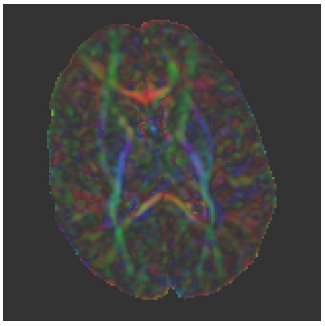

Figure 1: RGB-FA map at the level of the internal capsule. Color gives the direction of first eigenvector: red: L/R, green: A/P, blue: S/I.

Material and Methods

Data acquisition: The study was performed on spontaneously asleep 3 months old healthy babies, 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 = 3mm, FOV = 24cm, matrix = 128x128, b = 0 and 700s.mm^{-2}, TE = 108ms, TR = 9.7s). Diffusion gradients were applied in 11 directions without repetitions, leading to a total acquisition time of 2.5min. Data processing: Geometric distortions due to eddy currents were first corrected referring to the T2 image [5]. The diffusion tensor parameters were then estimated in each voxel using Brainvisa software [6]. Maps of apparent diffusion coefficient (ADC), fractional anisotropy (FA) and FA-weighted color-coded directionality (RGB-FA) were generated. Regions of interest (ROIs) were positioned on individual white matter tracts (meanly 12 voxels were considered) and ADC and FA were evaluated. Fiber tracking was performed using the FACT algorithm [7]. ROIs were positioned on the RGB-FA map and all fibers bundles passing through a ROI were tracked.

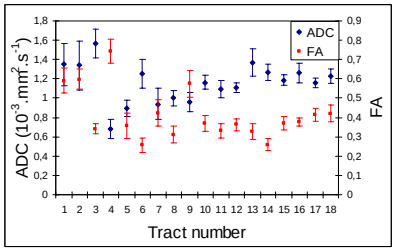

Figure 2: Mean ADC and FA over the tract ROIs defined in the text. Standard deviations were measured over the ROIs.

Results and Discussion

Data obtained from a 53 weeks GA baby are presented here. The T2-w image SNR was 39, higher than in adults due to the longer baby's brain T2 relaxation time. Figure 1 presents the high-quality RGB-FA map obtained at the level of the internal capsule. Several white matter fascicules could be identified: corpus callosum genu (1), splenium (2), body (3), middle (4) and superior (5) cerebellar peduncles, posterior commissure (6), spino-thalamic tracts and medial lemniscus (7), cortico-spinal fibers in the mid-brain (8), posterior (9) and anterior (10) limbs of the internal capsule, external capsule (11), corona radiata (12), optic (13) and acoustic radiations (14), superior (15) and inferior (16) longitudinal fasciculi, cingulum (17), uncinate or occipito-frontal fasciculus (18). Bundle 18 was limited to the frontal region, preventing distinction between the uncinate or the occipito-frontal fasciculus. The myelination of these fibers is known to begin earlier in 1-9, 12-14 than in 10-11 and 15-18. ADC and FA measurements are presented in Figure 2. As expected FA is higher in more mature tracts (1, 2, 4, 9). To reduce CSF partial volume effects at the level of bundle 3, acquiring thiner slices seems necessary. Fiber tracking could be performed for most of the tracts, except 6, 14 and 17 tracts, whose track fiber length was too short. Figures 3 (a, b, c) display 3D tracts obtained for ROIs positioned at the level of bundles a: 1, 2, 5, 13, 8, 9, 12; b: 15; c: 9, 11.

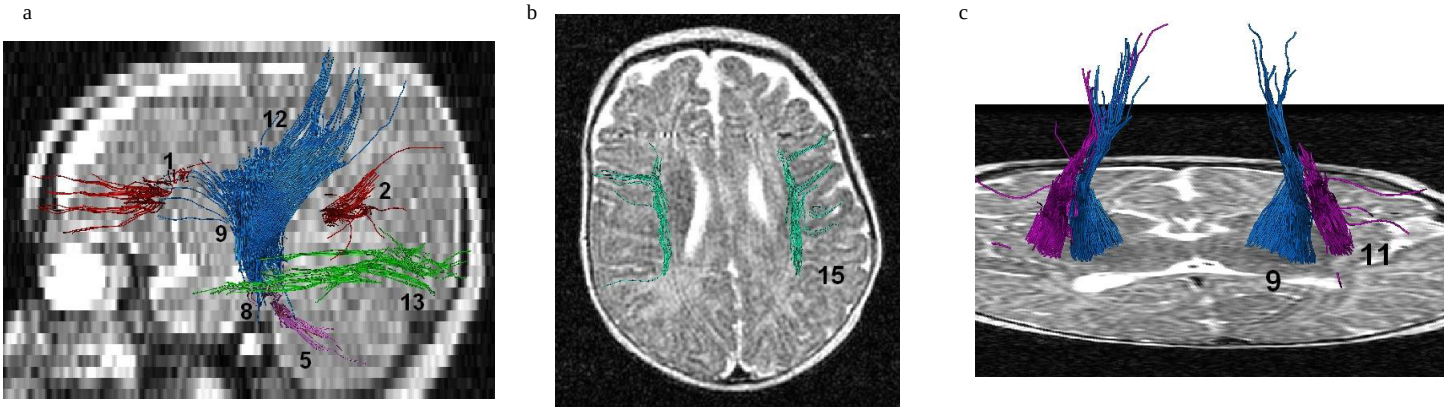

Figure 3: 3D fiber tracts of bundles defined in the text, projected on a sagittal (a) or axial (b, c) view of axial T2 images.

Conclusion

This study demonstrates the feasibility of tracking thin white matter fibers in babies with unachieved myelination and diffusion FA as low as 0.33. A specific acquisition protocol customized to the unmature baby brain was successfully used to accurately map major white matter tracts. ADC and FA measurements were in agreement with the known stages of myelination and the values reported in newborns [2]. Main fiber bundles seem to be already in place around 3 months after birth. DTI appears as a promising tool to detect the early presence of white matter bundles in very young babies, as well as pathological (absent or delayed) white matter development (for instance, the absence of the left anterior limb of the internal capsule in a 2 month old baby whith a perinatal left frontal stroke -data not shown).

References [1] Paus *et al* Brain Res Bull 2001, 54:255-266. [2] Neil *et al* NMR in Biomed 2002, 15:543-522. [3] Huppi *et al* Pediatr Res 1998, 44:584-590. [4] Wimberger *et al* J Comp Assist Tomog 1995, 19:28-33. [5] Mangin *et al* Med Image Anal 2002, 6:191-198. [6] Cointepas *et al* Neuroimage 2003, 19:S810, http://brainvisa.info/. [7] Mori *et al* Ann Neurol 1999, 45:265-269.