White matter maturation of normal human fetal brain-An in vivo diffusion tensor imaging tractography study

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Objective : To demonstrate the ability of magnetic resonance diffusion tensor imaging (DTI) tractography, to assess *in vivo* and *in utero* a crucial stage of human fetal brain development: the white matter (WM) maturation.

Methods: The study was approved by the local committee on ethics in biomedical research. High quality *in utero* DTI images (Figure 1) of 17 normal living human fetuses (mean age 32 +/- 4 weeks of gestation (range, 23-38 weeks) among 61 were selected. DTI was performed on a 1.5T MR scanner (Symphony Siemens, Erlangen, Germany) using a phased array coil (4 anterior elements and 2 to 3 posterior spinal elements) and consisted in 3 series of single-shot SE-EPI sequence (TR 8900ms; TE 105 ms; 50 contiguous slices with 2.2 mm thickness; matrix 128; FOV 256 mm; 12 directions, b values of 1000 s/mm^2). Tractography (Figure 1) was performed using Runge Kutta algorithm (order 4, FA threshold 0.08 adapted to the immaturity of the fetal tracts, Max Angle 70° adapted to the curved geometry of the optic radiations). The average values of the ADC, the FA, the $\lambda_{//}$ and the $\lambda_{\perp}$ along each bundle were extracted and normalized (Z-scores).

Results: Evolution of diffusion characteristics during gestation were different for cortical spinal tract, optic radiations, anterior, middle and posterior part of corpus callosum (Anova $p<0.05$ corrected for multiple comparisons), reflecting the presence of structural heterogeneity between these large WM tracts during gestation. Non-linear curve fittings of normalized longitudinal and radial water diffusivities as a function of age identify 3 different phases of maturation with specific dynamics for each WM bundle type (Fig 2).

Discussion and Conclusion: The 3 phases correspond to distinct cellular events previously reported by immunostaining studies such as i) axonal organization (phase 1 ending at 25-28.5 GW depending of WM bundles) reflected by increased $\lambda_{//}$, a large increase in longitudinal diffusivity concomitant to a slow increase in radial diffusivity causing significant increases in ADC and FA; ii) myelination gliosis (phase 2 ending at 32.5 GW for CST, 34.5 for OR but not finished before birth for genu of CC) characterized by similar and concomitant slow decreases in longitudinal and radial diffusivity, causing no change in FA and decreased ADC and iii) myelination (phase 3) related to slow decrease in longitudinal diffusivity and concomitant fast decrease in radial diffusivity.

Conclusion: DTI tractography provides access to a better understanding of fetal WM maturation and is shown to be a promising tool for prenatal diagnosis of brain development disorders.

Fig 1: in utero DTI tractography

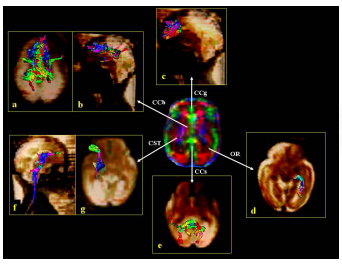

Figure 2: In utero maturation of CST and OR assessed by DTI tractography