Atlas-based analysis of neurodevelopment from infancy to adulthood using Diffusion Tensor Imaging

A. V. Faria[1,2], J. Zhang[1], K. Oishi[1], X. Li[3], H. Jiang[1], K. Akhter[1], K. Sakai[1], L. Hermoye[4], S-K. Lee[5], M. I. Miller[6], P. van Zijl[1,3], and S. Mori[1]

[1]Radiology, Johns Hopkins Medical Institutes, Baltimore, MD, United States, [2]Radiology, State University of Campinas, Campinas, SP, Brazil, [3]Kennedy Krieger Institute, Baltimore, MD, United States, [4]Université Catholique de Louvain, Belgium, [5]Yonsei University, Seoul, Korea, [6]Center for Imaging Studies, Johns Hopkins University, Baltimore, MD, United States

INTRODUCTION: Quantification of normal brain maturation is a crucial step to understand developmental abnormalities in the brain anatomy and functions. There are a large number of previous studies based on T1 and T2 images, in which volumetric changes of the gray and white matter were characterized. In these conventional MRI studies, the white matter (WM) is usually treated as a single compartment. By providing contrasts within the WM, Diffusion Tensor Images (DTI) has proved to be a useful method for monitoring intra-WM changes. For brains at 24 months and older, developmental changes become subtle and accurate brain registration is required to detect small but consistent time-dependent changes. Here we used a nonlinear warping algorithm based on large deformation, diffeomorphic metric mapping (LDDMM) to register DTI images of normal pediatric participants into common coordinates and time-dependent changes were investigated. The recently established white matter atlas was then used to automatically segment the entire white matter into 176 structures. Various anatomical and DTI parameters in each structure were then measured and the correlations with the ages were accessed. This enables us to investigate differences in maturation processes in different regions of the white matter, which has not been extensively studied in the past.

METHODS: 26 children and 9 healthy adult were included in this study. DTI were acquired using a 1.5 T scanner with b=700 s/mm^2. After linear affine transformation, dual-contrast LDDMM was performed to register each subject's data to the JHU atlas using FA and b0 images simultaneously. Using the parcellation map in the atlas, the brain was automatically segmented to 176 regions. In each region, following parameters were measured: size, fractional anisotropy (FA), apparent coefficient diffusion (ADC), parallel diffusivity ($\lambda||$, the major eigenvalue) and perpendicular diffusivity ($\lambda\perp$, the average of the smallest eigenvalues). Relative volume of each region was obtained by dividing the volume of each region by the total brain volume. Age related changes in each region were investigated using linear and polynomial regression. We considered significant p value less than 0.05 after correction for multiple comparisons by setting the false discovery ratio (FDR).

RESULTS and DISCUSSION: Whole brain analysis: We observed linear increase of the whole brain, white matter and CSF volumes with age, and a tendency to decrease cortex volume in agreement with previous studies. Regional analysis: In the Atlas-based analysis, most regions have relationship with age. However the extent of the change varies for relative size, FA and ADC and they have different 'velocities' of changes, represented by the slopes (Fig. 1)

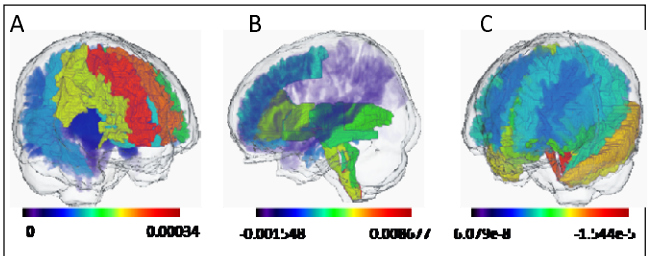

Figure1: 3D representation of regions where relative size (A), FA (B) and ADC (C) were statistically significant related to the age. Color scales represent the slopes of linear regression (red are the biggest and blue, the smallest ones).

The relative size of white matter and subcortical gray matter increased with age while most part of cortical areas decreased (except for the amygdala and the hippocampal cortex), although not significant. Fig. 2 shows the results of the statistical analysis of the regional size changes and time-dependency plots for two representative areas. The change in the cortex is modulated by an inverted U-shape. This type of curve was described before in higher-level association cortical areas, recognized by slow maturation.

Positive relation between FA and age was found in the subcortical WM as well as the thalamus and the anterior part of corona radiata (Fig. 3). Both perpendicular and parallel diffusion decreased in many white matter regions, indicating ongoing myelinization process and/or increasing compactness of axonal bundles. In the brainstem, there were clear increases in the relative size and FA and decrease in perpendicular diffusivity of the corticospinal tract (CST). Significant shortening of the central conduction time during childhood and adolescence has been observed, functionally supporting that myelination of CST fibers in this phase. The decrease of the perpendicular diffusivity, thus, may reflect the extension of the myelination.

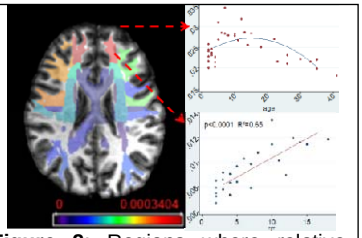

Figure 2: Regions where relative size where significant related to age. In superior frontal gyrus, polynomial curve modulated cortex while linear modulated white matter.

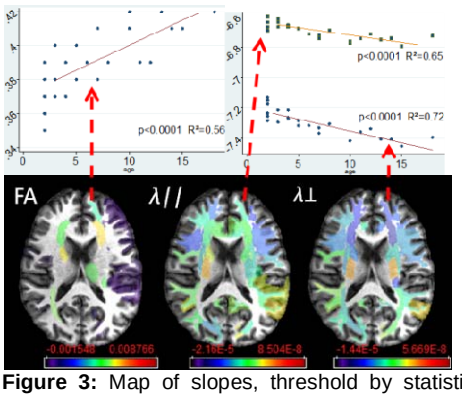

Figure 3: Map of slopes, threshold by statistical significant values, superimpose on axial images at the level of corona radiata and scatter plots of FA and $\lambda\perp$ and λ|| (in log) versus age

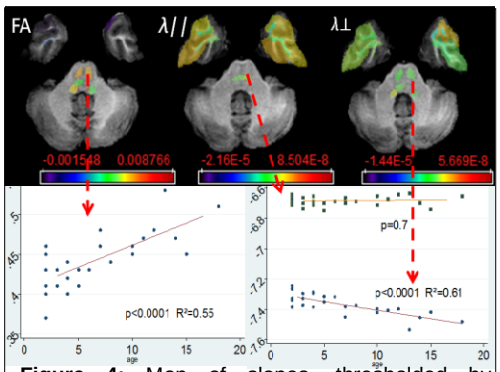

Figure 4: Map of slopes, thresholded by statistical significant values, superimpose on axial images at the level of CST and scatter plots of FA and $\lambda\perp$ and λ|| (in log) versus age.

CONCLUSION: LDDMM and atlas-based analyses of DTI allowed us comprehensive investigation of brain development in 176 pre-segment regions. Each segmented area showed distinctive maturation processes in term of its size, FA, and diffusivity. The quantitative and regional characterization of normal maturation process is the important first step to characterize abnormal brain development. The reported tools and data should provide important information about the normal values and variability among normal subjects, which are essential for experimental designs for future pathological studies.

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