

Development of Multi-Contrast Human Neonatal Brain Atlas

K. Oishi¹, P. Donahue², L. Anderson³, S. Buchthal³, T. Ernst³, A. Faria¹, H. Jiang^{1,4}, X. Li⁴, M. Miller⁵, P. van Zijl^{1,4}, S. Mori^{1,4}, and L. Chang³

¹Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ²Department of Pediatrics, Johns Hopkins University School of Medicine, ³Neuroscience and Magnetic Resonance Research Program, John A. Burns School of Medicine, University, ⁴F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, ⁵Department of Biomedical Engineering, Johns Hopkins University

Introduction Normalization-based image analysis, which has been widely used in adult and children's studies, is one of the most effective methods for image quantification and statistical comparison. However, the application of normalization-based analysis to neonatal brain MRI is scarce. One of the difficulties is the rapid change in T1 and T2 contrasts during early development, as well as the lack of anatomical contrasts, which prohibits accurate cross-subject image registration. Diffusion tensor imaging (DTI) provides rich and stable anatomical contrasts in neonatal brains. Because of its quantitative nature, DTI is an ideal technology with which to evaluate the normal and abnormal neonatal brain anatomy using normalization-based image analysis. In this study, we developed neonatal brain atlases with detailed anatomic information derived from DTI and co-registered anatomical MRI images. Combined with a highly elastic non-linear transformation of large deformation diffeomorphic metric mapping (LDDMM), we attempted to normalize neonatal brain images to the atlas space and three-dimensionally parcellate the images into 122 brain structures. The accuracy level of the normalization was measured by the agreement with manual segmentation. This method was applied to 33 normal subjects, ranging from ages 37 to 53 post-conceptual weeks, to characterize developmental changes. Future applications of this atlas will include investigations of the effect of prenatal events and preterm birth or low birth weights, as well as clinical applications, such as determining imaging biomarkers for various neurological disorders.

Methods (1) Atlas creation: 25 normal-term neonatal MRI scans (38 – 41 post-conceptual weeks at the scan) were used to create the atlases. DWIs were acquired with co-registered MPRAGE and double-echo FSE using a 3T scanner equipped with 8.0 G/cm gradient units. DTIs were calculated using the software DTIStudio¹. AC-PC aligned images were averaged to create the initial template; then, each image was linearly transformed to the initial template and averaged. This procedure was repeated twice to create a linear atlas. A single-subject MRI scan with the shape closest to the linear atlas was selected and linearly transformed it to create a single-subject atlas. This latter atlas was parcellated three-dimensionally to 122 structures for further analyses. (2) Application to the infant DTIs: DTI scan from 33 additional neonates (ages 37 – 53 post-conceptual weeks), acquired at 3T, were non-linearly normalized to the single-subject atlas. Nonlinear transformations between each subject's data and a single-subject atlas were obtained using the software, DiffeoMap² using a fractional anisotropy (FA) map and a mean diffusivity (MD) map, based (dual contrast) LDDMM. By overlaying the parcellation atlas on each normalized image, we measured specific parameters, such as the FA and MD of each structure. The transformation-based segmentation was examined for accuracy by comparing the results with manual segmentation.

Results and Discussion: Fig. 1 demonstrates some images from the linear atlas and the single-subject atlas. The gray/white matter contrasts of T1- and T2- weighted images are opposite to those of adults, and there was poor contrast inside the white matter. Conversely, DTI provides far superior contrasts to reveal the white matter anatomy. The rightmost column shows the parcellation map overlaid on the single-subject atlas. This parcellation map works as a set of pre-defined ROIs for automated brain parcellation after the normalization. Fig. 2 shows the original neonate images and the images normalized to the single-subject atlas, overlaid by the parcellation map that can qualitatively demonstrate the registration accuracy. The reliability of the segmentation, measured by Kappa analysis, was more than 0.8 for most areas, which indicates "almost perfect" agreement based on Landis and Koch criteria. From the normalized images, we could perform both voxel-based and atlas-based regression analyses as a function of age. Fig.3 demonstrates the areas with significant positive correlation between FA and age.

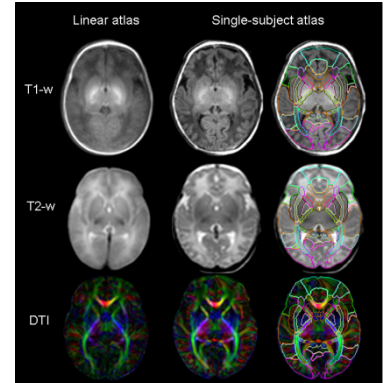


Fig. 1: Atlases created in this study. The upper row shows a T1-weighted atlas, the middle row shows a T2-weighted atlas, and the lower row shows a DTI atlas

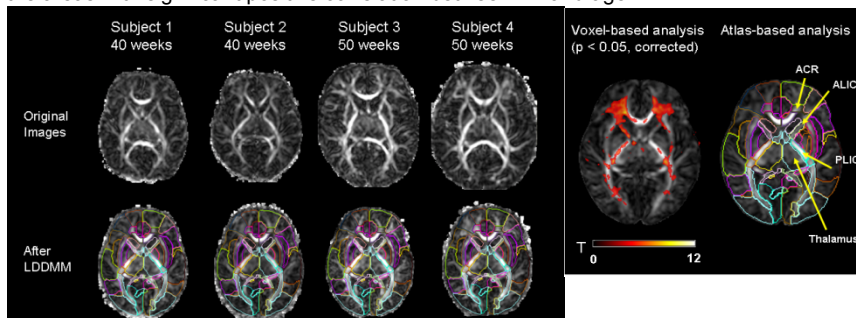


Fig. 2: Examples of the normalization using multi-channel LDDMM. The original neonatal images from 40 and 50 post-conceptual weeks are shown in the upper row.

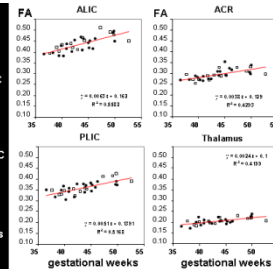


Fig. 3: Voxel-based regression analysis between FA and age (left) and atlas-based analysis (right). Results of the atlas-based FA measurement were shown as scatterplots with linear-fitting. Black dots: girls; white dots: boys

Conclusion: The neonatal MRI atlases developed here are the first step toward the whole-brain quantitative evaluation of neonatal MRI, which is important for visualizing structural specificity, and was lacking in past studies. These basic studies will lead to more clinical investigations, such as determining imaging biomarkers for various neurological disorders.

Bibliography: ¹Jiang, H. and Mori, S.; Johns Hopkins University, www.MriStudio.org; ² Li, X.; Jiang, H. and Mori, S.; Johns Hopkins University, www.MriStudio.org; This study was supported by ADRC, Johns Hopkins University and NIH grants: R21AG033774 / P50AG05146 / RO1AG20012 / P41RR015241/ 1U54NS56883 / 2K24DA16170 and F05NS059230