Quantitative Characterization of Mouse Brain Development Using MR Microimaging and Large Deformation Metric

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Introduction: Brain undergoes considerable morphological changes during developmental process and its characterization has been difficult due to lack of imaging techniques that can non-invasively delineate the internal structures. Our previous work using diffusion tensor microimaging successfully monitored evolution of brain tissue structures, including both gray matter and white matter structures, from early embryonic stages to adult stage. In this study, we studied the possibility of using MRI to quantitatively measure morphological variations and normal brain development. High resolution diffusion tensor (DT) images of embryonic and postnatal mouse brains were acquired. Quantitative morphological measurements based on large deformation metric (LDM) were obtained by landmark matching based on DT images. To characterize the morphological change, 3D growth vector fields were computed.

Methods: C57BL/6J mice at embryonic stages (E12 to E18) and postnatal stages (P0 to adult) were perfused and fixed using 4% paraformaldehyde and were left in fixation solution for at least a month. Experiments were performed on a 9.4T GE Omega spectrometer. Samples were placed in plastic tubes with fomblin inside. Images were acquired using 3D multiple spin echoes with twin navigator echoes. Imaging resolution ranged from 0.08mm to 0.12mm per pixel in all three directions, depending on the size of samples. Diffusion weighted images were acquired with TE of 37ms, TR of 900ms, and a b value of 1200 s/mm^2. High-resolution T_2-weighted images (0.04~0.06mm per pixel) were also acquired. Images from different samples were aligned using rigid landmark matching algorithm. Deformation maps between postnatal mouse brains were computed based on 270 landmarks were placed in forebrain regions. Morphological variations were computed from variations of deformation maps. Three dimensional (3D) growth vector fields were obtained for a series of postnatal mouse brains from P7 to P30. For mouse brains at embryonic stages, deformation maps were computed based on 20 landmarks.

Results and Discussion: Figure 1 shows normal mouse brain morphological variations measured at P7, P30 and P80. DT and T_2-weighted images were acquired from four mouse brain samples at each stage. Coronal DT images of three individual mouse brains were shown in columns A, B and C, with several structures labeled in images in column A. Similarities among mouse brains at the same stage and morphological changes due to development can be appreciated. Quantitative measurements of morphological variations of normal mouse brains were shown in column D, which shows the magnitude of local variations at each stage, with high intensity areas correspond to regions with large morphological variations. Boundaries of various tissue compartments were overlaid on these images, and the results showed that cortical regions often experienced higher degree of variations. Column E showed principle directions of variations, as red color represents variations along anterior-posterior direction, green represents variations along lateral-medial direction, and blue for variations along dorsal-ventral direction. These results provided quantitative measurements of normal variations and may form the basis for characterizing abnormal morphology.

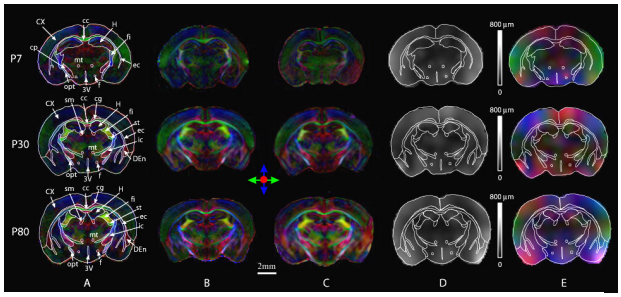

Fig. 1: Morphological variations of normal mouse brains.

Figure 2 shows vector visualization of growth vector fields during postnatal development obtained by landmark matching. Growth vector fields were overlaid on three orthogonal cross-sections of diffusion weighted images at P7 (A), P10 (B) and P20 (C). Vector's color reflects the rate of growth. These results suggested that the growth rates varied in different brain compartments. Cortical regions often had higher growth rate then thalamic regions. Growth vector fields in the cortical regions were shown in D (P7), E (P10), and F (P20). At P7, anterior and posterior regions of cortex showed the rapid growth. At P10, posterior region of cortex continued its rapid growth while anterior cortical regions showed slow growth. At P20, growth rates in both regions were slowed to approximately 0.2 mm/week.

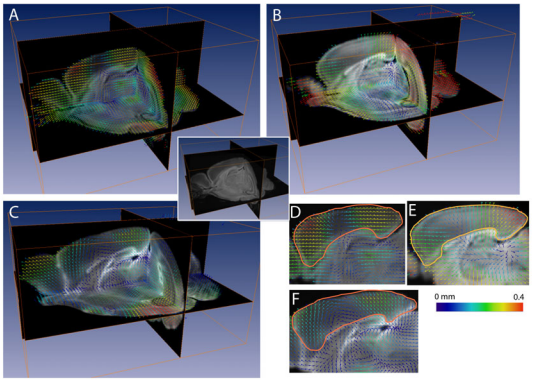

Fig. 2: 3D growth vector fields in normal mouse brains.

Conclusion: MR microimaging provided necessary contrast and resolution for global characterization of tissue morphological changes during mouse brain development. It revealed complex patterns of mouse brain development. With LDM, quantitative measurement of brain development is achievable.

References:

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