Measurement of Brain Development in the First Two Years of Life

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Introduction: Major brain development occurs in the early years. With rapid development of MR imaging and processing techniques, the quantitative volumetric analysis of human brain in early ages becomes possible. For achieving precise longitudinal measurement of global and local brain development, it requires not only the appropriate design of longitudinal data acquisition protocol, but also the suitable segmentation and registration methods for extracting brain tissues and further matching brain structures across different times. In this study, MR images were collected three times within the first two years of life for each subject, and a set of advanced tissue segmentation and longitudinal image registration algorithms were integrated for studying structure changes in the developing brains.

Methods: A total of 28 subjects (with 18 females and 10 males) participated in this study. Each subject has 3 time-point MR brain images scanned at the gestational age of 41±1, 95±3, and 144±7 weeks, referred to as postnatal age of several weeks, one year and two years, respectively. For each subject, T1 and T2 MR brain images were collected using a 3T Siemens scanner. All images were first skull stripped before performing tissue segmentation. The segmentation of brain tissues from the MR images of one year and two years can be completed by using a conventional tissue segmentation technique developed for adult brain images, such as fuzzy segmentation algorithms [1]. However, for neonatal brain images of several weeks, the tissue contrast is generally very low and intensity inhomogeneity is a serious problem, which make all current tissue segmentation methods (or even the population-atlas based segmentation methods) fail. To overcome this problem, we developed a subject-specific atlas for segmenting brain tissues in the neonatal images by taking the advantage of our longitudinal study [2]. In particular, we warp the tissue probability maps generated from one- or two-year-old image to the neonatal image space, and then use these probability maps to guide the tissue segmentation for the neonatal image. Moreover, the tissue segmentation result from neonatal image is further used to refine the registration between the neonatal image and one- or two-year-old image, for better bringing the one- or two-year-old tissue probability maps to the neonatal image space and thus achieving better tissue segmentation. These two steps of image warping and atlas-based tissue segmentation are repeated until convergence. After completing tissue segmentations on all three time-point images of each subject, we used a 4-dimensional nonlinear registration algorithm [3] to consistently register all three time-point images within the same framework, and obtain the deformation fields between any two time-point images. From these estimated deformation fields, tissue density maps (of GM, WM, and CSF) can be calculated for each voxel or brain region, to represent the local/global volume changes across different time points.

Results: Based on the tissue density maps, the overall global and local volume changes from all 28 subjects can be estimated. As shown in Fig. 1a, the growth ratio of the cerebellum is 291% in the first year, which is much larger than that of cerebrum (103%). The growth ratio of the cerebellum drops to 17% in the second year, and becomes similar to that of cerebrum (15%). The percentage of cerebellum volume relative to the whole brain volume is small (6.1%) at several weeks, and it reaches the adult level in the first year (11.1%), as shown in Fig. 1b. A similar trend can be observed for the GM volume. The GM volume grows fast in the first year (137%), and then it slows down (10%) in the second year. In contrast, the growth ratio of WM is relatively stable, with 53% growth in the first year and 31% in the second year. Accordingly, the percentage of total WM volume in the whole brain drops from 33% at several weeks to 24% at one year old, and then goes back to 27% (Fig. 1d). On the other hand, since our tissue density maps captures voxel-wise volume changes between any two different times, we can also measure the volume changes in the cortical regions, as shown in Fig. 2. On average, the brain cortex inflates at a mean growth ratio of 112% from several weeks to one year; in particular, the temporal lobe and parietal lobe have higher growth rates than other lobes. From one year to two years, the development of brain cortex slows down, especially in the temporal lobe, while the parietal lobe and frontal lobe have relatively higher growth rates than other lobes (Fig. 2).
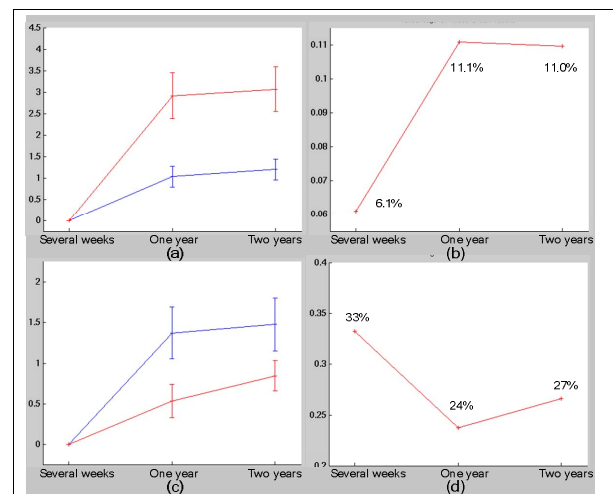

Fig. 1. Global brain development. (a) Growth rates of cerebrum (blue) and cerebellum (red). (b) Percentage of cerebellum volume relative to the whole brain volume. (c) Growth rates of GM (blue) and WM (red). (d) Percentage of WM volume relative to the whole brain.

Discussion and Conclusion: As reported in animal experiments and human studies, brain growth is heterochronous [4]. Different brain regions reach maximal development rates at different time, which are then followed by relatively steep declines towards adult level. In this study, cerebellum, which plays an important role in the integration of sensory perception and motor control, is found to be largely developed in the first year of life. The temporal lobe grows fast in first year and then slows down in the second year. However, the parietal lobe maintains a relatively higher growth rate in the first two years. Only a small part of prefrontal cortex has high growth rate in the first year and a larger part of frontal lobe grows faster in the second year, which is in harmony with the fact that synapse numbers are known to peak until 4-5 years of age [5]. In summary, brain growth is investigated for the first two years of life in this study, and both global and local volume growth are quantitatively measured. The results indicate that cerebellum reaches adult level in the first year, and that different lobes manifest heterochronous growth patterns.
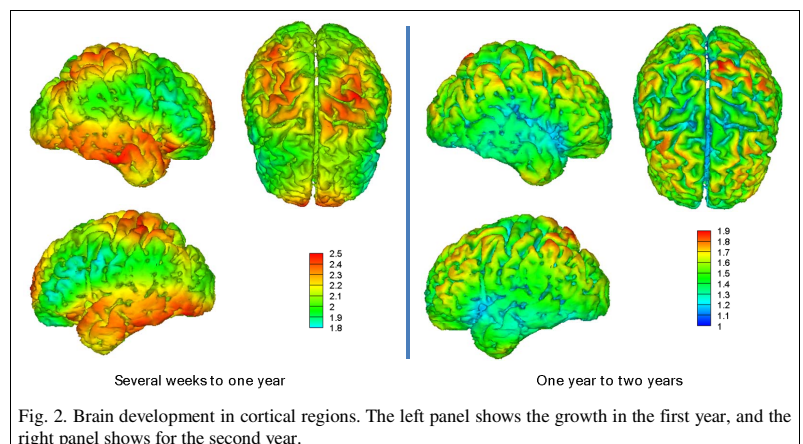

Fig. 2. Brain development in cortical regions. The left panel shows the growth in the first year, and the right panel shows for the second year.

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