

Longitudinal Regional Brain Development in Infants from Four to Nine Months of Age

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Introduction

We report normal developmental changes in regional brain tissue volumes in children from four to nine months of age. This is a longitudinal study where the growth of each child is individually studied. This data will be useful in mapping the trajectory of normal brain development during the child's first year, which is usually accompanied by rapid growth.

Method

Sixty subjects (33 males and 27 females) in the age range of 3-5 months were imaged with a MPAGE sequence on a 3T Siemens scanner. IRB permission was obtained from the parents and no sedation was used. Out of these sixty subjects 14 were also scanned when they were in the range 8 – 10 months. This is a longitudinal study and our plan is to increase the pool of 3-5 months to 75 and follow at least 50 of them to 4 years of age.

The data processing consisted of a) trimming the brain images below the neck and applying BET (FSL) for extracting the brain; b) Applying FAST (FSL) for segmenting the images into CSF, gray matter (GM) and white matter (WM), c) Spatially normalizing the extracted brain image to a 9 month infant template [1] with FLIRT (FSL) and storing the transformation T , d) Segmenting the 9 month template into 8 broad regions which have been separated into left and right to give 16 regions [2], f) Applying the inverse of the transformation T (found in step c) to the ROI atlas so that it is mapped back to the acquisition space f) In each region calculate the volumes CSF, GM, and WM based on the FAST segmentation (Step b) above.

Figure 1 explains the method. Fig. 1A is the template and Fig. 1B shows the 8 regions. These are 1) Dorsolateral prefrontal (DLPF), 2) Orbitofrontal cortex (OF), 3) Premotor (PM), 4) Subgenual (SG), 5) Sensorimotor (SM), 6) Parieto-occipital (PO), and 7) Inferior occipital (IO). Fig. 1C is a 4 month infant and the same infant at 9 months is shown in Fig. 1E. The corresponding atlases after inverse mapping are shown in Figures 1D and 1F respectively.

The longitudinal data was analyzed with a one parameter fit ($x(9m) = x(4m) (1 + \alpha)$) for each subject to calculate the mean growth rate. If MRI data is only available at two time points then it is just a one parameter fit, if on the other hand multiple time points are available (because the scan had to be repeated to complete a partial scan) then a least squares fit was done.

Results

The mean volumes for females were smaller than those of males but the difference was not significant at $p = 0.05$. Males and females are analyzed together. Treating the two groups of children at 4 months and 9 months as two separate groups, the mean growth in total brain volume was 20%, for CSF was 13%, for gray matter 34%, and for white matter was 7%, with the growth being significant at $p = 0.05$. The corresponding boxplots are shown in Figure 2. We had 14 infants who were imaged both at 4m and at 9m. The mean growth rate for all the eight regions was calculated from the growth rate of each child. The growth rates are not the same across the different regions. The following table gives the regions with the minimum and the maximum growth rate. The gray matter had high growth rates for all regions with the highest growth for the gray matter being in the subgenual region (SG), and the highest growth for the white matter in the DLPF region.

Volumes	Total	CSF	GM	WM
Minimum rate (region)	20% (SG)	-1.5% (SG)	28% (PM)	0.5% (SG)
Maximum rate (region)	26% (IO)	23% (IO)	69% (SG)	29% (DLPF)

The minimum rates for CSF and WM in the subgenual (SG) region are not significantly different from zero.

Conclusions

The data allows us to study the normal trajectory of brain development. The average growth in brain volume was 20% with the gray matter having the fastest growth of 34%. In the paired analysis for the longitudinal analysis the gray matter had the fastest growth in the subgenual regions (69%), and the white matter had the fastest growth in the DLPF region (29%).

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2. Limperopoulos, C., et al., *Cerebellar injury in the premature infant is associated with impaired growth of specific cerebral regions*. Pediatr Res, 2010. **68**(2): p. 145-50.

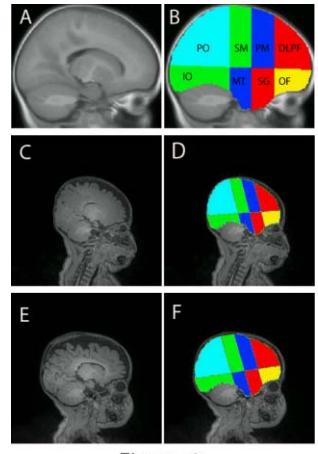


Figure 1

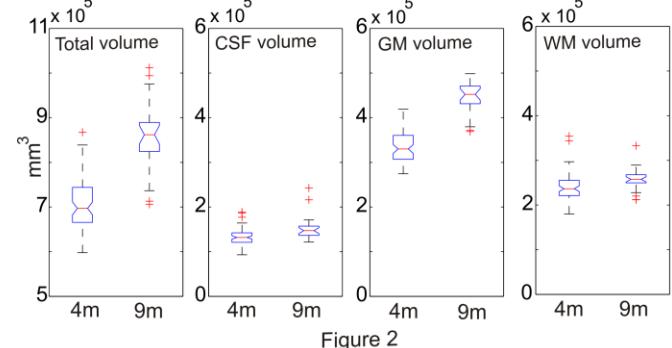


Figure 2