Influence of prematurity on local cortical development

Laura Gui[1], François Lazeyras[2], Lana Vasung[1], Anita Truttmann[3], Cristina Borradori-Tolsa[1], and Petra Hüppi[1]
[1]Pediatrics, Children's Hospital, Geneva, Geneva, Switzerland, [2]Radiology, Geneva University Hospitals, Geneva, Geneva, Switzerland, [3]Pediatrics, Children's Hospital, Lausanne, Vaud, Switzerland

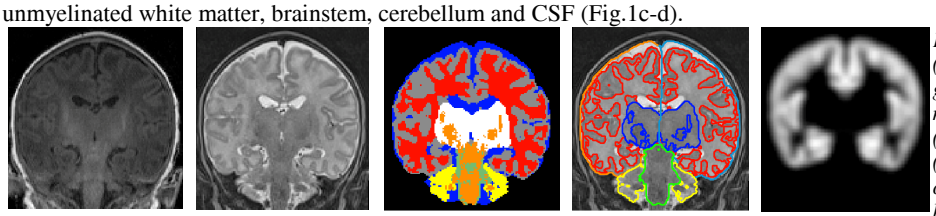
Introduction

Premature birth increases infants' risk for adverse neurodevelopmental outcome[1]. The goal of this study is to investigate the effect of prematurity on local cortical structure via morphometric analysis, capitalizing on the availability of good quality MR scans of the newborn brain and on the recent development of automated tools for neonatal brain image segmentation[2]. Such analyzes have the potential of identifying structural markers of atypical neurodevelopment, allowing for early detection of infants at risk, and the development of adequate intervention strategies.

Material and Methods

MR acquisition: Brain MR images of 50 preterm infants (GA 27.6±1wks) and 11 term-born infants (GA 40.4±1.1wks) were acquired at term-equivalent age (GA 40.5±1.5wks) on a Siemens Trio 3T. For each infant, T1- and T2-weighted images covering the whole head were obtained using the MPRAGE protocol (3D), TE = 2.5 ms, TI = 1100 ms, TR = 2200 ms for the T1 image, and the turbo spin echo protocol (2D coronal slices), TE = 150 ms, TR = 4600 ms for the T2 image, with resolution 0.8x0.8x1.2mm^3 for both scans (Fig.1a-b).

Data post-processing: T1 and T2 images of each infant were segmented with a novel atlas-free automatic method based on morphological constraints[2]. The following tissues and structures were segmented: the two hemispheres, cortical & subcortical gray matter, myelinated & unmyelinated white matter, brainstem, cerebellum and CSF (Fig.1c-d).



(a) (b) (c) (d) (e)

Figure 1. (a,b) T1 and T2 images of the newborn brain; (c) segmentation labels (gray/white – cortical/subcortical gray matter, orange/red – myelinated/unmyelinated white matter, yellow – cerebellum, green – brainstem (unmyelinated), blue – CSF); (d) segmentation contours (red/blue – cortical/subcortical gray matter, yellow – cerebellum, green – brainstem, orange and light blue – the hemispheres); (e) average of the smoothed coregistered gray matter masks of our cohort (coronal).

Morphometry analysis: T2 images of each infant were registered to a T2 template of the neonatal brain, obtained by averaging 20 coregistered T2 brain images of infants scanned at term-equivalent age, with the same protocols described above. Image registration was performed by affine registration, followed by nonlinear registration using the SPM8 software[3]. The registration transformation of each T2 image was also applied to its corresponding cortical mask resulted from the segmentation. This was followed by multiplication of the aligned mask with the inverse of the Jacobian determinants of the deformation field (to preserve the amount of cortical tissue from the original image) and smoothing with a Gaussian kernel of 4x4x4mm^3 (FWHM). A visual confirmation of the segmentation and registration quality is offered by the average of smoothed coregistered gray matter masks of our cohort (Fig.1e). Next, we performed voxel-based morphometry (VBM) analysis on the resulted images, using SPM8. We used a multiple regression model for each voxel, with gestational age (GA) at birth and intracranial volume as covariates. Significance level was set to a P-value of 0.05 after family-wise error (FWE) correction.

Results

Our morphometry analysis revealed a significant positive dependence on GA at birth (P<0.05 FWE corrected) of two main cortical regions: one in the gyrus rectus (bilaterally) and one in the left calcarine fissure (Fig. 2).

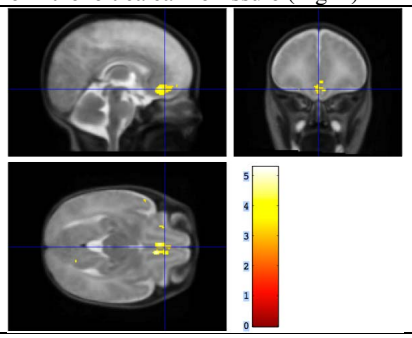
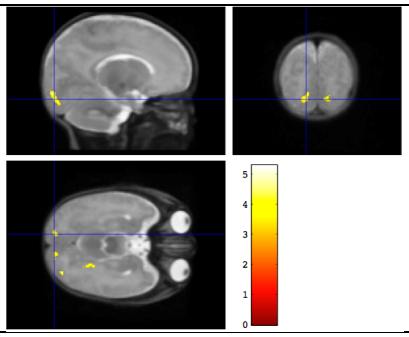
Regions with a significant positive dependence on GA at birth, superposed on the neonatal T2 template.		
Region localization	Gyrus rectus (bilaterally)	Left calcarine fissure
P-value (FWE corrected)	0.041	0.035
Number of voxels in cluster	465	227

Figure 2. Cortical regions showing a significant positive dependence on GA at birth.

Conclusion

We used a novel automatic method to segment the cortical gray matter from MR images of a cohort of preterm and term-born neonates examined at term-equivalent age. Then we performed a morphometric analysis of the cortex, which reflected a deficit of cortical density for neonates of lower GA at birth in the gyrus rectus (bilaterally) and in the left calcarine fissure. The gyrus rectus is a primary olfactory area, and the calcarine fissure is a primary visual area, thus our results suggest an altered development of these areas associated with prematurity. These results concord with the findings of M. Groppo et al.[4], which indicate a significant correlation between GA at birth and impaired development in the optic radiation (measured as reduced fractional anisotropy by Diffusion Tensor Imaging).

References 1. B. Larroque et al., *Neurodevelopmental disabilities and special care of 5-year-old children born before 33 weeks of gestation (the EPIPAGE study): a longitudinal cohort study*. Lancet 2008. **2.** L. Gui et al., *Morphology-driven automatic segmentation of MR images of the neonatal brain*, Medical Image Analysis 2012. **3.** SPM8, 2009. http://www.fil.ion.ucl.ac.uk/spm/. **4.** M. Groppo et al., *Development of the optic radiations and visual function after premature birth*, Cortex 2012.