Detection and mapping of delays in early cortical folding in fetuses with ventriculomegaly from in utero MRI

P. A. Habas[1], J. A. Scott[1], V. Rajagopalan[1], K. Kim[1], A. J. Barkovich[1], O. A. Glenn[1], and C. Studholme[1]
[1]University of California San Francisco, San Francisco, CA, United States

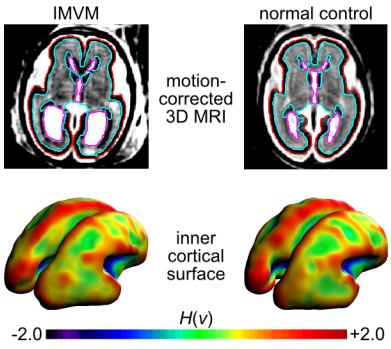
INTRODUCTION

During normal in utero brain development, early cortical folding occurs according to a very specific spatio-temporal schedule. The timing of the appearance of the primary and secondary sulci is so precise that they are used as reliable landmarks in estimation of gestational age. The pattern of cortical convolutions is also a good phenotypic marker of overall brain development and an indicator of functional maturity [1]. Magnetic resonance (MR) imaging of the human fetus has recently become an important tool for clinical assessment of brain growth in utero, including the analysis of early cortical folding. During visual evaluation of 2D MR slices, fetal neuroradiologists from our institution observed that the parieto-occipital sulcus is more shallow in fetuses with isolated mild ventriculomegaly (IMVM) compared with normal controls, indicating abnormal sulcation of this region in IMVM subjects [2]. In this study, we present an application of a dedicated image analysis framework [3] for spatially unconstrained detection and mapping of delays in early cortical folding in fetuses with IMVM.

METHODS

Clinical MR imaging was performed without sedation on a 1.5T scanner for 16 fetuses with IMVM at 22.00-25.43 gestational weeks and 22 age-matched fetuses with normal brain development (normal controls, NC). For each subject, multiple stacks of single-shot fast spin-echo (SSFSE) T2w slice images (TR = 3000-9000ms, TE = 91ms, in plane pixel size 0.5x0.5mm, slice thickness ~3mm, no gap between slices) were obtained in the approximately axial, sagittal and coronal planes with respect to the fetal brain. All stacks were acquired in an interleaved manner to reduce saturation of spins in adjacent slices. To account for spontaneous between slice fetal motion during scanning, the MR slice images of each subject were registered using the slice intersection motion correction (SIMC) technique [4] and reconstructed into high-resolution 3D volumes with isotropic voxel size of 0.5mm (Fig. 1). The reconstructed MR volumes were automatically segmented into individual tissues using an atlas-based approach [5] with age-specific tissue probability maps generated from a spatio-temporal atlas of the fetal brain [6]. The resulting maps of developing white matter were spatially normalized using linear registration and tessellated into triangular meshes to reconstruct the inner cortical surface of the fetal brain. To quantify local surface geometry, mean curvature (H) was calculated at each mesh vertex. For temporal modeling of early cortical folding, mean curvature measurements from individual subject surfaces were mapped onto a population-average surface obtained via group-wise registration of tissue maps. Age-related changes in local surface curvature at each vertex v were modeled as $H(v,t) = H_n(v,t) + H_d(v) = b_0(v) + b_1(v)t + b_2(v)t^2 + a_0(v)$ with coefficients found through joint least squares fitting to mean curvature measurements $H(v,t)$ mapped from normal controls and IMVM subjects with gestational ages t. The quadratic term $H_n(v,t) = b_0(v) + b_1(v)t + b_2(v)t^2$ represented the temporal pattern of normal cortical folding at vertex v whereas the constant delay term $H_d(v) = a_0(v)$ captured the vertex-specific difference in local surface curvature of IMVM subjects with respect to normal controls. The statistical significance of the folding delay term $H_d(v)$ at each vertex v was evaluated using permutation testing.

Figure 1



RESULTS

Figure 1 shows multiple views of the population-average inner cortical surface with values of the folding delay term $H_d(v)$ estimated at each vertex v. Cool colors indicate regions of the brain surface with lesser concavity (delayed sulcation) in IMVM subjects with respect to normal controls; warm colors indicate regions with lesser convexity (delayed gyrification) in IMVM subjects with respect to normal controls.

Figure 2

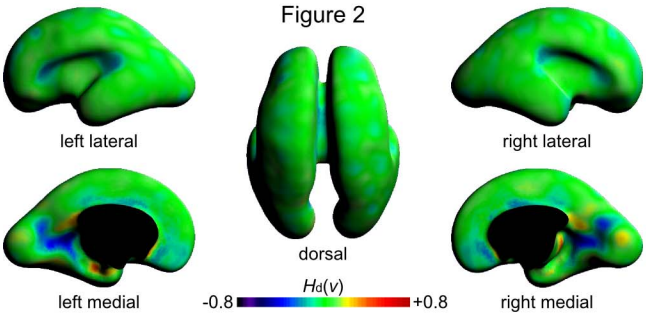


Figure 3

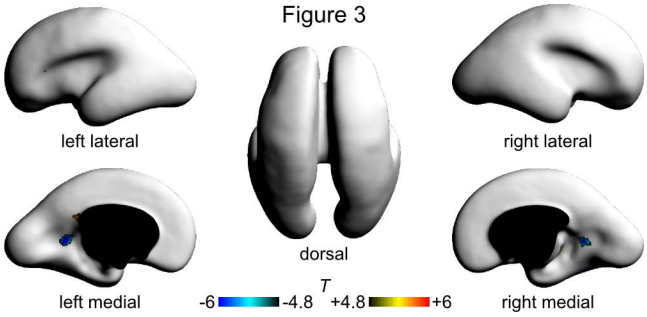


Figure 2 shows the T-statistic map of the folding delay term $H_d(v)$ thresholded at $p = 0.05$ (corrected). Significant delays in early cortical folding in fetuses with IMVM were detected bilaterally in the region of the parieto-occipital sulcus, confirming previous qualitative findings of the fetal neuroradiologists. Delays in early cortical folding at other locations, although visible in Fig. 1, were not significant indicating that the differences between the IMVM group and normal controls were not larger than the variability present among subjects with normal brain development.

CONCLUSIONS

Local alterations in early cortical folding occur in fetuses with IMVM compared with subjects with normal brain development. Additional analysis with older fetuses is needed to determine whether these differences in sulcation are transient or persist into later gestation. Further studies on a larger population will analyze the correlation between delays in cortical folding detected from antenatal MRI and postnatal neurodevelopmental outcomes.

REFERENCES

[1] Barkovich et al. Radiology (1988) [2] Habas et al. OHBM (2009) [3] Habas et al. SPIE Medical Imaging: Image Processing (2011) [4] Kim et al. IEEE Trans Med Imaging (2010) [5] Habas et al. Hum Brain Mapp. (2010) [6] Habas et al. NeuroImage (2010)