Cortical Folding Analysis for Normal Fetuses

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Introduction

Significant cortical folding is one of the most noticeable characteristics of human brains. The folding process starts at the end of the second trimester of pregnancy and is regarded as one important component of neurodevelopment. In this work, we have applied 8 existing cortical folding measures to the MRIs of 41 normal fetuses of varied gestational ages. Various folding measures have been proposed in the literature and applied to children or adults, but they have not been evaluated for fetuses *in vivo*. Reliable MRI measures of normal cortical folding in its initial stage of brain development will aide in the detection of altered brain development in fetal pathological states such as congenital heart defects [3] and diaphragmatic hernias. Fetal neural images, however, bring more challenges to the cortical folding analysis, such as motion corruption, difficult tissue segmentation and low image resolution. We address these issues by a processing pipeline and obtain some preliminary results.

Data description

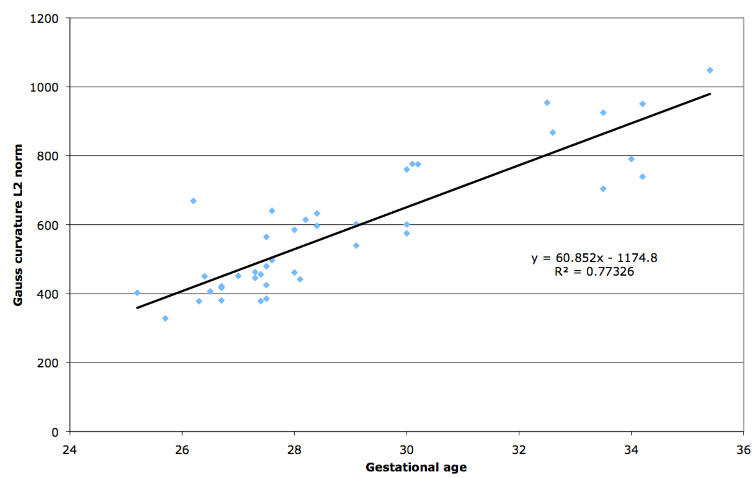
We collected T2-weighted magnetic resonance images on 49 pregnant subjects [3]. 8 subjects were excluded from analysis due to their flawed brain masks. The estimated gestational ages of the fetuses range from 25.2 to 35.4 weeks. All the fetuses, 23 males and 18 females, are healthy. MRI scans were performed using a 1.5 Tesla scanner (Achiva, Philips Medical System, Netherlands) and a 5-channel phased array cardiac coil. Multiplanar single shot turbo spin echo imaging (SSTSE, TE 120 ms; TR 12500 ms; number of signal averages 0.625; field of view 330 mm; slice thickness 2mm with no interslice gap; acquisition matrix 256 X 204; acquisition time: 30-60 seconds) was performed. For each subject, brain masks were generated by investigators who did not involve in the data analysis.

Proposed method

The fetal images were processed in the following pipeline: (1) The images were de-noised and intensity inhomogeneity was corrected. (2) 3D fetal images were corrupted by spontaneous fetal motion so there was intensity discontinuity between adjacent slices although each slice was usually free from motion effect. We performed slice-to-slice rigid registration based on mutual information to alleviate the misalignment. (3) Intracranial space was extracted by manual cerebral masks. We performed fuzzy tissue segmentation to separate white matter and gray matter from cerebrospinal fluid (CSF). The interface of gray matter and CSF was regarded as the cortical surface. (4) A level set was fitted to the cortical surface (up-sampled beforehand to eliminate cortical self-intersections) and 8 folding measures were computed on the surface. Those measures are curvedness (C), shape index (S), Gaussian curvature L^2 norm (GC), mean curvature L^2 norm (MC), extrinsic curvature index (EC), intrinsic curvature index (IC), isoperimetric index (IP) and sulcal depth sum (SD). The definitions of them can be found in [1], [2] and the reference thereof.

Experimental results

We correlated all the measures with the gestational age (GA) in order to inspect which measures were well correlated with the development of fetal brain. We also performed linear regression and calculated the squared cross correlation (R^2) to indicate the linearity. The larger R^2 is, the more linear the correlation is. The table below lists the squared cross correlations between each measure and the gestational age. Besides, the chart on the right shows one example of the plot of one measure, GC, over GA and the regression line.



Measures	C	S	GC	MC	EC	IC	IP	SD
R^2	.63	.06	.77	.64	.27	.79	.05	.42

Discussion and conclusion

We find that the correlations between the 8 folding measures and gestational age vary significantly. Half the measures (C, GC, MC and IC) have relatively good correlations. 2 measures (EC and SD) have low correlations and the other 2 (S and IP) almost do not correlate to GA. In theory, all these measures should be positively related to the time since the folding of fetal brains during this stage is developing significantly. In practice, the imperfection in the motion correction, under-sampling of the fetal brain due to motion and inaccuracy in the cortex extraction may cause some measures to drift on some subjects. Gaussian curvature and intrinsic curvature index tend to be both more sensitive to noise in curvature calculation than mean curvature and curvedness because the former two measures are the product of principal curvatures while the latter two get values close to the mean of principal curvature.

Generally speaking, Gaussian curvature and intrinsic curvature are more consistently correlated with gestational age even though inter-subject variance exists in fetal cortexes. This indicates that the two folding measures may be helpful in characterization of normal cortical development and in diagnosis of abnormal brain growth in fetuses.

Reference

[1] S. Awate, P. Yushkevich, Z. Song, D. Licht, J. Gee, “Multivariate High-Dimensional Cortical Folding Analysis, Combining Complexity and Shape, in Neonates with Congenital Heart Disease”, Information Processing in Medical Imaging (IPMI) 2009, pp 552-563, Springer LNCS 5636

[2] P. Batchelor, A. Castellano-Smith, D. Hill, D. Hawkes, T. Cox, A. Dean, “Measures of folding applied to the development of the human fetal brain”. IEEE Transactions on Medical Imaging 21(8), 953–965 (2002)

[3] C. Limperopoulos, *et al.* “Impaired third trimester brain growth and metabolism in the fetus with congenital heart disease detected by quantitative magnetic resonance imaging”, Circulation, in press.