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Simultaneous and consistent labeling of longitudinal dynamic developing cortical surfaces in infants

Gang Li [a], Li Wang [a], Feng Shi [a], Weili Lin [a], Dinggang Shen [a,b,*]

[a] Department of Radiology and BRIC, University of North Carolina at Chapel Hill, NC, USA
[b] Department of Brain and Cognitive Engineering, Korea University, Seoul, Republic of Korea

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ABSTRACT

The human cerebral cortex develops extremely dynamically in the first 2 years of life. Accurate and consistent parcellation of longitudinal dynamic cortical surfaces during this critical stage is essential to understand the early development of cortical structure and function in both normal and high-risk infant brains. However, directly applying the existing methods developed for the cross-sectional studies often generates longitudinally-inconsistent results, thus leading to inaccurate measurements of the cortex development. In this paper, we propose a new method for accurate, consistent, and simultaneous labeling of longitudinal cortical surfaces in the serial infant brain MR images. The proposed method is explicitly formulated as a minimization problem with an energy function that includes a data fitting term, a spatial smoothness term, and a temporal consistency term. Specifically, inspired by multi-atlas based label fusion, the data fitting term is designed to integrate the contributions from multi-atlas surfaces adaptively, according to the similarities of their local cortical folding with that of the subject cortical surface. The spatial smoothness term is then designed to adaptively encourage label smoothness based on the local cortical folding geometries, i.e., allowing label discontinuity at sulcal bottoms (which often are the boundaries of cytoarchitecturally and functionally distinct regions). The temporal consistency term is to adaptively encourage the label consistency among the temporally-corresponding vertices, based on their similarity of local cortical folding. Finally, the entire energy function is efficiently minimized by a graph cuts method. The proposed method has been applied to the parcellation of longitudinal cortical surfaces of 13 healthy infants, each with 6 serial MRI scans acquired at 0, 3, 6, 9, 12 and 18 months of age. Qualitative and quantitative evaluations demonstrated both accuracy and longitudinal consistency of the proposed method. By using our method, for the first time, we reveal several hitherto unseen properties of the dynamic and regionally heterogeneous development of the cortical surface area in the first 18 months of life.

1. Introduction

The human cerebral cortex develops dynamically in both structure and function in first years of life (Lyall et al., 2014; Nie et al., 2012, 2013a). At term birth, all primary and secondary cortical folding are present (Hill et al., 2010), resembling the morphology of the adult brain, and are then well preserved during the dynamic postnatal cortex development (Li et al., 2013a). For example, in the first year of life, the cortical gray matter volume doubles (Gilmore et al., 2012) and the cortical surface area expands 1.8 times (Li et al., 2013a). Increasing evidence suggests that many neurodevelopmental disorders are likely the results of abnormal development in this critical stage of rapid cortex growth (Gilmore et al., 2012; Lyall et al., 2014). Thus, studying the dynamic cortex development during this stage using MR images would greatly increase our limited knowledge on normal early brain development and also provide important insights into neurodevelopmental disorders (Gilmore et al., 2012; Li et al., 2014c; Lyall et al., 2014).

Cortical surface-based analysis is particularly suitable for studying the dynamic development of the highly-folded and thin cortex, as these methods respect the topology of the cortex and facilitate the alignment, analysis, functional mapping and visualization of buried sulcal regions (Dale et al., 1999; Van Essen et al., 2001). Moreover, cortical surface-based measurements, such as the surface area, cortical thickness, sulcal depth, cortical folding, and cortical gyrification, provide a very detailed picture on how the cortex develops (Li et al., 2014a). Parcellation of cortical surfaces into a set of Regions of Interest (ROIs) is of fundamental importance in

* Corresponding author. Address: Radiology and BRIC, UNC-CH School of Medicine, MRI Building, CB #7513, 130 Mason Farm Road, Chapel Hill, NC 27599, USA.
E-mail address: dgshen@med.unc.edu (D. Shen).

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localizing structural/functional regions and mapping regional cortex development. However, manual parcellation of the highly-folded cortical surface is extremely tedious, time-consuming, and subject to inter-rater variation. Accordingly, many methods have been proposed for cortical surface parcellation in the cross-sectional adult studies, based on the sulcal–gyral folding geometries from structural MR images (Cachia et al., 2003; Desikan et al., 2006, 2010; Fischl et al., 2004; Hu et al., 2010; Joshi et al., 2012; Klein and Hirsch, 2005; Klein and Tourville, 2012; Li et al., 2009, 2013c; Liu et al., 2004; Lohmann and von Cramon, 2000; Nie et al., 2007; Rettmann et al., 2002; Shi et al., 2013; Van Essen et al., 2012; Wan et al., 2008; Yang and Kruggel, 2008; Yeo et al., 2008; Zhang et al., 2010).

Recently, longitudinal neuroimaging studies of the dynamic brain development in the first years of life have received increasing attention (Almli et al., 2007; Fan et al., 2011; Gilmore et al., 2012; Li et al., 2013a, 2014b; Nie et al., 2013b; Shi et al., 2010, 2011). Because these longitudinal studies can uniquely capture the dynamic developmental trajectory of each individual and are also less influenced by the confounding effects of inter-subject variation, compared with the cross-sectional studies (Bernal-Rusiel et al., 2012; Li et al., 2014a). Due to the highly convoluted and variable cortical folding (Li et al., 2010b; Nie et al., 2010; Zhang et al., 2009), cortical surface parcellation often involves the highly complex nonlinear optimization, thus subtle changes of the cortical folding could lead to significantly different parcellation results. Hence, applying existing cross-sectional methods to each longitudinal infant cortical surface independently is likely to generate the longitudinally-inconsistent surface parcellation, especially for those small-sized cortical regions and ambiguous cortical regions. This will eventually lead to inaccurate measurements of longitudinal cortex development in infants. Therefore, a method for accurate and consistent parcellation of longitudinal dynamic infant cortical surfaces is essential to understand the early brain development in both healthy and high-risk infant populations.

To ensure the longitudinal consistency of cortical surface parcellation, one can first parcellate the cortical surface of a selected time point (e.g., typically the first or the last time point) by using an existing cross-sectional method, and then propagate its parcellation result onto the cortical surfaces of other time points. However, this type of parcellation results would be biased by the selected time point, in addition to the propagation of potential labeling errors. Accordingly, efforts have been made recently towards unbiased and temporally consistent parcellation of longitudinal cortical surfaces from adult serial MR images (Reuter et al., 2012). For example, in the longitudinal pipeline of FreeSurfer (Reuter et al., 2012), a within-subject template is first built by rigidly aligning all longitudinal images of a subject to its median time-point image. Then the cortical surfaces of the within-subject template are reconstructed and parcellated using the conventional cross-sectional method (Fischl et al., 2004). Next, the parcellated cortical surfaces of the within-subject template are rigidly transformed back to the space of each longitudinal image as the initialization. Finally, the initialized cortical surface parcellation is further refined independently for each time point to achieve the longitudinal consistency (Reuter et al., 2012). Although this independent refinement of each longitudinal surface might be suitable for the adult brains with small longitudinal changes (Reuter et al., 2012), it becomes problematic when applied to the infant brains with dynamic longitudinal development.

In this paper, we present a new method for accurate, consistent, and simultaneous parcellation of longitudinal dynamic cortical surfaces from serial infant brain MR images. The proposed method is explicitly formulated as a minimization problem of an energy function, which includes a data fitting term, a spatial smoothness term, and a temporal consistency term. Inspired by the recent success of multi-atlas based labeling, the data fitting term is designed to integrate the contributions from multiple atlas surfaces adaptively, according to the similarities of their local cortical folding with that of the subject cortical surface. The spatial smoothness term is designed to adaptively encourage the label smoothness based on the local cortical folding geometries. The temporal consistency term is further designed to adaptively encourage longitudinal label consistency based on the temporal similarities of local cortical folding. The energy function is efficiently minimized by the alpha-expansion graph cuts method (Boykov and Kolmogorov, 2004). In our method, all longitudinal cortical surfaces of the same infant are treated equally and labeled jointly, thus the longitudinal surface parcellation results are unbiased (not dominated by any specific time-point). Since adaptive temporal constraints are imposed in our method, the longitudinal surface parcellation results are temporally consistent, with no temporally-unrealistic (bumpy) changes. The proposed method has been applied to label the longitudinal cortical surfaces of 13 healthy infants, each with 6 serial MRI scans at 0, 3, 6, 9, 12 and 18 months of age. Both qualitative and quantitative evaluation results demonstrate the accuracy and consistency of the proposed method.

A preliminary version of this work was presented at the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI) (Li et al., 2013b). This paper significantly extends the preliminary version with more details on introduction of methodology and also more extensive validations and discussions. Moreover, by using the proposed method, this paper reveals several hitherto unseen properties of the dynamic, age-related, and regionally heterogeneous development of the cortical surface area in the first 18 months of life.

2. Materials and methods

2.1. Subjects and MR image acquisition

This study was approved by the Institutional Review Board of the University of North Carolina (UNC) School of Medicine. Pregnant mothers were recruited during the second trimester of pregnancy from the UNC hospitals. Informed consent was obtained from both parents. Exclusion criteria included abnormalities on fetal ultrasound, or major medical or psychotic illness in the mother. Infants in the study cohort were free of congenital anomalies, metabolic disease, and focal lesions. No sedation was employed and all infants were imaged during natural sleep. A physician or nurse was present during each scan, and a pulse oximeter was used to monitor heart rate and oxygen saturation. More information on subjects can be found in Li et al. (2014a), Nie et al. (2012), and Wang et al. (2012b). Each infant was planned to be scanned every 3 months from birth till year 1 and again at 18 months. 13 healthy infants (9 males/4 females), each with 6 serial MRI scans (acquired at 2 weeks, 3, 6, 9, 12 and 18 months of age, respectively), were used in this study.

Serial T1-, T2-, and diffusion-weighted MR images of each infant were acquired using a Siemens 3T head-only MR scanner with a 32 channel head coil. T1 images (144 sagittal slices) were acquired with the following imaging parameters: TR = 1900 ms, TE = 4.38 ms, flip angle = 7, acquisition matrix = 256×192, and voxel resolution = $1 \times 1 \times 1$ mm^3. T2 images (64 axial slices) were acquired with the imaging parameters: TR/TE = 7380/119 ms, flip angle = 150, acquisition matrix = 256×128, and voxel resolution = $1.25 \times 1.25 \times 1.95$ mm^3. Diffusion-weighted images (DWI) (60 axial slices) were acquired with the parameters: TR/TE = 7680/82 ms, acquisition matrix = 128×96, voxel resolution = $2 \times 2 \times 2$ mm^3, 42 non-collinear diffusion gradients, and diffusion weighting $b = 1000$ s/mm^2. More information on image