sulcal pattern, brain development, in-vivo MRI,
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CORTICAL PATTERN DETECTION FOR THE DEVELOPING BRAIN: A 3D VERTEX LABELING AND SKELETONIZATION APPROACH

Normal brain development is associated with expansion and folding of the cerebral cortex in a normal sequence of gyral-sulcal formation. We propose a global approach for measuring the cortical folding pattern of the developing brain. Our method measures geometric features directly on the cortical surface mesh, based on vertex labeling and skeletonization. The resulting extraction provides an accurate representation of global cortical organization. We applied this method to 17 young infants in order to characterize the evolution of cortical organization in the developing brain.

1. INTRODUCTION

The ability to quantify normal developmental patterns of the immature brain is needed in order to characterize the nature, timing, and progression of abnormal brain development. In recent years, a growing number of investigators have focused on the study of cerebral cortical development, given that the cerebral cortex has been shown to be very important in microscopic structure [1, 2], macroscopic arrangement [3, 4, 5] and functional organization [6]. Recent studies have emphasized the importance of considering not only the cortical structures, but also their relative organization, in order to integrate the intrinsic nature of the cortical ribbon. These studies have incorporated a structural approach to studying the brain [3] that overcomes issues that are inherent to studies that use localization approaches [7]. These limitations include inconsistencies in the topography of sulci across individuals or inaccurate matching between homologous areas. These structural methods make use of architectural information about the brain while performing inter-subject studies.

The notion of a stable scheme of cortical organization, appearing very early in gestation, has been supported by several studies [1, 8]. The ability to obtain quantitative structural information of the growing brain is critical for understanding normal and abnormal brain development. The principal challenge lies in the type of information used to characterize brain organization. Several studies have used the extraction of local information [9, 10] to enable cortex anatomical description.

In this paper, we propose an approach for globally quantifying cortical development in the immature brain. Relying on an original feature extraction technique, applied directly to the cortical surface, the proposed method aims to delineate the global scheme of cortical organization.

2. OVERVIEW AND PREVIOUS WORK

The study of sulcal development focuses on extraction of local structures, the most common being the sulcus. However, their extraction must be consistent with cortical organization. The relative location of the cortical folds is of great importance both from a developmental and functional perspective [1, 11].

The study of sulcal organization is important for understanding inter-individual variability. This approach is based on certain anatomical and developmental assumptions. Several studies have studied the natural organization of the cortical folds [12, 11], and have described a folding model that is stable across individuals. A tension-based theory [13] has also been proposed, in which the gyrification and the relative

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mechanical constraints during growth are elucidated. Other studies have focused on the stability of certain anatomical markers during growth and development [8, 9]. At a macroscopic level, cortical sub-units have been described as being stable across individuals. Moreover [8], this method also describes a natural orthogonal organization of these sub-units. At a microscopic level, the notion of a stable organization of the sulcal anatomy has been reported [1], in which cortical maps are proposed. These cortical maps were created from information transportation by the cells during the brain formation, providing a stable pattern for the upcoming macroscopic maturation.

When assessing cortical organization in the developing brain, it is important to determine what anatomical features should be considered. In [9], the extraction of the cortical sub-units has been performed, as such structures reflect the emergence of cortical organization. A great strength in this approach is that it overcomes the inter-individual variability occurring at the sulcal level. However, the extraction and the labeling of such structures have been shown to be a non-trivial problem [12]. Another approach relies on sulci extraction to provide a macroscopic description of the brain folding. In [14], a description of the cortical folding was proposed, and the primary and secondary folds appearing through the first weeks of ex-uterine life in premature babies was delineated. In a more recent paper, an atlas of the newborn term brain has been proposed, describing the sulcal folds across 14 subjects [15]. However, these studies do not provide a description of the global cortical pattern. It is also important to note that the sulcal description that is presented in these papers is limited by the inter-variability of the sulci between patients, in shape, location and topology.

To tackle these issues, we propose herein the extraction of a global sulcal pattern (i.e. on the entire cortical surface), relying on 3D vertex labeling and skeletonization performed over the cortical surface. This method allows measuring the cortical folding at a global scale, overcoming the issue of single anatomical structures that can be very variable across individuals, and therefore inconsistent. We applied our method to data from young infants, in order to get a description of the average gyrification process.

3. METHOD

3.1. DATA ACQUISITION AND PROCESSING

We applied our approach to the study of cortical surfaces extracted from in-vivo healthy infant MRI studies. Infant data came from healthy controls in the NIH MRI Study of Normal Brain Development [16]. All MRI studies included T1-weighted acquisitions (2D T1W multi-slice spin echo sequence, TR = 500 ms, TE = 12 ms, 1x1x3 mm, time = 3-5 min), performed on a 1.5 Tesla scanner without sedation. Our cohort consisted of 17 infants and was subdivided as follows: The first group included 6 subjects (all subjects were 12 weeks old, standard deviation = 0). The second group included 11 subjects (mean age = 16.81 weeks, range: 15-22 weeks, standard deviation = 2.04). We divided our cohort in two groups (described above) in order to evaluate the folding pattern at two different developmental ages.

The pre-processing stages included intensity non-uniformity correction, normalization, and linear alignment to a common target. Each linearly registered volume was then segmented. The segmentation was automated for the young infants using the FSL FAST segmentation tool [17] (the *a-priori* volume used in the Expectation-Maximization algorithm was a pediatric volume manually segmented). Extraction of cortical surfaces for each hemisphere was then performed using CLASP [18].

3.2. SULCAL PATTERN DESCRIPTION

The local geometry of a surface can be described by differential quantities of second-order such as principal curvatures (k_1 and k_2 with $|k_1| > |k_2|$) and principal directions ($\vec{t}_1$ and $\vec{t}_2$). Two shape descriptors are then defined; *mean* curvature H and *Gaussian* curvature K where:

$$H = \frac{k_1 + k_2}{2} \text{ and } K = k_1 \cdot k_2 \quad (1)$$

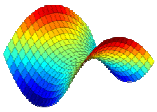
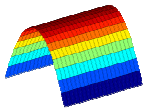
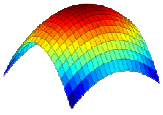
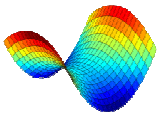
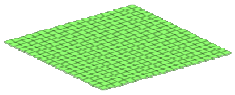
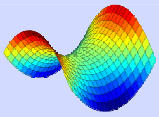
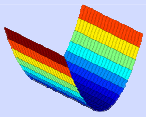
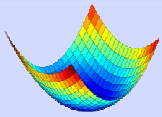
Combining the signs of H and K, it is possible to enumerate eight types of basic shapes (see Table 1).

Traditional techniques for features detection generally rely on higher order differential quantities such as curvature derivatives (*i.e.*, third-order estimation). However, these derivatives are very sensitive to noise. Thus, it produces feature networks with a lack of connectivity [19]. Therefore, the method proposed in this paper directly uses the curvatures and morphological operators to extract the sulcal pattern and ensure connectivity between features.

The first step of our method is to label each point of the surface according to their curvature values. There is no mutual agreement on the best way to compute curvatures. Among the existing curvature estimators, we chose to use the method proposed in [20] due to its quality and stable results [21]. It consists of locally fitting, in the least squares sense, the surface by a bi-cubic polynomial:

$$f(x,y) = \frac{A}{2}x^2 + Bxy + \frac{C}{2}y^2 + Dx^3 + Ex^2y + Fxy^2 + Gy^3 \tag{2}$$

Table 1. Basic shapes defined by the signs of mean and Gaussian curvatures.

	$K < 0$	$K = 0$	$K > 0$
$H < 0$	Saddle ridge 	Ridge 	Peak 
$H = 0$	Minimal surface 	Plane 	*Not possible*
$H > 0$	Saddle valley 	Valley 	Pit 

In order to assert the smoothness of the curvature tensor, a pre-processing step is required. In our case, we applied a *Laplacian* smoothing on the point coordinates.

Sulci are located in the *concave* parts of the surface characterized by $H > 0$ (depicted in blue on Table 1). Each point p_i of the surface is then labeled as:

$$Label(p_i) = \begin{cases} 1 \text{ if } H > 0, \\ 0 \text{ otherwise.} \end{cases} \tag{3}$$

From this point, the local geometry is transformed into a binary map corresponding to regions of interest [22]. The labeled points represent candidate points belonging to sulcal pattern.

The second step of our method is to extract sulcal lines from the binary map and therefore find for each region the *centerline*. This problem of centerline extraction can be referred to *skeletonization* [23]. The extraction of the sulcal pattern through a skeletonization algorithm may be discussed. Theoretically, there is no specific reason for the skeleton to lie on sulci. However, the points comprising the skeleton are a subset of candidate points (*i.e.*, corresponding to concave areas). Thus keeping any of these labeled points would be a good option, given that they characterize a smooth and connected line. However, the best representation of the regions of interest is the skeleton because it is a well-known global center of a shape and thus it is theoretically justified to consider it.

In order to obtain the skeleton directly on the mesh surface, we chose to use operators proposed in [24], which is an extension of the well-known 2D image operators, with slight modifications. The skeleton is computed by thinning. It consists in an iterative process of erosions that deletes the outer layer

of a shape without altering its topology. In our case, it is a notable property since we want to guarantee the connectivity of the extracted sulcal pattern.

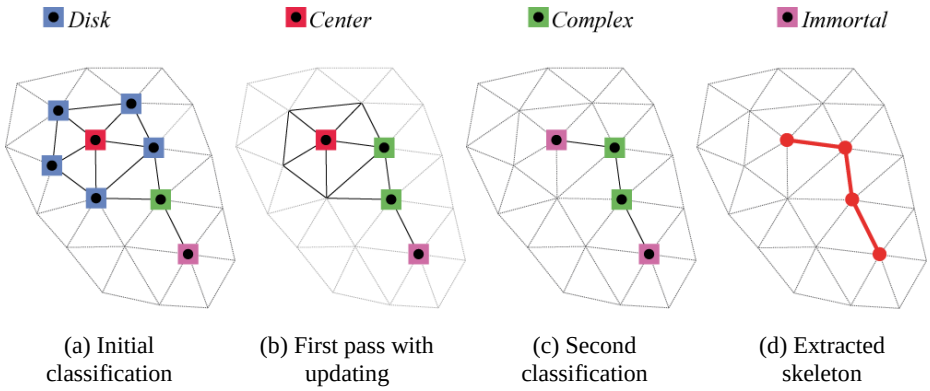
For the sake of clarity, we denote F the set of labeled points to 1, p a point of the surface and q_i its direct neighbours. All the points of F are classified into four categories: *disk*, *center*, *complex* and *immortal* (Figure 1a).

p is considered as *center* if p and all its neighbours q_i belong to F. In this case, all q_i are marked as *disks*. It corresponds to the definition of a *simple point* (*i.e.*, a point that does not change the topology if it is removed). Conversely, p is a *complex* point when there are at least four *transitions* among its neighbours q_i. A *transition* exists if:

$$Label(q_i) \neq Label(q_{i+1}) \tag{4}$$

Lastly, all the remaining points of F are flagged as *immortal* points. The thinning process deletes, until convergence, the *disk* points since they do not modify the topology. During this sequence, for each point deleted, the states of its neighbours q_i are updated to ensure connectivity of detected sulcal lines.

The last step of the method is to prune the smallest branches which generally correspond to artifacts. A similar mechanism is applied: all *immortal* points with at least two neighbours belonging to F are deleted.



(a) Initial classification | (b) First pass with updating | (c) Second classification | (d) Extracted skeleton

Fig. 1. Illustration of the skeletonization process.

4. RESULTS AND EXPERIMENTATION

The feature extraction method was applied to two groups of young infants described earlier. Our method extracted the global sulcal pattern of the developing brain, showing the deep cortical organization on a global scale. Figure 2 shows the resulting probability maps of sulci locations for the two groups, mapped on the average left hemisphere for each group (right hemispheres were flipped on the x axis). In order to get a better sense of the folding process for the two studied groups, we computed an unbiased average surface of each cohort (see figure 2), using the methodology presented in [25]. Such average surfaces allow to represent with more clarity the average shape of a specific population. Suci location probability maps were then super-imposed on these surfaces. The resulting cortical pattern was consistent between the subjects, and enabled us to characterize the gyrification process across in early infancy (12-22 week range maturational stage). For comparison, we applied our method to an adult average surface, computed from the normative ICBM adult database (figure 3) [25, 26]. All cortical surfaces averages were computed using the unbiased population average computation method presented in [25].

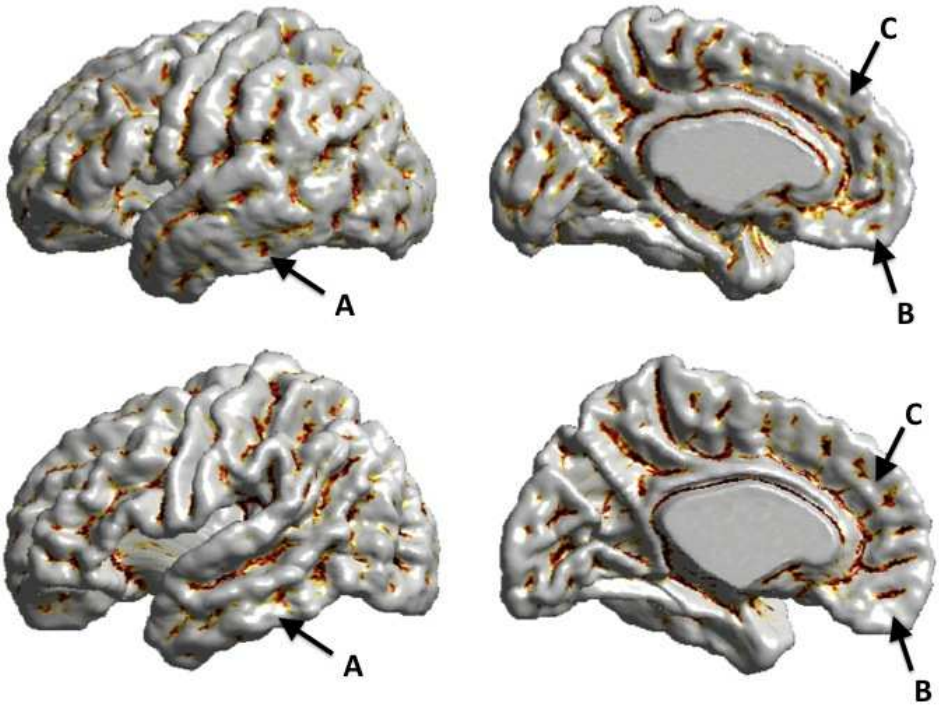


Fig. 2. Probability maps of sulcal pattern after features extraction, in two groups of infants: Top: 12 weeks old subjects. Bottom: 16.8 weeks (mean) old subjects.

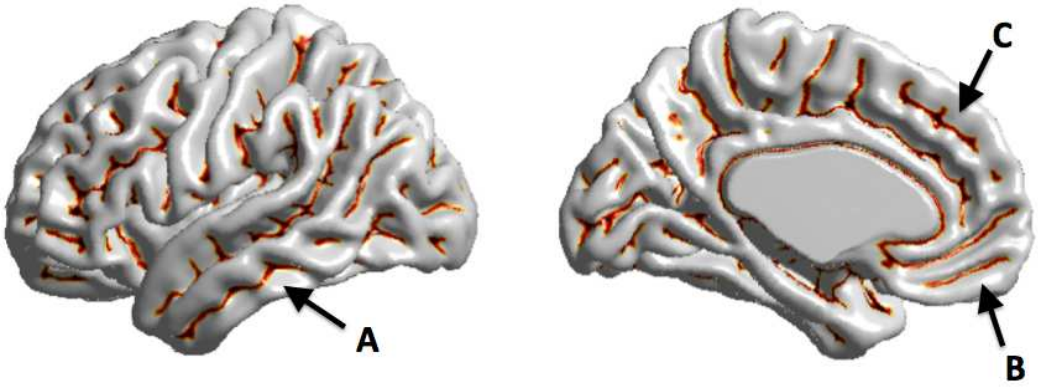


Fig. 3. Sulcal pattern extraction on an average surface of 135 adults.

The cortical pattern for young infants is principally depicting primary and secondary sulci organization. For example, the mid-temporal sulcus (A), the folds in the medial orbito-frontal gyrus (B) or in the superior frontal gyrus (C) are not yet well formed at early stages of development, resulting in a sulcal pattern that is less consistent in these areas. Conversely, primary folds such as the central sulcus, superior temporal sulcus or the cingulate sulcus are stable through a period of growth. The high connectivity between the extracted features allows us to capture and to compare the global folding pattern at each stages of brain maturation.

5. CONCLUSION

The work we present herein aims to extract the global cortical pattern of the developing brain. The geometrical approach chosen is based on vertex labeling and skeletonization, which allows us to capture this folding pattern in the developing human cortex. The extraction algorithm uses direct curvature values and morphological operators. Thus, it ensures a high connectivity between features and is robust to noise. This promising method enabled us to begin characterizing the evolution of early life sulcal development

in young infant, and provides a novel approach for quantifying the gyrification process and sulcal organization of the developing brain, using *in-vivo* MRI data.

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