SPATIAL DISTRIBUTION AND LONGITUDINAL DEVELOPMENT OF DEEP CORTICAL SULCAL LANDMARKS IN INFANTS

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ABSTRACT

Sulcal pits, the locally deepest points in sulci of the cerebral cortex, are found to be spatially highly consistent across human adult individuals. It is suggested that sulcal pits are genetically controlled and have close relationship with functional areas. To date, most imaging studies of sulcal pits are focused on adult brains, yet little is known about the spatial distribution and temporal development of sulcal pits in the first 2 years of life, the most dynamic period of postnatal brain development. Studying sulcal pits during this period would enrich our current limited understanding of the developmental trajectories of sulcal pits and provide insights into neurodevelopmental disorders, i.e., with abnormal cortical folding patterns. In this paper, by using surface-based morphometry, for the first time, we systemically investigated the spatial distribution and temporal development of sulcal pits in major sulci from 73 healthy infants, each with longitudinal 3T MR scans at term birth, 1 year, and 2 years of age. Our results suggest that the consistency of spatial distribution of sulcal pits in major sulci across subjects has already existed at term birth and this spatial distribution pattern is relatively stable during cortex development in the first 2 years, despite that the cortex expands dramatically and the sulcal depth increases considerably.

Index Terms— infant, cortical surface, sulcal depth, sulcal pits, longitudinal development

1. INTRODUCTION

The human cerebral cortex is highly folded and variable across individuals. Sulcal pits are the locally deepest points along sulcal lines in the cerebral cortex [1]. During human brain development, the deepest parts of primary sulci are the first places to develop in an embryo's brain and then change least as the cortex growing [1]. Quantitative MR imaging studies provide strong evidences that the deeper parts of sulci are more genetically controlled than the superficial parts [12]. Abundant studies [1, 2, 3] indicate that there is a particularly spatial relationship between the deepest parts of sulci and functional areas.

Accordingly, sulcal pits have drawn increasingly more attentions in neuroimaging studies in the past few years. Gabriele Lohmann *et al.* [1] first examined sulcal pits in volumetric MR images and observed that the spatial distribution of sulcal pits in major sulci was strikingly regular across adult individuals, despite their highly variable cortex folding. Kiho Im *et al.* [4] proposed a more reliable sulcal pits extraction approach on the cortical surfaces reconstructed from MR images. Based on the sulcal depth, they used watershed algorithm to partition the cortical surface into many basins, and then identified the deepest point in each basin as the sulcal pit after pruning basins with shallow depth or small size. Kiho Im *et al.* [4] confirmed the observations in [1], and further investigated hemispherical asymmetries of both frequency and distribution of sulcal pits. Based on these studies, sulcal pits in major sulci were considered as reliable anatomical landmarks and could potentially be helpful for the challenging problem of inter-subject brain MR image registration.

However, to our knowledge, most previous imaging studies of sulcal pits were focused on adult brains, while little is known about the spatial distribution and temporal development of sulcal pits in infants from birth to 2 years of age. The first 2 years of life is the most dynamic and critical period of postnatal brain structural and functional development, with the cortical surface area expansion 1.8 times in the first year and 1.2 times in the second year [5]. Thus, studying sulcal pits during this period would increase our current limited understanding of the developmental trajectories of sulcal pits and also provide important insights into neurodevelopmental disorders, i.e., with abnormal cortical folding patterns. In this paper, by using the cortical surface-based morphometry, for the first time, we systemically study the spatial distribution of sulcal pits and their temporal development from 73 healthy infant subjects, each with longitudinal 3T MR scans at term birth, 1 year, and 2 years of age. Our results suggest that the consistency of spatial distribution of sulcal pits in major sulci across subjects has already existed at term birth. Our results also show that, though the cortex expands dramatically and the sulcal depth increases considerably, the spatial distributions of major sulcal pits are relatively stable during cortex development in the first 2 years.

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2. MATERIALS AND METHOD

2.1. Subjects and MRI Acquisition

T1-weighted (resolution=1×1×1mm^3) and T2-weighted (resolution=1.25×1.25×1.95mm^3) MR images were acquired on a Siemens head-only 3T scanner from 73 healthy infant subjects, including 42 males and 31 females. For each subject, data were longitudinally collected at 3 time points: birth, 1 year, and 2 years of age. For more information on subjects and MRI acquisition, please refer to [5, 6].

2.2. Method

Which steps are manual? I assume bias corr. and skull str. are the same as in [7], correct? Was the last step automatic?

2.2.1 Image Processing

All MR images are processed by the following pipeline: First, skull, cerebellum and brain stem were removed. Then, intensity inhomogeneity was corrected. Next, each image was rigidly aligned onto the age-matched infant atlas [7]. After that, tissue segmentation was performed by an infant-specific longitudinally-guided coupled level sets method [8]. Finally, non-cortical structures were marked and filled, and each brain was separated into left and right hemispheres.

2.2.2 Cortical Surface Reconstruction and Registration

Does [5] produce the topology correct tesselation?

For each hemisphere of each image, cortical inner and outer surfaces were reconstructed using a deformable surface method [5]. Specifically, the topology-corrected white matter was first tessellated as a triangular mesh and then deformed by preserving its initial topology. The inner cortical surface of each hemisphere was smoothed, inflated and mapped to a standard sphere [9]. To establish inter-subject cortical correspondences, all cortical surfaces of the same hemisphere at the same age were aligned to the age-matched surface-based atlases [5], using Spherical Demons [10]. To establish longitudinal cortical correspondences, the cortical surfaces at birth were aligned to the corresponding cortical surfaces at 1 year of age, and the cortical surfaces at 1 year of age were aligned to the corresponding cortical surfaces at 2 years of age, using Spherical Demons [10].

2.2.3 Sulcal Pits Extraction

Does "20 times" refer to "20 iterations"?

For each vertex on the cortical surface, the sulcal depth, defined as the distance from the vertex to the closest point on the cerebral hull surface, was computed using the method in [6]. Herein, we adopted the inner cortical surface for sulcal pit analysis for a close comparison with existing studies in adults [1, 4]. To eliminate noises on the cortical surface, the sulcal depth map was smoothed 20 times using an *anisotropic* smoothing method on the cortical surface, in contrast to the existing *isotropic* smoothing in the previous studies [4], since the sulci have clear orientations. Specifically, the *anisotropic* smoothing of the sulcal depth was formulated as:

$$d(i,t+1)=\left(d(i,t)+\frac{\sum_{j\in N(i)} d(j,t)\cdot S(\mathbf{n}(i)\cdot\mathbf{n}(j))\cdot\|\mathbf{p}(i)-\mathbf{p}(j)\|^{-1}}{\sum_{j\in N(i)} S(\mathbf{n}(i)\cdot\mathbf{n}(j))\cdot\|\mathbf{p}(i)-\mathbf{p}(j)\|^{-1}}\right)\times 0.5 \quad (1)$$

At the vertex i, $d(i,t)$ is the sulcal depth at the iteration t, $\mathbf{p}(i)$ is the 3D coordinate position, and $\mathbf{n}(i)$ is the normal direction. $S(\mathbf{n}(i)\cdot\mathbf{n}(j))$ is defined as: if $\mathbf{n}(i)\cdot\mathbf{n}(j)>0$, $S(\mathbf{n}(i)\cdot\mathbf{n}(j))=\mathbf{n}(i)\cdot\mathbf{n}(j)$; otherwise, $S(\mathbf{n}(i)\cdot\mathbf{n}(j))=0$. $N(i)$ is the N-ring neighborhood of the vertex i. In our application, N was set as 10 experimentally. In this formulation, vertices along the sulci will have larger weights, as their normal directions are similar to that of the current vertex; while vertices perpendicular to the sulci will have smaller weights due to large difference of their normal directions.

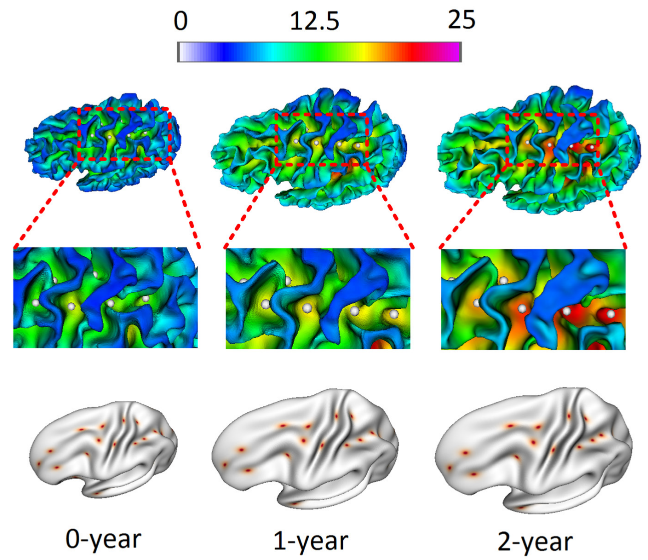

Fig. 1. The sulcal pits extraction from a representative infant. In the first row, cortical surfaces are color-coded by the sulcal depth (mm), with white points indicating sulcal pits. In the second row, sulcal pits (red points) are mapped onto the inflated cortical surfaces for better inspection.

A watershed algorithm was then applied to the smoothed sulcal depth map on the surface mesh. Specifically, 1) a vertex with the currently largest depth was picked out; 2) if none of its neighbor was labeled, the vertex was selected as a sulcal pit, and then assigned with a new label; if it had a labeled neighbor, the vertex was assigned with the same label; if it had at least 2 neighbors with different labels, the vertex was assigned by the label of the closest pit; 3) the steps 1 and 2 were repeated until the sulcal depth of the currently picked vertex was less than a certain threshold T, since we only concerned the sulcal pits in deep sulci. For adults with relatively stable brain size across subjects, T could be set as a fixed value for all subjects. However, the variation of brain size across different subjects at different ages is large in infants, hence there is no such fixed T suitable for all cortical surfaces. In our experiments, we performed a linear regression based on the relationship between experimentally set T and the max sulcal depth d_{max}

on the cortical surface from a subset of randomly selected subjects, to adaptively define the threshold T based on the following equation:

$$T = 0.75 \times d_{\max} - 7.85 \tag{2}$$

After the watershed procedure, noisy sulcal pits were removed as done in [4], by pruning the basins with shallow depth or small size.

3. RESULTS

We extracted sulcal pits from the cortical surfaces for all 73 infants at each age. **Fig. 1** shows the sulcal pits extraction results on cortical surfaces of a representative infant at 0, 1, and 2 years of age. The first row shows the original inner surfaces color-coded by the sulcal depth and the extracted sulcal pits (white points). Sulcal pits are hard to observe because of the convoluted folding, hence the sulcal pits are mapped onto the partially inflated cortical surfaces for better inspection, as shown in the second row of **Fig. 1**. As can be seen from **Fig. 1**, although cortical surface grows dramatically from 0 to 2 years of age, the spatial distribution of major sulcal pits is temporally consistent.

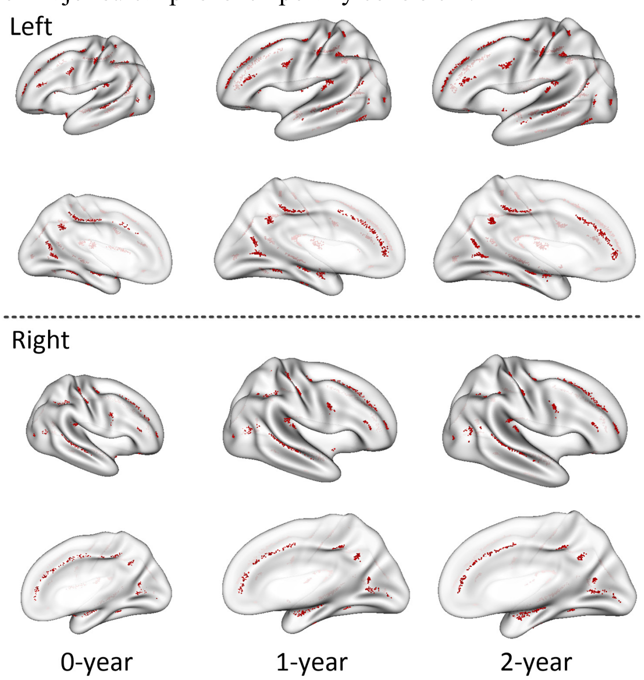

Fig. 2. Spatial distributions of sulcal pits (red points) in major sulci of 73 infants at 0, 1 and 2 years of age, mapped onto the age-matched inflated surface atlases.

To further examine the spatial distribution of sulcal pits across individuals at each age, we mapped all the sulcal pits from 73 infants to the age-matched inflated surface atlas, as shown in **Fig. 2**. We can see that the sulcal pits (red points) of the infant population are concentrated in some specified regions, in line with the results in adult studies [1]. For example, in the central sulcus, we can clearly identified two clusters of sulcal pits, which is consistent with the results in adults [1, 12] and preterm newborns [11]. Moreover, the sulcal pits in the superior part of the central sulcus are more variable than those in the inferior part, consistent with the results in adults [12].

During the dynamic cortex development from 0 to 2 years of age, the concentration regions keep almost unchanged. These results suggest that the consistency of spatial distribution of sulcal pits in major sulci across subjects has already existed at term birth, and their spatial distributions are relatively stable during the cortex development in the first 2 years.

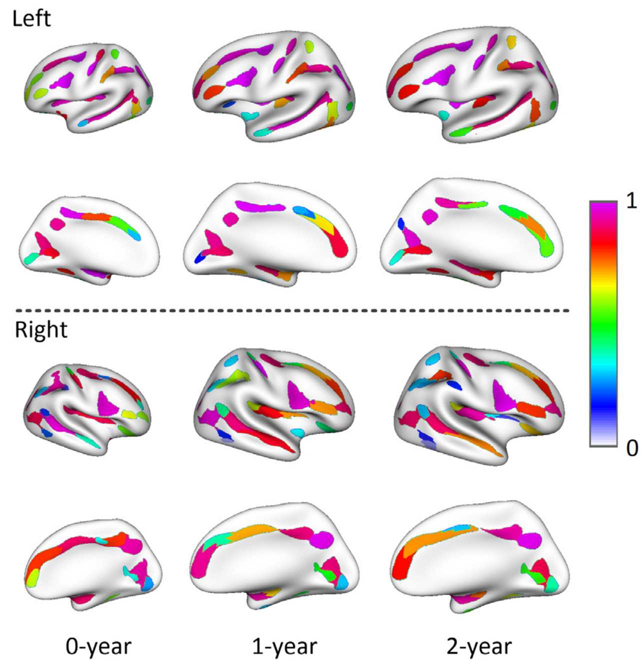

Fig. 3. Sulcal pits concentrated regions and their frequencies in 73 infants at 0, 1 and 2 years of age.

We further partitioned the cortical surface into regions based on the distribution of sulcal pits and computed the frequency that a sulcal pit appeared in the corresponding region, as done in [4]. Specifically, 1) each vertex in an infant cortical surface was assigned a density value. If a vertex was a sulcal pit, its density was set to 1; otherwise, its density was set to 0. 2) The density map was smoothed 175 times using a nearest neighboring method, while keeping the density of pits as always 1. 3) The smoothed density maps of all infants were mapped to the age-matched surface atlases and summed together. 4) A watershed method was performed on each summed density map of the population to partition the surface atlas into regions. The watershed was stopped once the summed density value was lower than 0.8, 1.0 and 1.2, respectively, for the 0, 1 and 2 year surface atlases. To compute the frequency, if a sulcal pit in an infant surface was mapped into a region of the corresponding surface atlas, the frequency of that region increased by one; if more than one pit from the same infant were mapped into the same region, only one pit was counted. **Fig. 3** shows the sulcal pits concentrated regions and their frequencies in 73

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infants from 0 to 2 years of age. As can be seen, although the frequency across ages is not strictly the same, it is temporally consistent in major sulci. High frequency regions were consistently found in major sulci, such as central, precentral, postcentral, superior temporal, superior frontal, cingulate, parieto-occipital and calcarine sulci, consistent with the results in [4].

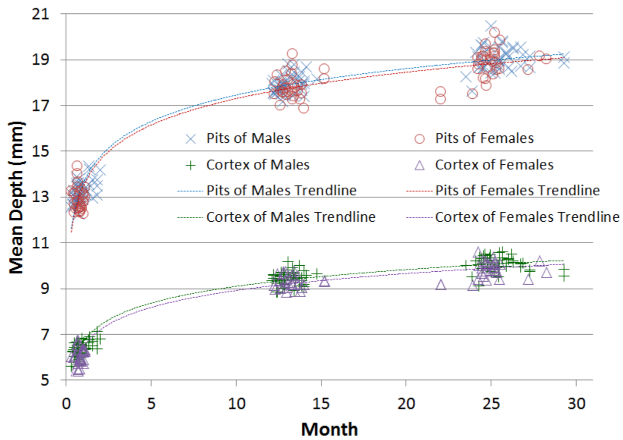

Fig 4. The distributions of longitudinal mean depths of both sulcal pits and whole cortices in the left hemispheres of 73 infants.

Table 1. The mean depths (mm) of both sulcal pits and whole cortices of left hemispheres, at 0 to 2 years of age.

	0-year		1-year		2-year	
	Pits	Cortex	Pits	Cortex	Pits	Cortex
Male	13.22	6.42	17.94	9.45	19.11	10.10
Female	12.91	6.10	17.80	9.29	18.96	9.92

Table 2. The growth percentages of the mean depths for sulcal pits and whole cortices in the left hemispheres, at 0 to 2 years of age.

	0~1 year		1~2 year		0~2 years	
	Pits	Cortex	Pits	Cortex	Pits	Cortex
Male	35.68	47.21	6.51	6.88	44.50	57.34
Female	37.86	52.37	6.51	6.80	46.83	62.73

We also investigated the gender differences on the sulcal pits during the cortex development. For each cortical surface, we compute the mean depths for all sulcal pits and the whole cortex, respectively, as shown in **Fig. 4**. **Table 1** gives the mean depths (mm) of the sulcal pits and the whole cortices in left hemispheres, at 0 to 2 years of age. And **Table 2** further provides the growth percentages of the mean depths of sulcal pits and the whole cortices of left hemispheres from 0 to 2 years of age, for male and female respectively. The mean depth of sulcal pits increases dramatically in the first 2 years, with the values of 36.8% in the first year and 6.5% in the second year for male and female together. While the mean depth of the whole cortex increases 49.8% in the first year and 6.8% in the second year for male and female together. The mean depth of sulcal pits in males is consistently larger than that of females at 0, 1 and 2 years of age, with the p-values consistently smaller than 0.05, suggesting that gender difference on sulcal pits has existed already at birth and is kept during cortex development in the first 2 years.

4. CONCLUSION

For the first time, we systemically studied the spatial distribution and temporal development of major cortical sulcal pits in infants from birth to 2 years of age. Our results reveal that the consistency of spatial distribution of sulcal pits in major sulci across subjects has already largely existed at term birth and is kept relatively stable during cortex development in the first 2 years, despite that the cortex expands dramatically and also the sulcal depth increases considerably during this period. Therefore, these spatially and temporally consistent sulcal pits could be potentially used as anatomical landmarks for guiding both longitudinal and cross-sectional brain MR image registration in the future.

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