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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 highly convoluted and variable cerebral cortex, are found to be spatially consistent across human adult individuals. It is suggested that sulcal pits are genetically controlled and have close relationships with functional areas. To date, the existing imaging studies of sulcal pits are mainly 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, which is the most dynamic and critical period of postnatal brain development. Studying sulcal pits during this period would greatly enrich our limited understandings of the origins and developmental trajectories of sulcal pits, and would also provide important insights into many neurodevelopmental disorders associated with abnormal cortical foldings. 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 cortical sulci from 73 healthy infants, each with three longitudinal 3 T MR scans at term birth, 1 year, and 2 years of age. Our results suggest that the spatially consistent distributions of sulcal pits in major sulci across individuals have already existed at term birth and this spatial distribution pattern keeps relatively stable in the first 2 years of life, despite that the cerebral cortex expands dramatically and the sulcal depth increases considerably during this period. Specially, the depth of sulcal pits increases regionally heterogeneously, with more rapid growth in the high-order association cortex, including the prefrontal and temporal cortices, than the sensorimotor cortex in the first 2 years of life. Meanwhile, our results also suggest that there exist hemispheric asymmetries of the spatial distributions of sulcal pits in several cortical regions, such as the central, superior temporal and postcentral sulci, consistently from birth to 2 years of age, which likely has close relationships with the lateralization of brain functions of these regions. This study provides detailed insights into the spatial distribution and temporal development of deep sulcal landmarks in infants.

Introduction

The human cerebral cortex is highly convoluted and variable across adult individuals (Li et al., 2009; Ono et al., 1990). Sulcal pits are the locally deepest points along sulcal bottom lines in the cerebral cortex (Lohmann et al., 2008). During the human brain development, the deepest parts of primary sulci are thought as the first places to develop in an embryo's brain and then change least as the cortex grows (Lohmann et al., 2008). Quantitative MR imaging studies provide strong evidence that the deepest parts of sulci are more genetically controlled than the superficial parts (Le Goualher et al., 1999; Lohmann et al., 1999; McKay et al., 2013). Abundant studies also indicate that there are particularly spatial relationships between the deepest parts of sulci and functional areas (Lohmann et al., 2008; Piao et al., 2004; Rakic, 1988, 2004; Smart and McSherry, 1986; Welker, 1990).

Accordingly, sulcal pits have drawn increasing attentions in neuroimaging studies in the past few years (Im et al., 2010, 2013; Lohmann et al., 2008; McKay et al., 2013). Lohmann et al. 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 foldings (Lohmann et al., 2008). Then Im et al. proposed a more reliable sulcal pits extraction approach on cortical surfaces reconstructed from MR images (Im et al., 2010, 2013). In this method, a watershed algorithm based on the sulcal depth was used to partition the cortical surface into many basins, and then the deepest point in each basin was identified as the sulcal pit, after pruning basins with shallow sulcal depths or small sizes. The results in Im et al. (2010) confirmed the observations in Lohmann et al. (2008), and further revealed the hemispheric asymmetries of sulcal pits. According to these studies, sulcal pits

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in major cortical sulci were considered as reliable anatomical landmarks and some of them could be potentially helpful for the challenging problem of inter-subject brain MR image registration (Li et al., 2010; Lohmann et al., 2008). Im et al. (2013) further investigated the relationships between the presence of sulcal pits and intelligence, and found that in the left posterior inferior frontal sulcus and the right posterior inferior temporal sulcus, the number of sulcal pits of young adults with high IQ was significantly different from that of young adults with average IQ. McKay et al. (2013) specifically studied the central sulcus in adults and found that most adult individuals had two peaks in the sulcal depth position profiles, close to the hand and mouth regions, where the peak genetic heritability of the sulcal depth occurred. By tracking the cortical surface development of four neonates between birth and 4 weeks of age, Lefevre et al. (2009) found that the cortical surfaces grew in a radial manner from some growth seeds. They suggested that the concepts of growth seeds, sulcal roots (Regis et al., 2005) and sulcal pits might be merged into one kind of entity that could be stable across individuals.

However, to our knowledge, most existing imaging studies of sulcal pits were mainly focused on adult brains, while little is known about the spatial distribution and temporal development of sulcal pits in the normal infants from birth to 2 years of age. Note that the first 2 years of life is the most dynamic and critical period of the postnatal brain structural and functional development (Knickmeyer et al., 2008; Li et al., 2014c; Lyall et al., in press; Nie et al., 2012b, in press), with the cortical surface area expansion 1.8 times in the first year and 1.2 times in the second year (Li et al., 2013), although major cortical sulci are already present at term birth (Chi et al., 1977; Dubois et al., 2008; Hill et al., 2010a). Increasing evidence also suggests that many neurodevelopmental disorders are likely the results of abnormal brain development during this critical period of rapid cortex growth (Gilmore et al., 2012). Thus, studying sulcal pits during this period would greatly increase our currently limited understanding of the developmental trajectories of sulcal pits and also provide important insights into the neurodevelopmental disorders associated with abnormal cortical foldings. In this paper, by using the cortical surface based morphometry, for the first time, we systematically study the spatial distribution of sulcal pits and their temporal development from 73 healthy infants, each with three longitudinal MR scans at term birth, 1 year, and 2 years of age. Our results suggest that the spatially consistent distributions of sulcal pits in major sulci across subjects have already existed at term birth. Meanwhile, though the cortex expands dramatically and the sulcal depth increases considerably, the spatial distributions of major sulcal pits keep relatively stable in the first 2 years. Importantly, the depth of sulcal pits exhibits a regionally heterogeneous growth, with more rapid growth in the high-order association cortex, including the prefrontal and temporal cortices, than the sensorimotor cortex in the first 2 years of life. Moreover, our results reveal certain hemispheric asymmetries in infants.

Materials and methods

Subjects

This study was approved by the Institutional Review Board of the University of North Carolina (UNC) School of Medicine. The UNC hospitals recruited pregnant mothers during their second trimesters of pregnancy, with the informed consents obtained from both parents. Subjects were excluded if the fetal ultrasound was abnormal or the mother had major medical diseases or psychotic illness. The infants in the study cohort did not have any congenital anomaly, metabolic disease or focal lesion. Before scanning, the infants were fed, swaddled, and fitted with ear protection, and none of them was sedated (Gilmore et al., 2012; Li et al., 2013; Shi et al., 2011).

MR images were longitudinally acquired for all 73 healthy infants at 0, 1 and 2 years of age. Specifically, the study group consisted of 31 singletons (including 20 males and 11 females) and 42 twins (including 22 males and 20 females). For the twins, there were 7 monozygotic twin pairs, 10 dizygotic twin pairs and 8 "single" twins (Gilmore et al., 2012). The mean gestational age at birth for all the 73 infants was 37.9 ± 1.6 weeks. The mean age at each scanning time point is provided in Table 1. No gender difference of ages at scanning was found at any of the three time points. This dataset has been used in prior studies of the development of the cortical gray matter volume (Gilmore et al., 2012), the expansion of the cortical surface area (Li et al., 2013), and the hemispheric asymmetries of the cerebral cortex (Li et al., 2014b) in infants.

To closely compare sulcal pits in infants to those in adults, we also studied a cohort of 64 healthy young adults, including 29 males and 35 females. Young adult data were obtained from a subset of the Pediatric MRI Data Repository (Release 4.0) created for the NIH MRI Study of Normal Brain Development (Evans, 2006), a multi-site project aimed at providing a normative database to characterize healthy brain maturation in relation to behavior (Nie et al., 2013a). The average age of these young adults was 18.9 ± 1.4 years.

MR image acquisition

For infants, MR images were acquired by using a Siemens head-only 3 T scanner with a circular polarized head coil. For T1-weighted images, 160 sagittal slices were acquired with the three-dimensional magnetization-prepared rapid gradient echo (MPRAGE) sequence: TR = 1900 ms, TE = 4.38 ms, inversion time = 1100 ms, flip angle = 7°, and resolution = $1 \times 1 \times 1$ mm^3. For T2-weighted images, 70 transverse slices were acquired with turbo spin-echo (TSE) sequences: TR = 7380 ms, TE = 119 ms, flip angle = 150°, and resolution = $1.25 \times 1.25 \times 1.95$ mm^3 (Gilmore et al., 2012; Shi et al., 2011). The T2-weighted image was linearly aligned onto its counterpart of T1-weighted image and then resampled to the resolution of $1 \times 1 \times 1$ mm^3.

For young adults, a three-dimensional T1-weighted Spoiled Gradient Recalled (SPGR) echo sequence from 1.5 T scanners was obtained on each participant, with 1 mm isotropic data acquired sagittally from the entire head. Slice thickness of 1.5 mm was allowed for GE scanners due to their limit of 124 slices. Total acquisition time was about 25 min and was often repeated when indicated by the scanner-side quality control process. More details on image acquisition can be found in Evans (2006).

Image preprocessing

All MR images were preprocessed by the following pipeline. First, skull, cerebellum and brain stem were automatically removed (Shi et al., 2012). Second, intensity inhomogeneity was corrected using N3 method (Sled et al., 1998). Third, each image was rigidly aligned to the age-matched brain atlas (Shi et al., 2011). Fourth, tissue segmentation of MR images was performed by using a longitudinally guided coupled level-sets method (Wang et al., 2013a, 2013b). Fifth, non-cortical structures were automatically masked and filled, and each brain was further separated into left and right hemispheres. More details on image preprocessing can be found in Li et al. (2014b, 2014c).

Cortical surface reconstruction and registration

For each hemisphere of each image, a topologically correct and geometrically accurate cortical surface was reconstructed using a deformable surface method (Li et al., 2012, 2014a). Herein, we adopted the

Table 1
The mean ages at the MR scanning of the 73 infants at 0, 1 and 2 years of age, as well as 64 young adults.

	0 year (days)	1 year (days)	2 years (days)	Adults (years)
Male	27.3 ± 13.1	390.0 ± 21.6	765.4 ± 37.4	18.7 ± 1.4
Female	23.0 ± 6.1	396.6 ± 22.4	748.2 ± 37.4	18.9 ± 1.4
All	25.5 ± 10.8	392.8 ± 22.1	758.1 ± 38.1	18.9 ± 1.4