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Characterization of the central sulcus in the brain in early childhood

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Abstract

Characterization of the developing brain during early childhood is of interest for both neuroscience and medicine, and in particular, is key to understanding what goes wrong in neurodevelopmental disorders. In particular, the cortex grows rapidly in the first 3 years of life, and creating a normative atlas can provide a comparison tool to diagnose disorders at an early stage, thereby empowering early interventional therapies. Zooming in on specific sulci may provide additional targeted information, and notably, an understanding of central sulcus growth can provide important insight on the development of laterality. However, there currently do not exist any atlases of

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specific changes in sulci as the brain grows. In this pilot study, we explore regional differences in the depth of the central sulcus between two and three year old infants using brain magnetic resonance images.

I. Introduction

The brain grows rapidly from birth to childhood, reaching 95% of its final volume by 6 years of age. Cortical folding begins at the gestational age of 16 weeks in the normal brain, but continues to evolve rapidly into early childhood [16]. Sulci are major landmarks of the cortex, and it has been shown that their depth can be a marker of functional specificities [6] or of developmental pathologies [15]. The patterns of these folds are impacted by genetic as well as environmental factors [2,14]. While there exists a lot of variation in the cortex between individuals, some consistent patterns are found in the cortical folds of healthy individuals, and it has been shown that subtle abnormalities in the folding pattern are associated with cognitive disorders such as schizophrenia, bipolar disorder, ADHD, Williams' syndrome and autism [9,17]. For example, [17] found that autistic and control children exhibit strikingly different relationships with age in terms of changes in brain morphology; the central, intraparietal and frontal medial sulci showed a significant and consistent pattern of abnormalities across different geometrical indices, such as the length and depth of the sulcus.

Understanding healthy cortical folding in early childhood is important to establish a baseline for normal cortical maturation. A few studies delve into cortical folding and growth in infancy [12, 16], however, the study of normal cortical development using MRI in early childhood is still at its early stages. Until recently, the potential for more accurate, quantitative in vivo diagnoses was hampered by the lack of large systematic studies of normal development from in vivo data, with which to compare abnormal cases. Several large databases of healthy children's brain MRI are currently being created, including for example the NIH MRI Study of Normal Brain Development [1], the Pediatric Imaging, Neurocognition, and Genetics Study [20], and the Advanced Baby Imaging Lab database that we will use here [14]. All of these databases are being funded to answer different questions about normal brain development, but in spite of all the new data coming in, cortical sulcal development is still poorly understood. Here we focus specifically on the evolution of the central sulcus, taking advantage of the large early childhood structural MRI dataset acquired as part of the Baby Imaging Lab (BIL) study of normal brain development [19]. This work inscribes itself as part of a larger study that we are currently undertaking to determine the development of major sulci in children 0–4 years old using the BIL dataset.

II. METHOD

A. Data

The brain volumes were chosen randomly from the Advanced Baby Imaging Lab's healthy children database. In this pilot study, the data used consists of T1-weighted brain MRIs of 2 and 3 year olds subjects, with 8 and 9 subjects in each group respectively. More precisely, the dataset used consists of high-resolution MP-RAGE images of healthy children, with

inclusion criteria including: singleton birth between 37 and 42 weeks gestation with no abnormalities on fetal ultrasound and no reported history of neurological events or disorders in the infant. Additional details on the data acquisition can be found in [7, 8]. Each subject or their guardian was informed of the goals of the study and signed a formal consent. The studies were approved by the Institutional Review Board of Brown University. All data was de-identified.

B. Processing

The brain volumes were first skull stripped using BrainSuite [18] and then intensity corrected using the N4 intensity correction in ANTs [3]. We then resampled the brain volumes to $1 \times 1 \times 1 \text{ mm}^3$ space and performed tissue segmentation using the BrainVisa Morphologist pipeline (<http://brainvisa.info>) [11]. Histogram analysis was tuned manually in some cases to achieve optimum results. After tissue segmentation and surface modeling, the pipeline produces a graph that contains meshes of each of the cortical sulci. A sulcal parameterization process was then applied to the left and right central sulci of each subject and depth was measured at each position along the sulcus, which resulted in a depth curve for each central sulcus, as described in [5, 6]. This method detects the dorsal and ventral extremities and provides a smooth isometric parameterization that, for every point on the sulcus, indicates its relative position between the two extremities [5]. For each position within [0 100], the depth at this position is estimated by measuring the length of the corresponding isoparametric lines. The resulting sulcal depth profiles have shown good inter-subject reproducibility for morphological statistical studies [4,6]. We computed the mean and standard deviation of the sulcal depth in the 2 and 3 year old subjects. To investigate the differences in the central sulcus depth between the two and three year old brains, we conducted a Mann Whitney test at each of the 101 positions. We then corrected for multiple comparisons via permutation testing.

III. RESULTS

The figures below contain the mean and standard deviation of the central sulcus of the 2 and 3 year old datasets for the left and right central sulci. Although the standard deviation is high, we see that the general shape is maintained and is similar to that seen in adults [6]. We also see in Fig. 2 that the right central sulcus of the 3 year old group has less variation in its depth profile.

The Mann-Whitney test performed to compare the distribution between the 2 age groups yielded significance ($p < 0.05$) in 11 locations between positions 67 to 82 in the right central sulcus. The same test yielded significance at 6 positions between 77 and 94 for the left central sulcus. The plots of the p-values are shown in Fig. 3. The overall p-value for the right central sulcus is 0.0077 and for 0.0262 for the left central sulcus.

IV. DISCUSSION

As with the adult data in [6], in Fig. 1 and Fig. 2, we see a steep incline in the depth profile from position 1 to around position 20, where we see a first peak. There is then a gradual increase in the depth profile until the next peak at around position 61, after which the curves

decline steeply. The average depth curve at age 3 is indeed very much like the adult one. However the curve at age 2 is not. After an increase to the first peak (superior peak) [6], it keeps on increasing to the second one (inferior peak). Both of these points are located in the vicinity of the somatotopic upper limb representation in the primary sensorimotor cortex, according to the approximate Talairach z-coordinates [6].

In adults there is a depth minimum between the two peaks, called the ‘Pli de Passage Fronto-parietal Moyen’ or PPFM, which is a buried gyrus that connects the frontal and parietal lobes through the central sulcus. This seems to really start to emerge between the ages of 2 and 3. Hence, our pilot study indicates that the shape of the depth profile is similar to the adult profile even at early ages. The main differences we see between the 2 and 3 year old subjects are in regions 67 to 82, past the inferior peak, towards the sulcal fundus. This is confirmed by testing for multiple comparisons. The entire central sulcus separates the primary motor and primary somatosensory cortices, hence, it is likely that the central sulcus will change as motor functions develop. We will investigate this in further detail adding covariates related to motor skills to better understand this finding. For example, it was shown in [10] that the middle and deep Mouth and Tongue Area activations are found along the anterior bank of the CS. Language develops rapidly in that age range, hence, it is possible that the differences seen are due to the acquisition of motor skills and development of the tongue between 2 and 3 years of age. In addition, significance in the right central sulcus was higher than on the left, though this may be due to increased variability on the left. More subjects need to be added into the study to confirm these results. We are also in the process of adding earlier ages in order to obtain a picture of early central sulcus development.

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Figure 1. Mean profile of the depth curves of the central sulcus of 2 year old data. Top: Right central sulcus, Bottom: Left central sulcus

Figure 2.
Mean profile of the depth curves of the central sulcus of 3 year old data. Top: Left central sulcus, Bottom: Right central sulcus

Figure 3.

The p-values plotted for each sulcal position. The green line represents the p-value of 0.05 and the red line represents $p = 0.01$. Top: Left Central Sulcus, Bottom: Right central sulcus.