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Central sulcus development in early childhood

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Abstract

Mapping out the development of the brain in early childhood is a critical part of understanding neurological disorders. The brain grows rapidly in early life, reaching 95% of the final volume by age 6. A normative atlas containing structural parameters that indicate development would be a powerful tool in understanding the progression of neurological diseases. Although some studies have begun exploring cortical development in pediatric imaging, sulci have not been examined extensively. Here, we study the changes in the Central Sulcus (CS), which is one of the earliest sulci to develop from the fetal stage, at early developmental age 1–3 years old using high resolution magnetic resonance images. Parameterization of the central sulcus was performed and results show us that the CS change corresponds to the development of the mouth and tongue regions.

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I. Introduction

Normal development of the brain is of key interest in both neuroscience and medicine. The brain develops rapidly during early childhood and cortical folding, which begins at 16 weeks gestational age keeps progressing. Hence, it can provide valuable insight into brain development [1]. Cortical folding parameters such as sulcal depth can be a marker of functional specificities or developmental pathologies [2], [3]. Some studies have shown that sulcal depth varies for right handed and left handed participants in the central sulcus [4], [5]. While cortical folds and sulcal parameters can be affected by genetics and environmental factors, there is consistent similarity in the patterns of folds and sulci of healthy individuals. As shown in a study of handedness [4], the central sulcus starts and ends in similar locations and has dips in similar positions along the sulcal path. Subtle abnormalities in cortical folding patterns can be indicative of diseases such as ADHD, schizophrenia, autism or bipolar disorder [6], [7]. It is therefore important to establish a baseline of normal cortical maturation, especially in order to gain more insight into the structural changes in neurological diseases. A few studies have investigated cortical folding patterns in childhood [1], [8], however, the study of normal cortical folding in early infancy is still in the beginning stages.

There exist several important challenges to characterizing normal cortical. First, biological differences with the adult brain that make it harder to use methods developed in adults, During early stages of life, the contrast and ratio of the white matter and gray matter also change rapidly, making it difficult to assess magnetic resonance images [9]. Additionally, there is a shortage of largescale systematic studies using in-vivo data. Currently, several large databases of healthy pediatric brain MRI are being generated including the NIH MRI Study of Normal Brain Development [10], the Pediatric Imaging, Neurocognition and Genetics Study (http://pingstudy.ucsd.edu), the University of North Carolina at Chapel Hill [11], and the Advanced Baby Imaging Lab database that we will use here (www.babyimaginglab.com).

Here, we focus on the changes that occur in the central sulcus (CS). Although some studies have shown cortical folding changes in early childhood [12], few studies investigate the various parameters of the individual sulci. The CS is one of the earliest sulci that develops at 21 weeks gestational age and is situated in between the motor and somatosensory cortices. Many functions associated with this sulcus develop rapidly in the early childhood period, including language and motor skills [13]. Previously we investigated the CS in two and three year old children and found differences in the CS in regions that corresponds to the tongue area, indicating language development [14]. In this study, we aim to comprehend better the changes in the CS corresponding to motor and sensory function development by including a younger age group of 1 year old subjects and also by exploring the growth pattern of the central sulcus with respect to age through means of linear regression.

II. Method

A. Data

We chose 12 brain volumes from the 1 year old, 2 year old and 3 year old groups from the Advanced Baby Imaging Lab database (www.babyimaginglab.com). The data used consisted of high resolution T1 MP-RAGE MRI scans (1.4–1.8mm^3) of healthy normal children with the following inclusion criteria: 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. Data acquisition details can be found in [15], [16]. 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 and all data was de-identified. The handedness of the subjects are not assessed in this study, as handedness can not be determined with certainty in the 1 year old group.

B. Processing

Brain volumes were first skull-stripped using the BrainSuite [17] software. The data was resampled to a common resolution, and linearly registered with 6 degrees of freedom to an age matched template using FSL FLIRT [18], [19].

The brain volumes were then intensity corrected using either the N4 intensity correction in ANTs [20][21] or geodesic intensity mapping [22] and resampled to a 1×1×1mm^3 space. Next, we used the BrainVisa morphologist pipeline [23] to perform tissue segmentation. The histogram of the gray and white matter was manually tuned to achieve an accurate brain mask and hemisphere split. Once the tissue segmentation and surface modeling were complete, the BrainVisa pipeline produced graphs containing the cortical sulci meshes. Using these graphs, we manually chose the CS. We then applied the sulcal parameterization pipeline in BrainVisa to the left and right central sulci of each subject, which resulted in a depth measure at each position along the sulcus. The sulcal parameterization process detects the dorsal and ventral extremities of the CS and computes a smooth isometric parameterization for the sulcus. This gives us a relative position between the two extremities for each point on the sulcus. The depth at each position between [0, 100] is computed by measuring the length of the corresponding isoparametric lines as shown in Figure 1.

In previous morphological statistical studies, the resulting sulcal depth profiles have shown good inter-subject reproducibility. We then computed the mean and standard deviation for each group (1, 2 and 3 year old groups) of the sulcal depth. The differences of the CS between the 1 year old and 2 year old groups and between the 2 year old and 3 year old groups was explored by conducting a Mann Whitney test at each of the 101 positions and then corrected for multiple comparisons via permutation testing using all the sulcal depth points along the central sulcus. The Mann Whitney test is used as we do not assume a Gaussian distribution of the sulcal depth.

Finally, to determine age-based trajectories, linear regression was then done using MATLAB to see how the CS changes at each of the 100 position within the ages of one to three.

III. Results

Fig. 2 shows the mean sulcal depth curve of the left and right CS in each group. In all three groups and on both hemispheres, there is a steep increase in the depth profiles from the superior part of the CS (position 1) to around position 30 (the superior peak). There is then a gradual increase in the depth profile until the next peak (the inferior peak) at around position 65, after which the curves decline steeply. We also notice a dip for the 3 year old age group at around position 50.

The Mann-Whitney test results along with permutation testing to correct for multiple comparisons showed significant difference ($p<0.05$) in the depth profile between the two and three year old group mostly within positions 67–84 in the right CS and within positions 6–29 in the left CS. The same test, when done to compare the one and two year old groups, showed significant difference ($p<0.05$) in the depth profile mostly within positions 65–78 in the left CS only.

The linear regression results, shown in Fig. 3, were averaged for two separate areas of the sulcus to explore specific ROIs. Here, the positions between 70–77 (corresponding to the mouth and tongue area, circled in red) and 13–19 (corresponding to the trunk/neck area, circled in red) were chosen and linear regression was performed for these specific areas. Fig. 3 shows the slope of change of each sulcal position for the left and right hemispheres.

The linear regression results of the mouth and tongue ROI yielded significant p-values of 0.0113 for the left CS and 0.0022 for the right CS, while the p-values for the trunk/neck ROI was 0.0037 and 0.0127 for the left and right CS respectively.

IV. Discussion

This study shows the progression of the CS in three different age groups. In all cases the overall shape of the depth profile is similar to that of the adult [2], however, the three year old group is much more similar to it.

The linear regression plots in Fig. 3 show significance in regions around positions between 6 and 30 as well as positions in between 65 and 80 in both left and right central sulci. It is also interesting to note that between positions 70 and 80, the slopes are of similar values in both hemispheres. The dip we see around position 50 in Fig. 2 for the 3 year old group is called the ‘Pli de Passage Fronto-parietal Moyen’, or PPFM, a buried gyrus connecting the frontal and parietal lobes through the central sulcus. This is seen in the adult CS quite clearly as well [2]. It is also interesting to note the negative slope shown in the same position around 50 in Fig. 3 as well. This may indicate the emergence of the buried gyrus, making the depth of the CS lesser, whereas the depth of the CS in the circled regions get larger.

The linear regression results of the mouth and tongue ROI and trunk/neck ROI also indicate significance showing there is a strong trend in development in these regions, as can be observed in the CS.

V. Conclusion

The CS may play an important role in understanding development as progression through various ages can be tracked. More subjects will be needed to improve statistical significance and to understand the development trajectory more accurately. In addition, handedness information will also be added in future studies investigating sulcal development differences in older age groups (36 months and above), when handedness is determined easily.

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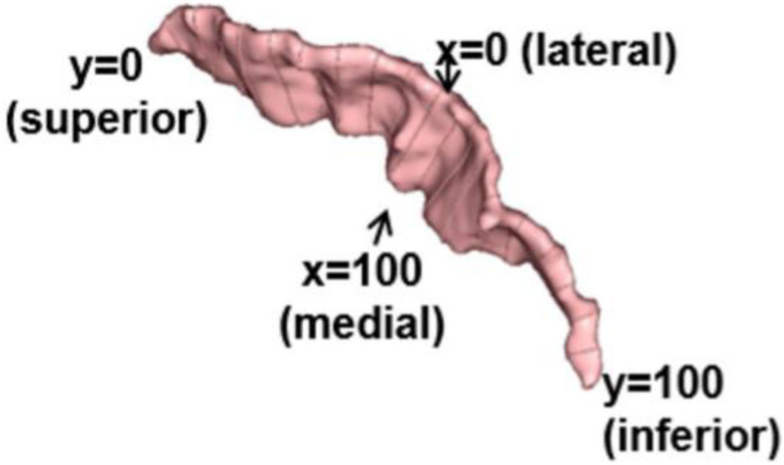

Figure 1.
An example of the central sulcus after parameterization using Brainvisa.

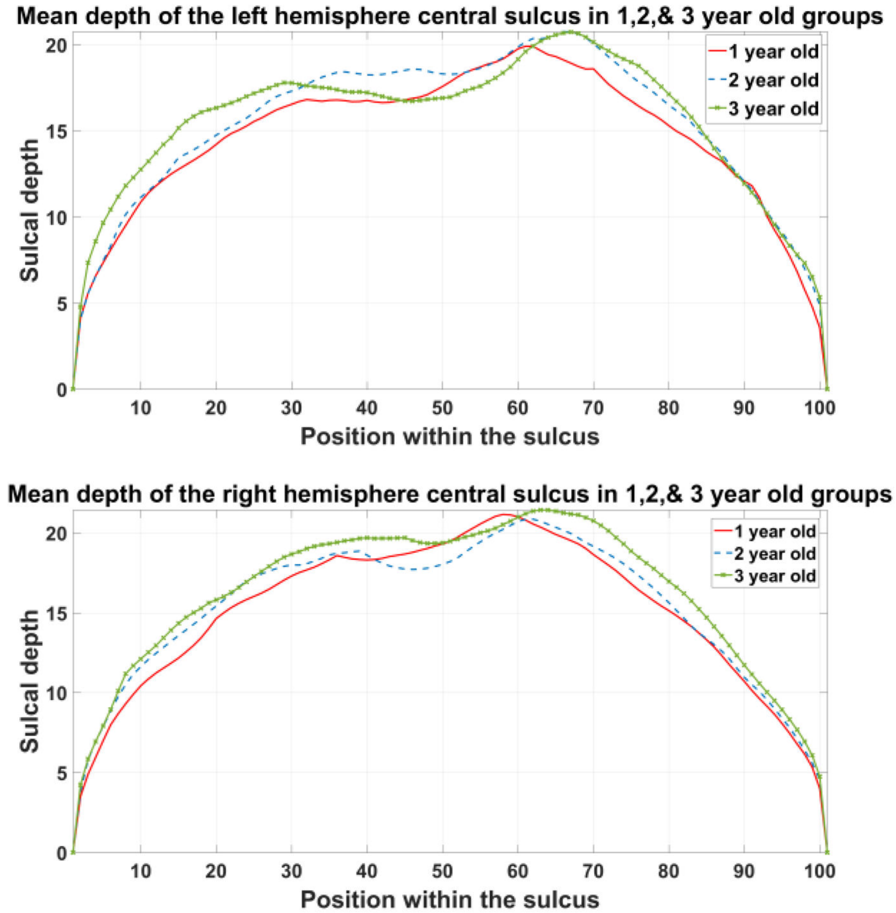

Figure 2.

The sulcal depth profiles of the left and right CS for 1, 2, and 3 year old groups. Top and Bottom: Left CS and right CS depth curves respectively.

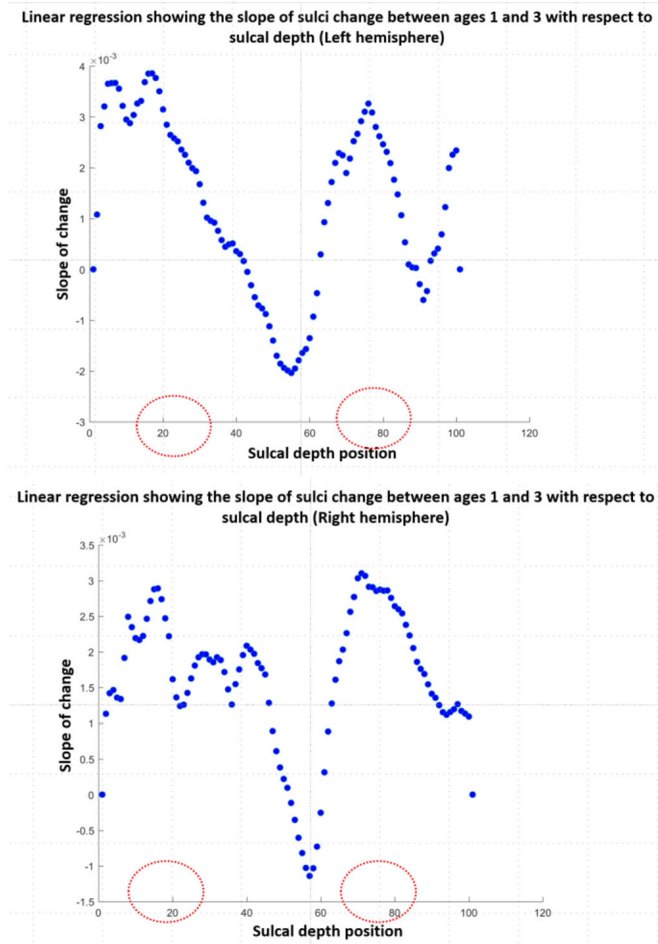

Figure 3.

Linear regression results showing the slope of change for all the sulcal positions in the CS in the left and right hemispheres. Top: Left hemisphere, Bottom: Right hemisphere. The red circles indicate the region of selected ROIs. The left circles indicate the trunk/neck region and the right circle indicate the mouth and tongue area.