Mapping primary gyrogenesis. In-utero, high-resolution structural MRI study of brain development in fetal baboons

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Introduction

Primary Gyrogenesis (PG) is a developmental process that transforms the lissencephalic cortex of a maturing mammalian brain toward its mature, gyrencephalic state by sculpting an intricate pattern of folds (gyri) and burrows (sulci). Although PG putatively emerges from and bears on other important ontogenic processes such as neuronal migration and differentiation, formation of functional associations and hemispheric lateralization is still poorly understood. This is partly because precise structural measurements of the morphological changes during primary PG are difficult to obtain. We demonstrate that a novel *in utero* MRI protocol developed specifically for high-resolution imaging of fetal brain can be used for precise tracking of the progress of global and regional gyrification in fetuses of a non-human primate (baboons).

Methods

Six pregnant dams with pregnancy terms from 17 to 25 weeks were imaged during a total of 10 sessions. All imaging was performed at the Research Imaging Institute, UTHSCSA using a Siemens 3 T Tim Trio MRI scanner (Siemens, Erlangen, Germany). High-resolution (isotropic 500µm), high gray matter/white matter/CSF/amniotic fluid contrast images of fetal cerebra were acquired using a 3D, balanced steady-state free precession (bSSFP) protocol with respiratory gating and retrospective motion-correction. The progress in cerebral maturation was tracked by global and regional measurements: the brain volume, cortical surface area, gyrification index (GI) and length and depth of ten primary cortical sulci.

Results

The cortical surface at 17 weeks was mostly lissencephalic with the GI of 1.04 (Figure 1). Only two cortical structures, the *sylvian* and *superior temporal fissure*s, were distinguishable at that age. However, shortly thereafter, at 20 weeks, an-adult like pattern of gyrification was observed for every brain. This change was accompanied by an accelerated growth in cerebral brain volume and cortical surface area. Analysis of the rate of growth in the average sulcal length was higher than that of the average sulcal depth (3.3±0.4mm/week vs. 0.68±0.1 mm/week) even when the rates of change were normalized as a percentage of the average adult values (8.0±1.1% vs. 5.2±0.9% per week). The apparent consequence of this was that at the 24th week the average sulcal length was at nearly 80% of its adult value; compared to only 47% for the average sulcal depth. Therefore, postnatal development is responsible for only ~20% of changes in the sulcal length and for over 50% in the changes in sulcal depth.

Discussion

Aspects of these trends in gyrification have previously been reported [1], but the findings of a contrast between rates of growth in sulcal length are novel. This finding is believed to a manifestation of the difference between primary and secondary gyrification. Primary gyrification is responsible for elongation of the cortex and growth of sulci along the long (length) axis while the secondary gyrification is responsible radial expansion and growth of the gyral crowns due to myelination of the underlying white matter.

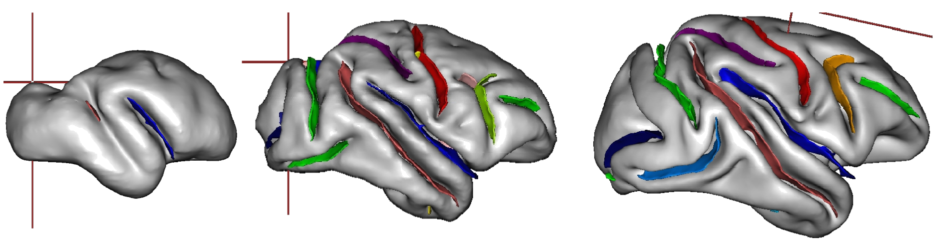

Figure 1. Fetal images were analyzed at weeks 17, 20 and 25.

Conclusion

We used high-resolution 3D MRI to quantify some of the global and regional fetal cerebral ontogenic changes in baboons during primary gyrogenesis (weeks 17-25 of fetal development). During this period, the fetal cerebrum undergoes a rapid transformation from the lissencephalic to the gyrencephalic state and this is accompanied by accelerated growth in brain volume and cortical surface and folding of the cortex to form primary sulci and gyri. Our findings indicate that primary gyrogenesis is a complex process and that changes in sulcal length and depth are influenced by diverse factors with the former being changed by expansion of the cortex along the tangential direction, while the latter being influenced by radial expansion of cortical surface, possibly due to myelination of gyral white matter.

Acknowledgment: This work was supported, in part, by the K01 #EB006395, NIH #P51-RR013986, 1R01AG029412-01, P01 HD047675 and R24 RR013632.

Reference

[1] Smart IH, McSherry GM. Gyrus formation in the cerebral cortex in the ferret. I. Description of the external changes. *J Anat* 1986; **146**: 141-152.