Observation of Intrinsic and Extrinsic Mechanisms during Cortical Convolution Development

L. Srinivasan[1,2], H. Xue[1,2], S. J. Counsell[1], J. M. Allsop[1], J. A. Fitzpatrick[1], G. Durighel[1], A. D. Edwards[1], M. A. Rutherford[1], D. Rueckert[2], and J. V. Hajnal[1]

[1]Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College London, London, London, United Kingdom, [2]Department of Computer Sciences, Imperial College London, London, London, United Kingdom

Introduction: During evolution the cortex has expanded enormously in surface area leading to a gyrencephalic brain in humans. This process is recaptured during the third trimester; i.e. a smooth cortex at 24 weeks is transformed in to a highly folded surface by 40 weeks gestation. As convolutions are closely related to functional cortical units (1), the study of gyrification in preterm infants will not only provide important insights into the underlying mechanistic processes, but may also assist in deciphering the functional deficits seen in these infants. The intrinsic theory proposed by Griffin LD (2) explains cortical convolutions by changes in the intrinsic geometry of the cortical surface whereas the extrinsic theory of Van Essen DC (3) hypothesises that extrinsic mechanical tension of white matter tracts would pull strongly connected cortical regions and form folds. These theories imply quite different cortical developmental patterns and can be explored by studying the geometric properties of MRI derived cortical surfaces.

Aim: To determine the intrinsic and extrinsic geometric curvatures of the cortex in a group of preterm infants during the third trimester.

Methods: 120 preterm infants born < 34 weeks gestation were recruited from Hammersmith Hospital neonatal unit. T_2-weighted pseudo-volumes [TR 7578ms, TE 160 ms, FOV 220 mm,1 NEX and voxel dimension 0.86 x 0.86 x1 mm] were acquired after ethical approval on a 3 T Philips Achieva System using an 8 channel head coil. The cortex was automatically segmented and extracted using an extended Expectation maximisation method with MRF field constraint and correction of mis-classified tissue class caused by partial volume effects (4). Curvature analysis was performed on the inner cortical surface reconstructed using level set method. This surface was chosen as it is most robust against loss of detail in the sulcal fundi. The surface area (SA) was obtained from the triangular mesh fitted on the white matter segmentation and the volume from the cortical segmentation.

Curvature indices: Isoperimetric ratio (IPR) was calculated as $SA/volume^{2/3}$ and measures the excess surface area for given volume. The two principle curvatures *k*max and *k*min were computed at each point of the level set function for the whole area *A*, from which GLN and ECI were computed. **L_2 norm of Gaussian curvature (GLN)** is the sum of squares of the Gaussian curvature K where $K = k\max \times k\min$ and measures the intrinsic geometry of a curvature. **Folding index or extrinsic curvature index (ECI)** is computed as $1/4\pi \iint k\max(k\max - k\min)/dA$ and measures the extrinsic curvature.

Results: The median gestational age at birth was 28.1 weeks. These infants were scanned between 25 and 50 weeks post menstrual age. The median weight and head circumference at scan were 1.65 kg and 29.7 cms respectively. 15 infants had significant cerebral or cerebellar lesions clearly seen on their images. The surface area and cortical volume showed exponential growth during the third trimester; however the isoperimetric ratio increased only until 36 weeks gestation after which it plateaued off (fig 1.a). The cortical surface was further explored using the curvature measurements; the ECI was relatively static until 36 weeks gestation after which it increased (fig 1.b), whereas the GLN linearly increased throughout the third trimester (fig 1.c). Multiple regression showed that the SA was more strongly related to ECI ($p<0.0001$) than GLN ($p=0.0002$). In the presence of lesions both the surface area and volume were proportionally reduced with the ECI and not the GLN being significantly reduced.

Discussion: These results showed a rapid increase in the cortical surface area for a given volume until 36 weeks. During this period the extrinsic curvature was relatively static whereas the GLN increased with gestational age. This suggested that the surfeit in SA changed the intrinsic geometry of the cortex and caused fissuration similar to Griffin's observations. After 36 weeks the IPR plateaued off and coincided with an increase in ECI. This suggested that the proportional increase in SA and volume lead to changes in the extrinsic curvature and caused folding possibly due to tension between the interconnected cortical regions as implicated by Van Essen. These findings were confirmed by analysis of a cohort of infants with lesions, where proportional reduction in SA and volume were related to reduction in ECI and not the GLN.

Conclusions: A combination of both intrinsic and extrinsic mechanisms appear active during cortical convolution formation albeit at different phases of cortical gyrification; the key developmental factor being differential growth of cortical SA and volume.

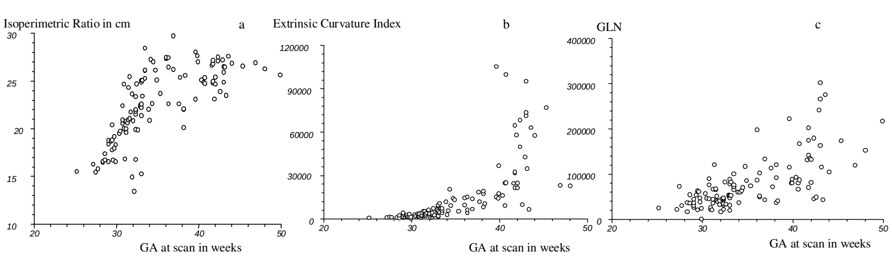

Figure 1: Depicts the IPR (a), ECI (b) and GLN (c) of preterm infants between 25 and 50 weeks of development.

References: 1.Brodmann K. Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Barth, Germany; 1909. 2.Griffin LD. The intrinsic geometry of the cerebral cortex. J Theor Biol 1994 Feb 7;166(3):261-73. 3. Van E. A tension-based theory of morphogenesis and compact wiring in the central nervous system. Nature 1997 Jan 23;385(6614):313-8. 4.Xue H, Srinivasan L, Jiang S, Rutherford M, Edwards AD, Rueckert D, et al. Automatic segmentation and reconstruction of the cortex from neonatal MRI. Neuroimage 2007 Nov 15;38(3):461-77.