Cortical curvature and allometric scaling of cerebral cortex in preterm infants

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Introduction: The survival of preterm infants is increasing due to developments in neonatal care. However, premature delivery creates a major environmental stress during a period when the architectonic and connectional specification of the human cerebral cortex is developing rapidly, and many preterm infants develop significant neurodisability including cognitive delay, language disturbances and behavioral abnormalities. The main feature of third trimester cortical development is a striking increase in the folding and surface area of the cortex similar to that seen during mammalian evolution. Allometric analysis show that during evolution the cortical surface area is related to the total cerebral volumes by a scaling exponent of more than one and a recent study using a simple slice wise analysis described a similar allometric scaling during brain growth in preterm infants [1]. To investigate cortical development further we have used a new approach for cortical segmentation and reconstruction to study the cortical thickness, surface area, gyrification (measured as mean curvature) and volume in relation to total brain volume, re-estimating the scaling exponent and testing the hypothesis that as cortical surface area and mean curvature increases there is no change in cortical thickness.

Methods: MR Image Acquisition: MRI scans were performed on a 3T Philips Intera system (Best, The Netherlands) after ethical approval and parental consent. Preterm infants were sedated using chloral hydrate and monitored with pulse oximetry and electrocardiographic monitoring. Infants had ear protection and were stabilised using a suction-evacuated pillow. T1 weighted MPRage (TR17/TE 4.6 ms, FOV 210, matrix 256 x 256, flip angle 30°) volume datasets; voxel size of 0.86 x 0.86 x 0.86 mm and T2-weighted fast spin echo pseudo-volumes (TR 11712 /TE 160ms, FOV 220, matrix 224x224, flip angle 90°); voxel size of 0.86 × 0.86 × 2 mm with 50% slice overlap were obtained.

Brain segmentation: Gray matter, white matter, CSF and deep gray matter segmentation was performed using a modified Gaussian mixture model (GMM) and expectation-maximization (EM) scheme. A knowledge based rule was developed and integrated into the classic EM approach to correct mislabeled partial volume (MLPV) voxels resulting from the inverted gray-white contrast seen in neonatal brain images. If a voxel was recognized to be misclassified, the prior probability of the incorrect tissue class was decreased and other tissue classes were favored by increasing their prior probabilities.

Cortical reconstruction: Cortical reconstruction was performed from the resulting segmentation using a level set method based on resolving the standard level set equation. More details of this algorithm and validation results can be found in [2,3]. Cortical surface area and mean curvature were calculated from the inner cortical surface and thickness was determined from the difference between the inner and outer surfaces fitted to the cortical segmentation Total cortical volume was calculated from thickness and surface area measurements. Total cerebral volumes were calculated after subtracting the CSF and non brain voxels from a total brain mask.

Results: 21 preterm infants born at a median age of 27.86 (range 24.43- 32.71) weeks, were scanned at a median gestational age of 33.86 (range: 27.17-44.1) weeks. Median birth weight of the infants was 1.16 (range: 0.62-1.8) kg and the median head circumference was 26.3 (range: 20.5-29.5) cm. The median weight and head circumference at scan were 1.72 (range: 0.8- 3.68) kg and 29 (range 24.3-37) cm respectively. 2 infants were scanned serially thrice. The median thickness of the cortex was 1 mm (range of 0.86-1.13mm). The median of the mean cortical curvatures of all the infants was 0.55 (range 0.38-0.97). The median cerebral volume, cortical surface area and cortical volume were 224.27 cm^3 (range 133-443.24 cm^3); 594.47 cm^2 (range 288.15-1514.96 cm^2); 52.77 cm^3 (range 26.6-118.17 cm^3) respectively. All these measures were linearly related to gestational age at scan. The mean cortical surface area, cortical volumes and cerebral volumes were log transformed to assess scaling relationships. Figure 1 shows that the log-log plot of cortical surface area against total cerebral volume is linear indicating a power law relationship and a random effects generalised auto regression showed a scaling exponent of 1.4 (95% 1.35-1.57). The cortical volume is linearly related to total cerebral volume (r=0.988, p=0.0001). Cortical thickness did not show any relationship with gestational age at scan.

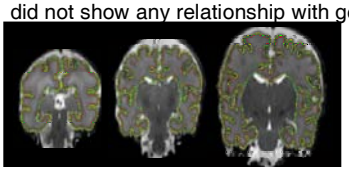
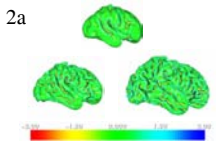


Fig 1: Inner (red), middle (green) and outer (yellow) cortical surface reconstruction in a coronal T2W scan of an infant scanned at 29.86, 34, 39.86 weeks.



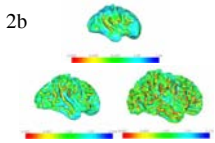
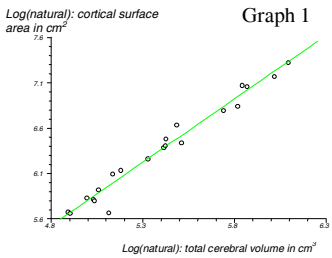
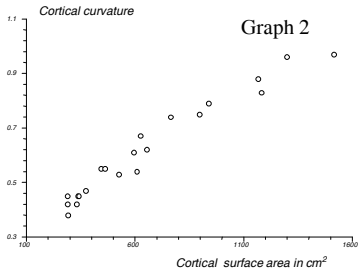


Fig 2 (a): 3D rendering of middle cortical surface at 29.86, 34 and 39.86 weeks with a colour coded scale of the mean curvature showing an increasing in the mean curvature and surface area and (b) colour coded scale of thickness at the same gestations.





Graph 1: Depicts a log- log plot of the cortical surface area on the y-axis and total cerebral volume on the x-axis. The regression equation is given by Log(natural): cortical area in cm^2 = 1.397787 Log(natural): total cerebral volume in cm^3 -1.182856
Graph 2: Illustrates the linear relationship between increase in surface area in cm^2 and cortical curvature (r=0.97, p=0.0001)

Discussion: The previous estimation of a surface area to volume scaling exponent of 1.29 (95% confidence limit 1.25-1.33) in preterm infants was imprecise because it measured surface area and volume by counting voxels on individual slices rather than a reconstructing a continuous smooth cortical surface [3]. The present study used an automated cortical segmentation and surface reconstruction program to estimate a more accurate scaling exponent of 1.42 (double that of a sphere) and showed that cortical growth is achieved by increasing gyrification without increase in cortical thickness, confirming that surface area is a biologically useful measurement of cortical size in allometric studies [4].

References: [1] 0.Kapellou, et al PLOS Medicine 2006 [2&3]. H. Xue, et al submitted to ISMRM 2007. [3.[4].C.F. Stevens Nature 2001.