Investigating the spatial folding pattern of very preterm neonatal cortex scanned at term-equivalent age

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Introduction Advances in neonatal care have improved the survival of infants born prematurely; the rates of disability and neurodevelopmental problems in survivors remain unchanged [1]. Advanced MR techniques have revealed a common neuroimaging phenotype of infants born very preterm compared with term born controls. MR biomarkers of disability and neurodevelopmental problems have the potential to improve neonatal intensive care, and target post discharge interventions to the babies at highest risk of adverse outcomes. This work analyses the cortical surface properties of 92 babies born before 32 weeks gestational age (GA). High-resolution T1-weighted data are segmented using an automated, adaptive expectation maximisation algorithm and the grey matter and white matter interface optimised using a level-set. The curvature properties of this interface are analysed to investigate differences in the spatial pattern of cortical folding.

Method: 92 high-resolution T1-weighted term-equivalent MRI of very preterm neonates (T1/T2=17*ms*/6*ms,* FA=21°, 0.39x0.39x1*mm,* mean GA 27.1±2.7wks, mean birthweight: 973±364g, M/F 48/44). We use a modified expectation maximisation segmentation algorithm [2] that makes use of adaptive tissue class priors to simultaneously estimate the grey and white matter segmentation and define the registration mapping from the space of the priors to the data. We subsequently use a cortical surface analysis based on [3] using a level-set routine to define the grey/white matter surface. The curvature of any point on this surface can be summarised by two values, the shape index and curvedness, and we can form a two-dimensional histogram from the distribution of these values over an arbitrary region. Since gyrification is mostly complete by term equivalent age, to analyse folding in individual lobular regions we register the MNI atlas [4] to the space of the priors and propagate onward to the individual data using the registrations found by the segmentation method, thus we can use the intersection of the major atlas lobes with the segmentation result to analyse lobular cortical regions (see Figure 1). By correlating the cortical surface histograms found for each lobe across all 92 subjects we can investigate the spatial pattern of cortical folding using non-linear dimensionality reduction (Isomap).

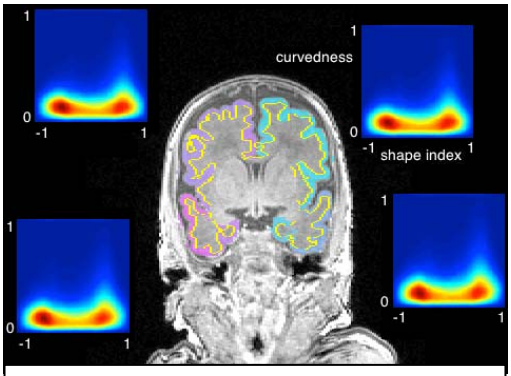

Fig 1) Compound image for a single subject T1-weighted MR. Grey/white matter boundary shown in yellow and grey-matter lobular segmentation shown in pastel. Associated with each lobe is a 2D histogram of shape index vs curvedness, the two peaks correspond to gyral

Results: To investigate the inter-relationships between histograms we looked for major trends in the data revealed on a learned manifold; distances between histograms were defined by the cross-correlation between histograms and this approach yields visually clearer results than a standard Euclidean analysis. The data is plotted in two coordinates of the learned manifold and color-coded by a given property of interest. The cortical histograms were shown to represent the underlying white/grey matter ratio (Fig. 2a). Figure 2b shows that there is an anterior-posterior trend in complexity from frontal region (red) to occipital region (magenta). This pattern is dominant along the anterior-posterior axis, the corresponding medial-lateral trend is found to be strongly symmetric with high histogram similarity between corresponding lobes on opposing hemispheres. The anterior-posterior trend in cortical complexity may reflect the emerging adult pattern of cortical folding.

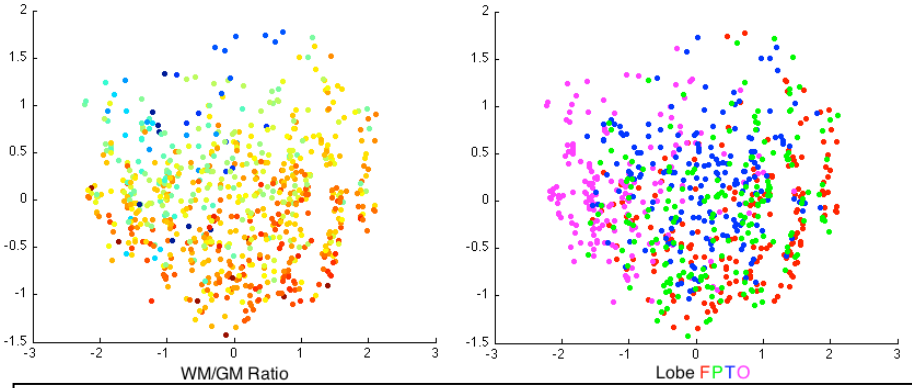

Fig. 2) Histogram data plotted by the first two coordinates found by Isomap color-coded by A) white/grey matter volume ratio found from the image segmentation and B) color-coded by corresponding lobe from posterior to anterior (**F**rontal, **P**arietal, **T**emporal, **O**ccipital).

Conclusion: This work has revealed consistent spatial patterns in the cortical surface in a cohort of 92 very preterm infants scanned at term. The lobular cortical folding pattern is correlated with position on the anterior-posterior axis and also the grey/white matter volume ratio. The spatial pattern of folding in preterm neonates has a generic phenotype and further work will determine to what extent it is predictive of the emerging adult folding pattern.

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