Analysing the cortical folding pattern of very preterm neonates scanned at term-equivalent age: correlations with diffusion tensor tractography

Andrew Melbourne[1], Giles S Kendall[2], Manuel J Cardoso[1], Nicola J Robertson[2], Neil Marlow[2], and Sebastien Ourselin[1]
[1]*University College London, London, United Kingdom,* [2]*University College Hospital, London, United Kingdom*

Introduction: Infants born prematurely are at increased risk of adverse neurodevelopmental outcome. The measurement of white matter structure and features of the cortical surface can help define biomarkers for neurodevelopmental outcome. This work analyses the cortical surface and white matter diffusion properties of 19 infants born very preterm (less than 32 weeks gestational age). High-resolution T1-weighted data are segmented and the grey matter / white matter interface extracted. The local folding properties of this interface are correlated with indices of deep grey matter connectivity using probabilistic diffusion tensor tractography.

Method: 22 infants born very preterm (<32weeks gestation) underwent an MRI at term equivalent age. High resolution T1-weighted imaging (Figure 1A) and 30 directional diffusion tensor imaging ($b=600s.mm^{-2}$) were acquired alongside an un-weighted image. Segmentation of the T1 weighted images was performed using a modified expectation-maximisation segmentation [1] to extract the cortical and deep grey matter (Figure 1B/C) followed by a level-set driven cortical surface analysis [2] (Figure 1D). We also used a fast-marching algorithm on the grey/white matter interface, so that at any point on the cortical surface we can extract properties of the local folding pattern (marked red in Figure 1D). Each region corresponds to about 1.5% of the total surface area. Segmentation data is aligned with an affine transform to the diffusion data (Figure 1E), and the deep grey matter segmentation is used as a seed mask for probabilistic tractography [3]. Tractography was performed for every deep grey matter voxel (example shown in Figure 1F). For each tract that meets the cortical surface we find the corresponding local cortical surface properties in the form of a 2D histogram [2], which are then combined to generate a weighted summation of the cortical folding properties associated with each deep grey matter voxel. The cortical complexity may be summarised by the entropy of this histogram. This process results in a deep grey matter segmentation, coded by the cortical folding properties of the surface to which it is connected. Finally we correlate the connectivity results of the cortical folding pattern with properties of the specific tract system (average FA found within the tract and number of cortical connections) emerging from each deep grey matter voxel.

Results: Correlating the cortical surface histogram entropy with the connectivity results reveals some interesting trends. Higher tract-average FA is found in the projective cortico-spinal tracts; these tracts form early in gestation and are some of the first regions to become myelinated. In addition increased tract FA correlates with increasing numbers of connections to the cortex (although this result might reflect the difficulty of tractography in regions of low FA). However, we do find strong linear relationships between the number of connections to the cortex, the tract volume and the average tract FA. The intra-subject relationship of the number of connections to the cortex to cortical folding is found to be highly non-linear; the average result of Spearman tests for all 18 cases finds a correlation of $\rho=-0.30\pm0.11$, thus entropy is found to decrease with increased connections to the cortex.

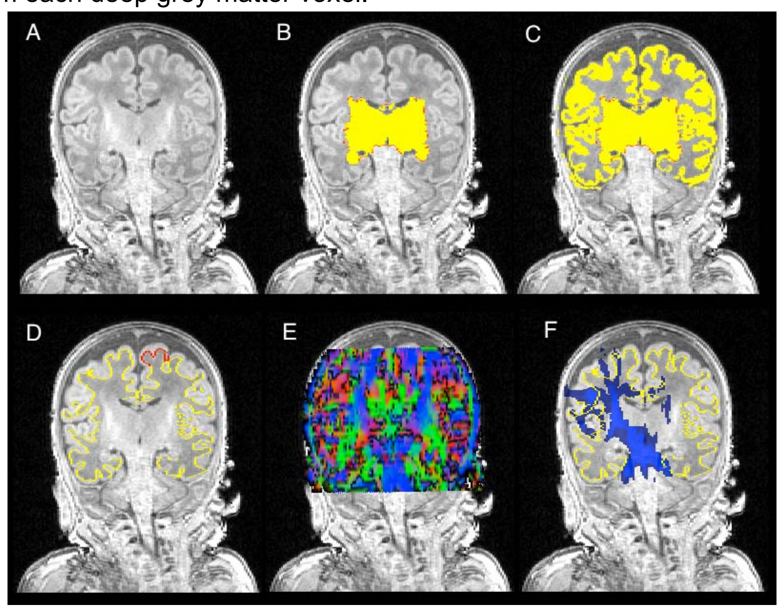

Fig 1) A) T1-weighted term-equivalent MRI B & C) deep and cortical grey matter segmentations D) grey/white matter interface E) DTI registered to T1-weighted space F) Corticospinal tractography in T1-weighted space.

Conclusion: This work has developed a methodology to link the cortical folding pattern with the underlying pattern of white matter connectivity. The spatial pattern may allow inference on the connectivity and thus the integrity of the deep grey matter. The use of this work is two-fold: the negative correlation of the cortical surface entropy with connection strength implies that when the number of connections to the cortex is high, the cortical complexity is lower. As the cortical surface entropy is likely to be reduced in proximity to substantial deep sulci this finding would be in keeping with the predictions of the axonal tension hypothesis in which major sulci are expected to correlate with stronger connections. Subtleties in the combined connectivity-cortical folding pattern might be linked to underlying pathology, such as the biological manifestation of white matter damage. Further work will investigate how the cortical and white matter patterns represent the underlying notion of a combined thalamocortical system.

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