Variegation in the adolescent cortical folding pattern in preterm and control populations

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Introduction: Preterm birth is associated with reduced cognitive performance persisting from birth, through childhood to adolescence. Recent studies have suggested that reduced white matter volumes [1] and a delayed pattern of cortical folding are two potential determinants of cognitive and neurodevelopmental outcomes. This work investigates the associations between the volume of white matter and the morphology of cortical convolutions in a group of adolescents born preterm and a group of controls. We aim to measure to what extent the preterm phenotype persists at adolescence in order to better understand the processes underlying cortical maturation in the preterm population and develop robust biomarkers for future intervention studies.

Method: Data from a cohort of 50 adolescents born preterm (14-16 years, born at <33 weeks gestation, mean 27.5 weeks, 27 with positive cranial ultrasound findings at birth) and 39 term born controls, matched for age and sex, are included in this study [1]. Volumes of grey and white matter (GM/WM) are calculated from 3D-FLASH images acquired at 1mm isotropic resolution using an automated iterative segmentation routine [2]. The GM/WM boundary is used to initialise a level set. The surface defined by this level set allows the concavity to be used to define a cortical sulcation ratio defined as the number of voxels found to be on a sulcus relative to the total number of voxels [3,5]. A regional sulcation ratio can be defined by combination with a regional parcellation generated by a multi-atlas technique and label fusion strategy [4] (see figure 1). The multiple labels from this atlas are grouped into lobe-based regions defining the frontal, temporal, parietal and occipital regions on both left and right hemispheres.

Results: Figure 1 summarises the key results found in this cohort. Both grey and white matter volumes are found to be significantly reduced. The sulcation ratio calculated over the surface defined by the level set is found to be lower and more variable in the preterm population ($p<0.0001$). The sulcation ratio found on each lobe reveals a strong anterior-posterior trend with group differences most pronounced over parietal and temporal regions. Sulcation ratios are found to be higher in the left compared to right hemispheres-in both groups. Sulcation ratio was highly correlated with WM volume ($R>0.7$) and with GM volume ($R=0.46$) in both groups.

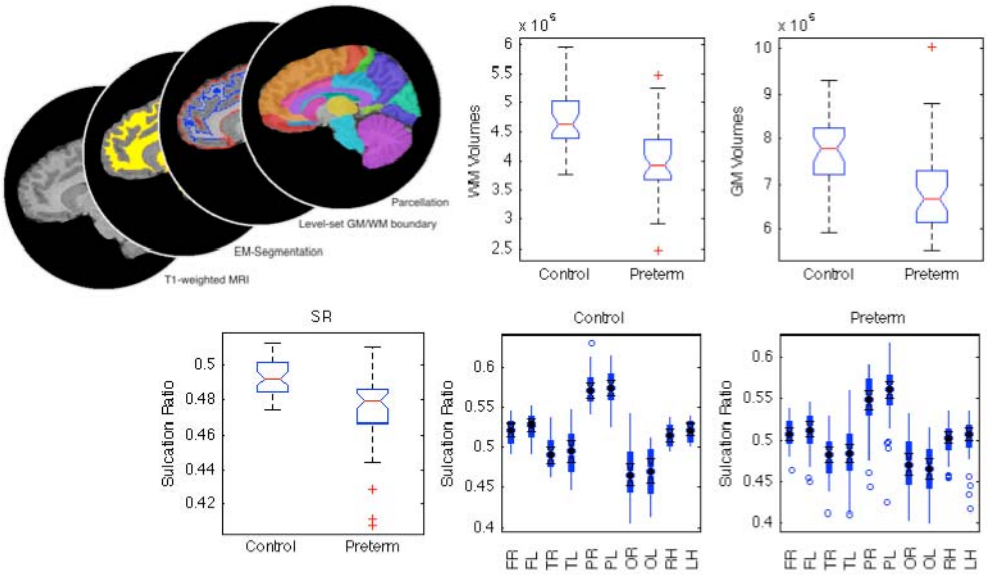

Fig 1) Example segmentation, cortical folding and parcellation followed by a) WM volumes, b) GM volumes and c) the global sulcation ratio for all 89 infants. d) & e) regional sulcation ratios found on gross lobar regions for **F**rontal, **T**emporal, **P**arietal and **O**ccipital (**L**eft/**R**ight) for control and preterm groups.

Conclusion: This study provides a quantitative analysis of the cortical folding pattern in human preterm brain at adolescent age. By comparing these findings to findings in preterm newborns, a clearer picture on the developmental trajectory in the preterm population can be made. For example, the strong correlation of sulcation ratio to WM volume in adolescence could be of potential value in predicting cognitive development from cortical folding obtained in infancy. In addition, differences in SR are largest over the parietal and temporal lobes, both regions known to develop during the preterm period [5]. Since it is of clinical importance to determine if the cortical folding pattern can be used as biomarkers of later cognitive outcome, future work will investigate how the cortical folding analysis in newborns [5] contributes to accurately predicting both the appearance of the adolescent preterm cortical folding pattern and scores in longitudinal neurodevelopmental assessments, potentially allowing earlier diagnosis and targeted interventions at a young age.

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