# Cortical folding patterns in extremely preterm born young adults

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**Synopsis:** Preterm born individuals may be subject to abnormal gyrification, associated with behavioural-cognitive deficit. In this work we perform a cortical folding analysis of the white-grey matter boundary in extremely preterm born young adults when compared to their term born peers, through a groupwise analysis using joint spectral matching. The results show that there are significant differences in folding in the temporal lobe, results which could be connected with poor executive function and language deficits in the extremely preterm cohort.

**Introduction:** Extremely preterm birth overlaps with a period of major changes in cortical anatomy, when the brain develops from a lissencephalic state to a highly folded one. Due to this timing, most of the gyrification has to take place under the altered conditions of the extrauterine environment. Abnormal gyrification patterns have been associated with cognitive-behavioural deficits among subjects [1]. Previous studies have shown differences in cortical folding between preterm and term born infants [2]. Some of these differences may persist into adulthood, thus it is important to study cortical folding group differences between adults born extremely preterm and controls. Being able to map these differences might illuminate our understanding of brain development during this crucial period and its correlation with psychological outcome.

**Methods:** We acquired T1-weighted MR data from 43 young adults born at an average gestational age of 24.83±0.84 weeks (28 females + 15 males) and 18 control subjects (10 females + 8 males), all aged 19. We segmented the scans of each patient into 6 tissue classes (white matter, grey matter, cerebrospinal fluid, deep grey matter, cerebellum and brainstem) using the GIF framework [3]. To study the cortical folding, we looked at the white-grey matter boundary and used the white matter segmentations to obtain smooth triangle-based meshes of this boundary. For each group (preterm and control) we chose a random subject as initial template and mapped all of the other surfaces using joint spectral matching [4] with a CPD initialisation. We used the mappings to create mean shapes of the white matter surfaces for both extremely preterm and control cohorts. Morphological changes between the two groups were then investigated by computing the vertex displacements in the mean surfaces after another step of joint spectral matching. We computed the Hotelling $T^2$ two sample metric to assess local group difference and derive local statistical p-values for all corresponding points [5]. We fitted a multivariate general linear model to our data, correcting for white matter volume and gender, computed the vertex-wise T-statistics using a random field theory multiple-comparison correction to yield an equivalent p-value of 0.05 and finally generated the map of groups difference.

**Results:** The white matter volume of the mean shapes is larger in control subjects (436.34±41.02 $cm^3$) than in preterm subjects (403.59±46.77 $cm^3$). The vertex displacement map shows local shape differences in cortical folding between control and preterm groups mainly in the temporal lobe and frontal-parietal region, while there are just small variations in the prefrontal and occipital regions (Figure 1). Moreover, there seems to be asymmetry, there being larger variations in the left hemisphere than in the right, especially in the parietal region. After correcting for white matter volume and gender, the folding group shape significance maps show that the differences in the temporal lobe are statistically significant at a $p=0.05$ significance level between the preterm and control groups. The left-right asymmetry is not significant.

**Discussion/Conclusion:** In this study we investigated the differences in cerebral folding between extremely preterm and term born adolescents by looking at the vertex displacements after matching the white-grey matter surfaces using spectral matching. Vertex displacements differences are larger in the temporal and frontal-parietal regions, however, after correcting for gender and white matter volume, which is smaller in preterm born individuals, only the differences in the temporal lobe remain statistically significant. This result is consistent with previous studies that found reduction in white and grey matter volumes of the temporal lobes in other preterm cohorts [2] [5], usually connected with neurological deficits, poor executive function and language deficits. Our future work will analyse the possible functional implications of the shape differences with cognitive and language performance, as well as investigating the inter-relationship between cortical white matter volume and shape and the specific physical links of the temporal lobe with regions to which it is connected including the basal ganglia.


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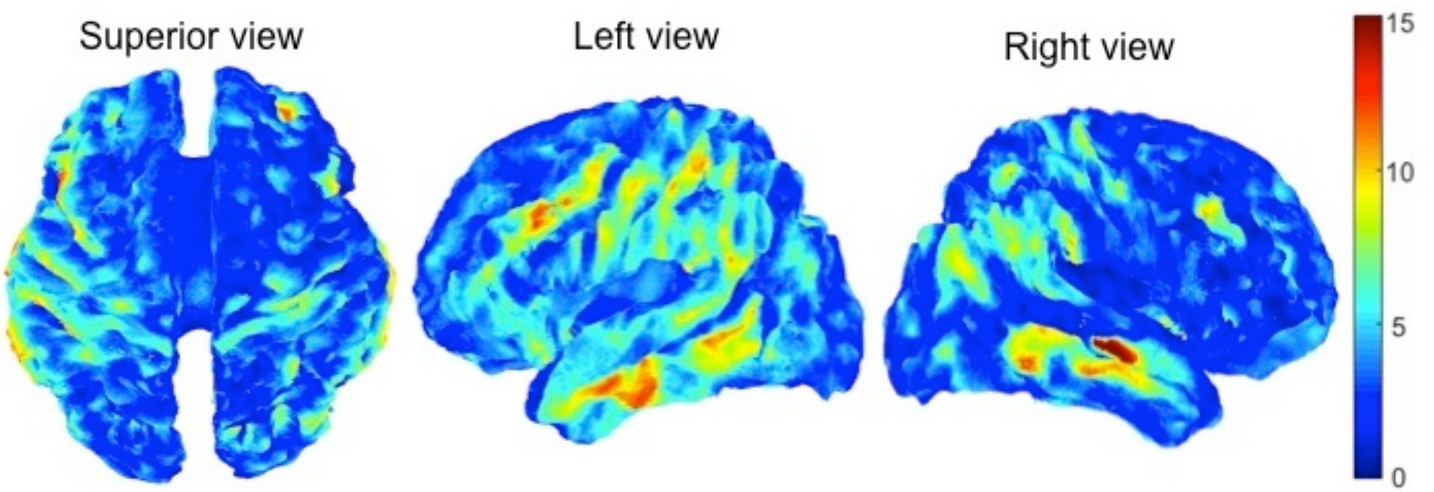


**Figure 1. Local shape differences between the preterm and term mean white-grey matter boundary. Units of scale are mm.**

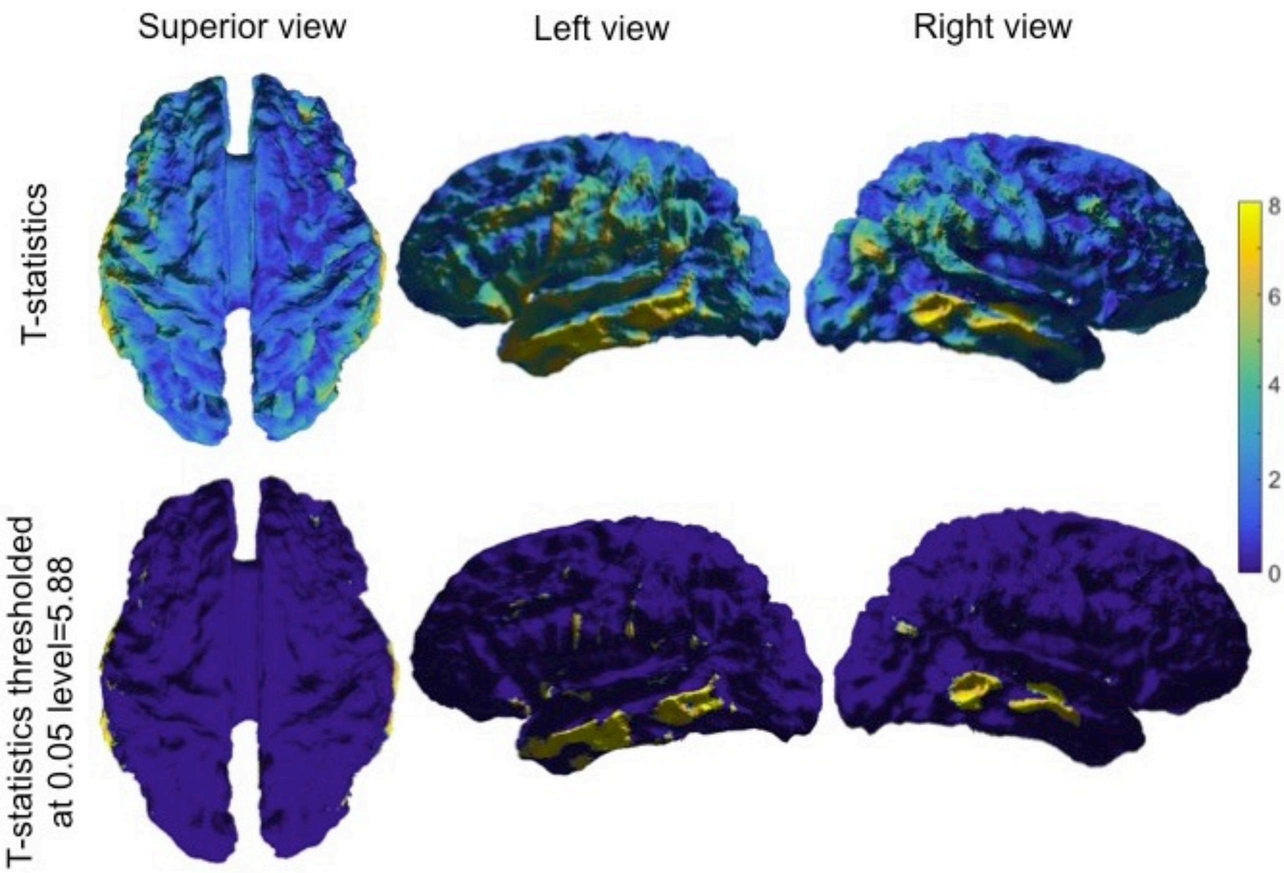


**Figure 2. Significance of folding group difference controlling for white matter volume and gender. P-value of 0.05 corresponds to a T-stat of 5.8802, hence regions with T-stat values greater than 5.8802 will pass the random field theory based multiple comparison thresolding at 0.05 significance level.**