Local shape analysis of the thalamus in extremely preterm born young adults

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Synopsis: Alterations of thalamic structures may cause disruptions in thalamic-cortical-thalamic circuitry and affect cognition. In this work we present a local shape analysis of the thalamus in extremely preterm born young adults when compared to their term born peers. We perform a groupwise shape analysis after spectral matching registration. After correcting for gender and thalamic volume, it resulted that the anterior and superior thalamic regions, connected to regions responsible for executive function, working memory, language and verbal memory, show most shape variations.

Introduction: The last trimester of pregnancy is a period of major brain development, with changes in volume, appearance and connectivity of the foetal brain. Birth before 27 weeks (extremely preterm) implies that this development will take place outside the mother's womb and these infants are prone to increased rates of adverse neurological outcome[1]. The thalamus is an important part of the brain and alterations of the thalamic structure are likely to cause disruption in the thalamic-cortical-thalamic circuitry and thus may affect cognitive performance. It has been shown that the size and structure of the thalamus are affected by preterm birth[2] and we hypothesis that these difference may persist into adulthood. Mapping differences between extremely preterm and term born adults can provide us with an understanding of the long-term structural impact of extreme prematurity.

Methods: T1-weighted MR data was acquired from 62 young adults born at <26 weeks of gestation (38 females + 24 males) and 47 control subjects (28 females + 19 males). All subjects were 19 year old adults born in 1995. We segmented the thalamus of each subjects using the GIF framework[3]. Thalamus segmentations were used to obtain smooth triangle-based meshes of the thalamus. For each group (preterm and control) we chose a random subject as template, to which we mapped all other surfaces using joint spectral matching with a CPD initialisation. The mappings were used to create a mean shape for each of the two groups. Morphological changes between the groups were then investigated by computing the difference in vertex position (displacement maps) of the mean shapes thalamic surfaces after another step of joint spectral matching. This pipeline was repeated to investigate differences between the groups by gender. Groupwise shape analysis using spectral matching has previously been shown to give reliable results[4]. We used the Hotelling T^2 two sample metric to derive a local group difference metric and local statistical p-values for all corresponding points[5]. After fitting a multivariate general linear model to our data, correcting for thalamic volume and gender, we computed the vertex-wise T-statistics using a random field theory multiple-comparison correction to yield an equivalent p-value of 0.05 and we then generated a map of group difference.

Results: Firstly, we notice that the mean thalamic volume is larger in control subjects (12.46±1.17 cm^3) than in the preterm population (10.46±1.22 cm^3). Secondly, the local shape differences between control and preterm groups are larger in the anterior part of the thalamus than in the posterior part (Figure 1). Furthermore, these differences are larger in the left hemisphere than in the right.

When separating the subjects by gender, we notice that the mean thalamic volume is smaller in females than males: 10.29±1.17 cm^3 and 10.80±1.21 cm^3 in the preterm population for female and male, respectively and 11.29±1.03 cm^3 and 13.28±0.92 cm^3 for the control population for female and male, respectively. Local shape differences between the preterm and term females are quite constant with no noticeable asymmetry (Figure 2). The local shape differences between the preterm and term males are large, especially in the anterior part of the thalamus (Figure 3). The differences are greater in the left hemisphere than in the right.

The group shape significance map, corrected for thalamic volume and gender (Figure 4), shows that the shape of the superior-lateral part of the thalamus is significantly different between the preterm and control groups, with a slight non-significant left-right asymmetry.

Discussion/Conclusion: We investigated differences in thalamus shape and volume between preterm and term-born young adults by performing a group comparison on vertex displacement, with matching carried out using

joint spectral matching. The thalamus was smaller in preterm-born individuals with differences mainly in the anterior thalamus and these differences were more pronounced in male subjects. The anterior thalamus connects to brain regions with roles in executive function, working memory, problem solving, mood and motivation[6]. Thalamic shape differences were more pronounced in the superior part, which has substantial connections to the temporal lobe[7], with role in language and verbal memory. Similar anterior and superior thalamic differences have been found in studies on ADHD subjects[7] and it may be interesting to explore the links further between thalamic shape, composition and the influence on an extreme prematurity-ADHD correlation[8]. Our future work will explore this possibility making use of the results of a neurocognitive assessment battery.

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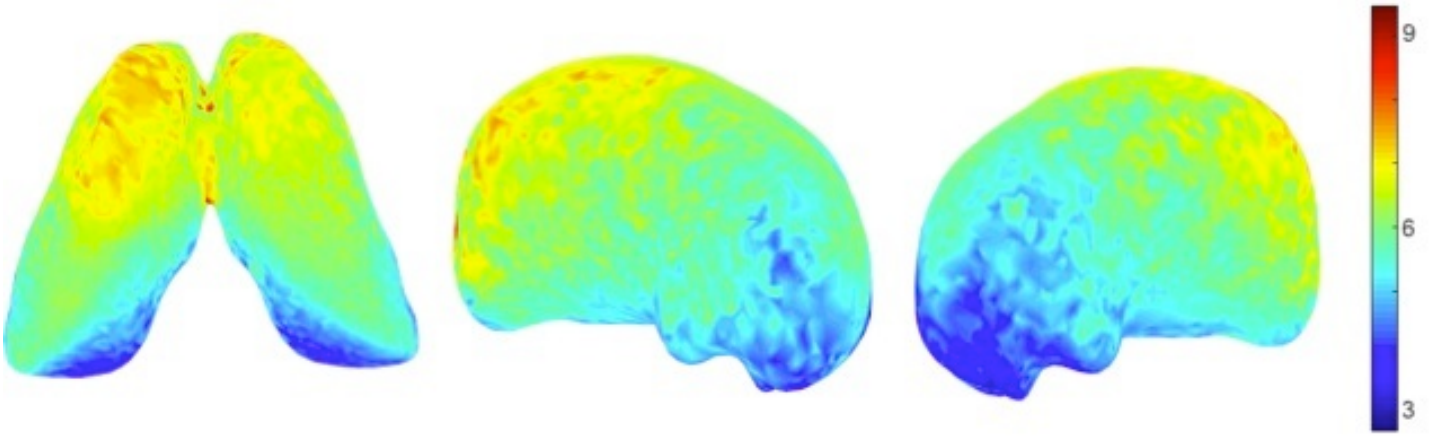

Figure 1. Local shape differences between the preterm and term mean thalamus: superior aspect and lateral aspect (left and right). Units of scale are mm.

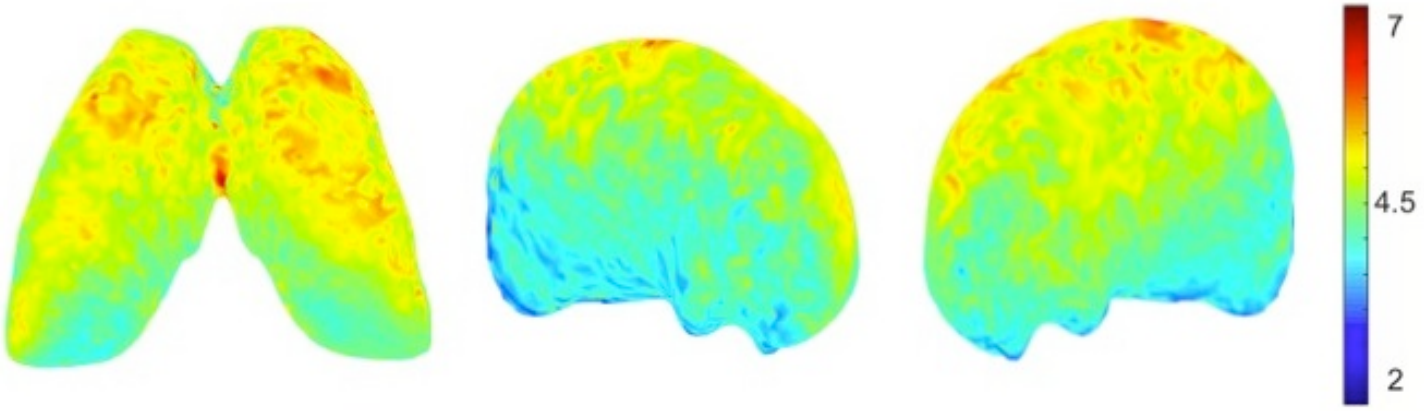

Figure 2. Local shape differences between the female preterm and female term mean thalamus: superior aspect and lateral aspect (left and right). Units of scale are mm.

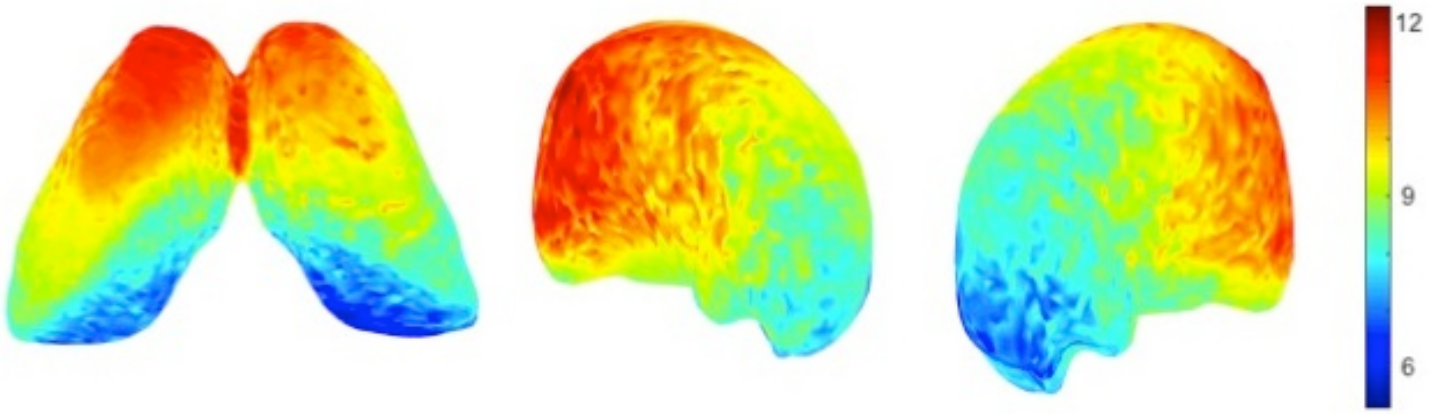

Figure 3. Local shape differences between the male preterm and term mean thalamus: superior aspect and lateral aspect (left and right). Units of scale are mm.

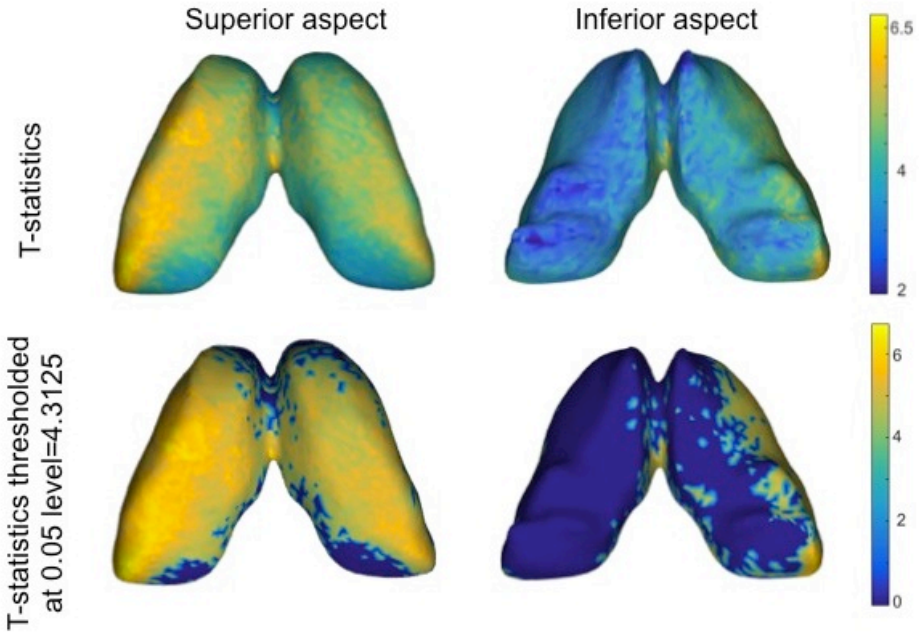

Figure 4. Significance of thalamus group difference controlling for thalamic volume and gender. P-value of 0.05 corresponds to a T-stat of 4.3125, hence regions with T-stat values greater than 4.3125 will pass the random field theory based multiple comparison thresholding at 0.05 significance level.