COMPARATIVE IN AND EX UTERO THALAMIC VOLUMETRIC GROWTH AND THE EFFECT OF PRETERM BIRTH

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Background: Preterm birth is associated with grey and white matter abnormalities, which represent a common imaging phenotype related with adverse neurodevelopment[1]. Specifically, thalamo-cortical development is disrupted with reduction in thalamic volume at term equivalent age[2,3]. Our aim is to compare thalamic growth trajectories of the fetal, term and preterm populations.

Materials and Methods: Informed parental consent and research ethics committee approval was obtained prior to MRI scanning. Fetal (n= 53) and term control (n= 11) populations were obtained from our normal control database. The preterm infants (n= 39) were recruited as part of an on going research study assessing preterm brain development. Fetuses with congenital brain and heart abnormalities, intrauterine growth restriction (IUGR) and twin pregnancies were excluded. Term control, preterm and fetal groups had normal brain MRI appearances. Fetal patients and neonates were scanned at Philips Achieva MRI scanners (Best, the Netherlands) operating at 1.5Tesla and 3.0Tesla respectively, using imaging parameters and radiography techniques as previously published [2,4]. Manual thalamic segmentations (Fig.1), were obtained from axial T2-weighted data sets using the ITK SNAP v.2.1.4 [5]. Original T2 weighted MRI datasets were corrected for patient motion using the Snapshot-to-Volume reconstruction (SVR) algorithm [6]. Previously described thalamic anatomical delineations were used for the term and preterm groups [7]. Additional information for fetal thalamic delineation was supplemented with an anatomical atlas [8]. Close anatomical proximity of the thalamus with other smaller brain structures (upper thalamic margin neighbours the choroid plexus, lower thalamic margin is in close anatomic relation with the mesencephalon at the level of the sub-thalamic nuclei ,lateral thalamic margins abut the posterior limb of the internal capsule) as well as image contrast and resolution may limit accurate manual segmentation of this structure. Clearly defined upper margins (at the level of the inferior aspects of the choroids plexus within the body of the lateral ventricle) and lower borders (at the level of the superior aspect of the superior colliculi) were prescribed. Interobserver (two experienced independent observers) and intraobserver agreement as assessed in 16 and 10 measurements respectively were high: Intraclass co-efficient (ICC) was 0.79 for interobserver and 0.87 for intraobserver measurements. Linear regression analyses of thalamic volumes against age were performed using STATA statistical analysis software program.

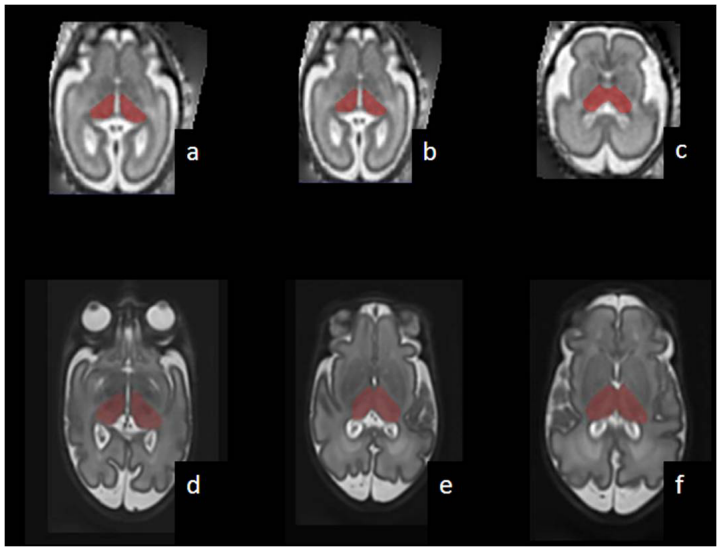

Fig.1. Thalamic manual segmentation on SVR motion corrected T2-w data sets. Top row (a-c): 27-week fetal brain: thalamic volume segmentation (red area) at (a) low, (b) mid and (c) upper levels. Bottom row(d-f): 35-week neonatal brain: thalamic volume segmentation (red area) at (d) low, (e) mid and (f) upper levels.

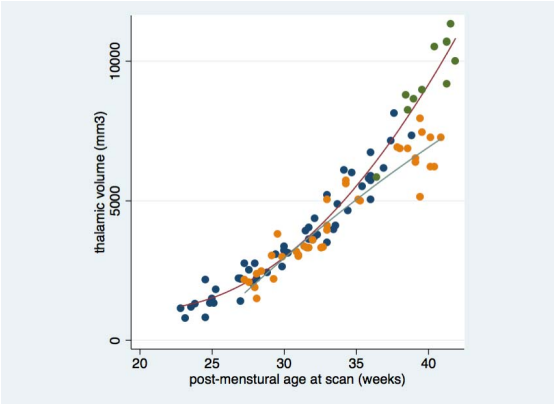

Fig.2. Regression analysis demonstrates curvilinear relationship between thalamic volume and age for fetal and term populations (red curve). Comparable thalamic volumes for fetal and preterm groups during mid gestation and statistically significant (p=0.03) deviation in thalamic

Results: The median gestational age of the fetal, term control and preterm populations were 30.0 wks (range 22.9 - 38.9 wks), 40.4 wks (range 36.4 - 41.9 wks) and 32.7 wks (range 27.7 - 40.9 wks) respectively. Regression analyses of growth trajectories were log transformed for interpretation. The volumetric growth trajectory curves for the fetal and term groups were non exponential. There were no statistically significant differences in the growth trajectories between the fetal and term control groups (p =0.767) and thalamic growth was not disrupted by the birth process. Statistically significant differences (p = 0.03) between the coefficients of the growth curves of the fetal and term controls were demonstrated when compared to the preterm population (Fig.2).

Conclusion: Thalamic growth trajectories during in- and ex- utero periods have been successfully obtained. Notable features of the results are that the development of the thalamus in the combined fetal and term populations can be consistently modelled with a single growth curve. In contrast, the preterm group were found to have a thalamic growth curve consistent with the fetal group only during mid gestation (28- 35 weeks), with a reduction in thalamic growth beyond 35 weeks potentially indicating a critical period at which growth deviation occurs. Future work will need to focus on recruiting and analysing more subjects (fetuses, preterm and term born infants) with gestational age in the 33-37 week range to allow further investigation of these findings.

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