Thalamic development in preterm infants during the third trimester

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Introduction: The deep grey matter has become an important focus of investigation as information to and from the cortex is relayed and modulated by the thalamus. In preterm infants at term equivalent age with diffuse WM disease, reductions in deep grey matter have been shown by both automated cerebral segmentation technique and deformation based morphometry compared to term born controls (1;2). Manual volumetry has also confirmed this reduction in lentiform nuclei and thalamic volume at term age (3) and showed that this reduction was especially pronounced in the presence of supratentorial focal WM lesions. However the rate of growth of the thalamus and whether these thalamic abnormalities are present prior to term equivalent age is unknown.

Aim: The aim of this study was to determine the thalamic development in the presence and absence of white matter injury during the third trimester.

Methods: 80 preterm infants, born <33 weeks gestation, were scanned between 25 and 45 weeks corrected age. T_1 weighted magnetization prepared rapid acquisition gradient echo volumes: TR17 ms/TE 4.6 ms, FOV 210, matrix 256 x 256, flip angle =30, 1 NEX and voxel size of 0.86 x 0.86 x 0.8mm were acquired. Image *J* (version 1.37) software was used for manual segmentation. Thalamic landmarks: Each thalamus is situated between the head and the tails of the caudate nucleus. The third ventricle forms the medial border and the posterior limb of the internal capsule forms the lateral border; the posterior border is formed by the lateral ventricle; and the sub-thalamic nuclei along with the geniculate bodies form the inferior border. An example of the manual segmentation of the thalamus at several anatomical levels is shown in figure 1.

Results: Multiple linear regression showed that the gestational age (GA) at birth, birth weight, head circumference (HC) at birth, weight, HC and age at scan were significantly correlated to total thalamic volume. Principle component analysis was performed to show that GA at scan explained most of the variance seen in the thalamic volume and therefore thalamic volume and its relationship to GA at scan was investigated further. This showed that the total thalamic volume increased from 1.61-12.1cm^3 during the third trimester and that the rate of thalamic growth was 0.49 cm^3/week. The thalamic growth in infants with lesions was 0.25 cm^3 per week. Covariance analysis showed that the growth lines of infants with and without lesions were not parallel and that there was a significant vertical distance between the lines of -2.3cm^3 (95% CI -3.05 to -1.5cm^3 p<0.001).

It also showed that the rate of thalamic growth in infants with lesions was significantly reduced compared infants without lesions (p=0.0017).

These finding were further explored in a group of 47 preterm infants longitudinally scanned twice or three times during neonatal period. All the clinical variables such as GA at scan, weight, HC were correlated to thalamic volume at that time point. However as the weights and head circumferences were dependent on GA at scan, principle component analysis was performed, which showed that GA at scan explained most of the statistical variance at each time point. General linear model for repeated measurements was carried out between GA at scan and thalamic volumes. Interactions of sex and lesions were also analysed. It showed that gestation at scan, sex and lesions had an effect on the thalamic volume. Lesions had a significant effect on both the total volume and rate of growth of thalamus during the developmental period. However, as males had more lesions when the interactions of lesions and sex were combined, their effect on the thalamic volume was lost.

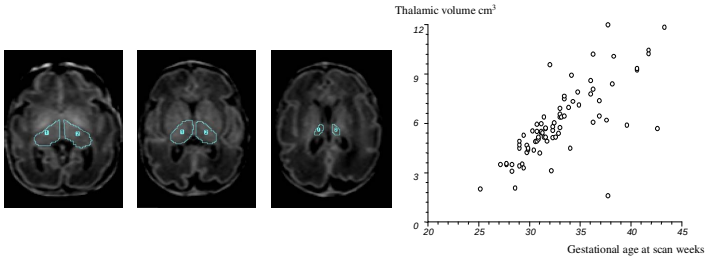

Figure 1: T_1 weighted axial images of preterm infant at 29 weeks gestation showing thalamus manually segmented at a low, middle and high section of the basal ganglia.
Figure 2. Increase in thalamic volume with increasing gestational age is depicted in the graph.

Effect	Value	F	Sig.	Partial Eta Squared
volume	.900	17.986(a)	.010	.900
volume * ga	.878	14.444(a)	.015	.878
volume * lesion	.850	11.345(a)	.022	.850
volume * sex	.841	10.566(a)	.025	.841
volume * lesion * sex	.000	.(a)	.	.

Table 1. Multivariate thalamic volume analysis. The thalamic volume was tested for interactions with sex, lesions and gestational age at scan. As expected the Partia Eta squared values showed significant interactions between gestational age, lesions and sex. However as lesions were present in mostly in males when both lesions and sex were taken into account, the interactions on thalamic volume were lost.

Conclusions: This study showed using serial and longitudinal imaging of infants that the absolute thalamic volume and rate of growth of thalamus were significantly decreased in infants with lesions compared to infants without lesions due to both reduction in total volumes and rate of thalamic growth. Thus these results suggests that the combined reduction in total thalamic volume and rate of growth may lead to the reduction in thalamic volume seen in preterm infants at term equivalent age in the presence of lesions compared to term born controls.

References: 1. Boardman JP, Counsell SJ, Rueckert D, Kapellou O, Bhatia KK, Aljabar P, et al. Abnormal deep grey matter development following preterm birth detected using deformation-based morphometry. Neuroimage 2006 Aug 1;32(1):70-8. 2. Inder TE, Warfield SK, Wang H, Huppi PS, Volpe JJ. Abnormal cerebral structure is present at term in premature infants. Pediatrics 2005 Feb;115(2):286-94. 3.Srinivasan L, Dutta R, Counsell SJ, Allsop JM, Boardman JP, Rutherford MA, et al. Quantification of deep gray matter in preterm infants at term-equivalent age using manual volumetry of 3-tesla magnetic resonance images. Pediatrics 2007 Apr;119(4):759-65.