In-vivo subplate development in preterm infants

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Introduction: The subplate is a transient laminar layer of the cortex consisting of the first post mitotic neurons embedded in a rich abundant extracelluar matrix. It is necessary for the migration, laminar location and areal specification of the thalamocortical fibres to different functional cortical areas(1). Kostovic et al (2) demonstrated that the subplate had a low signal intensity on T_1 weighted images, due to the increased hydrophilic extracelluar matrix. However the subplate has not been systematically quantified in-vivo using MR images.

Aim: The aim of this study was to quantify the subplate development in preterm infants during the third trimester and to compare the subplate between preterm infants at term age and term born controls.

Methods: 80 preterm infants born < 34 weeks gestation were recruited from Hammersmith Hospital neonatal unit after ethical approval. T_2 -weighted pseudo-volumes [TR 7578ms, TE 160 ms, FOV 220 mm, 1 NEX and voxel dimension 0.86 x 0.86 x1 mm] were acquired on a 3 Tesla Phillips Achieva System using an 8 channel head coil. **Manual measurements:** Image J program was used for manual 2D measurements. The length (horizontal region of interest [ROI]), depth (vertical ROI) and the signal intensity within the ROI were measured in the sagittal plane of the frontal, parietal, temporal and occipital lobes. Vertical ROI -subplate depth (fig 1) was defined as the perpendicular distance between the outer subplate border (demarcation between low signal intensity (SI) cortex and high SI subplate) and inner subplate border (demarcation between high SI subplate and medium SI immature white matter). Horizontal ROI -subplate length was defined as the maximal length of continuous subplate without any interruptions (fig 2). Both ROIs were measured in all the four individual lobes. ROI T_2-intensity ratio was determined as the ratio of the mean signal intensity within the subplate ROI divided by the mean signal intensity of adjacent cerebrospinal fluid. Intra-observer variability was calculated for both the vertical and horizontal subplate ROI after 20 repeated measurements.

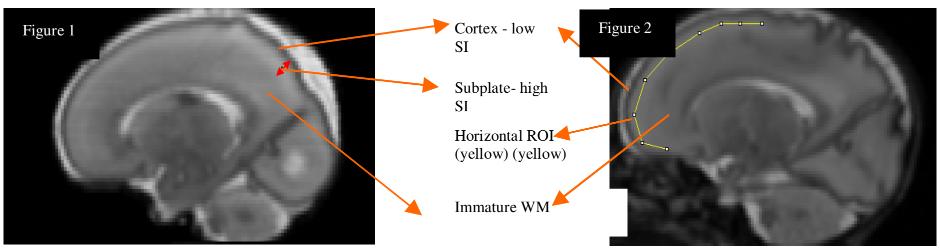

Figure 1 Parietal vertical ROI is depicted on a T2 weighted scan at 28 weeks gestation. Vertical subplate ROI is the perpendicular distance between the outer subplate border (border of low signal intensity (SI) cortex and high SI subplate) and inner subplate border (demarcation of high SI of subplate and medium SI immature white matter).
Figure 2. . Frontal horizontal ROI is depicted on a T2-weighted scan at 34 weeks gestation. Horizontal ROI is defined as the maximal length of continuous subplate without any interruptions

Results: 80 preterm infants born < 33 weeks gestation, were scanned between 25 and 45 weeks post menstrual age. The intra-observer variability error for the vertical and horizontal ROI subplate measurements were 1.6 and 1.5% respectively. **Visual analysis:** 12 of the 67 infants had subplate present both in gyri and sulci on qualitative visual analysis. The median gestational age at scan of these infants was 30 weeks. **Subplate depth:** There was no relationship between gestational age at birth or at scan and vertical ROI of the subplate in all the four regions. There was regional variation, with the temporal lobe having the greatest depth and T_2-intensity ratio and occipital subplate having the least depth and T_2-intensity ratio. In infants with lesions, the T_2-intensity ratio and depth of the subplate was significantly lower compared to infants without lesions especially in the parietal and occipital regions. **Subplate length:** This decreased with increasing gestational age at scan. The mean length was maximal in the frontal region (35.8 cm) and was statistically increased compared to the other regions. The mean horizontal ROI of the parietal, temporal and occipital region were 10. 9, 10.9 and 11.2 cms respectively and were not significantly different. **Preterm at term and term born controls:** 10 preterm infants at term age and 10 term born controls were analysed at a median gestation age of 41 weeks. In all infants the subplate was restricted to the gyral crests. The term controls showed a significantly lower vertical ROI, T_2-intensity ratio and horizontal ROI of the subplate in all 4 lobes compared to preterm infants at term age.

Discussion and conclusions: This in-vivo study of subplate development showed that subplate was maximal below 30 weeks gestation due to it's presence in both gyral and sulcal regions, after which it was restricted to gyral crests. Although the length of the subplate decreased between 25 weeks and term age due to sulcal formation, the depth of the subplate remained constant. Regional variation probably reflected the structural/ functional maturation of the overlying cortex. In infants with lesions the depth and T_2 intensity of the subplate was decreased. These results suggested that the subplate length is an important marker of maturity, whereas the depth was a marker of abnormality during development. By term age the length, depth and T_2 intensity were increased in preterm infants compared to term born controls, suggesting a combination of delayed and abnormal subplate maturation in preterm infants. Although the intra-observer variation was minimal, the main drawback of this study was the subjective nature of manual subplate ROI placement. However automated methods for extraction of the subplate are very difficult and require significant manual editing.

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