Specific white matter diffusion characteristics in the newborn period correlate with either neuromotor or neurocognitive outcome at 2 years. A voxel based Analysis

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Introduction

Full attainment of brain function is dependent on cortical integrity and fully myelinated white matter. Myelination is an important process of brain development. This process takes place in the foetal period and is mostly completed by the age of 2. Preterm birth can lead to delay and deficits in brain myelination with consequences for neuromotor and neurocognitive capacities in early child development and later in life. Developmental difficulties after preterm brain are characterized by motor deficits and neurocognitive delay in attention control, language development and executive functions. Early structural correlates of these deficits are missing. Diffusion MRI provides insight into brain development and the quantitative indices of diffusion and of apparent diffusion coefficient (ADC) are related to brain maturation [1]. ADC values in particular decrease with brain myelination [2]. Studies that correlate regional MRI diffusion changes in the newborn period to early childhood outcome are still lacking. Thus, this study presents results of a voxel based analysis of ADC in the newborn period and the neuromotor and neurocognitive outcome of preterm infants at 2 years of age.

Material and Methods

Patients and outcome scores

58 premature newborns (mean gestational age - GA: 29.39, range: 25.14w-36.57w) were included in the study. We monitor preterm infants from birth to 24 months. We examined children with Bayley scales of infant development to analyse neuromotor and neurocognitive development at 24 months. Bayley scales include a mental developmental index (MDI) evaluating mainly neurocognitive development and a psychomotor development index (PDI) evaluating mainly neuromotor development.

MR acquisition MRI were performed at 1.5T (Philips Intera) and 3T (Siemens Trio) scanners. Axial slices covering the whole brain were imaged by diffusion-EPI sequence using 6 orthogonal directions (b=700 s/mm^2) with a spatial resolution of 2x2x2 mm^3.

Data post-processing All data were processed off line using diffusion toolkit [3], which provided ADC maps for each infant. Data analysis was performed using SPM (4). A template was built on a subset of 21 normal newborn's brains at term using reference (b=0) EPI images (figure 1). This template was further used for normalization, which consisted of affine and non-linear transformation. The transformation matrix was applied to the ADC maps. ADC maps were compared using a multiple regression analysis using MDI and PDI scores as effects of interest and the MR scanner (Philips or Siemens) as covariate. A p-value of 0.001 (uncorrected) was considered as statistically significant.

Results

MDI effect An inverse relation was found between ADC values and MDI scores at 24 months (Figure 2 left graphic). ADC decreases when MDI increases and this was specific for certain brain regions. These regions include mainly bilateral frontal white mater (figure 2 left). These areas anatomically correspond to the longitudinal fasciculus, which is involved in different brain functions such as language and executive functions. Bilateral parieto-occipital areas (not shown) were also found. This area represents angular gyrus, which is linked again to language functions.

PDI effect As for MDI values, there was a inverse relation between ADC values and PDI scores. ADC values were increased with decreased PDI in the pre-central motor region, more pronounced on the left side (figure 2 right). Additional areas with significant inverse relationship were found in the occipital region, areas of visuomotor control

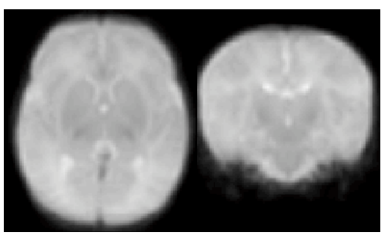

Figure 1: Template used for SPM normalisation. It was created with 21 normal infant's brain at term. A 4-mm gaussian kernel filter was used.

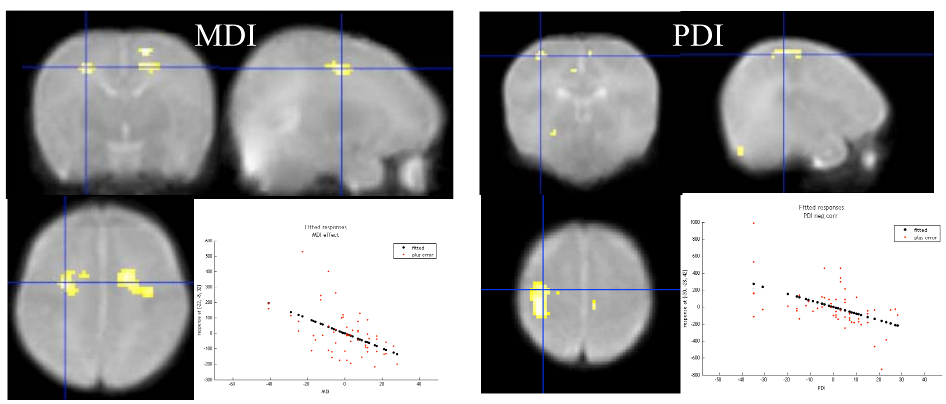

Figure 2: Regions with increased ADC in relation with low MDI score (left) and low PDI score (right)

Discussion and Conclusion

All observed ADC changes were negatively correlated with MDI and PDI. The most prominent areas showing negative correlation between ADC and the neurocognitive score of MDI at 2 years were found in areas linked to a dedicated language subcircuit, which involves postero-temporal areas, supramarginal and angular gyri, Broca's area, and the superior longitudinal fasciculus. Areas showing strong negative correlation between ADC and the neuromtor score of PDI were located in the precentral white matter linked to the motor pathways and some occipital regions linked to visuomotor pathways. These data indicate that delayed myelination, assessed by ADC in white matter pathways linked to early motor control in the newborn will lead to delayed neuromotor development at age 2. In addition delay in pre-myelination changes in the frontal and parietoccipital areas of language pathways in the newborn leads to delays in composite mental developmental scores at age 2. Further assessment of fiber tract integrity, using FA will provide further insight into these changes.

References

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