Longitudinal Analysis of Tissue Property Changes in Multi-modal MRI of the Developing Preterm Brain

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Introduction

Between 24 and 44 weeks postmenstrual age (PMA), the brain undergoes significant changes in size, shape and structure, but longitudinal quantitative markers of development are limited. Changes in the magnetic resonance signal intensity (SI) may reflect maturational changes in water content [1] and changing tissue characteristics associated with myelination and pre-myelination events [2]. The aim of our work is to quantify T1 and T2 weighted signal intensity changes in a unified way during this developmental period.

Methods

This study was carried out using T1 and T2 weighted MR images from 116 premature neonates acquired between 29-44 weeks PMA (mean PMA at birth 29^{+4} weeks, range 24^{+5}-35^{+2}). Sequence parameters were: T1 images: MPRAGE, TR 17ms, TE 4.6ms, Flip angle 13°, FoV 210mm, Matrix 256 x 256; T2 images: multi-slice FSE pseudo-volume TR 14000ms, TE 160ms, slice thickness 2mm, 50% overlap, FoV 220mm, Matrix 256 x 256. The first steps in the proposed framework are masking of non-brain tissues and correction of MR intensity inhomogeneity. Next, the pairs of T1W and T2W scans acquired in each session are rigidly co-registered. Each T2W scan is then affinely aligned to the reference template of a 4D atlas [3] at the same time point. The resulting affine transformation is then used to transform both the T1W and T2W scans to the reference template. After matching each T1W-T2W pair with their respective time-point in the atlas, they were subsequently aligned to a single time-point reference, the atlas average intensity template at 37 weeks GA. Longitudinal registrations were carried out in two steps: A global transformation was first estimated using affine registration. Subsequently, using the result of the affine transformation as the starting point, a non-rigid registration step was carried out using the method of *Rueckert et al.* [4]. In order to perform voxel-wise intensity comparisons across different scans, after mapping them to a common coordinate space, images with a common intensity range are required. T1W scans were normalized using the high intensity of fatty tissue between the skull and the skin. T2W scans were normalized using high intensity values of CSF. Intensity normalization is followed by per-voxel kernel regression. The changes over time in T1W and T2W signal intensity were measured in sub-cortical grey matter and white matter to create a 3-dimensional change map.

Results

Figure 1 shows spatio-temporal patterns of intensity change that reflect maturational processes between 29-44 weeks postmenstrual age. Our results indicate differing patterns of spatio-temporal signal change in T1W (A-B) and T2W (C-D) MR images. Figure 2 (upper panels) shows the intensity change trajectories of the cross-section of the posterior limb of internal capsule (marked by square in Fig. 1) in both T1W and T2W MRI. As expected the T1W intensities increase as a function of age whereas T2W intensities decrease with age. However, as shown in the bottom panel of Figure 2 the temporal trajectories of the lateral aspect of the lentiform nucleus (marked by an ellipse in Fig. 1) show a delay in the phase of rapid change with age and suggest an initial increase in the T2W signal before the longer term trend to lower signal commences. The error bars represent the standard deviation at each time-point.

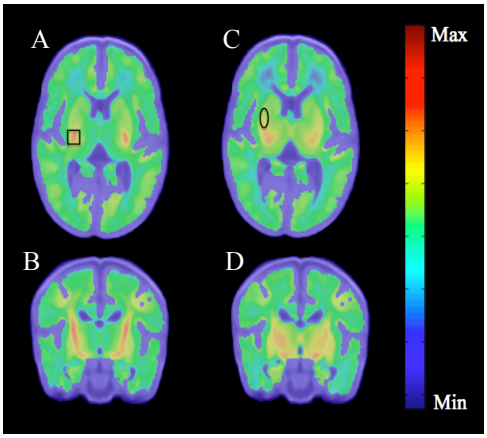

Figure 1

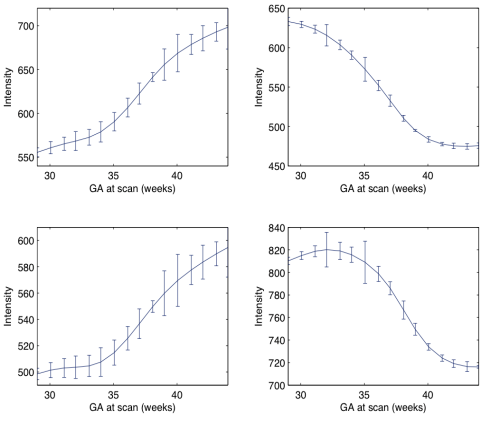

Figure 2

Conclusion and Future Work

We have quantified spatio-temporal signal intensity changes during early development using multi-modal MR imaging, atlasing and non-rigid registration. The results demonstrate signal changes consistent with the expected maturational processes in tissue characteristics from 29 weeks onwards following preterm birth which are likely to represent myelination and pre-myelination [2] changes and alterations in water content [1]. The approach provides a consistent framework for exploring brain changes during development allowing patterns of signal intensity change to be mapped as well as the more usual assessment of anatomical development. The patterns of change identified may be useful in providing age-specific norms for mechanistic studies of preterm brain injury and for studying the effects of interventions designed to improve outcome following preterm birth. While our analysis framework is reliant on normalization accuracy, the results demonstrated are promising and more accurate normalization methods will be investigated. Future work will also make use of other modalities within our analysis framework as well as tracking signal intensity change in other brain structures. The extension from signal intensities to quantitative mapping of T1W and T2W values is also of great interest.

References

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