Groupwise atlas construction for the identification of neuroanatomical changes associated with preterm birth

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INTRODUCTION

Preterm delivery affects around 5% of all deliveries and its consequences contribute to significant individual, medical and social problems. The principle morbidity among survivors is neurological, resulting from the profound effect of preterm birth on the developing brain: neurodevelopmental and neuropsychiatric problems are common in later life[1]. In order to study the structural correlates of the cognitive and behavioural impairments, anatomical atlases of the brain of preterm and term-born infants can be constructed using MR images acquired at equivalent time points.

This requires the construction of a representative atlas for each group. Non-rigid registration can be used to do this by aligning all subjects to a common coordinate system. Typically, a subject is chosen from the population to act as a reference, and deformation fields mapping this to all other subjects individually are found[2] (pairwise registration). This creates an atlas in the coordinate system of the chosen reference. However, in a group with wide variation in shape (eg: preterm infants), it can be difficult to select a representative reference subject. A better method, which is less biased, would be to register to the *average shape* of the population. This study aims to create unbiased atlases, which represent the average shape of the brain in preterm and term-born neonates at term-equivalent age, using a groupwise non-rigid registration algorithm, and to compare the structural differences between these two groups.

METHOD

Subjects: 3D MR images were acquired from 16 preterm infants at term-equivalent age (median GA: 29.71 weeks, 24-34 weeks), and 16 term-born controls (median GA: 40.43 weeks, 37-44.57 weeks). Infants with parenchymal lesions were excluded.

Image acquisition: A 1.5 Tesla Eclipse MR system was used to acquire high resolution T1-weighted (TR=30ms, TE=4.5ms, flip angle=30°), volume datasets in contiguous sagittal slices (in-plane matrix size 256x256, field of view = 25cm), with a voxel size of 1.0x1.0x1.6mm, in addition to conventional T1 and T2-weighted images.

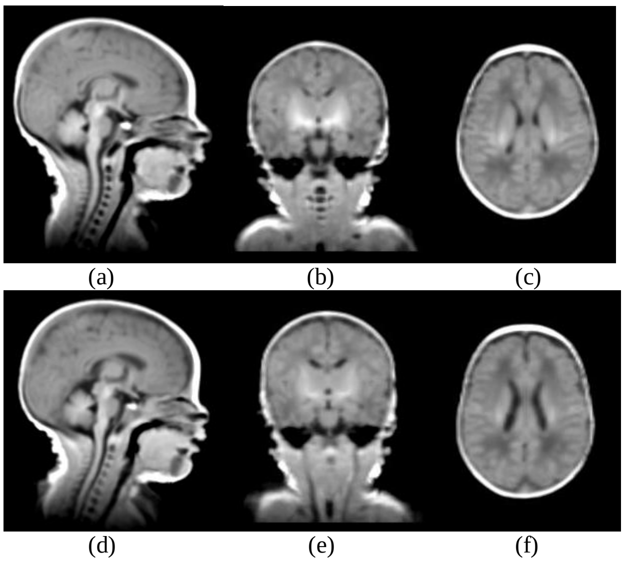
Groupwise non-rigid registration for atlas construction: A consistent, groupwise, registration algorithm[3] based on B-splines is used to *simultaneously* register all subjects in the population to a reference space representing the average shape of the population. This is done by overlaying a mesh of uniformly-spaced control points onto each of the images; deforming the control points deforms the underlying images. Although the average shape is not known beforehand, it is calculated implicitly by constraining the sum of all the deformations to be equal to zero: the method therefore does not rely on the use of any anatomical reference. The control points are manipulated until the similarity between all the images is maximised.

Evaluating the similarity of n *images using Normalised Mutual Information (NMI)*: Using NMI for n images would require an n-dimensional histogram, making its evaluation computationally infeasible. Instead, one arbitrary image, X_{ref}, is selected to be an intensity – but not anatomical – reference. All corresponding intensity pairs are added to the same joint histogram, which can be used to evaluate the similarity by: $S = \left(H(X_{ref}) + H(X_{group})\right) / H(X_{ref}, X_{group})$ in the same way as for two images.

Optimization and efficiency: To constrain the sum of deformations to equal zero, the Gradient Projection Method[4] for constrained optimization is used. To increase the efficiency of the algorithm, deformation fields are first produced using pairwise registration. These deformation fields are then concatenated with their mean, forming an initial set of deformations satisfying the constraint[5]. Groupwise registration is then used to update these in order to remove any bias caused by the initial choice of reference.

RESULTS

Figure 1 shows atlases constructed for 16 preterm infants at term-equivalent age and 16 term-born controls. Qualitative comparison of the atlases shows expected differences between the two groups: there is a scaphocephalic appearance to brain shape, and enlargement of the lateral ventricular system among preterm infants at term equivalent age (c and f). Myelination in the internal capsule was more pronounced in the control group (b) than in the preterm at term-equivalent age atlas (e).



(a) (b) (c) (d) (e) (f)

Figure 1: corresponding locations in atlases of 16 term-born controls (a-c) and 16 preterm neonates (d-f)

CONCLUSION

We have used groupwise registration to create atlases of preterm and term-born neonates representing the average shape of each population, and used these to detect structural differences at term-equivalent age. These atlases could be used as templates for morphometric studies of the human brain in the perinatal period.

REFERENCES

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