

Diffusion tensor imaging with tract-based spatial statistics (TBSS) reveals local white matter abnormalities in preterm infants at term equivalent age

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Introduction

Infants born preterm have a high incidence of neurodevelopmental impairment in later childhood,^{1,2} often associated with poorly defined cerebral white matter abnormalities. Diffusion tensor imaging (DTI) quantifies the diffusion of water within tissues and has been used to assess micro-structural abnormalities in the cerebral white matter in this group of infants.³⁻⁵ Tract based spatial statistics (TBSS)⁶ is an automated observer independent method of aligning fractional anisotropy (FA) images from multiple subjects to assess group-wise microstructural differences in the major white matter pathways of the brain.

Aim

The aim of this study was to determine if TBSS could be implemented in the preterm population, and to test the hypothesis that preterm infants have microstructural differences in cerebral white matter compared to term born control infants in the absence of major focal abnormalities such as cystic periventricular leukomalacia (cPVL) or haemorrhagic parenchymal infarction (HPI) on conventional MRI.

Methods

Ethical approval for this study was granted by the local Research Ethics Committee and written parental consent was obtained prior to scanning. We studied 26 preterm infants (11 female, 15 male) of median (range) gestational age at birth = 28.9 (25.7-32.6) weeks at term equivalent age (post-menstrual age at scanning = 41.3 (38.1-45.3) weeks) and 6 healthy term-born control infants (2 female, 4 male) imaged at 41.7 (41.0-46.0) weeks post-menstrual age. In the subgroup of 11 preterm infants (4 female, 7 male) who were born at 28 weeks gestation or less, the median (range) gestational age of the infants at birth = 26.7 (25.7-28.0) weeks, and the median (range) post-menstrual age at imaging was 41.0 (38.1-44.0) weeks.

MRI was performed on a Philips 3 Tesla system using a phased array head coil. 3D MPRAGE and T2 weighted FSE images were obtained prior to DTI. Single shot echo planar DTI was acquired in 15 non-collinear directions using the following parameters; TR = 8000ms, TE = 79ms, slice thickness = 2mm, voxel size = 1.75 x 1.75 x 2 mm³, NSA = 2, *b* value = 750 s/mm², SENSE factor = 2. Distortions due to eddy currents were minimized by registering the diffusion weighted images to the *b* = 0 image using affine transformations. Fractional anisotropy, λ_1 , λ_2 and λ_3 maps were generated using FDT.⁷ Voxelwise statistical analysis of the FA data was carried out using TBSS.⁶ All subjects' FA data were aligned into a common space using a non-linear registration algorithm (www.doc.ic.ac.uk/~dr/software). The mean FA image was then created and thinned to create a mean FA skeleton which represented the centres of all tracts common to the group. This was thresholded to FA ≥ 0.20 to include the major white matter pathways but exclude peripheral tracts where there was significant inter-subject variability and/or partial voluming with grey matter. Each subject's aligned FA data was then projected onto this skeleton and the resulting data was fed into voxelwise cross-subject statistics. TBSS analysis was also applied to the λ_1 , λ_2 and λ_3 maps.

Results

There were no significant differences in age at scanning ($p = 0.24$) or in gender ($p = 0.53$) between the preterm-born group and the term-born controls. There were no significant differences in age at scanning ($p = 0.14$) or in gender ($p = 0.47$) between the subset of preterm infants born ≤ 28 weeks gestational age and term-born control infants.

We found that regions within the centrum semi ovale, frontal white matter and the genu and isthmus of the corpus callosum had a significantly lower FA in preterm infants imaged at term equivalent age compared to term-born controls (Figure 1a-d). Those infants born at or before 28 weeks gestational age ($n = 11$) displayed additional reductions in FA in the posterior aspect of the posterior limb of the internal capsule, external capsule and within the optic radiations, and had larger regions of reduced anisotropy within the centrum semi ovale, frontal white matter and genu of the corpus callosum (Figure 1e-h). The decreased FA values in these regions could be explained by increases in λ_2 and λ_3 (radial diffusivity) in the preterm-born group.

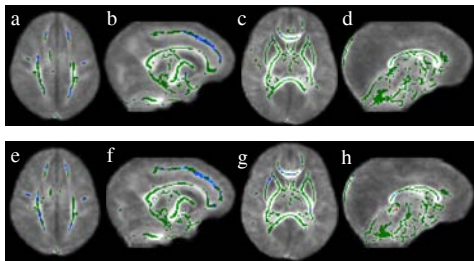


Figure 1: The effect of preterm birth on FA at term equivalent age

Mean FA skeleton overlaid on the mean FA image. Regions of the mean FA skeleton in green represent areas where there were no significant differences in FA values in the preterm-born infants imaged at term compared to the term-born controls. Areas in blue are regions where the FA was significantly lower in the preterm group (first row), and can be observed in the centrum semi-ovale (a), frontal white matter (b), genu (c) and isthmus (d) of the corpus callosum. Those infants born ≤ 28 weeks gestational age (second row) displayed additional reductions in FA in the posterior aspect of the posterior limb of the internal capsule (g), external capsule (h) and the optic radiations.

Discussion

This study demonstrates that TBSS is able to demonstrate abnormalities in many white matter regions in the preterm brain at term equivalent age. Those infants born ≤ 28 weeks gestational age had more extensive regions of abnormality. This technique promises to be a useful tool for group-wise assessment of the preterm brain.

References

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