Identification and interpretation of microstructural abnormalities in motor pathways in adolescents born preterm

S. Groeschel[1], J-D. Tournier[2], G. Northam[3], T. Baldeweg[3], J. Wyatt[4], B. Vollmer[5,6], and A. Connelly[2]

[1]Experimental Pediatric Neuroimaging and Developmental Medicine & Child Neurology, University Children's Hospital, Tuebingen, Germany, [2]Brain Research Institute, Melbourne, Australia, [3]UCL Institute of Child Health, London, United Kingdom, [4]UCL Hospitals, London, United Kingdom, [5]Karolinska Institute, Stockholm, Sweden, [6]University of Southampton, United Kingdom

Introduction

With the increasing prevalence of preterm birth, understanding preterm brain injury and its long-term effects on brain structure has become a focus in imaging research. Neuromotor impairments ranging from minor motor difficulties to cerebral palsy (CP) are frequent in survivors of preterm birth (see e.g. Saigal & Doyle, 2008). Quantifying microstructural changes in motor pathways using diffusion tensor imaging (DTI) has therefore been a major interest, although this remains challenging. A significant challenge comes from the fact that the tensor model is based on the assumption of only one fibre orientation per voxel, while in reality around 90% of voxels contain more than one fibre population (Jeurissen et al. 2010). This is especially problematic for the study of preterm brain injury since a common location for white matter injury is in the periventricular WM, which has particularly complex crossing-fibre characteristics.

The objective of the present study is to investigate diffusion parameters along motor pathways in adolescents born preterm. The main aim is to measure diffusion parameters along motor tracts identified using high angular resolution diffusion imaging (HARDI) data in conjunction with Constrained Spherical Deconvolution (CSD) (Tournier et al. 2007) and a probabilistic tracking algorithm to define the local fibre orientations. It is hypothesized that in survivors of preterm birth, the microstructure of motor tracts is abnormal, and can be detected more sensitively by measuring DTI parameters than on visual inspection of conventional structural MRI. Moreover, it is hypothesized that the interpretation of diffusion parameters along the fibre tracts is dependent on the underlying fibre architecture.

Methods

45 preterm adolescents (aged 15.6 years ± 1.3; born <33 weeks) were studied, together with 31 term-born healthy controls of similar age. Neurological examination revealed CP in 3 of the preterm children, and a further 12 had unspecific neurological findings (such as mild muscular hypo- or hypertonia, or clumsiness). MRI included a HARDI acquisition (Siemens 1.5T Avanto, 64 diffusion directions, b-value 3000 s/mm^2, voxel size 2x2x3mm).

Image analysis consisted of definition of seed and target regions for tractography in a template image generated from all subjects. These regions were then spatially warped to each individual's images. Warping and template creation were done using large deformation symmetric normalization (ANTS) accounting for possible ventricular dilatation and improving registration accuracy (Avants et al. 2008). Tractography of motor pathways was performed using Constrained Spherical Deconvolution (Tournier et al. 2007) and probabilistic streamlines. To sample diffusion tensor derived parameters, equivalent positions along motor tracts were defined in template space, which were spatially warped to each individual's native space to provide ROIs for measurement of diffusion parameters.

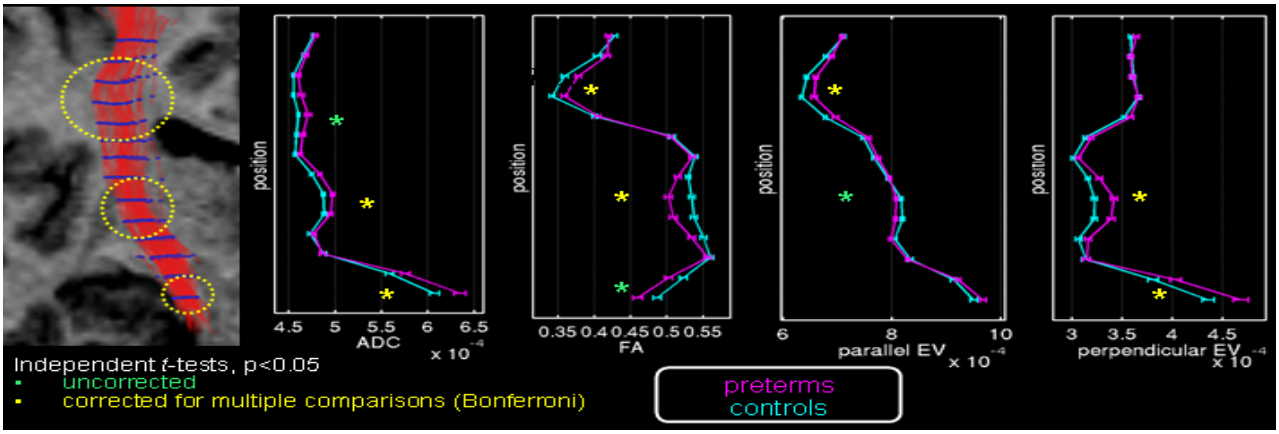

Figure 1

Diffusion parameters (ADC, FA, and parallel and perpendicular eigenvalues) along the cortico-spinal tract. Yellow circles indicate regions in which significant differences were observed

Results

Diffusion parameters were significantly different between preterms and controls at several levels along the corticospinal tract, thalamo-cortical and transcallosal pathways. In the centrum semiovale (top circle, Fig 1), FA and ADC were significantly increased compared to controls. In contrast, within the highly organized WM regions of the corpus callosum (data not shown) and internal capsule (Fig 1), ADC was found to be increased whilst FA was decreased. The major contributor to reduced FA in preterms in predominantly single fibre regions (e.g. internal capsule) was the increased radial eigenvalue (Fig 2). In predominantly crossing-fibre regions, the tensor eigenvalues are not meaningful, and the observed increase in FA is likely to be due to a decrease in anisotropy in one of the contributing fibre bundles (Fig 2). These differences were also observed after excluding radiologically abnormal preterms, although they were less pronounced.

Discussion

White matter microstructure was found to be altered in motor pathways in adolescents born preterm. These changes affect diffusion parameters differently in crossing fibre regions (periventricular WM) than in highly organized WM pathways such as the corpus callosum and internal capsule (figure 2).

The major finding in this study is that disruption of WM microstructure in a single fibre region with resulting higher radial diffusivity leads to *lower* FA, whereas selective disruption of one fibre population in a crossing fibre region may lead to *higher* FA (figure 2). These findings challenge the common simplistic interpretation of FA as a measure of WM tract integrity.

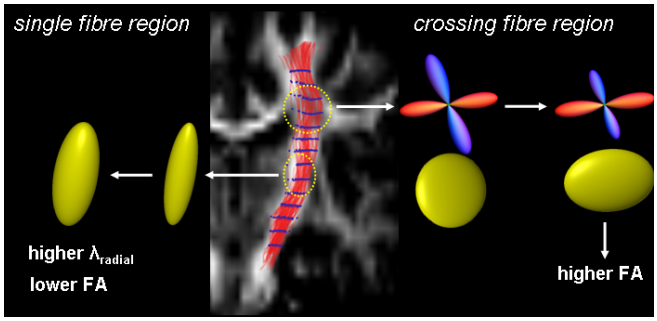

Figure 2

Changes of the tensor (illustrated in yellow) in predominantly single (left) and crossing (right) fibre regions along the cortico-spinal tract and resulting changes in FA. CSD derived FODs are illustrated for crossing-fibre region.

References

Avants BB et al. 2008, Med.Image Anal., 12 (1), 26-41.
Jeurissen B et al. 2010, ISMRM, 573.
Saigal & Doyle, 2008 , Lancet, 371(9608):261-9.
Tournier JD et al. 2007, Neuroimage., 35 (4), 1459-1472.