Voxel based analysis of diffusion tensor imaging in Newborns with Intrauterine Growth Restriction

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Introduction:

Intrauterine growth restriction (IUGR) is known to affect brain development. IUGR is associated with neurological and behavioural deficits in children. Advanced quantitative volumetric three-dimensional MRI techniques demonstrated a reduction of cerebral cortical gray matter volume in IUGR preterm infants secondary to placental insufficiency (Tolsa CB et al. Pediatr Res 2004). The aim of this study was to evaluate the effect of intrauterine growth restriction on microstructural brain development using DTI with a novel voxel based analysis approach.

Methods :

Subjects :

6 IUGR preterm infants born (n=6, GA 33 wks ± 1.7, birth weight <10%tile 1310 g ± 210) were compared with 9 preterm infants with a normal growth (n=9, GA 31.5 wks ± 2.6, birth weight 1730 g ± 460). Infants studied were free of prematurity-associated cerebral pathology, such as intraventricular hemorrhage, ventriculomegaly or periventricular leukomalacia.

MRI acquisition:

MR imaging was performed at 40 weeks of gestation without sedation (IUGR: 40.7 ± 0.8 wks, Controls 40.5 ± 1.2 wks) using a 1.5 T Philips MR system. Conventional 3D T1 and T2-weighted MR scans were obtained using continuous, 1.5 mm, coronal sections. The field of view was 180 mm, yielding 0.703 x 0.703 mm in-plane resolution. DTI consisted of a single-shot echo planar imaging (EPI), multisection spin echo with a FOV of 200 mm, an in plane resolution of 1.56 x 1.56 mm and a slice thickness of 4 mm. 6 non-linear gradient directions with a b value of 700 s/mm2 were applied.

MRI processing:

Corrections for eddy current distortions were computed with BrainVISA software (http://brainvisa.info/). Thereafter the diffusion tensor was calculated on a pixel by pixel basis. Spatial normalization for each case was performed using its reference image (b=0) to a T2-weighted template constructed from a collection of 14 healthy babies in a common stereotaxic space in SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/); this transformation matrix was applied to FA maps. FA maps were smoothed with a 3 mm full width half-maximum isotropic kernel. Regions of significant difference with cluster size above 150 were retained for further analysis. FA values in IUGR were then compared to control cases on a voxel-by-voxel basis using a two samples *t*-test in SPM2 software with a threshold set to $p < 0.05$. The correction of the *p*-value was based on a volume of interest centered on the cerebellar white matter.

Results:

Voxel-by-voxel comparisons of the anisotropy maps revealed decreased anisotropy in the white matter of the cerebellum of the IUGR preterm infants (Figure 1). The left side seems to be predominantly affected (Right side: x y z = 13 –11 –46; T= 3.40; *P* FDR-corr = 0.048; Left side: x y z = –14 –12 –51; T = 5.68; *P* FDR-corr = 0.003).

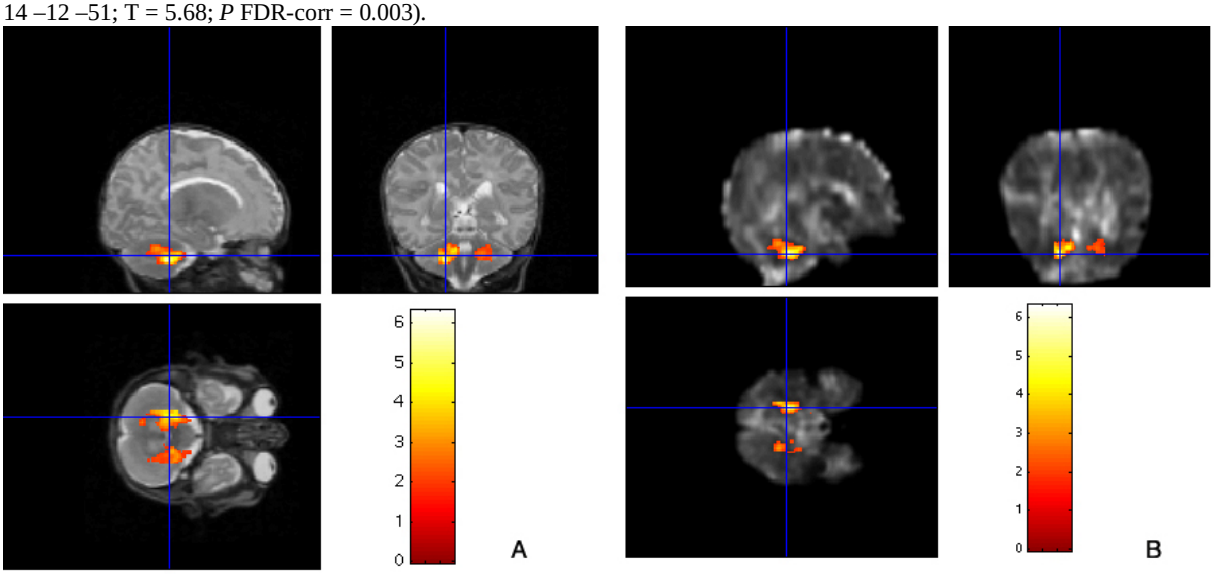

Figure 1 : Visualisation of the regions of significant reduction in FA values in IUGR infants. A : overlaid on T2-weighted image B: overlaid on FA map

Discussion/Conclusions:

Using a voxel-based approach of DTI analysis without an a priori hypothesis, we were able to show microstructural changes in the cerebellar white matter of IUGR preterm infants, which corresponds to changes observed in the cerebellum in IUGR animal models. Mallard et al. (Mallard C Neuroscience 2000) specifically showed a reduction in the volume of the cerebellar white matter and a reduction of the number of the Purkinje neurons. IUGR was further associated with a reduction of myelination in the cerebellum with myelin sheaths, which were disproportionately reduced relative to axon diameter (Nitsos I, Rees S. 1990). This microstructural alteration might well explain our finding of reduced anisotropy in the bilateral cerebellar white matter in IUGR infants.