White Matter Diffusion Anisotropy in Adolescents Born Prematurely

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INTRODUCTION

Premature birth is linked to an increased risk of minor brain dysfunction. Present knowledge points to two main causes; disturbed brain maturation and local ischemic events. Due to the blood vessel organization the latter has a predilection to specific "watershed" areas in periventricular white matter. The main aim of the present study was to investigate if diffusion tensor imaging (DTI) using fractional anisotropy (FA) maps could detect differences in white matter areas between a group of adolescents with previous premature birth and an age matched control group.

METHODS

The subjects are divided into three groups, the very low birth weight group (VLBW), consisting of those with a birth weight under 1500 g, the small for gestational age (SGA) group, consisting of children with a birth weight below the 10th percentile for gestational age, and a control group consisting of children born at term and with a normal birth weight. The results presented here are based on 158 subjects that underwent MRI examination at the age of 15. 28 of the MRI examinations were excluded from analysis because of image artifacts or unsuccessful scans, leaving 132 subjects divided into 36 VLBWs, 42 SGAs, and 52 controls.

All subjects were scanned on a 1.5 T Siemens Magnetom Symphony with Quantum gradients (30 mT/m). The protocol consisted of a structural T1-weighted sagittal MPRAGE sequence (TR/TE/TI 7.1/3.45/1000 ms, flip angle 7°), FOV 256 x 256 x 170 mm, in-plane resolution 1 x 1 mm, slice thickness 1.33 mm, and a single-shot balanced-echo [1] EPI (TR/TE 6000/97 ms) DTI sequence with 20 contiguous transversal slices covering all but the topmost part of the brain, FOV 228 x 228 mm, in-plane resolution 1.78 x 1.78 mm, and slice thickness 5 mm. For each slice one image without diffusion weighting (S_0 image), and 6 images with diffusion gradients applied along six non-collinear directions (b = 1000 s/mm^2) was acquired. The DTI scan was repeated 6 times for increased SNR.

Motion correction was applied to the DTI data using a mutual information cost function implemented in FSL/FLIRT [2], before averaging, diagonalization of diffusion tensor and calculation of FA maps. To allow for statistical analysis, the FA maps were normalized to a T1 weighted pediatric template from the Imaging Research Center at Cincinnati Children's Hospital Medical Center [3]. Normalization was done by first coregistering the S_0 images to the structural volume, bringing FA images in registrer with the structural scan. The structural scan was then normalized to the template, and the same transformation applied to the FA images. Normalization and subsequent statistical analysis was done with SPM2 (Wellcome Department of Cognitive Neurology, London, UK). Group comparisons (between VLBW, SGA and control) of the FA maps were performed using a threshold of FA > 0.15, thus confining our analysis to white matter [4]. Two-sample t-tests with a FDR-corrected confidence level of $p < 0.05$ were used for group comparisons.

RESULTS

Comparison between the VLBW and control group detected several areas where the VLBW group have significantly lower FA, Figure 1. The largest clusters of reduced FA in the VLBW group were in the capsula interna. Using the opposite contrast, that is areas with larger FA values in the VLBW group compared to the control, also detected some areas with significant differences, Figure 2.

Group comparison between the SGA group and the control, detected no voxels of statistically significant difference. Group comparison between the VLBW group and the SGA group detected several significant clusters, in roughly the same areas as the group comparison between the VLBW and control group.

a) coronal -8 mm b) coronal -16 mm c) transversal 16 mm

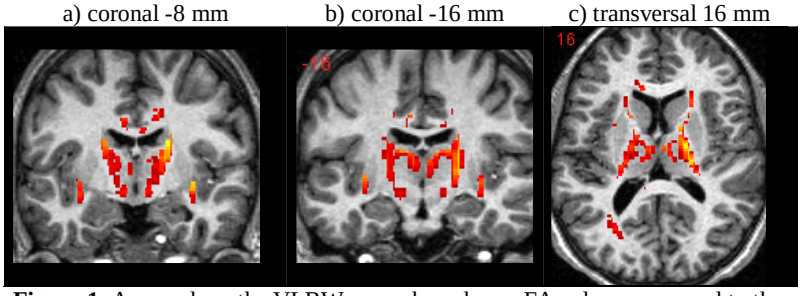

Figure 1. Areas where the VLBW group have lower FA values compared to the control group. (The right side of the images is the subject's right side.)

a) transversal 13 mm d) coronar 0 mm e) sagittal 26 mm

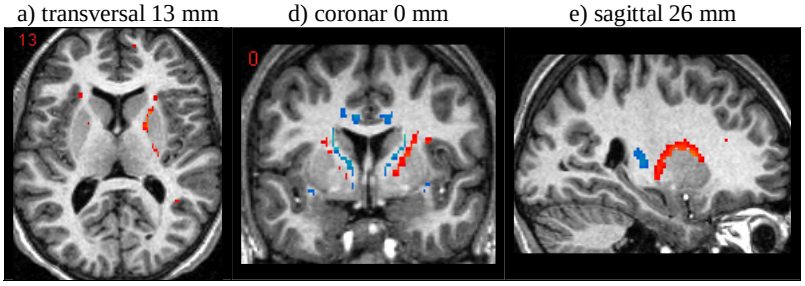

Figure 2. Areas where the VLBW group have higher FA values compared to the control group (in red). The opposite contrast is shown in blue for comparison.

DISCUSSION

DTI was able to detect differences in fractional anisotropy in white matter between adolescents with premature birth and controls. These areas, which included the capsula interna, the centrum semiovale, occipital periventricular white matter and the corpus callosum, are known predilection areas for periventricular leukomalacia in VLBW newborns. Compared with standard MRI, DTI may give additional information about white matter injury that may influence neurodevelopment in VLBW children

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