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Regional white matter anisotropy and general intelligence in preterm born children: a voxelwise analysis

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Introduction:

Premature born are at risk of white matter injury which may in turn be a contributory factor to impaired cognition. Fractional anisotropy (FA), a biomarker of white matter injury, is reduced in multiple white matter regions in preterm compared to term newborns (1, 2). Significant correlations have been found between cognitive indices and FA in specific white matter regions in the normal pediatric population (3). In a cohort of very low birth weight (<1500 grams) preterm born children (<37 weeks gestation), we tested for regions of significant correlations between white matter fractional anisotropy and Wechsler full-scale IQ scores using a voxelwise analysis technique to determine if similar associations exist.

Methodology:

Twenty-two children (12 male, 10 female, age range 9.2 yrs- 11.5 yrs, all right handed) who were born very low birth weight preterm were recruited for diffusion tensor MR imaging (DTI) studies and intelligence quotient tests using the Wechsler full-scale IQ (FSIQ), performed within nine months of each other. Children requiring sedation for MR imaging and those with congenital brain malformations or ventriculomegaly on conventional MR imaging, and cerebral palsy were excluded. DTI was performed using a 1.5T imager with a standard head coil in 25 gradient encoding directions using single-shot echo-planar imaging (TR=10000ms, TE=100ms, acquisition matrix=128 x 128, field of view =28cm, slice thickness of 5mm with 1.5mm gap, b factor=1200s/mm^2). Fractional anisotropy (FA) maps were created (FUNCTOOL, GE Medical Systems). Using SPM2 (Wellcome Dept of Cognitive Neurology, Institute of Neurology, UK), the T1W image of the subjects was co-registered to the non-diffusion weighted DTI image (b0) and this was spatially affine normalized to the pediatric T1W template CCHMC2_fp (Cincinnati Children's Hospital Medical Center, OH, USA). The normalization parameter derived was applied to T1 and FA images. Each normalized T1 image was segmented to give probability maps of gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF). A high probability WM binary mask of each subject was created using the equation (i2>i1)&(i2>i3)&(i2>(1–i1–i2–i3)) in function ImCalc, where i1, i2 and i3 represented probability maps of GM, WM and CSF, respectively. All the masks were averaged and smoothed with a 12mm-isotropic Gaussian filter and binarized at >0.5. The FA images were smoothed with 12mm-isotropic Gaussian filter. Using multiple regression analysis in SPM2, with analysis confined to white matter using the mask created, we tested regions of significant correlation of FA with FSIQ after adjusting for the effects of age and gender (FDR corrected p<0.05 and cluster size > 30 contiguous voxels). For the regions that correlated with FA, scatterplots were generated and partial correlations of the mean FA values of the region-of-interest (ROI) with FSIQ was performed.

Results:

Patient demographic data and FSIQ scores are summarized in Table 1. Regions of statistically significant positive correlations of FA with FSIQ scores were found in six white matter regions that were bilaterally symmetrical (Fig. 1, 2). The regions were in the right and left; occipito-temporal, temporo-parietal and frontal lobes. The largest and most significant region (Fig. 2) was in the left occipito-temporal lobe (FWE-corrected p=0.025, FDR corrected p < 0.001, Talairach coordinates -50, -53, -4). No region was found with significantly negative correlation with FSIQ. Partial correlations of the ROI mean FA values and FSIQ confirmed the significant correlations observed in the voxelwise analysis (Fig. 3).

	Min	Max	Mean	SD
Age (years)	9.2	11.5	10.2	0.7
Birth weight (Grams)	650.0	1475.0	1110.2	202.1
Gestational age (weeks)	24	34	28.9	2.7
FSIQ	79	131	105.5	12.7

Table 1 showing patient demographic data (*n=22*)

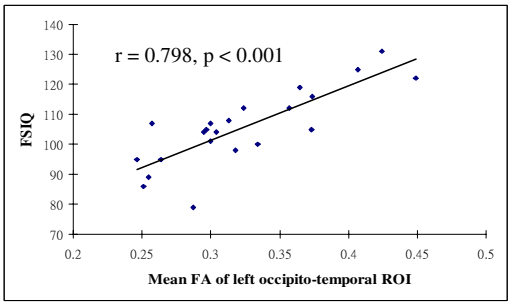

Fig. 3 showing scatterplot of FSIQ vs mean FA of left occipito-temporal ROI

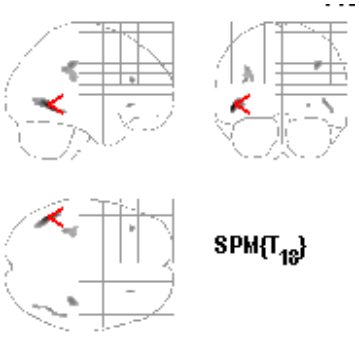

Fig. 1 standard SPM glass brain projections showings 6 clusters of significant correlations between FA and

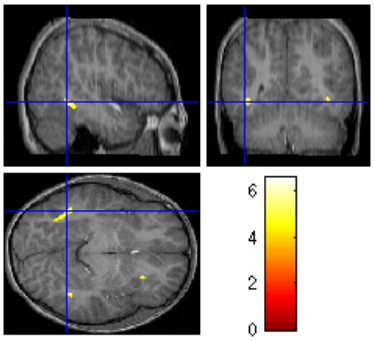

Fig. 2 voxelwise analysis showing statistically significant correlations between FA in bilateral occipito-temporal regions and FSIQ

Conclusion:

There are regionally specific white matter areas of positive correlation of FA with FSIQ in preterm born children and these areas overlap with those found in the normal pediatric population. These similar findings suggest that fiber organization/integrity in specific white matter regions underlie general intelligence.

References:

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