Cerebral Myelin Content Correlation with Mathematical Abilities in Young Children

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Introduction.— Some fMRI studies have reached the conclusion that the parietal cortex plays a significant role in computation based tasks [1, 2]. However, most studies to date have focused on the adult population; age-related changes in activation have been described in the parietal and prefrontal cortices suggesting the specialization of brain circuits for math related tasks over time [3]. Recently, diffusion tensor imaging has been used to investigate structural differences in white matter (WM) associated with reduced mathematical abilities in children. Barnea-Goraly et al. [4] studied this relationship in a group of individuals with velocardiofacial syndrome and van Eimeren et al. [5] analyzed this connection in a group of typically developing children, both finding significant white matter structures associating frontal and parietal regions.

The analysis of multi-exponential T_2 decay has been established as a reliable measure of myelin integrity [6]. Myelin mapping was performed on 20 young subjects (grade 4) who each completed the Calculation and Applied Problems subtests of the Woodcock Johnson Third Edition Tests of Achievement. The selected participants had average reading skills and spoke English as their first language. The group was composed of 16 males and 4 females, of which 16 subjects were right-handed. Correlation analysis was performed using a voxel-wise approach in a study-specific standard space.

Data Collection and Post-processing.— All magnetic resonance scans were acquired in a 3T Phillips Achieva whole body MRI scanner using an 8 channel Philips Sense head-coil. A GRASE sequence was used for the T_2 decay curve collection with TR = 1000ms, TE = 8ms, and ΔTE = 8ms. The reconstructed image resolution was 192 x 192 x 10 (field-of-view = 211mm x 211mm x 44mm). The decay of the magnitude image at each voxel was fitted assuming a multi-exponential behaviour [7]. The T_2 components were logarithmically spaced between 10ms and 2s. The exponentials' coefficients were calculated using a non-negative least squares algorithm to minimize the sum of χ^2 and a regularizing energy constraint. The fraction of area below 40ms in the T_2 distribution was classified as the myelin water fraction (MWF).

An adult structural template applied in a voxel-based analysis of pediatric data could lead to possible tissue type misclassifications and potentially require unnecessary warping to account for differences in structural anatomy across age groups [8, 9, 10]. All linear and non-linear transformations were generated using FSL 4.1.4 (FMRIB, Oxford, UK). A study-specific template was produced by normalizing all structural images to a particular subject whose brain appeared to best represent the average. All structural images were visually inspected for gross structural abnormalities such as lesions, which would cause undesirable warping. Each subject's structural scan was linearly registered to said individual's brain using 12 degrees-of-freedom (DoF), sinc interpolation and a mutual information cost function. The registered images were averaged to produce a whole brain, first pass template. This normalizing process was iterated 5 times in total, using each iteration's output template as the reference image for the next iteration's registration. The iterative process had the effect of reducing the sensitivity of the template to the subject used to seed the normalization process.

To transform the MWF images to the template space, each person's T_2 image was first linearly registered to their respective structural scan. The co-registered T_2 images were visually inspected for accuracy. Non-linear registration normalized each subject's structural image space to the template image space. Default configuration parameters meant for normalization with the well known MNI152 template were used. The T_2-to-structural and structural-to-template transformations were applied to the MWF images resulting in MWF images in a standard space with isotropic voxel dimensions of 1.1mm x 1.1mm x 1.1mm.

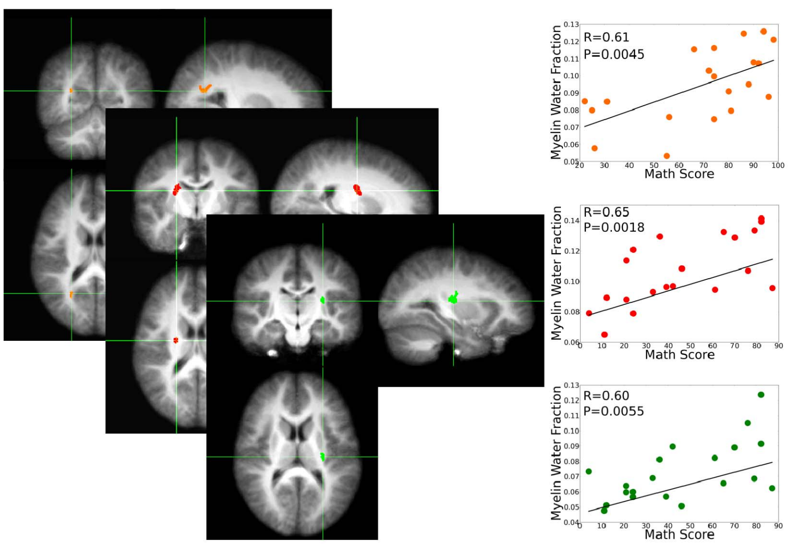

Figure 1 - Three clusters displaying significance and high correlation in white matter alongside a linear regression for the most correlated voxel in each cluster. Cluster color is matched with the corresponding scatter plot. Images are displayed using the radiological convention.

Results and Discussion.—Voxel-wise correlation of white matter and math score was performed, generating two statistical maps, one for each math test. A 5x5x5 mean filter was applied to the myelin images before calculating Pearson correlation coefficients (R) to increase signal-to-noise. R values were only calculated for Voxel classified as WM for all subjects. The statistical images were thresholded to only account for significant voxels ($P < 0.05$) with high correlation ($R \geq 0.5$). A cluster size thresholded was set at 100 contiguous voxels to remove random areas of high correlation appearing as artifacts of the registration process.

Three groupings of voxels met the outlined statistical significance criteria. Figure 1 displays the clusters overlaid with the study-specific template as well as the MWF distribution for the most significant voxel in each group. The clusters found in the left external capsule (green) and the right anterior limb of the internal capsule (red) are highly correlated regions with the Calculation Problems test. The right lateralized cluster is made up of 201 voxels (R=0.56 ± 0.04), while the left lateralized cluster consists of 156 voxels (R=0.54 ± 0.03). The right occipital/parietal white matter cluster (orange) was highly correlated with the Applied Problems test; it is composed of 135 voxels (R=0.54 ± 0.02). This region is in close proximity with the right intraparietal sulcus, which has been implicated with numerical magnitude processing [3]. A cluster in this region compliments the findings of decreased right parietal matter in children with developmental dyscalculia [11].

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