

Voxelwise Analysis of White Matter Integrity in Healthy Adolescents

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Background: Fractional Anisotropy (FA), as measured by diffusion tensor imaging (DTI), increases with age and intelligence during normal development, however, this is understudied in developing adolescents. Giedd et al [1], and Clayden et al [2], showed that there is a general trend of white matter maturation as adolescents age, particularly in the range from 8 to 18 years. Giedd et al [1] also demonstrated that the posterior portion of the corpus callosum and the splenium show the areas of most maturation.

Methods: *MRI Data Acquisition:* DTI datasets from 33 healthy children, aged 9 to 17 (mean age 13.4 years, 21 females), were acquired on a 3.0 T GE Signa Excite MRI scanner. Fifteen diffusion directions were used with 2 mm² in plane resolution and a slice thickness of 2 mm.

Image Analysis: The Tract-Based Spatial Statistics (TBSS) package from FSL was used to warp all images into a common space [3]. This was performed by first fitting a tensor model to the raw diffusion data, and then extracting the brain from the rest of the data. All subjects' FA data were aligned into a common space by choosing the most regular image from the given data, nonlinearly warping the subject data to that image, and then linearly warping the resulting images into MNI-152 space. Next, the Randomise package from FSL was used to perform a voxelwise regression analysis of the group-wise FA strength. To generate correlation maps only within white matter, the maps output by Randomise were reduced to the white matter tracts using the FMRIB Automated Segmentation Tool (FAST).

Results: At a threshold of $p < 0.1$ (FWE corrected), significant correlations were found in several areas of the brain as age increased in the subjects, which reflects increasing FA as subjects aged. Of particular interest is the corpus callosum and splenium, which showed very strong correlations. Significant correlations were also found throughout the entire body of white matter as IQ increased in the subjects as well, for $p < 0.05$ (FWE corrected). These correlations also regressed out any correlations that could be

due to subject age. The subject IQ ranged from 74 to 150, with a mean IQ of 108.5. Intellectual functioning in subjects was determined by the Wechsler Abbreviated Scale of Intelligence (WASI) two-subtest short form.

Discussion: The analysis of white matter integrity with respect to age shows a significant increase in FA. This is probably related to ongoing myelination of axons by oligodendrocytes, following a pattern throughout the brain of inferior to superior and posterior to anterior. Corpus callosum size, in particular, has been shown to continue to increase in size due to ongoing myelination, especially the posterior regions of the corpus callosum [4]. Childhood IQ and white matter integrity also have important implications for the development and integrity of white matter tracts. Other work has suggested that childhood IQ is linked to both IQ and white matter integrity in old age, implying that stronger connections in childhood can lead to a healthier life throughout adult life [5].

References: [1] Giedd, et al. *Prog Neuropsychopharmacol Biol Psychiatry*, 23:571–588, 1999.

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