A DTI Study of Developmental Brain Changes During Puberty

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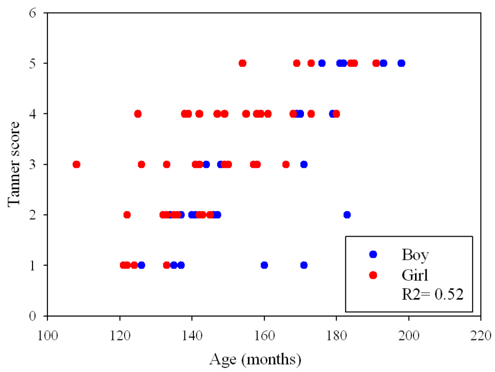
Introduction

Diffusion tensor imaging (DTI) is highly sensitive to microstructural changes in the brain throughout the normal lifespan. The period of pre-adolescence and early adolescence is a profound stage of development with significant hormonal, behavioral, and physical developmental changes. In this study a cohort of typically developing subjects were imaged with DTI on several occasions between the ages of 9 and 16 years (108-198 months) of age. Physical and hormonal changes associated with puberty were characterized using Tanner score measurements at each time point. To investigate microstructural changes with age and development in this sample, a voxel-based analysis was performed using methods of nonlinear co-registration, FNIRT-FSL *http://www.fmrib.ox.ac.uk/fsl/fnirt/index.html*, white matter segmentation, and correction of partial volume blurring effects with T-SPOON [1]. Tract-based spatial statistics (TBSS – FSL [2]) was also applied for comparison. These methods were applied to 96 data sets. Group comparisons were performed for FA, mean diffusivity (MD), radial diffusivity (Dr) and axial diffusivity (Da).

Methods



Data: DTI data from 20 males and 20 females were acquired using a single-shot spin echo EPI sequence with diffusion-tensor encoding (12 directions, b=1000s/mm^2, voxels = 1.88 x 1.88 x 3mm). Subjects were scanned between 1 and 4 times with at least one year between scans, resulting in 96 data sets from 40 subjects. Intra-subject scan correlations were ignored. The average age was 148.9 months old, and the standard deviation was 19.9 months. Tanner scores were measured by a physician as an indication of physical development. A plot of age and tanner scores is shown on the left. The DTI data were corrected for head motion, eddy currents static field inhomogeneities using a combination of FSL field map correction and in-house software. RESTORE [3] built in Camino *http://www.cs.ucl.ac.uk/research/medic/camino/index.htm* was used to process DTI.

TBSS: TBSS analysis was done using FSL 4.1.4 described in Smith et al [2]. The template for nonlinear warping was from one subject whose age (149 months old female) was about the mean and the FA data was transformed to be co-registered with FMRIB58_FA_1mm

T-SPOON: Using the same nonlinear warping transformation that was used for the TBSS above, white matter segmented mask, and DTI measurements (FA, MD, Dr, Da) were transformed and smoothed using Gaussian smoothing (FWHM 4mm) to create T-SPOON data.

Statistics: The voxel-wise statistical analysis was done using an FSL function 'randomise', which is a non-parametric permutation test. Group difference between Tanner score 1 group (10 data sets, mean age: 135.5 months old, std: 16.1) vs. Tanner score 3 and 4 group (13 data sets, mean age: 135.5 months old, std: 11.3) or vs. Tanner score 5 (17 data sets, mean age: 179.2 months old, std: 11.7) results were investigated using TFCE [4] using optimization parameters (--T2 for the skeleton and -T for the T-SPOON data) and a threshold of TFCE (Threshold-free cluster enhancement) p value < 0.01. Since the comparison of Tanner score 1 vs. Tanner score 3 &4 was based on age matched data, ANOVA was used. Comparing Tanner score 1 and Tanner score 5, age was used as a covariate in the model first, and then a simple ANOVA was tested again. Finally a linear correlation of DTI measurements (FA, MD, Dr, and Da) and age using 96 sets of the whole data were investigated.

Results

In general, the linear correlation of age and DTI appears to be quite diffuse over much of the white matter. An example of correlation maps of FA, MD, and Dr with age is shown in the top row of Fig 2. The linear regression of FA vs. age for one voxel is plotted in Fig 1. Da has much smaller (-) linear correlation values with age than Dr with age. When testing group differences there was no significant difference between two groups (age matched); Tanner score 1 vs. Tanner score 3 and 4. Also no significant difference was found between Tanner score 1 group and Tanner score 5 group when controlling for age. However, when age was not considered an ANOVA test of Tanner score 1 group and Tanner score 5 group revealed a significant difference as shown in the bottom row of Fig 2.

Discussion

From the correlation of age and DTI study, all eigenvalues reduce over the period of puberty, but Dr decreases more than Da, which leads to increasing FA over the age. Tests of comparing different Tanner score groups showed no significant difference whenever controlling for age, which may indicate that changes in DTI measurements over age are not driven by puberty-related changes directly.

References

[1] Lee J et al. NeuroImage 44:870 (2009). [2] Smith S et al. NeuroImage 31:1487 (2006). [3] Chang et al. MRM 53:1358 (2005) [4] Smith and Nichols. NeuroImage 44:83 (2009).

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Fig 1

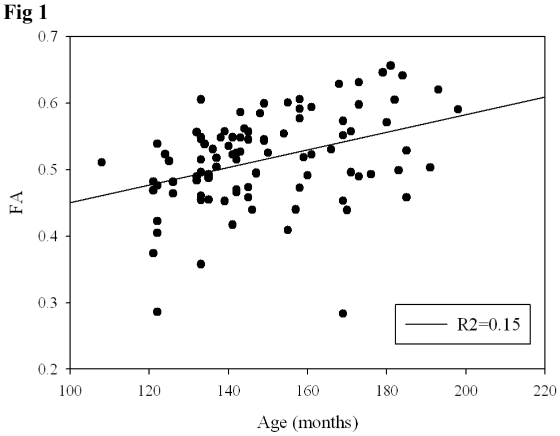

Fig 2

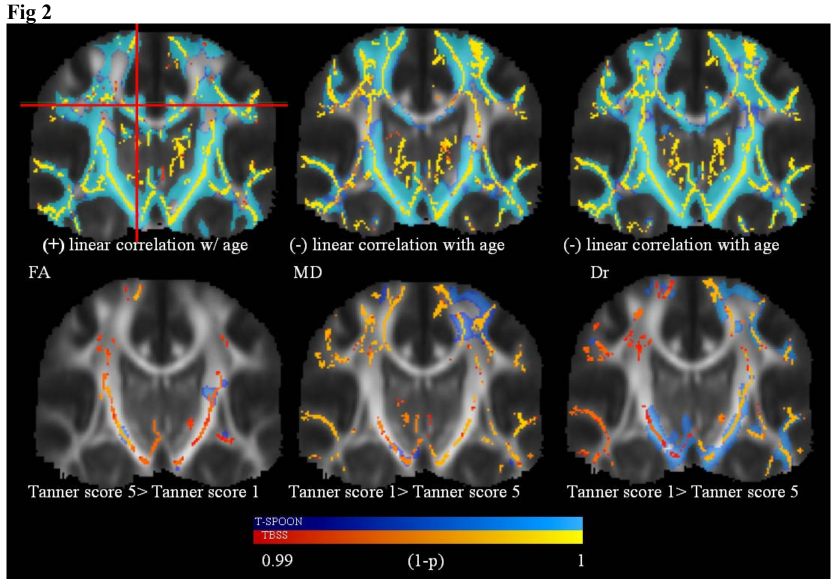

Fig 1. A linear regression of FA and age at the crosshair in Fig 2.

Fig 2. VBA results for linear correlation of DTI and age in the top row. The bottom row is ANOVA of Tanner score 1 vs. Tanner score 5. All results are thresholded at TFCE p<0.01.