Voxel Based Analysis of ADC, FA and Hemispheric Asymmetry in Normal Aging

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Introduction:

Understanding the normal brain aging process provides important insights into mechanisms of pathologic brain decline. Several groups have attempted to study the effect of normal aging on brain employing diffusion tensor imaging [1, 2]. These studies rely either on global or regional histogram analysis or region based comparative analysis. However ROI based studies may not be particularly effective when changes are subtle and localized to many anatomical locations as in aging and requires a priori hypothesis of the anatomical location. A global (and automated) exploratory strategy is more appropriate in this situation. Voxel based analysis (VBA) that tests each voxel for statistical differences between population cohorts offers a convenient method for automated analysis. Here, we examine age related alteration in diffusion parameters using the image volumes acquired at high magnetic field (3.0 T). We adapt a strategy based on free-form transformation to generate a template to represent average shape model of population under study. VBA was performed with all subjects transformed to the co-ordinate system of the template. Our voxel-based methodology was evaluated against selective ROI analysis. Adapting a similar approach we also examined the inter-hemispheric FA asymmetry among young and middle age population employing both voxel-based and ROI based analysis.

Method:

For this study twenty healthy adult volunteers aged 26-69 years were recruited. The participants were divided into two age groups: Young age (mean age of 31 ± 3 years, range of 26 – 36 years, 8 males and two females) and middle-aged (mean age of 56 ± 9 years, range of 43-69, 3 males and 5 females). All the subjects were right handed except one in the middle age group. The data were acquired at 3.0 T (Magnetom Trio®, Siemens Medical Solutions, Erlangen, Germany) with a 8-element head coil array, using spin-echo single shot EPI with parallel acquisition (GRAPPA; acceleration factor of 2). The spatial resolution was 1.3 mm x 1.3 mm x 2 mm, and 18 averages were used to increase SNR. The geometric distortion associated with EPI acquisition was corrected utilizing a constrained free form registration algorithm based on optic flow developed in our lab [3].

An average parametric (FA, ADC) MRI brain atlas extending the work by Guimond and et al. [4] was created. Parametric maps from individual subjects were transformed to the coordinate of the average template utilizing affine and constrained free form transformations. Spatially normalized FA and ADC maps were smoothed using 3D spatial Gaussain filter with full with half maximum of 4 mm and compared by voxel based two sample *t*-test with handedness as covariance across the two age groups utilizing SPM2 software. To create a template for inter-hemispheric asymmetry voxel based analysis a mirror image of the original image volumes were generated. The flipped images were aligned to the original images utilizing affine and free form transformations. Once the flipped images registered to the original image, a common template was created. For hemispheric asymmetry study, a paired "t" test was utilized to compare subjects in each age group separately. Only right-handed subjects were recruited for this study (10 subjects for young age group and 9 subjects for middle age group). The multiple comparison test was addressed by false discovery rate (FDR) approach. Six ROIs, genu and splenium of corpus callosom, anterior and posterior limbs of internal and external capsules were outlined by one operator on FA template on each hemisphere separately. The ROIs were then transferred to the spatially normalized individual volumes where they were relocated, if necessary, to ensure maximum homology across subjects. For each particular ROI the size and shape were kept constant across subjects. The statistical significance for the age related differences were examined for individual hemispheres by implementing the one tailed two-sample student "t" test. Asymmetry effects were determined statistically by employing two tailed paired student "t" test. All ROI based analysis was performed on the right-handed subjects.

Results:

VBA of FA with age demonstrates regions of decline in genu and body of corpos callosum, posterior limb of internal capsule, anterior and posterior limbs of external capsule, frontal white matter and cingulum (Fig. 1). Voxel based asymmetry evaluation of FA for young age group revealed significant right-greater-than-left asymmetry in genu, splenuim and body of corpus callosum and left-greater-than-right asymmetry in anterior limb of external and posterior limb of internal capsule, thalamus and cerebral peduncle (Fig. 2). The asymmetry for the middle age group was reduced and limited to right-greater-than-left asymmetry in anterior limb of external capsule and left-greater-than-right asymmetry in posterior limb of internal capsule (Fig. 2). VBA and ROI analysis agreed fairly well for age related FA changes.

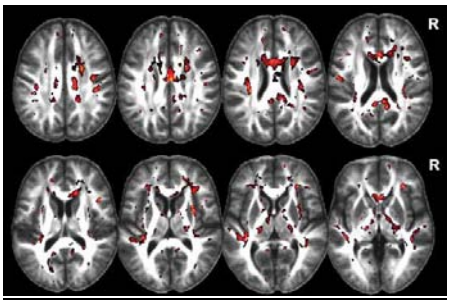

Fig. 1. Map of voxel-based significance of FA decline with aging. The map was generated by computing the voxel level *t*-tests between young and middle age groups. In each row, the planes are separated by 4 mm. The color scale represents the significance of FA decline with aging measured in *t* values with yellow representing the most significant area. ($t \geq 3.23$ or $p \leq 0.025$).

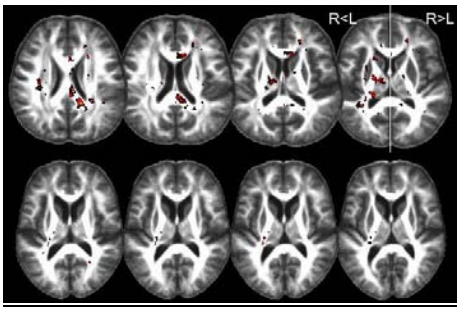

Fig.2. Map of voxel-based significance of FA asymmetry for the young age (top) and middle age (bottom) groups. Note the significant reduction in asymmetry with aging. The map was generated by computing the voxel level paired *t*-tests between corresponding points in right and left hemispheres. In each row, the planes are separated by 4 mm. The color scale represents the significance of FA change measured in *t* values with yellow representing the most significant area. ($t \geq 4.49$ or $p \leq 0.025$).

Conclusions:

In contrast to ROI based techniques, the approach in this study is to utilize a sophisticated spatial normalization technique to establish a one-to-one correspondence between all the imaging studies, enabling VBA to measure the changes in ADC and FA values with aging. The results of the VBA compared favorably to conventional ROI based analysis on genu and splenium and anterior and posterior limbs of internal and external capsules. Hemispherical asymmetry of the two populations were also evaluated by VBA and compared to ROI analysis on the same structures listed above. This paper is the first to report reduction in hemispheric asymmetry of fractional anisotropy with age.

References:

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