Diffusion Tensor Imaging in Normal Aging Brain : Analysis of Voxel-wise Statistical Maps and White Matter Tractography

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Synopsis

Brain structural changes associated with normal aging lead to alterations in water diffusivity measurements. Previous work revealed age-related declines in white matter anisotropy with analysis of specified regions-of-interest. In this work, we investigated mean diffusivity and diffusion anisotropy in the brains of 45 normal aging populations using voxel-wise statistical analysis. In addition, a study of white matter tractography was performed to help understanding anatomical connectivity of white matter tracts which were altered with normal aging.

Introduction

Normal aging is accompanied by white matter structural change as well as loss of gray matter volume. Previous work revealed age-related declines in white matter anisotropy in the corpus callosum, centrum semiovale, and bilateral frontal and parietal pericallosal areas by means of a region-specific analysis targeting several pre-selected areas of normal healthy brains [1][2]. As an alternative approach, a voxel-wise statistical analysis allows mapping spatially distributed statistical results in a standardized coordination system. However the quantitative analysis using this method is still challenging due to residual anatomical variability after image registration process. It is known that the statistical reliability of voxel-based methods can be improved by use of large sample size. In this work, we analyzed whole brain apparent diffusion coefficient (ADC) and fractional anisotropy (FA) values on a voxel-by-voxel basis using relatively large number of normal aging subjects. In addition, a study of white matter tractography was performed to help understanding anatomical connectivity of white matter tracts which altered with normal aging.

Methods

We studied a group of 45 normal healthy subjects composed of 16 men and 29 women aged 20 to 86 years (mean±S.D.=40.91±20.29). Diffusion tensor (DT)-MRI were acquired on a 3T Magnetom Allegra (Siemens, Erlangen, Germany) system equipped with 40mT/m amplitude and 400 mT/m/s slew rate gradients and a standard circulary-polarized head coil. A single-shot spin-echo EPI with a twice-refocused balanced echo sequence was used to reduce eddy current distortions [3] (TR/TE=5800/87ms, FOV=20cm, acquisition matrix=128x96, reconstruction matrix=128x128, number of averaging=8, diffusion sensitizing orientations=12, b=1000s/mm^2, 45 contiguous axial slices with 3mm section thickness). To minimize effects from blood flow and CSF pulsation, image scanning was gated with peripheral arterial pulse. The susceptibility induced geometric distortions were corrected using a 1-D correction algorithm along the phase-encoding direction with a separately acquired field map [4]. Linear estimation of diffusion tensor was followed by calculations of FA and ADC maps. Data preprocessing and statistical parametric map (SPM) calculations were performed using SPM2 (Wellcome department of Cognitive Neurology, UK). Data were spatially normalized into an MNI (Montreal Neurologic Institute) stereotaxic space with 2x2x2 isotropic voxel dimension and were smoothed using 8mm 3D Gaussian kernel. Each ADC and FA maps of the group were linearly fitted using simple regression model with age regressor on a voxel-by-voxel basis. SPM was thresholded with criteria of familywise error corrected *p*-value 0.001 (t=7.14, df=43) and cluster size of 50 voxels. Finally, a tensor deflection tractography [5] seeded from the thresholded activation clusters was performed and was visually inspected to correlate with a priori knowledge of neuroanatomy.

Results

The areas of increased ADC were observed in the white matter of precentral, superior and middle temporal areas, and in the gray matter of insula, inferior parietal lobule, parahippocampal, medial frontal, anterior cingulate, and postcentral gyri, bilaterally (Fig.1A). The areas of decreased FA were detected only at the frontal pericallosal white matter, bilaterally (Fig. 1B). Correlation coefficients (r) at the global maxima of SPM were measured 0.86 of ADC and -0.83 of FA, respectively. No areas with declined ADC or elevated FA with age were observed. Tractography results demonstrated the white matter tracts connected to the areas of declined anisotropy, including corpus callosum, frontal forceps and uncinate fasciculi, bilaterally (Fig.2).

Conclusion

We reproduced similar diffusivity changes in normal aging brains reported in previous work. However, using voxel-based analysis of the whole brain, our work provided a useful map of normal aging process. We expect that our results can contribute understanding cognitive and functional changes in the geriatric population.

Reference

[1] Pfefferbaum A, et al. Magn Reson Med 2003;49:953-961
[2] Abe O, et al. Neurobiol Aging 2002;23:433-441
[3] Reese T, et al. Magn Reson Med 2003;49:177-182
[4] Jezzard P, et al. Magn Reson Med 1995;34:65-73
[5] Weinstein DM, et al. IEEE Visualization Proc, p249-253, 1999

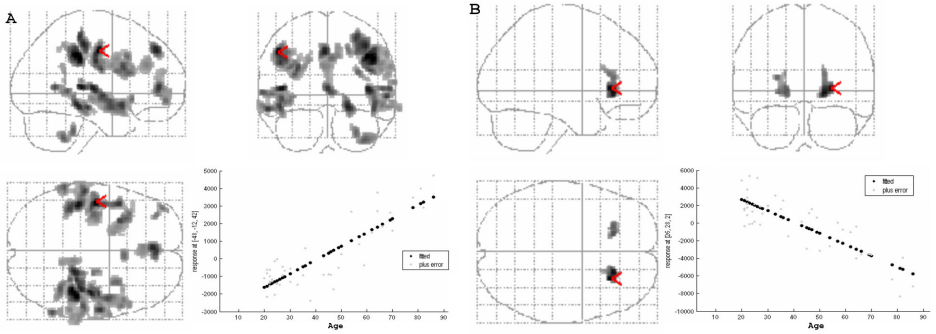

Figure 1. Projected statistical parametric maps (SPM) (corrected p<0.001) and regression plots from simple linear regression analyses (A) apparent diffusion coefficient (ADC) (B) fractional anisotropy (FA). The voxels of global maxima in the SPM (red brackets) were selected to demonstrate the fitted plots.

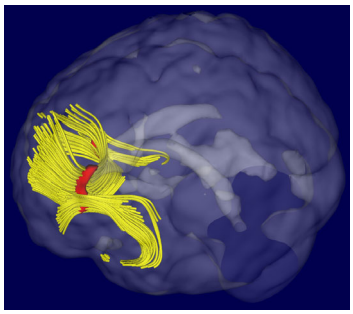

Figure 2. Tractography demonstrates the white matter tracts connecting areas of less anisotropy, including corpus callosum, frontal forceps and uncinate fasciculi, bilaterally.