Semi-automated Voxelwise Analysis of Fractional Anisotropy Changes in Multiple Sclerosis Patients

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Abstract

Diffusion Tensor Imaging (DTI) is a noninvasive technique that is used to assess the microstructure of the cerebral tissue in a variety of neurological diseases. Recently, diffusion tensor studies have provided new insights into tissue changes occurring in normal appearing white matter (NAWM) in multiple sclerosis (MS). However, the region-of-interest (ROI) analyses used in these studies to obtain this DTI information have several drawbacks in terms of speed of analysis and reproducibility and accuracy of ROI placement. The purpose of this study was to investigate the use of a semi-automated voxelwise analysis of fractional anisotropy (FA) maps in a standard neuroanatomical space in MS patients.

Introduction

Several studies have recently shown changes in diffusion anisotropy in NAWM in MS.[1-3] These include changes not only in regions distant from the plaques but also in the peri-plaque regions, potentially leading to a reevaluation of the true size of lesions.[2,3] However, in many, if not all, of these studies researchers have manually delineated ROIs on their images in order to carry out their analyses. This is usually a time-consuming process and is rather arbitrary in terms of deciding where these regions are to be drawn. Furthermore, given the same data set, it is questionable whether the same results could be reproduced. Some groups have addressed this issue by utilizing the theory, methodology, and tools from the computational neuroanatomy and functional magnetic resonance imaging communities.[4-9] In this study we have developed a semi-automated method to facilitate this analysis by spatially normalizing the images into a standard neuroanatomical space and then statistically comparing the images at the level of individual voxels. In this preliminary study, we investigated the utility of this approach in the detection of diffusion anisotropy changes in MS patients.

Methods

DTI was performed on 10 normal controls and 6 patients with MS lesions. We acquired DTI by collecting diffusion-weighted images using a spin-echo echo planar imaging sequence. Diffusion sensitizing gradients were applied in six non-collinear directions with a b value of 1000 sec/mm^2. An image without diffusion weighting (b = 0 sec/ mm^2) was also collected. Twenty axial slices (with 6mm thickness and in-plane resolution of 1.8 x 1.8 mm) covering the entire brain were imaged using a 1.5 T scanner. The imaging parameters included: TR = 6000 ms, TE = 100 ms, FOV = 240 mm, 98x128 and 4 acquisitions. FA images were then created using an in-house modified diffusion tensor toolbox of SPM99 (Wellcome, UK). The FA maps were then spatially normalized (via an affine transformation) into the space of the EPI template available in SPM99. (The b=0 image was used to determine the transformation parameters). The FA maps were then smoothed using a 4x4x12 mm Gaussian kernel. A normal FA atlas was created using the 10 normal subjects. The FA map of each of the patients was then compared voxelwise with the FA atlas of the group of normals in a two sample t-test (uncorrected p value of 0.05).

Results

The statistical maps showing regions of significant FA differences were compared with routine T1, T2, and fluid attenuated inversion recovery (FLAIR) images. Figure 1 shows an example of a typical result observed in this study. As seen in the figure, there were numerous regions of statistically significant (p=0.05) FA differences that were readily seen on the statistical map but not visible on the routine MR image. Please note that the large lesion (arrow) on the statistical map in the left hemisphere corresponds well in location with the lesion (arrow) shown on the FLAIR image. It can be seen that the center of the lesion (yellow) exhibits more significant FA changes than the peripheral portions (orange). Similar findings were observed on the other five MS cases analyzed as well. In two cases, however, there were lesions visible on routine MRI that did not show significant FA changes. Additionally, in one of the cases (not shown), in which longitudinal patient data was available, some of the lesions shown in the statistical map later appeared in the routine images. This is consistent with previous published findings that showed that diffusion changes in NAWM (more specifically, increases in average apparent diffusion coefficient (ADC_{av})) precede the appearance of Gd-DTPA enhancing lesions. [10]

Discussion and Conclusion

Voxel-wise analysis of spatially normalized FA maps has the potential to significantly improve the analysis of diffusion tensor data in terms of speed, reproducibility, and accuracy. In addition, FA changes can be readily visualized in the whole brain rather than simply being quantified (without the ability for visualization) in isolated regions as is done with ROI analyses. Furthermore, this method has the potential to both characterize quantitatively the extent of MS lesions and abnormal FA in NAWM. Such analysis of FA data using a standard anatomical atlas will greatly help in longitudinal follow-up of these MS patients as well. However, care must be taken in interpreting the regions of FA differences. Some of these may be due to misregistration of images, leading to a comparison of different tissue types. This phenomenon should generally be more pronounced at tissue interfaces, such as in the periventricular regions and the grey-white interfaces. Future work will address these issues and attempt to more definitively interpret the pathological significance of regions of FA change in the NAWM. This may be facilitated by the availability of patient data at multiple points in time. These preliminary results are very encouraging and warrant further investigation.

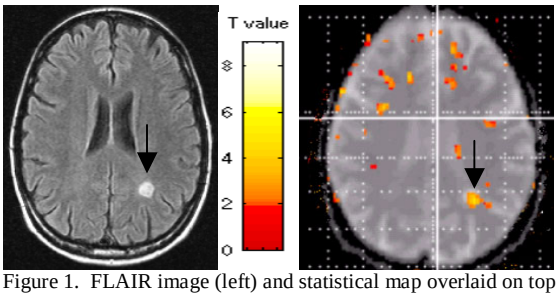

Figure 1. FLAIR image (left) and statistical map overlaid on top of the b=0 diffusion weighted image (right).

References:

1. Ciccarelli, O. et al. 2001. Neurology 56:926-933.
2. Guo et al. 2002. Radiology 222(3):729-736.
3. Kealey et al. 2004. American Journal of Roentgenology 183(2):497-503.
4. Park, Hae-Jeong et al. 2004. Neuroimage 23: 213-223.
5. Barnea-Goraly, N. et al. 2003. American Journal of Medical Genetics 118B(1): 81-88.
6. Barnea-Goraly, N. et al. 2003. American Journal of Psychiatry 160:1863-1869.
7. Eriksson, S.H. et al. 2001. Brain 124(3): 617-626.
8. Rugg-Gunn et al. 2001. Brain 124(3): 627-636.
9. Sach, M. et al. 2004. Brain 127:340-350.
10. Werring, D.J. et al. 2000. Brain 123:1667-1676.