The Analysis of the Water Diffusivity within White Matter Tract in Cuprizone-Induced Mouse Model using Various Indices by the Diffusion Tensor Ellipsoid

C-Y. Lin[1,2], P-C. Chang[2], C-Y. Hong[2], J-H. Chen[1], C. Chang[2]

[1]Interdisciplinary MRI/MRS Lab, Department of Electrical Engineering, National Taiwan University, Taipei, Taiwan, [2]Functional and Micro-MRI Center, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

Synopsis

The goal of this study is to explore the ability of various diffusion tensor indices in detecting the abnormality of white matter tract (WMT) in cuprizone-induced mouse model. The results demonstrate that the analysis of size, shape and similarity of diffusion tensor ellipsoid are able to provide the different insight in tissue architecture which is promising for monitoring the changes of white matter structure in the development, aging and disease.

Introduction

Diffusion-tensor MRI (DT-MRI) is widely used to investigate tissue pathology and morphology noninvasively [1]. The DT was derived by matrix diagonalization, and three pairs of eigenvalues and eigenvectors were calculated and can be used to form an ellipsoid mathematical model. There are several indices derived from the DT ellipsoid have been previously proposed [2,3]. These indices can be classified into 3 categories that were size, shape and similarity, respectively. However, there are no systematic comparisons among these indices as to which category or which index in specific category is more sensitive and appropriate for particular applications. The purpose of the present study is thus to have a comparison of inter- and intra-categories in pathological tissue. A well-established cuprizone-induced model of experimental demyelination in corpus callosum in a mouse brain was used for the current study.

Material and Methods

Animal

A male (8-week-old) C57BL/6 mouse was treated on a diet of 0.2% cuprizone through mixed into milled chow and was maintained on the cuprizone diet until 10 weeks.

DTI data acquisition and analysis

Mouse was anesthetized with isoflurane/oxygen mixture (isoflurane at 5 % for induction and 1% for maintenance) and examined in a 4.7T Biospec 47/40 spectrometer. A spin echo imaging sequence was employed for acquisition of the required series of diffusion-weighted images with TR of 1.5 s, TE of 36.5 ms, Δ of 15 ms, δ of 8 ms, 8 averages, slice thickness 0.8 mm, FOV of 2 cm, data matrix 256x256 and b values of 0 and 1100 mm^2/s applied along six directions:[Gx, Gy, Gz] = [1,1,0],[1,0,1],[0,1,1],[-1,1,0],[0,-1,1], and [1,0,-1]. Images were acquired before and at 4th, 10th week after treating with cuprizone diet. Quantitative indices, including the analysis of DT size utilizing trace (Tr (D)), trace2 (Tr (D^2)) and volume (Vol); DT shape utilizing fractional anisotropy (FA), relative anisotropy (RA) and Skewness (Sk); similarity utilizing direction correlation (DC) and normalized tensor scalar product (NTSP), were derived pixel-by-pixel using Matlab (MathWorks, Natick, MA, USA) as defined by the following equations:

$$\mathbf{Tr(D)} = \lambda_1 + \lambda_2 + \lambda_3,\quad \mathbf{Tr(D^2)} = \lambda_1^2 + \lambda_2^2 + \lambda_3^2,\quad \mathbf{Vol} = \lambda_1 \times \lambda_2 \times \lambda_3;$$

$$\mathbf{FA} = \sqrt{3\sum_{i=1}^{3}(\lambda_i - \mathbf{Tr(D)}/3)^2 / 2\mathbf{Tr(D^2)}},\quad \mathbf{RA} = \sqrt{\sum_{i=1}^{3}(\lambda_i - \mathbf{Tr(D)}/3)^2} / \sqrt{3}(\mathbf{Tr(D)}/3),\quad \mathbf{Sk} = \sqrt{\sum_{i=1}^{3}(\lambda_i - \mathbf{Tr(D)}/3)^2} / \mathbf{Tr(D^2)};$$

$$\mathbf{DC}_{ij} = \mathbf{V}_{i1} * \mathbf{V}_{ij},\quad \mathbf{NTSP(D_1, D_2)} = \sum_{i=1}^{3}\sum_{j=1}^{3}\lambda_{1i}\lambda_{2j}\varepsilon_{1i}\varepsilon_{2j} / |\mathbf{Tr(D_1)}||\mathbf{Tr(D_2)}|$$

In the case of similarity, the initial point was assigned as indicated by the red arrow in Figure C1. In size and shape categories, the contrast-to-noise ratio (CNR) was calculated by following formula: CNR = |(SI of corpus callosum – SI of cortex)| / SI of cortex. ROI selection was shown in Figure B1

Results

The quantitative indices of DT size, shape and similarity at the indicated time points are shown in Figures A1-A3, B1-B3 and C1-C2, respectively. The CNR analyses of size and shape indices are illustrated in Figure A4 and B4, respectively, whereas the values of DC and NTSP are represented as Figure C3. In size category, Tr (D) and Tr (D^2) show 2 to 3-fold CNR difference in the CC (arrowheads) at different time points whereas Vol provides the best contrast between low- and high- anisotropy. In shape category, FA and RA exhibit the comparable CNR with each other while Sk yields the best contrast between isotropy and anisotropy. In addition, prolate DT ellipsoid has positive skewness while oblate DT ellipsoid has negative skewness. In similarity category, NTSP calculated by the inner product of diffusion tensor instead of principal diffusion direction, in contrast to DC, is more sensitive to detect subtle changes of WMT.

Conclusion

The present results demonstrate that the size indices are able to detect where the lesion is and shape indices provide the high contrast between isotropy and anisotropy, especially in Sk index which can be used to classify white matters from gray matters, while similarity of DT is more sensitive to reveal the changes of orientation and diffusivity in the abnormality of WMT.

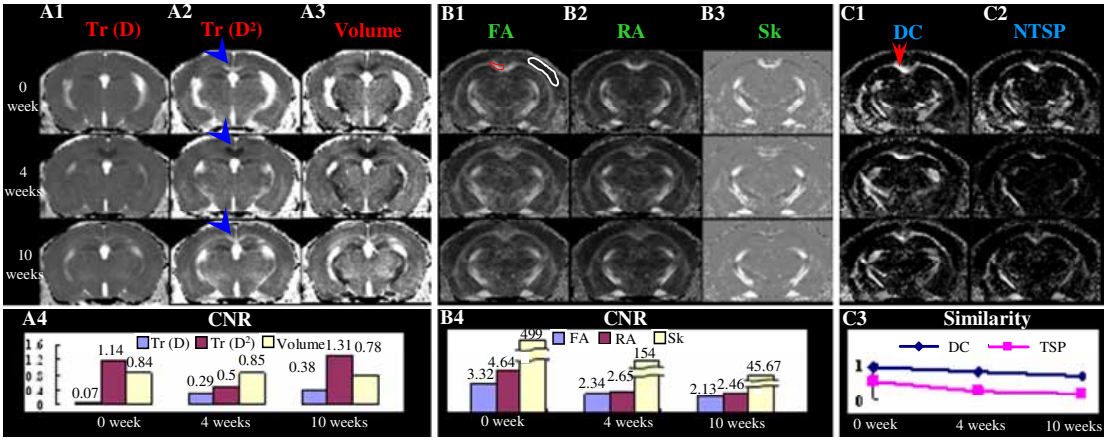

Figure A. The size maps of DT and CNR at indicated time points. Figure B. The shape maps of DT and CNR at indicated time points. Figure C. The similarity maps and quantitative analysis of DC and NTSP at indicated time points.

References

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