A Spatial normalized study of diffusion tensor imaging in clinically isolated syndrome and multiple sclerosis patients

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Introduction

Diffusion tensor imaging (DTI) is unique in its non-invasive capability to reveal a set of physiological parameters related to water diffusion, such as fractional anisotropy (FA), apparent diffusion coefficient (ADC), axonal (L1, the largest eigen-value) and axial (L2, the average of the two least eigen-values) diffusivities. Numerous publications have observed changes of these parameters in MS patients [1,2,3], we applied a spatial normalized based analysis to examine these parameters voxel by voxel. Our analysis does not require predefined ROI calculations and this may suit better the diffuse nature of MS.

Materials and Methods

This is an IRB approved study. T1 weighted (1mm^3 in voxel size) and DTI images (6 different encoding directions and 2mm^3 in voxel size, total 46 slices) were collected for all the subjects on a Siemens 3T head only scanner. Written consents were obtained from all subjects prior to image acquisition. 28 normal volunteers (15M, 13F, 34.39±6.08 years old) were recruited for building the normal DTI statistics of four scalar DTI components (FA, ADC, L1 and L2). The DTI results from 35 CIS (8M, 27F, 40.40±9.85 years old) and 16 MS (3M, 13F, 39.88±10.66 years old) patients were compared with the corresponding normal DTI statistics for significance analysis. The inter-subject warping was performed with a B-spline model based registration carried on T1. A 3D rigid registration was used to align DTI with the T1 from the same subject, so that DTI results can be spatially transformed towards the common template through the T1 across-subject registration. The "abnormal" volume of each patient was computed by summing up all the voxels, whose deviation from the normal mean exceeds two standard deviations either positively (positive abnormal volume, PAV) or negatively (negative abnormal volume, NAV). The "abnormal" volume of a normal volunteer was obtained by comparing his DTI parameters with the templates built without him (leave-one-out). For each DTI parameter, Kruskal-wallis multiple groups tests were performed on the global variables such as the "abnormal" volumes and the locations of quartiles (25%, 50% and 75%)of the histogram. Local Kruskal-wallis tests were also performed in the spatially normalized DTI maps for all the voxels with brain. Using brain segmentation, the statistically significant findings can be categorized into both white matter (WM) and gray matter (GM) regions.

Results

One slice of the mean and standard deviation maps of FA and ADC from normal population was given in Figure 1. The significant regions (red area overlapped upon the anatomical images) identified with voxel based multiple group comparison were demonstrated in Figure 2. The significant different areas between normal and CIS (left column), normal and MS (middle column), and CIS and MS (right column) from FA (upper row) and ADC (lower row) statistics were given in Figure 2. Significant findings in the histogram and "abnormal" volume analysis in both GM and WM were summarized in the table. Even though significant differences were identified between normal and the patient groups, no significance was found between CIS and MS groups.

	(Mean ± SD) of normal, CIS and MS groups	P values
DTI parameter histogram quartile locations		
GM FA 1st	(0.099 ± 0.007) (0.091 ± 0.013) (0.090 ± 0.012)	<0.01
GM L1 3rd	(1.224 ± 0.053) (1.274 ± 0.083) (1.265 ± 0.105)	<0.05
GM L2 3rd	(0.998 ± 0.060) (1.049 ± 0.088) (1.048 ± 0.112)	<0.05
WM FA 1st	(0.224 ± 0.020) (0.212 ± 0.021) (0.201 ± 0.020)	<0.01
WM ADC 3rd	(0.824 ± 0.022) (0.846 ± 0.033) (0.845 ± 0.038)	<0.02
WM L1 3rd	(1.215 ± 0.030) (1.244 ± 0.039) (1.229 ± 0.041)	<0.01
WM L2 3rd	(0.705 ± 0.024) (0.722 ± 0.034) (0.728 ± 0.038)	<0.05
NAV and PAV for DTI parameters		
GM FA NAV	(1.68±0.72) (3.70±1.22) (4.18±1.58)	<0.00001
WM FA NAV	(9.39±6.26) (16.91±7.31) (21.27±9.15)	<0.00001
GM ADC PAV	(23.33± 10.55) (39.99±18.44) (39.44±22.38)	<0.001
GM ADC PAV	(17.56±9.45) (40.23±25.75) (40.16±29.50)	<0.0001
GM L1 NAV	(2.03±1.36) (4.72±3.57) (4.90±3.90)	<0.01
GM L1 PAV	(22.51± 9.68) (38.72±19.68) (37.18±21.35)	<0.01
WM L1 NAV	(6.25±4.52) (9.55±4.85) (10.89±6.75)	<0.01
WM L1 PAV	(16.52±7.34) (31.94±17.09) (28.77±16.14)	<0.001
GM L2 PAV	(16.63±9.33) (34.00±19.06) (37.79±25.13)	<0.0001
WM L2 PAV	(21.64±10.06) (38.26±17.42) (37.93± 21.48)	<0.001

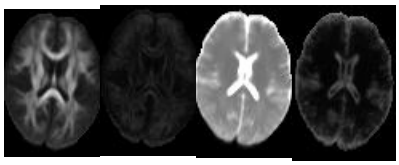

Figure 1

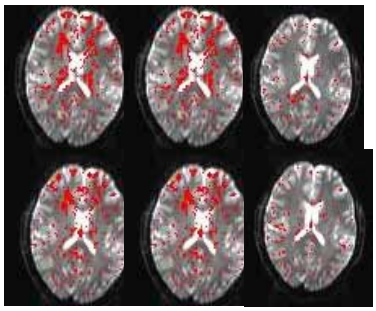

Figure 2

Discussion

The spatial normalization based approaches were capable to differentiate CIS and MS from the normal population using both histogram, and voxel based analysis, but not between CIS and MS groups. Histogram analysis of both WM and GM regions revealed significantly lower 1st quartile FA, and significantly higher 3rd quartile L1 and L2 statistics in both MS and CIS groups. ADC histograms only showed differences within the WM at the 3rd quartile. This is consistent with previous findings that FA is reduced, while diffusivities are elevated in MS patients. The DTI "abnormal" volumes demonstrated statistical significance for all WM and GM measures for both the CIS and MS groups compared to the normal group. The statistical differences are greater than histogram analysis. This difference may attribute to that each voxel is studied before they are summated, whereas in histogram analysis all voxels are averaged together before calculations of statistical significance are made. L1 demonstrated both NAV and PAV significance. This may be caused by the co-existence of inflammation and axonal/myelin loss synchronously occurring in the brain. The lack of statistically significant differences between the CIS and MS groups may indicate that either imaging techniques or clinical criteria for MS diagnosis are not sensitive enough for differentiation. If later is the case, DTI may play a greater role in diagnosis of MS. As for the potential significant areas (the red regions in Figure 2) identified with voxel based multi-group comparison, more efforts are still needed before any conclusion can be made. Possibly, individual sequential voxel based analysis may help determine if we can differentiate over time between individual CIS and MS patients.

References

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