The improved detection of corticospinal tract degeneration in amyotrophic lateral sclerosis using the combination of color-coded DTI maps and 3D fiber tracking

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Background and Objectives

In our previous study to employ diffusion tensor MRI in ALS, we demonstrated that fractional anisotropy (FA) and mean diffusivity (MD) were significantly reduced and elevated, respectively in ALS patients versus normal control in the cerebral peduncle (1). Although the analytic method used in our previous work showed such significant group differences, the sensitivity (43.6% for FA, 18.8% for MD) of the DTI was not enough for clinical application on an individual basis. We speculated that the low sensitivity may originate from the inadvertent inclusion of adjacent white matter tracts having a similar orientation but not belonging to the corticospinal tracts in the manually drawn region of interest (ROI). We hypothesized that selective inclusion of the corticospinal tracts might improve the detection of the corticospinal degeneration in ALS and employed a so-called two-ROI approach in which 3D fiber bundle tracking was performed using two reference ROIs.

Materials and Methods

We investigated 11 ALS patients (M:F=6:5, 55.5 ± 10.4 years) included in our pervious study, thus their histories and MR measurement protocol in DTI were the same in our previous study (1); their diagnoses were established according to the criteria of El Escorial in the revised form of Airlie House (2) and the UMN signs were estimated in all patients according to the same criteria used for the diagnosis of ALS. We determined simply the presence or absence of UMN dysfunction in each limb and bular region and counted the number of regions having the definite evidence of UMN involvement. All patients and the 7 healthy age and sex-matched controls (mean age 58.0±8.3 years old; M:F=3:4) gave informed consent. The pyramidal tract was identified on color-coded fractional anisotropy maps (FA threshold of 0.3) of fiber direction, which helped to identify pyramidal tracts and exclude voxels containing anisotropic fibers with orientations inconsistent with known pyramidal tract orientation. Regions of interest (ROIs) were manually drawn in the left and right pyramidal tracts on the cerebral peduncle at the level slightly above the red nucleus (ROI-1) and the lower pons (ROI-2). SubROI was determined at the region of ROI-1 with tract portions that passed through a ROI-2 in all tracts obtained from seed points in a ROI-1, i.e., by two-ROI analysis (Fig. 1). Fiber-tracking was performed using a home-made program based on the FACT method proposed by Mori. The 3D tracking results were superimposed within the ROI-1 on FA map (Sub-ROI) for quantitative analyses of diffusion properties of corticospinal tracts. Repeated measure ANOVA (General linear model) was first used to assess the effect of parcellation, group (patient versus control), and of possible interaction between these factors on FA. FA and MD values were averaged in the right and left ROI-1, ROI-2 and sub-ROI, and group comparisons were made using the Kormogorov-Smirnov test. Correlation between FA in the sub-ROI and clinical extent of UMN signs was investigated by Spearman's correlation analysis.

Results

Table 2 showed FA was significantly lower in ALS versus normal control only in sub-ROI, but MD was not significantly different between ALS and normal control in all ROIs. In sensitivity of DTI as a diagnostic tool of upper motor neuron dysfunction, on an individual basis, five patients (45.5%) and no control had an average FA value of less than the average FA-2 S.D. in the control group (<0.587), while three patients (27.3%) and no control had an average MD value of greater than the average MD+2 S.D. in the control group (>1079 mm^2/s). There were significant group (ALS vs normal control, p=0.002) and parcellation effect (p<0.001). There was also significant interaction between group and parcellation (p=0.15), which means that the elevation of FA values by parcellation was different between ALS and normal control (Fig 2, left and middle). Including all subjects and by scoring the extent of UMN signs of normal controls as "0", we found a significant inverse correlation between FA in the sub-ROI and the clinical extent of UMN signs (spearman correlation analysis, r = -0.75, p<0.001, Fig. 2, right).

Conclusion

The corticospinal tracts could be delineated reliably using our two-ROI approach. Compared with the method of visual inspection and manual drawing of ROI, combination of color-coded DTI maps and automated 3D fiber tracking may improve the detection of corticospinal tract degeneration in ALS.

References

1) Hong YH, Lee KW, Sung JJ, Chang KH, Song IC. J Neurol Sci, In press. 2) Brooks BR, Miller RG, Swash M, Munsat TL. Amyotroph Lateral Scler Other Mot Neuron Disord 2000;1:293 – 9.

Table 2. Averages of the left and right mean fractional anisotropy and mean diffusivity in the cerebral peduncle (ROI-1), the lower pons (ROI-2) and sub-ROI within ROI-1.

	Fractional anisotropy			Mean diffusivity (mm^2/sec)		
	Normal control	ALS	p	Normal control	ALS	p
ROI-1	0.557±0.031	0.520±0.026	0.072	1102±63	1197±97	0.277
ROI-2	0.403±0.027	0.372±0.031	0.063	895±82	902±49	0.535
Sub-ROI	0.667±0.040	0.597±0.046	0.013*	949±65	1022±122	0.108

Kolmogorov-Smirnov test, *, p<0.05

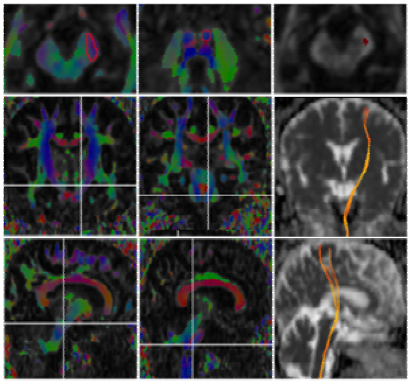

Figure 1. Sub-ROI parcellation (right and first row) within the cerebral peduncle (ROI-1) by tractography which connects ROI-1 (red line in left and first row) and ROI-2 (red line in middle and first row)

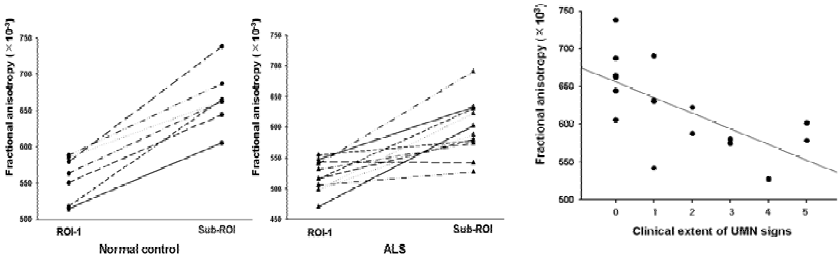

Figure 2. (Left and middle) Repeated measures ANOVA (Geneal Linear Model) Significant group effect (ALS vs normal control), p=0.002; Significant parcellation effect, p<0.001 ; Group×parcellation interaction effect, p=0.15, (Right) Inverse correlation between fractional anisotropy (FA) averages in the sub-ROI within the cerebral peduncle (ROI-1) and the clinical extent of UMN signs (r = -0.75, p<0.001).