Diffusion Tensor MRI as a Diagnostic Tool of Upper Motor Neuron Involvement in Amyotrophic Lateral Sclerosis

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Background and objective
Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease affecting both upper and lower motor neurons. Clinical identification of upper motor neuron (UMN) dysfunction in amyotrophic lateral sclerosis (ALS) is often difficult, particularly early in the course of disease or when lower motor neuron dysfunction is very prominent. Diffusion tensor imaging (DTI) can provide unique information on the axonal organization by measuring the anisotropy of diffusion as well as the directionally independent diffusion. The purpose of this study is to assess water diffusion changes along pyramidal tracts of the brainstem in patients with ALS and possible correlations between the changes of diffusion properties and clinical parameter.

Materials and Methods
We studied 16 patients (M:F=9:7, mean age 50.5±12.4 years) with definite, probable or laboratory-supported probable ALS according to El Escorial criteria as defined by clinical and electrophysiological examination (1). The clinical extent of UMN signs was estimated in all patients by determining the number of extremities with clinical signs of upper motor neuron involvement, defined by the existence of the Babinski sign, increased tendon reflexes, spasticity or well-preserved tendon reflexes in an extremity with advanced muscular atrophy. The bulbar region was considered as one “extremity”, so that the clinical extent of UMN signs in a subject was scored from “0” (control group) to “9” (bulbar and four limbs). They were compared with 11 healthy, age and sex-matched controls (M:F=5:6, mean age 54.5±9.9 years). Diffusion-tensor magnetic resonance imaging using a single shot SE-EPI with 25 noncollinear diffusion gradient directions (b=1000 sec/mm²) and also with no diffusion gradient was performed on a 3.0 Tesla MR system. The diffusion-weighted images were initially smoothed using a Gaussian filter with a FWHM of 4 pixels to preserve information within the image while reducing the effects of noise. Properties of the diffusion tensor matrix were then computed pixel by pixel using SVD method and displayed as images. The diffusion parameters we investigated were the mean diffusivity (MD) and the fractional anisotropy (FA). Region of interests (ROIs) were manually drawn on the left and right pyramidal tract in the brainstem. FAs were collectively averaged in four anatomical regions (cerebral peduncle 3 slices, upper pons 3 slices, lower pons 3 slices, medulla 3 slices) and compared between groups. At the level of the midbrain, we further evaluated the extent of anisotropy and mean diffusivity using FA threshold of 0.5 to avoid partial volume contamination of the pyramidal tract within ROIs.

Results
In the analysis using multifactorial ANOVA, the effects of the group and anatomical level on FA and MD were significant (p<0.001 for both diffusion parameters), whereas the effect of side and interactions between factors (group by side, and group by anatomical level) were not (p>0.05). In all subjects, FA was highest in the cerebral peduncle, lowest in the caudal pons and intermediate in the medulla and highly variable even between contiguous slices in the pons and medulla, whereas relatively constant FA values were noted at the level of the midbrain. We found a significant decrease of FA and increase of MD in patients compared with normal controls in the midbrain, but not in the pons and medulla (Mann-Whitney U test with a Bonferroni adjustment, p<0.001 for FA, p=0.001 for MD, Fig. 1). When only the voxels having FA above 0.5 were included in the analysis at the level of the midbrain, FA continued to be significantly reduced in patients compared with normal controls (p<0.001). Bivariate correlation analysis revealed significant inverse relationships between FA value and the degree of UMN signs (spearman’s rho = -0.81, p=0.001, Fig. 2).

Discussions and Conclusions
Our observations in the brainstem, consistent with the finding of the previous work (2), support the potential of DTI as a noninvasive in vivo diagnostic tool of UMN involvement in motor neuron disease and that DTI may be useful to document an UMN affection objectively and quantitatively in ALS. Another interesting finding of this study was that only the cerebral peduncle, as an optimal region for demonstrating “pathological” changes in ALS, showed a strong link between anisotropy and clinical extent of UMN signs, which is consistent with the observations by Ellis et al., who also reported negative correlations between anisotropy and spasticity scales. In conclusion, we suggest that in the brainstem, the cerebral peduncle would be the optimal region in order to investigate the pathological changes of the pyramidal tract using DTI in ALS. A strong negative correlation between anisotropy values in the cerebral peduncle and the clinical extent of UMN signs supports the potential role of DTI for detecting and monitoring the UMN involvement in ALS.

References

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