White matter impairment in Amyotrophic Lateral Sclerosis (ALS): Diffusion Tensor imaging and high b-value DWI study

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Background/ Aims:

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder of the motor system causing damage to both the upper and lower motor neurons (UMN/LMN). Previous diffusion tensor imaging (DTI) studies reported reduced fractional anisotropy (FA) in the cortico-spinal tracts (CST) as measured by region of interest analysis and using tractography to build up the entire fiber[1]. The purpose of this study was to quantitative evaluating the cerebral pyramidal tracts using DTI and high b-value diffusion weighted imaging (DWI).

Methods:

Study group: Twenty-three ALS patients, (8 women, mean age, 50+/- 23 years old) were included. ALS patients where clinical evaluated by the ALS functional rating scale (ALSFRS-R). Mean ALSFRS-R of Patients was 35.5±25. Mean disease duration (months since appearance of first symptoms) was 30.35 ± 60 months. *Control group*: Twenty two healthy subjects (12 women, mean age, 44+/- 16 years old) were included .

MRI protocol: MRI was conducted on a 3.0T GE MRI system. The MRI protocol included T1, T2, FLAIR, DTI and high b value DWI sequences. DTI data set was acquired in axial direction along 15 diffusion gradients with a b value of 1000 s/mm^2. High b-value cardiac gated coronal DTI data sets were acquired along six gradient directions with 15 b values incremented from 0 to12,000 s/mm^2.

Image Processing: Motion and eddy current correction were performed using FSL program (FMRIB Software Library). DTI analysis was performed on the axial slices according to Bassar et al [2] using DTIStudio software and fractional anisotropy (FA) was calculated. q-space analysis was performed on the set of the coronal high b value DW images, by a Fourier transform of the non-mono-exponential signal decay, using an in-home Matlab® program to produce two maps of probability (Prob) and displacement (Disp) (see Figure 1). Tractography was done using DTIStudio for reconstruction the corticospinal fiber (CST). Motor and sensory fibers were reconstruct separately, and on each hemisphere. Fibers were calculated going through three ROIs: at the level of posterior (motor) or inferior (sensory) to the central sulcus, posterior limb of the internal capsule, and anterior (motor) posterior (sensory) regions in the thalamus – midbrain. On the coronal slices - fibers were similarly prescribed without separation to motor and sensory. Mean values of FA, Prob and Disp were calculated for each fiber.

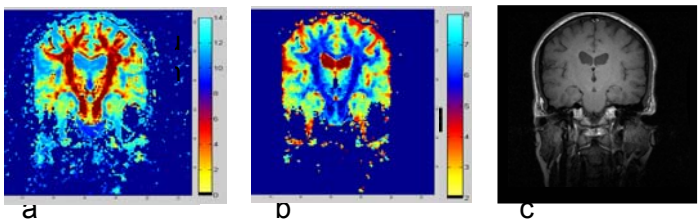

Figure 1: (a) Displacement map (b) probability for zer displacement map and (c) T_1 weighted image of a typical control subject.

Results and Discussion:

Significant reduction in FA was detected in the CST in both axial and coronal data sets ($p<0.05$) for both sensory and motor fibers, between the study group and the control group. Table 1 summarizes values of FA obtained for the two groups obtained from the axial data set. Significant increase in displacement values were also detected in the left CST but not on the right or with the Prob values. Table 2 summarizes values of Prob and Disp for the two groups. Correlations between FA, eigen values and Prob and disease duration was obtained only within a subgroup of patients with bulbar onset (n=5) but not for the whole group of ALS patients. On histogram analysis significant reduction in restriction was observed for Disp and Prob in the gray matter peak only ($p<0.05$).

	M - R	M - L	S - R	S - L
Control	0.55±0.04	0.55±0.04	0.55±0.04	0.55±0.06
Patients	0.51±0.05	0.51±0.05	0.52±0.03	0.52±0.04

Table1: FA values as detected in the study group compared to the control group ($p<0.05$) in both the R-right and L-left M -motor and S - sensory fibers.

	Disp (μm)	Prob (a.u)
Control	2.14±0.79	6.65±0.69
Patients	2.30±0.88	6.51±0.63

Table2 : Prob and Disp values obtained from q-space high b-value analysis.

Our findings provide quantifiable information regarding to the CST degeneration that occurs in ALS. The results showed damage to the white matter as well as to the gray matter, and show damage to the extra motor

References [1] *Assaf Y et al , 2000. Magn Reson Med 44:713-722* [2] *Basser PJ et al ,1994. J Magn Reson B 103:247-254*