Longitudinal Changes in Amyotrophic Lateral Sclerosis Detected by Diffusion Tensor Imaging and MR Spectroscopy

S. Wang[1], S. Chawla[1], J. H. Woo[1], L. B. Elman[2], L. F. McCluskey[2], H. Poptani[1], and E. R. Melhem[1]

[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Neurology, University of Pennsylvania, Philadelphia, PA, United States

Introduction

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease selectively affecting motor neurons. Earlier studies have demonstrated the diagnostic value of diffusion tensor imaging (DTI) and MR spectroscopy (MRS) [1-4]. However, it would also be valuable to monitor disease progression and response to therapy in these patients. The purpose of this study was to determine longitudinal changes in diffusion and metabolite concentrations as potential biomarkers for assessing disease progression in patients with ALS.

Materials and Methods

Seven patients (4 M, 3 F, age 42-63) with definite or probable ALS according to El Escorial criteria and one healthy subject (F, age 56) were included in this study. Clinical severity was measured using ALSFRS-R. Each subject was scanned twice over a period ranging from 10 to 23 months. MR study was performed on a 3.0 T whole body scanner (Trio, Siemens, Erlangen, Germany) using a product transmit-receive coil. DTI was acquired with a 12 direction, single shot, spin-echo, echo planar sequence (TR/TE = 6500/99, b = 1000 sec/mm^2). Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values were measured from the corticospinal tract at the level of internal capsule using a tractography-based approach[2]**.** 2D CSI was performed using a spin echo sequence (TR/TE = 1700/30). The VOI (80 x 80 – 90 x 90 mm) was centered on the central sulcus with a section thickness of 20 mm, resulting in an approximate voxel size of 11 x 11 x 20 mm^3. Average NAA/Cr and NAA/Cho ratios were measured from voxels covering at least 50% precentral gyrus by using a spectral fit program LC Model. Absolute metabolite concentrations of NAA, Cr and Cho were calculated in two patients using unsuppressed water signal as an internal reference.

Results

The longitudinal changes are shown in Table 1. All the patients with ALS deteriorated over time as measured by ALSFRS-R and exhibited reduced FA on follow-up. Four out of seven patients showed increased ADC. On MRS, 6/7 patients demonstrated decreased NAA/Cr ratios, whereas 5/7 patients showed reduced NAA/Cho ratios. Absolute concentration of NAA and Cr was measured using LC Model in two patients and in both cases a decrease of NAA (12-20%) and Cr (12-15%) was noticed, whereas Cho concentration was found to be slightly elevated (7-11%, Fig 1). In the normal healthy control (Table 1, subject 8), no changes were observed in any of these parameters.

Table 1: Longitudinal Changes in MR parameters from Patients with ALS

Subject	Duration (months)	ALSFRS-R		FA		ADC (10^{-4}mm/s)		NAA/Cr		NAA/Cho	
		1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd
1	23	46	31	0.65	0.64	7.56	7.53	1.69	1.46	4.97	4.02
2	20	40	20	0.61	0.59	7.25	7.53	1.65	1.42	3.95	4.26
3	19	45	35	0.65	0.62	7.17	7.01	1.44	1.38	4.85	4.36
4	16	40	33	0.59	0.59	7.85	7.73	1.70	1.46	5.19	5.34
5	15	47	36	0.63	0.57	7.37	7.41	1.67	1.25	5.20	4.74
6	10	40	34	0.63	0.59	7.21	7.70	1.64	1.69	6.14	4.85
7	14	34	31	0.66	0.58	7.38	7.54	1.56	1.42	6.13	4.59
8	20	48	48	0.67	0.66	7.41	7.47	1.70	1.68	6.23	6.43

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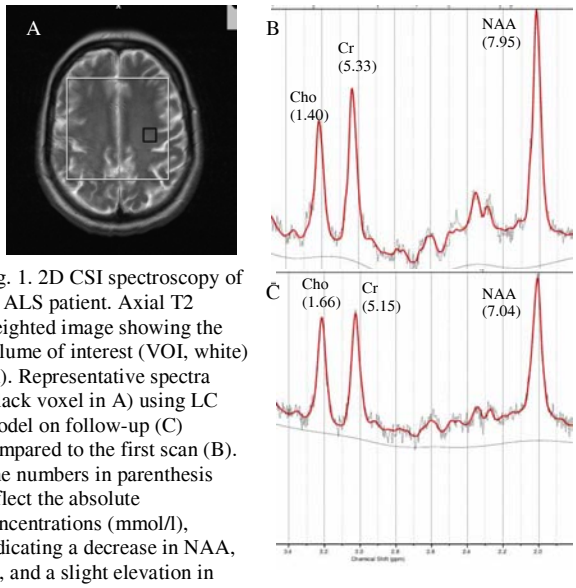

Fig. 1. 2D CSI spectroscopy of an ALS patient. Axial T2 weighted image showing the volume of interest (VOI, white) (A). Representative spectra (black voxel in A) using LC Model on follow-up (C) compared to the first scan (B). The numbers in parenthesis reflect the absolute concentrations (mmol/l), indicating a decrease in NAA, Cr, and a slight elevation in Cho.

Discussion

FA value in the posterior limb of internal capsule appears to be sensitive to progressive corticospinal tract degeneration in ALS. Reduction of relative and absolute NAA concentrations was observed in the motor cortex on follow-up. Decrease in NAA and Cr concentrations may be due to the progressive neurodegeneration, reflecting the need for measuring absolute metabolite concentrations. An increased Cho level has been previously interpreted to represent degradation of membrane phospholipids [5]. This preliminary study indicates the potential of DTI and MRS in monitoring the progression of ALS. Such studies might aid in monitoring response to therapy as well.

Reference

1. Ellis CM, et al. Neurology 1999; 53:1051
2. Wang S, et al. Radiology 2006; 238:831
3. Graham JM, et al. Neurology 2004; 63:2111
4. Pohl C, et al. Arch Neurol 2001; 58:729
5. Suhy J, et al. Neurology 2002; 58 773