Proton magnetic resonance spectroscopy (1H-MRS) on the spinal cord in Amyotrophic Lateral Sclerosis (ALS) at 3T

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Introduction

The purpose of this study was to compare ^{1}H magnetic resonance spectroscopy (MRS) metabolite measurements in the cervical spine of amyotrophic lateral sclerosis (ALS) patients to healthy volunteers. ALS is a fatal neurodegenerative disorder characterized by a degeneration of both upper and lower motor neurons in the brain, brainstem, and spinal cord. This study was motivated by the need to characterize upper motor neuron (UMN) dysfunction and potentially detect early changes in UMNs. Early detection is supported by brain metabolic changes, in an ALS mouse model, that precede pathology evident by structural imaging[1]. Metabolite measurements in the spinal cord hold great promise for early monitoring of ALS since neuronal damage occurs first distally and progresses towards the cell body[2].

Materials and Methods

Spectroscopy measurements were performed on 8 ALS patients (mean age 52.5 ± 13.7y, 4 females) and 9 healthy controls (mean age 31.8 ± 5.6y, 4 females) who provided informed consent. This study was approved by our institutional review board. Imaging was performed on a 3T whole-body system (TIM Trio; Siemens Medical Solutions, Malvern, PA). Spinal cord ^{1}H-MRS examinations were performed with a point-resolved spectroscopy (PRESS) spin-echo sequence, with TR = 2000 ms and TE = 35 ms. Water spectra were collected to assess the quality of shimming through line width (<15 Hz) and shape. A three-pulse chemical shift selective (CHESS) saturation sequence suppressed the water signal. A rectangular voxel (≈9x7x35 mm^3) was placed along the main axis of the cord with the lower boundary at the inferior aspect of the C2 vertebra. A total of 256 water-suppressed signal accumulations were acquired during a total spectrum acquisition time of 9 min. MRS data were analyzed with the software LCModel (v6.1-A, SW Provencher).

Results

The average and standard deviations of the main metabolites and metabolite ratios in the spinal cord of patients and healthy controls are given in Table 1. The NAA+NAAG, NAA+NAAG/Cre and NAA+NAAG/water values showed a significant difference between the two groups, with p-values equal to 0.005, 0.003 and 0.010 respectively. Age did not provide a significant additional contribution to the variance of the observed data when age is included as a covariate. The average of the Glu+Gln, Glu+Gln/Cre, Glu+Gln/water, mI, mI/Cre and mI/water values, while higher in patients, were not significantly different than controls.

Table 1: Metabolites and metabolite ratios of the spinal cord of ALS patients and healthy controls

		Cre (mM)	mI (mM)	GPC+PCh (mM)	NAA+NAAG (mM)	Glu+Gln (mM)
ALS (8)	Ave(SD)	3.69 (0.97)	5.16 (2.19)	1.51 (0.50)	**3.43 (1.08)**	4.96 (3.07)
Healthy controls (9)	Ave(SD)	3.59 (0.87)	4.32 (0.99)	1.56 (0.36)	**5.29 (1.26)**	3.07 (1.07)
		mI/Cre	**GPC+PCh/Cre**	**NAA+NAAG/Cre**	**Glu+Gln/Cre**	**Cre/GPC+PCh**
ALS (8)	Ave(SD)	1.40 (0.33)	0.41 (0.14)	**0.87 (0.35)**	1.47 (1.09)	2.64 (0.75)
Healthy controls (9)	Ave(SD)	1.22 (0.20)	0.44 (0.09)	**1.52 (0.42)**	0.91 (0.38)	2.33 (0.42)
		Cre/water	**mI/water**	**GPC+PCh/water**	**NAA+NAAG/water**	**Glu+Gln/water**
ALS (8)	Ave(SD)	7.04(1.58)	9.57(2.86)	2.85 (0.99)	**5.94(2.04)**	9.30 (5.86)
Healthy controls (9)	Ave(SD)	6.36 (2.02)	7.69 (2.54)	2.81 (0.96)	**9.40 (2.79)**	5.42 (2.19)

Discussion and Conclusion

The present study showed the feasibility of the MRS applied to the spinal cord of ALS patients with a standard PRESS sequence. To our knowledge, this is the first study of MRS in the ALS spine. The findings of metabolite changes, relative to controls, were consistent with the results of previous studies using ^{1}H-MRS for the brain, medulla, and brainstem metabolism analysis of ALS patients[3,4,5]. Ongoing work includes increasing the number of subjects and longitudinal measurements.

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