Echo planar Spectroscopic Imaging in Patients with Amyotrophic Lateral Sclerosis

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Introduction: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by degeneration of the motor neurons in the cerebral cortex, brainstem and causes damage to the corticospinal tracts (CST)[1]. Proton magnetic resonance spectroscopy (^{1}H-MRS) studies have been focused on the motor cortex reporting reduced NAA/Cr and increased Cho/Cr in ALS patients[2-4]. However, the extent of brain damage beyond the motor cortex is evidenced by changes in apparent diffusion coefficient and fractional anisotropy along the CST [2]. The published ^{1}H-MRS literature has been limited by the use of single voxel or single slice multivoxel acquisition methods that encompass only a limited area of the brain. Echo planar spectroscopic imaging (EPSI) has recently been developed to map metabolite distribution throughout the brain with excellent spectral resolution and quality[5,6]. The purpose of present study was thus to evaluate the potential of EPSI in assessing metabolic alterations in regions of brain beyond the motor cortex of ALS patients.

Materials and Methods: Magnetic resonance imaging and EPSI were performed on a 3 Tesla MR system using a 12-channel head array coil. Ten patients (mean age =60.8±14.3, 8M/2F) diagnosed with ALS, based on EI Escorial criteria, were recruited in this study. Conventional imaging protocol included acquisition of T2, T1 and PD weighted images with standard parameters. The spin echo EPSI data was acquired with chemical shift-selective (CHESS) water suppression pulses and lipid inversion nulling using an inversion time of 198 ms. The typical acquisition parameters were: TR/TE=1710/70ms, 50x50x18 phase encoding steps, excitation angle=73°, voxel size=5.6x5.6x10mm^3, field of view=280x280x180mm^3. The sequence also included an interleaved water reference acquisition scan obtained using a gradient-echo acquisition with 20°excitation angle and echo time =6.3 ms. All data were processed offline using the automated MIDAS tool described previously[7], which included k-space extrapolation, B_0 correction, eddy current correction and parametric spectral analysis using Gaussian line-shape for fitting signals. Area under the curves for N-acetylaspartate (NAA), total creatine (Cr) and total choline (Cho) were measured from both hemispheres of occipital region (OR), precentral gyrus (PreCG), postcentral gyrus (postCG) and posterior limb of internal capsule (IC) in all patients. The OR was used as internal control as this region has been reported to be relatively spared from atrophy and metabolic abnormalities in ALS patients[8, 9]. Ten voxels were averaged from each hemisphere of the OR, PreCG and PostCG and 4 voxels were averaged from each IC hemisphere. The averaged NAA/Cr and Cho/Cr ratios from each region were computed and comparisons were made across brain regions by one-way analysis of variance (ANOVA). If an ANOVA test was found to be significant ($p<0.05$), a post-hoc test (Bonferroni test) was performed.

Results: Representative summed voxels and corresponding spectra from the different locations of an ALS patient are shown in Fig 1. Significant reductions in NAA/Cr were observed from the preCG and IC from both the hemispheres. Significantly higher Cho/Cr ratios were also observed from the preCG, postCG and IC regions in comparison to the control OR (Fig 2).

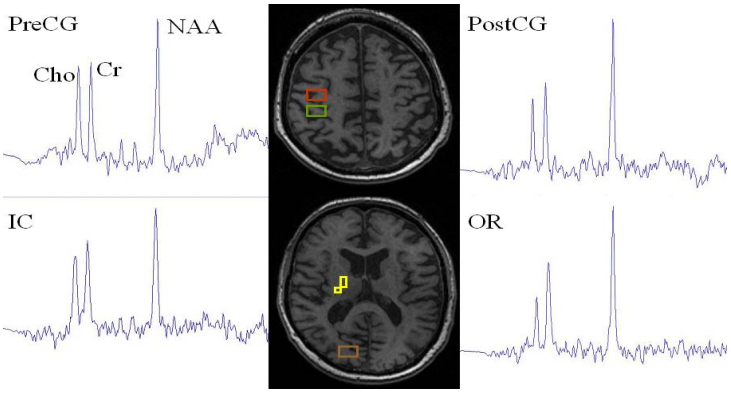

Fig 1. T1 weighted image demonstrating voxels from preCG (red), postCG (green), IC (yellow) and OR (orange). Corresponding spectra from these different regions are also shown.

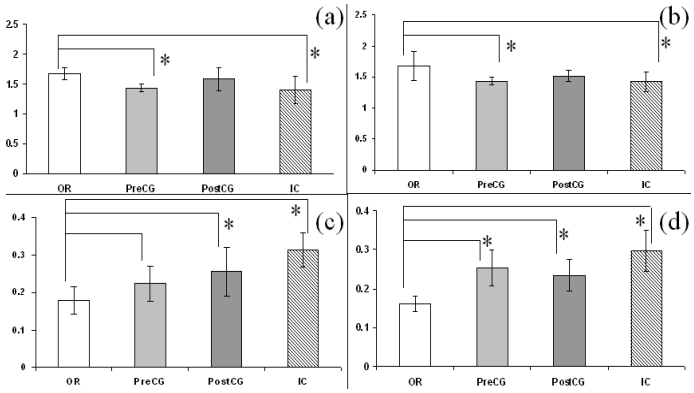

Fig 2. NAA/Cr from right (a) and left hemisphere (b) and Cho/Cr from right (c) and left hemisphere (d) of the OR, preCG, postCG and IC regions (* indicates significant difference).

Discussion: These results demonstrate the ability of EPSI in assessing neuronal damage from ALS patients beyond the motor cortex and into the cortico-spinal tract, confirming the diffused nature of this disease. Reduction of NAA/Cr from the PreCG and IC reflects loss or dysfunction of neurons and axons. In fact, histologic studies from ALS patients and animal models have demonstrated loss of the giant pyramidal Betz cells along with vacuolation and astrogliosis in the cortical layers and the length of CST. Significantly higher Cho/Cr observed from these regions of ALS patients may be due to the combined effect of increased membrane turnover caused by degeneration of neurons and variable degree of gliosis.
In conclusion, EPSI is an ideal spectroscopic sequence for studying metabolite alterations from different locations of a brain in ALS patients and can potentially be used for other pathologies that diffusely affect the brain.

Acknowledgements: The work was supported by NIH grant 1R21NS063111 (JHW).

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