

Whole-brain Proton MRSI in ALS: Changes in the Distribution of Metabolites by Brain Lobes and Tissue Types

V. Govind¹, K. R. Sharma², S. Sheriff¹, and A. A. Maudsley¹

¹Radiology, University of Miami, Miami, Florida, United States, ²Neurology, University of Miami, Miami, Florida, United States

INTRODUCTION: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder that was long considered to affect the motor cortex, corticospinal tracts, brain stem and spinal cord. Findings from recent pathological [1], neuroimaging [2] and neuropsychological [3] studies have also shown alterations in the non-motor brain regions. Whereas MRS studies using single-voxel and 2D-multivoxel methods have indicated potential for observing metabolic changes with ALS in a few selected brain regions, the availability of whole-brain MRS data facilitates evaluation of metabolite alterations from a much larger volume. The aim of this study was to use a whole-brain MRSI acquisition method to evaluate the spatial extent of changes in the brain metabolites, N-acetyl aspartate (NAA), total-choline (Cho) and total-creatine (Cr) of ALS patients, with characterization by brain lobar regions and tissue-types.

METHODS: MRI and MRSI data were acquired at 3T from 27 patients with definite-ALS (mean age: 54±12 years, age range: 24-68 y) and 62 controls. The MRSI data were obtained from the whole-brain using a volumetric EPSI sequence (FOV: 280x280x180 mm³, 50x50_px18_s encodes, TR/TE=1710/70 ms, 135 mm slab, nominal voxel size: 5.6x5.6x10 mm³, Tacq: 26 min.). Data were processed using the MIDAS package [4] and the processing steps included spatial registration to a simulated MNI T1-MRI, segmentation of T1-MRI and calculation of voxel tissue-type content [5]. Metabolite ratios (NAA/Cr, Cho/Cr and Cho/NAA) from the eight hemispheric lobar regions (frontal lobe - left (LF) and right (RF), temporal lobe - left (LT) and right (RT), parietal lobe - left (LP) and right (RP) and occipital lobe - left (LO) and right (RO) were obtained for the white matter (WM) and gray matter (GM) by selecting spectra with fitted metabolite linewidths between 2 Hz and 12 Hz and averaging over the selected spectra of voxels within each region. Metabolite ratios from the cerebellum were calculated by averaging over GM and WM values. The metabolite ratios were compared between the control and ALS groups using the 2-tailed t-test assuming unequal variance, and p-values of ≤ 0.05 and ≤ 0.01 were considered significant and highly significant, respectively.

RESULTS: The mean±SD of the metabolite ratios from the WM of the 8 hemispheric lobes are presented in Figure 1 and the regions that showed significant difference from the controls are indicated with asterisk(s). In the ALS group as compared to controls, NAA/Cr showed a consistent decreased trend in all the lobes for WM and GM, and Cho/NAA showed an increased trend across the lobes only in WM. In GM, significant differences were found in the left frontal- and left parietal lobes for NAA/Cr, and bilateral frontal lobe for Cho/NAA. For cerebellum, NAA/Cr (p=0.08) and Cho/NAA (p=0.07) were approaching towards significance.

DISCUSSION: The results indicate that significant and widespread alterations of NAA/Cr and Cho/NAA occurred in the WM of ALS patients in all, but Cho/NAA in the right temporal, lobar regions. In GM, the significant changes in NAA/Cr and Cho/NAA of ALS patients were limited to the frontal and parietal lobes. The observed metabolite changes in the ALS group can be attributed to varying degree of axonal degeneration throughout the brain that results in decreased NAA and increased Cho. The decreased NAA/Cr could also be caused by increased Cr or altered relaxation times of NAA or Cr. This study demonstrates that widespread alterations of proton MRS-observed metabolites occur throughout the brain, providing MRS-evidence that ALS is a multisystem disorder, affecting the whole brain. In conclusion, the whole-brain MRSI data acquisition and analyses by lobar and tissue-type levels provide an approach to evaluate diffuse metabolite changes in ALS with greater sensitivity.

ACKNOWLEDGEMENTS: This work is supported by NIH grants R01 NS060874 and EB000822.

REFERENCES: [1] Y. S. Piao *et al.*, Brain pathol.13: 10-22 (2003), [2] C. M. Ellis *et al.*, Neurology 57: 1571-8 (2001), [3] S. Abrahams *et al.*, Neurology 64: 1222-6 (2005), [4] A.A. Maudsley, *et al.*, NMR Biomed, 19: 492-503 (2006), [5] A.A. Maudsley *et al.*, Magn. Reson. Med. 61: 548-559 (2009).

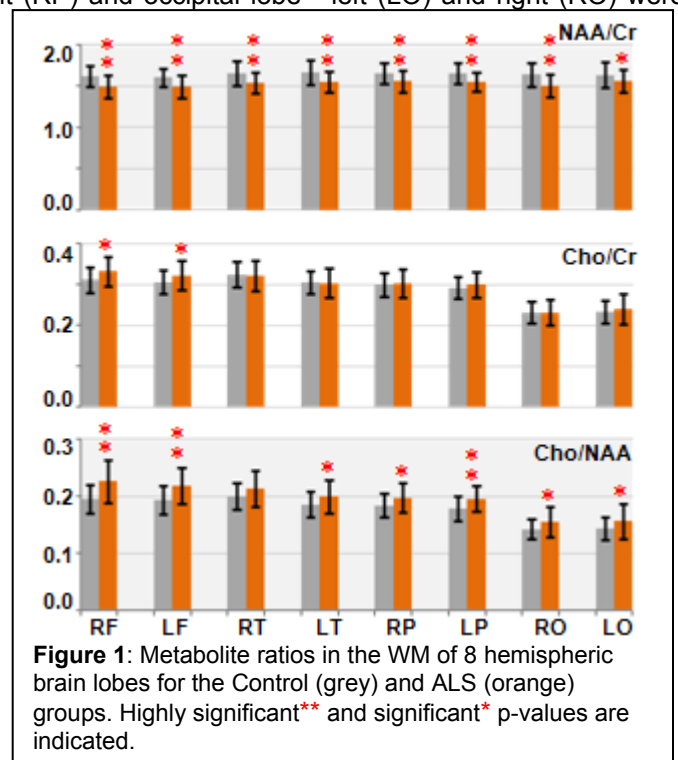


Figure 1: Metabolite ratios in the WM of 8 hemispheric brain lobes for the Control (grey) and ALS (orange) groups. Highly significant** and significant* p-values are indicated.