Comprehensive analysis of brain metabolites in the CST of ALS patients

Varan Govind[1], Khema Sharma[2], Andrew A Maudsley[1], Kristopher L Arheart[3], Gaurav Saigal[1], and Sulaiman Sheriff[1]
[1]*Radiology, University of Miami, Miami, Florida, United States,* [2]*Neurology, University of Miami,* [3]*Epidemiology and Public Health, University of Miami*

INTRODUCTION: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease which is characterized by the loss of motor neurons in the cerebral cortex, brain stem and spinal cord, and degeneration of the corticospinal cord (CST). In previous studies, quantification of proton MR-observed brain metabolites along the length of the CST was performed by defining regions-of-interest (ROIs) manually at few select locations along the tract. Such an approach is bound to have subjectivity in data sampling. In this study, a comprehensive analysis of brain metabolite (N-acetyl aspartate (NAA), total-creatine (Cre) and total-choline (Cho)) alterations in the CST of subjects with ALS was performed using a 3D CST atlas.

METHODS: MRI and MRSI data were obtained at 3T from 38 subjects with sporadic definite-ALS (mean age: 52.3±8.8 years, age range: 34-65 years) and 70 age-range matched controls. The MRSI data was obtained from the whole-brain using a volumetric EPSI sequence (TR/TE=1710/70 ms, 135 mm slab, T_{acq}= 26 min.; details in [1]). Data was processed using the MIDAS package [2, 3]. After 3D spatial smoothing, the processed MRSI data was zero-padded to 64x64x32 mm^3 with the resultant voxel volume of ~1 mL. The data was then spatially registered with the MNI template. For identifying the CST, a single-subject probabilistic CST atlas [4] in MNI space with both the left and right whole-CST defined in 3D volumes was chosen. We modified this atlas for our data analysis by only including voxels with probability values >0.20 (Figure 1A). Data analysis was performed for i) the whole-CST and ii) 5 anatomically relevant segments along the length of the CST. The five segments are at the levels of: precentral gyrus (PCG), centrum semiovale (CS), corona radiata (CR), posterior limb of internal capsule and cerebral peduncle (CP). In each of the left and right CSTs, spectral quality was controlled by including only spectra from voxels with fitted linewidths of ≤ 12 Hz and voxel tissue volume ≥70%. NAA, Cre and Cho values (in institutional units) and Cho/NAA ratio were compared between the groups using ANCOVA with age as the covariate. A multiple comparison adjusted p-value of <0.05 was considered significant.

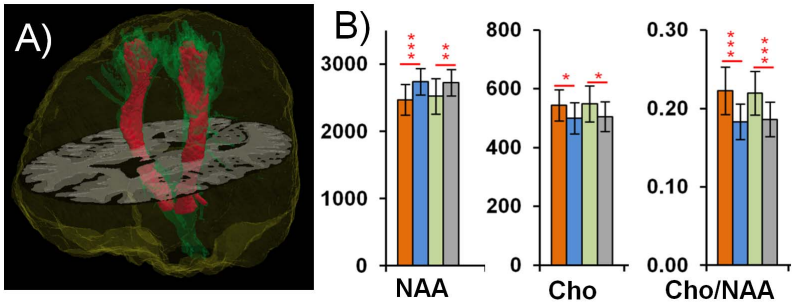

Figure 1: (A) The CST atlas [4] with full (green) and >0.20 (red) probability values. (B) NAA, Cho and Cho/NAA in the whole-CST of ALS (left –orange and right –green) and controls (left -blue and right-gray). Mean ± SD and p-values (*p<0.05, **<0.001, ***p<0.0001) are provided.

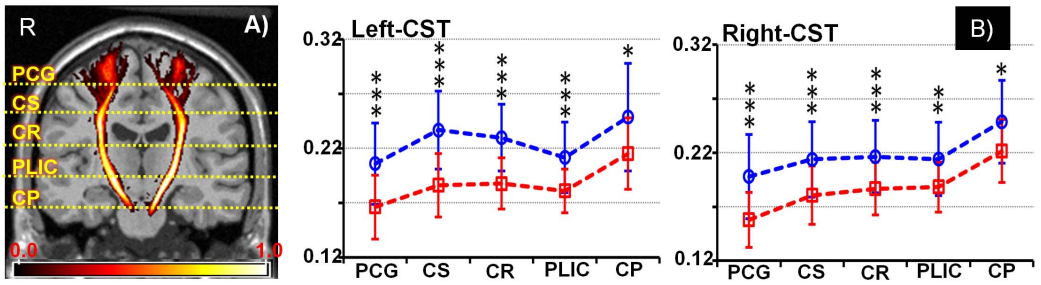

Figure 2: (A) Five segments along the length of CST. (B) Cho/NAA in the left and right CST of the groups of ALS (blue) and Control subjects (red). Mean ± SD and p-values (*p< 0.05, **< 0.001, ***p<0.0001) are provided.

RESULTS AND CONCLUSIONS: In Figure 1 are shown a) the CST atlas and b) the metabolite value comparisons between the groups of ALS and control subjects. As seen, significant (p <0.05) or highly significant (p <0.001 or 0.0001) metabolite group differences were observed for NAA, Cho and Cho/NAA in both sides of the whole-CST. There were no significant differences observed between the groups for Cre (data not shown). In Figure 2 are shown a) the 5 segments along the length of CST (between the PCG and CP) and b) Cho/NAA comparison between the ALS and Control groups along the 5 segments in both sides of the CST. Significant differences were observed for Cho/NAA in all the segments in both the sides. The results of this study show that significant alterations of proton MRS-observed metabolites occur in the CST of patients with ALS and these alterations can be quantified relative to age-matched control group values using atlas-guided analysis methods.

ACKNOWLEDGEMENTS: This work is supported by NIH grants R01 NS060874 and R01EB000822.

REFERENCES: [1] Govind V et al. *J Neurotrauma* 27:483-496 (2010); [2] Maudsley AA et al. *NMR Biomed* 19:492-503 (2006); [3] Maudsley AA et al Magn. Reson. Med. 61:548-559 (2009); [4] Oishi K et al *NeuroImage* 46:486-499 (2009).