Comparison of Global T2 Values and Globus Pallidal T1-weighted Signal Changes in Sub-Clinical Hepatic Encephalopathy

A. M. Thomas[1], R. Kumar[2], B. Sawale[3], A. Huda[4], S. Han[5]

[1]Radiological Sciences, University of California Los Angeles (UCLA) School of Medicine, Los Angeles, CA, United States, [2]Neurobiology, UCLA School of Medicine, Los Angeles, CA, United States, [3]Radiological Sciences, UCLA School of Medicine, Los Angeles, CA, United States, [4]Physics, California State University at Fresno, Fresno, CA, United States, [5]Digestive Diseases, UCLA School of Medicine, Los Angeles, CA, United States

Introduction: Hepatic Encephalopathy (HE) is a common neuropsychiatric disorder identified in patients with liver cirrhosis. Bilateral symmetric enhanced signal intensity in the globus pallidus (GP) region has been reported in patients with chronic liver failure on T_1-weighted imaging (1-2). T_2-weighted signal changes were also reported in the white matter before and normalization after liver transplant (3), however, no such study is available correlating T_2 relaxation values and T_1 signal changes in GP region. The objective of this study was to calculate T_2 values and T_1-weighted signal intensities in GP region to compare with sub-clinical HE and control cohorts, and to assess overall disease load in sub-clinical HE using T2-relaxometry.

Methods: A Siemens 1.5 Tesla Avanto MRI scanner (Siemens Medical Systems, Erlangen, Germany), having maximum gradient amplitude of 45mT/m, using a receive-only 12-channel phased array head matrix coil was used. Seven patients with sub-clinical HE (mean age = 52.9 yrs; 4male/3female) and 12 healthy controls (mean age = 52.5 yrs; 4males/8females) were investigated. Foam pads were used either side of head to reduce the motion. High-resolution T_1-weighted images using a magnetization prepared rapid acquisition gradient-echo (MPRAGE) sequence (TR = 1,660 ms; TE = 3.9 ms; inversion time = 900 ms; average = 1; matrix size = 256 × 256; FOV = 230 × 230 mm^2; slice thickness = 1.2 mm; number of slices = 176) were collected. Proton-density (PD) and T_2-weighted images were also collected using a dual-echo turbo spin-echo sequence (TR = 7,500 ms; TE_1, TE_2 = 17, 134 ms; flip angle = 150°; matrix size = 256 × 256; FOV = 230 × 230 mm^2; slice thickness = 4.0 mm; number of slices = 42; average = 1).

Data were processed using the statistical parametric mapping package SPM2 (Wellcome Department of Cognitive Neurology, UK), and Matlab-based (The MathWorks Inc, Natick, MA) custom software. Using T_2 and PD-weighted images, T_2 maps were computed voxel-by-voxel using the following equation: $T_2 = (TE_2 - TE_1)/\ln(SI_1/SI_2)$, where TE_1 and TE_2 were the echo times for PD and T_2-weighted images, and SI_1, SI_2 were the signal intensities from the PD and T_2-weighted images, respectively. T_2 maps were constructed using the T_2 relaxation times calculated for each voxel, in which voxel intensity corresponded to the calculated T_2 relaxation time. Using SPM2, T_2 maps of each subject were spatially normalized to the standard Montreal Neurological Institute (MNI) T_2-weighted template. High- resolution T_1-weighted images were also normalized to MNI T_1-weighted template. Bilateral whole GP masks were created manually using normalized T_1-weighted image and T_2 map from a control subject. Median signal intensity from T_1-weighted images and median T_2 values from T_2 maps were calculated in each subject using these masks. Relative change in T_1 signal intensity in patient group compare to controls was calculated. Median T_2 relaxation values calculated from GP region were compared between patients and control subjects to see any difference using paired t-test. For assessment of whole brain disease load, normalized T_2 maps of all patients and control subjects were smoothed and compared voxel-by-voxel using analysis of covariance (false discovery rate correction for multiple comparison, $p < 0.05$, age as a covariate).

Results and Discussion: The GP signal intensities and T_2 relaxation values were calculated bilaterally in six patients and 12 controls since one HE patient was excluded due to the existence of a suspicious mass in the temporal lobe. The enhanced T_1 signal was 21.9% in left GP, 23.7% in right GP, and 22.8% in averaged bilateral GP (Figure 1). The averaged median T_2 values in the left GP region was 91.85 ms and 92.95 ms in the right GP of HE patients, and 91.13 ms in left GP and 95.33 ms in right GP of healthy subjects. Although, these values were not significantly different between the groups but trend was declining in patient cohort compared to controls. Whole brain voxel-by-voxel analysis showed several abnormal regions with increased T_2 values in patient group compared to controls including anterior, mid, posterior cingulate cortices, ventral frontal cortex, bilateral insular cortices, and bilateral cerebellar cortex (Figure 2a, b).

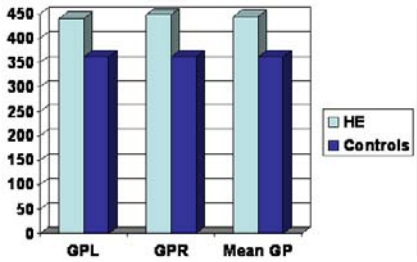

Figure 1: GP signal intensities calculated from T_1-weighted MRI.

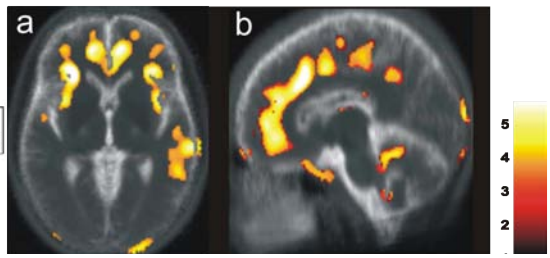

Figure 2. Global T_2 changes presented on the axial (a) and sagittal (b) slices.

Increased signal intensity in the T_1-weighted MRI of HE patients is suggestive of deposition of paramagnetic substances in GP region (2). The region with paramagnetic substance would be expected with decrease T_2 relaxation values in patients compared to control subjects. Other regions showing increased T_2 relaxation values in patients could be due to mild cerebral edema in HE patients.

Conclusion: The GP hyper-intensity increase in patients was approximately 23% compare to healthy controls consistent with previous reports (2, 3). The T_2 relaxation values have been quantitated first time and they showed decreased trend in the GP region of patients suggesting deposition of paramagnetic substances. In other brain regions, increased T_2 values are suggestive of mild brain edema in HE.

References:

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