Correlation Studies of Multiple Sclerosis Using ^{1}H MRS, Volumetric MRI, and Cognitive Test

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Abstract

The goal of this study is to assess the relationships between brain metabolite levels, cerebral atrophy, and cognitive functions of patients with multiple sclerosis (MS). ^{1}H MRS, volumetric MRI, and neuropsychological testing were performed on 15 MS patients. In the posterior periventricular regions, ratios of NAA/Cr and NAA/Cho were positively correlated with cognitive performance, but inversely associated with central CSF volume fraction. The central cerebral atrophy was inversely related to cognitive functions. The findings suggest that axonal damage or injury coincides with progression of atrophy and decline in cognition in MS.

Introduction

Multiple sclerosis (MS) is the most common inflammatory demyelinating disease of the CNS, characterized by repeated cycles of white matter (WM) damage, recovery, and injury. ^{1}H MRS studies (1-4) of patients with MS have shown decreased N-acetylaspartate (NAA) levels in brain lesions and normal appearing WM (NAWM), which is related to the axonal damage or dysfunction. Volumetric MRI studies (5-6) have shown that compared to healthy controls, MS patients have significant cerebral atrophy which progresses at a significantly higher rate, reflecting the ongoing destructive pathologic processes in this disease.

In this preliminary study, we measured brain metabolite levels and atrophy in MS patients with one MR protocol, using ^{1}H MRS and volumetric MRI. The findings from the MR measurements were correlated with cognitive functions of the patients.

Methods

15 MS patients (age range 32-53 yrs, mean ± SD = 45 ± 7 yrs) were recruited for this study. They were clinically described as relapsing remitting (n = 8), primary (n = 2) and secondary (n = 5) progressive MS patients. They were evaluated with expanded disability status scale (EDSS) and the scores ranged from 0 to 6.5 with mean ± SD = 3.8 ± 2.1. Each MS patient underwent a modified version of the Brief Repeatable Battery (BRB) of neuropsychological tests for assessment of the cognitive functions.

MRI/MRS scanning sessions were performed using a 1.5 T Marconi Edge whole-body scanner with the body coil as the transmitter and a birdcage head coil as the receiver. A 3D SPGR sequence was employed to acquire T_1-weighted axial images covering the whole brain with 30° flip angle, TE = 5 ms, TR = 30 ms, 1.5 mm slice thickness, 24 cm FOV, and 256x 256 matrix size. A 3D EXPRESS sequence with fat suppression was used to collect T_2-weighted axial images with the same acquisition location and parameters except for TE = 95 ms, TR = 4000 ms, and ETL = 136. 3D FLAIR images were also acquired from each patient with the same slice location, slice number, slice thickness, and FOV. Single slice multi-voxel ^{1}H MRS was performed with a PRESS sequence with TE = 135 ms, TR = 1500 ms, 16 cm FOV, 2D phase encoding (16x16), and 2 scan averages. The slice of interest with 2 cm thickness was taken through the posterior and anterior aspects of the corpus callosum (2). The total MRI/MRS scanning time was less than one hour.

The 3D T_2-weighted images were used for stripping away the skull/scalp and extracting a brain mask volume. A multi-spectral segmentation scheme based on a hidden Markov random field model and Expectation Maximization algorithm (7) was then applied to both T_1- and T_2-weighted images for classifying voxels within the mask, resulting in volumes of gray matter (GM), WM, and total CSF, from which central ventricular CSF (CV-CSF) volume was extracted. The FLAIR images were used to define the locations of the lesions that appeared hypo-intense on T_1-weighted images, avoiding overestimation of the CSF volume.

Proton spectra from the left and right posterior periventricular (LPPV and RPPV) voxels were processed with 3 Hz line broadening, given the prevalence of lesions in periventricular tissue in MS (2). The periventricular voxels were selected through elimination of voxels with greater than 30% CSF and by anatomical placement. A proton spectrum from a NAWM voxel was also processed. Resonance peaks of NAA, total creatine (Cr) and choline compounds (Cho) were identified and their peak area ratios were calculated.

Correlation analysis between brain atrophy, metabolite ratios, and cognitive functions was performed using Pearson correlations.

Results

Figs. 1 and 2 shows the significant positive correlations between RPPV NAA/Cho, NAA/Cr and BRB scores, respectively. Fig. 3 shows the significant inverse relationship between CV-CSF volume fraction (of the total brain and CSF volume) and BRB scores. Fig. 4 shows that RPPV NAA/Cho was inversely associated with CV-CSF volume fraction. The same relationship was found between RPPV NAA/Cr and CV-CSF volume fraction ($r = -0.65$, $p < 0.01$). After controlling for age and education, LPPV NAA/Cho and NAA/Cr were also found to be positively related to BRB scores ($p < 0.05$).

Discussion

In this ongoing study, we combined results from MRI/MRS measurements with those from neuropsychological tests to evaluate the relations between periventricular metabolite levels, cerebral atrophy, and cognition in MS patients. The inverse relationships between CV-CSF volume fraction and cognitive functions indicate that the loss of periventricular brain tissue is associated with progressive deterioration of cognition in MS patients. Axonal integrity can be assessed by NAA levels (2). The findings of positive correlations between NAA/Cho, NAA/Cr and cognitive functions, and the inverse relationships between NAA/Cho, NAA/Cr and CV-CSF volume fraction suggest that axonal damage or injury coincides with loss of periventricular WM and decline in cognition.

References

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