Proton Magnetic Resonance Spectroscopy for Monitoring Disease Progression and Response to Treatment in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is an autoimmune neurodegenerative disorder characterized by demyelination, axonal loss, inflammation, gliosis and edema.1,2 MS is further sub-classified as relapsing-remitting, primary-progressive and secondary-progressive according to the course of the disease.2 Increasing evidence is suggestive of metabolite alterations not only in the areas of the plaque but also involving normal appearing white matter (NAWM) regions.3 In the present study, proton magnetic resonance spectroscopy (1H MRS) was used to monitor disease progression following the administration of an immuno-modulating drug (interferon- 1β) in the plaque and NAWM regions of relapsing remitting MS patients.

Materials and Methods: Magnetic resonance (MR) imaging and three dimensional multivoxel magnetic resonance spectroscopic imaging (1H MRSI) were performed on a 3 Tesla MR system. Ten patients with clinical definite MS (relapsing-remitting, with at least two episodes of relapses or attacks) and ten controls were recruited in this study. First study (baseline study) was performed prior to treatment and subsequent studies (3,6,9 and 12 months) were performed after drug administration. MR imaging protocol included acquisition of T2 weighted, T1 weighted and FLAIR images with standard parameters. Multivoxel 1H MRSI was acquired using PRESS sequence (TR/TE/NEX=1700ms/30ms/3) using a voxel size of 10x10x10mm3. 1H MRSI data were analyzed from 6 voxels encompassing the NAWM of normal controls and 34 MS plaques. In addition, one voxel thick NAWM regions surrounding the plaques from MS patients were also analyzed at each time point. Absolute concentration of NAA, Cr, Cho and ml were computed using a spectral fit program [Linear Combination (LC) Model]. A two-tailed student t-test was performed to look for group differences (between controls and MS patients at baseline) in metabolite concentrations. One-way ANOVA and Bonferroni tests were performed to look for group differences (between baseline study and subsequent studies) in metabolite concentrations in the MS patients.

Results: At baseline, significant reduction in NAA along with significant elevations in Cho and ml were observed in the NAWM and plaque regions of patients compared to controls (Fig 1). Changes in the NAA, Cr, Cho, and ml concentrations from the NAWM and plaque at different time points are shown in figure 2. Both the plaques and the NAWM demonstrated reduced NAA initially (3 months) followed by a slow recovery. A significant elevation in Cr concentration was observed at the 9th and 12th month within plaques and at 12th month in NAWM compared to baseline. There was a significant increase in ml concentration at months 6th, 9th and 12th within plaques and at month 12th in NAWM. No change in the Cho concentration was observed within the MS plaques and NAWM.

Discussion: Initial reduction in NAA in both MS plaques and NAWM of patients reflects neuronal degeneration and axonal loss.4 However, an increase in NAA after 3 months indicates that early damage is partially reversible.5 Increase in Cr at 9th month may be attributed to the synergistic effect of repopulation of MS plaques and NAWM with oligodendrocytes and remyelination. Initial elevation in ml, both in plaques and NAWM compared to controls and further increase at 6th month in plaques and 12th month in NAWM may be due to diseased glial cells or gliosis.6

Conclusion: 1H MRS may be helpful in understanding the underlying pathophysiological events occurring at different time points during the long term clinical course in MS patients.

References: