Acetyl content in skeletal muscle of multiple sclerosis patients

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Introduction

Multiple sclerosis (MS) is a degenerative disease central nervous system. Individuals with MS have compromised muscle function [1] and excess fatigue [2]. However, the underlying mechanisms of muscular fatigue remains unclear and warrants further study because it is the most prominent complaint in MS. Proton magnetic resonance spectroscopy (^{1}H-MRS) is gaining favor in the non-invasive study of skeletal metabolism in both health and disease. Kreis and colleagues were the first to report acetylcarnitine in muscle of healthy subjects at rest. Acetylcarnitine supplementation has been used to treat fatigue in neuromuscular diseases however, the mechanisms are somewhat unclear. Acetylcarnitine efficacy may be mediated by its capacity to normalize central and peripheral energy metabolism [3]. Muscle acetylcarnitine levels have not been determined in patients with MS. Therefore, the purpose of this study was to identify baseline levels of acetylcarnitine in MS subjects over a range of disability and fatigue scores.

Subjects and Methods

Fourteen females (45.3 ±11.7) (Mean ± SD) with MS and mean disability score (EDSS) of 4.0 ± 1.3 ranging from 1.0 to 6.5 participated in this study [4]. Subjects using immunomodulators (i.e., Interferon β, and Glatiramer acetate) were included while those using prednisone or anti-spasmotic drugs were excluded. Subjects' percent body fat was assessed using the three-site skinfold technique [5]. Fatigue was assessed using the modified fatigue impact scale (MFIS) [6].

***^{1}H-MRS*:** ^{1}H-MRS was performed on a 3T whole body magnet (GE, SIGNA, Milwaukee, WI) on the limb most affected by MS. Subject's leg was positioned parallel to the to B_o field. A 15 mm^3 PROBE-P voxel was selected in the mid-vastus lateralis of the thigh (Figure 1), which was positioned in home-made extremity coil. Water suppressed proton spectra (TE=45ms, 25ms; TR=2s, 128 average) were obtained at rest (Figure 2). The data were processed using jMRUI [7]. Acetyl group levels in muscle were estimated using an unsuppressed internal water reference from the same voxel [8].

Results

Our subjects had a mean percent body fat of 31.5±7.6 and body mass index (BMI) of 25.8±5.1. Acetylcarnitine was present at rest (5.9 x 10^5 ± 4.7 x 10^5 au) in most of the subjects although the range was quite variable (7.8 x 10^4 - 1.71 x 10^6 au). Pearson product moment correlations revealed significant correlations between body fatness, BMI and fatigue (MFIS) r=.625, and r=0.53, respectively. Acetyl group accumulation was weakly correlated with EDSS r=0.478 (P<0.05). There was no correlation between fatigue and acetylcarnitine accumulation.

Discussion and Conclusion

The level of acetylcarnitine varies in MS patients and was weakly correlated with disability but not fatigue. Determination of metabolic characteristics of skeletal muscle in MS will assist in tracking disease progression as well as identifying the influence of therapeutic interventions on muscle metabolism.

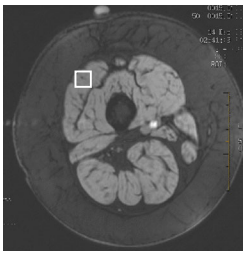

Figure 1. MRI of and MS subject's vastus lateralis displaying 1.5 cm^3 PROBE-P voxel

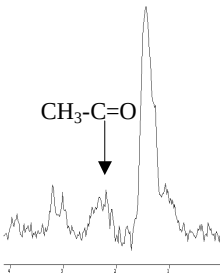

Figure 2. ^{1}H-MRS of an MS subject with acetylcarnitine resonance at 2.13 ppm

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