Reduced muscle strength and proton metabolites in patients with multiple sclerosis

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Introduction

Multiple sclerosis (MS) causes progressive degeneration of the central nervous system and is the most common neurological disorder of young adults. Muscle weakness and fatigue [1] are the most frequently observed symptoms in MS which contribute to a decline physical activity and quality of life. Studies have shown lower isometric and isokinetic force and total work of the quadriceps in MS patients compared to healthy controls [2,3]. However, the impact of the disease versus physical inactivity remains unclear [4,5]. Therefore, MS patients and controls matched for age, BMI, gender and activity level were compared using measures of leg strength and *in vivo* ^{1}H-MR spectroscopy to assess skeletal muscle creatine and trimethylamine (TMA) groups. The relationship between muscle biochemical properties, strength and disability were also explored.

Subjects and Methods

Six individuals with MS and disability score (EDSS) [6] from 1 to 5.5 and 6 controls matched for age, gender, BMI and activity level volunteered as subjects. Both MS and control subjects were recreationally active (1-3 x/wk for previous 3 mo). Individuals using disease modifying agents were included while those using prednisone or antispasmotic drugs were excluded.

Muscle Strength: Quadriceps and hamstring muscle strength were assessed using a Kin-Com isokinetic dynamometer. Following a light warm-up, subjects performed three maximal trials of leg extension and leg curl and the highest value was used for statistical comparison. Muscle strength is expressed as Newtons per kilogram fat free mass (N/kg FFM) to account for muscle mass difference between subjects.

***^{1}H localized and MRS*:** For thirty minutes prior to ^{1}H-MRS, subjects remained supine to alleviate fluid accumulation in the lower extremities. ^{1}H-MRS was performed on a 3T whole body system (General Electric, SIGNA, Milwaukee, WI) on the limb most affected by MS. Subject's leg was positioned parallel to the to B_o field. A 1.5cc^{3} PROBE-P voxel was selected in the mid-vastus lateralis of the thigh (Figure 1), which was positioned in home-made extremity quadrature birdcage coil. Water suppressed proton spectra (TE=45ms, 25ms; TR=2s, 128 average) were obtained at rest (Figure 2). The data were further processed using jMRUI ver. 2.1 [7]. Change in metabolite contents were estimated using unsuppressed using internal water reference from the same voxel [9].

Results

Quadriceps (5.09 ± 1.2 vs. 7.38 ± 1.72 N/kg FFM) and hamstring (2.47 ± 0.70 vs. 3.46 ± 1.07 N/kg FFM) muscle strength, creatine ($1.50 \times 10^{6} \pm 6.02 \times 10^{5}$ vs. $3.25 \times 10^{6} \pm 6.20 \times 10^{5}$ au) and TMA ($1.41 \times 10^{6} \pm 6.92 \times 10^{5}$ vs. $3.36 \times 10^{6} \pm 2.01 \times 10^{6}$ au) levels were significantly lower in MS ($P<0.01$) compared with controls, respectively. Pearson product correlations were used to determine the relationship between muscle metabolites and strength. Creatine level was correlated with quadriceps ($r=0.727$) and hamstring strength (0.733)($P<0.05$) in MS. Disability score was inversely correlated with creatine ($r=-0.74$) and TMA ($r=-0.90$) (both $P<0.05$).

Discussion and Conclusion

MS subjects had significantly lower (~30%) strength (both absolute and relative to fat free mass) and total creatine (PCr + Cr) than matched controls. Since PCr levels influence the power generating capacity during muscle contractions [10], reduced creatine content observed in MS may help explain the decrements in strength. Since muscle creatine uptake is influenced by the sodium-dependent creatine transporters [11], any reduction in muscle total creatine may reflect changes in the quality or quantity of creatine transporters in skeletal muscle of MS subjects. Trimethylamines represent carnitine and choline metabolites. Since carnitine is closely related to long chain fatty acid metabolism in skeletal muscle, a reduction in carnitine could reflect a decreased capacity for fat metabolism in MS. The results indicate that reduced muscle creatine is likely a covariate of functional loss in MS.

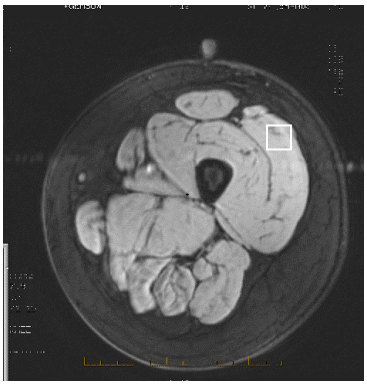

Figure 1. 1.5 cc^{3} voxel in the mid-vastus lateralis of the thigh.

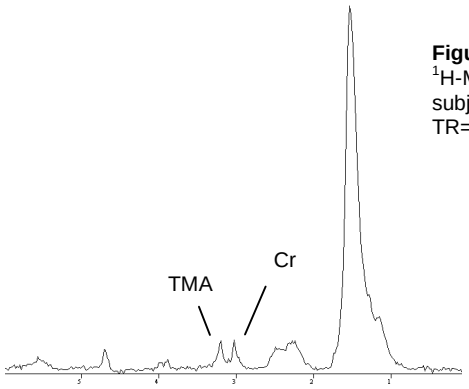

Figure 2. Example of ^{1}H-MRS from a typical MS subject. PRESS (TE=45ms, TR=2 s, 128 avg).

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Acknowledgments

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