Muscle Lipid Content in Multiple Sclerosis Subjects

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Abstract Multiple sclerosis (MS) is a progressive demyelinating disease of the central nervous system. Subjects with multiple sclerosis typically present with symptoms of increased muscle weakness, fatigue and spasticity. Clinicians generally rely on subjective questionnaires to classify disease status. The questionnaires commonly employed are the expanded disability status scale (EDSS), modified fatigue impact scale (MFIS). The specific aim of this investigation was to evaluate intramyocellular lipid (IMCL) content in subjects with multiple sclerosis prior to an exercise intervention. Significant association between spectral characteristics and measures of disease status would provide clinicians with a quantitative tool to track disease progression. Proton (^{1}H) magnetic resonance spectroscopy (^{1}H-MRS) was performed on seven female and one male subject. Spectra were acquired from the vastus lateralis in a 3T whole body scanner. IMCL at baseline was evaluated using the water content in the same voxel as an internal reference and arbitrary units. The underlying contribution of IMCL and EMCL to skeletal muscle metabolism as it relates to whole body vigor remains unknown.

Introduction Increased levels of IMCL have been found in diabetes, generalized lipodystrophy, and in certain exercised populations [1-3]. In contrast, reduced or absent levels of IMCL in post-polio residual paralysis patients correlated with the degree of disease severity. This current investigation is the first to report on IMCL levels in multiple sclerosis patients. Disease progression in MS is a highly variable entity. The current clinical diagnosis and treatment of disease states relies heavily on subjective ratings by the patient and clinician. Quantitative analysis of disease progression and regression are necessary to track the efficacy of therapeutic interventions. Second, the sequestering of lipid within the myocyte serves as a substrate for energy metabolism. MS patients are limited in activities of daily living due to excessive fatigue. Lipid serves as the primary fuel source at rest [4] and during low to moderate intensity exercise [5]. A portion of lipid used during exercise may be from IMCL sources [6,7]. ^{1}H-MRS has been used to measure IMCL non-invasively. The purpose of this investigation is to examine the possible involvement of IMCL and EMCL to overall energy metabolism in multiple sclerosis and its relationship to clinical measures of disease severity.

Materials and Methods Eight subjects were evaluated for IMCL content of the vastus lateralis. The subjects characteristics are as follows: (44.9 ± 4.2, mean ± SE yrs, 3.7 ± 0.3 EDSS, 26.9 ± 2.3 kg/m^2, 33.5 ± 3.2 %body fat). Subjects reported for their trial in a fasted state. Dietary prescriptions were made two days prior to testing to ensure homogenous dietary intake (total fat < 30%, carbohydrate 50-60%, protein 10-15%). Subjects kept dietary logs during these days as well. Thirty minutes prior to ^{1}H-MRS subjects assumed a supine position to alleviate fluid accumulation in the lower extremities. ^{1}H-MRS was conducted on the limb most affected by MS.

^{1}H localized MRS: Proton MR spectroscopy was done on the 3 T whole body system (General Electric, SIGNA-VH2, Milwaukee, WI). A 1.5x1.5x1.5 cc PROBE-P voxel was selected in the mid-vastus lateralis muscle of the right leg mode (**Figure 1**), which was positioned in the extremity quadrature birdcage coil A set of pads was devised in order to reproduce the leg angulation with respect to the B_o field. Water suppressed proton spectra (TE=45ms, 25ms; TR=2s, 128 average) were obtained at rest (**Figure 2**). The data were further processed using jMRUI [8]. The IMCL and EMCL concentrations were evaluated using internal water reference from the same voxel [9].

Results and Discussion Multiple sclerosis patients contained 2.08 x 10^7 arbitrary units of IMCL. EMCL levels in multiple sclerosis patients were reported as 2.57 x 10^7 arbitrary units. Pearson product correlations were used to determine the relationship between EMCL and IMCL with parameters affecting functional capacity in MS patients. IMCL/water ratio was significantly correlated to knee flexion strength ($p<0.05$). EMCL was weakly associated with knee flexion and plantarflexion strength ($p<0.10$). However, IMCL and EMCL levels were not correlated with percent body fat, modified fatigue impact scale, central activation ratio or EDSS score ($P>0.05$).

In this study, IMCL/water ratio was associated with knee flexion strength. However, we did not find any further association between IMCL levels expressed as arbitrary units or arbitrary units/water and disability status, body fat, or fatigue in multiple sclerosis individuals. Moreover, the ability to quantify changes in IMCL content has widespread application in identification of treatment regimens able to alter disease status. Completed analysis of control subjects matched for age and physical activity status are warranted. Further studies to evaluate muscle bioenergetics during exercise may provide additional insight into muscle characteristics contributing to weakness and fatigue. ^{1}H-MRS may be a powerful tool to assess biochemical alterations in skeletal muscle associated with theraupeutic interventions used in MS. The present investigation is the first to report IMCL and EMCL levels in MS patients. However, the contribution of IMCL and EMCL to skeletal muscle metabolism in patients as it relates to whole body vigor in patients with MS is unknown.

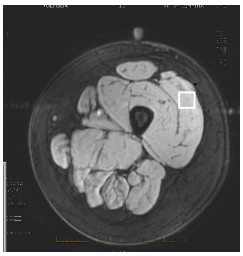

Figure 1. 1.5^3 cc voxel in the mid-vastus lateralis of the thigh.

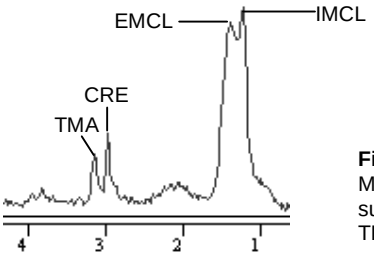

Figure 2. Example of ^{1}H-MRS from a typical MS subject. PRESS (TE=45ms, TR=2 s, 128 avg).

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