859 Board #120 May 30 2:00 PM - 3:30 PM

Seric Musclin is not Increased in Patients with Metabolic Syndrome and Insulin Resistance

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(No relevant relationships reported)

Skeletal muscle has now been recognized as an endocrine tissue, through the production and secretion of myokines. Musclin is a myokine mainly secreted by fibers type II (FT-II) that induces insulin resistance (IR) in both cellular and murine models. We hypothesize that musclin could be involved in pathophysiology of metabolic syndrome (MS) in humans.
PURPOSE: to evaluate the relationships among IR, seric musclin, area occupied by FT-II and muscle mass in adults with and without MS.
METHODS: analytical study in adults with and without MS. Homeostatic model assessment (HOMA-IR) was used as indicator of IR, musclin was measured by ELISA, area of FT-II in right vastus lateralis muscle by proton magnetic resonance spectroscopy and both fat and lean mass of the body and the right thigh (absolute values in Kg, or indexes in Kg/m^2 and Kg/Kg body mass) by dual X-ray absorptiometry. Data presented as mean±standard deviation.
RESULTS: 23 subjects with and 10 without MS, comparable in age (51.6±5.7 with MS vs 53.5±6.3 without MS; P>0.05) and gender were included. Subjects with MS had higher values of insulin (18.3±7.4 vs 6.7±2.5 µU/ml; P<0.05) and HOMA-IR (4.6±2.2 vs 1.6±0.6; P<0.05). There were no differences between groups regarding glycaemia (99.1±8.8 vs 93.2±12.7), musclin (609.9±203.4 pg ml^{-1} vs 657.9±240.5 pg ml^{-1}), area of FT-II (51.4±23.2% vs 49±26.7%) or absolute values or indexes of muscle mass. There were positive correlations between HOMA-IR and both body fat mass or thigh fat mass (r>0.46; P<0.05), between musclin and indexes of total lean mass (Kg m^{-2}, r=0.51; P<0.05) and thigh lean mass (Kg m^{-2}, r>0.54; P<0.05), also between area of FT-II and indexes of total lean mass (r>0.49; P<0.05). There was a negative trend between total lean mass and HOMA-IR (r=-0.34; P=0.07). We did not find correlation between HOMA- IR and musclin or area of FT-II.
CONCLUSIONS: lean mass seems to determine seric musclin, however, this myokine was not associated to IR in our patients. These findings are in controversy with previous ones reported for cellular models. COLCIENCIAS 111562638757. CODI 2605. Interinstitucional 2016-1341. Colciencias doctoral scholarships 727-2015.

860 Board #121 May 30 2:00 PM - 3:30 PM

Ketone Bodies Induce Mitochondrial Biogenesis In Skeletal Muscle Cells

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(No relevant relationships reported)

Previous studies have shown that a long-chain fatty acid-rich diet as well as endurance exercise induce increase in muscle mitochondria and enhance endurance capacity in rodents. We previously showed that a medium-chain fatty acid (MCFA)-rich diet increases mitochondrial protein levels in the skeletal muscles of non-obese rodents. However, its mechanism remains unclear. Most MCFAs are converted to ketone bodies, which are thereafter released into the blood.
PURPOSE: The purpose of this study was to examine whether β-hydroxybutyrate (β-OHB), a ketone body, increases the levels of mitochondrial proteins in muscles (Exp. 1). We also evaluated the binding of β-OHB to peroxisome proliferator-activated receptors (PPARs), which regulate the expression of mitochondrial genes (Exp. 2).
METHODS: Exp. 1: C2C12 mouse skeletal muscle cells were grown in Dulbecco's modified Eagle's medium (DMEM) with 10% fetal bovine serum and 1% penicillin/streptomycin (PS), and differentiated in DMEM with 2% donor bovine serum and 1% PS. After 5 days, the cells were treated with different concentrations (0.05, 0.1, 0.25, 0.5, or 1 mM) of β-OHB for 24 h. The levels of voltage-dependent anion channel (VDAC) and complex-IV (COX-IV) were then measured by western blotting. Exp. 2: PPARs-ligand-binding domain were incubated with buffer containing either agonists or β-OHB, and then with fluorescein-labeled coactivator peptide and terbium-labeled anti-GST antibodies. The fluorescence intensity was measured using time- resolved fluorescence resonance energy transfer.
RESULTS: Exp. 1: Treatment of the cells with 0.25 mM, 0.5 mM, and 1 mM β-OHB increased VDAC levels compared with those in the control (3.5-, 2.6-, 3.7-fold, $p < 0.05$, respectively). Similarly, treatment with 0.25 mM and 0.5 mM β-OHB increased COX-IV expression compared with that in the control (2.0-, 2.5-fold, $p < 0.05$, respectively). Exp. 2: GW7674, an agonist of PPARα (EC50; 6.2±0.4 nM), and GW501516, an agonist of PPARδ (EC50; 10.3±3.6 nM), increased the fluorescence intensity ratio (520/495 nm). Treatment with β-OHB, however, did not increase the 520/495 nm ratio for either PPARα or PPARδ.
CONCLUSION: The results indicate that β-OHB induces the expression of mitochondrial proteins in skeletal muscle cells of mice via a pathway different from the one associated with PPARs.

861 Board #122 May 30 2:00 PM - 3:30 PM

Cancer-Related Fatigue and Mitochondrial Function in Cancer Survivors

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(No relevant relationships reported)

Cancer-Related Fatigue (CRF) is a commonly reported symptom of cancer survivors during or after treatment and can contribute to decreased quality of life (QOL). The cause of CRF is largely unknown and is likely multifactorial. CRF has long been hypothesized to result from decreased energy production due to impaired mitochondrial function.
PURPOSE: To investigate if impaired mitochondrial function contributes to CRF.
METHODS: Ten cancer survivors (CA, Prostate, Breast, Ovarian), reporting CRF to varying degrees and 5 control subjects with no history of cancer (C), participated in this pilot cross-sectional study. The following measurements were obtained from all subjects: CRF (FACIT-F), depression (CES-D), QOL (PROMIS Global Well-Being (GWB)). Physical function was indicated by handgrip strength (HG), 30 Seconds Sit-to-Stand (STS), timed 6 min walk test (6MWT), and Godin Leisure Time Questionnaire (Godin). Mitochondrial oxidative capacity of the wrist flexor muscles was indicated by the time constant (T_C) of muscle mVO_2 recovery measured with near-infrared spectroscopy (NIRS). The upper limb was chosen so to be relatively independent from ambulation or activity. Analyses were by unpaired T-tests. Pearson Correlations were obtained for variables that differed between groups. Sig. $p \leq 0.05$. Data are mean (SD).
RESULTS: No significant group differences (all ≥ 0.3) were noted in age (CA = 53.8 (10.3), C = 48.6 (10.5) yr.), height (CA = 168.7(7.2), C= 166.6(9.0) cm), weight (CA=81.7 (13.2), C=73.8(13.6) kg), or body fat (CA=28.7 (4.45), C=33.14(8.6) %, bioelectrical impedance). Significant differences or trends were noted between CA and C groups in FACIT-F (Ca = 36 (11), C = 49 (2), p =0.01), CES-D (Ca = 11 (9), C = 4 (4), p = 0.05), PROMIS-GWB (CA = 37 (7), C =46 (3), p =0.02), HG (Ca = 27 (9), C = 38 (7) kg, p = 0.04), and 30STS (Ca = 15 (4), C = 22 (4), p =0.01)), and Tc (Ca = 46 (9), C = 36 (9) s, p = 0.07). Significant correlations were noted between: FACIT-F and CESD (r = -0.84), PROMIS-GWB (r = 0.90), STS (r = 0.72), and Tc (r = -0.52). PROMIS-GWB was also correlated to HG (r = 0.57), STS (r = 0.74), and CES-D (r = -0.93).
CONCLUSIONS: Mitochondrial oxidative capacity (i.e. Tc) may be lower in Ca reporting fatigue compared to C and contribute to CRF (i.e. FACIT-F). Further, Tc may mediate QOL through CRF.

862 Board #123 May 30 2:00 PM - 3:30 PM

Impaired Mitochondrial Function May Contribute to Disability and Symptoms of Multiple Sclerosis

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(No relevant relationships reported)