EA.07 - Glucocorticoids decrease the thermogenic capacity and increase the triacylglycerol synthesis by glycerokinase activation in brown adipose tissue of rats

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The maintenance of adequate triacylglycerol (TAG) stores is essential for normal brown adipose tissue (BAT) functioning and requires a continuous supply of glycerol-3-phosphate (G3P). This study aimed to investigate the effects of glucocorticoids on thermogenic capacity and in G3P generation pathways for TAG synthesis in interscapular brown adipose tissue (IBAT) of rats. Male Hannover rats received a single daily injection of dexamethasone (DEXA) (1 mg/Kg) or saline 0,9% during 7 days (CEUA protocol 195/2018). The mitochondrial proteins content, the temperature after noradrenaline stimulation, and noradrenaline content were measured in IBAT. The generation of G3P was evaluated by glycolysis, glyceroneogenesis, and direct phosphorylation of glycerol, respectively, by 2-deoxyglucose uptake, phosphoenolpyruvate carboxykinase (PEPCK) activity and pyruvate incorporation into TAG-glycerol, and glycerokinase (Gyk) activity and glycerol incorporation into TAG in IBAT. DEXA treatment increases the IBAT mass and lipid content probably by increasing the de novo fatty acid (FA) synthesis, evaluated by increased glucose-6-phosphate dehydrogenase and ATP citrate lyase activities (79% and 48% respectively), compared to control. DEXA increases the content (~55%) and activity (~41%) of Gyk, without affecting the glucose uptake and glyceroneogenesis. DEXA reduces the glycerol incorporation into TAG (~54%), the AQP7 content (~50%), and the rate of basal glycerol release (~54%) in IBAT. In addition, DEXA decreases the thermogenic capacity of IBAT, evidenced by a reduction in the content of mitochondrial proteins, including UCP-1, and the respiratory complexes, reduction in the noradrenaline content (53%), and the capacity of IBAT to increase the temperature after noradrenaline stimulation. Our data suggest that direct phosphorylation of glycerol by Gyk may be responsible for maintaining the supply of G3P for the increased esterification of FA and TAG synthesis in IBAT from DEXA-treated rats. The reduction of IBAT thermogenic capacity in these animals could be probably due to reduced sympathetic stimulation of IBAT. **Keywords:** Brown adipose tissue, Glucocorticoids, Glycerokinase

EA.08 - High-density lipoprotein remodeling associates with COVID-19 severity: a quantitative proteomic study

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Coronavirus disease 2019 (COVID-19) has caused more than 4 million deaths worldwide. Alterations in lipid profile, including lower levels of high-density lipoprotein (HDL)-cholesterol and high levels of triglycerides have been linked to disease severity. Although important for lipid metabolism, HDL may also play a role in immune response in infectious diseases. Due to its very complex protein composition, HDL proteome is altered in several diseases, including metabolic, inflammatory and infectious diseases. We used quantitative proteomics to test whether alterations in HDL proteome associate with COVID-19 severity. COVID-19 patients (n=41) were divided into two groups according to disease severity (hospitalized and non-hospitalized subjects). Levels of 29 HDL proteins were quantified by high resolution mass spectrometry. We showed levels of five proteins were increased by more than 50% in hospitalized patients when compared to non-hospitalized ones. Those proteins were serum amyloid A 1 and 2 (SAA1 and SAA2), pulmonary surfactant-associated protein B (SFTPB), apolipoprotein F (APOF) and inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4). On the other hand, phospholipid transfer protein (PLTP) and apolipoproteins A2 (APOA2) and L1 (APOL1) were reduced by more than 30% in those same hospitalized patients. Apolipoprotein M (APOM) levels within HDL negatively associated with odds of death due to COVID-19. Furthermore, HDL proteins were able to classify COVID-19 subjects into those two groups (error rate of 5%). Our results indicate an inflammatory remodeling of HDL proteome which reflects the severity of COVID-19 infection and contribute to the putative role of HDL in infectious diseases.
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