BROWN ADIPOSE TISSUE MITOCHONDRIAL PHYSIOLOGY IN OBESE YOUNG MICE OVERFED DURING LACTATION

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Introduction and Objectives: The Brown adipose tissue (BAT) has a high oxidative capacity and is involved in the regulation of whole-body energy expenditure and adiposity. Studies showed that the excess of energy substrates in obesity can lead to mitochondrial dysfunction in adipose tissue. Study the mitochondrial physiology in interscapular BAT of obese young mice overfed during lactation.

Materials and Methods: To induce obesity, Swiss male mice were submitted to litter size reduction during lactation. At 21 days (weaning) we evaluated in the control group (CG) and overfed group (OG): body weight, fat weight, liver weight and fasting glucose. The mitochondrial function was evaluated by High-resolution Respirometry (Oxygraph-2k) and the protein content analyzed by Western Blotting. Data are given as the mean ± SD; analyzed using Student’s t-test. P < 0.05 was considered statistically significant. N = 6/group.

Results and Conclusions: We showed that overnutrition increased body weight, visceral fat, BAT weight, liver weight and fasting glucose in OG compared to CG (P < 0.001). UCP1 content was increased in BAT of OG (P < 0.05) while pAMPK/AMPK ratio and PGC1α content were decreased (P < 0.05). No difference was observed in the insulin signaling pathway (IRβ, IRS1, PI3K, AKT, pAKT, GLUT4 e GLUT1). High-resolution Respirometry showed BAT mitochondrial impairment in OG with significant reduction in the maximum ADP-stimulated respiration rate (State 3) in carbohydrate protocol, indicating a reduction in carbohydrate oxidation capacity compared to CG (P < 0.05). In addition, RCR (respiratory control ratio) for carbohydrate protocol was decreased in OG BAT suggesting a lower mitochondrial coupling. Our data suggest that the impairment in BAT mitochondrial function might be associated with accumulation of visceral fat content and unfavorable metabolic outcomes in obese pups overfed during early postnatal life, which likely increases susceptibility to obesity in adulthood.

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Key Words: Brown adipose tissue; Obese mice; Mitochondrial physiology.