Exercise Biochemistry Review

Proceedings of IBEC 2018, Beijing, China, October 23-25
PO-201

Aging attenuates the effect of aerobic capacity in muscle and serum metabolic profile but not in white adipose tissue

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Objective Aerobic capacity is a quantitative predictor of the morbidity and mortality in many diverse patient populations. While aging is the main factor affecting aerobic capacity. The present study aimed to assess the effect of aerobic capacity and aging on metabolic profile in rats and to investigate the metabolic interactions between white adipose tissue (WAT), muscle and serum.
Methods In this study, we used rat models that were selectively bred to differ in maximal running capacity (High capacity runners (HCR) and Low capacity runners (LCR)). Part of the rats were sacrificed after 9 months and the rest at 21 months. The effect of aerobic capacity on metabolic profile was assessed from 9 months old young rats (HCR-Y and LCR-Y), while the effect of aging on the metabolic profile in different capacity rats was determined comparing 9 months to 21 months old rats (HCR-O and LCR-O). Nuclear magnetic resonance (NMR) spectroscopy was performed to detect the metabolomics of WAT, muscle and serum. Partial least-squares-discriminant analysis (PLS-DA) was used for pattern recognition between HCR-Y and LCR-Y and between HCR-O and LCR-O. Metabolites with variable influence on projection (VIP) >1.0 and $p<0.05$ were classified as significantly different metabolites between groups. Spearman correlation was used to assess the metabolic interactions between white adipose tissue (WAT), muscle and serum.
Results HCR-Y rats had significantly higher skeletal muscle mass-to-body mass ratio ($p<0.001$), while lower body mass ($p<0.001$), fat mass ($p<0.001$), skeletal muscle mass ($p=0.035$) and fat mass to body mass ratio ($p=0.004$) than LCR-Y rats. The running capacity of HCR-Y rats was 132.7% (best running speed) better than LCR-Y rats ($p<0.001$). However, with age, the difference between body compositions between the two capacity groups became insignificant. HCR-O only had significantly lower body mass than the LCR-O ($p=0.02$). Running capacity ($p=0.06$) was 86.4% (best running speed) higher in the HCR-O rats than that of the LCR-O rats. PLS-DA revealed marked effects of aerobic capacity on metabolic profile in all three tissue types between HCR-Y and LCR-Y. The metabolic profile classification and prediction was best (i.e. sharper) in muscle than in WAT and serum. In addition, muscle and serum contained more significantly different metabolites than WAT in HCR-Y than in LCR-Y. Pathway analysis of the significantly different metabolites between HCR-Y and LCR-Y revealed that all the pathways belong to the lipid metabolism and amino acid metabolism in muscle while in serum it is only amino acid metabolism. However, in the case of the old groups, the PLS-DA gave reversed results. It revealed that WAT performed best in terms of classification and prediction of metabolites between HCR-O and LCR-O and had the most significantly different metabolites out of the three tissue types. The significantly different metabolites' pathways belong to lipid metabolism in WAT. When assessing the metabolic interaction between different tissue types, all significantly different metabolites between HCR and LCR rats in young and old groups were moderately or strongly correlated (Spearman correlation between 0.45-0.9) with one or more metabolites in any of the three tissues.
Conclusions In this study, we assessed the metabolic profile and body composition of WAT, muscle and serum in young and old rats with different aerobic capacities. We found that aerobic capacity greatly impacts body composition and the metabolic profile in muscle and serum in young rats, however the impact is attenuated with age. In addition, it is aging and not aerobic capacity that had

the most influence on WAT metabolites. This suggest that WAT has more important role in aging process than previously assumed.