Description for the general public (in English)

The effect of physical activity on the tissue nitric oxide (NO•) bioavailability and mitochondrial biogenesis in skeletal muscle and in the heart of the transgenic mice (Tgαq*44) with chronic heart failure

Heart failure (HF) is a clinical syndrome characterized by progressive deterioration of the pump function leading to the decrease in capacity of the heart to meet the body requirements for blood flow. Heart failure patients are characterized by low exercise tolerance, which is related not only to the diminished heart function but also to the skeletal muscle weakness. Endothelial dysfunction and reduced nitric oxide (NO•) signaling are recognized as a major feature of the pathophysiology of that disease. Nitrate supplementation, leading to an increase in nitric oxide bioavailability improves cardiac contractility as well as augments skeletal muscle contractile properties. This leads to an increase in quality of life in heart failure patients. Interestingly, physical activity itself has been found to increase the systemic NO• bioavailability, hence it might be an effective non-pharmacological therapeutic strategy in improving the skeletal muscle performance and exercise tolerance in patients with heart failure. Physical activity provides several beneficial effects in various organs of human body, nevertheless; the underlying physiological mechanisms remain largely unknown. An increase in mitochondrial enzymes activities and mitochondrial content is a key adaptive response in skeletal muscles in endurance training resulting in an enhancement of exercise tolerance and resistance to fatigue. Nitric oxide has been indicated as one of the major factors involved in intensification of mitochondrial biogenesis. Even though endurance training has been found to increase the plasma NO• bioavailability, far less is known about the training-induced changes in tissue nitrite pool (a physiological storage of NO•) in heart failure condition in relation to the mitochondrial biogenesis and exercise tolerance.

Therefore, in the present study we aimed to determine the effect of the physical activity on the tissue nitric oxide (NO•) bioavailability (tissue nitrite pool), mitochondrial biogenesis, oxidative stress and antioxidant defence in striated muscles with varied mitochondria and myoglobin content *i.e.* in slow (*m. soleus, S*) and in fast (*m. tibialis anterior, TA*) locomotory muscles as well as in heart in physiological (wild-type mice and rats) and pathophysiological conditions (transgenic mice model of chronic heart failure and myoglobin deficient mice). The main aim of this study is to determine the effect of 8 weeks of forced endurance training in rats as well as 8 weeks of voluntary physical exercise in the running wheels (which mimics moderate-intensity exercise in humans) on the tissue nitrite pool in relation to mitochondrial biogenesis in skeletal muscles and in the heart of the mice with chronic heart failure (HF) using the model of transgenic mice (Tgαq*44).

The results of this study can extend our basic knowledge concerning the significance of the training-induced changes in the tissue nitrite pool in the locomotors muscles (fast vs slow) and in the heart for exercise tolerance in physiological conditions and in heart failure. Moreover, we are aiming to establish the impact of myoglobin content on the tissue nitric oxide bioavailability (nitrite pool) in varied type of muscles at rest and during exercise. Furthermore, this study might have also practical implications since it can provide some new basic research evidence on the impact of moderate intensity and higher intensity of physical activity on the tissue nitrite pool in relation to mitochondrial biogenesis in the heart as well as in the slow and fast skeletal locomotors muscles, needed for deeper understanding of the mechanism underling the deterioration of physical exercise capacity in chronic heart failure.