

Summary

Fatigue during intense exercise in human skeletal muscle is complex and several factors can be involved in the process depending on intensity and duration of the exercise performed. Disturbances in ion homeostasis and especially accumulation of interstitial potassium are thought to induce membrane depolarization during intense exercise and thereby lead to fatigue development. Skeletal muscle ion transport proteins are probably important for the ability to sustain changes in ion homeostasis and thus postpone development of muscle fatigue during exercise. The present PhD-thesis is based on five papers and these experiments aimed at changing the protein expression by either dexamethasone treatment or different training and inactivity interventions to examine the effects of ion regulation on fatigue development and exercise performance. In addition, molecular mechanisms involved in the increased skeletal muscle Na^+/K^+ pump activity observed in transition from rest to exercise was examined as an important part of the thesis.

Western blotting was performed as the main analysis to determine changes in protein expression and phosphorylation in the included experiments and some general methodological considerations in relation to these analyses are presented. Optimization of several steps in the analysis procedure decreases the overall method variation, but biological variation, which differs between proteins, affects the method sensitivity and seems to influence the risk of conducting type II errors.

A connection between phospholemman (FXYP1) phosphorylation and the expected increase in skeletal muscle Na^+/K^+ pump activity at onset of intense exercise was examined by acute exercise in humans and electrical stimulation in rat skeletal muscle cells. After 30 s of high intensity exercise overall FXYP1 phosphorylation is increased from the resting level. Subsequent moderate intense exercise in human skeletal muscles induce higher phosphorylation of FXYP1 at serine 63, serine 68 and probably threonine 69 as well, indicating an important role for FXYP1 phosphorylation in Na^+/K^+ pump activity regulation. An increase in PKC α activity may be the link between FXYP1 phosphorylation and the exercise induced Na^+/K^+ activity increase.

Dexamethasone treatment and speed endurance training in already trained subjects were successfully used as interventions to manipulate the protein expression in human skeletal muscles. Especially the Na^+/K^+ pump α -subunit are increased in response to intense exercise training, indicating an increase in Na^+/K^+ pump content, while the lactate and H^+ transporters are generally not altered. In addition, intensified training increase and training cessation decrease, respectively, the resting FXYP1ser68 phosphorylation level compared to before the intervention in soccer players. Concomitant with these protein alterations intensified training in already trained runners and soccer players induces better performance in a broad range of intense exercise tests as well as maintain and even improve long-term performance for some of the endurance trained runners. Thus, alterations in expression of proteins involved in ion transport and primarily potassium regulation may influence intense exercise performance, but further research is needed in order to understand the exact mechanisms of muscular fatigue and to evaluate the specific influence of ion disturbances in this process.