Rutgers Equine Science Center

Research Updates

Exercise-Related Factors Affecting Skeletal Muscle Metabolism and Physiologic Performance Measures in Standardbred Horses

Recent Ph.D. graduate Dylan Klein, under the direction of Drs. Tracy Anthony and Ken McKeever investigated the effects of acute exercise, training and detraining on the unfolded protein response and its role in the beneficial adaptations of skeletal muscle to exercise in research funded by the Equine Science Center.

The Research Project

Exercise improves health and increases athletic performance in part through changes in skeletal muscle metabolism and function. The horse possesses an innate ability to exercise and has a large proportion of its body mass as skeletal muscle. As such, horses position themselves as a unique model to understand how exercise impacts skeletal muscle performance and health.

Findings from our studies have revealed novel molecular changes in equine skeletal muscle in response to exercise and training. These changes suggest that repeated bouts of exercise decrease markers of muscle injury and damage and increase markers related to muscle's capacity for turnover and repair. In addition, training alters muscle metabolism towards a profile that is suggestive of an increased ability to produced energy and resist fatigue.

Taken together, training confers metabolic adaptations in skeletal muscle that may allow for increased performance and the ability to better recover from strenuous exercise.

Chronic exercise training leads to improved health as well as increased muscle mass and function. A potential mechanism that has been proposed to govern the beneficial cellular adaptations to exercise in mice and humans is a tripartite collection of signal transduction events emanating from the endoplasmic or sarcoplasmic reticulum collectively known as the unfolded protein response (UPR).

The sarcoplasmic reticulum (SR) is a membrane-bound structure found within muscle cells that is similar to the endoplasmic reticulum in other cells.

Dr. Klein used ultrasound to measure rump fat thickness, which was then used to calculate percent body fat and fat-free mass. Using these measurements he was able to figure out the baseline and post-training physiological and performance characteristics of each horse.

The main function of the SR is to store calcium ions (Ca2+). Cellular activities regulated by the UPR include general protein synthesis and turnover, gene-specific translation and altered gene expression with the ultimate goal to regain sarcoplasmic reticulum (SR) homeostasis.

The UPR is activated in response to cellular stressors such as calcium disturbances, exercise, hypoxia, and energy deprivation that affect the SR. If initial attempts to regain SR homeostasis via UPR activation cannot be achieved, the UPR can then become hyper-reactive, promoting cell death (i.e. apoptosis) through a network of transcriptional regulators. Thus, the SR and UPR are critical links between the appropriate cellular responses and adaptations to exercise.

Unaccustomed exercise has been shown to activate the UPR in human and rodent skeletal muscle, whereas training habituates this response. As such, the sarcoplasmic –endoplasmic reticulum has been implicated as a potential governor of the beneficial adaptations that occur in skeletal muscle in response to exercise. However, no such research has been conducted in the horse. In the present study, acute incremental exercise, regardless of training status, had no effect on UPR or UPP-related gene expression in skeletal muscle.

However, 12 weeks of exercise training did result in alterations in basal gene expression related to the UPR and UPP. These results suggest that acute high-intensity exercise does not induce the transcriptional UPR or UPP in equine skeletal muscle, but that exercise training does alter the basal expression of certain genes, particularly those related to apoptosis, muscle atrophy, and protein turnover. These changes may contribute to the positive biological effects of exercise on skeletal muscle in response to stressors.

Habitual exercise leads to improvements in overall health, in part through changes in skeletal muscle's phenotype. The horse, being over 50% skeletal muscle mass and innately athletic, uniquely positions itself as a model to understand the effects of exercise and training on muscle metabolism.

Using an untargeted metabolomics approach in the muscle biopsies of eight Standardbred horses we identified novel metabolic adaptations related to the early and late post-exercise recovery periods, as well as training status. Alterations largely centered on the branched-chain amino acids, microbial-derived xenobiotics, and a variety of lipid and nucleotide metabolites that occurred alongside an increased resistance to fatigue in the trained state.

BCAAs provide several metabolic and physiologic roles. Metabolically, BCAAs promote protein synthesis and turnover, signaling pathways, and metabolism of glucose. There is limited information regarding the changes in equine skeletal muscle branched-chain amino acid (BCAA) metabolism following exercise and training.

Interestingly, training also increased the relative abundances of lipid metabolites in skeletal muscle that have been previously shown to be associated with obesity and insulin resistance in humans. This was accompanied by increased plasma branched-chain amino acids and phenylalanine, another metabolic hallmark that is predictive of insulin resistance in humans. However, given our previous findings regarding the transcriptional UPR and UPP, these changes may be reflective of a beneficial expansion of the plasma amino acid pool for the purposes of meeting the increased protein turnover demands of skeletal muscle.

Further, acute exercise decreased the relative abundances of almost all lipid species in skeletal muscle by 24 hours post-exercise, indicating higher turnover and a greater reliance on lipids as a fuel source in the trained state. Thus, while these results highlight novel exercise-related metabolomic changes in skeletal muscle of the athletic horse, they also underscore the complexity of certain metabolites and their relationships in health and disease.

While training is employed by trainers to increase equine athletic performance, due to injury, behavioral issues and/or overtraining, horses may be removed from physical activity for extended periods of time. Nonetheless, they are still expected to compete at a high level afterwards. As such, it is important to characterize the physiologic and performance changes that occur during extended periods of training and detraining so that the appropriate decisions can be made concerning retraining and the successful resumption of competitive endeavors.

Our studies also showed that exercise training in horses results in a rapid and sustained increase in aerobic and athletic capacities. However, these changes occurred without any improvement in body composition. Interestingly, during the initial 12 weeks of training, geldings outperformed mares during exercise, possibly due to differences in overall fat mass (approximately 30kg).

Given a longer training period (72 weeks), exercise performance is maximally sustained in both sexes and is ultimately not hindered by the accumulation body fat. Following 20 weeks of confinement to dry lot paddocks, it was shown that aerobic capacity was maintained over the detraining period and performance during exercise was not compromised. As such, horses can maintain their athletic capabilities even during prolonged rest periods.

These, results suggest that a long retraining period may not be required following detraining given that the rest period is preceded by a training period that produces maximal aerobic and exercise capacities.

Conclusions and Future Directions:

Results from three studies funded by the Equine Science Center suggest that acute high-intensity exercise does not induce the transcriptional UPR or UPP in equine skeletal muscle, but that exercise training does alter the basal expression of certain genes, particularly those related to apoptosis, muscle atrophy, and protein turnover. These changes may contribute to the hormetic effects of exercise on skeletal muscle.

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Meet the Researchers

Dr. Dylan J. Klein
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Dr. Dylan J. Klein is a graduate of Rutgers University where he earned his Bachelor's of Science in nutritional sciences, and recently earned his Ph.D. from the Nutritional Sciences Graduate Program under the guidance of Drs. Ken McKeever and Tracy Anthony.

Much of Klein's research interests utilize the equine athlete as a comparative model for understanding exercise physiology and metabolism.

Using transcriptional and metabolomic bioinformatic approaches, his work focused on the molecular and cellular adaptations that govern the beneficial effects of exercise in skeletal muscle, and improve performance and promote health. Further, his research characterizes the relationship between body composition and maximal aerobic capacity over periods of training and detraining. A better understanding of the mechanisms that mediate skeletal muscle adaptations with exercise and relative inactivity can lead to better nutrition, exercise, and management-related interventions that can improve health and reduce the risk of injury and disease.

The journey that led Klein to work with horses is one of irony – and possibly fate. He grew up in central NJ where his best friend's father owned and raced Thoroughbred horses. Moreover, in middle school, he worked at the once active Standardbred breeding farm, Perretti Farms, as a summer farmhand.

If that wasn't coincidence enough, Dylan's grandfather – who always wanted to be a jockey – asked that upon his death, he be cremated and his ashes spread at the Monmouth Park Racetrack. It is there that he and his family would visit every Father's Day to watch the horse races in honor of his grandfather and his favorite sport.

Yet, it wasn't until his second year of graduate school that Klein ever handled a horse. Nonetheless, he felt right at home and considered himself extremely lucky to be working with such an amazing animal.

Since graduating in May Dr. Klein has assumed a new Assistant Professorship in Health and Exercise Science at Rowan University.

Further Readings:

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