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A Novel Role Of ASICs In Immediate Exercise-Induced Pain And Exercise Performance

Tahsin Khataei1, Anne S. Harding2, Mahyar Jahanmadi1, Maram El-Genediy1, Hamid Rajabi1, Peter M. Snyder1, Kathleen A. Sluka1, Christopher Benson1.

1University of Iowa, Iowa City, IA. 2Shahid Beheshti University of Medical Sciences, Tehran, Iran, Islamic Republic of. 3Karazani University, Tehran, Iran.

Email: tahsin-khataei@uiowa.edu

(No relationships reported)

INTRODUCTION: Exercise training is an effective therapy for many pain-related conditions, and there is a difference in pain perception between athletes and unconditioned people. The mechanisms by which exercise modulates pain are poorly understood. Painful conditions can be associated with elevated levels of protons, metabolites and inflammatory factors, which can activate receptors and/or ion channels on nociceptive sensory neurons including acid sensing ion channels (ASICs) and transient receptor potential cation channel subfamily V member 1 (TRPV1). Additionally, strenuous exercise also causes the release of similar chemical signals, and ASICs within muscle afferents may mediate immediate exercise-induced pain (IEP) and fatigue, as well as reflex hemodynamic changes. We hypothesized that ASICs and TRPV1 have role in IEP and maximal exercise performance.

METHOD: First, C57BL/6 mice were divided into sedentary (SED), low-intensity continuous training (LICT) and high-intensity interval training (HIIT) groups. Mice were trained on a treadmill every other day for 4 weeks. SED mice were placed on a non-moving treadmill for similar periods of time. After 4 weeks, exercise performance, ASIC and TRPV1 mRNA levels with lumbar dorsal root ganglion (DRG) were measured. In a separate group, we measured IEP at baseline and following exhaustive exercise before and after HIIT. In a third study, we compared the IEP and exercise performance in ASIC3−/− versus wild type (WT) mice.

RESULTS: We found HIIT improved exercise performance compared to LICT and sedentary groups, diminished ASICs and TRPV1 mRNA levels in lumbar DRG, and reduced IEP. We also found a negative relationship between mRNA levels of ASICs and TRPV1 and exercise performance (r = -0.59, p < 0.001). In addition, ASIC3−/− showed a significant lower IEP compared to WT mice while there was no difference in maximal exercise performance between groups.

CONCLUSION: In summary, ASIC is required for IEP following exhaustive exercise, and exercise training downregulates ASICs and TRPV1 in muscle afferents and diminishes IEP. These findings suggest a possible role of ASICs in benefits of exercise training for many pain and fatigue conditions such as fibromyalgia and chronic fatigue syndrome conditions. Supported by Department of Veterans Affairs.

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Pain Modulation Is Associated With Moderate Physical Activity In Gulf War Veterans With Chronic Pain

Stephanie M. Van Riper1, Aaron J. Stegner1, Jacob V. Ninneman1, Alexander Borouch1, Jacob B. Lindheimer1, Ryan J. Dougherty1, Neda E. Almassi1, Laura D. Ellingson, FACSM1, Patrick J. O'Connor, FACSM1, 2University of Wisconsin - Madison, Madison, WI. 4William S. Middleton Veterans Memorial Hospital, Madison, WI. 4Western Oregon University, Monmouth, OR. 1University of Georgia, Athens, GA.

Email: svanriper@wisc.edu

(No relationships reported)

Veterans of the Persian Gulf War (GV) suffer unresolved widespread chronic musculoskeletal pain (CMP) that significantly impacts their functional ability and quality of life. Pain modulation is impaired in some groups with CMP and can be augmented with acute exercise. Further, we have shown that physical activity behaviors in women with fibromyalgia are positively associated with pain modulation. Whether this relationship occurs in GV with CMP is unknown.

PURPOSE: To examine the relationships between self-reported and accelerometer measures of physical activity and pain modulation in GV with CMP.

METHODS: Sixty-eight GV with CMP were recruited and 55 completed physical activity assessments that included completing the International Physical Activity Questionnaire and wearing an Actigraph accelerometer for one week. Psychophysical pain testing was used to assess pain modulation. Painful heat stimuli were delivered alone and during completion of a distracting cognitive task, the Stroop Color and Word Test. Participants rated pain intensity and unpleasantness using Gracy Box Scales (0-20). Multiple linear regression analyses were used to determine whether physical activity significantly predicted pain responses during the distracting cognitive task while controlling for age (years), body mass index (BMI), pain symptom severity (McGill Pain Questionnaire), and mood (Profile of Mood States).

RESULTS: Forty-three GV with CMP were included in the analyses (age = 50.0 (SD 6.7) years; weight = 100.7 (SD 37.2) kg; height = 1.7 meters (SD 8.3); Average Widespread Pain Index scores = 7.0 (SD 3.3)). Moderate physical activity (β=0.45), based on accelerometer measurements, was a significant predictor of pain responses during distraction (F (5, 37) = 2.572, p = 0.05); adjusted R² = 0.16. Relevant covariates (age, BMI, mood and pain symptom severity) were not significant predictors of pain ratings. Self-reported physical activity (β=0.08) was not a significant predictor of pain responses during distraction (F (5, 45) = 1.298, p > 0.05).

CONCLUSION: These results suggest that being physically active may help maintain pain regulatory mechanisms in GV with CMP, but the strength of the relationship was weak and requires further research. Supported by US Department of Veterans Affairs grant #I01CX000383.

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Acute Exercise Increases Pain Threshold And Subjective Psychosocial Mood State

John J. Guers1, Evan L. Matthews2, Casey Wrabley1, Lauren Kerner1.

1Rider University, Lawrenceville, NJ. 2Montclair State University, Montclair, NJ.

Email: jguers@rider.edu

(No relationships reported)

Prescription pain medication can be addictive and have long-term health consequences. Alternative pain-relieving strategies are becoming increasingly sought after. Exercise is known to have a pain-relieving effect which is thought to be mediated through the dopaminergic system.

PURPOSE: To examine the relationships between minimum pain threshold (MPT), exercise blood lactate (EBL), and the self-reported psychosocial effects of exercise based on questions from the Morphine-Benzodiazepine Group, Morphine and Excitement subscales of the Addiction Research Center Inventory (ARCI) following acute exercise in college aged students.

METHODS: Twelve college aged students (age = 20.9 ± 0.5yr) underwent 5 minutes of light leg cycling as a warmup. Following the warmup, they cycled for 20 minutes at 8 METS with an additional 5-minute cooldown. Measurements were taken prior to exercise and just before the cool down. EBL was collected as a measure of relative exercise intensity. The MPT was measured using a Wagner “Pain Test” algometer on the extensor carpi radialis. Results were assessed using a Student’s T-Test.

RESULTS: Following exercise the MPT was increased by 62.1% ± 2.8 (P<0.001). Women had a greater increase in MPT (25.7 ± 9.1%) relative to men (15.8 ± 9.4%; P<0.05). EBL increased from an average of 1.8 ± 0.6 mMol/L at baseline to 4.1 ± 0.7 mMol/L following exercise (P<0.01). There was a positive linear correlation between MPT and EBL (r²=0.59; P<0.05). Indicating greater EBL levels were related to increased MPT. Positive responses from the ARCI subscale increased by 27 ± 3.3% following exercise (P<0.05). There was no effect of sex nor EBL on positive responses on the ARCI.

CONCLUSIONS: These data suggest moderate intensity exercise can increase MPT and to a greater extent in women. Further, MPT correlated with increased EBL indicating that greater relative exercise intensity may modulate a greater increase MPT. Moderate intensity exercise increased positive responses on the ARCI providing evidence that the dopaminergic system may drive changes to MPT. However, positive responses did not correlate to EBL which may suggest another variable may augment pain reduction with increased exercise intensity.