Department of Biological Sciences Seminar Blog

Seminar Date: January 26, 2018
Speaker: Dr. Kathleen A. Sluka, University of Iowa
Seminar Title: *"Exercise: Does it Hurt or Help? Underlying Mechanisms and Clinical Implication"*

Walking Your Way to Freedom: Exercise and Chronic Pain

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Dr. Kathleen Sluka is currently a Professor at the University of Iowa. Prior to earning her doctorate degree, she was clinically trained as a physical therapist. During her clinical experience, she was able to see the symptoms of chronic pain in patients. Her clinical experience and the gap in effective treatments for chronic pain inspired her to return to graduate school. Dr. Sluka now specializes in studying how exercising and physical movement can aid in helping to treat various chronic pain conditions.

Chronic pain is a disease that affects many Americans; in fact, it affects more Americans than cancer, heart disease and diabetes combined. As the opioid epidemic continues to wreak havoc across the nation, the Center for Disease Control (CDC) Opioid Prescribing Guidelines have suggested that the most preferred way to treat this condition would be with a nonpharmacological therapy (1). It has been found that one of the most effective treatments for chronic pain is exercise. Individuals that suffer from chronic pain have high levels of inactivity; this inactivity likely contributes to additional pain in a feedforward cycle.

Throughout her career, Dr. Sluka has published over 200 publications in various journals that span her research area. While she focuses mainly on the mechanisms of exercise and how they function to generally help

relieve pain, she also has devoted time to studying and reviewing specific chronic pain disorders, such as fibromyalgia. Dr. Sluka, with other colleagues, has analyzed if fibromyalgia is primarily caused by changes in the central nervous system or if there are changes in the peripheral nervous system as well (2). Dr. Sluka does not solely focus on studying fibromyalgia though. Her research spans multiple chronic pain centered diseases. Her current research focuses on how exercise can be a course of treatment for chronic pain and the impact of exercise as a front-line treatment for patients (3).

Interestingly, although exercise is broadly used for analgesia, exercise itself can induce pain. Such exercise-induced pain is associated with fatigue and is a serious problem in chronic patients who exhibit significant inactivity. To understand the mechanisms of this phenomenon, Dr. Sluka has developed a murine model of fatigue-induced pain. Two injections of a mildly acidic saline solution (pH=5.0) are administered directly into the mouse's muscle. The injection does not disrupt the muscle structure and alone does not cause any pain. Only in the context of fatigue (or electrical stimulation of the muscle) prior to the second injection do mice exhibit pain-like behavior. Depending on the conditions, the hyperalgesia persists for 24 hours or up to five weeks.

From this exercise-induced pain model, Dr. Sluka and her colleagues were able to look at various peripheral mechanisms that likely drive the hyperalgesia. The lab's first hypothesis focused on nociceptors. It was thought that the nociceptors were being activated by multiple different fatigue metabolites, such as ATP or lactate. One of the most interesting peripheral mechanisms that they identified was relative balance of different types of macrophages that are found in the exercise-induced model.

It is known that there are pro-inflammatory (M1) and anti-inflammatory (M2) cytokines. In sedentary animals following the acid injection injury, there were more M1 than M2 macrophages at the site of injury. However, in animals that previously exercised prior to injury, there were more M2 than M1 macrophages and these animals exhibited less pain-like behavior. These data suggest that the balance of M1 versus M2 macrophages contributes to protective effects of consistent exercise before an injury and the negative effects of acute fatigue on pain. They are continuing to study this system to identify why this occurs and to see if it can be utilized in treatments for chronic pain.

In addition to various peripheral mechanisms, central mechanisms were also assessed. The lab conducted varying immunohistochemistry experiments to identify where NR1, a subunit on the N-methyl-D-aspartate (NMDA) receptor found in nerve cells, was phosphorylated (2). It is believed that the phosphorylation of NR1 leads to enhanced conductance and trafficking of the receptor to the synapse. However, when there is decreased expression of NR1, there appears to be no hyperalgesia present in the murine model. On the other hand, overexpression leads to hyperalgesia.

Excitingly, Dr. Sluka and her colleagues do not just stay confined to the bench top. They also conduct clinical studies to identify different ways that they can encourage individuals to continue exercise regiments to reduce their pain. Their biggest concern with using exercise as a treatment method is the adherence of patients to the exercise intervention. To improve patients' adherence, they focus on education and catering to the needs of each patient. This can include involving their families to motivate them to continue their prescribed regiment and designing specific exercise plans that target the affected body part or area where their chronic pain is presenting.

Dr. Sluka continues to work towards trying to find a way to help those who are still suffering from chronic pain. Even though acute exercise causes acute pain, it is imperative that global society realizes that regular exercise can help to reduce pain. Given that society is typified by more physical inactivity than physical activity, it is important that the message about exercise reaches the ears of all who need it. The benefits of exercise extend well beyond pain including effects on someone's entire well-being. For those who currently exercise regularly, it is important that they understand the effect that exercise can have presently and how it can help prevent other diseases in the future. It is possible that performing minimal exercise, like a 30-minute walk three times a week, can help treat chronic pain and possibly other co-morbid diseases that arise in the context of chronic pain. Indeed, you can "walk" your way to freedom and start to experience everything that your chronic pain causes you to miss out on!

References

1. Opioid Overdose [Guidelines for Prescribing Opoids for Chronic Pain] 2017. Centers for Disease Control and Prevention. URL https://www.cdc.gov/drugoverdose/prescribing/guideline.html (accessed 2.15.18).

2. Lima, L.V., Abner, T.S.S., Sluka, K.A., 2017. Does exercise increase or decrease pain? Central mechanisms underlying these two phenomena. The Journal of Physiology 595, 4141–4150.

3. Sluka, K.A., Clauw, D.J., 2016. Neurobiology of fibromyalgia and chronic widespread pain. Neuroscience 338, 114–129.