Dynamic Chiropractic

CHRONIC / ACUTE CONDITIONS

Normal Activity, Inflammatory Mediators, Chronic Pain and Diet

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Does normal activity lead to the release of inflammatory mediators? Is this related to chronic pain? And is there a dietary connection? There is a growing perception that chronic pain is caused by an overactive central nervous system. I partially to mostly disagree with this view because convincing evidence has yet to be presented that would lead us to discount ongoing peripheral inflammation and nociception.

The traditional view of injury and inflammation contends that "acute inflammation" occurs after injury, which is then followed by the repair and remodeling phases. Pain supposedly should resolve as acute inflammation subsides, so long as care is taken not to mechanically strain the injured tissues. However, when pain does persist and becomes chronic, despite appropriate resolution of acute inflammation, often we are left looking for an explanation.

The Misbehaving CNS

It commonly assumed that peripheral tissues are structurally sound and thus incapable of generating nociceptive impulses, so a common conclusion is that the problem must involve the central nervous system. The perpetuated story goes something like this: The initial injury excited the spinothalamic neurons, which led to the injury-induced pain. For some reason which is typically unexplained, the initial excitation is said to be perpetuated by the CNS, such that spinothalamic neurons keep firing after the peripheral injurious/inflammatory stimulus slows and eventually stops because the injured musculoskeletal tissues healed.

Different terms are used to describe the state of the misbehaving CNS. It is said to *hyperexcitable, sensitized, facilitated* or "*wound up*." There are multiple problems associated with laying the blame exclusively on the central nervous system. A key error in the "misbehaving nervous system" theory is that, at present, there is no gold-standard method for identifying the nature of "healthy" peripheral low back tissues, as an example, despite the present of chronic low back pain that would allow us to impugn the CNS without considering low back tissues. Understanding the "biomechanical" chemistry of normal musculoskeletal tissues can help us to develop a better understanding about the potential nature of theoretically "normal" peripheral tissues that are associated with ongoing pain.

Biomechanical Chemistry

Most are aware that prostaglandins participate in the generation of peripheral nociceptive signals. Typically, prostaglandin E2 (PGE2) is incorrectly viewed solely as a pain/inflammation producer released as a consequence of tissue injury. Research published over the past decade demands that we reconsider this notion.

In 1999, researchers utilized a microdialysis technique to collect fluid from the Achilles tendons of subjects who performed intermittent isometric plantar flexion exercises that mimicked the force

generation that occurs during normal walking.[1] The researchers demonstrated that supposedly painful PGE2 is *normally* released during this activity. Not surprisingly, the subjects in this study did not experience any pain. So, why was PGE2 released? The reason is that PGE2 creates vasodilation in the Achilles tendon and other tissues, which is needed during physical activity.

In 2004, Wang, et al., decided to look at which mediators are released when tendon fibroblasts are stretched.2 It turns out that fibroblasts release PGE2, which demands that we discard the notion that only classic immune cells release inflammatory mediators in response to injury. We now know that connective tissue cells release so-called inflammatory mediators during normal activities.[1-2]

In 2003, research was published that provided us with a unique view of the PGE2 that is produced during the previously mentioned plantar flexion exercise that mimics normal walking.[3] Researchers compared the release of PGE2 without medication with a COX-2 inhibitor (Celebrex), and with indomethacin and aspirin, which inhibit COX-1 and COX-2.

As a quick review, *both* cyclo-oxygenase (COX) enzymes convert dietary omega-6 arachidonic acid into PGE2, which is a well-known fact, but one that is rarely discussed in the context of treating pain and inflammation. Well-known in nutrition circles is the fact that the same COX enzymes convert dietary anti-inflammatory omega-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) into non-inflammatory mediators.[4] This means that the "inflammatory activity" of the COX enzymes can be influenced by the omega-6 and omega-3 fatty acids present within the cell membrane.

In the 2003 study, PGE2 production in the Achilles tendon was determined at rest, during exercise (simulated walking) and in the recovery period. Even at rest, PGE2 production exists, which increases during exercise. An increase in PGE2 production occurred during exercise. This increase did not take place while taking Celebrex, which means that "walking" stimulates the COX-2 enzyme.

The key point to embrace from this research is that we normally produce so-called "painful" PGE2 at rest and we activate so-called "inflammatory" COX-2 by non-injurious stimuli, such as light isometric exercise that simulates walking. In other words, we are always producing a mediator that is typically viewed to be inflammatory and pain promoting, and it makes no difference whether the tissue is injured or not. And so, even if tissue healing theoretically occurs after a low back injury, there is no evidence to suggest that the local tissue chemistry is not pro-inflammatory and capable of perpetuating nociceptive input.

Diet-Derived Arachidonic Acid/PGE2 and Chronic Pain?

Osteoarthritis is an example of a painful condition that is known to be associated with an increased level of arachidonic acid within joint tissues; this has been known since 1975.[5] In 1991, research demonstrated that young joints do not contain arachidonic acid, which only accumulates as we age[6] because of a dietary excess of omega-6 fatty acids. In 2004, high levels of arachidonic acid were measured in cancellous bone of the femoral head in patients undergoing hip surgery.[7] The above chemistry studies in osteoarthritis demonstrated that arachidonic acid levels increase in connective tissues as we age. Consequently, we cannot firmly state that the periphery is not involved in the generation of pain simply because we choose to assume that musculoskeletal tissues have repaired after an injurious event.

It is certainly possible that a critical threshold will be reached regarding diet-derived arachidonic

acid levels in musculoskeletal tissues. At this point, the "normal state" is pro-inflammatory and pro-nociceptive, which is why a patient will continually rescue with NSAIDs. In this case, the sensitized dorsal horn would be perpetually stimulated by ongoing nociceptive input in the absence of overt pathoanatomy.

In short, a great deal more work needs to be done before we proclaim peripheral tissue health and impugn the CNS. The nutrition-inflammation connection may be a key determining factor.

References

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