When Moving Hurts

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GLOBAL YEAR AGAINST MUSCULOSKELETAL PAIN

OCTOBER 2009 – OCTOBER 2010

Basic Aspects of Muscle Pain

Introduction

- Musculoskeletal disorders are the leading causes of pain in every population.
- Pain from muscles and pain from the skin are subjectively and objectively distinct.
- Muscle pain is aching and cramping, and cutaneous pain is sharp and pricking. In contrast to cutaneous pain, muscle pain is referred to other deep somatic structures.
- The neuronal pathways of nociceptive information from muscle and skin are different in the central nervous system (CNS).

Morphology and Functional Properties of Muscle Nociceptors

- Muscle nociceptors are free nerve endings that are connected to the CNS by thin myelinated (group III) or unmyelinated (group IV) fibers.
- Nociceptive muscle afferents are not blocked by tetrodotoxin (TTX), which indicates the presence of TTX-resistant sodium channels.
- Group III and IV fibers comprise high-threshold mechanosensitive (presumably nociceptive) and low-threshold mechanosensitive (presumably non-nociceptive) muscle receptors. The latter probably mediate pressure sensations from muscle.
- Dorsal root ganglion cells projecting in a muscle nerve contain neuropeptides such as substance P, calcitonin gene-related peptide (CGRP), and somatostatin.

Effective Stimuli for Peripheral Muscle Nociceptors

- Effective stimulants are adenosine triphosphate (ATP) and protons (low pH). These substances excite muscle nociceptors at (patho)physiological concentrations.
- Receptor molecules are P2X2–5 for ATP and ASIC3/TRPV1 for protons. Most muscle nociceptors are polymodal and respond to both noxious pressure stimulation and pain-producing substances.
- In lesioned muscle, nociceptors lower their mechanical threshold and respond to weak stimuli. This change in threshold may be the basis of muscle tenderness.
- Repeated intramuscular injections of acidic solutions induce generalized muscle pain.
- The density of innervation with free nerve endings increases in inflamed muscle.

Central Effects of Nociceptive Activity from Muscle

- Nociceptive input from muscle is more effective in inducing central neuroplastic changes than is input from the skin.
- Every long-lasting input from muscle nociceptors to the CNS increases the excitability of central neurons, leading to pain, hyperalgesia, and pain referral. The referral is probably due to the opening of silent synapses.
- The postsynaptic receptor molecules responsible for central sensitization include *N*-methyl D-aspartate (NMDA) and neurokinin-1 receptors.
- Even subthreshold synaptic activity sensitizes dorsal horn neurons. This mechanism may be essential for some cases of occupational muscle pain.
- Glial cells, microglia in particular, are activated by a muscle lesion and release sensitizing factors such as ATP, prostaglandins, and brain-derived neurotrophic factor.

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