Stress-Induced Hyperalgesia: Clinical Implications for the Physical Therapist

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INTRODUCTION
Following a motor vehicle accident, my patient, Ms. S, carried her daughter into an emergency room unaware of her own injuries. Only after learning that her daughter’s injuries were not life threatening did she experience the pain in her feet from glass fragments lodged in her shoes. Years later, Ms. S was diagnosed with fibromyalgia and now struggles with the opposite impact of stress on pain. Daily life stress increases her pain. Her two experiences demonstrate the paradoxical role stress plays in pain perception.

The intensity or aversiveness of a stressor may influence the amplification or suppression of pain. Highly intense stress may inhibit pain. Termed “stress-induced analgesia,” this phenomena was first described by Dr. Henry Beecher, a military anesthesiologist, who collected data on pain complaints of severely wounded soldiers during World War II. (1) Two thirds of the men with extensive soft tissue injuries, penetrating wounds or compound fractures said they had little or no pain. Only 27% requested pain medication. Recent research demonstrates that both opioid and non-opioid intrinsic pain inhibitory systems activate to suppress pain under intense-stress conditions. (2)

Stress may also amplify pain conditions. In clinical settings, stress is implicated in the transition from acute to chronic back pain (3), plays a role in the exacerbation of fibromyalgia (4), rheumatoid arthritis (5), pelvic pain (6) and irritable bowel syndrome (7), and can have an adverse effect on surgical outcomes. (8) In addition, individuals with a history of abusive childhoods are at an increased risk of chronic pain in adulthood relative to individuals not reporting childhood abuse. (9)

STRESS-INDUCED HYPERALGESIA
An increase in pain sensitivity caused by stress, termed “stress-induced hyperalgesia” (SIH), is an area of current laboratory research. In rodent studies, hyperalgesia has been shown to result from repeated exposure to stress such as swim (10) and sound stress (11), chronic restraint (12) and social defeat. (13) In rats, water avoidance stress produced mechanical hyperalgesia in skeletal muscle and an approximate 34% decrease in the mechanical threshold of muscle nociceptors, 65% increase in the number of action potentials produced by a fixed intensity suprathreshold stimulus and 67% increase in nerve conduction velocity. (14) Rats subject to neonatal stress demonstrated persistent mechanical hyperalgesia and nociceptor sensitization in adulthood. (15) In the mature rats, mechanical threshold of muscle nociceptors was reduced nearly 31% and conduction velocity increased by approximately 28%.
NERVOUS SYSTEM MECHANISMS CONTRIBUTING TO SIH

Peripheral mechanisms contributing to SIH
Catecholamines, secreted by the adrenal medulla in response to stress, may act in the periphery to promote hyperalgesia. In rats, local administration of epinephrine induces transient mechanical hyperalgesia in the absence of nerve injury via action of the beta-adrenergic receptors. (16) Exposure to elevated levels of epinephrine has also been shown to enhance the pro-nociceptive effects of immune mediators (17) and induce IL-6 synthesis in skeletal muscle. (18) IL-6 synthesis is significant because of its role in producing mechanical hyperalgesia in skeletal muscle and possible contribution to the transition from acute to chronic pain. (19)

Central mechanisms contributing to SIH
Chronic social stress in rats has been shown to induce spinal neuroinflammation, resulting in a decrease in mechanical nociceptor threshold, sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. (13) Forced swim stress in rats has been shown to induce mechanical hyperalgesia and a shift in excitatory and inhibitory mechanisms at the spinal level. (10) A decrease and delayed inhibitory neurotransmitter release in the spinal cord initiated hyperalgesia, while an increase excitatory neurotransmitter release maintained the SIH.

The dorsomedial nucleus of the hypothalamus (DMH) plays a critical role in neuroendocrine responses to stress and has direct and indirect connections to the rostral ventralmedial medulla (RVM), a brainstem region active in the descending modulation of nociceptive transmission in the dorsal horn. (20) In rats, disinhibition of the DMH triggered behavioral hyperalgesia and a robust activation of pain-facilitating neurons and suppression of pain-inhibiting neurons in the RVM. (21)

CLINICAL IMPLICATIONS OF SIH
Physical therapy interventions for the treatment of pain depend on an accurate understanding of underlying mechanisms. These mechanisms are complex, multifactorial and under continual clinical and laboratory investigation. Current evidence suggests stress plays a contributing role in hyperalgesia and chronic pain. Although mechanisms underlying SIH come from rodent studies, results of these laboratory investigations combined with evidence of the role of stress in clinical populations invite a thoughtful consideration of the role stress plays in the pain complaints of patients. SIH could contribute to an elevated pain level and more prolonged healing process than expected in a stressed patient. Pain from an injury in a stressed individual could persist because of SIH and potentially contribute to a chronic pain condition.

Physical therapists may wish to consider a patient’s stress level when evaluating and assessing mechanisms of a pain complaint. Inquiring about stress levels may be a judicious choice when pain complaints appear more severe than would otherwise be expected for the mechanism of injury or pain persists beyond a reasonable time frame for healing. Also, should a patient disclose a history of childhood abuse, physical therapists need to be aware that preliminary findings suggest the possibility that early trauma may have an enduring impact on the nociceptive system.
The direct influence of a patient’s stress level on pain is not easily identified and quantified. A patient’s self-report of stress is limited by his or her self-awareness and self-assessment skills. Some patients may accurately identify and be comfortable discussing life stressors and their limited skills to manage stress. Others may not recognize or be willing to disclose difficult life circumstances or suggest their coping is impaired. A short assessment tool, such as the Perceived Stress Scale, may help both patient and clinician identify a patient’s stress level. The Perceived Stress Scale is a valid, reliable and widely-used 10-item measure of self-appraised stress. (22, 23)

If a patient acknowledges high stress levels and/or the physical therapist makes the clinical judgment that stress plays a role in the patient’s pain complaints, treatment choices to address the pain escalating influences of stress should be included in a plan of care. The following treatment approaches warrant consideration:

1. Pain neurophysiology education.
   Pain neurophysiology education provides patients with an understanding of key factors that give rise to the experience of pain. Topics covered include the anatomy of the nervous system, peripheral and central sensitization and how the brain processes and regulates nociceptive information. A recent systematic review of pain neurophysiology education concludes that for chronic musculoskeletal disorders, this education strategy may have a positive impact on pain, disability, catastrophizing and physical performance. (24) This comprehensive educational approach could, in part, reduce a patient’s stress level.

2. Progressive muscle relaxation training
   Progressive muscle relaxation has been shown to reduce subjective and physiological indices of stress (25) and may help patients increase coping and control of pain. (26) In addition, authors of a Cochrane Database Review conclude moderate evidence exists in favor of progressive relaxation for providing a large positive effect on pain and behavioral outcomes in patients with chronic low back pain. (27)

3. Diaphragmatic breathing
   Preliminary investigations suggest slow, deep breathing may contribute to a reduction in sympathetic nervous system activity and pain perception. (28, 29) This treatment strategy may prove especially helpful to patients with fibromyalgia, a population shown to have smaller chest expansion measurements and lower maximal inspiratory and expiratory pressures compared to healthy controls. (30)

4. Body awareness training
   A patient’s ability to be aware of the body is necessary for the self-regulation of the nervous system. Many patients have little or no body awareness. Others are afraid to pay attention to their physical experience because of pain. Unable to bring awareness to the body in a skillful manner, they are unable to observe and successfully modulate the stress reaction. Strategies that promote body awareness such as the mindful body scan (31), gentle yoga (32) and tai chi (33), promote a healthy mind-body relationship and may contribute to a patient’s ability to observe and reduce the stress reaction.

5. Aerobic exercise
   Aerobic exercise has been shown to improve mood and reduce anxiety and panic. (34) In addition, physical fitness may act to mitigate adverse effects of psychosocial stress and
reduce inflammatory cytokine response to acute mental stress. (35)
6. Psychosocial interventions tailored for delivery by physical therapists.
Physical therapists providing standard physical therapy treatment combined with a
psychosocial intervention to patients with low back pain was shown to reduce risk factors
for pain and disability, reduce the use of the health care system, reduce the use of pain
medication and improve return-to-work outcomes. (36) This physical therapist-delivered,
psychosocial intervention included the targeted treatment of psychosocial risk factors,
graded activity setting, exposure to feared activity, goal setting, problem solving and
motivational enhancement. This structured psychosocial intervention could conceivably
contribute to reducing a patient’s stress level.

In addition, physical therapists may consider referring patients to additional stress
management resources including cognitive behavioral therapy (37) and mindfulness
based stress reduction programs. (31, 38)

CONCLUSION
Stress is recognized to both suppress and amplify pain. Intense, life-threatening stress
may inhibit pain, while mild or moderate stress may amplify pain. Recent evidence from
laboratory investigations of SIH suggests stress can amplify nociceptive system
sensitivity through both peripheral and central nervous system mechanisms. Physical
therapists have the opportunity to employ evidence-based stress reduction strategies to
reduce possible SIH in patients with persistent pain conditions. Additional physical
therapy treatment approaches to reduce patient stress and the impact of those strategies
on pain and function create an opportunity for future research.

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