Chronic Musculoskeletal Pain: Emerging Mechanisms and the Chiropractic Opportunity

A Mechanistic Link Between Spinal Degeneration and Neurogenic Inflammation in Muscle

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Chronic pain constitutes a global epidemic and ranks among the most pressing challenges confronting contemporary healthcare systems. Physiologically distinct from acute, transient pain, chronic pain does not resolve with tissue healing; instead, it persists and induces progressive structural and functional remodelling of the nervous system. Its prevalence increases significantly with advancing age, such that the majority of older adults experience some form of symptomatic chronic musculoskeletal disease (Davis, 1988). Consequently, the societal and clinical burden of chronic musculoskeletal pain is projected to increase exponentially in as the global population ages.

This workshop provides a structured overview of an emerging mechanistic framework that links spinal degeneration to the development of neurogenic inflammation within skeletal muscle. Drawing upon foundational and emerging empirical evidence, the presentation critically examines the scientific basis for this linkage and explores its broader implications. In doing so, it highlights how this body of research provided the biological plausibility for a central role of chiropractors in the management and prevention of chronic musculoskeletal pain. This collective body of research makes the strong argument for chiropractors as primary gatekeepers in addressing this escalating public-health concern.

The Nervous System in Chronic Pain: Central Sensitization

Acute pain serves a protective physiological function. It signals tissue injury and typically resolves following tissue healing. Chronic musculoskeletal pain, by contrast, is fundamentally a different physiological construct. Its hallmark is central sensitization, a neuroadaptive process in which neurons within the central nervous system exhibit heightened responsiveness. Clinically, this state is expressed through spreading hyperalgesia beyond the original injury site (expansion of receptive fields), altered somatosensory response to innocuous stimuli (allodynia), and pain that persists in the absence of identifiable tissue damage (Meeus & Nijs, 2007; Srbely et al., 2010a). Advancing age further exacerbates susceptibility to sensitization, as endogenous pain-

inhibitory mechanisms progressively decline, thereby rendering older adults more susceptible to the development and maintenance of central sensitization and, ultimately, to chronic musculoskeletal pain (Gibson & Farrell, 2004).

The Biochemical Signature of Chronic Myofascial Pain

A central question follows from this framework: if chronic musculoskeletal pain is a manifestation of a sensitized nervous system, what facilitates that sensitized state in the tissues? The foundational insight came from the early work of Shah and colleagues, who used in vivo microdialysis to sample the biochemical environment of myofascial trigger points directly (Shah & Gilliams, 2008). Shah and colleagues showed that active, painful trigger points are characterized by a distinctive biochemical milieu, one predominated by sensitizing and pro-inflammatory substances that is not observed in healthy muscle. For the first time, the pain of chronic myofascial disease was linked to a unique pro-inflammatory and sensitizing signature in the affected muscle, establishing that these painful nodules are sites of biochemical activity rather than passive regions of muscular tension. The broader clinical significance of this signature is reinforced by additional work showing that individuals with active trigger points differ from those without pain across physical findings, sleep, mood, disability, and overall quality of life (Gerber et al., 2013). Although this early evidence identified the inflammatory nature of chronic myofascial pain, it did not establish the origin of that inflammation.

From Spine to Muscle: Preclinical Evidence for Neurogenic Inflammation

The question of origin has been addressed by emerging preclinical research in the Srbely lab, and its answer points to the central role of the spine in health and disease. The relevant mechanism is neurogenic inflammation, which is defined as inflammation generated by the nervous system itself. When sensory nerves are activated, they release signaling molecules such as glutamate and substance P into the dorsal horn. If this is allowed to persist, dorsal horn sensitization can lead to dorsal root reflexes (DRR) that evokes an antidromic release of proinflammatory neuropeptides substance P and calcitonin gene-related peptide (CGRP) into the neurosegmentally linked tissues. This DRR can occur in both somatic and visceral tissues, producing an inflammatory response in the absence of local injury (Ustinova, 2007). Furthermore, using a controlled preclinical model, Srbely and colleagues experimentally induced osteoarthritis in the facet joints of the spine and examined its consequences in neurosegmentally linked muscle (Duarte et al., 2021). Animals subjected to spinal facet osteoarthritis in this study developed the sensory hallmarks of central sensitization together with elevated levels of neurogenic inflammatory biomarkers, including substance P and calcitonin gene-related peptide, specifically in the muscles that shared the affected spinal segments. Muscles that were not neurologically linked to the degenerated segments exhibited no such changes.

This finding provides further support to the emerging role of spinal degeneration in the pathophysiology of chronic musculoskeletal pain. It provides direct experimental

evidence that degenerative spine disease can generate neurogenic inflammation in remote but segmentally connected muscle, thereby providing the causal link to support the earlier biochemical work by Shah and colleagues. Together, these two lines of investigation converge onto an emerging body of foundational mechanistic work supporting the role of the spine in the pathogenesis and pathophysiology of chronic musculoskeletal pain.

The Neurogenic Hypothesis and the Spine as a Primary Driver

These findings give empirical support to the Neurogenic Hypothesis (Srbely, 2008). According to this hypothesis, chronic myofascial/musculoskeletal pain is not primarily a disorder of the symptomatic muscle; instead, it's a downstream secondary expression of central sensitization arising from a distinct, remote source of persistent nociception that shares the same spinal segment as the symptomatic muscle (Srbely et al., 2010b). This supports a unified framework whereby degeneration of the spine and its joints may represent a primary driver of chronic musculoskeletal pain in the aging population. It's theoretical framework arose from the observation that chronic myofascial pain and degenerative spinal disease both increase with advancing age, with spinal degeneration producing the persistent, segmentally organized nociceptive source needed to evoke persistent neurogenic responses the model predicts. Complementary theoretical work describes how this process can also lead to impaired clearance of inflammatory mediators from tissue, including fascia, thereby creating a mechanism for sustained nociceptor activation and central sensitization (Tuckey et al., 2021). Additional studies have proposed diagnostic frameworks for conditions such as nonspecific low back pain, identifying the underlying drivers of neurogenic inflammation rather than addressing symptoms in isolation (Sikdar et al., 2023). Viewed in this light, the spine becomes an important consideration in the diagnosis, management and prevention of chronic musculoskeletal pain.

Two Clinically Impactful Levers for Chiropractic: Treatment and Prevention

The clinical implications of this mechanistic perspective rest on two primary opportunities. The first is therapeutic. Spinal manipulation appears to exert its effects not through mechanical means alone, but by attenuating central sensitization in the treated segment. Controlled trials have shown that manipulation produces measurable reductions in the sensitivity of myofascial trigger points that are specific to the treated segment (Srbely et al., 2013), and independent experimental work confirms that segmental manipulation attenuates experimentally induced central sensitization and secondary hyperalgesia (Bialosky et al., 2014; Gevers-Montoro et al., 2021). If sensitization and its associated neurogenic inflammation are the processes that sustain chronic pain, then manipulation offers an effective, non-invasive, low cost intervention for attenuating those processes at their segmental source.

The second, and perhaps more consequential, opportunity is preventive. If spinal degeneration does, in fact, initiate the mechanistic cascade that culminates in chronic pain, then preventative measures to slow that degeneration should be prioritized. Prevention is most appropriately considered at three levels across the lifespan. *Primary prevention* acts before disease becomes established, through the optimization of spinal mechanics and movement, patient education, ergonomic and lifestyle guidance, and maintenance care, with the aim of mitigating the onset and progression of degeneration. *Secondary prevention* addresses early and frequently asymptomatic degeneration, identifying and correcting biomechanical and myofascial dysfunction before they mature into an entrenched and sensitized pain state. *Tertiary prevention* manages established chronic musculoskeletal pain to limit disability, optimize function, and reduce reliance on medication and more costly and potentially invasive interventions. Because biomechanical joint dysfunction is a primary determinant of degenerative joint disease (Roos et al., 2011) and manipulation optimizes joint mechanics and alters the neurophysiology of the treated segment (Pickar, 2002), spinal care represents a critical component of a lifelong strategy to mitigate degeneration and its chronic musculoskeletal pain sequelae.

The Chiropractor as a Gatekeeper of Chronic Musculoskeletal Pain

Collectively, these findings offer a coherent and well supported framework for the essential role of chiropractors in the current and future health delivery system. Chronic musculoskeletal pain is maintained by central sensitization, and that sensitization is sustained by neurogenic inflammation in muscle. The early biochemical work of Shah established the inflammatory signature of this process, and the emerging preclinical work of Srbely and colleagues identifies degeneration of the spine as an important nociceptive source in the causal pathway of chronic musculoskeletal pain. This body of mechanistic evidence places the spine, and therefore the chiropractic profession, at the center of chronic musculoskeletal pain management and prevention. Chiropractors are positioned to intervene therapeutically, using manipulation to modulate the sensitization that perpetuates and amplifies chronic musculoskeletal pain, and to intervene preventively across the lifespan, slowing the degeneration that sets this process in motion. This growing evidence-based body of work presents the chiropractic profession with a unique opportunity to establish itself as the gatekeepers of chronic musculoskeletal pain moving forward.

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