Myofascial Trigger Points and Central Sensitization in Chronic Pelvic Pain and Endometriosis: New Research Approaches

Jay P. Shah, MD
Senior Staff Physiatrist
Rehabilitation Medicine Department
Mark O. Hatfield Clinical Research Center
jshah@mail.cc.nih.gov
Learning Objectives:

1. Examine the unique neurobiology of muscle pain and the dynamic interplay of muscle nociceptors and endogenous biochemicals in the initiation, amplification and perpetuation of peripheral and central sensitization.

2. Demonstrate that an active MTrP has elevated levels of inflammatory mediators, neuropeptides, and cytokines, etc. – substances known to be associated with persistent pain states, sensitization and inflammation.

3. Demonstrate that MTrPs are stiffer than surrounding tissue and that active MTrPs can be distinguished from latent MTrPs by their high-resistance blood flow.

4. Demonstrate that the presence of abdominal MTrPs in women with chronic pelvic pain may be indicative of an underlying visceral disease process, or may have resulted from previous visceral disease.

5. Demonstrate that women with chronic pelvic pain show signs of central sensitization (allodynia and hyperalgesia) and myofascial dysfunction.

Introduction

Myofascial pain is a specific condition - non-inflammatory in nature – which should be distinguished from other soft tissue pain disorders such as fibromyalgia, tendonitis, or bursitis. Typical symptoms and signs include regional pain, often accompanied by increased tension and decreased flexibility in muscle and related fascia. The most important physical finding is one or more myofascial trigger points (MTrPs)—hard, discrete, tender, hyperirritable nodules palpable in a taut band of skeletal muscle (Figure 1). Active MTrPs are a source of spontaneous pain while latent MTrPs are painful only on deep palpation. Both latent and active MTrPs can cause muscle dysfunction, muscle weakness, and limit range of motion. MTrPs are the most common, and yet most under-diagnosed and under-treated component of non-articular musculoskeletal pain disorders.
Figure 1: Schematic of a trigger point complex. CTrP identifies the central trigger point that is found in the endplate zone and contains numerous contraction knots and electrically active loci among normal fibers. A taut band of muscle fibers extends from the trigger point to the attachment (ATrP) at each end of the involved fiber. (Adapted from Simons, D.G., Travell, J.G. Myofascial Pain and Dysfunction: The Trigger Point Manual, vol. 1; second ed., and Anva ndare: Chrizz.)

Unique neurobiology of muscle pain
Muscle pain has a unique neurobiology which helps to explain its clinical presentation. In contrast to cutaneous pain, (1) muscle pain causes an aching, cramping pain that is difficult to localize and is often referred to deep and distant somatic tissues; (2) muscle pain activates unique cortical structures in the central nervous system; (3) muscle pain is inhibited more strongly by descending pain-modulating pathways; and (4) activation of muscle nociceptors is much more effective at inducing maladaptive neuroplastic changes in dorsal horn neurons. These neuroplastic changes are important harbingers of a chronic pain disorder.

Peripheral and central sensitization
Peripheral and central sensitization is responsible for the transition from normal to aberrant pain perception—that is, when the CNS experience of pain outlasts the noxious stimulus coming from the periphery. Muscle pain is especially effective at driving central sensitization. Continuous activation of muscle nociceptors increases the ‘afferent drive’—that is, the impulses per second bombarding dorsal horn neurons in the spinal cord. This may lead to changes in function and connectivity of sensory dorsal horn neurons via central sensitization. This process can spread to adjacent neurons, leading to structural changes and maladaptive neuroplastic alterations in the central nervous system. The clinical consequences are (1) allodynia (pain in response to a normally non-painful stimulus), (2) hyperalgesia (increased sensitivity to pain), and (3) expansion of the receptive field of pain.

There is a biochemical basis to the development of peripheral and central sensitization in muscle pain. For example, sensitizing agents released in muscle may up-regulate or increase the activity of receptor molecules on the nociceptor terminal. Continuous activation of muscle nociceptors leads to the co-release of
substance P and glutamate at the pre-synaptic terminals of the dorsal horn. This can eventually lead to maximal opening of calcium-permeable ion channels, which hyperexcites nociceptive neurons and induces apoptosis of inhibitory neurons.

Moreover, prolonged noxious input may lead to long-term changes in gene expression, somatosensory processing and synaptic connections in the spinal cord and other higher structures. These mechanisms of peripheral and central sensitization lower the activation threshold of afferent nerves and their central terminals, allowing them to fire even in response to daily innocuous stimuli. Consequently, even non-noxious stimuli such as light pressure and muscle movement can cause pain.

**Active myofascial trigger points have a unique biochemical milieu**

Acute muscle injury has obvious signs of bleeding and inflammation. In contrast, the pathophysiology of myofascial pain is quite obscure. Our research studies sought to determine if there are biochemical aspects that differentiate active MTrPs (spontaneously painful) from latent MTrPs (non-painful), and muscle without MTrPs. To address this common yet poorly understood entity, my co-investigators and I developed a novel microdialysis needle (Figures 2A and 2B) to safely and quantitatively measure the local biochemical environment of muscle *in vivo*.

Our microanalytical technique enables continuous, real-time sampling from soft tissue in extremely small quantities of approximately 0.5 microlitres. Moreover, it allows us to directly sample the biochemical milieu of MTrPs, as well as to investigate the bioactive substances (e.g. inflammatory mediators, neuropeptides, catecholamines, and cytokines, etc.) that are released from and act on muscle, nerve, and connective tissue.
We found that subjects with neck pain secondary to an MTrP in the upper trapezius had significantly elevated levels of the aforementioned substances in the local muscle biochemical milieu compared to carefully matched controls. These results were published in the *Journal of Applied Physiology*\(^9\). Additional studies conducted in our laboratory have confirmed that active MTrPs have a unique biochemical milieu of substances that are known to be associated with chronic pain states. Furthermore, compared to controls, subjects with active MTrPs in the upper trapezius have elevated levels of these biochemicals in a remote, unaffected muscle\(^10\).

The various types of inflammatory mediators, cytokines, and neuropeptides etc. which were found to be elevated in active MTrPs are known to be associated with persistent pain states\(^6\). High concentrations of these substances are able to cause both peripheral and central sensitization. Our biochemical findings may explain why active MTrPs are acutely painful, tender, and a source of referred pain.

**Dry needling and the local twitch response**

Trigger point dry needling may be performed using either a superficial or deep dry needling technique, depending upon the depth of needling and the clinician’s experience and preference. Elicitation of one or more LTRs is a goal of deep dry needling.

While the mechanism of the LTR is unknown, our studies suggest a biochemical component. We found that the levels of two biochemicals dropped significantly
from their initial baseline levels immediately following the successful induction of a LTR. The decrease in local concentrations of substance P and calcitonin gene-related peptide may correlate with the symptomatic reduction of pain following deep dry needing. It is possible that these concentration drops are due to a small, localized increase in blood flow, and/or nociceptor and mechanistic changes associated with an augmented inflammatory response.

**Visualisation and characterization of myofascial trigger points**

Despite the high prevalence, there are currently no imaging criteria for the diagnosis of MTrPs or for assessing the clinical outcome of treatments. Our laboratory recently began using three types of ultrasound diagnostic imaging techniques—grayscale (2D ultrasound), vibration sonoelastography, and Doppler—to differentiate tissue characteristics of MTrPs in the upper trapezius muscle compared to surrounding soft tissue. We found that MTrPs appeared as focal, hypoechoic regions on 2D ultrasound, indicating local changes in tissue echogenicity, and as focal regions of reduced vibration amplitude on vibration sonoelastography, indicating a localized area of stiffer tissue (Figure 3).

We have shown that ultrasound is feasible for imaging MTrPs and that MTrPs exhibit different echogenicity compared to surrounding muscle. Furthermore, vibration sonoelastography shows differences in relative stiffness between MTrPs and normal (uninvolved) muscle. That is, sites containing MTrPs have significantly greater relative stiffness compared to normal tissue. Figure 4 shows the color variance image of the upper trapezius muscle that was normal on physical examination. The entire region of the muscle appears to vibrate with approximately uniform amplitude, as indicated by the uniform color.

Doppler ultrasound was also able to show differences in the microcirculation in and around active MTrPs compared to latent MTrPs and normal tissue. For example, blood flow waveform characteristics can be used to differentiate active and latent MTrPs. Retrograde flow on diastole was associated with active MTrPs, indicating a very high resistance vascular bed and possible blood vessel compression. Details and results of our ultrasound investigations are discussed in our paper titled ‘Novel Applications of Ultrasound Technology to Visualize and Characterize Myofascial Trigger Points and Surrounding Soft Tissue’.

![Figure 3: Upper trapezius muscle with a palpable MTrP. A hypoechoic region and a well-defined focal decrease of color variance indicating a localised stiffer region are visible.](image-url)
Myofascial dysfunction in the pelvis

Many gynecologists and patients believe that chronic pelvic pain associated with endometriosis is caused by the endometriosis lesion. However, a causal link has not been established. Furthermore, severity of the pain does not correlate well with severity of disease. Likewise, there is little correlation between the location of the pain and that of the ectopic growths. Although analgesics, hormonal therapies, and surgery are standard treatments, there is often recurrence of pain, which is not necessarily associated with the return of endometriosis lesions.

Jarrell became interested in the contributions of MTrPs to chronic pelvic pain syndromes because he noted that 25-40% of all cases of laparoscopy done for pelvic pain do not demonstrate an identifiable visceral cause for the pain. Specifically, his hypothesis is that pelvic pain cannot only be due to MTrPs, but that MTrPs may also be a sign of underlying organic disease.

In his study, fifty-five consecutive patients with pelvic pain were evaluated in a cross-sectional design. Eligible subjects had to present with chronic pelvic pain and be found to have, as a component of their condition, evidence of myofascial dysfunction in one or more areas of the abdomen and pelvis. Jarrell’s objective was to describe subjects with myofascial dysfunction and pelvic pain more carefully in terms of the number of MTrPs and their relationship to age, parity, treatment, and any underlying visceral disease. Subjects were considered to have evidence of visceral disease if they had received treatment for a surgically confirmed visceral cause of pain in the past or had evidence documenting current visceral disease.

Interestingly, Jarrell found that the only variable that correlated with visceral disease was the presence of an abdominal wall MTrP. This finding predicted evidence of visceral disease in 90 percent of subjects. Conversely, if an MTrP was not present, this finding was associated with no visceral disease in 64 percent of the subjects. Furthermore, he found that the presence of MTrPs in the
perineum or intrapelvic muscles was not associated with previous or current visceral disease. He does offer a caveat that - because of a strict bias in patient selection - these correlations would not necessarily be seen in a more general group of women with chronic pelvic pain.

The presence of abdominal wall MTrPs in women with chronic pelvic pain may indicate an underlying visceral disease process. On the other hand, abdominal MTrPs may be secondary to previous visceral disease. Accordingly, these findings suggest that if one treats only the MTrPs, then the underlying diagnosis (e.g., visceral disease could be overlooked. Either way, this study supports the classic osteopathic concepts of somatovisceral and viscerosomatic interactions.

Central nervous system sensitization in women with chronic pelvic pain and endometriosis

Introduction

In Chronic Pelvic Pain (CPP) associated with endometriosis, pain intensity is not correlated with disease severity nor is pain location with lesion site. To better understand the pathophysiology of CPP in relation to endometriosis, we investigated signs of central nervous system (CNS) sensitization in women with CPP and endometriosis (CPP+E), CPP alone (CPP), and healthy volunteers (HV).

Materials and Methods

Allodynia and hyperalgesia were assessed bilaterally from T9 to S2. Pain pressure threshold (PPT) was measured along the supraspinous ligament in the same region. CNS sensitization was defined as the presence of allodynia, hyperalgesia, or a lowered PPT (≤9lbs) in half of the sites tested. Myofascial trigger points (MTrPs) and their PPTs were examined in 7 pelvic muscles. Myofascial dysfunction was defined as having an MTrP associated with a lowered PPT (≤4lbs) in 4 or more muscles. Subjects rated their pain level on a visual analog scale (VAS) from 0 (no pain) to 10 (worst pain imaginable), today and within the last month. A VAS of ≥4 was a criterion for presence of pain. Endometriosis was confirmed by biopsy upon laparoscopic surgery. Data were analyzed using Jonckheere-Terpstra tests for trend.

Results

Sensitization, as defined by all three criteria (allodynia, hyperalgesia, and lowered PPT), showed the same segmental pattern in each individual. Those with CPP had a statistically significant higher rate of sensitization (82% CCP+E vs 75% CPP vs 17% HV; p=0.001) (Table 1). Myofascial dysfunction was significantly more common with CPP (100% CCP+E vs 88% CPP vs 17% HV; p<0.0001) or lowered PPTs in MTrPs (36%, 13%, and 0%, respectively; p=0.03).
The CPP+E group experienced the highest pain levels over the last month (p<0.0001).

Table 1. CNS Sensitization in the pelvic region by study group

<table>
<thead>
<tr>
<th></th>
<th>CPP+E N=11 n (%)</th>
<th>CPP N=8 n (%)</th>
<th>HV N=12 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allodynia</td>
<td>9 (82)</td>
<td>6 (75)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>8 (73)</td>
<td>4 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Lowered PPT</td>
<td>7 (64)</td>
<td>3 (38)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Myofascial dysfunction (MTrPs)</td>
<td>11 (100)</td>
<td>7 (88)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Lowered PPT in TrPs</td>
<td>4 (36)</td>
<td>1 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Pain today</td>
<td>4 (40)</td>
<td>4 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Pain in last month</td>
<td>9 (90)</td>
<td>5 (63)</td>
<td>0</td>
</tr>
</tbody>
</table>

1 p=0.001; 2 p=0.0003; 3 p=0.007; 4 p<0.0001; 5 p=0.03

Discussion

CNS sensitization, and myofascial dysfunction, both common signs of regional pain syndromes, were found in women with CPP, and may be exacerbated in those with endometriosis. These physical findings provide objective evidence of a subjective pain complaint. This comprehensive assessment may help clinicians identify pain processes that likely have contributed to difficulty in successfully treating these patients.

Summary

MTrPs are a ubiquitous and highly underdiagnosed component of many acute and chronic pain complaints, such as chronic pelvic pain. However, they are also a common physical finding in asymptomatic individuals. This dichotomy challenges and behoves pain management practitioners to learn how to palpate the soft tissue and distinguish active from latent MTrPs. Making this distinction is critical in order to adequately identify and treat a myofascial component of chronic pelvic pain.

Histological, neurophysiological, biochemical, ultrasound imaging and somatosensory studies of MTrPs have found objective abnormalities. Together with observed motor and sensory abnormalities, they implicate peripheral and central mechanisms in the development of myofascial pain and associated MTrPs. Future clinical research studies should focus on identifying the mechanisms responsible for the pathophysiology of myofascial pain. Successful treatment depends upon identifying and targeting these mechanisms.
and addressing the perpetuating factors that sustain this pain syndromes such as chronic pelvic pain.

References


