New Frontiers in the Pathophysiology of Myofascial Pain: Enter the Matrix

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Myofascial pain is a specific non-inflammatory condition which is distinguished from other soft tissue pain disorders such as fibromyalgia, tendonitis, or bursitis[8]. It presents as regional pain, often accompanied with increased tension and decreased flexibility in muscle and related fascia. The most important physical finding is of one or more myofascial trigger points (MTrPs)—a discrete hyperirritable nodule in a taut band of muscle which is palpable during physical examination (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 underdiagnosed and under-treated component of non-articular musculoskeletal pain disorders[1,3,4].

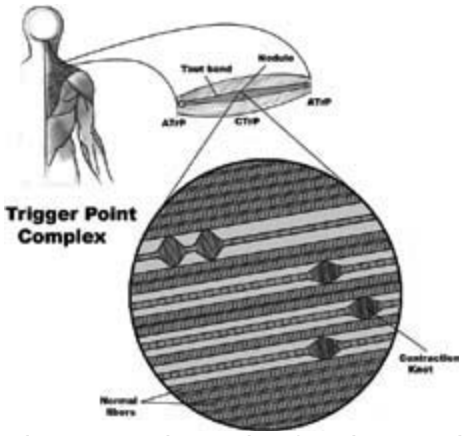

Figure 1: Schematic of a trigger point complex. CTrP identifies the central trigger point that is found in the endplate zone and contains numerous contraction knots and electrically active loci among normal fibers. A taut band of muscle fibers extends from the trigger point to the attachment (ATrP) at 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[13] ; (3) muscle pain is inhibited more strongly by descending pain-modulating pathways[15,2]; and (4) activation of muscle nociceptors is much more effective at inducing maladaptive neuroplastic changes in dorsal horn neurons[14]. 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[12]. This process can spread to adjacent neurons[5], 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[7].

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.

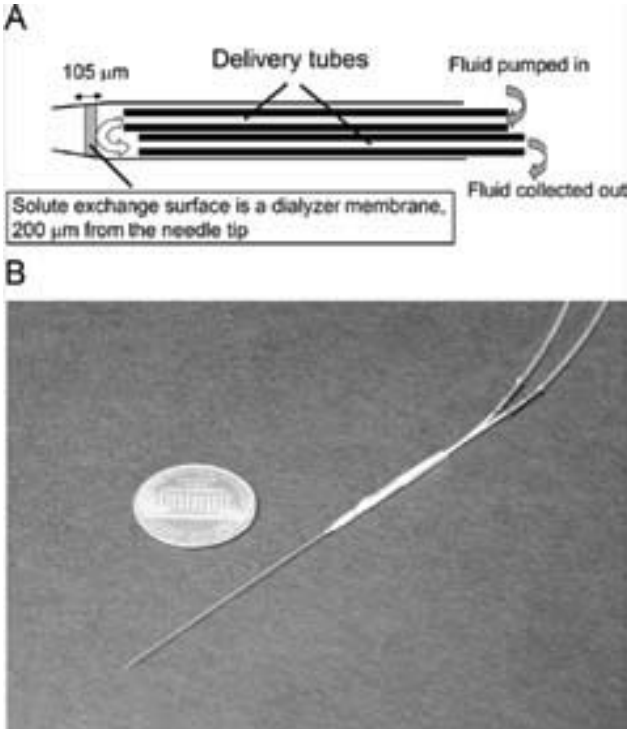

Figure 2. A: schematic of microdialysis needle construction. B: microdialysis needle.

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'. The paper has been accepted for a 2009 publication date in the *Archives of Physical Medicine and Rehabilitation*[11].

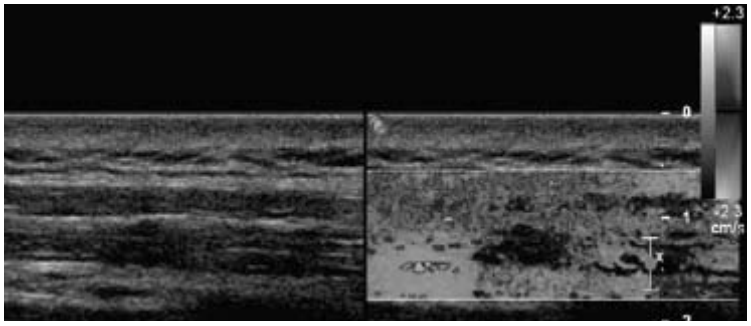

Figure 3: Upper trapezius muscle with a palpable MTrP. A hypoechoic region and a well-defined focal decrease of colour variance indicating a localised stiffer region are visible.

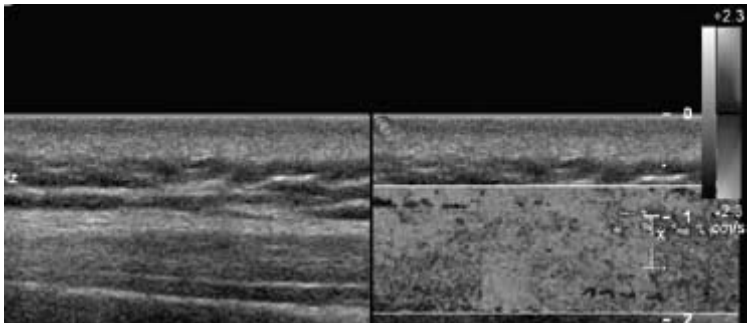

Figure 4: Normal upper trapezius muscle. A myofascial trigger point is not palpable and the normal muscle appears isoechoic and has uniform color variance.

Future studies

We are working towards developing a model for the peripheral and central mechanisms involved in myofascial pain. Now that we have identified objective differences which distinguish active MTrPs from latent MTrPs and normal tissue, we wish to investigate the development of MTrPs over time.

• Do the biochemical milieu, stiffness properties and local blood flow of active MTrPs change over time with respect to the natural history of myofascial pain?

• Does the biochemical milieu of active MTrPs correlate with changes in the severity of pain, presence or absence of physical findings, or degree of local tenderness over time?

• What are the levels of anti-inflammatory substances (e.g. IL-4, IL-10), neurotrophins (e.g. Nerve Growth Factor) and analgesic substances (e.g. β-endorphin) in the local biochemical milieu of muscle with and without MTrPs?
• What are the local effects (e.g. on the biochemical milieu, stiffness properties and blood flow) of physical medicine treatments such as dry needling of active MTrPs?

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