New frontiers in the pathophysiology of myofascial pain

By Jay Shah

Myofascial pain is a specific non-inflammatory condition which is distinguished from other soft tissue pain disorders such as fibromyalgia, tendonitis, or bursitis. It presents as regional pain, often accompanied with increased tension and decreased flexibility in muscle and related fascia. Myofascial pain may be diagnosed as a part of a clinical complex of pain disorders, but comes with its own set of signs and symptoms, the most important of which is the finding of one or more myofascial trigger points (MTrPs).

An MTrP is 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.

Most of our scientific knowledge about pain mechanisms is derived from studies of cutaneous pain, and incorrectly applied to pain of muscular origin. This misunderstanding commonly leads to misdiagnoses and inadequate treatment of muscle pain conditions. MTrPs are the most common, and yet most under-diagnosed and under-treated component of non-articular musculoskeletal pain disorders.

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 localise and is often referred to deep and distant somatic tissues; (2) muscle pain activates unique cortical structures in the central nervous system, particularly those which are associated with the affective or emotional components of pain; (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.

Despite the fact that muscle makes up more than 50 per cent of the body by weight, there is no organised focus (at least in the United States) on student training or research dealing with muscle pain. Due to a lack of understanding, therefore, clinicians are trained to treat the *symptoms* of muscle pain (e.g. with medications) rather than the *cause*, which is often MTrPs

The primary reason that muscle pain is given little consideration is because the accurate diagnosis of myofascial pain depends exclusively

on the palpation skills and experience of the examiner. Since most physicians and physical therapists in the USA are not trained in these diagnostic techniques, pain of myofascial origin is often overlooked, misdiagnosed, and untreated.

Peripheral and central sensitisation

Peripheral and central sensitisation 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 sensitisation. In animal models of pain, nociceptive input from skeletal muscle is much more effective at inducing neuroplastic changes in the spinal cord than noxious input from the skin. 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 sensitisation.

This process can spread to adjacent neurons, leading to structural changes and maladaptive neuroplastic alterations in the central nervous system. For example, there may be loss of inhibitory neurons at segmental levels affected by the persistent noxious input. 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. These clinical signs of central sensitisation—which result in an intensified pain experience—are very distressing to patients.

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There is a biochemical basis to the development of peripheral and central sensitisation in muscle pain. For example, sensitising 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. In addition, previously silent synapses may become effective. These mechanisms of peripheral and central sensitisation 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

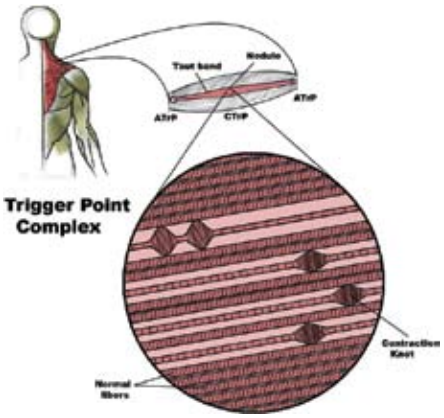

Figure 1: Schematic of a trigger point complex. CTrP identifies the central trigger point that is found in the endplate zone and contains numerous contraction knots and electrically active loci among normal fibers. A taut band of muscle fibers extends from the trigger point to the attachment (ATrP) at 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.)

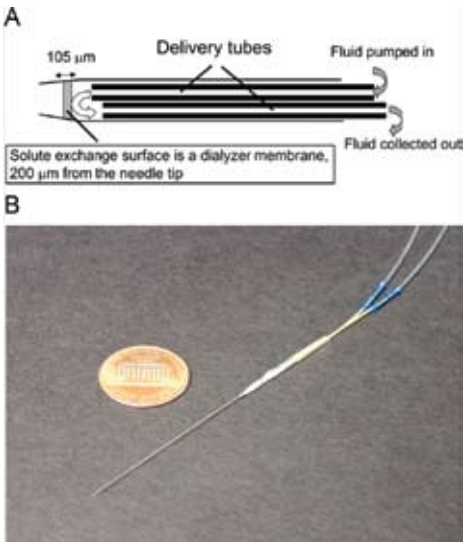

Figure 2. A: schematic of microdialysis needle construction. B: microdialysis needle.

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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*. This microdialysis needle has the same size, shape and handling characteristics of an acupuncture needle.

Our microanalytical technique enables continuous, real-time sampling from soft tissue in extremely small quantities—about 0.5 microlitres (approximately one 10 000th of a level teaspoon). 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 utilised this microdialysis needle in combination with novel microanalytical techniques to safely sample and measure the biochemical milieu of muscles with and without MTrPs.

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* (Shah et al. 2005). 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. Interestingly, the local biochemical milieu appears to change with a local twitch response (LTR). These results have been published in the *Archives of Physical Medicine and Rehabilitation* (Shah et al. 2008).

Our studies demonstrate the existence of objective biochemical differences between active MTrPs compared to latent MTrPs and normal muscle. 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. High concentrations of these substances are able to cause both peripheral and central sensitisation. Our biochemical findings may explain why active MTrPs are acutely painful, tender, and a source of referred pain.

The findings also suggest that when a clinician identifies an active MTrP in the upper trapezius, he/she is identifying an area of muscle with an objective biochemical abnormality.

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. In clinical practice, eliciting multiple LTRs seems to provide maximal benefit from dry needling therapy. 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, localised increase in blood flow, and/or nociceptor and mechanistic changes associated with an augmented inflammatory response.

Visualisation and characterisation 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. Therefore, it remains a clinical diagnosis based exclusively on history and physical examination. Accordingly, there is a need to develop objective, repeatable and reliable diagnostic tests for evaluating MTrPs and determining treatment outcome measures. Such measures can be used to properly diagnose and understand the natural history of MTrPs. 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 localised area of stiffer tissue. (Figure 3).

We have shown that ultrasound is feasible for

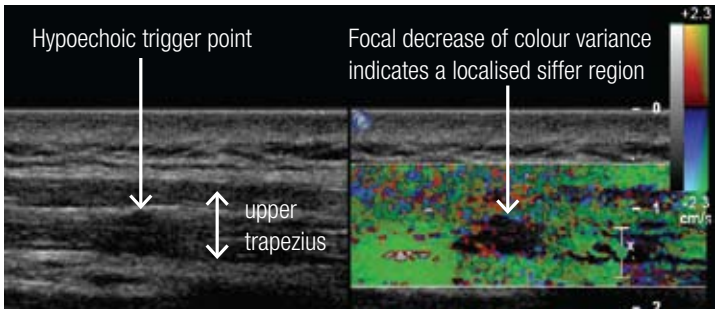

Figure 3: Upper trapezius muscle with a palpable MTrP. A hypoechoic region and a well-defined focal decrease of colour variance indicating a localised stiffer region are visible.

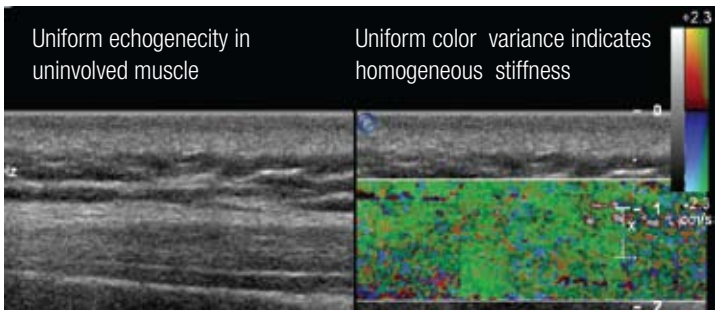

Figure 4: Normal upper trapezius muscle. A myofascial trigger point is not palpable and the normal muscle appears isoechoic and has uniform color variance.

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 colour 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 colour.

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*.

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. Among the questions we would like to address are:

- 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?

Summary

MTrPs are a ubiquitous and highly under-diagnosed component of many acute and chronic pain complaints. 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 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 syndrome.

Jay P Shah. MD is a senior staff physiatrist in the Rehabilitation Medicine at the NIH Clinical Center. His clinical research interests include the pathophysiology of myofascial pain and the integration of physical medicine techniques with promising complementary approaches in the management of neuromusculoskeletal pain and dysfunction. He is the Director of the Medical Rehabilitation Training Program for Rehabilitation Medicine and a well-known lecturer on the mechanisms of chronic pain, myofascial pain, acupuncture techniques and other related topics. Jay and his co-investigators at the NIH are utilising novel microanalytical techniques to study the unique biochemical milieu of myofascial trigger points.

Jay is a keynote speaker for SPA and the ADNG at the 2009 Conference where he will be presenting at a one-day post-conference workshop called 'New Frontiers in the Matrix of Neuromusculoskeletal Pain: Integrating Pain Mechanisms with Objective Physical Findings and Needling Strategies.'