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John L. Quintner

Mount Claremont, jqu33431@bigpond.net.au

Geoffrey M. Bove

University of New England, gbove@une.edu

Milton L. Cohen

St Vincent's Clinical School

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A CRITICAL EVALUATION OF THE “TRIGGER POINT” PHENOMENON

John L. Quintner, MB BS FFPMANZCA. Rheumatology and Pain Medicine, Mount Claremont,
Perth, Western Australia*

Geoffrey M. Bove, DC, PhD. Associate Research Professor, University of New England,
Biddeford, Maine, USA

Milton L. Cohen, MD FRACP FFPMANZCA. Pain Medicine and Rheumatology, St Vincent’s
Clinical School, UNSW Australia, Sydney, New South Wales, Australia

*Corresponding Author:

John L. Quintner

28 Bentley Close, Mount Claremont, WA 6010 Australia

Phone: [+61 \(0\)8 93842895](tel:+61(0)893842895)

Mobile: [+61 0419956418](tel:+610419956418)

Email: jqu33431@bigpond.net.au

Running Title: The “trigger point” phenomenon

Abstract

The theory of myofascial pain syndrome (MPS) caused by trigger points (TrPs) seeks to explain the phenomena of muscle pain and tenderness in the absence of evidence for local nociception. Although it lacks external validity, many practitioners have uncritically accepted the diagnosis of MPS and its system of treatment. Furthermore, rheumatologists have implicated TrPs in the pathogenesis of chronic widespread pain (fibromyalgia syndrome). We have critically examined the evidence for the existence of myofascial TrPs as putative pathological entities and for the “vicious cycles that are said to maintain them. We find that both are inventions that have no scientific basis, whether from experimental approaches that interrogate the suspect tissue or empirical approaches that assess the outcome of treatments predicated on presumed pathology. Therefore the theory of MPS caused by TrPs has been refuted. This is not to deny the existence of the clinical phenomena themselves, for which scientifically sound and logically plausible explanations based on known neurophysiological phenomena can be advanced.

Key messages:

1. The theory of “myofascial pain” based on “trigger points” is conjecture that has been put forward as established knowledge.
2. The key phenomenon of muscle tenderness demands a robust plausible explanation based on neurobiology..
3. The context in which treatment is carried out influences the outcome.

Keywords: nerve; muscle; referred pain; pain mechanisms; philosophy of science

Introduction

The phenomena of muscle pain and tenderness in the absence of obvious disease are well recognized but poorly understood. Myofascial pain syndrome (MPS) is a popular explanatory model, which posits a local (muscle) origin of nociception called the trigger point (TrP) and advocates local treatment, primarily direct manipulation of TrPs using manual pressure or needles, the latter with and without injectate [1, 2]. These forms of treatment are being practised worldwide by physicians, physical therapists, chiropractors, and various unlicensed and unregulated practitioners [3].

But does the evidence support these concepts? Are the hypotheses generated by MPS theory scientifically sound? And are treatments based on this theoretical model beneficial?

This article will show that the theory is flawed both in reasoning and in science. In seeking a resolution two testable hypotheses are identified, which point the way to neuroscientific explanations for the observed clinical phenomena.

Evolution of MPS Theory

The belief that muscle pain might originate from focal lesions within connective tissues harbouring low-grade inflammation that activated sensory fibres innervating muscle spindles and the interstitial tissues between muscle fibres has long been entertained [4,5]. The initial description put forward by Stockman was of “fibrositic” nodules, which were suggested to harbour low-grade inflammation that activated sensory fibres innervating muscle spindles and

the interstitial tissues between muscle fibres[6]. The initial claim that “*the essential lesion is a chronic inflammatory hyperplasia of white fibrous tissue in patches*” was never confirmed [6,7].

An infective aetiology of such nodules was proposed but other conjectures included micro-trauma, exposure to environmental extremes, nerve root irritation, and psychoneurosis [8-9].

Kraus (cited by Simons [3]) speculated that palpable muscle hardenings of unknown cause could set up a reflex increase in muscle tension resulting in a “pain-reflex-pain self-perpetuating cycle” that could be disrupted by ethyl chloride sprayed onto the overlying skin or by local injections of anaesthetic. Pain theorists William Livingstone [10] and John Bonica [11] favoured this “vicious circle” hypothesis, as did others [12,13].

These speculations took a new turn when Travell and Rinzler [4] conceptualised that pain felt in voluntary muscles is “myofascial” in origin. Their claim that “trigger areas in myofascial structures can maintain pain cycles indefinitely” was reminiscent of the “vicious circle” hypothesis.

Travell and Simons [14] formalised the construct of “myofascial pain arising from trigger points.” Not only were TrPs described in exactly the same way as fibrositic nodules had been, but also it was asserted that they could potentially develop within every voluntary muscle and in multiple locations within a given muscle.

The theory of MPS comprised two essential components: (i) the TrP, a localised area of tenderness or hyperirritability deep within voluntary muscle; and (ii) a predictable discrete zone of deep aching pain, which could be located in the immediate region of or remote from the TrP, and which was worsened by palpation of the TrP [4, 14].

Travell and Simons [14] composed anatomical charts of trigger points, and their “characteristic” pain referral patterns. However, it appears that their diagrams had “*sometimes been chosen arbitrarily, there being no accepted standard*” [15].

Located within palpable “taut bands,” TrPs were said to represent shortened (“contractured” [16]) muscle fibres. On “snapping” palpation or insertion of a needle, a local twitch response could be elicited, which was accompanied by an “irritable” electromyographic response [14]. In contrast to a normal muscle, one containing a TrP was said to exhibit both analgesic inhibition when tested for its strength and intolerance to passive stretch.

To explain the puzzling onset of pain in ostensibly lesion-free tissues, Travell and Simons [14] found it necessary to invent the “latent” TrP, a site of potential tenderness within a muscle unassociated with spontaneous pain but having the potential to be activated by a myriad of factors, within or outside the body. In an attempt to extend the theory to explain more widespread pain, they claimed that TrPs could self-propagate to become “secondary” TrPs in other muscles and even to “metastasise” throughout the bodily musculature.

The recent conjecture that peripheral pain generators can reside within muscles (i.e. myofascial tissues), and be responsible not only for spontaneous pain but also for the initiation and maintenance of profound changes within the central nervous system (known as central sensitisation) rests upon these dubious premises [17, 18]. Similarly, prominent rheumatologists are amongst those who maintain that TrPs are responsible for the initiation and maintenance of the syndrome of chronic widespread pain (Fibromyalgia) [17-23].

Beliefs in TrP theory and the associated concept of MPS continue to be strongly held [24], despite the fact that such beliefs exemplify circular reasoning: TrPs cause myofascial pain because painful muscles contain them [25].

Review of the evidence

Clinical diagnosis

An extensive review identified at least 19 different sets of diagnostic criteria used for the MPS/TrP syndrome, and concluded there was a lack of consistency and consensus on case definition [26]. The authors suggested that until reliable diagnostic criteria had been established, *“there is a need for greater transparency in research papers on how a case of MTrP (sic) pain syndrome is defined, and claims for effective interventions in treating the condition should be viewed with caution.”* A similar study found that the diagnosis of MPS from putative TrPs was based on a clinical test of unknown reliability and validity with no accepted reference standard [27].

In studies of inter-examiner reliability, examiners were given the muscle to palpate, with or without an accompanying diagnosis [28-31]. In one study, extensive training coupled with the use of an algometer resulted in examiner agreement that the phenomenon could be localized [29]. Another study reported that the assessments of an individual examiner were consistent from one test to another [31] and that more experience in assessment leads to better inter-examiner agreement [30]. These studies suggest that when shown where a problem may exist, examiners may agree. However, when blinded as to diagnosis, those who claimed expertise in the field were unable to detect putative TrPs in the majority of subjects with a MPS diagnosis [32]. In this study there was virtually no inter-examiner reliability for either putative TrPs or taut bands. This finding questions the reliability of the diagnostic criteria used by these experts. More recent studies [33, 34] have also reported poor inter-examiner diagnostic reliability and poor methodological quality [35].

In summary, physical examination cannot be relied upon to diagnose a condition that is supposed to be defined by that physical examination. That is, the pathognomonic criterion for making the diagnosis of MPS is unreliable.

Pathology

The first histological analysis of “fibrositic nodules” reported diffuse inflammatory changes [9]. These findings were not confirmed, although tender muscles contained increased extracellular fluid [36]. The authors suggested that the resulting turgor might explain the observed finding of mechanical tenderness.

The term “myogelosis” describes a change in muscle structure analogous to TrPs [37]. Samples taken from unfixed cadavers following detection of such areas showed altered histology, [37] but the clinical relevance to the findings on palpation is unknown.

Tissue biochemistry

Shah et al. [38, 39] employed micro-dialysis to sample tissue fluid within and near to a palpated “trigger” zone in trapezius muscles in patients with a diagnosis of TrPs and in normal pain-free subjects. Samples were taken from the following regions: normal (no pain, no TrP), active (pain and TrP detected) and latent (no pain, TrP detected). Samples were also taken from asymptomatic gastrocnemius muscles. Elevated levels of CGRP, SP, norepinephrine, TNF-alpha, IL-1, IL-6 and low pH were reported in fluid from all sampled regions of symptomatic patients. However, elevated levels were also found in uninvolved, control muscle areas.

These reported alterations in biochemical milieu are consistent with inflammation due either to tissue damage or to altered peripheral nerve function, in contrast to pathology necessarily being in the tissue sampled [40, 41].

Electromyographic studies

In one study, electromyographic examination (EMG) of TrPs failed to provide evidence of ongoing denervation or focal muscle spasm [42]. But another study did report spontaneous electrical activity (i.e. endplate noise and spikes) in regions considered to be TrPs in patients with chronic tension headache and pericranial muscle tenderness [43].

Simons et al. addressed the question whether endplate noise and spikes arise from “normal” endplates by performing EMG on 25 patients who met the American College of Rheumatology 1990 criteria for fibromyalgia [44] and 8 pain-free subjects in whom “latent” TrPs had been identified by manual palpation of taut bands and characteristic referral of pain (*sic*) [45, 46]. Unfortunately the researchers conflated the TrPs of MPS and the “tender points” of fibromyalgia, another issue yet to be resolved [47]. They concluded that endplate noise is characteristic of but not restricted to TrPs, and that the finding could not be considered a reliable diagnostic criterion [45, 46].

An alternate interpretation of these EMG findings is that insertional and spontaneous activity (i.e. “end plate noise”) from single muscle fibres generated by the activation of intramuscular nerve terminals irritated by the needle was being recorded [48]. Nonetheless, it is still asserted that spontaneous electrical activity is one of the characteristics of myofascial TrPs [49].

Imaging studies

Seven patients with a 3-year history of “myofascial pain” associated with the presence of a taut band in the upper trapezius muscle were examined using magnetic resonance elastography [50]. A “signature” chevron-like pattern was reported, with its leading edge coincident with the physician-identified taut band. The authors did not offer diagnostic criteria, nor make any comment on the relationship of a “taut band” to a TrP. A subsequent study of 8 subjects, 4 of whom were said to have MPS and 4 who did not, is open to the same criticism [51].

Attempts were made to visualise TrPs using diagnostic ultrasound of the anterior abdominal wall of 10 patients [52]. The points in question appeared as a “mixed echoic area in the rectus abdominis muscle that *became prominent* on injection of local anesthetic solution” (italics by authors). They conceded that the findings could have been coincidental. Also the image presented is consistent with the normal sonographic appearance of abdominal muscles [53].

In another study, 44 patients with acute cervical pain and at least one putative TrP identified by palpation in the upper trapezius were evaluated using sonoelastography and Doppler imaging [54]. The authors claimed to have measured trigger point size and to have distinguished normal muscle from active and latent TrPs. Although the data on which these assertions were made were not presented, the authors found no correlation between claimed TrP area and pain pressure threshold. The absence of pain-free control subjects is yet another flaw. These methodological concerns do not lend credibility to the findings.

Animal models

Animal models are often informative about pathophysiology in ways that are impossible to demonstrate in humans. To be considered relevant, models must have symptomatic and/or pathological similarities to the condition being studied. For TrP research, no such model exists.

Simons and Stolov [55] biopsied ostensibly normal canine muscles, seeking to correlate palpated taut bands with morphological and histological changes. The findings were negative, given that there was no indication of pain or a pathological condition present prior to these studies. The researchers observed: “rubbing palpation produced a transient contraction which could be

primarily responsible for the sensation of a hardness palpated in the dog muscles.” This is the myotatic reflex, which correlates to the “twitch response” also evocable on palpation of normal human muscle [56].

Based upon the conjecture that “... latent TrPs can be identified in almost all skeletal muscles of normal adults”[14], a rabbit model of TrPs was proposed [57, 58]. Rabbit leg muscles were palpated until they exhibited a myotatic reflex. Such muscles were considered to contain taut bands and, by assumption, TrPs. A number of papers have since been published using this “model” [58-65]., but have not offered evidence of clinical relevance.

Delayed Onset Muscle Soreness

Studies of delayed onset muscle soreness (DOMS) have been undertaken using eccentric exercise to cause symptoms, in both humans and animals. Although DOMS has been related to TrPs in only one study [66], this model was proposed for MPS [67]. The relevant experiment was performed in humans, and used eccentric exercise of the extensor digitorum of the middle finger [66]. Following the development of DOMS, the muscle was palpated, revealing a tender band judged to be taut. However, since the muscle itself is a band, relating the description to TrPs seems meaningless. It should be noted that DOMS is self-limiting, whereas whatever phenomenon is occurring with chronic muscle-related pain is not. The relevance of DOMS to TrPs remains unclear.

Integrated hypothesis

Dommerholt et al. [68,69] postulated that low-level isometric muscle contraction or eccentric or sub-maximal concentric contractions could result in muscle dysfunction or damage, and that the formation of TrPs would follow. According to Gerwin et al., [70] an excessive release of acetylcholine from dysfunctional neuromuscular endplates might be responsible for the “taut band” phenomenon (i.e. focal muscle contraction modulated by muscle spindle afferents) and that these bands could in turn produce muscle ischemia, apparently by compressing adjacent capillaries supplying the muscle. This physiological process could precipitate an “energy crisis” in the relevant working muscle, which would respond by releasing pro-inflammatory molecules, thereby activating nociceptive neurons. Although there is no experimental evidence in support of this hypothesis, others [71,72] have accepted the “motor end plate” and the “energy crisis” theories of tonic muscle hyperactivity and TrP formation.

Recent studies of induced muscle pain in humans did not provide evidence for a reflex increase in fusimotor drive and spindle discharge [73, 74]. In fact persistent musculoskeletal pain is associated with decreased agonist muscle tone [75]; in other words, digital pressure or other stimuli that evoke pain will decrease the tone of the muscle stimulated. The validity of the paradigm that correlates endplate activity or noise with pain arising from the TrP became further suspect when it was reported that injection of Botulinum toxin A in the region of a TrP had no effect on pain intensity or mechanical pain thresholds, but did significantly reduce motor endplate activity and EMG interference pattern [76]. Finally, the “vicious circle” hypothesis has now been laid to rest by microneurographic recordings in humans performed during sustained muscle pain [73, 74].

The integrated hypothesis remains conjecture in the face of conflicting data.

Treatment

Non-invasive interventions that have been advocated include compression of the TrP, “spray and stretch”, transcutaneous electrical stimulation (TENS) and, more recently, high-intensity focused ultrasound [79]. Invasive treatments have included injection of local anaesthetic agents, injection of corticosteroids, injection of botulinum toxin, needle acupuncture, and dry needling [80].

In their systematic review Cummings and White [81] were unable to find evidence that needling therapies have any specific effect.. Their later review of 1517 studies found only 7 that were of high enough quality for meaningful analysis [82]. Rickards [83] also found limited strength of evidence for any treatment of TrPs.

Another review remarked upon the heterogeneity of the populations being treated, and the lack of widely accepted standard diagnostic criteria for MPS [84]. This review also concluded that there was insufficient evidence to support the use of most interventions.

A systematic review of botulinum toxin A for TrP treatment located 21 RCTs, with 12 eligible for consideration but only 5 suitable for inclusion, and concluded that the current evidence does not support any therapeutic value [85]. Again, these authors reported that the data were limited and that the patient populations were heterogeneous.

These studies provide little evidence that dry needling of TrPs is associated with a treatment effect compared with standard care [3]. They are based on small sample sizes, uncertainty as to

whether TrPs were the sole cause of pain, as well as neglect of technical issues such as the variability in the location of TrPs and the depth of needle insertion.

With these results in mind, why do many clinicians insist that their treatments “work?” One explanation is that the treatments are rarely performed in an isolated fashion; that is, treatment is accompanied by manual therapy, home exercises, and stretching.

Contextual effects could explain the plethora of anecdotal responses to treatment [86, 87]. This is not unexpected when a medical treatment with high face validity is based solely on practical experience rather than reflecting a rational approach based on pathogenesis. Apparent effectiveness of any treatment may be attributed to the natural history of the particular problem being treated, regression to the mean, and the expectation of *something* being done to the area in question. This can lead to the fallacy known as *post hoc ergo propter hoc* (“after this therefore because of this”), when the treatment offered in fact had nothing to do with the pathogenesis of the condition towards which it was directed. A recent study comparing dry needling with manual compression, where there was no control group, exemplifies this critical methodological issue [88].

One common factor shared by most therapies is that they elicit pain at the site of their application; that is, they are noxious stimuli. If they do “work,” this similarity suggests a common mechanism of action. One possible mechanism is counter-irritation, or application of a competing noxious stimulus [89]. It is not surprising that a noxious stimulus applied in the region where pain is experienced, whether or not there is local pathology present at that site, would

elicit a transient reduction in pain intensity by recruiting those higher order brain regions responsible for anti-nociception [90-92].

In conclusion, the vast majority of studies and meta-analyses do not support the prediction from MPS theory that focal treatment of TrPs is effective.

An impasse

In 1976 Simons [1] hoped that “It would now appear possible to resolve much of the conflicting data of the past by carefully distinguishing trigger from reference zones, and acute from chronic lesions using modern electrodiagnostic, biochemical, histochemical, and ultramicroscopic techniques.” Some three decades later, he conceded that acceptance of the concept of TrPs had been hampered by two outstanding considerations: the lack of a diagnostic gold standard and the lack of generally recognised pathogenesis [93].

We propose that sufficient research has been performed to allow TrP theories to be discarded. The scientific literature shows not only that diagnosis of the pathognomonic feature of MPS (the TrP) is unreliable but also that treatment directed to the putative TrP elicits a response that is indistinguishable from the placebo effect. As these conclusions refute MPS, formulating a plausible scientific explanation for pain perceived by patients as coming from their muscles remains a challenge.

Towards explaining the clinical phenomena

In our opinion current neuroscientific hypotheses can form the basis for collaborative scientific investigation to explain the clinical phenomena. We offer two for consideration, neither of which relies on local pathophysiology.

Neuritis Model

Nerve inflammation as a source of pain was discussed in the 19th century [95-100], but focused research on nerve inflammation as a primary disease aetiology has been limited.

Quintner and Cohen [25] hypothesised that the TrP was an area of what was then called secondary hyperalgesia occurring in muscles that are structurally and physiologically unimpaired. Noting the remarkable proximity of TrPs to known peripheral nerves, these authors argued that sensitization of the axons within the nerves, possibly by inflammation, may inform the underlying mechanism. Subsequent research has emerged in support of this hypothesis.

Focal inflammation of peripheral nerves leads to ectopic axonal mechanical sensitivity and spontaneous discharge of some but not all of the nociceptors within the inflamed nerve [101-104]. These changes can be expected to lead to focal areas of neurogenic inflammation and possibly to sensitization in the muscle innervated. If confirmed, they can inform further investigation that might be highly relevant to explaining the phenomenon of chronic muscle pain.

Referred pain and tenderness (allodynia)

Kellgren [105-107] reported the critical observation that, in addition to referred pain, referred tenderness could be induced by targeted injections of hypertonic saline into tissues such as

interspinous ligaments, periosteum, cancellous bone, or voluntary muscle. His studies and those of others [108, 109] showed that localised muscle pain and tenderness could originate from pathologies within other deep tissues that produce nociceptor activation. This relegates the TrP to being a site of secondary allodynia reflecting altered central nociceptive mechanisms [110].

CONCLUSION

The construct of MPS caused by TrPs remains conjecture. All working hypotheses derived from this conjectures have been refuted and therefore the theory can be discarded. By contrast, evolving insights into the neurobiology of nociception and pain suggest plausible hypotheses that form a basis for advancing knowledge and therapeutics in this challenging area.

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