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Review Article

MYOFASCIAL PAIN SYNDROME: UPDATED INSIGHTS ON CLINICAL FEATURES, CAUSES, DIAGNOSIS, AND EVIDENCE-BASED TREATMENT APPROACHES

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ABSTRACT

Myofascial pain syndrome (MPS) is a widespread musculoskeletal disorder characterized by localized pain, tenderness, and dysfunction arising from myofascial trigger points (MTrPs). This examines offers a modified synopsis of clinical views within MPS, stresses their epidemiology, pathogenesis, diagnostic standards, and evidence-based management methods. Epidemiological statistics reveal a variety of prevalence in general societies and higher rates in chronic pain clinics, oncology patients, and patients with comorbid conditions such as fibromyalgia. Hazard variables: Duration material, systemic, psychological, and lifestyle. Etiopathogenesis involves an intertwined mechanism involving MTrP formation arranged for peripheral nociception, fundamental sensitization magnifying pain and neurogenic inflammation, preserving muscle hyperirritability. In clinical practice, MPS can be described as localized pain caused by contact with the body, restriction of movement, and partner sleep disturbance. Trust in standardized standards, clinical palpation of MTrPs, and rejection of mimics. Pharmacological therapy, such as non-steroidal anti-inflammatory drugs, antidepressants, and muscle relaxants, has modest efficacy, while non-pharmacological interventions, such as dry needling, manual therapy, and neuromuscular techniques, have more evidence of lowering pain and improving function. However, growth therapy appreciates shockwave therapy and neuromodulation, which still require validation. A multimodal, patient-centered strategy integrating pharmacological and non-pharmacological modes of action according to the profile of the patient and the comorbidities should be highlighted. Although progress has been made, differences remain in the understanding of long-term effects, optimal treatment planning, and biomarker designation. Future research should prioritize large-scale randomized trials, biomarker discovery, and personalized medicine frameworks to enhance clinical decision-making and patient outcomes. This review underscores the need for a holistic, evidence-driven strategy to address the complex interplay of biopsychosocial factors in MPS.

Keywords: Myofascial pain syndrome, Trigger points, Central sensitization, Multimodal therapy, Evidence-based practice.

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INTRODUCTION

Myofascial pain syndrome (MPS) is a common, recurring or alternatively chronic musculoskeletal condition that significantly impacts the quality of life for the long term and poses major challenges for the healthcare system. The designation "myofascial" refers to the intricate relationship of the muscle tissue (myo) and the surrounding connective tissues (fascia). MPS may be distinguished by localized pain and tenderness in specific areas of muscle and fascia, particularly associated with hyperirritable nodules, term myofascial gun trigger scores (MTrPs). These MTrPs are classified either as active or latent: Active trigger scores produce spontaneous pain, while latent individuals are clinically silent and respond only to stimuli that cause pain, such as palpation or needling. MTrPs can limit the extent of gestures range of motion (ROM), cause muscle failure, and contemporary together with a distinctive form of nearby and touched pain, motor dysfunction, and autonomic symptoms (Fig. 1). In addition to frequent symptom overlap with other musculoskeletal pain conditions, MPS clinical presentation is complicated by underdiagnosis and misdiagnosis. The lack of understanding of the MPS underlying mechanism and the absence of a globally accepted diagnostic standard make this ambiguity worse. As a consequence, different patients are aware of unsuitable or otherwise delayed treatment, with a high incidence of chronic pain, functional impairment, and decreased health. To clarify the pathophysiology of MPS, stress the position of persistent muscle contraction, biochemical adaptations, and neuromuscular dysfunction in the formation of gun trigger scores and related pain. A comprehensive, evidence-based strategy integrating pharmacologic therapy, corporeal and manual intervention, and, where appropriate, psychological support, all geared to simultaneously relieve symptoms and implicit support variables, is needed to lead MPS productively. This review article provides updated insights into the clinical features, causes, diagnostic complexities, and evidence-based treatment approaches for MPS, synthesizing the latest research and ongoing debates to inform best practices in patient care.

EPIDEMIOLOGY AND PREVALENCE

Estimates of the prevalence of MPS in general inhabitants are commonly subjected to incompatibility with diagnostic standards and methodological approaches. However, statistics consistently indicate that MPS is a useful subscriber in terms of musculoskeletal pain. Prevalence rates have been reported between 37% for gentlemen and 65% for women, with even higher estimates – up to 85% – in adults over 65 years of age [1]. Further occupational surveys, together with individual reports, show that 15.2% of female sewists have neck and shoulder muscles compared to 9.0% of males in control [2].

MPS is much more common in clinical practice. The general intrinsic medicine delved into the development that 29.6% of patients who show symptoms together with pain were diagnosed with MPS, which is the main cause of pain in this cohort [3]. Specialized pain clinics even report a more dramatic figure: 85% of their patients were diagnosed with MPS, and another focused program resulted in 93% of patients who had musculoskeletal pain having myofascial trigger points (MTrPs), together with 74% determining MTrPs as a primary pain foundation.

Prevalence is similarly high in specific subpopulations. A retrospective study of MPS in 61% of human beings with complicated regional pain syndrome, while a prospective study of atop patients with non-specific neck pain found that 100% had MTrPs [4]. MPS appears to

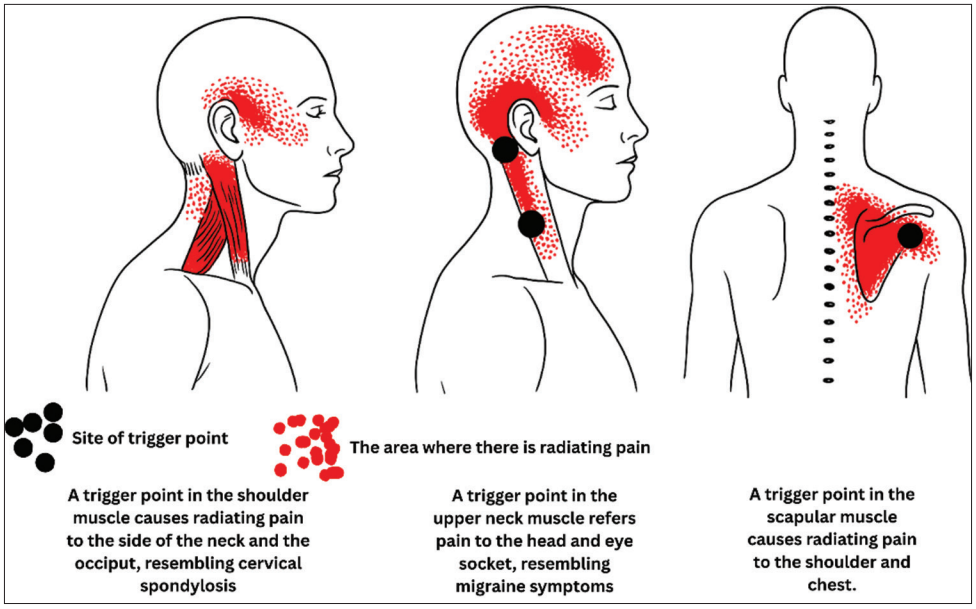

Fig. 1: Trigger points and referred pain patterns associated with myofascial pain syndrome

be widespread in oncology settings: 45% of breast cancer survivors develop MPS indoors 1 year after surgery [5], and 11.9% of head-and-neck cancer patients are proficient with MPS, particularly after surgery or radiation [6].

RISK FACTORS

MPS is a complex and multifactorial condition caused by the interaction between body, psychological, systemic, and lifestyle factors. Despite the fact that the above threat variables predispose people to the development of MPS, they also contribute to its continuity and resistance to care. Physically, a major subscriber is persistent strain, muscle overuse, injury, and impoverished position, particularly in the context of work and other human beings with inadequate ergonomics [7]. Systemic environments such as hypothyroidism, Vitamin D deficiency, and connective tissue abnormalities are also implicated as implicit in subscribers' muscle dysfunction and formation of MTrPs [8].

Psychological factors, including stress, anxiety, and depression, are frequently detected in MPS patients and may combine with other symptoms caused by increased muscle tension and decreased pain threshold; [9] these components regularly develop a cyclical connection whenever pain increases psychological distress and frailty. Furthermore, insomnia and sleep disturbances are independently associated with an increased risk of developing MPS. A long-term study shows that people with insomnia have about double the risk of developing MPS compared with those who do not have sleep concerns and suggests that inadequate sleep quality may impair muscle recovery and increase sensitization [10].

Lifestyle-related factors such as sedentary behavior, lack of corporeal work, and needy body mechanics. Furthermore, smoke and subpar hydration are likely to reduce tissue oxygenation and healing capacity while facilitating the progression of gun trigger poiny [11]. Together, these multifaceted risk factors magnify the need for a complete method of diagnosing and monitoring MPS, individuals who do not only experience localized muscle dysfunction but also many biopsychological conditions that manifest the syndrome (Fig. 2).

Physical contributors

Muscle overexploitation remains one of the most well-established etiological variables in the development of MPS, particularly in the middle of people engaged in occupations otherwise undertakings which involve with repetitive, strong, or prolonged muscle contraction [12].

Fig. 2: A biopsychosocial model outlining four primary categories of risk contributors in myofascial pain syndrome: (1) physical contributors, (2) systemic contributors, (3) psychological contributors, and (4) lifestyle contributors

Persistent mechanical vibrations may result in localized ischemia, metabolic strain, and microtrauma, fostering a neuromuscular environment conducive to the development of MTrPs [13]. The growing sign implies that the method involves a dysfunctional motor endplate project and excessive acetylcholine (ACh) release, establishing a localized zone of sustained muscle fiber contraction and biochemical sensitization [14]. Overuse-related MTrPs are often detected in muscles involved in postural care, otherwise clear work, including the upper trapezius, levator scapula, and lumbar paraspinals, particularly in those exposed to repetitive strain in tournament, manual labor, or sedentary desk project [15].

Acute muscle injury, similar to a bruise or strain, can also initiate MTrP formation by disrupting the normal muscle structure and

neuromuscular signal nerve pathway, causing a cascade of nociceptive and inflammatory events that persist beyond tissue repair [15]. At the same time, chronic postural imbalances, particularly those associated with a prolonged inactive position such as forward head position, pectoral kyphosis, or pelvic tilt, magnify the abnormal load of some muscle groups and predispose them to persistent mechanical overload and gun trigger formation [16]. Moreover, spinal and joint pathologies, similar to osteoarthritis or scoliosis, may produce a slanting or compensatory motion, principally to exploit synergies or stabilize muscles and to create a milieu ripe for chronic myofascial pain [17].

Recent investigations have further implicated fascial tension and myofascial chain dysfunctions in the propagation of MTrPs beyond localized zones. Myofascial continuity suggests that deformity of a single area, such as a cut off hamstring, may add strain in a company with a connected fascial plane, possibly leading to problems in distant but biomechanically connected areas, similar to a low support [18]. These findings underline the need for a comprehensive biomechanical assessment of the patient, together with the MPS, to establish the location and systemic body subscriber responsible for their pain presentation.

Systemic contributors

Systemic and metabolic components have emerged as important contributors to the pathogenesis and continuity of MPS. Among these, Vitamin D deficiency has been highlighted for its ability to disrupt muscle metamorphosis, immune regulation, and neuromuscular function. Research suggests that a significant proportion of chronic pain patients, including MPS patients, with current and insufficient serum Vitamin D stages, which correlate with decreased body function and increased analgesia requirements, are also affected by chronic pain [19,20]. Moreover, coexisting magnesium deficiency may exacerbate neuromuscular excitability and pain sensitivity in Vitamin D-deficient individuals [21].

Thyroid disorders, especially hypothyroidism, may be another systemic factor correlated with MPS. Hypothyroidism is a major cause of general fatigue, stiffness, and increased susceptibility to the formation of the MTrP [22]. Furthermore, iron deficiency is associated with muscle hypoxia and impaired oxygen transport, both of which may contribute to MTrP development in premenopausal women. Trace element imbalances, such as decreased zinc, magnesium, and Vitamin B12 serum levels, have also been implicated in MPS patients, together with evidence of a strong correlation between a lack of micronutrients and symptoms, pain threshold, and psychological responsibility [23].

Psychological contributors

Psychiatric stress has become increasingly recognized as a key participant in the initiation, continuity, and aggravation of MPS [24]. Continuing psychological stress, anxiety, and sentimental tension may disrupt the hypothalamic–-pituitary–adrenal axis and sympathetic nervous system, resulting in sustained muscle contraction, particularly in stress-prone areas such as the trapezius, sternocleidomastoid, and masseter muscle [25]. The present persistent muscle hyperactivity contributes to the development and treatment of MTrPs, which continue a vicious cycle of pain, dysfunction, and psychological distress. Furthermore, stress has been shown to decrease the threshold for nociceptive activation and increase essential sensitization, thus increasing the subjective experience of pain [26].

Beyond stress, passionate perturbations such as depression and anxiety disorders are common among patients with MPS. Depression not only coexists with chronic pain syndrome but also looks to modulate the perception of pain through the serotonergic and noradrenergic nerve pathways, which are also involved in descending pain resistance [27]. A bidirectional link has been recognized in the presence of persistent myofascial pain: patients with persistent myofascial pain are extra anticipated to develop depressive symptoms scheduled to functional restriction and decreased life satisfaction. During extant depression, probably increases the affective dimension of pain and reduces coping ability [28]. Neuroimaging investigations, in addition to propose that MPS patients with comorbid depression display changes in brain tasks in the prefrontal cerebral cortex and anterior cingulate gyrus—regions involved in intense and pain processing-indicating a neurobiological interface in the midst of temper and pain management [29].

Ultimately, addressing psychological and emotional factors is essential for effective MPS management. Integrated biopsychosocial interventions – such as cognitive-behavioral therapy, mindfulness-based stress reduction, and pharmacological treatments targeting mood and stress – may not only alleviate emotional distress but also reduce myofascial pain severity and improve overall function.

Lifestyle contributors

Lifestyle and behavioral factors are critical yet often underappreciated contributors to the onset and persistence of MPS. Sedentary lifestyles significantly increase the threat of MPS by promoting muscular deconditioning, rigidity, and a restricted ROM. These investigations have shown that corporeal inactivity and related metabolic disorders, such as fleshiness and micronutrient deficiency, create a biochemical and mechanical environment favorable to the progress of the MTrP [30,31]. Conversely, regular material handling only enhances muscle elasticity and, in spite of this, may reduce systemic inflammation and support neuromuscular recovery, thus alleviating the symptoms of MPS and the recurrence of MPS [32].

Oral parafunctional behaviors, such as bruxism and jaw clenching, are very common and play an important role in the pathogenesis of MPS place in the orofacial region. These relentless, involuntary projects overstrain the masticatory muscle, particularly the masseter and temporalis muscle, promoting MTrP activation and the dissemination of the recommended pain [33,34]. Lifestyle counseling focused on modifying eating, sleeping, and chewing behaviors has demonstrated efficacy in reducing orofacial symptoms, further supporting the behavioral etiology of MPS in this region [35].

In addition, sleep disturbances, notably insomnia and disconnection of sleep, constitute a significant risk factor for chronic MPS. The underprivileged sleep is associated with decreased muscle recovery, increased focal sensitization, decreased pain threshold, and a joint increase in the sensitivity to the trigger [36]. Managing sleep standardly through cognitive-behavioral therapy or alternatively pharmacologic agents can significantly increase pain effects and should continue to be integrated into a multidisciplinary method for managing MPS.

ETIOPATHOGENESIS

Pathophysiological mechanisms

The pathophysiology of MPS, including dynamic interaction among peripheral and essential mechanisms, is complex and incompletely understood. Kellgren, who demonstrated that stimulation of the deep muscular and fascial systems by hypertonic saline solution produces a place and pointed out pain form, proposed a spinal segmental mechanism underlying referred pain [37]. Hockaday and Whitty further supported this finding, demonstrating that the injection of the interspinous ligament could retroflex the form of the affected area [38-40]. Mense *et al*. [38] extend this work in animal models, highlighting the obligation to release excessive ACh close to the motor plate, a prerequisite for the prolongation of sarcomere contraction and the formation of a taut band characteristic of MTrPs [40]. A leading theory – the "integrated hypothesis–" proposes that muscle overload leads to excessive ACh release, prolonged sarcomere shortening, and localized ischemia, stimulating inflammatory mediators (e.g., bradykinin, substance P, calcitonin gene-related peptide [CGRP]) that sensitize nociceptors and maintain pain. This biochemical environment not only initiates pain but also sensitizes a significant nociceptive nerve pathway, explaining allodynia and hyperalgesia in MPS. Recent electrophysiological studies have connected spontaneous electrical projects near malfunctioning motor endplates to the neurogenic and contractile core of MTrPs.

Essential sensitization, which includes increased nociceptive data from spinal and supraspinal compositions, also maintains chronic MPS. Continuous activation of the trigger at the apex disrupts the descending inhibitory system and facilitates pain through the nerve pathway, such as the periaqueductal gray and the anterior cingulate cortex. The interaction between peripheral nociceptor sensitization and essential amplification structures, a peripheral-central continuum in MPS etiology (Table 1). Knowledge that these mechanisms are important for therapy, including dry needling, neuromodulation, and pharmacologic transition of the nociceptive nerve pathway.

A leading theory – the "integrated hypothesis–" proposes that muscle overload leads to excessive ACh release, a prolonged sarcomere shortening, and community-based ischemia [41], which in turn stimulates the release of inflammatory mediators such as bradykinin, matter P, and CGRP, sensitizing the community nociceptors and maintaining pain. The present biochemical environment plays a role not only in the establishment of pain but also in the sensitization of the central nociceptive nerve pathway, explaining phenomena such as allodynia and hyperalgesia in MPS patients. Recent electrophysiological studies have shown that spontaneous electrical projects originate from a dysfunctional motor plate of MTrPs, which contributes to their neurogenic and contractile foundation [42].

Importantly, essential sensitization, where spinal anesthesia and supraspinal structures increase nociceptive input, also plays a key role in chronic MPS. The persistent activation of gun trigger grades is directed toward lower descending inhibitory regulation and facilitation of pain through arrangements such as the periaqueductal gray and the anterior cingulate cortex [43]. The current double engagement of peripheral nociceptor sensitization and key amplification establishes the principle of the peripheral-central continuum in the etiopathogenesis of MPS [44]. Knowledge of such mechanisms is essential for targeted curative schemes, such as dry needling, neuromodulation, and pharmacologic transition of the nociceptive nerve pathway.

Trigger point formation

The formation of MTrPs has been extensively explained by Simons' Integrated Trigger Point Hypothesis, which elucidates the underlying pathophysiological mechanisms contributing to localized muscle pain and dysfunction [56,57]. Based on this model, repetitive mechanical stress or microtrauma to skeletal muscle fiber disrupts normal neuromuscular function, with a strong preference for an excessive release of ACh at the motor endplate [58]. This hypersecretion continues the constant depolarization and spontaneous electrical activity, which is regularly detected as endplate noise and spike, forming a palpable, hyperirritable nodule in a tense muscle mass [59]. Sustained contracture limits local blood flow, causing an energy crisis that enhances the nociceptive signal. The consequences of an ischemic microenvironment include a significant decrease in the pH of the acidic environment, as well as the release of vasoactive substances and an inflammatory mediator identical to bradykinin, histamine, serotonin, and prostaglandins [60]. These substances sensitize nociceptors, perpetuating the local pain cycle characteristic of active MTrPs.

Emerging evidence from metabolomic and imaging studies has validated the biochemical signature of active MTrPs, identifying elevated levels of substance P, CGRP, and protons (H+), which correlate strongly with pain intensity and chronicity [61]. Moreover, studies using microdialysis and sonography confirm the presence of hypoxia and inflammatory activity in MTrP regions, supporting the notion of self-sufficient nociceptive cringle [62]. These views only reinforce Simon's physiologic plausibility

Table 1: Key mechanistic hypotheses and pathophysiological processes in the etiopathogenesis of myofascial pain syndrome (MPS), integrating peripheral and central mechanisms

Mechanistic hypothesis	Central or peripheral mechanism	Key features	Proposed pathophysiological process
Cinderella hypothesis [45,46]	Peripheral	Sustained low-level muscle contractions Continuous activation of type I fibers Metabolic overload Calcium homeostasis disruption Cytokine release (e.g., IL-6) Muscle pain onset	Repetitive low-force muscle use leads to metabolic stress, calcium imbalance, cytokine release, and persistent pain.
Neuromuscular junction dysfunction [47]	Peripheral	Abnormal motor endplate activity Spontaneous electrical activity at trigger points Excessive ACh release Increased endplate potentials Taut bands	Excess acetylcholine causes continuous muscle contraction, ATP depletion, and formation of taut bands/trigger points.
Integrated trigger point hypothesis [48,49]	Peripheral	Repetitive microtrauma Excessive ACh and low pH Persistent contraction Inflammatory mediator release (e.g., bradykinin, CGRP) Localized pain	Muscle overload triggers a cascade: excess ACh→sustained contraction→ischemia→mediator release→local pain and sensitization.
Central sensitization [50]	Central	Increased CNS neuron responsiveness Amplified pain signaling Persistent input from trigger points Substance *P* release Pain spread	Chronic nociceptive input alters spinal/supraspinal pathways, amplifying pain and spreading symptoms beyond the original site.
Neurogenic inflammation [51-53]	Central and Peripheral	Inflammatory mediator release (substance P, histamine) Vasodilation Increased vascular permeability Nociceptor sensitization Hyperalgesia/allodynia	Nerve endings release mediators, sensitizing nociceptors and perpetuating both peripheral and central pain responses.
Fascia densification [54,55]	Peripheral	Pathological fascia changes Altered biomechanics Reduced contractile force Increased inflammation Extracellular matrix/fibroblast changes	Chronic muscle stress induces myofibroblast transformation, fascia thickening, reduced flexibility, and heightened pain sensitivity.

CNS: Central nervous system, IL-6: Interleukin-6

but also propose new curative targets such as neuromodulators, proton pump inhibitors, and anti-inflammatory peptides for MTrP deactivation and myofascial pain management.

Central sensitization

Central sensitization is a hallmark of chronic MPS, representing a state where neurons in the central nervous system (CNS) – notably in the dorsal horn of the spinal cord – exhibit heightened responsiveness to nociceptive input from peripheral tissues such as MTrPs. This neuroplastic procedure is directed at amplifying the pain signal, resulting in hyperalgesia (expansion of pain caused by stimulation without pain), allodynia (pain caused by stimulation without pain), and global sensory hyperresponsiveness, where the patient may report pain caused by touch, strain, or even exposure to bright light and loud noise. Analytic analysis has shown that frequent activation of peripheral nociceptors by MTrPs heads leads to the release of neuropeptides, admire material P and glutamate in the dorsal horn, which induces long-term potentiation and synaptic facilitation, thus reducing the pain threshold and expanding the receptive meadows of the second-order nerve cell [63,64].

Quantitative sensory testing and neuroimaging studies provide objective evidence for central sensitization in MPS. For example, patients with active MTrPs show significantly lower pain pressure thresholds and larger referred pain areas compared to controls, indicating central amplification of pain processing. In one study, the size of vasomotor reactivity within the referred pain zone was markedly higher in patients with latent trigger points (11.1±10.96%) versus controls (0.8±0.6%, $p<0.05$), supporting the involvement of abnormal autonomic nervous system activity in central sensitization [65]. Functional magnetic resonance imaging (MRI) and positron-emission tomography imaging have revealed increased activation in brain regions involved in pain modulation, such as the anterior cingulate cortex and insula, in patients with chronic MPS [63].

Importantly, primary sensitization may prevail even in the absence of continuous peripheral contributions due to chemical, organizational, and functional changes in the CNS, including glial cell activation and neuroinflammation [63]. The present persistent declaration underlies not only chronic widespread pain but also related symptoms such as fatigue, sleep disturbances, cognitive impairment, and mood changes, collectively known as fundamental sensitization syndrome or chronic overlap pain conditions. The presence of increased algogenic substances (bradykinin, substance P, CGRP, tumor necrosis factor-alpha [TNF-α], interleukin [IL]-1β, serotonin, norepinephrine) and decreased pH in active MTrPs is more closely associated with the magnitude of focal sensitization and pain chronicity [64].

Neurogenic factors

Neuromuscular junction (NMJ) dysfunction

NMJ dysfunction is becoming more and more known as a fundamental mechanism for the progression and continuity of MTrPs in MPS. MTrPs are presumed to be caused by a physiologic abnormality at the motor plate, where the motor nerve cells meet the muscle fiber. Electromyographic recordings consistently show spontaneous electrical activity, particularly endplate noise and spikes, localized to the MTrP site, which is notably absent from adjacent, unaffected muscle tissue [66,67]. At first presumed to be a malfunctioning muscle spindle, this anomalous project was soon understood to be caused by excessive ACh release near the NMJ, aiming at increasing the miniature end-plate potential [68].

The present persistent ACh release concept is intended to cause a sustained depolarization of the muscle membrane resulting in local contraction, metabolic stress, and the formation of taut bands—marks of active MTrPs. ACh and related metabolite concentrations in MTrP territories compared to normal muscle were revealed by recent analytical surveys using microdialysis, which supports the notion of NMJ hyperactivity as a biochemical driver of trigger top formation and maintenance. These results not only clarify the electrophysiological and biochemical underpinnings of MPS but also suggest that therapy targeting NMJ functions, such as botulinus toxin injection or agent-modified cholinergic transmission, may provide a novel avenue of proficient involvement [69].

Neurogenic inflammation

Neurogenic inflammation is a key participant in the pathophysiology of MPS, acting as a joint stimulator and amplifier of pain through the sensitization of the spinal cord and peripheral tissues. This method is triggered when the nociceptive sensory nerve fibers release neuropeptides such as Material P, calcitonin gene-related peptide (CGRP), and histamine from the regional muscle tissue [70]. The release of these mediators leads to vasodilation, increased vascular permeability, and recruitment of immune cells, which in turn intensifies the local inflammatory reaction [71]. In particular, the resultant pro-inflammatory environment reduces the threshold for the activation of the nociceptors, facilitating peripheral sensitization and the development of allodynia and hyperalgesia [72]. Analytical data from microdialysis studies have demonstrated significantly elevated levels of inflammatory cytokines (e.g., IL-1β, TNF-α), neuropeptides, and decreased pH in the vicinity of active MTrPs compared to non-affected muscle [73]. Importantly, neurogenic inflammation can persist independently of ongoing muscle damage, specifically following focal sensitization, and may even facilitate the establishment of MTrPs [73]. The fact that chronic inflammatory conditions may not be used in academic writing to prolong pain but rather underpins the transition from acute to chronic MPS stresses the need for curative measures targeting equally neurogenic and immune-mediated nerve pathways [74].

Densification of fascia

Densification of fascia has emerged as a novel and increasingly recognized mechanism contributing to the pathophysiology of MPS. The fascia, a specialized connective tissue network enveloping muscles, plays a crucial role in force transmission, proprioception, and structural integrity. Under conditions of mechanical overload, repetitive strain, or microtrauma, the fascia can undergo pathological densification—a process characterized by increased viscosity and stiffness of the extracellular matrix [75]. This densification is primarily attributed to alterations in the composition and organization of hyaluronan and collagen fibers, which reduce the gliding capacity between fascial layers and impair muscle flexibility and contractile efficiency [76].

Recent histological and imaging studies have demonstrated that densified fascia exhibits increased fibroblast activity, myofibroblast transformation, and extracellular matrix remodeling, leading to the formation of fibrotic adhesions and localized tissue stiffness [77]. In addition, an inflammatory mediator released during neurogenic inflammation, such as cytokines and growth factors, may contribute to fibroblast proliferation and collagen production. The aforementioned pathological changes not only restrict muscle movement, but they also add persistent pain by increasing the mechanical stress on the nociceptors implanted in the fascia. Importantly, the compaction of the fascia may explain the chronic, widespread pain and decreased responsiveness of some patients with MPS in combination with chronic pain caused by muscle fiber [78]. As an adjunctive treatment for MPS, interventions such as manual fascial release, target stretching, and therapy aimed at reinforcing fascial hydration and elasticity are being investigated, with the clinical importance of resolving fascial pathology in complete pain management strategies (Fig. 3).

DIAGNOSIS

The diagnosis of MPS remains a complex and evolving system, essentially due to the lack of universally accepted, objective, and standard diagnostic criteria. The clinical diagnosis is typically grounded in subjective findings, including patient-reported pain, exclusion of alternative pathologies, and the palpation of MTrPs [79]. The diagnosis

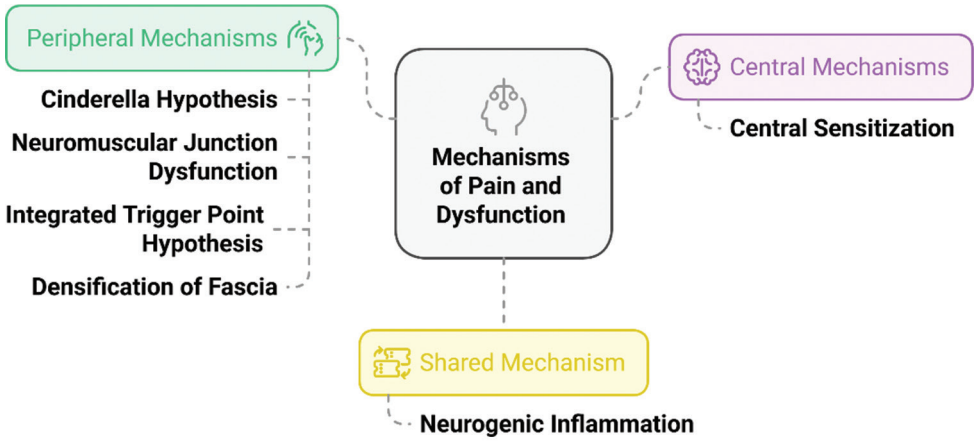

Fig. 3: Mechanisms of pain and dysfunction in myofascial pain syndrome, adapted to highlight peripheral, central, and shared pathophysiological factors

of MPS remains a complex and evolving system, essentially due to the lack of universally accepted, objective, and standard diagnostic standards. The clinical diagnosis is typically anchored by subjective findings, including patient-reported pain, expulsion of alternative pathologies, and the palpation of MTrPs [80].

Physical examination remains the cornerstone of diagnosis, palpating the taut set and determining the vital abilities of allergic muscae volitantes. Confirmatory observations, such as arousing a nearby twitch response, which may also indicate pain in the compaction, may also support the diagnosis, and the presence of spontaneous electrical projects by MTrPs may continue to be confirmed by electromyography [81]. Despite these clinical signs, questions show useful inter-rater variability, particularly in deep muscle, and there is a continuing debate on the minimal standard required for definitive diagnosis. The recent expert consensus states that the designation of the gun trigger apex should remain in place alongside the slightest duo outwards of the three features: taut band, allergic topographic point, and recommended pain otherwise sensation-although the individual symptom response is not considered to be essential for the diagnosis of MPS [82].

As a result of these limitations, research has increasingly focused on objective diagnostic methods. To assess pain sensitivity and significant pain working, supply realizations among centripetal abnormalities associated with MPS: Quantitative Centripetal Testing, Algometry, and Conditional Pain Transition [83]. The ability to visualize organizational and functional muscle transformations as well as the rate of blood flow and tissue rigidity, is a prerequisite for image approaches identical to ultrasound, MRI, magnetic resonance elastography, and infrared thermal imaging. For instance, vibration elastography provides a non-invasive technique to quantify the stiffness differences between taut sets characterized by neighboring well tissue. Despite their promises, such advanced diagnostic instruments are rarely used in everyday clinical practice, often due to their high costs, restricted use, and the need for dedicated training [84].

Differential diagnosis is essential since MPS may present symptoms that are associated with other musculoskeletal and pain disorders, particularly fibromyalgia. While MPS is typically quality by regional pain and distinct palpable MTrPs, fibromyalgia donation together by widespread pain, absence of taut group, and tender points which do not produce any local twitch response, but which do not provoke any local twitch response, also point out pain on palpation [85]. MPS involves localized changes in peripheral tissues and inflammatory mediators close to MTrPs, whereas fibromyalgia is associated with significant sensitization and does not show similar peripheral results. This emphasizes the need to carry out a comprehensive clinical assessment and, at the same time, use the evolving objective modality for improving diagnostic accuracy and promoting target leadership approaches.

Differential diagnosis of MPS

The differential diagnosis of MPS presents a significant clinical challenge due to its symptom overlap with several other chronic pain conditions, including fibromyalgia, neuropathic pain disorders, temporomandibular joint dysfunction, and various musculoskeletal or inflammatory joint diseases [86]. A frequent misdiagnosis or a delay in treatment can be caused by the above-mentioned overlap features, such as widespread pain, fatigue, tenderness of the trigger point, and restricted mobility [87]. Table 2 describes in a nutshell Common diagnostic aids for MPS.

A structured, evidence-based diagnostic workflow is needed to assist clinicians in separating MPS from other chronic pain disorders. A complete clinical report, body examination, and biochemical testing, for instance, abnormal glycosaminoglycans (otherwise GAGs), enzyme activity evaluation, and high-tech diagnostic imaging identical including MRI, infrared thermal imaging, and vibration elastography [87]. Moreover, molecular ancestral testing may be used to confirm the presence of an infectious mutant, while inherited metabolic disorders, such as mucopolysaccharidoses (MPS), are suspected of a derived function [88].

Fig. 2 illustrates a proposed clinical diagnostic algorithm that guides healthcare professionals through the systematic evaluation of suspected MPS cases, incorporating both biochemical and genetic assessments as well as multidisciplinary evaluation to establish an accurate diagnosis and initiate appropriate disease management strategies.

MPS versus neuropathic pain disorders

MPS is often mistaken for a neuropathic pain condition, such as radiculopathies and peripheral neuropathies, due to the similar clinical signs of radiating or referred pain. For correct diagnosis and treatment, however, insight into the crucial differentiation is essential [89]. Radiculopathies, which usually result in pain, numbness, and muscle weakness, also show a precise dispersion of the nerve branches. Peripheral neuropathies include damage to the peripheral nervous system and symptoms such as burning, tingling, or an electric shock under the additional grip [90]. In contrast, MPS originates from MTrPs and misses the dermatomal sensory deficit, muscle failure, or the usual change reflex seen in neuropathic pain. Moreover, neuropathic pain follows specific nerve pathways, often aligning with dermatomes, whereas MPS-related referred pain does not correspond to these neural distributions. Fig. 4 discusses a proposed clinical diagnostic flowchart for patients with suspected mucopolysaccharidosis. For optimal clinical differentiation, a comprehensive cognitive assessment is essential to detect centripetal deficiency, autonomic changes, and motor weakness - hallmarks of neuropathic environments. In addition

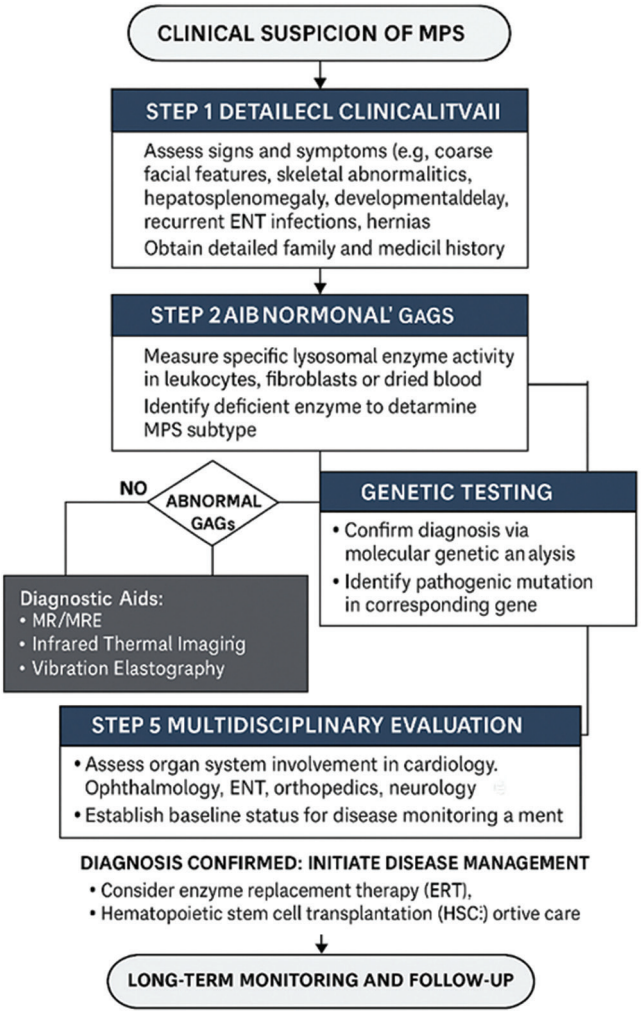

Fig. 4: A proposed clinical diagnostic flowchart for patients with suspected mucopolysaccharidosis. The process begins with clinical suspicion and involves five structured steps: (1) detailed clinical evaluation, (2) abnormal glycosaminoglycan screening, (3) confirmatory genetic testing, (4) multidisciplinary evaluation to assess organ involvement, and (5) implementation of disease-specific management. The diagram also highlights the role of diagnostic aids such as magnetic resonance imaging/MRE, infrared thermal imaging, and vibration elastography, followed by long-term monitoring and follow-up

to providing more instruments for the detection of the aforementioned pain syndromes, the recent progress in neuroimaging and quantitative sensory tests provides new opportunities for research and patient-specific management strategies [91].

MPS versus joint disorders

MPS is frequently associated with joint disorders such as osteoarthritis, bursitis, tendinopathies, and temporomandibular joint disorder (TMJD), as these conditions can present together with localized musculoskeletal pain, frequently making clinical differentiation difficult [92]. MPS and joint conditions may also cause pain when moving, and their symptoms may be similar, especially when pain occurs near a joint [93]. Nevertheless, the presence of discrete MTrPs, which are allergic muscae volitantes in muscle tissue, which may produce a pointed pain form directly related to joint pathology, is a distinguishing feature of MPS. For instance, shoulder pain in MPS may come from the trigger points of the trapezius or infraspinatus muscle rather than the glenohumeral joint itself [13].

In contrast, joint disorders are usually TMJD, which is usually contemporaneous with pain in the joint and commonly associated with joint-specific dysfunctions such as clicking, locking, or a reduced ROM [83]. TMJD pain is principally associated with the temporomandibular joint, while MPS-related pain radiates from the jaw, neck, or commonly refers to gun trigger points in a muscle such as the masseter, temporalis, or sternocleidomastoid. In particular, TMJD and MPS may coexist, complicating diagnosis and management [94].

For the diagnosis of MPS from joint disorders, a comprehensive clinical assessment is necessary. In MPS, palpation of MTrPs typically reproduces the characteristic pain form of the tolerant, whereas in joint conditions, pain is more closely associated with joint motion and load [83]. The radiographic signs of joint degeneration or inflammation, which can be distinguished by muscle contraction and tautness, are normally observed in joint disorders but not in MPS, which can be distinguished alternatively by muscle contraction and tautness. The knowledge of such distinctions is essential for the correct diagnosis and targeted therapy, particularly in view of the significant overlap between clinical presentations and the potential for comorbidities [95].

MPS versus fibromyalgia

MPS and Fibromyalgia are duo-dominant chronic pain disorders which regularly present alongside similar symptoms, complicating differential diagnosis due to the lack of validated gold standard criteria [96]. A finely detailed narrative and material analysis are the cornerstones of characterization within this syndrome. MPS are typically distinguished by regionally dispersed pain associated with distinct MTrPs, which are palpable allergic nodules within a tight muscle fiber network. Compaction of these MTrPs produces stereotypical pain forms and may cause a municipal twitch reaction, together with pain that responds rapidly to target local treatment [97].

Conversely, fibromyalgia is defined by widespread, chronic pain persisting for more than 3 months, with symmetrically distributed tender points located in soft tissues rather than within taut muscle bands. Such delicate dots do not cause prescribed pain, lack a domestic twitch response to palpation, and are largely insensitive to local therapy [98]. Fibromyalgia is also closely associated with a wide spectrum of symptoms, including fatigue, sleep disturbances, cognitive impairment (fibro fog), and temper disorders, mirroring a systemic process likely caused by an unbalanced fundamental pain processing [99].

Pathophysiologically, MPS are correlated with localized peripheral tissue variations, such as increased levels of inflammatory mediators in MTrPs, whereas fibromyalgia is thought to be caused primarily by focal sensitization without any obvious signs of peripheral inflammation in relation to tenderness scores [100]. The fact that chronic, regional pain syndromes may progress to a more widespread pain syndrome that resembles fibromyalgia makes the diagnostic problem even more pressing. In clinical practice, it is useful to classify patients who have regional pain free of focal sensitization, regional pain with significant sensitization, or widespread pain accompanying central sensitization [101].

NON-PHARMACOLOGICAL TREATMENT

Effective treatments for MPS span physical therapies, lifestyle changes, electrotherapies, medications, and invasive techniques such as dry needling and trigger point injections. Evidence supports a multimodal approach that includes stretching, exercise, massage, nonsteroidal anti-inflammatory drugs (NSAIDs), and localized interventions such as botulinum toxin or ultrasound therapy [102-105].

Physical therapy approaches

Physical therapy is a cornerstone in managing MPS, using techniques such as gun trigger compaction, myofascial release, kinesiology tape, and precise stretching to restore function and alleviate pain. Trigger apex compaction increases blood and lymph flow while reducing an

inflammatory mediator [106]. Myofascial release and spray-and-stretch approaches improve mobility and reduce sensitivity of muscle trigger points [107]. Kinesiology taping supports skin and lymphatic flow and alleviates pain by means of the gate control mechanism. In addition, in order to be able, techniques such as foam peal, ischemic compaction, and cross collision massage are described [108].

Physical therapy is a proven intervention for managing MPS, with multiple techniques showing measurable benefits. Trigger point compression significantly increases pain pressure threshold and reduces visual analog pain scores, with improvements up to 3–5 points on visual analog scale (VAS) and 2 kg/cm^2 in pressure pain threshold (PPT) [108,109]. Kinesiology taping led to significant improvements in cervical ROM and disability scores over 14 days, with flexion ROM increasing by over 10° and disability scores dropping by >30% [110]. Manual therapies such as myofascial release, spray-and-stretch, and foam rolling provide significant short-term pain relief and functional gains [106,107]. These data support a multimodal approach to restoring muscle function and reducing pain (Table 3).

PHARMACOLOGICAL TREATMENT

Needling therapies: Trigger point injections (TPIs)

Botulinum toxin type A (BTX-A) in MPS

BTX-A eases myofascial pain by blocking nerve movement to the muscles and regulating two neuropeptides connected to pain. Research shows that BTX-A helps improve symptoms in patients with both pelvic floor and masticatory forms of MPS [126]. Those with pelvic floor MPS experienced pain reduction and better mental health for approximately 3 months after injection, whereas those with jaw MPS saw improved jaw movement and relief from pain for almost 6 months [127].

BTX-A's effect on stopping spasticity is inconsistent with that of the placebo. Among the four high-quality randomized controlled trials (RCTs), the Cochrane review found a significant pain reduction in only one trial compared with placebo [128]. In addition, when compared directly to LA injections, BTX-A often underperformed, particularly in the short term (Table 4).

Local anesthetics (LA)

LA injections are a highly effective treatment for MPS, acting by blocking sodium channels in peripheral nerves to interrupt pain signal transmission. Analyses of 33 controlled trials reported that LA injections markedly reduce painful symptoms across several months, and these findings are better than dry needling or BTX-A in most comparisons. While these pharmaceuticals help a lot with quick pain relief, they do not reliably improve flexibility in your neck or mood, especially in controlled studies with no cues. While these benefits are robust in terms of short-term analgesia, their impact on cervical ROM or psychological factors is less consistent, particularly in double-blinded studies. In masticatory MPS, LA injections have been shown to significantly improve maximum mouth opening when compared to placebo, especially in patients with localized rather than referred pain [128]. Moreover, receiving LA several times can give patients more steady pain relief than from a single injection, as several trials have shown an extra 22–34% decrease in pain over time. The research proves that LA injections are a common, economical, and proven treatment for many MPS conditions [128].

Table 2: Common diagnostic aids for MPS

Diagnostic aid	Description	Clinical utility
Patient history and clinical exam	Assessment of pain characteristics, exclusion of other causes, palpation for MTrPs	First-line, subjective; identifies regional pain, taut bands, and referred pain
Manual palpation	Identification of taut bands, hypersensitive spots, and local twitch response	Essential for detecting trigger points, but inter-examiner reliability varies
Algometry	Measures pressure pain threshold at suspected trigger points	Provides quantitative assessment of tenderness
Ultrasound Imaging	Visualizes muscle structure, identifies hypoechoic regions, and taut bands	Non-invasive, aids in confirming MTrPs and differentiating from other disorders
Magnetic resonance imaging (MRI)	Assesses muscle morphology and detects changes in tissue composition	Useful for complex or unclear cases; research tool
Magnetic resonance elastography	Measures tissue stiffness and visualizes chevron patterns in taut bands	Objective assessment of muscle elasticity and taut bands
Infrared thermal imaging	Evaluates tissue blood flow, metabolism, and temperature changes	Supports detection of active MTrPs through local heat changes
Electromyography (EMG)	Detects spontaneous electrical activity at MTrPs	Identifies abnormal endplate activity, supports diagnosis
Biomarkers	Analysis of inflammatory mediators (e.g., substance P, bradykinin, cytokines) in tissues	Research tool; may help differentiate active MTrPs in future
AI-assisted diagnosis	Utilizes machine learning to analyze imaging, EMG, and clinical data for pattern recognition	Emerging tool; may improve diagnostic accuracy and standardization

MPS: Myofascial pain syndrome, MTrPs: Myofascial trigger points

Table 3: Summary of therapeutic physical modalities for MPS

Modality	Key findings	References
TENS (transcutaneous electrical nerve stimulation)	Provides short-term pain relief and improved ROM; not consistently superior to sham or alternative treatments. FREMS may be more effective than TENS for longer-term benefits.	[111,112]
Magnetic stimulation (MS)	Reduces pain and improves cervical/pelvic ROM; benefits are maintained up to 3 months in some cases.	[113-115]
Ultrasound therapy (US)	Improves pain, PPT, and quality of life; continuous US more effective than pulsed for resting pain.	[116-118]
Laser therapy (LLLT)	Effective for pain, ROM, and function; results vary by application parameters.	[119,120]
Extracorporeal shock wave therapy (ESWT)	Improves pain and function short-term; not consistently superior to other active treatments.	[121,122]
Manual therapy	Effective for short-term pain and ROM; no clear advantage over alternative modalities like dry needling or KT.	[123]
Kinesio taping (KT)	Reduces pain and improves ROM in the short term; benefits often diminish over time.	[124,125]

MPS: Myofascial pain syndrome, ROM: Range of motion

Table 4: Comparative effectiveness of local anesthetics versus BTX-A for myofascial pain syndrome

Feature	Local anesthetics (LA)	Botulinum toxin type A (BTX-A)	References
Mechanism of action	Blocks sodium channels, inhibiting pain transmission	Inhibits ACh release; reduces muscle activity and pain mediators (Substance P, CGRP)	[116,117]
Short-term pain relief	Effective within hours to days; consistent across studies	Mixed results; generally slower onset (≥1 week)	[134]
Long-term pain relief	Up to 8–16 weeks (especially with repeated injections)	Up to 6 months in select cases (e.g., masticatory MPS)	[135]
Functional improvement	Modest; some effect on ROM, less on psychological scores	More noticeable in select domains (e.g., mouth opening, dyspareunia)	[136]
Efficacy versus placebo	Consistently superior	Inconclusive; only 1 of 4 RCTs showed a significant effect	[137]
Efficacy versus each other	LA consistently outperforms BTX-A in pain relief and cost-effectiveness	Less effective for short-term pain, more costly	[131]
Cost consideration	Inexpensive and widely accessible	High cost; often×3 higher than LA	[131]
Best indications	General MPS, neck, shoulder, pelvic, and masticatory MPS	Chronic localized MPS, masticatory or pelvic floor pain not responsive to LA	[138]

ROM: Range of motion

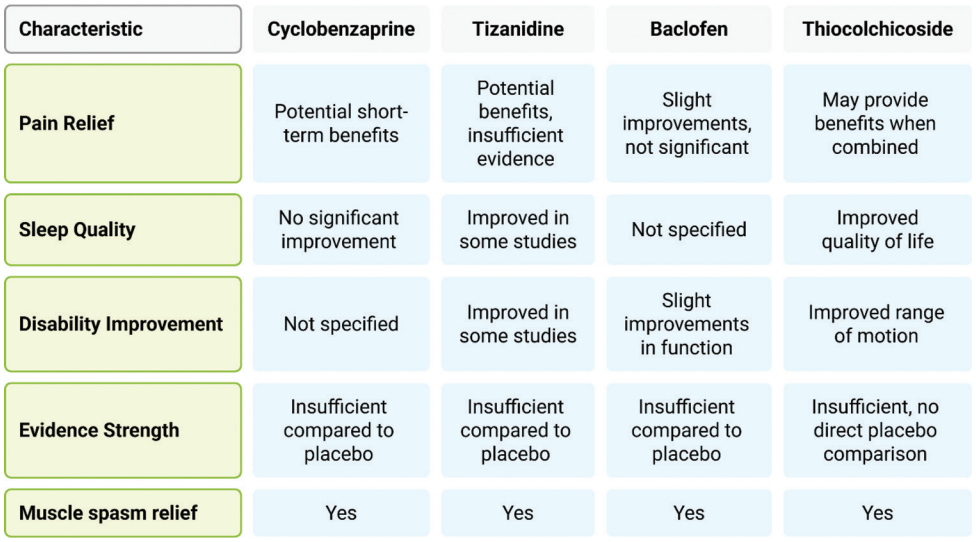

Fig. 5: Comparative analysis of muscle relaxants in myofascial pain syndrome based on clinical outcomes including pain relief, sleep quality, functional disability improvement, evidence strength, and muscle spasm relief. Data synthesized from recent studies and systematic reviews

Beyond their primary analgesic effects, LA injections also demonstrate favorable safety and accessibility profiles, making them suitable for widespread clinical use in both outpatient and multidisciplinary pain settings. Unlike more complex or cost-intensive interventions such as BTX-A, LA agents such as lidocaine and bupivacaine are inexpensive, easy to administer, and associated with a low incidence of adverse effects when proper technique is used. Furthermore, in conditions like pelvic floor or shoulder MPS, LA injections not only reduce the number of active trigger points but also lead to measurable improvements in pain pressure thresholds and patient-reported outcomes such as sleep quality and daily activity tolerance [125]. While long-term structural benefits may be limited, repeated LA injections combined with physical therapy or behavioral interventions could enhance outcomes by addressing both peripheral and central pain mechanisms. As such, LA injections not only offer a potent standalone therapy but also serve as a valuable component of multimodal MPS management strategies.

Anticonvulsants

Gabapentin

Many doctors give gabapentin, a chemical that works much like GABA, to patients with neuropathic pain due to its capability to connect with the α2δ1 part of voltage-gated calcium channels, lower neuronal activity, and cease certain overactive nerve messages. Although RCTs for gabapentin and MPS have not been done yet, a study of 42 patients with continuous facial MPS showed that 36.8% of people who struggled to improve on TCAs found significant pain decreases with 974 mg of gabapentin [128]. In contrast, 43% of TCA responders experienced similar pain relief, suggesting that gabapentin may be particularly effective in TCA-resistant patients.

From a stepped treatment approach, the combined use of TCAs followed by gabapentin led to 50% pain relief in over one-half (54.8 %) of all participants in that test, stressing that gabapentin is a second-line option for patients who are not responsive to treatment. In particular, gabapentin showed a dose-efficient response under MPS compared to neuropathic pain tests. However, gabapentin has low response rates and is not as effective as monotherapies when compared to TCAs directly [128].

Although limited by the absence of RCTs, these findings suggest gabapentin may be a valuable adjunctive therapy in MPS, especially in patients with widespread pain or comorbid conditions who do not tolerate or respond to antidepressants. Further studies are needed to confirm its comparative effectiveness and to identify ideal patient subgroups for targeted use.

Muscle relaxants

Muscle relaxants play a key role in relieving pain and improving the functioning of patients suffering from MPS. Cyclobenzaprine, tizanidine, baclofen, and thiocolchicoside, together with a distinct

mechanism regulating the essential nervous structure, project to minimize involuntary muscle contraction and hypertonicity [123]. These medicines target spinal interneurons, otherwise the supraspinal nerve pathway, which effectively disrupts the pain-spasm-pain cycle characteristic of MPS [110]. Fig. 5 depicts Comparative analysis of muscle relaxants in myofascial pain syndrome based on clinical outcomes including pain relief, sleep quality, functional disability improvement, evidence strength, and muscle spasm relief. Data synthesized from recent studies and systematic reviews.

Although robust evidence supports the efficacy of muscle relaxants in general musculoskeletal disorders [128], clinical trials focusing specifically on MPS remain limited in scale and scope. For instance, a 2023 RCT involving 78 MPS patients demonstrated that cyclobenzaprine (10 mg nightly for 14 days) significantly reduced the VAS pain scores by 38%, compared to 22% with placebo ($p<0.05$) [128]. Similarly, tizanidine showed promise in a pilot crossover study by improving PPT and sleep quality, although sedation was a notable adverse effect [18].

Fig. 1 summarizes the comparative clinical impact of four commonly used muscle relaxants in MPS, highlighting their effects on pain relief, sleep quality, disability improvement, and evidence strength across trials.

CONCLUSION

MPS remains a prevalent and complex musculoskeletal disorder, characterized by the interplay of physical, systemic, psychological, and lifestyle factors that contribute to its onset, persistence, and clinical variability. Advances in understanding the pathophysiology of MPS—particularly the roles of MTrPs, central sensitization, and neurogenic inflammation—have informed the development of more nuanced diagnostic and therapeutic strategies. While pharmacological treatments such as NSAIDs, muscle relaxants, and tricyclic antidepressants offer modest symptomatic relief, the evidence increasingly supports the superiority of non-pharmacological interventions, including dry needling, manual therapy, electrotherapies, and exercise-based modalities, in reducing pain and improving function. Innovative approaches, such as regenerative medicine, advanced imaging, wearable technologies, and artificial intelligence, are poised to further personalize and optimize care for MPS patients. Importantly, a multimodal, patient-centered approach that integrates both pharmacological and non-pharmacological therapies—tailored to individual patient profiles and comorbidities—emerges as the most effective strategy for long-term management. Despite significant progress, challenges remain in standardizing diagnostic criteria, understanding long-term outcomes, and identifying reliable biomarkers for MPS. Future research should focus on large-scale RCT, biomarker discovery, and the integration of personalized medicine frameworks to enhance clinical decision-making and improve patient outcomes. Ultimately, a holistic, evidence-based approach that addresses the biopsychosocial dimensions of MPS is essential for advancing both the science and the clinical management of this challenging condition.

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CONFLICT OF INTEREST

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