Review article

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THE SIGNIFICANCE OF QUANTITATIVE SENSORY TESTING IN PATIENTS WITH CHRONIC MUSCULOSKELETAL PAIN

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Quantitative Sensory Testing (QST) provides objective, reproducible data, which can help confirm a diagnosis or monitor treatment outcomes in patients with chronic musculoskeletal pain (CMSP). QST has the potential to become an integral part of routine clinical evaluations in a variety of chronic musculoskeletal conditions. QST can detect early sensory changes before they are clinically obvious. QST procedures are non-invasive, making them suitable for repeated assessments and monitoring over time. The standardization of testing protocols is essential for obtaining reliable results. Impaired Conditioned Pain Modulation (CPM) could serve as a biomarker for central sensitization in chronic pain conditions, helping clinicians identify patients whose pain is centrally mediated. QST has the potential to become an integral part of routine clinical evaluations in a variety of chronic musculoskeletal conditions. QST is particularly useful for evaluating the impact of physical therapies, exercise programs, and psychological interventions.

Key words: central sensitization, chronic pain, musculoskeletal pain

Pregledni rad

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ZNAČAJ PRIMENE KVANTITATIVNOG SENZORNOG TESTIRANJA KOD PACIJENATA SA HRONIČNIM MIŠIĆNO-KOŠTANIM BOLOM

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Kvantitativno senzorno testiranje (QST) pruža objektivne, ponovljive podatke koji mogu pomoći u potvrđivanju dijagnoze ili praćenju ishoda lečenja kod pacijenata sa hroničnim mišićno-skeletnim bolom (CMSP). QST ima potencijal da postane sastavni deo rutinskih kliničkih evaluacija kod različitih hroničnih mišićno-skeletnih stanja. QST može otkriti rane senzorne promene pre nego što postanu klinički očigledne. QST procedure su neinvazivne, što ih čini pogodnim za ponovljene procene i dugotrajno praćenje. Standardizacija protokola testiranja je ključna za dobijanje pouzdanih rezultata. Oslabljena modulacija bola uslovljena kondicioniranjem (CPM) mogla bi poslužiti kao biomarker za centralnu senzitizaciju kod hroničnih bolnih stanja, pomažući kliničarima da identifikuju pacijente čiji je bol centralno posredovan. QST ima potencijal da postane sastavni deo rutinskih kliničkih evaluacija kod različitih hroničnih mišićno-skeletnih stanja. QST je posebno koristan za procenu uticaja fizičkih terapija, programa vežbanja i psiholoških intervencija.

Ključne reči: centralna sensitizacija, hronični bol, mišićno-koštani bol

Introduction

Chronic musculoskeletal pain (CMSP) is a widespread condition that affects millions globally, contributing significantly to disability and diminishing quality of life. The International Association for the Study of Pain (IASP) defines musculoskeletal pain as stemming from occupational injuries, repetitive stress, or overuse, encompassing disorders that induce pain in muscles, bones, joints, or adjacent tissues, such as lumbar and cervical pain, tendinopathy, neuropathic syndromes, muscular pain, and stress fractures (1). The IASP further categorizes chronic pain as persistent discomfort that is present over three months. However, in cases like fibromyalgia or nonspecific low-back pain, it may be reclassified as a standalone condition termed "chronic primary pain", reflecting its complexity and recognition as a neurological disorder (2). CMSP, conversely, is termed "chronic secondary pain", where discomfort initially arises as a symptom of an underlying pathology (2). Current clinical frameworks advocate for a mechanism-based management approach, distinguishing between adaptive and physiological pain, such as nociceptive or inflammatory pain, and maladaptive and pathological pain, such as neuropathic or nociplastic pain, each necessitating tailored therapeutic strategies (3). Notably, research highlights central sensitization, marked by abnormal pain processing, as a critical predictor of poor clinical outcomes in CMSP (4).

Quantitative Sensory Testing (QST) has emerged as a promising diagnostic tool to objectively evaluate the sensory functions of the nervous system, enhance diagnostic accuracy, and inform treatment strategies in patients with CMSP. Over recent decades, QST has gained significant traction in clinical practice, offering valuable insights into sensory disturbances linked to diverse chronic pain conditions including osteoarthritis, fibromyalgia, chronic low back pain (CLBP), myofascial pain syndrome, and complex regional pain syndrome (CRPS) (5, 6, 7). QST can help clinicians tailor interventions to the specific pain mechanisms present in a patient, such as nociceptive pain, neuropathic pain, or central sensitization (8). Central to chronic pain are the phenomena of peripheral sensitization and central sensitization. Peripheral sensitization arises from heightened excitability of nociceptors, resulting in hyperalgesia. QST detects peripheral sensitization through reduced thermal (heat and cold) pain thresholds (9). Central sensitization is a condition where the central nervous system becomes hyper-responsive to stimuli, which results in increased pain perception and chronic pain states in patients with chronic musculoskeletal pain (osteoarthritis, lumbar and cervical syndrome, fibromyalgia, rheumatoid arthritis, complex regional pain syndrome, tendinopathies, etc.) (10, 11, 12). Central

sensitization represents a mechanism for the development of nociplastic pain. In patients with CMSP, persistent inflammation causing prolonged nociceptive pain increases the risk of nociplastic pain, which may manifest in isolation or alongside other types of pain (13). QST identifies central sensitization via temporal summation, where administering rapid, repeated mechanical or thermal stimuli intensifies perceived pain. Importantly, QST-measured central sensitization differs from symptom-based assessments, such as those assessed by the Central Sensitization Inventory (CSI) (14).

QST measurement principles

The QST method allows for the assessment of sensory processing in both large and small afferent nerve fibers, as well as other ascending pathways, by modulating various sensory stimuli (15, 16).

QST involves the systematic application of controlled sensory stimuli to assess the integrity of sensory pathways, both peripheral and central. Developed by the German Research Network on Neuropathic Pain, QST serves as a standardized framework for assessing thermal and mechanical sensory functions (Rolke). This approach involves applying a battery of standardized tests that enable clinicians to objectively evaluate somatosensory responses mediated by both large-diameter (Aβ) and small-diameter (Aδ and C) nerve fibers (17).

These stimuli can include mechanical (touch or pressure), thermal (temperature changes), and electrical (nerve conduction) stimuli. The responses are quantitatively measured, typically via threshold detection or response amplitude, allowing for a detailed, objective evaluation of reduced sensory capacity, such as hypoesthesia and hypoalgesia, or increased sensitivity, such as hyperesthesia, hyperalgesia and allodynia (18).

QST and central sensitization

QST is a crucial tool for identifying central sensitization through the use of tests like Conditioned Pain Modulation (CPM), Temporal Summation of Pain (TSP), and wind-up phenomenon.

1. Conditioned Pain Modulation (CPM)

Blunted CPM responses are a key indicator of central sensitization, which is often found in chronic musculoskeletal pain conditions like fibromyalgia or chronic low back pain. A reduced CPM response can signal that the patient's body is not able to inhibit pain signals as it should, leading to increased pain perception. CPM is a reliable test, but its reliability varies depending on the protocols and methodology used. The most reliable test stimulus is the pressure pain threshold, while among the conditioning stimuli, cold water is the most effective (19). Literature data show that the combination of determining the pressure pain threshold with an algometer as the test stimulus and cold water as the conditioning stimulus has demonstrated the highest reliability (20).

CPM testing is significant in determining the pain modulation profile, where individuals with a pro-nociceptive profile exhibit pain facilitation, indicating a less effective CPM and a higher risk for developing pain conditions (9). Pain modulation profiles are variable throughout life and represent a dynamic phenomenon that can become pro-nociceptive during pain conditions and later return to normal (21, 22).

2. Temporal Summation and Wind-Up Phenomenon

QST can measure temporal summation (the increasing pain response over time), which can help identify patients who are particularly sensitive to repeated or prolonged stimuli. The wind-up phenomenon refers to an exaggerated pain response when stimuli are presented in rapid succession, which can occur in conditions like myofascial pain syndrome and fibromyalgia. QST consists of tests which assess pain thresholds and temporal summation. Using thermal and mechanical modalities, QST can identify patients who are particularly sensitive to repeated or prolonged stimuli. Pain thresholds represent the transition point at which a sensation, such as pressure, becomes painful, while temporal summation describes the progressive escalation in perceived pain following repeated application of stimuli such as heat or pressure (23). Studies suggest that temporal summation reflects endogenous facilitatory pain pathways, characterized by amplified pain perception despite constant stimulus intensity during repeated or prolonged noxious input (24). Wind-up is a phenomenon connected to central sensitization. It is "a frequency-dependent increase in the excitability of spinal cord neurones, evoked by electrical stimulation of afferent C-fibers". In humans, temporal summation of second pain reflects the wind-up phenomenon (25).

Clinical significance of QST

QST has significant applications in determining personalized treatment, as well as in monitoring its effectiveness (9, 24).

QST can also help clinicians decide whether pharmacological treatments are appropriate (25). If QST indicates the presence of peripheral nociceptive pain, therapies with local anti-inflammatory effects are recommended, such as NSAIDs, local injections, or physical therapy (26).

In patients with central sensitization or reduced CPM, medications are recommended that are effective effective in modulating central sensitization and improving pain perception (duloxetine, gabapentin, or pregabalin). If the pain is centrally mediated, opioid analgesics might be less effective, and non-opioid therapies like antidepressants or anticonvulsants (e.g., gabapentinoids) could be better choices (26).

Before initiating treatment, a baseline QST can help identify pain thresholds, sensory deficits, and central sensitization markers. Monitoring QST after therapy is essential for assessing treatment effectiveness through evaluating pain modulation (e.g., improvement in CPM response, reduced temporal summation, increased pressure pain thresholds) (27, 28).

Some studies show that patients with less effective CPM respond better to certain medications, such as SNRIs (serotonin-noradrenaline re-uptake inhibitors), which enhance descending inhibition, compared to patients with effective CPM (21, 29).

If conditioned pain modulation is impaired, interventions that focus on modulating central pain processing, such as exercises, graded motor imagery (GMI), cognitive-behavioral therapy (CBT), biofeedback or peripheral nerve stimulation, should be included (30, 31, 32, 33, 34). In patients central sensitization (hypersensitivity or heightened pain perception) it is necessary to apply treatments targeting pain modulation (e.g., mindfulness-based stress reduction, medication management, exercise therapy targeting central sensitization) (35, 36, 37).

In patients with normal pain thresholds, conservative treatments like manual therapy, stretching exercises, or strengthening programs can be effective (38). If a high pain threshold is identified in patients with CMSP, physical therapies and rehabilitation that improve mobility and motor control are highly significant, as well as techniques that enhance sensory processing (e.g., sensory discrimination training) (39).

If a patient undergoes a multidisciplinary program combining exercise therapy and CBT, QST can reveal whether the CPM response improves, suggesting that the treatment is addressing central sensitization effectively. The improvements in mechanical or thermal pain thresholds can indicate recovery or responsiveness to interventions, while worsening thresholds can suggest disease progression (17).

Conclusion

Quantitative Sensory Testing (QST) provides a comprehensive tool for understanding the pain processing mechanisms in patients with chronic musculoskeletal pain (CMP). By providing insights into how a patient's nervous system processes pain, QST can an essential role in diagnosing, monitoring, and tailoring treatment strategies. As part of a multidisciplinary approach, QST can significantly enhance the management of chronic musculoskeletal pain.

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