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## *Review Article*

# Can Quantitative Sensory Testing Move Us Closer to Mechanism-Based Pain Management?

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### Abstract

**Objective. This review summarizes the scientific literature relating to the use of quantitative sensory testing (QST) for mechanism-based pain management.**

**Design. A literature search was undertaken using PubMed and search terms including quantitative sensory testing, pain, chronic pain, response to treatment, outcome measure.**

**Settings and Patients. Studies including QST in healthy individuals and those with painful disorders were reviewed.**

**Measures. Publications reported on QST methodological issues including associations among measures and reliability. We also included publications on the use of QST measures in case-control studies, their associations with biopsychosocial mechanisms, QST measures predicting clinical pain, as well as predicting and reflecting treatment responses.**

**Results. Although evidence suggests that QST may be useful in a mechanism-based classification of pain, there are gaps in our current understanding that need to be addressed including making QST more applicable in clinical settings. There is a need for developing shorter QST protocols that are clinically predictive of various pain subtypes and treatment responses without requiring expensive equipment. Future studies are needed, examining the clinical predictive value of QST including sensitivity and specificity for pain classification or outcome prediction. These findings could enable third-party payers' reimbursement, which would facilitate clinical implementation of QST.**

**Conclusions. With some developments, QST could become a cost-effective and clinically useful component of pain assessment and diagnosis, which can further our progress toward the goal of mechanism-based personalized pain management.**

**Key Words. Quantitative Sensory Testing; QST; Pain; Sensory Function; Phenotypes; Pain Management**

### Introduction

The vast majority of effective pain treatments produce clinically meaningful improvements only in a minority of the patients that receive them. Many authors have suggested that one factor contributing to this state of affairs is the prevailing approach to pain classification [1–4]. At present, pain diagnosis is based primarily on signs and symptoms, sometimes combined with evidence of disease, structural damage, or injury. However, the clinical diagnosis typically provides limited information regarding the pathophysiological mechanisms underlying the pain experience that may guide choice of treatment. Because treatments exert their clinical benefits by impacting the mechanisms underlying pain, an important goal for enhancing pain care is to incorporate assessment of pain mechanisms into the patient evaluation. One potentially promising method for assessing the mechanisms that contribute to the development and/or maintenance of chronic pain is quantitative sensory testing (QST). Over the last two decades, QST protocols have been developed to complement and extend the bedside neurological examination [5–9]. QST collectively refers to a group of procedures that assess the

**Table 1** Common quantitative sensory testing stimulus modalities and their characteristics

| | Electrical | Contact Thermal | Mechanical | Thermal Immersion | Ischemic | Chemical |
|---|---|---|---|---|---|---|
| Tissue depth | Variable | Superficial | Superficial and deep | Superficial and deep | Deep | Variable |
| Anatomical structure* | S, M, V | S | S, M, V | S, M | M | S, M |
| Afferent selectivity | Poor | Good | Moderate | Moderate | Moderate | Good |
| Duration | Phasic | Phasic or Tonic | Phasic or Tonic | Tonic | Tonic | Tonic |
| Repeatable | Yes | Yes | Yes | No | No | No |
| Clinical relevance | Poor | Moderate | Moderate | Moderate | Good | Good |

* S = skin, M = muscle, V = viscera.

perceptual responses to systematically applied and quantifiable sensory stimuli for the purpose of characterizing somatosensory function or dysfunction. QST assesses the integrity of the entire neural axis from receptor to brain and complements clinical neurophysiological studies (e.g., nerve conduction) that can only assess sensory large fiber function. Thus, QST can provide information regarding large myelinated A-beta, thinly myelinated A-delta, and small unmyelinated C fiber function, and their corresponding central pathways, although it cannot provide information on the exact source of somatosensory dysfunction. QST represents a useful, noninvasive method to assess both loss and gain of sensory function that may contribute to our understanding of pathophysiological mechanisms. It can be also used to evaluate a condition's natural history and may predict and/or reflect treatment responses. Although QST provides quantifiable sensory measures, similar to other psychophysical methods, it can be affected by variations in the subject's concentration, attention, and disposition, and by procedural variability. Thus, performance of QST requires training and the use of standardized protocols. The present article provides an introduction to QST, including a focused discussion of methods and evidence regarding the relationship of QST findings to clinical pain. For more detailed information, the reader is referred to other recent reviews [10–13].

## QST Methodological Issues

### *Stimulus Modalities and Target Tissues*

A variety of stimulus modalities are commonly used to assess experimental pain responses, and these modalities engage different nerve endings, nerve fibers, and central nervous system pathways involved in somatosensory transmission and processing. The modalities of stimulation typically include thermal (heat, cold), mechanical (tactile, pressure, vibration) stimuli, but electrical, ischemic, and chemical stimulation can also be employed (see Tables 1 and 2). Thermal stimuli are commonly applied to the skin surface using Peltier elements (i.e., semiconductor junctions that produce a temperature gradient between the upper and lower stimulator surfaces produced by the passage of an electric current). Other less standardized methods may also be used to cool or heat the skin such as radiant heat or ice application or via limb water immersion. Although most QST methods involve cutaneous stimulation, QST stimuli can also target other tissues, including muscle, hollow visceral organs (e.g., rectum, bladder, and esophagus), body cavities (i.e., oral cavity), and genitalia. Common models of muscle pain include induction of ischemia, the intramuscular infusion of various chemicals, and performance of eccentric muscle

**Table 2** Peripheral afferents selectively activated by common quantitative sensory testing (QST) stimuli

| Stimulus Type | Afferents | Central Pathways | Possible Bedside QST |
|---|---|---|---|
| Thermal | | | |
| Cold (25°C) | Aδ | Spinothalamic | Cold and warm metallic rollers or test tubes |
| Warmth (41°C) | C | Spinothalamic | |
| Heat pain (>45°C) | Aδ, C | Spinothalamic | |
| Cold pain (<5°C) | Aδ, C | Spinothalamic | |
| Mechanical | | | |
| Static light touch | Aβ | Dorsal-columns | Cotton swab |
| Vibration | Aβ | Dorsal-columns | Tuning fork |
| Brushing | Aβ | Dorsal-columns | Brush |
| Pinprick | Aδ, C | Spinothalamic | Pin |
| Blunt pressure | Aδ, C | Spinothalamic | Examiner's thumb |

Adapted from Backonja et al. and Campbell et al. [11,111].

exercise that causes delayed onset muscle soreness after 24–48 hours [14]. Other nonstandard QST methods can be used to assess visceral pain, for example, by distending the rectum with an inflatable balloon [15]. Similarly, intradermal capsaicin injection and ultraviolet radiation can provide additional human experimental models of hyperalgesia [16,17].

Another commonly used model is the nociceptive flexion reflex (NFR), which is comparable with the withdrawal reflex used in animal experiments. In humans, electrical stimulation of the sural nerve at the ankle is performed along with recording of the electromyogram at the biceps femoris muscle of the hamstring to detect a withdrawal reflex. Given that it occurs within 150 milliseconds of stimulation, the NFR represents a spinal reflex. The linear correlation between the pain ratings and the magnitude of the withdrawal reflex have led to its use as a measure of spinal nociceptive transmission while avoiding more complex supraspinal processes part of the pain experience [5]. However, there is evidence that supraspinal factors can significantly influence and modulate NFR responses ostensibly through descending modulation of spinal circuitry [18]. The NFR model can be used to differentially examine the influence of different primary afferent types on the reflex (i.e., RII for A-beta activation and RIII for A-delta activation).

*QST Response Measures*

In parallel to the multiple stimulus modalities available for QST, several output measures can be assessed in order to characterize the functioning of the somatosensory system in response to standardized sensory stimuli. Perceptual responses include measures reflecting nonpainful sensations (e.g., sensation detection thresholds—the point of transition from any lack of sensation to the first perceived sensation), which are typically assessed in order to identify loss of sensory function. QST also includes measures of pain response ranging from the pain threshold (i.e., the minimum stimulus intensity required to evoke a painful percept) to suprathreshold magnitude estimates (e.g., ratings of discrete stimuli pulses) to pain tolerance (i.e., the maximum stimulus intensity the subject is willing or able to tolerate).

A number of methodologies can be used to measure sensory detection or pain thresholds, but the most common is the method of limits due to its ease and quick administration. In this method, a stimulus is gradually increased to a point at which the subject reports detection of the sensation (detection threshold) or the experience of pain (pain threshold) or conversely, a stimulus can be gradually decreased to a point at which the subject no longer perceives the stimulus or the pain. A limitation of this method is its dependence on reaction time. In healthy individuals, the neurotransmission delay adds a negligible amount of error that can be reduced by using a slow temperature change [19,20]. However, reaction time may become of greater concern in older adults or in particular patient populations (e.g., Parkison's disease, spinal cord injury). A common reaction time-exclusive method is the method of constant stimuli including the method of levels, where a stimulus of predefined intensity is administered and the subject reports it as painful or not. The next presented stimulus may be increased or decreased to identify the threshold. However, this method can be time-consuming, making it less practicable for clinical use. Previous studies have reported similar sensitivity and test-retest reliability between the method of constant stimuli and method of limits [21–23]; therefore, the latter has been used almost exclusively.

Recent years have witnessed increased interest in QST methods that assess the dynamics of the pain processing system, particularly pain facilitation and inhibition. Characterization of temporal and spatial summation responses provide information about facilitatory mechanisms underlying nociceptive processing in healthy and diseased states. Temporal summation refers to an increase in pain perception after application of a series of noxious stimuli delivered at sufficient frequency and intensity (usually 0.3 Hz with fixed stimulus intensity) and is presumed to be the psychophysical manifestation of wind-up. Wind-up is a phenomenon where repetitive stimulation of C primary afferents at rates greater than 0.3 Hz produces a slowly increasing response of second-order neurons in the spinal cord [24–27]. The underlying mechanism is dependent on activation of the N-methyl-D-aspartate receptor [28,29]. Temporal summation can be examined using heat, mechanical, and electrical stimulus modalities by delivering repetitive stimuli at a fixed intensity and assessing the ensuing increase in perceived pain. The temporal dynamics of pain can also be evaluated using long duration stimuli (15–120 seconds), and continuous pain ratings can be electronically obtained to model time-dependent changes in pain perception [30–32]. Another form of pain facilitation, spatial summation, occurs when enlargement of the stimulus area produces an increase in pain perception. Spatial summation results from the central integration of nociceptive information from multiple peripheral afferents and can occur across large body areas. This integration between multiple painful stimuli is present within [33,34] and across dermatomes [34–36] suggesting the involvement of complex peripheral and central nervous system mechanisms [34].

Other QST paradigms can be used to characterize the endogenous inhibitory capacity of the nociceptive system, disruption of which may contribute to some chronic pain conditions. Conditioned pain modulation (CPM) refers to the reduction in pain from one stimulus (the test stimulus) produced by concurrent application of a second pain stimulus at a remote body site (the conditioning stimulus). CPM is believed to reflect the perceptual manifestation of diffuse noxious inhibitory controls (DNICs) [37], whereby ascending projections from one noxious stimulus activate supraspinal structures, triggering descending inhibitory projections to the dorsal horn, which are opioidergic, serotonergic, and noradrenergic in nature. A more recently observed form of endogenous inhibition is offset analgesia, whereby a small reduction in the temperature of a

painful heat stimulus triggers a disproportionate decrease in pain ratings [38]. Offset analgesia has been proposed as a temporal contrast filtering mechanism for nociceptive information involving the periaqueductal grey, rostroventromedial medulla and locus coeruleus [39] that appears to be mostly opioid-independent [40].

Thus, multiple QST methodologies are available, including numerous stimulus modalities and ranging from unidimensional approaches, such as sensory or pain threshold, to more complex dynamic measures of endogenous pain modulatory function. The specific QST methods applied in any given setting should be based on the specific clinical and research questions being asked.

*Relationships across QST Measures*

QST measures have been shown to be only moderately correlated across stimulus modalities or outcomes in most studies [41–47], although stronger associations have been reported among threshold-level measures across different modalities [48]. In line with the organization of the somatosensory system, previous research has supported the use of multimodal pain assessments to evaluate all aspects of somatosensory function that may be of clinical relevance [44,46,47]. Consistent with this idea, the German Research Network on Neuropathic Pain (DFNS) has developed and validated a standardized comprehensive QST battery to profile somatosensory function at affected and unaffected pain sites [8,9]. A recent study by the DFNS investigators assessed mechanical and thermal sensory responses in 1,236 patients with various peripheral and central neuropathic pain conditions [49]. For all diagnostic groups, different patterns of QST responses emerged, with some patients within each group showing no change, sensory losses, sensory gains, or both. Two important conclusions may be drawn from these findings: 1) within a diagnostic group, different patterns of sensory abnormalities emerge, suggesting the influence of distinct underlying pain mechanisms; and 2) across diagnostic groups, similar patterns of sensory abnormalities can be observed, suggesting that similar mechanisms may be operating even among patients with different pain diagnoses. Similarly, multiple QST profiles have been observed in other pain conditions such as temporomandibular disorders (TMDs) [50], back pain [51], and osteoarthritis (OA) [52]. These findings reflect the substantial heterogeneity in somatosensory function and dysfunction that exists within and across chronic pain conditions [53], further supporting the need for mechanism-based pain assessment, necessary to enable mechanism-targeted therapies.

*Reliability of QST Measures*

Although some variability in psychophysical measures is expected, an important characteristic of an outcome or diagnostic measure is its consistent reproduction under the same conditions. Several studies have found sufficient test-retest reliability between sessions for mechanical [54,55], vibration [56–59], and thermal detection thresholds [54,56,58–63], but reliability of thermal pain threshold measurements has been lower, particularly for cold pain [55,62,64]. A recent large study from the DFNS [65] examined the test-retest and interrater reliability of QST measures in 60 patients with peripheral and central lesions across four study centers with multiple measures at affected and control sites over 2 days. Twelve QST measures showed at least moderate test-retest and interrater reliability ($r > 0.60$) with most measures having excellent ($r > 0.80$) reliability coefficients. Only paradoxical heat sensations had poor reliability coefficients. Similar results were obtained when reliability was examined for intraoral QST [66]. In general, studies support the reliability of QST measures when standardized protocols are followed and when careful experimenter and subject training is performed.

## Clinical Findings

Several lines of research provide evidence that QST may be useful in the assessment of clinical pain and ultimately in moving toward mechanism-based pain classification (for examples, see Table 3). First, QST can be used to distinguish patients with chronic pain from pain-free controls and may be useful in subgrouping chronic pain patients. Second, similar biopsychosocial mechanisms appear to influence both clinical pain and QST responses. Third, QST measures can predict future development or severity of clinical pain. Fourth, QST measures can both predict and reflect responses to pain treatment. Each of these lines of research will be briefly discussed later.

*QST in Case-Control Studies*

QST measures have consistently differentiated between individuals with and without pain [67]. In the "Orofacial Pain: Prospective Evaluation and Risk Assessment" study, standardized odds ratios for experimental pain sensitivity measures (adjusted for age, sex, race/ethnicity, and study site) distinguished TMD cases from controls [68]. OA patients with severe clinical pain (visual analog scale [VAS] rating >6) and mild-to-moderate clinical pain (VAS rating <6) showed significantly greater temporal summation of pressure pain compared to controls both at the knee and at the tibialis anterior [69]. Similarly, fibromyalgia patients require less frequent stimulation for temporal summation than healthy controls [36,70]. More recently, QST measures showed high predictive value in separating individuals with and without post-herpetic neuralgia [71]. Similarly, pressure pain sensitivity demonstrated good ability to differentiate between people with OA and healthy controls. Lower pressure pain thresholds in persons with OA in affected and remote sites may suggest peripheral and central sensitization states supporting it as a tool for phenotyping persons with OA pain [72]. Additionally, OA patients with high pain and low levels of radiographic disease severity showed greater sensitivity to mechanical, heat, and cold pain tested at unaffected body sites [73]. Similar results have been reported in other large samples of symptomatic OA participants [74]). Similarly, endogenous pain modulation has consistently differed between healthy controls and individuals with chronic pain states such as irritable bowel syndrome (IBS) and TMD patients.

**Table 3** Examples of the relationship between various quantitative sensory testing measures predicting response or treatment outcome that may aide in the targeting of therapeutic interventions

| Stimulus Modality | Common Measures | Examples |
|---|---|---|
| Thermal (heat and cold) | Pain threshold<br>Pain tolerance<br>Suprathreshold ratings<br>Temporal summation | Baseline heat pain thresholds predicted response to opioid treatment, but not responses to amitriptyline, in patients with post-herpetic neuralgia [103] |
| Mechanical (blunt and punctate) | Pain threshold<br>Pain tolerance<br>Suprathreshold ratings<br>Temporal summation | Pressure pain thresholds increased after total knee replacement in patients with knee osteoarthritis [107] |
| Chemical (capsaicin, hypertonic saline, glutamate) | Pain ratings<br>Pain area<br>Allodynia<br>Hyperalgesia | Analgesic efficacy of clonidine over placebo depended on the presence of functional capsaicin-responsive nociceptors in the skin in patients with painful diabetic neuropathy [112] |
| Electrical | Pain threshold<br>Pain tolerance<br>Suprathreshold ratings<br>Temporal summation<br>Nociceptive flexion reflex | Electrical pain detection was predictive for pregabalin effect with high sensitivity and specificity in patients with painful chronic pancreatitis [106] |
| Conditioned pain modulation (CPM)—often with cold or heat as conditioning stimulus and heat or pressure as test stimulus | | Baseline CPM response predicted duloxetine efficacy on patients with painful diabetic neuropathy [104] |

For example, healthy controls showed greater reductions of heat pain on the hand when their foot was concurrently immersed in a cold water bath, indicating more robust pain inhibition among controls compared with both TMD and IBS patients [75]. A recent meta-analysis further demonstrates that across multiple clinical conditions, CPM is compromised among individuals with chronic pain [76]. Finally, QST profiles in patients with cervical radiculopathy were distinct from those in patients with non-specific neck-arm pain and in patients with fibromyalgia [77]. On the other hand, a recent meta-analysis suggests that static QST measures (i.e., pain thresholds) are weakly correlated with self-reported pain intensity and disability in people with spinal pain [13]. Even so, evidence is beginning to emerge supporting specific QST measures and modalities for diagnostic purposes within a specific pain condition [78].

### *QST Associations with Biopsychosocial Mechanisms*

The recognized interindividual variability in clinical pain experiences is paralleled by interindividual differences in QST responses. Moreover, as with clinical pain, individual differences in QST responses have been associated with multiple biopsychosocial mechanisms, which have also been found to influence clinical pain. For example, individuals who rated a heat pain stimulus as particularly painful showed more robust heat pain-related activation in the somatosensory (S1), anterior cingulate cortex, and prefrontal cortex compared with people who provided low heat pain ratings [79]. Altered activity in these brain regions has also been implicated in clinical pain conditions [80]. In addition, several genetic markers have been associated with QST responses. The mu-opioid receptor gene has been associated with sensitivity to multiple pain modalities [81–83]. This gene has also recently been associated with prognosis following lumbar disc herniation [63]. Similarly, the catechol-O-methyltransferase (*COMT*) gene has been related to multiple experimental pain measures [84,85], as has the guanosine triphosphate cyclohydrolase gene [86,87], and both of these genes have been associated with clinical pain conditions [88,89]. Recent evidence supports the association of experimental pain phenotypes with the *COMT* gene in persons with fibromyalgia [90].

Psychosocial variables similarly influence both clinical pain and QST responses. For example, reactive and depressive affect balance style (ABS) subgroups were previously reported to be more frequent in a fibromyalgia sample compared with controls [91], and recently, ABS style was associated with ischemic experimental pain responses among healthy adults [92]. Also, situational pain catastrophizing is associated with greater pain ratings as well as greater sensitivity to experimental pain in healthy, arthritis, and TMD individuals [93]. Similarly, studies have supported the relationship between high levels of optimism and lower pain sensitivity in healthy [94,95] and TMD individuals [96]. Interestingly, interactions of genetic and psychological factors can influence both clinical pain and QST responses. Indeed, the *COMT* gene interacted with pain catastrophizing to impact clinical shoulder pain as well as experimentally-induced shoulder pain [97,98].

*QST Predicting Clinical Pain*

QST measures have been used in multiple studies to predict the future occurrence or severity of clinical pain. Reduced endogenous pain inhibition has been proposed as a risk factor for chronic post-thoracotomy pain [99]. In that study, DNIC significantly predicted development of chronic pain (pain rating >20) 7 months after thoracotomy. Patients with long-lasting whiplash symptoms after motor vehicle accidents had lower cold pressor pain tolerance 1 week after injury compared with recovered patients and a comparison group of patients with ankle injury [100]. Greater mechanical temporal summation preoperatively predicted higher evoked pain (upon arm elevation and coughing) following thoracotomy [101]. Likewise, mechanical temporal summation at the hand and the knee significantly predicted weekly diary ratings of average pain in individuals with knee OA [102]. Thus, emerging evidence suggests that QST measures may have value for predicting future experiences of both acute and chronic pain.

*QST Predicting and Reflecting Treatment Responses*

QST responses have been found to predict responses to pain treatments, and QST may also represent a useful marker of treatment outcome [12]. Baseline heat pain thresholds predicted response to opioid treatment, but not responses to amitriptyline, in patients with postherpetic neuralgia [103]. Similarly, patients with painful diabetic neuropathy who had poorer pain inhibitory function (i.e., less efficient CPM) at baseline showed greater duloxetine efficacy (i.e., patient rating of the overall effect of the drug on their pain) [104]. An interesting case report was recently reported where QST was performed in a person with bilateral at-level pain at T9 following spinal cord injury [105]. The patient described the pain on both sides identically as burning and pricking with a severity of 8 out of 10. On the right side, the patient had normal sensation and cold hyperalgesia (i.e., central sensitization), while on the left side, the patient had loss of thermal and mechanical sensations with a loss of intraepidermal nerve fiber density (i.e., deafferentation). Interestingly, pregabalin treatment greatly reduced the at-level pain on the right but not the left side, suggesting that pregabalin was effective for the pain mediated by central sensitization but not the pain due to deafferentation. Similarly, in patients with painful chronic pancreatitis, electrical pain detection ratio (pancreas to control site) predicted the effect of pregabalin, with 87.5% sensitivity and 80.0% specificity [106]. Thus, limited evidence suggests that QST may predict responses to treatment, but as noted in a recent meta-analysis, additional research is needed before QST can be recommended for this purpose [12].

With regard to QST as a marker of treatment outcome, QST was performed in 48 knee OA patients before and after total knee replacement (TKR) and in 21 healthy controls [107]. Before surgery, OA patients showed greater pain sensitivity than controls at both affected and unaffected body sites. Pressure pain thresholds increased in OA patients after knee replacement on both the affected and unaffected sides of the body. Before surgery, OA patients failed to show CPM in contrast with controls. However after TKR, CPM was normalized in OA patients consistent with the pain reduction. These findings corroborate similar results previously reported by Kosek and Ordeberg [108,109]. In these studies, QST appears to reveal that the dysfunctional pain processing both resulting from and contributing to the clinical pain has been corrected by successful treatment. Similarly, QST measures have been predictive of analgesic responses in healthy subjects [110].

## Challenges and Future Directions

Although evidence suggests that QST may be useful in a mechanism-based classification of pain, there are gaps in our current understanding that need to be addressed. First, the psychometric characteristics of many QST measures are still poorly characterized. This is particularly true for ischemic and chemical modalities, but also for many of the dynamic QST measures (e.g., CPM, offset analgesia), and reliability data within specific subject populations and settings are often unavailable. Second, it is currently unclear which of the QST measures may be most useful for characterizing pain mechanisms. Specifically, if the large interindividual differences in pain sensitivity are modality specific (e.g., there are subgroups of individuals that are specifically more or less sensitive to heat vs pressure vs ischemic pain), then selecting the correct QST battery remains a challenge. Other logistical issues such as the space and expense of the equipment required for some QST measures, as well as the time required to complete the assessments, may be a barrier to implementation in clinical settings.

It is also important to recognize that QST findings cannot pinpoint specific mechanisms underlying clinical pain in individual patients. For example, findings of generalized hypersensitivity to painful stimuli in a patient with knee OA could reflect multiple mechanisms, including alterations of endogenous opioid function, changes in serotonergic and noradrenergic processes, altered cerebral pain processing, and high levels of pain catastrophizing. Moreover, these mechanisms are not mutually exclusive and likely interact in many cases. Nonetheless, it seems potentially valuable to know whether a patient with knee OA expresses widespread hypersensitivity, as this may indicate the involvement of different pathophysiological mechanisms and thus the need for different treatments compared with a patient with localized pain and normal sensory function. It is hoped that ultimately QST profiles will be used to identify subgroups of patients based on underlying mechanisms, which could inform more personalized pain treatment designed to target specific pathophysiological processes. Thus, QST may offer potential value for classifying individuals with chronic pain, and continued research in this area is needed in order to further improve the clinical utility of QST.

The following developments would serve to make QST more applicable in the clinical setting. First, "bedside" QST protocols that require less time and do not require cumbersome and expensive equipment are needed (see Table 2 for examples). Second, standardized normative values are needed for the bedside QST protocols in healthy and pain populations. Third, while an impressive QST battery has been developed for neuropathic pain, additional protocols need to be developed for other pain conditions, such as musculoskeletal and visceral pains. Fourth, additional evidence regarding the clinical predictive value of QST is needed, including sensitivity and specificity for classification or outcome prediction. Finally, third-party payers often do not reimburse for QST, and this will need to change if QST is to be clinically implemented. With these additional developments, QST could become a cost-effective and clinically useful aspect of pain assessment and diagnosis, which can further our progress toward the goal of mechanism-based personalized pain management.

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