

Comprehensive review

## Relationship between quantitative sensory testing and pain or disability in people with spinal pain—A systematic review and meta-analysis

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### ABSTRACT

Sensitization of the nervous system can present as pain hypersensitivity that may contribute to clinical pain. In spinal pain, however, the relationship between sensory hypersensitivity and clinical pain remains unclear. This systematic review examined the relationship between pain sensitivity measured via quantitative sensory testing (QST) and self-reported pain or pain-related disability in people with spinal pain. Electronic databases and reference lists were searched. Correlation coefficients for the relationship between QST and pain intensity or disability were pooled using random effects models. Subgroup analyses and mixed effects meta-regression were used to assess whether the strength of the relationship was moderated by variables related to the QST method or pain condition. One hundred and forty-five effect sizes from 40 studies were included in the meta-analysis. Pooled estimates for the correlation between pain threshold and pain intensity were  $-0.15$  (95% confidence interval [CI]:  $-0.18$  to  $-0.11$ ) and for disability  $-0.16$  (95% CI:  $-0.22$  to  $-0.10$ ). Subgroup analyses and meta-regression did not provide evidence that these relationships were moderated by the QST testing site (primary pain/remote), pain condition (back/neck pain), pain type (acute/chronic), or type of pain induction stimulus (eg, mechanical/thermal). Fair correlations were found for the relationship between pain intensity and thermal temporal summation (0.26, 95% CI: 0.09 to 0.42) or pain tolerance ( $-0.30$ , 95% CI:  $-0.45$  to  $-0.13$ ), but only a few studies were available. Our study indicates either that pain threshold is a poor marker of central sensitization or that sensitization does not play a major role in patients' reporting of pain and disability. Future research prospects are discussed.

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## 1. Introduction

Pain sensitization, in which nociceptive neurons become sensitized by nociceptive input, manifests as pain hypersensitivity (eg, hyperalgesia, allodynia) and may contribute to clinical pain [82]. A common assumption of the central sensitization model is that people with enhanced pain sensitivity also report higher levels of pain and/or disability [40,70]. Preliminary research has shown that both evoked and spontaneous pain (ie, pain experienced by patients without stimulation) can induce changes in pain sensitivity and brain activity that are associated with the pain experienced by the participant [3,4,16,66,74]. In healthy volunteers, neuroimaging research has shown that capsaicin-induced central sensitization

increases brain activity that correlates with the perception of pain intensity induced by an experimental pain stimulus [45].

Sensory disturbances such as pain sensitivity are frequent features of chronic pain [5,25,48,56]. For example, the presence of cold hyperalgesia characterizes people with lateral epicondylalgia, who have higher pain and disability levels [12]. In patients with spinal pain, sensitivity to painful stimulation can be associated with the individuals' experience of pain intensity and disability [11,63,66]. Furthermore, increased pain sensitivity in the primary area of pain (local pain) is considered a sign of predominantly peripheral pain sensitization, whereas pain sensitivity in areas anatomically remote from the primary area of pain is thought to reflect a more central phenomenon [31,66,82].

The assessment of sensory function using quantitative sensory testing (QST) has been advocated to explore the mechanisms underlying local and widespread musculoskeletal pain [13,58,83]. Several studies using QST (mechanical/thermal pain thresholds) have found that compared with healthy control subjects, patients

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with acute or chronic spinal pain (neck pain, low back pain [LBP]) show evidence of pain hypersensitivity. This has been interpreted as reflective of peripheral and/or central nociceptive sensitization [7,20,31,37,55,56]. However, the current evidence for the association between measures of QST and reported pain intensity and/or disability in spinal pain is inconsistent. Findings of no correlation or weak to moderate correlations may depend on the site of testing, the pain induction stimulus (eg, mechanical, thermal), the pain condition (LBP, neck pain, whiplash), the pain type (acute, chronic), and the outcome measured (eg, threshold, tolerance, temporal summation, pain or disability) [11,29,40,42,63,66,79]. A better understanding of the relationship between clinical features of spinal pain and sensitivity, as well as of the impact of potential moderators on this relationship, is vital to understand the role that central sensitization plays in pain and disability.

The first objective of this systematic review and meta-analysis was to examine the relationship between established QST measures and pain or disability in spinal pain. The second objective was to assess whether the strength of the relationship was moderated by variables related to the QST method and pain condition.

## 2. Methods

### 2.1. Study selection

The current study is reported in accordance with the PRISMA statement for the reporting of systematic reviews and meta-analyses [51]. A computerized search for articles published between the years 1966 and October 2012 was performed in the following databases: MEDLINE (OvidSP), EMBASE (OvidSP), CINAHL (EBSCO host), PsycINFO (OvidSP), Cochrane Central Register of Controlled Trials (OvidSP). Furthermore, reference lists of all retrieved articles were manually checked for additional studies.

The updated search strategies of the Cochrane Back Review Group ([http://back.cochrane.org/sites/back.cochrane.org/files/uploads/PDF/CBRG\\_searchstrat\\_Jun2011.pdf](http://back.cochrane.org/sites/back.cochrane.org/files/uploads/PDF/CBRG_searchstrat_Jun2011.pdf)) were used to identify studies of LBP and neck pain. In addition, the search for self-reported measures of pain and disability included a combination of subject headings and text words using keywords such as: pain, disability, function\$, Visual Analogue Scale (or VAS), Oswestry, Neck Disability Index (or NDI). The search for QST included keywords such as quantitative sensory testing, hyperalgesia, pressure algometry, central/peripheral sensitization, hypersensitivity. The MEDLINE search strategy is provided in [Appendix A](#).

To be eligible, studies had to meet the following selection criteria: cross-sectional or longitudinal study; randomized controlled trial (RCT) or nonrandomized controlled clinical trial (CCT) (baseline data/no treatment arm); participants' ages at least 18 years; acute (less than 6 weeks), subacute (6 to 12 weeks) or chronic (12 weeks or more) LBP or neck pain with or without referred pain including idiopathic pain, whiplash-associated disorder (WAD), myofascial pain syndrome, degenerative joint or disc disease, and spondylolisthesis. Each study was required to assess both QST and pain and/or disability using standardized and valid measures eg, VAS, numeric rating scale (NRS), NDI.

QST was defined as a method that quantifies the magnitude of physical stimuli (eg, pressure, heat, cold, vibration, electrical current) that is required to determine a specific pain perception (ie, pain threshold, pain tolerance, temporal summation, pain magnitude rating) [83]. The application of the physical stimulus had to be standardized and the physical stimulus had to be expressed in quantitative terms eg, pressure: kg/cm<sup>2</sup>; heat/cold: °C. Likewise, the evoked sensory and pain perception had to be reported quantitatively (eg, pressure: kg/cm<sup>2</sup>; heat/cold: °C; intensity ratings using VAS or NRS). Studies using invasive forms of QST (eg, noxious

stimulation of the intervertebral disc) were excluded. Correlation coefficients (Pearson's  $r$  or Spearman's  $\rho$ ) for the relationship between QST measured locally and/or at a remote site and pain/disability had to be reported or could be calculated from the data reported in the study or from data obtained from the study authors. Studies that only provided correlations between pain/disability and QST composite scores, ie, local and remote site combined, were excluded.

Two reviewers applied the inclusion criteria independently to select the potentially relevant trials from the titles, abstracts, and keywords of the retrieved literature. Articles that met the selection criteria as well as articles with abstracts that were imprecise concerning the selection criteria were considered for full-text analysis. Studies involving participants with nonspinal pain caused by other conditions (eg, metastasis, neoplasm, fracture, infection, inflammation, osteoporosis, fibromyalgia, temporomandibular joint disorder, rheumatoid arthritis, headache) or previous spinal surgery were excluded. Studies were also excluded if they were conducted on mixed populations (eg, acute/subacute/chronic, LBP/neck pain) unless correlation coefficients could be obtained for the separate populations. Studies that included participants with neck pain and WAD were eligible.

### 2.2. Data extraction

Data extraction from the included studies was performed by one author (M.H.) using standard extraction forms and independently cross-checked by 2 of 3 other authors (A.L., N.M., T.R.). Study characteristics and outcome data of interest included study design, length of follow-up, number of participants, participants' characteristics (age, sex, diagnosis, duration of symptoms), pain or disability scores, QST measure, and correlation coefficient and other relevant information such as  $P$  value and confidence intervals (CIs). For longitudinal studies, data collected at baseline and the last follow-up were selected for reporting cross-sectional correlations for each time point if the 2 time points fell into different pain stages (ie, acute/subacute versus chronic). Otherwise, cross-sectional correlations of baseline data or longitudinal correlations between baseline QST data and follow-up pain or disability scores were used. If necessary, up to 3 attempts were made to contact study authors via email to request missing or additional data.

Disagreements between the reviewers regarding the selection of studies and the data extraction were resolved by discussion and consensus. Persisting disagreements were discussed in a consensus meeting of all authors to make the final decision.

### 2.3. Data synthesis and analysis

Included studies were grouped into acute/subacute (less than 12 weeks) or chronic ( $\geq 3$  months) according to the duration of pain [27]. Measurement areas of QST were grouped into local or remote. Local was defined as the primary area of pain, eg, over the lumbar spine in LBP, over the cervical spine in neck pain, and/or a site adjacent to the primary area of pain that was reportedly painful, eg, gluteal muscle in LBP, trapezius muscle in neck pain. Remote was defined as a site that was anatomically distant from the primary area of pain, eg, tibialis anterior muscle or thumb in spinal pain. When QST was measured at several distant sites, the most unrelated site was chosen, such as the tibialis anterior muscle instead of the thumb for neck pain or thumb instead of tibialis anterior muscle for LBP. When QST was measured at multiple sites within the same area and thus several correlation coefficients were available for this area, eg, C2/3 and C5/6 in neck pain, the strongest coefficient was chosen. If tender and nontender points were tested locally, ie, in the primary area of pain, the highest correlation

coefficient was used, regardless of whether it was a tender or non-tender point.

The results of comparable studies were pooled by using a random effects model. We first divided studies into those that investigated pain threshold, pain tolerance, temporal summation/wind-up, or pain magnitude rating. Then, as we wanted to investigate the effect of several potential predictors on the size of the correlations, we explored correlation coefficients for subgroups of studies, categorized by the following study characteristics: (1) QST testing site (local, remote), (2) pain condition (LBP, neck pain), (3) pain type (acute/subacute, chronic), and (4) type of pain induction stimulus (cold, heat, pressure, etc.).

Pearson's  $r$  or Spearman's  $\rho$  were synthesized together. Heterogeneity was examined using the Cochran's  $Q$  test and the  $I^2$  statistic, which is the percentage of total variation across studies due to heterogeneity rather than chance [36]. We considered  $P$  values of  $<0.1$  as indicating significant heterogeneity and  $I^2$  values of 25%, 50%, and 75% as corresponding to low, moderate, and high heterogeneity, respectively [36].

Given sufficient availability of data, mixed effects meta-regression was used to formally assess the effect of the potential categorical predictors (QST testing site, pain condition, pain type, type of pain induction stimulus) on the strength of the relationship between pain threshold and pain intensity/disability. The effect of each categorical predictor was tested in a separate meta-regression. The variation in effect size (correlation coefficient) explained by the categorical model ( $Q_M$  or  $Q_B$ ) was calculated and tested against a  $\chi^2$  distribution. More than 1 effect size could have been included in the meta analysis from an individual study due to different types of pain induction stimuli (eg, heat, cold, pressure) and QST testing sites (ie, at the primary area of pain or a remote site) [24,73].

As a guideline, we used 0.25, 0.5, and 0.75 as cut-off points to interpret the strength of the relationship as little or zero (0.00 to 0.25), fair (0.25 to 0.50), moderate to good (0.50 to 0.75), and good to excellent (above 0.75) [60]. Statistical analyses were performed using the Comprehensive Meta-Analysis (version 2.2) and Meta-Win (version 2.1) software.

### 3. Results

The search strategy retrieved 1516 studies, from which 228 full-text articles were assessed to determine eligibility (Fig. 1). Eighty-four authors were contacted (132 articles), and 28 authors provided additional data (36 articles) that could not be extracted from the articles. Finally, 43 articles met the inclusion criteria and were further considered for this review.

#### 3.1. Description of included studies

Studies were included for LBP, chronic neck pain, and acute and chronic WAD. The main characteristics of the included studies are presented in Appendix B. Nineteen studies included 934 participants with LBP: 15 studies on chronic LBP [1,6–9,11,16,28,29,35,41,49,59,65,81], 4 subacute LBP [20–23]. The mean sample size for the 19 studies ranged from 16 to 180. Studies included mostly female (61%) participants. The mean age ranged from 32 to 53 years. Eleven studies used a cross-sectional design, 1 study was a longitudinal design, and 7 studies were RCTs. The longitudinal study provided cross-sectional correlation analyses of baseline data.

Nineteen studies included participants with chronic neck pain [14,15,18,38,43,44,46,47,53,54,68,72,76,77] and chronic WAD [19,39,40,62,75]. Sample sizes ranged from 22 to 151, with 1043 total participants from all studies. Studies included mostly female

(82%) participants. The mean age ranged from 29 to 58 years. One study [66] involved a mix of patients with chronic neck pain ( $N = 20$ ) and chronic WAD ( $N = 29$ ). Ten studies used a cross-sectional design, 1 study was a longitudinal design, and 8 studies were RCTs. The longitudinal study provided cross-sectional data on participants with chronic WAD at 3-month follow-up.

Five studies included participants with acute WAD [40,63,80] and acute/subacute neck pain and WAD [78,79]. Sample sizes ranged from 24 to 146, with 352 participants in total across all studies. Studies included mostly female (70%) participants. The mean age ranged from 35 to 40 years. Three studies used a cross-sectional and 2 studies used a longitudinal design. One longitudinal study provided cross-sectional data on participants with acute WAD, and another one provided longitudinal correlations between baseline QST and follow-up disability scores.

In LBP, the most commonly used instruments to assess pain and disability were the VAS (9 studies), the NRS (5 studies), and the Oswestry Disability Index (7 studies). One study used the SF-36 pain and physical functioning subscales, and another used the Hannover Functional Ability Questionnaire. In neck pain and WAD, pain and disability were typically assessed using the VAS (14 studies), NRS (4 studies), and NDI (13 studies). Two studies used the Northwick Park neck pain questionnaire, and 1 study used the patient-specific functional scale.

The most commonly reported QST measure was pressure pain threshold (28 studies), followed by cold pain threshold (9 studies) and heat pain threshold (8 studies). Only 1 study reported electrical current to assess detection and pain thresholds. Studies assessing pain tolerance used either pressure (2 studies) or cold stimuli (2 studies), and 1 study used electrical current. Studies that assessed summation of pain (temporal summation/wind-up) in response to repetitive stimuli used heat in 3 studies and pin-prick in 2 studies. Pain magnitude rating of 1 suprathreshold heat pulse (first pulse response, FPR) was tested in 2 studies. Appendix C contains an outline of all QST measures reported in the included studies.

#### 3.2. Meta-analysis

Overall, pain thresholds were little correlated with pain intensity or disability in spinal pain. Fair correlations were found for the relationship between pain intensity and heat-evoked temporal summation or pain tolerance.

##### 3.2.1. Correlation between pain threshold and pain intensity

The pooled estimate (72 coefficients, 34 studies) for the correlation between pain threshold and pain intensity was  $-0.15$  (95% CI:  $-0.18$  to  $-0.11$ ), indicating that lower thresholds demonstrated little or zero correlation with higher pain levels. Heterogeneity was not significant ( $P = .20$ ,  $I^2 = 12.0\%$ ).

##### 3.2.2. Correlation between pain threshold and disability

The pooled estimate (52 coefficients, 23 studies) for the correlation between pain threshold and disability was  $-0.16$  (95% CI:  $-0.22$  to  $-0.10$ ), indicating that lower thresholds demonstrated little or zero correlation with higher disability levels. There was evidence for moderate heterogeneity ( $P < .01$ ,  $I^2 = 57.2\%$ ).

##### 3.2.3. Correlation between pain tolerance and pain intensity

The pooled estimate (9 coefficients, 7 studies) for the correlation between pain tolerance and pain intensity was  $-0.30$  (95% CI:  $-0.45$  to  $-0.13$ ), indicating that lower pain tolerance was fairly correlated with higher pain levels. Although not significant, there was evidence for moderate heterogeneity ( $P = .07$ ,  $I^2 = 45.2\%$ ).

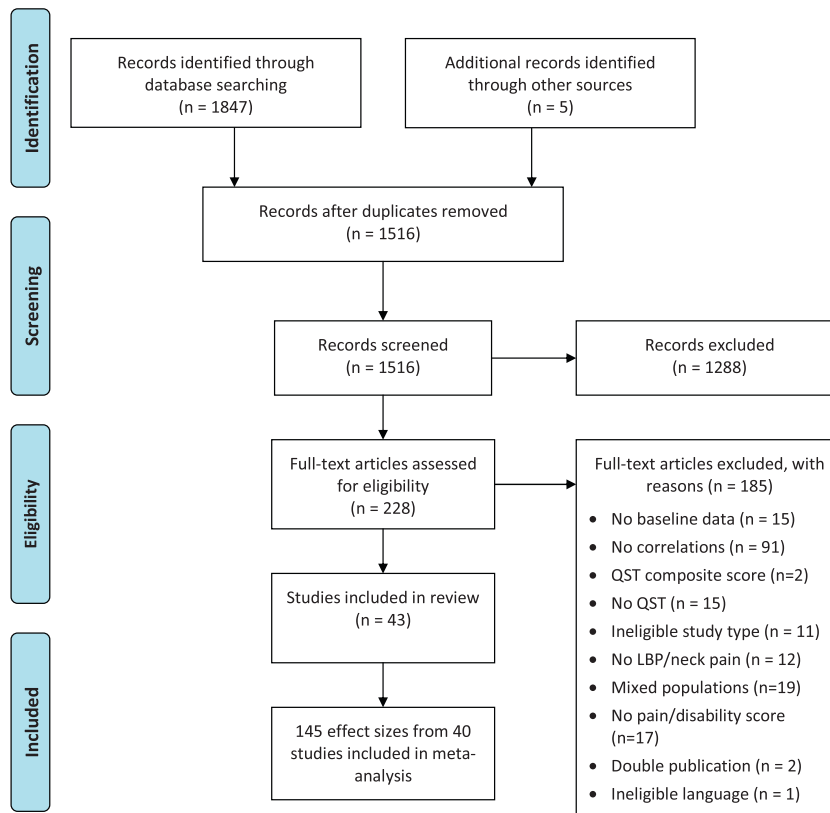


Fig. 1. PRISMA flow chart of the study selection process.

### 3.2.4. Correlation between pain tolerance and disability

The pooled estimate (2 coefficients, 2 studies) for the correlation between pain tolerance and disability was  $-0.32$  (95% CI:  $-0.69$  to  $0.17$ ), indicating that lower pain tolerance was fairly but not significantly correlated with higher disability levels. There was evidence for high heterogeneity ( $P = .04$ ,  $I^2 = 75.4\%$ ).

### 3.2.5. Correlation between temporal summation/wind-up and pain intensity

The pooled estimate (8 coefficients, 5 studies) for the correlation between temporal summation/wind-up and pain intensity was  $0.16$  (95% CI:  $0.02$  to  $0.29$ ), indicating that higher temporal summation/wind-up demonstrated little or zero correlation with higher pain levels. Heterogeneity was not significant ( $P = .34$ ,  $I^2 = 12.1\%$ ).

### 3.2.6. Correlation between FPR and pain intensity

The pooled estimate (4 coefficients, 2 studies) for the correlation between FPR and pain intensity was  $0.25$  (95% CI:  $-0.16$  to  $0.66$ ), indicating that higher intensity ratings (NRS) of the heat stimulus were fairly but not significantly correlated with higher pain levels. Although not significant, there was evidence for moderate heterogeneity ( $P = .34$ ,  $I^2 = 47.6\%$ ).

### 3.2.7. Subgroup analyses

The results of the exploratory subgroup analyses are presented in Tables 1–4. In summary, similar to the overall estimates, the subgroup analyses revealed little or zero correlations for correlations between pain threshold and pain intensity/disability. Regarding the temporal summation/wind-up and pain intensity relationship, the subgroup analysis showed a stronger correlation for the heat-evoked temporal summation/wind-up compared with the pinprick-evoked. Forest plots for the correlations between pain

threshold, pain tolerance, or temporal summation/wind-up and pain intensity/disability by pain condition (LBP, neck pain) are given in Appendix D.

### 3.2.8. Meta-regression

None of the selected predictors was significantly associated with the strength of the correlation coefficients between pain threshold and pain intensity ( $P \geq .44$ ) or pain threshold and disability ( $P \geq .65$ ).

## 4. Discussion

This systematic review and meta-analysis quantified the strength of the relationship between QST measures and pain or disability in people with spinal pain. The main finding from our meta-analysis was that the relationship between pain threshold and pain or pain-related disability was weak. Pain threshold measures explained around 2% of the variance in pain or disability in both neck and low back pain. Furthermore, 95% confidence intervals of the point estimates exclude the possibility of any meaningful correlation. Somewhat stronger correlations were found for the relationship between pain intensity and heat-evoked temporal summation or pain tolerance. Those measures explained around 7% or 9%, respectively, of the variance in pain or disability.

The results of the exploratory subgroup analyses and meta-regression for pain threshold did not provide evidence that the relationships found were moderated by the QST testing site, pain condition, pain type, or type of pain induction stimulus. This means that the relationship was the same whether the QST testing was performed in the primary area of pain or at a remote site. Furthermore, the strength of the relationship did not differ either between people with LBP or neck pain or among those with acute/subacute or chronic pain. Although the correlations seemed to be slightly

**Table 1**  
Summary of correlation coefficients between pain threshold and pain intensity by subgroups.

| Group                 | No. of studies | No. of effect sizes | Sample size | Correlation (95% confidence interval) |
|-----------------------|----------------|---------------------|-------------|---------------------------------------|
| <i>QST site</i>       |                |                     |             |                                       |
| Local                 | 29             | 40                  | 2187        | −0.14 (−0.19 to −0.09)                |
| Remote                | 23             | 32                  | 1390        | −0.15 (−0.20 to −0.10)                |
| <i>Pain condition</i> |                |                     |             |                                       |
| LBP                   | 17             | 40                  | 1709        | −0.13 (−0.18 to −0.08)                |
| Neck pain             | 17             | 32                  | 1823        | −0.16 (−0.21 to −0.11)                |
| <i>Pain type</i>      |                |                     |             |                                       |
| Acute/subacute        | 7              | 12                  | 932         | −0.19 (−0.25 to −0.12)                |
| Chronic               | 27             | 60                  | 2645        | −0.13 (−0.18 to −0.09)                |
| <i>QST modality</i>   |                |                     |             |                                       |
| PPT                   | 28             | 46                  | 2747        | −0.17 (−0.21 to −0.13)                |
| CPT                   | 4              | 8                   | 314         | −0.07 (−0.18 to 0.04)                 |
| HPT                   | 7              | 12                  | 446         | −0.07 (−0.17 to 0.03)                 |
| MPT                   | 2              | 4                   | 130         | −0.08 (−0.26 to 0.10)                 |
| EPT                   | 1              | 2                   | 78          | −0.25 (−0.45 to −0.02)                |

Note: A negative correlation indicates that lower pain threshold was correlated with a higher level of pain.

QST = quantitative sensory testing; LBP = low back pain; PPT = pressure pain threshold; CPT = cold pain threshold; HPT = heat pain threshold; MPT = mechanical pain threshold; EPT = electrical pain threshold.

**Table 2**  
Summary of correlation coefficients between pain threshold and disability by subgroups.

| Group                 | No. of studies | No. of effect sizes | Sample size | Correlation (95% confidence interval) |
|-----------------------|----------------|---------------------|-------------|---------------------------------------|
| <i>QST site</i>       |                |                     |             |                                       |
| Local                 | 22             | 33                  | 1839        | −0.16 (−0.23 to −0.08)                |
| Remote                | 17             | 19                  | 1039        | −0.16 (−0.27 to −0.06)                |
| <i>Pain condition</i> |                |                     |             |                                       |
| LBP                   | 13             | 18                  | 785         | −0.17 (−0.27 to −0.05)                |
| Neck pain             | 16             | 34                  | 2063        | −0.16 (−0.23 to −0.09)                |
| <i>Pain type</i>      |                |                     |             |                                       |
| Acute/subacute        | 6              | 11                  | 593         | −0.24 (−0.33 to −0.15)                |
| Chronic               | 19             | 41                  | 2255        | −0.13 (−0.22 to −0.06)                |
| <i>QST modality</i>   |                |                     |             |                                       |
| PPT                   | 29             | 36                  | 3015        | −0.17 (−0.24 to −0.10)                |
| CPT                   | 5              | 9                   | 439         | −0.22 (−0.34 to −0.09)                |
| HPT                   | 4              | 5                   | 202         | −0.02 (−0.25 to 0.11)                 |
| MPT                   | 1              | 2                   | 46          | −0.01 (−0.30 to 0.30)                 |

Note: A negative correlation indicates that lower pain threshold was correlated with a higher level of disability.

QST = quantitative sensory testing; LBP = low back pain; PPT = pressure pain threshold; CPT = cold pain threshold; HPT = heat pain threshold; MPT = mechanical pain threshold.

**Table 3**  
Summary of correlation coefficients between pain tolerance and pain intensity by subgroups.

| Group               | No. of studies | No. of effect sizes | Sample size | Correlation (95% confidence interval) |
|---------------------|----------------|---------------------|-------------|---------------------------------------|
| <i>QST site</i>     |                |                     |             |                                       |
| Local               | 2              | 2                   | 63          | −0.26 (−0.57 to 0.12)                 |
| Remote              | 7              | 7                   | 203         | −0.32 (−0.49 to −0.11)                |
| <i>QST modality</i> |                |                     |             |                                       |
| CPTol               | 2              | 2                   | 48          | −0.30 (−0.61 to 0.10)                 |
| EPTol               | 1              | 2                   | 78          | −0.12 (−0.44 to 0.23)                 |
| HPTol               | 2              | 2                   | 47          | −0.27 (−0.60 to 0.14)                 |
| PPTol               | 2              | 3                   | 93          | −0.44 (−0.66 to −0.16)                |

Note: All studies involve participants with chronic low back pain. A negative correlation indicates that lower pain tolerance was correlated with a higher level of pain.

QST = quantitative sensory testing; CPTol = cold pain tolerance; EPTol = electrical pain tolerance; HPTol = heat pain tolerance; PPTol = pressure pain tolerance.

higher for pressure pain thresholds, we did not find that the stimulus modality predicted the strength of the relationship.

The results from this study are interesting given the large volume of data pertaining to QST measures in chronic pain conditions. The presence of sensory hypersensitivity has been reported in many chronic pain conditions with decreased pain thresholds as well as pain-related disability often reported in LBP [20,30,55,61],

neck pain [38,79], and whiplash [10,33,66]. Preliminary evidence has suggested that sensory hypersensitivity is particularly common in those with higher levels of pain and disability [11,26,70,71], and accordingly, the results from this review are surprising as a stronger relationship between pain thresholds and pain and/or pain-related disability was expected. The weak relationship indicates that pain intensity or disability is not solely

**Table 4**

Summary of correlation coefficients between temporal summation/wind-up and pain intensity.

| Group               | No. of studies | No. of effect sizes | Sample size | Correlation (95% confidence interval) |
|---------------------|----------------|---------------------|-------------|---------------------------------------|
| <i>QST site</i>     |                |                     |             |                                       |
| Local               | 2              | 2                   | 59          | 0.30 (0.03 to 0.53)                   |
| Remote              | 5              | 6                   | 195         | 0.11 (−0.04 to 0.14)                  |
| <i>QST modality</i> |                |                     |             |                                       |
| TS, heat            | 3              | 4                   | 127         | 0.26 (0.09 to 0.42)                   |
| TS, (WUR), pinprick | 2              | 4                   | 130         | 0.05 (−0.13 to 0.23)                  |

Note: All studies involve participants with chronic low back pain. A positive correlation indicates that higher temporal summation/wind-up was correlated with higher levels of pain.

QST = quantitative sensory testing; TS = temporal summation; WUR = wind-up ratio.

accounted for by the degree of pain sensitivity. It is conceivable that numerous other factors, including pain-related psychological variables, also account for the variability in pain intensity or disability [17]. Previous studies identified variables such as pain catastrophizing, pain self-efficacy, depression, and anxiety as predictors for pain intensity and disability in chronic pain including LBP [50,52,67]. Theoretically this indicates that patients with low levels of hypersensitivity relative to other patients, but still high levels of hypersensitivity compared with pain-free control subjects, can report high pain intensity and disability because of their psychological status or other factors. In summary, even though pain threshold might help to discriminate between groups (pain versus no pain), the ability of pain threshold to predict the intensity of the pain or the severity of disability in patients seems limited. However, the ability of QST to discriminate between groups according to their diagnosis was beyond the scope of our review and is potentially a fruitful area for future research.

QST is a measure of large and small afferent fiber function, depending on the modality used, their respective spinal pathways (spinothalamic and dorsal column), as well as supraspinal centers; the presence of lowered pain thresholds has been considered to reflect sensory gain in these pathways [34,64]. Sensitization is essentially an augmentation of neural signaling resulting in pain hypersensitivity (lowered pain thresholds) [82], which may occur within the central nervous system (central sensitization) or peripheral nervous system (peripheral sensitization). Should lowered pain thresholds be evident at the site of primary pain, sensitization could be local (peripheral) or a combination of both peripheral and central. Should lowered pain thresholds be evident at sites remote from the primary site of pain, then the argument for the presence of central sensitization is stronger. If central sensitization is a key neurophysiologic mechanism underlying chronic musculoskeletal pain and assuming that pain threshold is a valid marker of central sensitization, it is conceivable that the relationship between pain threshold and pain intensity/disability would be at least fair. However, we did not find evidence for such a relationship. A number of explanations exist for the poor relationship found in our review.

One possible explanation for the lack of a relationship may relate to the validity of QST as a marker of sensitization. Because established criteria for determining the presence of central sensitization are lacking [82], care must be taken when interpreting QST findings as reflective of sensitization in the absence of other clinical information. The development of more objective biomarkers and of reliable and valid diagnostic criteria of central sensitization is highly desirable, and would likely aid the evaluation of the validity of QST.

QST represents a method for evoking pain, and is used to examine the presence of pain hypersensitivity. However, evoked pain may not necessarily reflect the clinical experience of pain. In this respect, the results from a recent study by Parks et al. [57] are important to consider. This study outlined differences recorded in cortical responses between evoked and spontaneous pain in

people with osteoarthritis of the knee. In addition to the typical areas of the brain activated during somatosensory nociceptive processing, spontaneous pain, ie, pain experienced by patients without stimulation, engaged the prefrontal limbic structures, ie, the area of the brain more associated with an emotional state, whereas evoked pain did not. This may mean that evoked pain, such as that measured by thermal and mechanical pain thresholds, does not measure the same construct of pain experienced by patients, and may in part explain the finding that pain threshold correlated poorly with measures of pain and pain-related disability in our review.

If we assume that QST is a reasonable measure of pain sensitivity and the presence of lowered pain thresholds accurately reflects the presence of sensitization, the absence of a correlation between lowered pain thresholds and pain/disability may be explained by the fact that in many of the participants in the included studies, central processes did not or did not predominantly contribute to pain hypersensitivity. Results from a recent clinical study involving 464 people with chronic LBP identified 106 (23%) of the participants as having central sensitization as their dominant pain mechanism [69], with the remaining 358 (77%) deemed (clinically) to present with a dominance of nociceptive or neuropathic pain. If the results from Smart et al. [69] are generalizable, it is quite conceivable that the majority of participants in the studies included in this review did not present with clinical manifestations of central sensitization, and as such, a link between sensitization as measured by QST and their pain and /or disability would not necessarily be expected. It would be interesting to investigate the correlation between QST as a measure of sensitization and pain intensity and disability in a subgroup of people who are deemed to have evidence of central sensitization based on valid (clinical) assessment. This would help to ascertain whether QST measures add in any way to the clinical assessment of pain and sensitization.

A strength of this review is that although we only found a small number of studies that reported correlations, we were eventually able to include 43 studies after contacting authors, therefore including as many correlations as possible in the meta-analysis. However, there are several limitations that have to be acknowledged. The majority of studies included in this review used pain threshold. It has recently been suggested that this static QST measure identifies 1 point on a scale of sensations and is thus limited in its capacity to capture the complexity of the pain-processing system [2]. Measures derived from dynamic QST are thought to better capture a sensitized nociceptive system by assessing the temporal and spatial summation as well as descending modulation of pain [2]. In addition, pain magnitude rating for a suprathreshold stimulus allows for the study of suprathreshold pain processing [2]. Indeed, we found a stronger relationship between heat-evoked temporal summation and pain intensity and a trend toward a stronger relationship between magnitude rating (ie, FPR) and pain intensity. However, because of the small number of included studies employing temporal summation or suprathreshold ratings, the

relationship between dynamic QST measures and pain intensity/disability in spinal pain should be ascertained in future studies.

As mentioned before, most of the studies showed moderate heterogeneity. We had too few studies using tolerance, temporal summation, or magnitude rating to formally examine the source of heterogeneity. Furthermore, heterogeneity between trials of pain thresholds could not be explained by meta-regression assessing the effect of the potential categorical predictors QST i.e. testing site, pain condition, pain type, or type of pain induction stimulus. It has to be acknowledged that other differences in methodological features of studies related to sample size, sampling methods, study populations, diversity of QST protocols, and measures of pain intensity and disability might have influenced the strength of the relationship found in our review. For instance, most studies had small sample sizes, only 12 studies had 50 or more and 6 studies had 100 or more participants. Sampling methods were often not described, which hampers appraisal of the generalizability of study findings. Many studies did not provide sufficient details on the QST protocols used, including information on standardization of instructions, training/experience of assessors, or test order. Furthermore, the pain tolerance tests presumably involve more affective/motivational aspects of pain than threshold tests [32], which might affect their reliability.

In conclusion, this systematic review and meta-analysis did not show any meaningful correlations between pain threshold and pain or disability in spinal pain. There may be a number of explanations for this. First, this finding probably reflects that both methods measure different constructs that may not be directly interrelated. Second, assuming that central sensitization manifests itself in pain hypersensitivity that contributes to clinical pain and related disability, our study indicates that pain threshold is either a poor marker of central sensitization or sensitization does not play a major role in the participants' reporting of pain or disability. The reliance on threshold as the only valid measure of central or peripheral sensitization is thus questionable. However, studies using other methods, such as measures derived from dynamic QST or pain magnitude rating, are limited. Future studies are required to elucidate the relationship between tests of suprathreshold pain processing, central integration, or descending control and clinical features of spinal pain.

### Conflict of interest statement

There are no conflicts of interest.

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### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.pain.2013.05.031>.

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