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Comprehensive review

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

Markus Hübscher [a,*], Niamh Moloney [a], Andrew Leaver [a], Trudy Rebbeck [a], James H. McAuley [b], Kathryn M. Refshauge [a]

[a] Faculty of Health Sciences, The University of Sydney, Sydney, New South Wales, Australia
[b] Neuroscience Research Australia and The University of New South Wales, Sydney, New South Wales, Australia

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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.

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

* Corresponding author. Address: 75 East Street, Lidcombe, NSW 2141, Australia. Tel.: +61 2 9351 9013; fax: +61 2 93 51 9601.
E-mail address: markus.huebscher@sydney.edu.au (M. Hübscher).

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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) 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^2; heat/cold: °C. Likewise, the evoked sensory and pain perception had to be reported quantitatively (eg, pressure: kg/cm^2; 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 ρ) 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 ($\geqslant$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