The Modulatory Effect of Quantitative Sensory Testing in Shoulder Pain

A Systematic Review and Meta-Analysis

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Shoulder Pain, Quantitative Sensory Testing, Intervention, Modulation

Background

The underlying mechanisms for shoulder pain (SP) are still widely unknown. Previous reviews report signs of altered pain processing in SP measured using quantitative sensory testing (QST). Evidence suggests that QST might hold predictive value for SP after intervention, yet it is not known whether QST profiles can be modulated in response to different treatments. Therefore, this systematic review and meta-analysis aimed to assess if QST-parameters can be modified by interventions for patients with SP.

Methods

Three databases were searched to identify eligible studies. Eligible studies had a prospective design, with at least one QST variable as an outcome in conjunction with an intervention measured before and after intervention. Studies that involved SP caused by spinal or brain injury and studies looking at combined chronic neck/shoulder pain were excluded.

Results

19 studies investigating SP were eligible for inclusion for this review. Pressure pain threshold (PPT) was the most frequently used QST-parameter investigating local and widespread hyperalgesia. A meta-analysis was performed with data from 10 studies with a total of 16 interventions. Results demonstrated an overall acute effect (<24 hours after intervention) of interventions in favour of local decreased pain sensitivity and of remote decreased pain sensitivity comparing PPTs before and after interventions.

Conclusions

This study demonstrates that interventions such as exercise and manual therapy can modulate PPTs acutely both locally and remotely in patients with shoulder pain. Further research investigating the acute and long-term modulatory ability of these interventions on other QST-parameters is needed in patients with shoulder pain.

Introduction

Shoulder pain is one of the most common reasons for musculoskeletal pain and has a 1-month prevalence of 7-26% in the general population (1). Additionally, shoulder pain is the third most frequent cause of musculoskeletal pain in primary care (2,3). Shoulder pain is prevalent in both the sports active population and in a variation of occupations with physical factors such as work with highly repetitive movement in difficult positions, and work that includes heavy lifting for extensive periods (4). The etiology of shoulder pain can originate from pathologies in the glenohumeral joint, acromioclavicular joint, rotator cuff muscle, joint capsule or other soft tissue in and around the shoulder girdle (4). Studies have found localized and widespread pressure hyperalgesia in subpopulations of patients with shoulder pain, which indicate sensitization of central pain mechanisms (5,6).

Quantitative sensory testing (QST) is a quantifiable method to assess the sensory function of the nervous system and has been utilized to investigate peripheral and central pain mechanisms in patients with various musculoskeletal pain conditions, including shoulder pain (7-10). QST can be assessed using different modalities including mechanical, thermal, tactile and electrical stimuli (11-13). QST protocols have been developed to contain both static measures, such as pain pressure threshold and dynamic measures, such as conditioned pain modulation (CPM) to mechanistically investigate the pain profiles (14,15).

Studies have found a predictive value of QST for pain related outcomes after pharmacological treatments (16,17), surgery (18-20) and exercise-based therapy (21,22) but a recent review highlights that the predictive value of QST is poor to moderate and that it is important to understand factors modulating central pain mechanisms (23).

Preliminary studies have demonstrated that pharmacological interventions such as duloxetine (a serotonin-noradrenaline reuptake inhibitor) can modulate CPM in patients with painful diabetic neuropathies and that ketamine (a NMDA-antagonist) can modulate temporal summation of pain (TSP) in patients with fibromyalgia, but this has yet to be investigated within the field of shoulder pain (24,25). Therefore, this review aims at investigating the modulatory effect of all types of interventions for shoulder pain on QST.

Methods

This systematic review was conducted in accordance with PRISMA guidelines for reporting systematic reviews and meta-analysis (26).

Systematic literature search

The databases PubMed, Embase, and Cochrane Central Register of Controlled Trials were systematically searched by one reviewer with assistance from a research librarian in March 2020. Additionally, reference lists and citation tracking from the included full texts was checked for relevant articles using Google Scholar. Literature searches can be seen in the supplementary material.

Eligibility Criteria

In this review all studies were included that investigated the effect of interventions where QST was used to assess patients with shoulder pain (i.e., traumatic and non-traumatic). Diagnosis such as rotator cuff tears, subacromial pain syndrome (or similar terms such as non-specific shoulder pain, impingement syndrome etc.) and glenohumeral instability were therefore eligible for this review. All types of interventions (e.g. manual therapy, exercise, surgery, acupuncture, taping, pharmacological) were eligible for this review, as multiple interventions are often used to manage shoulder pain and since both surgical (27, 28), pharmacological (29) and non-surgical and non-pharmacological intervention (30) have been found to modulate QST parameters in other chronic pain conditions.

Prospective studies were considered eligible for inclusion if they contained data from at least one well described QST paradigm (e.g., thermal and mechanical stimuli, CPM) and an intervention in patients with shoulder pain (systematic reviews and meta-analysis, pilot-studies and case-report studies were not included). Studies that included participants with shoulder pain caused by injuries to the spinal cord or brain (i.e., paraplegia, hemiplegia, quadriplegia/tetraplegia or stroke) or studies who included patients with combined neck and shoulder pain (or similar disorders) and/or pain originating from neurological diseases or cancer were excluded from this review. Animal studies or any studies that investigated the pain by experimental induced methods were excluded. Papers were not excluded due to publication year but was limited to literature in English.

Review Process

A single investigator (KDL) imported all studies identified by the search strategy to Endnote, version X9 (Thomson Reuters, Philadelphia, PA, USA). After importing all studies, they were cross referenced, and duplicates were deleted. The remaining were then divided between KDL and JBBT and screened for eligibility, firstly after read though of title or abstract secondly after full-text reading. If any disagreements would occur between KDL and JBBT, the senior author (KKP) was consulted and provided a final decision of inclusion or exclusion.

Data Extraction

The following study characteristics were extracted: Publication details (author, year, and study design) characteristics of the participants (shoulder pain condition, gender, age and number of participants allocated to each intervention), outcome measures (e.g. QST parameter) and a short summary of the main findings from each paper was extracted. The primary outcomes baseline and post-intervention measures were extracted from the included articles by the first reviewer (KDL).

Data were first entered into Excel and then into RevMan (Review Manager v5.4, The Nordic Cochrane Centre, Copenhagen, Denmark) for meta-analysis.

Quality Assessment

The quality of each study was evaluated using the risk of bias tool: QUality In Prognostic Studies (QUIPS) from the Cochrane Handbook for Systematic Reviews of Interventions (27). QUIPS consists of four domains: Issues to consider for judging overall rating of “Risk of Bias”; Study Methods and Comments; Rating Reporting, and Rating of “Risk of Bias” under which each study is evaluated through 34 items listed in six categories with the headlines: Study Participants; Study Attrition; Prognostic Factor Measurement; Outcome measurement; Study Confounding, and Statistical Analysis and Reporting. Each item was scored as low risk, unclear risk, and high risk and judged from the “Criteria for judging risk of bias” from the Cochrane Handbook (31). Physiotherapy Evidence Database quality scale (PEDro scale) was used to evaluate the quality of the interventions used in the included randomized control trials (32). The PEDro scale consists of 11- items, and score <7/10 equals high quality, a score between 4-6/10 equals moderate quality and a score >4 equals low quality. The methodological and the overall quality of the included studies were assessed by two reviewers (KDL and JBBT).

Data Analysis

Findings were summarized narratively in tables to enable an overview of the modulatory effect of different interventions after different durations of treatment periods and QST modality. The data were analyzed based on condition, study design, number of participants, intervention(s), intervention duration and outcome/QST parameter(s). Data were narratively synthesized with interventions being categorized as acute (< 24 hours after intervention), sub-acute (24 hours to 3 months) or long-term (>

3 months follow-up) to provide an overview. Meta-analysis was conducted with focus on pre- and post-intervention QST parameters for all data combined and for the subcategories for intervention length. If data were available from two defined subgroups of patients, but with no statistical difference in outcome measures, data were pooled following the Cochrane Handbook Guidelines (31). The overall effect size (Z statistics) was calculated for post-intervention versus baseline and expressed as standardized mean difference (SMD), using an inverse variance random-effects (to account for between-study heterogeneity) model, for each intervention (independent if two or three interventions were tested considering that none of the included interventions in the meta-analysis had overlapping patient populations). Effect sizes (SMD) were calculated for all studies and interpreted as small (SMD < 0.20), medium (SMD = 0.21-0.79), and large (SMD > 0.80). The heterogeneity between comparable studies was assessed by between-study variance (Chi^2) and inconsistency (I^2). If Chi^2 test was < 0.1, statistically significant heterogeneity was present, and if I^2 was above 60%, substantial heterogeneity was considered present.

Results

The systematic literature search identified 876 papers. Citation tracking revealed three additional records. Duplicates were then removed, resulting in 775 papers, and 662 papers were excluded based on screening of titles and abstracts. Based on the full-text assessment of 113 studies, 95 studies were excluded, and 19 studies were identified and included in the final analysis (33-51) (Figure 1). The 19 studies consisted of 11 randomized control trials and eight prospective cohort studies. All the studies included examined either subacromial impingement syndrome (or similar terms such as subacromial pain syndrome) or chronic shoulder pain. Pressure pain threshold (PPT) was the most used QST assessment and was assessed in 15 out of 19 (78%) of the included studies (33-44,49,50); CPM was assessed in three out of 19 (15%) studies (47,50,51); heat pain threshold (HPT) was assessed in two out of 19 (10%) studies (37,51); and temporal summation of pain (TSP) was assessed in 2 studies

(10%) (37, 46). Eleven different treatment strategies were used, with exercise as the most frequent (55%). Findings from all studies are summarized in table 1.

Figure 1 here

Table 1 here

Methodological Quality Assessment

An agreement of 90% was found between raters after evaluating the risk of bias in the studies with Cochrane's QUality In Prognostic Studies-tool (QUIPS) (27). All discrepancies were resolved using the senior author (KKP). QUIPS data is shown in table 2. Fifteen studies were rated as being of low risk of bias, three studies were rated as being of moderate risk of bias and one study was rated as being of high risk of bias. An agreement of 100% was found between raters on the PEDro scale assessing the respective interventions used in the included RCT studies. Ten RCT studies (35-40,42,44,48,49) were rated as having low risk of bias and the remaining two RCT studies were rated as having high risk of bias (34,45), see table 3.

Table 2 here

Table 3 here

Narrative Synthesis

The Modulatory Effect on QST

Acute modulatory changes of QST (<24 hours) were assessed in 15 studies (<24hrs) (34-40,42-45,48,49), four studies looked at the sub-acute changes of QST (>24 hours - <3 months) (33,41,49) and six studies investigated the long-term changes of QST (>3 months) (33,38,46-48,51).

The Acute Modulatory Effect on QST (<24hrs)

Pressure Pain Threshold - Local

PPTs were reported in all studies investigating the acute modulatory effect of treatment on QST. Ten out 15 studies (9 different treatment strategies) reported a local significant increase in PPTs after acute interventions. A local increase in PPTs were demonstrated after TENS, heat therapy and a combination of the two (34), manipulation to the cervical spine (37), shoulder exercises (36,42,45), exercise of non-painful muscles (43), manual therapy (36,44,48). Kamali et al. found a local increase in PPT after dry-needling and Calvo-Lobo et al. found significant changes after treatment with dry needling in the active and latent triggerpoint group and in the active triggerpoint only group (35,39). No acute modulatory effects were found after taping in conjunction with mobilization (49) and manipulation (40). Ultrasound-guided percutaneous electrolysis in combination with exercise and manual therapy did not demonstrate significant changes in PPTs compared to exercise and manual therapy (38).

Pressure Pain Threshold – remote

Remote locations for the measurement of PPT was reported in 7 studies (35-38,42-44), in which five studies (9 different treatment strategies) reported a significant increase in PPTs after acute interventions. Significantly increased PPTs were found at the m. extensor carpi radialis brevis after dry-needling (35), at m. tibialis anterior after cervical thrust manipulation or shoulder thrust manipulation or exercise (37), at m. quadriceps and m. tibialis after either a physical task or an emotional task (42), at the m. tibialis anterior after mobilization (44), and at the m. tibialis anterior after ultrasound-guided percutaneous electrolysis in combination with exercise, manual therapy or exercise, and manual therapy only (38). No change in PPTs were reported bilaterally at m. tibialis anterior after either exercise only or exercise and manual therapy (36), or at the contralateral trapezius after thoracic manipulation or sham thoracic manipulation. Lannersten and Kosek found that an acute bout of exercise of the painful area did not lead to an increase in PPT at remote sites, but that exercise of a non-painful area (i.e. m. quadriceps) lead to an increase in remote PPT (43).

Temporal Summation of Pain

The acute modulatory effect of temporal summation of pain (TSP) was reported in Coronado et al., which found that cervical manipulations and exercise significantly decreased TSP (37).

Sub-Acute Modulatory Effect on QST (>24 hours <3 months).

Pressure Pain Threshold

The sub-acute modulatory effect of PPTs was reported in four studies (33,39,41,49) with three studies reporting significant increases in PPTs after treatment. One study reported a local increase in PPTs after three weeks of high-intensity laser therapy in combination with exercise and also reported an increase in PTTs following sham-laser and exercise (33). Another study reported a local increase of PPTs following three days of dry needling (39). Similarly, a study reported a local increase of PPTs after 3-4 days of dry needling but demonstrated no effects on the contralateral shoulder (41). Finally, one study reported no effect on PPTs of mobilizations with movement in conjunction with tape after 7 days of intervention (49).

Long Term Modulatory effect of QST (>3 months)

Pressure Pain Threshold

The long-term modulatory effect of interventions on PPT was reported in two studies (33,38) with both studies reporting significant increases after treatment. One study found increased PPTs after three months of high-intensity laser therapy in combination with exercise and reported an increase in PPTs after sham-laser and exercise (33). Another study found increased localized PPTs in a group receiving ultrasound-guided percutaneous electrolysis in combination with exercise and manual therapy for three months and increased localized PPTs in a group receiving manual therapy and exercise (38).

Temporal Summation of Pain

TSP was assessed in one study, which found no significant long-term modulatory effect after arthroscopic subacromial decompression (46).

Heat Pain Threshold

Heat pain threshold was reported in one study with no long-term modulatory effect (three months) after arthroscopic surgery in both the group which improved in pain and the group which did not (51).

Conditioned Pain Modulation

Conditioned pain modulation (CPM) was reported in three studies (47,50,51). Simon et al. separated participants into low risk and high-risk groups of chronic postoperative pain prior to arthroscopic surgery and demonstrated increased CPM after surgery in the low-risk group, but not in the high-risk group (47). Another study found no significant modulatory effect on CPM, three months after arthroscopic surgery (50). Valencia et al. reported no significant change in CPM from baseline to 3 months in an improved pain group and a decreased effect in a non-improved pain group after arthroscopic surgery (51).

Meta-analysis

PPT – Local and remote effects

The acute effects (<24hrs) on local and remote PPT were analyzed on pooled data from 7 randomized control trials with a total of 16 interventions and 5 cohort studies with a total of 11 interventions. There was an overall effect in favor of local decreased PPTs (SMD = -0.38; 95%CI: -0.54, -0.23, $p < 0.0001$; Figure 2). Similarly, an overall effect in favor of remote decreased PPTs were found (SMD

= -0.33; 95%CI: -0.6, -0.06, p = 0.02; Figure 3). A meta-analysis on the subacute and remote long-term data was not possible due to lack of available studies.

Figure 2 here

Figure 3 here

Conditioned pain modulation effect at 3 to 6 months follow-up

Pooled data from three eligible prospective cohort studies investigating the effect of surgery on shoulder pain demonstrated no significant effect on CPM effect at 3 months follow-up (SMD = 0.01; 95%CI: -0.26, 0.29, p = 0.94, Figure 2). Likewise, data from 2 eligible prospective cohort studies demonstrated no significant effect of surgery on CPM effect after 6 months (SMD = -0.09; 95%CI: -0.39, 0.22, p = 0.58; Figure 3). Only one study assessed the CPM effect 12 months after surgical intervention, and a meta-analysis was therefore not performed.

Temporal summation of pain and Heat Pain Threshold

TSP and HPT were reported in separate, single studies and were therefore not included in the meta-analyses.

Heterogeneity in the compared studies

For the acute local and remote PPT, no significant heterogeneity was found for local PPT (χ^2 (10) = 18.9, I^2 = 21%, p = 0.21) and substantial heterogeneity was found for remote PPT (χ^2 (10) = 25.31, I^2 = 60%, p = 0.005). For the remote PPT, the majority of this heterogeneity can be attributed to true variance between study results, as expected given the known heterogeneity in study sample sizes, muscle choice, and protocols used. Substantial heterogeneity was found for the CPM effect (I^2 = 70%,

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p = 0.04) at 3 months and near substantial at 6 months (I^2 = 58%, p = 0.12), but not acutely (I^2 = 0%, p = 0.82).

Discussion

This systematic review synthesized evidence from 19 studies on the modulatory effect on QST of different interventions. The narrative review identified significantly increased PPTs in local (10/15 studies) and widespread (5/7 studies) sites to acute interventions, increased PPTs in local sites (3/4 studies) to subacute interventions and increased PPTs in local sites (1/2 studies) to long-term interventions. The meta-analysis demonstrated an overall effect on local and remote PPTs favoring decreased pain sensitivity to acute interventions. For other QST-parameters, mixed results were found and only one out of three studies were suggestive of an increased long-term CPM effect after intervention whereas one out of two studies suggested that intervention could decrease TSP acutely.

The Modulatory Ability of QST

It seems evident that some patients with chronic pain are more pain sensitive than others (19,52,53). Studies suggest a link between QST and e.g. development of chronic postoperative pain (18, 54-57) or responses to pharmacological interventions (17,24,29,58), although other studies find no association (23). It is currently not clear why some patients are more pain sensitive than others but factors such as longer pain duration (59), higher pain intensities (52,60), high levels of pain catastrophizing (61,62), prolonged use of opioids (63) or poor sleep (64,65) may affect pain sensitivity. It is hypothesized that treatments targeting some of these mechanisms might reduce pain sensitivity. Some studies have demonstrated that a reduction in clinical pain intensity after e.g. total hip (28) or knee (27) arthroplasty leads to normalization of CPM and pressure pain thresholds after 6-12 months. Similarly, a recent study demonstrated that a five weeks upper trapezius eccentric training program decreased clinical pain and improved PPTs and CPM in females with neck and shoulder pain (66). The current review indicates that short- and long-term pain relief might improve PPTs the evidence supporting modulations of HPT, TSP and CPM is lacking for patients with SP.

Quality assessment

In this systematic review, the included studies overall demonstrated a low risk of bias measured using the QUIPS-tool and the included RCT studies showed an overall low risk of bias measured using the PEDro scale. Inadequate description of the source population, lack of assessor blinding and adjusting for confounders were among the most common reasons for methodological compromise. Lack of blinding was a common bias often caused by the difficultness of blinding due to the methodological nature of some of the different interventions (e.g., exercise or manual therapy). Despite this, the lack of blinding might hamper the trustworthiness of the findings and questions the specificity of the effects of the different interventions.

Clinical implications

The use of QST in clinical trials has increased over the last decade and accumulating evidence suggests that patients with chronic pain are pain sensitive when compared to healthy age- and gender-matched subjects (5). Studies have demonstrated that pain relief is associated with a normalization of QST parameters (24,27,28), but recent evidence does suggest that this is not always the case (18,58), suggesting that normalization of QST parameters is independent of clinical pain intensities. Emerging evidence suggests that proxy assessments for central pain sensitization (such as widespread hyperalgesia, TSP and CPM) might hold predictive value for e.g. surgical (19, 54-57, 67), pharmacological (16, 17, 58, 68) and exercise-based (21, 22) therapies and therefore pretreatment modulation of QST parameters is hypothesized to lead to better treatment outcomes. The current systematic review and meta-analysis provide evidence that some treatments might normalize QST parameters and future research should combine QST modulating treatments with standard care to investigate if this yield better treatments outcomes for patients with chronic pain.

Limitations

This study did not include studies from other languages than English, and it is therefore possible that relevant studies have been excluded. The current meta-analysis was conducted to test whether the included interventions affected the primary outcomes, but not whether one was more effective than the other. Therefore, a baseline and post-intervention effect size was calculated for each independent intervention and aggregated in the overall meta-analysis. The meta-analysis is limited by the lack of studies investigating central pain mechanisms such as TSP and CPM and therefore future research should identify if these factors are modifiable in patients with SP.

Conclusion

This systematic review and meta-analysis provides preliminary evidence for a modulatory ability of localized and widespread pressure hyperalgesia after pain relieving interventions in patients with shoulder pain. This systematic review and meta-analysis were limited by the lack of studies investigating central pain mechanisms and therefore future research should identify if these are modifiable in patients with shoulder pain.

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Conflict of interest

The authors have no conflicts of interest to declare.

Informed consent

Not applicable.

Ethical approval

Not applicable.

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Table Legends

Table 1: Summary

Table 2: QUIPS

Table 3 - Physiotherapy Evidence Database appraisal tool (PEDro)

Figure Legends

Figure 1: Flow diagram of included studies.

Figure 2: Meta-analysis results of localized and remote pressure hyperalgesia in people with subacromial pain syndrome. CI = confidence interval; PPT = Pressure Pain Threshold.

Figure 3: Meta-analysis results of conditioned pain modulation in people with subacromial pain syndrome. CI = confidence interval; CPM = conditioned pain modulation.

Tables

Table 1: Summary

Summary of Findings

Reference	Condition	Study design	Participants (n)	Intervention (duration)	Outcome (QST)	Main findings
Aceituno-Gómez 2019	SPS	Control trial with alternate allocation	46	HILT and ET (3 weeks)	PPT	High-intensity laser therapy + exercise is not better than exercise alone to improve PPTs measured after 3 weeks.
Başkurt 2006	SPS	RCT	92	TENS and Heat Therapy (< 24 hours)	PPT	No significant difference in PPT was found before and after TENS and Heat Therapy compared to a control group.
Calvo-Lobo 2018	SPS	RCT	66; 23 m; 43 f; >65 yrs	Dry needling in active and latent TrP or only active TrP (1 week)	PPT	Both groups experienced an increase in PPTs after intervention, but a significant difference was found in favor of the active+latent TrP-group. This was the case immediately after intervention and after one week.
Camargo 2015	SPS	RCT	46; 24 m; 22 f >18 yrs	ET and MT or ET alone (4 weeks)	PPT	Local PPTs, but not remote PPT, improved in both groups after 4 weeks of intervention. There was no significant difference in improvement across groups.
Coronado 2015	SPS	RCT	78; 42 m; 36 f; 18-65 yrs	Cervical thrust manipulation and ET (2 weeks)	PPT & HPT	Both groups experienced an increase in PPT and HPT after intervention, but no significant difference between groups were reported.
de Miguel Valtierra 2018	SPS	RCT	50; 23 m; 27 f; 18-65 yrs	MT + ET + Ultrasound guided Electrolysis (5 weeks)	PPT	US-guided percutaneous electrolysis, manual therapy, and exercise did not provide significant differences in pressure pain sensitivity compared with control group.
Kamali 2019	Unilateral SIS	RCT	40; 20 m; 20 f; 18-60 yrs	Dry Needling in Upper Trapezius MTrP (< 24 hours)	PPT	No significant effect on PPTs was found after dry needling in either muscles.
Kardouni 2015	SPS	RCT	45; 22 m; 23 f; 18-60 yrs	Thoracic spinal manipulative therapy or sham manipulation (< 24 hours)	PPT	No significant differences between groups in pre-to post-treatment changes in PPT was reported. Similarly, no differences was found in PPT within groups.
Koppenhaver 2016	Unilateral subacromial syndrome	RCT	57	Dry needling to bilateral infraspinatus muscles (< 24 hours, 3-4 days after)	PPT	PPT and ROM significantly increased 3–4 days, but not immediately after dry needling only in the symptomatic shoulder.
Kuppens 2015	SPS	RCT (cross-over)	24; 10 m; 14 f; 18+ yrs	Isometric exercise (< 24 hours)	PPT	Increase in PPTs in the shoulder region following physical task was reported, but not following emotionally stressful task.

Lannersten 2010	Unilateral Shoulder Myalgia	Case-control	20 (+20 healthy)	Isometric exercise (< 24 hours)	PPT	Patients with shoulder pain showed lower PPTs locally, but not remotely, compared to healthy controls. Exercise of an remote muscle increased PPTs, but exercise of local muscles did not increase PPTs in patients with shoulder myalgia.
Lluch 2018	Chronic shoulder pain	RCT	31; 18 m; 13 f; 18-60 yrs	Mobilization (< 24 hours)	PPT	PPT in the affected shoulder increased significantly following both the treatment and manual contact conditions. Shoulder AP joint mobilization also increased PPT at distal, non-painful site.
Persson 2003	Unilateral chronic shoulder pain	RCT	19	Isometric exercise (< 24 hours)	PPT	Subjected to a static endurance test of the shoulder muscles on the most painful side, a long-standing decreased sensitivity to pressure pain was found, particularly on the activated side similar to those found in a healthy group.
Simon 2016	shoulder pain, musculoskeletal dysfunction	Prospective Cohort Study	179	Arthroscopic surgery (3 and 6 months)	TS	Older adults had higher movement-evoked pain intensity and increased temporal summation at three months compared to young and middle-aged adults, but not at six months.
Simon 2019	shoulder pain eligible for shoulder surgery	Prospective Cohort Study	148	Arthroscopic surgery (3, 6, and 12 months)	CPM	Low-risk group had a similar CPM response after 12 months compared to baseline. The high-risk subgroup demonstrated decreased CPM response when compared to baseline.
Teys 2008	SPS	RCT (cross-over)	25; 15 m; 10 f; 18+ yrs	Mobilization (< 24 hours)	PPT	Significant and clinically improvements in PPT occurred immediately after post treatment, which was significantly higher compared to sham and a control group.
Teys 2013	Pain in antero-superior aspect of one shoulder	RCT (cross-over)	30	Mobilization, Taping (< 24 hours, 24 hours and 1-week)	PPT	No significant effect on PPTs were found after either intervention.
Valencia 2013	SPS	Prospective Cohort Study	324	Surgery (3 months)	CPM;	CPM response were present both before and after surgery. This response was lower three months after surgery compared to baseline. The stability of CPM was differed by sex.
Valencia 2014	SPS	Prospective Cohort Study	78	Surgery (3 months)	TSP CPM	Surgery showed no significant changes on CPM in either the pain-improved group or the pain-unimproved group after three months.

Table 2: QUIPS

QUality **I**n **P**rognostic **S**tudies (QUIPS)	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis	Overall Risk of Bias
Aceituno-gómez 2019	Low	Low	Low	Low	Moderate	Low	Low
Baskurt 2006	Moderate	High	High	High	High	High	High
Calvo-lobo 2018	Low	Moderate	Low	Low	Moderate	Low	Moderate
Camargo 2015	Low	Low	Low	Low	Low	Low	Low
Coronado 2015	Moderate	Low	Low	Low	Low	Low	Low
de Miguel Valtierra 2018	Low	Low	Low	Low	Low	Low	Low

Kamali 2019	Low	Low	Low	Low	Moderate	Moderate	Moderate
Kardouni 2015	Low	Low	Low	Low	Low	Low	Low
Koppenhaver 2016	Low	Low	Low	Moderate	Moderate	Low	Moderate
Kuppens 2016	High	Low	Low	Low	Moderate	Low	Low
Lannersten 2010	Moderate	Low	Low	Low	Low	Low	Low
Lluch 2018	Low	Low	Low	Low	Low	Low	Low
Persson 2003	Low	Low	Low	Low	Low	Low	Low
Simon 2016	Low	Low	Low	Low	Low	Low	Low
Simon 2019	Low	Low	Low	Low	Low	Low	Low
Teys 2008	Low	Low	Low	Low	Low	Moderate	Low
Teys 2013	Low	Low	Low	Low	Low	Moderate	Low
Valencia 2013	Low	Low	Low	Low	Low	Low	Low
Valencia 2014	Low	Low	Low	Low	Low	Low	Low

Table 3: PEDro

Table 3 - Physiotherapy Evidence Database appraisal tool (PEDro) Legend: 1 = yes; 0 = no

Reference/Item	1	2	3	4	5	6	7	8	9	10	11	Total
Baskurt 2006	RCT	1	0	1	0	0	0	1	1	0	0	4
Calvo-lobo 2018	RCT	1	1	1	0	0	1	1	1	1	1	8
Camargo 2015	RCT	1	1	1	0	0	0	1	1	1	1	7
Coronado 2015	RCT	1	1	1	0	0	1	1	1	1	1	8
de Miguel Valtierra 2018	RCT	1	1	1	0	0	1	1	1	1	1	8
Kamali 2019	RCT	1	0	1	0	0	1	1	1	1	1	7
Kardouni 2015	RCT	1	1	1	0	0	1	1	1	1	1	8
Kuppens 2016	RCT	1	0	1	0	0	1	1	1	1	1	7
Lluch 2018	RCT	1	1	1	1	0	1	1	1	1	1	9
Persson 2003	RCT	1	0	0	0	0	0	0	0	1	1	3
Teys 2008	RCT	1	1	1	1	0	1	1	0	1	1	8
Teys 2013	RCT	1	1	1	0	0	1	1	1	1	1	8

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Figure 1: PRISMA Flowchart

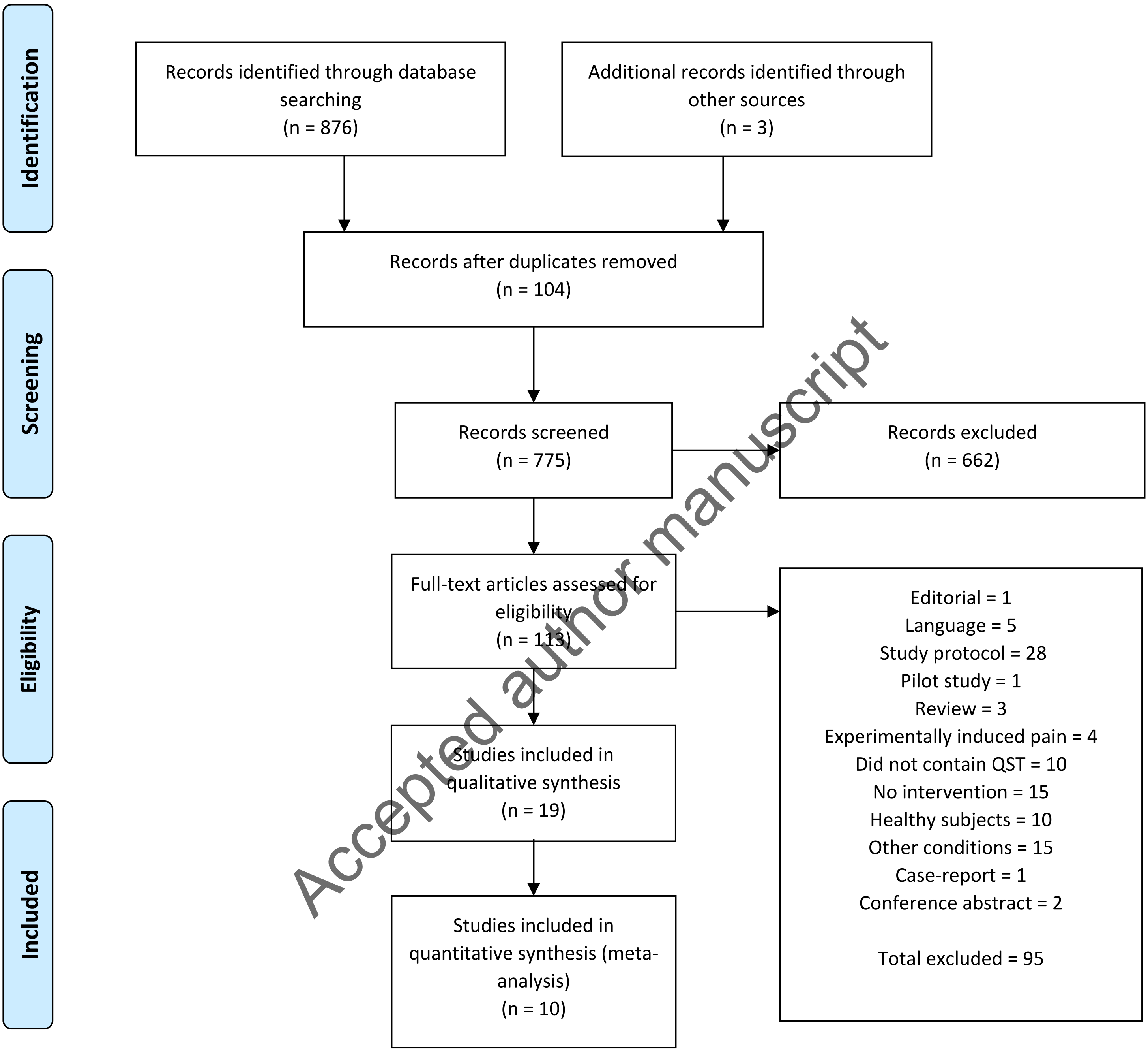

Figure 2:

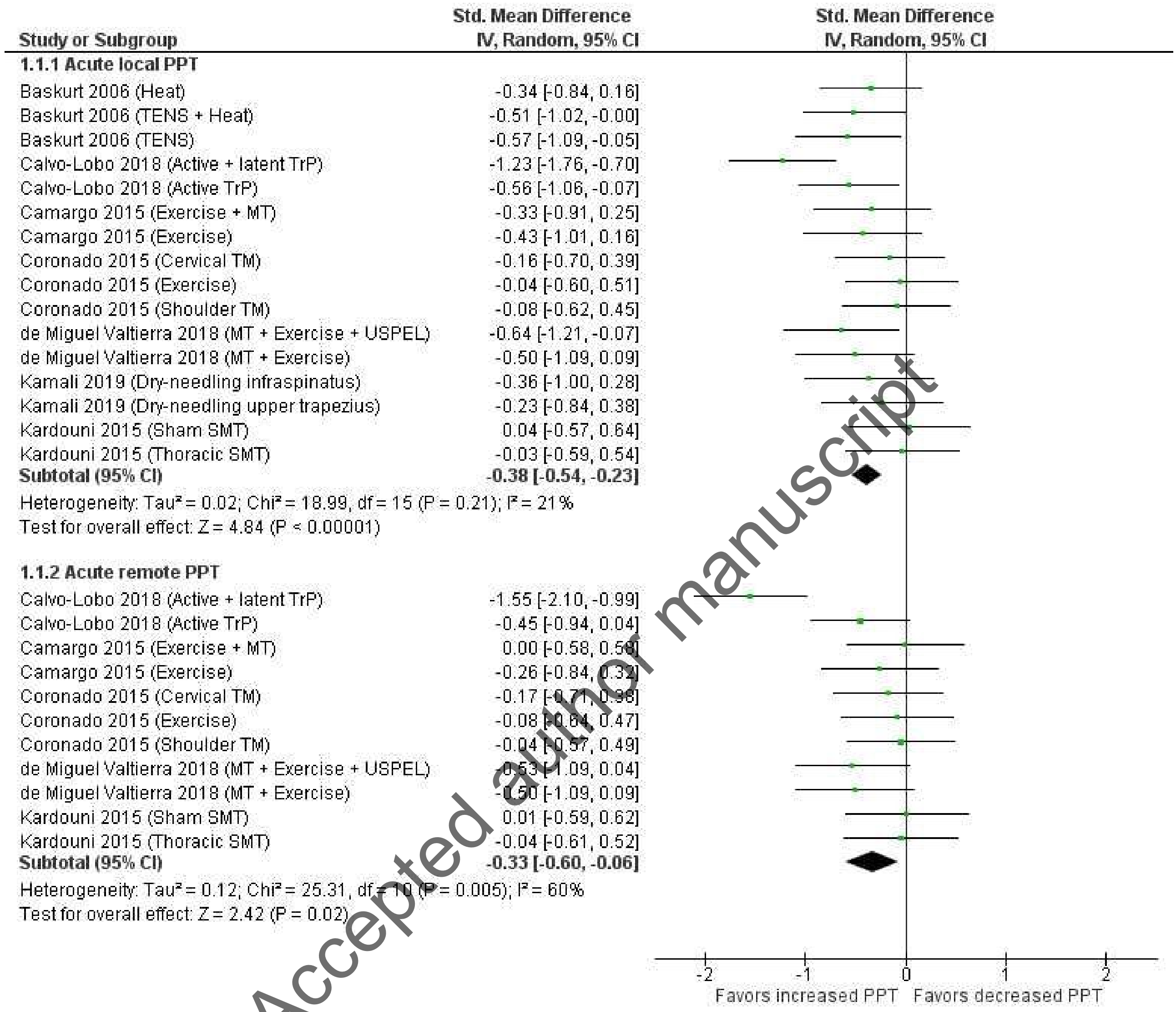

Figure 3: