

## Critical Review

# Is Tactile Acuity Altered in People With Chronic Pain? A Systematic Review and Meta-analysis

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**Abstract:** Impaired tactile acuity in people with chronic pain conditions has been suggested to reflect altered cortical representation of the painful body part, and treatments that aim to improve tactile acuity in these conditions have shown clinical benefit. Whether abnormalities in tactile acuity are a consistent feature of chronic pain remains largely unknown. The aim of this review was to systematically evaluate the literature and use meta-analysis to establish whether tactile acuity is altered in people with chronic non-neuropathic pain. We systematically searched the literature for studies that investigated tactile acuity in people with chronic non-neuropathic pain and compared it to an appropriate control group. Sixteen studies, reporting data from 5 chronic pain conditions, were included. Data were available for 18 chronic pain populations (n = 484) and 15 control populations (n = 378). Our results suggest that tactile acuity is diminished in arthritis, complex regional pain syndrome, and chronic low back pain but not in burning mouth syndrome. The strength of the available evidence is weakened by somewhat inconsistent results and the high risk of bias observed in all of the included studies.

**Perspective:** This systematic review synthesizes the evidence for tactile acuity deficits in people with chronic non-neuropathic pain. The findings suggest that tactile acuity deficits may be characteristic of chronic pain. That tactile acuity training may benefit those with chronic pain disorders suggests that clinical trials may be warranted.

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**Key words:** Tactile acuity, 2-point discrimination, chronic pain, sensory training, reorganization.

Tactile acuity refers to the precision with which we can sense touch,<sup>18</sup> and this precision is thought to be impaired in some chronic pain conditions.<sup>48</sup> However, these impairments cannot be explained by deficits in tactile detection<sup>45,68</sup> or transmission<sup>63</sup> and thus

are thought to reflect cortical changes, including a functional reorganization of the response profile of neurons in the primary somatosensory cortex (S1).<sup>17,39,64</sup> Discriminative ability is dependent on the integrity of S1<sup>12</sup>; hence, in some chronically painful conditions, cortical reorganization appears to manifest as reduced tactile acuity at the affected body region. Whether tactile acuity deficits and cortical reorganization characterize all pain conditions remains largely unknown.

This is important because treatments that aim to improve tactile acuity have shown clinical benefit in a number of chronic pain conditions.<sup>16,46,47,69,70</sup> There seems to be a growing view that tactile acuity deficit is a generic finding in chronic pain,<sup>48,65</sup> irrespective of pathology or condition. If so, tactile acuity training might have a greater generic applicability than has

Supplementary data accompanying this article are available online at [www.jpain.org](http://www.jpain.org) and [www.sciencedirect.com](http://www.sciencedirect.com).

M.J.C. and C.B. are supported by an Australian post-graduate award. G.L.M. is supported by the National Health and Medical Research Council of Australia ID 1061279. This study was supported by National Health and Medical Research Council of Australia Project Grant ID 1008017.

All authors report no conflicts of interest.

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1526-5900/

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<http://dx.doi.org/10.1016/j.jpain.2014.06.009>

currently been demonstrated. Despite this growing interest, there has been no attempt to systematically synthesize the evidence of tactile acuity deficits in chronic pain.

We aimed to systematically evaluate the literature and use meta-analysis to establish whether tactile acuity is consistently altered in people with chronic pain. We focused our review on non-neuropathic pain conditions, as peripheral lesions of the somatosensory pathways may disrupt the transmission of tactile stimuli from the periphery and thus account for diminished acuity evident in neuropathic pain conditions.<sup>26,57,62</sup> Primarily, we sought to determine whether tactile acuity is altered at the site of pain and/or at regions remote from the site of pain. Our secondary aims were to determine whether deficits in tactile acuity relate to pain intensity or to the duration of pain.

## Methods

A systematic review of the peer-reviewed scientific literature was undertaken to locate studies that reported tactile acuity data for people with chronic pain. A review protocol was designed a priori in accord with the *Cochrane Handbook for Systematic Reviews*<sup>24</sup> and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>44</sup> guidelines.

## Data Sources

Candidate studies were identified in June 2013 via a computer search of online bibliographic databases (AMED, CINAHL, Cochrane Library, Embase, Medline, PsycINFO, Scopus, and Web of Science). Each database was searched separately from its inception, and the search string proximity operators and expanders were appropriately customized for each database (see [Supplemental Information](#) for the Medline search string). No restrictions were placed on the language of the articles or the publication date. All duplicates were removed.

## Study Selection

All titles and abstracts (where available) were initially screened independently by 2 reviewers (M.J.C. and C.B.) to identify eligible articles. The full-text articles of the potentially relevant studies were retrieved and reviewed independently by the same pair of reviewers. Study eligibility was compared at each stage and any discrepancies were resolved by discussion between the 2 reviewers; if agreement could not be reached, a third reviewer (N.E.O.) would arbitrate.

Studies were included if they potentially reported tactile acuity data on a population of chronic pain patients. Studies were excluded if tactile acuity data were not reported for a definable chronic pain group (pain persisting for 3 months or longer<sup>42</sup>); control data (from a separate control group or the unaffected side) were not reported; the sample included people diagnosed with a central neurologic disorder (eg, stroke, multiple sclerosis), demonstrable nerve injuries (includes nerve compression injuries diagnosed electrophysiologically),

or repairs; or the presented data were duplicated from an existing study. The reference lists of all relevant studies were examined and cross-referenced to identify additional studies.

## Outcome Measures

Measures of tactile acuity were the primary outcomes of interest in this review. Comparable measures included tests of 2-point discrimination, tactile spatial localization, and grating orientation tasks. Comparisons of graphesthesia were not considered because they are task performance based rather than distance based. Secondary outcome measures were pain duration and pain intensity (eg, visual analog scale, numerical rating scale [NRS], McGill Pain Questionnaire [MPQ]).

## Risk of Bias Assessment and Data Extraction

Two reviewers (M.J.C. and C.B.) independently assessed the included studies for risk of bias. The form used was based on the STROBE statement<sup>66</sup> and relevant items for case-control study designs from the Cochrane Collaboration's tool for assessing bias (see [Supplemental Information](#)).<sup>4,24</sup>

Data extraction was completed independently by the 2 reviewers (M.J.C. and C.B.) using a customized data extraction sheet. The data extraction sheet was piloted on several studies before the commencement of the search. The following descriptive data were extracted from each included study: age, gender, sample size, chronic condition, region of pain, region assessed, pain intensity, pain duration. Extracted outcome measures were mean (standard deviation [SD]) tactile acuity, assessment protocol, assessment tool, body region of pain (for the patient group), body region assessed, and any association data comparing tactile acuity and pain intensity and/or pain duration. Reviewer differences were resolved through discussion; if an agreement could not be reached, a third reviewer (N.E.O.) would arbitrate.

The authors of the included studies were contacted to clarify the details of their study and to request raw data, which included measures of pain intensity and/or pain duration. Raw data were entered into SPSS Statistics (v21.0.0.0; IBM Corporation, New York, NY). Tactile acuity data were entered in millimeters, and pain duration data were entered in months.

## Data Analysis and Synthesis

### Comparing Tactile Acuity Between People With Chronic Pain and Controls

Studies that compared the tactile acuity of people with chronic pain to the tactile acuity of controls were first split into 2 groups: studies that compared tactile acuity assessed at the painful region and studies that compared the tactile acuity at a site remote from the painful region. The study data were then subgrouped by chronic pain condition (determined a priori) for comparison. Quantitative analysis was conducted using Review manager software (Revman v5.2.5; The Nordic Cochrane

Centre, Copenhagen, Denmark). Studies were excluded from the quantitative analysis if they did not report sufficient data and the necessary data could not be obtained from the authors. When possible, mean and SD values were calculated from raw data. To simplify the comparison, in studies that included raw data for bilateral pain conditions, the mean (SD) of the left and right sides was compared with the control data. In instances where the same study reported several results on the same sample, the weighting was adjusted by dividing the sample size by the number of regions presented for that subgroup. Studies were pooled by the inverse variance method with a random effects model using the standardized mean difference (SMD) as the measure of effect size (Hedge's *g*). SMD was used instead of the weighted mean difference to better account for the predicted variation in acuity levels between studies of different body regions. Effect estimates were interpreted as small (.2), moderate (.5), or large (>.80).<sup>9</sup> To further aid the interpretation of the pooled effect sizes, the SMD of subgroups in which all assessments were conducted at skin regions of comparable receptive field densities were back-transformed to a mean difference in millimeters using the averaged (mean) SD from the control data. The mean difference was then expressed as a percentage of the control group tactile acuity. As this calculation uses the averaged SD, taken from studies that used differing protocols and assessment tools, the results should be considered an estimate.

All forest plots were visually inspected and a sensitivity analysis was conducted if the effect estimate of a data set within a subgroup appeared substantially different from the other studies and thus may have influenced the pooled effect estimate.

### Comparing Tactile Acuity Between the Affected and Unaffected Sides of People With Unilateral Chronic Pain Conditions

The tactile acuity of the affected and unaffected sides of people with unilateral chronic pain was compared. The study data were grouped by chronic pain condition and the analysis was conducted as for the aforementioned comparisons.

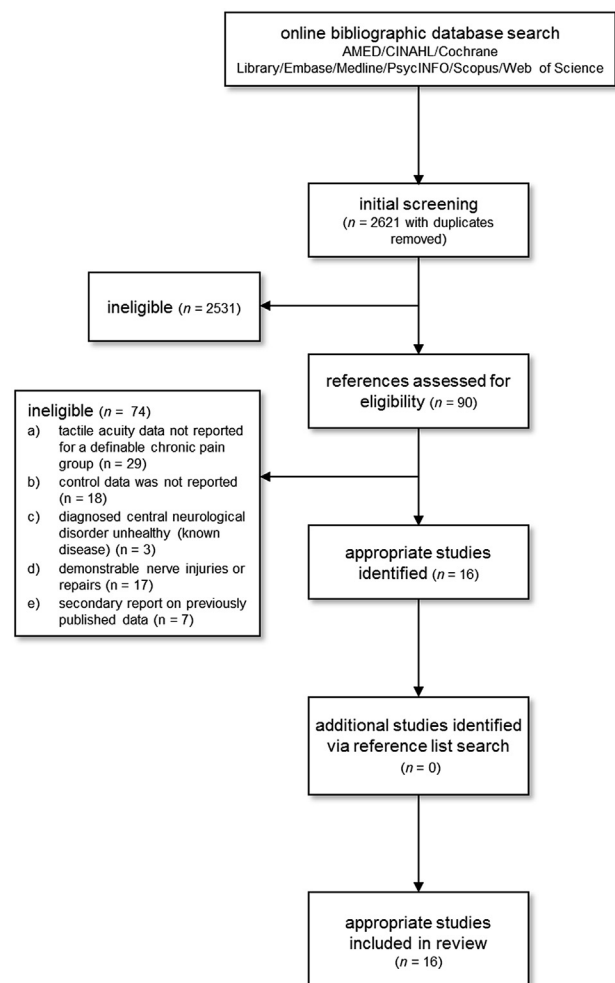
### Relationship Between Tactile Acuity and Pain Intensity and Duration

Correlational data were extracted and presented. For studies in which raw data were available, correlation coefficients were calculated. Furthermore, a Spearman's correlation coefficient ( $r_s$ ) was calculated to estimate the overall relationship between tactile acuity and the intensity and duration of pain. Tactile acuity data were transformed into z-scores and pooled. Average pain intensity data were converted to the most commonly used scale (eg, 0–100 mm visual analog scale converted to 0–10 NRS), and the pain duration data were converted into months. Scatterplots displaying the relationship between tactile acuity and pain intensity and/or duration were generated using MYSTAT 12 for Windows (v12.02.00; SYSTAT Software Inc, Chicago, IL).

## Results

Fig 1 outlines the results of the systematic review process (PRISMA flow chart). The initial search identified 2,621 studies. Of these, 2,531 were excluded in the initial screening of titles and abstracts. A further 74 were excluded following the review of the full text. The most common reason for exclusion was a lack of control data (unaffected side or independent healthy sample). Other common reasons for exclusion included peripheral nerve injuries, central nervous system disorders, or secondary analyses. No additional studies were identified from searching the reference lists of the eligible studies. In total, 16 studies—reporting data for 484 people with chronic pain and 378 control individuals—were included in the analysis.

All the authors of the 16 included studies were contacted for their raw data and to clarify some details of their studies that were not clear from the study report. The authors of 5 studies<sup>3,20,58–60</sup> did not respond. The raw data for 3 studies were unobtainable because they had been destroyed<sup>51</sup> or the authors reported that they were currently inaccessible.<sup>32,50</sup> Raw data were obtained for the remaining 8 studies.<sup>2,34,37,45,54,55,61,68</sup>



**Figure 1.** Flow diagram describing the review and screening process.

**Table 1. Summary of Study Demographics**

STUDY	YEAR OF PUBLICATION	CHRONIC PAIN CONDITION	REGION OF PAIN	REGION ASSESSED	CHRONIC PAIN PARTICIPANTS	
					SAMPLE SIZE (FEMALES)	AGE (MEAN [SD])
Ayhan et al <sup>2</sup>	2011	RA and OA	Hands	Index finger	RA: 28 (28); OA: 43 (43)	RA: 55.9 (9.5); OA: 58.9 (4.8)
Batterman <sup>3</sup>	1966	Chronic arthritis	?	Forearm	58 (?)	?
Grushka et al <sup>20</sup>	1987	Burning mouth syndrome	Mouth (unspecified)	Tongue, palate, lip, cheek	72 (61)	Males: 45.5 (11.2); females: 59.0 (9.9)
Lewis and Schweinhardt <sup>32</sup>	2012	Unilateral CRPS	Upper limb	Index finger	22 (15)	50.6 (10.6)
Luomajoki and Moseley <sup>34</sup>	2011	CLBP	T10–L5	L1 and iliac crest	45 (25)	43.0 (15.0)
Maihöfner and DeCol <sup>37</sup>	2007	Unilateral CRPS	Upper limb	Index finger	12 (10)	50.9 (3.9)
Moseley <sup>45</sup>	2008	CLBP	Lumbar region	T4–gluteal folds	6 (3)	43.8 (11.1)
Peltz et al <sup>50</sup>	2011	Unilateral CRPS	Upper limb	Index finger	30 (19)	50.9 (12.3)
Peters and Schmidt <sup>51</sup>	1991	CLBP	Back (unspecified)	Lateral forearm	20 (10)	43.6 (range 21–55)
Pleger et al <sup>54</sup>	2006	Unilateral CRPS	Hand (including digits)	Index finger	17 (10)	40.1 (9.5)
Reiswich et al <sup>55</sup>	2012	CRPS	Upper limb (unspecified)	Index finger	16 (10)	51.8 (10.8)
Saeidian et al <sup>58</sup>	2011	Lumbosacral radiculopathy	Low back (unspecified)	L4–S1	20 (20)	Range 40–58
Seltzer and Seltzer <sup>59</sup>	1986	Chronic pain	Low back, neck, arm, leg, generalized	Lateral forearm	19 (?)	?
Seltzer et al <sup>60</sup>	1992	Unspecified chronic pain	?	Lateral forearm	20 (?)	?
Stanton et al <sup>61</sup>	2013	OA and CLBP	Knee; low back (unspecified)	Medial and lateral knee; L1–iliac crest	20 (14) OA knee; 17 (14) back	68 (9); 45 (15)
Wand et al <sup>68</sup>	2010	CLBP	Low back (unspecified)	Transverse process at L3	19 (11)	41 (12.5)

Abbreviations: NPSI, Neuropathic Pain Symptom Inventory; VAS, visual analog scale.

NOTE. ?, not reported.

\*Current pain intensity unless specified.

†Calculated from raw data (not reported in manuscript).

## Study Characteristics

Table 1 summarizes the study characteristics of the 16 included studies. Fifteen studies compared people with chronic pain to control individuals, including 5 studies<sup>32,37,50,54,61</sup> that also compared tactile acuity at the site of pain to that of the contralateral unaffected region. One study<sup>58</sup> only compared tactile acuity at the site of pain to that of the contralateral unaffected region and did not include a healthy control group. Data were available for 18 chronic pain samples, representing 5 specific chronic pain conditions (burning mouth syndrome  $n = 72$ , complex regional pain syndrome [CRPS]  $n = 97$ , chronic low back pain [CLBP]  $n = 127$ , osteoarthritis [OA]  $n = 121$ , rheumatoid arthritis [RA]  $n = 28$ ), some unspecified chronic pain patients ( $n = 39$ ), and 16 control samples ( $n = 378$ ).

All of the included studies used the 2-point discrimination threshold (TPDT) as a measure of tactile acuity.

Eleven studies<sup>2,20,32,34,45,51,58-61,68</sup> used commercially available clinically applicable tools, whereas 5 studies<sup>3,37,50,54,55</sup> used custom-made assessment tools. Two studies<sup>3,58</sup> failed to clarify (or adequately reference) their protocols sufficiently for replication; attempts to contact these authors were unsuccessful. Whether tactile acuity was assessed directly within the painful region was unclear.

Six studies used recognized diagnostic criteria. Maihöfner and DeCol,<sup>37</sup> Pleger et al,<sup>54</sup> and Lewis and Schweinhardt<sup>32</sup> used the International Association for the Study of Pain Diagnostic Criteria for CRPS.<sup>43</sup> Peltz et al<sup>50</sup> and Reiswich et al<sup>55</sup> used the Budapest Research Criteria<sup>22</sup> for CRPS. Stanton et al<sup>61</sup> used the Altman et al<sup>1</sup> criteria to diagnose OA.

## Risk of Bias

Table 2 displays the results of the risk of bias assessment. The risk of bias was high across multiple domains

**Table 1. Continued**

CHRONIC PAIN PARTICIPANTS		CONTROL PARTICIPANTS			
PAIN INTENSITY* (MEAN [SD])	PAIN DURATION (MO)	CONTROL TYPE	SAMPLE SIZE (FEMALES)	AGE (MEAN [SD])	RAW DATA PROVIDED
RA: 4.3 (1.2)	RA: 117.1 (102.5); OA: 34.0 (12.0)	Healthy sample	39 (39)	56.6 (5.8)	✓
?	?	Healthy sample	27 (12)	?	x
MPQ: mean 2.3	39.6 (36.0)	Healthy sample	43 (36)	Males: 47.7 (13.8); females 58.1 (7.5)	x
NPSI: 20.34 (12.5)	37.2 (53.7)	Healthy sample and unaffected side	22 (?)	43.0 (14.2)	x
?	?	Healthy sample	45 (25)	41.0 (10.0)	✓
0–100 NRS: 40.8 (5.6)	5.4 (1.5)	Healthy sample and unaffected side	12 (8)	48.2 (3.5)	✓
MPQ-PRI: 22.2 (4.9)	52.2 (36.1)	Upper limb pain patients	10 (5)	42.3 (11.3)†	✓
100 mm VAS: 47.2 (12.5)					
MPQ: 24.6 (15.0)	16.8 (12.6)	Healthy sample and unaffected side	?	?	x
0–100 NRS: 39.2 (16.3)	103.2 (12–360)	Healthy sample	20 (10)	43.6 (range 20–60)	x
?					
NRS: 5.4 (2.1) current; 4.0 (1.4) sustained	17.1 (20.6)	Healthy sample and unaffected side	17 (10)	40.2 (10.0)	✓
NRS: 3.0 (1.1)	12.4 (12.7)	Healthy sample	47 (27)	43.9 (15.8)	✓
VAS (unspecified): 8.5 (1.7)	?	Unaffected side	NA	NA	x
?	?	Healthy sample	19 (?)	?	x
?	?	Healthy sample	20 (?)	?	x
100 mm VAS: 21.9 (25.5); 34.1 (22.4)	90.5 (168.1); 30.9 (72.1)	Healthy sample and unaffected side	20 (12) hand controls; 18 (12) back controls	37 (16); 41 (11)	✓
NRS: 3.2 (3.0)	108 (117.6)	Healthy sample	19 (14)	34 (12.1)	✓

in all of the included studies. Although most studies reported the sampling method (81%), all but 2 studies used samples of convenience, with only Moseley<sup>45</sup> recruiting consecutive patients and Saeidian et al<sup>58</sup> using an undisclosed random sampling technique. Only 6 studies recruited participants using recognized diagnosis criteria (38%) and of these, only 4 of the 6 excluded controls on the same basis. Although most studies reported the protocol used to assess tactile acuity, none of the studies reported or cited reliability indices for their protocols. Of the 15 studies that compared people with chronic pain to control individuals, only 8 (53%) attempted to age-match their control group. Only 3 of the included studies (19%) used appropriately sized samples, and none of the studies justified the size of their samples. Critically, all but 1 study<sup>45</sup> (94%) failed to blind the assessor to the group.

**Outcomes**

**Is Tactile Acuity Altered at the Painful Region in People With Chronic Pain?**

Eleven studies<sup>2,7,20,32,34,37,45,50,54,55,68</sup> assessed tactile acuity at the painful region and compared it with the same region in controls. The forest plot shown in Fig 2 compares the tactile acuity of people with chronic pain (n = 296) to that of controls (n = 341). The pooled results of all comparisons suggest that TPDTs are larger at the site of pain in people with chronic pain than they are in controls. A large, significant effect estimate of 1.02 (95% confidence interval [CI]: .59 to 1.46, P < .0001) in favor of worse tactile acuity in people with chronic pain was noted. However, heterogeneity was high (I<sup>2</sup> = 81.8%, P = .0009) and there were apparent differences between diagnostic subgroups.

**Table 2. Risk of Bias in Included Studies**

	SELECTION BIAS		DETECTION BIAS		REPORTING BIAS				PERFORMANCE BIAS		
	REPLICABLE SAMPLING METHOD	REPRESENTATIVE OF CASES	RECOGNIZED DIAGNOSIS CRITERIA	DIAGNOSIS CONTROLS	APPROPRIATE SAMPLE SIZE	AGE MATCHED CONTROLS	NO MISSING DATA	MISSING DATA DESCRIBED	BLINDED ASSESSOR	ASSESSMENT PROTOCOL REPORTED	RELIABLE ASSESSMENT
	Ayhan et al <sup>2</sup>	X	X	?	?	✓	✓	X	X	?	X
Batterman <sup>3</sup>	X	X	?	?	X	X	X	X	?	X	X
Grushka et al <sup>20</sup>	✓	X	?	?	✓	X	X	X	?	✓	X
Lewis and Schweinhardt <sup>32</sup>	✓	X	✓	✓	X	?	X	NA	?	✓	X
Luomajoki and Moseley <sup>34</sup>	✓	X	X	✓	✓	✓	X	X	?	✓	X
Maihöfner and DeCol <sup>37</sup>	✓	X	✓	✓	X	✓	✓	NA	?	✓	X
Moseley <sup>45</sup>	✓	✓	X	X	X	X	X	X	✓	✓	X
Peters and Schmidt <sup>51</sup>	✓	X	X	?	X	✓	X	X	X	✓	X
Peltz et al <sup>50</sup>	✓	✓	✓	✓	X	?	X	NA	X	✓	X
Pleger et al <sup>54</sup>	X	X	✓	✓	X	✓	X	X	?	✓	X
Reiswich et al <sup>55</sup>	✓	?	✓	X	X	X	✓	NA	?	✓	X
Saeidian et al <sup>58</sup>	✓	✓	X	NA	X	✓	X	X	X	X	X
Seltzer and Seltzer <sup>59</sup>	✓	X	X	?	X	?	X	X	X	✓	X
Seltzer et al <sup>60</sup>	✓	X	X	?	X	?	X	X	?	✓	X
Stanton et al <sup>61</sup>	✓	X	✓	?	X	✓	✓	NA	?	✓	X
Wand et al <sup>68</sup>	✓	X	X	✓	X	✓	X	X	X	✓	X

NOTE. ✓, yes (low risk of bias); X, no (high risk of bias); ?, unclear; NA, criterion not applicable.

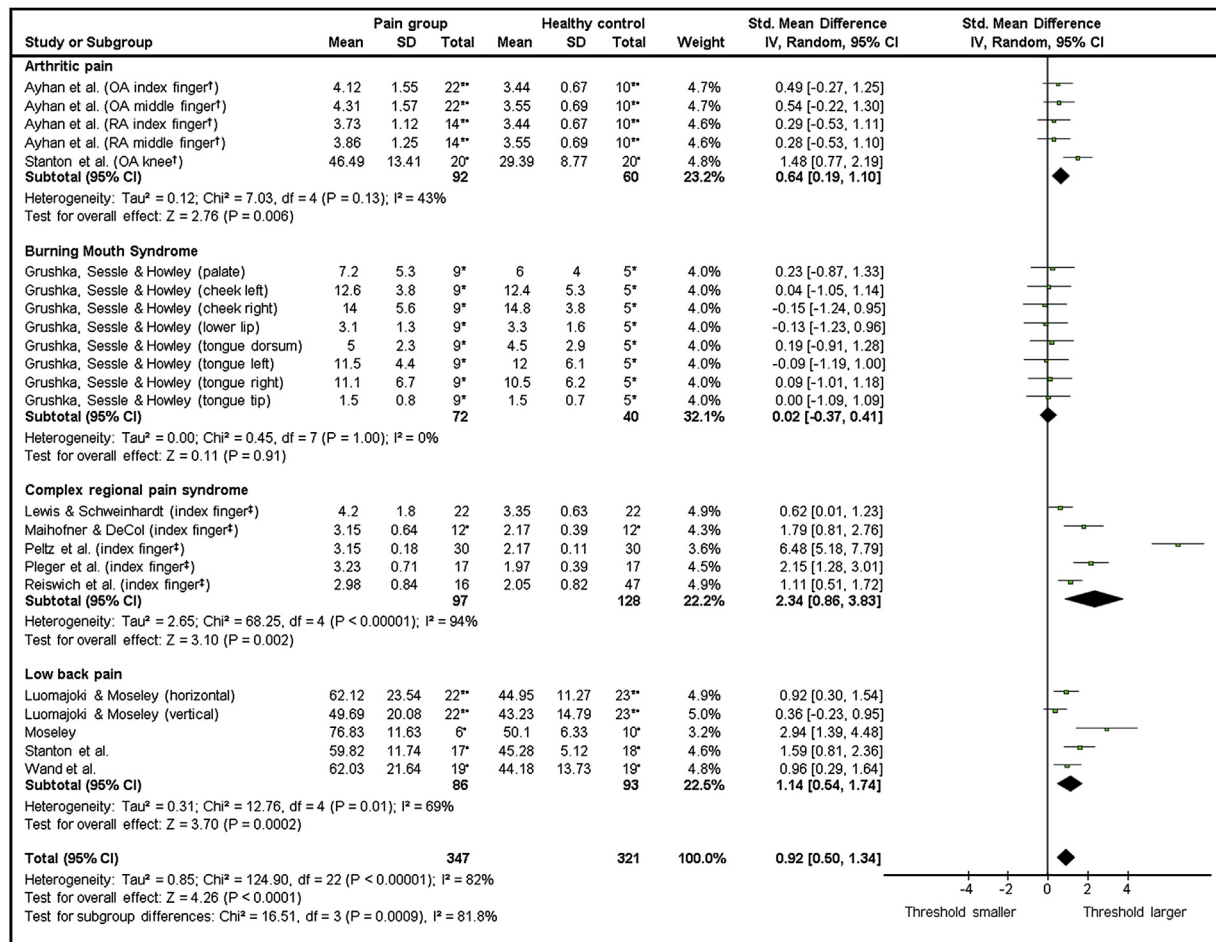
**Arthritic Pain.** Two studies<sup>2,61</sup> compared the tactile acuity of people with chronic arthritic pain to that of controls. Despite differences in protocols and assessment tools used, heterogeneity within this subgroup was not statistically significant ( $P = .13$ ). The pooled results of 5 comparisons suggest that TPDTs are larger at the site of pain than they are in controls, a large, significant effect estimate of 1.48 (95% CI: .77 to 2.19,  $n = 24$ ) in favor of worse tactile acuity in people with arthritis. However, the results appear inconsistent, with a difference in acuity observed at the knee in people with knee OA but no differences in acuity at the fingertip in people with hand OA and RA.

**Burning Mouth Syndrome.** One study<sup>20</sup> compared the tactile acuity of people with burning mouth syndrome to that of controls. The pooled results of 8 oral regions assessed suggest that TPDTs are not altered in people with burning mouth syndrome (effect estimate .02, 95% CI: -.37 to .41, with no heterogeneity). This equates to a difference of .1 mm (95% CI: -1.4 to 1.6 mm), or a percentage difference of 0% (95% CI: -18% to 19%) between the people with burning mouth syndrome and controls.

**CRPS.** Five studies<sup>32,37,50,54,55</sup> compared the tactile acuity of people with CRPS to that of controls. The pooled results of 5 comparisons suggest that TPDTs are larger at the site of pain in people with CRPS than they are in controls; a large, significant effect estimate of 2.34 (95% CI: .86 to 3.83,  $P = .002$ ) in favor of worse tactile acuity in people with CRPS was noted. This equates to a difference of 1.1 mm (95% CI: .4 mm to 1.8 mm), or a percentage difference of 47% (95% CI: 17% to 76%) between the people with CRPS and

controls. However, substantial heterogeneity was observed for this comparison ( $I^2 = 94%$ ,  $P < .00001$ ) even though all of the included studies demonstrated statistically significant differences in TPDTs. The results of Peltz et al<sup>50</sup> had much lower variance than the other studies, which may have contributed to their remarkably large effect size (6.48, 95% CI: 5.18 to 7.79; see [Appendix](#) for further discussion of the Peltz et al<sup>50</sup> study). Considering this discrepancy and several anomalies found in their data, sensitivity analyses with the Peltz et al<sup>50</sup> data excluded were undertaken (see [Supplementary Fig 1](#)). The pooled results of the remaining 4 studies suggest that TPDTs are larger at the site of pain in people with CRPS (effect estimate 1.35, 95% CI: .69 to 2.01,  $P < .0001$ ), and although heterogeneity remained significant, it was lower with the Peltz et al<sup>50</sup> study removed ( $I^2 = 69%$ ,  $P = .02$ ). This equates to a difference of .8 mm (95% CI: .4 mm to 1.1 mm), or a percentage difference of 31% (95% CI: 16% to 47%) between the people with CRPS and controls.

**CLBP.** Four studies<sup>34,45,61,68</sup> compared the tactile acuity of people with CLBP to that of controls. The pooled results of 5 comparisons suggest that TPDTs are larger in people with CLBP; a large, significant effect estimate of 1.14 (95% CI: .54 to 1.74,  $P = .0002$ ) in favor of worse tactile acuity in people with CLBP was noted. This equates to a difference of 11.7 mm (95% CI: 5.5 mm to 17.8 mm), or a percentage difference of 26% (95% CI: 12% to 39%) between the people with CLBP and controls. Substantial heterogeneity for this comparison was observed ( $I^2 = 69%$ ,  $P = .01$ ).



**Figure 2.** Forest plot comparing tactile acuity, assessed at the painful region, of people with chronic pain and healthy pain-free controls. All included studies used the TPDT as a measure of acuity; hence, larger thresholds indicate worse acuity. Abbreviations: IV, inverse variance; CI, confidence interval. Note: †, bilateral limb pain (mean TPDT); ‡, unilateral limb pain (affected side TPDT); \*, sample size reduced to adjust study weighting; ●, calculated from raw data.

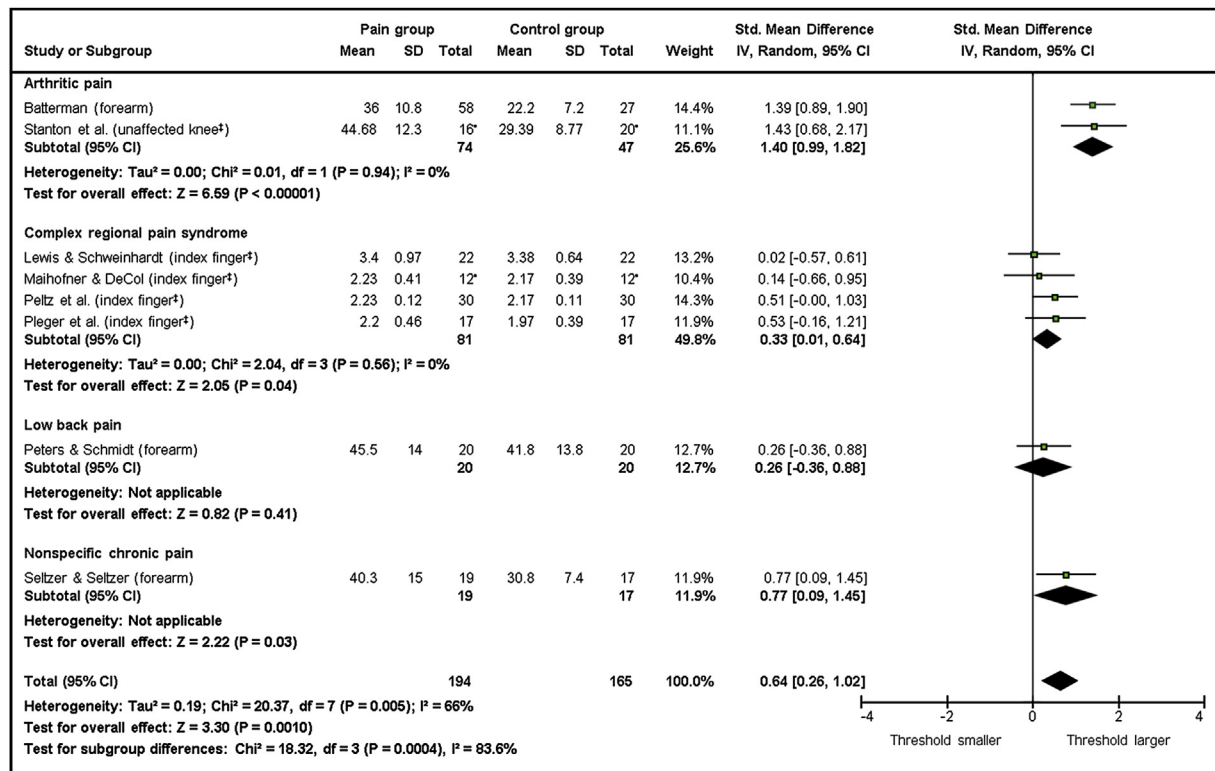
### Is Tactile Acuity Altered in Regions Remote From the Region of Pain, in People With Chronic Pain?

Eight studies<sup>3,32,37,50,51,54,59,61</sup> assessed tactile acuity at a site remote from the region of pain. The remote locations where tactile acuity was assessed are described in the forest plot in Fig 3. The plot compares the tactile acuity of people with chronic pain (n = 194) to that of controls (n = 165). The pooled results of 8 comparisons suggest that TPDTs are larger at regions remote from the site of pain in people with chronic pain in comparison with healthy pain-free people; a moderate, significant effect estimate of .64 (95% CI: .26 to 1.02) in favor of worse tactile acuity in people with chronic pain was noted. Again, tactile acuity was not consistently altered in all of the included conditions, and the differences between subgroups was substantial (I<sup>2</sup> = 83.6%, P = .0004).

**Arthritic Pain.** Two studies<sup>3,61</sup> compared the tactile acuity of people with chronic arthritic pain to that of controls. The pooled results of 2 comparisons suggest that TPDTs are larger at regions remote from the site of pain in people with chronic arthritic pain; a large,

significant effect estimate of 1.40 (95% CI: .99 to 1.82, P < .00001) in favor of worse tactile acuity in people with arthritis was noted. Despite differing protocols (ie, Batterman<sup>3</sup> assessed the TPDT with a custom-built air jet apparatus) and differing clinical presentations (ie, Batterman<sup>3</sup> did not report which joints were affected), heterogeneity was not detected (I<sup>2</sup> = 0%, P = .94).

**CRPS.** Four studies<sup>32,37,50,54</sup> compared the tactile acuity of people with CRPS to that of controls. The pooled results of 4 comparisons suggest that TPDTs are larger at regions remote from the site of pain in people with CRPS; a small, significant effect estimate of .33 (95% CI: .01 to .64, P = .04) in favor of worse tactile acuity in people with CRPS was noted. This equates to a difference of .13 mm (95% CI: 0 mm to .24 mm), or a percentage difference of 5% (95% CI: 0% to 10%) between the people with CRPS and controls. Heterogeneity was not detected (I<sup>2</sup> = 0%, P = .56) but a sensitivity analysis was conducted with the Peltz et al<sup>50</sup> study excluded (see Supplementary Fig 2). The pooled results of the remaining 3 studies suggest that TPDTs are not altered at regions remote from the site of pain in people with CRPS (95% CI: -.17 to .61, P = .28), which



**Figure 3.** Forest plot comparing tactile acuity, assessed at a location remote from the painful region, of people with chronic pain and healthy pain-free controls. All included studies used the TPDT as a measure of acuity; hence, larger thresholds indicate worse acuity. Abbreviations: IV, inverse variance; CI, confidence interval. Note: †, unilateral limb pain (unaffected side TPDT); •, calculated from raw data.

suggests that the significant pooled effect was probably carried by the Peltz et al<sup>50</sup> data.

**CLBP.** One study<sup>51</sup> compared the tactile acuity of people with CLBP to that of controls. The results suggest that TPDTs are not altered at regions remote from the site of pain in people with CLBP (95% CI: -.26 to .88).

**Nonspecific Chronic Pain.** One study<sup>59</sup> compared TPDTs at the forearm in people with chronic pain in various body regions to the forearm TPDTs of controls. The results suggested that TPDTs at the forearm are larger in people with chronic pain; a moderate, significant effect estimate of .77 (95% CI: .09 to 1.45,  $P = .03$ ) in favor of worse tactile acuity in people with chronic pain was noted. This equates to a difference of 5.7 mm (95% CI: .7 mm to 10.7 mm), or a percentage difference of 19% (95% CI: 2% to 35%) between the people with nonspecific chronic pain and controls. However, these data included people with pain in the arm and generalized pain.

An additional study not included in the overall analysis<sup>60</sup> compared TPDTs at the forearm in patients with unspecified chronic pain (ie, patient condition was not reported) to the forearm TPDTs of controls. They noted a significant difference ( $t[12] = 2.78$ ,  $P < .02$ ), but insufficient data were reported for its inclusion in the meta-analysis.

### Comparing Tactile Acuity of the Affected and Unaffected Sides of People With Chronic Pain

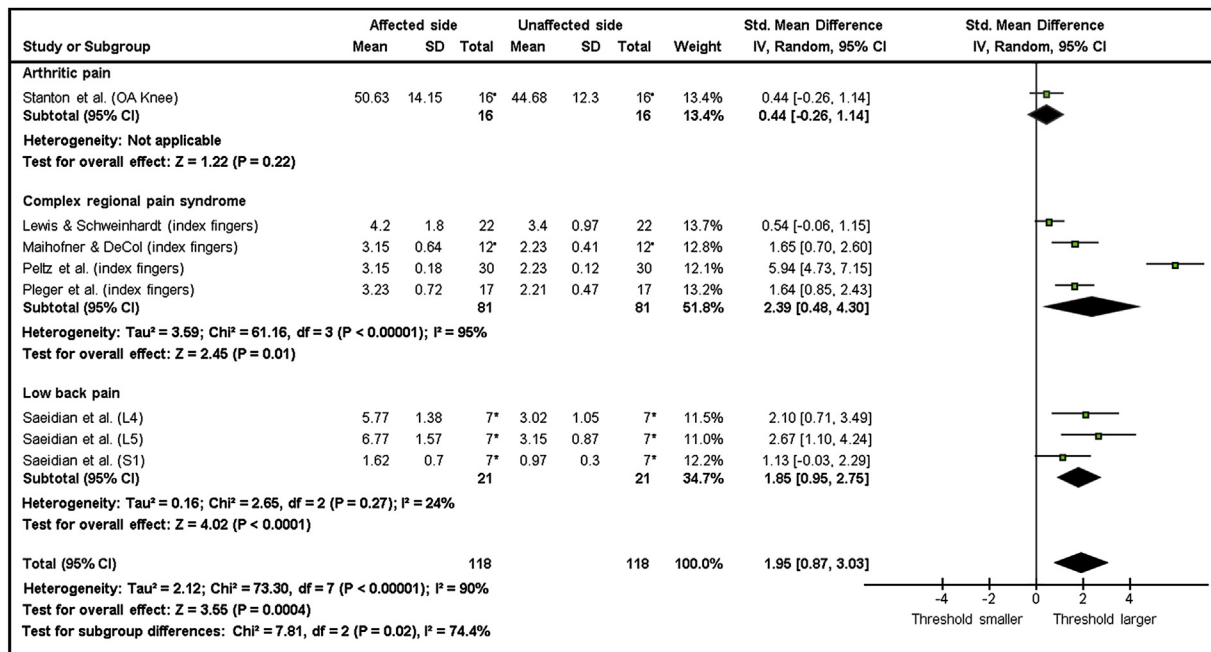
Six studies<sup>37,50,52,54,58,61</sup> measured tactile acuity in people with unilateral chronic pain ( $n = 118$ ). The forest plot shown in Fig 4 compares tactile acuity at the

region of pain with the contralateral unaffected region. The overall pooled results of 8 comparisons suggest that TPDTs are larger at the site of pain in comparison with the contralateral unaffected region; a large, significant effect estimate of 1.95 (95% CI: .87 to 3.03) in favor of worse tactile acuity at the site of pain was noted. Once again, tactile acuity was not consistently altered in all of the included conditions, and the differences between subgroups was substantial ( $I^2 = 74.4%$ ,  $P = .02$ ).

**Arthritic Pain.** One study<sup>61</sup> compared the tactile acuity of the affected and unaffected knees of people with chronic knee OA. The results suggest that the TPDT of the affected side is not altered in comparison with the unaffected side (95% CI: -.26 to 1.14).

**CRPS.** Four studies<sup>32,37,50,54</sup> compared the tactile acuity of the affected and unaffected limbs of people with CRPS. The pooled results of 4 comparisons suggest that TPDTs are larger at the site of pain in comparison with the contralateral unaffected region; a large, significant effect estimate of 2.39 (95% CI: .48 to 4.30) in favor of worse tactile acuity at the site of pain was noted. This equates to a difference of 1.2 mm (95% CI: .2 mm to 2.2 mm), or a percentage difference of 47% (95% CI: 10% to 87%) between the affected and unaffected sides. As noted above, substantial heterogeneity was observed for this comparison ( $I^2 = 95%$ ,  $P < .00001$ ), probably because of the results of the Peltz et al<sup>50</sup> study, which had an effect size 3.5 times the pooled estimate. A sensitivity analysis was conducted with the Peltz et al<sup>50</sup> data excluded (see





**Figure 4.** Forest plot comparing the tactile acuity of the painful region to the tactile acuity of the contralateral unaffected region in people with chronic pain. All included studies used the TPDT as a measure of acuity; hence, larger thresholds indicate worse acuity. Abbreviations: IV, inverse variance; CI, confidence interval. Note: \*, sample size reduced and rounded to nearest whole number to adjust study weighting; ●, calculated from raw data.

Supplementary Fig 3). The overall pooled results of the remaining 3 comparisons suggest that TPDTs are larger at the site of pain in comparison with the contralateral unaffected region (effect estimate 1.22, 95% CI: .43 to 2.02). This equates to a difference of .8 mm (95% CI: .3 mm to 1.2 mm), or a percentage difference of 29% (95% CI: 10% to 46%) between the affected and unaffected sides.

**CLBP.** One study<sup>58</sup> compared the tactile acuity of the affected and unaffected sides of people with unilateral CLBP. The pooled results of 3 comparisons suggest that TPDTs are larger at the site of pain in comparison with the contralateral unaffected region; a large, significant effect estimate of 1.85 (95% CI: .95 to 2.75,  $P < .00001$ ) in favor of worse tactile acuity at the site of pain was noted. This equates to a difference of 1.4 mm (95% CI: .7 mm to 2.0 mm), or a percentage difference of 58% (95% CI: 29% to 86%) between affected and unaffected sides.

### Relationship Between Tactile Acuity and Pain Intensity

Seven studies<sup>32,37,50,54,55,61,68</sup> reported the relationship between tactile acuity and pain intensity, and the relationship could be calculated from the raw data of 1 further study.<sup>45</sup> Table 3 shows the correlation data for the 8 studies, and Fig 5 compares tactile acuity and current pain intensity for the 6 studies that provided raw tactile acuity and pain intensity data.

A significant positive relationship between tactile acuity and pain intensity was noted in 3 of 7 studies, all in CRPS samples. Maihöfner and DeCol<sup>37</sup> (n = 12) reported a statistically significant relationship between

tactile acuity and current pain intensity ( $r = .70, P < .05$ ) using the MPQ pain rating index (MPQ-PRI) but not for spontaneous pain intensity measured with a 0 to 100 NRS ( $r = -.10, P > .05$ ). Peltz et al<sup>50</sup> (n = 30), using the same measures, reported results identical to those of the Maihöfner and DeCol<sup>37</sup> study (see Appendix). Pleger et al<sup>54</sup> (n = 17) noted a statistically significant relationship between tactile acuity and average pain intensity ( $P = .001$ ) but not current pain intensity ( $P = .157$ ), both using the NRS. Analysis of the pooled data showed no significant association between tactile acuity and pain intensity ( $P = .218$ ).

### Relationship Between Tactile Acuity and Pain Duration

Two studies<sup>61,67</sup> reported the relationship between tactile acuity and pain duration. Raw data were available for both of these studies and for a further 3 studies<sup>2,45,54</sup> that did not report the relationship. Fig 6 plots the data for people with OA (hands and knee), RA (hands), CRPS, and CLBP.

Stanton et al<sup>61</sup> noted that pain duration was not related to TPDTs in people with knee OA (n = 20,  $P = .60$ ) or CLBP (n = 17,  $P = .61$ ). Wand et al<sup>68</sup> (n = 19) also found no significant correlation between TPDTs and the duration of CLBP (partial  $r = -.169, P = .516$ ). The raw data from the Ayhan et al<sup>2</sup> (n = 43 OA, 28 RA), Moseley<sup>45</sup> (n = 6), and Pleger et al<sup>54</sup> (n = 17) studies were analyzed, and no further significant relationships were identified between TPDTs and pain duration ( $P > .90$ ). Analysis of the pooled data showed no significant association between tactile acuity and pain duration ( $P = .242$ ).

**Table 3. Relationship Between Tactile Acuity and Pain Intensity**

STUDY	CONDITION	N	PAIN MEASURE	RELATIONSHIP (PEARSON'S R)	SIGNIFICANCE (P)
Lewis and Schweinhardt <sup>32</sup>	CRPS	22	NPSI (average; past 24 h)	.31	>.05
Maihöfner and DeCol <sup>37</sup>	CRPS	12	NRS	-.01	>.05
			MPQ-PRI	.70	<b>&lt;.05</b>
Moseley <sup>45</sup>	CLBP	6	VAS (current)	.278*†	.298
			VAS (usual)	-.213*†	.428
Peltz et al <sup>50</sup>	CRPS	30	MPQ-PRI (current)	.70	<b>&lt;.05</b>
			NRS (posttesting)	-.10	>.05
Pleger et al <sup>54</sup>	CRPS	17	NRS (average; past 4 wk)	.71	<b>.001</b>
			NRS (current)	.36	.157
Reiswich et al <sup>55</sup>	CRPS	16	DASH (average; past 4 wk)	.39	>.05
			NRS (current)	-.03	>.05
Stanton et al <sup>61</sup>	OA knee	20	NRS (current)	?*	.170
			NRS (average; past 48 h)	?*	.160
	CLBP	17	NRS (current)	?*	.870
			NRS (average; past 48 h)	?*	.610
Wand et al <sup>68</sup>	CLBP	19	NRS (usual)	.03	.914
			NRS (current)	.015	.955
			NRS (worst)	.032	.907

Abbreviations: VAS, visual analog scale; DASH, Disabilities of the Arm, Shoulder and Hand questionnaire.

NOTE. **Bold** highlights significant relationship.?, correlation coefficient calculated but not reported in study.

\*Spearman's rho.

†Calculated from raw data.

## Discussion

We aimed to systematically evaluate the literature and use meta-analytical methods to establish whether tactile acuity is altered in people with non-neuropathic chronic pain. The overall pooled results suggest that the tactile acuity of people with non-neuropathic chronic pain is worse at both the site of pain and regions remote from the site of pain in comparison to control individuals. However, the reduction in acuity observed at remote sites is only clearly present in the arthritis data. Although tactile acuity deficits were not evident in all of the included chronic pain conditions, none of the included studies associated chronic pain with an enhancement of tactile acuity.

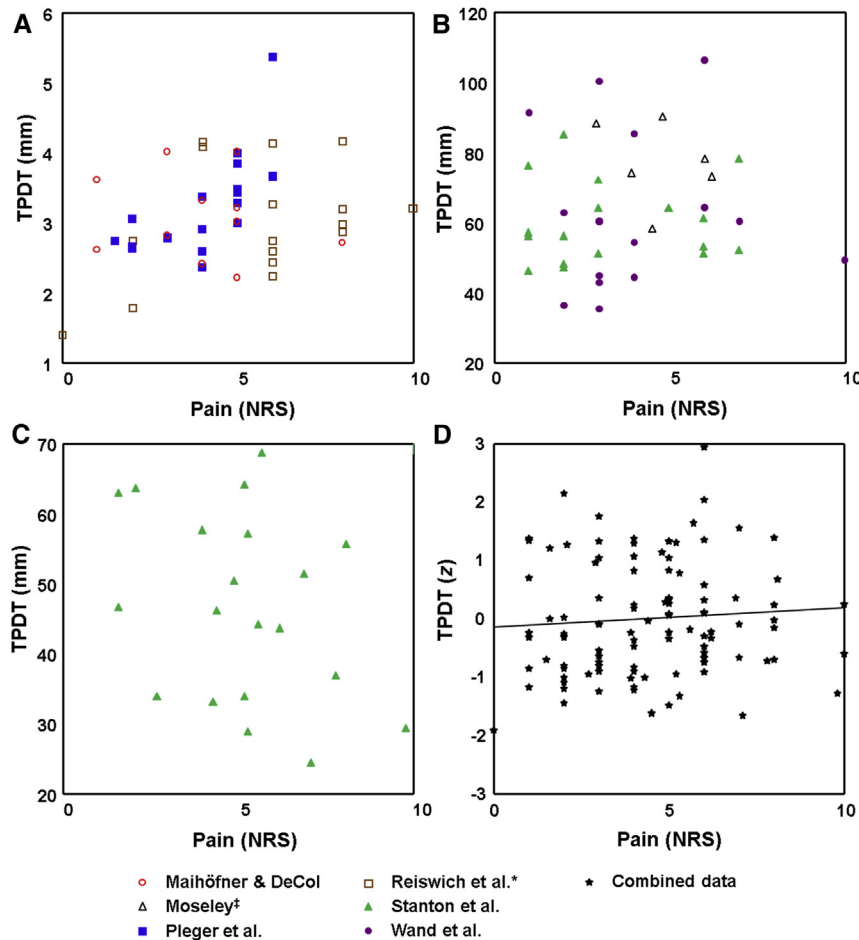
In CRPS, there is consistent evidence showing that tactile acuity, assessed at the fingertip, is worse in the affected hand than in both the unaffected hand and the hands of pain-free controls, suggesting that the impairment is restricted to the area of pain. Given the association between tactile acuity and S1 representation,<sup>12</sup> these findings are in keeping with evidence of an altered cortical representation of the affected hand, as compared to the unaffected hand, in people with CRPS<sup>28,36</sup> (see Di Pietro et al<sup>11</sup> for a review).

We found consistent evidence to suggest that tactile acuity deficits in people with CLBP are restricted to the painful back region. As with the CRPS data, these findings appear to be consistent with cortical reorganization at the back<sup>14</sup>; however, we are not aware of any data to suggest that S1 representation is normal in unaffected regions.

In arthritic conditions, we found evidence of altered acuity at both the site of pain and remote regions, suggesting that acuity is generally altered across the body. However, Stanton et al<sup>61</sup> categorized the contralateral knee as

unaffected if it was pain free at the time of testing. That many of the participants reported a history of pain in the unaffected knee<sup>61</sup> and that current pain intensity does not correlate with tactile acuity may account for the deficits observed in the remote region. Furthermore, Batterman<sup>3</sup> failed to report which joints were affected, and it is possible that joints near the assessment site on the forearm (ie, the wrist) were affected and inflated the size of the difference at the remote site. Although cortical changes are thought to contribute to the pain associated with OA and RA,<sup>31,49</sup> we are not aware of any evidence of cortical reorganization in these conditions. That deficits in acuity may not be isolated to the region of pain suggests that S1 reorganization alone may not account for the impairment and that other cortical or subcortical areas might be involved. Nonetheless, arthritic conditions are associated with altered touch perception<sup>23</sup> and pain thresholds,<sup>23,25,40</sup> indicative of peripheral and central sensitization,<sup>41,56</sup> and hyperalgesia, a marker of central sensitization, directly relates to the extent of cortical reorganization in other chronic pain conditions.<sup>36</sup> Further studies, using appropriate protocols and remote sites, are needed to further interrogate this phenomenon in arthritic conditions.

Only 1 study<sup>20</sup> investigated tactile acuity in burning mouth syndrome and found no differences in comparison to healthy controls. This poorly understood condition is thought to be mediated centrally,<sup>19</sup> but to date there is no evidence of cortical reorganization in the burning mouth syndrome literature. That no differences between touch perception or tactile acuity were observed suggests that burning mouth syndrome is not associated with peripheral neural abnormalities or disruption of the sensory neuraxis.



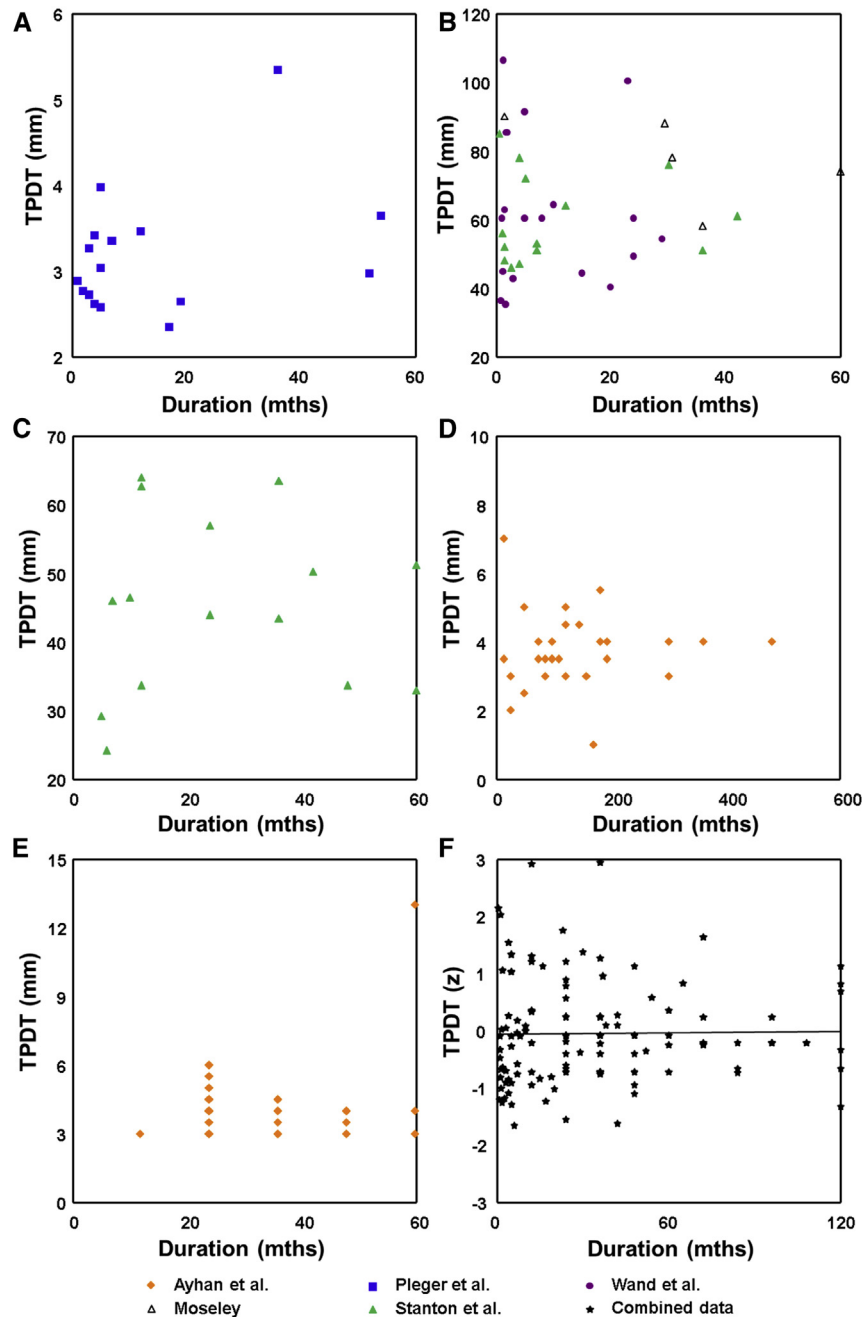
**Figure 5.** Scatterplots showing the relationship between the TPDT and pain intensity (11-point NRS) for people with (A) CRPS; (B) CLBP; (C) chronic knee OA; and (D) combined data (z scores). Note: \*, 6-point (0–5) scale Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire (question 24) converted to 11-point NRS; ‡, 0–100 mm visual analog scale converted to 11-point NRS.

Tactile acuity does not appear to worsen as pain worsens or persists in the period 3 months after the initial injury. We found little evidence of a relationship between tactile acuity and pain intensity. A significant relationship between tactile acuity and pain intensity was noted only in 3 studies, each in CRPS samples. The identical findings of Maihöfner and DeCol<sup>37</sup> and Peltz et al<sup>50</sup> suggested a significant relationship between acuity and current pain intensity. Conversely, Pleger et al<sup>54</sup> reported a significant relationship between acuity and average pain intensity but found no relationship between acuity and current pain intensity. These conflicting results, and the fact that no further relationships were identified in our analysis of 5 additional data sets, suggest that tactile acuity deficits may be independent of the perceived intensity of the pain. This is surprising given the relationship between tactile acuity and S1 representation<sup>12</sup> and between the extent of S1 reorganization and average pain intensity in both CRPS<sup>36,38,53</sup> and phantom limb pain.<sup>13,15,21</sup> Although S1 hyperactivity increases with chronicity in CLBP,<sup>14</sup> we found no evidence of a relationship between pain duration and tactile acuity. These findings suggest that tactile acuity does not worsen as pain persists and imply that S1 hyperactivity is not directly related to deficits in tactile acuity.

However, the available data regarding these relationships are limited. It is, nonetheless, plausible that the changes in tactile acuity occur in the acute and subacute phases and we were unable to detect a relationship because we only included studies of participants with pain that has persisted for greater than 3 months.

Although some chronic non-neuropathic pain conditions appear to be associated with deficits in tactile acuity, the point at which a deficit becomes clinically meaningful remains unknown. However, previous studies have addressed the issue of assessment and provided guidelines as to the size of the difference needed to be distinguishable from measurement error.<sup>71</sup>

All of the included studies used the TPDT as a measure of tactile acuity, and the differences between the assessment protocols and tools likely contributed to the observed heterogeneity. The TPDT is the most common measure of tactile acuity<sup>26</sup> as it is easy to assess and is appropriate for use in regions of high and low acuity.<sup>8</sup> However, it has been criticized for the unexplained variability observed within subjects,<sup>71</sup> between subjects, and between studies,<sup>27</sup> and some researchers argue that it should not be used as a scientific measure of acuity.<sup>10</sup> It is vulnerable to bias insofar as most protocols require the assessor to make a subjective judgment as to when



**Figure 6.** Scatterplots showing the relationship between the TPDT and pain duration (months) for people with (A) CRPS; (B) CLBP; (C) chronic knee OA; (D) chronic hand OA; (E) RA; and (F) combined data (z scores).

the threshold has been determined. Future studies should consider other measures of tactile acuity such as grating orientation tasks<sup>18</sup> and consider the influence of assessor bias and test-retest reliability. Nonetheless, despite wide variability and small sample sizes, most of the studies included in this review reported statistically significant findings.

All of the included studies were at risk of bias, primarily because of nonconsecutive recruitment, the lack of exclusion based on recognized diagnosis criteria, and the use of nonblinded assessors. Furthermore, although it is well documented that tactile performance declines with age,<sup>30,72</sup> few studies reported age-matching their

control group. It is thus plausible that the effect estimates reported in this review may overestimate the true disparity in acuity between people with chronic pain and controls. The fact that all of the included studies that hypothesized that tactile acuity would be altered because of cortical reorganization were statistically significant,<sup>32,34,37,45,50,54,55,61,68</sup> despite the small samples and the wide variability associated with tests of acuity, suggests that a publication bias may also have influenced our results.<sup>33</sup>

Several limitations may have influenced our findings. We only excluded studies that provided explicit evidence of overt peripheral neuropathy. Impaired touch

perception can be indicative of nerve injury<sup>35</sup> and will likely impair tactile acuity, yet only 4 studies<sup>2,20,45,68</sup> provided evidence of normal sensory detection. Additionally, none of the CRPS studies included nerve conduction velocity or electromyographic assessments to exclude nerve lesions, which suggests that CRPS (type 2) cannot be ruled out definitively.<sup>5</sup> We also did not restrict the age range of the participants, and several of the studies included older adults. Tactile acuity progressively declines across the life span,<sup>6,29</sup> and age-matching was not consistently achieved. It is plausible that some of the observed deficits in acuity were due to peripheral abnormalities or due to age-related changes. Two of the studies used controls that were not pain free,<sup>45,61</sup> and 1 study did not include a control group.<sup>58</sup> It is unknown whether these data inflated the differences between the groups or reduced them. Finally, the tactile acuity data reported by Peltz et al<sup>50</sup> differed substantially from the other CRPS studies. The effect sizes from that study were up to 5 times larger than the pooled estimates, and well beyond .8, which is the generally accepted size of a "large" effect.<sup>9</sup> The authors assured us that the anomalies in that data (see Appendix) were coincidental, but the possibility of reporting errors cannot be excluded. We undertook sensitivity analyses with the Peltz et al<sup>50</sup> data removed to ensure that these outlying results did not carry the main finding. Although the pooled effect sizes and heterogeneity were reduced, the findings remained consistent, with the exception of

the finding that tactile acuity was altered at sites remote from the painful site. The sensitivity analysis suggested that TPDTs are not altered at remote sites, and we thus contend that the most prudent position is to conclude that a difference between acuity at sites remote from the site of pain probably does not exist.

In summary, the current evidence suggests that tactile acuity is altered in several chronic pain conditions. However, the strength of the available evidence is weakened by the inconsistent results and the high risk of bias observed in the included studies. Nonetheless, the current findings suggest that tactile acuity deficits may be characteristic of chronic pain in general. Tactile acuity training may be of benefit to the wider range of chronic pain disorders, and clinical trials of this possibility appear warranted.

## Acknowledgments

The authors would like to thank Elena Krumova, Hannu Luomajoki, Christian Maihöfner, Burkhard Pleger, Tasha Stanton, and Benedict Wand for kindly providing their raw data and responding rapidly to other inquiries.

## Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.jpain.2014.06.009>.

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## Appendix

The tactile acuity data reported by Peltz et al<sup>50</sup> differed substantially from the other CRPS studies and several anomalies were observed. Although they followed the same protocol described in the group's earlier study, Maihöfner and DeCol,<sup>37</sup> they reported much smaller variability; .18 SD compared with .64 SD (note that the Maihöfner and DeCol data was calculated from raw data). Interestingly, the mean values for both the patients and healthy controls were identical in these 2 studies and the standard deviations reported by Peltz et al<sup>50</sup> were identical to the standard error of the means reported by Maihöfner and DeCol.<sup>37</sup> Intriguingly, the pain intensity data differed, yet the relationship between the TPDT and pain intensity (as measured by the MPQ and NRS) in the 2 studies were identical (see [Table 3](#)). We contend that this would seem impossible and we therefore suspect an error in reporting. The

raw data for the Peltz et al<sup>50</sup> study was unfortunately unavailable, but the authors assured us that the data came from separate cohorts and the several identical values were coincidental. We would contend, however, that these data represent an anomaly and have thus contributed to an overestimation of the acuity deficits in the pooled analyses. As such, we thought it prudent to include the Peltz et al<sup>50</sup> data but also undertake sensitivity analyses (see [Suppl Figs 1–3](#) in the Supplementary Material) to ensure that the outlying results from Peltz et al<sup>50</sup> did not carry the main finding. Although the pooled effect sizes and heterogeneity were reduced, the findings remained consistent, with the exception of the finding that tactile acuity was altered at sites remote from the painful site. The sensitivity analysis suggested that TPDTs are not altered at remote sites, and we thus contend that the most prudent position is to conclude that a difference between acuity at sites remote from the site of pain probably does not exist.