# Attentional Bias to Somatosensory Stimuli in Chronic Pain Patients: A Systematic Review and Meta-Analysis

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# Abstract

This systematic review and meta-analysis aimed to evaluate the evidence pertaining to attentional bias for painful and non-painful somatosensory stimuli in individuals with chronic pain. Eligible studies were identified via searches of Medline, PsycINFO, CINAHL, Web of Science, Scopus, and Cochrane Library databases. Search terms were words and phrases organised into three concept blocks: pain condition, cognitive process and stimuli/paradigm. The search identified 29 eligible studies (reporting 32 eligible experiments), of which quantitative meta-analysis was possible for 16 studies (19 experiments). The meta-analysis found that chronic pain patients, excluding somatoform pain patients, showed significantly greater attentional bias to stimuli in the somatosensory modality than healthy controls (*k* = 9, *g* = 0.34). Additionally, meta-analysis of studies that used a temporal order judgement task found that patients with unilateral chronic pain showed a spatial attentional bias away from somatosensory stimuli (*k* = 7, effect estimate = 22.43 milliseconds) and visual stimuli (*k* = 2, effect estimate = 13.75 milliseconds) on or near the painful body side. Most studies of attentional bias to the somatosensory modality recruited samples of patients with fibromyalgia whereas most studies of spatial attentional bias assessed patients with complex regional pain syndrome. The extent to which these results generalise to other pain conditions is therefore unclear. We recommend future research test spatial and modality attentional biases across chronic pain conditions and examine the psychometric properties of attentional bias measurement paradigms for use with chronic pain populations. PROSPERO registration number CRD42019124510.

Attentional Bias to Somatosensory Stimuli in Chronic Pain Patients: A Systematic Review and Meta-Analysis

A biopsychosocial approach to the understanding and treatment of chronic pain is currently advocated [22; 37], which highlights, amongst others, the importance of cognitive factors in the experience of pain, including biases in information processing. More specifically, attentional bias (AB), which can be defined as selective attention to pain and pain-related information over other information, has been frequently explored in chronic pain populations [e.g. 47; 57].

Theoretical models posit that AB contributes to chronic pain onset and maintenance. According to the Fear-Avoidance Model, pain hypervigilance develops from fear of pain and contributes to activity disruption and disability in chronic pain [78]. The Threat Interpretation Model of Pain (TIMP) makes more specific predictions for the time-course of AB, positing that vigilance-avoidance pattern of AB to threatening and pain-related information promotes pain chronicity [66]. Providing a broader context of pain-related AB, an Integrated Contextual-Functional Framework of Pain-Related Cognitive Biases suggests that AB fits within a network of cognitive biases, which are functional, interrelated, and influenced by context and motivation [74]. In reference to somatosensory information, the Embodied Defence Model posits that pain captures attention in level two of the protection system of the human body, and only if physiological adaption in level one cannot reduce the threat without awareness. Furthermore, if pain avoidance is not possible (such as in chronic pain) dissociation from pain occurs in level three [14].

A relatively large body of research has investigated visual AB toward pain-related information, notably pain-related words and facial expressions, using numerous paradigms such as modified versions of the Stroop task [e.g. 50], spatial cueing task [e.g. 58], visual-probe task [e.g. 39; 55], visual-search task [e.g. 38; 54], and change detection paradigm [e.g. 56]. Several meta-analyses of pain-related AB have found that chronic pain patients show greater AB toward pain-related information than healthy individuals, particularly for stimuli associated with the sensory dimension of pain. However, effect sizes are generally small and the results of individual studies inconsistent [11; 57; 67].

While carefully selected linguistic and pictorial stimuli may be symbolic representations of pain, they are nevertheless not equivalent to the individual’s actual subjective experience of pain. Somatosensory stimuli, defined as stimuli which can evoke a sensation (e.g. pressure, pain, or warmth) anywhere on the body, may be better suited to assess AB to information related to one’s own actual pain [9; 57; 67; 73]. Chronic pain affects how somatosensory stimuli are processed [e.g. 7] but AB to somatosensory stimuli has not to date been systematically reviewed.

This systematic review and meta-analysis aimed to evaluate ABs for painful and non-painful somatosensory stimuli in individuals with chronic pain. We additionally investigated AB to visual stimuli in peripersonal space around a pain-affected body region [5; 17] because a scoping search identified this as a pertinent extension to the research question. More specifically, we addressed the following questions (depicted schematically in Figure 1): 1) Do chronic pain patients show AB to somatosensory modality stimuli over other modalities of stimuli? 2) Do patients with unilateral chronic pain show spatial AB to somatosensory stimuli near the location of pain? 3) Do chronic pain patients show spatial AB to visual stimuli in the peripersonal space around a pain-affected body region? Somatosensory modality AB and spatial AB were compared between chronic pain patients and healthy controls. Spatial AB was also compared between pain-affected and pain-unaffected sides of the body.

# Method

The protocol for this systematic review and meta-analysis was registered on PROSPERO CRD42019124510 [2].

## Search Strategy

 The search was conducted in seven databases: Web of Science (title); MEDLINE, PsycINFO, and CINAHL (title, subject terms, abstract); PubMed (title/abstract); Scopus (title); and Cochrane Library databases (title, abstract, keywords). The grey literature was searched using the OpenGrey database (main search field). The database search was conducted on 18th October 2019 with studies from database inception until this date eligible for inclusion.

 Search terms were developed from previous systematic reviews of AB [11; 57; 67], original studies of AB to somatosensory stimuli identified in a scoping search [e.g. 17; 25; 43; 46] and consultation with a University of Southampton Research Librarian. The scoping search was conducted in Google Scholar and the above databases using search terms related to AB, relevant stimuli and tasks, and authors with previous publications in this area of research. The search terms were organised into three concept blocks, which were combined with the ‘AND’ operator:

1. Pain condition: (chronic AND (pain OR \*ache)) OR fibromyalgia OR “complex regional pain syndrome” OR CRPS OR migraine OR arthritis OR abdominal OR musculoskeletal.
2. Cognitive process: \*attention\* OR attend\* OR \*vigilan\* OR detect\* OR bias\* OR process\*.
3. Stimuli/paradigm: (visual OR visuospatial OR somat\* OR \*tactile OR \*cutaneous OR electric\* OR pressure OR thermal OR mechanic\* OR vibrat\* OR laser OR “temporal order judgement\*” OR “change detection” OR “body scanning reaction time” OR “dual task” OR oddball).

Titles and abstracts were screened by PB and a random sample of 10% of the records were independently screened by DS. All records would have been screened independently had disagreements been evident in this 10%, but this was not the case. PB and DS independently reviewed the full text of all potentially relevant records with any disagreements resolved by discussion with CL.

## Inclusion and Exclusion Criteria

Studies had to meet the following criteria for inclusion in this review:

1. Recruited participants of any age with any type of chronic pain, defined as pain lasting three months or longer.
2. Assessed attention to somatosensory stimuli (defined as stimuli that can evoke a sensation anywhere on the body) using an attentional task.
3. Compared either chronic pain patients to healthy controls, or compared pain-affected to pain-unaffected body regions in chronic pain patients.
4. The full text was available in the English language.

This review included studies which investigated attention to somatosensory sensations in isolation as well as studies which investigated attention to somatosensory sensations with a concurrent task in another modality. This was based on the rationale that attention has a limited capacity and can be directed to many different internal or external stimuli even without a specific task [8]. Therefore, greater attention to stimuli in the somatosensory modality implies reduced attention to other modalities of stimuli.

Studies which assessed attention to somatosensory stimuli using a neuroimaging method without an attentional task were excluded because in these studies it’s difficult to isolate whether they measured attention or other processes. Studies which assessed AB with a questionnaire were also excluded. All study designs were eligible. Studies published in peer-reviewed journals or as part of PhD theses were eligible for inclusion, whereas studies published as conference abstracts or as MSc theses were ineligible due to lack of rigorous peer-review for these types of reports.

## Data Extraction

 PB and DS independently extracted the following data from eligible studies: Author and year of publication; country in which the study was conducted; domain of AB measured; participant demographics and medical characteristics including sample size, chronic pain condition, gender, age, pain duration, pain intensity; scores from questionnaires administered in the study; body region to which the somatosensory stimuli were presented; paradigm; type of stimuli; results relevant to the outcomes of this systematic review; and correlations between outcomes and participant characteristics. Where the necessary data for meta-analysis were not reported in the article, the corresponding author was contacted up to two times via email to request these data.

## Risk of Bias

 PB and DS independently assessed the risk of bias for included studies. No currently existing tool was appropriate for this review, therefore risk of bias was assessed using items based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [79] and the Cochrane Collaboration’s Risk of Bias Tool [26], in an approach similar to a previous systematic review of tactile acuity in chronic pain patients [7]. The risk of bias assessment tool included the following items: Replicable sampling method; recognised diagnosis inclusion criteria or diagnosis made by a professional; controls matched for age and gender; researcher blinded to group; method could be replicated; paradigm used to assess AB was previously checked for reliability and validity; *a priori* power calculation; no missing data or missing data dealt with adequately; and all assessed outcomes reported.

All items were rated as either: (i) Yes (clearly described or appropriately referenced within paper), (ii) No (clearly reported but criteria not met), or (iii) ? (not reported or description unclear). Comments were provided to justify each rating or ‘NA’ was stated if the item was not applicable to a particular study. Inter-rater reliability was calculated and any disagreements were resolved by discussion between PB and DS, and with CL where necessary.

 Confidence in the cumulative evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria [24]. This cumulative confidence rating was based on the imprecision, inconsistency, indirectness, risk of bias, and publication bias across included studies. Publication bias, defined as the probability of non-publication for small sample studies that found small or negative effects, was evaluated using funnel plots and Egger’s regression test [15]. However, this test is not reliable for fewer than 10 studies due to inadequate statistical power to distinguish asymmetry representative of true publication bias from chance results. Funnel plots were also visually inspected to determine whether the asymmetry indicated by Egger’s test was in a pattern indicative of publication bias (i.e. if small studies always show large effect sizes in one direction) or whether this asymmetry was instead caused by true effect size heterogeneity, reporting bias, methodological quality or chance [64].

## Data Synthesis

 Eligible studies were combined in a narrative synthesis that considered the overall evidence for each outcome organised by chronic pain condition, paradigm, and stimuli type. The terminology/diagnosis used in the original study to describe participants’ chronic pain conditions is retained in the present review.

Quantitative meta-analysis was conducted in R version 3.5.1 with the package ‘meta’ [59]. Random effects models were used, allowing for a distribution of true effect sizes due to within-study and between-study variance [1]. Hedges’ *g* was computed for between-group comparisons, and single means from the temporal order judgement (TOJ) task were pooled based on inverse variance and compared to a null effect of zero [59]. Where measures of variance were not available [46], these were calculated from the *t* statistic [27].

Data for spatial AB were analysed separately for somatosensory stimuli and visual stimuli. We compared chronic pain patients with healthy controls, and also compared the pain-affected side with the unaffected side of patients with unilateral chronic pain. For modality AB, separate meta-analyses were conducted for painful and non-painful stimuli, as well as for attentional interference and distraction efficacy in order to assess these aspects of AB individually. Data from adults and children would have been analysed separately had behavioural data from at least two paediatric studies been available. Heterogeneity was assessed with Cochrane’s *Q* and  *I2* statistics. These statistics complement one another: Q indicates whether heterogeneity is present whereas I2 indicates the extent of heterogeneity. Therefore both were computed to provide a comprehensive assessment of heterogeneity [29]. Sensitivity analyses were conducted when heterogeneity was significant, and studies were removed based on this analysis when there was theoretical rationale. Subgroup analyses were conducted by chronic pain condition and paradigm where possible. Correlations between participant characteristics and the outcomes were extracted from the data, with the plan to conduct meta-regression; however, too few studies assessed correlations between the same variables to allow adequate power for meta-regression [27]. The correlations between questionnaire measures and attentional task measures of AB are discussed in the narrative synthesis.

## Meta-Analysis Methodological Decisions

 It was necessary to make several methodological decisions throughout the meta-analytic process:

1. Only behavioural data were analysed because the data from neuroimaging measures were too heterogeneous to be included in the meta-analysis [12; 13; 25; 30; 33; 40; 63; 65; 80]. Neuroimaging evidence was evaluated in the narrative synthesis.
2. Where a study conducted more than one experiment or more than one condition with the same participants [5; 17; 41-44; 48; 72], the meta-analysis included only the experiment or condition most relevant to the assessed outcome.
3. For spatial AB, positive values indicate bias away from the pain-affected location. For modality AB, greater values indicate greater somatosensory hypervigilance. As recommended by the Cochrane Handbook [27], values were multiplied by -1 where the paradigm produced results in the opposite direction, such as reaction time measures of task performance [12; 62; 63; 71; 75; 77].
4. The TOJ task produces one mean, which was compared to zero [17; 42-44; 48; 68], whereas other measures of spatial AB such as the spatial cueing task [19; 61] and digit discrimination task [20; 33; 34] produce two means (e.g. reaction time to the affected and unaffected sides). These types of studies could not be combined in meta-analysis and were therefore analysed separately.

In addition, to evaluate overall AB to the somatosensory modality:

1. Where a study tested both painful and non-painful stimuli and provided adequate behavioural data for meta-analysis [62], the painful condition was included in the overall meta-analysis.
2. Where results from a common task and primary task were reported, a measure of attentional interference (task performance when experiencing pain as compared to task performance without pain) was included in the overall meta-analysis instead of a measure of distraction efficacy (the pain rating with the attentional task as compared to pain rating without the attentional task).

# Results

The database searches yielded 23,725 records after duplicate removal, of which 40 were potentially relevant. Two further potentially relevant studies were identified by scanning reference lists [20; 34]. Following full-text screening of these 42 studies, 29 studies (reporting 32 experiments) were included in the systematic review (Figure 2). Two studies met the criteria for two outcomes of this systematic review [17; 33] and one study reported three eligible experiments [44]. Of the included studies, 18 assessed AB to the somatosensory modality, eight assessed spatial AB for somatosensory stimuli, and five assessed spatial AB for visual stimuli. Twenty-five studies reported case-control designs whereas four reported single group observational designs [17; 20; 43; 48]. Table 1 summarises the characteristics of included studies, with all data extracted available in Supplementary Table 1. Table 2 provides descriptions of all paradigms from included studies.

## Outcome 1: AB to the Somatosensory Modality

 Eighteen studies assessed AB to the somatosensory modality (chronic pain *N =* 683, healthy *N =*  426) [12; 13; 25; 30; 33; 34; 40; 41; 45; 46; 62; 63; 65; 71; 72; 75; 77; 80].

### Between-group chronic pain patients vs healthy controls: Behavioural evidence.

Sixteen studies reported behavioural measures of AB to somatosensory stimuli, of which five found significant differences between chronic pain patients and healthy controls [12; 33; 34; 62; 77]. Patients with CRPS [33; 34] and migraine [12] showed significantly less AB to the somatosensory modality than healthy controls as indicated by significantly more errors on a digit discrimination task [33; 34] and significantly worse spatial discrimination of somatosensory stimuli [12]. In contrast, two other studies found indications that chronic pain patients had greater somatosensory modality AB than controls. An attentional task was associated with a significantly smaller increase in pain threshold and a significantly smaller decrease in pain ratings for patients with chronic unexplained pain than for healthy controls, indicating greater attention to painful somatosensory stimuli for the chronic pain patients in this study [62]. In addition, patients with fibromyalgia made significantly fewer neglect errors on a vicarious somatosensory experience paradigm than healthy controls indicating fewer lapses of attention to somatosensory stimulation, although the between-group difference in the number of vicarious somatosensory experiences was not significant [77]. No other studies found significant between-group differences in measures of AB to somatosensory modality stimuli. Overall, the behavioural evidence was inconsistent as to whether chronic pain patients showed greater or less AB to somatosensory modality stimuli than healthy controls.

Across the literature there was no consistent evidence that painful stimuli were associated with AB more than non-painful stimuli. Three studies found significant between-group differences with non-painful stimuli [33; 34; 77] whereas two studies found significant between-group differences with painful stimuli [12; 62].

### Between-group chronic pain patients vs healthy controls: EEG and fMRI evidence.

 Nine studies used neuroimaging measures of attention to somatosensory stimuli [12; 13; 25; 30; 33; 40; 63; 65; 80]. The EEG evidence is presented for each component followed by the fMRI evidence.

#### N1.

N1 represents selective attention to basic stimulus characteristics and initial discrimination [31]. Zohsel et al. [80] found that N150 was similar for children with chronic migraine and healthy children in response to laser stimuli during a concurrent oddball task. However, Iacovelli et al. [30] found that children with migraine or tension type headaches showed a significantly greater increase in N140 amplitude than healthy controls when instructed to attend to, rather than ignore, mechanical stimuli during concurrent electrical stimuli. Similarly, during a digit discrimination task the negativity-polarity cluster on the contralateral side at 132ms was significantly greater for CRPS patients than healthy controls and was also greater on the pain-affected side than the pain-unaffected side. However, the results were highly variable between CRPS patients, suggesting that this finding may not generalise to all CRPS patients [33].

#### N2.

N2 responds to deviance from normal stimuli and requires attention for modulation to occur. Interpretations of N2 include an attentional orienting response, stimulus discrimination, and target selection [31]. An attentional task significantly reduced the amplitude of N2 in response to laser stimuli for healthy controls but not for chronic migraine patients [12]. However, in another primary task paradigm study, N260 did not significantly differ between children with chronic migraine and healthy children in response to mechanical stimuli with a concurrent oddball task [80].

#### P2.

P2 is related to selective attention, stimuli change, feature detection, and short-term memory [31]. An attentional task significantly reduced the amplitude of P2 for healthy controls but not for chronic migraine patients [12]. In addition, Hermann et al. [25] found that, during an attentional task, reduction in P2 latency from the painful condition to the non-painful condition was significantly less for children with chronic abdominal pain than for healthy children.

#### N2-P2.

Attentional tasks reduced the amplitude of N2-P2 significantly more for healthy controls than chronic migraine patients from a comparison condition of presentation of the stimuli alone [13] and a somatosensory discrimination task [12].

#### P3.

P3 represents attention to an unexpected stimulus and only occurs when participants attend and respond to a stimulus. Attention allocation, availability of processing resources, and the probability and relevance of a stimulus can all modulate P3 [31]. Children with chronic migraine or chronic abdominal pain, as compared to healthy controls, showed a significantly greater P3 amplitude and significantly shorter P3 latency in response to painful and non-painful stimuli which were presented concurrent to an oddball task [25; 80]. Similarly, adults with CRPS showed a significantly greater P3 than healthy controls in response to non-painful tactile stimuli, specifically a positive-polarity fronto-central (motor area) cluster at 268ms. This between-group difference was only present when participants were engaged in a digit discrimination task, not under conditions of no task demands, which is as expected because P3 requires attention and response to the stimulus [33].

#### Gamma oscillations.

Gamma oscillations, which are thought to be related to selective attention, did not significantly differ between fibromyalgia patients and healthy controls in response to pain or visual stimuli during concurrent laser pain stimuli and a visual reaction time task [65].

#### fMRI.

Under conditions of a concurrent attentional task and thermal pain stimulus, chronic migraine patients showed significantly less task-related activity and more pain-reduction brain activity. Furthermore, when the concurrent painful stimulus was removed and the task was completed without this stimulation, chronic migraine patients showed significantly less deactivation than healthy controls in areas related to pain regulation [40].

A Stroop task with concurrent thermal pain stimuli, as compared to the pain stimuli alone, significantly decreased functional connectivity between the medial prefrontal cortex and the anterior insula for healthy participants but not for participants with somatoform pain. This reduction in functional connectivity may relate to shifting attention away from painful and non-painful somatosensory stimuli, therefore its impairment in chronic pain patients might indicate difficulty disengaging attention from somatosensory stimuli [63].

Overall, neuroimaging evidence indicates that chronic pain patients show greater AB to somatosensory modality stimuli than healthy controls.

## Outcome 2: Spatial AB to Somatosensory Stimuli

 Eight studies [17; 20; 33; 42-44; 48; 68], which reported the results of 10 experiments (three experiments with different participants were reported by Moseley et al. [44]), assessed spatial AB to somatosensory stimuli (chronic pain *N =* 180, healthy *N =* 55).

### Within-group pain-affected vs unaffected side.

Eight studies [17; 20; 33; 42-44; 48; 68] compared attention to somatosensory stimuli on the pain-affected and pain-unaffected sides of the body in samples of participants with unilateral chronic pain. In six of the eight studies at least one outcome measure showed significant AB away from the pain-affected side of the body [17; 20; 33; 42-44; 48; 68].

Five studies that used the TOJ task [42; 43; 48] or digit discrimination task [20; 33] with CRPS patients found significant AB away from the pain-affected side of the body. In the only other study of CRPS patients, this bias was non-significant but in the same direction [17]. One report of three experiments consistently found AB away from the pain-affected body side for patients with unilateral low back pain [44]. The only report of a bias toward somatosensory stimuli at the pain-affected location was conducted with a sample of orofacial pain patients and the finding was not statistically significant [68].

Three studies with CRPS patients [17; 42; 43] have repeated the somatosensory TOJ task with arms crossed over the midline. Two studies that tested this configuration [17; 42; 43] found that CRPS patients showed AB away from the usual location of the pain-affected limb, rather than its current location. This indicates that spatial AB is relative to the location of limbs in space, rather than the limbs themselves. In these studies, there was a significant difference in point of subjective simultaneity (PSS) when arms were crossed as compared to uncrossed [42; 43]. However, one study found no significant difference in PSS between the arms crossed and uncrossed conditions [17].

Overall, the data indicates that chronic pain patients show spatial AB away from somatosensory stimuli on the pain-affected side of the body.

### Between-group chronic pain patients vs healthy controls.

Four studies [33; 42; 44; 68] compared spatial AB to somatosensory stimuli between chronic pain patients and healthy controls using a TOJ task [42; 44; 68] or digit discrimination task [33]. Three studies of CRPS [33; 42] or low back pain patients [44] found at least one indication that AB away from the pain-affected side was greater than AB away from the matched side for healthy controls. No significant between-group differences were found in a TOJ task with chronic orofacial patients and healthy controls [68]. Overall, the evidence suggests that chronic pain patients show greater AB away from somatosensory stimuli on the pain-affected side as compared to the matched side for healthy controls.

## Outcome 3: Spatial AB to Visual Stimuli

Five studies [5; 16; 19; 32; 61] reported investigations of spatial AB to visual stimuli relative to the pain-affected area of the body (chronic pain *N =* 111, healthy *N =* 73).

### Within-group pain affected vs unaffected side.

Two of the five studies which assessed this outcome found a significant AB to visual stimuli relative to the location of pain [5; 17]. Both showed AB to visual stimuli on the side of the body unaffected by pain, although this bias was only significant when hands were out of sight in the study by Bultitude and colleagues [5], and when the visual stimuli were in near space next to the participant’s hands in the study by Filbrich and colleagues [17]. These were the only studies to use a TOJ task and both tested a sample of CRPS patients. Two spatial cueing task studies found no significant difference in attention to visual stimuli on the pain-affected as compared to pain-unaffected sides of the body for patients with unilateral CRPS [19] or migraine with unilateral prodromes [61]. In a neglect test, patients with CRPS and other pain in an upper limb showed slightly faster reaction times to visual stimuli on the pain-unaffected side as compared to the pain-affected side but there was no significant difference between sides [32].

Filbrich et al.[17] found that the PSS was greater when hands were located near to the visual stimuli rather than close to the body. This is somewhat in contrast with the results of Bultitude et al. [5], in which bias was greater when hands were out of sight than when they were near the visual stimulus, although it is noted that the difference in PSS between the no hands and uncrossed hands conditions was not significant in this study.

Overall, the evidence is inconclusive, showing AB away from visual stimuli on the pain-affected side but only for CRPS patients using the TOJ task.

### Between-group chronic pain patients vs healthy controls.

Four studies compared spatial AB to visual stimuli between patients with unilateral chronic pain and healthy controls [5; 19; 32; 61]. One TOJ study found a significantly greater bias to the pain-unaffected side for CRPS patients than the matched side for healthy controls but this difference did not remain in the crossed hands condition [5]. No significant between-group differences were found in studies that used a spatial cueing task or neglect test [19; 32; 61].

Similar to the within-group analysis, the evidence is inconclusive. One study of CRPS patients using the TOJ task found greater AB away from the pain-affected side as compared to the matched side for healthy controls but all other results were non-significant.

## Risk of Bias

Risk of bias assessment revealed that, in some aspects, a large number of studies showed a low risk of bias. All studies reported the results of all measures detailed in the methods section; however, it is possible that unreported measures could have been omitted from the methods section. Twenty-six studies recruited chronic pain patients using published criteria or diagnosis by an appropriately qualified clinician [5; 12; 13; 17; 19; 20; 25; 30; 32-34; 40-43; 46; 48; 62; 63; 65; 68; 71; 72; 75; 77; 80]. Twenty-four studies reported the method with adequate detail to allow for replication [5; 12; 13; 17; 19; 25; 30; 32; 33; 40-42; 44-46; 62; 63; 65; 68; 71; 72; 75; 77; 80] and 19 used a sampling method which could be replicated [5; 12; 13; 30; 32-34; 40; 45; 46; 61-63; 65; 68; 72; 75; 77; 80]. Healthy participants were matched to chronic pain patients by age and gender in 13 studies [5; 12; 13; 19; 32; 33; 40; 42; 45; 46; 62; 65; 72] and this item was inapplicable in another four cases due to single group designs [17; 20; 43; 48]. However, for other items, risk of bias was high in the majority of cases. Only two studies fulfilled the criteria for each of the following items: Conducted an a priori power analysis [44; 68]; used an unbiased method for dealing with missing data (or had no missing data) [5; 44]; and blinded the researcher who analysed the data to whether each participant was part of the chronic pain or healthy group [12; 42]. No study used a paradigm for which the psychometric properties had been tested in the same population. Cohen’s kappa indicated good inter-rater agreement for risk of bias (weighted kappa = 0.93, unweighted kappa = 0.86). Risk of bias for all studies is shown in Supplementary Table 2 and depicted in Figure 3.

## Meta-Analyses

 All between-group meta-analysis results are displayed in Table 3 and all within-group results in Table 4. See Supplementary Material for forest plots of all subgroup analyses.

### AB to the somatosensory modality: between-group chronic pain vs healthy participants.

A large number of studies in the review (*N =* 18) compared AB to the somatosensory modality between chronic pain patients and healthy controls. Ten of these studies provided adequate behavioural data for meta-analysis [12; 41; 46; 62; 63; 65; 71; 72; 75; 77]. Overall, there was no significant difference between chronic pain patients and healthy controls in AB to the somatosensory modality (Figure 4) (*k* = 10, chronic pain *N =* 269, healthy *N =* 266, Hedges’ *g* = 0.27, 95% CI [-0.04, 0.58], *Z* = 1.68, *p* = .093). However, heterogeneity was significant and substantial (Cochrane’s *Q* = 26.99, *p* = .001; *I2* = 66.7%). Only two studies in the meta-analysis found that participants showed (non-significantly) less AB somatosensory stimuli than controls [41; 63]. The study with the most extreme effect in this direction recruited patients with somatoform pain, a diagnostic group which may differ from patients with other chronic pain conditions in their physical and psychological characteristics. A sensitivity analysis excluding this study [63] found a significant between-group difference, with chronic pain patients showing significantly greater somatosensory hypervigilance than controls (*k* = 9, chronic pain *N =* 256, healthy *N =* 253, Hedges’ *g* = 0.34, 95% CI [0.05, 0.64], *Z* = 2.26, *p* = .024). Heterogeneity was reduced but remained substantial (*Q* = 21.08, *p* = .007; *I2* = 62.1%).

Subgroup meta-analysis of the six studies that assessed AB to painful stimuli [12; 41; 62; 63; 65; 75] found no significant between-group difference (*k* = 6, chronic pain *N =* 129, healthy *N =* 134, Hedges’ *g* = 0.28, 95% CI [-0.28, 0.84], *Z* = 0.97, *p* = .331) but there was significant heterogeneity between studies (*Q* = 22.87, *p* < .001; *I2*  = 78.1%). For the reasons detailed above, a sensitivity analysis excluding Stankewitz et al. [63] was conducted but there remained no significant difference between chronic pain patients and healthy controls (*k* = 5, chronic pain *N =* 116, healthy *N =* 121, Hedges’ *g* = 0.45, 95% CI [-0.10, 1.00], *Z* = 1.60, *p* = .110). Heterogeneity remained significant (*Q* = 15.53, *p* = .003; *I2*  = 74.2%).

Five studies reported adequate data for meta-analysis of AB to non-painful stimuli [46; 62; 71; 72; 77]. This subgroup analysis indicated that chronic pain patients also showed significantly greater AB to non-painful stimuli than healthy controls (*k* = 5, chronic pain *N =* 156, healthy *N =* 148, Hedges’ *g* = 0.26, 95% CI [0.03, 0.48], *Z* = 2.22, *p* = .026) with low heterogeneity (*Q* = 3.64, *p* = .456; *I2*  = 0.0%).

In the subset of studies which tested fibromyalgia patients [41; 46; 65; 72; 75; 77], there was no significant difference in AB to the somatosensory modality between chronic pain patients and healthy controls (*k* = 6, chronic pain *N =* 204, healthy *N =* 205, Hedges’ *g* = 0.32, 95% CI [-0.06, 0.71], *Z* = 1.67, *p* = .095). Heterogeneity was significant and substantial (*Q* = 18.00, *p* = .003; *I2*  = 72.2%).

In the subgroup of studies that used the common task paradigm, no significant difference between chronic pain and healthy control groups was found for distraction efficacy (k = 4, chronic pain *N =* 86, healthy *N =* 86, Hedges’ *g* = 0.17, 95% CI [-0.39, 0.72], *Z* = 0.59, *p* = .556). Heterogeneity approached significance in this subgroup of studies (Cochrane’s *Q* = 7.64, *p* = .054; *I2* = 60.8%). Excluding the study of somatoform patients [63], the meta-analysis still showed no significant difference between chronic pain patients and healthy controls in distraction efficacy (k = 3, chronic pain *N =* 73, healthy *N =* 73, Hedges’ *g* = 0.36, 95% CI [-0.10, 0.83], *Z* = 1.53, *p* = .127). Heterogeneity was not significant (*Q* = 3.07, *p* = .215; *I2*  = 34.9%).

In the subgroup of studies that used a primary task paradigm [41; 65; 75], attentional interference by pain was not significantly different between chronic pain patients and healthy controls (k = 3, chronic pain *N =* 92, healthy *N =* 97, Hedges’ *g* = 0.34, 95% CI [-0.48, 1.17], *Z* = 0.82, *p* = .413). Heterogeneity was significant and considerable (*Q* = 14.58, *p* < .001; *I2*  = 86.3%).

In summary, chronic pain patients (excluding somatoform pain patients) showed significantly greater AB to somatosensory modality stimuli than healthy controls. In subgroup analysis, this result was significant for non-painful stimuli but non-significant for painful stimuli. Subgroup analyses grouped by task and chronic pain condition were not significant.

### Spatial AB to somatosensory stimuli: within-group affected vs unaffected sides for chronic pain patients.

Six studies assessed spatial AB to somatosensory stimuli on the affected and unaffected body sides of patients with unilateral chronic pain. Five studies, reporting seven experiments, provided adequate data for meta-analysis [42-44; 48; 68]. All studies used the TOJ task so a single group meta-analysis was conducted on PSS means with the pooled mean compared to a null effect of 0. The overall effect was significant, (*k* = 7, *N =* 91, effect estimate = 22.43, 95% CI [15.79, 29.06], *Z* = 6.62, *p <* .001) (Figure 5). This result indicates that patients with unilateral chronic pain show AB away from somatosensory stimuli on the pain-affected side (or towards the pain-unaffected side). Heterogeneity was significant and substantial (*Q* = 31.59, *p* < .001; *I2* = 81.0%). A sensitivity analysis indicated that Van Damme et al. [68] had the largest effect size and may be a statistical outlier. A meta-analysis excluding this study showed a significant effect in the same direction (*k* = 6, *N =* 71, effect estimate = 25.37, 95% CI [21.21, 29.53], *Z* = 11.94, *p* < .0001) and heterogeneity was greatly reduced (*Q* = 10.61, *p* = .060; *I2* = 52.9%). However, the aim of this meta-analysis was to evaluate AB across chronic pain conditions. It is possible that the finding of Van Damme and colleagues represents a real effect of bias toward the location of pain for participants with orofacial pain, which may also exist in other chronic pain conditions. Therefore, the study has been retained for the final result of this meta-analysis.

Subgroup analysis for each chronic pain condition was conducted where possible. The analyses showed significant bias away from the affected side for patients with CRPS (*k =* 3, *N =* 33, effect estimate = 23.52, 95% CI [18.28, 28.77], *Z* = 8.79, *p* < .0001) and lower back pain (*k =* 3, *N =* 26, effect estimate = 30.11, 95% CI [23.40, 36.82], *Z* = 8.79, *p* < .0001). Results were more heterogeneous for CRPS patients than lower back pain patients (CRPS subgroup: *Q* = 7.23, *p* = .027; *I2* = 72.3%; lower back pain subgroup: *Q* = 1.11, *p* = .574, *I2* = 0.00%).

Congruent with the conclusion of the narrative review, the meta-analysis showed significant spatial AB away from the pain-affected side of the body for somatosensory stimuli. Subgroup analysis showed that this findings was significant for CRPS and back pain.

### Spatial AB to somatosensory stimuli: between-group chronic pain vs healthy participants.

Five studies compared spatial AB to somatosensory stimuli between chronic pain patients and healthy controls, three of which provided adequate data for meta-analysis [42; 44; 68]. There was no significant between-group difference in spatial AB to somatosensory stimuli (k = 3, chronic pain *N =* 42, healthy *N =* 42, Hedges’ *g* = 0.60, 95% CI [-0.63, 1.83], *Z* = 0.96, *p* = .338). Heterogeneity was high (*Q* = 13.47, *p =* .001; *I2* = 85.1%) and sensitivity analysis indicated that Van Damme et al. [68] might be an outlier. With this study omitted, chronic pain patients showed a significantly greater bias away from the affected side than healthy controls (*k* = 2, chronic pain *N =* 22, healthy *N =* 22, Hedges’ *g* = 1.20, 95% CI [-0.55, 1.86], *Z =* 3.61, *p* < .001) and heterogeneity was reduced (*Q* = 0.02, *p* = .890; *I2* = 0.00%). However, as reasoned above, Van Damme et al. [68] will not be omitted from the final result. Therefore, in summary, spatial AB to somatosensory stimuli was not significantly different between chronic pain patients and healthy controls.

### Spatial AB to visual stimuli: within-group affected vs unaffected sides for chronic pain patients.

Five studies assessed AB to visual stimuli on the affected and unaffected sides of the body in patients with unilateral chronic pain. Only TOJ studies were included in the meta-analysis (*k* = 2) [5; 17] because they produced a single mean and could not be statistically combined with measures that produce two means such as the spatial cueing task. The analysis revealed a significant AB away from the pain-affected side for visual stimuli (Figure 6) (*k* = 2, *N =* 38, effect estimate = 13.75, 95% CI [7.05, 20.46], *Z* = 4.02, *p* < .001). Heterogeneity was low (*Q* = 0.03, *p* = .867; *I2* = 0.00%). In accordance with the narrative review, the meta-analysis found AB away from visual stimuli on the pain-affected side but only for CRPS patients using the TOJ task.

### Spatial AB to visual stimuli: between-group chronic pain vs healthy participants.

Two of the four studies that assessed spatial AB to visual stimuli in chronic pain patients and healthy controls provided adequate data for meta-analysis; however, one study used a TOJ task so produced one mean (the PSS) [5] whereas the other used a neglect task which produced two means (performance on the affected and unaffected sides) [32], therefore the studies could not be statistically combined in meta-analysis.

## Correlations between Questionnaire and Attentional Task Measures of AB

Two questionnaires were used by the included studies to assess somatosensory AB. These were the Pain Vigilance and Awareness Questionnaire (PVAQ) [49] and the Body Vigilance Scale (BVS) [51]. The PVAQ is a 16 item questionnaire that measures attention to pain. Participants rate the items on a 6-point scale from 0 (never) to 5 (always) based on their behaviour over the past 2 weeks [49]. The BVS assesses body vigilance, defined as attention to internal bodily sensations, and was originally designed to assess body vigilance in panic disorder. The questionnaire is comprised of 4 items which participants rate from 0 (not at all like me) to 10 (extremely like me) according to how they have felt over the past week [51].

In six of the included studies participants completed the PVAQ [49]. Higher scores on the PVAQ significantly predicted faster detection of electrical stimuli in the single task condition of a body scanning reaction time task (in a multiple regression model: left leg β = -.423, p = .035, right leg β = .474, p =.017) [46]. In addition, higher PVAQ scores were significantly correlated with tactile accuracy (r = .37, p < .05) [71]. However, scores on the PVAQ were not significantly associated with tactile suppression (r = -.29) or tactile intensity (r = .16) [71]. There was also no significant correlation between the PVAQ and primary task reaction times (r = .06, p = .71) [65]; number of vicarious somatosensory errors (r = -.03) or number of neglect errors (r = -.03) [77]; accurate change detection in the predictable (valid trials: r = -.13, p = .437; invalid trials: r = -.07, p = .657) or unpredictable (r = -.06, p = .721) conditions of a change detection task [72]; or PSS in a TOJ task (r = .17) [68]

 The BVS [51] was included in five studies. Higher scores on the BVS were significantly positively correlated with faster detection in body scanning task but only when the stimulus was presented on the right arm (no regression coefficient reported) [46]. Furthermore, scores on the BVS were significantly associated with tactile intensity (r = .42) [71]. BVS scores were not significantly correlated with reaction time to a primary task (no regression coefficient reported) [45]; tactile suppression (r = -.00), or tactile accuracy (r = .13) [71]; accurate change detection in the predictable condition (valid trials: r = .23, p = .142; invalid trials: r = .17, p = .293) or unpredictable condition of a change detection task (r = .28, p = .077) [72]; distraction efficacy (r = -.10) or task interference (r = -.01) [75].

## Meta-Biases

 The evidence in this systematic review and meta-analysis was from observational studies, therefore certainty in the evidence must be adjusted from a baseline of ‘low quality’ according to GRADE [24]. We considered there to be a moderate risk of bias in this systematic review because some items on the risk of bias tool had few studies rated as high risk of bias whereas others had many. We considered inconsistency a moderate concern; although many studies had overlapping confidence intervals, heterogeneity was high in some analyses. Indirectness was possibly the strongest reason to decrease confidence in the evidence because most paradigms used indirect measures of AB and therefore the outcomes could have been affected by multiple confounding factors.

The optimal information size criterion (OIS) was calculated to determine the precision of the systematic review. To meet the OIS criterion the number of participants in the meta-analysis must be greater than the number of participants needed a for single trial with adequate power, as determined by a sample size calculation [23]. The OIS was calculated with *α* = 0.05, power (1 – *β*) = 0.8 and the effect sizes of the meta-analyses. Independent t-tests were conducted for between-group effects and one sample t-tests for the TOJ within-group effects. Sample sizes were greater than the OIS for all main meta-analyses (between-groups modality AB: *OIS* = 535, *N* = 436; between-groups spatial AB to somatosensory stimuli: *OIS* = 82, *N* = 84; within-group spatial AB to somatosensory stimuli: *OIS* = 8, *N* = 91; within-group spatial AB to visual stimuli: *OIS* = 31, *N* = 38). The OIS criterion was met and therefore imprecision was not a great cause of concern for this review [23].

Publication bias was tested using funnel plots and Egger’s regression test for plot asymmetry [15]. Between-group and within-group effect sizes were tested separately because single means from the TOJ task could not be meaningfully combined with standardised mean difference effect sizes. No evidence of publication bias was revealed by visual inspection of funnel plots (Figure 7) or by Egger’s test for between-group modality AB effect sizes (*t* (8) = -0.84, *p* = .424) between-group spatial AB effect sizes (*t* (1) = 5.03, *p* = .125) or within-group spatial AB effect sizes (*t* (7) = -1.23, *p* = .259). However, tests of publication bias for spatial AB contained fewer than 10 studies so Egger’s test may be unreliable in these cases [15]. Overall, there may be reason to downgrade the rating of evidence quality due to the overall probabilities of risk of bias, inconsistency, and indirectness.

# Discussion

 This systematic review and meta-analysis investigated whether chronic pain patients show AB to somatosensory stimuli over other stimuli modalities and relative to the spatial location of pain. The meta-analysis found that chronic pain patients, excluding somatoform pain patients, showed significantly greater AB to somatosensory modality stimuli than healthy controls (*k* = 9, Hedges’ *g* = 0.34). Considering spatial AB, meta-analysis of TOJ task results found that patients with unilateral chronic pain showed significant AB away from somatosensory stimuli (*k* = 7, effect estimate = 22.43ms) and visual stimuli (*k* = 2, effect estimate = 13.75ms) on the pain-affected side of their body. The majority of studies that contributed to this outcome recruited patients with CRPS, therefore the extent to which this finding generalises to other chronic pain conditions is unclear. Meta-analysis of between-group effects indicated that spatial AB to somatosensory stimuli did not differ between chronic pain patients and healthy controls (*k* = 3, *g* = 0.60), reflecting the effect direction inconsistency between studies [42; 44; 68]. There was not a consistent correlation between questionnaire and attentional task measures of AB. This is perhaps unsurprising because it may be difficult for self-report questionnaires to fully assess automatic and unintentional attentional processes such as hypervigilance [10; 70].

AB to somatosensory sensations may contribute to chronic pain maintenance through the mechanisms described by the Attentional Gain Control Model of Hypervigilance [28], which was developed from research with fibromyalgia patients. This model argues that patients monitor sensations indicative of pain and therefore direct more attention to these sensations, amplifying their perception and contributing to the maintenance of chronic pain. This systematic review only found limited evidence for somatosensory hypervigilance in fibromyalgia in one study [77], and the subgroup meta-analysis of fibromyalgia patients was not significant (*g* = 1.67, *p* = .095). However, neuroimaging evidence from the systematic review indicates that AB to the somatosensory modality may exist in other chronic pain conditions including migraine and tension type headache in adults [12; 40] and children [30; 80], somatoform pain [63], and paediatric abdominal pain [25]. For example, the amplitudes of ERP components associated with attention to somatosensory stimuli were reduced by an attentional task to a lesser extent for chronic pain patients than healthy controls. This indicates that chronic pain patients, including paediatric patients [25; 80], attend to somatosensory stimuli over other task demands, which may contribute to difficulty using distraction as a pain management technique [12; 13; 25; 33; 80].

Considering spatial AB, a body of previous research has found that CRPS patients show symptoms of inattention relative to their affected limb, similar to symptoms of hemi-spatial neglect [21]. Therefore, it is unsurprising that this meta-analysis found that CRPS patients show AB away from somatosensory or visual stimuli near their affected limb. However, AB away from the pain-affected location was also found for unilateral low back pain patients [44], suggesting that symptoms of inattention may also be involved in other chronic pain conditions.

In contrast to patients with CRPS and low back pain, previous research has found that healthy participants show AB toward the location of experimentally-induced pain [69; 76]. This difference is not surprising given the extent to which chronic pain differs from experimental pain and may be theoretically explained by the Embodied Defence Model [14], which posits that the protection system of the human body has three levels. At the first level, physiological adaption reduces the threat without awareness, whereas at level two pain captures attention and urges a protective response. Level three is entered when avoidance of pain is not possible, in this level a person dissociates from pain and ignores the urge to engage in protective behaviour [14]. Level two of the model describes the experience of experimentally-induced pain whereas chronic pain is more characteristic of level three, although there is likely to be overlap between these levels dependent on context and intrapersonal factors. AB away from the painful region of the body, as found by this review, may be an example of dissociation in level three.

As described above, this review found that chronic pain patients showed spatial AB away from the location of pain but greater overall AB to somatosensory modality stimuli; these results could be considered conflicting evidence. However, these findings can be integrated within the Threat Interpretation Model of Pain (TIMP) [66], which predicts vigilance to pain-related stimuli during early stages of attention but avoidance of pain-related, threatening stimuli during later stages of attention. Studies of somatosensory modality AB mostly used indirect measures of AB, such as reaction times or neuroimaging indices, which assess initial orienting. In contrast, most studies of spatial AB used the TOJ task, which requires an untimed response from the participant. This response may be subject to demand characteristics and self-presentation biases given the additional time available to the participant, and therefore results from the TOJ task may represent attention during its later stages [18]. Stimuli on the pain-affected side of the body are likely to be interpreted as more pain-related and threatening than stimuli on the unaffected side. Accordingly, spatial AB away from the pain location, as measured by a TOJ task, may indicate avoidance of threatening stimuli during later stages of attention, supporting the vigilance-avoidance pattern of AB that the TIMP predicts to facilitate pain chronicity.

 Attentional bias modification (ABM) interventions have attempted to train attention away from pain-related words and images, with the aim of reducing pain and improving functioning for chronic pain patients, and have shown promising results [6; 35; 36; 53; 60]. Somatosensory stimuli may be more relevant to the experience of pain than words or images, and therefore ABM with somatosensory stimuli could address biases more directly. However, the current review highlights the need for caution in the direction of bias modification and the importance of specificity. ABM interventions must be tailored to the targeted chronic pain condition, a one-size-fits-all approach would not be appropriate. For instance, chronic pain conditions including CRPS and chronic low back pain already show AB away from the pain location [42; 43; 48]. Therefore, ABM which trains attention away from somatosensory stimuli may be ineffective or even detrimental. Indeed, treatments for CRPS including mirror box therapy and prism adaptation involve reintegrating the affected limb into the body schema, directing attention toward, as opposed to away from, the pain-affected limb [4].

 It is important to note that this review included numerous chronic pain conditions, which differ in physical and psychological characteristics. Many of the meta-analyses included a mixture of chronic pain conditions and this is likely to have contributed, at least in part, to the high statistical heterogeneity found in several analyses. Additional heterogeneity may be accounted for by the differences between the numerous tasks included in this review. For example, the primary task paradigm and common task paradigm both involve a concurrent somatosensory stimulus and attentional task which compete for attention and therefore both were considered measures of AB to the somatosensory modality. However, one study that compared measures of attentional interference and distraction efficacy from primary and common task paradigms found no significant correlation between the measures, highlighting the possibility that these may be independent constructs rather than related measures of AB [75]. Where possible, subgroup and sensitivity analyses were conducted to investigate the heterogeneity between chronic pain conditions and tasks. Relatedly, it should be noted this review included tasks that met the inclusion criteria even if they did not explicitly refer to AB. Due to changes in terminology and in our understanding of the construct of AB over time, studies that did not mention AB may have used identical methods to those described as measuring AB, and therefore their exclusion would have rendered the review incomplete.

Another source of heterogeneity in this review lies in the inclusion of both adults and children. Previous studies of cognitive biases to pain-related information have indicated that factors related to developmental stage, including inhibitory control, may influence AB [3]. However, developmental variables were not considered in the current review due to the low number of eligible studies that recruited children [25; 30; 80]. Studies of children were not included in any meta-analyses, due to lack of behavioural data, but were included in the narrative synthesis.

A further limitation of this review is that many assessments of AB to somatosensory modality stimuli did not provide the necessary behavioural data for meta-analysis and therefore the meta-analytic effect size may not be representative of the whole body of evidence. Additionally, only three chronic pain conditions (CRPS, back pain, and orofacial pain) were represented in the evaluation of spatial AB. Therefore, the results of the spatial AB meta-analysis may not generalise to other chronic pain conditions.

 The findings of this review have generated multiple questions for this area of research. First, the risk of bias assessment highlighted the need to investigate the psychometric properties of paradigms that assess attention to somatosensory stimuli to ensure their reliability and validity with chronic pain populations.

 Second, this review has indicated that patients with some types of chronic pain show a significant spatial AB away from the location of pain but it is not yet known whether this bias generalises across chronic pain conditions. Further, as only one study assessed orofacial pain and found an effect in the opposite direction [68], it is unclear whether this finding reflects an outlier or whether patients with chronic orofacial pain (and possibly other unilateral chronic pain conditions) consistently show AB toward their pain-affected side. Future research could assess spatial AB to somatosensory and visual stimuli across a range of chronic pain conditions to clarify the direction and mechanism of spatial AB for each condition.

 Third, future research could investigate the link between AB to somatosensory stimuli and AB to pain-related words and images. This association is theoretically supported by schema theories, which posit that AB is shown to information in schemas related to pain because AB is already shown to pain itself [47], and could have important clinical implications for bias modification interventions.

Finally, recent models of cognitive biases in chronic pain [66; 74] provide theoretical rationale that AB interacts with other types of cognitive bias including interpretation bias and memory bias. Preliminary investigations into the interactions between cognitive biases have been conducted, from our lab, with pain-related words and images [52; 58] but no research has yet investigated these associations with somatosensory stimuli. Research into the interactions between cognitive biases to visual and somatosensory stimuli could provide a broader understanding of the cognitive changes associated with chronic pain and their role in the onset and maintenance of pain.

# Conclusion

 A systematic review of all included studies showed limited behavioural evidence for somatosensory hypervigilance in chronic pain conditions; however, findings from neuroimaging studies provided evidence in support of AB to somatosensory sensations in CRPS, migraine, and abdominal pain. The meta-analysis found that chronic pain patients, excluding somatoform pain patients, showed AB to somatosensory sensations. In addition, meta-analysis of spatial AB studies found that patients with unilateral CRPS and low back pain showed AB away from somatosensory and visual stimuli on their pain affected side, although the extent to which this finding generalises across chronic pain conditions was unclear.

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*Figure 1.* A visual representation of the types of attentional bias investigated by this systematic review of attentional bias to somatosensory stimuli. 1. a) Attentional bias to somatosensory modality stimuli over stimuli in other modalities; 1. b) Attentional bias to somatosensory stimuli on a pain-affected body region as compared to an unaffected body region; 2. Attentional bias to visual stimuli in the peripersonal space of a pain-affected body region as compared to the peripersonal space of a pain-unaffected body region. 1. b) and 2. will be compared between pain-affected and unaffected body regions. All types of attentional bias will be compared between chronic pain patients and healthy controls.

*Figure 2.* PRISMA diagram of the method followed by this systematic review of attentional bias to somatosensory stimuli in chronic pain patients.

*Figure 3.* Risk of bias assessment across included studies (k = 29). The x axis shows the percentage of studies that were rated low, high and unclear risk of bias for each item on the risk of bias tool. The y axis shows the items on the risk of bias tool.

*Figure 4.* Forest plot of somatosensory modality attentional bias compared between chronic pain patients and healthy controls. A positive standardised mean difference (SMD) indicates greater AB for chronic pain patients than healthy controls. The central points of the horizontal lines are the SMD effect sizes from each study. The horizontal lines are the 95% confidence intervals of the effect sizes. The grey squares around the effect sizes indicate the weightings of each study in the meta-analysis; a larger square indicates a greater weighting. The grey diamond indicates the overall weighted effect size.

*Figure 5.* Forest plot of spatial attentional bias to somatosensory stimuli compared between the ipsilateral (pain-affected) and contralateral (pain-unaffected) sides of the body for chronic pain patients with unilateral chronic pain.

*Figure 6.* Forest plot of spatial attentional bias to visual stimuli in peripersonal space compared between the ipsilateral (pain-affected) and contralateral (pain-unaffected) sides of the body for chronic pain patients with unilateral chronic pain.

*Figure 7.* Funnel plots and contour-enhanced funnel plots of studies included in the meta-analyses of between-group modality attentional bias (*k* = 10), between-group spatial attentional bias (*k* = 3) and within-group spatial attentional bias (*k* = 9). Each point represents a study, the x axis shows the effect size from the meta-analysis, and the y axis shows the study precision expressed in standard error units. In the basic funnel plots the vertical line indicates the pooled effect size from the meta-analysis and the inverted funnel shows the 95% confidence interval of the effect. The contour-enhanced funnel plots are centred on the null effect of zero. In the contour-enhanced plots, the white zones include effects *p* > .1, the dark blue zones include effects between *p* = .1 and *p* = .05, the light blue zones include effects between *p* = .05 and *p* = .01, the grey zones include effects *p* < .01.

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| *Table 1* |  |
| Characteristics of studies included in this systematic review of attentional bias to somatosensory stimuli in chronic pain patients  |  |
| **Study** | **Study design** | **Domain of attentional bias (AB) measured** | **Sample size (chronic pain group)** | **Chronic pain condition** | **Paradigm(s)** | **Results** |
| Sinforiani et al. [61]  | Case-control | Visuospatial AB | 46 (26) | Migraine | Spatial cueing task | There was no significant difference between migraine patients and healthy controls in reaction times to targets on the pain-affected side as compared to the side unaffected by pain.  |
| Peters et al. [46] | Case-control  | Somatosensory modality AB | 60 (30) | Fibromyalgia | Body scanning reaction time, dual task  | There was no significant difference between fibromyalgia patients and healthy controls in reaction times on either task. |
| Peters et al. [45] | Case-control  | Somatosensory modality AB | 54 (36) | Low back pain | Primary task, dual task | No significant difference between low back pain patients and healthy controls in reaction times on either task. Low back pain patients with high fear of pain responded slower in all conditions of the primary task.  |
| De Tommaso et al. [13] | Case-control | Somatosensory modality AB | 55 (25)  | Migraine | Primary task | ERPs (N2a-P2) to laser stimuli were reduced significantly less by a primary task for migraine patients than healthy controls.  |
| Förderreuther et al. [20] | Single group | Somatosensory spatial AB | 73 (73) | CRPS | Digit discrimination task | CRPS patients were significantly more likely have difficulty identifying a finger on the affected side than the unaffected side. |
| De Tommaso et al. [12] | Case-control | Somatosensory modality AB | 16 (8) | Migraine | Primary task, common task | There was no significant difference between pain ratings with an attentional task and pain ratings without the task for migraine patients or healthy controls. ERPs (N2 and P2 but not N1) to laser stimuli were reduced significantly less by a primary task for migraine patients than healthy controls. |
| Hermann et al. [25] | Case-control | Somatosensory modality AB | 29 (14) | Abdominal pain | Oddball  | Children with RAP showed significantly greater P3 (but not P2 or N1) amplitudes to painful and non-painful stimuli than healthy controls.  |
| Zohsel et al. [80] | Case-control | Somatosensory modality AB | 31 (16) | Migraine | Oddball  | Children with migraine showed significantly greater P300 (but not P260 or N150) amplitudes to painful and non-painful stimuli and at a shorter latency than healthy controls.  |
| Moseley et al. [43] | Single group  | Somatosensory spatial AB | 10 (10) | CRPS | Temporal order judgement | CRPS patients perceived tactile stimuli on the unaffected arm 25ms faster than tactile stimuli on the affected arm when arms were uncrossed. With arms crossed, CRPS patients perceived stimuli on the affected arm 18ms before stimuli on the unaffected arm. The difference in PSS was significantly different between the crossed and uncrossed conditions. |
| Snijders et al. [62] | Case-control | Somatosensory modality AB | 32 (16) | Chronic unexplained pain | Common task  | Pain thresholds were increased by a distraction task significantly less for patients with chronic unexplained pain than for healthy controls. For painful stimuli, distraction increased VAS scores for chronic pain patients but decreased VAS scores for healthy controls, this was a significant between-group difference. For non-painful stimuli, there was no between-group difference.  |
| Iacovelli et al. [30] | Case-control | Somatosensory modality AB | 38 (28) | Migraine, tension type headache  | Gauze ball test  | The increase in N140 from the neutral to the selective attention condition was significantly greater for children with migraine or tension type headache than healthy children.  |
| Kolb et al. [32] | Case-control | Spatial AB for visual stimuli | 60 (40) | CRPS, other chronic pain in upper extremity | Neglect test | There was no significant differences between CRPS patients, other pain patients and healthy controls in response time on the pain-affected side or the unaffected side.  |
| Moseley et al. [42] | Case-control | Somatosensory spatial AB | 20 (10)  | CRPS | Temporal order judgement | Under conditions with (and without) vision of the arms, CRPS patients perceived tactile stimuli on the unaffected arm 17ms (without vision: 16ms) faster than tactile stimuli on the affected arm when arms were uncrossed. With arms crossed, CRPS patients perceived stimuli on the affected arm 9ms (without vision: 8ms) faster than stimuli on the unaffected arm. The difference in point of subjective PSS was significantly different between the crossed and uncrossed conditions. Healthy controls did not show any significant bias.  |
| Moseley et al. [44]Experiment 1 | Case-control | Somatosensory spatial AB | 24 (12) | Back pain | Temporal order judgement  | Low back pain patients perceived tactile stimuli faster on the unaffected side than the affected side when stimuli were on the back (25ms) or on hands positioned 3cm behind the back (17ms). No significant bias was shown when hands were positioned in front. No significant bias was found in any condition for healthy controls. |
| Moseley et al. [44]Experiment 2 | Single group | Somatosensory spatial AB | 7 (7) | Back pain | Temporal order judgement  | One hand in front of body and one behind. On affected side, tactile stimuli were perceived 36ms faster on the hand in front than the hand behind. There was no difference between hands on the unaffected side. |
| Moseley et al. [44]Experiment 3 | Single group | Somatosensory spatial AB | 7 (7) | Back pain | Temporal order judgement  | Low back pain patients perceived tactile stimuli on the lower back 30ms faster on the unaffected side than the affected side. For tactile stimuli on the upper back there was no significant bias. |
| Tiemann et al. [65] | Case-control | Somatosensory modality AB | 41 (19)  | Fibromyalgia | Primary task  | A painful stimulus affected task performance and neutral gamma oscillations similarly for fibromyalgia patients and healthy controls.  |
| Van Damme et al. [71] | Case-control  | Somatosensory modality AB | 54 (30) | Back pain | Tactile suppression task | Tactile suppression on the back was similar for back pain patients and healthy controls.  |
| Vandenbroucke et al. [77] | Case control design  | Somatosensory modality AB | 77 (39) | Fibromyalgia | Vicarious somatosensory experience paradigm | Fibromyalgia patients made significantly fewer neglect errors than healthy controls. There was no significant difference in the number of vicarious somatosensory experiences between fibromyalgia patients and healthy controls. |
| Filippopulos et al. [19]Experiment 2 | Case-control | Visuospatial AB | 18 (9) | CRPS | Spatial cueing task  | CRPS patients showed no significant difference between saccade latency to targets on the side affected by pain and saccade latency to targets on the unaffected side. There was no significant difference between latency of saccades to the affected side in CRPS patients and latency of saccades healthy controls.  |
| Mathur et al. [40] | Case-control | Somatosensory modality AB | 28 (14) | Migraine | Primary task  | During an attentional task with concurrent experimentally induced heat pain, migraine patients showed less task-related neural activity than healthy controls but more reductions in pain-related activity than healthy controls. |
| Van Damme et al. [72] | Case-control | Somatosensory modality AB | 81 (41)  | Fibromyalgia | Tactile change detection task  | There was no significant difference between fibromyalgia patients and healthy controls in accuracy of tactile change detection. |
| Reid et al. [48]Experiment 2  | Single group | Somatosensory spatial AB | 13 (13) | CRPS | Temporal order judgement | CRPS patients perceived tactile stimuli on the hand of the unaffected side 27ms faster than tactile stimuli on the pain-affected hand. |
| Bultitude et al. [5] | Case-control | Visuospatial AB | 48 (24) | CRPS | Temporal order judgement | CRPS patients perceived visual stimuli on the unaffected side of the body faster than visual stimuli on the affected side when hands were not visible or uncrossed. Bias was similar to healthy controls when hands were crossed. Across conditions bias was 15ms for CRPS patients and 6ms for healthy controls.  |
| Filbrich et al. [17]Visual task | Single group | Visuospatial AB. | 14 (14) | CRPS | Temporal order judgement | CRPS patients perceived visual stimuli in the near space of the unaffected limb 13ms faster than visual stimuli in the near space of the affected limb.  |
| Filbrich et al. [17]Somatosensory task | Single group | Somatosensory spatial AB | 12 (12) | CRPS | Temporal order judgement | The PSS was not significantly different to zero and there were no significant differences between the arms crossed conditions and the arms uncrossed condition.  |
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| Kuttikat et al. [34] | Case-control | Somatosensory modality AB | 313 (253)  | CRPS, fibromyalgia, rheumatoid arthritis, low back pain, fracture,  | Digit discrimination task | There was a significantly higher prevalence of accuracy <10 or time required >20 seconds (previously determined cut off points) among CRPS patients than patients with other chronic pain conditions or healthy controls.  |
| Kuttikat et al. [33]Experiment 1  | Case-control | Somatosensory spatial AB | 26 (13)  | CRPS | Digit discrimination task | CRPS patients were significantly less accurate on the affected side than the unaffected side and were overall less accurate and had slower response times than healthy controls. Patients showed less neural activity than controls in the superior parietal lobe and precuneus in both the task condition and no task condition, but greater activity than controls in the superior frontal lobe in the task condition. Patients showed a greater P300 response in the supplementary motor area in the task condition as compared to controls. |
| Stankewitz et al. [63] | Case-control | Somatosensory modality AB | 26 (13) | Somatoform pain | Common task  | A Stroop task reduced VAS pain intensity and unpleasantness ratings a similar amount for chronic pain patients and healthy controls. During thermal pain and Stroop, healthy controls showed a decrease in functional connectivity between the medial prefrontal cortex and anterior insula from when they experienced thermal pain alone, but this decrease was not shown by somatoform pain patients. |
| Van Damme et al. [68] | Case-control | Somatosensory spatial AB | 40 (20)  | Orofacial pain | Temporal order judgement | The PSS of orofacial pain patients was not significantly different to zero or the PSS of healthy controls.  |
| Van Ryckeghem et al. [74] | Case-control | Somatosensory modality AB | 98 (49) | Fibromyalgia | Primary task, common task  | The difference in reaction times between the condition with concurrent painful stimuli and the condition with concurrent non-painful stimuli was similar for fibromyalgia patients and healthy controls. The difference in pain ratings between visual modality trials and somatosensory modality trials was similar for fibromyalgia patients and healthy controls. |
| Moore et al. [41] | Case-control | Somatosensory modality AB | 50 (24) | Fibromyalgia | Primary task | Induced pain had similar effects for fibromyalgia patients and healthy controls on performance in attentional tasks.  |

*Note.* AB = attentional bias, CRPS = complex regional pain syndrome, ERP = event-related potential, PSS = point of subjective simultaneity, RAP = recurrent abdominal pain, VAS = visual analogue scale.

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| *Table 2* |  |  |
| Paradigms used by studies included in a systematic review of attentional bias to somatosensory stimuli |
| **Paradigm** | **Description of paradigm** | **Measure of attentional bias** |
| Body scanning reaction time.[46] | Somatosensory stimuli are presented at one of several body locations. Participants indicate the location of the stimulus as quickly and accurately as possible. | **Response time to somatosensory stimuli.** A shorter response time indicates greater AB to the somatosensory modality. |
| Common task. [12; 62; 63; 75] | Participants complete an attention-demanding task while being presented with task-irrelevant painful stimuli. | **Difference in pain intensity rating between the conditions with and without attentional task.**A smaller reduction in pain intensity with the task, as compared to without, indicates greater AB to the somatosensory modality.  |
| Digit discrimination task.[20; 33; 34] | Tactile stimuli presented to the tips of fingers. Participants indicate which finger has been stimulated.  | **Accuracy of digit discrimination.** More accurate digit discrimination indicates greater AB to the somatosensory modality.  |
| Dual task.[45; 46] | A somatosensory response time task and a response time task in another modality are presented simultaneously.  | **Difference in response time between single and dual task.**A smaller increase for the somatosensory task than the other task indicates greater AB to the somatosensory modality.  |
| Gauze ball test.[30] | Painful electrical stimuli are presented and participants are asked to either count brief non-painful mechanical stimuli made with a gauze ball (selective attention condition) or just to ignore the painful stimuli (neutral condition). | **Difference in ERPs to the painful stimuli between neutral and selective attention conditions.**  |
| Oddball standards task (with event-related potential measurement)[25; 80]  | Participants respond to rare targets in one modality (e.g. auditory tones) while experiencing task irrelevant noxious or innocuous somatosensory stimuli which participants are instructed to ignore. Event-related potentials (ERPs) are recorded in response to the somatosensory stimuli.  | **Amplitude and latency of ERPs to somatosensory stimuli with concurrent oddball task.**Larger amplitude and shorter latency of P3 indicate greater AB to the somatosensory modality.  |
| Primary task.[12; 13; 40; 41; 45; 65; 75] | Participants complete an attention-demanding task. For some trials of the task irrelevant noxious or innocuous somatosensory stimuli are presented (distraction trials).  | **Difference in task performance between the conditions with and without the somatosensory stimuli.** Decreased task performance to the primary task on distraction trials indicates greater AB to the somatosensory modality. Task performance measured as task accuracy (1) or reaction time (2).  |
| Tactile change detection task.[72] | Two patterns of tactile stimuli are presented consecutively. Participants indicate whether they detected a change between the two patterns.  | **Accuracy of tactile change detection.**Attention improves tactile change detection so greater accuracy indicates greater AB to the somatosensory modality.  |
| Tactile suppression task.[71] | Participants make arm or back movements while tactile stimuli are presented to the arm, back, or chest.  | **The difference in tactile detection between movement and no movement conditions.** A lower index of tactile suppression (less tactile suppression while moving that body area) indicates greater AB to tactile stimuli in that area.  |
| Vicarious somatosensory experience paradigm.[77] | Participants view videos of painful experiences (i.e. hands and knives) while experiencing somatosensory stimuli. Participants indicate when they perceive the somatosensory stimuli.  | **Neglect of somatosensory stimuli (1) and vicarious somatosensory experiences (2).**More vicarious somatosensory experiences (somatosensory perception while observing videos of pain but no actual somatosensory stimulation) and fewer neglect errors (both hands stimulated but only perceive somatosensory stimuli on the side of the pain video). |
| Temporal order judgement. [5; 17; 42-44; 48; 68] | Stimuli are presented at two locations on the body (e.g. one on/near each hand) at various stimulus onset asynchronies (SOAs) meaning that one stimulus is presented at varying lengths of time before the other (this is also known as the inter-stimulus interval). Participants indicate which stimulus they detected first (or second).  | **Point of subjective simultaneity (PSS).**The point at which ‘right stimulus first’ or ‘left stimulus first’ are reported equally often, otherwise described as the point at which the stimuli are perceived as occurring simultaneously. A PSS significantly greater than zero indicates spatial AB toward the side of the stimulus which was presented latest in time.  |
| Neglect test.[32] | Numbers are scattered across a computer screen. Participants indicate when they notice a number flicker.  | **Reaction time.**A faster reaction time to a number flickering on one side of the screen as compared to the other indicates spatial AB to that hemifield.  |
| Spatial cueing task.[19; 61] | A cue is displayed on one side of the computer screen and this is followed by a target either on the same side of the screen or the opposite side.  | **Saccade latencies (1) or reaction times (2).**A shorter saccade latency to targets on one side of the screen indicates spatial AB to visual stimuli in that hemifield.  |

*Note.* (1) indicates first choice of measure to be included in systematic review, (2) indicates second choice if first is not available. AB = attentional bias, ERP = event-related potential, PSS = point of subjective simultaneity.

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| *Table 3* |  |  |  |  |  |  |  |
| Between-groups meta-analyses of attentional bias to somatosensory stimuli in chronic pain versus healthy participants |
| **Description** | ***N* Included studies** | ***N* Chronic pain** | ***N* Healthy** | **Hedges’ *g* (95% CI)** | **Test for overall effect, *Z* and *p*** | **Cochrane’s *Q* and *p*** | ***I2*** |
| AB to the somatosensory modality: chronic pain vs healthy participants.  | 10 [12; 41; 46; 62; 63; 65; 71; 72; 75; 77] | 269 | 266 | 0.27 (-0.04, 0.58) | 1.68, *p* = .093 | 26.99, *p* = .001 | 66.7% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Sensitivity analysis omitting Stankewitz et al. [63].  | 9 [12; 41; 46; 62; 65; 71; 72; 75; 77] | 256 | 253 | 0.34 (0.05, 0.64) | 2.26, *p* = .024 | 21.08, *p* = .007 | 62.1% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used painful stimuli. | 6 [12; 41; 62; 63; 65; 75] | 129 | 134 | 0.28 (-0.28, 0.84) | 0.97, *p* = .331 | 22.87, *p* < .001 | 78.1% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used painful stimuli, omitting Stankewitz et al. [63]. | 5 [41; 62; 63; 65; 75] | 116 | 121 | 0.45 (-0.10, 1.00) | 1.60, *p* = .110 | 15.53, *p* = .003 | 74.2% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used non-painful stimuli. | 5 [46; 62; 71; 72; 77] | 156 | 148 | 0.26 (0.03, 0.48) | 2.22, *p* = .026 | 3.64, *p* = .456 | 0.0% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies with fibromyalgia patients. | 6 [46; 65; 72; 75; 77] | 204 | 205 | 0.32 (-0.06, 0.71) | 1.67, *p* = .095 | 18.00, *p* = .003 | 72.2% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used the common task paradigm. | 4 [12; 62; 63; 75] | 86 | 86 | 0.17 (-0.39, 0.72) | 0.59, *p* = .556 | 7.64, *p* = .054 | 60.8% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used the common task paradigm, omitting Stankewitz et al. [63]. | 3 [12; 62; 75] | 73 | 73 | 0.36 (-0.10, 0.83) | 1.53, *p* = .127 | 3.07, *p* = .215 | 34.9% |
| AB to the somatosensory modality: chronic pain vs healthy participants. Subgroup analysis of studies that used the primary task paradigm. | 3 [41; 65; 75] | 92 | 97 | 0.34 (-0.48, 1.17) | 0.82, *p* = .413 | 14.58, *p* < .001 | 86.3% |
| Spatial AB to somatosensory stimuli chronic pain vs healthy participants. | 3 [42; 44; 68] | 42 | 42 | 0.60 (-0.63, 1.83) | 0.96, *p* = .338 | 13.47, *p* = .001 | 85.1% |
| Spatial AB to somatosensory stimuli chronic pain vs healthy participants. Sensitivity analysis omitting Van Damme et al. [68].  | 2 [42; 44] | 22 | 22 | 1.20 (0.55, 1.86) | 3.61, *p* < .001 | 0.02, *p* = .890 | 0.00% |

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| --- | --- | --- | --- | --- | --- | --- |
| *Table 4* |  |  |  |  |  |  |
| Within-groups meta-analyses of attentional bias to somatosensory stimuli in chronic pain patients |  |  |
| **Description** | ***N*  Included studies** | ***N* Chronic pain** | **Pooled mean (95% CI) (MS)** | **Test for overall offect, *Z* and *p*, null effect = 0**  | **Cochrane’s *Q* and *p*** |  ***I2*** |
| Spatial AB to somatosensory stimuli affected vs unaffected sides for chronic pain patients. | 7 [42-44; 48; 68] | 91 | 22.43 (15.79, 29.06) | 6.62, *p* < .001 | 31.59, *p* < .0001 | 81.0% |
| Spatial AB to somatosensory stimuli affected vs unaffected sides for chronic pain patients. Sensitivity analysis omitting Van Damme et al. [68]. | 6 [42-44; 48] | 71 | 25.37 (21.21, 29.53) | 11.94, *p* < .001 | 10.61, *p* = .060 | 52.9% |
| Spatial AB to somatosensory stimuli affected vs unaffected sides for chronic pain patients. Subgroup analysis of studies with CRPS patients. | 3 [42; 43; 48] | 33 | 23.52 (18.28, 28.77) | 8.79, *p* < .001 | 7.23, *p* = .027 | 72.3% |
| Spatial AB to somatosensory stimuli affected vs unaffected sides for chronic pain patients. Subgroup analysis of studies with back pain patients. | 3 [44] | 26 | 30.11 (23.40, 36.82) | 8.79, *p* < .001 | 1.11, *p* = .574 | 0.00% |
| Spatial AB to visual stimuli: affected vs unaffected sides for chronic pain patients. | 2 [5; 17] | 38 | 13.75 (7.05, 20.46) | 4.02, *p* < .001 | 0.03, *p* = .867 | 0.00% |

*Note.* AB = attentional bias.