A systematic review with subset meta-analysis of studies exploring memory recall biases for pain-related information in adults with chronic pain

Review

Daniel E. Schoth, Kanmani Radhakrishnan & Christina Liossi

Pain Research Laboratory, School of Psychology, University of Southampton, Southampton, UK

Corresponding author: Daniel Schoth, Pain Research Laboratory, School of Psychology, University of Southampton, Highfield, Southampton, SO17 1BJ, UK. E-mail: D.E.Schoth@soton.ac.uk, Tel: 0044 023 8059 4518.

**Abstract**

Pain-related memory biases have been frequently explored in individuals with chronic pain, and along with attentional and interpretation biases are hypothesised to contribute to the onset and/or maintenance of chronic pain. The aim of this review is to provide a systematic review and synthesis of studies exploring memory recall biases for pain-related information in individuals with chronic pain relative to healthy controls and the recall of neutral information. Studies were identified via a search of Medline, PsychINFO, Web of Science, CINAHL, Cochrane Library and Open Grey databases. Search terms were *memory*, *recall*, *recognition*, and *bias*\*, intersected with *pain*. Eighteen studies meeting the inclusion criteria were included. Sub-set meta-analyses are also reported from 12 studies with relevant between-groups data (comparing recall in chronic pain versus healthy control groups) and 12 studies with relevant within-groups data (for example comparing recall of pain-related/emotional versus neutral words). Between-groups analysis revealed significantly weaker recall bias for affective-pain words in individuals with chronic pain relative to healthy controls, but only when non-depressed chronic pain individuals were included. No significant differences were found between groups in the recall of sensory-pain, illness-related or depression-related words. Within-groups analysis revealed individuals with chronic pain show a significant recall bias favouring sensory-pain words relative to neutral and affective-pain words, and a bias for illness-related words relative to depression-related words. A recall bias favouring neutral words was found in healthy individuals. Evidence for the presence of pain-related memory biases in patients with chronic pain is inconclusive. Further methodologically rigorous research is required.

Keywords: Chronic pain; Memory bias; Pain-related information; Meta-analysis; Systematic review

**Introduction**

Individuals with chronic pain show pain-related attentional [17; 86; 101] and interpretation [88] biases compared to healthy individuals. Theoretical accounts of emotional processing and chronic pain also predict memory biases favouring the recall of pain-related information in people with chronic pain [4; 5; 72], and it has been argued different forms of cognitive bias interact and influence one another [28; 40]. The Threat Interpretation Model [100] proposes an interpretation bias favouring the pain-related meaning of ambiguous information is necessary, but not sufficient, for an attentional bias to be observed. Biases in memory have not been incorporated into this model, although memory, attention and interpretation processes interact with each other [14; 41]. More recently van Ryckeghem and colleagues [102] have argued the relationship between pain-related attentional, interpretation and memory biases is bidirectional, which is likely due to shared underlying mechanisms (i.e., motivational and contextual variables), and that the co-occurrence of multiple forms of bias may have cumulative effects on pain-related outcomes. Further to testing these predictions and contributing to a more comprehensive theoretical model of pain-related cognitive biases, an understanding of memory biases in chronic pain is important as it has been speculated they may exacerbate or maintain the experience of pain (e.g., [46; 58]). Across the broader literature evidence of memory bias has been reported in meta-analyses of anxious [37; 59] and depressed [56] populations, and the causal role of such biases in the development of anxiety and depression debated. A review of existing evidence for memory biases in chronic pain will make an important contribution to the chronic pain cognitive bias field, and help guide future research into their clinical implications.

Pincus and Morley [72] provided an excellent narrative review of the cognitive bias literature up to 2001. In their review of the memory bias literature, which included five studies with adults and two studies with children, they explored recall biases for pain-/illness-related words. A meta-analysis was not conducted, nor were specific between-groups effect sizes comparing chronic pain versus pain-free controls computed. Only within-groups effect sizes were calculated where possible comparing recall for pain-related words versus control words, although insufficient information is provided on the exact procedures undertaken. For adults with chronic pain, effect sizes pertaining to the recall of sensory-pain versus neutral words were small to large across two studies (0.33 to 0.78). Nevertheless, and in the absence of between-groups meta-analyses, Pincus and Morley concluded there to be robust evidence for memory biases in chronic pain patients. The specificity of bias and comorbidity of depression were also considered by the authors in their narrative review, concluding that biases exist towards sensory-pain words in chronic pain patients, along with biases towards broader health- and illness-related words in patients who were concurrently depressed or distressed. Considering the overall cognitive bias literature (i.e., attention, interpretation and memory biases), they concluded patients with chronic pain demonstrated preferential processing of sensory-pain stimuli in particular. Numerous studies have been published since this review however. A more recent review from Rusu and colleagues [84] also highlighted evidence of memory biases in individuals with chronic pain, in particular towards sensory-pain words. It was noted however that more recent studies have not replicated this finding, and that future research is needed exploring the influence of moderating variables such as patient depression on memory biases. While informative and timely, neither a systematic search nor a meta-analysis was conducted as part of this review.

The aim of this systematic review is to provide an updated synthesis of studies exploring memory biases for pain-related (sensory-pain, affective-pain, pain images), illness-related and emotional (depression-related, negative) information in adults with chronic pain, and a subset meta-analysis comparing memory biases in patients with chronic pain relative to healthy, pain-free individuals, and also relative to the recall of neutral words. While there is a growing body of research exploring the influence of memory on pain and pain outcomes in children and adolescents (e.g., [66; 67]), a review of the paediatric cognitive bias literature specifically has recently been published [49], with a further systematic review and meta-analysis of this literature currently underway [52]. The present review will therefore focus on the adult memory bias literature only, addressing the following questions: (i) Are adults with chronic pain characterised by a memory bias specifically favouring the recall of pain-related information compared to healthy controls? (ii) Are adults with chronic pain characterised by a memory bias favouring the recall of pain-related information relative to neutral information?

**Methods**

**Literature Search**

PRISMA guidelines were followed [60], and although the protocol was not registered with PROSPERO [78] is available on request. Studies were identified via a search of Web of Science (title), Medline, PsychINFO and CINAHL (title, subject terms), Cochrane Library (title, abstract, keywords) and Open Grey (main search field) databases (the full search strategy is provided in Supplementary Material 1). Search terms were *memory*, *recall*, *recognition*, and *bias*\*, intersected with *pain*. The names of known researchers in the chronic pain cognitive bias field were also used as search terms in the databases. Lastly, reference lists of all obtained articles were inspected. All searches were made from database inception. The initial literature search was conducted by DS, and all potentially eligible records were independently reviewed by DS and CL with any disagreements resolved by discussion.

**Inclusion and Exclusion Criteria**

For inclusion in the review each study was required to meet the following criteria:

1. Available in English language until 12th November 2019.
2. Explored memory recall biases for presented pain-related or illness-related information and provided relevant data.
3. Included a sample of adults (≥ 18 years old) with chronic pain lasting 3 months or longer.

Cognitive biases may differ between children and adults, and therefore studies recruiting a paediatric sample [43; 46] were not included. Patterns of cognitive bias in adult populations may be confounded by recurrent episodes of pain and pain management attempts [49], and developmental factors may also affect patterns of cognitive bias. Indeed, adolescence is a sensitive period of brain development [31], and is associated with improvements in attentional shift, response inhibition, processing speed and emotional capacity [107]. A separate systematic review of the paediatric pain-related cognitive bias literature is therefore currently underway from our research group [52], in the same way separate systematic reviews of anxious youth have been published (e.g., [24; 54]). The present review also only includes studies assessing memory biases for symbolic representations of pain in the form of visually presented pain-related words or images or words presented aurally, in line with recent attentional [17; 86; 101] and interpretation bias [88] reviews. Several reviews of the relationship between working memory and long-term memory and chronic pain have been published. Berryman and colleagues [7] concluded individuals with chronic pain perform worse on working memory tests than healthy controls, with moderate effects found consistently across studies and paradigms. Mazza and colleagues [57] found evidence of moderate declines in both working memory and long-term memory performances in patients with chronic pain. Although it could not be concluded there were long-term storage impairments, patients with chronic pain exhibited more specifically encoding or retrieving difficulties compared to controls.

**Data Extraction** Data from eligible studies was extracted into standardized, pre-piloted forms (developed by CL and DS) by DS which were subsequently checked for accuracy by CL. Where data were unavailable or insufficient for analysis, study authors were contacted via email requesting missing data.

**Study Quality Assessment**

Various bespoke tools have been used in former chronic pain cognitive bias reviews to assess study quality, featuring items relevant to the particular form of cognitive bias under review [17; 81; 86; 88]. We therefore developed a tool to assess quality of memory bias studies specifically, which was based partly on these previously used tools and partly on a tool recently developed for cross-sectional studies [23]. A preliminary version of this tool was piloted, and further feedback obtained from an independent expert in the chronic pain cognitive bias field (see Acknowledgements). The tool includes 15 items covering a range of issues relevant to empirical research in general (e.g., clear description of samples recruited, reporting of *A priori* power calculation) and memory bias research specifically (e.g., appropriate paradigm and stimuli used to assess memory bias, stimuli rated on valence and arousal). Assessment was based on information in the report. Two authors (DS and KR) independently performed the risk of bias assessment (Kappa = .784), with disagreements resolved by discussion where necessary with the third author (CL) (Table S1). A discussion of the results is provided, although a summary score was not computed as these have been found to be unreliable, are not always transparent, and pose difficulties in assigning weightings to different items [38; 39].

According to the GRADE working group if the total number of participants in a systematic review is less than that required for a single adequately powered intervention (a threshold known as the optimal information size OIS)) the quality of evidence may be downgraded [34]. While proposed in relation to clinical interventions, the OIS is nevertheless a useful criterion to evaluate quality of evidence. Power calculations were therefore conducted in GPower [27] for both small (*d* = .30) and medium (*d* = .50) effect sizes, using commonly accepted conventions (two-tailed [30], power level of .80 [16], alpha of .05 [62; 98]).

**Meta-Analytic Procedures**

For inclusion in meta-analysis each study had to provide independent data pertaining to, or enabling the calculation of, effect sizes and standard deviations of appropriate memory bias measures. The magnitude of memory bias was explored via between-groups and within-groups analyses [59]. Between-groups analyses examined differences between chronic pain and healthy control groups in the recall of pain-related/emotional information. Within-groups analyses examined differences between the recall of pain-related/emotional and neutral information in chronic pain and healthy control groups separately. These two types of analysis address different forms of bias, and it may be argued both are required to infer the presence of memory biases in a specific population [59; 83]. In order to explore the bias specificity in more depth [53], within-groups analyses were also conduced where possible comparing recall of sensory-pain versus affective pain words, and recall of pain-related/illness-related versus negative/depression-related words.

 **Between-groups procedures**. Hedges’ adjusted *g* effect sizes (standardized mean difference) for between-group comparisons (chronic pain group versus healthy control group) were computed using group means and standard deviations in Review Manager 5.3 [80]. A random-effects model was used, which assumes the average effect size varies between studies, and therefore heterogeneity is to be expected [10]. Although random-effects models have less statistical power than fixed-effects models, results may be generalised to similar studies not included in the actual analysis [10; 82]. Cochrane’s Q and the I² statistic were used to assess study heterogeneity. With Cochrane’s Q, a significant result is indicative of heterogeneity. The I² statistic describes the percentage of variability in effect estimates due to heterogeneity as opposed to sampling error [39]. Where evidence of significant heterogeneity was found sensitivity analyses were conducted to explore the robustness of findings and with all decisions fully documented [39].

 **Within-groups procedures**. Cohen’s *d* effect sizes were computed for within-group analyses (e.g., recall for pain-related versus neutral words) based on study means and standard deviations. Based on recent recommendations [18; 48] the average standard deviation was used in these computations, as correlations between measures were not available. A random-effects analysis was used to compute average effect sizes using ESCI [18]. Based on the recommendation of Cumming [18] an unbiased estimate of the population effect size, referred to as *d*unb, was computed in ESCI and used in within-groups analyses. This adjustment is advocated as *d* overestimates the population effect size, especially for smaller sample sizes [18; 19; 36]. A positive effect indicates greater recall for pain-related words than neutral words, whereas a negative effect indicates the opposite recall pattern. Cochrane’s Q and the I² statistic were used to assess study heterogeneity, and where significant sensitivity analyses were conducted to explore the robustness of findings and with all decisions fully documented [39].

**Meta-regression.** Meta-regression was planned to explore whether memory bias scores were significantly predicted by individual difference variables such as current pain intensity, anxiety or depression. It was not possible to perform any meta-regression however as none of the analyses included data from ten or more studies as recommended by the Cochrane Collaboration [39].

**Meta-Analytic Methodological Decisions**

A number of methodological decisions were made further to the stated inclusion and exclusion criteria, and which are provided in Supplementary Material 2.

**Results**

**Search Results**

The literature search and study selection process is shown in the PRISMA flow diagram in Figure 1. From an initial identification of 6357 records, 18 studies meeting the inclusion criteria were retained for the review, of which 12 provided data for inclusion in the subset meta-analyses (see Table 1 for study characteristics). Data from 12 studies were available for use in the between-groups meta-analysis, and 12 studies the within-groups meta-analyses.

**Methodological Quality**

All studies clearly stated their aims or objectives, recruited samples representative of the intended population, and provided sufficient details on methods and statistical analyses that would allow for replication. All but one study specified in the methods section the analyses to be conducted which were subsequently reported in the results ([75] reported all details in the results section). The chronic pain group was clearly defined in nine studies [13; 25; 44; 65; 73; 79; 85; 90; 91], and the control group in seven studies [13; 44; 73; 79; 85; 90; 104]. In 17 studies all participants completed the experiment as intended, or the protocol for handling missing data was provided and followed as intended. In the remaining study [26] the protocol for handling missing data at follow-up was not provided. Authors’ conclusions were justified by the results in all studies, although authors did not discuss study limitations in two studies [25; 73]. Seven studies assessed and reported anxiety and depression, and considered potential or actual influences on patterns of memory bias [21; 69; 71; 75; 85; 90; 91].

A number of particularly notable limitations were identified. Only two controlled studies matched their chronic pain and control groups on age, sex, and education [44; 70]. No study rated their stimuli on valence and arousal and reported the data, and only three studies performed a power calculation and reported the results [44; 79; 91]. An appropriate and identical testing environment was only clearly specified in two studies [69; 75]. No study was deemed to have used an appropriate paradigm and stimuli which were described clearly. This item had two subsections, which required both to be answered ‘yes’ in order for the overall item to be rated as ‘yes’. Twelve studies matched their stimuli on relevant dimensions [21; 25; 26; 44; 65; 71; 73-75; 85; 90; 91], although importantly none used a paradigm that has been trialled, piloted, or published previously and reported psychometric properties. While there were broad similarities between the free recall tasks adopted in the studies, the majority differed on important features such as mode of stimuli presentation (computer, audio, written), completion of prior tasks featuring the stimuli (Stroop, homophone, sentence generation, visual-probe, spatial cueing tasks), task instructions (explicit recall, surprise recall after an endorsement task [type of endorsement also varied]), presence of absence of a distractor task, and time allocated for recall. In many instances aspects of the methodology were altered from previous studies without any reported piloting. This, coupled with the lack of reporting of paradigm psychometric properties, resulted in all studies being rated as ‘no’ for this item.

**Systematic Review**

To address the two research questions in turn the narrative synthesis first discusses between-groups results followed by within-groups results.

 **Between-groups biases.** Sensory-pain words were the most common type of stimuli used. Three without an explicit self-endorsement task reported significantly greater recall of sensory-pain words in chronic pain patients relative to healthy controls [70; 71; 90], whereas four found no significant differences between groups [13; 25; 44; 85]. Karimi and colleagues [44] combined sensory- and affective words and found patients with an endurance response pattern recalled significantly more pain-related words than patients with a fear-avoidance response pattern and healthy controls.

Some studies have explored recall following a prior endorsement task, two of which presented participants with a cue question to facilitate encoding of words in relation to the self (*Describes your pain?* *Describes you?*). Wells and colleagues [104] found chronic pain patients who had not received a medical diagnosis recalled significantly fewer sensory-pain words than a healthy control group of medical professionals and patients with ankylosing spondylitis. Another study presented participants with negative illness words which were encoded in self-referent (*Describes you?*) and other-referent (*Describes your best friend?*) conditions, and later divided into sensory-pain and disability categories. No evidence was found for enhanced recall of sensory-pain words in those with chronic pain relative to healthy controls [21]. Pincus and colleagues [74] presented participants with word lists, and for each word required the participant to imagine either themselves (self-referent condition) or another person (other-referent condition) in a situation involving that word. No differences in recall were found between chronic pain and healthy control groups. Overall across the reviewed studies there is no evidence of a significant between-groups effect favouring enhanced sensory-pain recall in chronic pain patients following a prior endorsement task.

No evidence of an enhanced recall bias for affective-pain words (e.g., *cruel, punishing, horrible*) specifically has been reported in chronic pain patients relative to healthy controls [25; 26; 44; 71; 74] (no study included an endorsement task). Broader categories of pain-, illness- and health-related words have also been used (for simplicity this category is referred to as ‘illness-related’). Considering studies without a prior endorsement task, one showed significantly greater recall of illness-related (e.g., *die*, *pain*, *heal*) words in chronic pain patients than healthy controls [75]. Another found no evidence of recall bias in patients with chronic headache relative to healthy controls for ambiguous words with disability and neutral meanings (e.g., *disorder*, *invalid*, *handicap*) [90]. Two studies have explored memory biases in patients diagnosed with somatoform pain disorders. Pauli and Alpers [69] found patients with somatoform pain disorders and hypochondriasis recalled significantly more pain-related words (e.g., *stinging*, *unpleasant*, *miserable*) than patients with somatoform pain disorders only and a patient control group (i.e., patients without somatoform disorder and one or two practice visits within the past 3 months). Nikendei and colleagues [65] recruited somatoform patients with low-back pain and a predominately organic illness attribution (SPP-O), somatoform patients with low-back pain and a predominately psychosocial illness attribution (SPP-P), and pain free controls. Memory for words related to organic causes (e.g., *weak bones*, *strain*, *rheumatism*) and psychosocial causes (e.g., *emotional stress*, *depression*, *divorce*) were explored. The results showed no significant differences in recall between the three participant groups.

Two studies using a prior endorsement task reported chronic pain patients to recall significantly more negative illness-related words than healthy controls. Pincus and colleagues [73] found depressed chronic pain patients to recall significantly more negative pain-related words (e.g., *hurting*, *vulnerable*, *uncomfortable*) encoded in the self-referential condition compared to non-depressed chronic pain patients and healthy controls. Clemmey and Nicassio [15] found patients with rheumatoid arthritis with depression to recall significantly more negative illness-related words (e.g., *sick*, *diseased*, *painful*) than healthy controls, but no difference was found between patients with rheumatoid arthritis without depression and healthy controls. Denton and colleagues reported no evidence of bias for negative illness words (e.g., *hurting*, *aching*, *vulnerable*) in patients with rheumatoid arthritis or systemic lupus erythematosus, although post-hoc analysis found depressed patients to recall a significantly greater proportion of disability-related words than healthy controls and non-depressed patients [21]. Two studies reported no significant differences between participant groups [79; 104].

 For depression/negative words, two studies without an explicit self-endorsement task have not reported any significant biases in chronic pain patients relative to healthy controls [69] [70]. Of those studies featuring an endorsement task, Wells and colleagues found diagnosed chronic pain patients recalled significantly fewer depression-related words than ankylosing spondylitis patients, although no differences were found to healthy controls [104]. The remaining three studies found no evidence of bias towards depression/negative words relative to healthy controls [21; 73; 79].

One study explored memory bias for pain-related images. Busch and colleagues [13] used a computerised memory game involving 12 image pairs randomised and presented ‘face down’ in a 6 x 4 grid. Participants revealed each image by selecting it with the mouse. The task of the participant was to match identical images in as few moves (i.e., mouse clicks) as possible. Participants completed one game featuring pain-related images (images of models displaying pain behaviours, including holding their head/neck/back in pain) and one game featuring neutral images (nature scenes). Chronic pain patients performed significantly worse in the pain-related game than healthy controls, taking more moves to solve the game.

**Within-groups biases.** For sensory-pain words, two studies without an explicit self-endorsement task reported significantly greater recall of sensory-pain words relative to neutral words in those with chronic pain [70; 90]. Another found patients with chronic pain without depression recalled significantly more sensory-pain words than neutral and affective-pain [25]. An uncontrolled study revealed chronic pelvic pain patients prior to surgery recalled significantly more pain-related words than non pain-related words, although sensory- and affective-pain word categories were combined. Six months following surgery, half of the patients were completely pain-free, and the results showed a greater number of non pain-related words recalled than pain-related words [26]. Also combining sensory- and affective-pain words, one study found chronic pain patients recalled fewer pain-related words than neutral words [44].

Considering studies using a prior endorsement task, one reported patients with ankylosing spondylitis and healthy controls to recall significantly more sensory-pain words than neutral, illness-related, and depression-related words [104]. One uncontrolled study found chronic pain patients with diagnostic certainty, and patients with diagnostic uncertainty, to recall significantly more sensory-pain words than neutral words [91]. Pincus and colleagues [74] found chronic pain patients recalled significantly more sensory-pain words encoded in a self-referent condition than those encoded in an other-referent condition, but reported no difference in recall compared to neutral words. Three studies reported no significant within-groups biases for sensory-pain words relative to neutral words [13; 21; 71], although one reported that a significantly greater proportion of sensory-pain words were recalled than neutral words across both chronic pain and healthy control groups [85].

 Regarding affective-pain words, as noted one study showed chronic pelvic pain patients to recall significantly more pain-related words than non pain-related words, with the pain-related words comprising sensory- and affective-pain adjectives [26]. Another reported chronic pain patients recalled fewer pain-related words (sensory and affective-pain words combined) than neutral words [44]. Three studies reported no significant biases for affective-pain words relative to neutral words in patients with chronic pain [25; 71; 74]. Of those studies using illness-related words without a prior endorsement task, one uncontrolled study found chronic pain patients with diagnostic uncertainty recalled significantly more illness-related adjectives (e.g., *suffering*, *disabled*, *dependent*) than neutral words [91]. No other study without [65; 69; 75; 90] or with [15; 21; 73; 79; 104] an endorsement task found evidence of bias for illness-related words relative to neutral words.

Considering studies using depression/negative words without an explicit self-endorsement task, one study found chronic pain patients recalled significantly more negative words than neutral words during immediate recall, but not during delayed (five minute) recall [70]. Another reported no significant recall biases for depression/negative words relative to neutral words [69]. Considering studies featuring an endorsement task, Wells and colleagues found diagnosed chronic pain patients recalled significantly fewer depression-related words than neutral words [104]. The remaining three studies reported no significant recall biases for depression/negative words relative to neutral words [21; 73; 79; 91]. In the only study to use pain-related images Busch and colleagues found that, contrary to their hypothesis, chronic pain patients took significantly more moves to solve the pain-related game than the neutral game [13].

**Meta-Analysis Results**

**Between-Groups Analyses**

Meta-analyses are presented comparing patients with chronic pain to healthy controls on recall memory biases for pain-related (sensory-pain and affective-pain combined), sensory-pain, affective-pain, illness-related, depression-related and negative words. Full details for each analysis is provided in Table 2, and data is presented in a series of forest plots in Figure 2. Additional analyses exploring biases with depressed and non-depressed chronic pain groups separately are provided in Supplementary Material 3 and Table S2. A power calculation revealed the optimal information size for between-groups analyses to be 128 participants for a medium effect size, and 352 participants for a small effect size.

**Pain-related words.** Three studies included data from both sensory- and affective-pain word categories [25; 44; 74]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 1: chronic pain *n =* 87, healthy control *n* = 71;Hedges’ *g* = 0.05, *p* = .84).

**Sensory-pain words.** Eight studies included data from sensory-pain words [13; 25; 44; 70; 74; 85; 90; 104]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 2: chronic pain *n =* 257, healthy control *n* = 212; Hedges’ *g* = 0.10, *p* = .50). Significant heterogeneity was found and therefore a sensitivity analyses was conducted excluding the only study to recruit a control group comprised of medical professionals [104]. Between-group differences remained non-significant (Analysis 3: chronic pain *n =* 185, healthy control *n* = 178; Hedges’ *g* = 0.19, *p* = .16).

**Affective-pain words.** Three studies included data from affective-pain words [25; 44; 74]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 4: chronic pain *n =* 87, healthy control *n* = 71; Hedges’ *g* = -0.30, *p* = .13).

**Illness-related words.** Six studies included data from illness-related (illness-related, negative pain, organic-related causes of pain) words [21; 65; 73; 79; 90; 104]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 5: chronic pain *n =* 231, healthy control *n* = 134 Hedges’ *g* = -0.04, *p* = .79). An additional analysis was conducted excluding studies recruiting control groups comprised of medical professionals/students [79; 104] and which was non-significant (Analysis 6: chronic pain *n =* 99, healthy control *n* = 75; Hedges’ *g* = -0.11, *p* = .68). Another analysis was conducted excluding the only study to recruit patients with a diagnosis of somatoform pain disorder [65] and which again was non-significant (Analysis 7: chronic pain *n =* 203, healthy control *n* = 120; Hedges’ *g* = 0.04, *p* = .82).

**Depression-related words.** Four studies included data from depression-related words [21; 73; 79; 104]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 8: chronic pain *n =* 186, healthy control *n* = 100; Hedges’ *g* = -0.02, *p* = .89). An additional analysis were conducted excluding studies recruiting control groups comprised of medical professionals/students [79; 104] and which was non-significant (Analysis 9: chronic pain *n =* 54, healthy control *n* = 41; Hedges’ *g* = -0.04, *p* = .84).

**Negative words.** Four studies included data from negative words [21; 73; 79; 104]. No significant differences in recall were found between chronic pain and healthy control groups (Analysis 10: chronic pain *n =* 186, healthy control *n* = 100; Hedges’ *g* = 0.20, *p* = .12). An additional analysis was conducted excluding studies recruiting control groups comprised of medical professionals/students [79; 104] and which was non-significant (Analysis 11: chronic pain *n =* 54, healthy control *n* = 41; Hedges’ *g* = 0.32, *p* = .14).

**Within-Groups Analyses**

Meta-analyses are presented comparing memory recall biases for pain-related (sensory- and affective-pain combined), sensory-pain and affective-pain words relative to neutral words in patients with chronic pain and healthy individuals separately. Analysis was not conducted with illness-related words as only one study included neutral words [65]. Analyses were not conducted for depression and negative words as studies using this word categories included negative and/or positive adjectives as control words rather than neutral words specifically [21; 73; 79; 104]. Full details for each analysis is provided in Table 3, and data for chronic pain patients (where applicable including depressed and non-depressed patients combined) is presented in a series of forest plots in Figure 3. Sufficient data were also available to perform analyses comparing recall biases for sensory-pain relative to affective-pain words, illness-related relative to negative words, and illness-related to depression-related words. Additional analyses exploring biases with depressed and non-depressed chronic pain groups separately are provided in Supplementary Material 3 and Table S3.

**Pain-related words versus neutral words.** Three studies included data from both sensory- and affective-pain word categories along with neutral words [25; 44; 74]. No significant recall bias was found for chronic pain patients (Analysis 1: *n* = 87; *d*unb = 0.18, *p* = .09) or healthy controls (Analysis 2:  *n* = 71; *d*unb = -0.20, *p* = .09).

**Sensory-pain words versus neutral words.** Seven studies included data from sensory-pain and neutral words [13; 25; 44; 70; 74; 85; 90]. Significant recall bias was found for chronic pain patients favouring the recall of sensory-pain words (Analysis 3: *n =* 185; *d*unb = 0.53, *p* = .001), but no significant bias was observed in healthy controls (Analysis 5: *n =* 178; *d*unb = -0.09, *p* = .52). Significant heterogeneity was found in each analysis, and therefore sensitivity analyses excluding the study with the largest effect size that could potentially be an outlier ([90] for chronic pain patient analysis, and [85] for healthy control analysis). Recall bias remained significant for chronic pain patients (Analysis 4: *n =* 168; *d*unb = 0.42, *p* = .001). Bias was also significant for healthy controls favouring recall of neutral words over sensory-pain words (Analysis 6: *n =* 144; *d*unb = -0.22, *p* = .02).

**Affective-pain words versus neutral words**. Three studies included data from affective-pain and neutral words [25; 44; 74]. No significant recall bias was found for chronic pain patients (Analysis 7: *n* = 87; *d*unb = 0.03, *p* = .78) or healthy controls (Analysis 8: *n* = 71; *d*unb = 0.03, *p* = .78).

**Sensory-pain words versus affective-pain words.**  Three studies included data from sensory- and affective-pain words [25; 44; 74]. Significant recall bias was found favouring sensory-pain words for chronic pain patients (Analysis 9: *n* = 87; *d*unb = 0.23, *p* = .03). No significant bias was found for healthy controls (Analysis 10: *n* = 71; *d*unb = -0.18, *p* = .15).

**Illness-related versus negative words**. Five studies included data from illness-related and negative words [21; 73; 79; 91; 104]. No significant recall bias was found for chronic pain patients (Analysis 11: *n* = 254; *d*unb = 0.14, *p* = .08). No significant difference was found for healthy controls (Analysis 12: *n* = 100; *d*unb = 0.25, *p* = .23), nor after removal of the study with the largest effect size which could potentially be an outlier (Analysis 13: *n* = 78; *d*unb = 0.08, *p* = .64).

**Illness-related versus depression-related words**. Five studies included data from illness-related and negative words [21; 73; 79; 91; 104]. Significant recall bias was found favouring illness-related words for chronic pain patients (Analysis 14: *n* = 254; *d*unb = 0.41, *p* = .01). This effect remained significant in a sensitivity analysis removing the study with the largest effect size which could potentially be an outlier (Analysis 15: *n* = 216; *d*unb = 0.19, *p* = .01). No significant recall bias was found for healthy controls (Analysis 16: *n* = 100; *d*unb = 0.41, *p* = .12), nor after removal of the study with the largest effect size which could potentially be an outlier (Analysis 17: *n* = 78; *d*unb = 0.13, *p* = .34).

**Publication Bias**

The inspection of funnel plots is not recommended when fewer than 10 studies are included in the meta-analysis [39]. Therefore no funnel plots were inspected in the present meta-analyses, which included at most eight studies.

**Discussion**

The aim of this systematic review was to determine whether adults with chronic pain are characterised by a memory bias specifically favouring the recall of pain-related information. Between-groups analysis revealed patients with chronic pain, relative to healthy controls, show significantly weaker memory recall bias for affective-pain words. This result was only significant with the inclusion of the non-depressed chronic pain group from Edwards and colleagues however [25]. Within-groups analysis showed patients with chronic pain had a significant recall bias for sensory-pain words relative to neutral words and affective-pain words, and a significant recall bias for illness-related words relative to depression-related words. Healthy individuals showed significantly greater recall bias for neutral words relative to sensory-pain words. No significant evidence of memory recall bias was found when sensory- and affective-pain related words were combined.

Inconsistent evidence for the presence of pain-related memory biases have been found when comparing the results of the between- and within-groups meta-analyses, and there is also variation between the results of individual studies. These differences are likely due in part to a number of methodological limitations identified in the individual studies included in this review. For example, none of the studies rated their stimuli on valence and arousal, although emotion has a complex relationship with memory [6] and research has shown arousing and highly valanced words are better recalled than neutral words [45]. It is important researchers therefore include detailed information on stimuli characteristics such as these in their reports. Furthermore, few studies reported using an appropriate and identical testing environment for all participants, although different testing environments could potentially influence recall due to the presence or absence of environmental cues (for example hospital or clinical environments may contain more pain-related cues than university laboratories). Few studies also reported matching chronic pain and control groups on age, sex, and education level, although individual difference variables such as these may also influence memory either individually or through their interaction [20; 33; 94].

Overall, the present results provide only partial support for the predictions of relevant theoretical models (e.g., [5; 72]), and are not in line with the overall conclusion from Pincus and Morley [72] that robust evidence for memory biases exist in chronic pain. It is not uncommon for systematic reviews to reach different conclusions however [42; 61], especially if they are not directly compatible, as is the case in this instance. More specifically: (i) Pincus and Morley included studies from both adult and paediatric samples, including two paediatric studies which reported evidence of significant sensory-pain memory biases [43; 46]; (ii) only the present review included a meta-analysis of study effect sizes (although Pincus and Morley did report within-groups effect sizes where possible); (iii) the present review included ten additional studies published since Pincus and Morley’s review that have reported mixed results; and (iv) the present review clearly separated within- and between-groups effects. The results of the present review are more akin with the review from Rusu and colleagues [84], who note evidence of memory biases has been found in individuals with chronic pain, yet results are not consistent and more recent studies have not replicated this finding.

The only conclusion shared by all three reviews is the existence of an enhanced recall bias favouring sensory-pain words relative to neutral words in adults with chronic pain, which itself is supportive of the view that such words are particularly relevant to patients and favour enhanced processing [17; 35; 72; 100]. Affective-pain words may be less threatening than sensory-pain words, and threat is argued as an important component in the salience of pain-related information and whether cognitive biases are shown [100]. Patients may therefore find it easier to avoid affective-pain words than sensory-pain words, although unfortunately no study included in this review provided ratings on arousal or threat. Although sensory and affective dimensions of pain are intimately related they are nevertheless distinguishable [47; 77], and the existence of different patterns of cognitive bias is not surprising (as shown in the attentional bias literature [17]).

The present review also found individuals with chronic pain showed significantly greater recall bias for sensory-pain words than affective-pain words. It is therefore unsurprising no bias was found when sensory- and affective pain words were combined. A significant between-groups effect revealing weaker biases for affective-pain words in patients with chronic pain was only found when the non-depressed chronic pain group from Edwards and colleagues [25] was included; no difference was found with the inclusion of the depressed chronic pain group or when both depressed and non-depressed groups were combined. This result is difficult to interpret and should be considered with caution as the analysis included only three studies with evidence of moderate heterogeneity. Nevertheless emerging research suggests avoidance of affective-pain information may have negative outcomes. A prospective study of acute and sub-acute low back pain patients showed attentional avoidance of affective-pain information at baseline predicted chronicity at 3 and 6 months [93]. Another study with healthy individuals found training attention towards affective-pain words, compared to training attention away, resulted in significantly greater experimental pain threshold but also greater distress at tolerance [99]. It is feasible attentional avoidance of affective-pain words would lead to a poorer recall of such stimuli [8; 28]. Further research exploring the potential clinical implications of avoiding affective-pain information, as measured via different forms of cognitive bias, is warranted.

Between-groups analysis found no evidence of significant bias for sensory-pain words in patients with chronic pain relative to healthy controls. Research shows poorer memory performance in patients with chronic pain relative to healthy controls [22; 68], and such differences may at least partly explain the lack of between-group effects. Considering evidence shows declines in working memory with increasing age [29], chronic pain and healthy control groups should be matched for age. This was only reported for two studies included in the sensory-pain meta-analysis however [44; 70], and for one study relatively large differences were apparent [25]. Healthy samples were also recruited from a variety of locations, and included psychology students, hospital staff and individuals from evening classes and a community centre, yet only two studies in this analysis reported matching control and chronic pain groups on education [44; 70]. Healthy individuals were found to show significantly greater recall of neutral words than sensory-pain words, although considering the heterogeneity within these samples we recommend caution in the interpretation of this result. Overall, and similar to the attentional [17; 86] and interpretation bias [88] literature, patterns of within- and between-group biases can vary within the same study, and we encourage researchers to be explicit when describing their results.

A number of studies used broader categories of words reflecting illness and organic-related causes of pain (referred to as ‘illness-related’; for example, four studies included in the meta-analysis used the words *vulnerable*, *ill*, *suffering*, and *uncomfortable*). The meta-analysis showed no significant between-group effects.The narrative review suggests additional individual difference variables may be important however, as a number of studies reported recall biases in depressed chronic pain patients relative to controls, but not in patients without depression relative to controls [15; 21; 73]. Within-groups analysis showed individuals with chronic pain to recall significantly more illness-related words than depression-related words (an effect remaining significant with the inclusion of patients with and without depression). Interpretation biases for broader illness-related information has been observed in patients with chronic pain relative to controls [88]. In contrast, between-group differences have not been observed in the attentional bias literature for words and images reflecting antecedents or consequences of pain [17; 87]. We agree with other researchers that it is important for future studies to continue exploring the specificity of cognitive biases in chronic pain and their clinical implications [100], including differences between sensory-pain and broader illness-related stimuli.

 Potential clinical implications of pain-related attentional and interpretation biases have been raised (e.g., [51; 88; 92]). Facilitated recall of pain-related information may enhance emotional distress, which in turn may encourage pain behaviours [74]. Of the five studies reporting correlational analyses between pain-related recall specifically and patient functioning, three reported no significant associations [13; 21; 71]. Pincus and colleagues [73] found, in non-depressed chronic pain patients, 56% of the variance of recall of self-referential negative pain-related words was accounted for by pain at time of testing, maximum pain that week, physical damage ratings (provided by a physician for each patient on a 5 cm visual analogue scale), and chronicity. For depressed chronic pain patients however, significant negative correlations were found between recall of self-referential negative pain-related words and pain at time of testing, maximum pain that week, damage ratings, and activity. In a subsequent study, the proportion of illness-related homophones recalled was significantly and positively correlated with maximum pain intensity from the previous week [75]. Longitudinal research is particularly needed exploring causal relationships between recall biases with pain characteristics and pain-related distress.

Evidence of attentional [17; 86] and interpretation [88] biases have been found in patients with chronic pain, and it has been argued that normal cognitive processes are cyclical in nature [64] and that different forms of cognitive bias influence and interact with one another [40; 100]. Despite this, conclusive evidence for pain-related memory biases does not currently exist in the chronic pain literature. Between-groups analyses found no evidence of biases for sensory pain words, although significant within-group effects were found relative to neutral words. It should be noted however that not all studies in the present review reported matching pain-related and neutral words on length and frequency of use. Considerable research has explored how word length and frequency influence recall, with evidence that shorter words are better recalled than longer words [2], and high frequency words better recalled than low frequency words [76]. These effects are not always consistently reported however [12; 63], and important variations in study design and sample characteristics can influence the pattern of results found. While it is beyond the scope of this review to discuss this literature in detail, it is important to emphasise that researchers should consider stimulus properties such as these when developing their stimuli lists and carefully report such details.

Furthermore, ‘neutral’ is a rather broad term which can be misleading, as in two studies which labelled negative adjectives (e.g., obnoxious, crude, thoughtless) as neutral [91; 104]. As noted, it is important to carefully match emotional and neutral information in memory bias studies, and future research should always assess stimuli on valence and arousal. Significant within-groups bias was also shown for sensory-pain words relative to affective-pain words, although again limitations are apparent as the word categories were not matched on length or frequency. It is also important to acknowledge that the source of bias is not clear when comparing two emotional/threatening categories of information [3], although comparisons with neutral stimuli in the same study can help explain these effects.

Much like attentional [17] and interpretation [89] biases, differing methods may be used to explore memory recall biases, including surprise and explicit tasks. These two different approaches have not been directly compared in the chronic pain field, nor have the reliability of such paradigms been assessed. The latter is important however, as between-group effects may not be detected should the paradigms used be unreliable [59]. Furthermore, the self-reference effect has been extensively documented [96; 97], although only three studies included in the meta-analysis explored whether self-referent encoding facilitates greater recall for pain-related information than other-referent encoding [21; 73; 74]. While only one found evidence supporting the self-reference effect [74], this nevertheless remains an avenue for future investigation. Lastly, one study in this review used a novel computerised memory game with pictures that recorded manual responses (i.e., number of mouse clicks), in addition to immediate recall of a list of memorised words [13]. Although some evidence was shown for differences in performance between the two paradigms (i.e., chronic pain patients performed significantly worse than healthy controls in the computerised memory experiment but not the free recall task), the inclusion of different stimuli makes such comparisons difficult. We encourage researchers to further develop and explore alternatives to the use of simple word lists when researching memory biases, although once again it is important that reliability and psychometric properties are fully assessed.

Experimental [32] and clinical research [66] has shown memory of previous pain significantly contributes to the subsequent experience of pain, while clinical assessment of chronic pain is largely based on the patient’s ability to recall their pain experience [50]. Memory for pain has been extensively studied for many decades, although there is still debate regarding the accuracy of patients’ memories of pain [1]. Nevertheless, some research has shown patients with chronic pain overestimate their pain during later recall [11; 95]. One possibility is that patients who overestimate their previous pain episodes may also demonstrate significantly greater recall biases for pain-related information (i.e., representations of pain). The relationship between biased recall of pain and memory recall biases for pain-related information has yet to be explored however.

Further to recall of symbolic representations of pain, research has also explored the relationship between autobiographical memory and pain. Liu and colleagues [55] administered the Autobiographical Memory Test [105] which presents a series of negative and positive cue words to participants, who for each word were asked to describe what it reminded them of. Chronic pain patients retrieved significantly more overgeneral memories, significantly slower, than healthy controls. Vucurovic and colleagues [103] recruited participants with fibromyalgia and healthy controls, who were instructed to describe five self-defining memories of events from at least one year earlier. Participants with fibromyalgia retrieved less specific self-defining memories (similar to the results of Liu and colleagues [55]) with a more negative emotional valence than healthy controls, although the number of pain memories retrieved did not differ between the two groups. Divergent findings have been reported however. Wright and Morley [106] presented participants with pain-related and neutral cue words, who then subsequently retrieved a personal event from their past associated with the cue. Patients with chronic pain retrieved significantly more memories incorporating elements of physical pain, which was attributable to memories of themselves in chronic pain. This between-group effect was not due to chronic pain patients showing differential sensitivity to pain-related cues specifically however. Although contrasting to the results of Vucurovic and colleagues [103], these two studies used different methodologies with different patient groups, and therefore direct comparison should be avoided. Although it is beyond the scope of the present review to discuss this literature in depth, this body of research nevertheless highlights differences in retrieval of autobiographical memories between individuals with chronic pain and healthy controls. One possibility for future research is to investigate whether recall biases for symbolic representations of pain are associated with, or are predicted by, biases in retrieval of autobiographical memories.

 Unfortunately data was not available from all studies for inclusion in the subset meta-analyses, and in some instances meta-analysis was conducted with as few as three studies. The optimal information size for between-groups analyses was 128 participants for a medium effect size which was met in all but six analyses. The optimal information size was 352 participants for a small effect size however which was not met in 28 of the between-group analyses. The limited number of studies also prevented the use of meta-regression to explore the potential influence of covariates such as pain intensity at the time of testing however [9; 39]. It should also be noted that while all studies included in this review met our inclusion and exclusion criteria, specific pain diagnosis varied between studies and within the analyses conducted. While we are unable to ascertain any consistent evidence that certain pain diagnoses are more likely to be associated with memory recall biases than other pain diagnoses, this is a difficult assessment to make given that studies included in this review differed not only on pain diagnosis but also the precise stimuli and methods employed. A limitation of the present review is that it was not registered on PROSPERO [78]. Although PROSPERO is mainly used for registering systematic reviews of interventions, it good practice to register all systematic reviews in some capacity online. In summary, inconclusive evidence is presented for pain-related memory biases in chronic pain. Numerous methodological limitations have been raised pertaining to the studies included in the present review however, and it is apparent that further, rigorous research is needed.

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**Figure Legends**

Figure 1. Flow of records for inclusion in the narrative review and meta-analysis of memory biases in chronic pain
Figure 2. Between-groups forest plots created in Review Manager showing overall effect sizes for individual studies for pain-related, sensory-pain, affective pain, illness-related, depression-related and negative words ordered by publication date
Figure 3. Within-groups forest plots created using ESCI for chronic pain patients’ recall bias effect sizes

**Tables**

Table 1. Characteristics of chronic pain memory bias studies included in the systematic review and summary of main results

Table 2. Between-groups meta-analysis effect sizes for the recall of pain-related, illness-related, depression-related and negative words

Table 3. Within-groups meta-analyses effect sizes for the recall of pain-related, sensory-pain, and affective pain words relative to neutral words, sensory-pain relative to affective-pain words, and illness-related relative to negative and depression-related words

**List of Supplemental Digital Content**

Supplementary Material 1 – Search Strategy

Supplementary Material 2 – Meta-Analytic Methodological Decisions

Supplementary Material 3 – Additional meta-analyses

Table S1: Quality assessment tool ratings

Table S2: Additional between-groups meta-analysis effect sizes for pain-related, illness-related, depression-related and negative stimuli conducted separately where possible for depressed and non-depressed chronic pain groups

Table S3: Additional within-groups meta-analysis effect sizes for the recall of pain-related, sensory-pain, and affective pain words relative to neutral words, sensory-pain relative to affective-pain words, and illness-related relative to negative and depression-related words