



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

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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 through 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. Subset meta-analyses are also reported from 12 studies with relevant between-groups data (comparing recall in chronic pain vs healthy control groups) and 12 studies with relevant within-groups data (eg, comparing recall of pain-related/emotional vs 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 nondepressed 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

1. Introduction

Individuals with chronic pain show pain-related attentional^{17,86,101} and interpretation⁸⁸ biases compared with 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 Model¹⁰⁰ 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 et al.¹⁰² have argued the relationship between pain-related attentional, interpretation, and memory biases is bidirectional, which is likely due to shared underlying mechanisms (ie, 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 because it has been speculated they may exacerbate or maintain the experience of pain.^{46,58} Across the broader literature, evidence of memory bias has been reported in meta-analyses of anxious^{37,59} and depressed⁵⁶ 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 Morley⁷² provided an excellent narrative review of the cognitive bias literature up to 2001. In their review of the

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memory bias literature, which included 5 studies with adults and 2 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 vs pain-free controls computed. Only within-groups effect sizes were calculated where possible comparing recall for pain-related words vs 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 vs neutral words were small to large across 2 studies (0.33–0.78). Nevertheless, and in the absence of between-groups meta-analyses, Pincus and Morley concluded there to be robust evidence for memory biases in patients with chronic pain. 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 patients with chronic pain, along with biases towards broader health- and illness-related words in patients who were concurrently depressed or distressed. Considering the overall cognitive bias literature (ie, attention, interpretation, and memory biases), they concluded patients with chronic pain demonstrated preferential processing of sensory-pain stimuli in particular. However, numerous studies have been published since this review. A more recent review from Rusu et al.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. Although there is a growing body of research exploring the influence of memory on pain and pain outcomes in children and adolescents,^{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: (1) Are adults with chronic pain characterised by a memory bias specifically favouring the recall of pain-related information compared with healthy controls? and (2) Are adults with chronic pain characterised by a memory bias favouring the recall of pain-related information relative to neutral information?

2. Methods

2.1. Literature search

PRISMA guidelines were followed,⁶⁰ and although the protocol was not registered with PROSPERO,⁷⁸ it is available on request. Studies were identified through a search of Web of Science (title), MEDLINE, PsychINFO and CINAHL (title, subject terms), Cochrane Library (title, abstract, key words), and Open Grey (main search field) databases (the full search strategy is provided in supplementary material 1, available at <http://links.lww.com/PR9/A62>). 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. Finally, 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 D.E.S. and C.L. with any disagreements resolved by discussion.

2.2. Inclusion and exclusion criteria

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

1. Available in the English language until November 12, 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 development³¹ 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.^{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 bias⁸⁸ reviews. Several reviews of the relationship between working memory and long-term memory and chronic pain have been published. Berryman et al.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 et al.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 with controls.

2.3. Data extraction

Data from eligible studies were extracted into standardized, prepiloted forms (developed by C.L. and D.E.S.) by D.E.S. which were subsequently checked for accuracy by C.L. Where data were unavailable or insufficient for analysis, study authors were contacted through email requesting missing data.

2.4. 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 (eg, clear description of samples recruited, reporting of a priori power calculation) and memory bias research specifically

(eg, 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 (D.E.S. and K.R.) independently performed the risk of bias assessment (Kappa = 0.784), with disagreements resolved by discussion where necessary with the third author (C.L.) (Table S1, <http://links.lww.com/PR9/A62>). 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 Although proposed in relation to clinical interventions, the OIS is nevertheless a useful criterion to evaluate quality of evidence. Power calculations were therefore conducted in GPower²⁷ for both small ($d = 0.30$) and medium ($d = 0.50$) effect sizes, using commonly accepted conventions (2-tailed,³⁰ power level of 0.80,¹⁶ alpha of 0.05^{62,98}).

2.5. 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 SDs of appropriate memory bias measures. The magnitude of memory bias was explored through 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 2 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} To explore the bias specificity in more depth,⁵³ within-groups analyses were also conducted where possible comparing recall of sensory-pain vs affective-pain words and recall of pain-related/illness-related vs negative/depression-related words.

2.5.1. Between-groups procedures

Hedges' adjusted g effect sizes (standardized mean difference) for between-group comparisons (chronic pain group vs healthy control group) were computed using group mean values and SDs 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 I^2 statistic were used to assess study heterogeneity. With Cochrane's Q , a significant result is indicative of heterogeneity. The I^2 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

2.5.2. Within-groups procedures

Cohen's d effect sizes were computed for within-group analyses (eg, recall for pain-related vs neutral words) based on study mean values and SDs. Based on recent recommendations,^{18,48} the

average SD 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 (Exploratory Software for Confidence Intervals).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 I^2 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

2.5.3. 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, because none of the analyses included data from 10 or more studies as recommended by the Cochrane Collaboration.³⁹

2.6. 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, available at <http://links.lww.com/PR9/A62>.

3. Results

3.1. 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.

3.2. 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 (Ref. 75: reported all details in the results section). The chronic pain group was clearly defined in 9 studies,^{13,25,44,65,73,79,85,90,91} and the control group in 7 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 2 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 2 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 3

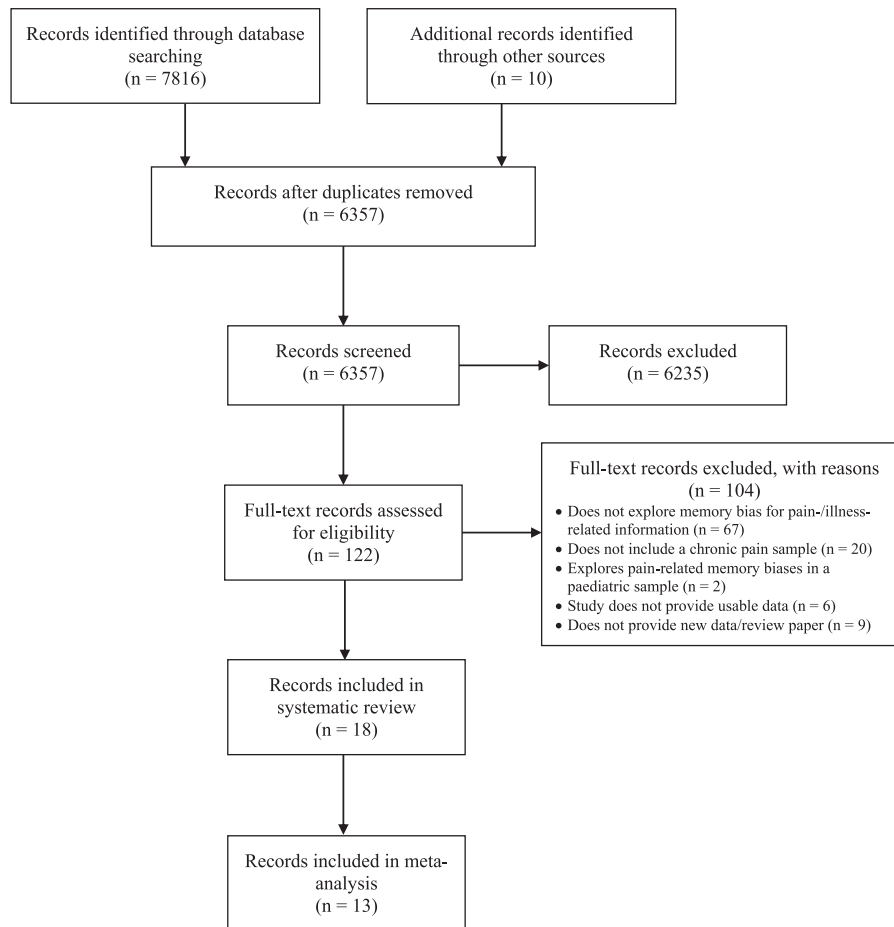


Figure 1. Flow of records for inclusion in the narrative review and meta-analysis of memory biases in chronic pain.

studies performed a power calculation and reported the results.^{44,79,91} An appropriate and identical testing environment was only clearly specified in 2 studies.^{69,75} No study was deemed to have used an appropriate paradigm and stimuli which were described clearly. This item had 2 subsections, which required both to be answered “yes” 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 trialed, piloted, or published previously and reported psychometric properties. Although 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 previous 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.

3.3. Systematic review

To address the 2 research questions in turn, the narrative synthesis first discusses between-groups results followed by within-groups results.

3.3.1. 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 patients with chronic pain relative to healthy controls,^{70,71,90} whereas 4 found no significant differences between groups.^{13,25,44,85} Karimi et al.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 after a previous endorsement task, 2 of which presented participants with a cue question to facilitate encoding of words in relation to the self (Describes your pain? Describes you?). Wells et al.¹⁰⁴ found patients with chronic pain 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 et al.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

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

Study	Country	Paradigm	Stimuli category	Sample (age and sex)	Summary of main study results
Pearce et al., ⁷⁰ —Experiment 1*	United Kingdom	Explicit recall task immediately after presentation of words and a delayed recall task after a 5-minute distractor	Sensory-pain, negative, and neutral words	25 patients with chronic pain 25 healthy controls (mean age across both groups 50.36 [15.73]; 52% male)	In the immediate recall condition, patients with chronic pain recalled significantly more sensory-pain words than neutral words and significantly more negative words than neutral words In the immediate recall condition, a significant interaction revealed patients with chronic pain to recall more sensory-pain words, and fewer neutral words, than healthy controls. In the delayed recall condition, patients with chronic pain recalled significantly more sensory-pain words than negative and neutral words. In the delayed recall condition, patients with chronic pain recalled fewer words overall compared with healthy controls. In both recall conditions, patients with chronic pain were significantly more likely to falsely recall the word "pain" than healthy controls.
Edwards et al. ^{25,*}	United Kingdom	Explicit free recall task and a recognition task	Sensory-pain, affective-pain, and neutral adjectives	19 chronic pain patients without depression (45.79 [14.80]) 16 chronic pain patients with depression (52.38 [8.54]) 18 patients with depression (45.39 [14.56]) 19 healthy controls (39.42 [9.89]) (sex ratio unclear)	Chronic pain patients without depression recalled significantly more sensory-pain than affective-pain and neutral words. Depressed patients recalled significantly fewer affective-pain words than sensory-pain and neutral words. Analysis of recognition task data suggests both chronic pain groups to have poorer true memory performance than healthy controls.
Pincus et al. ^{74,*}	United Kingdom	Explicit recall task and a word recognition task, after an encoding task during which participants had to imagine either themselves (self-referent condition) or a fictional doctor/nurse (other-referent condition) "in a situation in which something, or someone, is [target word]." Participants then rated the likelihood of this situation occurring on a 5-point scale.	Sensory-pain, affective-pain, and neutral adjectives	21 patients with chronic pain (attending a rheumatology clinic) (43.9 [12.33]; 8 male, 13 female) 21 healthy controls (50.7 [15.97]; 8 male, 13 female)	Patients with chronic pain recalled significantly more sensory-pain words, and significantly fewer neutral words, encoded in the self-referent condition than the other-referent condition. Healthy controls recalled significantly more affective-pain words encoded in the self-referent condition than the other-referent condition. Across both groups, better recognition memory and a shift in response criterion was found for self-referent words compared with other-referent words and also for sensory-pain words compared with affective-pain and neutral words.

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Table 1 (continued)

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

Study	Country	Paradigm	Stimuli category	Sample (age and sex)	Summary of main study results
Pincus et al. ^{73,*}	United Kingdom	Surprise free recall task, after an endorsement task (Describes you? Describes your best friend?)	Pain-related, depression-related, and control adjectives, each split into negative and positive valence categories. Separate word lists for self-referent and other-referent endorsement task questions.	19 nondepressed chronic pain patients (15 rheumatoid arthritis, 4 osteoarthritis) (49.00 [12.28]; 12 male, 7 female) 19 depressed chronic pain patients (14 rheumatoid arthritis, 5 osteoarthritis; 12 male, 7 female) (49.05 [12.03]) 19 healthy controls (48.50 [9.92]; 12 male, 7 female)	Depressed chronic pain patients recalled significantly more negative pain-related words encoded in the self-referential condition compared with nondepressed chronic pain patients and healthy controls. Depressed chronic pain patients recalled significantly more positive pain-related words encoded in the self-referential condition compared with healthy controls. In the nondepressed chronic pain group, 56% of variance of recall of self-referential negative pain-related words was accounted for by pain at time of testing, maximum pain that week, damage ratings, and chronicity.
Edwards et al. ²⁶	United Kingdom	Recall task	Sensory-pain, affective-pain, neutral, and gardening-related words. The first 2 categories were subsequently combined to form a pain-related category, and the latter 2 categories were subsequently combined to form a non-pain-related category	24 female chronic pelvic pain patients undergoing hysterectomy and oophorectomy (35.96 [6.16])	Before surgery, patients recalled more pain-related than non-pain-related words. Six months after surgery, patients recalled more non-pain-related words than pain-related words. However, the interaction between word category and time of testing only revealed a trend for significance ($P = 0.08$).
Pincus et al. ⁷⁵	United Kingdom	Surprise free recall task, after an interpretation bias task	Illness-related homophones (which also have neutral associations) and nonhomographic neutral words	20 patients with chronic pain (including patients with limb, back, and shoulder, and abdominal pain) (47.6 [11.12]; 55% female) 20 healthy controls (48.7 [10.26]; sex not provided, although "matched as closely as possible")	Patients with chronic pain recalled significantly more illness-related words than healthy controls. Chronic pain patients' proportion of illness-related words recalled was positively correlated with maximum pain intensity for the previous week. Patients with chronic pain, compared with healthy controls, interpreted significantly more ambiguous homophones as illness-related.
Clemmey and Nicassio ¹⁵	United States	Incidental free recall task and a recognition task, after a self-description task where participants indicated if each word was descriptive of themselves	Negative illness-related words, positive illness-related words (ie, words representing good health, eg, strong and healthy)	25 rheumatoid arthritis patients with depression (RAD) (61.2 [14.3]; 22 female, 3 male) 25 rheumatoid arthritis patients without depression (RAN) (59.4 [10.4] 22 female, 3 male) 25 depressed patients without rheumatoid arthritis (DEP) (61.1 [13.6] 22 female, 3 male) - 25 healthy controls (NON) (62.4 [9.6] 22 female, 3 male)	The RAD group (1) recalled and (2) falsely recognized significantly more negative illness-related words than the RAN and NON groups. The RAN group recalled significantly more positive illness-related words than the RAD group. Within-group analysis showed the RAD group recalled and falsely recognized significantly more negative illness-related words than positive illness-related words. Within-group analysis showed RAN and NON groups recalled and falsely recognized significantly more positive illness-related words than negative illness-related words. The DEP group (1) recalled and (2) falsely recognized significantly more negative illness-related words than the NON group. Regression analysis revealed negative illness self-schema (a composite index of recall scores, false recognition scores, stimuli rated as self-descriptive, and past and future illness behaviours) accounted for 9% unique variance in functional disability scores.

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Table 1 (continued)

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

Study	Country	Paradigm	Stimuli category	Sample (age and sex)	Summary of main study results
Pincus et al. ⁷¹ —Experiment 1	United Kingdom	Free recall task, after a Stroop task	Sensory-pain, affective-pain, neutral, and colour words.	20 patients with chronic pain (8 female, 12 male) 20 healthy controls (8 female, 12 male) (age information not provided)	Patients with chronic pain recalled significantly more sensory-pain words than healthy controls.
Pauli and Alpers ⁶⁹	Germany	Four word-sets were presented, with an immediate recall task after each. Delayed recall task 20 minutes after final word-set. Recognition test (48 stimulus words plus 48 - additional words from matching categories).	Pain-related, negative, positive, and neutral adjectives (3 of each per word-set)	8 patients with somatoform disorder (SP-only) (38.3 [9.3]; 4 female, 4 male) 14 patients with hypochondriasis and somatoform pain disorder (HH & SP) (38.8 [8.7]; 11 female, 3 male) 6 patients with hypochondriasis disorder (HH-only) (44.2 [5.1]; 4 female, 2 male) 14 patient controls (ie, patients from the same medical practice without somatoform disorder and one or 2 practice visits with past 3 mo due to well-defined minor complaint) (36.6 [5.2]; 8 female, 6 male)	Patients with HH & SP immediately recalled significantly more pain-related words than SP-only patient and patient control groups. Patient controls immediately recalled significantly more positive words than all other participant groups. Averaged across immediate and delayed recall, patients with hypochondriasis (HH and SP, and HH-only) recalled significantly fewer positive, and significantly more pain words, than patients without hypochondriasis (SP-only and patient controls). Recognition test showed patients with hypochondriasis to have less conservative criteria for the recognition of pain-related and negative adjectives than patients without hypochondriasis (ie, more likely to recognise such words although they were not part of the originally presented stimuli).
Wells et al. ^{104,*}	United Kingdom	Surprise free recall task, after an endorsement task (Describes your pain? Describes you?)	Sensory-pain, illness-related, depression-related, and neutral† adjectives	15 diagnosed chronic pain patients 21 undiagnosed chronic pain patients 36 ankylosing spondylitis patients 34 healthy controls (hospital staff) (age information not provided) (sex not provided)	Nondiagnosed chronic pain patients recalled significantly fewer sensory-pain words than the ankylosing spondylitis and healthy control groups Diagnosed chronic pain patients recalled significantly fewer depression-related words than ankylosing spondylitis patients. Diagnosed chronic pain patients recalled significantly fewer depression-related words than sensory-pain, illness-related, and neutral words. Ankylosing spondylitis patients recalled significantly more sensory-pain words than depression-related, illness-related, and neutral words. Healthy controls recalled significantly more sensory-pain words than depression-related, illness-related, and neutral words. Further analysis revealed this to be significant only for controls hypothesised to show a frequency effect (eg, doctors and nurses, n = 21).

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Table 1 (continued)

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

Study	Country	Paradigm	Stimuli category	Sample (age and sex)	Summary of main study results
Read and Pincus ^{79,*}	United Kingdom	Free recall task, after an endorsement task (Describes you now? Describes you in the future?)	Ill-health, depression-related, and control adjectives, each split into negative and positive valence categories. Separate word lists for current and future endorsement task questions	35 nondepressed chronic low back pain patients (55.97 [17.51]; 15 male, 20 female) 25 depressed chronic low back pain patients (51.40 [16.37]; 12 male, 13 female) 25 healthy controls (student osteopaths) (30.92 [6.85]; 13 male, 12 female)	Depressed chronic pain patients recalled significantly more ill-health words than depression-related words encoded in the current (Describes you now?) endorsement condition. No significant differences in recall bias were found between any of the 3 participant groups.
Denton et al. ^{21,*}	Australia	Free recall task, after an endorsement task (Describes you? Describes your best friend?)	Pain-related, depression-related, and control adjectives, each split into negative and positive valence categories. Separate word lists for self-referent and other-referent endorsement task questions. Pain-words were subsequently split into sensory-pain and disability categories	16 patients with rheumatoid arthritis (58.7 [11.8]; 2 male, 14 female) 26 patients with systemic lupus erythematosus in a flare (SLE flare) (40.2 [12.1]; 0 male, 26 female) 17 SLE patients not in a flare (SLE nonflare) (50.8 [9.7]; 1 male, 16 female) 22 healthy controls (44.0 [13.8]; 1 male, 21 female)	No significant differences were found between the 4 participant groups in the proportion of words recalled. Patients were combined and then split into depressed and nondepressed groups. The nondepressed group of patients recalled significantly fewer positive control words than depressed patients and healthy controls. Depressed patients recalled significantly more disability illness words compared with both nondepressed patients and healthy controls.
Busch et al. ^{13,*}	Sweden	(1) Computerised memory experiment of the classic card game "concentration." Twelve image pairs are included, face down, and participants must find matched pairs in as few attempts as possible (2) Immediate free recall of memorised words	(1) Images of people depicting pain behaviours and facial expressions of pain and neutral images of nature (2) Sensory-pain and neutral (ie, sound) adjectives	28 chronic myofascial pain syndrome patients (neck pain) (33 yrs, 18–50; all female) 28 healthy controls (29 yrs, 19–44; all female)	Patients with chronic pain performed significantly worse in the pain-related computerised memory experiment compared with healthy controls, taking more attempts to solve the game. Patients with chronic pain performed significantly worse in the computerised memory experiment featuring pain images than neutral images, taking more attempts in the former. No significant differences were found between chronic pain and healthy control groups in the word recall task.
Nikendei et al. ^{65,*}	Germany	Four word-sets were presented, with an immediate recall task after each. Recognition test (48 stimulus words plus 48 additional words from matching categories).	Organic-related pain words, psychological-related pain words, and neutral words	14 somatoform patients with low back pain and a predominately organic illness attribution (SPP-O) (47.8 yrs; 3 male, 11 female) 14 somatoform patients with low back pain and a predominately psychosocial illness attribution (SPP-P) (46.4 yrs; 3 male, 11 female) 14 pain-free controls. (age and sex not provided)	No significant differences in free recall were found between the 3 participant groups. The SPP-O group, compared with SPP-P and control groups, recalled significantly fewer correct words in the recognition test. The SPP-O group, compared with SPP-P and control groups, showed significantly poorer ability to discriminate between previously presented words and new words in the recognition test.

(continued on next page)

Table 1 (continued)

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

Study	Country	Paradigm	Stimuli category	Sample (age and sex)	Summary of main study results
Serbic and Pincus ⁹¹	United Kingdom	Surprise free recall task, after an endorsement task (Describes your pain? Describes you?)	Pain-related, illness-related, depression-related and neutral† adjectives	36 chronic lower back pain patients certain about diagnosis (50.00 [10.73]; 63.9% female) 32 chronic lower back pain patients uncertain about diagnosis (49.45 [11.50]; 53.1% female)	Patients with diagnostic certainty recalled significantly more pain-related adjectives than neutral adjectives. Patients with diagnostic uncertainty recalled significantly more pain-related adjectives and illness-related than neutral adjectives. Patients with diagnostic uncertainty responded significantly slower, and endorsed significantly more adjectives, than patients with diagnostic certainty.
Karimi et al. ^{44,*}	Germany	Explicit free recall task	Sensory-pain, affective-pain, and neutral words	31 chronic low back pain patients (43.30 [13.3]; 12 male, 19 female) 31 healthy controls (43.00 [13.00]; 12 male, 19 female)	Patients with chronic pain recalled fewer pain-related words than neutral words. Patients with an endurance response pattern to pain recalled significantly more pain-related words than patients with a fear-avoidance response patterns and healthy controls
Schoth et al. ^{90,*}	United Kingdom	Surprise free recall task	Sensory-pain, disability, and neutral words	17 chronic headache patients (38.76 [13.66]; 1 male, 16 female) 20 healthy controls (35.55 [13.78]; 6 male, 14 female)	Chronic headache patients recalled a significantly greater proportion of sensory-pain words relative to healthy controls Chronic headache patients recalled a significantly greater proportion sensory-pain words than neutral words
Schoth et al. ^{85,*}	United Kingdom	Surprise free recall task	Sensory-pain and neutral words	28 chronic headache (39.11 [19.70]; 22 female, 6 male) 34 healthy control (37.44 [17.88]; 24 female, 10 male)	No significant differences in recall for sensory-pain or neutral words were found between chronic pain and healthy control group. Across both groups, a significantly greater proportion of sensory-pain words were recalled than neutral words.

* Data available for inclusion in meta-analysis.

† Although these adjectives have been labelled by the authors as neutral, they are in fact negative adjectives (eg, obnoxious, crude, and thoughtless).

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 patients with chronic pain after a previous endorsement task.

No evidence of an enhanced recall bias for affective-pain words (eg, cruel, punishing, and horrible) specifically has been reported in patients with chronic pain 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 previous endorsement task, one showed significantly greater recall of illness-related (eg, die, pain, and heal) words in patients with chronic pain 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 (eg, disorder, invalid, and handicap).⁹⁰ Two studies have explored memory biases in patients diagnosed with somatoform pain disorders. Pauli and Alpers⁶⁹ found patients with somatoform pain disorders and hypochondriasis recalled significantly more pain-related words (eg, stinging, unpleasant, and miserable) than patients with somatoform pain disorders only and a patient control group (ie, patients without somatoform disorder and one or 2 practice visits within the past 3 months). Nikendei et al.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 (eg, weak bones, strain, and rheumatism) and psychosocial causes (eg, emotional stress, depression, and divorce) was explored. The results showed no significant differences in recall between the 3 participant groups.

Two studies using a previous endorsement task reported patients with chronic pain to recall significantly more negative illness-related words than healthy controls. Pincus et al.⁷³ found depressed chronic pain patients to recall significantly more negative pain-related words (eg, hurting, vulnerable, and uncomfortable) encoded in the self-referential condition compared with nondepressed chronic pain patients and healthy controls. Clemmey and Nicassio¹⁵ found patients with rheumatoid arthritis with depression to recall significantly more negative illness-related words (eg, sick, diseased, and painful) than healthy controls, but no difference was found between patients with rheumatoid arthritis without depression and healthy controls. Denton et al.²¹ reported no evidence of bias for negative illness words (eg, hurting, aching, and 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 nondepressed patients. Two studies reported no significant differences between participant groups.^{79,104}

For depression/negative words, 2 studies without an explicit self-endorsement task have not reported any significant biases in patients with chronic pain relative to healthy controls.^{69,70} Of those studies featuring an endorsement task, Wells et al.¹⁰⁴ found diagnosed chronic pain patients recalled significantly fewer depression-related words than ankylosing spondylitis patients, although no differences were found to healthy controls. The remaining 3 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 et al.¹³ used a computerised memory game involving 12 image pairs randomised and presented “face down” in a 6 × 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 (ie, 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). Patients with chronic pain performed significantly worse in the pain-related game than healthy controls, taking more moves to solve the game.

3.3.2. Within-groups biases

For sensory-pain words, 2 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 before surgery recalled significantly more pain-related words than non-pain-related words, although sensory- and affective-pain word categories were combined. Six months after 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 patients with chronic pain recalled fewer pain-related words than neutral words.⁴⁴

Considering studies using a previous 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 et al.⁷⁴ found patients with chronic pain 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 with 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 patients with chronic pain 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 previous endorsement task, one uncontrolled study found chronic pain patients with diagnostic uncertainty recalled significantly more illness-related adjectives (eg, suffering, disabled, and 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 patients with chronic pain recalled significantly more negative words than neutral words during immediate recall, but not during delayed (5-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 et al.¹⁰⁴ found

diagnosed chronic pain patients recalled significantly fewer depression-related words than neutral words. The remaining 3 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 et al.¹³ found that, contrary to their hypothesis, patients with chronic pain took significantly more moves to solve the pain-related game than the neutral game.

4. Meta-analysis results

4.1. 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 are provided in **Table 2**, and data are 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, available at <http://links.lww.com/PR9/A62>. A power calculation revealed the OIS for between-groups analyses to be 128 participants for a medium effect size and 352 participants for a small effect size.

4.1.1. 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' $g = 0.05$, $P = 0.84$).

4.1.2. 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' $g = 0.10$, $P = 0.50$). Significant heterogeneity was found, and therefore, sensitivity analyses was conducted excluding the only study to recruit a control group comprising medical professionals.¹⁰⁴ Between-group differences remained nonsignificant (analysis 3: chronic pain $n = 185$, healthy control $n = 178$; Hedges' $g = 0.19$, $P = 0.16$).

4.1.3. 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' $g = -0.30$, $P = 0.13$).

4.1.4. 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' $g = -0.04$, $P = 0.79$). An additional analysis was conducted excluding studies recruiting control groups comprising medical professionals/students^{79,104} and which was nonsignificant (analysis 6: chronic pain $n = 99$, healthy control $n = 75$; Hedges' $g = -0.11$, $P = 0.68$). Another analysis was conducted excluding the

only study to recruit patients with a diagnosis of somatoform pain disorder⁶⁵ and which again was nonsignificant (analysis 7: chronic pain $n = 203$, healthy control $n = 120$; Hedges' $g = 0.04$, $P = 0.82$).

4.1.5. 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' $g = -0.02$, $P = 0.89$). An additional analysis were conducted excluding studies recruiting control groups comprising medical professionals/students^{79,104} and which was nonsignificant (analysis 9: chronic pain $n = 54$, healthy control $n = 41$; Hedges' $g = -0.04$, $P = 0.84$).

4.1.6. 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' $g = 0.20$, $P = 0.12$). An additional analysis was conducted excluding studies recruiting control groups comprising medical professionals/students^{79,104} and which was nonsignificant (analysis 11: chronic pain $n = 54$, healthy control $n = 41$; Hedges' $g = 0.32$, $P = 0.14$).

4.2. 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 are provided in **Table 3**, and data for patients with chronic pain (where applicable including depressed and nondepressed patients combined) are 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 nondepressed chronic pain groups separately are provided in supplementary material 3 and Table S3, available at <http://links.lww.com/PR9/A62>.

4.2.1. Pain-related words vs 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 patients with chronic pain (analysis 1: $n = 87$; $d_{\text{unb}} = 0.18$, $P = 0.09$) or healthy controls (analysis 2: $n = 71$; $d_{\text{unb}} = -0.20$, $P = 0.09$).

4.2.2. Sensory-pain words vs neutral words

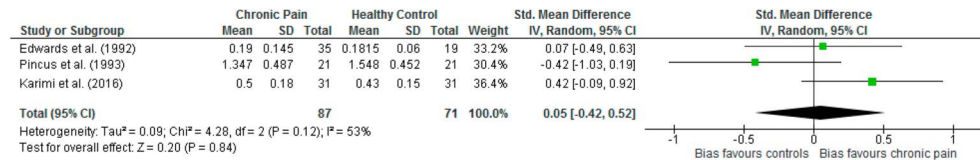
Seven studies included data from sensory-pain and neutral words.^{13,25,44,70,74,85,90} Significant recall bias was found for patients with chronic pain favouring the recall of sensory-pain words (analysis 3: $n = 185$; $d_{\text{unb}} = 0.53$, $P = 0.001$), but no significant bias was observed in healthy controls (analysis 5:

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

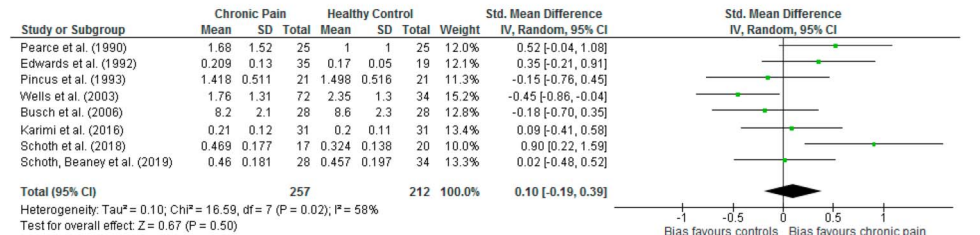
Analysis	Notes	No. of included studies (citation)	No. participants in the chronic pain group	No. participants in the control group	Effect size (95% CI)	Test for overall effect (Z and P)	Cochrane's Q	I ² (%)
Pain-related words (sensory- and affective-pain words)								
1	Depressed and nondepressed chronic pain groups combined from Ref. 25	3 ^{25,44,74}	87	71	0.05 (−0.42 to 0.52)	0.20, P = 0.84	4.28, P = 0.12	53
Sensory-pain words								
2	Depressed and nondepressed chronic pain groups combined from Ref. 25	8 ^{13,25,44,70,74,85,90,104}	257	212	0.10 (−0.19 to 0.39)	0.67, P = 0.50	16.59, P = 0.02	58
3	Sensitivity analysis of analysis 4 excluding Ref. 104 which was the only study to recruit a control group comprising medical professionals	7 ^{13,25,44,70,74,85,90}	185	178	0.19 (−0.08 to 0.46)	1.41, P = 0.16	9.58, P = 0.14	37
Affective-pain words								
4	Depressed and nondepressed chronic pain groups combined from Ref. 25	3 ^{25,44,74}	87	71	−0.30 (−0.69 to 0.09)	1.52, P = 0.13	2.89, P = 0.24	31
Illness-related words (illness-related, negative pain, organic-related causes of pain)								
5	Depressed and nondepressed chronic pain groups combined from Refs. 73,79	6 ^{21,65,73,79,90,104}	231	134	−0.04 (−0.35 to 0.26)	0.27, P = 0.79	9.35, P = 0.10	47
6	Sensitivity analysis of analysis 13 excluding Refs. 79,104 which were the only studies to recruit a control groups comprising medical professionals/students	4 ^{21,65,73,90}	99	75	−0.11 (−0.63 to 0.41)	0.41, P = 0.68	8.16, P = 0.04	63
7	Sensitivity analysis of analysis 13 excluding Ref. 65 which was the only study to recruit patients with a diagnosis of somatoform pain disorder	5 ^{21,73,79,90,104}	203	120	0.04 (−0.27 to 0.35)	0.23, P = 0.82	6.79, P = 0.15	41
Depression-related words								
8	Depressed and nondepressed chronic pain groups combined from Refs. 73,79	4 ^{21,73,79,104}	186	100	−0.02 (−0.26 to 0.23)	0.13, P = 0.89	0.69, P = 0.88	0
9	Reanalysis of analysis 21 excluding Refs. 79,104 which were the only studies to recruit a control groups comprised of medical professionals	2 ^{21,73}	54	41	−0.04 (−0.46 to 0.38)	0.20, P = 0.84	0.64, P = 0.42	0%
Negative words								
10	Depressed and nondepressed chronic pain groups combined from Refs. 73,79	4 ^{21,73,79,104}	186	100	0.20 (−0.05 to 0.45)	1.56, P = 0.12	1.57, P = 0.67	0
11	Reanalysis of analysis 27 excluding Refs. 79,104 which were the only studies to recruit a control groups comprised of medical professionals	2 ^{21,73}	54	41	0.32 (−0.11 to 0.74)	1.47, P = 0.14	0.23, P = 0.63	0

The standardized mean difference and random-effects model were used for all analyses.

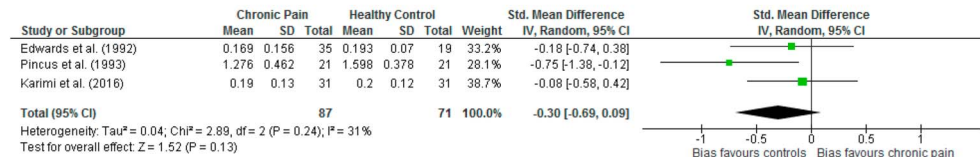
Pain-related (sensory- and affective-pain) words



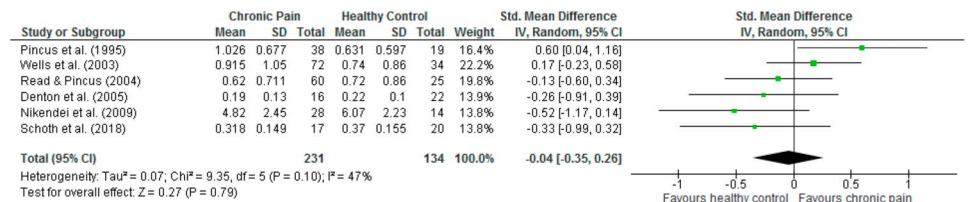
Sensory-pain



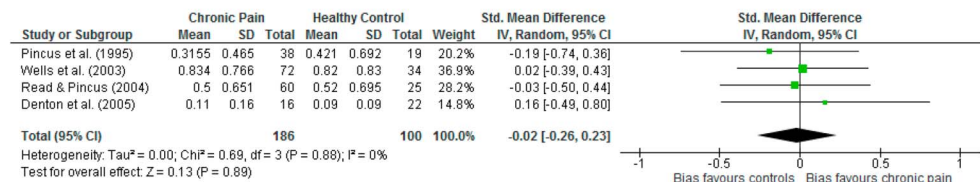
Affective-pain words



Illness-related words



Depression-related words



Negative words

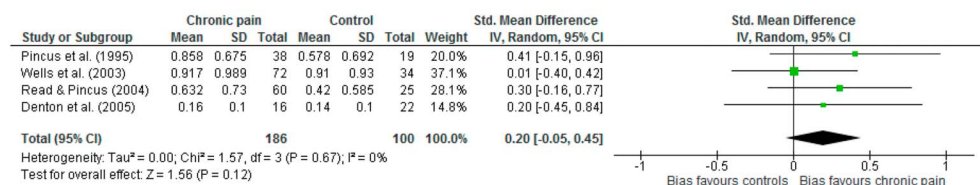


Figure 2. Between-groups forest plots created in Review Manager showing overall effect sizes for individual studies for pain-related, sensory-pain, affective-pain, illness-related, depression-related, and negative words ordered by publication date.

n = 178; $d_{unb} = -0.09$, $P = 0.52$). 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 (Ref. 90 for chronic pain patient analysis, and Ref. 85 for healthy control analysis). Recall bias remained significant for patients with chronic pain (analysis 4: n = 168; $d_{unb} = 0.42$, $P = 0.001$). Bias was also significant for healthy controls

favouring recall of neutral words over sensory-pain words (analysis 6: n = 144; $d_{unb} = -0.22$, $P = 0.02$).

4.2.3. Affective-pain words vs neutral words

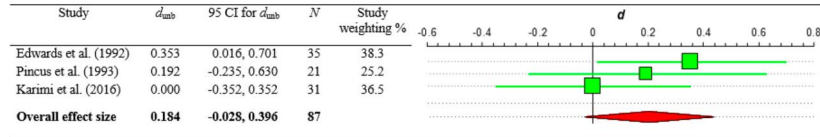
Three studies included data from affective-pain and neutral words.^{25,44,74} No significant recall bias was found for patients

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.

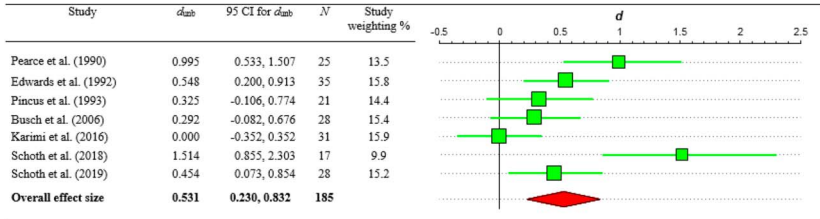
Analysis	Notes	No. of included studies (citation)	No. participants	d_{umb} effect size (95% CI)	Test for overall effect (t and P)	Cochrane's Q	I^2 (%)
Pain-related words (sensory- and affective-pain words) vs neutral words							
1	Depressed and nondepressed chronic pain groups combined from Ref. 25	3 ^{25,44,74}	87	0.18 (−0.03 to 0.40)	1.70, $P = 0.09$	2.09, $P = 0.35$	4
2	Healthy controls	3 ^{25,44,74}	71	−0.20 (−0.43 to 0.03)	1.71, $P = 0.09$	1.45, $P = 0.49$	0
Sensory-pain words vs neutral words							
3	Depressed and nondepressed chronic pain groups combined from Ref. 25	7 ^{13,25,44,70,74,85,90}	185	0.53 (0.23 to 0.83)	3.46, $P = 0.001$	22.51, $P = 0.001$	73
4	Sensitivity analysis of analysis 3 excluding Ref. 90 which had the largest effect size and could be an outlier	6 ^{13,25,44,70,74,85}	168	0.42 (0.17 to 0.67)	3.27, $P = 0.001$	12.6, $P = 0.03$	60
5	Healthy controls	7 ^{13,25,44,70,74,85,90}	178	−0.09 (−0.38 to 0.19)	0.64, $P = 0.52$	22.73, $P = 0.001$	74
6	Sensitivity analysis of analysis 5 excluding Ref. 85 which had the largest positive effect size and could be an outlier	6 ^{13,25,44,70,74,90}	144	−0.22 (0.40 to −0.03)	2.32, $P = 0.02$	6.46, $P = 0.26$	23
Affective-pain words vs neutral words							
7	Depressed and nondepressed chronic pain groups combined from Ref. 25	3 ^{25,44,74}	87	0.03 (−0.18 to 0.24)	0.28, $P = 0.78$	2.13, $P = 0.35$	6
8	Healthy controls	3 ^{25,44,74}	71	0.03 (−0.19 to 0.26)	0.28, $P = 0.78$	0.74, $P = 0.69$	0
Sensory-pain words vs affective-pain words							
9	Depressed and nondepressed chronic pain groups combined from Ref. 25	3 ^{25,44,74}	87	0.23 (0.02 to 0.44)	2.19, $P = 0.03$	0.29, $P = 0.86$	0
10	Healthy controls	3 ^{25,44,74}	71	−0.18 (−0.43 to 0.07)	1.44, $P = 0.15$	2.35, $P = 0.31$	15
Illness-related words vs negative words							
11	Depressed and nondepressed chronic pain groups combined from Refs. 73,79	5 ^{21,73,79,91,104}	254	0.14 (−0.02 to 0.29)	1.77, $P = 0.08$	5.87, $P = 0.21$	32
12	Healthy controls	4 ^{21,73,79,104}	100	0.25 (−0.16 to 0.65)	1.19, $P = 0.23$	12.29, $P = 0.007$	76
13	Sensitivity analysis of analysis 11 excluding Ref. 21 which had the largest effect size and could be an outlier	3 ^{73,79,104}	78	0.08 (−0.26 to 0.43)	0.47, $P = 0.64$	4.87, $P = 0.09$	59
Illness-related words vs depression-related words							
14	Depressed and nondepressed chronic pain groups combined from Refs. 73,79	5 ^{21,73,79,91,104}	254	0.41 (0.08 to 0.73)	2.46, $P = 0.01$	23.41, $P < 0.001$	83
15	Sensitivity analysis of analysis 14 excluding Ref. 73 which had the largest effect size and could be an outlier	4 ^{21,79,91,104}	216	0.19 (0.06 to 0.32)	2.77, $P = 0.01$	2.55, $P = 0.47$	0
16	Healthy controls	4 ^{21,73,79,104}	100	0.41 (−0.10 to 0.93)	1.56, $P = 0.12$	18.19, $P < 0.001$	84
17	Sensitivity analysis of analysis 14 excluding Ref. 21 which had the largest effect size and could be an outlier	3 ^{73,79,104}	78	0.13 (−0.13 to 0.38)	0.96, $P = 0.34$	2.74, $P = 0.25$	27

A random-effects model was used for all analyses.

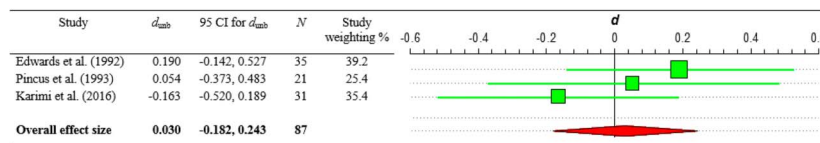
Pain-related (sensory- and affective-pain) words relative to neutral words



Sensory-pain words relative to neutral words



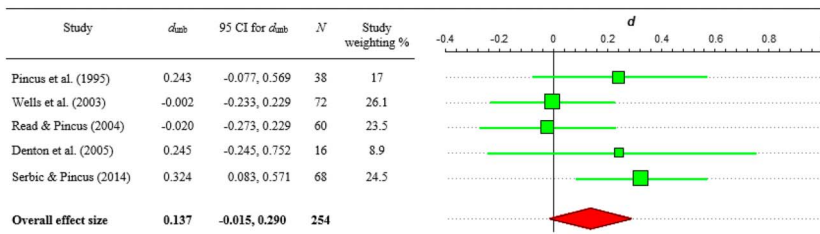
Affective-pain words relative to neutral words



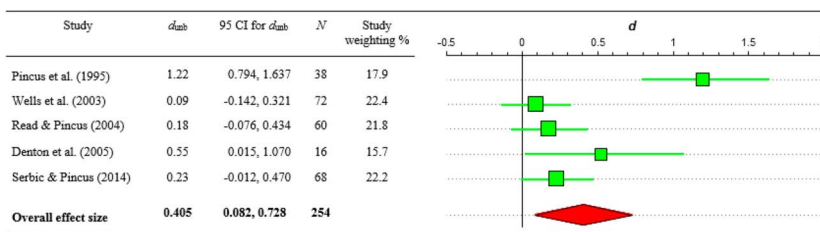
Sensory-pain words versus affective-pain words



Illness-related versus negative words



Illness-related versus depression-related words



Note: for each figure a positive d indicates greater recall of the first category of stimuli indicated in each analysis

Figure 3. Within-groups forest plots created using ESCI for chronic pain patients' recall bias effect sizes.

with chronic pain (analysis 7: $n = 87$; $d_{\text{unb}} = 0.03$, $P = 0.78$) or healthy controls (analysis 8: $n = 71$; $d_{\text{unb}} = 0.03$, $P = 0.78$).

4.2.4. Sensory-pain words vs 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 patients with chronic pain (analysis 9: $n = 87$; $d_{\text{unb}} = 0.23$, $P = 0.03$). No significant bias was found for healthy controls (analysis 10: $n = 71$; $d_{\text{unb}} = -0.18$, $P = 0.15$).

4.2.5. Illness-related vs negative words

Five studies included data from illness-related and negative words.^{21,73,79,91,104} No significant recall bias was found for patients with chronic pain (analysis 11: $n = 254$; $d_{\text{unb}} = 0.14$, $P = 0.08$). No significant difference was found for healthy controls (analysis 12: $n = 100$; $d_{\text{unb}} = 0.25$, $P = 0.23$) nor after removal of the study with the largest effect size which could potentially be an outlier (analysis 13: $n = 78$; $d_{\text{unb}} = 0.08$, $P = 0.64$).

4.2.6. Illness-related vs 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 patients with chronic pain (analysis 14: $n = 254$; $d_{\text{unb}} = 0.41$, $P = 0.01$). This effect remained significant in a sensitivity analysis removing the study with the largest effect size which could potentially be an outlier (analysis 15: $n = 216$; $d_{\text{unb}} = 0.19$, $P = 0.01$). No significant recall bias was found for healthy controls (analysis 16: $n = 100$; $d_{\text{unb}} = 0.41$, $P = 0.12$) nor after removal of the study with the largest effect size which could potentially be an outlier (analysis 17: $n = 78$; $d_{\text{unb}} = 0.13$, $P = 0.34$).

4.3. 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 8 studies.

5. 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. However, this result was only significant with the inclusion of the nondepressed chronic pain group from Edwards et al.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-pain- and affective-pain-related words were combined.

Inconsistent evidence for the presence of pain-related memory biases has 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 memory⁶ and research has shown arousing and highly valenced 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 (eg, 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,^{5,72} and are not in line with the overall conclusion from Pincus and Morley⁷² 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: (1) Pincus and Morley included studies from both adult and paediatric samples, including 2 paediatric studies which reported evidence of significant sensory-pain memory biases^{43,46}; (2) only the present review included a meta-analysis of study effect sizes (although Pincus and Morley did report within-groups effect sizes where possible); (3) the present review included 10 additional studies published since Pincus and Morley's review that have reported mixed results; and (4) 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 et al.,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 3 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 literature¹⁷).

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 nondepressed chronic pain group from Edwards et al.²⁵ was included; no difference was found with the inclusion of the depressed chronic pain group or when both depressed and nondepressed groups were combined. This result is difficult to interpret and should be considered with caution as the analysis

included only 3 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 subacute 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 with 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 through 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. However, this was only reported for 2 studies included in the sensory-pain meta-analysis,^{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 2 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 bias⁸⁸ 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"; eg, 4 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 have been observed in patients with chronic pain relative to controls.⁸⁸ By 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.^{51,88,92} Facilitated recall of pain-related information may enhance emotional distress, which in turn may encourage pain behaviours.⁷⁴ Of the 5 studies reporting correlational analyses between pain-related recall specifically and patient functioning, 3 reported no significant

associations.^{13,21,71} Pincus et al.⁷³ found, in nondepressed 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 interpretation⁸⁸ biases has been found in patients with chronic pain, and it has been argued that normal cognitive processes are cyclical in nature⁶⁴ 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 However, these effects are not always consistently reported,^{12,63} and important variations in study design and sample characteristics can influence the pattern of results found. Although 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 stimulus lists and carefully report such details.

Furthermore, "neutral" is a rather broad term which can be misleading, as in 2 studies which labelled negative adjectives (eg, obnoxious, crude, and 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 2 emotional/threatening categories of information,³ although comparisons with neutral stimuli in the same study can help explain these effects.

Much like attentional¹⁷ and interpretation⁸⁹ biases, differing methods may be used to explore memory recall biases, including surprise and explicit tasks. These 2 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, because between-groups 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 3 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} Although only one found evidence supporting the self-reference effect,⁷⁴ this nevertheless remains an avenue for future investigation. Finally, one study in this review used

a novel computerised memory game with pictures that recorded manual responses (ie, 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 2 paradigms (ie, patients with chronic pain 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.

Experimental³² and clinical research⁶⁶ 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 (ie, representations of pain). However, the relationship between biased recall of pain and memory recall biases for pain-related information has yet to be explored.

Further to recall of symbolic representations of pain, research has also explored the relationship between autobiographical memory and pain. Liu et al.⁵⁵ administered the Autobiographical Memory Test¹⁰⁵ 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. Patients with chronic pain retrieved significantly more overgeneral memories, significantly slower, than healthy controls. Vucurovic et al.¹⁰³ recruited participants with fibromyalgia and healthy controls, who were instructed to describe 5 self-defining memories of events from at least 1 year earlier. Participants with fibromyalgia retrieved less-specific self-defining memories (similar to the results of Liu and et al.⁵⁵) with a more negative emotional valence than healthy controls, although the number of pain memories retrieved did not differ between the 2 groups. However, divergent findings have been reported. Wright and Morley¹⁰⁶ 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. However, this between-group effect was not due to patients with chronic pain showing differential sensitivity to pain-related cues specifically. Although contrasting to the results of Vucurovic et al.,¹⁰³ these 2 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 were not available from all studies for inclusion in the subset meta-analyses, and in some instances, meta-analysis was conducted with as few as 3 studies. The OIS for between-groups analyses was 128 participants for a medium effect size which was met in all but 6 analyses. The OIS 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.^{9,39} It should also be noted that although all studies included in this review met our inclusion and exclusion criteria, specific pain diagnosis varied between studies and within the analyses conducted. Although 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 used. 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. However, numerous methodological limitations have been raised pertaining to the studies included in the present review, and it is apparent that further, rigorous research is needed.

Disclosures

The authors have no conflicts of interest to declare.

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Appendix A. Supplemental digital content

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