Attentional, interpretation and memory biases for sensory-pain words in individuals with chronic headache

**Abstract**

**Introduction**: Cognitive biases in attention, interpretation and less consistency memory have been observed in individuals with chronic pain, and play a critical role in the onset and maintenance of chronic pain. Despite operating in combination cognitive biases are typically explored in isolation. **Aims**: The primary aim of this study was to explore attentional, interpretation, and memory biases and their interrelationship in individuals with chronic headache. **Methods**: Twenty-eight participants with chronic headache and 34 healthy controls completed paradigms assessing attentional, interpretation and memory biases with ambiguous sensory-pain and neutral words. **Results**: Individuals with chronic pain showed significantly greater pain-related attentional and interpretation biases relative to controls, with no differences in memory bias. No significant correlation was found between any of the three forms of cognitive bias assessed. **Discussion and conclusions**: The clinical implications of cognitive biases in individuals with chronic pain remain to be fully explored, although one avenue for future research would be specific investigation of the implications of biased interpretations considering the consistency of results found across the literature for this form of bias.

**Key words:** Chronic headache, cognitive biases, attentional bias, interpretation bias, memory bias

**Introduction**

 Individuals with chronic pain show attentional[1](#_ENREF_1), [2](#_ENREF_2), interpretation[3](#_ENREF_3) and less consistently memory biases for pain-related information (e.g.,[4](#_ENREF_4), [5](#_ENREF_5)). The majority of studies in this field have explored cognitive biases in isolation, although there has recently been greater consideration given to the inter-relationships between different forms of bias. The Threat Interpretation Model[6](#_ENREF_6) notes the ambiguous nature of pain related information (for example words such as *Sharp* and *Tender)*, and proposes that an interpretation bias favouring the pain-related meaning of information is necessary, but not sufficient, for an attentional bias to be observed. In the broader anxiety and depression literature it has been suggested that cognitive biases influence and interact with one another (e.g.,[7](#_ENREF_7), [8](#_ENREF_8)), and different possibilities for the temporal pattern of their occurrence have been proposed (for example, Everaert and colleagues[9](#_ENREF_9) speculate that in depression attentional bias precedes interpretation biases).

 Only Schoth and colleagues[4](#_ENREF_4) have explored combined pain related attentional, interpretation and memory biases. Individuals with chronic headache, relative to healthy controls, showed significantly greater interpretation and memory biases favouring ambiguous sensory-pain words, and also an interpretation bias favouring ambiguous disability words. Surprisingly, no evidence of an attentional bias using the spatial cueing task for sensory-pain or disability words was found. The aim of the present study was therefore to further explore attentional, interpretation, and memory biases and their interrelationship in individuals with chronic headache, and provide a preliminary test of the Threat Interpretation Model. The visual-probe task was used to assess attentional biases. As per former research stimuli presentation times of 500 and 1250 ms were included to measure biases in initial orienting of attention and maintained attention respectively[2](#_ENREF_2), [10](#_ENREF_10). It was predicted that individuals with chronic headache, relative to healthy controls, would show significant attentional, interpretation, and memory biases for sensory-pain words. More specifically, based on the Threat Interpretation Model, a significant positive correlation was predicted between pain-related interpretation and attentional biases only in individuals who would show interpretation biases.

**Methods**

**Participants**

 Participants were recruited from the South of England via press announcements and word of mouth. For the chronic headache group inclusion criteria were: (a) experiencing primary tension-type headache or migraine, and satisfying the criteria stated in the International Classification of Headache Disorders 3rd edition beta version (ICHD-3) for chronic headache, (b) aged 18 or over, (c) normal or corrected-to-normal vision. Exclusion criteria were: (a) a psychiatric disorder, currently or within the past five years, (b) any other chronic pain. For the control group inclusion criteria were: (a) aged 18 or over, (b) normal or corrected-to-normal vision. Exclusion criteria were: (a) a psychiatric disorder, currently or within the past five years, (b) chronic pain (in terms of headache frequency, experiencing more than 7 headaches per month[4](#_ENREF_4), [11-13](#_ENREF_11)), (c) taking any psychotropic or analgesic medication regularly. Eligibility was established via a short telephone interview prior to recruitment.

Sixty-two participants were recruited, 28 with chronic headache (mean age = 39.11, *SD* = 19.70, range 18 – 73; 79% female) and 34 healthy controls (mean age = 37.44, *SD* = 17.88, range 19 – 70; 71% female). The chronic headache and healthy control groups reported on average 20.86 (*SD* = 5.77, range 15 – 30 days) and 1.63 (*SD* = 1.52, range 0 - 5 days) headache days per month respectively. Participants with chronic headache reported living with chronic headache for a mean duration of 15.5 years (*SD* = 17.22, range 4 months to 61 years). Within this group, 16 (57%) had tension-type headache, and 12 (43%) had migraine. Eighteen (64%) reported at least one relative to also suffer from regular headache. As indexed by their MIDAS (migraine disability assessment) scores, 22 (79%) indicated severe disability as a consequence of their headaches. All but two (93%) were taking regular analgesic medication for the management of their headaches.

**Measures**

 The following questionnaires were used: Hospital Anxiety and Depression Scale[14](#_ENREF_14); State-Trait Anxiety Inventory[15](#_ENREF_15); McGill Pain Questionnaire[16](#_ENREF_16); Brief Pain Inventory-Short Form[17](#_ENREF_17); Migraine Disability Assessment Questionnaire[18](#_ENREF_18). Full details are provided in the Supplementary Questionnaire Information file (Supplementary Material 1).

**Experimental Stimuli**

Experimental stimuli (Table S1) included nine sensory-pain words associated with the sensory dimension of headache, and nine neutral words unrelated to pain. These words were used in a prior chronic pain combined cognitive bias investigation[4](#_ENREF_4). Due to the exploration of interpretation biases, each word was either a homograph (words which have identical spelling but different meanings and etymologies) or a pseudo-homograph (also referred to as polysemes; words which have identical spelling but different meanings, although stem historically from the same source)[19](#_ENREF_19), [20](#_ENREF_20). Sensory-pain words were selected to have pain-related and neutral associations, and neutral words were selected to have multiple neutral associations. Although ambiguous, sensory-pain words were nevertheless relevant to headache, and are commonly used by patients to describe their pain; all but one of the sensory-pain words are included in the McGill Pain Questionnaire[16](#_ENREF_16), and the only word not included is specifically relevant to headache (i.e., tension). Sensory-pain and neutral words were matched on length and Kucea-Francis written frequency using the MRC Psycholinguistic Database[21](#_ENREF_21), and on word set size (i.e., number of strong associations a word has) using the University of Florida Free Association Norms database[20](#_ENREF_20).

**Experimental Paradigms**

**Visual-probe task**. The visual-probe task[22](#_ENREF_22) was used to explore attentional biases, and was based on versions used in former chronic headache attentional bias research (e.g.,[13](#_ENREF_13), [23](#_ENREF_23), [24](#_ENREF_24)). The task began with eight practice trials featuring random letter strings as stimuli. This was followed by a single block of 72 experimental trials, each of which featured one sensory-pain and one neutral word. Each trial began with a fixation cross in the centre of the screen for 500 ms, followed by a randomly selected word-pair presented vertically (i.e., one above the initial fixation cross, the other below) for either 500 ms or 1250 ms. Immediately after the disappearance of the word-pair, a visual-probe was randomly displayed in either the upper or lower location replacing one of the former words. Participants indicated the location of this probe as quickly as possible, using a two-button response-box (with ‘U’ and ‘L’ labels for upper and lower respectively) to provide their response. Following a randomly determined inter-trial interval of either 1000 or 1500 ms, the next trial began with the display of the initial fixation cross.

The two stimuli presentation times were applied in a randomised order over all trials. Each of the nine word-pairs were presented eight times; four times for 500 ms and four times for 1250 ms. Within each exposure duration, each sensory-pain word appeared twice in the upper location and twice in the lower location. The probe location (upper or lower) was counterbalanced across both locations, resulting in an equal number of congruent (probe replacing the sensory-pain word) and incongruent (probe replacing the neutral word) trials.

**Sentence Generation Task**.The sentence generation task[25](#_ENREF_25) was used to explore interpretation biases, which has been adopted in previous studies exploring biases in anxious[26](#_ENREF_26) and chronic pain [4](#_ENREF_4) populations. The task included 18 experimental trials featuring the same sensory-pain and neutral stimuli as the visual-probe task[4](#_ENREF_4). Trials were presented in a new randomised order for each participant. Each trial began with a fixation cross for 1000 ms. A single word presented in size 40 Times New Roman font subsequently replaced the cross, remaining on the screen until the end of the trial. Participants read the word and used a keyboard to type a single sentence featuring the word once only. Text appeared in size 18 Times New Roman font below the experimental word as the participant typed. Backspace and delete keys were used to correct spelling mistakes or make amendments as necessary, and the F12 key to submit the response. The next trial began after 120 seconds if no response was submitted. Trials followed one another automatically, with all 18 trials presented in a single block. Two practice trials were initially presented to familiarise participants with the requirements of the task, featuring the words *running* and *dancing*.

**Free Recall Task**. A pen and paper version of the free recall task was used to explore memory biases, and which has been commonly adopted in former research exploring memory biases in anxious (e.g.,[27](#_ENREF_27), [28](#_ENREF_28)) and chronic pain (e.g.,[4](#_ENREF_4), [29](#_ENREF_29)) populations. Participants were unexpectedly asked to write down as many words as possible from the visual-probe and sentence generation tasks in 3 minutes.

**Apparatus and Procedure**

Ethics approval was obtained from the University of Southampton Research Ethics Committee. Visual-probe and sentence generation tasks were developed in Presentation® (version 12.2, Neurobehavioural Sciences) and run on a personal computer with a 15 inch colour monitor with all text, fixation crosses, probes and cursors presented in white against a black background. The visual-probe task was completed first, followed by the sentence generation task after a short break. The surprise free recall task was administered last, after a brief distractor task (i.e., counting backwards from 400 in units of 7 for two minutes) which was included to control for recency effects influencing subsequent recall. A second break was provided at this point, after which the participants completed the study questionnaires which were presented in a new randomised order for each participant. The total experimental duration was approximately 60 minutes (visual-probe task = 10 minutes, sentence generation task = 8 minutes, free recall task = 3 minutes).

**Data Reduction and Analytic Plan**

Analyses were conducted in IBM SPSS Statistics for Windows 22. For the visual-probe task, practice and experimental trials with incorrect responses were excluded from the analysis. Box and whisker plots for overall data showed outliers to be any response time less than 200 ms or greater than 1100 ms, which were removed. Mean response times for each participant were then calculated, and any response time 3 standard deviations above or below this mean were also removed as outliers [4](#_ENREF_4), [13](#_ENREF_13), [23](#_ENREF_23), [30](#_ENREF_30). Attentional bias scores were then calculated for each participant at each exposure duration (i.e., 500 ms and 1250 ms) using the following formula: attentional bias score = ((TuPl – TlPl) + (TlPu – TuPu))/2. Where T = threatening stimulus, P = probe, u = upper position, l = lower position. A positive bias score indicates a shift of attention towards the location of threatening words relative to neutral words. A negative bias score indicates a shift of attention away from the location of threatening words towards neutral words[24](#_ENREF_24).

For the sentence generation task, two raters independently and blindly categorised participant response sentences as either pain-related (e.g., *He had a pressing pain in his head*) or benign (e.g., *The boy was pressing the buttons in the lift*). Benign responses included both neutral and positive sentences. The initial inter-rater agreement was 97%, and after discussion consensus was reached on 100% of ratings. The proportion of interpretations made were used in the analyses[4](#_ENREF_4), [31](#_ENREF_31), [32](#_ENREF_32). For the free recall task, the proportion of words recalled per stimuli category was computed and used in the analyses[4](#_ENREF_4), [32](#_ENREF_32), [33](#_ENREF_33).

Between-groups differences for demographic characteristics and self-report questionnaires were explored via *t*-tests and χ2 for continuous and categorical variables respectively. A 2 (group; chronic headache, healthy control) x 2 (presentation time: 500 ms, 1250 ms) mixed-designs ANOVA was conducted on attentional bias scores, and a 2 (group; chronic headache, healthy control) x 2 (stimuli category; sensory-pain, neutral) mixed-designs ANOVA conducted on the proportion of participant responses classified as sensory-pain (interpretation bias) and the proportion of words correctly recalled for each stimuli condition (memory bias). *T*-tests were used as required in post-hoc analyses to clarify significant effects and explore patterns of bias in greater detail. Effect sizes for ANOVA and *t*-tests were quantified using partial eta-square p2 and Cohen’s *d* respectively. ESCI (Exploratory Software for Confidence Intervals)[34](#_ENREF_34) was used to compute Cohen’s *d* and associated 95% confidence intervals. For ANOVA analyses, the alpha level was set at .05, two-tailed. Pearson’s correlation coefficients were selectively conducted to assess the relationship between different types of sensory-pain cognitive bias, along with 95% confidence intervals using the bias-corrected and accelerated (BCa) bootstrap method (1000 samples), which corrects for bias and skewness in the distribution of bootstrap estimates [35](#_ENREF_35). For correlational analyses, the alpha level was set at .01 (two tailed) due to the number of correlations performed and in order to reduce the possibility of making a type 1 error.

**Results**

 Data from self-report measures, attentional bias scores, the proportion of pain and benign interpretations made for each word category, and the proportion of words correctly recalled for each stimuli condition are provided in Table 1.

**Group Comparisons**

Chronic headache (*n* = 28) and healthy control groups (*n* = 34) did not significantly differ in terms of age [*t*(60) = 0.35, *p* = .729, *d*  = 0.09, CI of *d* [-0.41, 0.59] sex [chronic headache = 79% female (22); healthy control = 71% female (24); χ2 = 0.51, *p* = .475] or years of education [chronic headache = 16.44 (3.26); healthy control = 18.39 (8.86); *t*(58) = 1.08 , *p* = .283]. The chronic headache group reported significantly higher state and trait anxiety and depression than the healthy control group. These variables were not included as covariates as this is not appropriate for analyses with pre-existing, non-randomised groups and does not ‘control’ for any potential differences[36](#_ENREF_36), [37](#_ENREF_37).

**Attentional Bias**

The chronic headache group did not significantly differ from the healthy control group in mean reaction time [chronic headache = 641.32 ms (*SD* = 113.33); healthy control = 644.67 ms (*SD* = 145.71); *t*(60) = 1.08, *p* = .914, *d* = 0.03, CI of *d* (-0.47, 0.53)], number of incorrect responses made [chronic headache = 0.93 (*SD* = 1.22); healthy control = 0.59 (*SD* = 0.93); *t* (60) = 1.25, *p* = .215, *d* = 0.31, CI of *d* (-0.19, 0.82)] or number of outliers removed [chronic headache = 1.64 (*SD* = 1.66); healthy control = 1.94 (*SD* = 2.97); *t* (60) = 0.47, *p* = .638, *d* = 0.12, CI of *d* (-0.38, 0.62)]. The main effect of group was not significant, *F* (1, 60) = 2.19, *p* = .145, ηp2= .035, nor the main effect of presentation time, *F* (1, 60) = 0.96, *p* = .332, ηp2= .016, or the group by presentation time interaction, *F* (1, 60) = 2.07, *p* = .155, ηp2= .033.

Participants with chronic headache showed significantly greater bias towards sensory-pain words than healthy controls when stimuli were presented for 500 ms, *t*(60) = 2.08, *p* = .042, *d* = 0.53, CI of *d* (0.02, 1.04). No difference was found between groups at the 1250 ms presentation time, *t*(60) = 0.15, *p* = .884, *d* = 0.04, CI of *d* (-0.46, 0.54). Bias scores were also compared to 0 which denotes equal attentional engagement of both threatening and neutral words. The chronic headache group showed significant bias towards pain-related words presented for 500 ms, *t*(27) = 2.35, *p* = .027.

**Interpretation Bias**

The chronic headache group did not significantly differ from the healthy control group in the number of valid interpretations made [both groups = 18:00, SD = 0.00]. The main effect of stimuli category was significant, *F* (1, 26) = 88.68 *p* < .001, ηp2= .773, as was the main effect of group, *F* (1, 26) = 88.09, *p* < .001, ηp2= .772, and the stimuli category by group interaction, *F* (2, 55) = 8.60, *p* = .007, ηp2= .249. Chronic headache participants, relative to healthy controls, provided significantly more pain responses to sensory-pain words, *t*(59) = 3.64, *p* = .001, *d* = 0.58, CI of *d* (0.06, 1.09). There was no difference between the two groups in the proportion of pain responses to neutral words, *t*(59) = 0.287, *p* = .775, *d* = 0.08, CI of *d* (-0.43, 0.58).

**Memory bias**

The chronic headache group did not significantly differ from the healthy control group in the number of total words recalled [chronic headache = 7.46 (*SD* = 2.84), healthy control = 7.21 (*SD* = 2.59); *t*(60) = 0.38, *p* = .709, *d* = 0.10, CI of *d* (-0.41, 0.60)] or the number of incorrect words recalled [chronic headache = 0.93 (*SD* = 1.27), healthy control = 1.00 (*SD* = 1.13); *t*(60) = 0.34, *p* = .816, *d* = 0.06, CI of *d* (-0.44, 0.56)]. The main effect of stimuli category was significant, *F* (1, 60) = 11.36, *p* = .001, ηp2 = .159. Pairwise comparison showed participants recalled a significantly greater proportion of sensory-pain words (.459, *SE* = .024) than neutral words (.355, *SE* = .025). The main effect of group was not significant, *F* (1, 60) = 0.132, *p* = .717, ηp2= .002, nor the group by stimuli category interaction, *F* (1, 60) = 0.137, *p* = .713, ηp2= .002.

**Correlation Analysis**

 Across all participants no significant correlations were found between sensory-pain attentional, interpretation and memory biases (Table S2). In order to specifically test our hypothesis derived from the Threat Interpretation Model, thirteen participants who provided only benign interpretations of the ambiguous stimuli were removed from the analysis as there was no evidence they had interpreted any of the words as anything other than neutral/benign. Once again, no significant correlations were found between sensory-pain attentional, interpretation and memory biases. At the request of an anonymous reviewer depression was correlated specifically with the proportion of sensory-pain words recalled. No significant correlations were found for individuals with chronic headache (*r* = -.052, *p* = .793), healthy controls (*r* = -.061, *p* = .739) or when all participants were combined (*r* = -.047, *p* = .722).

**Discussion and conclusions**

 In partial support of the first hypothesis, evidence of attentional and interpretation biases for ambiguous sensory-pain words was found in individuals with chronic headache relative to healthy controls. No significant difference was found between the two groups in the recall of ambiguous sensory-pain words however. The second hypothesis was not supported, as no significant correlation was found between pain-related interpretation and attentional biases in participants who made at least one pain interpretation. Considering attentional biases, both between- and within-groups biases were found at the 500 ms stimuli presentation time only. This contrasts somewhat with the results of our former chronic headache research which showed more pronounced biases at 1250 ms[13](#_ENREF_13), [24](#_ENREF_24), [38](#_ENREF_38). As noted, biases at 500 and 1250 ms may reflect processes of initial orienting of attention and maintained attention respectively[10](#_ENREF_10). Given that the present study used words specifically selected for their ambiguity direct comparison with the results of former studies should be made with caution, especially as personal relevance has been shown to be an important factor in determining whether attentional biases are observed[39](#_ENREF_39), and also because we could not include certain obvious and relevant words as they did not meet our inclusion criteria (e.g., pain, aching, throbbing).

Despite these cautions in making direct comparisons, it is possible that ambiguous words are less likely to maintain attention or lead to difficulties disengaging attention as they are simply deemed less threatening than the pain-related words typically used in former studies. This is in alignment with the Threat Interpretation Model[6](#_ENREF_6) which suggests that participants will easily disengage from low threat. Although we did not include a stimuli rating task in the present study, as part of a larger independent project we have collected ratings on valence (i.e. pleasantness) and arousal for a large selection of words from 16 healthy participants using a computerised version of the Self-Assessment Manikin (SAM) task[40](#_ENREF_40) (See Supplementary Material 2 for further details). Data were available for the sensory-pain words used in the present study (arousal mean = 2.89, *SD* = 0.43; valence mean = 4.90, *SD* = 0.36). We compared to a previous publication from our lab which used sensory-pain words specifically selected for their relevance to chronic headache[24](#_ENREF_24) (arousal mean = 3.61, *SD* = 1.00; valence mean = 4.21, *SD* = 0.97). Words in the former study were rated as possessing significantly higher arousal (*t*(19) = 2.33, *p* = 0.31) and significantly lower valence (*t*(18) = 2.40, *p* = .029) than words in the present study.

An alternative possibility for the present pattern of results is that participants had resolved the ambiguity of the words by 1250 ms in favour of their neutral meaning. Overall, despite some inconsistencies regarding the time-course of attentional bias, these results are nevertheless in alignment with those of former research showing pain-related attentional biases exist in individuals with chronic pain relative to healthy controls, a meta-analysis providing evidence of significant bias at presentation times of 300 to 500 ms[2](#_ENREF_2" \o "Schoth, 2012 #30), and another meta-analysis showing significant bias at times of 500 to 1000 ms[1](#_ENREF_1" \o "Crombez, 2013 #470). One possibility for future research would be to include a broader selection of pain-related stimuli varying in ambiguity, and to examine more directly whether patterns of attentional (and memory) bias differ in the same chronic pain sample according to the ambiguity of such words.

 In line with all former studies[4](#_ENREF_4), [31](#_ENREF_31), [32](#_ENREF_32), [41-44](#_ENREF_41) using a variety of paradigms[25](#_ENREF_25), the present investigation found biases in the interpretation of ambiguous pain-related information in individuals with chronic pain relative to healthy controls. Maladaptive interpretations of pain are implicated in the development of chronic pain[45](#_ENREF_45), [46](#_ENREF_46), as they increase fear and anxiety which in turn promotes an avoidance of potentially pain-provoking situations[47](#_ENREF_47). An argument has therefore been made for research exploring the potential therapeutic benefits of modifying biased interpretations in patients with chronic pain[44](#_ENREF_44), especially as supporting evidence has been provided in the anxiety and depression literature[48](#_ENREF_48), [49](#_ENREF_49). We are in agreement with this suggestion, and echo the need for research exploring the clinical implications of biased interpretations specifically in chronic pain. Future research may also benefit from the use of indirect measures of interpretation such as the incidental learning task[44](#_ENREF_44), [50](#_ENREF_50), which measures relatively implicit processes and thus likely reduces demand characteristics and response biases[25](#_ENREF_25), [50](#_ENREF_50). Like most direct measures of biased interpretations, responses provided in the sentence generation task may not necessarily reflect the initial interpretation which came to mind[25](#_ENREF_25), [50](#_ENREF_50). It is also possible that some participants may actually provide benign interpretations as a form of avoidance, although we were unable to test this in the present study.

 The wider memory bias literature has reported inconsistent results, finding significant bias for sensory-pain words relative to neutral words in those with chronic pain, but no difference between chronic pain and healthy control groups[51](#_ENREF_51). The present study found no evidence of memory bias for ambiguous sensory-pain words in the chronic headache group specifically, relative either to the healthy control group or the recall of neutral words. Recall biases are predicted by theories of emotional processing (e.g.,[52](#_ENREF_52)) and chronic pain[53](#_ENREF_53) however, and the current results contrast those of a recent study using the same stimuli and research design which did report significant biases in the chronic headache group[4](#_ENREF_4). Nevertheless, the present study did find a main effect of stimuli condition, whereby participants across both groups recalled a significantly greater proportion of ambiguous sensory-pain than neutral words. This result is in alignment with research showing people typically demonstrate improved recall of emotional than neutral material (e.g.,[54](#_ENREF_54), [55](#_ENREF_55)). It could be argued that the main effect of stimuli condition in the memory bias analysis also points towards an emotionality effect. The significant differences observed between groups in attention and interpretation may also stem from the fact that the sensory-pain words were simply threatening, rather than because they had pain-related connotations specifically. This possibility should be explored as it has been recently in the attentional bias literature[30](#_ENREF_30).

 The present study is only the second following the investigation of Schoth and colleagues[4](#_ENREF_4) to explore all three forms of cognitive bias in the same chronic pain sample. Specific comparison between the two studies is therefore warranted. As noted, our former investigation found individuals with chronic headache, relative to healthy controls, showed significantly greater interpretation and memory biases favouring ambiguous sensory-pain words. It is unsurprising that interpretation bias results were consistent across both studies considering that the same stimuli and paradigm were used. Differences in attentional bias results may be partly explained by the different paradigms used. The spatial cueing task used in our previous study enabled us to include three stimuli categories (sensory-pain, disability, and neutral) each with the same number of words (an equal number of words per category, shown the same number of times, is essential to ensure a valid comparison of results). The spatial cueing task has been used infrequently in the pain literature with limited success (one study reported pain-related biases in patients with irritable bowel syndrome [56](#_ENREF_56) but another did not [57](#_ENREF_57)), and a review of research with anxious populations showed a very small, non-significant between-group effect size for studies using this paradigm (Bar-Haim et al., 2007). In regards to memory biases, we have noted above the discrepancy between the two investigations, and have also noted the general inconsistency in the broader literature.

Support was not found for the prediction of the Threat Interpretation Model[6](#_ENREF_6) that an interpretation bias favouring the pain-related meaning of ambiguous stimuli is necessary for an attentional bias to be observed. The present study did not provide the optimal test of the prediction however, which was cross-sectional in nature and also measured attentional biases prior to interpretation biases. Further research is needed specifically testing the temporal relationship between these two forms of bias. It has also been suggested that memory biases may form the basis for attention and interpretation biases, although the alternative is possible with recall biases arising as a result of biases in attention and/or interpretation[58](#_ENREF_58). Longitudinal research will be able to address these specific questions, and also ascertain the effects inducing one form of bias has on other forms of bias[3](#_ENREF_3), [4](#_ENREF_4), [7](#_ENREF_7). Such research is also vital for interventions aimed at modifying cognitive biases[58](#_ENREF_58), [59](#_ENREF_59), and of which there is evidence for the benefits of attentional bias modification in the literature broadly[60](#_ENREF_60) and in chronic pain specifically[61-64](#_ENREF_61).

As anticipated and in line with previous studies (e.g., [43](#_ENREF_43)) only a proportion of words in the sensory-pain category were interpreted as pain-related (26% of words for individuals with chronic headache and 17% of words for healthy controls). While many attentional and memory bias studies take their stimuli from validated self-report measures such as the McGill Pain Questionnaire (e.g., [4](#_ENREF_4), [65](#_ENREF_65)), potential ambiguity is not typically assessed. We therefore encourage researchers to consider degree of ambiguity in their cognitive bias research regardless of whether they assess interpretation bias specifically or not. Furthermore, the present study recruited individuals with chronic headache, although the majority of former studies assessing interpretation [3](#_ENREF_3) and memory biases [51](#_ENREF_51) have recruited individuals with musculoskeletal pain. It is important that stimuli of relevance to the particular chronic pain condition experienced by participants are developed, and indeed for this reason we recommend against the recruitment of mixed chronic pain samples in cognitive bias research.

 A number of limitations may be raised. First, for between-groups comparisons a post-hoc power calculation using GPower [66](#_ENREF_66) revealed 12%, 49%, and 87% probabilities of correctly rejecting the null hypothesis for small (0.2) medium (0.5) and large (0.8) effect sizes respectively. Second, we did not counter-balance the order of the attentional and interpretation bias tasks, although this would have allowed us to explore whether the time-course of pain-related attentional bias varies based on previous stimuli exposure. It would also allow exploration as to whether attentional biases are more pronounced towards ambiguous stimuli already seen and interpreted in a pain-related than a neutral manner. Third, the psychometric properties of the visual-probe task, including its reliability, have been questioned[67](#_ENREF_67), [68](#_ENREF_68). Attentional biases have nevertheless been frequently found with this paradigm[1](#_ENREF_1), [2](#_ENREF_2) and confirmed with other paradigms (e.g.,[12](#_ENREF_12), [69](#_ENREF_69), [70](#_ENREF_70)). Fourth, while medium effect sizes were found for between-groups attentional (500 ms) and interpretation bias scores, confidence intervals were nevertheless broad in both instances.

Furthermore, although the two participant groups did not differ on age, sex or years of education, it would have nevertheless been preferable to match participants one to one between the two groups on these variables. The chronic headache group reported significantly higher anxiety and depression than the healthy control group. A meta-analysis of the attentional bias literature by Crombez and colleagues[1](#_ENREF_1) reported negligible, non-significant correlations between sensory-pain attentional biases and several variables including state anxiety, trait anxiety and depression when included as continuous variables. There were also no significant differences between groups when participants were dichotomised into high and low groups on these variables. Despite this, considering the potential role of threat on cognitive biases[6](#_ENREF_6), and also the influence of anxiety and depression on threat perceptions[71](#_ENREF_71), [72](#_ENREF_72), researchers may wish to consider if and how variations in such variables influence patterns of combined cognitive biases in future chronic pain research. In conclusion, the present study found evidence of attentional and interpretation biases for ambiguous sensory-pain words in individuals with chronic headache.

**Declaration of Conflicting Interests**

The Authors declare that there is no conflict of interest.

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References

1. Crombez G, Van Ryckeghem D, Eccleston C, Van Damme S. Attentional bias to pain-related information: a meta-analysis. Pain. 2013;154(4):497-510.

2. Schoth DE, Delgado Nunes V, Liossi C. Attentional bias towards pain-related information in chronic pain; a meta-analysis of visual-probe investigations. Clin Psychol Rev. 2012;32(1):13 - 25.

3. Schoth DE, Liossi C. Biased interpretation of ambiguous information in patients with chronic pain: A systematic review and meta-analysis of current studies. Health Psychol. 2016;35(9):944-56.

4. Schoth DE, Parry L, Liossi C. Combined cognitive biases for sensory-pain and disability information in individuals with chronic headache. J Health Psychol. in press.

5. Serbic D, Pincus T. Diagnostic uncertainty and recall bias in chronic low back pain. Pain. 2014;155(8):1540-6.

6. Todd J, Sharpe L, Johnson A, Nicholson Perry K, Colagiuri B, Dear BF. Towards a new model of attentional biases in the development, maintenance, and management of pain. Pain. 2015;156(9):5189-1600.

7. Hirsch CR, Clark DM, Mathews A. Imagery and interpretations in social phobia: Support for the combined cognitive biases hypothesis. Behav Ther. 2006;37(3):223-36.

8. Everaert J, Koster EHW, Derakshan N. The combined cognitive bias hypothesis in depression. Clin Psychol Rev. 2012;32(5):413-24.

9. Everaert J, Tierens M, Uzieblo K, Koster EH. The indirect effect of attention bias on memory via interpretation bias: Evidence for the combined cognitive bias hypothesis in subclinical depression. Cognition and Emotion. 2013;27(8):1450-9.

10. Bradley BP, Mogg K, Falla SJ, Hamilton LR. Attentional bias for threatening facial expressions in anxiety: Manipulation of stimulus duration. Cognition and Emotion. 1998;12(6):737 - 53.

11. Liossi C, Schoth DE, Godwin HJ, Liversedge SP. Using eye movements to investigate selective attention in chronic daily headache. Pain. 2014;155(3):503-10.

12. Schoth DE, Godwin HJ, Liversedge SP, Liossi C. Eye movements during visual search for emotional faces in individuals with chronic headache. Eur J Pain. 2015;19(5):722 - 32.

13. Schoth DE, Liossi C. Specificity and time-course of attentional bias in chronic headache: a visual-probe investigation. Clin J Pain. 2013;29(7):583-90.

14. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67(6):361-70.

15. Spielberger CD, Gorsuch RL, Lushene RE. State Trait Anxiety Inventory. Palo Alto, California: Consulting Psychologists Press; 1970.

16. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. Pain. 1975;1(3):277-99.

17. Cleeland CS, Ryan KM. Pain assessment: Global use of the brief pain inventory. Annals of the Academy of Medicine, Singapore,. 1994;23:129-38.

18. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. Neurology. 2001;56:S20 - S8.

19. Drury DA. Homographs and pseudo-homographs. Word Ways The Journal of Recreational Linguisatics. 1969;2(3):146-54.

20. Nelson DL, McEvoy CL, Schreiber TA. The University of South Florida free association, rhyme, and word fragment norms. Behav Res Methods Instrum Comput. 2004;36(3):402-7.

21. Wilson M. MRC Psycholinguistic Database: Machine-usable dictionary, version 2.00. Behav Res Methods Instrum Comput. 1988;20(1):6-10.

22. MacLeod C, Mathews A, Tata P. Attentional Bias in Emotional Disorders. J Abnorm Psychol. 1986;95(1):15 - 20.

23. Schoth DE, Liossi C. Attentional bias towards pictorial representations of pain in individuals with chronic headache. Clin J Pain. 2010;26(3):244 - 50.

24. Liossi C, Schoth DE, Bradley BP, Mogg K. Time course of attentional bias for pain-related cues in chronic daily headache sufferers. Eur J Pain. 2009;13(9):963 - 9.

25. Schoth DE, Liossi C. A systematic review of experimental paradigms for exploring biased interpretation of ambiguous information with emotional and neutral associations. Front Psychol. 2017;8(171).

26. Taghavi MR, Moradi AR, Neshat-Doost HT, Yule W, Dalgleish T. Interpretation of ambiguous emotional information in clinically anxious children and adolescents. Cognition & Emotion. 2000;14(6):809-22.

27. Russo R, Fox E, Bellinger L, Nguyen-Van-Tam DP. Mood-congruent free recall bias in anxiety. Cognition & Emotion. 2001;15(4):419-33.

28. Reidy J, Richards A. Anxiety and memory: A recall bias for threatening words in high anxiety. Behav Res Ther. 1997;35(6):531-42.

29. Pincus T, Fraser L, Pearce S. Do chronic pain patients 'Stroop' on pain stimuli? Br J Clin Psychol. 1998;37:49 - 58.

30. Liossi C, Schoth DE. Attention toward interpersonal stimuli in individuals with and without chronic daily headache. Journal of Neurology and Neurosurgery. 2016;3(3):1-7.

31. Pincus T, Pearce S, McClelland A, Farley S, Vogel S. Interpretation bias in responses to ambiguous cues in pain patients. J Psychosom Res. 1994;38(4):347-53.

32. Pincus T, Pearce S, Perrott A. Pain patients' bias in the interpretation of ambiguous homophones. Br J Med Psychol. 1996;69(3):259-66.

33. Karimi Z, Pilenko A, Held SM, Hasenbring MI. Recall bias in patients with chronic low back pain: individual pain response patterns are more important than pain itself! Int J Behav Med. 2016;23(1):12-20.

34. Cumming G. Understanding the new statistics: effect sizes, confidence intervals, and meta-analysis. New York: Routledge; 2012.

35. Efron B. Better bootstrap confidence intervals. Journal of the American statistical Association. 1987;82(397):171-85.

36. Miller GA, Chapman JP. Misunderstanding analysis of covariance. J Abnorm Psychol. 2001;110(1):40.

37. Field A. Discovering Statistics using IBM SPSS Statistics. London: Sage; 2013.

38. Liossi C, White P, Schoth DE. Time-course of attentional bias for threat-related cues in patients with chronic daily headache–tension type: Evidence for the role of anger. Eur J Pain. 2011;15(1):92 - 8.

39. Dear BF, Sharpe L, Nicholas M, Refshauge K. Pain-related attentional biases: The importance of the personal relevance and ecological validity of stimuli. J Pain. 2011a;12(6):625-32.

40. Bradley MM, Lang PJ. Measuring emotion: the Self-Assessment Manikin and the semantic differential. J Behav Ther Exp Psychiatry. 1994;25:49-59.

41. Edwards LC, Pearce SA. Word completion in chronic pain: evidence for schematic representation of pain? J Abnorm Psychol. 1994;103(2):379-82.

42. Griffith J, McLean M, Pearce SA. Information processing across three different chronic pain groups. In Abstracts of 8th World Congress on Pain; Seattle, WA: International Association for the Study of Pain; 1996. p. 75.

43. McKellar JD, Clark ME, Shriner J. The cognitive specificity of associative responses in patients with chronic pain. Br J Clin Psychol. 2003;42(1):27-39.

44. Khatibi A, Sharpe L, Jafari H, Gholami S, Dehghani M. Interpretation biases in chronic pain patients: an incidental learning task. Eur J Pain. 2015;19(8):1139-47.

45. Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull. 1999;125(3):356 - 66.

46. Asmundson GJG, Vlaeyen JWS, Crombez G. Understanding and treating fear of pain. USA: Oxford University Press; 2004.

47. Jones EB, Sharpe L. The effect of Cognitive Bias Modification for Interpretation (CBM-I) on avoidance of pain during an acute experimental pain task. Pain. 2014;155(8):1569-76.

48. Hallion LS, Ruscio AM. A meta-analysis of the effect of cognitive bias modification on anxiety and depression. Psychol Bull. 2011;137(6):940-5.

49. MacLeod C, Mathews A. Cognitive bias modification approaches to anxiety. Annu Rev Clin Psychol. 2012;8:189-217.

50. Khatibi A, Schrooten MG, Vancleef LM, Vlaeyen JW. An experimental examination of catastrophizing-related interpretation bias for ambiguous facial expressions of pain using an incidental learning task. Front Psychol. 2014;5(Article number: 1002):1-10.

51. Schoth DE, Radhakrishnan K, Liossi C. A systematic review with subset meta-analysis of studies exploring memory recall biases for pain-related information in adults with chronic pain. in preperation.

52. Beck AT. Cognitive therapy and the emotional disorders. New York: American Library; 1976.

53. Pincus T, Morley S. Cognitive-processing bias in chronic pain: a review and integration. Psychol Bull. 2001;127(5):599 - 617.

54. Reisberg D, Heuer F. Remembering emotional events. In: Hertel DRP, editor. Memory and Emotion. New York: Oxford University Press. ; 2004.

55. Adelman JS, Estes Z. Emotion and memory: A recognition advantage for positive and negative words independent of arousal. Cognition. 2013;129(3):530-5.

56. Chapman S, Martin M. Attention to pain words in irritable bowel syndrome: increased orienting and speeded engagement. Br J Health Psychol. 2011;16(1):47-60.

57. Martin M, Chapman SCE. Cognitive processing in putative functional gastrointestinal disorder: rumination yields orientation to social threat not pain. Eur J Pain. 2010;14(2):207-13.

58. Van Ryckeghem DM, Vervoort T. Towards an integrative view of cognitive biases in pain. Eur J Pain. 2016;20(8):1201-2.

59. Liossi C. Attentional biases in chronic pain: do they exist and does it really matter? Pain. 2012;153(1):9-10.

60. Jones EB, Sharpe L. Cognitive bias modification: A review of meta-analyses. J Affect Disord. 2017;223:175-83.

61. Schoth DE, Georgallis T, Liossi C. Attentional bias modification in people with chronic pain: a proof of concept study. Cogn Behav Ther. 2013;42(3):233-43.

62. McGowan N, Sharpe L, Refshauge K, Nicholas M. The effect of attentional re-training and threat expectancy in response to acute pain. Pain. 2009;142(1):101-7.

63. Carleton RN, Richter AA, Asmundson GJG. Attention Modification in Persons with Fibromyalgia: A Double Blind, Randomized Clinical Trial. Cogn Behav Ther. 2011;40(4):279-90.

64. Sharpe L, Ianiello M, Dear BF, Nicholson Perry K, Refshauge K, Nicholas MK. Is there a potential role for attention bias modification in pain patients? Results of 2 randomised, controlled trials. Pain. 2012;153(3):722-31.

65. Asmundson GJG, Wright, K, D., & Hadjistavropoulos, H. D. Hypervigilance and attentional fixedness in chronic musculoskeletal pain: consistency of findings across modified Stroop and dot-probe tasks. J Pain. 2005;6(8):497 - 506.

66. Faul F, Erdfelder E, Lang A-G, Buchner A. G\* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175-91.

67. Dear BF, Sharpe L, Nicholas M, Refshauge K. The psychometric properties of the dot-probe paradigm when used in pain-related attentional bias research. . J Pain. 2011b;12:1247 - 54.

68. Sharpe L, Haggman S, Nicholas M, Blake DF, Refshauge K. Avoidance of affective pain stimuli predicts chronicity in patients with acute low back pain. Pain Headache. 2014;155:45-52.

69. Schoth DE, Ma Y, Liossi C. Exploring attentional bias for real-world, pain-related information in chronic musculoskeletal pain using a novel change detection paradigm. Clin J Pain. 2015;31(8):680 - 8.

70. Taylor AM, Harris AD, Varnava A, Phillips R, Hughes O, Wilkes AR, et al. Neural responses to a modified Stroop paradigm in patients with complex chronic musculoskeletal pain compared to matched controls: an experimental functional magnetic resonance imaging study. BMC Psychology. 2016;4(1):5.

71. Muris P, Luerman J, Merckelbach H, Mayer B. Danger is lurking everywhere. The relationship between anxiety and threat perception abnormalities in normal children. J Behav Ther Exp Psychiatry. 2000;31(2):123-36.

72. Sussman TJ, Jin J, Mohanty A. Top-down and bottom-up factors in threat-related perception and attention in anxiety. Biol Psychol. 2016;121:160-72.