Combined cognitive biases for pain and disability information in individuals with chronic headache: A preliminary investigation

**Abstract**

Pain-related cognitive biases have been demonstrated in chronic pain patients, yet despite theoretical predictions are rarely investigated in combination. Combined cognitive biases were explored in individuals with chronic headache (*n*=17) and pain-free controls (*n*=20). Participants completed spatial cueing (attentional bias), sentence generation (interpretation bias), and free recall tasks (memory bias), with ambiguous sensory-pain, disability, and neutral words. Individuals with chronic headache, relative to controls, showed significantly greater interpretation and memory biases favouring ambiguous sensory-pain words, and interpretation bias favouring ambiguous disability words. No attentional bias was found. Further research is needed exploring the temporal pattern of cognitive biases.

**Key words:** Pain, Chronic Illness, Cognitive Processing, Health Psychology, Quantitative Methods

**Introduction**

Cognitive biases are frequently explored in people with chronic pain, with evidence for pain-related attentional (Crombez et al., 2013; Schoth et al., 2012), interpretation (Schoth and Liossi, in press), and memory biases (Pincus and Morley, 2001). Rather than existing in isolation however, different forms of bias may influence and interact with one another (Hirsch et al., 2006). Schema theory (Beck et al., 1985; Beck and Haigh, 2014) predicts dysfunctional schemata result in a selective processing of schema-congruent information, with biases existing across various forms of information processing that are largely considered in parallel. Within the depression literature, it has been speculated that attentional allocation and rumination over negative information precedes a negative interpretation bias, with evidence for an indirect effect between attentional and memory biases, with interpretation bias as a mediating variable, found (Everaert et al., 2013). Considering pain, the Threat Interpretation Model (Todd et al., 2015) highlights the ambiguity of certain words used in attentional bias paradigms (e.g., sharp-pain, sharp-cleaver), and argues an interpretation bias favouring pain-related meanings is necessary, but not sufficient, for attentional bias to be observed. Although the co-existence of cognitive biases is therefore often mentioned in the literature, theoretical perspectives differ in their conceptualisation of the sequential nature of biases.

Research with chronic pain patients typically explores cognitive biases in isolation, with no study to date assessing attentional, interpretation, and memory biases in the same sample. Of the few studies exploring two forms of bias, one found evidence for both interpretation and memory biases for illness-related words, although the proportion of illness-related interpretations made was not correlated with recall scores (Pincus et al., 1996). Another study reported memory bias for sensory-pain words, but not attentional bias measured via the emotional Stoop task; correlations between attentional and memory bias were not reported (Pincus et al., 1998). Comparison between these studies is difficult due to the different pairs of cognitive bias explored, and the different stimuli categories used. Related to this latter issue, it is uncertain whether combined cognitive biases are shown for pain-related information specifically, or also for more general disability-related information. Research using the visual-probe task has found pronounced attentional biases in individuals with chronic pain toward sensory-pain words but not disability words (e.g., (Dehghani, 2003; Sharpe et al., 2009)), whereas one study reported interpretation biases for both sensory-pain and disability words (McKellar et al., 2003). While some studies have found memory biases for sensory-pain words (e.g., (Serbic and Pincus, 2014)), none to date have used a category of disability words specifically.

The aim of the present study was to provide a preliminary investigation of attentional, interpretation, and memory biases for disorder-specific sensory-pain words and more general disability words in individuals with chronic headache. Considering attentional biases in chronic pain are particularly pronounced at longer stimuli presentation times associated with rumination (Crombez et al., 2013; Schoth et al., 2012), attentional biases were assessed prior to interpretation biases. Based on the theoretical models highlighted and the results of former research, it was hypothesised that individuals with chronic headache, relative to pain-free controls, would show significant attentional, interpretation, and memory biases for sensory-pain words.

**Methods**

Ethics approval was obtained from the University of Southampton Research Ethics Committee. In accordance with regulations of the University and guidelines of the Declaration of Helsinki participants provided informed consent prior to taking part.

**Participants**

Participants were recruited from the South of England via press advertisements. For the chronic headache group inclusion criteria were: (a) suffering from primary tension-type headache or migraine, and satisfying the criteria stated in the International Classification of Headache Disorders 3rd edition beta version (ICHD-3), (b) aged 18 or over, (c) having normal or corrected-to-normal vision. Exclusion criteria were: (a) having a diagnosis or receiving treatment for any psychiatric disorder, either currently or within the past five years, (b) suffering from any other form of chronic pain including secondary headache. For the control group inclusion criteria were: (a) aged 18 or over, (b) having normal or corrected-to-normal vision. Exclusion criteria were: (a) having a diagnosis or receiving treatment for any psychiatric disorder, either currently or within the past five years, (b) suffering from any form of chronic or regular pain (in terms of headache frequency, more than 7 headaches per month), (c) taking any psychotropic or analgesic medication regularly. Eligibility was established via telephone interview prior to recruitment.

Thirty-seven participants were recruited, including 17 with chronic headache (mean age = 38.76, *SD* = 13.66, range 21 - 59) and 20 healthy controls (mean age = 35.55, *SD* = 13.78, range 21 - 62). The majority of participants were female (30; 81%). Participants with chronic headache reported on average 21.53 (*SD* = 6.37, range 15 – 30 days) headache days per month, while healthy controls reported on average 1.95 (*SD* = 1.61, range 0 - 5 days) headache days per month. Participants with chronic headache reported living with chronic headache for a mean duration of 14.12 years (*SD* = 11.40, range 1 to 35 years). Within this group, 6 (35.3%) had tension-type headache, and 11 (64.7%) had migraine. Nine (52.9%) reported at least one relative to also suffer from regular headache. As indexed by their MIDAS (migraine disability assessment) scores, 11 (64.7%) indicated severe disability as a consequence of their headaches. All but three (82.4%) were taking regular analgesic medication for the management of their headache.

**Measures**

 The following questionnaires were used: Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983); State-Trait Anxiety Inventory (Spielberger et al., 1970); McGill Pain Questionnaire (Melzack, 1975); Brief Pain Inventory-Short Form (Cleeland and Ryan, 1994); Migraine Disability Assessment Questionnaire (Stewart et al., 2001). Full details are provided in Supplementary Questionnaire Information and Data.

**Experimental Stimuli**

Experimental stimuli (Supplementary Table 1) included nine sensory-pain words, reflecting the sensory dimension of headache pain; nine disability words, reflecting longer-lasting potential consequences of pain; and nine neutral words, unrelated specifically to pain or ill-health. As interpretation biases were explored, all words were either homographs (i.e., words which have identical spelling but different meanings and etymologies) or pseudo-homographs (also referred to as polysemes; i.e., words which have identical spelling but different meanings, although stem historically from the same source) (Drury, 1969). All words therefore have multiple meanings and associations, as indexed by the Merriam-Webster dictionary (merriam-webster.com) and the University of Florida Free Association Norms database (Nelson et al., 2004). Sensory-pain and disability words have neutral associations as well as pain-related/disability associations, and neutral words have multiple neutral associations. Words across the three conditions were matched on length and Kucea-Francis written frequency using the MRC Psycholinguistic Database (Wilson, 1988). Using the University of Florida Free Association Norms database, words were also matched on word set size, which is an index of how many strong associations the word has (Nelson et al., 2004).

**Experimental Paradigms**

**Spatial Cueing Task**. The exogenous spatial cueing task (Supplementary Figure 1) was modelled on those used in recent studies exploring biases in depressed and pain populations (Baert et al., 2010; Martin and Chapman, 2010; Everaert et al., 2013). The task included 216 experimental trials, presented in a new randomised order for each participant. The task began with 8 practice trials featuring nonsense strings of consonants (e.g., Ghtxyw). Experimental trials were split into two 108 trial blocks, each of which was immediately preceded by two buffer trials (featuring nonsense strings). Each trial began with a fixation cross in the centre of the screen for 1000 ms, flanked to the left and right by two rectangular boxes. A single word (size 40 Times New Roman font) was then presented for 100 or 1500 ms in either the left or right box. Fifty milliseconds after the disappearance of the word, a probe (the cue) (1 cm in diameter) appeared in the left or right box. Participants indicated the location of the probe as quickly and accurately as possible using a two-button response box to provide their responses. Trials followed one another automatically, with the inter-trial interval varying randomly between either 1000 or 1500 ms. If a response was not provided after 2000 ms of the probe being displayed, the trial ended automatically.

Trials in which the probe replaces the word are ‘valid’ trials, and trials in which the probe appears in the opposite location to the word are ‘invalid’ trials. An equal number of valid and invalid trials were included, divided equally across the three word conditions and two presentation times. Words were therefore not predictive of the probe location. Participants were instructed to focus on the fixation cross as much as possible; in reality however the presentation of the word is difficult to ignore and typically engages attention (Fox et al., 2001), the extent of which can be compared across participant groups and stimuli categories. Six catch trials (three per block) were also included and interspersed randomly among the experimental trials, which reinforced the instruction to focus on the centre of the screen. During each catch trial, a number (1, 2, or 3) replaced the fixation cross. Participants pressed the corresponding number key on the keyboard as soon as they saw the number, and then placed their thumbs again on the buttons on the response box. Following each catch trial, the subsequent experimental trial began automatically after 2500 ms. Text, fixation crosses, and probes were presented in white against a black background. The spatial cueing task lasted approximately 20 minutes.

**Sentence Generation Task**.The sentence generation task (Taghavi et al., 2000) included 27 experimental trials featuring the same sensory-pain, disability, and neutral stimuli as the spatial cueing task (Supplementary Figure 1). 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 then replaced the cross, which remained on the screen until the end of the trial. Participants were instructed to read the word, and using the keyboard 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 when satisfied the participant pressed the F12 key to submit their response. If no answer was submitted, the next trial began after 120 seconds. Trials followed one another automatically, and all 27 trials were 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*. Text, fixation crosses, and cursors were presented in white against a black background. The sentence generation task lasted approximately 12 minutes.

**Free Recall Task**. Participants were unexpectedly given three minutes to write down as many words as possible from the spatial cueing and sentence generation tasks.

**Apparatus and Procedure**

Spatial cueing and sentence generation tasks were developed in Presentation® (version 12.2, Neurobehavioural Sciences) and run on a personal computer with a 15 inch monitor. Participants first completed the spatial cueing task, and after a short break completed the sentence generation task. This task order is the same as that used in a recent study exploring combined cognitive biases in subclinical depression (Everaert et al., 2013), and reflects the notion that attentional allocation and rumination over negative/threatening information precedes a bias favouring negative/threatening interpretations of ambiguous information. Immediately following this, participants were instructed to count backwards from 400 in units of 7 for two minutes. This distractor task was used to reduce the possibility of recency effects influencing subsequent recall. Participants then completed the surprise free recall task. After a short break participants completed the questionnaires, which were presented in a new randomised order for each participant. The total experimental duration was approximately 60 minutes.

**Data Reduction and Analytic Plan**

Analyses were conducted in IBM SPSS Statistics for Windows 22. For the spatial cueing task, practice trials were excluded from final analysis, along with experimental trials with incorrect responses. Box and whisker plots for overall data revealed outliers to be any response latencies falling below 200 or above 1500 ms, which were removed. After this, mean response times were calculated for each participant individually, with any response >3SD away from their individual mean also removed as outliers. Response times from valid trials were subtracted from invalid trials to form a cue validity index for each stimuli category at both presentation times (Koster et al., 2010). An overall attentional bias index was then calculated by subtracting the cue validity index of neutral words from the cue validity index of sensory-pain and disability words at 100 ms and 1500 ms presentation times (Everaert et al., 2013). A positive score indicates greater attentional engagement of sensory-pain/disability words relative to neutral words, whereas a negative value indicates greater attentional engagement of neutral words relative to sensory-pain/disability words. This attentional bias index was used in the statistical analyses.

For the sentence generation task, as per former research (McKellar et al., 2003) two raters independently and blindly categorised participant response sentences as either pain-related (i.e., describing the experience of pain – *He had a pressing pain in his head*), disability (i.e., describing the consequences of pain or illness – *His lack of mobility was a pressing matter*) or benign (i.e., describing situations or events unrelated to pain or disability – *The boy was pressing the buttons in the lift*). Benign responses include 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 was used in the analysis (Pincus et al., 1994; Pincus et al., 1996). For the free recall task the proportion of words recalled per stimuli category was computed (Karimi et al., 2016; Pincus et al., 1996).

Between-groups differences for demographic characteristics and self-report questionnaires were explored via *t*-tests and χ2 for continuous and categorical variables respectively. Mixed-designs analysis of variance (ANOVA) was used to compare chronic headache and healthy control groups on attentional bias indices, sentence generation responses, and proportion of words recalled. ANOVAs and *t*-tests were used as required in post-hoc analyses to clarify significant effects. Effect sizes for ANOVA and *t*-tests were quantified using partial eta-square p2 and Cohen’s *d* respectively. Cohen’s d and associated 95% confidence intervals were calculated via ECSI (Cumming, 2012). For ANOVA analyses, the alpha level was set at .05, two-tailed. Pearson’s correlation coefficients were conducted selectively to assess the relationship between different types of sensory-pain and disability cognitive bias.

**Results**

**Group Comparisons**

Chronic headache (*n* = 17) and healthy control groups (*n* = 20) did not differ significantly in age [*t*(35) = 0.71, *p* = .482, *d*  = 0.23, CI of *d* [-0.42, 0.88] or sex [chronic headache = 94% female (16); healthy control = 70% female (14); χ2 = 3.48, *p* = .062]. Questionnaire data is provided in Supplementary Questionnaire Information and Data. Independent *t*-tests were conducted on measures completed by both groups. The chronic headache group reported significantly higher trait anxiety than the healthy control group. Trait anxiety was not included as a covariate in the analyses conducted as this was not predictive of cognitive bias for sensory-pain or disability words.

**Spatial Cueing Task: Attentional Bias**

Mean reaction times across the three stimuli conditions did not significantly differ, *F* (2, 72) = 2.08, *p* = .133, ηp2= .055 [sensory-pain = 624 ms, disability = 619 ms, neutral = 621 ms]. Chronic headache and healthy control groups did not significantly differ in mean reaction time [chronic headache = 664.97 ms (*SD* = 139.00); healthy control = 584.63 ms (*SD* = 120.18); *t*(35) = 1.89, *p* = .068, *d* = 0.62, CI of *d* (-0.05, 1.28)], number of incorrect responses made [chronic headache = 2.24 (*SD* = 1.72); healthy control = 2.10 (*SD* = 2.17); *t* (35) = 0.21, *p* = .837, *d* = 0.07, CI of *d* (-0.58, 0.72)] or number of outliers removed [chronic headache = 4.06 (*SD* = 3.21); healthy control = 3.10 (*SD* = 1.62); *t* (35) = -1.17, *p* = .249, *d* = 0.39, CI of *d* (-0.27, 1.04)].

Attentional bias index scores are presented in Table 1. A 2 (group; chronic headache, healthy control) x 2 (stimuli type; sensory-pain, disability) x 2 (presentation time; 100 ms, 1500 ms) mixed-designs ANOVA was conducted on attentional bias scores. No significant main effects or interactions were found, for example: group, *F* (1, 35) = 0.22, *p* = .639, ηp2= .006; group by stimuli type by presentation time, *F* (1, 35) = 2.62, *p* = .115, ηp2= .070. Although the lack of significant results did not warrant the comparison of groups via independent samples *t*-tests, Cohen’s *d* effect sizes for between-groups differences are given here for information purposes: sensory-pain 100 ms *d* = 0.13, CI of *d* (-0.52, 0.77); sensory-pain 1500 ms *d* = 0.19, CI of *d* (-0.46, 0.83); disability 100 ms *d* = 0.28, CI of *d* (-0.37, 0.93); disability 1500 ms *d* = 0.16, CI of *d* (-0.49, 0.80). Full results are presented in Supplementary Table 2.

INSERT TABLE 1 HERE

**Sentence Generation Task: Interpretation Bias**

Chronic headache and healthy control groups did not differ significantly in the number of valid interpretations made [chronic headache = 26.65 (*SD* = 0.70), healthy control = 26.55 (*SD* = 1.00); *t* (35) = -0.34, *p* = .739, *d* = 0.11, CI of *d* (-0.54, 0.76)]. The proportion of pain, disability, and benign interpretations made for each category of words are presented in Table 1. A 2 (group; chronic headache, healthy control) x 3 (stimuli type; sensory-pain, disability, neutral) x 3 (response; pain, disability, benign) mixed-designs ANOVA was conducted on the proportion of participant responses classified as sensory-pain, disability or benign for each stimulus category. The main effect of response was significant, *F* (2, 55) = 1208.79, *p* < .001, ηp2= .972, along with a significant group by response interaction, *F* (2, 35) = 10.18, *p* < .001, ηp2= .225, and stimuli type by response interaction, *F* (4, 140) = 102.04, *p* < .001, ηp2= .745. These results were qualified by a significant group by stimuli type by response interaction, *F* (4, 140) = 6.34, *p* = .002, ηp2= .153.

Independent *t*-tests were conducted to clarify the significant three-way interaction. Chronic headache participants, relative to healthy controls, provided significantly more pain responses to sensory-pain words, *t*(35) = 3.64, *p* = .001, *d* = 1.19, CI of *d* (0.48, 1.88), and significantly more disability responses to disability words, *t*(35) = 2.14, *p* = .040, *d* = 0.71, CI of *d* (0.03, 1.37). In contrast, healthy controls, relative to chronic headache participants, provided significantly more benign responses to sensory-pain words, *t*(35) = 3.63, *p* = .001, *d* = 1.20, CI of *d* (0.49, 1.90), and significantly more benign responses to disability words, *t*(35) = 2.11, *p* = .042, *d* = 0.71, CI of *d* (0.04, 1.37). No significant differences between groups were found for the neutral stimuli category.

**Free Recall Task: Memory Bias**

Chronic headache and healthy control groups did not differ significantly in the number of total words recalled [chronic headache = 8.88 (*SD* = 2.62), healthy control = 9.25 (*SD* = 3.31); *t*(35) = 0.370, *p* = .714, *d* = 0.12, CI of *d* (-0.53, 0.77)] or the number of incorrect words recalled [chronic headache = 0.65 (*SD* = 1.06), healthy control = 0.70 (*SD* = 1.22); *t*(35) = 0.14, *p* = .890, *d* = 0.05, CI of *d* (-0.60, 0.69)]. The proportion of the total correct recall accounted for by each stimuli condition are provided in Table 1. A 2 (group; chronic headache, healthy control) x 3 (stimuli type; sensory-pain, disability, neutral) mixed-designs ANOVA was conducted. The main effect of stimuli type was significant; *F* (2, 70) = 5.00, *p* = .009, ηp2 = .125, as was the group by stimuli type interaction; *F* (2, 70) = 4.27, *p* = .018, ηp2= .109. Independent *t*-tests were conducted to clarify the significant interaction. Chronic headache participants, relative to healthy controls, recalled a significantly greater proportion of sensory-pain words, *t*(35) = 2.81, *p* = .008, *d* = 0.92, CI of *d* (0.24, 1.60). There was a trend for healthy controls, relative to chronic headache participants, to recall more neutral words, although this was not statistically significant, *t*(35) =1.90, *p* =.066, *d* = 0.63, CI of *d* (-0.04, 1.28). The two groups did not differ in the proportion of disability words recalled, *t*(35) =1.04, *p* =.306, *d* = 0.35, CI of *d* (-0.31, 1.00)]. One-way ANOVAs were also conducted on stimuli type for each group independently. A main effect of stimuli type was found for the chronic headache group only, *F* (2, 32) = 7.61, *p* = .002, ηp2= .322. Pairwise comparisons revealed a significantly greater proportion of words recalled were from the sensory-pain category than the neutral category (mean difference = .256, *p* = .006).

**Correlation Analysis**

 Correlation matrices can be found in Supplementary Tables 3a to 3f. Across all participants, the proportion of pain interpretations made for sensory-pain words was positively correlated with the proportion of sensory-pain words recalled, *r* = .391, *p* = .017. For the healthy control group, the proportion of pain interpretations made for sensory-pain words was positively correlated with attentional biases for sensory-pain words presented at 100 ms, *r* = .500, *p* = .025.

**Discussion**

 Partly supporting the study hypothesis, individuals with chronic headache, relative to controls, showed significantly greater interpretation and memory biases for sensory-pain words. The two groups did not differ in patterns of attentional bias for sensory-pain words. The results also revealed a significant interpretation bias for disability words in those with chronic headache relative to controls.

Interpretation biases have been infrequently explored in chronic pain, although all former studies showed significantly more frequent pain-related/illness-related interpretations of ambiguous words or images in those with chronic pain relative to pain-free controls (Schoth and Liossi, in press). The specificity of such biases is a notable issue, as some studies used broader stimuli categories reflecting ill-health rather than pain specifically (e.g., (Pincus et al., 1996; Pincus et al., 1994)). The present results provide some clarification, showing individuals with chronic headache demonstrate interpretation biases for both disorder-specific sensory-pain words and general disability words. The majority of participants experienced pain for many years and reported severe disability, and therefore biases for disability words is unsurprising. These results also align with those of McKellar and colleagues, who reported pain- and disability-related interpretation biases in individuals with chronic pain. In contrast, studies using the visual-probe task have reported attentional biases for sensory-pain but not disability words (e.g., (Dehghani, 2003; Sharpe et al., 2009)). This is supported by a meta-analysis showing significant biases for sensory-pain words, but not words associated with consequences of pain (including disability-related words), in chronic pain patients (Crombez et al., 2013). Furthermore, research recruiting a chronic headache sample with similar levels of disability found attentional bias for pain-related images but not general health-threat images (Schoth and Liossi, 2013). This pattern of results therefore suggests interpretation biases exist for a broader range of stimuli than do attentional biases, although it is premature at present to try and explain why this should be so.

Evidence for sensory-pain memory biases in chronic pain patients have been reported in some studies (e.g., (Serbic and Pincus, 2014)) but not others (e.g., (Busch et al., 2006)). Although disability-related words have not been used specifically, broader categories of words reflecting ill-health have been used, again with some studies reporting memory biases (e.g., (Serbic and Pincus, 2014)) and others not (e.g., (Nikendei et al., 2009)). Numerous methodological differences exist within this literature which likely account for the inconsistency of results, including whether the recall task is made explicit or is unexpected by participants. If unexpected, there is also variation in the conditions and instructions under which encoding takes place. Interestingly, the present study found evidence of a pronounced memory bias for sensory-pain but not disability words in those with chronic headache. Within-group analysis also showed a significantly greater proportion of words recalled by the chronic headache group were from the sensory-pain category than the neutral category, although no difference was found between disability and neutral categories. While a specificity of memory bias was observed, future research should aim to replicate these findings under a variety of experimental conditions, including explicit and unexpected tasks.

Attentional bias was measured via the spatial cueing task. As this paradigm presents one stimulus per trial, it may be addressed whether the presence of threat has a slowing or inhibition effect on motor responses (Mogg et al., 2008); overall there was no evidence of such effects in the present study. Stimuli presentation times of 100 and 1500 ms were used to explore initial orienting of attention and maintained attention respectively. While the former is associated with hypervigilance for threat (Beck et al., 1985), the latter has been linked to processes of excessive elaboration and rumination (Donaldson et al., 2007). No evidence of attentional bias for sensory-pain words was found however, which is inconsistent with former studies recruiting chronic headache samples that have reported pain-related biases via visual-probe (e.g., (Schoth and Liossi, 2013; Liossi et al., 2009)), visual scanning (Liossi et al., 2014), and visual search tasks (Schoth et al., 2015). The spatial cueing task has been infrequently used in pain samples, with evidence for pain-related biases in one study with patients with irritable bowel syndrome (Chapman and Martin, 2011) but not another (Martin and Chapman, 2010). A recent study reported evidence of attentional biases towards health and somatic threat cues in low pain catastrophisers, but not high pain catastrophisers as predicted (Schrooten et al., 2015). Furthermore, a review of research with anxious populations showed a very small, non-significant between-group effect size for studies using the spatial cueing task (Bar-Haim et al., 2007), and between-group effect sizes were also small in the present study. Related to this, for between-groups comparisons a post-hoc power calculation using GPower (Faul et al., 2007) revealed only 9%, 31%, and 65% probabilities of correctly rejecting the null hypothesis for small (0.2) medium (0.5) and large (0.8) effect sizes respectively. The paradigm used, in combination with the small sample size, likely explains the null attentional bias findings in the present study.

As two experimental conditions were included in the current study, a neutral match was required for each experimental word. The spatial cueing task was therefore used instead of the visual-probe task, as the latter would necessitate either twice as many neutral words, or the same set of neutral words paired with both sensory-pain and disability words. Both are problematic for the later exploration of memory biases, which requires an equal number of words per category, shown the same number of times, to allow for a valid comparison of results (i.e., if neutral words are displayed twice as often, memory for this category of words will likely improve). This problem is avoided by the use of the spatial cueing task, which presents words from each stimuli category the same number of times. Considering the null findings however, follow up studies will explore combined cognitive biases using the visual-probe task with a single experimental stimuli category of sensory-pain words (matched with neutral words).

The Threat Interpretation Model (Todd et al., 2015) predicts a relationship between pain-related interpretation and attentional biases. For healthy controls, an interpretation bias favouring the pain-related meaning of ambiguous words with sensory-pain and neutral meanings is associated with a hypervigilance for such words. Surprisingly this effect was not found for the chronic headache group. Across all participants the proportion of pain interpretations made for sensory-pain words was positively correlated with the proportion of sensory-pain words recalled. As pain is important for survival (Williams, 2002), it unsurprising that across all individuals a tendency to interpret ambiguous information as pain-related is associated with enhanced recall of such information. Specific testing of the predictions raised by the Threat Interpretation Model is required however, although this latter correlation does highlight the possibility of modifying this model to also include memory biases.

Further research is required to explore the temporal pattern of cognitive biases, especially as the effects of attentional and interpretation biases on the experience of pain are being explored (Schoth et al., 2013; Jones and Sharpe, 2014; Sharpe et al., 2012; Carleton et al., 2011). While Todd and colleagues predict interpretation biases to precede attentional biases, schema theory largely considers cognitive biases in parallel (Beck and Haigh, 2014), and the combined cognitive bias hypothesis states “a number of biased cognitive processes often operate simultaneously and/or in succession” (Hirsch et al., 2006)(p. 223). As noted, research exploring combined biases in subclinical depression postulates that attentional allocation and rumination over negative information precedes a negative interpretation bias (Everaert et al., 2013). Counterbalancing the order of attentional and interpretation bias tasks in future research would help elucidate the precise relationship between these forms of cognitive bias. Longitudinal research may also be used to address whether induction of one form of bias has resulting effects on other forms of bias (Schoth and Liossi, in press; Hirsch et al., 2006).

Limitations may be highlighted with the current investigation. Due to the small sample size the study was underpowered, and the results of the spatial cueing task and the correlational analysis should be interpreted with caution. The study also did not explore the relationship between pain characteristics, such as intensity and duration of episodes, on patterns of cognitive bias. While there is inconsistent evidence for such relationships in the existing literature, there is a need to explore the impact of such characteristics in future combined cognitive bias research. Furthermore and as noted, this present study did not set out to specifically test the predictions raised by the Threat Interpretation Model (Todd et al., 2015). Rather, the aim was to provide a preliminary investigation into combined cognitive biases in chronic pain, an area which has received little attention. In conclusion, the results contribute to a growing body of chronic pain research, providing evidence for interpretation and memory pain-related biases in individuals with chronic headache.

**Declaration of Conflicting Interests**

The Authors declare that there is no conflict of interest

**Funding**

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**Acknowledgements**

The authors would like to thank Dr Jin Zhang, PhD (Senior Experimental Officer, Academic Unit of Psychology, University of Southampton, Southampton, Hampshire) for developing the spatial cueing and sentence generation tasks used in this investigation, and for her continued technical support.

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Table 1.
*Attentional, interpretation, and memory biases mean scores (SD) for chronic headache and healthy control groups*

|  |  |  |
| --- | --- | --- |
| Bias index | Chronic Headache Group (*n* = 17) | Healthy Control Group (*n* = 20) |
| Attentional bias (bias index scores)  |  |  |
|  Sensory-pain 100 ms | 16.14 (64.38) | 9.79 (33.60) |
|  Sensory pain 1500 ms | 4.97 (42.95) | -1.88 (30.73) |
|  Disability 100 ms | 17.41 (74.09) | 1.79 (34.79) |
|  Disability 1500 ms | -5.17 (47.19) | 1.70 (40.20) |
|  |  |  |
| Interpretation bias (proportion of responses) |  |  |
|  Pain responses to sensory-pain words | .275 (.153) | .114 (.116) |
|  Disability responses to sensory-pain words | .000 (.000) | .000 (.000) |
|  Benign responses to sensory-pain words | .726 (.153) | .886 (.116) |
|  |  |  |
|  Pain responses to disability words | .022 (.048) | .022 (.046) |
|  Disability responses to disability words | .419 (.180) | .310 (.127) |
|  Benign responses to disability words | .560 (.183) | .668 (.124) |
|   |  |  |
|  Pain responses to neutral words | .000 (.000) | .006 (.025) |
|  Disability responses to neutral words | .020 (.044) | .028 (.049) |
|  Benign responses to neutral words | .980 (.044) | .967 (.063) |
|  |  |  |
| Memory bias (proportion of words recalled) |  |  |
|  Sensory-pain words | .469 (0.177) | .324 (0.138) |
|  Disability words | .318 (0.149) | .370 (0.155) |
|  Neutral words | .213 (0.144) | .306 (0.153) |

Supplementary Table 1.

*Sensory-pain, disability, and neutral words used in the cognitive bias tasks*

|  |  |  |
| --- | --- | --- |
| **Sensory-pain** | **Disability** | **Neutral** |
| Tension | Bedroom | Setting |
| Pounding | Disorder | Boarding |
| Pressing | Terminal | Inclined |
| Splitting | Dependent | Promotion |
| Piercing | Unstable | Animated |
| Drilling | Handicap | Compound |
| Tight | Wound | Grasp |
| Pulsing | Disable | Banking |
| Squeeze | Invalid | Trailer |

Supplementary Table 2.

*Analysis of variance results for the attentional bias analysis from the spatial cueing task data*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Source of Variance | *F*  | *df* | *p* | ηp2 |
| Group | 0.224 | 1, 35 | .639 | .006 |
| Stimuli type | 0.732 | 1, 35 | .398 | .020 |
| Presentation time | 1.604 | 1, 35 | .214 | .044 |
| Group x Stimuli type | 0.083 | 1, 35 | .776 | .002 |
| Group x Presentation time | 0.375 | 1, 35 | .544 | .011 |
| Stimuli type x Presentation time |  < 0.001 | 1, 35 | .990 | < .001 |
| Group x Stimuli type x Presentation time | 2.617 | 1, 35 | .115 | .070 |

Supplementary Table 3a. Pearson’s correlation coefficients between sensory-pain cognitive bias indices for all participants (*n* = 37)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Sensory-pain 100 ms | Sensory-pain 1500 ms | Pain responses to sensory-pain words |
| Sensory-pain 100 ms (attentional bias) |  |  |  |
| Sensory pain 1500 ms (attentional bias) | .196 |  |  |
| Pain responses to sensory-pain words (interpretation bias) | .142 | .071 |  |
| Sensory-pain words recalled (memory bias) | -.018 | -.028 | .391\* |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Sensory-pain 100 ms | Sensory-pain 1500 ms | Pain responses to sensory-pain words |
| Sensory-pain 100 ms (attentional bias) |  |  |  |
| Sensory pain 1500 ms (attentional bias) | .154 |  |  |
| Pain responses to sensory-pain words (interpretation bias) | -.046 | -.113 |  |
| Sensory-pain words recalled (memory bias) | -.160 | -.037 | .114 |

Supplementary Table 3b. Pearson’s correlation coefficients between sensory-pain cognitive bias indices for chronic headache participants (*n* = 17)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Sensory-pain 100 ms | Sensory-pain 1500 ms | Pain responses to sensory-pain words |
| Sensory-pain 100 ms (attentional bias) |  |  |  |
| Sensory pain 1500 ms (attentional bias) | .282 |  |  |
| Pain responses to sensory-pain words (interpretation bias) | .500\* | .242 |  |
| Sensory-pain words recalled (memory bias) | .171 | -.135 | .362 |

Supplementary Table 3c. Pearson’s correlation coefficients between sensory-pain cognitive bias indices for healthy participants (*n* = 20)

\* Correlation is significant at the .05 alpha level. \*\* Correlation is significant at the .01 alpha level.

Supplementary Table 3d. Pearson’s correlation coefficients between disability cognitive bias indices for all participants (*n* = 37)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Disability 100 ms | Disability 1500 ms | Disability responses to disability words |
| Disability 100 ms (attentional bias) |  |  |  |
| Disability 1500 ms (attentional bias) | .263 |  |  |
| Disability responses to disability words (interpretation bias) | -.118 | -.129 |  |
| Disability words recalled (memory bias) | -.039 | .081 | .093 |

Supplementary Table 3e. Pearson’s correlation coefficients between disability cognitive bias indices for chronic headache participants (*n* = 17)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Disability 100 ms | Disability 1500 ms | Disability responses to disability words |
| Disability 100 ms (attentional bias) |  |  |  |
| Disability 1500 ms (attentional bias) | .337 |  |  |
| Disability responses to disability words (interpretation bias) | -.285 | -.184 |  |
| Disability words recalled (memory bias) | -.058 | -.007 | .165 |

Supplementary Table 3f. Pearson’s correlation coefficients between disability cognitive bias indices for healthy participants (*n* = 20)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Disability 100 ms | Disability 1500 ms | Disability responses to disability words |
| Disability 100 ms (attentional bias) |  |  |  |
| Disability 1500 ms (attentional bias) | .188 |  |  |
| Disability responses to disability words (interpretation bias) | .083 | -.004 |  |
| Disability words recalled (memory bias) | .055 | .140 | .168 |

\* Correlation is significant at the .05 alpha level. \*\* Correlation is significant at the .01 alpha level.

Supplementary Figure 1. Schematic representation of a trial in the spatial cueing task (above) and a trial in the sentence generation task (below)

A single word is presented in either the left or right box for either 100 or 1500 ms

A fixation cross, flanked to the left and right by rectangular boxes, is presented for 1000 ms

Fifty milliseconds after the disappearance of the word, a probe (i.e., the cue) appears in either the left or right box

 Splitting

A single word replaces the fixation cross and remains displayed while the participant provides their response

A fixation cross is presented for 1000 ms

 Splitting

The splitting headache was getting worse by the minute.

**Supplementary Questionnaire Information and Data**

The Hospital Anxiety and Depression Scale (HADS; ([Zigmond and Snaith, 1983](#_ENREF_13)) rates the severity of seven symptoms of anxiety and seven symptoms of depression over the past week. Scores are summed for anxiety and depression subscales, each with a range of 0 – 21; higher scores indicating higher levels of anxiety or depression. A review has supported the internal consistency of anxiety (.68 - .93, mean .82) and depression (.67 - .90, mean .82) subscales ([Bjelland et al., 2002](#_ENREF_2)). Cronbach’s alpha in the current investigation for the anxiety and depression subscales were .88 and .82, respectively.

The State-Trait Anxiety Inventory (STAI; ([Spielberger et al., 1970](#_ENREF_9)) is a 40-item measure of state (i.e., how the respondent currently feels) and trait (i.e. how the respondent generally feels) anxiety. Answers are selected from a four-point Likert scale, with scores ranging between 20 and 80 for both state and trait subscales; higher scores indicate more intense or frequent feelings of anxiety. A review of 45 articles reporting psychometric properties of state and trait subscales found high levels of internal consistency (.91 and .89 respectively) and test-retest reliability (.70 and .88 respectively; ([Barnes et al., 2002](#_ENREF_1))). Cronbach’s alpha in the current investigation for the state and trait subscales were .86 and .62, respectively.

The McGill Pain Questionnaire (MPQ; ([Melzack, 1975](#_ENREF_8)) assesses characteristics of pain and pain intensity using verbal descriptors. The pain rating index of the MPQ features 78 descriptors of pain across 20 categories, assessing sensory, affective, evaluative, and miscellaneous characteristics of pain. Participants select one descriptor per category best describing their pain. The rank order of descriptors selected are summed to form the four characteristics of pain, and a total sum score. The MPQ also includes a 5-point measure of Present Pain Intensity (PPI), ranging from *no pain* to *excruciating pain*. The MPQ is one of the most common measures of pain used, with support for its psychometric properties ([Jensen, 2003](#_ENREF_5)), including good test-retest reliability (total sum score *r* = .83) ([Love et al., 1989](#_ENREF_6)). Cronbach’s alpha in the current investigation for total sum score was .64.

The Brief Pain Inventory-Short Form (BPI; ([Cleeland and Ryan, 1994](#_ENREF_3)) is a measure of pain intensity and pain interference. Pain intensity is assessed via 4 items asking patients to rate their worst pain, least pain, and average pain over the past week, along with their current pain, on an 11-point numeric rating scale (0 = no pain, 10= pain as bad as you can imagine). The average of these four items forms the Pain Intensity Scale. Pain interference is assessed via 7 items asking the degree to which pain has interfered with general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life over the past week, which are assessed on an 11-point numeric rating scale (0 = does not interfere, 10 = completely interferes). The average of these seven items forms the Pain Interference Scale. The BPI also includes a single item assessing how much relief pain treatments and medications have provided over the past week, and a body map so patients can graphically indicate the location of their pain. The psychometric properties of the BPI are well supported ([Cleeland and Ryan, 1994](#_ENREF_3); [Jensen, 2003](#_ENREF_5)), including internal consistency of pain intensity and interference items (Cronbach’s alpha .85 and .88 respectively ([Tan et al., 2004](#_ENREF_12)). Cronbach’s alpha in the current investigation were .79 and .90 for Pain Intensity and Pain Interference scales respectively.

The Migraine Disability Assessment (MIDAS) Questionnaire ([Stewart et al., 2001](#_ENREF_10)) assesses headache-related disability. Participants answer five questions, scoring the number of days, in the past 3 months, of activity limitations due to headache. The overall score is categorized to yield four grades of increasing disability. The MIDAS is internally consistent, highly reliable, valid, and correlates with physicians’ clinical judgment ([Stewart et al., 1999](#_ENREF_11); [Stewart et al., 2001](#_ENREF_10)), and was applied to all participants with chronic headache regardless of type, in line with current clinical practice ([Harpole et al., 2005](#_ENREF_4); [Matchar et al., 2008](#_ENREF_7)). Cronbach’s alpha in the current investigation was .78.

|  |
| --- |
| Table 1.*Means* (*SD*) *for questionnaire measures completed by chronic headache and healthy control groups* |
| Measure | Chronic Headache Group (*n* = 17) | Healthy Control Group (*n* = 20) | Mean difference | *t* | *df* | *p* | Cohen’s *d* | 95% CI of *d* |
| HADS anxiety | 6.88 (4.65) | 6.60 (3.19) | 0.28 | 0.20 | 35 | .842 | 0.07 | -0.58, 0.71 |
| HADS depression | 4.41 (3.37) | 3.50 (3.19) | 0.91 | 0.84 | 35 | .404 | 0.28 | -0.37, 0.93 |
| STAI state anxiety | 34.65 (14.52) | 28.80 (8.53) | 5.85 | 1.54 | 35 | .132 | 0.51 | -0.15, 1.16 |
| STAI trait anxiety | 45.47 (11.83) | 37.20 (10.82) | 8.27 | 2.22 | 35 | .033 | 0.73 | 0.06, 1.40 |
| BPI pain intensity scale | 4.62 (2.05) |  |  |  |  |  |  |  |
| BPI pain interference scale | 4.28 (2.67) |  |  |  |  |  |  |  |
| MPQ sensory | 33.82 (15.81) |  |  |  |  |  |  |  |
| MPQ affective | 8.18 (5.00) |  |  |  |  |  |  |  |
| MPQ evaluative | 3.06 (1.52) |  |  |  |  |  |  |  |
| MPQ miscellaneous  | 8.00 (3.59) |  |  |  |  |  |  |  |
| MPQ total | 53.06 (21.59) |  |  |  |  |  |  |  |
| MPQ present pain intensity | 3.36 (0.93) |  |  |  |  |  |  |  |

STAI = State Trait Anxiety Inventory; HADS = Hospital Anxiety and Depression Scale; BPI = Brief Pain Inventory; MPQ = McGill Pain Questionnaire

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