**The Association between Attentional Bias to Experimentally-Induced Pain and to Pain-Related Words in Healthy Individuals: The Moderating Role of Interpretation Bias**

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**Abstract**

Attentional bias to pain-related information may contribute to chronic pain maintenance. It is theoretically predicted that attentional bias to pain-related language derives from attentional bias to painful sensations; however, the complex interconnection between these types of attentional bias have not yet been tested. This study aimed to investigate the association between attentional bias to pain words and attentional bias to the location of pain, as well as the moderating role of pain-related interpretation bias in this association. Fifty-four healthy individuals performed a visual-probe task with pain-related and neutral words, during which eye movements were tracked. In a subset of trials, participants were presented with a cold pain stimulus on one hand. Pain-related interpretation and memory biases were also assessed. Attentional bias to pain words and attentional bias to the pain location were not significantly correlated, although the association was significantly moderated by interpretation bias. A combination of pain-related interpretation bias and attentional bias to painful sensations was associated with avoidance of pain words. In addition, first fixation durations on pain words were longer when the pain word and cold pain stimulus were presented on the same side of the body, as compared to on opposite sides. This indicates that congruency between the locations of pain and pain-related information may strengthen attentional bias. Overall, these findings indicate that cognitive biases to pain-related information interact with cognitive biases to somatosensory information. The implications of these findings for attentional bias modification interventions are discussed.

**The Association between Attentional Bias to Experimentally-Induced Pain and to Pain-Related Words in Healthy Individuals: The Moderating Role of Interpretation Bias**

Pain-related attentional bias is defined as selective attention to pain-related information. This can facilitate avoidance of harm in situations involving acute pain [39; 51] but, in chronic pain, pain-related attentional bias can excessively disrupt attention and interfere with functional activities, which may reduce quality of life and contribute to pain chronicity [51; 63; 72].

Meta-analyses have found that individuals with chronic pain show significant attentional bias to pain-related information, including pain-related words and images [10; 51; 64], whereas individuals in acute or experimentally-induced pain do not [10; 64], indicating that attentional bias is specifically involved in pain chronicity. However, for both acute and chronic pain, effect sizes were mostly small and the results of individual studies inconsistent [10; 51; 64]. Previous research has also investigated attentional bias to painful sensations, finding that healthy individuals showed attentional bias toward tactile [70] and visual stimuli [16; 44; 69] near the pain location. Contrastingly, individuals with complex regional pain syndrome or back pain showed significant attentional bias away from tactile and visual stimuli near the pain location [8].

Theoretical models predict that pain-related attentional bias interacts with biases in interpretation and memory [63; 67]. For instance, the Threat Interpretation Model of Pain (TIMP) predicts that a vigilance-avoidance pattern of attentional bias is shown toward stimuli interpreted as pain-related and threatening, and contends that this attentional pattern facilitates chronic pain development [63]. However, empirical studies to date have produced limited support for this prediction [45; 52; 62].

Research has not yet investigated the interaction between cognitive biases to somatosensory sensations and cognitive biases to visual, pain-related information. This interaction is theoretically supported by schema theories, which posit that biases for pain-related information are derived from biases for pain [3; 39]. Furthermore, according to the associative network theory [5], the activation of one schema partially activates nearby (similar) schemas. Therefore, chronic activation of the pain schema would provoke cognitive biases to pain-related visual information, as well as to somatosensory sensations. Investigating this interaction could also generate meaningful clinical insights, such as whether modification of attentional bias using pain-related words and images [9; 29] could also modify attention to painful sensations [1; 23; 56].

Based on this theoretical and clinical rationale, the current experiment aimed to investigate the association between attentional bias to experimentally-induced painful sensations and to pain-related words in healthy individuals, defined here as individuals without chronic pain, as well as the role of interpretation bias is this association. It was hypothesised that:

1. Attentional bias to ambiguous pain words would be positively associated with attentional bias to the location of pain.
2. This association would be stronger for participants with higher levels of pain-related interpretation bias.
3. Attentional bias to pain words would be stronger when their location was congruent with the location of experimentally-induced pain.

Furthermore, the theoretically predicted associations between attention, interpretation, and memory biases [39; 67] were investigated in additional exploratory analysis at the word-level and participant-level as this is a current line of investigation in our lab [52].

# Method

Approval was obtained from the University of Southampton Research Ethics Committee prior to data collection (ERGO ID 52104).

## Participants

Participant inclusion criteria were: (i) aged 18-50 years inclusive; (ii) normal or corrected to normal vision; and (iii) fluency in the English language. Participant exclusion criteria were: (i) a diagnosis of any type of chronic pain or psychiatric condition; or (ii) currently experiencing pain.

Participants were recruited via social media, word-of-mouth, posters around the University of Southampton campus, and the website ‘efolio’, which is used to recruit undergraduate Psychology students for research studies at the University of Southampton. Psychology students at the University of Southampton received partial course credit for participating, other participants received £9.

A power analysis was conducted in GPower [15] to ensure that the sample size was adequate to test Hypothesis 1. This showed that a sample size of 55 was required to detect a medium effect size (0.3) in a linear regression at 80% power and alpha level .05. To allow for 10% drop-out or technical problems, 60 participants were recruited.

## Questionnaires

 Questionnaires assessed the psychological and demographic characteristics of the sample. The constructs assessed by the questionnaires in this study have previously been found to interact with cognitive biases.

Participants completed the Hospital Anxiety and Depression Scale [78] because anxiety and depression are associated with cognitive biases to negative and threatening information, which may interact with pain-related cognitive biases [2; 12]. Fear of pain was assessed with the Fear of Pain Questionnaire – III [35]. There is a strong, positive association between fear of pain and disability [77] and individual studies have found greater pain-related attentional bias for individuals with a high fear of pain [26; 55], although meta-analysis revealed no significant association between fear of pain and attentional bias [10]. Additionally, participants completed a demographic questionnaire that assessed age, occupation, sex, and years in education because these variables may influence pain-related biases [25; 64]. As handedness may influence spatial attentional bias, the Edinburgh Handedness Questionnaire – Short Form [71] was also completed by participants. Questionnaire information can be found in Supplementary File 1.

Correlational analysis was conducted to assess whether the constructs assessed by these questionnaires were associated with cognitive biases in the current study.

## Linguistic Stimuli

Pain-related and neutral homographs were used as stimuli in the sentence generation task, the testing phase of the incidental learning task, and trials of the visual-probe task that contained pain and neutral words. Pain homographs had sensory pain and neutral meanings, and were derived from the McGill Pain Questionnaire [36]. Neutral homographs had multiple neutral meanings. The neutral and pain homographs used in this study were matched on length and written frequency according to the MRC Psycholinguisic Database [74] and on number of strong associations according to the University of Florida Free Association Norms Database [37]. These stimuli have previously been used in attention, interpretation and memory bias research from our lab [45; 52].

Unambiguous pain words were used in the learning phase of the incidental learning task and these were matched on length and written frequency with the other word categories. Trials of the visual-probe task that contained only neutral words used neutral words that were matched on length and written frequency within their pair and with the other word stimuli (see Table 1).

A pilot word rating study was conducted prior to data collection to assess the valence, arousal and pain-relatedness of the words. The sample for this pilot study consisted of nine postgraduate and undergraduate students, five females and four males, with a mean age of 27.06 years (SD = 7.24). The participants had on average 18.11 years of education (SD = 1.26). For each word, valence and arousal were rated on the Self-Assessment Manikin (SAM) scale [6] and pain-relatedness was assessed directly by asking participants ‘How well does this word represent pain?’ on a scale of 1 (‘Not at all’) to 9 (‘Very well’). For further details see Supplementary File 2.

## Experimental Paradigms

### Attentional bias.

Attentional bias to pain words and attentional bias the pain location were both assessed using eye-tracking during a modified visual-probe task [33] (see Figure 1). Response times were also recorded as a secondary measure of attentional bias.

In each trial of the visual-probe task, a central point was displayed until the participant fixated on it. Two words were then shown, one on the left side of the screen and one on the right. After 2000 ms the two words disappeared and a dot appeared in the location where one of the words was previously located. Attentional bias was inferred from eye tracking indices. Specifically, bias in attentional orienting was inferred from a greater proportion of initial fixations and shorter time to the initial fixation on the pain word. Bias in maintained attention was inferred from longer mean fixation duration, mean first fixation duration, and total fixation time on the pain word, as well as a greater number of fixations and visits to the pain word. Attentional bias to the pain location was inferred from the same eye tracking indices for the word ipsilateral to the location of pain. These indices were decided upon *a priori,* as recommended by Skinner and colleagues [58] to decrease the risk of selective reporting.

As the response time measure of attentional bias, participants were asked to respond to the location of the dot as quickly as possible using the left and right arrow keys. Faster responses indicated that attention was already directed toward the location of the dot. Therefore, faster responses to dots that replaced pain-related words or words ipsilateral to the pain location indicated pain-related attentional bias [51]. Response times are still the most common method of assessing attentional bias [64], and inclusion allows for comparison to published literature.

### Interpretation bias.

The sentence generation task was conducted as a direct measure of interpretation bias and the incidental learning task as an indirect measure of interpretation bias. Direct measures have been used more commonly in studies of pain-related interpretation bias and therefore using a direct measure facilitates comparison with previous research [49]. However, direct assessment of word interpretation is susceptible to social desirability and response biases from the participant [50]. Indirect measures of interpretation bias, which do not ask participants to interpret a stimulus but infer interpretation bias from a seemingly unrelated behavioural task, reduce the possibility of response biases [50].

#### Sentence generation task.

In each trial of the sentence generation task participants were presented with a word and instructed to write the first meaningful sentence that came to mind containing that word [50]. After two practice trials and the opportunity for questions, there were 18 trials in the main block, presented in a randomised order. In nine trials, a pain-related homograph was presented and in the other nine trials a neutral homograph was presented.

#### Incidental learning task.

The incidental learning task [27] consisted of a learning phase and a testing phase (see Figure 1). In the learning phase, after a central fixation cross presented for 500 m, an unambiguous pain word or a neutral word was presented centrally for 675 ms. Following pain words, the dot was presented on one side of the screen (e.g. the left) for 80% of trials and on the other side for 20% of trials. The opposite was the case for neutral words. Participants responded to the location of the dot as quickly as possible using the left and right arrows on the keyboard. The side associated with pain words was counterbalanced between participants. There was an inter-trial interval of either 800 ms or 1200 ms, varying randomly. The same series of events occurred in the test phase except an ambiguous pain word was shown in the centre of the screen and the dot had an equal chance of appearing on the left or right. Faster responses to dots on the side previously predicted by pain words indicates pain-related interpretation bias.

Each word was presented four times, therefore there were 72 trials in the learning phase and 36 trials in the testing phase. The trials in each phase were presented in a randomised order. Participants completed 10 practice trials with neutral words and had the opportunity to ask questions before the start of the main block of trials.

### Memory bias.

Memory bias was assessed with a surprise free recall task [45; 52]. Participants were asked to recall as many words as possible from the previous tasks within a three-minute period, using the full time period for the task. The free recall task is one of the most commonly used assessments of pain-related memory bias and therefore was selected to facilitate comparison with previous research [53].

## Apparatus

Cold pain stimuli were produced and delivered through a Neurosensory Analyser Model TSA-II. The thermode had a contact area of 3cm2 and was attached to the thenar eminence of the participant’s hand with a Velcro strap.

Eye movements were recorded using an SR-Research Eyelink 1000 eye tracker. The experiment was programmed and run with SR-Research Experiment Builder. Eye movements were recorded from the corneal reflection of the right eye and sampled at 1000 Hz. Before each block of trials the eye tracker was calibrated and validated within spatial accuracy of 0.5° using a nine point calibration.

## Procedure

The experiment took place in the Pain Research Laboratory at the University of Southampton. Lighting was dimmed and the room temperature was 22°C for all participants. Participants gave informed consent before the study commenced.

The experimental session began with cold pain threshold assessment. Cold pain rather than heat pain was selected for this experiment because it is likely to be experienced less frequently in everyday life and therefore would be more novel. Furthermore, cold pain is mediated to a greater extent by C fibres and therefore induces predominantly second pain, which is more representative of acute or chronic pain [59]. The thermode was attached to the thenar eminence and decreased in temperature at a rate of 1°C/sec from baseline 32°C. Participants indicated the very first moment the temperature became painful by clicking a mouse button. At this point the temperature of the thermode did not decrease further and returned to the baseline temperature at a rate of 8°C/second. This process was repeated three times on each hand, with hand order randomised. The mean of the three trials was used as the intensity for the pain stimulus in subsequent tasks.

Participants then completed the incidental learning task, followed by the sentence generation task. Next, participants completed the visual-probe task during which eye movements were tracked. The visual-probe task was conducted under three different conditions. All three were conducted with the thermode on one hand then repeated with the thermode on the other hand. Hand order was counterbalanced between participants. Overall, there were six blocks of trials with 32 trials in each block. The trial order in each block was randomised for each participant. A diagram of the experimental setup for the visual probe task is shown in Figure 1.

In *Condition 1*, no cold pain was administered. In each trial, an ambiguous pain word and a neutral word were presented. Each ambiguous pain word was presented four times in the block: Twice on the left and twice on the right, for each side the dot replaced the pain word once (a congruent trial) and the neutral word once (an incongruent trial).

In *Condition 2*, all words were neutral and the cold pain stimulus was applied to the thenar eminence. The study used a threshold level cold pain stimulus because pilot testing indicated that participants would not tolerate a more intense stimulus for the duration of the visual-probe task. The stimulus cooled down to the pain threshold before the start of the block and remained at threshold level for the duration of the block. The dot was presented an equal number of times on the left and right.

In *Condition 3*, an ambiguous pain word and a neutral word were presented in the same method as Condition 1 and the cold pain stimulus was presented as in Condition 2.

Following this, participants counted backward from 300 in units of seven for two minutes, similar to Schoth et al. [45]. This distractor task prevented participants using rehearsal strategies to remember information from previous tasks. The surprise free recall test was then conducted. Finally, participants completed the questionnaires before being thanked and debriefed. The Edinburgh Handedness Questionnaire [71]was completed online after study participation.

## Design

Hypotheses one and two were tested with a single group observational design. Hypothesis three was investigated with a 2 (word type: pain, neutral) x 2 (pain location: left, right) within-subjects design.

## Data preparation

 All data cleaning and analyses were conducted using RStudio [43] with Rversion 4.0.2 [41].

### Visual-probe task eye-tracking data.

Fixation data were extracted using SR Research DataViewer. The interest period began with the onset of the two words and ended with the offset of the words. Rectangular interest areas of width 265 pixels and height 250 pixels were created around each word.

Data was organised and fixation contingencies were computed using the organise functions in in eyeTrackR [19]. Trials with incorrect or no response were excluded (3.25% of trials which contained 3.73% of all fixations). Fixations less than 60 ms or greater than 1500 ms were removed (4.63% of fixations). Values more than three standard deviations from the mean were removed for each eye movement measure. This data processing protocol is the same as that of other eye-tracking research from our lab [30; 47; 54] and these data cleaning limits are similar to previous eye-tracking research with the visual-probe task [14; 60; 75; 76]. Histograms were inspected to ensure that these limits were appropriate for our data.

The proportion of initial fixations and time to the initial fixation on the interest area were calculated as indices of attentional orienting. Mean fixation duration, mean first fixation duration, total fixation time, number of fixations on the interest area, as well as number of visits to the interest area, were calculated as indices of maintained attention. These indices were computed using the analyse functions in eyeTrackR [19]. All measures were grouped by word type (pain or neutral) and/or location relative to pain (pain side or neutral side). Only fixations within the interest areas were included in the data analysis. For all eye movement indices, the difference between the value for the pain side/word and the value for the non-pain side/word were calculated for later use in correlation and regression analyses. This followed the same formula as the attentional bias index:

$$Eye tracking attentional bias index= Ip -Inp$$

 Where *Ip* = eye tracking index on the pain word/side and *Inp* = eye tracking index on the non-pain word/side. For all indices, a positive index indicates attentional bias to pain. To ensure this consistency, the sign was changed for time to first fixation because a lower value of this index indicates greater attentional bias.

### Visual-probe task response times.

Histograms and box-and-whisker plots showed that response times less than 200 ms or greater than 800 ms were outliers and therefore these data points were excluded (2.44% of trials). Response times more than three standard deviations outside each participant’s mean response time were excluded (1.06% of trials). This cleaning process was based on previous research with the visual-probe task [31; 45; 48].

An attentional bias index was calculated from response times to the location of the dot according to the following formula:

$$Response time attentional bias index = ((PrDl-PlDl) + (PlDr-PrDr))/2$$

Where *P* = pain word (or pain side), *D* = dot, *r* = right, *l* = left [51]. According to this formula, response times on congruent trials (pain word/stimulus and dot on the same side) were subtracted from response times on incongruent trials (pain word/stimulus and dot on opposite sides). Therefore, a positive index indicates attentional bias to pain words/location whereas a negative index indicates attentional bias away from pain words/location.

### Incidental learning task.

Data from the incidental learning task were cleaned in the same way as the visual-probe data. Trials with incorrect or no response were excluded (learning phase: 0.86%, testing phase: 0.42%). Histograms and boxplots showed that response times less than 200ms or greater than 800ms were outliers so these were removed (learning phase: 1.13%, testing phase: 0.88%). Response times more than three standard deviations outside each participant’s mean response time were excluded (learning phase: 1.18%, testing phase: 1.11%).

The congruency effect was calculated with data from the learning phase. A positive congruency effect indicates a faster response when the dot appears on the predicted side of the screen, indicating that the contingency has been learnt.

$$Congruency effect = RTi - RTc$$

Where *RTi* = mean response time on incongruent trials and *RTc* = mean response time on congruent trials. The interpretation bias index was calculated from response times in the test phase, as in previous research [27; 28]. A positive interpretation bias index indicates pain-related interpretation bias.

$$Interpretation bias index = RTn - RTp$$

 Where *RTn* = mean response time to targets in the location associated with neutral words and *RTp* = mean response time to targets in the location associated with pain words.

### Sentence generation task.

Two researchers (DES and PB) independently categorised sentences from the sentence generation task into pain-related or benign and then calculated the proportion of pain-related sentences out of total meaningful sentences generated, as in previous research [50]. The proportion of self-referent pain-related sentences was also calculated. The working definition for pain-related interpretations was: 'describes a painful experience or a situation usually associated with pain'; the working definition for benign interpretations was: 'describes an experience or situation unrelated to pain' [45; 52]. The researchers had 98.33% agreement (Cohen’s kappa = 0.91). Discrepancies were resolved by discussion to reach 100% agreement. Seven sentences (0.65%) were either missing or not meaningful.

### Free recall task.

The proportion of pain words out of all recalled words was calculated.

### Questionnaires.

Questionnaires were scored according to their scoring instructions [35; 71; 78]. No data was missing from the Hospital Anxiety and Depression Scale, one participant was missing values for two items on the Fear of Pain Questionnaire and therefore their score was excluded from further analyses.

## Statistical Analysis

For all analyses the significance level was *p* = .05 and two-tailed. No correction for multiple comparisons was applied for several reasons. Firstly, it is noted that the hypothesis-testing analyses did not meet the criteria for applying the Bonferroni correction. These criteria include a universal null hypothesis of interest, the same test in multiple subsamples, and searching for significant associations without *a priori* hypotheses [38]. Furthermore, our research followed a novel paradigm and therefore adjustment for multiple comparisons may have resulted in accepting the null hypothesis too readily and missing potentially important research leads [18; 42]. An additional consideration was that previous eye tracking attentional bias research has not adjusted for multiple comparisons [e.g. 20; 22; 34]. Therefore, using a similar data analysis strategy facilitates comparison with previous research. The results section is clearly split into exploratory and hypothesis-testing analyses to indicate which results are theory-driven and which are data-driven.

Descriptive statistics were calculated for the demographic characteristics and individual differences variables of the participants.

To assess interpretation bias, response times to the testing phase of the incidental learning task were compared between the pain-associated and neutral-associated locations using a paired-samples t-test. To assess attentional bias, response times and eye movement measures from the visual-probe task were compared between pain-related words and neutral words, as well as between the pain location and the neutral location, considering the left and right sides separately and aggregated in a series of paired-samples t-tests. Correlations between biases and demographic variables were explored using the Rpackage ‘corrplot’ for the statistics and graphics [73].

The extent to which attentional bias to the pain location statistically predicted attentional bias to pain words was investigated with linear regression models for each of the eye movement and response time indices. The moderating effects of interpretation bias on this association were then investigated using multiple regression models and simple effects analysis was conducted with theRpackage ‘interactions’ [32]. Additional exploratory analysis investigated the moderating role of fear of pain in the association between attentional bias to the pain location and attentional bias to pain words as well as, at the suggestion of one anonymous reviewer, the moderating role of memory bias in this association.

To investigate the relative influences of concurrently presented pain words and pain stimuli on attentional bias, a 2 (location: pain side vs non-pain side) x 2 (word type: pain vs neutral) repeated measures ANOVA was computed for each of the eye-tracking and response time measures using theRpackage ‘rstatix’ [24]. Post-hoc paired samples t-tests were computed where the ANOVA result was significant.

# Results

For inferential statistics, all results are reported in tables but only significant results are discussed in the text. Data and analysis scripts have been deposited in the UK Data Service ReShare repository.

## Preliminary Analysis

### Sample descriptive statistics.

Sixty participants healthy individuals were recruited. The participants had a mean age of 22.29 years (SD = 5.47), 35 female and 25 male. All were undergraduate or postgraduate students with a mean of 15.88 years in education (SD = 2.52). Handedness information was provided by 52 participants, the mean score of the Edinburgh Handedness Questionnaire Short Form was 125.48 (SD = 133.62), indicating that participants gave preference to their right hand on average (0 indicates no preference between hands). The mean cold pain threshold was 8.29°C (SD = 7.30). On average, pain threshold on the left hand was significantly colder (M = 7.48, SD = 7.42) than pain threshold on the right hand (M = 9.11, SD = 7.77), *t* (59) = -2.98, *p* = .004. Descriptive statistics for questionnaire scores are shown in Table 2.

 Eye movements could be tracked for 54 participants, this subset was comprised of 32 females and 22 males, had a mean age of 22.12 years (SD = 5.50), a mean of 15.76 years in education (SD = 2.58), and a mean handedness score of 131.91 (SD = 128.93).

### Absolute measures of attention, interpretation, and memory biases.

#### Interpretation bias: Sentence generation task.

Out of all sentences generated, the mean proportion of pain-related sentences was 0.11 (SD = 0.10) and the mean proportion of pain-related self-referent sentences was 0.06 (SD = 0.07).

#### Interpretation bias: Incidental learning task.

In the learning phase, the mean reaction time to probes was significantly faster in the congruent location (M = 300.06 ms, SD = 37.19) than the incongruent location (M = 305.14 ms, SD = 38.09), *t* (59) = 3.47, *p* < .001. This indicates that participants learnt the contingency between word type and probe location.

In the testing phase, there was no significant difference between reaction times to probes in the location previously predicted by pain words (M = 300.56 ms, SD = 38.61) and probes in the location previously predicted by neutral words (M = 301.57 ms, SD = 36.85), *t* (59) = 0.30, *p* = .767. As expected this demonstrates that healthy individuals do not show a pain-related interpretation bias.

#### Attentional bias: Pain vs neutral words with no experimentally-induced pain.

Participants made on average fewer fixations on pain-related words (M = 2.65, SD = 0.66) than neutral words (M = 2.74, SD = 0.72), *t* (53) = 2.24, *p* = .029. No other eye-tracking measure showed significant differences between pain words and neutral words (see Table 3). The mean attentional bias index for pain words was not significantly different from zero (M = -4.77, SD = 28.48), *t* (53) = -1.23, *p* = .224.

#### Attentional bias: Pain side vs non-pain side with neutral words.

When the pain stimulus was on the left, time to first fixation was significantly faster to the pain side (M = 320.17, SD = 176.96) than the non-pain side (M = 514.14, SD = 424.71) , *t* (45) = 3.68, *p* < .001. However, when the pain stimulus was on the right there was no significant difference in time to first fixation between the pain side and non-pain side, *t* (47) = 1.55, *p* = .129.

When the pain stimulus was on the right hand, mean fixation duration was significantly longer on the pain side (M = 353.18, SD = 121.14) than the non-pain side (M = 313.92, 76.14), *t* (51) = 2.88, *p* = .006. Similarly, with the pain stimulus on the right hand, mean first fixation duration was significantly longer on the pain side (M = 328.17, SD = 121.31) than the non-pain side (M = 302.85, SD = 97.76), *t* (51) = 2.05, *p* = .045. With the pain stimulus on the left hand there was no significant difference between sides in mean fixation duration or mean first fixation duration. Independent of the pain location, participants showed a leftwards bias characterised by significantly more first fixations on the left than right and significantly more visits to the word on the left than right. See Table 4 for all eye-tracking indices. This pattern of results was found for right and left handed participants, see Supplementary File 3.

The mean attentional bias index for pain location was negative (M = -7.03, SD = 18.52) and significantly different from zero, *t* (52) = -2.76, *p* = .008. This indicates that participants responded faster to dots that were on the opposite side to the experimental pain stimulus.

#### Memory bias: Free recall task.

Eighteen pain-related words and 29 neutral words were available for participants to recall from the tasks. Participants recalled a mean of 4.68 pain words (SD = 1.31) and 4.92 neutral words (SD = 2.37). Relative to the total number of words of each type, on average participants recalled a greater proportion of pain words (M = 0.26, SD = 0.07) than neutral words (M = 0.17, SD = 0.08), *t* = 6.91, *p* < .001. Relative to the total number of words recalled by each participant, the mean proportion of pain words recalled was 0.51 (SD = 0.14). Participants were not exposed to each word for an equal duration. For instance, ambiguous pain words were shown in the sentence generation, incidental learning and visual probe tasks, whereas neutral words that comprised the neutral-neutral word pairs were only shown in the visual-probe task. Therefore, these measures of memory bias can be used for between-participant comparisons but cannot be taken as a measure of absolute memory bias.

### Correlations

As expected, the eye-tracking indices of attentional bias to pain words were inter-correlated, for further details see Supplementary File 4. Attentional bias to pain words and attentional bias to the pain side were mostly non-significantly correlated. However, proportion of first fixations to pain words had a significant negative correlation with speed of first fixations to the pain side, *r* = -.35, *p* = .022.

There were also correlations between cognitive biases. Notably, there was not a significant correlation between the direct and indirect measures of interpretation bias, *r* = .08, *p* = .700. The proportion of pain sentences generated in a sentence generation task had a significant positive correlation with total fixation time on pain words, *r* = .28, *p* = .024. Additionally, the incidental learning task index had a significant positive association with speed of first fixation on pain words, *r* = .43, *p* = .003. See Supplementary File 5 for the interaction between pain-related interpretations and self-referent interpretations in their associations with attentional bias. Memory bias had a significant negative correlation with time to first fixation on the pain side, *r* = -.33, *p* = .033. See Supplementary File 6 for the moderating effect of memory bias on the association between attentional bias to the pain location and attentional bias to pain words.

There were several correlations between cognitive biases and participant characteristics. The proportion of pain sentences generated in a sentence generation task had a significant negative correlation with depression, *r* = -.23, *p* = .012 but a significant positive correlation with age, *r* = .12, *p* = .030. Anxiety had a significant positive correlation with pain side response time index, *r* = .30 , *p* = .025. Depression had significant negative correlations with speed of first fixation on the pain side, *r* = -.21, *p* = .029, and number of visits to the pain side, *r* = -.28, *p* = .048. See Supplementary File 7 for the interaction between fear of pain and attentional bias to painful stimuli in their associations with attentional bias to pain words.

There were also correlations within participant characteristics. Anxiety had a significant positive correlation with depression, *r* = .35, *p* < .001. Depression had a significant negative correlation with age, *r* = -.18, *p* = .014.

See Figure 2 for a heatmap of the strength and direction of all correlations.

### Exploratory word-level analysis: The association between pain-related interpretation of a word with subsequent measures of attentional bias and memory bias.

 Words that were interpreted as pain-related in the sentence generation task were more likely to be recalled (55.17%) than not recalled (44.83%). In contrast, words that were interpreted as neutral were less likely to be recalled (45.24%) than not recalled (54.76%). This difference approached significance, *χ2* (1) = 3.60, *p* = .058. There were no significant findings with measures of attentional bias, see Table 5 for full results.

## Hypothesis Testing Analyses

### Hypothesis 1: Attentional bias to ambiguous pain words will be positively associated with attentional bias to the location of pain.

Linear regression models with attentional bias to the location of pain as the predictor variable and attentional bias to pain words as the outcome variable were tested for all eye movement and response time indices. None of the models explained a significant amount of variance and scatterplots indicated no association between the variables. See Table 6.

### Hypothesis 2: This association will be stronger for participants with a large pain-related interpretation bias.

Multiple regression models were constructed with interpretation bias, attentional bias to the pain side, and the interaction between these variables predicting attentional bias to pain words. When an indirect measure of interpretation bias (incidental learning task index) was included as the moderator, this interaction was significant for several indices of attentional bias including time to first fixation, number of fixations, total fixation time, number of visits, and response time. When a direct measure of interpretation bias (proportion pain-related sentences generated) was included as the moderator, there were significant interactions for mean first fixation duration and the response time index. Full results are shown in Tables 7 and 8. Simple effects analyses were conducted to examine these interactions and are reported below.

#### Attentional orienting: Time to first fixation.

At one standard deviation below the mean (-1SD) of incidental learning task index, time to first fixation on the pain side did not significantly predict time to first fixation on pain words, *b* = 0.16, standard error (SE) = 0.14, *t* = 1.14, *p* = .260. However, at one standard deviation above the mean (+1SD) of the incidental learning task index, there was a significant negative association between attentional bias to the pain side and attentional bias to pain words, *b* = -0.46, SE = 0.16, *t* = -2.93, *p* = .006.

#### Maintained attention: Number of fixations.

At -1SD incidental learning task index, more fixations on the pain side significantly predicted more fixations on pain words, *b* = 0.46, SE = 0.21, *t* = 2.19, *p* = .034. However at +1SD incidental learning task index, more fixations on the pain side significantly predicted fewer fixations on pain words, *b* = -0.61, SE = 0.21, *t* = -2.93, *p* = .005.

#### Maintained attention: Total fixation time.

At -1SD incidental learning task index, greater total fixation time on the pain side (non-significantly) predicted greater total fixation time on pain words, *b* = 0.44, SE = 0.22, *t* = 1.98, *p* = .054. At +1SD incidental learning task index, greater total fixation time on the pain side predicted shorter total fixation time on pain words, *b* = -0.47, SE = 0.18, *t* = -2.57, *p* = .013. See Figure 3 for a graphical representation of this interaction.

#### Maintained attention: Number of visits.

 At -1SD incidental learning task index there was a positive but non-significant association between number of visits to the pain side and to pain words, *b* = 0.39, SE = 0.30, *t* = 1.32, *p* = .194. At +1SD there was a negative association between number of visits to the pain side and number of visits to pain words, *b* = -1.15, SE = 0.29, *t* = -4.01, *p* < .001.

#### Maintained attention: Mean first fixation duration.

At -1SD of proportion pain sentences generated, there was a non-significant positive association between first fixation duration to the pain side and to pain words, *b* = 0.24, SE = 0.15, *t* = 1.59, *p* = .119. At +1SD of proportion pain sentences generated, there was a non-significant negative association between first fixation duration to the pain side and to pain words, *b* = -0.55, SE = 0.29, *t* = 1.88, *p* = .067.

#### Attentional bias response time index

 At -1SD incidental learning task index there was a significant negative association between the attentional bias response time index (AB index) to the pain side and AB index to pain words, *b* = -0.62, SE = 0.30, *t* = -2.09, *p* = .042. At +1SD of the incidental learning task index there was no significant association between AB pain side index and AB pain word index, *b* = 0.08, SE = 0.26, *t* = 0.31, *p* = .759.

 In contrast, at -1SD proportion pain sentences there was a positive association between pain side AB index and pain word AB index that was approaching significance, *b* = 0.52, SE = 0.28, *t* = 1.88, *p* = .066. At +1SD proportion pain sentences there was a significant negative association between pain side AB index and pain word AB index, *b* = -0.91, SE = 0.32, *t* = -2.89, *p* = .006.

Overall, all but one of these interactions showed that the association between attentional bias to the pain location and attentional bias to pain words was positive for participants with lower levels of pain-related interpretation bias, but negative for participants with higher levels of pain-related interpretation bias.

### Hypothesis 3: Word type (pain vs neutral) and pain location (pain side vs non-pain side) will interact in their effect on attentional bias indices; a stronger attentional bias is predicted when pain words are on the same side of the body as experimentally-induced pain.

2 (location: pain side vs non-pain side) x 2 (word type: pain vs neutral) repeated measures ANOVAs were conducted on each of the eye-tracking and response time indices from Condition 3 of the visual-probe task. See Table 9 for all results.

There was a significant main effect of word for mean fixation duration (*F* (1, 51) = 12.23, *p* < .001), mean first fixation duration (*F* (1, 51) = 7.02, *p* = .011) and total fixation time (*F* (1, 51) = 9.27, *p* = .004). This indicates that, controlling for pain location, participants spent longer fixating on pain words than neutral words while experiencing concurrent cold pain.

For the mean first fixation duration, there was a significant interaction between word type and pain location. Post-hoc paired t-tests showed that, mean first fixation durations on pain words were non-significantly longer on the pain side (M = 321.59, SD = 91.29) than the neutral side (M = 311.76, SD = 77.78), *t* (51) = -1.94, *p* = .058. In contrast, mean first fixation durations on neutral words were non-significantly longer on the non-pain side (M = 311.22, SD = 81.85) than the pain side (M = 300.58, SD = 75.42), *t* (51) = 1.07, *p* = .290. See Figure 4.

# Discussion

This study aimed to investigate the association between attentional bias to painful sensations and attentional bias to pain-related language. Healthy individuals showed significant attentional bias to the pain location but not to pain words, consistent with the results of previous meta-analyses [10; 64]. Hypothesis 1 was not supported because there was not a significant correlation between attentional bias to pain words and attentional bias to the pain location. Contrary to the prediction of Hypothesis 2, this association was significantly moderated by interpretation bias in such a way that the association was negative for higher levels of pain-related interpretation bias and positive for lower levels. This finding was consistent across eye tracking indices of attentional orienting and maintained attention, specifically time to first fixation, number of fixations, mean first fixation duration, total fixation time, and number of visits. Hypothesis 3 was partially supported as the interaction between word type and pain location was significant only for mean first fixation duration: first fixation durations on pain words were longer when the locations of the pain word and cold pain stimuli were congruent, as compared to incongruent.

In the current study, the direction and strength of eye movement indices differed from response time indices in most cases. Differences in attentional bias results are not uncommon between eye tracking and reaction time measures. Notably, reaction time tasks tend to show greater bias toward pain-related stimuli during maintained attention [51] whereas some eye-tracking research reveals avoidance of pain-related stimuli during later stages of attention [e.g. 34; 40] (but not all [e.g. 14; 17]). Eye movements provide a more direct and continuous measure of overt attention than reaction times [58] but are limited in that they provide no indication of covert attention [40].

The findings of this study have several implications for theory. The Threat Interpretation Model of Pain (TIMP) [63] predicts a vigilance-avoidance pattern of attentional bias to stimuli interpreted as pain-related and threatening, and posits that this pattern of attentional bias facilitates chronic pain development. The current study found avoidance of pain words among participants with high levels of attentional bias to the pain location and pain-related interpretation bias. Attentional bias to the location of painful sensations could indicate heightened awareness of pain, possibly due to greater perceived threat [39; 65]. Therefore, one interpretation of these results is that participants who feel threatened by pain and interpret ambiguous words as pain-related show attentional bias away from those words. This supports the prediction of the TIMP that words interpreted as pain-related and threatening are avoided in later stages of attention.

Schema models posit that cognitive structures called schemas guide how information from the environment is processed [3; 4]. Theoretically, similar schemas are linked together and activation of one schema (e.g. painful sensations) partially activates associated schemas (e.g. pain-related language) [5]. The links between schemas are strengthened by multiple associations. Participants in the current study did not experience chronic pain and are therefore unlikely to make frequent schema associations between painful sensations and pain-related language. This weak association between schemas may underlie the lack of statistically significant association between attentional biases to pain and pain words.

Interactions between attention, interpretation and memory biases are theoretically predicted by models including the Combined Cognitive Bias Hypothesis [13] and the Integrated Functional-Contextual Framework of Cognitive Bases in Pain [67]. The interconnectedness of cognitive biases to pain words was partially supported by the current study, which found associations between attentional and interpretation biases. It is likely that attentional and memory biases also influence one another. Memory has limited capacity and therefore attention determines what will be encoded, while memory from past experience guides what should be attended. The interaction between attention and memory bias was investigated in exploratory analysis (Supplementary File 6) but could be investigated in hypothesis-driven analysis in future research.

The current findings also have clinical implications for attentional bias modification interventions. This study reports longer first fixations on pain words when they are displayed ipsilateral to the pain location, as compared to contralateral. In this case, attentional bias to the pain location may compound attentional bias to pain words, producing a larger bias. Accordingly, training attention away from pain-related information may be more difficult when it is presented nearer to the location of pain. Therefore, the location of pain should be considered in intervention design.

Existing attentional bias modification interventions for individuals with chronic pain have attempted to train attention away from pain-related information [11; 21; 46; 56; 57; 61; 68]. However, the current study found that a combination of attentional bias to painful sensations and high pain-related interpretation bias was associated with attentional bias away from pain words, which may indicate avoidance of pain-related information. If this pattern were present in a participant of a cognitive bias modification intervention, rather than further directing attention away from pain words, the biases may be better addressed by attempting to reduce pain-related interpretation bias [e.g. 23] or an acceptance-based approach of directing attention toward pain-related language without the associated threat of pain [66; 67].

A further consideration is that the results from this study may be more applicable to interventions for acute or procedural pain than chronic pain due to differing patterns of attentional bias. More specifically, attentional bias is shown toward the location of acute pain but away from the location of chronic pain [8; 16]. Therefore, it might be predicted that individuals with chronic pain would show less attentional bias to pain words near the location of pain, a prediction that could be tested in future research.

 The methods of the current study were novel in several ways. This study was the first to assess attentional bias to both pain words and the pain location with a visual probe task, reducing the effect of task differences on their measurement and facilitating concurrent measurement. Additionally, this study was the first to use the incidental learning task with pain-related words. A significant congruency effect was achieved indicating that the testing phase assessed pain-related interpretation bias successfully. Identical word stimuli were used to assess attention and interpretation biases, minimising the effects of stimuli differences on the association between biases. Additionally, this study was conducted in a controlled laboratory environment with standardised temperature and lighting brightness to maximise consistency and accuracy of measurement.

Nonetheless, this study had limitations. Participants were able to stop the pain stimulus at any time, resulting in higher perceived control over pain than is typical for procedural or acute pain. Furthermore, participants were aware that the research was related to pain and therefore been subject to unintentional priming or demand characteristics. Additionally, this study used a young, student sample, whereas the beneficiaries of attentional bias modification interventions are likely to be older, as the likelihood of chronic pain increases with age [7]. Previous research has found that, although overall response times increase with age, there is no evidence of a significant association between age and attentional bias [10; 51; 64]. Therefore, similar results are likely to have been obtained with an older sample, although this should be tested in future research. To consider a further limitation, the study used a threshold level cold pain stimulus because pilot testing indicated that participants would not tolerate a more intense stimulus for the duration of the visual-probe task. However, a suprathreshold stimulus may have strengthened the activation of bottom-up attentional processes and therefore elicited greater attentional bias.

There were also procedural limitations to the current study. Notably, due to an oversight, handedness information was collected online after study completion and therefore was not obtained from several participants. In addition, the horizontal display of stimuli in the visual-probe task resulted in an inevitable leftward bias of attention, similar to previous studies [e.g. 44]. However, comparable biases also influence attention to vertical stimuli displays [51].

 The results of this study have prompted several suggestions for future research. Firstly, future studies could investigate the association between attentional bias to pain and attentional bias to pain-related language in a sample with chronic pain. Secondly, whereas this study investigated the association between attentional biases to pain-related language and painful sensations, future research could investigate this association for interpretation biases. This line of research could improve understanding of how interpretation bias modification interventions using pain-related language could affect perception of ambiguous bodily sensations [e.g. 23]. Finally, due to the connections between interpretation and attentional biases in the current study, future research could investigate whether modifying interpretation bias for pain-related language alters attentional bias to pain-related words.

## Conclusion

An experimental study of healthy individuals found that attentional bias to pain words and attentional bias to the pain location were not significantly correlated. However, a combination of attentional bias to painful sensations and high pain-related interpretation bias was associated with attentional bias away from pain words, which may indicate avoidance of pain-related information. Additionally, first fixation durations were greater when the locations of pain and pain-related information were congruent, as compared to incongruent, indicating that this congruency may strengthen attentional bias.

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*Figure 1.* A schematic diagram of the experimental setup for the investigation into the association between attentional bias to experimentally-induced pain and to pain-related words using a visual probe task with eye-tracking. Visual-probe task: 1. A central fixation point was presented until the participant fixated on it. 2. Two words were presented for 2000 ms, either one ambiguous pain word and one neutral word or two neutral words, depending on the condition. 3. The dot had an equal chance of replacing the pain word and neutral word as well as an equal chance of appearing on the left and right. Incidental learning task learning phase: 1. A central fixation point was presented for 500 ms. 2. An unambiguous pain word or a neutral word was shown in the centre of the screen for 675 ms. 3. Pain words were followed by a dot on one side of the screen (e.g. the left) on 80% of trials and by a dot on the other side on 20% of trials. Neutral words were followed by a dot on the other side of the screen (e.g. the right) on 80% of trials and by a dot on the other side on 20% of trials. Training phase: 1. A central fixation point was presented for 500 ms. 2. An ambiguous pain word was shown in the centre of the screen for 675 ms. 3. The dot had an equal chance of appearing on the left or right. Note that the eye tracker and thermode were only present during the visual-probe task.

*Figure 2.* Pearson’s r correlations between cognitive biases to pain words, attentional bias to the side of pain, and participant characteristics. Blue indicates a positive correlation whereas red indicates a negative correlation. Greater colour saturation and larger circles indicate a stronger correlation. A grey asterisk indicates that the correlation was significant at *p* < .05. No correction for multiple correlations was applied and therefore statistical significance may not necessarily indicate a meaningfully significant correlation. ‘Word’ at the end of a variable name indicates that the eye tracking index refers to attentional bias to pain words. ‘Side’ at the end of a variable name indicates that the eye tracking index refers to attentional bias to the side of the painful stimulus.

*Figure 3.* The association between total fixation time bias for words ipsilateral to the pain location and total fixation time bias for pain words, moderated by the interpretation bias index from the incidental learning task. Note +1SD = one standard deviation above the mean, -1SD = one standard deviation below the mean.

*Figure 4.* Violin plots showing first fixation duration bias for pain words and for the location of experimentally-induced pain, when both are presented concurrently in a visual-probe task. The width of the violin plots represents the density of the data at each value, with wider sections indicating higher density. Unfilled dots indicate the mean first fixation duration for each individual participant, the black dot indicates the mean across participants, and the error bars represent ±2 standard deviations.