

Threat, cognitive biases and pain outcomes

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RUNNING HEAD: THREAT, COGNITIVE BIASES AND PAIN OUTCOMES

The effect of threat on cognitive biases and pain outcomes: An eye-tracking study

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Abstract

Background: Theoretical accounts of attentional and interpretation biases in pain suggest that these biases are interrelated and are both influenced by perceived threat. A laboratory-based study was conducted to test whether these biases are influenced by threat, their interrelationship, and whether attention or interpretation biases predict pain outcomes.

Methods: Healthy participants (n=87) received either threatening or reassuring pain information, and then completed questionnaires, interpretation and attentional bias tasks (with eye-tracking), and a pain task (the cold pressor).

Results: There was an interaction effect for threat group and stimuli type on mean dwell time for face stimuli, such that there was an attentional bias towards happy faces in the low but not high threat group. Further, high threat was also associated with shorter pain tolerance, increased pain, and distress. In correlational analyses, avoidance of affective pain words was associated with increased pain. However, no relationship was found between attention and interpretation biases, and interpretation biases were not influenced by threat or associated with pain.

Conclusions: These findings provide partial support for the threat interpretation model and the importance of threat and affective pain biases, yet no relationship between cognitive processing biases was found, which may only occur in clinical pain samples.

Key Words: Pain; attentional bias; interpretation bias; eye-tracking; cognitive; threat

Introduction

There is evidence that pain tends to capture attention and is prioritised (Eccleston & Crombez, 1999), leading to a bias towards cognitive processing of signals of pain. Cognitive processing biases include preferential attending to pain-related information, and an increased threat interpretation bias of pain information. Pincus and Morley (2001) conducted the first systematic review of cognitive biases in pain, and found that memory, attention, and interpretation biases can influence the behavioural and affective experience of pain beyond its physical properties. In the ensuing years, the study of attentional biases in pain has proliferated.

Two recent meta-analyses have provided evidence that individuals with chronic pain demonstrate an attentional bias towards pain-related stimuli such as sensory pain words (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013; Schoth, Nunes, & Lioffi, 2012). In contrast, relatively little research has examined interpretation bias in pain. Among existing literature, chronic pain patients have shown larger interpretation biases relative to healthy individuals (Edwards & Pearce, 1994; Khatibi, Sharpe, Jafari, Gholami, & Dehghani, 2015; McKellar, Clark, & Shriner, 2003; Pincus, Pearce, McClelland, Farley, & Vogel, 1994; Pincus, Pearce, & Perrott, 1996). Further, interpretation biases have been found in high compared to low catastrophizers (Khatibi, Schrooten, Vancleef, & Vlaeyen, 2014), and have moderated experimental pain outcomes following manipulation (Jones & Sharpe, 2014).

Theoretical accounts suggest that it is the interpretation of pain as harmful, and resulting pain-fearfulness, that drives patients to be hypervigilant to pain (Vlaeyen & Linton, 2000). Hence, theories predict that interpretation and attentional biases should be strongly linked, at least in some paradigms (Todd et al., 2015).

The threat interpretation model is a recent account of the role of attentional biases in pain (Todd et al., 2015). The basic assumptions are that attentional biases depend on the

interpretation of stimuli as both pain-related and threatening, and that attentional biases change over the time course of stimuli presentation. Because the words that are usually used as pain stimuli in attentional bias tasks such as the dot-probe are actually ambiguous (e.g. sharp, boring), there is a potential overlap with interpretation bias, in that classifying the ambiguous stimuli as pain-related requires interpretation of these stimuli as being pain-related. As such, attentional bias on this type of task should be associated with interpretational bias.

The present research was designed to test the threat interpretation model of pain. Specifically, threat was manipulated in order to examine the impact on interpretation and attention biases and pain outcomes. Based on this model, it was hypothesised that those in the high threat group would show greater interpretation biases, and would have faster attentional bias reaction times at both early and late stages of attentional processing (indicating initial vigilance and speeded avoidance respectively) than those in the low threat group. In addition, those in the high threat group were expected to show worse pain outcomes (greater hesitance, quicker threshold and shorter tolerance for pain, and higher pain ratings) than those in the low threat group. Finally, it was hypothesized that larger attentional biases would be associated with larger interpretation biases.

Method

Participants and Design

Participants were 87 first year university students, recruited over a single semester at the University of Sydney. Ethical approval was obtained from the University of Sydney's human research ethics committee. Inclusion criteria were: being over 18 years of age, proficient in English, having no instances of prolonged pain in the 3 months prior to testing, and no current acute pain (current pain ratings of $<4/10$). Participation was voluntary and in

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exchange for course credit. The study was conducted at a single time point and used a two group experimental design.

Materials

Threat Manipulation

The threat manipulation consisted of two written descriptions of the cold pressor task (high threat, low threat), as previously described by Boston and Sharpe (2005). The high threat information described the cold pressor as a vasodilation task and used technical, biomedical language. It was outlined that the task was designed to stimulate the sympathetic nervous system, the process of which was likened to frostbite. In contrast, in the low threat condition, the task was described as a cold pressor task, and medical language was not used. The process was described as being similar to reaching into a bucket of ice for a cold drink. In addition, throughout the information statement and cold pressor task instructions, the cold pressor was similarly described as either a vasodilation task or a cold pressor task, for the high and low threat groups respectively.

Incidental Learning Task (Interpretation Bias Measure)

The interpretation bias task was adapted from the incidental learning task developed by Khatibi et al. (2015), using identical face stimuli and cue presentation times. The task was programmed using Affect 4 software package (Spruyt, Clarysse, Vansteenwegen, Baeyens, & Hermans, 2010). Stimuli were 16 happy and 16 painful facial expressions that were matched on emotion intensity. A further 16 facial expressions were included that were morphed from an additional 16 pairs of happy and painful facial expressions, which have previously been identified as being the most ambiguous morph of each photograph pair (Khatibi et al., 2015). Split-half reliability analysis was conducted for the ambiguous trials, and the items were considered sufficiently reliable (Spearman-Brown coefficient= .779).

The task consisted of a learning phase and a testing phase. A black fixation cross was first presented for 500ms. During the learning phase, a facial expression (happy or pain) was then presented for 675ms, in the centre of the screen. The facial expression was then followed by a target letter “H” presented for 1500ms on the left or right of the screen; the location of which was consistently determined by the facial expression (e.g. happy faces-target left; pain faces-target right). The side of the pain target was counterbalanced across participants. The testing phase followed a similar procedure to the learning phase, except that morphed faces were presented and followed by a target letter “H” appearing equally on the left or the right of the screen. An interpretation bias was considered to be present if ambiguous faces were responded to as if pain-related; i.e. if responses were faster when the target appeared on the side previously associated with painful expressions and slower when the target appeared on the side previously associated with happy expressions.

Participants were given written instructions on the computer screen, as well as the following verbal instructions: *“You will now complete a(nother) computer task. Please keep your head in the head rest and remain as still as possible. For this task, you will be presented with a picture of a face, which will be followed by a letter ‘H’ that will appear on the left or the right hand side of the screen. You will be using the mouse (point to mouse) to respond to the faces, using the left mouse button to respond when the ‘H’ appears on the left and the right mouse button when the ‘H’ appears on the right. Pay attention to the type of facial expressions because the type of facial expression will determine which side the ‘H’ will appear for most trials, and I will be asking you about this relationship at the end of the study. Do you have any questions?”* In this way, they were given explicit instructions about the target-cue contingency and that the relationship was determined by facial expression.

To assess explicit awareness of the training direction, at the end of the study participants were asked 1) whether they thought that it was facial expression, gender, or age

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that determined the association, 2) what kinds of facial expressions they were aware of, and 3) whether the pain (happy) faces were most often followed by a target on the left, right, or equally often in either location.

Dot Probe Task (Attentional Bias Measure)

Attentional bias was assessed using a computer-based dot-probe task (MacLeod, Mathews, & Tata, 1986). The dot-probe was programmed using E-Prime 2.0 to interface with the Tobii TX300 integrated eye tracker. The stimuli for the dot probe were presented on a 23-inch TX300 screen unit, with a 1920 x 1080 pixel resolution and a 60 Hz refresh rate.

To begin each trial, a fixation point ‘.’ was presented in the middle of the screen. The trial continued once eye movement fixation was detected. A word or face pair then replaced the fixation point, with one stimulus appearing above where the fixation point had been and the other below. Each stimulus pair was presented for 1500 ms and was followed by a probe of either the letter ‘p’ or ‘q’, appearing in the upper or lower position. Participants were required to respond to the letter using two buttons (i.e. ‘p’ or ‘q’) on a Cedrus RB-530 response pad. Each trial ended upon response or after 1500 ms had elapsed. All data was recorded via the E-Prime 2.0 software.

Participants were given written instructions on the computer screen, as well as the following verbal instructions: *“Now we will start the (next) computer task. The computer will automatically monitor your eye movements. Please keep your head in the chin rest. On each trial a dot will appear in the centre of the screen, which you need to fixate on in order for the task to continue. After you fixate on it, the dot will disappear and two words or pictures of faces will appear, one above where the dot was, and one below. When you see words, it is important that you read both words silently, and when you see the faces it is important that you look at both faces. After the words or faces disappear, either a ‘p’ or a ‘q’ will appear on the screen. Simply press the ‘p’ key with your right hand as fast as you can when you see ‘p’*

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on the screen, and press the 'q' key as fast as you can with your right hand when you see 'q' on the screen. It will be easier if you place your fingers near the keys before the test starts. You will be given on-screen instructions at different points throughout the task – please read all instructions carefully. You will also be given five practice trials before you start. Do you have any questions?"

The experimental word stimuli for the dot-probe task were developed by Dehghani, Sharpe, and Nicholas (2003) and consisted of 10 sensory pain and 10 affective pain words, each matched to a neutral word of equal length and frequency. As such, a total of 20 stimulus pairs were used, and were the same word stimuli used by Sharpe, Johnson, and Dear (2015) in a similar sample.

The experimental face stimuli were developed by Sharpe et al. (2015), who previously used this stimuli on a similar population of healthy adults. The face stimuli consisted of black and white photographs of 10 faces (equal genders), each posing three expressions (pain, happy and neutral). Each pain and each happy expression was matched with the neutral expression from that person, creating 10 pain/neutral pairs and 10 happy/neutral pairs. Each image was 52 mm x 38 mm, with only basic features of the face were visible.

The 20 word pairs and 20 face pairs were used in four different presentation combinations (target up/probe down; target up/probe up; target down/probe down; target down/probe up), resulting in a total of 160 trials. Congruent trials occurred when both the target stimuli and probe appeared in the same location, and incongruent trials occurred when the target stimuli and probe appeared in opposite locations, i.e. one on the upper screen and one on the lower screen. The trials were presented in a random order for each participant. Participants were able to take a break for up to 60 seconds after each set of 40 stimuli. Five practice trials were presented prior to the start of the task.

Eye-tracking Software

Eye-tracking software was used to track eye movements throughout the dot probe task, in a similar manner to Yang, Jackson, Gao, and Chen (2012). Saccades that remained stable within a one degree visual angle for at least 100ms were classified as fixations on that position. Duration and frequency of these saccades was recorded. Fixations on the cue were counted if they occurred at least 100ms after stimulus onset, and if fixation was not on the location of the cue prior to onset. As measures of early attention, percentage of instances in which first fixation was on the pain cue, length of time to first pain cue fixation, and mean dwell time of first fixation on the pain cue were collected. As measures of sustained attention, length of first pain cue fixation, and mean dwell time on the pain cue were collected.

Questionnaires

The Fear of Pain Questionnaire (FPQ; McNeil & Rainwater, 1998) was used to measure pain-related fear, and has previously been found to have good internal consistency and test-retest reliability (McNeil & Rainwater, 1998). In the current study, the FPQ was found to be reliable, $\alpha = .92$. The Pain Catastrophizing Scale (PCS; Sullivan, Bishop, & Pivik, 1995) was used to measure pain catastrophizing, or exaggerated negative interpretations of pain and the outcomes of pain. The PCS has been used extensively in previous research with good validity within university student and community samples (Osman et al., 2000; Sullivan et al., 1995), and had good internal consistency in the current study ($\alpha = .90$). The Depression Anxiety Stress Scale (DASS; Lovibond & Lovibond, 1995) was used as a measure of anxiety and depression within the current study, as this scale has been found to have good internal consistency and validity, and reliably distinguish these symptoms both within clinical and community samples (Antony, Bieling, Cox, Enns, & Swinson, 1998). The depression ($\alpha = .95$), anxiety ($\alpha = .82$), and stress ($\alpha = .91$) subscales were found to have acceptable internal consistency in the current study.

Threat Manipulation Check

In order to assess the effects of the threat manipulation, participants completed four brief questions immediately prior to the cold pressor task. Participants were asked to indicate how worried they were about the cold pressor task, how likely it is to be painful, how likely it is that they could cope with the task, and how likely it is that the task would cause harm. Questions were rated on an 11 point Likert scale, from *not at all* to *extremely*. The manipulation was intended to make participants more worried about the task and rate the task as more harmful, and themselves as less able to cope. However, participants were led to expect the same level of pain and therefore this item was included to ensure that there were no differences in expected pain.

The Cold Pressor Task

The cold pressor has been previously used as a pain task in attentional bias research (Boston & Sharpe, 2005; McGowan, Sharpe, Refshauge, & Nicholas, 2009). Participants first placed their right arm in a tank of water set at 37°C for 30 seconds, to regulate arm temperature. They then placed the same arm in a second tank set between 5 +/-0.5°C for as long as they could, which was within the optimal temperature range to observe the pain caused by vasoconstriction followed by vasodilatation of the blood vessels in the arm (Ahles, 1983). The temperature of the tanks was maintained throughout the experiment by a thermostat that could heat or cool the water as necessary. The arm was withdrawn at tolerance (i.e. when participants could no longer keep their arm in the water) or at a maximum of 4 minutes. Five measures of pain were collected: hesitance (i.e. the length of time until the arm was placed in the cold pressor); pain threshold (i.e. the length of time it takes to register pain); pain tolerance (i.e. the length of time that participants keep their arm in the tank for); pain rating (i.e. the intensity of pain from 0- no pain to 10- extreme pain) at threshold, after 30 seconds of immersion, and at tolerance; and distress at threshold (i.e. the level of distress experienced, from 0- no distress to 10- extreme distress). Participants who

kept their arm in the tank for the full 4 minutes were recorded as having a tolerance time of 240 seconds. Pain levels at tolerance were recorded at the end of that four minute period.

Procedure

The study took place in a research lab in single sessions of 40-60 minutes. Upon arrival, participants were randomly allocated to either a high threat or low threat group via a computer-based random number generator. After reading a detailed information statement outlining the study and their right to withdraw at any time without penalty, individuals were given the option to sign the consent form and participate in the study. Participants were then given the threat manipulation information about the cold pressor task to be completed. Following the threat manipulation, participants completed the questionnaires on a second computer with no eye-tracking function. Participants were then instructed to sit 60cm from the TX300 computer screen, with their head in a head rest to ensure accurate perception and recording of eye movements. From this position, participants completed the interpretation bias task and the dot probe task, with the ordering counterbalanced. Prior to the dot probe task, the eye tracker was calibrated. The dot probe task began with the five practice trials, followed by the 160 experimental trials.

Once the processing bias tasks were complete, participants were asked the four threat manipulation check questions, were reminded of their right to withdraw from the study at any time, and then completed the cold pressor task. Instructions for the cold pressor task varied with threat group. The task was again described as a painful vasodilation task designed to stimulate the sympathetic nervous system for the high threat group. In the low threat condition, the task was described as a cold pressor task, and participants were reassured that although the task would be painful, it would not be harmful.

Finally, participants were asked a series of questions to assess their explicit awareness of the training contingency in the interpretation bias tasks, which was followed by a verbal and written debrief.

Power and Data Analysis

We powered the study in order to be able to determine moderate correlations between attentional and interpretation biases, and a medium effect of the threat manipulation. An a-priori power analysis based on the ANOVA threat main effect indicated that in order to detect medium effects ($f=.3$; based on Boston & Sharpe, 2006) at 80% power and $p<.05$, 90 participants would be needed. An a-priori power analysis based on the correlations indicated that in order to detect medium effects ($r=.3$) at 80% power and $p<.05$, 84 participants would be needed.

For interpretation bias task, responses $<150\text{ms}$ or $>750\text{ms}$ or that were incorrect were deleted, and average reaction time for remaining trials was used. The interpretation bias data was excluded when participants had 50% or more errors on the ambiguous trials. These participants were retained in analyses that did not involve interpretation bias. For the dot probe task, responses $<200\text{ms}$ or $>1500\text{ms}$ or that were incorrect were also excluded, as per previous research (Dear, Sharpe, Nicholas, & Refshauge, 2011b), and attentional biases were calculated based on the average of the remaining trials. Trial outlier exclusion criteria were set a-priori and differed between the two tasks because of the different levels of cognitive processing required. Whilst the interpretation bias task requires processing of a single visual stimulus followed by localisation of a probe, the dot probe attentional bias task requires processing of two visual stimuli followed by localisation and then discrimination of the type of probe.

An overall attentional bias reaction time index was calculated for each type of attentional bias stimuli (sensory pain words, affective pain words, pain faces, happy faces)

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using the formula: bias index = $((tupl - tlppl) + (tlpu - tupu))/2$; where t = target stimulus, p = probe, u = upper location, and l = lower location. Positive scores indicate attentional biases towards the target, whilst negative scores indicate attentional biases away from the target. In addition, eye-tracking data measures of early attentional processing (mean time to first fixation on the test stimuli, mean percentage of time spent fixating on the test stimuli, and duration of fixation on the test stimulus within the first 250 msec) and sustained attentional processing (mean time spent in first fixation on the test stimuli, and overall mean length of time of fixation on the test stimuli) were calculated.

Results

Descriptive Statistics

Of the 87 participants who signed up to the study, one was excluded because of a base pain level above 3/10, leaving a sample of 86 first year psychology students, with equal numbers in both threat groups. Other participants were excluded from individual analyses where data was missing but were still retained in the other analyses and overall sample. This was the case for the interpretation bias index ($n=4$; excluded from outlier analysis). Data was missing from the cold pressor pain at 30 seconds measure for some participants ($n=6$ participants removed their arm before 30 seconds, $n=1$ participant indicated pain threshold after 30 seconds); however these values were imputed based on their tolerance and threshold ratings, respectively.

Participants had a mean age of 19.9 years ($SD=4.7$; range 18-54 years), of whom 48.8% were female. Participants most commonly identified as of Australian/New-Zealand (55.8%) or of Asian (27.9%) ethnicity, the majority lived at home with their parents (75.6%) and had an intermediate or higher managerial, administrative or professional head of household (69.8%). On average, participants fell within the normal range for DASS depression ($M=6.3$, $SD=7.9$), anxiety ($M=5.5$, $SD=4.9$) and stress ($M=10.0$, $SD=7.4$;

Lovibond & Lovibond, 1995), and scored similarly to other healthy samples for fear of pain ($M=83.9$, $SD=16.7$; McNeil & Rainwater, 1998; Osman, Breitenstein, Barrios, Gutierrez, & Kopper, 2002) and pain catastrophizing ($M=18.2$, $SD=9.3$; Osman et al., 2000; Sullivan et al., 1995). The average level of pain of participants at baseline was 0.23 ($SD= 0.52$) out of ten. For the cold pressor task, a total of 24 participants reached the full task time of 240 seconds.

The attention and interpretation bias indices were relatively normally distributed, with histograms available from the authors upon request. Congruent and incongruent attentional bias indices (and corresponding variance) were comparable to those reported in other healthy samples (e.g. Dehghani et al., 2003), and some chronic pain samples (Sharpe, Dear, & Schrieber, 2009). Interpretation bias reaction times and standard deviations were similar to those reported in healthy samples (Khatibi et al., 2014), but substantially smaller than those reported in chronic pain samples (Khatibi et al., 2015).

There were no significant effects of the cognitive bias task order on any pain, bias, or psychological outcomes ($ps >.05$). There were also no significant differences between high and low threat groups on any of the psychological measures, gender distribution, age, or initial pain ratings ($ps >.05$). For the interpretation bias task, 94% of participants were explicitly able to identify the training direction. Using independent samples t tests, the interpretation bias index for those who were unable to identify the training direction compared with those who were was not significant ($p>.9$), and therefore the data from all participants was retained.

Independent samples t-tests were used to compare threat groups for the manipulation check questions. Significant differences were found for worry ($t_{(84)} = 2.78$, $p = .007$) and for harm ($t_{(84)} = 6.36$, $p <.001$), such that those in the high threat group were more worried about the task than those in the low threat group, and those in the high threat group also believed that the task was likely to be more harmful than those in the low threat group. No significant

differences were found for expected pain or coping ($ps >.05$), indicating that threat was effectively manipulated, but participants expected the same level of pain and felt equally able to cope with it. Results are reported in Supplementary Table 1.

In order to determine whether the cognitive processing biases that were identified were absolute or relative biases, a series of one sample t tests were used to determine whether the attentional bias and interpretation bias reaction time indices differed significantly from zero. The happy face index ($M=-1.65$, $SD= 49.03$; $t_{(85)} = -0.31$, $p =.755$), pain face index ($M=65.37$, $SD= 48.61$, $t_{(85)} = 1.03$, $p =.308$), affective pain word index ($M=1.32$, $SD= 47.49$, $t_{(85)} = 0.26$, $p =.797$), and sensory pain word index ($M=3.95$, $SD= 45.75$, $t_{(85)} = 0.80$, $p =.425$) were not statistically significant, nor was the interpretation bias index ($M=4.71$, $SD= 62.40$, $t_{(81)} = 0.68$, $p =.496$). Therefore, there was no evidence of absolute biases in this healthy sample. For cognitive bias means, by threat group and stimuli type, see Tables 1-3.

Threat Manipulation

To explore the effect of threat on attentional bias measures, a series of mixed design 2 x (2) ANOVA were conducted separately for face and for word stimuli, with threat (high threat, low threat) as a between subjects variable, and attentional bias stimuli type (happy faces, pain faces OR affective pain words, sensory pain words) as a within subjects factor, for the three eye-tracking measures of early attentional processing, the two eye-tracking measures of sustained attentional processing, and the attentional bias reaction time index. There were no significant findings for early processing eye-tracking measures ($ps >.05$).

Regarding sustained attention eye-tracking measures, overall mean duration of fixation on test stimuli appeared important. For face stimuli, a threat x stimuli interaction was observed ($F_{(1,84)}=6.04$, $p =.016$, $\eta_p^2=.067$). The simple effects were tested with paired samples t-tests conducted separately for the high and low threat groups. For the low threat group, participants spent more time looking at the happy faces than the pain faces ($t_{42}=3.00$,

$p=.005$; 95% CI [6.97, 35.56]). In contrast, for the high threat group, participants spent a similar amount of time looking at the happy faces as the pain faces ($t_{(42)}=0.76$, $p=.45$; 95% CI [-11.29, 24.96]). For word stimuli, a stimuli main effect was observed ($F_{(1,84)}=4.31$, $p=.041$; 95% CI: [0.35, 16.14]), such that participants spent longer looking at the affective pain words than they did looking at the sensory pain words, with no threat by stimuli interaction.

Regarding the attentional bias reaction time indices, for word stimuli, there was no main effect of threat group or stimuli type; however there was an interaction effect, ($F_{(1,84)}=4.10$, $p=.046$, $\eta_p^2=.047$). Under low threat, there was a bias away from affective stimuli and towards sensory stimuli, whilst under high threat, there was a bias towards affective stimuli and a bias away from sensory stimuli, although the simple slopes were not significant. There were no main or interaction effects for face stimuli ($ps>.05$). For full analyses of the effects of the threat manipulation on attentional biases, see Supplementary Table 2.

For the interpretation bias reaction time measures, a mixed design 2 x (2) ANOVA were used, with threat (high threat, low threat) as a between subjects variable, and ambiguity resolution (happy face resolution, pain face resolution) as a within subjects factor. There was a main effect of threat, ($F_{(1,82)}=5.94$, $p=.017$, $\eta_p^2=.068$), such that participants were generally slower to respond to ambiguous faces under conditions of high threat compared to low threat, regardless of whether the probe indicated a happy or pain resolution. However, the main effect of ambiguity resolution ($F_{(1,82)}=0.28$, $p=.599$) and the threat-ambiguity resolution interaction ($F_{(1,82)}=1.06$, $p=.306$) were not significant.

To explore the effects of the threat manipulation on pain outcomes, a 2-group MANOVA analysis was used, with cold pressor pain measures as outcome variables. The overall model was significant ($F_{(7,78)}=2.69$, $p=.015$, $\eta_p^2=.195$). As displayed in Table 4, The individual pain measures that were significant were tolerance rating ($F_{(1,84)}=9.79$, $p=.002$, $\eta_p^2=.104$), tolerance time ($F_{(1,84)}=5.40$, $p=.023$, $\eta_p^2=.060$) and tolerance distress ($F_{(1,84)}$

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$=7.47, p = .008, \eta_p^2 = .082$), indicating that those in the high threat group had shorter pain tolerance time, higher pain tolerance rating, and higher distress at tolerance than those in the low threat group.

As tolerance time differs for each participant, an ANOVA analysis was performed to further explore the effect of threat on tolerance pain rating, controlling for tolerance time. The results were significant; ($F_{(1,83)} = 4.65, p = .034, \eta_p^2 = .053$), suggesting that even after controlling for tolerance time, those in the high threat group had a higher pain ratings at tolerance than those in the low threat group. An additional ANOVA analysis was performed to further explore the effect of threat on threshold pain rating, controlling for threshold time, however the results were not significant, ($F_{(1,83)} = 3.05, p = .085, \eta_p^2 = .035$).

Correlations

Correlations between cognitive processing biases and pain outcomes were measured, controlling for threat group. For the full analyses, see Supplementary Tables 3 and 4. Correlations between psychological measures cognitive processing biases and pain outcomes were not a focus of this study, but are reported in Supplementary Table 5 for ease of comparison with other research.

For reaction time measures, the affective pain word bias index was associated with threshold time ($r_{(79)} = -.232, p = .037$), indicating that those who had biases away from affective pain words took longer to reach their pain threshold. The other reaction time measures were not significant ($ps > .05$)

For early processing eye-tracking variables, percentage of first fixations on the test stimuli was associated with hesitancy for affective pain stimuli ($r_{(79)} = -.261, p = .019$) happy face stimuli ($r_{(79)} = -.228, p = .041$) and pain face stimuli ($r_{(79)} = -.271, p = .014$), such that those who had a greater proportion of their first fixations on these forms of stimuli hesitated for less time prior to placing their arm in the cold pressor. Percentage of first fixations was also

associated with threshold time for affective pain stimuli ($r_{(85)}=-.235, p=.035$), such that those who had a greater proportion of first fixations on affective pain stimuli took longer to reach their pain tolerance. Time to first fixation was associated with hesitancy ($r_{(79)}=-.233, p=.036$) for happy faces, such that those who took longer to orient towards the happy faces hesitated for less time.

Regarding later stage processing variables, length of first fixation on happy faces was associated with threshold time ($r_{(79)}=-.225, p=.044$), such that those who spent longer looking at the happy faces registered the cold pressor as painful more quickly. Mean dwell time was associated with hesitancy for affective pain words ($r_{(79)}=-.279, p=.012$) and for happy faces ($r_{(79)}=-.244, p=.028$), such that those who spent longer looking at the affective pain word or happy face stimuli hesitated for less time before completing the cold pressor task. Finally, mean dwell time was associated with tolerance pain for pain faces ($r_{(79)}=.226, p=.042$), such that those who spend longer looking at pain faces rated the task as more painful at tolerance.

No other cognitive processing biases were associated with pain outcomes, and there were no associations between attention and interpretation biases ($ps>.05$). Scatter plots of the attentional bias-interpretation bias associations revealed an even distribution of spread, with no other patterns of association evident, and are available from the authors on request.

Discussion

The aim of this study was to test the threat interpretation model (Todd et al., 2015). We hypothesized that threat would increase pain-related interpretation and attention biases. However, there were no effects of threat on interpretation biases, suggesting that pain threat does not increase the propensity for healthy people to interpret ambiguous facial expressions as painful. Further, threat had no impact on *early* attentional processes assessed by eye-tracking measures. This is surprising, since the eye-tracking literature has consistently found that early stage processing (i.e. hypervigilance) differentiates between chronic pain patients

and controls (Lioffi, Schoth, Godwin, & Liversedge, 2014; Yang, Jackson, & Chen, 2013) and between those with high and low fear of pain (Vervoort, Trost, Prkachin, & Mueller, 2013; Yang et al., 2012).

There was an impact of threat on later stage attentional processing, whereby the low threat group spent less time looking at pain faces than happy faces, whilst there were no significant differences for the high threat group. Further, there was an interaction between threat and stimuli for words, indicating a relative bias away from affective pain words and towards sensory pain words under low threat, but a bias towards affective pain words and away from sensory pain words under high threat. These findings are consistent with the meta-analysis by Schoth et al. (2012) who observed larger effects for later processing than early processing. The threat interpretation model predicts a curvilinear relationship between threat and attentional biases. At low levels of threat, biases away from pain-related stimuli are expected in later stage attentional processes. As threat increases, individuals are argued to have difficulty disengaging from pain-related stimuli, until the threat becomes high where avoidance ensues. Here, the pattern is similar to what would be expected at moderate levels of threat. In this case, a bias towards happy faces can be considered consistent with a bias away from pain faces. A similar argument has been made previously (Lautenbacher et al., 2010). For the reaction time word stimuli, the pattern of avoidance at lower threat and difficulty disengaging at higher threat is consistent for the affective stimuli, although this does not account for the opposite pattern observed for the sensory stimuli. Further, other predictions from the model were not supported.

The threat manipulation was also associated with poorer pain outcomes. Under high threat, lower pain tolerance, and increased pain and distress at tolerance was observed. This is consistent with previous research that has found threat manipulation effects on tolerance, but not other pain outcomes (Sharpe et al., 2010), and supports the idea that threat is important

for later pain and cognitive processes. Furthermore, that participants withdrew their arm more quickly under high threat supports models such as the fear-avoidance model, where fear of pain and pain catastrophizing lead to greater pain-related avoidance (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012).

The relationship between cognitive biases and pain outcomes demonstrated that avoidance of affective pain words was associated with higher pain ratings. Although meta-analyses confirm that the relationship between attentional bias and pain outcomes are not robust (Crombez et al., 2013), there is evidence to suggest that it is avoidance of affective pain stimuli that leads to worse pain outcomes in pain samples (Sharpe, Haggman, Nicholas, Dear, & Refshauge, 2014). This fits with the work of Pincus and Morley (2001), who also found that the experience of pain extended beyond sensory aspects. They suggested that affective biases may be particularly relevant where there is an enmeshment of self, illness, and pain schemas. However, whilst under low threat avoidance of affective pain words was observed, under high threat there was a pattern of difficulty disengaging from affective pain words relative to sensory pain words. Despite this inconsistency, these findings point to a dissociation between attentional biases to sensory and affective pain stimuli.

An unexpected finding was that hesitancy was negatively associated with percentage of first fixations on happy and pain faces, and affective pain words. Hesitance is an indication of behavioural avoidance (Jones & Sharpe, 2014). These results may indicate an avoidance of engaging with emotionally salient stimuli in preference for neutral stimuli, or a general slowing of responsiveness associated with avoidance.

Interpretation biases were, however, not associated with pain outcomes. Only one previous study has investigated this relationship, and found that inducing interpretation biases towards pain increased hesitance, but not other aspects of pain (Jones & Sharpe, 2014). These findings suggest that interpretation bias as measured with the incidental learning task may not

be important in the experience of pain in healthy samples, although this relationship should be more fully explored in pain samples and where interpretation biases are present.

Further, although we expected to find an association between attentional and interpretation biases, they were not significantly correlated. As this relationship has not been measured before, this finding provides preliminary evidence that these biases may not be related in healthy people about to complete a painful task. However, the small effects and low variance for the interpretation bias task, compared to chronic pain samples (Khatibi et al., 2015), may explain the lack of association.

It is also possible that reaction time measures of interpretation bias do not have sufficient sensitivity to detect effects, and alternative tools could be considered. Further, a distinction has recently been made between the interpretation of stimuli as pain-related and the interpretation of pain as threatening (Todd et al., 2015). Whilst research tends to focus on the threat interpretation of pain information (e.g. Asmundson, 2012; Boston & Sharpe, 2005), the incidental learning task is based on the categorisation of faces as pain-related. Thus, in order to understand these processes, there has been a call for a greater research focus on the role of interpretation bias for pain (Crombez, Heathcote, & Fox, 2015).

There were limitations to the study that should be borne in mind. Firstly, the interpretation bias task was not significant in any of the analyses. As there is little other research into pain interpretation biases, it is difficult to determine whether this is a true null result representing interpretation biases, or whether this is a task-specific finding. In addition, the interpretation bias task does now allow for differentiation of positive and pain-related biases; alternative tasks such as the word recognition task can allow for comparison of pain interpretations and benign/neutral interpretations (Jones & Sharpe, 2014) and should be investigated.

We did not assess relevance of the cognitive bias stimuli to this particular. However, these stimuli have been used previously in similar samples (e.g. Sharpe et al., 2015) and there is evidence that personal relevance is more important to pictorial, than word, stimuli (Dear, Sharpe, Nicholas, & Refshauge, 2011a). Unfortunately, attentional bias reliability analyses were not feasible given the nature of the eye-tracking data. Hence, potential problems with reliability of the eye-tracking data cannot be discounted. Further, it is possible that the pain ratings during the cold pressor task served as a distraction however such iatrogenic effects are difficult to eliminate.

Consistent with a recent meta-analysis (Crombez et al., 2013) and some theoretical accounts (Pincus & Morley, 2001), the present study found that healthy participants do not display cognitive processing biases to pain-related stimuli. Previous research has found evidence of interpretation biases in those high in pain-related fear (Khatibi et al., 2014) and that manipulating threat in pain-free individuals can influence attentional biases (Boston & Sharpe, 2005; McGowan et al., 2009) but these findings have not been confirmed in meta-analyses (Crombez et al., 2013). The effect of threat on interpretation biases has not previously been studied. Nonetheless, these results add to the literature that fails to find an impact of threat on pain-related cognitive processes in healthy people.

Finally, we used many parameters of attention and the correlations would no longer be significant if a Bonferroni correction were applied. Hence, the findings must not be over-interpreted. However, it does increase confidence in the lack of association between biases that was demonstrated in these studies.

Implications and Conclusions

Our research investigated the effect of threat on cognitive processing biases and the experience of pain. This is the first research in the pain literature to explore the relationship between attention and interpretation biases, and also adds to the small number of studies that

have used eye-tracking measures to more thoroughly explore attentional processes. No association between attentional and interpretation biases was found. In addition, the threat manipulation did not influence interpretation bias. However, there was evidence that threat is associated with difficulty disengaging from painful facial expressions relative to happy facial expressions using the dot probe task, providing partial support for the threat interpretation model (Todd et al., 2015). Understanding the precise nature of attentional and interpretation biases is important in the context of a growing literature investigating the application of these technologies to modify biases with a view to improving outcomes (Jones & Sharpe, 2014; McGowan et al., 2009; Sharpe et al., 2012; Sharpe et al., 2015; Sharpe et al., 2010).

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Author Contributions:

JT, LS, and BC conceptualised and designed the study. LS provided the dot probe task and threat manipulation, and AK provided the incidental learning task and adapted it for use in this study. JT collected data. JT and LS analysed the results and drafted the manuscript. BC and AK provided feedback on the manuscript.

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Table 1

Means (standard deviations) of attentional bias eye-tracking measures

Variable	Stimuli category	Stimuli type	low threat	high threat	average
Percent first fixation	Faces	Happy	50.98 (7.93)	48.40 (6.53)	49.69 (7.34)
		Pain	48.32 (4.79)	48.30 (6.84)	48.31 (6.30)
	Words	Affective	47.34 (5.84)	48.53 (6.81)	47.94 (6.34)
		Sensory	46.75 (8.22)	49.54 (5.98)	48.14 (7.28)
Dwell time first 250ms	Faces	Happy	2.66 (3.09)	2.00 (2.92)	2.33 (3.01)
		Pain	2.55 (2.68)	2.37 (3.59)	2.45 (3.15)
	Words	Affective	0.43 (1.11)	0.47 (1.35)	0.45 (1.22)
		Sensory	0.26 (0.56)	0.26 (0.80)	0.26 (0.68)
Mean dwell time	Faces	Happy	459.64 (79.09)	439.74 (70.65)	449.69 (75.21)
		Pain	438.38 (70.00)	446.58 (93.67)	442.48 (82.30)
	Words	Affective	348.75 (88.65)	353.62 (80.21)	351.18 (84.07)
		Sensory	336.63 (91.15)	349.25 (71.88)	342.94 (81.84)
Duration first	Faces	Happy	221.66 (47.15)	220.10 (46.73)	220.88 (46.67)

Threat, cognitive biases and pain outcomes

fixation		Pain	216.24 (52.86)	228.17 (58.50)	222.21 (55.75)
	Words	Affective	206.85 (62.87)	217.48 (49.65)	212.16 (56.57)
		Sensory	206.13 (63.41)	221.17 (43.10)	213.65 (54.40)
Time to first	Faces	Happy	676.22 (135.21)	695.14 (112.68)	685.68 (124.09)
fixation		Pain	663.55 (141.05)	703.20 (129.98)	683.37 (136.29)
	Words	Affective	646.73 (172.82)	681.64 (108.72)	664.18 (144.59)
		Sensory	633.69 (164.52)	696.96 (94.10)	664.33 (136.98)

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Table 2

Means (standard deviations) of attentional bias reaction time measures

Stimuli category	Stimuli type	Low threat (n=43)			High threat (n=43)			Average (n=86)		
		Congruen t	Incongrue nt	Bias index	Congruen t	Incongrue nt	Bias index	Congruen t	Incongrue nt	Bias index
Faces	Happy	669.15 (94.59)	668.37 (87.90)	-0.78 (52.89)	683.03 (109.29)	680.50 (93.62)	-2.52 (45.47)	676.09 (101.84)	674.44 (90.47)	-1.65 (49.03)
	Pain	657.50 (99.05)	667.16 (91.40)	9.65 (41.88)	683.44 (104.31)	684.53 (104.15)	1.10 (54.69)	670.47 (101.95)	675.85 (97.80)	5.37 (48.61)
Words	Affective	673.87 (103.52)	666.74 (102.24)	-7.13 (51.91)	683.12 (97.98)	692.90 (105.82)	9.77 (41.52)	678.50 (100.30)	679.82 (104.27)	1.32 (47.49)
	Sensory	667.32 (90.30)	676.12 (87.92)	8.80 (38.09)	687.79 (105.99)	686.90 (103.03)	-0.89 (52.32)	677.55 (98.41)	681.51 (95.36)	3.95 (45.75)

Table 3

Means (standard deviations) of interpretation bias reaction times to ambiguous faces

Probe location	low threat	high threat	average
Happy	392.69 (73.34)	432.28 (63.78)	412.49 (71.15)
Pain	403.26 (75.74)	428.88 (60.81)	416.07 (69.47)
Bias index	10.56 (64.88)	-1.44 (59.88)	4.71 (62.40)

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Table 4

Pain outcome means (standard deviations) and MANOVA comparisons by threat group

Outcome	Low threat	High threat	f	p	η_p^2
Hesitancy (secs)	2.17 (1.48)	3.15 (3.23)	3.30	.073	.038
Pain at threshold (0-10)	4.44 (1.71)	5.09 (1.76)	3.02	.086	.035
Threshold time (secs)	10.94 (8.29)	12.58 (7.18)	0.96	.331	.011
Pain at 30 secs (0-10)	6.73 (1.50)	7.02 (1.83)	0.65	.422	.008
Pain at tolerance (0-10)	7.29 (2.00)	8.42 (1.28)	9.79	.002	.104
Tolerance time (secs)	136.5 (87.08)	94.53 (80.21)	5.40	.023	.060
Distress at tolerance (0-10)	4.80 (2.22)	6.03 (1.95)	7.47	.008	.082

Notes: n=86