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ATTENTIONAL AVOIDANCE IS ASSOCIATED WITH INCREASED PAIN SENSITIVITY IN PATIENTS WITH CHRONIC POSTTRAUMATIC PAIN AND COMORBID POSTTRAUMATIC STRESS

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ABSTRACT

Objectives: Posttraumatic stress disorder (PTSD) is common in chronic posttraumatic pain. Theoretical models suggest that attentional biases (AB) contribute to the development and maintenance of chronic pain and PTSD, however, the influence of AB on clinical and heat pain sensitivity in chronic posttraumatic pain patients is unknown. This study investigated AB for linguistic pain- and trauma-related stimuli, and clinical and thermal sensitivity in patients with chronic posttraumatic pain with and without PTSD.

Methods: Thirty-four patients with chronic posttraumatic cervical pain performed the visual attentional probe task assessing patterns of selective attentional responding to trauma cues and to pain cues. The task used short (500ms) and long (1250ms) stimulus exposure durations to ensure sensitivity to both the orienting and maintenance of attention. Heat pain threshold (HPT) was assessed at the non-painful hand. Clinical pain intensity, psychological distress (anxiety, depression, and disability), and PTSD symptomatology were assessed with questionnaires.

Results: The Pain/PTSD group (N=14) demonstrated increased clinical and heat pain sensitivity as well as psychological distress compared with the Pain/No-PTSD group (N=20; p<0.05). AB scores were significantly different between groups (p=0.04). Irrespective of stimulus exposure duration, the Pain/PTSD group demonstrated attentional bias away from trauma and pain cues (avoidance) whereas the Pain/No PTSD group demonstrated attentional bias towards pain cues (vigilance). Attentional avoidance of pain cues was associated with increased pain intensity and heat pain sensitivity (p<0.02).

Discussion: These results suggest that attentional avoidance is associated with increased chronic posttraumatic pain. The causal contribution of attentional avoidance to pain outcomes remains unclear.

Keywords: Posttraumatic stress, PTSD, chronic posttraumatic pain, attentional bias, pain sensitivity
1. INTRODUCTION

Posttraumatic stress disorder (PTSD) is common in chronic posttraumatic pain [1-3]. Coexistence of chronic pain and PTSD is associated with increased clinical and experimental pain sensitivity [4, 5], disability and distress [4, 6, 7]. Moreover the existence of chronic pain and comorbid PTSD has been found to complicate treatment [8, 9].

Theoretical models suggest that attentional biases (AB) contribute to the development and maintenance of chronic pain and PTSD [10, 11]. Currently, AB in patients with chronic posttraumatic pain has been investigated by Beck and colleagues who, using the emotional Stroop task, obtained findings consistent with a greater attentional bias towards pain and trauma cues in pain patients with comorbid PTSD, compared to patients without PTSD and asymptomatic controls [12]. However, the Stroop task has been criticized as a measure of selective attention to threat, as observed effects could instead reflect only general motor slowing in the presence of threat information, rather than attentional vigilance for such information [13, 14]. The attentional probe task [13] was developed to yield a more direct measure of AB that is not influenced by such general slowing of motor responding. This task measures the difference in speed to process visual probes that appear either proximal to or distal from the location where threat cues (e.g. pain or trauma words) are presented on a computer screen. Attentional vigilance for threat cues is indicated by a relative speeding to process probes that are proximal to such threat cues relative to distal probes, while attentional avoidance of threat cues is indicated by a relative slowing to process probes that are proximal to threat cues relative to probes distal from such cues. Several attentional probe investigations have found evidence of an attentional bias towards pain-related cues in chronic pain [15-19] and towards trauma-related cues in PTSD [20-23]. However, some studies have instead obtained findings that suggest attentional avoidance of threat cues in PTSD [24-26].
Similarly, longitudinal studies have revealed attentional avoidance of affective pain-cues (or focus on positive cues) in patients with chronic postoperative pain [24] and chronic back pain [25].

A number of attentional probe studies have varied the exposure duration of the threat cues, in order to distinguish between initial attentional orienting responses and sustained attention to such stimuli. Such work suggests biased attentional processing of pain cues may be particularly evident in maintained attention (assessed using 1250 milliseconds stimulus exposure duration) [18, 19]. Biased attentional responding to pain-related information has been implicated as a vulnerability factor for increased pain and disability [27, 28]. The few studies that previously have explored the influence of pain-related biases have mostly employed short stimulus exposures (typically 500 ms), which are often considered to reveal AB in initial attentional orienting. Findings from such studies suggest that attentional orienting towards pain cues may predict increased pain sensitivity in healthy volunteers [29], but reduced chronicity in acute pain patients [30, 31]. Without also employing longer stimulus exposure durations, it is not possible to distinguish the role of biased attentional orienting and biased attentional maintenance in predicting pain experience.

Currently, no studies have yet used the attentional probe task to assess AB in subjects with chronic pain and comorbid PTSD, and so the influence of AB on clinical and experimental pain sensitivity in patients with chronic posttraumatic pain is unknown. Thus, the primary aims of this study were 1) to investigate attentional bias towards pain cues and trauma cues, in posttraumatic chronic pain patients with comorbid PTSD compared with patients without PTSD, using the attentional probe task, and employing different stimulus exposure durations (500 and 1250 ms) to distinguish attentional orienting and maintained attention; and 2) to investigate associations between attentional bias to pain cues and pain
severity, assessed by measuring both clinical pain intensity and thermal sensitivity. It was hypothesized that, compared to pain patients without PTSD, those with comorbid PTSD would exhibit greater AB to pain cues and trauma cues, greater clinical pain intensity, and lower heat pain threshold.

2. MATERIALS AND METHODS

2.1 Patients

Forty-four patients referred to interdisciplinary pain treatment, during the period from August 2015 to April 2016, were given information about the research project. All these patients were experiencing accident-related chronic nonmalignant pain in the cervical spine, and the onset of this pain was associated with a traffic accident. Thirty-seven patients consented to participate. Two patients were later excluded from further assessment, when they were identified as fulfilling the PTSD cluster criteria but being below the cut-off in terms of their PTSD score obtained on the ICD-11 Trauma Questionnaire (see section 2.2.1) and thermal sensitivity and attentional bias was not performed in these patients. In total, thirty-five patients (mean age: 44.1 years [range: 23-69]; 30 women), were included in this study. The present study was completed while these individuals were on a wait-list to commence interdisciplinary pain treatment. All patients completed questionnaires via an electronic software system (PainData, Denmark) to provide the following pain related data: duration of pain, and intensity of average clinical pain measured using a 0-10 numerical rating scale (NRS) with 0 defined as “no pain” and 10 as “worst pain imaginable” during the previous 24 hours [32]. Participants also completed questionnaires assessing PTSD symptomatology (ICD-11 Trauma Questionnaire) [33], and levels of anxiety (Generalized Anxiety Disorder, GAD-7) [34], depression (Patient Health Questionnaire, PHQ9) [35] and disability (Pain Disability Index, PDI) [36]. Pain sensitivity was assessed using a heat pain induction
procedure, and the attentional probe task was completed to assess biased attentional responding to pain cues and trauma cues. The study was approved by the local ethical committee (S-20150081) and all patients provided written informed consent.

2.2 Questionnaire Assessment

2.2.1 PTSD

PTSD symptomatology was measured using the ICD-11 Trauma Questionnaire, Part 1 [33]. This questionnaire consists of 7 items, assessing the core clusters of PTSD symptoms as outlined by the ICD-11 model; re-experiencing (3 items), avoidance (2 items) and sense of threat (2 items). Responses to questionnaire items are made using a 5-point Likert scale, ranging from 0 = “not at all” to 4 = “extremely”. The ICD-11 criteria for PTSD are met if a participant endorses at least one symptom from each of the three clusters, as indicated by scores ≥ 2. In addition a total PTSD symptom score was calculated by summing responses across item (potential score range 0-28). The factor structure of the ICD-11 model of PTSD is consistent across multiple trauma types, and the instrument had good concurrent validity, with excellent model of fit having been obtained in six of seven trauma samples in Denmark [37]. Evidence supports the discriminant and convergent validity, as well as the clinical utility of the ICD-11 Trauma Questionnaire when assessing trauma-exposed populations [38]. Based on the cluster criteria and the total score on ICD-11, participants were divided into two groups (Pain/PTSD and Pain/No-PTSD). Chronic pain and PTSD share a number of symptoms and response patterns (e.g., increased arousal, attentional bias, avoidance, anxiety sensitivity) [37]. Given that both groups in this study presented with highly heterogeneous conditions, an ICD-11 Trauma Questionnaire score cut-off was established to separate the two groups, such that they did not overlap in PTSD symptom severity. This cut-off criterion was guided by the data from a recent study (Vaegter et al, under review), which found that
pain patients without PTSD exhibited ICD-11 Trauma Questionnaire scores of 6.9±4.9, while pain patients with PTSD exhibited scores of 18.1±5.9. In the present study, therefore, patients were classified as belonging to the Pain/PTSD group only if in addition to fulfilling the cluster criteria, their ICD-11 Trauma Questionnaire score was ≥ 12, and were classified as belonging to the Pain/No-PTSD group only if in addition to not fulfilling the cluster criteria, their ICD-11 Trauma Questionnaire score was below 12.

2.2.2 Anxiety

The 7-item Generalized Anxiety Disorder (GAD-7) questionnaire [34] was employed to measure anxiety symptoms. The scale contains 7 questions that ask patients how often, during the last two weeks, they have been bothered by each option. The questionnaire is assessed using a 4-point Likert scale, ranging from 0 = “not at all” to 3 = “nearly every day”. The GAD-7 is a validated screening and severity measure for the most common anxiety disorders in primary care, with excellent internal consistency reliability (α = .92), as well as good test-retest reliability (r = .83). Additionally, the scale has shown good procedural validity (r = .83) as compared to health-professional administered versions of the scale [34], and the GAD-7 has been frequently used to assess anxiety in chronic pain populations [39].

2.2.3 Depression

The 9-item Patient Health Questionnaire (PHQ-9) [35] was employed as a measure of depression severity. Each question is assessed on a 4-point Likert scale, ranging from 0 = “not at all” to 3 = “nearly every day”. The PHQ-9 has been demonstrated to be a valid instrument to measure depressive symptoms in primary care patients, with excellent internal consistency reliability (α = .89). Additionally, the PHQ-9 has shown good procedural validity (r = .84) as compared to health-professional administered versions of the scale [35], and the scale has been widely used to measure depressive symptoms in chronic pain populations [39].
2.2.4 Pain intensity

Pain intensity was measured using the Numeric Rating Scale (NRS) [32] which is designed to measure the individuals’ subjective experience of pain intensity. The scale is rated on a single 11-item numeric rating scale, ranging from 0 = "no pain" to 10 = "worst pain imaginable". In this study, patients were asked to record their average levels of pain during the last 24 hours, and this score defined average pain intensity. The NRS has shown good test-retest reliability in patients with rheumatoid arthritis \( r = .96, p < .05 \) [40].

2.2.5 Pain disability

The Pain Disability Index (PDI) [36] is a 7-item self-report measure to assess the degree to which chronic pain interferes with daily activities. The scale is constructed on an 11-item numeric rating scale in which 0 = “no disability” and 10 = “worst disability”. The original version of the PDI measures 2 factors: 1) voluntary activities (items 1 to 5) and 2) obligatory activities (item 6 and 7). The PDI has shown excellent internal consistency \( (\alpha = .86) \), good concurrent, criterion-related and discriminate validity, and satisfactory test-retest reliability \( r = .44 \) [41]. However, some psychometric analyses indicates that the obligatory activation subscale has inadequate internal reliability [42], and the voluntary subscale alone has been found to provide sufficient information regarding the degree of disability associated with chronic pain. Thus, the present study considered only the 5 items measuring disability to voluntary activities were included, which yielded a pain disability score of between 0-50.

2.3 Assessment of thermal sensitivity

A Somedic Thermostat apparatus (MSA Thermal Stimulator) connected to a PC with SenseLab, version 2.22 Software (Somedic AB, Hørby, Sweden) was used to assess thermal sensitivity. Assessments were performed by the same experienced male assessor. Prior to
assessments, patients were thoroughly introduced to the assessment procedures using pictorial illustrations as well as verbal instructions. A thermode with a 2.5 x 5.0 centimetre surface was placed on the thenar eminence of the left hand. The baseline temperature was 32°C and increased by 1.0°C/s to a maximum of 50°C. Patients were instructed to press a handheld switch as soon as they detected a change in heat sensation, thereby revealing their warmth detection threshold (WDT). After assessment of WDT, heat pain threshold (HPT) was assessed. Patients were instructed to press the handheld switch as soon as the heat sensation was defined as the first sensation of pain. The peak temperature was stored and the thermode decreased its temperature (3.0°C/s) to the baseline temperature. Test stimuli were repeated three times, and the averages of WDT and HPT were used as the measures of warmth detection threshold and heat pain threshold, respectively. Breaks between WDT and HPT ramp stimuli were 3 seconds.

2.4 Assessment of attentional bias to pain and trauma cues

2.4.1 Generation of pain and trauma cues

An initial pool of 30 candidate pain-related words was generated from the Danish version of the McGill Pain Questionnaire (MPQ) [43] and drawing upon existing pain-related stimuli in the literature [12]. In addition, 30 candidate trauma-related words were generated from existing trauma- and accident-related stimuli in the literature [12, 44]. These words were then translated from English to Danish. The same procedure was used to generate a set of 30 candidate neutral words. Each word-pair was matched based on word-frequency and word-length using the Korpus 90 frequency list (available at: www.dsl.dk).

All candidate stimulus words were presented to 20 independent judgers not participating in the present study, including 12 chronic pain patients and 8 healthy controls. The valence of each word was rated on a 9-point scale, in which 1 = “very negative”, 5 =
“neutral” and 9 = “very positive”. On the basis of mean ratings, two sets of threat-related (pain and trauma) and neutral word-pairs were selected. The final word sets each included word pairs in which a negative member had a mean valence rating less than 3.5, and a neutral member had a mean valence rating between 4 and 6.5. The Pain Cue subset (Supplementary material Table S1, Supplemental Digital Content 1, http://links.lww.com/CJP/A431) comprised 16 word pairs in which the negative member was a pain-relevant word and the other was a length and frequency matched neutral word (mean rating difference 2.94; p < 0.001). The Trauma Cue subset comprised 16 word pairs in which the negative member was a trauma-relevant word and the other was a length and frequency matched neutral word (mean rating difference 3.38; p < 0.001).

2.4.2 Attentional probe task procedure

This study employed a modified version of the attentional probe task developed by MacLeod et al [13]. Each trial within the attentional probe task commenced with the presentation of a white central fixation cross, that appeared on the black screen background for 1000 ms. One of the stimulus word pairs then was presented, in white letters, with the members spatial separated by a distance of 3 cm. One member appeared above and one below the location where the fixation cross has just been shown and, for critical stimulus pairs, the threatening member of the pair (pain cue or trauma cue) appeared equally often in the upper and in the lower location. This word pair remained on screen for either 500 ms or 1250 ms, depending on the stimulus exposure duration condition. Then both words disappeared and a light grey “probe” stimulus, which was either the symbol “<” or “>” appeared in the location where either the upper or lower member of the preceding word pair has just been presented. Participants were required to discriminate the identity of this probe, and to respond by correctly pressing the corresponding key (left arrow or right arrow) on the keypad as quickly
as possible. The speed and accuracy of this probe discrimination response was recorded. Following the participant’s response, the probe disappeared and, after an inter-trial interval of 500 ms, the next trial began.

Thus each of the critical word pairs could be presented in any of 8 unique experimental conditions, reflecting the nested combination of the experimental factors Threat Word Position (pain or trauma cue top vs bottom), Probe Position (probe top vs bottom) and Stimuli Exposure Duration (500 ms vs 1250 ms). The assumption underpinning this assessment approach is that participants will be quickest to discriminate the identity of probes that appear where they are already attending. Thus attention vigilance towards the threat members of the critical word pairs will be revealed by speeding to discriminate probes that appear in the locus of these threat stimuli, relative to probes that appear in the locus of the neutral pair members. Conversely, attentional avoidance of these threat cues will be revealed by slowing to discriminate probes that appear in the locus of these threat stimuli, relative to probes that appear in the locus of the neutral pair members.

A 16 trial practice version of the probe task, using only neutral stimuli, was delivered first, to familiarise participants with the required probe discrimination. This was followed by 384 trials, using the above described stimulus pairs. Hence, 128 of these were filler trials (using the filler word pairs), and 256 were the experimental trials of interest that presented the critical word pairs containing the threat cues (128 trials presenting pairs containing a pain cue, and 128 trials presenting pairs containing a trauma cue). These 384 trials were delivered in 8 blocks of 48 trials, within which every stimulus word-pair was presented once. Within each block, one eighth of the trials presenting each type of word pair was given in each of the 8 unique experimental conditions described above. For each participant, the assignment of each word-pair to these 8 conditions rotated across blocks, such that by the end of the 384
trials, every word-pair had been presented once in each of the 8 conditions. Across participants, the condition that each word pair was assigned on the first block also was rotated, such that after every 8 participants had been tested, each word pair had been presented 8 times in each of the 8 unique conditions, once in each block positions.

Participants were tested individually in a secluded, dimly lit room. Written instructions were provided on the computer screen. These instructions told participants to correctly indicate the probe identity on each trial as quickly as possible, but did not direct participants to attend specifically to either of the words presented. Participants were not informed about the rationale of the study prior to completing the task. Three self-paced breaks were evenly spread through task, being given after every 96 trials. Time taken to complete the attentional probe task was approximately 20 minutes.

2.4.3 Computation of attentional bias indices

Probe discrimination latencies from practice and filler trials were discarded. In keeping with standard practice for maintaining data integrity for this task [45, 46], trials with extremely short (< 200 ms) and long (> 2000 ms) response times were removed, as these reflect anticipatory responding and lapses of concentration, respectively. Four attentional biases indices were then calculated for each participant, expressing the degree to which they displayed attentional vigilance for each type of threat cue (pain cues and trauma cues) at each stimulus exposure duration (500 ms and 1250 ms). In each case, this attentional bias index expressed speeding to discriminate probes proximal to these threat cues, relative to probes distal from these threat cues, by subtracting the mean discrimination latency for probes appearing in the same location as threat-related words from the mean discrimination latency for probes appearing in the opposite location to the threat-related words. Thus, a positive value on the each resulting attentional bias index reflected an AB towards the threat cue (i.e.,
threat vigilance), whereas a negative value reflected an AB away from the threat cue (i.e., threat avoidance).

2.5 Statistical analyses

Data are reported as means and standard deviations (SD). All statistical analyses were run using SPSS Statistics (Version 21; IBM, Armonk, NY, USA). Tests for normality showed that all data were normally distributed (Shapiro-Wilk test; P > 0.05). Between group differences in demographic variables, psychological distress, pain intensity, use of analgesics, and heat sensitivity between groups were tested using Chi-square test and independent samples t-tests for categorical and continuous variables, respectively. In addition, a sensitivity analysis was conducted to investigate whether clinical pain outcomes were different between the two groups if excluded subjects were maintained in the analysis. P-values less than 0.05 were considered significant. The effect sizes of group differences on continuous variables were calculated based on Hedges’ g, due to dissimilar group sizes. Effects sizes were classified as small (g = 0.20), medium (g = 0.50), and large (g = 0.80). In order to test the hypothesis that the two groups would display differing patterns of selective attentional responding to the threat cues, a mixed model repeated measures analysis of variance (RM-ANOVA) was conducted on the attentional bias index scores computed from the attentional probe task data, with threat cue type (pain cue; trauma cue), and stimulus exposure duration (500ms; 1250ms) as within-subject factors, and group (Pain/No-PTSD; Pain/PTSD) as the between subject factor. Mauchley’s Test of Sphericity showed no violation (p=0.96). Subsidiary analyses conducted to reveal the nature of significant effects used Bonferroni corrections for multiple comparisons. In order to examine whether there was an association between selective attentional responding to pain cues and pain sensitivity, Pearson correlation analyses were used to determine the relationship between the AB index scores reflecting
attentional bias to pain cues and the measures of both clinical and heat pain sensitivity. As no significant difference in attentional bias index scores reflecting selective attentional responding to pain cues was found between the two stimulus exposure durations, the mean attentional bias scores computed across both stimulus exposure duration (500ms; 1250ms) were used in the correlation analyses. To reduce the risk of type I error due to multiple correlational analyses, the level of statistical significance of the correlation coefficients was adjusted by dividing the alpha level by the number of correlations [47], such that a p-value equal to or less than 0.025 (0.05 / 2) was considered significant in the correlational analyses.

3. RESULTS

3.1 Group characteristics

Group 1 (Pain/No-PTSD) included 20 patients with chronic pain who did not meet criteria for PTSD. Group 2 (Pain/PTSD) comprised 15 patients with chronic pain who all met the criteria for PTSD and were above the pre-determined cut-off. However, one subject was excluded from this latter group because this individual exhibited no accuracy on the attentional probe task (error rate > 50%, which represents below chance performance). Therefore 34 patients were included in the final analyses. Obviously the two groups differed significantly in PTSD score (Table 1; t(32) = 8.98, p < 0.001), as the ICD-11 Trauma Questionnaire was used to subdivide the patients. No significant differences were found in distribution of women and men (X^2 = 0.49, p = 0.48) or age (t(32) = 0.23, p = 0.82) between groups.

3.2 Psychological distress and pain disability

Patients with PTSD had significantly higher scores of anxiety (Table 1; t(32) = 3.52, p = 0.001), depression (t(32) = 2.95, p = 0.006), and disability (t(32) = 2.78, p = 0.009) compared with patients without PTSD. Sensitivity analyses including all 37 patients confirmed the
findings for anxiety (t(35) = 3.78, p = 0.001), depression (t(35) = 3.11, p = 0.004), and disability (t(35) = 2.31, p = 0.027).

3.3 Pain intensity
Clinical pain intensity tended to be higher in the PTSD group than in the no-PTSD group, though this difference fell slightly short of statistical significance (Table 1; t(32) = 1.90, p = 0.06). Sensitivity analysis including all 37 patients confirmed the findings (t(35) = 1.91, P = 0.065).

3.4 Thermal sensitivity
No significant group difference was found for warmth detection threshold (Table 1; t(32) = 0.23, p = 0.82) but there was a significant group difference in the heat pain threshold (t(32) = 2.10, p = 0.046), with lower pain threshold being observed in the PTSD group compared with the no-PTSD group.

3.5 Attentional bias to pain and trauma cues
Accuracy on the attentional probe task was generally high, with errors and outliers resulting in elimination of only 3.1% of the probe discrimination latency data. The groups did not differ significantly in terms of their error rates on the attentional probe task t(32) = 1.60, p = 0.14, nor in terms of number of outlying discrimination latencies t(32) = 1.60, p = 0.41, nor in their mean probe discrimination latencies t(32) = 0.35, p = 0.53.

The ANOVA carried out on the AB index scores revealed a significant main effect of group (Fig. 1; F(1, 32) = 4.57, p = 0.04), with post-hoc test showing that the Pain/No-PTSD group demonstrated greater relative vigilance towards the threat cues (displaying positive AB scores) than was the case for the Pain/PTSD group (who instead displayed negative AB scores). No other effects were significant. Hence, the group difference in attentional responding to threat cues was not moderated by either threat cue type (F(1, 32) = 2.16, p =
0.15) or stimulus exposure duration (F(1, 32) = 0.44, p = 0.51), indicating that this group difference was equally evident regardless of whether the threat stimulus was a pain cue or a trauma cue, and regardless of whether it was presented at the short or long exposure duration.

3.5 Associations between biased attentional responding to pain cues and pain symptomatology

A significant positive correlation was found between the AB index score to pain cues and heat pain threshold (r = 0.41, p = 0.016), indicating that greater attentional avoidance of pain cues was associated with lower heat pain threshold. A significant negative correlation between this same index score, and clinical pain intensity was also found (r = -0.44, p = 0.009), indicating that greater attentional avoidance of pain cues was associated with increased clinical pain intensity.

4. DISCUSSION

4.1 Summary of findings

This study investigated the relationship between biased attentional responding for pain or trauma cues and pain symptoms, reflecting clinical pain severity and heat pain threshold, in patients with chronic posttraumatic pain. The results indicate that individuals with chronic pain and PTSD symptoms following a physical injury displayed greater attentional avoidance of pain and trauma cues relative to chronic pain patients without PTSD, who instead showed responses consistent with attentional vigilance for such cues. This group discrepancy in attentional bias did not differ for pain and trauma cues, and was equally evident at both the short stimulus exposure duration employed to assess attentional orienting and the long stimulus exposure duration employed to assess maintained attention. Moreover, heightened attentional avoidance of pain cues was significantly associated with increased clinical pain intensity and heat pain threshold. These latter findings suggest that attentional avoidance of
pain cues, may contribute to increased pain experience and symptomatology in patients with chronic posttraumatic pain.

Todd et al. [27] have argued that the tendency to exhibit attentional avoidance of threat cues may be increased when threat severity is high. It is plausible that pain cues and trauma cues both could be perceived as more highly threatening by those individuals, whose posttraumatic chronic pain is accompanied by PTSD-symptom severity, explaining why the Pain/PTSD group alone displayed attentional avoidance of such threat cues. An attentional bias away from threat cues is consistent with the avoidance cluster of PTSD, and there is evidence that the tendency to display attentional avoidance of threat cues may increase the risk of developing PTSD symptomatology following exposure to potentially traumatic situations [26, 48]. Although attentional avoidance of some types of threat may be adaptive under certain situations, the present results suggest that attentional avoidance of pain cues may contribute to more negative pain experiences in chronic pain patients. In line with this, prospective studies have shown that attentional avoidance of pain-cues is a strong predictor in the development of chronic pain [30, 31], suggesting that such attentional avoidance may represent a maladaptive pain-coping strategy.

4.2 Clinical implications

The present findings may be of relevance to pain-rehabilitation programs that emphasise the central role of cognition in adjustment to chronic pain. PTSD and chronic pain share a number of symptoms and response patterns, including increased arousal, anxiety, depression, ABs and avoidance-behaviours [11, 18]. It has been suggested that clinical treatment protocols for people who experience combined chronic pain and PTSD should target the symptoms common to these two problems in order to provide an integrated treatment for both conditions [3]. Given the present finding that attentional avoidance of pain cues may
contribute to increased pain sensitivity and symptomatology, clinicians may focus on integrating interventions that teach patients how to reduce attentional avoidance of pain cues.

Of course, whether or not such procedures designed to directly modify selective attentional responding to pain cues is likely to deliver therapeutic benefits in clinical cohorts will depend upon whether or not the presently observed association between greater attentional avoidance of pain cues and heightened pain sensitivity/severity, in pain patients with PTSD, is causal in nature, such that this attentional avoidance functionally contributes to pain sensitivity and clinical pain severity. An alternative possibility proposed by some researchers is that, rather than AB causally influencing the experience of pain, the experience of pain instead may modulate attention to pain cues [49]. Only cross-section data were collected in this study, and this does not allow for conclusions concerning the causal direction of the observed association. Indeed it is possible that this relationship may not reflect any causal association between attentional avoidance of pain cues and pain experience, but instead may result from each of these variables sharing an independent association with some third factor, such as emotional distress. Only by directly modifying selective attentional responding to pain cues, and observing the consequences of this attentional manipulation on pain sensitivity and severity, is it possible to establish whether by this attentional bias functionally contributes to pain experience, and whether the attenuation of the bias can therapeutically attenuate pain experience.

One promising intervention approach that may operate by reducing biased attentional responding to pain cues is mindfulness, which by encouraging recipients to accept and experience their moment to moment sensations has proven capable of reducing their experience of pain [50]. Another approach that may hold special promise is attentional bias modification (ABM), specifically targeting the maladaptive pattern of attentional bias that
predicts increased pain sensitivity and chronic pain symptomatology [51]. The result of the current study may guide future ABM investigations, as it highlights potentially important distinctions in attentional processing of threat cues in pain patients with and without PTSD. Although ABM protocols traditionally rely on the premise that beneficial effects result from training attention away from threat, recent findings suggest that this may not be true of all clinical conditions characterised by biased attentional responding to threat. For example, there is recent evidence that the risk of PTSD can be significantly attenuated by employing ABM procedures to increase attentional bias towards threat cues in people who subsequent experience traumatic events [52, 53]. Similar findings have been reported in relation to pain, with higher pain thresholds on the cold pressor task resulting from an ABM procedure configured to increase attentional bias towards affective pain cues, in healthy volunteer [54].

Consistent with a number of previous studies [4, 6, 7], the Pain/PTSD group in the present experiment showed higher levels of anxiety and depression than did the Pain/No-PTSD group. Given that depression and anxiety have been associated with biased attentional responding to threat stimuli [55], it also is important to consider the potential influence of these emotional variables on chronic pain. However, due to the limited sample size, this present study could not determine whether the observed association between AB and pain experience was moderated by anxiety or depression.

4.4 Limitations and Strengths

Several limitations of the current study should be borne in mind when considering the reported findings. First, this study had a small sample size of only 34 participants. An a priori power analysis showed that to test the hypothesis that the Pain/PTSD group demonstrated increased pain sensitivity, assuming a large effect size, a sample size of at least 21 participants within each group would be necessary to reduce the probability of Type I and
Type II error to satisfactory levels. It may be that with larger samples, other significant effects may emerge. Furthermore, although previous studies have shown that the use of self-report measures and clinical interviews may be comparable when identifying PTSD in patients following a physical injury [56], this study would be strengthened by including a diagnostic interview. Additionally, the PTSD questionnaire cut-off score employed in addition to fulfilling the cluster criteria may affect the generalizability of the results. The present study could also have benefited from including a healthy control group, and it also would have been valuable to have assessed pain sensitivity in the deeper musculoskeletal structures potentially affected in our pain patients. The pain-induction procedure was administered prior to the attentional assessment which differs from other studies. Although participants were no longer experiencing induced pain at the time of the attentional assessment, it is possible that the order in which the pain induction procedure and the attentional assessment procedure were delivered may influence the nature of the observed association between such measures. This issue cannot be addressed using the present data, and nor could it have been addressed if we had instead employed the reverse fixed ordering. Future research could systematically manipulate the order of attentional assessment and pain induction, to empirically determine whether this moderates the nature and/or strength of the observed association between the resulting measures. Clearly, the results from the present study now need to be replicated in a larger sample, and these additional issues can usefully be addressed within such future work, which also should assess the therapeutic impact of modifying attentional avoidance of pain cues in pain patients with PTSD within clinical settings. These preliminary findings provide a strong justification for such future extensions of the present work.
It was a strength of this study that participants were carefully selected based on the presence of a pain/trauma association, but differed in terms of PTSD comorbidity (with no group differences in age and gender). Including a trauma-exposed but resilient sample allowed for the investigation of whether patterns of biased attentional responding to pain and trauma cues, and the association between such AB and pain experience, were consistent across people who has experienced trauma exposure, or differed as a function of PTSD symptomatology. Furthermore, including a measure of heat pain threshold, in addition to a measure of clinical pain severity, represents a further strength of the study.

4.5 Conclusions

Patients with chronic posttraumatic pain and comorbid PTSD demonstrated increased clinical pain intensity and heat pain sensitivity, as well as higher levels of anxiety and depression, compared to those whose chronic posttraumatic pain was not comorbid with PTSD. The Pain/PTSD group also displayed greater attentional avoidance of pain cues and trauma cues than was exhibited by pain patients without PTSD. Moreover, across all patients attentional avoidance of pain cues was associated with increased clinical and heat pain sensitivity. These findings reveal both a difference in attentional responding to pain and trauma cues between posttraumatic pain patients with and without PTSD, while also indicating that across all such patients attentional avoidance may be a cognitive marker associated with increased chronic posttraumatic pain symptoms. In terms of clinical implications, the results from this study point to the potential value of specifically targeting biased attentional responding to such threat cues in the context of rehabilitation for patients with chronic posttraumatic pain, with and without comorbid PTSD.
References


**Figure legends**

Figure 1: Mean (±SEM) attentional bias index scores towards pain cues and trauma cues, in posttraumatic chronic pain patients with comorbid PTSD (N = 14) and patients without PTSD (N = 20), using the attentional probe task, and employing different stimulus exposure durations (500 and 1250 ms) to distinguish attentional orienting and maintained attention. Significant difference between groups (*, p < 0.05).

**Table 1:** PTSD-score, demographics, clinical pain, analgesics, psychological distress, and thermal sensitivity in chronic posttraumatic pain patients with and without comorbid PTSD. ‘NRS’: Numerical Rating Scale. ‘GAD7’: Generalized anxiety disorder. ‘PHQ9’: Patient health questionnaire. ‘PDI’: Pain Disability Index. ‘WDT’: Warmth Detection Threshold. ‘HPT’: Heat Pain Threshold.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Variable</th>
<th>Pain/No-PTSD (n=20)</th>
<th>Pain/PTSD (n=14)</th>
<th>P-value</th>
<th>Effect size (Hedge’s g)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PTSD</strong></td>
<td>Total PTSD sumscore (ICD-11: 0-28)</td>
<td>4.8±3.3 (range: 0-10)</td>
<td>17.5±5.0 (range: 12-26)</td>
<td>&lt;0.001</td>
<td>2.99</td>
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<tr>
<td><strong>Demographics</strong></td>
<td>Gender (F/M)</td>
<td>17/3</td>
<td>13/1</td>
<td>0.48</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Age (years)</td>
<td>43.8±11.5</td>
<td>44.6±8.5</td>
<td>0.82</td>
<td>-</td>
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<tr>
<td><strong>Clinical pain</strong></td>
<td>Pain duration (years)</td>
<td>9.1±9.3</td>
<td>7.4±5.5</td>
<td>0.55</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>Pain intensity (NRS: 0-10)</td>
<td>6.4±1.6</td>
<td>7.4±1.5</td>
<td>0.06</td>
<td>0.64</td>
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<tr>
<td></td>
<td>Analgesic users (Y/N)</td>
<td>17/20</td>
<td>13/14</td>
<td>0.48</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Opioid users (Y/N)</td>
<td>(85.0%)</td>
<td>(92.9%)</td>
<td>0.41</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(20%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antidepressant users (Y/N)</td>
<td>10/20</td>
<td>9/14</td>
<td>0.34</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(50.0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anticonvulsive users (Y/N)</td>
<td>3/20</td>
<td>4/14</td>
<td>0.16</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(15%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NSAID users (Y/N)</td>
<td>4/20</td>
<td>3/14</td>
<td>0.08</td>
<td>-</td>
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<td>Paracetamol users (Y/N)</td>
<td>3/20</td>
<td>5/14</td>
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<tr>
<td></td>
<td>(15%)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Muscle relaxants (Y/N)</td>
<td>15/20</td>
<td>11/14</td>
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<tr>
<td></td>
<td>(75.0%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0%)</td>
<td></td>
<td></td>
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<td><strong>Psychological distress</strong></td>
<td>Anxiety (GAD7: 0-21)</td>
<td>6.0±4.1</td>
<td>11.6±5.2</td>
<td>0.001</td>
<td>1.20</td>
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<td>Depression (PHQ9: 0-28)</td>
<td>10.2±6.2</td>
<td>15.9±4.7</td>
<td>0.006</td>
<td>1.04</td>
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<td>Disability (PDI: 0-50)</td>
<td>34.2±9.1</td>
<td>41.9±5.8</td>
<td>0.009</td>
<td>1.01</td>
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<tr>
<td><strong>Experimental pain sensitivity</strong></td>
<td>WDT Hand (32-50°C)</td>
<td>34.3±3.1</td>
<td>34.2±1.0</td>
<td>0.82</td>
<td>0.10</td>
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<td></td>
<td>HPT Hand (32-50°C)</td>
<td>42.4±4.3</td>
<td>39.4±3.6</td>
<td>0.046</td>
<td>0.76</td>
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