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RUNNING HEAD: Attentional biases in pain

Towards a new model of attentional biases in the development, maintenance and management of pain

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Towards a new model of Attentional Biases in the Maintenance and Management of Pain

1. Introduction

There are numerous models of the development and/or maintenance of chronic pain that suggest that attentional biases are important in chronic pain [1; 7; 11; 12; 41]. While these models attribute slightly different roles to attentional processes, the broad assumption is that when people are in pain and are highly fearful or threatened by the pain, they over-attend to pain-related stimuli. Pain is known to capture attention, which interferes with activity, leads to avoidance of the pain-provoking activity and consequently is associated with processes that exacerbate disability [7; 41].

There is also a large and growing body of research exploring the relationship between attentional processes and pain. Two recent meta-analyses have summarised this research. Schoth et al. [30] found evidence of attentional biases in those with chronic pain compared to healthy controls ($g = 0.45$). Results differed with the time at which biases were assessed with differences in attentional biases being greater with longer presentation times (e.g. > 1000 msec) than at shorter durations (e.g. 500 msec). Another recent meta-analysis conducted by Crombez et al. [8] confirmed that attentional biases were present in chronic pain groups ($d = 0.13$). However, only attentional biases towards sensory pain words were unique to patients with chronic pain compared with healthy controls. Crombez et al. [8] also found that attentional biases towards signals of impending pain were present in healthy participants ($d = 0.68$).

Despite confirmation of the presence of attentional biases once someone has developed chronic pain, the mere presence of attentional biases is not sufficient to confirm that they actually *influence* pain [20]. Theories typically assign a potentially causal role to attentional biases, such that those who over-attend to pain are more likely to subsequently avoid activity and become more disabled, creating a vicious cycle of chronicity [41]. However, the specific role of attentional processes in the development of chronic pain remains poorly understood. For example, in their meta-analysis, Crombez et al. [8] found that in cross-sectional studies, attentional biases were not consistently associated with important theoretical constructs, such as fear of pain, state/trait anxiety or depressive mood, nor were they associated with pain outcomes.

To date, no systematic reviews have focussed on the types of studies which can be used to test the causal nature of attentional biases in chronic pain: prospective studies and experimental studies. Prospective studies can determine whether attentional biases present prior to the development of pain actually precede and predict subsequent pain outcomes; which are necessary but not sufficient conditions to establish causation. Experimental studies that manipulate attention and then assess pain outcomes can directly test whether attentional processes have a causal role in people's response to pain. The present study therefore sought to systematically review the available prospective and experimental studies concerning attentional biases and chronic pain, as well as develop a hypothesis generating model, which can be used to direct future research into attentional biases in pain.

2. Systematic Review Methodology

The search was conducted in November 2014. Suitable studies were identified through a search of Medline, PsycInfo and CINAHL databases. A broad range of search terms were used to obtain titles and abstracts relevant to both attentional bias and pain. The search was restricted to human studies published since January 2001 to cover the period since Pincus and Morley's [27] review, which did not identify any studies that met the current inclusion criteria. A sample of articles was independently screened at the title and abstract stage and full text articles were determined by two authors. For search terms and an example of the full database search, see

Supplementary 1. The following journals were also manually searched: *European Journal of Pain*, *Pain*, *Cognitive Behaviour Therapy*, *British Journal of Health Psychology*, *The Clinical Journal of Pain*, *Pain Medicine*, and *The Journal of Pain.* In addition, reference lists from relevant reviews and articles were searched, using the ancestry method for additional articles, and key authors were contacted to provide in press and recently accepted publications. These strategies were used to reduce the risk of bias across studies.

For the initial search, 1941 titles and abstracts were screened and 187 full-texts were retrieved for further screening. A sample of 100 titles and abstracts were independently screened by two authors with good inter-rater reliability (Kappa= .76). The remaining full-text articles were screened and resulted in a consensus between two authors that eleven studies were eligible for inclusion in the current systematic review and an additional article was identified through searching relevant journals. The study selection flow diagram is outlined in Figure 1.

[FIGURE 1 NEAR HERE]

Studies were eligible for inclusion in this systematic review if they assessed attentional bias to pain using standard experimental paradigms including the modified Stroop task, the dot-probe paradigm, Posner's visual cuing task or an adapted spatial cuing task, or an attentional eye-blink task. Prospective and predictive studies were required to assess attentional biases using one of these standard paradigms *and* examine their predictive relationship with at least one measure or rating of subsequent pain. We included, therefore, studies that assessed pain after the assessment of attention biases, but not in the same session as we considered these cross-sectional. Experimental studies were included if the outcome of an intervention, which specifically targeted attention, was reported in comparison with a control intervention. Clinical and laboratory studies of pain and pain-free samples were included, as long as a measure of pain was included in the outcomes reported. Only controlled studies were included in order to maintain a higher quality of research. Where available pre-post intervention attentional bias and pain change scores were extracted, as were other pain-related secondary outcomes (such as disability and fear of pain), although these outcomes were not the main focus of the review.

The three types of intervention that were included were: (1) Attention Bias Modification (ABM); (2) Wells' attention re-training; and (3) mindfulness. Although other forms of attention training exist in the literature, only studies using these interventions met inclusion criteria. In ABM paradigms, the dot-probe task is used to implicitly train participants to either attend towards or away from pain-related stimuli. Participants are presented with two stimuli (either words or pictures/faces), one that is pain-related and one that serves as a control. One of these stimuli is then followed by a probe, which the individual has to respond to. In ABM, the probe either consistently follows the pain stimuli (training toward) or the control stimuli (training away). Change in attentional biases are the primary target of the intervention, and for this reason, all studies that used the dot-probe as a training paradigm were included regardless of whether attentional biases were assessed at pre and post-training.

Wells' attention re-training was originally designed for use in the treatment of panic disorder [42]. This paradigm involves deliberately training people to have more control over the direction of their attention and to subsequently use this control to attend away from threatening pain-related information. Whilst this intervention is focused primarily on attention, the mechanisms behind Wells' attention re-training have not been investigated and it is possible that this paradigm works to target aspects of the pain experience other than attention. Therefore, to be included, in addition to pain outcomes, studies needed to measure attentional bias outcomes.

Unlike Well's attention training and ABM, mindfulness does not focus on drawing attention away from pain, but on enabling focused attention to bodily sensations whilst at the same time reducing judgment and catastrophic interpretations of these sensations. Although attention is a core component of mindfulness, other mechanisms are thought to also be important, and therefore attentional bias outcomes and pain outcomes were necessary for mindfulness interventions to be included in this review.

Two authors independently performed a quality assessment of each study included in the systematic review (see Tables 1 and 2) using the criteria specified by Schoth et al. [30] in their meta-analysis of the dot-probe task investigating attentional biases in pain. This was adapted from the criteria used by Roelofs, Peters, Zeegers, and Vlaeyen [29] in their earlier meta-analysis. Additional criteria were adapted from the EPHPP Quality Assessment Tool for Quantitative Studies [26]. Inter-rater reliability for each individual criterion for the quality assessment was acceptable (Kappa = .60), and discrepancies were resolved via discussion. For quality assessment criteria and results, see Supplementary 2.

Effect sizes were included in order to explore the magnitude of significant results. For predictive studies, correlations were used as the primary effect size, except in the case where the outcome measure was categorical, in which case odds ratio was used, or in the case where the predictor was categorical, in which case Cohen's D was used as an indicator of effect size. For experimental studies, Cohen's D was used as the primary effect size. Effect size categories (small, medium, large) were determined based on recommendations in the literature [6]. Effect size confidence intervals were calculated by the authors based on available information. Researchers were contacted to provide further information where effect sizes were not present or able to be calculated from the text.

Importantly, effect sizes were not combined into a meta-analysis for three key reasons. First, the primary and a priori goal of the review was to descriptively summarise studies in order to understand patterns in the available data. Second, as argued in previous literature [13], the current literature is marked by considerable heterogeneity and it is not meaningful to create an aggregate of studies in this situation. Third, the small number of studies available meant there was insufficient information for the necessary moderator analyses to be employed for meta-analysis.

3. Results

3.1. Do Attentional Biases Predict Subsequent Pain?

Regarding whether attentional biases predict subsequent pain, only six articles reporting five prospective studies were identified that met the inclusion criteria [17-19; 25; 31; 38]. Two articles reported on the same study with an overlapping sample, although the follow-up outcome length differed [18; 19]. Of the five studies, three investigated individuals who were awaiting an acute medical procedure likely to cause pain, namely, minor gynaecological surgery, cancer surgery, or correction of chest malfunction, whilst one tested individuals with acute and sub-acute low back pain, and one tested individuals with chronic pain. Three of the studies used the dot-probe, one used the Stroop, and one used a modified spatial cueing task. In the three studies of individuals awaiting surgery, a measure of attentional bias was taken prior to surgery. Across the six articles, outcomes were assessed immediately post-surgery (n=3), 2 days later (n=1), or 3 and 6 months later (n=2). Tables 1 and 2 provide a summary of the descriptives and results of prospective studies reviewed, respectively. Overall quality of the articles was good, indicating low risk of bias.

[TABLE 1 NEAR HERE]

[TABLE 2 NEAR HERE]

All six articles included an assessment of pain, which was the primary outcome, and was measured either as pain intensity or the presence or absence of chronicity or clinically meaningful pain. In four of the six articles, some aspect of attentional bias directly predicted pain, although effect sizes ranged from negligible to small, with the exception of a medium effect size for the one study that reported a categorical pain outcome (high vs low pain intensity). Munafò and Stevenson [25] were the only ones to find, as predicted, that a bias *towards* pain-related words predicted future pain. They showed that those with greater attentional biases reported greater post-operative pain. In their version of the modified Stroop, physical pain words were presented at 100ms with masked presentation and hence this finding indicates that biases in initial orientation of attention to pain-related words predicted future pain.

Van Ryckeghem et al. [38] conducted the only study using the modified spatial cueing task. At stimuli presentation times of 200ms, attentional biases predicted average pain severity recorded over a two week period; however, when prior pain levels and demographic variables were controlled for, this association was no longer significant.

The four remaining articles that used the dot-probe to assess attentional biases all used longer presentation durations (500ms), but there were different patterns of findings. In a group of patients awaiting surgery for the correction of a chest malfunction, Lautenbacher et al. [18] found that biases away from pain words were the strongest predictors of post-operative pain, whilst positive and social threat words did not predict pain outcomes. In the same sample, Lautenbacher et al. [19] found that attentional biases did not predict pain outcomes at the three month follow-up. However, attentional bias towards positive (non-pain) stimuli predicted whether patients had clinically meaningful pain six months later, whilst there was no effect found for pain-related words or social threat words. At face value these findings appear conflicting, and it is difficult to determine which mechanisms and factors might be contributing to these mixed findings. However, it might be that biases towards positive stimuli and away from salient negative stimuli are different facets of the same process. Biases away from pain stimuli may, for example, signify an avoidance of pain and, in an effort to increase distraction away from pain, a bias towards positive stimuli may be observed. Indeed, this is not a new idea, and has been argued previously by Lautenbacher et al. [19] based on the findings of several studies [18; 19]. While this is a potentially contentious claim, if one makes this assumption, then Sharpe et al.'s [31] study is no longer inconsistent with Lautenbacher's claim. That is, Sharpe et al. found that biases away from affective pain words predicted chronicity of pain in acute and sub-acute low back pain patients, whilst biases towards sensory, disability and threat words were not significant predictors of chronicity. Finally, in an independent sample of cancer patients awaiting surgery, Lautenbacher et al. [17] found that attentional biases to pain, social threat, and positive words did not predict acute post-operative pain in a sample of patients undergoing surgery for cancer. However, it was notable that a bias away from pain words did predict analgesic use, which may partly explain the lack of relationship between biases and pain.

3.1. Disability as an outcome

In addition to pain, three articles measured disability as an outcome. In two of these studies disability was significantly predicted, although effect sizes were small. Sharpe et al. [31] found that affective pain word biases measured using the dot probe were negatively associated with disability both three and six months later; however, this relationship was no longer significant when other variables were controlled for in a regression analysis. Sensory pain, disability, and threat word biases did not predict disability at either time point. Similarly, Lautenbacher et al. [19] found that dot probe attentional biases towards pain, social threat, and positive words did not predict disability three and six months post-surgery. In contrast, Van Ryckeghem et al. [38] found that whilst a conditioned attentional bias was not a direct predictor of disability two weeks later, the pain-severity-attentional bias interaction was a significant predictor of disability. When taken together, these findings suggest that attentional biases alone may not account for pain-related disability, but rather that for individuals who have high levels of attentional bias, the experience of pain may be more likely to lead to disability.

3.2. Other outcome measures

Two studies measured amount of post-operative analgesia used as an outcome. Lautenbacher et al. [18] found that biases away from pain words were the strongest predictors of analgesia used in the two days post-operatively, whilst pain and positive word biases were not predictive. In an independent sample, Lautenbacher et al. [17] found that attentional biases towards pain words were a significant predictor of post-operatively requested analgesia one week post-surgery, whilst social threat and positive word biases were not predictive.

Other outcome measures were only measured in single studies. For example, Sharpe et al. [31] did not find attentional biases predictive of depression, anxiety or stress scores at three or six months. Finally, whilst Van Ryckeghem et al. [38] did not find attentional biases directly predictive of pain avoidance behavior or distractibility, there was a significant interaction between pain severity and attentional biases that predicted distractibility, such that for those with greater attentional biases, pain was a stronger predictor of distractibility.

3.3. Presence of attentional biases

When the presence of attentional bias was measured, it was included in the secondary analyses, even though biases may not necessarily be directly observable in healthy samples.

Munafò and Stevenson [25] conducted the only study using the Stroop task. Under masked presentation at 100ms, hypervigilance was found such that attentional biases towards physical pain words were observed within a healthy sample. However, attentional biases were not found with other stimuli presentations, such as neutral, positive and social threat words, nor for unmasked presentations of any stimuli. In the remaining five articles using the modified spatial cueing task [38] and the dot probe task [17-19; 31], attentional biases were not found to be significantly different from zero. However, in the only dot probe task study to use a pain sample at baseline, Sharpe et al. [31] found a significant difference in affective biases between the chronic pain group and the comparison group, with greater avoidance of affective pain words for those with chronic pain compared to those in the comparison group.

3.4. Can Modifying Attention Biases Impact the Experience of Pain?

Regarding attentional bias modification and the impact on pain, six articles reporting seven studies that met criteria were identified [4; 23; 32-35]. Most studies tested ABM via the modified dot-probe task (*n*=5), while one study used Wells's attention training task (ATT) and another used mindfulness. Six of the seven studies assessed attentional biases before and after the treatment. Four studies applied interventions in the laboratory on pain-free individuals and assessed the effect of these interventions on the cold pressor task (an acute experimental pain paradigm). The remaining three studies investigated the efficacy of the interventions on patients with fibromyalgia (*n*=1), chronic pain patients (*n*=1), or acute pain patients (*n*=1). Of the five dot-probe ABM studies, three studies compared ABM with placebo, and two compared ABM with a paradigm that trained participants towards pain-related stimuli. One dot-probe ABM study evaluated its efficacy as an adjunct to cognitive-behavioural therapy for chronic pain. Both the mindfulness and the ATT studies compared the tasks to a progressive muscle relaxation task.

Tables 3 and 4 provide a summary of the descriptives and main findings of these studies, respectively. The overall quality of the articles was good, indicating low risk of bias.

[TABLE 3 NEAR HERE]

[TABLE 4 NEAR HERE]

3.4.1. Effects of attention training on clinical pain outcomes

In the clinical samples, only one of three studies found evidence of an effect on pain outcomes. In an acute pain sample, Sharpe, et al. [32] found positive benefits of a single session of ABM. Compared with the placebo group, the ABM group reported less current and average pain (large effect sizes), and fewer days in pain three months later. This study differed from the other two studies in that it used acute pain patients and pain was one of the nominated primary outcomes. In contrast, the other two studies used chronic pain samples and did not find an effect on pain using ABM training [4; 32]; although Carleton et al. [4] found a trend approaching significance ($p = 0.06$). They both, however, found an effect on other measures of anxiety sensitivity, and Sharpe et al. [32] also found effects on disability.

Importantly, despite these clinical outcomes, none of the studies were able to document a training effect (although Carleton et al. [4] did not assess biases before and after treatment) and only in the acute pain sample [32] was change in bias correlated with pain outcomes. Hence, the mechanism of treatment is unclear.

3.4.2. Effects of attention training on laboratory pain outcomes

In the laboratory, all four studies assessed biases before and after treatment and used three measures from a cold pressor task: threshold (time to register pain), tolerance (length of time of pain tolerance), and pain intensity (at threshold, 30 seconds, and/or tolerance). Regarding intervention effects on attention, three of the four studies demonstrated the predicted training effects following treatment, such that the two ABM studies both found changes in attentional biases, and the ATT study found reductions in hypervigilance towards pain-related stimuli. The fourth study of mindfulness did not produce changes in attentional bias when compared with relaxation, and also did not produce changes in any of the pain outcomes [35]. Effect sizes ranged from negligible to medium, but were generally small.

For the three studies that did show evidence of changes in attentional processes [23; 33; 34], all three found that following the attention training participants took longer to register pain compared to the control condition. Only one of the three studies showed an impact of ABM on pain intensity, and none showed an impact of attentional training on tolerance. Hence, it seems that treatments that are able to successfully change attentional processes appear to influence how quickly participants identify pain, which is arguably a behavioural indicator of hypervigilance to pain-related sensations. Although changes in pain threshold were consistently found in studies where attentional processes changed, which shows greater confidence in the proposed mechanism than is available in clinical studies, it remains the case that only McGowan et al. [23] found associations between changes in attentional biases and pain outcomes.

3.4.3. ***Effects of attention training on secondary outcomes***

Two experimental studies included secondary outcome measures in addition to pain outcomes. Carleton et al. [4] measured fear of pain, anxiety sensitivity, injury sensitivity, and pain anxiety, and found significant reductions in fear of pain and anxiety sensitivity in the ABM experimental group, with small effect sizes. However, these findings must be interpreted with caution as the ABM group was not directly compared to the control group, a one-tailed test was used and the sample size was small (n=8 for each group). Sharpe et al.'s [32] second study included a range of secondary outcomes including disability, anxiety sensitivity, fear of pain, and mood that were measured both immediately post and 6 months following ABM training. Post intervention, significant improvements in disability in the ABM group in comparison to the control group were observed. These improvements in disability were maintained at 6 months follow-up. Furthermore, at 6 months, significant improvements in anxiety sensitivity and fear of movement were also observed. These effects ranged from small to medium in size.

3.5. Summary of Results

Overall, the prospective studies were mostly consistent in finding that some aspect of attentional bias predicted pain outcomes; however, the pattern of findings differed across studies. One possible explanation for this pattern of results is the vigilance-avoidance hypothesis for which there is mounting evidence in the anxiety disorders [24]. According to the vigilance-avoidance hypothesis, anxious individuals under high threat show immediate vigilance towards threat, which is supported in the only study that assessed early attentional processes [25]. This initial vigilance is then followed by an avoidance of threat; an avoidance of negative (or focus on positive) stimuli was identified in the remaining studies, although the precise stimuli to which biases were observed differed between studies. Whilst speculative, if Lautenbacher et al.'s [19] premise that biases towards positive stimuli is another facet of biases away from pain stimuli is accepted, the vigilance-avoidance hypothesis appears to fit the available data. Preoperative biases consistently predict pain in some instances up to six months after surgery [17; 19], suggesting that attentional biases have an important role in the development of pain. However, further research is warranted to determine the mechanisms behind these effects.

The attention modification literature shows some promise, particularly in laboratory settings. These studies have shown that interventions that change attentional processes are generally effective, particularly in changing pain threshold (i.e. how quickly a person recognises pain). However, while the clinical applications have been promising, it is premature to conclude that ABM is consistently efficacious. All three clinical studies reported effects on at least one outcome. However, given the variety of populations, measures, stimuli and parameters, if one looks at individual outcomes (e.g. pain), the data are less compelling. Similarly, the lack of a plausible mechanism is problematic. This is particularly the case, since if the process that is identified in prospective studies is vigilance-avoidance, then it is unclear that the training away paradigms employed in ABM studies to date should be efficacious. The reliability of measurement tasks such as the dot-probe has also been questioned [10], and more direct measurement of attentional bias (such as eye tracking) may help to elucidate the mechanisms of change. Researchers have called for further exploration and improvement of attentional bias modification procedures until these procedures can consistently modify biases [5]. Measuring cognitive change through pre-post attentional bias assessments (which was present in most studies reviewed), as well as systematically manipulating task parameters have also been recommended in order to better understand and improve modification procedures [22].

4. Discussion

The Proposed Threat Interpretation Model

Although previous theories have all highlighted an important role for attentional biases in pain, theories to date have not considered the exact nature of attentional processes and the way in which they may contribute to the experience of pain. The aim of the *Threat Interpretation Model* (see Figure 2) proposed here is to provide, on the basis of available evidence, a hypothesis-generating model that can guide and be evaluated in future attention bias research.

[FIGURE 2 NEAR HERE]

In cross-sectional studies, it is the spatial cueing task which has found the most robust attention biases towards pain-related stimuli [8]. This is perhaps unsurprising, since the bias tested here is in response to somatosensory stimuli, which is most ecologically valid in terms of the pain experience [36]. In contrast, the most widely used tasks to assess attention bias have been the dot-probe and Stroop tasks using word stimuli. These tasks arguably measure a bias towards words that represent aspects of the pain. In order for participants to be able to respond to these words as pain-related, they firstly have to categorize these stimuli as pain-related. That is, these paradigms rely on the interpretation of sometimes ambiguous word stimuli (e.g. sharp, boring) as pain-related. Hence, in understanding the available literature, one would assume that interpretation biases that favour pain-related interpretations are necessary, although not sufficient, for attentional biases to pain-related word stimuli to be observed. This interpretation bias may be less relevant for other types of stimuli (e.g. faces, [15; 16], or pictures [9]), although may be present to varying degrees.

Once the stimuli are categorized as pain-related, the degree to which someone will demonstrate a bias towards that stimulus is likely to depend upon the salience of that stimulus to the individual. Most theories of pain suggest that the salience is determined by the degree to which participants find the pain experience threatening or fearful [e.g. 11; 41]. Hence, we would anticipate that it is not the experience of pain alone that necessarily influences attentional biases, but the degree to which the pain is interpreted as threatening.

There is now good meta-analytic evidence that there are biases towards sensory pain stimuli on reaction time tasks in chronic pain patients *and* healthy controls, although this is marginally greater for chronic pain patients [8]. The meta-analytic findings give only a snapshot of where attention is placed at the time of the assessment and therefore eye tracking studies can help to disentangle the processes more clearly. Recent eye tracking studies have found an engagement bias and a pattern of initial vigilance to pain-related words even in healthy participants [28; 43]. Interestingly, both studies found that this initial vigilance was followed by faster disengagement from pain-related stimuli than other neutral stimuli (i.e. avoidance). The authors of these studies argued that there may be benefit to immediate orientation towards pain-related stimuli and, when that stimulus has no threat value, to disengaging from it quickly to maintain positive mood [28]. Other studies investigating the time-course of attentional processes have also found similar patterns of speeded orientation followed by avoidance [2]. This pattern of vigilance-avoidance in healthy participants appears consistent with the previous interpretation of prospective studies, such that initial vigilance and then subsequent avoidance of salient negative information (or focus on positive) was associated with a range of outcomes across studies. It therefore appears that vigilance and avoidance could potentially indicate a *vulnerability* to the experience of subsequent pain (and associated disability). What is particularly interesting is that previous meta-analytic research [30] suggests that, for the *maintenance* of chronic pain, difficulty disengaging may be a more relevant attentional process. Although the pattern proposed here would need be further investigated and remain preliminary, when taken together with the meta-analytic findings it appears that different patterns of attentional processes may be important at different stages of the development and maintenance of chronic pain.

Previous theoretical models are consistent with the vigilance-avoidance hypothesis. For example, within the fear of (re)injury model [41] and its successor the fear avoidance model [7], It is proposed pain-related fear leads to hypervigilance towards pain, as well as an avoidance of further pain and injury. However, the time course of these processes is not specified, and nor is the role of attention and interpretation made explicit. One advantage of the *Threat Interpretation Model* is that it generates testable predictions, particularly about the role that these attentional processes play, and how these attentional processes are influenced by interpretation.

In addition to looking at the pattern of attention over time and the role of interpretation, it is important to determine in what way high levels of threat might impact this vigilance-avoidance pattern. Threat is not a new construct in the pain literature, and has been incorporated into previous theoretical models such as the cognitive affective model of attention and pain [11]. The cognitive affective model suggests that while it is usual for pain to capture attention, individuals have difficulty disengaging from pain stimuli under conditions of threat. The failure to disengage effectively from painful stimuli is thought to interfere with efforts to engage in appropriate goal-directed function, which contributes to the risk of increasing disability. The *Threat Interpretation Model* differs in that it proposes that avoidance rather than difficulty disengaging is important in high threat environments. Other researchers have also indicated the importance of threat [37], particularly explaining how attentional bias influences pain through threat mechanisms rather than attentional deficits. However, to date the *Threat Interpretation Model* is the first to explicitly outline this relationship and propose that the mechanism underlying the influence of threat on attention is interpretation. Furthermore, the model proposes that different levels of threat may influence attentional processes differently.

Evidence from a number of sources suggests that, under high levels of threat, initial orientation or vigilance continues to increase as the level of threat increases, at least to sensory pain words. In available eye-tracking studies comparing chronic pain to healthy controls, greater vigilance has been demonstrated to pain stimuli [21; 43]. This is also the case for those studies that have compared high vs. low fear of pain in both chronic pain [43] and healthy participants

[44]. Further, in the only prospective study, to date, examining orientation biases (masked presentation at 100msec), Munafo and Stevenson [25] confirmed that biases towards pain stimuli were associated with future pain. Further, this is potentially consistent with the meta-analytic data [8; 30]. Hence, there appears to be relatively strong evidence from a variety of sources indicating that orientation biases increase under conditions of threat, at least for sensory aspects of pain.

What is less clear is the nature of biases of sustained attention that are relevant to the development or maintenance of pain. This is where the cross-sectional and prospective data is conflicting. That is, cross-sectional data indicates larger attentional biases at longer presentation intervals, which has been interpreted as difficultly disengaging, whereas it has been the avoidance of pain-related and other salient negative information (or a focus on positive) which has predicted future pain in prospective studies. Eye tracking literature has found biases in orientation indicating vigilance, but also found earlier disengagement from pain words amongst chronic pain patients compared to controls indicative of avoidance [43]. While Liossi et al. [21] did not find this effect, there was also a trend towards avoidance in their study. Yang et al. [44] found the same pattern for high fear of pain participants in another study, as did Vervoort [39; 40] with parents of children with pain who were high in catastrophizing. Indeed, avoidance increased as the severity of the pain faces increased (i.e. increasing threat of the stimuli). Thus, there is increasing evidence to suggest that when threat is sufficiently high, the attentional biases towards threat switch to a mechanism of avoidance (see Figure 3). The primary predictions from the Threat Interpretation Model are further outlined in Table 5.

[FIGURE 3 NEAR HERE]
[TABLE 5 NEAR HERE]

Although this potentially links prospective and experimental studies, what remains unclear is why then would modifying attentional biases by training people away from pain-related stimuli lead to improved pain, if avoidance is the putative mechanism through which attentional biases result in poorer outcomes. One possibility is that it may be the stimuli which are important. In Pincus and Morley's [27] seminal paper, they differentiated between sensory and affective components of pain and argued that sensory aspects of pain would be preferentially attended to by all pain patients, whereas only those who are depressed would attend towards affective pain words. While that prediction has not been borne out, there is evidence that affective and sensory pain words play different roles. For example, Sharpe et al. [31] found that acute pain patients did demonstrate a bias towards sensory pain words, as previously demonstrated [14], but that avoidance of affective pain words predicted subsequent chronicity. In the laboratory it has also been shown that threat can influence training effects. Boston and Sharpe [3] found that attending to sensory aspects of pain was helpful under condition of low threat, relative to affective pain, whereas the opposite was true under high threat. Therefore, it may be that different stimuli produce a different pattern of attentional processes. To date, the majority of ABM studies have trained towards either all pain words (e.g. sensory pain, affective pain, threat, disability) or sensory pain words only. It seems that it is avoidance, particularly of the affective components of pain, which might be important. Therefore, it is possible that ABM protocols are effective by training only one aspect of attention (e.g. reduced vigilance), or from changes in biases towards some stimuli but not others.

4.1. Recommendations and Conclusions

Given that the literature reviewed is widely varied and still emerging, any conclusions that are drawn from the *Threat Interpretation Model* generated remain tentative. In addition, the small number of studies and variations in training paradigms, stimuli, samples and outcomes mean that conclusions drawn from this research remain preliminary and require further testing. Nonetheless, the prospective literature appears to generally fit a pattern of vigilance followed by avoidance, and the proposed *Threat Interpretation Model*, whilst preliminary, generates testable hypotheses about attentional processes. For example, interpretation biases should be associated with attention biases, particularly to words on the dot-probe paradigm. In addition, under conditions of threat, a pattern of increasing vigilance is likely to be observed. Finally, whilst avoidance may be helpful under conditions of low threat as the individual can disengage to carry out other tasks, avoidance under high threat may be detrimental and contribute to poor pain outcomes. These predictions should be tested, and, if found to hold, could be used to build theory based interventions. Intervention tools may integrate ABM strategies, cognitive-behavioural approaches, and other strategies that target not only attention but also threat and interpretation, which would be in keeping with recent recommendations in the literature [38].

To summarize, the aim of this article was to answer the question recently posed about attentional biases: do they matter [20]? On the basis of available evidence it appears that attentional biases do matter, but are the product of a complex relationship between the nature of the pain, threat interpretation and other individual factors, and characteristics of the task used to assess the attentional biases. The primary pattern of biases that predicted pain under conditions of high threat was initial vigilance, followed by avoidance of negative stimuli (or a focus on positive stimuli). Further, manipulating biases through attention bias modification showed some promise in the management of pain in a range of settings in which it has been trialled, although these changes did not consistently map changes in attentional biases. For this reason, Clarke et al. [5] have made a call for better training paradigms that can reliably change attentional biases.

The use of different stimuli, different directions of training and eye tracking technology could help to disentangle the processes involved and thereby maximize the efficacy of ABM protocols.

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TABLES

Table 1

Summary of prospective research descriptives and quality ratings

	Population	N	Task	Word stimuli used	Stimuli presentation time	Quality assessm rating/
Lautenbacher et al. (2011)	Undergoing surgery, primarily for cancer	58	Dot-probe	Affective pain, affective positive, social threat	500ms	7
Lautenbacher et al. (2009)	Undergoing corrective surgery for chest malformation	54	Dot-probe	Affective pain, affective positive, social threat	500ms	7
Lautenbacher et al. (2010)	Undergoing corrective surgery for chest malformation	84	Dot-probe	Affective pain, affective positive, social threat	500ms	8
Munafo & Stevenson (2003)	Undergoing gynaecological surgery	47	Dot-probe	Physical threat, social threat	100ms	8
Sharpe, Haggman et al. (2014)	Individuals with acute/sub-acute lower back pain	100	Stroop	Sensory pain, affective pain, disability pain, threat pain	500ms	9
Van Ryckegham et al. (2013)	Individuals with chronic pain	69	Modified spatial cueing task	N/A	200ms	10

Note. AB= attentional bias.

Table 2a

Summary of prospective research with attentional bias predicting pain outcomes

Article	**Outcome; follow up length**	**Attentional Bias Stimuli**				**Direction of bias; notes**	**Effect size**			
		Pain	**Disability**	**Social threat**	**positive**		**Value**	**Size[+]**	**95% CI**	
									Lower	**Upper**
Lautenbacher et al. (2011)	Post-operative pain intensity (11pt NRS); < 1 day	NS	-	NS	NS					
Lautenbacher et al. (2009)	Post-operative pain intensity (11pt NRS); 1 week	**Y**	-	NS	NS	Away from general pain	R=-0.292	Small	-0.519	-0.026
Lautenbacher et al. (2010)	Post-operative pain intensity (11pt NRS); 3 months	NS	-	NS	NS		D=0.507	Medium	*	*
	Post-operative	NS	-	NS	**Y**	Towards	D=0.648	Medium	*	*

	pain intensity (11pt NRS); 6 months					affective bias				
Munafo & Stevenson (2003)	Pain intensity (SF-MPQ); < 1 day	**Y**	-	-	-	Towards physical threat	r=-0.251++	Small	-0.502	0.039
Sharpe et al. (2014)	Chronicity (dichotomous); 3 months	**Y**	NS	NS	-	Away from affective pain	OR=0.98	Negligible	0.97	1.00
	Chronicity (dichotomous); 6 months	**Y**	NS	NS	-	Away from affective pain	OR=0.98	Negligible	0.95	1.00
Van Ryckegham et al. (2013)	Pain severity (MPI); 2 weeks	**Y**/NS	-	-	-	NS when other measures controlled for				

Note: AB= attentional bias, SF-MPQ= Short Form McGill Pain Questionnaire, NRS= numerical rating scale, MPI= multidimensional pain inventory, m= months, NS= not significant. +Descriptor based on Cohen's [1] classifications of effect sizes.

++ Effect sizes not available or calculable from text, provided by authors

Table 2b

Summary of predictive research with attentional bias predicting disability

Article	Outcome; Follow up length	Attentional Bias Stimuli				Direction of bias; notes	Effect Size			
		Pain	**Disability**	**Social threat**	**Positive**		**Value**	**Size**$^{+}$	**95% CI**	
									Lower	**Upper**
Lautenbacher et al. (2010)	Disability; 3 months	NS	-	NS	NS					
	Disability; 6 months	NS	-	NS	NS					
Sharpe et al. (2014)	Disability; 3 months	**Y**/NS	NS	NS	-	Away from affective pain; NS when other measures controlled for	r=0.177	Small	-0.021	0.362
	Disability; 6 months	**Y**/ NS	NS	NS	-	Away from affective pain; NS when other	r=0.217	Small	0.020	0.397

						measures controlled for				
						Towards sensory pain; NS when other measures controlled for	r=0.210	Small	0.013	0.391
Van Ryckegham et al. (2013)	Disability; 2 weeks	NS	-	-	-	NS; but AB significant moderator of pain/disability	r=0.18	Small	-0.051	0.392

Note: AB= attentional bias, NS= not significant. +Descriptor based on Cohen's [1] classifications of effect sizes. ++ Effect sizes not available or calculable from text, provided by authors

Table 2c

Summary of predictive research with other outcomes, by attentional bias stimuli

Article	Outcome	Attentional Bias Stimuli				Direction of bias; notes	Effect Size		
		Pain	Disability	Social	Affective		Value	Size+	95% CI

				threat	positive				Lower	Upper
Lautenbacher et al. (2011)	Analgesics; 2 days	N	-	**Y**	NS	Away	*	*	*	*
Lautenbacher et al. (2009)	Analgesics; 1 week	**Y**	-	NS	NS	Away	r=-0.157	Small	-0.408	0.116
Sharpe et al. (2014)	D/A/S; 3 months	NS	NS	NS	-					
	D/A/S; 3 months	NS	NS	NS	-					
Van Ryckegham et al. (2013)	Avoidance behavior; 2 weeks	NS	-	-	-					
	Distractibility; 2 weeks	NS	-	-	-	NS; but AB significant moderator of pain/ distractibility	r=0.17	Small	-0.061	0.444

Note: AB= attentional bias, D/A/S= DASS depression anxiety stress scale, Analgesics= amount of requested analgesics NS= not significant.

+Descriptor based on Cohen's [1] classifications of effect sizes. ++ Effect sizes not available or calculable from text, provided by authors

Table 3

Summary of experimental research descriptives and quality ratings

	Population	N	Biases measured pre/post treatment	Nature of training	Training compared with	Quality assessment rating/10
Carleton et al. (2011)	Fibromyalgia patients	17	No	Dot-probe ABM	Dot-probe placebo	7
McGowan et al. (2009)	University students	104	Yes	Dot-probe ABM	Trained away from pain stimuli	8
Sharpe et al. (2012) - Study 1	Individuals with acute pain	54	Yes	Dot-probe ABM	Dot-probe placebo	10
Sharpe et al. (2012) - Study 2	Individuals with chronic pain	34	Yes	Dot-probe ABM	Dot-probe placebo	10
Sharpe, Johnson & Dear (Submitted)	University students	128	Yes	Dot-probe ABM	Trained away from pain stimuli	9
Sharpe et al. (2010)	University students	103	Yes	Wells' attention training	Progressive muscle relaxation	8
Sharpe et al. (2013)	University students	140	Yes	Mindfulness	Progressive muscle relaxation	8

Note: ABM= attentional bias modification

Table 4a

Summary of experimental research- clinical pain outcomes

Article	Effects on AB	Direction of effect	Outcome; follow up length	Effects on pain	Direction of effect	Effect Sizes			
						Value	Size	95% CI	
								Lower	Upper
Carleton et al. (2011)	N/A	Not measured	Pain severity	NS					
Sharpe et al. (2012) - Study 1	NS		Pain severity; Post	NS					
			Pain severity; 3 months	**Y**	Improvements in ABM group vs. placebo	D=-0.602	Large	-1.461	-0.342
			Average pain severity; 3 months	**Y**	Improvements in ABM group vs. placebo	D=-0.926	Large	-1.487	-0.365
			# days in pain; 3 months	**Y**	Improvements in ABM group vs. placebo	D=-0.070	Negligible	-0.603	0.464
Sharpe et al. (2012) - Study 2	NS		Pain severity; Post	NS					
			Pain severity; 6 months	NS					

Notes: AB= attentional biases, ABM = attentional bias modification

Table 4b

Summary of experimental research- laboratory pain outcomes

Article	**Effects on AB**	**Description**	**Pain Outcome**	**Effects on pain**	**Description**	**Effect Sizes**			
						Value	**Size**	**95% CI**	
								Lower	**Upper**
McGowan et al. (2009)	NS		CP threshold	**Y**	Training towards pain stimuli reduced threshold compared to neutral training	-0.393	Small	-0.781	-0.005
			CP 30s pain	**Y**	Training towards pain stimuli increased pain compared to neutral training	0.417	Small	0.029	0.806
			CP tolerance	NS					
			CP tolerance pain	NS					

Sharpe et al. (2010)	**Y**	*Hypervigilance:* 3 way (group, time, stimuli) interaction: ATT reduced hypervigilance towards sensory pain words over time, whilst relaxation group became more hypervigilant to sensory pain words. No changes for affective words. *Disengagement:* no effects	CP threshold	**Y**	ATT group slower to register pain than relaxation group	0.427	Small	0.038	0.816
			CP 30s pain	NS					
			CP tolerance	NS					
			CP tolerance pain	NS					
Sharpe et al. (2013)	**Y**	3 way (threat, time, group) interaction: increased bias towards painful words for	CP threshold	NS					
			CP tolerance	NS					

		relaxation high threat group, and for those in mindfulness low threat group. No change over time for relaxation high threat or mindfulness low threat	CP average pain rating	NS					
Sharpe et al. (In Press)	**Y**	*Pain stimuli:* 2 way (time, group) interaction: increased bias towards pain stimuli when trained towards; increased bias away from pain stimuli when trained away	CP threshold	**Y**	Improvements in ABM training away from vs. training towards pain	Pain faces: D=-0.001	Negligible	-0.516	0.514
						Pain words D=-0.787	Medium	-1.339	-0.222
		Happy stimuli: no effects	CP tolerance	NS					
			CP average pain rating	NS					

Notes: CP = cold pressor, AB = attentional biases, ABM = attentional bias modification, ATT = Well's attention training

Table 4c

Summary of experimental research- other outcomes

Article	Effects on AB	Description	Pain Outcome	Effects on pain	Description	Effect Sizes			
						Value	Descriptor	95% CI	
								Lower	Upper
Carleton et al. (2011)	N/A	Not measured	Fear of pain	**Y**	Significant fear of pain reductions for experimental group; no changes in control group (groups not compared directly)	D=0.262	Small	-0.775	1.299
			Anxiety sensitivity	**Y**	Significant anxiety sensitivity reductions for experimental group; no changes in control group (groups not compared directly)	D=0.202	Small	-0.833	1.238
			Injury sensitivity	NS					

			Pain anxiety	NS					
Sharpe et al. (2012) - Study 2	NS		Disability (post)	**Y**	Significant improvements in disability for experimental group compared to control group	D=0.45	Small	0.26	1.42
			Anxiety sensitivity (post)	NS					
			Fear of pain (post)	NS					
			Mood (post)	NS					
			Disability (6 months)	**Y**	Significant improvements in disability for experimental compared to control group	D=0.55	Medium	0.33	1.35
			Anxiety sensitivity (6 months)	**Y**	Significant improvements in anxiety sensitivity for	D=0.75	Medium	0.05	1.66

			experimental compared to control group				
	Fear of pain (6 months)	NS					
	Fear of movement (6 months)	**Y**	Significant reductions in fear of movement for experimental compared to control group	D=0.65	Medium	0.28	1.4
	Mood 6 months)	NS					

Notes: AB= attentional biases

Table 5

Hypotheses arising from the Threat Interpretation Model

Impact of threat and interpretation:	
Interpretation biases	As threat increases, interpretation biases increase (i.e. more likely to interpret pain stimuli as threatening)
Initial vigilance	As threat interpretation increases, initial vigilance towards pain-related stimuli will increase.
Sustained attention	The relationship between threat and sustained attention will be non-linear (see below)
Sustained attention and threat:	
Low threat	Participants will disengage easily from threat (i.e. low levels of attention bias)
Moderate threat	Participants will have difficulty disengaging from threat (i.e. high levels of AB)
High threat	Participants will avoid threatening stimuli (i.e. negative levels of AB)
Relationship between interpretation bias and attention bias:	
Interpretation biases will be associated with attentional biases to ambiguous stimuli (e.g. pain-related words)	
The relationship between threat and attentional biases should be mediated by interpretation biases	
The relationship between interpretation biases and AB will be higher under conditions of high threat	
The relationship between interpretation biases and pain outcomes should be mediated by attentional biases	

FIGURES

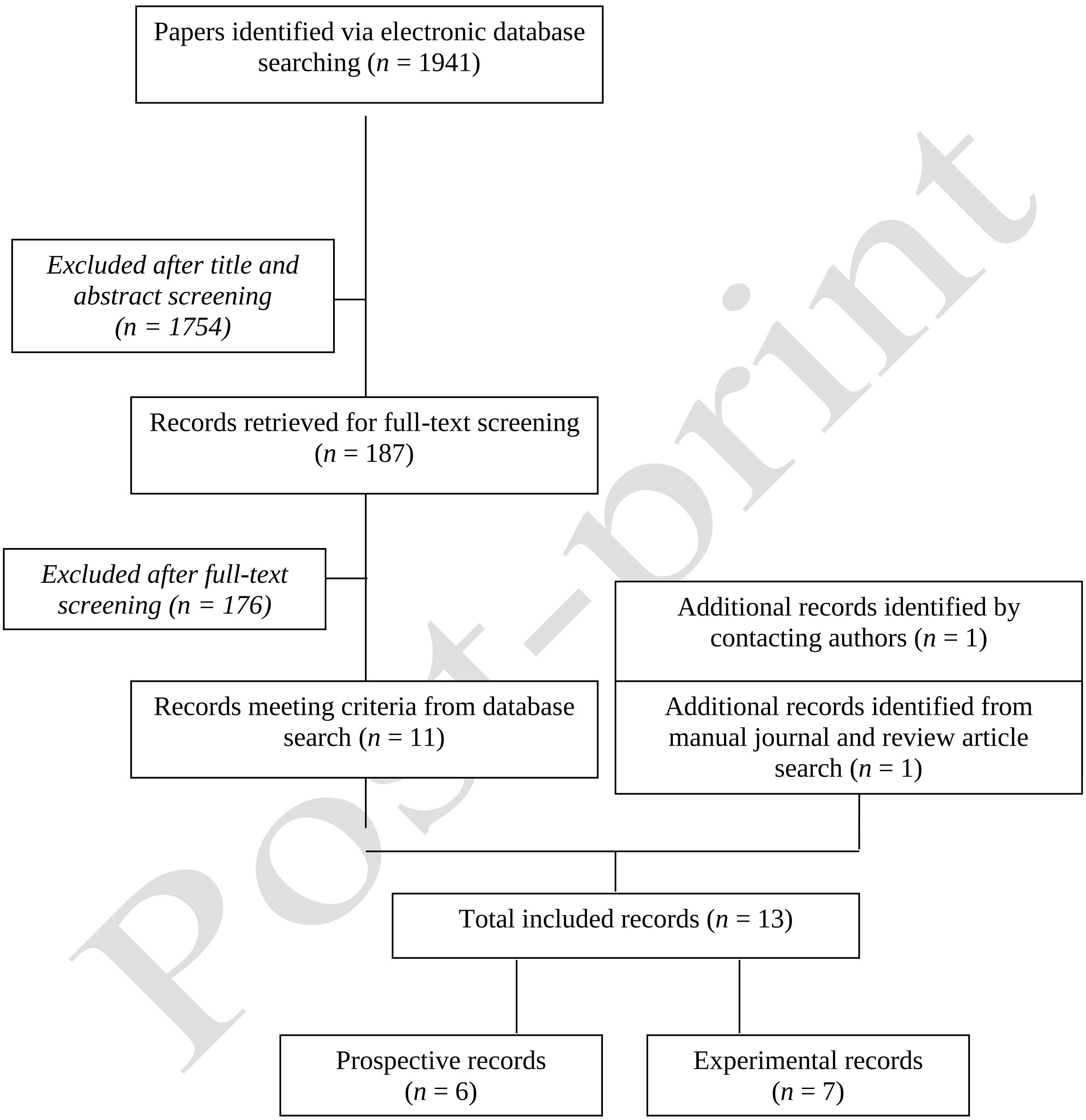

Figure 1. Flowchart outlining the screening and study selection process.

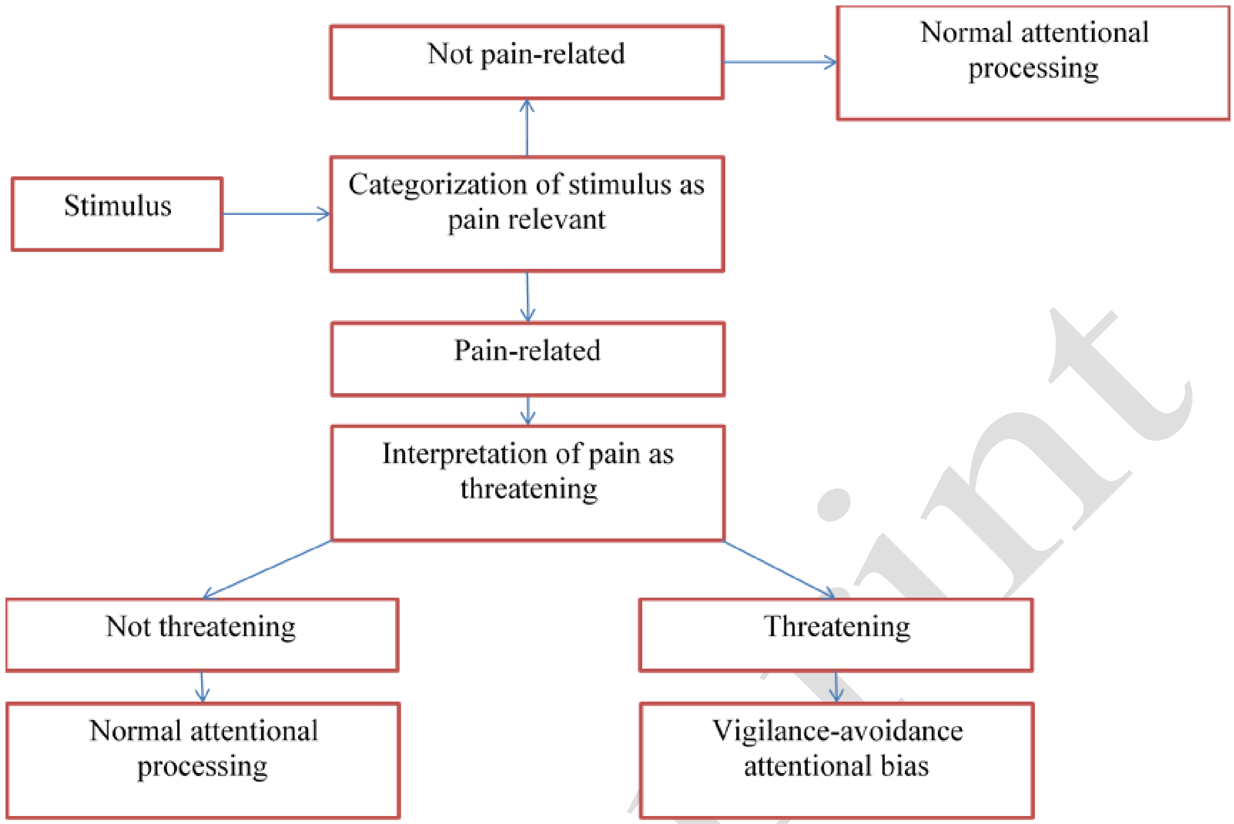

Figure 2. An integrated threat interpretation model of attentional biases to pain

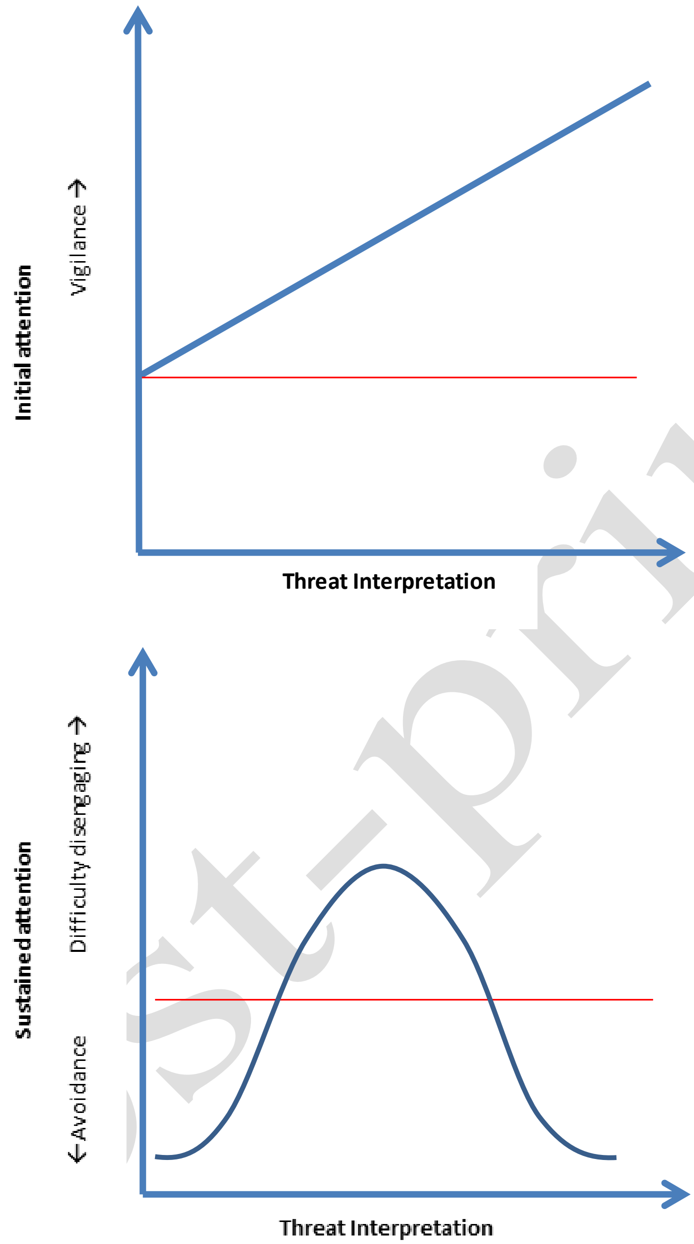

Figure 3. The vigilance-avoidance hypothesis within the Threat Interpretation Model