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Attentional bias modification and pain: The role of sensory and affective stimuli

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Word count: 7107

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Keywords: Attentional bias modification; pain; intervention; attention

ABSTRACT

There is growing evidence to support attentional bias modification (ABM) techniques such as the modified dot-probe task within the pain literature. Such techniques can help to inform theoretical models of pain by identifying the causal role of attentional bias constructs. The aim of this research was to explore the effects of dot-probe ABM that trains individuals towards (+) or away from (-) sensory (S) and affective (A) pain words, on attentional biases, interpretation biases, and pain outcomes. Healthy undergraduate students (N= 106) completed questionnaires, an attentional bias dot-probe task, and an interpretation bias task before and after ABM, one of four ABM versions that differed in training direction (S+A+, S-A+, S+A-, S-A-), and pain outcomes using the cold pressor task. Those trained towards affective pain words were found to have a greater pain threshold but also greater distress at tolerance. However, mechanisms of change could not be established, as ABM did not affect attentional or interpretation bias, even though changes in attentional bias were associated with pain outcomes. These findings provide partial support for the threat interpretation model and highlight the utility of affective pain ABM, although further investigation of causal mechanisms is warranted.

Introduction

Research exploring the role of attentional biases in the experience of pain is growing rapidly, with a number of recent systematic reviews (Pincus & Morley, 2001; Todd et al., 2015) and meta-analyses (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013; Schoth, Nunes, & Liossi, 2012) having been published. Importantly, although most researchers agree that attentional biases play a role in pain, the specific nature of these attentional biases is still yet to be determined and research to date remains somewhat inconsistent regarding the best parameters under which to detect these biases. For example, in Crombez et al.'s (2013) meta-analysis of cross-sectional studies, the strongest attentional biases were observed for sensory pain stimuli (e.g. shooting, burning), with biases towards sensory pain words being present in chronic pain patients in comparison with healthy participants. They did not however find any relationship between attentional biases and pain outcomes. Conversely, we recently reviewed prospective studies and found that avoidance of salient stimuli or a bias towards positive stimuli predicted chronicity (Todd et al., 2015).

A number of models have implicated cognitive processing biases such as attentional bias in the development and maintenance of chronic pain. For example, within the fear of (re)injury model (Vlaeyen & Linton, 2000) and subsequent fear-avoidance model (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012), it is proposed that chronic pain is maintained through a process of catastrophic pain interpretation and pain-related fear, which leads to attentional hypervigilance in an attempt to avoid further pain, which in turn contributes to increased depression and disability.

The role of attentional bias in pain has also been investigated using attentional bias modification (ABM) procedures, which is often based on a modified dot-probe task (MacLeod, Mathews, & Tata, 1986). Dot-probe ABM, in the context of pain research, involves training individuals to pay attention towards or away from pain-related information, and as such is designed to specifically reduce pain by influencing attentional processes that are thought to underlie how pain-related information is processed. To date there has been some success in using ABM to improve pain outcomes or associated disability in both chronic and acute pain samples (Sharpe et al., 2012) and in laboratory research (McGowan, Sharpe, Refshauge, & Nicholas, 2009; Sharpe, Johnson, & Dear, 2015). Our recent review of prospective pain literature suggested that whilst ABM is promising and generally leads to improvement on at least one primary pain outcome, the mechanisms of this improvement are less clear (Todd et al., 2015). However, despite improvements in pain outcomes, ABM training does not consistently bring about changes in attentional biases, the assumed mechanism, particularly in clinical samples (Todd et al., 2015).

ABM procedures training *away from* pain-related information have tended to result in improvements in pain outcomes in comparison with training towards pain-related information (McGowan et al., 2009; Sharpe et al., 2015). These ABM procedures have been developed from the predictive research in which individuals with chronic pain tend to exhibit a bias *towards* sensory pain information that is not present in healthy participants (Crombez et al., 2013). However, some research has found an opposite pattern; particularly for affective pain stimuli. For example, although acute pain patients exhibit the same biases towards sensory pain words that have been identified in chronic pain patients, these biases do not predict subsequent pain. Rather, biases *away from* affective pain stimuli (e.g. unbearable, vicious) have been found to

predict the development of chronicity in acute pain patients (Sharpe et al., 2014). If one were to rely on the prospective literature to develop ABM protocols, it would be expected that ABM procedures training *towards* affective pain-related information would be more effective. Whilst training towards affective pain-related information has not been investigated for pain, training individuals towards threat stimuli has been applied to PTSD, where evidence that avoidance is a putative attentional process also exists. For example, Bar-Haim et al. (2010) found that amongst those exposed to real bomb threats, those who avoided threatening stimuli showed increased distress. Similar results were found by Wald et al. (2011), whereby those who avoided threatening stimuli during real threats of rocket attacks had increased risk of PTSD. Based on the existing ABM findings for threat, Wald et al. (In Press) developed an ABM protocol that trained Israeli soldiers to attend *towards* threatening stimuli. The results indicated that ABM training towards threat was associated with fewer PTSD symptoms following deployment in comparison to a placebo control group.

Whilst attentional biases towards threat and pain are not identical, it is important to note that the patterns of attentional avoidance of threat described in relation to PTSD appear to most closely match studies exploring attentional processes in relation to affective pain stimuli. That is, in pain there is evidence of a bias towards sensory pain words, but it appears that avoidance of affective pain is subsequently associated with poorer outcomes. Within the pain literature, it has tended to be sensory pain biases that have been modified with ABM (Schoth & Liossi, 2010; Sharpe et al., 2015) or a combination of sensory, affective, threat and disability words has been used with no ability to distinguish stimulus specific effects (McGowan et al., 2009; Sharpe et al., 2012). There is very little research comparing the effectiveness of training with different types of stimuli and comparing training towards and away from these stimuli. Therefore, we wanted to

investigate the efficacy of training towards versus training away from both sensory and affective pain words in a laboratory pain paradigm.

Another complicating factor for ABM pain research is that attentional bias is a dynamic rather than a single static construct that is assessed using reaction time responses to the dot-probe paradigm (Crombez, Heathcote, & Fox, 2015). More recently, eye tracking measures have been successfully used to determine different attentional components that may be present (Priebe, Messingschlager, & Lautenbacher, 2015; Yang, Jackson, & Chen, 2013; Yang, Jackson, Gao, & Chen, 2012) and have been argued to be more accurate and reliable than traditional reaction time measures of attention (Cooper & Langton, 2006; Sharpe, 2014).

The time course of attentional biases has been further explored in the threat interpretation model (Todd et al., 2015), which was recently developed from the available prospective and experimental research. The threat interpretation model makes a number of predictions, including that as threat increases, attentional biases will be characterised by increased attentional vigilance at early stages of attentional processing. At later stages of attentional processing, it is proposed that there will be a pattern of effective disengagement with low threat, difficulty disengaging with moderate threat, or avoidance with high threat levels. Further, the threat interpretation model suggests that attentional biases are likely to depend on whether or not pain information is interpreted as threatening. Interpretation biases are defined as the interpretation of ambiguous information as being threatening (or painful) in the absence of sufficient contextual cues (Pincus & Morley, 2001). Therefore, according to the threat interpretation model it is expected that ABM procedures may have some effect on interpretation biases, as has been found in anxiety literature (White, Suway, Pine, Bar-Haim, & Fox, 2011), but is yet to be tested for pain. Cross-sectional research has found an association between pain-related attentional bias and questionnaire

measures of interpretation bias (Keogh & Cochrane, 2002). There has also been one study that has investigated this relationship using a computer based reaction time measure of biased interpretation, however that study failed to find an association (Todd, Sharpe, Colagiuri, & Khatibi, In Press). To date, no study has manipulated attentional bias to determine the effects on interpretation bias.

The current research was designed to determine the effectiveness of different forms of ABM on attentional biases, interpretation biases, and pain outcomes. Given the limited amount of ABM interventions in the pain literature, the study was broadly-speaking exploratory. However, as it has generally been found that biases towards sensory pain words but away from affective pain words play some role in explaining pain outcomes, it would be expected that ABM training away from sensory and towards affective pain words would be the most effective in reducing attentional biases and improving pain outcomes. Further, we sought to explore which components of attentional bias change with ABM training, and whether these changes in attention mediate the effects of ABM on pain outcomes. In particular, the components of attention that we were interested in were early and later stages of processing, which were assessed using eye-tracking technology in addition to traditional reaction time measures.

Method

Participants and Design

Participants were 106 first year university students. Inclusion criteria were: being over 18 years of age, being proficient in English, having no instances of prolonged pain in the 3 months prior to testing, and not currently experiencing acute pain (pain ratings of <4/10 on a numerical rating scale). Participation was voluntary and in exchange for course credit. A randomised controlled trial design was used, with both researchers and participants blind to group allocation.

Participants were randomly allocated to one of the four training conditions (A+S+, A+S-, A-S+, A-S-; where A= affective pain stimuli, S= sensory pain stimuli, + = training towards pain stimuli, - = training away from pain stimuli; such that A+S- is training towards affective pain stimuli but away from sensory pain stimuli). Random allocation was achieved by firstly allocating participants to a unique random number via a list of computer-generated numbers (www.randomizer.org), which was then fed into the ABM program where participants were allocated to a group based on this number. Therefore, allocation to group did not occur until the ABM task was commenced and was concealed from the researchers. This study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000793617).

Materials

Dot-probe Task and Attentional Bias Training

The dot-probe paradigm, as originally described in the anxiety literature (MacLeod et al., 1986) and adapted for use in pain research (Dehghani, Sharpe, & Nicholas, 2003) was used to assess attentional biases towards pain words, and was administered as a computer task. Programming of the dot-probe was carried out using E-Prime 2.0 to interface with the Tobii TX300 integrated eye tracker. The stimuli for the dot-probe were presented on a 23-inch TX300 integrated LCD display, at 1920 x 1080 pixel resolution and 60 Hz refresh rate.

We chose to use word stimuli rather than pictorial stimuli because words can be used to compare sensory and affective pain stimuli more easily than pictures. Meta-analytic results show no difference in attention bias for word versus pictorial pain stimuli (Crombez et al., 2013), and a further meta-analysis shows that ABM protocols using word stimuli are more effective than those using facial expressions for anxiety (Hakamata et al., 2010). Recent evidence in the pain literature also directly compared ABM protocols using words versus facial expressions, and

found that pain threshold was significantly improved when words were used as stimuli, in a similar sample to the present study (Sharpe et al., 2015). Therefore, a word-based ABM protocol was selected for the present study.

Participants were presented with a fixation point '.' in the middle of the computer screen for 500 ms. A word pair then replaced the fixation point, with one stimulus appearing above where the fixation point had been and the other below. In both pre-training and post-training trials, each stimulus pair remained on the screen for 1250ms before being replaced immediately by a probe of either the letter 'p' or 'q'. For the training trials, the stimulus pair display time was 500ms. Participants were instructed to indicate which letter appeared on the screen using a Cedrus RB-530 response pad. Responses and reaction times were recorded and no feedback was given. Each probe disappeared as soon as a response was recorded or after 1500ms.

Before the start of the task, five practice trials were presented to familiarise participants with the task. For the pre-training and post-training trials used to measure attentional bias, twenty word pairs (10 affective/neutral; 10 sensory/neutral) were used. For each word pair, four different presentation combinations were presented (target up/probe down, target up/probe up, target down/probe down, target down/probe up; where target is the pain word in the stimuli pair). This equated to 80 presentations for both pre- and post-training. Two of these combinations were congruent, whereby both the target word and the probe appeared in the same location. The other two combinations were incongruent whereby the target word and probe appeared in opposite locations, one on the upper screen and one on the lower screen.

ABM training stimuli consisted of twenty word pairs (10 affective/neutral; 10 sensory/neutral). When attention was trained towards pain stimuli, all trials were congruent, and where attention was trained away from pain stimuli, all trials were incongruent. Trials varied

both in type of stimuli (sensory or affective pain words) and also direction of training (towards or away from pain stimuli). For each block, participants were presented with a random selection of 20 affective/neutral word pairs, and 20 sensory/neutral word pairs, presented in a random order. Each participant completed a total of 320 training trials across eight blocks. Participants were given a 1 minute break after the pre-training block and after each training block. The task concluded after the post-training block.

The pre- and post-training word stimuli for the dot-probe task were the same as those used by Dehghani et al. (2003). For the training stimuli, 10 sensory and 10 affective pain words from McGowan et al. (2009) were used. Pain words in all trials were matched with a neutral word of equal length and frequency from Keogh, Dillon, Georgiou, and Hunt (2001).

Eye-tracking software

Gaze behaviour data were recorded using a Tobii TX300 integrated eye tracker, with a sampling rate of 300 Hz. For each trial, an area of interest was designated 6.2° x 1° visual angle. A fixation was defined as a period of at least 100ms in which the participant held their gaze within an area of 0.5° radius. Duration and frequency of these saccades was recorded. Fixations on the cue were counted if they occurred at least 100ms after stimulus onset, and if fixation was not on the location of the cue prior to onset. As measures of early attention, percentage of instances in which first fixation was on the pain word, length of time to first fixation on the pain word, and mean dwell time on the pain word during the first 250ms were collected. As measures of sustained attention, length of first fixation on the pain word, and mean dwell time on the pain word were used.

Questionnaires

The Fear of Pain Questionnaire (FPQ; McNeil & Rainwater, 1998) was used to measure pain-related fear, and has previously been found to have good internal consistency and test-retest reliability (McNeil & Rainwater, 1998). In the current study, the FPQ was found to be reliable (α= .925). The FPQ scores were also used to calculate the values for the FPQ short form (SF; Asmundson, Bovell, Carleton, & McWilliams, 2008), to enable comparison with other studies using this version. The FPQ-SF also had acceptable reliability (α= .896). The Pain Catastrophizing Scale (PCS; Sullivan, Bishop, & Pivik, 1995) was used to measure pain catastrophizing, or exaggerated negative interpretations of pain and the outcomes of pain. The PCS has been used extensively in previous research with good validity within university student and community samples (Osman et al., 2000; Sullivan et al., 1995), and had good internal consistency in the current study (α= .905). The Depression Anxiety Stress Scale (DASS; Lovibond & Lovibond, 1995) was used as a measure of anxiety and depression within the current study, as this scale has been found to have good internal consistency and validity, and reliably distinguish these symptoms both within clinical and community samples (Antony, Bieling, Cox, Enns, & Swinson, 1998). The depression (α= .917), anxiety (α= .786), and stress (α= .904) subscales were found to have acceptable internal consistency in the current study.

Interpretation Bias Task

Interpretation bias, or the tendency to interpret pain related information as threatening, was measured using the incidental learning task as described by Khatibi, Sharpe, Jafari, Gholami, and Dehghani (2015). Stimuli were 16 happy and 16 painful facial expressions that were matched on emotion intensity. A further 16 facial expressions that were morphed from an additional 16 pairs of happy and painful facial expressions were included, which have previously

been identified as being the most ambiguous morph of each photograph pair (Khatibi et al., 2015).

The task consisted of a learning phase and a testing phase. A black fixation cross was first presented for 500ms. During the learning phase, a facial expression (happy or pain) was then presented for 675ms, either on the left or the right of the screen. The facial expression was then followed by a target letter "H" presented for 1500ms. The location of the target letter was consistently determined by facial expression (e.g. happy faces-target left; pain faces-target right, counterbalanced). Participants were informed of the facial expression-target location association both verbally and via written instructions on the computer screen. During the task, participants were required to respond to the side that the "H" appeared by pressing the corresponding mouse button. The testing phase followed a similar procedure to the learning phase, except that morphed faces were presented and followed by a target letter "H" appearing equally often on the left or the right of the screen. An interpretation bias was considered to be present if ambiguous faces were responded to as if they were pain- related; i.e. responses were faster when the target appeared on the side previously associated with painful expressions and slower when the target appeared on the side previously associated with happy expressions. The incidental learning task was completed twice, before and after the ABM training, using identical versions of the task (i.e. maintaining the same consistent face-target side across both times).

Pre-Cold Pressor Task Expectations

Four items were used to measure expectations of the cold pressor task; each rated on an 11-point numerical scale (0-10). The questions related to perceived harm and worry about the task, predicted level of pain, and perceived self-efficacy to cope with the task.

The Cold Pressor Task

The Cold Pressor has previously been used as a pain outcome task in attentional bias research (McGowan et al., 2009). Participants first placed their right arm in a tank of water set at 37°c for 30 seconds, to regulate arm temperature. They then placed the same arm in a second tank set between 5+/-0.5°c for as long as they could, which was within the optimal temperature range to observe the pain caused by vasoconstriction followed by vasodilatation of the blood vessels in the arm (Ahles, 1983). The temperature of the tanks was maintained throughout the experiment by a thermostat that could heat or cool the water as necessary. The arm was withdrawn at tolerance (i.e. when participants could no longer keep their arm in the water) or at a maximum of 4 minutes.

A total of five pain measures were taken: hesitance, pain threshold, pain tolerance, distress at tolerance and level of pain. Hesitance is the time taken (in seconds) for the participant to fully submerge their arm in the cold pressor tank following the instructions to do so. Pain threshold indicates the time taken (in seconds) for the participant to first register pain after placing their arm in the cold pressor. Tolerance is the amount of time (in seconds) participants hold their arm in the cold pressor. Distress at tolerance is self-reported distress rated on an 11-point numerical scale, with zero being no distress and 10 being extreme distress, measured at the time of tolerance. Pain levels were self-reported on an 11-point numerical scale, with zero being no pain and 10 being extreme pain. Pain levels were recorded at three time points; when the participant first registered pain (threshold), 30 seconds after placing their arm in the tank, and when the participant withdrew their arm from the tank (tolerance), with the average of these pain level ratings used as an indicator of overall pain. Consistent with previous research (Sharpe et al., 2015), pain threshold and average pain ratings were considered primary outcomes, and hesitance and distress at tolerance were considered secondary outcomes.

Procedure

The study took place in a research laboratory, and the duration of the experiment was approximately one hour. See Figure 1 for the study flow diagram. Participants read a detailed information statement and signed the consent form, after which they completed the computer-based questionnaires. Participants were then instructed to sit 60cm from the TX300 computer screen, with their head in a head rest to ensure accurate perception and recording of eye movements. The chin rest additionally ensured each participant had a maximum gaze angle less than 35°. From this position, participants first completed the interpretation bias task, followed by the dot-probe task. They were then randomly allocated to one of four experimental groups (A+S+, A+S-, A-S+, A-S-), completed ABM, and then again completed the dot-probe task and interpretation bias task. Prior to the dot-probe task, the eye tracker was calibrated. Participants were then given verbal and written instructions on the computer about the dot-probe task, which were identical to previous dot-probe tasks (Dehghani, Sharpe, & Nicholas, 2004; Dehghani et al., 2003). Once the processing bias tasks were complete, participants completed the four cold pressor expectation questions, and then completed the cold pressor task.

FIGURE 1 NEAR HERE

Power and Data Analysis

Based on the medium effect size (Cohen's $d = 0.65$) found in McGowan et al. (2009), for the primary outcome of pain threshold and using a 2 x 2 ANOVA exploring experimental effects on pain outcomes, power analysis indicated that 98 participants in total would be sufficient to detect medium effects at 80% power and $p<.05$. Other studies with a similar design have found a similar sample size sufficient for detecting effects (McGowan et al., 2009; Sharpe et al., 2015).

For the interpretation bias task, responses <150ms or >750ms or that were incorrect were deleted as per previous research (Todd et al., In Press). For participants who had 50% or more errors on the ambiguous trials, their interpretation bias data was excluded (n=4). The average reaction time for the remaining trials was used. For the dot-probe task, responses <200ms or >1500ms or that were incorrect were excluded in accordance with previous research (Dear, Sharpe, Nicholas, & Refshauge, 2011). Outlier exclusion criteria for trials differed between the tasks because whilst the interpretation bias task requires processing of a single visual stimulus followed by localisation of a probe, the dot-probe attentional bias task requires processing of two visual stimuli followed by localisation and then discrimination of the type of probe.

Attentional bias indices were calculated for each type of attentional bias stimuli (sensory pain words, affective pain words) and at each time point (pre training, post training) using the formula: Bias index = ((*tupl* - *tlpl*) + (*tlpu* – *tupu*))/2; where *t* = target stimulus, *p* = probe, *u* = upper location, and *l* = lower location, which has been used in previous research (Keogh et al., 2001). As such, the bias index is the difference between the average of incongruent trials and the average of congruent trials, and provides an indication of the relative reaction time saving when the probe appears in the same location as the target stimuli compared to when they appear in different locations (Boston & Sharpe, 2005). Positive scores indicate attentional biases towards the target, whilst negative scores indicate attentional biases away from the target. Additional eye-tracking data variables were also used as secondary attentional bias outcomes.

A series of mixed (2) x 2 ANOVA were conducted to determine the difference in time (pre, post) and training direction (towards, away) on attentional bias measures. These ANOVA were conducted for sensory training effects on sensory pain words, affective training effects on affective pain words, sensory training effects on affective pain words, and affective training

effects on sensory pain words. Attentional bias reaction time and eye tracking measures formed outcomes.

To determine experimental effects on primary pain outcomes, a 2x2 between-subjects MANOVA was used, with stimuli (sensory pain words, affective pain words), and direction of training (towards, away) as independent variables, and pain variables (hesitancy, threshold time, tolerance time, average pain rating, and distress at tolerance) as outcomes. Partial eta squared (η_p^2) was included as an effect size for the MANOVA analyses, with the following guidelines: .01= small, .06= medium, .14= large (Cohen, 1969; Richardson, 2011).

Finally, bivariate correlations were used to explore the association between psychological variables (DASS, FPQ, PCS) and attentional biases. In addition, correlations between attentional bias change variables and pain outcomes were explored to determine whether the change in attentional biases over the course of the experiment predicted pain outcomes, with correlation effect size guidelines of .10=small, .30=medium, .50=large (Cohen, 1992). Cognitive bias change variables were calculated by subtracting the post-ABM bias measures from the pre-ABM bias measures for both bias indices and eye tracking variables.

Results

Descriptive Statistics

A total of 106 healthy university students agreed to participate in this study. Of these, three were excluded as they had pain ratings of >3/10 at baseline, one was excluded due to a technical issue with the questionnaire software, and seven were excluded as there were technical difficulties with the eye tracking equipment which interfered with the dot-probe task. This left a final total of 96 participants. Participants were on average 20 years old, with a range of 18-50

years old, and 45% identified as female. From the questionnaire data, participants scored an average of 86.19 (SD=16.80) on the FPQ and 55.00 (SD= 11.25) on the FPQ-SF. These scores were slightly higher but within one standard deviation of similar healthy and undergraduate samples for both the FPQ (McNeil & Rainwater, 1998; Osman, Breitenstein, Barrios, Gutierrez, & Kopper, 2002) and the FPQ-SF (Carleton & Asmundson, 2009). Participants scored an average of 17.48 (SD=9.41) on the PCS, which is similar to the average found in other healthy samples (Osman et al., 2000; Sullivan et al., 1995). On the DASS, participants scored an average of 5.38 (SD=6.19) for depression, 4.39 (SD=4.39) for anxiety, and 9.55 (SD=7.45) for stress, indicating that they were within the normal range (Lovibond & Lovibond, 1995). There were no significant baseline group differences in age or gender, nor in FPQ, PCS, and DASS scores ($p>.05$).

To determine whether cognitive processing biases were present at baseline, a series of single sample t tests were conducted. The sensory and affective attentional bias indices, and the interpretation bias index were not significantly different from zero at baseline ($p>.05$). A series of repeated measures t tests was also conducted to compare pain and neutral words in attentional bias eye tracking measures, however these were also not significant ($p>.05$), indicating that no cognitive processing biases were present at baseline. This was expected as attentional biases are not consistently found in pain free samples (Crombez et al., 2013).

Effects of ABM on pain outcomes

Effects of ABM on pain outcomes were found, with main effects displayed in Table 1. Those who were trained towards affective pain words had a longer latency to threshold than those trained away from affective pain words ($F_{1,94}=6.07$, $p=.016$, $\eta_p^2=.063$). That is, it took

longer for those trained towards affective pain words to report pain after they immersed their arm in the cold water tank. However, those trained towards affective pain words also displayed greater distress at tolerance than those trained away from affective pain words ($F_{1,94}$ =5.19, *p* =.025, η_p^2 =.054). There were no effects of affective pain training on pain levels or tolerance time. No effects of sensory training were found on pain outcomes, nor were there any significant interaction effects between sensory and affective training, as had been predicted.

INSERT TABLE 1 NEAR HERE

Effects of ABM on cognitive biases

The effect of ABM on attentional bias was explored with a series of (2) x 2 ANOVA. The primary outcome of interest was the interaction effects between time and ABM training direction; however, this was not significant for any of the analyses. There were main effects over time for latency to first fixation with both word types (sensory: $F_{1,94}$ =5.69, *p* =.019, η_p^2= .057; affective: $F_{1,94}$ =12.32, *p* =.001, η_p^2= .116) and mean dwell time with both word types (sensory: $F_{1,94}$ =7.09, *p* =.009, η_p^2=.070; affective: $F_{1,94}$ =8.50, *p* =.004, η_p^2=.083), such that over time participants became faster at orienting towards pain stimuli but also disengaged more quickly, regardless of treatment group. There was also a significant difference between sensory training groups for percentage of first fixation towards sensory pain words ($F_{1,94}$ =5.00, *p* =.028, η_p^2= .050), but as this was not moderated by time, this occurred independently of treatment. No other attentional bias results were significant, and there was no significant effect of ABM training on interpretation bias. Given that ABM did not result in significant group differences in attentional bias over time, the minimum requirements for attentional bias to mediate the ABM training-pain

outcome relationship were not met, and therefore the planned mediation analyses were not conducted.

Relationship between cognitive bias change and pain outcomes

Correlations between cognitive bias change (pre-ABM to post-ABM) variables and pain outcomes were explored, as shown in Table 2. For attentional bias eye tracking measures, change in percentage of first fixations on affective stimuli (r=.249, p=.014), and change in mean dwell time for affective (r=.202, p=048) and for sensory (r=.218, p=.042) stimuli were all associated with latency to pain threshold, such that those who had an increase in percentage of first fixations on the affective stimuli, or an increase in the average dwell time of either sensory or affective stimuli, took longer to register pain. In addition, change in latency to first fixation for affective stimuli was associated with distress ratings (r=.216, p=.035), such that those who took longer to orient towards affective pain words reported increased distress at tolerance. The attentional bias reaction time change indices were, however, not associated with pain outcomes.

The interpretation bias change index was associated with latency to pain threshold (r=.247, p=.027) and pain tolerance (r=.226, p=.044), as well as average pain rating (r=-.254, p=.023), such that those who had an increase in pain interpretation reported a higher pain threshold, higher pain tolerance and a reduction in pain ratings.

INSERT TABLE 2 NEAR HERE

Discussion

The present study explored the effects of four versions of dot-probe ABM on attentional biases, interpretation biases, and pain outcomes. ABM training towards and away from affective

pain words (but not sensory pain words) was successful in influencing pain outcomes. Consistent with expectations, those trained towards affective pain words had a higher pain threshold, yet they did not report lower pain and also reported greater distress at tolerance than those trained away from affective pain words. However, the hypothesized interaction between sensory and affective training was not significant, nor did the sensory training alone bring about changes in pain outcomes. Against predictions, ABM did not result in changes to attentional biases, as measured by either reaction time data or eye tracking. Even so, small associations between change in cognitive processes and pain outcomes were found. Those who initially fixated on affective pain stimuli more frequently, and those who spent longer looking at both affective and sensory pain stimuli tended to take longer to report pain on the cold pressor task.

As those who received ABM training towards affective pain stimuli, and those who had an increase in time looking at (primarily affective) pain stimuli tended to take longer to register pain, the findings of the present research are somewhat consistent. Further, those who took longer to orient towards affective stimuli also showed increased distress at tolerance. Taken together, the ABM training and correlational results suggest that increasing focus on affective stimuli at both early and later stages of attentional processing can serve to delay the time taken to register pain. However, in contrast to the rest of the findings, ABM training towards affective stimuli also increased distress, which requires further investigation.

Whilst it cannot be conclusively stated that ABM is successful in changing pain outcomes through changing attentional biases, as only two of the three requirements for mediation were satisfied, it does appear that attentional bias modification and attentional biases more generally do have some role in the experience of pain. This is not the first study to find ABM training effects on pain or on attentional bias that do not satisfy mediation requirements

(e.g. Sharpe et al., 2012). This lack of mediation has been discussed by Todd et al. (2015) as being an issue for this area of research, and various explanations have been put forth. Sharpe et al. (2012) suggested that in the typical ABM study, at most 50% of the dot-probe trials are 'active' ABM trials, as the dot-probe is also used to assess attentional biases prior to and following ABM. In assessment trials, pain stimuli are no longer followed consistently by a probe in the same location. Therefore, assessment trials may serve to dilute the ABM effects on the allocation of attention during test phases. However, the dilution explanation cannot explain why ABM effects on pain outcomes still occur. Another explanation is that ABM may affect certain attentional mechanisms but not others (e.g. hypervigilance vs. difficulty disengaging), which an overall attentional bias index cannot detect. However, the specific effects explanation does not seem to hold in the present study, as a strength of the present research was that eye tracking was used to better measure specific attentional processes. Finally, Sharpe et al. suggest that individual differences may account for the discrepant effects of ABM, where ABM is successful for some individuals but not others. The possibility that the efficacy of ABM is affected by individual differences should be explored further, as change in attentional bias was associated with a number of pain outcomes, suggesting that where change occurs, it can be relevant to pain.

The present study failed to find effects of ABM on interpretation bias, nor an association between attention and interpretation bias. However, change in interpretation bias was associated with pain outcomes, such that those with an increased pain interpretation had lower pain ratings, and longer latency to pain threshold and pain tolerance on the cold pressor task. Interestingly, this pattern of association between interpretation bias and pain outcomes was opposite to what was expected, as previous research has found biases towards pain interpretation are present in individuals with chronic pain compared to healthy participants, (Pincus & Morley, 2001; Pincus,

Pearce, McClelland, Farley, & Vogel, 1994; Pincus, Pearce, & Perrott, 1996), and pain interpretation biases are therefore thought to be implicated in the development of chronic pain. However, whilst chronic pain may be associated with an increased reliance on a pain-based schema interpretation (Pincus & Morley, 2001), cognitive bias processes may play a different role for healthy individuals, particularly under conditions of low threat. As interpretation biases were not present at baseline, a small increase in pain interpretation may be an appropriate response given the pain-related focus of the study, whereas continuing to interpret ambiguous information as not pain related could indicate avoidance. However, the 'appropriate response' explanation is speculative and would require further exploration, particularly to determine which levels of pain interpretation are helpful. Even so, the association between interpretation bias and pain found in the present study provides some support for the role of interpretation biases in pain, which has to date received little attention.

The threat interpretation model (Todd et al., 2015) makes predictions about the role of interpretation bias in pain that were not supported. Contrary to predictions, greater interpretation bias was associated with improved pain outcomes. Further, although stipulated in the model, no association between attention and interpretation bias was found, suggesting that cognitive biases biases are not as closely related as first thought, at least within healthy pain-free samples. Although unexpected, the lack of association between cognitive biases is consistent with another recent study, which failed to find an association between attention and interpretation biases for pain (Todd et al., In Press).

Overall, the present research provides only partial support for the threat interpretation model (Todd et al., 2015) and the vigilance-avoidance hypothesis (Crombez et al., 2012; Mogg, Bradley, Miles, & Dixon, 2004). Both models stipulate a pattern of attentional bias indicating

initial vigilance, followed by difficulty disengaging (at moderate levels of threat in the case of the threat interpretation model), or followed by avoidance (in the case of the vigilance-avoidance hypothesis, or at high or low threat levels in the case of the threat interpretation model). It appears that both models are supported in indicating that, at least in healthy participants, avoidance of primarily affective stimuli at later stages of attentional processing may be problematic, as indicated by the association between shorter dwell times and poorer pain outcomes. However, it also appears that avoidance can occur early in attentional processing. Early avoidance, rather than vigilance as proposed by the models, may be equally problematic, as reduced initial fixations and delayed orienting towards affective stimuli were also associated with poorer outcomes in the present study. It is notable, however that there are inconsistencies in this field of research, and some studies have found avoidance of sensory pain stimuli but difficulty disengaging from affective pain stimuli to be present in chronic pain patients, based on reaction time data (Carleton, Asmundson, Collimore, & Ellwanger, 2006). Further investigation is therefore warranted to replicate the pattern of avoidance of affective pain stimuli across the attentional time-course that was observed in this study. Use of alternative methodologies to reaction time measures, such as eye tracking, will help to clarify these processes.

Strengths and Limitations

Whilst the present study found ABM group differences in pain outcomes, at least for affective pain word training, and associations between attentional biases and pain outcomes, mechanisms of change were not able to be established as ABM failed to produce changes in attentional biases. However, the absence of an identifiable training mechanism does not preclude the importance of this research and other studies with similar findings. In particular, that changes in pain outcomes were found with a single session of ABM in a sample of healthy participants

suggests that ABM does indeed have some merit in the field of pain (MacLeod, Koster, & Fox, 2009; Sharpe, 2012). Further, the current study was the first to use eye tracking to better explore the effects of ABM on specific attentional processes, and as such, some potential explanations for the lack of identifiable mechanisms of change in ABM were able to be dismissed. Further efforts to identify the processes by which this change occurs should be the focus of future research.

It is worth noting that overall, participants became quicker at orienting towards both sensory and affective pain stimuli, and also disengaged more quickly from these stimuli, and this effect was not dependent on treatment group. When considered alongside the lack of effect of ABM on attentional biases, alternative mechanisms of change to attentional bias modification should be explored. A habituation effect to the task itself may have served to dilute any between group effects. It is possible that a shorter task with less ABM or dot-probe trials would be more effective; however, as the reliability of the dot-probe has been called into question (Dear et al., 2011), a balance is necessary in designing a task that is both reliable and effective.

Another alternative explanation is that participants are exposed to pain-relevant stimuli through both the dot-probe and ABM, and thus there may be improvement in outcomes with increased trials, regardless of training direction. Indeed, although Sharpe et al. (2015) found expected effects of ABM on pain threshold, there was also evidence that mere exposure to painful facial expressions led to lower reports of pain regardless of the direction of training. The possibility that exposure alone may improve outcomes could help to explain why, in some research, ABM is no more effective than matched control tasks (Heeren, Mogoaşe, Philippot, & McNally, 2015). A second suggestion that has been cited in the literature is that attentional control may be the mechanism through which ABM protocols exert their effect, rather than

direction of attentional training (e.g. Carleton et al., 2015; Enock, Hofmann, & McNally, 2014; Heeren, Mogoaşe, McNally, Schmitz, & Philippot, 2015). For example, research has found that ABM training towards and away from threat can be equally effective, compared to a control task with no training direction (Klumpp & Amir, 2010). Both the exposure and attentional control hypotheses could be considered relevant in the present study, as over time participants became quicker at both orienting to the stimuli, and disengaging from it, regardless of treatment group, which could equally occur through stimuli exposure or through increased attentional control. Exposure and attentional control are interesting ideas that should be further explored and compared, in order to clarify the mechanisms of change in tasks such as the dot-probe ABM. Measures of attentional control before and after training might help to disentangle these effects.

Whilst a number of individual difference variables such as depression, anxiety, fear of pain, and catastrophising were measured in the present study as control variables, these were not the primary focus of the present research. Future research could explore the relationship between these variables or other individual difference variables (such as the pain anxiety symptoms scale, PASS; McCracken & Dhingra, 2002) and attentional bias and pain. However, it is worthwhile to note that anxiety and depression did not correlate with attentional bias and pain outcome measures that were affected by ABM (see Supplementary Table). In addition, including post-intervention measures could help to determine the effects of ABM on these individual difference variables.

Conclusions

The current study explored the effectiveness of ABM that trained individuals towards or away from sensory and affective pain words, in order to delineate the way in which sensory and

affective pain stimuli may differently affect pain outcomes. This study challenges earlier research in that it was the affective rather than sensory bias training that was most important for pain outcomes, and therefore further comparison of the role of sensory and affective pain biases is warranted. Further, this study was the first to use eye tracking measures of attentional bias to explore the effects of ABM on specific attentional processes, although no training effects were found. Finally, this was also the first study to test the effects of ABM on interpretation biases, although there did not appear to be any effects, at least on healthy participants under conditions of low threat. Even so, these findings provide partial support for the threat interpretation model, and in particular the vigilance-avoidance pattern of attentional bias in pain, as well as providing some avenues for continued research into the mechanisms of ABM.

Acknowledgements:

Thanks are due to Ali Khatibi, for providing the incidental learning task for use in this research.

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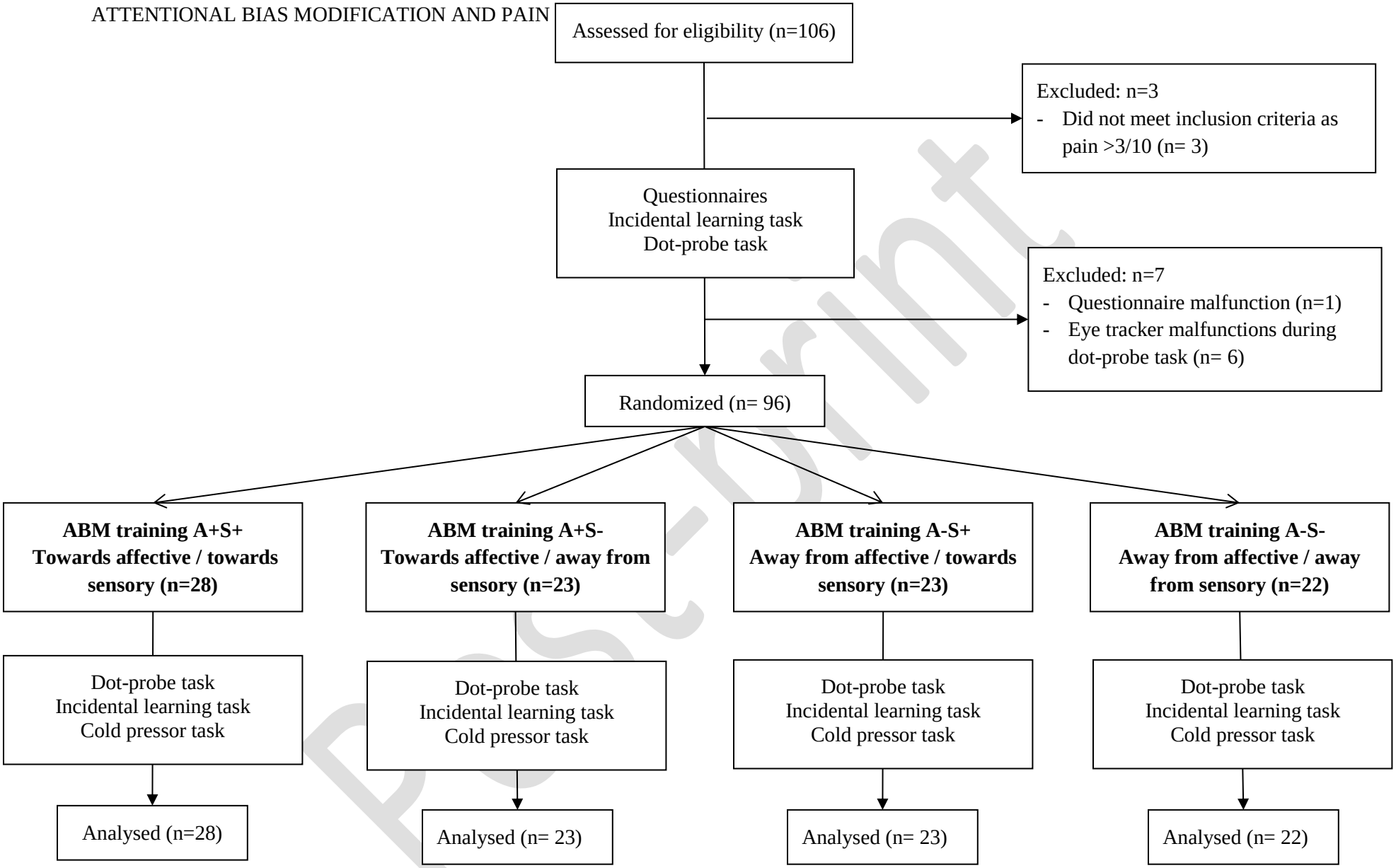

Figure 1. Study Flow Diagram

Table 1

ABM group differences in pain outcomes

	Training group mean (SD)				
Outcome	Towards (n=50)	Away (n=45)	f	p	η_p^2
Affective pain words					
Hesitancy (secs)	2.48 (1.67)	2.04 (1.45)	1.85	.178	.020
Threshold time (secs)	15.89 (11.98)	10.97 (6.60)	6.07	.016	.063
Tolerance time (secs)	97.42 (85.73)	95.76 (84.62)	0.01	.934	.000
Average pain (0-10)	6.52 (1.48)	6.06 (1.37)	2.36	.128	.025
Distress at tolerance (0-10)	4.37 (2.88)	3.13 (2.62)	5.19	.025	.054
Sensory pain words					
Hesitancy (secs)	2.30 (1.92)	2.24 (1.11)	0.02	.879	.000
Threshold time (secs)	13.13 (11.19)	14.05 (8.73)	0.25	.622	.003
Tolerance time (secs)	91.79 (79.56)	102.01 (90.79)	0.37	.544	.004
Average pain (0-10)	6.49 (1.23)	6.09 (1.63)	1.73	.192	.019
Distress at tolerance (0-10)	3.94 (2.66)	3.61 (2.99)	0.38	.539	.004

Table 2

Correlations between attentional bias change measures and pain outcomes

	Bias Indices			Orientation				Avoidance				Disengagement	
	Attention		Interpretation	Mean time to first fixation		Percentage of first fixation		Mean duration of first fixation		Mean duration in first 250ms		Mean dwell time	
	S	A		S	A	S	A	S	A	S	A	S	A
Hesitancy	.007	-.016	-.135	-.082	-.012	-.063	.014	-.094	.035	.013	-.024	.052	.127
Threshold	-.012	-.035	.247*	.187	.136	.170	.249*	.054	.026	.017	-.093	.208*	.202*
Tolerance	.025	.070	.226*	.098	-.059	.060	.099	.045	-.193	.154	-.161	.090	-.009
Pain Average	-.050	-.073	-.254*	.008	.088	-.060	-.170	.057	.130	-.074	-.019	-.030	-.110
Distress	.037	-.079	.018	.110	.216*	-.030	-.144	.082	.087	.021	.071	.134	-.002

Notes: *p<.05, S= sensory bias, A= affective bias. All biases are change scores, with post-training values subtracted from pre-training values.