The impact of modifying attentional bias on vulnerability to pain

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Abstract

The preferential deployment of attention to noxious versus benign information in the internal and external environment - "attentional bias" - is thought to confer vulnerability to pain. The current thesis tested this putative mechanism by modifying the bias using the visual-probe task (attentional bias modification; ABM) and examining effects of this experimental manipulation on attentional bias and critical pain outcomes. Drawing on recent evidence that the impact of pain on attentional bias varies across its temporal components, this thesis additionally tested the component stages of attentional bias implicated in pain experience by manipulating the duration for which visual-probe stimuli were presented. Study 1 confirmed that both rapid and slower attentional orienting was biased in individuals with persistent musculoskeletal pain. Results from Studies 2 and 3 indicated that acute experimentally-induced pain modified the faster bias and that participants whose fast bias was modified had reduced vulnerability to cold pressor pain, in comparison with control participants. This suggested that mechanisms of initial orienting were more active in the acute pain experience. Studies 4 and 5 revealed that concurrently retraining fast and slower bias was optimal for persistent musculoskeletal pain. Results of a systematic review and meta-analysis indicated a small overall statistical effect of ABM on pain severity. Critically, however, whereas ABM had been effective at reducing acute pain severity, this was not the case for persistent pain. Overall, these findings suggest that the faster bias influenced vulnerability to acute pain, indicating a potential therapeutic target for future research. However, retraining the earlier stage of attention alone did not influence persistent pain outcomes, where there appeared to be greater involvement of the slower bias. It was concluded that not only could attentional bias influence critical pain outcomes, but that the optimal timings may vary across temporal pain classifications.

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Chapter 1

Introduction

1.1 A cognitive understanding of pain: From basic science to public health

The current examination of the influence of modifying attentional bias on vulnerability to pain draws on a rich theoretical and scientific background. In the first part of this Chapter (Section 1.1), the basic behavioural science of pain will be introduced. Next, pain classifications and epidemiology will be described (1.1.2). The comparatively recent conceptualisation of pain as subjective experience has led to improvements in scientific understanding of the complex neurocognitive and psychological processes that characterise and control pain. This thesis focusses on the role of component stages of attention in pain experience, and specifically on attentional bias. As such, it is rooted in cognitive and experimental psychology. In the second part of the Chapter (Section 1.2), an overview of theories of attention (including its time course) and emotional processing will be provided, with an emphasis on competition models of selective attention that underpin attentional bias research. In recent years, specialised models of the attentional processing of pain have been developed, and these will be introduced in Section 1.3. The increasing understanding of the importance of psychological factors in pain experience has led to advances in pain medicine, and the development of psychological approaches for the management of acute and persistent pain that incorporate attentional strategies; these will be described in Section 1.3.3. Finally, innovative experimental investigations of pain-related attentional bias will be introduced (Section 1.4), with particular emphasis on the use of the visual-probe task, which will be utilised in the present programme of work, to test, characterise, and modify the bias.

1.1.1 The biopsychosocial perspective and neurocognitive models of pain

Pain, which has been defined as “a sensory and emotional experience associated with actual tissue damage, or described in terms of such damage” (Merskey & Bogduk, 1994, p. 210), performs an essential protective function, warning the individual of actual or potential bodily harm. Its critical role is illustrated by the condition ‘congenital insensitivity to pain’, a rare genetic disorder characterised by an abnormality of interpretation of painful stimuli (Verheyen & Castelein, 2007). Affected individuals retain a sense of touch but do not experience sensations as unpleasant and painful, and as a result are at greater risk of injury (e.g. Protheroe, 1991). In addition to illustrating the protective function of pain, clinical reports of this condition fed into the theoretical distinction between its sensory and affective components (Melzack & Casey, 1968; Nagasako, Oaklander, & Dworkin, 2003). Pain theorists realised that discomfort does not always occur in the presence of nociception, defined as central and peripheral nervous system activity produced by pressure, chemical or temperature stimuli that possess the potential to cause tissue damage (Legrain, Iannetti, Plaghki, & Mouraux, 2011b; Sherrington, 1906). Similarly, the nonlinear relationship

between nociception and pain was suggested by the occurrence of pain felt in the absence of nociception (Tracey & Mantyh, 2007). Studies examining this dissociation revealed abnormalities in the central processing of pain stimuli, which included cognitive and emotional factors, such as attentional and interpretive processing styles, and levels of comborbid depression and anxiety (Berna et al., 2010; Jarcho, Mayer, Jiang, Feier, & London, 2012; Legrain, Perchet, & Garcia-Larrea, 2009a; Legrain et al., 2011b; Tracey & Mantyh, 2007). Such findings pointed to a more complex understanding of pain than unidirectional stimulus-response mechanisms suggested by earlier theorists.

The biopsychosocial model (Engel, 1977, 1981) was proposed in response to prevailing limitations of the biomedical model of health, which suggested somatic symptoms could be fully explained in terms of biological factors, measurable using biomedical tests. The model suggested that symptoms (e.g. aching and discomfort) could influence and be influenced by psychological factors (e.g. anxiety and biased attention to pain) and social context (e.g. family and healthcare interactions), as well as biological (e.g. disc degeneration) disease mechanisms (Engel, 1981; Pincus, 2013). There was no question that disease states have biological determinants. What was challenged was the assumption that the 'disease' (defined as the objectively verifiable evidence of pathology) fully explained the 'illness' (the experience of ill health) and that the relationship between them was linear and unidirectional (Drossman, 2005; Engel, 1977, 1981). Since the model's initial publication (Engel, 1977), research has offered further examples of disease occurring without illness (such as asymptomatic ulcers; Drossman, 2005) and illness occurring without obvious pathophysiology (such as, for many individuals, chronic low back pain; e.g. Pincus et al., 2013). The biopsychosocial model provided a template for these findings according to which biological and psychosocial factors could affect both the disease and the illness (Drossman, 2005). Crucially, illness, which itself had effects that could in turn affect the disease process or the clinical outcome, resulted from complex, mutually reciprocal relationships, between biological, psychological, and social factors (Drossman, 2005; Engel, 1977; Gatchel, Peng, Peters, Fuchs, & Turk, 2007).

The original formulation of the biopsychosocial model (Engel, 1977, 1981) used systems theory to mitigate the observed limitations of 'reductionism' applied to medicine (the view that 'all behavioural phenomena of disease must be conceptualised in terms of physicochemical principles'; Engel, 1977, p. 2). He argued that each 'level' of the system (e.g. the cells of an organism, organs, nervous system, individual, their family and community and social context; Engel, 1981) was linked hierarchically, and that each system level contributed to symptom expression. However, the model failed to explain how the system levels interacted with one another, and provide testable mechanisms for empirical research (Malmgren, 2005). Indeed, it can be argued that its value lay not as a 'model' per

se, but in its identification for the vital need for new theoretical models of illness (Malmgren, 2005). Crucially, the 'biopsychosocial perpective' thereby fuelled the development of behavioural science in the latter part of the twentieth century, during which time new theories of health psychology were developed. Thus, the approach has been highly influential, and remains the dominant heuristic for conceptualising the aetiology and prognosis for illness and pain (Gatchel et al., 2007).

In particular, the biopsychosocial perspective has been powerfully applied to low back pain (Waddell, 1987) and chronic pain (Gatchel et al., 2007). So applied, the biological disruption of nociceptive receptors, the psychological status of the individual, and their sociocultural context are all considered important, interrelating, determinants of the subjective pain experience and clinical outcomes, such as disability (Gatchel et al., 2007). The description of persistent pain as a biopsychosocial phenomenon helped explain how pain can often persist in the absence of known aetiology (Gatchel et al., 2007; Tracey & Mantyh, 2007), and contributed to the development of interdisciplinary management approaches for refractory pain (Gatchel et al., 2007, Gatchel, McGeary, McGeary, & Lippe, 2014; multimodal pain management approaches will be more fully discussed in Section 1.3.3). In the current Section, models and theories concerning the neurobiology of nociception and associated neural processes of pain, and their interaction, will be described. Explanations of the pre-twentieth and early twentieth centuries introduced below were rooted in a biomedical perspective, tending to proffer biological or mechanical accounts of its peripheral apparatus sending signals to the brain. More recent theories, such as the pain neuromatrix (Melzack, 1999), which additionally described the central processing of pain stimuli, provided a testable theoretical framework for the biopsychosocial perspective (Gatchel et al., 2007). These theories fuelled numerous experimental studies on the psychological determinants of pain, which have produced considerable evidence supporting the importance of psychological factors (cognitive and emotional) to pain experience. Research on psychological processes considered relevant to pain experience (the 'psychological' component of the biopsychosocial perspective) will be discussed in more detail in Section 1.3.2.

Contemporary thinking has moved on considerably from early theories that viewed pain as a straightforward input to the central nervous system, whereby sensation was thought to travel from the point of contact with the stimulus (e.g. the fingertip touching something hot) to sensory regions in the brain. Descartes (1664, English translation Hall, 1972) was the first to develop a mechanical explanation of pain. He developed the concept of a pain pathway linking the periphery of the body with the brain, and thereby set the stage for scientific investigation into pain physiology. Later, 'specificity theory' (von Frey, 1895, in Moayedi & Davis, 2013) suggested that pain was a specific sensation that was independent

from other sensations and had its own central and peripheral apparatus. Specialised peripheral sensory receptors for pain were thought to respond to damage and send signals through pathways in the nervous system directly to a pain centre in the brain. However, the theory could not account for pain that occurred in the absence of noxious stimulation, and vice versa, noxious stimulation that did not produce pain. The 'pattern theory' of pain sensation (Goldscheider, 1920 in Gatchel, 1999; Nafe, 1929; Sinclair, 1955; Weddell, 1955) was proposed in reaction to some of the limitations of specificity theory (Hertling & Kessler, 2006).

Proponents of pattern theory (e.g. Nafe, 1929) posited that, in conjunction with stimulus intensity, central integration of the perceived stimulus determined pain. They suggested that strong and weak stimuli of the same sensory modality produced different patterns of neural activity. Critically, it was not the direct stimulation of specific pain receptors (all nerve endings were considered alike), but the transmission of patterns of neural firing coded at the periphery that gave rise to the pain sensation (Hertling & Kessler, 2006). A key aspect of pattern theory was that it provided a preliminary explanation for phenomena such as phantom limb pain, which is pain that appears to arise in a body part that has been lost through amputation (Hertling & Kessler, 2006). The theory was criticised, however, because it overlooked evidence of nerve fibre specialisation (Hertling & Kessler, 2006; Melzack & Wall, 1965). Other theorists of the mid-twentieth century emphasised the importance of central integration as a determinant of pain. For example, Noordenbos (1959) attempted to explain how rubbing an affected area could alleviate pain intensity, putting forward a concept of pain in which afferent impulses were modified. According to this view, tactile impulses transmitted from an injured region along large diameter fibres could inhibit pain impulses transmitted from the same site along thinner fibres. Hence, pain intensity was determined by the ratio of thick to thin fibre input from the affected site.

Yet, these earlier theories were unable to fully account for a paradox in the study of pain. Commentators (e.g. famously, Beecher, 1946) had noted that sometimes there could be severe damage and little experience of pain when severely injured soldiers had escaped the battlefield, which he attributed to the relief of having escaped. Conversely, there could be severe pain with little evidence of a noxious stimulus, as in conditions such as peripheral neuropathy (where gentle stimulation of 'normal skin' can also trigger severe pain; Melzack & Wall, 1965), and phantom limb pain. Melzack and Wall (1965) proposed a theory that provided an explanation for this apparent paradox, and changed the way that people thought about pain. Their 'gate-control' theory retained the premise of specificity theory that some cells are specialised to detect and transmit noxious input. In so doing, they rejected the premise of pattern theory that all nerve endings are alike. However, they additionally rejected the premise of specificity theory that this entails the cells are specialised 'pain

receptors'. Crucially, they realised that nociception is neither necessary nor sufficient for pain perception. To fully understand pain perception, it is necessary to explain how psychological variables (such as attention and beliefs) can modulate pain experience. The present thesis will investigate the relationship between attention and pain.

In providing an account of how central processes can modulate pain perception, Melzack and Wall (1965) proposed that the transmission of impulses from the body (it was supposed the skin contained receptors that have specific physiological properties by which they may transmit particular types and ranges of stimuli in the form of impulse patterns) into the central nervous system is modulated or gated in the spinal cord. Within the spinal cord, nociceptive neurons, which have small-diameter axons, make synaptic contact with other neurons. They tend to excite these second neurons in the sequence, a type of interneuron called 'transmission cells', which then transmit action potentials to the thalamus. Nociceptive neurons release two excitatory neurotransmitters (glutamate and substance P). A given amount of activity in a nociceptive neuron can trigger different amounts of activity in a transmission cell, depending on events occurring around the synapse. This helps to explain how a given amount of tissue damage can be associated with very different reported pain intensities. Using the analogy provided by the gate control theory, it is as if there is a gate within the spinal cord. When the gate is open, the nociceptive message can pass through, but, when the gate is closed, the message gets no further than the axon terminal of the nociceptive neuron in the spinal cord. Large nerve fibre impulses impede pain transmission (shuts the gate), whereas small fibre impulses facilitate transmission (opens the gate). Critically, this gating mechanism in the spinal cord is affected by descending impulses from the brain. Large fibres may activate specific cognitive processes, which, in turn, may influence the gate by downregulating the impulse (Melzack, 1993). Hence, the theory provided a mechanism by which psychological factors could exert real influence on pain perception. The term 'gate' is of course only a metaphor; however, the chemical process that opens and closes the nociceptive pathway has been identified (Hunt & Mantyh, 2001).

Research has since supported the hypothesis that psychological effects arising in the brain are able to block the transmission of nociceptive information. For example, several studies have indicated that distraction techniques, which explicitly require participants to direct their attention away from a painful stimulus, towards a benign stimulus (such as a pleasant picture), can reduce pain intensity ratings during medical procedures (Diette, Lechtzin, Haponik, Devrotes, & Rubin, 2003; Malloy & Milling, 2010; see also Section 1.3.3 for its role in persistent pain management). Moreover, when participants' brains were imaged during an experimental pain induction (heat) with and without distraction, regions of the network of pain areas implicated in pain processing (the 'pain matrix'; e.g. the thalamus (lateral and medial) and anterior insular and cingulate cortices) were more strongly activated

in the no distraction condition. In contrast, in the distraction condition, the pain matrix showed less activation, and increased activity in areas associated with top-down attentional control over incoming stimuli (e.g. the prefrontal cortex) was reported (Valet et al., 2004). According to this physical measure of pain, the amount of attention allocated to the pain stimulus modulated pain intensity. According to gate control theory, the transmission of the noxious heat stimulus through the nociceptive pathway was blocked by a descending pathway from the brain when attention was paid to the distractor during the pain induction, which closed a 'gate' in the spinal cord and impeded the incoming information from further processing. The gate-control theory was revolutionary in that it suggested that psychological factors such as attention and emotion can influence pain perception and response to pain by acting on the gate-control system. However, whilst it suggested a central role for the brain in pain processing, it was unable to describe in any detail the neural pathways via which pain is processed. In addition, although it provided a foundation for understanding the role of cognitive processing in pain and explicitly postulated that attention was directly implicated in pain perception, it could not explain in detail how attention influences pain experience. This thesis will seek to develop understanding of the role of attentional processing in pain.

Subsequent theories have attempted to redress the theoretical gap. Melzack (1999, 2005) proposed the 'neuromatrix' theory, which sought explicitly to understand brain function. The theory posited a large multimodal "network of neurons that generates patterns, processes information that flows through it and ultimately produces the pattern that is felt as a whole body possessing a sense of self" (Iannetti & Mouraux, 2010; Melzack, 2005, p. 87). It connected somatosensory, limbic and thalamocortical regions, underpinning the sensory-discriminatory, cognitive-affective and evaluative-motivational components of pain experience (Melzack, 1999). Critically, the theory posited that the characteristic 'neurosignature' pattern of neural processing that occurs in pain can be activated by nociceptive inputs, but can also be activated in their absence (Melzack, 1999). In addition, as the widespread network links diverse regions of the brain, its output is subject to multidimensional somatosensory and cognitive-affective influences (Melzack, 2005).

The existence of a neuromatrix (or 'pain matrix') has been tested in numerous studies, typically exploring the relationship between nociceptive stimuli of graded intensity, and the magnitude of brain response within the proposed network. These studies predominantly employ Positron Emission Tomography (PET) and functional magnetic resonance imaging (fMRI) techniques. For example, using fMRI, Büchel et al. (2002) demonstrated that the magnitude of responses in the insular and perigenual anterior cingulate and ventral perigenual anterior cingulate cortices reliably predicted the intensity of pain perceived, as well as the intensity of the nociceptive stimuli (brief radiant pulses applied to participants' skin). These findings suggested the neuromatrix may be a specialised network

for processing pain-related information (e.g. Tracey & Mantyh, 2007). However, whilst it is broadly agreed that certain key regions are implicated in pain experience, as the neuromatrix theory suggests, this does not necessarily entail that the identified regions are specialised 'pain processors' that signify a direct representation of the conscious experience of pain at the neural level. An alternative explanation of the data is that the identified 'hubs', such as the anterior cingulate cortex, are multimodal processors that deal with different types of incoming sensory information other than and including pain (e.g. Legrain et al., 2011b).

There is accumulating evidence that, in a number of circumstances, the magnitude of the responses in the network may be dissociated from the subjective intensity of pain, as well as the physical intensity of the nociceptive input (Legrain et al., 2011b). For example, Iannetti, Hughes, Lee, & Mouraux (2008) found that the magnitude of nociceptive stimulus-related event-related potentials (ERPs) decreased significantly with repetition, although the perception of pain intensity remained constant (Iannetti & Mouraux, 2010; Legrain et al., 2011a, b). Moreover, research investigating the effect of attention in the context of pain processing has indicated that, irrespective of whether the stimulus was noxious or not, regions were activated in the dorsal anterior cingulate cortex (Büchel et al., 2002; Peyron et al., 1999), suggesting that some neural activity within the pain matrix could represent attentional processing dealing with the salience of somatosensory stimuli, rather than nociception per se (Iannetti & Mouraux, 2010; Legrain et al., 2009b, 2011b). A stimulus's salience is characterised by its ability to stand out relative to background and neighbouring stimuli, with nociceptive stimuli included in the class of salient stimuli due to their noxious nature (Iannetti & Mouraux, 2010; Yantis, 2008). Thus, Iannetti and Moruaux (2010) and Legrain et al. (2009b, 2011b) have argued that the network's identified cortical regions process salient, but not necessarily nociceptive material. Their theory refutes the view that its sole function is to directly represent pain perception and perceived intensity. Rather, it reconceptualises the pain matrix as a multimodal network primarily involved in salience detection, attentional orientation and prioritisation of cortical processing activities, irrespective of sensory modality (Legrain et al., 2009b; Van Damme, Legrain, Vogt, & Crombez, 2010). The salience-detection model is appealing from an evolutionary perspective, positing that hardwired into the neural architecture is a basic defensive system through which potentially dangerous events for the body's integrity are detected. It is somewhat vague, however, in characterising how stimulus salience uniquely activates the posited detection system, and how different types of salience are differentiated. It also does not explain where the "hurt" is situated, and how pain has its own particular unique salience content. Whilst there is ongoing debate over how to interpret the neuromatrix (as pain or non-pain specific), there is a degree of consensus that the regions of the brain associated with cognitive processing, selective attention and salience regulation, including the anterior

cingulate, prefrontal, and insular cortices, in conjunction with the somatosensory cortex, play a central role in pain experience (e.g. Apkarian, Bushnell, Treede, & Zubieta, 2005; Legrain et al., 2011b; Tracey & Mantyh, 2007).

Before considering the role of attention in pain experience in more depth, pain classifications and prevalence will be introduced.

1.1.2 Pain classifications and epidemiology

Persistent pain is typically identified as a distinct phenomenon from acute pain (Merskey & Bogduk, 1994). Whereas acute pain duration usually corresponds roughly to the continued existence of disturbance to the body, persistent pain lasts beyond normal tissue healing time (Bonica, 1953; Merskey & Bogduk, 1994). For nonmalignant pain, the usual point of division between acute and persistent pain is three months, such that chronicity is typically indicated when pain has been experienced for three months or more. In practice, many conditions are treated as examples of chronic pain even though normal healing has not occurred, such as osteoarthritis, or where the 'injury' recurs frequently, as with migraine (Merskey & Bogduk, 1994). Hence, persistent pain can also be understood as refractory pain that is not readily amenable to treatments or routine methods of pain control, such as pharmaceutical analgesics (Merskey & Bogduk, 1994). Such pain becomes a problem in its own right.

Pain (acute and chronic) is a pervasive problem, with chronic pain alone affecting an estimated twenty percent of people worldwide (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). The revised version of the International Classification of Diseases for its Eleventh edition (ICD-11) will include seven categories of the most common chronic pain disorders: primary pain disorders, cancer pain, postsurgical pain, musculoskeletal pain, visceral pain, neuropathic pain, and headache (IASP, 2014; Rief et al., 2010; World Health Organisation, 2014). In the present thesis, the studies investigating attentional bias and its modification in persistent pain will sample participants from the musculoskeletal pain population. Persistent musculoskeletal pain is pain that occurs in the bones, joints, muscles, or surrounding structures. The most common site of pain is the lower back, with 18% of adults reporting long-term discomfort in this region (Breivik et al., 2006; IASP, 2009). Disorders of the musculoskeletal system can result from overuse, repetitive strain injuries, and work-related disorders (IASP, 2009). This category of persistent pain carries the greatest economic burden, accounting for 29% of lost workdays due to ill health, surpassed only by cardiovascular disease (IASP, 2009). Symptoms can be localised, as in the lower back, or widespread, as in fibromyalgia, a prevalent (estimated prevalence 1.2% to 5.4% UK; Jones et al., 2014a) long-term condition characterised by diffuse pain of the muscles and joints (Wolfe et al., 2010). Common across disorders characterised by musculoskeletal pain include symptoms of tenderness, peripheral nerve irritation, weakness, limited motion, and

stiffness (IASP, 2009). These symptoms can be exacerbated by psychological factors such as work-related and personal stress (IASP, 2009). Research has identified other cognitive factors, such as fear of pain, as important in maintaining chronicity beyond usual tissue healing time (Nijs et al., 2013). The fear-avoidance model of musculoskeletal pain suggests that fear of pain increases hypervigilance for pain-related stimuli at the cost of information pertaining to activities of daily life, and also increases avoidance behaviour, which leads to disuse and deconditioning, and escalates pain-related disability and distress (Vlaeyen & Linton, 2000, 2012). Hence, current models indicate that attentional bias can play an important role in maintaining persistent musculoskeletal pain, which will be investigated in the current thesis (see also Section 1.3.1 Introduction).

For the majority of those affected, living with pain comes at a high social and emotional cost, affecting almost every aspect of their daily lives and the lives of their significant others. A recent survey found that one third of people with persistent pain could not work as a result of their pain and nearly one quarter found it more difficult to maintain relationships with family and friends (Breivik et al., 2006). Individuals with acute pain, including pain due to medical diagnostic and therapeutic procedures, often also suffer from pain despite medical and pharmacological intervention (Bradshaw, Brown, Cepeda, & Pace, 2011; Strassels, Chen, & Carr, 2002). Overall, uncontrolled pain creates a huge emotional and financial burden to the individual, their family and health-care organisations. Effective non-pharmacological methods as adjuvants to or alternatives for biomedical treatments for pain are in great need (Tan, Yowler, Super, Fratianne, 2010). In terms of the current thesis, improving understanding of basic underpinning cognitive-affective mechanisms of action in pain experience could feed the development of novel intervention approaches to pain management, based on bias modification techniques.

1.2 Attentional theories and the cognitive understanding of emotion

In understanding the cognitive approach to pain, and specifically the role of attentional processing in pain that underpins this thesis, it will be useful briefly to consider the development of theories of selective attention. These theories were extended to explain maladaptive patterns of attentional processing in psychological conditions such as anxiety, which has informed the cognitive approach to pain processing. The most relevant cognitive models of emotional processing, which suggested how the aberrant deployment of attention is implicated in the development and maintenance of psychological conditions, will be introduced.

1.2.1 Overview of theories of selective attention

Whilst the precise meaning of the term “attention” is still contested (e.g. Mole, Smithies, & Wu, 2011), there is broad consensus that attention involves the selection of some information from the internal and external environment for further processing, and the

inhibition of other information from receiving this processing (Chun, Golomb, & Turk-Browne, 2011). Theories and models of selective attention have sought to explain the mechanisms by which information is selected, drawing on observations that cognitive resources are limited, cognitive and behavioural events can occur automatically (i.e. without the need for conscious guidance or monitoring; Bargh, 1994; Scullin, McDaniel, & Shelton, 2013), and that performing more than one task at a time (e.g. listening to a lecture whilst people are talking near you) can be difficult (Eccleston & Crombez, 1999). Using the metaphor of communications technology, Broadbent's (1958) filter theory proposed that, due to capacity limitations of the central nervous system, information was filtered for attention at an early stage from the incoming processing stream based on physical properties, such as, in the auditory domain, the tone and loudness of the stimulus, whereas unattended information was disregarded. Treisman's (1964) attenuation model agreed with Broadbent's (1958) filter theory that attentional selection occurred early in the processing stream; however, instead of this filter blocking out all unattended stimuli, the model suggested that it merely attenuated them based on their physical properties. Thus, it was still possible for the attenuated stimulus to be processed further according to its more complex attributes; in the case of a verbal stimulus, these were, in hierarchical order, its syllables, syntax, and semantic content. In addition, the signal detectors ("dictionary units") for different stimuli possessed different thresholds, whereby some units, which responded to biologically or emotionally important stimuli, had lower thresholds. Hence, the theory allowed that even highly attenuated, pre-attentive stimuli could activate a unit that was tuned to that signal. This helped to explain how biologically important information (e.g. a baby's cry) might be given a pre-attentive advantage for neural activation in a nearby individual, readily recruiting their attentional resources. The pertinence model (Deutsch & Deutsch, 1963; Norman, 1968) countered that, instead of there being a serial filter governing attentional input based on the physical properties of stimuli, all stimuli were analysed in parallel, and the selection for attention was based on what was most relevant or pertinent to the individual. Hence, the model helped explain how the attentional filter could be biased towards certain stimuli based on prior experience and learning. However, it was criticised on the basis that for all stimuli to be fully analysed at all times would be too resource-intensive and demanding (Lavie, 1995).

In an attempt to resolve the discrepancies between the early and late selectionist views, Lavie's (1995) theory of perceptual load drew on elements from both standpoints. It suggested that the efficiency of attentional selection (that is, whether it occurred earlier or later) was determined by task difficulty, and the amount of cognitive resources available to the selective mechanism (Lavie, 1995). Empirical support for the theory was provided by the computer-based response competition paradigm, in which participants were instructed to

respond using the keyboard to onscreen target letters. Simultaneously presented were distractor letters that were either the same as (compatible) or different to (incompatible) the target. In addition, the target letter either appeared alone (low perceptual load) or was embedded in a six letter string (high perceptual load). Lavie (1995) concluded that when perceptual load was high, depleting the available cognitive resources, the task-distractors (i.e. the displayed letters that were irrelevant to the task in hand) were filtered out based on their low-level, physical properties (early selection). Whereas, when perceptual load was low, leaving more resources available for attentional selection, the task-distractors were filtered out at a later stage, after their more complex properties had been processed (Lavie, 1995). Later, the theory was extended to account for the different effects of different types of cognitive load (Lavie, Hirst, de Fockert, & Viding, 2004). It was found that whereas high perceptual load reduced the interference of task-irrelevant distractors, working memory load (which represented greater burden on processes of cognitive control) had the opposite effect, and increased distractor interference. The observed dissociation suggested the attentional effects had not been a general function of task difficulty. Instead, it was proposed that attentional selection is governed by two mechanisms. In conditions of high perceptual load, a bottom-up, stimulus driven perceptual selection mechanism allows for distractor elimination from early perceptual processes. Whilst, in conditions of low perceptual load, a top-down cognitive control mechanism downregulates the task-irrelevant distractors even after they have been perceived, governing response options in accordance with current concerns (Lavie et al., 2004). The notion that mechanisms of prefrontal cognitive control help determine attentional selection has been well supported (Bishop, Duncan, Brett, & Lawrence, 2004; Bushnell, Čeko, & Low, 2013; Derryberry & Reed, 2002; Lavie et al., 2004; Holmes, Mogg, de Fockert, Nielsen, & Bradley, 2014; Hou et al., 2014). Overall, Lavie's (1995, 2004) theory retained the assumption that attentional processing occurred in a temporally linear fashion that can be divided into earlier and later stages, and suggested that the error of the earlier theories was to suppose that the selective mechanism (which was still understood as the passage of information through a limited capacity bottleneck) had a stable location; instead, the bottleneck was located in different places, depending on factors such as the task's perceptual characteristics and cognitive demands for the participant (Mole et al., 2011).

Allport (1989) argued against the Broadbentian linearity assumption in favour of a multi-channel hypothesis to explain the complexities of selective attention. He also challenged the inherent assumption that there would be little need for attention if the brain had infinite capacity. Crucially, he claimed that the primary purpose of the attentional system was to ensure the coherence of behaviour through maintaining attention on any given focal task, whilst retaining the ability to divert attention away from this task and respond to

changing external and internal events that are unpredictable and potentially dangerous (Allport, 1989; Allport, Antonis, & Reynolds, 1972). Thus, attentional selection serves to manage the conflicting requirements of behavioural continuity, such as when attention is maintained on a current goal, and interruptibility, as occurs when attention is diverted from the current task to an environmental threat (Allport, 1989). This 'selection for action' view has influenced models of attention and pain (see Section 1.3.1), and suggested that pain can be characterised by its capacity to interrupt attention and initiate escape behaviour, which can become maladaptive in chronic pain (Eccleston & Crombez, 1999). In contrast with the Broadbentian assumption that attentional selectivity derives from the management of limited capacity bottlenecks, this view claims that it derives from capacity excess, as it enables cognitive coherence in a system that otherwise would be unable to focus on multiple discrete and incompatible messages (Mole et al., 2011; Mole, 2009; Neumann, 1987).

Other theorists observed that the attentional demands of tasks vary. Shiffrin and Schneider (1977) distinguished between automatic and controlled attentional processing. Whereas the automatic stage is fast, capacity-free and not reliant on conscious processes, the controlled stage is slower, limited, and more volitional in nature. Opposing a dichotomous classification, parallel distribution models of information processing suggested that automatic and controlled processes might be better construed as a continuum such that, with varying weightings, they can jointly determine action (Cohen, Dunbar, & McClelland, 1990). A wealth of evidence suggests that stimuli can influence behaviour (e.g. manual response time) at a relatively automatic level of processing (e.g. Chen & Bargh, 1999), and that automatic processes can be strategically modulated (e.g. Carlisle & Woodman, 2011). Through examination of the time course of attentional change in pain experience, the current thesis will gain insight into the relative importance of faster, more automatic, versus slower, more regulatory, processing streams in acute and persistent pain (Cisler & Koster, 2010).

In the last two decades of the twentieth century, the use of connectionist networks to model cognitive processes received particular research attention. Within this context, the focus shifted to the role of competitive mechanisms in attentional selectivity. In their competition model of selective attention, Desimone and Duncan (1995) proposed that, at multiple points between initial input and response output, coexisting stimuli compete for limited processing capacity and control of behaviour. Crucially, the competition outcome was determined by the relative influence of bottom-up mechanisms that responded to the stimulus salience, and top-down mechanisms that selected objects of relevance to current priorities (Desimone & Duncan, 1995). A competition-based view of attentional selection has been supported by neuroimaging studies which suggest that competition between stimuli occurs throughout the human cortex, and that a large distributed network of neuronal regions contributes to the outcome of these competitions (Kastner & Ungerleider, 2000). According

to these data, when a stimulus 'wins' the competition for representation in the visual cortex, it gains access to additional processing systems (Duncan, Humphreys, & Ward, 1997; Kastner & Ungerleider, 2000).

1.2.2 Models of emotional processing

Cognitive models of anxiety extended biased competition models of selective attention (Mathews & Mackintosh, 1998; Mogg & Bradley, 1998). These models drew on findings from empirical studies that had measured biased attentional allocation in anxiety. For example, MacLeod, Mathews, and Tata (1986) adapted the visual-probe task (also known as the dot-probe task) from computer-based experimental psychology paradigms which showed that spatial attention could be measured based on reaction times to visual-probes (Mogg & Bradley, 1998; Navon & Margalit, 1983; Posner, 1980). Speeded detection of a probe (e.g. a directional arrow) indicated the attended region of the visual display. Findings suggested that when two words (one threat-related and one neutral) were presented simultaneously onscreen, highly anxious individuals reliably responded more rapidly to probes replacing the threat-related versus the neutral word (attentional bias; MacLeod et al., 1986). These findings have been replicated on numerous occasions (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007). According to biased competition models, this observed attentional capture by threat was determined by the competitive interplay between the threat-related distractors (words) and task-relevant stimuli (arrows), with input from both a pre-attentive evaluation of threat and mechanisms of top-down control determining the outcome of this competition (Bishop, 2008; Mathews & Mackintosh, 1998; Mogg & Bradley, 1998).

More specifically, Mathews and Mackintosh (1998) proposed that when two or more stimuli were presented simultaneously (e.g. dot-probe task word pairs), their attributes (e.g. meaning) were processed in parallel, prior to full awareness of their identity. These initial, pre-attentive attribute representations competed for attentional resources. Crucially, emotional valence was accessed prior to awareness, and the threat value of the stimulus was computed automatically, at a very early stage of processing (Mathews & Mackintosh, 1998). Early representations of threat-related attributes were stored in a 'threat evaluation system' (TES), which was broadly construed as an ancient mechanism that, when threat cues were detected, initiated physiological arousal and directed attention to the possible source of danger, thereby interrupting ongoing activities (Mathews & Mackintosh, 1998). All perceptual input was automatically evaluated for affective significance in the TES, and when it matched stored threat attributes, received attentional priority (Mathews & Mackintosh, 1998). Thus, information pertaining to threat stored in the TES could be accessed pre-attentively via a fast, automatic processing route that would confer evolutionary advantage in enabling the rapid detection of cues signalling danger to the organism, and instigating a

response. In addition, elevated anxiety levels amplified the TES activation of initial threat representations, lowering the threshold at which they were evaluated as signalling danger. This meant that when anxiety was high, signals which would have previously been insufficient to capture attention would now do so in the same way as severe threat cues. However, critically, top-down control processes could oppose and downregulate this attentional capture. That is, efforts to attend to a specific stimulus could increase activation of the target representation, and inhibit the threat distractor representation (Cohen et al., 1990; Mathews & Mackintosh, 1998). Thus, the presence or absence of a threat-related attentional bias was determined by the balance between the threat value of the distractor, and the extent of target activation via task demand effects (Mathews & Mackintosh, 1998). Lavie et al's (2004) theory of perceptual load would further suggest that this ability to downregulate task distractors is reduced when cognitive load is high. Hence, a maladaptive attentional bias may become more prominent through greater stimulus-driven, bottom-up, attentional capture by aversive versus benign stimuli when cognitive control resources are depleted, such as when a person is tired or pressured (Holmes et al., 2014).

Mechanisms of biased competition continue to underpin contemporary accounts of selective attention in emotion (e.g. Vuilleumier and Driver, 2007) and pain (Legrain et al., 2009b, 2011b). The reconceptualisation of the pain matrix by Legrain et al. (2009b, 2011b), referred to in Section 1.1, proposed that the output from the salience detection system (and hence the attentional priority assigned to a sensory stimulus relative to competing attentional demands) was determined by the interplay between bottom-up, stimulus-driven processes (e.g. the intensity, novelty, and threat-value of a nociceptive stimulus) and top-down factors (e.g. catastrophic beliefs an individual holds about the stimulus, such as that it will be unbearably painful; Legrain et al., 2009b; Sullivan, Bishop, & Pivik, 1995). According to the theory, individuals with persistent pain will display a pain-related attentional bias due to the possession of stored information about pain (such as beliefs and fears) that makes it more difficult to downregulate the incoming perceptual input, and facilitates the somatosensory representation for additional processing (Legrain et al., 2009b, 2011b). Hence, adverse antecedent stored knowledge and content about pain, associated with pain chronicity, could lead to the top-down facilitation of afferent input and inhibition of non-pain input, resulting in the biased allocation of attentional resources to noxious information. In spite of its theoretical basis, few studies have explored the nature of the proposed bias. Particular questions concern its temporal components, whether the stage of attention affected is consistent across pain classifications (e.g. acute and chronic), and whether biased attention is causally implicated in vulnerability to pain. The present thesis will examine the impact of attentional bias in earlier versus later attention on acute experimental and persistent pain experience.

1.2.3 Dual-process accounts of cognitive vulnerability

As outlined in the previous section, biased competition models of anxiety (e.g. Mathews & Mackintosh, 1998) and pain (e.g. Legrain et al., 2011b) suggest that the deployment of attention to threat and discomfort is determined by biasing signals from two systems: a bottom-up subcortical system, and a top-down cortical control system (Browning Holmes, Murphy, Goodwin, & Harmer, 2010b; Legrain et al., 2011b).

These accounts share principles with the class of dual-process models, which suggest there are two coexisting but qualitatively distinct processing streams (Carver, Johnson, & Joormann, 2008). Whilst an associate stream recruits fast, bottom-up, reflexive processing that depends on acquired associations; a reflective stream recruits slower, top-down, effortful processing that relies on symbolic rules (Beevers, 2005; Browning et al., 2010b; Carver et al., 2008). Dual-process models have been widely applied in social and cognitive psychology (for an overview see Chaiken & Trope, 1999). More recently, clinical application of the approach has provided a powerful explanatory framework for cognitive vulnerability to anxiety (Ouimet, Gawronski, & Dozois, 2009), depression (Beevers, 2005), and addiction (Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013). This section extends the aforementioned prior clinical applications of the dual-process perspective to pain, with a view to providing a conceptual framework for understanding the pain-related attentional bias examined in this thesis.

As mentioned above, fundamental to dual-process accounts is that there are two distinct streams of processing, and these streams are thought to occur simultaneously and interact with one another (Carver et al., 2008). Associative (automatic) processing works rapidly through matching the salient characteristics of a current stimulus with previously encoded stimuli. It is thought to operate at a preconscious level of processing, such that the individual is aware of the output of the associative stream, without being aware of the mechanism by which the output was generated (Beevers, 2005). Past experience can, in this way, reflexively influence how current information is processed. Unchecked noxious associative processing can be detrimental to an individual's well-being. In particular, cognitive biases are considered to develop associatively through conditioned learning (Hertel & Mathews, 2011). These biases have been well documented in anxiety (towards threat; e.g. Bar-Haim et al., 2007 for a review) and depression (towards negative self-referent information; e.g. Peckham, McHugh, & Otto, 2010 for a review), where they are implicated in the development and maintenance of the conditions (e.g. MacLeod & Mathews, 2012; Van Bockstaele et al., 2014). There is growing evidence that persistent pain is also associated with condition congruent processing biases (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013a; Schoth, Nunes, & Liossi, 2012 for reviews), although evidence for their causal influence on pain is at present sparse (e.g. McGowan, Sharpe,

Refshauge, & Nicholas, 2009; this will be discussed further in Section 1.4 and Chapter Two).

Controlled (reflective) processing is comparatively slow and therefore temporally distinguishable from associative processing (Browning et al., 2010b). It is thought to be slower in part because it operates sequentially (following a series of steps) rather than in parallel (multiple concurrent events; Beevers, 2005). Unlike associative processing, it makes use of symbolic rules and explicit strategies to direct processing and, as a result, it is more effortful and takes longer to complete (Beevers, 2005; Wiers et al., 2013). For example, cognitive behavioural therapy (CBT; this will be described more fully in Section 1.3.3) teaches individuals effortfully to practise countering automatic negative thoughts that could be triggered in certain situations. Back pain may trigger the automatic thought "I cannot cope", which, with effort, the individual counteracts through searching for evidence to the contrary. In this way, the individual intentionally learns to counter the output of the associative stream and must consciously acquire the techniques taught in therapy to apply them in the future. The potential for reflective processing to modulate the associative stream is suggested by studies which have shown an impact of CBT on attentional bias in pain (Dehghani, Sharpe, & Nicholas, 2003). However, as the reflective stream is effortful and capacity limited (Carver et al., 2008), it is less likely to be helpful when resources are depleted, such as when under time pressure or when tired, when more automatic thoughts will take hold (Beevers, 2005; Holmes et al., 2014). This notion is supported by studies that have experimentally diminished executive resources using working memory load manipulations and demonstrated a resultant increase in noxious bias, suggesting that downregulation of the associative bias was impeded by the cognitive load (e.g. Wenzlaff, Rude, Taylor, Stultz, & Sweatt, 2001).

Critically, cognitive vulnerability to persistent pain might occur when an individual possesses the relatively automatic, associative bias (e.g. attentional) favouring noxious information that is not corrected by top-down executive control processes. As has been discussed in other sections, it is thought that uncorrected noxious bias can be damaging. In depression, reflective processing that focusses on mood congruent information, and does not challenge it, can reinforce the toxic bias and maintain the noxious mood-state (Beevers, 2005). In pain, reflective processing that might contribute to its maintenance includes catastrophic thinking and fearful thoughts and beliefs about pain (e.g. Swinkels-Meewisse, Roelofs, Oostendorp, Verbeek, & Vlaeyen, 2006; Sullivan & Martel, 2012). These elaborative thoughts might serve to upregulate the pain-congruent associative bias (Section 1.3.2), and contribute to impaired disengagement from, and maintained attention on, pain content (Van Damme, Crombez, & Eccleston, 2002, 2004a).

A dual-process account of vulnerability to pain suggests that any impairment in top-down modulation could result in a more pronounced bias, and more severe pain. Severe or prolonged pain might, in turn, diminish cognitive recourses, which could create a vicious spiral, whereby the co-occurrence of increased pain and reduced executive resources makes it more difficult to disengage from pain-related content, and engage with corrective processes, leading to a negative feedback loop (Beevers, 2005; Donaldson, Lam, & Mathews, 2007; Van Damme, Crombez, & Lorenz, 2007; Van Damme et al., 2002; Van Damme et al., 2004a). In line with this account, contemporary models of pain processing suggest that hypervigilance can heighten pain experience, and that pain can increase hypervigilance (e.g. Vlaeyen & Linton, 2000, 2012). There is a scarcity of experimental evidence on the influence of attentional bias on vulnerability to pain, which the current thesis aims to redress; however, one study has suggested that inducing a pain bias in attention leads to decreased pain threshold and increased pain severity (McGowan et al., 2009; see also Section 1.4). This is in line with the suggested dual-process account of vulnerability to pain, which emphasises that unchecked pain-related bias can influence an individual's perception regarding a pain stimulus. Overall, this account highlights the importance of investigating methods to reduce the bias and optimise mechanisms of cognitive control over the associative stream.

1.2.4 Cognitive accounts of emotion

In his associative network theory, Bower (1981) posited a network model of emotion and associative spreading activation. The model conceptualised emotions as nodes within a semantic network, such that when an individual becomes anxious or depressed, the emotion facilitates the retrieval of mood-congruent information through the activation of associated information across the semantic network. Whilst the model principally dealt with mood state dependent memory, Bower (1981) stated that emotion could influence other cognitive processes based on the same underlying principles. For example, he claimed that emotion could influence selective attention through its effects on the salience of mood-congruent information (Bower, 1981). The model predicted, for instance, that negative words would 'pop out' for depressed individuals due to the mood congruency effect, and that a depressed individual would spend more time looking at negative words in a multiple stimulus display, which, in turn, could lead to a negative feedback loop (Bower, 1981). Whilst the model provided a powerful theoretical framework for cognition and emotion research, it has been criticised on a number of grounds. First, the conceptualisation of emotions as nodes within a semantic network is considered an over simplification (Eysenck, 2013; Power & Dalgleish, 1999). In actuality, emotion is more that the constituent of a semantic network; it is readily distinguishable from cognition, and, as such, requires additional explanation than is provided by the model (Eysenck, 2013). Second, whereas the

pattern of automatic activation is likely to vary across different types of emotion (e.g. anxiety, depression), the model treated all emotion in the same way and thus cannot provide a more nuanced account of the cognitive processing of emotionally salient information (Eysenck, 2013). Third, the model suggested that mood-congruent processing biases exclusively resulted from bottom-up, stimulus driven, associative mechanisms, and did not allow for the dual influence on attentional competition of bottom-up sensory mechanisms responsive to stimulus salience and their modulation by top-down control mechanisms that promote task relevant activity, whereas contemporary research has supported the importance of this interaction (Bishop, 2008; Eysenck, 2013).

Biased competition models of anxiety (e.g. Mathews & Mackintosh, 1998) and pain (e.g. Legrain et al., 2009b, 2011b) proposed that an individual's prior experience can modulate bottom-up attentional capture and contribute to attentional bias (Sections 1.1.1 and 1.2.2). Beck (1976) and Beck and Clark's (1988) schema theory provided a cognitive account of how an individual's stored representations could influence the development and maintenance of psychological conditions such as anxiety and depression. They proposed that cognitive schemas, defined as "functional structures of relatively enduring representations of prior knowledge and experience" (Beck & Clark, 1988, p. 24), influence multiple processing systems, including attention, perception, and memory. Importantly, pre-existent maladaptive schemas (e.g. in anxiety, of threat-related content) could produce cognitive biases in which the processing of schema-congruent information was prioritised (Beck & Clark, 1988). This preferential allocation of resources to information congruent with antecedent maladaptive schemas, it was proposed, increased vulnerability to anxiety and depression. Tending to be latent, schemas particularly influenced an individual's thinking and behaviour in times of stress. Being in an anxious or depressed state activated the threat-related or negative self-schemas, which in turn led to negative automatic thoughts and cognitive distortions. One such cognitive distortion was termed 'catastrophising', whereby anxious individuals who possessed maladaptive threat-related schemas were more likely to focus on the worst possible outcome of a situation, and over-estimate the probability of its occurrence (Beck & Clark, 1988; Eysenck, 1997).

The idea that maladaptive schemas exert top-down influences on the cognitive processing of schema-congruent information has been influential. Contemporary cognitive-affective models of pain, such as the schema-enmeshment model (Pincus & Morley, 2001; this model will be discussed in Section 1.3.1 below) continue to invoke functional networks of associated content that bias processing resources towards noxious information, in explaining aspects of pain chronicity. In line with Beck's cognitive account of emotional processing, numerous empirical studies have demonstrated that anxious individuals disproportionately attend to threat-related information (attentional bias; for a review see Bar-

Haim et al., 2007) and tend to interpret ambiguous information in a threat-related way (interpretative bias; Mathews & Mackintosh, 2000). However, limitations of the theory have also been highlighted (e.g. Eysenck, 1997; Williams, Watts, MacLeod, & Mathews, 1988). In particular, whilst the theory predicts that individuals with anxiety and depression will exhibit multi-modal processing biases in attention, interpretation, and memory, this has not been consistently demonstrated. In actuality, the pattern of biases associated with anxiety and depression differs more than was suggested by schema theory (Mogg & Bradley, 2005; Eysenck & Keane, 2010). For instance, even considering attentional bias on its own, the collective evidence suggests that whereas anxiety is reliably associated with an early, relatively automatic attentional bias towards external threat-related information, this bias is not typical of depression (Mogg & Bradley, 2005). In depression, the attentional bias has typically been demonstrated for self-relevant information that is presented under conditions that permit later, more elaborative processing of the stimulus (Mogg & Bradley, 2005). In addition explicit memory biases have typically been reported in depression, but not anxiety (e.g. Mogg, Mathews, & Weinman, 1987). These findings led to the suggestion that anxiety and depression might be characterised by different types of cognitive bias, which differ in the extent to which they resulted from earlier, associative, or later, more conceptual, information processing (Williams et al., 1988; Mogg, Bradley, Williams, & Mathews, 1993).

In their integrative model, Williams et al. (1988) sought to explain the observed differences in processing biases in emotion. Since pain has an emotional component (Merskey & Bogduk, 1994) and cognitive mechanisms that determine processing biases of emotionally salient information in anxiety and depression are thought to be extendable to other conditions (e.g. Mathews & Mackintosh, 1998; LeDoux, 1996, 2003), it will be useful to consider their account here. In essence, Williams and colleagues (1988) suggested that attentional and memorial processing involve both an automatic and strategic component. Emotional processing biases could involve one stage, without relying on the other stage, and emotions could differentially influence automatic and strategic subsystems according to their individual characteristics. Threat detection was facilitated by fast, relatively automatic, stimulus-driven ‘perceptual’ processes, whereas depression involved ‘conceptual’ top-down mechanisms that were slower, and more strategic, in nature, forming links between the semantic content of incoming and stored representations, and thereby guiding the allocation of cognitive resources through more reflective processing.

Given that the function of anxiety is thought to be to alert an organism to actual or potential harm, the perceptual subsystems could rapidly assign attentional priority to processing threat-related over benign stimuli in anxious individuals, and hence this helped explain how the bias could be detected at relatively short stimulus durations (Mogg, Bradley, De Bono, & Painter, 1997; Williams et al., 1988). Since depression involved reflective

subsystems that were used for elaborative processing, early attentional bias would not typically be evident in this population (Mogg & Bradley, 2005; Williams et al., 1988). The model explained that the slower, more strategic allocation of resources to negative self-referent material in depression would result in a bias in later, and not earlier, attention (Williams et al., 1988). This latter prediction is supported by a number of experimental studies reporting depression-congruent biases in maintained attention (e.g. Koster, De Raedt, Goeleven, Franck, & Crombez, 2005). Drawing on these insights from the emotion domain, the present thesis will examine the temporal dynamics of attentional bias in pain processing.

In distinguishing between automatic and strategic processes in bias acquisition, the model of Williams et al. (1988) provided a plausible account of the various experimental findings concerning cognitive biases in different disorders, which previous theories had been unable to explain (e.g. Beck, 1976). However, the model had a number of limitations. In particular, some studies have suggested that anxiety could also influence elaborative processing (e.g. Williams, Mathews & Hirsch, 2014). For example, having initially oriented to a threating cue, anxious participants may then deliberately favour benign information, thereby minimising their conscious processing of, and disturbance by, the threat (e.g. Mogg, Bradley, Miles, & Dixon, 2004a). Conversely, the tendency for depressed individuals to make negative appraisals may become more automated over time (e.g. Beevers, 2005; Gotlib & Joormann, 2010). Such observations led some theorists to suggest that a combination of automatic and elaborative processes is involved in various emotions (e.g. Mogg et al., 1993; Beevers, 2005), and the theoretical distinction between these components of processing contributed to the development of biased competition models of selective attention in emotion (e.g. Mathews & Mackintosh, 1998, discussed in Section 1.2.2). The present thesis will explore the impact of pain on initial orienting and maintained attention, and test the comparative effects on pain of training the earlier versus later stages of attention.

1.2.5 Time course of attention

As indicated above, central to the present thesis is examination of whether different temporal aspects of attentional bias have consistent influences on pain. This section will therefore consider in more detail the time course of attentional orienting.

Research has supported the notion that attentional selection has component processes that can be temporally divided based on where they occur in the processing stream, drawing a distinction between mechanisms involved in the shifting and maintenance of attention (Allport, 1989; LaBerge, 1995; Mogg & Bradley, 1999; Williams et al., 1988). According to this view, initial orienting is a relatively fast process which can be assessed when stimuli are presented to participants for comparatively short exposure durations ($\leq$ 500 ms; Mogg & Bradley, 1998). For example, many visual-probe studies have demonstrated that participants display an attentional bias for threat-related information presented for 500

ms, suggesting a relatively heightened vigilance to these danger-signalling stimuli. In some instances, a pattern of vigilance-avoidance has been demonstrated, whereby initial orientation to the threatening stimulus is followed by an attentional shift favouring competing benign content (e.g. presented for 1250 ms; Mogg, et al., 1997). Biases in maintained attention can be revealed when stimuli are presented for longer durations (e.g. ≥ 1200 ms; Mogg & Bradley, 1998), which is thought to be sufficient time to allow more elaborative processing of stimulus content (Koster et al., 2005; Mogg & Bradley, 1998, 1999). For example, several studies have suggested that depressed individuals display an attentional bias when condition congruent information is presented for 1250 ms (Koster et al., 2005), suggesting that later attentional processes, such as difficulty shifting attention away from the stimulus (disengaging), or inhibiting its aversive content, are implicated in attentional biases in depression (e.g. Koster et al., 2005; Leyman, De Raedt, Schacht, & Koster, 2007; Joormann & D'Avanzato, 2010; Sass et al., 2014).

Supporting neuroimaging evidence suggests that distinguishable neural subsystems underpin attentional shifting and maintenance. Whereas early vigilance is thought to rely primarily on early sensory processing brain regions, such as the visual cortex and amygdala, later maintained attention is thought chiefly to rely on cortical and prefrontal regions, also associated with attentional control (Bishop, 2008; Gotlib & Joormann, 2010; Sass et al., 2014). Hence, examining the time course of pain-related attentional processing speaks to the relative degree to which early vigilance and later elaborative mechanisms of cognitive control are involved in biasing attention to noxious stimuli (Sass et al., 2014). In the present thesis, attentional bias in earlier and later attention will be measured by manipulating the duration of presented stimuli (e.g. Mogg & Bradley, 1998; Liossi, Schoth, Bradley, & Mogg, 2009; Liossi, White, & Schoth, 2011).

1.3 The role of attention in experimental, acute and chronic pain

1.3.1 Cognitive-affective models of attention and pain

In addition to the fear-avoidance model referred to in Section 1.1.2, four key theoretical models seek to explain the relationship between pain and attention at the level of the individual; these will be introduced below. Although only one of these models was developed to provide an explanation for the development of pain-related cognitive bias (the Schema Enmeshment Model of Pain; Pincus and Morley, 2001), they have each provided valuable insights into the inexorable links between attentional and pain processing, and as such will inform the current programme of research.

First, the cognitive-affective model of the interruptive function of pain (Eccleston & Crombez, 1999) proposes that the primary function of pain is to disrupt attention and initiate escape behaviour, and that persistent pain should be redefined as persistent interruption. The model is based on three principles: the first defines attention as selection for action, and

states that the urge to escape is intrinsic to the attentional selection of pain. Hence, the model draws on the theoretical approach to attention of Allport (1972, 1989), who claimed that the attentional system serves primarily to enable both the coherence of cognition and behaviour through maintained attention on a focal task (such as reading a text) and the shifting of resources to unpredictable cues (such as the smell of smoke), thereby enabling the initiation of protective action through disruption of the original behaviour. Applying this conceptual framework of priority reassignment specifically to signals of bodily sensation, the second principle states that pain selection interrupts attention and behaviour, imposing a new behavioural priority of stopping the pain. The third principle indicates that this interruption is moderated by several factors concerning the pain itself, such as its intensity, novelty, predictability and perceived threat-value, and the pain environment, such as concomitant emotional arousal (Eccleston & Crombez, 1999).

Thus, the model describes how pain, understood as a warning of bodily danger to the organism (Eccleston & Crombez, 1999; Öhman, 1979), occurs in an environment of multiple non-noxious competing demands. In the absence of pain, attention can be engaged on a focal task (they give the example of listening to a friend's story at a party). In spite of other demands on attention (such as distant conversations), a coherent engagement in the story is maintained (Eccleston & Crombez, 1999). This behavioural coherence is achieved via the prioritisation of 'action programs' concerning listening to the story, and the control of sensory inputs from the internal and external environment. If in this scenario a painful stimulus is encountered (the example is given of consuming something hot), then new action programs aimed at abating the noxious stimulus are prioritised over those concerned with listening to the story (Eccleston & Crombez, 1999). Attention is rapidly shifted to the pain, enabling fast action aimed at dealing with the noxious stimulus and preventing excessive tissue damage.

This attentional shift from the focal task to pain is modulated by a number of factors relating to the pain stimulus (such as its intensity) and its internal (e.g. beliefs an individual holds about pain) and external (e.g. how interesting the story was) context, as suggested by the third principle of the model. A stimulus of high intensity (very hot) is more likely to disrupt attention than a low intensity stimulus. Supporting this claim, Eccleston (1994) found that performance on a task that required controlled effortful command of attentional focus (the numerical interference task) was interfered with more in participants given high levels (versus low levels) of pain, as indicated by poorer performance. Concerning the pain context, an individual listening to an interesting story, who has low fear of pain and does not tend to think catastrophically about pain (such as wondering whether something serious will happen; Sullivan et al., 1995), will be less disturbed by a pain stimulus of the same severity as someone who is listening to a dull story, is highly fearful of pain and tends to have

catastrophic thoughts whenever they experience pain. These predictions have been supported by studies indicating reduced attentional capture by pain when the focal task is cognitively engaging (Legrain, Perchet, & Garcia-Larrea, 2008) and greater pain-related attentional capture in participants with high versus low fear of pain, and pain catastrophising (e.g. Keogh, Ellery, Hunt, & Hannent, 2001b; Vancleef & Peters, 2006, respectively). The model has provided a useful framework for understanding the importance to pain experience of attentional interruption. In characterising persistent pain as persistent interruption it highlights that, over and above its sensory qualities, pain has the capacity to repeatedly disrupt and interfere with an individual's goals when it is habitually processed at the expense of competing non-noxious information (Eccleston & Crombez, 1999). It also suggests that reducing this pain-related attentional bias and inducing a bias towards benign content might help inhibit pain processing, thereby reducing persistent pain severity and interference with daily life, although this possibility has received little research attention. The impact of modifying attentional bias on vulnerability to pain will be examined in experimental Studies Three, Four, and Five of this thesis.

Second, the motivational account of pain (Van Damme et al., 2010) similarly views pain in the context of goal pursuit. Like Eccleston and Crombez (1999), it states that to fully understand why and how people attend to pain requires taking into account the motivational context in which it occurs (Legrain, Crombez, & Mouraux, 2011a; Van Damme et al., 2010). They highlight that central to Allport's (1989) view of attention was that its deployment is influenced by goals, which they further define as the 'mental representation of a desired end state that differs from the current state of an individual' (Van Damme et al., 2010, p. 205, with reference to Austin & Vancouver, 1996; Fishbach & Ferguson, 2007). Task goals can lead to the voluntarily and involuntary capturing of attention through modifying attentional control settings based on volitional strategy and task demands (e.g. instructions), respectively (Van Damme et al, 2010). Importantly, the focussing of attention on goal-relevant stimuli results in the inhibition of goal-irrelevant stimuli, such that even salient information can be missed (Simons & Chabris, 1999; Van Damme et al., 2010). According to this view, the likelihood that pain will divert attention from a current task or goal is reduced when the task is highly engaging, in which case an afferent noxious stimulus might be inhibited and ignored. On the other hand, in situations where the current goal is pain-related (e.g. seeking medical treatment; Eccleston & Crombez, 2007), then the opposite might occur, wherein top-down mechanisms facilitate the afferent sensation and inhibit pain irrelevant stimuli, resulting in a pain-related attentional bias (Van Damme, et al., 2010). Hence, the model suggests that differentiating between whether pain is goal relevant (top-down facilitation) or irrelevant (bottom-up interruption), as well as consideration of the

nature of concurrent goals (how engaging they are), will help account for patterns of pain-related attentional capture in pain.

The concept applied in the motivational account of attention to pain (Van Damme et al., 2010) that the seeking of medical treatment for pain can itself become problematic draws on the misdirected problem solving model of chronic pain (Eccleston & Crombez, 2007). This third model highlights that individuals with long-term pain often seek medical cessation of their discomfort in vain because, despite improved diagnostics and greater access to sophisticated medical interventions, symptoms can persist in spite of treatment (Eccleston & Crombez, 2007; Turk, 2002). Instead of alleviating pain, the ongoing search for a diagnosis and solution to the problem increases levels of arousal and draws biomedical content into focal attention, biasing attention towards pain and potentially sensitising the individual to multiple somatic complaints (Eccleston & Crombez, 2007; Pincus & Morley, 2001). Supporting this hypothesis, one study reported that individuals whose goal it was to control a conditioned pain stimulus reported more pain than a comparison group who were given a different goal (Notebaert et al., 2011). This study was conducted with healthy volunteers in an acute experimental pain context, and hence the generalisability of findings to individuals with persistent pain may be limited. Nevertheless, it suggests that the possession of an attentional set (defined as the mental set of stimulus features that participants used to identify goal-relevant information; Notebaert et al., 2011) relating to pain (here pain control), which has been separately reported in persistent pain populations (Eccleston & Crombez, 2007), could facilitate the top-down attentional prioritisation of noxious stimuli (Notebaert et al., 2011).

A number of other studies have investigated mechanisms of attentional capture by pain through manipulating the relevance of the nociceptive stimulus to the focal goal of the participant. Studies examining attentional processing when pain was irrelevant to the focal goal employed the primary task paradigm (e.g. Crombez, Baeyens, & Eelen, 1994). In this task, the extent to which performance on a non-painful task (such as auditory detection and/or discrimination) was disrupted by pain was an indirect measure of its bottom-up attentional demand. In line with the model of Crombez & Eccleston (1999), findings consistently demonstrated that pain led to decrements in task performance, providing evidence for bottom-up, stimulus-driven attentional capture by pain. However, the effect was typically transient and participants rapidly switched back to the primary task, suggesting reorientation to the focal goal (e.g. auditory detection; Crombez et al., 1994; Van Damme et al., 2010). Also widely used is the Posner exogenous cueing task (e.g. Posner, 1978, 1980), which measures participants' performance when responding to targets at either cued (valid) or uncued (invalid) locations. Experiments making use of this task typically reported reaction times were faster to detect targets when the cue was painful (Van Damme et al.,

2007) or signalled forthcoming pain (Van Damme, Crombez, & Eccleston, 2004b). As such, these studies supported theoretical models that additionally predicted the top-down modulation of attentional capture by task-irrelevant pain stimuli (e.g. Crombez & Eccleston, 1999; Van Damme et al., 2010). Furthermore, research has suggested that attention to non-painful stimuli (such as visual) can decrease pain and change pain-related brain activity (e.g. Bantick et al., 2002). In keeping with Van Damme et al.'s (2010) account, it is thought that cognitive engagement to a focal task decreases attentional capture by pain by inhibiting the sensory analysis of nociceptive inputs (Legrain et al., 2009a). Attentional processing when pain is goal-relevant (i.e. participants perform a task that is related to pain, such as detection, discrimination and evaluation) has also been investigated using cueing paradigms (Spence & McGlone, 2001; Van Damme et al., 2004a), and supported the notion that attention can upregulate pain processing when it is relevant to the focal goal.

Fourth, the schema-enmeshment model of pain (SEMP; Pincus & Morley, 2001) provides the only explicit explanation for the occurrence of cognitive processing biases in persistent pain. It suggests that three self-schemas relating to pain (its sensory features), illness (negative health, behavioural and emotional consequences), and self (a multifaceted structure that includes evaluation of self-worth) are active in persistent pain experience. Crucially, it is the degree to which aspects of the self are 'enmeshed' with pain, represented in the interaction between these three schemas, which determines the level of cognitive bias towards pain-related information, and how well an individual adapts to pain.

The SEMP makes four key predictions. First, that processing priorities depend not only on the salience of stimuli, but also on the content of schemas; second, that all pain patients exhibit preferential processing of pain-related information; third, self-referential material, particularly when congruent with the self-schema, is preferentially processed; and fourth, cognitive biases towards self-referential health and pain-related information are a feature of persistent pain. The latter is particularly true of depressed chronic pain patients, as in this group illness information is supposedly enmeshed with pain and the self. In light of these predictions, and considering the model as a whole, a key hypothesis is that individuals with comorbid depression exhibit a greater overlap and enmeshment of the three schemas, leading to increased pain-related distress and disability (Pincus & Morley, 2001; Rusu & Pincus, 2012). To date, two studies have directly tested this hypothesis by examining whether depressed individuals with persistent pain display a tendency to generate sentences with negative health and pain content. The first study (Pincus, Santos, & Morley, 2007) compared responses on a sentence completion task between four groups (depressed pain; non-depressed pain; healthy controls; osteopath controls) to explore the types of thoughts that depressed chronic pain patients experienced. As predicted, negative health meanings were more prevalent among the depressed chronic pain group in comparison with the other

three groups, whereas non-depressed pain patients focussed on health, but not necessarily in a negative way. However, interpretation of the findings was limited because the study did not code for separate health and pain content and there was no non-pain depressed control group and no analysis of self-denigration. Consequently, it was not possible to tell whether health-pain cognitive specificity occurred, given that the excess of negative health meanings could have been a function of a discrete, psychiatric depression and not the pain-related depression predicted by enmeshment of the self, pain and illness schemas. A subsequent study delineated these constructs in the design and provided further support for a discrete, pain-related depression that is qualitatively different from psychiatric depression, indicating that the posited schemas may be active in pain-related distress (Rusu & Pincus, 2012). However, researchers unconnected with the model's development also need to test its hypotheses, to avoid any unintended experimenter bias.

One problem with the SEMP is that it has been almost entirely based on cross-sectional studies that have examined possible vulnerability markers for the development and maintenance of chronic pain, such as attentional bias, anxiety and depression and fear of pain. Consequently, it remains unclear whether processing biases result from exposure to pain over time, or do indeed signify a cognitive vulnerability that can amplify pain experience and result in its maintenance. Future research therefore needs to employ a longitudinal design, and investigate whether fluctuation in processing bias impacts on pain. The impact of an induced neutral attentional bias on persistent pain experience will be investigated in the present thesis.

Limitations that apply to each of the models (Eccleston & Crombez, 1999, 2007; Pincus & Morley, 2001; Van Damme et al., 2010) include that they do not specify the mechanisms by which attention is captured by pain, such as the extent to which pain impacts on the earlier versus later stage of attentional processing in acute and persistent pain (and whether this differs), and what impact these temporal components of attention have on pain experience. In measuring attentional bias at different stimulus durations (500 versus 1250 ms), and assessing the impact of inducing a neutral bias in earlier versus later attention, relative to controls, on pain (acute experimental and persistent), the current programme of research will address these questions.

1.3.2 Cognitive factors and pain

The theoretical models discussed in the previous section highlighted the prominent role of cognitive factors in pain experience. Experimental studies have supported the notion that maladaptive cognitive profiles, such as ones characterised by fear of pain and hypervigilance, can represent a risk factor for the development of persistent pain in individuals with acute or subacute pain, and, in persistent pain, can increase pain-related disability and distress (Main, Kendall, & Hasenbring, 2012). These cognitive constructs

could help explain the exceptional heterogeneity of pain phenotypes such that individuals can present with comparable pathology (such as joint involvement in musculoskeletal pain) and experience very different levels of distress and disability.

Researchers have sought to reduce this heterogeneity through characterising how maladaptive psychological factors are associated with poorer pain outcomes, thereby informing the clinical selection of optimal treatment strategies. Indeed, in line with the biopsychosocial model of chronic pain (Gatchel et al., 2007; cf. Section 1.1.1 Introduction), psychosocial factors have been found to be stronger predictors of treatment outcome than biomedical factors (Carleton & Asmundson, 2012; Crombez, Vlaeyen, Heuts, & Lysens, 1999), such that the identification and reduction of maladaptive pain-related cognitions can be a valuable and effective treatment approach (Carleton, Richter, & Asmundson, 2011; see also Section 1.3.3). In the present section, key predispositional traits that the hitherto research has implicated in vulnerability to pain will be introduced. As the present thesis concerns the influence of attentional bias on pain vulnerability, the focus of this section will be on cognitive factors that have been associated with attention to pain, and adverse pain outcomes.

Chapman (1978) was the first to apply the concept of hypervigilance to the pain literature, defining it as a constant scanning of the body for somatic sensations that might be pain or preface pain (Roelofs, Peters, McCracken, & Vlaeyen, 2003a; Van Damme, Crombez, Eccleston, & Roelofs, 2004c). Whereas increased somatosensory attention to pain and related signals was termed 'specific hypervigilance', heightened attention towards other, non-pain signals was termed 'general hypervigilance' (Chapman, 1978; Roelofs et al., 2003a). This overalertness for pain was thought to be an emergent characteristic of pain's inherent threat value, such that individuals who appraised somatic sensations as harmful or dangerous, were considered to be more likely to develop a tendency for scanning the internal and external environment for pain-related sensations and information (Chapman, 1978; Van Damme et al., 2004c). As detailed in Section 1.3.1 of the Introduction, Eccleston and Crombez (1999) proposed that, in functioning as a signal of potential danger and bodily harm, pain diverts attention from ongoing activities and enables an individual to respond quickly with protective action. Furthermore, this interruptive function is mediated by affective characteristics of pain pertaining to its threat value (Eccleston & Crombez, 1999). Supporting this view, cognitive and affective factors that increase the perceived threat value of pain have been found to exacerbate its attentional interruption, which, in turn, leads to central amplification of the afferent input and is associated with poorer pain outcomes (e.g. Van Damme et al., 2002, 2007). Hence, attention has been identified as a critical mechanism by which cognitive factors, such as being fearful of and thinking catastrophically about

somatic and painful sensations (these will be discussed in more detail below), can impact on pain experience (Sullivan & Martel, 2012).

Pain catastrophising has been broadly defined as an exaggerated negative orientation to actual or anticipated pain, comprising elements of excessive focus on pain-related stimuli (rumination), exaggeration of the threat-value of pain (magnification) and negative evaluation of one's ability to deal with pain (helplessness; Sullivan et al., 2001; Sullivan & Martel, 2012). Central to pain catastrophising is how somatic and painful sensations are appraised, placing it within the theoretical context of prominent cognitive models of emotional processing (e.g. Beck, 1976). As discussed earlier in the Introduction (Section 1.2.4), these models propose that negative appraisals will lead to emotions such as fear and anxiety (Sullivan & Martel, 2012). This approach was elaborated in the fear avoidance model of pain, which described how catastrophic thinking about pain could lead to increased fear of pain and pain-related hypervigilance or attentional bias, resulting in avoidance and escape behaviours and problematic pain outcomes (Vlaeyen & Linton, 2000, 2012). Numerous studies have supported the hypotheses that pain catastrophising predicts response to acute pain (e.g. Roelofs, Peters, van der Zijden, & Vlaeyen, 2004), and pain severity, distress and disability in persistent pain populations (e.g. Turner, Jensen, Warms, & Cardenas, 2002).

Several studies have reported the anticipated association between raised pain catastrophising and attentional bias or hypervigilance for pain (e.g. Crombez, Eccleston, Baeyens, & Eelen, 1998a, b; Vancleef & Peters, 2006). However, findings have been mixed, with other studies failing to find evidence for the predicted relationship (e.g. Van Damme et al., 2008; Van Ryckeghem, Crombez, van Hulle, & Van Damme, 2012). Using the dot-probe task, Van Ryckeghem et al. (2012) presented sensory pain and neutral word pairs (n = 5) on screen for 500 ms, and found no association between this index of attentional bias and pain catastrophising in a healthy undergraduate sample. This absence of association could have occurred for a number of reasons: the very small number of word pairs and use of a single stimulus presentation time might each have reduced the sensitivity of the attentional bias test. Measuring attentional bias in earlier and/or later attention, and utilising a greater stimulus set, might uncover an association between the two constructs (which will be tested in the current programme of research). The importance of employing longer stimulus presentation times when measuring attentional bias in pain has been suggested by a number of studies (see Crombez et al., 2013a; Schoth et al., 2012 for reviews). For example, using the primary task paradigm, Van Damme et al. (2002) demonstrated that, whilst pain catastrophising does not necessarily lead participants to orient attention towards pain, once attention has been captured by pain, it is more difficult for them to disengage attention from the pain stimulus. This disengagement deficit was enhanced when levels of pain

catastrophising were high, suggesting that negative pain appraisals made it more difficult for participants to shift their attention away from the word 'pain', as indexed by slowed response times to a subsequent auditory tone. Whilst these findings (the study employed a healthy undergraduate sample with mean age of 19) cannot be easily generalised to clinical pain populations, a recent review found that individuals with persistent pain who scored highly on measures of pain catastrophising were less likely to engage in coping strategies such as distraction, and reported higher pain severity, supporting the implication that the tendency to negatively appraise pain may make it more difficult to disengage from pain, and engage with other, competing, activities (Edwards, Bingham, Bathon, & Haythornthwaite, 2006). The relationship between pain catastrophising, attentional allocation and distraction efficacy was further supported by two recent studies which suggested that high catastrophisers reported lower engagement with a distraction task administered whilst their arm was immersed in freezing cold water (Van Damme, Crombez, Wever, & Goubert, 2008), and that participants were less responsive to distraction from experimentally induced electrocutaneous pain when they possessed a baseline attentional bias towards pain stimuli (Van Ryckeghem et al., 2012). However, as discussed above, this latter study failed to find the anticipated association between pain catastrophising and attentional bias, which could be due to methodological factors.

Closely related to the concept of catastrophising, anxiety sensitivity (AS) has been defined as the fear of anxiety-related sensations that arise from beliefs the sensations will have adverse consequences such as serious illness and death (Reiss, 1991). AS was one of the first psychological constructs suggested to be a potentially critical vulnerability factor for the development and maintenance of persistent musculoskeletal pain (Asmundson & Taylor, 1996; Asmundson & Norton, 1995; Carleton & Asmundson, 2012; Carleton, Sharpe, & Asmundson, 2007). Originally understood in the context of anxiety disorders, AS was thought to amplify fear reactions, and thereby contribute to the development of clinical anxiety and panic attacks (Asmundson & Taylor, 1996; Reiss, 1991). More specifically, an individual may be subject to an anxiety provoking situation, such as chest pain, which they appraise as signifying a harmful event, such as a heart attack; this catastrophic appraisal sensitises them to the symptoms of anxiety, and they become anxious of being anxious. Around this time, research had pointed to the importance of fear of pain to the behaviour of individuals with persistent pain (e.g. McCracken, Zayfert, & Gross, 1992), and anxiety sensitivity was considered a potentially contributory factor to pain fear and avoidance behaviours, which, in turn, reinforce the fearful appraisals (Asmundson & Taylor, 1996; Carleton & Asmundson, 2012). Crucially, higher levels of anxiety sensitivity are thought to contribute to catastrophic misinterpretations of physical sensations related to pain, or general

arousal, which is associated with increased sensitivity to pain (Carleton & Asmundson, 2012).

Studies have supported the relationship between AS, particularly the component of AS that concerns somatic symptoms, and pain (Asmundson, Norton, & Norton, 1999). This relationship has been demonstrated both in acute pain and persistent musculoskeletal pain samples (Asmundson & Norton, 1995; Keogh & Cochrane, 2002; Norton & Asmundson, 2004; Thompson, Keogh, French, & Davis, 2008). Moreover, AS might be related to cognitive biases for physically threatening and pain related stimuli (Keogh & Birkby, 1999), although findings have been somewhat mixed (Keogh & Cochrane, 2002; Vancleef & Peters, 2006). These mixed findings could be because pain-related attentional bias is specific to pain stimuli, whereas anxiety sensitivity is a more general concept that incorporates social and cognitive, as well as somatic, concerns (Vancleef & Peters, 2006). For instance, using the dot-probe task, Keogh and Birkby (1999) found that healthy individuals with elevated AS displayed an increased attentional bias for physically threatening stimuli. In a subsequent study, Keogh and Cochrane (2002) found that participants completing the cold pressor task (CPT) who had higher baseline AS reported lower pain threshold and tolerance, and higher pain severity than those with lower AS. In addition, AS was significantly associated with pain threshold and affective pain scores, such that individuals with higher AS noticed pain more quickly and reported higher levels of affective pain. However, whilst the relationship between AS and pain severity was found to be mediated by cognitive bias (in this case interpretive), the prediction that attentional bias would mediate AS and pain severity was not supported. Hence, these findings supported the notion that the maladaptive processing of pain-related information could exacerbate pain experience, but the precise relationship between pain hypervigilance and AS was left unclear. This could have been in part due to its purely retrospective assessment of pain severity (attentional bias was measured before or after the CPT, counterbalanced), which might have recruited more interpretive processing of the nociceptive event, and hence interpretive bias was found to mediate the relationship. In addition, the dot-probe stimuli were presented for the single duration of 500 ms, leaving it possible that earlier and/or later attention might have mediated the relationship had it been assessed. Other studies have suggested that AS may exacerbate negative pain experience through its contribution to fear of pain, which has been more reliably associated with pain hypervigilance (e.g. Keogh et al., 2001b; Yang, Jackson, & Chen, 2013).

Several studies have provided evidence for the relationship between anxiety sensitivity, fear of pain, and deleterious pain outcomes, such that individuals with persistent pain who have elevated AS are more likely to experience higher levels of distress and disability than individuals with lower AS and comparable pain severity (Asmundson & Norton, 1995; McCracken & Keogh, 2009; Norton & Asmundson, 2004). For instance,

using structural equation modelling, Asmundson and Taylor (1996) and Norton and Asmundson (2004) found that AS directly exacerbated fear of pain and indirectly increased avoidance behaviour, through its effects on fear of pain, in individuals with persistent musculoskeletal pain and recurrent headache, respectively. It should be noted that a limitation of these studies was that, through their use of structural equation modelling, the predictions were not tested through experimental manipulation, but through modelling of the extant dataset (Asmundson et al., 1999). Nevertheless, two recent meta-analyses have provided overall support for the relationship between AS and pain, such that AS was found to increase pain-related fear, which, in turn, was associated with lower pain threshold and tolerance in acute experimental pain (Ocañez, McHugh, & Otto, 2010), and increased disability in persistent pain (Martin, McGrath, Brown, & Katz, 2007; Ocañez et al., 2010).

The above findings are in line with the fear avoidance model of persistent musculoskeletal pain (Vlaeyen & Linton, 2000, 2012). Numerous studies have specifically measured fear of pain (typically administering questionnaires in the laboratory, such as the 'Fear of Pain Questionnaire'; Asmundson, Bovell, Carleton, & McWilliams, 2008), and supported its relationship with acute pain outcomes (e.g. Fritz & George, 2002; Sieben, Vlaeyen, Tuerlinckx, & Portegijs, 2002; Swinkels-Meewisse et al., 2006), and the development and maintenance of persistent pain (e.g. Crombez et al., 1999; Crombez, Viane, Eccleston, Devulder, & Goubert, 2013b). A recent study extended these findings and measured fear of pain and pain severity in a persistent musculoskeletal pain sample using experience sampling methodology in the home environment, thereby introducing greater ecological validity to the results than those attained from laboratory studies. Their results indicated a strong positive association between higher pain fear and severity ratings (Crombez et al., 2013b). Moreover, they found that higher fear of pain was associated with increased attention to somatic and painful sensations, which was, in turn, associated with worse pain (Crombez et al., 2012). This finding supports the view that fear of pain can bring about an attentional state of hypervigilance for pain cues, which can, in turn, exacerbate somatosensory symptoms. Overall, fear of pain, which is amplified by anxiety sensitivity, is considered an important diathetic construct, and, in persistent pain, is thought to be more disabling than pain severity itself (Crombez et al., 1999; Carleton & Asmundson, 2012; Vlaeyen & Linton, 2012).

In summary, cognitive factors such as pain catastrophising, anxiety sensitivity, and fear of pain can modulate acute and persistent pain experience, and hypervigilance is considered to be an important underpinning mechanism in this relationship. This raises the possibility that interventions which seek to retrain attention could impact on pain experience, which will be explored in the present thesis. Whereas research has suggested that fearful and catastrophic thinking about pain can lead to the diminution of cognitive resources involved

in distracting oneself from pain, thereby reducing the efficacy of this important coping strategy, the current thesis will explore an implicit technique for retraining attention which, it is thought, does not rely on conscious strategic mechanisms of top-down control, and hence could be a useful adjunct to individual strategies for coping with pain and existing therapeutic techniques.

1.3.3 Psychological approaches to pain management

Currently, one of the main psychological approaches for persistent pain management is cognitive behavioural therapy (CBT), which is based on the concept that thoughts, feelings and behaviours are causally interconnected. It emphasises the important role of patient cognitions (e.g. appraisals, beliefs, expectancies) as mediators between situational stimuli and physiological, emotional and behavioural responsiveness (Turner & Chapman, 1982).

CBT for persistent pain has a good evidence-base, with research demonstrating that it can often result in reductions in pain outcomes, pointing to a causal role for cognitive factors in pain experience. Cognitive-behavioural models are based on the observation that beliefs and expectations concerning pain play an important role in perception and adjustment. Drawing on these models, CBT aims to create feelings of coping and self-efficacy (Keefe, Abernethy, & Campbell, 2005). In a typical CBT for pain protocol, participants complete a number of modules over a series of sessions, such as education, distraction techniques, relaxation training, and cognitive restructuring (Aggarwal et al., 2011). First, participants may be given a rationale for how the programme could help control pain, which might include education on central pain processing. Second, they are taught explicit self-regulatory strategies to divert attention from pain, and to create affectively positive images and visualise positive scenes (distraction). Third, they may be taught relaxation techniques. Fourth, in cognitive restructuring, participants are taught how to challenge negative thoughts that accompany pain, such as the tendency to attribute their disabilities to a reality characterised by loss of control (e.g. Main & Watson, 2013). Unchallenged, these self-statements may reinforce demoralisation, inactivity and sensitisation to nociception. Hence, in CBT, patients learn explicitly how to counter negative self-appraisals about their ability to perform certain motor activities, such as climbing the stairs or lifting heavy objects, and how to counter catastrophic thoughts, such as ‘this pain in my spine is terrible, it must be damaged’ (Buhrman et al., 2013). For example, patients with non-cardiac chest pain undergoing CBT who learned to reattribute the cause of their pain to stress instead of a heart problem exhibited a reduction in reported chest pain (Looper & Kirmayer, 2002).

A recent Cochrane review of psychological interventions for the management of persistent pain concluded that, in comparison with treatment as usual, CBT resulted in small

to moderate reductions in pain severity, mood (anxiety and depression), disability and pain catastrophising at post-intervention (standardised mean differences = -0.21 to -0.53). However, the effects of the intervention, which relies on participants effortfully identifying and challenging their maladaptive beliefs (e.g. Mathews, 2006), had diminished at six-month follow-up (Williams, Eccleston, & Morley, 2012). Research in the anxiety domain has suggested that thinking styles can be successfully targeted at a relatively automatic level of processing. In particular, cognitive biases have been modified using more implicit cognitive bias modification (CBM) techniques (e.g. the visual-probe paradigm, which will be discussed in Section 1.4 below). Tackling these maladaptive processing styles at a more habitual level might assist in the transfer of intervention effects to real life (Bowler et al., 2012). However, the application of such CBM techniques to persistent pain has received little research attention, and will be tested in the current programme of research.

1.4 Attentional bias in pain and its modification

Despite the reported success of multidisciplinary pain management programmes for persistent pain compared with unimodal approaches and non-intervention control groups, a surprisingly high proportion of individuals do not realise significant gains (40 – 60%), while others fail to maintain improvements attained during treatment (Buhrman, Fältenhag, Ström, & Andersson, 2004; Mckellar, Clark, & Shriner, 2003; Turk, 1990; Williams et al., 2012). This divergence in intervention outcomes has led to investigation of the underlying process variables that could be influencing the mechanisms of treatment. As such, features of cognitive processing in acute and persistent pain have been examined. A wealth of research has suggested that when two or more processing options are present, individuals with persistent pain will systematically attend to the pain-related option, e.g. a distressed face, in favour of the benign option (attentional bias; e.g. Chapman & Martin, 2011; Dehghani et al., 2003; Haggman, Sharpe, Nicholas, & Refshauge, 2010) and perceive pain-related meanings when presented with ambiguous information (interpretative bias; e.g. McKellar et al., 2003). To date, fewer studies have examined interpretative bias in pain, which occurs when an individual preferentially selects the pain-related meaning from two or more possible interpretations of an ambiguous stimulus. There is, however, evidence that, when presented with pain-related homophones using headphones (words that sound the same but have at least one pain-related and one neutral meaning, e.g. pain/pane; moan/mown; slay/sleigh), chronic pain patients will systematically interpret the stimuli as pain-related compared with non-pain controls (e.g. Pincus, Pearce, & Perrott, 1996). It is worth noting, though, that the studies to date concerning interpretive bias in pain have relied on the use of explicit measures like the homophone task, and as a result it remains unclear whether the bias operates at a strategic or more automatic level of processing (Rusu & Pincus, 2012).

Two cognitive paradigms have predominantly been used to investigate attentional bias in pain: the emotional Stroop task and the visual-probe task (or dot-probe paradigm). In the emotional Stroop task (adapted from Stroop, 1935), participants are required to name the colours of word stimuli as quickly as possible whilst ignoring their content, which is either pain-related or neutral. Response times on trials with valenced content are then compared with non-valenced trials. When a participant takes longer to name the colours of stimuli with pain content than neutral stimuli, it is inferred that the stimulus has captured attention, which has interfered with the colour naming task and slowed response time (attentional bias). Findings using the Emotional Stroop Task have been mixed. Whilst some studies have produced evidence for attentional bias in chronic pain patients relative to non-pain controls (Pearce & Morley, 1989), others have found no such evidence of bias in pain (Asmundson, Wright, & Hadjistavropoulos, 2005b), or have only found within-group bias towards pain versus non-pain stimuli, and not a significant difference with non-pain controls (e.g. Crombez, Hermans, & Adriaensen, 2000; Schoth et al., 2012). Within the context of other Stroop research, such discrepancy suggests methodological limitations need to be considered before drawing firm conclusions from the results. In particular, inconsistencies have been found in Stroop task research in other conditions, including PTSD and panic disorder (e.g. Buckley, Blanchard, & Hickling, 2002); spider phobia (e.g. Thorpe & Salkovskis, 1997) and snake phobia (Wilkström, Lundh, Westerlund, & Hogman, 2004; see Cisler, Bacon, & Williams, 2009 for a review). Given the considerable evidence for processing biases within these disorders (e.g. see Beard, 2011, for a review), the sporadic failure to detect bias is likely to reflect methodological weakness, wherein the task is not sensitive enough to consistently reveal biases when they are present (Cisler et al., 2009). The extent to which the Stroop task measures selective attention has been questioned, with some theorists suggesting that the observed interference is due to a momentary increase in emotional arousal, and not preferential attentional allocation (e.g. Mogg & Bradley, 1998). Moreover, the concurrence of stimulus input and response output factors within the Stroop paradigm leave unclear whether the colour naming interference results from input competition at the stage of attentional allocation or output competition at the stage of response generation (Donaldson et al., 2007; Mogg, Millar, & Bradley, 2000). In spite of these limitations, a meta-analysis of five Stroop studies provided preliminary evidence that individuals with chronic pain selectively attend to sensory and affective pain words in comparison with healthy controls, with significant mean difference estimates identified between groups (Roelofs, Peters, Zeegers, & Vlaeyen, 2002b; Schoth et al., 2012).

The presence of attentional bias in pain has been supported by numerous studies using the more sophisticated means of assessment, the visual-probe (or dot-probe) task (MacLeod et al., 1986). Unlike the Stroop task, in this task the presentation of the probe

follows the critical stimulus presentation, such that the response selection is made after the stimulus has disappeared from screen (Donaldson et al., 2007). More specifically (and as indicated in Section 1.2.2), the dot-probe paradigm is a computer-based task in which individuals are presented with pairs of stimuli, typically words or images, on screen, with each pair containing one valenced and one non-valenced item. In the attentional bias test, the stimulus pair disappears and is immediately replaced with a visual probe, which appears in the prior location of either the valenced or neutral stimulus with equal probability. The participant's task is to indicate the probe position (probe-positional version) or type (probe-classification version) as quickly and accurately as possible, using the keypad. Faster reaction times to the probe when it is in the prior location of the valenced (e.g. pain-related) stimulus are indicative of an attentional bias toward that class of stimuli. For example, Dehghani et al. (2003) showed that individuals with chronic musculoskeletal pain respond more rapidly to probes presented in the prior location of sensory pain words than threat, disability and neutral stimuli, in comparison with healthy controls. Consistent with this, Asmundson, Carleton, & Ekong (2005a) reported that, in comparison with pain free controls, individuals with chronic headache disproportionately attend to sensory and affective pain words over neutral words.

Theoretically, the presence of multimodal cognitive processing biases (i.e. of interpretation as well as attention) is predicted both by Beck's schema theory (Beck, 1976; Beck, Emery, & Greenberg, 1985; Beck & Clark, 1997), and the Schema Enmeshment Model of Pain (Pincus & Morley, 2001), which proposed that biases of encoding and interpretation are produced by cognitive networks of associated concepts (schemas), which function to organise information, and make salient domain congruent content. Previous research has supported the idea that pain-related schemata may build up over time in persistent pain. McKellar et al. (2003), for instance, reported that chronic pain participants tended to produce more pain based responses to ambiguous homographs (words with one spelling that have two or more possible meanings, e.g. beat: overcome/hit, batter: food mix/assault) than acute pain participants, suggesting a downstream interpretive bias that is not influenced by state fluctuations in pain levels. Meanwhile, evidence for attentional bias in initial orienting for sensory pain words has been found in acute pain (Haggman et al., 2010), indicating that it may be the experience of pain itself rather than its cumulative experience that elicits this early processing bias. Indeed, the notion that pain captures and demands attention, serving as a powerful survival mechanism, is well established in pain theory (Eccleston & Crombez, 1999). Several studies have used the dot-probe paradigm to investigate the time course of attentional bias in persistent pain. In these studies, which recruited participants with chronic headache, initial orienting was operationalised as a stimuli presentation time of 500 ms, whilst to assess maintained attention the stimulus pair

was presented on screen for 1250 ms (Liossi et al., 2009, 2011; Schoth & Liossi, 2013). Findings supported the hypothesis that persistent pain (in this case headache) is associated with an attentional bias towards pain-related information, and suggested that the duration for which stimuli are presented can affect the reliability of detection. Whereas the presence of attentional bias towards pain-related information was not reliably demonstrated in initial orienting (500 ms), in each study the bias was detected in maintained attention (1250 ms), in comparison with pain free controls (Liossi et al., 2009, 2011; Schoth & Liossi, 2013). Critically, a recent meta-analysis of findings suggested that, although present at initial orienting (effect size = .29), the magnitude of attentional bias in persistent pain is greater within maintained attention (effect size = .42; Schoth et al., 2012), indicating that pain chronicity is particularly associated with more ruminative processes. A further meta-analysis supported the finding that stimulus duration is an important consideration when measuring attentional bias in persistent pain, with effects larger when stimuli were presented for over 1000 milliseconds (Crombez et al., 2013a). However, the weight of evidence to date is associative in nature and does not speak to the causal role of attentional bias in vulnerability to pain. In addition, these studies exclusively concern persistent pain, such that the possibility that the role of the faster and slower bias differs across acute and persistent pain classifications has not been explored. These questions will be addressed in the current thesis.

In order to test the causal influence of attentional bias on pain vulnerability, the bias will have to be manipulated first, and the effects of this experimental manipulation on attentional bias and pain outcomes examined. CBM is a comparatively recent experimental technique that erodes noxious attentional bias through repeated computer-based practice in disengaging from the adverse stimuli (attentional bias modification: ABM) or interpreting emotional ambiguity in a benign direction (cognitive bias modification for interpretation: CBM-I). Like the assessment of attentional bias, ABM uses the dot-probe paradigm. Participants are presented with pairs of words or images on the computer screen. Shortly afterwards, the stimulus pairs disappear to be replaced by a visual probe in the prior location of one of the stimuli, and the participant is required to indicate the either the probe position (probe-positional version) or type (probe classification version) as quickly and accurately as possible, using the keypad. The critical difference between the test and active training is that in ABM the probe is reliably located in the prior position of the neutral stimulus, training participants implicitly to direct their attention towards that location, speeding their response time to the probe. Near-transfer of training effects is said to occur when there is procedural and contextual overlap between the training and transfer phase, such as for the visual-probe test of attentional bias (Ellis, 1965; Hertel & Mathews, 2011). In contrast, far-transfer of training effects is demonstrated when the cognitive procedures of training are recruited for transfer but the contexts in which they are applied differ greatly, such as when retrained bias

influences actual somatosensory hypervigilance (Hertel & Mathews, 2011). As such, repeated ABM trials are hypothesised to set up a strategy for attending to more benign information that may transfer to everyday life and disrupt pain perception, reducing later vulnerability to pain (e.g. Carleton et al., 2011; McGowan et al., 2009; Sharpe, Ianiello, Dear, Perry, Refshauge, & Nicholas, 2012).

To date, though, only five studies have investigated ABM for pain; two of these studies assessed the impact of attentional bias modification on acute pain (McGowan et al., 2009; Sharpe et al., 2012 Study 1) and three on chronic pain (Carleton et al., 2011; Schoth, Georgallis, & Liossi, 2013; Sharpe et al., 2012 Study 2). Four of these studies trained participants using programs in which word pairs remained on screen for 500 ms (Carleton et al., 2011; McGowan et al., 2009; Sharpe et al., 2012 Study 1, Study 2), and one study used randomised stimulus presentation times of 500 and 1250 ms (Schoth et al., 2013). Overall, all of the studies reported at least some therapeutic benefits of ABM for pain. Carleton et al. (2011) found post-ABM reductions in self-reported current levels of chronic musculoskeletal pain among fibromyalgia patients relative to healthy controls, although the reduction in pain from pre to post treatment in the ABM group was of trend-level significance only. Also found were large reductions in anxiety sensitivity and pain-related fear in the intervention group, compared with the control group. Whilst encouraging, Carleton et al. (2011) employed a very small sample size, and did not incorporate a test of attentional bias, so mechanisms of action were unclear.

Meanwhile, Sharpe et al. (2012) reported two randomised controlled trials of attentional bias for pain: the first was for new back or neck pain injury experienced less than 12 weeks previously; the second was for chronic benign pain or arthritis. Both studies found evidence to support the efficacy of ABM. In the first study, participants in the active intervention group reported fewer days in pain and less average and current pain than those who received placebo (no contingency or 'sham') training. In the second study, chronic pain participants reported significant reduction in disability after four sessions of ABM compared with sham training controls. Crucially, however, Sharpe et al. (2012) were unable to identify an attentional bias at baseline, and in a mixed model ANOVA, found no time by training group interaction, suggesting that the predicted training effect on attentional bias had not occurred. This could have been partly attributable to the fact that they used threat and disability words as part of their training stimuli (50%), when prior studies have indicated that pain participants do not selectively attend to these classes of words, favouring sensory and affective pain stimuli (as used by Carleton et al., 2011). Moreover, attentional bias was modified and assessed in initial orienting only, whereas emerging evidence suggests that attentional bias in persistent pain is more evident in maintained attention (Schoth et al., 2012). This raises the possibility that ABM for pain would be optimised were longer

stimulus durations to be included in the retraining procedure. Indeed, there is preliminary evidence to support this prediction (Schoth et al., 2013). In this single case series (N = 8 participants), individuals with heterogeneous persistent pain who were trained to attend to neutral information presented for 500 and 1250 ms reported significantly lower pain severity and reduced pain interference at post-training. However, the comparative influence of targeting initial orienting and maintained attention on the temporal components of attentional bias, and on pain outcomes, has not been examined. The current thesis will provide the first systematic investigation of the optimal timings for ABM, and assessment of the causal influence of the faster and slower attentional bias on vulnerability to pain.

1.5 Thesis aims

The primary aim of this thesis is to assess the impact of modifying attentional bias in initial orienting and maintained attention on critical pain outcomes. This will provide insights concerning the relative weightings of top-down and bottom-up processes in pain-related attentional deployment. In addition, it will provide important information on the potential therapeutic efficacy of this novel, implicit, attentional retraining technique for acute and persistent adult pain. The timings of attentional bias will be investigated through manipulation of the durations for which stimuli are presented in the test and modification programs, using the visual-probe task. It is predicted that retraining both initial orienting (500 ms) and maintained attention (1250 ms) will influence vulnerability to acute experimental pain; however, since no previous studies have tested the impact of ABM for maintained attention on experimentally induced pain, it is difficult to make firm predictions in that regard. Based on previous findings and theoretical models, it is hypothesised that individuals with persistent pain will display an attentional bias in initial orienting, and maintained attention, and that the bias will be more evident at the later than earlier stage of attention. Correspondingly, it is hypothesised that retraining both temporal stages of attention will benefit individuals with persistent pain (in terms of reductions in pain outcomes), and that ABM may be particularly efficacious for adult persistent pain when the training stimuli are presented in sustained attention, permitting more elaborative processing of their schematic content. However, it is similarly difficult to make strong predictions concerning the relative efficacy of modifying attentional bias in initial orienting versus maintained attention for persistent pain, in the absence of any previous studies comparing the influence of inducing biases at both stimulus durations on long-term pain. It is possible that modifying attentional bias at the shorter stimulus duration will transfer to attentional bias in maintained attention (and vice versa), which would, theoretically, render the inclusion of both stimulus durations optimal for modifying attentional bias in this population. A corollary aim of the current thesis is to examine the mechanism of action of neutral ABM (i.e. ABM that trains attention towards benign stimuli); it is generally

considered that ABM works through inducing the ability to preferentially select neutral information over competing noxious content, at a comparatively automatic level of attentional processing. Hence, each study will measure attentional bias in initial orienting and maintained attention at pre and post-training, and the effects of retraining attention on the temporal components of attentional bias, and pain symptom outcome measures, will be assessed. Some theorists have contested that ABM does not rely on a change on attentional bias for its therapeutic effects to be realised, and that it instead functions primarily through its influence on mechanisms of attentional control. Consequently, perceived attentional control will also be measured in Studies One, Two, Three, and Five. This will help account for potential baseline differences in this variable, and potential pre to post-training alterations in perceived attentional control will be considered in the final study. In the next Chapter, a systematic review and meta-analysis of ABM for adult pain will be conducted, to examine in detail the current state of the evidence for its efficacy, and therapeutic potential, in preparation for the experimental studies.

Chapter 2

Assessing the efficacy of attentional bias modification for adult pain: A systematic review and meta-analysis

2.1 Introduction

Biased attentional processing has been theorised to play a central role in pain experience. Attentional bias modification (ABM) is a computer-based experimental technique that was developed to test causal models of attentional bias in anxiety through inducing an attentional bias towards neutral/positive or aversive stimuli, using the visual-probe task (MacLeod et al., 1986, 2002; Mathews & MacLeod, 2002). Past research in the emotion domain suggests that this type of computer-based training can alleviate threat-related attentional bias in anxious participants and reduce vulnerability to anxiety (see Hakamata et al., 2010 for a review). Drawing on cognitive-affective models of pain processing (e.g. Eccleston & Crombez, 1999; Pincus & Morley, 2001), recent research has adapted ABM techniques to test the hypothesis that modifying pain-related attentional bias will influence pain experience (e.g. Schoth et al., 2013; Sharpe et al., 2012). There has been no systematic review and meta-analysis of ABM for pain, however; this chapter aims to redress this gap in the literature and provide the first such review. This will, in turn, help situate the current programme of research within its empirical context.

ABM rests on the theoretical premise that attention is selective, and that which information is syphoned from the incoming stream of stimuli for further processing can have profound effects on an individual's well-being. Competition models of selective attentional processing propose that individuals achieve cognitive unison through competition between bottom-up (the relatively automatic evaluation of the threat status of incoming information) and top-down (executive control) processes (Mathews & Mackintosh, 1998; Mole et al., 2011). Resolution for each one of these struggles is hypothesised as being biased by a top-down attention-specific signal that prioritises relevant information, congruent with an individual's concerns, for additional handling (Desimone & Duncan, 1995, Reynolds & Desimone, 2001). For instance, individuals who are prone to persistent pain are more likely to allocate their attention to pain-related information (Crombez et al., 2013a; Schoth et al., 2012). Attentional bias generally operates outside an individual's conscious awareness, and has been implicated in the development and maintenance of conditions such as anxiety, depression, and more recently with vulnerability to pain chronicity (MacLeod & Mathews, 2012).

Noxious biased attentional processing is assumed to lead to exaggerated perceptions of pain and negative appraisals, which can increase vulnerability to pain, and establish a vicious cycle of cause and effect (Eccleston & Crombez, 1999; Kamping & Flor, 2012; Yiend et al., 2014). Experimental findings to date have supported this view, demonstrating

that attentional bias toward adverse information is associated with recognised pain vulnerability factors such as fear of pain (Keogh, Thompson, & Hannent, 2003), pain catastrophising (Vancleef & Peters, 2006), and the experience of acute and chronic pain (Haggman et al., 2010). Mechanisms of attentional bias may compromise adjustment to pain by making it more difficult to disengage attention from pain stimuli and focus attention on goal-relevant tasks in daily life. Supporting this hypothesis, a prospective study suggested that attentional bias moderated the relationship between daily pain severity and functional impairment, as well as daily pain severity and pain distractibility (Van Ryckeghem et al., 2013). These advances have led to the suggestion that pain management interventions that seek to directly target attentional bias towards pain-related information may be effective at reducing key pain outcomes such as severity, distress and disability (Liossi et al., 2011; Sharpe et al., 2012; Van Ryckeghem et al., 2013).

As discussed in Chapter One ('Introduction'), improving understanding of pain processing mechanisms is important given that, each year, millions of people are affected by acute and chronic pain, and for a great many their pain is inadequately managed (IASP/EFIC 2004; Bradshaw et al., 2011; Breivik et al., 2006). For the majority of those affected, living with pain comes at a high social and emotional cost, affecting almost every aspect of their daily lives and the lives of their significant others (Turk, Wilson, Cahana, 2011). Approximately one third of individuals with persistent pain report they can no longer work as a result of it, and nearly one quarter are less able to maintain relationships with family and friends (Breivik et al., 2006). Avoiding activities and social contact can itself have unfavourable consequences, leading to less activity and social withdrawal and an almost complete focus of attention on pain. This tendency may lead to a vicious circle of pain, lack of activity, fear of renewing activity and depression, and more pain (Traue, Jerg-Bretzke, Pfingsten, & Hrabal, 2010).

Described in Chapter One ('Introduction'), and repeated here for clarity, ABM describes techniques that aim to help participants redirect their attention away from pain-related information towards more neutral stimuli through repeated practice at shifting attention from one type of stimulus to another. Typically, ABM uses the dot-probe task (e.g. Sharpe et al., 2012). In this computer-based task individuals are presented with pairs of stimuli, such as words or pictures, on screen, with each pair containing one pain-related and one neutral item. After the onscreen presentation time for the stimulus pair has elapsed (e.g. 500ms, 1250ms), it is replaced with a visual probe (e.g. a left versus right facing arrow) in the prior location of either the pain-related or neutral stimulus. The participant's task is either simply to indicate the location of the visual probe using the keypad (probe-positional version) or to make a decision about its shape or orientation (e.g. to press the right arrow key when a right-facing arrow is displayed; probe classification version). Although slightly more

difficult, the probe-classification version is generally considered as superior to the probe-positional version of the dot-probe task as it promotes a more consistent monitoring of the visual display (Mogg & Bradley, 1999). In active (as opposed to control or 'sham') ABM, instead of there being an equal distribution of the visual probe between the pain-related and neutral cues, the probe is reliably located in the prior position of the neutral information, training participants implicitly to direct their attention away from the pain stimuli towards the neutral stimuli in order to do well on the task. Drawing on current models, repeated trials of this type might help the individual to disengage from pain and threat-related information and facilitate engagement with more benign information, potentially reducing vulnerability to pain should the effects transfer to everyday life.

ABM has previously been found to be effective in alleviating anxiety, with effect sizes comparable to some pharmacological and cognitive-behavioural interventions (Hakamata et al., 2010). Here, a general picture has emerged that ABM is associated with a decrease in noxious-stimulus evoked responses in the brain areas associated with unpleasant stimuli and, in some cases, in increased activity in areas associated with top-down control over these signals (Browning et al., 2010b; Legrain, Perchet, & Garcia-Larrea, 2009a). Hence, repeated practice at attending away from pain stimuli and towards neutral stimuli, as in ABM, may reduce the potency of task irrelevant pain distractors and make it more likely that pain-related information can be downregulated, enabling preferential selection of the benign processing option. However, to date, only four published papers have reported the impact of modifying attentional bias on pain outcomes, and of these studies, findings have been somewhat mixed. For instance, a significant impact of ABM on post-training pain severity has been reported in some studies (e.g. Schoth et al., 2013) and not others (e.g. Sharpe et al., 2012). A systematic review and meta-analysis is therefore considered necessary to formally assess the extent of the literature-base (including unpublished research), evaluate the hitherto methodological approaches to ABM and outcome measurement, and assess the efficacy of ABM for pain. The findings of this review will inform the current research programme.

The presence of attentional bias is typically measured using the same computer-based dot-probe task as ABM (MacLeod et al., 1986, 2002). An attentional bias is indicated by an individual's response times to the visual probe when it is in the prior location of the pain versus neutral stimuli. Like training, the test can constitute either a probe positional or classification version of the task. An attentional bias index can be calculated by subtracting congruent reaction times (RTs; when the visual probe is in the same spatial location as the target pain stimulus) from incongruent trial RTs (when the visual probe is in the opposite spatial location to the target pain stimulus; e.g. RTIncongruentPain − RTCongruentPain). Higher scores on the attentional bias index indicate facilitated attention towards pain cues,

while lower scores indicate attentional prioritisation of neutral stimuli. Although studies have reported that modifying attentional bias can improve pain outcomes, the mechanism of action remains unestablished, with a general failure to find the expected impact of training on attentional bias (e.g. Schoth et al., 2013; Sharpe et al., 2012). This could be due to methodological factors, such as the type of pain targeted (e.g. acute versus persistent pain) and the presentation duration of the training and test critical stimuli. To date, different studies have targeted different pain populations, and the temporal stage of attention targeted using ABM techniques has not been systematically explored. Within the present review, consideration will be given to methodological differences such as these in determining the efficacy of ABM for pain-related attentional bias and symptom outcomes.

The ability to experimentally manipulate the preconscious deployment of attentional resources to pain-related information has thus suggested a potential therapeutic application, which could provide a novel and effective intervention for pain. Furthermore, there has been some evidence that a pronounced attentional bias to pain can hamper other common explicit intervention techniques like distraction therapy (Van Ryckeghem et al., 2012). A technique that directly targets attentional bias may therefore be of particular use. However, whilst attentional retraining research has supported its efficacy for key outcomes such as reduction in pain severity and disability (e.g. Carleton et al., 2011), findings have been somewhat mixed (e.g. Sharpe et al., 2012), and the efficacy of ABM to reduce pain severity and contribute to analgesic requirements, together with the mechanism of action, has not been established. Mixed findings may be in part due to methodological limitations and associated risk of bias. A systematic review is needed to assess the overall efficacy of ABM for pain, and as such whether or not the approach does indeed have potential as a novel therapeutic intervention. The current objective was to provide the first quantitative review of attentional bias modification for pain in adults.

2.2 Method

2.2.1 Search strategy

Relevant studies were identified for this review through a computerised search of the OVID Medline, CINAHL, PsychInfo, and Cochrane Library CENTRAL databases. A detailed search strategy was developed for each electronic database. The first database searched was Medline, and the search strategy was revised for each subsequent search to meet the requirements of the other databases. The subject search used a combination of controlled vocabulary (MeSH) and free text terms based on the search strategy developed for Medline (see Appendix A1). Search terms and keywords entered in PsychInfo, CINAHL and the CENTRAL databases were combinations of *cognitive bias modification, attention* bias modification, attention* train*, attention retrain*, bias modification, visual*, dot* and*

probe paired with *pain, arthriti*, fibromyalgia, headache** and *migraine**. Since the dot-probe paradigm, used for the measurement and modification of attentional bias, was first introduced twenty-eight years ago (MacLeod et al., 1986), the search was restricted to studies conducted between 1986 and 2014. Only studies that were published in English and fully accessible were included in the review. In addition to the database searches, the reference lists for all relevant articles and review reference sections were examined for further relevant articles not yet identified. Papers were filtered by title for relevance, and then at abstract and article level in accordance with inclusion and exclusion criteria.

2.2.2 Inclusion/exclusion criteria

Participants

Studies that tested adults aged 18 years and over of any gender, nationality or socioeconomic class who were either exposed to acute experimental pain, had recently received an acute pain injury such as whiplash and were still self-reporting pain at the start of the study, or who were self-reporting pain that had lasted for three months or more, were included in the review. Persistent pain conditions included, but were not limited to, musculoskeletal conditions (e.g. low back pain, ankylosing spondylitis, osteoarthritis, and fibromyalgia), and migraine. Selection of studies was not restricted on the basis of study settings, and hence could comprise participants' homes, primary care practices, outpatient clinics, hospital inpatient facilities, and university-based testing facilities.

Study design

Randomised controlled trials and quasi-randomised controlled trials that assessed the effects of ABM on pain-related attentional bias and/or reduction in levels of pain severity, pain-related distress, or disability, were included in the review. The study included at least one experimental group in which attentional bias to pain was modified, as well as at least one control group. If a control bias modification procedure was administered to the comparison group, this training was designed to be inert (i.e. it comprised sham or neutral training), or it was designed to have the opposite effect relative to the training for the active experimental condition (e.g. to induce a pain-related bias; Hallion & Ruscio, 2011). Studies or outcomes that administered another active intervention (e.g. relaxation therapy) in conjunction with ABM, or as the primary control condition, were not included in the review, as this would prevent the isolation of ABM effects. Blinding was not part of the eligibility criteria, given that it is often not possible to blind a participant to an ABM condition. Where studies contained inadequate information and/or data for inclusion in the review, the study authors were contacted for elucidation

Attentional bias modification method

Included studies evaluated and reported the effects of modifying attentional bias using the dot-probe paradigm on attentional bias, pain severity, pain-related distress, or

disability. Training stimuli included pain-related images (e.g. facial expressions) or words (e.g. sensory pain descriptors), paired with matching neutral images (e.g. a neutral facial expression) or words (e.g. household objects). It was essential that attentional bias was directly targeted through training. Hence, studies that manipulated attentional bias using a different method to direct training using the dot-probe task (e.g. cognitive behavioural therapy), were not eligible for the present review (Hallion & Ruscio, 2011).

Pain outcome and attentional bias assessment

The following primary and secondary symptom outcomes were selected because they are commonly assessed in the pain literature. Studies were included in the systematic review when at least one of the below primary or secondary outcomes was measured and reported. For the meta-analysis, effect sizes were calculated based on the primary outcome measure at post-training in each study. If a primary outcome was not specified in the article, a validated clinician/researcher administered, self-report, and/or behavioural measures assessing the pain outcome(s) of interest, administered at least once after ABM, was used (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Thomson & Page, 2007). Table 2.1 provides a list of the pain measures used by each study.

Primary outcome

1. Pain severity

Secondary outcomes

2. Attentional bias to pain
3. Pain-related distress (anxiety and depression)
4. Pain-related disability

It was anticipated that different studies would use different outcome measures, and hence studies were not excluded on the basis of outcome measures used. Outcomes were instead transformed to a common scale using standardised means before pooling. Where attentional bias was assessed, included studies provided data for at least post intervention.

Outcomes were categorised into short-term (where measurement was taken immediately after completion of the ABM program; ≤ 1 week), medium term (> 7 days ≤3 months post ABM) and long-term (> 3 months post ABM). It was anticipated that all of the above self-report outcomes would be assessed using published and validated measures, such as the Depression and Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995), and the Anxiety Sensitivity Index-3 (ASI-3; Taylor et al., 2007). Attentional bias was measured using the computer-based attention bias test, based on the dot-probe paradigm, which has been implemented in numerous published studies (see Schoth et al., 2012 for a review). Instrument validity was explicitly reported in the results section.

Available data

For inclusion in the meta-analysis, the study needed to provide sufficient detail to calculate an effect size comparing the active ABM and control groups on attentional bias and/or pain outcomes after training. Effect sizes were determined using group means, standard deviations and sample sizes reported in the text (Borenstein, Hedges, Higgins, & Rothstein, 2005; Hallion & Ruscio, 2011; Lipsey & Wilson, 2001). When these data were not reported in the article text, authors were contacted for additional data (n = 1). It was not necessary to exclude any studies due to the absence of necessary data.

2.2.3 Risk of bias assessment

Each study included in the meta-analysis was assessed for quality using the Cochrane 'risk of bias tool' (Higgins & Green, 2008). This tool requires the researcher to assess each study across seven domains: i) risk of selection bias due to the method of randomisation; ii) risk of selection bias due to the method of allocation concealment; iii) risk of performance bias due to the masking status of participants and study personnel; iv) risk of attrition bias due to incomplete outcome data; v) risk of detection bias due to the blinding status of study personnel and outcome assessors; vi) risk of reporting bias due to selective reporting of results, and vii) other bias concerns (Andersson et al., 2014; Higgins & Green, 2008).

2.2.4 Meta-analytic approach

Data suitable for pooling were entered into RevMan 5.2 (RevMan, 2011) software, and findings from individual studies and their treatment effect were summarised in forest plots for each outcome and comparison. As discussed in the "Pain outcome assessment method" subsection above, given that multiple outcomes are typically assessed in pain intervention studies using multiple measurement tools, the specified pain-related outcomes measured and methods of assessment were recorded (Table 2.1). For each comparison, three outcomes were identified and labelled "Pain severity", "Disability", and "Distress". Following Eccleston, Williams, and Morley (2009) and Williams, Eccleston, and Morley (2012), the measure considered most appropriate from each trial for each of the three outcomes was selected. To guide the choice of outcome measure, two rules were applied. First, established outcome measures that are used more frequently in the literature were selected over more novel measures. Second, given a choice between single-item and multi-item self-report tools, multi-item tools were chosen on the basis of increased reliability (Eccleston et al., 2009).

Where study authors reported pain severity using visual analogue scales (VAS) or numeric rating scales (NRS), treatment effects were estimated using standardised mean differences (SMD) by extracting means, standard deviations, and sample size at post-treatment and/or follow-up (a sample data extraction sheet is included in Appendix A2).

Treatment effects were the SMD between experimental and control conditions for VAS and NRS outcomes measured on a 0 to 10 scale. The other continuous and response rate outcomes were treated similarly, and SMD treatment sizes calculated. If both per protocol and intention-to-treat data were reported, the latter estimate was used in the meta-analysis. Subgroup analyses were planned for type of pain (acute/experimental (of comparatively short duration, < 3 months), persistent (of longer duration, ≥ 3 months) and presentation time of the stimuli used for training and assessing attentional bias (e.g. 500 ms versus 1250 ms), with a view to assessing the differential impact of these variables on outcomes. Sensitivity analyses were conducted to investigate heterogeneous methodological factors that may have affected pooled results. Where possible, the primary analysis was repeated by substituting alternative values for methodological decisions that were identified as problematic (Higgins & Green, 2008). These secondary findings were reported in the summary of findings table.

2.2.5 Assessment of study heterogeneity

As part of a meta-analysis, it is important to evaluate whether the pooled effect sizes are estimates of the same population mean (Hallion & Ruscio, 2011; Lipsey & Wilson, 2001). Data were assessed for heterogeneity using the chi-square and I^2 statistics. A significant chi-square result provides evidence of heterogeneity of intervention effects (Higgins & Green, 2008). However, a non-significant result does not provide evidence of no heterogeneity, and hence it is also necessary to look at the I^2 statistic (Higgins & Green, 2008). The I^2 statistic quantifies the degree of heterogeneity by estimating the percentage of the variance that is attributable to between-studies variability, with a value above 40% indicating that moderate heterogeneity may be present (Andersson et al., 2014; Crowther, Lim, & Crowther, 2010; Higgins & Green, 2008). In the present review, some heterogeneity was expected given the notable differences between studies in characteristics such as the clinical status of participants, and number of ABM sessions administered (Hallion & Ruscio, 2011).

2.3 Results

2.3.1 *Study characteristics and systematic review*

The initial search generated 708 results after removal of duplicates (n = 109), of which 493 were excluded by title. Of the 215 search results screened by abstract and/or full text, four papers (five studies) met all review criteria and were included in the present narrative synthesis section of the systematic review. Of these, one study (N = 8; Schoth et al., 2013) did not include a control group, and could not be included in the meta-analysis. Figure 2.1 illustrates the inclusion/exclusion process.

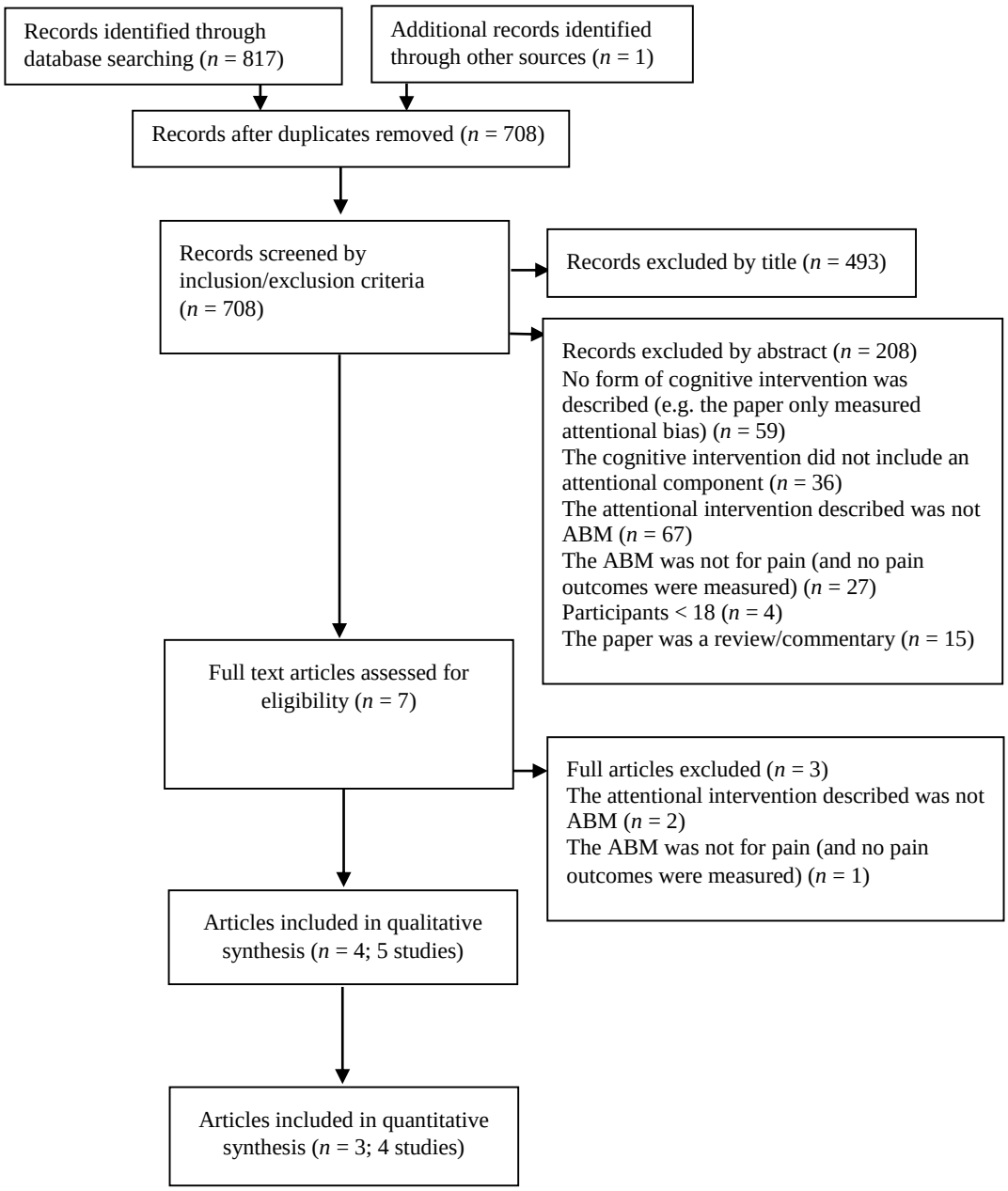


Figure 2.1 PRISMA flow diagram illustrating process of inclusion and exclusion.

A systematic review of the eligible studies was undertaken (see Table 2.1). All studies were published 2009 to 2013. The age of participants (N = 217) included in the systematic review and meta-analysis ranged between 18 and 78. All studies sampled both males and females. All five studies included in the systematic review assessed the impact of ABM on pain experience (Carleton et al., 2011; McGowan et al., 2009; Schoth et al., 2013; Sharpe et al., 2012 Study 1, Study 2); four out of five of the studies (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012 Study 1, Study 2) specified pain severity as the primary outcome, and the remaining study (McGowan et al., 2009) specified pain severity as a main outcome. In terms of the type of pain studied, three targeted persistent pain, defined as pain lasting more than three months (Carleton et al., 2011; Schoth et al., 2013; Sharpe et

al., 2012 Study 2), one targeted acute experimental pain (McGowan et al., 2009), and one targeted acute clinical pain (Sharpe et al., 2012 Study 1). Of the persistent pain samples, one study targeted a homogenous group of individuals with diagnosed fibromyalgia (Carleton et al., 2011) and two targeted heterogeneous persistent pain groups, with a range of conditions included (Schoth et al., 2013; Sharpe et al., 2012 Study 2). The experimental pain was induced using the cold pressor task (McGowan et al., 2009); while the acute clinical pain was resultant from an acute back or neck pain injury (Sharpe et al., 2012, Study 1).

Importantly, three of the studies (McGowan et al., 2009; Sharpe et al., 2012 Study 1, Study 2) were from the same research group in Sydney, Australia, highlighting the need for other research groups to investigate the role of attentional bias in pain experience, using ABM techniques. The smallest study had eight participants (Schoth et al., 2013), and the largest had 52 participants (McGowan et al., 2009). The studies targeting persistent pain had notably small sample sizes ranging from eight to 34 participants, with authors citing recruitment difficulties for this population as the primary obstacle (e.g. Carleton et al., 2011). Of the non-experimental pain studies, all three of the chronic pain experiments recruited participants solely through self-referral (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012 Study 2), while the acute pain study adopted a mix of self-referral and clinical recruitment (Sharpe et al., 2012 Study 1).

In terms of the ABM program administered, all five studies used the probe classification version of the dot-probe task (Carleton et al., 2011; McGowan et al., 2009; Schoth et al., 2013; Sharpe et al., 2012). Four of the studies used vertically aligned linguistic stimuli presented for 500 ms (Carleton et al., 2011; McGowan et al., 2009; Sharpe et al., 2012), while one study used linguistic and pictorial stimuli presented for 500 and 1250 ms, with words aligned vertically above and below the central fixation point, and images aligned horizontally, to the left and right of the central fixation point (Schoth et al., 2013). Four of the studies reported matching training word pairs for length and stimuli and/or had obtained their linguistic stimuli from studies in which matching had been reported (McGowan et al., 2009; Schoth et al., 2013; Sharpe et al., 2012). Two studies (McGowan et al., 2009; Sharpe et al., 2012 Study 1) administered a single session comprising 320 trials, and three studies reported a course of multiple sessions ranging from four times 320 trials to eight times 384 trials (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012 Study 2). Three studies reported that, excluding practice trials, one hundred percent of trials were critical (McGowan et al., 2009; Sharpe et al., 2012), while two studies indicated that the ABM/control program included trials in which both stimuli presented were neutral (Carleton et al., 2011; Schoth et al., 2013). Four studies included a control group (Carleton et al., 2011; McGowan et al., 2009; Sharpe et al., 2012); of these, one study reported that in the comparison program the probe replaced the pain-related stimuli for one hundred percent of the trials, while three

studies stated that the control group completed a sham training program, in which the probe replaced the pain versus neutral stimuli with equal probability (Carleton et al., 2011; Sharpe et al., 2012 Study 1, Study 2).

Four of the studies measured attentional bias at pre and post-training (McGowan et al., 2009; Schoth et al., 2013; Sharpe et al., 2012; post-training data were entered into the meta-analysis from the eligible studies). All investigations that measured attentional bias used the probe-classification version of the dot-probe task. Three of the studies used vertically aligned linguistic stimuli presented for 500 ms (McGowan et al., 2009; Sharpe et al., 2012), while one study used linguistic and pictorial stimuli presented for 500 and 1250 ms, with words aligned vertically above and below the central fixation point, and images aligned horizontally, to the left and right of the central fixation point (Schoth et al., 2013).

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
Carleton et al., 2011. "Attention bias modification in persons with fibromyalgia: a double blind randomized clinical trial." Regina, Canada	Participants were randomly allocated to condition. Method of randomisation was not reported. The study did not claim that condition allocation was concealed. It was reported that participants were blinded. Blinding of study personnel was unclear. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was four weeks, and took place in a University.	*N* = 17. Mean age = 51.2, *SD* = 6; age range 38 - 60. Male and female. Participants met the diagnostic criteria for fibromyalgia and pain had lasted more than three months. In addition, participants showed no evidence of suicide intent; no substance abuse; no evidence of current or past schizophrenia, bipolar disorder or mental disorder; were not currently receiving CBT, and had no change in other psychosocial treatments of medication in the past three months.	Persistent (> 3 months)	Two sessions per week for four weeks (eight sessions total). 240 trials per session. Completed on a lab PC. Number of participants per session not stated. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory pain; neutral assorted). Word pairs not matched for length and frequency. 66% of trials were critical. Probe replaced neutral words. Stimuli alignment not reported.	Sham training. Two sessions per week for four weeks (eight sessions total). 240 trials per session. Completed on a lab PC. Number of participants per session not stated. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory pain; neutral assorted). Word pairs not matched for length and frequency. 66% of trials were critical. Probe replaced pain and neutral words (50:50). Stimuli alignment not reported.	Yes – pain severity measured on a 100 mm visual analogue scale, anchored from "no pain" to "worst pain imaginable". This scale has been validated by previous research.	Anxiety Sensitivity Index – 3 Pain Anxiety and Stress Scale – 20 Fear of Pain Questionnaire – Short Form Illness/Injury Sensitivity Index-Revised State-Trait Anxiety Inventory	Attentional bias was not measured in this study.	Pain outcomes were assessed post-training.	Yes

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
McGowan et al., 2009. "The effect of attentional re-training and threat expectancy in response to acute pain" Sydney, Australia	Participants were randomly allocated to condition. The method of randomisation was an online random number sequence generator. The study did not claim that condition allocation was concealed, or any form of blinding. No measures taken to protect against contamination were reported. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was one hour (approx.), and took place in a University.	*N* = 104. Mean age = 21.53 (*SD* = 5.88). Age range 18 - 48. Male and female. Participants were healthy volunteers, recruited predominantly from first year psychology courses. Exclusion criteria were a current medical condition, recent use of analgesics, excessive caffeine intake in the preceding 24 hours, or current pain (> 4 VAS).	Experime-ntal (cold pressor pain)	Single session (approx. 30 minutes). 320 trials per session. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced neutral words. Stimuli presented vertically.	Sham training. Single session (approx. 30 minutes). 320 trials per session. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced pain words. Stimuli presented vertically.	A primary outcome was not specified.	Pain severity measured during the cold pressor task (CPT; at 30 seconds) on an 11 point (0 – 10) numerical rating scale (NRS). Anchors not reported. Pain severity measured when the participant withdrew their arm from the cold water (tolerance) on an 11 point (0 – 10) NRS. Anchors not reported. Pain threshold (time taken in seconds to first register pain). Pain tolerance (total time the participant kept their arm in the cold pressor). The NRS has been validated by previous research.	Attentional bias was measured using the dot-probe task. 80 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; assorted neutral). Word pairs matched for length and frequency. 100% of trials were critical. Stimuli presented vertically.	Pain outcomes were assessed at post-training (during CPT). Attentional bias was measured at post-training.	Yes

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
Schoth et al., 2013. "Attentional bias modification in people with chronic pain: a proof of concept study." Southampton, UK	This was a within-subjects design and hence participants were not randomly allocated to condition. Participants were informed "that the intervention aimed to improve their pain" (p. 237). There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was four weeks, and took place in a University.	*N* = 8. Mean age = 27, *SD* = 8.52; age range 20 – 47. Male and female. Volunteers were included who: i) were experiencing any type of chronic pain; ii) were aged between 18 and 60 years; iii) did not have a diagnosis of or were receiving treatment for any psychiatric disorder, either currently or within the past five years; and iv) were not currently receiving psychiatric therapy.	Persistent (> 3 months)	Two sessions per week for four weeks (eight sessions total). 384 trials per session. Completed on a lab PC. Number of participants per session not stated. Probe classification version of the dot-probe task. Stimuli presented for 500 ms and 1250 ms, randomised. Words (sensory, affective, disability, threat) and images (pain facial expressions, headache-related images, health-threat, general threat). Word pairs matched for length and frequency. 67% of trials were critical. Probe replaced neutral words/images. Words presented	No control condition.	Yes – pain severity measured on the Brief Pain Inventory pain severity subscale. This measure has been validated in past research.	Hospital Anxiety and Depression Scale (HADS) – anxiety and depression. Brief Pain Inventory pain interference subscale.	Attentional bias was measured using the dot-probe task. 384 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; assorted neutral). Word pairs not matched for length and frequency. 67% of trials were critical.	Pain outcomes were assessed post-training. Attentional bias was measured post-training.	No

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
				vertically; images presented horizontally.						
Sharpe et al., 2012. "Is there a potential role for attention bias modification in pain patients? Results of 2 randomised, controlled trials" Study 1 Sydney, Australia	Participants were randomly allocated to condition. The method of randomisation the SPSS Bernouli function. The study claimed that condition allocation was concealed, and that both participants and study personnel were blinded to condition. No measures taken to protect against contamination were reported. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was one hour	*N* = 54. Mean age = 41.02, *SD* = X; age range not reported. Male and female. Participants were recruited from 11 physiotherapy clinics. Eligibility criteria were i) new back or neck pain injury, with no red flag conditions as identified by the assessing physiotherapist, which they experienced less than 12 weeks previously; ii) no history of chronic pain or serious mental illness; iii) and be aged between 18 and 75 years. Participants who were unable to use both arms or had a brain injury were	Acute (< 3 months)	Single session (approx. 30 minutes). 320 trials per session. Completed on a laptop at the physiotherapy clinic. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced neutral words. Stimuli presented vertically.	Sham training. Single session (approx. 30 minutes). 320 trials per session. Completed on a laptop at the physiotherapy clinic. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced pain and neutral words (50:50). Stimuli presented vertically.	Yes – pain severity measured on a 100 mm visual analogue scale, anchored from "no pain" to "extreme pain". This scale has been validated by previous research.	Örebro musculoskeletal pain questionnaire Roland–Morris disability questionnaire Tampa scale for kinesiophobia. Depression, anxiety and stress scale (DASS). Average pain VAS Number of days in pain	Attentional bias was measured using the dot-probe task. 80 trials in each (pre/post) attentional bias test. Completed on a laptop at the physiotherapy clinic. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; assorted neutral). Word pairs matched for length and frequency. 100% of trials were critical. Stimuli presented	The primary outcome measure (pain severity) was measured at post-training and three month follow-up. Attentional bias was measured at post-training. The secondary outcome measures were administered at three month follow-up only.	Yes

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
	(approx.), and took place in a physiotherapy clinic.	excluded.						vertically.		
Sharpe et al., 2012. "Is there a potential role for attention bias modification in pain patients? Results of 2 randomised, controlled trials" Study 2 Sydney, Australia	Participants were randomly allocated to condition. The method of randomisation was the SPSS Bernouli function. The study claimed that condition allocation was concealed, and that both participants and study personnel were blinded to condition. No measures taken to protect against contamination were reported. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of	*N* = 34. Mean age = 45.6, *SD* = 14.54; age range 22 – 78. Male and female. Recruited from pain-related services and from participants from previous nontreatment studies. Eligibility criteria were: i) aged over 18 ii) experiencing chronic or recurrent pain (pain more days than not) for 3 months from either chronic benign pain or arthritis; iii) no other painful disease; iv) no severe mental illness, head injury; and v) did not live interstate.	Persistent or recurrent (> 3 months)	One session per week for four weeks (four sessions total). 320 trials per session. Completed on a PC at the University (two sessions) and on participants' PCs at home (via CD; two sessions). Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced neutral	Sham training. One session per week for four weeks (four sessions total). 320 trials per session. Completed on a PC at the University (two sessions) and on participants' PCs at home (via CD; two sessions). Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; neutral assorted). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced pain and	Yes – pain severity measured on a 100 mm visual analogue scale, anchored from "no pain" to "extreme pain". This scale has been validated by previous research.	Roland–Morris disability questionnaire Tampa scale for kinesiophobia. Depression, anxiety and stress scale (DASS). Fear of Pain Questionnaire-Revised Anxiety Sensitivity Index Pain Self-Efficacy Questionnaire	Attentional bias was measured using the dot-probe task. 80 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms. Word pairs (sensory and affective pain; assorted neutral). Word pairs matched for length and frequency. 100% of trials were critical. Stimuli presented	Post-training (included in meta-analysis). Post CBT and 6 month follow-up, post CBT (not included in meta-analysis).	Yes

Table 2.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)	Included in meta-analysis
	the study was four weeks and took place at a University and participants' homes.			words. Stimuli presented vertically.	neutral words (50:50). Stimuli presented vertically.			vertically.		

Four of the investigations reported matching test word pairs for length and stimuli and/or had obtained their linguistic stimuli from studies in which matching had been reported (McGowan et al., 2009; Schoth et al., 2013; Sharpe et al., 2012 Study 1, Study 2). In three of the studies, the attentional bias test comprised 80 trials (McGowan et al., 2009; Sharpe et al., Study 1, Study 2), and in one study it comprised 384 trials (Schoth et al., 2013). As with training, three studies reported that, excluding practice trials, one hundred percent of trials were critical (McGowan et al., 2009; Sharpe et al., Study 1, Study 2), while one study indicated that the attentional bias test included trials in which both stimuli presented were neutral (Schoth et al., 2013). Where measured, the assessment of attentional bias was always at pre and post-training; no studies included an assessment of attentional bias at follow-up. Only two studies measured pain outcomes at a prolonged follow-up of three months or more (Sharpe et al., 2012 Study 1, Study 2), and of these, one study (Sharpe et al., 2012, Study 2) administered cognitive behavioural therapy immediately following the post-training attentional bias and pain outcome assessment, preventing inclusion of these follow-up data in the meta-analysis.

Concerning the results of individual studies, findings were somewhat mixed. First, pain severity: one study reported a significant reduction in pain severity ratings from pre to post-training (Schoth et al., 2013), and one study stated that participants in the ABM group reported significantly lower pain severity than control participants at post-training (McGowan et al., 2009). One study reported a trend-level reduction in pain severity from pre to post-training, which was not significant in control participants (Carleton et al., 2011). This study additionally found a significant difference in the percentage of participants reporting clinically significant change in pain severity ratings between conditions, favouring the ABM group (Carleton et al., 2011). Two studies reported no significant effects of ABM on pain severity at post-training in comparison with control participants (Sharpe et al., 2012, Study 1, Study 2). The single study to measure the impact of ABM on pain severity at follow-up found a significant difference between groups, such that the ABM group rated their pain as less severe than the control group (Sharpe et al., 2012, Study 1). Second, disability: only two studies measured the impact of ABM on pain disability, one targeting acute pain and measured at three month follow-up (Sharpe et al., 2012, Study 1), and one targeting chronic pain and measured at post-training (Sharpe et al., 2012, Study 2). There was no difference between ABM and control group participants in the acute pain study (Sharpe et al., 2012, Study 1). In the study targeting chronic pain, it was reported that ABM had a significant impact on disability relative to the control group, with ABM participants reporting greater improvement in disability from pre to post-training than their placebo training counterparts (Sharpe et al., 2012, Study 2). Another of the studies targeting chronic pain measured the impact of ABM on pain interference at post-training, which assessed the extent to which

pain interfered with daily activities such as walking ability, and reported a significant reduction in pain inference ratings from pre to post ABM (Schoth et al., 2013). Hence, both studies assessing ABM effects on the extent to which persistent pain interfered with activities of daily living reported a significant effect at post-training, favouring the ABM group, whereas there was no effect found at follow-up for acute pain. Finally, three studies included a measure of pain-related distress (anxiety and depression) at post-training (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012, Study 2). In one study (Schoth et al., 2013), this measure was the HADS; in one study it was the DASS (Sharpe et al., 2012, Study 2) and in one study, it was the PASS-20 (Carleton et al., 2011). A further study included a measure of distress at three month follow-up only (Sharpe et al., 2012 Study 1). Of these, only one study reported a significant impact of ABM on pain-related anxiety and depression, with participants reporting lower distress levels from pre to post-training (Schoth et al., 2013).

2.3.2 Risk of bias assessment

Three of four studies included in the meta-analysis were assessed to have either low or unclear risk of bias across the seven domains, whilst one study (Careleton et al., 2011) was deemed to have high risk of bias across two domains (Figure 2.2; Tables for individual studies are presented in Appendix A3).

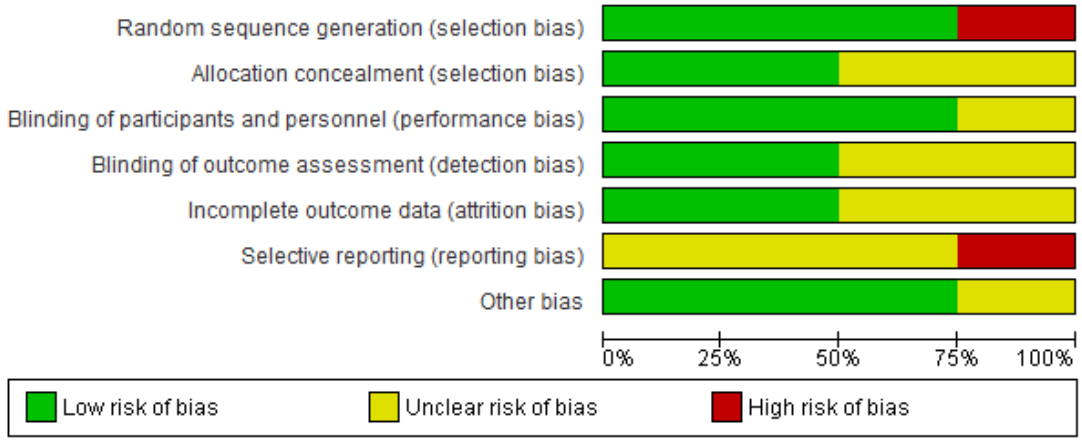


Figure 2.2 Risk of bias graph: review author's judgements about each risk of bias item presented as percentages across all included studies.

2.3.3 Data synthesis

Impact of ABM on pain severity

Homogeneity of the included studies was indicated by an I^2 value of 10%, $\chi^2(3) = 3.32$, $p = .35$, and therefore a fixed effects model was applied.[1] This model suggested that participants in the ABM group reported lower pain severity at post-training than control

[1] Results were very similar using a random effects model, $g = -0.21$, CI = -0.5 to 0.09, $Z = 1.37$, $p = 0.17$.

group participants, g = -0.22, CI – 0.5 – 0.05, however this difference was not significant, Z = 1.58, p = .11, as depicted in the first forest plot (Figure 2.3; Table 2.2). These findings were contrary to the hypothesis that neutral ABM at 500 ms would have concomitant effects on pain severity at post-training.

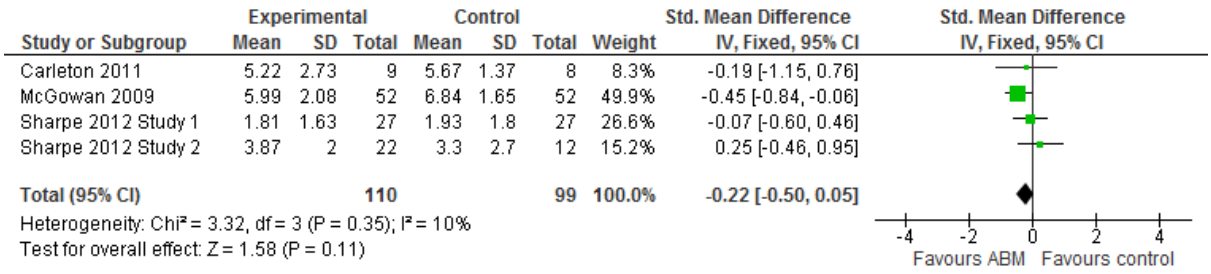


Figure 2.3 Forest plot displaying post-training pain severity effect sizes of studies comparing ABM with a control group.

Only one study (Sharpe et al., 2012, Study 1) measured pain severity at a later time-point than immediately post-training, and compared these findings with a sham training control group. When these data were entered into the meta-analysis, heterogeneity of the included studies was indicated by an I^2 value of 53%, χ^2 (3) = 6.37, p = .09, and therefore a random effects model was applied. Results of this model suggested that participants in the ABM group reported lower pain severity after training than control group participants, g = -0.38, CI = -0.83 to 0.06; however, this difference was significant at trend-level only, Z = 1.67, p = .09 (see Table 2.2). This slight difference in the sensitivity of studies to detect an interventional impact on pain severity suggests that the methodological factor of length of follow-up may have influenced this outcome, such that a difference in pain severity between the ABM group and control group was more evident when a gap was introduced between the last ABM session and measurement of pain severity.

Table 2.2

Summary of findings table

Outcomes	Comparative effect size (95% CI) Control	ABM	Alpha-level	No of Participants (studies)	Comments
Pain severity at post-training NRS and VAS	The mean pain severity ranged across control groups from 1.93 points to 6.84 points [NRS/VAS]	The mean pain severity in the ABM groups was -0.22 lower [-0.5 to 0.05]	p = .11	209	A lower pain severity score indicates that ABM participants reported lower current pain severity on the NRS/VAS at post-training, in comparison with control participants.
Pain severity at post-training/follow-up NRS and VAS	The mean pain severity ranged across control groups from 1.93 points to 6.84 points [NRS/VAS]	The mean pain severity in the ABM groups was -0.38 lower [-0.83 to 0.06]	p = .09	209	In this comparison, the single study (Sharpe et al., 2012 Study 1) to incorporate a follow-up (3 months) assessment of pain severity was entered into the meta-analysis.
Attentional bias Dot-probe task	The mean attentional bias index ranged across control groups from -0.82 to 8.6 [dot-probe]	The mean attentional bias index in the ABM groups was -0.4 lower [-0.69 to -0.1]	p = .008	184	A lower attentional bias indicates that ABM participants exhibited a greater tendency to attend away from pain stimuli towards neutral stimuli on the dot-probe task at post-training, in comparison with control participants.

The second outcome assessed was whether or not ABM impacted on attentional bias in comparison with placebo ABM. Homogeneity of the included studies was indicated by an I^2 value of 0%, χ^2 (2) = 1.52, p = 0.47, and so a fixed effects model was applied.[2] One study (Carleton et al, 2011) did not measure attentional bias, and could not be included in the meta-analysis for this outcome. The fixed effects model suggested that ABM impacted on attentional bias measured at post-training, Z = 2.63, p = .008, with participants in the ABM group exhibiting a significantly less pronounced pain-related attentional bias after training

[2] Results were identical using a random effects model, g = -0.4, CI = -0.69 to -0.10, Z = 2.63, p = .008.

than control group participants, *g* = -0.4, CI = -0.69 to -0.10 (see Figure 2.4; Table 2.2). These findings support the hypothesis that neutral ABM at 500 ms reduces attentional bias to pain in initial orienting.

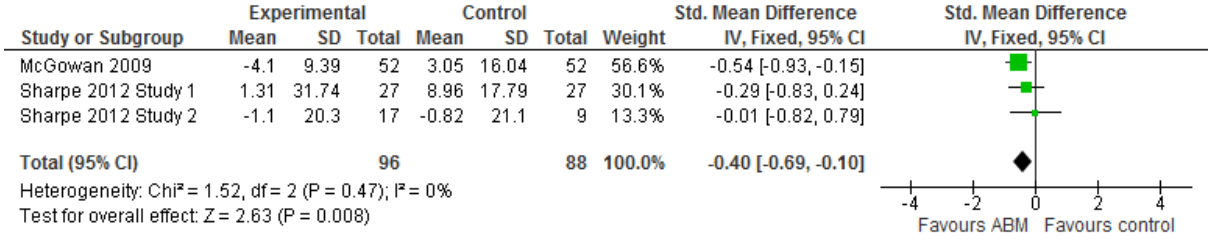


Figure 2.4 Forest plot displaying post-training attentional bias effect sizes of studies comparing ABM with a control group.

2.4 Discussion

The present review included a total of five studies (four published papers) that tested the effects of ABM on attentional bias and/or pain outcomes, and four studies (three published papers) were included in the meta-analysis. This meta-analysis revealed that ABM had a small significant effect on attentional bias, with attentional training successfully redirecting attention away from linguistic pain stimuli towards neutral stimuli (*g* = -0.4). Whilst attentional bias modification demonstrated near-transfer to attentional bias, the current data suggested that training effects did not result in far-transfer to pain severity, where a small trend-level effect was demonstrated at post-training and follow-up, favouring the ABM group (*g*s = -0.22 to -0.38). Hence, the findings from the meta-analysis provided clear evidence that ABM can ameliorate pain-related attentional bias. Meanwhile, the synthesised data failed to provide clear support for the hypothesis that modifying pain-related attentional bias in initial orienting would result in a post-training reduction in pain severity.

The systematic review highlighted a number of methodological differences between studies that could help explain the pain outcome findings, which could not be statistically explored through subgroup analyses in the meta-analysis due to the small number of studies conducted to date. The qualitative synthesis of studies suggested that the type of pain targeted differed across studies (one targeted acute pain; one experimental, and three persistent pain); as did the length of follow-up (only one study introduced a gap between the training program and pain assessment (Sharpe et al., 2012 Study 1)). Past research suggests that length of follow-up could be an important variable, with some studies indicating the impact of modifying attentional bias on symptom outcomes is only realised after the modified bias has interacted with participants' every day experience (e.g. Browning, Holmes, & Harmer, 2010a). In addition, techniques for targeting attentional bias differed in

a number of important ways, which could form the focus of future research addressing optimal techniques for modifying pain-related bias. For example, two studies administered a single session (320 trials; McGowan et al., 2009; Sharpe et al., 2012, Study 1); one study administered four sessions (each at 320 trials; Sharpe et al., 2012, Study 2), and two studies administered eight sessions (at 240 and 384 trials per session; Carleton et al., 2011; Schoth et al., 2013, respectively). It appears that single sessions have been administered for acute/experimental pain, while chronic pain participants have been administered multi-session courses, although this distinction in 'dosage' has not been explicitly stated in study reports, and the optimum 'dose-response' has not been empirically tested. Future research could explore the optimum number of sessions for different pain contexts (procedural/acute and clinical/chronic).

Moreover, the most recent study (that could not be included in the meta-analysis due to the absence of a control group) targeted attentional bias at two stimulus durations (500 ms and 1250 ms), while all of the other studies targeted attention at the shorter stimulus duration of 500 milliseconds. The methodological divergence of the latest study was due to important, contemporary, empirical findings. As discussed in Chapter One, drawing on cognitive theories that suggest attention is non-unitary in nature, and that it is important to distinguish between initial orienting and maintained attention (e.g. Allport, 1989; Mogg, Philippot, & Bradley, 2004b), some studies exploring attentional processing in persistent pain have suggested that it is maintained attention that is particularly biased in this population (e.g. Liossi et al., 2009, 2011; Schoth et al., 2012). This could be because, less likely in acute pain, when pain has been experienced over a long period of time, the development of more elaborative pain-related cognitions connected with the self and well-being, and overlapping networks of associated ideas (or pain and health schemata), contribute to the biasing of attention towards this incoming class of adverse stimuli in the processing stream (Pincus & Morley, 2001). Hence, it might be that targeting maintained attention would be particularly beneficial for alleviating persistent pain severity, whereas targeting initial orienting may be optimal for acute and experimental pain states. However, to date, no studies have explicitly addressed the question of which training stimulus duration is optimal for the far-transfer of training effects to acute and persistent pain outcomes, such as pain severity. This question will be addressed in the present thesis.

The present review had a number of limitations. First, a separate search strategy was not developed for the grey literature such that some unpublished studies could have been overlooked. However, the CINAHL database included unpublished dissertations, thereby incorporating an important subsection of the grey literature into the systematic search. Second, it was not possible to assess publication bias given the small number of published studies conducted to date that have implicitly trained pain-related attentional bias using the

visual-probe task. Third, three of the four studies were from the same research group, which could have introduced other bias, and demonstrates the need for other groups to explore the role of attentional bias in pain experience. Fourth, it was not possible to perform subgroup analyses due to the small number of studies (e.g. by pain type, number of sessions, length of follow-up, stimulus duration), although elucidated were several areas that could be the focus for future research.

These findings provided preliminary evidence that ABM can impact on pain-related attentional bias. In addition, the small, trend-level effect on pain severity indicated that modifying attentional bias towards neutral stimuli might have the potential to alleviate pain experience, as suggested by cognitive-affective models that propose noxious attentional biases can increase vulnerability to pain. However, the systematic review suggested that the ability of training effects to transfer to pain severity could be influenced by differences in techniques used to modify the bias, and variability in the applicability of those techniques to different pain populations, which has yet to be explored. To date, the small number of studies entails that more research is needed before firm conclusions can be drawn.

Chapter 3 Study 1

Pain-related attentional bias in a clinical persistent pain sample versus pain free controls: A between subjects comparison

3.1 Introduction

As discussed in Chapters One and Two, current models suggest that the attentional prioritisation of pain-related over benign information can become maladaptive, when it ceases to be protective for the individual (Eccleston & Crombez, 1999, Moore, Keogh, & Eccleston, 2012). The aim of this initial experimental study was to examine whether or not individuals with persistent musculoskeletal pain exhibit the putative pain-related attentional bias and provide information on its time course, before seeking to retrain attention in this population (Studies Four and Five). Around twenty studies have previously sought to assess whether or not this distorted pattern of attentional processing is evident in persistent pain, using the visual-probe task (Crombez et al., 2013a; Schoth et al., 2012). Most of these studies have been between-subjects comparisons of attentional bias in persistent pain participants versus healthy controls (e.g. Dehghani et al., 2003). Generally, results have suggested the presence of a pain-related attentional bias (particularly towards sensory pain-related words; e.g. Crombez et al., 2013a) in this population, although findings have been conflicting. Whilst most studies have measured bias at a relatively early stage of attention (typically presenting the visual-probe task stimuli for 500 ms), recent evidence suggests that a longer stimulus duration, thought to permit more elaborative processing of the presented information, may be necessary to detect attentional bias in persistent pain (for a review, see Schoth et al., 2012). The hitherto mixed findings point to important methodological considerations for the present research programme.

In one of the first studies to experimentally measure attentional bias in pain, Asmundson et al. (2005b) found no evidence of the bias using the linguistic probe-detection version of the dot-probe task in which word pairs were exclusively presented to participants for 500 ms, vertically aligned, and participants were asked to read the top word aloud. There are at least four factors that could have reduced the sensitivity and specificity of this early version of the test. First, the task-requirement to read the top word out loud promoted the attentional prioritisation of this region of the visual display, interrupting any valence-driven prioritisation of the competing stimuli for attentional selection (Mogg & Bradley, 1999). Second, the inclusion of unprobed neutral-neutral filler trials led to the potential for a learned contingency between the presence of a threat word and subsequent response probe, confounding response times (Mogg & Bradley, 1998). Third, this version simply required participants to indicate using the keypad whether or not a probe appeared on screen, whereas later versions required participants to make a forced choice response concerning either the position or the identity of the probe (i.e. the probe-positional and probe-classification

versions of the task, respectively; Mogg & Bradley, 1998). These later versions are thought to necessitate a more even monitoring of the visual display, and have been found to be more reliable at detecting attentional bias in psychopathology than the original version used by Asmundson and colleagues (Mogg & Bradley, 1998). Fourth, and crucially from a theoretical standpoint and to the present thesis (see also Chapters One and Two), stimuli were exclusively presented on screen for 500 ms, thereby measuring the bias at a comparatively early stage of attention that may be less relevant to persistent pain. Supporting this view, recent research has suggested that, although attentional bias is evident at this relatively early stage of attention, effect sizes are smaller, increasing the likelihood of making a Type II error (Crombez et al., 2013a; Schoth et al., 2012). Hence, consideration of the time course of attentional bias will be critical to developing understanding of attentional processes in persistent pain, and will be assessed using the probe-classification version of the visual-probe task.

In spite of its theoretical import, only a handful of published studies have explicitly examined the time course of attentional bias in adult chronic pain, in all cases in persistent headache (Liossi et al., 2009, 2011; Schoth & Liossi, 2010, 2013). Findings consistently suggested that the bias was particularly situated in later attention (1250 ms). In keeping with other studies reporting attentional bias in pain (e.g. Haggman et al., 2010), the time course studies used the more sophisticated probe-positional or probe-classification (as opposed to probe-detection) versions of the dot-probe task, and all trials were probed. For example, Liossi et al. (2011) found that an overall attentional bias was exhibited in comparison with pain free control participants, and that it was more pronounced at the later (d = 1.32) than the earlier (d = .12) stimulus duration. These findings suggest that the attentional profile of persistent pain may be similar to that noted in individuals with clinical depression, wherein ruminative processing is thought to lead to the top-down biasing of attentional resources towards condition congruent information (Beevers, 2005; Corbetta & Shulman, 2002; Koster et al., 2005; Mogg & Bradley, 2005; Schoth et al., 2012). Its presence was confirmed by a recent meta-analysis of visual-probe investigations of attentional bias in persistent pain which found an overall small to moderate significant effect (g = 0.36), such that these individuals attended more to pain than healthy control participants. In addition, the effect size for attentional bias in maintained attention (g = 0.42) was found to be almost twice as large as that in initial orienting (g = 0.29), supporting the hypothesis that the bias is more evident at this later stage of attention (Schoth et al., 2012). This finding was replicated for sensory pain words (but not images) in a subsequent meta-analysis, by a different research group (Crombez et al., 2013a). Hence, it seems that studies measuring attention in persistent pain exclusively at the earlier stimulus duration were missing an important part of the picture.

Based on the previous research, the current investigation of attentional bias in persistent pain will apply the linguistic probe-classification version of the visual-probe task, in which participants are required to key in the identity of the probe on screen (a left or right facing arrow), and measure attentional bias at two word durations. Thus, pairs of words will be presented on screen, and immediately after the offset of each word pair, a directional arrow probe will appear in the prior location of one of the words. The participant's task will be to key in the identity of the arrow as quickly and accurately as possible. Attentional bias for pain-related words will be indicated by faster response times to arrow-probes suddenly appearing in place of pain words than neutral words, as this signifies the attended region of the visual display (Mogg & Bradley, 1998; Posner, Snyder, & Davidson, 1980). Enabling comparison across visual-probe studies, and for reasons discussed in Chapter One, the selected stimulus durations will be 500 ms for the assessment of initial orienting, and 1250 ms for the assessment of maintained attention (Liossi et al., 2009, 2011). In addition, participants will complete self-report measures of pain severity (experimental group only), and pain catastrophising, anxiety, and depression (whole sample), to assess whether these key constructs are associated with the measured bias, as suggested by past research (e.g. Goubert, Crombez, & Van Damme, 2004; Chapter One). In consideration of the possibility that individual differences in attentional control may be associated with attentional bias development (e.g. Holmes et al., 2014), a measure of perceived attentional control will be administered to all participants to test this association.

As the prior studies examining the time course of attentional bias in persistent pain were conducted for headache, the time course of attentional bias in other types of persistent pain is yet to be investigated (Rusu & Pincus, 2012). Hence, in advance of seeking to modify attentional bias in the main body of the present thesis, the primary aim of this initial study was to replicate and extend previous findings, and test the hypothesis that individuals with persistent musculoskeletal pain will exhibit a pain-related attentional bias in comparison with a pain free control group, and that this bias will be particularly evident in maintained attention (1250 ms), in comparison with initial orienting (500 ms).

3.2 Method

3.2.1 Participants

A total of 101 participants (mean age = 32, *SD* = 15.49, range 18 - 78; 71.3% female) were recruited via posters, leaflets and invitation packs from an NHS pain management clinic, GP practices, and the wider Norwich community, as well as through campus-wide electronic advertisements. The dataset for the persistent pain sample are analysed in the current preparatory between-subjects comparison that sought to determine whether the predicted attentional bias was evident and characterise its time course, and are

also analysed in Study Five (Chapter Six), which sought to retrain the putative bias and examine the impact of this retraining procedure on attention and pain outcomes. Inclusion criteria for the experimental group were: diagnosed chronic benign musculoskeletal pain that had lasted for three months or more; native English speakers (due to the verbal nature of the tasks); aged 18 years and over; normal or corrected-to-normal vision; able to read and understand text displayed on a computer screen, and able to use a computer keyboard comfortably for 30 minutes with breaks. Exclusion criteria were: pain related to a progressive condition such as cancer; undergoing psychological treatment for pain, such as cognitive behavioural therapy, currently or within the past three months, and change in pain medication within the past three months.

Exclusion criteria for the control group were: current persistent pain that has lasted for three months or more, or a history of such pain; a current acute pain condition (e.g. a sprained ankle), and any other physical or mental health condition, either currently or within the past three months. Otherwise, inclusion criteria were identical to those reported for the experimental condition.

The resultant experimental group (n = 49) had a mean pain severity score at baseline of 54 (SD = 20.29; MPQ-SF VAS) out of a possible 100, which is indicative of moderate pain (Breivik et al., 2008; Hawker, Mian, Kendzerska, & French, 2011; Melzack,2011), and a pain interference score of 5.49 (SD = 2.43) out of a possible 10, which suggests moderate interference with daily life (Cleeland, 2009; see Table 3.2). The majority of participants (n = 35; 71.4%) reported persistent musculoskeletal pain in more than one site (14 participants; 28.6% had pain in a single site), and seven (14%) experienced widespread pain in six or more sites. Recruitment took place from August 2013 to August 2014.

3.2.2 Materials

Experimental stimuli

The test stimulus words were 24 pain-related words and 24 neutral words, matched for length and frequency of usage using the Brysbaert database (Brysbaert & New, 2009; see Table 3.1). The pain-related words were selected to be related to the sensory (e.g. “stabbing”) and affective (e.g. “wretched”) aspects of pain, and were taken from previous studies investigating attentional bias and its modification in pain (Asmundson et al., 2005a; Carleton et al., 2011; Keogh et al., 2001b; Liossi et al., 2009, 2011; Sharpe et al., 2012). To minimise the possible confound of category priming, all neutral words were related to the category of household items (Donaldson, Lam, & Mathews, 2007; Liossi et al., 2009; Mogg, Bradley, Williams, & Mathews, 1993). The resulting 24 word pairs were then divided into two test sets (each comprising 12 word pairs; in Study Five (Chapter Six) these different tests were administered at pre and post-training), and test administration was counterbalanced across experimental and control conditions.

Table 3.1

Matched pain and neutral words used in the attentional bias test

Pain word	Neutral word
cut	car
tearing	backyard
tightness	plasterer
stings	spoons
grinding	cassette
sharp	plate
gruelling	glassware
alarming	cabinets
unbearable	bathrooms
tortured	household
debilitating	floorboards
punishing	decorated
stiff	towel
tugging	textile
bruised	cutlery
stabbing	cushion
intense	grounds
sore	brush
wretched	storage
agitation	banister
panic	steps
exhaustion	microwaves
upset	table
agonising	bedclothes

Attentional bias test

The attentional bias test used a modified form of the probe classification version of the dot-probe paradigm adapted from MacLeod and colleagues (MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002), and was administered using E-Prime software (Schneider, Eschman & Zucolotto, 2002). The dot-probe task comprised 96 trials (12 word pairs randomly presented eight times). As illustrated in Figure 3.1, each trial began with a fixation point presented in the middle of the computer screen (48.26 cm/19 inch) for 500 milliseconds. This was followed immediately by the matched word pairs, each with one neutral meaning (e.g. “bookcase”) and one pain-related meaning (e.g. “piercing”). Words (black text on a white background) were separated by a vertical distance of 3 cm, with one word above and one below the prior position of the fixation point. Participants were seated approximately 60 cm from the monitor, affording a visual angle of 1.43º between the central fixation cross and each stimulus word (cf. See, MacLeod, & Bridle, 2009). The test featured two word pair stimulus onset asynchronies (SOA; 500 and 1250 ms) in randomised order. After either 500 or 1250 ms an arrow probe (“<” or “>” with equal frequency) appeared in the prior location of one of the words. The central fixation cross, stimulus words, and arrow probes were all presented in Arial size 11 font. There was a 50:50 distribution of probe

presentation in the position of the pain-related or neutral word, and they were presented with equal frequency above and below the central fixation point. Participants were required to press the left or right arrow key as quickly and accurately as possible, to indicate which direction the arrow was pointing. Faster reaction times (RTs) to probes in non-pain word positions (as opposed to probes in pain word positions) indicated a non-pain attentional bias (i.e. an ability to focus attention away from pain). The test lasted approximately five minutes.

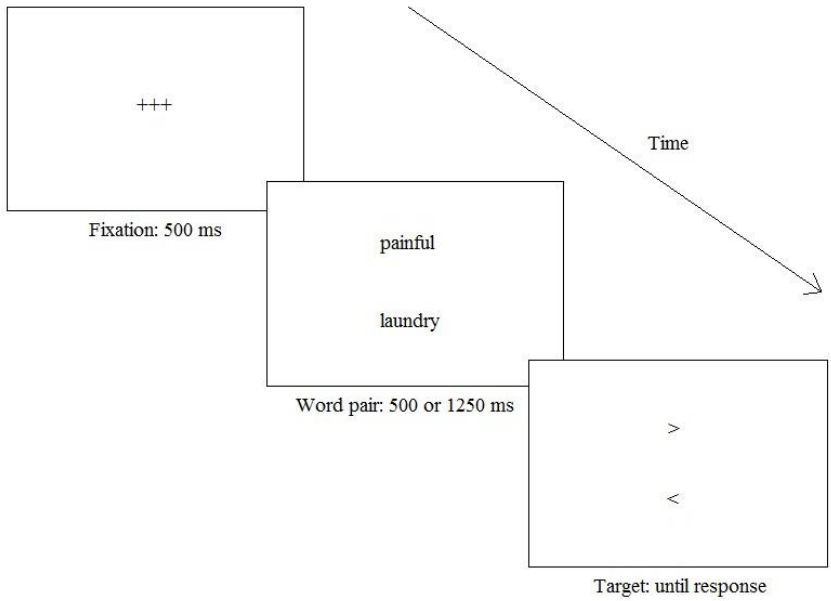


Figure 3.1 Sequence of events in the dot-probe attentional bias test.

Self-report questionnaires

Six standard questionnaires were administered to participants to characterise the sample and test the putative associations of key cognitive and affective variables with bias. In addition to a Demographic and Clinical Questionnaire, these were: the McGill Pain Questionnaire – Short-Form (MPQ-SF; Melzack, 1987); the Brief Pain Inventory (BPI; Cleeland & Ryan, 1994); the Hospital and Anxiety Depression Scale (HADS; Zigmond & Snaith, 1983); the Pain Catastrophizing Scale (PCS; Sullivan et al., 1995); the Pain Vigilance and Awareness Questionnaire (PVAQ; Roelofs et al., 2003a); and the Attentional Control Scale (ACS; Derryberry & Reed, 2002). These measures described the sample in terms of the sensory, cognitive, and affective dimensions of pain experience and vulnerability to pain. The PCS and ACS additionally tested the association between these variables and attentional bias.

The MPQ-SF (Melzack, 1987) is an established multidimensional measure of perceived pain for adults with persistent pain (Hawker et al., 1987). It contains three items: the pain rating index (PRI), visual analogue scale (VAS), and present pain intensity (PPI)

index. The PRI comprises fifteen descriptors; the first eleven of these describe the sensory aspects of pain (e.g. “stabbing”; sensory subscale range 0 - 33), and the last four describe the affective aspects of pain (e.g. “fear-causing”; affective subscale range 0 - 12). Participants are asked to rate the extent to which each word describes their pain during the past week on a scale from 0 (none) to 3 (severe). A total score for this item can be calculated by summing all ratings (range 0 – 45). The VAS is a 100 mm line on which participants are required to rate their pain intensity during the last week from “no pain” to “worst possible pain”. A higher score in millimetres indicates greater pain intensity. Finally, the PPI asks participants to rate their current pain intensity from 0 (“no pain”) to 5 (“excruciating”). A total score for the MPQ-SF is calculated by summing the totals for the first (PRI) and third (PPI) items. Good levels of internal consistency in persistent pain populations (Cronbach’s alpha = .78 to .89) have been reported (Burckhardt & Bjelle, 1994), along with good test-retest reliability (α = .93; Strand, Ljunggren, Bogen, Ask, & Johnsen, 2008), and content and construct validity (Burckhardt & Bjelle, 1994; Gandhi, Tsvetkov, Dhottar, Davey, & Mahomed, 2010; Hawker et al., 2011).

The BPI (Cleeland & Ryan, 1994) was developed to assess clinical pain severity and pain interference. Pain severity is assessed over four items that ask participants to rate their level of pain at its “worst”, “least”, “average” and “now” from 0 (“no pain”) to 10 (“pain as bad as you can imagine”). The pain severity score is the mean rating of these four items (range 0 – 10). Pain interference is assessed over seven items that ask participants to rate the extent to which pain has interfered with their daily life (e.g. general activity, mood, walking ability, sleep) from 0 (“does not interfere”) to 10 (“completely interferes”). The pain interference score is the mean rating of these seven items (range 0 - 10). Also included in the BPI is a single-item percentage measure of pharmaceutical relief from pain during the past twenty-four hours from 0 (“no relief”) to 100 (“complete relief”), although this item is typically not included in a composite score (Cleeland, 2009). Good levels of internal consistency for the pain severity and pain inference scales have been reported (α = .85 to .88, respectively; Tan, Jensen, Thornby, & Shanti, 2004).

The HADS (Zigmond & Snaith, 1983) was selected as the measure of pain-related distress (anxiety and depression, comorbid with persistent pain; e.g. Pincus & Morley, 2001) as it was developed for populations with physical health conditions. It does not include the somatic symptoms of depression that could be caused by physical illness, and is hence unlikely to fall foul of criterion contamination (Pincus & Williams, 1999). The measure has also been used extensively in past research on cognitive biases in persistent pain (e.g. Pincus et al., 2007; Rusu, Pincus, & Morley, 2012; Schoth et al., 2013). The HADS is a fourteen item measure, grouped on two seven-item subscales, that require participants to rate their levels of anxiety (e.g. “I get a sort of frightened feeling as though something awful is about

to happen") and depression (e.g. "I have lost interest in my appearance") during the past week, on four-point scales. Scores are calculated by summing items (range 0 – 21 for each subscale). Scores of seven or less on either subscale indicates no case; 8 – 10 possible case; and greater than or equal to 11 probable case (Zigmond & Snaith, 1983). Good levels of internal consistency in a persistent pain population for the anxiety subscale (α = .85) and depression subscale (α = .86) have been reported (Rusu & Pincus, 2012).

The PCS (Sullivan et al., 1995) is a thirteen item measure that asks participants to rate their level of catastrophic thinking (e.g. "I worry all the time about whether the pain will end") in response to pain on a five-point scale ranging from 0 ("not at all") to 4 ("all the time"), with a higher score representing higher levels of pain catastrophising (range 0 – 52). Three subscales address different dimensions of catastrophic thinking pertaining to rumination (range 0 - 16; e.g. "I anxiously want the pain to go away"); magnification (range 0 - 12; e.g. "I become afraid that the pain will get worse"), and helplessness (range 0 - 24; e.g. "It's awful and I feel that it overwhelms me"). Scores are calculated by summing items. Good levels of internal consistency for the total score (Cronbach's alpha = .95) and subscale scores (α range .66 to .87), and good factorial validity, have been reported (Osman et al., 2000; Sullivan et al., 1995).

The PVAQ (McCracken, 1997) provides an explicit measure of attention to pain. The sixteen item measure asks participants to rate their vigilance and awareness of pain (e.g. "I am quick to notice changes in pain intensity") over the past two weeks on a six-point scale ranging from 0 "never" to 5 "always", with a higher score representing greater pain vigilance (range 0 – 80). Scores are calculated by summing items, including two which are reverse scored. Good levels of internal consistency in chronic low back pain patients (α = .86) and healthy university students (α = .88), as well as good test-retest reliability in chronic pain (r = .80) and healthy (r = .77) participants have been reported (McCracken, 1997; Roelofs, Peters, Muris, & Vlaeyen, 2002a, respectively).

Lastly, the ACS (Derryberry and Reed, 2002) is a twenty item self-report questionnaire measuring two types of attention: attention focusing (items 1-9; e.g. "It's very hard for me to concentrate on a task when there are noises around") and attention shifting (items 10-20; e.g. "It takes me a while to get really involved in a new task"). Items are scored on a 4 point scale from 1 ("almost never") to 4 ("always"). A total score is summed across all items (following the reverse-scoring of eleven inversely coded items), with higher scores indicating greater perceived attentional control. Derryberry and Reed (2002) reported good reliability and validity for the measure.

3.2.3 Procedure

Ethical approval was obtained from the Tayside NHS Research Ethics Committee and University of East Anglia School of Psychology Research Ethics Committee (see

Appendix B). At the experimental session, participants were given a paper copy of the participant information sheet and consent form, together with condition-relevant copies of an eligibility criteria checklist. Having provided full written informed consent, willing participants completed the questionnaire measures (MPQ-SF; BPI; HADS; PCS; PVAQ; ACS) in accordance with their condition (control participants were not asked to complete the pain specific MPQ-SF and BPI), after which they completed the attentional bias test. Testing took place in small groups across two computer laboratories on campus. Finally, participants were debriefed verbally and in writing.

3.3 Results

3.3.1 Group characteristics

As shown in Table 3.2, a series of chi-square or independent samples *t*-tests indicated that the persistent pain and control groups did not differ in gender ratio, χ^2 (1, N = 101) = 1.66, p = .2, or perceived attentional control, t (99) = 1.06, p = .29, r = .11. Contrary to expectations, there was no difference between groups in pain catastrophising, t (99) = 0.39, p = .86, r = .04. The persistent pain group was significantly older than the control group, t (99) = 7.3, p < .001, r = .59, and consequently age was controlled for in the main between-subjects comparisons. As expected when comparing a clinical persistent pain sample with a healthy control group, individuals with persistent pain had significantly higher levels of comorbid anxiety, t (98) = 2.94, p = .004, r = .28, and depression, t (98) = 6.55, p < .001, r = .55, and reported greater vigilance and awareness of pain, t (99) = 3.51, p = .001, r = .33, relative to their pain free counterparts (see Table 3.2 for means and standard deviations).

Table 3.2

Descriptive Data: Means of Age, MPQ-SF Total, BPI-Interference, Anxiety, Depression, Pain Catastrophising, Pain Vigilance and Awareness, Attentional Control, and Attentional Bias with Standard Deviations, and Gender Ratio, by Condition

	Persistent pain *n* = 49		Control *n* = 52	
	M	*SD*	*M*	*SD*
Age	41.39	15.61	23.15	8.75
Female:Male[a]	17:32		12:40	
MPQ-SF	23.25	10.38		
BPI-Interference	5.49	2.43		
HADS-Anxiety	9.65	4.55	7.23	3.65
HADS-Depression	7.79	4.87	2.65	2.51
PCS	23.35	12.43	21.46	9.14
PVAQ	46.31	12.02	37.71	12.77
ACS	49.05	10.79	47.10	7.28
Attentional Bias-500	-14.95	62.01	-1.61	22.58
Attentional Bias-1250	-13.97	44.02	6.40	22.21

3.3.2 Statistical analysis and data reduction

First, with a view to minimising the influence of extreme reaction times on individual trials within the attentional bias test, median reaction times to each of the four critical trial types (probe up, pain word up; probe up, pain word down; probe down, pain word up; probe down, pain word down) at each stimulus presentation time (500 ms, 48 trials; 1250 ms, 48 trials; as well as overall, 500 and 1250 ms, 96 trials), for each participant, were extracted from E-Prime (MacLeod et al., 2002; Whelan, 2008). In addition, due to the instruction that participants with persistent pain could take a break at any point during the program, trials with RTs $\geq$ 3000 ms were not considered accurate measures of attentional bias, and hence, along with error trials, were discarded (3.45% data; MacLeod et al., 2002; Whelan, 2008). Second, in view of the hypotheses, and to facilitate interpretation, three attentional bias indexes (overall, and for each stimulus duration individually) were calculated by subtracting the mean (of the extracted medians) reaction times to neutral words from the mean (of medians) reaction times to pain-related words, such that a more negative value represented a more pain-related bias (MacLeod et al., 2002). Third, in light of the

difference in age (and age-related difference in mean reaction times between the persistent pain group, M = 595.75, SD = 136.92, and control group, M = 482.9, SD = 47.46), a bias proportion score was calculated by dividing each attentional bias index by the mean reaction time (across all trial types), and multiplying this value by one hundred. Hence, each score represented the proportion of the overall mean reaction time that was biased towards the pain versus neutral stimuli. These data formed the dependent variable for the main analyses.

The attentional bias data (extracted medians for each trial type and attentional bias proportion scores) and questionnaire scores were assessed for normality within each condition. Skewness and kurtosis coefficients were calculated by dividing each statistic by its corresponding standard error and screened for whether or not they fell within the recommended range of ± 2 (Curran, West, & Finch, 1996). Findings indicated positively skewed RT distributions at baseline for each trial type in the persistent pain group. Questionnaire data were normally distributed. Inspection of box and whisker plots across the different levels of the attentional bias data suggested three extreme outliers within the persistent pain group (two had extreme negative attentional bias indexes and proportion scores at 500 ms and one had an extreme negative bias index and proportion score at 1250 ms). The control group attentional bias data were normally distributed. No objective reasons for the occurrence of the three extreme values could be identified, and it was decided not to amend or exclude them due to the within-subject nature of the attentional bias data (Osborne & Overbay, 2004; Ratcliff, 1993; Tabachnick & Fidell, 2001). In the absence of a non-parametric equivalent for the main omnibus analysis, and in view of its reputed robustness, a mixed model analysis of variance (ANCOVA) was conducted on the untransformed data (Glass, Peckham, & Sanders, 1972; Lix, Keselman, & Keselman, 1996). Group (Persistent Pain, Control) was entered as the between-subjects factor, test stimulus presentation time (500 ms, 1250 ms) was the within-subjects factor, and age was the covariate. Where assumptions of homogeneity of variance were not met, the Huynh-Feldt correction to degrees of freedom was used, although unadjusted degrees of freedom were reported for clarity.

The primary outcome measure was attentional bias, measured at 500 ms and 1250 ms, to test the hypothesis that the persistent pain group would exhibit an overall attentional bias towards pain, in comparison with the control group, and that this bias would be particularly evident in maintained attention (1250 ms).

3.3.3 Main outcome analysis: mixed model ANCOVA

The experimental group (M = 1.4, SD = 1.48) and control group (M = 1.92, SD = 2.54) did not differ significantly in the percentage of trials that were discarded due to participant error, t (99) = -1.25, p = .22. Results of the main two (Group: Persistent Pain, Control) by two (Stimulus Duration: 500, 1250 ms) mixed model ANCOVA, with age as

covariate, indicated that, in line with the prediction that the persistent pain group would display a facilitated response time to probes replacing the pain-related words versus neutral words, in comparison with the control group, there was a significant between-subjects effect of group, F (1, 98) = 4.2, p = .043, η^2 = .041, such that individuals with persistent pain had a more pronounced pain-related attentional bias, measured at both stimulus presentation times (M = -2.02; SE = .77), than the pain free control participants (M = 0.41; SE = .75; see Figure 3.2). Contrary to expectations, there was no group by stimulus duration interaction, F (1, 98) = .15, p = .6, η^2 = .002, suggesting that the extent of attentional distortion did not differ as a function of word duration. Hence, whilst providing evidence for an overall pain-related attentional bias, these data did not support the hypothesis that, relative to attentional bias in initial orienting, the bias would be markedly more evident in maintained attention, in comparison with controls.

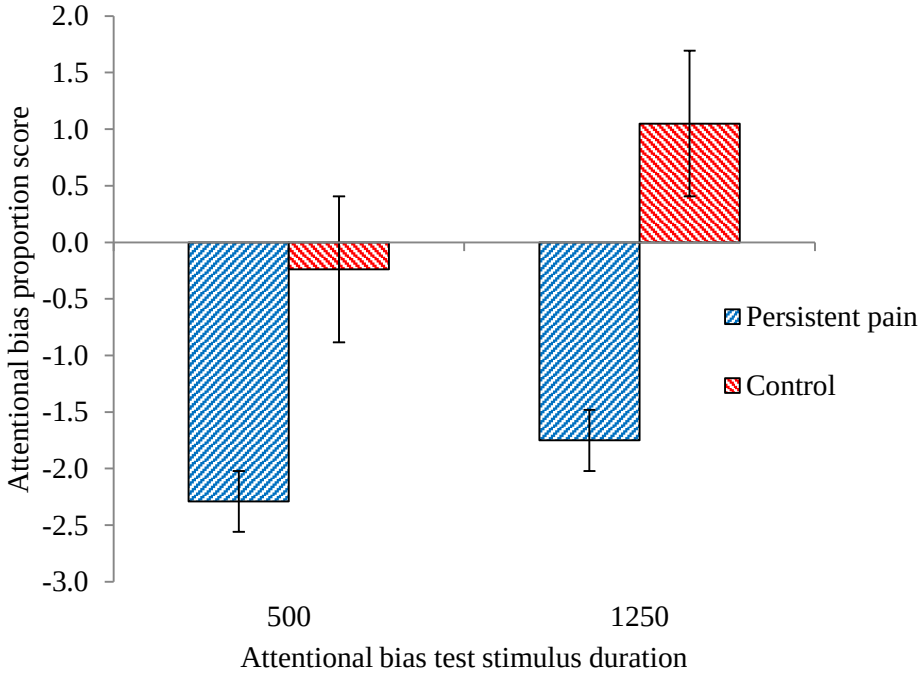


Figure 3.2 Graph illustrating pain-related attentional bias in persistent pain and control groups by test SOA (error bars are standard error of the mean).

Comparison with zero

Within the persistent pain group, two non-parametric one-sample Wilcoxon signed-ranked tests, comparing baseline attentional bias at test stimulus duration 500 ms (*mdn* = -5.50; range = 374.5), and 1250 ms (*mdn* = -7.25; range = 278.25), with the hypothesised median of zero, indicated that, in line with previous findings (e.g. Liossi et al., 2009), attention was biased towards pain words presented for the longer, Z (49) = -2.03, p = .042 (two-tailed), r = -.29, and not the shorter, Z (49) = -1.06, p = .136, r = -.15, time. Within the healthy control group, two one-sample t-tests, comparing baseline attentional bias at test

stimulus duration 500 ms (M = -1.61; SD = 22.58), and 1250 ms (M = 6.4; SD = 22.21), with the hypothesised mean of zero, indicated that, in line with expectations, no attentional bias was evident at the shorter stimulus duration, t (51) = -.51, p = .61 (two-tailed), r = .07, whilst at the longer stimulus duration, pain free participants in fact diverted their attention away from pain words, displaying a neutral attentional bias, t (51) = 2.08, p = .043 (two-tailed), r = .28.

Univariate ANCOVAs

In view of the hypothesis, based on previous literature (Schoth et al., 2012), that processes of maintained attention may be particularly implicated in persistent pain experience, two additional univariate ANCOVAs (with age as covariate) compared the attentional bias (proportion score) in initial orienting, and maintained attention, between groups. For the earlier stimulus duration, as anticipated, the result did not reach significance, F (1, 98) = 1.42, p = .24, η^2 = .014, suggesting that attentional bias in initial orienting did not differ markedly between groups. Whereas, in line with expectations, there was a significant difference in maintained attention, F (1, 98) = 4.43, p = .038, η^2 = .043, with the pain group displaying a more pain-related attentional bias than controls.

3.3.4 Correlations

To evaluate the relationship between the posited cognitive and affective risk factors for persistent pain and attentional bias, Spearman's correlation coefficients were calculated between each attentional bias index and the questionnaire measures. These correlations were conducted first for the whole sample, and then separately within the experimental group and control group. All reported p-values are two-tailed.

Whole sample

Contrary to expectations, no significant associations were identified between pain catastrophising, pain vigilance and awareness, anxiety, or depression and the attentional bias indexes (all ps > .10; see Table C1.1, Appendix C). There was a small negative association between the slower attentional bias and ACS, rs (101) = -.23, p = .024, indicating that participants with a more neutral attentional bias in maintained attention reported lower levels of perceived attentional control.

Persistent pain group

In line with expectations, there was a small significant negative association between pain severity during the past week (visual analogue scale of the MPQ-SF) and the faster attentional bias, rs (49) = -.31, p = .033, suggesting that individuals with a more neutral attentional bias in initial orienting reported experiencing less severe pain. Contrary to expectations, no further significant associations were identified (all ps > .30; Table C1.2, Appendix C).

Control group

No significant correlations were identified between the attentional bias indexes and questionnaire measures (all *p*s > .30; Table C1.3, Appendix C).

3.4 Discussion

The aim of this study was to test the prediction that the clinical persistent pain group would display an overall attentional bias (across initial orienting and maintained attention), favouring pain stimuli, in comparison with control participants. The significant main effect of group on attentional bias (measured at 500 and 1250 ms) provided clear support for this hypothesis. In addition, there was tentative evidence to support previous findings that the bias is more evident in maintained attention. As in previous work (e.g. Liossi et al., 2009, 2011; Schoth et al., 2012), within the persistent pain group, the effect size for attentional bias in maintained attention (r = -.29) was approximately twice as large as that in initial orienting (r = -.15), when compared with zero. However, unlike in three of these previous studies (Liossi et al., 2009, 2011; Schoth & Liossi, 2013, but not Schoth & Liossi, 2010), there was no overall group by stimulus duration interaction, suggesting that persistent musculoskeletal pain affects both component attentional stages. Importantly, these findings extend those of previous research to a persistent musculoskeletal pain population with predominantly widespread pain (i.e. in multiple sites).

The findings support those of Schoth and Liossi (2010), who found a significant main effect of group (persistent headache versus healthy control) on attentional bias, such that it was more pronounced in the context of persistent pain, but this bias did not differ as a function of stimulus presentation time. However, it is worth noting that, in keeping with the emerging overall pattern of findings, the bias was also more pronounced at the longer (12.83 s) than the shorter (4.21 s) stimulus duration in their study (Schoth & Liossi, 2010). The current results fit with those of a recent meta-analysis of visual-probe investigations of pain-related attentional bias, which found that the bias was evident in both initial orienting and maintained attention, but was more pronounced at the later stimulus duration (Schoth et al., 2012). Hence, the current absence of an overall group by stimulus duration interaction suggests that the observed temporal variation is in bias magnitude, and that processes of both earlier and particularly later attention are relevant to persistent musculoskeletal pain.

Correlational analyses were conducted to evaluate the relationship between the self-report measures and bias indexes, which were calculated for each of the measured temporal components of attentional bias. Within the persistent pain group, the questionnaire measures of pain interference, hypervigilance to pain, pain catastrophising, anxiety, and depression, were not significantly associated with the attentional bias indexes of the dot-probe task. These findings are in line with previous cross-sectional studies using implicit measures of

attentional bias, including the dot-probe (e.g. Baum, Huber, Schneider, & Lautenbacher, 2011; Roelofs, Peters, van der Zijden, Thielen, & Vlaeyen, 2003b; Schoth & Liossi, 2013) and Stroop (Roelofs et al., 2002b) tasks, that failed to find evidence of the predicted relationship with the explicit questionnaire measures, as assessed at a single time point. This discrepancy suggests that the different measurement types may be tapping into somewhat distinct processing streams (e.g. Baum et al., 2011; Beevers, 2005). For instance, whereas self-report measures rely on conscious awareness of the measured constructs, the visual-probe task was designed to measure relatively automatic patterns of attentional processing of which the individual is not necessarily aware (e.g. Mathews & Mackintosh, 1998).

Across the whole sample, a more neutral bias in maintained attention was associated with lower perceived attentional control, although the association was not evident within individual conditions. The overall association provides preliminary support for the relationship between bias magnitude and individual differences in attentional control. Critically, within the persistent pain group, the faster attentional bias was negatively associated with pain severity during the last week (such that more pain-related bias, as indexed by a more negative score, was associated with higher pain ratings). This supports the notion that the preferential selection of pain stimuli in early attention is associated with greater perceived pain. However, this finding should be interpreted with caution, as the large number of correlations conducted increases the likelihood of making a type I error.

The main findings of this study support cognitive models of pain chronicity which suggest that ongoing pain is characterised by attentional biases to condition congruent material (e.g. Pincus & Morley, 2001). These biases are thought to maintain or exacerbate pain experience in a number of ways. For example, attentional biases may increase the monitoring of physical sensations, hypervigilance, and increase maladaptive behaviours associated with pain interference (Rusu & Pincus, 2012). Here, both processes of initial orienting, and processes of maintained attention, were active in determining the allocation of attentional resources to the pain versus benign content. The relative prominence of the attentional bias at the later exposure duration suggests that more reflective processes of sustained attention were particularly active in diverting attention away from the competing target stimulus (e.g. Mogg & Bradley, 1998; Schoth et al., 2012). Current theory (e.g. Pincus & Morley, 2001) proposes that the observed bias may be determined by pain-schemata that facilitate the top-down attentional selection of condition congruent material (here indexed by the speeded response times to targets in the prior location of pain words versus neutral words) reflecting the individual's ongoing concerns (Beck, 1976; Mogg & Bradley, 1998; Pincus & Morley, 2001). Hence, repeated pain experience may lead to the build-up of enduring representations of pain and interconnected aversive content that make it more difficult to inhibit afferent impulses and pain-related information, and focus on non-pain

content. The cross-sectional nature of the present study could not determine the causal role of attentional bias in pain. Chapters Five and Six will test whether biased initial orienting and/or maintained attention is epiphenomenal to persistent pain experience, or is causally implicated in its maintenance, by manipulating the bias at both exposure durations, and testing the impact of the modified bias on key pain outcomes.

Importantly, this is the first study to report an attentional bias at later and earlier stages of attention in an adult heterogeneous persistent pain group, characterised by distributed musculoskeletal pain. Overall, the current results, obtained from a large sample, add to mounting evidence that attentional bias could represent a valid therapeutic target for conditions characterised by ongoing pain (e.g. Sharpe et al., 2012). This is additionally supported by psychological approaches for pain management that have alleviated pain-related attentional biases using explicit strategies that aim to increase cognitive control over pain-related distractors (Dehghani et al., 2003). Implicit strategies, like ABM, for targeting these relatively automatic processing biases (that do not rely on conscious processes, and therefore of which the individual is not necessarily aware) could prove a useful adjunctive technique for managing these maladaptive thought processes (Bowler et al., 2012; Sharpe, 2012; Sharpe et al., 2012). Therefore, the present thesis will assess the potential efficacy of modifying attentional bias for pain, with particular focus given to the optimal stimulus presentation duration.

In summary, evidence has been provided that individuals with clinical persistent musculoskeletal pain display an attentional bias towards pain in both initial orienting and maintained attention, in comparison with a healthy control group. In line with previous studies, this pain appeared to have particularly strong effects on maintained attention. Studies Three, Four and Five (Chapters Four to Six) will explore the effects of targeting attentional bias at the earlier and later stages of attention on attentional bias and pain outcomes.

Chapter 4 Studies 2 and 3

Attentional bias modification for acute experimental pain: A comparison of training effects at earlier versus later attention on pain severity, threshold and tolerance

4.1 Introduction

The findings from Study One (Chapter Three) supported theoretical models which suggest that the disproportionate allocation of attentional resources to pain-related cues over competing information (attentional bias; for a review see Crombez et al., 2013a; Schoth et al., 2012) increases vulnerability to pain. However, evidence explicitly testing the posited causal relationship is sparse (Chapter Two). The two experimental pain studies of this chapter will aim explicitly to address this issue and investigate the relationship between shifts in attentional bias, in initial orienting and maintained attention, and pain experience.

As outlined in the previous Chapters, in examining the causal relationship between attentional bias and pain, past research suggests that the time course of the induced bias will be an important consideration (e.g. Koster, Baert, Bockstaele, & De Raedt, 2010; Liossi et al., 2009). This line of research is based on substantial evidence that attention is not a unitary mechanism and that it is important to distinguish between processes involved in the initial orienting and maintenance of attention (Allport, 1989; LaBerge, 1995; Mogg et al., 2004b). In Chapter Three, it was found that individuals with persistent pain disproportionately attended to pain-related information, and this attentional bias was particularly evident within maintained attention (1250 ms), which is in line with previous research on the time course of attentional bias in pain (Liossi et al., 2009, 2011; Study One). These findings supported evidence from previous studies of attentional bias in chronic pain that elaborative processes relating to the meaning of the presented word to the individual are critical to the emergence of the observed bias (Crombez et al., 2013a; Schoth et al., 2012). These studies, however, leave unclear whether biased maintained attention also acts as a vulnerability factor to acute pain perception and response to pain, or whether it is specific to features of ongoing pain, which include emotional distress, repeated interference with activities of daily living, and disability (e.g. Pincus & Morley, 2001; Reid et al., 2011).

One way to disentangle the impact of attentional bias on these different dimensions of pain experience, which can be difficult to delineate in clinical groups, is to use experimental pain induction techniques with healthy participants. It would appear, however, that no studies to date have examined the time course of attentional bias using an experimental pain paradigm. The two experiments of this chapter will address these foundational questions. In Study Two, the impact of acute cold pressor pain on the earlier and later components of attentional bias will be tested and the resultant change in attentional bias from this experimental pain induction will be described. In Study Three, critical features of Study Two's procedure will be reversed. Using the dot-probe task (MacLeod, Mathews,

& Tata, 1986; MacLeod et al., 2002), attentional bias will be targeted at the earlier and later stages of attention through administering two training programs, characterised by their different stimulus exposure durations (500 versus 1250 ms). The impact of these different types of attentional bias modification on change in attentional bias at each stage of attention, and on pain experience and response to pain during the cold pressor task (CPT), will then be assessed, in comparison with a sham training control group.

Whilst studies have not examined the time course of the posited causal relationship between attentional bias and pain, some studies have measured and/or induced an attentional bias in healthy participants, using the visual-probe task, either before, during or after an acute pain induction (Burns et al., 2010; Keogh & Cochrane, 2002; McGowan et al., 2009). For example, Keogh & Cochrane (2002) separately administered the cold pressor task and cognitive bias tests of interpretation and attention to participants in a cross over trial. They found that participants with higher anxiety sensitivity (in comparison with participants with lower anxiety sensitivity) reported higher pain severity and lower pain threshold on the cold pressor task, and this effect was mediated by an adverse cognitive bias, in this case interpretive and not attentional. In addition, a greater pain-related attentional bias in initial orienting was positively correlated with greater post CPT sensory pain severity ratings (as reported on the McGill Pain Questionnaire – Short Form; Melzack, 1987) across the sample, suggesting a relationship between initial orienting to pain stimuli and recollection of worse pain immediately following the CPT. Burns et al. (2010) also measured attentional response to words presented in initial orienting (250 ms) during an ischemic pain induction (the tightening of a blood pressure cuff). Interestingly, results indicated that change in attentional bias across the acute pain induction differed as a function of participants' baseline anxiety profile, such that high anxious participants oriented away from sensory pain words during the pain task, whereas low anxious participants did not exhibit an attentional shift in relation to sensory pain words during this timeframe (from less than one minute to between one and two minutes into the pain task). Unfortunately, pain was not assessed within this study, and so it was not possible to determine whether change in attentional bias was associated with key pain outcomes such as severity. However, in a separate study, high anxious participants reported more severe pain two minutes after completing a cold pressor task, suggesting that greater anxiety at baseline was associated with poorer recovery following cold pressor immersion (Burns et al., 2010). Overall these findings suggest that recovery from acute pain could be impeded when dispositional anxiety is elevated.

Although there is a paucity of evidence concerning change in attentional bias from pre to post an acute pain experience, research from the analogous stress domain would suggest that healthy individuals who undergo an acute stress induction demonstrate an avoidant attentional shift, prioritising neutral over threat-related information following the

stressor, in comparison with beforehand. For example, Roelofs and colleagues (2007) reported that, whereas high glucocorticoid stress responders demonstrated a failure to inhibit threat-related distractors following a laboratory stress induction, low responders were able to filter out the aversive content at a relatively automatically level of processing, and instead selectively attended to neutral information (Roelofs, Bakvis, Hermans, van Pelt, & van Honk, 2007). This has led to the suggestion that the avoidance of noxious stimuli following the stressor may represent an adaptive response, supported by research demonstrating that individuals who reorient towards neutral stimuli have lower post-stressor cortisol levels than their threat biased counterparts (Ellenbogen, Schwartzman, Stewart, & Walker, 2002; Isaacowitz, 2005; van Honk et al., 2000). These findings broadly fit with the correlational findings of Keogh & Cochrane (2002), who found that a pain-related bias was associated with higher pain ratings after the CPT, but appear to diverge from those of Burns et al. (2010), who reported that high anxious participants avoided pain stimuli during the pain task. This discrepancy is probably due to the methodological differences; specifically, Burns et al. (2010) administered the attentional bias test during the pain stressor, whereas in the other studies it was administered subsequently. Overall, the findings suggest that healthy volunteers who experience an acute, experimental pain induction will orient increasingly towards neutral stimuli from pre to post pain task, as part of a normal, rehabilitative response to unpleasant stimuli (Andreotti, 2013; Ellenbogen et al., 2002). By contrast, it seems a maladaptive attentional response to pain may be characterised by the reverse, such that individuals with cognitive vulnerability factors for poor pain response (such as anxiety, e.g. Burns et al, 2010; Katz et al., 2005; Tang & Gibson, 2005), might orient increasingly towards pain-stimuli, and exhibit an attentional shift from neutral towards pain-related information from pre to post CPT (Hermans, Henckens, Joels, & Fernandez, 2014).

In line with the hypothesis that a maladaptive pattern of attentional processing may affect pain outcomes, some longitudinal studies have suggested that the responsiveness of the attentional system influences how pain is experienced: inducing an attentional bias towards pain words in initial orienting decreased pain threshold (the length of time in seconds it took participants to first register pain) and increased pain severity on the cold pressor task (McGowan et al., 2009). Crucially, this suggests that increasing pain-related attentional bias at the earlier stage of attention has a causal role in pain outcomes. In addition, Sharpe et al. (2012) administered a single session of neutral, linguistic, attentional bias modification, also in initial orienting, to individuals with acute low back pain. They calculated change scores, such that a higher score represented a greater shift in attentional bias towards neutral words over the course of an ABM program. Correlations, calculated within the ABM group, with these change scores and average patient pain ratings as the dependent variables, revealed moderate to large negative associations at three month follow-

up, suggesting that those whose biases had shifted the most towards neutral words reported the lowest pain ratings following ABM. In addition, participants in the neutral ABM group reported lower average and current pain severity at follow-up than control participants, who completed a sham training program. Together, these findings suggest that variation in attentional bias at the earlier stage of attention is causally implicated in acute pain perception and response to pain. Yet, no studies to date have assessed the causal role of maintained attention in acute pain experience in healthy participants. To address this gap in the literature, the next two experimental studies will make use of the cold pressor task (CPT) that has been applied successfully in previous experimental pain research (e.g. Keogh & Cochrane, 2002; McGowan et al., 2009), with a view to exploring the foundations of attentional allocation in pain.

To summarise, the aim of Study Two was to investigate the impact of the cold pressor task on change in attentional bias, in earlier versus later attention, as it occurs when pain is encountered. The first hypothesis was that the experience of pain during the CPT would induce an attentional bias either towards or away from pain-related information in healthy participants, and that this may differ as a function of baseline anxiety. The second hypothesis was that pre to post CPT change in attentional bias would be evident at both the earlier and later stages of attention, although the absence of previous studies concerning the impact of acute experimental pain on the temporal components of attention entailed that these predictions were necessarily tentative. The third hypothesis was that change in attentional bias, at both stimulus durations, would be correlated with pain outcomes, both behavioural (i.e. pain measurements taken during the CPT) and self-report (i.e. McGill Pain Questionnaire-Short Form scores taken following the CPT), such that a greater shift towards neutral words will be associated with better pain outcomes (indexed by higher threshold and tolerance, and lower reported severity).

The main aim of Study Three was to conduct the first assessment of the effects of training attention away from pain-related cues towards neutral cues at earlier (500 ms) versus later (1250 ms) stages of attention on pain threshold, tolerance and severity on the cold pressor task. Drawing on attentional theories of pain (e.g. Legrain et al., 2011b), and previous research (e.g. Liossi et al., 2009, 2011; McGowan et al., 2009), it was predicted that participants in the active ABM conditions would attain higher pain threshold and tolerance and report lower levels of pain severity during the CPT, in comparison with a placebo ABM control group. Based on recent findings concerning the time course of attentional bias in pain, it was anticipated that vulnerability to pain would be modified when the faster and slower bias were retrained, although the absence of previous studies concerning the optimal time course of ABM for pain entailed that this prediction was necessarily tentative.

4.2 Study Two

4.2.1 Method

4.2.1.1 Participants

Thirty students and staff from the University of East Anglia completed the study in exchange for either course credit or payment. Two participants who did not finish the cold pressor task (one withdrew their arm at 34.5 s, and one at 13.0 s) were excluded from the main analyses, as this difference in task adherence could confound results (Verhoeven et al., 2010). This left 28 participants for analysis (mean age = 20.54, *SD* = 2.76; 19 females; see Table 4.1). All participants were asked to complete an eligibility criteria checklist upon entering the study. Inclusion criteria were: aged 18-35 (this comparatively low age cut off was selected for the present studies with healthy participants in view of age-related changes in attention; e.g. Allard & Kensinger, 2014); fluent English speaker (due to the verbal nature of the task); normal or corrected-to-normal vision; and able to read and understand text displayed on a computer screen. A number of exclusion criteria were applied to ensure suitability of the cold pressor task: current acute (> 4/10 VAS) or chronic pain or history of chronic pain within the past six months; history of cardiovascular disorder; history of fainting or seizures; history of frostbite; presence of open cuts or sores on the left hand or forearm; history of Raynaud's syndrome; any current medical condition; and recent use of analgesics (within the past six hours; cf. von Baeyer, Piira, Chambers, Trapanotto, & Zeltzer, 2005). Data collection took place over a period of five weeks from March to May 2014.

4.2.1.2 Materials

Cold pressor task (CPT)

The cold pressor apparatus comprised a Techne B-18 stainless steel water bath (L530 mm by W375 mm by H172 mm) with TE-10D thermoregulator and RU-200 dip cooler, which maintained the circulating deionised water temperature at 5 °C (set point accuracy ± 1 °C; temperature stability ± .01 °C; Bibby Scientific, 2013; see Figure 4.1). This set-up adhered to published recommendations for laboratory cold pressor equipment (Von Baeyer, Torvi, Hemingson, & Beriault, 2011), and has been implemented in other experimental pain studies using student and adult samples (e.g. Verhoeven et al., 2010). The water was continuously circulated to ensure no localised warming occurred around the arm. A second tank was used where water was maintained at room temperature (20.3 °C, ± 0.7 °C). To standardise skin temperature prior to cold pressor immersion, all participants first submerged their left arm in the room temperature water tank for one minute. Participants were then instructed to lower their left arm into the cold water to a depth of 8 cm above the wrist (the appropriate point was indicated to the participant by the experimenter) and to "leave it in the water until (the experimenter) tells you to take it out".

They were also asked to keep their hand open while it was in the water, and to avoid touching the sides and the bottom of the water bath. A fixed immersion paradigm was employed, wherein participants were required to immerse their arm in the cold water for a fixed period of time (45 seconds). This ensured that the post CPT measures of attentional bias and pain were not confounded by tolerance time (Verhoeven et al., 2010). Participants were aware in advance that the maximum duration would be 45 seconds. Past research has indicated that contact with cold can induce a complex pain experience (Davis, 1998). Specialised cold-resistant ion channels operate within peripheral nociceptors to sense pain at very low temperatures and protect the body from frost-damage (Jarvis et al., 2007); in addition, it is thought cold-induced vasoconstriction of the blood vessels produces ischemic pain during the CPT (Ahles, Blanchard, & Leventhal, 1983; Jones & Sharpe, 2014b).

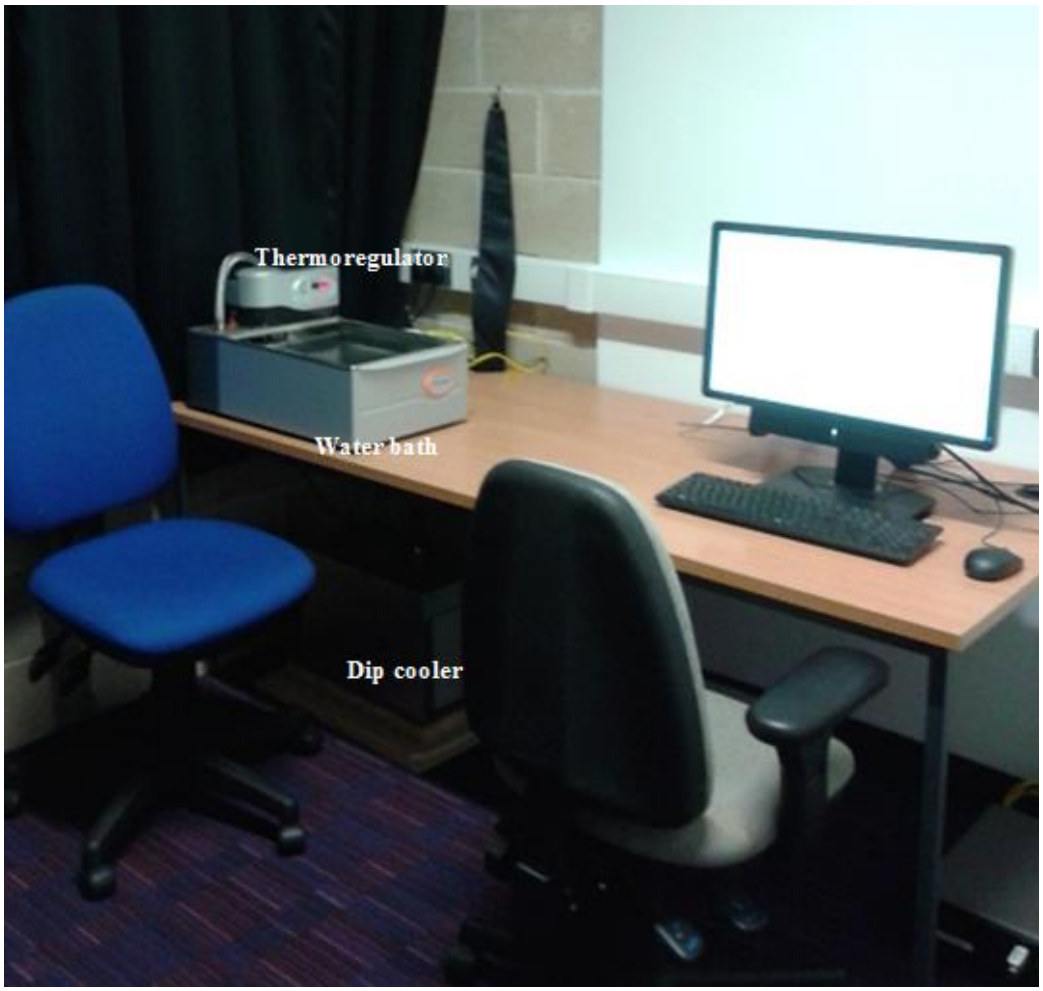


Figure 4.1 Photograph of cold pressor apparatus set up for participant use with adjacent computer for dot-probe task administration.

Experimental stimuli

The experimental stimulus words were identical to those used in Study One (Chapter Three), although details are repeated here for convenience. They comprised 24 pain-related words and 24 neutral words matched for length and frequency of usage in the

Brysbaert database (Brysbaert & New, 2009; see Table 3.1). The pain-related words were selected to be related to the sensory (e.g. "aching") and affective (e.g. "tiring") aspects of pain, and were taken from previous studies investigating attentional bias and its modification in pain (Asmundson et al., 2005a; Carleton et al., 2011; Keogh et al., 2001b; Liossi et al., 2009, 2011; Sharpe et al., 2012). To control for potential priming of the target word group, all neutral words were related to the category of household items (Donaldson et al., 2007; Liossi et al., 2009; Placanica, Faunce, & Soames Job, 2002). The resulting 24 word-pairs were then divided into two test sets (each comprising 12 word pairs; see Table 3.1).

Attentional bias test

The attentional bias test was identical to that used in Study One (Chapter Three). As described there, and repeated here for convenience, it used a modified form of the probe classification version of the dot-probe paradigm adapted from MacLeod and colleagues (MacLeod et al., 2002), and was administered using E-Prime software (Schneider et al., 2002). The dot-probe task comprised 96 trials (12 word pairs randomly presented eight times) with new words presented at pre and post-training and order of test administration counterbalanced across conditions. Each trial began with a fixation point presented in the middle of the computer screen (58.42 cm/23 inch) for 500 ms. This was followed immediately by the matched word pairs (black text on a white blackground), each with one neutral meaning (e.g. "plate") and one pain-related meaning (e.g. "sharp"). Words were separated by a vertical distance of 3 cm, with one word above and one below the prior position of the fixation point. Participants were seated approximately 60 cm from the monitor, affording a visual angle of 1.43º between the central fixation cross and each stimulus word (cf. See et al., 2009). The test featured two word pair stimulus onset asynchronies (SOA; 500 and 1250 ms) in randomised order. After either 500 or 1250 ms an arrow probe ("<" or ">" with equal frequency) appeared in the prior location of one of the words. The central fixation cross, stimulus words, and arrow probes were all presented in Arial size 11 font. There was a 50:50 distribution of probe presentation in the position of the pain-related or neutral word position, and they were presented with equal frequency above and below the central fixation point. Participants were required to press the left or right arrow key as quickly and accurately as possible, to indicate which direction the arrow was pointing. Faster reaction times (RTs) to probes in non-pain word positions (as opposed to probes in pain word positions) indicated a non-pain attentional bias (i.e. an ability to focus attention away from pain). Each test lasted approximately five minutes.

Pain measurements during the CPT

Pain measures were adapted from the only study to date that has investigated the impact of ABM on CPT pain (McGowan et al., 2009). In the current experiment, these were: pain threshold (time taken in seconds for the participant to first register pain), and perceived

pain severity at 30 seconds and 45 seconds into the task, as rated on an 11-point (0-10) numerical rating scale. These measurements were taken to assess the hypothesised association between pain outcomes and attentional bias.

Self-report measures

Eight standard questionnaires were administered at either baseline or following the cold pressor task. After a Demographics questionnaire, the first six of these measured cognitive and emotional factors that have been identified by past research as vulnerabilities for pain experience. Anxiety sensitivity was measured using the Anxiety Sensitivity Index (ASI-3; Taylor et al., 2007). Fear of pain was measured using the Fear of Pain Questionnaire-Short Form (FPQ-SF; Asmundson et al., 2008). As in Study One (Chapter Three), anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). Pain catastrophising was assessed using the Pain Catastrophizing Scale (PCS; Sullivan et al., 1995), and vigilance to pain was gauged using the Pain Vigilance and Awareness Questionnaire (PVAQ; McCracken, 1997). The final baseline measure assessed perceived attentional control using the Attentional Control Scale (ACS; Derryberry & Reed, 2002), as previous studies have suggested that attentional control may affect an individual's ability to downregulate task irrelevant attentional distractors (e.g. Derryberry & Reed, 2002; Sharpe et al., 2012).

Psychometric properties of the HADS, PCS, PVAQ, and ACS were reported in Study One (Chapter Three), and will not be repeated here. Those questionnaires that were either not administered in Study Two (Chapter Three), or were adapted for present purposes, are herein described. The ASI-3 (Taylor et al., 2007) is an eighteen item questionnaire that asks participants to rate their sensitivity to anxiety-related sensations (e.g. "It scares me when my heart beats rapidly") on a scale from 0 ("very little") to 4 ("very much"), with a higher score representing greater anxiety sensitivity (range 0 – 72). Three six-item subscales (range 0 - 24) address the physical (e.g. "When I feel pain in my chest, I worry that I'm going to have a heart attack"), cognitive (e.g. "It scares me when I am not able to keep my mind on a task") and social (e.g. "It is important for me not to appear nervous") aspects of anxiety sensitivity. Scores are calculated by summing items. Good levels of internal consistency (Cronbach's alphas range from .76 to .86 for physical concerns; .79 to .91 for cognitive concerns, and .73 to .86 for social concerns), and good test-retest reliability, have been reported (Taylor et al., 2007).

The FPQ-SF (Asmundson et al., 2008) is a twenty item measure that asks participants to rate their fear of pain associated with various situations (e.g. "breaking your arm") on a scale from 1 ("not at all") to 5 ("extreme"), with a higher score representing greater fear of pain (range 20 - 100). Four subscales address fear related to minor (range 8 - 40; e.g. "biting your tongue while eating"); severe (range 6 - 30; e.g. "breaking your leg");

injection (range 3 - 15; e.g. “receiving an injection in your arm”) and dental pain (range 3 - 15; e.g. “having a tooth pulled”). Scores are calculated by summing items. High levels of internal consistency for the total score (Cronbach’s alpha = .91) and subscale scores (α range .83 to .9), and good factorial validity, have been reported (Asmundson et al., 2008; Carleton & Asmundson 2009).

The MPQ-SF (Melzack, 1987) is an established multidimensional measure of perceived pain; although typically used with persistent pain populations, it can be used to assess acute pain as well (Hawker et al., 2011; Strand, Ljunggren, Bogen, Ask, & Johnsen, 2008). In the present study, participants were asked to base their responses on any pain they experienced during the CPT (James & Hardardottir, 2002). The MPQ-SF comprised two items: the pain rating index (PRI), and present pain intensity (PPI) index. The PRI comprises fifteen descriptors; the first eleven of these describe the sensory aspects of pain (e.g. “stabbing”; sensory subscale range 0 - 33), and the last four describe the affective aspects of pain (e.g. “fear-causing”; affective subscale range 0 - 12). Participants are asked to rate the extent to which each word describes their pain during the past week on a scale from 0 (“none”) to 3 (“severe”). A total score for this item can be calculated by summing all ratings (range 0 – 45). The PPI asks participants to rate their current pain intensity from 0 (“no pain”) to 5 (“excruciating”). A total score for the MPQ-SF is calculated by summing the totals for the first (PRI) and second (PPI) items. Good levels of internal consistency (α = .78 to .89) have been reported (Burckhardt & Bjelle, 1994), along with good test-retest reliability (*r* = .93; Strand et al., 2008), and content and construct validity (Burckhardt & Bjelle; Gandhi et al., 2010; Hawker et al., 2011). The MPQ-SF was administered to assess the association between the sensory and affective dimensions of pain and attentional bias.

Lastly, current pain severity was measured using an 11-point numerical rating scale for pain, which went from 0 (“no pain”) to 10 (“unbearable pain”). This was administered at three time points: at baseline, to ensure that the participant was not currently experiencing pain, 30 seconds into the cold pressor task, and at 45 seconds, the end of the task. The pain NRS has high reported test-retest reliability (*r* = .96; Hawker et al., 2011) and construct validity, in relation to both healthy participants completing the cold pressor task at 5 °C (*r* = .79 to .81; Ferreira-Valente, Pais-Ribeiro, & Jensen, 2011), and chronic pain patients (*r* = .86 to .95; Downie et al., 1978; Ferraz et al., 1990; Hawker et al., 2011).

4.2.1.3 Procedure

Ethical approval for the study was obtained from the University of East Anglia School of Psychology Research Ethics Committee. After completing the eligibility criteria checklist and providing informed written consent, participants completed paper versions of the questionnaire measures. These were always presented in the same order (Demographics; ASI-3; FPQ-II; HADS; PCS; PVAQ; ACS; NRS). Next, participants were administered the

first attentional bias test on the computer, adjacent to the cold pressor apparatus (either version one or two, according to counterbalancing). This was followed immediately by the cold pressor task. First, they immersed their left arm in the room temperature water tank for one minute, followed immediately by the cold water tank, until asked to remove their arm by the experimenter. Verbal instructions for the task were given from a script, ensuring they were standardised across participants (see Appendix D1). These instructions were developed in accordance with published guidelines for effective and ethical administration of the task with children, adapted for present use with an adult population (von Baeyer et al., 2005). Pain threshold was recorded with a stopwatch. Using the NRS, participants verbally reported pain severity at 30 seconds into the task, and at 45 seconds, the end of the task. Following the CPT, participants completed a second attentional bias test (the different version to pre CPT), followed by the MPQ-SF. Finally, they were debriefed both verbally and in writing. Participants were tested individually for 30 minutes, and all sessions were completed in the same laboratory on campus.

4.2.2 Results

4.2.2.1 Group characteristics

Two one-sample *t*-tests, comparing attentional bias data at test stimulus duration 500 ms (M = -3.86; SD = 20.77), and 1250 ms (M = -5.93; SD = 20.95), with zero, indicated that, as expected in a healthy sample, participants did not exhibit a pain-related attentional bias at either the shorter, t (27) = -.98, p = .33 (two-tailed), r = .19 , or longer, t (27) = -1.5, p = .15 (two-tailed), r = .28, stimulus presentation time. Means and *SD*s for anxiety sensitivity, fear of pain, anxiety and depression, pain catastrophising, pain vigilance and awareness, attentional control and attentional bias at baseline are presented in Table 4.1.

Table 4.1

Descriptive Data: Means of Age, Anxiety Sensitivity, Anxiety, Depression, Fear of Pain, Pain Catastrophising, Pain Vigilance and Awareness, Attentional Control and Attentional Bias with Standard Deviations, Gender Ratio and Handedness by Condition

	M	*SD*
Age	20.54	2.76
Female:Male	19:9	
Right:Left handed	26:2	
ASI-3	18.39	9.03
HADS-Anxiety	8.29	3.34
HADS-Depression	2.79	1.85
FPQ-SF	51.21	11.32
PCS	19.39	8.74
PVAQ	40.82	8.25
ACS	48.46	7.59
Attentional Bias-500	-3.86	20.77
Attentional Bias-1250	-5.93	20.95

4.2.2.2 Statistical analysis and data reduction

With a view to minimising the influence of extreme reaction times on individual trials within the attentional bias tests (pre - post), median reaction times to each of the four critical trial types (probe up, pain word up; probe down, pain word down; probe down, pain word up; probe down, pain word down) at each stimulus presentation time (500 ms, 48 trials; 1250 ms, 48 trials; as well as overall, 500 and 1250 ms, 96 trials), for each participant, were extracted from E-Prime (MacLeod et al., 2002; Whelan, 2008). An accuracy filter was applied during the data extraction and trials with errors were discarded (2.56% of the data; MacLeod et al., 2002).

Next, in view of the hypotheses, and to facilitate interpretation, three attentional bias indexes were calculated (overall, and for each SOA individually), by subtracting the mean (of the extracted medians) reaction time to neutral words from the mean (of medians) reaction time to pain-related words, such that a more negative score represented a more pain-related attentional bias (MacLeod et al., 2002).

The attentional bias data (extracted medians for each trial type and derived bias indexes) were checked for normality within each condition. Findings indicated that these data were normally distributed, with skewness and kurtosis coefficients (i.e. the skewness and kurtosis values divided by the corresponding standard errors) at both assessment points (pre, post CPT) for both SOAs (500, 1250) and word types (pain, neutral) falling within the recommended range of ± 2 (Curran et al., 1996). Parametric tests on the raw data were therefore performed.

To assess whether there was an association between change in attentional bias over the CPT pain induction and the key pain outcome measures, attentional bias change scores were calculated by subtracting the relevant attentional bias index at baseline from the equivalent bias index at post CPT (MacLeod et al., 1986). A positive score indicated that attentional bias had shifted from pain words to neutral words from pre to post CPT, whereas a negative score suggested that attention had shifted from neutral words to pain words. As these data were normally distributed, Pearson's correlations are reported.

Preparatory correlational analyses were performed to assess whether the baseline individual differences in vulnerability to pain were significantly associated with the dependent variable (pre - post CPT change in attentional bias). These analyses indicated there was a significant moderate negative association between anxiety at baseline and change in attentional bias at 500 ms, r (28) = -.45, p = .016 (two-tailed), suggesting that the more anxious participants were, the more biased they became towards detecting targets replacing pain words, presented for the shorter stimulus duration, across the CPT pain induction.[3] This finding corresponds with previous research on attentional responsiveness to pain (e.g. Burns et al., 2010). It was therefore considered appropriate to include anxiety as a covariate in a repeated measures analysis of covariance (ANCOVA), thereby increasing test sensitivity for the predicted effects in comparison with the same model without anxiety included as covariate (Asmundson & Katz, 2009; Hinkle, Wiers, & Jurs, 2003). Hence, the main analysis was performed using a repeated measures ANCOVA with baseline anxiety as the covariate and time (pre, post CPT), stimulus duration (500, 1250 ms), target position (behind pain word, behind neutral word) and pain word position (top, bottom) as the within-subjects factors.

4.2.2.3 Main outcome analyses: impact of CPT pain on attentional bias

Repeated measures ANCOVA

To test the central hypothesis of this study that acute pain experience would significantly impact on attentional bias at both the earlier (500 ms) and later (1250 ms)

[3] A significant negative correlation was additionally found between anxiety at baseline and post CPT attentional bias at 500 ms, r (28) = -.449, p = .017 (two-tailed), suggesting that higher baseline anxiety was associated with increased attentional bias to pain words after the cold pressor task.

stages of attention, the above described repeated measures ANCOVA was performed on the attentional bias data. Results indicated that, in line with predictions, the only significant effects were a significant two-way time by target position interaction, F (1, 26) = 4.27, p = .049, η^2 = .14, suggesting that participants responded at different speeds to targets replacing pain words versus neutral words from pre to post CPT. This interaction was qualified by a significant three-way time by stimulus duration by target position interaction, F (1, 26) = 4.52, p = .043, η^2 = .15, indicating that reaction times were differently speeded to targets replacing pain versus neutral words from pre to post CPT, as a function of stimulus duration (see Figure 4.2).[4]

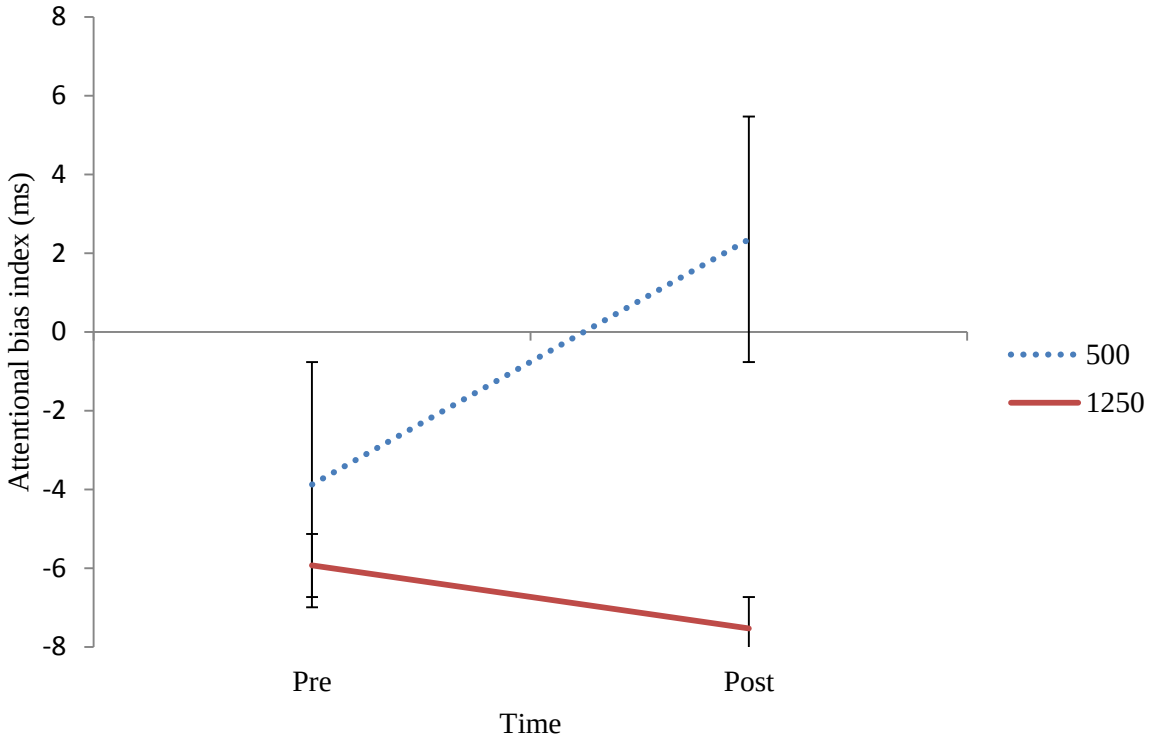


Figure 4.2 Line graph illustrating pre to post CPT change in attentional bias at 500 ms and 1250 ms.

Inspection of means (see Table 4.2) indicated that participants became faster at detecting targets replacing neutral words presented for 500 ms, whereas this was not the case

[4] The results of a repeated measures ANOVA performed on the same data, with time (pre, post), stimulus duration (500, 1250), target position (behind pain word, behind neural word) and pain word position (top, bottom) as the within-subjects factors, indicated that the critical time by target position interaction was not significant, F (1, 27) = .144, p = .71, η^2 = .005, suggesting that the speed of reaction times to targets replacing pain words in comparison with neural words did not change as a function of assessment point. The only significant effect, not directly relevant to current hypotheses, was a significant time by pain word position interaction, F (1, 27) = 5.44, p = .027, η^2 = .17, with means suggesting that participants became faster to respond to targets replacing all word types, across stimulus durations, when pain words were presented at the top, from pre (M = 465.22 ms) to post (M = 450 ms) CPT, whereas this was not the case when pain words were presented at the bottom of the visual display (Ms = 455.49 and 458.67 ms, respectively).

for words presented for 1250 ms. At the later SOA, participants conversely became faster at detecting targets replacing pain words. This suggests that after receiving a noxious stimulus, participants showed a significant shift in attentional bias in initial orienting away from pain-related words and towards neutral words.

Table 4.2

Mean Reaction Times for Each Stimulus Duration at Pre and Post CPT

	Pre		Post	
Attentional bias test	*M*	*SD*	*M*	*SD*
500 neg	458.88	54.44	456.73	57.54
500 neut	462.73	63.86	454.38	54.04
1250 neg	456.94	49.88	449.35	50.10
1250 neut	462.87	55.00	456.88	45.89
500 bias index	-3.86	20.77	2.35	25.40
1250 bias index	-5.93	20.95	-7.53	19.51

Median split baseline anxiety: repeated measures ANOVAs on higher vs lower anxious participants

As noted above, the impact of pain on attentional bias was significant when anxiety was introduced as a covariate. To explore further the relationship between baseline anxiety and how pain impacted on attentional bias, a median split was performed on the HADS-Anxiety scores. For ease of interpretation, analyses were conducted on the two attentional bias indexes (thereby collapsing the target position and word position conditions).

A two (time: pre, post) by two (SOA: 500, 1250) by two (word type: pain, neutral) repeated measures ANOVA was performed within the less anxious group (mean HADS-Anxiety score = 5.12, *SD* = 2.02). Results indicated no main effect of time, F (1, 11) = 4.09, p = .068, η^2 = .271, a significant main effect of SOA, F (1, 11) = 10.42, p = .008, η^2 = .486, and, crucially, a significant two-way time by SOA interaction, F (1, 11) = 4.95, p = .048, η^2 = .311. Follow-up paired samples *t*-tests suggested that the less anxious participants attended significantly more to neutral words when they were presented for 500 ms after the cold pressor task (*M* = 19.48, *SD* = 21.63) than beforehand (*M* = -9.63, *SD* = 20.37), t (11) = -2.64, p = .023 (two-tailed), r = .62, whereas there was no evidence of attentional shift in maintained attention from pre (*M* = -12.9, *SD* = 19.73) to post CPT (*M* = -4.44, *SD* = 18.18) at 1250 ms, t (11) = -.872, p = .402 (two-tailed), r = .25 (means and *SD*s are presented in Table 4.2; see Figure 4.3).

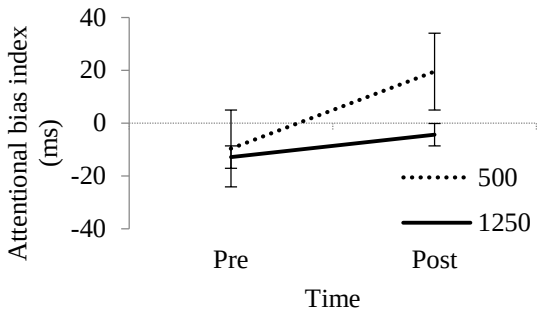


Figure 4.3 Line graph illustrating pre to post CPT change in attentional bias at 500 ms and 1250 ms in participants (n = 12) with lower baseline anxiety as defined by a median split.

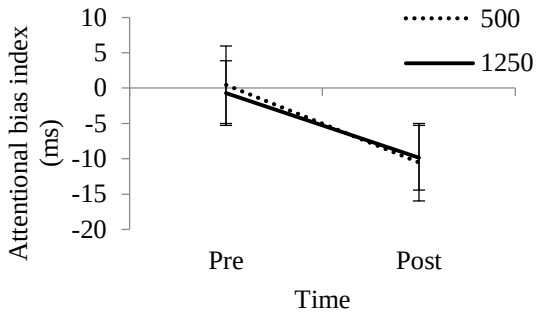


Figure 4.4 Line graph illustrating pre to post CPT change in attentional bias at 500 ms and 1250 ms in participants (n = 16) with higher baseline anxiety as defined by a median split.

However, within the more anxious group (mean HADS-Anxiety score = 10.44, *SD* = 2.37), results from the repeated measures ANOVA indicated no main effect of time, F (1, 15) = 2.24, p = .155, η^2 = .13, no main effect of SOA, F (1, 15) = .003, p = .957, η^2 = < .001, and no time by SOA interaction, F (1, 15) = .065, p = .802, η^2 = .004 (see Table 4.2 and Figure 4.4). Together, these findings suggest that the shift towards neutral stimuli was driven solely by the individuals with lower levels of baseline anxiety.

4.2.2.4 Correlational analyses

Change in attentional bias and pain outcomes

To test the hypothesis that change in attentional bias would be associated with perceived pain severity during the cold pressor task, a series of correlations was performed with pre to post CPT attentional bias index change scores (500 and 1250 ms) and CPT pain outcomes, followed by the MPQ-SF total and subscale scores, as the dependent variables. All reported p-values for these correlations are two-tailed.

Contrary to predictions, no significant correlations were found between change in attentional bias at 500 ms and pain severity at 30 s, r (28) = -.063, p = .75, pain severity at 45 s, r (28) = .028, p = .89, or threshold, r (27) = .19, p = .34, or between attentional bias at 1250 ms and pain severity at 30 s, r (28) = -.059, p = .77, pain severity at 45 s, r (28) = .085, p = .67, or threshold, r (27) = .086, p = .67, as measured during the CPT.

However, in line with predictions, results suggested that change in attentional bias was significantly associated with MPQ-SF pain severity ratings at both the earlier and later stages of attention. A significant moderate negative correlation was found between change in attentional bias at 500 ms and the MPQ-SF total score, r (28) = -.482, p = .009, and MPQ-SF descriptors total score, r (28) = -.497, p = .007, suggesting that development of a more neutral attentional bias at this stimulus duration was associated with lower pain ratings. More specifically, a significant moderate negative correlation was identified between change

in attentional bias at 500 ms and the MPQ-SF sensory pain score, r (28) = -.521, p = .004, but not between change in attentional bias at 500 ms and the MPQ-SF affective pain score, r (28) = -.243, p = .212, suggesting that greater initial orienting to neutral words was particularly associated with lower sensory pain (see Figures 4.5 and 4.6). Diverging with hypotheses, however, the correlation between change in attentional bias at 500 ms and pain intensity (MPQ-SF item 2) did not reach significance, r (28) = -.201, p = .31.

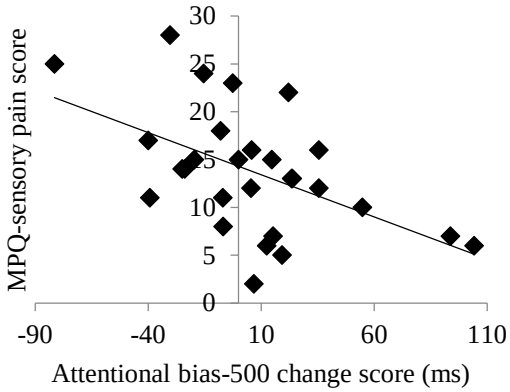


Figure 4.5 Scattergraph illustrating significant moderate negative correlation between change in attentional bias at 500 ms and MPQ-SF sensory pain ratings post CPT.

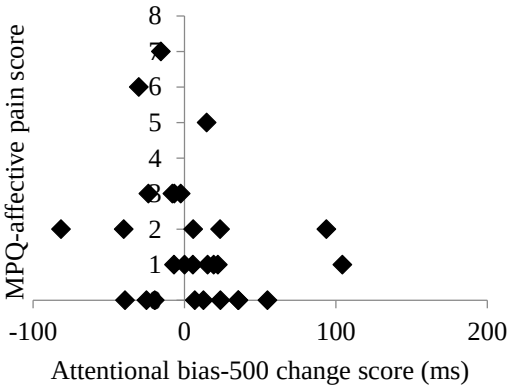


Figure 4.6 Scattergraph illustrating null correlation between change in attentional bias at 500 ms and MPQ-SF affective pain ratings post CPT.

As indicated above, the same pattern of results was observed for attentional bias at 1250 ms. A significant negative correlation was identified between change in attentional bias at 1250 ms and the MPQ-SF total score, r (28) = -.398, p = .036, and MPQ-SF descriptors total score, r (28) = -.416, p = .02, suggesting that a greater neutral attentional bias in maintained attention was associated with lower pain ratings. More specifically, a significant negative correlation was found between change in attentional bias at 1250 ms and the MPQ-SF sensory pain score, r (28) = -.423, p = .025, but not between change in attentional bias at 1250 ms and the MPQ-SF affective pain score, r (28) = -.251, p = .197, suggesting that greater maintained attention to neutral words was particularly associated with lower sensory pain (see Figures 4.7 and 4.8). Again, contrary to hypotheses, the correlation between change in attentional bias at 1250 ms and pain intensity did not reach significance, r (28) = -.112, p = .57.

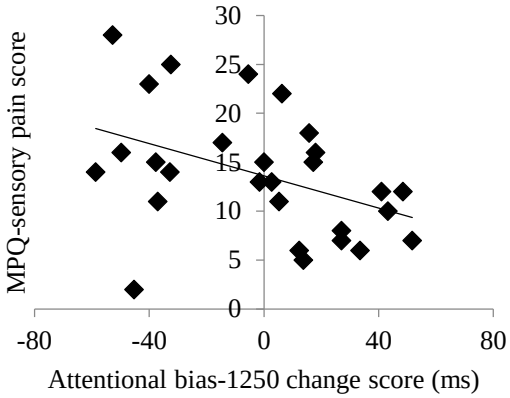


Figure 4.7 Scattergraph illustrating significant weak negative correlation between change in attentional bias at 1250 ms and MPQ-SF and sensory pain ratings post CPT.

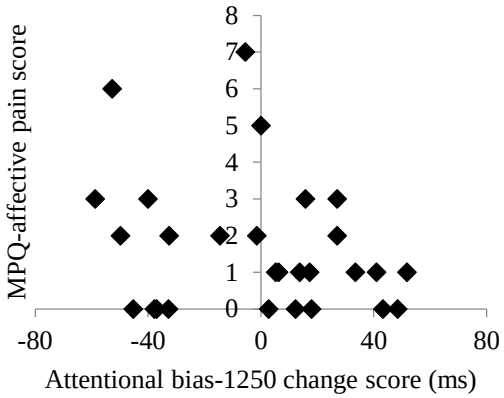


Figure 4.8 Scattergraph illustrating null correlation between change in attentional bias at 1250 ms and MPQ-SF affective pain ratings post CPT.

Baseline attentional control and change in attentional bias

To examine the relationship between dispositional attentional control and change in attentional bias from pre to post CPT, a series of correlations was performed with baseline ACS scores and attentional bias index change scores (500 and 1250 ms) as the dependent variables. All reported *p*-values are two-tailed. Findings indicated the anticipated positive association at trend-level between baseline control over attentional focussing and neutral bias acquisition in initial orienting, r (28) = .361, p = .059, suggesting there was a trend for individuals with higher ACS-F scores at baseline to shift their faster attention to neutral words after the acute pain induction. Although all in the predicted positive direction, the associations between ACS-Shifting, r (28) = .189, p = .335, and ACS-Total, r (28) = .306, p = .114, and AB-500 change, and ACS-Shifting, r (28) = .28, p = .149, ACS-Focussing, r (28) = .305, p = .115, and ACS-Total, r (28) = .327, p = .089, and AB-1250 change, did not reach significance.[5]

4.2.3 Interim discussion

The findings of Study Two were two-fold. First, when baseline anxiety was included as a covariate, earlier (at 500 ms) and not later (at 1250 ms) attention shifted away from pain-related information, towards neutral information, following the acute pain experience. Contrary to expectations, there was no impact of pain experience on attentional bias when baseline anxiety was not partialled out of the analysis, suggesting that elevated anxiety levels affected participants' ability to disengage from pain stimuli in the recovery phase.

[5] When the two participants who withdrew their arm from the cold water early were included in this ACS correlational series, the only significant association was between baseline ACS-F and the faster neutral bias acquisition, r (30) = .372, p = .043, all other $rs < .20$, $ps > .10$.

Second, the more biased participants' attention became towards neutral words (that is, the faster they became at detecting targets replacing neutral words in comparison with pain words) from pre to post CPT, the less pain they reported on the MPQ-SF (total scores and sensory pain score) after the pain induction. These associations were evident at both 500 and 1250 ms. Contrary to predictions, however, there was no association between change in attentional bias and the behavioural measures of pain, taken during the CPT.

The first finding fits with previous research that reported healthy participants disengaged from threat stimuli in the wake of a social stressor and engaged with neutral information in early attention (290 ms; Ellenbogen et al., 2002). Current findings suggest that acute sensory pain can similarly lead healthy participants to divert early attention away from pain words towards neutral words. Having additionally presented critical word pairs for the longer stimulus duration (1250 ms), the present study can add that the pain-induced attentional avoidance of pain stimuli was not evident in maintained attention, and was evident only in initial orienting. This suggests that the observed neutral attentional bias was a relatively automatic stress response mechanism that did not rely on more elaborative, strategic mechanisms of effortful control (e.g. Sass et al., 2014; Tully, Lincoln, & Hooker, 2014). The overall pattern of findings fits with current models that propose the cognitive-affective response to acute stressors is associated with two brain-wide, cross-modal, neuronal networks (the salience processing network and executive control network), which interoperate in a biphasic manner, in response to acute stressors like nociceptive events (Hermans et al., 2014; Legrain et al., 2011b). Supporting these models, empirical data suggest that stressful events can increase hypervigilance and the selective allocation of attentional resources to a range of salient aversive stimuli, including threat and pain (e.g. Burns et al., 2010; Schwabe & Wolf, 2010). It is posited that the two networks regulate the stress response such that, in the acute phase, neural resources are allocated towards the salience network, whereas the executive control network is actively suppressed (Hermans et al., 2014). This results in a transient, hypervigilant state. Whereas, in the recovery phase, this effect is reversed by allocating resources to the executive control network, and suppressing the salience network (Hermans et al., 2014). This can lead to an avoidant state, evident at a relatively automatic stage of processing, whereby attention is allocated away from the noxious stimuli after the stressor has abated, and homeostasis is restored (Andreotti, 2013; Bijleveld, Custers, & Aarts, 2009; Ellenbogen et al., 2002; Hermans et al, 2014). Thus, the accumulating data and theoretical picture suggest that the observed neutral shift in attentional bias might represent a fundamental, adaptive response to acute stressors that include physical pain.

In contrast, the absence of an association between pain-induced attentional bias and mid CPT pain outcomes suggests that the relative timing of the attentional bias test and pain

measurements was crucial. The completion of the attentional bias test only after the acute pain stimulus had terminated might have prevented the detection of an association with pain outcomes measured during the CPT, when the relative allocation of attentional resources to pain and neutral stimuli could have differed to that exhibited in the recovery phase (Burns et al., 2010; Hermans et al., 2014). This could be addressed in future investigations on the impact of pain on selective attention by administering a dot-probe task concurrent with pain measurements, during an acute pain induction.

The avoidant effect of pain on attentional bias was only evident when anxiety was partialled out of the analysis. Together with the findings from the median split (that attentional bias became significantly more neutral pre to post CPT at 500 ms, and not 1250 ms, only in the low anxiety group), it appears that less anxious participants were more able to prioritise neutral stimuli in early attention following the physical stressor than their high anxious counterparts. Past research would suggest individuals with higher baseline dispositional anxiety might have found it harder than those with lower anxiety to regulate the intrusion of competing pain-related task distractors following acute pain (Mathews & Mackintosh, 1998). Thus, theoretically, elevated anxiety levels may have led to a post stressor breakdown of attentional control over aversive stimuli, as suggested by the trend-level pre to post CPT shift towards a pain-related attentional bias in the more anxious group (Bishop et al., 2004; Derryberry & Reed, 2002; Hou et al., 2014; Mathews & Mackintosh, 1998). The importance of attentional control in attentional bias regulation was also suggested by the correlational analyses conducted across the whole sample between baseline attentional control and bias acquisition from pre to post acute pain induction. In particular, the finding that greater dispositional ACS-F was associated with greater acquisition of the faster neutral bias (at trend-level) lends preliminary support to the notion that the associative bias is subject to top-down regulatory mechanisms of attentional control (e.g. Beevers, 2005; Chapter One Introduction Section 1.2.3).

The second finding was of a negative correlation between neutral pre to post CPT attentional shift at 500 ms and 1250 ms and subsequent total and sensory MPQ-SF pain ratings, irrespective of baseline anxiety. This provided preliminary indication that the earlier and later attentional prioritisation of incoming neutral information in the wake of acute pain could be protective, insofar as the more biased attention became towards neutral stimuli at both stages of attention, the lower the severity of sensory (but not affective) pain recalled following the nociceptive event. However, it could equally have been the case that the lower the severity of pain recalled, the more able participants were to divert their attention towards neutral stimuli at post CPT. Study Three will extend current findings, and test the causal basis of the apparent association between an induced neutral bias and reduced vulnerability to pain. It will do so by assessing the impact of experimentally inducing a benign attentional

bias in earlier versus later attention on critical pain outcomes measured during the cold pressor task, in comparison with a control group, in which no bias is trained.

To summarise, the findings from Study Two suggested that acute pain results in a potentially adaptive neutral attentional bias in initial orienting in low anxious individuals that may be impaired in high anxious individuals. In addition, a neutral shift in attentional bias (in both initial orienting and maintained attention), irrespective of baseline anxiety level, suggested a protective, rehabilitative role for the neutral allocation of attentional resources following pain, as indexed by its association with lower post CPT pain severity ratings (Hermans et al., 2014). However, before firm conclusions can be drawn, the causal influence of inducing a neutral attentional bias (at each stimulus duration) on vulnerability to CPT pain needs to be assessed; this will be the focus of Study Three.

4.3 Study Three

As discussed in the general introduction to this chapter, recent studies have suggested a causal role for attentional bias to pain-related information in pain experience (McGowan et al., 2009; Sharpe et al., 2012), such that individuals who have an attentional bias induced in initial orienting towards pain words have a lower pain threshold and report higher pain severity than participants who are trained to attend to neutral words (pain and neutral words were presented for 500 ms). These findings have led some commentators to argue that modifying attentional bias could have therapeutic potential for pain (e.g. Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012). However, the absence of a control group, in which attentional bias was not manipulated, in McGowan et al.'s (2009) study, meant that it was not possible to infer whether the induced attentional prioritisation of pain stimuli in the pain-ABM group led to an increase in pain vulnerability, or that the converse occurred, and the induction of a neutral attentional bias in the neutral-ABM group led to a decrease in pain vulnerability (or both). Hence, the causal role of an induced neutral attentional bias in alleviating vulnerability to acute experimental pain has not been directly tested. In addition, the critical time course for targeting pain-related attentional bias remains unclear, with studies that have presented stimuli for a single stimulus duration (typically 500 ms) suggesting that attentional bias towards pain stimuli is evident at an earlier stage of attention (e.g. McGowan et al., 2009; Sharpe et al., 2012). Meanwhile, studies that measured attentional bias at more than one stimulus duration have suggested that it is particularly evident at a later stage of attention (1250 ms; e.g. Liossi et al., 2009, 2011). Indeed, experimental pain studies have not investigated the causal role of attentional bias in maintained attention in vulnerability to acute pain, although there is good evidence that biased maintained attention is associated with, and may causally contribute to, persistent pain (Liossi et al., 2009, 2011; Sharpe et al., 2012). Thus, the aim of Study Three was to test

whether training participants to attend away from pain-related words, and towards neutral words, presented for 500 ms versus 1250 ms, increased pain threshold and tolerance and decreased self-reported pain severity during the cold pressor task, in comparison with a sham training control group (where no bias was trained).

4.3.1 Method

4.3.1.1 Participants

Seventy-five students from the University of East Anglia completed the study in exchange for course credit. Three participants were excluded, leaving a total of 72 for analysis (mean age = 20.04, *SD* = 2.26; age range 18 - 28; 54 females).[6] All participants were asked to complete an eligibility criteria checklist upon entering the study. Inclusion criteria were identical to those described in Study Two. Using an online research randomiser program (www.randomizer.org) participants were randomly allocated to one of three conditions: ABM-500 (*n* = 23); ABM-1250 (*n* = 23); and ABM-Placebo (*n* = 26). Participants were unaware of their condition allocation. Data collection took place over a period of six weeks in February and March 2014.

4.3.1.2 Materials

Cold pressor task (CPT)

The cold pressor apparatus was as described in Study Two (see Figure 4.1). Instructions were similar to those administered in the previous experiment: as before, having immersed their left arm in the room temperature water for one minute, participants were instructed to lower their left arm into the cold water to a depth of 8 cm above the wrist (the appropriate point was indicated to the participant by the experimenter). However, to enable assessment of the hypothesis that, in comparison with sham training, neutral ABM would increase pain tolerance, participants were instructed to "leave (their) arm in the water for as long as possible". As in Study Two, they were asked to keep their hand open while it was in the water, and to avoid touching the sides and the bottom of the water bath. An uninformed ceiling of four minutes was enforced for participant safety, after which time results can become confounded due to numbing (von Baeyer et al., 2005).

Experimental stimuli

The attentional bias test and experimental stimuli were identical to those described in Study Two (see Table 3.1 for test presented word pairs). An additional twenty-four word pairs for the attentional bias modification program were selected and matched in the same

[6] Apparatus could not be set up in accordance with the study protocol for two participants due to technical problems, and one session was interrupted by building work. In addition, some individuals who did not fulfil inclusion criteria attended the experiment and were demonstrated aspects of the procedure in exchange for course credit, in accordance with School regulations; any resultant data from these individuals were not subject to analysis.

way, using the Brysbaert database (Brysbaert & New, 2009; these stimuli are presented in Table 4.3).

Attentional bias modification

Past research has suggested that a single session of ABM is sufficient to impact on attentional bias and response to acute stressor tasks, including the cold pressor task (e.g. McGowan et al., 2009). A single session of ABM was therefore administered comprising 192 trials, using E-Prime software (Schneider et al., 2002). The critical difference between the attentional bias test and training program was that in the active ABM conditions the probe always replaced the neutral word in each word pair. This was intended to train attention away from the pain-related stimuli. The twenty-four word pairs were randomly presented eight times in each of the four possible combinations (left arrow top/target top; right arrow top/target top; left arrow bottom/target bottom; right arrow bottom/target bottom). Stimuli are presented in Table 4.3. Participants were instructed to fixate their gaze on the centre of the screen throughout and indicate as quickly and as accurately as possible whether a left or right facing arrow appeared on screen using the corresponding arrow keys on the keyboard. The arrow probe disappeared as soon as it was keyed in or after one second. The identity of the arrow probe was randomised for each trial. Participants were not given any indication that the ABM procedure may affect their experience of pain during the cold pressor task. Within the ABM-500 program, there was 500 ms, and within the ABM-1250 program, there was 1250 ms, before the probe appeared (stimulus duration).

The ABM-Placebo program was identical to the attentional bias test (the pain/non-pain words were probed equally), and used the same word pairs as in the active ABM programs (Table 4.3), with 500 and 1250 ms stimulus durations.

Table 4.3

Matched Pain and Neutral Words Used for Attentional Bias Modification

Training set	
Pain word	Neutral word
painful	laundry
sting	porch
tender	carpet
pinching	polished
agony	timer
spasm	stair
squeezing	wallpaper
grinds	mopped
ache	cork
freezing	electric
heavy	floor
biting	sponge
interfere	magazine
suffer	drawer
killing	window
troublesome	telephones
terrible	kitchen
vicious	ceiling
distressing	disinfectant
harmful	pyjamas
upsetting	fireplace
worry	room
nausea	coaster
fearful	stables

Pain measurements taken during the CPT

As in Study Two, pain measures were adapted from the only other study to date that has investigated the impact of ABM on CPT pain (McGowan et al., 2009). These were: pain threshold (time taken in seconds for the participant to first register pain); pain tolerance (maximum time in seconds the participant was able to keep their arm submerged in the cold water before withdrawing it minus threshold); and perceived pain severity at 30 seconds into the task and at tolerance, as rated on an 11-point (0-10) numerical rating scale.

Self-report measures

Baseline self-report measures were identical to those administered in Study Two. Unlike Study Two, however, there was no post CPT questionnaire, as the focus of hypotheses was to test the impact of neutral versus sham ABM on perceived pain and response to pain (severity, threshold and tolerance) during the cold water immersion.

4.3.1.3 Procedure

Ethical approval for the study was obtained from the University of East Anglia School of Psychology Research Ethics Committee. Two data collectors (JB and KB) were counterbalanced across conditions. After completing the eligibility criteria checklist and giving informed written consent, participants completed paper versions of the questionnaire measures. These were always presented in the same order (Demographics; ASI-3; FPQ-II; HADS; PCS; PVAQ; ACS; NRS). Next, participants were administered the first attentional bias test (either version one or two according to counterbalancing). This was followed immediately by one of the ABM programs (500, 1250, or Placebo) depending on condition, and finally by the post-training attentional bias test (the different version to pre-training).

Next, participants completed the cold pressor task; first they immersed their left arm in the room temperature water tank for one minute, followed immediately by the cold water tank for as long as possible. As in Study Two, verbal instructions for the task were given from a script so they were standardised across experimenters and conditions (Appendix D1), and pain threshold and tolerance were recorded with a stopwatch. Using the numerical rating scale, participants verbally reported pain severity at 30 seconds into the task and again at tolerance. Where applicable, at four minutes the researcher asked participants to remove their arm from the water (n = 7).

After the cold pressor task, participants were asked to dry their arm thoroughly and flex their fingers to ensure circulation was fully restored. Finally, they were debriefed both verbally and in writing. Participants were tested individually for one hour. All sessions were completed in the same laboratory on campus (which was the same laboratory as in Study Two).

4.3.2 Results

4.3.2.1 Group characteristics

A series of one-way ANOVAs indicated that randomisation had been successful and there were no significant differences between groups at baseline in age, anxiety sensitivity, anxiety and depression, fear of pain, pain catastrophising, pain vigilance and awareness, perceived attentional control and attentional bias, all Fs < 1. A series of chi-squares indicated no significant differences in gender, χ^2 (2, N = 72) = 3.62, p = .164, or handedness, χ^2 < 1. Means and SDs are reported in Table 4.4.

Two one-sample t-tests, comparing attentional bias data at test stimulus duration 500 ms (M = -1.3; SD = 20.05), and 1250 ms (M = -1.68; SD = 22.8), with zero, indicated that, as expected in a healthy sample, participants did not exhibit a pain-related attentional bias at either the shorter, t (71) = -.551, p = .583 (two-tailed), r = .06, or longer, t (71) = -.624, p = .535 (two-tailed), r = .07, stimulus duration.

Table 4.4

Descriptive Data: Means of Age, Anxiety Sensitivity, Anxiety, Depression, Fear of Pain, Pain Catastrophising, Pain Vigilance and Awareness, Attentional Control and Attentional Bias with Standard Deviations, Gender Ratio and Handedness by Condition

	ABM-500 (*n* = 23)		ABM-1250 (*n* = 23)		ABM-Placebo (*n* = 26)		
	M	*SD*	*M*	*SD*	*M*	*SD*	*F*-value
Age	20.04	2.29	20.13	2.14	19.96	2.41	0.03
Female:Male[a]	14:9		19:4		21:5		3.62
Right:Left handed	21:2		21:2		23:3		0.15
ASI-3	19.78	10.25	19.7	10.4	20.87	10.44	0.10
HADS-Anxiety	7.70	3.08	8.35	4.02	7.31	3.47	0.53
HADS-Depression	3.04	2.38	2.52	2.71	1.96	1.40	1.47
FPQ	49.91	7.74	51.96	11.00	52.58	10.49	0.48
PCS	20.65	7.92	19.78	8.50	19.81	10.02	0.07
PVAQ	36.22	13.59	35.66	10.30	37.49	10.42	0.17
ACS	47.11	5.85	47.53	8.63	48.29	7.16	0.17
Attentional Bias-500	-3.53	21.3	-2.83	16.87	2.02	21.77	0.56
Attentional Bias-1250	-0.99	28.95	3.14	21.12	-6.55	17.32	1.12

Note:[a] All between-groups comparisons at baseline were non-significant ($p > .10$). As gender and handedness are dichotomous variables, chi-squares were conducted.

4.3.2.2 Statistical analysis and data reduction

The approach to statistical analysis and data reduction was similar to that reported in Study Two. First, median reaction times were extracted and trials with errors were discarded (1.69% of the data). Next, the attentional bias data (extracted medians for each trial type and derived bias indexes) were checked for normality within each condition. Findings indicated that these data were normally distributed, with skewness and kurtosis coefficients (i.e. the skewness and kurtosis values divided by the corresponding standard errors) at both assessment points (pre, post ABM) for both SOAs (500, 1250) and word types (pain, neutral) falling within the recommended range of ± 2 (Curran et al., 1996). Parametric tests on the raw attentional data were therefore performed.

Next, the CPT pain outcomes were assessed for normality in the same way. Results indicated that, whereas the Numerical Rating Scale data were normally distributed, with

skewness and kurtosis coefficients falling within the recommended ± 2 range (Curran et al., 1996), the threshold and pain tolerance data exhibited positive skew and kurtosis within all three conditions (see Table 4.5). Inspection of box and whisker plots indicated there were three extreme outliers in the threshold data, and four extreme outliers in the tolerance data (one of which was overlapping with the threshold data). In view of these findings, extreme outliers that fell more than three standard deviations from the group mean were replaced with the next extreme plus one (Tabachnick & Fidell, 2001). However, these imputations failed to normalise the data (see Table 4.5). Therefore, homogeneity of variance assumptions for the Kruskal-Wallis test were checked by calculating absolute values of the residuals and performing a one-way ANOVA on these data (Nordstokke, Zumbo, Caims, & Saklofske, 2011), which indicated that test assumptions had been violated ($p < .001$).

Table 4.5

Skewness and kurtosis coefficients for CPT pain threshold and tolerance

Group	Pain outcome	Skewness coefficient	Kurtosis coefficient	Skewness coefficient[a]	Kurtosis coefficient[a]
ABM-500	Threshold	6.36	11.54	3.13	1.30
	Pain tolerance	1.48	-1.41	1.48	-1.41
ABM-1250	Threshold	2.20	0.45	0.53	-1.66
	Pain tolerance	4.87	11.76	3.36	1.60
ABM-Placebo	Threshold	6.33	9.76	0.63	-1.75
	Pain tolerance	5.16	4.91	3.55	1.92

[a] After data imputations

The main analyses were therefore a series of one-way analyses of variance (ANOVAs) conducted on the dataset in which, as described above, three extreme values had been replaced with the next extreme plus one (Babu, Padmanabhan, & Puri, 1999; Glass et al., 1972; Lix et al., 1996; Tabachnick & Fidell, 2001). In addition, given their positively skewed distribution, the raw CPT threshold and tolerance data were log-transformed, and the one-way ANOVAs repeated to see if results were comparable (Ratcliff, 1993; Whelan, 2008).

Next, to test the hypothesis that ABM-500 and ABM-1250 would modify attentional bias in comparison with sham training, the attentional bias data were analysed using a mixed model ANOVA with group (ABM-500, ABM-1250, ABM-Placebo) as the between subjects factor. In the first instance, time (pre, post-training), stimulus duration (500, 1250 ms), target position (behind pain word, behind neutral word) and pain word position (top, bottom) were included as the within-subjects factors. Where relevant, significant interactions were

followed up with mixed model ANOVAs and *t*-tests conducted on the attentional bias indexes (MacLeod et al., 1986).

Finally, to test the hypothesis that there would be an association between change in attentional bias over the training period and change in the key pain outcome measures, attentional bias 'improvement' scores were calculated by subtracting the relevant attentional bias index at pre-training from the corresponding index at post-training, such that a more positive value represented a greater shift towards a more neutral attentional bias (MacLeod et al, 1986; Sharpe et al., 2012). Where outcomes were not normally distributed (the change scores were normally distributed, whilst, as discussed above, the threshold and tolerance data were positively skewed), Spearman rho correlations are reported.

The primary outcome measures for the present study were the CPT pain measurements (pain severity at 30 s; threshold; tolerance); the secondary outcome measure was the relative change in attentional bias at each test stimulus duration (500 ms; 1250 ms) between training groups, which tested the posited mechanism of action.

4.3.2.3 Main outcome analyses: impact of ABM at 500 versus 1250 ms on CPT pain outcomes

Numerical Rating Scale at 30 seconds

Some participants (n = 20) reached tolerance and withdrew their arm from the water before 30 seconds leaving data for 53 participants available for analysis. A chi-square confirmed CPT withdrawal did not vary between groups, χ^2 (2, N = 72) = .514, p = .773. To test the hypothesis that ABM (in initial orienting and maintained attention) would decrease perceived pain severity at 30 seconds, in comparison with the control group, a one-way ANOVA with condition (ABM-500, ABM-1250, ABM-Placebo) as the independent variable and NRS at 30 seconds as the dependent variable was performed on the relevant NRS data. Results indicated that, in line with predictions, there was a significant difference between groups, F (2, 50) = 3.44, p = .04. Follow-up LSD contrasts suggested that participants in the ABM-500 group (n = 18) rated their pain as less severe (M = 5.1, SD = 1.23) than participants in the ABM-1250 group (n = 17; M = 6.35, SD = 1.41, p = .013), and there was a trend towards the ABM-500 group reporting less severe pain than the control group (n = 18; M = 5.94, SD = 1.63, p = .083), whereas there was no difference between the ABM-1250 and control group, p = .4 (see Figure 4.9). Hence, these findings provided tentative support for the prediction that participants in the ABM-500 would report less severe pain than control participants, whereas there was no evidence that training attentional bias in maintained attention impacted on perceived pain severity, in comparison with controls. In fact, participants who were trained to attend to neutral words (and away from pain words) in initial orienting reported significantly less severe pain than the equivalently trained participants in maintained attention.

Numerical Rating Scale at Tolerance

It was not expected that ABM would impact on perceived pain severity at tolerance in comparison with Placebo Bias Modification (PBM), as previous research has suggested that participants reach an average of 7 to 8 out of 10 on the NRS before they feel the need to withdraw their arm (McGowan et al., 2009). It was expected, however, that the length of time it took for participants' pain ratings to reach that point would differ between groups. In line with the previous findings, a one-way ANOVA with condition (ABM-500, ABM-1250, ABM-Placebo) as the independent variable and NRS at tolerance as the dependent variable revealed no significant difference in mean ratings between the ABM-500 (M = 7.09, SD = 1.78; ABM-1250 (M = 7.26, SD = 1.42) and ABM-Placebo (M = 7.19, SD = 1.7) groups, $F < 1$ (see Figure 4.9).

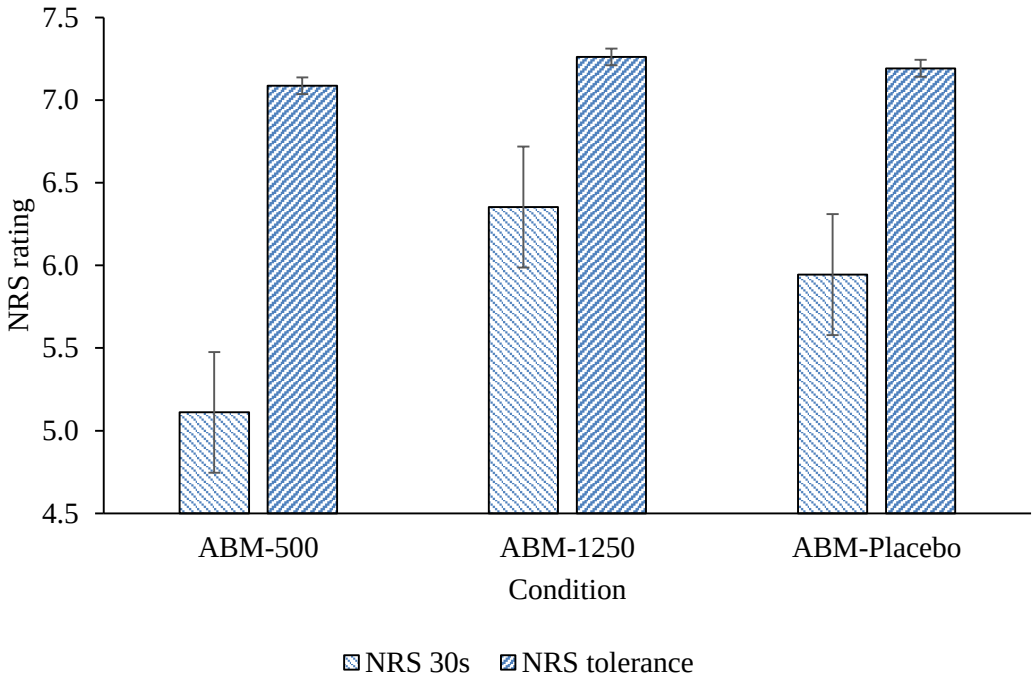


Figure 4.9 Mean pain NRS rating at 30 seconds and tolerance by ABM condition (500 ms, 1250 ms, Placebo). Error bars represent ± 1 standard error.

Pain threshold

Using the three standard deviations from the mean approach, two extreme outliers were identified and replaced with the next extreme plus one (Tabachnick & Fidell, 2001).[7] To test the hypothesis that ABM (in initial orienting and maintained attention) would increase pain threshold, in comparison with the control group, a one-way ANOVA with condition (ABM-500; ABM-1250; ABM-Placebo) as the independent variable and threshold

[7] Results of the one-way ANOVAs performed on the log-transformed CPT data were similar to the original findings, reported in the main text, such that there was a significant difference between the ABM and PBM groups in threshold, F (2, 71) = 3.43, p = .038, and pain tolerance, F (2, 71) = 3.49, p = .036.

(s) as the dependent variable was conducted on these data. As expected, results indicated a significant difference between groups F (2, 69) = 4, p = .023. Follow-up LSD contrasts suggested that participants in the ABM-500 group had a higher pain threshold (M = 17.54, SD = 13.39) than participants in the ABM-1250 group (M = 11.63, SD = 7.26, p = .039) and control group (M = 10.19, SD = 6.72, p = .009), whereas there was no difference between the ABM-1250 and control group, p = .597 (see Figure 4.10). Hence, these results supported the prediction that participants in the ABM-500 would have a higher pain threshold than control participants. Whereas, corresponding with the perceived pain severity at 30 seconds findings, there was no evidence that training attentional bias in maintained attention affected pain threshold, in comparison with controls; instead, the findings suggested that ABM in initial orienting was superior to ABM in maintained attention for increasing this outcome.

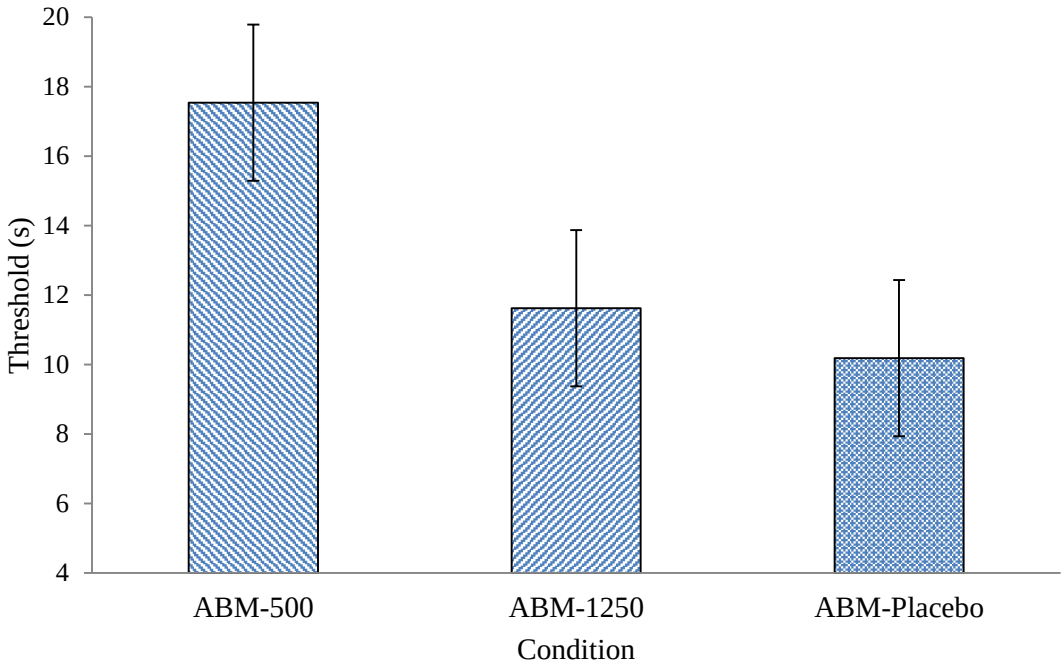


Figure 4.10 Mean threshold (s) by ABM condition (500 ms, 1250 ms, Placebo). Error bars represent ± 1 standard error.

Pain tolerance

One extreme outlier was identified using the three standard deviations from the mean method and replaced with the next extreme plus one (Tabachnick & Fidell, 2001). To test the hypothesis that ABM (in initial orienting and maintained attention) would increase pain tolerance, in comparison with the control group, a one-way ANOVA with condition (ABM-500; ABM-1250; ABM-Placebo) as the independent variable and pain tolerance (s) as the dependent variable was performed on these data. Results indicated that, as expected, there was a significant difference between groups F (2, 69) = 5.28, p = .007. Follow-up LSD contrasts suggested that participants in the ABM-500 had a higher pain tolerance (M = 96.54, SD = 91.41) than participants in the ABM-1250 group (M = 35.51, SD = 29.52, p =

.003) and control group (M = 50.95, SD = 63.68, p = .019), whereas there was no difference between the ABM-1250 and control group, p = .42 (see Figure 4.11).[8] These results supported the hypothesis that participants in the ABM-500 would have a higher pain tolerance than control participants, whereas, corresponding with the perceived pain severity at 30 seconds and threshold findings, there was no evidence that training attentional bias in maintained attention affected pain tolerance, in comparison with controls, and ABM in initial orienting appeared superior to ABM in maintained attention for increasing CPT pain tolerance.

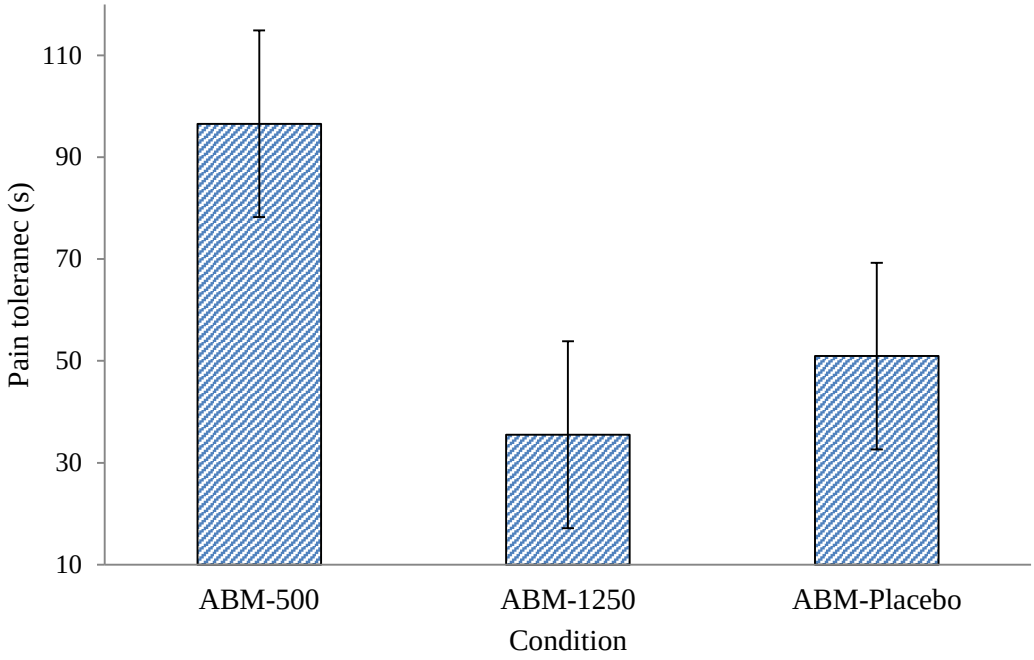


Figure 4.11 Mean pain tolerance (s) by ABM condition (500 ms, 1250 ms, Placebo). Error bars represent ± 1 standard error.

Controlling for gender

Although the difference between groups was not significant, inspection of gender ratios suggested that more males had been randomly allocated to the ABM-500 group than the ABM-1250 group and ABM-Placebo group. A recent systematic review of studies examining gender and pain suggested that, on the cold pressor task, two of the dependent variables of interest (threshold and pain severity) did not differ between genders (Racine et al., 2012). However, gender can potentially impact on CPT tolerance, with males tolerating the cold water for longer than females (Racine et al., 2012; Thompson, Keogh, Chen, &

[8] In view of the previous literature reporting the impact of dispositional anxiety on pain and attentional function, four post hoc one-way ANCOVAs were conducted for each of the above significant CPT outcomes, with baseline anxiety and physical anxiety sensitivity included as covariates (Burns et al., 2010; Keogh & Cochrane, 2002). Results were comparable with the original findings, reported in the main text.

French, 2012). In line with this evidence-base, in the current dataset, only tolerance was significantly correlated with gender (see Figure D2.1, Appendix D). It was therefore decided to rerun analyses with gender included as a covariate, and this was performed for all CPT outcomes as a precaution. The overall pattern of results was comparable with the one-way ANOVAs, with significant effects of group on pain threshold, F (2, 68) = 4.66, p = .013, η^2 = .121, and pain tolerance, F (2, 68) = 3.68, p = .027, η^2= .10. For NRS at 30 s, results indicated that gender did not significantly affect pain severity ratings, F (1, 49) = 0.705, p = .405, η^2 = .014, and there remained a trend-level difference between conditions, F (2, 49) = 2.79, p = .071, η^2 = .102. Inspection of means suggested that both male and female participants reported slightly lower levels of pain at 30 s in the ABM-500 group (*Ms* = 4.86, 5.27, *SDs* = 1.21, 1.27) than in the ABM-1250 group (*Ms* = 6.33, 6.36, *SDs* = 1.53, 1.45) and control group (*Ms* = 5.33, 6.07, *SD* = 1.53, 1.67, respectively).

4.3.2.4 Impact of ABM on attentional bias

The ABM-500 (pre and post *M*s = 5.09, 5.26; *SD*s = 1.24, 1.74), ABM-1250 (*M*s = 5.52, 5.70; *SD*s = 1.50, 1.45) and control (*M*s = 5.70, 6.50; SDs = 1.61, 2.30) groups did not differ significantly in the percentage of trials discarded due to participant error at pre, F (2, 71) = .719, p = .491, or post, F (2, 71) = 2.74, p = .072, training. To test the hypothesis that ABM would differentially impact on reaction times to targets replacing pain words in relation to neutral words at each test SOA, in comparison with sham training, a two (time: pre, post) by two (test SOA: 500, 1250) by two (target position: behind pain, behind neutral) by two (word position: top, bottom) by three (group: ABM-500, ABM-1250, ABM-Placebo) mixed model ANOVA was conducted on the median reaction time data, with between-subjects on the last factor.

Results indicated there was no main effect of time, F (1, 69) = 2.23, p = .14, η^2 = .031, suggesting that participants' reaction times, irrespective of stimulus type and duration, did not change across the single session of ABM, and no time by group interaction, F (2, 69) = 2.77, p = .07, η^2 = .074, indicating there was no overall effect of group on response times from pre to post ABM.

The only significant interactions with time, and hence relevant to hypotheses, was a three-way time by test stimulus duration by group interaction, F (2, 69) = 4.98, p = .01, η^2 = .126, which was further qualified by the critical four-way time by test SOA by target position by group interaction, F (2, 69) = 4.45, p = .015, η^2 = .114, suggesting that, thus far in line with predictions, active ABM, in comparison with PBM, had a differential impact on reaction times to targets replacing pain words versus neutral words, when they were presented for 500 ms versus 1250 ms.

To follow up this four-way interaction, three separate repeated measures ANOVAs were conducted within each condition with time (pre, post) and test stimulus duration (500,

1250 ms) as the within subjects factors. Contrary to expectations, findings indicated that the interaction effect appeared to be driven by increased dwelling in maintained attention on neutral words within the placebo ABM group. Specifically, within the ABM-500 group, results of the repeated measures ANOVA indicated that there was no main effect of time, $F < 1$, and the crucial time by stimulus duration interaction was non-significant, F (1, 22) = .252, p = .621, η^2 = .011, suggesting that, whilst attentional bias in initial orienting means (although not in maintained attention) shifted in the expected directions (see Table 4.6), there was no impact of ABM-500 on either initial orienting or maintained attention.

Table 4.6

Mean Reaction Times for Each Stimulus Duration at Pre and Post ABM

	ABM-500 n = 23		ABM-1250 n = 23		ABM-Placebo n = 26	
Attentional bias test	*M*	*SD*	*M*	*SD*	*M*	*SD*
Pre-500 neg	459.76	43.13	443.92	53.58	452.73	63.75
Pre-500 neut	463.29	37.95	446.75	51.19	450.71	58.11
Post-500 neg	438.18	42.94	452.67	42.99	445.49	59.02
Post-500 neut	438.66	40.42	450.40	40.47	446.49	54.97
Pre-1250 neg	459.65	48.77	446.65	50.35	448.59	53.49
Pre-1250 neut	460.64	50.17	443.51	50.39	455.13	49.24
Post-1250 neg	448.54	44.62	445.35	31.59	458.11	58.63
Post-1250 neut	449.95	46.14	444.90	39.06	448.77	59.65
Pre-500 bias index	-3.53	21.30	-2.83	16.87	2.02	21.77
Post-500 bias index	-0.48	19.22	2.27	19.25	-1.00	24.13
Pre-1250 bias index	-0.99	28.95	3.14	21.12	-6.55	17.32
Post-1250 bias index	-1.40	22.89	0.45	16.60	9.34	15.57

Within the ABM-1250 group, results of the repeated measures ANOVA similarly suggested that, contrary to expectations, there was no main effect of time, F (1, 22) = .079, p = .782, η^2 = .004, and the crucial time by stimulus duration interaction was non-significant, F (1, 22) = 1.17, p = .29, η^2 = .051, suggesting that, as above, whilst attentional bias in initial orienting (although not in maintained attention) means shifted in the expected directions (see Table 4.6), there was no impact of ABM-1250, on either maintained attention or initial orienting.

Within the PBM group, results of the repeated measures ANOVA suggested that, as would be expected in this group, there was no main effect of time, F (1, 25) = 1.75, p = .198, η^2 = .066, suggesting that attentional bias did not shift significantly in either direction (towards pain or neutral words), from pre to post sham training. However, contrary to expectations, the crucial time by stimulus duration interaction was significant, F (1, 25) = 8.01, p = .009, η^2 = .244. Inspection of means (see Table 4.6) suggested that, reflecting the inverse of the pattern of findings observed within the ABM groups, attentional bias in initial orienting exhibited a slight shift towards pain words, although this change was not significant, t (24) = .454, p = .65 (two-tailed), r = .093. Hence, the overall interaction effect appears to have been driven by an unexpected speeding of reaction times to targets replacing neutral words presented in maintained attention, from pre (M = -6.55, SD = 17.33) to post (M = 9.34, SD = 15.57) sham training, t (25) = -3.16, p = .004 (two-tailed), r = .54.[9]

4.3.2.5 Correlations

Attentional control and change in attentional bias in active ABM groups

To examine the relationship between dispositional attentional control and change in attentional bias from pre to post active ABM, a series of correlations was performed with baseline ACS scores and attentional bias index change scores (500 and 1250 ms) as the dependent variables. Contrary to expectations, no significant correlations were identified between baseline ACS-Total (or ACS-S, ACS-F) and the bias change scores, all rs < .2, all ps > .10 (see Table E1.2, Appendix E).

Change in attentional bias and CPT pain measurements

To test the predictions that improvements in attentional bias at each stimulus duration would be associated with improvements in CPT pain outcomes, a series of Spearman's correlations was conducted within each condition for those pain outcomes that were found to differ significantly between conditions (pain tolerane, severity at 30 s, and

[9] Based on the findings of Study Two that baseline levels of anxiety affected pain-related attentional bias in the context of the cold pressor task, and in view of the consideration that current anxiety levels could have been elevated by the upcoming pain induction (and hence during the attentional bias tests, the second of which immediately preceded the CPT), it was decided post hoc to rerun the mixed model ANOVA with baseline anxiety and physical anxiety sensitivity included as covariates (Burns et al., 2010; Keogh & Cochrane, 2002), to assess whether partialling anxiety out of the analyses affected the overall findings (as in Study Two). Results indicated that the overall three-way time by stimulus duration by group interaction remained significant, F (2, 67) = 4.56, p = .014, η^2 = .12. However, critically, follow-up univariate ANCOVAs on bias index difference scores indicated that this interaction was driven by a time by stimulus duration interaction in the PBM group only, F (1, 23) = 8.34, p = .008, η^2 = .27, which was in turn driven by an increased pain-related bias in initial orienting from pre (M = 2.02; SD = 21.77) to post (M = -1; SD = 21.14) sham training, F (1, 23) = 5.53, p = .028, η^2 = .19, whereas the change in attentional bias in maintained attention was no longer significant, F (1, 23) = .48, p = .49, η^2 = .021. As reported in the main text, there were no significant effects of ABM on attentional bias (i.e. no main effects of time, and no time by stimulus duration interactions) in the ABM-500 and ABM-1250 groups, all ps > .12. Together, these findings suggest that detection of the predicted ABM effects on attentional bias may have been overshadowed by the proximal cold pressor task.

threshold), with attentional bias change scores (500 ms, 1250 ms) and the relevant CPT pain measurements, as the dependent variables. All reported *p*-values are two-tailed.

ABM-500 group

In line with hypotheses, significant moderate positive correlations were found between improvement in the training-congruent attentional bias at 500 ms and pain tolerance, *rs* (23) = .468, *p* = .024 (see Figure 4.12), suggesting that greater initial orienting to neutral words over the course of ABM-500 was associated with greater pain tolerance on the cold pressor task. Also, providing limited support for predictions, a trend-level moderate negative correlation was found between improvement in attentional bias at 500 ms and pain severity ratings at 30 s, *rs* (18) = -.447, *p* = .063, suggesting that greater initial orienting to neutral words over the course of ABM-500 was marginally associated with lower pain ratings. Contrary to hypotheses, however, no correlation was found between change in attentional bias at 500 ms and threshold, *rs* (23) = -.084, *p* = .705. In addition, change in attentional bias at 1250 ms was not associated with pain severity, threshold or tolerance outcomes within this condition (all *ps* > .50), suggesting that the observed relationship between attentional bias improvement and reduced vulnerability to CPT pain was evident when the ABM and test stimulus durations were congruent.

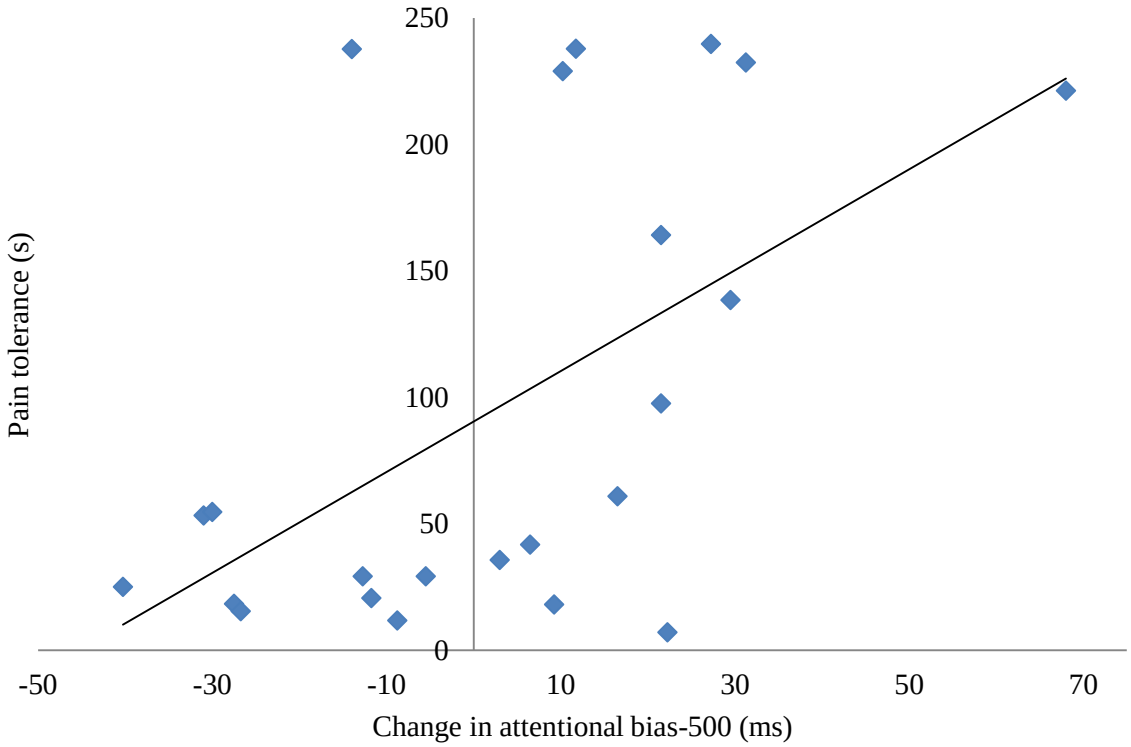


Figure 4.12 Scattergraph illustrating a moderate positive correlation between change in attentional bias at 500 ms and pain tolerance (s) in the ABM-500 group.

ABM-1250 group

Supporting the original hypothesis that pre to post ABM improvement in attentional bias would be associated with improved pain outcomes, a significant moderate positive correlation was found between change in the training-congruent attentional bias at 1250 ms and pain tolerance, *rs* (23) = .469, *p* = .024. However, contrary to predictions, there was no association between change in maintained attentional bias and pain severity, *r*s (17) = -.18, *p* = .5, or threshold, *r*s (23) = .31, *p* = .15. The only other association within this group was a near-significant moderate positive correlation between change in attentional bias at 500 ms and pain tolerance, *rs* (23) = .41, *p* = .053, suggesting that greater initial orienting to neutral words was marginally associated with greater pain tolerance in the training incongruent condition. Nevertheless, adding support to the speculative hypothesis that improvements in pain outcomes would be strongest where stimulus durations were congruent, there was no association between pre to post ABM-1250 change in attentional bias at 500 ms and pain severity ratings at 30 s, *rs* (17) = -.082, *p* = .76, or threshold, *rs* (23) = -.007, *p* = .98.

ABM-Placebo group

In line with predictions, there was no significant association between change in attentional bias at 500 ms or 1250 ms and pain severity ratings at 30 s, *rs* (18) = .213, *p* = .396; and *rs* (18) = -.053, *p* = .835, respectively. However, somewhat surprisingly, significant moderate negative correlations were identified between change in attentional bias at 500 ms and threshold, *rs* (26) = -.41, *p* = .038, and pain tolerance, *rs* (26) = -.426, *p* = .03, suggesting that greater initial orienting towards neutral words from pre to post sham training was associated with lower threshold and tolerance times. Similarly, a significant negative moderate correlation was identified between change in attentional bias at 1250 ms and threshold, *r* (26) = -.557, *p* = .003, suggesting greater maintained attention towards neutral words from pre to post sham training was associated with decreased threshold. Corresponding with expectations, no associations were found between change in attentional bias at 1250 ms and pain tolerance, *r*s (26) = -.204, *p* = .317, within the placebo group.

Differences in correlations

Analyses were conducted to examine whether those significant correlations identified in the ABM-500 group between improvement in attentional bias at 500 ms and pain outcomes differed from the equivalent correlations in the control group. Findings indicated that, in line with expectations, these correlations were significantly different when compared between conditions for pain tolerance, Z (*N* = 49) = 3.15, *p* = .002, and there was a near significant difference for pain severity at 30 s, Z (*N* = 36) = -2.31, *p* = .056 (Soper, 2014).

4.3.3 Discussion

The aim of Study Three was to assess the relative efficacy of modifying attentional bias at 500 ms versus attentional bias at 1250 ms on perceived pain severity, threshold, and tolerance during the cold pressor task, in comparison with a sham training control group. Findings suggested that training initial orienting, and not maintained attention, towards neutral words produced significant increases in pain threshold and tolerance, and there was a trend-level reduction in perceived pain severity at 30 seconds, in comparison with controls. As expected, ABM at neither stimulus duration impacted on pain ratings at tolerance, with all groups reporting a mean rating of seven out of ten, suggesting that attentional training in initial orienting modulated the length of time that participants could withstand the cold pressor immersion, and not the pain level at which tolerance occurred. Hence, in the present study, therapeutic effects were evident only when attention was implicitly diverted to words presented for 500 ms (and not 1250 ms), suggesting the shorter stimulus duration was optimal for this type of attentional retraining

The present findings extended those of McGowan et al. (2009), who found that inducing a pain-related bias in initial orienting (also 500 ms) decreased pain threshold and increased cold pressor pain severity ratings at 30 seconds, but did not affect pain ratings at tolerance, in comparison with a neutral ABM group. The current study was the first to compare the effects of neutral ABM on acute experimental pain in comparison with a placebo training control group. In comparing pain versus neutral ABM, the previous study was unable to specify from which condition the experimental effects derived. In contrast, the current inclusion of a placebo ABM control group permits the inference that retraining initial orienting to neutral information alleviates vulnerability to experimentally induced pain. The current study also compared two ABM stimulus durations, which added that initial orienting may be particularly implicated in acute pain experience. The current effects of modifying the faster bias on CPT pain were additionally corroborated by the correlational evidence of a relationship between increased initial orienting to neutral words, decreased pain and increased tolerance, which differed significantly from the control group.

Both the study by McGowan et al. (2009) and the current study found a significant impact of ABM-500 on pain threshold, strengthening evidence that the faster bias influences this outcome. Both studies also reported small effects in the expected directions on pain severity at 30 seconds. However, unlike in this study, there was no difference in tolerance between groups in the prior experiment. This could be in part due to methodological differences in the maximum length of cold water immersion imposed: whereas participants kept their arm immersed in the cold water for up to ten minutes in McGowan et al.'s (2009) experiment, in the present study participants were subjected to an uninformed ceiling of four minutes, after which time it is thought tolerance results become less meaningful due to

numbing (von Baeyer et al., 2005). Overall, the replicated and extended findings that ABM for initial orienting modifies pain threshold and severity align with studies reporting therapeutic effects of ABM for persistent pain (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012), providing crucial evidence that neutral attentional retraining in initial orienting affects fundamental pain processes that can be difficult to delineate in clinical pain populations. These results are consistent with the idea that selective attentional deployment may be a common process in acute and persistent pain experience (Pincus & Morley, 2001; Sharpe et al., 2012).

However, the predicted training effects on attentional bias were not found: in neither of the active ABM groups was a significant increase in neutral attentional bias found in comparison with the sham training group. Relatedly, the expected association between baseline ACS and neutral bias acquisition from pre to post ABM was not evident. Noteworthy is that when baseline anxiety was included as a covariate, it was only the PBM group who exhibited a significant increase in pain-related attentional bias in initial orienting, in comparison with the ABM groups. It is likely that the detection of ABM effects on attentional bias was overshadowed by the proximity of the dot-probe to the cold pressor task, both spatially and temporally. This explanatory hypothesis is supported by the finding that it was only when anxiety, which might have been exacerbated by the proximal physical stressor, was partialled out of the attentional bias analysis that the predicted training effects started to emerge, in this case in the form of preventing the development of an equivalent pain-related attentional bias in initial orienting in the ABM groups.

Importantly, the current attentional bias data also correspond with those of McGowan et al. (2009), whose reported training effects on attentional bias in initial orienting were evident when their measure of distress (the Depression, Anxiety and Stress Scale, DASS; Lovibond & Lovibond, 1995) was included as a covariate, suggesting that, where attentional bias modification and test procedures immediately preceded an acute pain induction, it was important to consider the potential impact of anxiety on task performance (see also Burns et al., 2010). In spite of the failure of ABM to induce the predicted attentional bias relative to controls, the correlational evidence supported hypotheses that, within the ABM-500 group, improvement in attentional bias at 500 ms was associated with improved pain outcomes, which was consistent with some other studies that have reported associations between change in attentional bias in initial orienting and pain experience (e.g. Keogh & Cochrane, 2002; Sharpe et al., 2012). On the other hand, within the ABM-Placebo group, no association was found between the bias improvement score at 500 ms and pain perception and response to pain on the cold pressor task. Interestingly, within this group, a more neutral bias at 500 ms and 1250 ms was associated with decreased pain threshold and tolerance, suggesting that, whilst sham training impacted on attentional bias, as has been

observed in a number of other studies (e.g. Carlbring et al., 2012; Sharpe et al., 2012), these changes did not translate to the real world and failed to improve participants' experience of pain.

The present study had a number of limitations. First, there was a non-significant difference in gender ratios between groups, and pain tolerance (but not pain severity or threshold) was correlated with gender (Appendix D2). When this was statistically controlled for in an analysis of covariance findings remained significant. Nevertheless, in view of evidence that gender can affect pain tolerance (e.g. Racine et al., 2012), this result in particular should be interpreted with caution, and requires replication before firm conclusions can be drawn. Second, the dot-probe paradigm was used to measure (as well as modify) attentional bias. Consequently, the nature and stability of any resultant attentional change is arguably subject to the reliability of the dot-probe task itself (Browning et al., 2011). Whilst some commentators have questioned its reliability and validity for measuring attentional bias in psychopathology (e.g. Crombez et al., 2013a; Staugaard, 2009), there is recent evidence of its reliability and sensitivity in assessing change in attentional bias in depression and anxiety (Browning et al., 2011). Importantly, the dot-probe task has a large evidence-base that spans the emotion and pain literature (see e.g. Hakmata et al., 2010 and Schoth et al., 2012 for reviews) that enables comparison across studies, and hence will continue to be used in the current programme of research. Third, the generalisability of findings was limited by the student sample. Future studies should seek to extend these findings across a wider age range and socioeconomic demographic.

The findings of Study Three are consistent with cognitive-affective and information processing models of pain that suggest attention modulates perception of and response to pain, such that decreased attention to noxious information can increase the length of time it takes before pain is first registered and extent of pain experienced (e.g. Eccleston and Crombez, 1999; Pincus & Morley, 2001). In terms of clinical implications, the findings concerning threshold are noteworthy. Reduced pain threshold has been reported in individuals with persistent pain (e.g. Herren-Gerber et al., 2004) and is indicative of somatosensory hypervigilance (Van Damme et al., 2014). Greater somatosensory hypervigilance is, in turn, thought to lead to increased avoidance of pain-causing activities, deconditioning and depression, and increased likelihood of pain, creating a vicious circle (Vlaeyen & Linton, 2000, 2012). As such, quelling excessive attention to pain (increased threshold) and decreasing avoidance behaviours (increased pain tolerance) could help reduce deconditioning and pain-related depression, and improve adjustment to pain. However, the generalisability of ABM effects to persistent pain requires systematic examination, which will form the focus of Studies Four and Five. Nevertheless, the ability to increase acute pain threshold could have therapeutic potential for acute procedural pain. The critical role of

attention in acute, including procedural, pain experience is supported by the current evidence base for distraction therapies (e.g. Diette et al., 2003). Interestingly, unlike distraction, which is an explicit strategy for diverting attention from pain, ABM is an implicit strategy for attentional diversion that is thought to work at a relatively automatic level of processing (Hertel & Mathews, 2011). Recent research has suggested that the efficacy of explicit strategies like distraction might be reduced when there is a pre-existing attentional bias to pain (Van Ryckeghem et al., 2012), indicating that the two might work in different and potentially complementary ways; future research could address this question.

In summary, the present study has suggested that shorter exposure to the critical stimulus trials is relatively more efficacious in promoting transfer of attentional retraining effects to a real-world pain-stressor task, in comparison with both the longer stimulus duration and placebo-ABM.

4.4 Additional analyses: Data from Studies Two and Three combined

4.4.1 Participants

Combining the data from Studies Two and Three resulted in a total of 102 participants with complete data for analysis (mean age = 20.25, *SD* = 2.5; age range 18 – 30; 27 male, 75 female).

4.4.2 Results

4.4.2.1 Group characteristics

A series of one-way ANOVAs indicated there were no significant differences between groups at baseline in age, anxiety and depression, fear of pain, pain catastrophising, pain vigilance and awareness, perceived attentional control and attentional bias, all *F*s < 1.5, *p*s > .20. However, there was a significant difference between groups in attention to changes in pain, F (3, 98) = 5.06, p = .003, such that the no training control group (Study Two participants) had significantly higher scores (M = 18.73, SD = 3.38) than the ABM-500 (M = 14.96, SD = 5.01; p = 001) and ABM-1250 (M = 15.11, SD = 4.42; p = .002), although not ABM-Placebo (M = 17.10, SD = 3.68; p = .14) groups. Pain vigilance and awareness was therefore included as a covariate in the main analyses. A series of chi-squares confirmed there were no significant differences in gender (number of males per group: ABM-500 = 9; ABM-1250 = 4; PBM = 5; No Training = 9), χ^2 (3, N = 102) = 3.76, p = .289, or handedness, $\chi^2 < 1$, between groups.

Two one-sample *t*-tests, comparing attentional bias data at test stimulus duration 500 ms (M = -2.72; SD = 20.36), and 1250 ms (M = -3.26; SD = 22.23), with zero, indicated that, as expected in a healthy sample, participants did not exhibit a pain-related attentional

bias at either the shorter, t (101) = -1.35, p = .181 (two-tailed), r = .13, or longer, t (101) = -1.48, p = .142 (two-tailed), r = .13, stimulus duration.

4.4.2.2 Statistical analysis

Two one-way ANCOVAs with Helmert contrasts, with baseline pain vigilance and awareness (PVAQ total score) included as a covariate, were conducted on the combined dataset to test the hypothesis that, drawing on the findings from Study Three, participants in the ABM-500 group would have lower pain ratings at 30 seconds (as measured on the above described Numerical Rating Scale) and higher pain threshold in seconds, during the cold pressor immersion, than the three other groups (ABM-1250; ABM-Placebo; No Training control).

4.4.2.3 Main outcome analyses: pain severity and threshold

Results of the one-way ANCOVA conducted on the pain severity data, with condition (ABM-500; ABM-1250; ABM-Placebo; No Training) as the independent variable and NRS rating at 30 seconds as the dependent variable, indicated a trend-level difference between groups, F (3, 77) = 2.21, p = .094, η^2 = .079. In view of the hypothesis, and previous findings (Study Three) suggesting that ABM-500 modulated perceived pain severity, the follow-up Helmert contrasts were pursued. These suggested that, as predicted, participants in the ABM-500 group (M = 5.11, SD = 1.23) reported lower pain severity than participants in the ABM-1250 (M = 6.35, SD = 1.41), ABM-Placebo (M = 5.94, SD = 1.63) and No Training control (M = 6.24, SD = 2.01; p = .017) groups (see Figure 4.13). No further significant differences were identified (ps > .41).

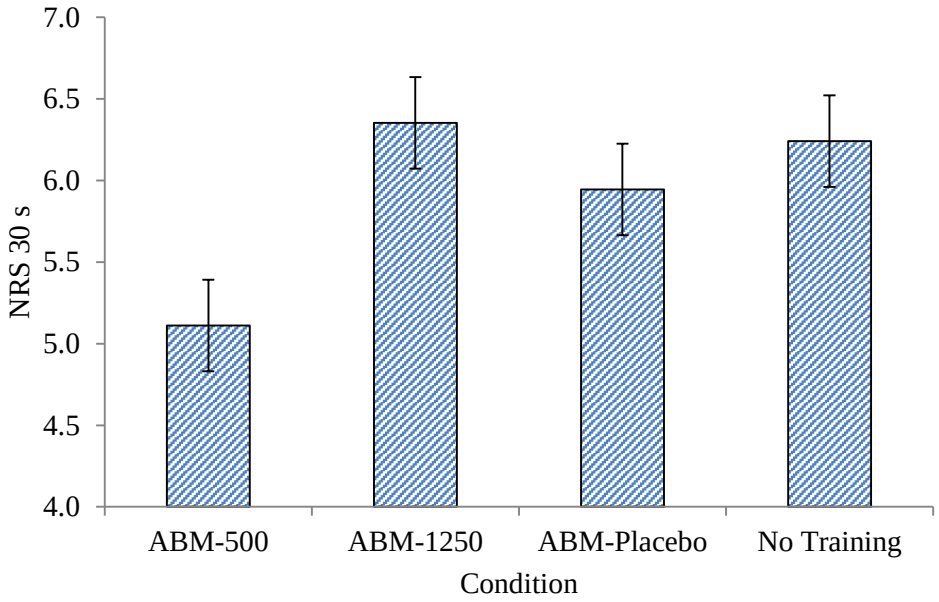


Figure 4.13 Mean pain severity rating at 30 seconds by ABM condition (500 ms, 1250 ms, Placebo, No Training). Error bars represent ± 1 standard error.

Results of the one-way ANCOVA conducted on the threshold data, with condition (ABM-500; ABM-1250; ABM-Placebo; No Training) as the independent variable and threshold (s) as the dependent variable, indicated the predicted significant difference between groups, F (3, 97) = 3.91, p = .011, η^2 = .11. Follow-up Helmert contrasts suggested that, as hypothesised, participants in the ABM-500 group had a higher pain threshold (M = 17.54, SD = 13.39) than participants in the ABM-1250 (M = 11.63, SD = 7.26), ABM-Placebo (M = 10.19, SD = 6.72), and No Training control (M = 10.06, SD = 5.71; p = .001) groups, whereas no further significant differences between groups were identified (ps > .50). Overall, these results provide additional support for the findings from Study Three (see Figure 4.14).[10]

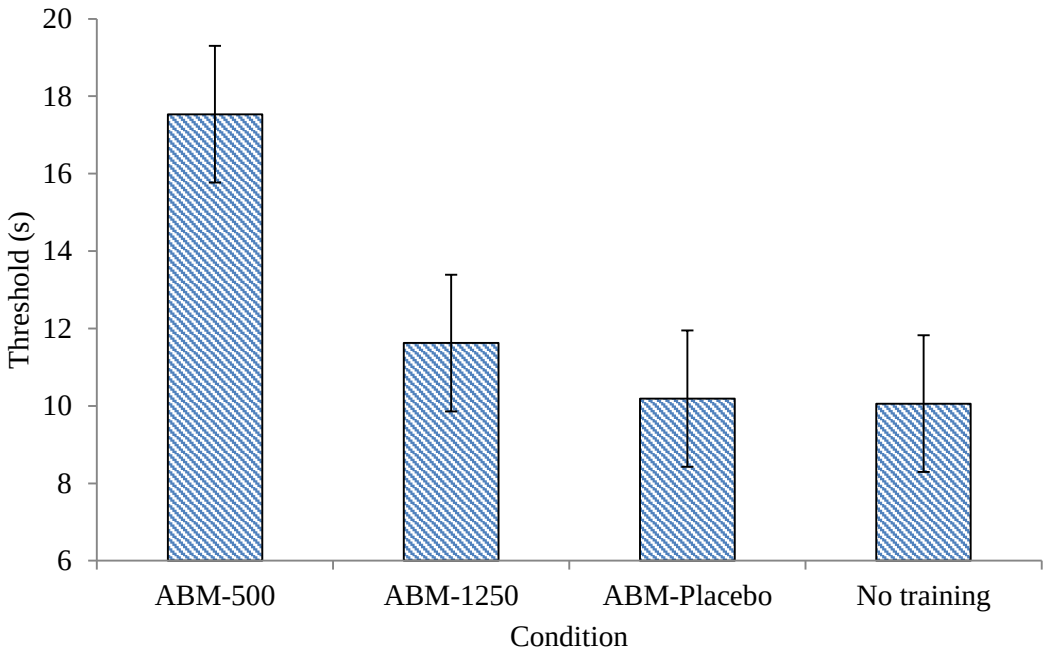


Figure 4.14 Mean threshold (s) by ABM condition (500 ms, 1250 ms, Placebo, No Training). Error bars represent ± 1 standard error.

4.5 General discussion

Overall, the findings from Studies Two and Three suggested that, first, acute pain impacts on initial orienting, redirecting early attention to neutral stimuli in the recovery phase (immediately after the acute pain induction) and second, that training initial orienting reduced vulnerability to acute pain. These symmetrical effects were not evident in maintained attention. Here, only correlational evidence suggested a relationship between

[10] These findings were comparable when a one-way ANCOVA was conducted on the raw threshold data after it had been log-transformed, F (3, 96) = 3.16, p = .028, η^2 = .09, with Helmert contrasts indicating that, as reported in the main text, the ABM-500 group had significantly higher threshold than the ABM-1250, ABM-Placebo and No Training groups (p = .003), whereas there were no significant differences between the non ABM-500 conditions (ps > .50).

increased maintained attention to neutral stimuli and lower MPQ-SF pain severity ratings after the CPT in Study Two; while in Study Three, the association was with increased pain tolerance. When the data from both studies were combined, findings provided general support for the analgesic effects of targeting attentional bias in initial orienting, and not maintained attention, on acute pain severity and threshold in comparison with a no training control group. Hence, across both experiments, the weight of evidence suggests that attentional bias in initial orienting can both be affected by and causally influence acute pain experience, whereas maintained attention does not have a key active role in modulating this type of pain.

The combined findings of Studies Two and Three provide clear support for cognitive-affective models of pain that suggest attentional processes play a critical role in pain experience (e.g. Eccleston & Crombez, 1999; Pincus & Morley, 2001). The experimental pain paradigm employed has demonstrated that early attentional processes modulate key aspects of acute pain perception including pain severity and threshold. Future research should explore how attention modulates persistent pain, and whether the time course of ABM for persistent pain is the same as, or differs from, these experimental pain findings. Whereas evidence was not found here that maintained attention impacts on acute pain experience, it is possible that maintained attention takes on a more prominent role in modulating persistent pain, where the experience of pain over a longer period of time might recruit more ruminative processes (e.g. Schoth et al., 2012). The next study (Four) will investigate whether targeting attentional bias in initial orienting or maintained attention (or both) is optimal for alleviating attentional bias, and pain outcomes, in persistent pain.

Chapter 5 Study 4

Attentional bias modification for persistent pain: A comparison of training initial orienting versus maintained attention on attentional bias, anxiety sensitivity, pain severity and disability

5.1 Introduction

Studies Two and Three suggested three points that warrant further consideration: first, that pain significantly impacts on attentional bias, such that participants selectively attend to neutral words after an acute pain experience, and that this effect is particularly evident at 500 ms following cue onset (Study Two); second, that training attention towards neutral words in initial orienting (500 ms) significantly alleviates acute pain outcomes in healthy participants (Study Three); third, that change in attentional bias at *both* 500 ms and 1250 ms SOAs towards neutral words is significantly associated with lower acute pain ratings (Studies Two and Three).

The next study will attempt to extend these foundational findings from the acute, experimental pain studies with a community-based sample of people with persistent pain, and further specify the optimal time course of attentional bias modification for pain.

As was replicated in Study One, individuals with persistent pain, such as low back pain, tend to exhibit an adverse attentional bias. Overall, findings have indicated they are more likely to preferentially attend to information in the environment that is related to pain (attentional bias; Pincus & Morley, 2001; Schoth et al., 2012). In addition, overall findings (including those from Study One) suggest that individuals with persistent pain exhibit a faster (500 ms) and slower (1250 ms) attentional bias to pain-related information, and that the magnitude of this bias is larger for the longer stimulus duration (e.g. Liossi et al., 2009). As was discussed in the first chapter, one of the main limitations of the extant research on attentional bias in persistent pain is that it is largely cross-sectional in nature. A number of studies have associated attentional bias with identified risk factors for developing chronicity, such as anxiety sensitivity (Keogh, Dillon, Georgiou, & Hunt, 2001a), and fear of pain (Keogh et al., 2001b), as well as with poor pain outcomes and maintaining chronicity, such as pain-related disability (Dehghani et al., 2003). However, these studies leave unclear whether attentional bias is epiphenomenal to the maladaptive emotional states, results from long-term exposure to pain, or is a vulnerability indicator that results in the onset and maintenance of persistent pain (Rusu & Pincus, 2012).

Cognitive-affective models of persistent pain suggest that attentional bias could increase vulnerability to pain, and that this distortion in cognitive processing might play a key role in the development and maintenance of chronicity (e.g. Eccleston & Crombez, 1999; Legrain, Iannetti, Plaghki, & Mouraux, 2011b; Pincus & Morley, 2001). An important consideration in the understanding of cognitive biases in pain is its evolutionary origin

(Eccleston & Crombez 1999). For example, it is thought that the main function of pain, and its associated emotional states, such as fear of pain (Vlaeyen & Linton, 2000, 2012), is to facilitate the detection of potential danger to the integrity of the physical organism, alert the organism of the potential danger through the interruption of ongoing activities, and initiate analgesic behaviour (Eccleston & Crombez, 1999; Eccleston, 2013; Legrain et al., 2011b). The attentional system is fundamental in providing the mechanism for detecting and monitoring environmental and interoceptive stimuli which are relevant to the ongoing state of the individual (Mogg & Bradley, 1998). Thus, these models suggest that distorted attentional processing of pain content can disrupt attentional and behavioural engagement with life goals, increase the access of pain content into focal attention, and thereby increase pain severity and related distress and disability (Eccleston & Crombez 1999; Pincus & Morley 2001).

Hence, one of the putative cognitive mechanisms implicated in vulnerability to persistent pain is the attentional prioritisation of aversive stimuli. Contemporary literature in the analogous emotion domain has demonstrated that attentional bias plays a causal role in the development and maintenance of anxiety (e.g. Mathews & Mackintosh, 2000; MacLeod et al., 2002). In light of the importance of attentional processes in chronic pain experience, and the theoretical overlap between anxiety and pain, it is reasonable to predict that attentional bias may also have a causal role in persistent pain, and thus constitute a valid therapeutic target (Goubert et al., 2004; Vlaeyen & Linton, 2000). Yet, to date, only three published studies have tested the impact of modifying attentional bias on persistent pain experience (Carleton et al., 2011; Schoth et al., 2013; Sharpe et al., 2012). As discussed in Chapters One and Two, attentional bias modification (ABM) is a recently developed technique that aims to implicitly erode pain-related attentional bias through repeated computer-based practice at disengaging from pain stimuli using a visual-probe task. Initial studies have suggested that this approach can be efficacious at reducing key pain outcomes. For example, Carleton et al. (2011) investigated the impact of ABM on self-reported musculoskeletal pain in individuals with fibromyalgia. They found that administering two short sessions (240 trials at 500 ms SOA per session) of linguistic ABM per week for four weeks resulted in significant reductions in anxiety sensitivity and fear of pain, and a trend-level reduction in pain severity in the ABM group, whereas no such changes were found in a sham training control group. Broadly consistent with this, Sharpe et al. (2012) found that four linguistic ABM sessions (320 training trials at 500 ms per session; course timeframe unclear) administered to a heterogeneous sample of individuals self-reporting persistent pain (minimum three months duration) resulted in a significant post-training reduction in self-reported disability, and reductions in disability, anxiety sensitivity, and fear of injury at six-month follow-up, relative to a sham training control group. However, whilst means

suggested that pain severity fell more in the ABM group than the control group, the omnibus comparison was not significant. Finally, Schoth et al. (2013) administered an innovative ABM program to eight individuals with heterogeneous chronic pain that combined linguistic (four sessions; 384 trials per session) and pictorial (four sessions; 192 trials per session) stimuli that were presented for a mixture of stimulus presentation durations (500 and 1250 ms, randomised) across a total of eight sessions, spread over six weeks. Measures of attentional bias, pain severity, pain interference, anxiety and depression were taken at pre and post-training, with pain intensity identified as the primary outcome measure. Results indicated that statistically and clinically significant reductions in pain intensity, interference, anxiety and depression occurred within the ABM group, although there was no significant change in attentional bias (Schoth et al., 2013). These findings supported those of Carleton et al. (2011) and Sharpe et al. (2012) in providing preliminary indication that ABM can reduce pain severity and improve emotional functioning across a range of conditions characterised by chronic pain, although the mechanism of action was not specified.

Whilst such an intervention has clear therapeutic potential for the persistent pain population, research into the underlying mechanisms of action remains in its infancy. Building on the converging findings that attentional bias is particularly situated in maintained attention in persistent pain (Study One), and that modifying attentional bias can directly affect the pain experience (Study Three), a next logical step is to investigate whether training attention at an earlier (e.g. 500 ms) versus a later (e.g. 1250 ms) stage of attention is optimal for reducing pain-related attentional bias and symptoms in a chronic pain sample. It is interesting to note that both of the two studies to date that have measured training-induced modifications in attentional bias in persistent pain have failed to find any significant changes (Schoth et al., 2013; Sharpe et al., 2012), in spite of reported changes in symptoms. In the study by Schoth and colleagues, the pain bias was again situated at 1250 ms (baseline bias = -20.04 ms) and not 500 ms (8.29 ms), suggesting that the failure to find an overall effect of training on attentional bias could have been due to differential activity at each training and test SOA. The study by Sharpe et al. (2012), on the other hand, only trained and measured attention at 500 ms, which may not have been optimal for capturing attentional effects in this population. To date, there are no published studies that have systematically addressed this issue, and assessed the relative efficacy of training attention at an earlier versus later stage of attention for persistent pain. Because of known perceptual asymmetries (Asmundson & Stein, 1994; Thomas & Elias, 2011; Vuilleumier, 2005), it will also be prudent to analyse the attentional data as a function of vertical hemispace, which has not been considered in previous persistent pain ABM research. Hence, the present study aims to establish whether ABM works to alleviate long-term pain through a change in attentional bias, and to specify which stage(s) of attentional processing is modified by the training procedure.

To summarise, based on the previous findings that attentional bias is particularly situated in maintained attention in chronic pain, which has been operationalised at 1250 ms (Liossi et al., 2009, 2011; Schoth et al., 2012; Study One), it was hypothesised that directly targeting this stage of attention, by presenting the stimuli for 1250 ms within the training program, might result in a training-congruent reduction in attentional bias at 1250 ms, in comparison with the placebo training control groups. Since no previous studies have systematically tested the optimal timings of ABM for pain, it was difficult to make firm predictions whether this training would be superior to the usual training at 500 ms, as it is possible that training at the earlier stage of attention could transfer to attentional bias at 1250 ms. It was, however, predicted that the induction of a neutral attentional bias at 1250 ms would lead to reductions in self-reported pain severity (primary pain outcome) and anxiety sensitivity and distress (secondary pain outcomes) in the ABM-1250 group (and possibly the ABM-500 group as well, if the training transfers to the other SOA), in comparison with two sham training control groups.

5.2 Method

Power analysis

An *a priori* power calculation was conducted using G*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009). On the basis of prior ABM effect sizes, and applying a recent ABM interaction effect size for anxiety sensitivity in long-term pain (d = .56; Sharpe et al., 2012), a minimum sample size of 12 participants per group will be necessary to achieve 80% power at $\alpha = .05$ for mixed model ANOVA analyses; the critical F value will be $F = 2.3$.

5.2.1 Participants

A total of 68 participants were recruited via posters and advertisements from the University of East Anglia and the wider Norwich community. Inclusion criteria were: self-reported chronic benign musculoskeletal pain that had lasted for three months or more (this population was selected as past research has associated attentional bias towards pain words with persistent musculoskeletal pain, e.g. Dehghani et al., 2003); fluent English speakers (due to the verbal nature of the tasks); aged 18-70 years; normal or corrected-to-normal vision; able to read and understand text displayed on a computer screen, and able to use a computer keyboard comfortably for 30 minutes. Exclusion criteria were: pain related to a progressive disease such as cancer; undergoing psychological treatment for pain, such as cognitive behavioural therapy, currently or within the past three months, and change in pain medication within the past three months. Recruitment took place from May 2012 to May 2013.

Individuals who expressed interest were screened according to these criteria via email and only those who were deemed eligible were invited to take part. Of these, 11 (16.1%) subsequently dropped out (see Figure 5.1). Fifty-seven participants, 15 males and 42 females (mean age = 42.46, *SD* = 16.33, range 18-70; mean approximate pain duration = 123.19 months, *SD* = 110.63) completed the study and were each given £5 as a thank you for taking part. Overall, the sample had a mean pain severity score at baseline of 45.9 (*SD* = 20.53; MPQ-SF VAS) out of a possible 100, which is indicative of moderate pain (Breivik et al., 2008; Hawker et al., 2011), and pain disability score of 26.56 (*SD* = 16.26; PDI) out of a possible 70, which suggests moderate disability (Chibnall & Tait, 1994). The majority of participants (*n* = 47; 82.5%) reported persistent musculoskeletal pain in more than one site (10 participants; 17.5% had pain in a single site), and seven (12.3%) experienced widespread pain in six or more sites. The distribution of musculoskeletal pain by primary pain site was as follows (Dehghani et al., 2003; Merskey & Bogduk, 1994). Thirty-nine participants (68.4%) had low back pain; five (8.8%) had thoracic back pain; five (8.8%) had cervical pain; one (1.8%) had thoracic (chest wall) pain; one (1.8%) had upper limb pain; four (7%) had lower limb pain; one (1.8%) had hip pain; and one (1.8%) had shoulder pain.

Participants were randomly allocated (via the online research randomiser website, www.randomizer.org) to one of four conditions: attentional bias modification at 500 ms (ABM-500; *n* = 15); attentional bias modification at 1250 ms (ABM-1250; *n* = 14); placebo bias modification at 500 ms (PBM-500; *n* = 14), and placebo bias modification at 1250 ms (PBM-1250; *n* = 14).

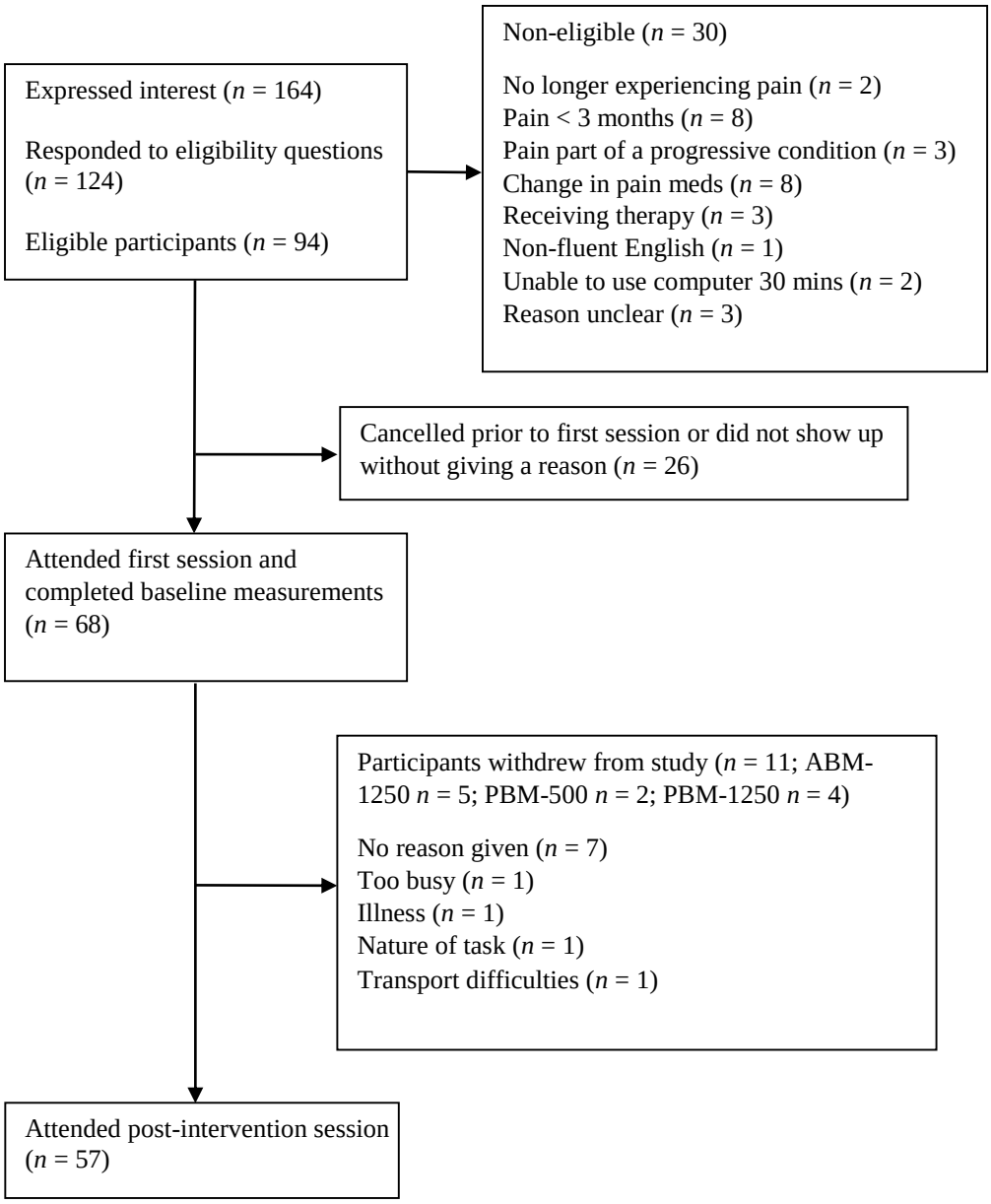


Figure 5.1 Flow of participants through study.

5.2.2 Materials

Experimental stimuli

The critical stimulus words were 84 pain-related words and 84 household-related neutral words, which, as in Studies Two to Four, were matched for length and frequency using the Brysbaert database (Brysbaert & New, 2009; see Table 5.1). The pain-related words were selected to be related to the sensory (e.g. “aching”) and affective (e.g. “tiring”) aspects of pain, and were taken from previous studies investigating attentional bias and its modification in pain (Asmundson et al., 2005a; Carleton et al., 2011; Keogh et al., 2001b; Liossi et al., 2009, 2011; Sharpe et al., 2012). The resulting 84 word-pairs were then divided

into two test sets (each comprising 12 word pairs) and one master training set (60 word pairs). Order of test administration (pre - post) was counterbalanced across conditions.

Theoretical models suggest that ABM should aim to directly target the pain schema of the individual experiencing persistent pain, from which it is thought the attentional bias derives (Pincus & Morley, 2001). This suggests that the personal relevance of the words used to modify the attentional bias is key, and this inference is supported by some empirical research (Dear, Sharpe, Nicholas, & Refshauge, 2011). Thus, with a view to ensuring the relevance of the training stimuli to each individual participant's pain experience, an idiographic lexical selection procedure was applied (Amir, Beard, Burns, & Bomyea, 2009). Before training, participants were asked to rate the master training set of words "according to how related" they thought they were to their pain, on a scale of -3 to +3, where -3 was "not at all related", and +3 was "very much related" to their pain (Amir et al., 2009). The 24 words that were rated most negatively (and thus pain relevant) by that participant from the training set were then used as the pain words in the ABM or PBM program, depending on the participant's condition allocation.

Table 5.1

Matched Pain and Neutral Words Used for Attentional Bias Test and Modification

Training set				Test set	
Pain word	Neutral word	Pain word	Neutral word	Pain word	Neutral word
aching	aerial	radiating	shrubbery	tugging	textile
burning	jacket	painful	laundry	tearing	backyard
hurting	garage	sting	baked	tightness	plasterer
pain	seat	tender	carpet	stings	spoons
piercing	dwelling	pinching	shelters	grinding	cassette
pounding	pancakes	agony	timer	aggravating	videotaping
pulsating	balconies	spasm	stair	gruelling	fabrics
sharp	walls	squeezing	cushion	indescribable	installations
splitting	recorder	grinds	mopped	unbearable	bathrooms
throbbing	ornament	ache	cork	tortured	household
searing	trouser	beating	cooking	debilitating	supermarkets
choking	mansion	freezing	electric	punishing	decorated
cramps	yogurt	heavy	address	stiff	roses
gnawing	tidying	biting	freezer	exploding	toothpaste
penetrating	mantelpiece	smarting	saucepans	bruised	earring
victim	market	depressing	bedtime	cut	car
invasion	curtains	uncontrollable	extinguisher	intense	grounds
defenceless	pillowcase	worry	money	sore	brush
interfere	magazines	tiring	sprouts	wretched	biscuits
suffer	guests	suffocating	binoculars	agitation	artichoke
killing	window	harmful	pyjamas	nagging	shelves
troublesome	telephones	helpless	clothing	exhausting	housewives
terrible	radio	irritated	housework	difficult	upstairs

Table 5.1

Matched Pain and Neutral Words Used for Attentional Bias Test and Modification

Training set				Test set	
Pain word	Neutral word	Pain word	Neutral word	Pain word	Neutral word
vicious	ceiling	failing	wardrobe	agonising	bedclothes
griping	timbers	apprehension	videotapes		
harm	roof	angry	glass		
nausea	coaster	dreadful	cabinet		
fearful	stables	guilty	bottle		
hopeless	roommate	devastating	decorating		
frustration	sunglasses	distressing	disinfectant		

Attentional bias test

As in the previous studies, the attentional bias test used a modified form of the probe classification version of the dot-probe paradigm adapted from MacLeod and colleagues (MacLeod et al., 2002), and was administered using E-Prime software (Schneider et al., 2002). The dot-probe task comprised 192 trials (12 word pairs randomly presented 16 times), with new words presented at pre and post-training. The sequence of events was identical to the test administered in Studies One to Three, and is repeated here for convenience. Each trial began with a fixation point presented in the middle of the computer screen (48.26cm/19 inch) for 500 milliseconds. This was followed immediately by the matched word pairs, each with one neutral meaning (e.g. "spoons") and one pain-related meaning (e.g. "stings"). Words (black text on a white background) were separated by a vertical distance of 3 cm, with one word above and one below the prior position of the fixation point. Participants were seated approximately 60 cm from the monitor, affording a visual angle of 1.43º between the central fixation cross and each stimulus word (cf. See et al., 2009). The test featured two word pair SOAs (500 and 1250 ms) in randomised order. After either 500 or 1250 ms, an arrow probe ("<" or ">" with equal frequency) appeared in the prior location of one of the words. The central fixation cross, stimulus words, and arrow probes were all presented in Arial size 11 font. There was a 50:50 distribution of probe presentation in the position of the pain-related or neutral word position, and they were presented with equal frequency above and below the central fixation point. Participants were required to press the left or right arrow key as quickly and accurately as possible, to indicate which direction the arrow was pointing. Faster reaction times (RTs) to probes in non-pain word positions (as opposed to probes in pain word positions) indicated a non-pain attentional bias (i.e. an ability to focus attention away from pain). Each test lasted around ten minutes.

Attentional bias modification

Past research has reported that four sessions of ABM for persistent pain is sufficient to impact on pain outcomes (Sharpe et al., 2012). Four sessions of ABM, each comprising

384 trials, were therefore administered over a period of two weeks (at two sessions per week) using E-Prime software (Schneider et al., 2002). The critical difference between the attentional bias test and sham training programs, and the active training programs, was that in the active ABM conditions the probe always replaced the neutral word in each word pair. This was intended to train attention away from the pain-related stimuli. The 24 word pairs were randomly presented 16 times in each of the four possible combinations (left arrow top/neutral word top; right arrow top/neutral word top; left arrow bottom/neutral word bottom; right arrow bottom/neutral word bottom). In the sham training conditions, the 24 word pairs were randomly presented eight times in each of eight possible combinations (the above, and: left arrow top/neutral word bottom; right arrow top/neutral word bottom; left arrow bottom/neutral word top; right arrow bottom/neutral word top).

In view of the persistent pain population, participants were informed that they could take a break at any point during the program if they so wished, in addition to an inbuilt break after ten minutes. They were then instructed to fixate their gaze on the centre of the screen throughout and indicate as quickly and as accurately as possible whether a left or right facing arrow appeared on screen using the corresponding arrow keys on the keyboard. The arrow probe remained onscreen until response, disappearing as soon as a response option was keyed. The identity of the arrow probe was randomised for each trial. As in the acute, experimental pain study (Chapter Four), participants were not given any indication that the ABM program may affect their pain experience. In the ABM-500 program, each word pair remained on screen for 500 ms before the probe appeared, and in the ABM-1250 program, 1250 ms elapsed before the probe appeared.

The two ABM-Placebo programs were matched to the two active ABM programs such that, in the PBM-500 program, there was 500 ms, and in the PBM-1250 program, there was 1250 ms, before the probe replaced the word pairs, respectively. In structure, the PBM programs were identical to the attentional bias test (the pain/non-pain words were probed equally). The same idiographic stimulus selection procedure was applied, using the same master training word set, as in the two active ABM-conditions. All training programs (ABM/PBM) lasted approximately 20 minutes.

Self-report questionnaires

Six standard questionnaires were administered at pre and post-training. These were: the Anxiety Sensitivity Index (ASI-3; Taylor et al., 2007); the Fear of Pain Questionnaire – Short-Form (FPQ-SF; Asmundson et al., 2008); the Hospital and Anxiety Depression Scale (HADS; Zigmond & Snaith, 1983); the McGill Pain Questionnaire – Short-Form (MPQ-SF; Melzack, 1987); the Pain Disability Index (Pollard, 1984), and the Pain Medication Questionnaire (PMQ; developed for the present study).

The ASI-3, FPQ-SF, HADS, and MPQ-SF were described in detail in Chapter Three (Study Two), and will therefore not be repeated here. In the current study, the PDI (Pollard, 1984) assessed the impact of ABM on disability associated with persistent pain experience. This particular pain disability measure was selected as it was designed for use with multiple types of pain conditions, including those characterised by persistent musculoskeletal pain (Tait & Chibnall, 2005). It is a brief seven-item measure that assesses the extent persistent pain interferes with seven different domains of an individual's life (e.g. family, social activities, occupation, sleep; Tait, Pollard, Margolis, Duckro, & Krause, 1987). On each of the domains participants are asked to rate level of interference on an 11-point scale from 0 ("no disability") to 10 ("worst disability"). Good internal consistency ($\alpha = .86$; Rusu & Pincus, 2012), and test-retest reliability (Chibnall & Tait, 1994; Soer et al., 2013), have been reported.

Past research has suggested that anxiolytics and antidepressants can reverse cognitive biases in distressed patients (e.g. Browning et al., 2011). It is reasonable to suppose that analgesics could similarly impact on patterns of distorted cognitive processing in persistent pain. The PMQ was therefore developed for the present study to control for pain medication intake. The first part of the measure comprises two items concerning the number of doses of prescription medication and over-the-counter medication participants have taken during the past week, respectively. The second part asks the names of prescription and over-the-counter medications consumed. The score is a sum of the first two items. As it was developed for present purposes, there are no reliability and validity data available for this measure.

5.2.3 Procedure

Ethical approval for the study was obtained from the University of East Anglia School of Psychology Research Ethics Committee. After providing informed written consent, participants were asked to rate the master training set of 60 pain descriptors for relevance to their pain. Next, participants completed paper versions of the questionnaire measures (baseline). Questionnaires were always given in the same order (ASI-3; FPQ-SF; HADS; MPQ-SF; PDI; PMQ). Whilst questionnaires were being completed, the researcher entered the top third most highly rated pain descriptors into E-Prime, tailoring each training program to the individual participant's pain experience (Amir et al., 2009; Crombez et al., 2013a; Dear et al., 2011).

Next, participants completed the attentional bias test (baseline), immediately followed by the first ABM (at 500 or 1250 ms) or PBM (at 500 or 1250 ms) program, depending on condition. In total, the first session lasted approximately two hours.

Of the 57 participants who completed the study, the majority ($n = 51$; 89.5%) completed it within the prescribed 14 ± 2 days. One participant (PBM-500 group) completed

it in eleven days; three participants (ABM-500; PBM-500 and PBM-1250 groups) completed it in 17 to 18 days, and two participants (ABM-500 and ABM-1250 groups) completed it in 22 days. The latter, prolonged duration, was due to a one week gap between sessions three and four in both cases. At the post-intervention session, the attentional bias test was administered first, followed by the six pen and paper questionnaires, after which participants were debriefed. Participants in the control conditions were given the opportunity to complete the active ABM-500 program if they so wished. The post-intervention session lasted approximately 1.5 hours. All participants, with the exception of one (due to the laboratory being updated), were tested in the same computer laboratory on campus, in groups of one to four.

5.3 Results

5.3.1 Group characteristics

A series of independent-samples *t*-tests (and Mann-Whitney U or chi-square tests) indicated there were no significant differences between those who completed the study and those who dropped out in baseline demographics, pain presentation, and condition allocation (all *ps* >.10; see Table F1.1, Appendix F). For the complete-case sample, as shown in in Table 5.2, the groups were well matched at baseline on demographics and measures of pain, anxiety, depression, disability, medication consumption, and attentional bias (all *p*s > .10). Two non-parametric one-sample Wilcoxon signed-ranked tests, comparing baseline attentional bias at test SOA 500 ms (*mdn* = -2.50; range = 169.8), and 1250 ms (*mdn* = -5.75; range = 138.5), with the hypothesised median of zero, indicated that, in line with previous findings, attention was biased towards pain words presented for the longer, Z (57) = -2.03, *p* = .042 (two-tailed), *r* = -.27 , and not the shorter, *Z* (57) = -.862, *p* = .389, *r* = -.11, stimulus duration.

Table 5.2

Descriptive Data: Means of Age, Anxiety Sensitivity, Fear of Pain, Anxiety, Depression, MPQ-SF Total, Pain Disability, Pain Medication Consumption and Attentional Bias with Standard Deviations, and Gender Ratio, by Condition

	ABM-500 *n* = 15		ABM-1250 *n* = 14		PBM-500 *n* = 14		PBM-1250 *n* = 14		
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*F*-value
Age	40.33	15.31	38.31	18.62	43.21	14.95	47.86	16.68	0.88
Female:Male[a]	10:5		13:1		10:4		9:5		3.71
ASI-3	23.07	10.83	21.21	14.19	26.21	10.41	19.43	13.36	0.78
FPQ-SF	46.80	14.90	47.71	13.85	51.29	13.86	51.57	13.13	0.44
Anxiety	9.80	3.14	9.21	4.92	11.57	3.63	8.21	3.21	1.94
Depression	5.00	3.55	3.93	2.62	6.64	4.43	5.57	4.48	1.22
MPQ-SF	18.53	6.50	15.92	6.63	16.93	8.65	14.08	3.75	1.09
PDI	31.60	14.87	21.43	15.24	27.21	19.22	25.64	15.49	0.97
PMQ	10.07	12.19	8.57	13.17	15.43	26.85	10.93	12.87	0.41
AB-500[b]	-0.53	34.53	0.64	38.56	-10.64	14.69	-5.48	27.89	0.41
AB-1250[b]	1.03	24.80	-4.84	26.15	-9.46	14.31	3.46	29.32	0.81

Note: All between-groups comparisons at baseline were non-significant ($p > .10$). [a] As gender is a dichotomous variable, a chi-square was conducted.[b] Kruskal-Wallis tests confirmed there were no significant differences at baseline in the attentional data, all *p*s > .10.

5.3.2 Statistical analysis and data reduction

A complete-case analysis in which only participants with all data points complete were included was used to analyse the data following a missing values analysis, which suggested these data were missing at random (Little & Rubin, 1987).[11] In addition, for the attentional bias data, adherence to protocol is necessary for putative ABM mechanisms to take effect (e.g. Bowler et al., 2012; Kuyken et al., 2010).

As in previous Studies, to minimise the influence of extreme reaction times on individual trials within the attentional bias tests (pre - post), median reaction times to each of the four critical trial types (probe up, pain word up; probe up, pain word down; probe down, pain word up; probe down, pain word down) at each stimulus presentation time (500 ms, 96 trials; 1250 ms, 96 trials; as well as overall, 500 and 1250 ms, 192 trials), for each participant, were extracted from E-Prime (MacLeod et al., 2002; Whelan, 2008). In addition, due to the instruction that participants could take a break at any point during the program, trials ≥ 3000 ms were not considered accurate measures of attentional bias, and hence, along with error trials, were discarded (2.78% data; MacLeod et al., 2002; Whelan, 2008). Next, in view of the hypotheses, and to facilitate interpretation, three attentional bias indexes (overall, and for each SOA individually) were calculated by subtracting the mean (of the extracted medians) reaction times to neutral words from the mean (of medians) reaction times to pain-related words, such that a more negative value represented a more pain-related bias (MacLeod et al., 2002).

The attentional bias data (extracted medians for each trial type and attentional bias indexes) and questionnaire scores were assessed for normality within each condition. Skewness and kurtosis coefficients were calculated by dividing each statistic by its corresponding standard error, which indicated positively skewed distributions at baseline for each trial type, a common characteristic of reaction time data (Baayen & Milin, 2010; Ratcliff, 1993). Inspection of box and whisker plots across the different levels of the dependent variable suggested four extreme outliers (one in the ABM-500; two in the ABM-1250, and one in the PBM-1250 group). Possible objective reasons were identified for the occurrence of two of these extreme values (one had been tested in a different room to the rest of the sample for technical reasons; and one had reported a concurrent emotional disturbance unrelated to pain at the last session), whilst causes for the remaining values were unclear. On balance, it was decided not to amend or exclude any outliers due to the within-subject nature of the attentional bias data (Osborne & Overbay, 2004; Ratcliff, 1993; Tabachnick & Fidell, 2001). In the absence of a non-parametric equivalent for the main omnibus analysis, and in view of its reputed robustness, a mixed model analysis of variance

[11] A chi-square for these data was non-significant, indicating there was no discernible pattern to the missing data (i.e. they were missing at random), χ^2 (114, N = 68) = 124.28, p = .24.

(ANOVA) was conducted on the untransformed data (Glass et al., 1972; Lix et al., 1996). Hence, the main analysis was performed using a mixed model ANOVA with the between-subjects factors of ABM type (active neutral versus placebo sham) and ABM stimulus SOA (500 versus 1250 ms). In the first instance time (pre, post), target position (behind pain word, behind neutral word), word position (top, bottom) and test SOA (500, 1250 ms) were included as the within-subjects factors. Where assumptions of homogeneity of variance were not met, the Huynh-Feldt correction to degrees of freedom was used, although unadjusted degrees of freedom were reported for clarity (e.g. Browning, Holmes, Charles, Cowen, & Harmer, 2012). Where relevant, significant interactions were followed up with analyses conducted using the attentional bias indexes (Macleod et al., 1986). In addition, given their positively skewed distribution, trial type data were log-transformed, attentional biases recalculated based on the transformed data, and the ANOVAs re-run to see if results were comparable (Ratcliff, 1993; Whelan, 2008).

To assess whether there was an association between change in attentional bias over the training period and change in the key pain outcome measures, attentional bias improvement scores were calculated by subtracting the relevant attentional bias index at pre-training from the equivalent index at post-training, such that a more positive value represented a greater shift towards a more neutral attentional bias (MacLeod et al., 1986; Sharpe et al., 2012). Questionnaire change scores were also calculated by subtracting the value at pre-training from the post-training value, such that a more negative score represented a greater reduction in pain symptoms. Where outcomes were not normally distributed (the attentional bias-500 change scores were positively skewed in the ABM conditions and negatively skewed in PBM conditions, whilst the reverse was true for attentional bias at 1250 ms), Spearman rho correlations are reported.

The primary outcome measure for the present study was attentional bias (i.e. the relative dot-probe reaction times to pain-related and neutral words); the secondary outcome measures were the MPQ-SF total (drawing on previous findings that ABM can impact on pain severity, e.g. Schoth et al., 2013); and the PDI and ASI-3 totals (Sharpe et al., 2012).

5.3.3 Main outcome analyses: impact of ABM at 500 versus 1250 ms on attentional bias

Groups did not differ significantly in the percentage of trials that were discarded due to participant error (pre-training *M*s 0.41 to 2.9, *SD*s 0.8 to 7.03; post-training *M*s = 0.26 to 1.79, *SD*s 0.62 to 3.54) at pre, F (3, 56) = 1.43, p = .245, or post intervention, F (3, 56) = 1.93, p = .136. To test the hypothesis that type of attentional training would differentially impact on response times to the target replacing pain words in relation to neutral words at each test SOA, a two (time: pre, post) by two (test SOA: 500, 1250) by two (target position: behind pain word, behind neutral word) by two (word position: top, bottom) by two (training

SOA: 500, 1250) by two (ABM type: active, placebo) mixed model ANOVA was performed on the untransformed attentional bias data, with between-subjects on the last two factors.

Results indicated a main effect of time, F (1, 53) = 23.19, $p < .001$, $\eta^2 = .304$, suggesting that, as would be expected with increased task familiarity over the course of the study, reaction times were faster at the final session (M = 539.26 ms) than at the first session (M = 606.46 ms). There was also a main effect of test SOA, F (1, 53) = 5.89, $p = .019$, $\eta^2 = .1$, such that participants responded more quickly when words were presented for 1250 ms (M = 566.19 ms) than 500 ms (M = 579.53 ms), indicating a general response facilitation at the longer stimulus duration.

The overall, critical, time by test SOA by target position by ABM type by ABM SOA interaction, and time by test SOA by target position by word position by ABM type by ABM SOA interaction, were each non-significant, Fs < 1, suggesting that, contrary to the hypothesis that training attention at 1250 ms might particularly benefit the time-congruent attentional bias, one stimulus exposure was not generally superior to the other in modifying attentional bias (at either test SOA), in comparison with the placebo training groups.

The only significant interaction with time, and hence relevant to hypotheses, was a five-way time by test SOA by target position by word position by ABM type interaction, F (1, 53) = 4.61, $p = .036$, $\eta^2 = .8$, suggesting that active ABM, in comparison with PBM, had a differential impact on response times to targets replacing pain words versus neutral words, when they were presented in the upper versus lower region of the visual display.[12]

To decompose this interaction, separate attentional bias indexes were calculated for pain words presented in the upper and lower regions of the visual field (U/LVF), and two separate time by test SOA by ABM type mixed model ANOVAs were conducted on these data. In the UVF, the time by group interaction was non-significant, F (1, 55) = .6, $p = .44$, $\eta^2 = .01$, suggesting that ABM did not lead to an overall improvement in attentional bias in this region in comparison with PBM. Crucially, however, the anticipated time by test SOA by ABM type interaction was significant, F (1, 55) = 4.44, $p = .04$, $\eta^2 = .075$, suggesting that, in this part of the visual display, ABM had differentially reduced the impact of the distractors (pain words) on task performance, based on the duration (500 versus 1250 ms) for which the pain words were presented. By comparison, for pain words presented in the LVF, neither the time by group interaction, F (1, 55) = .61, $p = .44$, $\eta^2 = .01$, nor the time by test SOA by ABM type interaction, F (1, 55) = 3, $p = .089$, $\eta^2 = .052$, reached significance,

[12] Results of the omnibus mixed model ANOVA performed on the log-transformed data were similar to the original findings, reported in the main text, such that the only significant interaction with time was the five-way time by test SOA by target position by word position by training type effect, F (1, 53) = 5.67, $p = .021$, $\eta^2 = .097$, suggesting that active ABM in comparison with PBM had a differential impact on response times to targets replacing pain words versus neutral words, presented in the upper versus lower region of the visual display.

indicating that, in comparison with the placebo training, ABM had not reduced attentional capture by pain words presented in the lower region of the visual display (see Figure 5.2).[13]

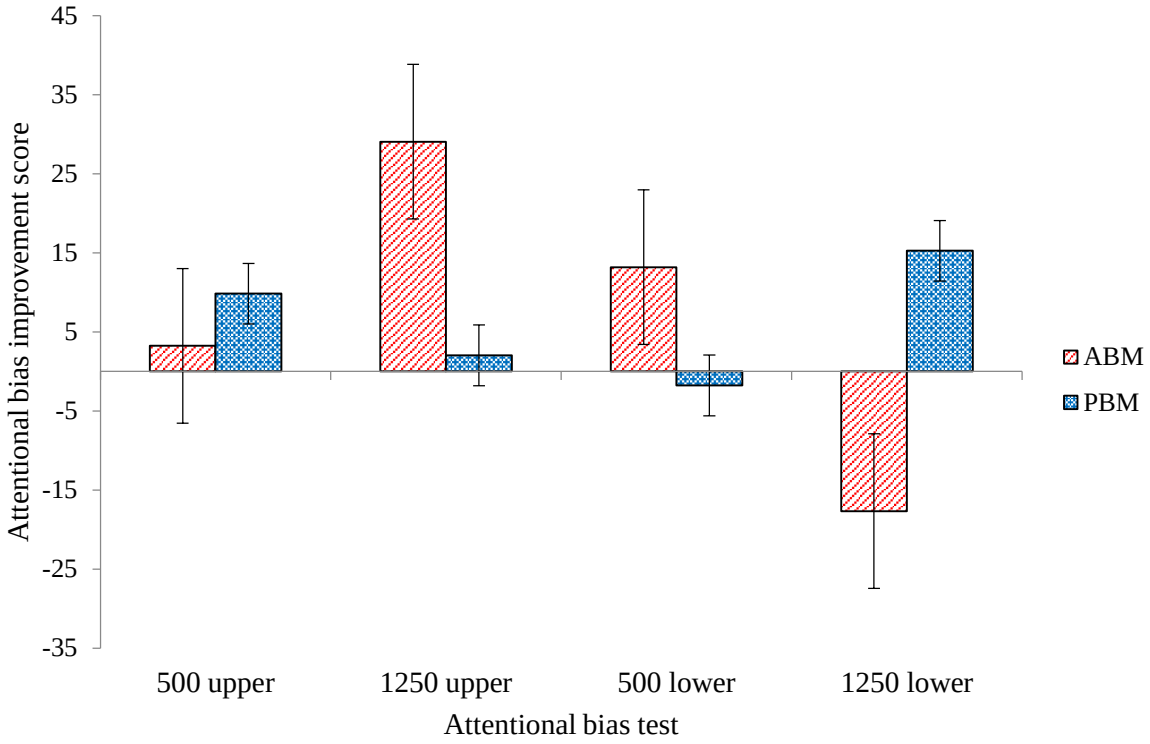


Figure 5.2 Graph illustrating attentional bias improvement scores (attentional bias index at post-training minus attentional bias index at pre-training; a more positive score represents a greater shift towards neutral words) as a function of test SOA and word position, by condition (ABM versus PBM). Error bars represent ± 1 standard error.

To follow-up the significant three-way interaction, Wilcoxon tests were conducted on the UVF bias scores at each test SOA, within the ABM and PBM conditions. Results indicated that, in line with original predictions, the only change in attentional bias from pre (*mdn* = -12.0, range = 431.5) to post (*mdn* = 7.0, range = 102) training, occurred at test SOA 1250 ms in the active ABM group, Z = -2.38, p = .017 (two-tailed), r = .45, suggesting a neutral bias in maintained attention was induced following ABM. Change in attentional bias at test SOA 500 ms from pre (*mdn* = 3.0, range = 174.5) to post (*mdn* = 3.0, range = 136.5)

[13] The follow-up analyses performed on the log-transformed data were also broadly comparable with the original findings, with a trend-level effect in the upper visual display, F (1, 55) = = 3.49, p = .07, n^2 = .06, such that, within the active ABM group, attentional bias at 1250 ms, t (28) = -2.28, p = .031 (two-tailed), r = .40, and not 500 ms, t < 1, p > .80, became more neutral from pre to post-training. Within the log-transformed data, there was also a trend level effect for the lower visual display (LVF), F (1, 55) = 3.51, p = .07, n^2 = .06, which appeared to be driven by an improvement in attentional bias at 1250 ms in the placebo group; however, paired samples t-tests assessing these changes did not reach significance at 1250, t (27) = -1.9, p = .07 (two-tailed), r = .34, or 500, t < 1, p > .70, ms. Within the ABM group, LVF changes in bias were also non-significant at both 1250, t < 1, p > .40, and 500, t (28) = -1.22, p = .23, r = .23, ms).

training in the ABM group was non-significant, Z = -.054, p = .96 (two-tailed), r = .01, and attentional bias was not modified at either SOA in the placebo training groups, ps > .45. These findings were similar when analyses were performed on the log-transformed data.[12] Overall, the results so far support the hypothesis that ABM for persistent pain improves maintained attentional bias at 1250 ms, but these effects are only detected for upper visual field probes, perhaps due to better coding of pain words in the UVF (Vuilleumier, 2005).

5.3.4 Impact of ABM on pain outcomes and correlations

ASI-3, MPQ-SF, PDI

Contrary to hypotheses there was no impact of ABM at either training SOA on pain severity, anxiety sensitivity, or disability. Whilst there was a main effect of time for anxiety sensitivity only, F (1, 53) = 6.24, p = .016, η^2 = .11, such that participants returned lower scores over the course of the training programme, none of the crucial time by group interactions were significant for anxiety sensitivity, F (1, 53) = 3.04, p = .09, η^2 = .05, pain severity, F < 1, or disability, F < 1. Similarly, no time by group by SOA effects were evident, all Fs < 1, suggesting that ABM effects did not transfer to pain symptoms as assessed at post-training.

Correlations

In view of the original hypotheses, a series of correlations was performed within each condition to assess whether or not there was a relationship between pre - post change in attentional bias at each stimulus presentation time and change in the pain outcomes (MPQ-SF; ASI-3; PDI). Previous literature concerning pharmaceutical analgesic effects has suggested that they may only become evident in moderate and severe pain (Bjune, Stubhaug, Dodgson, & Breivik, 2008; Breivik, Barkvoll, & Skovlund, 1999; Breivik et al., 2008). Therefore, it was decided to run these correlations on participants who reported experiencing moderate pain and above at baseline, which was defined as a score of 45 and above on the MPQ-SF visual analogue scale (n = 31; Hawker et al., 2011).

In the ABM-1250 group, contrary to expectations, there was no association between change in attentional bias and disability, rs (8) = .33, p = .42 (two-tailed). However, in line with predictions, there was a significant strong negative association between change in attentional bias at 1250 ms and change in pain severity, rs (8) = -.802, p = .017 (two-tailed), suggesting those whose pattern of attentional processing shifted the most from pain words to neutral words presented for 1250 ms over the course of ABM experienced the greatest reductions in pain severity. There was also a significant strong negative association between change in attentional bias at 1250 ms and anxiety sensitivity, rs (8) = -.81, p = .015 (two-tailed), indicating that the greater the shift towards a more neutral attentional bias at this SOA during ABM, the greater the reduction in anxiety sensitivity.

In the ABM-500 group, there were no significant associations between change in attentional bias (500, 1250) and change in pain outcomes (all *p*s > .20). Within the placebo ABM-500 group, there was a surprising, strong positive association between an increasing neutral bias at 500 ms and increased pain severity, *rs* (5) = .90, *p* = .037 (two-tailed), suggesting that a greater, sham training-induced, shift towards neutral words presented for 500 ms was associated with a greater increase in pain. None of the other associations were significant (*p*s > .35). Finally, in the PBM-1250 group, as expected, there were no significant associations between change in attentional bias at each SOA and pain severity, *r*s (7) = -.16, *p* = .73 (two-tailed), anxiety sensitivity, *r*s (7) = -.66, *p* = .11 (two-tailed), or pain disability, *r*s (7) = -.05, *p* = .91.

5.4 Discussion

The first aim of the present study was to assess the relative efficacy of training attention at 1250 versus 500 ms for alleviating the corresponding stages of attentional bias in persistent pain, in comparison with controls. A second, corollary, aim was to assess whether one type of ABM was superior to the other in improving pain outcomes, as compared to the control groups. Concerning attentional function, the results suggested that both ABM-500 and ABM-1250 improved attentional bias at 1250 ms (which, in line with Study One, is where attentional bias was situated at baseline) relative to the PBM groups. However, interestingly, this training effect was only evident when pain words were presented in the upper part of the visual display, suggesting that here the task distractors ceased to divert maintained attention, whereas their presence continued to divert maintained attention when presented in the lower region of the visual display (Feng & Spence, 2014; Rauss, Schwartz, & Pourtois, 2011).

Interpretation of condition related attentional shifts at each test SOA, from pre to post ABM, requires a four-way interaction between time (pre - post), target position (behind pain, behind neutral), test SOA (500, 1250), and training type (ABM, Placebo). In the present study, a five-way interaction, with the additional factor of word position (upper, lower) actively modulating the interaction, was observed, suggesting that the potency of pain-related task distractor differed from pre to post-training as a function of vertical hemispace. Based on theoretical models, the next inference would be that an attentional shift has occurred in the ABM group towards neutral words; and that such a shift has not occurred in the PBM group. This would be indicated by, at minimum, a significant time by target position interaction, within the ABM group. It would then be expected that the corresponding interaction in the PBM group is not significant. Contrary to expectations, the ABM group did not exhibit a shift in overall bias from pre to post-training, which is in fact in line with recent ABM studies for persistent pain that have also measured attentional bias

using the dot-probe task at pre and post-training (Schoth et al., 2013; Sharpe et al, 2012). In light of these contemporary findings, in conjunction with evidence that the attentional bias in persistent pain is situated in maintained attention, the present study additionally predicted that there would be an interaction with test SOA, such that the attentional shift is situated at 1250 ms and not 500 ms, which would be supported by the inclusion of test SOA in the repeated measures interaction within the ABM group.

This interaction did not reach significance in either the ABM group, or the PBM group, with evidence only of a trend-level shift in attention, that was, as anticipated, contingent on test SOA, in the ABM condition, *ps* $\leq$ .1. Fine-grained analyses suggested that, in line with the original prediction, active ABM had modified pain-related attentional bias at 1250 ms (and not 500 ms), but this effect was only evident in the upper region of the visual display, in comparison with the placebo group.

One putative explanation for the current findings is that, in this community-based sample, the dot-probe evaluation of attentional bias was more sensitive to participants' pre - post attentional shift in maintained attention, when words were presented in the upper part of the visual display, corresponding with the upper visual field (UVF). This superior test sensitivity for attentional shift at 1250 ms in the UVF could be attributable to perceptual asymmetries in the vertical meridian (Feng & Spence, 2014). Neuroimaging and behavioural evidence suggests that these vertical perceptual asymmetries, which have been observed across a range of attentional tasks, including the dot-probe assessment of physical threat-related attentional bias (Asmundson & Stein, 1994), could arise due to better coding of words (semantic content) presented in the UVF, in comparison with the LVF (Bocanegra, Huijding, & Zeelenberg, 2012; Drain & Reuter-Lorenz, 1996; Thomas & Elias, 2011; Vuilleumier, 2005). This explanatory hypothesis requires testing through the collection of data (neuroimaging/ERP) from participants with persistent pain whilst they perform the visual-probe task, for validation. As it stands, current findings offer one potential explanation for past reported failure to find an effect of ABM on attentional bias in persistent pain, in spite of within-subjects improvements in pain outcomes (Schoth et al., 2013; Sharpe et al., 2012), as neither study reported omnibus analyses of the attentional data across each of the trial types, having immediately collapsed the conditions through calculation of the attentional bias indexes. The present study is therefore the first to demonstrate that, as measured in the UVF, attentional bias modification can ameliorate attentional bias in maintained attention in persistent pain, in comparison with placebo training, as predicted by previous research (e.g. Carleton et al., 2011; McGowan et al., 2009; Pincus & Morley, 2001).

The second aim was to assess the relative efficacy of attentional training at each training SOA on pain outcomes, as compared with the control groups. In conjunction with

the near-transfer effects observed on attentional bias at 1250 ms, if evidenced, these far-transfer effects (i.e. the transmission of training effects to real world symptom outcomes) would indicate a causal link between the attentional bias in maintained attention exhibited at baseline, and pain reactivity (Hertel & Mathews, 2011). Contrary to predictions, the results of the mixed model analysis of variance suggested that ABM did not lead to greater improvements in symptoms, in comparison with PBM, at either training SOA. The absence symptom effects means that the expected causal role of attentional bias in persistent pain experience was not supported. This finding diverges from those of the previous ABM for persistent pain studies, which reported improvements in anxiety sensitivity, pain severity and pain disability (Carleton et al., 2010; Schoth et al., 2013; Sharpe et al., 2012). Two points arise here. First, only one of these studies included a between-subjects component in analyses, where an improvement in pain disability only (measured using the Roland-Morris Disability Questionnaire) was reported at post-training, relative to the sham training control group (Sharpe et al., 2012). Given the main effects of time, this leaves open the possibility that the current absence of between-groups training effects was in part attributable to the sham training also exerting an effect on symptoms, as has been reported in the anxiety literature (e.g. Carlbring et al., 2012). Second, in the Sharpe et al. (2012) study, effects on pain severity and anxiety sensitivity only became evident at follow-up. This finding fits in with a mounting body of evidence that suggests there is a window in which the modified bias interacts with participants' experience, which is fundamental to detecting the impact of changes in cognitive bias on symptoms (e.g. Browning et al., 2012). Future research assessing the causal role of cognitive bias in persistent pain should thus incorporate a follow-up period, for a more robust assessment of the posited interaction.

In spite of the absence of between group differences in pre to post symptom outcome means, the planned correlations indicated the anticipated association between improvement in attentional bias at 1250 ms and reductions in pain severity and anxiety sensitivity, but not disability, within the ABM-1250 group. This suggests that when maintained attention was trained at the corresponding SOA, the resultant change in attentional bias was associated with a reduction in pain severity and anxiety sensitivity over the course of training. These findings correspond with the foundational findings of Study Three (in which ABM preceded the cold pressor task), where, within the ABM groups, improvements in attentional bias were associated with improved pain outcomes (specifically higher threshold and tolerance, and, at trend-level, with lower pain severity ratings). Current findings also suggested an association between speeded reaction times to neutral (versus pain) words and improved pain outcomes (severity and anxiety sensitivity). Interestingly, in that study as well, 'improvement' in attentional bias in the placebo training group was associated with poorer pain outcomes, suggesting that sham training effects do not translate

to real-world improvement in pain experience in either an acute or persistent pain context. Differing from the acute pain findings, however, where attentional bias and pain associations were identified at both test SOAs, within both the ABM-500 and ABM-1250 groups, present findings suggested that the associations were situated at 1250 ms only, within the ABM-1250 group. This could reflect the greater involvement of ruminative processing, and maintained attention, in long-term pain experience (Schoth et al., 2012).

Thus, so far the findings have provided evidence of near-transfer of ABM effects to attentional bias at 1250 ms, and limited, correlational evidence only of the predicted far-transfer of training effects to pain outcomes. Importantly, the prediction that training would causally impact on persistent pain was not supported. This raises a significant question for the next study. Specifically, it could be explored whether the ABM paradigm can be augmented such that training effects are more robust, and far-transfer to clinical outcomes is promoted. One method to enhance CBM effects might be to add explicit task instructions (e.g. MacLeod & Mathews, 2012). Currently, participants are not given any information concerning the contingency between the stimulus valence and target location. However, whilst the absence of task guidance is striking, there is reason to believe that explicit instructions might in fact counteract far-transfer effects, in spite of augmenting effects on attentional bias, because the revised training (with explicit instructions) invokes a more strategic level of processing than usual ABM (Grafton, Mackintosh, Vujc, & MacLeod, 2014). Specifically, recruitment of explicit strategies to downregulate unwanted, cognitive interference (by emotional, and, by extension, pain-related cues) might lead to a paradoxical increase in their intrusion (e.g. Grafton et al., 2014; MacLeod, Koster, & Fox, 2009). This notion suggests that fundamental to CBM is that it targets attentional bias at a relatively automatic level of processing, and is supported by evidence that its effects are retained even when mechanisms of cognitive control are taken up by other processing activities (e.g. Bowler et al., 2012). Hence, a logical next step would be to test whether ABM-effects are augmented through the addition of an instruction that is designed to operate at a relatively automatic level of processing, such as an implementation intention (Gollwitzer & Sheeran, 2006; Webb, 2007), and will be pursued in Study Five (Chapter Six).

The present study had a number of limitations. First, the combination of attrition from the 68 participants recruited and the factorial design employed meant that each group contained only a quarter of the 57 participants who completed the study. This means that intricate effects of ABM, such as its differential impact on pain outcomes, may have been detectable if the sample size had been larger (Browning et al., 2012). Second, the recruited participants represented a relatively high-functioning community-based sample of convenience. As such, the study may have been relatively insensitive to changes in pain outcomes as assessed in the analysis of variance, as nearly half of the sample reported only

mild pain. To address this issue, the next study should aim to recruit a clinical sample with moderate to severe pain. Third, conclusions concerning ABM effects are contingent on the reliability of the dot-probe task, which has been called into question (e.g. Staugaard, 2009). The interaction of attentional response with the vertical meridian of display also suggests that the estimate of attentional bias may be influenced by features of the test procedure, potentially reducing its sensitivity. Nonetheless, recent data provide support for its reliability and sensitivity in determining attentional bias within the context of a long-term condition, depression (Browning et al., 2011). Fourth, the present study directly compared ABM with sham training, and did not include a non-training control group; hence, it cannot be ruled out that where hypotheses were not supported, such as in the absence of effects on pain outcomes, this was attributable to sham training effects, although the correlational findings suggest this is unlikely.

In summary, this study provides the first evidence that ABM (at 500 and 1250 ms) can reduce pain-related attentional bias, situated in maintained attention, in a persistent pain population. There was no evidence for far-transfer effects to pain outcomes at post-training, although a strong association was found between improvement in attentional bias in maintained attention and reductions in pain severity and anxiety sensitivity. Future research should investigate the augmentation of ABM with implementation intention instructions to promote real-world transfer effects, and assess these after a follow-up period, during which the induced changes in attentional bias have had time to interact with participants' pain experience.

Chapter 6 Study 5

A comparison of attentional bias modification with and without an added implementation intention instruction: Effects on attentional bias and pain outcomes in a clinical persistent pain sample

6.1 Introduction

Chapter Five (Study Four) provided initial evidence that ABM, which is designed to target earlier (stimulus duration 500 ms) and later (1250 ms) attention, can reduce pain-related attentional bias, situated in maintained attention, in a community-based persistent pain population. However, contrary to expectations, there was no evidence for far-transfer effects to pain outcomes at post-training, although a strong association was found between improvement in attentional bias in maintained attention and reductions in pain severity. This finding corresponded with a mounting body of evidence that suggests it is fundamental to detecting the impact of changes in cognitive bias on symptoms that there is a window in which the modified bias interacts with the participants' experience (e.g. Browning et al., 2012). It was also noted that the addition of participant instructions to the paradigm might enhance real-world transfer of training effects. The current study will assess the efficacy of augmenting the ABM paradigm with an instruction for clinical pain, examining its therapeutic impact after any resultant change in attentional bias has interacted with participants' daily pain experience for one week.

As discussed in Chapter Five, one method to enhance CBM effects might be to add explicit task instructions (e.g. MacLeod & Mathews, 2012); currently, participants are not given any information concerning the contingency between the stimulus valence and target location. One difficulty is that explicit instructions might in fact counteract far-transfer effects, in spite of augmenting effects on attentional bias, because the revised training (with explicit instructions) invokes a more strategic level of processing than usual ABM (Grafton, Mackintosh, Vujc, & MacLeod, 2014). Specifically, recruitment of explicit strategies to downregulate unwanted, cognitive interference (by emotional, and, by extension, pain-related cues) might lead to a paradoxical increase in their intrusion (e.g. Grafton et al., 2014; MacLeod et al., 2009). Hence, fundamental to CBM might be that it targets attentional bias at a relatively automatic level of processing, as supported by evidence that its effects are retained even when mechanisms of cognitive control are taken up by other processing activities (Bowler et al., 2012). Therefore, a logical next step is to test whether ABM-effects are augmented through the addition of an instruction that is designed to operate at a relatively automatic level of processing, such as an implementation intention (Gollwitzer & Sheeran, 2006; Webb, 2007).

Like ABM, the formation of implementation intention plans (IMPs), represents another route to the automatisation of response. This explicit self-regulatory strategy is

thought to automatise decision-making by linking a cue stimulus in the first 'if' clause of a proposition with the response in the 'then' clause of a proposition, giving rise to an if-then plan in the format: 'If situation x is encountered, then I will initiate response y''. In this way, implementation intentions are distinct from goal intentions that specify a desired performance or outcome and have the format: ''I intend to reach z'' - for example, ''I intend to exercise more''. Whereas goal intentions only designate desired end-states that the individual feels committed to attain, implementation intentions are designed to create a commitment to respond to a specified critical situation in a planned, goal-directed manner. For instance, ''If I am on the bus, then I will get off one stop early and walk the rest of the way!'' Implementation intentions are thus typically formed with a view to realising respective goal intentions (Sheeran, Webb, & Gollwitzer, 2005).

Whilst a wealth of research has suggested that forming implementation intentions can promote the achievement of behavioural goals (for a review see Gollwitzer & Sheeran, 2006), comparatively few studies have investigated the possibility that forming IMPs might also be an effective way to regulate feeling states. However, there is mounting evidence that these self-regulatory plans could attenuate emotion such as anxiety and anger (for a review see Webb, Schweiger Gallo, Miles, Gollwitzer, & Sheeran, 2012). In their meta-analysis, Webb et al. (2012) found that creating implementation intentions had a large effect on affective response, relative to no regulation instructions and a medium-sized effect relative to goal intention instructions. Current theory suggests that the formation of a plan increases the accessibility of the asserted cue and elicits strong cue-response links (Sheeran et al., 2005; Webb et al., 2012). By extension, the resulting 'if-then' plan could help to undermine attentional bias implicated in persistent pain experience by inhibiting the salience of the maladaptive stimulus.

Lending some support to this hypothesis, past research has indicated that anxiety-inhibiting IMPs can modify attentional bias in social anxiety (Webb, Ononaiye, Sheeran, Reidy, & Lavda, 2010). In the first of three studies, Webb et al. (2010) demonstrated that high socially anxious participants who formed the implementation intention "If I see a neutral word, then I will focus all of my attention on it!", prior to a dot-probe of assessment of threat-related attentional bias, had significantly reduced threat bias at post-intervention. Their subsequent studies further suggested that implementation intention formation helped individuals to provide more accurate evaluations of their performance on a speech stressor task, and self-report lower levels of anxiety during the speech than participants who had not formed an IMP (Webb et al., 2010). These findings suggest that an implementation intention instruction might complement ABM. Yet, interestingly, although both IMPs and ABM have sought to automatise responses on attentional switching tasks such as the dot-probe, they have not been combined and evaluated within a single study.

The present study aimed to address this gap in the literature through, first, testing the relative impact of usual ABM and ABM with an integrated salience-inhibiting IMP, which took the form of "If I see a neutral word, then I will focus all of my attention on it!", on attentional bias, in comparison with a no training control group (Webb et al., 2010). It was hypothesised that attentional bias to pain would be reduced in both ABM groups in comparison with controls, and that the greatest reduction in bias would be observed in the ABM-IMP condition. A measure of perceived attentional control was also included in the study with a view to examining its putative role in the underpinning mechanism of action, but which has not been directly tested in ABM-pain research (e.g. Bar-Haim, 2010; Everaert, Mogoaşe, David, & Koster, 2014; Mackintosh & Fox, 2014; Schoth et al., 2013). Specifically, some commentators have speculated that ABM may work through increasing attentional control, and thereby facilitate top-down control of pain-related distractors, in turn neutralising pain-related attentional bias (e.g. Bar-Haim, 2010). If this is the case, it is expected that levels of attentional control (Attentional Control Scale; ACS, Derryberry & Reed, 2002) scores will increase in the ABM and ABM-IMP groups relative to controls. Conversely, others have speculated that dispositional attentional control may affect ABM efficacy, such that those with higher attentional control are more likely to acquire the training-congruent bias, and do well on the task (e.g. Everaert et al., 2014). If this is true, it is expected there will be a positive correlation between baseline attentional control and neutral bias acquisition within the ABM groups.

Second, the impact of usual ABM and augmented ABM for pain on pain severity was compared to the control group from pre-training to post-training and follow-up. It was predicted that training effects on pain severity would particularly emerge during the follow-up period, and that the greatest reductions in pain outcomes (pain, pain interference and distress) would be observed in the ABM-IMP group.

6.2 Method

Power analysis

An *a priori* power calculation was conducted using G*Power 3.1 software (Faul et al., 2009). On the basis of prior ABM effect sizes, and applying a recent ABM interaction effect size for anxiety sensitivity in long-term pain (d = .56; Sharpe et al., 2012), it was determined that a minimum sample size of 14 participants per group would be required to achieve 80% power at $\alpha = .05$ for mixed model ANOVA analyses; the critical F value will be $F = 3.5$.

6.2.1 Participants

A total of 49 participants were recruited via leaflets, invitation packs, and posters from a local NHS pain management clinic (n = 18, 37%), GP practices (n = 16, 33%), and

the wider Norwich community (*n* = 15, 30%). The dataset for this sample was also reported in Study One (Chapter Three), where the attentional data were compared with a healthy pain free control group. As described in Chapter Three, and repeated here for clarity, inclusion criteria were: diagnosed chronic benign musculoskeletal pain that had lasted for three months or more (this population was selected as past research has associated attentional bias towards pain words with persistent musculoskeletal/neuropathic pain, e.g. Dehghani et al., 2003); native English speakers (due to the verbal nature of the tasks); aged 18 years and over; normal or corrected-to-normal vision; able to read and understand text displayed on a computer screen, and able to use a computer keyboard comfortably for 30 minutes with breaks. Exclusion criteria were: pain related to a progressive condition such as cancer; undergoing psychological treatment for pain, such as cognitive behavioural therapy, currently or within the past three months, and change in pain medication within the past three months. Recruitment took place from August 2013 to August 2014.

Individuals who expressed interest in the study (*N* = 104) were sent an electronic copy of the participant information sheet, together with an electronic consent form, which they were asked to fill in should they still wish to take part having read the study information. Of these, 55 (53%) returned the completed electronic consent form and were sent the word task in two parts. Fifty-three participants (51%) returned both parts of the word task. Of these, 49 (47%) attended the session with the researcher, in which they were given paper copies of the participant information sheet, eligibility criteria checklist and consent form, and all 49 participants (17 males and 32 females; mean age = 41.39, *SD* = 15.61, range 18 – 78; mean approximate pain duration = 137.5 months, *SD* = 134.2) were confirmed to meet eligibility requirements and completed the intervention session.

Overall, the sample (*N* = 49) had a mean pain severity score at baseline of 54 (*SD* = 20.29; MPQ-SF VAS) out of a possible 100, which is indicative of moderate pain (Breivik et al., 2008; Hawker et al., 2011), and a pain interference score of 5.49 (*SD* = 2.43) out of a possible 10, which suggests moderate inference with daily life (Cleeland, 2009). The majority of participants (*n* = 35; 71.4%) reported persistent musculoskeletal pain in more than one site (14 participants; 28.6% had pain in a single site), and seven (14%) experienced widespread pain in six or more sites. The distribution of musculoskeletal pain by primary pain site was as follows (Dehghani et al., 2003; Merskey & Bogduk, 1994). Eighteen participants (36.7%) had low back pain; 2 (4.1%) had thoracic back pain; four (8.2%) had head and face pain; one (2%) had pelvic pain; three (6.1%) had upper limb/shoulder pain; four (8.2%) had lower limb pain; and 17 (34.1%) had pain in more than three of the above major sites, 16 (32.7%) of whom also reported cervical pain.

Participants were randomly allocated (via the online research randomiser website, www.randomizer.org) to one of three conditions: attentional bias modification (ABM; *n* =

16); attentional bias modification with added implementation intention plan (ABM-IMP; *n* = 16), and a Control Task group (CT; *n* = 17). A chi-square suggested there was no difference between groups in the number of participants who were recruited from the pain management clinic, χ^2 (2, *N* = 49) = 1.73, *p* = .42.

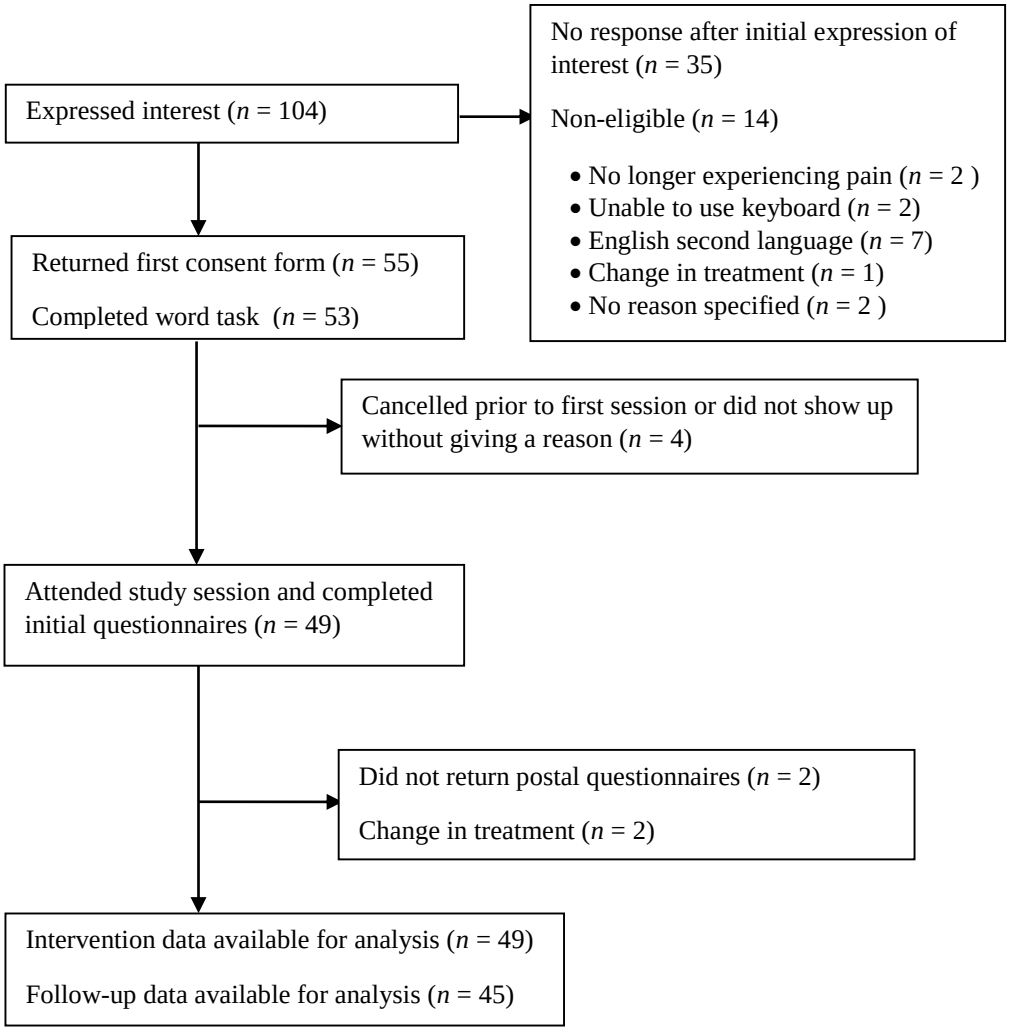


Figure 6.1 Flow of participants through study.

6.2.2 Materials

Experimental stimuli

The critical stimulus words were generated in the same way as described in Study Four, and comprised 84 pain-related words and 84 neutral words, which were selected from and matched for length and frequency of usage using the Brysbaert database (Brysbaert & New, 2009; see Table 6.1). The resultant set of word pairs was then divided into two test sets (each comprising 12 word pairs) and one master training set (60 word pairs). Order of test administration (pre - post) was counterbalanced across conditions.

A similar idiographic lexical selection procedure was applied as in Study Four (Chapter Five) to enhance the relevance of the training stimuli to each individual participant's pain experience (Amir et al., 2009). Before training, all participants were first

asked to generate as many words as they could (up to a maximum of twelve) that described their pain, writing them down as soon as they came to mind. The first six of these self-generated words were then matched with neutral words for length and frequency and added to the predetermined list of 60 word pairs, taken from previous studies. Participants were asked to rate the resultant list of 66 words for how related they were to their pain on a scale of -3 to +3, where -3 was "not at all related", and +3 was "very much related" (Amir et al., 2009). The 24 words that were rated most negatively (and thus related to their pain) by that participant from the training set were then used in the ABM or ABM-IMP program, depending on the participant's condition allocation. For both the test and master training sets, an equal number of the target words described the sensory (e.g. aching/aerial) and affective (invasion/cupboard) aspects of pain. Different stimuli were used for the pre and post attentional bias tests (counterbalanced) and words were not repeated between the attentional bias test and training programs.

Table 6.1

Matched pain and neutral words used for attentional bias test and modification

Training set				Test set	
Pain word	Neutral word	Pain word	Neutral word	Pain word	Neutral word
aching	aerial	radiating	shrubbery	cut	car
burning	jacket	painful	laundry	tearing	backyard
hurting	garage	sting	porch	tightness	plasterer
pain	seat	tender	carpet	stings	spoons
piercing	bookcase	pinching	polished	grinding	cassette
pounding	curtains	agony	timer	sharp	plate
pulsating	bedspread	spasm	stair	gruelling	glassware
sharp	walls	squeezing	wallpaper	alarming	cabinets
splitting	recorder	grinds	mopped	unbearable	bathrooms
throbbing	ornament	ache	cork	tortured	household
searing	roofing	beating	cooking	debilitating	floorboards
choking	mansion	freezing	electric	punishing	decorated
cramps	bleach	heavy	floor	stiff	towel
gnawing	tidying	biting	sponge	tugging	textile
penetrating	mantelpiece	smarting	saucepans	bruised	cutlery
victim	painted	depressing	toothbrush	stabbing	cushion
invasion	cupboard	frightening	refrigerator	intense	grounds
defenceless	pillowcase	worry	room	sore	brush
interfere	magazines	tiring	blinds	wretched	storage
suffer	drawer	upsetting	fireplace	agitation	banister
killing	window	harmful	pyjamas	panic	steps
troublesome	telephones	helpless	clothing	exhaustion	microwaves
terrible	kitchen	irritated	housework	upset	table
vicious	ceiling	failing	wardrobe	agonising	bedclothes
griping	timbers	apprehension	videotapes		
harm	roof	angry	glass		

Table 6.1

Matched pain and neutral words used for attentional bias test and modification

Training set				Test set	
Pain word	Neutral word	Pain word	Neutral word	Pain word	Neutral word
nausea	coaster	miserable	television		
fearful	stables	tormenting	Appliances		
hopeless	basement	devastating	decorating		
frustrating	toothpaste	distressing	disinfectant		

Attentional bias test and ABM

As in previous studies, the attentional bias test and modification program used a modified form of the probe classification version of the dot-probe paradigm adapted from MacLeod et al. (2002), and was administered using E-Prime software (Schneider et al., 2002). The pre and post attentional bias tests each comprised 96 trials, and were as described in Study Four. Building on the findings from Study Four, in which the ABM-500 and ABM-1250 training programs were found to have comparable efficacy for pain-related attentional bias, the ABM program featured two word pair stimulus onset asynchronies (SOA; 500 and 1250 ms) in randomised order, and was otherwise as detailed in that study (comprising 384 trials, with the set of 24 word pairs randomly presented 16 times).

Attentional bias modification with added implementation intention plan

The ABM component of the program was the same as above. For the IMP component, participants received onscreen instructions prior to the commencement of training to form an implementation intention in the format: "If I see a neutral word, then I will focus all of my attention on it!" (Webb et al., 2010, 2012). They were further instructed to repeat the implementation intention to themselves twice and type the instruction once prior to commencement of the attentional training.

Control program

Control group participants completed a categorisation task similar in design to the Implicit Association Test (IAT; Greenwald, McGhee, & Schwartz, 1998) and the control training used by Schoenmakers et al. (2010). In each trial of the control task, a target stimulus appeared in the centre of the screen. The participant's task was to press either the right or left arrow key to classify the target as being either pain-related or non pain-related (i.e. neutral), a number, or the name of a colour. This task was selected because it enables the same stimuli to be used as in the ABM program and engages participants in a similar activity to the experimental conditions with comparable feedback, without modifying attentional bias (Schoenmakers et al., 2010).

Self-report questionnaires

Seven standard questionnaires were administered at pre-training and post-training. In addition to a Demographic and Clinical Questionnaire administered at baseline, these were: the McGill Pain Questionnaire – Short-Form (MPQ-SF; Melzack, 1987); the Brief Pain Inventory (BPI; Cleeland & Ryan, 1994); the Hospital and Anxiety Depression Scale (HADS; Zigmond & Snaith, 1983); the Pain Catastrophizing Scale (PCS; Sullivan et al., 1995); the Pain Vigilance and Awareness Questionnaire (PVAQ; Roelofs et al., 2003a); the Attentional Control Scale (ACS; Derryberry & Reed, 2002), and a current pain severity Visual Analogue Scale (VAS), which was additionally administered at post-training (three time-points total). Also given at post-training was a VAS assessing level of training engagement (eng-VAS), to gauge whether this was comparable across the different types of training. Psychometric properties for the above standard questionnaires were reported in Chapters Three and Four.

6.2.3 Procedure

Ethical approval was obtained from the Tayside NHS Research Ethics Committee and University of East Anglia School of Psychology Research Ethics Committee (see Appendix B). Interested individuals were emailed an electronic copy of the participant information sheet and electronic informed consent form for the word-stimuli generation task. Consenting participants were asked via email to generate a list of words that described their pain. These words were added by the researcher to the master list of 60 pain descriptors taken from previous studies concerning attentional bias in pain, and participants were sent the word rating task. They were then invited to attend the experimental session.

At the experimental session, they were given a paper copy of the participant information sheet (Appendix B2) and completed paper copies of the eligibility criteria checklist and consent form (Appendix B3). Having provided full written informed consent, willing participants completed the battery of baseline questionnaires (MPQ-SF; BPI; HADS; PCS; PVAQ; ACS; VAS x 2). Next, they completed the attentional bias test and, depending on the condition to which they were randomised, ABM, ABM-IMP, or Control program. Next, participants completed the post-intervention measures (second attentional bias test; pain severity-VAS; engagement-VAS). At the end of the session, they were asked to complete a questionnaire pack at home exactly one week after the meeting with the researcher, and return it by post using an enclosed stamped addressed envelope. At one week follow-up, all participants were sent a reminder (via text/email) to return the questionnaires to the researcher. Participants were informed at the outset they would be randomised to condition. They were told that the study investigated "attention and pain" and "how people with long-term pain think", and were not told that any of the conditions sought to retrain attention and improve pain experience. At the end of the study, participants were fully

debriefed (Appendix B4), and those who were randomly allocated to the control condition were given the opportunity to complete the usual ABM program if they so wished. Overall, the session lasted approximately 1.5 hours; the total time commitment was approximately three hours, spread over the study.

6.3 Results

6.3.1 Group characteristics

As shown in Table 6.2, a series of one-way ANOVAs suggested the groups were well matched at baseline on age, and the pain characteristics of pain duration, number of GP visits in the past month, days absent from work due to pain, and number of medications taken per day for pain (all *p*s > .10). They were also well matched for the identified cognitive and affective vulnerability factors for pain of anxiety, depression, pain catastrophising, pain vigilance and awareness, attentional control and attentional bias (all *p*s > .10). In addition, a series of chi-squares suggested that the groups had equivalent gender ratio, χ^2 (2, *N* = 49) = 1.04, *p* = .60, marital status, χ^2 (8, *N* = 49) = 8.79, *p* = .36, and employment status, χ^2 (14, *N* = 49) = 12.81, *p* = .54.

As indicted in Study One (Chapter Three), two non-parametric one-sample Wilcoxon signed-ranked tests, comparing baseline attentional bias across the whole sample at test SOA 500 ms (*mdn* = -5.5; range = 374.5), and 1250 ms (*mdn* = -7.25; range = 278.25), with the hypothesised median of zero, indicated that, in line with findings from Study Four (Chapter Five), attention was biased towards pain words presented for the longer, Z (49) = -2.03, *p* = .042 (two-tailed), *r* = -.29 , and not the shorter, *Z* (49) = -1.06, *p* = .136, *r* = -.15, stimulus duration.

Table 6.2

Descriptive Data: Means of Age, Pain Duration, Number of GP Visits, Number of Days Absent, Number of Medications, MPQ-SF Total, BPI Total, Anxiety, Depression, Pain Catastrophising, Pain Vigilance and Awareness, Attentional Control, Current Pain Severity, and Attentional Bias with Standard Deviations, and Gender Ratio, by Condition

	ABM		ABM-IMP		Control		
	n = 16		*n* = 16		*n* = 17		
	M	*SD*	*M*	*SD*	*M*	*SD*	*F*-value
Age	38.63	18.21	40.56	13.63	44.76	15.00	0.66
Female:Male[a]	10:6		12:4		10:7		1.04
Pain duration months	134.19	147.93	140.44	128.52	137.88	134.27	0.008
GP visits	2.06	1.65	2.88	3.63	4.35	7.00	1.01
Days absent	6.33	8.59	1.80	3.55	4.44	13.33	0.58
No. medications	3.20	2.78	3.38	2.58	2.53	1.74	0.58
MPQ-SF	23.33	10.93	24.50	9.78	22.00	10.91	0.23
BPI	51.69	20.02	62.47	21.20	58.47	23.86	0.97
HADS-Anxiety	10.06	4.06	10.25	5.04	8.63	4.60	0.60
HADS-Depression	7.75	4.89	8.25	5.32	7.38	4.66	0.13
PCS	21.88	11.80	24.44	13.81	23.71	12.28	0.17
PVAQ	45.62	10.98	46.13	11.89	47.19	13.78	0.07
ACS	51.70	10.96	49.03	11.64	48.47	12.28	0.36
Pain severity VAS	48.06	21.36	58.06	24.79	50.18	22.31	0.85
Attentional Bias-500[b]	-7.77	61.80	-23.98	81.17	-13.21	40.53	0.28
Attentional Bias-1250	-32.00	58.12	-8.67	35.07	-2.00	31.44	2.19

Note [a] All between-groups comparisons at baseline were non-significant ($p > .10$). As gender is a dichotomous variable, a chi-square was conducted. [b] Kruskal-Wallis tests confirmed there were no significant differences at baseline in the attentional data, all *p*s > .20).

6.3.2 Statistical analysis and data reduction

As in Study Four, with a view to minimising the influence of extreme reaction times on individual trials within the attentional bias tests (pre - post), median reaction times to each of the four critical trial types (probe up, pain word up; probe up, pain word down; probe down, pain word up; probe down, pain word down) at each stimulus presentation time (500 ms, 48 trials; 1250 ms, 48 trials; as well as overall, 500 and 1250 ms, 96 trials), for each participant, were extracted from E-Prime (MacLeod et al., 2002; Whelan, 2008). In addition, due to the instruction that participants could take a break at any point during the program, trials with RTs ≥ 3000 ms were not considered accurate measures of attentional bias, and hence, along with error trials, were discarded (8.07% data; MacLeod et al., 2002;

Whelan, 2008). Next, in view of the hypotheses, and to facilitate interpretation, three attentional bias indexes (overall, and for each SOA individually) were calculated by subtracting the mean (of the extracted medians) reaction times to neutral words from the mean (of medians) reaction times to pain-related words, such that a more negative value represented a more pain-related bias (MacLeod et al., 2002).

The attentional bias data (extracted medians for each trial type and attentional bias indexes) and questionnaire scores were assessed for normality within each condition. Skewness and kurtosis coefficients were calculated by dividing each statistic by its corresponding standard error, which indicated positively skewed distributions at baseline for each trial type, which, as previously noted, is a common characteristic of reaction time data (Baayen & Milin, 2010; Ratcliff, 1993).

Inspection of box and whisker plots across the different levels of the dependent variable suggested three extreme outliers (two in the ABM group and one in the ABM-IMP group) at 500 ms (n = 2) and 1250 ms (n = 2; one participant had extreme scores at both stimulus presentation durations), who each had a very pain-related bias at baseline (< -150 ms), and one of whom retained an extreme negative score at post-training (ABM-IMP group). No objective reasons for the occurrence of these extreme values could be identified, and it was decided not to amend or exclude them due to the within-subject nature of the attentional bias data (Osborne & Overbay, 2004; Ratcliff, 1993; Tabachnick & Fidell, 2001). As discussed in Chapter Five, in the absence of a non-parametric equivalent for the main omnibus analysis, and in view of its reputed robustness, a mixed model analysis of variance (ANOVA) was conducted on the untransformed data (Glass et al., 1972; Lix et al., 1996).

Given the different types of ABM being tested, an additional measure of level of training engagement was taken using a visual analogue scale. Baseline analyses suggested that participants were comparably engaged with the ABM and ABM-IMP tasks (Ms = 60.81, 54.38, SDs = 25.77, 26.78 respectively), but more engaged with the control task (M = 80.31, SD = 17.64; F (2, 47) = 5.17, p = .009), perhaps due to the inherent semantic requirements of the implicit association test. However, as the purpose of the control task was to expose participants to equivalent stimuli and not induce any attentional bias, this should not have influenced outcomes. Nevertheless, the attentional data were analysed using a mixed model ANCOVA, with the between-subjects factor of ABM type (ABM, ABM-IMP, Control) and training engagement as the covariate. In the first instance Time (pre, post), Target Position (behind pain word, behind neutral word) and Word Position (top, bottom) were included as the within-subjects factors. Where assumptions of homogeneity of variance were not met, the Huynh-Feldt correction to degrees of freedom was used, although unadjusted degrees of freedom were reported for clarity. Where relevant, significant interactions were followed up with analyses conducted using the attentional bias indexes (Macleod et al., 1986).

The pain outcome data were analysed using a complete-case analysis, given the small number of participants who did not return the follow-up questionnaires as requested (n = 2), and in view of a missing value analysis conducted on the data, which confirmed it was reasonable to assume these values were missing at random (Little & Rubin, 1987).[14] As in ABM Studies Three and Four, to assess whether there was an association between change in attentional bias over the training period and change in the key pain outcome measures, attentional bias improvement scores were calculated by subtracting the relevant attentional bias index at pre-training from the equivalent index at post-training, such that a more positive value represented a greater shift towards a more neutral attentional bias (MacLeod et al., 1986; Sharpe et al., 2012). Questionnaire change scores were also calculated by subtracting the value at pre-training from the post-training value, such that a more negative score represented a greater reduction in pain symptoms. Where outcomes were not normally distributed, Spearman rho correlations were reported.

The primary outcome measure for the present study was the pain severity VAS, which was measured at three time points (pre, post and follow-up), testing the prediction that training effects for perceived pain might emerge at one-week follow-up. Secondary pain outcomes were pain experience measured using the MPQ-SF, pain interference (BPI) and distress (HADS), which tested the hypothesis that the ABM-IMP group would exhibit significant reductions in pain outcomes from baseline to one-week follow-up. The final secondary outcome was attentional bias (i.e. the relative dot-probe reaction times to pain-related and neutral words), which was measured at each test stimulus presentation duration (500 ms, 1250 ms) to test the hypothesis that ABM (both usual ABM and ABM-IMP) would reduce pain-related bias in initial orienting and maintained attention from pre to post-training in comparison with controls, and that this effect would be particularly evident in maintained attention in the ABM-IMP group.

6.3.3 Main outcome analyses: impact of usual ABM and ABM-IMP on pain severity

To test the hypothesis that type of attentional training would differentially impact on pain severity, a three (time: pre, post, follow-up) by three (group: ABM, ABM-IMP, Control) mixed model ANOVA was performed on the pain severity VAS data, with between-subjects on the last factor. Results indicated there was a main effect of time, F (2, 41) = 3.62, p = .036, η^2 = .15, suggesting that, on average, participants were in less pain at post-training (M = 48.51, SD = 24.32) and follow-up (M = 51.84, SD = 23.97) than at baseline (M = 52.33, SD = 23.1). This could have been due to a general benefit of study participation or demand characteristics, although the latter is unlikely as any training effects were entirely implicit. Critically, results of the multivariate analyses indicated a near-

[14] A chi-square for these data was non-significant, indicating there was no discernible pattern to the missing data (i.e. they were missing at random), χ^2 (151, N = 49) = 150.96, p = .49.

significant time by group interaction, F (4, 82) = 2.39, p = .058, η^2 = .104 (Roy's Largest Eigenvalue, F (2, 42) = 5.15, p = .01, η^2 = .197). Given the present hypothesis that group allocation would differentially influence change in pain severity across the three assessment points (pre, post, follow-up), the within-subjects effects and contrasts were inspected. Findings indicated that, as might be expected given the previous pre to post-training findings (Study Four) that suggested ABM is unlikely to immediately modify persistent pain experience, there was no overall within-subjects training effect on pain severity, F (4, 84) = 1.46, p = .24, η^2 = .065. However, crucially, within-subjects contrasts revealed a significant time by group quadratic interaction, F (2, 42) = 4.71, p = .014, η^2 = .18, suggesting that the impact of ABM on perceived pain severity differed as a function of condition and assessment point. Inspection of profile plots (see Figure 6.2) indicated that, as hypothesised, the differential impact of ABM on persistent pain severity emerged only during the one-week follow-up period, in comparison with the control group.

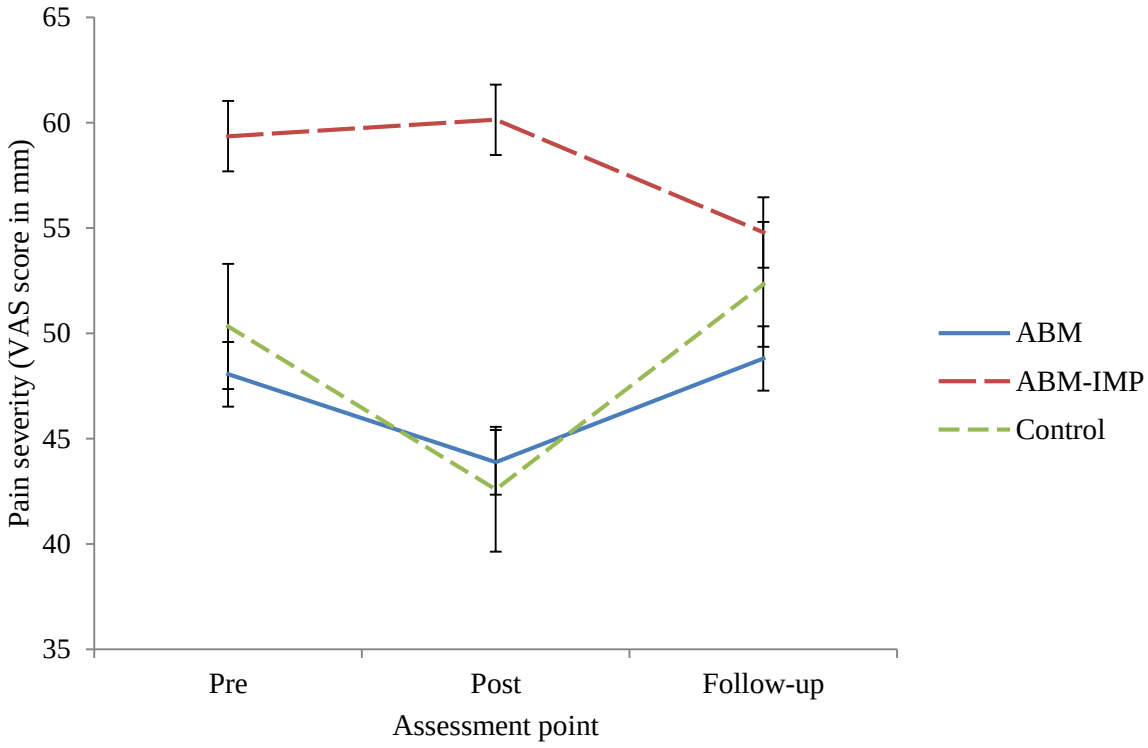


Figure 6.2 Line graph illustrating quadratic interaction.

The quadratic interaction was followed up with a series of one-way ANOVAs, with LSD contrasts, conducted on the pain severity improvement scores (calculated within each condition from baseline to post-training, and post-training to follow-up). Contrary to expectations, results indicated that from pre to post-training, the control group had exhibited a significantly greater reduction in pain severity (M = -7.73, SD = 10.14) than the ABM-IMP group (M = 0.79; SD = 8.93, p = .028), but was comparable with the ABM group (M = -4.19, SD = 10.93, p = .33). The cause of this comparative control group reduction in pain severity

during the session is unclear. During the critical follow-up period, as anticipated, only the ABM-IMP group reported a reduction in pain (M = -5.36, SD = 14.16), which was significantly different to the control group (M = 9.73, SD = 26.67; p = .033), but not the ABM group (M = 4.44, SD = 10.85; p = .14). The ABM group did not differ from the control group during the follow-up period, (p = .47), and no further significant effects were found.

Overall, these findings suggest that, relative to controls, attentional analgesia from post-training to follow-up was evident only in the augmented ABM-IMP group and not the usual ABM group, supporting the hypothesis that an added implementation intention instruction promotes the far-transfer of training effects to real-world persistent pain experience.

Secondary pain outcomes: changes in pain experience within each condition from baseline to one-week follow-up

Contrary to predictions, the time by group interactions did not reach significance for the MPQ-SF or HADS, Fs < 1, or BPI-Interference, F (2, 41) = 1.45, p = .25, η^2 = .066, measures, suggesting that ABM and ABM-IMP did not significantly improve these pain outcomes, relative to controls.

Given the relatively small sample size, further analyses were conducted as a precaution against making a type II error, and in accordance with the data analytic approach of Carleton et al. (2011), facilitating comparison between the studies (Carleton et al., 2011; Tabachnick & Fiddell, 2007). Therefore, to assess the hypothesis that the addition of an implementation intention would promote the transfer of ABM effects to reduction in pain outcomes from baseline to one-week follow-up, separate one-tailed paired-sample t-tests were performed within each condition, comparing the baseline measurements of pain (MPQ-SF), interference (BPI) and distress (HADS) to the corresponding final pain outcome measurements.

Within the control group, as expected, there was no change in pain, t (13) = 1.21, p = .12 (one-tailed), r = .32, pain interference, t (14) = 1.43, p = .09 (one-tailed), r = .36, or distress, t (13) = 0.97, p = .17 (one-tailed), r = .26. Within the usual ABM group, there was a small to moderate change in pain that approached significance, t (13) = 1.59, p = .069 (one-tailed), r = .40, but no change in pain interference, t (15) = 0.40, p = .35 (one-tailed), r = .10, or distress, t (15) = -1.05, p = .16 (one-tailed), r = .26. However, in line with expectations, within the ABM-IMP group, there was a small to moderate significant reduction in pain, t (13) = 1.81, p = .047 (one-tailed), r = .45, and moderate reduction in pain interference, t (13) = 3.14, p = .005 (one-tailed), r = .66, although there was no change in distress, t (13) = .513, p = .62, r = .14. Means and standard deviations are presented in Table 6.3.

Table 6.3

Means of the McGill Pain Questionnaire – Short Form, Brief Pain Inventory and Hospital Anxiety and Depression Scale scores at baseline and follow-up, with Standard Deviations, by Condition

	ABM		ABM-IMP		Control	
	n = 16		*n* = 14		*n* = 15	
	M	*SD*	*M*	*SD*	*M*	*SD*
MPQ-SF Pre	22.93	11.23	24.36	9.48	21.21	10.24
MPQ-SF Post	19.50	11.20	21.64	9.72	20.00	11.13
BPI-Interference Pre	4.87	2.34	6.25	2.43	5.68	2.66
BPI-Interference Post	4.73	2.89	5.23	2.43	5.08	2.80
HADS Pre	17.87	8.58	18.29	9.91	15.21	8.75
HADS Post	18.80	9.67	17.71	9.60	14.43	7.61

6.3.4 Impact of ABM on attentional bias and correlations

In spite of the above training effects on pain, the predicted effects of ABM on attentional bias were not found. The ABM (*M*s = 1.69, 1.43; *SD*s = 1.86, 1.25), ABM-IMP (*M*s = 1.37, 1.56; *SD*s = 1.36, 1.2) and Control (*M*s = 1.04, 0.98; *SD*s = 1.1, 1.63) groups did not differ significantly in the percentage of trials discarded due to participant error at pre, F (2, 48) = .814, p = .45, or post-training, F (2, 48) = .813, p = .45, respectively. To test the hypothesis that type of attentional training would differentially impact on response times to the target replacing pain words in relation to neutral words, two separate (one for each test stimulus presentation duration) two (time: pre, post) by two (target position: behind pain word, behind neutral word) by two (word position: top, bottom) by three (condition: ABM, ABM-IMP, Control) mixed model ANCOVAs were conducted on the untransformed attentional bias data, with between-subjects on the last factor, and training engagement included as a covariate.

For attentional bias at 500 ms, results indicated a main effect of time, F (1, 44) = 4.2, p = .046, η^2 = .087, such that participants were faster to key in the direction of the arrow probe replacing pain and neutral words at post (*M* = 561.38, *SD* = 102.24) than at pre (*M* = 603.07, *SD* = 142.45) training, perhaps due to increased task familiarity. Contrary to expectations, the overall time by target position by group, F < 1, and time by target position by word position by group, F (2, 44) = 1.23, p = .3, η^2 = .053, interactions were non-significant, suggesting that the ABM programs had comparable effects to the control task on attentional bias in initial orienting (see Figure 6.3).

For attentional bias at 1250 ms, results indicated no main effect of time, F (1, 44) = 2.39, p = .13, η^2 = .051, and, contrary to predictions, the overall time by target position by group, F (2, 44) = 1.87, p = .17, η^2 = .078, and time by target position by word position by group, F < 1, interactions did not reach significance, suggesting that, as for attentional bias in initial orienting, the ABM programs had comparable effects to the control task on attentional bias in maintained attention (see Figure 6.4). [15]

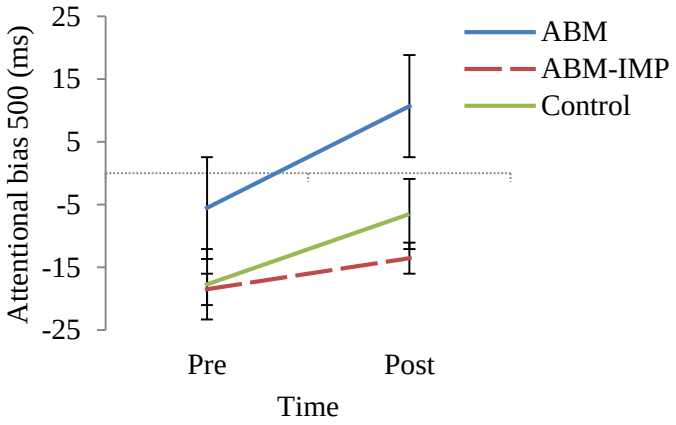


Figure 6.3 Line graph illustrating non-significant change in attentional bias in initial orienting from pre to post-training.

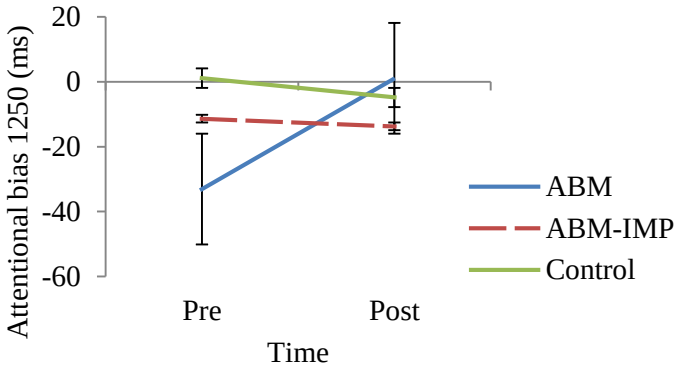


Figure 6.4 Line graph illustrating non-significant change in attentional bias in maintained attention from pre to post-training.

[15] When a mixed model ANCOVA was performed on the log-transformed attentional bias data, findings were similar to those reported in the main text. For AB-500, the time by target position by group, F < 1, and time by target position by word position by group, F (2, 44) = 1.77, p = .18, η2 = .075, interactions did not reach significance. Similarly, for AB-1250, there was no time by target position by group, F (2, 44) = 1.45, p = .25, η^2 = .062, and no time by target position by word position by group, F < 1, interaction, suggesting that the ABM programs had comparable effects to the control task on attentional bias at both stimulus durations.

As illustrated in Figure 6.4, although non-significant, there was a moderate effect of usual ABM on attentional bias at 1250 ms from pre (*M* = -32, *SD* = 58.12) to post (*M* = -1.03, *SD* = 32.38) training, suggesting that pain-related attentional bias in maintained attention had shifted in this group in the predicted direction. However, the pain outcome data indicated that these training effects did not transfer to persistent pain experience. Contrary to expectations, the addition of an implementation intention instruction did not enhance the effects of ABM on attentional bias in maintained attention, measured at post-intervention. Paradoxically, effects of augmented ABM on pain severity from post-training to follow-up were evident in this group, relative to controls, leaving the mechanism of action unclear at this stage.[16]

Correlations

First, to test the prediction that baseline attentional control may be related to training-induced bias acquisition, correlations were conducted within each group with baseline ACS scores and bias improvement scores as the dependent variables. Next, a series of correlations was conducted to test whether there was an association between pre - post change in attentional bias, for each test stimulus presentation duration, and change in pain severity over the past week, and pain interference, from pre-training to follow-up, as this is where within-subjects reductions were identified. All reported *p*-values are two-tailed.

Baseline ACS and bias acquisition

Separate correlations were conducted with ACS scores for each subscale (attentional shifting, attentional focussing), and total scores, and the attentional bias improvement scores for each test stimulus duration (500 ms, 1250 ms) as the dependent variables, within each condition. The only finding was of a trend-level moderate positive correlation between baseline perceived control of attentional shifting and improvement in maintained attentional bias within the ABM-IMP group, r (16) = .483, p = .058 (two-tailed), suggesting that higher baseline perceived attentional shifting control was moderately associated with greater improvement in attentional bias in maintained attention within the critical condition (see Table E1.3, Appendix E for full correlations). This finding provides preliminary support for the notion that dispositional attentional control (in this case of attentional shifting) may affect ABM efficacy (Everaert et al., 2014; Mackintosh & Fox, 2014).

[16] When complete-case analyses were conducted on the attentional bias data (i.e., only those participants who completed all study assessment points were analysed), and the three extreme outliers were excluded from analyses, the time by group interactions remained non-significant, *Fs* < 1, although changes in maintained attentional bias means from pre (ABM, ABM-IMP and Control *Ms* = -19.82, -0.23, 0.20, and *SDs* = 32.79, 19.51, 31.33) to post (*Ms* = -5.32, 7.12, 2.87; *SDs* = 28.43, 26.54, 30.62 respectively) training were in expected directions. A trend-level between-subjects effect of group, F (39, 1) = 2.91, p = .066, η^2 = .13, suggested that condition had an effect on attentional bias in maintained attention, but the effect of time on attentional bias was the same across conditions, which could be attributable to non-significant baseline differences in attentional bias.

Change in attentional bias and change in pain outcomes

ABM group

Within the ABM group, there was a moderate negative correlation between a more neutral bias in initial orienting and increased pain severity (MPQ-SF VAS), *rs* (16) = -.625, *p* = .01, suggesting that participants who were trained the most to attend away from pain-related stimuli, towards neutral stimuli, at the shorter stimulus duration from pre to post-training, also reported the greatest reductions in pain severity from pre-training to follow-up. The association between change in attentional bias in maintained attention and change in pain severity was non-significant, *rs* (16) = -.215, *p* = .212, and there was no association between change in attentional bias at 500 ms, *rs* (16) = .199, *p* = .416, or 1250 ms, *rs* (16) = .219, *p* = .415, and pain interference.

ABM-IMP group

Within the ABM-IMP group, there was a trend-level moderate negative correlation between a more neutral bias in maintained attention and increased pain interference (BPI), *rs* (14) = -.524, *p* = .054, suggesting that, as anticipated, participants who were trained the most to attend away from pain-related stimuli, towards neutral stimuli, at the longer stimulus duration from pre to post-training also reported the greatest reductions in pain interference from pre-training to follow-up. The association between change in attentional bias in initial orienting and change in pain interference was non-significant, *rs* (14) = -.145, *p* = .62, and there was no association between change in attentional bias at 500 ms, *rs* (14) = -.093, *p* = .753, and pain severity. Contrary to expectations, there was no relationship between change in bias at 1250 ms, *rs* (14) = .125, *p* = .671, and pain severity, either.

Control group

Within the Control group, there was a moderate positive correlation between a more neutral bias in maintained attention and increased pain severity (MPQ-SF), *rs* (15) = .683, *p* = .005, suggesting that participants who most diverted their strategic attention away from pain-related stimuli, towards neutral stimuli, from pre to post control task also reported the greatest increases in pain severity from pre control task to follow-up. As expected, the association between change in attentional bias in initial orienting and change in pain severity was non-significant, *rs* (15) = -.002, *p* = .994, and there was no association between change in attentional bias at 500 ms, *rs* (15) = -.188, *p* = .502, or 1250 ms, *rs* (15) = -.055, *p* = .846, and pain interference.

6.4 Discussion

The first aim of the current study was to assess whether the augmentation of attentional bias modification with an implementation intention could enhance the posited analgesic effects of ABM for clinical persistent pain, which it was expected might

particularly occur during the follow-up period. The second aim was to assess whether, as observed in Studies Three and Four, there was an association between the level of neutral bias induced during the ABM session, and changes in key pain outcomes. The third and final aim was to evaluate whether the augmented ABM program resulted in a more pronounced pre - post-training reduction in pain-related attentional bias (which it was anticipated would be particularly evident in maintained attention in this group), in comparison with both the usual ABM and Control groups, as a test of this putative mechanism of action (and to examine the role of perceived attentional control in ABM efficacy).

Concerning the first aim, the main finding was of a quadratic interaction that suggested, whereas, unlike the ABM-IMP group, usual ABM and control participants exhibited a slight reduction in pain severity from pre to immediately post-training, these groups' pain severity returned to approximately baseline levels during the follow-up period. In contrast, the ABM-IMP group reported a small but significant reduction in pain from post-training to follow-up, relative to the other two groups. These findings provided some support for the hypothesis that an added implementation intention would enhance the far-transfer of training-effects to pain reduction (relative to usual ABM and the control group), and that these effects would particularly emerge during the one-week follow-up period (as opposed to immediately post-training, during the session), when the training effects have interacted with participants' everyday experience. It is important to note, however, that, contrary to expectations, no overall reduction in current pain severity was reported from baseline to follow-up, and hence an alternative explanation of these data is that participants' pain severity scores were simply regressing to the mean at final assessment (e.g. Kahneman, 2011). However, deflecting this possible explanation, within-group analyses of the secondary pain outcomes (measured at baseline and follow-up only), suggested there were small to moderate reductions in pain (MPQ-SF) and pain interference (BPI), respectively, in the ABM-IMP group, that did not occur in the control group. These findings add to those of Carleton et al. (2011) and Schoth et al. (2013), who found that usual ABM resulted in within-subjects reductions in pain at post-training, and provide tentative evidence that this type of attentional retraining, with a simple added implementation intention instruction, can also alleviate pain after one-week. Larger studies are needed to establish the presence or absence of condition-level effects of ABM on these symptom outcomes, and validate these preliminary results, before firm conclusions can be drawn.

Findings from the correlational analyses supported the hypothesis that pre to post-training induced change in attentional bias in maintained attention would be associated with change in pain experience from baseline to one-week follow-up. Specifically, there was a trend-level (two-tailed) moderate negative correlation between improvement in attentional bias at 1250 ms and reduction in pain interference, but not pain severity, within the ABM-

IMP group, suggesting that when maintained attention was trained with the added implementation intention instruction, the resultant change in attentional bias was associated with a reduction in pain interference over the course of the study. Unlike in Study Four, the association between change in attentional bias at 1250 ms and reduction in pain severity in the ABM group did not reach significance (p = .21, two-tailed), although the small effect size (r = -.22) was in the predicted direction. In addition, there was a moderate association between the degree of induced neutral bias in initial orienting and pain reduction in the ABM, but not the ABM-IMP group. Overall, these findings suggest that change in attentional bias in initial orienting and maintained attention, induced during a single session of ABM and ABM-IMP (each with randomised stimulus durations of 500 and 1250 ms), is associated with change in pain outcomes at one-week follow-up, broadly corresponding with the correlational findings of Studies Three and Four. Interestingly, as in the current study, in both of these previous studies, 'improvement' in attentional bias in the control group was associated with poorer pain outcomes, supporting the notion that placebo effects on attentional bias do not translate to real-world improvement in pain experience, in either an acute or persistent pain (community-based and clinical) context.

Regarding attentional function, there were no significant pre to post ABM or ABM-IMP changes in pain-related attentional bias, relative to the control group, and the hypothesis that ABM-IMP would particularly result in speeded response times to targets replacing neutral words in comparison with pain words, relative to the other two groups, was not supported. As with previous studies, this calls into question that the mechanism of action is purely change in attentional bias (e.g. Schoth et al., 2013). Perceived attentional control was measured at baseline and follow-up to test the corollary hypothesis that ABM increases ACS, which may in turn facilitate the down regulation of pain distractors; however, there was no evidence to support this putative mechanism either. These findings add to increasing research (e.g. Boettcher et al., 2013; Boettcher, Hasselrot, Sund, Andersson, & Carlbring, 2014; Carlbring et al., 2012; Everaert et al., 2014; Rapee et al., 2013; Study Four) that has not replicated early findings which indicated a single session of ABM could alter attentional bias at the condition level (e.g. Amir, Weber, Beard, Bomyea, & Taylor, 2008).

As with previous studies (e.g. Everaert et al., 2014), there was large inter-individual variability in attentional bias, both within and across the training conditions, which suggests that ABM successfully modified attentional bias in a subset of the trained individuals (44% of participants had an overall neutral bias induced in each of the ABM groups). One possible explanation for these data is that ABM is most effective for those individuals in whom baseline attentional control is higher (Everaert et al., 2014; Mackintosh & Fox, 2014). This hypothesis was partially supported in the present study by a two-tailed trend-level moderate positive correlation between baseline perceived control of attentional shifting (which is

arguably the component of attention particularly pertinent to the dot-probe task) and pre to post-training improvement in attentional bias in maintained attention within the ABM-IMP group. This finding suggests that the higher participants' level of perceived control of attentional shifting was at baseline, the greater their pre - post shifts in maintained attention from pain stimuli towards neutral stimuli on the dot-probe task. More research is needed to investigate the importance of attentional control to ABM efficacy for pain and psychopathology. Finally, the current absence of evidence for training effects on attentional bias reignites previous doubts over the reliability of the dot-probe task for attentional bias measurement, potentially undermining the detection of training-induced changes in bias (Everaert et al., 2014; Schmukle, 2005). Nevertheless, this absence of evidence of ABM effects on pain-related attentional bias does not constitute evidence of absence of such effects, as corroborated by the current complete-case between-subjects effect size. Hence, future research should aim to optimise measurement of attentional bias in persistent pain populations, which will in turn facilitate understanding of the role of distorted attentional processing in chronic pain experience.

The present study had a number of limitations. First, while 55 participants joined the study, the combination of attrition and the factorial design meant that each condition contained only a third of the 45 participants who completed the study. This means that intricate effects of ABM and ABM-IMP, such as their differential impact on pain measurements relative to the control group at the condition level, may have been detectable if the sample size had been larger (Browning et al., 2012). Sample size was restricted by the challenges of recruiting a clinical persistent pain population, although the minimum sample size requirement was met. Second, the current aim was to provide a preliminary assessment of whether adding an IMP to an ABM program is feasible, together with initial evidence for whether or not the training impacts on attentional bias and pain outcomes. Since previous research had suggested that a single session of ABM was sufficient to modify attentional bias (e.g. Amir et al., 2008), it was decided to implement a single session of ABM with pre to post-training test trials, and one-week follow-up with postal questionnaires. A pragmatic advantage of this approach was that it minimised participant burden and attrition, with all the attentional data collected within a single laboratory session, and thereby retained greater power for more meaningful analyses. However, the success of the approach is contingent on the premise that a single session (in this case 384 ABM trials) is sufficient to induce the predicted changes. It may be the case that multiple sessions, spread over an extended period of time (e.g. four weeks) is required for full training effects to be realised at post-training and follow-up assessments, with more work on the optimal number of sessions needed. In addition, were the current study to be replicated and extended, it would be useful to include

a measure of attentional bias at follow-up, so that stability of any induced attentional bias can be tracked over time, and correlated with symptom outcomes.

In summary, this study provides initial evidence that the addition of an implementation intention instruction to an ABM program can enhance the transfer of protective training effects against vulnerability to some aspects of persistent pain experience (pain severity and pain interference, but not distress). In addition to the quadratic effect of ABM-IMP on current pain severity across the three assessment points, there were within group reductions in MPQ-SF scores and BPI-interference scores within the ABM-IMP group, and a strong association was found between improvement in attentional bias in maintained attention and reduction in pain interference. However, the absence of an overall linear reduction in current pain severity from baseline to follow-up, as well as time by group interactions for the secondary pain outcomes, entails that these findings must be interpreted with caution, and replication is needed. Future research could administer multiple sessions of augmented ABM and test its efficacy for persistent clinical pain in a larger sample, measure the impact of ABM-IMP on attentional bias using an alternative measure of attentional bias to the dot-probe, and further consider whether and how dispositional attentional control is active in ABM efficacy. Exploration along these avenues is needed to eliminate alternative explanations of the present findings. Nevertheless, it is noteworthy that a single session of implicit attentional retraining had small to moderate effects on persistent clinical pain after one week. This apparent potential for a straightforward, cost-effective intervention to have real impact on chronic pain experience clearly warrants further investigation.

Chapter 7

Assessing the efficacy of attentional bias modification for adult pain: Updated meta-analysis

7.1 Introduction

The current thesis explored the efficacy of attentional bias modification (ABM) for pain in adults, and, specifically, of targeting different stages of attention (initial orienting versus maintained attention) on key pain outcomes such as severity ratings, in both acute experimental and persistent pain. The impact of ABM on attentional bias in initial orienting versus maintained attention was also assessed. Three studies were conducted in which pain-related attentional bias was trained away from pain-related information and towards neutral information, using the visual-probe task. The effects of this attentional retraining on pain severity and attentional bias was compared with a placebo computer-based task. Building on previous research suggesting that biased processing in maintained attention may be particularly implicated in pain chronicity (e.g. Schoth et al., 2012), the present studies additionally manipulated the duration of the training stimulus presentation time. Findings indicated that training initial orienting (operationalised as a training stimulus presentation of 500 ms) may be particularly efficacious for acute experimental pain, while targeting both initial orienting and maintained attention (500 and 1250 ms) may be more beneficial for individuals with persistent pain. In Chapter Four, ABM at 500 ms resulted in healthy volunteers rating cold pressor pain as less severe in comparison with both ABM-1250 and placebo training groups, while in Chapter Five a community-based sample of individuals with persistent pain exhibited an attentional bias in maintained attention and not initial orienting at baseline, and there was no difference in the efficacy of the ABM at 500 and 1250 ms in successfully redirecting this attentional bias towards neutral stimuli, in comparison with a sham training control group. In spite of these apparent training effects in maintained attention, no evidence was found for an impact of ABM on pain severity at post-training. There was, however, a strong negative correlation between increased attending to neutral information at 1250 ms and decreased pain severity ratings at this time-point. It was hypothesised that effects of training on persistent pain severity may be more evident after a follow-up period, during which time the effects of ABM will have interacted with an individual's everyday experience. These predictions were supported in Chapter Six, where evidence of an impact of ABM-IMP (administered at both 500 and 1250 ms) on pain severity in a clinical persistent pain population emerged only at follow-up, one-week after the ABM session.

Thus, whilst there is empirical evidence at the individual-study level that supports the theoretical position which states that attentional bias impacts on pain experience, findings, including those outwith the current thesis, have been inconsistent and the

efficaciousness of ABM to reduce pain severity and contribute to analgesic requirements, together with the mechanism of action, has not been established (e.g. Sharpe et al., 2012). Although the initial meta-analysis (Chapter Two) demonstrated that ABM successfully reduced attentional bias at 500 ms, the effect on pain severity was unsupported, and there were insufficient studies to perform subgroup analyses that could more pointedly examine training effects. As discussed there, mixed findings may be in part due to methodological differences between studies. An updated meta-analysis, incorporating the studies of the present thesis, is needed to assess the combined effects on the defined temporal stages of attentional bias, and acute versus chronic pain experience. The aim of the present meta-analysis was to update the meta-analysis of Chapter Two, and quantitatively synthesise the findings of this thesis with those of studies by other researchers on this topic.

7.2 Method

The method applied was as reported in Chapter Two, with the same search strategy and inclusion and exclusion criteria applied. No further published studies were found as a result of the systematic search.

7.2.1 Meta-analytic approach

As described in Chapter Two, data suitable for pooling were entered into RevMan 5.2 software (RevMan, 2011), and findings from the individual studies and their treatment effect were summarised in forest plots for each outcome comparison. Whereas, in the first meta-analysis, it was not possible to carry out the planned subgroup analyses due to the limited number of studies, in the present meta-analysis, subgroup analyses were conducted for type of pain (acute/experimental, of comparatively short duration, < 3 months; persistent, of long duration, ≥ 3 months). As no studies were identified outside the current thesis that reported effects of ABM at 1250 ms on pain outcomes or measured attentional bias at 1250 ms post-training, in comparison with a control group, it was not possible to perform subgroup analyses by training and test stimuli duration.

Pain severity was again assessed using visual analogue scales (VAS) or numeric rating scales (NRS), and treatment effects were estimated using standardised mean differences (SMD) by extracting means, standard deviations, and sample size at post-treatment and/or follow-up. Treatment effects were the SMD between experimental and control conditions for VAS and NRS outcomes measured on a 0 to 10 scale. The other continuous and response rate outcomes were treated similarly, and SMD treatment sizes calculated. As in Chapter Two, where both per protocol and intention-to-treat data were reported, the latter estimate was used in the meta-analysis.

7.2.2 Assessment of study heterogeneity

Data were assessed for heterogeneity using the chi-square and I^2 statistics, with a value above 40% for this latter statistic indicating that moderate heterogeneity may be present (Andersson et al., 2014; Crowther et al., 2010; Higgins & Green, 2008).

7.3 Results

7.3.1 *Study and sample characteristics*

All three ABM studies conducted for the present thesis were eligible for inclusion in the meta-analysis, which, added to the studies deemed eligible for inclusion in Chapter Two, resulted in a total of seven studies (N = 365 participants). An overview of the studies added from the current thesis is presented in Table 7.1. The age of participants included ranged from 18 to 78, and all studies sampled both males and females.

Table 7.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)
PhD Study 3 "Attentional bias modification for acute experimental pain: A comparison of training effects at earlier versus later attention on pain severity, threshold and tolerance"	Participants were randomly allocated to condition. Method of randomisation was online randomiser. The study did not claim that condition allocation was concealed. Participants but not study personnel were blinded. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was one hour, and took place in a University.	*N* = 72. Mean age = 20.04, SD = 2.26; age range 18 - 28. Male and female. Participants were healthy volunteers, recruited predominantly from first year psychology courses. Inclusion criteria were: aged 18-35; fluent English speaker; normal or corrected-to-normal vision; and able to read and understand text displayed on a computer screen. Exclusion criteria were: current acute (> 4/10 VAS) or chronic pain or history of chronic pain within the past six months; history of cardiovascular disorder; history of fainting or seizures; history of frostbite; presence of open cuts or sores on the left hand or forearm; history of Raynaud's	Acute experimental pain (cold pressor).	Single session (approx. 30 minutes). 192 trials per session. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms versus 1250 ms. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced neutral words. Stimuli presented vertically.	Sham training – single session lasting approx. 30 minutes. 192 trials per session. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 ms versus 1250 ms. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced pain and neutral words with equal probability Stimuli presented vertically.	A primary outcome was not specified.	Pain severity measured during the cold pressor task (CPT; at 30 seconds) on an 11 point (0 – 10) numerical rating scale (NRS). Anchors not reported. Pain severity measured when the participant withdrew their arm from the cold water (tolerance) on an 11 point (0 – 10) NRS. Anchors not reported. Pain threshold (time taken in seconds to first register pain). Pain tolerance (total time the participant kept their arm in the cold pressor).	Attentional bias was measured using the dot-probe task. 96 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 and 1250 ms, randomised. Word pairs (sensory and affective pain; household neutral). Word pairs matched for length and frequency. 100% of trials were critical. Stimuli presented vertically.	Pain outcomes were assessed post-training (during the CPT).

Table 7.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)
		syndrome; any current medical condition; and recent use of analgesics (within past six hours).					The NRS has been validated by previous research.		
PhD Study 4 "Attentional bias modification for persistent pain: a comparison of training initial orienting versus maintained attention on attentional bias, anxiety sensitivity, pain severity and disability"	Participants were randomly allocated to condition. Method of randomisation was online randomiser. The study did not claim that condition allocation was concealed. Participants but not study personnel were blinded. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study. The duration of the study was two weeks, and took place in a	*N* = 57. Mean age = 42.46 (*SD* = 16.33). Age range 18 - 70. Male and female recruited from community. Inclusion criteria were: chronic benign musculoskeletal pain that had lasted for three months or more; fluent English speakers; aged 18-70 years; normal or corrected-to-normal vision; able to read and understand text displayed on a computer screen, and able to use a computer keyboard comfortably for 30 minutes. Exclusion criteria were: pain related to a progressive disease; undergoing	Persistent pain (≥ 3 months)	Two sessions per week for two weeks (four session total). 384 trials per session. Completed on a lab PC. Participants tested in small groups. Probe classification version of the dot-probe task. Stimuli presented for 500 ms versus 1250 ms. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were critical.	Sham training. Two sessions per week for two weeks (four session total). 384 trials per session. Completed on a lab PC. Participants tested in small groups. Probe classification version of the dot-probe task. Stimuli presented for 500 ms versus 1250 ms. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were critical. Probe replaced pain and	Yes - attentional bias index.	Anxiety Sensitivity Index – 3. Fear of Pain Questionnaire – Short-Form. Hospital Anxiety and Depression Scale (HADS) – anxiety and depression. McGill Pain Questionnaire – Short-Form. Pain Disability Index.	Attentional bias was measured using the dot-probe task. 192 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 and 1250 ms, randomised. Word pairs (sensory and affective pain; household neutral). Word pairs matched for length and frequency.	Pain outcomes were assessed post-training. Attentional bias was measured post-training.

Table 7.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)
	University.	psychological treatment for pain, such as cognitive behavioural therapy, currently or within the past three months, and change in pain medication within the past three months.		Probe replaced neutral words. Stimuli presented vertically.	neutral words with equal probability. Stimuli presented vertically.			100% of trials were critical. Stimuli presented vertically.	
PhD Study 5 "Attentional bias modification for persistent pain: clinical sample"	Participants were randomly allocated to condition. Method of randomisation was online randomiser. The study did not claim that condition allocation was concealed. Participants but not study personnel were blinded. There was no evidence of incomplete outcome data or systematic differences in withdrawals from the study.	*N* = 49. Mean age = 41.39, *SD* = 15.61; age range 18 – 78. Male and female. Inclusion criteria were: chronic benign pain of any origin that had lasted for three months or more and had received a diagnosis; fluent English speakers; aged 18 or over; normal or corrected-to-normal vision; able to read and understand text displayed on a computer screen, and able to use a computer keyboard comfortably for 30 minutes. Exclusion	Clinical persistent pain (≥ 3 months)	Single session (30 mins; 384 trials). Completed on a lab PC. Participants tested in small groups. Probe classification version of the dot-probe task. Stimuli presented for 500 ms versus 1250 ms. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were	Single session (30 mins; 192 trials). Completed on a lab PC. Participants tested in small groups. Adapted version of the implicit association test. Word pairs (sensory and affective pain; neutral household). Word pairs matched for length and frequency. 100% of trials were critical. Words presented in centre of screen.	Yes – attentional bias index and pain severity.	Brief Pain Inventory McGill Pain Questionnaire – Short-Form. Hospital Anxiety and Depression Scale (HADS) – anxiety and depression. Pain Catastrophizing Scale Attention Vigilance and Awareness Questionnaire Attentional	Attentional bias was measured using the dot-probe task. 96 trials in each (pre/post) attentional bias test. Completed on a lab PC. Participants tested individually. Probe classification version of the dot-probe task. Stimuli presented for 500 & 1250 ms. Word pairs (sensory and affective pain; assorted neutral). Word pairs matched	Pain outcomes were assessed post-training. Attentional bias was measured post-training.

Table 7.1

Characteristics of included studies

Study author, title and location	Methods	Participants	Pain type	ABM	Control task	Primary outcome specified?	Secondary pain outcomes	Attentional bias assessment	Outcome measurement time-point(s)
	The duration of the study was one week and took place in a University.	criteria were: pain related to a progressive disease; undergoing psychological treatment for pain, such as cognitive behavioural therapy, currently or within the past three months, and change in pain medication within the past three months.		critical. Probe replaced neutral words. Stimuli presented vertically			Control Scale	for length and frequency. 100% of trials were critical.	

7.3.2 Data synthesis

Impact of ABM on attentional bias in initial orienting

Homogeneity of the included studies was indicated by an I^2 value of 0%, χ^2 (5) = 2.96, p = .70, and therefore a fixed effects model was applied.[17] This model suggested that, overall, participants in the ABM group had a more neutral attentional bias in initial orienting after ABM than control group participants, g = -0.33, CI = -0.55 to -0.12, and this small effect size was significant, Z = 3.09, p = .002, as depicted in the first forest plot and summary of findings table (Figure 7.1; Table 7.2). Subgroup analyses indicated that the difference in effect sizes for attentional bias at 500 ms following ABM, in the acute pain versus chronic pain subgroups, was not significant, $\chi^2 < 1$, suggesting that the effect of ABM on attentional bias in initial orienting was comparable between these pain types.

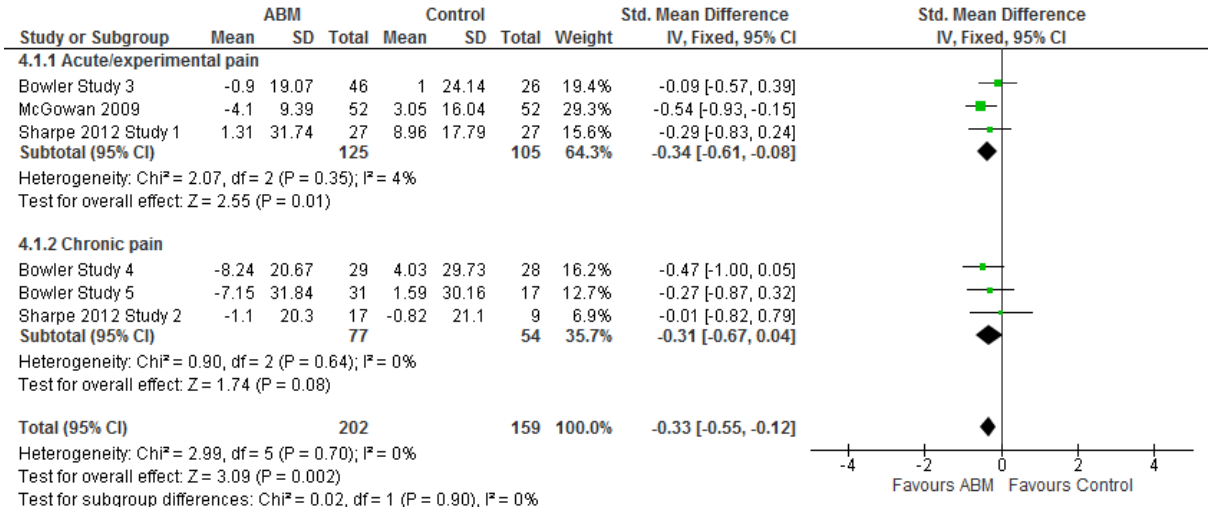


Figure 7.1 Forest plot displaying post-training attentional bias (500 ms) effect sizes of studies comparing ABM with a control group, divided into acute/experimental pain and chronic pain subgroups.

Impact of ABM on attentional bias in maintained attention

Results of a fixed effects model (I^2 = 15%; χ^2 (2) = 2.35, p = .31) indicated that, contrary to expectations, ABM did not produce an overall effect on attentional bias at 1250 ms across the three included studies to have measured attentional bias at this stimulus duration (PhD studies 3 - 5), g = 0.23, CI = -0.07 to 0.54, Z = 1.48, p = 0.14, suggesting that ABM failed to redirect pain-related attentional bias in maintained attention, as measured at post-training (see Table 7.2).[18]

[17] Results were very similar using a random effects model, with a significant overall effect of ABM on attentional bias in initial orienting, g = -0.33 [CI – 0.55 to – 0.12], Z = 3.09, p = .002. This effect was significant for the acute/experimental pain subgroup, g = -0.34 [CI – 0.61 to – 0.07], Z = 2.49, p = .01, and reached trend-level significance for the persistent pain subgroup, g = -0.31 [CI = -0.67 to 0.04], Z = 1.74, p = .08.

[18] Results were comparable using a random effects model, such that ABM did not reduce attentional bias at 1250 ms relative to controls, g = 0.23 [CI = -0.11 to 0.56], Z = 1.34, p = .18.

Table 7.2

Summary of findings

Outcomes	Illustrative comparative risks [95% CI]		*p-value*	No of participants (studies)	Comments
	Assumed risk	Corresponding risk			
	Control	ABM			
Pain severity NRS and VAS	The mean pain severity rating ranged across control groups from 1.93 to 6.84	The mean pain severity rating in the intervention groups was -0.27 lower [-0.48 to -0.06]	.01	364	A lower comparative pain severity score indicates that ABM participants reported lower current pain severity on the NRS/VAS, in comparison with controls.
Pain severity - acute/experimental pain NRS and VAS	The mean pain severity rating ranged across control groups from 1.93 to 6.84	The mean pain severity rating in the intervention groups was -0.48 lower [-0.76 to -0.2]	.0007	211	
Pain severity - persistent pain NRS and VAS	The mean pain severity rating ranged across control groups from 3.30 to 5.67	The mean pain severity rating in the intervention groups was 0.02 higher [-0.31 to 0.35]	.90	153	
Attentional bias 500 ms dot-probe task	The mean attentional bias index ranged across control groups from -0.82 to 8.96	The mean attentional bias index in the intervention groups was -0.33 lower [-0.55 to -0.12]	.002	361	
Attentional bias 500 ms - acute/experimental pain dot-probe task	The mean attentional bias index ranged across control groups from 1.00 to 8.96	The mean attentional bias index in the intervention groups was -0.34 lower [-0.61 to -0.08].	.01	231	A lower comparative attentional bias score indicates that ABM participants exhibited a greater tendency to attend away from pain stimuli presented for 500 ms towards neutral stimuli presented for 500 ms on the dot-probe task, in comparison with control participants.
Attentional bias 500 ms - persistent pain dot-probe task	The mean attentional bias index ranged across control groups from -0.82 to 4.03	The mean attentional bias index in the intervention groups was -0.31 lower [-0.67 to 0.04]	.08	131	
Attentional bias 1250 ms dot-probe task	The mean attentional bias index ranged across control groups from -9.33 to -1.93	The mean attentional bias index in the intervention groups was 0.23 higher [-0.07 to 0.54]	.14	177	A higher comparative attentional bias score indicates that control participants exhibited a greater tendency to attend away from pain stimuli presented for 1250 ms towards neutral stimuli presented for 1250 ms on the dot-probe task, in comparison with ABM participants.

Note: The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval

Impact of ABM on pain severity

Homogeneity of the included studies was indicated by an I^2 value of 36%, χ^2 (6) = 9.42, p = .15, and therefore a fixed effects model was applied.[19] This model suggested that, overall, participants in the ABM group reported lower pain severity than control group participants, g = -0.27, CI = -0.48 to -0.06, and this small effect size was significant, Z = 2.5, p = .01, as depicted in the below forest plot (Figure 7.2). Subgroup analyses revealed that acute pain (including experimental pain) was modulated by change in attentional bias, with ABM participants reporting less severe pain than controls, g = -0.48, CI = -0.76 to – 0.2, Z = 3.4, p = .0007. There were no effects of ABM on persistent pain severity, g = 0.02, CI = -0.31 to 0.35, Z = 0.12, p = .90. The difference between the subgroups was significant, χ^2 (1) = 5.3, p = .02, suggesting that ABM reduced acute but not persistent pain intensity.

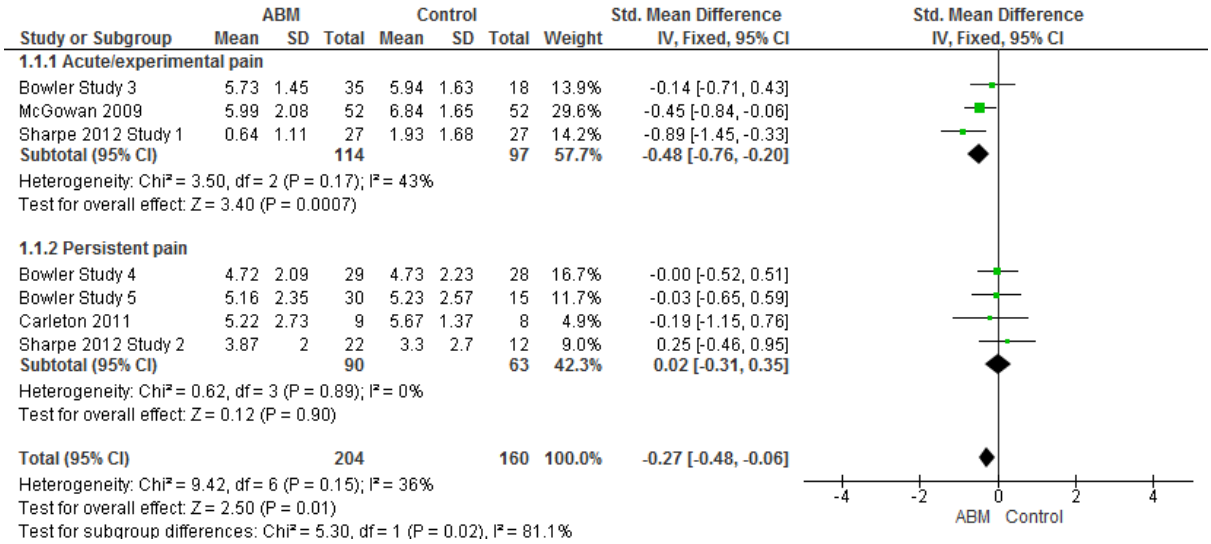


Figure 7.2 Forest plot displaying post-training/follow-up pain severity effect sizes of studies comparing ABM with a control group, divided into acute/experimental pain and chronic pain subgroups.

7.4 Discussion

The present meta-analysis updated the review of Chapter Two with the addition of the three thesis studies that tested ABM effects on attentional bias (in initial orienting and maintained attention) and pain severity. Importantly, results demonstrated that ABM successfully reduced attentional bias in initial orienting (herein 500 ms) and that training effects resulted in a reduction in acute pain severity. These findings support the hypothesis

[19] Results were comparable using a random effects model, with a trend-level overall effect of ABM on pain severity, g = -0.25 [CI -0.52 to 0.03], Z = 1.75, p = .08, that was evident in acute/experimental pain, g = -0.49 [CI -0.87 to -0.11], Z = 2.51, p = .01, and not persistent pain, g = 0.02 [CI -0.31 to 0.35], Z = .12, p = .90.

that biased attentional processing in initial orienting modulates acute pain severity, and provide evidence that it may represent a legitimate therapeutic target for this population.

The second main finding was that ABM did not reduce persistent pain severity. Even though there was a trend-level reduction in attentional bias at the shorter stimulus presentation time (500 ms) within the persistent pain subgroup, these training effects did not produce a concomitant reduction in pain ratings. This trend-level induction of a neutral bias in initial orienting and absence of analgesic effects suggests that targeting initial orienting alone may not be sufficient to exert a reliable therapeutic impact on persistent pain (Grafton et al., 2014). This may be because persistent pain is not cognitively characterised solely by a maladaptive pattern of initial orienting, but also a difficulty in disengaging from, and excessive dwelling upon, pain stimuli once they have captured attention (e.g. Sharpe, Dear, & Schrieber, 2009; Van Damme et al., 2004a). This view is supported by those empirical studies that have found a more pronounced attentional bias in maintained attention in this population (e.g. Liossi et al., 2009, 2011; Chapter Three) and that targeting biases in maintained attention in addition to initial orienting may help alleviate persistent pain (Schoth et al., 2013; Chapter Six). The limited number of studies meant that it was not possible to isolate this question in the current statistical synthesis. What was suggested was that the current paradigm did not reduce attentional bias in maintained attention, and hence it cannot be concluded that modifying attentional bias at this stimulus duration does not influence persistent pain, underscoring the need for further research on the role of sustained attention in persistent pain experience. Future studies of ABM for persistent pain should seek to develop techniques that modify maintained attentional bias, perhaps through incorporating a longer stimulus presentation duration as in Schoth et al. (2013) and Study Five, and additionally aim to test the effects of this intervention after a prolonged follow-up period.

The current meta-analysis had a number of limitations. First, it was not possible to perform all of the planned subgroup analyses due to the limited number of studies available. No studies have been published in 2014, and since the initial meta-analysis (Chapter Two), by other researchers addressing this topic. Second, it should be noted that subgroup analyses are entirely observational in their nature. These analyses were used to investigate identified differences between studies in the type of pain population recruited. Even though individuals were randomised to the experimental or control group within each study, they were not randomised to go into one study or another. Therefore, these analyses suffer the limitations of any observational investigation, such as potential bias, through confounding by other study-level characteristics (Higgins & Green, 2008).

In conclusion, the current meta-analysis of ABM for pain has provided clear evidence that ABM reduces pain-related bias in initial orienting and reduces vulnerability to acute pain, with small to moderate effect sizes comparable to those of some pharmaceutical

analgesics (e.g. Ong, Lirk, Seymour, & Jenkins, 2005). There was no effect of ABM on maintained attentional bias, which is the putative maladaptive stage of attention in persistent pain. Theoretically corresponding to this finding, there was no evidence for a therapeutic effect of ABM on persistent pain severity. Hence, implicit attentional strategies optimal for persistent pain management are likely to differ from those efficacious for acute or procedural pain.

Chapter 8

Overall discussion

8.1 Summary of studies

The current thesis aimed to investigate the temporal components of attentional bias in pain, and examine the influence of modifying biased initial orienting (500 ms) and maintained attention (1250 ms) on vulnerability to pain, using the dot-probe task. To test the thesis hypotheses (Introduction 1.5), the first two experimental studies measured the impact of persistent musculoskeletal pain (Study One) and acute cold pressor pain (Study Two) on the time course of attentional bias. Next, the optimal presentation duration for ABM stimuli was assessed. Participants were trained to favour the benign option of presented pain-neutral word pairs in initial orienting and/or maintained attention, and effects on pain experience (e.g. severity and interference) and response to pain (e.g. tolerance) were quantified (Studies Three, Four and Five). In each ABM study, attentional bias in initial orienting and maintained attention was measured at pre and post-training. This provided information concerning the temporal effects of ABM on attentional bias, in comparison with controls, and whether change in bias in earlier and/or later attention was associated with changes in pain outcomes (the posited mechanism of action). Individual differences in identified cognitive risk factors for pain were measured in all studies to describe samples and, where relevant to individual study aims, assess their association with attentional bias and training induced bias acquisition. A systematic review and meta-analysis was conducted (Chapter Two), which situated the current programme of research within its empirical context, and this was updated with the studies from this thesis in Chapter Seven.

Each study will be briefly summarised below to remind the reader of their specific aims and results. Next, their original contributions to the field will be integrated and interpreted in the context of the literature. Clinical implications concerning the application of ABM techniques for pain management will be discussed, which will be followed by consideration of the limitations of the collective studies, and suggestions for future research.

Chapter Two: Systematic review and meta-analysis

Prior to the experimental studies, Chapter Two presented the first systematic review and meta-analysis of attentional bias modification for adult pain. The aim of this review was to assess the efficacy of ABM for reducing pain severity and determine its effects on attentional bias. Findings suggested that ABM could reduce pain-related bias; however, the synthesised data failed to provide clear support for the hypothesis that modifying the bias would result in a post-training reduction in pain severity, with a small trend-level effect only that favoured the ABM-group. Importantly, a number of methodological factors were identified that helped to explain the absence of therapeutic effects, such as the timings of attentional bias modification for acute and persistent pain. The impact of pain (acute

experimental and chronic) on attentional bias in initial orienting and maintained attention, and the optimal ABM stimulus duration for pain, were explored in the experimental studies.

Chapter Three: Study One

The aim of the first experimental study was to replicate previous cross-sectional investigations of the time course of attentional bias in persistent headache, and extend these findings to a persistent musculoskeletal pain population. Study One tested the hypothesis that individuals with clinical persistent musculoskeletal pain would exhibit a pain-related bias in comparison with healthy controls, and examined whether this bias was evident in initial orienting and/or maintained attention, prior to seeking to retrain the bias in individuals with chronic musculoskeletal pain in Chapters Five and Six. Findings supported the hypothesis, providing evidence for the predicted significant overall attentional bias towards pain stimuli in the persistent pain group, in comparison with the control group. When compared with zero (no bias) within the persistent pain group, the bias effect size was almost twice as large in maintained attention (r = -2.9) than initial orienting (r = -1.5), in line with previous findings on its time course (Schoth et al., 2012 review). Hence, it was concluded that both earlier and later attention is biased towards noxious stimuli in persistent pain, and that maintained attention may be particularly implicated in persistent pain experience.

Chapter Four: Study Two

Study Two investigated the impact of acute cold pressor pain on attentional bias in initial orienting and maintained attention. The aim of this study was to test the hypothesis that the experimental pain induction, in non-clinical participants, would result in an attentional shift in both earlier and later attention. The influence of dispositional anxiety on attentional response to pain was also examined. Results indicated that, in participants with lower dispositional anxiety, initial orienting became biased towards neutral information from pre to post the cold pressor task (CPT), whereas there was no effect of pain on maintained attention. This early avoidant effect was not evident in more anxious participants. Contrary to expectations, correlational analyses indicated there was no association between change in attentional bias and pain outcomes measured during the CPT. However, negative correlations were identified between the pre to post CPT development of a more neutral attentional bias in initial orienting (moderate) and maintained attention (weak), and lower post CPT pain severity ratings. Overall, these findings provided initial evidence that the formation of a neutral attentional bias in initial orienting, in particular, may form part of an adaptive healing response to an acute pain stressor that is impaired in anxious individuals.

Chapter Four: Study Three

In the first of three ABM studies, Study Three examined the impact of retraining initial orienting versus maintained attention on cold pressor pain. In Study Two, pain had

impacted on attentional bias (in initial orienting), and this study was designed to test the reverse inference that modifying attentional bias would influence pain. More specifically, the aim was to test the hypothesis that training participants to attend away from pain-related words, and towards neutral words, presented for either 500 ms or 1250 ms, depending on condition, would each increase pain threshold and tolerance, and decrease pain severity, during the cold pressor task, in comparison with a sham training control group (where no bias was trained). Findings suggested that training initial orienting, ABM-500, and not maintained attention, ABM-1250, resulted in higher threshold and tolerance and lower pain severity ratings than the sham training group. However, the predicted effects of training on attentional bias were not found, which was in part attributed to the spatial and temporal proximity of the post-training attentional bias test to the cold pressor immersion. Neutral bias acquisition in initial orienting was positively correlated with higher tolerance (but not threshold), and negatively correlated with pain severity ratings, within the ABM-500 group, and these correlations differed significantly from those of the control group. Overall, it was concluded that training initial orienting was optimal for reducing vulnerability to acute experimental pain, although more work was needed to establish the underlying mechanism of action.

Chapter Five: Study Four

The aim of Study Four was to test the optimal stimulus duration (500 versus 1250 ms) for modifying pain-related attentional bias in a community-based sample of individuals with persistent musculoskeletal pain. Findings indicated that ABM stimulus durations of 500 ms and 1250 ms did not have significantly different effects on attention, each inducing a more neutral bias in maintained attention (but not initial orienting), relative to the control groups. Contrary to expectations, this ‘improvement’ in maintained attention did not translate into a condition-level reduction in pain outcomes at post-training. However, within the ABM-1250 group, a strong negative correlation was identified between the acquisition of a more neutral maintained attentional bias from pre to post-training, and reduction in pain severity. It was concluded that ABM, administered at both stimulus durations, can reduce the biased allocation of maintained attentional resources to pain content in a persistent musculoskeletal pain population. It was reasoned that allowing the induced bias to interact with an individual’s everyday pain experience might be necessary before full training benefits are realised. In addition, the correlational data provided preliminary indication that retraining maintained attention might have therapeutic potential. It was therefore decided to conduct a further study examining the effects of modifying attentional bias on persistent pain, in which the primary pain outcome was measured at baseline, post-training and one-week follow-up.

Chapter Six: Study Five

Study Five examined the efficacy of ABM in a clinical sample of individuals with persistent musculoskeletal pain. The first aim was to test the relative impact of usual ABM and ABM augmented with an added implementation intention plan (ABM-IMP) on pain-related attentional bias. Building on the findings from Study Four, the ABM programs included both the shorter and longer stimulus durations, randomised. It was hypothesised that attentional bias to pain would be reduced in both ABM groups in comparison with controls, and that the greatest reduction in bias would be in maintained attention in the ABM-IMP condition. To explore the intervention's mechanism of action, the relationship between perceived attentional control and bias acquisition was also assessed. The second aim was to test the impact of usual ABM and ABM-IMP on pain severity from pre-training to post-training and follow-up, in comparison with the control group. A quadratic interaction suggested that pain had been rated as less severe from post-training to follow-up (but not from pre to post-training, during the session) in the ABM-IMP group, in comparison with the usual ABM and control groups. However, the predicted training effects on attentional bias were not found, leaving the mechanism of action unclear. A moderate positive correlation between baseline perceived control of attentional shifting (ACS-S) and neutral bias acquisition in the ABM-IMP group suggested that individuals with high ACS-S were more likely to acquire a neutral bias over the course of training. In addition, neutral bias acquisition in maintained attention within the ABM-IMP group was moderately correlated with a reduction in pain interference, but not pain severity, from baseline to follow-up. Contrary to expectations, no significant effects were found for distress. It was concluded that the addition of an implementation intention instruction to an ABM program might enhance the far-transfer of protective training effects against vulnerability to some aspects of persistent pain experience (pain severity and interference).

Chapter Seven: Updated meta-analysis

The aim of this Chapter was to update the meta-analysis from Chapter Two with the ABM studies of the present thesis. Results indicated that ABM had successfully reduced pain-related attentional bias in initial orienting, and that post-training acute pain severity was lower in the ABM group than the control group. Hence, these findings suggested that modifying attentional bias in initial orienting can reduce vulnerability to acute pain. In persistent pain, there was no effect of ABM on maintained attentional bias, which was the putative maladaptive stage of attention in this population. Theoretically corresponding to this finding, there was no evidence for a therapeutic effect of ABM on persistent pain severity. It was concluded that implicit attentional strategies optimal for acute or procedural pain are likely to differ from those which prove beneficial for persistent pain, in having less reliance on mechanisms of sustained attention.

8.2 Integration

Points concerning the interpretation of findings have been made in the discussion sections of each individual chapter of this thesis. The aim of this chapter is to make additional, integrative points that help explain the overall findings concerning the influence of modifying attentional bias on vulnerability to pain, in the context of current literature.

8.2.1 Effects of modifying attentional bias on vulnerability to pain

The reported programme of research has met the primary aim of this thesis, which was to assess the impact of modifying attentional bias in initial orienting and maintained attention on vulnerability to critical pain outcomes. It has produced evidence concerning the effects of retraining earlier and later attention on pain experience, providing important information concerning the optimal stimulus duration (and thereby component stage of bias) at which attention can be targeted using this technique. Before this thesis, no studies had systematically examined the relative impact of modifying the different component stages of attentional bias on vulnerability to pain. Recent research had provided cross-sectional evidence that individuals with persistent headache exhibit an attentional bias towards headache related stimuli, and, crucially, that this bias is particularly evident in maintained attention (e.g. Liossi et al., 2009, 2011; Schoth et al., 2012, 2013). The current thesis extended these findings, providing original evidence on the causal role of the temporal components of attention in pain experience. As such, examination of the optimal timings for attentional bias modification drew on the theoretical premise that attention is non-unitary in nature, comprising ‘earlier’ and ‘later’ components (e.g. Allport, 1989; Mogg et al., 1997; Introduction Section 1.2.3). Attention to pain was also considered to be a particular instantiation of attention to threat (in this case bodily), inherently demanding attention to initiate protective action (Eccleston & Crombez, 1999; Van Damme et al., 2004c). According to this view, individuals may rapidly orient their attention towards pain stimuli owing to automatic attentional capture (Mogg et al., 1997; Van Damme et al., 2004c). This early diversion of attentional resources to pain was thought to enable the unpleasant sensation to act as an ‘alarm signal’, alerting the organism to possible corporeal harm (Eccleston & Crombez, 1999; Van Damme et al., 2004c, 2010).

Previous research had suggested that individuals with persistent pain may selectively attend to pain signals in initial orienting, and additionally maintain their attention on pain-related information, which could reflect a difficulty in disengaging from, and excessive dwelling upon, this content (Schoth et al., 2012). No studies had examined the impact of acute (including experimental) pain on maintained attention, leaving unclear whether the maintenance of attention on pain was a particular feature of pain chronicity, or pain in general. Moreover, at commencement of this thesis, very little research had been conducted examining the causal influence of modifying attentional bias on pain experience.

A single study had tested the impact of modifying attentional bias (in this case initial orienting) on pain (acute experimental; McGowan et al., 2009). No studies had sought to modify attentional bias in persistent pain. During the course of this thesis, studies have been published reporting trials of ABM-500 for persistent pain (Carleton et al., 2011; Sharpe et al., 2012). However, no research has systematically compared the effects of modifying initial orienting and maintained attention on acute and persistent pain experience; this thesis addresses that gap in the literature.

Overall, the findings of this programme of work support the hypothesis that modifying attentional bias influences vulnerability to pain, as indicated by the meta-analysis of Chapter Seven. This suggested that, following training, participants who undertook ABM reported lower pain severity and exhibited a more neutral attentional bias in initial orienting, in comparison with control participants, with each outcome yielding a significant overall effect size. Findings from the individual studies were somewhat mixed, however, pointing to important theoretical implications concerning the application of ABM for persistent pain populations, in particular, which will be discussed in due course. Mechanisms of initial orienting were activated in acute experimental (cold pressor) pain (Study Two) and retraining initial orienting reduced vulnerability to the cold pressor induction (Study Three). These findings extended those of McGowan et al. (2009), who found that inducing a pain-related bias reduced pain threshold and increased pain severity ratings during cold pressor immersion, relative to a neutral retraining group. In the absence of a placebo training control group, however, this study could not isolate treatment effects. In addition, the ABM program only included one stimulus duration (500 ms), leaving the role of maintained attention in acute pain experience untested (McGowan et al., 2009). The collective findings concerning threshold are particularly noteworthy, as they suggest that manipulating attentional bias in initial orienting, and not maintained attention, influences how rapidly individuals notice pain, which equates to a measure of actual pain hypervigilance. In Studies Three and Four (pain free participants), the absence of a baseline pain-related attentional bias supported the notion that hypervigilance to pain-related stimuli in chronic pain might emerge as the working of normal mechanisms, in an abnormal, persistent pain context (Van Damme et al., 2004c). In line with expectations, persistent musculoskeletal pain had a small impact on initial orienting (Study One) and a larger impact on maintained attention (Study One). Together, the findings of Studies Four and Five were in line with other studies of ABM for persistent pain which have failed to find a reliable, condition-level effect of ABM on attentional bias and symptom outcomes (e.g. Sharpe et al., 2012). These results were confirmed by the meta-analysis of Chapter Seven, where subgroup analyses revealed that the effects of ABM on attentional bias in initial orienting and pain severity were each significant for acute pain, whereas neither reached significance for persistent pain. These findings

suggest that mechanisms of initial orienting are causally implicated in acute pain experience, whereas the picture for persistent pain appears more complex.

8.2.2 Interpretation

Dual-process models of neural organisation provide a useful heuristic for interpreting the current findings concerning the relationship between attention and pain. As discussed in the Introduction (Chapter One, Section 1.2.3), these models propose that there are two distinct modes of processing: a relatively automatic mode that is fast and reflexive and a more strategic mode that is slower and effortful (Browning et al., 2010a; Carver et al., 2008; Gyurak, Gross, & Etkin, 2011, for reviews). The relatively automatic mode of processing is thought to rely on bottom-up mechanisms of associative memory; it is intuitive, uses short-cuts and heuristics and functions rapidly. This mode of processing is used for urgent acts (Carver et al., 2008). In contrast, the strategic system is thought to depend on top-down mechanisms of executive control, is broadly understood as the rational mind, uses symbolic representation, is reflective, and functions comparatively slowly (Carver et al., 2008; Wiers et al., 2013). This strategic mode of processing is used for planning and intentional behaviour. The distinction between bottom-up (driving) and top-down (modulatory) processes broadly parallels feedforward and feedback neural connections within the neocortex and related structures (Serre, Chikkerur, Kreiman, & Poggio, 2007). Importantly, the two modes of processing are thought to interact with one another such that their relative weightings determine emotion regulation (Gyurak et al., 2011) and behaviour (Carver et al., 2008; Deutsch & Strack, 2006). The findings of this thesis suggest that acute pain processing may particularly recruit relatively automatic, fast-acting, bottom-up processes of early vigilance. Moreover, they suggest that this rapid deployment of attention to pain is integral to the speed at which pain is detected and escape behaviour is initiated (Study Three). Here, retraining initial orienting (and not maintained attention) away from pain words, towards neutral words, increased pain threshold and tolerance, in comparison with the control group. These findings are in line with the suggestion of the cognitive-affective model of the interruptive function of pain that for healthy individuals, acute pain acts as an alarm signal, resulting in the rapid diversion of early attention to the nociceptive event, and that this early vigilance to pain facilitates pain perception and initiates protective action (Eccleston & Crombez, 1999). Importantly, they also suggest that in instances where the ‘alarm signal’ facet of pain is no longer needed, or it would be helpful to turn it down (such as in minor medical procedures), retraining initial orienting could potentially represent a valid therapeutic target, warranting further investigation in randomised controlled trials (see Section 8.3).

It is thought that the adaptive early vigilance for pain exhibited by healthy individuals can become maladaptive when it is prolonged, and at the expense of other

aspects of life (Carver et al., 2008; Crombez, Van Damme, & Eccleston, 2005; Van Damme et al., 2004c). Persistent pain can have a profound effect on the individual, negatively impacting on multiple spheres of their life (Breivik et al., 2006). This is reflected in the elevated levels of comorbid depression documented in clinical pain populations (Breivik et al., 2006; Pincus & Morley, 2001; Study Five). When considering the components of attentional bias active in persistent pain, the collective findings suggest that mechanisms of initial orienting are deployed to pain cues (this component can be likened to the 'alarm that won't switch off'; Van Damme et al., 2004c), and that concomitant elaborative processing might impede disengagement, resulting in the maintenance of attention on pain (Liossi et al., 2009, 2011; Schoth et al., 2013; Study One). The consistent finding that the use of longer stimulus durations results in the detection of a larger attentional bias in persistent pain suggests that it may be in part characterised by reflective processing of pain related content (Donaldson, Lam, & Mathews, 2007; Schoth et al., 2012). It has been noted with reference to depressed populations, who also exhibit an attentional bias (to negative information) in maintained attention, that this may impair attentional disengagement from the pain stimulus, as elaborative processes utilise information processing capacity, which may also be needed for shifting attention towards an alternative (Donaldson et al., 2007; Koster et al., 2005).

To assess the causal influence of the observed bias on persistent pain experience, this thesis provided the first longitudinal assessment of the impact of retraining initial orienting versus maintained attention (Study Four), which was followed by a study in which both initial orienting and maintained attention were retrained concurrently (Study Five). Recently, a single case series reported proof of concept of ABM for heterogeneous persistent pain (Schoth et al., 2013). Their successfully implemented ABM program also incorporated shorter and longer stimulus durations, lending further support to the approach of Study Five (Schoth et al., 2013). For the causal influence of attentional bias on persistent pain experience to be indicated, it would need to be demonstrated that a pre to post ABM change in pain-related attentional bias (in initial orienting and/or maintained attention) resulted in a change in symptom outcomes at post-training (Hill, 1965; Van Bockstaele et al., 2013). To date, no studies, including those of the current thesis, have demonstrated this relationship. In Study Four, the pre to post reduction in attentional bias in maintained attention in the ABM groups did not translate into a reduction in pain outcomes at post-training. One reason for this absence of far-transfer effects to symptoms could be that within the design (which sought primarily to determine the optimal stimulus duration for modifying attentional bias), participants were allocated to an ABM-500 group, or an ABM-1250 group, whereas it may be that retraining both initial orienting and maintained attention concurrently is central to producing the predicted effects. In addition, the impact of training on maintained attentional bias was only observed for stimuli presented in the upper visual field, suggesting that the

induced bias was not very robust. The suggestion of Study Four that retraining both earlier and later attention may be optimal for this population was partially supported by the findings of Study Five, in which some far-transfer effects of ABM (at 500 and 1250 ms) to pain outcomes were observed. Paradoxically, however, there were no effects of ABM on attentional bias in this study. These findings are in line with those of Schoth et al. (2013), who reported reductions in pain severity and pain interference from pre to post-training, whereas there were no effects of ABM on attentional bias. Overall, the meta-analysis of Chapter Seven (which could not include the aforementioned single case series design) suggested that ABM had not been successful in modifying attentional bias in maintained attention, and that there was no overall effect of ABM on persistent pain severity at post-training. Collectively, these findings cannot rule out the possibility that the documented attentional bias (in maintained and initial orienting) is causally implicated in persistent pain experience, and suggest that further work is needed at the conceptual level to understand mechanisms of attentional change (this will be discussed further in Section 8.2.7).

The results thus far raise the important question of why, when the modification of bias can influence experimental pain outcomes, are ABM effects not reliably evident for persistent pain outcomes. One possibility is that before the effects of an induced neutral bias can be reliably detected, it may need to interact with a stressor (Beevers & Carver, 2003; Hertel & Mathews, 2011). Central to this explanatory hypothesis is the notion that cognitive vulnerabilities like attentional bias can remain latent until they are activated or primed (Beevers & Carver, 2003; Segal & Ingram, 1994). In their prospective study, Beevers and Carver (2003) tested the prediction that elicited attentional bias (following a negative mood induction) would interact with life stress to predict increases in dysphoria at seven-week follow-up. It was expected that this effect would occur in remitted depressed undergraduates, compared with undergraduates who had never been depressed. The results of a hierarchical regression indicated that greater negative bias following the sad mood induction interacted with life stress to predict level of dysphoria at follow-up, explaining 12.4% of the variance. The study had a number of limitations; for example, it employed a student sample of convenience, and, perhaps not surprisingly in this non-clinical population, the effects of attentional bias on dysphoria were small and did not reach clinical significance (Donaldson et al., 2007). Nevertheless, the finding that attentional biases were more reliably detected when they were primed is consistent with some investigations of CBM effects on cognitive bias (e.g. Grey & Mathews, 2009). In addition, effects of an induced bias on symptom outcomes tend to be larger in response to a stressor (Hakamata et al., 2010). Thus, in explaining the absence of reliable effects of bias modification on persistent pain outcomes, it is notable that study designs to date have tended not to incorporate a follow-up period or stressor task after the completion of ABM (Carleton et al., 2011; Schoth et al.,

2013; Study Four). This prospect is lent preliminary support by the finding of Sharpe et al. (2012) that post ABM reductions in disability were larger at six month follow-up (d = .55), than at post-training (d = .09), and by the quadratic interaction described in Study Five.

8.2.3 Persistent pain sample characteristics and their association with attentional bias

This section will consider the cognitive and affective characteristics of the persistent pain samples, with a view to gaining additional insight into what factors may have affected the suitability of ABM for this population, based on the current data.

Individuals with persistent musculoskeletal pain (clinical sample) had significantly higher levels of anxiety and depression than the healthy pain free control group (Study One). This finding corresponds with a biopsychosocial conceptualisation of pain which suggests complex, mutually reciprocal, relationships exist between psychological factors such as distress levels and attentional bias, and pain experience, in this complex population (cf. Section 1.1.1 Introduction). The community (Study Four) and clinical groups (Study Five) were comparably anxious (with scores in the mild range); however, the community sample were not depressed (mean score fell within the normal range), whereas the clinical sample were mildly depressed. These data are in line with studies which suggest that anxiety is a prevalent comorbidity among both community (Raphael, Janal, Nayak, Schwartz, & Gallagher, 2006) and clinical (e.g. Gatchel, 2004) populations. The difference in depression levels may reflect the lower psychological comorbidity generally associated with community-based samples, than those with diagnosed pain conditions, recruited from clinics (e.g. Morley, Eccleston, & Williams, 1999).

It is worth noting that within the community and clinical pain groups, approximately one third of participants were below the recommended cut-off for anxiety (35 and 30% respectively), and a greater proportion did not reach the cut off for depression (70 and 55%, respectively). Individuals with persistent pain with and without psychological comorbidity are thought to exhibit different patterns of cognitive bias (Pincus & Morley, 2001). Supporting this idea, experimental investigations of the content of depressed cognitions suggested that, whereas individuals with comorbid persistent pain and depression preferentially recalled and generated meanings related to negative health and pain, clinical depression was characterised more by self-denigration (Pincus, Pearce, McClelland, & Isenberg, 1995; Pincus, Santos, & Morley, 2007; Rusu, Pincus, & Morley, 2012). It would appear that no studies have systematically investigated the content specificity of attentional bias in pain-related depression; however, theory would suggest that this may be similarly distinguishable from attentional bias in non-depressed persistent pain participants (Pincus & Morley, 2001). This, in turn, suggests that persistent pain participants with and without depression may optimally benefit from different attentional bias modification procedures (e.g. stimulus selection), which could be investigated in future research.

Within the clinical persistent pain sample (Study Five), there was a significant negative correlation between baseline pain severity (VAS) and attentional bias in initial orienting (visual-probe task), such that a more pain-related bias was associated with more severe pain over the last week (Chapter Three). This supports the notion that pain experience (in this case severity) is associated with the relatively automatic allocation of early attention to pain stimuli. There was no association between pain severity and maintained attentional bias, and no association between the PVAQ and pain severity. Contrary to expectations, little evidence was found for an association between attentional bias (as measured using the visual-probe task) and cognitive and affective traits that past research has suggested might increase vigilance to pain (e.g. fear of pain). In Study Five, there were no significant correlations between the self-report measures and visual-probe assessment of attentional bias (see Table G1.2, Appendix G). Similarly, post hoc exploratory analyses of the Study Four dataset (community persistent pain sample) revealed no significant associations between the baseline questionnaires (Fear of Pain, HADS-Anxiety, HADS-Depression) and attentional bias indexes (see Table G1.1, Appendix G). These findings are in line with other studies which have not found an association between self-report measures of anxiety and depression, fear of pain and pain catastrophising, and the baseline attentional bias test (e.g. Schoth & Liossi, 2013). The self-report measure of attentional bias (the PVAQ) was, however, significantly positively correlated with anxiety, depression, and pain catastrophising (rumination, magnification, and helplessness), supporting the notion that greater attention to pain is associated with greater negativity in this population. Collectively, these findings suggest that the implicit and explicit measures may tap into somewhat different processing streams. Whereas the PVAQ measures awareness of attentional allocation, the visual-probe task is designed to capture relatively automatic, unintentional, biases in attention that are thought to occur outside conscious awareness (Lautenbacher et al., 2009).

8.2.4 ABM responders versus non-responders in the persistent pain groups

It was noted when administering the ABM sessions that there were a range of participant responses concerning the acceptability of training, and perceived responsiveness to the tasks. This variability in participant perceptions has been reported by other researchers working with anxious populations (e.g. Beard, Weisberg, & Primack, 2012). In their study, participant reactions to ABM ranged from ‘enjoying and liking’ the program to finding it ‘boring’ and ‘frustrating’ (Beard et al., 2012, p. 624). It was not part of the current programme of research to conduct a qualitative investigation of ABM; however, anecdotally, participants gave both positive and negative feedback to the researcher. Positive comments relating to the acceptability of training included that ABM was ‘fun’ and ‘like a game’. On their perceived responsiveness to ABM, one participant even commented that they

'recreated the movement of their fingers on the keys in the evening' (and demonstrated moving their forefinger and thumb up and down slightly), as they felt it was helping and wanted to recreate doing the task at home. Another participant said it made 'a huge difference to how I feel', enabling them to 'relax more, which also helps with the reduction of pain'. Other participants had negative reactions, commenting that they 'can't see the point of all the arrows', the tasks were 'boring' and 'mesmerising' and 'do not relate to pain at all'. Several participants reported that their 'mind wandered' during the tasks, and that they 'counted the number of times (they) got it right' to pass the time. As research seeking to modify attentional bias in individuals with persistent pain is only just commencing, it is important to consider what factors may affect training acceptability, and participant responsiveness, to the tasks. These will be discussed below.

8.2.5 Perceived attentional control

According to dual-process models of emotional processing, individuals with diminished executive control may be particularly susceptible to associative cues (Carver et al., 2008). Pain-related attentional bias can be viewed as a powerful, cue driven bottom-up signal that automatically captures attention, combined with suboptimal strategic processing and cognitive control (Wiers et al., 2013). This suggests that individuals with lower levels of attentional control may be more likely to exhibit maladaptive attentional biases, and that interventions that seek to modify attentional biases may work through increasing attentional control (Bar-Haim, 2010). It was therefore decided to administer a measure of perceived attentional control (ACS) in the current programme of research (Studies One, Two, Three, and Five). As far as this researcher is aware, no previous studies of ABM for pain have examined this variable. The aim was to determine how this potentially important individual difference might relate to bias acquisition and ABM efficacy. Overall, findings suggested that baseline levels of perceived attentional control are associated with greater neutral bias acquisition in the context of pain (Studies Two and Five). Concerning the clinical persistent musculoskeletal pain population, the evidence suggested that ABM may utilise pre-existing mechanisms of executive control, such that when an individual possessed greater baseline ability, they benefitted more from the attentional retraining. These findings are in line with recent findings that ABM's therapeutic effects for anxiety were diminished when it was completed under working memory load, suggesting that its effects may depend on executive resources being available, at least during the learning phase (Booth, Mackintosh, Mobini, Oztop, & Nunn, 2014).

The present Section to 8.2.7 will revisit the current dataset to try and gain a deeper understanding of the mixed findings concerning ABM for persistent pain, in particular. This begins with an examination of attentional control, and its relationship with persistent pain experience. Research suggests that long-term pain can lead to reductions in executive control

function (e.g. Nes, Roach, & Segerstrom, 2009), and that this relationship could be bidirectional, such that impaired executive function is involved in the maintenance of the condition (e.g. Nes et al., 2009; Van Bockstaele et al., 2013). The current data support a relationship between ACS and pain severity (see Appendix G2). Significant moderate negative correlations were identified between baseline attentional control and measurements of pain (Table G2.1, Appendix G2), and, when a median split was performed on the persistent pain dataset using baseline ACS scores, individuals with lower ACS reported significantly higher pain for nearly all pain outcome measures, than did individuals with higher ACS (Table G2.2, Appendix G2).

These findings suggest an apparent paradox: bias is more likely to be retrained in individuals with higher ACS, while individuals with more severe pain, and therefore who might be more likely to benefit from an intervention, may have lower ACS, and be less receptive to ABM. Thus, the question becomes how to enhance training for individuals with lower ACS (and more severe pain), such that they can benefit more from the program (like those with higher ACS). As some participants had commented that their mind wandered during the ABM programs of Study Four, it was decided to introduce a measure of training engagement in Study Five. As far as this researcher is aware, this is the first ABM study that has measured level of participant engagement. In theory, lower levels of participant engagement with ABM during the session might have impaired the predicted training effects (reductions on measurements of attentional bias and pain experience). A series of correlations conducted within the ABM groups lend preliminary support to this idea, indicating a moderate positive correlation between level of attentional control at baseline and training engagement, and a weak positive correlation between training engagement and the development of a more neutral attentional bias in maintained attention (see Table G3.1, Appendix G3). Together, these associations suggest that individuals with lower ACS entering the study found ABM less engaging, and that the less engaged with ABM participants were, the less likely they were to acquire the trained bias. This suggests that enhancing ABM engagement for individuals who start a course with lower ACS, in particular, could improve responsiveness to the program, although this mechanism requires testing in future research. Crucially, higher engagement was also positively correlated with improved pain experience (MPQ-Total), pain interference (BPI-I), anxiety and depression (HADS), and pain catastrophising (PCS-Total) at follow-up. Overall, the extant data suggest that it could be critical to enhance engagement, if researchers are to successfully modify pain outcomes using this technique in clinical chronic pain populations.

8.2.6 Does ABM require a baseline attentional bias to be efficacious?

It was originally thought that for ABM to exert a therapeutic effect on condition outcomes (e.g. anxiety, depression, pain), it is necessary that there is a) a baseline bias

towards the condition-congruent material, and b) that this bias is reduced in a training-congruent direction (MacLeod & Clarke, 2015). However, several studies, including those of the current thesis, have suggested that change in symptoms can occur without change in bias (e.g. Schoth et al., 2013; Sharpe et al., 2012; Study Three; Study Five). As a result, both of these claims have been variously refuted, with some authors stating that a) there need not be a bias evident at baseline for ABM to be efficacious in terms of attentional bias or symptom reduction (Sharpe et al., 2012), and b) that ABM may work through mechanisms other than reduction in noxious bias (Bar-Haim, 2010; Sharpe et al., 2012). It was therefore decided to revisit the current dataset to examine, first, whether level of baseline bias was associated with ABM efficacy; and second, whether there is an alternative index of change that might better explain some of the inconsistent findings.

Visual inspection of the attentional bias indexes suggested that several of the persistent pain participants did not have a baseline pain-related attentional bias entering the study. To explore the above stated hypotheses a) and b), the persistent pain ABM groups (Studies Four and Five) were partitioned based on whether attentional bias in maintained attention (as this was where the significant effects of ABM on bias were identified in Study Four) became more neutral, or either did not change or became more pain-related, from pre to post-training. Interestingly, participants whose slower bias became more neutral over the course of training had significantly more biased maintained attention (but not initial orienting) towards pain at baseline than those whose bias stayed the same or became more pain-related (see Table G4.1, Appendix G4). This supports the idea that participants who have a predispositional noxious bias are more likely to acquire the trained neutral bias over the course of ABM.

8.2.7 How is attentional bias being trained?

As indicated above, ABM's putative mechanism of action is that it reduces a maladaptive bias, which otherwise serves to amplify afferent input (cf. Clarke, Notebaert, & MacLeod, 2014b; Hertel & Mathews, 2011). Supporting this hypothesis, there is mounting evidence that reduction in noxious attentional bias can result in a concomitant reduction in symptoms, in anxiety and acute pain in particular (Clarke et al., 2014b; Clarke, Browning, Hammond, Notebaert, & MacLeod, 2014a; Chapter Seven). In these populations, attentional retraining (at 500 ms) successfully reduced the faster bias (500 ms), which could indicate that it influenced participants' initial engagement with the aversive stimuli (Mogg et al., 1997; Posner & Petersen, 1990). In persistent pain (Study Four, Chapter Five), the preliminary finding that attentional retraining (at 500 and 1250 ms) successfully reduced the slower bias suggests that it may have influenced the later strategic processing of the pain content once triggered by initial orienting, without affecting the earlier engagement with pain (Wiers et al., 2013). It is possible that ABM works through conditioned learning (Hertel

& Mathews, 2011); through repeated computer-based practice, participants learn to associate a particular processing response with the presented cues. According to this view, central to the technique is that the programs present the pain and neutral stimuli concurrently and thereby enable the alternative response to be triggered when needed, in a bottom-up fashion, by the relevant stimuli (Wiers et al., 2013). This explanation also suggests that the use of domain specific and idiosyncratically selected stimuli (as in Studies Four and Five) might potentially enhance ABM effects, as these stimuli are more likely to trigger the benign response option outside the laboratory. Thus, ABM might in part work through training the automatic activation of control mechanisms that enable selection of a neutral alternative when required (Bijleveld et al., 2009; Wiers et al., 2013).

This raises the interesting possibility that, although it may contribute to reductions in symptoms, 'reduction' in pain-related attentional bias is not necessary for ABM effects to occur. If ABM works through the stimulus driven activation of domain specific control processes, then change in bias, in either direction, might index ABM responsiveness. This, in turn, could help explain how several studies have reported a change in symptoms, without finding the hypothesised reduction in pain bias; while other studies have reported both pain bias reduction and symptom improvement. Indeed, in the recent single case series of ABM for persistent pain (Schoth et al., 2013), it was noted that bias moved 'closer to zero' (p. 240), such that changes in attention were recorded in both directions. A similar phenomenon was true of the current persistent pain datasets (Studies Four and Five); in fact, within the clinical persistent pain sample, there was an equal partition of positive and negative maintained bias change scores within the ABM groups. Collectively, these data suggest that it will be important for future research to examine more closely the impact of ABM on mechanisms of attentional control, and its relationship with bias plasticity and symptom outcomes (see also Kuckertz & Amir, 2015).

8.3 Clinical implications

The findings of this thesis have a number of important implications concerning the potential therapeutic application of ABM for pain management. It is important to note that the use of the visual-probe paradigm in this thesis has been to experimentally investigate the putative causal influence of attentional bias on pain vulnerability. Ultimately, the findings can inform decisions of whether it is appropriate to conduct large-scale clinical randomised controlled trials that would seek to determine the therapeutic efficacy of ABM for pain. Indeed, an attractive feature of ABM is that it simultaneously provides a method for experimentally testing attentional bias, and the potential for a novel intervention approach should the experiments suggest that attentional retraining can improve pain outcomes. This section will evaluate the potential of this technique for clinical application based on current findings, consider how it might theoretically be implemented in a therapeutic context, and

discuss what advances would need to be made before it could be moved from the laboratory to the pain clinic.

8.3.1 Training acceptability

One of the prevailing participant criticisms of ABM, both within the current programme of research, and as noted by other researchers (e.g. Beard et al., 2012), is the lack of rationale for the task. Adding a rationale to training would be particularly important in a therapeutic context, and has been shown to increase treatment benefits in other domains (Grafton et al., 2014). Typically, ABM is administered implicitly; that is, without reference to the training contingency, and without informing participants that the program aims to retrain how they attend to pain-related information. It is thought that any observed effects occur at a relatively automatic level of processing; that is, they are activated without intention and do not depend on volitional control (Hertel & Mathews, 2011; Koster et al., 2010). It is possible that the implicit administration of the task is important for the automatisation of response activation. As discussed in Chapter Four, providing participants with explicit instructions for ABM has been shown paradoxically to impair its therapeutic effects on an acute stressor (Grafton et al., 2014). The explicit instruction may lead participants effortfully to try and focus their attention on something other than pain, which might recruit the strategic, intentional, processing stream that is capacity limited, and could be diminished in times of pain (e.g. Beevers, 2005; Holmes et al., 2014). In contrast, it has been argued, implicit ABM does not rely on volitional executive control because the training procedure automatises the reallocation of attention to an alternative (cf. Wiers et al., 2013). Collectively, these findings suggest the importance of developing a paradigm that incorporates an instruction, whilst retaining the automaticity of response, if it is to be optimised for clinical application.

Study Five (Chapter Six) provided the first test of one possible approach, with promising results. The aim of that study was to test whether the addition of an implementation intention plan to the ABM program could enhance its far-transfer effects to actual pain experience. It was considered this type of instruction could work well with ABM, as like ABM, implementation intentions are thought to automatise response selection through the linking of the desired outcome with a particular cue. This is accomplished by framing plans within a conditional proposition, such that the ‘cue’ is contained in the ‘if’ clause, and the desired outcome in the ‘then’ clause. In spite of their demonstrated success in realising goal intentions in relation to various health behaviours (such as exercising more, e.g. Prestwich, Lawton, & Conner, 2003), and emerging evidence that they can enhance emotion regulation (e.g. Webb et al., 2010), their potential to augment ABM effects had not be explored. In terms of clinical implications, the results of Study Five suggested that this type of instruction can be successfully added to ABM and administered to a clinical

persistent pain population, and that the effects of this augmented ABM transferred to pain outcomes at one-week follow-up. Hence, unlike the instruction that explicitly asked participants to practise their attention (Grafton et al., 2014), the addition of this instruction did not impair the generalisation of training effects to experience (in this case chronic musculoskeletal pain). This is noteworthy, as the explicit ("always quickly shift (your) attention away from the negative word towards the neutral word, on each trial"; Grafton et al., 2014, p. 9) and implicit ("If I see a neutral word, then I will focus all of my attention on it!"; Study Five) instructional forms of attention regulation were actually quite similar in their wording and impetus. The principal difference between them was therefore the linking of the cue with the response in the implementation intention. This adds strength to the notion that the divergence in outcomes (in terms of far-transfer effects) was attributable to the difference in approach to attention regulation (explicit versus implicit). Following Study Five's findings, it would be interesting to examine how different instructions in the implementation intention format (for example, "If I see a pain word, then I will focus my attention on the neutral word") might enhance ABM effects. These studies could also directly assess (by collecting participant feedback) whether training acceptability is increased by the instruction. Overall, findings to date suggest that adding an implementation intention could help optimise ABM for clinical application, meriting further investigation.

As discussed in Section 8.2.5, another clinical implication of the current findings is that it may be important to try and improve level of participant engagement with the program. Theoretically, individuals with lower levels of attentional control may find it more difficult to engage with ABM, which could, in turn, moderate the impact of training on pain outcomes (Derryberry & Reed, 2002). Initial support for this explanatory hypothesis was provided through an exploratory correlational analysis conducted on Study Five's dataset, and could be investigated in future research (Section 8.2.5; Appendix G3). The observation that a subsample of individuals find ABM 'boring' (Beard et al., 2012; current thesis) also suggests that it might be prudent to try and improve the user experience of ABM, if studies can also demonstrate that this aspect of the program (i.e. it being low-level, straightforward) is not integral to its efficacy. Data from Study Five suggested that adding an implementation intention was not sufficient to enhance participant engagement, relative to usual ABM. One possibility is to make the participants' task more like a game (Grafton et al., 2014). For example, feedback concerning accuracy could be added, participants could gain points, and instead of word pairs there could be a more complex visual array comprising pain and non-pain related stimuli. It might also be possible for changes in attentional bias to be operationalised as an outcome within the game (e.g. wealth) that participants aim to increase or decrease. Framing ABM as a game might improve the user experience, and provide added 'rationale' for completing the task in the form of the game's objectives. In theory, this

might, in turn, promote patient adherence to the prescribed course. Overall, different methods for optimising ABM delivery for clinical pain populations require systematic investigation in future studies.

8.3.2 Could ABM complement existing psychological approaches to pain management?

As discussed in Chapter One (Introduction, Section 1.3.3) distraction therapy is a commonly used explicit attentional strategy for managing acute procedural pain (e.g. during a medical procedure), in which sensory stimuli (e.g. nature scenes) are provided to patients in order to divert their attention from the unpleasant stimulus (Diette et al., 2003; Fernandez, 1986). Pain management programmes also teach distraction techniques, such as counting or the use of a focal point, with a view to helping persistent pain patients learn to divert attention away from pain during severe episodes (Kerns, Sellinger, & Goodin, 2011). An important limitation of the technique is that its efficacy is reduced when the distraction task is automatically interrupted by pain. As discussed throughout this thesis, pain-related attentional bias can increase the speed at which pain is noticed and lead to a decrement in pain outcomes (e.g. Van Damme et al., 2004c). It follows that pre-existing attentional bias might lead to greater attentional interruption by pain during the distraction task, and thereby reduce its therapeutic efficacy. Preliminary support for this hypothesis was provided by recent correlational evidence; greater dispositional attentional bias favouring pain cues was associated with more pain during auditory distraction from an experimental pain induction (Van Ryckeghem et al., 2012). This suggests that successfully retraining initial orienting could enhance distraction efficacy. This thesis (Study Three, Chapter Four) provided initial evidence that implicitly retraining initial orienting to favour neutral stimuli can increase the time elapsed before pain is first noticed (i.e. threshold), in comparison with a sham training control group. Hence, in conjunction with the other research, this important finding has the clinical implication that ABM-500 could reduce distraction task interference by acute pain, and thereby augment its therapeutic efficacy. This would be an interesting study for future research. It could also be investigated whether ABM (for earlier and later attention) enhances the effects of distraction techniques utilised by individuals with chronic pain.

Cognitive bias modification might similarly complement existing CBT protocols for teaching self-regulatory strategies for managing persistent pain. Despite the reported success of CBT for pain, a surprisingly high proportion of individuals do not realise significant gains (40 – 60%), while others fail to maintain initial post-treatment improvements (Buhrman et al., 2004; Mckellar et al., 2003; Turk, 1990; Williams et al., 2012). Tackling the aberrant deployment of attention to pain content at a more habitual level of processing might assist in the transfer of intervention effects to real life, and help maintain CBT effects over time. There is some evidence to support this notion; participants who completed four sessions of

ABM-500, prior to eight sessions of CBT, reported significantly less disability and anxiety sensitivity, although not pain severity, at six month follow-up, than participants in a sham training and CBT control group (Sharpe et al., 2012). More research, in the form of well-designed, high quality randomised controlled trials, is needed to assess whether ABM can work as a successful adjunct to existing CBT protocols.

8.3.3 General advantages of ABM

From a clinical perspective, ABM has a number of potential advantages. It is economical both in terms of cost and practitioner involvement, requiring minimal face to face contact time with a clinician (e.g. Schoth et al., 2013). In addition, patient burden is minimal, as sessions are typically short (approximately 20 minutes on average) and straightforward (Bar-Haim 2010; Schoth et al., 2013). It is also convenient, as participants can theoretically complete sessions at home or work: the program can be delivered via CD (e.g. Sharpe et al., 2012), on a PC connected to the internet (e.g. Carlbring et al., 2012), or via smartphone (e.g. Enock, Hofmann, & McNally, 2014). Importantly, however, only the CD method has been successfully implemented with pain patients (otherwise, ABM has been delivered online for anxiety). Furthermore, an environment with multiple distractions such as home or work might not be optimal for ABM practice (Booth et al., 2014; Cristea, Kok, & Cuijpers, 2015). Thus, in considering the potential clinical application of this computer-based intervention for pain, it will be important to ensure that participants allow 20 minutes to complete it free from situational diversions. More generally, it will be vital to test each of the various ways ABM can be administered (e.g. in clinic or remotely via the internet/smartphone) in high quality randomised controlled trials.

8.4 Limitations

The current programme of research had a number of overarching limitations, in addition to those discussed in individual chapters. First, words were used as the stimuli in all dot-probe tasks (tests and training). As symbolic representations of pain, linguistic stimuli have been criticised for having low ecological validity and ability to activate the posited pain schemata (Crombez et al., 2013a). Nevertheless, the consistent indication of the expected pre-existing pain-related attentional bias in Studies One, Four and Five (Chapters Five and Six) suggests the linguistic visual-probe tests were successful in measuring this pattern of attention. In addition, neuroimaging evidence has indicated that pain words (and not neutral, negative, or positive words) activate regions of the pain matrix commonly associated with pain processing (Richter et al., 2010), lending some support to their ability to tap into this system. Moreover, in this thesis, participants with persistent pain were asked to select and/or generate the words that were most related to their pain, thereby enhancing the relevance of the ABM stimuli to participants' individual pain experiences (Crombez et al., 2013a). As an alternative to linguistic stimuli, future studies could incorporate images as training stimuli

into ABM (as was recently applied by Schoth et al., 2013), or seek to develop somatosensory versions of the visual-probe tasks (Crombez et al., 2013a).

Second, all dot-probe tasks (tests and training) presented stimuli for 500 and/or 1250 milliseconds. These stimulus durations were selected based on previous research, and to facilitate comparison across studies. Whilst they have provided information on the time course of attentional bias and the optimal timings for its modification, patterns of attentional bias in very early attention (< 500 ms) and later maintained attention (> 1250 ms) are not known. It is possible that ABM effects on maintained attention might have been enhanced had a longer stimulus duration been employed. One study testing the efficacy of ABM for depression presented stimuli for as long as 4500 ms, which would have permitted fuller processing of the content of the stimuli, as the longer duration allows more elaborate conceptualisation of its meaning, and schemata activation (Mogg & Bradley, 2005; Wells & Beevers, 2010). Results of this study indicated that ABM resulted in a significant reduction in attentional bias in maintained attention, relative to a no training control group, and this change in bias mediated a reduction in depression at two-week follow-up (Wells & Beevers, 2010). Thus, future research should aim to test and retrain additional stimulus durations; in persistent pain, the effect of incorporating longer stimulus durations (> 1250 ms) on maintained attentional bias and pain outcomes at post-training, and after an extended follow-up period, would be particularly interesting.

Third, the dot-probe task measured attentional bias through reaction times to word stimulus pairs presented on screen for two pre-specified exposure durations. Two general limitations of this approach are that it provides only a proxy measure of attentional bias, and that the measurement represents only a glimpse of the bias (Mogg & Bradley, 2005; Schoth & Liossi, 2013). The addition of more stimulus durations to the task was decided against as this would have increased the task length, and consequently participant burden and fatigue. One possible solution to this limitation is to use eye-tracking technology during the visual-probe attentional bias test (Fashler & Katz, 2014; Mogg & Bradley, 2005; Yang, Jackson, Gao, & Chen, 2012; Yang et al., 2013). Three studies have adopted this approach, using pain words (presented for 2000 ms) to measure attentional bias in a healthy student sample split into lower and higher fear of pain groups (Yang et al., 2012), and student samples self-reporting heterogeneous persistent pain (Fashler & Katz, 2014; Yang et al., 2013). Broadly supporting the current visual-probe findings, results indicated that pain free fearful individuals oriented their very early attention towards sensory pain words (measured using eye-tracking), whereas both the eye-tracking and reaction time data suggested that participants did not sustain their attention on pain words for the longer stimulus duration (Yang et al., 2012). Also generally in line with current findings, Fashler & Katz (2014) reported that a large sample of 51 individuals with persistent pain (versus 62 pain free

controls) displayed significantly longer gaze durations on sensory pain words presented for 1000 to 2000 milliseconds, whereas in their study no significant differences were identified in initial orienting (0 to 500 ms inclusive), in comparison with the control group. These data help provide validation for the visual-probe task as a practical measurement of attentional bias that can inform future nuanced investigation of attentional allocation to pain-related information (this is discussed further in section 8.5.2).

Fourth, all of the studies of this thesis administered self-report questionnaires to measure pain, and the findings are therefore subject to the general limitations of self-report data, such as response bias and variation in introspective ability (e.g. Turk & Okifuji, 1994). Some have argued that measures which ask participants to recall their pain are inherently unreliable, as recall itself is a process of reconstruction that is prone to distort past experiences (Stone, Bachrach, Jobe, Kurtzman, & Cain, 1999; Stone et al., 2003). For example, recall of pain might be influenced by emotional state, both at the time of encoding, and when recollected (Mannion, Balagué, Pellisé, & Cedraschi, 2007). However, there is good evidence that asking participants to recall their average pain over the past week (as in the McGill Pain Questionnaire, for example) provides a reliable, valid and practical measurement of pain experience (e.g. Bolton, 1999). In addition, a review of pain self-report measures found that recall of critical persistent pain outcomes such as average severity and interference had acceptable validity for a recall period of at least three months (Mannion et al., 2007; Von Korff, Jensen, & Karoly, 2000). A second criticism of retrospective questionnaires is that they do not provide information about fluctuations in pain (Stone et al., 2003). The current studies aimed to assess changes in average levels of pain, and hence more fine-grained measurements of pain were beyond their scope. However, the findings of this thesis support more nuanced investigation of the impact of retraining attentional bias on persistent pain experience as it occurs throughout the day (see also Van Ryckeghem et al., 2013; although this study did not retrain bias and measured bias only at a single time point, followed by a two week online diary assessment of pain). Attentional bias and pain experience could be assessed at multiple time points, which could be accomplished using ecological momentary assessment or an experience sampling method (both of which require electronic diary completion several times per day).

Fifth, the assessment of attentional control also relied on self-report. As such, it cannot be ruled out that the construct measured was individual perception of attentional control abilities, and not actual control over attentional allocation. Future research could implement a behavioural measure of attentional control that does not depend on conscious reflection. One possibility is the antiscaccade task (Hallett, 1978). In this experimental paradigm, participants are asked to generate an eye movement (saccade) to the opposite side of a peripheral cue (hence, an antiscaccade). Abrupt onset cues are thought to capture

attention (indexed by eye movement) at a relatively automatic level of processing (Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001; Theeuwes, Kramer, Hahn, & Irwin, 1998). The participant's task requires controlled inhibition of the reflexive saccade towards the sudden onset cue (Nieuwenhuis et al., 2001). It is thought that antisaccade errors occur when neural systems involved in the prosaccade inhibition fail, and, as such, a higher error rate reflects greater impairment in top-down attentional control (Derakshan, Salt, & Koster, 2009; Hutton & Ettinger, 2006; Massen, 2004). The possibility of using the antiscaccade task to measure changes in attentional control from pre to post ABM was considered at the outset of this programme of research. It was decided that it would be prudent in the first instance to focus on the time course of attentional change, and that additional experimental tasks to the attentional bias test and modification programs could overly burden participants, particularly in a clinical population, whereas the questionnaire measure was comparatively straightforward to complete. Moreover, the ACS has been validated against the antisaccade task, with data suggesting that its subscales (shifting and focussing) are positively correlated with saccadic inhibition (Judah, Grant, Mills, & Lechner, 2014).

Lastly, efforts were made to optimise study quality through adherence to recommendations of the CONSORT statement for randomised controlled trials ('Consolidated Standards of Reporting Trials'; Schulz, Altman, & Moher, 2010). For example, all ABM studies randomised participants to condition using an online random sequence generator, and participants were not informed of their condition allocation until the end of the study. However, constraints in resources, and the educational nature of this project, meant that it was not possible to adhere to all CONSORT recommendations. For instance, it was not feasible to blind the data collector to the condition allocation during the data collection and analysis phases. This would be optimal as it minimises the risk of unknown bias, and hence, in an ideal world, it is something the researcher would have implemented.

8.5 Future research

Suggestions for future research have been made throughout this thesis, including within the body of this discussion; it is not the intention to repeat all of them here. This section will aim to draw together some of the aforementioned ideas with new suggestions, under two headings that this thesis suggests reflect some of the big areas for future investigation.

8.5.1 Understanding underpinning mechanisms of action: Attentional control and bias plasticity

First, given the possible role of attentional control in bias acquisition and ABM efficacy discussed in this thesis, research could administer, before and after ABM, a variant

of the antiscaccade task in which the sudden onset cue is pain-related or neutral. Based on the current findings, it would be predicted that individuals with persistent pain might show impaired performance when the to-be-inhibited stimuli are pain-related. Moreover, this approach would permit measurement of domain specific attentional control that was not measurable using the domain general ACS. It is possible that an adapted (i.e. pain specific) antisaccade task would detect the predicted increases in attentional control over pain content from pre to post ABM. Indeed, there is emerging evidence to suggest that ABM increases domain-specific attentional control measured using the antisaccade task in anxiety (see Chen, Clarke, Watson, MacLeod, & Guastella, 2015). Future studies could test whether control over automatic attentional capture by pain stimuli is enhanced from pre to post-training.

Second, studies could be designed which seek to examine how a baseline bias towards pain, as has been consistently demonstrated in persistent pain populations, might interact with bias malleability (that is, reactivity of the attentional system to environmental cues; cf. Fox et al., 2011), to provide a more nuanced explanation of ABM responsiveness, and vulnerability to pain. There is emerging evidence in the emotion literature that pre to post ABM change in attentional bias plasticity (measured in initial orienting) mediates the relationship between condition (neutral ABM versus sham training) and symptom reduction in PTSD (Kuckertz et al., 2014). Interestingly, in their study, whilst the mediation based on the usual method for calculating attentional bias change did not reach significance, level of baseline bias (but not baseline instability) moderated ABM effects (Kuckertz et al., 2014; Kuckertz & Amir, 2015). This suggests that individuals with a more pronounced bias at baseline were more likely to be amenable to the training effects on bias plasticity. Concerning pain, future studies might test whether those who benefit most from ABM (in terms of symptom reduction) are participants who a) present with a baseline bias, b) that is reduced, and c) demonstrate greater stability in attention over the course of training.

Third, future research could also assess the presence of particular genetic correlates and how these might affect individual responsiveness to ABM. There is interesting preliminary evidence for the genetic moderation of attentional retraining (in this case the 5-HTTLPR allele) in anxiety (Fox, Zougkou, Ridgewell, & Garner, 2011). One prospect is that ABM effects vary based on particular genetic polymorphisms that moderate neural plasticity (Fox et al., 2011; Wiers et al., 2013). According to this view, particular genotypes are associated with greater neural malleability, which, in turn, confer vulnerability to cognitive bias acquisition (towards salient positive or noxious information) through conditioned learning (e.g. Pischek-Simpson, Boschen, Neumann, & Waters, 2009). This, in turn, has the interesting implication that individuals who are the most vulnerable to exaggerated cognitive biases may also stand to gain the most from retraining interventions, as their neural systems

are more receptive to the induced change (Fox et al., 2011). There are no studies investigating the genetic correlates of vulnerability to pain-related bias acquisition, although it is plausible that these biases (like threat bias) develop through fear conditioned learning, and could be moderated by individual differences in neural plasticity (e.g. Beevers, Wells, Ellis, & McGeary, 2009; Eldar & Bar-Haim, 2010; Van Damme et al., 2004c). This could be examined in future studies.

Fourth, another approach to investigating the processes underlying ABM would be to study the impact of modifying attentional bias on brain function. An initial imaging study in anxiety suggested that inducing a threat-related versus neutral bias in initial orienting in healthy participants was related to altered activation of prefrontal regions to emotional stimuli, rather than to changes in subcortical systems (Browning et al., 2010b; Heeren, De Raedt, Koster, & Philippot, 2013). These findings lend support to the hypothesis that ABM works through mechanisms of top-down attentional control, typically associated with the prefrontal cortex (PFC; Browning et al., 2010b; DeRubeis, Siegle, & Hollon, 2008). However, training effects were tested by asking participants to violate the learned ABM rules and attend to training incongruent stimuli. As noted by the authors, this could have resulted in greater PFC activation associated with expectancy violation and effortful processing of the unpractised response (Beevers, 2005; Browning et al., 2010b). In addition, the study did not directly examine the impact of ABM on attentional control, which could be achieved through measuring within-subjects changes in prefrontal activation related to noxious stimuli from pre to post-training. Furthermore, studies which compare inducing a noxious bias with inducing a neutral bias do not permit isolation of effects, as either or both may influence attentional function (Browning et al., 2010b). As it is neutral attentional retraining that is thought to have therapeutic potential (Studies Three to Five, Chapters Four to Seven), future studies could compare the effects of benign ABM for pain and a control condition on brain function. To date, no studies have assessed the impact of ABM for pain on neural activity. Particular questions relating to persistent pain concern the impact of retraining earlier and later attention on attentional control systems, and whether ABM enhances prefrontal control over salient stimuli.

8.5.2 Optimising ABM and its potential clinical application

In addition to the suggestions made in Section 8.3.1 (concerning enhancing participant engagement with programs), there are a number of general questions concerning the optimisation of ABM for pain. First, the number of trials and sessions has varied widely across studies, ranging from one (320 trials) to eight (3072 trials) sessions. This leaves the optimal ‘dose’ for acute and persistent pain (and whether these differ) unknown, which could be systematically investigated in future research. Second, what is the optimal stimulus type; words, images, or both? It has been suggested that images may have greater ecological

validity than words as stimuli (e.g. Crombez et al., 2013a). On the other hand, words are able to depict the complexity of pain experience in a way that images (typically facial expressions of pain) may not be able to convey. Research that directly tests which stimulus type is optimal for ABM could be conducted; indeed, one study recruiting healthy pain free participants recently reported that linguistic ABM effects transferred to a pictorial attentional bias test, but not vice versa (Sharpe, Johnson, & Dear, 2015, see Appendix G5). These preliminary findings suggest that words may have greater transfer potential than images for modifying pain-related attentional bias; however, the findings need replicating and extending to persistent pain populations, in particular.

Third, further work on the optimal stimulus durations is also needed. The current thesis suggests that retraining initial orienting is optimal for acute pain, whereas retraining initial orienting and maintained attention may be better suited for persistent pain populations. Future research could aim to replicate and extend these findings, and explore the inclusion of stimulus durations other than 500 and 1250 ms within the ABM program. In addition, eye-tracking technology could be used alongside the visual-probe task to provide more nuanced information on the time course of attentional bias and modification effects. To date, eye-tracking findings have been somewhat mixed. For example, whereas Fashler and Katz (2014) reported prolonged gaze on sensory pain words in sustained attention, Yang et al. (2013) found no significant effects of persistent pain on gaze duration (also to words) in either initial orienting or maintained attention, in comparison with pain free controls. This inconsistency in results could be due to methodological differences between the studies; whereas Fashler and Katz (2014) temporally defined 'initial orienting' and 'maintenance' phases of visual attention, Yang et al. (2013), applied no such temporal distinction. In addition, the earlier study's sensory pain stimuli included non-sensory words such as 'indescribable' and 'incomprehensible', such that the test may have lacked sensitivity to detect pain bias (Asmundson et al., 2005a; Yang et al., 2013). Nevertheless, recently, other, non visual-probe studies have reported eye-tracking evidence of biased initial orienting, and not sustained attention, to pain-related images in persistent pain (headache) samples (Liossi, Schoth, Godwin, & Liversedge, 2014; Schoth, Godwin, Liversedge, & Liossi, 2014). Again, these discrepancies in findings could be due to procedural differences between studies, such as the use of different test paradigms (free scanning and visual search, respectively); however, more research is needed to clarify these issues. Moreover, future investigation of eye movements could provide a more fine-grained index of attentional change over the course of ABM.

Research, such as the above, that examines ABM effects at a conceptual level, could help refine and optimise implicit attentional retraining procedures for pain. This could, in turn, influence clinical research designs (Wiers et al., 2013). One consideration will be

whether the size of therapeutic effects for pain are sufficiently large to justify its use as a standalone intervention, or whether it would be better conceived as an adjunct treatment that fits with other more established therapies (cf. Van Bockstaele, 2013). In Section 8.2.7, it was suggested that one of the potential advantages of CBM over current treatment strategies, like CBT and distraction therapy, might be its automatic activation of control mechanisms that continue working even when executive resources are taken up with other processing activities (Bowler et al., 2012; Wiers et al., 2013). The implication was that implicit ABM might potentially complement explicit pain management techniques. This could be tested in future clinical research studies. For example, persistent pain participants could be randomised to ABM alone, learn a distraction technique, ABM and distraction technique, or a control group. Effects on critical pain outcomes could then be assessed over a follow-up period. If ABM is complementary to distraction, then effects on pain outcomes should be greatest in the combined intervention group, particularly when cognitive resources are depleted (e.g. in the context of concurrent life stresses during follow-up). Its potential clinical efficacy could similarly be explored in relation to distraction for acute pain, and as an adjunct to CBT.

There are a number of additional questions concerning the clinical potential of ABM. First, how long do training effects, on both attentional bias and pain outcomes, last? This could be tested in studies that include long-term follow-up assessments (such as one month, four months). Second, are there particular patient subgroups who respond better to ABM than others (for example, highly distressed persistent pain patients reportedly benefit less from CBT; McCracken & Turk, 2002)? Third, are there any particular adverse effects associated with ABM for persistent pain? There are no published data concerning adverse events, which may not be surprising as it is a low-intensity intervention that involves presenting stimuli that participants may encounter in their daily lives (Beard, 2011). It will nonetheless be important to measure and publish this information. It is possible that inducing a pattern of avoidance might impede habituation, which could exacerbate symptoms. Future randomised controlled trials could include a measurement of adverse events that is designed to assess this possibility. Fourth, does modifying pain-related attentional bias have downstream effects on other types of cognitive bias identified in pain, such as interpretive bias? To date, very few studies have tested interpretive bias in pain, although there is evidence that individuals with persistent pain tend to interpret ambiguous information in a pain-related way (e.g. Pincus, Pearce, McClelland, Farley, & Vogel, 1994; Vancleef, Peters, & De Jong, 2009). Theory suggests that interpretive bias could be a risk factor for chronicity and poor adaptation to pain (Pincus & Morley, 2001). Yet, no studies have assessed the possibility that modifying attentional bias may have cascading (therapeutic) effects on how an individual interprets ambiguous information relating to discomfort and health. Testing the

overlapping bias hypothesis in pain would be an interesting avenue for future research. Fifth, the current thesis examined ABM for adult pain; is it extendable to other populations, such as children and adolescents? Cognitive bias modification for attention has been successfully administered to a younger population in the emotion literature (e.g. Eldar et al., 2014; Shechner et al., 2014); however, no studies have tested its suitability for children and adolescents with pain. Its feasibility, acceptability and efficacy for this population could be investigated in future studies.

8.6 Conclusions

In conclusion, the current thesis tested the influence of defined temporal components of attentional bias on vulnerability to pain using attentional bias modification techniques. The stages of attention most implicated in acute and persistent pain were investigated through manipulation of the duration for which test and retraining stimuli were presented. This programme of research was driven by theory which suggests that pain can redirect attention to favour its processing over competing demands (e.g. Eccleston and Crombez, 1999), and that biased attentional processing can influence pain experience (e.g. Pincus & Morley, 2001). The findings from Study Two suggested that acute experimental pain diverted attention towards neutral information presented in initial orienting during the recovery phase. This finding complemented the findings of Study Three and the meta-analysis of Chapter Seven, which suggested that retraining initial orienting towards neutral information resulted in a reduction in critical acute pain outcomes. Together, these results supported the hypothesis that attentional bias has a key active role in acute pain experience, and added that this bias is particularly active in earlier, as opposed to later, attention. Drawing on dual-process models of attentional processing, this novel finding suggested that acute pain processing particularly recruits relatively automatic, fast-acting, bottom-up processes of early vigilance (e.g. Browning et al., 2010a; Legrain et al., 2011b).

Building on the foundational findings of Studies Two and Three, Studies Four and Five, together with the meta-analyses of Chapters Two and Seven, sought to examine the efficacy of ABM for persistent pain, and establish the optimal timings for retraining attention in this population. Recent cross-sectional data indicated that, in individuals with persistent headache, this maladaptive pattern of attentional processing is evident in both earlier and later attention, but is most pronounced in later, maintained attention (Liossi et al., 2009, 2011; Schoth et al., 2012; Schoth & Liossi, 2013). Study One replicated and extended these findings to a clinical persistent musculoskeletal pain population, where a significant attentional bias towards pain-related stimuli was evident in comparison with healthy controls, and this bias was most pronounced when stimuli were presented for 1250 (as opposed to 500) milliseconds. This finding added to the growing evidence-base that persistent pain particularly affects maintained attention, which, in turn, suggests that once

attended to, participants may find it difficult to disengage from pain content (Browning et al., 2010a, b; Schoth et al., 2012).

Prior to this thesis, no studies had investigated the optimal timings of ABM for persistent pain. The last two experimental studies of the current thesis explored whether, and at which temporal stage, attentional bias is causally implicated in vulnerability to persistent pain. Psychological models, such as the fear avoidance model, suggested that attentional bias is implicated in the maintenance of pain chronicity (Vlaeyen & Linton, 2000, 2012). It followed from these models that successfully retraining attention could alleviate the deleterious pain outcomes associated with pain hypervigilance and attentional selection. The current thesis provided the first evidence that retraining initial orienting and maintained attention has comparable ameliorative effects on pain-related attentional bias in maintained attention (Study Four). Furthermore, it contributed the original finding that ABM for both component stages of attention, augmented with an implementation intention instruction, can reduce pain severity from post-training to one-week follow-up, relative to a control group (Study Five). These latter findings additionally supported the prediction that training effects may be more evident once they have interacted with participants' everyday experience (e.g. Hallion & Ruscio, 2011). However, the mechanism of change remained unclear, as there was no definitive evidence of the expected neutral attentional shift in the active ABM groups in Study Five. What was evident was that individuals with higher perceived attentional control at baseline developed a more neutral attentional bias, indicating that this trait was associated with training-induced bias acquisition. These findings provided early support for theoretical accounts that suggest ABM (in this case neutral) may work in part through mechanisms of attentional control. Future research should explore the role of attentional control in bias acquisition, and seek to provide conceptual clarification on ABM's underlying processes. One possibility is that rather than reduction in noxious bias per se, ABM confers therapeutic benefit through impacting on mechanisms of attentional control and bias plasticity. It will also be important to investigate methods for optimising participant engagement with ABM, particularly for clinical pain populations.

Overall, the findings of the current thesis support the continued investigation of attentional bias modification for pain. Current evidence would suggest that modifying early orienting can influence vulnerability to acute pain, while persistent pain is characterised by an overall attentional bias that is particularly situated in maintained attention; as such, the optimal timings for modifying pain-related attentional bias are likely to differ across acute and persistent classifications.

Appendix A: Materials for systematic review and meta-analysis (Chapters 2 and 7)

A1 Ovid Medline detailed search strategy

A2 Sample data extraction sheet used for systematic review and meta-analyses

A3 Risk of bias tables for individual studies included in meta-analysis

Table A1.1

Ovid Medline detailed search strategy (search conducted 10.10.14)[20]

	Search term
1	"attention* bias modification".tw.
2	(attention* adj3 (bias* or modification*)).tw.
3	attention/
4	ABM.tw.
5	(attention* adj3 (train* or retrain*)).tw.
6	CBM-A.tw.
7	"cognitive bias modification".tw.
8	(cognitive adj3 bias*).tw.
9	((visual* or dot*) adj5 probe).tw.
10	or/1-9
11	exp Pain/
12	exp Headache Disorders/
13	Fibromyalgia/
14	exp Arthritis/
15	Pain Measurement/
16	(pain* or headache* or fibromyalgia or arthriti*).tw.
17	or/11-16
18	10 and 17
19	randomized controlled trial.pt.
20	controlled clinical trial.pt.
21	randomized.ab.
22	placebo.ab.
23	clinical trials as topic.sh.
24	randomly.ab.
25	trial.ti.
26	or/19-25
27	18 and 26
28	limit 28 to (English language and yr = "1986 - Current")

[20] The researcher wishes to acknowledge the Cochrane Pain, Palliative and Supportive care (PaPaS) review group for their help with devising the Medline search strategy.

A3 Sample data extraction sheet used for systematic review and meta-analyses[21]

Systematic Review
Data Extraction Form

PART A: PUBLICATION DETAILS

A1 Reviewer details

1	Reviewer Initials	
2	Date reviewed (DD/MM/YYYY)	

A2 Publication details

3	First Author	
4	Year of publication	
5	Title	
6	Key conclusions of the authors **(verbatim as reported in abstract)**	
7	Total number of studies reported	
8	Number of studies that meet all inclusion/exclusion criteria[1]	
9	Misc comments on A2	

A3 Correspondence-complete at end

10	Contact email (and name if not first author)			
11	Correspondence required (e.g. to request data not reported etc)	Yes	No	Undecided
12	Question numbers for which correspondence will be required (clarify if number is insufficient to make reason obvious)			

PART B: STUDY DETAILS

IMPORTANT: Copy and complete **all** of Part B for each study the publication reports that meets all inclusion/exclusion criteria[1].

B1 Study outline: risk of bias assessment (see p. 195 Higgins & Green, 2008).

Notes on Risk of Bias Tool (questions B1-6-24): Yes = low risk of bias; No = high risk of bias; Unclear = unknown risk of bias

1	Name of study (e.g. 'Study 1')				
2	Inclusion Criteria 1 met?[1]	Yes		No	
3	Inclusion Criteria 2 met?[1]	Yes		No	
4	Inclusion Criteria 3 met?[1]	Yes		No	
5	Design	Within-subjects	Between-subjects	Mixed	Unclear
6	Does the study claim randomisation?	Yes	No	Unclear	Not stated

[21] The researcher wishes to acknowledge Dr Ian Kellar for permitting adaptation of his data extraction sheet for the review reported in this thesis (Chapters 2 and 7), and its inclusion here.

	(nb in the case of within-subjects designs this should be to counterbalance order effects)				
If yes, go to 7. Otherwise, go to 9					
7	Unit of randomised allocation[3]	Individual	Group	Unclear	
8	Is the randomisation adequate?[4]	Yes	No	Unclear	
9	Does the study claim allocation concealment?	Yes	No	Unclear	
If yes, go to 10. Otherwise, go to 11					
10	Is the allocation adequate?[5]	Yes	No	Unclear	
11	Does the study claim any form of blinding?	Yes	No	Unclear	
If yes, go to 12. Otherwise, go to 20					
12	Does the study claim the participant is blinded?	Yes	No	Unclear	
13	Is the participant adequately blinded?[6]	Yes	No	Unclear	
14	Does the study claim the individual (experimenter/clinician, etc.) delivering the intervention is blinded?	Yes	No	Unclear	
15	Is the individual adequately blinded? [6]	Yes	No	Unclear	
16	Does the study claim that the data collector is blinded?	Yes	No	Unclear	
17	Is the data collector adequately blinded? [6]	Yes	No	Unclear	
18	Does the study claim the person doing data analysis **on the outcome measures** is blinded?	Yes	No	Unclear	
If yes, go to 19. Otherwise, go to 20					
19	Is data analyser adequately blinded?[6]	Yes	No	Unclear	
20	Does the study claim that measures have been taken to protect against contamination between conditions?	Yes	No	Unclear	
If yes, go to 21. Otherwise, go to 22					
21	Are these measures adequate	Yes	No	Unclear	
22	Is there any evidence of incomplete outcome data?[7] **E.g. data from participants who did not adhere to the intervention were not included in the analysis**	Yes	No	Unclear	Details:
23	Is there any evidence of systematic differences in withdrawals from the study?	Yes	No	Unclear	Details:
24	Were there any other sources of bias within the study?	Yes	No	Unclear	Details
25	Misc comments on B1				

B2 Recruitment

1	Sample population as described (verbatim)	
2	Geographic location of	City:

	research[8]	Country:		
3	Are comparisons made between conditions at baseline?	Yes	No	Unclear
If yes go to 4, Otherwise go to 6				
4	Are there significant differences between conditions at baseline?	Yes	No	Unclear
If yes go to 5, Otherwise go to 6				
5	Are adjustments made for these differences? (i.e. are these differences controlled for within subsequent analyses?)	Yes	No	Unclear
6	Attrition rate[9]			Not reported
7	Are comparisons made between participants that drop out and those that complete?	Yes	No	Unclear
If yes go to 8, Otherwise go to 9				
8	Are there differences between participants that drop out and those that complete?	No	Yes-results as follows:	Unclear
9	Is the attrition rate for each condition compared?	Yes	No	Unclear
If yes go to 10, otherwise go to 11				
10	Are there differences in attrition rates between conditions?	No	Yes-results as follows:	Unclear
11	Misc comments on B2			

B3 Summary of study conditions

1	Total number of conditions				
2	Number of conditions testing the effect of ABM on pain				
3	Setting	University		Medical	
		Community		Other	Unclear
4	Were participants told the study was testing a therapeutic intervention?	Yes	No	Unclear	
5	Misc comments on B3				

B6 Experimental Condition(s)

****IMPORTANT**:

- **Copy and complete B6 for each implementation intentions intervention group**
- **Relabel each row such that for each intervention group, the row number remains the same, but is followed by a different suffix.**
- **For example, for the 2nd intervention group, rows should read: '54b, 55b, 56b' and for the 3rd intervention group: '54c, 55c, 56c' and so on…**

1	Experimental (intervention) condition name as reported in paper	
2	Duration of the delivery of the intervention (weeks; days)	

	1 week = 7 days 6 hours = 0.25 days 1 month = 30.42 days				
3	Number of sessions				
4	Attrition rate of participants in the condition			Not reported	
5	Is the intervention delivered by PC/ internet?				
6	Who delivered the content of the intervention?		Unclear	Not stated	N/A
7	Was the intervention delivered to a group or individual?	All delivered to a group	Part group/ part individual	All delivered to individual	Not stated
8	What type of dot-probe task is used?	Probe-position	Probe-classification	Unclear	
9	What was the stimulus presentation time?	500	1250	Other:	
10	What were the stimuli?	Words	Images	Both	
11	What was the target stimulus valence?	Sensory	Affective	Both	Other:
12	What percentage of trials were critical?	100	< 100	If less than 100, specify:	
13	How were the stimuli aligned?	Vertical	Horizontal	Not stated	

B7 Comparison condition(s)

1	Condition name as reported in paper				
2	Duration of the delivery of the comparison condition (weeks; days) 1 week = 7 days 6 hours = 0.25 days 1 month = 365/12 days				
3	Number of sessions				
4	Attrition rate			Not reported	
5	Is the intervention delivered by PC/ internet?				
6	Who delivered the content of the comparison condition?		Unclear	Not stated	N/A
7	Was the comparison delivered to a group or individual?	All delivered to a group	Part group/ part individual	All delivered to individual	Not stated
8	What type of dot-probe task is used?	Probe-position	Probe-classification	Unclear	
9	What was the stimulus presentation time?	500	1250	Both	
10	What were the stimuli?	Words	Images	Both	

11	What was the control stimulus category valence?	Household	Neutral assorted	Other
12	Were the stimuli matched for length and frequency?	Yes	No	Unclear
13	What percentage of trials were critical?	100	< 100	If less than 100, specify:
14	How were the stimuli aligned?	Vertical	Horizontal	Not stated

B8 Pain outcome measure details
*****IMPORTANT*****

- **Copy and complete B8 for each outcome measure that tests the effects of the intervention (as described in B4)**
- **Re-label each copied box with the outcome number (second, third, fourth outcome).**

1	Is a primary outcome specified?	Yes	No	Unclear
2	First, second, third outcome definitions (verbatim)			
3	Subjective or objective	Subjective	Objective	Unclear
	If subjective go to 4, otherwise go to 5			
4	Is the measure reported validated by the authors or by previous research?	Yes	No	Unclear
5	Time interval between baseline and follow-up (**if there are multiple follow-ups then list each and average)		Unclear	
6	Is the outcome reported from a multi-item scale?	Yes	No	Unclear
	If yes go to 7, Otherwise go to B9-1			
7	Is the internal consistency of the outcome scale assessed?	Yes	No	Unclear
	If yes go to 141, Otherwise go to B9-1			
8	Is the internal consistency of the outcome scale adequate (i.e. alpha > .70)?	Yes	No	Unclear

B9 Attentional bias Outcome measure details
*****IMPORTANT*****

- **Copy and complete B9 for each measure that tests the effects of the intervention on attentional bias**

1	Outcome definition (verbatim)			
2	Subjective or objective	Subjective	Objective	Unclear
	If subjective go to 3, otherwise go to 4			
3	Is the measure reported validated by the authors or by previous research?	Yes	No	Unclear
4	Is the dot-probe task used to measure attentional bias?	Yes	No	Unclear
5	What type of dot-probe task is used?	Probe-position	Probe-classification	Unclear
6	How are the stimuli aligned?	Vertical	Horizontal	Other
7	Time interval between baseline and follow-up (**if there are multiple follow-ups then list each and average)		Unclear	

B10 Study Results

1	What type of analysis was conducted on the pain outcome(s)?[11]	Intention to treat	Per protocol	Unclear	
2	What type of analysis was conducted on the bias outome?[11]	Intention to treat	Per protocol	Unclear	N/A

B10 Study Results

IMPORTANT

- Copy and complete the relevant tables below for each condition and each outcome.

B10.1 Means reported (Experimental conditions)

Complete when **means** are reported in an **experimental** condition

1	Experimental condition number *should match answer to B6-1*								
2	Experimental condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol	Unclear		

1	Experimental condition number *should match answer to B6-1*								
2	Experimental condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol	Unclear		

1	Experimental condition number *should match answer to B6-1*	

2	Experimental condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

1	Experimental condition number *should match answer to B6-1*								
2	Experimental condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

B10.2 Means reported (Comparison conditions)

Complete when **means** are reported in a **comparison** condition

1	Comparison condition number *should match answer to B7-1*								
2	Comparison condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

1	Comparison condition number	

	should match answer to B7-1								
2	Comparison condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

1	Comparison condition number *should match answer to B7-1*								
2	Comparison condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

1	Comparison condition number *should match answer to B7-1*								
2	Comparison condition outcome *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	a	b	c	a	b	c	a	b	c
	N	Mean	Standard Deviation	N	Mean	Standard Deviation	N	Mean	Standard Deviation
4	What type of analysis does this constitute?[29]			Intention to treat		Per protocol		Unclear	

B10.3 Dichotomous values reported (Experimental conditions)

Complete when **dichotomous** values are reported in an **experimental** condition

1	Experimental condition number *should match answer to B6-1*								
2	Outcome measure *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	352a	353a	354a	355a	356a	357a	358a	359a	360a
	N	+ve outcome count (%)	-ve outcome count (%)	N	+ve outcome count (%)	-ve outcome count (%)	N	+ve outcome count (%)	-ve outcome count (%)
4	What type of analysis does this constitute?[29]		Intention to treat		Per protocol		Unclear		

B10.4 Dichotomous values reported (Comparison conditions)

Complete when **dichotomous** values are reported in a **comparison** condition

1	Comparison condition number *should match answer to B7-1*								
2	Outcome measure *should match B8-1*								
3	Pre-intervention/baseline			Post-intervention			Additional post-intervention/follow-up		
	364a	365a	366a	367a	368a	369a	370a	371a	372a
	N	+ve outcome count (%)	-ve outcome count (%)	N	+ve outcome count (%)	-ve outcome count (%)	N	+ve outcome count (%)	-ve outcome count (%)
4	What type of analysis does this constitute?[29]		Intention to treat		Per protocol		Unclear		

B11 Statistical analysis

- **Copy and complete B11 each time an effect size is calculated between an ABM condition and a control condition.**

1	**Name** and **number** of ABM condition			
2	**Name** and **number** of comparison condition			
3	Name of outcome measure			
4	Statistical technique used			
5	Does the technique adjust for confounds?	Yes	No	Unclear

6	Is an effect size reported?	Yes		No
If yes go to 7, If no go to 8				
7	Details of statistical analysis and effect size [21]			
8	Was mediation analysis undertaken?	Yes		No
9	Were moderator or subgroup analyses performed?	Yes		No
If yes to 10, go to 383, 11				
10	Details of analysis and results			
11	Misc comments on B10			

1	**Name** and **number** of ABM condition			
2	**Name** and **number** of comparison condition			
3	Name of outcome measure			
4	Statistical technique used			
5	Does the technique adjust for confounds?	Yes	No	Unclear
6	Is an effect size reported?	Yes		No
If yes go to 7, If no go to 8				
7	Details of statistical analysis and effect size [21]			
8	Was mediation analysis undertaken?	Yes		No
9	Were moderator or subgroup analyses performed?	Yes		No
If yes to 10, go to 383, 11				
10	Details of analysis and results			
11	Misc comments on B10			

1	**Name** and **number** of ABM condition			
2	**Name** and **number** of comparison condition			
3	Name of outcome measure			
4	Statistical technique used			
5	Does the technique adjust for confounds?	Yes	No	Unclear
6	Is an effect size reported?	Yes		No
If yes go to 7, If no go to 8				
7	Details of statistical analysis and effect size [21]			
8	Was mediation analysis undertaken?	Yes		No
9	Were moderator or subgroup analyses performed?	Yes		No
If yes to 10, go to 383, 11				
10	Details of analysis and results			
11	Misc comments on B10			

1	**Name** and **number** of ABM	

	condition			
2	**Name** and **number** of comparison condition			
3	Name of outcome measure			
4	Statistical technique used			
5	Does the technique adjust for confounds?	Yes	No	Unclear
6	Is an effect size reported?	Yes	No	
If yes go to 7, If no go to 8				
7	Details of statistical analysis and effect size [21]			
8	Was mediation analysis undertaken?	Yes	No	
9	Were moderator or subgroup analyses performed?	Yes	No	
If yes to 10, go to 383, 11				
10	Details of analysis and results			
11	Misc comments on B10			

NOTES

1. Inclusion Criteria:
Include if:

1: Paper reports a test of a method directly targeting pain-related attentional bias using the dot-probe task.
2: Paper states participants experience either experimental, acute, or chronic pain.
3: Paper reports "an effect size that estimates the impact of the attentional bias modification intervention (or information that enables an effect size to be derived)."

3. Individual allocation: participants are individually allocated to a particular condition. Group allocation: participants are allocated to a particular condition as a group. For example, employees at one workplace are allocated to one condition and employees at another workplace are allocated to a different condition.

4. Is the randomisation adequate?

Criteria for a judgement of 'YES' (i.e. low risk of bias).	The investigators describe a random component in the sequence generation process such as: • Referring to a random number table; • Using a computer random number generator; • Coin tossing; • Shuffling cards or envelopes; • Throwing dice; • Drawing of lots; • Minimization (Minimization may be implemented without a random element, and this is considered to be equivalent to being random.)
Criteria for the judgement of 'NO' (i.e. high risk of bias).	The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: • Sequence generated by odd or even date of birth;

	• Sequence generated by some rule based on date (or day) of admission;
	• Sequence generated by some rule based on hospital or clinic record number.
	• Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorization of participants, for example:
	  • Allocation by judgement of the clinician;
	  • Allocation by preference of the participant;
	  • Allocation based on the results of a laboratory test or a series of tests;
	  • Allocation by availability of the intervention.

Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Insufficient information

5. Is the method of allocation adequate?

Criteria for a judgement of 'YES' (i.e. low risk of bias).	Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: • Central allocation (including telephone, web-based, and pharmacy-controlled, randomization); • Sequentially numbered drug containers of identical appearance; Sequentially numbered, opaque, sealed envelopes.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: • Using an open random allocation schedule (e.g. a list of random numbers); • Assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); • Alternation or rotation; • Date of birth; • Case record number; Any other explicitly unconcealed procedure.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Insufficient information to permit judgement of 'Yes' or 'No'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

6. Was the blinding adequate?

Criteria for a judgement of 'YES' (i.e. low risk of bias).	Any one of the following: • No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding; • Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken; • Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.
Criteria for the judgement of 'NO' (i.e. high risk of bias).	Any one of the following: • No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding; • Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken; • Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	Any one of the following: • Insufficient information to permit judgement of 'Yes' or 'No'; • The study did not address this outcome.

7. Are there any other bias concerns?

Criteria for a judgement of 'YES' (i.e. low risk of bias).	The study appears to be free of other sources of bias.
Criteria for the judgement of 'NO' (i.e. high risk of bias)	There is at least one important risk of bias. For example, the study: • Had a potential source of bias related to the specific study design used; or • Stopped early due to some data-dependent process (including a formal-stopping rule); or • Had extreme baseline imbalance; or • Has been claimed to have been fraudulent; or Had some other problem.
Criteria for the judgement of 'UNCLEAR' (uncertain risk of bias).	There may be a risk of bias, but there is either: • Insufficient information to assess whether an important risk of bias exists; or Insufficient rationale or evidence that an identified problem will introduce bias.

Notes: 8. Only populate this box if the paper explicitly reports the geographic location in which the research was conducted. 9. Number of patients that dropped out between baseline and follow up reported as a percentage. If attrition rate not reported but can be calculated from available data, record here. 11. Mark as follows: Intention To Treat (ITT) - if all participants who were randomised to treatment are included in N for these means. Per Protocol (PP) analysis - if participants are excluded on the basis of their receipt of treatment

as per protocol e.g. if people who did not receive all of the intervention techniques that they should have done, these participants are excluded. Unclear - If neither of these fit, e.g. people are missing for no clear reason.

A3 Risk of bias tables for individual studies included in meta-analysis (Chapter 2)

Table A3.1

Carleton et al., 2011

Bias	Judgement	Support for judgement
Random sequence generation (selection bias)	High risk	The study reported that participants were randomised to condition; however, the method of randomisation was not described.
Allocation concealment (selection bias)	Unclear risk	It was not reported that condition allocation was concealed.
Blinding of participants and personnel (performance bias)	Low risk	The study reported that participants were blinded to condition.
Blinding of outcome assessment (detection bias)	Unclear risk	It was not clear whether the outcome assessor was blinded to condition. It was unlikely that the outcome measurement would be influenced by lack of blinding.
Incomplete outcome data (attrition bias)	Low risk	Intention-to-treat analyses were performed.
Selective reporting (reporting bias)	High risk	The difference that a trend-level baseline difference in PASS-20 scores could have made to results was not reported.
Other bias	Unclear risk	No further risks of bias were identified.

Table A3.2

McGowan et al., 2009

Bias	Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The study reported that participants were randomised to condition, and the method for randomisation was described (online random sequence generator).
Allocation concealment (selection bias)	Unclear risk	It was not reported that condition allocation was concealed.
Blinding of participants and personnel (performance bias)	Unclear risk	It was not reported that participants were blinded to condition. However, participant blinding was unlikely to affect outcomes due to task similarity of active and sham ABM.
Blinding of outcome assessment (detection bias)	Unclear risk	It was not reported that the outcome assessor was blinded to condition. However, the outcome measurement was unlikely to have been influenced by lack of blinding.
Incomplete outcome data (attrition bias)	Unclear risk	There was no evidence of incomplete outcome data.
Selective reporting (reporting bias)	Unclear risk	There was no evidence of selective outcome reporting.
Other bias	Low risk	No further risks of bias were identified.

Table A3.3

Sharpe et al., 2012 Study 1

Bias	Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The study reported that participants were randomised to condition, and the method for randomisation was described (online random sequence generator).
Allocation concealment (selection bias)	Low risk	Condition allocation was concealed from study personnel.
Blinding of participants and personnel (performance bias)	Low risk	Participants were unaware of their condition allocation.
Blinding of outcome assessment (detection bias)	Low risk	The study personnel responsible for administering the intervention were blinded to condition allocation.
Incomplete outcome data (attrition bias)	Unclear risk	There was no evidence of incomplete outcome data.
Selective reporting (reporting bias)	Unclear risk	There was no evidence of selective outcome reporting.
Other bias	Low risk	No further risks of bias were identified.

Table A3.4

Sharpe et al., 2012 Study 2

Bias	Judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The study reported that participants were randomised to condition, and the method for randomisation was described (online random sequence generator).
Allocation concealment (selection bias)	Low risk	Condition allocation was concealed from study personnel.
Blinding of participants and personnel (performance bias)	Low risk	Participants were unaware of their condition allocation.
Blinding of outcome assessment (detection bias)	Low risk	The study personnel responsible for administering the intervention were blinded to condition allocation.
Incomplete outcome data (attrition bias)	Low risk	Intention-to-treat analyses were performed.
Selective reporting (reporting bias)	Unclear risk	There was no evidence of selective outcome reporting.
Other bias	Low risk	No further risks of bias were identified.

Appendix B: NHS ethics materials for clinical persistent pain sample (Studies 1 and 5, Chapters 3 and 6)

B1 Letter of approval

B2 Participant information sheet

B3 Informed consent form

B4 Debrief information sheet ABM group

EoSRES

NHS SCOTLAND
Research Ethics Service

East of Scotland Research Ethics Service (EoSRES) REC 1
Tayside Medical Sciences Centre (TASC)
Residency Block C, Level 3
Ninewells Hospital & Medical School
George Pirie Way
Dundee DD1 9SY

Ms Jennifer Bowler
PhD Researcher
University of East Anglia
School of Psychology, EDU Building,
University of East Anglia, Norwich Research Park,
Norwich, NR4 7TJ

Date: 19 June 2013
Your Ref:
Our Ref: LR/DL/13/ES/0075
Enquiries to: Mrs Lorraine Reilly
Extension: Ninewells extension: 83878
Direct Line: 01382 383878
Email: eosres.tayside@nhs.net

Dear Ms Bowler

Study title: **Does the addition of an implementation intention plan enhance the effects of attention bias modification on attentional bias in persistent pain?**
REC reference: **13/ES/0075**
IRAS project ID: **108157**

The Proportionate Review Sub-committee of the East of Scotland Research Ethics Service REC 1 reviewed the above application on 17 June 2013.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Senior Co-ordinator Mrs Lorraine Reilly, lorraine.reilly@nhs.net.

Ethical opinion

There were no ethical issues noted.

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Regarding A50 of the application form - please justify why you are not going to register the research on a public database.

Regarding Participant Information Sheet (PIS) - a reference is made at A6-2 in the application that participants who suffer discomfort can take a break and return to the task when they are ready to do so. The Committee suggested that this should be added to the PIS in the section Eligibility criteria as it states in the 2nd bullet point " you are able to use a computer keyboard comfortably for 40 mins".

Please send a revised PIS with new version number and full date as a footer.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Approved documents

The documents reviewed and approved were:

Document	Version	Date	
Advertisement	1	19 April 2013	
Evidence of insurance or indemnity		23 April 2013	
Investigator CV			
Investigator CV			
Investigator CV		10 April 2013	
Investigator's Brochure			
Letter of invitation to participant	1	19 April 2013	
Other: VAS example			
Other: Attentional Control Scale			
Other: Checklist correspondence			
Document	**Version**	**Date**	

Other: Other (No Description Entered)			
Other: SF-MPQ			
Other: Word list for individual ratings			
Participant Consent Form	1	19 May 2013	
Participant Information Sheet	1	19 April 2013	
Protocol	1	19 April 2013	
Questionnaire: Brief Pain Inventory			
REC application		07 June 2013	
Referees or other scientific critique report		03 June 2013	

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.
Information is available at National Research Ethics Service website > After Review

13/ES/0075	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

Yours sincerely

L. Reilly

for **Mrs Sandra Forbes**
Vice-Chair

Email: eosres.tayside@nhs.net

Enclosures: List of names and professions of members who took part in the review
"After ethical review – guidance for researchers"

Copy to: Mrs Sue Steel
Dr Paul Mills, NHS Norfolk & Waveney

University of East Anglia

PARTICIPANT INFORMATION SHEET

AN INVESTIGATION OF ATTENTIONAL PROCESSING IN PERSISTENT PAIN

My name is Jennifer Bowler and I am a PhD student at the University of East Anglia. I would like to invite you to take part in a research study. Before you decide you need to understand the purpose of the research and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

The purpose of the study is to investigate how individuals who have long-term pain think. You are being invited to take part because you have a persistent pain that has lasted for three months or more.

This is an educational project which will be submitted in part fulfilment of a PhD degree.

Eligibility Criteria

If you meet the following eligibility criteria for the study and are aged 18 or over, then you may be eligible to take part in the study:

- You have had chronic benign pain, such as low back pain, for 3 months or more.
- You are able to use a computer keyboard comfortably for a total of 40 minutes. Please note that a break is built into the task approximately half-way through. In addition, should you experience any discomfort you can take a break at any time and return to the task when you are ready to do so.
- You are a native English speaker.
- You have normal or corrected-to-normal vision.
- You are able to read and understand text displayed on a computer screen.

What will your involvement entail?

If you choose to take part in this study, you will be invited to come and meet with the researcher at the University of East Anglia, as outlined below. You will also be asked to write down some words that describe your pain and rate how relevant some words (related to pain) are to you via email. The study will comprise a single meeting with the researcher, as well as completing some questionnaires at home.

Meeting with the researcher

i) At the start of the study you will be randomly allocated to a group (1, 2 or 3).

ii) You will be asked to fill in some questionnaires about your pain and your thoughts and feelings.

iii) You will complete a straightforward cognitive task (approximately 40 minutes duration) that requires you to press a key in response to a simple stimulus on screen.

It is estimated that the meeting with the researcher will last approximately 1.5 hours in total.

Questionnaires

All participants will also be given a pack of questionnaires together with a stamped addressed envelope to take home with them. These questionnaires should be completed exactly one week after the meeting with the researcher and returned to the researcher in the stamped addressed envelope. An email reminder will be sent to participants when it is time to return the questionnaires. You will also be given the option to complete the questionnaires via email if you would prefer to do so.

The study is taking place in the Elizabeth Fry Building, which is situated on the University of East Anglia campus in Norwich.

Data collection will take place July 2013-April 2014.

Anonymity, Privacy and Confidentiality

The researcher will ensure anonymity in the write-up and any final publication of the study.

The researcher will ensure individual privacy during each of the data collection sessions.

The data collected will be handled only by the researcher and her supervisors and will be completely anonymous when it is written-up. After the data has been written-up, all response sheets will be destroyed as agreed in the 'Participant Consent Form'.

During the data collection and write-up period the data collected will be stored securely in the School of Psychology at the University of East Anglia for a maximum of five years.

Withdrawal

Please remember that you are free to withdraw from the study at any time, for any reason and without prejudice. Due to the anonymous nature of the data it will not be possible to withdraw data once you have completed the study.

Ethical Approval

This research has been reviewed by a NHS Research Ethics Committee, which has responsibility for scrutinising proposals for medical research on humans. In this case, the reviewing committee was the East of Scotland Research Ethics Service REC 1, who have raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available to monitors from the University of East Anglia and NHS Norfolk, whose role is to check that this research is properly conducted and the interests of those taking part are adequately protected.

Compensation

The University of East Anglia holds insurance policies which apply to this study.

Travel expenses

Participants will be reimbursed with any travel expenses incurred as a result of taking part in the study up to a value of £7 per person. If you bring a car onto the UEA campus, you can also ask the researcher for a free parking permit.

Results dissemination

If you would like to receive a copy of the summary of the final results, please let me know and I will arrange for this to be emailed or posted to you.

Questions and concerns

Please do not hesitate to ask the Chief Investigator, Jennifer, or the Project Supervisor, Dr Andrew Bayliss, any questions you may have concerning the study.

If you wish to complain formally you can do so through the NHS Complaints Procedure. You can write, telephone e-mail or fax your complaint to:

Patient Liaison Manager
Level 2 East Block
Colney Lane
Colney
Norwich
Norfolk
NR4 7UY

Tel No: 01603 289 036
E-mail: PALS@nnuh.nhs.uk Fax:
01603 289 046

Contact Details

Jennifer Bowler (Chief Investigator); E-mail: j.bowler@uea.ac.uk

Dr Andrew Bayliss (Supervisor); E-mail: andrew.p.bayliss@uea.ac.uk;

Tel. 01603 597499

University of East Anglia

AN INVESTIGATION OF ATTENTIONAL PROCESSING IN PERSISTENT PAIN

CONSENT FORM

Centre Number:

Study Number:

Patient Identification Number for this study:

Name of Researcher: Jennifer Bowler

	Please initial box
1. I confirm that I have read and understand the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that data collected during the study may be looked at by individuals from the University of East Anglia and the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I agree to take part in the above study.	☐

Name of Patient	Date	Signature
Name of Person taking consent	Date	Signature

Consent Form Version 1.0, 19/04/13

University of East Anglia

Investigation of attentional processing in persistent pain

What is the purpose of the research?

Thank you for taking part in our study. We would now like to tell you a little bit more about the project. Many individuals experience pain on a daily basis that has lasted for many weeks, months or even years. In this research we are trying to understand how the brain processes information related to pain and what role this might play in the development and maintenance of the condition. Sometimes living with persistent pain is associated with distress and fear of pain, making the condition even more difficult to cope with.

How was this tested?

In this study we aimed to identify people who have experienced pain for three months or more to find out more about how the brain allocates attention to pain-related information, at a comparatively automatic level of processing (outside conscious awareness). To do this, we asked you to use a computer-based program that measured how you attend to pain.

In this computer program, each time a word pair was presented it consisted of a pain related word and a more benign word. The word pair then disappeared and was replaced by an arrow probe in the prior location of one of the words. In the first part of the program, the arrow probe replaced the pain-related word and neutral word with equal probability. Your task was to press the arrow key on the keyboard to indicate the direction of the arrow probe on screen. Some studies have suggested that in the context of persistent pain, individuals will press the corresponding arrow key more quickly when the arrow probe on screen replaces a pain-related word than when it replaces a neutral word, suggesting that attention is going more quickly towards pain-related information in comparison with neutral information. This is referred to as an ‘attentional bias’ in the literature. To find out whether an attentional bias is present, we will look at the reaction times on the computer program, and compare how quickly participants responded to pain-related words in comparison with neutral words.

We are also interested in finding out whether this pattern of attentional processing influences how pain is experienced. We tested this using a computer task that aims to directly target and modify attentional bias in pain. In the middle section of the computer program, the aim was to try and help you focus attention away from the pain relevant word on the computer screen and look instead at the benign word. We tried to do this by placing a small target (the arrow) consistently behind the benign word, and asking you to respond to the arrow. To do better on the task, we hope you might have started to focus more on the benign words than on the pain relevant words. Previous research has suggested that repeated practice at this type of

computerised attentional training may actually transfer to daily life and help people be able to focus their attention away from their pain and that this may help alleviate specific cognitive and emotional factors associated with persistent pain.

In order to evaluate the extent to which participants had been trained to attend to benign information, or not to attend to pain-related and adverse information, we repeated the measure of attentional bias in the third section of the program. In this final section, we asked all participants to complete a task in which new pain-neutral word pairs were equally replaced by a left or right facing arrow and measured how long it took you to indicate its direction using the keyboard.

We also wanted to know whether your experience of pain itself and emotions and feelings changed before and after the training so we asked you to complete some questionnaires at the beginning, immediately after the computer task, and end of the study and compared your responses with a group who completed a control computerised attentional task.

Where can I find information about persistent pain?

As we are researchers (the PhD student and her supervisor) and not a clinical service we cannot directly help you with specific difficulties that you may be experiencing; however included in this debriefing sheet is a section (please see below) on where to find information if you or someone you know is struggling with long-term pain.

Who can I contact should I have any further queries concerning the study?

If you have any further questions about the study, and/or if you would like to receive a summary of findings when the research is completed, please contact me, Jennifer Bowler, PhD researcher, by email: j.bowler@uea.ac.uk.

Alternatively you can contact my supervisor, Dr Andrew Bayliss, Senior Lecturer in Psychology, School of Psychology, UEA, by email, andrew.p.bayliss@uea.ac.uk or phone, 01603 597499.

Thank you for your participation in this research.

Information about persistent pain

If you are finding it difficult to cope with your pain condition we would recommend that you contact your GP in the first instance.

If you would like further information concerning chronic pain, please visit:

1. http://www.nhs.uk/Livewell/Pain/Documents/The%20pain%20toolkit%20-%20Oct%2010%20-%20READ.pdf. “The Pain Toolkit” is a free booklet approved by the NHS.

2. http://www.moodjuice.scot.nhs.uk/chronicpain.asp. This is a free self-help resource developed by NHS Forth Valley for individuals living with persistent pain.

Sources of support for UEA members

At UEA there are a number of options and information about them is available through the UEA website (please see below) or through Student Services. You can get in touch with the long-term medical conditions and chronic pain adviser, Debbie Sands, directly, or someone who knows you can make initial contact on your behalf, either by calling in to reception at the Dean of Students' Office (Upper Street, opposite Waterstones Bookshop), by telephone (01603 592761) or by email: debbie.sands@uea.ac.uk. The service is usually available Monday-Friday, 9am-5pm. You can also email the Dean of Students' Office reception at dos.reception@uea.ac.uk.

On the UEA Portal page, select the Help and Advice Tab.

Under the Dean of Students' Office heading you will find many useful links including:

'Disability' where you will find information about advice and support available at UEA, and 'Health Matters', where you will find the 'Medical Services Unit' and a route for contacting a GP for advice.

Appendix C: Tables of correlations (referred to in Chapter 3 Study 2).

A series of Spearman's Rho correlations was conducted with questionnaire scores and attentional bias indexes as the dependent variables (indexes non-normally distributed).

Table C1.1

Whole sample (49 persistent pain and 52 non-pain controls)

Questionnaire	AB-500		AB-1250	
N = 101	*rs*	*p*	*rs*	*p*
PCS	-.087	.39	.011	.92
HADS-Anxiety	-.040	.70	-.061	.55
HADS-Depression	.014	.87	-.149	.14
PVAQ	-.042	.67	-.131	.19
ACS	-.117	.24	-.225*	.024

Table C1.2

Persistent pain group only

Questionnaire	AB-500		AB-1250	
n = 49	*rs*	*p*	*rs*	*p*
MPQ-Total	-.067	.65	-.012	.94
MPQ-VAS	-.31*	.033	.018	.90
BPI-interference	-.11	.45	.011	.94
HADS-Anxiety	-.11	.48	-.010	.95
HADS-Depression	.007	.96	-.005	.98
PCS	-.12	.40	.039	.79
PVAQ	.037	.80	-.14	.36
ACS	-.15	.32	-.15	.31

Table C1.3

Healthy control group only

Questionnaire	AB-500		AB-1250	
n = 52	*rs*	*p*	*rs*	*p*
PCS	-.020	.89	-.010	.95
HADS-Anxiety	.050	.73	.039	.78
HADS-Depression	.035	.81	.13	.38
PVAQ	-.052	.71	.061	.67
ACS	-.071	.62	-.22	.11

*$p < .05$; **$p < .01$. *Note*: results were comparable for proportion scores.

Appendix D: Supplementary information for ABM cold pressor study (Chapter 4 Study 3)

D1 Cold pressor task instructions

Cold pressor task (CPT) instructions

To initiate CPT

Next, you are going to complete the cold pressor task, so if you could move your chair over here (indicate in front of room temp water container).

(Seat participant next to room temp water.) In preparation, you need to place your arm in some room temperature water first for one minute. (If necessary, ask participant to roll up sleeve of left arm to just above elbow and remove watch/jewellery.) I'll tell you and give you a signal when it's time to put your arm in the water. You'll put it in all at once, right up to here (indicate depth of immersion).

After that, please move to this chair (indicate seat in front of cold pressor apparatus) and I'll give you another signal when it's time to put your arm in the cold water.

Again, you'll put it in all at once, right up to here (indicate depth of immersion). Hold your hand face down. Avoid touching the sides and bottom of the water bath. Do not clench your fist.

Once you've put your arm in, leave it in the water for as long as possible.

Whilst you have your arm in the water, I will ask you for two measurements. First, tell me when you first feel pain. You can do this by saying "now". Second, I will ask you to rate your level of pain on this 0-10 rating scale (show participant the scale) from 0 (no pain) to 10 (unbearable pain) 30 seconds into the task. You can do this by saying the number out loud and do not need to write anything. I will ask you to repeat this rating when you withdraw your arm from the water. Remember to leave your arm in the water for as long as you can, and then take it out.

Do you have any questions about what you'll be doing?

Are you ready? Place your left arm in the water (indicate room temp water) now (give signal; start stopwatch).

(Whilst they have their arm in the warm water, remind participant to move to the other chair, immerse left arm, and to "tell me when you first feel pain by saying "now")

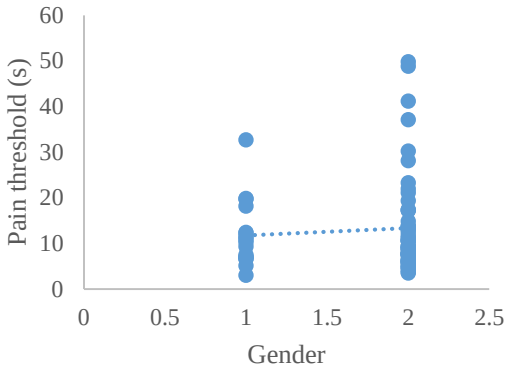
Place your left arm in the water (indicate cold water) now (give signal; start stopwatch).

After CPT

Thank you for completing the task. Dry your arm (indicate towel/paper towels) and, once it is dry, flex your fingers as well (demonstrate flexing fingers).

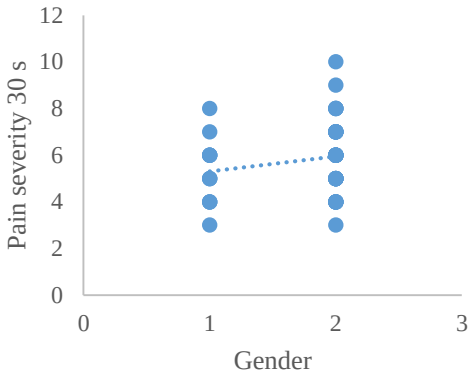
D2 Correlational analyses between gender and cold pressor task outcomes (referred to in Chapter 4 Study 4).

Threshold



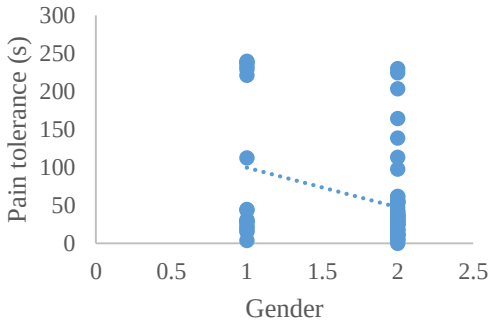
r = .073, *p* = .54

Pain severity



r = .186, *p* = .18

Pain tolerance



r = -.32, *p* = .006

Figure D2.1 Panel of scattergraphs illustrating point biserial correlations with gender and pain threshold, severity and tolerance (1 = male; 2 = female).

Appendix E: Tables of correlations

A series of correlations was conducted on the datasets from Studies 2, 3 and 5 with baseline attentional control scale (ACS) and bias change scores (post minus pre; a more negative score represents a more pain-related bias) as the dependent variables. These analyses were referred to in Chapter 8 ('Overall discussion') and individual study Chapters. All reported *p*-values are two-tailed.

Table E1.1

Chapter 4 Study 2: Pearson's correlations (normally distributed) ACS and bias acquisition

Attentional control	AB-500 change		AB-1250 change	
N = 30	*r*	*p*	*r*	*p*
ACS-Shift	.146	.442	.251	.181
ACS-Focus	.372*	.043	.195	.301
ACS-Total	.289	.122	.252	.179

*$p < .05$

Table E1.2

Chapter 4 Study 3: Pearson's correlations (normally distributed) ACS and bias acquisition

		AB-500 change		AB-1250 change	
Group	ACS	*r*	*p*	*r*	*p*
ABM-500	ACS-Shift	-.195	.372	-.144	.513
n = 23	ACS-Focus	.224	.305	.063	.773
	ACS-Total	.032	.885	-.044	.841
ABM-1250	ACS-Shift	-.091	.679	-.092	.676
n = 23	ACS-Focus	-.114	.606	.303	.160
	ACS-Total	-.118	.591	.106	.630
ABM-Placebo	ACS-Shift	-.099	.630	.336	.093
n = 26	ACS-Focus	.097	.638	.210	.304
	ACS-Total	-.008	.970	.321	.109

Table E1.3

Chapter 6 Study 5: Spearman's correlations (non-normally distributed) ACS and bias acquisiton

		AB-500 change		AB-1250 change	
Group	ACS	*rs*	*p*	*rs*	*p*
ABM	ACS-Shift	-.204	.449	-.213	.429
n = 16	ACS-Focus	-.092	.736	-.165	.541
	ACS-Total	.203	.450	.047	.862
ABM-IMP	ACS-Shift	-.035	.897	.483	.058
n = 16	ACS-Focus	.158	.559	.305	.251
	ACS-Total	.015	.957	.334	.206
Control	ACS-Shift	.185	.478	.244	.345
n = 17	ACS-Focus	.243	.347	.290	.258
	ACS-Total	.228	.378	.271	.293

Appendix F: Supplementary analyses comparing ABM completers versus drop-outs (Chapter 5 Study 4)

Table F1.1

Chapter 5 Study 4: Completers versus drop-outs (community-based persistent musculoskeletal pain sample)

	Completed (*n* = 57)		Dropped out (*n* = 11)			
Questionnaire	*M*	*SD*	*M*	*SD*	*t*	*p*
ASI	22.49	12.20	20.36	14.70	.512	.610
FPQ	50.18	12.41	44.73	8.47	1.391	.169
HADS-Anx	9.70	3.88	9.18	3.03	.420	.676
HADS-Dep	5.28	3.86	5.82	4.24	-.416	.679
MPQ-VAS	45.89	20.53	48.09	26.99	-.308	.759
MPQ-Total	16.45	6.67	18.40	9.64	-.789	.433
PDI	26.56	16.26	32.82	15.71	-1.175	.244
PMQ	11.23	17.02	16.45	21.20	-.896	.374

Appendix G: Overall discussion

The below sub appendices were all referred to in Chapter 8 (‘Overall discussion’).

G1 Correlations baseline attentional bias indexes and questionnaire pain measures persistent pain samples (Studies Four and Five, Chapters Five and Six).

G2 Baseline Attentional Control Scale and pain severity, persistent pain samples: correlations and median split analysis.

G3 Correlations Attentional Control Scale and training engagement

G4 ABM ‘responders’ versus ‘non-responders’: baseline AB-1250 differences within persistent pain samples.

G5 Sharpe, Johnson, & Dear (2015) paper

G1 Correlations bias indexes and questionnaire pain measures persistent pain samples

Table G1.1

Chapter 5 Study 4: Correlations baseline attentional bias indexes and questionnaire pain measures (community-based persistent pain sample)

Questionnaire	AB-500		AB-1250	
N = 57				
	rs	*p*	*rs*	*p*
ASI1-Physical	-.027	.841	-.047	.727
ASI1-Cognitive	-.123	.361	-.266*	.046
ASI1-Social	-.037	.783	-.169	.208
ASI1-Total	-.094	.487	-.205	.126
FPQ1-Minor	.064	.634	-.087	.52
FPQ1-Severe	.107	.43	-.083	.539
FPQ1-Injection	.093	.489	.009	.949
FPQ1-Dental	.098	.468	-.250	.061
FPQ1-Total	.077	.567	-.129	.34
HADS1-Anx	-.015	.909	-.328*	.013
HADS1-Dep	-.106	.433	-.151	.261
HADS1-Total	-.060	.657	-.278*	.037
MPQ1A-Sensory	.029	.833	-.168	.211
MPQ1A-Affective	.213	.112	-.035	.794
MPQ1A-Total	.110	.417	-.151	.263
MPQ1B	.244	.068	-.143	.287
MPQ1C	.229	.093	.062	.653
MPQ1-Total	.129	.347	-.111	.419
PDI1-Total	-.028	.837	.029	.828
PMQ1-Pres	.054	.689	.137	.309
PMQ1-OTC	.359**	.006	-.057	.672
PMQ1-Total	.170	.207	.102	.451
Pain duration months	-.254	.082	-.152	.303
Number sites msk pain	-.025	.851	-.090	.505
Number sites other pain	-.186	.171	-.020	.881
Total sites pain	-.072	.593	-.079	.557

*$p < .05$; ** $p < .01$

Table G1.2

Chapter 6 Study 5: Correlations baseline implicit attentional bias indexes, explicit PVAQ, and questionnaire pain measures (clinical persistent pain sample)

Questionnaire	AB-500		AB-1250		PVAQ	
N = 49						
	rs	*p*	*rs*	*p*	*rs*	*p*
MPQ1A-Sensory	-.086	.566	-.064	.67	.28	.06
MPQ1A-Affective	-.076	.606	.057	.701	.22	.138
MPQ1A-Total	-.142	.336	-.070	.637	.344*	.018
MPQ1B	-.305*	.033	.018	.9	.176	.231
MPQ1C	.112	.442	-.065	.657	.165	.262
MPQ1-Total	-.067	.65	-.012	.937	.307*	.036
BPI1-Sev	-.128	.379	.104	.477	.183	.214
BPI1-Int	-.112	.449	.011	.938	.259	.079
BPI1-Relief	.347*	.026	-.055	.733	-.142	.385
BPI1-Total	-.130	.379	.049	.743	.256	.082
HADS1-Anx	-.105	.476	-.010	.945	.414**	.004
HADS1-Dep	.007	.964	-.005	.975	.324*	.026
HADS1-Total	-.068	.648	-.010	.946	.404**	.005
PCS1-Rumination	-.200	.169	-.043	.77	.484**	< .001
PCS1-Magnification	.122	.404	-.020	.89	.552**	< .001
PCS1-Helplessness	-.132	.367	.104	.477	.338*	.019
PCS1-Total	-.123	.401	.039	.791	.491**	<.001
PVAQ1-ATP	.091	.534	.010	.947	/	/
PVAQ1-ATCP	-.034	.818	-.228	.115	/	/
PVAQ1-Total	.037	.802	-.135	.362	/	/
ACS1-Focussing	-.073	.619	-.188	.197	-.516**	< .001
ACS1-Shifting	.030	.841	-.109	.458	-.452**	.001
ACS1-Total	-.146	.317	-.149	.308	-.476**	.001
VASCurrentPainSeverity1	.016	.915	.094	.521	.226	.123
Number pain sites	-.020	.894	-.137	.348	.344*	.017
Pain duration months	.135	.355	-.129	.377	.053	.719
GP visits	-.084	.567	.145	.322	.137	.352
Days absent	.042	.834	-.178	.365	-.123	.534

*$p < .05$; **$p < .01$

G2 Clinical persistent pain sample: ACS and pain severity

Table G2.1

Chapter 6 Study 5: Correlations baseline ACS and pain measures

Pain measure *N* = 49	ACS-Shift	*p*-value	ACS-Focus	*p*-value	ACS-Total	*p*-value
MPQ1A-Sensory	-.301*	.040	-.270	.067	-.379**	.009
MPQ1A-Affective	-.297*	.041	-.311*	.031	-.291*	.045
MPQ1A-Total	-.284	.050	-.268	.066	-.331*	.021
MPQ1B	-.373**	.008	-.178	.221	-.358*	.012
MPQ1C	-.315*	.028	-.049	.737	-.240	.097
MPQ1-Total	-.330*	.022	-.298*	.040	-.375**	.009
BPI1-Sev	-.341*	.016	-.209	.149	-.381**	.007
BPI1-Int	-.305*	.035	-.258	.077	-.451**	.001

Table G2.2

Chapter 6 Study 5: Median split based on pre-training ACS scores

Pain measure *N* = 49	Lower ACS *n* = 24	SD	Higher ACS *n* = 25	SD	*t*-value	*p*-value
MPQ1A-Sensory	18.23	7.73	13.84	6.08	-2.18	.035
MPQ1A-Affective	6.57	4.07	4.04	3.63	-2.27	.028
MPQ1A-Total	23.78	10.41	17.88	8.99	-2.11	.041
MPQ1B	60.08	17.8	48.12	21.13	-2.14	.038
MPQ1C	2.33	0.70	2.04	0.79	-1.37	.176
MPQ-Total	26.87	10.36	19.92	9.40	-2.44	.019
BPI1-Sev	5.25	1.54	4.36	1.55	-2.02	.049
BPI1-Int	6.40	2.18	4.66	2.4	-2.62	.012

G3 Chapter 6 Study 5: ACS and training engagement

Table G3.1

Correlations between training engagement (VAS score) and dispositional ACS, change in attentional bias, and pain outcomes at follow-up, within ABM groups

Variable	Correlation type	*r or rs*	*p*-value
ACS-Shift	Pearson's	.421*	.016
ACS-Focus	Pearson's	.461**	.008
ACS-Total	Pearson's	.522**	.002
AB-500 change	Spearman's	.065	.723
AB-1250 change	Spearman's	.356*	.046
MPQ-Total	Pearson's	-.436*	.018
BPI-Severity	Pearson's	-.333	.072
BPI-Interference	Pearson's	-.395*	.031
HADS-Anxiety	Pearson's	-.567**	.001
HADS-Depression	Pearson's	-.463*	.010
PCS-Total	Pearson's	-.457*	.011

G4 ABM for persistent pain ‘responders’ versus ‘non responders’ differences in baseline attentional bias indexes, where ‘responder’ is defined as a reduction in pain-related bias, and increase in neutral bias (cf. MacLeod et al., 2002).

Table G4.1

Chapters 5 and 6, Studies 4 and 5: Community-based and persistent pain samples

Community-based persistent pain sample ABM groups						
	AB-1250 became more neutral (*n* = 18)	*SD*	AB-1250 became more pain-related (*n* = 11)	*SD*	*t*-value	*p*-value
Baseline AB-1250	-13.31	16.53	17.02	26.12	-3.85	.001
Clinical persistent pain sample ABM groups						
	AB-1250 became more neutral (*n* = 16)	*SD*	AB-1250 became more pain-related (*n* = 16)	*SD*	*t*-value*	*p*-value
Baseline AB-1250	-40.81	53.01	0.14	34.55	-2.59	.015

*Mann-Whitney-U = 19.5, $p < .001$

G5 Sharpe, L., Johnson, A., & Dear, B. F. (2015). Attention bias modification and its impact on experimental pain outcomes: Comparison of training with words versus faces in pain. *European Journal of Pain*.

At the end of this thesis, the above new ABM pain study was published (Sharpe et al., 2015) comparing the effects of retraining initial orienting using sensory pain words versus facial expressions on attentional bias (linguistic versus pictorial) and acute experimental (cold pressor task; CPT) pain outcomes. This section will briefly describe the study and how its results align with present findings.

In this study, 111 eligible first year undergraduate students were randomised (method of randomisation not reported) to receive a single session (320 trials) of either linguistic pain ABM, pictorial pain ABM, linguistic neutral ABM, or pictorial neutral ABM, which constituted the probe classification version of the visual-probe task. Attentional bias was measured at pre and post-training (80 trials per test; five stimuli per trial type) using the visual-probe task; however, 'happy' words and facial expressions were used, such that the probe replaced pain and happy stimuli with equal probability. CPT primary outcomes were threshold (time taken in seconds from immersion to first report pain) and pain intensity (measured on a 0 to 10 scale). Pain intensity was measured at three time points: threshold, 30 seconds after threshold, and at tolerance. However, the second measurement (pain intensity at threshold) was discarded, and the outcome analysed was an average of the pain intensity ratings at threshold and tolerance. Tolerance was also included as an outcome variable, and was defined as the total time from immersion until participants withdrew the arm from the water. An uninformed ceiling of threshold (M = 10 seconds) plus four minutes was applied.

Descriptive results indicated that there was a significant difference in age between groups, such that pain training participants were older than neutral training participants, and this effect was greater for those in the pictorial pain ABM group. The authors suggested that, as age was not correlated with pain outcomes, there was no need to control for this difference. Gender ratio across groups was not reported. Main attention analyses indicated that participants who were trained towards pain words or faces became more biased towards pain faces from pre to post-training, and those trained to attend towards neutral words or faces became more biased towards neutral faces. Pictorial ABM effects were significant for pictorial test trials only, and not linguistic trials. Main CPT outcome analyses suggested that participants in the neutral ABM groups had a higher pain threshold, and this effect was greatest for those allocated to the word condition. Effects for total tolerance time did not reach significance. For average pain intensity, participants in both pictorial conditions (whether trained towards or away from pain faces) reported less severe pain than participant

in the word conditions. Regression analyses did not find evidence to support the predictive value of change in attentional bias, measured in either modality, on CPT pain outcomes.

The results of this study are broadly in line with current findings. Importantly, they favour the present use of linguistic stimuli, although the interesting finding concerning pictorial training effects on average pain intensity warrants further investigation. They also align with the meta-analyses of Chapters Two and Seven, which suggested that ABM successfully modified attentional bias in initial orienting, and in particular in acute pain samples. Their CPT findings suggested that, unlike in Study Three, there was no impact of training on tolerance (although there was, as in Study Three, a significant correlation between reduced bias and increased tolerance; Sharpe et al., 2015). In line with Study Three, retraining initial orienting significantly impacted on pain threshold. Pain intensity was also lower in the neutral than pain linguistic ABM group, although, unlike present findings (and diverging from the findings of McGowan et al., 2009), this difference did not reach significance. This could have been due to the different way in which pain intensity was operationalised; whereas both Study Three and McGowan et al. (2009) measured pain severity at 30 seconds into the task, Sharpe et al. (2015) averaged pain intensity at threshold and tolerance. Overall, the collective findings of the three experimental ABM studies conducted to date (Chapter Four; McGowan et al., 2009; Sharpe et al., 2015) support the continued investigation of ABM for pain.

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